Merremoside D: De novo synthesis of the purported structure, NMR analysis, comparison of spectral data

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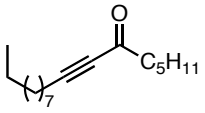
Supporting Information

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 3.30 ppm) or benzene-d_6 (δ 7.16 ppm) or pyridine-d_5 (δ 7.22, 7.58, 8.74 ppm) for ^{1}H NMR and $CDCl_3$ (δ 77.23 ppm) or CD_3OD (δ 49.05 ppm) or benzene-d_6 (δ 128.39 ppm) or pyridine-d_5 (δ 150.35, 135.91, 123.87 ppm) for ^{13}C NMR. In the case of ^{19}F NMR, trifluoroacetic acid (δ –76.55 ppm) was used as an external reference for Mosher ester analyses. Infrared (IR) spectra were obtained on a FT-IR spectrometer. Optical rotations were measured with a digital polarimeter in the solvent specified. Melting points were determined with a standard melting point apparatus. Flash column chromatography was performed on 60-200 or 230-400 mesh silica gel. Analytical thin-layer chromatography was performed with precoated glassbacked plates and visualized by quenching of fluorescence and by charring after treatment with panisaldehyde or potassium permanganate stain. R_f values were obtained by elution in the stated solvent ratios. 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.

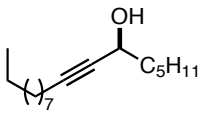
Section B: Experimental Procedures

Heptadec-7-yn-6-one 10 [1]



A solution of *n*-BuLi in hexane (30.40 mL, 0.08 mol) was added to a precooled solution of 1-undecyne **11** (11.50 g, 0.08 mol) in dry THF (138 mL) at –78 ºC under argon. After 30 min at this temperature slowly added hexanal **12** (6.90 g, 0.07 mol) and the resulting mixture was raised to room temperature over a period of 5 h. The reaction mixture was diluted with dichloromethane and quenched with saturated NH_4Cl at 0 ºC. The aqueous phase was extracted with CH_2Cl_2 (300 mL x 3). Combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 8-10% ethylacetate/hexane gave the racemic alkynol. The racemic alkynol was then dissolved in 173.00 mL DMSO and added Et_3N (57 mL, 41.90 mol). Cooled the mixture to –25 ºC and dropwise added a 173 mL DMSO solution of Py•SO_3 (33.20 g, 0.21 mol) via cannula. The reaction mixture was slowly raised to room temperature over 3h. Diluted with CH_2Cl_2 and quenched with 1N HCl at 0 ºC. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with saturated $NaHCO_3$ and brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 4% Et_2O/hexane gave **10** (13.70g, 78% over 2 steps). Faint yellow oil: R_f (5% hexanes/EtOAc) = 0.28, ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.84 (t, J = 6.5 Hz, 3H), δ 0.86 (t, J = 6.5 Hz, 3H), δ 1.23-1.38 (m, 18H), δ 1.53 (tt, J = 7.2, 7.2 Hz, 2H), δ 1.62 (tt, J = 7.2, 7.2 Hz, 2H), δ 2.31 (t, J = 7.6 Hz, 2H), δ 2.47 (t, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 188.6, 94.3, 81.0, 45.6, 31.9, 31.3, 29.5, 29.4, 29.2, 28.9, 27.8, 23.9, 22.8, 22.5, 19.0, 14.2, 13.9.

(*S*)-heptadec-7-yn-6-ol 13[1]

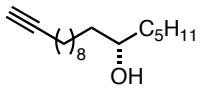


Propargyl ketone **10** (6.61 g, 26.40 mmol) was dissolved in 10 mL CH_2Cl_2 and added to a 1:1 mixture of HCOOH : Et_3N (45 mL). The reaction mixture was then degassed by bubbling argon

[1] Larson, D. P.; Heathcock, C.H. *J. Org. Chem*. **1997**, *62*, 8406.

through the solution for 15 min. Noyori-(*S*,*S*) catalyst (136.00 mg, 0.224 mmol) was added and the reaction mixture was stirred vigorously at room temperature for 12h. The reaction mixture was diluted with Et_2O and quenched with saturated $NaHCO_3$. The aqueous layer was extracted with Et_2O (100 mL x 3) and the combined organic layer was washed with saturated brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 3% EtOAc/hexane gave propargyl alcohol 1**3** (6.00 g, 90%). Light yellow oil: R_f (10% hexanes/EtOAc) = 0.54, $[\alpha]_D^{25}$ = –0.11 (*c* 1.14, CH_2Cl_2), ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, *J* = 7.6 Hz, 3H), δ 0.96 (t, *J* = 6.4 Hz, 3H), δ 1.25-1.72 (m, 21H), δ 1.89 (brs, 1H), δ 1.18 (ddd, *J* = 1.2, 5.2, 7.2 Hz, 2H), δ 4.33 (ddd, *J* = 2.0, 2.4, 6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 85.7, 81.6, 62.9, 38.4, 32.1, 31.7, 29.7, 29.4, 29.3, 29.0, 28.9, 25.1, 22.9, 22.8, 18.9, 14.3, 14.2.

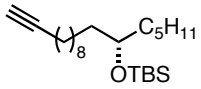
(*S*)-heptadec-16-yn-6-ol 13a[1,2]



A dry round-bottom flask was charged with KH (7.60 g, 0.19 mol). Hexane was removed by flowing argon through the flask. 1,3-diaminopropane (110 mL, 1.30 mol) was added dropwise and stirred for 90 min to give a homogeneous brown solution. Propargyl alcohol 1**3** (9.60 g, 0.04 mol) in 54 mL dry THF was added dropwise to the reaction mixture at 0 ºC and allowed to warm up to room temperature. After stirring for 2h at room temperature, the reaction mixture was cooled to 0 ºC and quenched by adding H_2O. The aqueous layer was extracted with CH_2Cl_2 (300 mL x 3) and the combined organic layer was washed with saturated $NaHCO_3$ and brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 5% EtOAc/hexane gave **13a** (6.70 g, 70%). White solid: R_f (5% hexanes/EtOAc) = 0.32, $[\alpha]_D^{25}$ = +1.1 (*c* 0.14, CH_2Cl_2), ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.84 (t, *J* = 6.6 Hz, 3H), δ 1.16-1.50 (m, 23H), δ 1.78 (brs, 1H), δ 1.89 (t, *J* = 2.8 Hz, 1H), δ 2.12 (ddd, *J* = 2.4, 6.8, 7.2 Hz, 2H), δ 3.52 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 84.8, 72.0, 68.2, 37.6, 37.5, 32.1, 29.8, 29.7, 29.6, 29.2, 28.9, 28.6, 25.8, 25.5, 22.8, 18.5, 14.2.

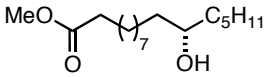
[2] Compound **13a** was involved in the transformation (**13** to **14**), which is not represented in Scheme 2.

(*S*)-*tert*-butyl(heptadec-16-yn-6-yloxy)dimethylsilane 14[1]



Alcohol **13a** (4.32 g, 17.20 mmol) was dissolved in 34 mL dry CH_3CN. DMAP (2.09 g, 17.20 mmol) was added to this solution and cooled to 0 ºC. At 0 ºC under argon, added DBU (7.70 mL, 51.40 mmol) followed by TBSCl (10.30 g, 68.50 mmol). The reaction mixture was raised up to room temperature over 2h. After consumption of starting material, reaction mixture was diluted with Et_2O and quenched with 1N HCl at 0 ºC. The aqueous layer was extracted with Et_2O (200mL x 3) and the combined organic layer was washed with saturated $NaHCO_3$ and brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 2-5% Et_2O/hexane gave **14** (6.30 g, quantitative). Colorless oil: R_f (1% hexanes/EtOAc) = 0.72, $[\alpha]_D^{25} = -0.04$ (*c* 5.0, CH_2Cl_2), ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.03 (s, 6H), δ 0.86 (t, *J* = 6.4 Hz, 3H), δ 0.88 (s, 12H), δ 1.28-1.56 (m, 23H), δ 1.89 (t, *J* = 3.2 Hz, 1H), δ 2.16 (ddd, *J* = 2.8, 4.4, 6.8 Hz, 2H), δ 3.61 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 84.7, 72.5, 68.3, 37.4, 32.4, 30.1, 29.8, 29.7, 29.4, 29.0, 28.7, 26.1, 25.5, 25.2, 22.9, 18.6, 14.3, –4.2.

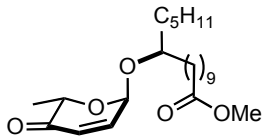
(*S*)-methyl 11-hydroxyhexadecanoate 7[1]



Alkyne **14** (7.23 g, 19.70 mmol) was dissolved in 65 mL benzene and 20 mL HOAc. The resulting solution was cooled to 0 ºC and added an aqueous solution of $KMnO_4$ (12.50 g, 0.08 mmol in 100 mL H_2O) dropwise via a dropping funnel. To this reaction mixture, added CTAB (1.44 g, 4.00 mmol) and stirred vigorously without replenishing ice over a period of 24h. Upon consumption of starting material, cooled the reaction to 0 ºC and slowly added 20 g Na_2SO_3 followed by 26 mL 1N HCl. Stirred for approximately 10 min until white precipitate formed and reaction turned colorless. The precipitate was dissolved by adding H_2O and the aqueous layer was subsequently extracted with CH_2Cl_2 (300 mL x 3). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude reaction mixture was passed through a pad of celite to obtain the corresponding carboxylic acid, which was carried to the next step without further purification. The crude carboxylic acid was dissolved in 300 mL MeOH and added 9.00 mL conc. H_2SO_4. The resulting reaction mixture was refluxed at 65 ºC for 2h. The

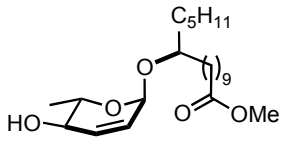
reaction was then cooled 0 ºC and added 10 g solid $NaHCO_3$. MeOH was removed under reduced pressure and the resulting ester was partitioned between EtOAc and H_2O. The aqueous layer was extracted with EtOAc (300 mL x 3) and the combined organic layer was washed with saturated brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 5-10% EtOAc/hexane gave jalapinolic ester **7** (3.36, 61%, 2 steps). White solid: mp: 38-40 ºC, R_f (10% hexanes/EtOAc) = 0.45, $[\alpha]_D^{25}$ = +1.0 (*c* 1.07, $CHCl_3$), (ref[1]: $[\alpha]_D$ = +0.9 ($CHCl_3$)), ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, *J* = 6.8 Hz, 3H), δ 1.20-1.45 (m, 22H), δ 1.60 (m, 2H), δ 2.29 (t, *J* = 7.6 Hz, 2H), δ 3.57 (m, 1H), 3.65 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.3, 72.0, 51.4, 37.5, 37.4, 34.1, 31.9, 29.6, 29.5, 29.3, 29.2, 29.1, 25.6, 25.3, 24.9, 22.6, 14.0. The enantiomeric excess (ee) was determined by Mosher ester analysis.

1-(Methoxycarbonyl)pentadec-10(*S*)-yl 2,3-didehydro-5-methyl-4-oxo-pyran 15



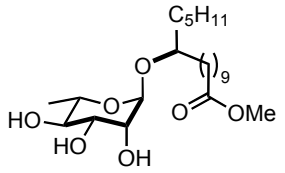
Jalapinolic ester **7** (236 mg, 0.82 mmol) was dissolved in 2.70 mL dry CH_2Cl_2. To this added α-L-Boc-pyranone **5** (282 mg, 1.24 mmol). The reaction mixture was cooled to 0 ºC and added a premixed solution of $Pd_2(dba)_3$•$CHCl_3$ (21.30 mg, 0.02 mmol) and PPh_3 (21.60 mg, 0.08 mmol) dissolved in CH_2Cl_2 via cannula under argon. The reaction mixture was stirred under argon at 0 ºC overnight. After consumption of starting materials, concentrated the reaction mixture under reduced pressure and flash chromatography with 12-14% Et_2O/hexane yielded the desired product **15** (318 mg, 97%). Colorless oil: R_f (10% hexanes/EtOAc) = 0.62; $[\alpha]_D^{25}$ = +13.8 (*c* 0.98, CH_2Cl_2); IR (thin film, cm^{-1}) ν 2928, 2855, 1739, 1700, 1158, 1079, 1025; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.85 (t, *J* = 7.2 Hz, 3H), δ 1.17-1.29 (m, 18H), δ 1.32 (d, *J* = 6.8 Hz, 3H), δ 1.44-1.58 (m, 6H), δ 2.25(t, *J* = 7.2 Hz, 2H), δ 3.64 (s, 3H), δ 3.68 (m, 1H), δ 4.56 (q, *J* = 6.4 Hz, 1H), δ 5.21 (d, *J* = 3.6 Hz, 1H), δ 6.02 (d, *J* = 10.4 Hz, 1H), δ 6.76 (dd, *J* = 3.2, 10.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 196.4, 174.6, 142.9, 128.1, 89.8, 72.2, 71.1, 51.7, 37.7, 37.6, 34.3, 32.1, 30.0, 29.9, 29.6, 29.4, 29.3, 25.8, 25.5, 25.1, 22.9, 15.6, 14.3; HRMS (ESI): calcd for $[C_{23}H_{40}O_5 + Na]^+$ 419.2773, found 419.2768.

1-(Methoxycarbonyl)pentadec-10(*S*)-yl 2,3-didehydro-α-L-rhamnopyranoside 16



Enone **15** (258 mg, 0.65 mmol) was dissolved in 1.30 mL dry CH_2Cl_2 and cooled to –78 ºC. To this cooled solution, added a 0.4 M solution of $CeCl_3$•MeOH (1.30 mL). After stirring for 10 min at this temperature, added solid $NaBH_4$ (37 mg, 0.98 mmol) in portions. The reaction mixture was stirred at –78 ºC for 2h. Quenched with saturated $NaHCO_3$ at low temperature, diluted with CH_2Cl_2 and warmed to 0 ºC. The aqueous layer was extracted with CH_2Cl_2 (50mL x 3) and the combined organic layer was washed with saturated brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 15-20% EtOAc/hexane gave enol **16** (255 mg, 98%). Colorless oil: R_f (10% hexanes/EtOAc) = 0.20; $[\alpha]_D^{25}$ = –29.5 (*c* 1.08, CH_2Cl_2); IR (thin film, cm^{-1}) ν 3460, 29.27, 28.55, 17.41, 1635, 1457, 1034, 668, 526; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.86 (t, *J* = 7.2 Hz, 3H), δ 1.18-1.30 (m, 21H), δ 1.34-1.48 (m, 4H, δ 1.61 (m, 2H), δ 2.27 (t, *J* = 8.0 Hz, 2H), δ 3.60 (m, 1H), δ 3.63 (s, 3H), δ 3.69 (dq, *J* = 2.4, 6.6 Hz, 1H), δ 3.77 (dd, *J* = 1.6, 7.2 Hz, 1H), δ 4.95 (s, 1H), δ 5.67 (ddd, *J* = 2.4, 5.2, 10.4 Hz, 1H), δ 5.89 (d, *J* = 10.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.5, 133.6, 127.0, 93.5, 78.8, 69.4, 68.2, 51.6, 35.3, 34.6, 34.2, 29.9, 29.7, 29.5, 29.4, 29.3, 25.5, 25.4, 25.1, 22.8, 18.0, 14.2; HRMS (ESI): calcd for $[C_{23}H_{42}O_5 + Na]^+$ 421.2924, found 421.2923.

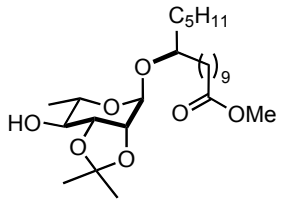
1-(Methoxycarbonyl)pentadec-10(*S*)-yl α-L-rhamnopyranoside 17



Allylic alcohol **16** (234 mg, 0.59 mmol) was dissolved in a 1:1 mixture of *t*-BuOH/acetone (0.60 mL) and the mixture was cooled to 0 ºC. To this added a 50% (v/v) solution of NMO/H_2O (0.60 mL). The reaction mixture was stirred at that temperature for 15 min and added OsO_4 (7.5 mg, 0.03 mmol). The resulting reaction mixture was stirred over night without replenishing ice from

0 ºC to rt. After consumption of starting material, the reaction was cooled back to 0 ºC, diluted with EtOAc and reduced the excess OsO_4 with saturated Na_2SO_3. The reaction mixture was then concentrated to remove acetone. The aqueous layer was extracted with EtOAc (30mL x 3) and the combined organic layer was washed with saturated brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 65-70% EtOAc/hexane gave triol **17** (212 mg, 83%). White solid: R_f (70% hexanes/EtOAc) = 0.21; mp: 56 ºC; $[\alpha]_D^{25}$ = –41.5 (*c* 0.66, CH_2Cl_2); IR (thin film, cm^{-1}) ν 3391, 2926, 2854, 1741, 1456, 1048, 668; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.86 (t, *J* = 7.2 Hz, 3H), δ 1.18-1.28 (m, 21H), δ 1.45 (m, 4H), δ 1.60 (m, 2H), δ 2.29 (t, *J* = 7.2 Hz, 2H), δ 2.49 (brs, 1H), δ 3.47 (m, 1H), δ 3.57 (m, 1H), δ 3.65 (s, 3H), δ 3.69-3.89 (m, 3H), δ 4.21 (brs, 1H), δ 4.82 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.7, 98.7, 78.1, 73.3, 72.2, 71.9, 68.4, 51.7, 34.6, 34.3, 44.3, 32.1, 30.0, 29.7, 29.5, 29.4, 29.3, 25.3, 25.1, 25.0, 22.8, 17.6, 14.3; HRMS (ESI): calcd for $[C_{23}H_{44}O_7 + Na]^+$ 455.2984, found 455.2979.

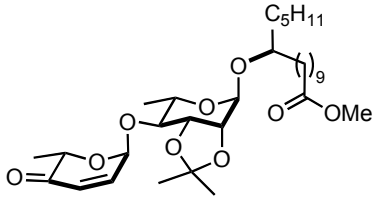
1-(Methoxycarbonyl)pentadec-10(*S*)-yl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside 18



Triol **17** (175 mg, 0.40 mmol) was dissolved in dry acetone (1.30 mL) and the mixture was cooled to 0 ºC. To this added 2,2-DMP (98 μL, 0.80 mmol) and *p*-TsOH (0.76 mg, 0.004 mmol). The reaction was stirred under argon from 0 ºC to rt over 2h. Then the reaction was quenched by adding few drops of Et_3N at 0 ºC. The quenched reaction mixture was concentrated under reduced pressure and purified by silica gel chromatography. Elution with 20-25% EtOAc/hexane gave **18** (170 mg, 90%). Colorless oil: R_f (20% hexanes/EtOAc) = 0.34; $[\alpha]_D^{25}$ = –23.38 (*c* 1.65, CH_2Cl_2); IR (thin film, cm^{-1}) ν 3459, 2928, 2855, 1741, 1457, 1380, 1219, 1071, 1051, 996, 861; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.87 (t, *J* = 7.4 Hz, 3H), δ 1.12-1.30 (m, 21H), δ 1.35 (s, 3H), δ 1.46 (m, 4H), 1.52 (s, 3H), δ 1.62 (m, 2H), δ 2.29 (t, *J* = 7.2 Hz, 2H), δ 2.64 (d, *J* = 3.6 Hz, 1H), δ 3.38 (m, 1H), δ 3.62 (m, 1H), δ 3.64 (s, 3H), δ 3.74 (dq, *J* = 6.0, 7.8 Hz, 1H), δ 3.09 (dd, *J* = 8.8, 7.8 Hz, 1H), δ 4.09 (d, *J* = 3.2 Hz, 1H), δ 5.02 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.6, 109.5, 95.7, 78.6, 76.6, 74.6, 66.2, 51.7, 34.6, 34.3, 33.1, 32.1, 30.0, 29.9, 29.7, 29.6,

29.4, 29.3, 28.2, 26.4, 25.4, 25.1, 25.0, 22.8, 17.5, 14.3; HRMS (ESI): calcd for $[C_{26}H_{48}O_7 + Na]^+$ 495.3292, found 495.3290.

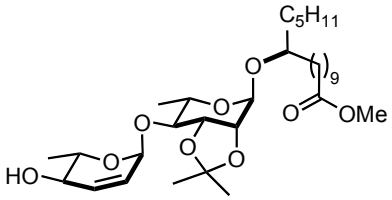
1-(Methoxycarbonyl)pentadec-10(*S*)-yl 2,3-didehydro-5-methyl-4-oxo-pyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside 18a[3]



Glycosyl acceptor **18** (2.11 g, 4.47 mmol) was dissolved in 15 mL dry CH_2Cl_2. To this added α-L-Boc-pyranone **5** (2.04 g, 8.95 mmol). The reaction mixture was cooled to 0 ºC and added a premixed solution of $Pd_2(dba)_3$•$CHCl_3$ (115.70 mg, 0.11 mmol) and PPh_3 (117.20 mg, 0.45 mmol) in CH_2Cl_2 via cannula under argon. The reaction mixture was stirred under argon at 0 ºC overnight. Concentrated the reaction mixture under reduced pressure and flash chromatography with 10% EtOAc/hexane yielded the desired product **18a** (2.60 g, quantitative). Colorless oil: R_f (20% hexanes/EtOAc) = 0.35; $[\alpha]_D^{25}$ = –13.52 (*c* 1.07, CH_2Cl_2); IR (thin film, cm^{-1}) ν 2928, 2855, 1734, 1700, 1669, 1576, 1540, 1457, 1045, 1020, 668; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.86 (t, *J* = 6.8 Hz, 3H), δ 1.19-1.32 (m, 22H), δ 1.35 (s, 3H), δ 1.37-1.51 (m, 6H), 1.56 (s, 3H), δ 1.59 (m, 2H), δ 2.87 (t, *J* = 7.6 Hz, 2H), δ 3.58-3.67 (m, 5H), δ 3.75 (m, 1H), δ 4.09 (d, *J* = 5.2 Hz, 1H), δ 4.21 (dq, *J* = 6.0, 8.2 Hz, 1H), δ 4.54 (q, *J* = 6.8, 1H), δ 5.05 (s, 1H), δ 5.77(d, *J* = 3.6 Hz, 1H), δ 6.08 (d, *J* = 10.4 Hz, 1H), δ 6.87 (dd, *J* = 3.6, 10.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.2, 174.5, 143.8, 127.2, 109.5, 95.5, 92.5, 79.1, 79.0, 76.9, 70.6, 64.4, 51.6, 34.6, 34.3, 33.2, 32.1, 29.9, 29.8, 29.7, 29.6, 29.4, 29.3, 28.2, 26.6, 25.4, 25.1, 25.0, 22.8, 17.7, 15.3, 14.3 ; HRMS (ESI): calcd for $[C_{32}H_{54}O_9 + Na]^+$ 605.3660, found 605.3659.

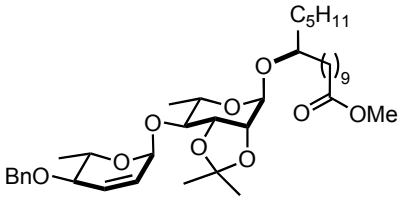
[3] Compound **18a** was involved in the transformation (**18** to **19**), which is not represented in Scheme 3.

1-(Methoxycarbonyl)pentadec-10(*S*)-yl 2,3-didehydro-α-L-rhamnopyranosyl -(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside 19



Enone **18a** (158 mg, 0.27 mmol) was dissolved in 0.50 mL dry CH_2Cl_2 and cooled to –78 ºC. To this added a 0.40 M solution of $CeCl_3$•MeOH (0.50 mL). After stirring for 10 min at this temperature, added solid $NaBH_4$ (15.40 mg, 0.41 mmol) in portions. The reaction mixture was stirred at to –78 ºC for 2h. Quenched with saturated $NaHCO_3$ at low temperature, diluted with CH_2Cl_2 and warmed to 0 ºC. The aqueous layer was extracted with CH_2Cl_2 (20mL x 3) and the combined organic layer was washed with saturated brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 20% EtOAc/hexane gave enol **19** (140 mg, 89%). Colorless oil: R_f (10% hexanes/EtOAc) = 0.21; $[\alpha]_D^{25}$ = –44.81 (*c* 1.69, CH_2Cl_2); IR (thin film, cm^{-1}) ν 3479, 2931, 2856, 1741, 1381, 1133, 1050, 1022, 987, 862; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.86 (t, *J* = 7.6 Hz, 3H), δ 1.16-1.29 (m, 22H), δ 1.33 (s, 3H), δ 1.42-1.49 (m, 6H), 1.52 (s, 3H), δ 1.59 (m, 2H), δ 1.91 (d, *J* = 8.0 Hz, 1H), δ 2.28 (t, *J* = 7.6 Hz, 2H), δ 3.56-3.75 (m, 7H), δ 3.82 (dd, *J* = 8.0, 8.0 Hz, 1H), δ 4.05 (d, *J* = 6.2 Hz, 1H), δ 4.17 (dd, *J* = 1.6, 6.2 Hz, 1H), δ 5.03 (s, 1H), δ 5.44 (s, 1H), δ 5.77 (ddd, *J* = 2.4, 4.4, 10.0 Hz, 1H), δ 5.92 (d, *J* = 10.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.6, 133.7, 126.8, 109.3, 95.5, 93.8, 79.2, 78.4, 77.3, 76.9, 69.6, 68.2, 64.5, 51.6, 34.6, 43.3, 33.1, 32.1, 29.9, 29.7, 29.5, 29.4, 29.3 28.2, 26.7, 25.4, 25.1, 25.0, 22.8, 17.9, 17.5, 14.3; HRMS (ESI): calcd for $[C_{32}H_{56}O_9 + Na]^+$ 607.3816, found 607.3814.

