

Supplementary data for the article:

Marjanovic Trajkovic, J.; Milanovic, V.; Ferjancic, Z.; Saicic, R. N. On the Asymmetric Induction in Proline-Catalyzed Aldol Reactions: Reagent-Controlled Addition Reactions of 2,2-Dimethyl-1,3-Dioxane-5-One to Acyclic Chiral  $\alpha$ -Branched Aldehydes. *European Journal of Organic Chemistry* **2017**, 2017 (41), 6146–6153.

<https://doi.org/10.1002/ejoc.201701073>

*Eur. J. Org. Chem.* **2017** • ISSN 1099–0690

<https://doi.org/10.1002/ejoc.201701073>

**SUPPORTING INFORMATION**

**Title:** On the Asymmetric Induction in Proline-Catalyzed Aldol Reactions: Reagent-Controlled Addition Reactions of 2,2-Dimethyl-1,3-dioxane-5-one to Acyclic Chiral  $\alpha$ -Branched Aldehydes

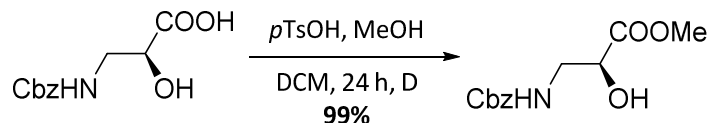
**Author(s):** Jasna Marjanovic Trajkovic, Vesna Milanovic, Zorana Ferjancic,\* Radomir N. Saicic\*

## Table of contents

1. Preparation of aldehyde <b>2b</b> .....	S1
2. Preparation of aldehyde <b>2d</b> .....	S3
3. Preparation of aldehyde <b>2e</b> .....	S5
4. Preparation of aldehyde <b>2f</b> .....	S6
5. Preparation of aldehyde <b>2h</b> .....	S6
6. $^1\text{H}$ and $^{13}\text{C}$ NMR spectra for all compounds and NOESY spectra for compounds <b>7</b> and <b>8</b> .....	S8

## 1. Preparation of aldehyde **2b**:

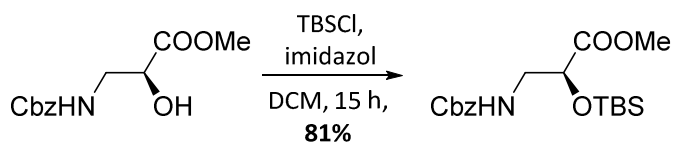
### (S)-Methyl 3-(benzyloxycarbonylamino)-2-hydroxypropanoate



To a solution of carboxylic acid (300.8 mg, 1.26 mmol) in dichloromethane (10.1 mL) was added methanol (6.26 mL) and *p*-toluenesulfonic acid (3.2 mg, 0.02 mmol). The reaction mixture was heated to reflux for 24 h, then diluted with water. The organic layer was separated, dried with anhydrous  $\text{MgSO}_4$ , filtered and concentrated under reduced pressure. The residue was purified by dry-flash chromatography ( $\text{SiO}_2$ ; petroleum ether/ethyl acetate = 4:6), to give methyl ester (313.9 mg, 99 %) as colorless oil.

$[\alpha]_D^{20} +19.0$  (*c* 1.00,  $\text{CH}_3\text{OH}$ );  $^1\text{H NMR}$  (200 MHz,  $\text{CDCl}_3$ )  $\delta$  7.30 (s, 5H), 5.70 – 5.55 (m, 1H), 5.06 (s, 2H), 4.27 (dd, *J* = 9.8, 5.0 Hz, 1H), 3.94 (d, *J* = 5.6 Hz, 1H), 3.70 (s, 3H), 3.56 – 3.44 (m, 2H);  $^{13}\text{C NMR}$  (50 MHz,  $\text{CDCl}_3$ )  $\delta$  173.2 (C), 156.6 (C), 136.2 (C), 128.3 (2xCH), 127.9 (2xCH), 127.9 (CH), 69.9 (CH), 66.7 ( $\text{CH}_2$ ), 52.4 ( $\text{CH}_3$ ), 44.0 ( $\text{CH}_2$ ); IR (ATR)  $\nu$  3362, 3036, 2952, 2930, 1749, 1727, 1693, 1538, 1450, 1302, 1262, 1233, 1206, 1126, 1105, 1066, 990, 973, 754, 698  $\text{cm}^{-1}$ ; HRMS (ESI) for  $\text{C}_{12}\text{H}_{15}\text{NO}_5\text{Na}$   $[\text{M}+\text{Na}]^+$  calculated: 276.0842; found: 276.0841.

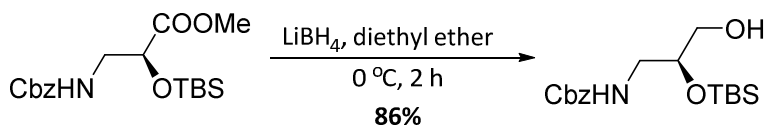
### (S)-Methyl 8,8,9,9-tetramethyl-3-oxo-1-phenyl-2,7-dioxo-4-aza-8-siladecane-6-carboxylate



To a solution of methyl ester (100.0 mg, 0.39 mmol) in cold (0 °C) dichloromethane (1.0 mL) was added imidazole (53.9 mg, 0.79 mmol) and TBSCl (58.5 mg, 0.39 mmol). The reaction mixture was stirred overnight at room temperature, then diluted with dichloromethane and water, organic layer washed with brine, dried with anhydrous  $\text{MgSO}_4$ , filtered and concentrated under reduced pressure. The residue was purified by column chromatography ( $\text{SiO}_2$ ; petroleum ether/ethyl acetate = 8:2), to give protected methyl ester (117.5 mg, 81%) as a colorless oil.

$[\alpha]_D^{20} -12.4$  (*c* 1.00,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 – 7.25 (m, 5H), 5.18 – 5.04 (m, 3H), 4.32 (t, *J* = 5.1 Hz, 1H), 3.71 (s, 3H), 3.58 – 3.50 (m, 1H), 3.49 – 3.42 (m, 1H), 0.90 (s, 9H), 0.10 (s, 3H), 0.06 (s, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  172.0 (C), 156.2 (C), 136.4 (C), 128.4 (2xCH), 128.0 (3xCH), 70.9 (CH), 66.7 ( $\text{CH}_2$ ), 52.0 ( $\text{CH}_3$ ), 44.8 ( $\text{CH}_2$ ), 25.6 (3x $\text{CH}_3$ ), 18.2 (C), -5.1 ( $\text{CH}_3$ ), -5.5 ( $\text{CH}_3$ ); IR (ATR)  $\nu$  3555, 3066, 3033, 2953, 2932, 2890, 2857, 1728, 1517, 1462, 1254, 1143, 1001, 838, 781  $\text{cm}^{-1}$ ; HRMS (ESI) for  $\text{C}_{18}\text{H}_{30}\text{NO}_5\text{Si}$   $[\text{M}+\text{H}]^+$  calculated: 368.1888; found: 368.1890.

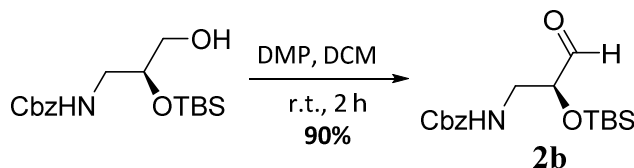
### (S)-Benzyl 2-(tert-butyldimethylsilyloxy)-3-hydroxypropylcarbamate



To a cold ( $0\text{ }^\circ\text{C}$ ) solution of protected methyl ester (63.4 mg, 0.17 mmol) in diethyl ether (2.0 mL) was added lithium borohydride (5.0 mg, 0.23 mmol) and the reaction mixture was stirred for 2 h at  $0\text{ }^\circ\text{C}$ . The reaction mixture was quenched by the sequential addition of water and extracted with diethyl ether. The combined organic extract was washed with brine, dried with anhydrous  $\text{MgSO}_4$ , filtered and concentrated under reduced pressure. Purification of the crude product by column chromatography ( $\text{SiO}_2$ ; petroleum ether/ethyl acetate = 7:3) afforded title alcohol (50.4 mg, 86%) as a colorless oil.

$[\alpha]_D^{20} +23.9$  ( $c$  1.00,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.44 – 7.31 (m, 5H), 5.17 – 5.08 (m, 3H), 3.94 – 3.80 (m, 1H), 3.59 – 3.43 (m, 3H), 3.22 (dt,  $J$  = 14.2, 5.0 Hz, 1H), 2.71 (bs, 1H), 0.91 (s, 9H), 0.10 (s, 6H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  157.6 (C), 136.5 (C), 128.8 (2xCH), 128.5 (CH), 128.4 (2xCH), 71.4 (CH), 67.2 ( $\text{CH}_2$ ), 63.6 ( $\text{CH}_2$ ), 43.6 ( $\text{CH}_2$ ), 26.0 (3x $\text{CH}_3$ ), 18.3 (C), -4.5 ( $\text{CH}_3$ ), -4.6 ( $\text{CH}_3$ ); IR (ATR)  $\nu$  3347, 3066, 3034, 2953, 2931, 2887, 2857, 1705, 1519, 1465, 1256, 1119, 1050, 1008, 836, 779  $\text{cm}^{-1}$ ; HRMS (ESI) for  $\text{C}_{17}\text{H}_{30}\text{NO}_4\text{Si}$   $[\text{M}+\text{H}]^+$  calculated: 340.1939; found: 340.1949.

### (S)-Benzyl 2-(tert-butyldimethylsilyloxy)-3-oxopropylcarbamate

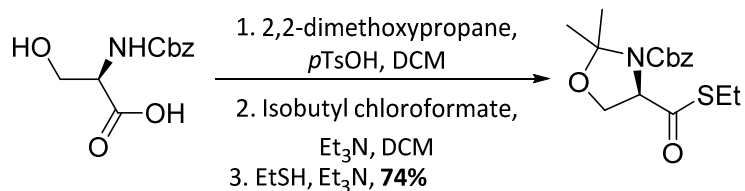


Dess-Martin's periodinane (181.1 mg, 0.42 mmol) was added to a solution of alcohol (70.5 mg, 0.21 mmol) in dichloromethane (4.3 mL) and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with dichloromethane, washed with 5%  $\text{Na}_2\text{S}_2\text{O}_3$  and sat. aq.  $\text{NaHCO}_3$ , dried over anhydrous  $\text{MgSO}_4$ , filtered and concentrated under reduced pressure. Purification of the residue by column chromatography ( $\text{SiO}_2$ ; petroleum ether/ethyl acetate = 7/3) afforded the title compound **2b** (63.0 mg, 90%) as a colorless oil.

$[\alpha]_D^{20} -4.4$  ( $c$  1.00,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  9.63 (s, 1H), 7.36 – 7.30 (m, 5H), 5.13 – 5.02 (m, 3H), 4.15 (t,  $J$  = 5.1 Hz, 1H), 3.54 – 3.41 (m, 2H), 0.92 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  201.5 (CH), 155.8 (C), 135.8 (C), 128.1 (2xCH), 127.7 (CH), 127.7 (2xCH), 75.9 (CH), 66.5 ( $\text{CH}_2$ ), 42.3 ( $\text{CH}_2$ ), 25.2 (3x $\text{CH}_3$ ), 17.7 (C), -5.3 ( $\text{CH}_3$ ), -5.5 ( $\text{CH}_3$ ); IR (ATR)  $\nu$  3349, 3065, 3034, 2953, 2931, 2890, 2857, 1710, 1518, 1465, 1257, 1124, 1007, 838, 780  $\text{cm}^{-1}$ ; HRMS (ESI) for  $\text{C}_{17}\text{H}_{28}\text{NO}_4\text{Si}$   $[\text{M}+\text{H}]^+$  calculated: 338.1782; found: 338.1776.

## 2. Preparation of aldehyde **2d**:

### (*R*)-Benzyl 4-(ethylthiocarbonyl)-2,2-dimethyloxazolidine-3-carboxylate

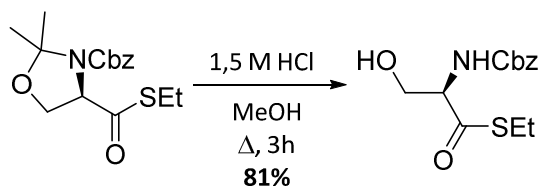


At first, 2,2-dimethoxypropane (4.3 g, 5.1 mL, 41.60 mmol) was added to a solution of carboxylic acid (1.65 g, 6.90 mmol) and *p*-toluenesulfonic acid (117.0 mg, 1.12 mmol) in dichloromethane (5.1 mL) and the solution was concentrated under reduced pressure, which caused it to turn red. The same procedure was repeated twice. The residue was diluted with ethyl acetate (30 mL), washed with water, dried over anhydrous MgSO<sub>4</sub>, and concentrated under reduced pressure, to give the crude product, as a pale yellow viscous oil, which was used in the next step without further purification.

Isobutyl chloroformate (1.46 g, 1.4 mL, 10.25 mmol) and triethylamine (1.31 g, 1.8 mL, 12.91 mmol) were added to a cold (0 °C) solution of aminoacetal (obtained from carboxylic acid 1.65, 6.90 mmol) in dichloromethane (29.0 mL) under an argon atmosphere. The reaction mixture was vigorously stirred for 30 min at 0 °C, then ethanethiol (1.16 g, 1.4 mL, 18.2 mmol) and triethylamine (1.31 g; 1.8 mL; 12.91 mmol) were added. The resulting solution was stirred for 30 min at 0 °C and 45 min at rt. The reaction mixture was diluted with dichloromethane (25 mL), washed with water (40 mL) and brine (30 mL), dried over anhydrous MgSO<sub>4</sub>, concentrated under reduced pressure and purified by column chromatography (SiO<sub>2</sub>; petroleum ether/EtOAc = 9:1), to give title compound (1.65 g, 74 %) as a pale yellow oil.

$[\alpha]_D^{20} +95.2$  (*c* 1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>, 338K) δ 7.50 – 7.19 (m, 5H), 5.15 (d, *J* = 12.1 Hz, 1H), 5.06 (bs, 1H), 4.72 – 4.59 (m, 1H), 4.23 (dd, *J* = 9.5, 7.3 Hz, 1H), 3.96 (dd, *J* = 9.5, 2.2 Hz, 1H), 2.84 (q, *J* = 7.4 Hz, 2H), 1.67 (s, 3H), 1.48 (s, 3H), 1.16 (t, *J* = 7.5 Hz, 3H); <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>, 338K) δ 199.3 (C), 151.2 (C), 135.9 (C), 127.9 (2xCH), 127.5 (CH), 127.1 (2xCH), 94.6 (C), 66.4 (CH<sub>2</sub>), 66.0 (CH<sub>2</sub>), 65.0 (CH), 24.8 (CH<sub>3</sub>), 22.9 (CH<sub>3</sub>), 22.2 (CH<sub>2</sub>), 13.9 (CH<sub>3</sub>); IR (ATR) ν 3064, 3033, 2984, 2936, 2880, 1712, 1681, 1454, 1402, 1347, 1264, 1243, 1208, 1094, 1055, 925, 840, 763 cm<sup>-1</sup>; HRMS (ESI) for C<sub>16</sub>H<sub>21</sub>NO<sub>4</sub>SNa [M+Na]<sup>+</sup> calculated: 346.1084; found: 346.1087.

### (*R*)-*S*-Ethyl 2-(benzyloxycarbonylamino)-3-hydroxypropanethioate

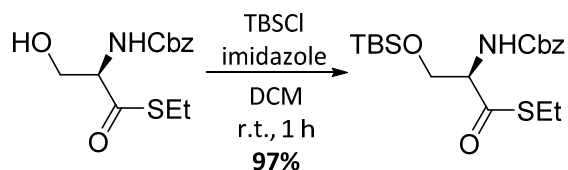


A solution of thioester (1.65 g, 5.10 mmol) in solvent mixture 1.5M HCl/methanol (40.0 mL, v/v= 1/1) was stirred and heated to reflux for 3 h. After the volatiles were removed under reduced pressure, the

residue was purified by dry-flash chromatography chromatography (SiO<sub>2</sub>; petroleum-ether/EtOAc = 7:3) to give title alcohol (1.18 g, 81%), as a white solid.

M.p. 55-56 °C;  $[\alpha]_D^{20} +26.9$  (c 1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>, 338K) δ 7.52 (bs, 1H), 7.43 – 7.28 (m, 5H), 5.09 (s, 2H), 4.77 (t, *J* = 6.0 Hz, 1H), 4.23 (ddd, *J* = 8.1, 6.2, 4.6 Hz, 1H), 3.73 – 3.65 (m, 2H), 2.81 (q, *J* = 7.4 Hz, 2H), 1.17 (t, *J* = 7.4 Hz, 3H); <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>, 338K) δ 199.6 (C), 155.7 (C), 136.6 (C), 127.9 (2xCH), 127.4 (CH), 127.3 (2xCH), 65.5 (CH<sub>2</sub>), 63.5 (CH), 61.1 (CH<sub>2</sub>), 22.1 (CH<sub>2</sub>), 14.0 (CH<sub>3</sub>); IR (ATR) ν 3354, 3064, 3034, 2967, 2933, 2879, 1686, 1524, 1456, 1412, 1328, 1264, 1062, 963, 752 cm<sup>-1</sup>; HRMS (ESI) for C<sub>13</sub>H<sub>18</sub>NO<sub>4</sub>S [M+H]<sup>+</sup> calculated: 284.0951; found: 284.0942.

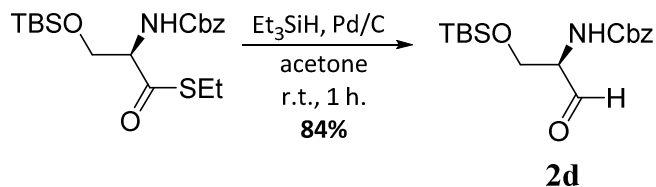
**(R)-S-ethyl 8,8,9,9-tetramethyl-3-oxo-1-phenyl-2,7-dioxa-4-aza-8-siladecane-5-carbothioate**



To a solution of alcohol (1.15 g, 4.06 mmol) in cold (0 °C) dichloromethane (7.7 mL) was added imidazole (539.0 mg, 7.92 mmol) and TBSCl (893.0 mg, 5.94 mmol). The reaction mixture was stirred for 1 h at room temperature, then diluted with dichloromethane, washed with water, dried with anh. MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. The residue was purified by dry-flash chromatography (SiO<sub>2</sub>; petroleum ether/EtOAc = 95:5), to give protected alcohol (1.55 g, 97 %) as a colorless oil.

$[\alpha]_D^{20} +17.3$  (c 1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.43 – 7.31 (m, 5H), 5.67 (d, *J* = 9.1 Hz, 1H), 5.17 (s, 2H), 4.41 (dt, *J* = 9.0, 3.1 Hz, 1H), 4.15 (dd, *J* = 10.2, 2.6 Hz, 1H), 3.78 (dd, *J* = 10.1, 3.6 Hz, 1H), 2.92 – 2.84 (m, 2H), 1.24 (t, *J* = 7.4 Hz, 3H), 0.85 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 200.4 (C), 155.9 (C), 136.2 (C), 128.6 (2xCH), 128.3 (CH), 128.2 (2xCH), 67.3 (CH<sub>2</sub>), 63.5 (CH<sub>2</sub>), 62.2 (CH), 25.7 (3xCH<sub>3</sub>), 23.4 (CH<sub>2</sub>), 18.2 (C), 14.4 (CH<sub>3</sub>), -5.6 (CH<sub>3</sub>), -5.7 (CH<sub>3</sub>); IR (ATR) ν 3443, 3336, 3065, 3034, 2954, 2931, 2882, 2857, 1730, 1685, 1499, 1464, 1255, 1214, 1113, 1063, 1007, 970, 839, 779 cm<sup>-1</sup>; HRMS (ESI) for C<sub>19</sub>H<sub>32</sub>NO<sub>4</sub>SSi [M+H]<sup>+</sup> calculated: 398.1816; found: 398.1806.

**(R)-Benzyl 1-(tert-butyldimethylsilyloxy)-3-oxopropan-2-ylcarbamate**



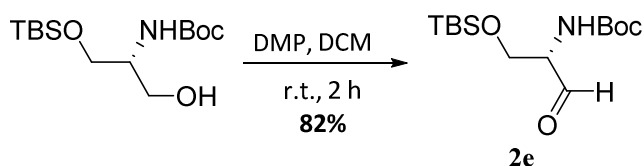
Triethylsilane (1.05 g, 1.45 mL, 9.08 mmol) was added over 15 min to a suspension of thioester (730.0 mg, 1.83 mmol) and 10% palladium on charcoal (406.0 mg; 0.43 mmol) in acetone (29.0 mL), at room temperature, under an argon atmosphere. Upon the completion of the addition, the reaction mixture was stirred for an additional 1 h, then filtered and concentrated under reduced pressure. The residue

was purified by dry-flash chromatography (SiO<sub>2</sub>; petroleum ether/EtOAc = 9:1) to give title aldehyde **2d** (524.2 mg, 84%) as a colorless oil.

[ $\alpha$ ]<sub>D</sub><sup>20</sup> -60.0 (c 1.08, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  9.65 (s, 1H), 7.46 – 7.28 (m, 5H), 5.63 (d, *J* = 7.4 Hz, 1H), 5.13 (s, 2H), 4.32 (dt, *J* = 7.7, 3.7 Hz, 1H), 4.21 (dd, *J* = 10.5, 3.1 Hz, 1H), 3.88 (dd, *J* = 10.5, 4.3 Hz, 1H), 0.85 (s, 9H), 0.03 (s, 3H), 0.03 (s, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  198.8 (CH), 156.0 (C), 136.1 (C), 128.5 (2xCH), 128.2 (CH), 128.1 (2xCH), 67.1 (CH<sub>2</sub>), 61.8 (CH), 61.2 (CH<sub>2</sub>), 25.7 (3xCH<sub>3</sub>), 18.1 (C), -5.7 (CH<sub>3</sub>), -5.7 (CH<sub>3</sub>); IR (ATR)  $\nu$  3277, 2956, 2933, 2881, 2858, 1765, 1466, 1392, 1254, 1221, 1129, 996, 839, 779, 746 cm<sup>-1</sup>; HRMS (ESI) for C<sub>17</sub>H<sub>28</sub>NO<sub>4</sub>Si [M+H]<sup>+</sup> calculated: 338.1782; found: 338.1772.

### 3. Preparation of aldehyde **2e**:

#### (S)-tert-butyl 1-(tert-butyldimethylsilyloxy)-3-oxopropan-2-ylcarbamate



Dess-Martin's periodinane (102.0 mg, 0.24 mmol) was added to a solution of alcohol<sup>1</sup> (30.0 mg, 0.10 mmol) in dichloromethane (2.4 mL) and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with dichloromethane, washed with 5% Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and sat. aq. NaHCO<sub>3</sub>, dried over anh. MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. Purification of the residue by column chromatography (SiO<sub>2</sub>; petroleum ether/ethyl acetate = 85/15) afforded the title compound **2e** (24.4 mg, 82%) as a colorless oil.

