

Supporting Information for:

# Oligomannan Synthesis Using Ionic Liquid Supported Glycosylation

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## Table of Contents

General Methods	Page 3
Experimental details of all new compounds and analytical data	Page 3
<sup>1</sup> H NMR spectrum of <b>3</b> in CDCl <sub>3</sub> at 300 MHz	Page 15
<sup>13</sup> C NMR spectrum of <b>3</b> in CDCl <sub>3</sub> at 75 MHz	Page 16
<sup>1</sup> H NMR spectrum of <b>4</b> in CDCl <sub>3</sub> at 300 MHz	Page 17
<sup>13</sup> C NMR spectrum of <b>4</b> in CDCl <sub>3</sub> at 75 MHz	Page 18
<sup>1</sup> H NMR spectrum of <b>5</b> in CDCl <sub>3</sub> at 300 MHz	Page 19
<sup>13</sup> C NMR spectrum of <b>5</b> in CDCl <sub>3</sub> at 75 MHz	Page 20

$^1\text{H}$ NMR spectrum of <b>6</b> in $\text{CDCl}_3$ at 300 MHz	Page 21
$^{13}\text{C}$ NMR spectrum of <b>6</b> in $\text{CDCl}_3$ at 75 MHz	Page 22
$^1\text{H}$ NMR spectrum of <b>7</b> in $\text{CDCl}_3$ at 300 MHz	Page 23
$^{13}\text{C}$ NMR spectrum of <b>7</b> in $\text{CDCl}_3$ at 75 MHz	Page 24
$^1\text{H}$ NMR spectrum of <b>8</b> in $\text{CDCl}_3$ at 300 MHz	Page 25
$^{13}\text{C}$ NMR spectrum of <b>8</b> in $\text{CDCl}_3$ at 75 MHz	Page 26
$^1\text{H}$ NMR spectrum of <b>9</b> in $\text{CDCl}_3$ at 300 MHz	Page 27
$^1\text{H}$ NMR spectrum of <b>10</b> in $\text{CDCl}_3$ at 300 MHz	Page 28
$^{13}\text{C}$ NMR spectrum of <b>10</b> in $\text{CDCl}_3$ at 75 MHz	Page 29
$^1\text{H}$ NMR spectrum of <b>11</b> in $\text{CDCl}_3$ at 300 MHz	Page 30
$^{13}\text{C}$ NMR spectrum of <b>11</b> in $\text{CDCl}_3$ at 75 MHz	Page 31
$^1\text{H}$ NMR spectrum of <b>12</b> in $\text{CDCl}_3$ at 300 MHz	Page 32
$^{13}\text{C}$ NMR spectrum of <b>12</b> in $\text{CDCl}_3$ at 75 MHz	Page 33
$^1\text{H}$ NMR spectrum of <b>13</b> in $\text{CDCl}_3$ at 300 MHz	Page 34
$^{13}\text{C}$ NMR spectrum of <b>13</b> in $\text{CDCl}_3$ at 75 MHz	Page 35
$^1\text{H}$ NMR spectrum of <b>14</b> in $\text{CDCl}_3$ at 300 MHz	Page 36
$^{13}\text{C}$ NMR spectrum of <b>14</b> in $\text{CDCl}_3$ at 75 MHz	Page 37
$^1\text{H}$ NMR spectrum of <b>1</b> in $\text{CDCl}_3$ at 300 MHz	Page 38
$^{13}\text{C}$ NMR spectrum of <b>1</b> in $\text{CDCl}_3$ at 75 MHz	Page 39

## General Methods.

The reactions were performed under a dry argon atmosphere and reaction temperatures were measured externally. Anhydrous solvents over molecular sieves were purchased from Fluka and used as such in reactions. Whenever necessary, compounds and starting materials were dried by azeotropic removal of water with toluene under reduced pressure. The reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel (60F<sub>254</sub>) plates (0.25 mm) from E. Merck and visualized using UV light (254 nm) and/or heating after spray with (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> solution (150 g ammonium sulfate, 30 mL H<sub>2</sub>SO<sub>4</sub>, 750 mL H<sub>2</sub>O). All solvents used for work-up and chromatography were reagent grade from Fischer. Flash column chromatography was carried out on silica gel 60 (230-400 Mesh). <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded at 300 MHz and 75 MHz respectively on JEOL300 Eclipse spectrometer. The coupling constants (*J*) are reported in Hz and chemical shifts ( $\delta$ ) are in ppm relative to a residual solvent peak (CDCl<sub>3</sub>) or an internal standard (TMS). The FABMS and HR-ESIMS spectra were recorded at Mass Spectrometry Laboratory, University of Illinois at Urbana-Champaign on Waters 70E-SE-4F and Waters Q-ToF Ultima API instruments respectively.

### ***p*-Thiotolyl 6-*O*-acetyl-2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranoside (3)**

To the dry CH<sub>2</sub>Cl<sub>2</sub> (50 mL) solution of compound **2** (15.0 g, 26.04 mmol) was added *p*-toluenethiol (3.88 g, 31.25 mmol). The reaction mixture was then cooled to 0 °C and stirred for 5 min followed by dropwise addition of BF<sub>3</sub>·Et<sub>2</sub>O (16.50 mL, 130.20 mmol) over a period of 20 minutes. After completion of addition ice bath was removed and the reaction mixture was stirred 6 h at room temperature. TLC showed complete conversion of the starting material to the product. The reaction mixture was again cooled to 0 °C and neutralized by the addition of Et<sub>3</sub>N

(18.30 mL, 130.20 mmol) and then poured into an ice-water mixture and extracted with CH<sub>3</sub>Cl (3 x 50 mL). The organic layer was then dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated to syrup. It was purified by column chromatography on silica gel using 5:1 Cyclohexane–EtOAc as eluent that produced glycoside **3** (15.33 g, 92% yield) as colorless solid. m.p. 65-67 °C. *R<sub>f</sub>* 0.42 (2:1 Cyclohexane–EtOAc). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): 8.08 (m, 2H, Ar), 7.99 (m, 2H, Ar), 7.84 (m, 2H, Ar), 7.50 (m, 9H, Ar), 7.27 (dd, 2H, *J* = 0.8, 6.9 Hz, Ar), 7.15 (d, *J* = 7.8 Hz, 2H, Ar), 5.99 (t, 1H, *J* = 9.9 Hz), 5.94 (dd, 1H, *J* = 1.5, 3.3 Hz), 5.84 (dd, 1H, *J* = 3.1, 10.0 Hz), 5.69 (d, 1H, *J*<sub>1,2</sub> = 1.2 Hz, H-1), 4.87 (ddd, 1H, *J* = 2.7, 5.4, 10.0 Hz), 4.40 (dd, 1H, *J* = 5.4, 12.0 Hz), 4.28 (dd, 1H, *J* = 2.7, 12.0 Hz), 2.34 (s, 3H, PhCH<sub>3</sub>), 2.06 (s, 3H, OAc). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): 170.64 (C=O), 165.68 (C=O), 165.55 (C=O), 165.42 (C=O), 138.70, 133.77, 133.73, 133.47, 132.96, 132.62, 130.18, 129.99, 129.87, 128.96, 128.75, 128.65, 128.49 (Ar), 86.35 (C-1), 71.93, 70.44, 69.69, 67.26, 62.94, 21.28 (PhCH<sub>3</sub>), 20.79 (OAc). HR-ESIMS: *m/z* 663.1659 [M+Na]<sup>+</sup> calcd for C<sub>36</sub>H<sub>32</sub>O<sub>9</sub>Na, found 663.1651.

#### **6-*O*-Acetyl-2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl fluoride (4)**

To the solution of *p*-thiotolyl 6-*O*-acetyl-2,3,4-tri-*O*-benzoyl-β-D-mannopyranoside **3** (8.0 g, 12.5 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (60 mL) was added diethylaminosulphur trifluoride (DAST) (2.30 mL, 18.8 mmol) at 0 °C followed by *N*-bromosuccinimide (NBS) (3.35 g, 18.8 mmol). The reaction mixture was stirred overnight during which time it was allowed to rise to room temperature. TLC indicated the total consumption of the starting material and the formation of the new compound. The solvent was removed under vacuum, and the resulting residue was purified by silica gel column chromatography (5:1 Cyclohexane–EtOAc) to obtain compound **4** (6.37 g, 95% yield) as a white foam. m.p. 47-50 °C. *R<sub>f</sub>* 0.48 (2:1 Cyclohexane–EtOAc). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): 8.10 (m, 2H, Ar), 7.97(m, 2H, Ar), 7.84 (m, 2H, Ar), 7.64 (t, 1H, *J* =

7.1 Hz, Ar), 7.46 (m, 6H, Ar), 7.27 (m, 2H, Ar), 6.04(1H, t,  $J = 9.9$  Hz), 5.87 (dd, 1H,  $^3J_{1,2} = 1.7$  Hz,  $^1J_{H,F} = 48.3$  Hz, H-1), 5.88 (ddd, 1H,  $J_{H,F} = 1.8$  Hz,  $J_{2,3} = 3.4$  Hz,  $J_{3,4} = 10.0$  Hz, H-3), 5.80 (dd, 1H,  $J_{H,F} = 0$  Hz,  $J_{1,2} = 1.8$  Hz,  $J_{2,3} = 3.4$  Hz, H-2), 4.50 (ddd, 1H,  $J = 3.2, 4.0, 9.9$  Hz), 4.38 (dd, 1H,  $J = 4.0, 11.5$  Hz), 4.33 (d, 1H,  $J = 3.0$  Hz), 2.12 (s, 3H, OAc).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ): 170.61 (C=O), 165.50 (C=O), 165.42 (C=O), 165.17 (C=O), 133.99, 133.79, 133.51, 130.04, 129.92, 129.86, 128.91, 128.81, 128.76, 128.65, 128.48 (Ar), 104.80 (d,  $^1J_{C,F} = 214.6$  Hz, C-1), 70.97 (C-3), 68.96, 68.53 (d,  $^2J_{C,F} = 38.8$  Hz, C-2), 65.91, 62.25, 20.74 (OAc). HR-ESIMS:  $m/z$  559.1380  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{29}\text{H}_{25}\text{O}_9\text{FNa}$ , found 559.1366.

***p*-Thiotolyl 2,3,4-tri-*O*-benzoyl- $\beta$ -D-mannopyranoside (5)**

Glycoside **3** (2.0 g, 3.1 mmol) was dissolved in a mixture of dry  $\text{CH}_2\text{Cl}_2$  (19 mL), dry MeOH (19 mL) and acetyl chloride (0.1 mL) at room temperature. It was stirred for 36 hrs at room temperature and the solvent was removed under vacuum. The resulting residue was purified by silica gel column chromatography (4:1 Cyclohexane–EtOAc) to produce 1.82 g (96% yield) of glycoside **5** as white foam. m.p. 130 °C.  $R_f$  0.36 (2:1 Cyclohexane–EtOAc).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.05 (m, 4H, Ar), 7.85 (m, 2H, Ar), 7.51 (m, 7H, Ar), 7.28 (m, 2H, Ar), 7.16 (d, 2H,  $J = 7.9$  Hz, Ar), 5.95 (m, 3H), 5.72 (s, 1H, H-1), 4.62 (dd, 1H,  $J = 4.6, 3.6$  Hz), 3.83 (m, 2H), 2.55 (dd, 1H,  $J = 6.9, 7.4$  Hz,  $\text{PhCH}_3$ ), 2.34 (s, 3H, OAc).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  166.55 (C=O), 166.57 (C=O), 165.53 (C=O), 138.64, 133.89, 133.75, 133.44, 132.85, 130.21, 130.07, 130.02, 129.85, 129.28, 129.01, 128.77, 128.73, 128.68, 128.47 (Ar), 86.45 (C-1), 72.13, 72.09, 7.012, 67.42, 61.46, 21.28 ( $\text{PhCH}_3$ ). HR-ESIMS:  $m/z$  621.1559  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{34}\text{H}_{30}\text{O}_8\text{SNa}$ , found 621.1570.

***p*-Thiotolyl 6-*O*-[6-*O*-acetyl-2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranosyl]-2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranoside (6)**

To a stirred suspension of 200 mg of freshly activated 4Å molecular sieves in dry CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was added AgClO<sub>4</sub> (174 mg, 0.84 mmol) and SnCl<sub>2</sub> (159 mg, 0.84 mmol). The mixture was cooled to 0 °C before a solution of compound **4** (225 mg, 0.42 mmol), compound **5** (299 mg, 0.50 mmol) and 2,6-Lutidine (49 µL, 0.42 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was added through a cannula. The reaction mixture was stirred overnight during which time it was allowed to rise to room temperature. TLC indicated the total consumption of the starting material and the formation of the new major compound. The mixture was filtered through a Celite pad, the solvent was removed under vacuum, and the resulting residue was dissolved in EtOAc (30 mL). The solution was washed with 1N HCl (10 mL), deionized water (15 mL), and finally with satd aq NaHCO<sub>3</sub> (15 mL). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, concentrated and the residue was purified by silica gel column chromatography (4:1 Cyclohexane–EtOAc) to give compound **6** (454 mg, 97%) as a white foam. m.p. 81-83 °C. *R*<sub>f</sub> 0.33 (2:1 Cyclohexane–EtOAc). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 8.18 (m, 2H, Ar), 8.05 (m, 6H, Ar), 7.89 (m, 4H, Ar), 7.45 (m, 20H, Ar), 7.20 (d, 2H, *J* = 7.9 Hz, Ar), 6.18 (t, 1H, *J* = 10.2 Hz), 6.04 (dd, 1H, *J* = 1.5, 3.2 Hz), 5.92 (m, 3H), 5.81 (br s, 1H), 5.75 (s, 1H, H-1), 5.13 (s, 1H, H-1'), 4.96 (dd, 1H, *J* = 3.3, 10.0 Hz), 4.14 (m, 4H), 3.77 (d, 1H, *J* = 11.0 Hz), 2.25 (s, 3H, PhCH<sub>3</sub>), 1.92 (s, 3H, OAc). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 170.54 (C=O), 165.68 (C=O), 165.64 (C=O), 165.60 (C=O), 165.33 (C=O), 165.21 (C=O), 138.61, 133.72, 133.63, 133.38, 133.22, 132.79, 130.30, 130.10, 129.96, 129.81, 129.43, 129.34, 129.21, 129.15, 129.02, 128.91, 128.66, 128.57, 128.45 (Ar), 98.01 (C-1'), 86.75 (C-1), 72.07, 70.67, 70.54, 70.19, 68.81, 67.08, 66.91, 66.80, 62.59, 21.20 (PhCH<sub>3</sub>), 20.57 (OAc). HR-ESIMS: *m/z* 1137.2979 [M+Na]<sup>+</sup> calcd for C<sub>63</sub>H<sub>54</sub>O<sub>17</sub>SNa, found 1137.2926.

