De Novo asymetric synthesis of the mezzettiaside family of natural products via the iterative use of a dual B-/Pd-catalyzed glycosylation

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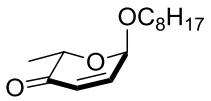
Supporting Information

Section A: General Information

^{1}H and ^{13}C NMR spectra were recorded on a 400, 500 or 600 MHz spectrometer. Chemical shifts were reported relative to internal tetramethylsilane (δ 0.00 ppm) or $CDCl_3$ (δ 7.26 ppm) or CD_3OD (δ 4.90 ppm) or benzene-d_6 (δ 7.44 ppm) for ^{1}H NMR and $CDCl_3$ (δ 77.00/77.23 ppm) or CD_3OD (δ 49.0 ppm) or benzene-d_6 (δ 128 ppm) for ^{13}C NMR. Infrared (IR) spectra were obtained on a FT-IR spectrometer. Optical rotations were measured with a digital polarimeter in the solvent specified. Flash column chromatography was performed on 60-200 or 230-400 mesh silica gel. Analytical thin-layer chromatography was performed with precoated glass backed plates and visualized by quenching of fluorescence and by charring after treatment with *p*-anisaldehyde or potassium permanganate stain. R_f values were obtained by elution in the stated solvent ratios. Acetonitrile, diethyl ether, tetrahydrofuran, methylene dichloride and triethylamine were dried by passing through activated alumina column with argon gas pressure. Commercial reagents were used without purification unless otherwise noted. Air- and/or moisture-sensitive reactions were carried out under an atmosphere of argon/nitrogen using oven- or flame-dried glassware and standard syringe/septa techniques.

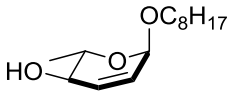
Section B: Experimental Procedures

1-Octyloxy-2,3-didehydro-5-methyl-oxo-pyran (15):



To a solution of Boc-pyranone **14** (5.0 g, 21.91 mmol) and octan-1-ol (4.28 g, 32.9 mmol) in 30 mL of CH_2Cl_2 at 0 ºC was added 4 Å molecular sieves (1.3 g) To this mixture was added $Pd_2(dba)_3$•$CHCl_3$ (567 mg, 2.5 mol %) and PPh_3 (576 mg, 10 mol %) solution in CH_2Cl_2. The reaction was stirred and warmed from 0 ºC to rt. After 2 h the reaction was quenched by adding 30 mL saturated $NaHCO_3$, followed by extraction with Et_2O (3 x 300 mL). The organic layers were combined, washed by 30 mL saturated brine solution, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 3-5% EtOAc/hexane to give pyranone **15** (4.9 g, 20.39 mmol, 93%): R_f (30% EtOAc/hexane) = 0.65; $[\alpha]^{25}_D$ = + 33.8 (c = 0.39, CH_2Cl_2); IR (thin film, cm^{-1}) 2928, 2857, 1733, 1702, 1467, 1375, 1158, 1086, 1041, 749; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 (dd, J = 10.4, 3.6 Hz, 1H), 6.01 (d, J = 10.0 Hz, 1H), 5.11 (d, J = 2.8 Hz, 1H), 4.52 (q, J = 6.4 Hz, 1H), 3.80 (ddd, J = 9.6, 7.2, 6.8 Hz, 1H), 3.54 (ddd, J = 9.6, 7.2, 6.8 Hz, 1H), 1.57 (m, 2H) 1.33 (d, J = 6.4 Hz, 3H), 1.26 (m, 10H), 0.87 (dd, J = 6.0, 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 143.8, 127.4, 93.2, 70.4, 69.7, 32.0, 29.8, 29.5, 29.4, 26.3, 22.8, 15.4, 14.3; HRMS (ESI) calcd for $[C_{14}H_{24}O_3 + H]^+$: 241.1745, Found: 241.1732.

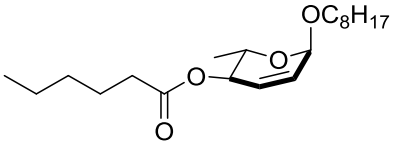
1-Octyloxy-2,3-didehydro-α-L-rhamnopyranoside (16):



To a solution of enone **15** (4.9 g, 20.40 mmol) in CH_2Cl_2 (20 mL) at –78 ºC was added $CeCl_3$/MeOH solution (0.4 M in MeOH, 21 mL) and $NaBH_4$ (926 mg, 24.5 mmol). The reaction mixture was stirred at –78 ºC for 3 h and quenched with 20 mL of saturated $NaHCO_3$ solution,

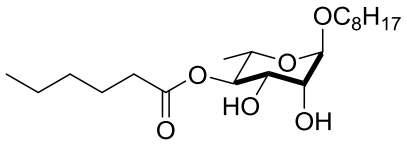
extracted with Et_2O (2 x 50 mL) at 0 ºC, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 10-12% EtOAc/hexane to give allylic alcohol **16** (3.94 g, 16.3 mmol, 80%): R_f (30% EtOAc/hexane) = 0.4; $[\alpha]^{25}_D = -62.5$ ($c = 1.51$, CH_2Cl_2); IR (thin film, cm^{-1}) 3391, 2926, 2857, 1459, 1379,1102, 1048, 1002, 887, 748, 724; ^1H NMR (400 MHz, $CDCl_3$) δ 5.90 (d, $J = 10.4$ Hz, 1H), 5.73 (ddd, $J = 10.4, 3.6, 2.0$ Hz, 1H), 4.89 (s, 1H), 3.79 (m, 1H), 3.75 (q, $J = 6.0$ Hz, 1H), 3.67 (ddd, $J = 9.6, 7.2, 6.8$ Hz, 1H), 3.48 (ddd, $J = 9.6, 7.2, 6.8$ Hz, 1H), 2.19 (m,1H), 1.59 (dd, $J = 7.3, 6.4$ Hz, 1H), 1.57 (dd, $J = 7.2, 6.4$ Hz, 1H), 1.30 (d, 3H), 1.26 (m, 9H), 0.87 (dd, $J = 6.0, 6.0$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.7, 126.8, 94.5, 68.8, 69.9, 68.1, 32.0, 30.0, 29.6, 29.5, 26.4, 22.9, 18.2, 14.3; HRMS–MALDI–TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{14}H_{26}O_3 + Na]^+$: 265.1774, Found: 265.1783.

1-Octyloxy-2,3-didehydro-4-*O*-hexanoyl-α-L-rhamnopyranoside (16a):



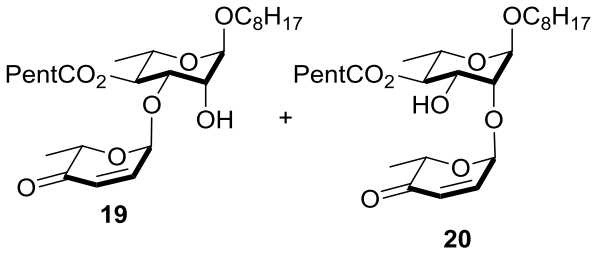
To a stirred solution of allylic alcohol **16** (4.41g, 18.2 mmol) in CH_2Cl_2 was added hexanoic acid (4.23g, 36.45 mmol) then added DCC (8.273g, 40.1 mmol) and DMAP (0.225g, 1.90 mmol). Stirred from 0 ºC to rt for 3 h, Reaction was completed, filtered to remove DCU. The filterate was washed with NaOH (0.5 N), concentrated under reduced pressure. The crude product was purified by using flash chromatography, eluting with 5% EtOAc/hexane to give ester **16a** (5.26 g, 15.47 mmol, 85%); R_f (10% EtOAc/hexane) = 0.7; $[\alpha]^{25}_D = -60.9$ ($c = 1.22$, CH_2Cl_2); IR (thin film, cm^{-1}) 2957, 2859, 1742, 1711, 1466, 1243, 1168, 1107, 1051, 1027, 749; ^1H NMR (400 MHz, $CDCl_3$) δ 5.78 (d, $J = 10.0$ Hz, 1H), 5.74 (dd, $J = 10.0, 10.0$ Hz, 1H), 5.00 (d, $J = 8.8$ Hz, 1H) 4.88 (s, 1H), 3.94 (dq, $J = 9.6, 6.6$ Hz, 1H), 3.72 (ddd, $J = 9.6, 7.2, 6.8$ Hz, 1H), 3.44 (ddd, $J = 9.6, 7.2, 6.8$ Hz, 1H), 2.27 (dd, $J = 7.2, 7.2$ Hz, 1H), 1.60 (m, 4H), 1.25 (m, 14H), 1.16 (d, $J = 6.8$ Hz, 3H), 0.83 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 129.8, 128.0, 94.5, 70.7, 68.8, 64.8, 34.5, 31.9, 31.4, 29.9, 29.5, 29.4, 26.3, 24.8, 22.8, 22.4, 18.1, 14.2, 14.0; HRMS–MALDI–TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{20}H_{36}O_4 + Na]^+$: 363.2506, Found: 363.2510.

1-Octyloxy-4-*O*-hexanoyl-α-L-rhamnopyranoside (17a):



To a stirred solution of ester **16a** (5.5 g, 16.20 mmol) in *t*-butanol/acetone (1:1, 16.1 mL) at 0 ºC was added a solution of *N*-methyl morpholine *N*-oxide/water (50% w/v) (8.1 mL) and OsO_4 (206 mg, 5 mol%). The reaction mixture was stirred at rt for 12 h and then concentrated. The residue was pipetted directly on to a silica gel column; the product was eluted with 10-15% EtOAc/hexane. Pure fractions were combined and concentrated to afford ester diol **17a** (5.3, 14.20 mmol, 88%); R_f (20% EtOAc/hexane) = 0.28; $[\alpha]^{25}_D$ = – 56 (c = 1.6, CH_2Cl_2); IR (thin film, cm^{-1}) 3321, 2956, 2925, 2857, 1732, 1459, 1379, 1246, 1178, 1104, 1085, 984, 835, 794, 645; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.80 (s, 1H), 4.77 (dd, J = 9.6, 9.6 Hz, 1H), 3.92 (d, J = 1.6 Hz, 1H), 3.88 (dd, J = 9.2, 3.2 Hz, 1H), 3.81 (dq, J = 9.6, 6.4 Hz, 1H), 3.68 (ddd, J = 9.6, 7.2, 6.8 Hz, 1H), 3.43 (ddd, J = 9.4, 6.4, 6.4 Hz, 1H), 2.39 (dd, J = 7.2, 7.6 Hz, 1H), 2.37 (dd, J = 7.2, 7.2 Hz, 1H) 1.66 (m, 2H), 1.56 (m, 2H) 1.33 (m, 14H), 1.21 (d, J = 6.0 Hz, 3H), 0.91 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 99.3, 75.6, 71.2, 70.6, 68.1, 65.5, 34.6, 32.0, 31.4, 29.6, 29.5, 29.5, 26.3, 24.8, 22.9, 22.5, 17.7, 14.4, 14.1; HRMS-MALDI-TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{20}H_{38}O_6 + Na]^+$: 397.2561, Found: 397.2594.

1-Octyloxy-2,3-didehydro-5-methyl-4-oxopyranosyl-(1→3)-4-*O*-hexanoyl-2-hydroxy-α-L-rhamnopyranoside (19 and **20):**



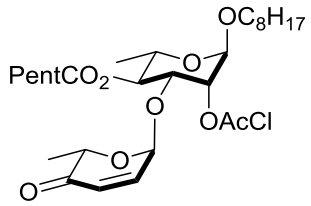
To a solution of diol **17a** (100 mg, 0.267 mmol) in toluene was added dibutyltinoxide (73 mg, 0.32 mmol, 1.1 eq.) and the reaction was refluxed for 4 h. After 4h, the toluene was evaporated and added dry CH_2Cl_2 (4 mL), stirred at 0 ºC for 15 min and then added Boc-pyranone **14** (68

mg, 0.29 mmol) followed by addition of $Pd_2(dba)_3$•$CHCl_3$ (7 mg, 2.5 mol%) and PPh_3 (7.1 mg, 10 mol%) solution in CH_2Cl_2. After 2 h the reaction was quenched by adding 1.5 mL saturated $NaHCO_3$, followed by extraction with EtOAc (3 x 10 mL). The organic layers were combined, washed by 2 mL saturated brine solution, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 10-15% EtOAc/hexane to give inseparable mixture of glycosylated product **19** and **20** as C-3 and C-2 regioisomer in the ratio (5:1) (88 mg, 0.18 mmol, 68%); R_f(20% EtOAc/hexane) = 0.5; $[\alpha]^{25}_D$ = – 31.3 (c = 0.5, CH_2Cl_2); IR (thin film, cm^{-1}) 3433, 2954, 2931, 2858, 1710, 1613, 1514, 1360, 1248, 1221, 1175, 1035, 819, 735, 529; Major Product **19**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.69 (dd, J = 10.4, 3.6 Hz, 1H), 6.10 (d, J = 10.4 Hz, 1H), 5.32 (d, J = 2.8 Hz, 1H), 5.11 (dd, J = 9.6, 9.6 Hz, 1H), 4.80 (s, 1H), 4.60 (q, J = 6.8 Hz, 1H), 4.10 (dd, J = 9.6, 2.8 Hz, 1H), 4.05 (br, 1H), 3.82 (dq, J = 9.6, 5.6 Hz, 1H), 3.69 (ddd, J = 9.6, 6.4, 6.4 Hz, 1H), 3.47 (ddd, J = 9.6, 6.4, 6.4 Hz, 1H), 2.37 (m, 2H), 1.66 (m, 4H) 1.40 (d, J = 6.8 Hz, 3H), 1.32-1.25 (m, 14H), 1.19 (d, J = 6.0 Hz, 3H), 0.90-0.88 (m, 6H); ^{13}C NMR (100MHz,$CDCl_3$) δ 196.3, 173.3, 142.5, 127.8, 99.3, 94.8, 77.9, 72.8, 71.3, 70.9, 68.2, 66.3, 34.6, 32.0, 31.5, 29.6, 29.5, 29.4, 26.3, 24.9, 22.8, 22.5, 17.6, 15.4, 14.3, 14.1; HRMS–MALDI-TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{26}H_{44}O_8 + Na]^+$: 507.2928, Found: 507.2934.

Alternative procedure for regioselective glycosylation at C-3 position:

To a stirred solution of diol **17a** (50 mg, 0.135 mmol) in CH_3CN/THF (1:0.1) (2.7 mL, 0.05M), was added boron catalyst ($Ph_2BOCH_2CH_2NH_2$) (4.5 mg, 30 mol%) at 0 ºC. After 15 min, was added Boc-pyranone (**14**) (37 mg, 0.16 mmol) followed by addition of previously mixed solution of $Pd_2(dba)_3$•$CHCl_3$ (3.5 mg, 2.5 mol%) and PPh_3 (3.6 mg, 10 mol%) solution in CH_3CN/THF. Reaction was monitored by TLC, completed in 4 h. Diluted with EtOAc, quenched with water and extracted. The organic layers were combined and evaporated under reduced pressure. The crude product was purified using silica gel to elute the desired product with 12-14% EtOAc/hexane to give inseparable mixture of glycosylated product as C-3 and C-2 regioisomer in the ratio (7.5:1) of **19** and **20** (48 mg, 0.10 mmol, 74%).

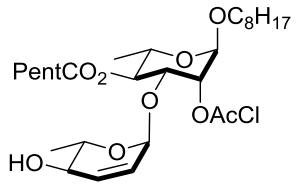
1-Octyloxy-2,3-didehydro-5-methyl-4-oxo-pyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (21):



To a mixture of enone **19** and **20** (80 mg, 0.16 mmol) in pyridine (0.33 mL) was added chloroacetic anhydride (98.8 mg, 0.58 mmol), 10% DMAP (2 mg, 0.016 mmol) at 0 ºC. Reaction was monitored by TLC, completed in 2 h. Diluted with EtOAc and quenched with dil. HCl (0.5N). Extracted the aqueous layer with ether (3 x 30 mL) and concentrated under reduced pressure. The crude product was subjected to column chromatography using silica gel eluting with 8-10% EtOAc/hexane to afford mixture **21** and its C-2 regioisomer (83.3 mg, 0.15 mmol, 90%); R_f(30% EtOAc/hexane) = 0.8 $[\alpha]^{25}_D$ = – 4.1 (*c* = 0.75, CH_2Cl_2); IR (thin film, cm^{-1}) 2956, 2926, 2856, 1747, 1704, 1463, 1377, 1238, 1166, 1133, 1088, 1040, 1007, 784; Major Product **21**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.61 (dd, *J* = 10.4, 2.8 Hz, 1H), 6.06 (d, *J* = 10.4 Hz, 1H), 5.32 (dd, *J* = 2.8, 1.2 Hz, 1H), 5.28 (d, *J* = 2.8 Hz, 1H), 5.08 (dd, *J* = 10.4, 9.6 Hz, 1H), 4.74 (d, *J* = 1.6 Hz, 1H), 4.52 (q, *J* = 6.4 Hz, 1H), 4.24 (dd, *J* = 9.6, 2.8 Hz, 1H), 4.14 (s, 2H), 3.84 (dq, *J* = 9.6, 6.4 Hz, 1H), 3.68 (ddd, *J* = 9.6, 7.2, 6.8 Hz, 1H), 3.47 (ddd, *J* = 9.6, 7.2, 6.8 Hz, 1H), 2.34 (m, 2H), 1.65 (m, 4H), 1.37-1.19 (m, 20H), 0.90 (brs, 3H), 0.88 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.5, 172.8, 167.2, 141.9, 127.9, 97.1, 95.5, 75.5, 73.8, 72.6, 70.8, 68.6, 66.7, 41.0, 34.5, 31.5, 29.9, 29.5, 29.4, 26.3, 24.9, 22.9, 22.5, 17.7, 15.1, 14.3, 14.1; HRMS–MALDI–TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{28}H_{45}O_9Cl + Na]^+$: 583.2644, Found: 583.2642.

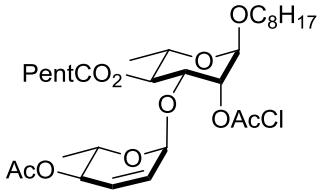
*(A MnO_2 oxidation was performed on compound **12** to provide pure enone **21**, which was fully characterized and the data is mentioned above in the supporting information). The assignment of the C-3 glycosylation was confirmed by using chloroacylation which in addition to serving as a protecting group, is also used to assign regioselectivity. The ^{1}H NMR for the chloroacylated major product **21** has a signal for the C-2 position (assigned by coupling constants, dd, J = 2.8, 1.2 Hz, 1H) that has moved downfield (5.32 ppm (**21**) from 4.05 ppm (**19**)) from the starting material (i.e., C-2 position of compound **19**). Further proof of the regioselectivity is provided by the conversion of **19** into the natural products, Mezzettiasides **2-11**).*

1-Octyloxy-2,3-didehydro-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (12):



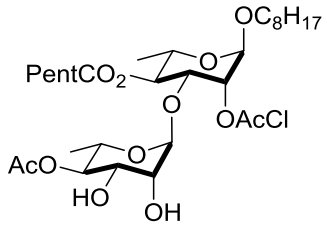
To a solution of enone **21** and its regioisomer (80 mg, 0.14 mmol) in CH_2Cl_2 (1.4 mL) at –78 ºC was added $CeCl_3$/MeOH solution (0.4 M in MeOH, 0.3 mL) and $NaBH_4$ (6.7 mg, 0.17 mmol). The reaction mixture was stirred at –78 ºC for 2 h and quenched with 2 mL of saturated aqueous $NaHCO_3$ solution, extracted with Et_2O (2 x 50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 18-20% EtOAc/hexane to give allylic alcohol **12** (68 mg, 0.12 mmol, 85%), the desired product was obtained in the pure form at this step; R_f (30% EtOAc/hexane) = 0.4; $[\alpha]^{25}_D$ = – 28.5 (*c* = 1.0, CH_2Cl_2); IR (thin film, cm^{-1}) 3454, 2928, 2859, 1744, 1275, 1260, 746; ^{1}H NMR (400 MHz, $CDCl_3$)) δ 5.91 (d, *J* = 10.4 Hz, 1H), 5.56 (ddd, *J* = 9.6, 6.6, 6.4 Hz, 1H), 5.26 (d, *J* = 3.2, 1.6 Hz, 1H), 5.02 (dd, *J* = 10.4, 9.6 Hz, 2H), 4.72 (d, *J* = 1.6 Hz, 1H), 4.19 (d, *J* = 5.2 Hz, 2H), 4.14 (dd, *J* = 9.6, 2.8 Hz, 1H), 3.82 (dq, *J* = 9.6, 6.4 Hz, 2H), 3.69 (ddd, *J* = 9.6, 7.2, 6.8 Hz, 1H), 3.63 (m, 1H), 3.46 (ddd, *J* = 9.6, 7.2, 6.8 Hz, 1H), 2.33 (m, 2H), 1.65 (m, 4H), 1.37-1.25 (m, 19H), 1.19 (d, *J* = 6.4 Hz, 3H), 0.90 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 167.4, 134.3, 125.8, 97.2, 96.7, 74.8, 74.6, 72.7, 69.7, 68.54, 68.54, 66.8, 41.2, 34.5, 32.1, 31.5, 29.6, 29.5, 26.3, 24.9, 22.90, 22.5, 18.0, 17.7, 14.4, 14.1; HRMS–MALDI–TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{28}H_{47}O_9Cl + Na]^+$: 585.2801, Found: 585.2830.

1-Octyloxy-2,3-didehydro-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (12a):



To a solution of allylic alcohol **12** (75 mg, 0.13 mmol) in pyridine (22 μL, 0.27 mmol) at 0 ºC was added acetic anhydride (25.2 μL, 0.27 mmol) and a catalytic amount of 4-dimethylaminopyridine (2.0 mg, 10 mol%). After being stirred for 2 h, the mixture was diluted with ether, washed with dil. HCl solution (1 mL) and the solvent was evaporated under reduced pressure. The crude product was purified by silica gel flash chromatography eluting with 5-7% EtOAc/hexane to give acetate **12a** (73 mg, 0.12 mmol, 91%) as oil: R_f (20% EtOAc/hexane) = 0.8; $[\alpha]^{25}_D = -28$ (*c* = 1.06, CH_2Cl_2); IR (thin film, cm^{-1}) 3591, 2928, 2857, 1746, 1376, 1234, 1165, 1133, 1083, 1039, 1001; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (d, *J* = 9.6 Hz, 1H), 5.61 (dd, *J* = 10.4, 2.0 Hz, 1H), 5.26 (d, *J* = 1.2 Hz, 1H), 5.04 (br, 1H), 5.02 (dd, *J* = 9.6, 9.6 Hz, 1H), 5.01 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.72 (s, 1H), 4.21 (d, *J* = 6.4 Hz, 2H), 4.15 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.83 (dq, *J* = 9.6, 6.4 Hz, 2H), 3.68 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 3.45 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 2.33 (m, 2H), 2.08 (s, 3H) 1.65 (m, 4H), 1.32-1.25 (m, 14H), 1.20 (d, *J* = 6.4 Hz, 3H), 1.19 (d, *J* = 6.4 Hz, 3H), 0.91 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 170.8, 167.3, 130.8, 126.8, 97.2, 96.8, 75.1, 74.5, 72.6, 70.8, 68.5, 66.7, 65.4, 41.2, 34.5, 32.0, 31.5, 29.5, 29.4, 26.3, 24.9, 22.9, 22.5, 21.3, 17.97, 17.69, 14.3, 14.0; HRMS (ESI) calcd for $[C_{30}H_{49}O_{10}Cl + Na]^+$: 627.2912, Found: 627.2918.

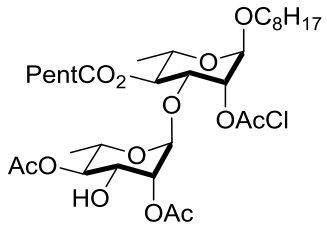
1-Octyloxy-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (12b):



To a stirred solution of acetate **12a** (70 mg, 0.12 mmol) in *t*-butanol/acetone (1:1, 0.6 mL) at 0 ºC was added a solution of *N*-methyl morpholine *N*-oxide/water (50% w/v) (50 μL) and OsO_4 (1.5 mg, 5 mol%). The reaction mixture was stirred at rt for 8 h and then concentrated. The crude product was purified using silica gel chromatography, eluting with 22-25% EtOAc/hexane. Pure fractions were combined and concentrated to afford desired diol **12b** (65.1 mg, 0.10 mmol, 88%); R_f (10% MeOH/CH_2Cl_2) = 0.45; $[\alpha]^{25}_D = -26.7$ (*c* = 2.4, CH_2Cl_2); IR (thin film, cm^{-1})

3493, 3394, 2955, 2928, 2858, 1742, 1454, 1376, 1235, 1164, 1132, 1084, 1036; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.19 (br, 1H), 5.06 (dd, *J* = 10.4, 10.4 Hz, 1H), 4.93 (s, 1H), 4.76 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.72 (s, 1H), 4.17 (s, 2H), 4.15 (dd, *J* = 9.6, 2.4 Hz, 1H), 3.80 (m, 3H), 3.67 (ddd, *J* = 9.6, 6.8, 6,8 Hz, 1H), 3.44 (ddd, *J* = 9.6, 6.8, 6,8 Hz, 1H), 2.31 (m, 2H), 2.13 (s, 3H), 1.62 (m, 4H), 1.30-1.24 (m, 14H), 1.19 (d, *J* = 5.6 Hz, 3H), 1.17 (d, *J* = 5.6 Hz, 3H), 0.90 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 172.7, 167.2, 101.4, 97.0, 75.5, 74.7, 73.8, 72.7, 71.1, 70.1, 68.6, 66.7, 66.6, 41.0, 34.5, 32.0, 31.5, 29.5, 29.4, 26.3, 24.8, 22.9, 22.5, 21.3, 17.6, 17.5, 14.3, 14.1; HRMS–MALDI-TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{30}H_{51}O_{12}Cl + Na]^+$: 661.2961, Found: 661.2994.

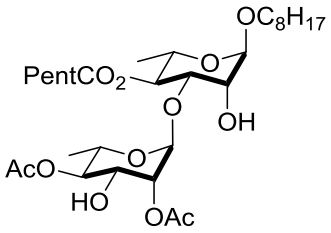
1-Octyloxy-2,4-*O*-diacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (22):



To a solution of diol **12b** (60mg, 0.09 mmol) in CH_2Cl_2 (0.45 mL) at 0 ºC was added triethylorthoacetate (51μL, 0.28 mmol) and *p*-TsOH·H_2O (3.0 mg). The reaction was stirred at 0 ºC for 1 h and then acetic acid (aq) (90%, 0.2 mL) was added, stirred for another 20 min. The reaction mixture was diluted with 10 mL EtOAc and washed with saturated aqueous $NaHCO_3$ solution, extracted with EtOAc (2 x 10 mL), dried Na_2SO_4, and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 20-22% EtOAc/hexane to give C-2 acetate **22** (54.5 mg, 0.08 mmol, 85%) as a thick oily liquid: R_f (20% EtOAc/hexane) = 0.8; $[\alpha]^{25}_D$ = – 30.8 (*c* = 2.3, CH_2Cl_2); IR (thin film, cm^{-1}) 3476, 2956, 2931, 2958, 1744, 1453, 1375, 1237, 1228, 1163, 1134, 1087, 1042, 986; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.16 (dd, *J* = 2.8, 1.2Hz, 1H), 5.07 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.91 (s, 1H) 4.85 (dd, *J* = 3.6, 1.2 Hz, 1H), 4.83 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.72 (s, 1H), 4.18 (d, 2H), 4.10 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.88 (dd, *J* = 10.4, 3.2 Hz, 1H), 3.79 (dq, *J* = 10.4, 6.0 Hz, 2H) 3.64 (ddd, *J* = 9.6, 6.4, 6.4 Hz, 1H), 3.42 (ddd, *J* = 9.6, 6.4, 6.4 Hz, 1H), 2.45 (m, 1H), 2.35 (m, 1H), 2.12 (s, 6H), 1.64

(m, 4H), 1.32-1.28 (m, 14H), 1.17 (m, 6H), 0.90 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 171.8, 170.4, 167.2, 99.4, 96.9, 75.4, 74.5, 73.7, 72.9, 72.1, 68.5, 68.2, 66.9, 66.8, 40.9, 34.1, 32.0, 31.47, 29.5, 29.4, 26.2, 24.7, 22.8, 22.5, 21.2, 21.1, 17.6, 17.4, 14.3, 14.1; HRMS (ESI) calcd for $[C_{32}H_{53}O_{13}Cl + H]^+$: 681.3253, Found: 681.3248.

Mezzettiaside-10 (10):

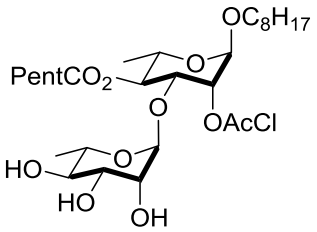


To a solution of diacetate alcohol **22** (30 mg, 0.04 mmol) in THF (0.4 mL) was added thiourea (21 mg, 0.264 mmol), $NaHCO_3$ (13 mg, 0.15 mmol) and *n*-Bu_4NI (8.2 mg, 0.02 mmol). The reaction mixture was stirred at 60 ºC for 3 h. The reaction solution was pipetted directly on to a silica gel column and eluted with 30-35% EtOAc/hexane to afford Mezzettiaside**-10** (**10**) (23 mg, 0.04 mmol, 86%) as a gum; R_f(50% EtOAc/hexane) = 0.3; $[\alpha]^{25}_D$ = – 48.1 (*c* = 0.10, $CHCl_3$); IR (thin film, cm^{-1}) 3515, 2922, 1740, 1378, 1325, 1266,845, 829, 721; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.07 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.94 (s, 1H), 4.91 (d, *J* = 1.6 Hz, 1H), 4.88 (dd, *J* = 9.6 9.6 Hz, 1H), 4.76 (s, 1H), 4.04 (dd, *J* = 9.6, 3.6 Hz, 1H), 3.96 (m, 3H), 3.77 (dq, *J* = 9.6, 6.0 Hz, 1H), 3.66 (ddd, *J* = 10.4, 6.8, 6.8 Hz, 1H), 3.41 (ddd, *J* = 10.4, 6.4, 6.4 Hz, 1H), 2.44 (m, 1H), 2.36 (m, 1H), 2.13 (s, 3H), 2.12 (s, 3H), 1.65 (m, 4H), 1.32-1.27 (m, 14H), 1.21 (d, *J* = 6.0 Hz, 3H), 1.18 (d, *J* = 6.0 Hz, 3H), 0.93 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 171.6, 170.5, 99.4, 99.2, 78.5, 74.5, 73.0, 72.0, 71.2, 68.3, 68.2, 67.0, 66.4, 34.3, 32.0, 31.5, 29.6, 29.5, 29.4, 26.3, 24.8, 22.9, 22.5, 21.20, 21.17, 17.6, 17.6, 14.3, 14.1; HRMS–MALDI–TOF (CCA) (m/z): [M + Na]$^+$ calcd for $[C_{30}H_{52}O_{12} + Na]^+$: 627.3351, Found: 627.3378.

NMR Data: ^{1}H NMR (400 MHz, C_6D_6 + CD_3OD (4:1)) δ 5.46 (dd, *J* = 10.4 Hz, 1H), 5.27 (dd, *J* = 10.0, 10.0 Hz, 1H), 5.21 (dd, *J* = 1.6 Hz, 1H), 5.01 (s, 1H), 4.86 (s, 1H), 4.40 (dd, *J* = 9.6, 3.6 Hz, 1H), 4.21 (m, 3H), 3.94 (dq, *J* = 10.6, 6.4 Hz, 1H), 3.62 (ddd, *J* = 9.6, 7.6, 7.8 Hz, 1H), 3.28 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 2.59 (m, 1H), 2.37 (m, 1H), 1.88 (s, 3H), 1.83 (s, 3H), 1.27 (m, 24H), 0.85 (m, 6H); ^{13}C NMR (100 MHz, C_6D_6 +CD_3OD (4:1)) δ 174.1, 171.3, 170.9, 100.6,

[1]100.2, 78.4, 74.6, 73.4, 73.0, 71.5, 68.2, 67.4 (2C), 67.2, 34.4, 32.2, 31.7, 29.8, 29.7, 29.6, 26.5, 24.9, 23.0, 22.7, 20.6, 20.4, 17.67, 17.51, 14.2, 14.0.

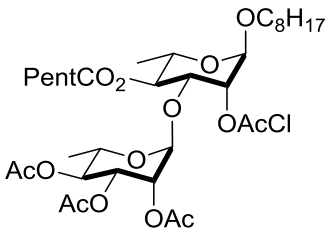
1-Octyloxy-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (12c):



To a stirred solution of allylic alcohol **12** (50 mg, 0.08 mmol) in *t*-butanol/acetone (1:1, 0.8 mL) at 0 ºC was added a solution of *N*-methyl morpholine *N*-oxide/water (50% w/v) (45 μL) and OsO_4 (1.2 mg, 5 mol%). The reaction mixture was stirred at rt for 12 h and then concentrated. The residue was pipetted directly on to a silica gel column and the product was eluted with 2-3 % MeOH/ CH_2Cl_2. Pure fractions were combined and concentrated to afford triol **12c** (42.5 mg, 0.07 mmol, 86%); R_f (10% MeOH/ CH_2Cl_2) = 0.45; $[\alpha]^{25}_D$ = – 32.4 (*c* = 2.1, CH_2Cl_2); IR (thin film, cm^{-1}) 3464, 3414, 2956, 2929, 2858, 1748, 1457, 1378, 1167, 1134, 1087, 1044, 987, 818; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.21 (br, 1H), 5.04 (dd, *J* = 10.4, 10.4 Hz, 1H), 4.87 (s, 1H), 4.72 (s, 1H), 4.26 (d, *J* = 11.6 Hz, 2H), 4.15 (dd, *J* = 10.4, 3.6 Hz, 1H), 3.81 (m, 2H), 3.67 (m, 3H), 3.44 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 2H), 2.33 (m, 2H), 1.62 (m, 4H), 1.37-1.25 (m, 17H), 1.17 (d, *J* = 6.4 Hz, 3H), 0.90 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 167.6, 101.7, 97.2, 74.2, 74.0, 73.4, 73.0, 71.6, 71.3, 69.3, 68.7, 66.7, 41.2, 34.7, 32.15, 31.6, 29.64, 29.55, 26.4, 25.0, 23.0, 22.6, 17.72, 17.70, 14.4, 14.2; HRMS–MALDI–TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{28}H_{49}O_{11}Cl + Na]^+$: 619.2856, Found: 619.2852.

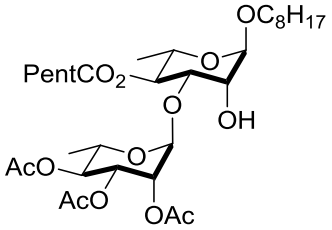
[1] Optical rotation for the isolated **Mezzettiaside-10**: $[\alpha]_D$ = – 54.4 (*c* = 0.10, $CHCl_3$) (Ref. 2).

1-Octyloxy-2,3,4-*O*-triacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (12d):



To a solution of triol **12c** (30 mg, 0.05 mmol) in CH_2Cl_2 (0.5 mL) was added pyridine (24.3 μL, 0.30 mmol) and acetic anhydride (19 μL, 0.20 mmol) at 0 ºC followed by addition of DMAP (0.7 mg, 10 mol%). Reaction was continued to stir for 3 h. Monitored by TLC and diluted with ether, quenched with dil. HCl (1 mL, 0.5N), dried over Na_2SO_4 and the crude product was purified using column chromatography eluting with 15-20% EtOAc/hexane to give triacetate product **12d** (34.2 mg, 0.05 mmol, 94%): R_f (30% EtOAc/hexane) = 0.8; $[\alpha]^{25}_D$ = – 17.8 (*c* = 2.3, CH_2Cl_2); IR (thin film, cm^{-1}) 2956, 2925, 2855, 1749, 1453, 1372, 1228, 1087, 1047, 749 ; ^1H NMR (400 MHz, $CDCl_3$) δ 5.20 (dd, *J* = 4.0, 2.4 Hz, 1H), 5.14 (dd, *J* = 9.6, 3.2 Hz, 1H), 5.09 (dd, *J* = 10.4, 10.4 Hz, 1H), 5.04 (dd, *J* = 9.6, 9.6 Hz, 1H), 5.01 (dd, *J* = 2.8, 1.2 Hz, 1H), 4.86 (s, 1H), 4.72 (s, 1H), 4.27 (dd, *J* = 15.6, 9.6 Hz, 2H), 4.14 (dd, *J* = 9.6, 3.6 Hz, 1H), 3.88 (dq, *J* = 9.6, 6.4 Hz, 1H), 3.78 (dq, *J* = 9.6, 6.2 Hz, 1H), 3.68 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 3.43 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 2.43 (m, 2H), 2.10 (s, 3H), 2.03 (s, 3H), 1.95 (s, 3H), 1.63 (m, 4H), 1.28 (m, 14H), 1.18 (m, 6H), 0.90 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 170.3, 170.1, 169.7, 167.4, 99.2, 96.9, 75.0, 73.4, 72.2, 70.9, 70.2, 68.6, 68.4, 67.5, 66.8, 41.0, 34.2, 32.0, 31.5, 29.5, 29.4, 26.2, 24.7, 22.8, 22.4, 21.0, 20.8, 17.6, 17.5, 14.3, 14.1; HRMS–MALDI–TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{34}H_{55}O_{14}Cl + Na]^+$: 745.3173, Found: 745.3188.

Mezzettiaside-11 (**11**)**:**



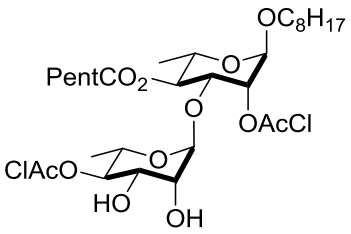
To a solution of the triacetate **12d** (20 mg, 0.028 mmol) in THF (0.28 mL) was added thiourea (6.4 mg, 0.083mmol), $NaHCO_3$ (9.3 mg, 0.11 mmol) and *n*-Bu_4NI (2.01 mg, 0.006 mmol). The reaction mixture was stirred at 60 ºC for 4 h. The reaction mixture was pipetted directly to a silica gel column and eluted with 20-25% EtOAc/hexane to afford Mezzettiaside-**11** (**11**) (14.7 mg, 0.023 mmol, 82%) as a gum: R_f (40% EtOAc/hexane) = 0.4; $[\alpha]^{25}_D$ = – 54.2 (c = 0.1, $CHCl_3$); IR (thin film, cm^{-1}) 3490, 2952, 2927, 1752, 1371, 1258, 1226, 1137, 1077, 764, 750; ^1H NMR (400 MHz, $CDCl_3$) δ 5.26 (dd, J = 10.4, 2.6 Hz, 1H), 5.10 (dd, J = 3.6, 1.6 Hz, 1H), 5.08 (dd, J = 10.4, 10.4 Hz, 1H), 5.05 (dd, J = 10.4, 10.4 Hz, 1H), 4.91 (s, 1H), 4.77 (s, 1H), 4.06 (dd, J = 9.6, 2.6 Hz, 1H), 3.96 (m, 2H), 3.78 (dq, J = 9.6, 6.4 Hz, 1H), 3.65 (ddd, J = 10.4, 7.2, 7.2 Hz, 1H), 3.42 (ddd, J = 10.4, 7.2, 7.2 Hz, 1H), 2.43 (m, 1H), 2.33 (m, 1H), 2.13 (s, 3H), 2.04 (s, 3H), 1.98 (s, 3H), 1.65 (m, 4H), 1.30-1.25 (m, 14H), 1.22 (d, J = 6.0 Hz, 3H), 1.19 (d, J = 5.6 Hz, 3H), 0.88 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 170.3, 170.1, 169.8, 99.3, 98.9, 78.3, 71.9, 71.2, 71.0, 70.2, 68.9, 68.2, 67.4, 66.6, 34.3, 32.0, 31.5, 29.59, 29.54, 29.45, 26.3, 24.7, 22.9, 22.5, 21.1, 21.0, 20.9, 17.7, 17.6, 14.3, 14.1; HRMS–MALDI–TOF (CCA) (m/z): [M + Na]$^+$ calcd for $[C_{32}H_{54}O_{13} + Na]^+$: 669.3457, Found: 669.3454.

NMR Data:^1H NMR (400 MHz, C_6D_6 + CD_3OD (4:1)) δ 5.65 (dd, J = 10.4, 2.8 Hz, 1H), 5.53 (dd, J = 10.4, 10.4 Hz, 1H), 5.40 (t, J = 9.6, 9.6 Hz, 1H), 5.38 (m, 1H), 4.96 (s, 1H), 4.89 (s, 1H), 4.37 (dq, J = 8.8, 6.4 Hz, 1H), 4.19 (m, 2H), 3.95 (dq, J = 9.6, 6.0 Hz, 1H), 3.63 (m, 1H), 3.29 (m, 1H), 2.51 (m, 1H), 2.33 (m, 1H), 1.72 (s, 3H), 1.68 (s, 6H), 1.50 (m, 2H), 1.30-1.20 (m, 22H), 0.88 (m, 6H); ^{13}C NMR (100 MHz, C_6D_6 + CD_3OD (4:1)) δ 173.7, 170.3, 170.29, 100.6, 99.8, 78.9, 72.7, 71.6, 71.3, 70.8, 69.6, 68.2, 67.5, 67.3, 34.4, 32.2, 31.7, 29.8, 29.7, 29.7, 26.6, 24.9, 23.0, 22.6, 20.23 (2C), 20.2, 17.7, 17.4, 14.2, 14.0.

[2]

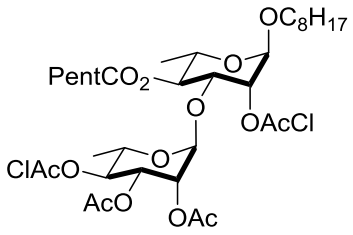
[2] Optical rotation for the isolated **Mezzettiaside-11**: $[\alpha]_D$ = – 48.6 (c = 0.10, $CHCl_3$) (Ref. 2).

1-Octyloxy-4-*O*-chloroacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (12e):



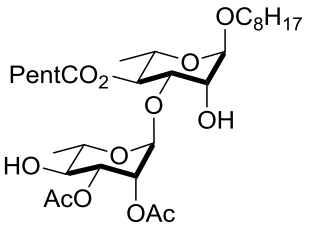
To a stirred solution of allylic alcohol **12** (80 mg, 0.14 mmol) in pyridine (40 μL) was added chloroacetic anhydride (73 mg, 0.43 mmol) and 4-dimethylaminopyridine (1.8 mg, 10 mol%). After stirring for 1 h, the mixture was diluted with ether, quenched with dil. HCl solution and the solvent was evaporated under reduced pressure. The crude product was directly used for carrying out dihydroxylation reaction. To a stirred solution of di-chloroacetate (74 mg, 0.12 mmol) in *t*-butanol/acetone (1:1, 1.1 mL) at 0 ºC was added a solution of *N*-methyl morpholine *N*-oxide/water (50% w/v) (115 μL) and OsO_4 (1.5 mg, 5 mol%). The reaction mixture was stirred at rt for 10 h and then concentrated under reduced pressure. The crude product was subjected to column chromatography with 22-25% EtOAc/hexane elution. Pure fractions were combined and concentrated to afford desired diol **12e** (73.7 mg, 0.11 mmol, 77%); $[\alpha]^{25}_{D}$ = – 48.4 (*c* = 0.32, CH_2Cl_2); IR (thin film, cm^{-1}) 3413, 2956, 2928, 2858, 1748, 1277, 1168, 1135, 1087, 1029, 764, 749; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.20 (dd, *J* = 2.8, 1.2 Hz, 1H), 5.06 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.93 (s, 1H), 4.87 (dd, *J* = 10.4, 10.4 Hz, 1H), 4.72 (s, 1H), 4.16 (s, 2H), 4.13 (d, *J* = 1.6 Hz, 2H), 3.82 (m, 5H), 3.67 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 3.45 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 2.33 (dd, *J* = 7.6, 7.2 Hz, 2H), 1.64 (m, 4H), 1.31-1.25 (m, 14H), 1.21 (m, 6H), 0.91 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 168.3, 167.2, 101.4, 97.0, 76.8, 74.8, 73.7, 72.7, 71.2, 69.8, 68.6, 66.6, 66.5, 41.0, 41.0, 34.5, 32.0, 31.5, 31.2, 29.5, 29.4, 26.3, 24.8, 22.9, 22.5, 17.6, 17.5, 14.3, 14.1; HRMS–MALDI–TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{30}H_{50}O_{12}Cl_2 + Na]^+$: 695.2572, Found: 695.2589.

1-Octyloxy-2,3-O-diacetyl-4-*O*-chloroacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (12f):



To a solution of diol **12e** (60 mg, 0.089 mmol) in pyridine (0.1 mL) at 0 ºC was added acetic anhydride (34 μL) and a catalytic amount of 4-dimethylaminopyridine (1.2 mg, 10 mol%). After stirring for 3 h the mixture was diluted with ether, washed with 1N dil. HCl solution (0.5 mL) and the solvent was evaporated. The crude product was purified by silica gel flash chromatography eluting with 12-14% EtOAc/hexane to give diacetate **12f** (63.9 mg, 0.084 mmol, 95%) as oil: R_f (20% EtOAc/hexane) = 0.6; $[\alpha]^{25}_D$ = – 45.6 (*c* = 0.9, CH_2Cl_2); IR (thin film, cm^{-1}) 2956, 2930, 2858, 1751, 1371, 1280, 1239, 1164, 1137, 1088, 1045, 749; ^1H NMR (400 MHz, $CDCl_3$) δ 5.22 (d, *J* = 1.6 Hz, 1H), 5.18 (dd, *J* = 9.6, 2.8 Hz, 1H), 5.10-5.04 (m, 3H), 4.89 (s, 1H), 4.73 (s, 1H), 4.23 (dd, *J* = 10.4, 2.0 Hz, 2H), 4.14 (dd, *J* = 9.6, 2.8 Hz, 1H), 4.03 (s, 2H), 3.94 (dq, *J* = 9.6, 6.4 Hz, 1H), 3.79 (dq, *J* = 9.6, 6.4 Hz, 1H), 3.67 (ddd, *J* = 9.6, 6.4, 6.4 Hz, 1H), 3.44 (ddd, *J* = 9.6, 6.4, 6.4 Hz, 1H), 2.42 (m, 2H), 2.13 (d, *J* = 2.0 Hz, 3H), 1.97 (d, *J* = 2.0 Hz, 3H), 1.61 (m, 4H), 1.30 (m,14H), 1.21 (d, *J* = 6.0 Hz, 3H), 1.91 (d, *J* = 6.0 Hz, 3H), 0.88 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 170.1, 169.8, 167.5, 167.0, 99.1, 97.0, 75.2, 73.4, 72.9, 72.2, 70.2, 68.5, 68.4, 67.1, 66.8, 41.0, 40.8, 34.2, 32.0, 31.5, 29.5, 29.5, 29.4, 26.3, 24.7, 22.9, 22.5, 21.0, 20.9, 17.6, 17.5, 14.3, 14.1; HRMS (ESI) calcd for $[C_{34}H_{54}O_{14}Cl_2 + H]^+$: 757.2969, Found: 757.3000.

Mezzettiaside-9 (9):

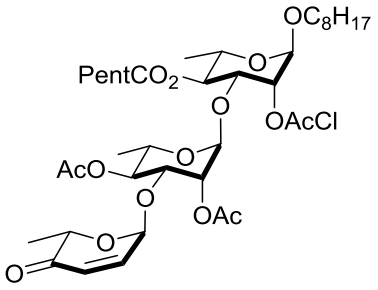


To a solution of diacetate **12f** (25 mg, 0.033 mmol) in THF (0.3 mL) was added thiourea (31 mg, 0.40 mmol), $NaHCO_3$ (17 mg, 0.20 mmol) and *n*-Bu_4NI (12.2 mg, 0.03mmol). The reaction mixture was stirred at 60 ºC for 3 h and then mixture was pipetted directly on to a silica gel column, eluting with 25-35% EtOAc/hexane to afford product Mezzettiaside-**9 (9)** (17.4 mg, 0.03 mmol, 87%) as a gummy oil: R_f(50% EtOAc/hexane) = 0.4; $[\alpha]^{25}_D = -47$ (*c* = 1.0, $CHCl_3$); IR (thin film, cm^{-1}) 3477, 2925, 2859, 1745, 1377, 1275, 1260, 1232, 1138, 1076, 1051, 764, 750; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.15 (dd, *J* = 10.0, 1.2 Hz, 1H), 5.10 (dd, *J* = 9.6, 9.6 Hz, 1H), 5.02 (dd, *J* = 2.8, 1.2 Hz, 1H), 4.87 (s, 1H), 4.78 (s, 1H), 3.98 (m, 1H), 3.93 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.90 (dq, *J* = 9.6, 6.4 Hz, 1H), 3.77 (dq, *J* = 9.6, 6.4 Hz, 1H), 3.67 (m, 2H), 3.43 (ddd, *J* = 8.8, 6.8, 6.8 Hz, 1H), 2.45 (m, 1H), 2.34 (m, 1H), 2.11 (s, 3H), 2.08 (s, 3H), 1.62 (m, 4H), 1.37-125 (m, 17H), 1.18 (d, *J* = 6.0 Hz, 3H), 0.90 (m, 6H); ^{13}CNMR(400MHz, $CDCl_3$) δ 173.3, 171.6, 170.1, 99.4, 99.1, 78.1, 72.1, 72.0, 71.6, 71.0, 70.5, 69.7, 68.1, 66.5, 34.3, 32.0, 31.5, 29.6, 29.6, 29.5, 26.3, 24.8, 22.9, 22.5, 21.1, 21.1, 17.8, 17.7, 14.3, 14.1; HRMS–MALDI–TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{30}H_{52}O_{12} + Na]^+$: 627.3351, Found: 627.3387. NMR Data: ^{1}H NMR (400 MHz, C_6D_6 + CD_3OD (4:1)) δ 5.52 (dd, *J* = 9.6, 2.8 Hz, 1H), 5.50 (dd, *J* = 10.4, 10.4 Hz, 1H), 5.36 (d, *J* = 2.4 Hz, 1H), 5.00 (s, 1H), 4.88 (s, 1H), 4.21 (m, 4H), 3.93 (m, 1H), 3.83 (dd, *J* = 9.6, 9.6 Hz, 1H), 3.61 (m, 1H), 2.51 (m, 2H), 1.83 (s, 3H), 1.73 (s, 3H), 1.47 (d, *J* = 6.0 Hz, 6H), 1.29 (m, 18H), 0.87 (m, 6H); ^{13}C NMR (100 MHz, C_6D_6 + CD_3OD (4:1)) δ 173.7, 171.1, 170.3, 100.6, 100.0, 78.4, 72.9, 71.9, 71.4, 71.3, 71.1, 69.9, 68.2, 67.3, 34.4, 32.2, 31.6, 29.8, 29.7, 29.7, 26.6, 24.9, 23.1, 22.7, 20.5, 20.3, 17.8, 17.7, 14.2, 14.0.