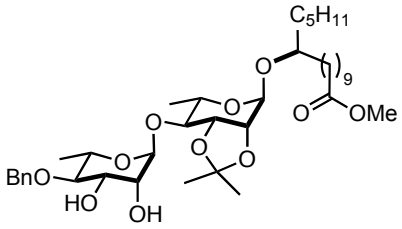
1-(Methoxycarbonyl)pentadec-10(*S*)-yl 2,3-didehydro-4-*O*-benzyl-α-L-rhamnopyranosyl -(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside 19a[4]



Allylic alcohol **19** (53.90 mg, 0.09 mmol) was dissolved in 0.50 mL dry DMF and cooled to 0 ºC. To this added BnBr (22.00 μL, 0.184 mmol) followed NaH (3.30 mg, 0.14 mmol). Ice bath was removed after addition of NaH and the reaction was stirred at rt for 2h. Upon consumption of starting material, the reaction was diluted with Et_2O and quenched with saturated $NaHCO_3$ at 0 ºC. The aqueous layer was extracted with Et_2O (20mL x 3) and the combined organic layer was washed with saturated brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 7-8 % EtOAc/hexane gave benzyl ether **19a** (58.3 mg, 96%). Faint yellowish oil: R_f (20% hexanes/EtOAc) = 0.50; $[\alpha]_D^{25}$ = −1.50 (*c* 0.10, CH_2Cl_2); IR (thin film, cm^{-1}) ν 2934, 2860, 1741, 1478, 1397, 1381, 1130, 1049, 981, 866; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, *J* = 7.6 Hz, 3H), δ 1.24-1.28 (m, 22H), δ 1.35 (s, 3H), δ 1.44-1.47 (m, 6H), 1.54 (s, 3H), δ 1.61 (m, 2H), δ 2.30 (t, *J* = 8.0 Hz, 2H), δ 3.58-3.77 (m, 8H), δ 4.04 (d, *J* = 5.2 Hz, 1H), δ 4.20 (dd, *J* = 1.2, 7.2 Hz, 1H), δ 4.67 (d, *J* = 11.6 Hz, 1H), 4.55 (d, *J* = 11.6 Hz, 1H), δ 5.04 (s, 1H), δ 5.46 (s, 1H), δ 5.81 (ddd, *J* = 2.4, 4.4, 10.8 Hz, 1H), δ 6.09 (d, *J* = 10.4 Hz, 1H), δ 7.28-7.34 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.5, 138.2, 130.9, 128.6, 128.1, 128.0, 126.9, 109.3, 95.4, 93.9, 79.3, 78.2, 77.0, 76.4, 71.2, 66.1, 64.6, 51.7, 43.6, 34.3, 33.2, 32.1, 30.0, 29.7, 29.6, 29.4, 29.3, 28.2, 26.7, 25.4, 25.1, 25.0, 22.8, 18.2, 17.5, 14.3; HRMS (ESI): calcd for $[C_{39}H_{62}O_9 + Na]^+$ 697.4292, found 697.4292.

[4] Compound **19a** was involved in the transformation (**19** to **8**), which is not represented in Scheme 3.

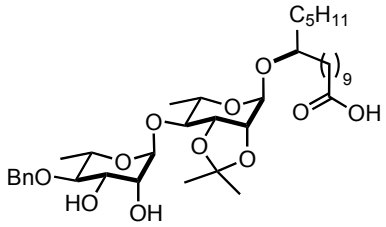
1-(Methoxycarbonyl)pentadec-10(*S*)-yl 4-*O*-benzyl-α-L-rhamnopyranosyl -(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside 19b[5]



Alkene **19a** (125.50 mg, 0.19 mmol) was dissolved in a 1:1 mixture of *t*-BuOH/acetone (0.50 mL) and the mixture was cooled to 0 ºC. To this added a 50% (v/v) solution of NMO/H_2O (0.50 mL). The reaction mixture was stirred at that temperature for 15 min and added OsO_4 (2.40 mg, 0.01 mmol). The reaction mixture was stirred overnight without replenishing ice from 0 ºC to rt. After consumption of starting material, cooled the reaction to 0 ºC, diluted with EtOAc and reduced the excess OsO_4 with saturated Na_2SO_3. The reaction mixture was then concentrated to remove acetone. The aqueous layer was extracted with EtOAc (20mL x 3) and the combined organic layer was washed with saturated brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 27-30 % EtOAc/hexane gave diol **19b** (115 mg, 87%). Colorless oil: R_f (30% hexanes/EtOAc) = 0.23; $[\alpha]_D^{25}$ = –76.50 (*c* 0.40, CH_2Cl_2); IR (thin film, cm^{-1}) ν 3391, 2920, 2854, 1741, 1478, 1387, 1393, 1130, 1047, 986, 866; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, *J* = 7.2 Hz, 3H), δ 1.22-1.33 (m, 22H), δ 1.34 (s, 3H), δ 1.46 (m, 6H), 1.53 (s, 3H),), δ 1.60 (m, 2H), δ 1.75 (brs, 1H), δ 2.29 (t, *J* = 8.0 Hz, 2H), δ 2.43 (d, *J* = 5.2 Hz, 1H), δ 2.55 (brs, 1H), δ 3.36 (dd, *J* = 8.8, 9.2 Hz, 1H), δ 3.50 (dd, *J* = 2.0, 9.6 Hz, 1H), δ 3.62 (m, 1H), δ 3.66 (s, 3H), δ 3.67-3.75 (m, 1H), δ 3.84 (dq, *J* = 6.0, 8.2 Hz, 1H), δ 3.96 (brs, 1H), δ 4.05 (d, *J* = 3.2, 1H), δ 4.15 (dd, *J* = 3.0, 7.6 Hz, 1H), δ 4.74 (s, 2H), δ 5.03 (s, 1H), δ 5.10 (s, CH_2Cl_2), δ 5.35 (s, 1H), δ 7.29-7.36 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.6, 138.4, 128.8, 128.4, 128.3, 128.2, 109.5, 98.4, 95.6, 81.7, 78.8, 75.3, 71.6, 71.5, 67.9, 64.3, 51.7, 34.6, 34.3, 33.2, 32.1, 30.0, 29.7, 29.6, 29.4, 29.3, 28.1, 26.7, 25.4, 25.1, 22.8, 18.1, 18.0, 14.3; HRMS (ESI): calcd for $[C_{39}H_{64}O_{11} + Na]^+$ 731.4312, found 731.4324.

[5] Compound **19b** was involved in the transformation (**19** to **8**), which is not represented in Scheme 3.

1-(Hydroxycarbonyl)pentadec-10(*S*)-yl 4-*O*-benzyl-α-L-rhamnopyranosyl -(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside 8[6]

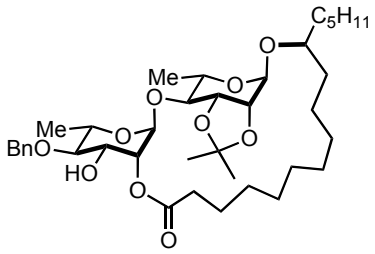


Methyl ester **19b** (114.90 mg, 0.16 mmol) was dissolved in a 9:1 mixture of MeOH/H_2O (1.60 mL). To the resulting mixture, added KOH (90.90 mg, 1.62 mmol) and refluxed at 55 ºC for 3h. Cooled the reaction mixture to 0 ºC, diluted with CH_2Cl_2 and quenched with 1N HCl. The aqueous layer was extracted with CH_2Cl_2 (30mL x 3) and the combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 30-35 % acetone/hexane gave diol-acid **8** (109 mg, 97%). Colorless oil: R_f (30% acetone/hexane) = 0.35; IR (thin film, cm^{-1}) ν 3469, 2986, 2864, 1741, 1715, 1470, 1383, 1038, 981, 862; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, *J* = 7.2 Hz, 3H), δ 1.21-1.32 (m, 22H), δ 1.33 (s, 3H), δ 1.46 (m, 6H), δ 1.53 (s, 3H), δ 1.61 (m, 2H), δ 2.32 (t, *J* = 7.2 Hz, 2H), δ 3.38 (dd, *J* = 9.2, 9.6 Hz, 1H), δ 3.50 (dd, *J* = 7.3, 10.0 Hz, 1H), δ 3.62 (m, 1H), δ 3.66-3.77 (m, 2H), δ 3.86 (dd, *J* = 2.8, 8.8 Hz, 1H), δ 3.96 (d, *J* = 2.8 Hz, 1H), δ 4.06 (d, *J* = 4.8 Hz, 1H), δ 4.16 (dd, *J* = 4.8, 7.6 Hz, 1H), δ 4.77 (d, *J* = 11.6 Hz, 1H), 4.73 (d, *J* = 11.6 Hz, 1H), δ 5.04 (s, 1H), δ 5.36 (s, 1H), δ 7.28-7.34 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 179.2, 138.3, 128.7, 128.2, 128.1, 109.5, 98.4, 95.6, 81.6, 78.8, 77.6, 77.5, 76.9, 75.3, 71.6, 68.0, 64.3, 34.6, 34.1, 33.1, 32.0, 29.9, 29.6, 29.5, 29.3, 29.2, 28.0, 26.6, 25.3, 25.0, 24.8, 22.7, 18.0, 17.9, 14.2.

[6] Zhu, X. M.; He, L. L.; Yang, G. L.; Lei, M.; Chen, S. S.; Yang, J. S. *Synlett*. **2006**, *20*, 3510.

Macrolactones 20 and 21[6]

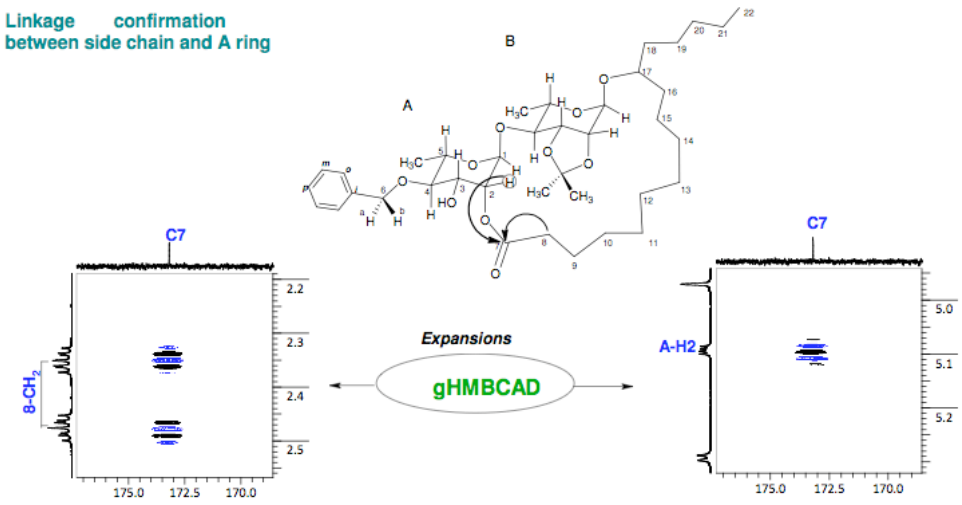
Diol acid **8** (150 mg, 0.22 mmol) was dissolved in dry/degassed toluene (5.40 mL). To the resulting mixture was added Py_2S_2 (228 mg, 1.13 mmol) and PPh_3 (295.60 mg, 1.13 mmol). The reaction was stirred at rt under argon for 5h. Upon consumption of starting material, it was diluted to 20 mL with dry/degassed toluene and loaded into a syringe. Using a syringe-pump, the mixture is added to boiling dry/degassed toluene (230 mL) over a period of 4 days. The reaction was then concentrated under reduced pressure and loaded directly on a column. Gradient elution with 12-13% EtOAc/hexane gave C-2-macrolactone **20** (80.9 mg, 54.3%) and elution with 14-15% EtOAc/hexane C-3-macrolactone **21** (17.2 mg, 11.5%).

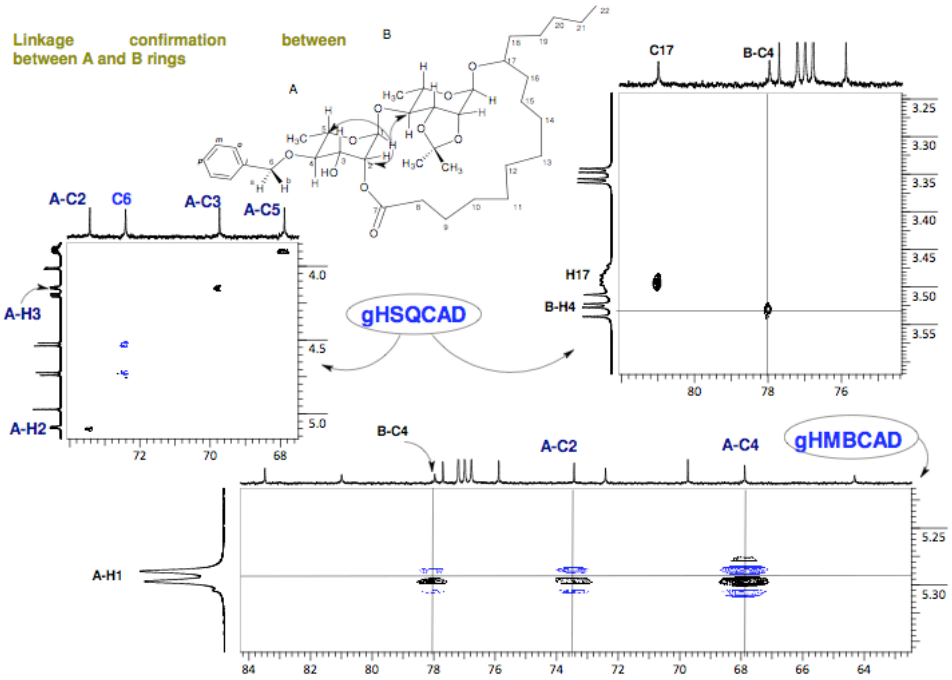


20:[7] Colorless oil; R_f (30% EtOAc/hexane) = 0.32; $[\alpha]_D^{25}$ = –24.6 (*c* 0.5, $CHCl_3$); IR (thin film, cm^{-1}) ν 3448, 2980, 2876, 1741, 1710, 1490, 1036, 980, 861; ^1H NMR ($CDCl_3$, 600 MHz): δ 0.88 (t, *J* = 7.2 Hz, 3H), δ 1.23 (d, *J* = 6.2 Hz, 3H), δ 1.28 (d, *J* = 6.4 Hz, 3H), 1.24-1.47 (m, 22H), δ 1.34 (s, 3H), δ 1.52 (s, 3H), 1.64-1.76 (m, 2H), δ 2.35 (m, 1H), δ 2.47 (m, 1H), δ 3.12 (d, $J_{(OH)}$ = 6.4 Hz, 1H), δ 3.35 (dd, *J* = 3.1, 8.2 Hz, 1H), δ 3.49 (m, 1H), δ 3.52 (dd, *J* = 7.3, 10.1 Hz, 1H), δ 3.85-3.94 (m, 2H), δ 4.01 (d, *J* = 5.4 Hz, 1H), δ 4.14 (dd, *J* = 3.0, 3.1 Hz, 1H), δ 4.19 (dd, *J* = 5.5, 7.0 Hz, 1H), δ 4.53 (d, *J* = 11.5 Hz, 1H), δ 4.73 (d, *J* = 11.5 Hz, 1H), δ 4.97 (s, 1H), δ 5.09 (dd, *J* = 3.0, 5.4 Hz, 1H), δ 5.29 (d, *J* = 5.4 Hz, 1H), δ 7.28-7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 173.2, 137.7, 128.4, 128.0, 127.9, 109.4, 96.5, 95.5, 83.5, 81.0, 77.9, 77.7, 75.9, 73.4, 72.4, 69.7, 67.9, 64.3, 34.9, 33.9, 32.8, 32.0, 29.4, 29.3, 28.1, 28.0, 27.7, 26.6, 25.6, 24.9, 23.0, 22.7, 22.6, 19.0, 17.7, 14.0; HRMS (ESI): calcd for $[C_{38}H_{60}O_{10} + Na]^+$ 699.4084, found 699.4079.

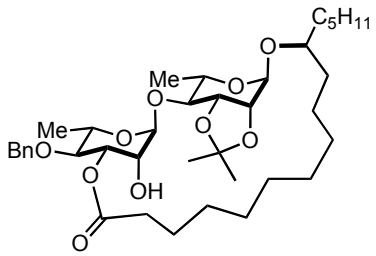
[7] C-2 macrolactone was assigned incorrectly as the C-3 macrolactone in reference 6

Position of macrolactone and sugar linkage[8]





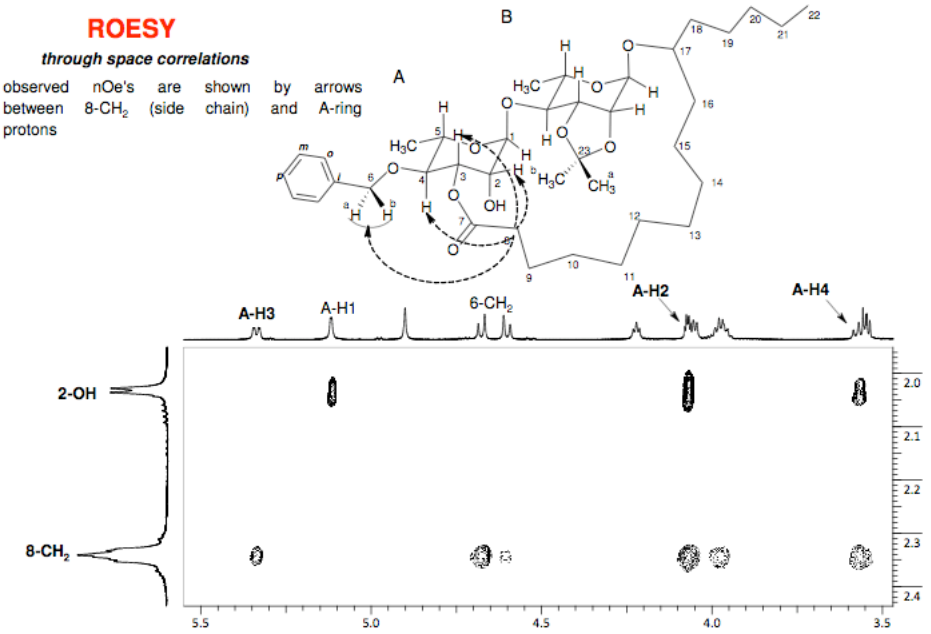
[8] See spectral data for full correlation studies

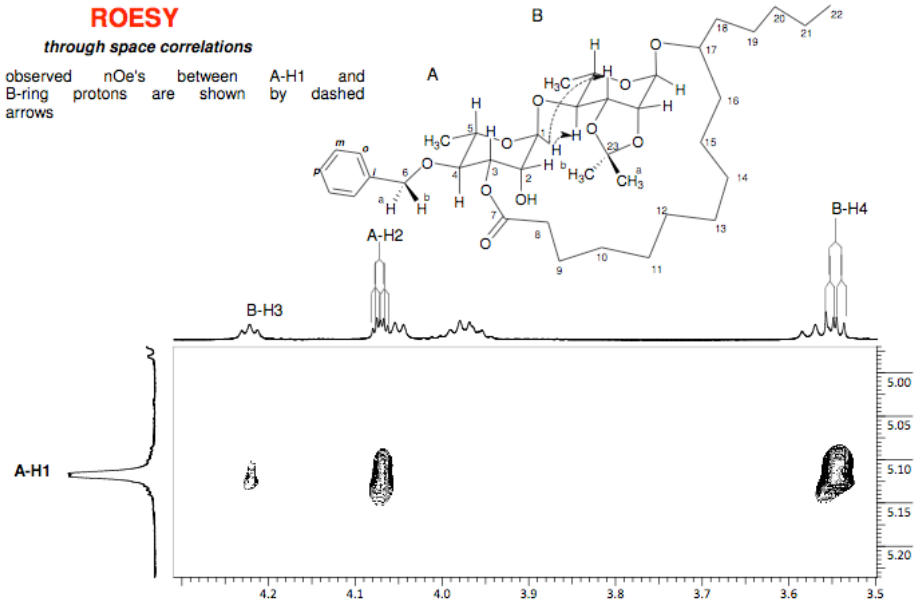


21:[9] Colorless oil; R_f (20% EtOAc/hexane) = 0.31; $[\alpha]_D^{25}$ = –9.1 (*c* 0.7, $CHCl_3$); IR (thin film, cm^{-1}) ν 3446, 2986, 2872, 1740, 1710, 1486, 1038, 984, 866; ^1H NMR ($CDCl_3$, 600 MHz): δ 0.87 (t, *J* = 7.2 Hz, 3H), δ 1.28 (d, *J* = 6.3 Hz, 3H), δ 1.32 (d, *J* = 6.3 Hz, 3H), δ 1.21-1.53 (m, 16H), δ 1.56-1.73 (m, 8H), δ 1.34 (s, 3H), 1.50 (s, 3H), δ 2.03 (d, $J_{(OH)}$ = 4.6 Hz, 1H), δ 2.34 (t, *J* = 6.4 Hz, 2H), δ 3.38-3.46 (m, 1H), δ 3.53-3.59 (m, 2H), δ 3.90-4.01 (m, 2H), δ 4.04-4.07 (m, 2H), δ 4.22 (dd, *J* = 5.5, 5.9 Hz, 1H), δ 4.60 (d, *J* = 11.2 Hz, 1H), δ 4.68 (d, *J* = 11.2 Hz, 1H), δ 4.90 (s, 1H), δ 5.12 (s, 1H), δ 5.34 (dd, *J* = 2.7, 9.2 Hz, 1H), δ 7.26-7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 173.2, 138.0, 128.3, 127.8, 127.7, 109.6, 98.0, 96.7, 80.3, 78.9, 78.5, 76.5, 74.7, 74.1, 73.9, 71.0, 69.2, 66.2, 34.2, 33.9, 32.0, 29.7, 29.5, 28.5, 27.7, 27.5, 27.0, 26.1, 25.9, 24.8, 23.8, 22.7, 22.6, 19.5, 17.8, 14.0. HRMS (ESI): calcd for $[C_{38}H_{60}O_{10} + Na]^+$ 699.4084, found 699.4079.

[9] C-2 macrolactone was assigned incorrectly as the C-3 macrolactone in reference 6

Position of macrolactone and sugar linkage[10]





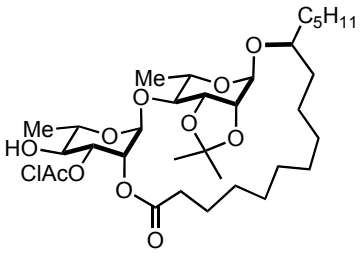
[10] See spectral data for full correlation studies

Lactone isomerization:

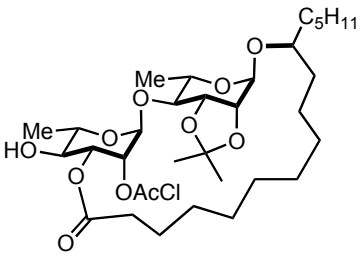
The C-2 macrolactone **20** (291 mg, 0.43 mmol) was dissolved in 25 mL dry toluene and cooled to 0 ºC. To this cold solution, 64.20 μL DBU was added and stirred under argon, slowly rising to ambient temperature. After 12h, the reaction mixture was cooled back to 0 ºC and diluted with Et_2O. A cold solution of 1N HCl was added and the aqueous layer was extracted with Et_2O. The combined organic layer was washed with $NaHCO_3$ and brine. Dried over Na_2SO_4 and concentrated under reduced pressure. ^1H NMR of the crude reaction mixture showed a 2:1 mixture of C-2 macrolactone **20** and C-3 macrolactone **21**. The mixture was taken to next step without further purification.

