

# Reductive cyclization of $\delta$ -hydroxy nitriles: a new synthesis of glycosylamines.

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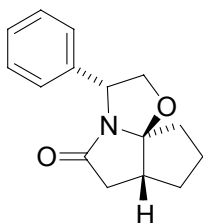
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## Supporting Information

General Experimental Details: Unless otherwise noted, starting materials were obtained from commercial suppliers and used without further purification. Tetrahydrofuran (THF), toluene, and dichloromethane (DCM) were dried by passing through activated alumina columns. All other solvents were analytical grade. Reactions were carried out under an atmosphere of nitrogen. Glassware, stir bars and needles were dried at 150 °C in an oven prior to use. Organic extracts were dried over MgSO<sub>4</sub>. Both reaction mixtures and chromatography fractions were analyzed on Merck silica gel 60 F<sub>254</sub> TLC plates. Compounds were detected by treating with ceric ammonium molybdate and heating at 200 °C. Flash column chromatography was carried out with ICN SiliTech 32-63 D 60 Å silica gel.

Instrumentation: Melting points are uncorrected and were determined on a Büchi melting point apparatus. FT-IR spectra were obtained on NaCl plates with an ATI Mattson Gemini spectrometer. Proton and carbon NMR spectra (<sup>1</sup>H NMR and <sup>13</sup>C NMR) were recorded in deuterated solvents on Bruker AM-400 or DRX-500 spectrometers and calibrated to the residual solvent peak. Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, m = multiplet, app = apparent. All NMR were recorded in CDCl<sub>3</sub>. Mass spectral data were obtained from the Micro-Mass Facility operated by the College of Chemistry, University of California, Berkeley.

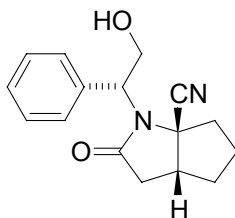
### (3*R*, 5*cR*, 8*bS*)-3-Phenylhexahydro-1-oxa-3a-azacyclopentalen-4-one (1).



To a solution of 5.67 g of 2-oxocyclopentane acetic acid (40.2 mmol) in 100 mL of toluene was added 5.25 g of (*R*)-(-)-2-phenylglycinol (38.3 mmol). The reaction mixture was heated at reflux for 12 h and concentrated *in vacuo*. Purification by silica gel

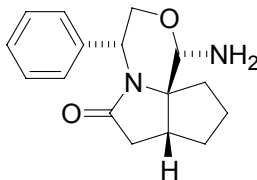
chromatography (3:1 hexanes:ethyl acetate) gave 8.75 g (94%) of **1** as a pale yellow oil. IR 1709  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz):  $\delta$  1.53-1.61 (m, 1H), 1.67-1.88 (m, 3H), 1.92-1.97 (m, 1H), 1.98-2.08 (m, 1H), 2.42-2.57 (m, 1H), 2.68-2.80 (m, 1H), 2.81-2.99 (m, 1H), 3.91-4.06 (m, 1H), 4.55-4.69 (m, 1H), 5.08-5.24 (m, 1H), 7.19-7.42 (m, 5H).  $^{13}\text{C}$  NMR (100 MHz):  $\delta$  24.59, 32.40, 36.72, 40.71, 41.44, 57.90, 73.51, 110.91, 125.61, 127.49, 128.77, 139.76, 180.38. HRMS (EI) Calcd for  $\text{C}_{15}\text{H}_{17}\text{NO}_2$  ( $\text{M}^+$ ): 243.1259. Found: 243.1263.

**(3b*R*, 6a*R*)-1-[(1*R*)-2-Hydroxy-1-phenylethyl]-2-oxohexahydrocyclopenta[*b*]pyrrole-6a-carbonitrile (2).**



To a solution of 2.00 g of **1** (8.23 mmol) in 100 mL of DCM was added 3.30 mL of trimethylsilyl cyanide (24.7 mmol). The reaction mixture was cooled to  $-78^\circ\text{C}$  and 16.5 mL of a 1.0 M solution of titanium(IV) chloride in DCM (16.5 mmol) was added. The reaction mixture was allowed to warm to room temperature over 12 h and washed with 1 N NaOH (3 x 100mL). The organic phase was dried, filtered and concentrated *in vacuo*. Recrystallization from hexanes/ethyl acetate afforded 1.74 g (79%) of **2** as a white solid. m.p. 139.1-141.2 $^\circ\text{C}$ . IR 3306, 2234, 1678  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz):  $\delta$  1.56-1.63 (m, 1H), 1.74-1.88 (m, 1H), 2.05-2.20 (m, 2H), 2.22-2.32 (m, 2H), 2.93-3.03 (m, 2H), 3.06-3.14 (m, 1H), 3.97-4.06 (m, 1H), 4.56-4.64 (m, 2H), 7.33-7.52 (m, 5H).  $^{13}\text{C}$  NMR (100 MHz):  $\delta$  25.34, 33.73, 36.70, 39.15, 41.08, 53.73, 67.90, 71.22, 125.67, 128.16, 128.93, 135.61, 172.94, 175.62. HRMS (FAB+) Calcd for  $\text{C}_{16}\text{H}_{19}\text{N}_2\text{O}_2$  ( $\text{M}+\text{H}^+$ ): 271.1447. Found: 271.1452.

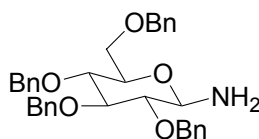
**(3a*R*, 6*R*, 9b*R*)-9-Amino-6-phenylhexahydro-8-oxa-5a-azacyclopenta[*c*]indene-5-one (3).**



To a solution of 100 mg of **2** (0.370 mmol) in EtOH (5.0 mL) was added 56 mg of sodium borohydride (1.4 mmol). The reaction mixture was stirred at reflux for 1 h, quenched with water and concentrated *in vacuo*. A 1:1 mixture of DCM/ 1 N NaOH (10 mL) was added to the crude residue and the aqueous phase was extracted with DCM (3 x 10 mL). The combined organic extracts were dried, filtered and concentrated. Purification by flash column chromatography (1:9 MeOH:ethyl acetate) gave 83 mg (82%) of **3** as a white solid. Recrystallization from hexanes/DCM afforded colorless, triangular, plate-

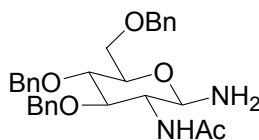
like crystals within 3 d. For X-ray crystallographic analysis, a fragment of a colorless plate crystal of **3** having approximate dimensions of 0.35 x 0.16 x 0.07 mm was mounted on a glass fiber using Paratone N hydrocarbon oil. m.p. 132.5-133.3 °C. IR 3391, 3333, 1674  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz):  $\delta$  0.88-0.96 (m, 1H), 1.32-1.50 (m, 4H), 1.82-1.94 (m, 3H), 2.18-2.25 (dd, 1H,  $J = 4.8, 18.0$  Hz), 2.49-2.59 (m, 1H), 2.70-2.79 (dd, 1H,  $J = 10.8, 17.6$  Hz), 3.86-3.94 (dd, 1H,  $J = 4.2, 12.4$  Hz), 4.02-4.10 (m, 1H), 4.62-4.66 (d, 1H,  $J = 12.4$  Hz), 5.30-5.32 (d, 1H,  $J = 4.2$  Hz), 7.27-7.36 (m, 3H), 7.54-7.58 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz):  $\delta$  25.24, 30.05, 33.89, 37.46, 38.78, 49.49, 66.92, 73.66, 88.97, 127.40, 127.95, 128.40, 139.64, 173.91. HRMS (EI) Calcd for  $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_2$  ( $\text{M}^+$ ): 272.1525. Found: 272.1524.

### 2,3,4,6-Tetra-*O*-benzyl- $\beta$ -D-glucopyranosylamine (**7**).



To a solution of 310 mg of 2,3,4,6-tetra-*O*-benzyl-D-gluconitrile **6** (0.575 mmol) in EtOH (18 mL) was added 86 mg of  $\text{NaBH}_4$  (2.29 mmol). The reaction mixture was stirred at room temperature for 2 h at which time a precipitate formed. The product was filtered, washed with cold EtOH and dried *in vacuo* to afford the pure  $\beta$  anomer **7** as a white solid (212.4 mg, 69%). IR 3387, 1644  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400MHz):  $\delta$  1.95 (d, 2H,  $J = 8.4$  Hz), 3.24 (t, 1H,  $J = 12.0$  Hz), 3.42-3.72 (m, 6H), 4.08 (d, 1H,  $J = 8.8$  Hz), 4.48-4.63 (m, 3H), 4.77-4.86 (m, 3H), 4.93-5.02 (m, 2H), 7.1-7.40 (m, 20H). Literature  $^1\text{H}$  NMR (90 MHz):  $\delta$  1.94 (s, 2H), 3.11-3.81 (m, 6H), 4.12 (d, 1H,  $J = 9.0$  Hz), 4.44-5.08 (m, 8H), 6.97-7.47 (m, 20H).  $^{13}\text{C}$  NMR (100MHz):  $\delta$  69.22, 73.78, 75.15, 75.20, 75.81, 75.91, 78.37, 83.71, 86.03, 86.48, 127.81, 127.86, 127.93, 127.95, 128.04, 128.14, 128.19, 128.26, 128.33, 128.42, 128.61, 128.73, 128.93, 138.12, 138.30, 138.84. Anal Calcd for  $\text{C}_{34}\text{H}_{37}\text{NO}_5$ : C, 75.67; H, 6.91; N, 2.60. Found: C, 75.32; H, 7.17; N, 2.60.