3

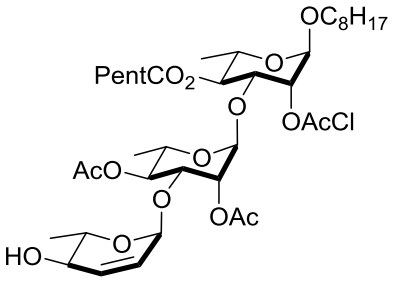
[3] Optical rotation for the isolated **Mezzettiaside-9**: $[\alpha]_D = -56.4$ (*c* = 0.10, $CHCl_3$) (Ref. 2).

1-Octyloxy-2,3-didehydro-5-methyl-4-oxopyranosyl-(1→3)-2,4-*O*-diacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (13):



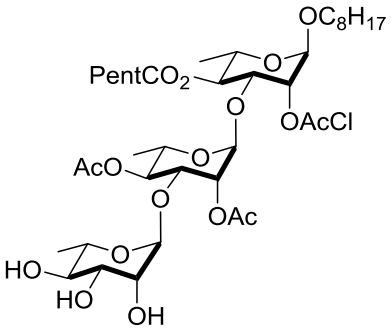
To a stirred solution of alcohol **22** (250 mg, 0.37 mmol) in CH_2Cl_2 (1.8 mL, 0.2M) at 0 ºC was added Boc-pyranone **14** (251.3 mg, 1.10 mmol) followed by addition of $Pd_2(dba)_3$•$CHCl_3$ (10.0 mg, 2.5 mol%) and PPh_3 (10.2 mg, 10 mol%) solution in CH_2Cl_2. The reaction was stirred and warmed from 0 ºC to rt. After 5 h, reaction was quenched by 10 mL saturated $NaHCO_3$ solution, followed by extraction with Et_2O (3 x 300 mL). The organic layers were combined, washed with 5 mL saturated brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 15-18% EtOAc/hexane to give trisaccharide enone **13** (198 mg, 0.25 mmol, 68%): R_f (30% EtOAc/hexane) = 0.8; $[\alpha]^{25}_D$ = – 34.4 (*c* = 0.3, CH_2Cl_2); IR (thin film, cm^{-1}) 3487, 2927, 2856, 1792, 1746, 1457, 1375, 1239, 1135, 1088, 1045, 987; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (dd, *J* = 10.4, 3.6 Hz, 1H), 6.05 (d, *J* = 10.4 Hz, 1H), 5.24 (d, *J* = 3.6 Hz, 1H), 5.20 (d, *J* = 1.2 Hz, 1H), 5.09 (m, 2H), 5.04 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.87 (s, 1H), 4.72 (s, 1H), 4.41 (q, *J* = 6.8 Hz, 1H), 4.21 (d, *J* = 8.0 Hz, 2H), 4.12 (dd, *J* = 10.4, 3.6 Hz, 1H), 4.09 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.81 (dq, *J* = 9.6, 5.6 Hz, 2H), 3.67 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 3.43 (ddd, *J* = 9.6, 5.6, 5.6 Hz, 1H), 2.45 (m, 1H), 2.35 (m, 1H), 2.09 (s, 6H), 1.64 (m, 4H), 1.33-1.16 (m, 17H), 1.19 (m, 6H), 0.89 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.7, 173.2, 170.4, 170.1, 167.3, 142.2, 127.8, 99.4, 97.0, 95.5, 75.5, 75.4, 73.6, 72.4, 72.1, 71.9, 70.8, 68.5, 67.6, 66.7, 41.0, 34.2, 32.0, 31.5, 29.5, 29.4, 26.3, 24.7, 22.9, 22.5, 21.2, 21.1, 17.59, 17.57, 15.0, 14.3, 14.1; HRMS (ESI) calcd for $[C_{38}H_{59}O_{15}Cl + H]^+$: 791.3621, Found: 791.3656.

1-Octyloxy-2,3-didehydro-α-L-rhamnopyranosyl-(1→3)-2,4-*O*-diacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (13a):



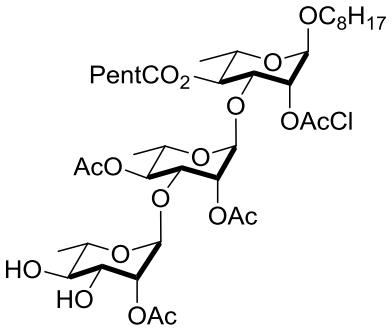
To a solution of trisaccharide enone **13** (150 mg, 0.19 mmol) in CH_2Cl_2 (1.5 mL) at – 78 ºC was added $CeCl_3$/MeOH solution (0.4 M in MeOH, 0.38 mL) and $NaBH_4$ (15 mg, 0.38 mmol). The reaction mixture was stirred at – 78 ºC for 3 h. The reaction mixture was quenched with 3 mL saturated $NaHCO_3$ solution, extracted with Et_2O (3 x 30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified using silica gel chromatography eluting with 22-25% EtOAc/hexane to give trisaccharide allylic alcohol **13a** (131mg, 0.17 mmol, 87%): R_f (30% EtOAc/hexane) = 0.4; $[\alpha]^{25}_D$ = – 36.6 (*c* = 1.8, CH_2Cl_2); IR (thin film, cm^{-1}) 3503, 2929, 2858, 1745, 1375, 1292, 1135, 1088, 1044, 986; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.90 (d, *J* = 10.4 Hz, 1H), 6.05 (ddd, *J* = 10.4, 3.0, 2.4 Hz, 1H), 5.20 (d, *J* = 1.2 Hz, 1H), 5.09 (dd, *J* = 9.6, 9.6 Hz, 1H), 5.02 (d, *J* = 1.2 Hz, 1H), 5.00 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.96 (s, 1H), 4.86 (s, 1H), 4.72 (s, 1H), 4.21 (d, *J* = 9.6 Hz, 2H), 4.11 (dd, *J* = 9.6, 3.2 Hz, 1H), 3.95 (dd, *J* = 10.0, 3.6 Hz, 1H), 3.80 (m, 3H), 3.67 (ddd, *J* = 9.6, 7.2, 7.2 Hz, 1H), 3.56 (dq, *J* = 8.8, 6.0 Hz, 1H), 3.43 (ddd, *J* = 9.6, 6.4, 6.4 Hz, 1H), 2.49-2.28 (m, 2H), 2.11 (s, 3H), 2.07 (s, 3H), 1.64 (m, 4H), 1.32-1.24 (m, 17H), 1.18 (m, 6H), 0.89 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 170.6, 170.2, 167.3, 134.0, 126.0, 99.4, 97.0, 96.7, 75.2, 74.7, 73.7, 72.6, 72.5, 72.1, 69.7, 68.5, 68.4, 67.7, 66.7, 41.0, 34.2, 32.0, 31.5, 29.5, 29.4, 26.3, 24.7, 22.9, 22.5, 21.3, 21.10, 17.8, 17.6, 14.3, 14.1; HRMS–MALDI–TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{38}H_{61}O_{15}Cl + Na]^+$: 815.3591, Found: 815.3575.

1-Octyloxy-α-L-rhamnopyranosyl-(1→3)-2,4-*O*-diacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (13b):



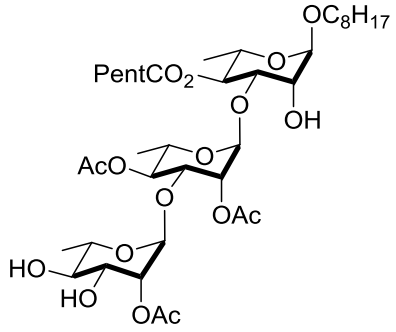
To a solution of allylic alcohol **13a** (120 mg, 0.15 mmol) in *t*-BuOH/acetone (1.5 mL) at 0 ºC was added a solution of (50% w/v) of *N*-methyl morpholine *N*-oxide / water (75 μL) followed by addition of crystalline OsO_4 (2 mg, 5 mol%), stirred for 8 h. The reaction mixture was concentrated and was pipetted directly on to a silica gel column using CH_2Cl_2, the crude product was purified using silica gel column chromatography eluting with 95% EtoAc/hexane to get triol **13b** (113.9 mg, 0.14 mmol, 91%) R_f (10% MeOH/DCM) = 0.55; $[\alpha]^{25}_D$ = – 52.1 (*c* = 1.17, CH_2Cl_2); IR (thin film, cm^{-1}) 3433, 3309, 2930, 2859, 1746, 1375, 1229, 1138, 1088, 1045, 987; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.18 (d, *J* = 2.4 Hz, 1H), 5.06 (dd, *J* = 10.4, 10.4 Hz, 1H), 4.98 (dd, *J* = 10.4, 10.4 Hz, 1H), 4.94 (s, 1H), 4.85 (brs, 1H), 4.82 (s, 1H), 4.71 (s, 1H), 4.26 (d, *J* = 12.4 Hz, 2H), 4.10 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.92 (dd, *J* = 9.6, 3.2 Hz, 1H), 3.78 (m, 3H), 3.66 (dq, *J* = 9.6, 6.4 Hz, 2H), 3.55 (dq, *J* = 8.8, 6.8 Hz, 1H), 3.42 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 2H), 3.31 (brs, 1H), 3.21 (brs, 1H), 2.48-2.34 (m, 2H), 2.11 (s, 3H), 2.08 (s, 3H), 1.63 (m, 4H), 1.29-1.22 (m, 17H), 1.20 (m, 6H), 0.88 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 170.6, 170.5, 167.4, 102.0, 99.4, 97.0, 75.4, 74.8, 73.7, 73.07, 72.6, 72.2, 71.9, 71.6, 71.2, 69.1, 68.5, 67.4, 66.7, 41.0, 34.2, 31.99, 31.47, 31.11, 29.48, 29.38, 26.2, 24.7, 22.82, 22.44, 21.1, 17.58, 17.47, 17.39, 14.2, 14.1; HRMS (ESI) calcd for $[C_{38}H_{63}O_{17}Cl + H]^+$: 827.3832, Found: 827.3837.

1-Octyloxy-2-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-*O*-diacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (13c):



To a solution of triol **13b** (32 mg, 0.04 mmol) in 1.0 mL CH_2Cl_2 was added *p*-TsOH·H_2O (2 mg) and triethylorthoacetate (22 μL, 0.12 mmol) at 0 ºC. After stirring at 0 ºC for 30 min, 0.1 mL 90% AcOH (aq.) was added and the reaction mixture was stirred for another 30 min at 0 ºC. The reaction mixture was diluted with 5 mL EtOAc and washed with 2 mL saturated $NaHCO_3$ solution, followed by washing with 3 mL saturated brine, dried over Na_2SO_4. The combined organic layers were concentrated under reduced pressure to give crude product. The crude product was purified by flash chromatography on silica gel eluting with 50-55% EtOAc/hexane to give diol **13c** (26.6 mg, 0.031 mmol, 79%): R_f (70% EtOAc/hexane) = 0.4; $[\alpha]^{25}_D$ = – 33.7 (*c* = 0.42, CH_2Cl_2); IR (thin film, cm^{-1}) 3462, 2955, 2927, 2858, 1745, 1479, 1376, 1235, 1138, 1046, 978, 749; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.18 (d, *J* = 2.4 Hz, 1H), 5.08 (dd, *J* = 10.4, 10.4 Hz, 1H), 5.03 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.93 (d, *J* = 3.2 Hz, 1H), 4.89 (d, *J* = 2.0 Hz, 1H), 4.85 (s, 1H), 4.84 (s, 1H), 4.72 (s, 1H), 4.20 (d, *J* = 7.2 Hz, 2H), 4.10 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.93 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.78 (dq, *J* = 9.6, 6.0 Hz, 3H), 3.67 (ddd, *J* = 9.6, 6.4, 6.4 Hz, 1H), 3.61 (dd, *J* = 9.6, 2.8 Hz, 1H), 3.44 (ddd, *J* = 9.6, 6.4, 6.4 Hz, 1H), 3.40 (m, 1H), 2.47-2.27 (m, 2H), 2.14 (s, 9H), 1.64 (m, 4H), 1.31-1.25 (m, 17H), 1.19 (m, 6H), 0.91 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 170.71, 170.42, 167.3, 99.57, 99.54, 97.0, 75.6, 74.7, 73.73, 73.48, 72.51, 72.27, 72.14, 71.9, 70.1, 68.98, 68.53, 67.6, 66.7, 41.0, 34.2, 32.0, 31.5, 29.92, 29.5, 29.43, 26.3, 24.7, 22.87, 22.51, 21.17, 21.07, 17.62, 17.51, 17.44, 14.3, 14.1; HRMS (ESI) calcd for $[C_{40}H_{65}O_{18}Cl + H]^+$: 869.3936, Found: 869.3936.

Mezzettiaside-8 (8):



To a stirred solution of diol **13c** (20 mg, 0.023 mmol) in THF (0.1 mL) was added thiourea (10.5 mg, 0.138 mmol), $NaHCO_3$ (6.8 mg, 0.08 mmol) and *n*-Bu_4NI (4.2 mg, 0.01 mmol). The reaction mixture was stirred at 60 ºC for 6 h. The reaction mixture was pipetted directly to a silica gel column and eluted with 65-70% EtOAc/hexane to afford Mezzettiaside-**8** (**8**) (15.5 mg, 0.019 mmol, 85%) as a gum: R_f (100% EtOAc/hexane) = 0.5; $[\alpha]^{25}_D = -40$ (*c* = 0.1, $CHCl_3$); IR (thin film, cm^{-1}) 3454, 2925, 2854, 1741, 1459, 1376, 1264, 1236, 1076, 1046, 736, 704; ^1H NMR (400 MHz, $CDCl_3$) δ 5.06 (dd, *J* = 9.6, 9.6 Hz, 1H), 5.04 (dd, *J* = 10.0, 10.0 Hz, 1H), 4.99 (dd, *J* = 3.2, 2.4 Hz, 1H), 4.88 (s, 3H), 4.76 (s, 1H), 4.06 (dd, *J* = 10.4, 3.6 Hz, 1H), 3.94 (m, 3H), 3.80 (m, 2H), 3.66-3.60 (2H), 3.45 (m, 2H), 2.42 (m, 1H), 2.34 (1H), 2.14 (s, 3H), 2.13 (s, 3H), 2.12 (s, 3H), 1.62 (m, 4H), 1.29 (m, 24H), 1.19 (m, 6H), 0.88 (brs, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 170.8, 170.7, 170.5, 99.5, 99.4 (2C), 78.9, 74.9, 73.4, 72.5,72.4, 71.9, 71.9, 71.2, 69.9, 69.1, 68.2, 67.5, 66.4, 34.3, 32.0, 31.5, 29.9, 29.9, 29.5, 29.4, 26.3, 24.7, 22.9, 22.5, 21.2, 21.0, 17.6, 17.4, 14.3, 14.1; HRMS (ESI) calcd for $[C_{38}H_{64}O_{17} + H]^+$: 793.4222, Found: 793.4253.
(^1H NMR (600 MHz, $CDCl_3$) δ 5.04 (dd, *J* = 9.7, 9.7 Hz, 1H), 5.04 (dd, *J* = 9.7, 9.7 Hz, 1H), 4.98 (dd, *J* = 3.4, 1.8 Hz, 1H), 4.89 (dd, *J* = 3.6, 1.6 Hz, 1H), 4.87 (d, *J* = 1.8 Hz, 1H), 4.87 (d, *J* = 1.6 Hz, 1H), 4.75 (d, *J* = 1.8 Hz, 1H), 4.04 (dd, *J* = 9.7, 3.4 Hz, 1H), 3.94 (dd, *J* = 9.9, 3.3 Hz, 1H), 3.93 (dd, *J* = 3.3, 1.5 Hz, 1H), 3.92 (dq, *J* = 9.7, 6.3 Hz, 1H), 3.78 (dd, *J* = 9.4, 3.5 Hz, 1H), 3.76 (dq, *J* = 9.7, 6.3 Hz,1H), 3.65 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 3.60 (dq, *J* = 9.6, 6.2 Hz, 1H), 3.43 (dd, *J* = 9.6, 9.4 Hz, 1H), 3.40 (ddd, *J* = 10.4, 6.8, 6.8 Hz, 1H), 2.42 (m, 1H), 2.36 (m, 1H), 2.14 (s, 6H), 2.12 (s, 3H), 1.62 (m, 4H), 1.29 (m, 24H), 1.19 (m, 6H), 0.88 (brs, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.0, 170.5, 170.4, 170.2, 99.3, 99.2, 99.2, 78.7, 74.7, 73.3, 72.5, 72.3, 71.9, 71.9, 71.0, 69.8, 69.1, 68.2, 67.3, 66.2, 34.1, 31.8, 31.3, 29.4, 29.3, 29.2, 28.1, 24.5, 22.6, 22.3, 21.0, 20.9, 20.8, 17.4, 17.2, 17.4, 14.1, 14.9.

NMR Data: (^{1}H NMR, CD_3OD + C_6D_6 (6:1)) δ 5.34 (dd, *J* = 9.6, 9.6 Hz, 1H), 5.22 (br, 1H), 5.19 (dd, *J* = 9.6 9.6 Hz, 1H), 5.07 (s, 1H) 4.98 (s, 1H), 4.97 (s, 1H), 4.85 (s, 1H), 4.42 (dd, *J* = 9.6 Hz, 1H), 4.24 (dq, *J* = 8.8, 6.8 Hz, 1H), 4.07 (m, 1H), 4.04 (d, *J* = 9.6 Hz, 1H), 3.94 (dq, *J* = 9.6, 6.0 Hz, 2H), 3.81 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 3.74 (dq, *J* = 8.8, 6.0 Hz, 1H), 3.56 (ddd, *J* = 9.6, 6.4, 6.4 Hz, 1H), 2.67 (m, 1H), 2.51 (m, 1H), 2.25 (s, 3H), 2.19 (s, 3H), 2.18 (s, 3H), 1.76 (m, 4H), 1.41 (m, 17H), 1.31 (brm, 6H), 1.02 (m, 6H); (^{13}C NMR, CD_3OD + C_6D_6 (6:1)) δ 173.9, 171.4, 171.0, 100.6, 100.3, 100.1, 78.7, 75.6, 73.3, 73.04, 72.98, 72.65, 72.57, 71.3, 69.8, 69.4, 68.1, 67.3, 67.1, 34.2, 32.2, 31.6, 30.0, 29.7, 29.6, 26.5, 24.8, 22.9, 22.6, 20.2, 20.1, 20.0, 17.2, 17.0, 13.8, 13.6.

4

[4] Optical rotation for the isolated **Mezzettiaside-8**: $[\alpha]_D$ = – 66.4 (*c* = 0.10, $CHCl_3$) (Ref. 1).

Mezzettiaside-8: Comparison of ^{13}C NMR spectra of isolated vs synthetic material

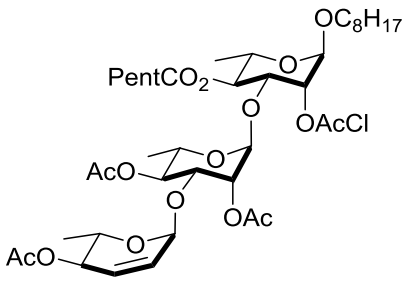
δ/ppm Natural $CD_3OD+C_6D_6$ (6:1)	δ/ppm Synthetic in $CD_3OD+C_6D_6$ (6:1) (100 MHz)	Difference (ppm)	δ/ppm Synthetic $CDCl_3$ (150 MHz)
173.1	174.6	-1.5	173.0
172.1	172.1	0.0	170.5
172.1	172.1	0.0	170.4
171.6	171.7	-0.1	170.2
101.3	101.3	0.0	99.3
101.0	101.1	-0.1	99.2
100.8	100.8	0.0	99.2
79.4	79.5	-0.1	78.7
76.3	76.3	0.0	74.7
74.1	74.1	0.0	73.3
73.8	73.8	0.0	72.5
73.7	73.7	0.0	72.3
73.4	73.4	0.0	71.9
73.3	73.3	0.0	71.9
72.0	72.0	0.0	71.0
70.5	70.5	0.0	69.8
70.1	70.1	0.0	69.1
68.0	68.8	-0.8	68.2
67.9	68.0	-0.1	67.3
67.8	67.8	0.0	66.2
34.1	34.9	-0.8	34.1
31.8	32.9	-1.1	31.8
31.3	32.4	-1.1	31.3
29.3	30.4	-1.1	29.4
29.1	30.4	-1.3	29.3
29.0	30.4	-1.4	29.2
26.1	27.3	-1.2	28.1
24.5	25.5	-1.0	24.5
22.7	23.7	-1.0	22.6
22.3	23.4	-1.1	22.3
21.0	20.9	0.1	21.0
21.0	20.9	0.1	20.9
20.8	20.8	0.0	20.8
17.4	17.9	-0.5	17.4
17.4	17.9	-0.5	17.2
17.2	17.7	-0.5	17.4
14.1	14.5	-0.4	14.1
13.9	14.3	-0.4	14.9

Note:- If we add (+ 0.7 ppm) to the above difference row, then everything falls within the range of +/- 0.8 ppm. We think the difference is due to the solvent ratio of the NMR used for the isolated material.

Mezzettiaside-8: Comparison of ^{1}H NMR spectra of isolated material vs synthetic.

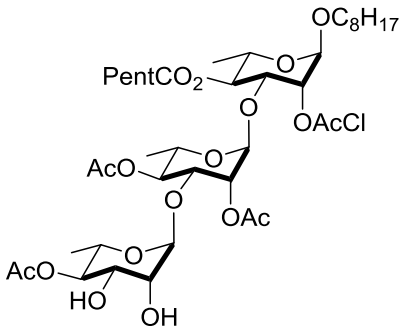
Natural Data δ/J ppm in C_6D_6+CD_3OD (1:6)	Synthetic data (δ/J ppm in C_6D_6+CD_3OD (1:6))	Synthetic data (δ/J ppm in 600 $CDCl_3$)
5.16 t, J = 9.7	5.34 (dd, J = 9.6, 9.6 Hz, 1H)	5.04 (dd, J = 9.7, 9.7 Hz, 1H)
5.05	5.22 (br, 1H)	5.04 (dd, J = 9.7, 9.7 Hz, 1H)
5.04 t, J = 9.9	5.19 (dd, J = 9.6 9.6 Hz, 1H)	4.98 (dd, J = 3.4, 1.8 Hz, 1H)
4.84 brs	5.07 (s, 1H)	4.89 (dd, J = 3.6, 1.6 Hz, 1H)
4.84 brs	4.98 (s, 1H)	4.87 (d, J = 1.8 Hz, 1H)
4.89 dd, J = 3.2, 1.5	4.97 (s, 1H)	4.87 (d, J = 1.6 Hz, 1H)
4.71 brs	4.85 (s, 1H)	4.75 (d, J = 1.8 Hz, 1H)
4.26 dd, J = 9.6, 3.4	4.42 (dd, J = 9.6 Hz, 1H)	4.04 (dd, J = 9.7, 3.4 Hz, 1H)
4.07 dq, J = 9.9, 6.2	4.24 (dq, J = 8.8, 6.8 Hz, 1H)	3.94 (dd, J = 9.9, 3.3 Hz, 1H)
3.92	4.07 (m, 1H)	3.93 (dd, J = 3.3, 1.5 Hz, 1H)
3.90	4.04 (d, J = 9.6 Hz, 1H)	3.92 (dq, J = 9.7, 6.3 Hz, 1H)
3.78 dq, J = 9.6, 6.3	3.94 (dq, J = 9.6, 6.0 Hz, 2H)	3.78 (dd, J = 9.4, 3.5 Hz, 1H)
3.74 dd, J = 9.6, 3.2	3.81 (ddd, J = 9.6, 6.8, 6.8 Hz, 1H)	3.76 (dq, J = 9.7, 6.3 Hz,1H)
3.57 dq, J = 9.6, 6.2	3.74 (dq, J = 8.8, 6.0 Hz, 1H)	3.65 (ddd, J = 9.6, 6.8, 6.8 Hz, 1H)
3.39 t, J = 9.6	3.56 (ddd, J = 9.6, 6.4, 6.4 Hz, 1H)	3.60 (dq, J = 9.6, 6.2 Hz, 1H)
1.27 d, J = 6.2	2.67 (m, 1H)	3.43 (dd, J = 9.6, 9.4 Hz, 1H)
1.16 d, J = 6.2	2.51 (m, 1H)	3.40 (ddd, J = 10.4, 6.8, 6.8 Hz, 1H)
1.15 d, J = 6.2	2.25 (s, 3H)	2.42 (m, 1H)
3.66 m	2.19 (s, 3H)	2.36 (m, 2H)
2.52 m	2.18 (s, 3H)	2.14 (s, 6H)
2.12 s	1.76 (m, 4H)	2.12 (s, 3H)
2.08 s	1.41 (m, 17H)	1.62 (m, 4H)
2.06 s	1.31 (brm, 6H)	1.29 (m, 24H)
1.68-1.15	1.02 (m, 6H)	1.19 (d, J = 5.2 Hz, 6H)
0.89 m		0.88 (brs, 6H)

1-Octyloxy-2,3-didehydro-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-*O*-diacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (13d):



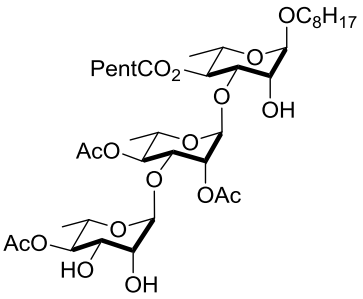
To a solution of allylic alcohol **13a** (60 mg, 0. 076 mmol) in CH_2Cl_2 (0.5 mL), added pyridine (15 μL), acetic anhydride (10.8 μL, 0.11 mmol) and 4-dimethylaminopyridine (1.0 mg, 10 mol%) at 0 ºC. After stirring for 2 h, the mixture was diluted with ether, washed with 1N dil. HCl solution (1 mL) and the solvent was evaporated under reduced pressure. The crude product was purified by silica gel flash chromatography eluting with 8-10% EtOAc/hexane to give allylic acetate **13d** (51.3 mg, 0.06 mmol 81%) as oil: R_f (30% EtOAc/hexane) = 0.75; $[\alpha]^{25}_D = -54.2$ (*c* = 0.67, CH_2Cl_2); IR (thin film, cm^{-1}) 2955, 2856, 1744, 1376, 1228, 1159, 1137, 1087, 1041, 1003; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (d, *J* = 10.0 Hz, 1H), 5.62 (d, *J* = 10.0 Hz, 1H), 5.20 (d, *J* = 1.2 Hz, 1H), 5.10 (dd, *J* = 9.6, 9.6 Hz, 1H), 5.02 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.99 (br, 2H), 4.96 (dd, *J* = 10.4, 10.4 Hz, 1H), 4.85 (s, 1H), 4.72 (s, 1H), 4.24 (d, *J* = 7.2 Hz, 2H), 4.12 (dd, *J* = 9.6, 3.6 Hz, 1H), 3.95 (dq, *J* = 10.4, 2.8 Hz 1H), 3.81 (dq, *J* = 10.4, 6.8 Hz, 3H), 3.67 (ddd, *J* = 9.6, 6.4, 6.4 Hz, 1H), 3.43 (9.6, 6.8, 6.8 Hz, 1H), 2.43-2.34 (m, 2H), 2.13 (s, 3H), 2.07 (s, 6H), 2.07 (s, 3H), 1.64 (m, 4H), 1.32-1.24 (m, 14H), 1.19 (m, 9H), 0.90 (br, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 170.7, 170.6, 170.1, 167.3, 130.5, 127.0, 99.3, 97.0, 96.9, 75.2, 74.9, 73.6, 72.5, 72.5, 72.1, 70.9, 68.5, 67.7, 66.7, 65.2, 41.0, 34.2, 32.0, 31.5, 29.9, 29.5, 29.4, 26.3, 24.7, 22.9, 22.5, 21.3, 21.1, 17.8, 17.6, 14.3, 14.1; HRMS (ESI) calcd for $[C_{40}H_{63}O_{16} + H]^+$: 835.3883, Found: 835.3919.

1-Octyloxy-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-*O*-diacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (23):



To a solution of allylic acetate **13d** (50 mg, 0.06 mmol) in *t*-BuOH/acetone (0.5 mL) at 0 ºC was added a solution of (50% w/v) of *N*-methyl morpholine *N*-oxide/water (60 μL) and crystalline OsO_4 (0.8 mg, 5 mol%). The reaction was stirred for 6 h. The reaction mixture was quenched with saturated sodium sulfite solution (0.1 mL), concentrated under reduce pressure and pipetted directly on to a silica gel column. The crude product was purified using silica gel column chromatography eluting with 40-45% EtOAc/hexane to get diol **23** (44.2 mg, 0.051 mmol, 85%) as liquid; R_f (70% EtOAc/hexane) = 0.5; $[\alpha]^{25}_D$ = – 53.3 (*c* = 0.8, CH_2Cl_2); IR (thin film, cm^{-1}) 3441, 2931, 2927, 1745, 1727, 1264, 1235, 749, 731, 702; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.15 (d, *J* = 1.6 Hz, 1H), 5.03 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.98 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.89 (d, *J* = 2.4 Hz, 1H), 4.83 (s, 1H), 4.82 (s, 1H), 4.77 (dd, *J* = 10.4, 10.4 Hz, 1H), 4.68 (s, 1H), 4.18 (d, *J* = 9.6 Hz, 2H), 4.07 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.91 (dd, *J* = 9.6, 3.2Hz, 1H), 3.75 (m, 2H), 3.74 (dd, *J* = 10.4 Hz, 1H), 3.67 (d, *J* = 2.8 Hz, 1H), 3.65 (m, 1H), 3.62 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 3.38 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 3.07 (brs, 1H), 2.44 -2.22 (m, 2H), 2.09 (s, 3H), 2.07 (s, 3H), 2.04 (s, 3H), 1.60 (m, 4H), 1.28-1.24 (m, 14H), 1.15 (m, 9H), 0.86 (brs, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 170.34, 170.31, 167.3, 101.7, 99.3, 96.9, 75.4, 74.8, 74.6, 73.5, 72.4, 72.1, 71.8, 71.1, 69.9, 68.4, 67.4, 66.7, 66.6, 40.9, 34.1, 31.9, 31.4, 29.4, 29.3, 26.2, 24.6, 22.8, 22.4, 21.2, 21.1, 21.0, 17.5, 17.4, 17.2, 14.2, 14.0; HRMS (ESI) calcd for $[C_{40}H_{65}O_{18}Cl + H]^+$: 869.3936, Found: 869.3936.

Mezzettiaside-4 (4):



To a solution of diol **23** (30 mg, 0.035 mmol) in THF (1.5 mL) was added thiourea (15.7 mg, 0.21 mmol), $NaHCO_3$ (10.1 mg, 0.12 mmol) and *n*-Bu_4NI (12.7 mg, 0.035 mmol) and the mixture was stirred at 60 ºC for 2 h. The reaction mixture was pipetted directly to a silica gel column and eluted with 55-60% EtOAc/hexane to afford Mezzettiaside**-4** (**4**) (22.5 mg, 0.028 mmol, 82%) as a gum: R_f (70% EtOAc/hexane) = 0.3; $[\alpha]^{25}_D = -56.9$ (c = 0.46, $CHCl_3$); IR (thin film, cm^{-1}) 3414, 3231, 2928, 2856, 1742, 1457, 1375, 1231, 1137, 1076, 1045, 980; ^{1}H NMR (400 MHz, $CDCl_3$) 5.06 (dd, J = 9.6, 9.6 Hz, 1H), 5.03 (s, 1H), 5.02 (dd, J = 9.6, 9.6 Hz, 1H), 4.97 (dd, J = 3.6, 1.2 Hz, 1H), 4.85 (s, 1H), 4.79 (s, 1H), 4.78 (dd, J = 9.6, 9.6 Hz, 1H), 4.18 (dd, J = 10.4, 3.6 Hz, 1H), 3.98 (m, 2H), 3.90 (dd, J = 9.6, 3.6 Hz, 1H), 3.85 (d, J = 2.0 Hz, 1H), 3.79 (dq, J = 9.6, 6.2 Hz, 1H), 3.73 (dd, J = 9.6, 3.2 Hz, 1H), 3.70 (dq, J = 9.6, 6.2 Hz, 1H), 3.65 (ddd, J = 9.6, 6.2, 6.2 Hz, 1H), 3.42(ddd, J = 9.6, 6.2, 6.2 Hz, 1H), 2.44-2.35 (m, 2H), 2.12 (s, 3H), 2.11 (s, 3H), 2.07 (s, 3H), 1.63 (m, 4H), 1.31 (m, 14H), 1.24 (m, 6H), 1.14 (d, J = 6.8 Hz, 3H), 0.89 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 172.3, 170.5, 170.3, 101.8, 99.7, 99.5, 79.4, 75.3, 75.2, 72.5, 72.3, 72.0, 71.2, 71.1, 69.9, 68.2, 67.4, 66.7, 66.4, 34.3, 32.0, 31.5, 29.6, 29.5, 29.4, 26.3, 24.7, 22.9, 22.5, 21.3, 21.2, 21.1, 17.62, 17.63, 17.3, 14.3, 14.1; HRMS (ESI) calcd for $[C_{38}H_{64}O_{17} + H]^+$: 793.4222, Found: 793.4226.

NMR Data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.04 (dd, J = 9.9, 9.8 Hz, 1H), 5.03 (dd, J = 9.9, 9.8 Hz, 1H), 5.01 (d, J = 1.6 Hz, 1H), 4.99 (dd, J = 3.4, 1.8 Hz, 1H), 4.86 (d, J = 1.8 Hz, 1H), 4.78 (d, J = 1.6 Hz, 1H), 4.75 (dd, J = 9.7, 9.7 Hz, 1H), 4.14 (dd, J = 9.9, 3.4 Hz, 1H), 3.96 (dd, J = 3.3, 1.6 Hz, 1H), 3.95 (dq, J = 9.8, 6.3 Hz, 1H), 3.90 (dd, J = 9.8, 3.3 Hz, 1H), 3.84 (dd, J = 3.5, 1.6 Hz, 1H), 3.77 (dq, J = 9.9, 6.3 Hz, 1H), 3.73 (dd, J = 9.7, 3.5 Hz, 1H), 3.70 (dq, J = 9.7, 6.3 Hz, 1H), 3.65 (ddd, J = 9.6, 6.8, 6.8 Hz, 1H), 3.41(ddd, J = 9.6, 6.8, 6.8 Hz, 1H), 2.44-2.35 (m, 2H), 2.12 (s, 3H), 2.11 (s, 3H), 2.07 (s, 3H), 1.63 (m, 4H), 1.31 (m, 14H), 1.24 (m, 6H), 1.14 (d, J = 6.8 Hz, 3H), 0.89 (m, 6H); ^{1}H NMR (150 MHz, $CDCl_3$) δ 173.5, 172.1, 170.2, 170.0, 101.4,

99.4, 99.3, 79.1, 75.1, 74.9, 72.3, 71.9, 71.7, 71.0, 71.0, 69.8, 67.2, 66.5, 66.2, 34.1, 31.8, 31.3, 29.4, 29.3, 29.2, 26.1, 24.5, 22.6, 22.3, 21.1, 21.0, 20.8, 17.4, 17.4, 17.3, 14.1, 13.9.

^{1}H NMR (500 MHz, CD_3OD + C_6D_6 (6:1)) δ 5.67 (dd, *J* = 10.0, 10.0 Hz, 1H), 5.58 (dd, *J* = 1.5, 1.5 Hz, 1H), 5.55 (dd, *J* = 10.0, 10.0 Hz, 1H), 5.47 (dd, *J* = 10.0, 10.0 Hz, 1H), 5.38 (s, 1H), 5.32 (s, 1H), 5.21 (s, 1H), 4.81 (dd, *J* = 9.5, 3.5 Hz, 1H), 4.61 (dq, *J* = 9.5, 6.0 Hz, 1H), 4.43 (m, 2H), 4.29 (m, 2H), 4.26-4.22 (dq, *J* = 9.5, 6.0 Hz, 2H) 4.15 (m, 1H), 3.89 (m, 1H), 2.94 (m, 1H), 2.84 (m, 1H), 2.54 (s, 3H), 2.51 (s, 6H), 2.12-2.03 (m, 4H), 1.84 (m, 14H), 1.66 (m, 9 H), 1.39 (m, 6H); ^{13}C NMR (100 MHz, CD_3OD + C_6D_6 (6:1)) δ 173.9, 171.7, 171.0, 170.9, 103.0, 100.7, 100.2, 78.9, 75.0, 74.6, 73.4 72.7, 72.5, 71.7, 71.4, 69.8, 68.1, 67.7, 67.4, 67.2, 34.3, 32.3, 31.7, 29.8, 29.7, 26.7, 24.9, 23.0, 22.7, 20.4, 20.2, 20.1, 17.4, 17.3, 17.1, 13.9, 13.7.

5

[5] Optical rotation for the isolated **Mezzettiaside-4**: $[\alpha]_D$ = – 54 (*c* = 0.46, $CHCl_3$) (Ref. 1).

Mezzettiaside-4: Comparison of ^{13}C NMR spectra of natural vs synthetic

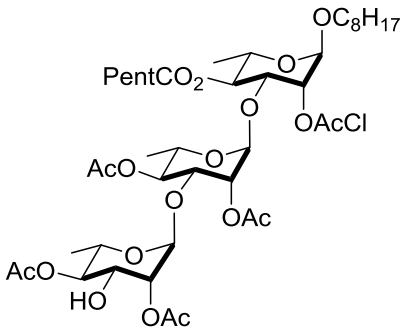
δ/ppm Natural $CD_3OD+C_6D_6$ (~ 6:1)	δ/ppm Synthetic in $CD_3OD+C_6D_6$ (6:1)	Difference (ppm)	δ/ppm Synthetic in (150 MHz $CDCl_3$)
173.9	173.9	0.0	173.5
171.8	171.7	0.1	172.1
170.9	171.0	-0.1	170.2
170.8	170.9	-0.1	170.0
103.1	103.0	0.1	101.4
100.8	100.7	0.1	99.4
100.4	100.2	0.2	99.3
79.4	78.9	0.5	79.1
75.4	75.0	0.4	75.1
75.1	74.5	0.5	74.9
73.6	73.4	0.2	72.3
73.1	72.7	0.4	71.9
72.8	72.5	0.3	71.7
72.0	71.7	0.3	71.0
71.9	71.4	0.5	71.0
70.3	69.4	0.5	69.8
68.3	68.1	0.2	67.2
67.9	67.7	0.2	66.5
67.9	67.4	0.5	66.2
67.4	67.2	0.2	34.1
34.8	34.3	0.5	31.8
32.4	32.3	0.1	31.3
31.9	31.7	0.2	29.4
30.1	29.8	0.3	29.3
29.9	29.7	0.2	29.2
29.8	29.7	0.1	26.1
26.8	26.6	0.2	24.5
25.2	24.9	0.3	22.6
23.2	23.0	0.2	22.3
22.9	22.7	0.2	21.1
20.9	20.3	0.5	21.0
20.7	20.1	0.5	20.8
20.4	20.1	0.3	17.4
17.9	17.3	0.5	17.4
17.8	17.1	0.5	17.3
17.6	17.1	0.5	14.1
14.4	13.9	0.5	13.9
14.2	13.7	0.5	

Note:- Here, if we substract 0.2 ppm from the above difference, the everything falls within a range of +/- 0.3 ppm.

Mezzettiaside-4: Comparison of ^{1}H NMR spectra of natural vs synthetic

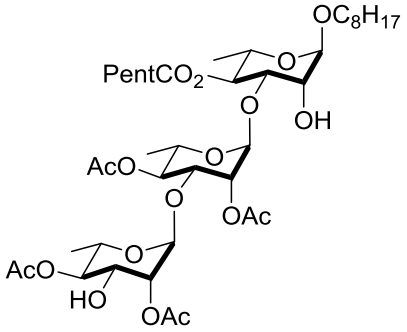
Natural Data δ/J ppm in C_6D_6+CD_3OD (1:6)		Synthetic data C_6D_6+CD_3OD (1:6)	Synthetic data (δ/J ppm in $CDCl_3$) (600 MHz)
5.67	9.8-9.9, 9.7-9.9	5.67 (dd, J = 10.0, 10.0 Hz, 1H)	5.04 (dd, J = 9.9, 9.8 Hz, 1H)
5.59	9.8-9.9, 9.7-9.9	5.58 (dd, J = 1.5, 1.5 Hz, 1H)	5.03 (dd, J = 9.9, 9.8 Hz, 1H)
5.53	3.0-3.5, 1.0-2.02	5.55 (dd, J = 10.0, 10.0 Hz, 1H)	5.01 (d, J = 1.6 Hz, 1H)
5.44	9.8-9.9, 9.7-9.9	5.47 (dd, J = 10.0, 10.0 Hz, 1H)	4.99 (dd, J = 3.4, 1.8 Hz, 1H
5.38	1.0-2.02	5.38 (s, 1H)	4.86 (d, J = 1.8 Hz, 1H)
5.21	1.0-2.02	5.32 (s, 1H)	4.78 (d, J = 1.6 Hz, 1H)
5.13	1.0-2.02	5.21 (s, 1H)	4.75 (dd, J = 9.7, 9.7 Hz, 1H)
4.75	9.7-9.9, 3.0-3.5	4.81 (dd, J = 9.5, 3.5 Hz, 1H)	4.14 (dd, J = 9.9, 3.4 Hz, 1H)
4.49	9.8-9.9, 6.1-6.4	4.61 (dq, J = 9.5, 6.0 Hz, 1H)	3.96 (dd, J = 3.3,1.6 Hz, 1H)
4.40	3.0-3.5, 1.0-2.02	4.43 (m, 2H)	3.95 (dq, J = 9.8, 6.3 Hz, 1H)
4.38	9.7-9.9, 3.0-3.5	4.29 (m, 2H)	3.90 (dd, J = 9.8, 3.3 Hz, 1H)
4.27	3.0-3.5, 1.0-2.02	4.26-4.22 (dq, J = 9.5, 6.0 Hz, 2H)	3.84 (dd, J = 3.5, 1.6 Hz, 1H)
4.26	9.7-9.9, 3.0-3.5	4.15 (m, 1H)	3.77 (dq, J = 9.9, 6.3 Hz, 1H)
4.23	9.8-9.9, 6.1-6.4	3.89 (m, 1H)	3.73 (dd, J = 9.7, 3.5 Hz, 1H)
4.17	9.8-9.9, 6.1-6.4	2.94 (m, 1H)	3.70 (dq, J = 9.7, 6.3 Hz, 1H)
3.84		2.84 (m, 1H)	3.65 (ddd, J = 9.6, 6.2, 6.2 Hz,
3.53		2.54 (s, 3H)	3.42(ddd, J = 9.6, 6.2, 6.2 Hz,
2.78		2.51 (s, 6H)	2.44-2.35 (m, 2H)
2.57		2.12-2.03 (m, 4H)	2.13 (s, 3H)
1.09		1.84 (m, 14H)	2.11 (s, 3H)
1.06		1.66 (m, 9 H)	2.08 (s, 3H)
2.18	s, 3H	1.39 (m, 6H)	1.63 (m, 4H)
2.06	s, 3H		1.31 (m, 14H)
1.96	s, 3H		1.24 (m, 6H)
1.57	6.1-6.4		1.14 (d, J = 6.8 Hz, 3H)
1.51	6.1-6.4		0.89 (m, 6H)

1-Octyloxy-2,4-*O*-diacetyl-α-L-rhamnopyranosyl-(1→3)-2,4-*O*-diacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (23a):



To a stirred solution of diol **23** (15mg, 0.017 mmol) in CH_2Cl_2 (0.2 mL) at 0 ºC was added triethylorthoacetate (9.5 μL, 0.052 mmol) and *p*-TsOH·H_2O (2 mg). The reaction was stirred at 0 ºC for 45 min and then aqueous acetic acid (90%, 0.15 mL) was added, stirred for another 20 min. The reaction mixture was diluted with 10 mL EtOAc and washed with saturated $NaHCO_3$ solution, extracted with EtOAc (2 x 10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 30-35% EtOAc/hexane to give desired acetate **23a** (13.0 mg, 0.014 mmol, 84%) as oily liquid: R_f (70% EtOAc/hexane) = 0.7; $[\alpha]^{25}_D$ = – 43.5 (*c* = 2.0, CH_2Cl_2); IR (thin film, cm^{-1}) 3470, 2937, 1754, 1745, 1612, 1584, 1231, 1139, 1093, 1042; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.17 (d, *J* = 2.0 Hz, 1H), 5.07 (dd, *J* = 9.2, 9.2 Hz, 1H), 5.02 (dd, *J* = 9.2, 9.2 Hz, 1H), 4.91 (d, *J* = 1.6 Hz, 1H), 4.86 (br, 2H), 4.83 (br, 1H), 4.79 (dd, *J* = 10.6, 10.6 Hz, 1H), 4.71 (s, 1H), 4.19 (d, *J* = 8.8 Hz, 2H), 4.09 (dd, *J* = 9.6, 2.8 Hz, 1H), 3.93 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.85 (dd, *J* = 10.4, 3.2 Hz, 1H), 3.78 (dq, *J* = 9.6, 6.8 Hz, 3H) 3.65 (ddd, *J* = 8.8, 6.4, 6.4 Hz, 1H), 3.41 (ddd, *J* = 9.6, 6.4, 6.4 Hz, 1H), 2.45 (m, 1H), 2.35 (m, 1H), 2.14 (s, 3H), 2.13 (brs, 6H), 2.11 (s, 3H), 1.63 (m, 4H), 1.28-1.15 (m, 23 H), 0.88 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 171.8, 170.7, 170.5, 170.4, 167.3, 99.5, 99.2, 96.9, 75.5, 74.7, 74.5, 73.6, 72.9, 72.2, 72.2, 71.8, 68.5, 68.4, 67.7, 66.9, 66.7, 40.9, 34.2, 32.0, 31.5, 29.49, 29.41, 26.2, 24.7, 22.8, 22.5, 21.2, 21.1, 21.0, 17.6, 17.5, 17.3, 14.3, 14.1; HRMS (ESI) calcd for $[C_{42}H_{67}O_{19}Cl + H]^+$: 911.4043, Found: 911.4037.

Mezzettiaside-2 (2):

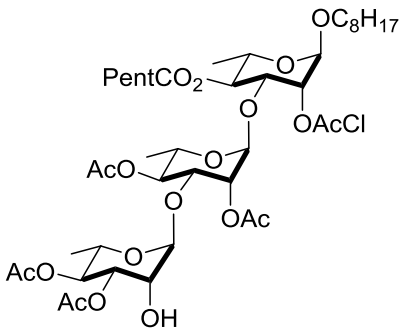


To a stirred solution of chloroacetate **23a** (10 mg, 0.011 mmol) in THF (0.1 mL) was added thiourea (5.0 mg, 0.0654 mmol), $NaHCO_3$ (3.2 mg, 0.038 mmol) and *n*-Bu_4NI (2.01 mg, 0.006 mmol). The mixture was stirred at 60 ºC for 4 h. The reaction solution was pipetted directly to a silica gel column and eluted with 38-40% EtOAc/hexane to afford Mezzettiaside-**2** (**2**) (7.1 mg, 0.009 mmol, 77%) as a gum: R_f (70% EtOAc/hexane) = 0.65; $[\alpha]^{25}_D$ = – 30.2 (c = 0.25, $CHCl_3$); IR (thin film, cm^{-1}) 3453, 2956, 2927, 2859, 1745, 1462, 1452, 1378, 1234, 1137, 1076, 986, 832, 764; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.08 (dd, J = 9.6, 9.6 Hz, 1H), 5.06 (dd, J = 9.6, 9.6 Hz, 1H), 4.97 (dd, J = 3.2, 1.6 Hz, 1H), 4.93 (s, 1H), 4.87 (dd, J = 3.6, 1.6 Hz, 1H), 4.86 (s, 1H), 4.83 (dd, J = 10.4, 9.6 Hz, 1H), 4.75 (s, 1H), 4.06 (dd, J = 9.6, 3.2 Hz, 1H), 3.93 (m, 2H), 3.91 (dd, J = 8.0, 3.6 Hz, 1H), 3.87 (dd, J = 10.4, 3.6 Hz, 1H), 3.78 (dq, J = 9.6, 6.4 Hz, 2H), 3.67 (ddd, J = 9.2, 6.4, 6.4 Hz, 1H), 3.42 (ddd, J = 9.2, 6.4, 6.4 Hz, 1H), 2.41 (m, 1H), 2.36 (m, 1H), 2.15 (s, 6H), 2.14 (brs, 3H), 2.13 (s, 3H), 1.64 (m, 4H), 1.32 (m, 23H), 0.88 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 171.8, 170.6, 170.5, 170.4, 99.4, 99.2, 78.9, 74.9, 74.5, 73.0, 72.3, 71.9, 71.8, 71.2, 68.4, 68.2, 67.6, 66.9, 66.4, 34.3, 32.0, 31.5, 29.6, 29.5, 29.4, 26.3, 24.7, 22.9, 22.5, 21.2, 21.2, 21.0, 17.6, 17.3, 14.3, 14.1; HRMS (ESI) calcd for $[C_{40}H_{66}O_{18} + H]^+$: 835.4327, Found: 835.4338.

NMR Data: ^{1}H NMR (400 MHz, C_6D_6 + CD_3OD (1:6)) δ 5.31 (dd, J = 9.6, 9.6 Hz, 2H), 5.21 (br, 2H), 4.95 (s, 1H), 4.85 (s, 1H), 4.81 (s, 1H), 4.47 (d, J = 10.0 Hz, 1H), 4.23 (m, 1H), 4.10 (br, 3H), 3.93 (dq, J = 7.2 Hz, 2H), 3.78 (m, 1H), 3.51 (m, 1H), 2.60 (m, 1H), 2.49 (m, 1H), 2.26 (s, 3H), 2.20 (s, 3H), 2.17 (s, 6H), 1.75 (m, 4H), 1.40 (brm, 17H), 1.30 (m, 6H), 1.02 (br, 6H); ^{13}C NMR (100 MHz, C_6D_6 + CD_3OD (1:6)) δ 174.5, 172.2, 172.1, 172.0, 171.5, 101.3, 101.0, 100.6,

79.7, 75.7, 75.0, 74.0, 73.8, 73.4, 73.1, 72.0, 68.8, 68.2, 68.1, 68.0, 67.8, 35.0, 32.9, 32.4, 30.41, 30.35, 27.3, 25.6, 23.7, 23.4, 20.9, 20.8, 20.7, 17.9, 17.7, 17.7, 14.5, 14.3.[6]

1-Octyloxy-3,4-*O*-diacetyl-α-L-rhamnopyranosyl-(1→3)-2,4-*O*-diacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (23b):

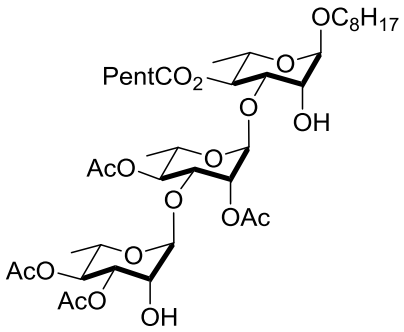


To a solution of trisaccharide diol **23** (19 mg, 0.02 mmol) in CH_3CN/THF (1:0.1, 0.1 mL), added boron catalyst ($Ph_2BOCH_2CH_2NH_2$) (0.7 mg, 15 mol%), the reaction was stirred at 0 ºC for 20 min. To the reaction then added acetyl chloride (2.3 μL, 0.033 mmol) followed by addition of DIPEA (5.7 μL, 0.033 mmol). The reaction mixture was stirred at at 0 ºC for 2 h then diluted with ethyl acetate and washed with water. The organic layers were combined, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 30-32% EtOAc/hexane to give alcohol as oil **23b** (14.2 mg, 0.016 mmol, 71%): R_f (70% EtOAc/hexane) = 0.8; $[\alpha]^{25}_D$ = – 45.4 (c = 0.32, CH_2Cl_2); IR (thin film, cm^{-1}) 3491, 2955, 2856, 1744, 1373, 1226, 1136, 1088, 1042, 987; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.18 (br, 1H), 5.08 (m, 2H), 5.03 (dd, J = 9.6, 9.6 Hz, 3H), 5.04 (br, 1H), 4.96 (br, 1H), 4.87 (brs, 2H), 4.72 (s, 1H), 4.20 (d, J = 7.2 Hz, 2H), 4.10 (dd, J = 9.6, 2.8 Hz, 1H), 3.98 (dd, J = 10.4, 2.8 Hz, 1H), 3.91 (d, J = 1.2 Hz, 1H), 3.80 (dq, J = 8.8, 6.8 Hz, 3H), 3.67 (ddd, J = 8.8, 6.4, 6.4 Hz, 1H), 3.43 (ddd, J = 8.8, 6.4, 6.4 Hz, 1H), 2.45 (m, 1H), 2.34 (m, 1H), 2.15 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 1.64 (m, 4H), 1.29 (m, 17H), 1.19 (m, 6H), 0.88 (br, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 170.5, 170.4, 170.3, 169.9, 167.4, 101.0, 99.4, 97.0, 75.5,

[6] Optical rotation for the isolated **Mezzettiaside-2**: $[\alpha]_D$ = – 31 (c = 0.25, $CHCl_3$) (Ref. 1).