### **2,3,4-Tri-*O*-benzoyl- $\alpha$ -D-mannopyranosyl fluoride (7)**

Fluoride glycoside **4** (6.0 g, 11.19 mmol) was treated with mixture of dry CH<sub>2</sub>Cl<sub>2</sub> (67 mL), dry MeOH (67 mL) and AcCl (0.6 mL) at room temperature overnight. The reaction mixture was concentrated under vacuum. Purification of crude syrup by column chromatography (3:1 Cyclohexane–EtOAc) yielded pure glycoside **7** (5.42 g, 98%) as colorless low melting solid. m.p. 49 °C. *R*<sub>f</sub> 0.38 (2:1 Cyclohexane–EtOAc). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  8.09 (m, 2H, Ar), 7.98 (m, 2H, Ar), 7.82 (m, 2H, Ar), 7.52 (m, 7H, Ar), 7.27 (m, 2H, Ar), 6.00 (ddd, 1H, *J* = 1.6, 3.0, 10.2 Hz), 5.93 (dd, 1H, *J* = 3.0, 10.1 Hz), 5.88 (dd, 1H, <sup>3</sup>*J*<sub>1,2</sub> = 1.8 Hz, <sup>1</sup>*J*<sub>H,F</sub> = 48.7 Hz, H-1), 5.84 (dd, 1H, *J* = 1.8, 3.0 Hz), 4.24 (ddd, 1H, *J* = 2.2, 2.8, 9.5 Hz), 3.91 (m, 1H), 3.78 (m, 1H), 2.69 (dd, 1H, *J* = 6.3, 7.4 Hz). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  166.58 (C=O), 165.46 (C=O), 165.32 (C=O), 134.01, 133.96, 133.51, 130.10, 130.06, 129.83, 128.83, 128.70, 128.47 (Ar), 105.11 (d, *J*<sub>C,F</sub> = 221.6 Hz, C-1), 73.39, 68.73 (d, *J*<sub>C,F</sub> = 40.08 Hz, C-2), 66.26, 60.90. HR-ESIMS: *m/z* 495.1455 [M]<sup>+</sup> calcd for C<sub>27</sub>H<sub>24</sub>O<sub>8</sub>F, found 495.1444.

### **2,3,4-Tri-*O*-benzoyl-6-*O*-chloroacetyl- $\alpha$ -D-mannopyranosyl fluoride (8)**

The glycoside **7** (5.0 g, 10.12 mmol) was dissolved in of dry CH<sub>2</sub>Cl<sub>2</sub> (15 mL) under argon atmosphere. The reaction mixture was then cooled in ice bath. A mixture of chloroacetylchloride (0.97 mL, 12.14 mmol) in dry pyridine (1.2 mL, 15.18 mmol) was added. It was left for stirring at 0 °C for 30 mins and TLC showed complete conversion. The reaction mixture was poured into an ice-water mixture and then extracted with CHCl<sub>3</sub> (2 x 25 mL). The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and then concentrated. The crude syrup was purified by column chromatography over silica gel G using 5:1 Cyclohexane–EtOAc as eluent to produce glycoside **8** (5.48 g, 95%) as colorless solid. m.p. 129 °C. *R*<sub>f</sub> 0.48 (2:1

Cyclohexane–EtOAc).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.09 (m, 2H, Ar), 7.95 (m, 2H, Ar), 7.82 (m, 2H, Ar), 7.52 (m, 7H, Ar), 7.27 (m, 2H, Ar), 6.02 (dd,  $J = 9.6, 9.3$  Hz, 1H), 5.89 (m, 1H), 5.85 (dd, 1H,  $J_{1,2} = 1.9$  Hz,  $J_{\text{F}, \text{H}-1} = 48.3$  Hz, H-1), 5.84 (dd, 1H,  $J = 1.9, 3.3$  Hz), 4.47 (m, 3H), 4.14 (d, 2H,  $J = 0.8$  Hz,  $\text{CH}_2\text{Cl}$ ).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  167.02 (C=O), 165.49 (C=O), 165.38 (C=O), 165.17 (C=O), 134.04, 133.89, 133.54, 130.06, 129.93, 129.85, 128.83, 128.75, 128.68, 128.56, 128.48 (Ar), 104.88 (d,  $J_{\text{C},\text{F}} = 224.0$  Hz, C-1), 70.88, 68.94, 68.50 ( $J_{\text{C},\text{F}} = 39.8$  Hz, C-2), 65.66, 63.53, 40.70 ( $\text{CH}_2\text{Cl}$ ). HR-ESIMS:  $m/z$  593.0991  $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{29}\text{H}_{24}\text{O}_9\text{FCINa}$ , found 593.1009.

**6-*O*-(1-methylimidazoliumhexafluorophospho)acetyl-2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranosyl fluoride (9)**

The glycoside **8** (5.4 g, 9.47 mmol) was dissolved in dry  $\text{CH}_3\text{CN}$  (30 mL) under argon atmosphere and to it was added *N*-methylimidazole (0.91 mL, 11.36 mmol). The reaction was refluxed overnight at 80 °C with stirring and TLC showed complete conversion. The reaction mixture was cooled to room temperature, potassium hexafluorophosphate ( $\text{KPF}_6$ ) (2.62 g, 14.20 mmol) was added and reheated overnight under reflux at 80 °C. The reaction mixture was filtered and concentrated under vacuum. The residue was dissolved in  $\text{CHCl}_3$  (50 mL) and undissolved solid was filtered off. The chloroform part was concentrated to a solid that was washed with diethylether (3 x 50 mL) and the solvent was removed by decantation. The solid residue was then dried under vacuum to get the pure IL-tagged donor glycoside **9** (5.90 g, 82% yield). m.p. 138 °C,  $R_f$  0.22 (5:1  $\text{CHCl}_3$ –MeOH).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.42 (s, 1H, Ar), 8.03 (m, 2H, Ar), 7.90 (m, 1H, Ar), 7.80 (m, 1H, Ar), 7.41 (m, 11H, Ar), 5.84 (m, 4H), 4.99



(s, 2H, CH<sub>2</sub>N), 4.55 (m, 2H), 4.36 (d, 1H,  $J = 11.5$  Hz), 3.77 (s, 3H, NCH<sub>3</sub>). HR-ESIMS:  $m/z$  617.1935 [M-PF<sub>6</sub>]<sup>+</sup> calcd for C<sub>33</sub>H<sub>30</sub>N<sub>2</sub>O<sub>9</sub>F, found 617.1926.

***p*-Thiotolyl 6-*O*-[(1-methylimidazoliumhexafluorophospho)acetyl-2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranosyl]-2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranoside (10)**

The acceptor glycoside **4** (862 mg, 1.44 mmol) and IL-tagged fluoride donor glycoside **9** (1.00 g, 1.31 mmol) were dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (15 mL) under Ar atmosphere in presence of activated 4Å molecular sieves (500 mg). The reaction mixture was then cooled to 0 °C and then the coupling reagents AgClO<sub>4</sub> (843 mg, 3.28 mmol) and Cp<sub>2</sub>HfCl<sub>2</sub> (547 mg, 1.44 mmol) were added. The reaction mixture was then left stirring overnight at room temperature. TLC (5:1 CHCl<sub>3</sub>–MeOH) showed complete consumption of acceptor glycoside. The reaction mixture was filtered and concentrated under vacuum. The residue was then washed with diethylether (3 x 25 mL) and the solvent was removed by decantation. The residue was finally dried under vacuum to give pure IL-tagged disaccharide **10** (1.76 g, 92% yield). m.p. 128-130 °C.  $R_f$  0.27 (5:1 CHCl<sub>3</sub>–MeOH). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): 8.54 (s, 1H, Ar), 8.16 (m, 2H, Ar), 7.99 (m, 6H, Ar), 7.86 (m, 4H, Ar), 7.45 (m, 24H, Ar), 7.17 (d, 3H,  $J = 8.5$  Hz, Ar), 6.18 (t, 1H,  $J = 10.2$  Hz), 6.02 (dd, 1H,  $J = 1.6, 3.0$  Hz), 5.97 (dd, 1H,  $J = 3.3, 10.2$  Hz), 5.88 (dd, 1H,  $J = 3.2, 10.0$  Hz), 5.79 (ddd, 2H,  $J = 4.1, 5.5, 10.4$  Hz), 5.71 (d, 1H,  $J = 1.4$  Hz, H-1), 5.10 (s, 1H, H-1'), 4.90 (m, 2H), 4.45 (dd, 1H,  $J = 4.5, 12.2$  Hz), 4.21 (m, 1H), 4.12 (dd, 1H,  $J = 4.4, 11.3$  Hz), 3.94 (d, 1H,  $J = 10.7$  Hz), 3.84 (s, 3H, NCH<sub>3</sub>), 3.73 (m, 1H), 2.23 (s, 3H, PhCH<sub>3</sub>). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): 166.21 (C=O), 165.64 (C=O), 165.32 (C=O), 165.12 (C=O), 138.73, 137.60, 133.94, 133.69, 133.44, 133.36, 133.07, 130.32, 130.09, 129.95, 129.79, 129.74, 129.28, 129.21, 128.93, 128.76, 128.50, 123.61, 123.30 (Ar), 98.17 (C-1), 86.82 (C-1'), 71.99, 70.72, 70.37, 70.12, 69.85, 68.51,

66.97, 66.36, 49.61 (NCH<sub>2</sub>), 36.54 (NCH<sub>3</sub>), 21.23 (PhCH<sub>3</sub>). HR-ESIMS:  $m/z$  1195.3534 [M-PF<sub>6</sub>]<sup>+</sup> calcd for C<sub>67</sub>H<sub>59</sub>N<sub>2</sub>O<sub>17</sub>, found 1195.3540.

***p*-Thiotolyl                  6-*O*-[2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranosyl]-2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranoside (11)**

IL-tagged disaccharide **10** (1.50 g, 1.12 mmol) was dissolved in bi-phasic solvent mixture diethyl ether–water (30 mL, 1:1 v/v). To it were then added saturated aqueous NaHCO<sub>3</sub> solution (12 mL) and Bu<sub>4</sub>N<sup>+</sup>I<sup>-</sup> (620 mg, 1.68 mmol). The reaction was left for stirring at room temperature for 8 hours. The ether layer was separated and washed with brine (2 x 10 mL). The ether layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, concentrated and the residue was further dried under high vacuum to produce disaccharide **11** as a colorless solid (1.20 g, 72% yield). m.p. 85-88 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): 8.17 (m, 2H, Ar), 8.04 (m, 6H, Ar), 7.87 (m, 4H, Ar), 7.50 (m, 14H, Ar), 7.29 (m, 6H, Ar) 7.19 (d, 2H,  $J$  = 8.2 Hz, Ar), 6.16 (t, 1H,  $J$  = 9.9 Hz), 6.04 (m, 2H), 5.89 (dd, 1H,  $J$  = 3.0, 10.2 Hz) 5.81 (m, 2H), 5.73 (s, 1H, H-1), 5.14 (s, 1H, H-1'), 4.94 (dd, 1H,  $J$  = 3.0, 10.0 Hz), 4.13 (dd, 1H,  $J$  = 4.7, 11.0 Hz), 3.94 (dd, 1H,  $J$  = 2.7, 9.9 Hz), 3.78 (dd, 1H,  $J$  = 1.6, 11.0 Hz), 3.53 (m, 2H), 2.34 (s, 3H, PhCH<sub>3</sub>). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  166.75 (C=O), 165.66 (C=O), 165.58 (C=O), 165.25 (C=O), 138.58, 133.79, 133.61, 133.35, 133.22, 132.78, 130.28, 130.11, 130.02, 129.96, 129.79, 129.41, 129.35, 129.23, 129.06, 129.99, 128.89, 128.70, 128.62, 128.43 (Ar), 98.20 (C-1'), 86.75 (C-1), 72.09, 71.05, 70.71, 70.60, 70.38, 69.80, 67.25, 67.16, 67.01, 61.06, 21.22 (PhCH<sub>3</sub>). HR-ESIMS:  $m/z$  1095.2874 [M+Na]<sup>+</sup> calcd for C<sub>61</sub>H<sub>52</sub>O<sub>16</sub>SNa, found 1095.2871.