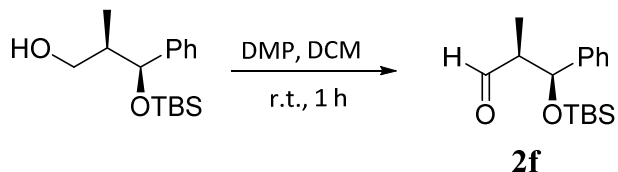
Data for aldehyde **2e**: [ $\alpha$ ]<sub>D</sub><sup>20</sup> +44.0 (c 1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  9.60 (s, 1H), 5.35 (bs, 1H), 4.27 – 4.08 (m, 2H), 3.83 (dd, *J* = 10.1, 3.6 Hz, 1H), 1.42 (s, 9H), 0.82 (s, 9H), 0.01 (s, 3H), 0.00 (s, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  199.4 (CH), 155.5 (C), 80.0 (C), 61.6 (CH), 61.4 (CH<sub>2</sub>), 28.3 (3xCH<sub>3</sub>), 25.7 (3xCH<sub>3</sub>), 18.2 (C), -5.6 (2xCH<sub>3</sub>). IR (ATR)  $\nu$  3404, 2955, 2931, 2888, 2858, 1700, 1505, 1470, 1391, 1368, 1304, 1253, 1166, 1114, 838, 779 cm<sup>-1</sup>; HRMS (ESI) for C<sub>14</sub>H<sub>29</sub>NO<sub>4</sub>SiNa [M+Na]<sup>+</sup> calculated: 326.1758; found: 326.1753.

1. Ref. S. Bhowmik, S. Batra, *Eur. J. Org. Chem.* **2013**, 7145–7151.



#### 4. Preparation of aldehyde **2f**:

##### (2S,3S)-3-((tert-butyldimethylsilyl)oxy)-2-methyl-3-phenylpropanal

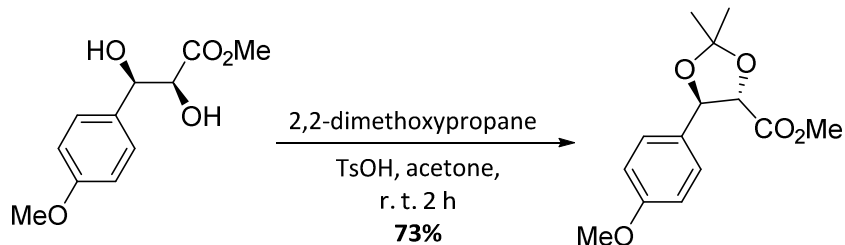


Dess-Martin's periodinane (91.0 mg, 0.21 mmol) was added to a solution of alcohol<sup>2</sup> (26.0 mg, 0.09 mmol) in dichloromethane (1.7 mL) and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with dichloromethane, washed with 5% Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and sat. aq. NaHCO<sub>3</sub>, dried over anh. MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. The residue was used in the next step without further purification.

2. N. Schläger, A. Kirschning, *Org. Biomol. Chem.* **2012**, 7721–7729.

#### 5. Preparation of aldehyde **2h**:

##### (4S,5R)-Methyl 5-(4-methoxyphenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate

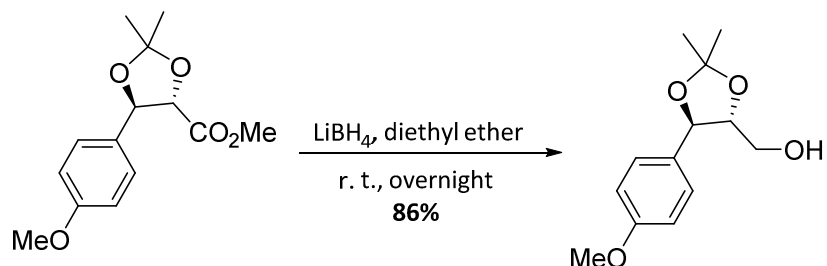


2,2-dimethoxypropane (34.0 mg; 40  $\mu$ L; 0.33 mmol) was added to a solution of diol<sup>3</sup> (50.0; 0.22 mmol) and *p*-toluenesulfonic acid (2.9 mg; 0.01 mmol) in acetone (0.6 mL). Reaction mixture was stirred at room temperature for 2 h and concentrated under reduced pressure. The residue was diluted with diethyl ether (30 mL), washed with brine, dried over anh. MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. Purification of the residue by column chromatography (SiO<sub>2</sub>; petroleum ether/ethyl acetate = 95:5) afforded the title compound (43.0 mg, 73%) as a colorless oil.

$[\alpha]_D^{20} +31.0$  (*c* 1.02, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.34 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 5.10 (d, *J* = 7.8 Hz, 1H), 4.33 (d, *J* = 7.8 Hz, 1H), 3.79 (s, 3H), 3.75 (s, 3H), 1.59 (s, 3H), 1.54 (s, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  170.8 (C), 159.9 (C), 129.5 (C), 128.0 (2xCH), 114.1 (2xCH), 111.4 (C), 81.3 (CH), 80.6 (CH), 55.3 (CH<sub>3</sub>), 52.4 (CH<sub>3</sub>), 27.0 (CH<sub>3</sub>), 25.9 (CH<sub>3</sub>); IR (ATR)  $\nu$  2990, 2954, 2938, 2839, 1758, 1615, 1587, 1516, 1460, 1440, 1378, 1300, 1248, 1208, 1175, 1098, 1033, 895, 831 cm<sup>-1</sup>.

3. A. Zhdanko, A. Schmauder, C. I. Ma, L. D. Sibley, D. Sept, F. Sasse, M. E. Maier, *Chem. Eur. J.* **2011**, *17*, 13349 – 13357.

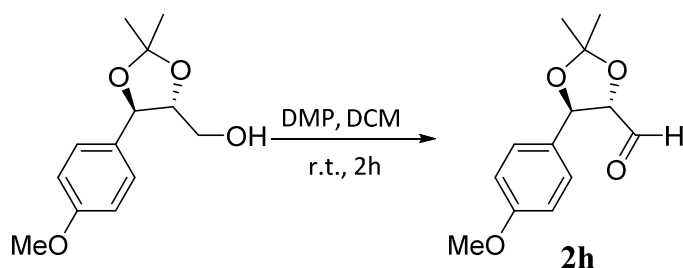
**((4R,5R)-5-(4-methoxyphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol**



To a cold (0 °C) solution of methyl ester (43.0 mg, 0.16 mmol) in diethyl ether (0.5 mL) was added lithium borohydride (6.0 mg, 0.27 mmol) and the reaction mixture was stirred overnight at room temperature. The reaction mixture was quenched by the sequential addition of water (0.6 mL) and extracted with diethyl ether. The combined organic extract was washed with brine, dried with anhydrous  $\text{MgSO}_4$ , filtered and concentrated under reduced pressure. Purification of the crude product by column chromatography ( $\text{SiO}_2$ ; petroleum ether/ethyl acetate = 8:2) afforded title alcohol (33.1 mg, 86%) as a colorless oil.

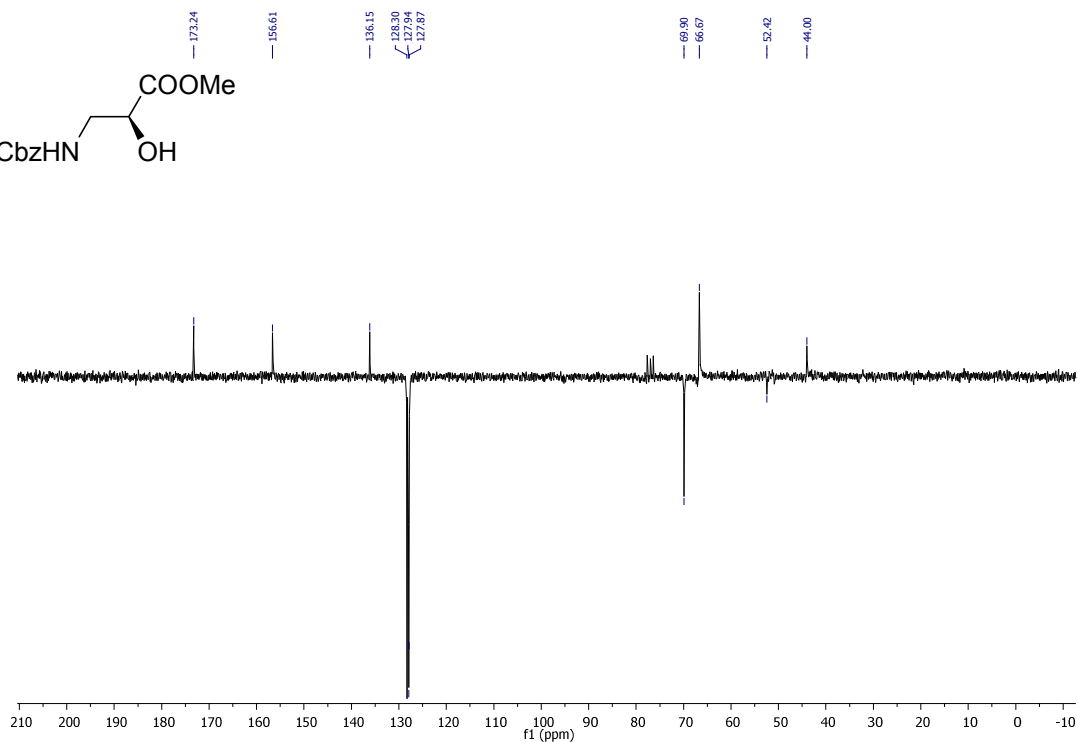
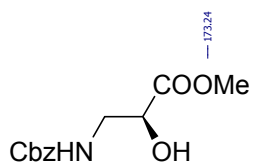
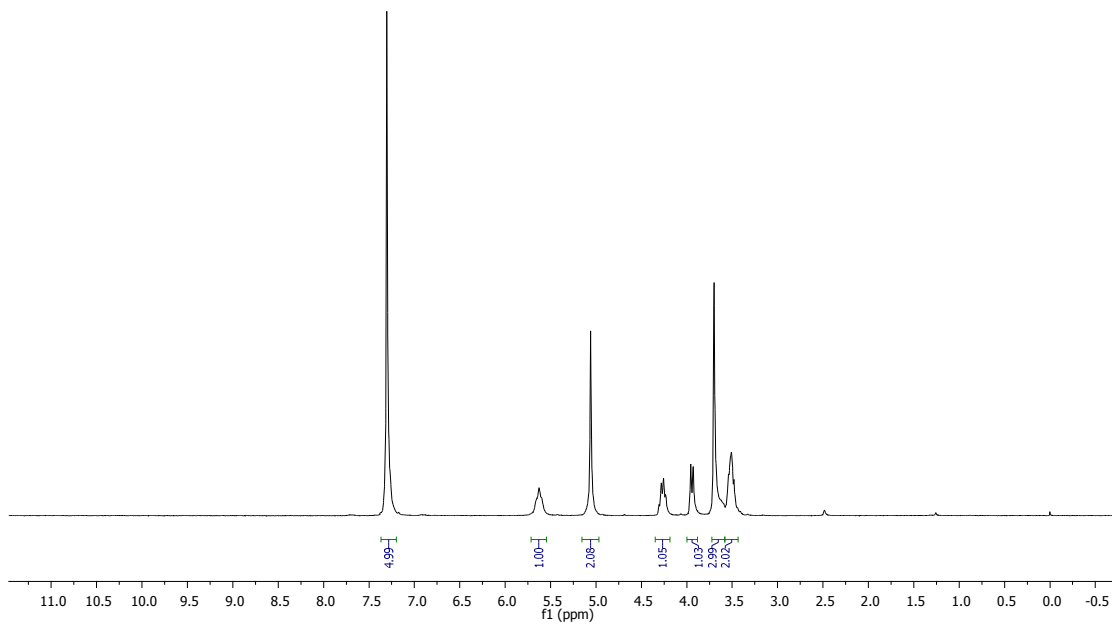
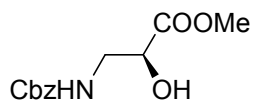
$[\alpha]_D^{20}$  -27.8 (c 1.00,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31 (d,  $J$  = 8.5 Hz, 2H), 6.90 (d,  $J$  = 8.8 Hz, 2H), 4.84 (d,  $J$  = 8.6 Hz, 1H), 3.87 – 3.80 (m, 2H), 3.80 (s, 3H), 3.63 – 3.56 (m, 1H), 2.33 – 2.27 (m, 1H), 1.57 (s, 3H), 1.51 (s, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  159.6 (C), 129.4 (C), 127.9 (2xCH), 114.0 (2xCH), 109.0 (C), 83.4 (CH), 78.4 (CH), 60.3 ( $\text{CH}_2$ ), 55.2 ( $\text{CH}_3$ ), 27.1 ( $\text{CH}_3$ ), 27.0 ( $\text{CH}_3$ ); IR (ATR)  $\nu$  3490, 2988, 2935, 2912, 2873, 2838, 1614, 1586, 1515, 1460, 1375, 1301, 1247, 1171, 1112, 1062, 1037, 830  $\text{cm}^{-1}$ ; HRMS (ESI) for  $\text{C}_{13}\text{H}_{17}\text{O}_3$   $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$  calculated: 221.1172; found: 221.1169.

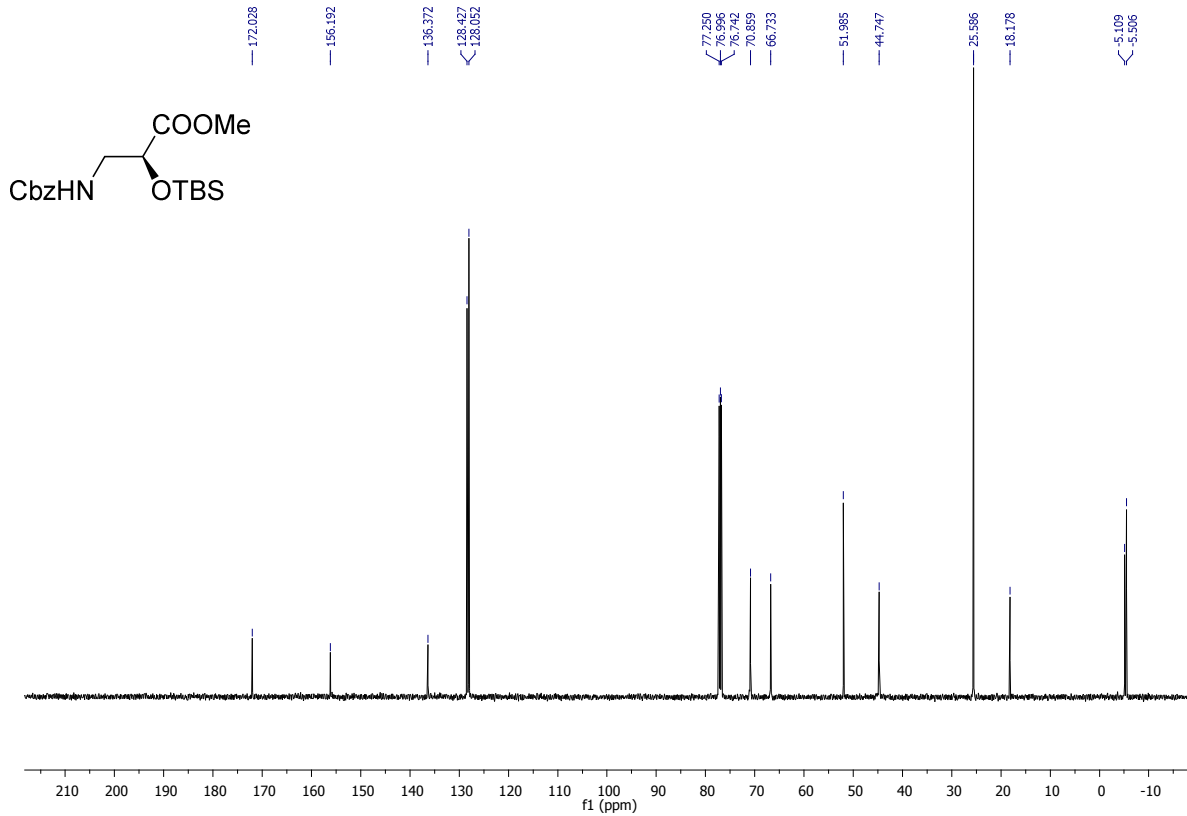
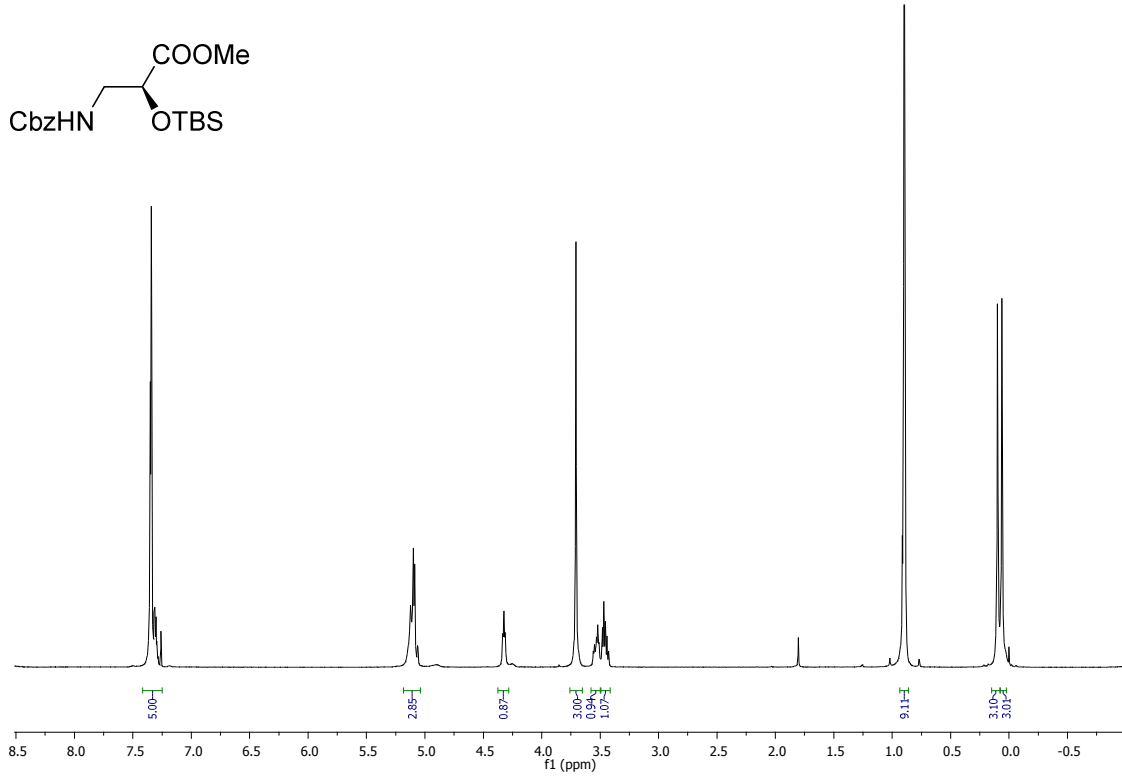
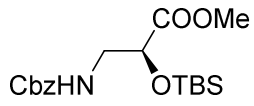
**(4S,5R)-5-(4-methoxyphenyl)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde**

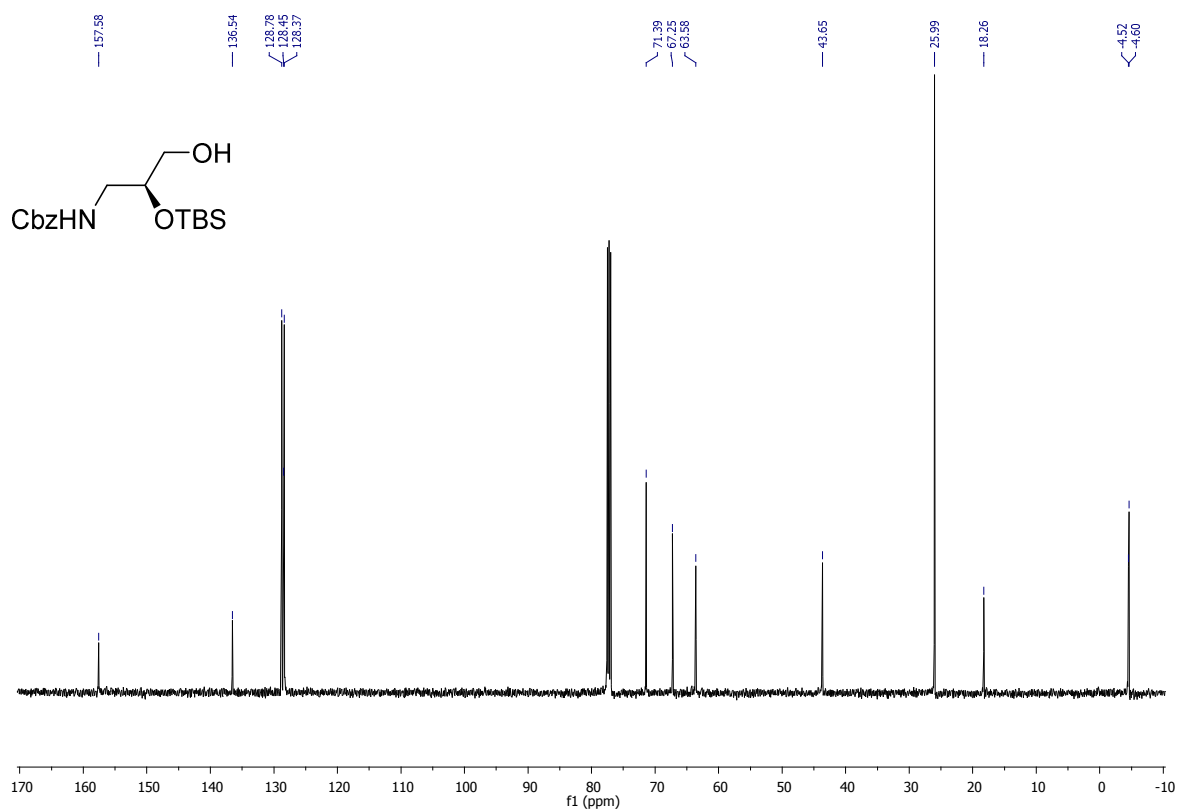
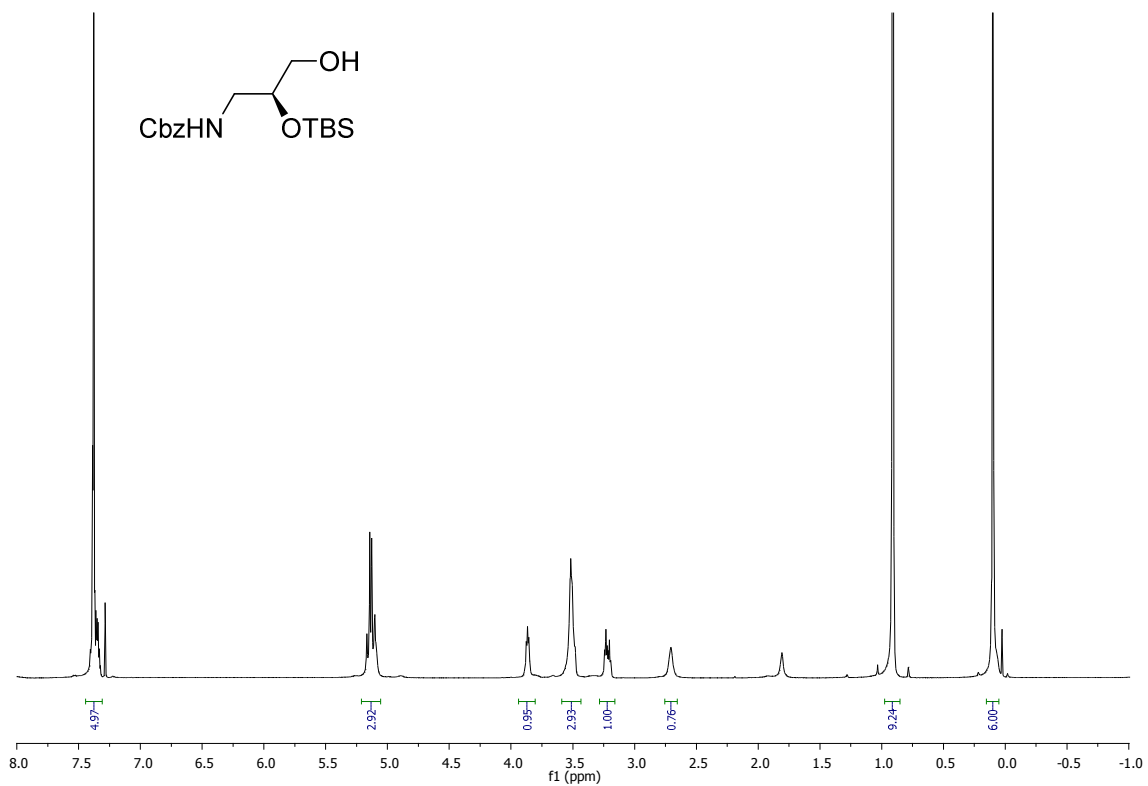