74.6, 73.7, 72.5, 72.2, 71.6, 71.2, 69.8, 68.5, 67.6, 67.3, 66.7, 41.0, 34.3, 32.0, 31.5, 29.5, 29.4, 26.3, 24.7, 22.9, 22.5, 21.2, 21.14, 21.1, 21.06, 17.6, 17.5, 17.4, 14.3, 14.3; HRMS–MALDI–TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{42}H_{67}O_{19}Cl + Na]^+$; 933.3857, Found: 933.3839.

Mezzettiaside-3 (3):



To a stirred solution of alcohol **23b** (11 mg, 0.012 mmol) in THF (0.5 mL) was added thiourea (5.51 mg, 0.072 mmol), $NaHCO_3$ (3.55 mg, 0.042 mmol) and *n*-Bu_4NI (2.2 mg, 0.006 mmol). The reaction mixture was stirred at 60 ºC for 1 h, then the mixture was diluted with ethyl acetate and extracted (3 x 5mL). The combined organic layers were concentrated and the crude product was purified using column chromatography, eluting with 40-42% EtOAc/hexane to afford Mezzettiaside-**3** (**3**) (8.3 mg, 0.01 mmol, 82%) as a gum: R_f (70% EtOAc/hexane) = 0.6; $[\alpha]^{25}_D$ = – 56.7 (*c* = 0.44, $CHCl_3$); IR (thin film, cm^{-1}) 3492, 3278, 2925, 2855, 1740, 1372, 1165, 1136, 1074, 1044, 987; ^1H NMR (500 MHz $CDCl_3$) δ 5.08 (m, 5H), 4.92 (d, *J* = 2.0 Hz, 1H), 4.89 (d, *J* = 2.0 Hz, 1H), 4.76 (d, *J* = 1.5 Hz, 1H), 4.12 (dd, *J* = 10.0, 3.5 Hz,1H), 3.96 (m, 3H), 3.92 (dd, *J* = 10.0, 3.0 Hz, 1H), 3.83 (dq, *J* = 10.0, 6.5 Hz, 2H), 3.67 (ddd, *J* = 9.5, 6.5, 3.0 Hz, 1H), 3.43 (ddd, *J* = 10.0, 6.5, 3.0 Hz, 1H), 2.45 (m, 1H), 2.35 (m, 1H), 2.16 (s, 3H), 2.08 (s, 3H), 2.06 (s, 3H), 2.03 (s, 3H), 1.65 (m, 4H), 1.32 (m, 17H), 1.20 (d, *J* = 6.0 Hz, 3H), 1.19 (d, *J* = 6.0 Hz, 3H), 0.88 (br, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 170.5, 170.4, 170.2, 170.1, 101.1, 99.4, 79.1, 74.7, 72.6, 71.9, 71.6 , 71.55, 71.2, 71.2, 69.7, 68.2, 67.4, 67.3, 66.4, 34.3, 32.0, 31.5, 29.5, 29.4, 26.3, 24.7, 22.9, 22.5, 21.2, 21.1, 21.1,17.6, 17.4, 14.3, 14.1; HRMS–MALDI-TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{40}H_{66}O_{18} + Na]^+$; 857.4141, Found, 857.4164.

NMR Data:^1H NMR (600 MHz, C_6D_6) δ 5.57 (dd, *J* = 10.0, 9.5 Hz, 1H), 5.54 (dd, *J* = 10.1, 9.7 Hz, 1H), 5.51 (dd, *J* = 9.6, 9.6 Hz, 1H), 5.45 (dd, *J* = 10.1, 3.2 Hz, 1H), 5.43 (dd, *J* = 3.5, 1.8 Hz, 1H), 5.19 (d, *J* = 1.7 Hz, 1H), 4.99 (d, *J* = 1.8 Hz, 1H), 4.88 (d, *J* = 1.6 Hz, 1H), 4.50 (dd, *J* =

10.0, 3.5 Hz, 1H), 4.25 (dq, *J* = 9.5, 6.3 Hz, 1H), 4.23 (dd, *J* = 3.2, 1.7 Hz, 1H), 4.22 (dq, *J* = 9.7, 6.2 Hz, 1H), 4.21 (d, *J* = 3.3, 1.6 Hz, 1H), 4.17 (dd, *J* = 9.9, 3.3 Hz, 1H), 4.01 (dq, *J* = 9.6, 6.2 Hz, 1H), 3.65 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 3.45 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 2.64 (m, 1H), 2.43 (m, 1H), 1.90 (s, 3H), 1.73 (s, 3H), 1.66 (s, 3H), 1.65 (s, 3H), 1.43 (m, 4H), 1.32 (m, 14H), 1.19 (m, 9H), 0.90 (m, 6H); ^{13}C NMR (150 MHz, C_6D_6) δ 173.4, 170.2, 169.8, 169.6, 169.6, 102.2, 101.7, 100.1, 79.8, 76.8 75.3, 72.7, 72.4, 72.2, 71.9, 71.8, 71.8, 71.5, 67.8, 67.8, 66.9, 34.5, 32.2, 31.7, 29.8, 29.7, 29.6, 26.5, 25.0, 23.0, 22.7, 20.5, 20.4, 20.4, 20.2, 17.8, 17.6, 17.4, 14.2, 14.1.

^{1}H NMR (400 MHz, C_6D_6 + CD_3OD) δ 5.77 (dd, *J* = 10.5, 9.6 Hz, 2H), 5.69 (dd, *J* = 9.6, 9.6 Hz, 1H), 5.62 (br, 1H), 5.61 (dd, *J* = 10.4, 3.6 Hz, 1H), 5.41 (s, 1H), 5.24 (s, 1H), 5.17 (s, 1H), 4.56 (d, *J* = 9.6 Hz, 1H), 4.53 (m, 5H), 4.24 (dq, *J* = 6.4 Hz, 2H), 3.89 (m, 1H), 2.85 (m, 1H), 2.63 (m, 1H), 2.24 (s, 3H), 2.13 (s, 3H), 2.05 (s, 3H), 1.98 (s, 3H), 1.75 (m, 4H), 1.62-1.47 (m, 23H), 1.21 (m, 6H); ^{13}C NMR (100 MHz, C_6D_6 + CD_3OD (4:1)) δ 173.7, 170.7, 170.7, 170.6, 170.6, 102.2, 100.5, 100.1, 79, 74.8, 73.2, 72.7, 72.3, 72.1, 71.5, 71.5, 69.3, 68.1, 67.7, 67.5, 67.1, 34.4, 32.1, 31.6, 30.1, 29.7, 29.7, 29.6, 26.5, 23.0, 22.6, 20.4, 20.3, 20.3, 20.2, 17.6, 17.4, 17.4, 14.2, 14.0.
[7]

[7] Optical rotation for the isolated **Mezzettiaside-3**: $[\alpha]^{20}_{D} = -49$ (*c* = 0.38, $CHCl_3$) (Ref. 1).

Mezzettiaside-3: Comparison of ^{13}C NMR spectra of natural vs synthetic

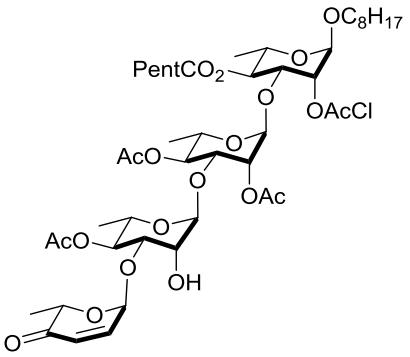
δ-values (ppm) Isolation Paper C_6D_6+CD_3OD (4:1)	δ-values (ppm) in C_6D_6+CD_3OD (~ 4:1) Ref. C_6D_6 (128 ppm)	Difference (ppm)	δ-values (ppm) Observed Data $CDCl_3$ (400 MHz)	δ-values (ppm) Observed Data C_6D_6 (150 MHz NMR)
173.5	173.7	-0.2	173.4	173.4
170.8	170.7	0.1	170.5	170.2
170.8	170.7	0.1	170.4	169.8
170.7	170.6	0.1	170.2	169.6
170.7	170.6	0.1	170.0	169.6
102.1	102.2	-0.1	101.0	102.2
100.4	100.5	-0.1	99.4	101.7
99.8	100.1	-0.3	79.1	100.1
78.9	79.0	-0.1	74.7	79.8
74.7	74.8	-0.1	72.6	76.8
73.1	73.2	-0.1	71.9	75.3
72.6	72.7	-0.1	71.6	72.7
72.2	72.3	-0.1	71.6	72.4
71.7	72.1	-0.4	71.2	72.2
71.4	71.5	-0.1	71.2	71.9
71.1	71.5	-0.4	69.7	71.8
69.2	69.3	-0.1	68.2	71.8
68.0	68.1	-0.1	67.4	71.5
67.6	67.7	-0.1	67.2	67.8
67.4	67.5	-0.1	66.4	67.8
66.9	67.1	-0.2	34.3	66.9
34.3	34.4	-0.1	32.0	34.5
32.0	32.1	-0.1	31.5	32.2
31.8	31.6	0.2	29.9	31.7
29.9	30.1	-0.2	29.6	29.8
29.9	29.7	0.2	29.5	29.7
29.5	29.7	-0.2	29.4	29.6
29.4	29.6	-0.2	26.3	26.5
26.3	26.5	-0.2	24.7	25.0
22.8	23.0	-0.2	22.9	23.0
22.4	22.6	-0.2	22.5	22.7
20.2	20.4	-0.2	21.2	20.5
20.1	20.3	-0.2	21.1	20.4
20.1	20.3	-0.2	21.1	20.4
20.0	20.2	-0.2	21.0	20.2
17.4	17.6	-0.2	17.6	17.8
17.2	17.4	-0.2	17.6	17.6
17.2	17.4	-0.2	17.4	17.4
14.3	14.2	0.1	14.3	14.2
14.1	14.0	0.1	14.1	14.1

Note:- If we add + 0.1 ppm to the above difference then everything falls under +/- 0.3 ppm range, we can account this difference to the reference peak, mixed solvent and the exact concentration.

Mezzettiaside-3: Comparison of ^{1}H NMR spectra of natural vs synthetic

δ-values (ppm) Isolation Paper C_6D_6+CD_3OD (4:1)		Synthetic data in C_6D_6+CD_3OD (4:1)	Observed Data δ/J ppm C_6D_6 (600 MHz)
5.82	9.9, 9.8	5.77 (dd, J = 10.5, 9.6 Hz, 2H)	5.57 dd, J = 10.0, 9.5 Hz, 1H)
5.82	9.8, 9.7	5.69 (dd, J = 9.6, 9.6 Hz, 1H)	5.54 (dd, J = 10.1, 9.7 Hz, 1H)
5.77	9.9, 9.9	5.62 (br, 1H)	5.5 (dd, J = 9.9, 9.6 Hz, 1H)
5.71	3.5, 1.7	5.61 (dd, J = 10.4, 3.6 Hz, 1H)	5.45 (dd, J = 10.1, 3.2 Hz, 1H)
5.68	9.9, 3.2	5.41 (s, 1H)	5.43 (dd, J = 3.5, 1.8 Hz, 1H)
5.49	2.1	5.24 (s, 1H)	5.19 (d, J = 1.7 Hz, 1H)
5.34	1.7	5.17 (s, 1H)	4.99 (d, J = 1.8 Hz, 1H)
5.26	1.4	4.56 (d, J = 9.6 Hz, 1H)	4.88 (d, J = 1.6 Hz, 1H)
4.91	9.9, 3.5	4.53 (m, 5H)	4.50 (dd, J =10.0, 3.5 Hz, 1H)
4.64	9.9, 6.3	4.24 (dq, J = 6.4 Hz, 2H)	4.25 (dq, J = 9.5, 6.3 Hz, 1H)
4.58	3.2, 2.1	3.89 (m, 1H)	4.23 (dd, J = 3.2,1.7 Hz, 1H)
4.54	3.3, 1.4	2.85 (m, 1H)	4.22 (dq, J = 9.7, 6.2 Hz, 1H)
4.51	9.7, 3.3	2.63 (m, 1H)	4.21 (dd, J = 3.3, 1.6 Hz, 1H)
4.49	9.8, 6.2	2.24 (s, 3H)	4.17 (dd, J = 9.9, 3.3 Hz, 1H)
4.32	9.8, 6.23.99	2.13 (s, 3H)	4.01 (dq, J = 9.6, 6.2 Hz, 1H)
3.66		2.05 (s, 3H)	1.44 (s, 3H)
2.91		1.98 (s, 3H)	1.37 (s, 3H)
2.71		1.75 (m, 4H)	1.26 (s, 3H)
2.34		1.62-1.47 (m, 23H)	
2.24		1.21 (m, 6H)	
2.17			
2.1			
1.86			
1.86			
1.71			
1.68			
1.68			
1.66			
1.62			
1.25			
1.25			

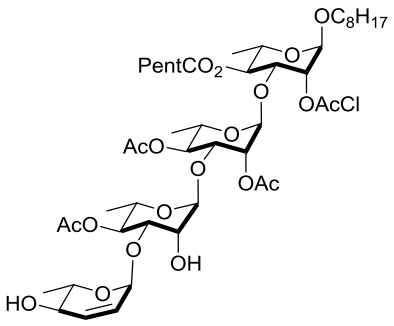
1-Octyloxy-2,3-didehydro-5-methyl-oxopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-*O*-diacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (24):



To a stirred solution of trisaccharide diol **23** (35mg, 0.040 mmol) in CH_3CN/THF (1:0.1) (0.8 mL) was added boron catalyst (1.4 mg, 15 mol%) and reaction stirred at 0 ºC for 20 min. To it then added Boc-pyranone (10.1 mg, 0.044 mmol) followed by addition of $Pd_2(dba)_3$•$CHCl_3$ (1.2 mg, 2.5 mol%) and PPh_3 (1.3 mg, 10 mol%) solution in CH_2Cl_2. The reaction mixture was stirred and warmed to rt, after 2 h, quenched by adding 0.5 mL saturated $NaHCO_3$ solution, followed by extraction with EtOAc. The organic layers were combined, washed with 2 mL saturated brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 22-25% EtOAc/hexane to give tetrasaccharide enone **24** (30 mg, 0.031 mmol, 76%) as a thick liquid oil: *Rf* (30% EtOAc/hexane) = 0.60; $[\alpha]^{25}_D$ = – 93.9 (*c* = 0.22, CH_2Cl_2); IR (thin film, cm^{-1}) 2976, 2360, 1755, 1275, 1260, 764, 750; ^1H NMR (400 MHz, $CDCl_3$) δ 6.68 (dd, *J* = 10.4, 3.6 Hz, 1H), 6.08 (d, *J* = 10.0 Hz, 1H), 5.29 (d, *J* = 3.2 Hz, 1H), 5.18 (d, *J* = 1.2 Hz, 1H), 5.08 (dd, *J* = 9.6, 9.6 Hz, 1H), 5.02 (dd, *J* = 9.6, 9.6 Hz, 1H), 5.00 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.98 (d, *J* = 3.2 Hz, 1H), 4.86 (s, 2H), 4.71 (s, 1H), 4.55 (q, *J* = 6.8 Hz, 1H), 4.19 (d, *J* = 6.8 Hz, 2H), 4.10 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.96 (m, 3H), 3.80-3.71 (dq, *J* = 9.6, 6.8 Hz, 3H), 3.66 (ddd, *J* = 9.6, 6.4, 6.4 Hz, 1H), 3.42 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 2.42 (m, 1H), 2.33 (m, 1H), 2.13 (s, 3H), 2.07 (s, 6H), 1.63 (m, 4H), 1.37 (d, *J* = 6.8 Hz, 3H), 1.31-1.15 (m, 20H), 1.13 (d, *J* = 6.0 Hz, 3H), 0.88 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.4, 173.1, 170.3, 170.2, 170.1, 167.3, 142.5, 127.8, 101.2, 99.3, 96.9, 94.8, 75.5, 75.0, 73.6, 73.6, 72.6, 72.4, 72.1, 71.7, 71.3, 70.9, 68.5, 67.5, 67.3, 66.7, 40.9, 34.2, 32.0, 31.5,

29.5, 29.5, 29.4, 26.2, 24.7, 22.8, 22.4, 21.2, 21.1, 21.1, 17.6, 17.5, 17.4, 15.3, 14.3, 14.1; HRMS (ESI) calcd for $[C_{46}H_{71}O_{20}Cl + H]^+$: 979.4305, Found: 979.4301.

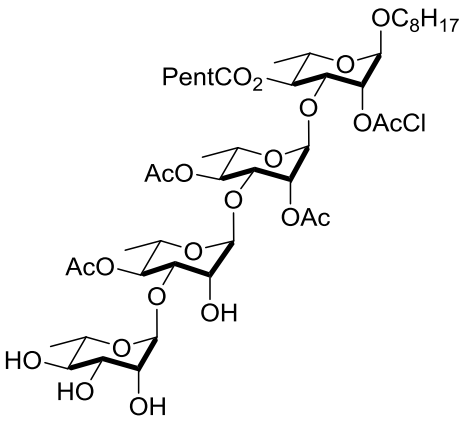
1-Octyloxy-2,3-didehydro-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-*O*-diacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (24a):



To a solution of enone **24** (25 mg, 0.026 mmol) in CH_2Cl_2 (0.25 mL) at –78 ºC was added $CeCl_3$/MeOH solution (0.4 M in MeOH, 25 μL) and $NaBH_4$ (1.5 mg, 0.038 mmol). The reaction mixture was stirred at –78 ºC for 2 h. The reaction mixture was quenched with 0.5 mL of saturated aqueous $NaHCO_3$, extracted with Et_2O (2 x 10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 40-45% EtOAc/hexane to give desired alcohol **24a** (21 mg, 0.021 mmol, 84%) as a gum: R_f (50% EtOAc/hexane) = 0.2; $[\alpha]^{25}_D$ = – 27.7 (*c* = 0.4, CH_2Cl_2); IR (thin film, cm^{-1}) 3488, 2928, 2856, 2351, 1792, 1748, 1717, 1457, 1375, 1231, 1137, 1089, 1044; ^1H NMR (400 MHz, $CDCl_3$) δ 5.94 (d, *J* = 10.4 Hz, 1H), 5.58 (d, *J* = 10.4 Hz, 1H), 5.19 (d, *J* = 1.2 Hz, 1H), 5.06 (dd, *J* = 10.4, 10.4 Hz, 1H), 5.01 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.99 (m, 2H), 4.94 (dd, *J* = 9.6, 9.6 Hz, 1H), 4.85 (s, 1H), 4.84 (s, 1H), 4.71 (s, 1H), 4.21 (d, *J* = 8.8 Hz, 2H), 4.09 (dd, *J* = 9.6, 2.8 Hz, 1H), 3.94 (dd, *J* = 10.4, 3.2 Hz, 1H), 3.86 (br, 1H), 3.83 (dd, *J* = 9.6, 3.2 Hz, 1H), 3.80 (m, 3H), 3.69 (dq, *J* = 8.8, 6.4 Hz, 2H), 3.64 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 3.41 (ddd, *J* = 9.6, 6.8, 6.8 Hz, 1H), 2.46 (m, 1H), 2.33 (m, 1H), 2.13 (s, 3H), 2.08 (s, 3H), 2.04 (s, 3H), 1.63 (m, 4H), 1.29 (m, 17H), 1.17 (m, 6H), 1.11 (d, *J* = 6.4 Hz, 3H), 0.89 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 170.5, 170.4, 170.3, 167.4, 134.4, 125.7, 101.3, 99.4, 96.9, 96.1, 76.8, 75.5, 74.9, 73.6, 72.8, 72.3, 72.1, 71.8, 71.6, 69.4, 68.5, 68.5, 67.5, 67.2, 66.7, 41.0, 34.2, 32.0,

31.5, 29.5, 29.5, 29.4, 26.2, 24.7, 22.8, 22.4, 21.2, 21.1, 21.1, 18.1, 17.6, 17.5, 17.3, 14.3, 14.1; ; HRMS–MALDI–TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{46}H_{73}O_{20}Cl + Na]^+$: 1003.4276, Found: 1003.4259.

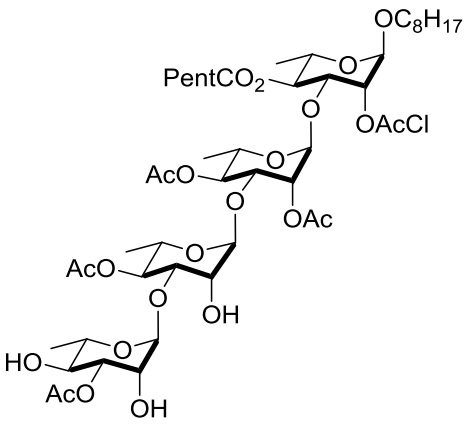
1-Octyloxy-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-*O*-diacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (25):



To a solution of allylic alcohol **24a** (18 mg, 0.018 mmol) in *t*-BuOH/acetone at 0 ºC was added a solution of (50% w/v) of *N*-methyl morpholine *N*-oxide/water (9.2 μL). Crystalline OsO_4 (0.3 mg, 5 mol%) was added and the reaction was stirred for 12 h. The reaction mixture was concentrated and was pipetted directly on to a silica gel column. The product was eluted with 3-5% MeOH/CH_2Cl_2 to afford triol **25** (16.2 mg, 0.016 mmol, 87%) as oil: R_f (10% MeOH/ CH_2Cl_2) = 0.3; $[\alpha]^{25}_D$ = – 31.6 (*c* = 0.2, CH_2Cl_2); IR (thin film, cm^{-1}) 3465, 2977, 2931, 2862, 1745, 1265, 1228, 1063, 733, 702; ^1H NMR (400 MHz, $CDCl_3$) δ 5.16 (s, 1H), 5.04 (dd, *J* = 10.0, 10.0 Hz, 1H), 5.01 (dd, *J* = 10.0, 10.0 Hz, 1H), 4.96 (dd, *J* = 10.2, 10.2 Hz, 1H), 4.94 (br, 1H), 4.84 (s, 1H), 4.80 (brs, 2H), 4.71 (s, 1H), 4.25 (d, *J* = 9.2 Hz, 2H), 4.09 (dd, *J* = 10.4, 3.2 Hz, 1H), 3.92 (dd, *J* = 9.6, 2.8 Hz, 1H), 3.86 (d, *J* = 8.8 Hz, 1H), 3.78 (m, 5H), 3.72 (dq, *J* = 8.8, 7.2 Hz, 2H), 3.64 (m, 1H), 3.44 (ddd, *J* = 9.6, 6.4, 6.4 Hz, 1H), 3.40 (m, 1H), 2.44 (m, 1H), 2.32 (m, 1H), 2.13 (s, 3H), 2.07 (s, 6H), 1.62 (m, 4H), 1.28 (m, 17H), 1.17 (m, 6H), 1.09 (d, *J* = 6.0 Hz, 3H), 0.88 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 171.5, 170.4, 170.3, 167.4, 102.1, 101.5, 99.5, 97.0, 76.8, 75.4, 74.7, 73.7, 73.0, 72.7, 72.3, 72.2, 71.7, 71.2, 69.1, 68.5, 67.5, 67.2,

66.7, 41.0, 34.2, 32.0, 31.5, 29.5, 29.4, 26.2, 24.7, 22.8, 22.4, 21.2, 21.2, 21.0, 17.6, 17.4, 17.3, 14.3, 14.1; HRMS–MALDI–TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{46}H_{75}O_{22}Cl + Na]^+$: 1037.4331, Found: 1037.4302.

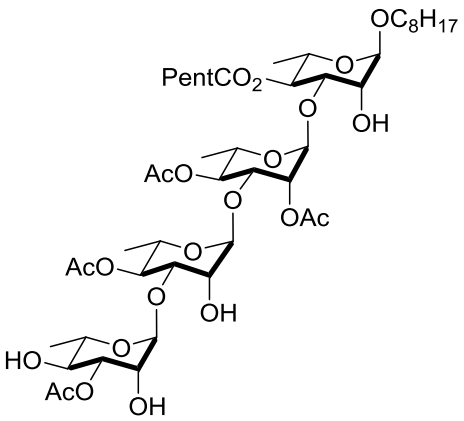
1-Octyloxy-3-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-*O*-diacetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-chloroacetyl-4-*O*-hexanoyl-α-L-rhamnopyranoside (25a):



To a stirred solution of triol **25** (12 mg, 0.012 mmol) in CH_3CN/THF (1:0.1) (0.22 mL) at 0 ºC was added boron catalyst (0.4 mg, 15 mol%), followed by addition of diisopropylethyl amine (DIPEA) (3.8 μL, 0.023 mmol) and acetyl chloride (1.5 μL, 0.023 mmol). Reaction was stirred at 0 ºC for 6 h. Monitored by TLC, reaction completed. Diluted with ethylacetate, washed with water, combined organic layers were concentrated under reduced pressure. The crude product was purified using silica gel chromatography, eluting with 55-60% EtOAc/hexane to get the desired product as oil **25a** (8.9 mg, 0.008 mmol, 71%): R_f (100% EtOAc) = 0.65; $[\alpha]^{25}_D$ = – 30.8 (c = 0.2, CH_2Cl_2); IR (thin film, cm^{-1}) 3453, 2927, 2825, 1745, 1379, 1258, 1232, 1137, 1087, 1046, 764, 750; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.18 (d, J = 1.5 Hz, 1H), 5.06 (dd, J = 9.6 Hz, 2H), 5.03 (dd, J = 9.6 Hz, 1H), 4.99 (br, 1H), 4.97 (br, 1H), 4.86 (br, 3H), 4.72 (s, 1H), 4.20 (d, J = 10.0 Hz, 2H), 4.09 (d, J = 9.6 Hz, 1H), 3.95 (d, J = 10.5 Hz, 1H), 3.90 (brs, 1H), 3.84 (m, 2H), 3.80 (dq, J = 9.2, 6.0 Hz, 3H), 3.71 (m, 1H), 3.66 (m, 1H), 3.62 (ddd, J = 9.6, 6.8, 6.8 Hz, 1H), 3.41 (ddd, J = 8.8, 5.6, 5.6 Hz, 1H), 2.43 (m, 1H), 2.33 (m, 1H), 2.15 (s, 3H), 2.13 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H), 1.63 (m, 4H), 1.33-1.25 (m, 17H), 1.18 (m, 6H), 1.12 (d, J = 6.0 Hz, 3H), 0.88 (br, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 171.8, 170.5, 170.4, 170.3, 167.4, 101.3, 101.0, 99.4, 97.0, 76.7, 75.6, 74.8, 74.7, 73.7, 72.7, 72.4, 72.1, 71.8, 71.4, 71.0, 69.8, 69.7, 68.5,

67.5, 67.3, 66.8, 41.0, 34.2, 32.0, 31.5, 29.5, 29.4, 26.3, 24.7, 22.9, 22.5, 21.3, 21.2, 21.1, 21.1, 17.7, 17.6, 17.5, 17.3, 14.3, 14.1; HRMS (ESI) calcd for $[C_{48}H_{77}O_{23}Cl + H]^+$: 1057.4622, Found:1057. 4635.

Mezzattiaside-5 (5):

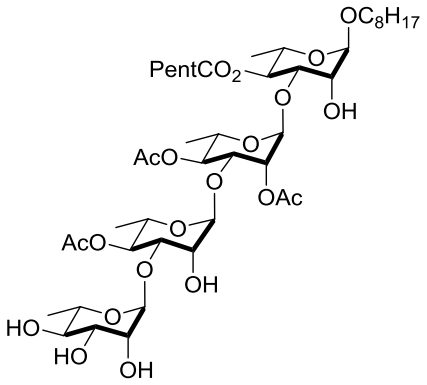


To a solution of tetrasaccharide triol **25a** (8 mg, 0.008 mmol) dissolved in THF (0.1 mL) was added thiourea (3.7 mg, 0.05 mmol), $NaHCO_3$ (2.4 mg, 0.03 mmol) and TBAI (1.5 mg, 0.004 mmol) and reaction was refluxed for 2 h. After 2 h, the reaction was brought to rt, diluted with ethyl acetate and washed with ammonium chloride solution (3 x 10 mL). Concentrated under reduced pressure and purified using silica gel chromatography, eluting with 65-70% EtOAc/hexane to give the desired product, Mezzattiaside-**5** (**5**) (6.5 mg, 0.007 mmol, 83%): R_f (100% EtOAc) = 0.5; $[\alpha]^{25}_D$ = – 69.3 (*c* = 0.35, $CHCl_3$); IR (thin film, cm^{-1}) 3455, 3338, 2958, 1741, 1264, 1044, 733, 704; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.12 (br, 1H), 5.07 (dd, *J* = 9.6, 9.6 Hz, 2H), 5.02 (dd, *J* = 10.4, 10.4 Hz, 1H), 5.01 (dd, *J* = 9.6, 2.4 Hz, 1H), 5.00 (d, *J* = 1.5 Hz, 1H), 4.88 (s, 1H), 4.84 (s, 1H), 4.81 (s, 1H), 4.24 (d, *J* = 9.6, 3.2 Hz, 1H), 3.96 (brm, 3H), 3.90 (m, 3H), 3.86 (dd, *J* = 9.6, 2.4 Hz, 1H), 3.80 (dq, *J* = 9.6, 6.4 Hz, 1H), 3.72 (dq, *J* = 9.6 6.4 Hz, 1H), 3.66 (ddd, *J* = 9.6, 6.4, 6.4 Hz, 1H), 3.57 (q, *J* = 9.6 Hz, 1H), 3.43 (ddd, *J* = 9.6, 6.4, 6.4 Hz, 1H), 3.14 (br, 2H), 2.47 (m, 1H), 2.39 (m, 1H), 2.16 (s, 3H), 2.15 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H), 1.63 (m, 4H), 1.36 (m, 6H), 1.29 (m, 12H), 1.19 (m, 6H), 1.10 (d, *J* = 6.0 Hz, 3H), 0.88 (br, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 172.0, 170.6, 170.3, 101.8, 100.9, 100.0, 99.4, 79.8, 75.9, 74.4, 72.6, 72.3, 72.2, 72.2, 71.6, 71.2, 71.0, 70.1, 69.6, 68.2, 67.3, 67.2, 66.3, 34.3, 32.0, 31.5, 29.6, 29.54, 29.45, 26.3, 24.7, 22.9, 22.5, 21.4, 21.3, 21.1, 21.0, 17.8, 17.7, 17.6, 17.3, 14.3,

14.1; HRMS–MALDI–TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{46}H_{76}O_{22} + Na]^+$: 1003.4720, Found:1003.4719.

NMR Data: ^{13}C NMR (100 MHz, $CD_3OD + C_6D_6$, (6:1)) δ 173.8, 171.8, 171.0, 170.9, 170.8, 102.8, 102.8, 100.6, 100.1, 78.9, 76.8, 75.3, 74.7, 73.1, 73.1, 72.7, 72.4, 71.3, 71.2, 70.4, 69.7, 69.2, 68.1, 68.0, 67.3, 67.1, 34.2, 32.2, 31.6, 29.7, 29.6, 29.6, 26.6, 24.8, 22.9, 22.6, 20.3, 20.2, 20.1, 17.2, 17.2, 17.0, 17.0, 13.8, 13.8.[8]

Mezzattiaside-7 (7):

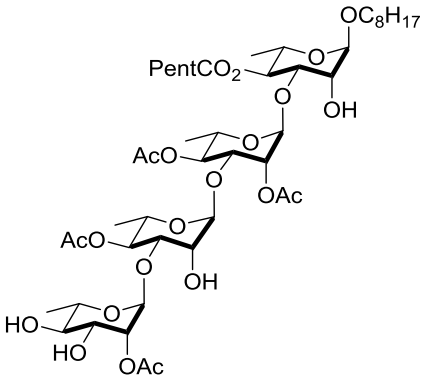


To a stirred solution of tetrasaccharide triol **25** (15 mg, 0.015 mmol) in THF (1 mL) was added thiourea (6.8 mg, 0.09 mmol), $NaHCO_3$ (4.4 mg, 0.05 mmol) and TBAI (2.7 mg, 0.007 mmol) and reaction refluxed for 3 h. The reaction was brought to room temperature and diluted with ethyl acetate, washed with saturated ammonium chloride solution extracted with EtOAc and concentrated under reduced pressure. The crude product was purified using column chromatography with 5% MeOH /DCM elution to get the desired product Mezzattiaside-**7** (**7**) (11.5 mg, 0.012 mmol, 83%): R_f(50% EtOAc/hexane) = 0.60; $[\alpha]^{25}_D = -55.6$ (*c* = 0.47, $CHCl_3$); IR (thin film, cm^{-1}) 3435, 2927, 1741, 1450, 1375, 1264, 1045, 896, 732, 703; ^1H NMR (500 MHz, $CD_3OD + C_6D_6$ (6:1)) δ 5.33 (dd, *J* = 9.5, 9.5 Hz, 1H), 5.25 (dd, *J* = 3.5, 2.0 Hz, 1H), 5.23 (dd, *J* = 10.5, 9.5 Hz, 1H), 5.23 (dd, *J* = 10.5, 9.5 Hz, 1H), 4.99 (s, 1H), 4.98 (d, *J* = 1.5 Hz, 1H), 4.96 (d, *J* = 1.0 Hz, 1H), 4.85 (d, *J* = 1.0 Hz, 1H), 4.44 (dd, *J* = 9.5, 3.5 Hz, 1H), 4.27 (m, 1H), 4.08 (m, 1H), 4.07 (m, 1H), 4.00 (m, 1H), 3.97 (dq, *J* = 9.5, 6.5 Hz, 1H), 3.94-3.91 (m, 4H), 3.90

[8] . Optical rotation for the isolated **Mezzettiaside-5**: $[\alpha]_D = -57$ (*c* = 0.37, $CHCl_3$) (Ref.1).

(m, 1H), 3.81 (ddd, *J* = 9.5, 7.0, 3.0 Hz, 1H), 3.59 (dd, *J* = 9.5, 9.5 Hz, 1H), 3.53 (ddd, *J* = 9.5, 6.5, 3.5 Hz, 1H), 2.65 (m, 1H), 2.52 (m, 1H), 2.20 (s, 3H), 2.19 (s, 3H), 2.16 (s, 3H), 1.77 (m, 4H), 1.45 (m, 17H), 1.31 (m, 6H), 1.28 (d, *J* = 6.0 Hz, 3H), 1.02 (m, 6H); ^{13}C NMR (100 MHz, $CD_3OD + C_6D_6$ (6:1)) δ 173.9, 171.1, 170.9, 170.8, 103.3, 102.8, 100.7, 100.2, 78.9, 76.9, 75.4, 73.2, 73.2, 73.1, 72.8, 72.4, 71.6, 71.4, 71.3, 69.6, 68.1, 68.0, 67.4, 67.2, 34.3, 32.2, 31.7, 29.7, 29.7, 26.6, 24.9, 23.0, 22.7, 20.2, 20.2, 20.2, 17.3, 17.2, 17.1, 17.0, 13.8, 13.7; HRMS–MALDI-TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{44}H_{74}O_{21} + Na]^+$: 961.4615, Found: 961.4645.
[9]

Mezzattiaside-6 (6):



To a solution of triol **25** (11 mg, 0.011 mmol) in 0.2 mL CH_2Cl_2 was added *p*-TsOH·H_2O (2 mg), triethylorthoacetate (19.5 μL, 0.11 mmol.) at 0 ºC. Stirred at 0 ºC for 1 h then added 0.1 mL 90% AcOH (*aq*). The reaction mixture was stirred for 30 min at 0 ºC and diluted with 5 mL EtOAc and washed with 2 mL saturated $NaHCO_3$ solution, then washed with 3 mL saturated brine, dried over Na_2SO_4. The organic layers were concentrated under reduced pressure to get the desired product. The crude product (9 mg) was further subjected directly to deprotection using thiourea (7.8 mg, 0.10 mmol), $NaHCO_3$ (5.0 mg, 0.06 mmol), *n*-Bu_4NI (3.1 mg, 0.01 mmol) in THF (0.1 mL) under reflux condition. Reaction was continued for 2 hr. Monitored by TLC, reaction completed, diluted with ethyl acetate and washed with saturated ammonium chloride solution.

[9] Optical rotation for the isolated **Mezzettiaside-7**: $[\alpha]_D = -63$ (*c* = 0.54, $CHCl_3$) (Ref.1).

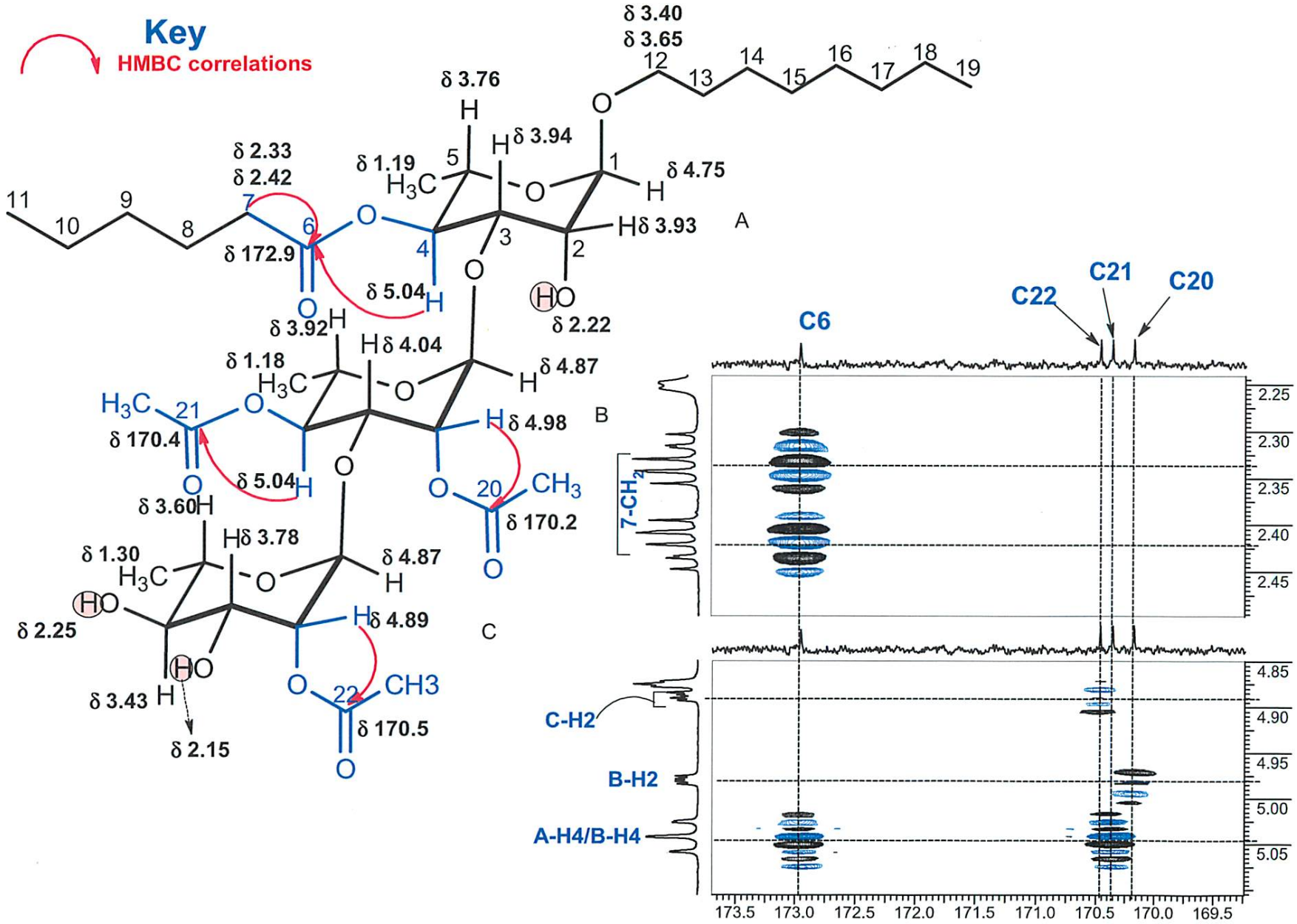
Washed with water and concentrated organic layer under reduced pressure. Finally, performed flash chromatography on silica gel eluting with 5-6% MeOH/ CH_2Cl_2 to give Mezzettiaside-**6** (**6**) (8.8 mg, 0.009 mmol, 83%): R_f (5% MeOH/ CH_2Cl_2) = 0.5; $[\alpha]^{25}_D = -37.6$ (c = 0.22, $CHCl_3$); IR (thin film, cm^{-1}) 3435, 2929, 2854, 1740, 1374, 1265, 1230, 1136, 1075, 1045, 733, 703; ^1H NMR (400 MHz, $CDCl_3$) δ 5.05 (dd, J = 9.6, 9.6 Hz, 1H), 5.03 (dd, J = 9.6, 9.6 Hz, 1H), 4.97 (br, 1H), 4.93 (dd, J = 10.4, 8.8 Hz, 1H), 4.92 (br, 1H), 4.86 (brs, 1H), 4.82 (br, 1H), 4.77 (brs, 2H), 4.18 (d, J = 9.6 Hz, 1H), 4.14 (d, J = 8.8 Hz, 1H), 3.94 (m, 2H), 3.91 (d, J = 10.4 Hz, 1H), 3.77 (m, 3H) 3.69-3.61 (m, 3H), 3.53 (dd, J = 9.6, 8.8 Hz, 1H), 3.42 (ddd, J = 9.6, 6.4, 6.4 Hz, 1H), 2.47 (m, 1H), 2.37 (m, 1H), 2.14 (s, 6H), 2.12 (s, 3H), 2.08 (s, 3H), 1.63 (m, 4H), 1.30 (m,17H), 1.19 (s, 6H), 1.12 (d, J = 6.0 Hz, 3H), 0.89 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 171.7, 171.4, 170.6, 170.0, 101.9, 99.85, 99.64, 99.4, 79.2, 78.4, 75.2, 73.2, 72.7, 72.6, 72.3, 72.1, 72.0, 71.3, 71.1, 69.04, 69.0, 68.2, 67.4, 67.3, 66.4, 34.3, 32.0, 31.5, 29.6, 29.5, 29.4, 26.3, 24.7, 22.9, 22.5, 21.4, 21.3, 21.1, 21.0, 17.7, 17.6, 17.5, 17.3, 14.3, 14.1; HRMS–MALDI-TOF (CCA) (m/z): $[M + Na]^+$ calcd for $[C_{46}H_{76}O_{22} + Na]^+$: 1003.4720, Found: 1003.4716.

^{13}C NMR (100 MHz, CD_3OD + C_6D_6, (6:1)) δ 173.9, 171.5, 171.4, 170.9, 170.8, 102.8, 100.6, 100.1, 100.1, 78.8, 76.9, 75.3, 73.4, 73.3, 73.1, 72.9, 72.7, 72.4, 71.3, 71.3, 69.5, 69.2, 68.1, 68.0, 67.3, 67.1, 34.2, 32.2, 31.6, 29.7, 29.6, 29.6, 26.6, 24.8, 22.9, 22.6, 20.3, 20.2, 20.1, 20.1, 17.2, 17.2, 17.0, 16.9, 13.8, 13.6.

[10]

[10] Optical rotation for the isolated **Mezzettiaside-6**: $[\alpha]_D = -35$ (c = 0.23, $CHCl_3$) (Ref.1).