***p*-Thiotolyl 6-*O*-[2,3,4-tri-*O*-benzoyl-6-*O*-{(1-methylimidazoliumhexafluorophospho)acetyl-2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranosyl]- $\alpha$ -D-mannopyranosyl]-2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranoside (12)**

The acceptor disaccharide **11** (1.16 g, 1.08 mmol) and IL-tagged fluoride donor glycoside **9** (746 mg, 0.98 mmol) were dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (15 mL) under argon atmosphere in presence of activated 4Å molecular sieves (500 mg). The reaction mixture was then cooled to 0 °C followed by addition of the coupling reagents AgClO<sub>4</sub> (681 mg, 2.65 mmol) and Cp<sub>2</sub>HfCl<sub>2</sub> (410 mg, 1.08 mmol). The reaction mixture was left stirring overnight at room temperature. The tlc (5:1 CHCl<sub>3</sub>–MeOH) showed complete consumption of acceptor glycoside. The reaction mixture was filtered and concentrated under vacuum. The residue was then washed with diethylether (3 x 25 mL) and the solvent was removed by decantation. The residue was finally dried under vacuum to give IL-tagged trisaccharide **12** (1.89 g, 85% yield). m.p. 93-95 °C. *R<sub>f</sub>* 0.56 (5:1 CHCl<sub>3</sub>–MeOH). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 8.54 (s, 1H, Ar), 8.21 (m, 2H, Ar), 8.14 (m, 2H, Ar), 8.06 (m, 6H, Ar), 7.89 (m, 8H, Ar), 7.53 (m, 18H, Ar), 7.30 (m, 13H, Ar), 8.25 (d, 2H, *J* = 8.2 Hz, Ar), 6.37 (t, 1H, *J* = 10.1 Hz), 6.03 (m, 4H), 5.93 (m, 2H), 5.79 (dd, 1H, *J* = 9.8, 10.1 Hz), 5.78 (s, 1H, H-1), 5.56 (m, 1H), 5.20 (s, 1H, anomeric H), 5.11 (d, 1H, *J* = 9.6 Hz), 4.95 (m, 2H), 4.80 (s, 1H, anomeric H), 4.45 (dd, 1H, *J* = 3.5, 12.2 Hz), 4.33 (dd, 1H, *J* = 3.5, 11.0 Hz), 4.22 (m, 2H), 4.01 (d, 1H, *J* = 11.5 Hz), 3.81 (s, 3H, NCH<sub>3</sub>), 3.90 (m, 4H), 3.39 (d, 1H, *J* = 10.1 Hz), 2.24 (s, 3H, PhCH<sub>3</sub>). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 166.23 (C=O), 165.83 (C=O), 165.77 (C=O), 165.67 (C=O), 165.63 (C=O), 165.55 (C=O), 165.35 (C=O), 165.24 (C=O), 138.54, 137.58, 134.07, 133.89, 133.75, 133.63, 133.37, 133.25, 132.85, 130.28, 130.14, 129.99, 129.86, 129.10, 128.98, 128.89, 128.76, 128.63, 128.47, 123.61, 123.41 (Ar), 98.24, 97.66 (C-1', C-1''), 86.86 (C-1), 72.10, 71.02, 70.63, 70.46, 70.36, 70.15, 69.68, 69.33, 68.62, 66.92, 66.80, 66.61,

66.29, 66.15, 49.71 (NCH<sub>2</sub>), 36.46 (NCH<sub>3</sub>), 21.19 (PhCH<sub>3</sub>). HR-ESIMS:  $m/z$  1669.4848 [M-PF<sub>6</sub>]<sup>+</sup> calcd for C<sub>94</sub>H<sub>81</sub>O<sub>25</sub>N<sub>2</sub>S, found 1669.4846.

***p*-Thiotolyl 6-*O*-[2,3,4-tri-*O*-benzoyl-6-*O*-(2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranosyl)- $\alpha$ -D-mannopyranosyl]-2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranoside (13)**

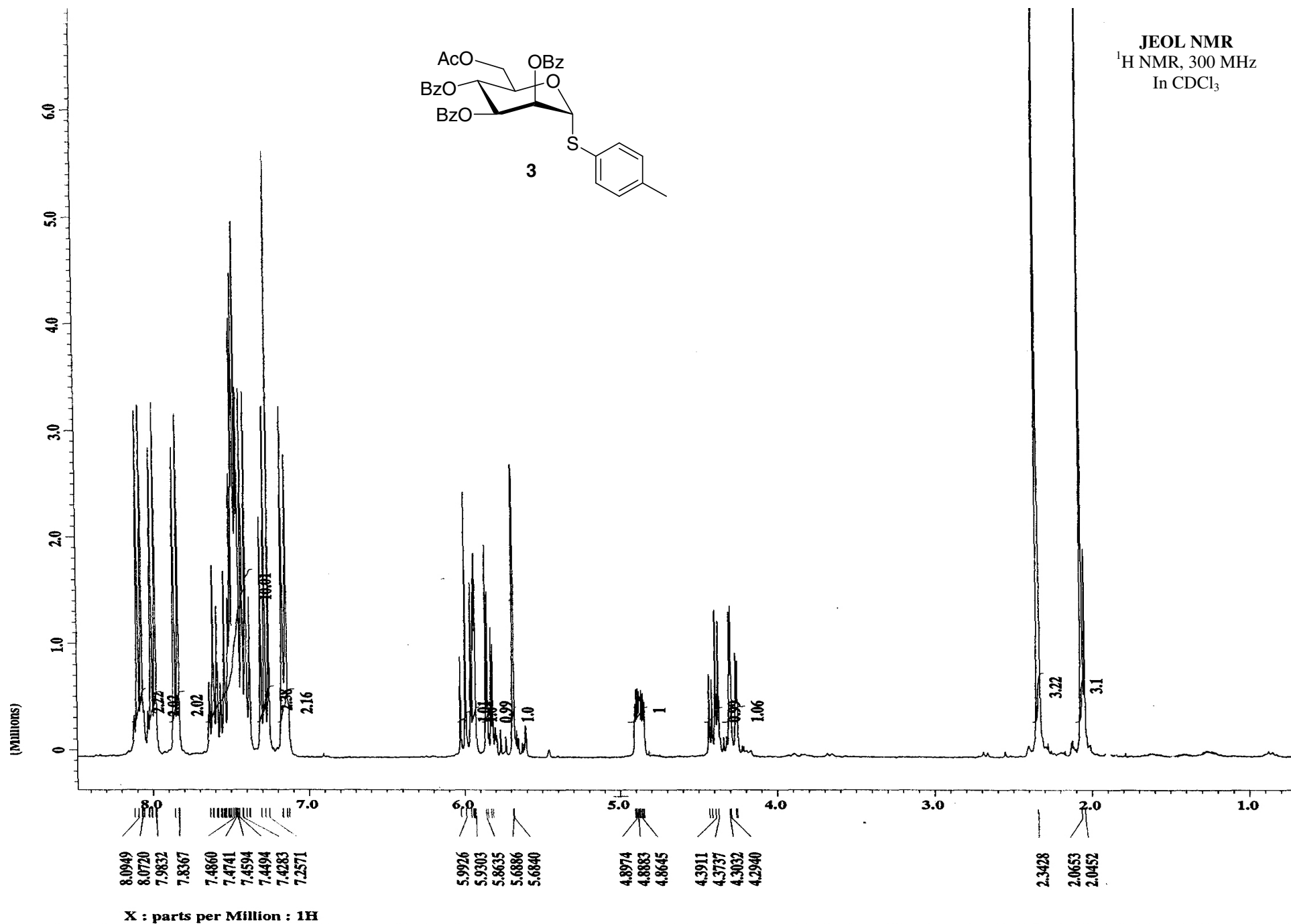
IL-tagged trisaccharide **12** (1.80 g, 0.79 mmol) was dissolved in bi-phasic solvent mixture diethyl ether–water (40 mL, 1:1 v/v). To it were added saturated aqueous sodium bicarbonate solution (16 mL) and Bu<sub>4</sub>N<sup>+</sup>T<sup>-</sup> (439 mg, 1.19 mmol). The reaction was left for stirring at room temperature for 8 hours. The ether layer was separated and washed with brine (2 x 10 mL). The ether layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, concentrated and residue was further dried under high vacuum to get the trisaccharide **13** as a colorless solid (1.21 g, 79% yield). m.p. 92-94 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  8.21 (m, 2H, Ar), 8.15 (m, 2H, Ar), 8.04 (m, 8H, Ar), 7.89 (m, 6H, Ar), 7.51 (m, 20H, Ar), 7.28 (m, 10H, Ar), 7.16 (dd, 2H,  $J$  = 7.9 Hz, Ar), 6.36 (dd, 1H,  $J$  = 9.9, 10.3 Hz), 6.03 (m, 4H), 5.93 (m, 2H), 5.77 (d, 1H,  $J$  = 1.3 Hz, H-1), 5.75 (dd, 1H,  $J$  9.8, 10.1 Hz), 5.56 (m, 1H), 5.16 (s, 1H, anomeric H), 5.09 (d, 1H,  $J$  = 7.9 Hz), 4.82 (s, 1H, anomeric H), 4.31 (dd, 1H,  $J$  = 4.1, 11.3 Hz), 4.21 (m, 1H), 3.84 (m, 3H), 3.50 (m, 2H), 3.36 (d, 1H,  $J$  = 9.6 Hz), 2.56 (m, 1H), 2.24 (s, 3H, PhCH<sub>3</sub>). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  166.77 (C=O), 165.75 (C=O), 165.71 (C=O), 165.65 (C=O), 165.56 (C=O), 165.32 (C=O), 138.47, 133.75, 133.63, 133.51, 133.31, 133.21, 133.15, 132.82, 132.67, 130.25, 130.13, 130.02, 129.92, 129.84, 129.47, 129.40, 129.18, 129.13, 128.93, 128.89, 128.84, 128.73, 128.65, 128.58, 128.43 (Ar), 98.27, 97.61 (C-1', C-1''), 86.87 (C-1), 72.10, 71.02, 70.62, 70.52, 70.36, 69.61, 69.40, 67.17, 66.78, 66.68, 65.94, 61.03, 21.21 (PhCH<sub>3</sub>). HR-ESIMS:  $m/z$  1569.4188 [M+Na]<sup>+</sup> calcd for C<sub>88</sub>H<sub>74</sub>O<sub>24</sub>SNa, found 1569.4243.

***p*-Thiotolyl 6-*O*-[2,3,4-tri-*O*-benzoyl-6-*O*-{2,3,4-tri-*O*-benzoyl-((1-methylimidazoliumhexafluorophospho)acetyl-2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranosyl)- $\alpha$ -D-mannopyranosyl]-2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranoside (**14**)**

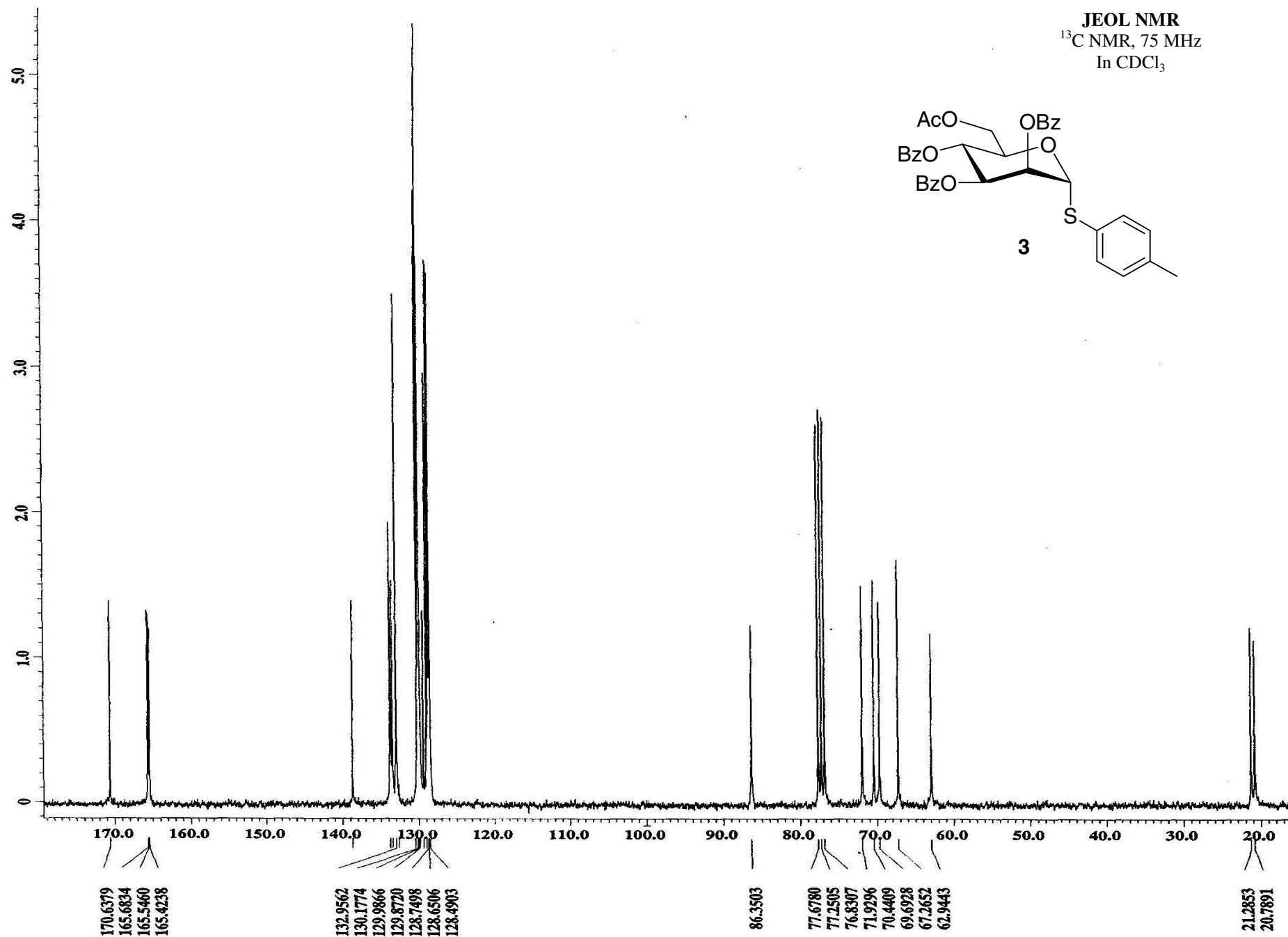
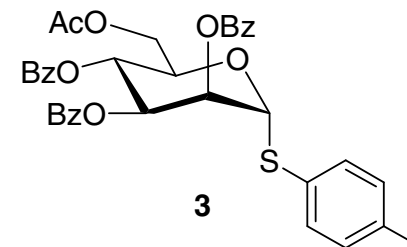
The acceptor trisaccharide **13** (1.10 g, 0.71 mmol) and IL-tagged fluoride donor glycoside **9** (495 mg, 0.65 mmol) were dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (15 mL) under argon atmosphere in presence of activated 4Å molecular sieves (400 mg). The reaction mixture was then cooled to 0 °C and coupling reagents AgClO<sub>4</sub> (419 mg, 1.63 mmol) and Cp<sub>2</sub>HfCl<sub>2</sub> (270 mg, 0.71 mmol) were added. The reaction mixture was left stirring overnight at room temperature. The tlc showed complete consumption of acceptor glycoside. The reaction mixture was filtered and concentrated under vacuum. The residue was then washed with diethylether (3 x 25 mL) and solvent was removed by decantation. The residue was finally dried under vacuum to give pure IL-tagged tetrasaccharide **14** (1.21 g, 81% yield). m.p. 112-115 °C. *R<sub>f</sub>* 0.37 (5:1 CHCl<sub>3</sub>–MeOH). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 8.57 (s, 1H, Ar), 7.99 (m, 22H, Ar), 7.41 (m, 42H, Ar), 7.12 (d, 2H, *J* = 8.3 Hz, Ar), 6.37 (dd, 1H, *J* = 9.8, 10.3 Hz), 6.09 (m, 4H), 5.94 (m, 4H), 5.79 (m, 2H), 5.75 (s, 1H, H-1), 5.65 (m, 1H), 5.20 (s, 1H, anomeric H), 5.11 (d, 1H, *J* = 7.7 Hz), 4.97 (m, 2H), 4.94 (s, 1H, anomeric H), 4.80 (s, 1H, anomeric H), 4.36 (m, 2H), 4.17 (m, 3H), 3.83 (m, 10H), 3.43 (m, 2H), 2.21 (s, 3H, PhCH<sub>3</sub>). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 166.29 (C=O), 165.74 (C=O), 165.58 (C=O), 165.42 (C=O), 165.29 (C=O), 165.23 (C=O), 165.09 (C=O), 138.50, 137.81, 134.06, 133.80, 133.66, 133.51, 133.30, 133.17, 132.88, 130.24, 130.12, 130.00, 129.89, 129.77, 129.48, 129.37, 129.31, 129.11, 128.94, 128.82, 128.73, 128.59, 128.43, 123.63, 123.15 (Ar), 98.28, 97.76 (C-1', C-1'', C-1'''), 86.86 (C-1), 72.07, 71.01, 70.63, 70.33, 70.23, 70.09, 69.78, 69.45, 69.34, 68.56, 66.98, 66.71, 66.51, 66.17, 65.94, 49.75 (NCH<sub>2</sub>), 36.56 (NCH<sub>3</sub>), 21.20 (PhCH<sub>3</sub>). ESIMS: *m/z* 2143.6 [M-PF<sub>6</sub>]<sup>+</sup> calcd for C<sub>121</sub>H<sub>103</sub>N<sub>2</sub>O<sub>33</sub>S, found 2143.1

