SUPPORTING INFORMATION

Versatile Strategy for the Divergent Synthesis of Linear Oligosaccharide Domain Variants of *Quillaja* Saponin Vaccine Adjuvants

Alberto Fernández-Tejada,[a,*] Derek S. Tan,[a,b,*] and David Y. Gin[a,b,¥]

[a]*Chemical Biology Program and* [b]*Tri-Institutional Research Program*
Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, New York 10065

¥Deceased March 22, 2011.

TABLE OF CONTENTS

A. MATERIAL AND METHODS

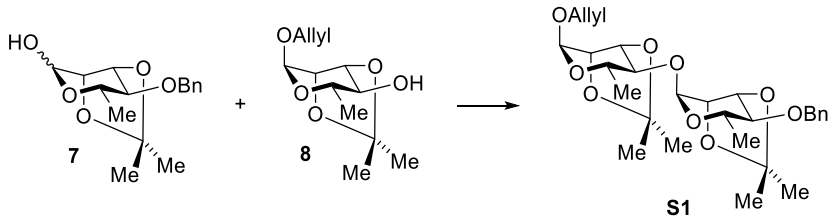
General Procedures. Reactions were performed in flame-dried sealed-tubes or modified Schlenk (Kjeldahl shape) flasks fitted with a glass stopper under a positive pressure of argon, unless otherwise noted. Air- and moisture-sensitive liquids and solutions were transferred via syringe. The appropriate carbohydrate reagents were dried via azeotropic removal of water with toluene. Molecular sieves were activated at 350 °C and were crushed immediately prior to use, then flame-dried under vacuum. Organic solutions were concentrated by rotary evaporation below 30 °C. Flash column chromatography was performed employing 230–400 mesh silica gel. Thin-layer chromatography was performed using glass plates pre-coated to a depth of 0.25 mm with 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm).

Materials. Dichloromethane, tetrahydrofuran, diethyl ether, and toluene were purified by passage through two packed columns of neutral alumina under an argon atmosphere.[1] Triethylamine and boron trifluoride diethyl etherate were distilled from calcium hydride at 760 Torr under N_2. All other chemicals were obtained from commercial vendors and were used without further purification unless noted otherwise.

Instrumentation. Infrared (IR) spectra were obtained using a Perkin Elmer Spectrum BX spectrophotometer or a Bruker Tensor 27. Data are presented as the frequency of absorption (cm^{-1}). Proton and carbon-13 nuclear magnetic resonance (^{1}H NMR and ^{13}CNMR) spectra were recorded on a Bruker Avance III instrument; chemical shifts are expressed in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual proton in the NMR solvent ($CDCl_3$: δ 7.26 for ^{1}H NMR, δ 77.00 for ^{13}C NMR; C_6D_6: δ 7.16 for ^{1}H NMR, δ 128.06 for ^{13}C NMR; CD_3OD: δ 3.31 for ^{1}H NMR, δ 49.15 for ^{13}C NMR). Data are presented as follows: chemical shift, multiplicity (s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet and/or multiple resonances), coupling constant in Hertz (Hz), integration. RP-HPLC purification and analyses were carried out on a Waters 2545 binary gradient HPLC system equipped with a Waters 2996 photodiode array detector, and absorbances were monitored at wavelengths of 210–600 nm.

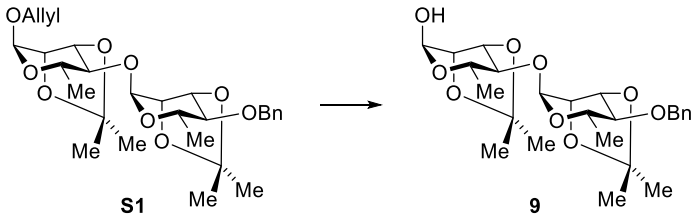
B . SYNTHESIS OF LINEAR OLIGOSACCHARIDE DOMAIN VARIANTS

1. SYNTHESIS OF DIRHAMNOSE VARIANT 4 (SQS-1-0-10-18)



***O*-Allyl 4-*O*-benzyl-2,3-di-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-isopropylidene-L-rhamnopyranoside (S1).** Trifluoromethanesulfonic anhydride (307 μL, 1.82 mmol, 2.0 equiv) was added to a solution of 4-*O*-benzyl-2,3-di-*O*-isopropylidene-L-rhamnopyranoside[2] (**7**) (268 mg, 0.91 mmol, 1.0 equiv), phenyl sulfoxide (737 mg, 3.64 mmol, 4.0 equiv) and 2,4,6-tri-*tert*-butylpyridine (1.13 g, 4.55 mmol, 5.0 equiv) in CH_2Cl_2 (33 mL) at –78 °C. The reaction was stirred at this temperature for 10 min and then transferred to a –45 °C bath for 90 min. After this time, a solution of *O*-allyl-2,3-di-*O*-isopropylidene-L-rhamnopyranoside[3] (**8**) (200 mg, 0.82 mmol, 0.9 equiv) in CH_2Cl_2 (3.0 mL) was added via cannula at –78 °C and the reaction temperature was slowly increased from –78 °C to −40 °C over 1 h and then to 21 ºC overnight. Triethylamine (1.0 mL) was then added to the reaction mixture, which was concentrated and purified by silica gel chromatography (hexanes to hexanes/ethyl acetate 4:1) to afford disaccharide **S1** (310 mg, 73% yield) as a white foam.

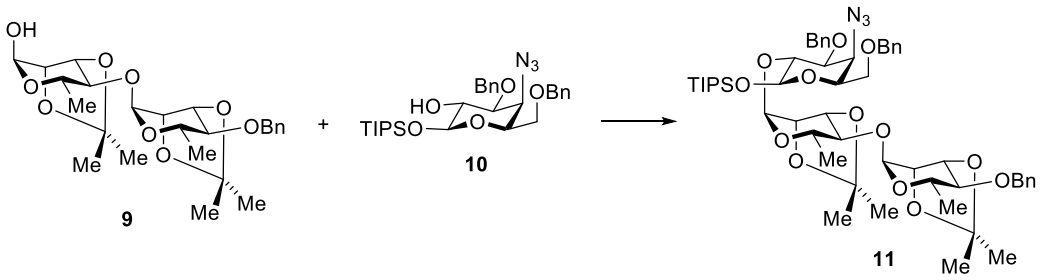
TLC: R_f 0.53 (4:1 hexanes/EtOAc). **IR** (neat film) cm^{-1} 3065, 3031, 2987, 2936, 2360, 2341, 2250, 1647, 1456, 1375, 1221, 1084, 914, 861, 740. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38–7.25 (m, 5H, Ar), 5.95–5.85 (m, 1H, CH_2CH=CH_2), 5.59 (s, 1H), 5.30 (dd, J = 17.2, 1.5 Hz, 1H), 5.21 (dd, J = 10.4, 1.3 Hz, 1H), 5.01 (s, 1H, H-1 Rha), 4.90 (d, J = 11.5 Hz, 1H), 4.64 (d, J = 11.5 Hz, 1H), 4.24–4.20 (m, 2H), 4.19–4.14 (m, 2H), 4.12 (d, J = 5.6 Hz, 1H), 4.02–3.97 (m, 1H), 3.72–3.64 (m, 2H), 3.58 (dd, J = 9.9, 7.4 Hz, 1H), 3.24 (dd, J = 9.8, 7.3 Hz, 1H), 1.54 (s, 3H), 1.51 (s, 3H), 1.37 (s, 3H), 1.32 (s, 3H), 1.27 (d, J = 6.3 Hz, 3H), 1.24 (d, J = 6.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 138.22, 133.55, 128.28, 128.08, 127.68, 117.81, 109.45, 109.01, 96.04, 95.52, 80.88, 78.55, 78.50, 76.49, 76.40, 76.09, 73.21, 67.91, 64.96, 64.02, 28.00, 27.89, 26.38, 26.32, 17.88, 17.51. **HRMS** (ESI) *m/z*: Calcd for $C_{28}H_{40}O_9Na$ $(M+Na)^+$ 543.2570, found 543.2559.



4-*O*-benzyl-2,3-di-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-isopropylidene-L-rhamnopyranoside (9). To a degassed solution of triphenylphosphine (101 mg, 0.38 mmol,

1.0 equiv), palladium acetate (18.0 mg, 77.0 μmol, 0.2 equiv) and diethylamine (0.48 mL, 4.61 mmol, 12 equiv) in CH_2Cl_2/methanol (1:1, 6 mL), a degassed solution of **S1** (200 mg, 0.38 mmol, 1.0 equiv) in CH_2Cl_2 (5.0 mL) was added via cannula. The reaction mixture was stirred in the dark at 21 °C for 27 h and then concentrated. Purification by silica gel chromatography (4:1 to 3:2 hexanes/ethyl acetate) afforded **9** (180 mg, 95% yield) as a yellow foam.

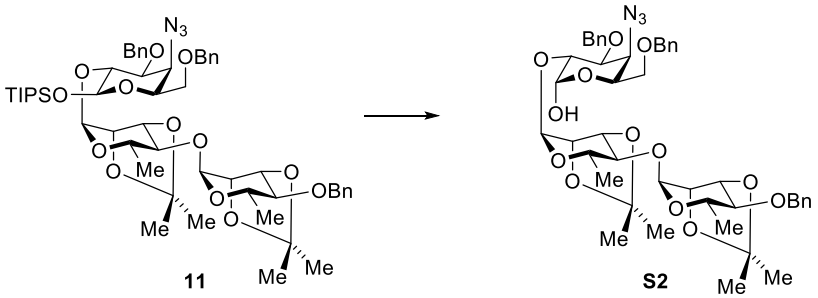
TLC: R_f 0.36 (7:3 hexanes/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38–7.26 (m, 5H), 5.59 (s, 1H), 5.39 (d, J = 1.6 Hz, 1H), 4.90 (d, J = 11.5 Hz, 1H), 4.64 (d, J = 11.5 Hz, 1H), 4.28–4.20 (m, 2H), 4.18–4.11 (m, 2H), 3.88 (dq, J = 12.5, 6.2 Hz, 1H), 3.69 (dq, J = 12.6, 6.3 Hz, 1H), 3.59 (dd, J = 9.7, 7.5 Hz, 1H), 3.24 (dd, J = 9.8, 7.4 Hz, 1H), 2.60 (d, J = 2.9 Hz, 1H), 1.54 (s, 3H), 1.51 (s, 3H), 1.38 (s, 3H), 1.33 (s, 3H), 1.27 (d, J = 6.3 Hz, 3H), 1.24 (d, J = 6.3 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 138.21, 128.30, 128.10, 127.70, 109.50, 109.04, 95.61, 91.97, 80.87, 78.50, 78.20, 76.39, 76.28, 76.08, 73.23, 65.00, 64.38, 28.01, 27.86, 26.36, 26.34, 18.02, 17.52. **HRMS** (ESI) *m/z*: Calcd for $C_{25}H_{36}O_9Na$ $(M+Na)^+$ 503.2257, found 503.2250.



***O*-Triisopropylsilyl 4-*O*-benzyl-2,3-di-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-isopropylidene-L-rhamnopyranosyl-(1→2)-4-azido-3,6-di-*O*-benzyl-4-deoxy-β-D-galactopyranoside (11).** To a solution of phenyl sulfoxide (65 mg, 0.32 mmol, 2.8 equiv) in CH_2Cl_2 (2.0 mL) at −78 ºC, trifluoromethanesulfonic anhydride (30 μL, 0.17 mmol, 1.5 equiv) was injected, and the mixture was stirred at this temperature for 30 min followed by another 40 min at −40 ºC. At this point, hemiacetal **9** (55 mg, 0.11 mmol, 1.0 equiv) in CH_2Cl_2 (4.0 mL) was added via cannula at −78 ºC and the solution was stirred for 10 min before warming it up to −40 ºC. 2,4,6-tri-*tert*-butylpyridine (74 mg, 0.30 mmol, 2.6 equiv) was then added and the mixture was stirred for 70 min at −40 ºC. After this time, a solution of **10**[4] (53 mg, 98.0 μmol, 0.86 equiv) in CH_2Cl_2 (3.0 mL) was cannula transferred into the reaction at −78 ºC, and the reaction was allowed to warm up to −40 ºC over 2 h and finally to 0 ºC over 4 h. Triethylamine (0.3 mL) was then added, and the contents were concentrated and purified by silica gel chromatography (hexanes to hexanes/EtOAc 4:1) to give 18 mg of recovered **10** and trisaccharide **11** (49 mg, 50% yield, 76% brsm) as a clear oil, which was directly advanced to the next reaction.

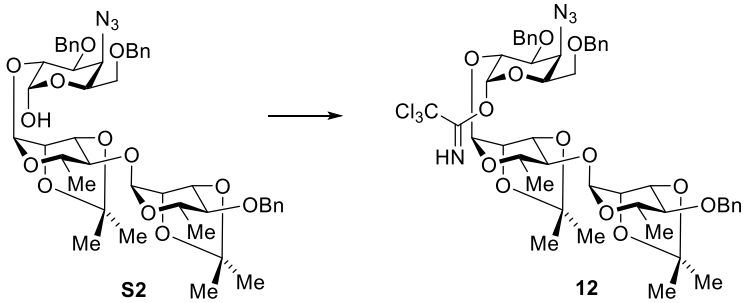
TLC: R_f 0.50 (4:1 hexanes/EtOAc). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40–7.27 (m, 15H), 5.65 (s, 1H), 5.54 (s, 1H), 4.89 (d, J = 11.6 Hz, 1H), 4.73 (d, J = 11.7 Hz, 1H), 4.64 (d, J = 11.6 Hz, 1H), 4.57–4.49 (m, 4H), 4.20–4.15 (m, 1H), 4.12–4.05 (m, 2H), 4.04–3.94 (m, 3H), 3.87 (dd, J = 9.3, 7.5 Hz, 1H), 3.70–3.62 (m, 3H), 3.61–3.55 (m, 2H), 3.52 (dd, J = 10.0, 7.4 Hz, 1H), 3.23 (dd, J = 9.8, 7.4 Hz, 1H), 1.51 (s, 3H), 1.50 (s, 3H), 1.37 (s, 3H), 1.32 (s, 3H), 1.26 (d, J = 6.2 Hz, 3H),

1.20 (d, J = 6.2 Hz, 3H), 1.11–1.00 (m, 21H). **HRMS** (ESI) *m/z*: Calcd for $C_{54}H_{77}N_3O_{13}SiNa$ $(M+Na)^+$ 1026.5123, found 1026.5157.



4-*O*-benzyl-2,3-di-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-isopropylidene-L-rhamnopyranosyl-(1→2)-4-azido-3,6-di-*O*-benzyl-4-deoxy-β-D-galactopyranoside (S2). To a solution of trisaccharide **11** (46 mg, 46.0 μmol, 1.0 equiv) in THF (5.0 mL) at 0 ºC was added acetic acid (3.2 μL, 5.5 μmol, 1.2 equiv) and tetrabutylammonium fluoride solution (1.0 M in THF, 64 μL, 1.4 equiv). The reaction mixture was stirred at 0 ºC for 2 h and at 21 ºC for 1 h before adding 4 mL methanol. The solvent was then removed and the residue was purified by silica gel chromatography (4:1 to 1:1 hexanes/EtOAc) to give **S2** (35 mg, 90% yield) as a white foam. This hemiacetal was then carried on forward to imidate formation.

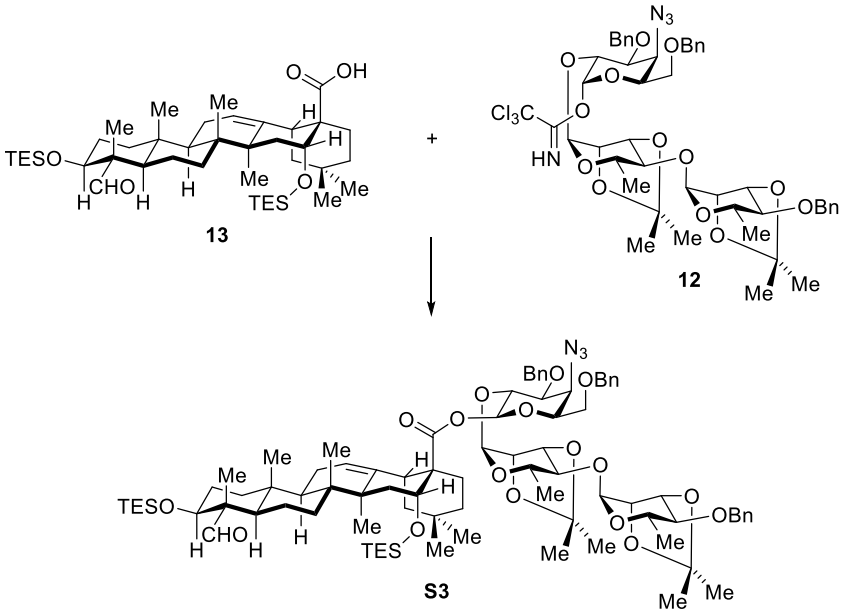
TLC: R_f 0.23 (7:3 hexanes/EtOAc). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.41–7.26 (m, 15H), 5.57 (s, 1H), 5.28–5.25 (m, 1H), 4.89 (d, J = 11.5 Hz, 1H), 4.76–4.70 (m, 1H), 4.67–4.60 (m, 2H), 4.59–4.50 (m, 2H), 4.24–4.11 (m, 5H), 4.09–4.03 (m, 2H), 4.02–3.98 (m, 1H), 3.77–3.60 (m, 3H), 3.59–3.55 (m, 2H), 3.23 (dd, J = 9.8, 7.3 Hz, 1H), 2.69 (d, J = 2.5 Hz, 1H), 1.52 (s, 3H), 1.51 (s, 3H), 1.37 (s, 3H), 1.31 (s, 3H), 1.26 (d, J = 6.1 Hz, 3H), 1.20 (d, J = 6.3 Hz, 3H). **HRMS** (ESI) *m/z*: Calcd for $C_{45}H_{57}N_3O_{13}Na$ $(M+Na)^+$ 870.3791, found 870.3777.



***O*-Trichloroacetimidoyl 4-*O*-benzyl-2,3-di-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-isopropylidene-L-rhamnopyranosyl-(1→2)-4-azido-3,6-di-*O*-benzyl-4-deoxy-β-D-galactopyranoside (12).** Trichloroacetonitrile (0.62 mL, 6.2 mmol, 150 equiv) and 1,8-diazabicycloundec-7-ene (31 μL, 0.21 mmol, 5 equiv) were added to a solution of hemiacetal **S2** (35 mg, 0.04 mmol, 1 equiv) in dichloromethane (8 mL) at 0 ºC. The reaction mixture was stirred for 2 h at that temperature followed by 1 h at 21 ºC and then concentrated and purified by silica

gel chromatography (4:1 hexanes/EtOAc with 1% triethylamine) to afford **12** (40 mg, 98% yield) as a white foam, to be directly used in the next glycosylation step.

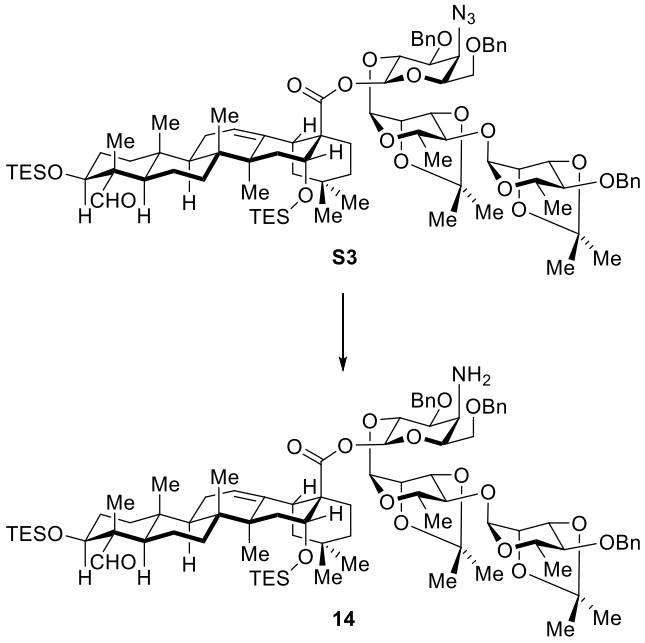
TLC: R_f 0.65 (3:1 hexanes/EtOAc). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.40–7.26 (m, 15H), 6.30 (d, *J* = 3.6 Hz, 1H), 5.53 (s, 1H), 5.24 (s, 1H), 4.89 (d, *J* = 11.5 Hz, 1H), 4.77 (d, *J* = 11.6 Hz, 1H), 4.68 (d, *J* = 11.7 Hz, 1H), 4.63 (d, *J* = 11.5 Hz, 1H), 4.57–4.50 (m, 2H), 4.23–4.15 (m, 3H), 4.13 (t, *J* = 6.8 Hz, 1H), 4.11–4.05 (m, 2H), 4.04–4.00 (m, 2H), 3.69–3.56 (m, 4H), 3.52 (dt, *J* = 10.0, 5.3 Hz, 1H), 3.22 (dd, *J* = 9.8, 7.3 Hz, 1H), 1.51 (s, 3H), 1.50 (s, 3H), 1.37 (s, 3H), 1.30 (s, 3H), 1.25 (d, *J* = 6.2 Hz, 3H), 1.17 (d, *J* = 6.2 Hz, 3H). **HRMS** (ESI) *m/z*: Calcd for $C_{47}H_{57}Cl_3N_4O_{13}Na$ $(M+Na)^+$ 1013.2885, found 1013.2933.



Protected dirhamnosyl-(4-azido-4-deoxygalactosyl) quillaic acid ester (S3)
{(2*S*,3*R*,4*S*,5*S*,6*S*)-5-azido-4-(benzyloxy)-3-(((3a*R*,4*S*,6*S*,7*S*,7a*R*)-7-(((3a*R*,4*S*,6*S*,7*S*,7a*R*)-7-(benzyloxy)-2,2,6-trimethyltetrahydro-4*H*-[1,3]dioxolo[4,5-*c*]pyran-4-yl)oxy)-2,2,6-trimethyltetrahydro-4*H*-[1,3]dioxolo[4,5-*c*]pyran-4-yl)oxy)-6-((benzyloxy)methyl)tetrahydro-2*H*-pyran-2-yl (4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-2,2,6a,6b,9,12a-hexamethyl-5,10-bis((triethylsilyl)oxy)-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2*H*)-carboxylate}.

To a solution of **13**[5] (28.5 mg, 39 μmol, 1.2 equiv) and imidate **12** (33 mg, 33 μmol, 1.0 equiv) in CH_2Cl_2 (5 mL) 30 mg powdered 4 Å molecular sieves was added and the mixture was stirred at 21 °C for 30 min. The reaction schlenk was then cooled to –35 °C and boron trifluoride diethyletherate (1.0 μL, 6.7 μmol, 0.23 equiv) was injected. The mixture was stirred for 30 min at –30 °C this temperature, quenched with 0.2 mL of triethylamine and concentrated. Purification of the residue by silica gel chromatography (0.2% triethylamine in benzene to 97:3 benzene/EtOAc) gave a colorless oil that was further chromatographed to afford the desired product **S3** (37 mg, 73% yield) as a white solid.

TLC: R_f 0.58 (9:1 benzene/EtOAc). **IR** (neat film) cm^{-1} 2950, 2876, 2360, 2341, 2107, 1733, 1456, 1374, 1221, 1082, 825, 736. **^{1}H NMR** (600 MHz, $CDCl_3$) characteristic resonances: δ 9.31 (s, 1H), 5.51 (s, 1H), 5.35–5.31 (m, 2H), 5.31–5.29 (s, 3H), 5.26 (s, 1H), 4.90 (d, *J* = 11.5 Hz, 1H), 4.75 (d, *J* = 11.3 Hz, 1H), 4.63 (d, *J* = 11.5 Hz, 1H), 4.60 (d, *J* = 11.3 Hz, 1H), 4.53–4.50 (m, 2H), 4.46 (s, 1H), 4.22 – 4.18 (m, 1H), 4.13–4.09 (m, 2H), 4.05 (d, *J* = 3.4 Hz, 1H), 4.02–3.98 (m, 1H), 3.91 (t, *J* = 8.7 Hz, 1H), 3.78 (dd, *J* = 11.1, 4.6 Hz, 1H), 3.56–3.52 (m, 2H), 3.47–3.43 (m, 1H), 3.22 (dd, *J* = 9.7, 7.4 Hz, 1H), 2.88 (dd, *J* = 14.1, 3.9 Hz, 1H), 2.21 (t, *J* = 13.5 Hz, 1H), 1.51 (s, 3H), 1.45 (s, 3H), 1.38 (s, 3H), 1.36 (s, 3H), 1.14 (d, *J* = 6.2 Hz, 3H), 1.05 (s, 3H), 0.70 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.45, 175.16, 143.19, 138.23, 137.46, 136.92, 128.64, 128.51, 128.32, 128.31, 128.24, 128.09, 128.00, 127.93, 127.90, 127.69, 121.77, 109.58, 109.04, 97.69, 95.50, 93.82, 80.83, 80.79, 78.54, 78.37, 76.53, 76.40, 75.68, 74.92, 73.77, 73.60, 73.21, 72.46, 71.94, 67.56, 66.49, 64.93, 58.88, 56.00, 53.42, 48.98, 47.91, 46.65, 46.56, 41.47, 40.68, 39.77, 38.22, 35.79, 35.17, 34.79, 32.70, 32.47, 30.80, 30.43, 28.01, 27.67, 26.80, 26.36, 26.04, 24.32, 23.31, 20.58, 18.17, 17.52, 17.03, 15.76, 9.51, 7.13, 6.82, 5.04, 4.90. **HRMS** (ESI) *m/z*: Calcd for $C_{87}H_{129}N_3O_{17}Si_2Na$ $(M+Na)^+$ 1566.8758, found 1566.8822.

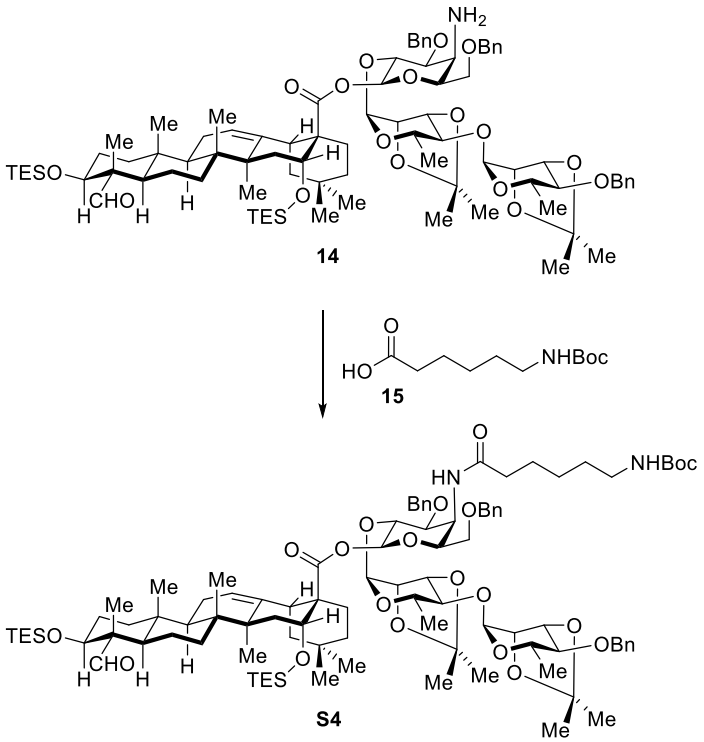


Protected dirhamnosyl-(4-amino-4-deoxygalactosyl) quillaic acid ester (14)
{(2*S*,3*R*,4*S*,5*S*,6*S*)-5-amino-4-(benzyloxy)-3-(((3a*R*,4*S*,6*S*,7*S*,7a*R*)-7-(((3a*R*,4*S*,6*S*,7*S*,7a*R*)-7-(benzyloxy)-2,2,6-trimethyltetrahydro-4H-[1,3]dioxolo[4,5-c]pyran-4-yl)oxy)-2,2,6-trimethyltetrahydro-4H-[1,3]dioxolo[4,5-c]pyran-4-yl)oxy)-6-((benzyloxy)methyl)tetrahydro-2H-pyran-2-yl (4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-2,2,6a,6b,9,12a-hexamethyl-5,10-bis((triethylsilyl)oxy)-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2H)-carboxylate}.

To **S3** (41 mg, 26 μmol, 1.0 equiv) dissolved in triethylamine (22 mL) was added a freshly prepared solution of phenyl selenol (0.81 mmol, 30 equiv) via cannula. Upon addition of phenyl

selenol a white precipitate was formed and the solution became bright yellow. The reaction was stirred for 4 h at 38 °C and the solution was then concentrated to afford a yellow-white solid. The crude mixture was purified by silica gel chromatography (9:1 to 7:3 toluene/EtOAc to afford the amine **14** (32 mg, 80% yield) as a glassy solid.

TLC: R_f 0.17 (9:1 benzene/EtOAc). **IR** (neat film) cm^{-1} 2951, 2876, 2360, 2341, 1734, 1456, 1381, 1242, 1221, 1085, 911, 817, 734. **^{1}H NMR** (600 MHz, $CDCl_3$) characteristic resonances: δ 9.31 (s, 1H), 5.54 (s, 1H), 5.38 (d, *J* = 8.0 Hz, 1H), 5.35–5.30 (m, 2H), 4.90 (d, *J* = 11.5 Hz, 1H), 4.66 (d, *J* = 11.4 Hz, 1H), 4.63 (d, *J* = 11.6 Hz, 1H), 4.58–4.51 (m, 3H), 4.48 (s, 1H), 4.20 (dd, *J* = 7.0, 5.9 Hz, 1H), 4.15–4.10 (m, 2H), 4.09–4.04 (m, 1H), 3.88–3.82 (m, 1H), 3.78 (dd, *J* = 11.2, 4.6 Hz, 1H), 3.71–3.67 (m, 1H), 3.58 (dd, *J* = 9.6, 5.6 Hz, 1H), 3.54–3.46 (m, 2H), 3.37 (d, *J* = 3.0 Hz, 1H), 3.23 (dd, *J* = 9.8, 7.3 Hz, 1H), 2.90 (dd, *J* = 14.2, 4.0 Hz, 1H), 2.22 (t, *J* = 13.6 Hz, 1H), 1.51 (s, 3H), 1.47 (s, 3H), 1.39–1.35 (m, 6H), 1.15 (d, *J* = 6.2 Hz, 3H), 1.05 (s, 3H), 0.87 (s, 3H), 0.72 (s, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.45, 175.25, 143.37, 138.23, 137.89, 137.38, 128.97, 128.58, 128.42, 128.29, 128.08, 128.05, 127.83, 127.77, 127.72, 127.68, 121.63, 109.50, 109.02, 97.40, 95.46, 94.23, 81.45, 80.81, 78.53, 78.38, 76.40, 75.89, 75.02, 73.82, 73.51, 73.37, 73.22, 73.18, 71.46, 68.09, 66.12, 64.92, 55.97, 49.01, 48.54, 47.91, 46.71, 46.52, 41.49, 40.59, 39.77, 38.19, 35.77, 35.20, 34.71, 32.68, 32.43, 30.87, 30.43, 28.00, 27.71, 26.79, 26.35, 26.34, 26.12, 24.36, 23.30, 20.56, 18.23, 17.50, 17.00, 15.75, 9.51, 7.13, 6.81, 5.03, 4.91. **HRMS** (ESI) *m/z*: Calcd for $C_{87}H_{132}NO_{17}Si_2$ $(M+H)^+$ 1518.9034, found 1518.9083.

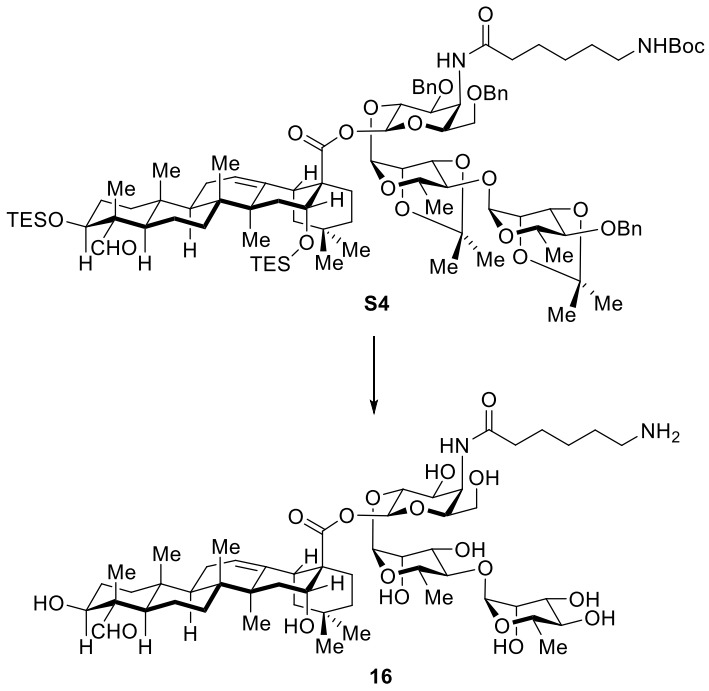


Protected dirhamnosyl-(4-(6-aminocaproamido)-4-deoxygalactosyl) quillaic acid ester (S4) {(2*S*,3*R*,4*S*,5*S*,6*S*)-4-(benzyloxy)-3-(((3a*R*,4*S*,6*S*,7*S*,7a*R*)-7-(((3a*R*,4*S*,6*S*,7*S*,7a*R*)-7-(benzyloxy)-2,2,6-trimethyltetrahydro-4*H*-[1,3]dioxolo[4,5-c]pyran-4-yl)oxy)-2,2,6-trimethyltetrahydro-4*H*-[1,3]dioxolo[4,5-c]pyran-4-yl)oxy)-6-((benzyloxy)methyl)-5-(6-((tert-

butoxycarbonyl)amino)hexanamido)tetrahydro-2*H*-pyran-2-yl (4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-2,2,6a,6b,9,12a-hexamethyl-5,10-bis((triethylsilyl)oxy)-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2*H*)-carboxylate}.

To a clear, colorless solution of 6-[(*t*-butoxycarbonyl)-amino]hexanoic acid (**15**) (26 mg, 0.11 mmol, 11.5 equiv) in tetrahydrofuran (1.5 mL) at 0 ºC was added triethylamine (125 µL, 0.90 mmol, 90 equiv) followed by ethyl chloroformate (9.6 µL, 0.10 mmol, 10.0 equiv). The turbid, white solution was stirred for 3 h at 0 °C and then added via cannula to amine **14** (15 mg, 0.01 mmol, 1.0 equiv). The reaction mixture was stirred at 0 ºC for 1 h, quenched with water (0.2 mL) and concentrated. Purification by silica gel chromatography (9:1 to 6:1 benzene/EtOAc with 0.2% triethylamine) afforded **S4** (16.5 mg, 94% yield) as a white glassy solid.

TLC: R_f 0.30 (85:15 benzene/EtOAc). **IR** (neat film) cm^{-1} 2937, 2876, 2360, 2341, 1717, 1684, 1507, 1456, 1366, 1171, 1083, 911, 863, 734. **^{1}H NMR** (600 MHz, $CDCl_3$) characteristic resonances: δ 9.31 (s, 1H), 5.65 (d, *J* = 7.9 Hz, 1H), 5.54 (s, 1H), 5.41 (d, *J* = 7.2 Hz, 1H), 5.33–5.28 (m, 2H), 4.90 (d, *J* = 11.5 Hz, 1H), 4.82 (dd, *J* = 9.9, 2.6 Hz, 1H), 4.78 (d, *J* = 10.9 Hz, 1H), 4.63 (d, *J* = 11.5 Hz, 1H), 4.53–4.46 (m, 3H), 4.44 (d, *J* = 10.7 Hz, 1H), 4.22–4.17 (m, 1H), 4.12 (d, *J* = 5.7 Hz, 1H), 4.11–4.08 (m, 2H), 3.81–3.75 (m, 2H), 3.72–3.59 (m, 4H), 3.55–3.45 (m, 3H), 3.23 (dd, *J* = 9.8, 7.3 Hz, 1H), 3.06–2.98 (m, 2H), 2.89 (dd, *J* = 14.2, 4.0 Hz, 1H), 2.21 (t, *J* = 13.6 Hz, 1H), 2.17–2.11 (m, 2H), 1.51 (s, 3H), 1.48 (s, 3H), 1.43 (s, 9H), 1.40–1.36 (m, 6H), 1.13 (d, *J* = 6.2 Hz, 3H), 1.05 (s, 3H), 1.00 (s, 2H), 0.98 (s, 4H), 0.97 (s, 2H), 0.89 (s, 3H), 0.87 (s, 3H), 0.72 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.43, 175.13, 172.81, 155.91, 143.49, 138.21, 137.66, 137.32, 128.43, 128.42, 128.38, 128.30, 128.10, 127.94, 127.80, 127.70, 121.53, 109.56, 109.06, 97.43, 95.49, 80.82, 79.04, 78.52, 78.32, 76.40, 76.02, 75.12, 74.14, 73.47, 73.24, 73.21, 73.00, 71.54, 68.35, 66.02, 64.94, 55.94, 49.07, 47.85, 46.74, 46.45, 45.99, 41.52, 40.51, 40.31, 39.78, 38.17, 36.58, 35.77, 35.19, 34.61, 32.65, 32.39, 30.91, 30.43, 29.75, 28.41, 28.00, 27.73, 26.77, 26.36, 26.35, 26.27, 26.15, 25.28, 24.32, 23.33, 20.56, 18.15, 17.51, 17.01, 15.81, 9.55, 7.13, 6.81, 5.03, 4.93. **HRMS** (ESI) *m/z*: Calcd for $C_{98}H_{151}N_2O_{20}Si_2$ $(M+H)^+$ 1732.0399, found 1732.0435.

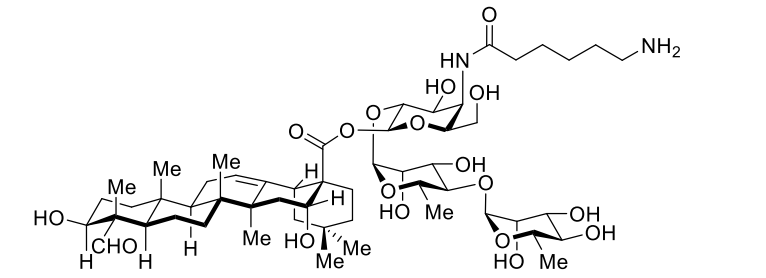


Dirhamnosyl-(4-(6-aminocaproamido)-4-deoxygalactosyl) quillaic acid ester (16)
{(2*S*,3*R*,4*S*,5*R*,6*S*)-5-(6-aminohexanamido)-3-(((2*S*,3*R*,4*S*,5*R*,6*S*)-3,4-dihydroxy-6-methyl-5-(((2*S*,3*R*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)-4-hydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl (4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-5,10-dihydroxy-2,2,6a,6b,9,12a-hexamethyl-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2*H*)-carboxylate}.

In a 25 mL round-bottom flask, **S4** (16 mg, 9.3 μmol, 1.0 equiv) was dissolved in tetrahydrofuran/ethanol (6 mL, 1:1) and 10% (dry basis) palladium on carbon, wet, Degussa type E101 NE/W (98.3 mg, 46.2 μmol, 5.0 equiv) was added. The reaction was stirred under hydrogen pressure (50 psi) for 11 h at 21 °C, and the suspension was filtered through a 0.45 μm nylon syringe filter, washed with methanol and concentrated. Successful debenzylation is assessed by the disappearance of aromatic resonances by ^{1}H NMR in CD_3OD. The residue was then dissolved in a precooled (0 ºC) solution of trifluoroacetic acid (4 mL, TFA/H_2O 3:1), stirred for 75 min in an ice bath, and evaporated to dryness. The crude residue was dissolved in 25% acetonitrile/water (10 mL) and purified via RP-HPLC on an XBridge Prep BEH300 C18 column (5 μm, 10 × 250 mm) using a linear gradient of 30–70% acetonitrile/water (0.05% TFA), over 15 min, at a flow rate of 5 mL/min. The 6-aminocaproic amide derivative **16** was obtained as a white powder (6.6 mg, 67% yield) after lyophilization.