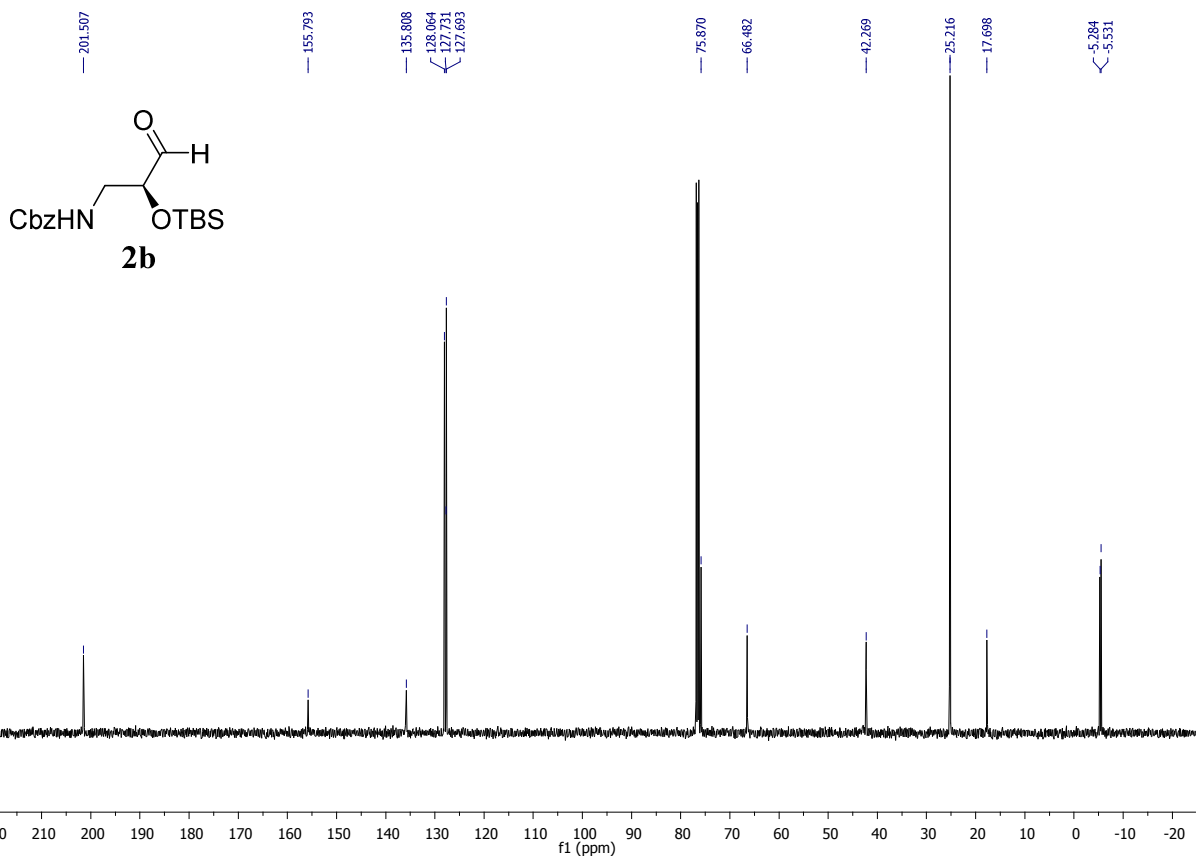
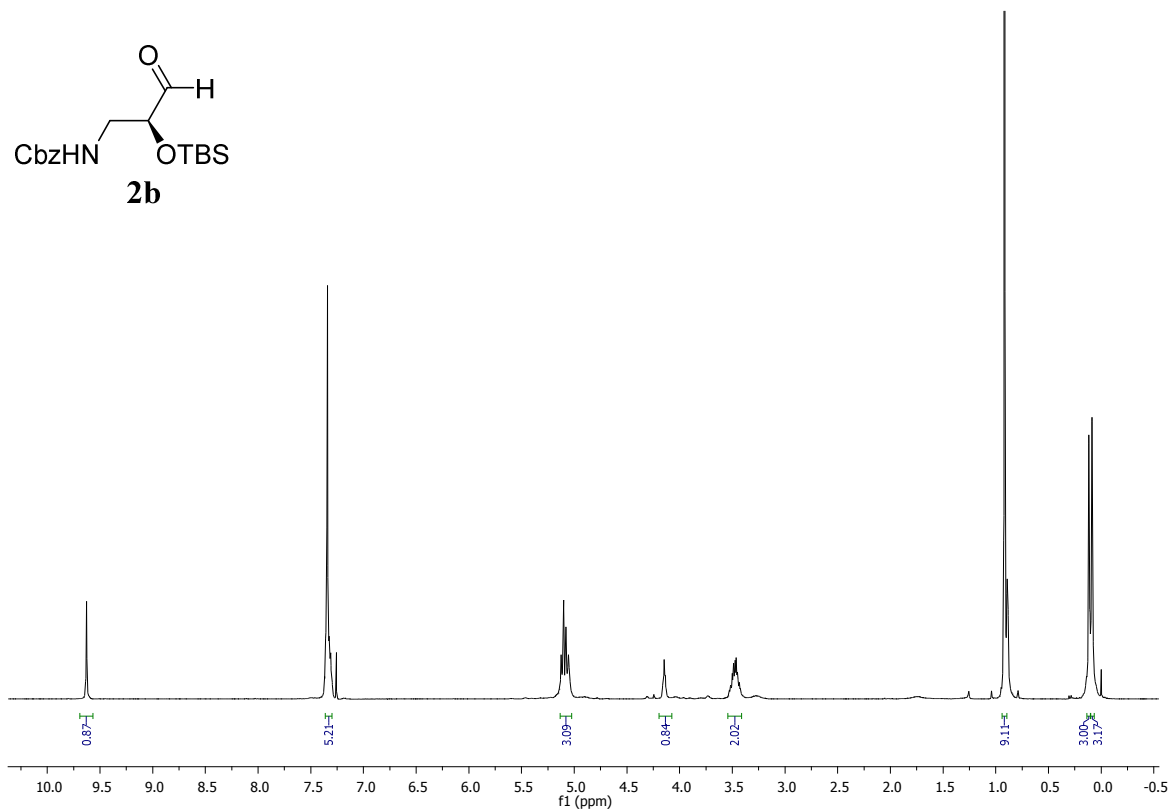
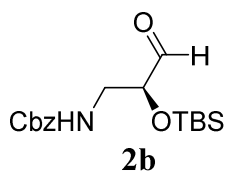
Dess-Martin's periodinane (400.0 mg, 0.94 mmol) was added to a solution of alcohol (80.0 mg, 0.34 mmol) in dichloromethane (5.0 mL) and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with dichloromethane, washed with 5%  $\text{Na}_2\text{S}_2\text{O}_3$  and sat. aq.  $\text{NaHCO}_3$ , dried over anhydrous  $\text{MgSO}_4$ , filtered and concentrated under reduced pressure. The residue was used in the next step without further purification.

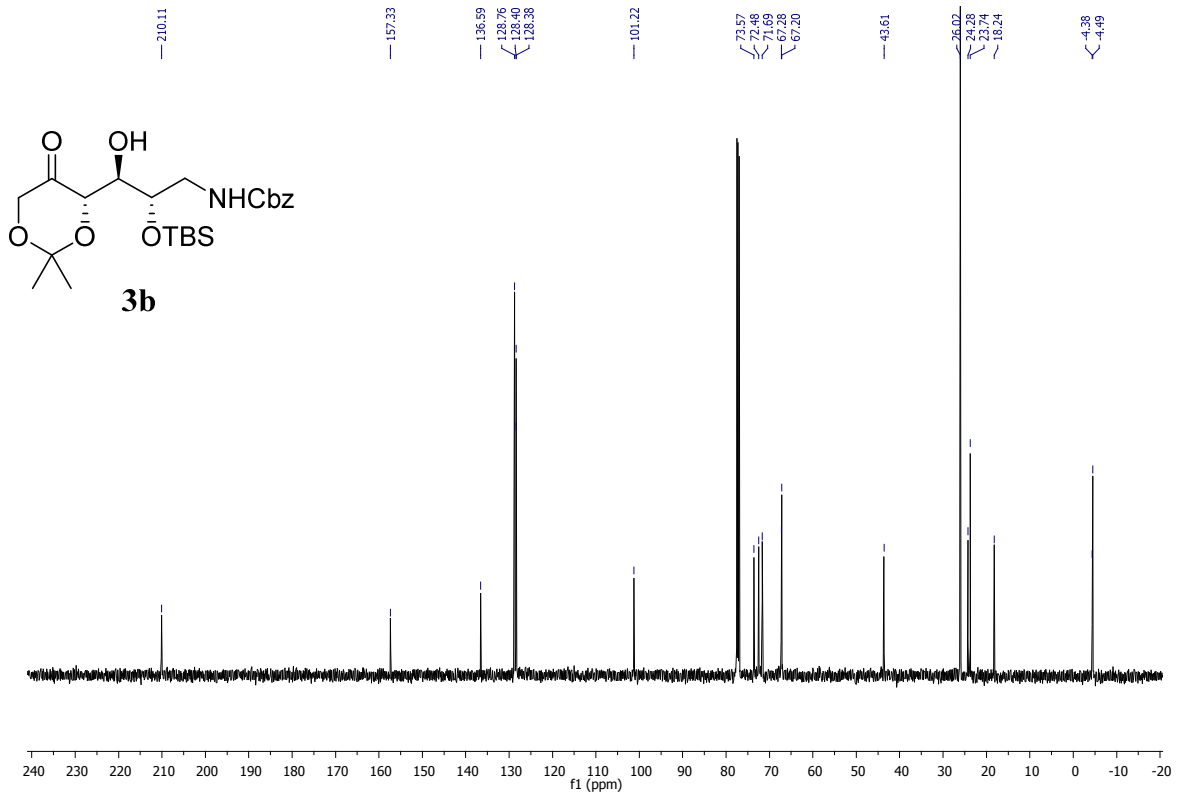
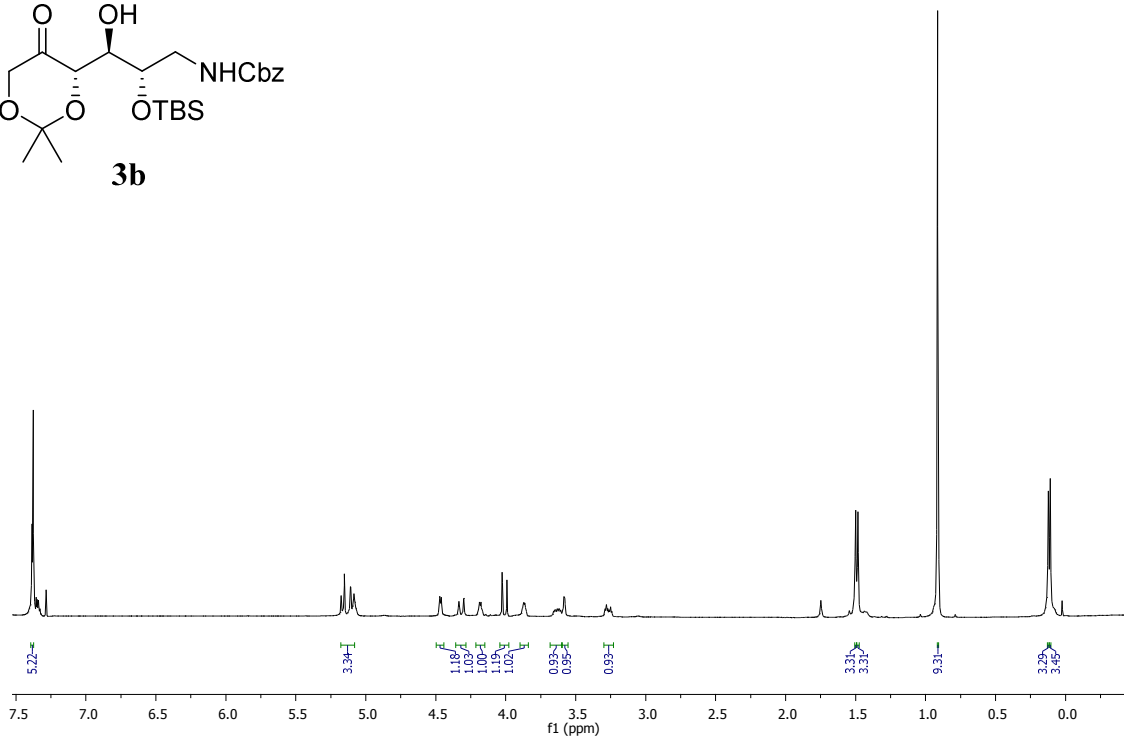
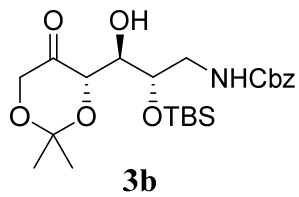
## 6. $^1\text{H}$ and $^{13}\text{C}$ NMR spectra for all compounds

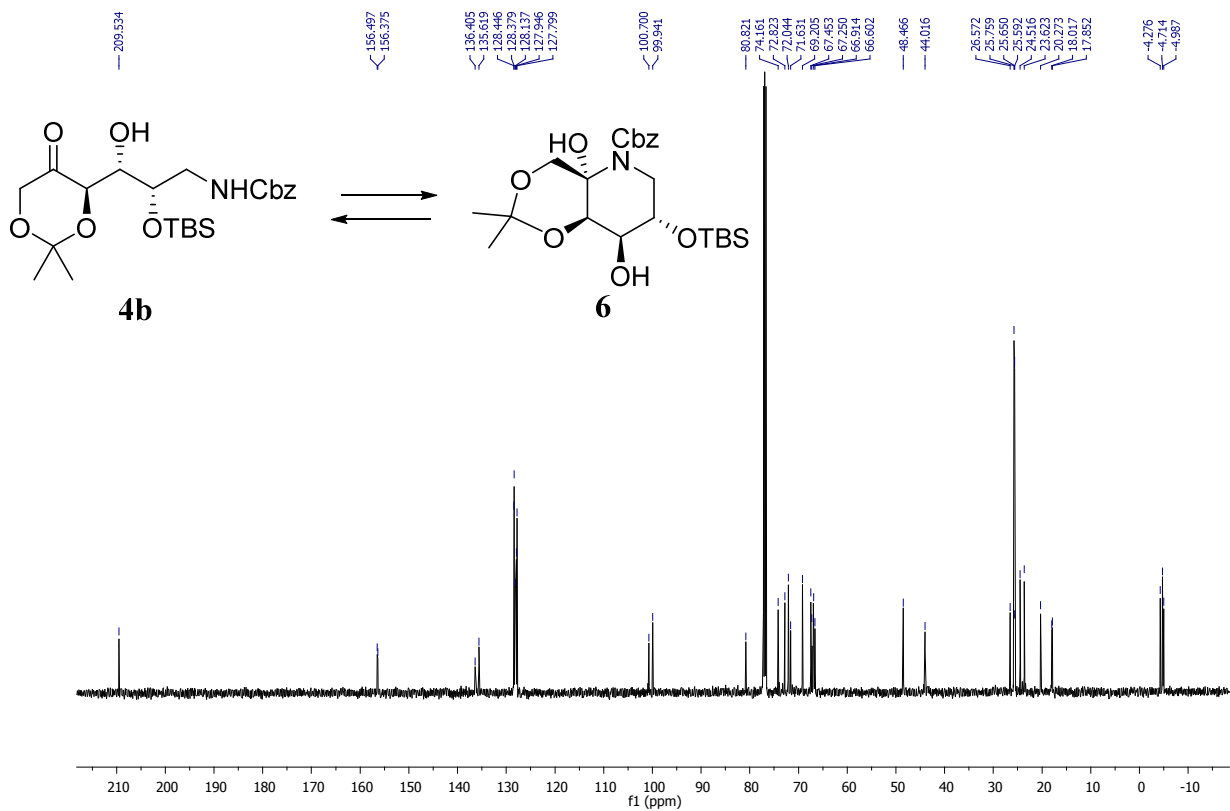
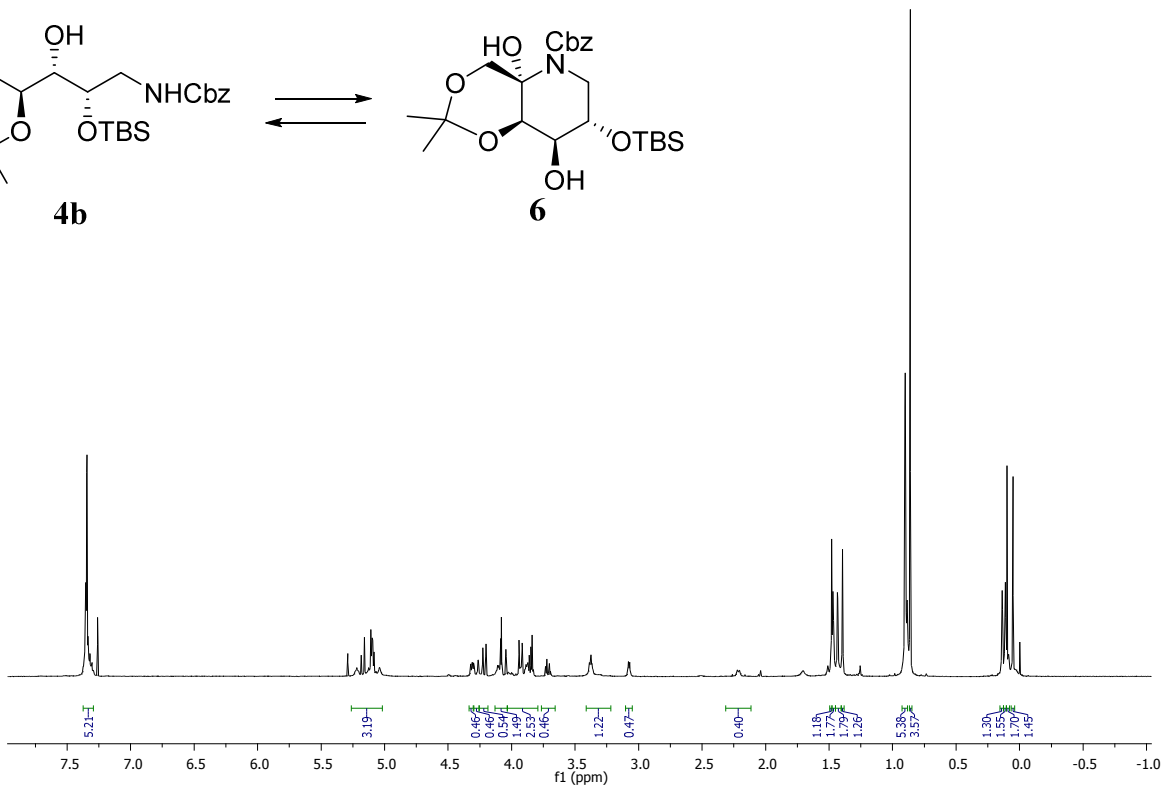
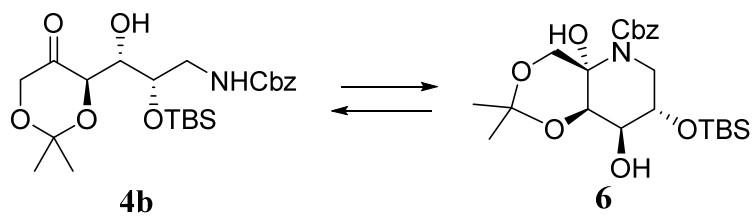




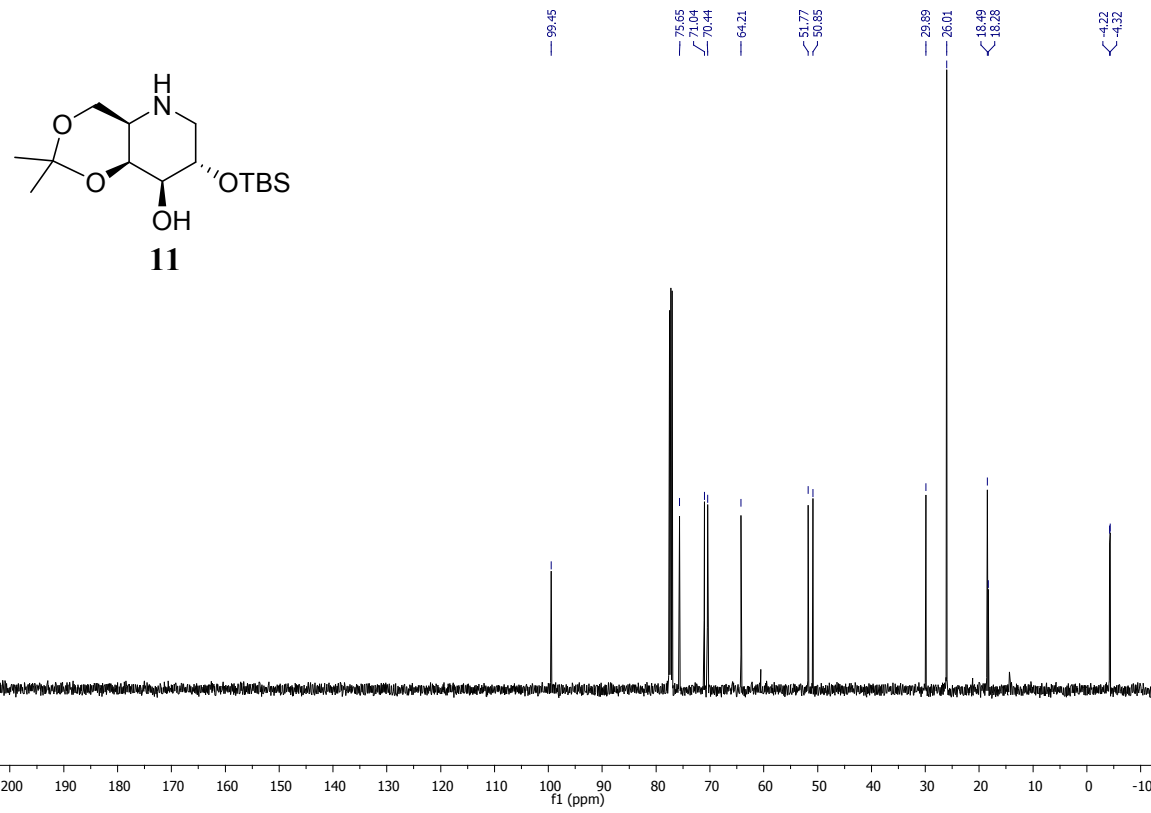
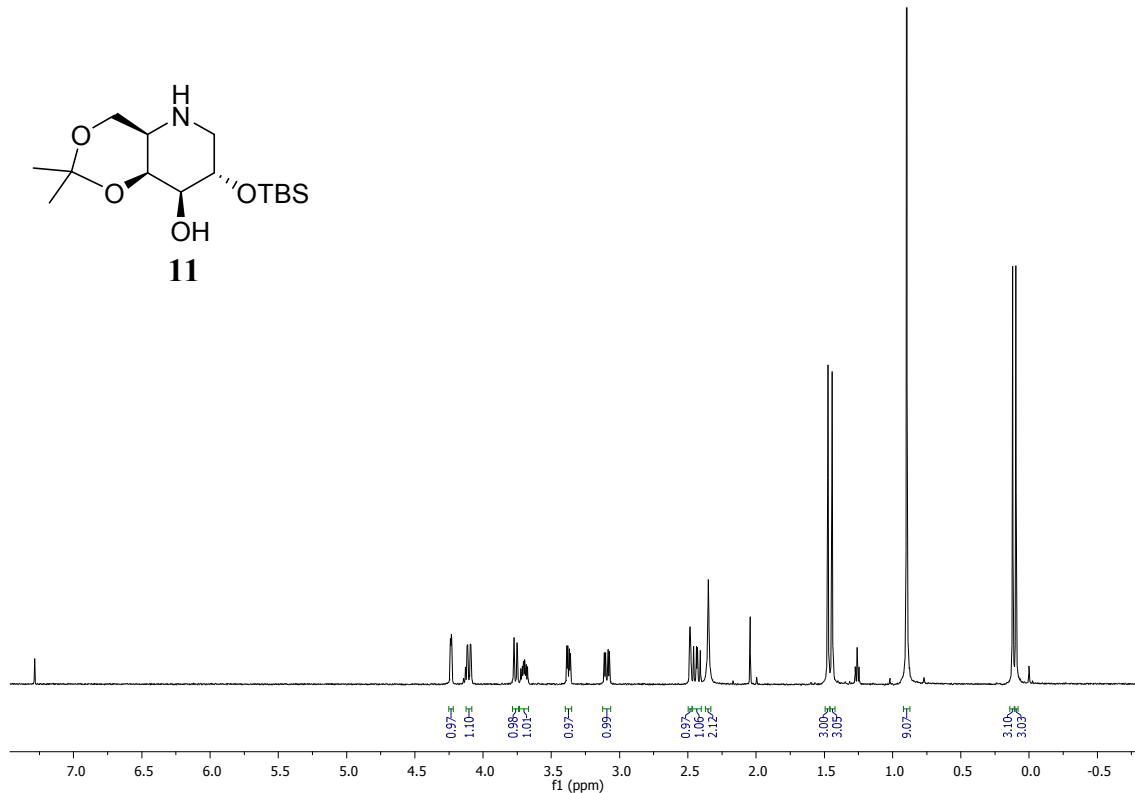
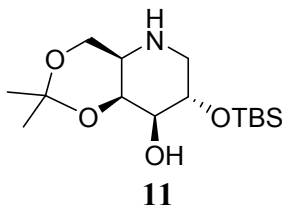