***p*-Thiotolyl 6-*O*-[2,3,4-tri-*O*-benzoyl-6-*O*-{2,3,4-tri-*O*-benzoyl-(2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranosyl)- $\alpha$ -D-mannopyranosyl}- $\alpha$ -D-mannopyranosyl]-2,3,4-tri-*O*-benzoyl- $\alpha$ -D-mannopyranoside (1)**

IL-tagged tetrasaccharide **14** (1.10 g, 0.48 mmol) was dissolved in bi-phasic solvent mixture diethylether–water (40 mL, 1:1 v/v). To it were added saturated aqueous NaHCO<sub>3</sub> solution (20 mL) and Bu<sub>4</sub>N<sup>+</sup>I<sup>−</sup> (266 mg, 0.72 mmol). The reaction was left for stirring overnight at room temperature. The ether layer was separated and washed with brine (2 x 15 mL). The ether layer was then dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, concentrated and residue was further dried under high vacuum to get the tetrasaccharide **1** as a colorless solid (844 mg, 86% yield). m.p. 142-145 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  8.19 (m, 6H, Ar), 8.07 (m, 8H, Ar), 7.93 (m, 10H, Ar), 7.41 (m, 38H, Ar), 7.14 (d, 2H, *J* = 8.3 Hz, Ar), 6.39 (t, 1H, *J* = 10.0 Hz), 6.15 (t, 1H, *J* = 10.0 Hz), 6.07 (m, 4H), 5.95 (m, 3H), 5.78 (m, 2H), 5.77 (s, 1H, H-1), 5.68 (m, 1H), 5.22 (s, 1H, anomeric H), 5.12 (dd, 1H, *J* = 2.5, 10.2 Hz), 5.01 (s, 1H, anomeric H), 4.81 (s, 1H, anomeric H), 4.37 (dd, 1H, *J* = 4.1, 11.3 Hz), 4.23 (m, 2H), 3.92 (m, 2H), 3.81 (m, 2H), 3.43 (m, 4H), 2.60 (br s, 1H), 2.23 (s, 3H, PhCH<sub>3</sub>). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  166.87 (C=O), 165.76 (C=O), 165.71 (C=O), 165.59 (C=O), 165.46 (C=O), 165.34 (C=O), 165.22 (C=O), 138.46, 133.80, 133.63, 138.48, 133.28, 133.12, 132.89, 130.15, 130.02, 129.92, 129.78, 129.42, 129.23, 129.13, 128.92, 128.82, 128.70, 128.61, 128.41 (Ar), 98.30, 98.18, 97.78 (C-1', C-1'', C-1'''), 86.86 (C-1), 72.10, 70.98, 70.64, 70.56, 70.35, 69.75, 69.46, 67.17, 66.92, 66.75, 66.42, 66.03, 65.94, 60.92 (CH<sub>2</sub>OH), 21.19 (PhCH<sub>3</sub>). FABMS: (*m/z*): 2043.5 [M+Na]<sup>+</sup> calcd for C<sub>115</sub>H<sub>96</sub>O<sub>32</sub>SNa, found 2043.3.



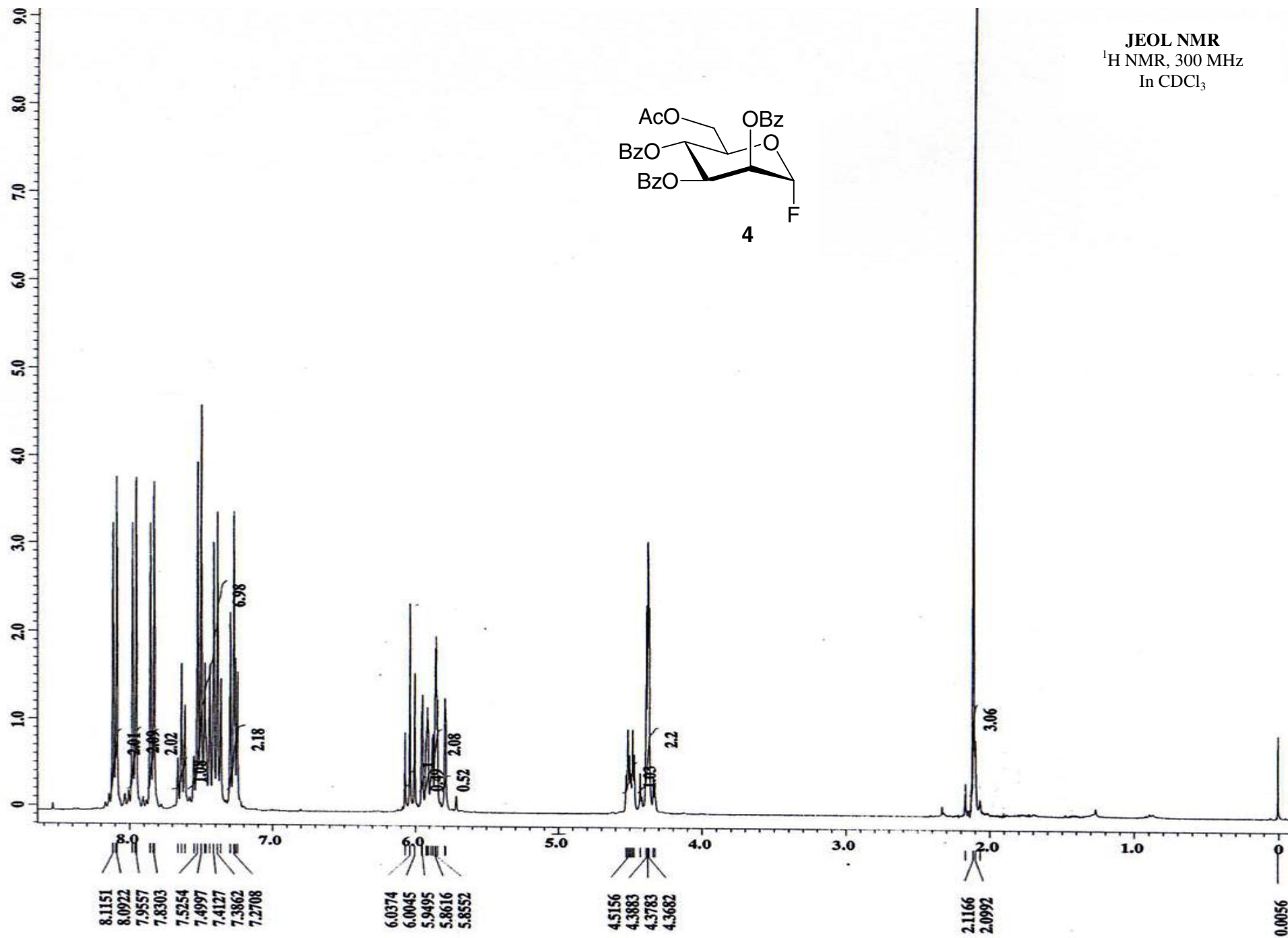
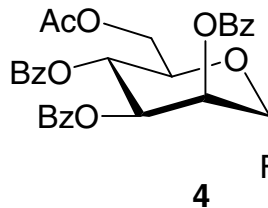
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 $^{13}\text{C}$  NMR, 75 MHz  
 In  $\text{CDCl}_3$



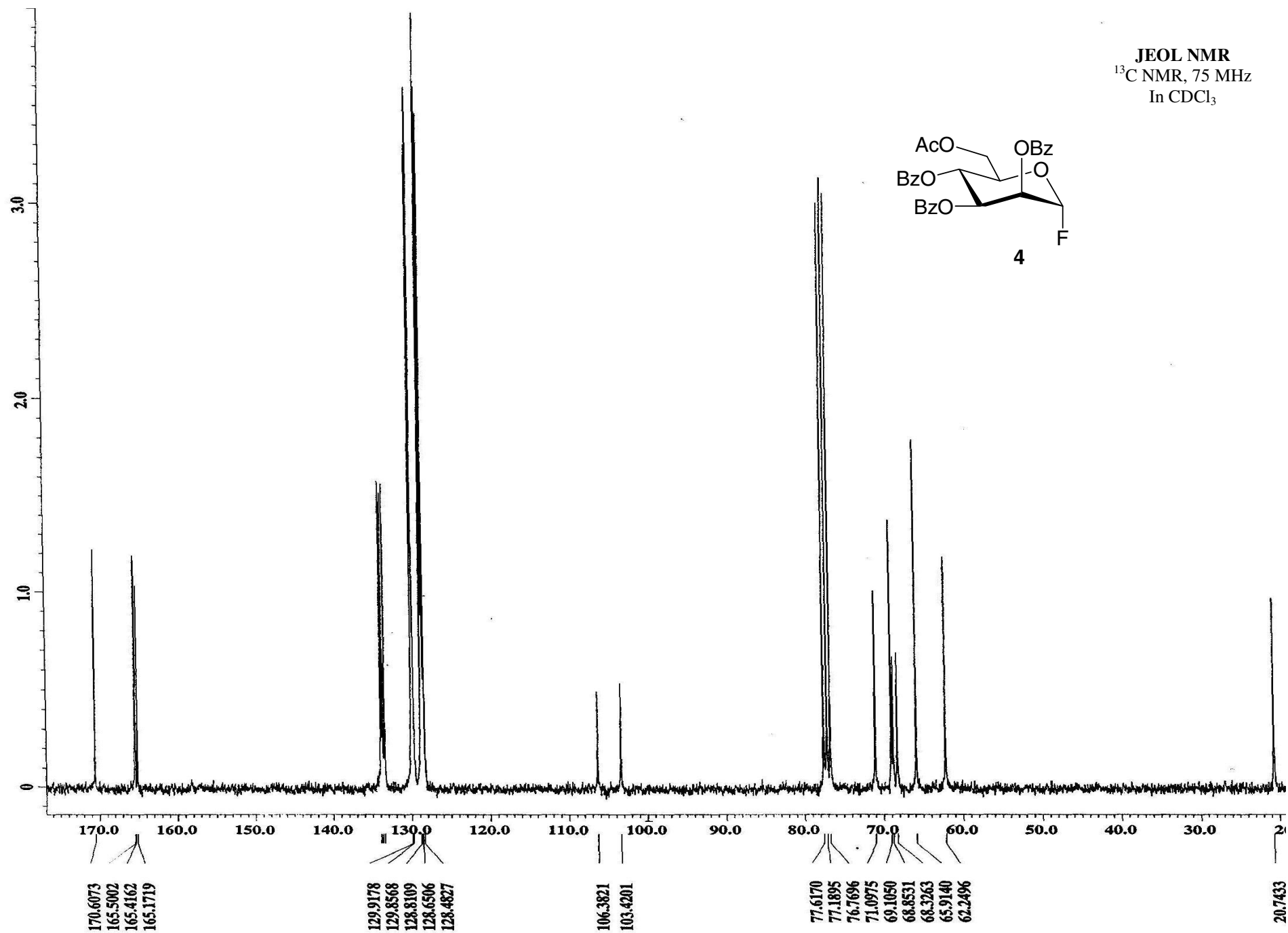
X : parts per Million :  $^{13}\text{C}$