Glycosyl acceptors 9 and 22

A mixture of C-2 macrolactone **20** and C-3 macrolactone **21** (300 mg, 0.44 mmol) was dissolved in dry CH_2Cl_2 (1.0 mL). The mixture was then cooled to 0 ºC and added pyridine (75 μL, 0.92 mmol) and chloroacetic anhydride (151 mg, 0.88 mmol). The resulting mixture was stirred under argon from 0 ºC to rt over 2h. Diluted with CH_2Cl_2 and quenched with 1N HCl at 0 ºC. The aqueous layer was extracted with CH_2Cl_2 (50mL x 3) and the combined organic layer was washed with saturated $NaHCO_3$ and brine. Dried over Na_2SO_4 and concentrated under reduced pressure. The reaction mixture was then passed through a short pad of silica gel to obtain crude chloroacetic ester, which was dissolved in EtOAc (5 mL) and few drops of MeOH. Pd/C (50 mg) was added and under H_2 balloon pressure the reaction was stirred for 3h. The solid Pd/C catalyst was removed by filtration through a celite pad. Filtrate was concentrated under reduced pressure and purified by silica gel chromatography. The C-3 glycosyl acceptor **9** (43 mg) was obtained using 12% EtOAc/hexane and the C-2 glycosyl acceptor **22** (202 mg) was obtained by using 18-20% EtOAc/hexane. The combined yield for 2 steps was 84%.



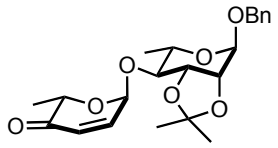
22: Colorless oil: R_f (20% acetone/hexane) = 0.45; $[\alpha]_D^{25}$ = –44.81 (*c* 1.69, CH_2Cl_2); IR (thin film, cm^{-1}) ν 3456, 3018, 2864, 1780, 1736, 1470, 1030, 976, 856; ^1H NMR (C_6D_6, 400 MHz): δ 0.90 (t, *J* = 7.2 Hz, 3H), δ 1.19-1.32 (m, 28H), δ 1.41 (d, *J* = 6.6 Hz, 3H), 1.46 (s, 3H), δ 1.71 (m, 2H), δ 1.94 (d, *J* = 5.2 Hz, 1H), δ 2.16-2.23 (m, 1H), δ 2.28-2.35 (m, 1H), δ 3.26 (brs, 1H), δ 3.41 (s, 2H), δ 3.47-3.52 (m, 1H), δ 3.96 (dd, *J* = 8.0, 9.6 Hz, 1H), δ 4.02 (dd, *J* = 6.0, 8.0 Hz, 1H), δ 4.18-4.23 (m, 2H), δ 4.63 (dd, *J* = 6.0, 6.4 Hz, 1H), δ 5.16 (s, 1H), δ 5.49 (dd, *J* = 2.8, 3.6 Hz, 1H), δ 5.54 (dd, *J* = 3.6, 5.2 Hz, 1H), δ 5.67 (d, *J* = 5.20 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.4, 167.6, 109.7, 96.1, 94.5, 80.8, 79.2, 76.6, 76.1, 75.3, 73.6, 70.6, 68.7, 64.1, 41.1, 34.9, 33.8, 33.1, 32.2, 29.9, 29.6, 29.3, 28.4, 28.3, 28.1, 26.9, 25.5, 25.2, 23.4, 22.8, 18.3, 18.0, 14.3; HRMS (ESI): calcd for $[C_{33}H_{55}ClO_{11} + Na]^+$ 685.3331, found 685.3315.



9: Colorless oil: R_f (20% acetone/hexane) = 0.26; $[\alpha]_D^{25}$ = –34.12 (*c* 1.69, CH_2Cl_2); IR (thin film, cm^{-1}) ν 3426, 3020, 2864, 1781, 1754, 1491, 1024, 976, 831, 659; ^1H NMR (C_6D_6, 400 MHz): δ 0.90 (t, *J* = 7.2 Hz, 3H), δ 1.21-1.42 (m, 29H), δ 1.47 (s, 3H), δ 1.49 (s, 3H), δ 1.64-1.74 (m, 1H), δ 2.08 (ddd, *J* = 4.4, 7.2, 14.6 Hz, 1H), δ 2.18 (ddd, *J* = 4.4, 7.0, 14.8 Hz, 1H), δ 2.57 (d, *J* = 5.2 Hz, 1H), δ 3.25 (m, 1H), δ 3.32 (d, *J* = 14.8 Hz, 1H), δ 3.43 (d, *J* = 14.8 Hz, 1H), δ 3.78-3.87 (m, 2H), δ 4.06 (dq, *J* = 6.0, 9.8 Hz, 1H), δ 4.19 (d, *J* = 6.0 Hz, 1H), δ 4.24 (dq, *J* = 6.8, 6.8 Hz, 1H), δ 4.44 (dd, *J* = 5.2, 6.0 Hz, 1H), δ 5.11 (s, 1H), δ 5.46 (dd, *J* = 2.8, 10.2 Hz, 1H), δ 5.48 (s, 1H), δ 5.68 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.7, 166.6, 110.2, 96.2, 95.7, 80.0,

79.4, 74.2, 73.5, 73.2, 71.7, 70.5, 65.8, 41.0, 34.4, 34.2, 33.9, 32.3, 29.9, 29.6, 28.9, 28.8, 28.5, 27.9, 27.8, 26.3, 25.4, 25.1, 25.0, 22.8, 19.8, 17.7, 14.3; HRMS (ESI): calcd for $[C_{33}H_{55}ClO_{11} + Na]^+$ 685.3331, found 685.3315.

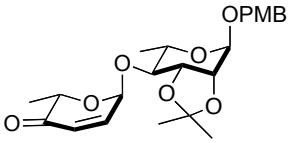
1-Benzyl-2,3-didehydro-5-methyl-4-oxo-pyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside 23a-i[11]



Glycosyl acceptor **23a** (2.17 g, 7.40 mmol) was dissolved in 15 mL dry CH_2Cl_2. To this added α-L-Boc-pyranone **5** (2.53 g, 11.10 mmol). The reaction mixture was cooled to 0 ºC and added a premixed solution of $Pd_2(dba)_3$•$CHCl_3$ (574 mg, 0.55 mmol) and PPh_3 (584 mg, 2.20 mmol) in CH_2Cl_2 via cannula under argon. The reaction mixture was stirred under argon at 0 ºC overnight. Concentrated the reaction mixture under reduced pressure and flash chromatography with 10% EtOAc/hexane yielded the desired product **23a-i** (3.02 g, 94%). Colorless oil: R_f (20% hexanes/EtOAc) = 0.6; $[\alpha]_D^{25} = -12.16$ (*c* 1.09, CH_2Cl_2); IR (thin film, cm^{-1}) ν 2854, 1741, 1680, 1154, 1071, 861; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.29 (d, *J* = 6.6 Hz, 3H), δ 1.34 (s, 3H), δ 1.38 (d, *J* = 6.8 Hz, 3H), δ 1.56 (s, 3H), δ 3.67-3.79 (m, 2H), δ 4.18 (d, *J* = 3.2 Hz, 1H), δ 4.25 (dd, *J* = 8.0, 8.4 Hz, 1H), δ 4.49-4.56 (m, 2H), δ 4.71 (d, *J* = 11.6 Hz, 1H), δ 5.08 (s, 1H), δ 5.77 (s, 1H), δ 6.07 (d, *J* = 9.6 Hz, 1H), δ 6.85 (dd, *J* = 3.0, 9.4 Hz, 1H), δ 7.29-7.34 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 196.9, 143.7, 137.1, 128.6, 128.3, 128.1, 127.1, 109.6, 96.2, 92.4, 78.9, 76.4, 70.5, 69.3, 64.3, 28.1, 26.5, 17.8, 15.2; HRMS (ESI): calcd for $[C_{22}H_{28}O_7 + Na]^+$ 427.1733, found 427.1720.

[11] Compound **23a-i** was involved in the transformation (**23a** to **4**), which is not represented in Scheme 5.

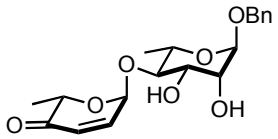
1-*p*-Methoxybenzyl-2,3-didehydro-5-methyl-4-oxo-pyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside 23b-i[12]



Compound **23b-i** was prepared from **23b** following the same procedure as for **23a-i**.

Colorless solid: R_f (15% hexanes/EtOAc) = 0.43; mp: 98 ºC; $[\alpha]_D^{25} = -12.84$ (*c* 2.32, CH_2Cl_2); IR (thin film, cm^{-1}) ν 2855, 1740, 1709, 1168, 1071, 866; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.29 (d, *J* = 6.0 Hz, 3H), δ 1.33 (s, 3H), δ 1.38 (d, *J* = 6.8 Hz, 3H), δ 1.55 (s, 3H), δ 3.67 (dd, *J* = 7.2, 9.2 Hz, 1H), δ 3.74 (dq, *J* = 6.0, 9.6 Hz, 1H), δ 3.79 (s, 3H), δ 4.14 (d, *J* = 3.2 Hz, 1H), δ 4.20 (dd, *J* = 3.0, 7.4 Hz, 1H), δ 4.51 (d, *J* = 11.6 Hz, 1H), δ 4.63 (d, *J* = 11.6 Hz, 1H), δ 4.54 (q, *J* = 7.2 Hz, 1H), δ 5.04 (s, 1H), δ 5.77 (d, *J* = 3.6 Hz, 1H), δ 6.07 (d, *J* = 9.6 Hz, 1H), δ 6.85 (dd, *J* = 3.8, 10.4 Hz, 1H), δ 6.89 (d, *J* = 8.8 Hz, 2H), δ 7.27 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.2, 159.6, 143.8, 130.2, 129.1, 127.2, 114.1, 109.7, 95.9, 92.4, 78.9, 78.8, 76.5, 70.6, 68.9, 64.3, 55.5, 28.2, 26.5, 17.9, 15.3; HRMS (ESI): calcd for $[C_{23}H_{30}O_8 + Na]^+$ 457.1838, found 457.1830.

1-Benzyl-2,3-didehydro-5-methyl-4-oxo-pyranosyl-(1→4)-α-L-rhamnopyranoside 4

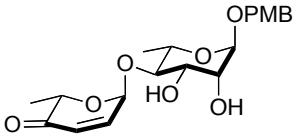


Acetonide protected *syn*-diol **23a-i** (1.0 g, 2.3 mmol) was dissolved in 24.70 mL CH_2Cl_2. Cooled to 0 ºC and slowly added 2.50 mL aqueous solution TFA (10:1). The reaction mixture was stirred at 0 ºC for 10 min and quenched with Et_3N. Water was added and the aqueous phase extracted with CH_2Cl_2 (100 mL x 3). The combined organic layer was washed with 1N HCl, saturated $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 50% EtOAc/hexane gave diol **4** (788 mg, 94%). Colorless oil: R_f (50% hexanes/EtOAc) = 0.31; $[\alpha]_D^{25} = -15.42$ (*c* 1.95, CH_2Cl_2); IR (thin film,

[12] Compound **23b-i** was involved in the transformation (**23b** to **24**), which is not represented in Scheme 5.

cm^{-1}) ν 3460, 3320, 2950, 1741, 1681, 1023, 964, 866; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.33 (d, *J* = 6.0 Hz, 3H), δ 1.37 (d, *J* = 6.8 Hz, 3H), δ 3.0 (d, *J* = 8.0 Hz, 1H), δ 3.1 (d, *J* = 4.4 Hz, 1H), δ 3.68 (dd, *J* = 9.6, 9.6 Hz, 1H), δ 3.75 (dq, *J* = 6.6, 9.6 Hz, 1H), δ 3.91 (s, 1H), δ 3.97 (dd, *J* = 3.2, 8.4 Hz, 1H), δ 4.46 (d, *J* = 11.6 Hz, 1H), δ 4.69 (d, *J* = 11.6 Hz, 1H), δ 4.57 (q, *J* = 6.8 Hz, 1H), δ 4.84 (s, 1H), δ 5.74 (d, *J* = 3.2 Hz, 1H), δ 6.06 (d, *J* = 10.0 Hz, 1H), δ 6.89 (dd, *J* = 2.0, 9.6 Hz, 1H), δ 7.29-7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.3, 143.8, 137.1, 128.6, 128.2, 128.1, 126.9, 98.8, 94.2, 79.6, 76.9, 72.5, 71.7, 70.7, 69.4,18.1, 15.2; HRMS (ESI): calcd for $[C_{19}H_{24}O_7 + Na]^+$ 387.1420, found 387.1418.

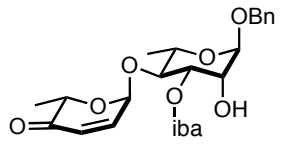
1-*p*-Methoxybenzyl-2,3-didehydro-5-methyl-4-oxo-pyranosyl-(1→4)-α-L-rhamnopyranoside 24



Compound **24** was prepared from **23b-i** following the same procedure as for **4**.

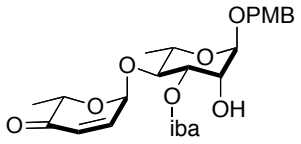
Colorless oil: R_f (50% hexanes/EtOAc) = 0.45; $[\alpha]_D^{25}$ = –22.56 (*c* 1.03, CH_2Cl_2); IR (thin film, cm^{-1}) ν 3469, 3305, 2950, 1741, 1680, 1168, 954, 864; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.34 (d, *J* = 6.0 Hz, 3H), δ 1.37 (d, *J* = 6.4 Hz, 3H), δ 2.69 (brs, 1H), δ 3.66 (dd, *J* = 8.8, 9.6 Hz, 1H), δ 3.75 (dq, *J* = 6.0, 9.6 Hz, 1H), δ 3.79 (s, 3H), δ 3.87 (dd, *J* = 1.6, 3.2 Hz, 1H), δ 3.96 (dd, *J* = 2.8, 8.8 Hz, 1H), δ 4.42 (d, *J* = 11.6 Hz, 1H), δ 4.62 (d, *J* = 11.6 Hz, 1H), δ 4.57 (q, *J* = 7.6 Hz, 1H), δ 4.82 (s, 1H), δ 5.74 (d, *J* = 3.6 Hz, 1H), δ 6.07 (d, *J* = 10.4 Hz, 1H), δ 6.86 (d, *J* = 8.8 Hz, 2H), δ 6.85 (dd, *J* = 4.0, 9.6 Hz, 1H), δ 7.24 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.2, 159.6, 143.8, 129.9, 129.1, 127.0, 114.0, 98.5, 94.2, 79.7, 72.5, 71.8, 70.8, 69.1, 66.7, 55.5, 18.1, 15.5; HRMS (ESI): calcd for $[C_{20}H_{26}O_8 + Na]^+$ 417.1525, found 417.1526.

1-Benzyl-2,3-didehydro-5-methyl-4-oxo-pyranosyl-(1→4)-3-*O*-isobutyral-α-L rhamnopyranoside 25a



The *syn*-diol **4** (1.8 g, 4.94 mmol) was dissolved in 82.30 mL toluene. The reaction mixture was stirred at rt for 10 min until all starting material dissolved. Bu_2SnO (1.48 g, 5.93 mmol) was added and refluxed for 3h under argon. During reflux, the reaction turned faint yellowish in color. Toluene was removed under reduced pressure and the residue was dried under high vacuum for 30 min. dissolved the residue in dry CH_3CN (49 mL) and cooled to 0 ºC. DIPEA (1.20 mL, 6.92 mmol) was added followed by slow addition of isobutyrylchloride (0.73 mL, 6.91 mmol). The reaction mixture was stirred at this temperature for 1h then diluted with CH_2Cl_2 and quenched with saturated $NaHCO_3$. The aqueous phase extracted with CH_2Cl_2 (100 mL x 2). The combined organic layer was washed with saturated brine, dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 25% EtOAc/hexane gave isobutyric ester **25a** (1.72 g, 80%). Colorless oil: R_f (40% hexanes/EtOAc) = 0.65; $[\alpha]_D^{25}$ = –20.10 (*c* 1.43, CH_2Cl_2); IR (thin film, cm^{-1}) ν 3327, 2930, 1814, 1756, 1638, 1168, 1071, 864; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.20 (d, *J* = 6.4 Hz, 6H), δ 1.35 (d, *J* = 6.2 Hz, 3H), δ 1.36 (d, *J* = 6.2 Hz, 3H), δ 2.19 (brs, 1H), δ 2.63 (septet, *J* = 6.8 Hz, 1H), δ 3.86 (dq, *J* = 6.4, 8.6 Hz, 1H), δ 3.94 (dd, *J* = 9.6, 9.6 Hz, 1H), δ 4.09 (s, 1H), δ 4.50 (d, *J* = 11.6 Hz, 1H), δ 4.53 (q, *J* = 6.8 Hz, 1H), δ 4.72 (d, *J* = 11.6 Hz, 1H), δ 4.81 (s, 1H), δ 5.25 (dd, *J* = 2.0, 9.2 Hz, 1H), δ 5.41 (d, *J* = 2.4 Hz, 1H), δ 6.07 (d, *J* = 10.4 Hz, 1H), δ 6.63 (dd, *J* = 3.2, 10.4 Hz, 1H), δ 7.27-7.33 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 196.7, 176.1, 142.6, 137.1, 128.6, 128.1, 127.4, 98.6, 94.3, 74.9, 70.7, 69.7, 69.4, 67.2, 34.3, 19.2, 19.1, 18.1, 15.0; HRMS (ESI): calcd for $[C_{23}H_{30}O_8 + Na]^+$ 457.1838, found 457.1833.

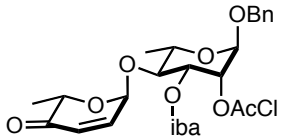
1-*p*-Methoxybenzyl-2,3-didehydro-5-methyl-4-oxo-pyranosyl-(1→4)-3-*O*-isobutyral-α-L rhamnopyranoside 25b



Compound **25b** was prepared from **24** following the same procedure as for **25a**.

Colorless oil: *Rf* (40% hexanes/EtOAc) = 0.62; $[\alpha]_D^{25}$ = –14.34 (*c* 0.97, CH_2Cl_2); IR (thin film, cm^{-1}) ν 3340, 2950, 2848, 1814, 1741, 1684, 1168, 1073, 864, 684; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.21 (d, *J* = 6.4 Hz, 6H), δ 1.33 (d, *J* = 6.4 Hz, 3H), δ 1.37 (d, *J* = 6.2 Hz, 3H), δ 2.04 (brs, 1H), δ 2.62 (septet, *J* = 6.8 Hz, 1H), δ 3.79 (s, 3H), δ 3.85 (dq, *J* = 6.0, 9.2 Hz, 1H), δ 3.90 (dd, *J* = 8.0, 9.2 Hz, 1H), δ 4.05 (s, 1H), δ 4.47 (d, *J* = 11.6 Hz, 1H), δ 4.54 (q, *J* = 5.6 Hz, 1H), δ 4.65 (d, *J* = 11.6 Hz, 1H), δ 4.80 (s, 1H), δ 5.19 (dd, *J* = 2.5, 9.0 Hz, 1H), δ 5.41 (d, *J* = 1.5 Hz, 1H), δ 6.01 (d, *J* = 7.6 Hz, 1H), δ 6.62 (dd, *J* = 1.6, 8.4 Hz, 1H), δ 6.86 (d, *J* = 6.4 Hz, 2H), δ 7.24 (d, *J* = 6.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 196.7, 176.1, 159.6, 142.6, 129.9, 129.1, 127.5, 114.0, 98.3, 94.3, 75.0, 70.8, 69.8, 69.1, 67.2, 55.5, 34.4, 19.3, 19.2, 18.1, 15.1; HRMS (ESI): calcd for $[C_{24}H_{32}O_9 + Na]^+$ 487.1944, found 487.1955.

1-Benzyl-2,3-didehydro-5-methyl-4-oxo-pyranosyl-(1→4)-2-*O*-chloroacetyl-3-*O*-isobutyral-α-L rhamnopyranoside 25a-i[13]

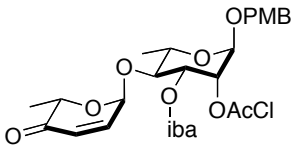


Alcohol **25a** (1.1 g, 2.53 mmol) was dissolved in dry CH_2Cl_2 (9.0 mL). The mixture was then cooled to 0 ºC and added pyridine (0.51 mL, 6.33 mmol), chloroacetic anhydride (866 mg, 5.06 mmol) and DMAP (154 mg, 1.26 mmol). The resulting mixture was stirred under argon from 0 ºC to rt over 2h. Diluted with CH_2Cl_2 and quenched with 1N HCl at 0 ºC. The aqueous layer was extracted with CH_2Cl_2 (50 mL x 3) and the combined organic layer was washed with saturated $NaHCO_3$ and brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel

[13] Compound **25a-i** was involved in the transformation (**25a** to **26a**), which is not represented in Scheme 5.

chromatography using 10-12% EtOAc/hexane to obtain **25a-i** (1.25 g, 97%). Colorless oil: R_f (20% acetone/hexane) = 0.60; $[\alpha]_D^{25}$ = –60.89 (*c* 1.05, CH_2Cl_2); IR (thin film, cm^{-1}) ν 2954, 2861, 1768, 1741, 1672, 1534, 1129, 1030, 866; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.17 (d, *J* = 6.4 Hz, 6H), δ 1.37 (d, *J* = 6.4 Hz, 3H), δ 1.39 (d, *J* = 6.4 Hz, 3H), δ 2.52 (septet, *J* = 7.2 Hz, 1H), δ 3.89 (m, 2H), δ 4.07 (d, *J* = 15.2 Hz, 1H), δ 4.15 (d, *J* = 15.2 Hz, 1H), δ 4.52 (d, *J* = 12.4 Hz, 1H), δ 4.72 (d, *J* = 12.4 Hz, 1H), δ 4.55 (q, *J* = 6.4 Hz, 1H), δ 4.79 (s, 1H), δ 5.35-5.40 (m, 3H), δ 6.08 (d, *J* = 9.6 Hz, 1H), δ 6.59 (dd, *J* = 3.2, 9.6 Hz, 1H), δ 7.34 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 196.3, 175.7, 166.6, 142.2, 136.6, 128.7, 128.2, 128.1, 127.5, 96.2, 94.5, 72.4, 71.9, 70.8, 69.6, 67.3, 40.8, 34.2, 18.9, 17.9, 15.0; HRMS (ESI): calcd for $[C_{25}H_{31}ClO_9 + Na]^+$ 533.1654, found 533.1660.

1-*p*-Methoxybenzyl-2,3-didehydro-5-methyl-4-oxo-pyranosyl-(1→4)-2-*O*-chloroacetyl-3-*O*-isobutyral-α-L rhamnopyranoside 25b-i[14]

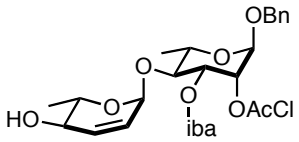


Compound **25b-i** was prepared from **25b** following the same procedure as for **25a-i**.

Colorless solid: R_f (30% acetone/hexane) = 0.82; mp: 118 ºC; $[\alpha]_D^{25}$ = –22.66 (*c* 0.48, CH_2Cl_2); IR (thin film, cm-1) ν 2954, 2864, 1768, 1736, 1682, 1534, 1030, 976, 866; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.16 (d, *J* = 6.4 Hz, 6H), δ 1.35 (d, *J* = 6.4 Hz, 3H), δ 1.39 (d, *J* = 7.2 Hz, 3H), δ 2.51 (septet, *J* = 7.2 Hz, 1H), δ 3.80 (s, 3H), δ 3.86-3.88 (m, 2H), δ 4.06 (d, *J* = 15.2 Hz, 1H), δ 4.13 (d, *J* = 15.2 Hz, 1H), δ 4.48 (d, *J* = 11.8 Hz, 1H), δ 4.64 (d, *J* = 11.8 Hz, 1H), δ 4.55 (q, *J* = 6.4 Hz, 1H), δ 4.76 (s, 1H), δ 5.32-5.35 (m, 2H), δ 5.40 (d, *J* = 3.6 Hz, 1H), δ 6.01 (d, *J* = 10.4 Hz, 1H), δ 6.62 (dd, *J* = 4.0, 10.4 Hz, 1H), δ 6.88 (d, *J* = 8.4 Hz, 2H), δ 7.26 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 196.4, 175.7, 166.7, 159.7, 142.2, 130.0, 128.6, 114.1, 95.9, 94.5, 72.4, 72.0, 70.8, 69.3, 67.3, 55.5, 40.8, 34.2, 29.9, 18.9, 18.0, 15.1; HRMS (ESI): calcd for $[C_{26}H_{33}ClO_{10}+Na]^+$ 563.1660, found 563.1671.

[14] Compound **25b-i** was involved in the transformation (**25b** to **26b**), which is not represented in Scheme 5.