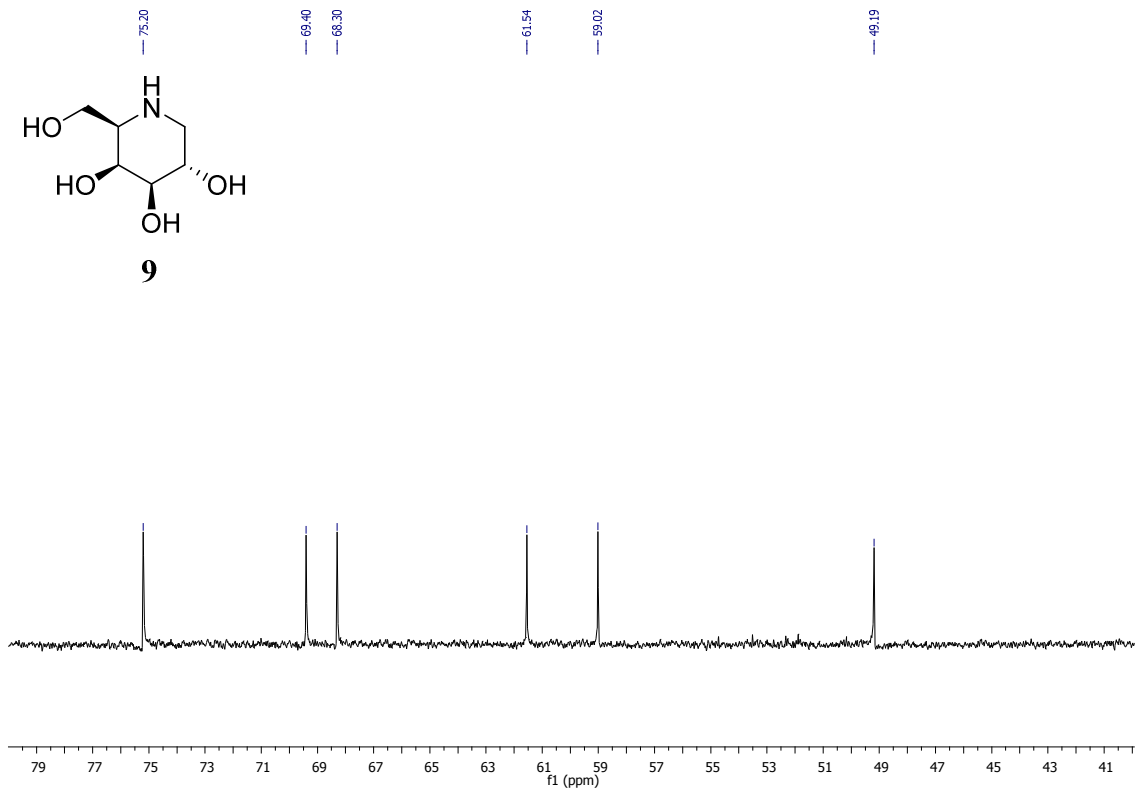
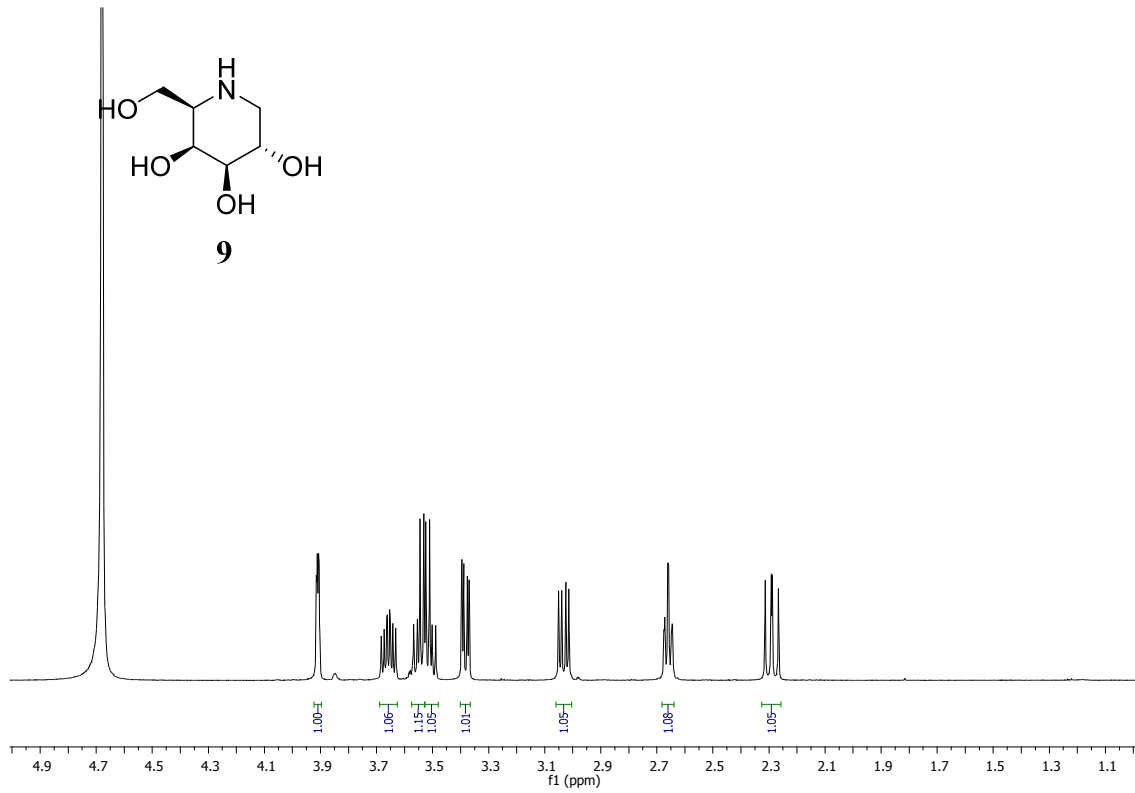


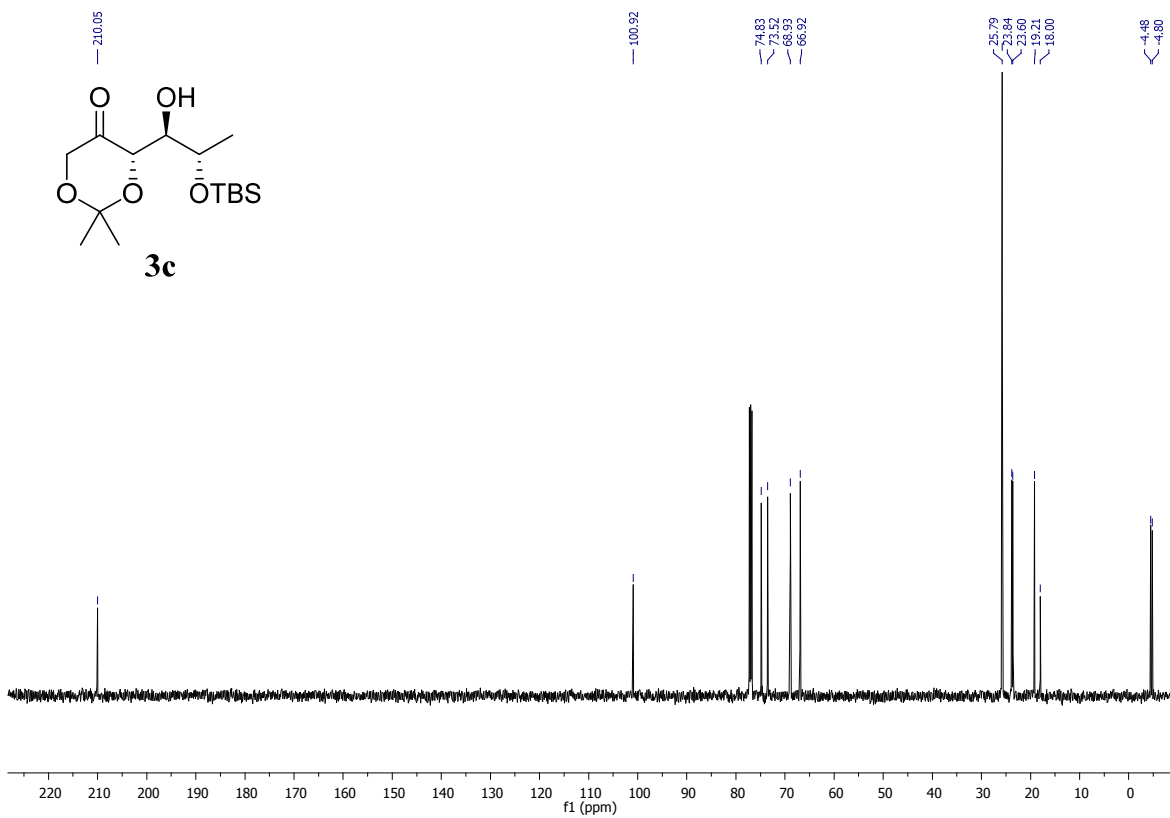
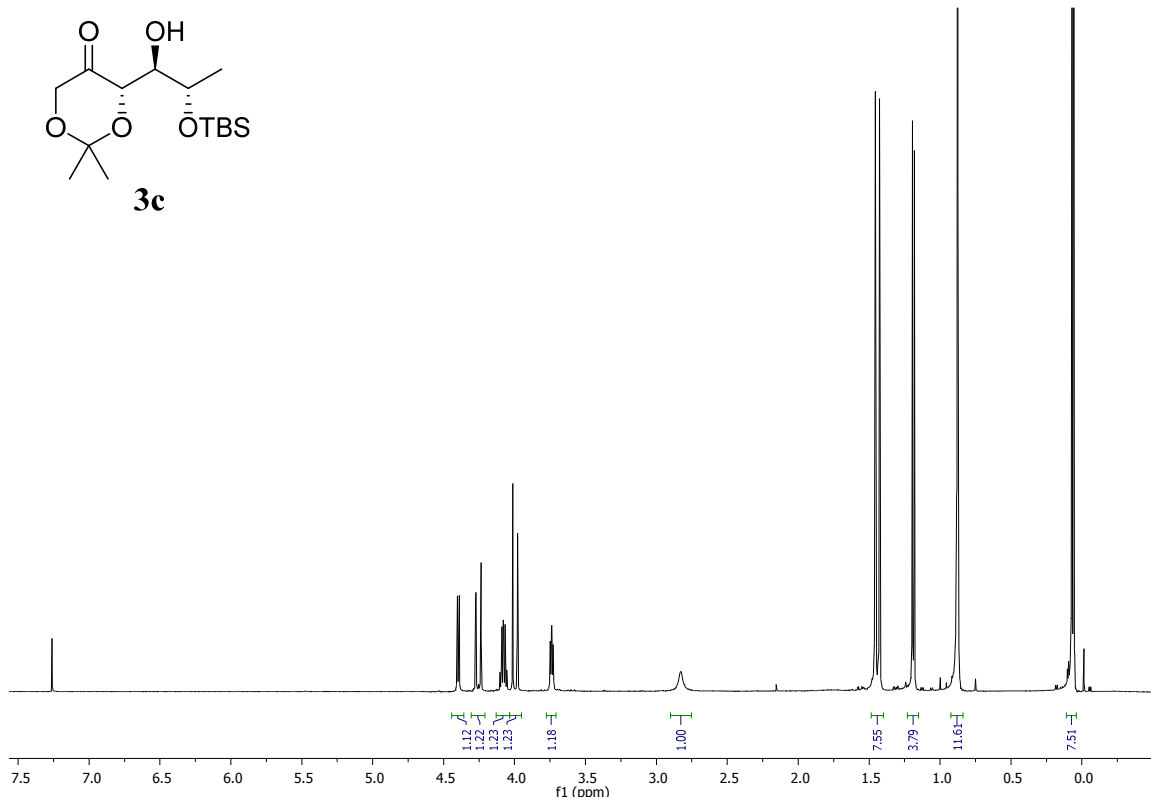


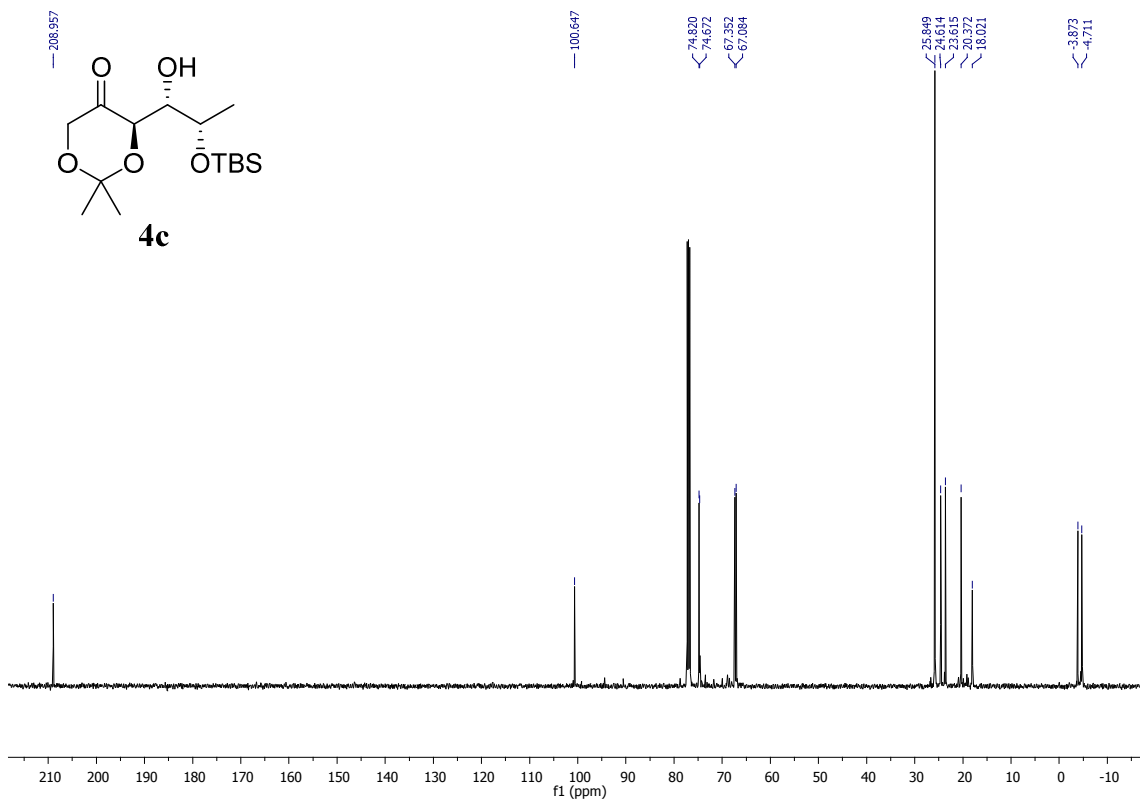
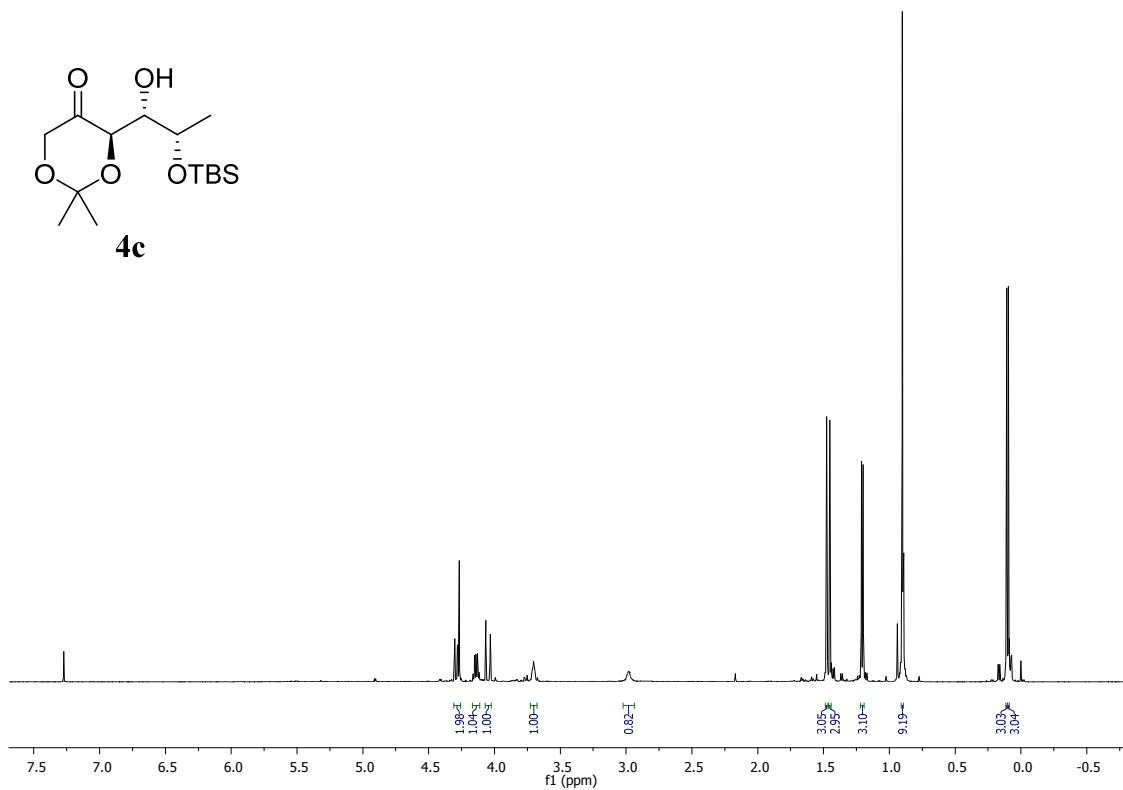
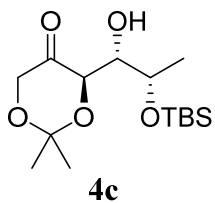


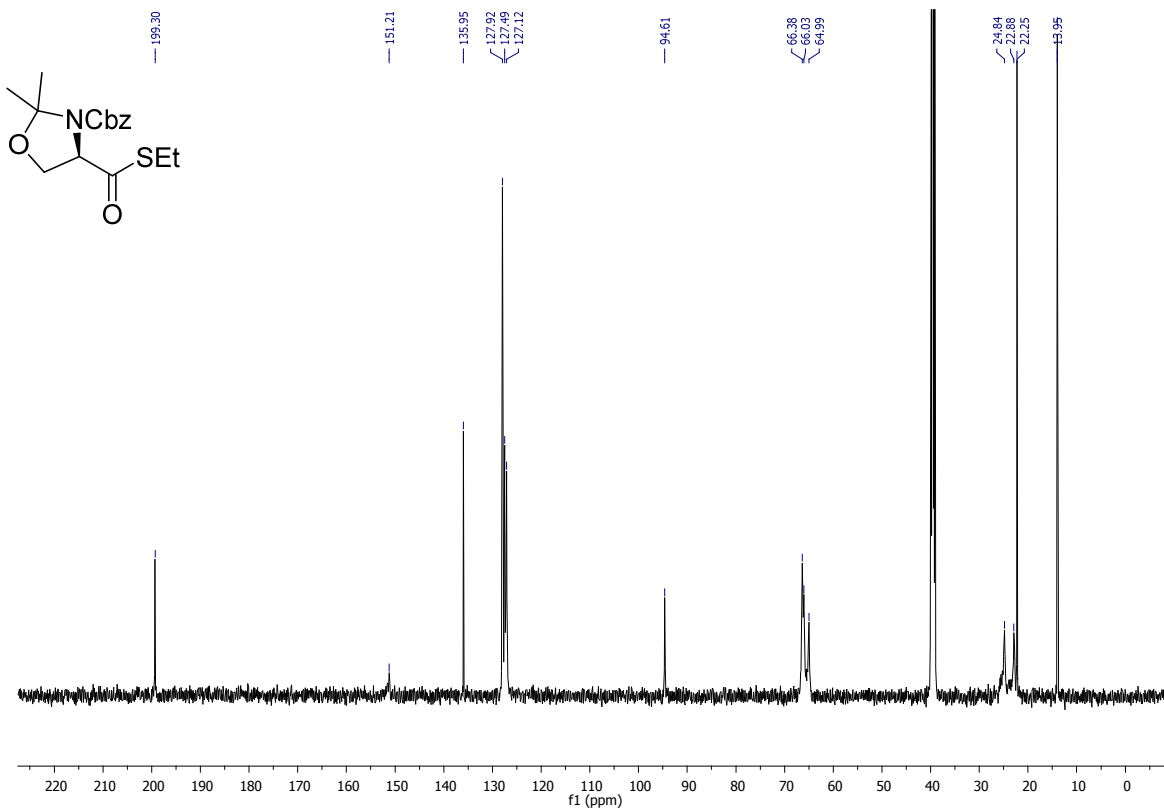
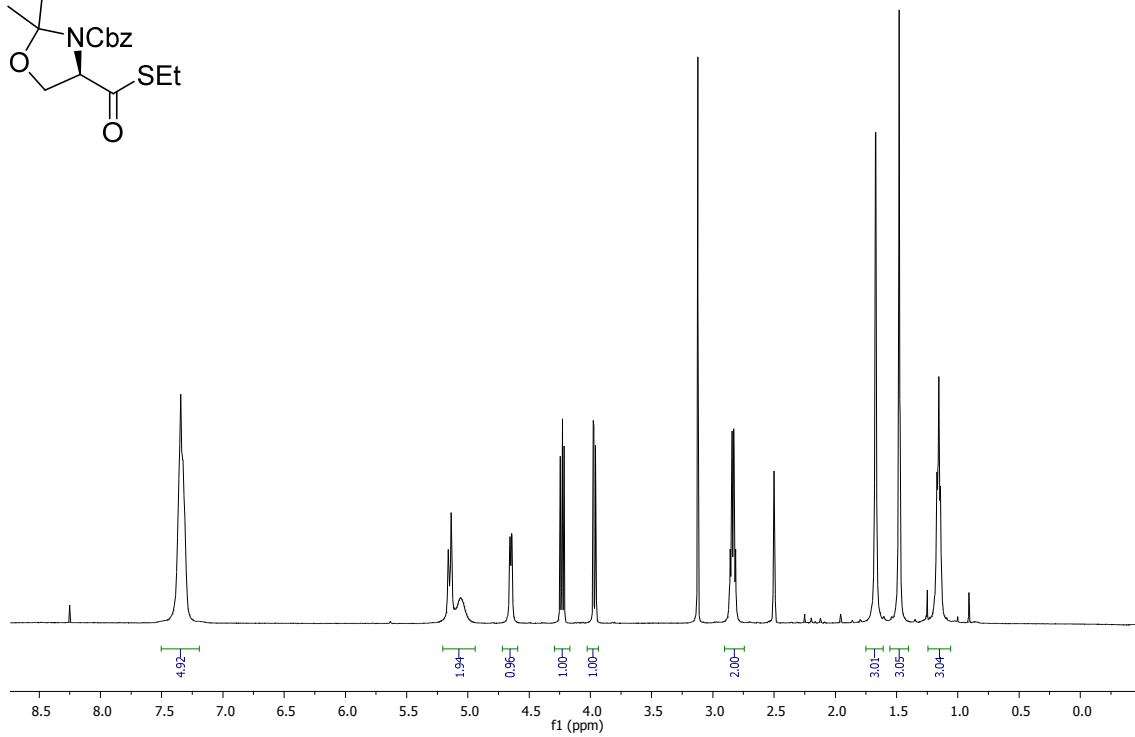
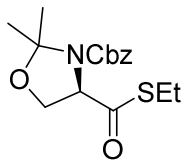