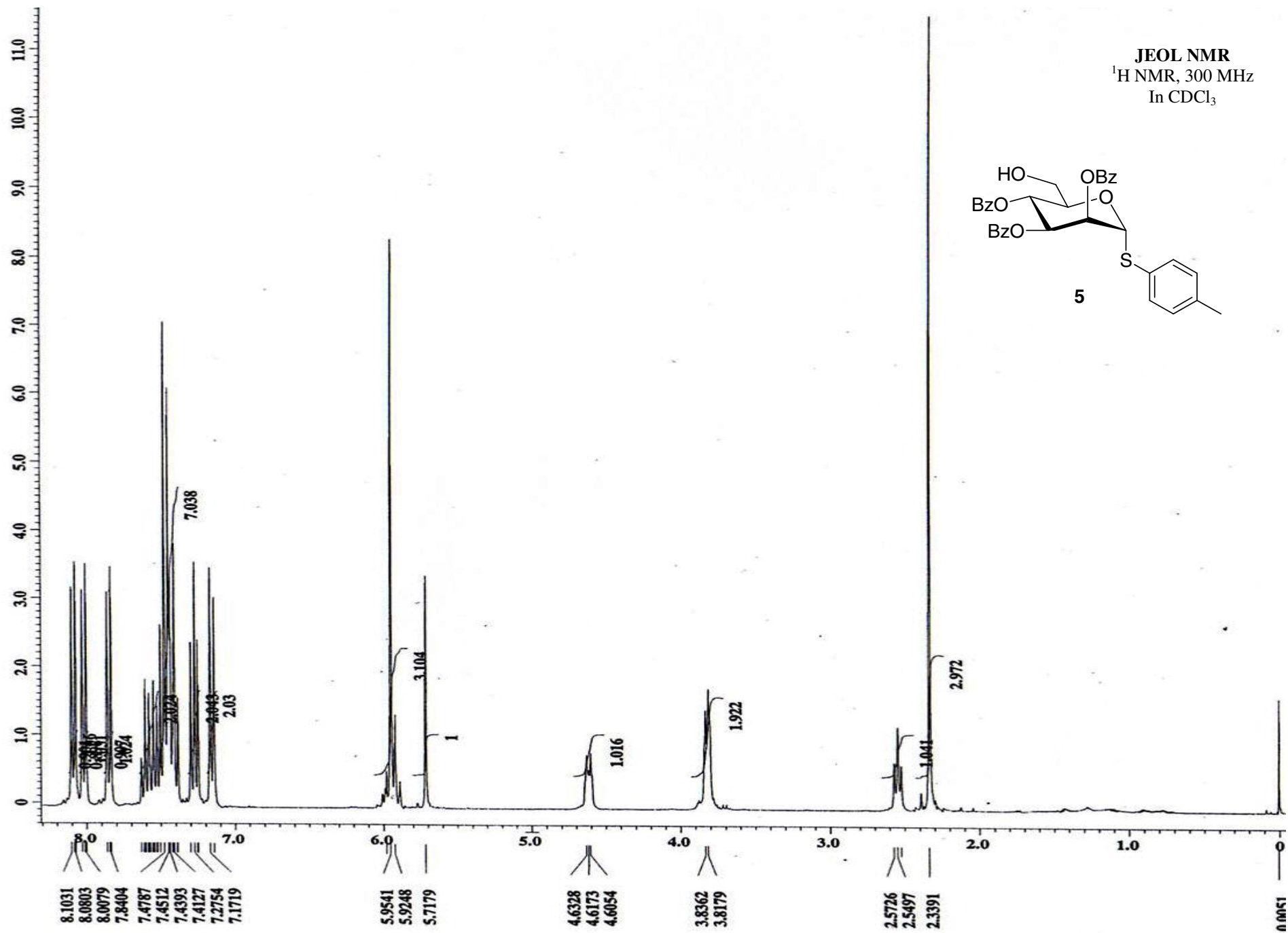


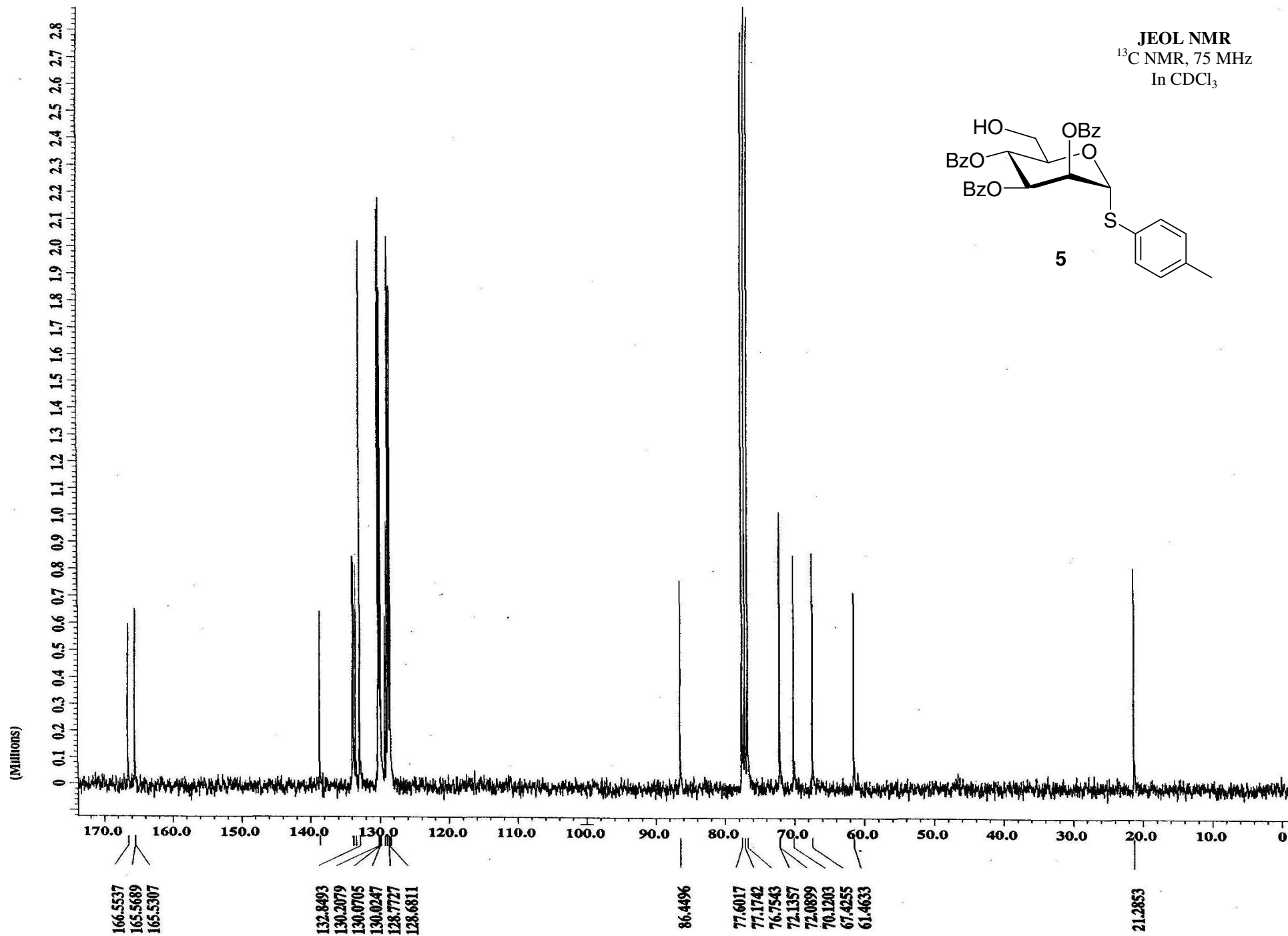
JEOL NMR  
<sup>1</sup>H NMR, 300 MHz  
 In CDCl<sub>3</sub>



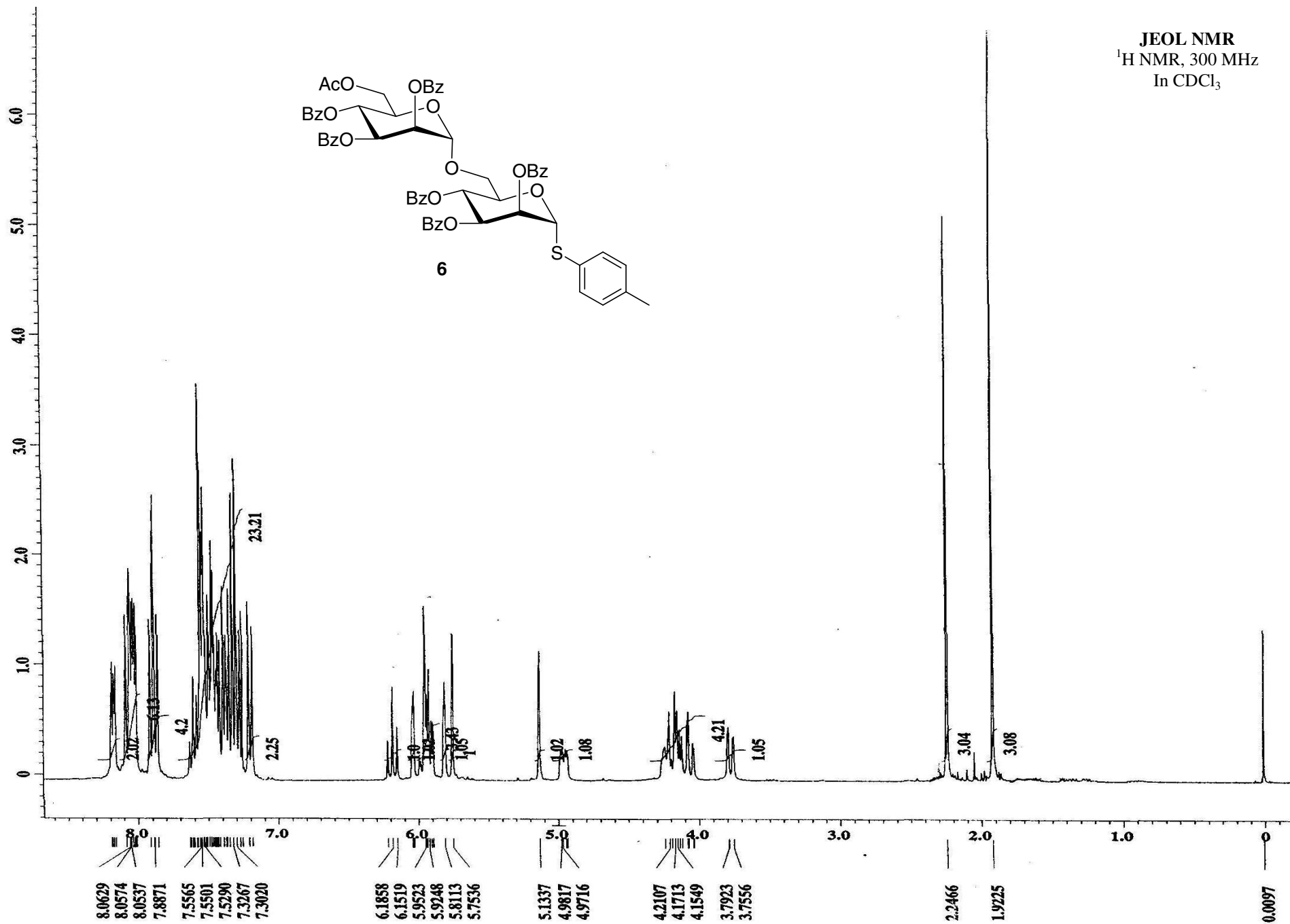
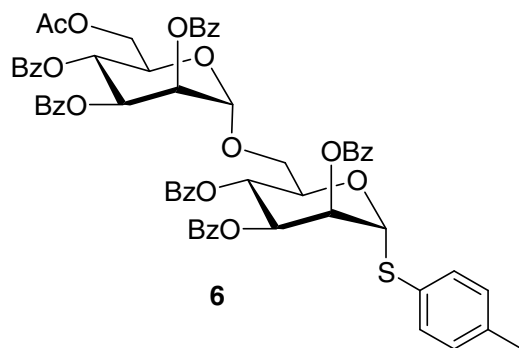
JEOL NMR  
<sup>13</sup>C NMR, 75 MHz  
In CDCl<sub>3</sub>