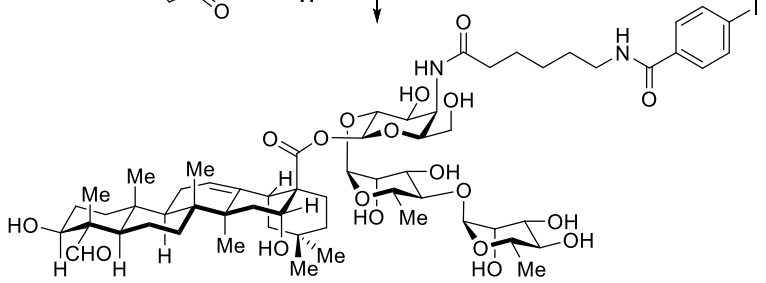
HPLC: t_{ret} = 7.08 min, λ_{max} = 210 nm. **^{1}H NMR** (600 MHz, CD_3OD) characteristic resonances: δ 9.29 (s, 1H), 8.01 (d, *J* = 9.3 Hz, 1H), 5.45 (s, 1H), 5.36 (d, *J* = 8.0 Hz, 1H), 5.33–5.29 (m, 1H), 5.19 (s, 1H), 4.48 (s, 1H), 4.40–4.30 (m, 1H), 3.96 (dd, *J* = 9.3, 4.6 Hz, 1H), 3.93–3.87 (m, 2H), 3.85 (s, 1H), 3.80–3.69 (m, 5H), 3.64 (dd, *J* = 9.4, 2.6 Hz, 1H), 3.57–3.50 (m, 2H), 3.45–3.37 (m, 2H), 3.00–2.89 (m, 3H), 2.42–2.31 (m, 3H), 2.03–1.88 (m, 4H), 1.43 (s, 3H), 1.37–1.31 (m, 5H), 1.25 (d, *J* = 6.1 Hz, 3H), 1.10–1.05 (m, 1H), 1.00 (s, 6H), 0.96 (s, 3H), 0.89 (s, 3H),

0.76 (s, 3H). **^{13}C NMR** (151 MHz, CD_3OD) δ 208.93, 178.03, 177.94, 176.94, 144.89, 123.50, 103.40, 101.60, 95.56, 80.18, 76.40, 75.39, 74.76, 74.32, 74.26, 73.30, 73.04, 72.76, 72.46, 72.26, 70.46, 68.97, 61.82, 57.01, 52.82, 52.74, 50.05, 50.00, 49.72, 48.13, 47.98, 42.97, 42.42, 41.29, 40.73, 39.65, 37.10, 36.98, 36.65, 36.40, 36.34, 34.01, 33.57, 32.37, 31.50, 28.47, 27.54, 27.13, 26.96, 26.53, 25.00, 24.60, 21.95, 19.21, 18.00, 17.87, 16.43, 9.51. **HRMS** (ESI) *m/z*: Calcd for $C_{54}H_{89}N_2O_{18}$ $(M+H)^+$ 1053.6110, found 1053.6107.



16

17



4 [SQS-1-0-10-18]

Dirhamnosyl-(4-(6-(4-iodobenzamido)caproamido)-4-deoxygalactosyl) quillaic acid ester (Dirhamnose variant 4, SQS-1-0-10-18)

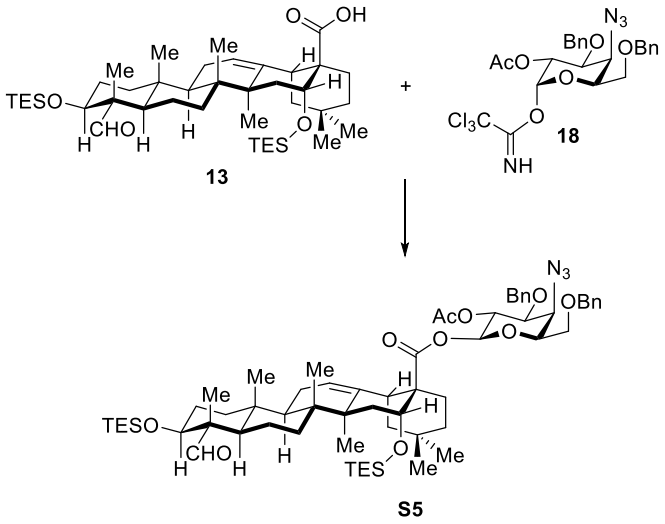
{(2*S*,3*R*,4*S*,5*R*,6*S*)-3-(((2*S*,3*R*,4*S*,5*R*,6*S*)-3,4-dihydroxy-6-methyl-5-(((2*S*,3*R*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)-4-hydroxy-6-(hydroxymethyl)-5-(6-(4-iodobenzamido)hexanamido)tetrahydro-2*H*-pyran-2-yl (4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-5,10-dihydroxy-2,2,6a,6b,9,12a-hexamethyl-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2*H*)-carboxylate}.

To a solution of **16** (6.6 mg, 6.3 µmol, 1.0 equiv) in *N,N'*-dimethylformamide (1.5 mL) was added triethylamine (17.6 µL, 0.13 mmol, 20 equiv) followed by dropwise addition of NHS ester **17** (10.8 mg, 31.3 µmol, 5.0 equiv) in *N,N'*-dimethylformamide (1.0 mL). After stirring for 2 h, the contents were diluted with 25% acetonitrile/water (0.05% TFA) (10 mL) and purified by RP-HPLC on an XBridge Prep BEH300 C18 column (5 µm, 10 x 250 mm) using a linear gradient of 30–70% acetonitrile/water (0.05% TFA), over 15 min, at a flow rate of 5 mL/min. Linear trisaccharide dirhamnose variant **4** (SQS-1-0-10-18) (6.0 mg, 75% yield) was obtained as a white powder after lyophilization.

HPLC: t_{ret} = 12.63 min, λ_{max} = 251 nm. **^{1}H NMR** (600 MHz, CD_3OD) characteristic resonances: δ 9.29 (s, 1H), 7.86–7.81 (m, 2H), 7.60–7.55 (m, 2H), 5.42 (d, *J* = 1.5 Hz, 1H), 5.36 (d, *J* = 7.7 Hz, 1H), 5.31 (t, *J* = 3.5 Hz, 1H), 5.18 (d, *J* = 1.5 Hz, 1H), 4.48 (br s, 1H), 4.36–4.31 (m, 1H), 3.96–3.92 (m, 2H), 3.90 (dd, *J* = 3.2, 1.8 Hz, 1H), 3.86 (dd, *J* = 3.2, 1.8 Hz, 1H), 3.79–3.71 (m, 4H), 3.69 (td, *J* = 6.9, 1.4 Hz, 1H), 3.63 (dd, *J* = 9.4, 3.3 Hz, 1H), 3.56–3.48 (m, 2H), 3.44–3.35 (m, 4H), 3.25–3.17 (m, 1H), 2.97 (dd, *J* = 14.2, 4.2 Hz, 1H), 2.39–2.31 (m, 3H), 1.84–1.75 (m, 2H), 1.47–1.40 (m, 6H), 1.32 (d, *J* = 6.1 Hz, 3H), 1.25 (d, *J* = 6.2 Hz, 3H), 1.06 (dd, *J* = 12.6, 3.2 Hz, 1H), 1.01–0.98 (m, 6H), 0.96 (s, 3H), 0.89 (s, 3H), 0.76 (s, 3H). **^{13}C NMR** (151 MHz, CD_3OD) δ 208.93, 178.39, 177.02, 169.48, 144.88, 139.04, 135.53, 130.17, 123.50, 103.41, 101.78, 99.18, 95.62, 80.34, 76.41, 75.08, 74.81, 74.25, 73.31, 73.00, 72.79, 72.48, 72.30, 70.46, 69.00, 61.85, 57.00, 52.69, 50.04, 50.00, 49.72, 48.14, 47.98, 42.95, 42.44, 41.31, 41.08, 39.66, 37.10, 36.90, 36.69, 36.63, 33.99, 33.59, 32.31, 31.52, 30.30, 27.69, 27.53, 27.14, 26.97, 25.05, 24.62, 21.95, 19.24, 18.02, 17.93, 16.45, 9.52, 9.36. **HRMS** (ESI) *m/z*: Calcd for $C_{61}H_{91}N_2O_{19}INa$ $(M+Na)^+$ 1305.5159, found 1305.5095.

---

2. SYNTHESIS OF LACTOSE VARIANT 5 (SQS-1-0-11-18)

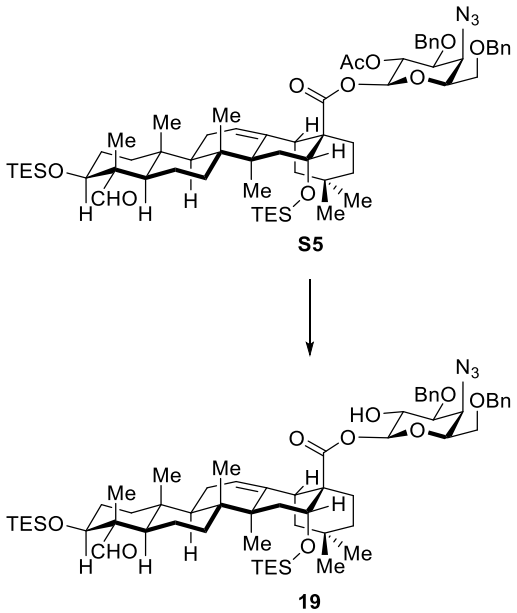


Protected 2-*O*-acetyl-4-azido-4-deoxygalactosyl quillaic acid ester (S5)
{(2*S*,3*R*,4*S*,5*S*,6*S*)-3-acetoxy-5-azido-4-(benzyloxy)-6-((benzyloxy)methyl)tetrahydro-2*H*-pyran-2-yl (4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-2,2,6a,6b,9,12a-hexamethyl-5,10-bis((triethylsilyl)oxy)-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2*H*)-carboxylate}.

Boron trifluoride diethyl etherate (4.5 μL, 36 μmol, 0.3 equiv) was added to a solution of imidate **18**[3] (92.0 mg, 0.16 mmol, 1.35 equiv) and acid **13**[5] (85 mg, 0.12 mmol, 1.0 equiv) with powdered 4 Å molecular sieves (200 mg) in CH_2Cl_2 (10 mL) at −78 ºC. After stirring for 15 min at this

temperature, the reaction was transferred to a –45 ºC bath (acetonitrile/CO_2), stirred for another 15 min and finally brought to 21 ºC for 2 min. The mixture was then cooled back to –78 ºC and additional boron trifluoride diethyl etherate (4.5 μL, 36 μmol, 0.3 equiv) was added. The previous temperature cycle was repeated twice and after that time, triethylamine (0.4 mL) was added at –78 ºC, and the reaction mixture was evaporated to dryness. Purification of the residue by silica gel chromatography (benzene with 0.2% triethylamine to 99:1 benzene/EtOAc) afforded **S5** (112 mg, 83% yield) as a white solid.

TLC: R_f 0.68 (9:1 benzene/EtOAc). **IR** (neat film) cm^{-1} 2952, 2876, 2360, 2341, 2108, 1756, 1456, 1227, 1055, 1008, 909, 818, 738. **^{1}H NMR** (500 MHz, $CDCl_3$) characteristic resonances: δ 9.30 (s, 1H), 5.35 (t, *J* = 3.5 Hz, 1H), 5.31–5.26 (m, 2H), 4.72 (d, *J* = 12.1 Hz, 1H), 4.58–4.48 (m, 3H), 4.43 (s, 1H), 4.07 (d, *J* = 2.9 Hz, 1H), 3.79 (dd, *J* = 10.7, 4.1 Hz, 1H), 3.71–3.63 (m, 2H), 3.62–3.53 (m, 2H), 2.90 (dd, *J* = 14.3, 4.0 Hz, 1H), 2.19 (t, *J* = 13.5 Hz, 1H), 1.94 (s, 3H), 1.79 (td, *J* = 12.8, 4.7 Hz, 1H), 1.35 (s, 3H), 1.04 (s, 3H), 0.86 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.31, 174.75, 168.56, 142.75, 137.41, 137.19, 128.53, 128.51, 128.31, 128.07, 128.01, 127.94, 127.60, 122.15, 92.19, 78.75, 74.42, 73.60, 73.14, 72.29, 72.07, 69.28, 67.47, 59.03, 56.03, 53.42, 48.69, 47.67, 46.49, 46.46, 46.29, 41.38, 40.20, 39.59, 38.15, 35.76, 35.05, 34.59, 32.65, 32.53, 30.93, 30.39, 26.74, 26.27, 24.11, 23.26, 20.80, 20.58, 16.93, 15.69, 9.41, 8.68, 7.09, 6.80, 5.03, 4.84. **HRMS** (ESI) *m/z*: Calcd for $C_{64}H_{97}N_3O_{10}Si_2Na$ $(M+Na)^+$ 1146.6610, found 1146.6572.

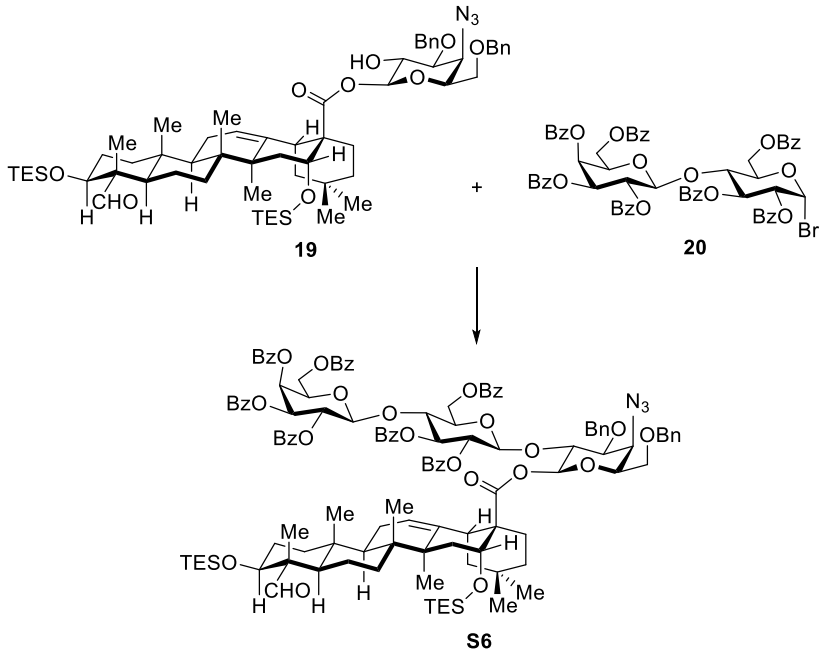


Protected 4-azido-4-deoxygalactosyl quillaic acid ester (19)

{(2*S*,3*R*,4*S*,5*S*,6*S*)-5-azido-4-(benzyloxy)-6-((benzyloxy)methyl)-3-hydroxytetrahydro-2*H*-pyran-2-yl (4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-2,2,6a,6b,9,12a-hexamethyl-5,10-bis((triethylsilyl)oxy)-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2*H*)-carboxylate}.

To a solution of **S5** (102 mg, 0.09 mmol, 1 equiv) in MeOH/CH_2Cl_2/H_2O (10:2:1, 26 mL), NaOMe (0.5 M in MeOH, 9.0 mL, 4.5 mmol, 50 equiv) was added gradually, and the reaction was stirred for at 21 ºC for 20 h. After this time, the mixture was diluted with CH_2Cl_2 (100 mL) and quenched with saturated $NaHCO_3$ (20 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 90 mL) and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. Purification by silica gel chromatography (98:2 to 97:3 benzene/EtOAc) afforded **19** (78 mg, 80% yield) as white solid.

TLC: R_f 0.63 (9:1 benzene/EtOAc). **IR** (neat film) cm^{-1} 3470, 2952, 2876, 2349, 2106, 1726, 1452, 1212, 1109, 1072, 1008, 910, 818, 735. **^{1}H NMR** (600 MHz, $CDCl_3$) characteristic resonances: δ 9.30 (s, 1H), 7.40–7.29 (m, 10H), 5.36–5.32 (m, 2H), 4.80 (d, *J* = 11.2 Hz, 1H), 4.59 (d, *J* = 11.2 Hz, 1H), 4.55 (s, 1H), 4.53 (s, 2H), 4.10 (d, *J* = 2.8 Hz, 1H), 3.85 (td, *J* = 9.4, 2.6 Hz, 1H), 3.79 (dd, *J* = 11.2, 4.6 Hz, 1H), 3.72 (t, *J* = 6.9 Hz, 1H), 3.61–3.55 (m, 3H), 2.95 (dd, *J* = 14.3, 4.1 Hz, 1H), 2.24–2.16 (m, 2H), 1.80 (td, *J* = 12.8, 4.5 Hz, 1H), 1.35 (s, 3H), 1.04 (s, 3H), 0.87 (s, 3H), 0.68 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.40, 174.90, 143.05, 137.44, 136.87, 128.74, 128.51, 128.38, 128.32, 128.12, 128.01, 127.96, 122.04, 93.82, 81.53, 74.86, 73.61, 73.16, 72.46, 72.42, 69.55, 67.58, 58.37, 56.06, 53.42, 48.77, 47.78, 46.57, 46.39, 41.40, 40.42, 39.68, 38.20, 35.77, 35.11, 34.49, 32.67, 32.36, 30.99, 30.45, 29.69, 26.77, 26.40, 24.20, 23.30, 20.60, 16.83, 15.71, 9.42, 7.11, 6.81, 5.03, 4.96. **HRMS** (ESI) *m/z*: Calcd for $C_{62}H_{95}N_3O_9Si_2Na$ $(M+Na)^+$ 1104.6505, found 1104.6527.



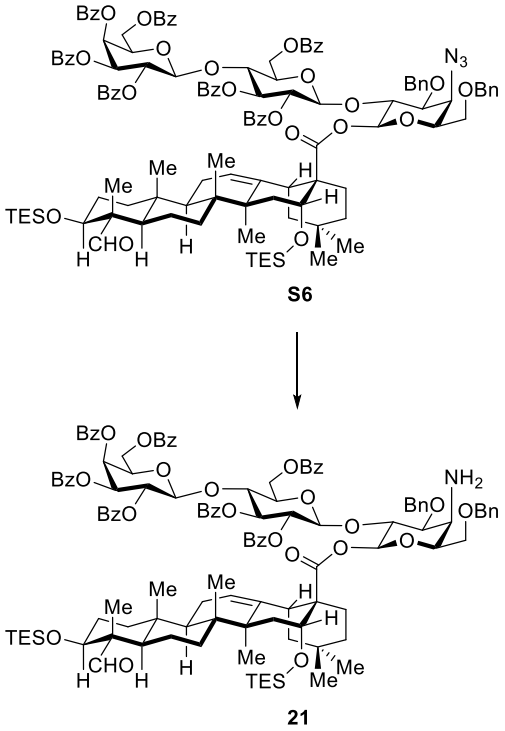
Protected lactosyl-(4-azido-4-deoxygalactosyl) quillaic acid ester (S6)

{(2*S*,3*R*,4*S*,5*S*,6*R*)-2-(((2*R*,3*R*,4*S*,5*R*,6*S*)-6-(((2*S*,3*R*,4*S*,5*S*,6*S*)-5-azido-4-(benzyloxy)-6-((benzyloxy)methyl)-2-(((4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-2,2,6a,6b,9,12a-hexamethyl-5,10-bis((triethylsilyl)oxy)-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-icosahydropicene-4a-

carbonyl)oxy)tetrahydro-2*H*-pyran-3-yl)oxy)-4,5-bis(benzoyloxy)-2-((benzoyloxy)methyl)tetrahydro-2*H*-pyran-3-yl)oxy)-6-((benzoyloxy)methyl)tetrahydro-2*H*-pyran-3,4,5-triyl tribenzoate}.

To a 25 mL schlenk containing alcohol **19** (31.5 mg, 29 μmol, 1.0 equiv), silver trifluoromethanesulfonate (18.6 mg, 72.5 μmol, 2.5 equiv), 2,4,6-tri-*tert*-butylpyridine (17.6 mg, 71 μmol, 2.45 equiv) and powdered 4 Å molecular sieves (70 mg) CH_2Cl_2 (1.6 mL) was added and the mixture was stirred in the dark at 21 ºC for 20 min. Hepta-*O*-benzoyl-α-lactosyl bromide **20**[6] {2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-α-D-glucopyranosyl bromide} (165 mg, 145 μmol, 5 equiv) in CH_2Cl_2 (2.4 mL) was then added via cannula at 0 ºC and the reaction mixture was stirred at 21 ºC for 24 h. After this time, additional silver trifluoromethanesulfonate (18.6 mg, 72.5 μmol, 2.5 equiv), and 2,4,6-tri-*tert*-butylpyridine (17.6 mg, 71 μmol, 2.45 equiv) were added and the suspension was allowed to stir at 21 ºC for 22 h and finally at 30 ºC for 2 h. The mixture was then filtered through Celite, rinsed with CH_2Cl_2 (15 mL), and concentrated. Purification by silica gel chromatography (99:1 to 97:3 benzene/EtOAc) afforded **S6** (50 mg, 80% yield) as a white solid.

TLC: R_f 0.68 (9:1 benzene/EtOAc). **IR** (neat film) cm^{-1} 2955, 2877, 2108, 1737, 1604, 1494, 1454, 1272, 1111, 1071, 1010, 913, 820, 738. **^{1}H NMR** (600 MHz, $CDCl_3$) characteristic resonances: δ 9.29 (s, 1H), 8.01 (d, *J* = 7.6 Hz, 2H), 7.97 (t, *J* = 7.6 Hz, 4H), 7.94 (d, *J* = 7.8 Hz, 2H), 7.90 (d, *J* = 7.8 Hz, 2H), 7.74 (d, *J* = 7.9 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.60–7.57 (m, 1H), 7.56–7.52 (m, 1H), 7.51–7.47 (m, 5H), 7.13 (t, *J* = 7.7 Hz, 2H), 5.77–5.69 (m, 3H), 5.45 (d, *J* = 8.1 Hz, 1H), 5.43–5.36 (m, 2H), 5.25 (d, *J* = 8.1 Hz, 1H), 5.01 (t, *J* = 3.6 Hz, 1H), 4.79 (d, *J* = 7.9 Hz, 1H), 4.61 (d, *J* = 10.7 Hz, 1H), 4.56–4.50 (m, 3H), 4.49–4.41 (m, 2H), 4.33 (dd, *J* = 11.5, 8.0 Hz, 1H), 4.22 (t, *J* = 8.8 Hz, 1H), 3.99 (t, *J* = 9.5 Hz, 1H), 3.93 (t, *J* = 6.8 Hz, 1H), 3.84–3.82 (m, 4H), 3.64 (dd, *J* = 11.3, 6.7 Hz, 1H), 3.61–3.55 (m, 3H), 3.44–3.36 (m, 2H), 2.94 (dd, *J* = 14.1, 3.8 Hz, 1H), 2.16 (t, *J* = 13.5 Hz, 1H), 1.28 (s, 3H), 1.03 (s, 3H), 0.78 (s, 3H), 0.72 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.27, 175.95, 165.83, 165.57, 165.37, 165.20, 164.88, 164.78, 142.50, 137.42, 136.71, 133.51, 133.33, 133.24, 133.17, 129.98, 129.81, 129.75, 129.69, 129.58, 129.54, 129.41, 128.84, 128.81, 128.62, 128.59, 128.56, 128.46, 128.43, 128.32, 128.24, 128.10, 127.92, 127.83, 122.15, 112.06, 101.19, 99.57, 92.57, 82.27, 75.31, 73.47, 73.34, 73.15, 73.09, 72.68, 72.19, 71.87, 71.76, 71.67, 71.39, 69.73, 67.49, 67.34, 63.38, 60.98, 59.27, 56.03, 48.80, 47.68, 46.45, 46.01, 41.22, 40.26, 39.72, 38.09, 37.66, 35.59, 34.69, 34.51, 32.63, 32.22, 31.21, 30.85, 30.47, 30.26, 26.74, 26.32, 24.73, 22.96, 20.58, 16.82, 15.61, 9.43, 7.11, 6.82, 5.03, 4.90. **HRMS** (ESI) *m/z*: Calcd for $C_{123}H_{143}N_3O_{26}Si_2Na$ $(M+Na)^+$ 2156.9396, found 2156.9302.

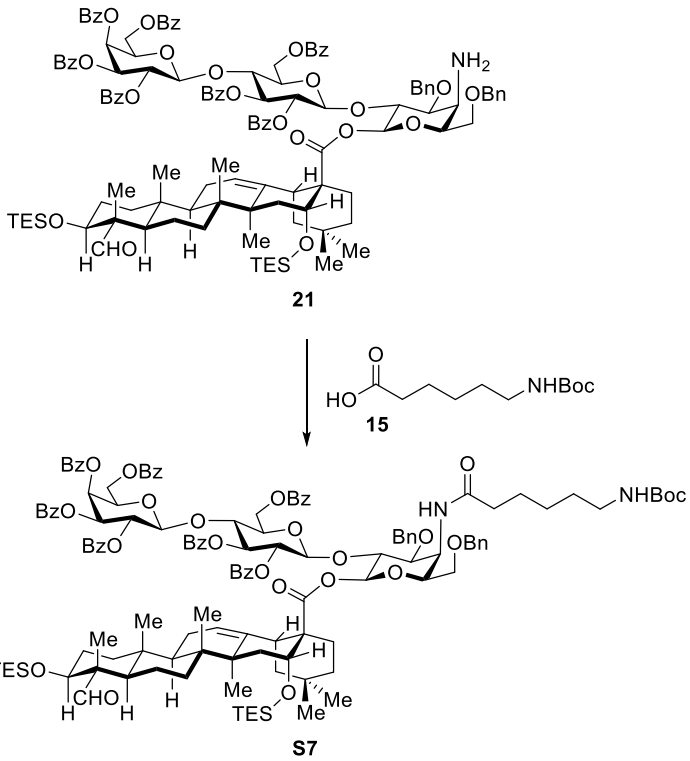


Protected lactosyl-(4-amino-4-deoxygalactosyl) quillaic acid ester (21)
{(2*S*,3*R*,4*S*,5*S*,6*R*)-2-(((2*R*,3*R*,4*S*,5*R*,6*S*)-6-(((2*S*,3*R*,4*S*,5*S*,6*S*)-5-amino-4-(benzyloxy)-6-((benzyloxy)methyl)-2-(((4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-2,2,6a,6b,9,12a-hexamethyl-5,10-bis((triethylsilyl)oxy)-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-icosahydropicene-4a-carbonyl)oxy)tetrahydro-2*H*-pyran-3-yl)oxy)-4,5-bis(benzoyloxy)-2-((benzoyloxy)methyl)tetrahydro-2*H*-pyran-3-yl)oxy)-6-((benzoyloxy)methyl)tetrahydro-2*H*-pyran-3,4,5-triyl tribenzoate}.

To **S6** (50 mg, 23.4 μmol, 1.0 equiv) dissolved in triethylamine (22 mL) was added a freshly prepared solution of phenyl selenol (0.70 mmol, 30 equiv) via cannula. Upon addition of phenyl selenol a white precipitate was formed and the solution became bright yellow. The reaction was stirred for 7 h at 38 °C and the solution was then concentrated to afford a yellow-white solid. The crude residue was purified by silica gel chromatography (9:1 to 85:15 toluene/EtOAc to afford the amine **21** (41 mg, 83% yield) as a glassy solid.

TLC: R_f 0.31 (85:15 toluene/EtOAc). **IR** (neat film) cm^{-1} 3064, 2952, 2876, 2361, 2341, 1735, 1602, 1492, 1452, 1270, 1177, 1095, 1070, 1028, 911, 826, 736. **^{1}H NMR** (600 MHz, $CDCl_3$) characteristic resonances: δ 9.30 (s, 1H), 8.04–7.95 (m, 8H), 7.94–7.88 (m, 4H), 7.77–7.71 (m, 2H), 7.65–7.60 (m, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.52–7.46 (m, 5H), 7.16 (t, *J* = 7.8 Hz, 2H), 5.79–5.68 (m, 3H), 5.46 (d, *J* = 8.1 Hz, 1H), 5.42–5.34 (m, 2H), 5.27 (d, *J* = 8.1 Hz, 1H), 5.14–5.09 (m, 1H), 4.79 (d, *J* = 7.9 Hz, 1H), 4.42 (d, *J* = 11.2 Hz, 1H), 4.37 (dd, *J* = 11.8, 7.1 Hz, 1H), 4.10 (t, *J* = 8.6 Hz, 1H), 4.04 (t, *J* = 9.5 Hz, 1H), 3.88 (t, *J* = 6.9 Hz, 1H), 3.78 (dd, *J* = 11.1, 4.8 Hz, 1H), 3.62–3.52 (m, 2H), 3.47–3.38 (m, 2H), 3.17 (s, 1H), 2.94 (dd, *J* = 14.2, 4.0 Hz, 1H), 1.31 (s, 3H), 1.04 (s, 3H), 0.78 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.67, 165.64, 165.50, 165.35, 165.35, 165.18, 164.85, 164.76, 142.98, 137.84, 137.22,

133.50, 133.31, 133.29, 133.26, 133.22, 133.18, 133.10, 131.44, 129.96, 129.78, 129.73, 129.66, 129.59, 129.57, 129.55, 129.53, 129.47, 129.38, 129.15, 129.00, 128.93, 128.80, 128.79, 128.60, 128.55, 128.48, 128.45, 128.37, 128.34, 128.24, 128.22, 128.19, 127.89, 127.80, 127.75, 127.70, 127.63, 126.94, 125.26, 121.87, 101.09, 99.41, 93.20, 83.10, 75.26, 73.49, 73.27, 73.18, 73.13, 72.32, 72.05, 71.73, 71.49, 71.29, 69.77, 67.97, 67.41, 63.21, 60.85, 56.00, 48.76, 48.60, 47.74, 46.47, 46.16, 41.29, 40.34, 39.72, 38.11, 35.63, 34.77, 34.49, 32.60, 32.21, 31.04, 30.92, 30.41, 29.67, 26.74, 26.35, 24.54, 23.13, 21.43, 20.57, 16.81, 15.63, 9.45, 7.12, 6.80, 5.02, 4.89. **HRMS** (ESI) *m/z*: Calcd for $C_{123}H_{146}NO_{26}Si_2$ $(M+H)^+$ 2108.9672, found 2108.9617.

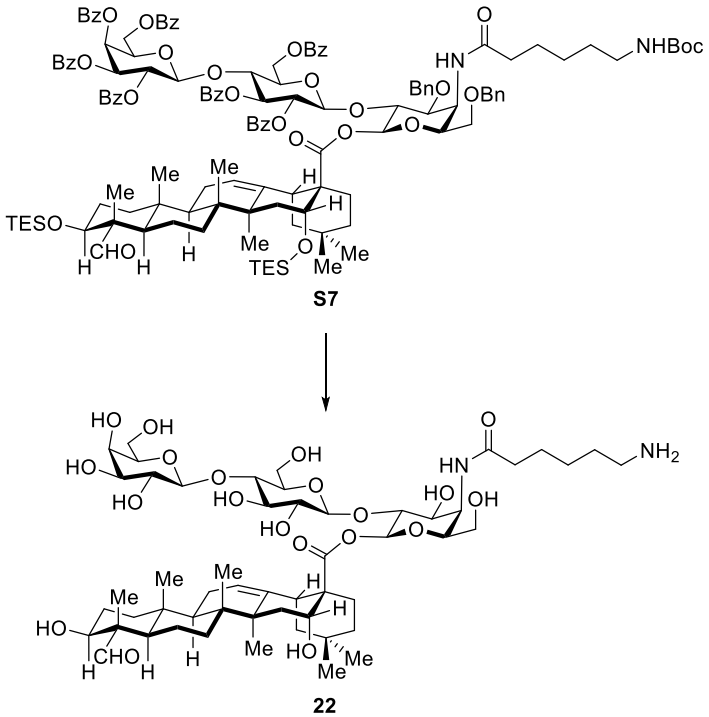


Protected lactosyl-(4-(6-aminocaproamido)-4-deoxygalactosyl) quillaic acid ester (S7) {(2*R*,3*S*,4*S*,5*R*,6*S*)-2-((benzoyloxy)methyl)-6-(((2*R*,3*R*,4*S*,5*R*,6*S*)-4,5-bis(benzoyloxy)-2-((benzoyloxy)methyl)-6-(((2*S*,3*R*,4*S*,5*S*,6*S*)-4-(benzyloxy)-6-((benzyloxy)methyl)-5-(6-((tert-butoxycarbonyl)amino)hexanamido)-2-(((4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-2,2,6a,6b,9,12a-hexamethyl-5,10-bis((triethylsilyl)oxy)-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-icosahydropicene-4a-carbonyl)oxy)tetrahydro-2*H*-pyran-3-yl)oxy)tetrahydro-2*H*-pyran-3-yl)oxy)tetrahydro-2*H*-pyran-3,4,5-triyl tribenzoate}.

To a clear, colorless solution of 6-((*t*-butoxycarbonyl)-amino)hexanoic acid (**15**) (34 mg, 0.15 mmol, 11.5 equiv) in tetrahydrofuran (2.0 mL) at 0 ºC was added triethylamine (160 µL, 1.15 mmol, 90 equiv) followed by ethyl chloroformate (12.2 µL, 0.13 mmol, 10.0 equiv). The turbid, white solution was stirred for 2.5 h at 0 °C and then added via cannula to amine **21** (27 mg, 12.8 µmol, 1.0 equiv). The reaction mixture was stirred at 0 ºC for 2 h, quenched with water (0.2 mL) and concentrated. Purification by silica gel chromatography (9:1 to 7:1

benzene/EtOAc with 0.2% triethylamine) afforded **S7** (28 mg, 94% yield) as a white glassy solid.

TLC: R_f 0.38 (85:15 benzene/EtOAc). **IR** (neat film) cm^{-1} 3064, 2952, 2875, 2361, 2341, 2251, 1736, 1602, 1501, 1452, 1315, 1268, 1177, 1094, 1070, 1028, 911, 736. **^{1}H NMR** (600 MHz, $CDCl_3$) characteristic resonances: δ 9.31 (s, 1H), 8.03–7.92 (m, 10H), 7.90–7.86 (m, 2H), 7.74–7.70 (m, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.22 (t, *J* = 7.9 Hz, 2H), 7.16 (t, *J* = 7.8 Hz, 2H), 5.81–5.65 (m, 4H), 5.43–5.36 (m, 2H), 5.32 (dd, *J* = 10.3, 3.4 Hz, 1H), 5.22–5.14 (m, 2H), 4.77–4.66 (m, 3H), 4.57–4.34 (m, 6H), 4.16–4.08 (m, 2H), 4.03 (t, *J* = 8.0 Hz, 1H), 3.83–3.75 (m, 2H), 3.71 (dd, *J* = 11.3, 6.2 Hz, 1H), 3.65–3.55 (m, 3H), 3.46 (dd, *J* = 8.9, 4.3 Hz, 1H), 3.39–3.28 (m, 2H), 3.08–2.99 (m, 2H), 2.85 (dd, *J* = 14.2, 3.9 Hz, 1H), 2.12 (t, *J* = 13.6 Hz, 1H), 1.66 (s, 4H), 1.45 (s, 9H), 1.32 (s, 3H), 1.06 (s, 3H), 0.84 (s, 3H), 0.83 (s, 3H), 0.75 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.37, 175.41, 172.74, 165.72, 165.46, 165.38, 165.30, 165.18, 165.13, 164.68, 155.90, 143.42, 137.52, 137.18, 133.49, 133.38, 133.30, 133.24, 133.18, 129.96, 129.87, 129.72, 129.64, 129.61, 129.57, 129.36, 129.32, 128.80, 128.74, 128.61, 128.54, 128.46, 128.37, 128.31, 128.26, 128.22, 127.77, 121.52, 100.95, 99.57, 81.50, 79.06, 76.04, 75.19, 73.49, 73.27, 73.19, 72.96, 72.93, 72.90, 71.96, 71.80, 71.35, 71.17, 69.75, 67.95, 67.32, 62.66, 60.76, 55.97, 48.87, 47.74, 46.43, 46.29, 45.61, 41.34, 40.34, 39.75, 38.13, 36.38, 35.70, 34.70, 34.44, 32.54, 32.18, 30.93, 30.73, 30.26, 29.71, 28.42, 26.75, 26.38, 25.15, 24.13, 23.27, 20.55, 16.76, 15.71, 9.52, 7.12, 6.80, 5.02, 4.87. **HRMS** (ESI) *m/z*: Calcd for $C_{134}H_{164}N_2O_{29}Si_2Na$ $(M+Na)^+$ 2344.0856, found 2344.0828.

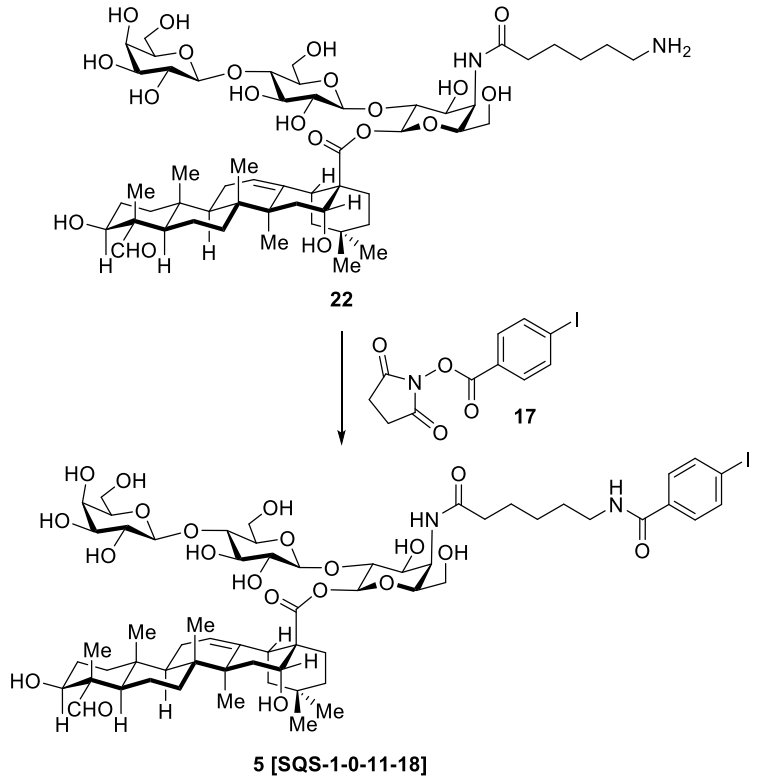


Lactosyl-(4-(6-aminocaproamido)-4-deoxygalactosyl) quillaic acid ester (22)
{(2*S*,3*R*,4*S*,5*R*,6*S*)-5-(6-aminohexanamido)-3-(((2*S*,3*R*,4*R*,5*S*,6*R*)-3,4-dihydroxy-6-(hydroxymethyl)-5-(((2*S*,3*R*,4*S*,5*R*,6*R*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-

pyran-2-yl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)-4-hydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl (4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-5,10-dihydroxy-2,2,6a,6b,9,12a-hexamethyl-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2*H*)-carboxylate}.

In a 25 mL round-bottom flask, **S7** (9.0 mg, 3.9 μmol, 1.0 equiv) was dissolved in tetrahydrofuran/ethanol (5 mL, 1:1) and 10% (dry basis) palladium on carbon, wet, Degussa type E101 NE/W (41.2 mg, 19.4 μmol, 5.0 equiv) was added. The reaction was stirred under hydrogen pressure (50 psi) for 10 h at 21 °C, and the suspension was filtered through a 0.45 μm nylon syringe filter, washed extensively with MeOH (2 × 20 mL) and CH_2Cl_2 (2 × 20 mL), and concentrated. Successful debenzylation is assessed by the disappearance of aromatic resonances by ^{1}H NMR in $CDCl_3$. The residue was then dissolved in a precooled (0 ºC) solution of trifluoroacetic acid (2.5 mL, TFA/H_2O 4:1), stirred for 2 h in an ice bath, and concentrated *in vacuo* to give a white solid residue. A solution of this crude product in methanol/water (10:1, 2.2 mL) was finally treated with NaOMe (0.5 M in MeOH, 0.2 mL, 97 μmol, 25 equiv) at 21 ºC and stirred for 6 h. After this time, the mixture was neutralized with Dowex 50-X8, filtered, washed thoroughly with MeOH and concentrated. The final residue was then dissolved in 30% acetonitrile/water (0.05% TFA) (6 mL) and purified by RP-HPLC on an XBridge Prep BEH300 C18 column (5 μm, 10 × 250 mm) using a linear gradient of 30−55% acetonitrile/water (0.05% TFA), over 15 min, at a flow rate of 5 mL/min. The 6-aminocaproic amide saponin **22** was obtained as a white powder (2.5 mg, 60% yield) after lyophilization.