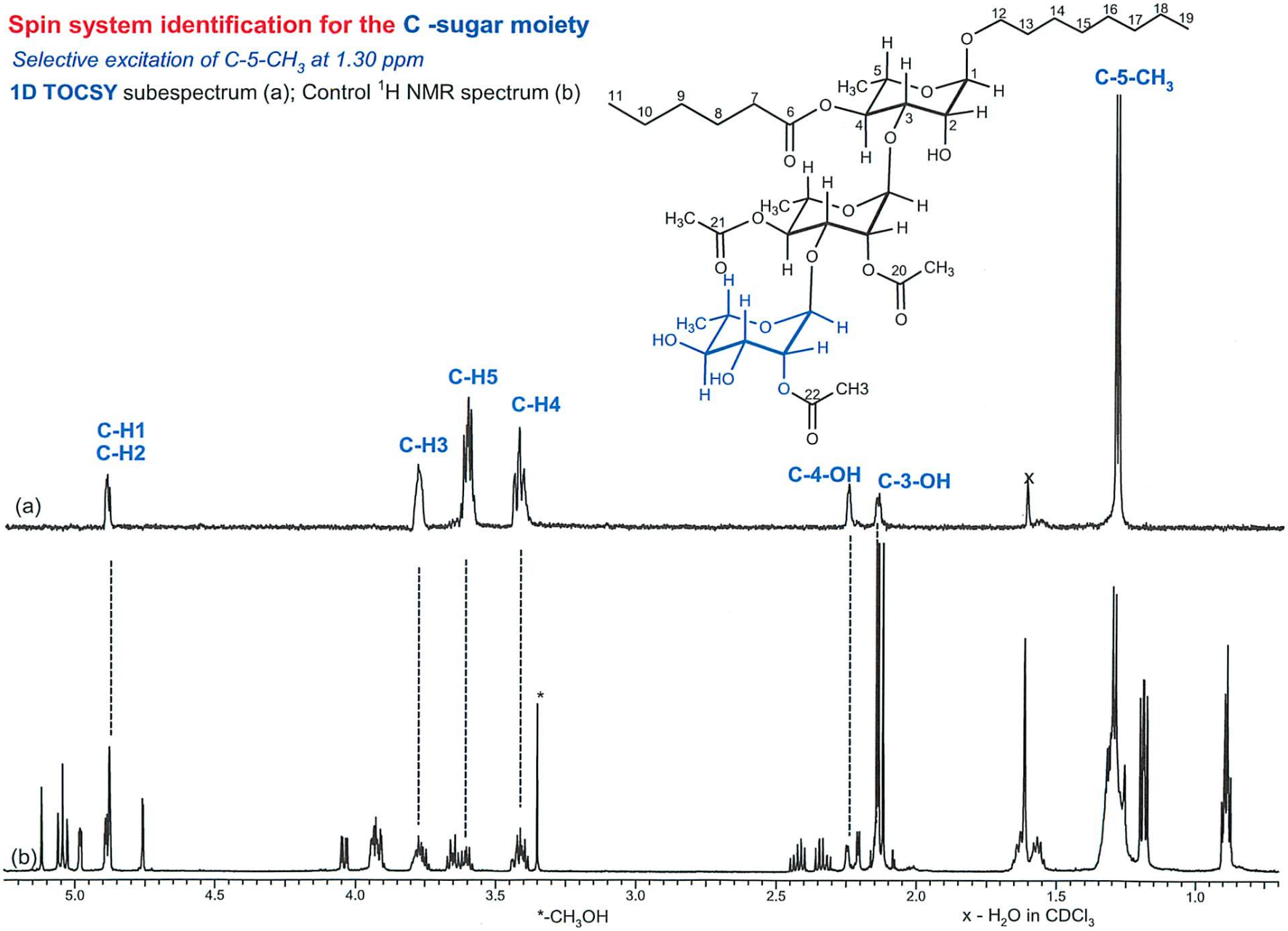
Mezzettiaside-8
(in $CDCl_3$, 600 MHz)



Spin system identification for the C -sugar moiety

Selective excitation of C-5-CH_3 at 1.30 ppm

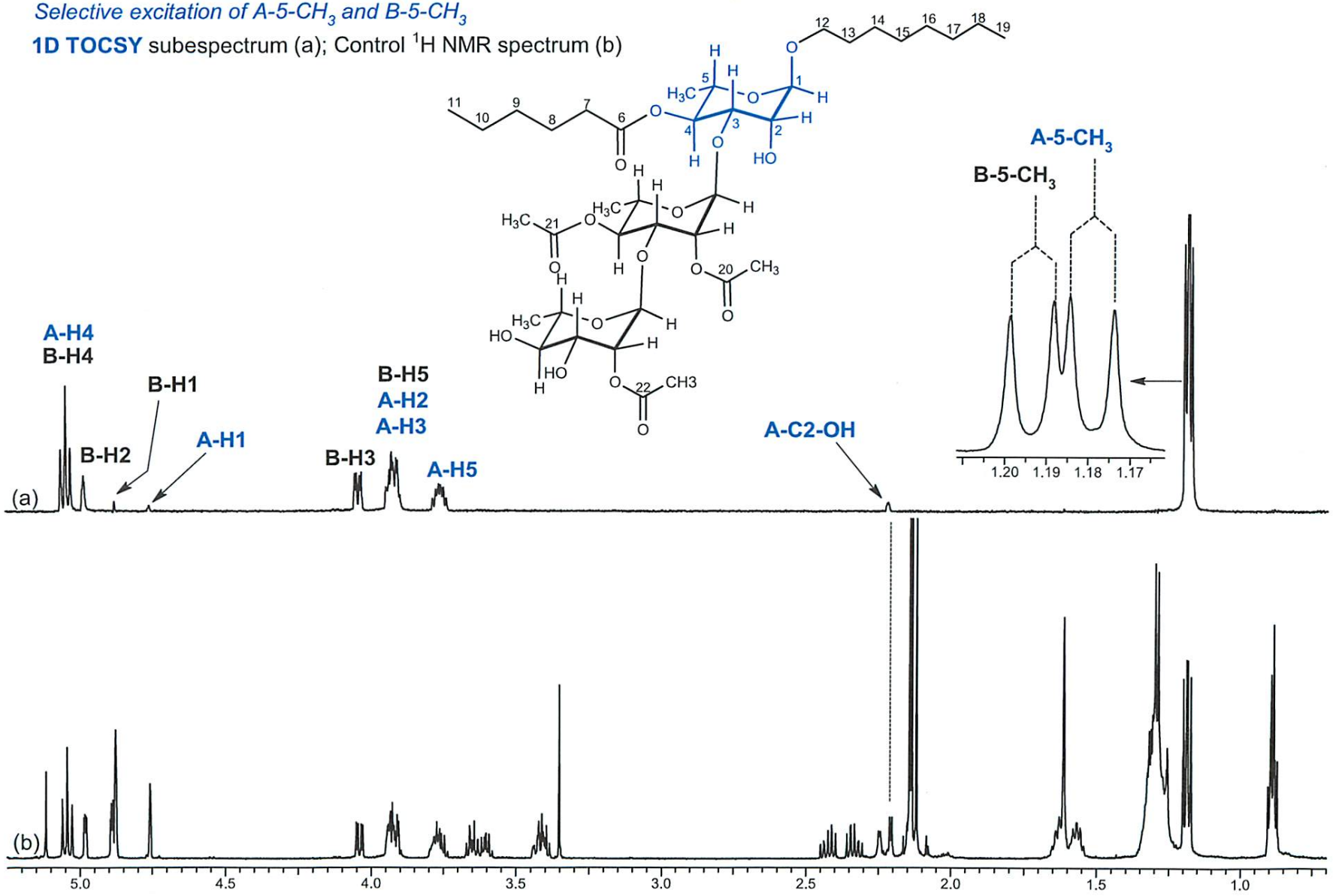
1D TOCSY subespectrum (a); Control ^{1}H NMR spectrum (b)

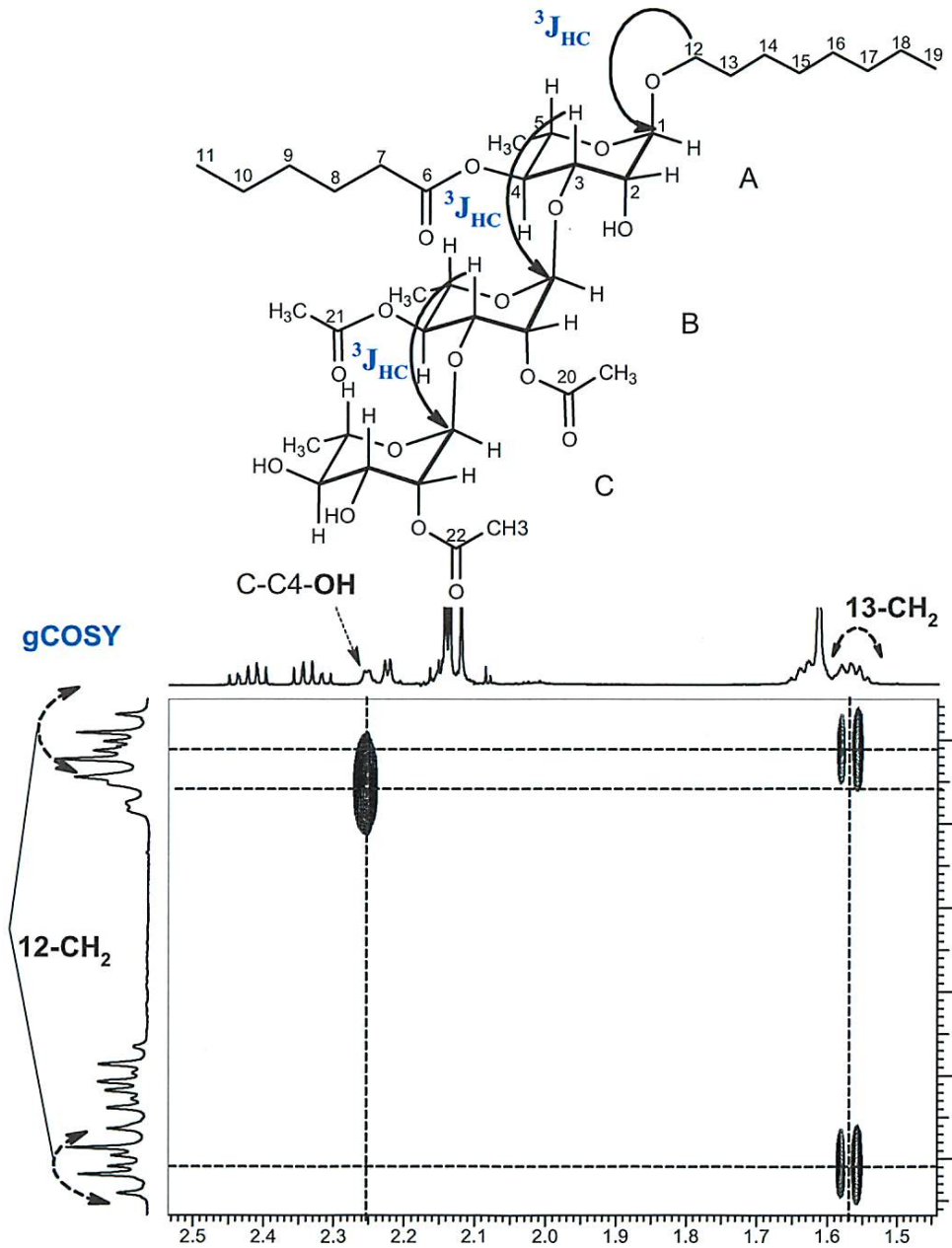


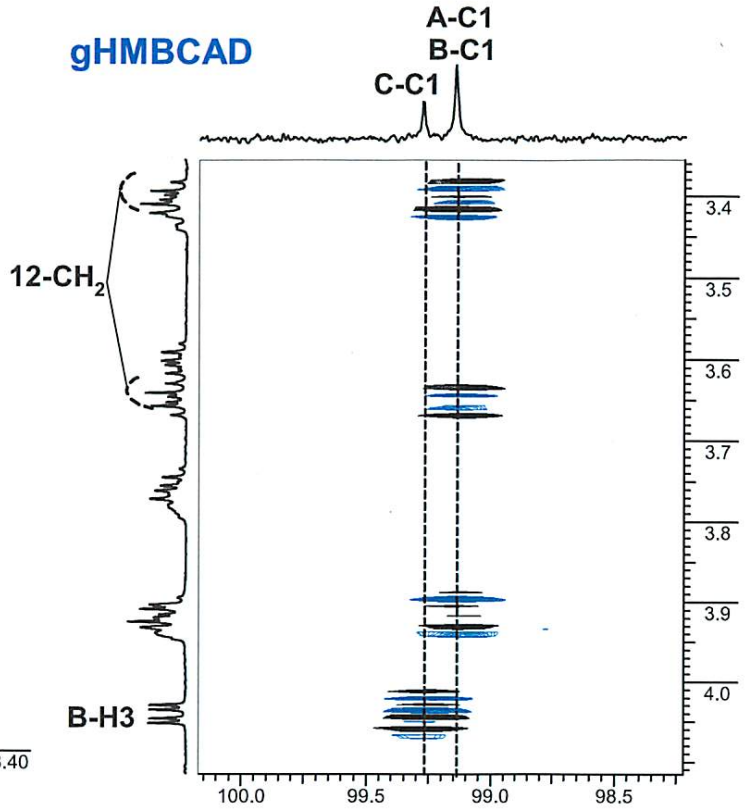
Spin system identification for the A -sugar moiety

Selective excitation of A-5-CH_3 and B-5-CH_3

1D TOCSY subespectrum (a); Control ^{1}H NMR spectrum (b)

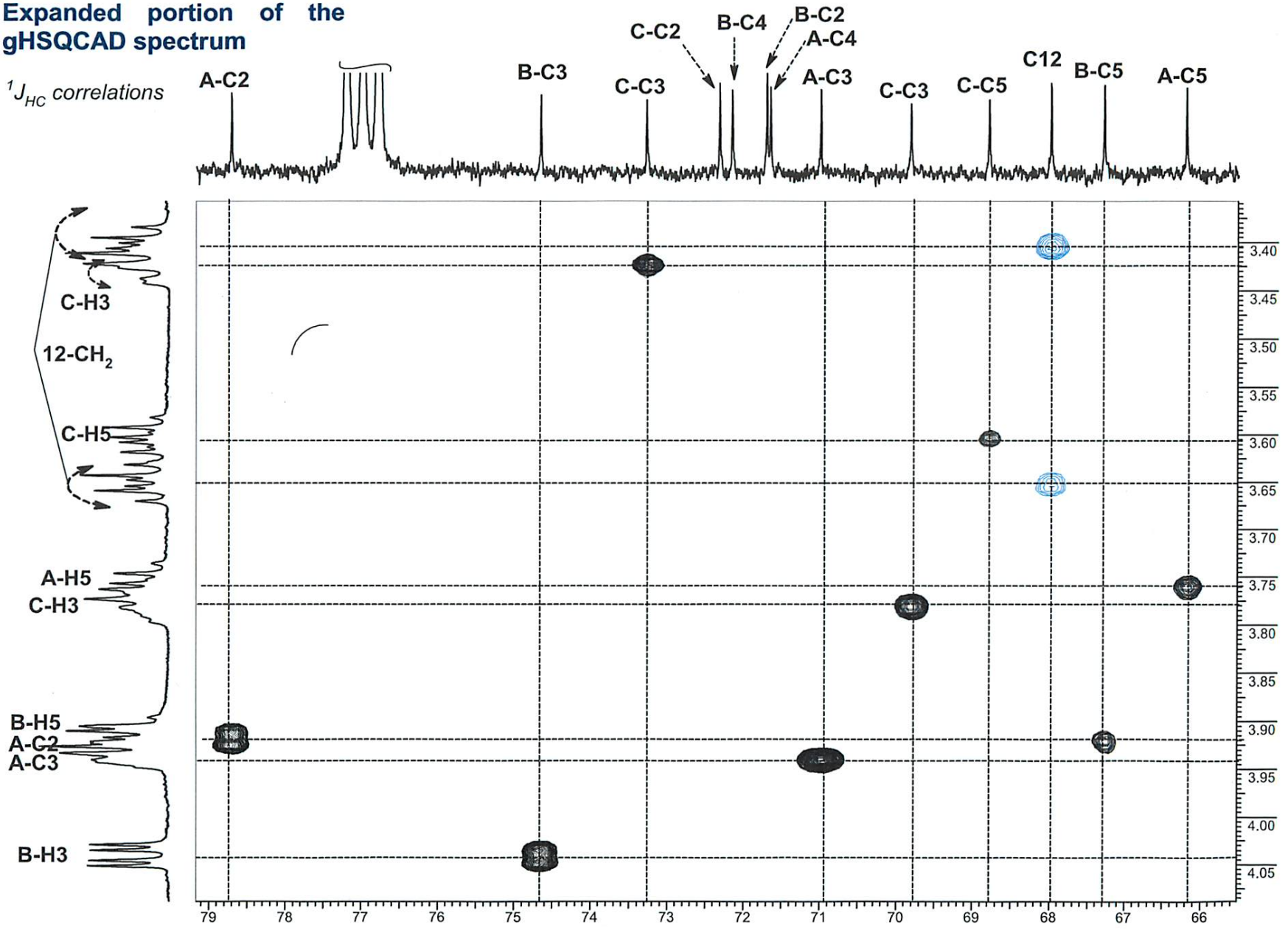



gCOSY
C-C4-OH
13-CH2
12-CH2
A
B
C
3J HC
3.40
3.45
3.50
3.55
3.60
3.65
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5

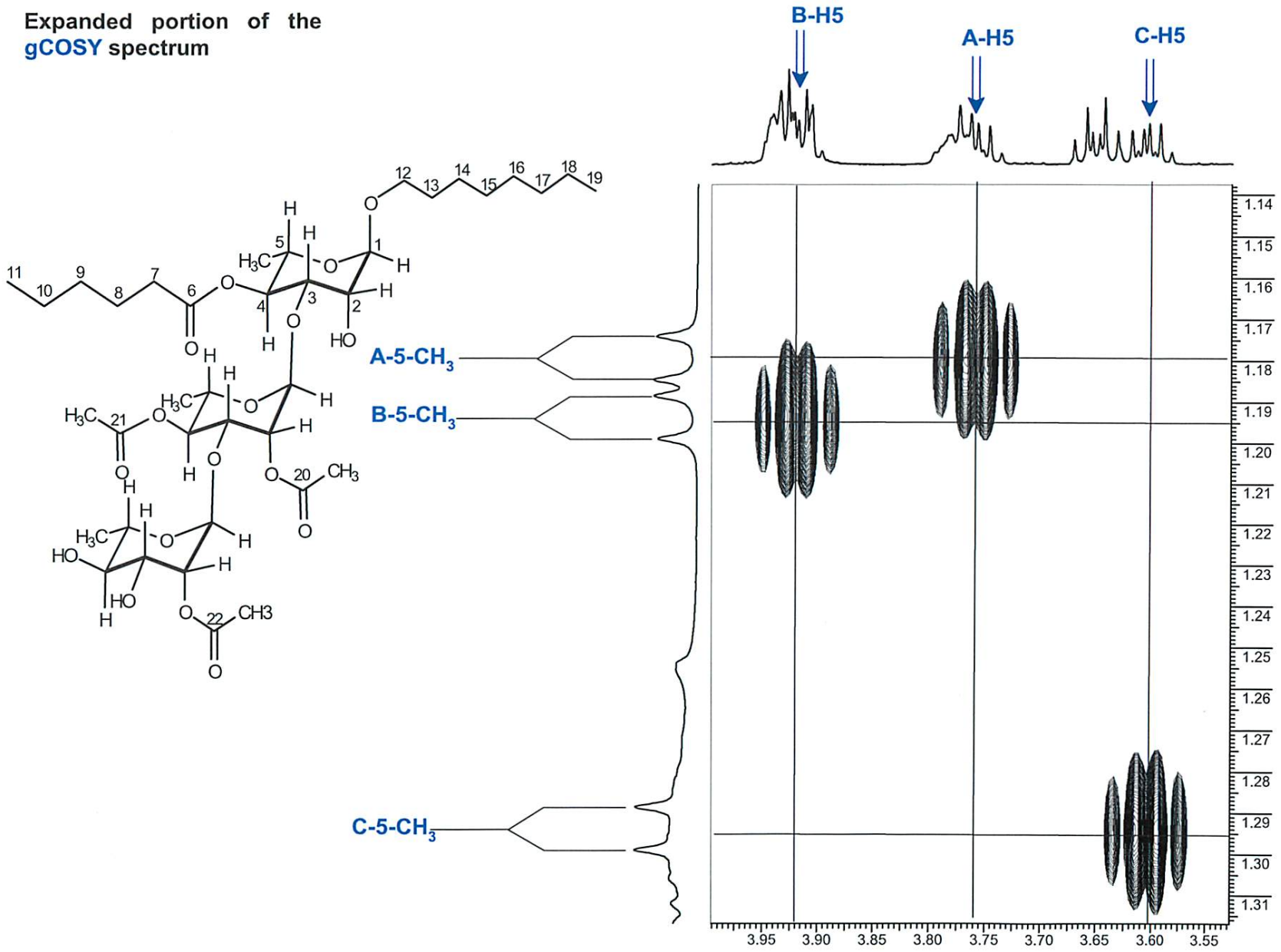

gHMBCAD
A-C1
B-C1
C-C1
12-CH2
B-H3
3.4
3.5
3.6
3.7
3.8
3.9
4.0
100.0
99.5
99.0
98.5

Expanded portion of the gHSQCAD spectrum

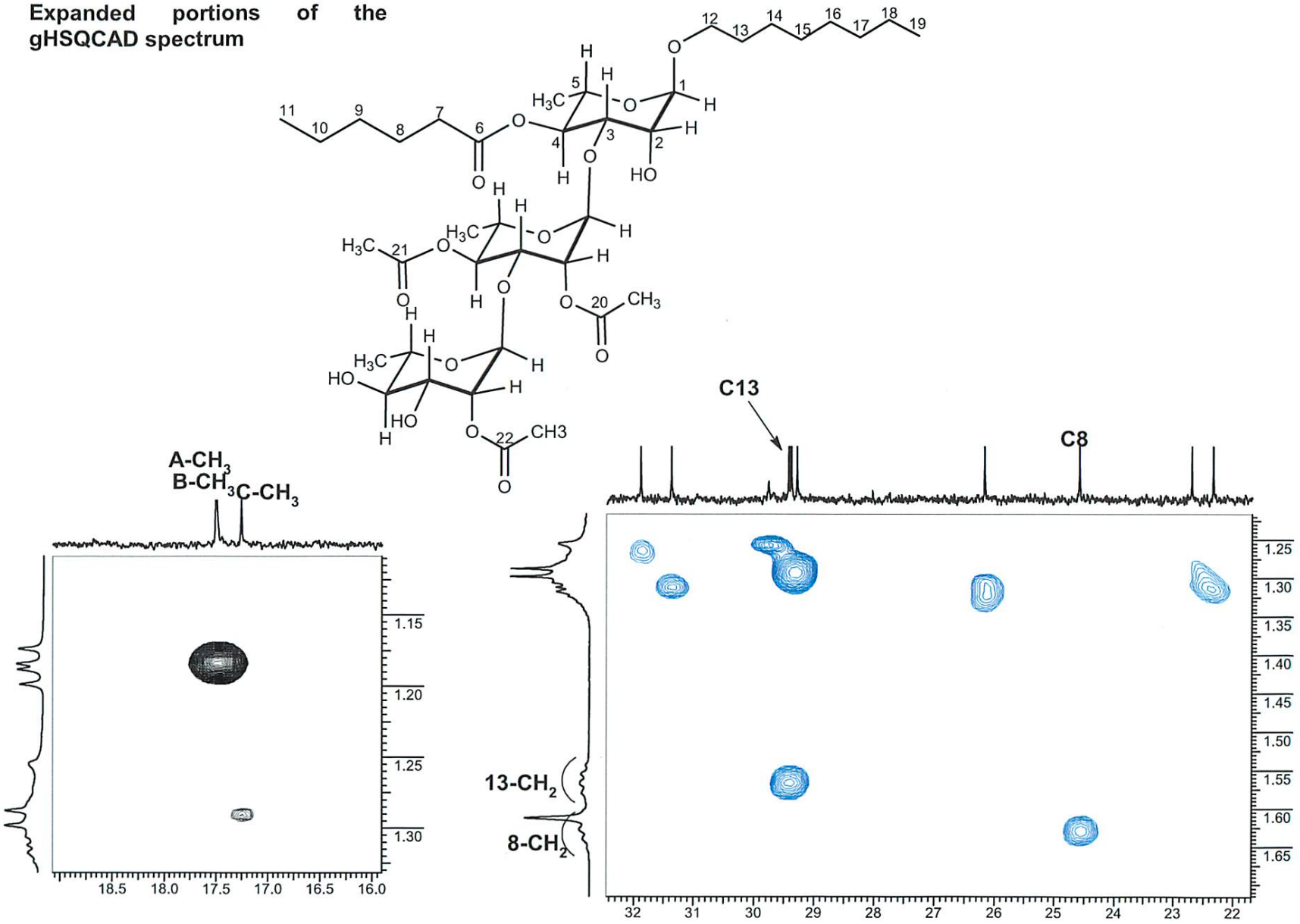
$^{1}J_{HC}$ *correlations*



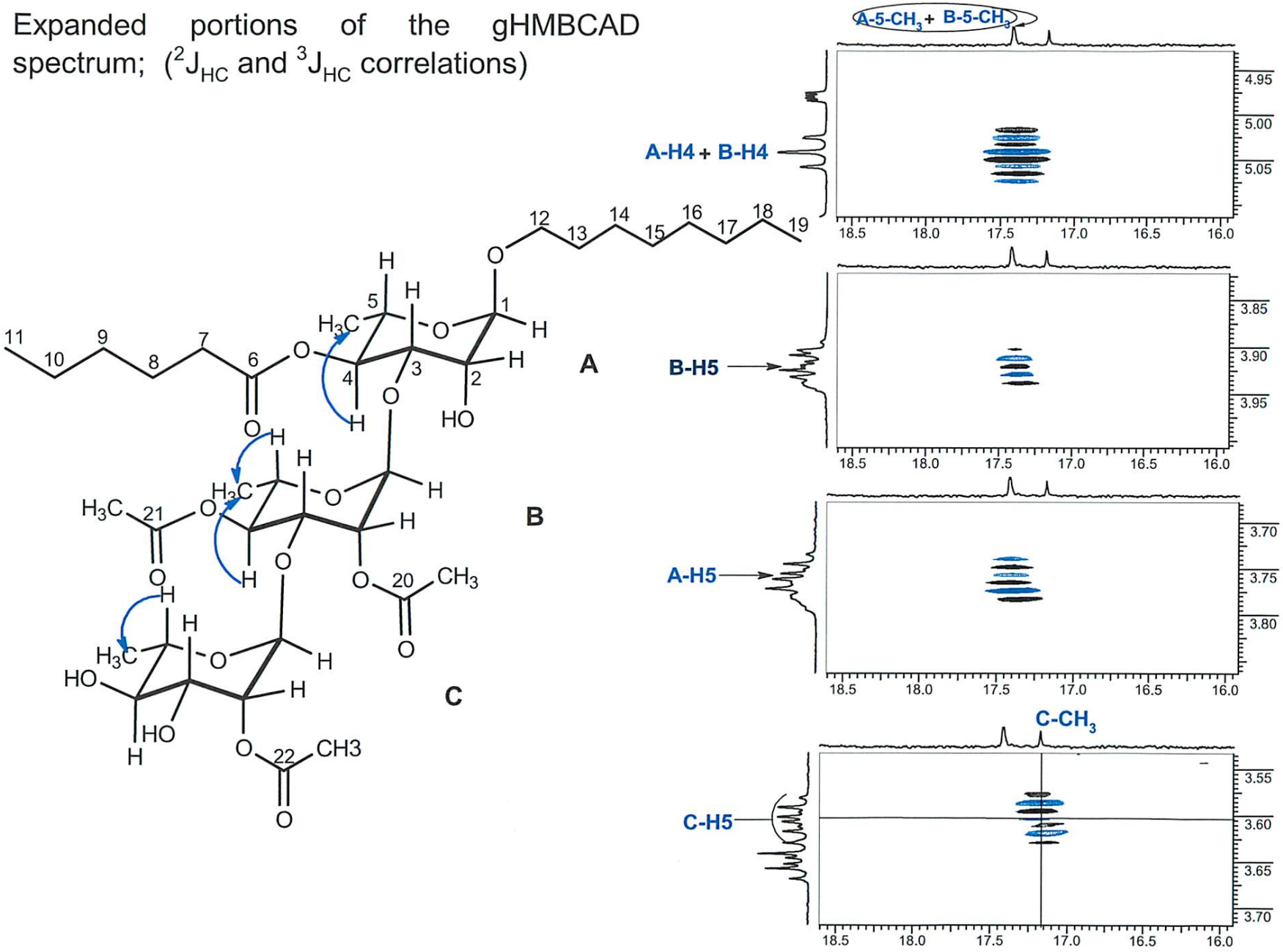
Expanded portion of the gCOSY spectrum

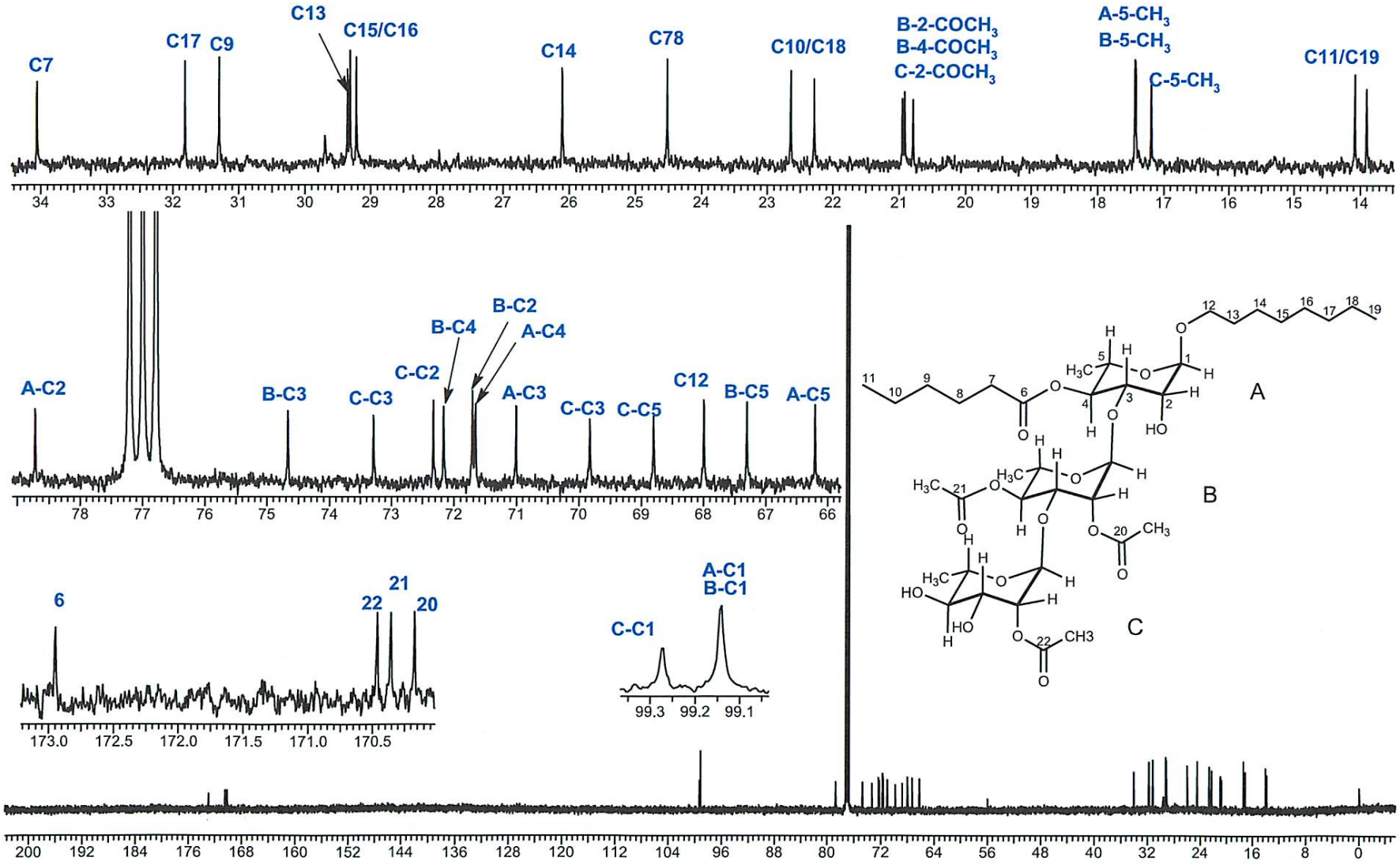


Expanded portions of the gHSQCAD spectrum



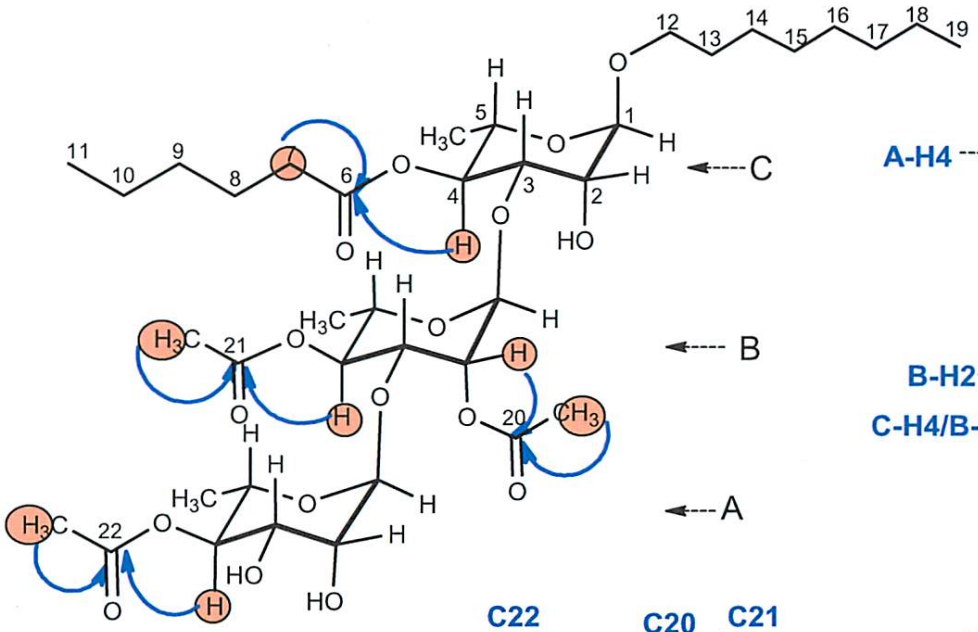
Expanded portions of the gHMBCAD spectrum; ($^2J_{HC}$ and $^3J_{HC}$ correlations)

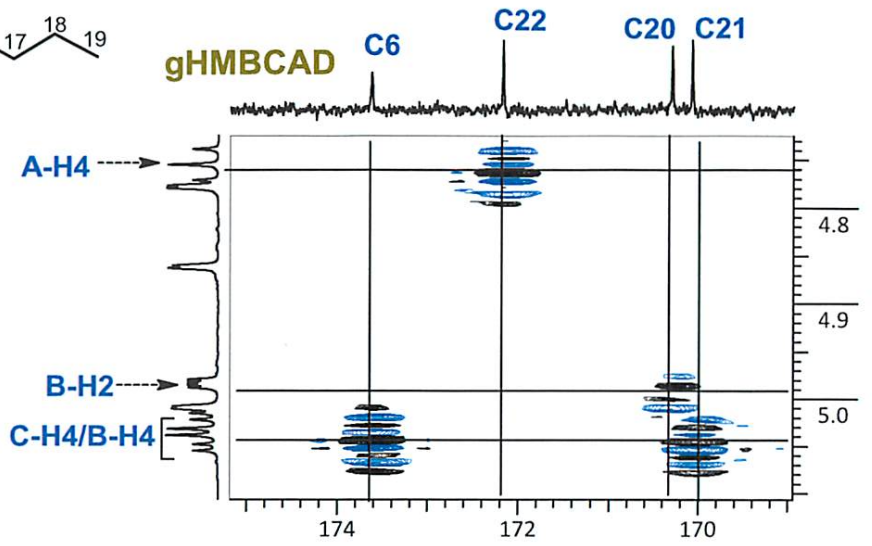


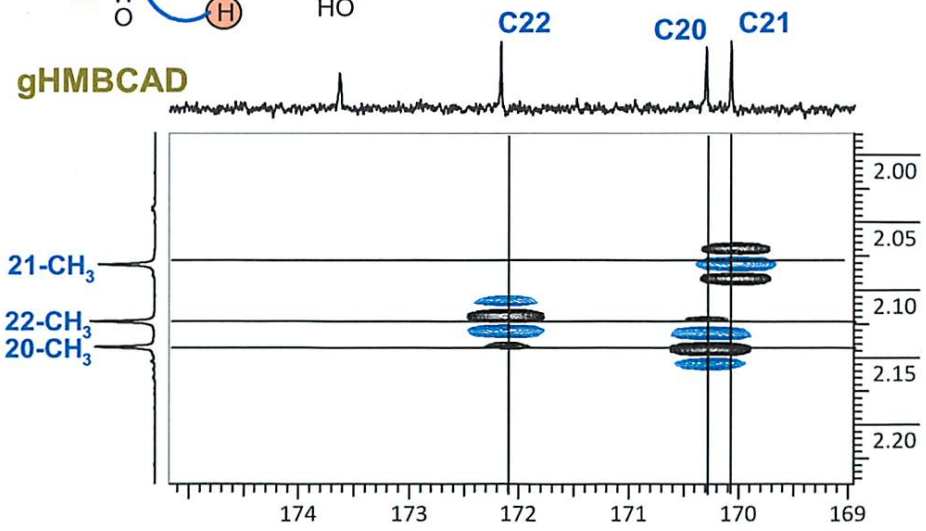

C7
C17
C9
C13
C15/C16
C14
C78
C10/C18
B-2-COCH3
B-4-COCH3
C-2-COCH3
A-5-CH3
B-5-CH3
C-5-CH3
C11/C19
A-C2
B-C3
C-C3
C-C2
B-C4
B-C2
A-C4
A-C3
C-C3
C-C5
C12
B-C5
A-C5
6
22
21
20
A-C1
B-C1
C-C1
A
B
C

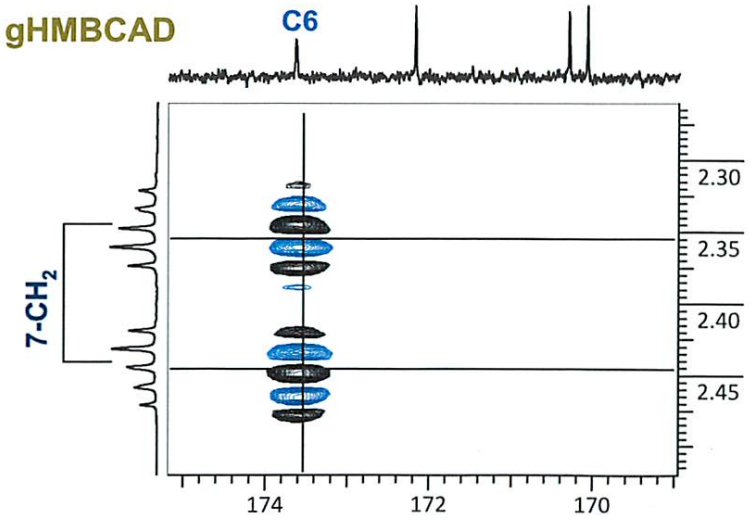
Mezzettiaside-4
(in $CDCl_3$, 600 MHz)

Proton and carbon chemical shift assigment for CO of three Acyl groups on the baisis of two and three bond HMBC correlations

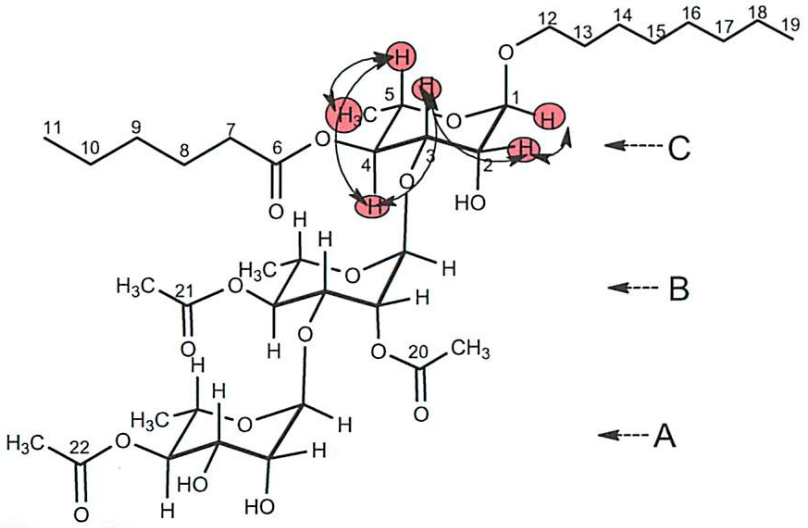


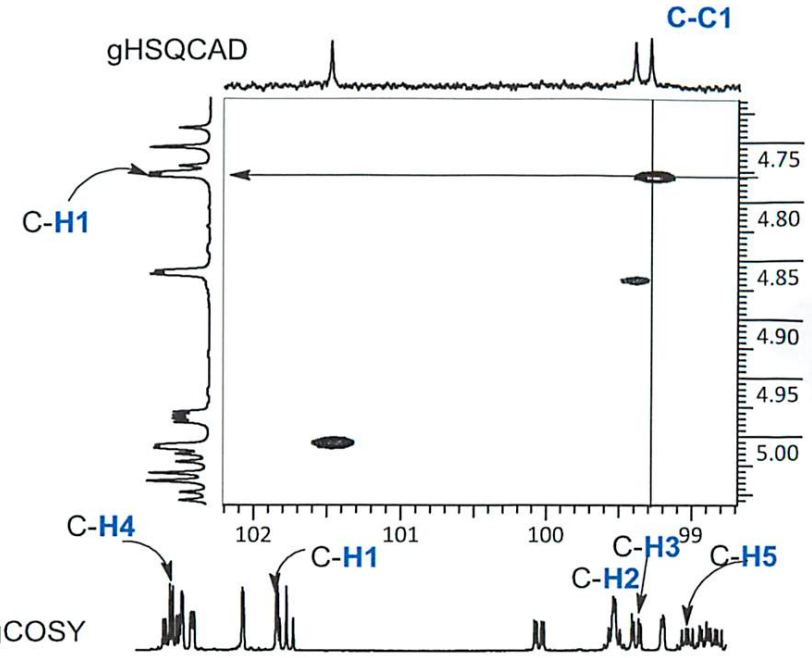




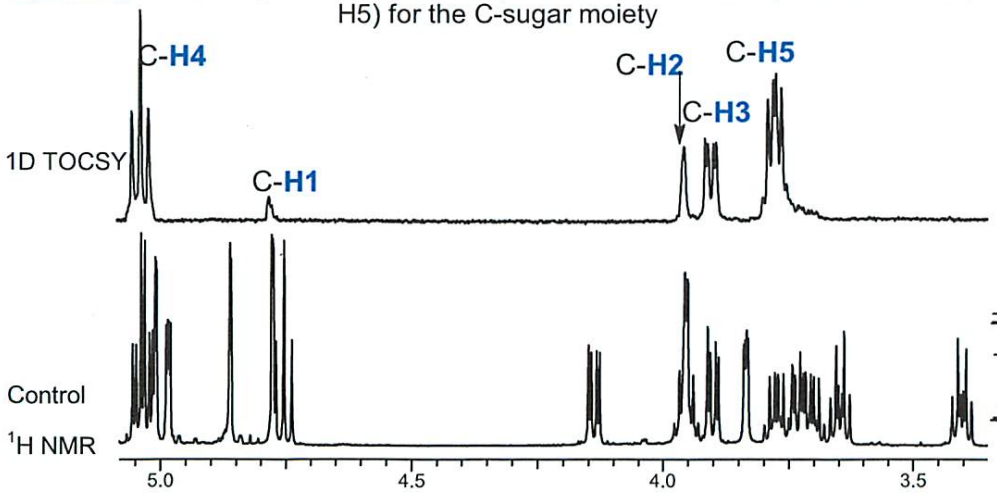


Step-2: assigment of C-**H1** (anomeric proton) on the basis of previously assigned **C-C1 at 99.22 ppm**



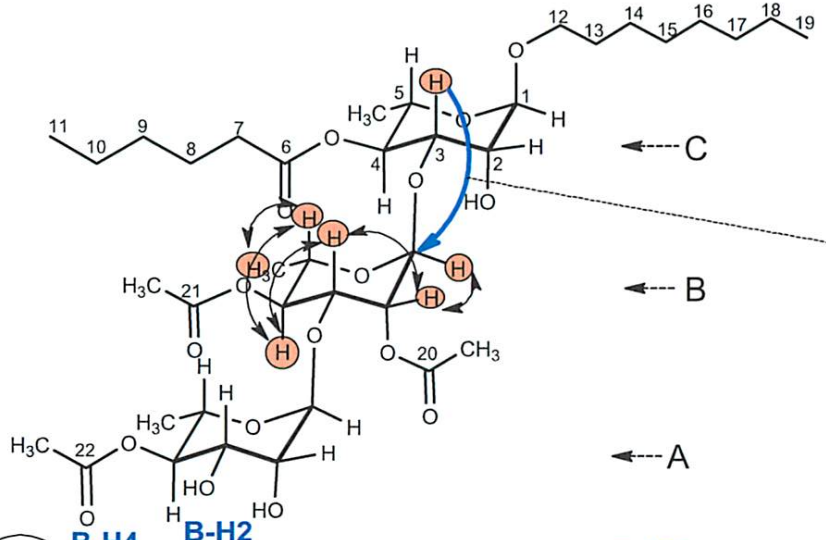


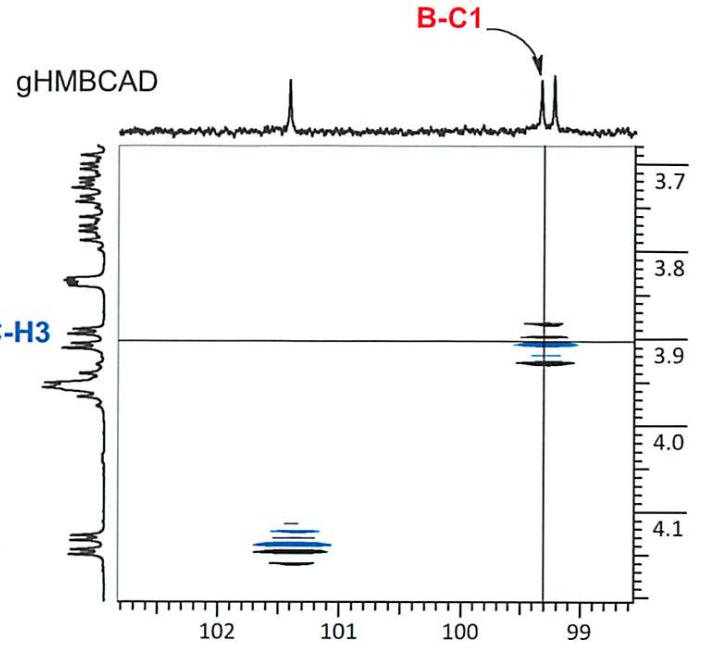
Step-3: on the basis of observed **COSY cross peaks** and **1D TOCSY spectrum** were assigned the remaining proton chemical shifts (H2, H3, H4, and H5) for the C-sugar moiety

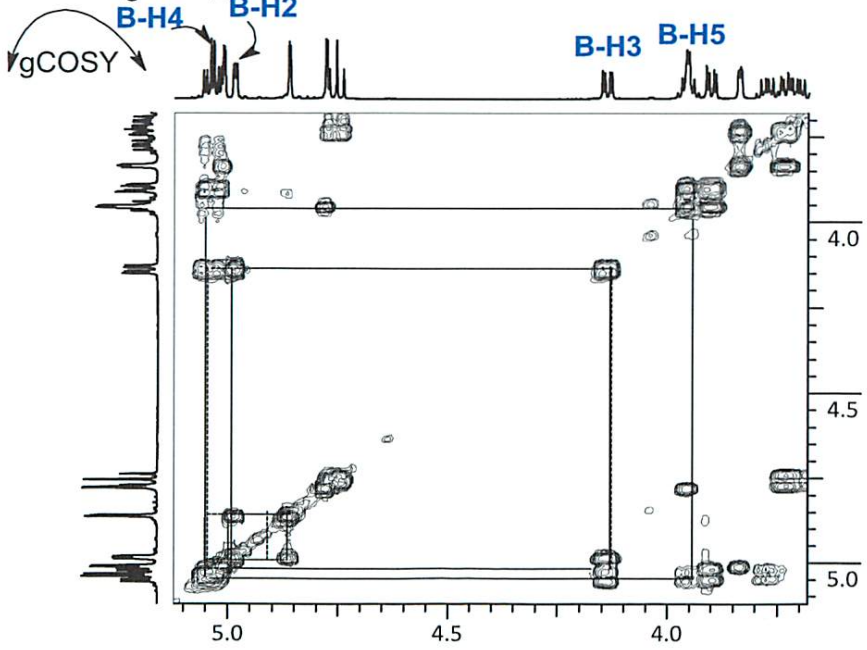


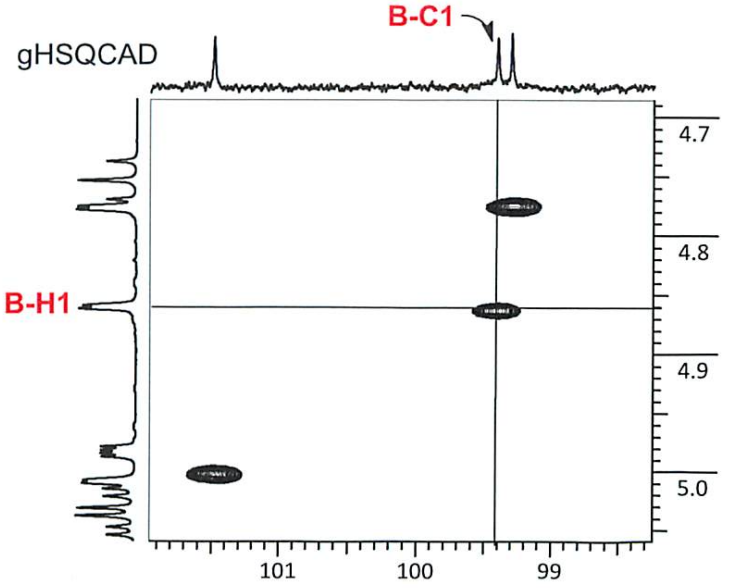
Continued

Step-5: linkage confirmation between **C and B sugar moieties**

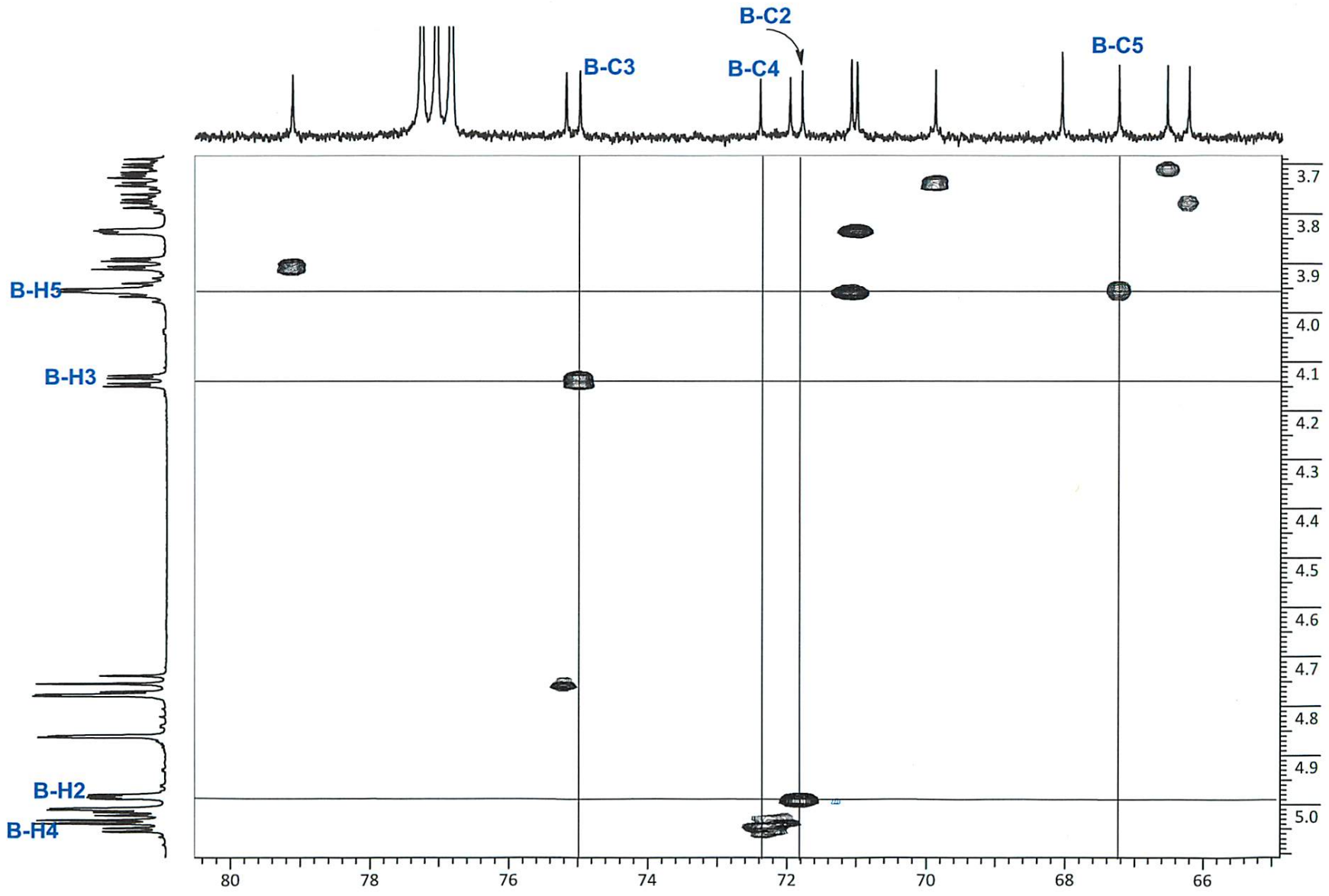






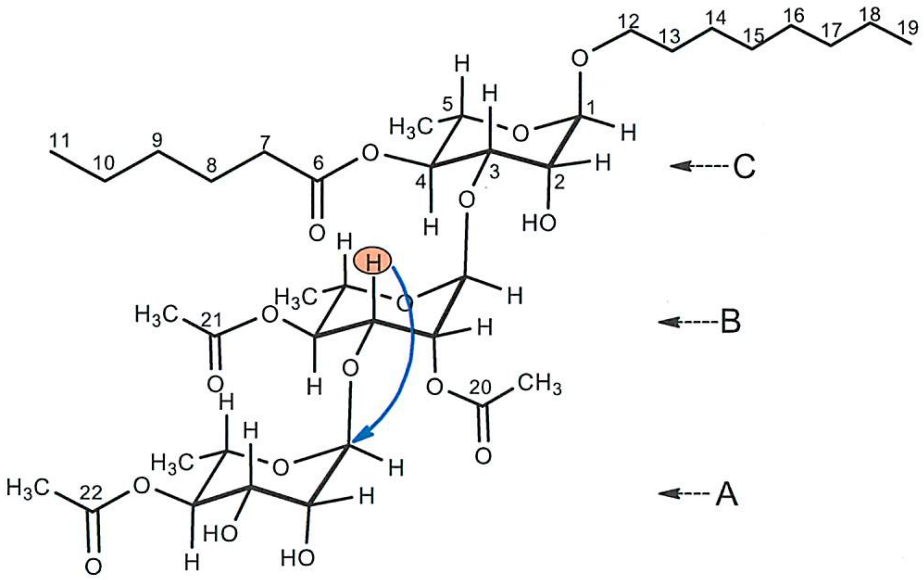


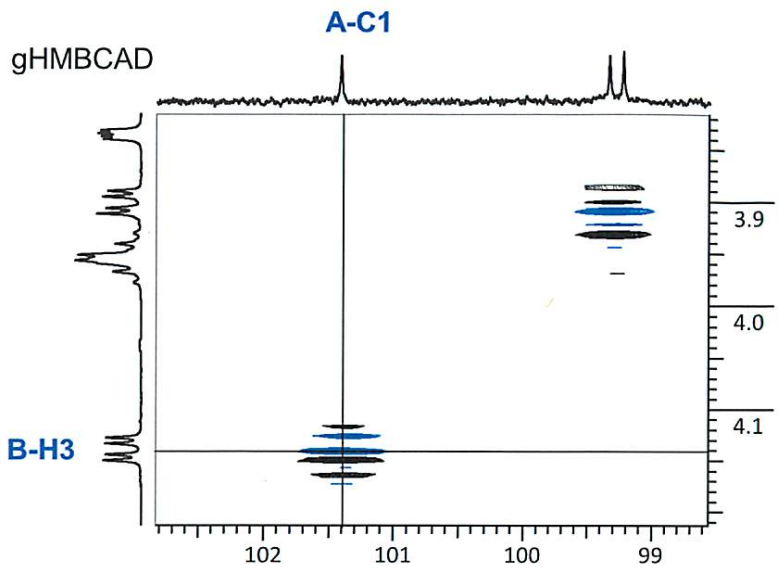
Step-6: carbon chemical shift assigments for the **B-sugar moiety**