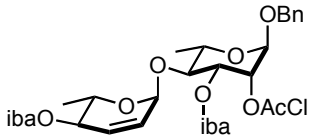
1-Benzyl-2,3-didehydro-α-L-rhamnopyranosyl-(1→4)-2-*O*-chloroacetyl-3-*O*-isobutyral-α-L rhamnopyranoside 25a-ii[15]



Enone **25a-i** (1.50 g, 2.94 mmol) was dissolved in 29.40 mL dry CH_2Cl_2 and cooled to –78 ºC. To this added a 0.4 M solution of $CeCl_3$•MeOH (5.90 mL). After stirring for 10 min at this temperature, added solid $NaBH_4$ (223 mg, 5.87 mmol) in portions. The reaction mixture was stirred at –78 ºC for 2h. Quenched with saturated $NaHCO_3$ at low temperature, diluted with CH_2Cl_2 and warmed up to 0 ºC. The aqueous layer was extracted with CH_2Cl_2 (100mL x 3) and the combined organic layer was washed with saturated brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography using 20% EtOAc/hexane to obtain allylic alcohol **25a-ii** (1.40 g, 93%). Colorless solid: R_f (20% acetone/hexane) = 0.25; mp: 146 ºC; $[\alpha]_D^{25}$ = –66.92 (*c* 0.80, CH_2Cl_2); IR (thin film, cm^{-1}) ν 3420, 3300, 2962, 1790, 1751, 1682, 1537, 1215, 1027, 966; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.13 (d, *J* = 7.0 Hz, 3H), δ 1.15 (d, *J* = 6.2 Hz, 3H), δ 1.33 (d, *J* = 6.0 Hz, 3H), δ 1.36 (d, *J* = 6.0 Hz, 3H), δ 1.65 (d, *J* = 5.2 Hz, 1H) δ 2.49 (septet, *J* = 7.6 Hz, 1H), δ 2.56 (dq, *J* = 6.4, 9.2 Hz, 1H), δ 3.78-3.89 (m, 3H), δ 4.06 (d, *J* = 14.8 Hz, 1H), δ 4.14 (d, *J* = 14.8 Hz, 1H), δ 4.54 (d, *J* = 12.0 Hz, 1H), δ 4.71 (d, *J* = 12.0 Hz, 1H), δ 5.78 (s, 1H), δ 5.14 (s, 1H), δ 5.34 (dd, *J* = 3.2, 8.8 Hz, 1H), δ 5.36 (s, 1H), δ 5.58 (dd, *J* = 2.0, 10.4 Hz, 1H), δ 5.94 (d, *J* = 10.4 Hz, 1H), δ 7.29-7.34 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 175.8, 166.7, 136.9, 134.3, 128.7, 128.2, 128.1, 125.8, 96.3, 95.5, 76.3, 72.4, 72.0, 69.5, 69.4, 68.5, 67.6, 40.8, 34.2, 18.9, 17.8, 17.7; HRMS (ESI): calcd for $[C_{25}H_{33}ClO_9 + Na]^+$ 535.1711, found 535.1704.

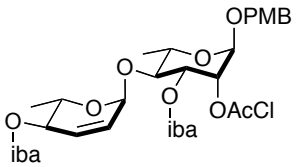
[15] Compound **25a-ii** was involved in the transformation (**25a** to **26a**), which is not represented in Scheme 5.

1-Benzyl-2,3-didehydro-4-*O*-isobutyral-α-L-rhamnopyranosyl-(1→4)-2-*O*-chloroacetyl-3-*O*-isobutyral-α-L rhamnopyranoside 26a



Allylic alcohol **25a-ii** (1.45 g, 2.83 mmol) was dissolved in dry CH_2Cl_2 (28.30 mL). The mixture was then cooled to 0 ºC and added pyridine (0.75 mL, 7.10 mmol), isobutyralchloride (0.59 mL, 5.65 mmol) and DMAP (173 mg, 1.42 mmol). The resulting mixture was stirred under argon from 0 ºC to rt over 2h. Diluted with CH_2Cl_2 and quenched with 1N HCl at 0 ºC. The aqueous layer was extracted with CH_2Cl_2 (50mL x 3) and the combined organic layer was washed with saturated $NaHCO_3$ and brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography using 10-15% EtOAc/hexane to obtain **26a** (1.60 g, 97%). Colorless solid: R_f (20% acetone/hexane) = 0.51; mp: 96 ºC; $[\alpha]_D^{25} = -88.54$ (*c* 0.70, CH_2Cl_2); IR (thin film, cm^{-1}) ν 2954, 1864, 1786, 1741, 1682, 1463, 11129, 1024, 864; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.13 (d, *J* = 6.2 Hz, 3H), δ 1.15 (d, *J* = 6.2 Hz, 3H), δ 1.16 (d, *J* = 6.0 Hz, 3H), δ 1.18 (d, *J* = 6.0 Hz, 3H), δ 1.22 (d, *J* = 6.0 Hz, 3H), δ 1.34 (d, *J* = 6.2 Hz, 3H), δ 2.45 (septet, *J* = 7.2 Hz, 1H), δ 2.56 (septet, *J* = 7.2 Hz, 1H), δ 3.79-3.94 (m, 3H), δ 4.06 (d, *J* = 14.4 Hz, 1H), δ 4.14 (d, *J* = 14.4 Hz, 1H), δ 4.55 (d, *J* = 12.0 Hz, 1H), δ 4.71 (d, *J* = 12.0 Hz, 1H), δ 4.79 (s, 1H), δ 5.04 (d, *J* = 3.0 Hz, 1H), δ 5.18 (s, 1H), δ 5.32 (dd, *J* = 3.0, 9.6 Hz, 1H), δ 5.36 (s, 1H), δ 5.62 (d, *J* = 10.4 Hz, 1H), δ 5.84 (d, *J* = 10.4 Hz, 1H), δ 7.29-7.34 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.6, 175.5, 166.6, 136.7, 130.9, 128.7, 128.2, 128.1, 126.7, 96.3, 95.6, 76.5, 72.4, 72.0, 70.2, 69.6, 67.5, 65.5, 40.8, 34.2, 19.1, 19.0, 18.9, 17.8, 17.7; HRMS (ESI): calcd for $[C_{29}H_{39}ClO_{10} + Na]^+$ 605.2129, found 605.2134.

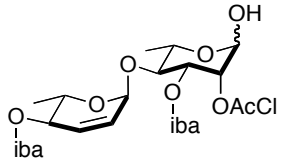
1-*p*-Methoxybenzyl-2,3-didehydro-4-*O*-isobutyral-α-L-rhamnopyranosyl-(1→4)-2-*O*-chloroacetyl-3-*O*-isobutyral-α-L rhamnopyranoside 26b



Enone **25b-i** (436 mg, 0.81 mmol) was dissolved in 8.1 mL dry CH_2Cl_2 and cooled to –78 ºC. To this added a 0.4 M solution of $CeCl_3$•MeOH (1.5 mL). After stirring for 10 min at this temperature, added solid $NaBH_4$ (46.17 mg, 1.22 mmol) in portions. The reaction mixture was stirred at to –78 ºC for 2h. Quenched with saturated $NaHCO_3$ at low temperature, diluted with CH2Cl2 and warmed to 0 ºC. The aqueous layer was extracted with CH_2Cl_2 (50mL x 3) and the combined organic layer was washed with saturated brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Crude allylic alcohol was passed through a pad of celite and carried to next step without further purification. The allylic alcohol thus obtained was dissolved in dry CH_2Cl_2 (9.0 mL). The mixture was then cooled to 0 ºC and added DIPEA (240 μL, 1.38 mmol), isobutyralchloride (135 μL, 1.28 mmol) and DMAP (10.5 mg, 0.086 mmol). The resulting mixture was stirred under argon from 0 ºC to rt over 2h. Diluted with $CH_2Cl_2$and quenched with 1N HCl at 0 ºC. Organic layer was extracted with CH_2Cl_2 (50mL x 3) and the combined organic layer was washed with saturated $NaHCO_3$ and brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography using 10% EtOAc/hexane to obtain **26b** (427 mg, 86%, 2 steps). Colorless solid: R_f (30% acetone/hexane) = 0.86; mp: 76 ºC; $[\alpha]_D^{25}$ = –92.24 (*c* 0.55, CH_2Cl_2); IR (thin film, cm^{-1}) ν 2962, 1864, 1790, 1764, 1652, 1537, 1117, 1029, 964, 863; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.12 (d, *J* = 6.8 Hz, 3H), δ 1.14 (d, *J* = 6.4 Hz, 3H), δ 1.16 (d, *J* = 6.2 Hz, 3H), δ 1.18 (d, *J* = 6.0 Hz, 3H), δ 1.22 (d, *J* = 6.8 Hz, 3H), δ 1.34 (d, *J* = 6.4 Hz, 3H), δ 2.45 (septet, *J* = 7.6 Hz, 1H), δ 2.56 (septet, *J* = 7.2 Hz, 1H), δ 3.80 (s, 3H), δ 3.82-3.94 (m, 3H), δ 4.09 (d, *J* = 14.8 Hz, 1H), δ 4.13 (d, *J* = 14.8 Hz, 1H), δ 4.44 (d, *J* = 12.0 Hz, 1H), δ 4.63 (d, *J* = 12.0 Hz, 1H), δ 4.78 (s, 1H), δ 5.04 (d, *J* = 8.4 Hz, 1H), δ 5.17 (s, 1H), δ 5.30 (dd, *J* = 2.8, 8.6 Hz, 1H), δ 5.32 (s, 1H), δ 5.60 (dd, *J* = 2.0, 10.4 Hz, 1H), δ 5.84 (d, *J* = 10.4 Hz, 1H), δ 6.87 (d, *J* = 8.8 Hz, 2H), δ 7.25 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.7, 175.8, 166.7, 159.6, 130.9, 129.9, 128.7, 126.7, 114.1, 95.9, 95.5, 76.5, 72.4, 70.2, 69.2, 67.4, 65.5, 55.5, 40.8,

34.2, 19.1, 19.0, 18.9, 17.8, 17.7; HRMS (ESI): calcd for $[C_{30}H_{41}ClO_{11}+Na]^+$ 635.2235, found 635.2230.

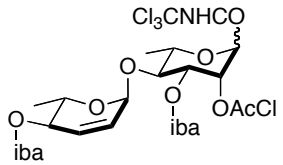
2,3-Didehydro-4-*O*-isobutyral-α-L-rhamnopyranosyl-(1→4)-2-*O*-chloroacetyl-3-*O*-isobutyral-α-L rhamnopyranoside 26b-i[16]



PMB ether **26b** (528 mg, 0.86 mmol) was dissolved in 3.0 mL aqueous CH_2Cl_2 (20:1) and cooled to 0 ºC. To this added solid DDQ (586.5 mg, 2.58 mmol) in portions. The reaction was allowed to rise to room temperature and stirred overnight at ambient temperature. Upon consumption of starting material, reaction was filtered through a short celite pad and subsequently washed with saturated $NaHCO_3$ at 0 ºC. The aqueous layer was extracted with CH_2Cl_2 (50mL x 3) and the combined organic layer was washed with saturated brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography using 18-20% EtOAc/hexane to obtain glycosyl donor **26b-i** (348 mg, 82%) as a mixture of diastereomers (9:1, α:β). Colorless solid: R_f (20% EtOAc/hexane) = 0.25; mp: 114-118 ºC; $[\alpha]_D^{25}$ = –65.54 (*c* 0.53, CH_2Cl_2); IR (thin film, cm^{-1}) ν 3454, 3110, 2973, 1851, 1780, 1652, 1598, 1220, 1136, 1029, 866; $_1$H NMR for the major diastereomes ($CDCl_3$, 400 MHz): δ 1.13 (d, *J* = 6.6 Hz, 3H), δ 1.15 (d, *J* = 6.2 Hz, 3H), δ 1.16 (d, *J* = 6.0 Hz, 3H), δ 1.18 (d, *J* = 7.0 Hz, 3H), δ 1.22 (d, *J* = 6.0 Hz, 3H), δ 1.37 (d, *J* = 6.0 Hz, 3H), δ 2.50 (septet, *J* = 6.4 Hz, 1H), δ 2.56 (septet, *J* = 6.4Hz, 1H), δ 3.13 (d, *J* = 3.6 Hz, 1H), δ 3.81 (dd, *J* = 9.6, 9.6 Hz, 1H), δ 3.92 (dq, *J* = 6.4, 9.6 Hz, 1H), δ 4.09 (dq, *J* = 6.4, 6.8 Hz, 1H), δ 4.12 (s, 2H), δ 5.04 (dd, *J* = 3.0, 9.2 Hz, 1H), δ 5.15 (d, *J* =3.2 Hz, 1H), δ 5.19 (s, 1H), δ 5.33-5.35 (m, 2H), δ 5.64 (d, *J* = 10.0 Hz, 1H), δ 5.85 (d, *J* = 10.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.8, 175.9, 166.9, 130.9, 126.8, 95.6, 91.9, 76.4, 72.3, 71.9, 70.3, 67.4, 65.6, 40.8, 34.3, 19.1, 19.0, 18.9, 17.9, 17.7; HRMS (ESI): calcd for $[C_{22}H_{33}ClO_{10}+Na]^+$ 515.1660, found 515.1662.

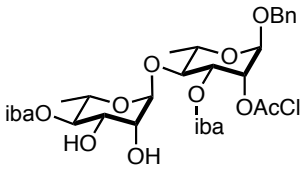
[16] Compound **26b-i** was involved in the transformation (**26b** to **28**), which is not represented in Scheme 5.

2,3-Didehydro-4-*O*-isobutyral-α-L-rhamnopyranosyl-(1→4)-2-*O*-chloroacetyl-3-*O*-isobutyral-α-L rhamnopyranosyl trichloroacetimidate 28



Glycosyl donor **26b-i** (50 mg, 0.10 mmol) was dissolved in 1.0 mL dry CH_2Cl_2 and cooled to 0 ºC. To this added Cl_3CCN (102 μL, 1.04 mmol) and NaH (0.24 mg, 0.01 mmol). The reaction was stirred at 0 ºC under argon for 3h. Upon consumption of starting material, reaction was directly loaded to a column (column diameter: 0.5 cm, packed with 2 cm celite and 3 cm silica gel). Elution with 5-10% EtOAc/hexane gave trichloroacetimidate **28** (56 mg, 88%) as a mixture of diastereomers (10:1, α:β). Colorless oil: R_f (20% EtOAc/hexane) = 0.75; $[\alpha]_D^{25}$ = –20.46 (*c* 0.05, benzene); IR (thin film, cm-1) ν 3430, 3120, 2964, 1851, 1780, 1652, 1556, 1136, 1031, 864; ^{1}H NMR for the major diastereomes (C_6D_6, 400 MHz): δ 0.99-1.03 (m, 9H), δ 1.07 (d, *J* = 6.4 Hz, 3H), δ 1.18 (d, *J* = 6.0 Hz, 3H), δ 1.44 (d, *J* = 5.6 Hz, 3H), δ 2.29-2.37 (m, 2H), δ 3.25 (d, *J* = 14.8 Hz, 1H), δ 3.35 (d, *J* = 14.8 Hz, 1H), δ 4.07 (dq, *J* = 2.8, 5.6 Hz, 1H), δ 4.14 (dd, *J* = 9.6, 9.6 Hz, 1H), δ 4.29 (dq, *J* = 4.0, 5.6 Hz, 1H), δ 5.27 (d, *J* = 8.8 Hz, 1H), δ 5.41 (s, 1H), δ 5.63 (d, *J* = 10.4 Hz, 1H), δ 5.71 (dd, *J* = 2.8, 10.0 Hz, 1H), δ 5.79 (d, *J* = 10.4 Hz, 1H), δ 5.85 (s, 1H), δ 6.39 (s, 1H), δ 8.47 (s, 1H); ^{13}C NMR (C_6D_6, 100 MHz): δ 176.2, 175.7, 166.6, 160.3, 131.3, 127.5, 96.2, 95.6, 91.4, 76.2, 72.9, 71.2, 70.8, 70.3, 66.2, 40.5, 34.5, 19.3, 19.2, 19.1, 18.4, 18.0; HRMS (ESI): calcd for $[C_{24}H_{33}Cl_4NO_{10} + Na]^+$ 658.0756, found 658.0767.

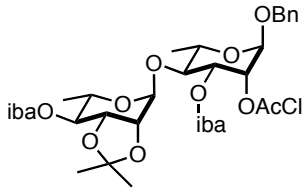
1-Benzyl-4-*O*-isobutyral-α-L-rhamnopyranosyl-(1→4)-2-*O*-chloroacetyl-3-*O*-isobutyral-α-L rhamnopyranoside 26a-i[17]



Alkene **26a** (1.65 g, 2.83 mmol) was dissolved in a 1:1 mixture of *t*-BuOH/acetone (6.00 mL) and the mixture was cooled to 0 ºC. To this added a 50% (v/v) solution of NMO/H_2O (6.00 mL). The reaction mixture was stirred at that temperature for 15 min and added OsO_4 (50 mg, 0.19 mmol). Stirred over night without replenishing ice from 0 ºC to rt. Cooled the reaction to 0 ºC, diluted with EtOAc and reduced the excess OsO_4 with saturated Na_2SO_3. The reaction mixture was then concentrated to remove acetone. The aqueous layer was extracted with EtOAc (50 mL x 3) and the combined organic layer was washed with saturated brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 35-40% EtOAc/hexane gave diol **26a-i** (1.47 g, 84%). White solid: R_f (40% hexanes/EtOAc) = 0.25; mp: 140-144 ºC; $[\alpha]_D^{25}$ = –117.40 (*c* 1.64, CH_2Cl_2); IR (thin film, cm^{-1}) ν 3390, 3054, 2864, 1741, 1680, 1624, 1478, 1391, 1130, 1042, 987, 866; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.14-1.21 (m, 15H), δ 1.36 (d, *J* = 6.0 Hz, 3H), δ 2.51 (septet, *J* = 7.2 Hz, 1H), δ 2.60 (septet, *J* = 7.2 Hz, 1H), δ 2.79 (d, *J* = 2.4 Hz, 1H), δ 3.12 (d, *J* = 4.4 Hz, 1H), δ 3.73 (dd, *J* = 9.0, 9.2 Hz, 1H), δ 3.76-3.91 (m, 4H), δ 4.05 (d, *J* = 15.6 Hz, 1H), δ 4.13 (d, *J* = 15.6 Hz, 1H), δ 4.55 (d, *J* = 11.6 Hz, 1H), δ 4.72 (d, *J* = 11.6 Hz, 1H), δ 4.75 (dd, *J* = 9.2, 9.2 Hz, 1H), δ 4.77 (s, 1H), δ 5.02 (s, 1H), δ 5.31 (dd, *J* = 3.2, 9.2 Hz, 1H), δ 5.35 (s, 1H), δ 7.29 -7.33 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.6, 176.0, 166.7, 136.6, 128.7, 128.3, 128.1, 101.3, 96.2, 78.3, 75.1, 71.9, 91.8, 71.2, 70.3, 69.5, 67.3, 66.7, 40.7, 34.3, 34.2, 19.2, 19.0, 18.9, 18.8, 18.2, 17.4; HRMS (ESI): calcd for $[C_{29}H_{41}ClO_{12} + Na]^+$ 639.2150, found. 639.2169.

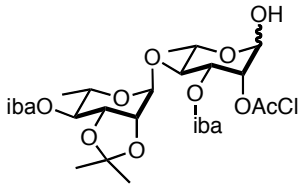
[17] Compound **26a-i** was involved in the transformation (**26a** to **27**), which is not represented in Scheme 5.

1-Benzyl-4-*O*-isobutyral-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→4)-2-*O*-chloroacetyl-3-*O*-isobutyral-α-L rhamnopyranoside 27



The *syn*-diol **26a-i** (700 mg, 1.13 mmol) was dissolved in dry CH_2Cl_2 (3.00 mL) and the mixture was cooled to 0 ºC. To this added 2,2-DMP (0.28 mL, 2.27 mmol) and *p*-TsOH (2.15 mg, 0.01 mmol). The reaction was stirred under argon from 0 ºC to rt over 2h. Diluted with CH_2Cl_2 and quenched by adding saturated $NaHCO_3$ at 0 ºC. The aqueous layer was extracted with CH_2Cl_2 (50 mL x 3) and the combined organic layer was washed with saturated brine. Dried over Na_2SO_4 and concentrated under reduced pressure. The product **27** (683 mg, 92%) was obtained by silica gel chromatography using 10% EtOAc/Hexane. Colorless solid: R_f (40% hexanes/EtOAc) = 0.25; mp: 132 ºC; $[\alpha]_D^{25}$ = –61.10 (*c* 1.05, CH_2Cl_2); IR (thin film, cm^{-1}) ν 2943, 2864, 1864, 1740, 1663, 1624, 1456, 1147, 1042, 978; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.14 (d, *J* = 7.0 Hz, 3H), δ 1.14 (d, *J* = 6.2 Hz, 3H), δ 1.15 (d, *J* = 6.0 Hz, 3H), δ 1.17 (d, *J* = 6.0 Hz, 3H), δ 1.18 (d, *J* = 6.6 Hz, 3H), δ 1.26 (s, 3H), δ 1.33 (d, *J* = 6.8 Hz, 3H), δ 1.52 (s, 3H), δ 2.52 (septet, *J* = 7.0 Hz, 1H), δ 2.57 (septet, *J* = 7.2 Hz, 1H), δ 3.73-3.87 (m, 3H), δ 3.99 (d, *J* = 3.2 Hz, 1H), δ 4.05-4.11 (m, 3H), δ 4.52 (d, *J* = 12.0 Hz, 1H), δ 4.71 (d, *J* = 12.0 Hz, 1H), δ 4.78 (d, *J* = 1.0 Hz, 1H), δ 4.83 (dd, *J* = 8.0, 9.0 Hz, 1H), δ 5.19 (s, 1H), δ 5.34-5.36 (m, 2H), δ 7.28-7.33 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.2, 176.0, 166.6, 136.7, 128.7, 128.2, 128.1, 109.7, 99.2, 96.3, 77.8, 76.3, 75.7, 73.8, 72.1, 71.9, 69.6, 67.3, 65.1, 40.7, 34.2, 27.7, 26.5, 19.2, 19.0, 18.9, 18.8, 17.9, 16.7; HRMS (ESI): calcd for $[C_{32}H_{45}ClO_{12} + Na]^+$ 679.2507, found 679.2521.

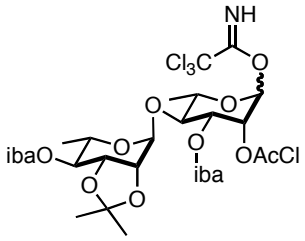
4-*O*-Isobutyral-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→4)-2-*O*-chloroacetyl-3-*O*-isobutyral-α-L rhamnopyranoside 27a[18]



Benzyl ether **27** (800 mg, 1.22 mmol) was dissolved in EtOAc (10 mL) and few drops of MeOH. To this solution, Pd/C (60 mg) was added and under H_2 balloon pressure the reaction was stirred for 3h at rt. The solid Pd/C catalyst was removed by filtration using a celite pad. Filtrate was concentrated under reduced pressure and purified by silica gel chromatography using 30-35% EtOAc/hexane to obtain **27a** (650 mg, 94%) as a mixture of diastereomers (10:1, α:β). White solid: R_f (30% hexanes/EtOAc) = 0.31; mp: 164 ºC; $[\alpha]_D^{25}$ = –22.80 (*c* 0.50, CH_2Cl_2); IR (thin film, cm^{-1}) ν 3360, 2985, 2833, 1851, 1741, 1663, 1456, 1147, 1040, 866; ^{1}H NMR of the major diastereomer in ($CDCl_3$, 400 MHz): δ 1.11-1.80 (m, 15H), δ 1.26 (s, 3H), δ 1.33 (d, *J* = 6.6 Hz, 3H), δ 1.51 (s, 3H), δ 2.48-2.62 (m, 2H), δ 3.73-3.87 (m, 3H), δ 3.99-3.4.17 (m, 5H), δ 4.82 (dd, *J* = 8.8, 8.8 Hz, 1H), δ 5.12 (s, 1H), δ 5.19 (s, 1H), δ 5.32-5.36 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.5, 176.3, 109.8, 99.1, 91.8, 77.8, 76.3, 75.7, 73.9, 72.3, 71.8, 67.1, 65.1, 40.8, 34.2, 27.8, 26.5 19.2, 19.0, 18.9, 18.8, 18.1, 16.7; HRMS (ESI): calcd for $[C_{25}H_{39}ClO_{12} + Na]^+$ 589.2008, found 589.2028.