HPLC: t_{ret} = 7.72 min, λ_{max} = 210 nm. **^{1}H NMR** (600 MHz, CD_3OD) characteristic resonances: δ 9.31 (s, 1H), 5.33 (d, *J* = 7.4 Hz, 1H), 5.30 (t, *J* = 3.4 Hz, 1H), 4.75–4.70 (m, 2H), 4.41–4.37 (m, 1H), 4.35 (d, *J* = 7.7 Hz, 1H), 4.07–3.96 (m, 3H), 3.89 (dd, *J* = 12.0, 4.8 Hz, 1H), 3.83 (d, *J* = 3.2 Hz, 1H), 3.80–3.75 (m, 2H), 3.60 (dd, *J* = 7.3, 4.9 Hz, 1H), 3.45 (dd, *J* = 12.8, 6.5 Hz, 1H), 3.24 (t, *J* = 8.3 Hz, 1H), 2.97–2.90 (m, 3H), 2.39–2.34 (m, 2H), 2.26 (t, *J* = 13.6 Hz, 1H), 1.39 (s, 3H), 1.07 (dd, *J* = 12.6, 3.4 Hz, 1H), 1.01 (s, 3H), 1.00 (s, 3H), 0.95 (s, 3H), 0.89 (s, 3H), 0.77 (s, 3H). **^{13}C NMR** (151 MHz, CD_3OD) δ 208.94, 177.68, 177.12, 145.15, 123.24, 105.46, 104.32, 94.72, 81.77, 77.27, 77.02, 76.91, 76.71, 75.55, 75.02, 74.56, 73.78, 73.01, 72.70, 70.38, 62.72, 62.58, 62.06, 56.97, 52.16, 50.00, 49.72, 48.24, 47.97, 42.76, 42.11, 41.33, 40.67, 39.61, 37.13, 36.92, 36.64, 36.29, 33.78, 33.46, 31.74, 31.44, 28.47, 27.48, 27.13, 27.03, 26.40, 25.08, 24.59, 24.36, 21.95, 17.92, 16.39, 9.57. **HRMS** (ESI) *m/z*: Calcd for $C_{54}H_{89}N_2O_{20}$ $(M+H)^+$ 1085.6009, found 1085.5994.



Lactosyl-(4-(6-(4-iodobenzamido)caproamido)-4-deoxygalactosyl) quillaic acid ester (Lactose variant 5, SQS-1-0-11-18)

{(2*S*,3*R*,4*S*,5*R*,6*S*)-3-(((2*S*,3*R*,4*R*,5*S*,6*R*)-3,4-dihydroxy-6-(hydroxymethyl)-5-(((2*S*,3*R*,4*S*,5*R*,6*R*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)-4-hydroxy-6-(hydroxymethyl)-5-(6-(4-iodobenzamido)hexanamido)tetrahydro-2*H*-pyran-2-yl (4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-5,10-dihydroxy-2,2,6a,6b,9,12a-hexamethyl-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2*H*)-carboxylate}.

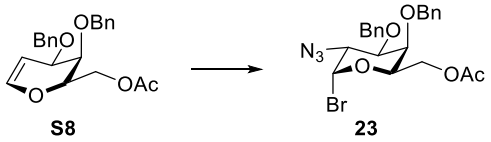
To a solution of **22** (3.2 mg, 3.0 μmol, 1.0 equiv) in *N,N′*-dimethylformamide (0.9 mL) was added triethylamine (8.2 μL, 59 μmol, 20 equiv) followed by dropwise addition of **17** (5.1 mg, 14.7 μmol, 5.0 equiv) in *N,N'*-dimethylformamide (0.6 mL). After stirring for 3 h, the contents were diluted with 30% acetonitrile/water (0.05% TFA) (6 mL) and purified by RP-HPLC on an XBridge Prep BEH300 C18 column (5 μm, 10 x 250 mm) using a linear gradient of 35–55% acetonitrile/water (0.05% TFA), over 18 min, at a flow rate of 5 mL/min. Lactose variant **5** (SQS-1-0-11-18) (3.1 mg, 80% yield) was obtained as a white powder after lyophilization.

HPLC: t_{ret} = 14.20 min, λ_{max} = 251 nm. **^{1}H NMR** (600 MHz, CD_3OD) characteristic resonances: δ 9.31 (s, 1H), 8.52 (t, *J* = 5.5 Hz, 1H), 8.01 (d, *J* = 9.3 Hz, 1H), 7.86–7.81 (m, 2H), 7.59–7.54 (m, 2H), 5.32 (d, *J* = 8.0 Hz, 1H), 5.30 (t, *J* = 3.4 Hz, 1H), 4.76–4.72 (m, 2H), 4.39–4.32 (m, 2H), 4.09–4.04 (m, 2H), 4.03–3.95 (m, 2H), 3.88 (dd, *J* = 12.0, 4.7 Hz, 1H), 3.83 (d, *J* = 3.1 Hz, 1H), 3.80–3.75 (m, 1H), 3.74–3.69 (m, 2H), 3.60 (dd, *J* = 7.0, 5.1 Hz, 1H), 3.23 (t, *J* = 8.4 Hz, 1H), 2.95 (dd, *J* = 14.2, 3.9 Hz, 1H), 2.40–2.30 (m, 2H), 2.26 (t, *J* = 13.6 Hz, 1H), 1.39 (s, 3H), 1.06 (dd, *J* = 12.9, 3.1 Hz, 1H), 1.01 (s, 3H), 0.99 (s, 3H), 0.95 (s, 3H), 0.89 (s, 3H), 0.77

(s, 3H). **^{13}C NMR** (151 MHz, CD_3OD) δ 208.96, 178.17, 177.17, 169.53, 145.16, 139.05, 135.55, 130.17, 123.23, 105.45, 104.27, 99.17, 94.71, 81.66, 77.24, 76.94, 76.84, 76.72, 75.53, 75.00, 74.54, 73.83, 73.02, 72.70, 70.39, 62.68, 62.58, 62.07, 56.98, 52.20, 50.03, 50.00, 49.72, 48.26, 47.98, 42.77, 42.12, 41.34, 41.07, 39.62, 37.13, 36.88, 36.72, 36.61, 33.78, 33.47, 31.68, 31.45, 30.29, 27.75, 27.48, 27.14, 26.95, 25.13, 24.60, 21.96, 17.95, 16.40, 9.57. **HRMS** (ESI) *m/z*: Calcd for $C_{61}H_{91}N_2O_{21}INa$ $(M+Na)^+$ 1337.5057, found 1337.5068.

---

3. SYNTHESIS OF 2-GALACTOSAMINE REGIOISOMERIC VARIANT 6 (SQS-1-0-12-18)

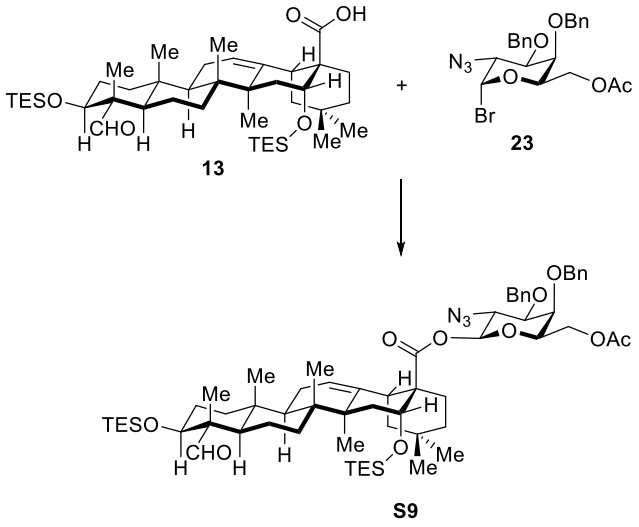


6-*O*-Acetyl-2-azido-3,4-di-*O*-benzyl-2-deoxy-α-D-galactopyranosyl bromide. A solution of 6-*O*-acetyl-3,4-di-*O*-benzyl-D-galactal **S8**[7] {((2*R*,3*R*,4*R*)-3,4-bis(benzyloxy)-3,4-dihydro-2*H*-pyran-2-yl)methyl acetate} (500 mg, 1.36 mmol, 1 equiv) in acetonitrile (6 mL) was added via cannula to a mixture of sodium azide (137 mg, 2.11 mmol, 1.55 equiv) and ceric ammonium nitrate (CAN) (2.24 g, 4.09 mmol, 3 equiv) at −25 ºC. After rinsing with additional acetonitrile (3 mL), the reaction was stirred between −20 ºC and −27 ºC for 5 h and then diluted with cold ether (80 mL). The mixture was washed with water (2 × 50 mL) and brine (50 mL), dried (Na_2SO_4), and concentrated. Purification by silica gel chromatography (9:1 to 7:1 hexanes/EtOAc with 0.2% triethylamine) afforded 263 mg (41%) of a clear oil as a mixture of azidonitrates (230 mg, α-anomer and 33 mg, β-anomer).

TLC: R_f 0.31 (α) and 0.18 (β) (8:2 hexanes/EtOAc). **^{1}H NMR** (500 MHz, $CDCl_3$) (α-anomer) δ 7.46–7.27 (m, 10H), 6.28 (d, *J* = 4.2 Hz, 1H), 4.93 (d, *J* = 11.2 Hz, 1H), 4.81–4.77 (m, 2H), 4.56 (d, *J* = 11.2 Hz, 1H), 4.31 (dd, *J* = 10.8, 4.2 Hz, 1H), 4.17 (dd, *J* = 10.9, 6.4 Hz, 1H), 4.11–4.03 (m, 2H), 3.97–3.94 (m, 1H), 3.87 (dd, *J* = 10.8, 2.5 Hz, 1H), 2.00 (s, 3H).

To a solution of α-azidonitrate (230 mg, 0.49 mmol, 1 equiv) in acetonitrile (2 mL) was added LiBr (211, 2.43 mmol, 5 equiv) and the reaction was stirred at 21 ºC for 4 h. The solution was diluted with cold CH_2Cl_2 (30 mL), this organic phase was washed with cold water (3 × 7 mL) and the aqueous layers extracted with CH_2Cl_2 (10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated to afford **23** as a yellow oil (220 mg, 92% yield). By ^{1}H NMR analysis, this product was judged to be sufficiently pure for use in the next step.

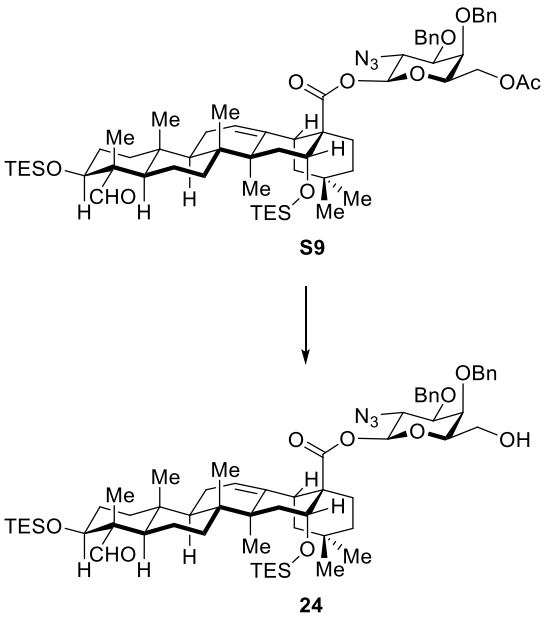
TLC: R_f 0.33 (8:2 hexanes/EtOAc). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.47–7.25 (m, 10H), 6.49 (d, *J* = 3.6 Hz, 1H), 4.93 (d, *J* = 11.2 Hz, 1H), 4.84–4.75 (m, 2H), 4.57 (d, *J* = 11.2 Hz, 1H), 4.21–4.10 (m, 4H), 4.03–3.93 (m, 2H), 2.02 (s, 3H). **HRMS** (ESI) *m/z*: Calcd for $C_{22}H_{24}BrN_3O_5Na$ $(M+Na)^+$ 512.0799, found 512.0820.



Protected 6-*O*-acetyl-2-azido-2-deoxygalactosyl quillaic acid ester (S9)
{(2*S*,3*R*,4*R*,5*R*,6*R*)-6-(acetoxymethyl)-3-azido-4,5-bis(benzyloxy)tetrahydro-2*H*-pyran-2-yl (4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-2,2,6a,6b,9,12a-hexamethyl-5,10-bis((triethylsilyl)oxy)-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2*H*)-carboxylate}.

To a solution of bromide **23** (75 mg, 0.15 mmol, 1.3 equiv) and acid **13** (84 mg, 0.12 mmol, 1 equiv) in EtOAc/water (6 mL, 1:1), were added K_2CO_3 (41 mg, 0.30 mmol, 2.5 equiv) and Bu_4NBr (57 mg, 0.18 mmol, 1.5 equiv). The mixture was stirred vigorously at 45 ºC for 5 h, and was then diluted with EtOAc (65 mL), and washed with water (20 mL) and brine (20 mL). The organic layer was dried over Na_2SO_4, filtered, and evaporated to give a residue that was purified by silica gel chromatography (98:2 benzene/EtOAc) to afford **S9** (112 mg, 84% yield) as a white solid.

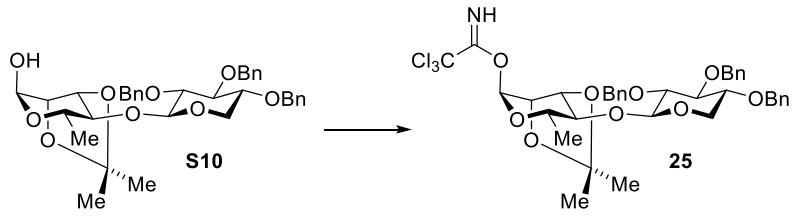
TLC: R_f 0.67 (9:1 benzene/EtOAc). **IR** (neat film) cm^{-1} 2951, 2360, 2341, 2113, 1736, 1458, 1365, 1238, 1053, 911, 818, 741. **^{1}H NMR** (600 MHz, $CDCl_3$) characteristic resonances: δ 9.34 (s, 1H), 5.40 (t, *J* = 3.3 Hz, 1H), 5.24 (d, *J* = 8.6 Hz, 1H), 4.95 (d, *J* = 11.6 Hz, 1H), 4.77 (s, 2H), 4.66–4.60 (m, 2H), 4.17 (dd, *J* = 11.2, 6.3 Hz, 1H), 4.05 (dd, *J* = 11.2, 6.4 Hz, 1H), 3.93 (dd, *J* = 10.1, 8.7 Hz, 1H), 3.85–3.79 (m, 2H), 3.60 (t, *J* = 6.4 Hz, 1H), 3.45 (dd, *J* = 10.2, 2.7 Hz, 1H), 3.00 (dd, *J* = 14.3, 4.0 Hz, 1H), 2.26 (t, *J* = 13.6 Hz, 1H), 1.96 (s, 3H), 1.42 (s, 3H), 1.07 (s, 3H), 0.76 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.23, 174.50, 170.27, 147.97, 143.01, 137.63, 137.13, 128.54, 128.36, 128.32, 128.26, 128.24, 128.17, 128.10, 128.08, 127.94, 127.85, 127.76, 126.72, 125.92, 125.67, 121.98, 92.82, 81.10, 74.78, 74.46, 73.13, 73.11, 73.04, 71.44, 62.42, 62.34, 55.96, 48.79, 47.78, 46.50, 46.40, 44.50, 41.35, 40.39, 39.60, 39.52, 38.14, 37.78, 35.71, 35.02, 34.38, 34.22, 32.61, 32.36, 30.88, 30.37, 29.43, 26.84, 26.72, 26.31, 26.09, 24.14, 23.61, 23.25, 22.58, 20.66, 20.58, 16.86, 15.64, 9.38, 7.06, 6.75, 4.98, 4.90. **HRMS** (ESI) *m/z*: Calcd for $C_{64}H_{97}N_3O_{10}Si_2Na$ $(M+Na)^+$ 1146.6610, found 1146.6643.



Protected 2-azido-2-deoxygalactosyl quillaic acid ester (24)
{(2*S*,3*R*,4*R*,5*R*,6*R*)-3-azido-4,5-bis(benzyloxy)-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl (4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-2,2,6a,6b,9,12a-hexamethyl-5,10-bis((triethylsilyl)oxy)-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2*H*)-carboxylate}.

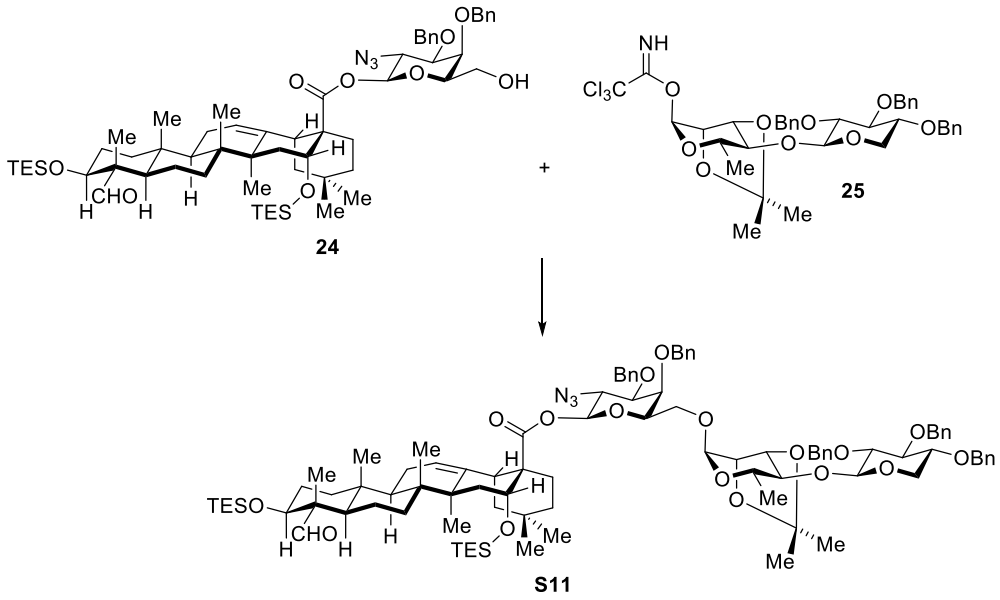
To a solution of **S9** (110 mg, 0.10 mmol, 1 equiv) in MeOH/CH_2Cl_2/H_2O (24 mL/7 mL/2.4 mL), NaOMe (0.5 M in MeOH, 2.9 mL, 1.47 mmol, 15 equiv) was added gradually, and the reaction was stirred at 21 ºC for 2 h. After this time, the mixture was diluted with CH_2Cl_2 (100 mL) and partitioned with saturated $NaHCO_3$ (25 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 80 mL) and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. Purification by silica gel chromatography (7:3 hexanes/EtOAc) afforded **24** (92 mg, 87% yield) as a white solid.

TLC: R_f 0.39 (9:1 benzene/EtOAc). **IR** (neat film) cm^{-1} 3504, 2953, 2911, 2877, 2349, 2114, 1734, 1456, 1240, 1111, 1078, 910, 818, 735. **^{1}H NMR** (600 MHz, $CDCl_3$) characteristic resonances: δ 9.32 (s, 1H), 5.37 (t, *J* = 3.4 Hz, 1H), 5.20 (d, *J* = 8.6 Hz, 1H), 4.92 (d, *J* = 11.7 Hz, 1H), 4.74 (s, 2H), 4.65–4.58 (m, 2H), 3.90 (dd, *J* = 10.1, 8.7 Hz, 1H), 3.84–3.77 (m, 2H), 3.72 (dd, *J* = 10.8, 6.2 Hz, 1H), 3.50–3.40 (m, 3H), 2.97 (dd, *J* = 14.3, 4.1 Hz, 1H), 2.24 (t, *J* = 13.6 Hz, 1H), 1.84 (td, *J* = 12.9, 4.6 Hz, 1H), 1.39 (s, 3H), 1.36 (dd, *J* = 14.9, 2.4 Hz, 1H), 1.08 (dd, *J* = 12.7, 3.2 Hz, 1H), 1.05 (s, 3H), 0.73 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.38, 174.71, 143.05, 137.72, 137.17, 128.62, 128.56, 128.50, 128.18, 128.16, 127.87, 122.04, 93.11, 81.15, 75.85, 74.83, 74.38, 73.15, 73.04, 71.30, 62.63, 61.45, 56.02, 48.82, 47.81, 46.52, 46.40, 41.38, 40.41, 39.66, 38.17, 35.76, 35.07, 34.25, 32.66, 32.38, 31.00, 30.42, 26.76, 26.36, 24.21, 23.28, 20.62, 16.88, 15.69, 9.42, 7.10, 6.79, 5.02, 4.94. **HRMS** (ESI) *m/z*: Calcd for $C_{62}H_{95}N_3O_9Si_2Na$ $(M+Na)^+$ 1104.6505, found 1104.6519.



***O*-Trichloroacetimidoyl 2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl-(1→4)-2,3-di-*O*-isopropylidene-L-rhamnopyranoside (25).** To a solution of hemiacetal **S10**[3] (50 mg, 0.082 mmol, 1.0 equiv) in CH_2Cl_2 (12 mL) at 0 ºC, trichloroacetonitrile (1.24 mL, 12.36 mmol, 150 equiv) and 1,8-diazabicyclo[5.4.0]undec-7-ene (62 μL, 0.41 mmol, 5.0 equiv) were added. The mixture was stirred at 0 ºC for 2 h and and at 21 ºC for 1 h, and then concentrated in vacuo. Purification by silica gel column chromatography (8:2 hexanes/EtOAc with 1% triethylamine) gave tricloroacetimidate **25** (60 mg, 97% yield) as a clear film, which was directly used in the subsequent glycosylation step.

TLC: R_f 0.48 (8:2 hexanes/EtOAc). **^{1}H NMR** (500 MHz, C_6D_6) δ 8.54 (s, 1H), 7.42 (d, *J* = 7.6 Hz, 2H), 7.35 (d, *J* = 7.5 Hz, 2H), 7.23–7.06 (m, 11H), 6.84 (s, 1H), 5.15 (d, *J* = 7.5 Hz, 1H), 4.96 (d, *J* = 11.4 Hz, 1H), 4.92 (d, *J* = 11.5 Hz, 1H), 4.86 (d, *J* = 11.5 Hz, 1H), 4.78 (d, *J* = 11.4 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 4.43–4.38 (m, 1H), 4.36 (d, *J* = 12.0 Hz, 1H), 4.26 (d, *J* = 4.9 Hz, 1H), 4.13 (dq, *J* = 12.2, 6.1 Hz, 1H), 4.04 (dd, *J* = 9.9, 7.3 Hz, 1H), 3.82 (dd, *J* = 11.5, 5.3 Hz, 1H), 3.64 (t, *J* = 8.8 Hz, 1H), 3.55 (td, *J* = 9.2, 5.4 Hz, 1H), 3.51–3.45 (m, 1H), 3.21–3.14 (m, 1H), 1.51 (d, *J* = 6.1 Hz, 3H), 1.45 (s, 3H), 1.17 (s, 3H). **HRMS** (ESI) *m/z*: Calcd for $C_{37}H_{42}Cl_3NO_9Na$ $(M+Na)^+$ 772.1823, found 772.1801.

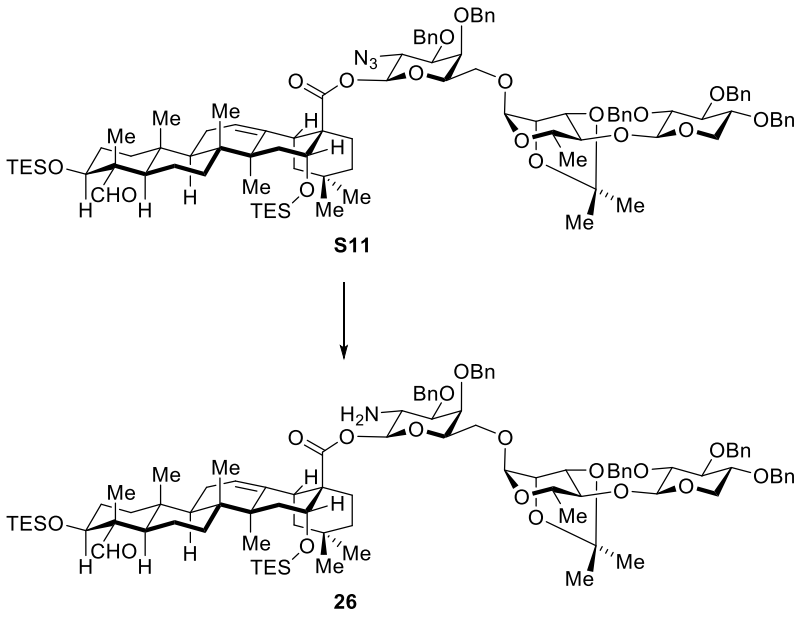


Protected xylosyl-rhamnosyl-(2-azido-2-deoxygalactosyl) quillaic acid ester (S11)
{(2*S*,3*R*,4*R*,5*R*,6*R*)-3-azido-4,5-bis(benzyloxy)-6-((((3a*R*,4*R*,6*S*,7*S*,7a*R*)-2,2,6-trimethyl-7-(((2*S*,3*R*,4*S*,5*R*)-3,4,5-tris(benzyloxy)tetrahydro-2*H*-pyran-2-yl)oxy)tetrahydro-4*H*-[1,3]dioxolo[4,5-c]pyran-4-yl)oxy)methyl)tetrahydro-2*H*-pyran-2-yl

(4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-2,2,6a,6b,9,12a-hexamethyl-5,10-bis((triethylsilyl)oxy)-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2*H*)-carboxylate}.

To a solution of alcohol **24** (51.6 mg, 47.7 μmol, 1.0 equiv) and disaccharide imidate **25** (43.0 mg, 57.3 μmol, 1.2 equiv) in CH_2Cl_2 (7 mL) with 50 mg powdered 4 Å molecular sieves at −45 ºC, trimethylsilyl trifluoromethanesulfonate (0.6 μL, 3.3 μmol, 0.07 equiv) was injected. The mixture was stirred at this temperature for 30 min, at which point additional trimethylsilyl trifluoromethanesulfonate (0.6 μL, 3.3 μmol, 0.07 equiv) was added. After stirring at −45 ºC for another 20 min, the reaction was quenched by addition of triethylamine (0.3 mL) and concentrated. The residue was redissolved in CH_2Cl_2 (6 mL), and lutidine (60 μL, 0.52 mmol) was injected at −20 ºC, followed by triethylsilyl trifluoromethanesulfonate (60 μL, 0.27 mmol). The mixture was stirred at this temperature for 20 min and then concentrated. Purification of the residue by silica gel chromatography (49:1 to 39:1 benzene/EtOAc) gave **S11** (40 mg, 50% yield) as a white solid.

TLC: R_f 0.60 (9:1 benzene/EtOAc). **IR** (neat film) cm^{-1} 2951, 2876, 2360, 2341, 2113, 1735, 1497, 1454, 1381, 1158, 1072, 818, 735. **^{1}H NMR** (600 MHz, $CDCl_3$) characteristic resonances: δ 9.31 (s, 1H), 5.35 (t, *J* = 3.2 Hz, 1H), 5.20 (d, *J* = 8.6 Hz, 1H), 4.95–4.79 (m, 6H), 4.74–4.67 (m, 3H), 4.66–4.58 (m, 3H), 4.55 (d, *J* = 11.4 Hz, 1H), 4.18–4.11 (m, 1H), 4.02 (d, *J* = 5.6 Hz, 1H), 3.93 (dd, *J* = 11.6, 4.2 Hz, 1H), 3.90–3.85 (m, 1H), 3.82–3.77 (m, 1H), 3.63–3.53 (m, 6H), 3.48 (td, *J* = 12.3, 6.1 Hz, 1H), 3.41 (dd, *J* = 10.2, 2.6 Hz, 1H), 3.28 (t, *J* = 8.1 Hz, 1H), 3.22–3.15 (m, 1H), 2.97 (dd, *J* = 14.2, 3.8 Hz, 1H), 2.23 (t, *J* = 13.6 Hz, 1H), 1.82 (td, *J* = 12.9, 4.4 Hz, 1H), 1.49 (s, 3H), 1.38 (s, 3H), 1.34 (s, 3H), 1.15 (d, *J* = 6.2 Hz, 3H), 1.04 (s, 3H), 0.73 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.39, 174.66, 143.09, 138.72, 138.62, 138.20, 137.81, 137.23, 128.57, 128.43, 128.35, 128.29, 128.08, 128.00, 127.97, 127.94, 127.89, 127.79, 127.77, 127.75, 127.57, 127.54, 122.02, 109.34, 102.07, 97.55, 92.98, 83.82, 82.02, 81.20, 78.11, 77.98, 77.92, 75.72, 75.59, 74.85, 74.73, 74.55, 74.25, 73.16, 72.96, 72.02, 65.86, 64.44, 63.77, 62.53, 56.05, 48.85, 47.83, 46.55, 46.45, 41.40, 40.44, 39.67, 38.21, 35.78, 35.07, 34.30, 32.68, 32.42, 31.02, 30.45, 29.69, 27.77, 26.79, 26.37, 24.25, 23.32, 20.66, 17.52, 16.94, 15.75, 9.43, 7.12, 6.81, 5.04, 4.96. **HRMS** (ESI) *m/z*: Calcd for $C_{97}H_{135}N_3O_{17}Si_2Na$ $(M+Na)^+$ 1692.9293, found 1692.9228.

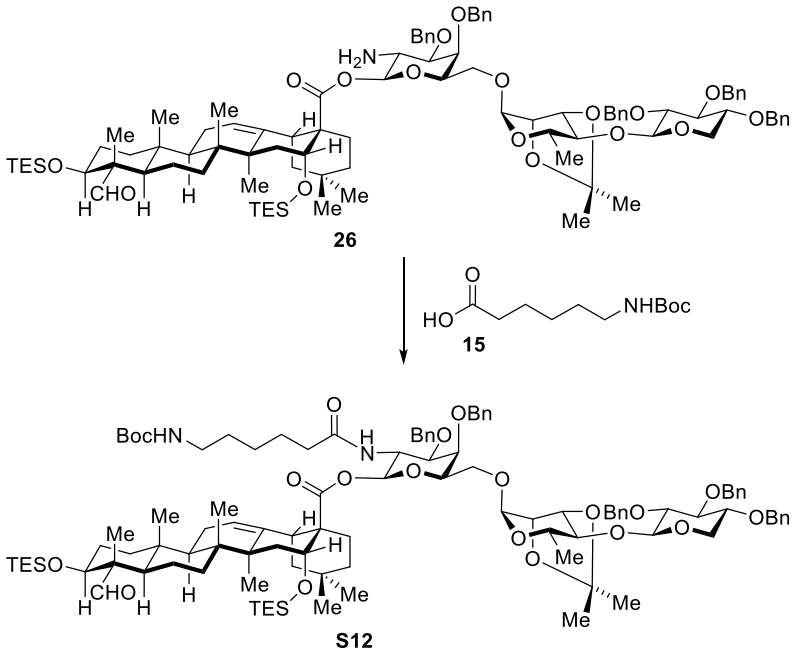


Protected xylosyl-rhamnosyl-(2-amino-2-deoxygalactosyl) quillaic acid ester (26) {(2*S*,3*R*,4*R*,5*R*,6*R*)-3-amino-4,5-bis(benzyloxy)-6-((((3a*R*,4*R*,6*S*,7*S*,7a*R*)-2,2,6-trimethyl-7-(((2*S*,3*R*,4*S*,5*R*)-3,4,5-tris(benzyloxy)tetrahydro-2*H*-pyran-2-yl)oxy)tetrahydro-4*H*-[1,3]dioxolo[4,5-c]pyran-4-yl)oxy)methyl)tetrahydro-2*H*-pyran-2-yl (4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-2,2,6a,6b,9,12a-hexamethyl-5,10-bis((triethylsilyl)oxy)-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2*H*)-carboxylate}.

To a solution of **S11** (49 mg, 29 μmol, 1.0 equiv) in triethylamine (25 mL) was added a freshly prepared solution of phenyl selenol (0.88 mmol, 30 equiv) via cannula. Upon addition of phenyl selenol a white precipitate was formed and the solution became bright yellow. The reaction was stirred for 12 h at 38 °C, and concentrated to afford a yellow-white solid. The crude residue was purified by silica gel chromatography (9:1 to 6:1 benzene/EtOAc to afford the amine **26** (37 mg, 77% yield) as a glassy solid.

TLC: R_f 0.28 (9:1 benzene/EtOAc). **IR** (neat film) cm^{-1} 2953, 2878, 2362, 2253, 1736, 1457, 1383, 1243, 1162, 1073, 913, 820, 737. **^{1}H NMR** (600 MHz, $CDCl_3$) characteristic resonances: δ 9.31 (s, 1H), 5.34 (t, *J* = 3.5 Hz, 1H), 4.95–4.80 (m, 6H), 4.77–4.69 (m, 2H), 4.67–4.60 (m, 2H), 4.58–4.51 (m, 2H), 4.20–4.15 (m, 1H), 4.06 (d, *J* = 5.6 Hz, 1H), 3.94 (dd, *J* = 11.6, 4.4 Hz, 1H), 3.85 (s, 1H), 3.79 (dd, *J* = 11.4, 4.5 Hz, 1H), 3.71–3.55 (m, 6H), 3.51 (dt, *J* = 15.1, 5.7 Hz, 1H), 3.44 (t, *J* = 8.9 Hz, 1H), 3.29 (dd, *J* = 8.9, 7.7 Hz, 1H), 3.23–3.17 (m, 1H), 2.97 (dd, *J* = 14.3, 3.9 Hz, 1H), 2.21 (t, *J* = 13.6 Hz, 1H), 1.50 (s, 3H), 1.38–1.33 (m, 6H), 1.15 (d, *J* = 6.2 Hz, 3H), 1.03 (s, 3H), 0.87 (s, 3H), 0.72 (s, 3H)). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.43, 174.98, 142.89, 138.72, 138.61, 138.20, 138.13, 137.33, 129.01, 128.63, 128.59, 128.42, 128.39, 128.27, 128.21, 128.07, 128.03, 127.99, 127.97, 127.94, 127.82, 127.78, 127.74, 127.70, 127.65, 127.56, 127.52, 127.47, 125.27, 122.12, 109.32, 102.08, 97.58, 83.81, 82.02, 78.16, 78.01, 77.92, 75.77, 75.58, 75.00, 74.73, 74.30, 74.10, 73.18, 73.15, 72.20, 71.06, 66.01, 64.41, 63.77, 56.03, 51.67, 48.98, 47.80, 46.56, 46.44, 41.43, 40.54, 39.72, 38.22, 35.75, 35.06, 34.59, 32.65, 32.44, 31.07, 30.46, 29.68, 27.78, 26.78, 26.37, 26.35, 24.34, 23.30, 21.45, 20.60, 17.50, 17.13, 15.76, 9.43,

7.11, 6.81, 5.03, 4.98, 4.96, 4.92. **HRMS** (ESI) *m/z*: Calcd for $C_{97}H_{138}NO_{17}Si_2$ $(M+H)^+$ 1644.9503, found 1644.9541.



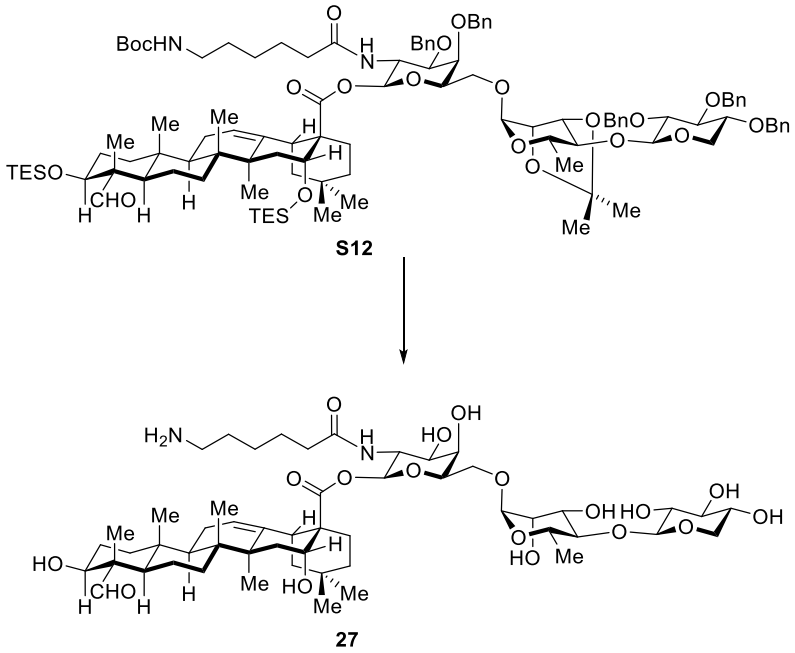
Protected xylosyl-rhamnosyl-(2-(6-aminocaproamido)-2-deoxygalactosyl) quillaic acid ester (S12)

{(2*S*,3*R*,4*R*,5*R*,6*R*)-4,5-bis(benzyloxy)-3-(6-((tert-butoxycarbonyl)amino)hexanamido)-6-((((3a*R*,4*R*,6*S*,7*S*,7a*R*)-2,2,6-trimethyl-7-(((2*S*,3*R*,4*S*,5*R*)-3,4,5-tris(benzyloxy)tetrahydro-2*H*-pyran-2-yl)oxy)tetrahydro-4*H*-[1,3]dioxolo[4,5-c]pyran-4-yl)oxy)methyl)tetrahydro-2*H*-pyran-2-yl (4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-2,2,6a,6b,9,12a-hexamethyl-5,10-bis((triethylsilyl)oxy)-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2*H*)-carboxylate}.

To a clear, colorless solution of 6-[(*t*-butoxycarbonyl)-amino]hexanoic acid (**15**) (38.8 mg, 0.17 mmol, 11.5 equiv) in tetrahydrofuran (2 mL) at 0 ºC was added triethylamine (183 µL, 1.31 mmol, 90 equiv) followed by ethyl chloroformate (14.0 µL, 0.15 mmol, 10.0 equiv). The turbid, white solution was stirred for 2.5 h at 0 °C and then added via cannula to amine **26** (24 mg, 14.6 µmol, 1.0 equiv) at 0 ºC. The reaction mixture was stirred at this temperature for 2 h, quenched with water (0.2 mL), and concentrated. Purification by silica gel chromatography (9:1 to 6:1 benzene/EtOAc with 0.5% triethylamine) afforded **S12** (22 mg, 81% yield) as a white glassy solid.

TLC: R_f 0.09 (9:1 benzene/EtOAc). **IR** (neat film) cm^{-1} 3333, 3030, 2950, 2876, 2360, 2341, 1732, 1455, 1365, 1242, 1165, 1090, 911, 863, 820, 735. **^{1}H NMR** (600 MHz, $CDCl_3$) characteristic resonances: δ 9.31 (s, 1H), 5.71 (d, *J* = 8.0 Hz, 1H), 5.34 (t, *J* = 3.1 Hz, 1H), 5.24 (d, *J* = 6.3 Hz, 1H), 4.73–4.67 (m, 2H), 4.66– 4.60 (m, 2H), 4.56–4.50 (m, 2H), 4.44 (d, *J* = 11.6 Hz, 1H), 4.20–4.14 (m, 1H), 4.05 (d, *J* = 5.6 Hz, 1H), 4.02–3.96 (m, 2H), 3.93 (dd, *J* = 11.6, 4.1 Hz, 1H), 3.88 (s, 1H), 3.79 (dd, *J* = 11.3, 4.3 Hz, 1H), 3.29 (t, *J* = 8.1 Hz, 1H), 3.23–3.17 (m,

1H), 2.94 (dd, *J* = 14.2, 3.7 Hz, 1H), 2.19 (t, *J* = 13.6 Hz, 1H), 1.49 (s, 3H), 1.44 (s, 9H), 1.35 (s, 6H), 1.16 (d, *J* = 6.1 Hz, 3H), 1.03 (s, 3H), 0.86 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.50, 174.93, 172.66, 155.96, 142.90, 138.73, 138.61, 138.21, 138.09, 137.62, 128.54, 128.42, 128.28, 127.99, 127.97, 127.94, 127.87, 127.78, 127.75, 127.70, 127.65, 127.55, 127.53, 122.05, 109.32, 102.09, 97.57, 92.15, 83.82, 82.03, 79.03, 78.61, 78.15, 78.04, 77.93, 75.77, 75.58, 74.85, 74.73, 74.37, 73.94, 73.22, 73.15, 72.06, 71.97, 66.05, 64.37, 63.77, 56.04, 52.33, 48.78, 47.72, 46.56, 46.40, 41.36, 40.24, 39.63, 38.18, 36.56, 35.76, 35.12, 34.62, 32.68, 32.50, 31.07, 30.46, 29.84, 28.41, 27.78, 26.77, 26.45, 26.39, 26.32, 24.98, 24.28, 23.28, 20.60, 17.51, 16.90, 15.75, 9.44, 7.14, 6.81, 5.03, 4.93. **HRMS** (ESI) *m/z*: Calcd for $C_{108}H_{156}N_2O_{20}Si_2Na$ $(M+Na)^+$ 1880.0688, found 1880.0662.