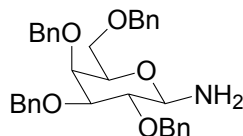
### 2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy- $\beta$ -D-glucopyranosylamine (**9**).



To a stirred solution of 535 mg (1.10 mmol) of 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy- $\beta$ -D-gluconitrile **8** in 10 mL of EtOH was added 166 mg (4.40 mmol) of  $\text{NaBH}_4$ . The mixture was stirred overnight, then concentrated to approximately 3 mL. The product precipitated out of solution and was collected by filtration to afford **9** as the pure  $\beta$  anomer (293 mg, 55%). m.p. 188-189°C. IR 3398, 3281, 1646  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz):  $\delta$  1.83 (s, 3H), 2.03 (s, 2H), 3.45-3.50 (m, 1H), 3.53-3.78 (m, 5H), 4.04 (d, 1H,  $J = 9.2$  Hz), 4.51-4.66 (m, 4H), 4.79 (d, 1H,  $J = 10.8$  Hz), 4.84 (d, 1H,  $J = 11.6$  Hz), 5.02 (d, 1H,  $J = 8.8$  Hz), 7.18-7.36 (m, 15H).  $^{13}\text{C}$  NMR (100 MHz):  $\delta$  23.74, 56.28, 69.24, 73.80, 74.52, 75.07, 76.04, 79.10, 82.26, 86.13, 127.94, 128.07, 128.16, 128.22, 128.58, 128.62,

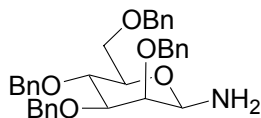
128.67, 128.75, 128.83, 138.14, 138.15, 138.49, 170.81. HRMS (FAB) Calcd for  $C_{29}H_{35}N_2O_5$  ( $M+H^+$ ): 491.2546. Found: 491.2534.

### 2,3,4,6-Tetra-*O*-benzyl-D-galactopyranosylamine (11).



To 100 mg of 2,3,4,6-tetra-*O*-benzyl-D-galactonitrile **10** (0.186 mmol) in EtOH (4 mL) was added 30 mg of  $NaBH_4$  (0.793 mmol). The reaction mixture was stirred for 9 hours. The solution was concentrated and the residue was dissolved in 10 mL of DCM. This was washed with 5% aqueous sodium bicarbonate solution (3 x 3 mL). The organic layer was dried with sodium sulfate and concentrated. The resulting oil was purified by flash column chromatography (3:2 hexane: ethyl acetate) to afford a mixture of anomers, ( $\alpha:\beta=1:4$ , 60 mg, 60%). IR 3408, 3340  $cm^{-1}$ .  $^1H$  NMR (500 MHz):  $\delta$  1.94 (s, 2H $\alpha$ , 2H $\beta$ ), 3.47 (m, 1H $\beta$ ), 3.55-3.63 (m, 2H $\alpha$ , 4H $\beta$ ), 3.85 (dd, 1H $\alpha$ ,  $J = 3.0$  Hz, 9.0 Hz), 3.91 (d, 1H $\beta$ ,  $J = 1.5$  Hz), 3.97 (t, 1H $\alpha$ ,  $J = 2.5$  Hz), 4.01 (dd, 1H $\alpha$ ,  $J = 4.0$  Hz, 9.0 Hz), 4.09 (d, 1H $\beta$ ,  $J = 8.0$  Hz), 4.34 (td, 1H $\alpha$ ,  $J = 2.0$  Hz, 6.5 Hz), 4.40-4.54 (m, 2H $\alpha$ , 2H $\beta$ ), 4.59 (d, 1H $\alpha$ ,  $J = 11.5$  Hz), 4.63 (d, 1H $\beta$ ,  $J = 11.5$  Hz), 4.67 (d, 1H $\alpha$ ,  $J = 12.0$  Hz), 4.72-4.79 (m, 2H $\alpha$ , 2H $\beta$ ), 4.83-4.88 (m, 1H $\alpha$ , 1H $\beta$ ), 4.97 (dd, 2H $\beta$ ,  $J = 7.5$  Hz, 11.0 Hz), 5.03 (d, 1H $\alpha$ ,  $J = 4.5$  Hz), 7.26-7.43 (m, 20H $\alpha$ , 20H $\beta$ ).  $^{13}C$  NMR (125 MHz):  $\delta$  69.34, 73.00, 73.06, 73.45, 73.50, 73.72, 74.04, 74.29, 74.41, 74.72, 74.86, 75.53, 77.08, 77.43, 78.17, 79.15, 79.31, 80.85, 83.60, 86.78, 127.64, 127.69, 127.74, 127.75, 127.77, 127.80, 127.92, 127.98, 128.05, 128.16, 128.38, 128.40, 128.41, 128.45, 128.48, 128.51, 128.52, 128.53, 128.56, 128.57, 128.60, 137.98, 138.32, 138.53, 138.65, 138.76, 138.78, 138.81, 138.82. HRMS (FAB) Calcd for  $C_{34}H_{38}NO_5$  ( $M+H^+$ ): 540.2750. Found: 540.2743.

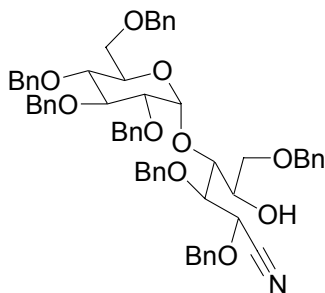
### 2,3,4,6-Tetra-*O*-benzyl- $\beta$ -D-mannopyranosylamine (13).



To 82 mg of 2,3,4,6-tetra-*O*-benzyl-D-mannonitrile **12** (0.153 mmol) in EtOH (10 mL) was added 25 mg of  $NaBH_4$  (0.661 mmol). The reaction mixture was stirred for 9 hours. The mixture was concentrated and the residue was dissolved in DCM (10 mL). The organic phase was washed with aqueous 5% sodium bicarbonate solution (3 x 3 mL). The organic layer was dried with sodium sulfate and concentrated. The oil obtained was purified by flash column chromatography (1:2 hexane: ethyl acetate) to afford the pure  $\beta$  anomer **13** (57 mg, 70%). IR 3400  $cm^{-1}$ .  $^1H$  NMR (500 MHz):  $\delta$  2.19 (s, 2H), 3.45-3.49 (m, 1H), 3.58-3.64 (m, 2H), 3.71 (dd, 1H,  $J = 1.5$  Hz, 10.0 Hz), 3.84 (t, 1H,  $J = 10.0$  Hz), 3.90 (d, 1H,  $J = 2.5$  Hz), 4.14 (s, 1H), 4.50 (d, 1H,  $J = 11.0$  Hz), 4.57 (dd, 2H,  $J = 12.5$  Hz, 18.0 Hz), 4.69 (d, 1H,  $J = 11.5$  Hz), 4.74 (dd, 2H,  $J = 11.5$  Hz, 18.5 Hz), 4.86 (d, 1H,

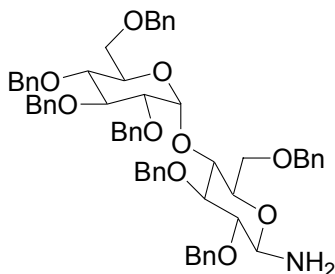
$J = 10.5$  Hz), 5.08 (d, 1H,  $J = 11.5$  Hz), 7.12-7.15 (m, 2H), 7.23-7.40 (m, 18H).  $^{13}\text{C}$  NMR (125 MHz):  $\delta$  69.75, 72.72, 73.64, 75.11, 75.26, 75.31, 76.43, 83.52, 84.65, 127.75, 127.81, 127.83, 127.85, 127.94, 128.16, 128.22, 128.24, 128.49, 128.51, 128.52, 128.67, 138.33, 138.35, 138.37, 138.76. HRMS (FAB) Calcd for  $\text{C}_{34}\text{H}_{37}\text{NO}_5 + \text{Li}^+$  ( $\text{M} + \text{Li}^+$ ): 546.2832. Found: 546.2843.

