A General Synthetic Strategy and Anti-Proliferation Property of Natural Phenylethanoid Glycosides

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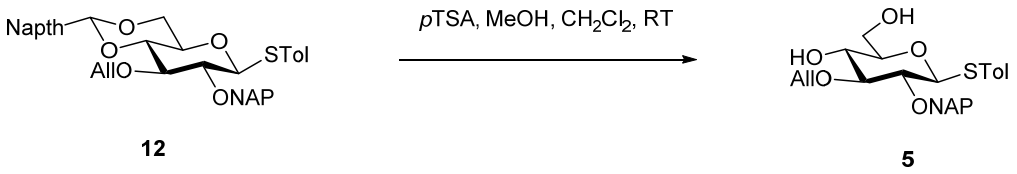
Supporting Information

General experimental:

Reagent-grade chemicals were purchased from commercial vendors and used without further purification. Dichloromethane (CH_2Cl_2) was dried by Asianwong solvent purification system (AWS-1000). *N*,*N*-Dimethylformamide (DMF) was stocked with flame-dried molecular sieves (MS) under N_2. Progress of reactions was monitored by thin layer chromatography on silica gel 60 F-254 plate and visualized under UV illumination and/or by staining with acidic ceric ammonium molybdate or *p*-anisaldehyde. Silica gel (Geduran Si-60, 0.063-0.200 mm) for chromatography was obtained from Merck. NMR spectra were recorded at 400 MHz and 100 MHz spectrometers in Varian console or 500 MHz and 125 MHz spectrometers in Varian console or 600 MHz and 150 MHz in Varian console as specified. Coupling constants in Hz was calculated from chemical shifts of ^{1}H NMR spectra.

Preparation of 2-(3,4-bis(*tert*-butyldimethylsilyloxy)phenyl-ethanol **8**[S1] and 3,4-bis(*tert*-butyldimethylsilyloxy) protected caffeic acid **9**[S2] were prepared according to literature procedure.

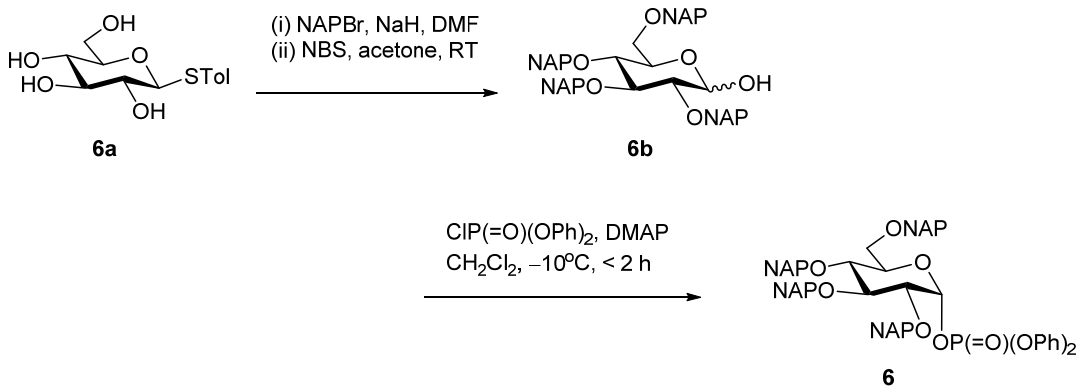
***p*-Tolyl 3-*O*-Allyl-2-*O*-(2-naphthyl)methyl-1-thio-β-D-glucopyranoside (5) (Scheme 1a in article):**



12 **5**

To a solution of thioglucoside **12** (4.0 g, 7.35 mmol) in CH_2Cl_2/MeOH (1:1, 60 mL) was added *p*-TsOH (5.6 g 29.41 mmol) at room temperature and reaction mixture was stirred for 6 h. After completion of reaction it was brought to 0 ˚C and neutralized by Et_3N and concentrated. The residue obtained was dissolved in CH_2Cl_2 (250 mL) and washed with water (2 × 100 mL), dried ($MgSO_4$) concentrated and purified by flash column chromatography (Elution: Hexane/EtOAc, 1/1) over silica gel to furnish thioglucoside **5** (2.6 g, 86%) as off white solid. For thioglucoside **5**, R_f = 0.40 (Hexane:EtOAc, 1:1); $[\alpha]_D^{25}$ = –22.4 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84-7.81 (m, 4H, Ar*H*), 7.56 (dd, J = 8.4, 1.6 Hz, 1H, Ar*H*), 7.46-7.42 (m, 4H, Ar*H*), 7.10 (d, *J* = 8.0 Hz, 2H, Ar*H*), 5.99-5.89 (m, 1H, allylic-*H*), 5.26 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.17 (dd, *J* = 10.4, 1.2 Hz, 1H), 5.06 (d, *J* = 10.4 Hz, 1H), 4.88 (d, *J* = 10.4 Hz, 1H), 4.68-4.66 (m, 1H), 4.42 (ddt, *J* = 12.4, 5.2, 1.2 Hz, 1H), 4.26 (ddt, *J* = 12.8, 6.0, 1.2 Hz, 1H), 3.91-3.88 (m, 1H), 3.81-3.75 (m, 1H), 3.60-3.57 (m, 1H), 3.46-3.40 (m, 2H), 3.36-3.32 (m, 1H), 2.93 (bs, 1H, O*H*), 2.32 (s, 3H, CH_3), 1.9 (bs, 1H, O*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.0, 135.5, 134.9, 133.3, 133.1, 132.8, 132.5, 129.86, 129.80, 129.7, 128.2, 128.0, 127.7, 126.9, 126.2, 126.1, 126.0, 117.4 (allylic-*C*), 88.1 (C-1), 85.9, 80.8, 79.2, 75.4, 74.3, 70.4, 62.6, 21.1 (*C*H_3); HRMS-EI (*m/z*): $[M + Na]^+$ calcd. for $C_{27}H_{30}NaO_5S$, 489.1706; found, 489.1724.

2,3,4,6-Tetra-*O*-(2-naphthyl)methyl-α-D-glucopyranosyl diphenylphosphate (6) (Scheme 1b in article):



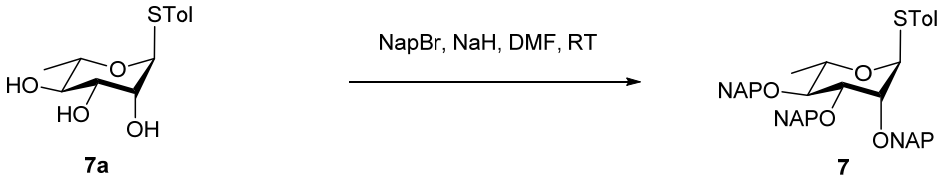
To a solution of thioglucoside **6a** (6.5 g, 22.72 mmol) and 2-(bromomethyl)-naphthalene (24.1 g, 109.09 mmol) in DMF (100 mL), NaH (4.5 g, 113.63 mmol) was added at 0 ˚C. The reaction mixture was stirred at RT for 4 h. Upon completion of reaction as monitored by TLC, the reaction mixture was brought to 0 ˚C and then quenched by addition of ice-water (10 mL). The resulting mixture was poured to H_2O (300 mL) to precipitate the product. The precipitate was filtered and washed with H_2O, followed by hexane, and then dried under vacuum to obtain the NAP-protected thioglucoside (16.6 g, 88%), which was directly undertaken deprotection after standard workup and purification. The per-*O*-NAP thioglucoside (11.0 g, 13.22 mmol) was suspended in acetone (60 mL), followed by addition of 1:1 CH_2Cl_2:H_2O mixture (12.0 mL). Then the reaction mixture was cooled at 0 ˚C and NBS (4.7 g, 26.40 mmol) was added. After stirring for 30 min, the reaction mixture was warmed to RT. After reaction at RT for 3 h, the reaction mixture was diluted by H_2O (60 mL), and the acetone was removed under reduced pressure and the residual aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL). Combined CH_2Cl_2 organic phase was dried over $MgSO_4$, filtered, and concentrated for flash chromatography purification over silica gel to furnish the desired glucosyl hemiacetal **6b** (7.0 g, 89%) as an off-white powder. For glucosyl hemiacetal **6b**, R_f = 0.25 (Hexane:EtOAc, 2.2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80-7.62 (m, 13H, Ar*H*), 7.53-7.37 (m, 14H, Ar*H*), 7.09 (dd, *J* = 8.4, 1.6 Hz, 1H, Ar*H*), 5.30 (t, *J* = 2.8 Hz, 1H),

5.16-5.09 (m, 1H), 5.03-4.87 (m, 4H), 4.81 (dd, *J* = 7.2 , 55.2 Hz, 0.4 H), 4.75 (d, *J* = 12.4 Hz, 1H), 4.68-4.58 (m, 2H), 4.12-4.06 (m, 2H), 3.78-3.68 (m, 4H), 3.54-3.50 (m, 0.36 H), 3.06 (d, *J* = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.3, 135.6, 135.4, 135.33, 135.30, 133.4, 133.3, 133.28, 133.22, 133.19, 133.10, 133.0, 132.9, 128.4, 128.36, 128.32, 128.2, 128.17, 128.13, 128.06, 128.04, 127.9, 127.8, 127.77, 127.74, 127.6, 127.1, 127.0, 126.94, 126.90, 126.58, 126.53, 126.47, 126.41, 126.3, 126.28, 126.23, 126.19, 126.16, 126.07, 126.02, 126.00, 125.9, 125.87, 125.85, 125.81, 125.7, 97.7, 91.4, 84.6, 83.1, 81.8, 80.0, 77.8, 77.7, 77.4, 75.8, 75.7, 75.1, 74.93, 74.90, 73.77, 73.73, 73.4, 70.5, 68.9, 68.6.

The glucosyl hemiacetal **6b** was directly used for phosphate preparation. To a solution of hemiacetal **6b** (6.0 g, 9.95 mmol) in CH_2Cl_2 (36 mL) were added DMAP (4.2 g, 34.82 mmol) and diphenyl chlorophosphate (4.1 mL, 19.90 mmol) at −10 ˚C and the reaction mixture was stirred for 2.0 h and 30 min at 0 ˚C. After the completion of reaction as monitored by TLC, the reaction mixture was brought to RT and diluted with CH_2Cl_2 (150 mL) and washed with aq. $NaHCO_3$ (100 mL), H_2O (2 × 100 mL), dried ($MgSO_4$), and concentrated. The residue obtained was purified by column chromatography (Elution: Hexane/EtOAc, 4/1) to afford glucosyl phosphate donor **6** (7.6 g, 85%) as a white glassy solid. For glucosyl phosphate **6**, R_f = 0.50, (Hexane/EtOAc, 2/1 v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80-7.63 (m, 13H, Ar*H*), 7.56 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.52 (d, J = 7.2 Hz, 1H, Ar*H*), 7.47-7.37 (m, 12H, Ar*H*), 7.26-7.20 (m, 6H, Ar*H*), 7.16-7.03 (m, 5H, Ar*H*), 6.15 (dd, *J* = 6.8, 3.2 Hz, 1H, H-1), 5.11 (d, *J* = 11.6 Hz, 1H), 4.97-4.92 (m, 3H), 4.79 (d, *J* = 11.6 Hz, 1H), 4.69 (d, *J* = 12.4 Hz, 1H), 4.61 (d, *J* = 11.2 Hz, 1H), 4.52 (d, *J* = 12.0 Hz, 1H), 4.01 (t, *J* = 8.8 Hz, 1H), 3.86- 3.80 (m, 2H), 3.76 (dt, *J* = 9.6, 3.2 Hz, 1H), 3.69 (dd, *J* = 10.4, 1.2 Hz, 1H), 3.40 (d, *J* = 10.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.63, 150.60, 150.56, 150.53, 136.1, 135.4, 135.2, 134.9, 133.3, 133.26, 133.24, 133.21, 133.15, 133.10, 133.03, 132.9, 129.7, 129.6, 128.3, 128.18, 128.10, 128.0, 127.9, 127.77, 127.74, 127.72, 127.6, 127.1, 126.9, 126.5, 126.4, 126.23, 126.21, 126.12, 126.10, 126.0, 125.9, 125.7, 125.3, 120.55, 120.50, 120.28, 120.23, 97.08

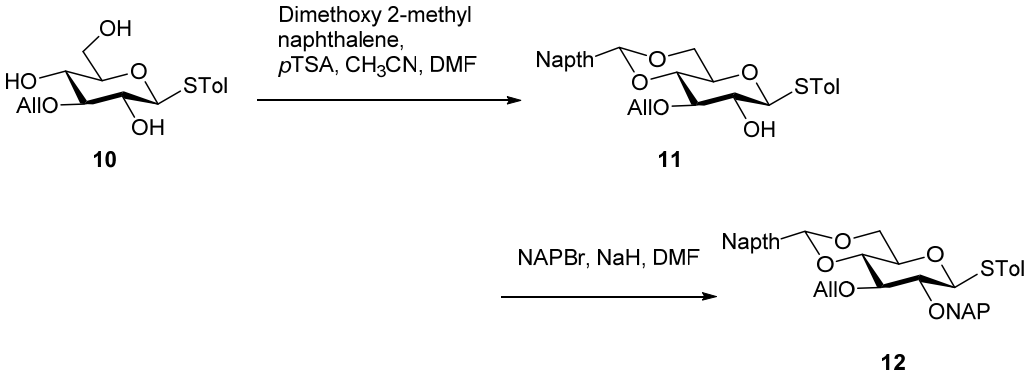
(C-1,d, $J_{c\text{-}p}$ = 6.0 Hz), 81.1, 76.7, 75.8, 75.2, 73.6, 73.2, 72.8, 67.5. The phosphate donor **6** was unstable to MS analysis and was directly used for next glycosylation.

***p*-Tolyl 2,3,4,6-Tetra-O-(2-naphthyl)methyl-1-thio-α-L-rhamnopyranoside (7) (Scheme 2a in article)**:



To a solution of rhamnose thioglycoside **7a** (2.0 g, 7.40 mmol) and 2-(bromomethyl)-naphthalene (5.8 g, 26.6 mmol) in DMF (25 mL), NaH (1.2 g, 29.6 mmol) was added at 0 ˚C. The reaction mixture was stirred at RT for 3 h. Upon completion of reaction as monitored by TLC, the reaction mixture was brought to 0 ˚C and quenched by ice-water (5mL) further reaction mixture was poured in H_2O (75 mL). Aqueous layer was extracted with EtOAc (3 × 50 mL). Combined organic layers were washed with brine (3 × 50 mL), dried over $MgSO_4$, filtered, and concentrated for flash chromatography purification over silica gel to furnish the desired product **7** (4.7 g, 92%) as a white amorphous solid. For compound **7**, R_f = 0.40 (Hexane:EtOAc, 4:1); $[\alpha]_D = -34.6$ (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81-7.65 (m, 12H, Ar*H*), 7.50-7.40 (m, 9H, Ar*H*), 7.18 (dd, *J* = 6.4, 1.6 Hz, 2H, Ar*H*), 6.98 (dd, *J* = 8.0, 0.4 Hz, 2H, Ar*H*), 5.44 (d, *J* = 1.6 Hz, 1H), 5.16 (d, *J* = 11.2 Hz, 1H), 4.88 (d, *J* = 8.4 Hz, 1H), 4.85 (d, *J* = 7.2 Hz, 1H), 4.79 (d, *J* = 7.6 Hz, 2H), 4.75 (d, *J* = 12.0 Hz, 1H), 4.23-4.16 (m, 1H), 4.05 (dd, *J* = 2.8, 1.6 Hz, 1H), 3.96 (dd, *J* = 9.2, 3.2 Hz, 1H), 3.80 (t, *J* = 9.2 Hz, 1H), 2.27 (s, 3H, C*H*$_3$), 1.40 (d, *J* = 6.2 Hz, 3H, C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.5, 136.1, 135.8, 135.3, 133.38, 133.34, 133.2, 133.1, 133.0, 132.0, 130.7, 129.8, 128.3, 128.2, 128.1, 128.03, 128.00, 127.75, 127.74, 127.71, 126.9, 126.58, 126.55, 126.14, 126.12, 126.06, 126.04, 126.01, 125.9, 125.8, 86.3 (C-1), 80.7, 80.1, 76.5, 75.5, 72.3, 72.2, 69.5, 21.1 (*C*H$_3$), 18.1 (*C*H$_3$); HRMS-EI (*m/z*): $[M + Na]^+$ calcd. $C_{46}H_{42}NaO_4S^+$, 713.2696; found, 713.2689.

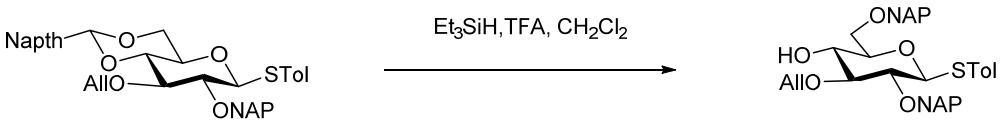
***p*-Tolyl 3-*O*-Allyl-4,6-*O*-(2-naphthyl)methylene-1-thio-β-D-glucopyranoside (11) and *p*-tolyl 3-*O*-allyl-2-*O*-(2-naphthyl)methyl-4,6-*O*-(2-naphthyl)methylene-1-thio-β-D-glucopyranoside (12) (Scheme 1a in article):**



To a solution of thioglucoside **10** (13.0 g, 0.0398 mol) in CH_3CN/DMF (9:1, 150 mL) were added 2-(dimethoxymethyl)-naphthalene (12.0 g, 0.059 mol) and *p*TSA (1.5 g, 0.008 mol) at 0 ˚C and the reaction mixture was stirred at RT for 3 h. Upon completion of reaction as monitored by TLC, the reaction mixture was poured in H_2O (300 mL) and the product was precipitated. The precipitate was washed with briefly with H_2O, followed by hexane, and then dried under vacuum to obtain the desired thioglucoside **11** (17.0 g, 92% yield.). For thioglucoside **11**, R_f = 0.45 (Hexane/EtOAc, 2/1); $[\alpha]_D$ = +42.3 (*c* 0.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (s, 1H, Ar*H*), 7.78-7.74 (m, 3H, Ar*H*), 7.48 (dd, *J* = 8.4, 1.6 Hz, 1H, Ar*H*), 7.43-7.36 (m, 4H, Ar*H*), 7.07 (d, *J* = 8.0 Hz, 2H, Ar*H*), 5.92-5.82 (m, 1H, allyl-*H*), 5.60 (s, 1H, naphthalidene-C*H*), 5.22 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.12-5.09 (m, 1H), 4.51 (d, *J* = 9.6 Hz, 1H), 4.37-4.32 (m, 2H), 4.21 (ddt, *J* = 12.4, 6.0, 1.2 Hz, 1H), 3.74 (t, *J* = 10.2 Hz, 1H), 3.56-3.52 (m, 2H), 3.48-3.37 (m, 2H), 2.57 (s, 1H, O*H*), 2.28 (s, 3H, C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.8, 134.8, 134.6, 133.9, 133.6, 132.9, 129.9, 128.4, 128.1, 127.7, 127.2, 126.5, 126.2, 125.5, 123.6, 117.6 (allyl-*C*), 101.4 (naphthalidene-*C*), 88.7 (C-1), 81.4, 81.2, 73.8, 72.1, 70.8, 68.7, 21.2 (*C*H$_3$). To a solution of the thioglucoside **11** (17.0 g, 0.036 mol) and 2-(bromomethyl)-naphthalene (9.7 g, 0.043 mol) in DMF (170 mL), NaH (2.0 g, 0.051 mol) was added was added at 0 ˚C. The reaction mixture was stirred for 2 h at RT. Upon completion of reaction as monitored by TLC, the reaction mixture was again

cooled at 0 ˚C, quenched by ice-water (5 mL) further reaction mixture was poured in H_2O (400 mL), solid precipitated was filtered and washed with H_2O (200 mL) after removal of water solid obtained was washed with hexane (300 mL) and dried under vacuum to obtained the desired thioglucoside **12** (20.0 g, 91%). For thioglucoside **12,** R_f = 0.40, (Hexane:EtOAc, 4:1); $[\alpha]_D^{25}$ = −11.4 (*c* = 0.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (s, 1H, Ar*H*), 7.78 -7.72 (m, 7H, Ar*H*), 7.52 (dd, *J* = 8.4, 2.0 Hz, 1H, Ar*H*), 7.49 (dd, *J* = 8.4 Hz, 2.0 Hz, 1H, Ar*H*), 7.41-7.36 (m, 6H, Ar*H*), 7.03 (dd, *J* = 8.4, 0.4 Hz, 2H, Ar*H*), 5.92-5.85 (m, 1H, allylic-*H*), 5.62 (s, 1H, naphthalidene-*H*), 5.21 (dq, J = 17.2, 1.6 Hz, 1H), 5.09-5.06 (m, 1H), 4.96 (d, *J* = 10.8, Hz, 1H), 4.91 (d, J = 10.8 Hz, 1H), 4.65 (d, *J* = 9.6 Hz, 1H), 4.39-4.31 (m, 2H), 4.21 (ddt, *J* = 12.8, 5.8/ 5.6, 1.6 Hz, 1H), 3.75 (t, *J* = 10.2 Hz, 1H), 3.67 (dd, *J* = 9.2, 8.4 Hz, 1H), 3.60 (t, *J* = 9.2 Hz, 1H), 3.46-3.36 (m, 2H), 2.25 (s, 3H, C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.2, 135.6, 135.0, 134.6, 133.6, 133.3, 133.1, 133.0, 132.9, 129.8, 129.2, 128.4, 128.16, 128.13, 128.0, 127.75, 127.73, 126.9, 126.4, 126.3, 126.2, 126.0, 125.9, 125.5, 123.7, 117.1 (allylic-*C*), 101.3 (naphthalidene-*C*), 88.6 (C-1), 82.8, 81.4, 80.5, 76.0, 74.2, 70.3, 68 .8, 21.2 (*C*H$_3$); HRMS-EI (*m/z*): $[M + Na]^+$ calcd. for $C_{38}H_{36}NaO_5S^+$, 627.2176; found 627.2176.

p-Tolyl 3-O-Allyl-2,6-di-O-(2-naphthyl)methyl-1-thio-β-D-glucopyranoside (13) (Scheme 1a in article):

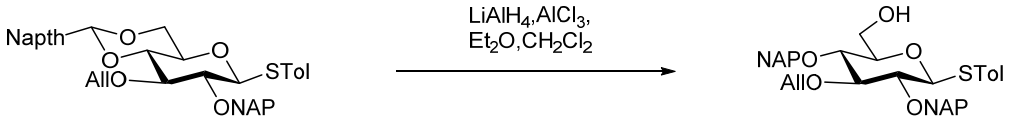


12 **13**

To a suspension of compound **12** (15 g, 24 mmol) and activated molecular sieves (AW300, 10 g) in CH_2Cl_2 (225 mL) were added. triethylsilane (39.5 mL, 248 mmol) and TFA (18.5 mL, 248 mmol) at 0 ˚C and reaction mixture was stirred for 1 h at RT. Upon completion of reaction as monitored by TLC, the reaction mixture was filtered from celite bed, subsequently diluted with CH_2Cl_2 (100 mL) and washed by $NaHCO_{3(aq)}$ (2 × 200mL) and H_2O (3 × 200 mL). The resulting

mixture was dried over $MgSO_4$, filtered, and concentrated for flash chromatography purification (Elution: Hexane/EtOAc, 4/1) over silica gel to furnish the desired product **13** (11.0g, 73% yield) as a white glassy solid. For thioglucoside **13**, R_f = 0.30 (Hexane:EtOAc, 4:1); $[\alpha]_D^{25}$ = −40.2 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83-7.81 (m, 7H, ArH), 7.78 (s, 1H, ArH), 7.57 (d, *J* = 8.8 Hz, 1H, ArH), 7.47-7.44 (m, 7H, ArH), 7.00 (d, *J* = 8.4 Hz, 2H, ArH), 5.99-5.90 (m, 1H, allylic-*H*), 5.26 (dd, *J* = 17.6, 2.0 Hz, 1H), 5.16 (d, J = 10.4 Hz, 1H), 5.05 (d, *J* = 10.4 Hz, 1H), 4.87 (d, *J* = 10.8 Hz, 1H), 4.73 (dd, *J* = 15.2, 12.0 Hz, 2H), 4.65 (d, *J* = 9.2 Hz, 1H), 4.42-4.37 (m, 1H), 4.31-4.26 (m, 1H), 3.87-3.78 (m, 2H), 3.67-3.62 (m, 1H), 3.52-3.41 (m, 3H), 2.76-2.73 (m, 1H), 2.25 (s, 3H, C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.7, 135.6, 135.4, 135.0, 133.37, 133.33, 133.1, 133.0, 132.5, 129.8, 129.7, 128.2, 128.1, 128.0, 127.9, 127.7, 126.9, 126.5, 126.3, 126.18, 126.10, 125.9, 125.7, 117.3 (allylic-*C*), 88.0 (C-1), 86.0, 80.5, 78.1, 75.4, 74.4, 73.8, 71.7, 70.4, 21.1 (*C*H_3); HRMS-EI (*m/z*): $[M + Na]^+$ calcd. for $C_{38}H_{38}NaO_5S^+$, 629.2332; found, 629.2326.