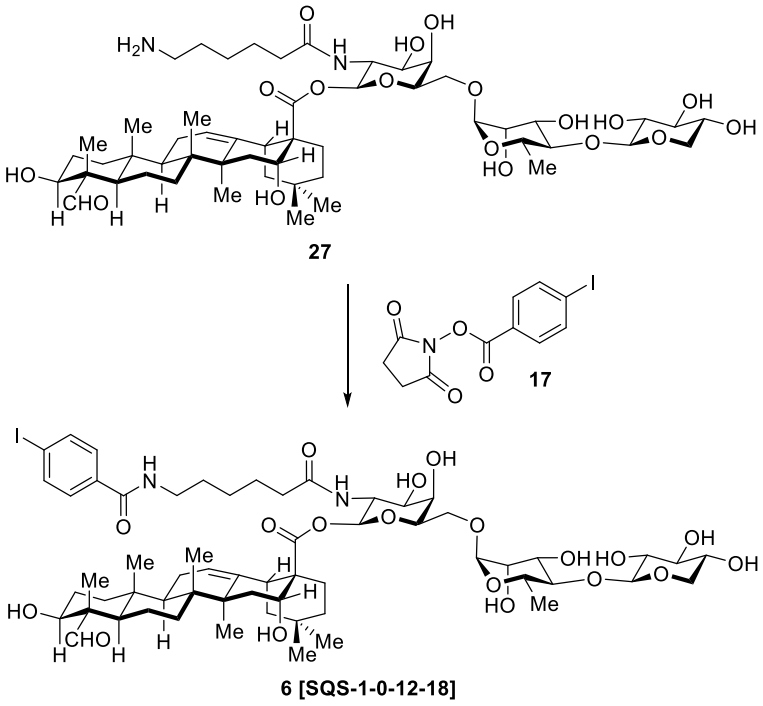


Xylosyl-rhamnosyl-(2-(6-aminocaproamido)-2-deoxygalactosyl) quillaic acid ester (27)
{(2*S*,3*R*,4*R*,5*R*,6*R*)-3-(6-aminohexanamido)-6-((((2*R*,3*R*,4*S*,5*R*,6*S*)-3,4-dihydroxy-6-methyl-5-(((2*S*,3*R*,4*S*,5*R*)-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)methyl)-4,5-dihydroxytetrahydro-2*H*-pyran-2-yl (4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-5,10-dihydroxy-2,2,6a,6b,9,12a-hexamethyl-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2*H*)-carboxylate}.

In a 10 mL round-bottom flask, **S12** (4.3 mg, 2.3 μmol, 1.0 equiv) was dissolved in tetrahydrofuran/ethanol (2 mL, 1:1) and 10% (dry basis) palladium on carbon, wet, Degussa type E101 NE/W (25 mg, 11.6 μmol, 5.0 equiv) was added. The reaction was stirred under hydrogen atmosphere (balloon) at 21 ºC for 12 h, and the suspension was filtered through a 0.45 μm nylon syringe filter, washed with methanol (25 mL) and concentrated. Successful debenzylation is assessed by the disappearance of aromatic resonances by ^{1}H NMR in CD_3OD. The crude mixture was then dissolved in a pre-cooled (0 ºC) solution of trifluoroacetic acid (0.4 mL, TFA/H_2O 3:1) and stirred at 0º C for 65 min. The reaction was evaporated to dryness at 0 ºC to

afford a white solid that was dissolved in 30% acetonitrile/water (2.5 mL) and purified via RP-HPLC on an XBridge Prep BEH300 C18 column (5 μm, 10 × 250 mm) using a linear gradient of 30–70% acetonitrile/water, over 15 min, at a flow rate of 5 mL/min. The amine-functionalized derivative **27** eluted was obtained as a white powder (1.4 mg, 60% yield) after lyophilization.

HPLC: t_{ret} = 5.40 min, λ_{max} = 210 nm. **^{1}H NMR** (600 MHz, CD_3OD) characteristic resonances: δ 9.30 (s, 1H), 5.37 (d, *J* = 8.9 Hz, 1H), 5.33 (t, *J* = 3.5 Hz, 1H), 4.69 (s, 1H), 4.52 (d, *J* = 7.8 Hz, 1H), 4.43 (s, 1H), 4.17 (t, *J* = 9.8 Hz, 1H), 3.89–3.76 (m, 6H), 3.75–3.66 (m, 2H), 3.63–3.52 (m, 3H), 3.49–3.40 (m, 2H), 3.22–3.14 (m, 3H), 2.98 (d, *J* = 14.4 Hz, 1H), 2.93–2.86 (m, 2H), 2.33–2.15 (m, 3H), 1.97–1.87 (m, 4H), 1.39 (s, 3H), 1.29 (d, *J* = 6.2 Hz, 3H), 1.00 (s, 6H), 0.95 (s, 3H), 0.88 (s, 3H), 0.77 (s, 3H). **^{13}C NMR** (151 MHz, CD_3OD) δ 208.78, 177.09, 176.15, 163.46, 163.23, 163.00, 144.69, 123.65, 106.70, 101.90, 94.64, 83.66, 78.35, 76.18, 75.82, 74.73, 72.97, 72.71, 72.17, 71.28, 69.58, 68.55, 67.41, 67.15, 56.95, 52.39, 50.00, 48.16, 47.88, 42.81, 41.93, 41.21, 40.81, 39.54, 37.26, 37.14, 36.55, 36.51, 33.81, 33.52, 32.30, 31.49, 28.87, 27.32, 27.24, 27.12, 26.20, 25.17, 24.57, 21.88, 18.55, 18.24, 18.17, 16.44, 9.55. **HRMS** (ESI) *m/z*: Calcd for $C_{53}H_{87}N_2O_{18}$ $(M+H)^+$ 1039.5954, found 1039.5957.



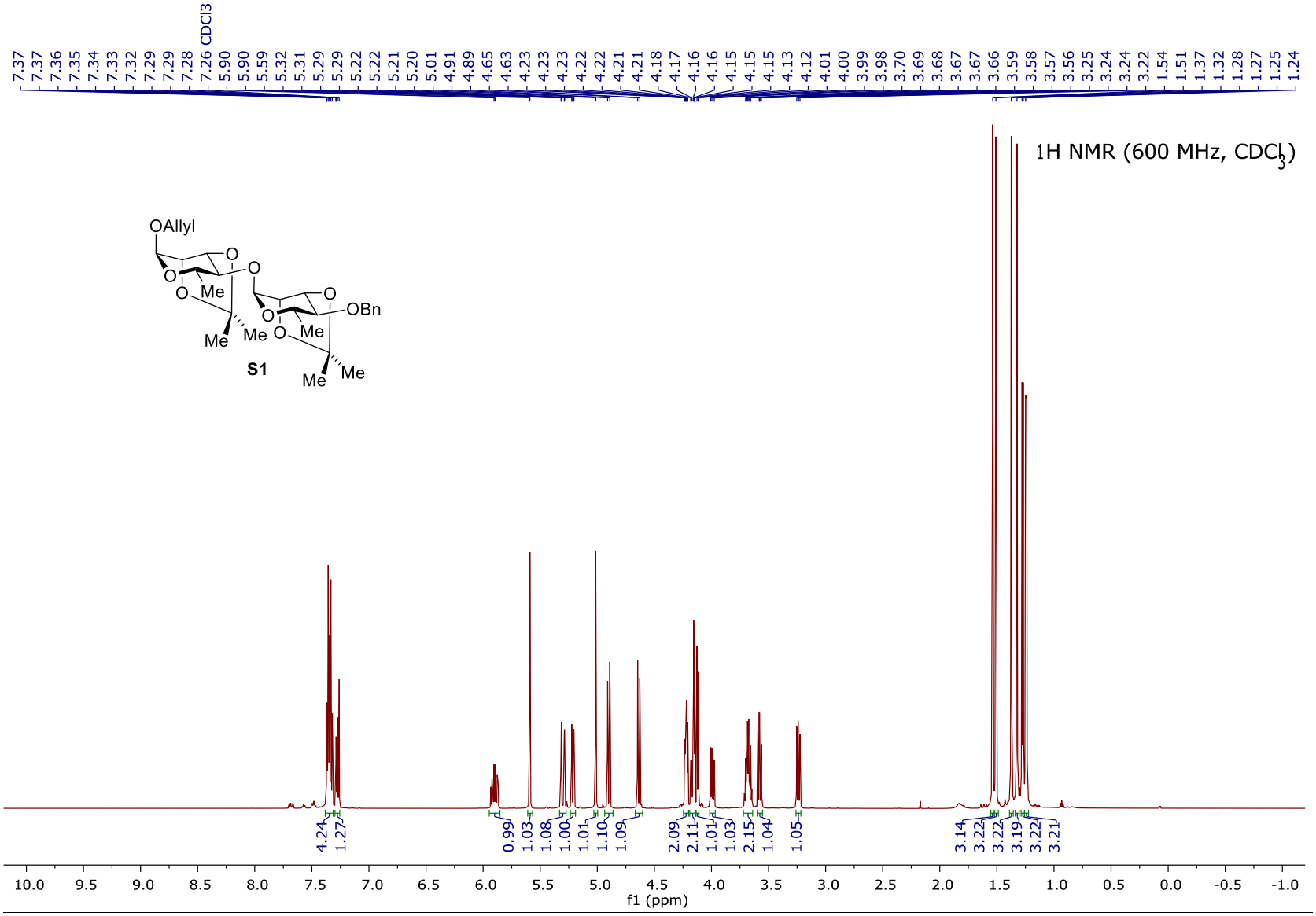
Xylosyl-rhamnosyl-(2-(6-(4-iodobenzamido)caproamido)-2-deoxygalactosyl) quillaic acid ester (2-Galactosamine regioisomeric variant 6, SQS-1-0-12-18)
{(2*S*,3*R*,4*R*,5*R*,6*R*)-6-((((2*R*,3*R*,4*S*,5*R*,6*S*)-3,4-dihydroxy-6-methyl-5-(((2*S*,3*R*,4*S*,5*R*)-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)methyl)-4,5-dihydroxy-3-(6-(4-iodobenzamido)hexanamido)tetrahydro-2*H*-pyran-2-yl (4a*R*,5*R*,6a*S*,6b*R*,8a*R*,9*S*,10*S*,12a*R*,12b*R*,14b*S*)-9-formyl-5,10-dihydroxy-2,2,6a,6b,9,12a-hexamethyl-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(2*H*)-carboxylate}.

To a solution of **27** (3.2 mg, 3.1 μmol, 1.0 equiv) in *N,N'*-dimethylformamide (0.9 mL) at 0 ºC was added triethylamine (8.6 μL, 62.0 μmol, 20 equiv) followed by dropwise addition of **17** (5.3 mg, 15.4 μmol, 5.0 equiv) in *N,N'*-dimethylformamide (0.6 mL). The reaction mixture was stirred at 21 °C for 3 h. After this time, the contents were diluted with 30% acetonitrile/water (5 mL) and purified by RP-HPLC on an XBridge Prep BEH300 C18 column (5 μm, 10 x 250 mm) using a linear gradient of 30–70% acetonitrile/water, over 15 min, at a flow rate of 5 mL/min. 2-Galactosamine regiosiomeric variant **6** (SQS-1-0-12-18) (2.0 mg, 51% yield) was obtained as a white powder after lyophilization.

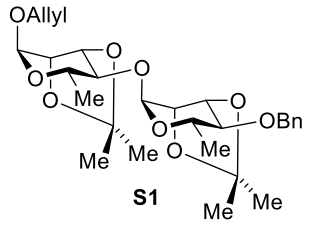
HPLC: t_{ret} = 11.87 min, λ_{max} = 251 nm. **^{1}H NMR** (600 MHz, CD_3OD) characteristic resonances: δ 9.28 (s, 1H), 7.87–7.83 (m, 2H), 7.60–7.55 (m, 2H), 5.38 (d, *J* = 8.9 Hz, 1H), 5.32 (t, *J* = 3.3 Hz, 1H), 4.69 (d, *J* = 1.1 Hz, 1H), 4.52 (d, *J* = 7.7 Hz, 1H), 4.41 (s, 1H), 4.15 (dd, *J* = 10.6, 8.9 Hz, 1H), 3.87–3.80 (m, 5H), 3.79–3.75 (m, 1H), 3.74–3.66 (m, 2H), 3.63–3.52 (m, 3H), 3.21–3.15 (m, 2H), 2.97 (dd, *J* = 14.4, 4.0 Hz, 1H), 1.37 (s, 3H), 1.29 (d, *J* = 6.2 Hz, 3H), 1.03 (dd, *J* = 13.1, 3.5 Hz, 1H), 0.98 (s, 6H), 0.94 (s, 3H), 0.87 (s, 3H), 0.76 (s, 3H). **^{13}C NMR** (151 MHz, CD_3OD) δ 208.73, 177.14, 176.52, 169.47, 144.73, 139.06, 135.50, 130.19, 123.59, 106.69, 101.89, 99.21, 94.68, 83.62, 78.34, 76.17, 75.79, 74.74, 72.95, 72.70, 72.18, 71.27, 69.61, 68.54, 67.40, 67.14, 56.92, 52.43, 50.00, 49.72, 48.15, 47.90, 42.83, 42.01, 41.22, 40.98, 39.58, 37.63, 37.13, 36.54, 33.81, 33.52, 32.22, 31.48, 30.27, 27.82, 27.33, 27.12, 26.51, 25.19, 24.56, 21.90, 18.24, 18.15, 16.46, 9.60. **HRMS** (ESI) *m/z*: Calcd for $C_{60}H_{89}N_2O_{19}INa$ $(M+Na)^+$ 1291.5002, found 1291.4962.

C. ^{1}H NMR AND ^{13}C NMR SPECTRA

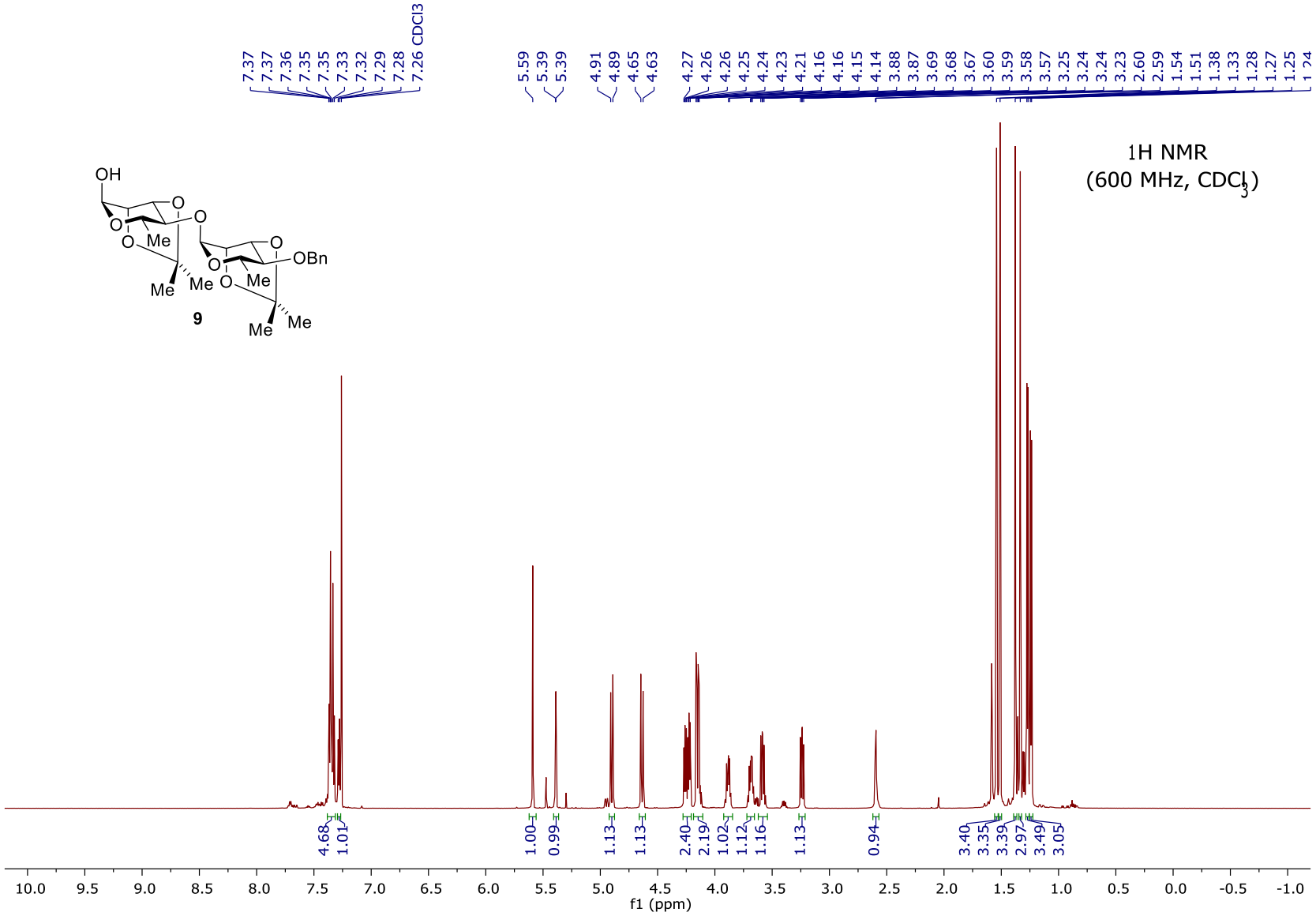
Synthesis of Linear Oligosaccharide Domain Variants


1H NMR (600 MHz, CDCl3)
CDCl3
OAllyl
OBn
Me
S1
f1 (ppm)

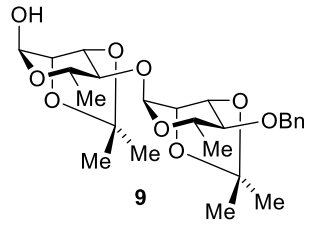
^{13}C NMR (151 MHz, $CDCl_3$)



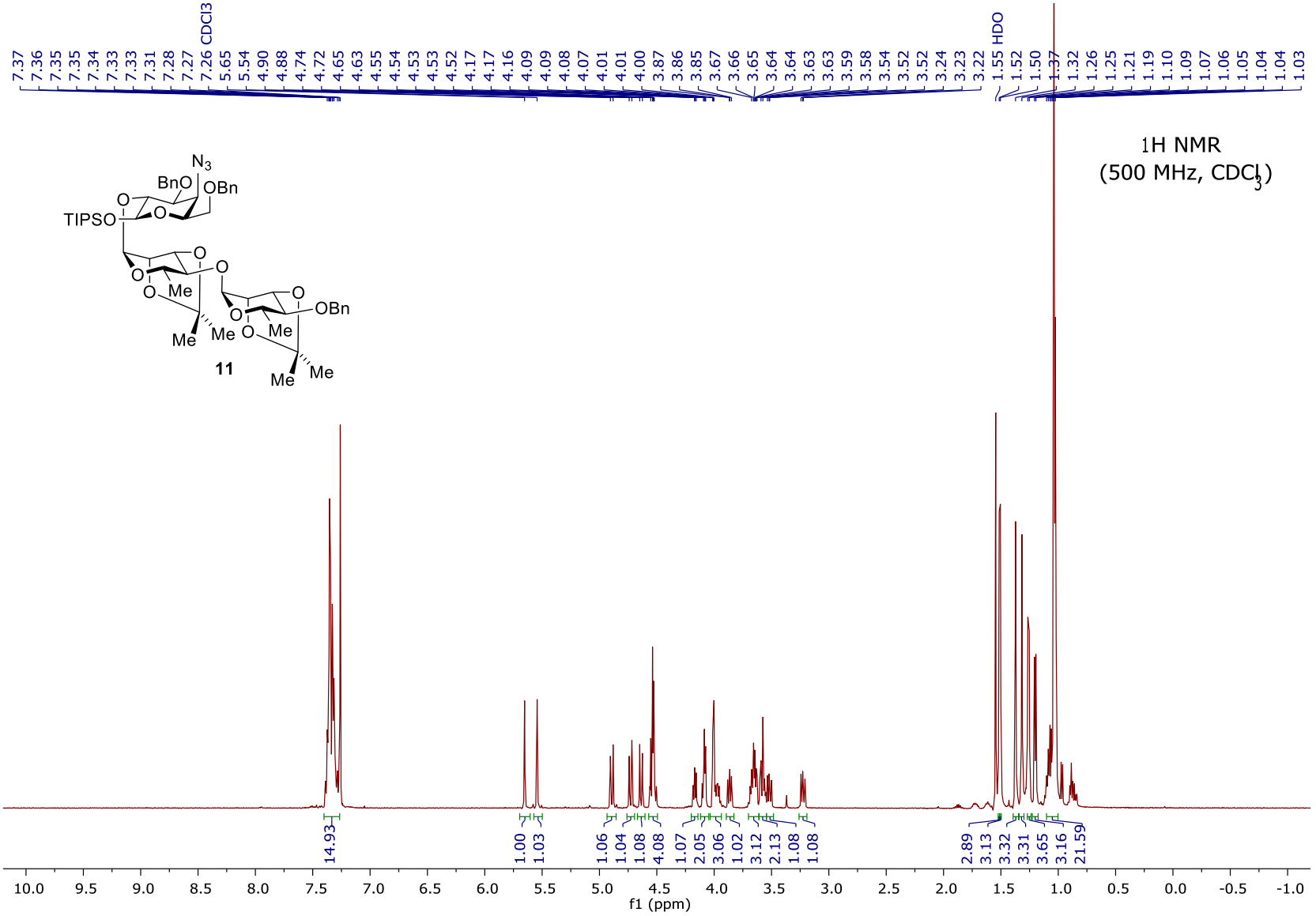
S1

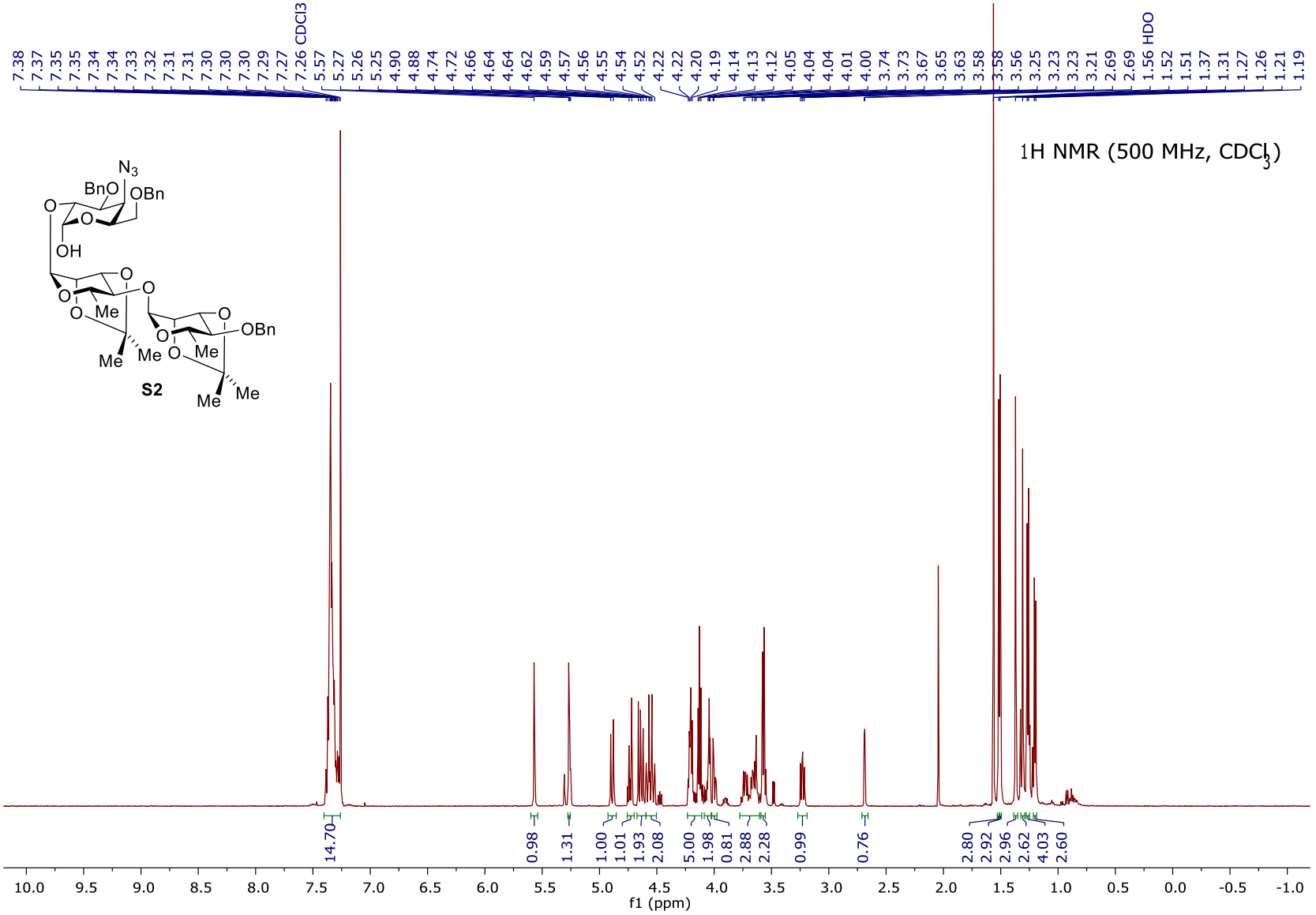

7.37
7.37
7.36
7.35
7.35
7.33
7.32
7.29
7.28
7.26 CDCl3
5.59
5.39
5.39
4.91
4.89
4.65
4.63
4.27
4.26
4.26
4.25
4.24
4.23
4.21
4.16
4.16
4.15
4.14
3.88
3.87
3.69
3.68
3.67
3.60
3.59
3.58
3.57
3.25
3.24
3.24
3.23
2.60
2.59
1.54
1.51
1.38
1.33
1.28
1.27
1.25
1H NMR
(600 MHz, CDCl3)
OH
O
O
O
O
Me
O
OBn
Me
Me
Me
O
Me
Me
Me
9
4.68
1.01
1.00
0.99
1.13
1.13
2.40
2.19
1.02
1.12
1.16
1.13
0.94
3.40
3.35
3.39
2.97
3.49
3.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

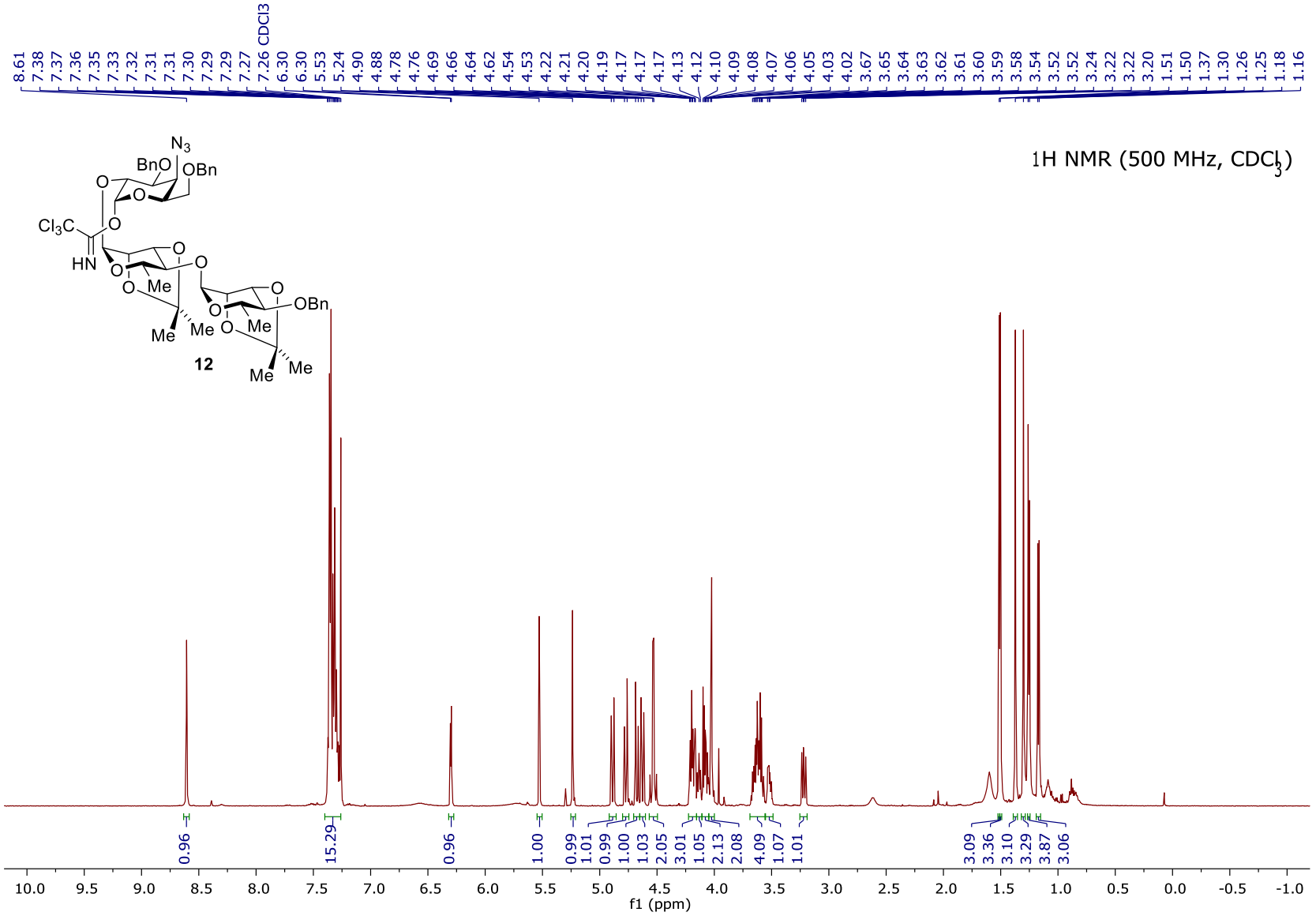
^{13}C NMR (151 MHz, $CDCl_3$)

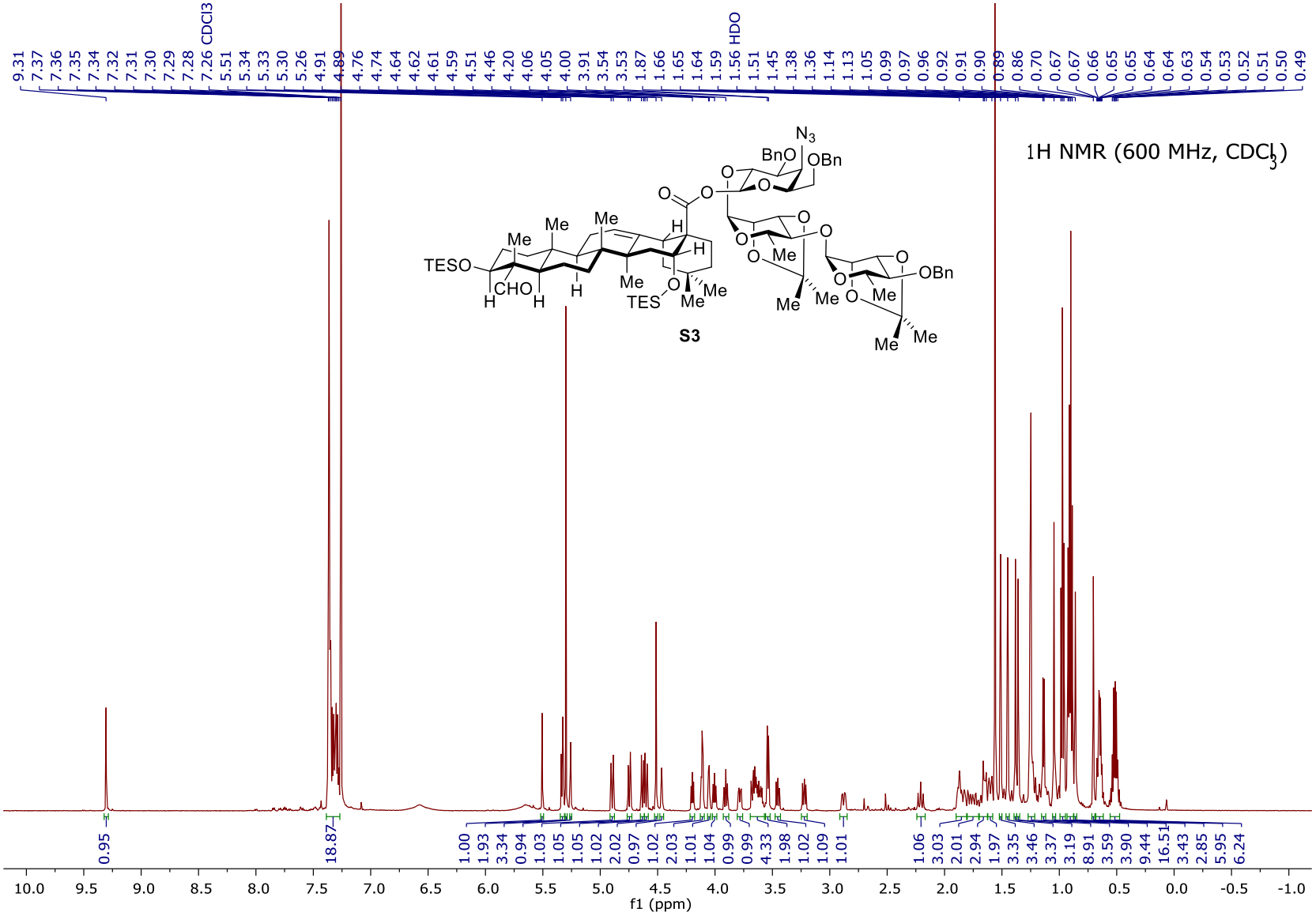


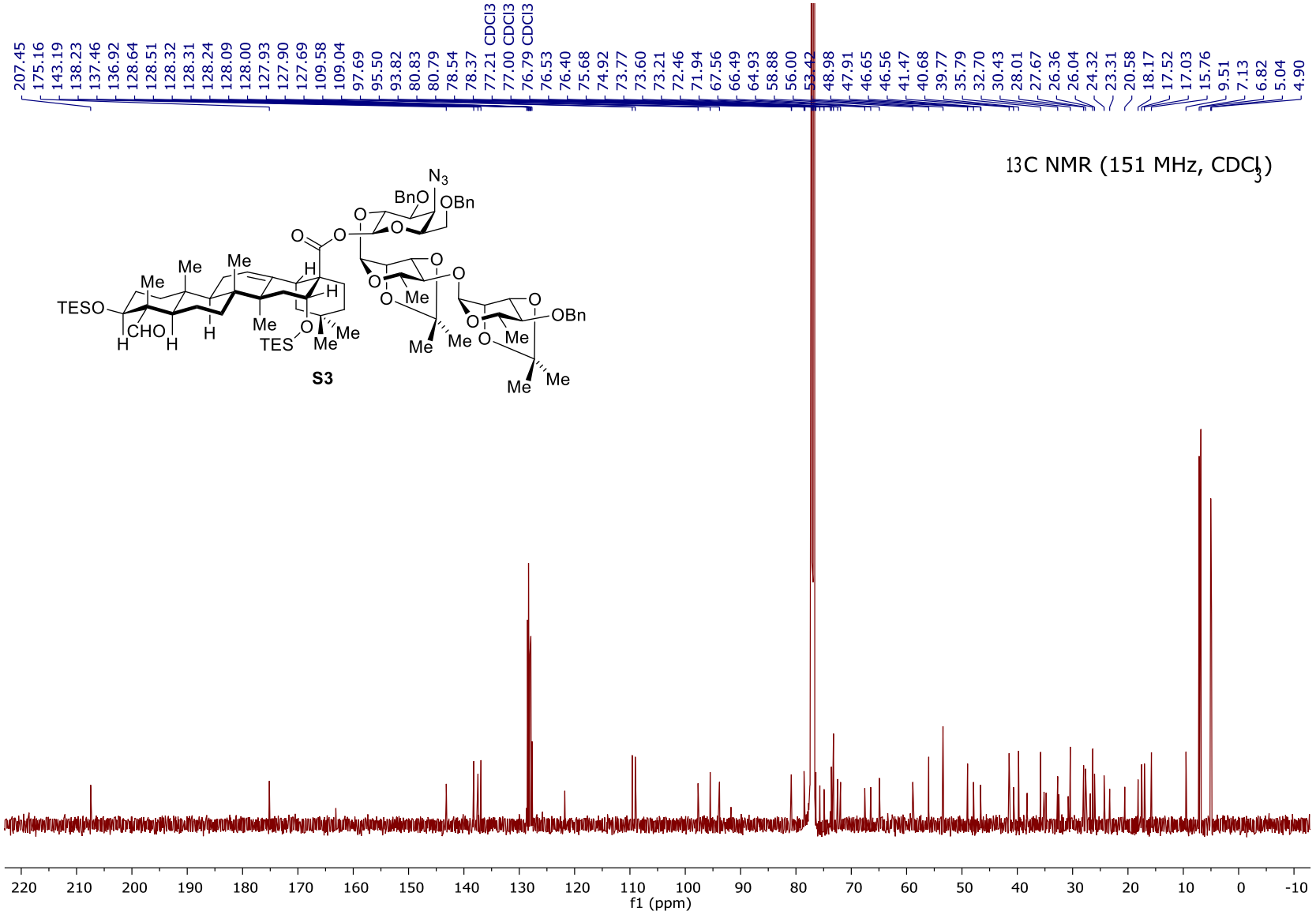
9

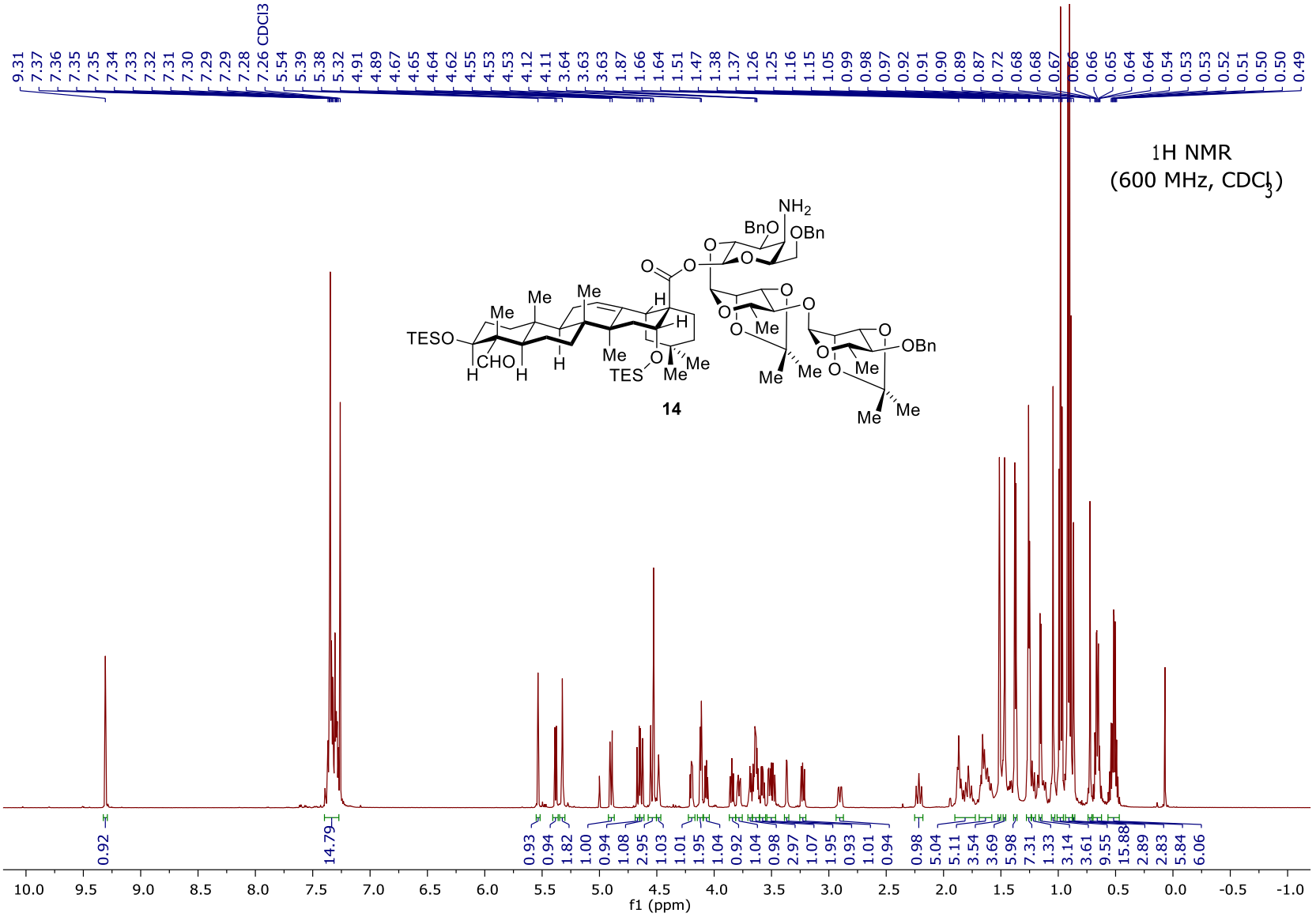

1H NMR
(500 MHz, CDCl3)
11
CDCl3
HDO
f1 (ppm)