**2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl- $\alpha$ -D-glucopyranosyl)-D-gluconitrile (15).**



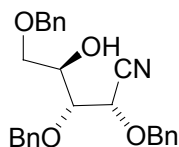
To a solution of 342 mg of 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl- $\alpha$ -D-glucopyranosyl)-D-glucose oxime **14** (0.346 mmol) and 192 mg of  $\text{PPh}_3$  (0.730 mmol) in MeCN (3 mL) was added 200 mg of  $\text{CBr}_4$  (5.96 mmol) in MeCN (1 mL). This was stirred for 30 minutes. Then 48 mg of  $\text{PPh}_3$  (0.183 mmol) in MeCN (2 mL) and MeOH (5.2 mL). Stirring was continued for 30 minutes and then the solution was concentrated. The oil obtained was purified by flash column chromatography (4:1 hexane: ethyl acetate) to afford **15** as a yellow oil (145 mg, 43%). IR 3511, 2251  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz):  $\delta$  3.41 (bs, 1H), 3.52 (dd, 1H,  $J = 6.0$  Hz, 10.0 Hz), 3.58 (m, 3H), 3.66 (d, 1H,  $J = 10.0$  Hz), 3.70 (dd, 1H,  $J = 4.0$  Hz, 10.5 Hz), 4.00 (t, 1H,  $J = 9.5$  Hz), 4.06 (dd, 1H,  $J = 3.0$  Hz, 5.5 Hz), 4.10 (d, 2H,  $J = 11.0$  Hz), 4.15 (dd, 2H,  $J = 3.0$  Hz, 7.5 Hz), 4.42-4.64 (m, 7H), 4.74 (d, 1H,  $J = 11.5$ ), 4.79-4.90 (m, 5H), 4.98 (d, 1H,  $J = 11.0$  Hz), 5.05 (d, 1H,  $J = 3.5$  Hz), 7.16-7.43 (m, 35H).  $^{13}\text{C}$  NMR (125 MHz):  $\delta$  68.60, 70.97, 71.02, 71.24, 71.42, 72.86, 73.47, 73.61, 74.34, 75.20, 75.40, 75.72, 78.10, 80.19, 80.42, 80.65, 82.07, 100.77, 117.57, 127.77, 127.87, 127.88, 127.91, 127.99, 128.04, 128.06, 128.09, 128.11, 128.12, 128.21, 128.35, 128.53, 128.58, 128.59, 128.60, 128.63, 128.64, 128.66, 128.67, 136.32, 137.48, 137.70, 137.73, 138.02, 138.03, 138.10, 138.25, 138.35, 138.90. HRMS (FAB) Calcd for  $\text{C}_{61}\text{H}_{63}\text{NO}_{10}\text{Li}$  ( $\text{M} + \text{Li}^+$ ): 976.4612. Found: 976.4646.

**2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl- $\alpha$ -D-glucopyranosyl)-D-glucopyranosyl amine (**16**).**



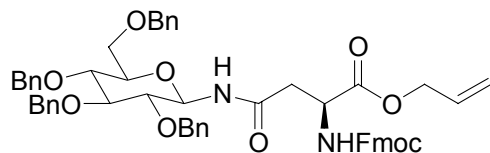
To 26 mg of 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl- $\alpha$ -D-glucopyranosyl)-D-gluconitrile **15** (0.026 mmol) in EtOH (4 mL) was added 7 mg of NaBH<sub>4</sub> (0.185 mmol). The reaction was stirred overnight and then concentrated. The residue was dissolved in DCM (10 mL) and washed with 5% aqueous sodium bicarbonate solution (2 x 2 mL). The organic layer was dried with sodium sulfate and concentrated. The resulting oil was purified by flash column chromatography (1:1 hexane: ethyl acetate) to afford **16** as a mixture of anomers ( $\alpha$ : $\beta$ =1:4, 13 mg, 50%). IR 3417 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz):  $\delta$  1.64 (bs, 2H $\alpha$ ), 1.98 (bs, 2H $\beta$ ), 3.27 (t, 1H $\beta$ ,  $J$  = 8.5 Hz), 3.39-5.02 (m, 27H $\alpha$ , 26H $\beta$ ), 5.58 (d, 1H $\alpha$ ,  $J$  = 5.0 Hz), 5.66 (d, 1H $\beta$ ,  $J$  = 5.0 Hz), 7.10-7.40 (m, 35H $\alpha$ , 35H $\beta$ ). <sup>13</sup>C NMR (125 MHz):  $\delta$  66.04, 68.42, 71.27, 73.52, 73.56, 73.69, 75.18, 75.36, 75.73, 76.98, 77.48, 79.51, 82.23, 126.74, 127.69, 127.70, 127.84, 127.89, 127.91, 127.98, 128.06, 128.22, 128.44, 128.47, 128.49, 128.51, 128.54, 128.55, 138.15, 138.40, 139.04. HRMS (FAB) Calcd for C<sub>61</sub>H<sub>66</sub>NO<sub>10</sub> (M+H<sup>+</sup>): 972.4687. Found: 972.4713.

**2,3,5-Tri-*O*-benzyl-D-ribonitrile (**21**).**



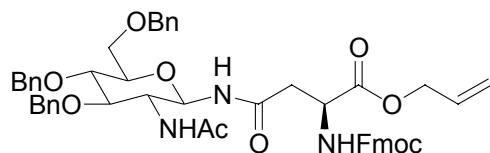
To a solution of 1.33 g of 2,3,5-tri-*O*-benzyl-D-ribose oxime (3.19 mmol), and 1.67 g of PPh<sub>3</sub> (6.38 mmol) in MeCN (25.5 mL) was added 2.64 g CBr<sub>4</sub> (7.97 mmol) in MeCN (10 mL). This was stirred for 20 minutes. Then 0.42 g of PPh<sub>3</sub> (1.59 mmol) in MeCN (12.5 mL) and MeOH in (35.8 mL) was added. The solution was stirred for an additional 15 minutes and concentrated. The oil obtained was purified by flash column chromatography (3:1 hexane: ethyl acetate) to afford **21** as an oil (820 mg (62%). IR 3557, 3467, 3089, 3067, 3033, 2915, 2871, 2253, cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz):  $\delta$  2.48 (s, 1H), 3.55 (dd, 1H,  $J$  = 4.5 Hz, 9.5 Hz), 3.59 (dd, 1H,  $J$  = 3.0 Hz, 9.5 Hz), 3.83-3.90 (m, 2H), 4.46 (dd, 2H,  $J$  = 12.0 Hz, 28 Hz), 4.57 (t, 2H,  $J$  = 11.5 Hz), 4.70 (d, 1H,  $J$  = 3.0 Hz), 4.91 (dd, 2H,  $J$  = 8.0 Hz, 11.0 Hz), 7.26-7.41 (m, 15H). <sup>13</sup>C NMR (125 MHz):  $\delta$  69.89, 70.12, 71.21, 73.04, 73.61, 74.64, 78.95, 116.54, 128.12, 128.16, 128.18, 128.40, 128.49, 128.59, 128.66, 128.71, 128.86, 136.01, 137.59, 137.72. HRMS (FAB) Calcd for C<sub>26</sub>H<sub>27</sub>NO<sub>4</sub> Li (M+Li<sup>+</sup>): 424.2100. Found: 424.2097.

**$\beta$ -N-9-fluorenylmethyloxycarbonyl- (N-2,3,4,6-Tetra-*O*-benzyl- $\beta$ -D-glucopyranosyl) aspartic acid allyl ester (27).**



To 110 mg of 2,3,4,6-tetra-*O*-benzyl- $\beta$ -D-glucopyranosylamine **7** (0.20 mmol) and 97 mg of *N*- $\alpha$ -Fmoc-L-aspartic acid  $\alpha$ -allyl ester **26** (0.24 mmol) in 10 mL of THF at  $-15^{\circ}\text{C}$  was added 28 mg of HOBT (0.20 mmol) and 51 mg of DCC (0.24 mmol) in 5 mL of THF. The reaction mixture was stirred at  $-15^{\circ}\text{C}$  for 1 hour, then was allowed to warm to room temperature. Stirring was continued at room temperature overnight. The reaction was filtered, DCM (50 mL) was added to the filtrate, and the resulting solution was washed successively with 5% aqueous citric acid (3 x 8 mL), 5% aqueous sodium bicarbonate (3 x 8 mL), and water (3 x 8 mL). The organic layer was dried and concentrated. The solid obtained was purified by flash column chromatography (5:1 hexane: ethyl acetate) to afford **27** (89.2 mg, 49%). m.p.  $199\text{--}200^{\circ}\text{C}$ . IR 3301, 1739, 1699, 1665,  $1073\text{ cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz):  $\delta$  2.43 (dd, 1H  $J = 4.0$  Hz, 16.5 Hz), 2.72 (dd, 1H,  $J = 4.0$  Hz, 16.5 Hz), 3.21–3.25 (m, 1H), 3.39 (d, 1H,  $J = 8.0$  Hz), 3.56–3.68 (m, 4H), 4.13 (t, 1H,  $J = 7.3$  Hz), 4.20 (dd, 1H,  $J = 7.5$  Hz, 10.5 Hz), 4.29–4.62 (m, 8H), 4.70–4.74 (m, 2H), 4.82 (s, 2H), 4.93 (t, 1H,  $J = 9.0$  Hz), 5.15 (d, 1H,  $J = 10.5$  Hz), 5.24 (d, 1H,  $J = 17.0$  Hz), 5.35 (d, 1H,  $J = 8.5$  Hz), 5.78–5.86 (m, 1H), 5.96 (d, 1H,  $J = 8.5$  Hz), 7.02–7.04 (m, 2H), 7.10–7.31 (m, 22H), 7.52 (d, 2H,  $J = 7.5$  Hz), 7.67 (d, 2H,  $J = 7.5$  Hz).  $^{13}\text{C}$  NMR (125 MHz):  $\delta$  37.79, 47.25, 50.61, 66.52, 67.46, 68.15, 73.73, 74.64, 75.16, 75.99, 76.49, 77.64, 78.85, 79.27, 86.30, 118.84, 120.13, 125.40, 125.46, 127.27, 127.85, 127.86, 127.96, 127.98, 127.99, 128.01, 128.09, 128.24, 128.55, 128.59, 128.67, 128.95, 129.19, 131.82, 137.82, 138.01, 138.13, 138.43, 141.41, 141.43, 143.98, 144.04, 156.36, 170.36, 170.76. HRMS (FAB) Calcd for  $\text{C}_{56}\text{H}_{56}\text{N}_2\text{O}_{10}$  ( $\text{M}+\text{H}^+$ ): 917.4013. Found: 917.4011.