***p*-Tolyl 3-*O*-allyl-2,4-di-*O*-(2-napthyl)methyl-1-thio-β-D-glucopyranoside (14) (Scheme 1a in article):**



12 **14**

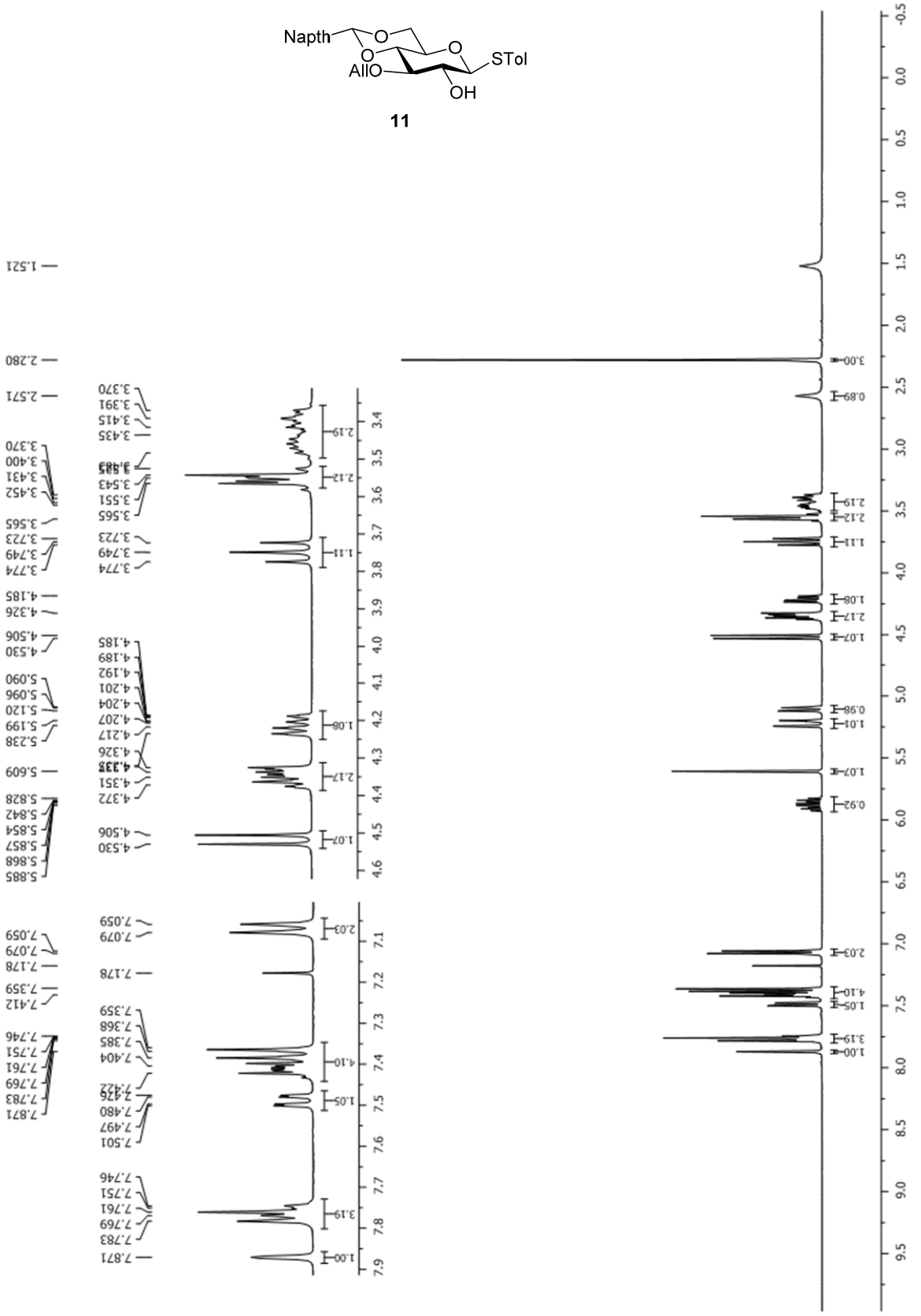
$LiAlH_4$ (245 mg, 6.62 mmol) was added to a solution of thioglucoside **12** (1.0 g, 1.65 mmol) in CH_2Cl_2/Et_2O (1:1, 50 mL), and mixture was slowly heated to its boiling point. $AlCl_3$ (1.5 g, 11.5 mmol) in Et_2O (20 mL) was added to hot solution over 30 min. Reaction mixture was heated at reflux for 2 h. Upon completion of reaction as monitored by TLC, the reaction mixture was poured to EtOAc (250 mL) and quenched by supersaturated Na_2SO_4. The resulting mixture filtered, and concentrated for flash chromatography purification over silica gel (Hexane:Et_2O, 3:1)to furnish the desired product (750 mg, 75%). For **14**, R_f = 0.35 (Hexane: Et_2O, 1:1); $[\alpha]_D^{25}$ = +1.040 (*c* 0.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85-7.80 (m, 7H, ArH), 7.76 (s, 1H, ArH), 7.58 (dd, *J* =

8.4, 1.5 Hz, 1H, ArH), 7.49-7.41 (m, 7H, ArH), 7.10 (d, *J* = 7.9 Hz, 2H, ArH), 6.03-5.94 (m, 1H), 5.32-5.26 (m, 1H), 5.17 (dq, *J* = 10.3, 1.2 Hz, 1H), 5.06 (d, *J* = 10.5 Hz, 1H), 5.00 (d, *J* = 11.1 Hz, 1H), 4.92 (d, *J* = 10.5 Hz, 1H), 4.81 (d, *J* = 11.1 Hz, 1H), 4.65 (d, *J* = 9.7 Hz, 1H), 4.42 (ddt, *J* = 12.4, 5.5, 1.4 Hz, 1H), 4.37 (ddt, *J* = 12.4, 5.5, 1.4 Hz, 1H), 3.88 (ddd, *J* = 11.9, 6.3, 2.6 Hz, 1H), 3.70 (ddd, *J* = 12.0, 7.,1 4.9Hz, 1H), 3.64-3.54 (m, 2H), 3.47 (dd, *J* = 9.7, 8.5 Hz, 1H), 3.39-3.34 (m, 1H), 2.32 (s, 3H), 1.98 (t, *J* = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.0, 135.5, 135.4, 135.0, 133.37, 133.32, 133.16, 133.11, 132.6, 129.8, 129.5, 128.3, 128.2, 128.03, 128.00, 127.7, 127.0, 126.9, 126.3, 126.2, 126.11, 126.10, 126.04, 126.00, 117.0, 87.8, 86.2, 81.1, 79.3, 77.6, 75.6, 75.2, 74.6, 62.3, 21.2; HRMS (*m/z*): $[M + Na]^+$ calcd. for $C_{38}H_{38}NaO_5S^+$, 629.2332; found, 629.2329.

Inhibition of human hormone-refractory prostate cancer PC-3 cells:

Human hormone-refractory prostate cancer PC-3 cells were seeded in 96-well plates in medium with 5% FBS. After 24 h, cells were fixed with 10% trichloroacetic acid (TCA) to represent cell population at the time of PhG compound addition (T_0). After additional incubation of 0.1% dimethylsulfoxide (DMSO) or the PhG compound (**1**, **2**, or **3**) for 48 h, cells were fixed with 10% TCA and SRB at 0.4% (w/v) in 1% acetic acid was added to stain cells. Unbound SRB was washed out by 1% acetic acid and SRB bound cells were solubilized with 10 mM Trizma base. The absorbance was read at a wavelength of 515 nm. Using the following absorbance measurements, such as time zero $[t_0]_{abs}$, control growth $[Ctrl]_{abs}$, and cell growth in the presence of the PhG compound $[t_{24h}]_{abs}$ after 24 h incubation, the percentage growth was calculated at each of the compound concentrations levels. Percentage growth inhibition was calculated as:

$$[1 - ([t_{24h}]_{abs} - [t_0]_{abs})/([Ctrl]_{abs} - [t_0]_{abs})] \times 100\%.$$



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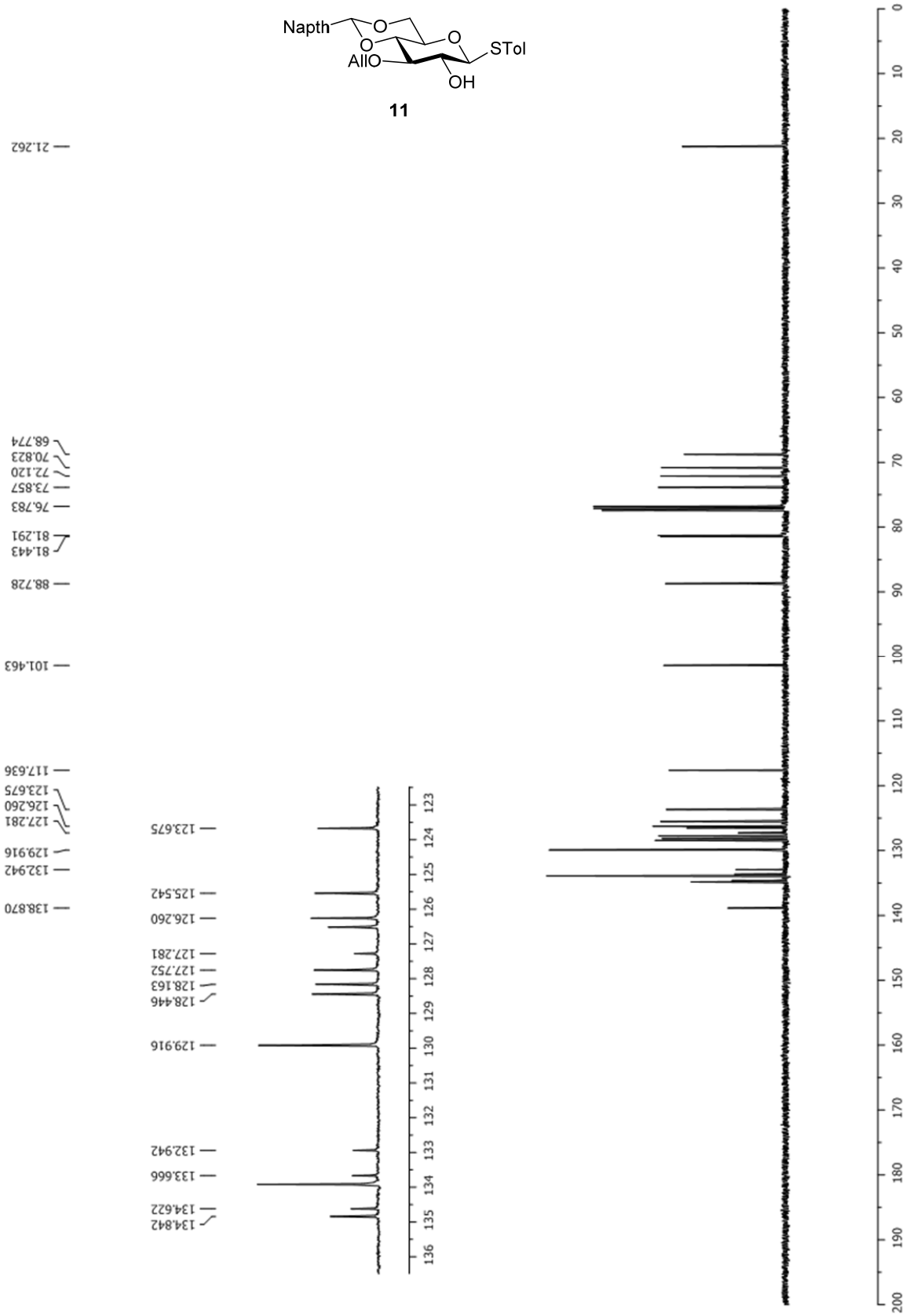
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O
O
AllO
STol
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81.291
81.443
88.728
101.463
117.636
123.675
126.260
127.281
129.916
132.942
138.870
123.675
125.542
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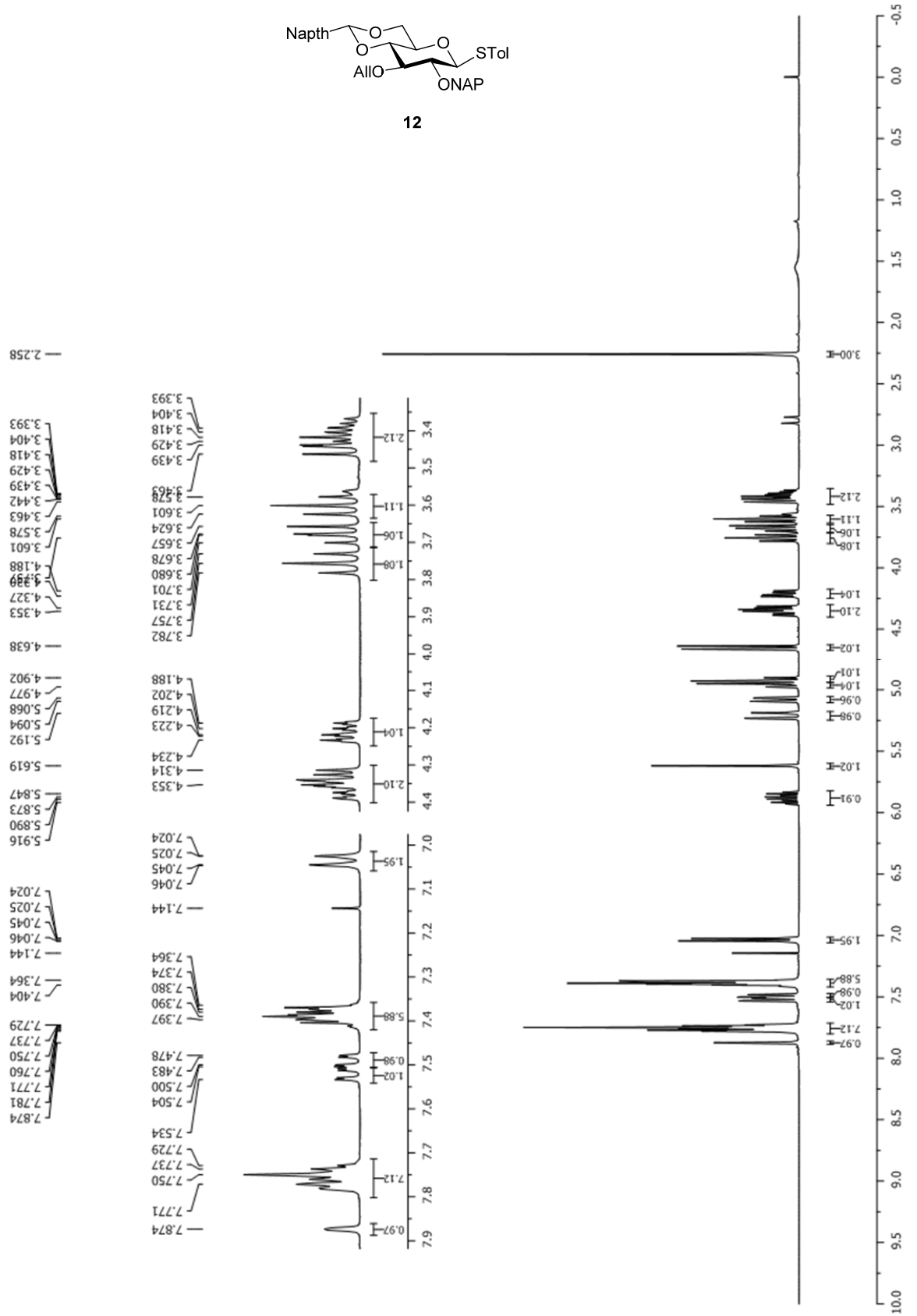
127.281
127.752
128.163
128.446
129.916
132.942
133.666
134.622
134.842