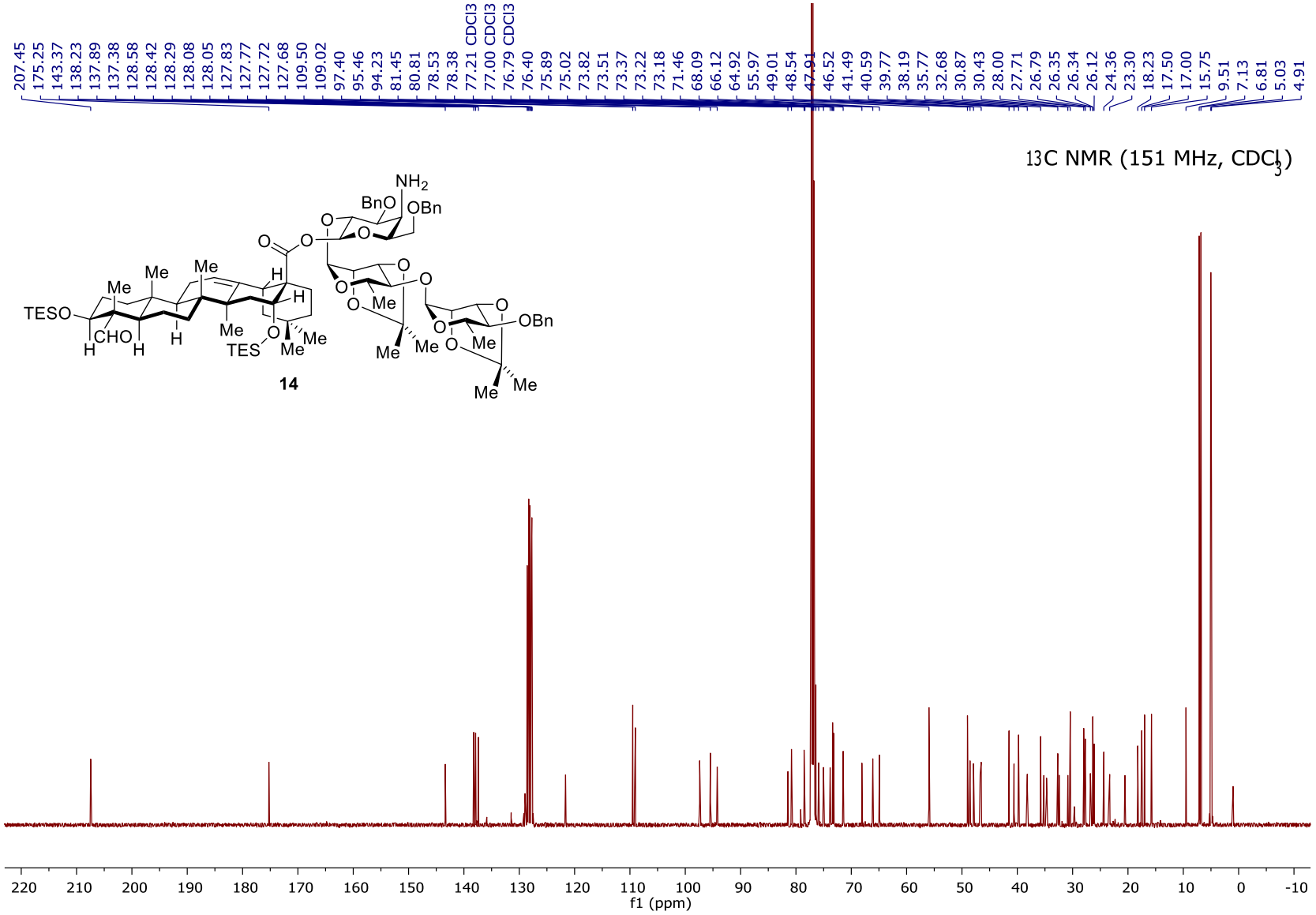

1H NMR (500 MHz, CDCl3)
S2
CDCl3
HDO
14.70
0.98
1.31
1.00
1.01
1.93
2.08
5.00
1.98
0.81
2.88
2.28
0.99
0.76
2.80
2.92
2.96
2.62
4.03
2.60
f1 (ppm)

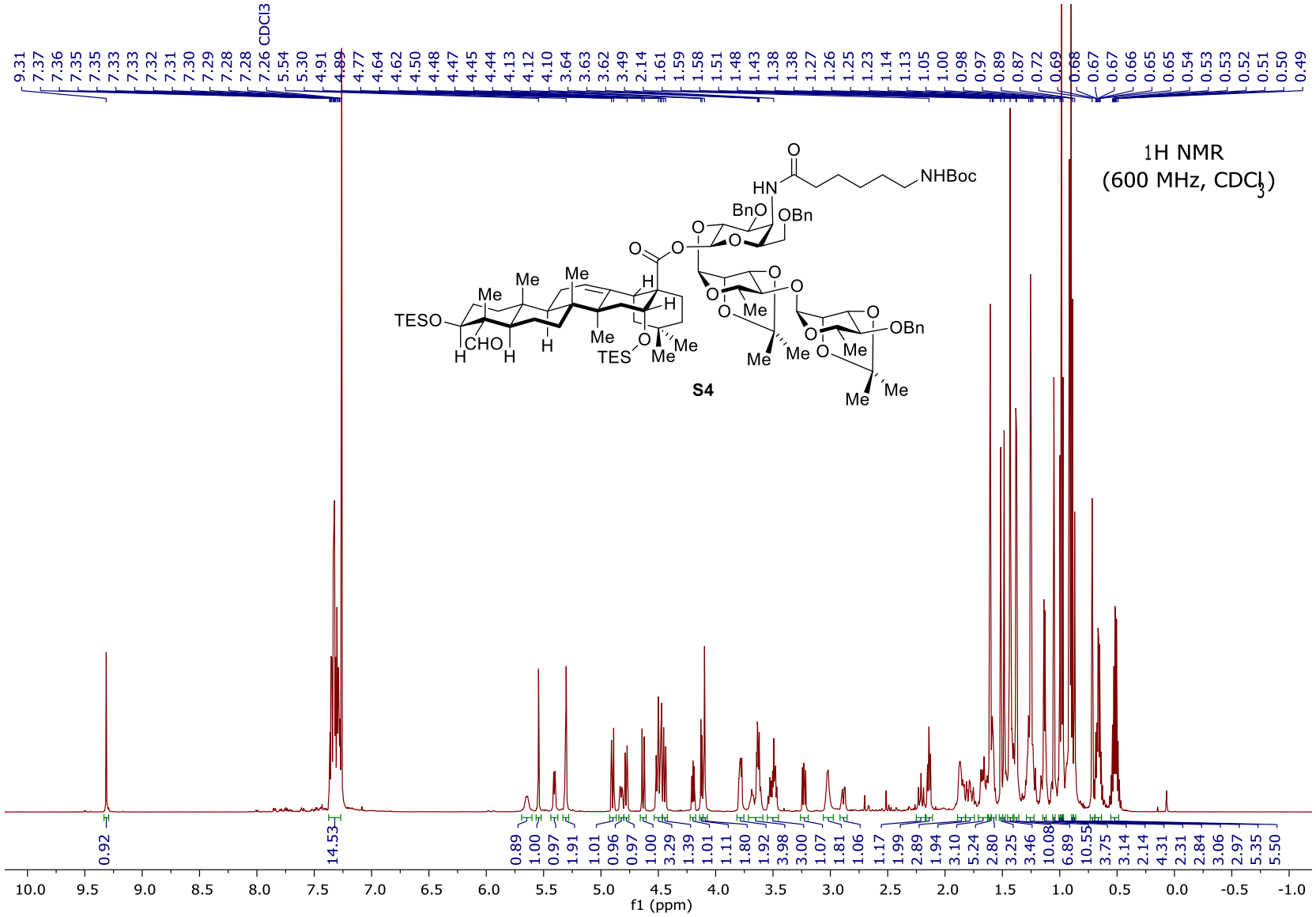

8.61 7.38 7.37 7.36 7.35 7.33 7.32 7.31 7.31 7.30 7.29 7.29 7.27 7.26 CDCl3 6.30 6.30 5.53 5.24 4.90 4.88 4.78 4.76 4.69 4.66 4.64 4.62 4.54 4.53 4.22 4.21 4.20 4.19 4.17 4.17 4.17 4.13 4.12 4.10 4.09 4.08 4.07 4.06 4.05 4.03 4.02 3.67 3.65 3.64 3.63 3.62 3.61 3.60 3.59 3.58 3.54 3.52 3.52 3.24 3.22 3.20 1.51 1.50 1.37 1.30 1.26 1.25 1.18 1.16
1H NMR (500 MHz, CDCl3)
N3
BnO
OBn
Cl3C
HN
Me
OBn
12
0.96 15.29 0.96 1.00 0.99 1.01 0.99 1.00 1.03 2.05 3.01 1.05 2.13 2.08 4.09 1.07 1.01 3.09 3.36 3.10 3.29 3.87 3.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

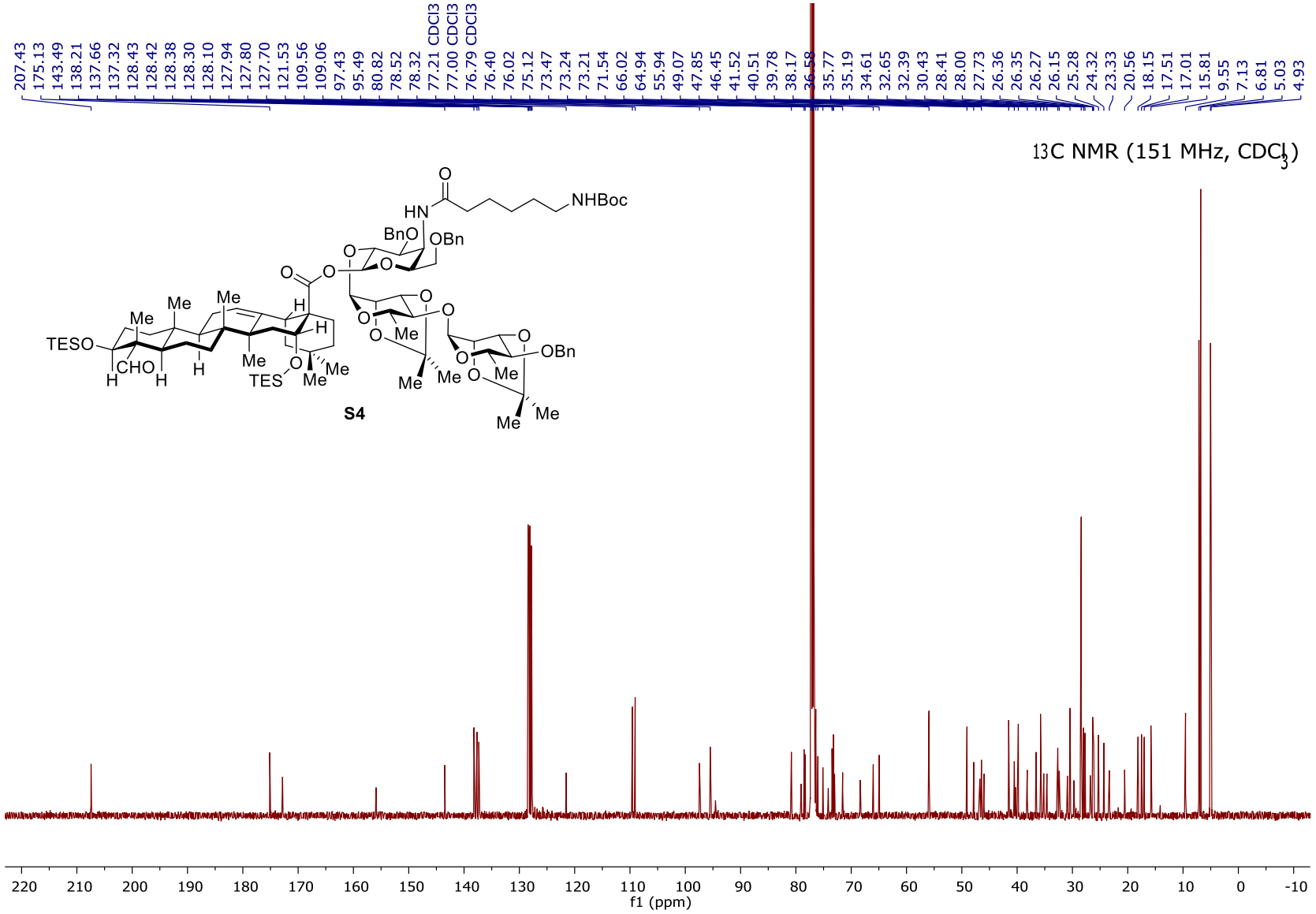

1H NMR (600 MHz, CDCl3)
S3
f1 (ppm)

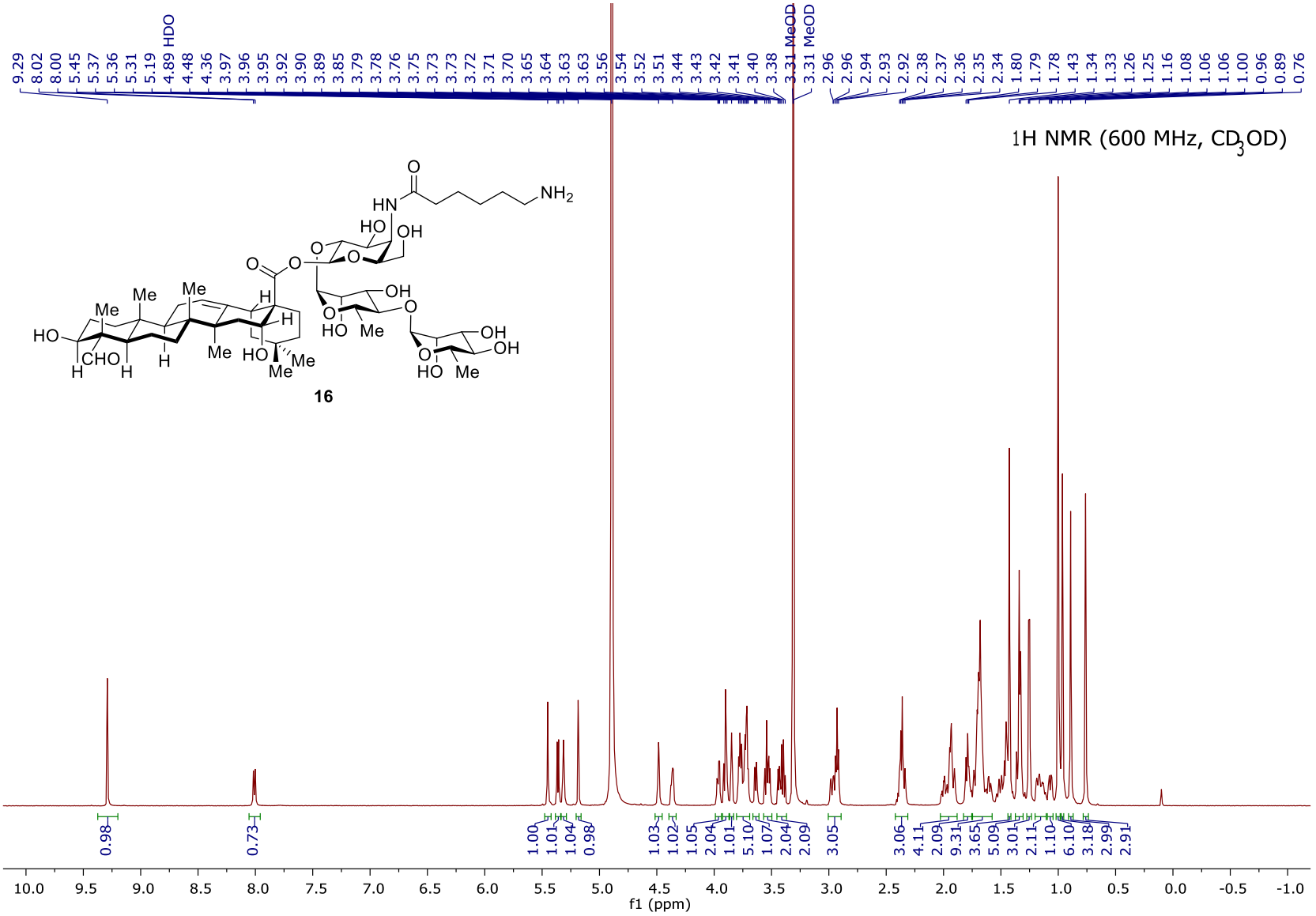

207.45
175.16
143.19
138.23
137.46
136.92
128.64
128.51
128.32
128.31
128.24
128.09
128.00
127.93
127.90
127.69
109.58
109.04
97.69
95.50
93.82
80.83
80.79
78.54
78.37
77.21 CDCl3
77.00 CDCl3
76.79 CDCl3
76.53
76.40
75.68
74.92
73.77
73.60
73.21
72.46
71.94
67.56
66.49
64.93
58.88
56.00
53.42
48.98
47.91
46.65
46.56
41.47
40.68
39.77
35.79
32.70
30.43
28.01
27.67
26.36
26.04
24.32
23.31
20.58
18.17
17.52
17.03
15.76
9.51
7.13
6.82
5.04
4.90
13C NMR (151 MHz, CDCl3)
S3
f1 (ppm)

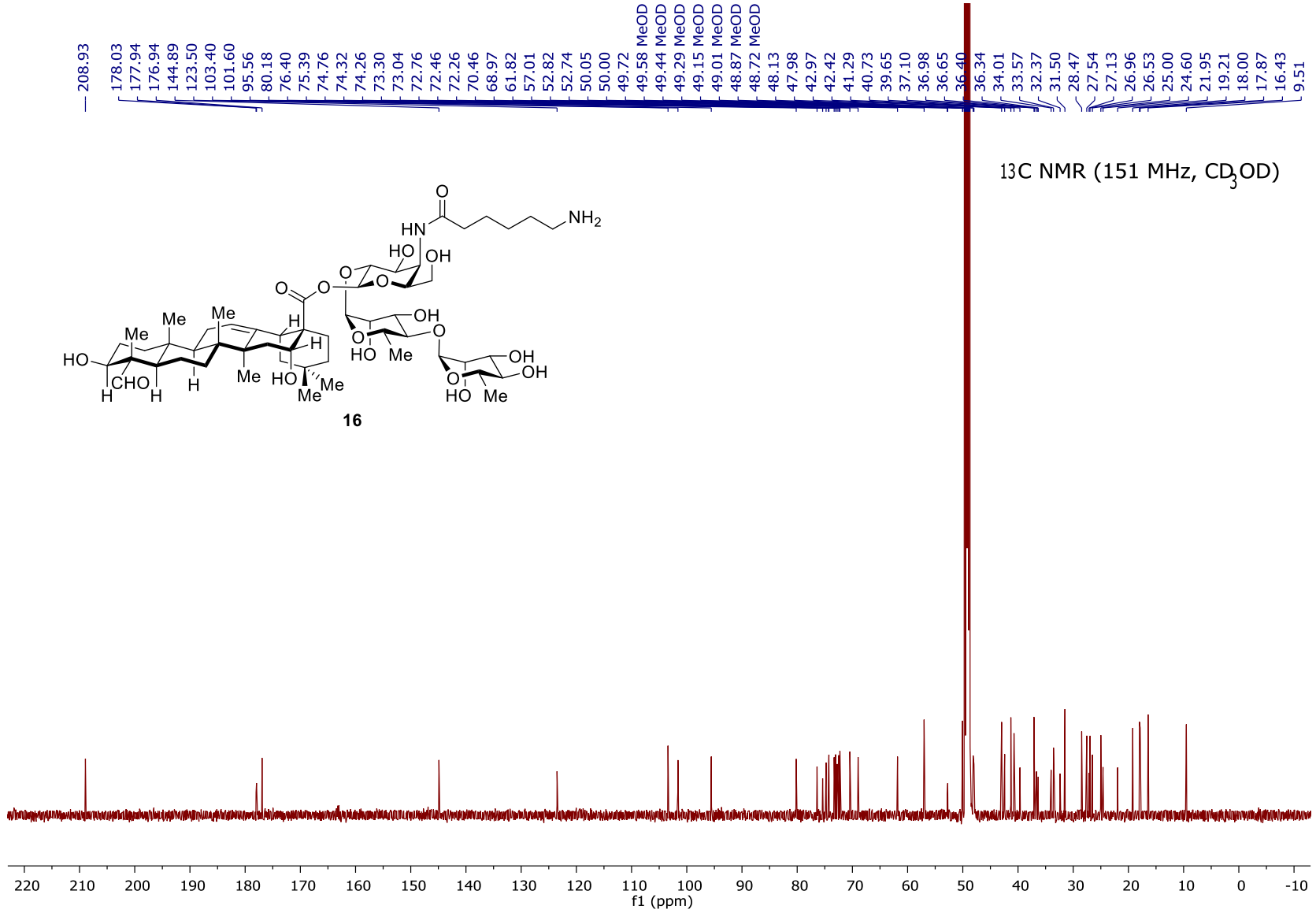

1H NMR
(600 MHz, CDCl3)
14
f1 (ppm)


207.45 175.25 143.37 138.23 137.89 137.38 128.58 128.42 128.29 128.08 128.05 127.83 127.77 127.72 127.68 109.50 109.02 97.40 95.46 94.23 81.45 80.81 78.53 78.38 77.21 CDCl3 77.00 CDCl3 76.79 CDCl3 76.40 75.89 75.02 73.82 73.51 73.37 73.22 73.18 71.46 68.09 66.12 64.92 55.97 49.01 48.54 47.91 46.52 41.49 40.59 39.77 38.19 35.77 32.68 30.87 30.43 28.00 27.71 26.79 26.35 26.34 26.12 24.36 23.30 18.23 17.50 17.00 15.75 9.51 7.13 6.81 5.03 4.91
13C NMR (151 MHz, CDCl3)
14
f1 (ppm)

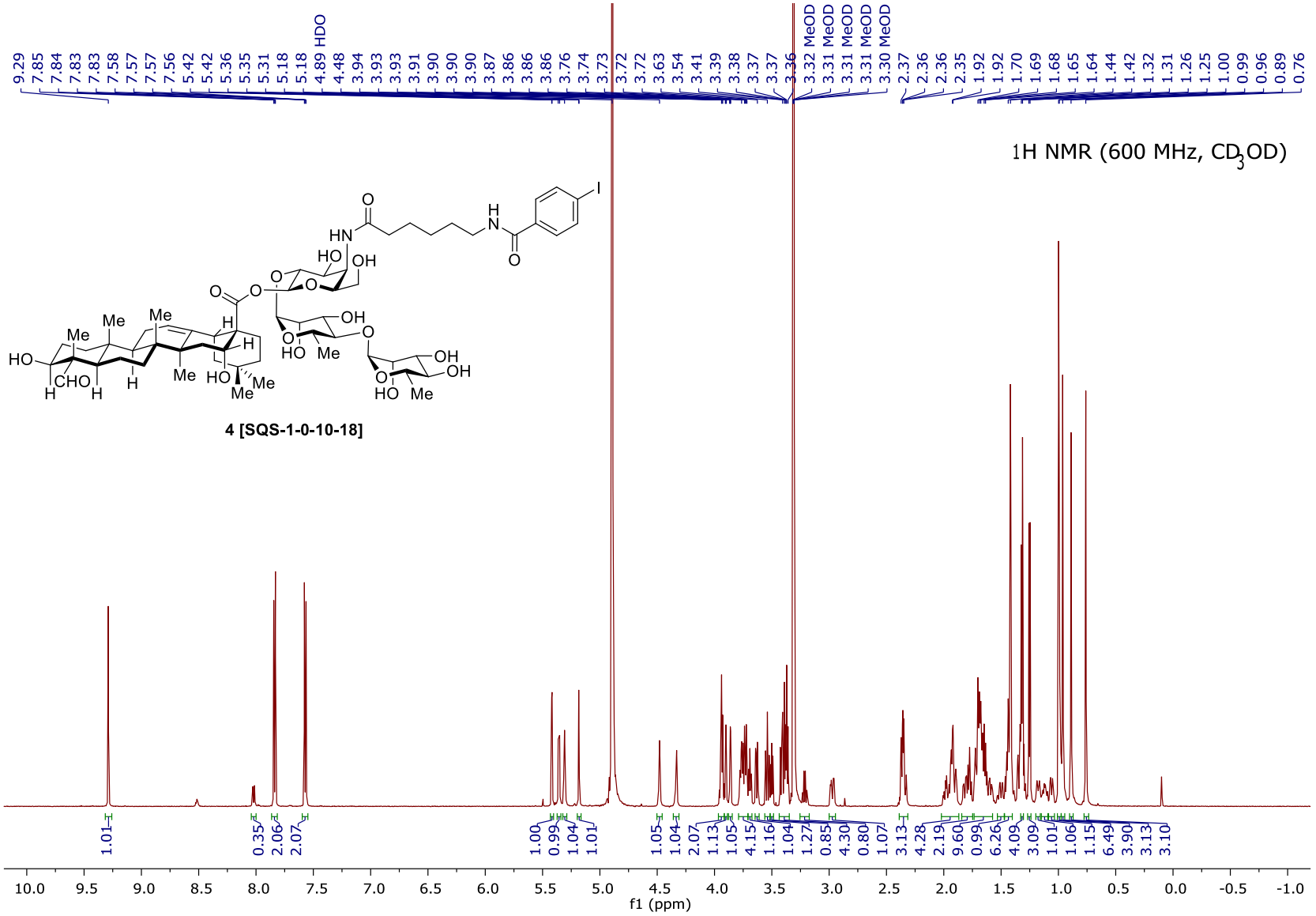

1H NMR
(600 MHz, CDCl3)
S4
f1 (ppm)

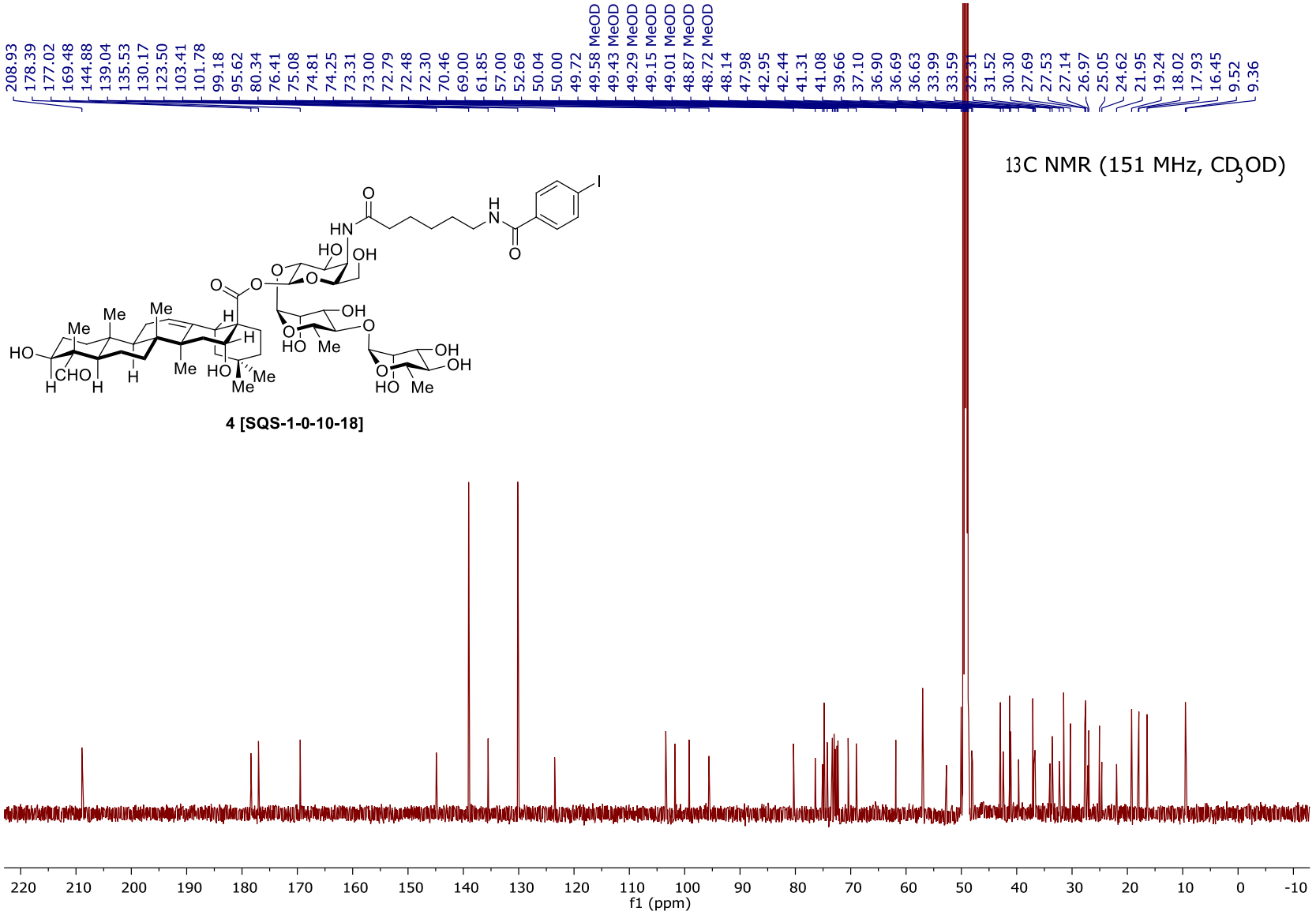

207.43
175.13
143.49
138.21
137.66
137.32
128.43
128.42
128.38
128.30
128.10
127.94
127.80
127.70
121.53
109.56
109.06
97.43
95.49
80.82
78.52
78.32
77.21 CDCl3
77.00 CDCl3
76.79 CDCl3
76.40
76.02
75.12
73.47
73.24
73.21
71.54
66.02
64.94
55.94
49.07
47.85
46.45
41.52
40.51
39.78
38.17
36.58
35.77
35.19
34.61
32.65
32.39
30.43
28.41
28.00
27.73
26.36
26.35
26.27
26.15
25.28
24.32
23.33
20.56
18.15
17.51
17.01
15.81
9.55
7.13
6.81
5.03
4.93
13C NMR (151 MHz, CDCl3)
NHBoc
HN
BnO
OBn
TESO
CHO
TES
OBn
S4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

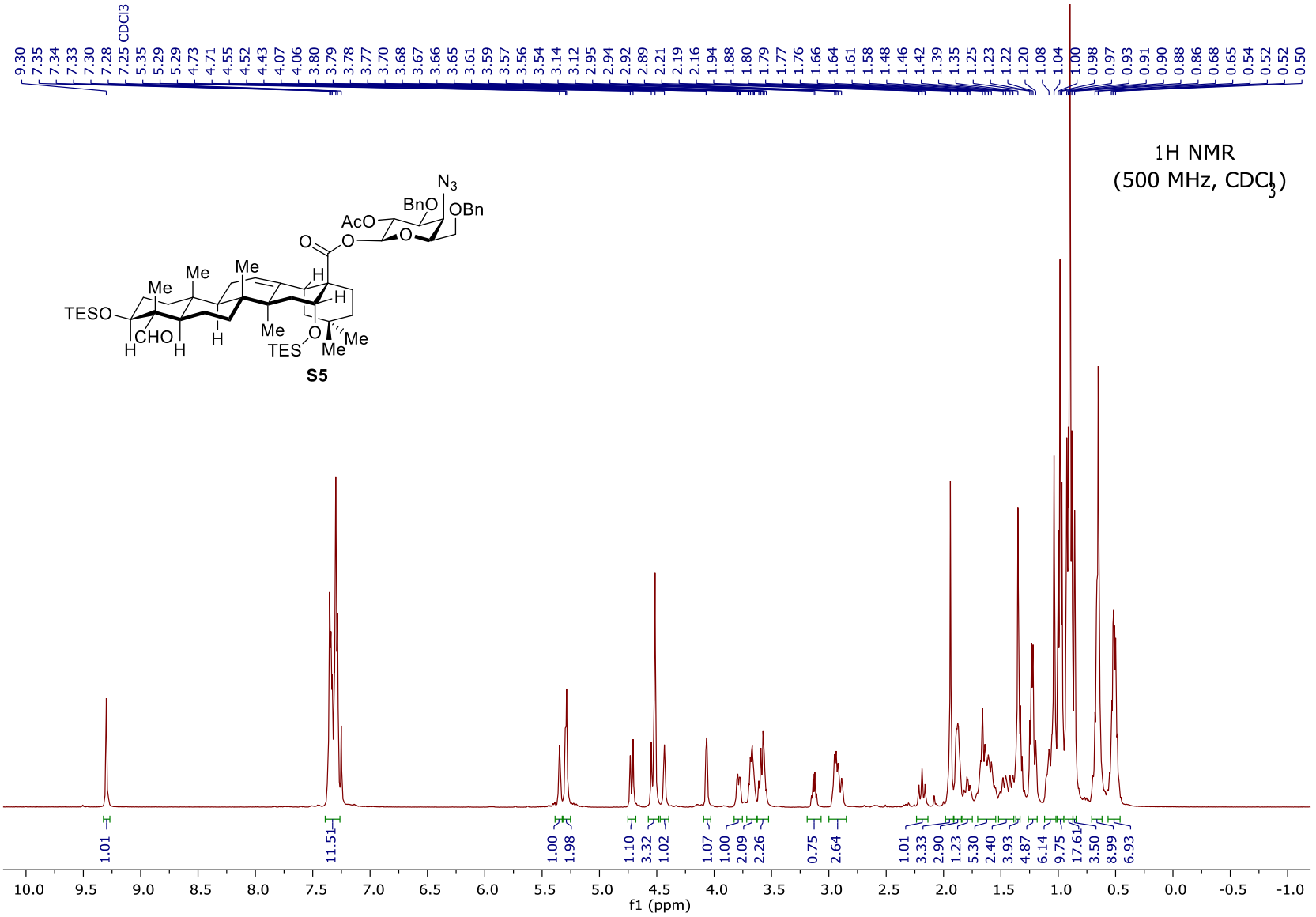

1H NMR (600 MHz, CD3OD)
16
f1 (ppm)

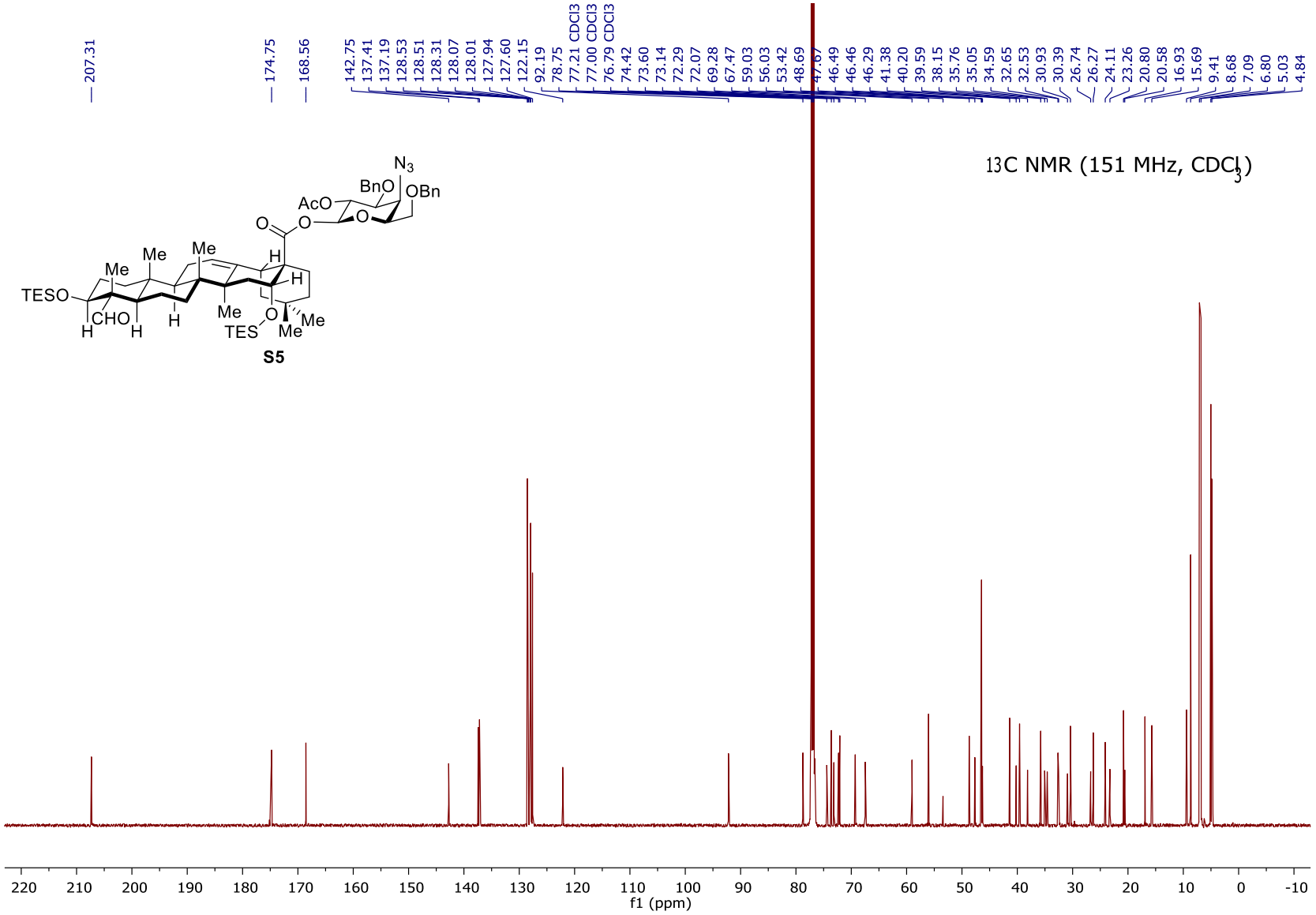

208.93
178.03
177.94
176.94
144.89
123.50
103.40
101.60
95.56
80.18
76.40
75.39
74.76
74.32
74.26
73.30
73.04
72.76
72.46
72.26
70.46
68.97
61.82
57.01
52.82
52.74
50.05
50.00
49.72
49.58 MeOD
49.44 MeOD
49.29 MeOD
49.15 MeOD
49.01 MeOD
48.87 MeOD
48.72 MeOD
48.13
47.98
42.97
42.42
41.29
40.73
39.65
37.10
36.98
36.65
36.40
36.34
34.01
33.57
32.37
31.50
28.47
27.54
27.13
26.96
26.53
25.00
24.60
21.95
19.21
18.00
17.87
16.43
9.51
13C NMR (151 MHz, CD3OD)
f1 (ppm)