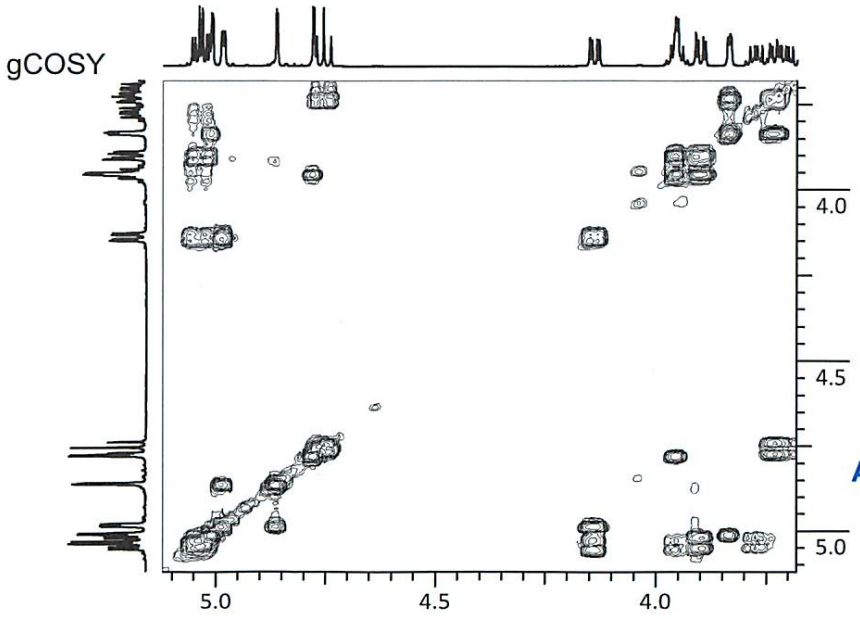


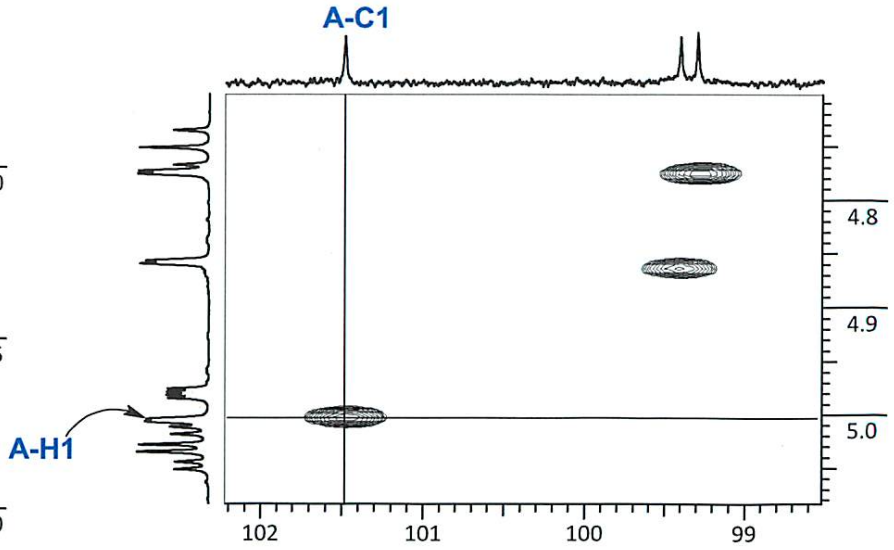
Continued

Step-7: linkage confirmation between **B and A sugar moieties**

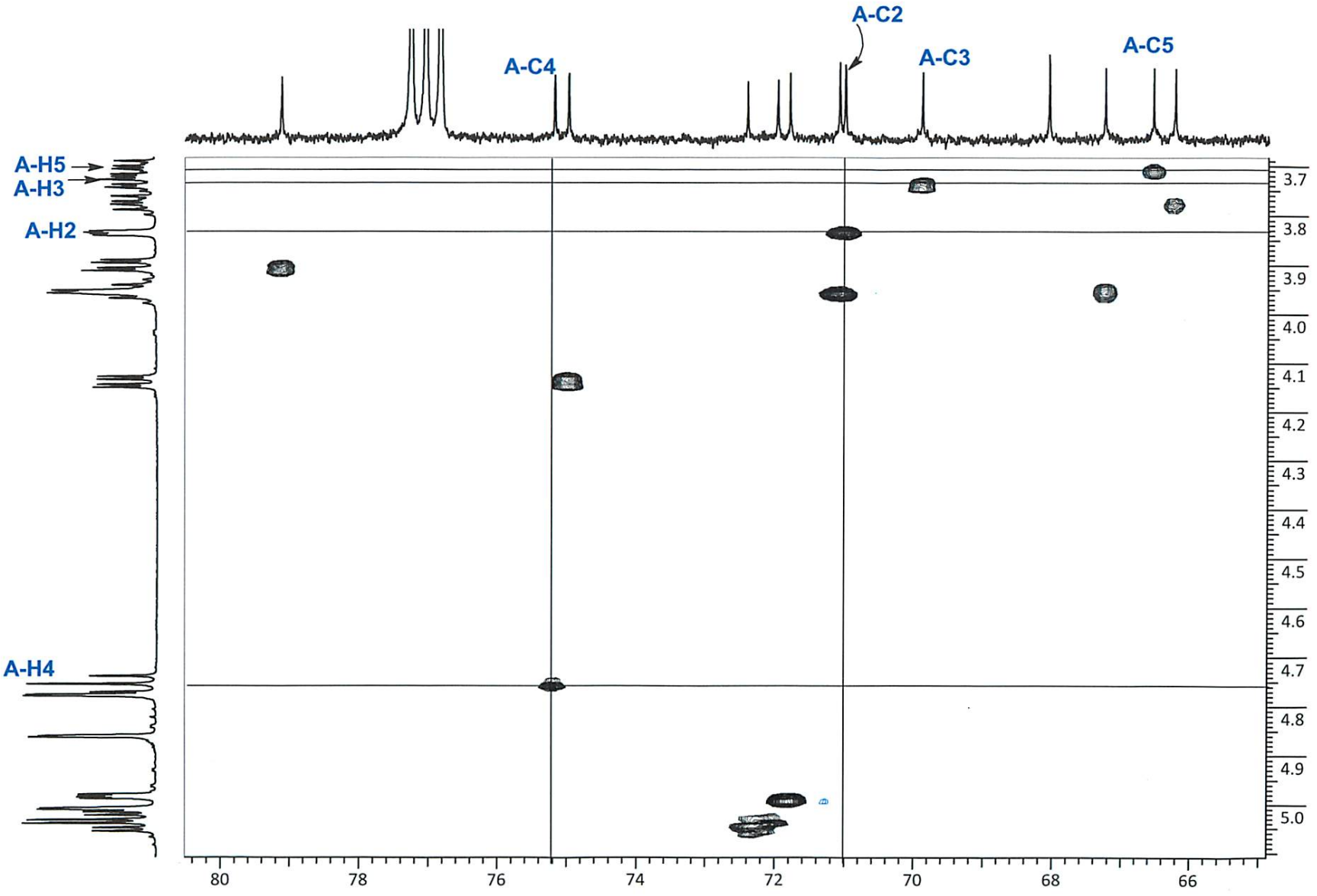


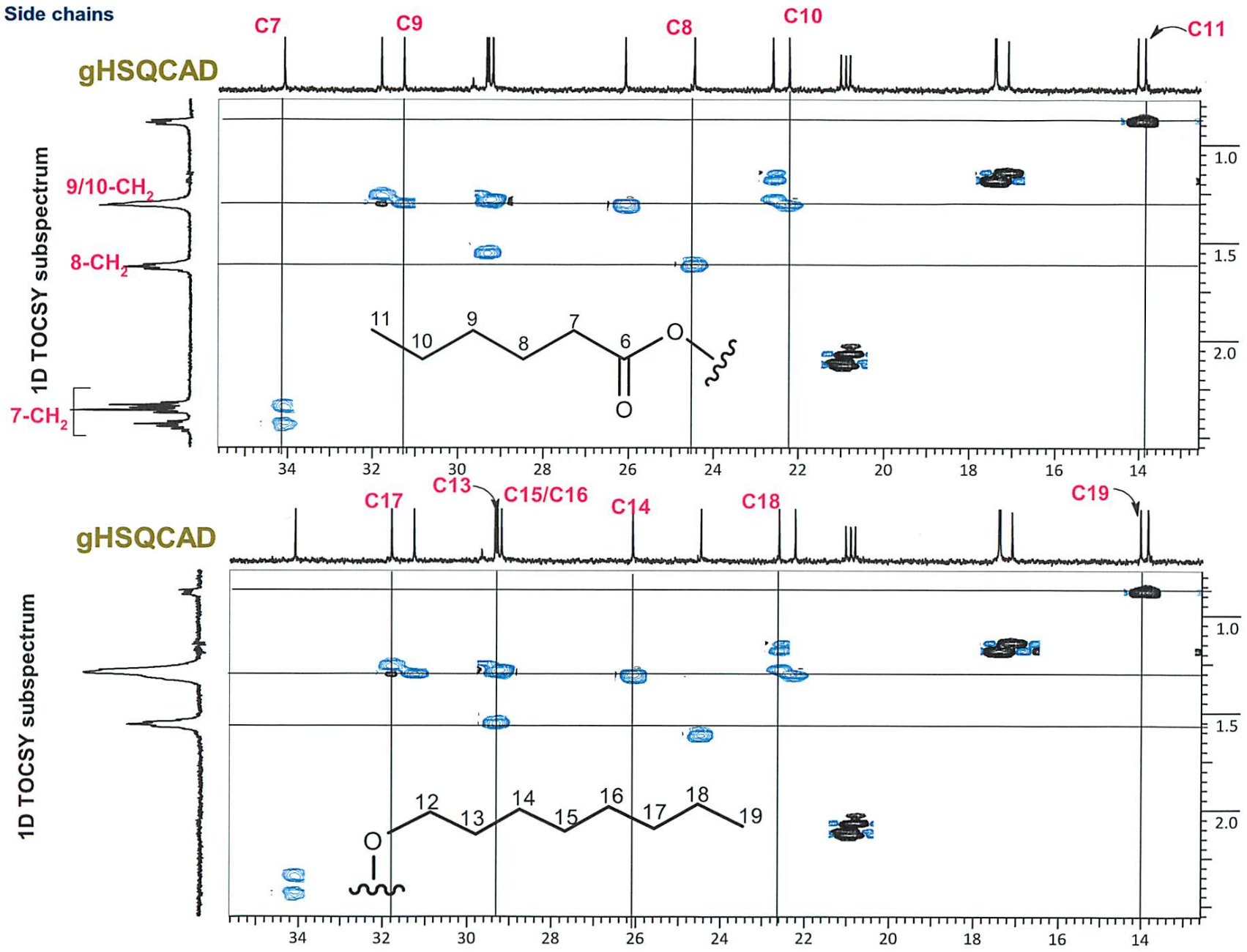






Step-7: carbon chemical shift assigments for the **A-sugar** moiety

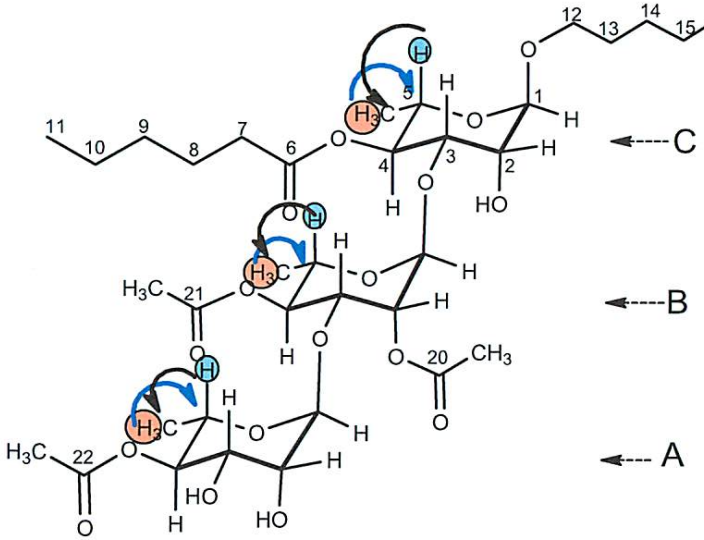


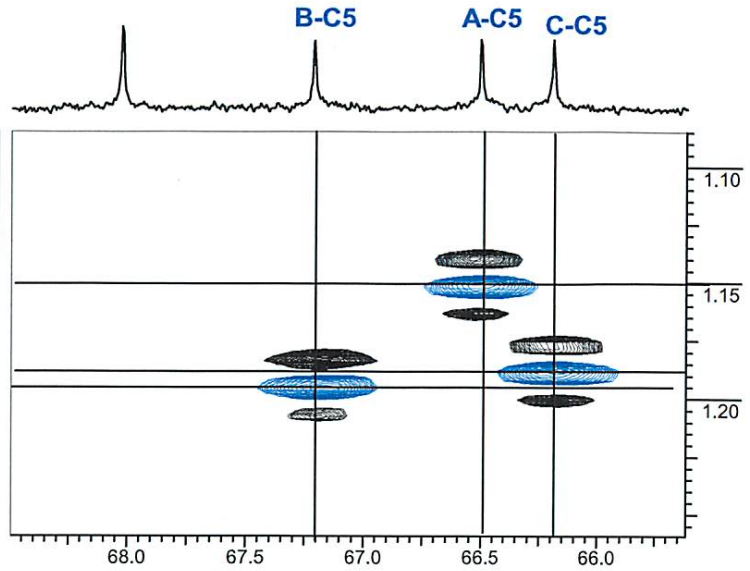

Side chains
gHSQCAD
C7
C9
C8
C10
C11
1D TOCSY subspectrum
9/10-CH2
8-CH2
7-CH2
11
10
9
8
7
6
O
O
1.0
1.5
2.0
34
32
30
28
26
24
22
20
18
16
14
gHSQCAD
C17
C13
C15/C16
C14
C18
C19
1D TOCSY subspectrum
12
13
14
15
16
17
18
19
O
1.0
1.5
2.0
34
32
30
28
26
24
22
20
18
16
14

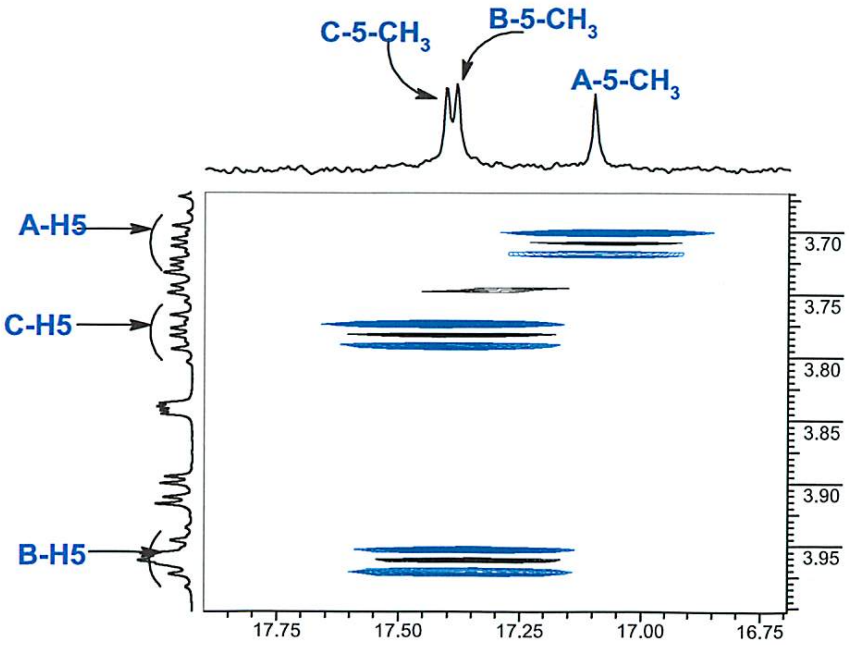
Carbon chemical shift assigment of C5 for A, B, and C sugar moities based on the two bond

CRISIS-gc2h2bc

correlations







Carbon chemical shift assigment for 5-CH_3's for A, B, and C sugar moities based on the two bond

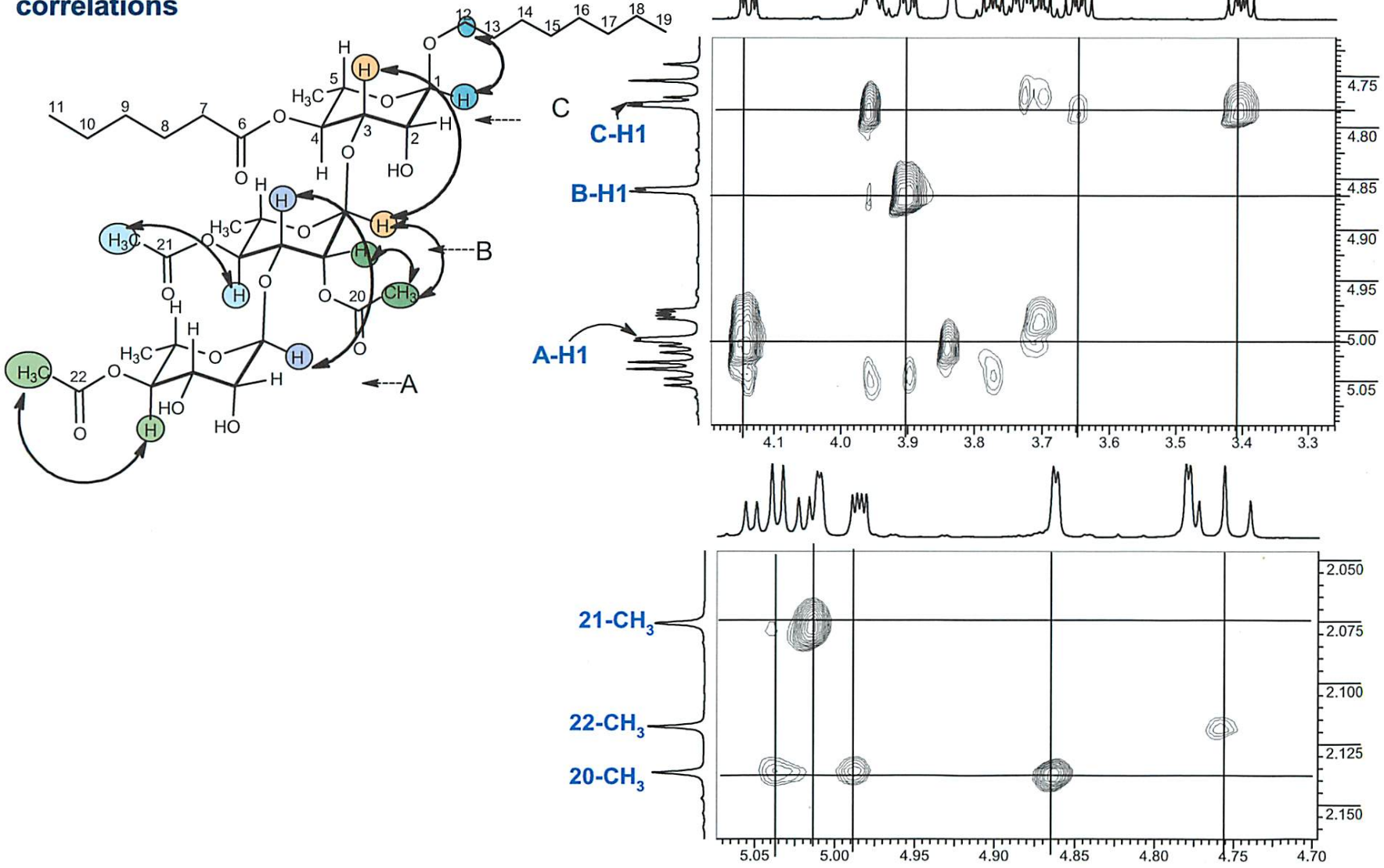
CRISIS-gc2h2bc

correlations

Key through space

ROESYAD

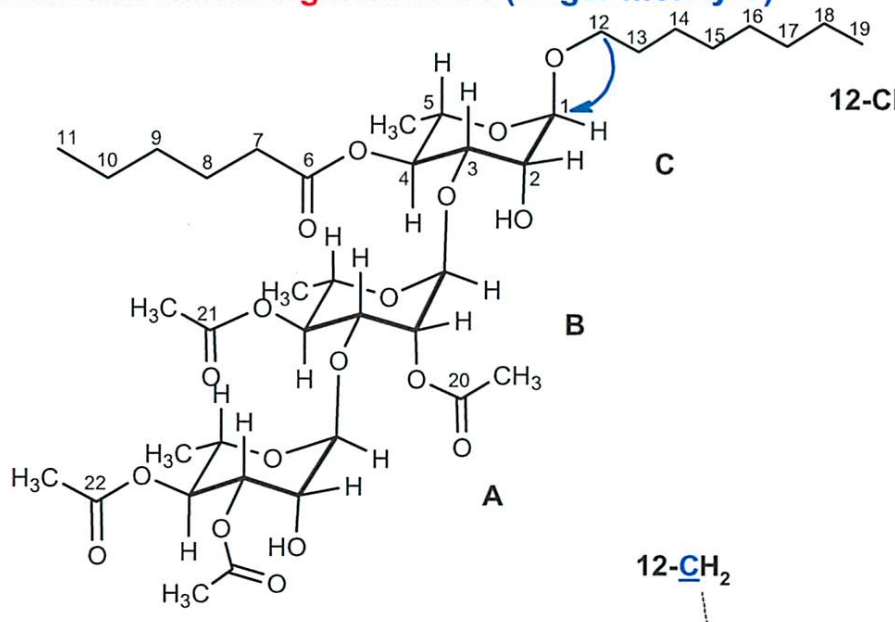
correlations



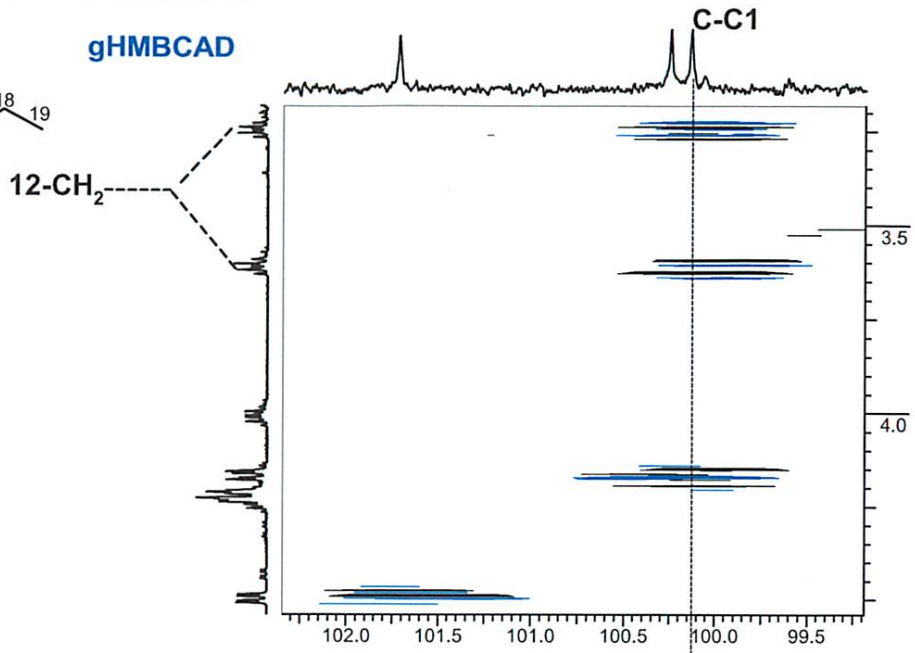
Mezzettiaside-3
(in C_6D_6, 600 MHz)

Step 1:

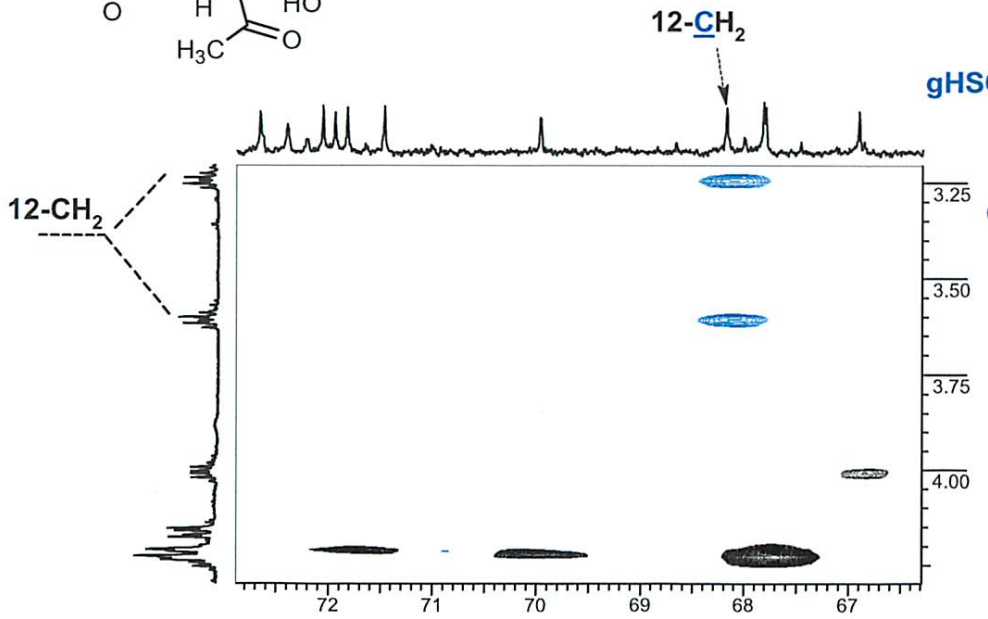
Chemical shift assigment of C1 (Sugar moiety C)

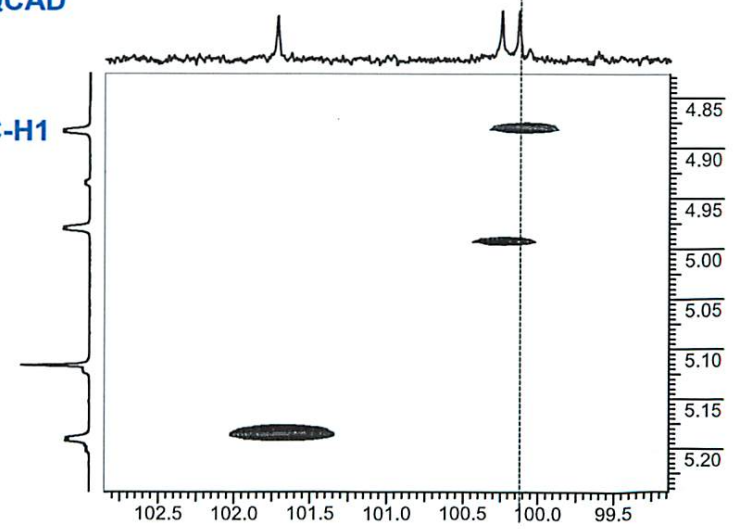


gHMBCAD



gHSQCAD

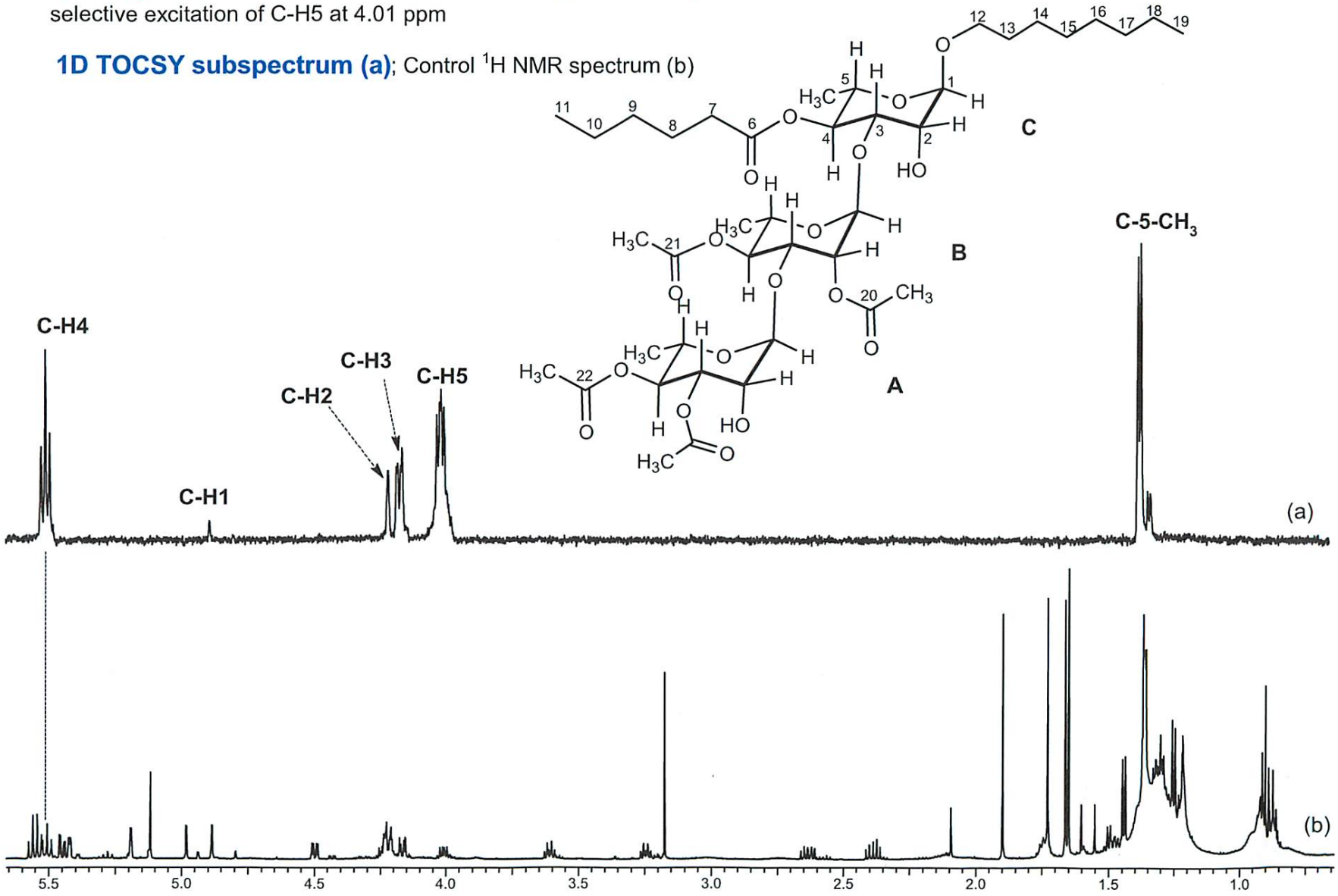


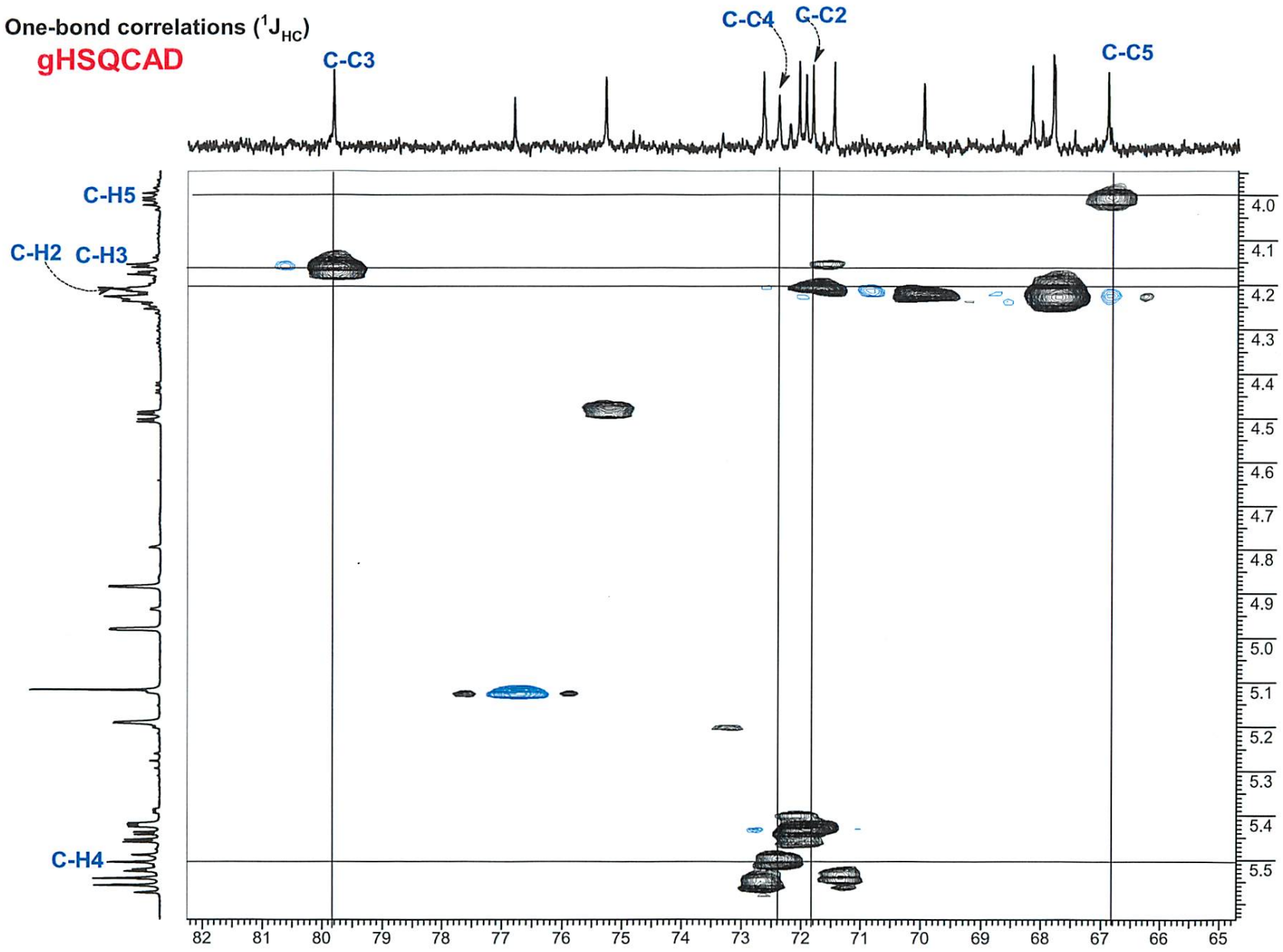


Spin system identification for the sugar moiety C

selective excitation of C-H5 at 4.01 ppm

1D TOCSY subspectrum (a); Control ^{1}H NMR spectrum (b)

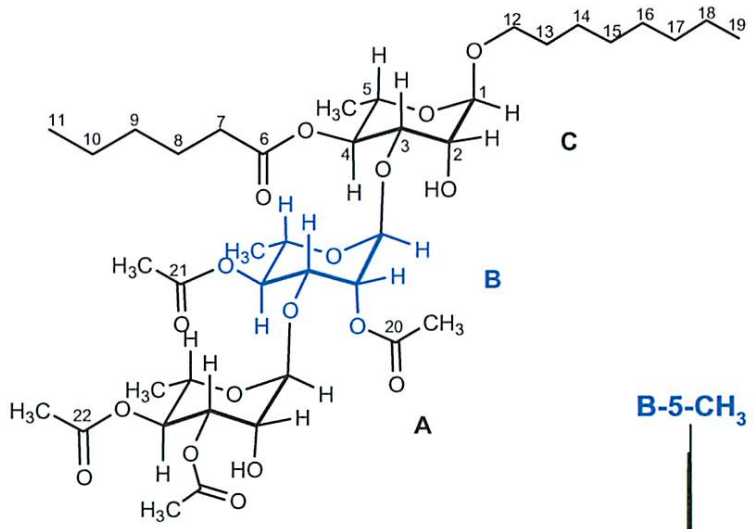


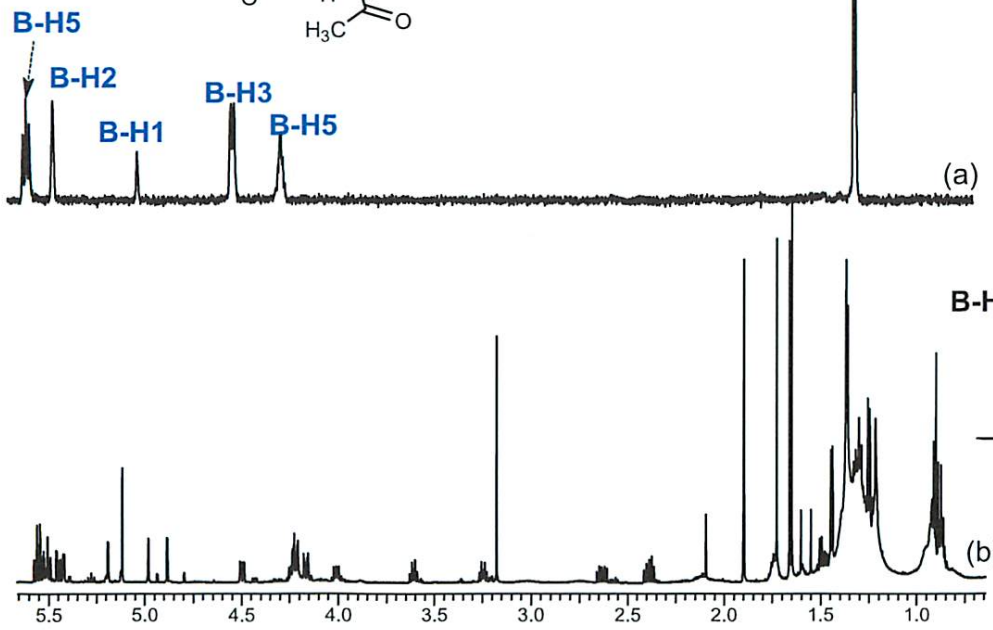

One-bond correlations ($^1J_{HC}$)
gHSQCAD
C-C3
C-C4
C-C2
C-C5
C-H5
C-H2
C-H3
C-H4
4.0
4.1
4.2
4.3
4.4
4.5
4.6
4.7
4.8
4.9
5.0
5.1
5.2
5.3
5.4
5.5
82
81
80
79
78
77
76
75
74
73
72
71
70
69
68
67
66
65

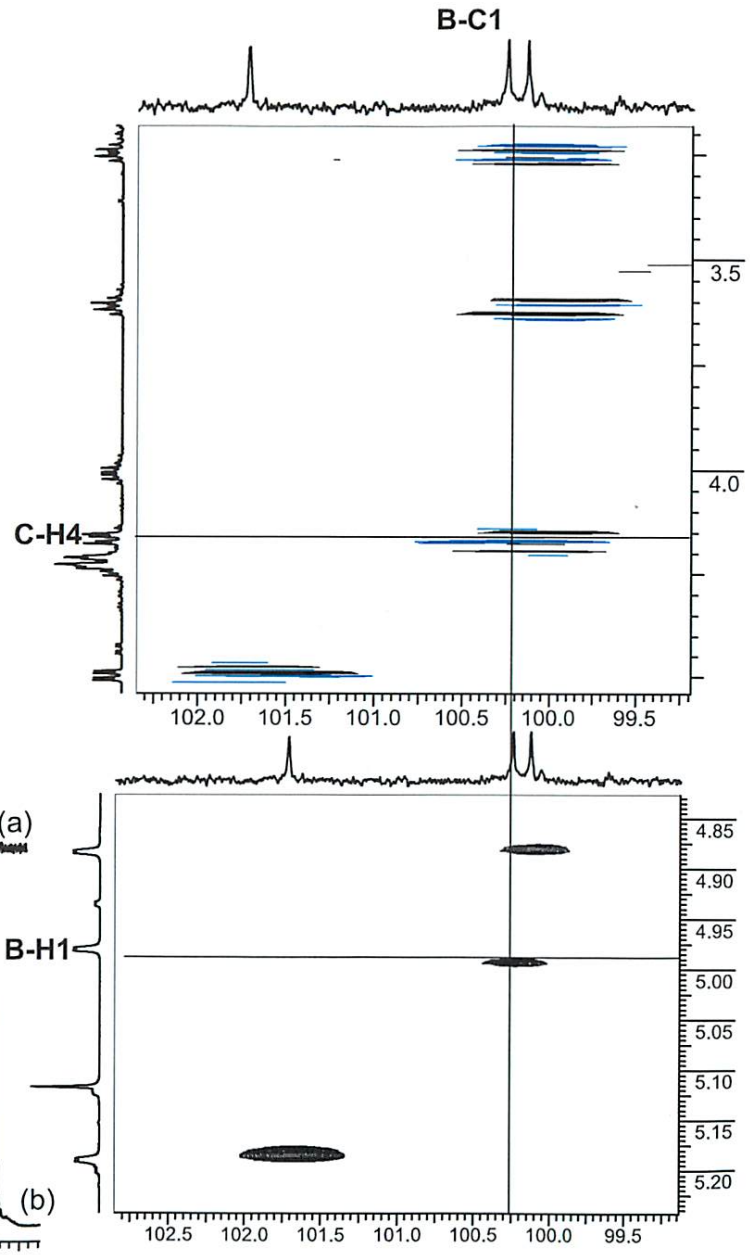
Spin system identification for the sugar moiety B

selective excitation of B-H3 at 4.50 ppm

1D TOCSY subspectrum (a); Control ^{1}H NMR spectrum (b)



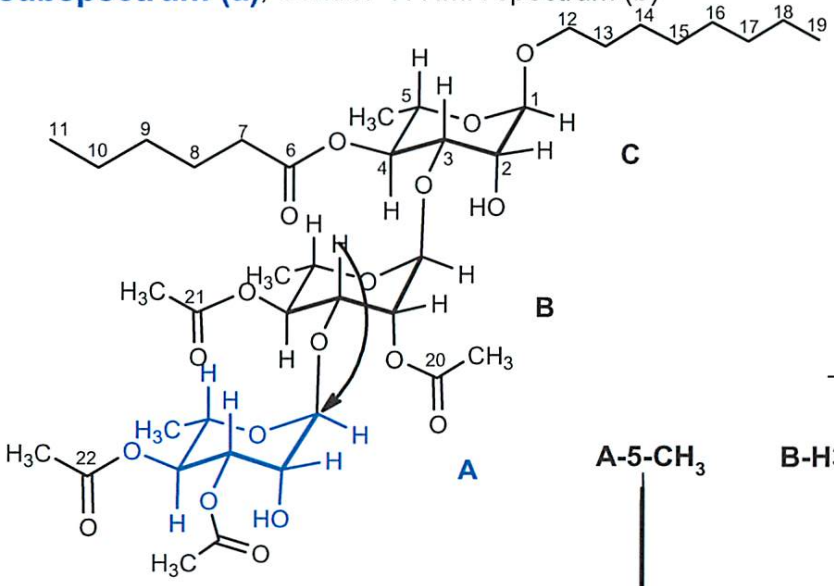


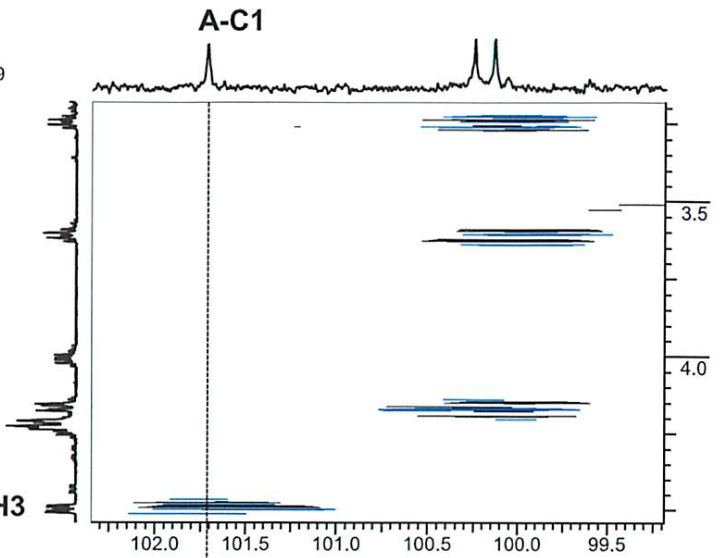


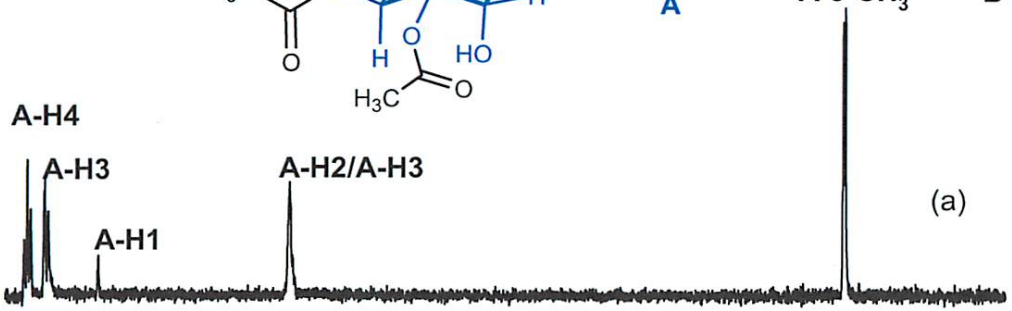
Spin system identification for the sugar moiety A

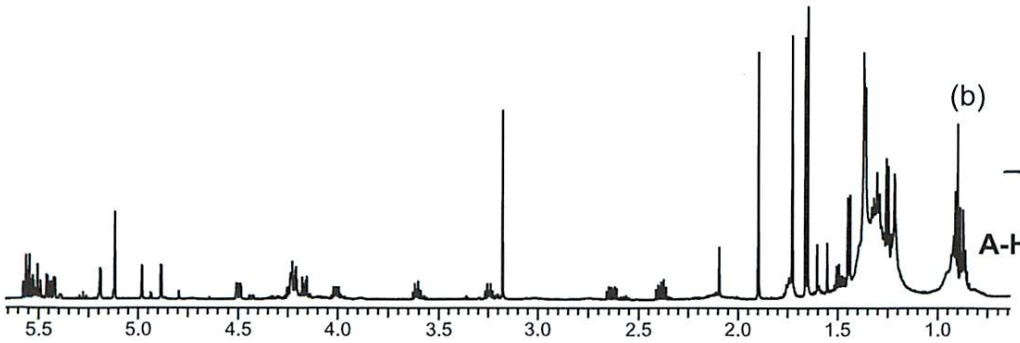
selective excitation of B-5-CH_3 at 1.44 ppm

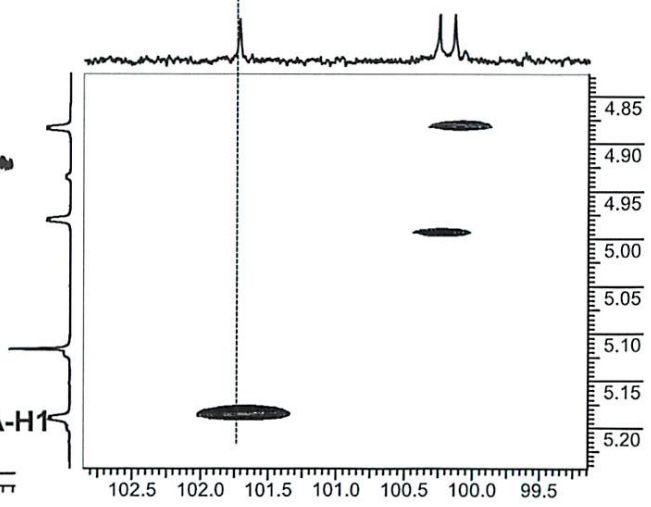
1D TOCSY subspectrum (a); Control ^{1}H NMR spectrum (b)