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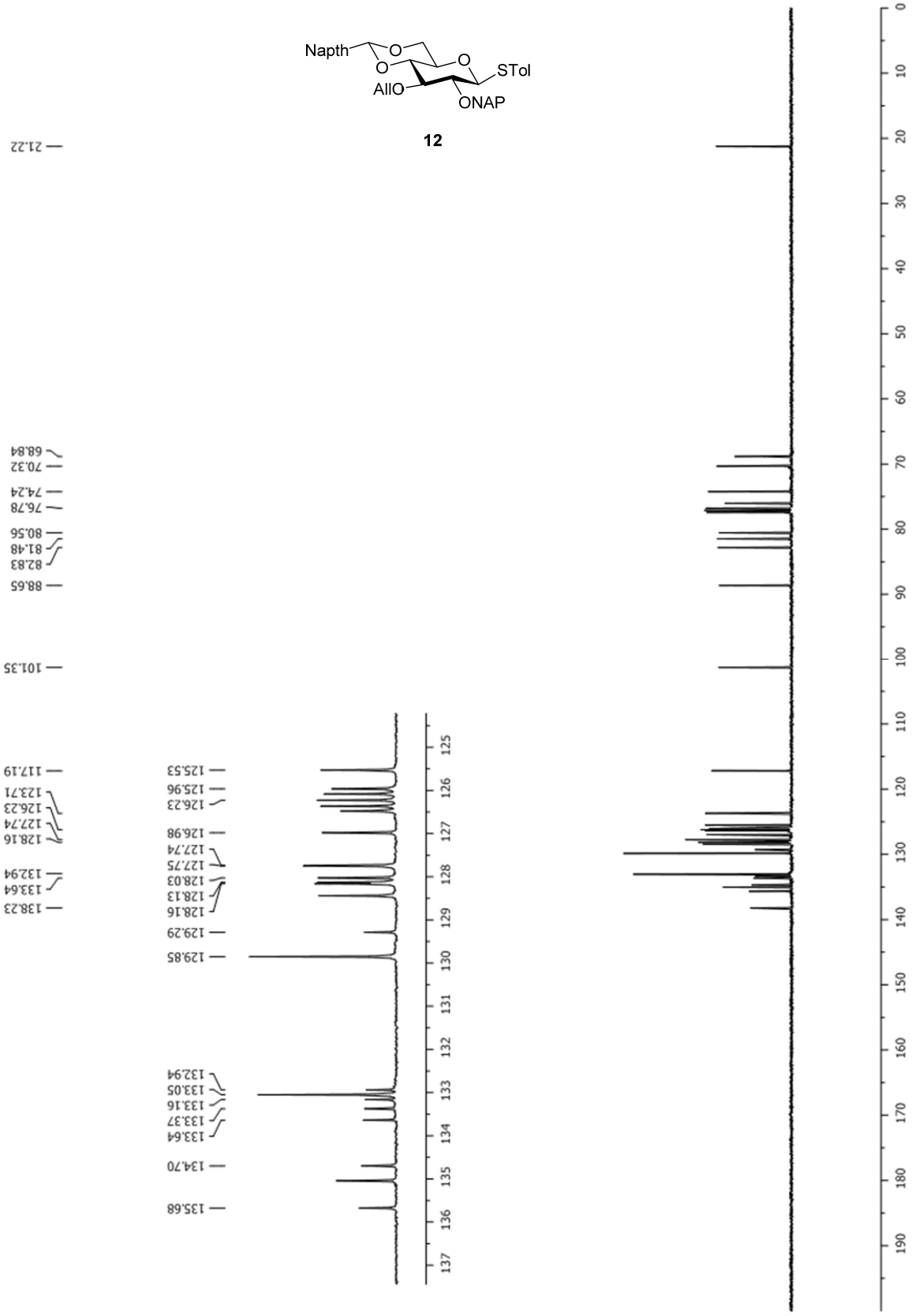
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O
O
O
STol
AllO
ONAP
12
21.22
68.84
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76.78
80.56
81.48
82.83
88.65
101.35
117.19
123.71
126.23
127.74
128.16
132.94
133.64
138.23
125.53
125.96
126.23
126.98
127.74
127.75
128.03
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129.85
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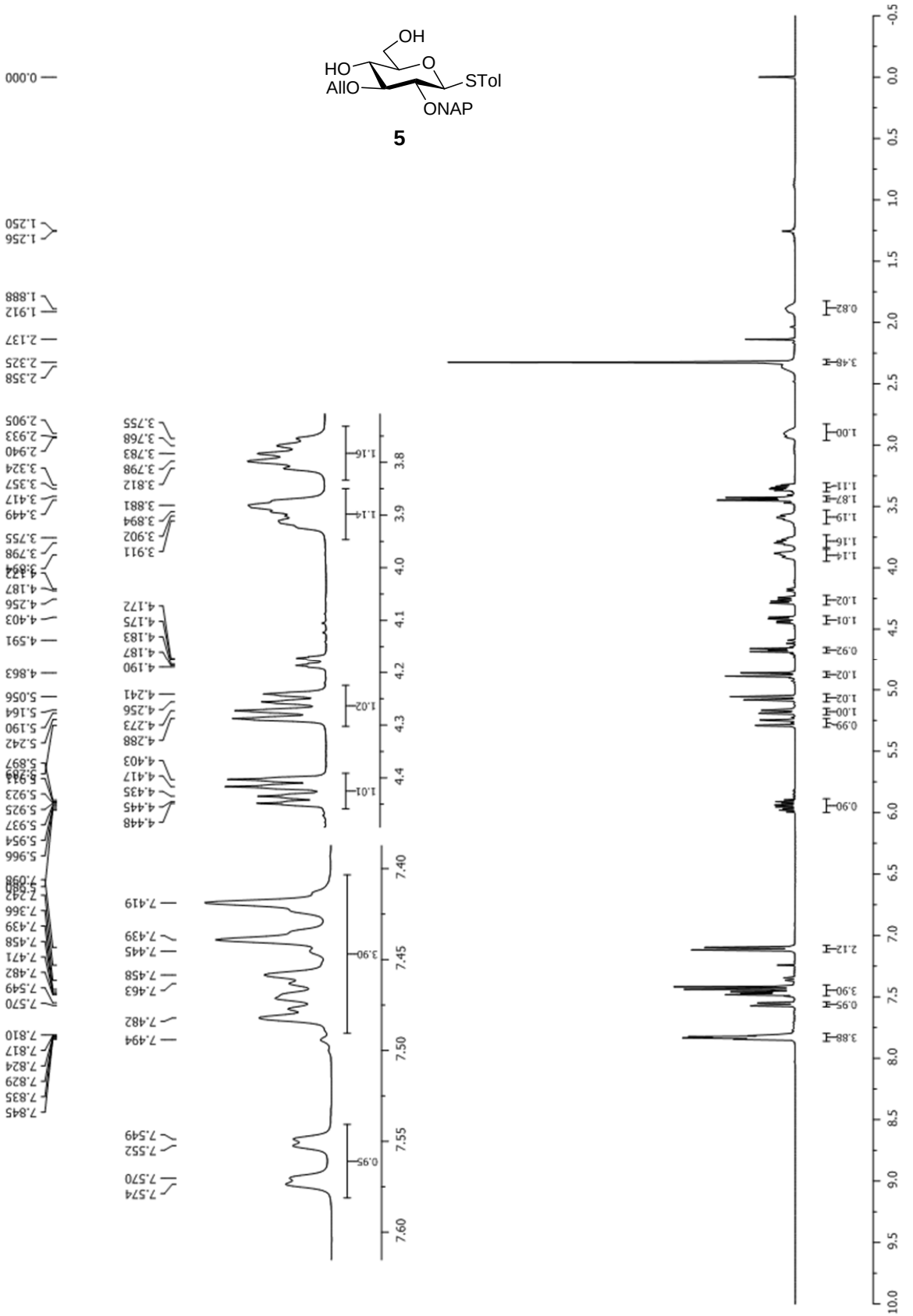
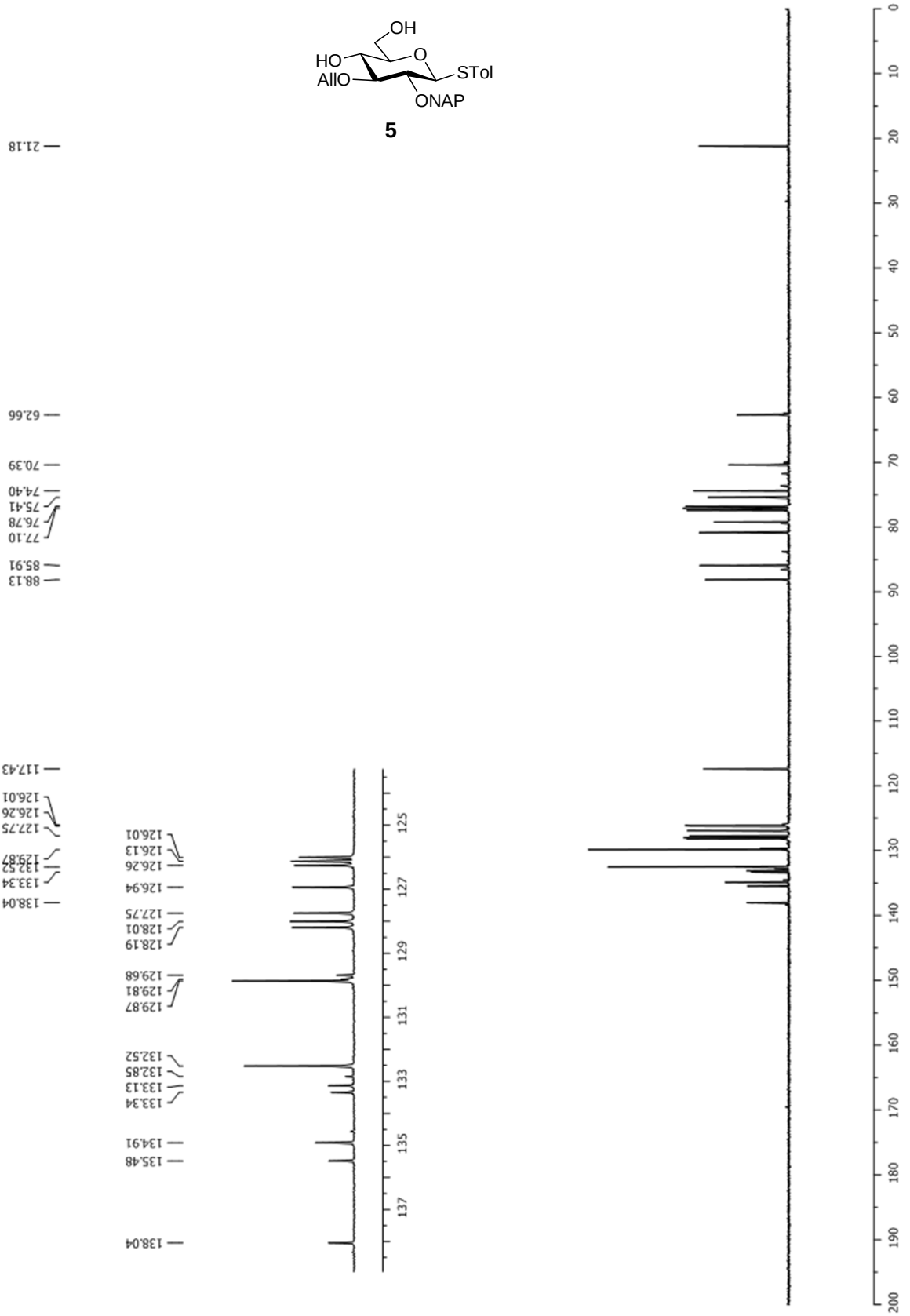
133.05
133.16
133.37
133.64
134.70
135.68


OH
HO
O
STol
AllO
ONAP
5


OH
HO
O
STol
AllO
ONAP
5
21.18
62.66
70.39
74.40
75.41
76.78
77.10
85.91
88.13
117.43
126.01
126.26
127.75
129.87
133.34
132.52
138.04
138.04
135.48
134.91
133.34
133.13
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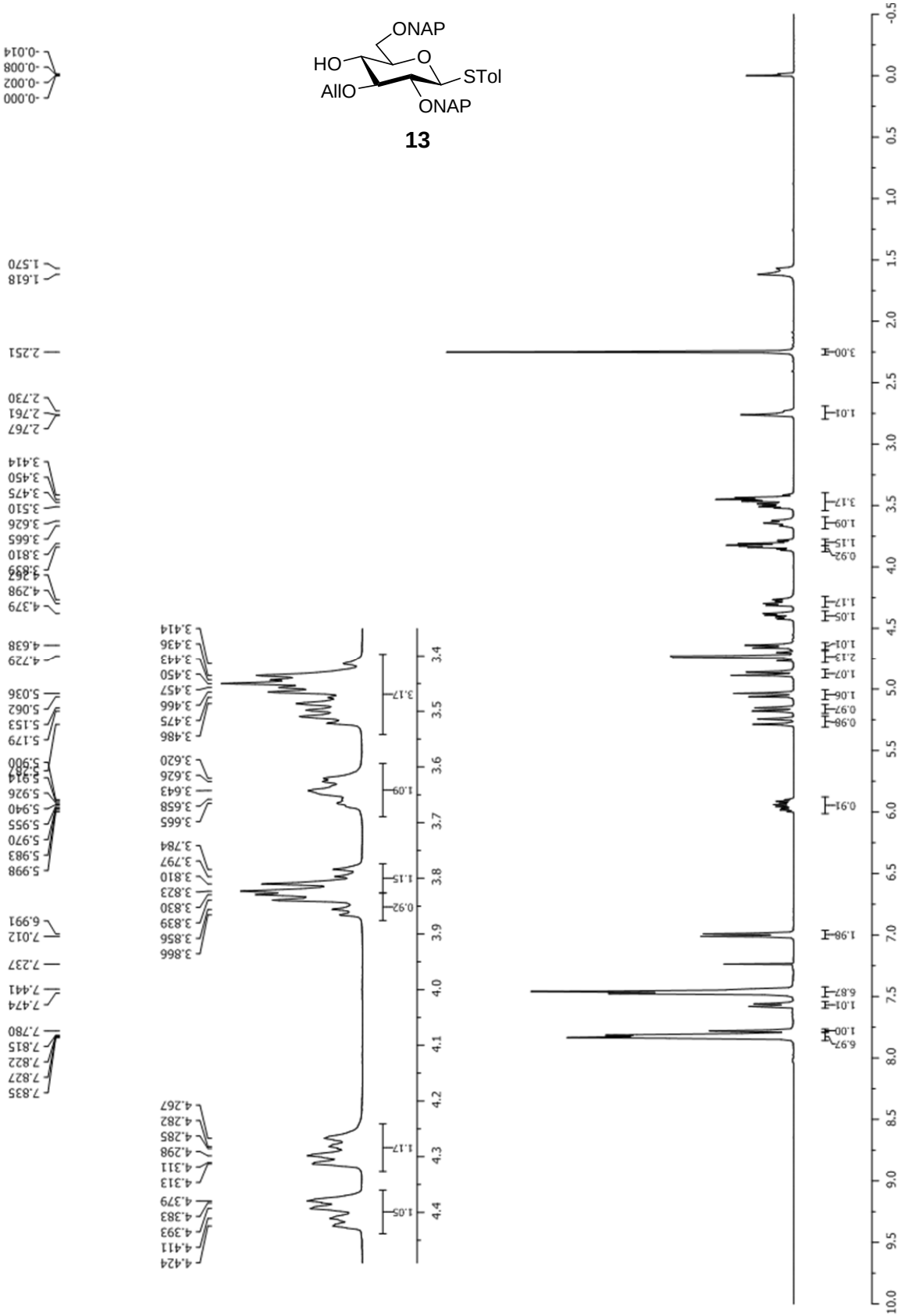
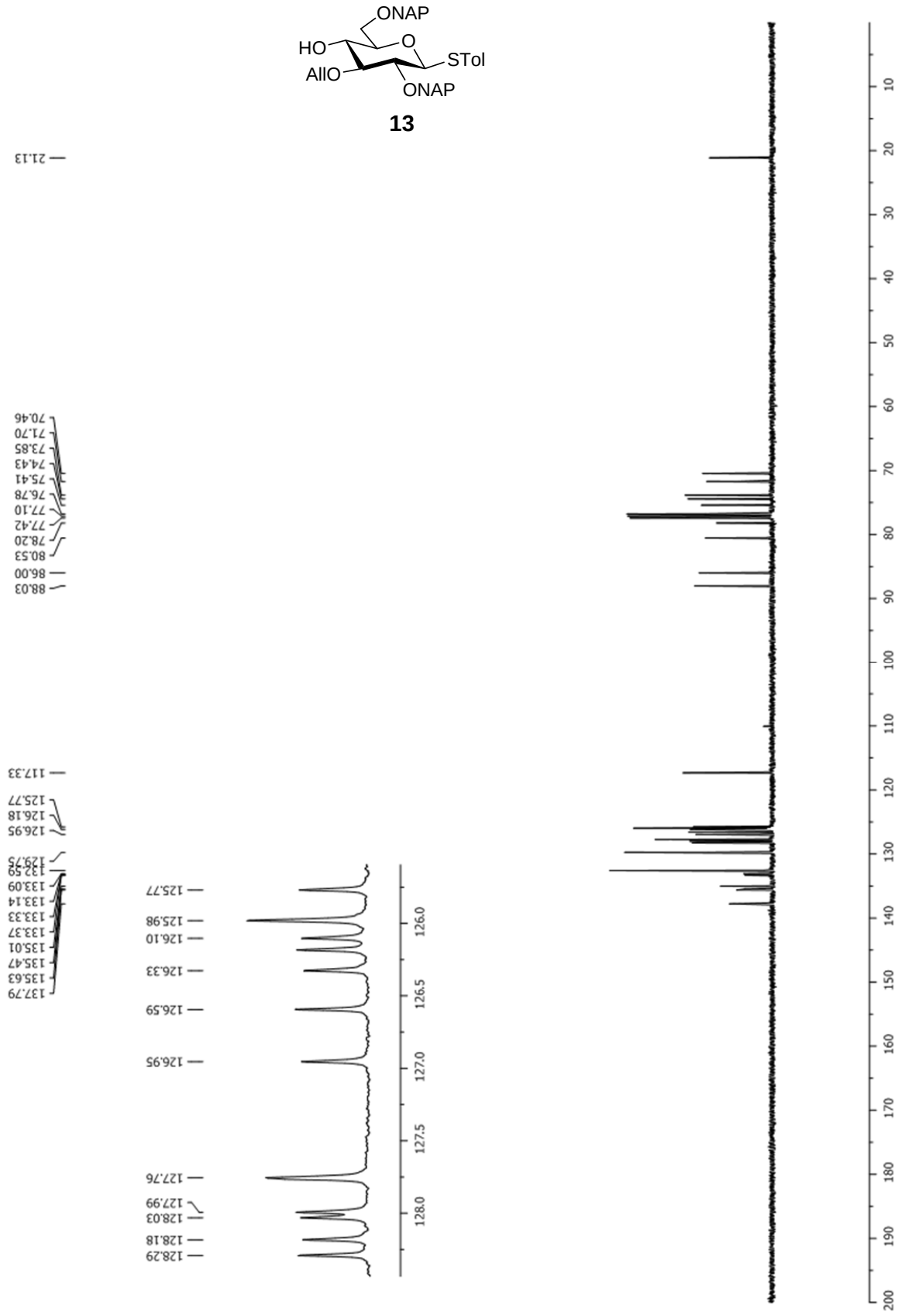
129.68
128.19
128.01
127.75
126.94
126.26
126.13
126.01


ONAP
HO
O
STol
AllO
ONAP
13


ONAP
HO
O
STol
AllO
ONAP
13
21.13
70.46
71.70
73.85
74.43
75.41
76.78
77.10
77.42
78.20
80.53
86.00
88.03
117.33
125.77
126.18
126.95
129.75
132.59
133.09
133.14
133.33
133.37
135.01
135.47
135.63
137.79
125.77
125.98
126.10
126.33
126.59
126.95
127.76
127.99
128.03
128.18
128.29
126.0
126.5
127.0
127.5
128.0
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140
150
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180
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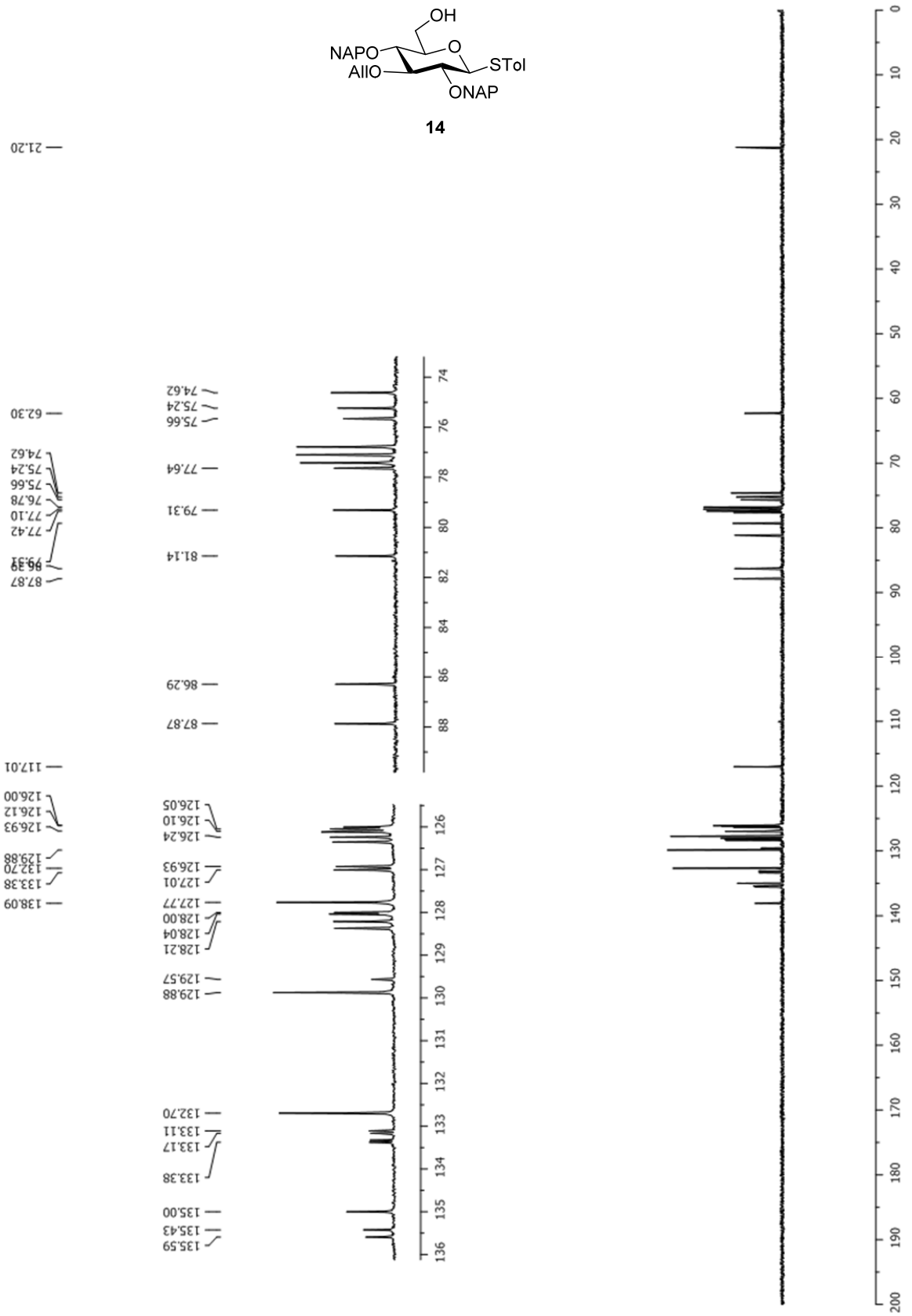
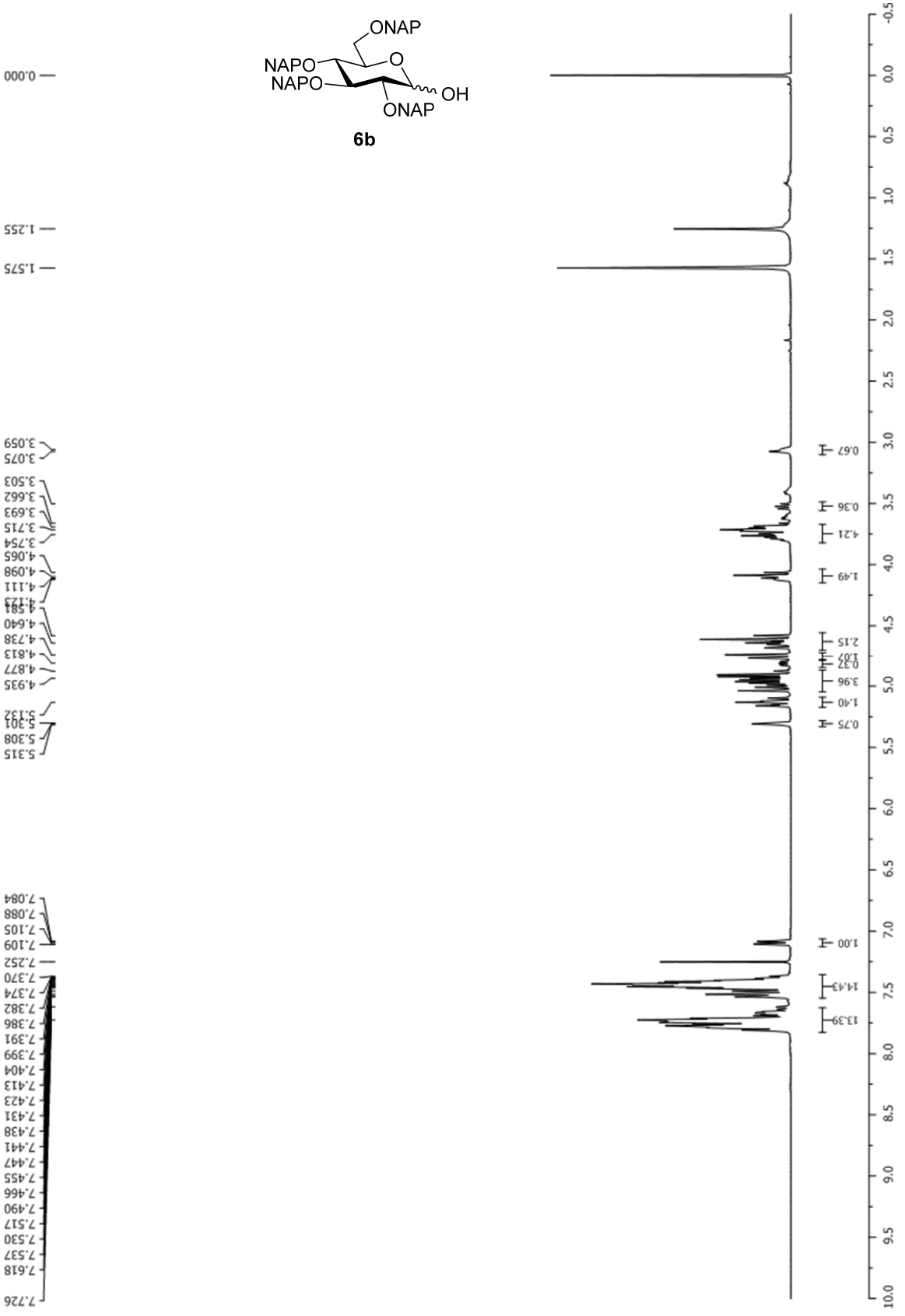
200