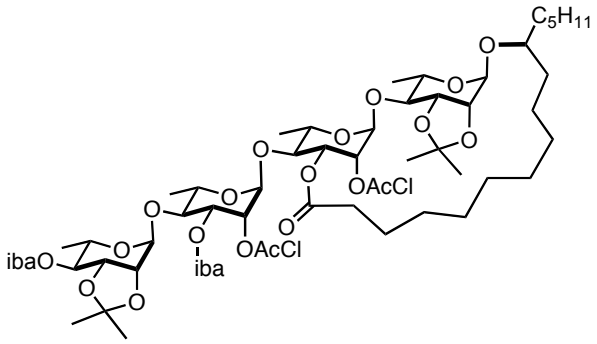
[18] Compound **27a** was involved in the transformation (**27** to **3**), which is not represented in Scheme 5.

4-*O*-Isobutyral-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→4)-2-*O*-chloroacetyl-3-*O*-isobutyral-α-L rhamnopyranosyl trichloroacetimidate 3



Anomeric alcohol **27a** (64 mg, 0.11 mmol) was dissolved in 1.10 mL dry CH_2Cl_2 and cooled to 0 ºC. To this added $CNCCl_3$ (113 μL, 1.13 mmol) and NaH (0.3 mg, 0.01 mmol). The reaction was stirred at 0 ºC under argon for 3h. Upon consumption of starting material, reaction was directly loaded to a column (column diameter: 0.50 cm, packed with 3.00 cm silica gel topped with a 2.00 cm celite pad). Elution with 10-15% EtOAc/hexane gave trichloroacetimidate **3** (55 mg, 70%) as a mixture of diastereomers (12:1, α:β). Colorless oil: R_f (20% EtOAc/hexane) = 0.50; $[\alpha]_D^{25}$ = –224.80 (*c* 0.50, benzene); IR (thin film, cm^{-1}) ν 3415, 3206, 2837, 1846, 1781, 1652, 1523, 1158, 866; ^{1}H NMR for the major diastereomes (C_6D_6, 400 MHz): δ 1.03-1.13 (m, 15H) δ 1.17 (d, *J* = 6.0 Hz, 3H), δ 1.39 (d, *J* = 6.6 Hz, 3H), δ 1.55 (s, 3H), δ 2.39 (septet, *J* = 6.8 Hz, 1H), δ 2.47 (septet, *J* = 7.6 Hz, 1H), δ 3.27 (d, *J* = 14.8 Hz, 1H), δ 3.26 (d, *J* = 14.8 Hz, 1H), δ 3.84 (dq, *J* = 6.6, 9.4 Hz, 1H), δ 4.04-4.14 (m, 3H), δ 4.29 (dq, *J* = 6.4, 9.2 Hz, 1H), δ 5.27 (dd, *J* = 9.6, 10.4 Hz, 1H), δ 5.53 (s, 1H), δ 5.73 (dd, *J* = 2.8, 10.4 Hz, 1H), δ 5.84 (s, 1H), δ 6.40 (s, 1H), δ 8.51 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.0, 166.5, 160.2, 110.2, 100.2, 95.5, 91.4, 77.7, 77.0, 76.5, 74.4, 72.7, 70.9, 70.2, 65.9, 40.5, 43.6, 34.5, 28.2, 26.9, 19.4, 19.3, 19.2, 19.1, 18.6, 17.1; HRMS (ESI): calcd for $[C_{27}H_{39}Cl_4NO_{12} + Na]^+$ 732.1124, found 732.1118.

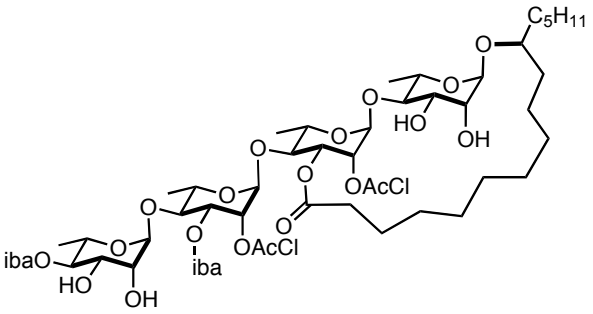
Tetrasaccharide 2



Glycosyl acceptor **9** (45 mg, 0.07 mmol) and glycosyl donor **3** (91 mg, 0.13 mmol) were separately dried azeotropically with benzene and under high vacuum for 3h. Acceptor **9** was dissolved in dry CH_2Cl_2 (1.00 mL) and transferred to the flask containing the donor **3** via cannula. Freshly activated molecular sieves (60 mg) was added and stirred under argon for 15 min. The reaction mixture was then cooled to –78 ºC and dropwise added a CH_2Cl_2 solution of TMSOTf (2.80 mL, 0.02 mmol in 0.3 mL CH_2Cl_2). The reaction was stirred from –78 ºC to 0 ºC over 1.50 h and subsequently quenched with Et_3N. Water was added and the aqueous phase extracted with CH_2Cl_2 (20 mL x 3). The combined organic layer was washed with 1N HCl, saturated $NaHCO_3$ and brine. The pooled organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 10-12% EtOAc/hexane gave tetrasaccharide **2** (60 mg, 71%). Colorless oil: R_f (20% EtOAc/hexane) = 0.5; $[\alpha]_D^{25}$ = –26.34 (*c* 2.4, CH_2Cl_2); IR (thin film, cm^{-1}) ν 2864, 1781, 1740, 1680, 1666, 1485, 1213, 1156, 1036, 1023, 948, 866, 788; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.87 (t, *J* = 6.6 Hz, 3H), δ 1.12-1.14 (m, 9H), δ 1.17 (d, *J* = 7.2 Hz, 3H), δ 1.19 (d, *J* = 6.4 Hz, 3H), δ 1.25-1.36 (m, 34H), δ 1.47 (s, 3H), δ 1.52 (s, 3H), δ 1.54-1.61 (m, 3H), δ 1.70 (m, 2H), δ 2.21 (ddd, *J* = 4.2, 7.2, 14.2 Hz, 1H), δ 2.39 (ddd, *J* = 4.4, 7.0, 14.2 Hz, 1H), δ 2.47-2.61 (m, 2H), δ 3.45 (brs, 1H), δ 3.49 (dd, *J* = 5.2, 7.2 Hz, 1H), δ 3.69 (dd, *J* = 9.6, 9.6 Hz, 1H), δ 3.74-3.79 (m, 2H), δ 3.89-3.95 (m, 2H), δ 3.98-4.04 (m, 2H), δ 4.08 (m, 4H), δ 4.12 (s, 2H), δ 4.22 (dd, *J* = 5.2, 6.0 Hz, 1H), δ 4.83 (dd, *J* = 8.8, 8.8 Hz, 1H), δ 4.91 (s, 1H), δ 4.94 (s, 1H), δ 5.13 (s, 1H), δ 5.15 (brs, 1H), δ 5.18 (s, 1H), δ 5.25 (dd, *J* = 3.2, 9.6 Hz, 1H), δ 5.32 (brs, 1H), δ 5.45 (dd, *J* = 2.8, 10.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.3, 175.8, 173.4, 166.5, 166.4, 110.1, 109.8, 99.1, 98.9, 96.4, 95.8, 80.3, 80.2, 78.7, 77.6, 76.8, 76.3, 75.8, 74.4, 73.9, 73.3, 72.2, 71.5, 71.4, 68.5, 68.1, 65.8, 65.2, 40.9, 40.7, 34.6, 34.2, 34.1, 33.1, 32.3, 30.1, 29.9, 28.6, 27.9, 27.8, 27.7, 27.6, 26.6, 26.4, 26.1, 25.1, 22.8,

19.5, 19.2, 19.0, 18.8, 18.3, 17.9, 16.7, 14.3; HRMS (ESI): calcd for $[C_{58}H_{92}Cl_2O_{22} + H]^+$ 1211.5536, found 1211.5562.

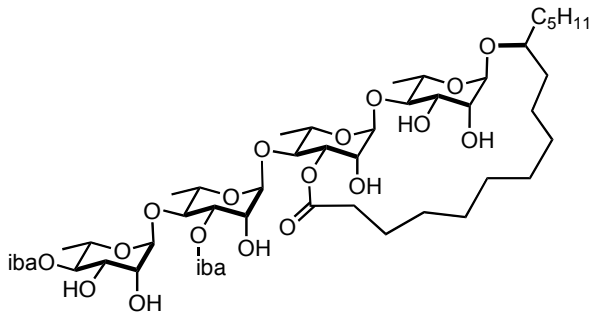
Macrocyclic tetraol 29



The bis-acetonide protected tetrasaccharide **2** (35 mg, 0.029 mmol) was dissolved in 0.40 mL of CH_2Cl_2 and cooled to 0 ºC. The reaction mixture was stirred for 10 min at this temperature and dropwise added 60 μL aqueous solution TFA (10:1). The reaction mixture was stirred at 0 ºC for 30 min and quenched with saturated $NaHCO_3$. Water was added and the aqueous phase extracted with CH_2Cl_2 (20 mL x 3). The combined organic layer was washed with brine and dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 35-40% EtOAc/hexane gave **29** (23.50 mg, 72%). Colorless oil: R_f (40% EtOAc/hexane) = 0.32; $[\alpha]_D^{25}$ = –54.3 (*c* 0.4, CH_2Cl_2); IR (thin film, cm^{-1}) ν 3350, 3300, 2912, 1764, 1741, 1684, 1536, 1491, 1216, 1026, 951, 866; ^1H NMR ($CDCl_3$, 500 MHz): δ 0.89 (t, *J* = 7.0 Hz, 3H), δ 1.14 (d, *J* = 7.0 Hz, 3H), δ 1.15 (d, *J* = 7.0 Hz, 3H), δ 1.89 (d, *J* = 7.0 Hz, 3H), δ 1.20 (d, *J* = 6.5, 3H), δ 1.21 (d, *J* = 6.5 Hz, 3H), δ 1.25-1.33 (m, 22H), δ 1.35 (d, *J* = 6.5 Hz, 3H), δ 1.36 (d, *J* = 6.0 Hz, 3H), δ 1.45-1.54 (m, 5H), δ 2.43 (ddd, *J* = 2.5, 8.0, 16.5 Hz, 1H), δ 2.34 (ddd, *J* = 3.0, 9.0, 16.7 Hz, 1H), δ 2.44 (d, *J* = 5.5 Hz, 1H), δ 2.51 (septet, *J* = 7.0 Hz, 1H), δ 2.61 (septet, *J* = 6.5 Hz, 1H), δ 2.68 (s, 1H), δ 2.86 (d, *J* = 8.0 Hz, 1H), δ 3.10 (d, *J* = 4.5 Hz, 1H), δ 3.42 (dd, *J* = 9.0, 9.0 Hz, 1H), δ 3.47 (m, 1H), δ 3.68 (dd, *J* = 9.5, 9.5 Hz, 1H), δ 3.75-3.79 (m, 4H), δ 3.85-3.99 (m, 5H), δ 4.09 (s, 2H), δ 4.11 (s, 2H), δ 4.75 (dd, *J* = 9.5, 9.5 Hz, 1H), δ 4.82 (d, *J* = 2.0 Hz, 1H), δ 4.92 (d, *J* = 1.5 Hz, 1H), δ 5.0 (s, 1H), δ 5.18 (dd, *J* = 2.5, 2.5 Hz, 1H), δ 5.22 (dd, *J* = 3.0, 9.5 Hz, 1H) δ 5.24 (d, *J* = 2.0 Hz, 1H), δ 5.41 (dd, *J* = 3.0, 10.5 Hz, 1H), δ 5.53 (dd, *J* = 2.0, 2.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.7, 175.8, 173.9, 167.0, 166.5, 101.2, 99.0, 98.9, 97.2, 82.1, 81.2, 78.7, 78.1, 75.3, 73.4, 72.2, 72.1, 72.0, 71.4, 71.3, 71.1, 70.4, 68.5, 68.1, 66.8, 66.7,

41.0, 40.7, 34.3, 34.2, 33.7, 33.1, 32.3, 30.3, 29.9, 28.6, 27.7, 27.6, 26.6, 25.6, 25.2, 22.8, 22.6, 19.2, 10.0, 18.8, 18.5, 18.4, 18.1, 17.4, 14.2; HRMS (ESI): calcd for $[C_{52}H_{84}Cl_2O_{22} + Na]^+$ 1153.4724, found 1153.4744.

Merremoside D (1)



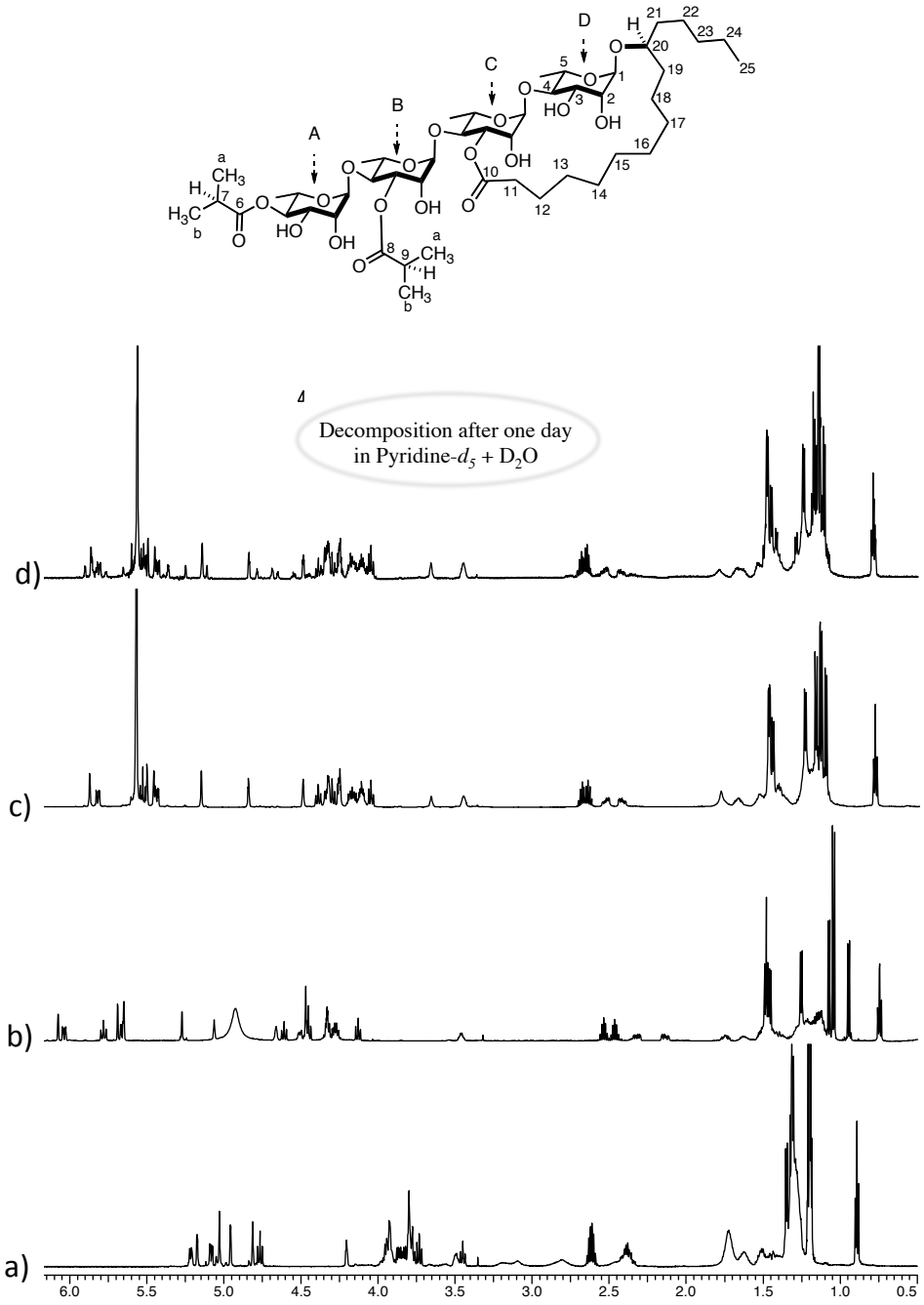
The bis-chloroacetate **29** (23.5 mg, 0.02 mmol) was dissolved in THF (1.0 mL). To this added thiourea (19.0 mg, 0.25 mmol), $NaHCO_3$ (11.0 mg, 0.13 mmol) and TBAI (4.0 mg, 0.01 mmol). The reaction mixture was then refluxed at 55 ºC under argon for 3h. Upon consumption of starting material, the reaction was cooled 0 ºC and diluted with EtOAc and H_2O. The aqueous phase extracted with EtOAc (10 mL x 3) and combined organic layer was washed with water (7-10 times to remove thiourea and TBAI) and saturated brine. Dried over Na_2SO_4 and concentrated under reduced pressure. Silica gel chromatography with 5% MeOH/$CHCl_3$ gave merremoside D (**1**), (16 mg, 78%). White solid, mp: 140 ºC, (ref[19] mp: 138-139 ºC); R_f (5% MeOH/$CHCl_3$) = 0.3; $[\alpha]_D^{25}$ = –68.6 (*c* 0.83, MeOH), (ref[19]: $[\alpha]_D$ = –77 (*c* 1.1, MeOH)) IR (thin film, cm^{-1}) ν 3330, 3300, 2910, 2850, 1741, 1730, 1864, 1514, 1236, 1026, 941, 866; HRMS (ESI): calcd for $[C_{48}H_{82}O_{20} + H]^+$ 979.5478, found 979.5457.

^1H and ^{13}C NMR spectrums were recorded in $CDCl_3$, Pyridine-d_5 and Pyridine-d_5 + D_2O. Due to instability of the compound in Pyridine-d_5 + D_2O, full NMR assignments were carried out in $CDCl_3$ and Pyridine-d_5.[20] The analyses are listed in following table for both solvents.

Stability of merremoside D (1) in different solvents (^{1}H NMR, 600 MHz)

[19] I. Kitagawa, N. I. Baek, K. Kawashima, Y. Yokokawa, M. Yoshikawa, K. Ohashi, H. Shibuya, *Chem. Pharm. Bull.* **1996**, *44*, 1680

[20] See comparison of ^{1}H NMR of merremoside D (**1**) in different solvents.



a) $CDCl_3$, b) Pyridine-d_5, c) Pyridine-d_5 + D_2O (5:1), d) Merremoside D (**1**) decomposed in Pyridine-d_5 + D_2O (5:1) after one day.

Complete ^{1}H NMR assignments in $CDCl_3$ (600 MHz)

Position	δ/ppm	J/Hz
25-CH_3	0.890	t, *J* = 7.2
5-CH_3^b-sugar A	1.189	d, *J* = 6.2
7-CH_3^a-iba	1.196	d, *J* = 7.0
7-CH_3^b-iba	1.197	d, *J* = 7.0
9-CH_3^a-iba	1.204	d, *J* = 7.0
9-CH_3-iba	1.206	d, *J* = 7.0
12-19, 21-24-CH_2's	1.24-1.77	m
5-CH_3-sugar D	1.308	d, *J* = 6.4
5-CH_3-sugar B	1.322	d, *J* = 6.4
5-CH_3-sugar C	1.349	d, *J* = 6.3
11-CH_2	2.33-2.43	m
9-H	2.61	septet, *J* = 7.0
7-H	2.62	septet, *J* = 7.0
6 x OH	2.56-3.45	m
4-H-sugar D	3.447	dd, *J* = 9.1, 9.1
20-H	3.47-3.51	m
4-H-sugar B	3.730	dd, *J* = 8.5, 9.1
4-H-sugar C	3.774	dd, *J* = 8.3, 8.8
3-H-sugar A	3.788	dd, *J* = 2.6, 9.3
2-H-sugar D	3.797	dd, *J* = 2.0, 2.8
2-H-sugar A	3.799	dd, *J* = 1.6, 2.6
5-H-sugar B	3.830	dq, *J* = 6.4, 9.1
5-H-sugar A	3.863	dq, *J* = 6.2, 9.5
2-H-sugar B	3.925	dd, *J* = 2.5, 3.1
5-H-sugar D	3.930	dq, *J* = 6.4, 9.1
5-H-sugar C	3.939	dq, *J* = 6.3, 8.8
3-H-sugar D	3.940	dd, *J* = 2.8, 9.1
2-H-sugar C	4.200	dd, *J* = 2.5, 2.9
4-H-sugar A	4.762	dd, *J* = 9.3, 9.5
1-H-sugar D	4.811	d, *J* = 2.0
1-H-sugar B	4.955	d, *J* = 2.5
1-H-sugar A	5.026	d, *J* = 1.6
3-H-sugar B	5.080	dd, *J* = 3.1, 8.5
1-H-sugar C	5.171	d, *J* = 2.9
3-H-sugar C	5.214	dd, *J* = 2.5, 8.3

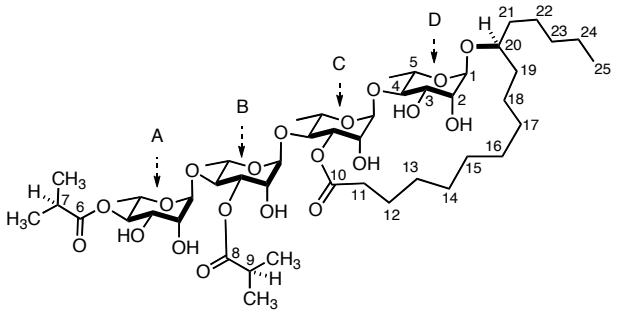
Complete ^{13}C NMR assignments in $CDCl_3$ (150 MHz)

Position	δ/ppm
C-6, C=O-iba	178.32
C-8, C=O-iba	176.11
C-10, C=O-macrolactone	173.97
C-1, sugar A	100.51
C-1, sugar B	100.33
C-1, sugar C	98.64
C-1, sugar D	98.51
C-4, sugar D	81.43
C-20	80.91
C-4, sugar B	78.14
C-4, sugar C	77.71
C-4, sugar A	74.99
C-3, sugar C	74.48
C-3, sugar B	73.67
C-2, sugar A	71.34
C-3, sugar D	71.33
C-2, sugar D	71.02
C-2, sugar C	70.31
C-3, sugar A	70.13
C-2, sugar B	69.65
C-5, sugar C	68.39
C-5, sugar B	67.67
C-5, sugar A	66.51
C-5, sugar D	66.35
C-7, C-9	34.11, 34.09
C-11	33.90
C-23	32.01
C-13	27.30
C-12	23.53
C-24	22.58
C-14 to C-19, C-21, C-22	33.89, 33.43, 29.66, 28.65 27.97, 27.73, 24.97, 24.91
4 x CH_3-iba	19.04, 18.96, 18.77, 18.73
CH_3, sugar C	18.39
CH_3, sugar D	18.10
CH_3, sugar B	18.04
CH_3, sugar A	17.16
C-25	14.01

Complete ^{1}H NMR assignments in Pyridine-d_5 (600 MHz)

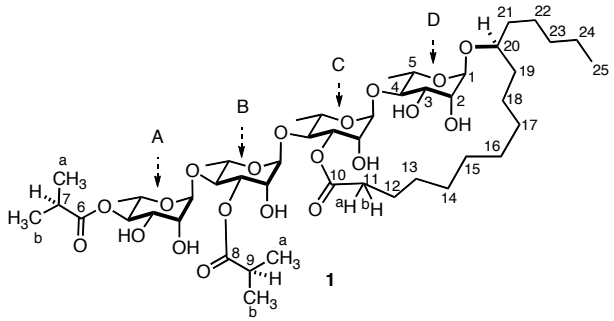
Position	δ/ppm	J/Hz
25-CH_3	0.86	t, J = 7.3
9-CH_3^a-iba	1.06	d, J = 7.0
7-CH_3^a-iba	1.15	d, J = 7.0
9-CH_3^b-iba	1.16	d, J = 7.0
7-CH_3^b-iba	1.18	d, J = 7.0
13-19, 21-24-CH_2's	1.20-1.65	m
5-CH_3-sugar A	1.36	d, J = 6.3
5-CH_3-sugar C	1.56	d, J = 6.2
5-CH_3-sugar D	1.58	d, J = 6.4
5-CH_3-sugar B	1.59	d, J = 6.4
12-H^a	1.68-1.77	m
12-H^b	1.82-1.88	m
11-H^a	2.23	ddd, J = 16.0, 9.5, 3.1
11-H^b	2.41	ddd, J = 16.0, 8.0, 3.1
20-H	3.51-3.55	m
9-H	2.56	septet, J = 7.0
7-H	2.62	septet, J = 7.0
4-H-sugar D	4.18	dd, J = 8.6, 8.6
5-H-sugar B	4.327	dq, J = 6.4, 9.5
5-H-sugar A	4.333	dq, J = 6.3, 9.5
2-H-sugar D	4.37	dd, J = 2.0, 3.3
5-H-sugar D	4.38	dq, J = 6.4, 8.6
5-H-sugar C	4.39	dq, J = 6.2, 9.5
4-H-sugar B	4.49	dd, J = 9.1, 9.5
2-H-sugar A	4.50	dd, J = 1.8, 2.7
3-H-sugar A	4.51	dd, J = 2.7, 9.1
3-H-sugar D	4.56	dd, J = 3.3, 8.6
4-H-sugar C	4.66	dd, J = 9.5, 9.8
2-H-sugar B	4.71	dd, J = 1.8, 3.2
2-H-sugar C	5.11	dd, J = 2.2, 2.5
1-H-sugar D	5.31	d, J = 2.0
1-H-sugar B	5.68	d, J = 1.8
3-H-sugar B	5.69	dd, J = 3.2, 9.1
1-H-sugar A	5.72	d, J = 1.8
4-H-sugar A	5.81	dd, J = 9.5, 9.5
3-H-sugar C	6.06	dd, J = 2.5, 9.8
1-H-sugar C	6.10	d, J = 2.2