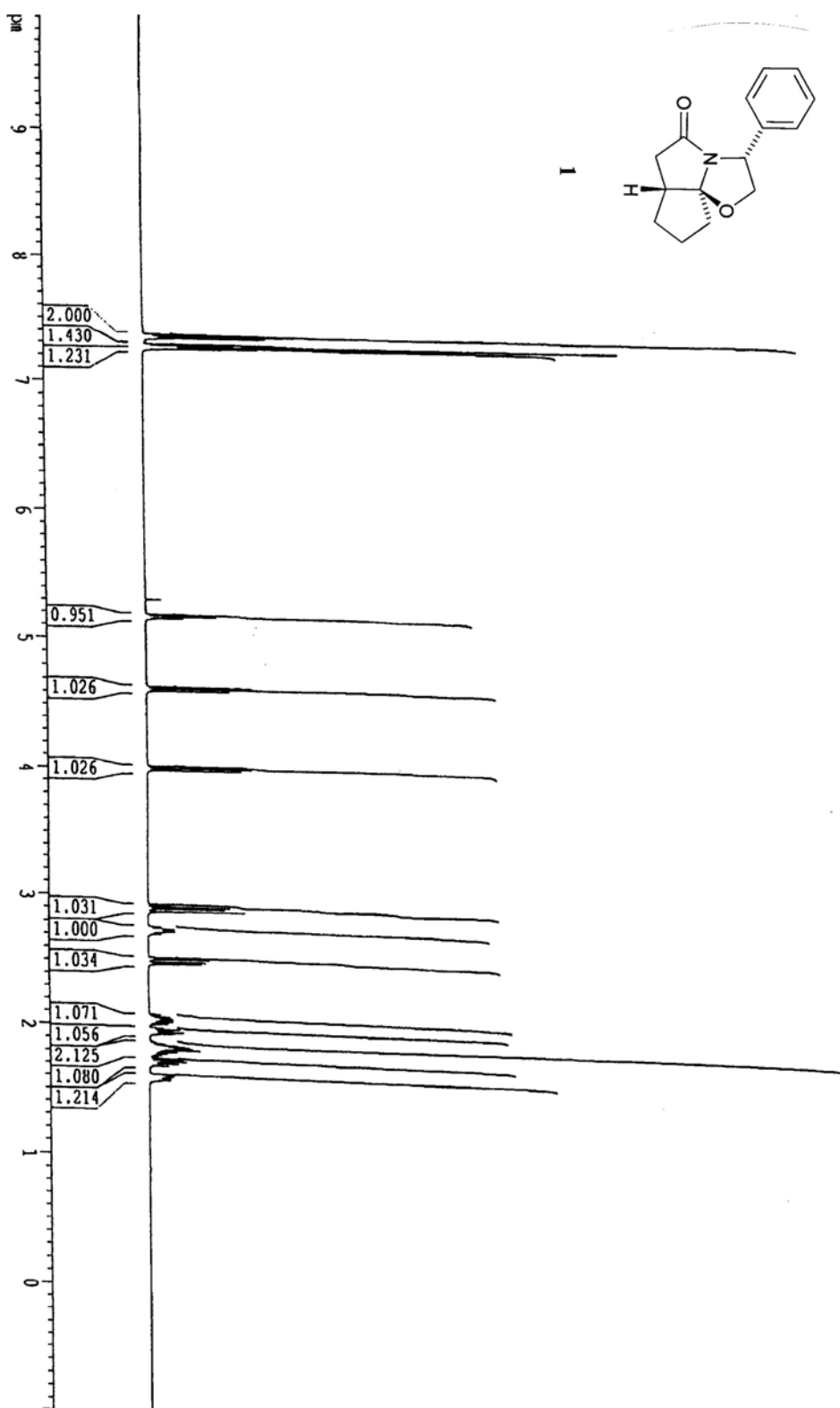
**$\beta$ -N-9-fluorenylmethyloxycarbonyl-(*N*-2-acetamido-3,4,6-tri-*O*-benzyl- $\beta$ -D-glucopyranosyl) aspartic acid allyl ester (28).**