14


OH
NAPO
O
STol
AllO
ONAP
14



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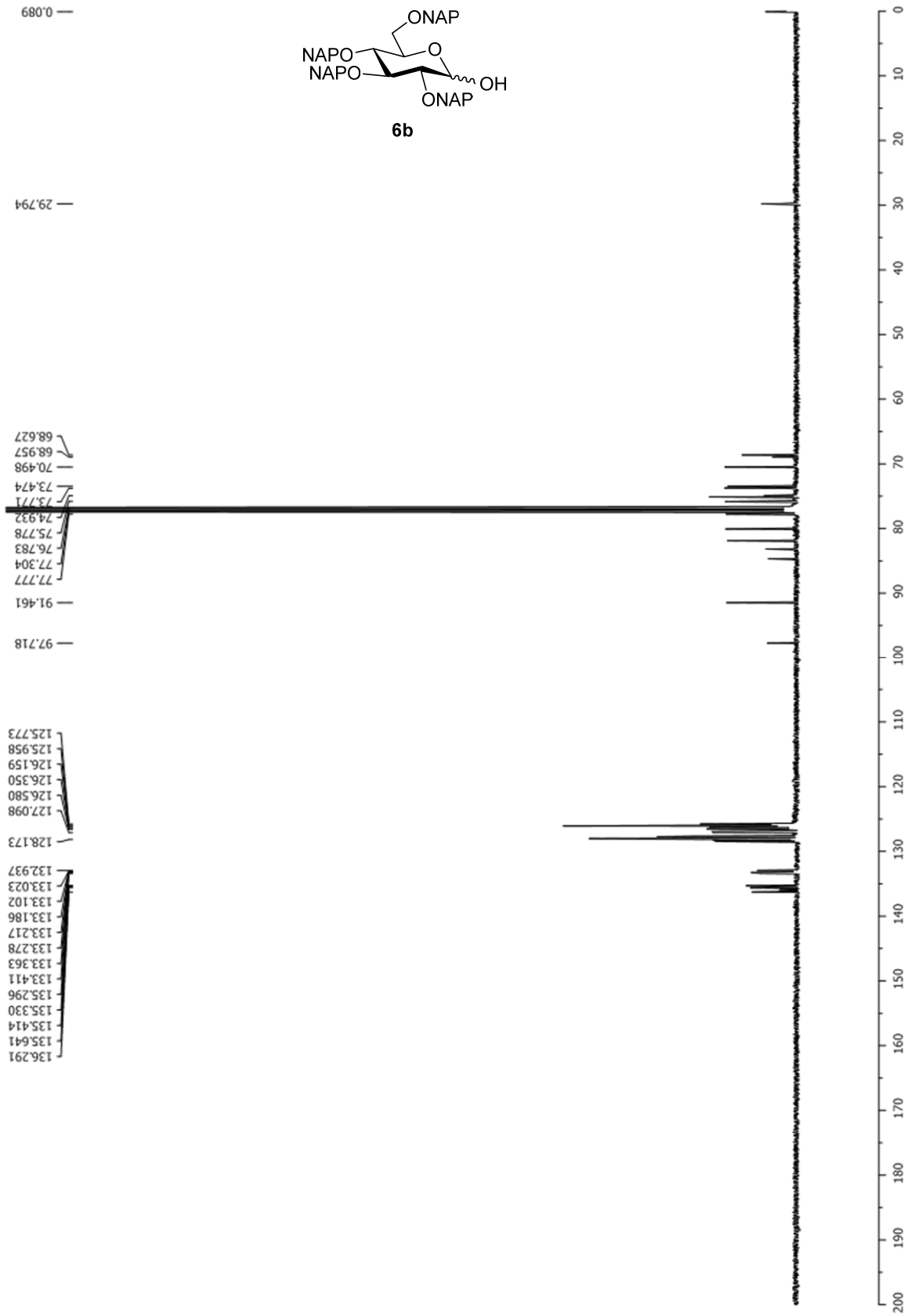
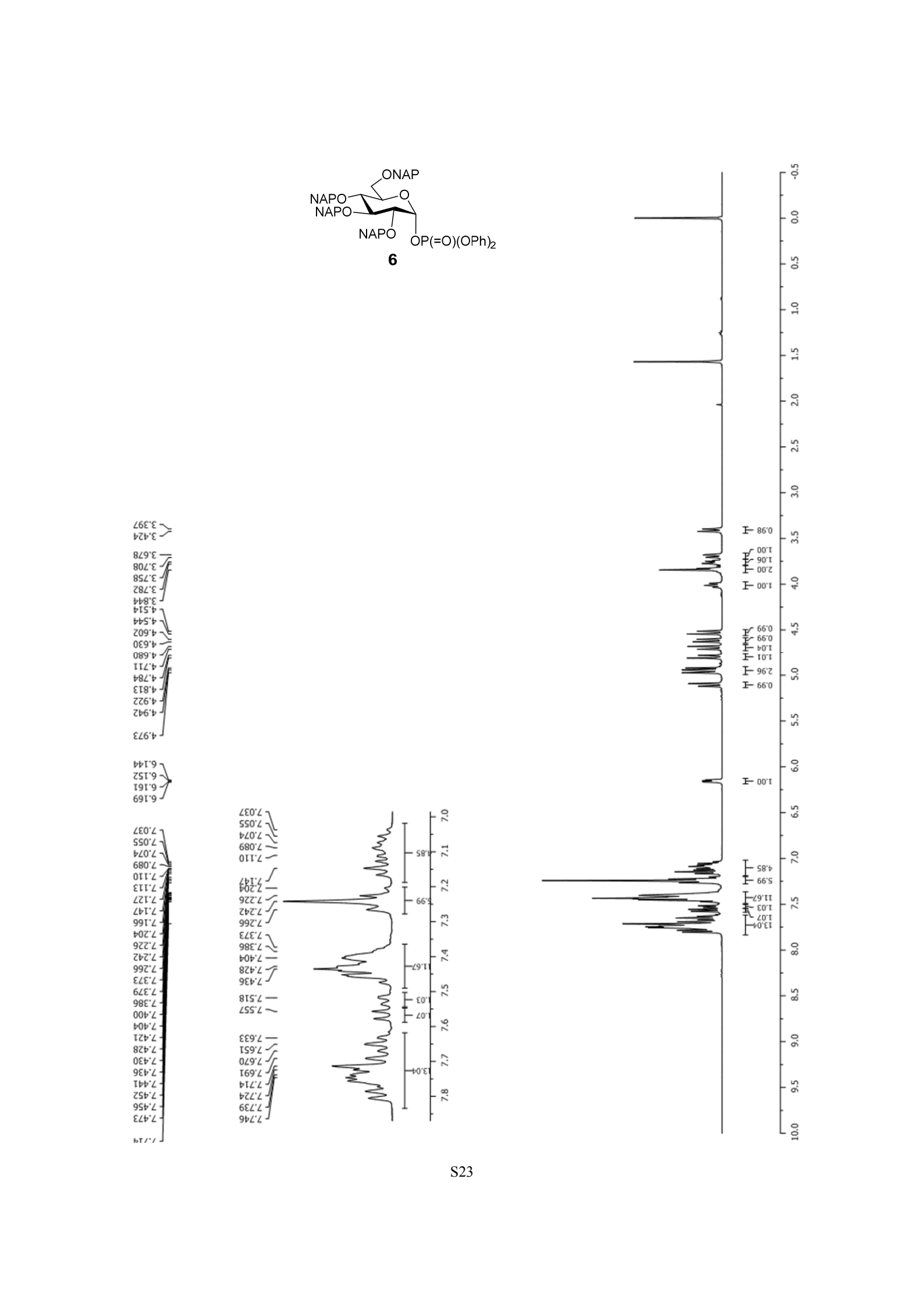
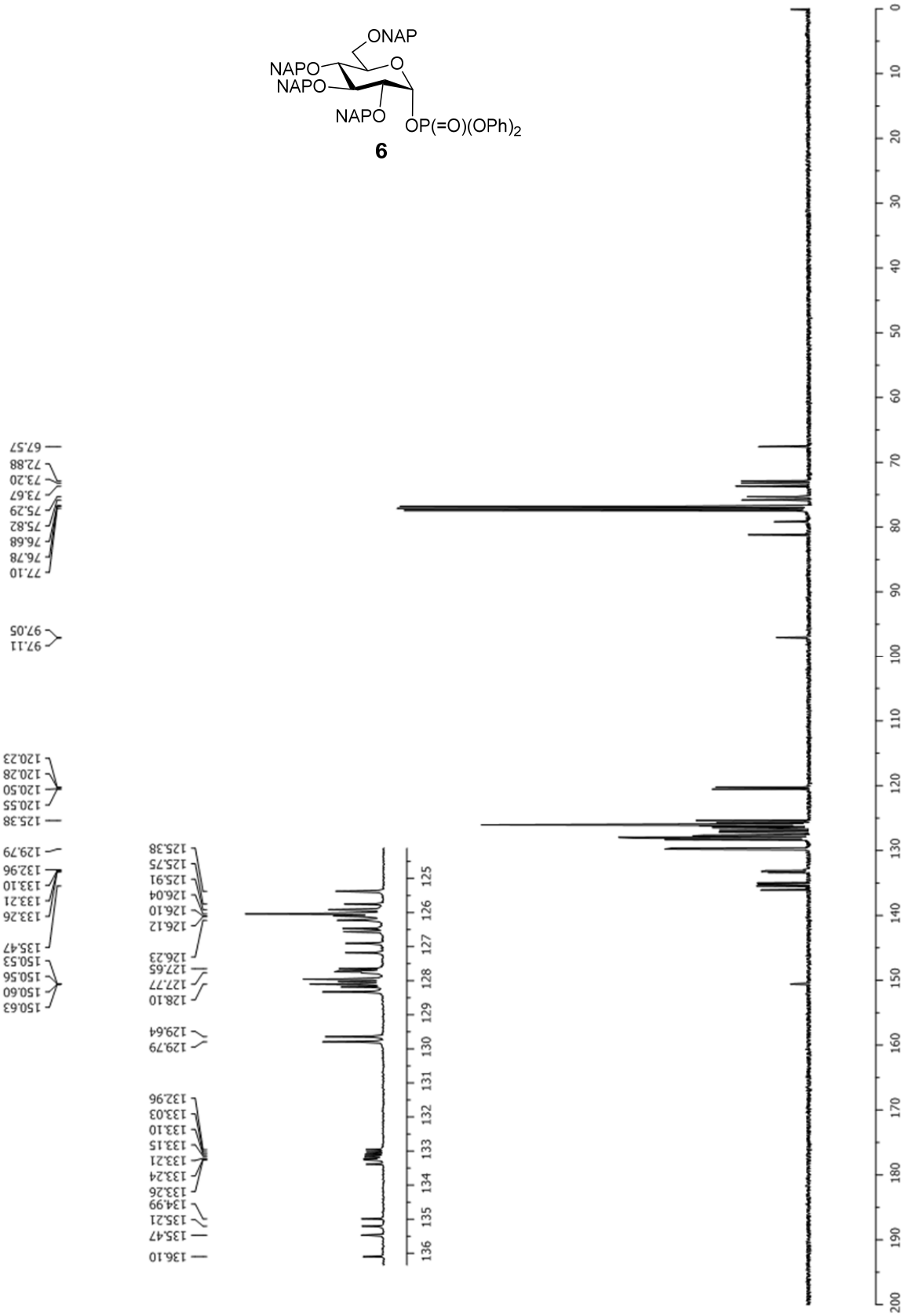