Complete ^{13}C NMR assignments in Pyridine-d_5 (150 MHz)



Position	δ/ppm
C-6, C=O-iba	176.73
C-8, C=O-iba	176.38
C-10, C=O-macrolactone	173.77
C-1, sugar A	103.30
C-1, sugar B	103.01
C-1, sugar C	101.79
C-1, sugar D	100.24
C-4, sugar D	82.43
C-20	79.28
C-4, sugar C	77.96
C-3, sugar C	76.22
C-3, sugar B	75.75
C-4, sugar A	74.95
C-4, sugar B	74.96
C-3, sugar D	73.00
C-2, sugar A	72.71
C-2, sugar B	72.70
C-3, sugar A	71.59
C-2, sugar C	71.60
C-2, sugar D	70.15
C-5, sugar C	69.45
C-5, sugar B	68.74
C-5, sugar A	68.25
C-5, sugar D	68.17
C-11	33.72
C-23	32.41
C-13	27.18
C-12	23.30
C-24	22.95
C-14 to C-19, C-21, C-22, C-7, C-9, 4 x CH_3-iba	34.96, 34.51, 34.47,34.46, 30.46, 29.05, 28.08, 20.05, 26.28, 25.35, 19.37, 19.12, 19.11, 18.99
CH_3, sugar C	19.13
CH_3, sugar D	19.07
CH_3, sugar B	18.79
CH_3, sugar A	17.90
C-25	14.28

Comparison of limited reported ^{1}H chemical shifts and coupling constants with our NMR analysis in Pyridine-d_5+D_2O (5:1):



Position	Natural **1**[i]	Synthetic **1**[ii]	Δ^{iii} = **1**$_{nat}$ – **1**$_{syn}$
25-CH_3	0.79 (t, *J* = 7.0)	0.79, (t, *J* = 7.3)	0.00
CH_3^b-iba	1.18 (d, *J* = 7.0)	1.11, (d, *J* = 7.0)	0.07
CH_3^a-iba	1.19 (d, *J* = 7.0)	1.14, (d, *J* = 7.0)	0.05
CH_3^b-iba	1.20 (d, *J* = 7.0)	1.15, (d, *J* = 7.0)	0.05
CH_3^a-iba	1.23 (d, *J* = 7.0)	1.17, (d, *J* = 7.0)	0.06
5-CH_3-sugar D	1.32 (d, *J* = 6.1)	1.24, (d, *J* = 6.2)	0.08
5-CH_3-sugar C	1.50, (d, *J* = 6.4)	1.45, (d, *J* = 6.2)	0.05
5-CH_3-sugar B	1.56, (d, *J* = 6.1)	1.48, (d, *J* = 6.1)	0.07
5-CH_3-sugar A	1.57, (d, *J* = 6.1)	1.49, (d, *J* = 6.2)	0.08
11-H^a	2.16, (ddd, *J* = 14.6, 6.9, 3.0)	2.43, (ddd, *J* = 15.8, 8.9, 3.2)	– 0.27
11-H^b	2.41, (ddd, *J* = 14.6, 6.9, 3.0)	2.54, (ddd, *J* = 15.8, 8.9, 3.2)	– 0.13
9-H	2.66, (m)	2.65, (septet, *J* = 7.0)	0.01
7-H	2.67, (m)	2.69, (septet, *J* = 7.0)	– 0.02
20-H	3.87, (m)	3.43-3.48, (m)	0.41
1-H-sugar D	5.33, (brs)	5.51, (d, *J* = 1.7)	– 0.18
1-H-sugar A	5.60, (brs)	5.47, (d, *J* = 1.7)	0.13
3-H-sugar C	5.61, (dd, *J* = 3.0, 9.5)	5.45, (dd, *J* = 2.7, 9.4)	0.16
3-H-sugar B	5.65, (dd, *J* = 3.0, 9.5)	5.83, (dd, *J* = 2.8, 10.0)	– 0.18
4-H-sugar A	5.67, (dd, *J* = 9.5, 9.5)	5.54, (dd, *J* = 9.8, 9.8)	0.13
1-H-sugar B	5.80, (brs)	5.51, (d, *J* = 1.6)	0.29
1-H-sugar C	6.29, (brs)	5.88, (d, 1.9)	0.41

i) Concentration of **1** and the ratio of Pyridine-d_5/D_2O is not known, ^{1}H NMR was acquired in 500 MHz spectrometer; ii) ^{1}H NMR was recorded in 600 MHz spectrometer by dissolving 7.5 mg of **1** in 0.5 mL Pyridine-d_5 and 100 μL D_2O; iii) Chemical shift difference which are ≥ 0.1 ppm are highlighted in red.

Reassigned chemical shifts of reported data and comparison with our assigned chemical shifts in Pyridine-d_5+D_2O (5:1):

Position	Natural **1**[i]	Synthetic **1**[ii]	Δ^{iii} = $\mathbf{1}_{nat}$ – $\mathbf{1}_{syn}$
25-CH_3	0.79 (t, *J* = 7.0)	0.79, (t, *J* = 7.3)	0.00
CH_3^b-iba	1.18 (d, *J* = 7.0)	1.11, (d, *J* = 7.0)	0.07
CH_3^a-iba	1.19 (d, *J* = 7.0)	1.14, (d, *J* = 7.0)	0.05
CH_3^b-iba	1.20 (d, *J* = 7.0)	1.15, (d, *J* = 7.0)	0.05
CH_3^a-iba	1.23 (d, *J* = 7.0)	1.17, (d, *J* = 7.0)	0.06
5-CH_3-sugar D	1.32 (d, *J* = 6.1)	1.24, (d, *J* = 6.2)	0.08
5-CH_3-sugar C	1.50, (d, *J* = 6.4)	1.45, (d, *J* = 6.2)	0.05
5-CH_3-sugar B	1.56, (d, *J* = 6.1)	1.48, (d, *J* = 6.1)	0.07
5-CH_3-sugar A	1.57, (d, *J* = 6.1)	1.49, (d, *J* = 6.2)	0.08
11-H^a	2.41, (ddd, *J* = 14.6, 6.9, 3.0)	2.43, (ddd, *J* = 15.8, 8.9, 3.2)	– 0.03
11-H^b	2.16, (ddd, *J* = 14.6, 6.9, 3.0)	2.54, (ddd, *J* = 15.8, 8.9, 3.2)	– 0.38
9-H	2.66, (m)	2.65, (septet, *J* = 7.0)	0.01
7-H	2.67, (m)	2.69, (septet, *J* = 7.0)	– 0.02
20-H	3.87, (m)	3.43-3.48, (m)	0.41
1-H-sugar D	5.60, (brs)	5.51, (d, *J* = 1.7)	0.09
1-H-sugar A	5.33, (brs)	5.47, (d, *J* = 1.7)	– 0.14
3-H-sugar C	5.61, (dd, *J* = 3.0, 9.5)	5.45, (dd, *J* = 2.7, 9.4)	0.16
3-H-sugar B	5.65, (dd, *J* = 3.0, 9.5)	5.83, (dd, *J* = 2.8, 10.0)	– 0.18
4-H-sugar A	5.67, (dd, *J* = 9.5, 9.5)	5.54, (dd, *J* = 9.8, 9.8)	0.13
1-H-sugar B	6.29, (brs)	5.51, (d, *J* = 1.6)	0.78
1-H-sugar C	5.80, (brs)	5.88, (d, 1.9)	– 0.08

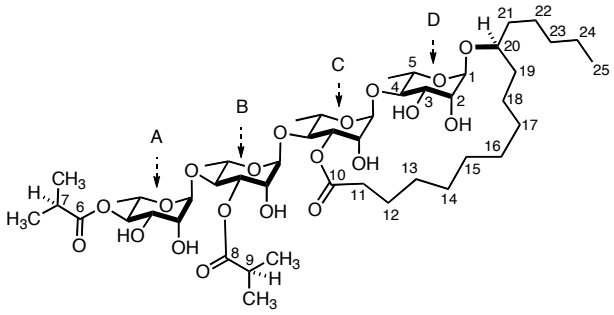
i) Reassigned reported chemical shifts for **1** (concentration of **1** and the ratio of Pyridine-d_5/D_2O is not known, ^{1}H NMR was acquired in 500 MHz spectrometer); ii) ^{1}H NMR was recorded in 600 MHz spectrometer by dissolving 7.5 mg of **1** in 0.5 mL Pyridine-d_5 and 100 μL D_2O; iii) Chemical shift difference which are ≥ 0.1 ppm are highlighted in red.

Comparison of limited reported ^{1}H chemical shifts and coupling constants in Pyridine-d_5 + D_2O (5:1) with our NMR analysis in Pyridine-d_5:

Position	Natural **1**[i]	Synthetic **1**[ii]	Δ^{iii} = $\mathbf{1}_{nat}$ – $\mathbf{1}_{syn}$
25-CH_3	0.79 (t, *J* = 7.0)	0.86, (t, *J* = 7.3)	– 0.07
CH_3^b-iba	1.18 (d, *J* = 7.0)	1.06, (d, *J* = 7.0)	0.12
CH_3^a-iba	1.19 (d, *J* = 7.0)	1.15, (d, *J* = 7.0)	0.04
CH_3^b-iba	1.20 (d, *J* = 7.0)	1.16, (d, *J* = 7.0)	0.04
CH_3^a-iba	1.23 (d, *J* = 7.0)	1.18, (d, *J* = 7.0)	0.05
5-CH_3-sugar D	1.32 (d, *J* = 6.1)	1.58, (d, *J* = 6.4)	– 0.26
5-CH_3-sugar C	1.50, (d, *J* = 6.4)	1.56, (d, *J* = 6.2)	– 0.06
5-CH_3-sugar B	1.56, (d, *J* = 6.1)	1.59, (d, *J* = 6.4)	– 0.03
5-CH_3-sugar A	1.57, (d, *J* = 6.1)	1.36, (d, *J* = 6.3)	0.21
11-H^a	2.16, (ddd, *J* = 14.6, 6.9, 3.0)	2.23, (ddd, *J* = 16.0, 9.5, 3.1)	– 0.07
11-H^b	2.41, (ddd, *J* = 14.6, 6.9, 3.0)	2.41, (ddd, *J* = 16.0, 9.5, 3.1)	0.00
9-H	2.66, (m)	2.56, (septet, *J* = 7.0)	0.10
7-H	2.67, (m)	2.62, (septet, *J* = 7.0)	0.05
20-H	3.87, (m)	3.51-3.55, (m)	0.34
1-H-sugar D	5.33, (brs)	5.31, (d, *J* = 2.0)	0.02
1-H-sugar A	5.60, (brs)	5.72, (d, *J* = 1.8)	– 0.12
3-H-sugar C	5.61, (dd, *J* = 3.0, 9.5)	5.06, (dd, *J* = 2.5, 9.8)	0.55
3-H-sugar B	5.65, (dd, *J* = 3.0, 9.5)	5.69, (dd, *J* = 3.2, 9.1)	– 0.03
4-H-sugar A	5.67, (dd, *J* = 9.5, 9.5)	5.81, (dd, *J* = 9.5, 9.5)	– 0.14
1-H-sugar B	5.80, (brs)	5.68, (d, *J* = 1.8)	0.12
1-H-sugar C	6.29, (brs)	6.10, (d, *J* = 2.2)	0.19

i) Reported chemical shifts and coupling constants for **1** (concentration of **1** and the ratio of Pyridine-d_5/D_2O is not known, ^{1}H NMR was acquired in 500 MHz spectrometer); ii) ^{1}H NMR was recorded in 600 MHz spectrometer by dissolving 7.5 mg of **1** in 0.5 mL Pyridine-d_5; iii) Chemical shift difference which are ($\Delta \geq 0.1$) ppm are highlighted in red.

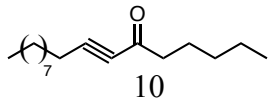
Comparison of limited reported ^{13}C chemical shifts and our completely assigned chemical shifts in Pyridine-d_5:



Position	Natural[i] **1**	Synthetic[ii] **1**	Δ[iii] (**1**$_{syn}$ – **1**$_{nat}$)
C-6, C=O-iba	176.5	176.7	0.2
C-8, C=O-iba	175.7	176.4	0.7
C-10, C=O-aglycon	174.1	173.8	– 0.3
C-1, sugar A	103.0	103.3	0.3
C-1, sugar B	102.3	103.0	0.7
C-1, sugar C	102.1	101.8	0.2
C-1, sugar D	99.8	100.2	– 0.4

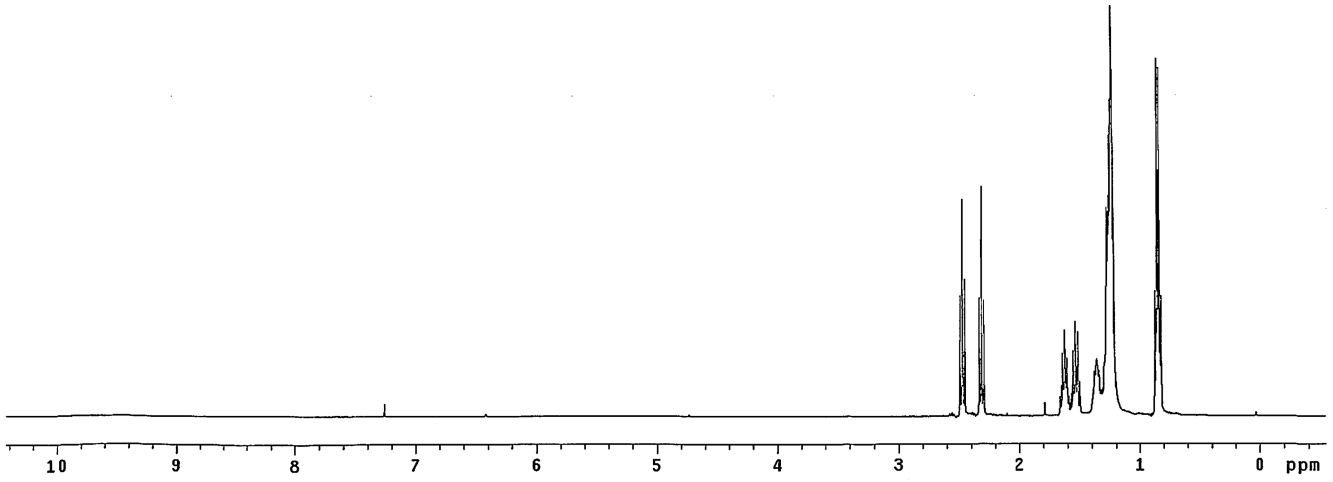
i) Limited reported ^{13}C NMR shifts in Pyridine-d_5 in descending order recorded in 125 MHz spectrometer; ii) Completely assigned ^{13}C NMR shifts recorded in 150 MHz spectrometer; iii) chemical shift difference ($\Delta \geq 0.5$) are highlighted in red.

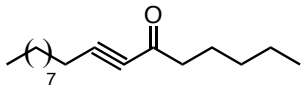
Section C: ^{1}H, ^{13}C NMR Spectra and Correlation Studies



10

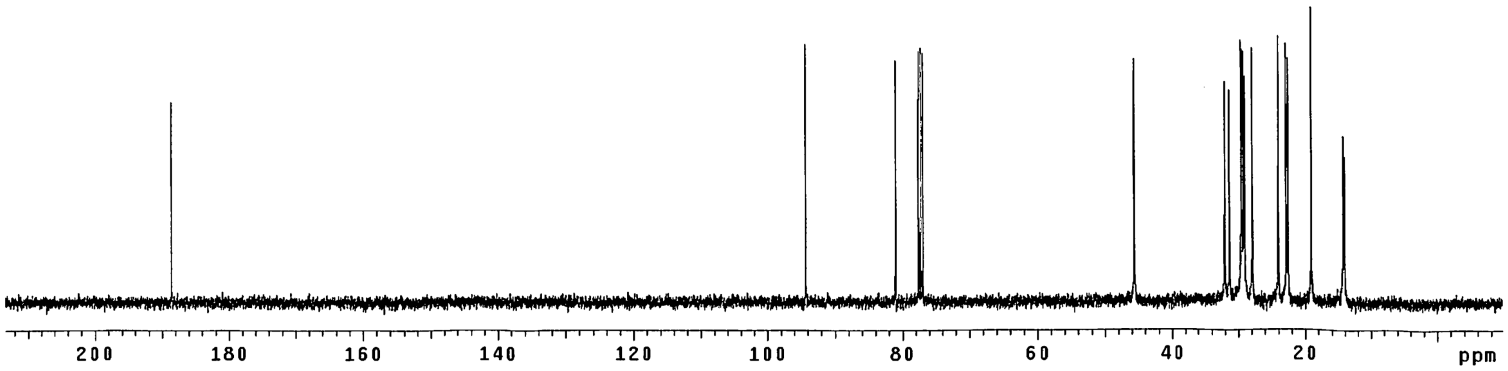
^{1}H NMR ($CDCl_3$, 400 MHz)

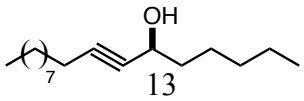




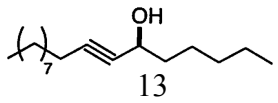
10

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



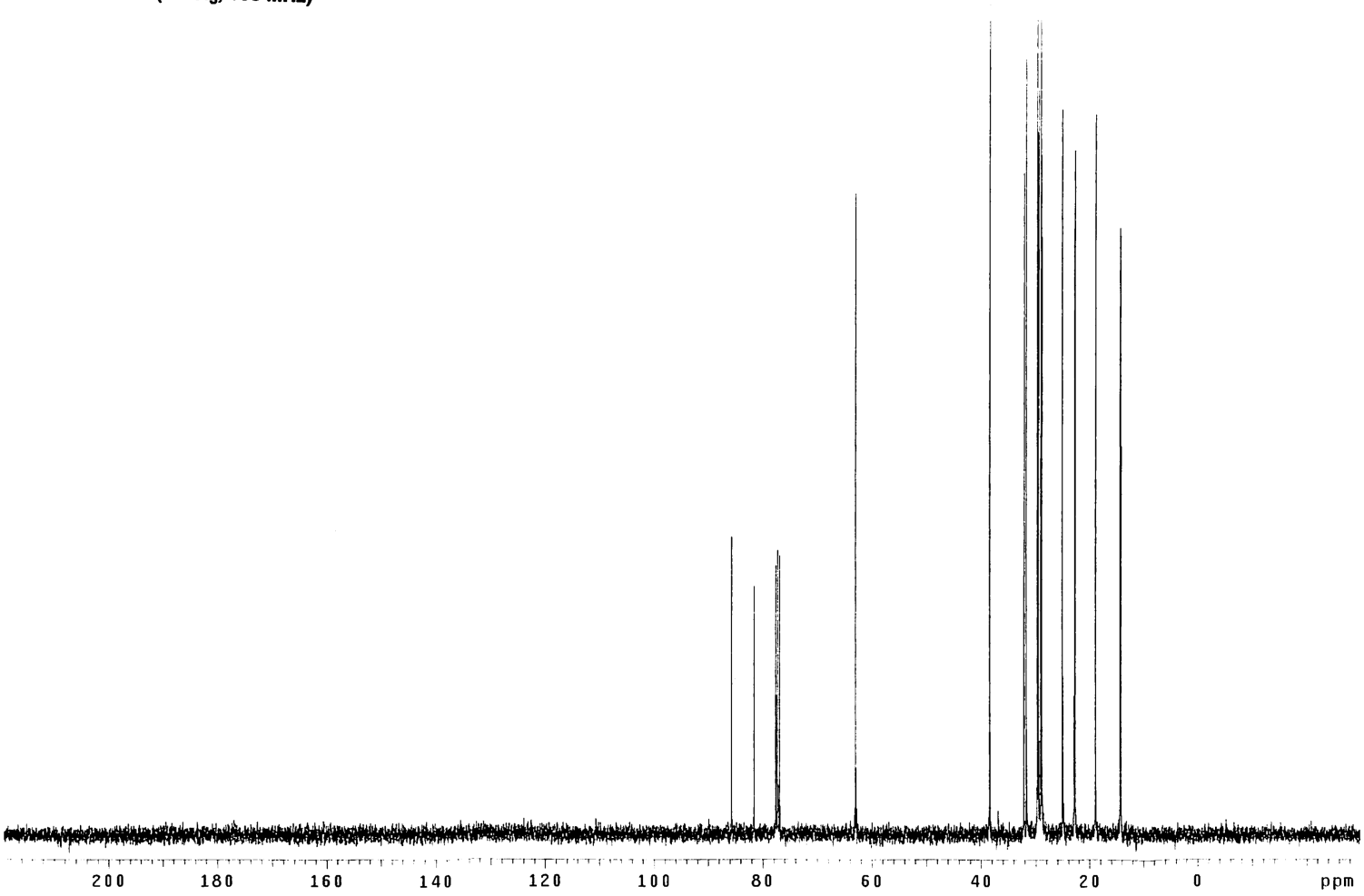


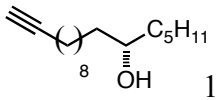
^{1}H NMR ($CDCl_3$, 400 MHz)



13

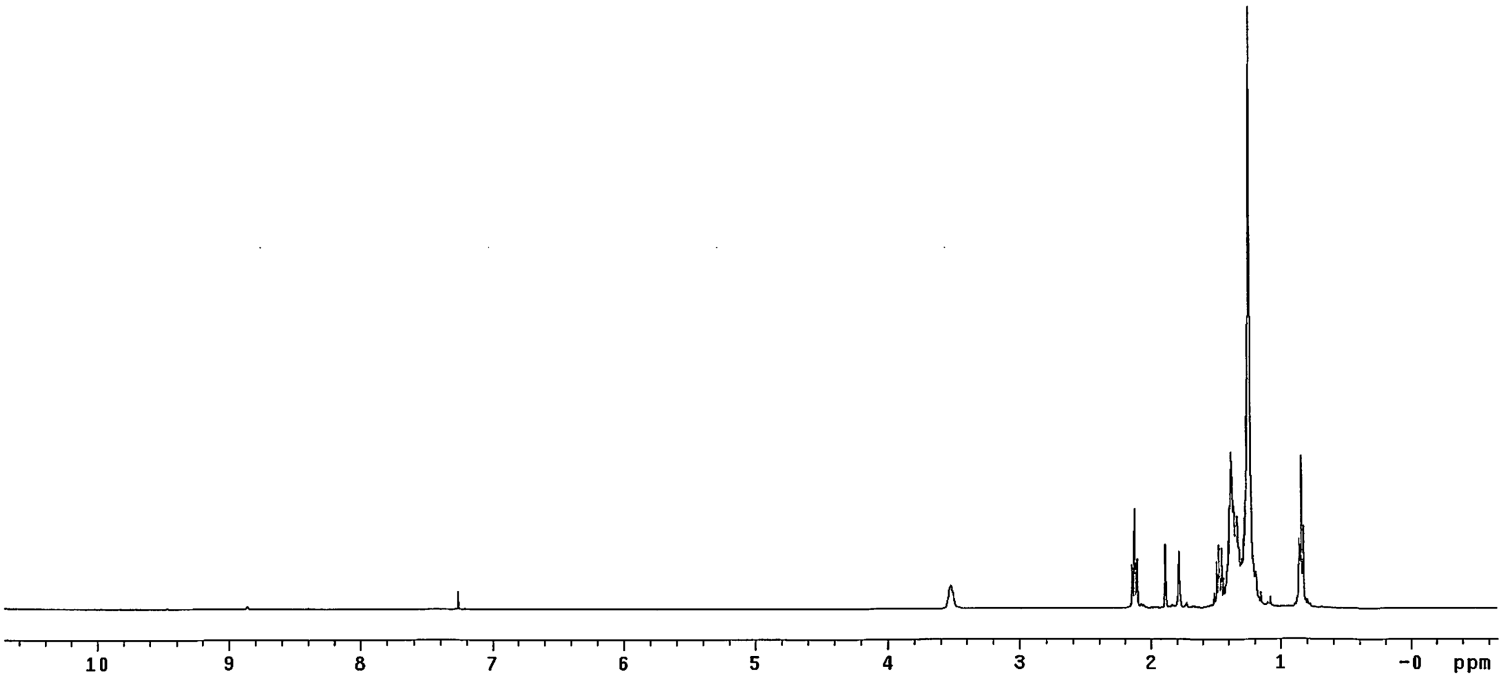
^{13}C NMR ($CDCl_3$, 100 MHz)