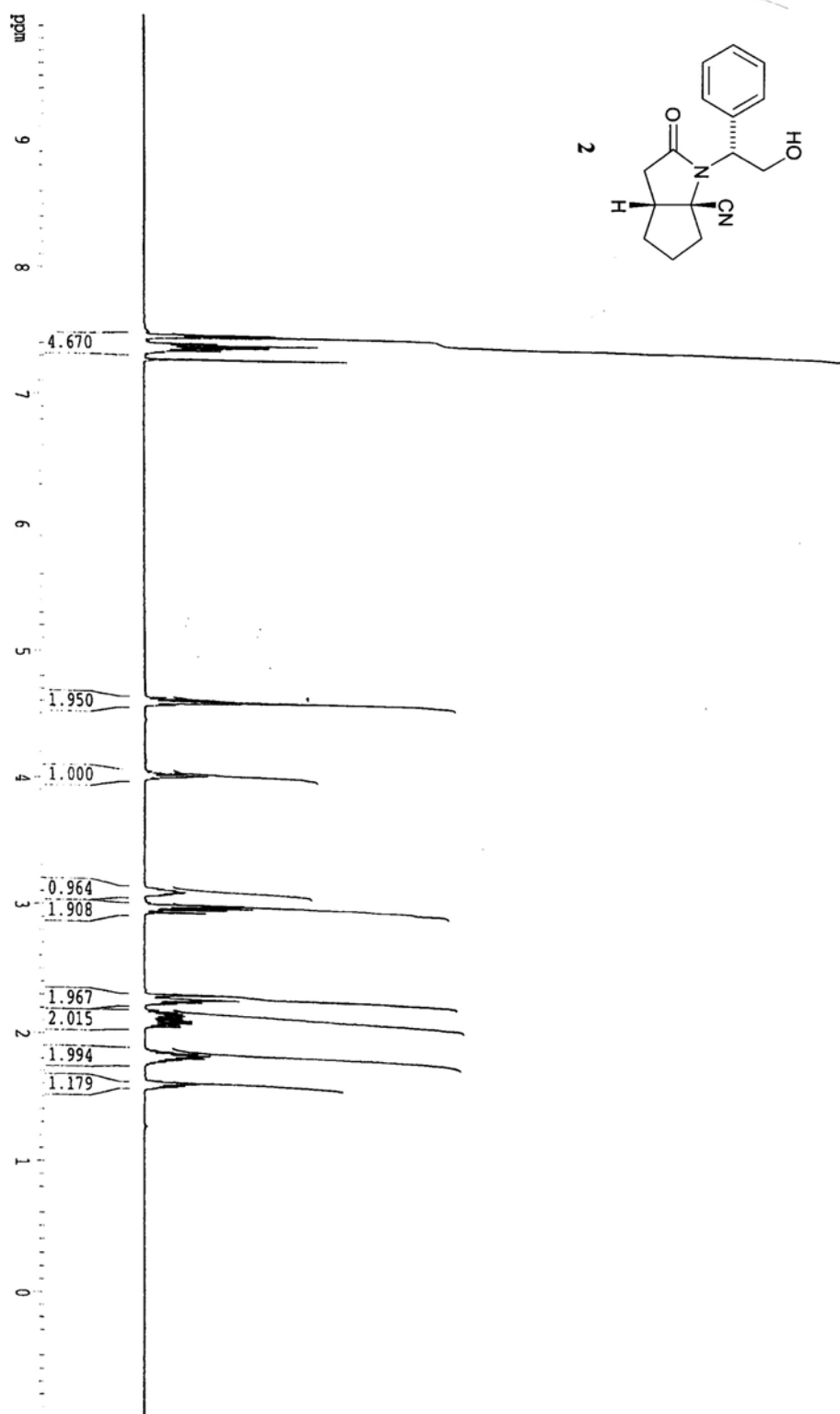


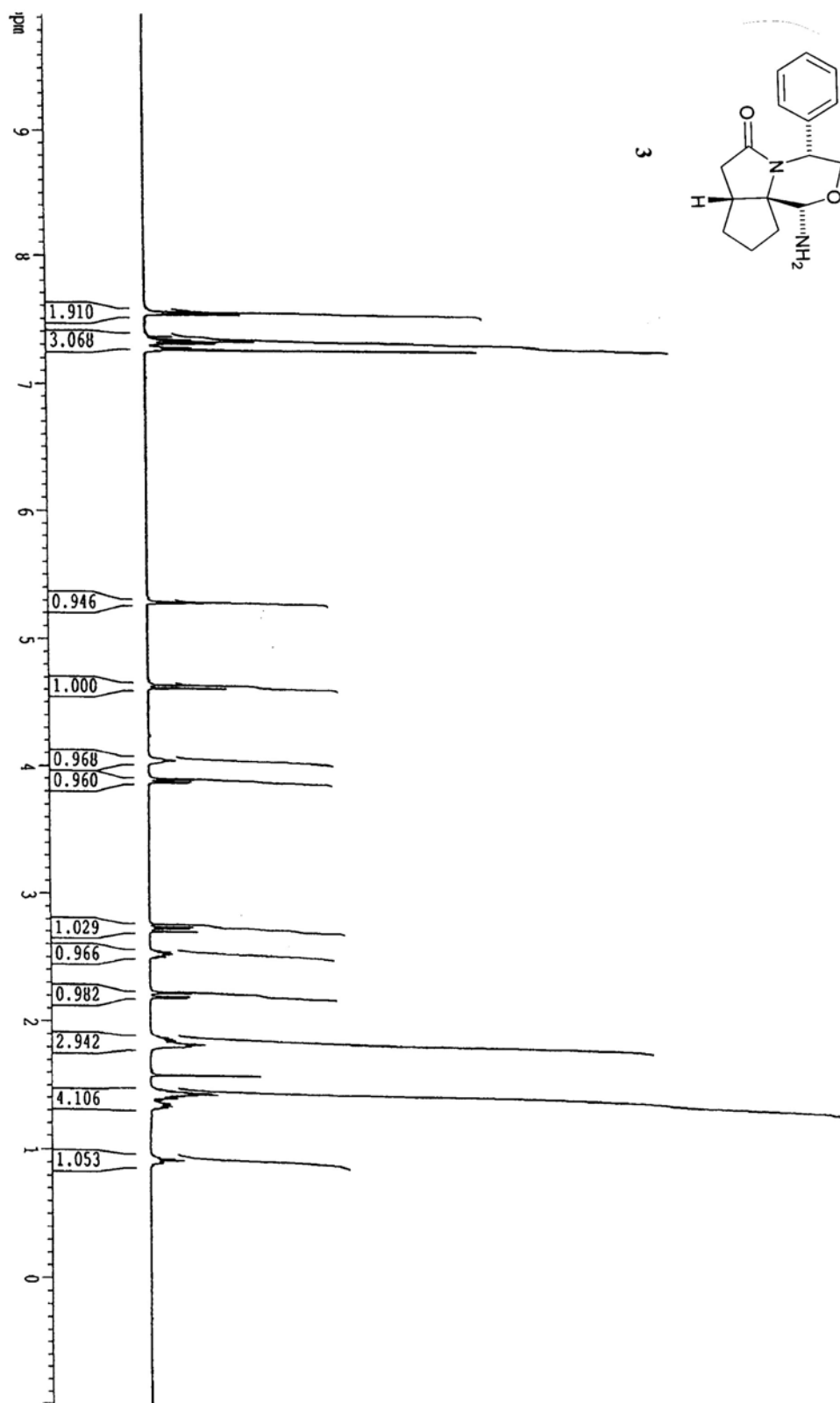
80 mg of *N*- $\alpha$ -Fmoc-L-aspartic acid  $\alpha$ -allyl ester **26** (0.204 mmol) and 62 mg of 2-isobutoxy-1-isobutoxycarbonyl-1,2-dihydroquinoline (IIDQ) (0.204 mmol) were dissolved in DCM (15 mL) and the mixture was stirred for 2 minutes. To this mixture was added 50 mg of 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy- $\beta$ -D-glucopyranosylamine (0.102 mmol) and stirring was continued for 1 h. The reaction was monitored by TLC (1:9 hexane: ethyl acetate). After 1 h the reaction mixture was concentrated and the solid was redissolved in DCM (40 mL) and this solution was extracted with 5% aqueous

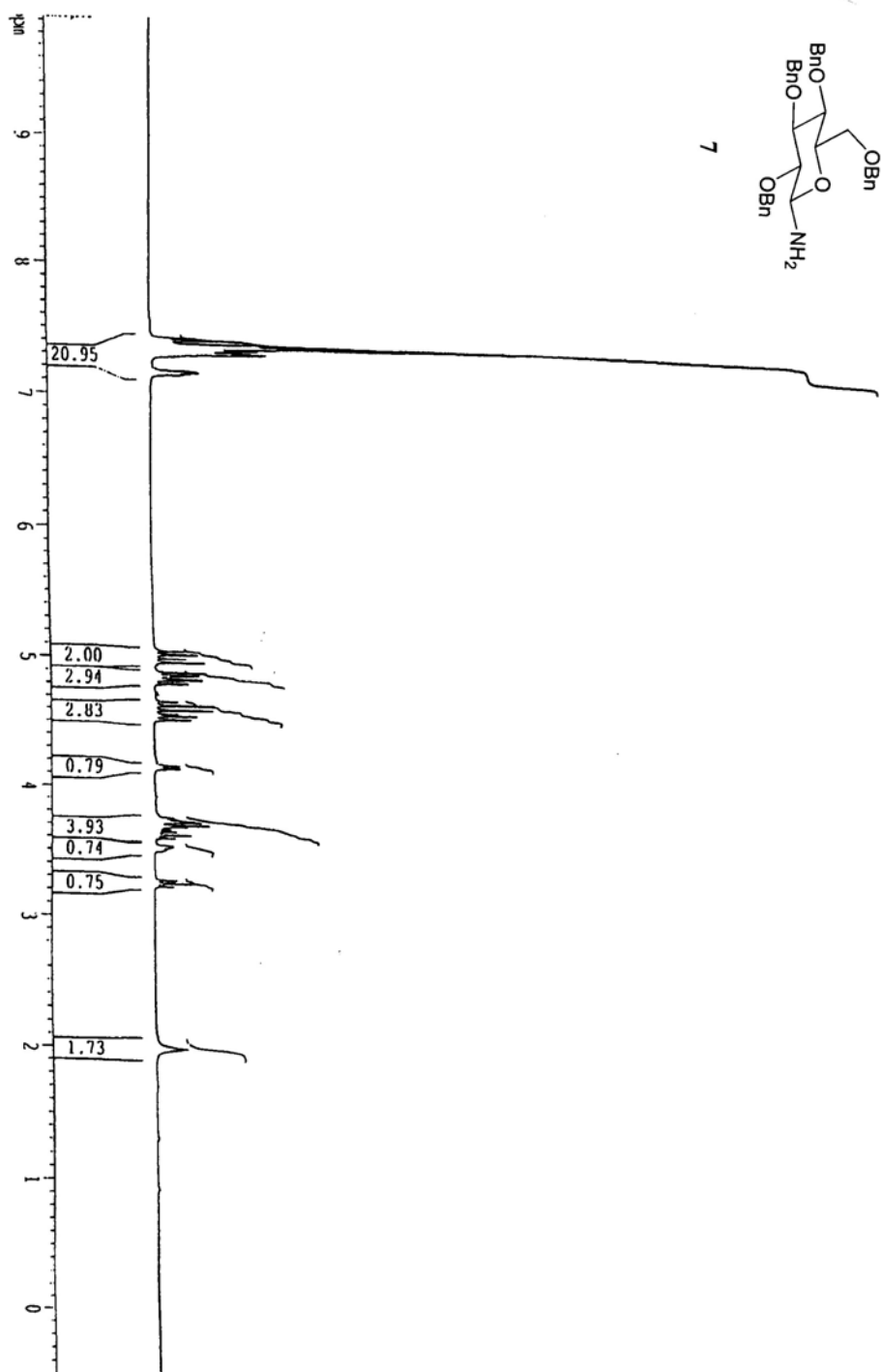
sodium bicarbonate solution (7 x 8 mL) and water (4 x 8 mL). The organic layer was dried and concentrated. The product was crystallized from acetone to remove unreacted starting material and afford the  $\beta$  linked **28** (45 mg, 50%). m.p. 233-235 °C.  $^1\text{H}$  NMR (500 MHz):  $\delta$  1.68 (s, 3H), 2.69 (dd, 1H,  $J$  = 4.0 Hz, 16.5 Hz), 2.88 (dd, 1H,  $J$  = 4.5 Hz, 16.5 Hz), 3.41 (dd, 1H,  $J$  = 8.5 Hz, 10.5 Hz), 3.47 (d, 1H,  $J$  = 9.5 Hz), 3.71-3.87 (m, 4H), 4.22 (t, 1H,  $J$  = 7.5 Hz), 4.28 (dd, 1H,  $J$  = 7.5 Hz, 10.5 Hz), 4.41 (dd, 1H,  $J$  = 7.0 Hz, 10.5 Hz), 4.47 (d, 1H,  $J$  = 12.5 Hz), 4.56-4.68 (m, 8H), 4.74 (dd, 1H,  $J$  = 8.5 Hz, 9.0 Hz), 4.79 (d, 1H,  $J$  = 11 Hz), 4.86 (d, 1H,  $J$  = 12.5 Hz), 5.17 (dd, 1H,  $J$  = 1.5 Hz, 10.5 Hz), 5.26 (dd, 1H,  $J$  = 1.5 Hz, 18 Hz), 5.81-5.89 (m, 1H), 6.06 (d, 1H,  $J$  = 9.5 Hz), 7.17-7.40 (m, 19H), 7.59 (d, 2H,  $J$  = 7.2 Hz), 7.74 (d, 2H,  $J$  = 7.6 Hz).  $^{13}\text{C}$  NMR (125 MHz):  $\delta$  23.27, 37.67, 47.31, 53.65, 66.32, 67.50, 68.18, 73.88, 74.45, 75.33, 76.72, 77.43, 78.57, 80.29, 80.95, 118.51, 120.15, 127.30, 127.88, 127.89, 128.03, 128.26, 128.31, 128.36, 128.64, 128.76, 128.86, 129.26, 129.28, 131.86, 137.86, 138.09, 141.44, 141.48, 171.02, 171.20, 172.39, 172.67. HRMS (FAB) Calcd for  $\text{C}_{51}\text{H}_{53}\text{N}_3\text{O}_{10} + \text{Li}^+$  ( $\text{M} + \text{Li}^+$ ): 874.3891. Found: 874.3914.