ONAP
NAPO
NAPO
O
OH
ONAP
6b

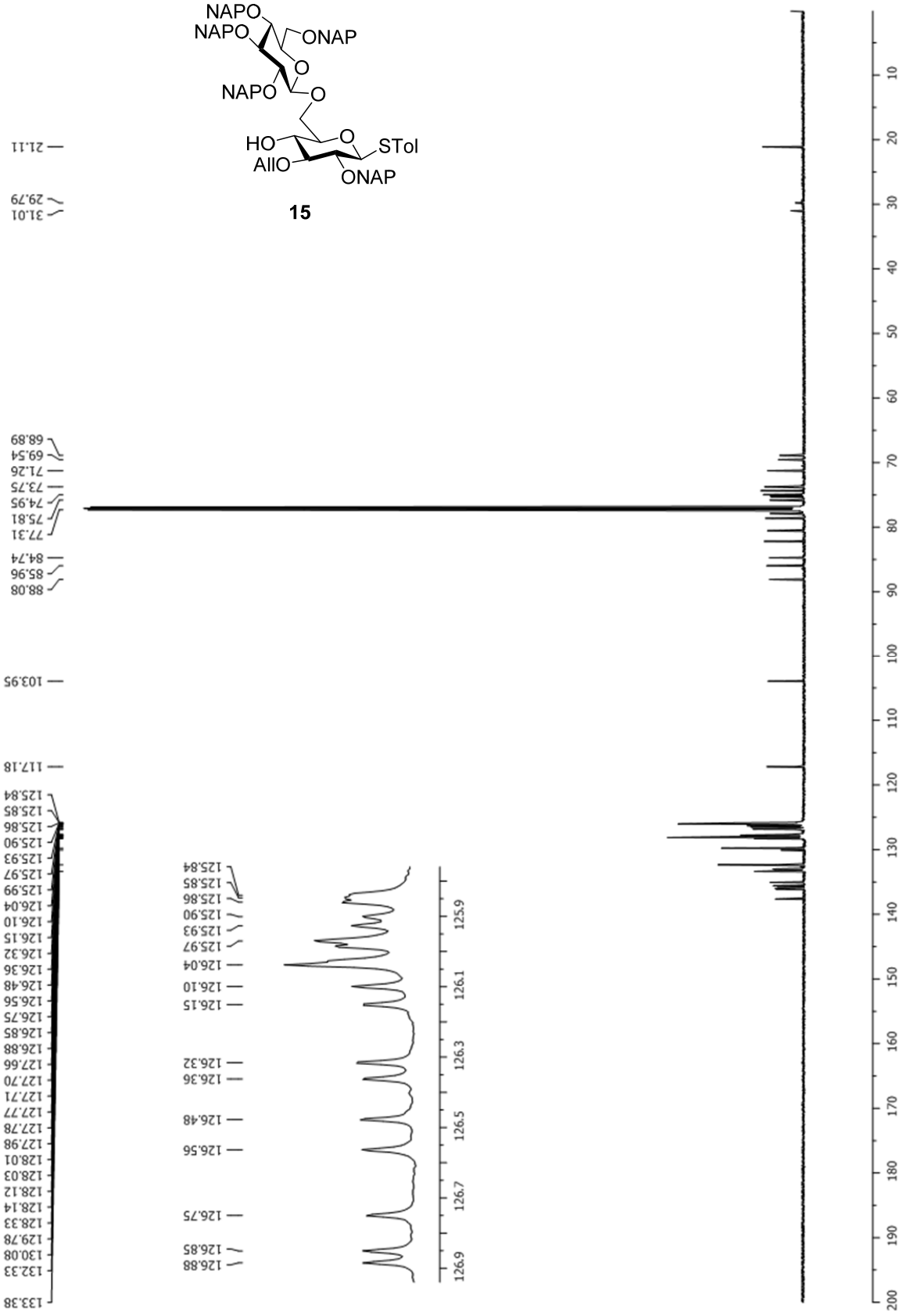

ONAP
NAPO
NAPO
NAPO
O
OP(=O)(OPh)2
6

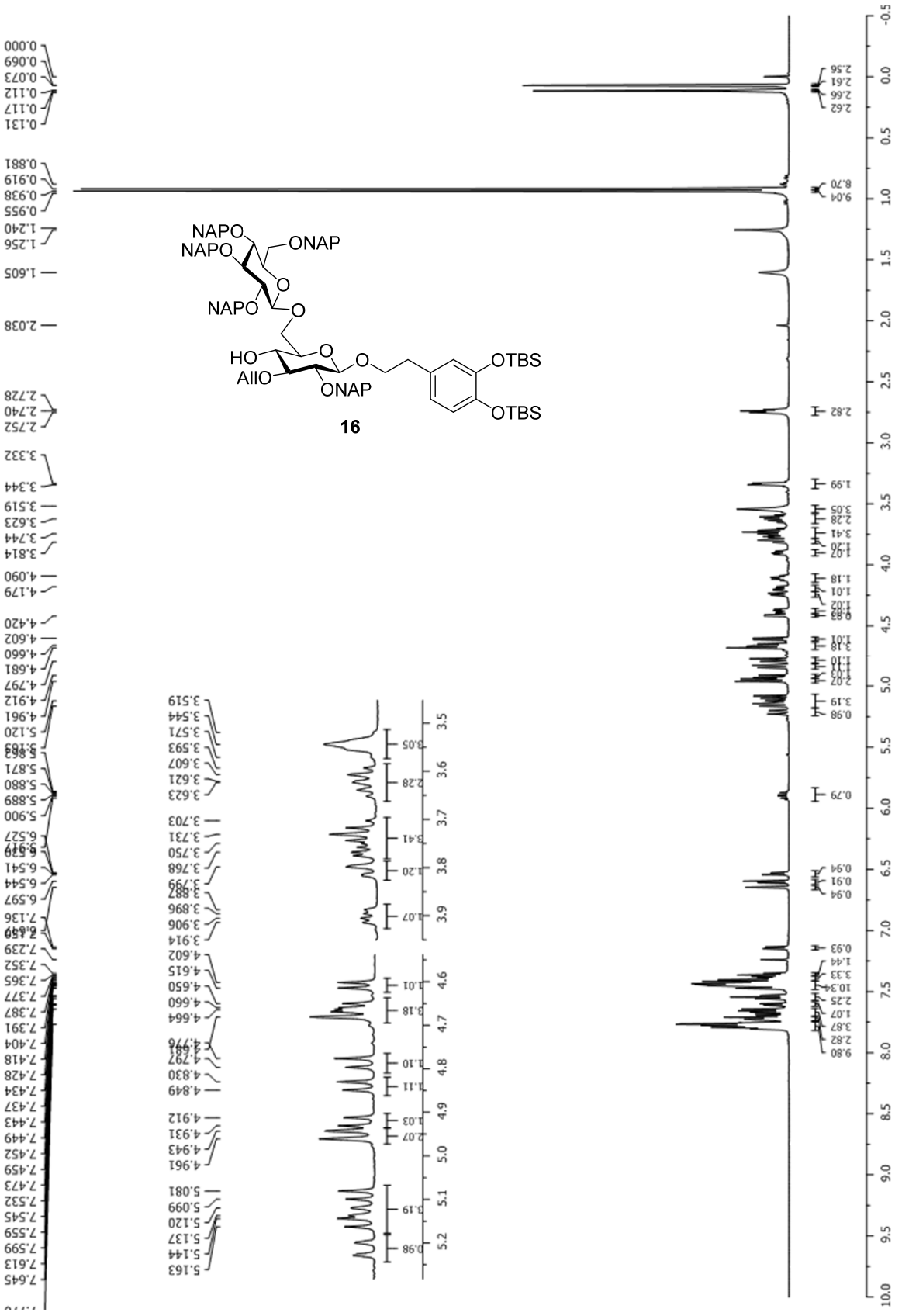

ONAP
NAPO
NAPO
O
NAPO
OP(=O)(OPh)2
6

7

STol
NAPO
O
NAPO
ONAP
7

15


NAPO
NAPO
ONAP
O
NAPO
O
HO
O
STol
AllO
ONAP
15



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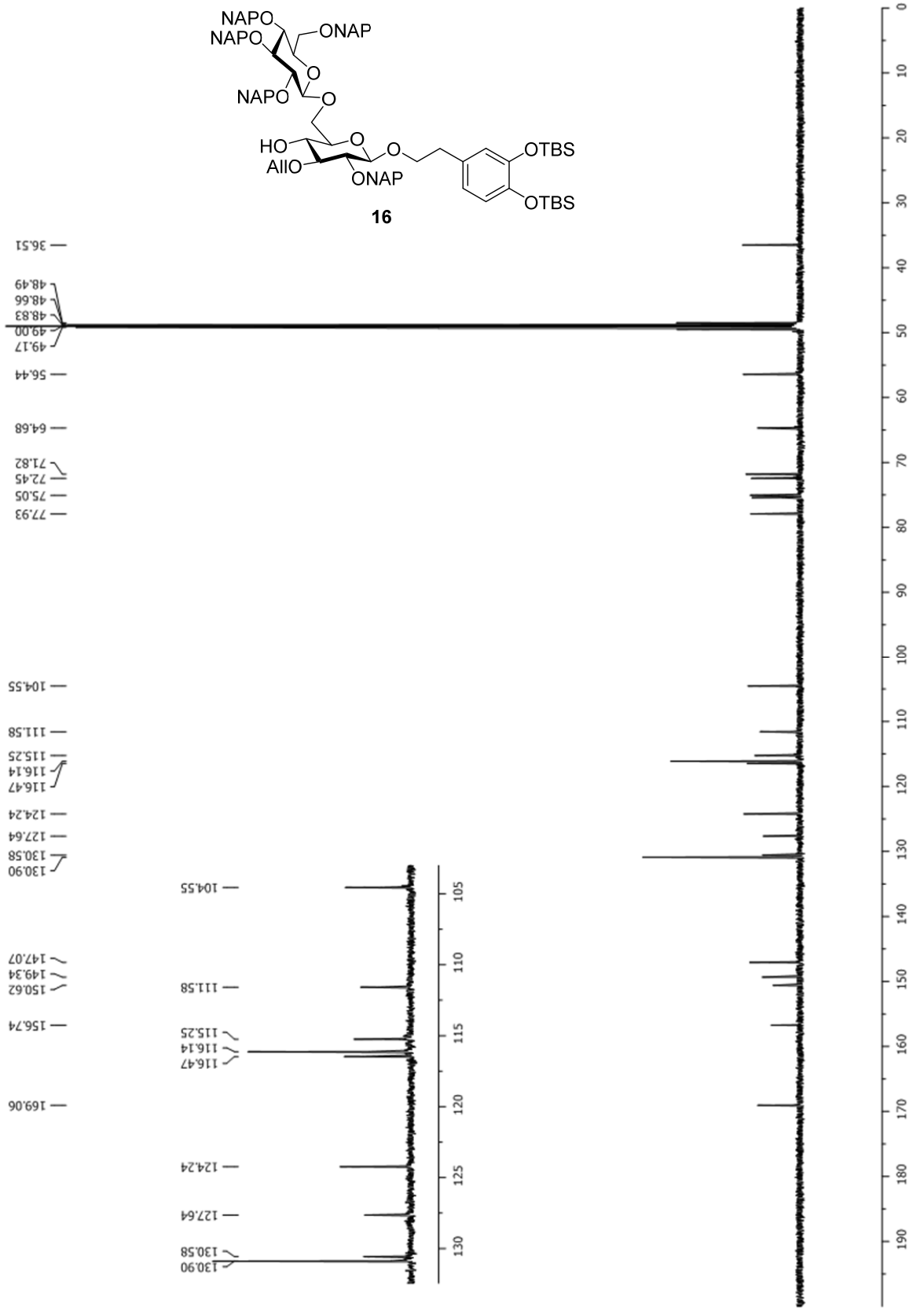
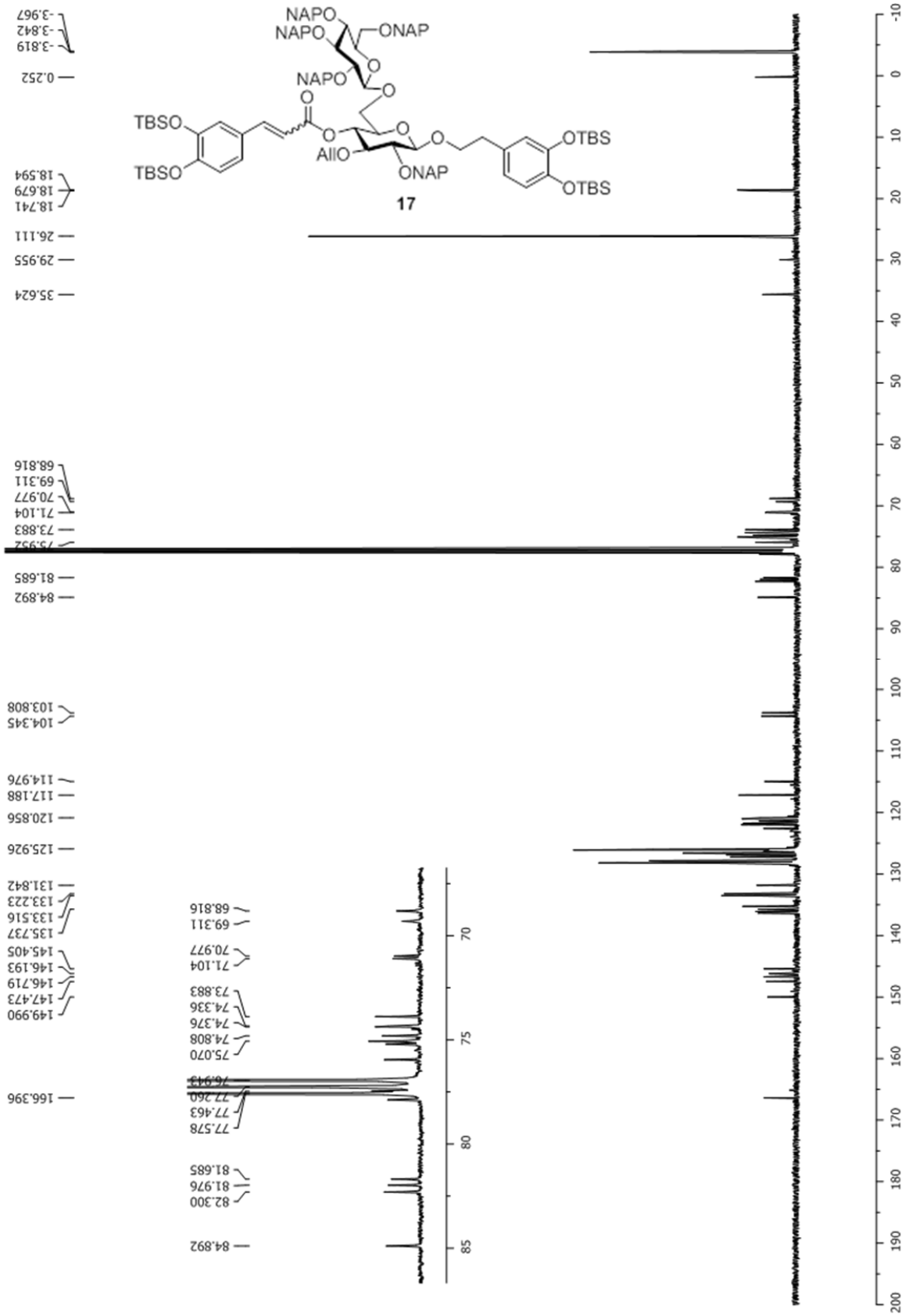

NAPO
NAPO
ONAP
O
NAPO
O
HO
O
O
OTBS
AllO
ONAP
OTBS
16
36.51
48.49
48.66
48.83
49.00
49.17
56.44
64.68
71.82
72.45
75.05
77.93
104.55
111.58
115.25
116.14
116.47
124.24
127.64
130.58
130.90
147.07
149.34
150.62
156.74
169.06

NAPO
NAPO
ONAP
NAPO
TBSO
TBSO
AllO
ONAP
OTBS
OTBS
17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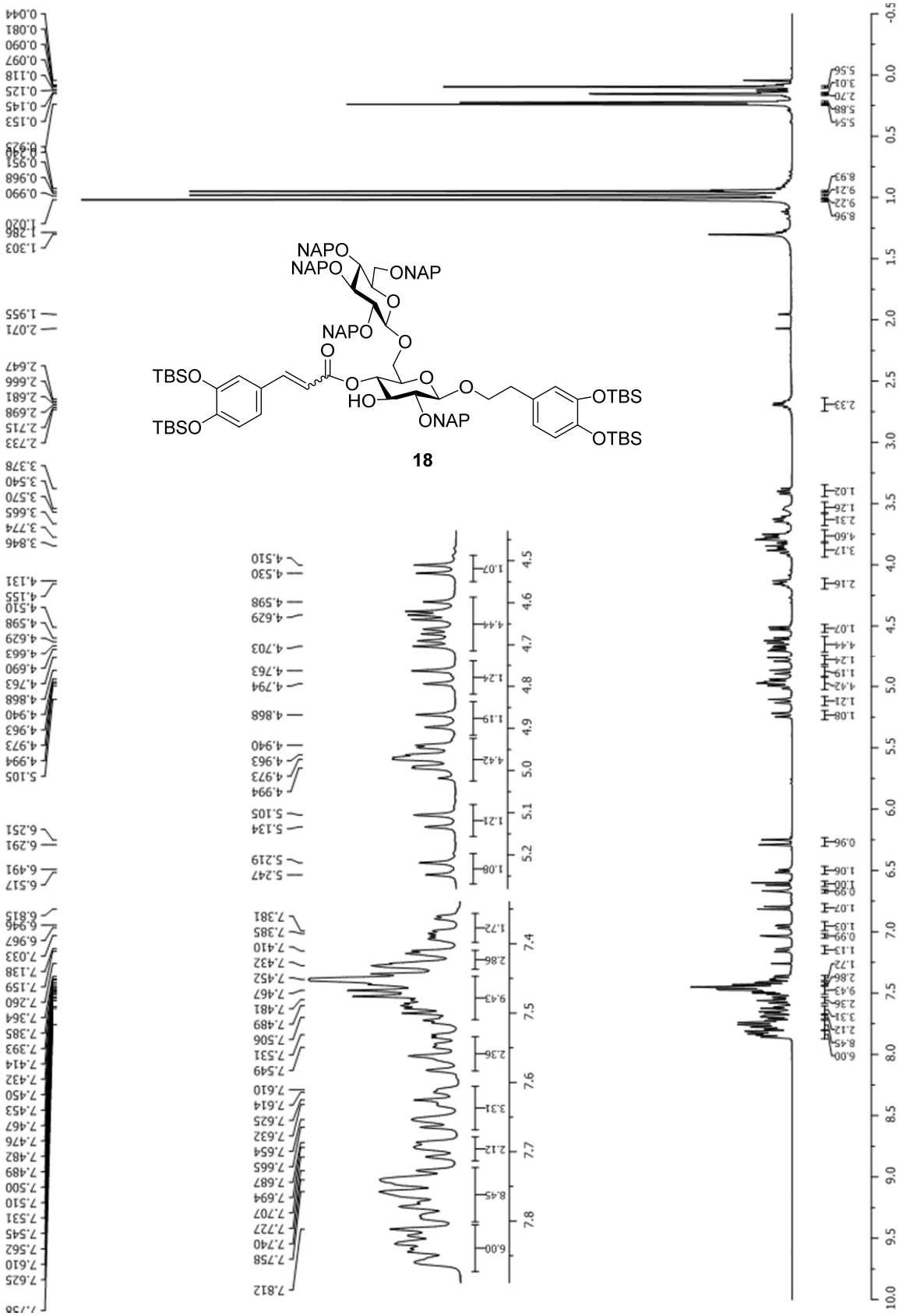
ONAP
NAPO
O
TBSO
TBSO
O
O
AllO
ONAP
O
OTBS
OTBS
17



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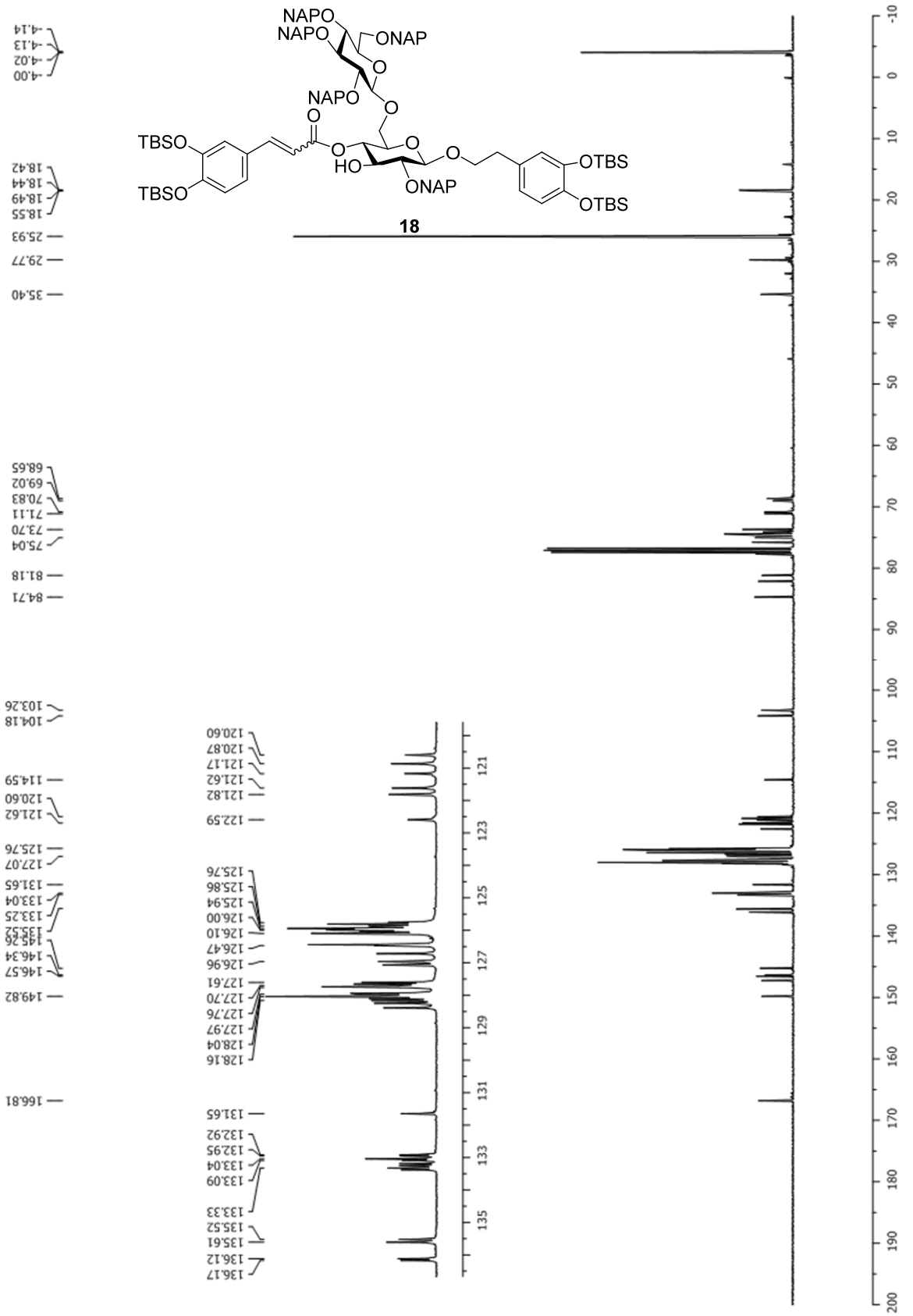
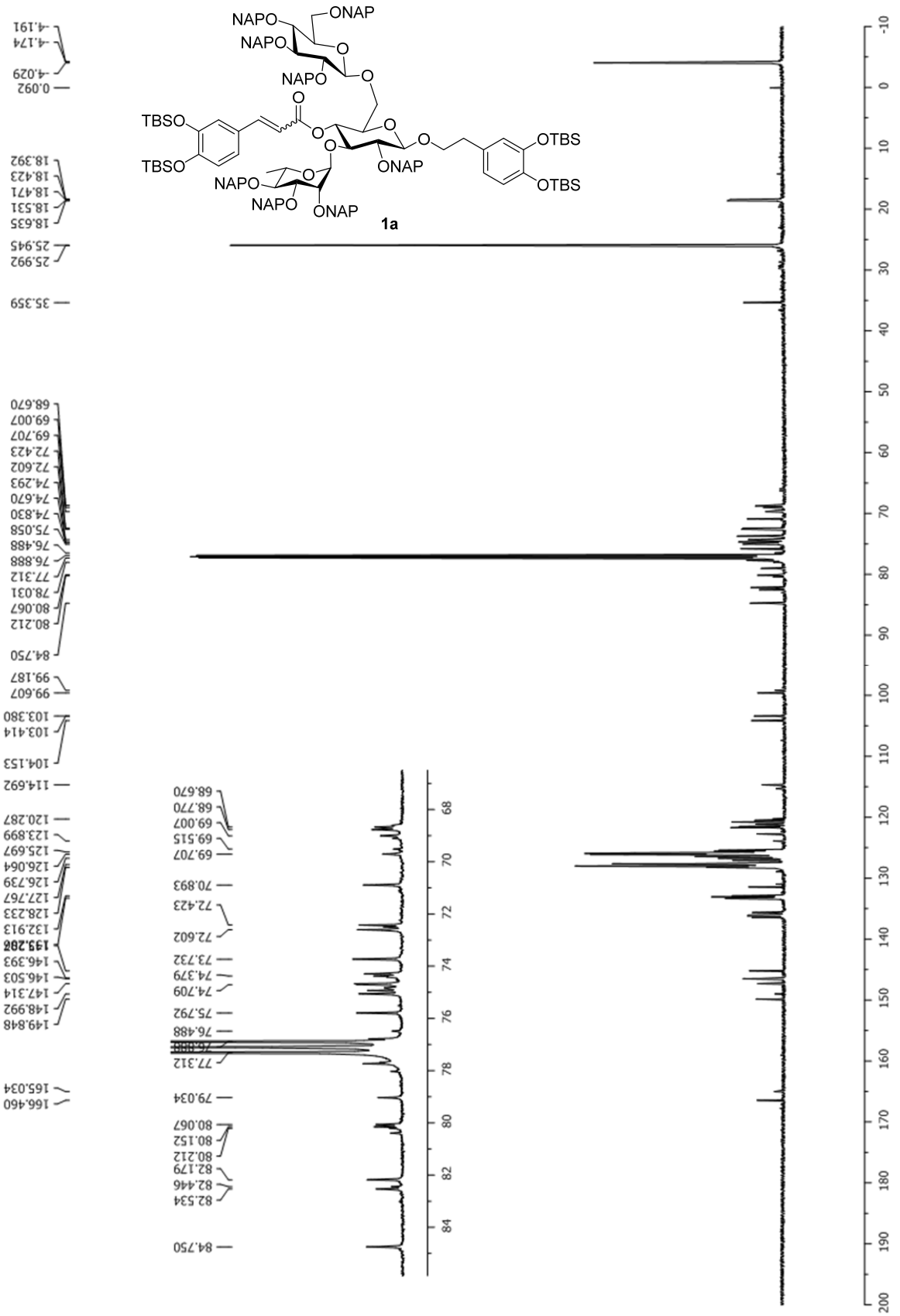