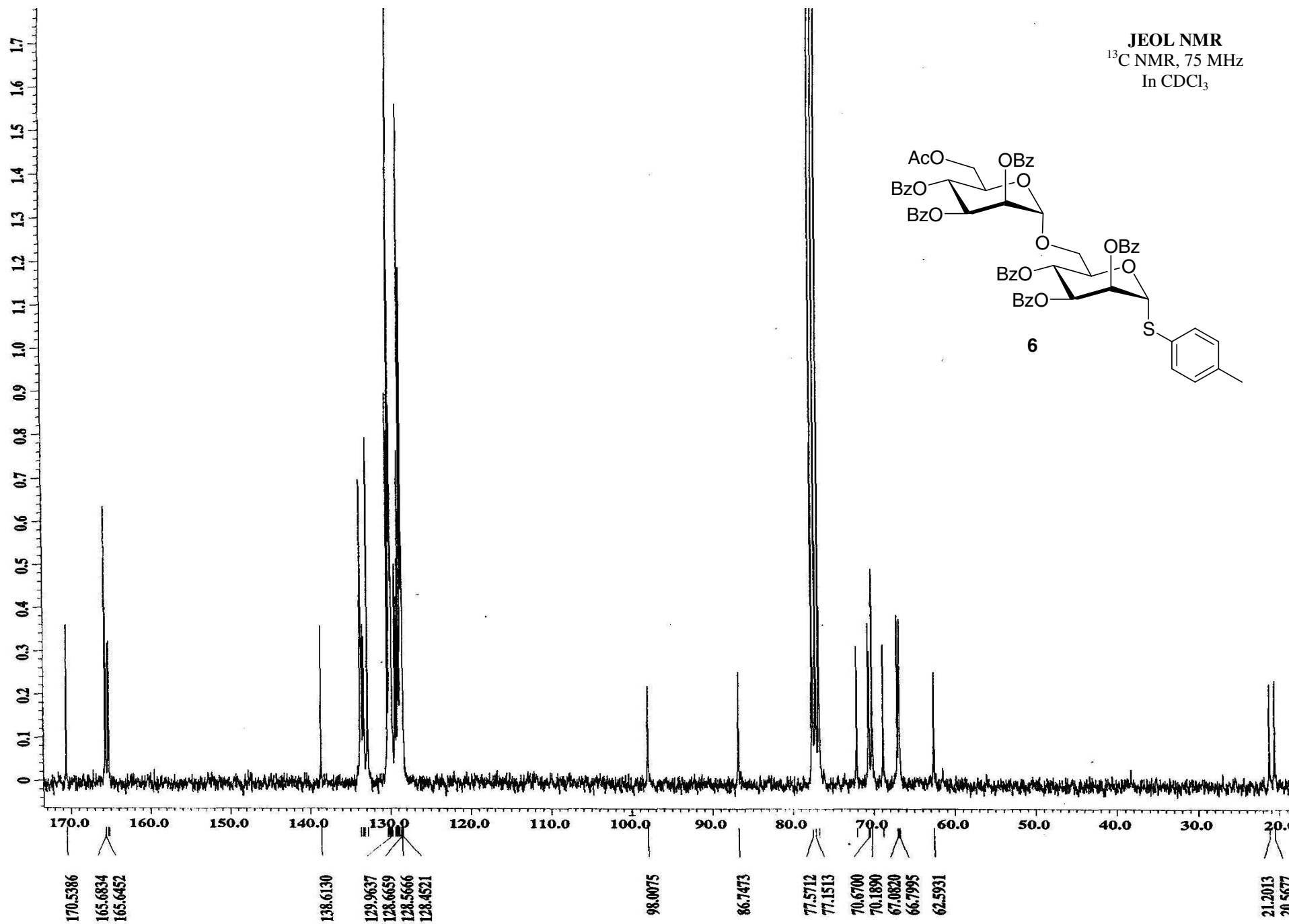




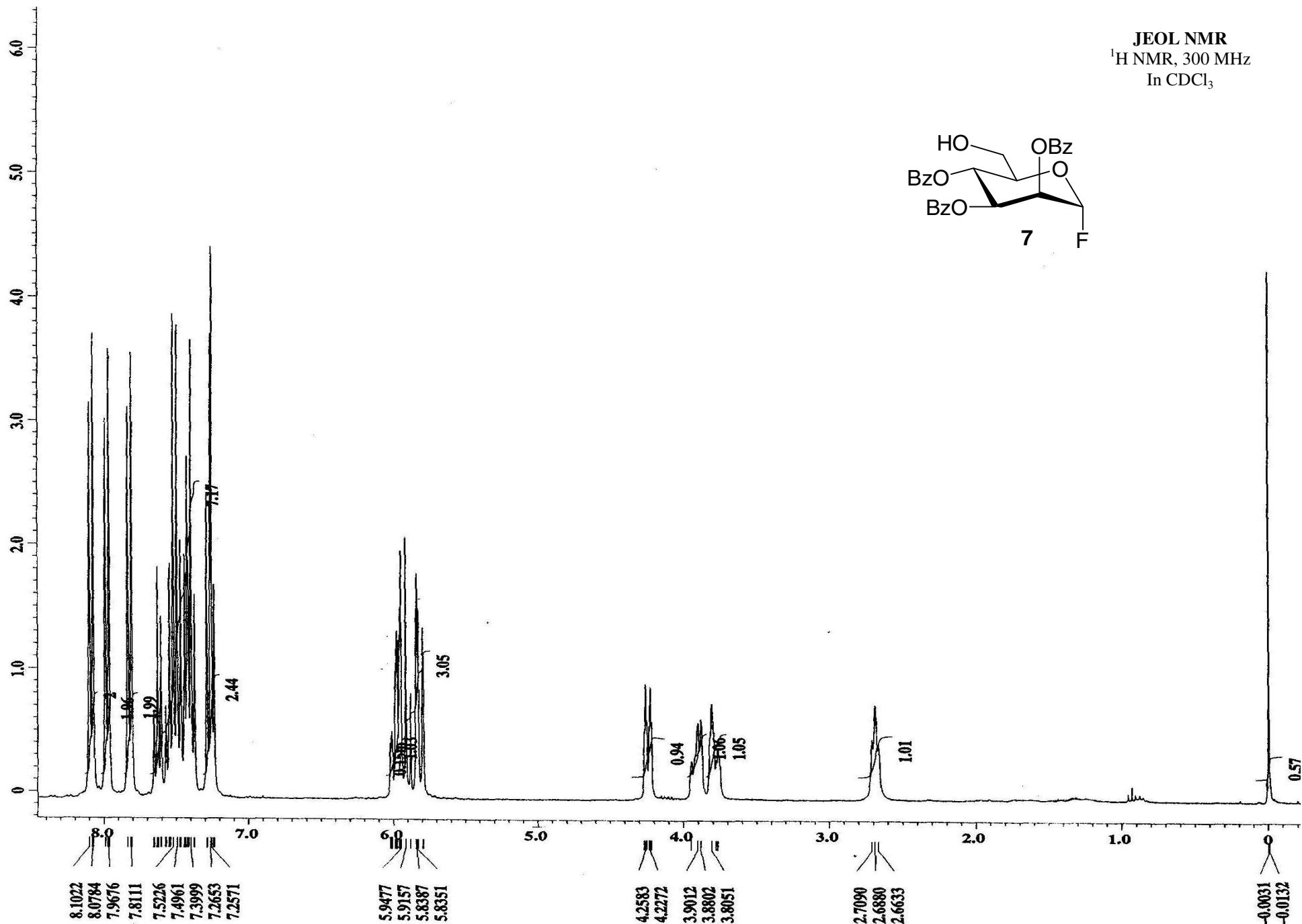
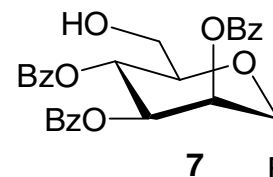
JEOL NMR  
<sup>1</sup>H NMR, 300 MHz  
 In CDCl<sub>3</sub>



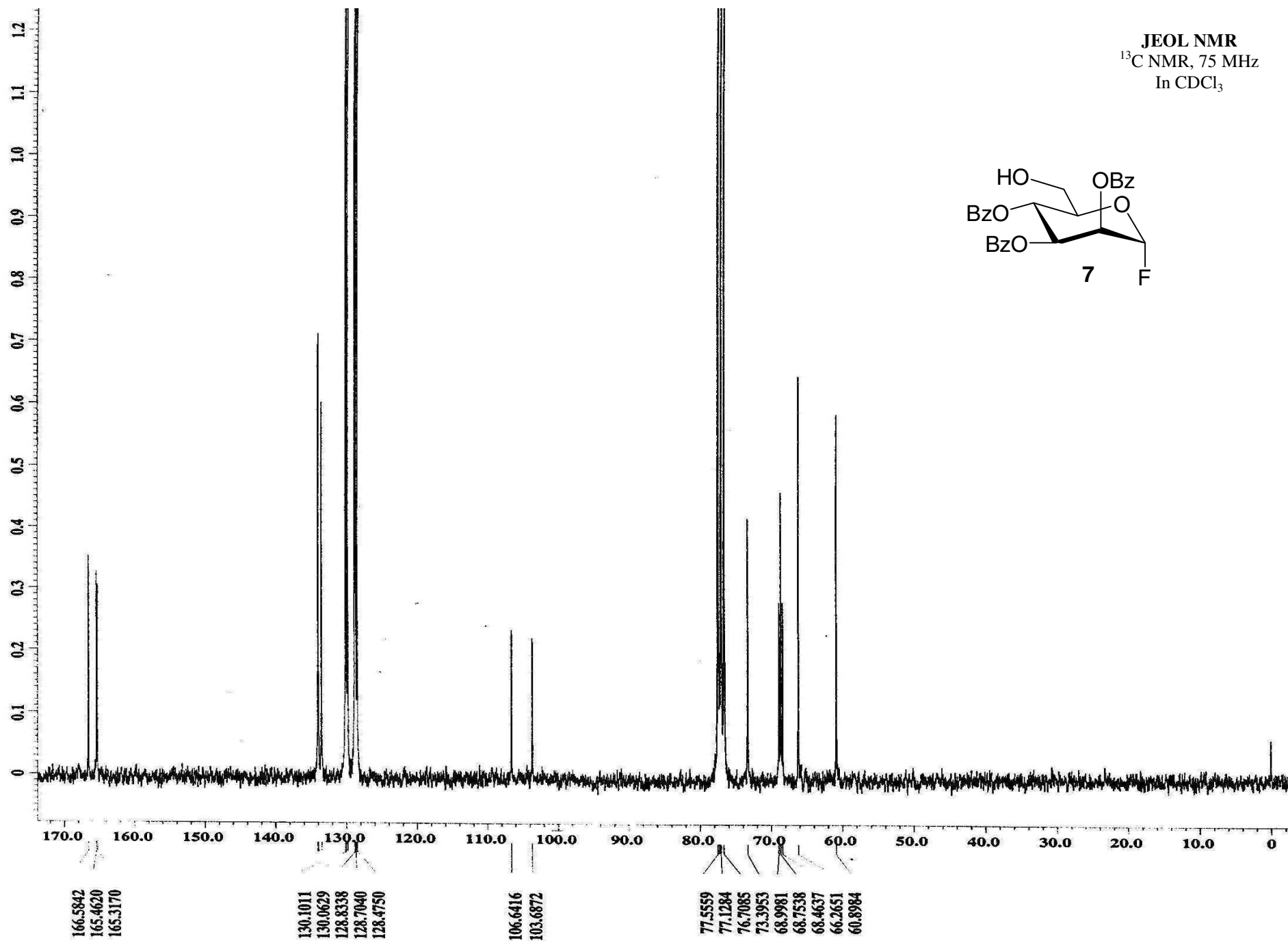
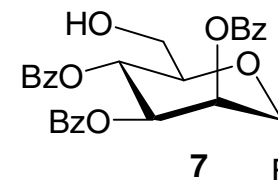
JEOL NMR  
 $^{13}\text{C}$  NMR, 75 MHz  
 In  $\text{CDCl}_3$



JEOL NMR  
<sup>1</sup>H NMR, 300 MHz  
 In CDCl<sub>3</sub>

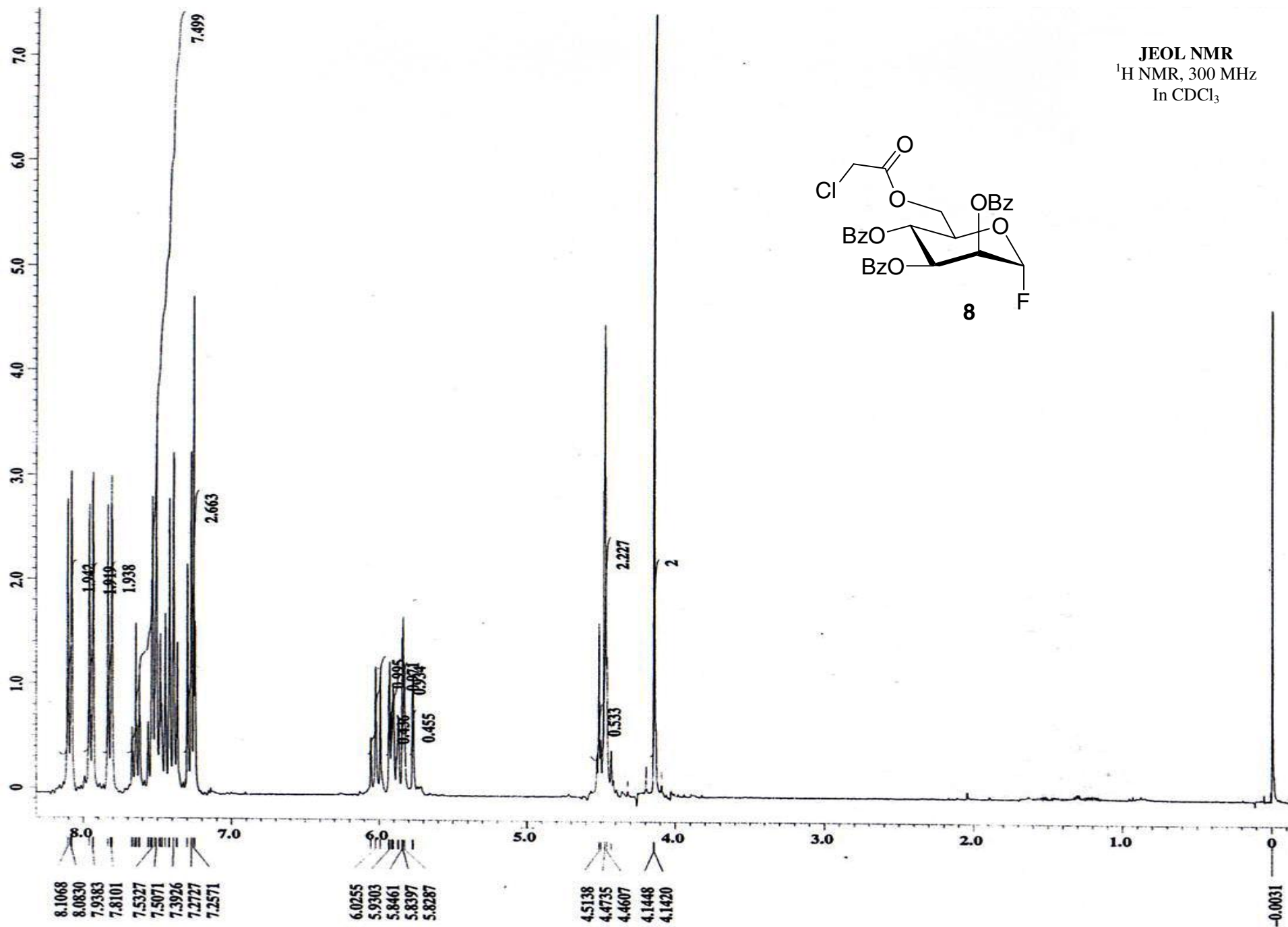
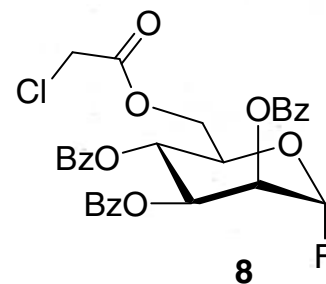