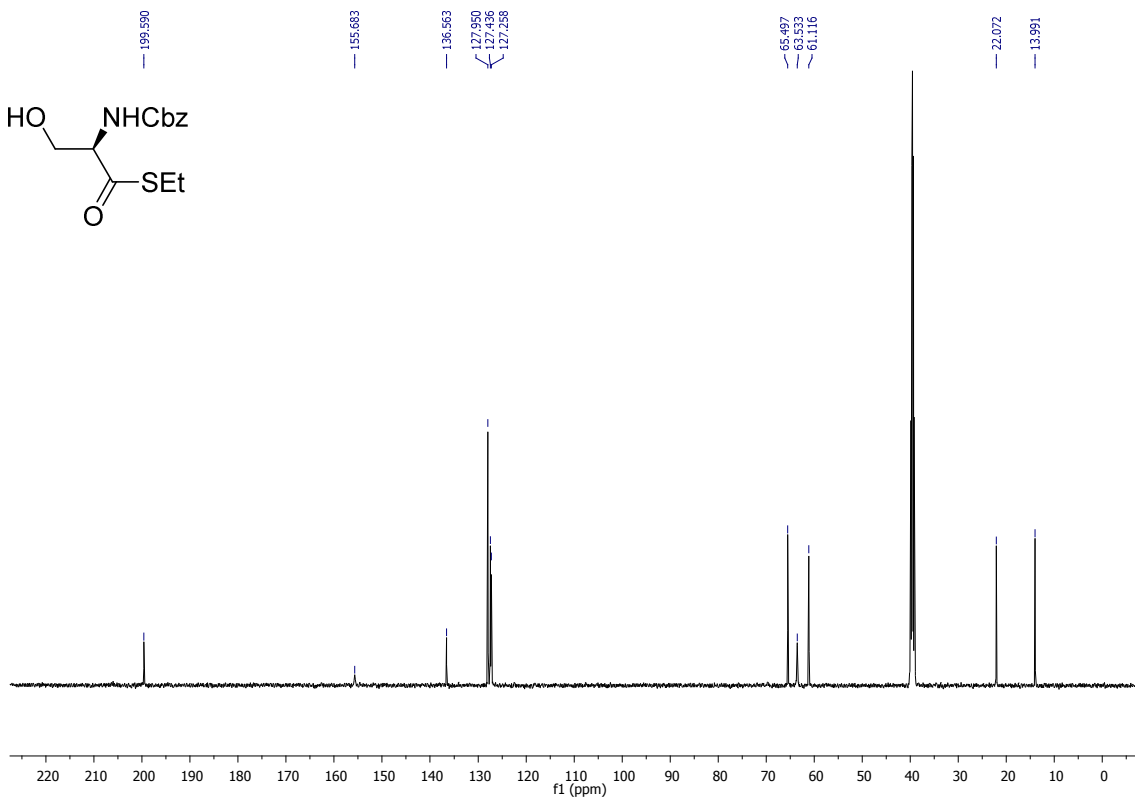
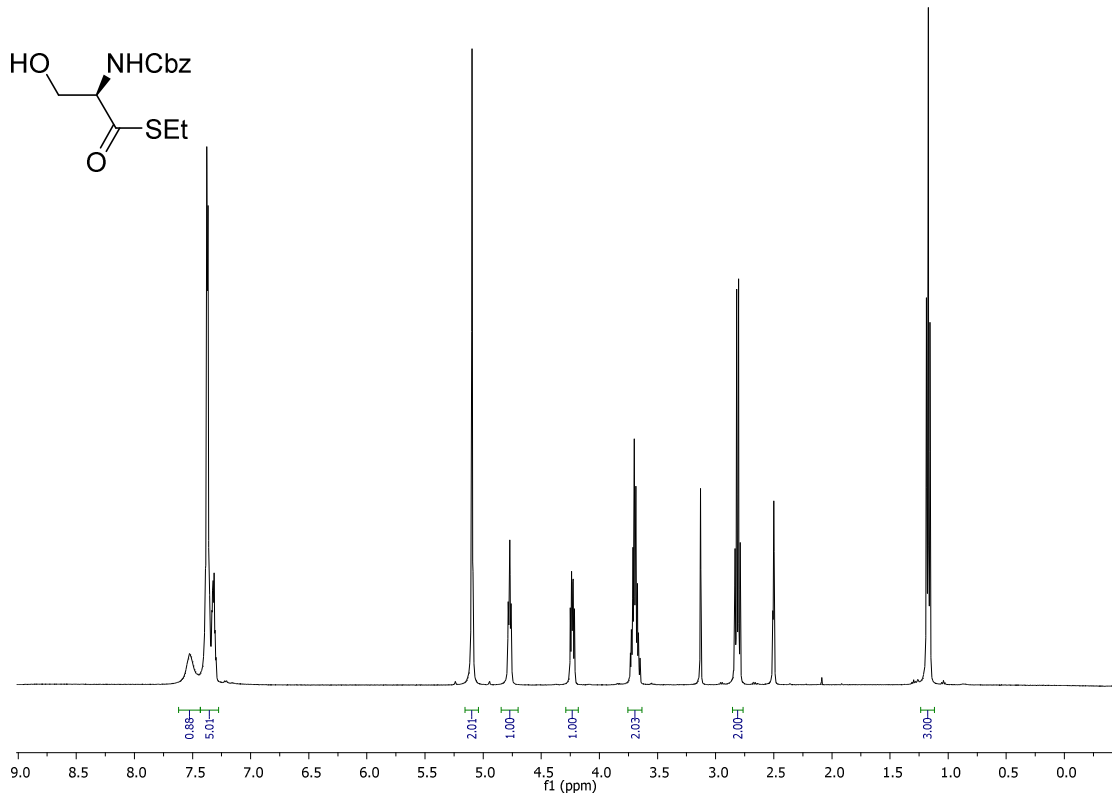


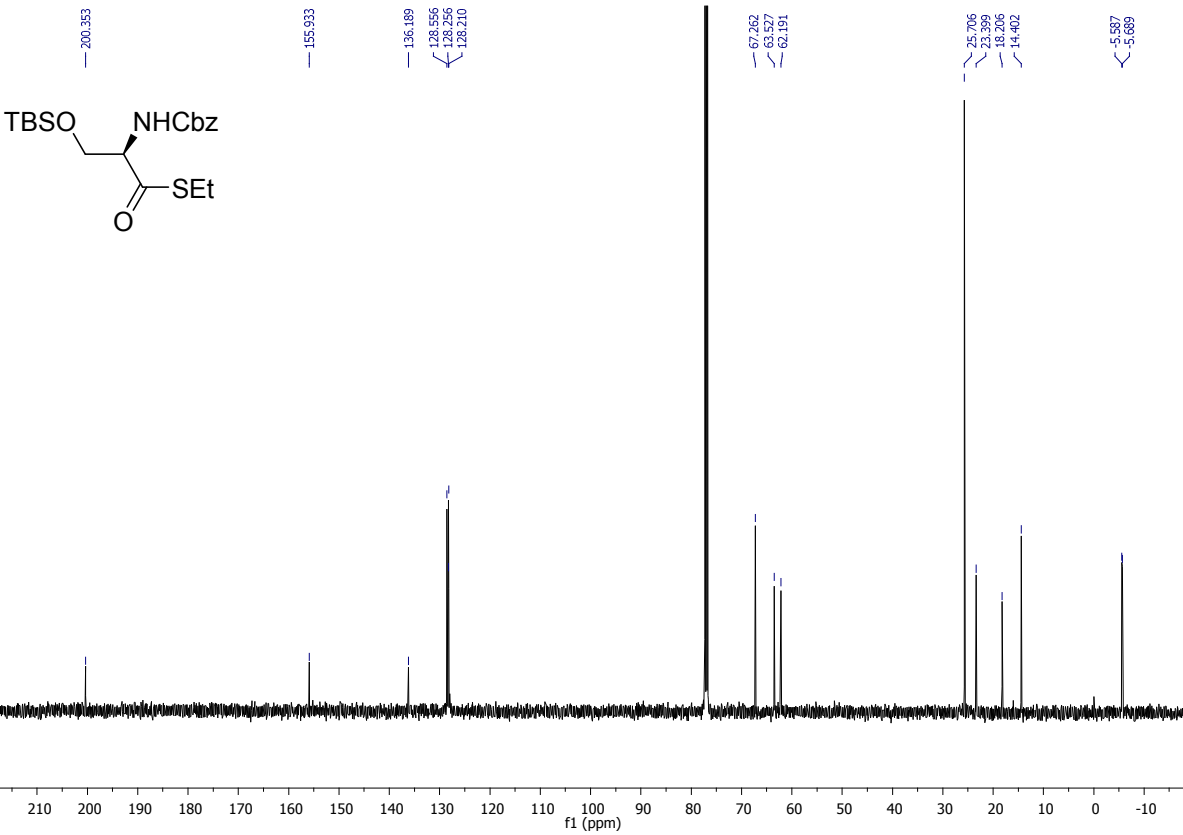
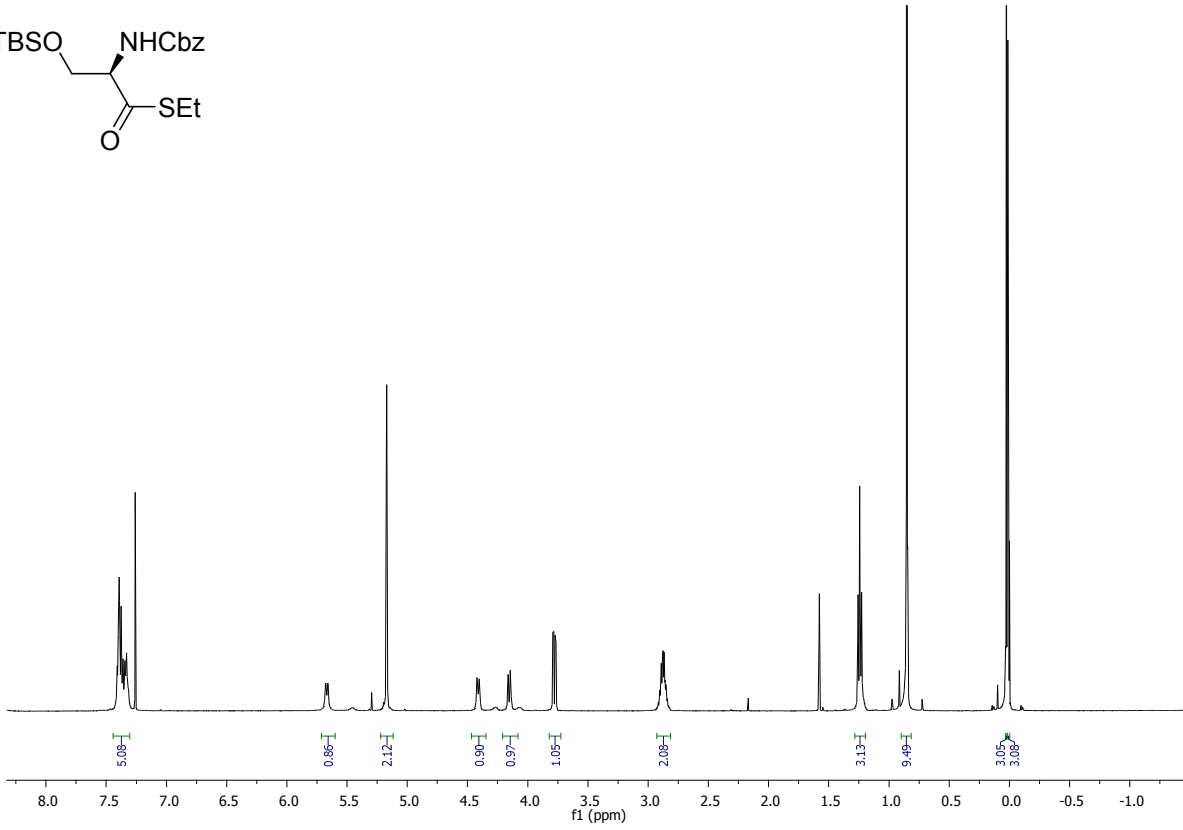
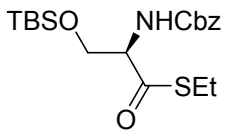


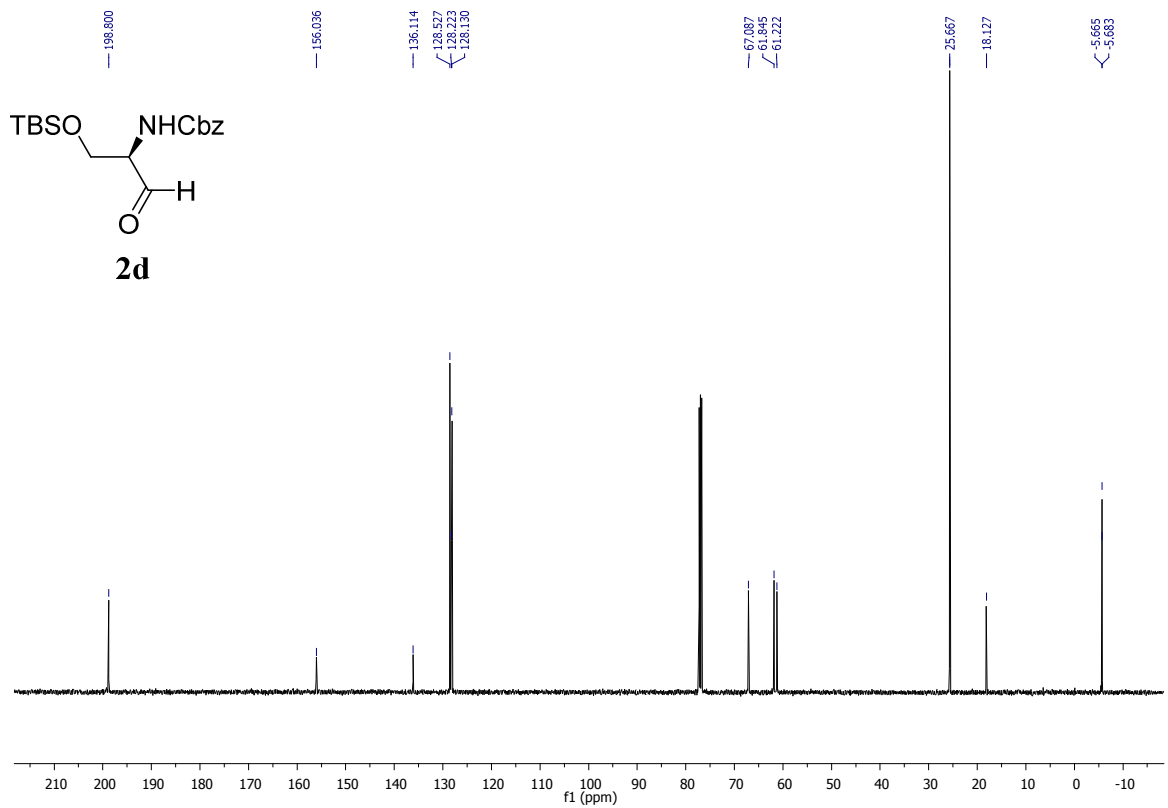
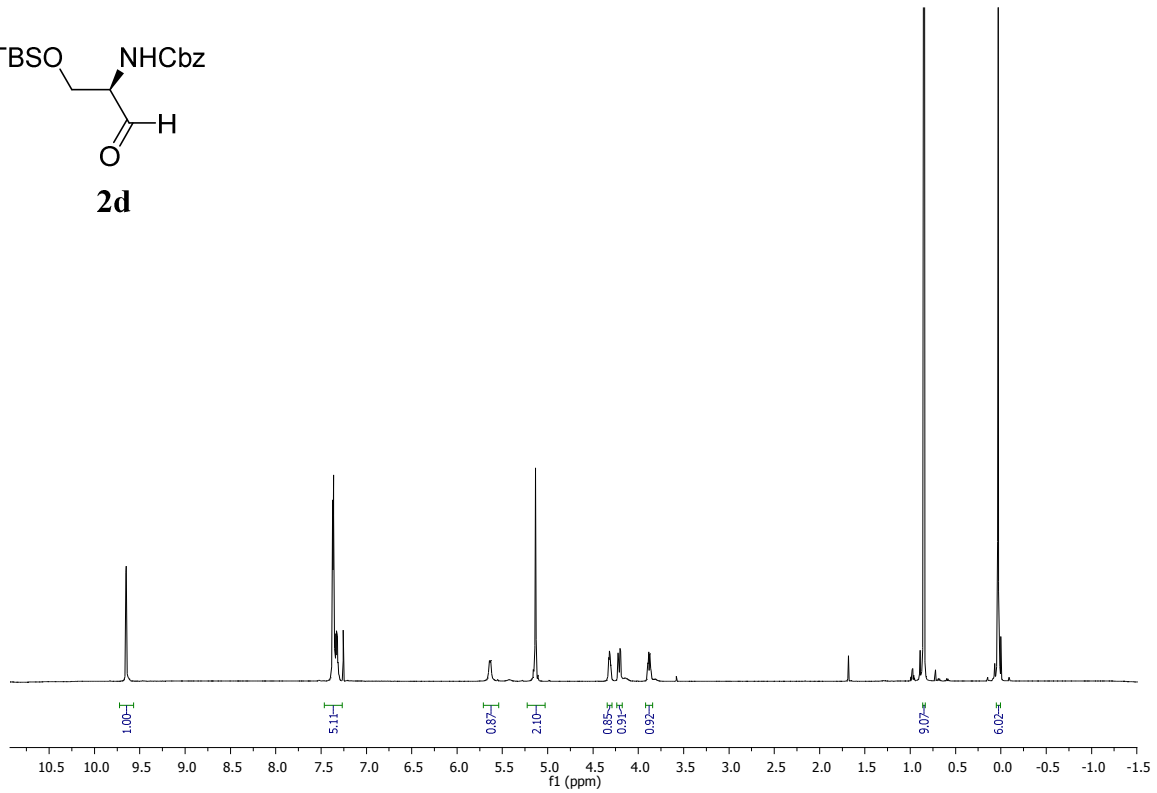
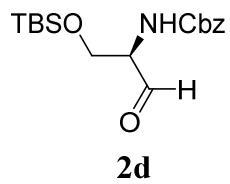




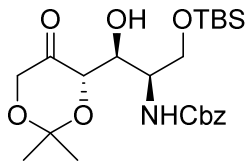




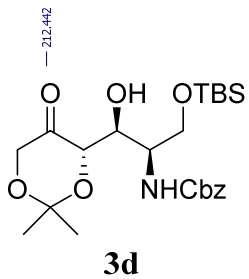
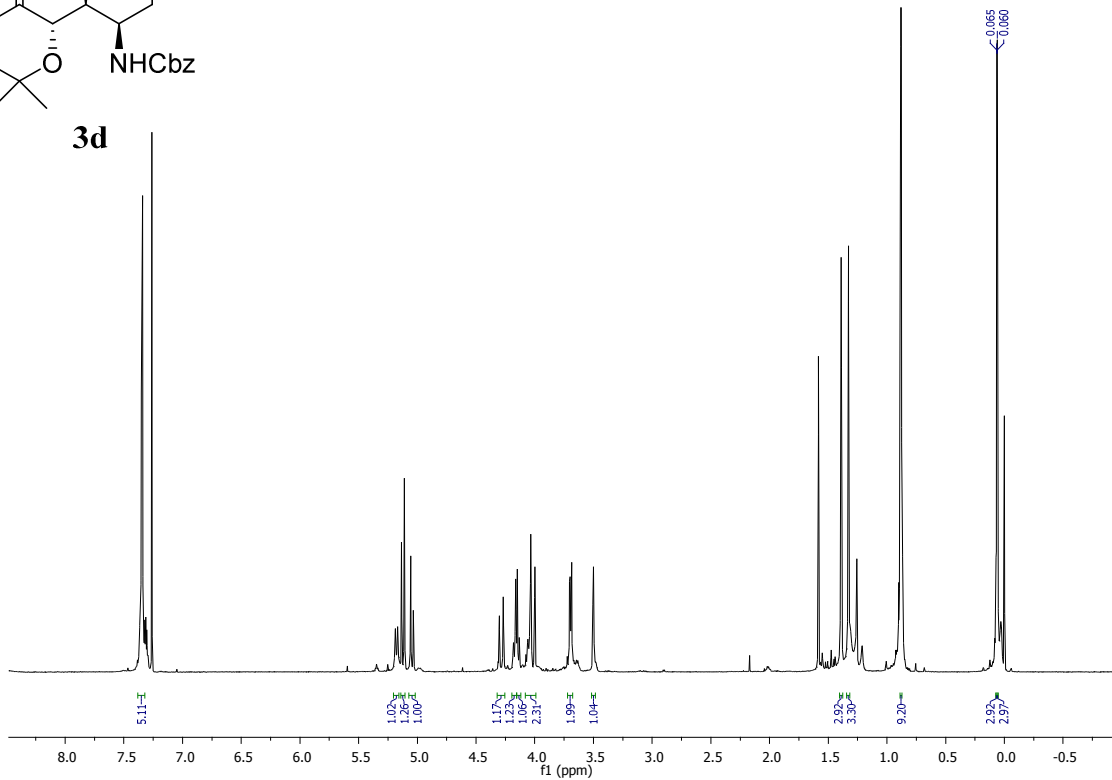