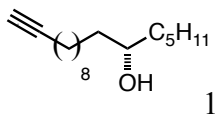




13a

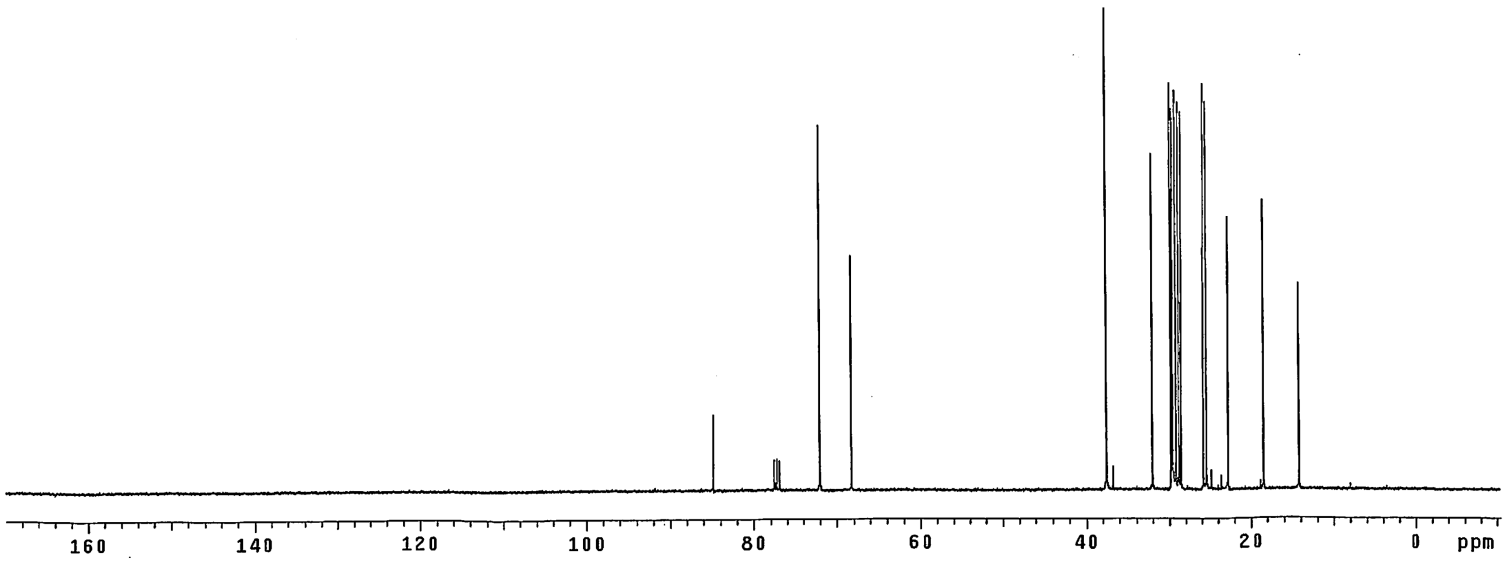
^{1}H NMR ($CDCl_3$, 400 MHz)

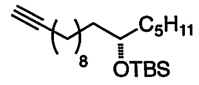




13a

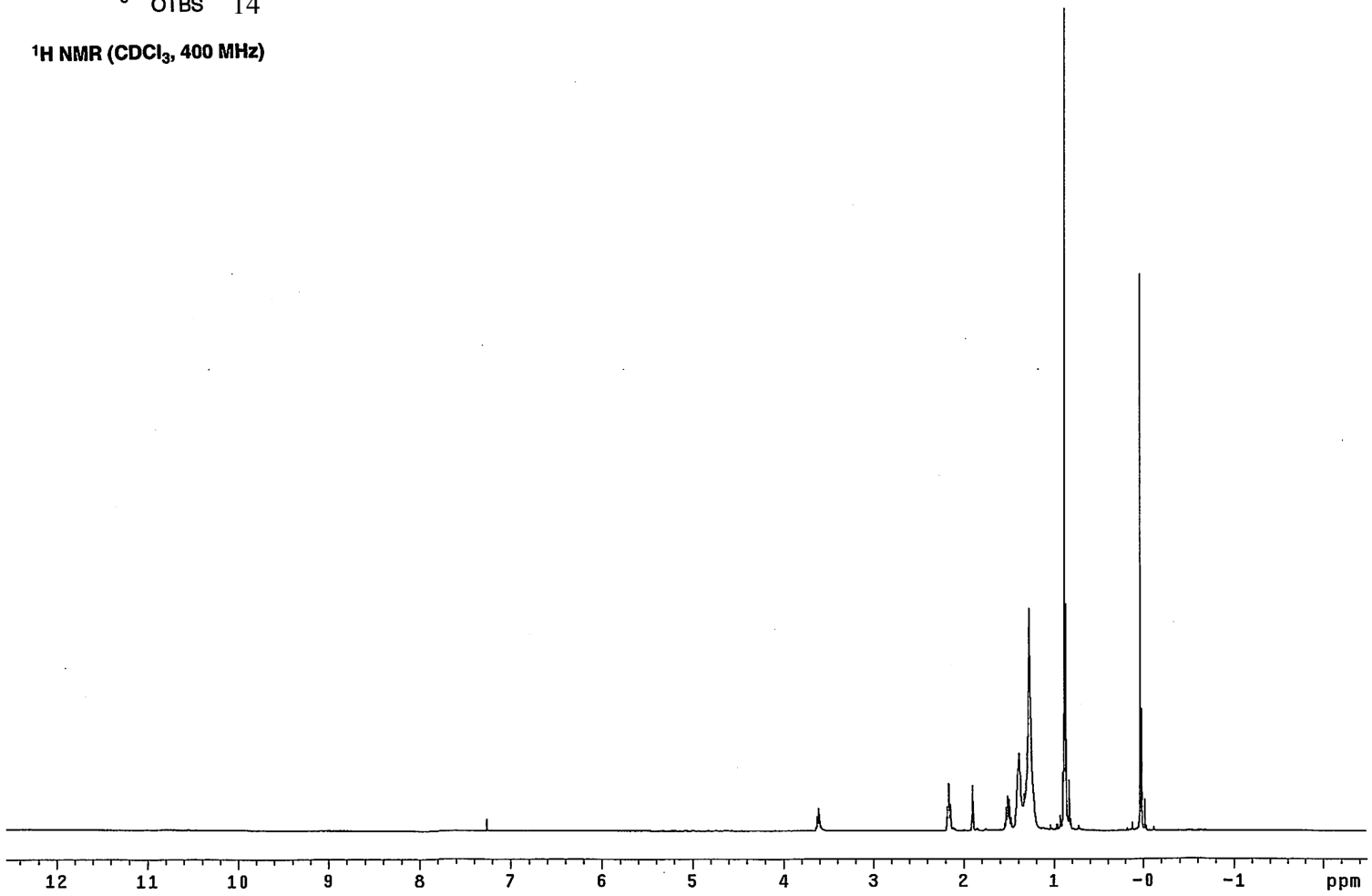
^{13}C NMR ($CDCl_3$, 100 MHz)

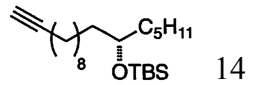




14

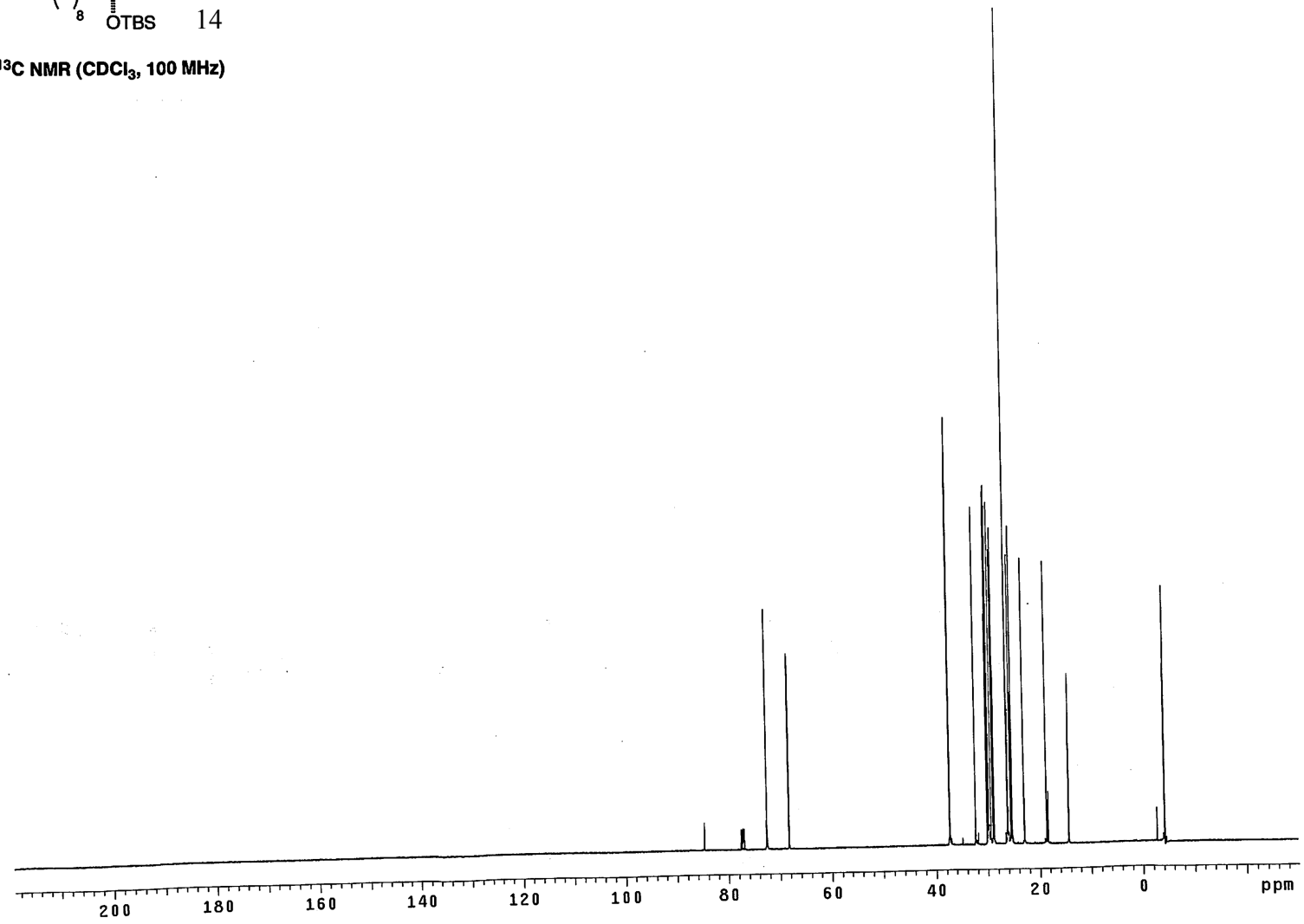
^{1}H NMR ($CDCl_3$, 400 MHz)

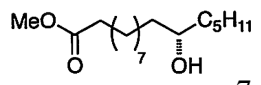




14

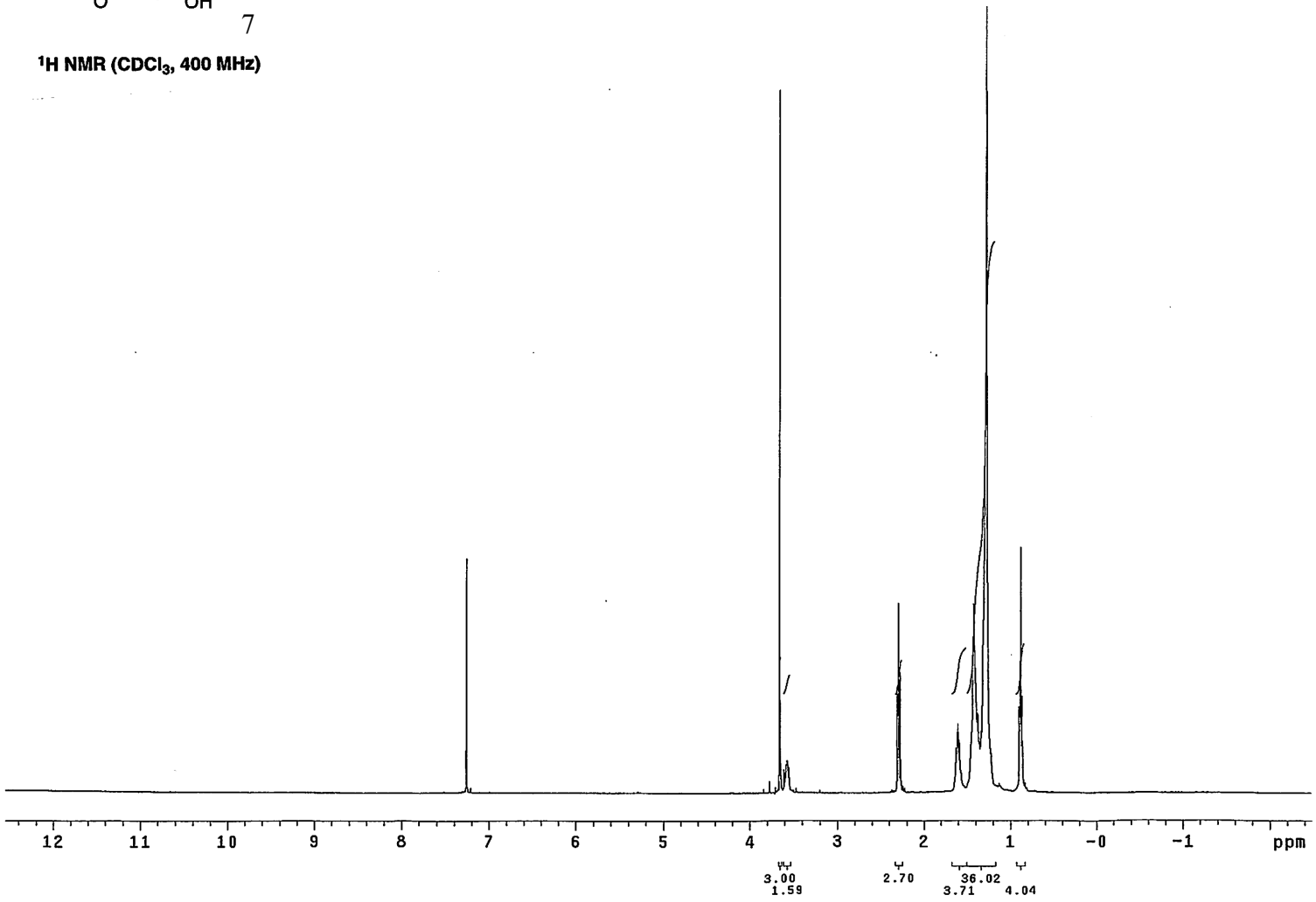
^{13}C NMR ($CDCl_3$, 100 MHz)

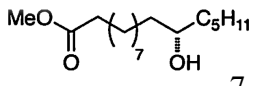




7

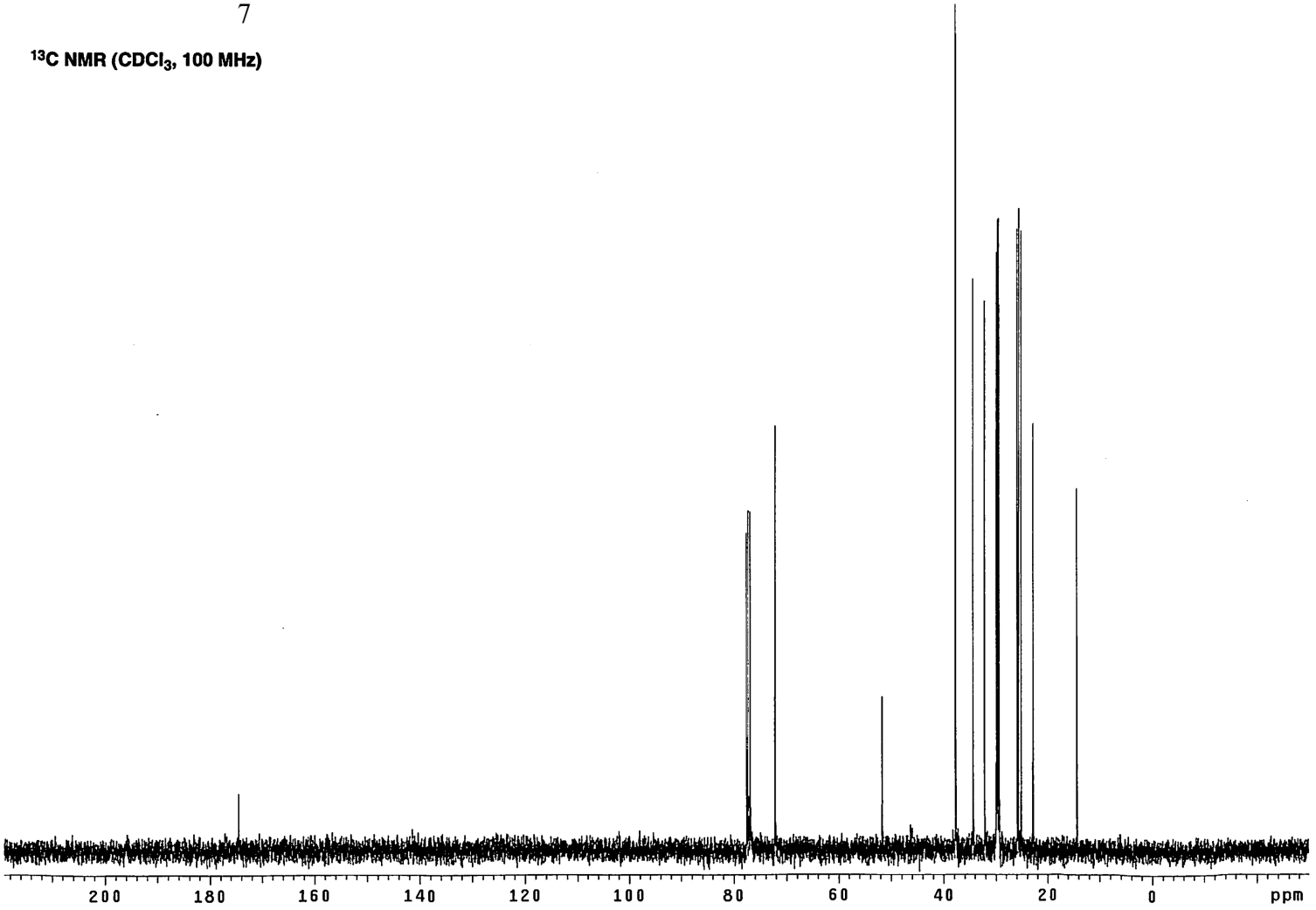
^{1}H NMR ($CDCl_3$, 400 MHz)

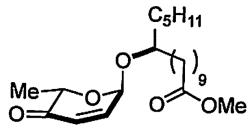




7

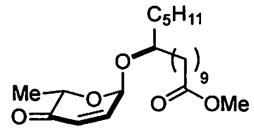
^{13}C NMR ($CDCl_3$, 100 MHz)





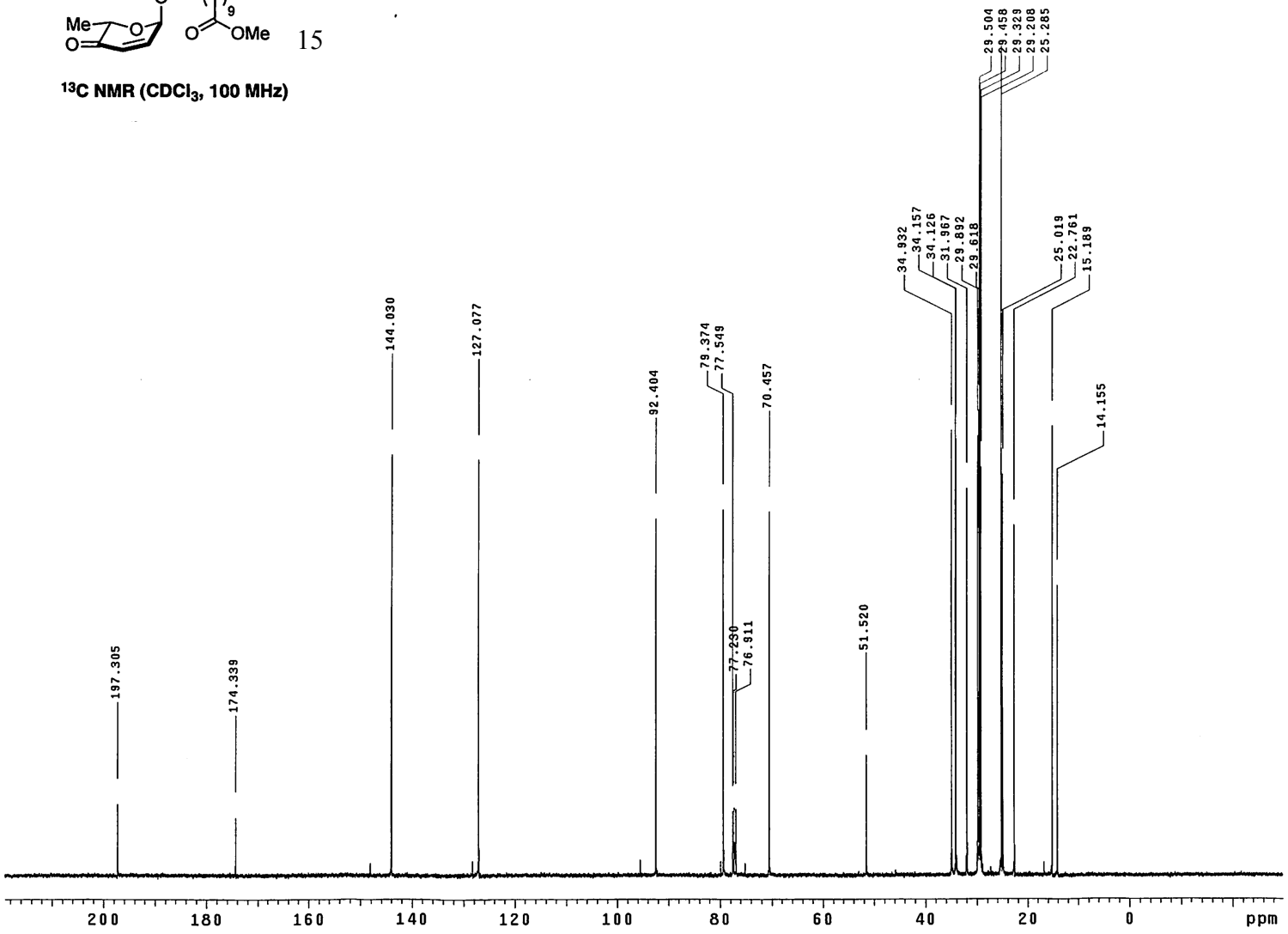
15

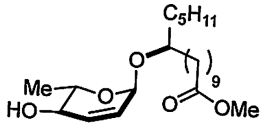
^{1}H NMR ($CDCl_3$, 400 MHz)