NAPO
NAPO
ONAP
O
NAPO
O
O
TBSO
TBSO
O
O
HO
O
O
ONAP
OTBS
OTBS
18

1a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NAPO
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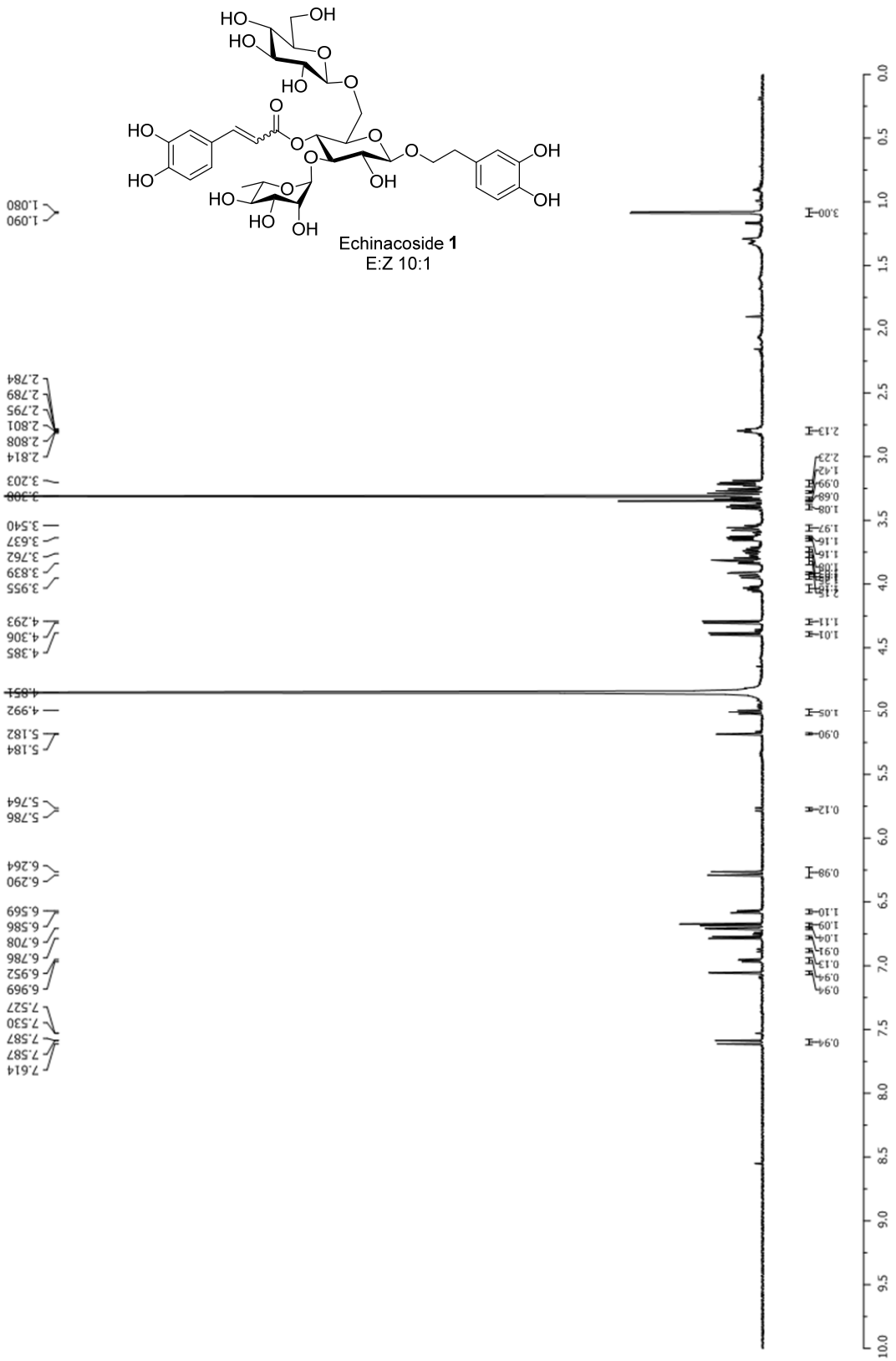
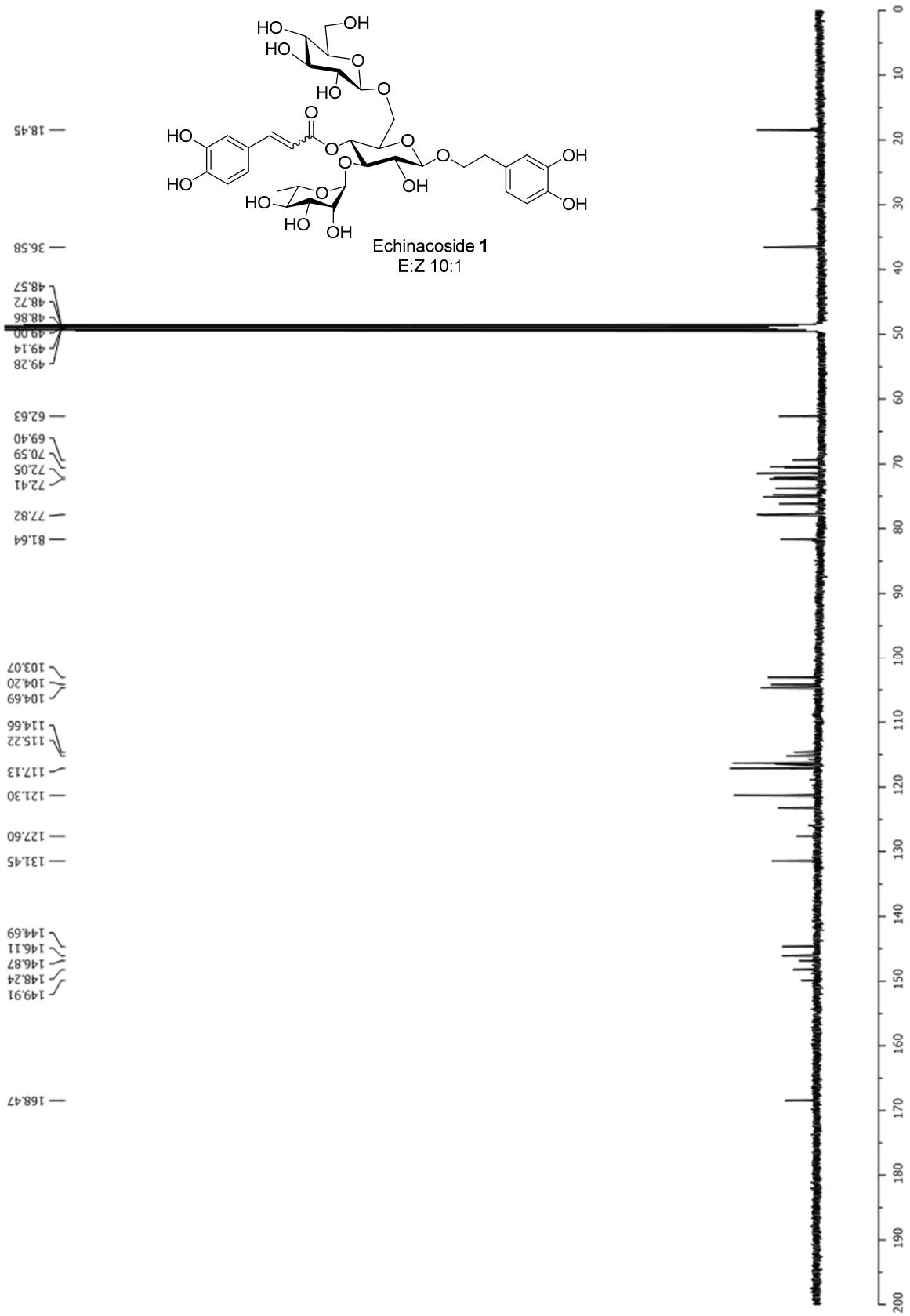
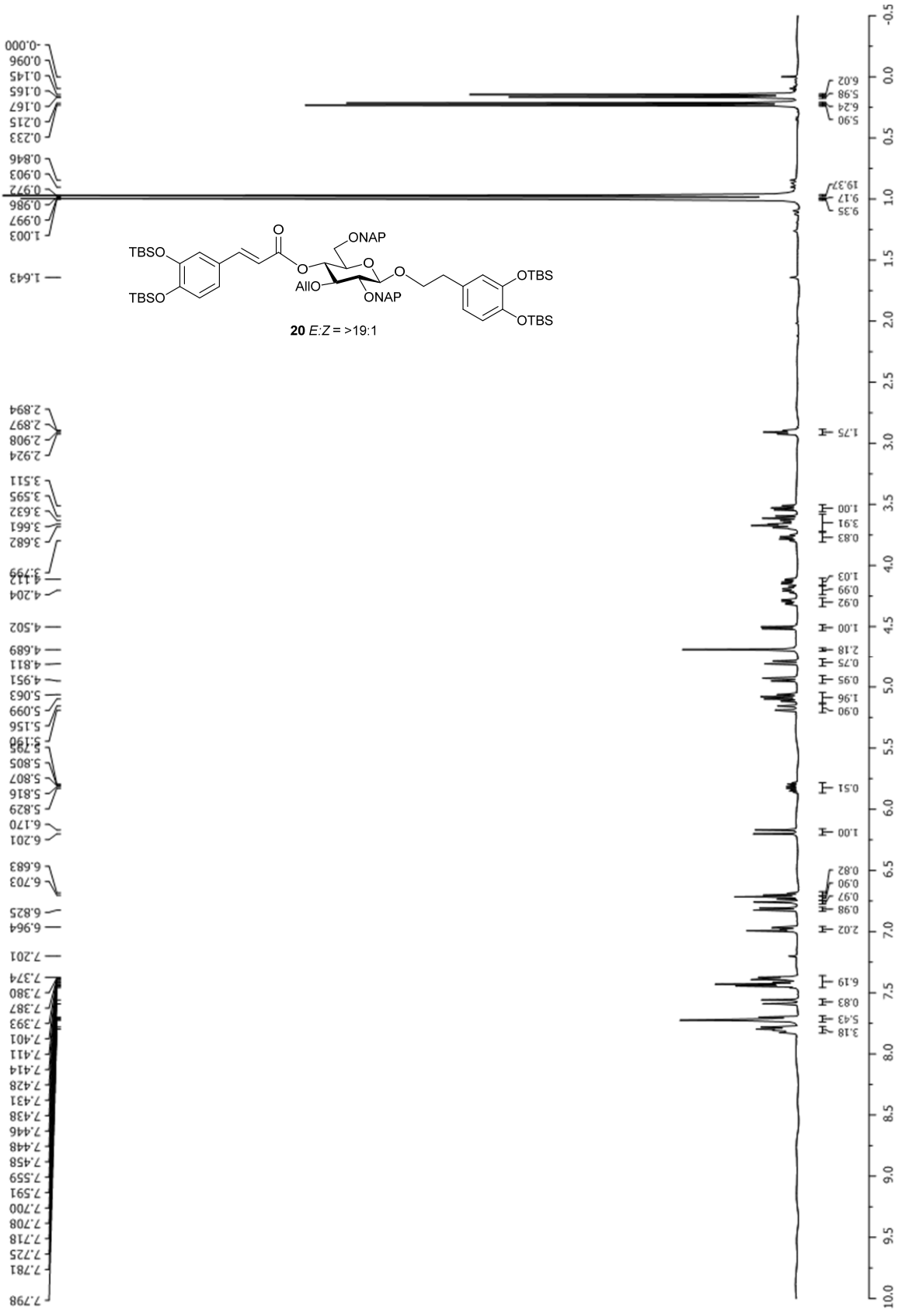
TBSO
OTBS
OTBS
ONAP
NAPO
NAPO
ONAP
1a


Echinacoside 1
E:Z 10:1


Echinacoside 1
E:Z 10:1

ONAP
HO
AllO
O
O
ONAP
OTBS
OTBS
19

ONAP
HO
O
O
AllO
ONAP
OTBS
OTBS
19



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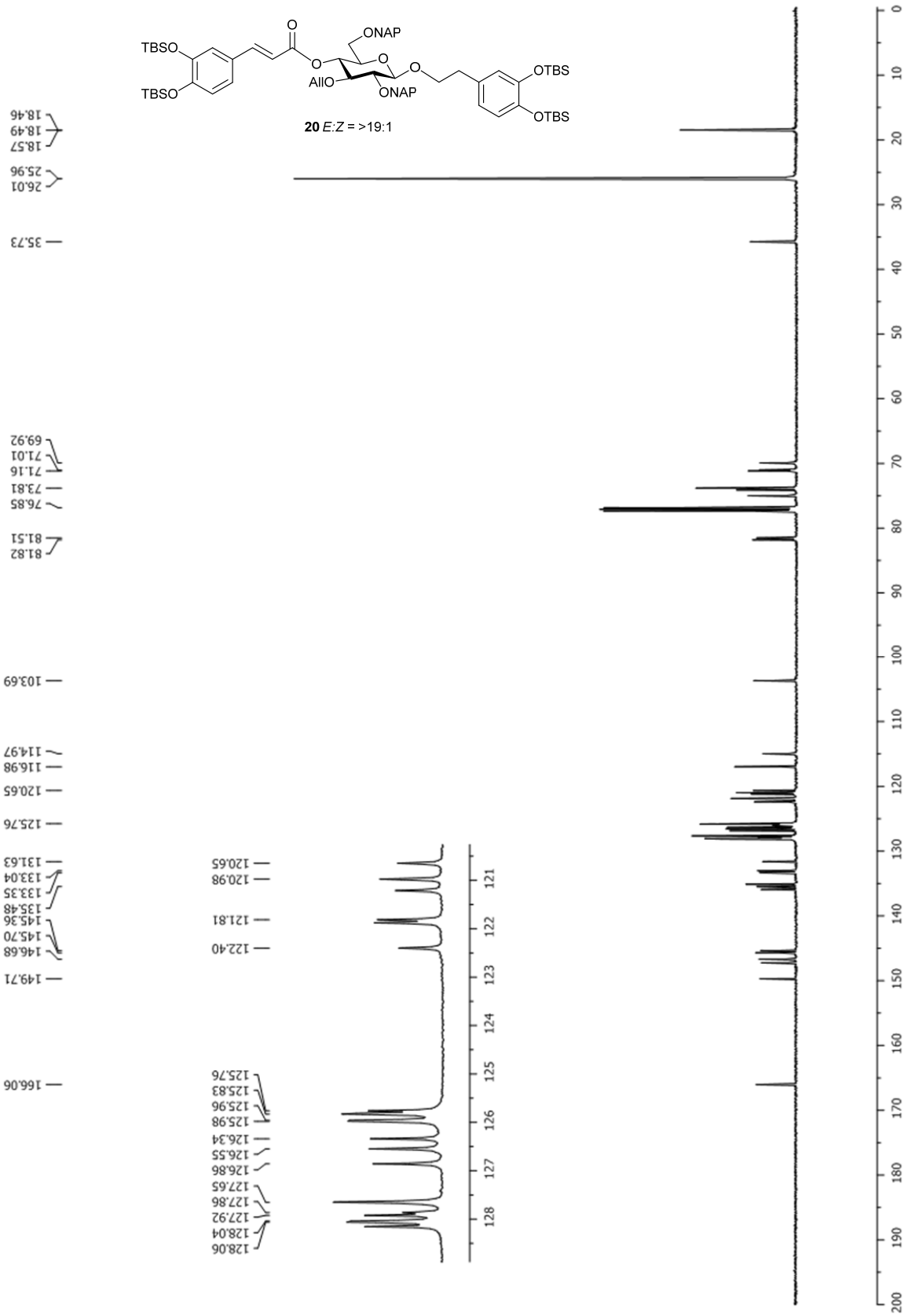
TBSO
TBSO
O
O
ONAP
O
AllO
ONAP
O
OTBS
OTBS
20 E:Z = >19:1
18.46
18.49
18.57
25.96
26.01
35.73
69.92
71.01
71.16
73.81
76.85
81.51
81.82
103.69
114.97
116.98
120.65
125.76
131.63
133.04
133.35
135.48
145.36
145.70
146.68
149.71
166.06
120.65
120.98
121.81
122.40
125.76
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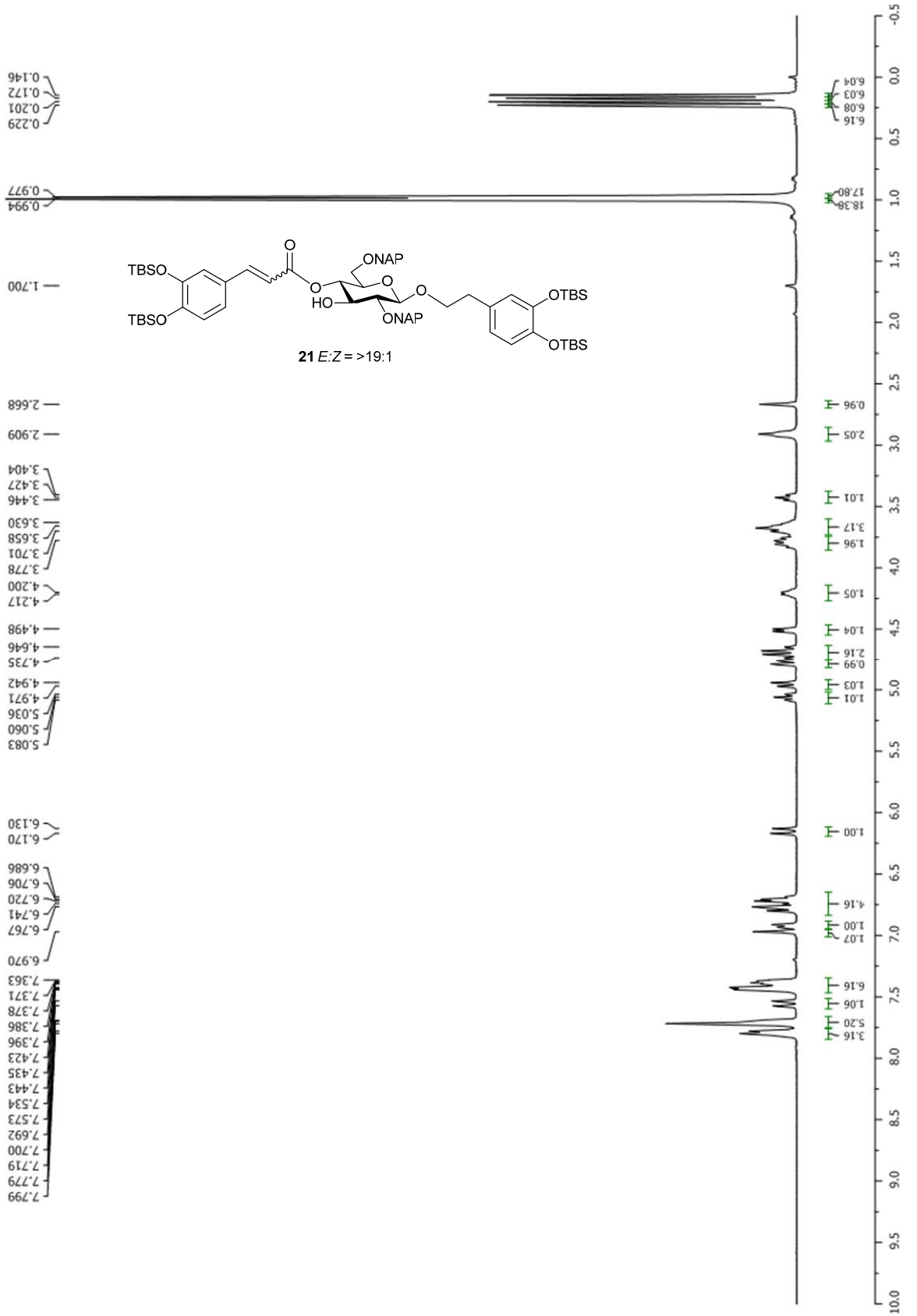
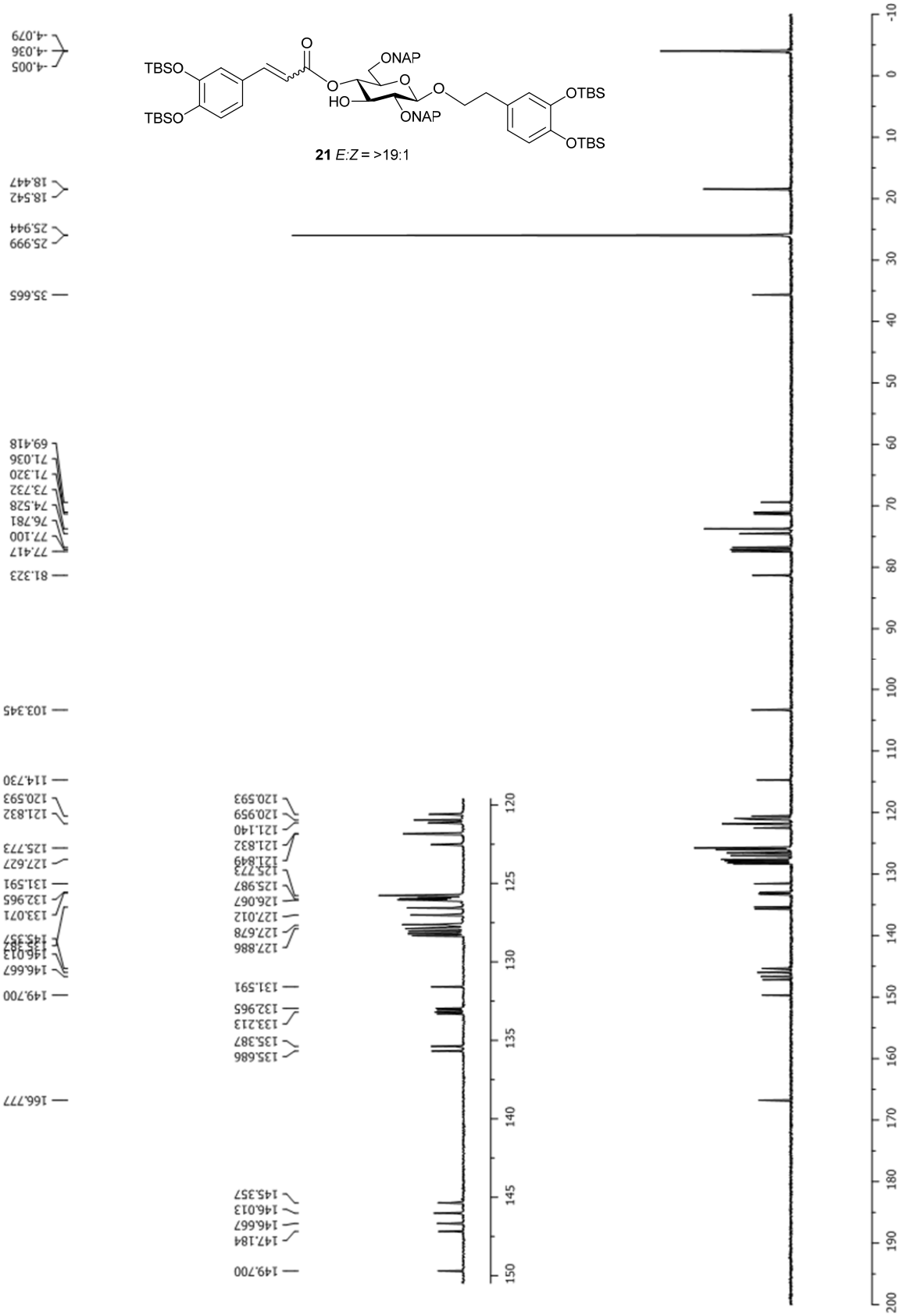
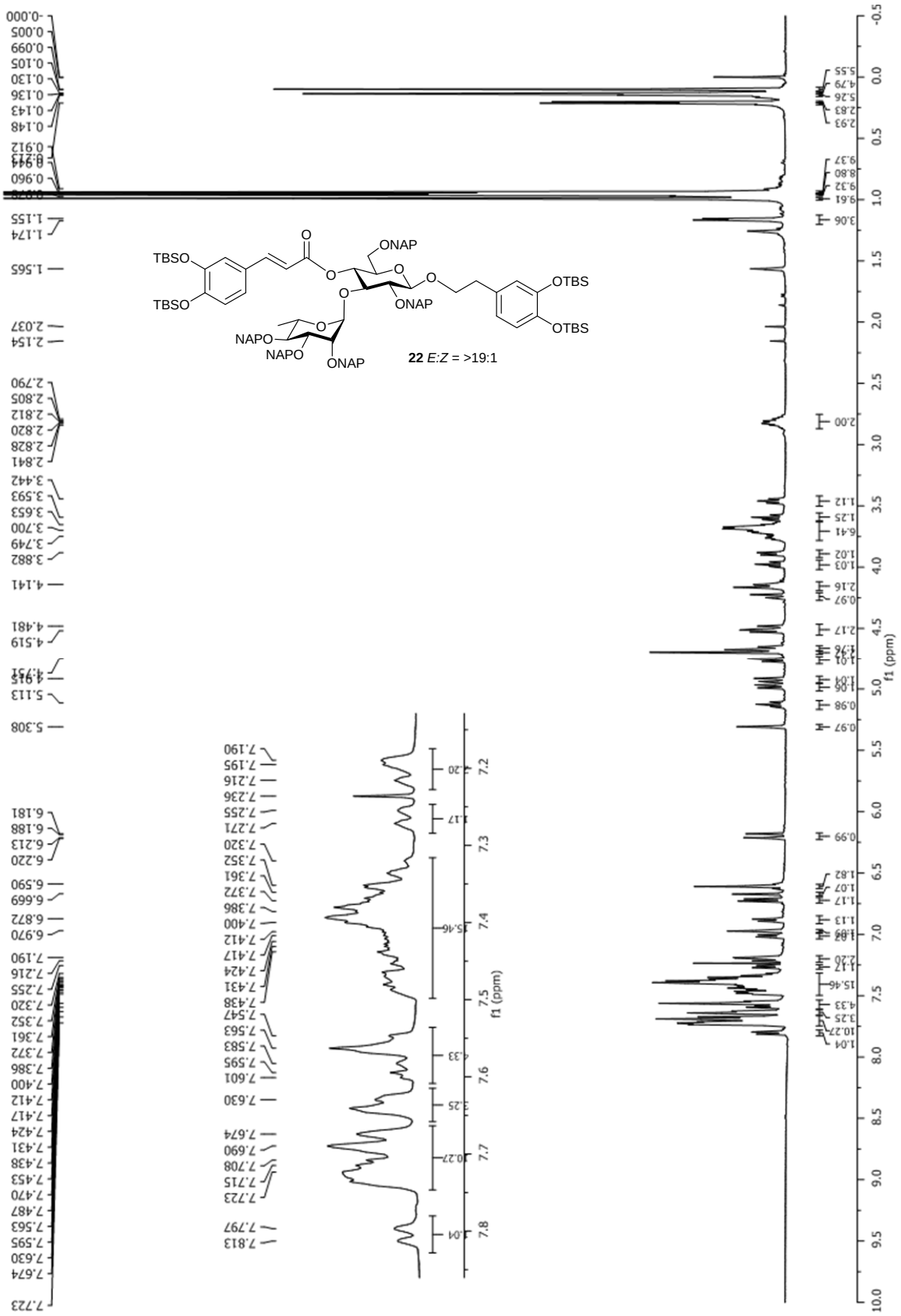
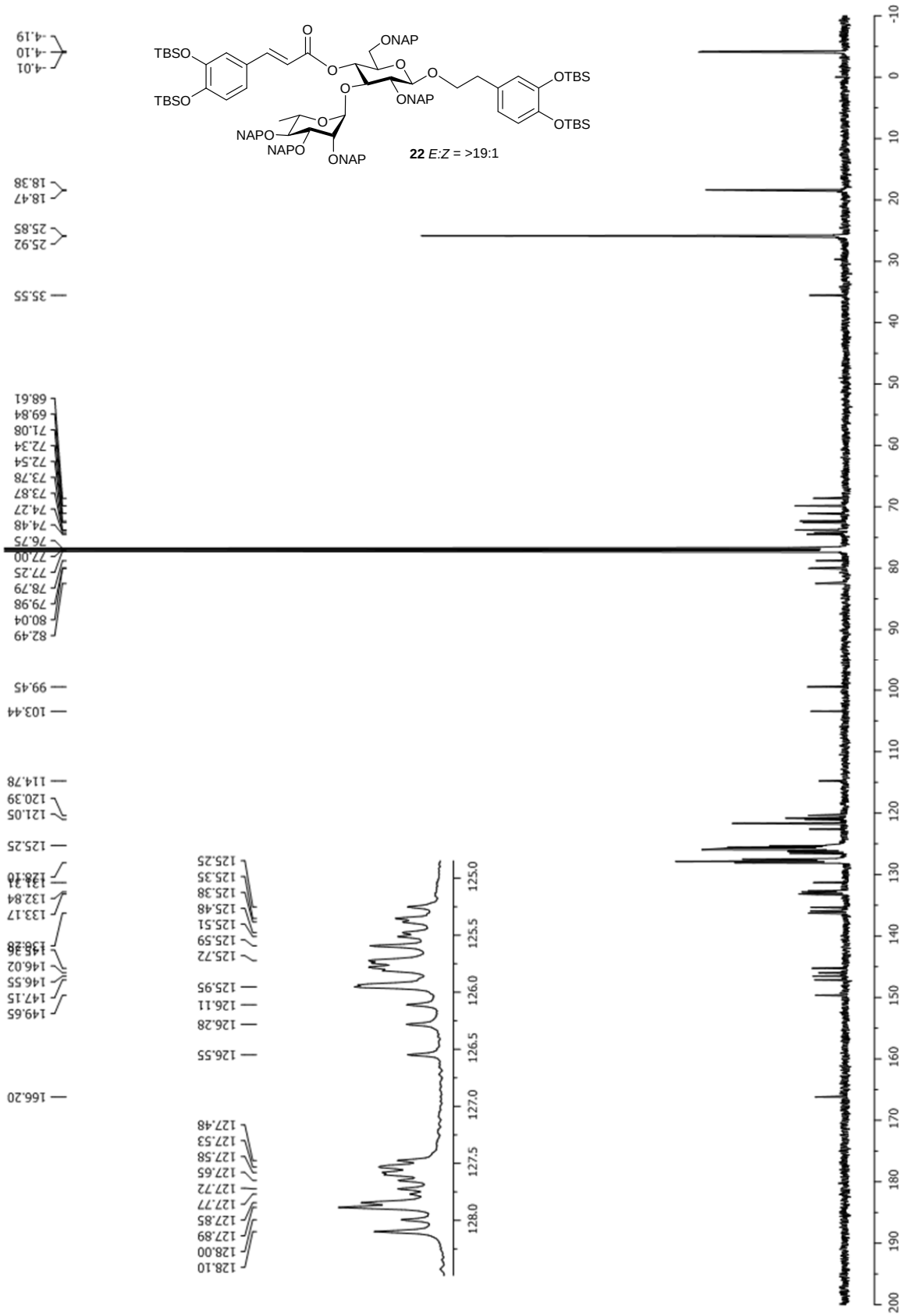
127.65
127.86
127.92
128.04
128.06