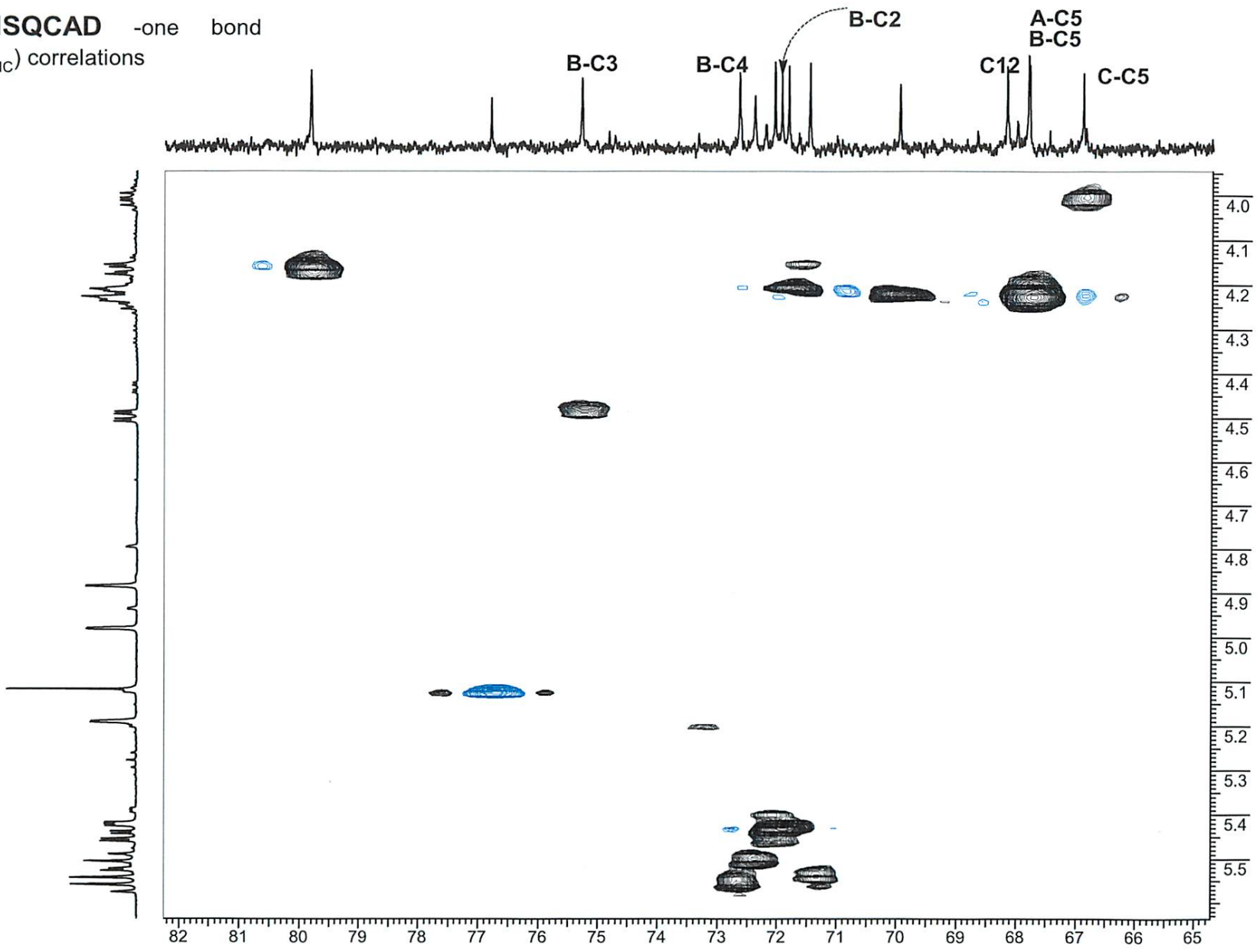




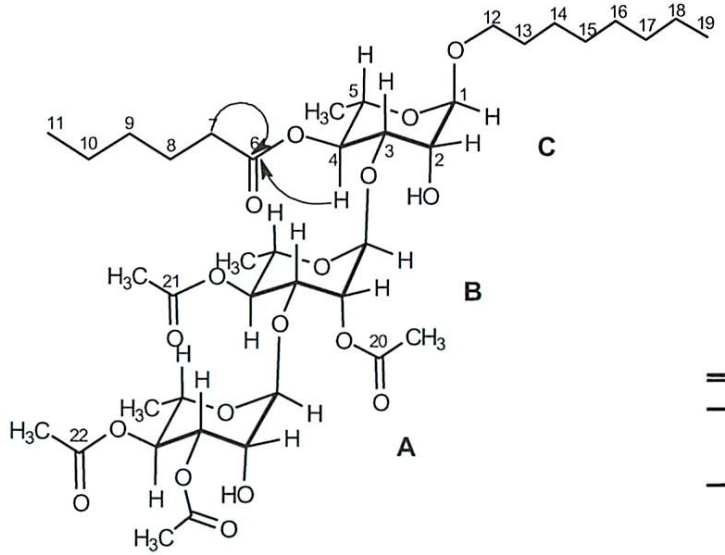


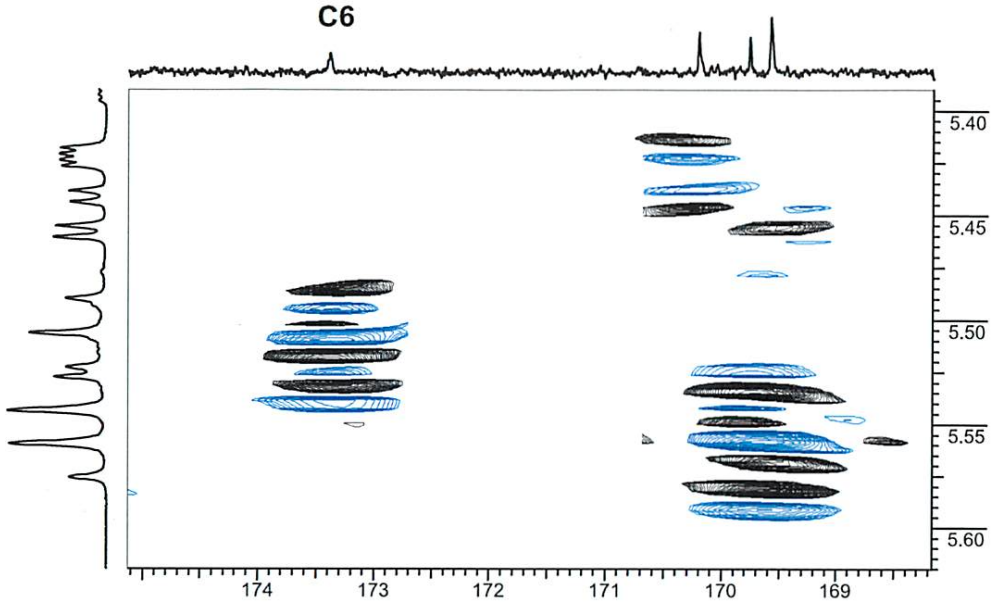


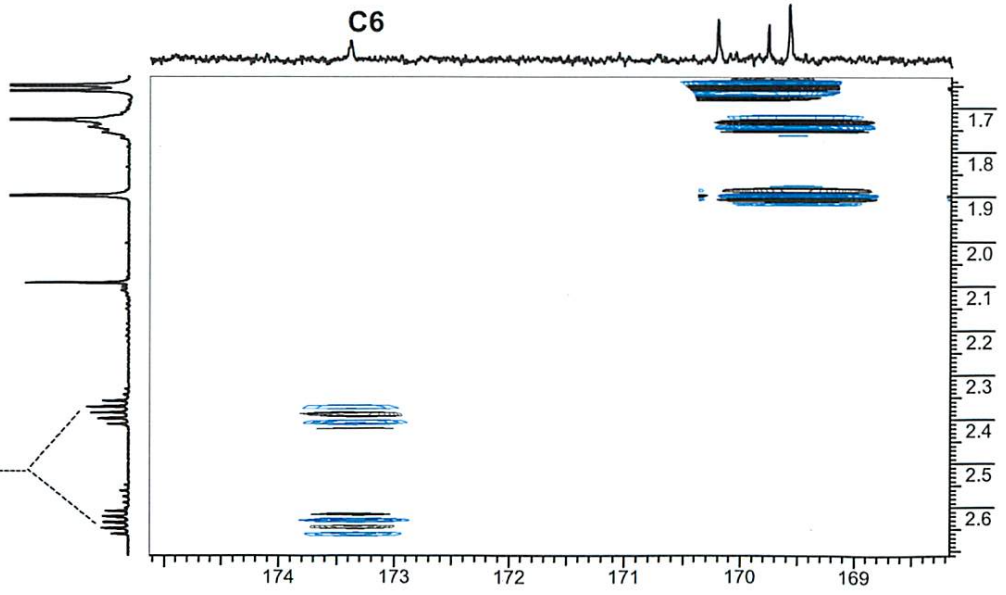
gHSQCAD -one bond
($^1J_{HC}$) correlations

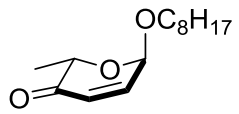


gHMBCAD

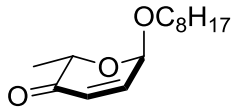

11
10
9
8
7
6
5
4
3
2
1
12
13
14
15
16
17
18
19
21
20
22
HO
HO
C
B
A


C6
5.40
5.45
5.50
5.55
5.60
174
173
172
171
170
169

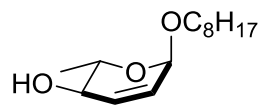

C6
7-CH2
1.7
1.8
1.9
2.0
2.1
2.2
2.3
2.4
2.5
2.6
174
173
172
171
170
169



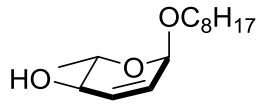
^{1}H NMR of (15)
(400 MHz, $CDCl_3$)



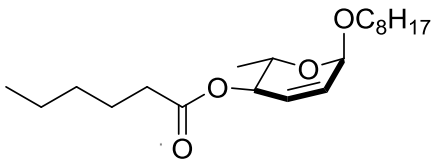
^{13}C NMR of (15)
(100 MHz, $CDCl_3$)



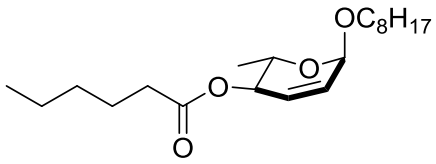
^{1}H NMR of (16)
(400 MHz, $CDCl_3$)



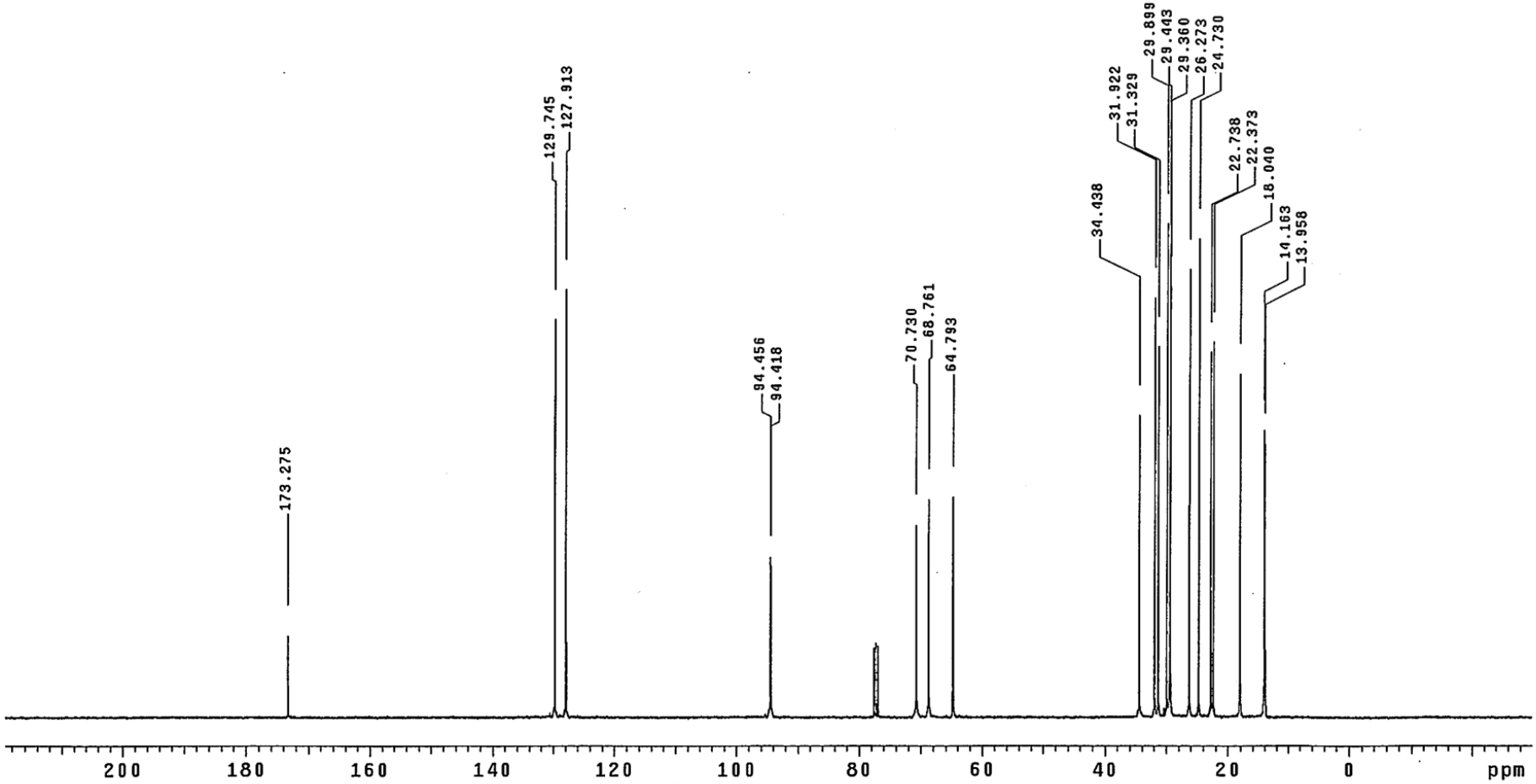
^{13}C NMR of (16)
(100 MHz, $CDCl_3$)

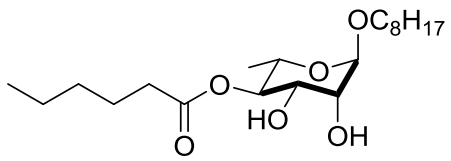


^{1}H NMR of (16a)
(400 MHz, $CDCl_3$)

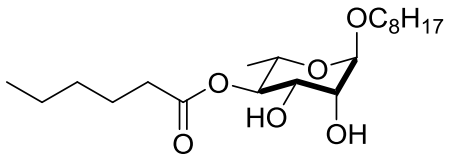


^{13}C NMR of (16a)
(100 MHz, $CDCl_3$)

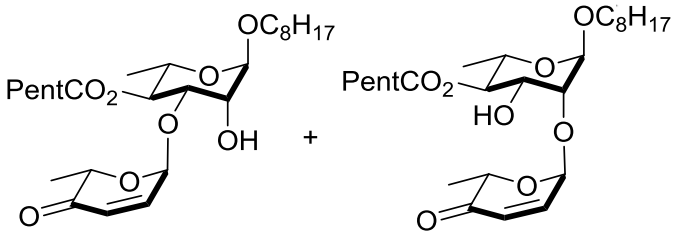




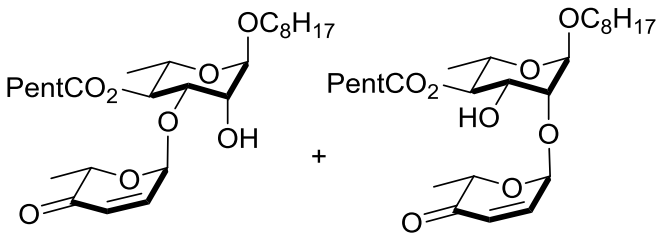
^{1}H NMR of (17a)
(400 MHz, $CDCl_3$)



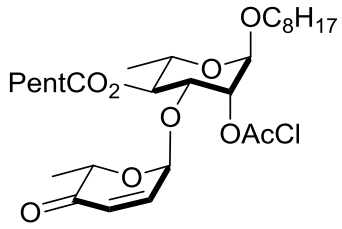
^{13}C NMR of (17a)
(100 MHz, $CDCl_3$)



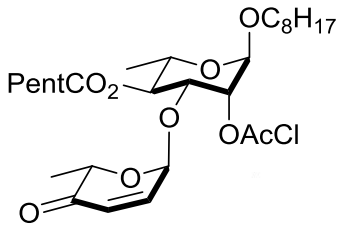
^{1}H NMR of (19 & 20)
(400 MHz, $CDCl_3$)



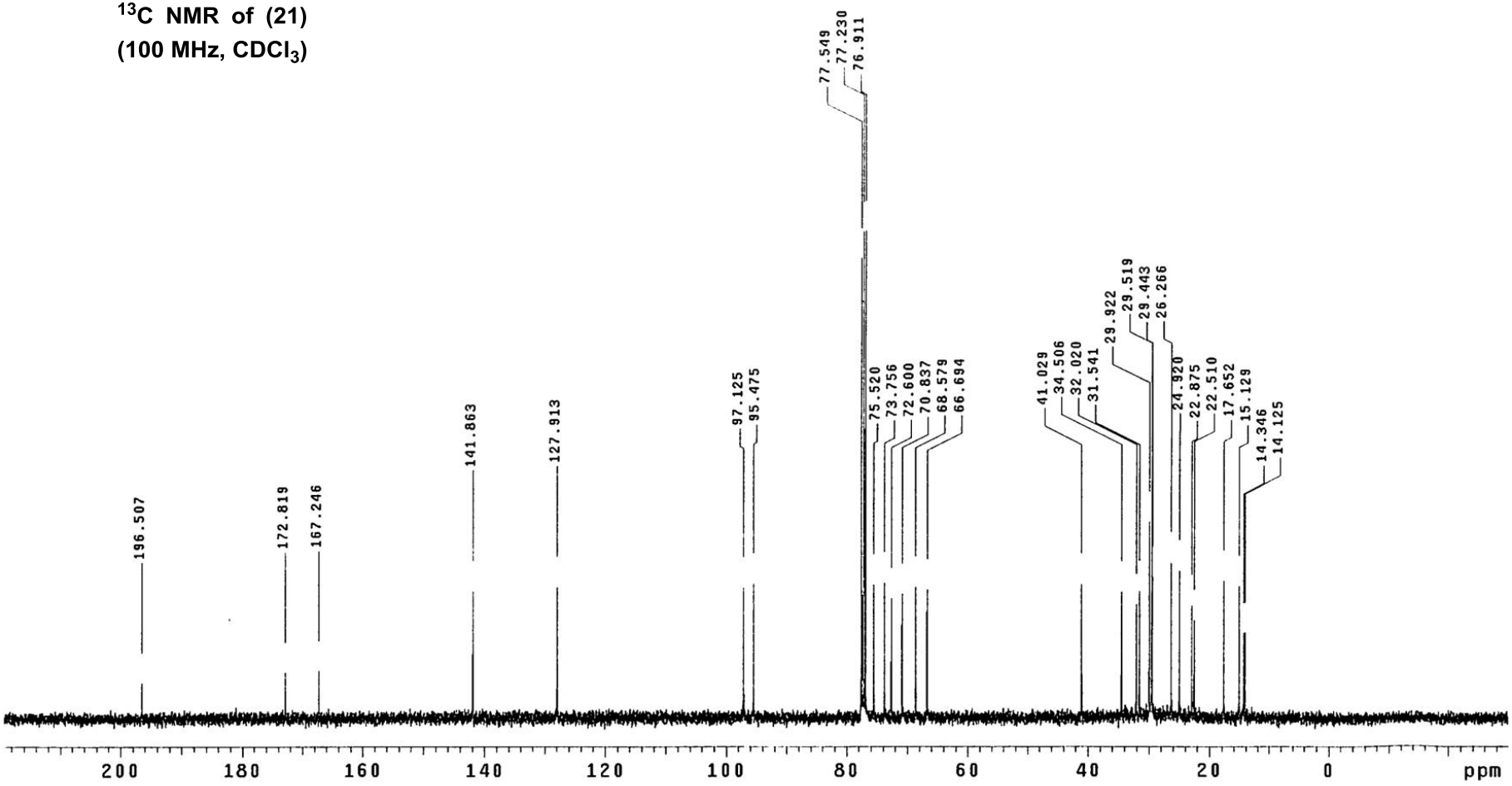
^{13}C NMR of (19 & 20)
(100 MHz, $CDCl_3$)

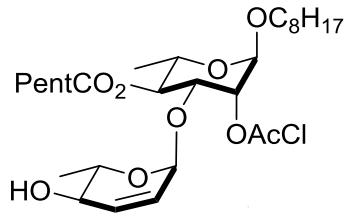


^{1}H NMR of (21)
(400 MHz, $CDCl_3$)

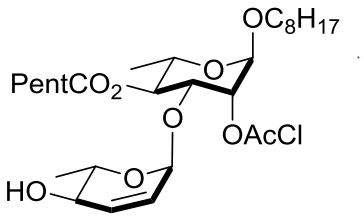


^{13}C NMR of (21)
(100 MHz, $CDCl_3$)

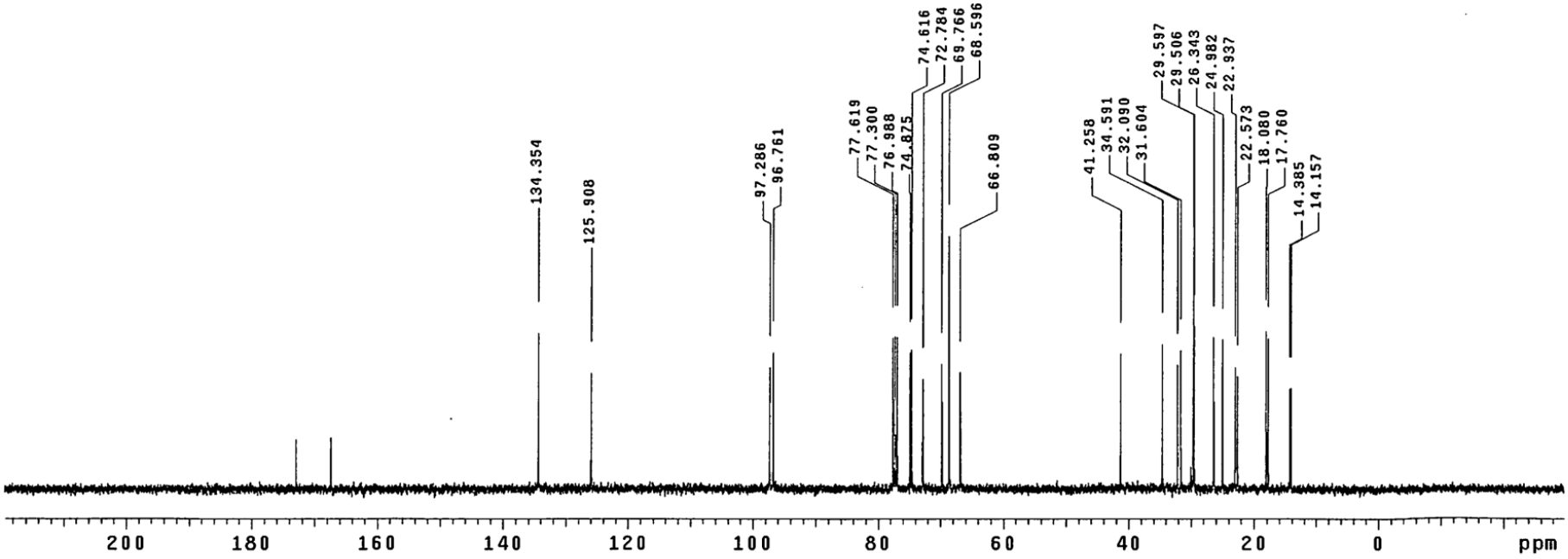


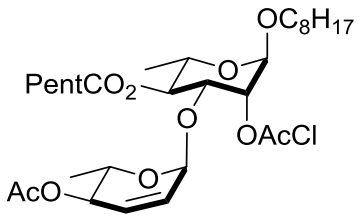


^{1}H NMR of (12)
(400 MHz, $CDCl_3$)

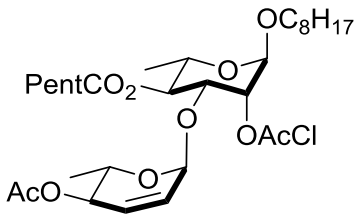


^{13}C NMR of (12)
(100 MHz, $CDCl_3$)

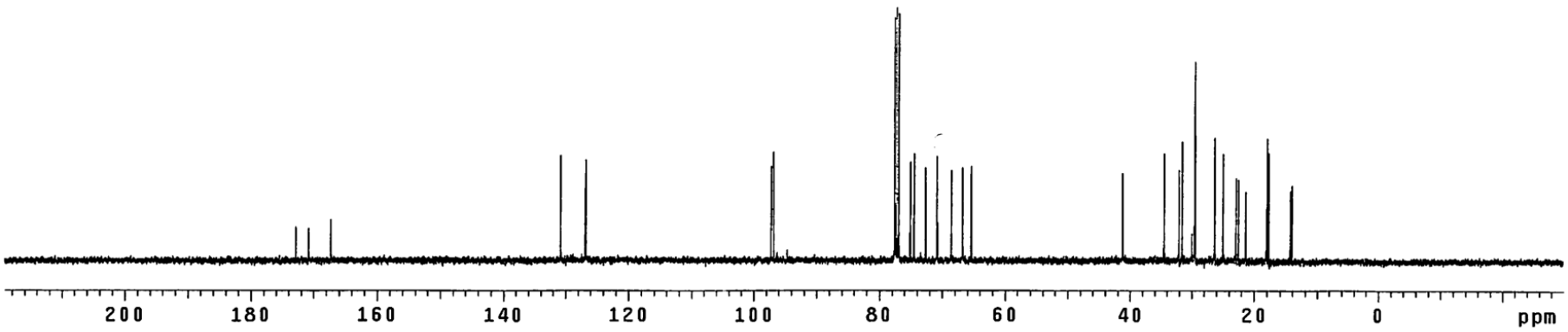


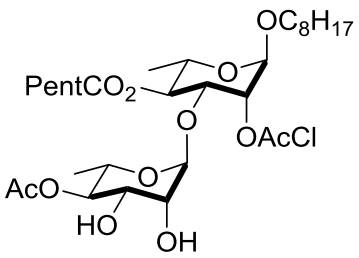


^{1}H NMR of (12a)
(400 MHz, $CDCl_3$)

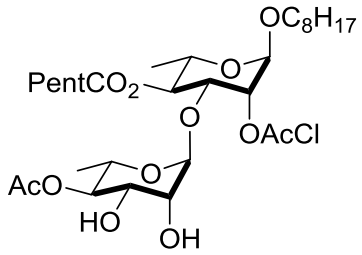


^{13}C NMR of (12a)
(100 MHz, $CDCl_3$)

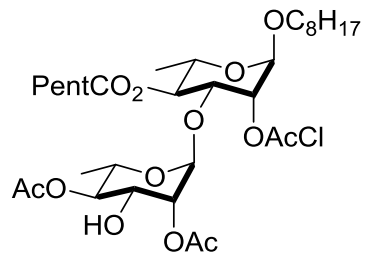




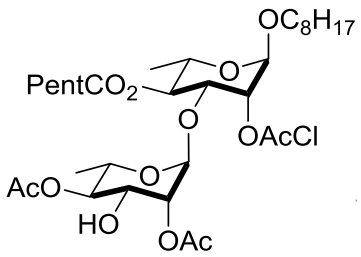
^{1}H NMR of (12b)
(400 MHz, $CDCl_3$)



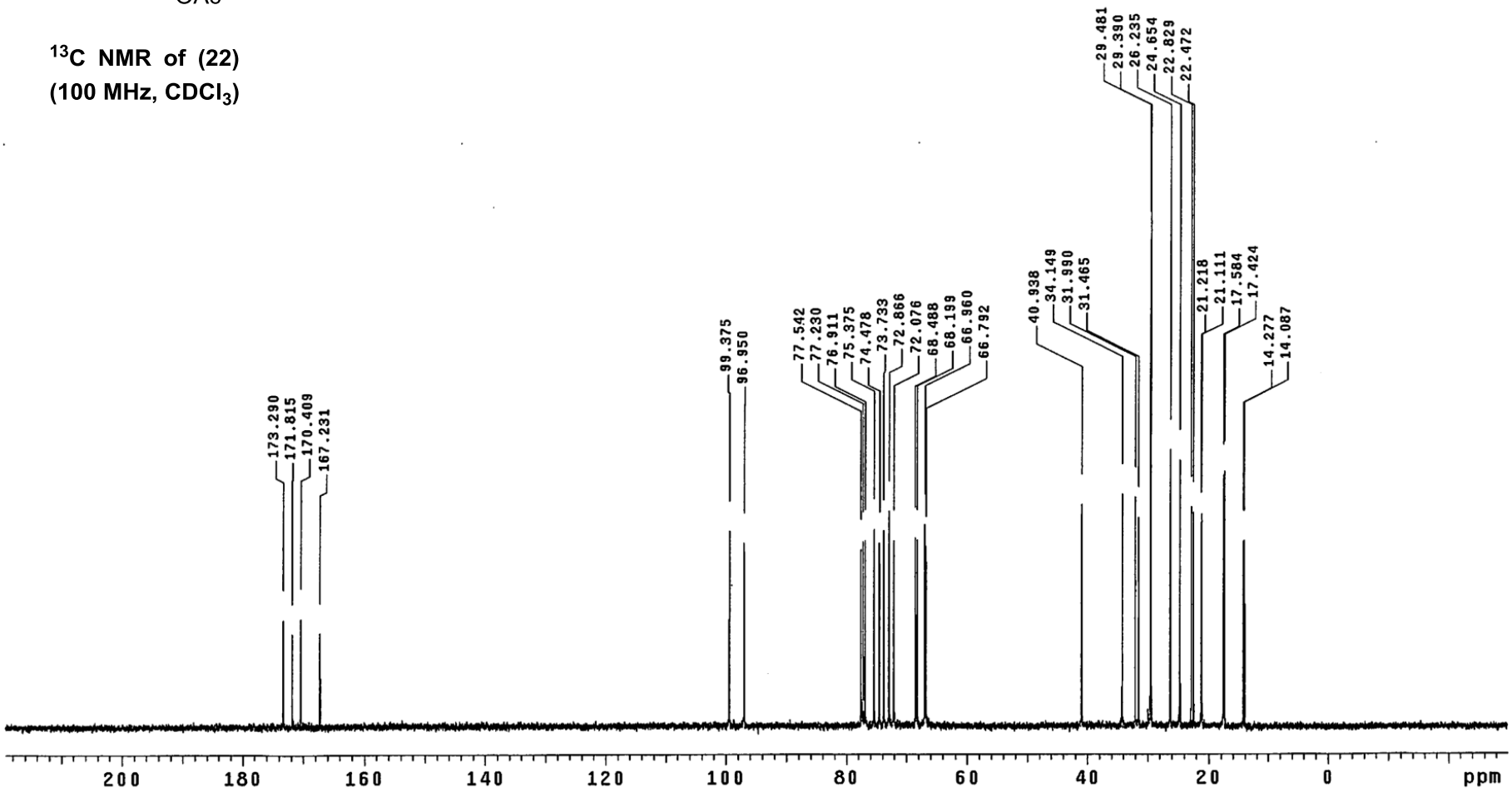
^{13}C NMR of (12b)
(100 MHz, $CDCl_3$)

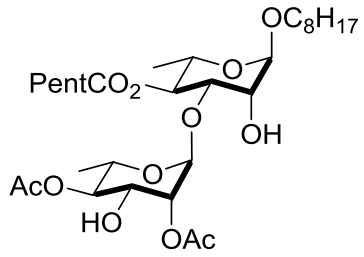


^{1}H NMR of (22)
(400 MHz, $CDCl_3$)

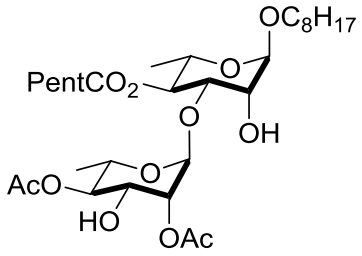


^{13}C NMR of (22)
(100 MHz, $CDCl_3$)

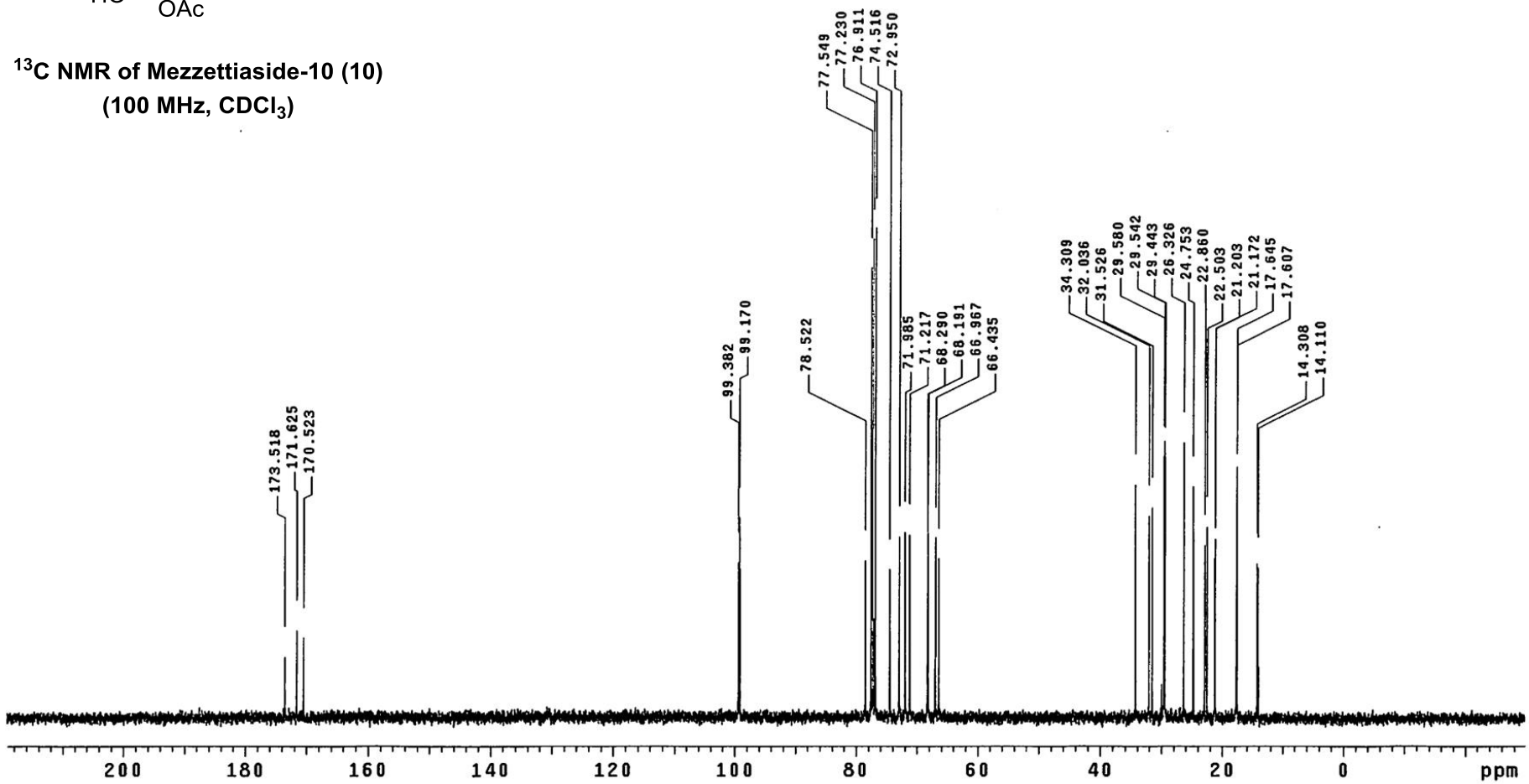


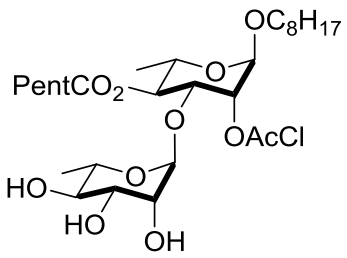


^{1}H NMR of Mezzettiaside-10 (10)
(400 MHz, $CDCl_3$)

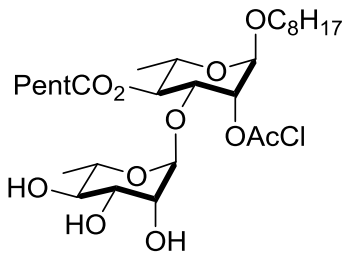


^{13}C NMR of Mezzettiaside-10 (10)
(100 MHz, $CDCl_3$)

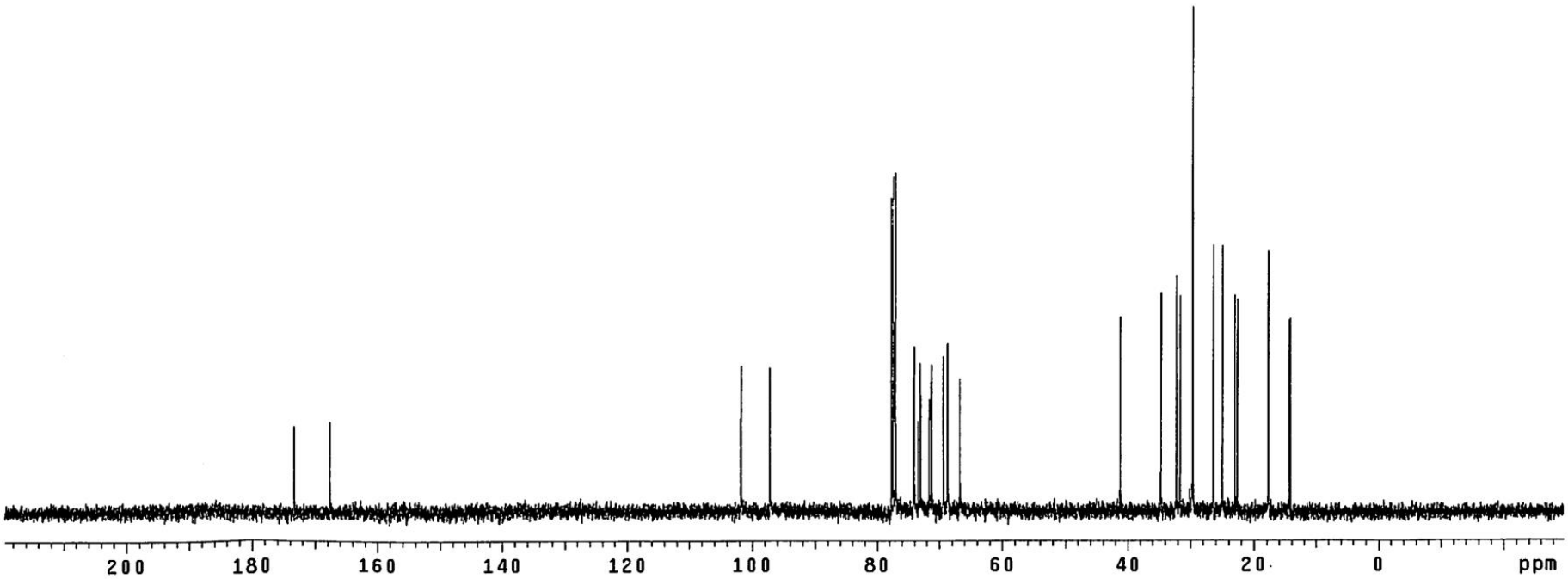


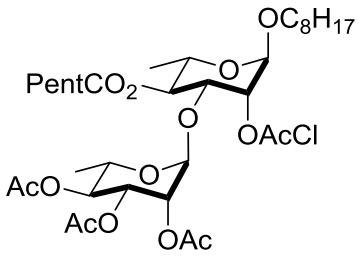


^{1}H NMR of (12c)
(400 MHz, $CDCl_3$)

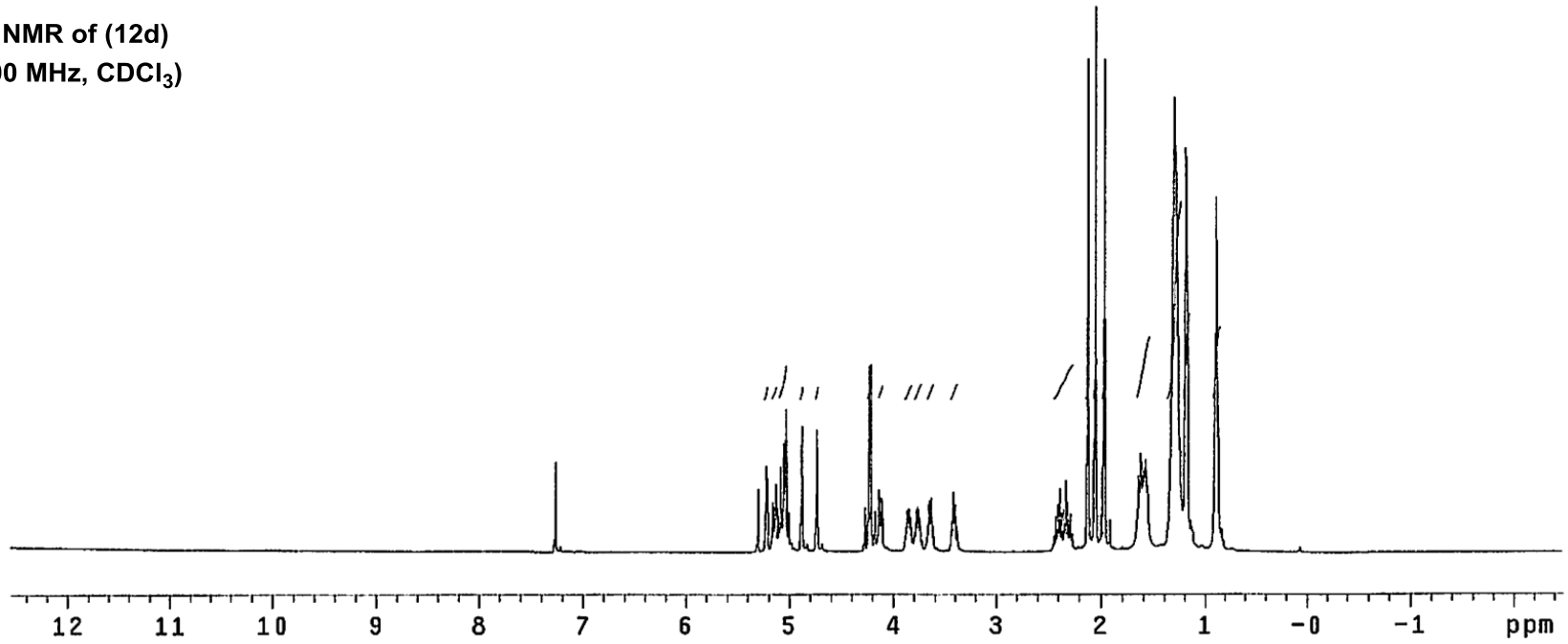


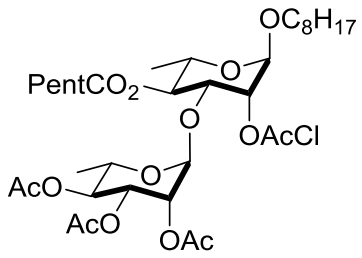
^{13}C NMR of (12c)
(100 MHz, $CDCl_3$)



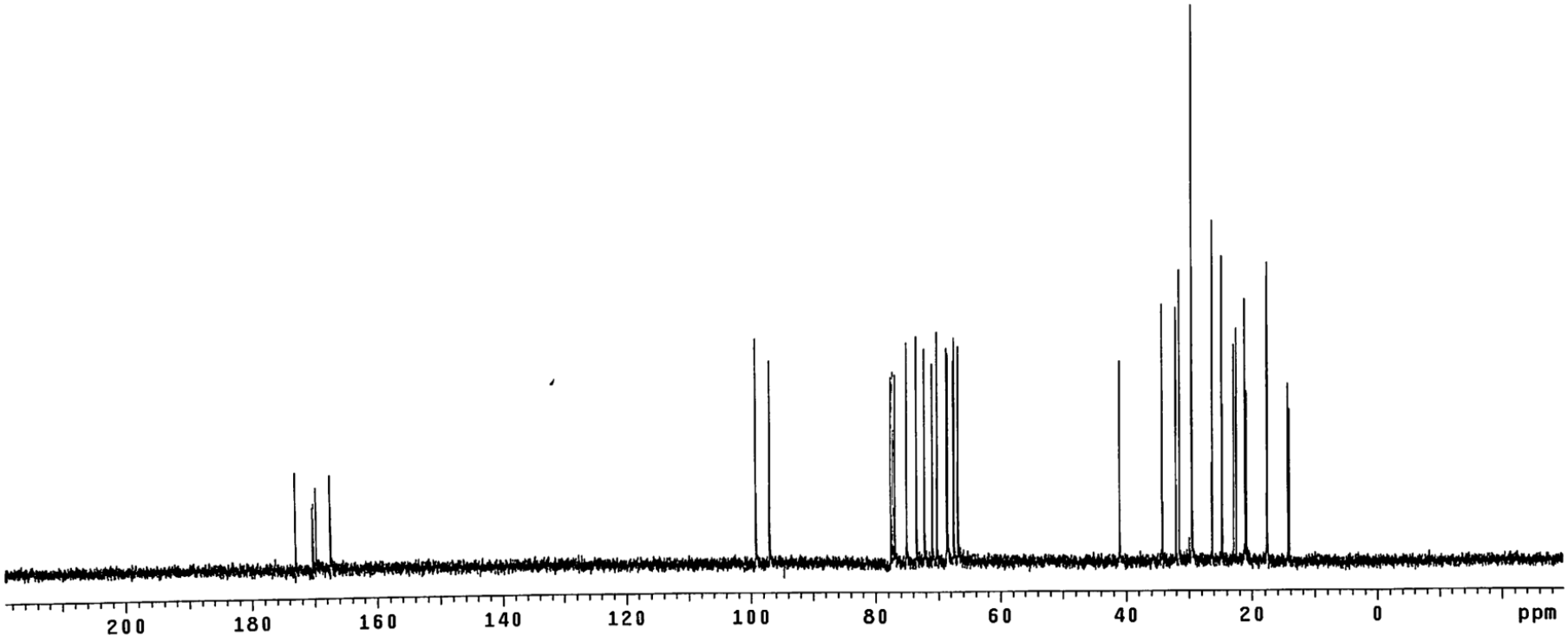


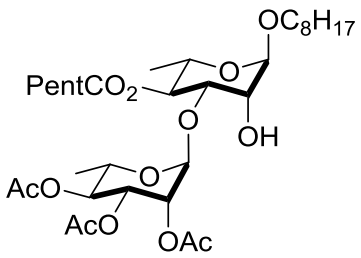
^{1}H NMR of (12d)
(400 MHz, $CDCl_3$)



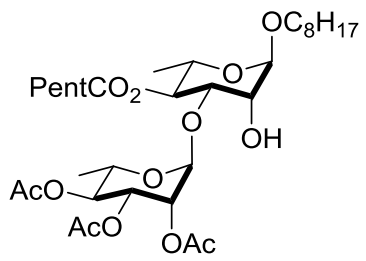


^{13}C NMR of (12d)
(100 MHz, $CDCl_3$)

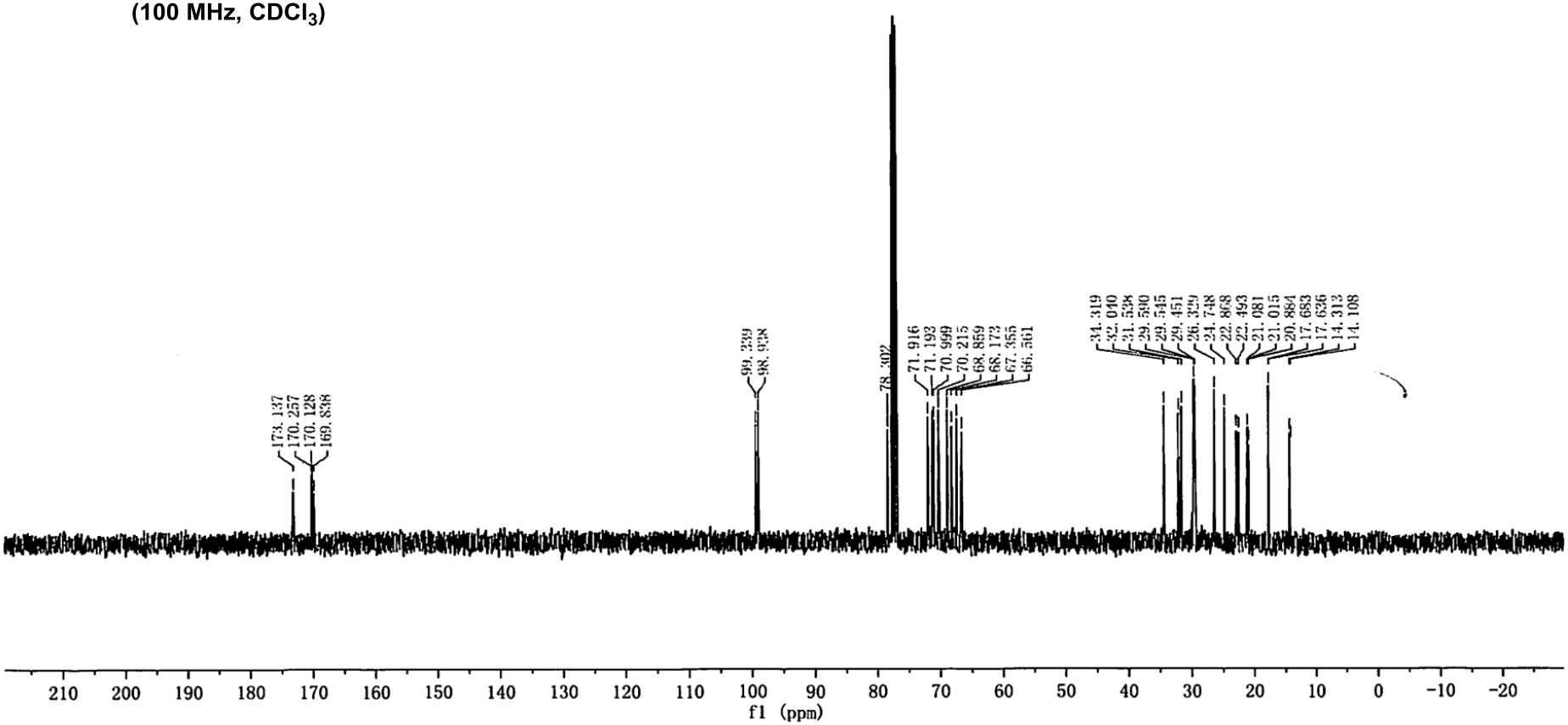


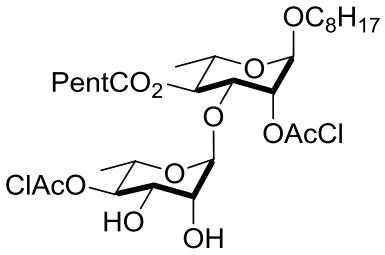


^{1}H NMR of Mezzettiaside-11 (11)
(400 MHz, $CDCl_3$)

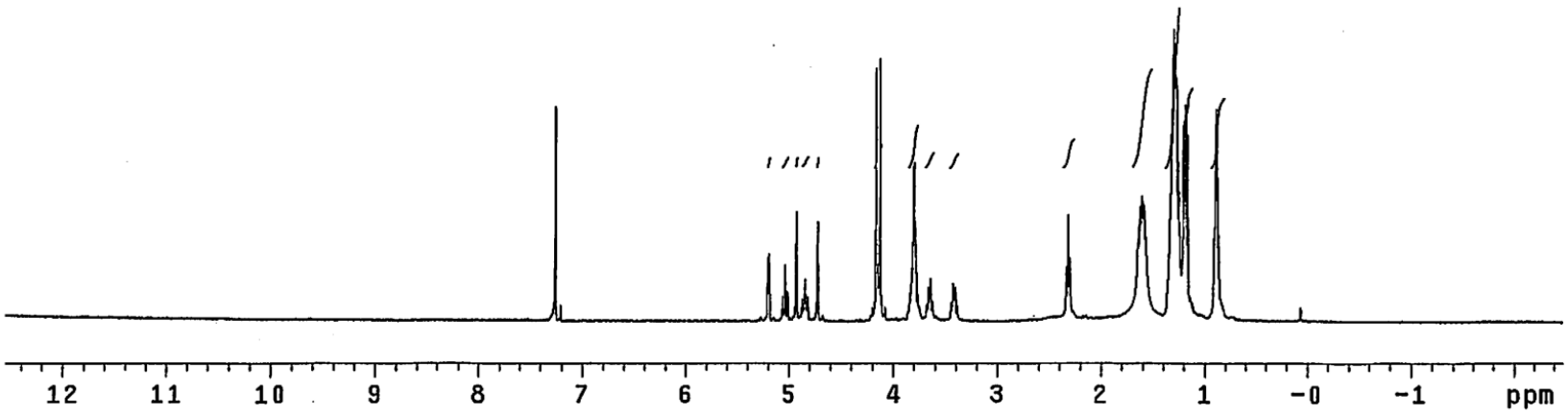


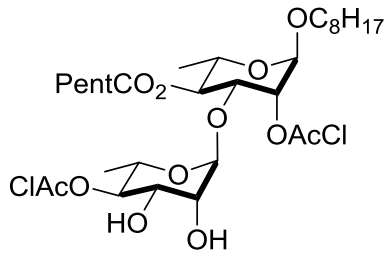
^{13}C NMR of Mezzettiaside-11 (11)
(100 MHz, $CDCl_3$)



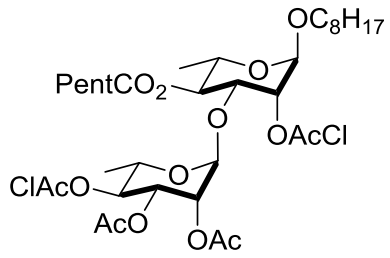


^{1}H NMR of (12e)
(400 MHz, $CDCl_3$)