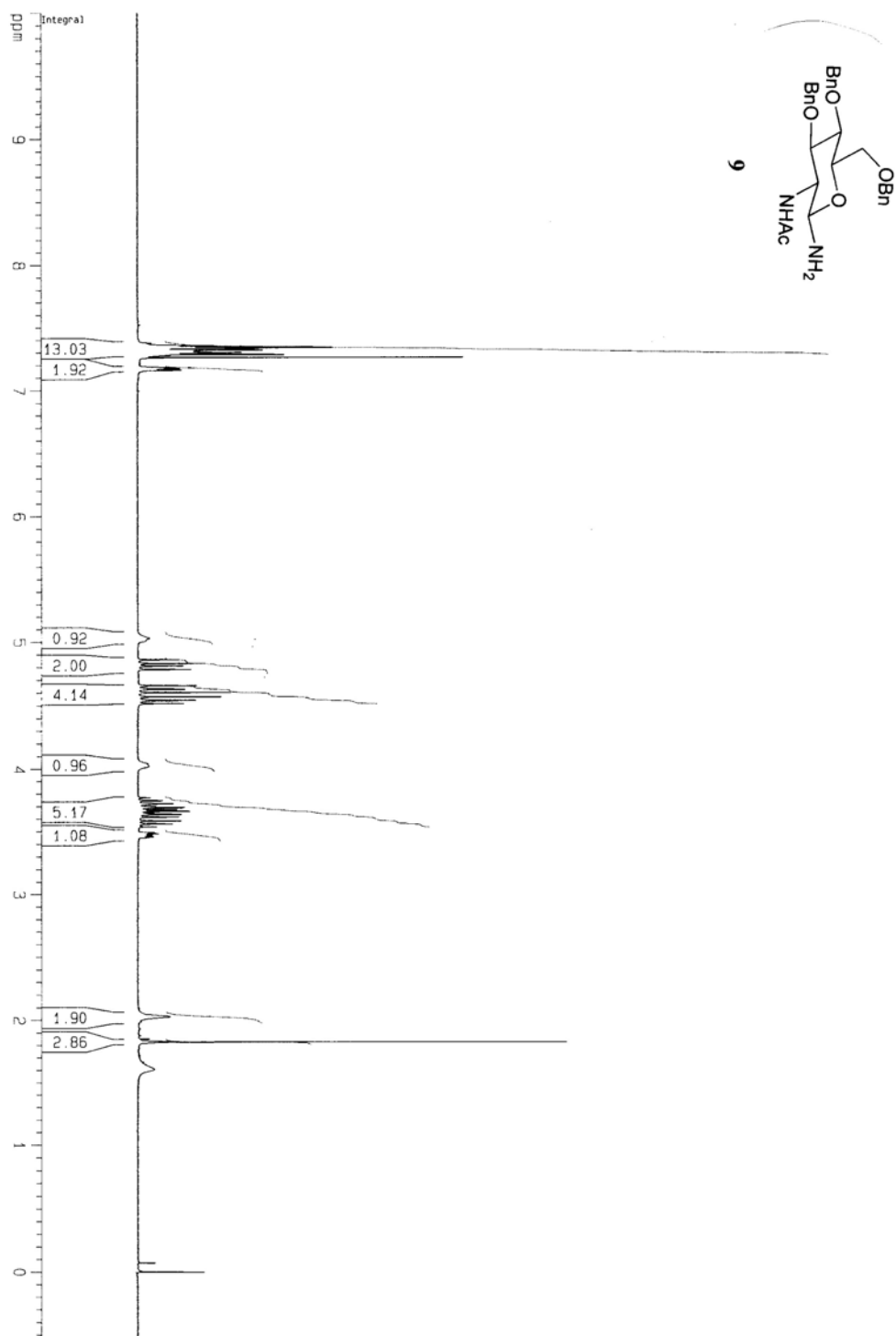


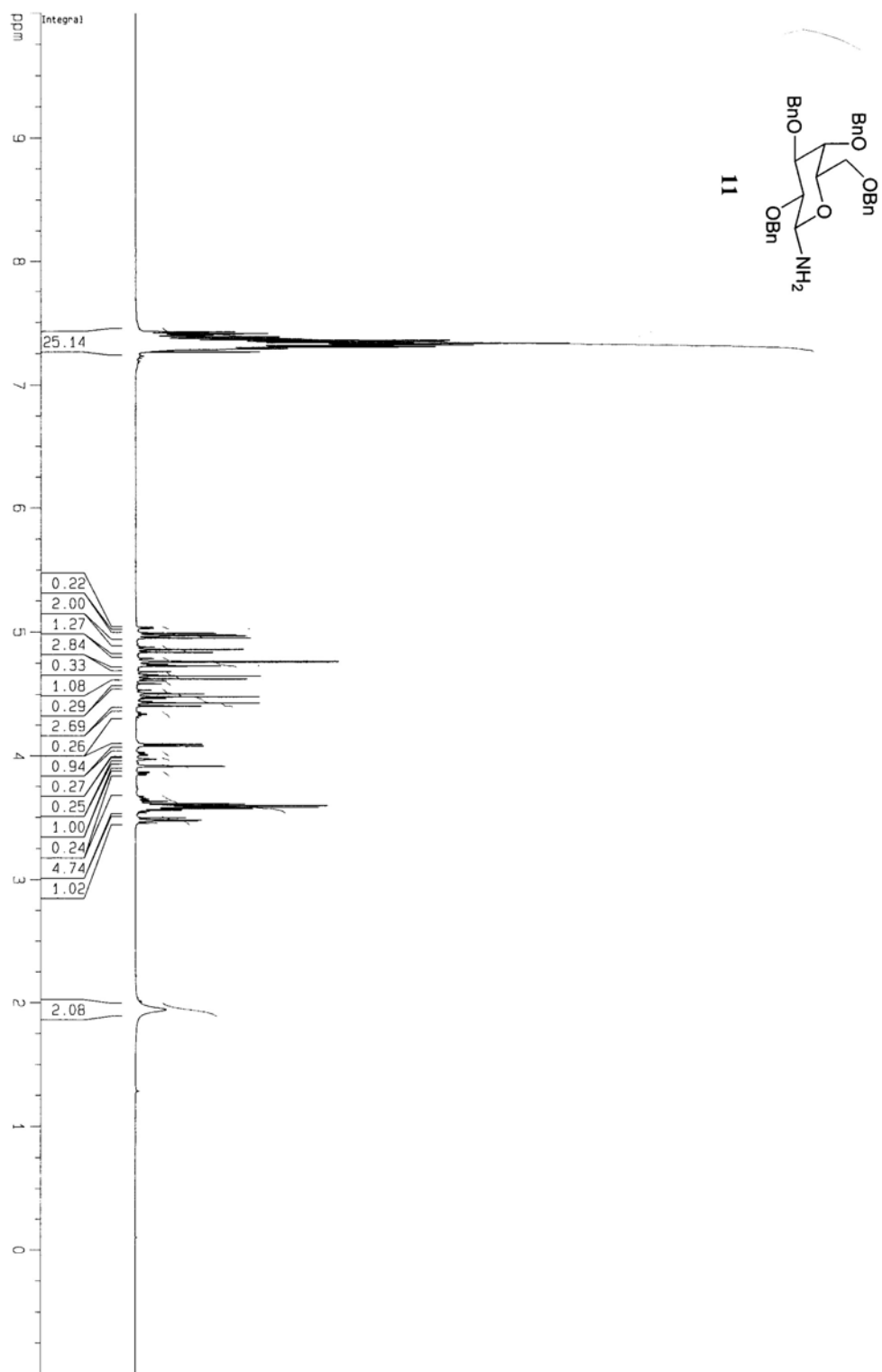


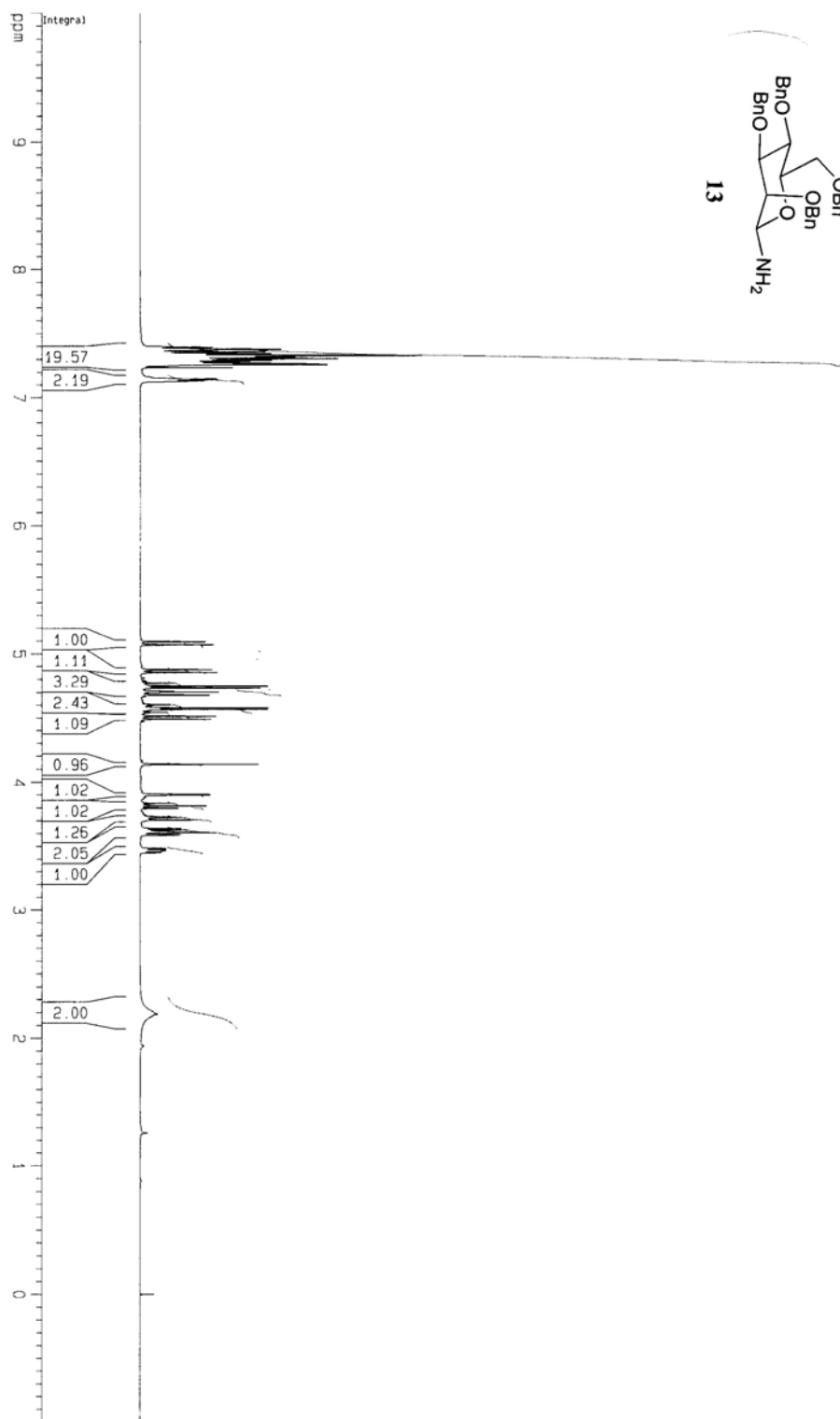
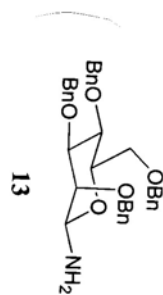