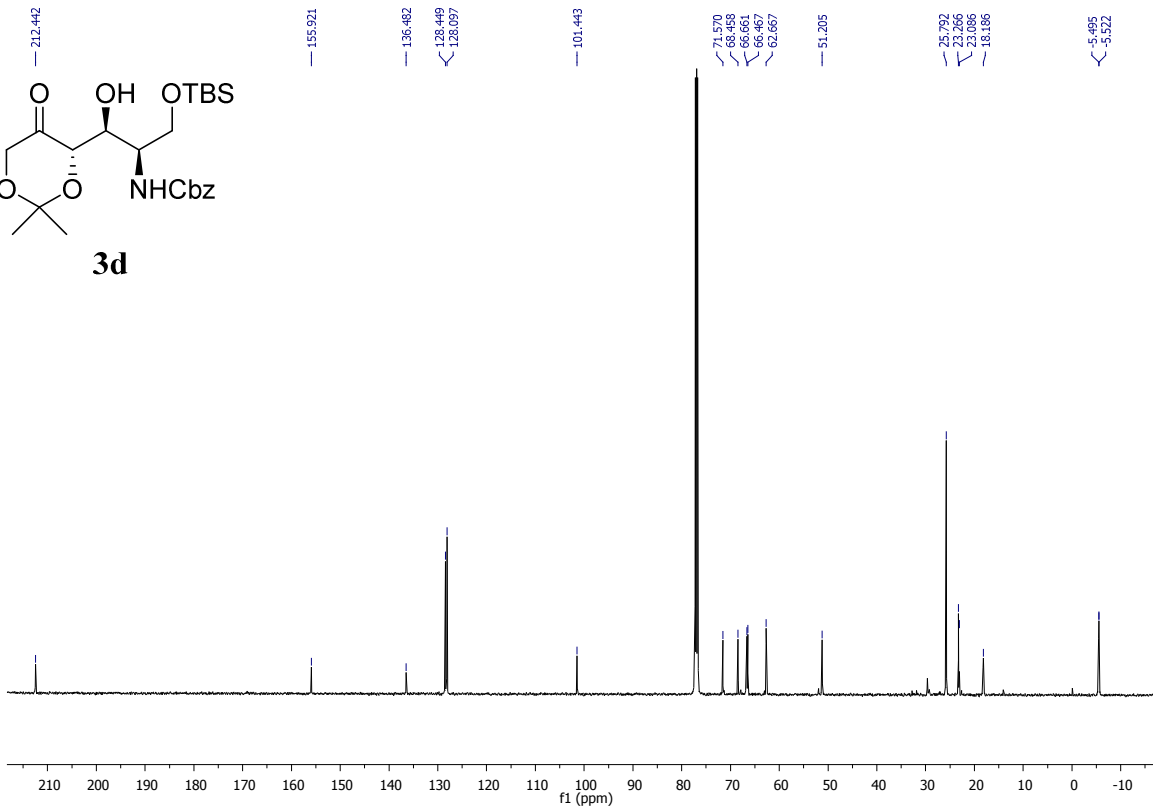


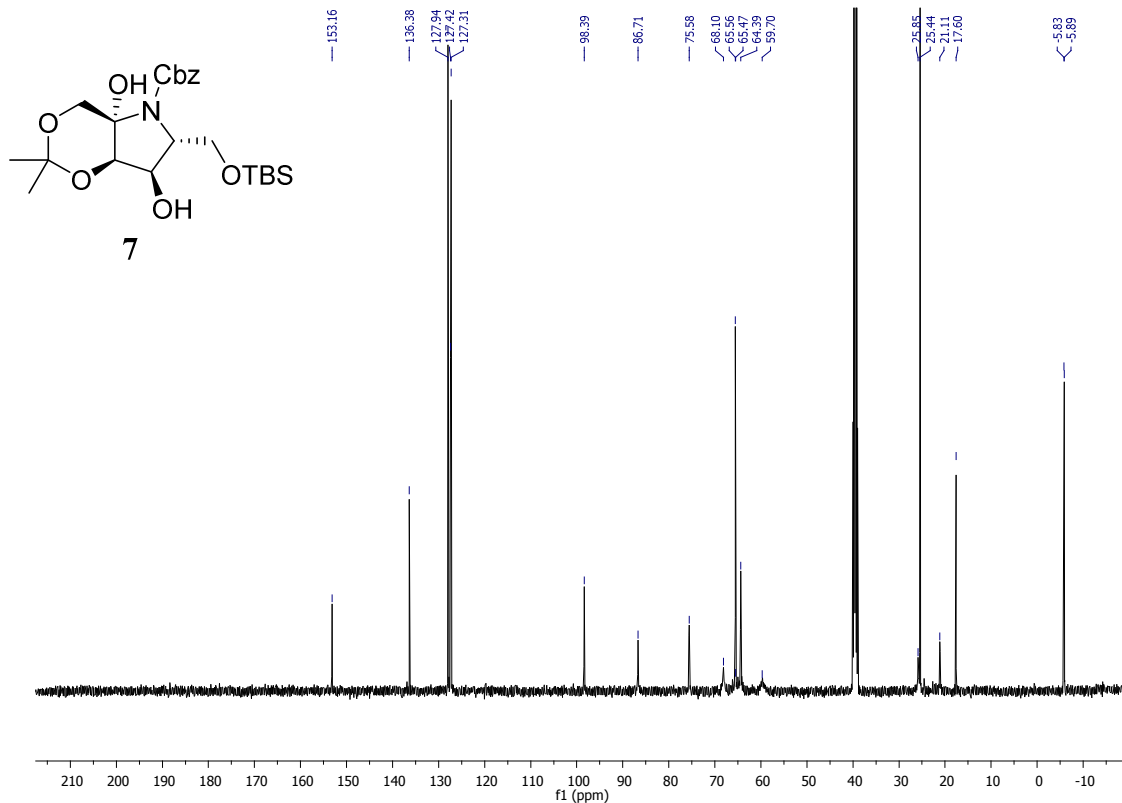
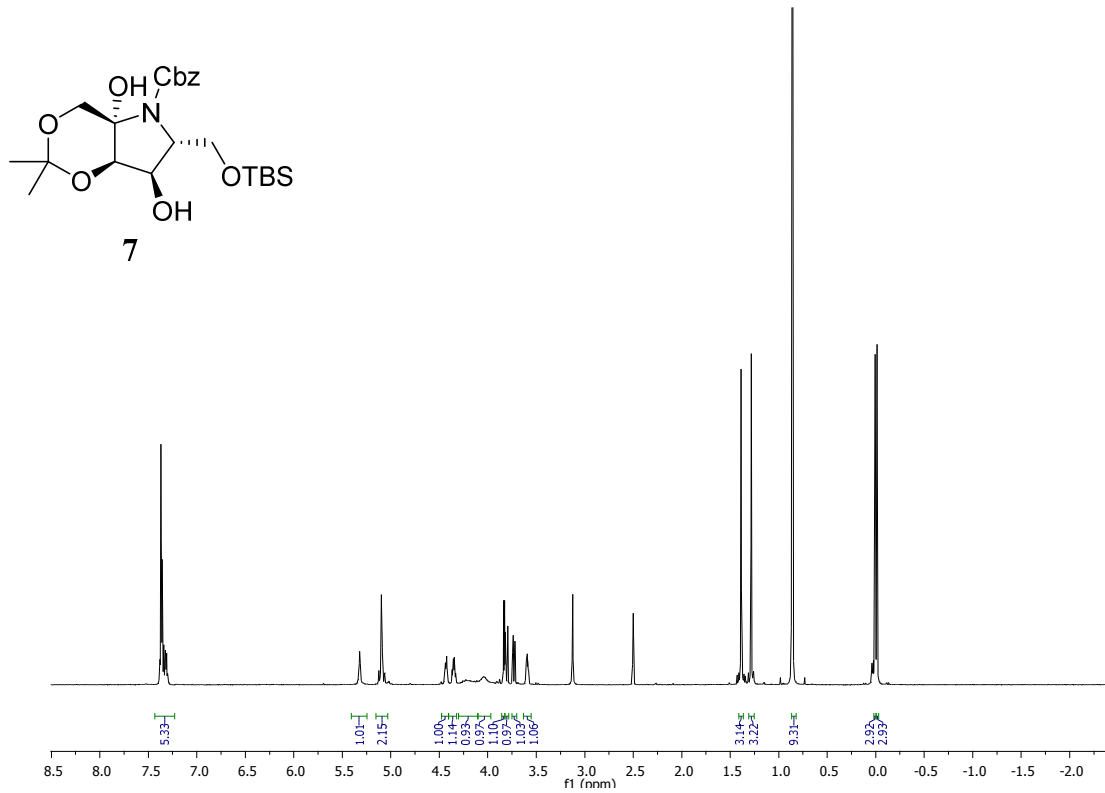


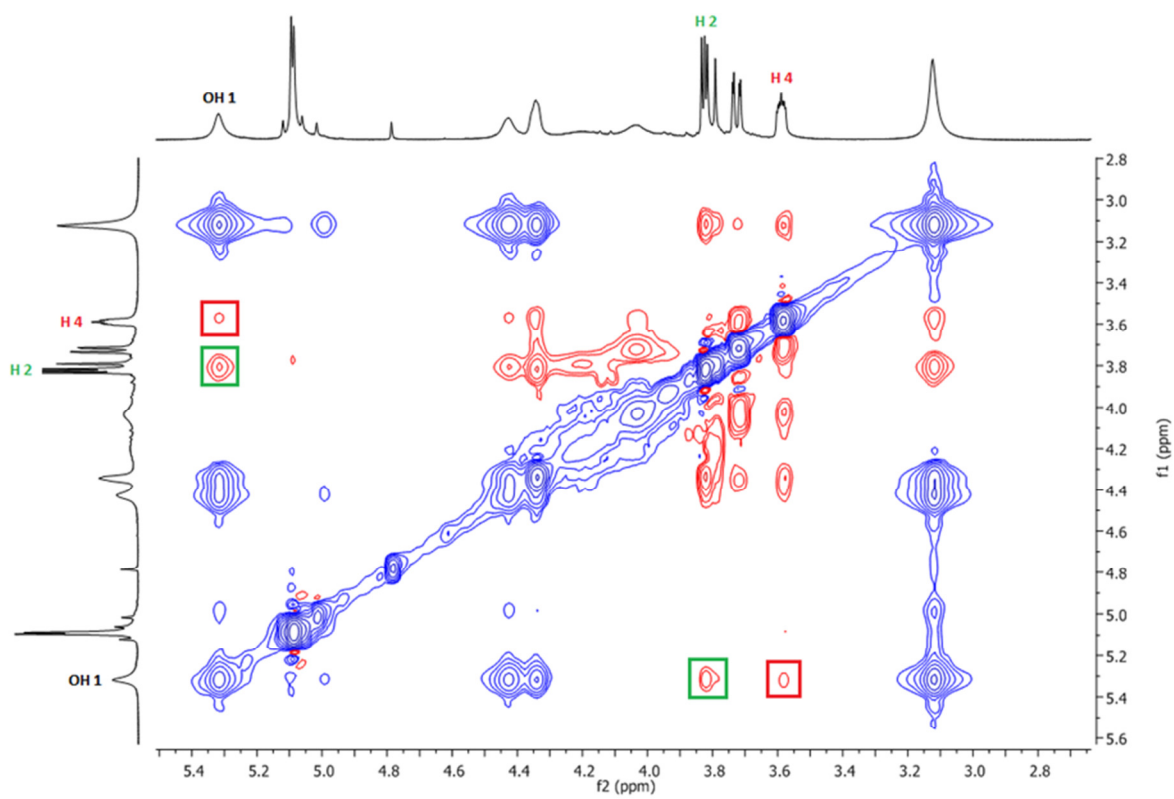
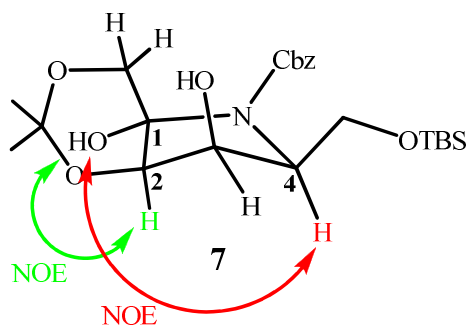
**3d**

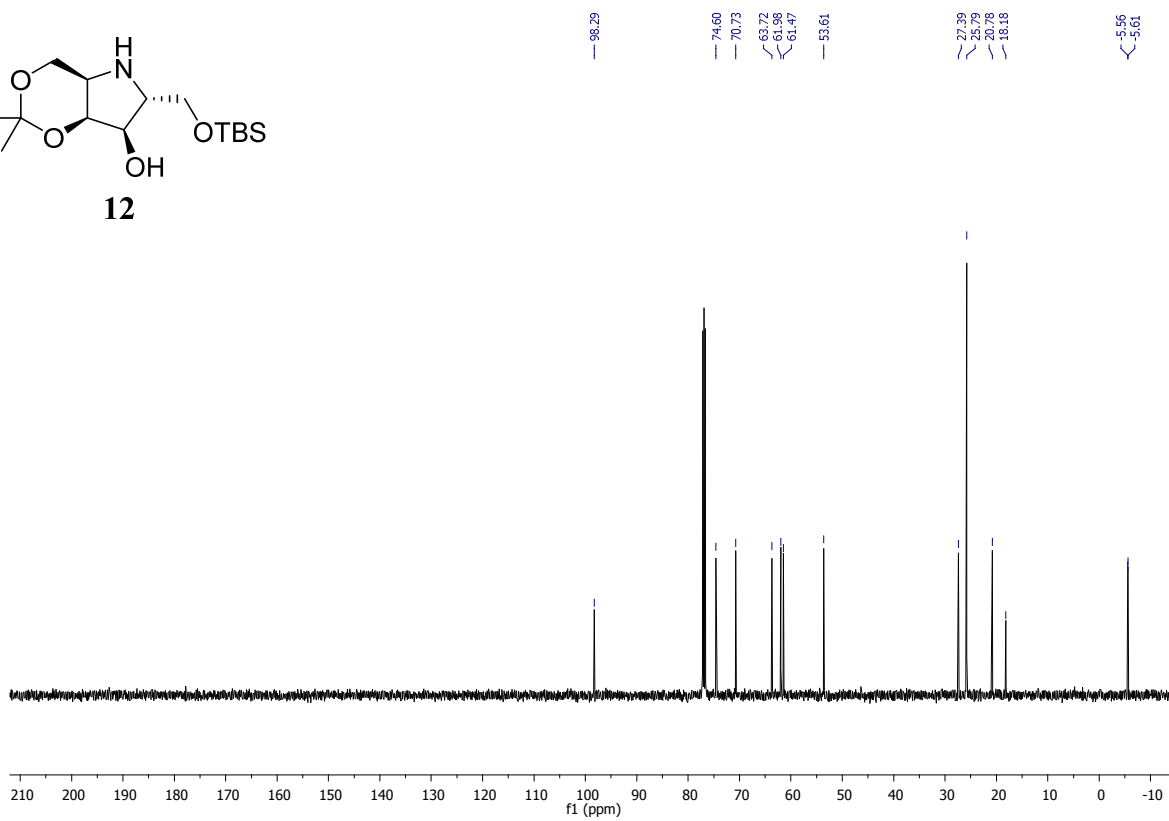
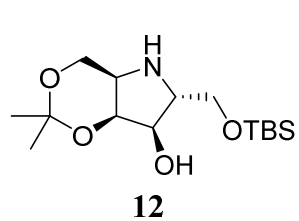
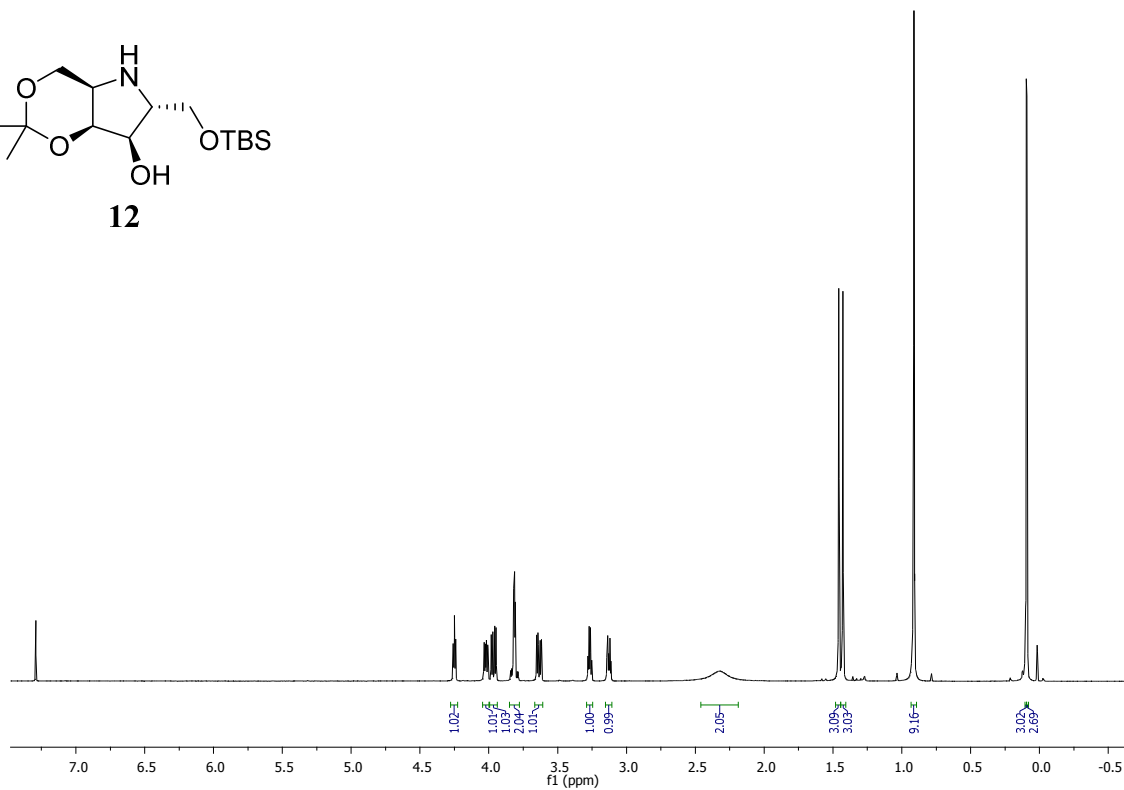
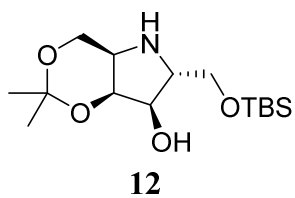


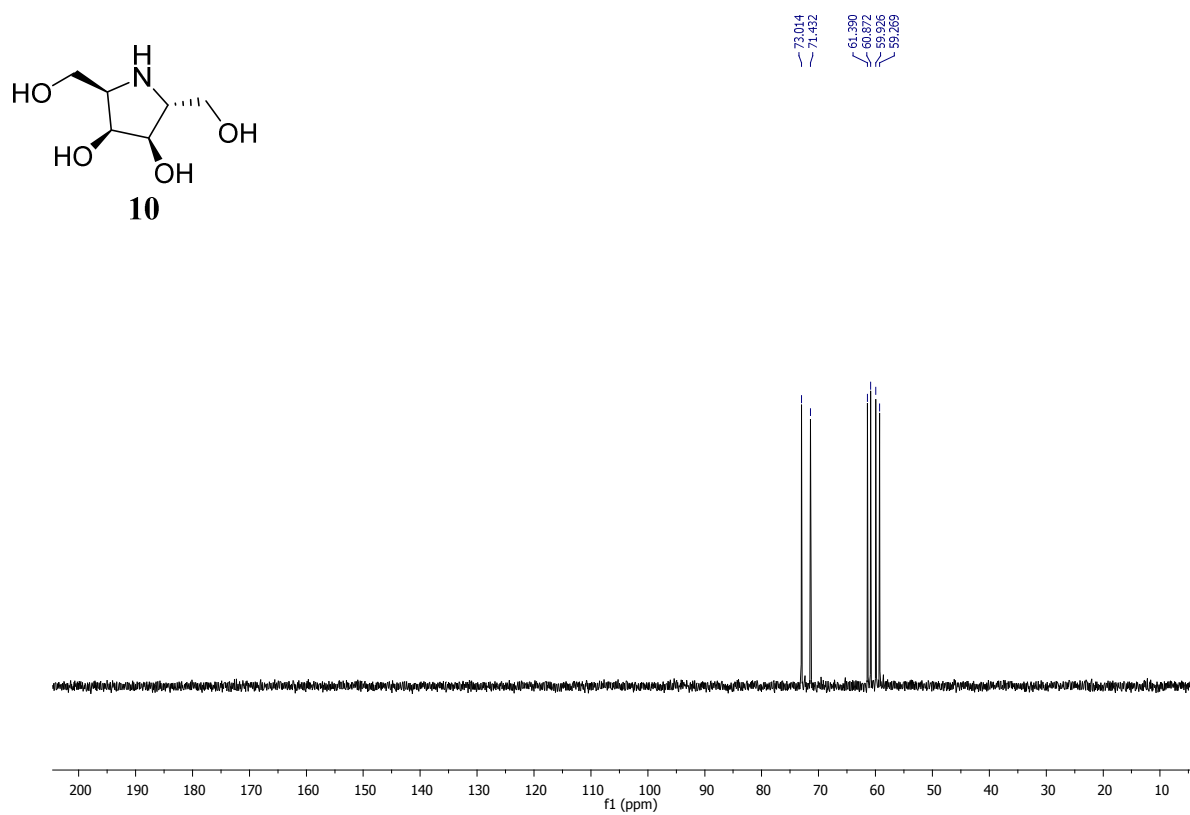
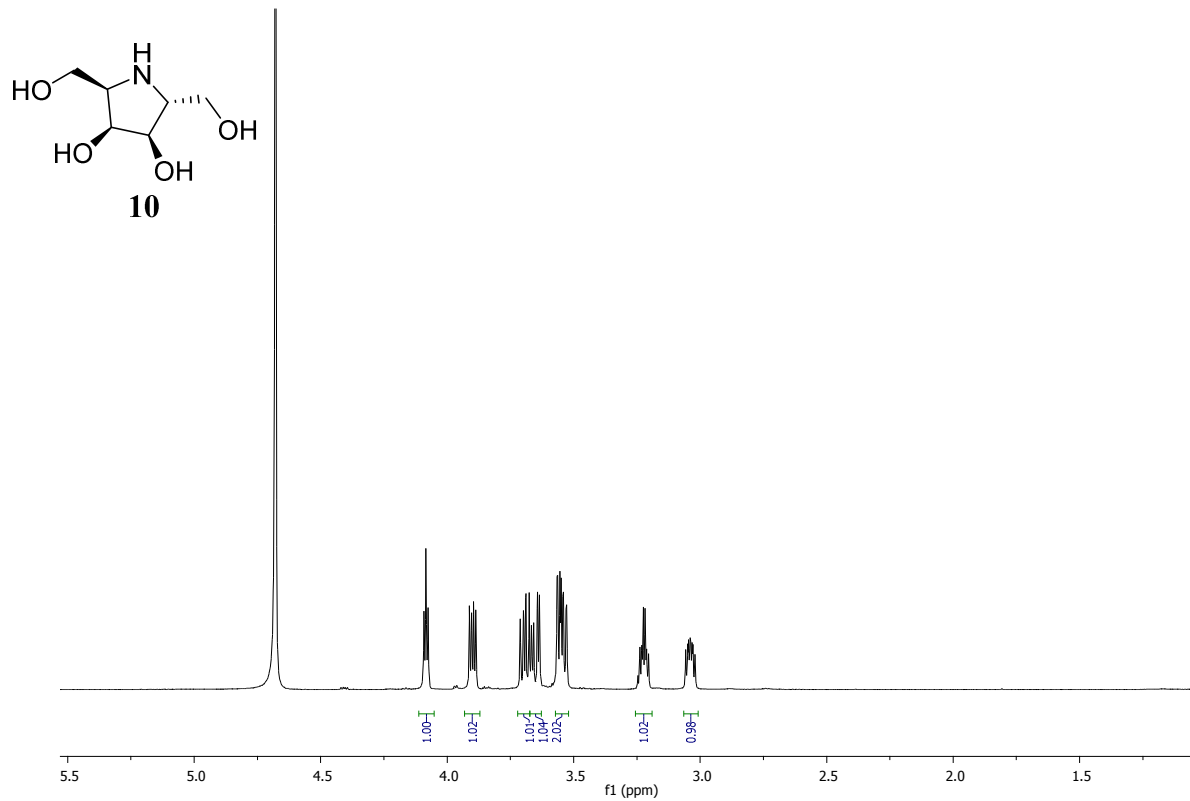
**3d**