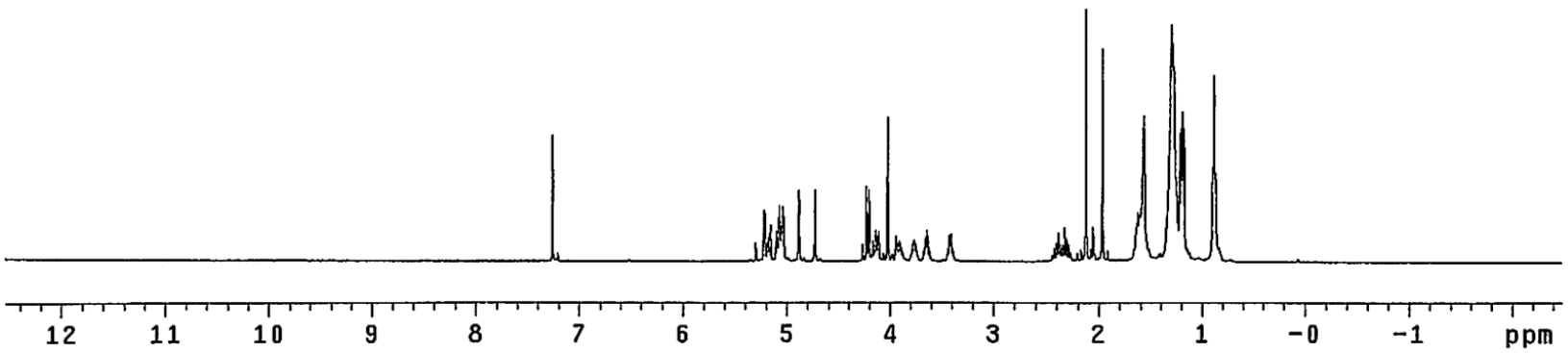


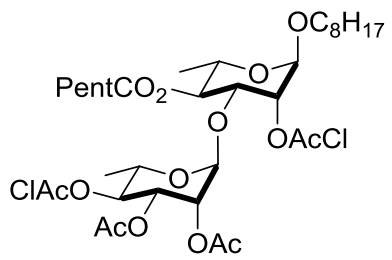


^{13}C NMR of (12e)
(100 MHz, $CDCl_3$)

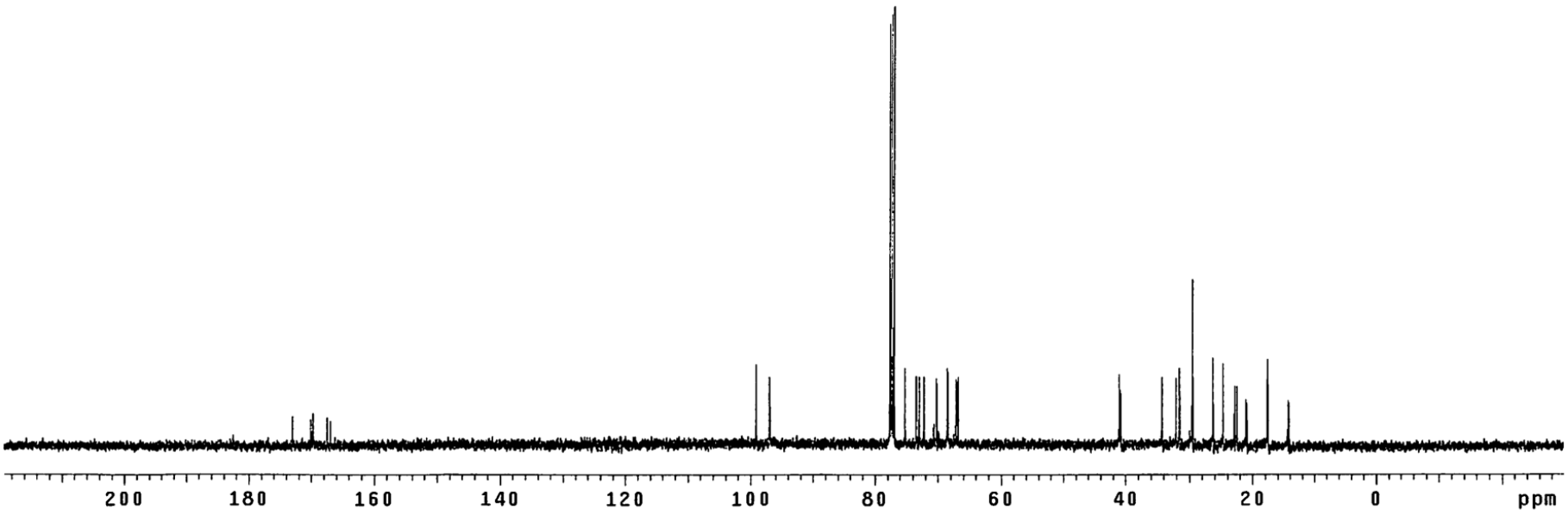


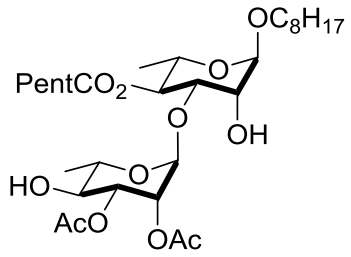
^{1}H NMR of (12f)
(400 MHz, $CDCl_3$)



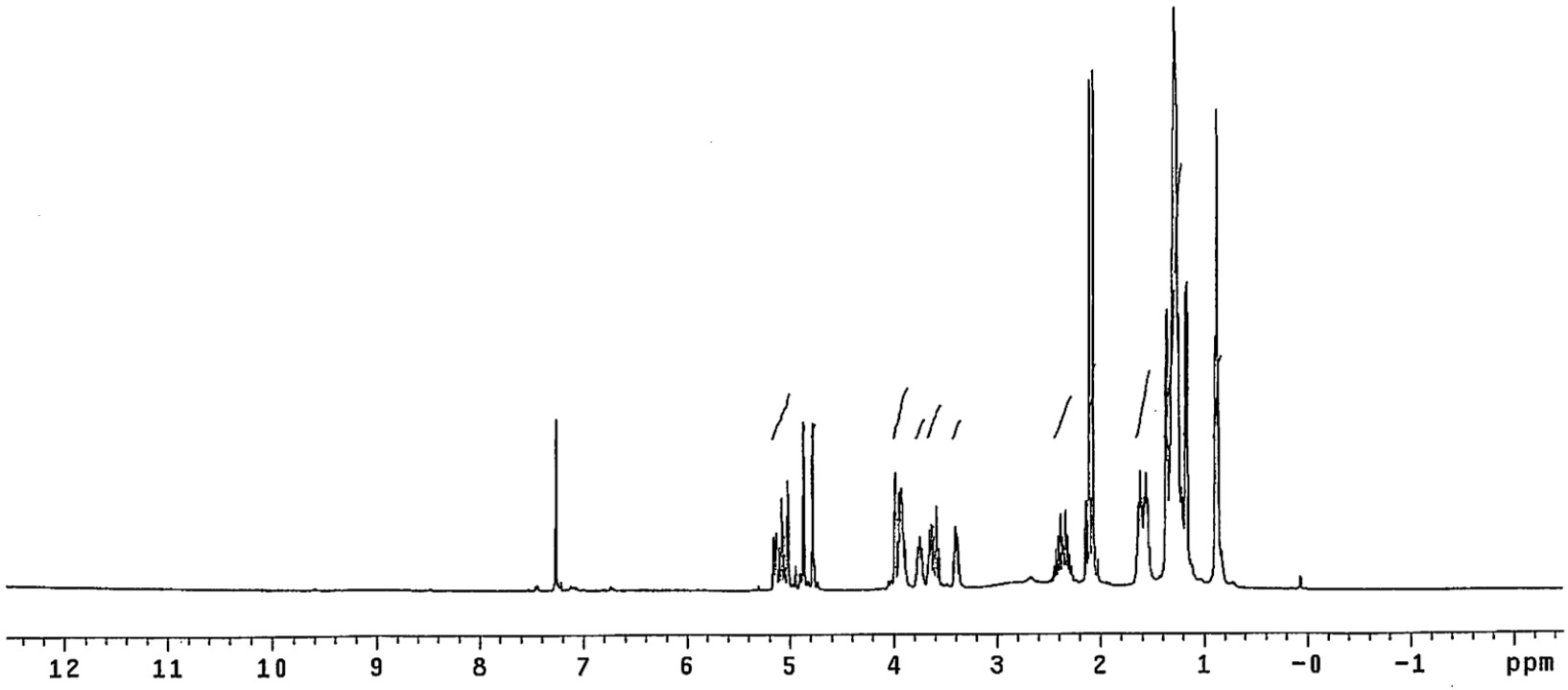


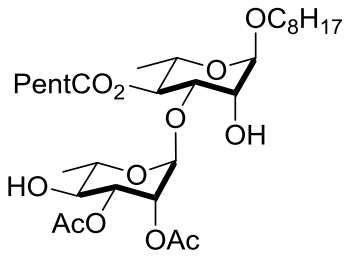
^{13}C NMR of (12f)
(100 MHz, $CDCl_3$)



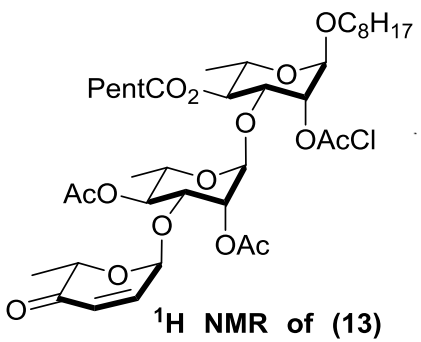


^{1}H NMR of Mezzettiaside-9 (9)
(400 MHz, $CDCl_3$)

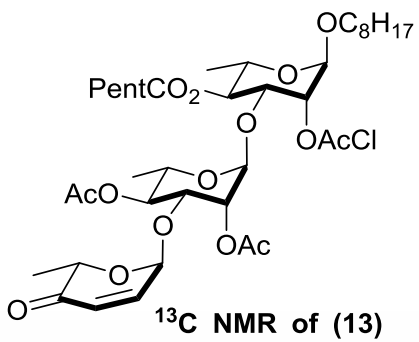




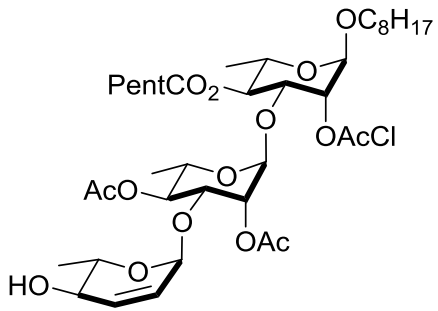
^{13}C NMR of Mezzettiaside-9 (9)
(100 MHz, $CDCl_3$)



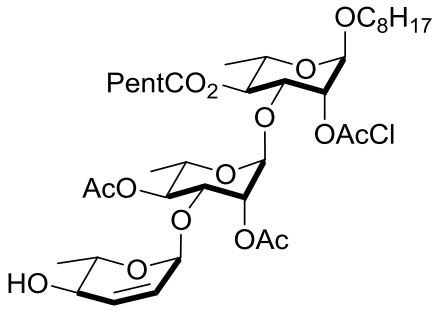
^{1}H NMR of (13)
(400 MHz, $CDCl_3$)



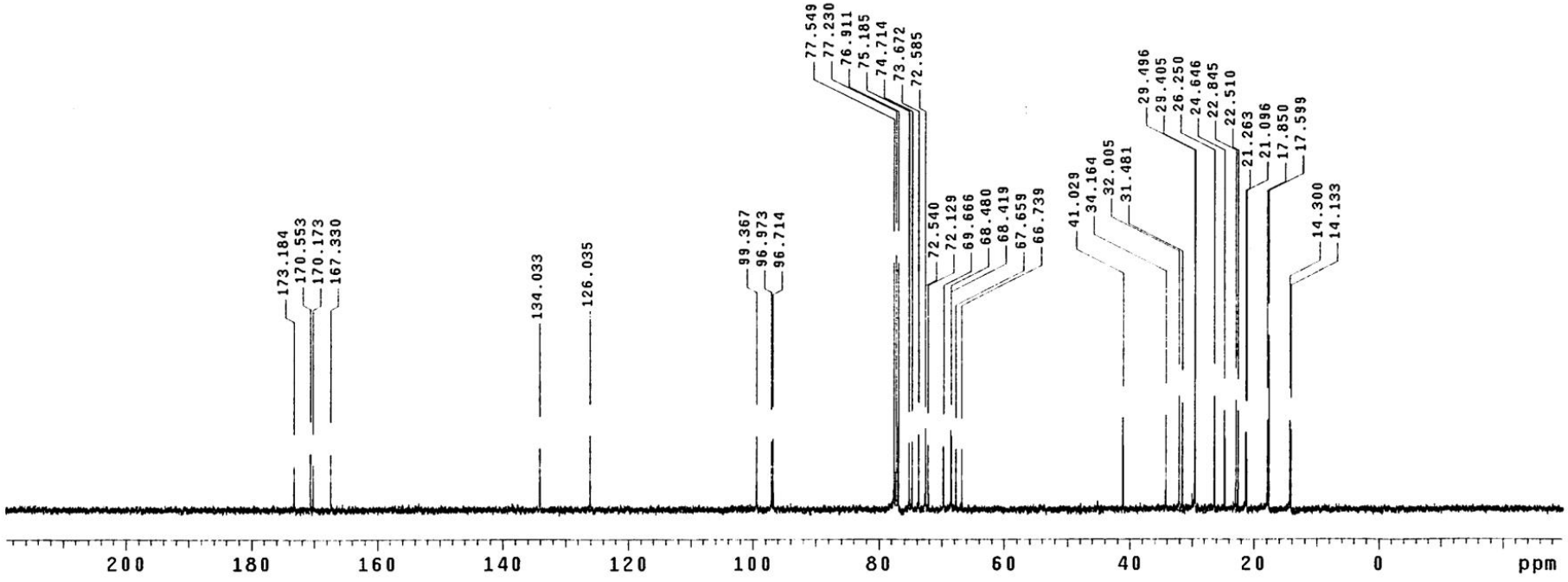
^{13}C NMR of (13)
(100 MHz, $CDCl_3$)

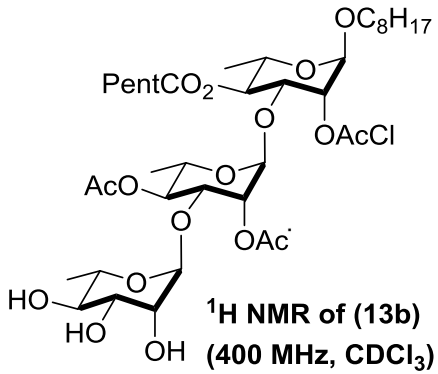


^{1}H NMR of (13a)
(400 MHz, $CDCl_3$)

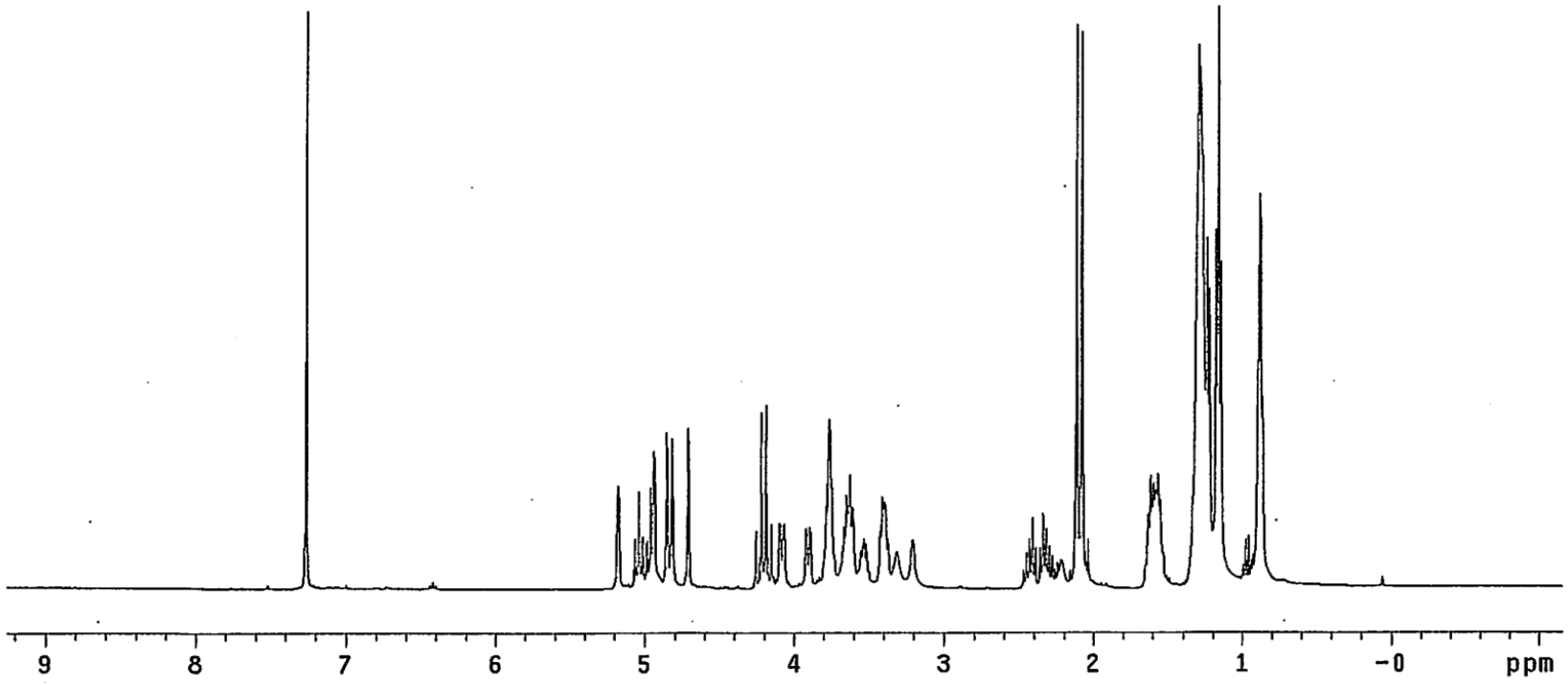


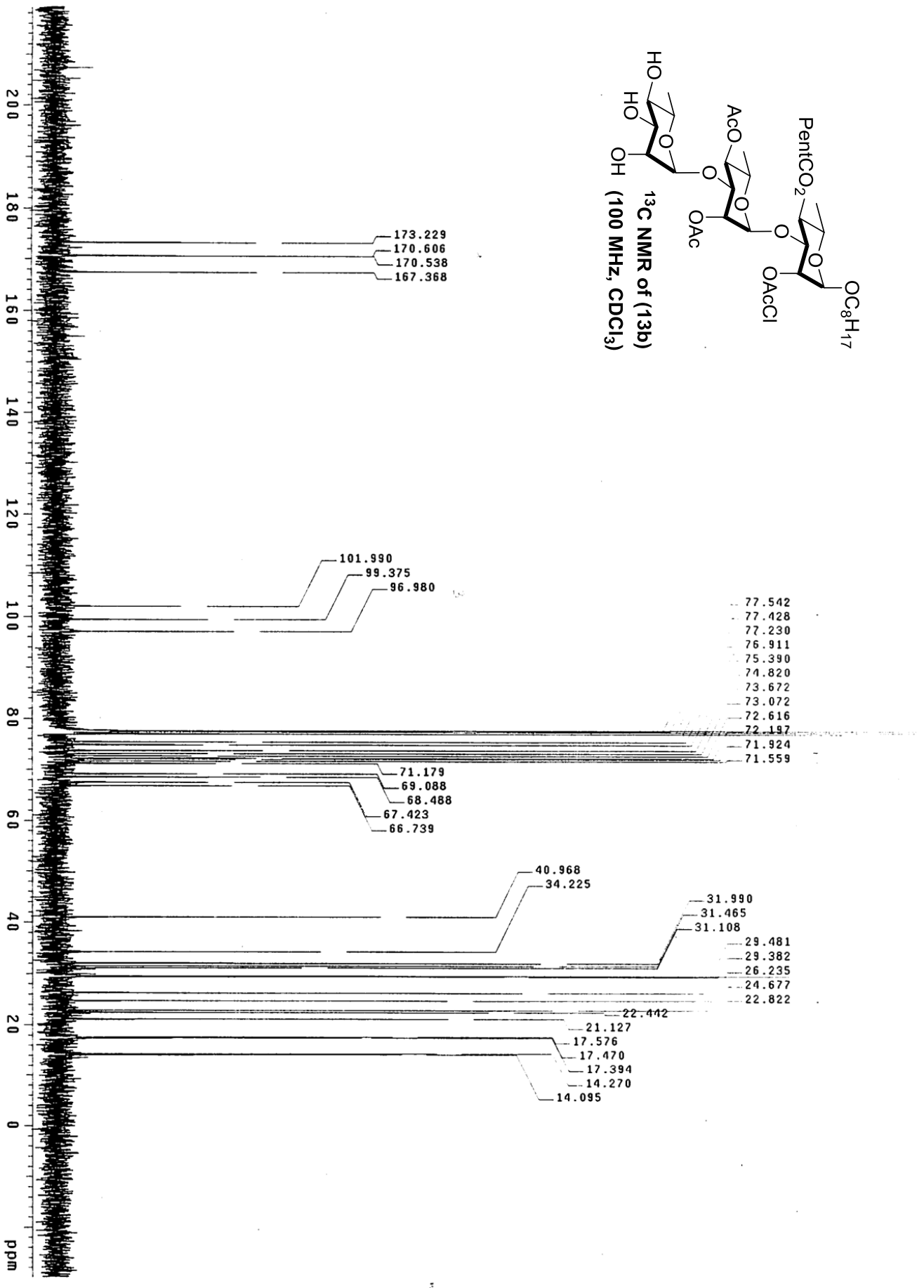
^{13}C NMR of (13a)
(100 MHz, $CDCl_3$)

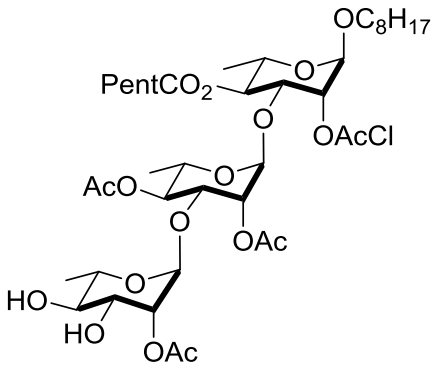




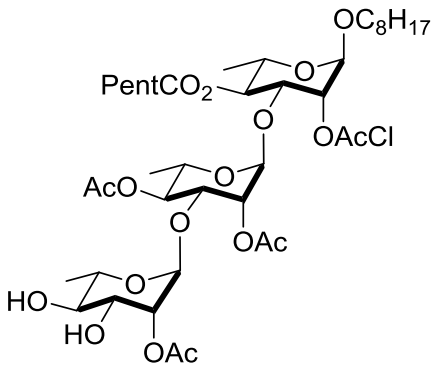
^{1}H NMR of (13b)
(400 MHz, $CDCl_3$)



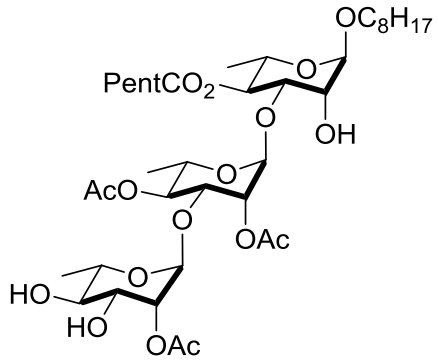

HO
HO
OH
AcO
OAc
PentCO2
OAcCl
OC8H17
13C NMR of (13b)
(100 MHz, CDCl3)
173.229
170.606
170.538
167.368
101.990
99.375
96.980
77.542
77.428
77.230
76.911
75.390
74.820
73.672
73.072
72.616
72.197
71.924
71.559
71.179
69.088
68.488
67.423
66.739
40.968
34.225
31.990
31.465
31.108
29.481
29.382
26.235
24.677
22.822
22.442
21.127
17.576
17.470
17.394
14.270
14.095
200
180
160
140
120
100
80
60
40
20
0
ppm



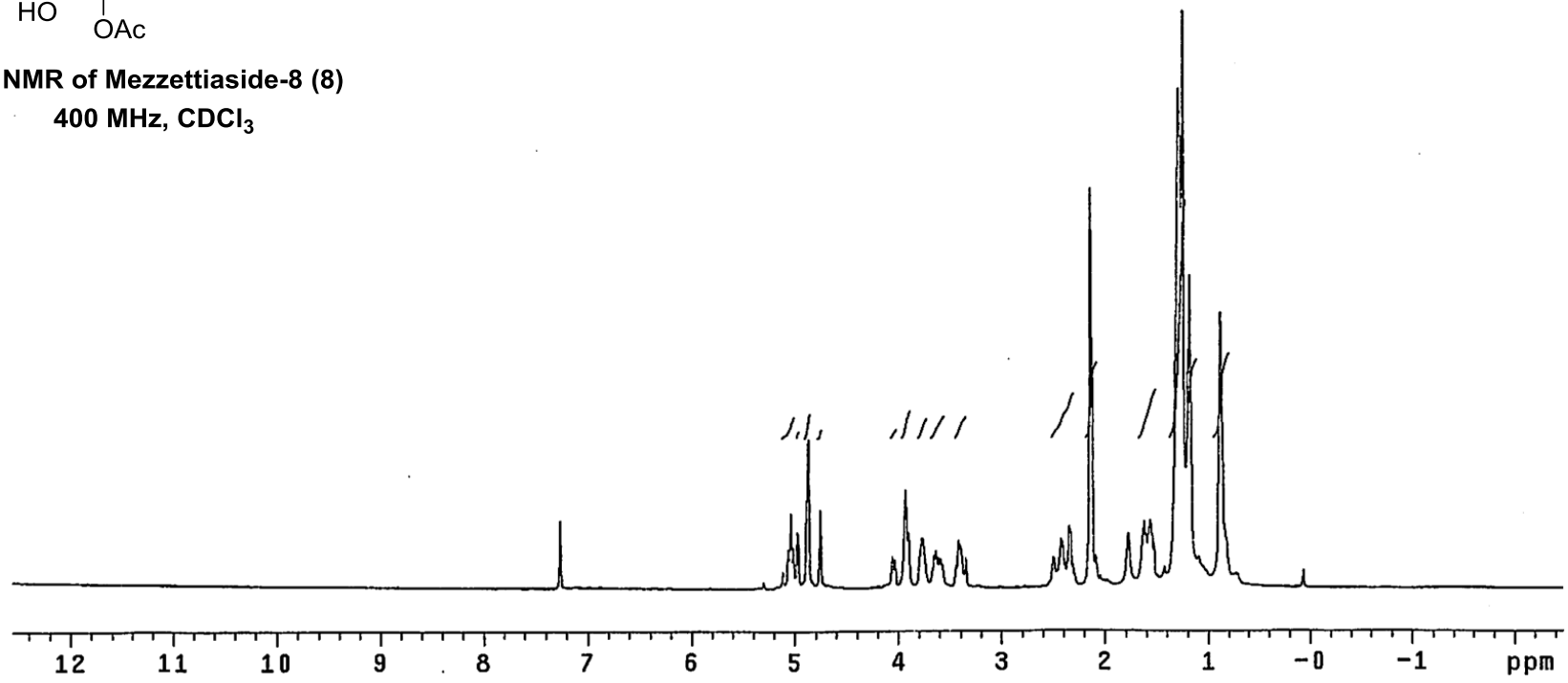
^{1}H NMR of (13c)
(400 MHz, $CDCl_3$)

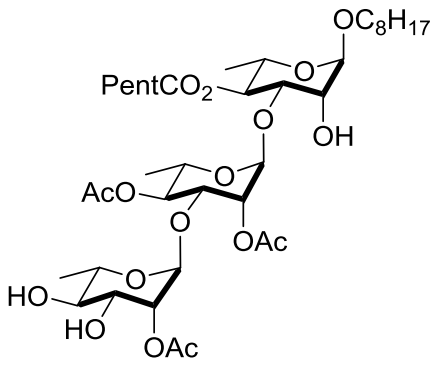


^{13}C NMR of (13c)
(100 MHz, $CDCl_3$)

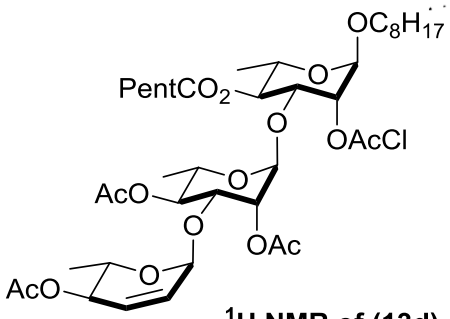


^{1}H NMR of Mezzettiaside-8 (8)
400 MHz, $CDCl_3$

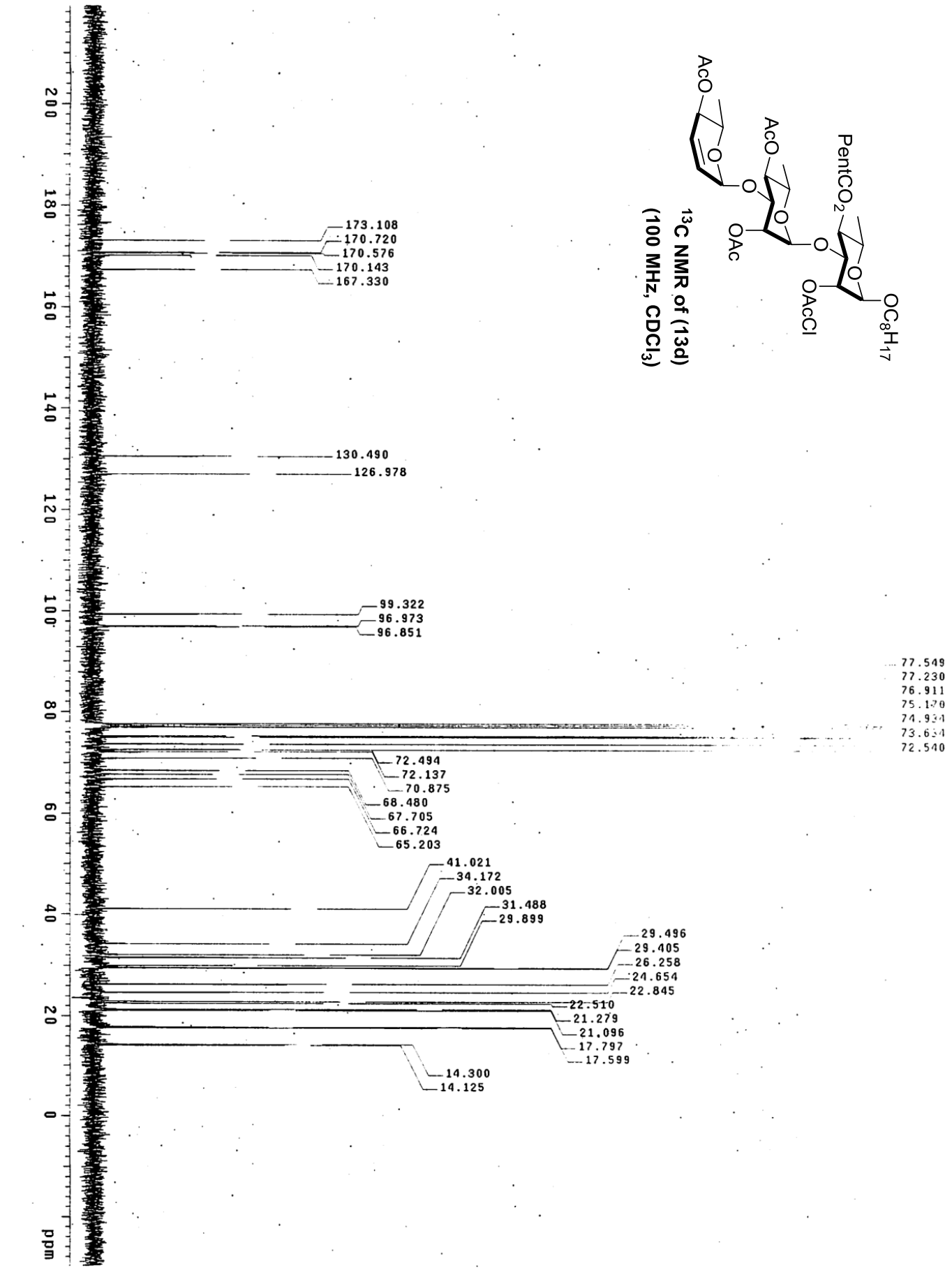


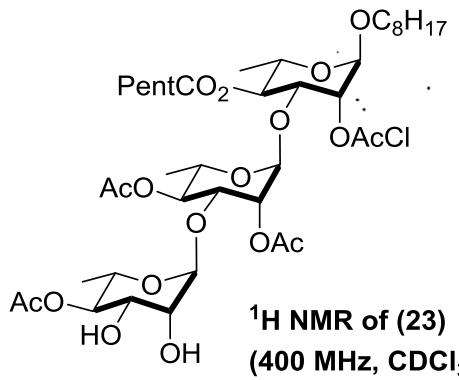


^{13}C NMR of Mezzettiaside-8 (8)
(100 MHz, $CDCl_3$)

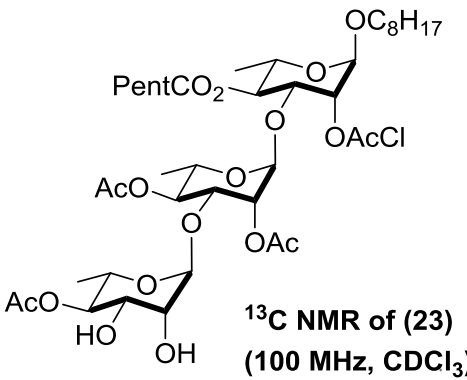


^{1}H NMR of (13d)
(400 MHz, $CDCl_3$)

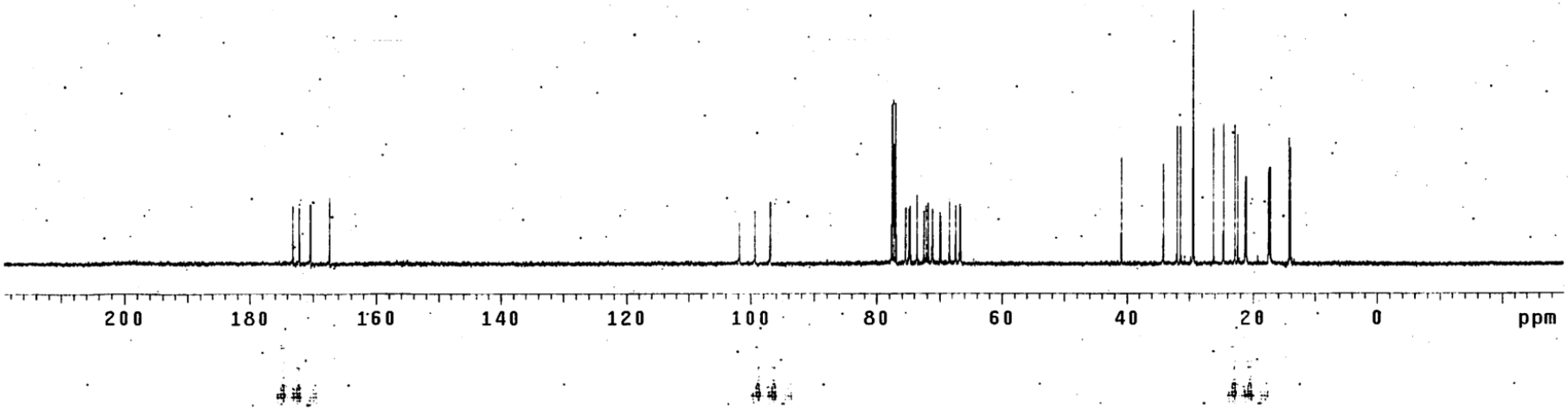

AcO
AcO
PentCO2
OAc
OAcCl
OC8H17
13C NMR of (13d)
(100 MHz, CDCl3)
173.108
170.720
170.576
170.143
167.330
130.490
126.978
99.322
96.973
96.851
77.549
77.230
76.911
75.170
74.934
73.634
72.540
72.494
72.137
70.875
68.480
67.705
66.724
65.203
41.021
34.172
32.005
31.488
29.899
29.496
29.405
26.258
24.654
22.845
22.510
21.279
21.096
17.797
17.599
14.300
14.125
200
180
160
140
120
100
80
60
40
20
0
ppm

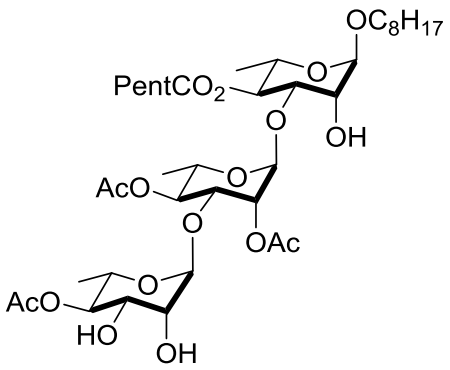


^{1}H NMR of (23)
(400 MHz, $CDCl_3$)

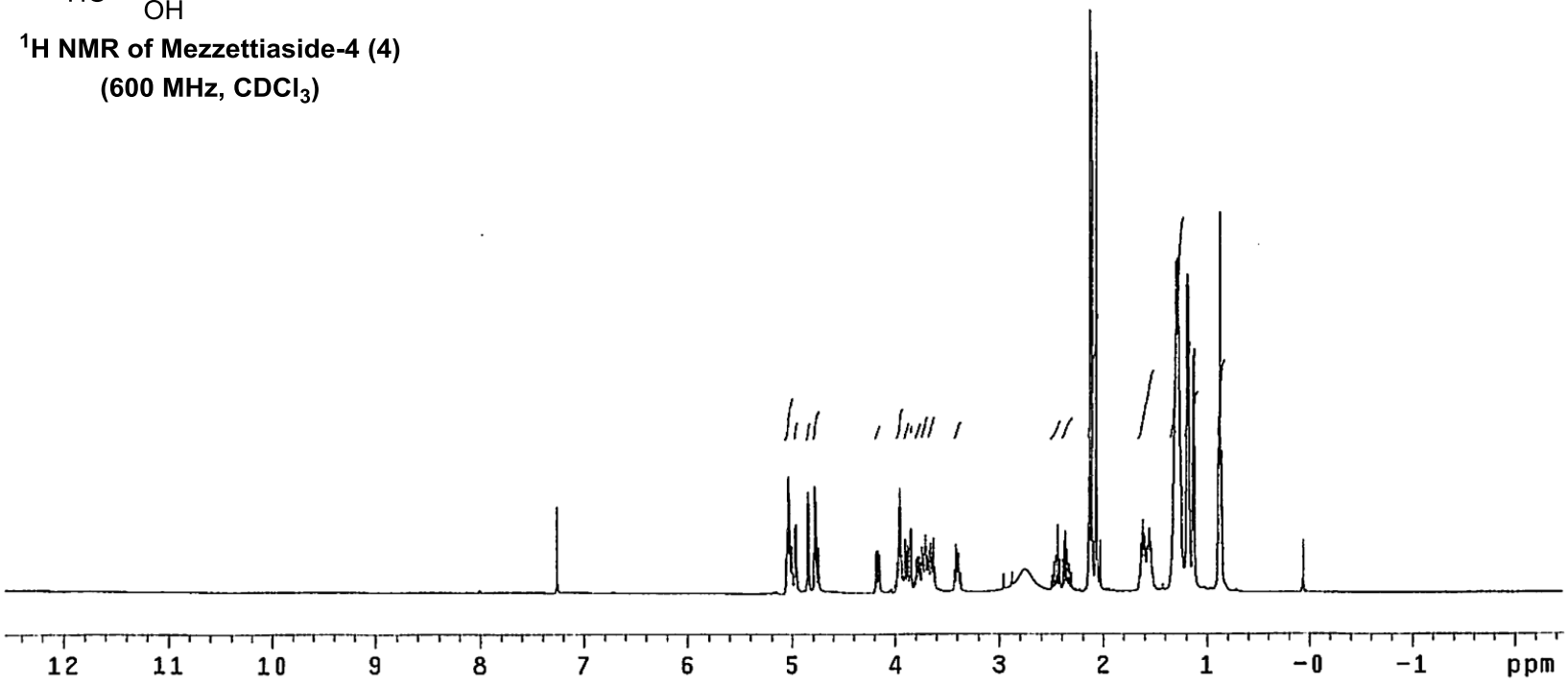


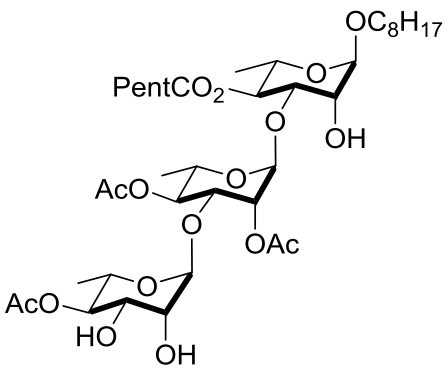
^{13}C NMR of (23)
(100 MHz, $CDCl_3$)



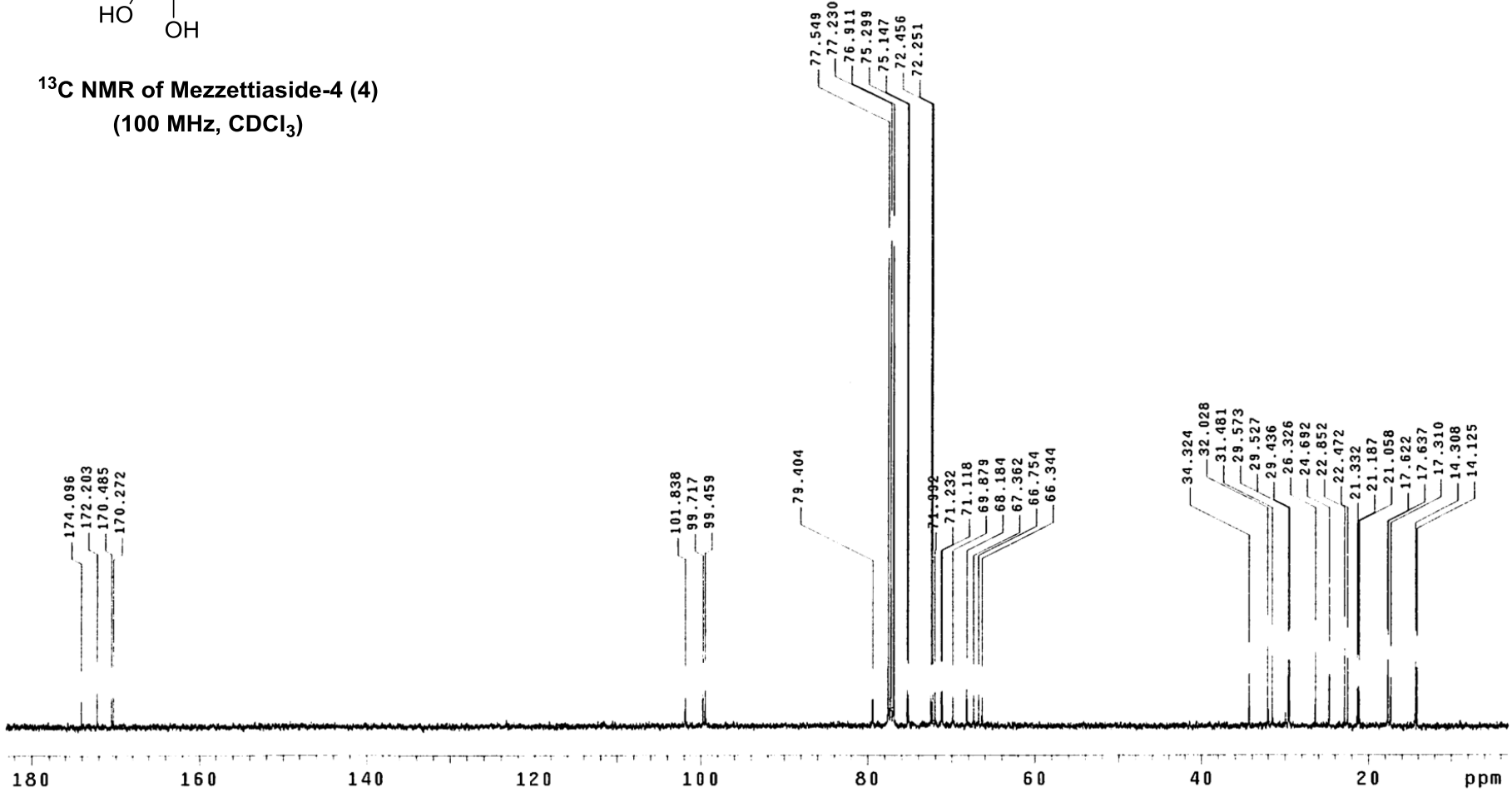


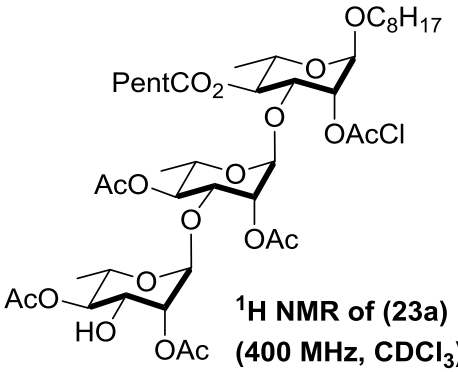
^{1}H NMR of Mezzettiaside-4 (4)
(600 MHz, $CDCl_3$)



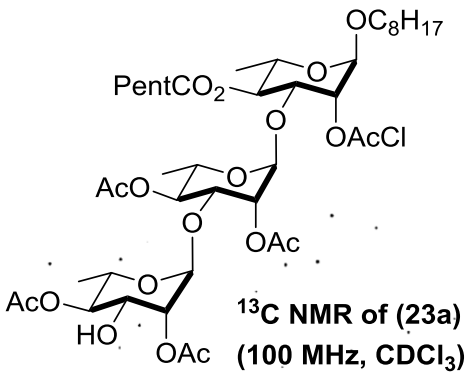


^{13}C NMR of Mezzettiaside-4 (4)
(100 MHz, $CDCl_3$)

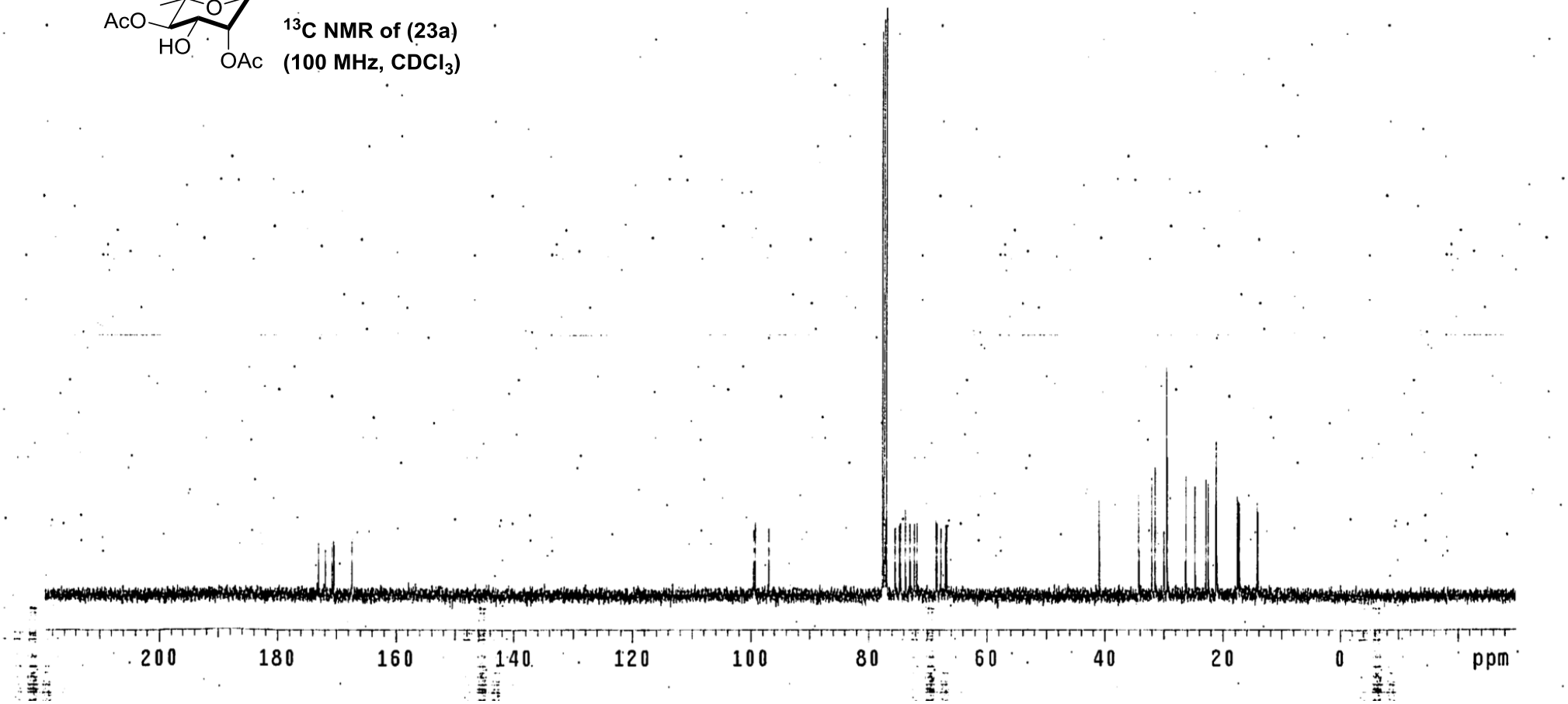


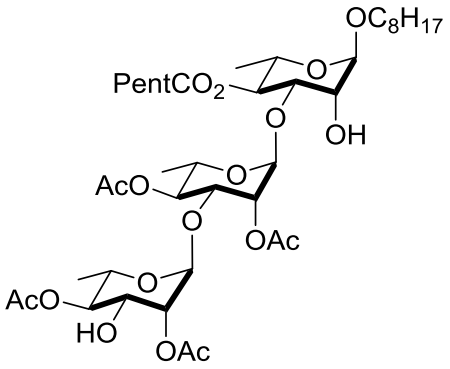


^{1}H NMR of (23a)
(400 MHz, $CDCl_3$)