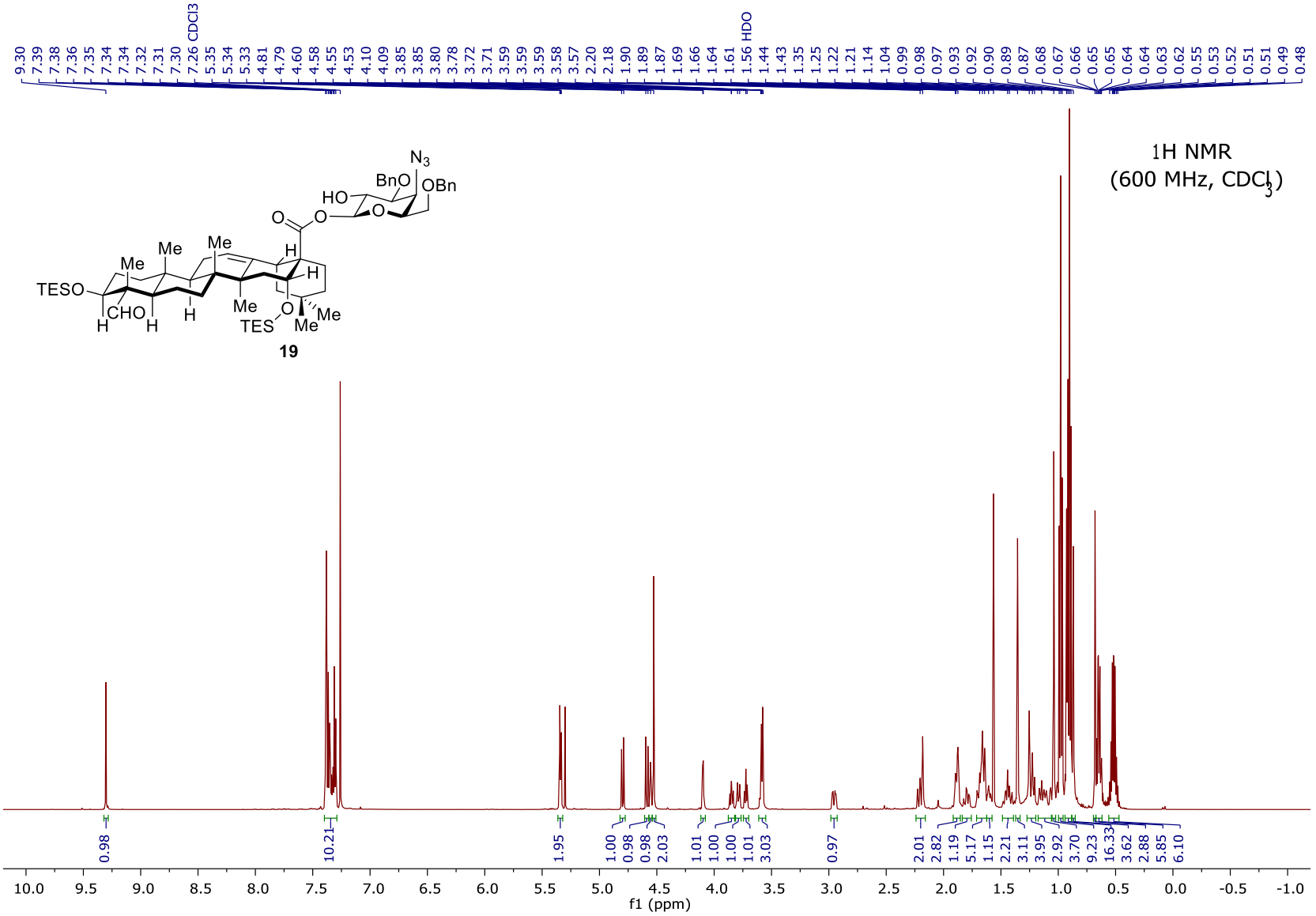
16

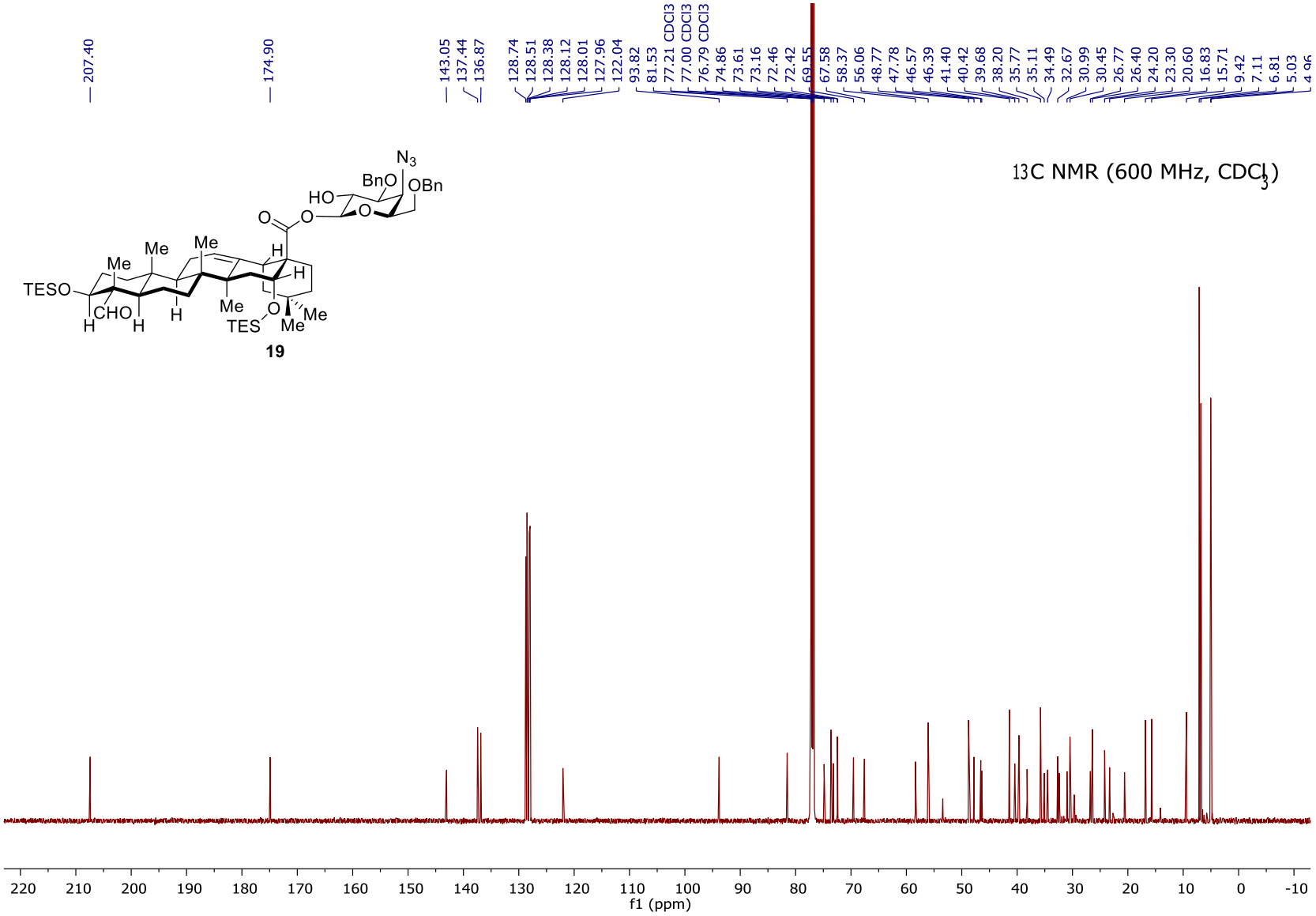

1H NMR (600 MHz, CD3OD)
4 [SQS-1-0-10-18]
f1 (ppm)

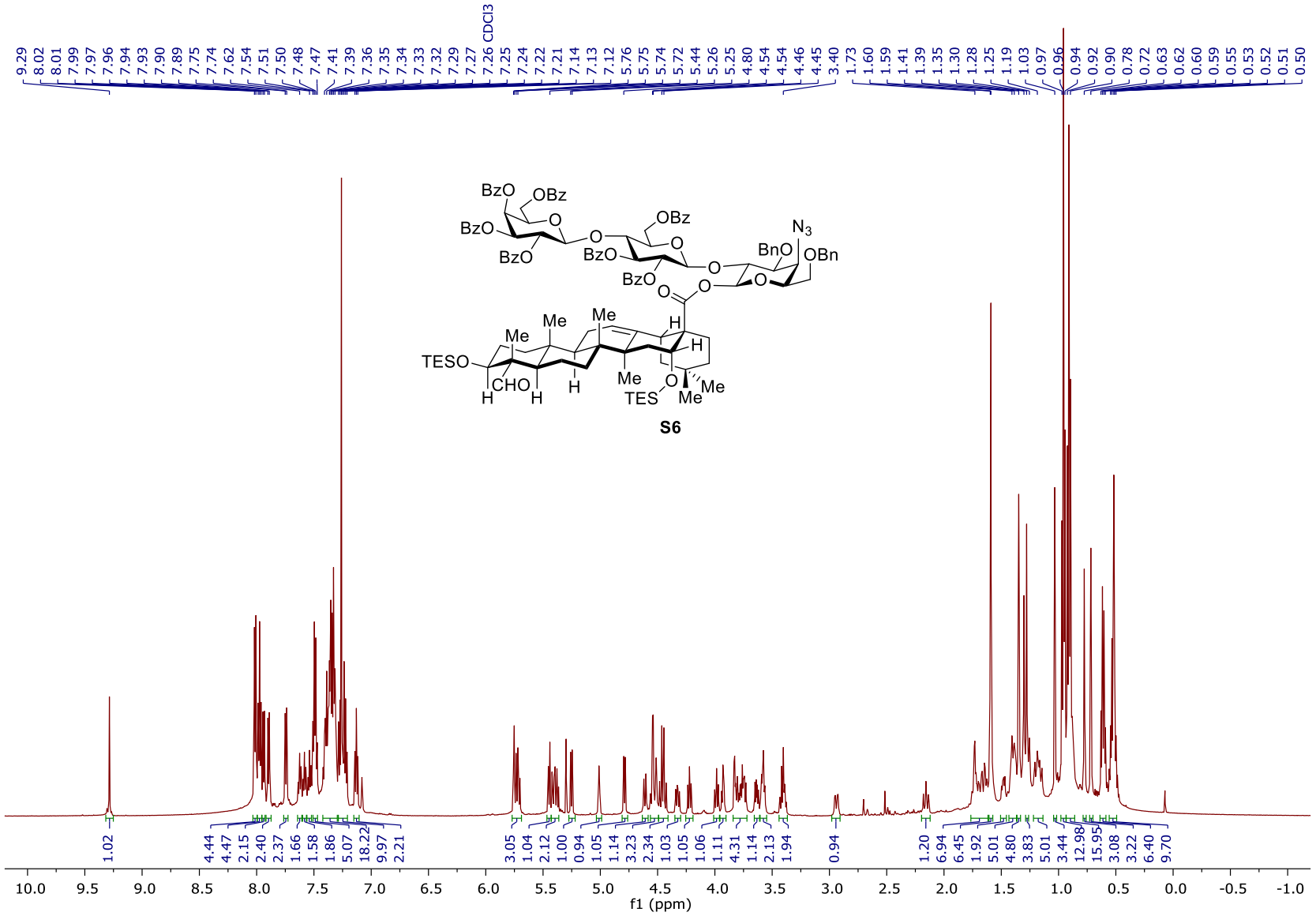

208.93
178.39
177.02
169.48
144.88
139.04
135.53
130.17
123.50
103.41
101.78
99.18
95.62
80.34
76.41
75.08
74.81
74.25
73.31
73.00
72.79
72.48
72.30
70.46
69.00
61.85
57.00
52.69
50.04
50.00
49.72
49.58 MeOD
49.43 MeOD
49.29 MeOD
49.15 MeOD
49.01 MeOD
48.87 MeOD
48.72 MeOD
48.14
47.98
42.95
42.44
41.31
41.08
39.66
37.10
36.90
36.69
36.63
33.99
33.59
32.31
31.52
30.30
27.69
27.53
27.14
26.97
25.05
24.62
21.95
19.24
18.02
17.93
16.45
9.52
9.36
13C NMR (151 MHz, CD3OD)
4 [SQS-1-0-10-18]
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

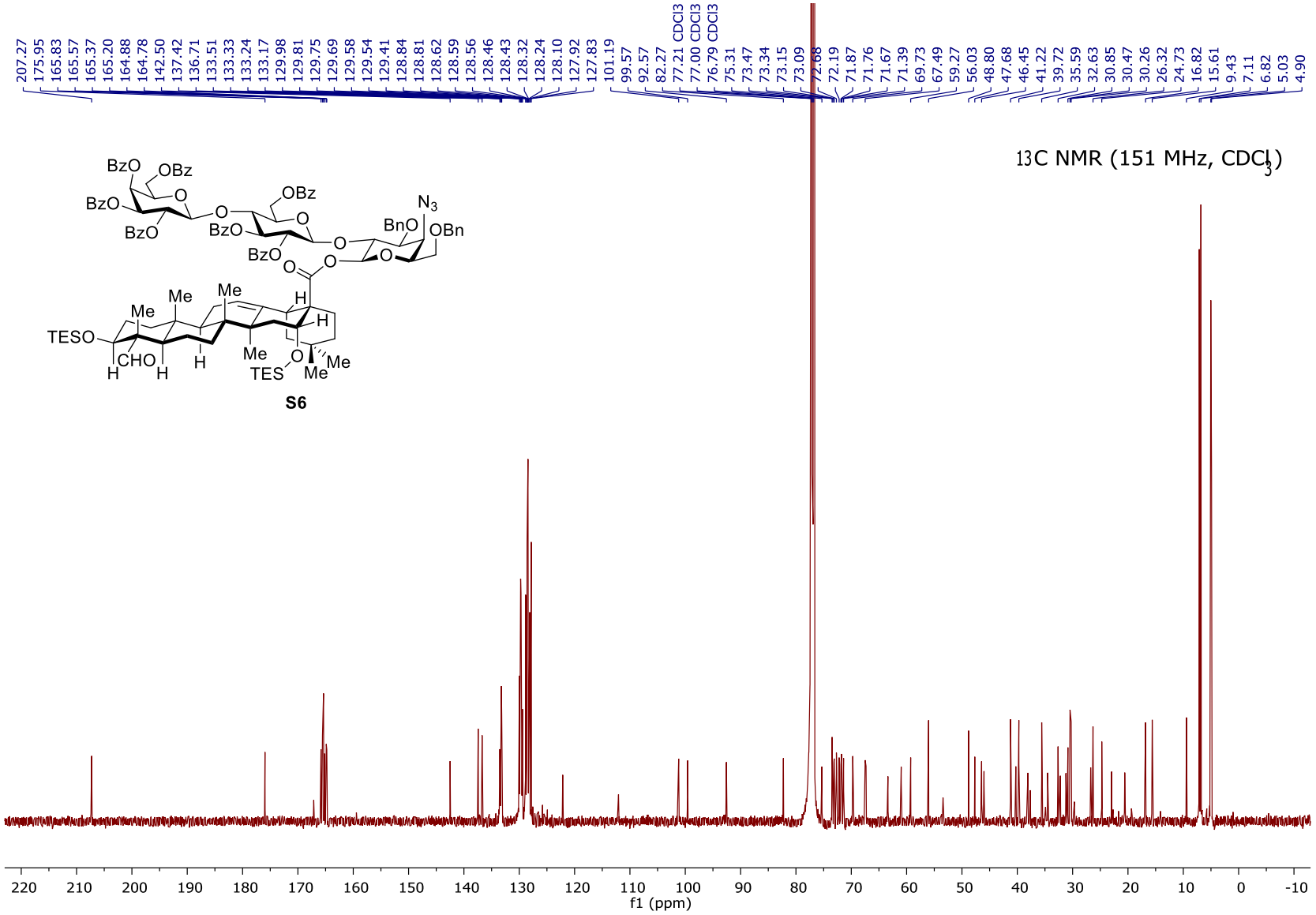

1H NMR
(500 MHz, CDCl3)
S5
f1 (ppm)

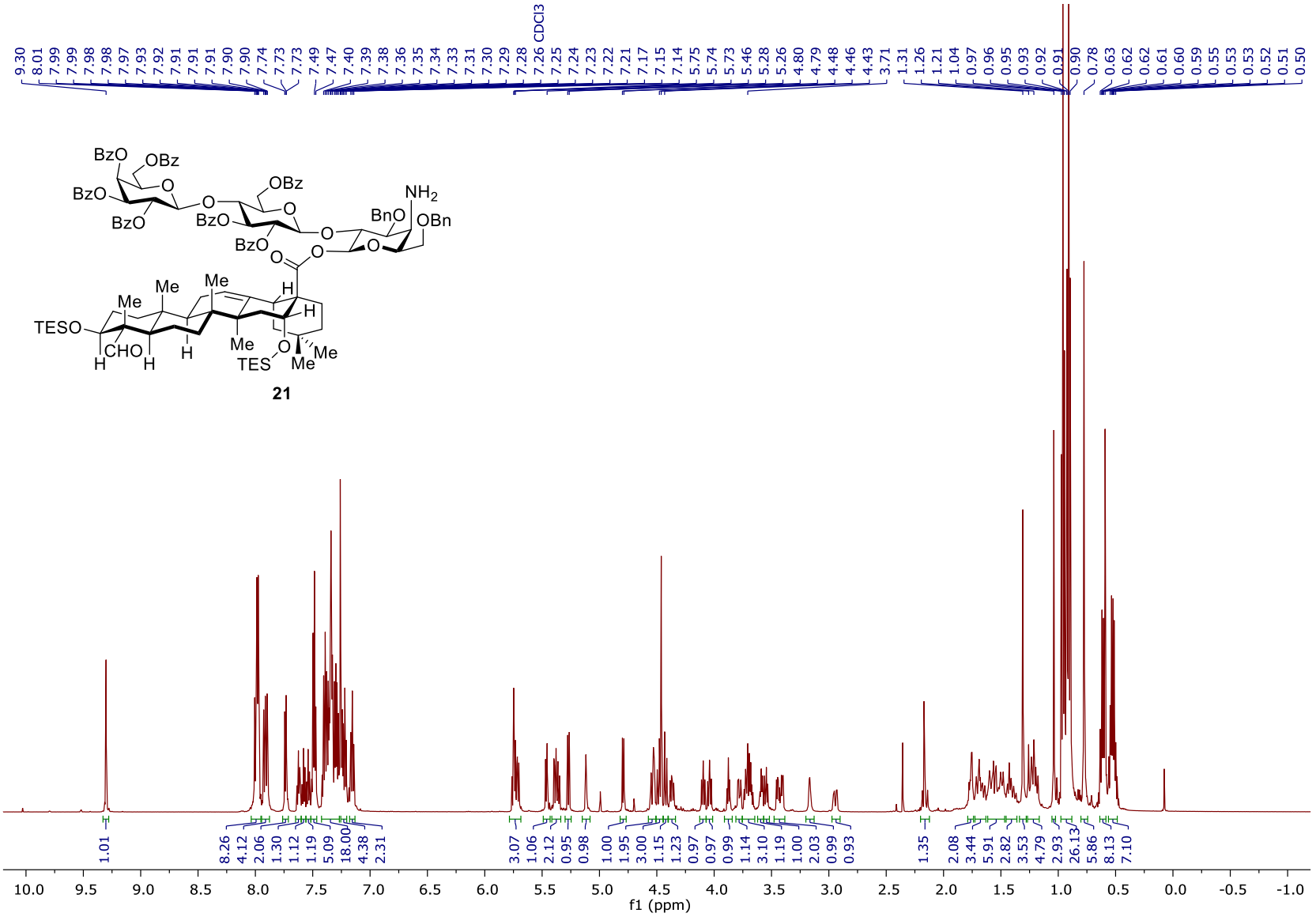

207.31
174.75
168.56
142.75
137.41
137.19
128.53
128.51
128.31
128.07
128.01
127.94
127.60
122.15
92.19
78.75
77.21 CDCl3
77.00 CDCl3
76.79 CDCl3
74.42
73.60
73.14
72.29
72.07
69.28
67.47
59.03
56.03
53.42
48.69
47.67
46.49
46.46
46.29
41.38
40.20
39.59
38.15
35.76
35.05
34.59
32.65
32.53
30.93
30.39
26.74
26.27
24.11
23.26
20.80
20.58
16.93
15.69
9.41
8.68
7.09
6.80
5.03
4.84
13C NMR (151 MHz, CDCl3)
N3
BnO
OBn
AcO
O
O
O
Me
Me
Me
H
H
TESO
CHO
H
H
H
Me
O
Me
TES
Me
S5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

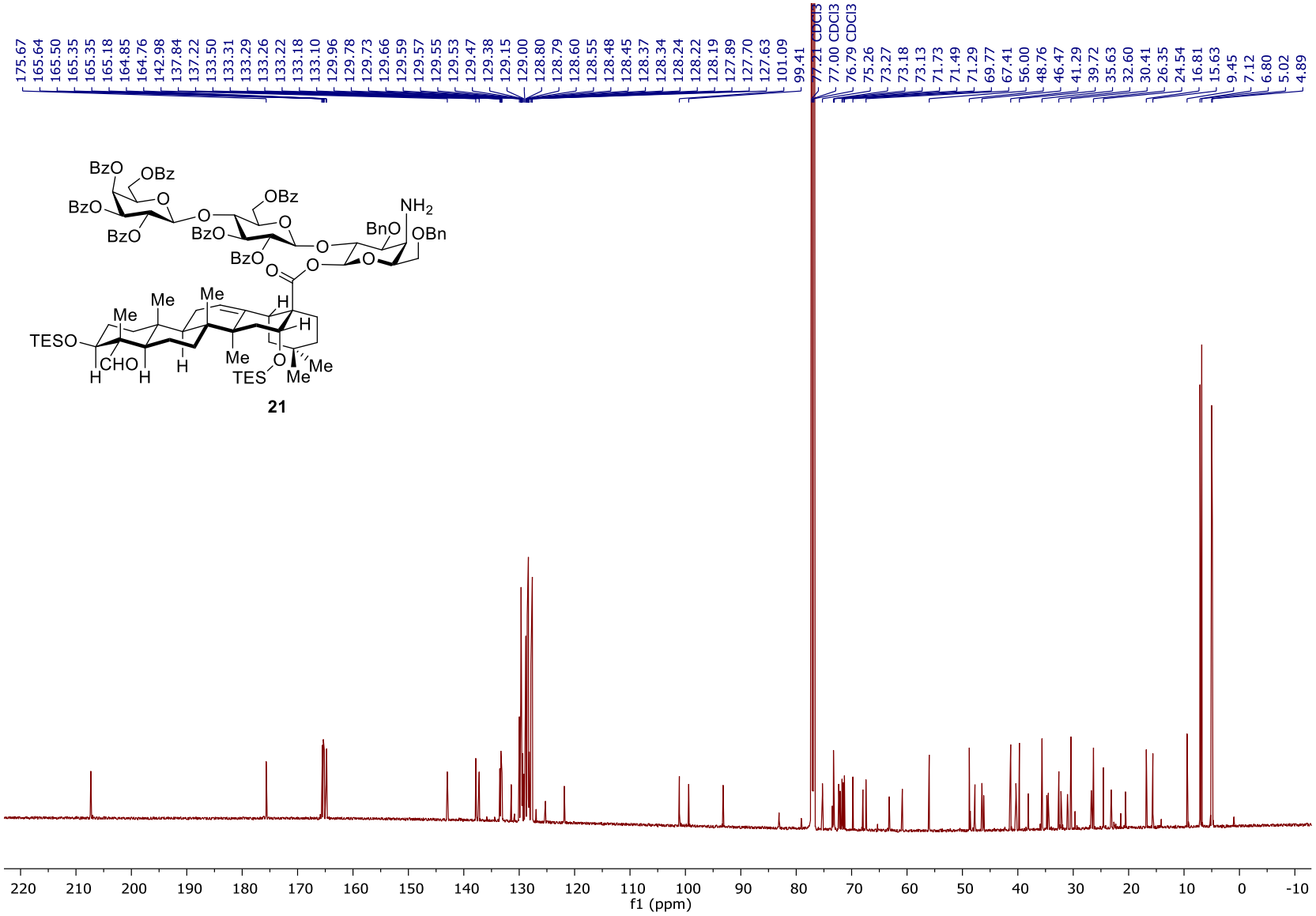

1H NMR
(600 MHz, CDCl3)
19
f1 (ppm)

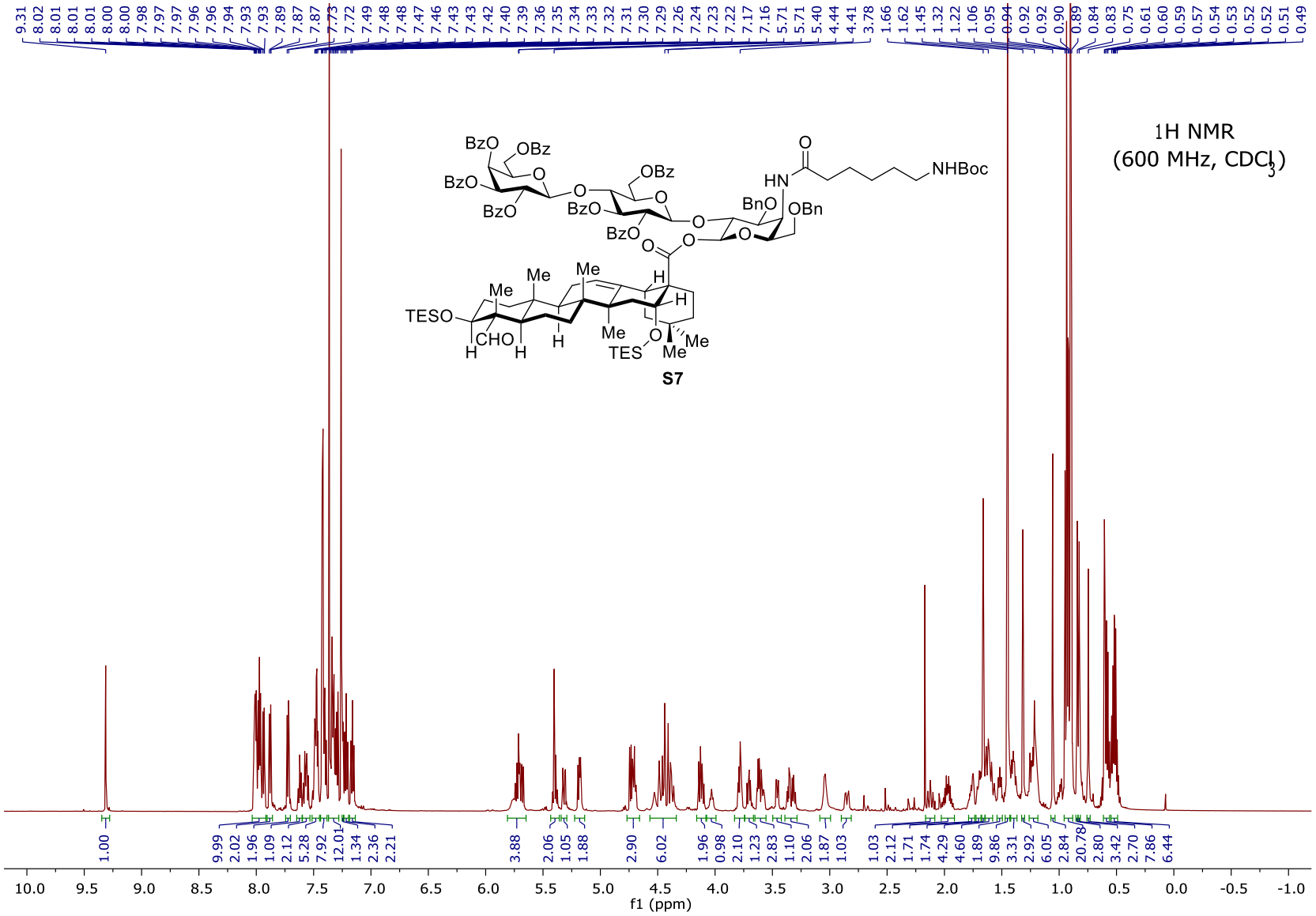

207.40
174.90
143.05
137.44
136.87
128.74
128.51
128.38
128.12
128.01
127.96
122.04
93.82
81.53
77.21 CDCl3
77.00 CDCl3
76.79 CDCl3
74.86
73.61
73.16
72.46
72.42
69.55
67.58
58.37
56.06
48.77
47.78
46.57
46.39
41.40
40.42
39.68
38.20
35.77
35.11
34.49
32.67
30.99
30.45
26.77
26.40
24.20
23.30
20.60
16.83
15.71
9.42
7.11
6.81
5.03
13C NMR (600 MHz, CDCl3)
N3
BnO
OBn
HO
O
O
O
TESO
Me
Me
Me
H
H
CHO
H
H
H
Me
TES
O
Me
Me
19
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

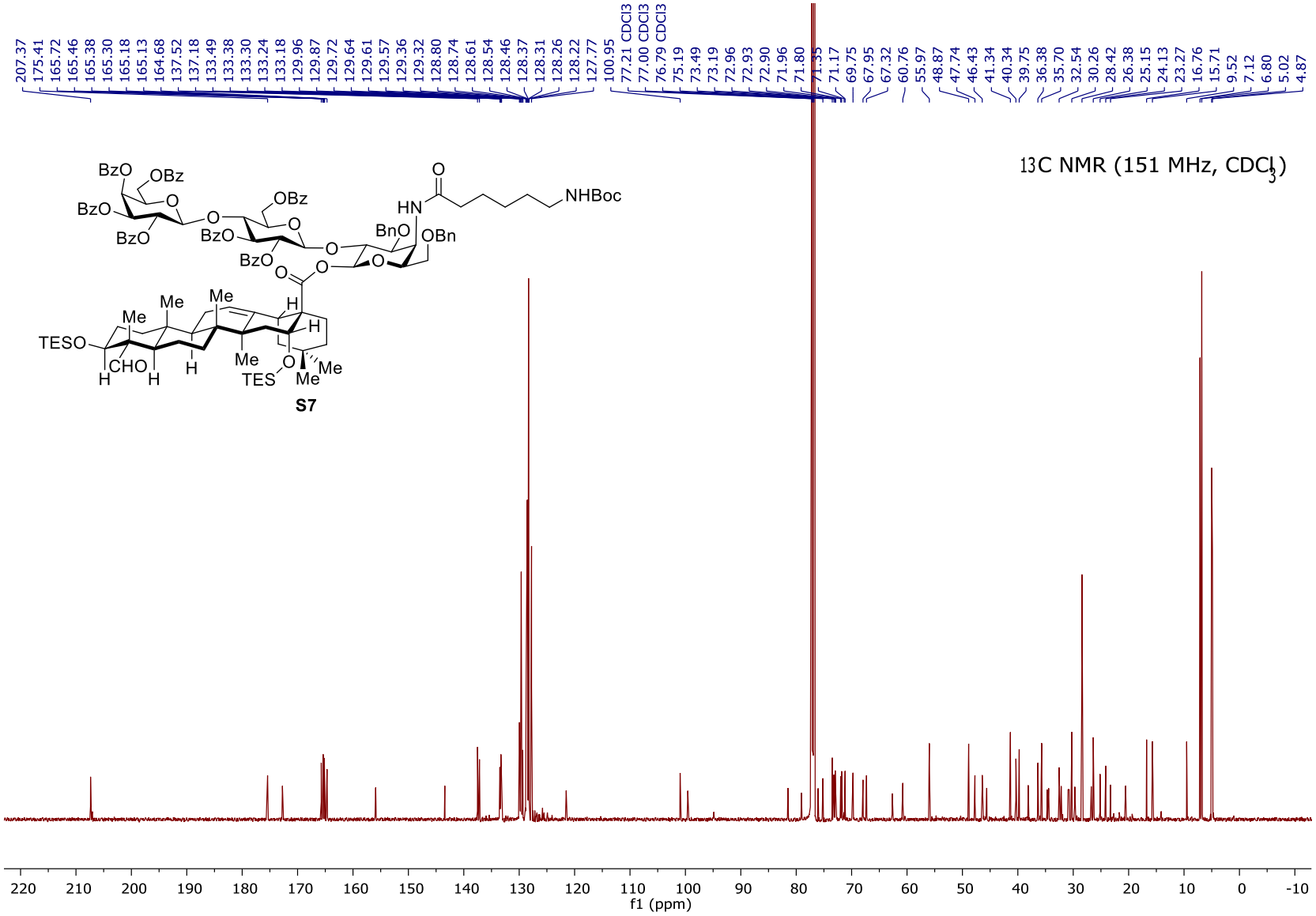

9.29 8.02 8.01 7.99 7.97 7.96 7.94 7.93 7.90 7.89 7.75 7.74 7.62 7.54 7.51 7.50 7.48 7.47 7.41 7.39 7.36 7.35 7.34 7.33 7.32 7.29 7.27 7.26 CDCl3 7.25 7.24 7.22 7.21 7.14 7.13 7.12 5.76 5.75 5.74 5.72 5.44 5.26 5.25 4.80 4.54 4.54 4.46 4.45 3.40 1.73 1.60 1.59 1.41 1.39 1.35 1.30 1.28 1.25 1.19 1.03 0.97 0.96 0.94 0.92 0.90 0.78 0.72 0.63 0.62 0.60 0.59 0.55 0.53 0.52 0.51 0.50
BzO OBz BzO BzO OBz BzO BzO N3 BnO OBn
Me Me Me H H TESO CHO H H Me TES O Me Me
S6
1.02 4.44 4.47 2.15 2.40 2.37 1.66 1.58 1.86 5.07 18.22 9.97 2.21 3.05 1.04 2.12 1.00 0.94 1.05 1.14 3.23 2.34 1.03 1.05 1.06 1.11 4.31 1.14 2.13 1.94 0.94 1.20 6.94 6.45 1.92 5.01 4.80 3.83 5.01 3.44 12.98 15.95 3.08 3.22 6.40 9.70
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

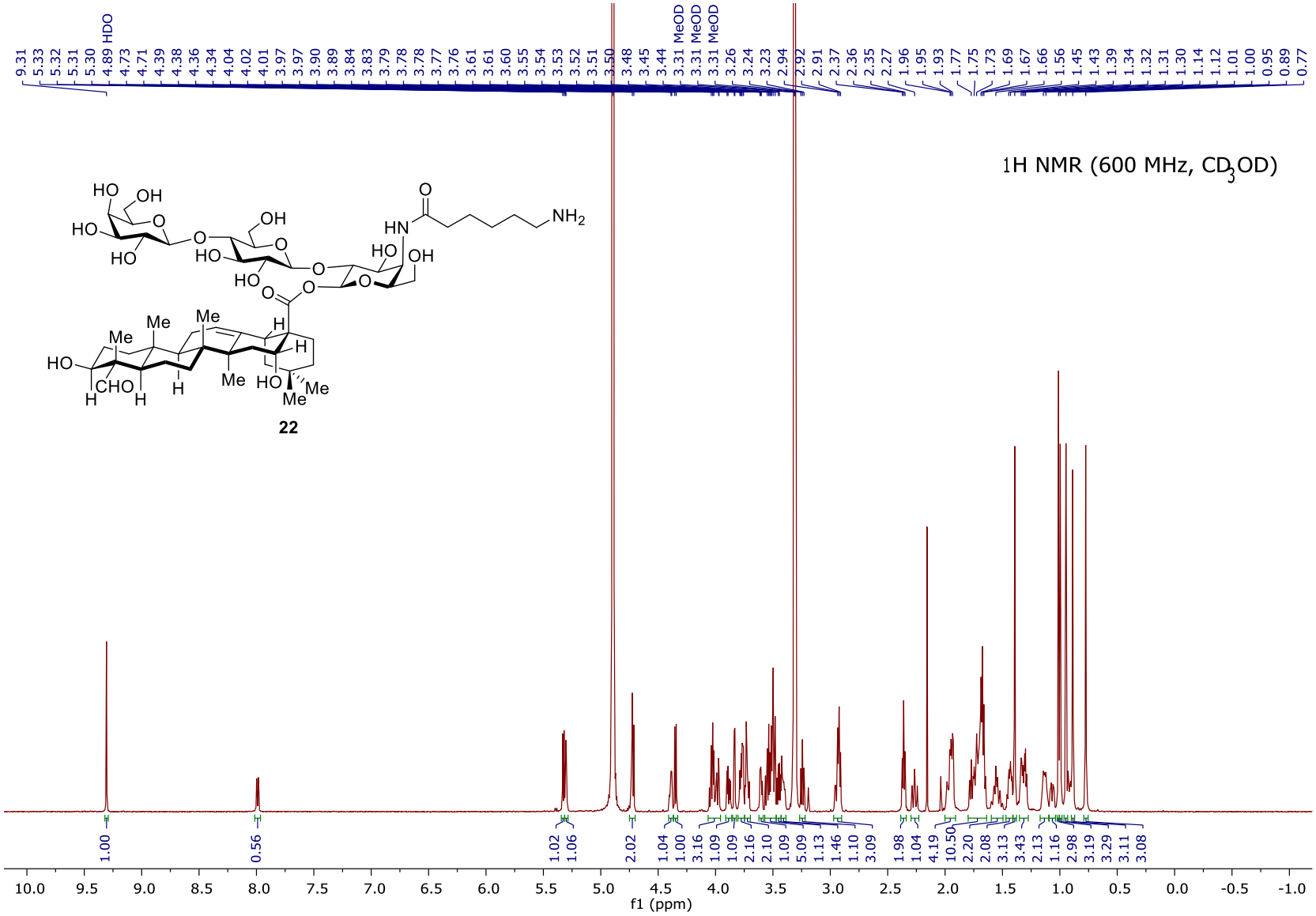

207.27
175.95
165.83
165.57
165.37
165.20
164.88
164.78
142.50
137.42
136.71
133.51
133.33
133.24
133.17
129.98
129.81
129.75
129.69
129.58
129.54
129.41
128.84
128.81
128.62
128.59
128.56
128.46
128.43
128.32
128.24
128.10
127.92
127.83
101.19
99.57
92.57
82.27
77.21 CDCl3
77.00 CDCl3
76.79 CDCl3
75.31
73.47
73.34
73.15
73.09
72.68
72.19
71.87
71.76
71.67
71.39
69.73
67.49
59.27
56.03
48.80
47.68
46.45
41.22
39.72
35.59
32.63
30.85
30.47
30.26
26.32
24.73
16.82
15.61
9.43
7.11
6.82
5.03
4.90
13C NMR (151 MHz, CDCl3)
BzO
OBz
BzO
BzO
O
OBz
BzO
O
BzO
O
N3
BnO
OBn
O
O
O
Me
Me
Me
H
H
TESO
CHO
H
H
H
Me
O
Me
TES
Me
S6
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

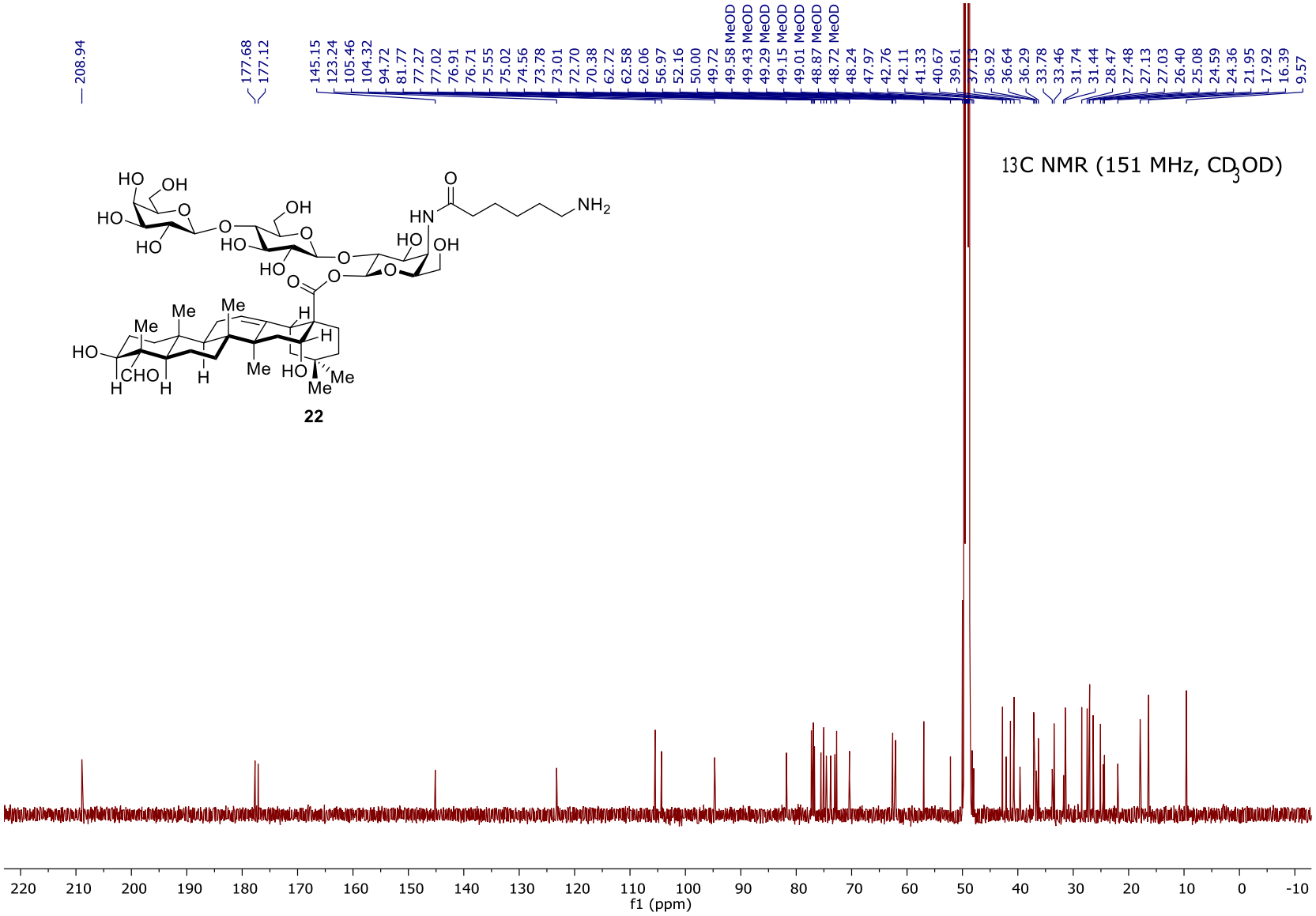

9.30 8.01 7.99 7.99 7.98 7.98 7.97 7.93 7.92 7.91 7.91 7.91 7.90 7.90 7.74 7.73 7.73 7.49 7.47 7.40 7.39 7.38 7.36 7.35 7.34 7.33 7.31 7.30 7.29 7.28 7.26 CDCl3 7.25 7.24 7.23 7.22 7.21 7.17 7.15 7.14 5.75 5.74 5.73 5.46 5.28 5.26 4.80 4.79 4.48 4.46 4.43 3.71 1.31 1.26 1.21 1.04 0.97 0.96 0.95 0.93 0.92 0.91 0.90 0.78 0.63 0.62 0.62 0.61 0.60 0.59 0.55 0.53 0.53 0.52 0.51 0.50
BzO
OBz
BzO
O
BzO
OBz
O
BzO
O
BzO
O
O
O
NH2
BnO
OBn
O
Me
Me
Me
H
H
TESO
CHO
H
H
H
Me
TES
O
Me
Me
21
1.01
8.26
4.12
2.06
1.30
1.12
1.19
5.09
18.00
4.38
2.31
3.07
1.06
2.12
0.95
0.98
1.00
1.95
3.00
1.15
1.23
0.97
0.97
0.99
1.14
3.10
1.19
1.00
2.03
0.99
0.93
1.35
2.08
3.44
5.91
2.82
3.53
4.79
2.93
26.13
5.86
8.13
7.10
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