21 *E*:*Z* = >19:1


TBSO
TBSO
O
ONAP
O
O
HO
ONAP
O
OTBS
OTBS
21 E:Z = >19:1


TBSO
TBSO
ONAP
NAPO
NAPO
ONAP
OTBS
OTBS
22 E:Z = >19:1
f1 (ppm)


TBSO
TBSO
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ONAP
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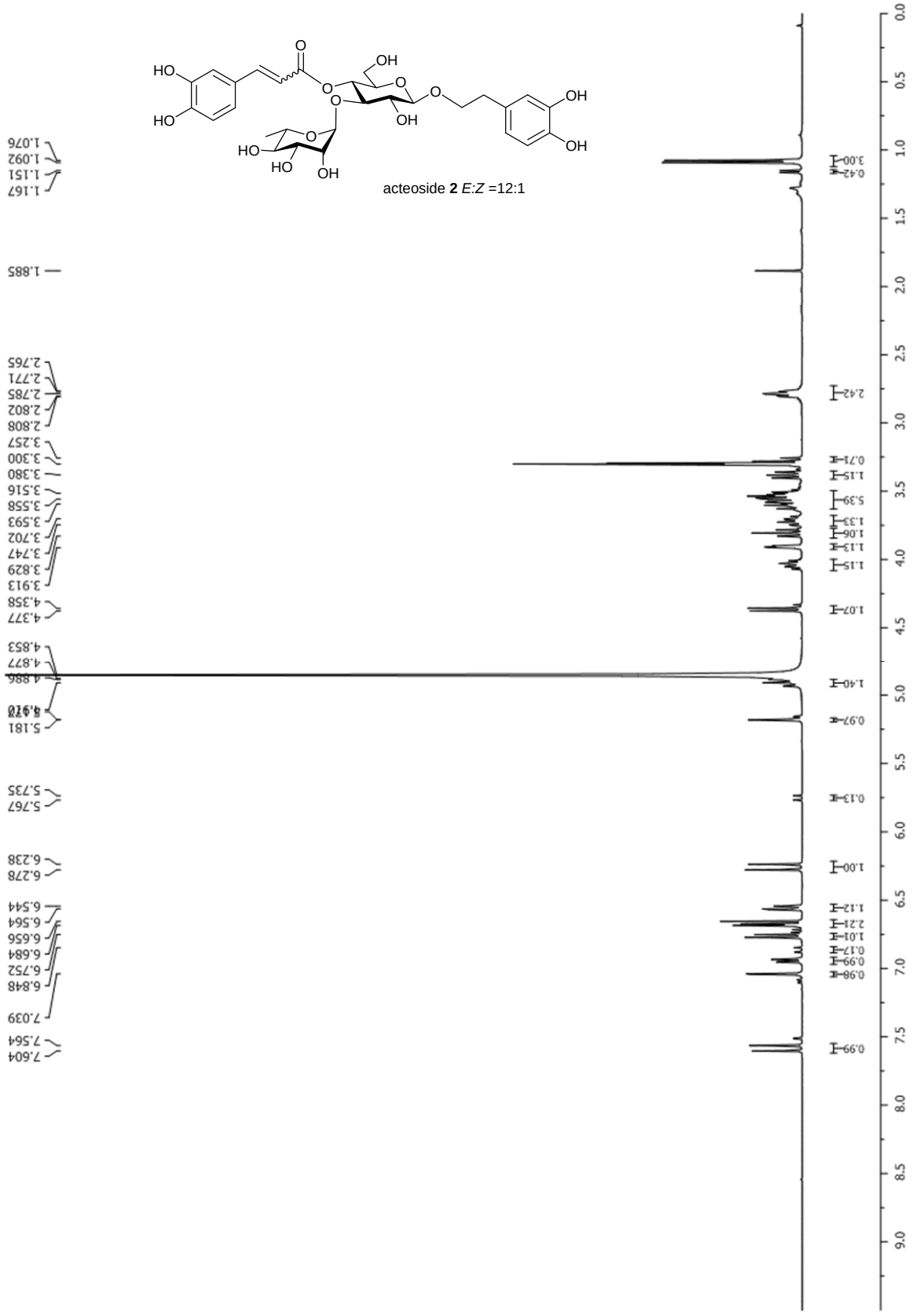
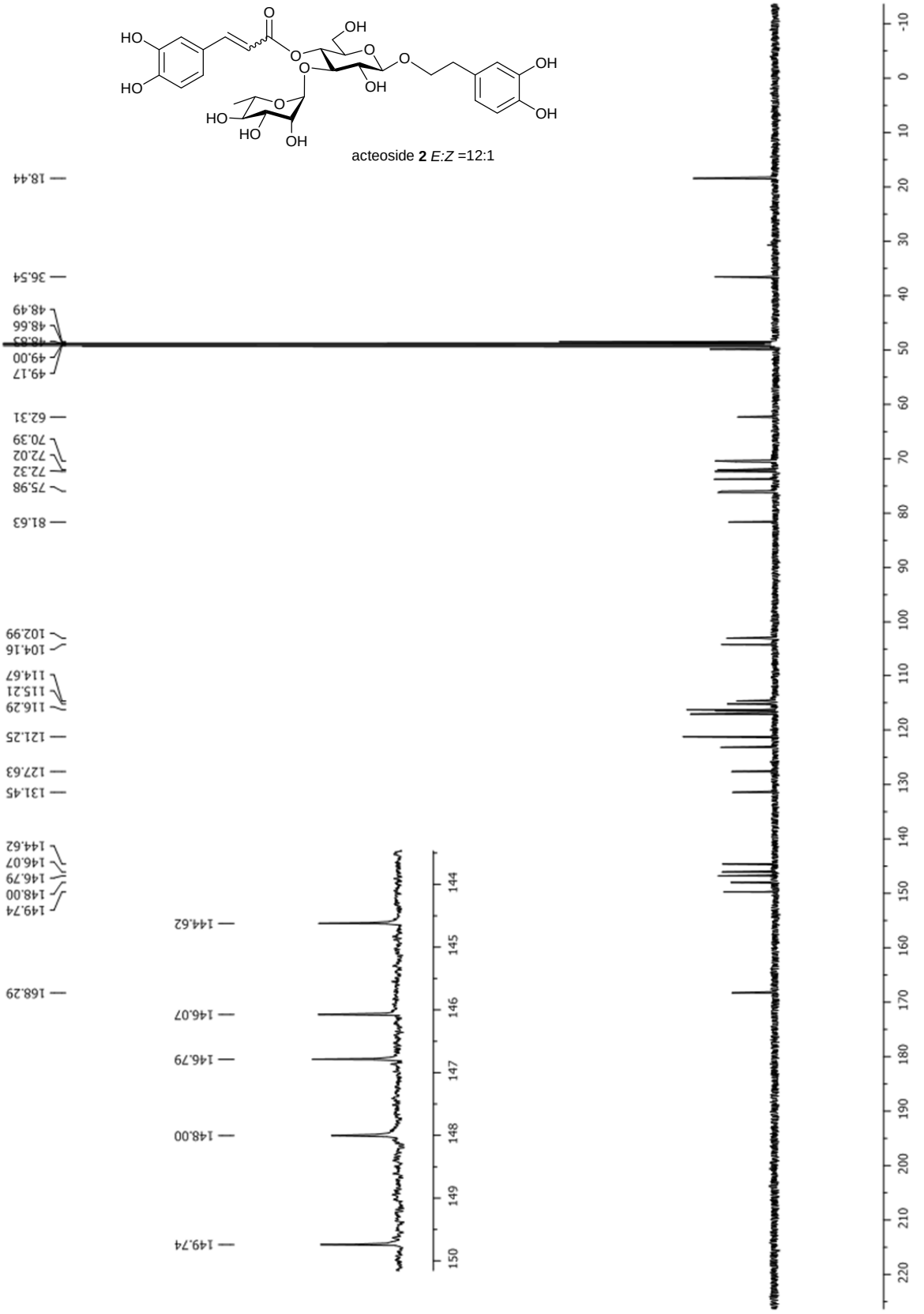
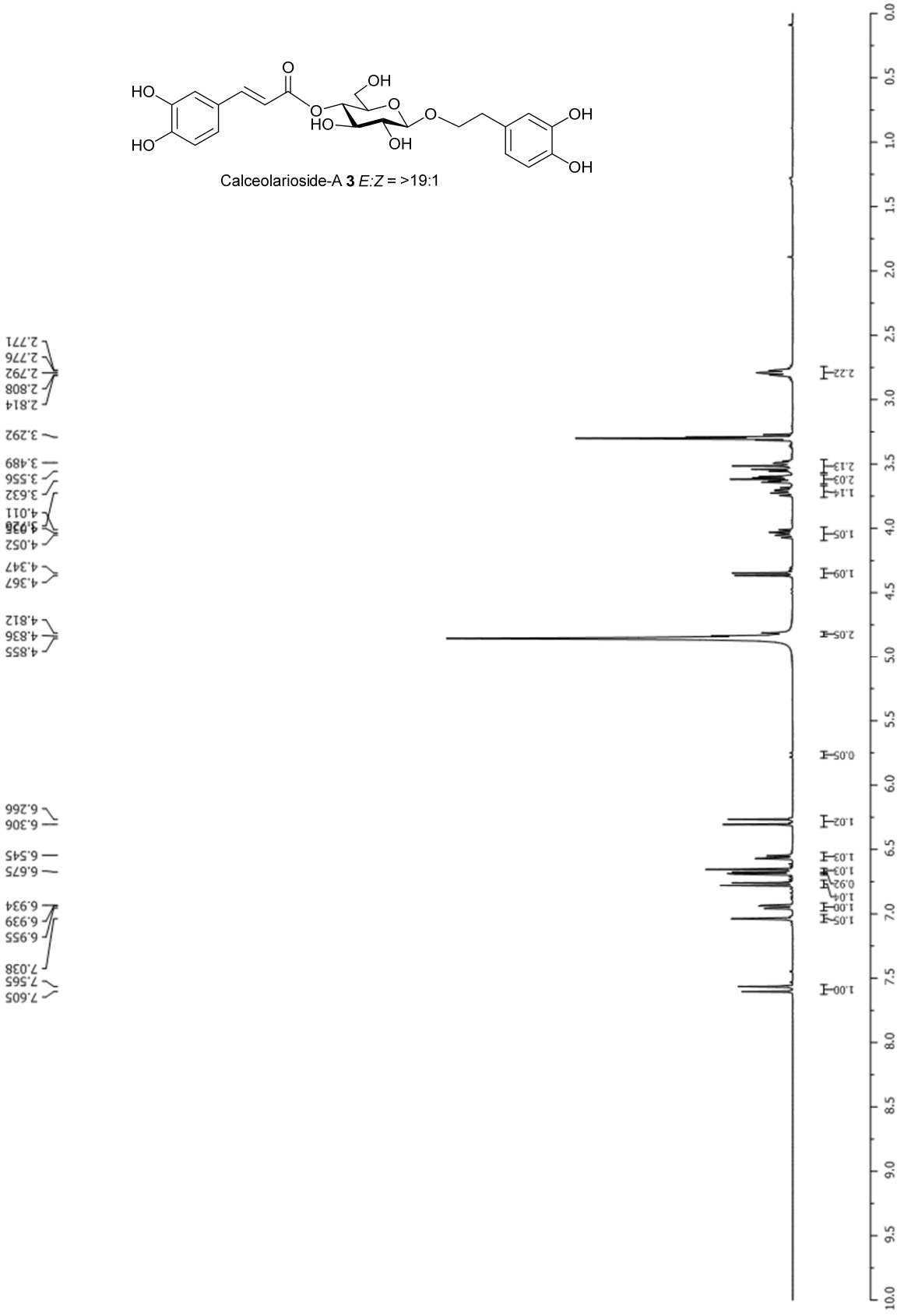
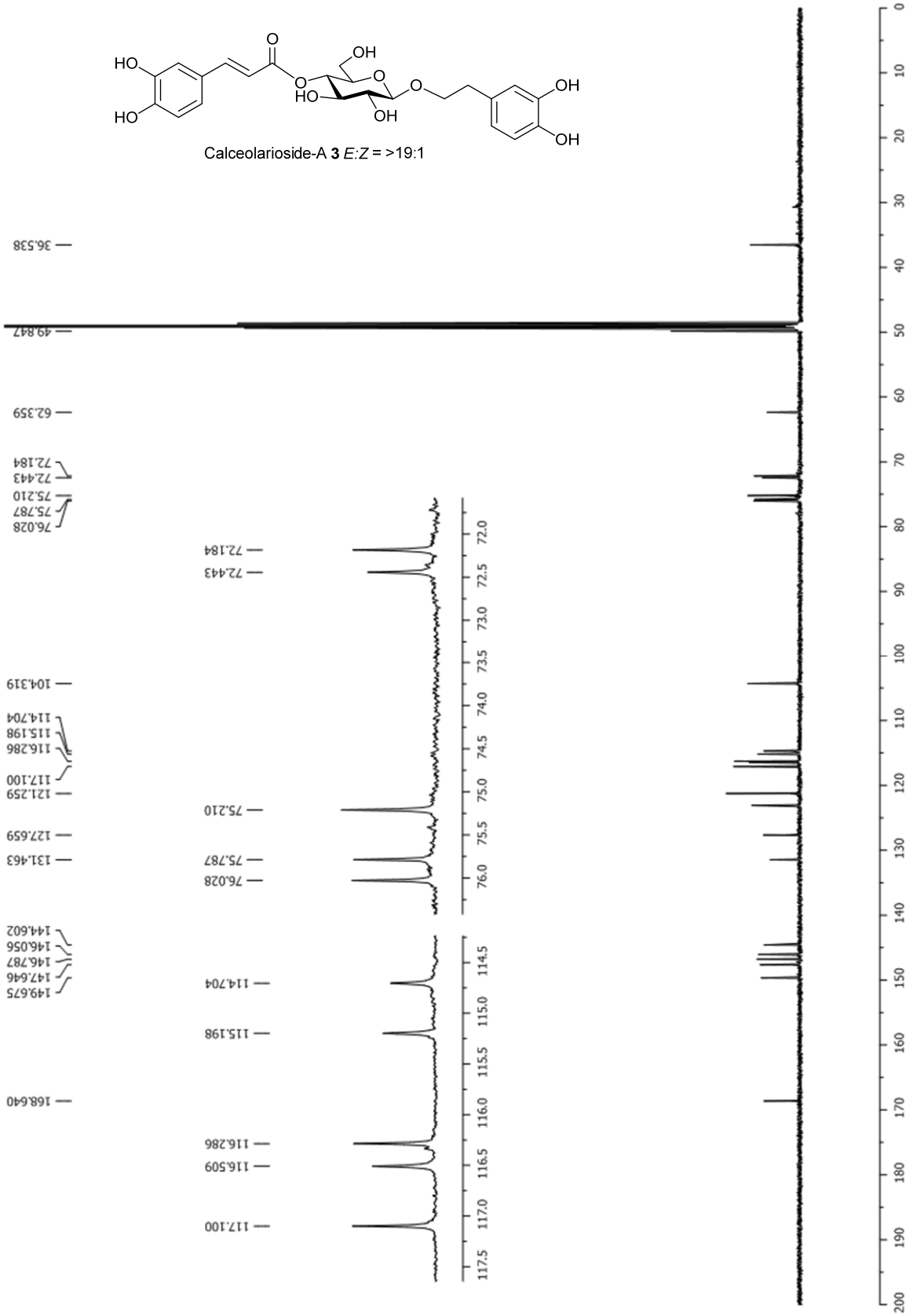
O
O
O
ONAP
OTBS
OTBS
O
NAPO
NAPO
ONAP
22 E:Z = >19:1


HO
HO
O
O
OH
O
O
OH
O
OH
HO
HO
OH
OH
acteoside **2** *E:Z* =12:1

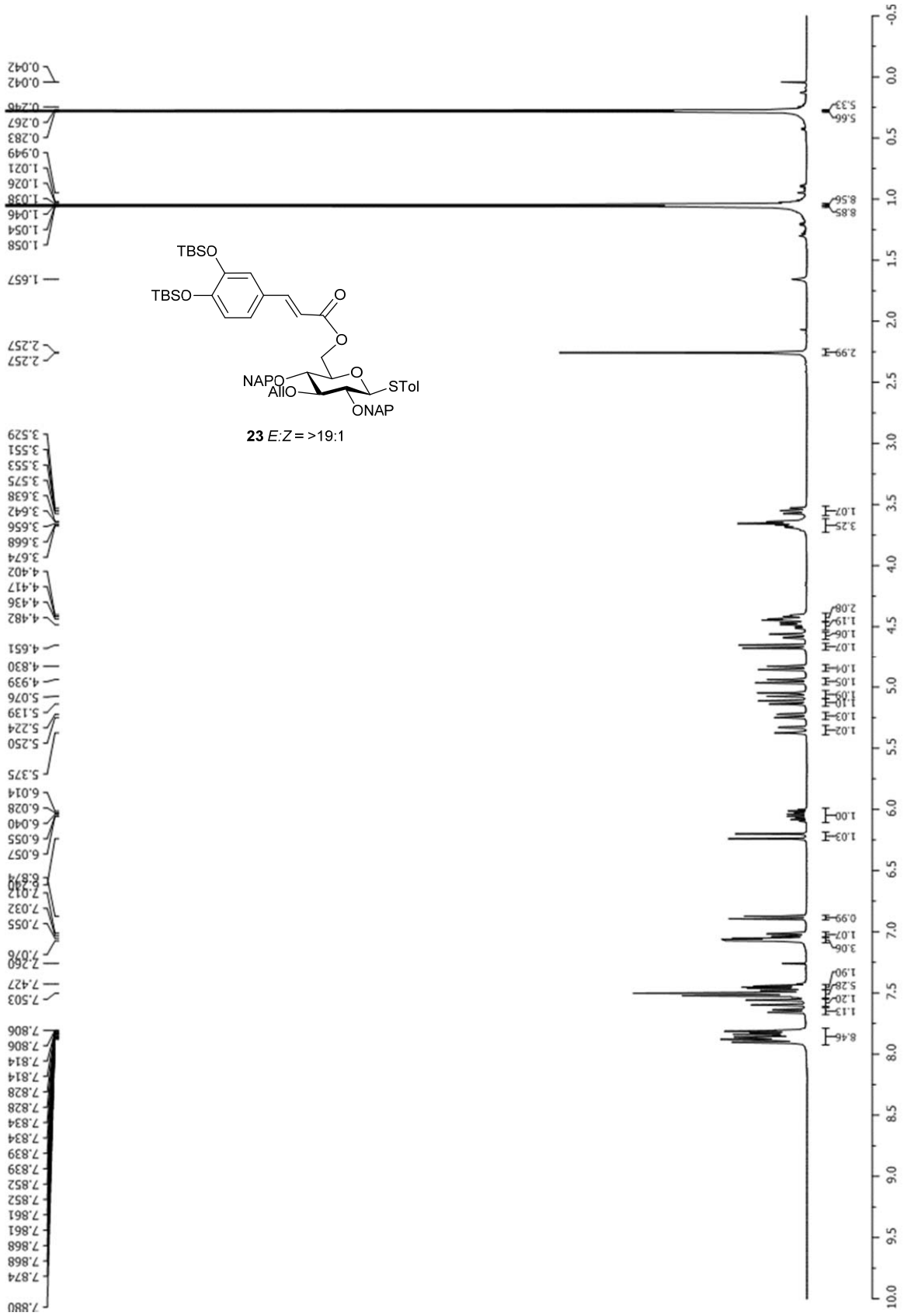

HO
HO
O
O
OH
O
O
O
OH
HO
HO
O
OH
OH
OH
acteoside **2** *E*:*Z* =12:1
18.44
36.54
48.49
48.66
48.83
49.00
49.17
62.31
70.39
72.02
72.32
75.98
81.63
102.99
104.16
114.67
115.21
116.29
121.25
127.63
131.45
144.62
146.07
146.79
148.00
149.74
168.29