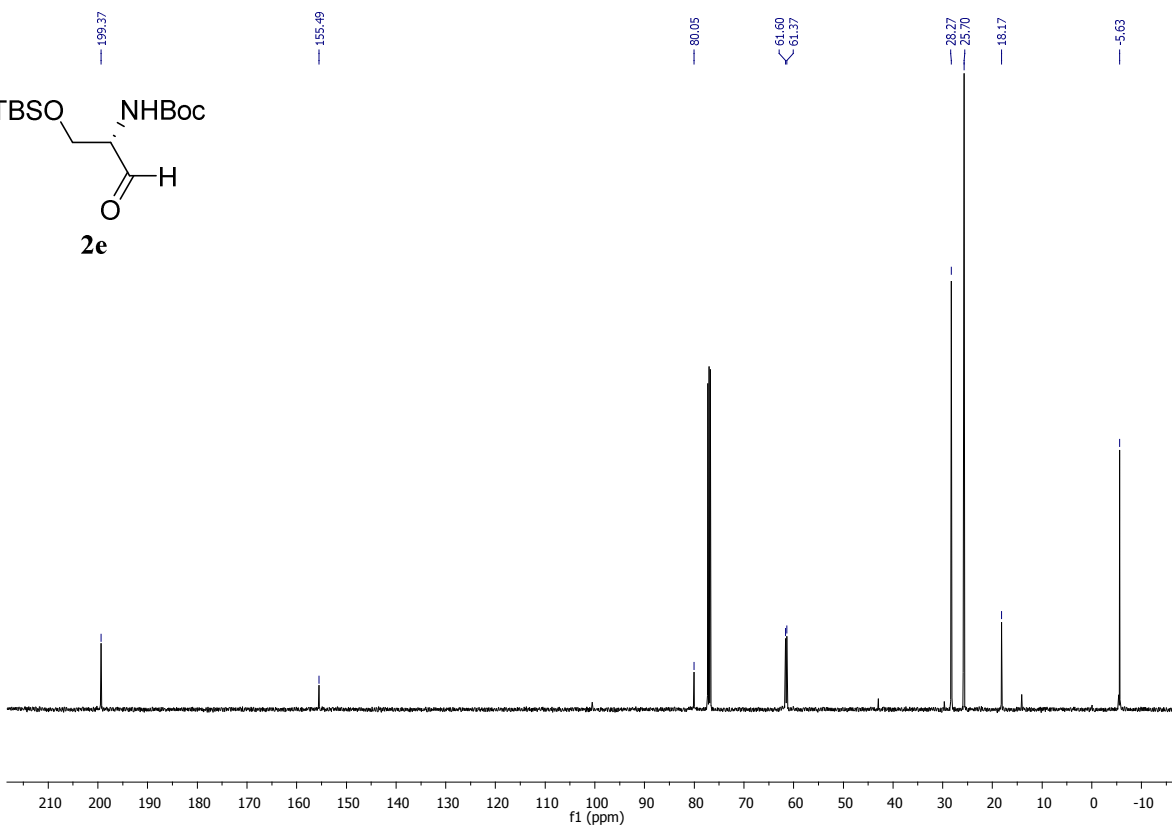
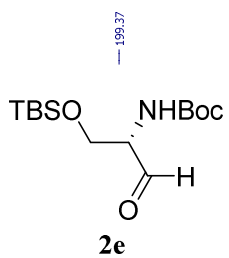
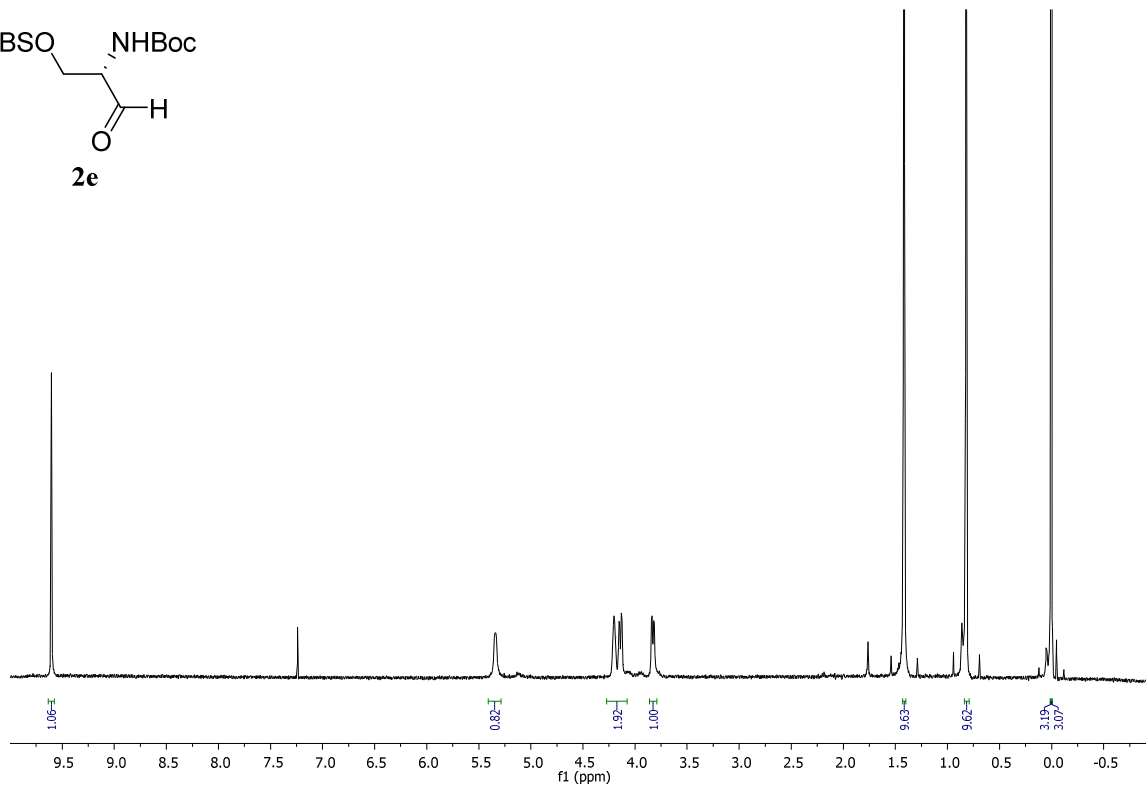
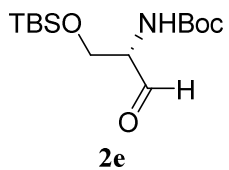


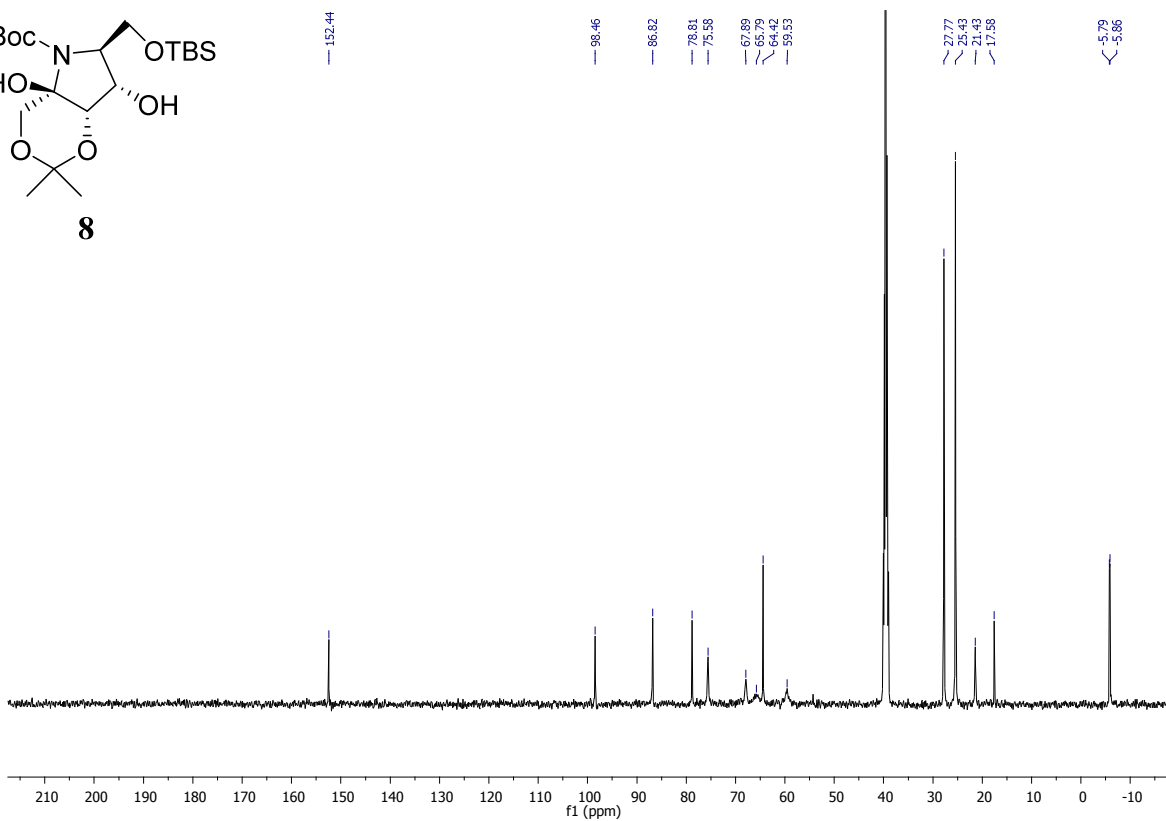
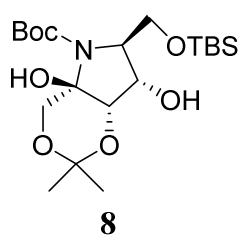
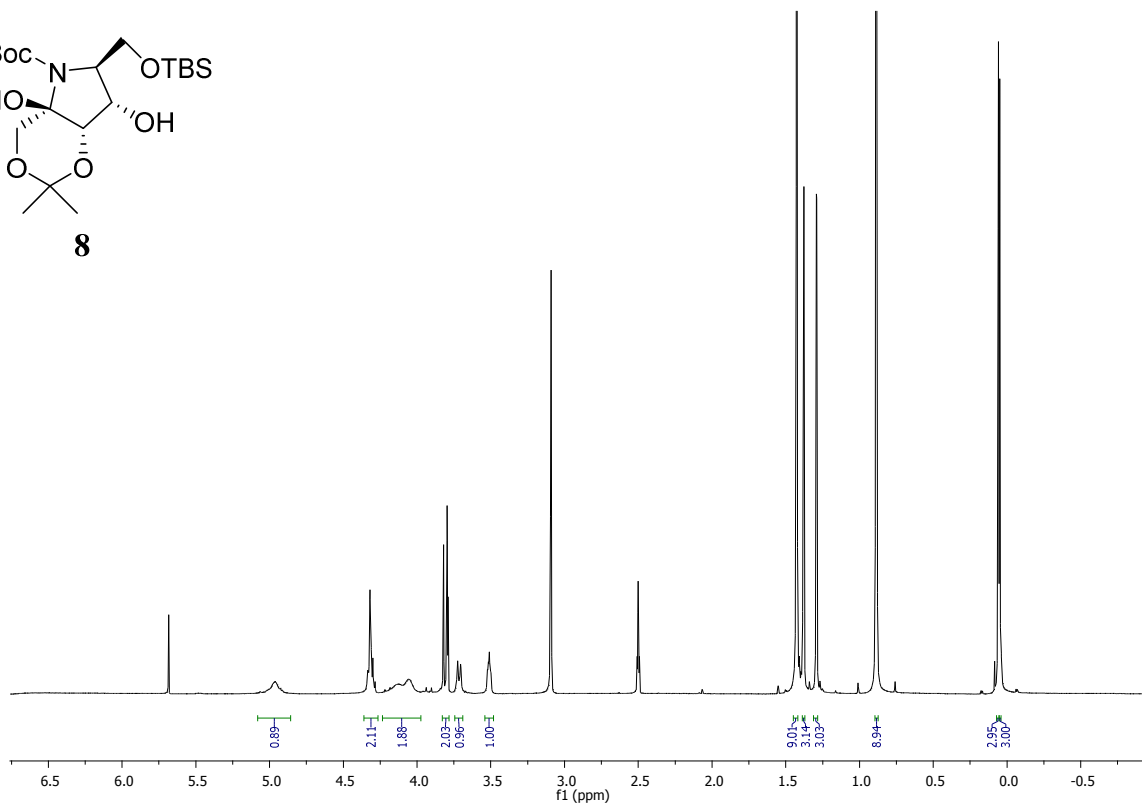
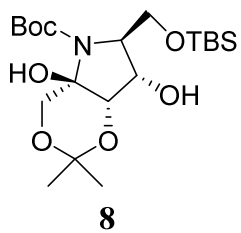


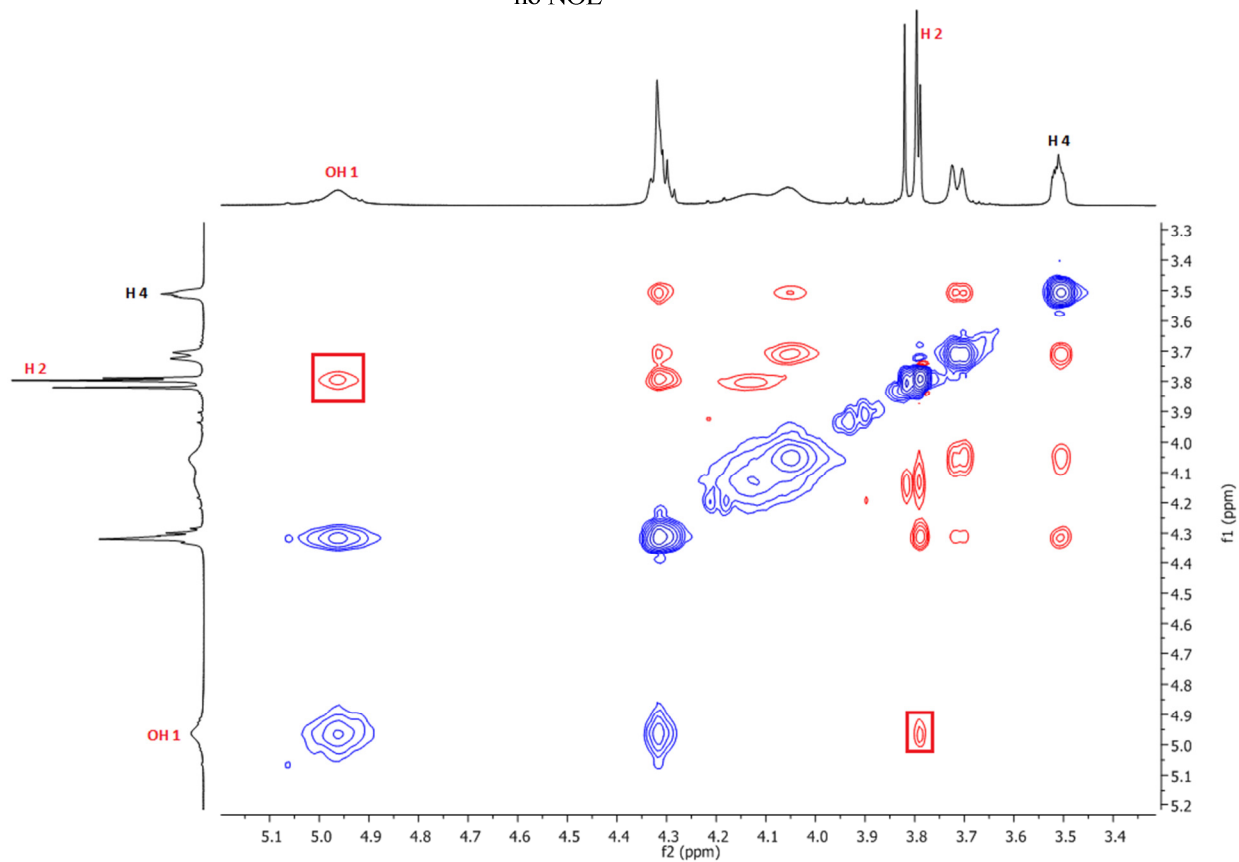
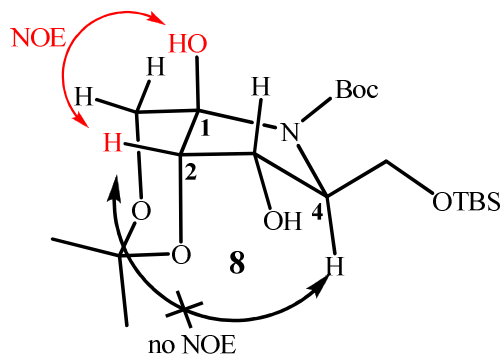




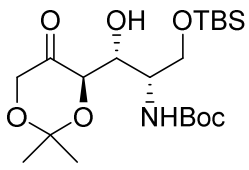




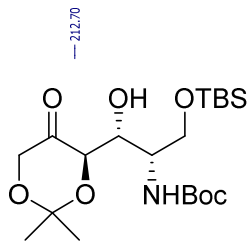
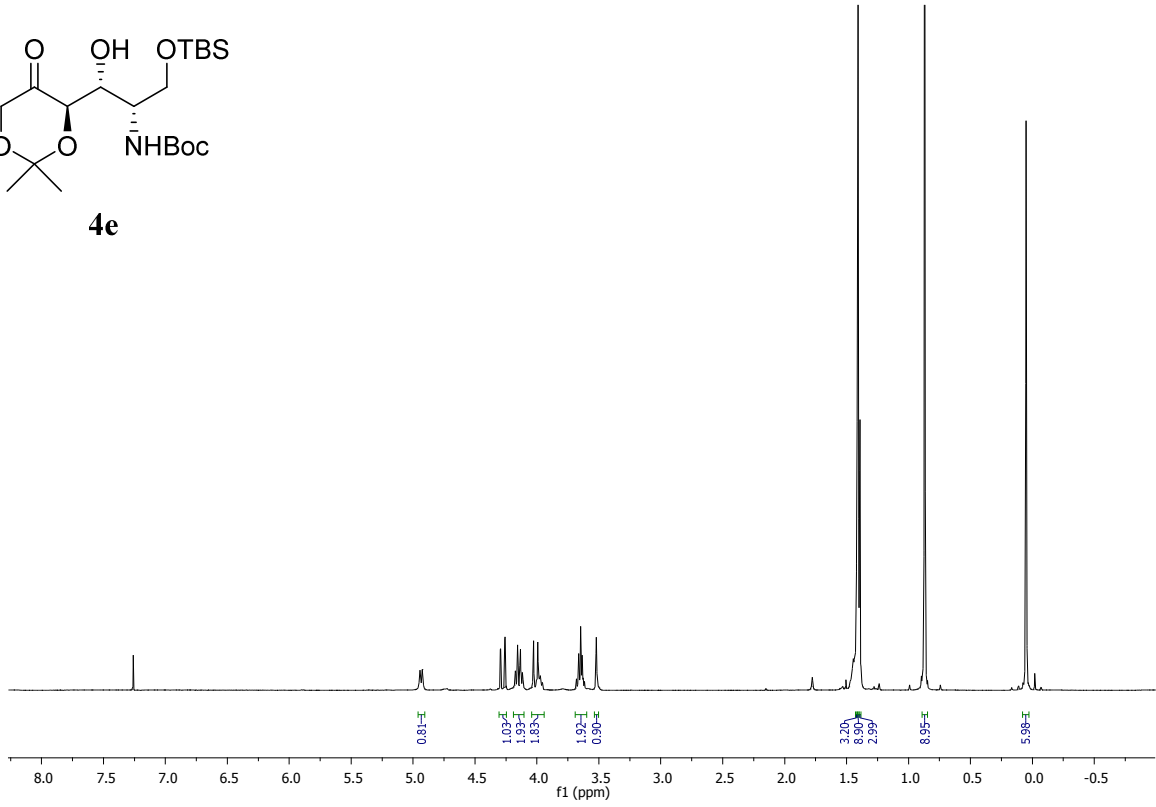