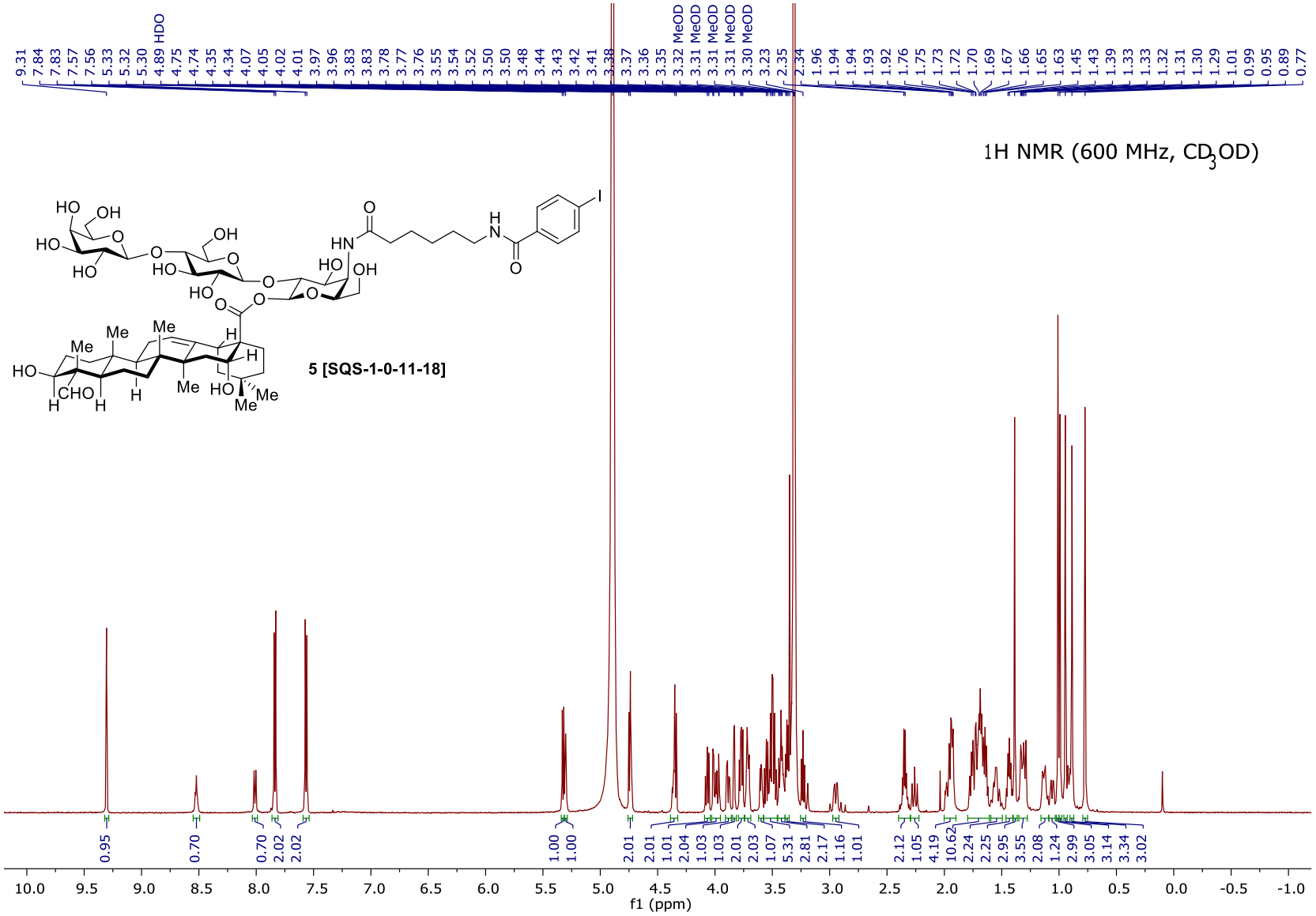

175.67
165.64
165.50
165.35
165.35
165.18
164.85
164.76
142.98
137.84
137.22
133.50
133.31
133.29
133.26
133.22
133.18
133.10
129.96
129.78
129.73
129.66
129.59
129.57
129.55
129.53
129.47
129.38
129.15
129.00
128.80
128.79
128.60
128.55
128.48
128.45
128.37
128.34
128.24
128.22
128.19
127.89
127.70
127.63
101.09
99.41
77.21 CDCl3
77.00 CDCl3
76.79 CDCl3
75.26
73.27
73.18
73.13
71.73
71.49
71.29
69.77
67.41
56.00
48.76
46.47
41.29
39.72
35.63
32.60
30.41
26.35
24.54
16.81
15.63
9.45
7.12
6.80
5.02
4.89
BzO
OBz
BzO
O
BzO
O
OBz
BzO
O
BzO
O
O
O
O
NH2
BnO
OBn
Me
Me
Me
H
H
TESO
CHO
H
H
H
Me
TES
O
Me
Me
21
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

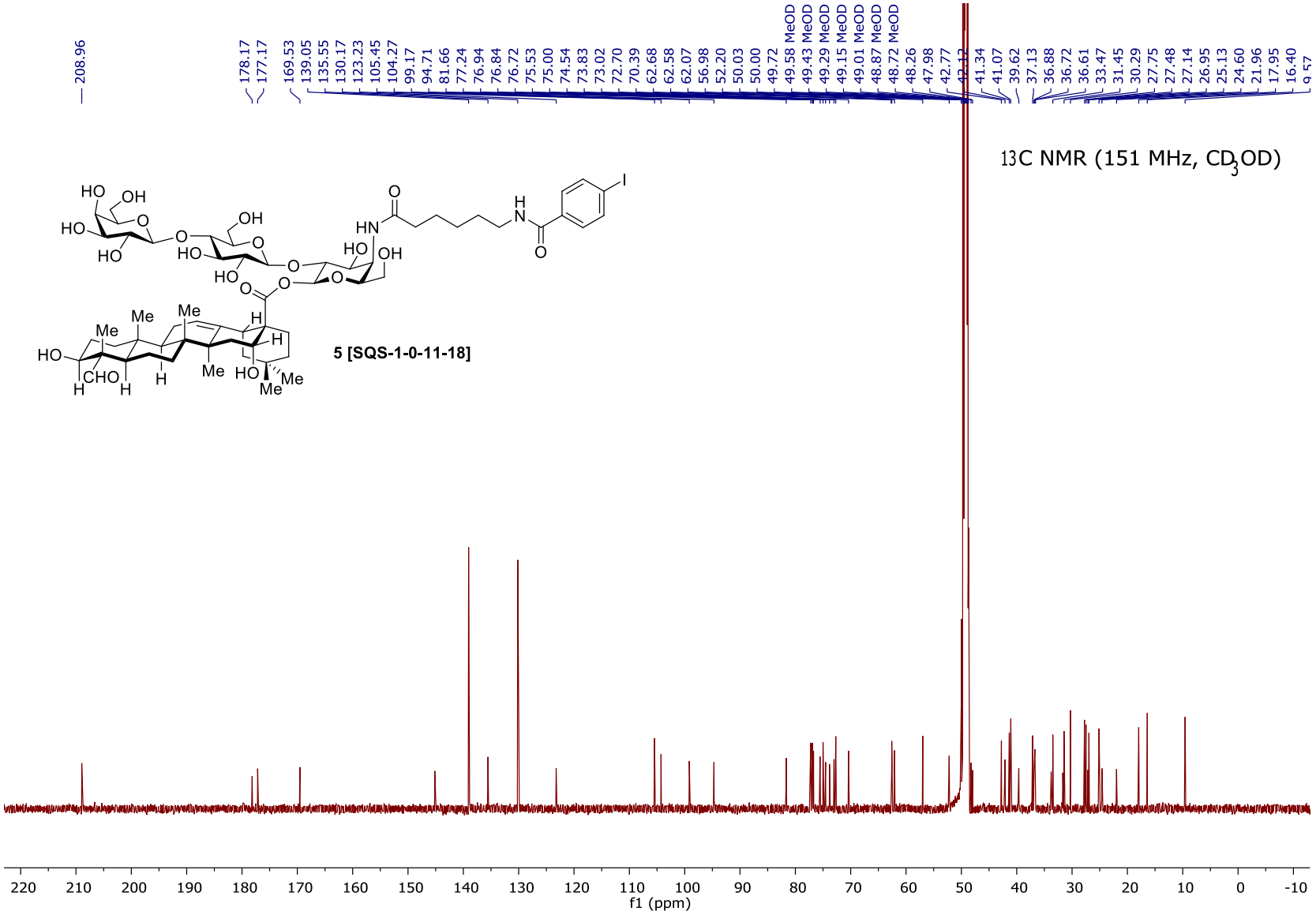

1H NMR
(600 MHz, CDCl3)
S7
f1 (ppm)

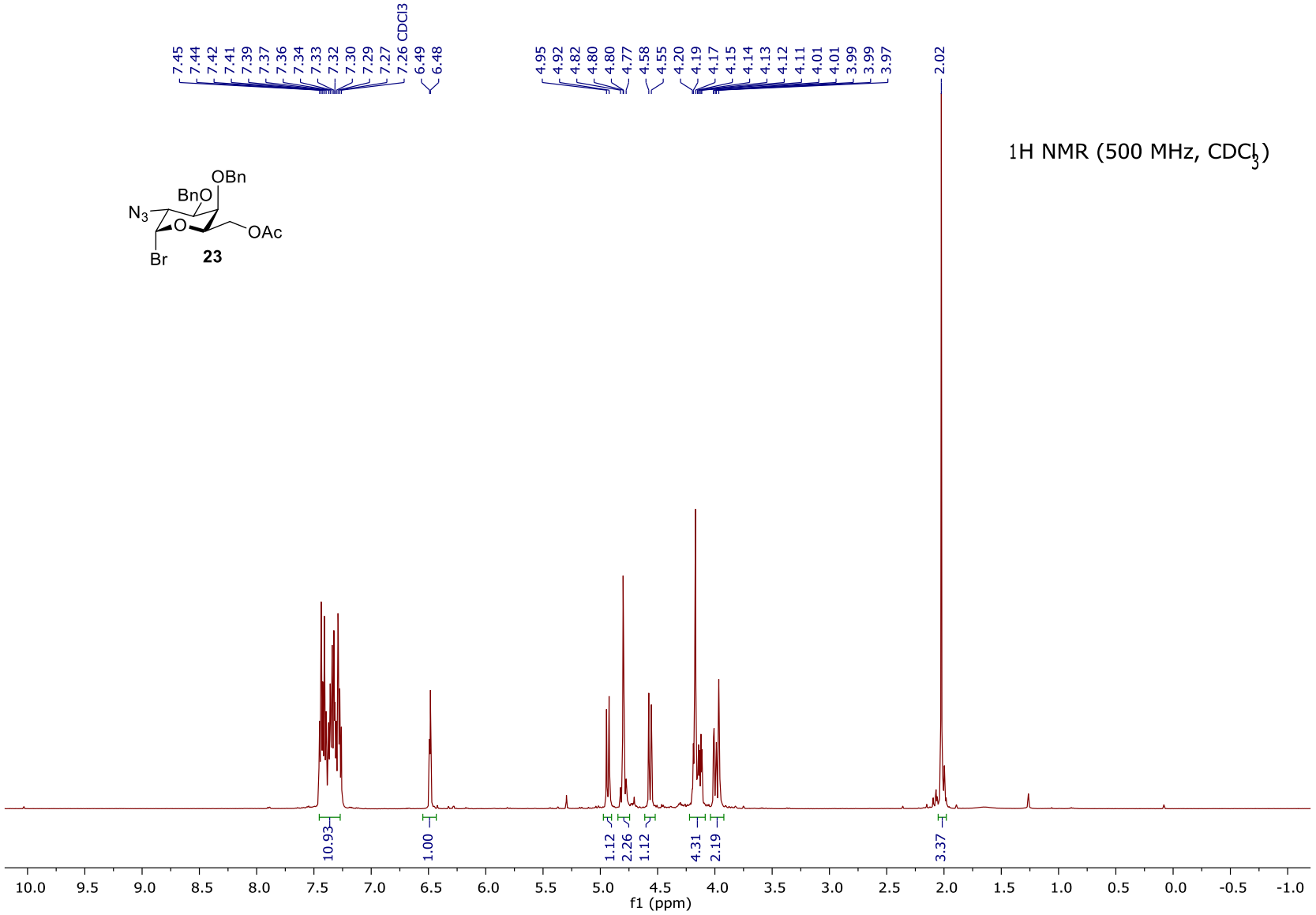

207.37
175.41
165.72
165.46
165.38
165.30
165.18
165.13
164.68
137.52
137.18
133.49
133.38
133.30
133.24
133.18
129.96
129.87
129.72
129.64
129.61
129.57
129.36
129.32
128.80
128.74
128.61
128.54
128.46
128.37
128.31
128.26
128.22
127.77
100.95
77.21 CDCl3
77.00 CDCl3
76.79 CDCl3
75.19
73.49
73.19
72.96
72.93
72.90
71.96
71.80
71.35
71.17
69.75
67.95
67.32
60.76
55.97
48.87
47.74
46.43
41.34
40.34
39.75
36.38
35.70
32.54
30.26
28.42
26.38
25.15
24.13
23.27
16.76
15.71
9.52
7.12
6.80
5.02
4.87
13C NMR (151 MHz, CDCl3)
BzO
OBz
BzO
O
BzO
O
OBz
BzO
O
BzO
O
O
O
HN
O
NHBoc
BnO
OBn
O
Me
Me
Me
H
H
TESO
CHO
H
H
H
Me
O
Me
TES
Me
S7
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

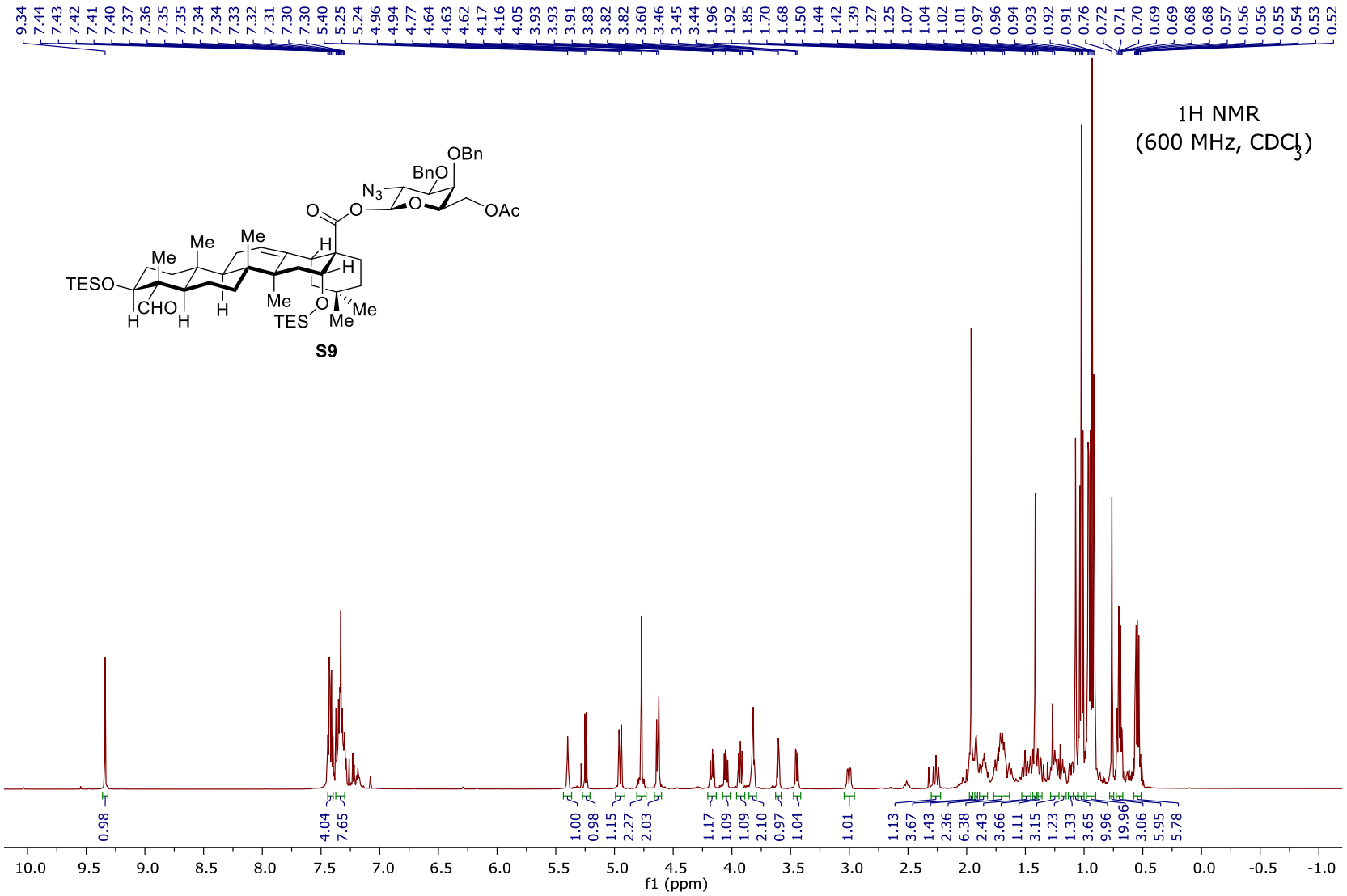

1H NMR (600 MHz, CD3OD)
22
f1 (ppm)

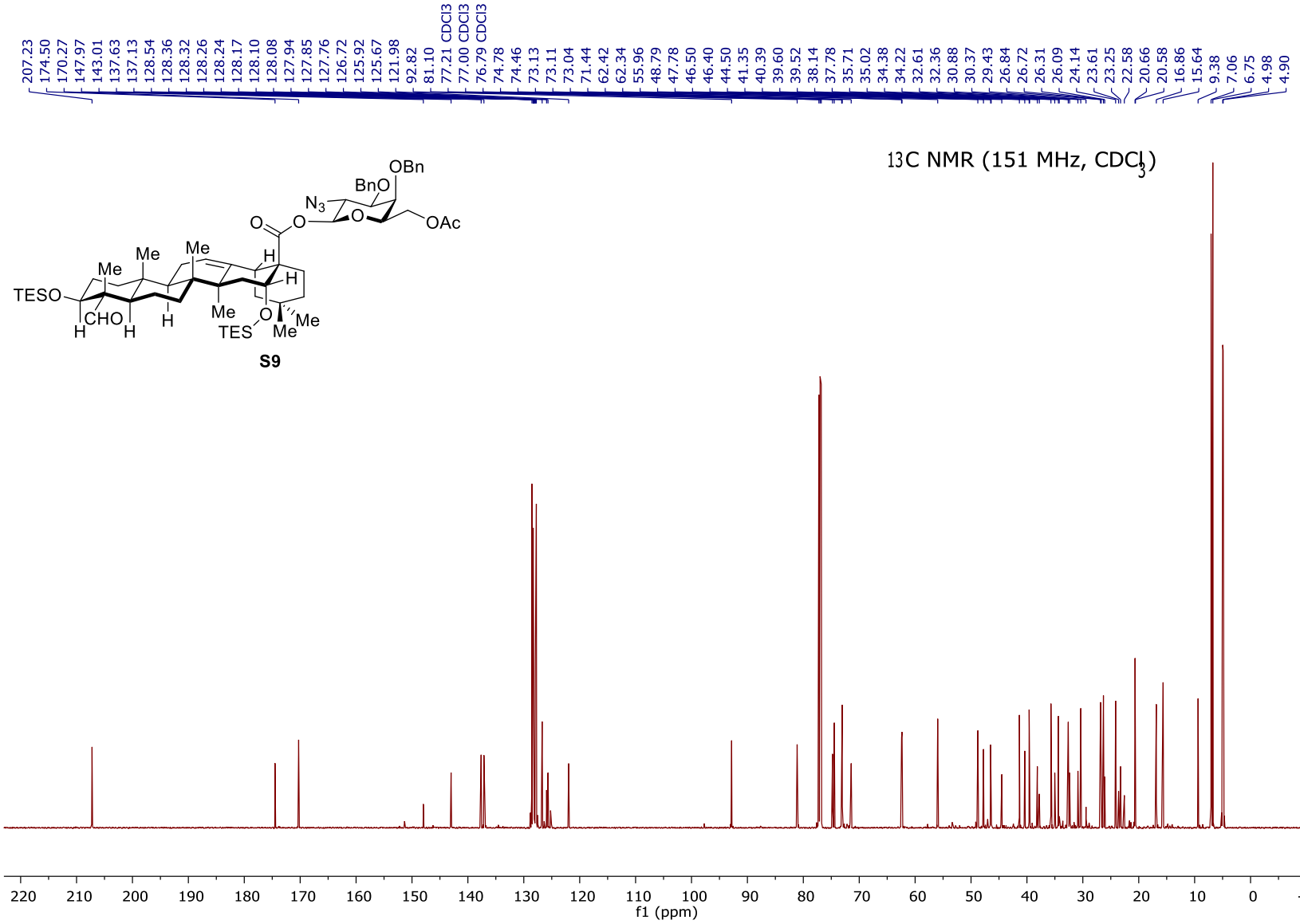

208.94
177.68
177.12
145.15
123.24
105.46
104.32
94.72
81.77
77.27
77.02
76.91
76.71
75.55
75.02
74.56
73.78
73.01
72.70
70.38
62.72
62.58
62.06
56.97
52.16
50.00
49.72
49.58 MeOD
49.43 MeOD
49.29 MeOD
49.15 MeOD
49.01 MeOD
48.87 MeOD
48.72 MeOD
48.24
47.97
42.76
42.11
41.33
40.67
39.61
37.13
36.92
36.64
36.29
33.78
33.46
31.74
31.44
28.47
27.48
27.13
27.03
26.40
25.08
24.59
24.36
21.95
17.92
16.39
9.57
13C NMR (151 MHz, CD3OD)
22
f1 (ppm)

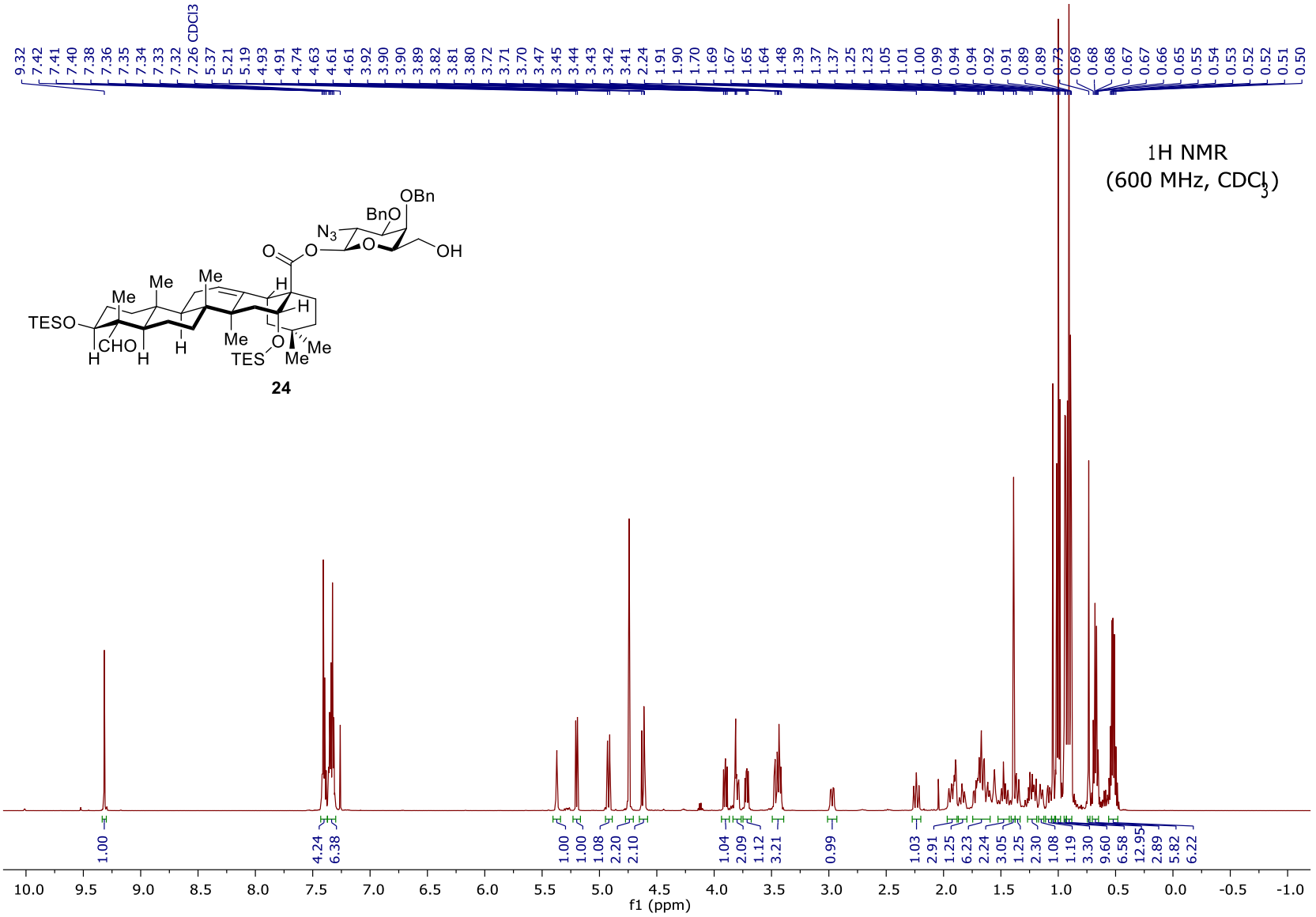

1H NMR (600 MHz, CD3OD)
5 [SQS-1-0-11-18]
f1 (ppm)

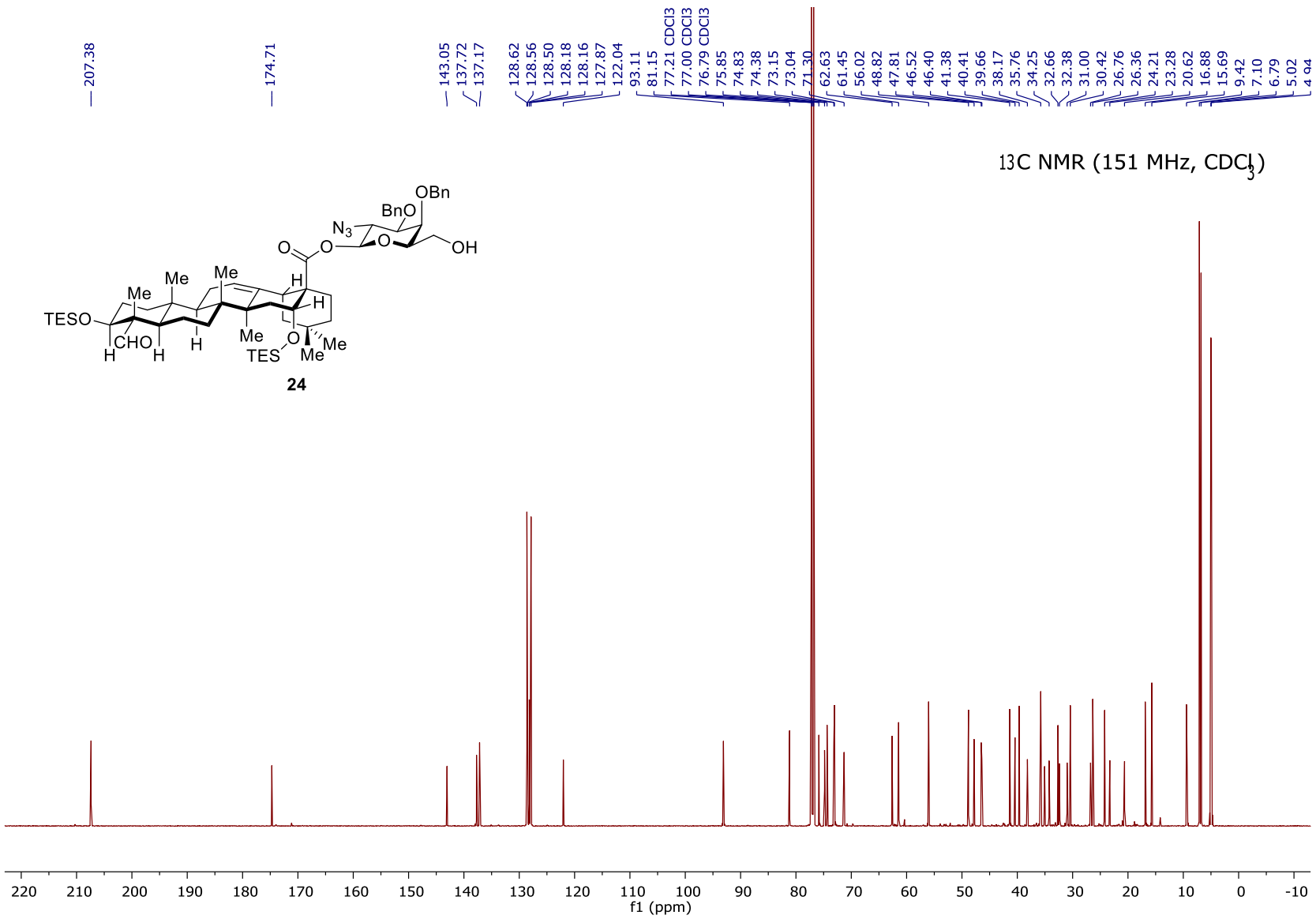

208.96
178.17
177.17
169.53
139.05
135.55
130.17
123.23
105.45
104.27
99.17
94.71
81.66
77.24
76.94
76.84
76.72
75.53
75.00
74.54
73.83
73.02
72.70
70.39
62.68
62.58
62.07
56.98
52.20
50.03
50.00
49.72
49.58 MeOD
49.43 MeOD
49.29 MeOD
49.15 MeOD
49.01 MeOD
48.87 MeOD
48.72 MeOD
48.26
47.98
42.77
42.12
41.34
41.07
39.62
37.13
36.88
36.72
36.61
33.47
31.45
30.29
27.75
27.48
27.14
26.95
25.13
24.60
21.96
17.95
16.40
9.57
13C NMR (151 MHz, CD3OD)
5 [SQS-1-0-11-18]
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

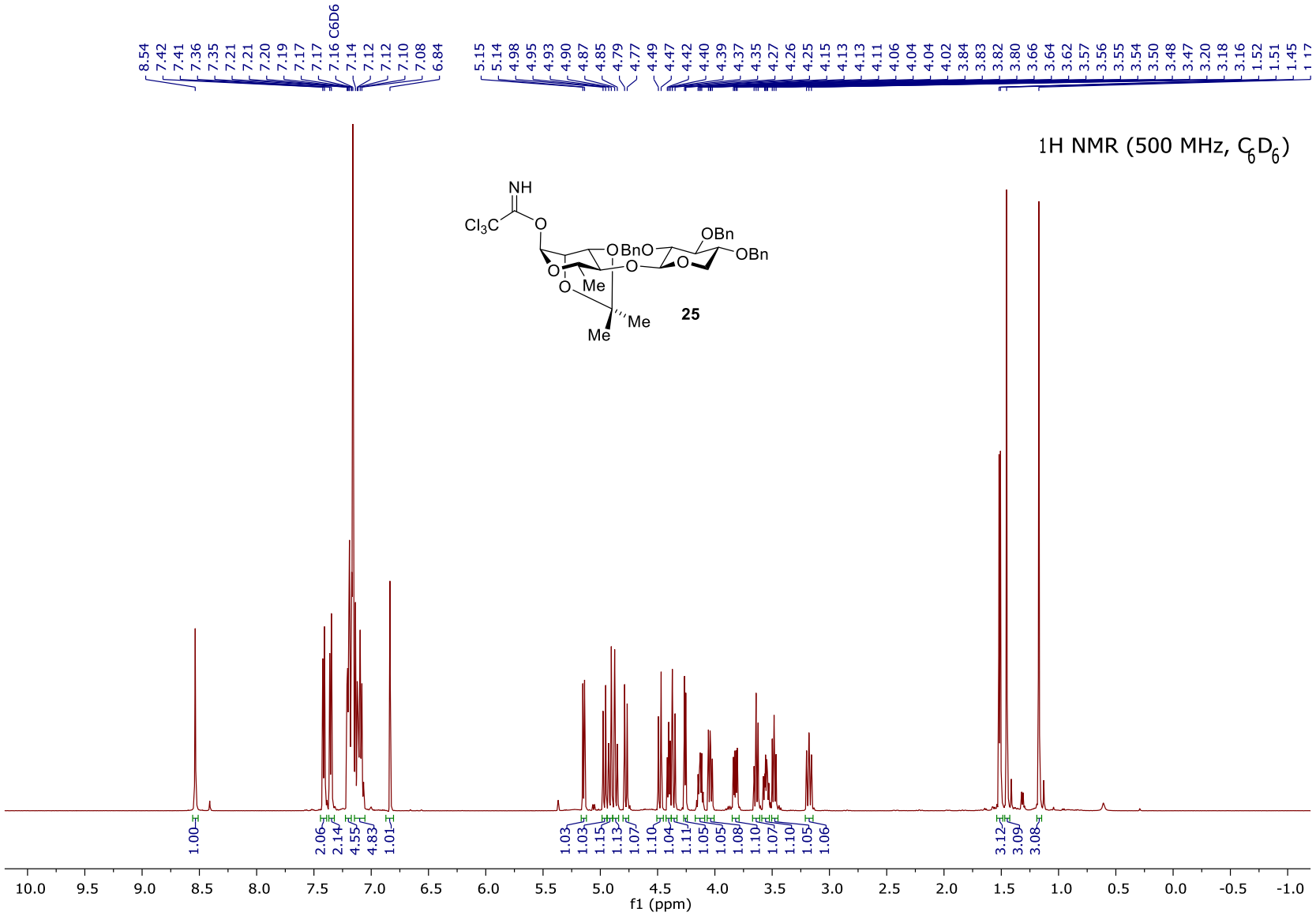

7.45
7.44
7.42
7.41
7.39
7.37
7.36
7.34
7.33
7.32
7.30
7.29
7.27
7.26 CDCl3
6.49
6.48
4.95
4.92
4.82
4.80
4.80
4.77
4.58
4.55
4.20
4.19
4.17
4.15
4.14
4.13
4.12
4.11
4.01
4.01
3.99
3.99
3.97
2.02
1H NMR (500 MHz, CDCl3)
OBn
BnO
N3
O
OAc
Br
23
10.93
1.00
1.12
2.26
1.12
4.31
2.19
3.37
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

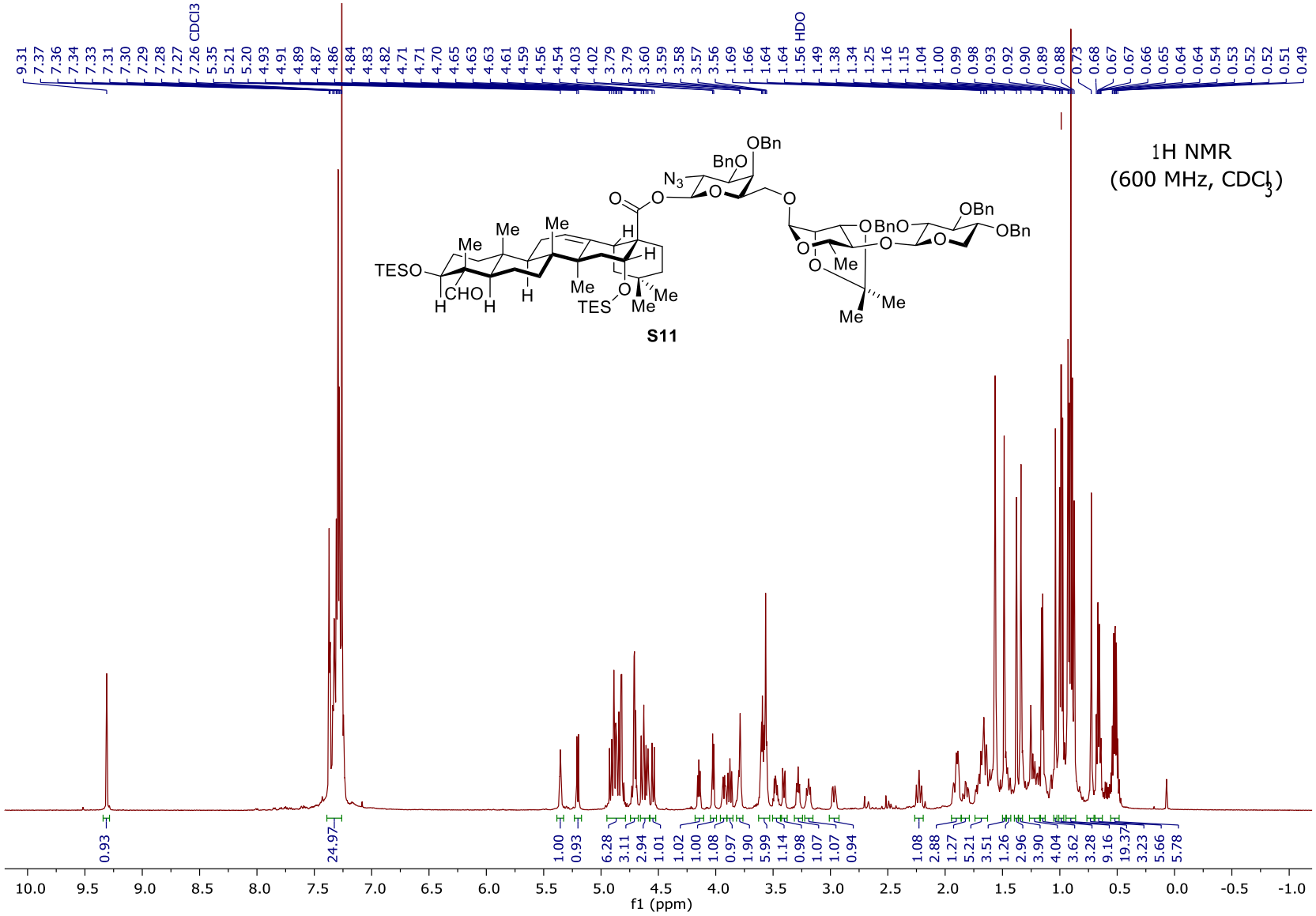

1H NMR
(600 MHz, CDCl3)
OBn
BnO
N3
O
O
O
OAc
TESO
Me
Me
Me
H
H
CHO
H
H
Me
O
Me
TES
Me
S9
f1 (ppm)