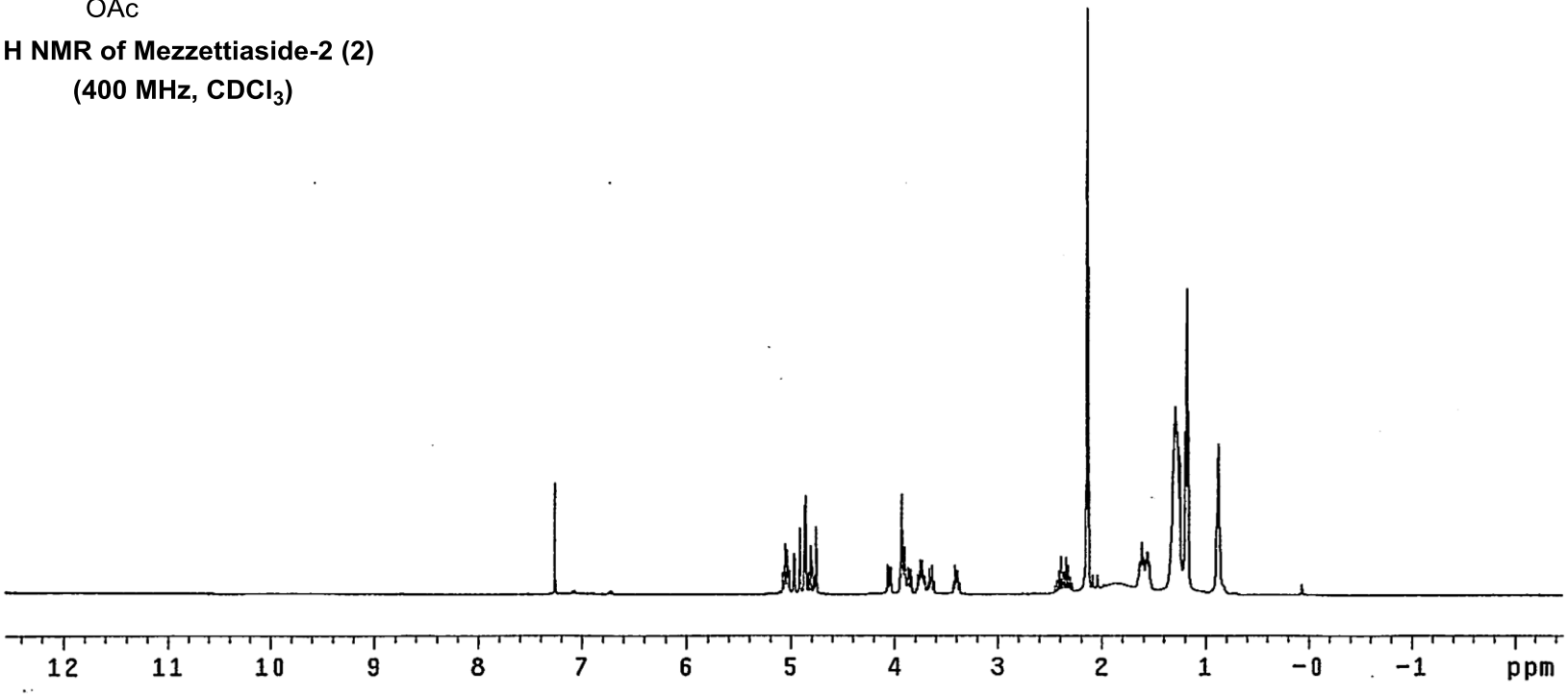


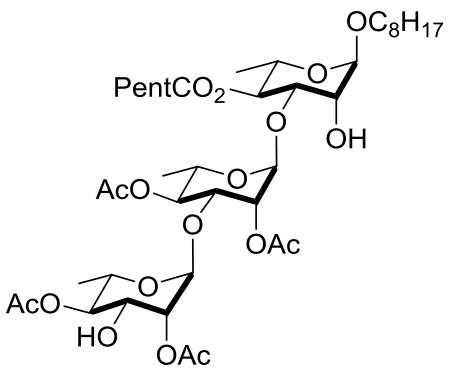
^{13}C NMR of (23a)
(100 MHz, $CDCl_3$)



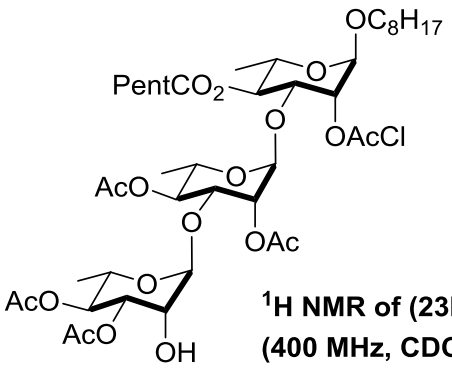


^{1}H NMR of Mezzettiaside-2 (2)
(400 MHz, $CDCl_3$)

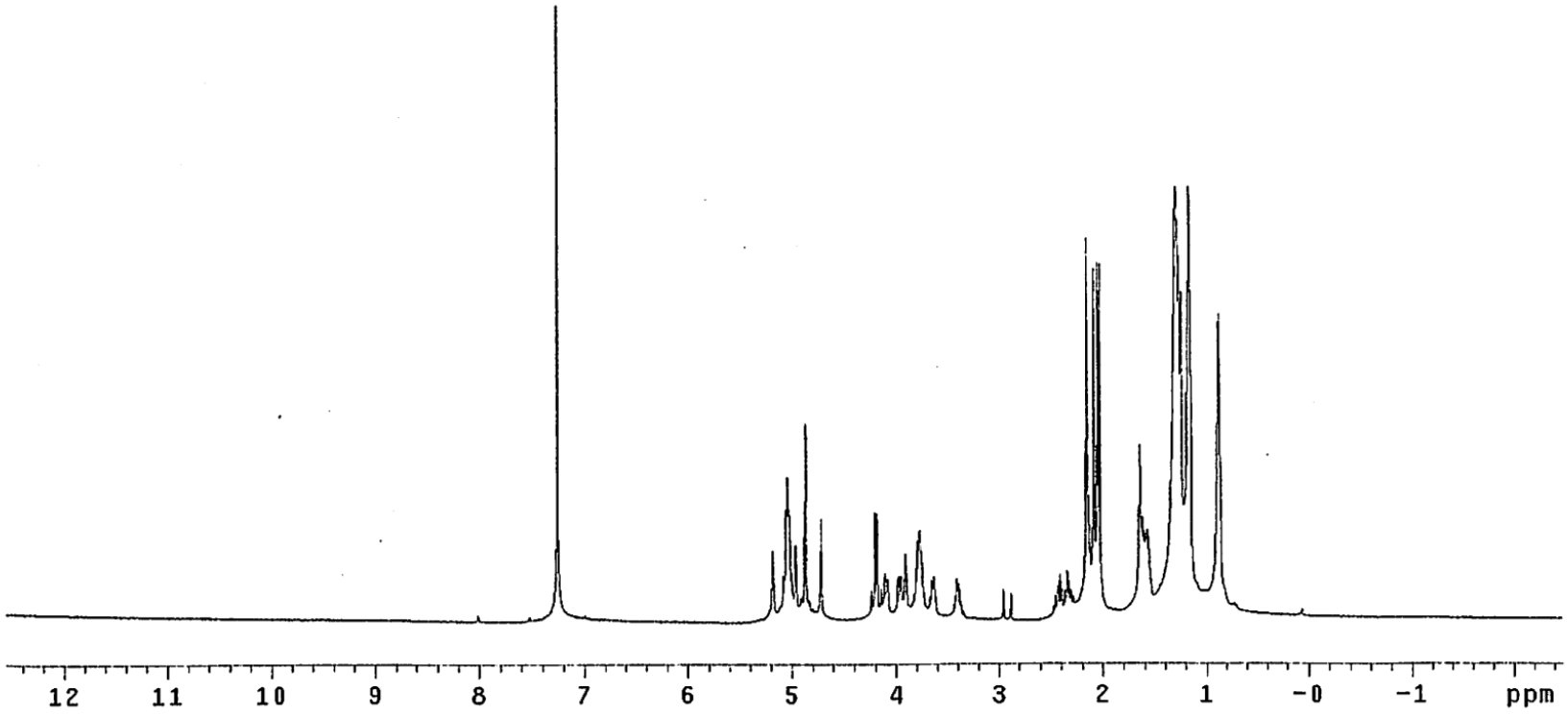


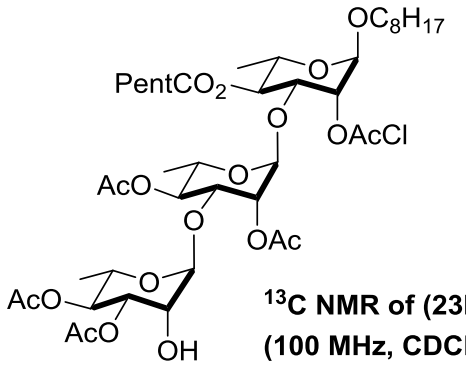


^{13}C NMR of Mezzettiaside-2 (2)
(100 MHz, $CDCl_3$)

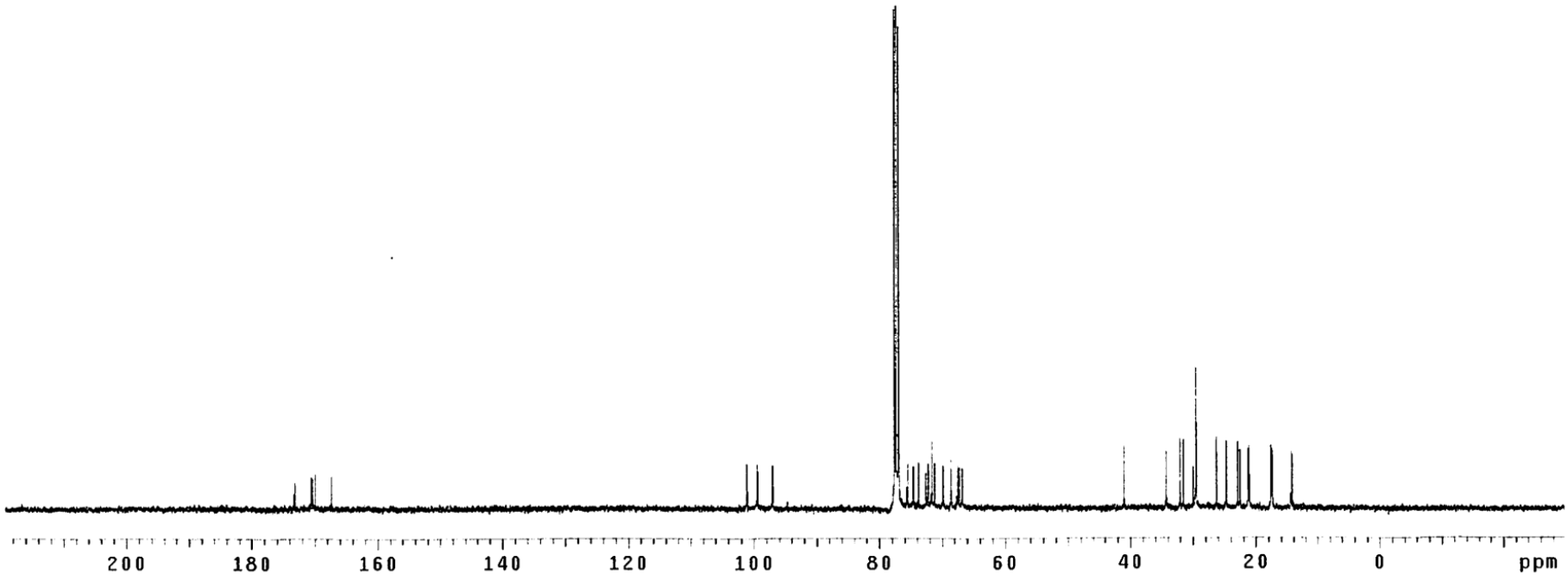


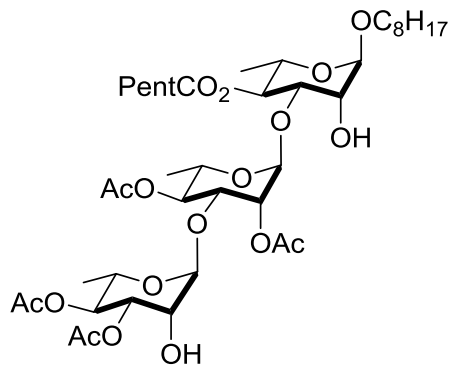
^{1}H NMR of (23b)
(400 MHz, $CDCl_3$)



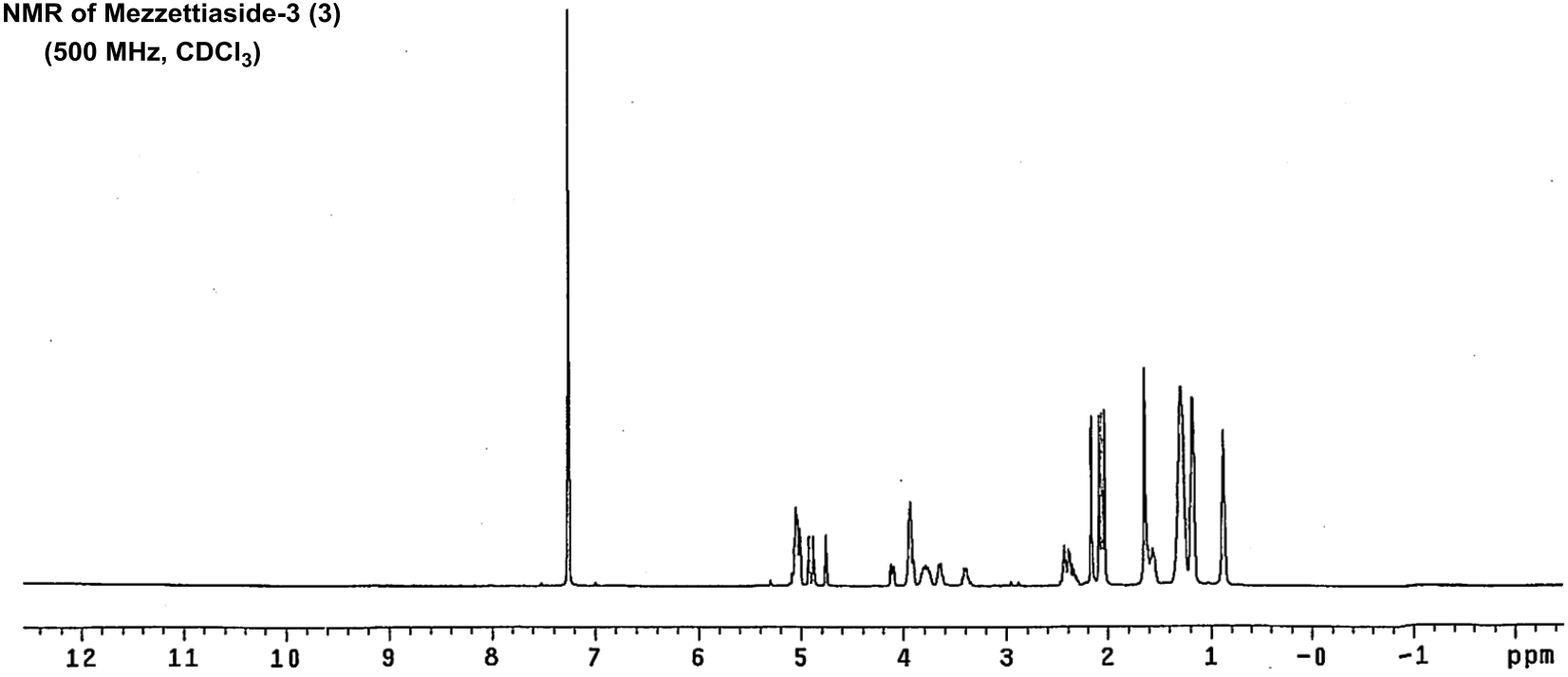


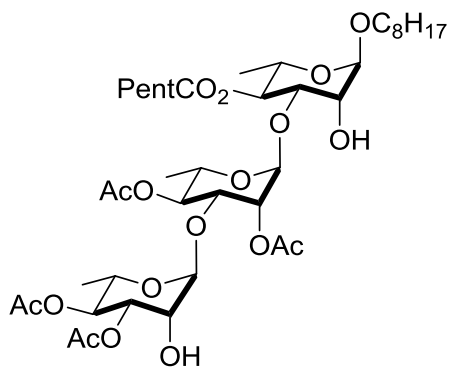
^{13}C NMR of (23b)
(100 MHz, $CDCl_3$)



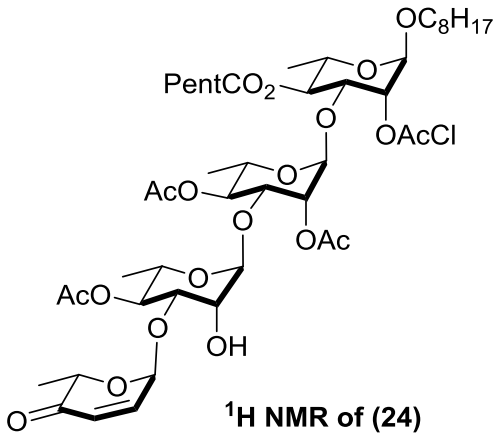


^{1}H NMR of Mezzettiaside-3 (3)
(500 MHz, $CDCl_3$)

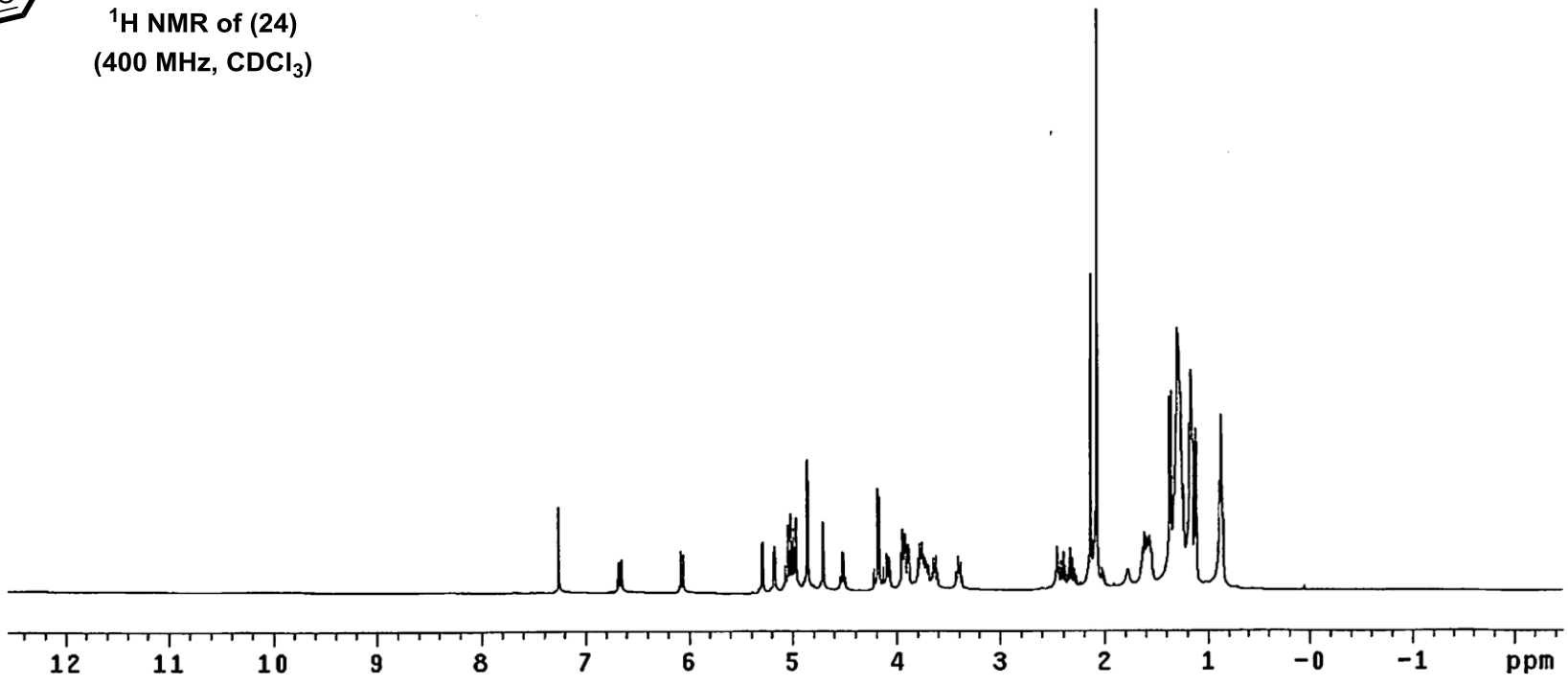


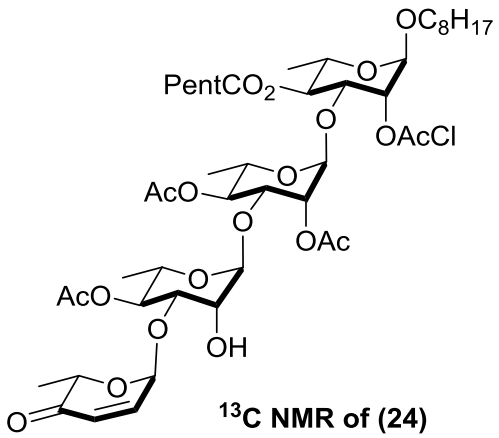


^{13}C NMR of Mezzettiaside-3 (3)
(100 MHz, $CDCl_3$)

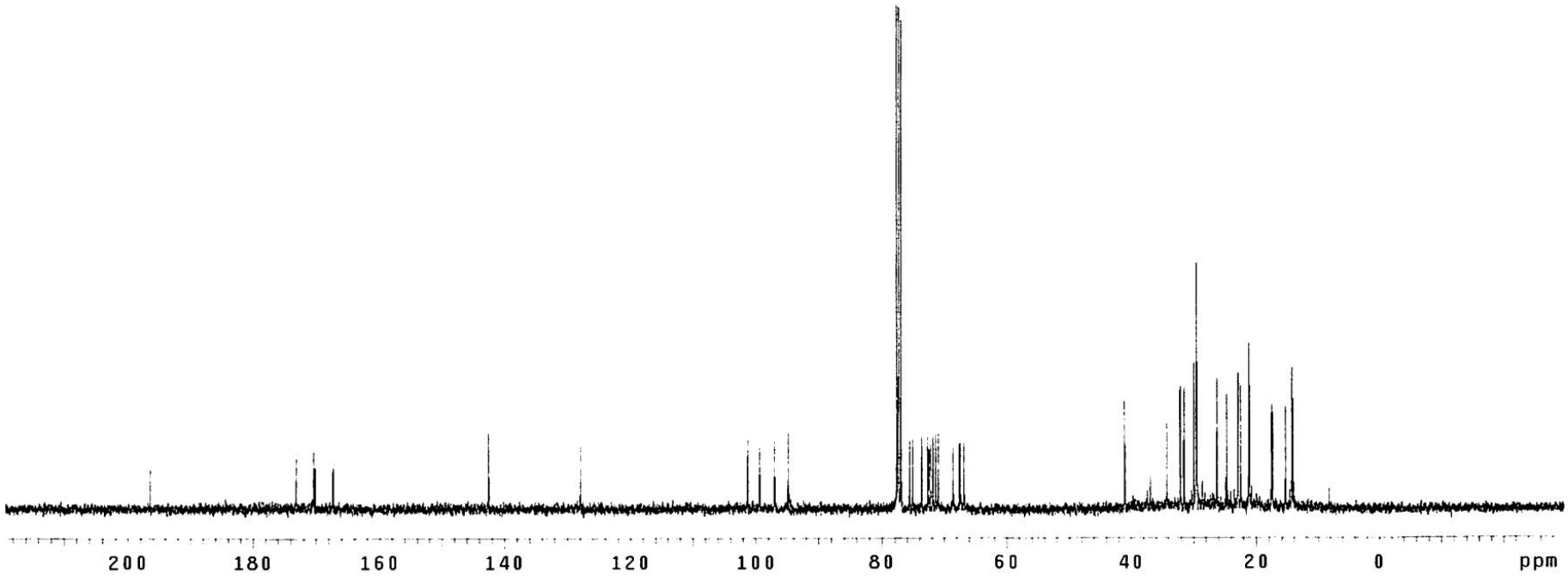


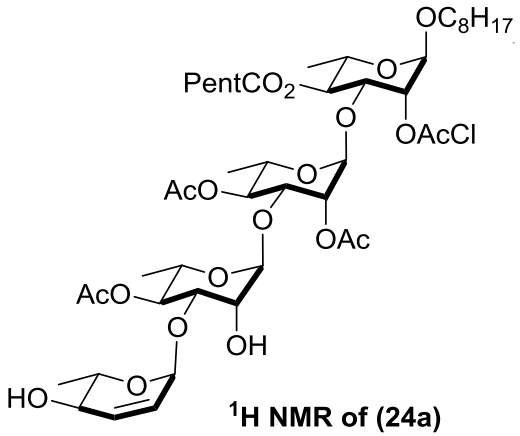
^{1}H NMR of (24)
(400 MHz, $CDCl_3$)



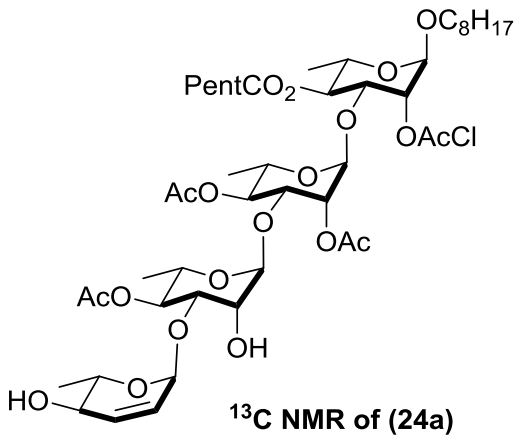


^{13}C NMR of (24)
(100 MHz, $CDCl_3$)

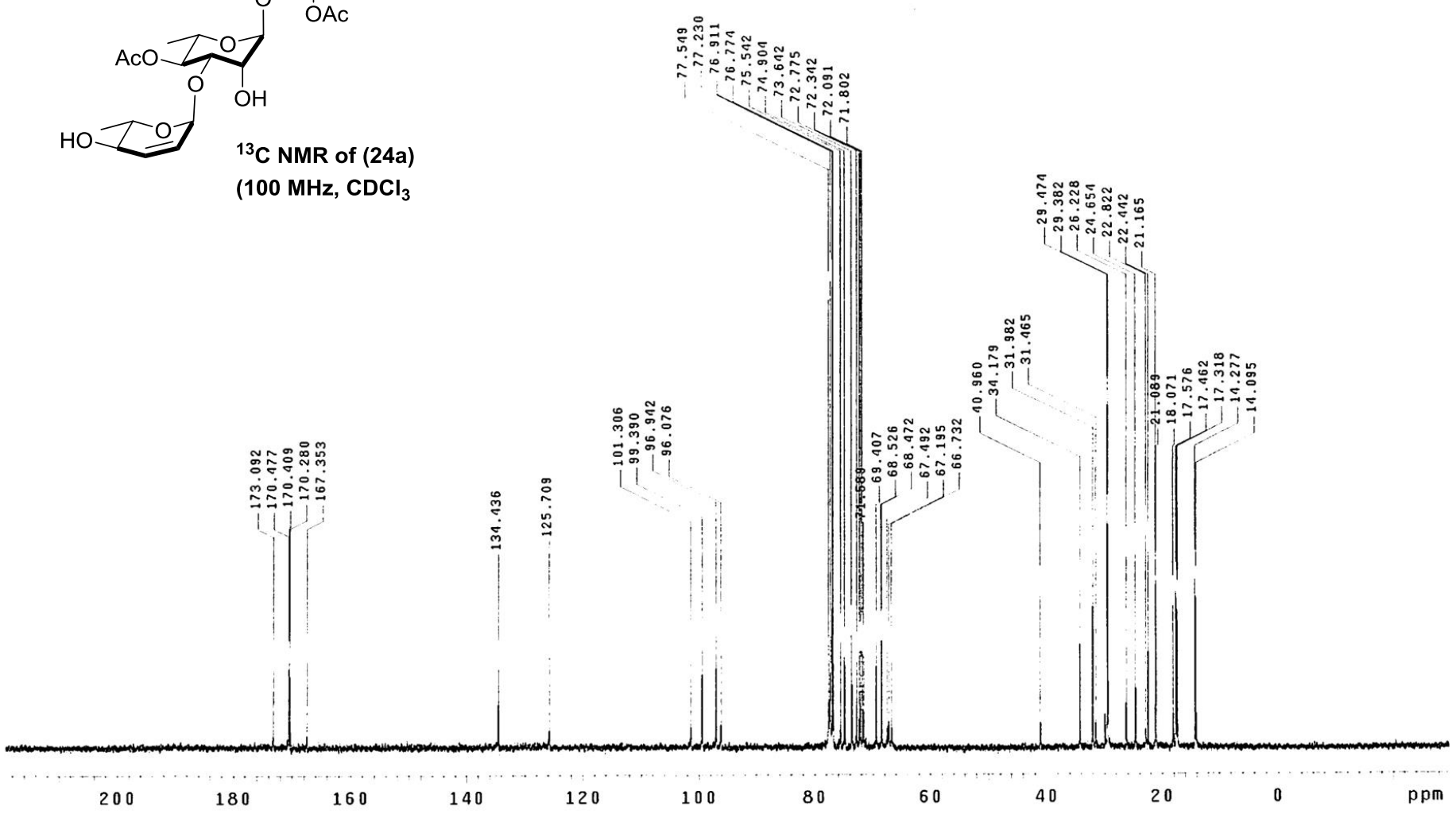


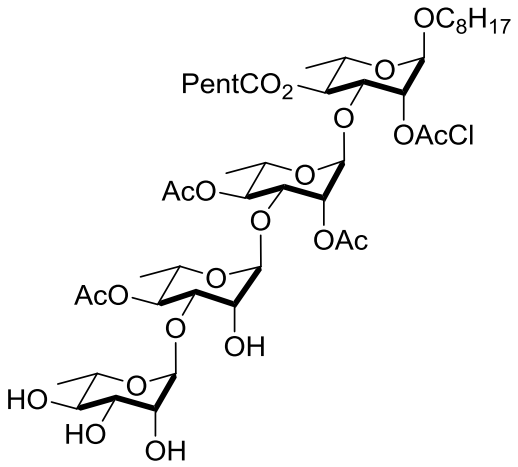


^{1}H NMR of (24a)
(400 MHz, $CDCl_3$

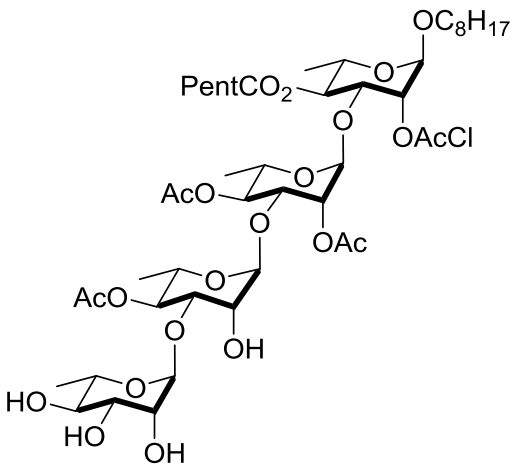


^{13}C NMR of (24a)
(100 MHz, $CDCl_3$

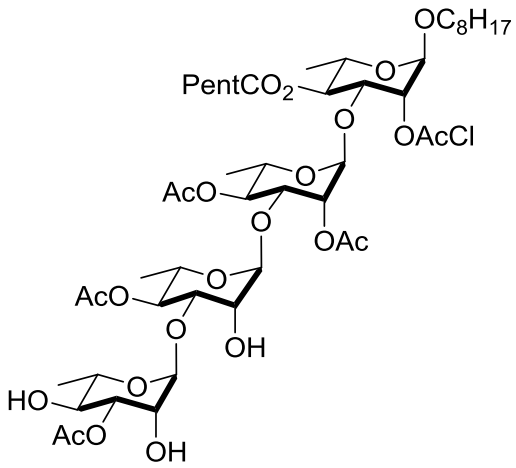




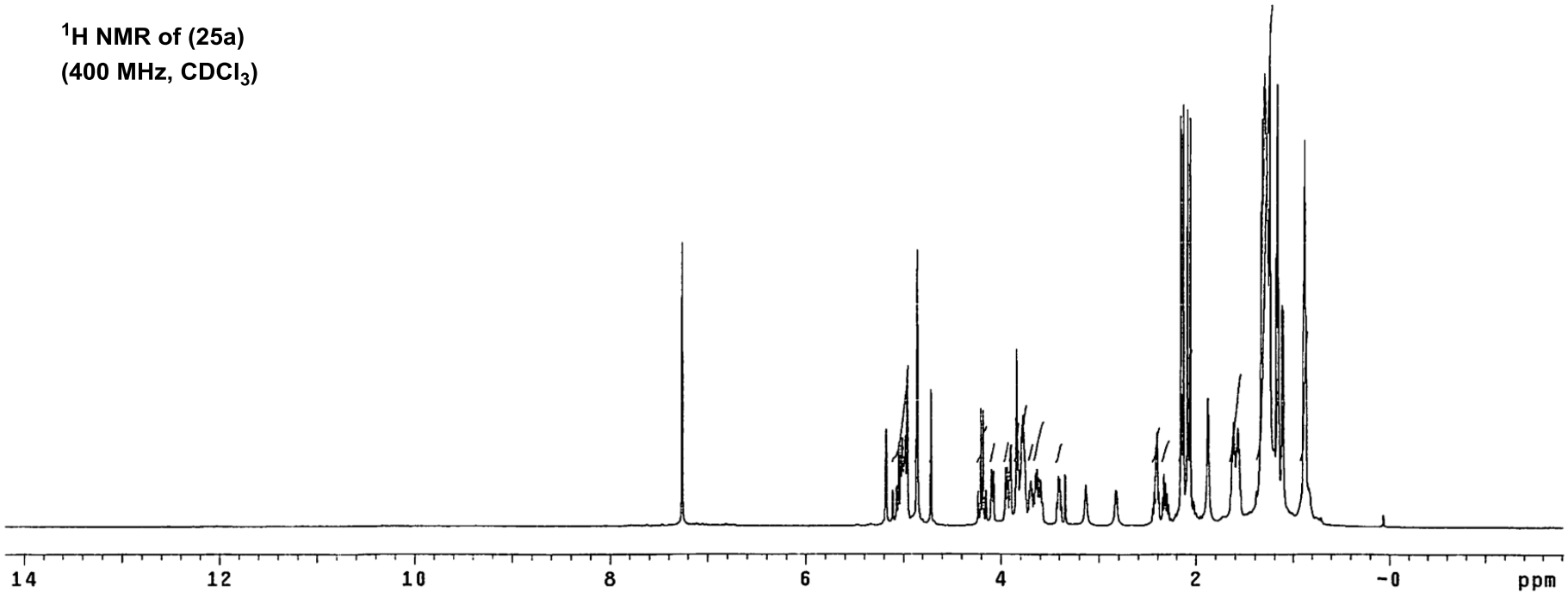
^{1}H NMR of (25)
(400 MHz, $CDCl_3$)

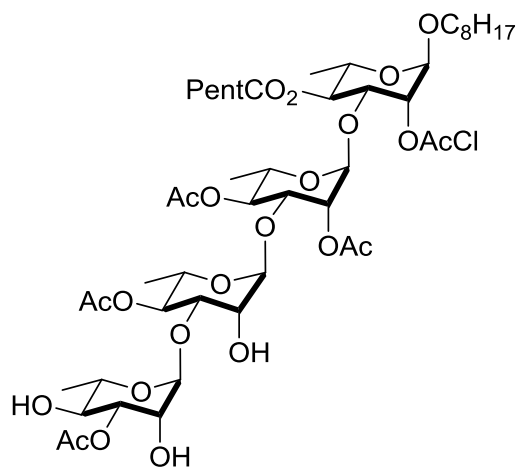


^{13}C NMR of (25)
(100 MHz, $CDCl_3$)

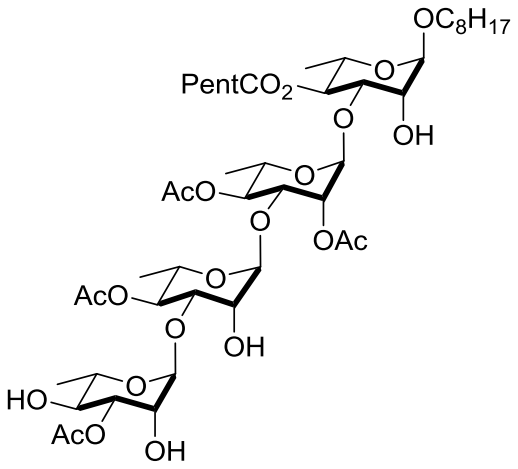


^{1}H NMR of (25a)
(400 MHz, $CDCl_3$)

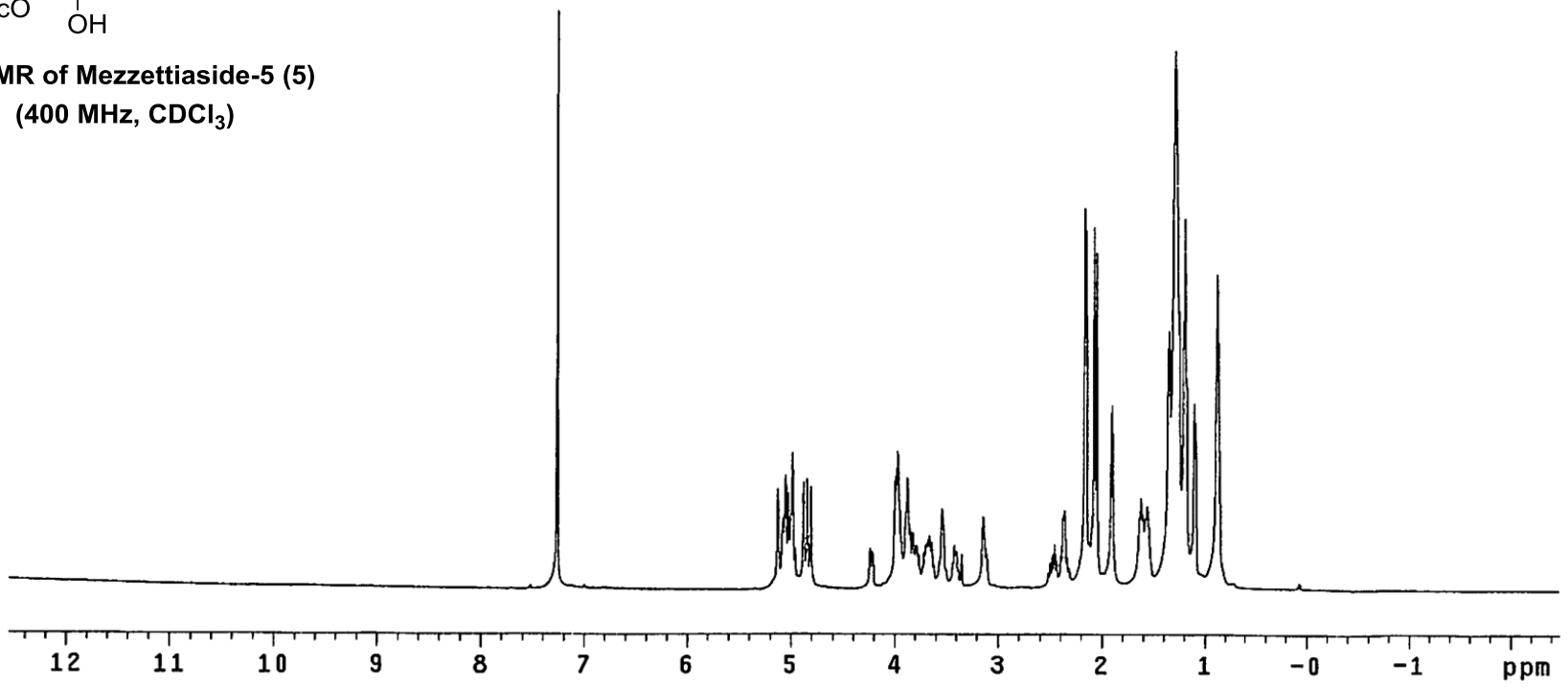


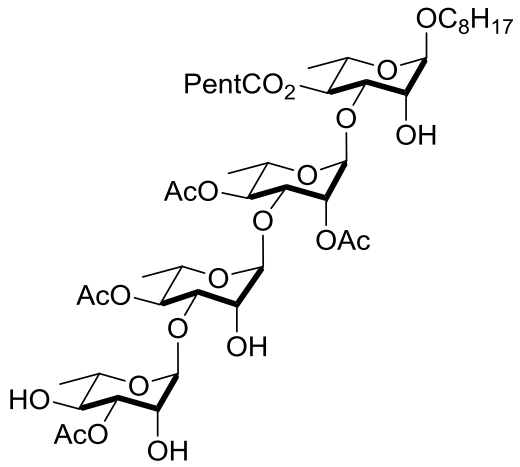


^{13}C NMR of (25a)
(100 MHz, $CDCl_3$)

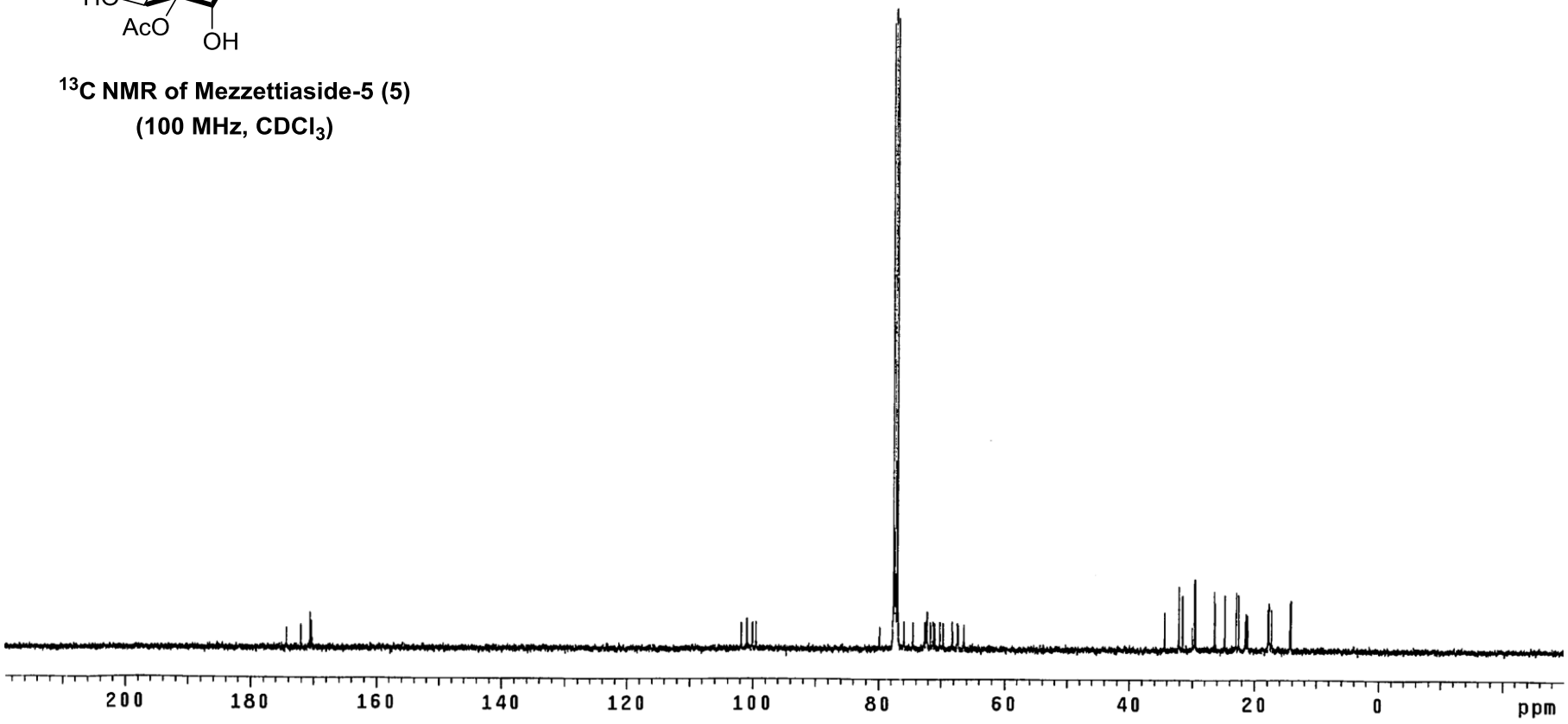


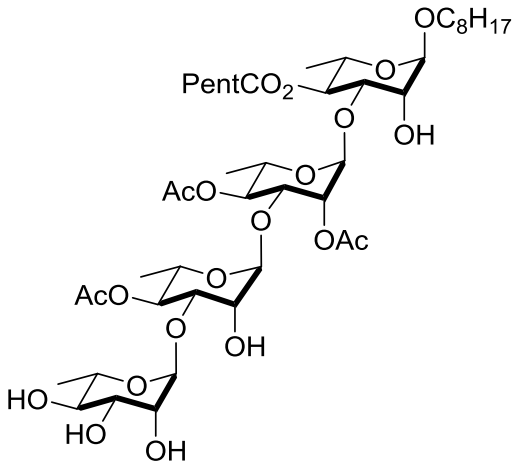
^{1}H NMR of Mezzettiaside-5 (5)
(400 MHz, $CDCl_3$)



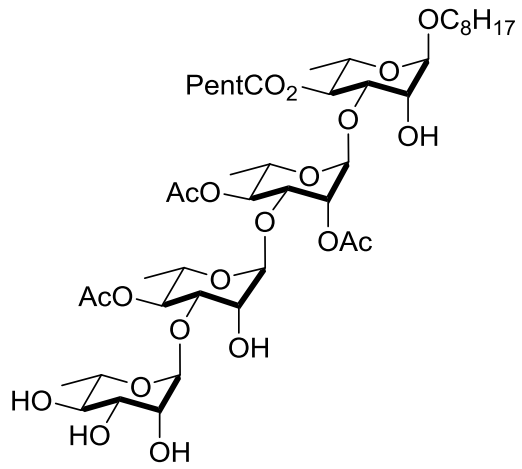


^{13}C NMR of Mezzettiaside-5 (5)
(100 MHz, $CDCl_3$)

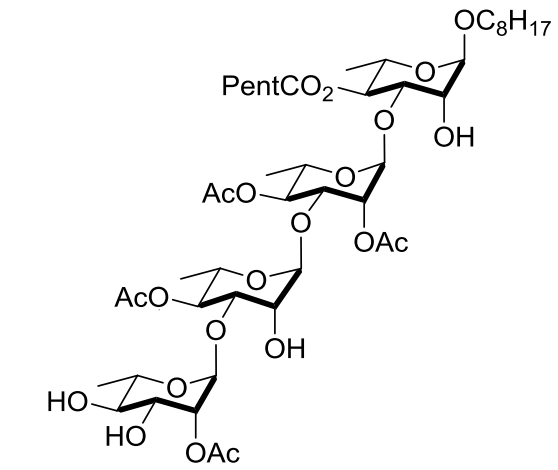




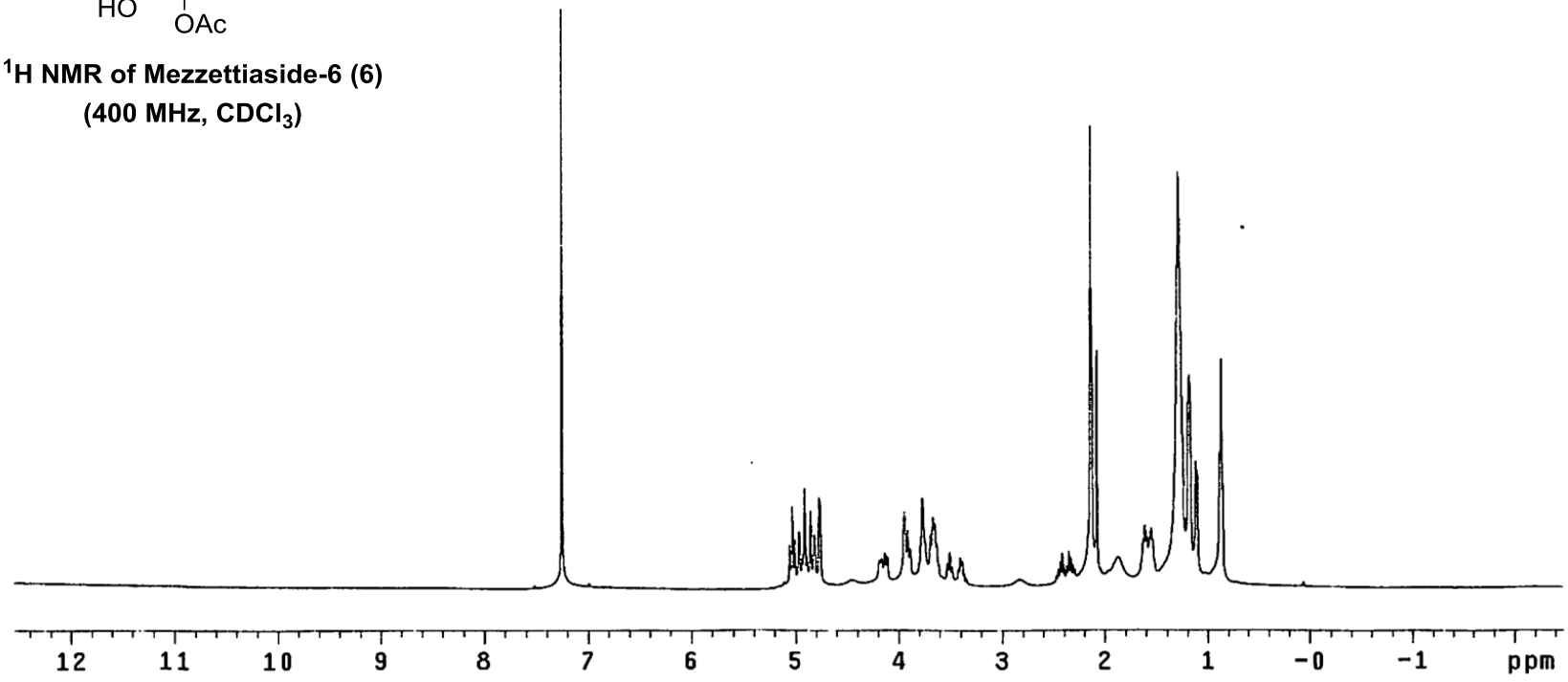
^{1}H NMR of Mezzettiaside-7 (7)
(500 MHz, CD_3OD + C_6D_6 (6:1))

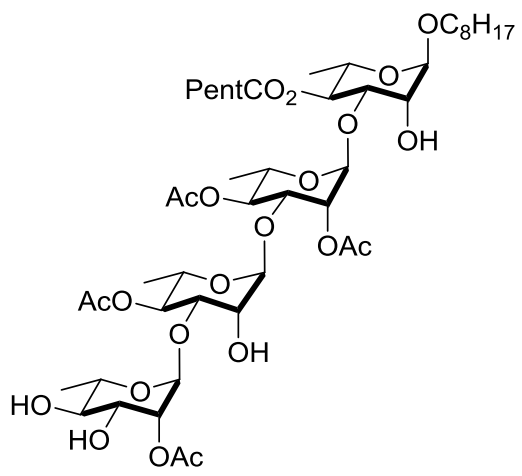


^{13}C NMR of Mezzettiaside-7 (7)
(100 MHz, CD_3OD + C_6D_6 (6:1))



^{1}H NMR of Mezzettiaside-6 (6)
(400 MHz, $CDCl_3$)





^{13}C NMR of Mezzettiaside-6 (6)
(100 MHz, $CDCl_3$)