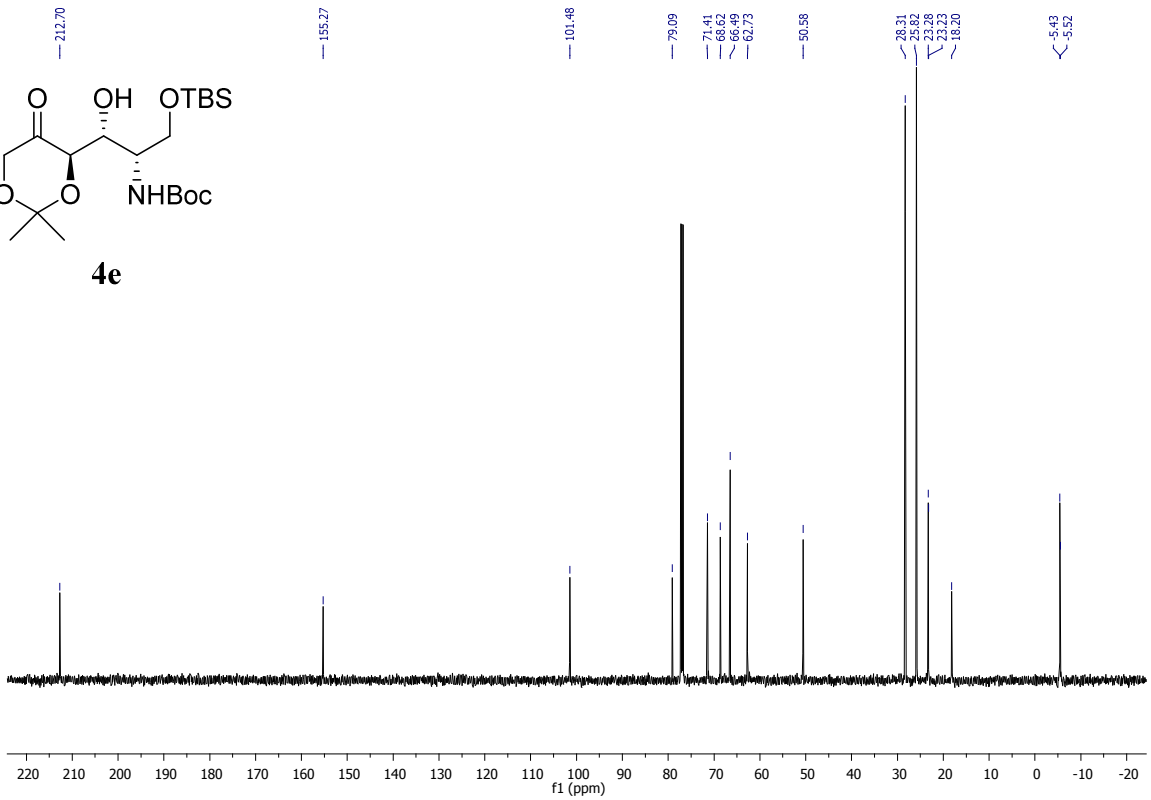


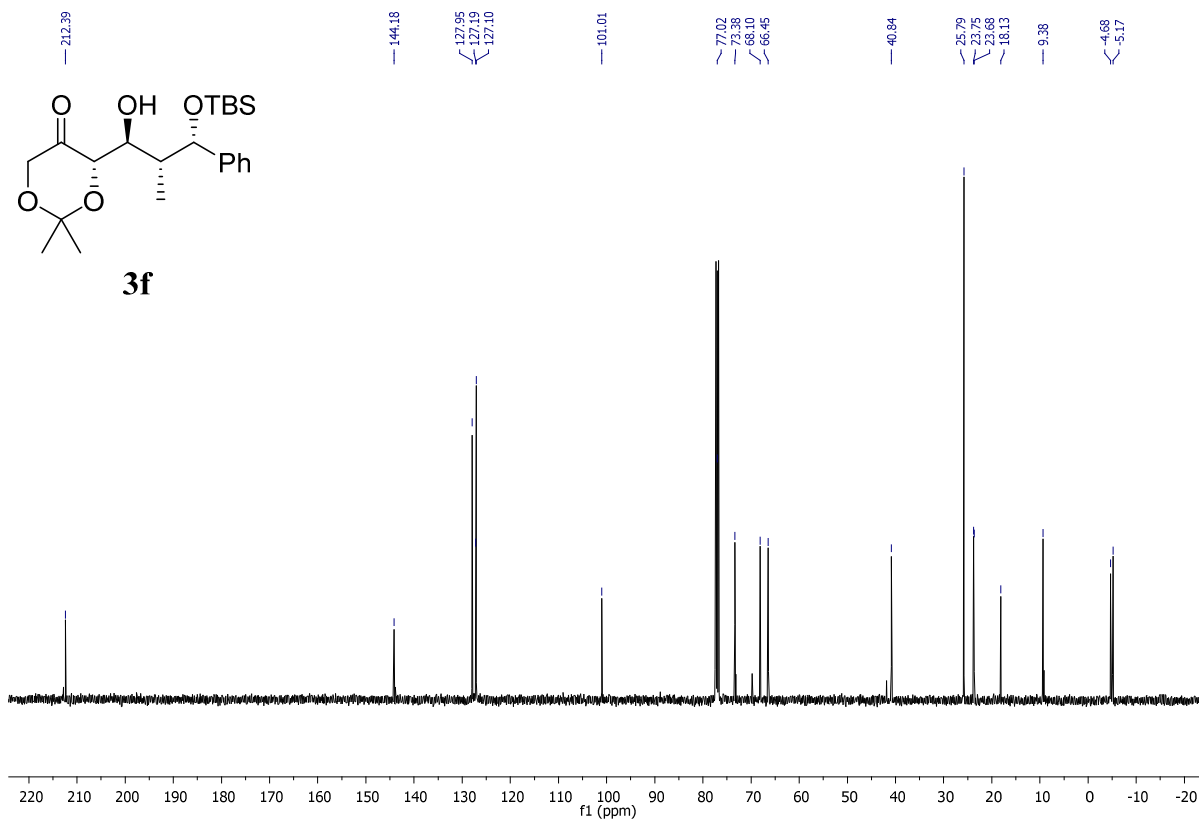
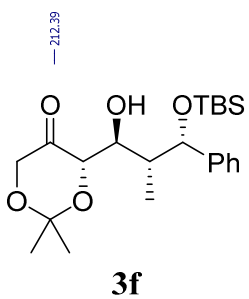
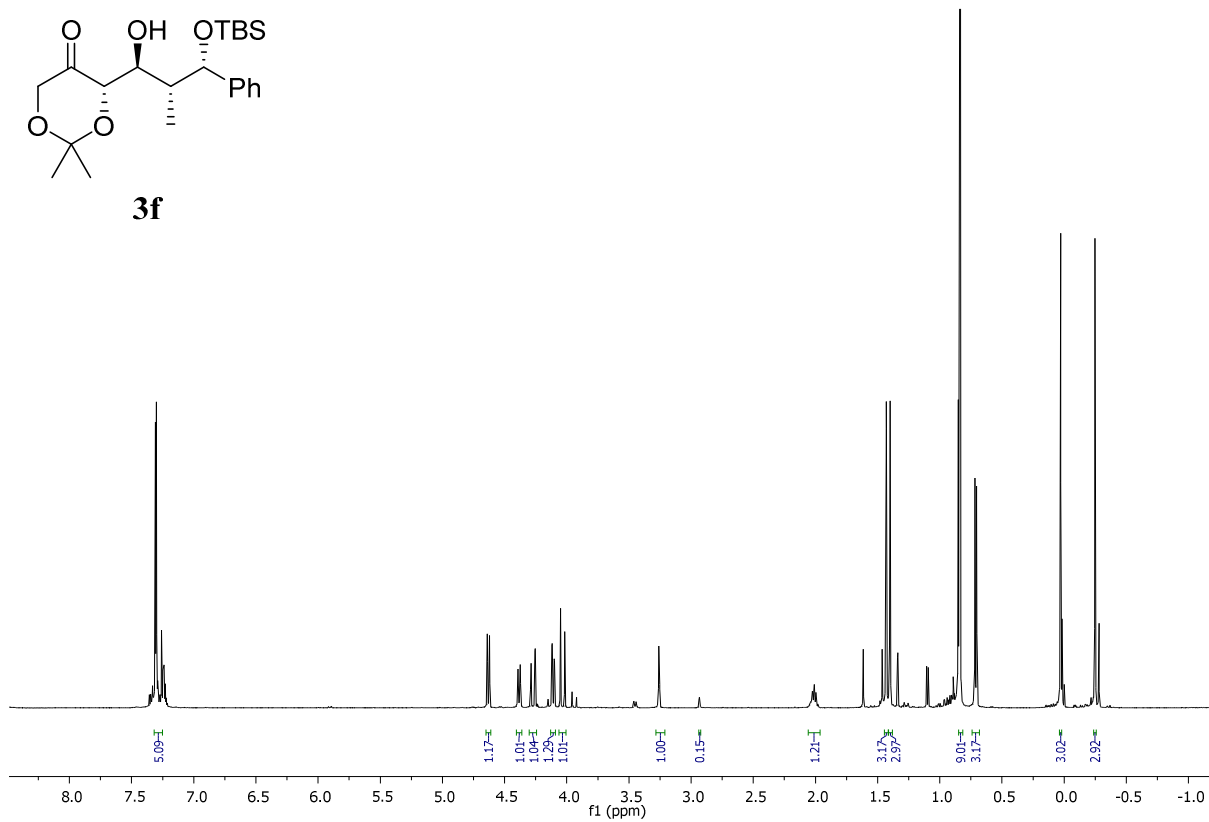
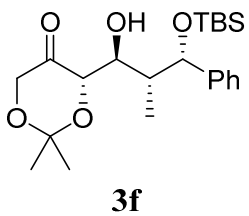


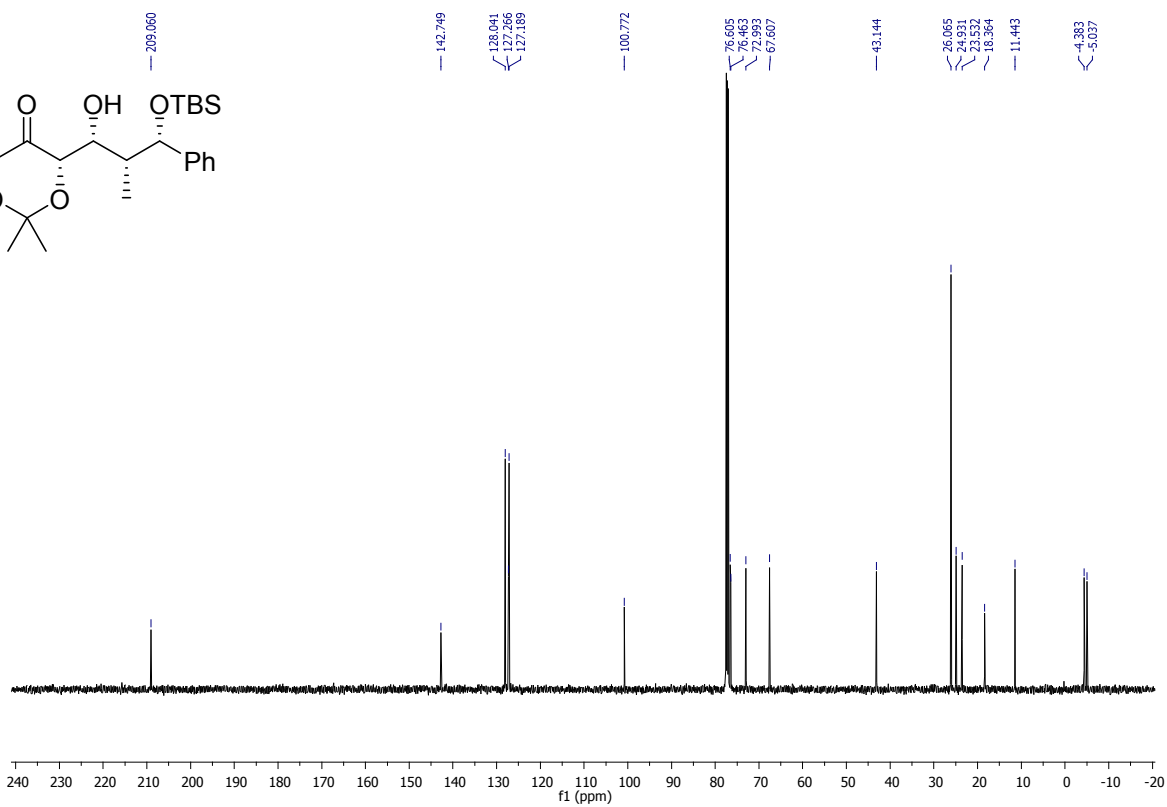
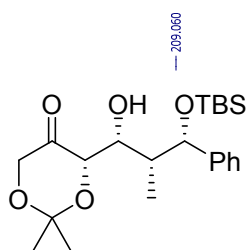
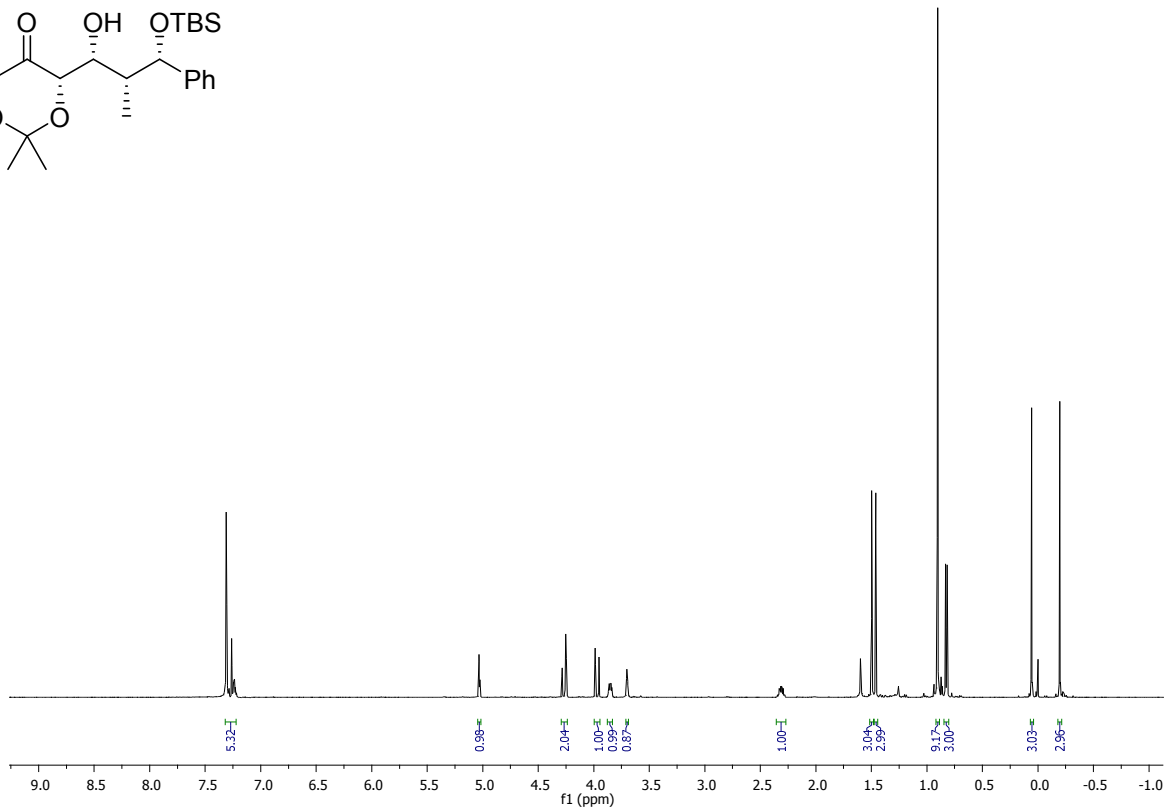
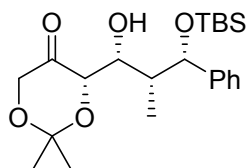
**4e**

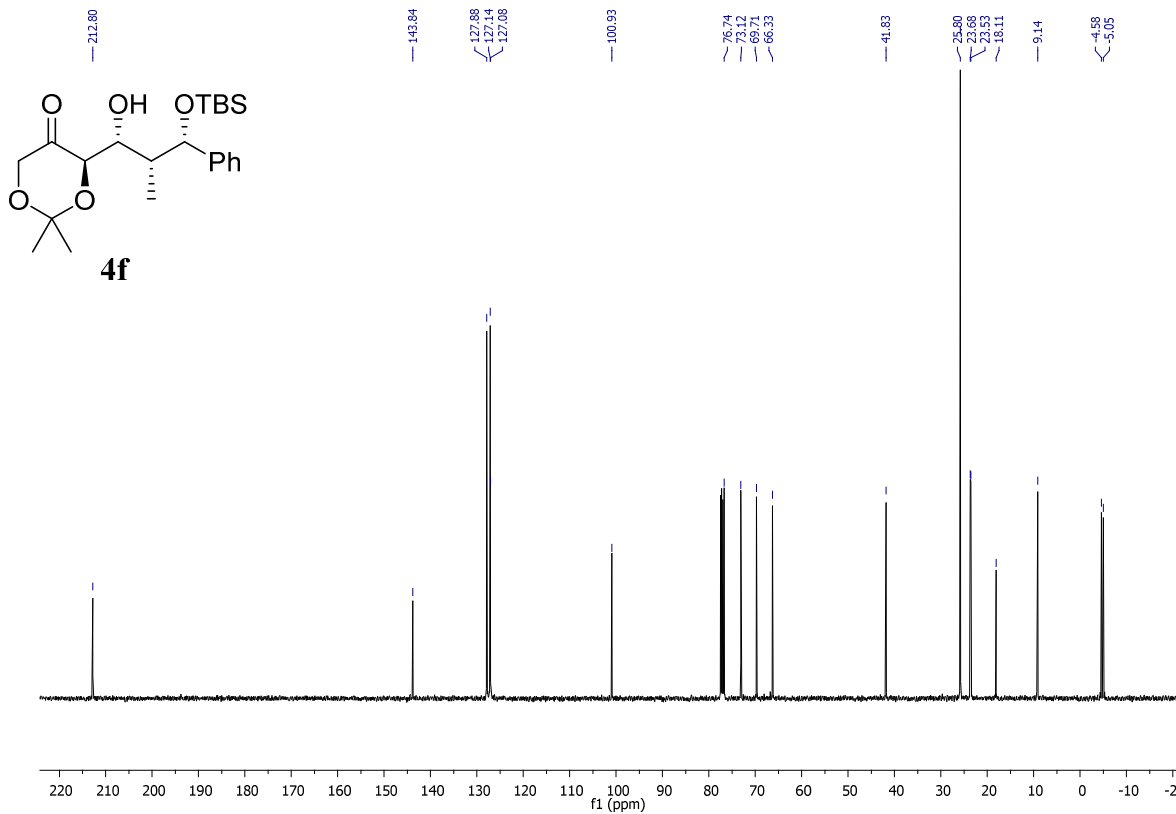
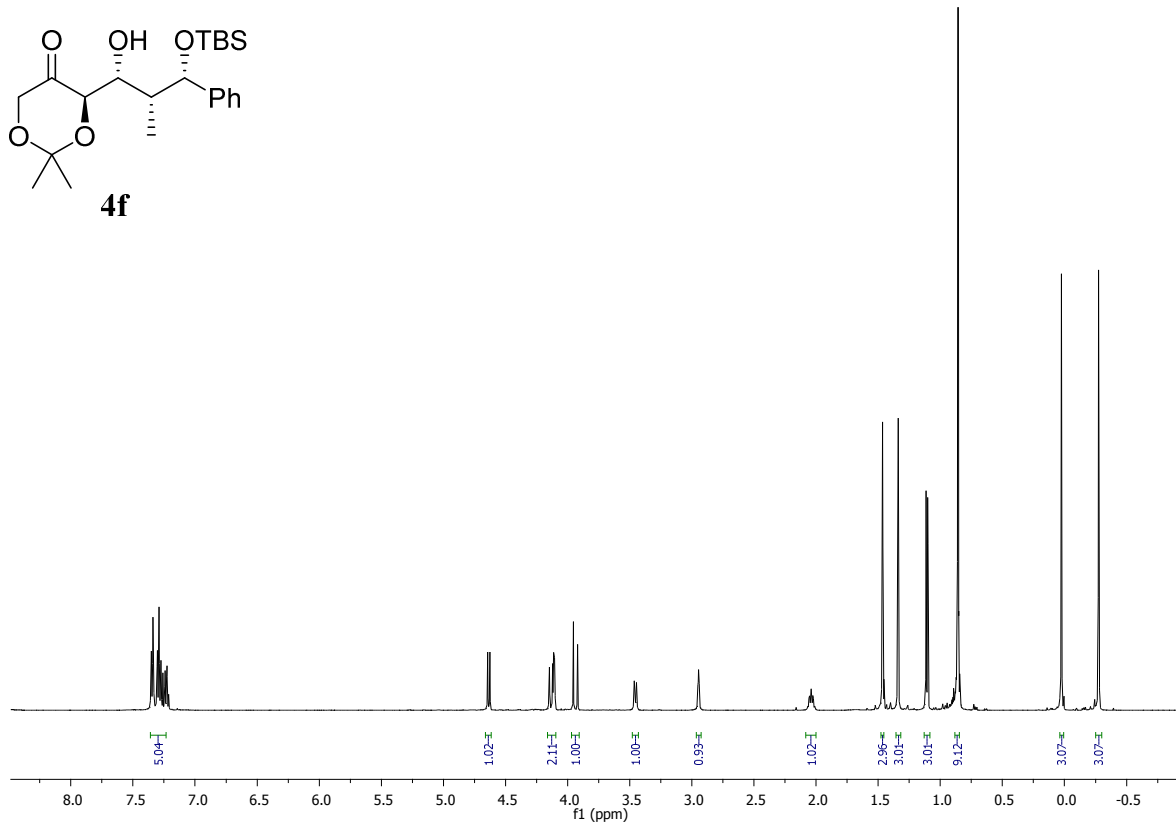
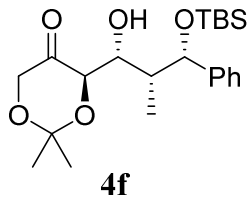


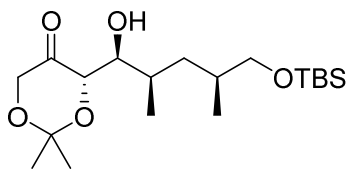
**4e**



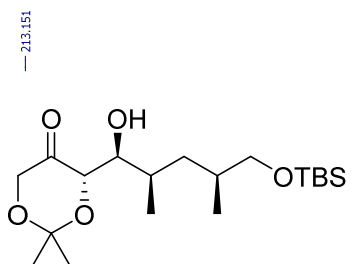
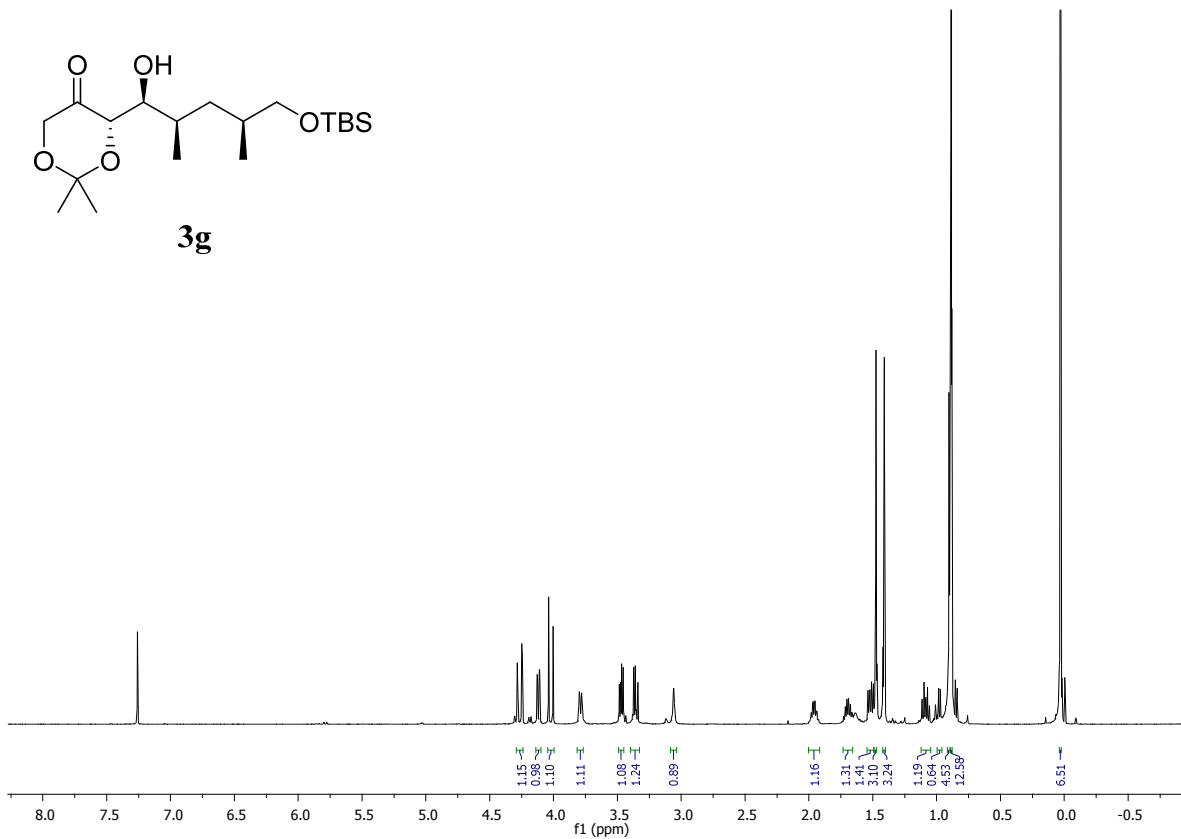








**3g**



**3g**