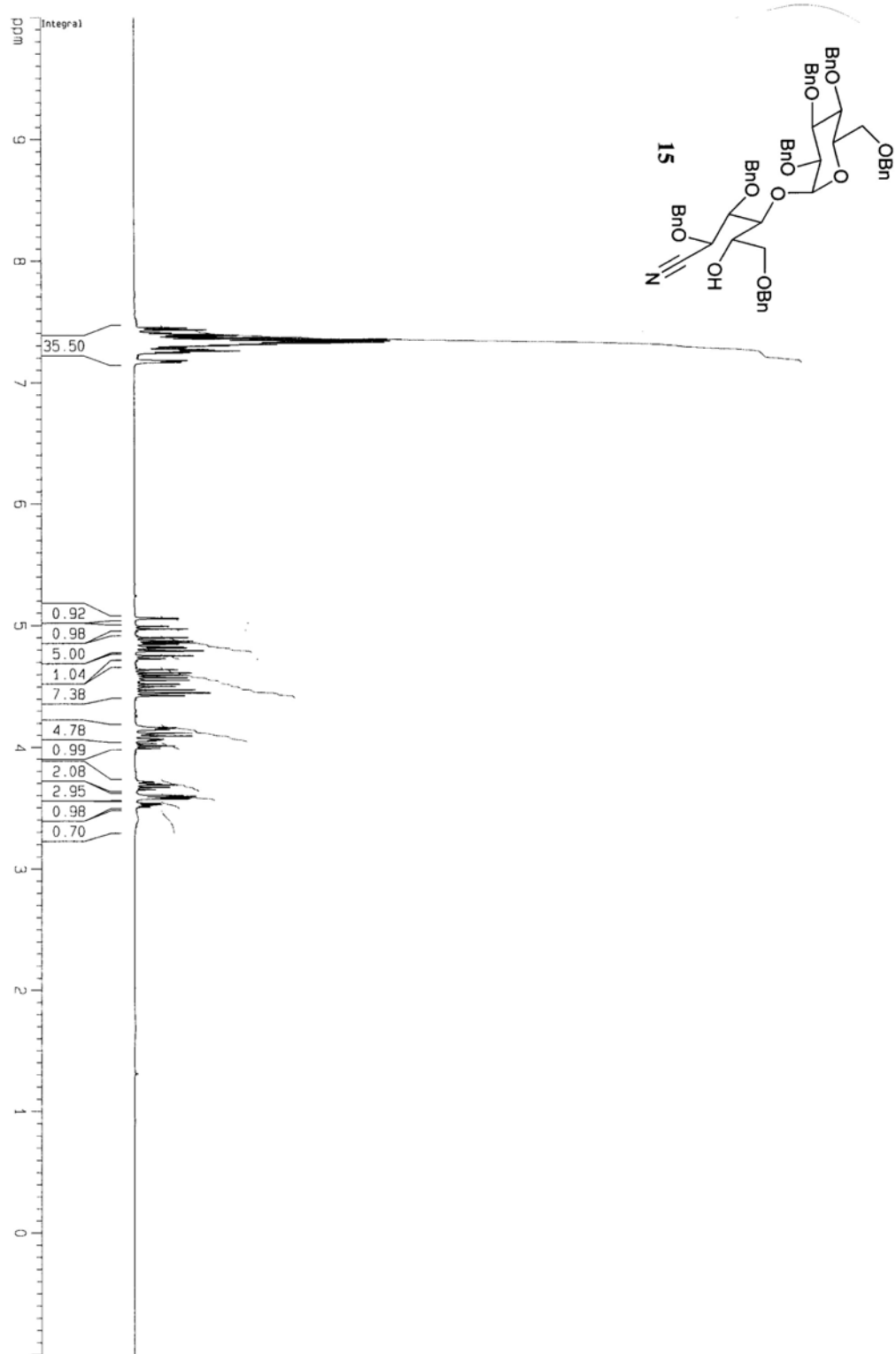




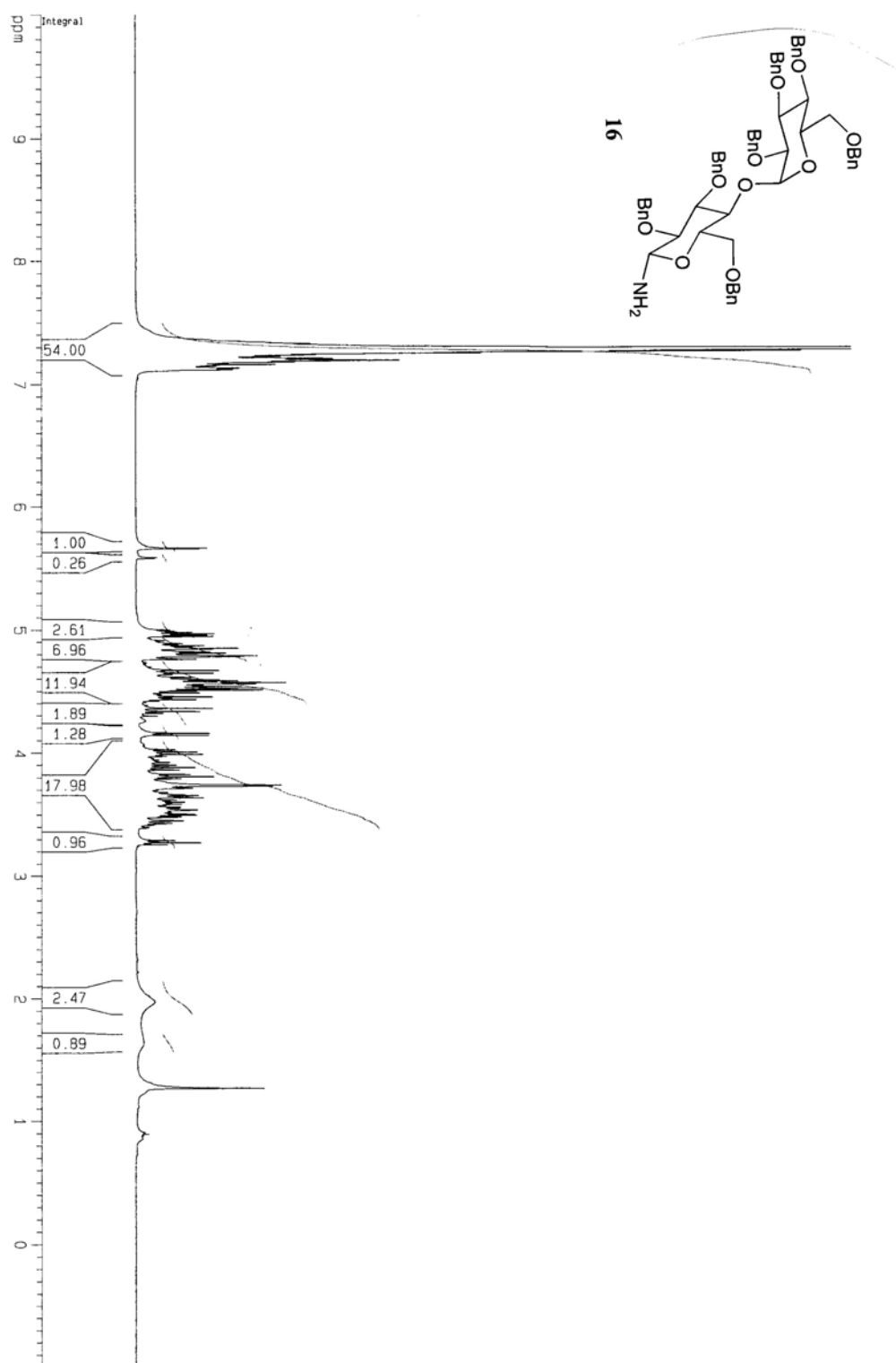


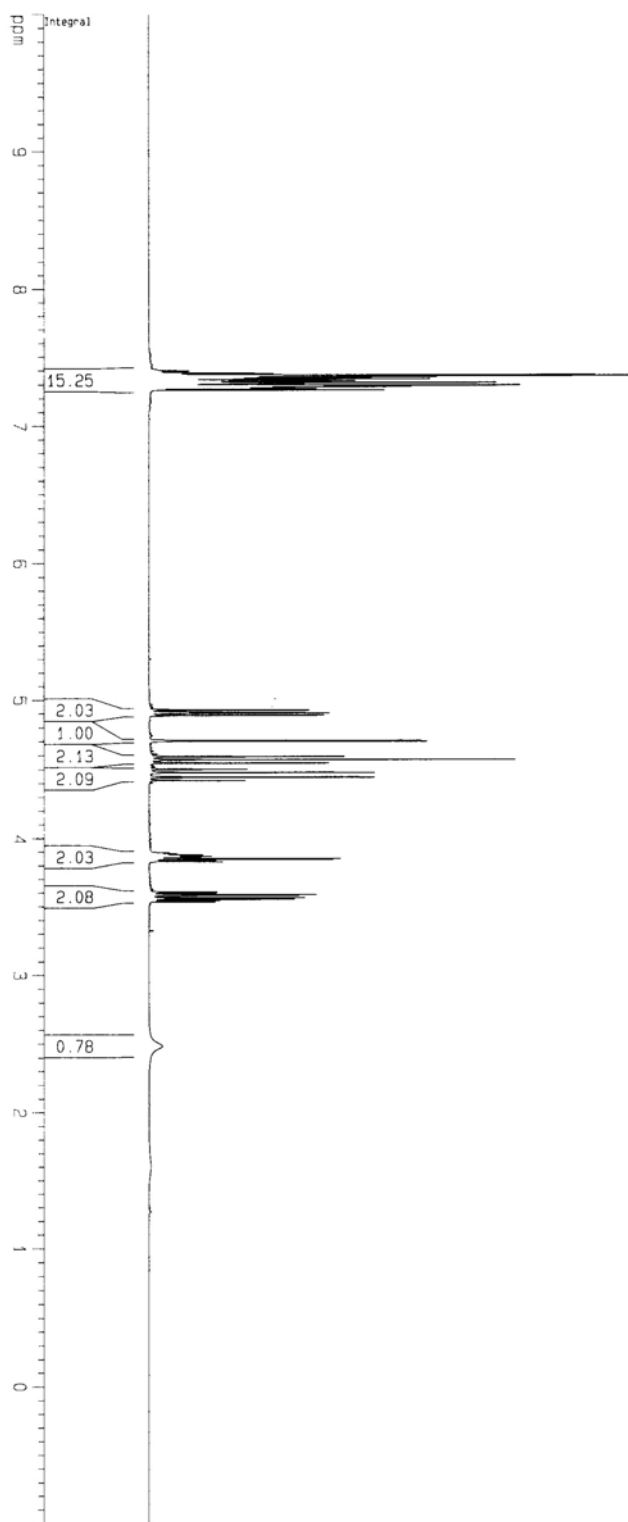
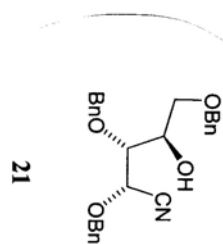