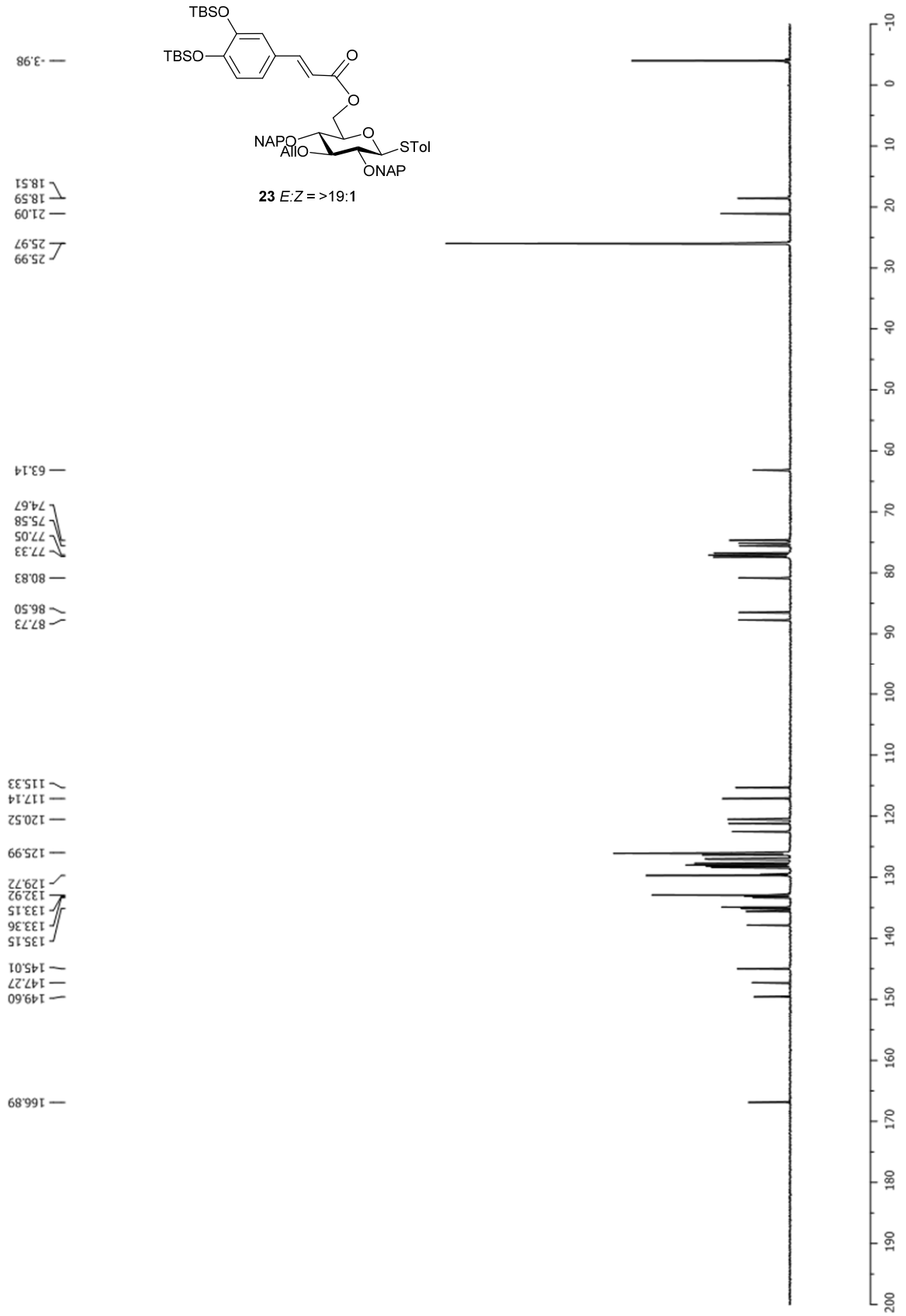
Calceolarioside-A **3** *E*:*Z* = >19:1

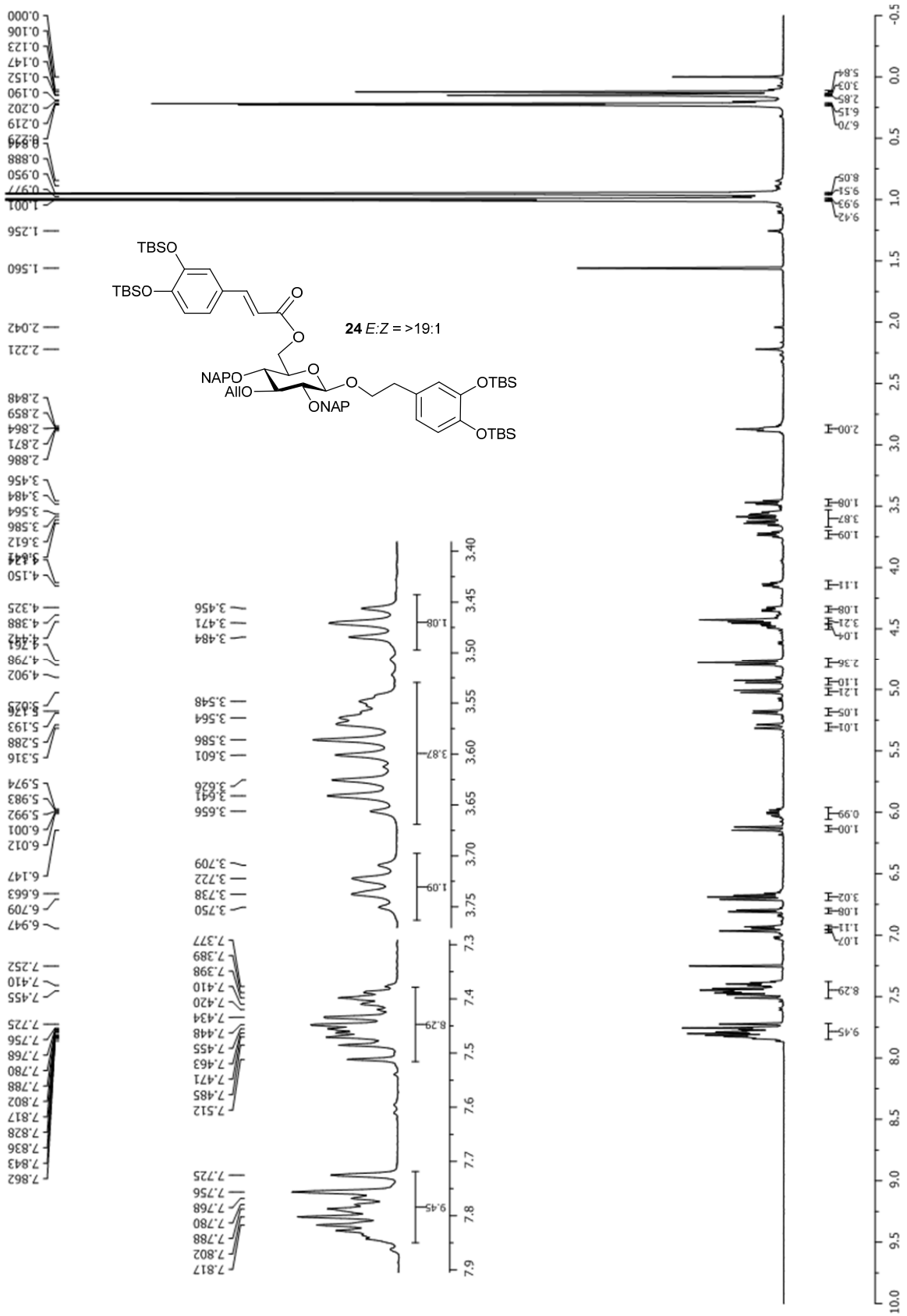


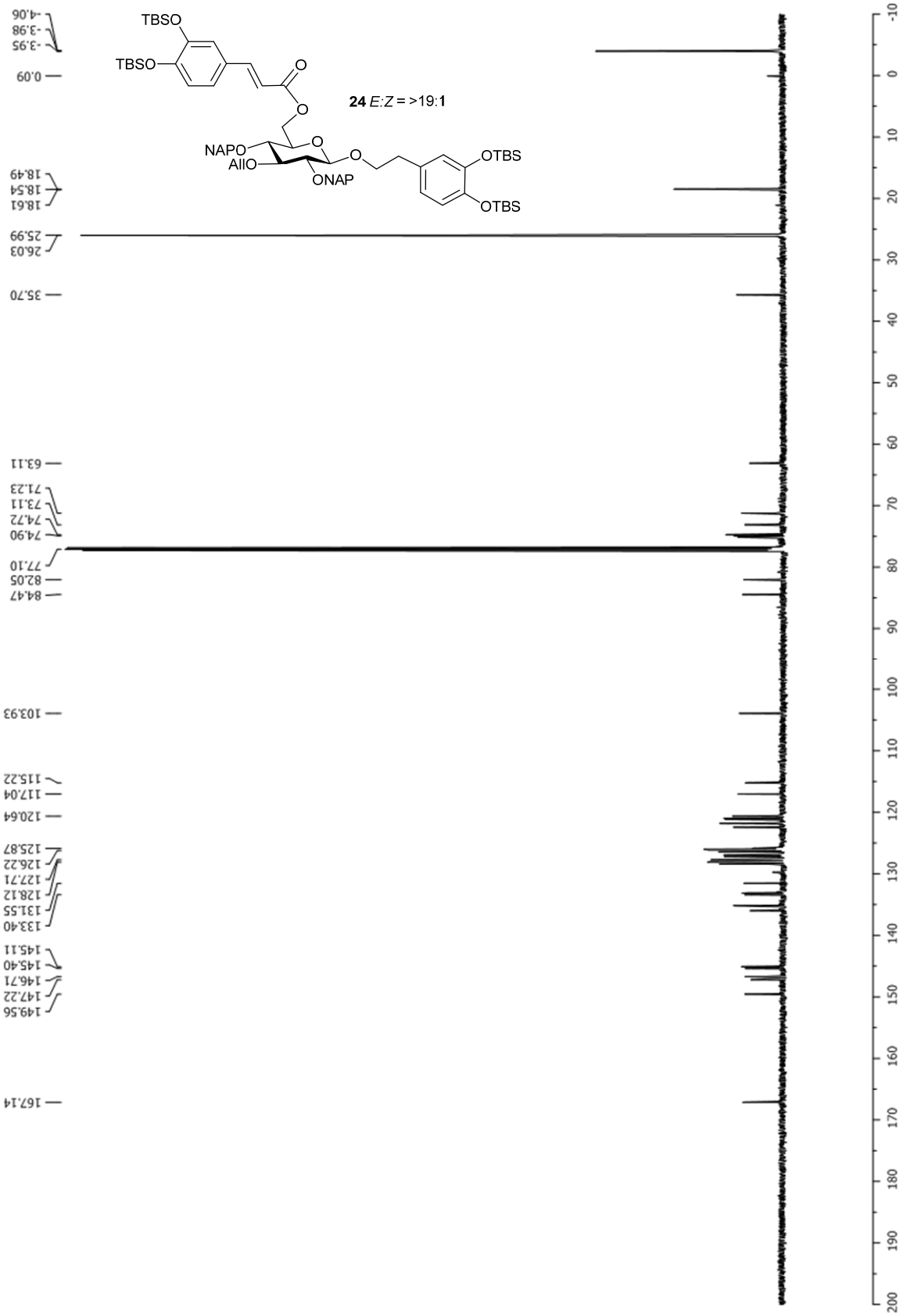
Calceolarioside-A **3** *E:Z* = >19:1

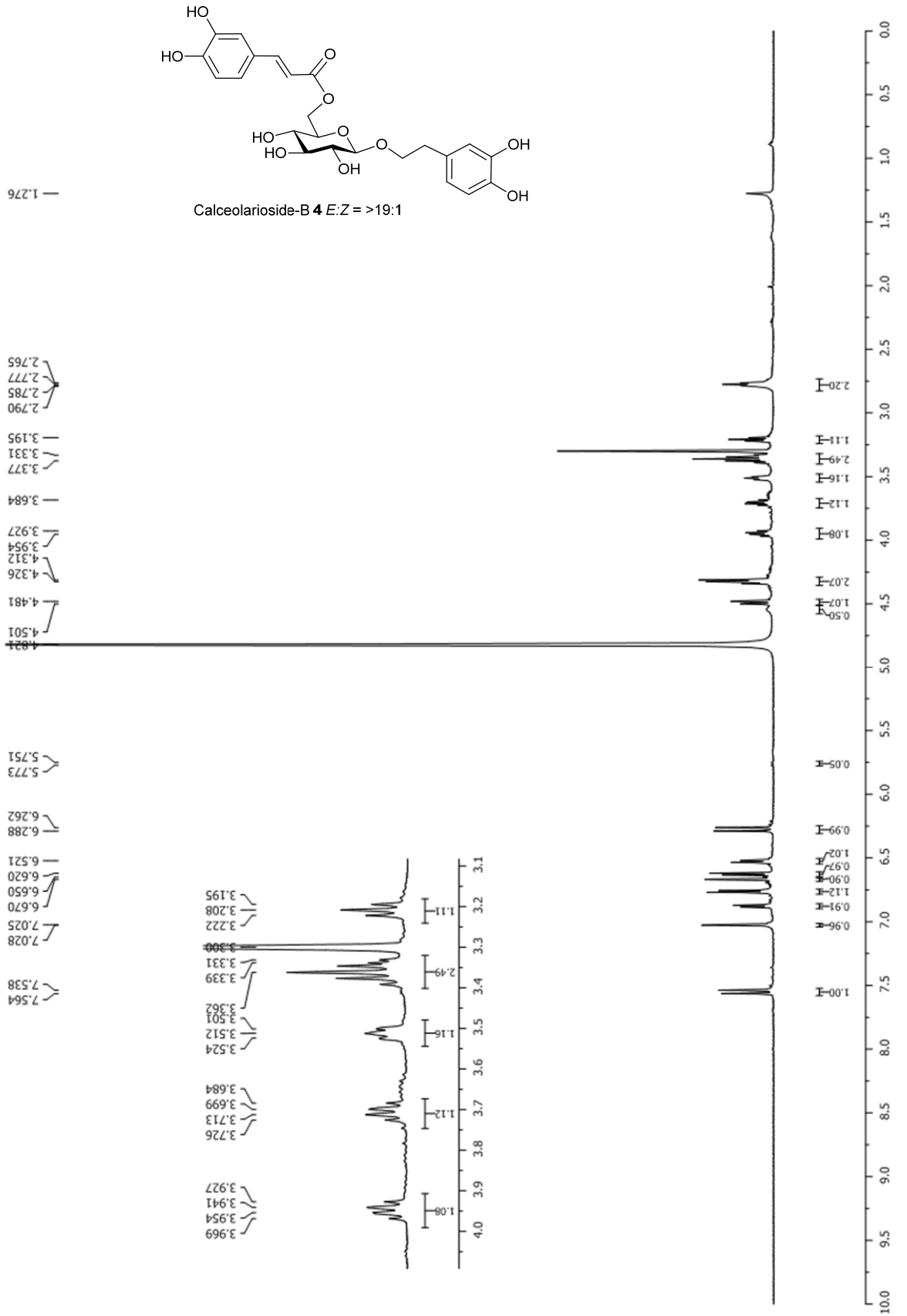


23 *E:Z* = >19:1

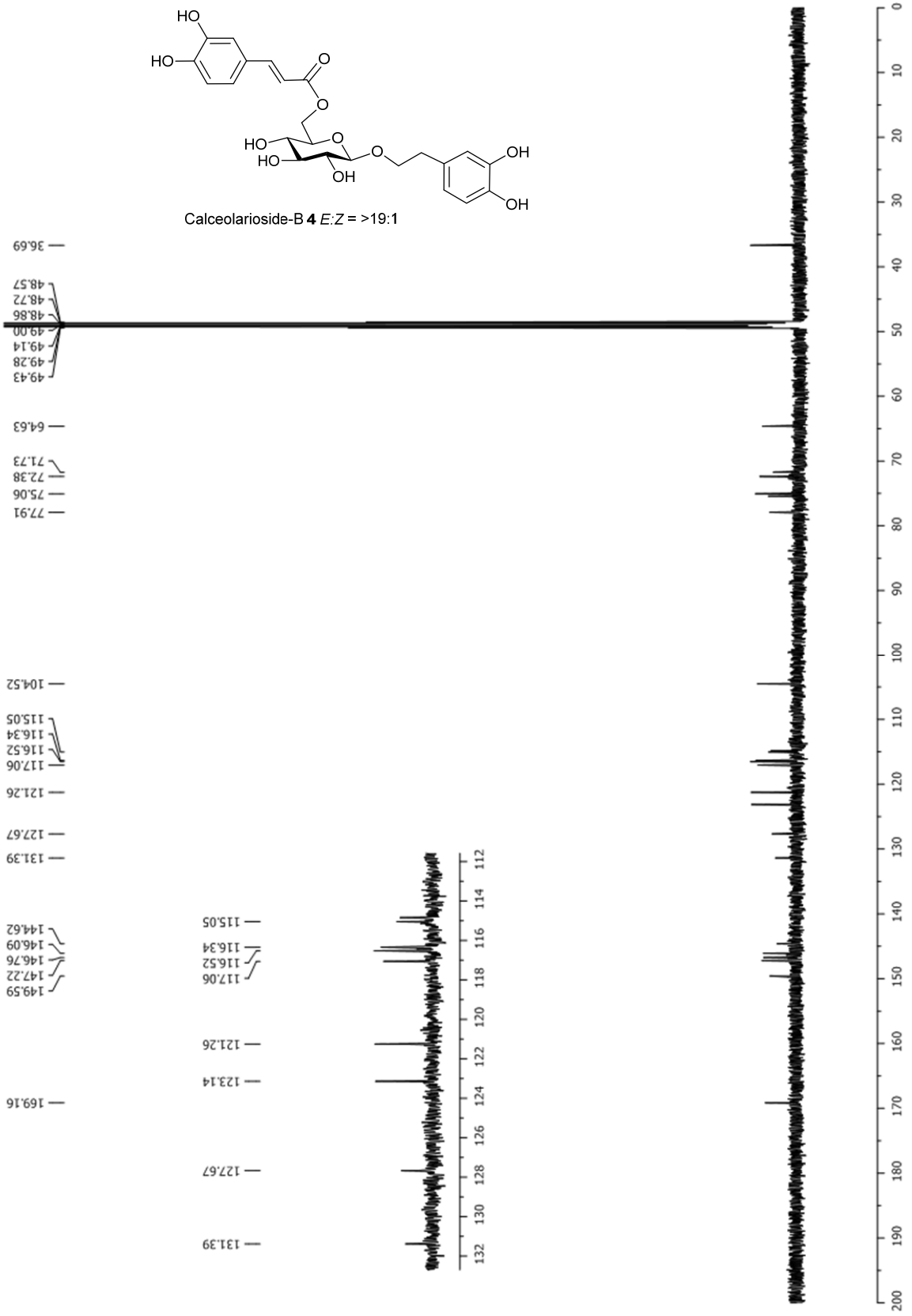

TBSO
TBSO
O
O
O
NAPO
AllO
STol
ONAP
23 E:Z = >19:1
-3.98
18.51
18.59
21.09
25.97
25.99
63.14
74.67
75.58
77.05
77.33
80.83
86.50
87.73
115.33
117.14
120.52
125.99
129.72
132.92
133.15
133.36
135.15
145.01
147.27
149.60
166.89


TBSO
TBSO
O
O
NAPO
AllO
O
ONAP
O
OTBS
OTBS
24 E:Z = >19:1


TBSO
TBSO
O
O
24 E:Z = >19:1
NAPO
AllO
O
O
ONAP
OTBS
OTBS
-4.06
-3.98
-3.95
0.09
18.49
18.54
18.61
25.99
26.03
35.70
63.11
71.23
73.11
74.72
74.90
77.10
82.05
84.47
103.93
115.22
117.04
120.64
125.87
126.22
127.71
128.12
131.55
133.40
145.11
145.40
146.71
147.22
149.56
167.14



Calceolarioside-B **4** *E*:*Z* = >19:**1**


HO
HO
O
O
HO
HO
O
O
OH
OH
OH
Calceolarioside-B 4 E:Z = >19:1
36.69
48.57
48.72
48.86
49.00
49.14
49.28
49.43
64.63
71.73
72.38
75.06
77.91
104.52
115.05
116.34
116.52
117.06
121.26
127.67
131.39
144.62
146.09
146.76
147.22
149.59
169.16

References:

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S2. D. E. Bogucki, J. L. Charlton, *Can. J. Chem.* **1997**, *75*, 1783-1794.

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