JEOL NMR  
 $^{13}\text{C}$  NMR, 75 MHz  
 In  $\text{CDCl}_3$

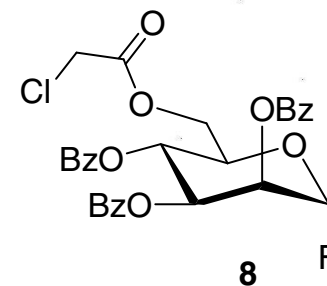
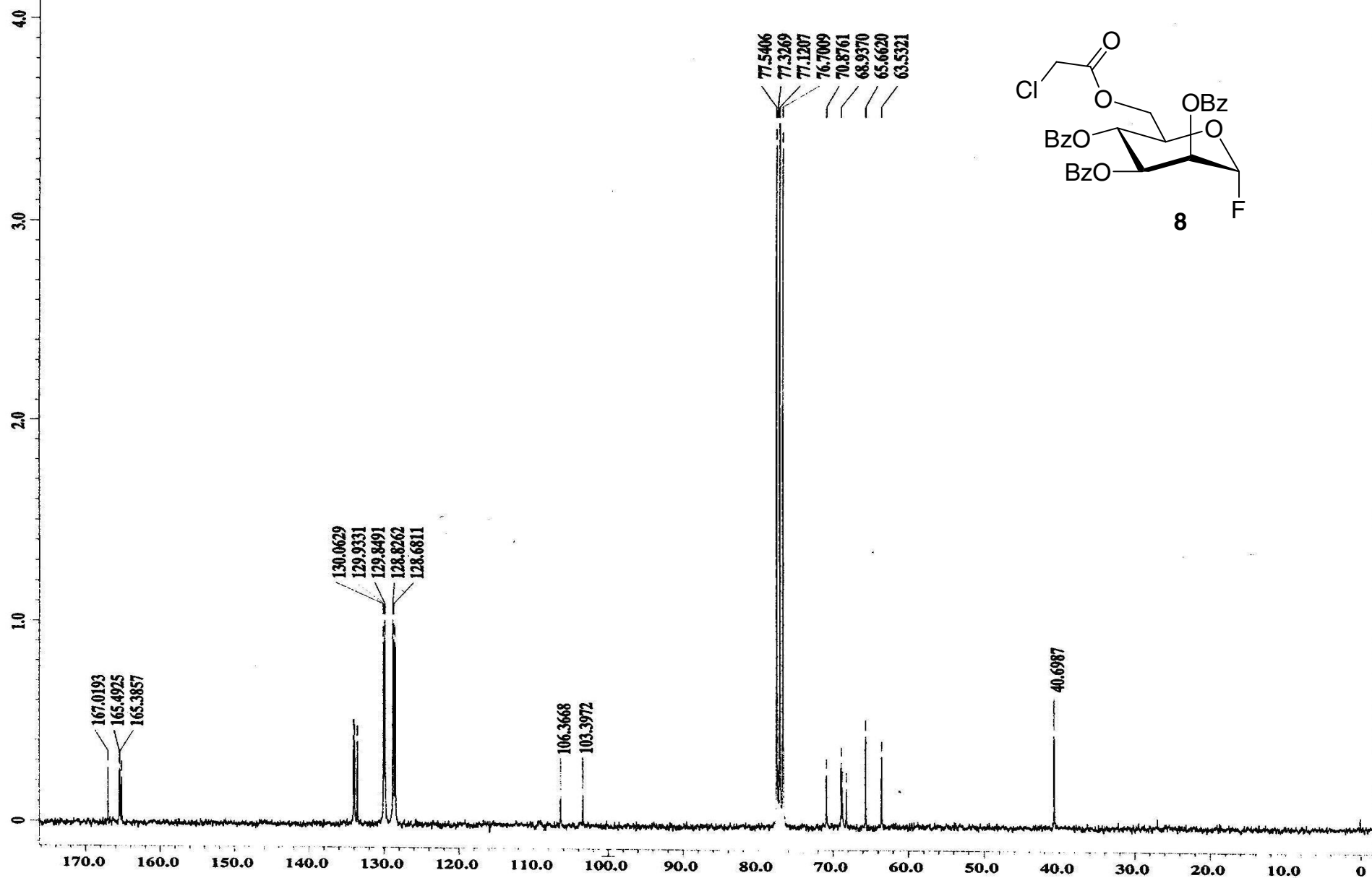




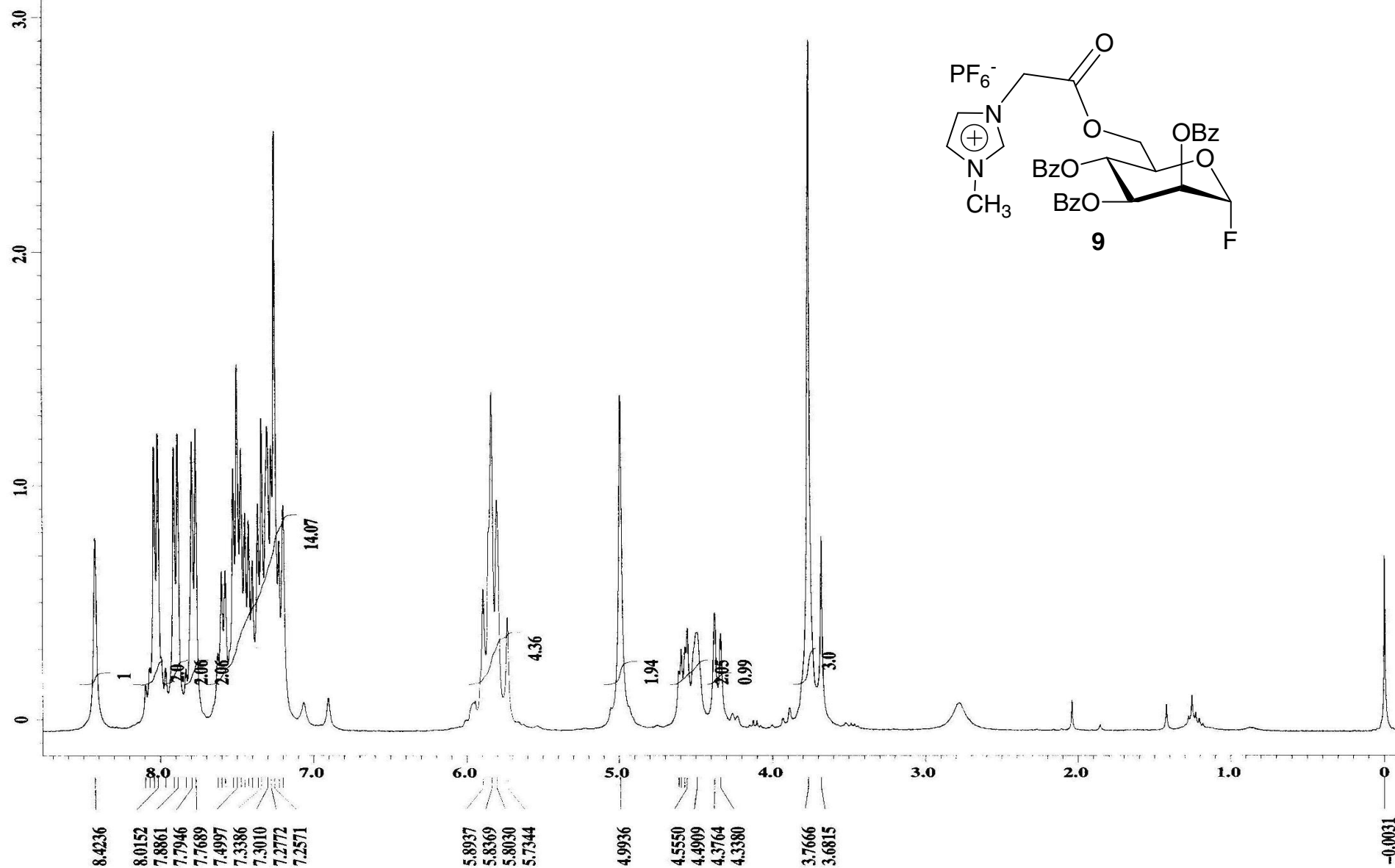
JEOL NMR  
<sup>1</sup>H NMR, 300 MHz  
 In CDCl<sub>3</sub>



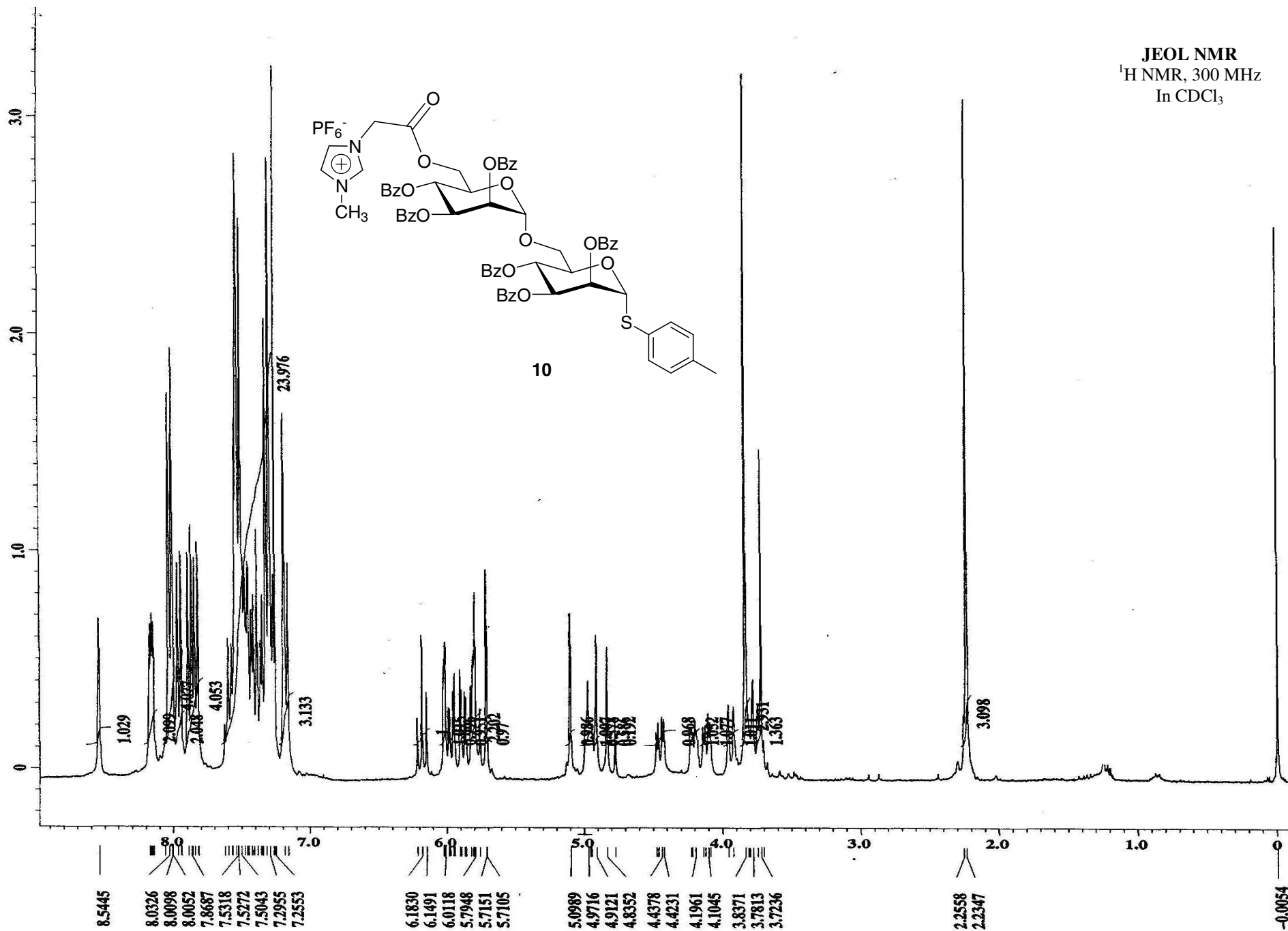
JEOL NMR  
<sup>13</sup>C NMR, 75 MHz  
 In CDCl<sub>3</sub>



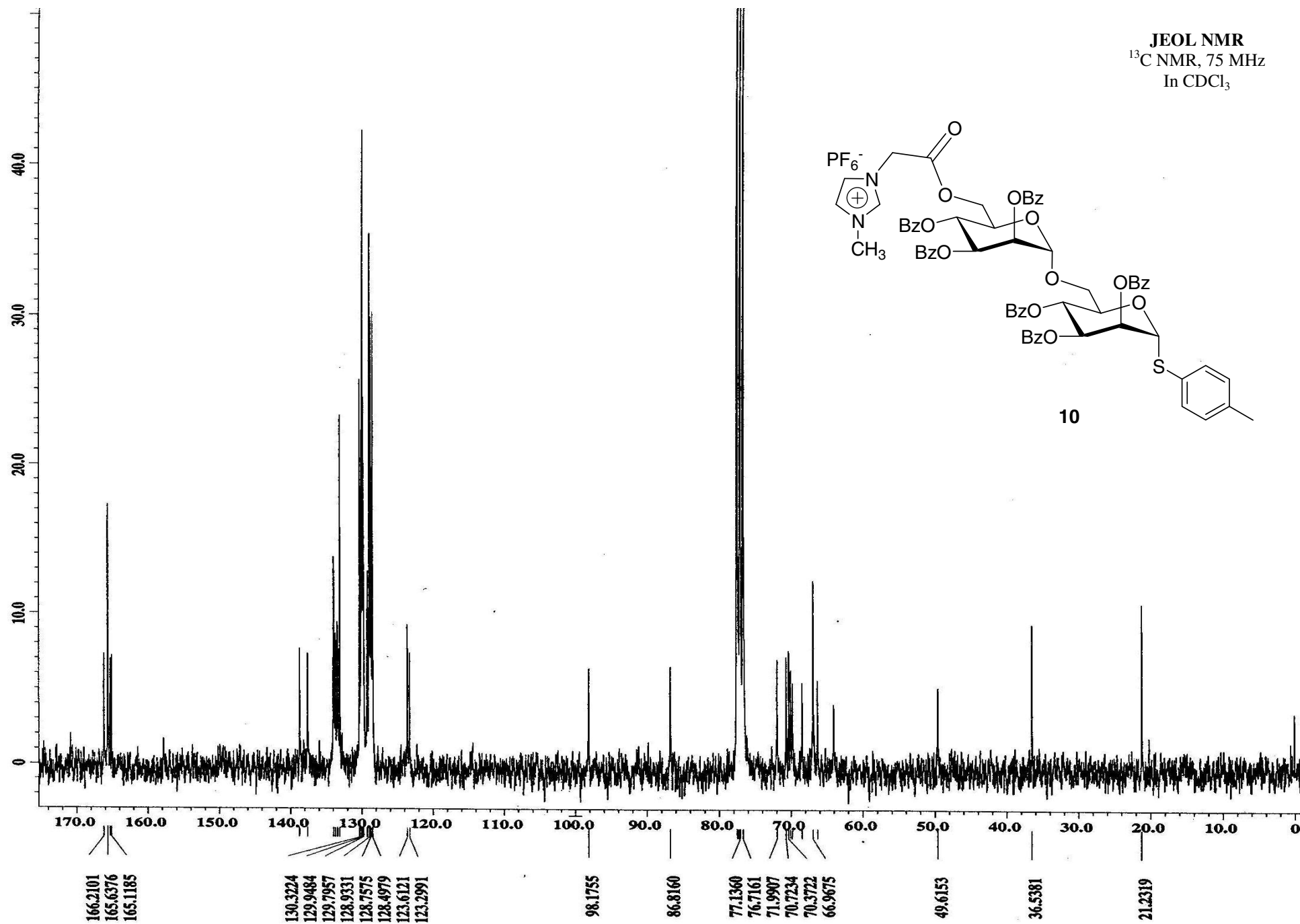
JEOL NMR  
<sup>1</sup>H NMR, 300 MHz  
 In CDCl<sub>3</sub>