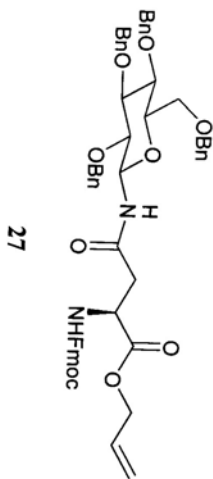


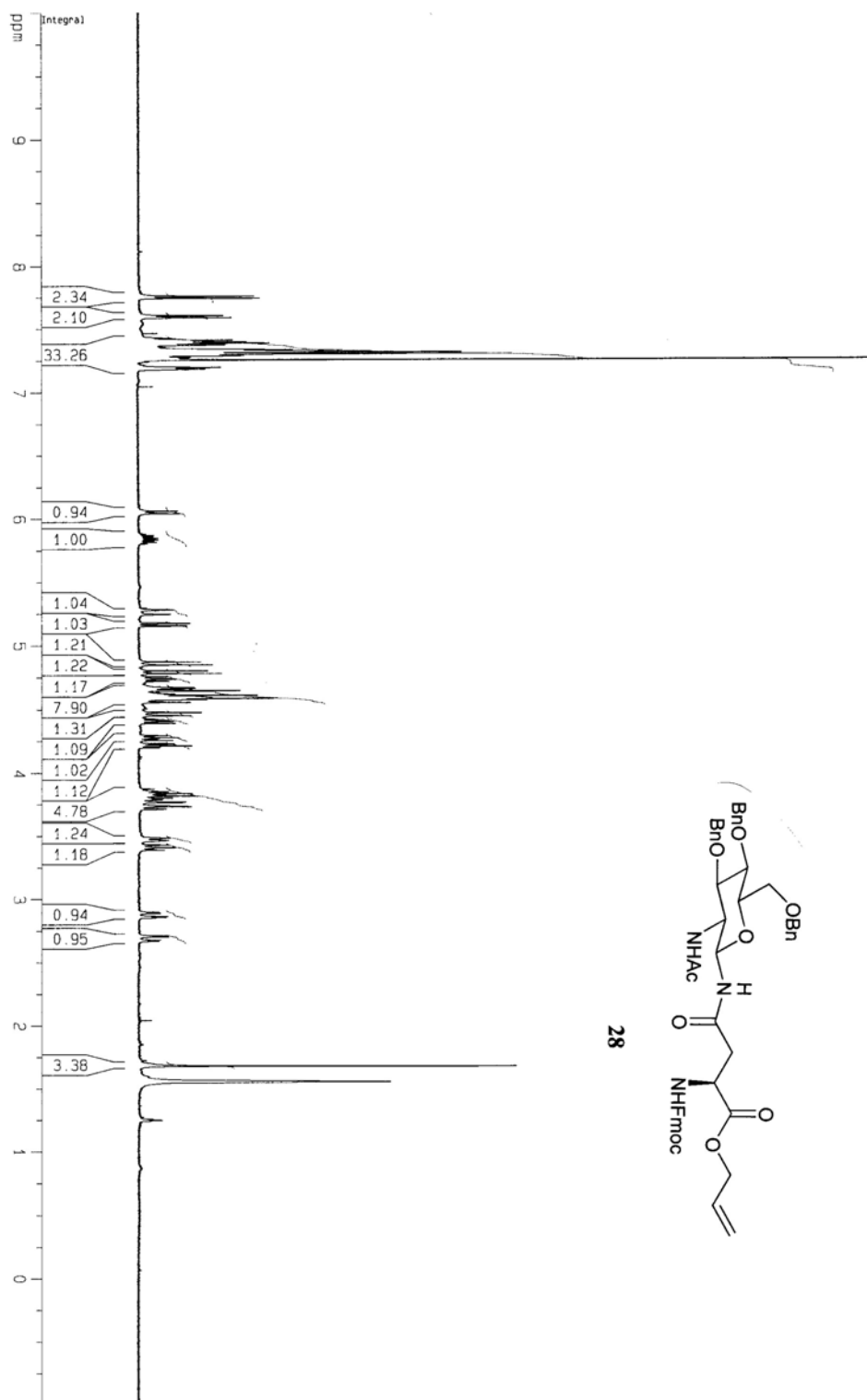












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