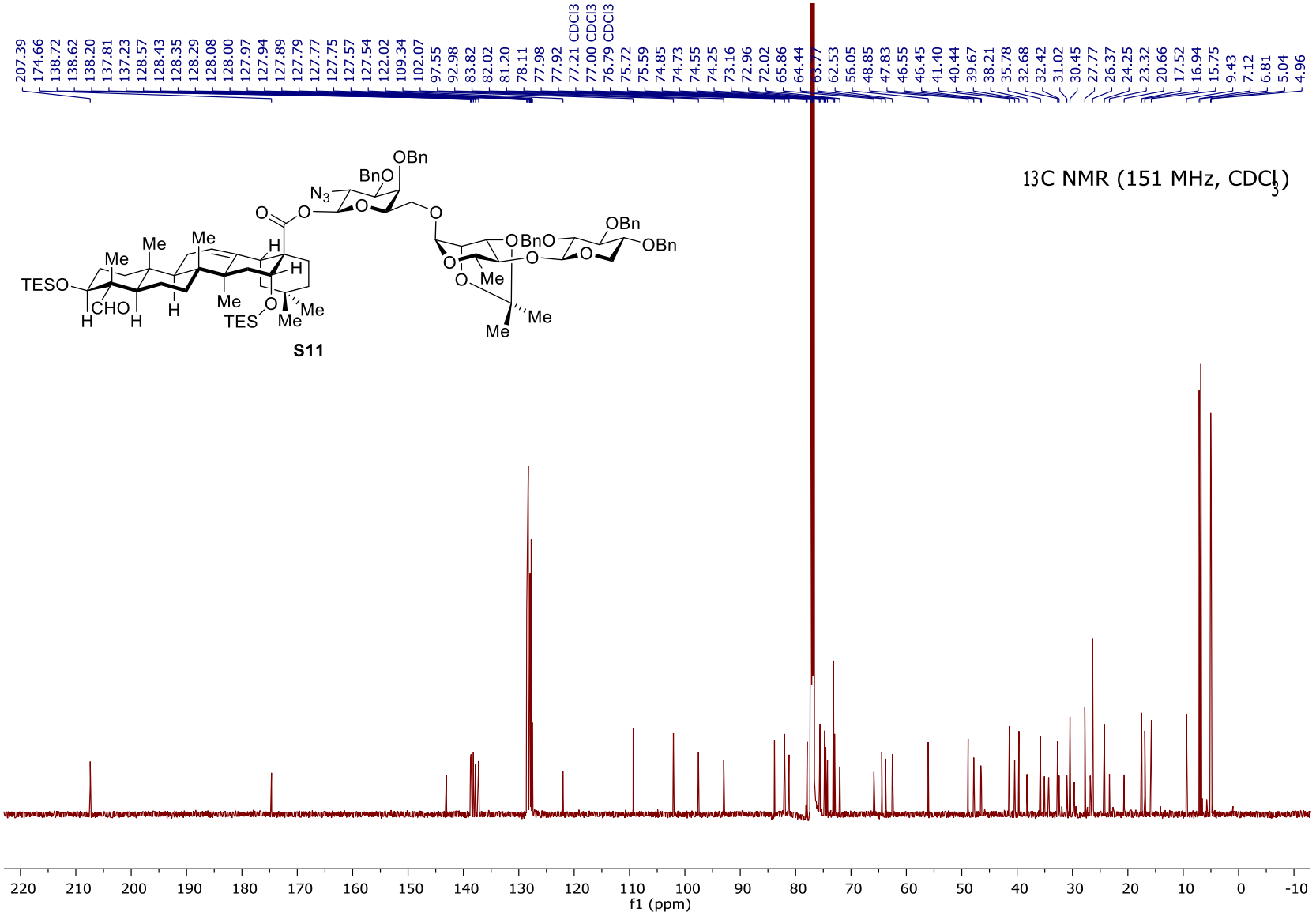

207.23
174.50
170.27
147.97
143.01
137.63
137.13
128.54
128.36
128.32
128.26
128.24
128.17
128.10
128.08
127.94
127.85
127.76
126.72
125.92
125.67
121.98
92.82
81.10
77.21 CDCl3
77.00 CDCl3
76.79 CDCl3
74.78
74.46
73.13
73.11
73.04
71.44
62.42
62.34
55.96
48.79
47.78
46.50
46.40
44.50
41.35
40.39
39.60
39.52
38.14
37.78
35.71
35.02
34.38
34.22
32.61
32.36
30.88
30.37
29.43
26.84
26.72
26.31
26.09
24.14
23.61
23.25
22.58
20.66
20.58
16.86
15.64
9.38
7.06
6.75
4.98
4.90
13C NMR (151 MHz, CDCl3)
OBn
BnO
N3
O
O
O
OAc
Me
Me
Me
H
H
TESO
CHO
H
H
H
Me
O
Me
TES
Me
S9
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

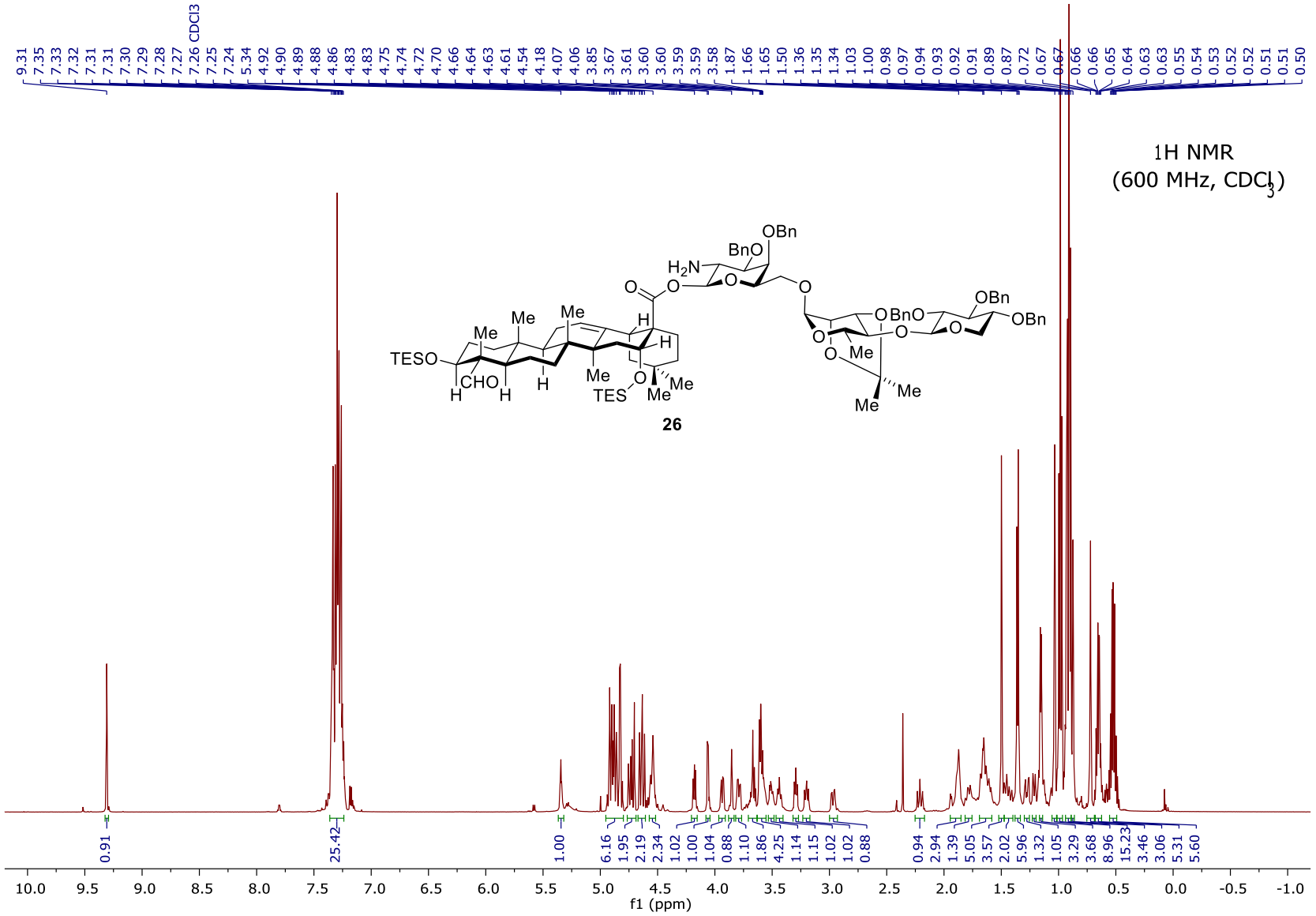

1H NMR
(600 MHz, CDCl3)
24
f1 (ppm)

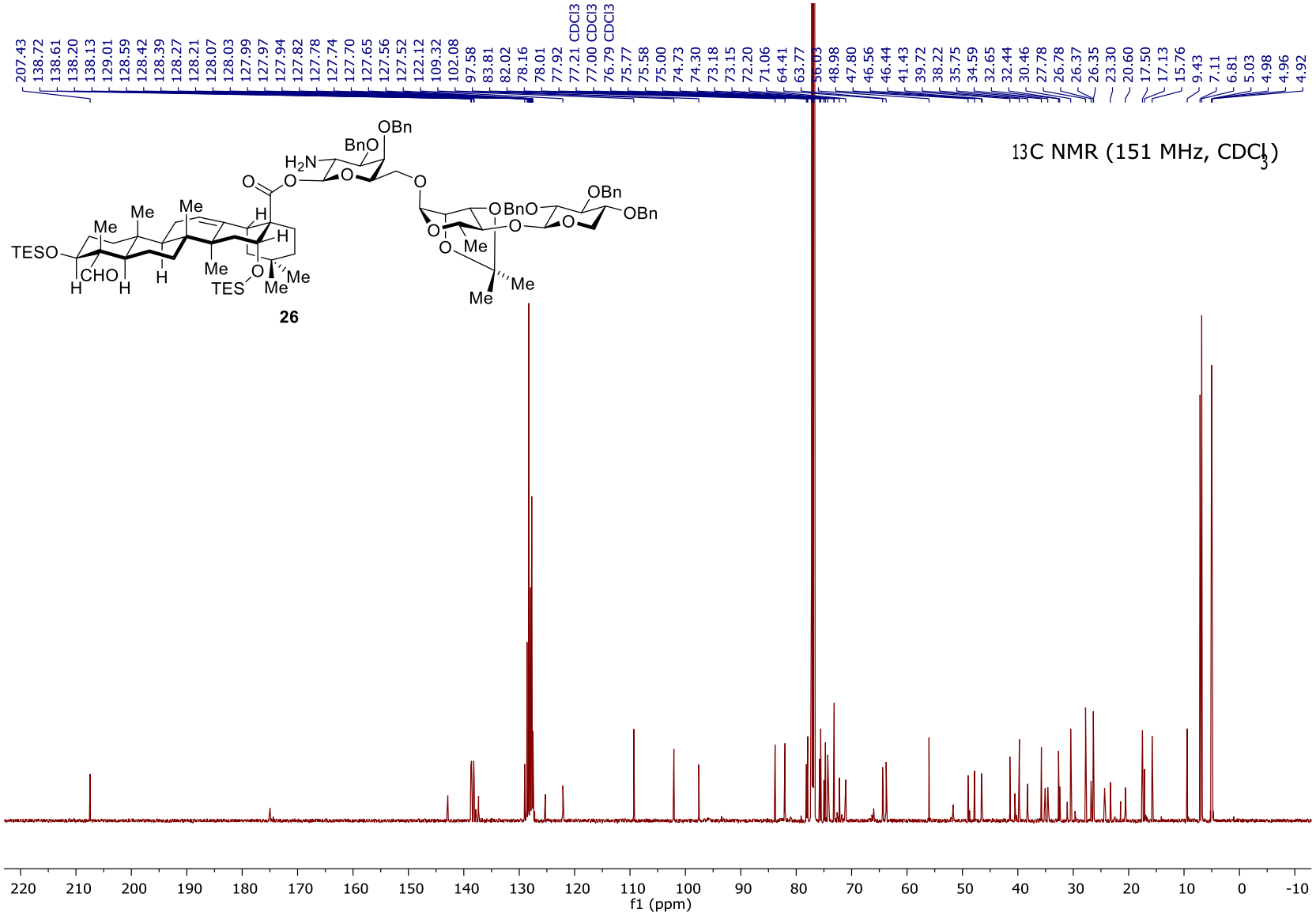

207.38
174.71
143.05
137.72
137.17
128.62
128.56
128.50
128.18
128.16
127.87
122.04
93.11
81.15
77.21 CDCl3
77.00 CDCl3
76.79 CDCl3
75.85
74.83
74.38
73.15
73.04
71.30
62.63
61.45
56.02
48.82
47.81
46.52
46.40
41.38
40.41
39.66
38.17
35.76
34.25
32.66
32.38
31.00
30.42
26.76
26.36
24.21
23.28
20.62
16.88
15.69
9.42
7.10
6.79
5.02
4.94
13C NMR (151 MHz, CDCl3)
OBn
BnO
N3
O
O
O
OH
Me
Me
Me
H
H
TESO
CHO
H
H
H
Me
O
Me
TES
Me
24
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

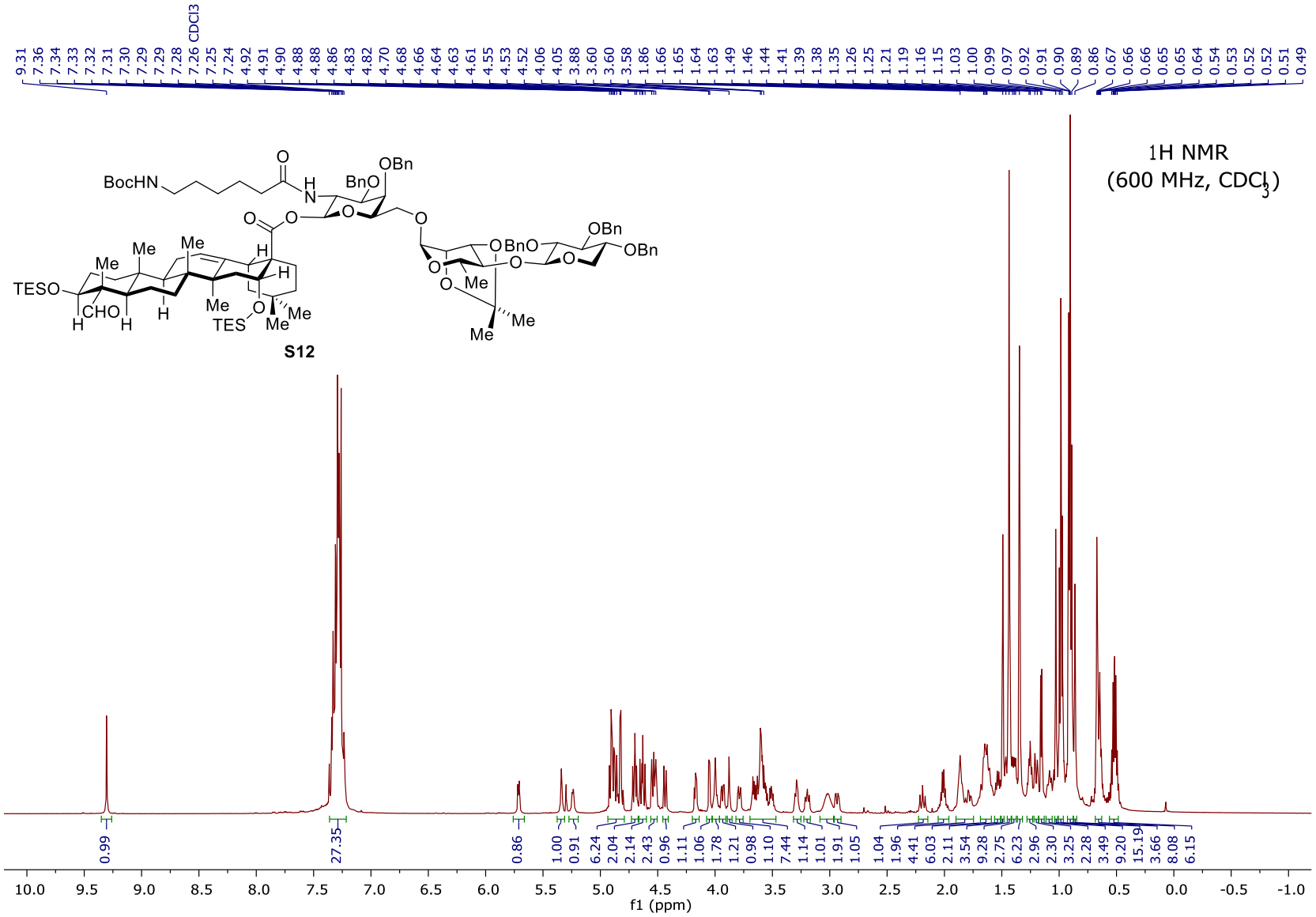

1H NMR (500 MHz, C6D6)
NH
Cl3C
O
OBnO
OBn
OBn
O
O
O
O
Me
Me
Me
25
f1 (ppm)

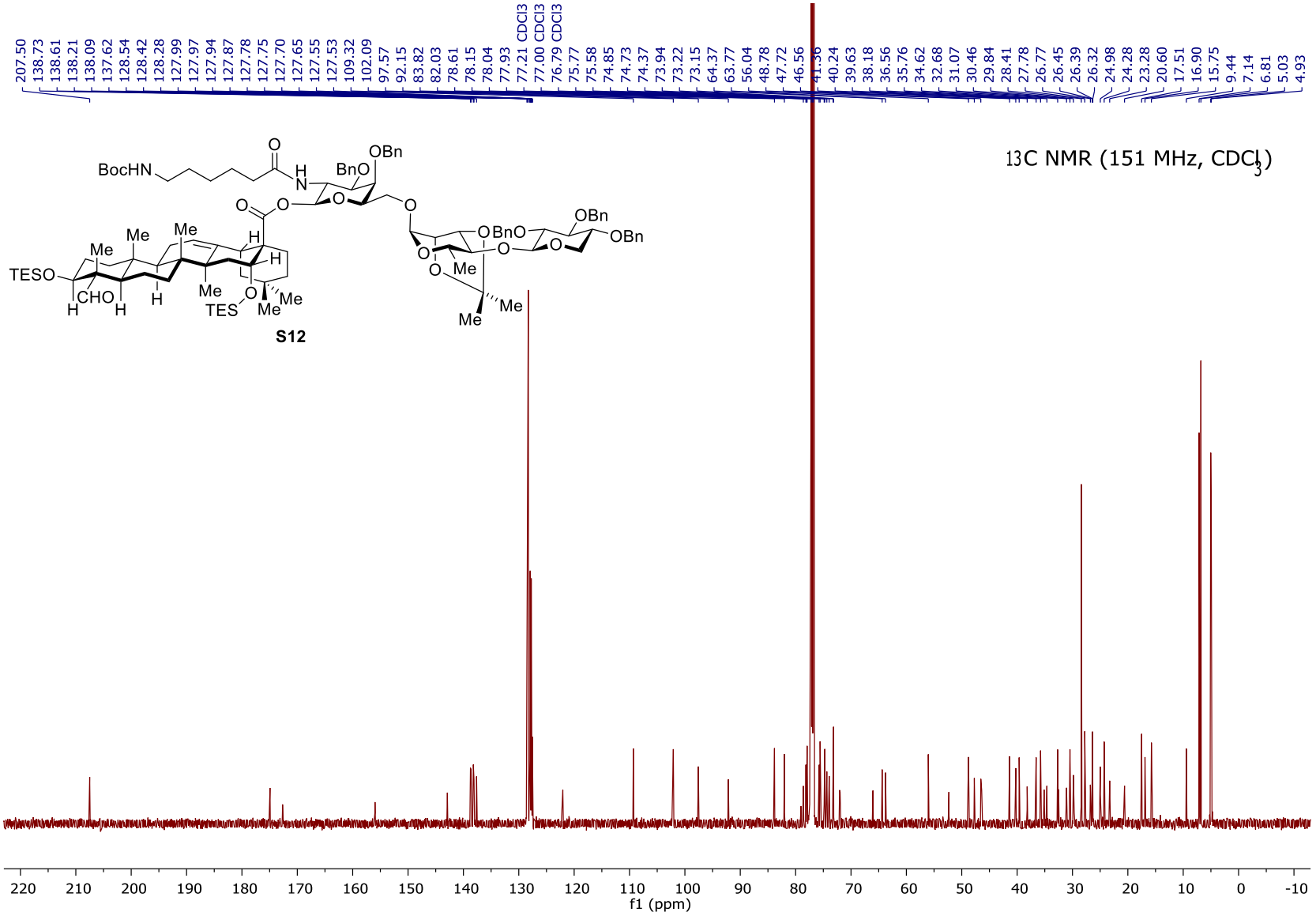

1H NMR
(600 MHz, CDCl3)
S11
f1 (ppm)

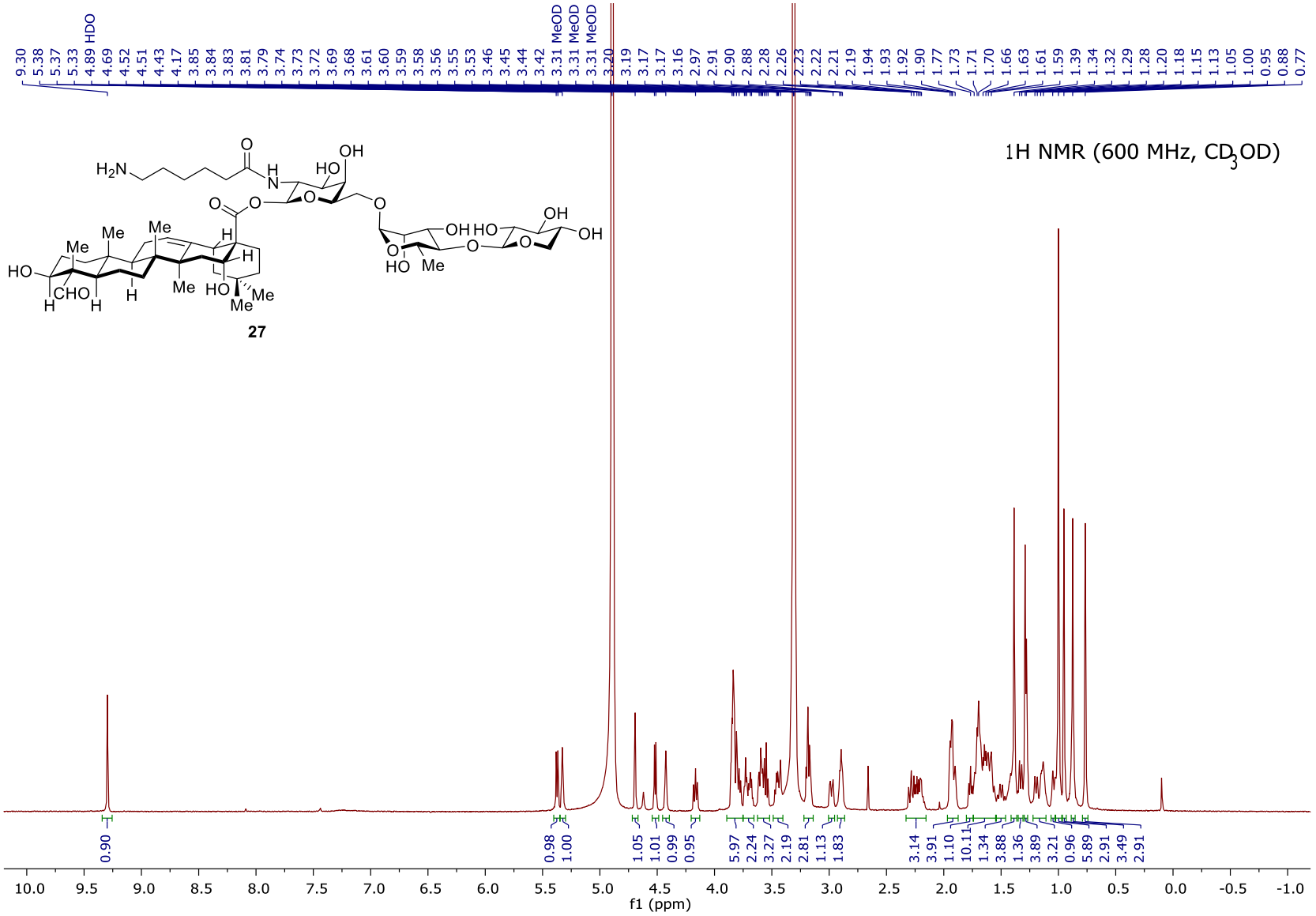

207.39
174.66
138.72
138.62
138.20
137.81
137.23
128.57
128.43
128.35
128.29
128.08
128.00
127.97
127.94
127.89
127.79
127.77
127.75
127.57
127.54
122.02
109.34
102.07
97.55
92.98
83.82
82.02
81.20
78.11
77.98
77.92
77.21 CDCl3
77.00 CDCl3
76.79 CDCl3
75.72
75.59
74.85
74.73
74.55
74.25
73.16
72.96
72.02
65.86
64.44
63.77
62.53
56.05
48.85
47.83
46.55
46.45
41.40
40.44
39.67
38.21
35.78
32.68
32.42
31.02
30.45
27.77
26.37
24.25
23.32
20.66
17.52
16.94
15.75
9.43
7.12
6.81
5.04
4.96
13C NMR (151 MHz, CDCl3)
S11
f1 (ppm)

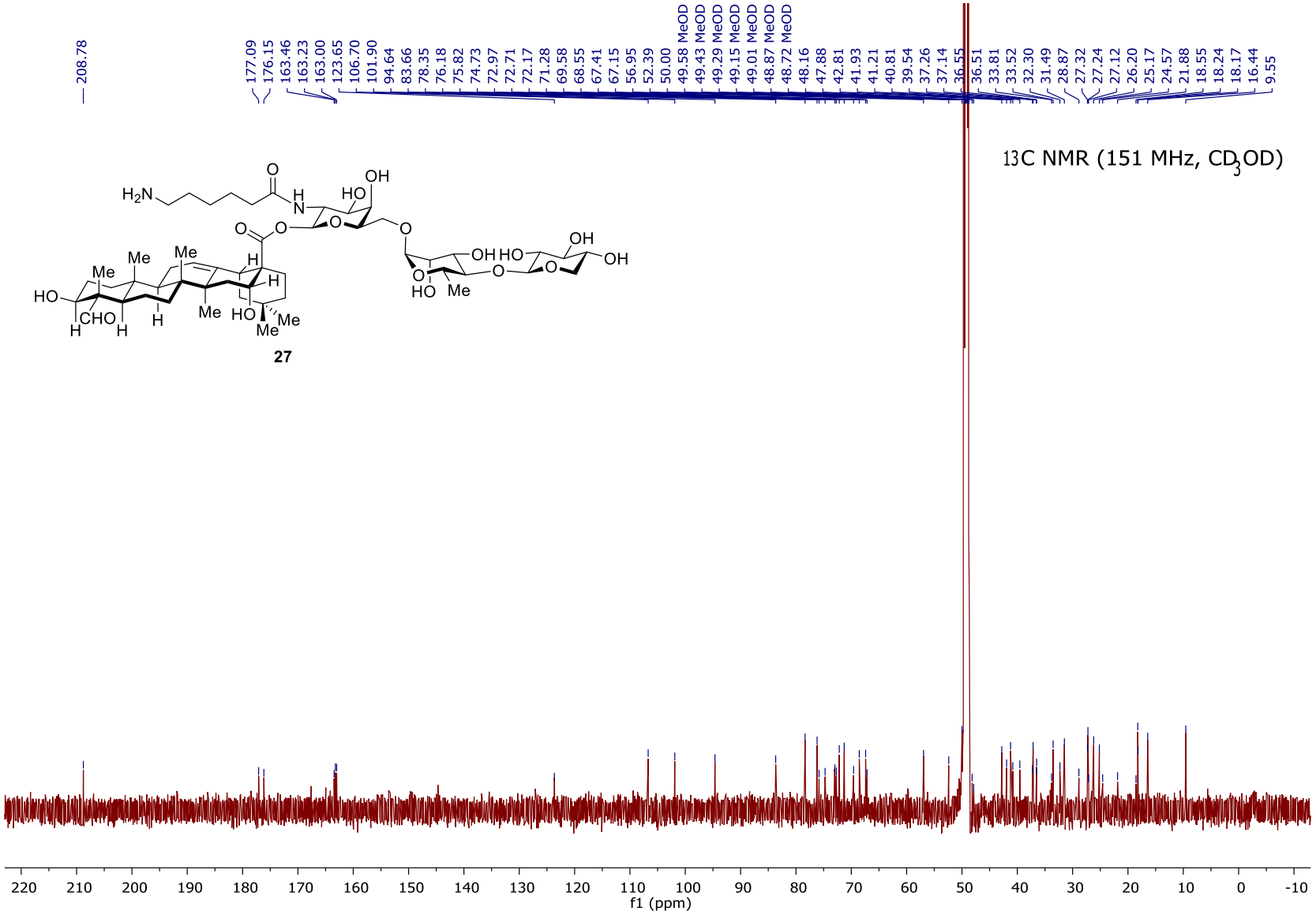

1H NMR
(600 MHz, CDCl3)
26
f1 (ppm)

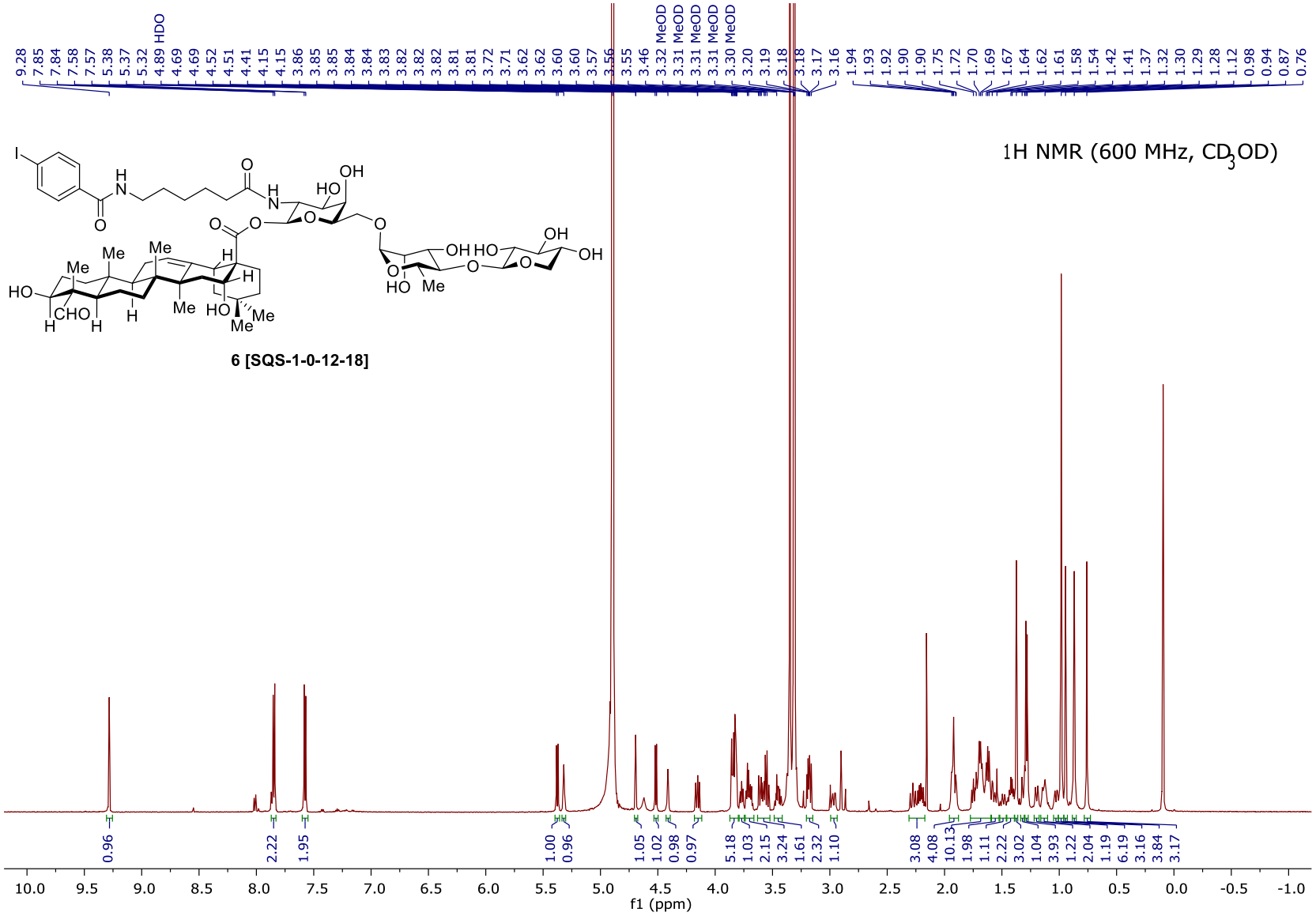

207.43
138.72
138.61
138.20
138.13
129.01
128.59
128.42
128.39
128.27
128.21
128.07
128.03
127.99
127.97
127.94
127.82
127.78
127.74
127.70
127.65
127.56
127.52
122.12
109.32
102.08
97.58
83.81
82.02
78.16
78.01
77.92
77.21 CDCl3
77.00 CDCl3
76.79 CDCl3
75.77
75.58
75.00
74.73
74.30
73.18
73.15
72.20
71.06
64.41
63.77
56.03
48.98
47.80
46.56
46.44
41.43
39.72
38.22
35.75
34.59
32.65
32.44
30.46
27.78
26.78
26.37
26.35
23.30
20.60
17.50
17.13
15.76
9.43
7.11
6.81
5.03
4.98
4.96
4.92
13C NMR (151 MHz, CDCl3)
26
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

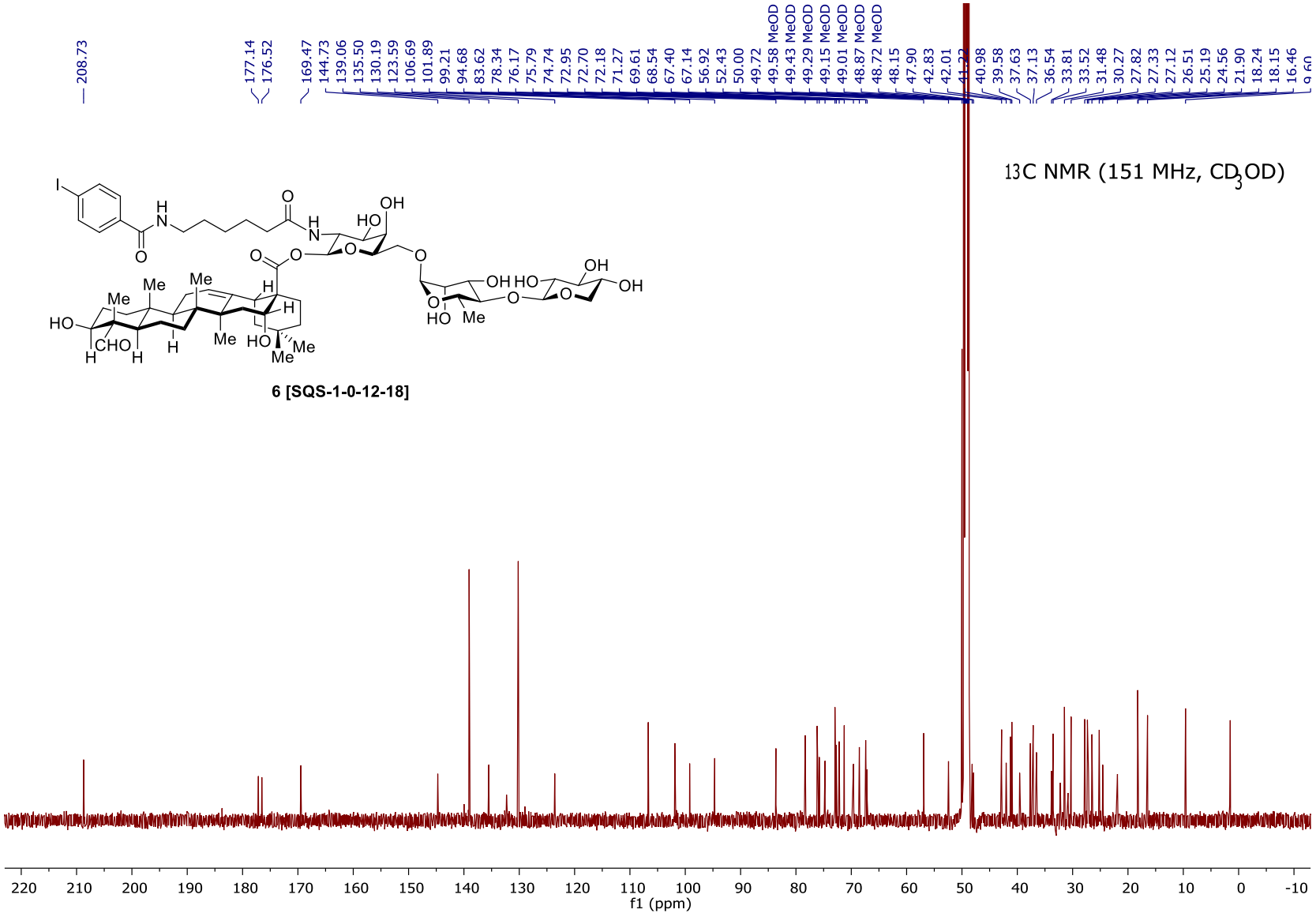

1H NMR
(600 MHz, CDCl3)
S12
f1 (ppm)


207.50 138.73 138.61 138.21 138.09 137.62 128.54 128.42 128.28 127.99 127.97 127.94 127.87 127.78 127.75 127.70 127.65 127.55 127.53 109.32 102.09 97.57 92.15 83.82 82.03 78.61 78.15 78.04 77.93 77.21 CDCl3 77.00 CDCl3 76.79 CDCl3 75.77 75.58 74.85 74.73 74.37 73.94 73.22 73.15 64.37 63.77 56.04 48.78 47.72 46.56 41.36 40.24 39.63 38.18 36.56 35.76 34.62 32.68 31.07 30.46 29.84 28.41 27.78 26.77 26.45 26.39 26.32 24.98 24.28 23.28 20.60 17.51 16.90 15.75 9.44 7.14 6.81 5.03 4.93
13C NMR (151 MHz, CDCl3)
BocHN
OBn
BnO
TESO
CHO
TES
S12
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


1H NMR (600 MHz, CD3OD)
27
f1 (ppm)


208.78
177.09
176.15
163.46
163.23
163.00
123.65
106.70
101.90
94.64
83.66
78.35
76.18
75.82
74.73
72.97
72.71
72.17
71.28
69.58
68.55
67.41
67.15
56.95
52.39
50.00
49.58 MeOD
49.43 MeOD
49.29 MeOD
49.15 MeOD
49.01 MeOD
48.87 MeOD
48.72 MeOD
48.16
47.88
42.81
41.93
41.21
40.81
39.54
37.26
37.14
36.55
36.51
33.81
33.52
32.30
31.49
28.87
27.32
27.24
27.12
26.20
25.17
24.57
21.88
18.55
18.24
18.17
16.44
9.55
13C NMR (151 MHz, CD3OD)
27
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


1H NMR (600 MHz, CD3OD)
6 [SQS-1-0-12-18]
f1 (ppm)


208.73
177.14
176.52
169.47
144.73
139.06
135.50
130.19
123.59
106.69
101.89
99.21
94.68
83.62
78.34
76.17
75.79
74.74
72.95
72.70
72.18
71.27
69.61
68.54
67.40
67.14
56.92
52.43
50.00
49.72
49.58 MeOD
49.43 MeOD
49.29 MeOD
49.15 MeOD
49.01 MeOD
48.87 MeOD
48.72 MeOD
48.15
47.90
42.83
42.01
40.98
39.58
37.63
37.13
36.54
33.81
33.52
31.48
30.27
27.82
27.33
27.12
26.51
25.19
24.56
21.90
18.24
18.15
16.46
13C NMR (151 MHz, CD3OD)
6 [SQS-1-0-12-18]
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

D. SUPPORTING INFORMATION REFERENCES

(1) A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen and F. J. Timmers, *Organometallics* 1996, **15**, 1518.

(2) H. M. Nguyen, J. L. Poole and D. Y. Gin, *Angew. Chem. Int. Ed.* 2001*,* **40**, 414.

(3) E. K. Chea, A. Fernández-Tejada, P. Damani, M. M. Adams, J. R. Gardner, P. O. Livingston, G. Ragupathi and D. Y. Gin, *J. Am. Chem. Soc*. 2012, **134**, 13448.

(4) M. M. Adams, P. Damani, N. R. Perl, A. Won, F. Hong, P. O. Livingston, G. Ragupathi and D. Y. Gin, *J. Am. Chem. Soc.* 2010, **132**, 1939.

(5) A. Fernández-Tejada, E. K. Chea, C. George, N. Pillarsetty, J. R. Gardner, P. O. Livingston, G. Ragupathi, J. S. Lewis, D. S. Tan and D. Y. Gin, *Nature Chem*. 2014, **6**, 635.

(6) (a) F. W. Lichtenthaler, E. Kaji and S. Weprek, *J. Org. Chem.* 1985, **50**, 3505; (b) V. P. Kamath, R. E. Yeske, J. M. Gregson, R. M. Ratcliffe, Y. R. Fang and M. M. Palcic, *Carbohydr. Res*. 2004, **339**, 1141.

(7) N. V. Bovin, S. E. Zurabyan and A. Y. Khorlin, *J. Carb. Chem*. 1983, **2**, 249.