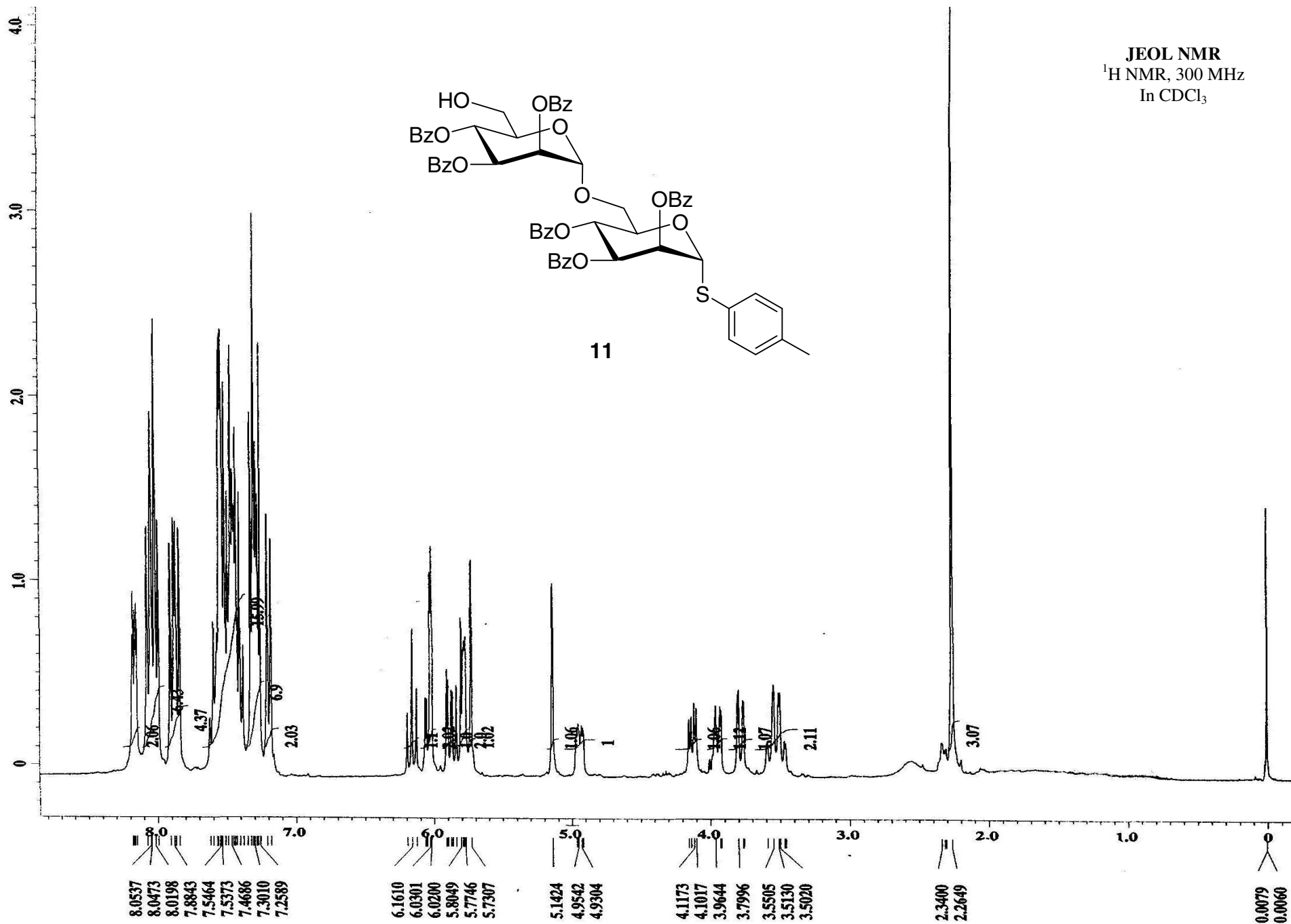
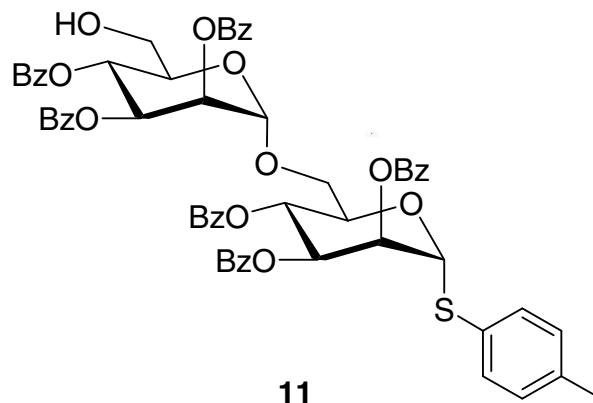
JEOL NMR  
<sup>1</sup>H NMR, 300 MHz  
 In CDCl<sub>3</sub>



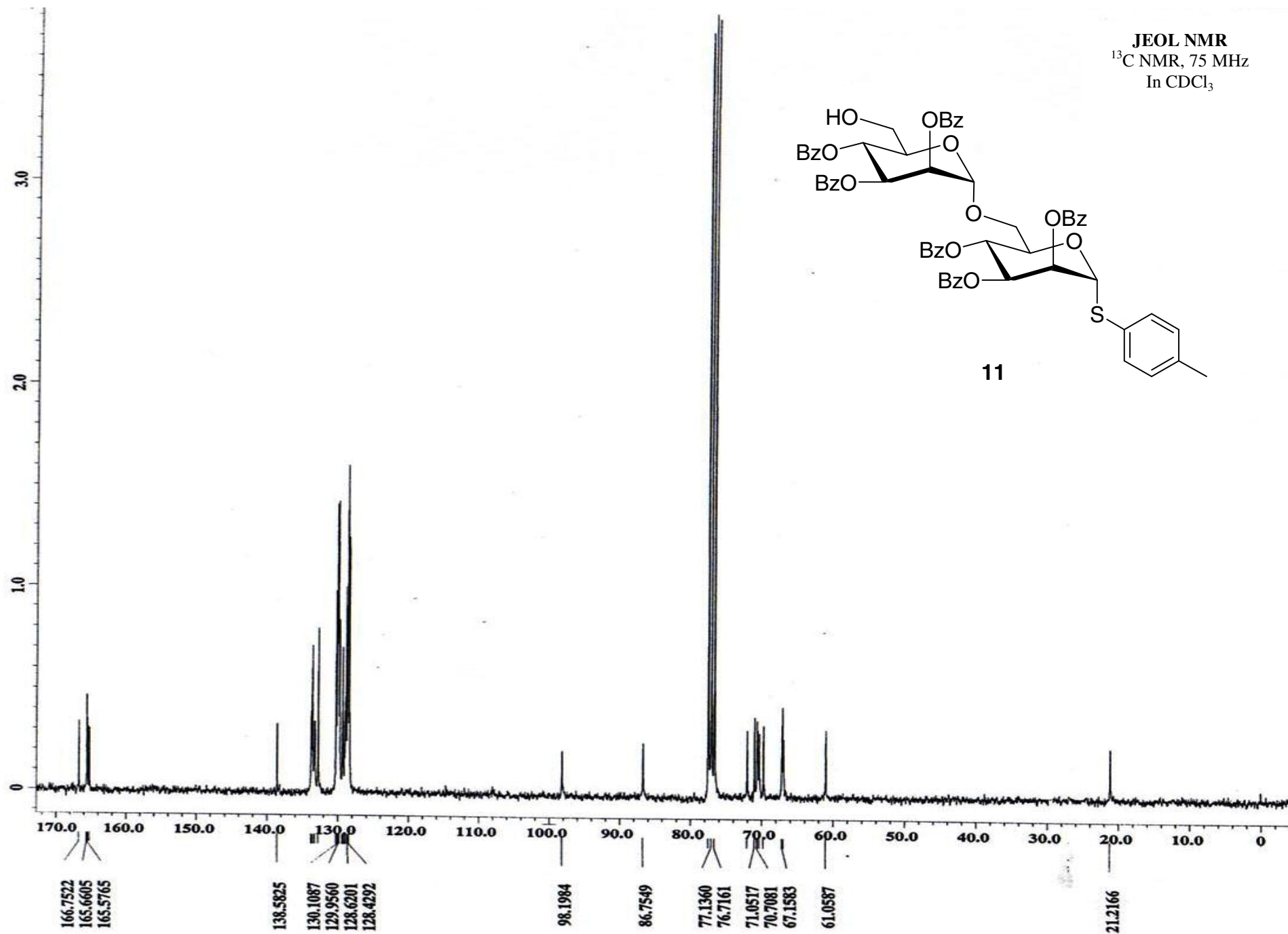
JEOL NMR  
<sup>13</sup>C NMR, 75 MHz  
 In CDCl<sub>3</sub>



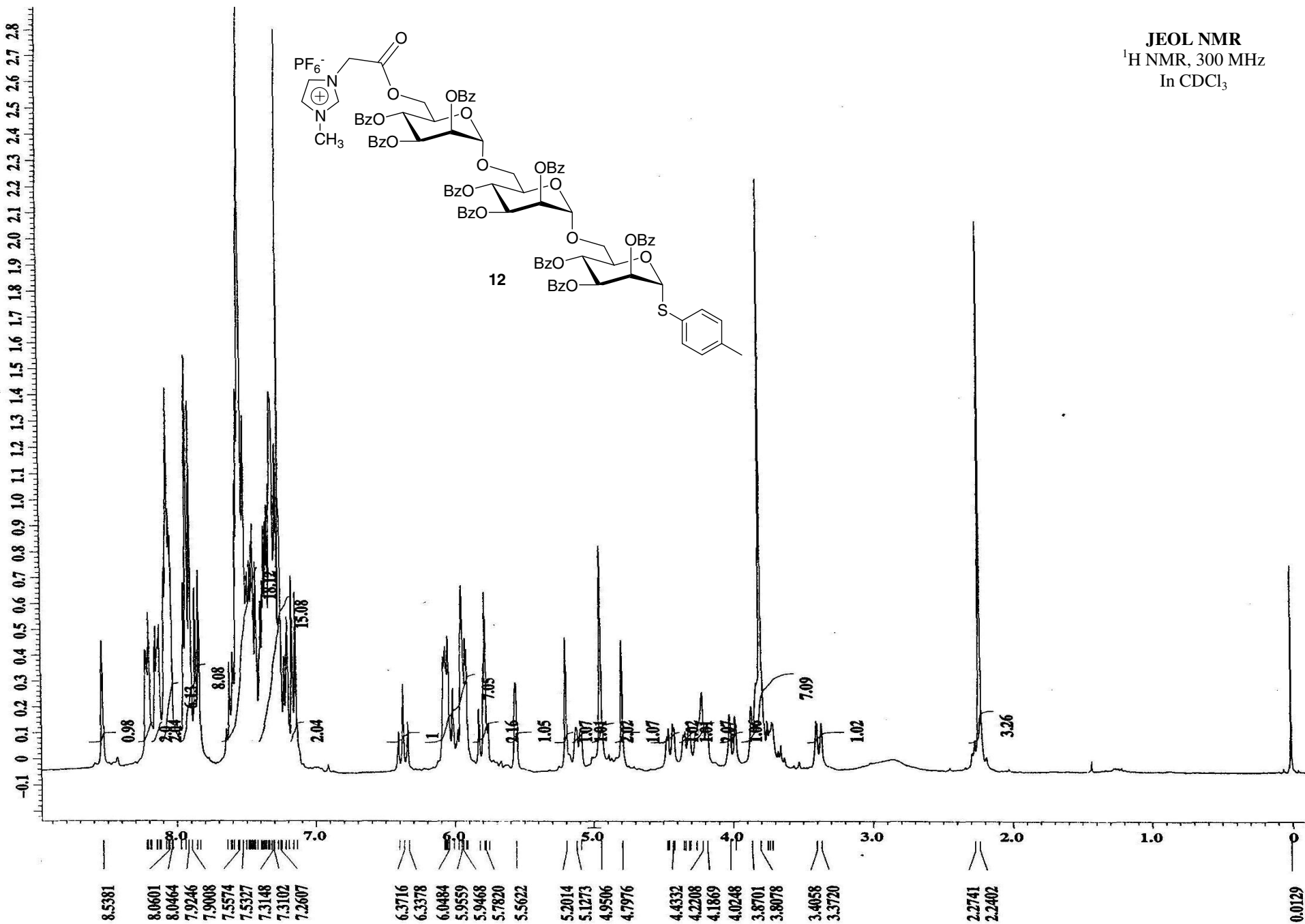
JEOL NMR  
<sup>1</sup>H NMR, 300 MHz  
 In CDCl<sub>3</sub>



JEOL NMR  
<sup>13</sup>C NMR, 75 MHz  
 In CDCl<sub>3</sub>



JEOL NMR  
<sup>1</sup>H NMR, 300 MHz  
 In CDCl<sub>3</sub>





JEOL NMR  
<sup>13</sup>C NMR, 75 MHz  
 In CDCl<sub>3</sub>