15

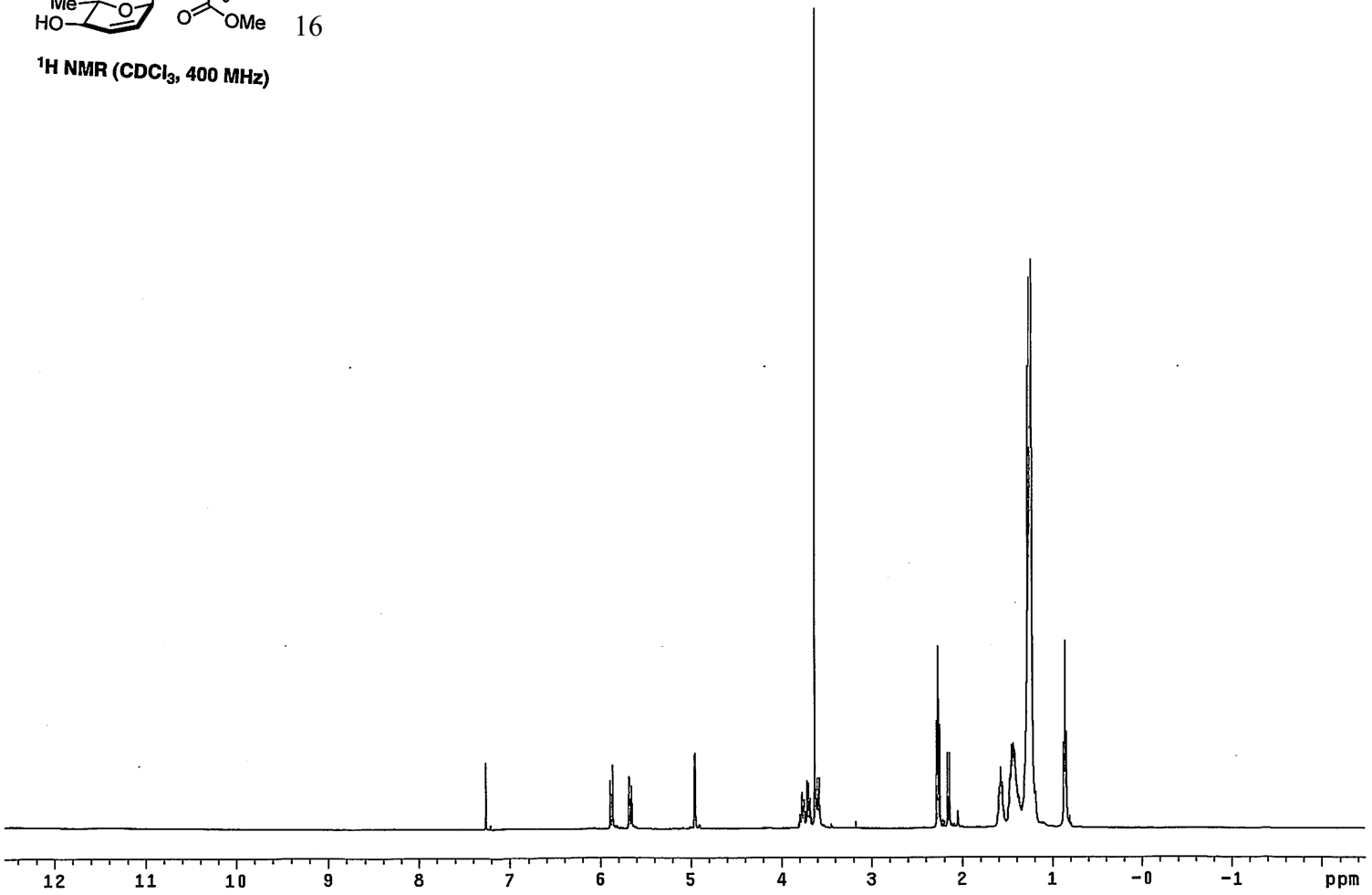
^{13}C NMR ($CDCl_3$, 100 MHz)

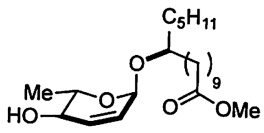




16

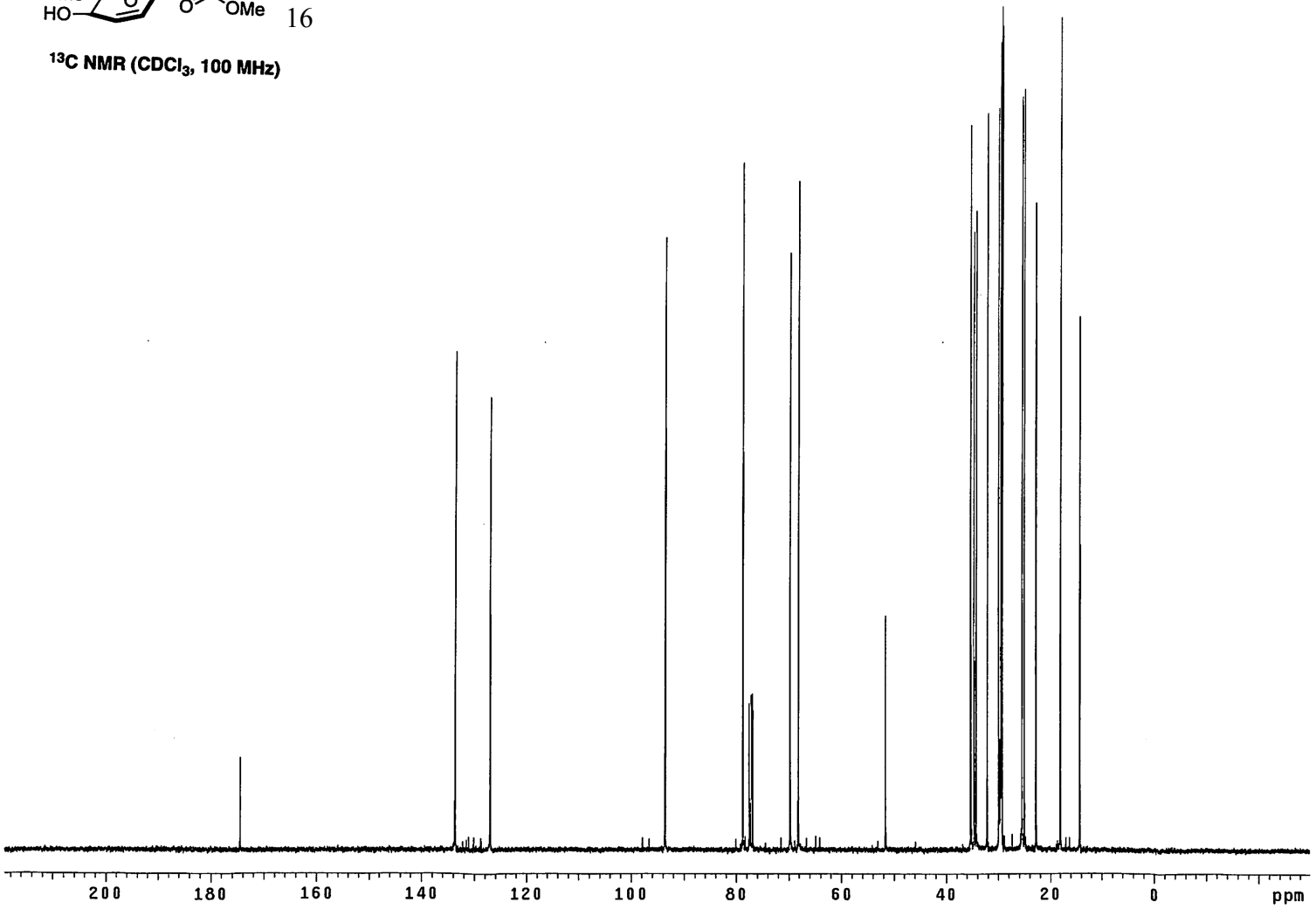
^{1}H NMR ($CDCl_3$, 400 MHz)

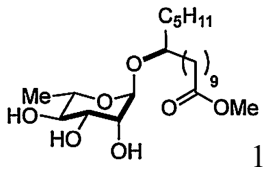




16

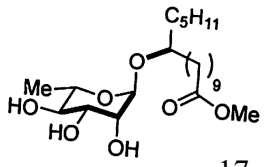
^{13}C NMR ($CDCl_3$, 100 MHz)





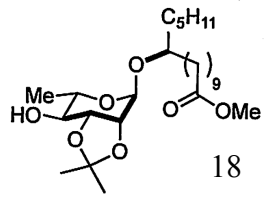
17

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



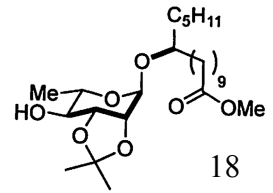
17

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



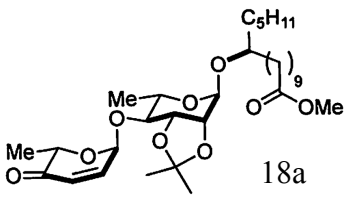
18

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



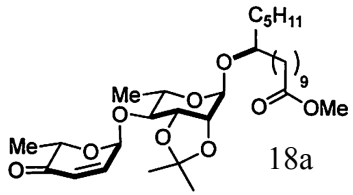
18

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



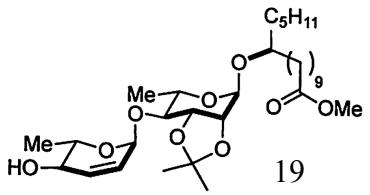
18a

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



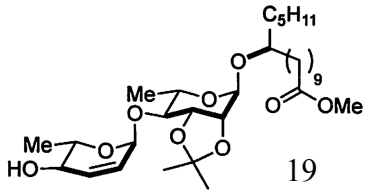
18a

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



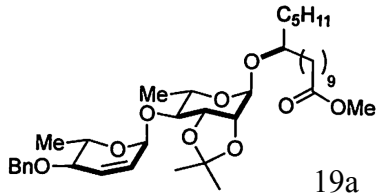
19

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



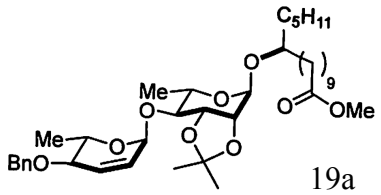
19

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



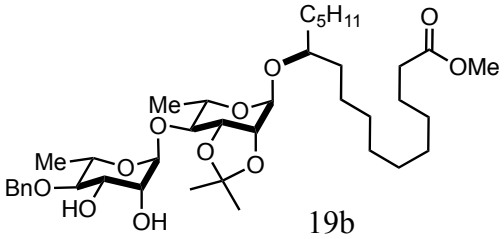
19a

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



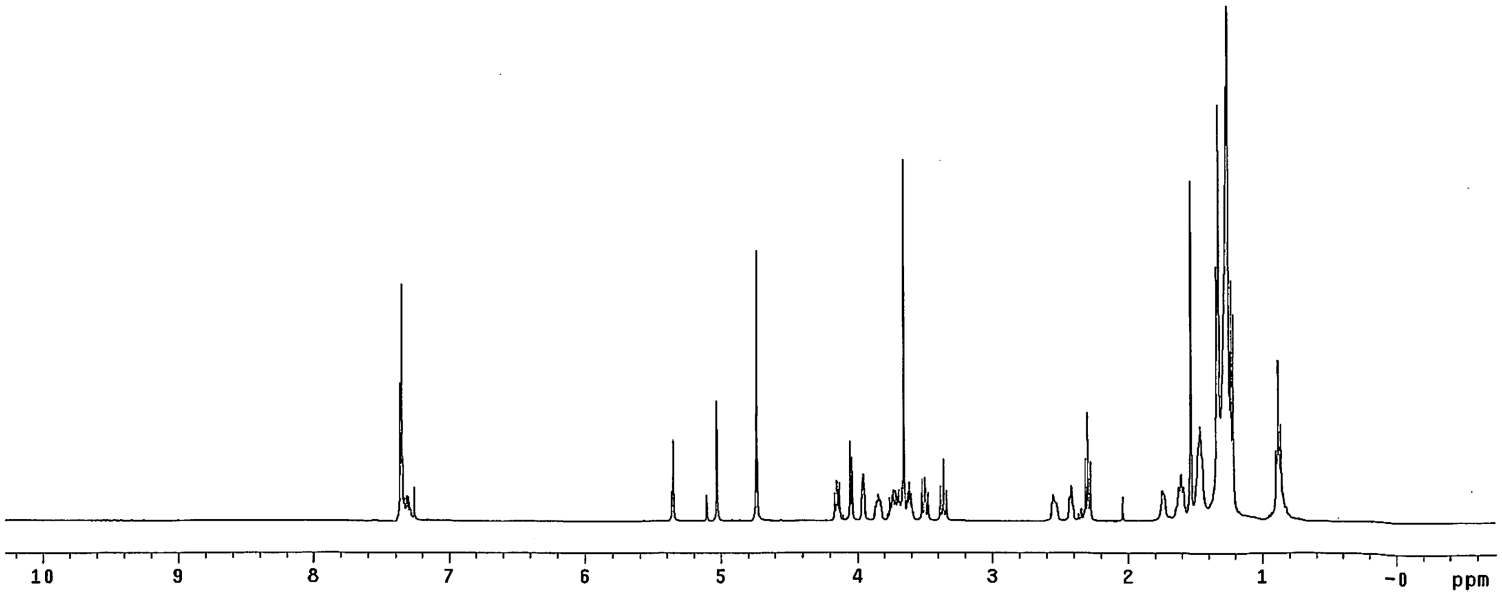
19a

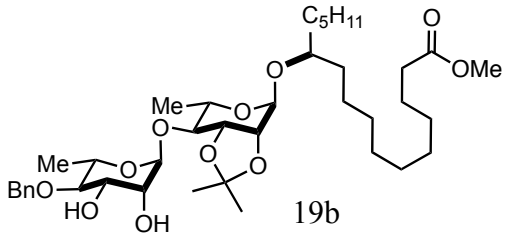
^{13}C NMR ($CDCl_3$, 100 MHz)



19b

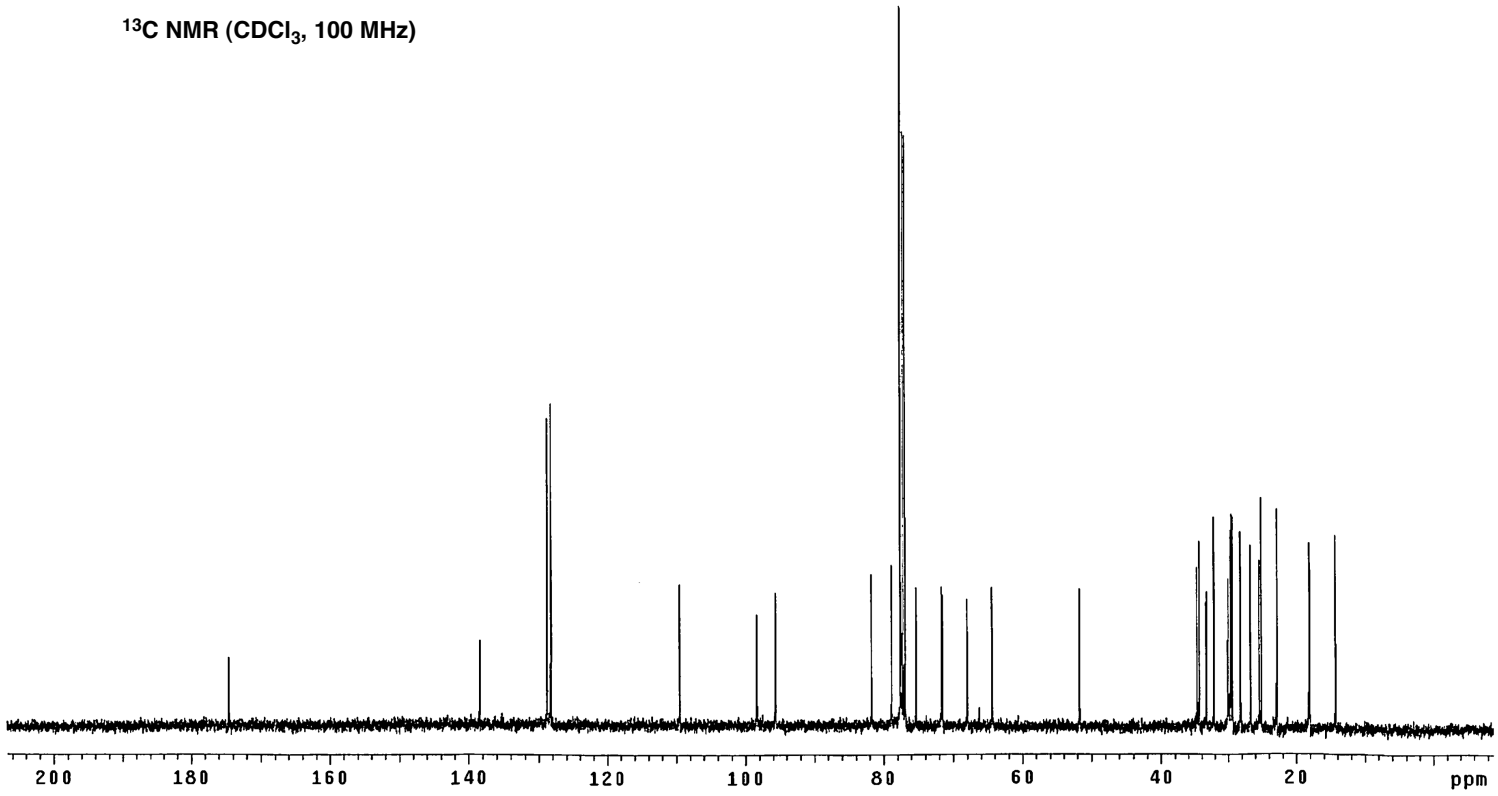
^{1}H NMR ($CDCl_3$, 400 MHz)

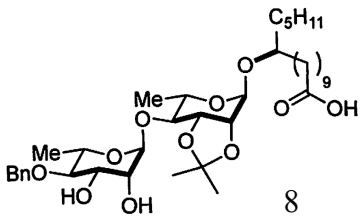




19b

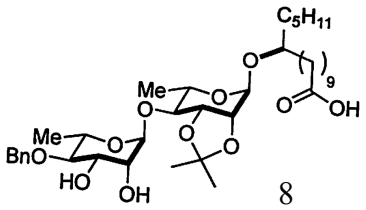
^{13}C NMR ($CDCl_3$, 100 MHz)





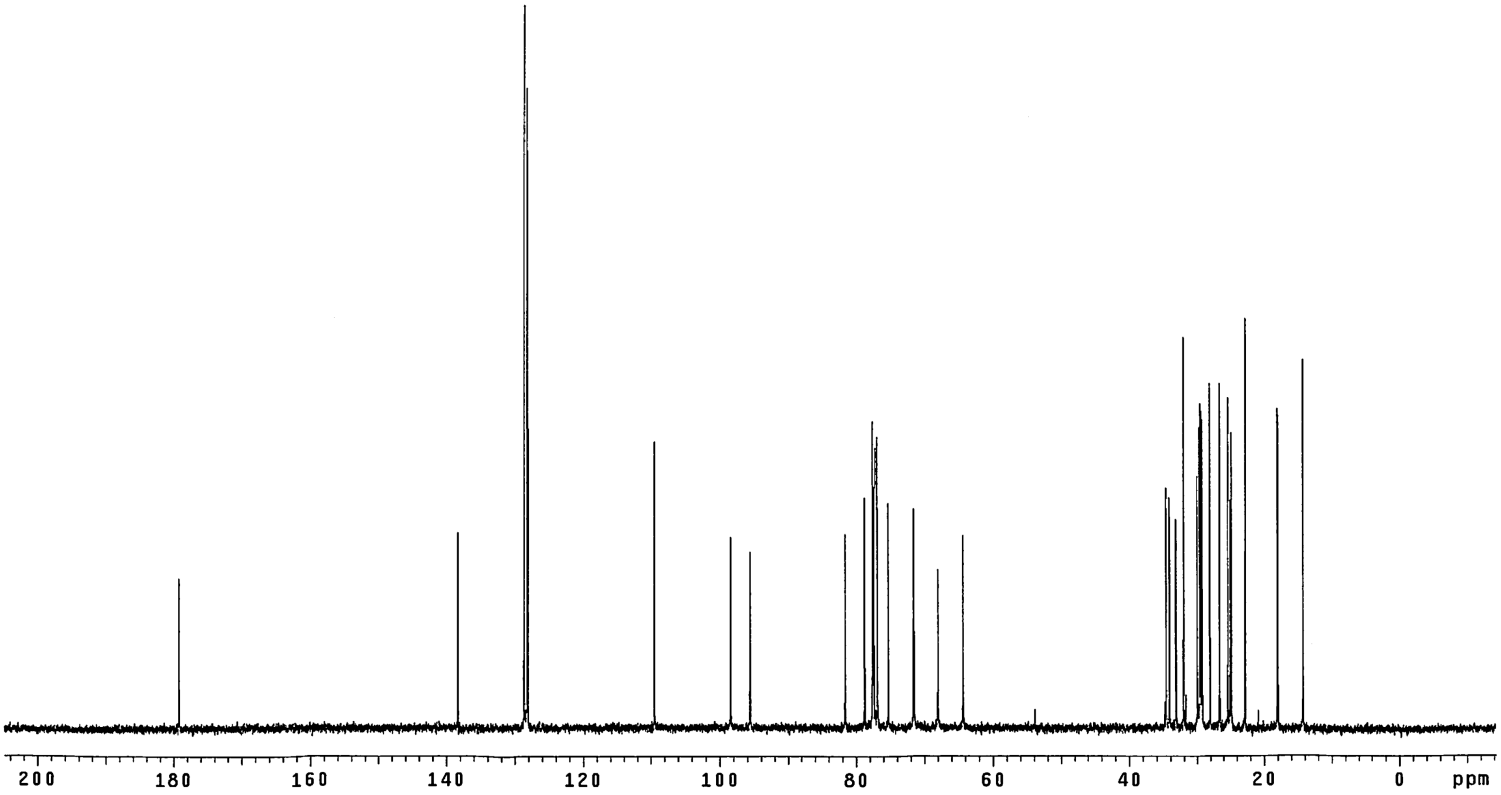
8

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

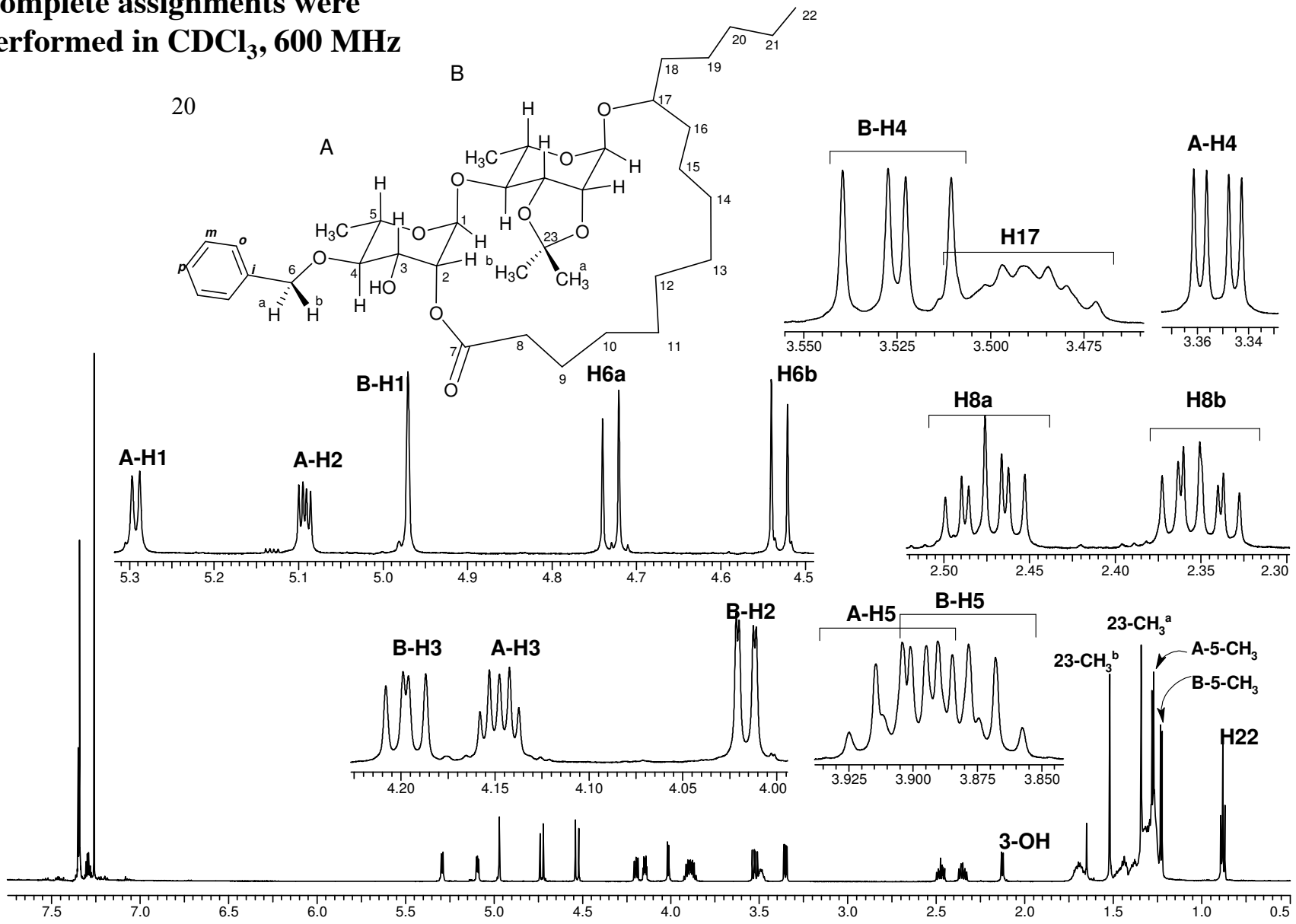


8

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

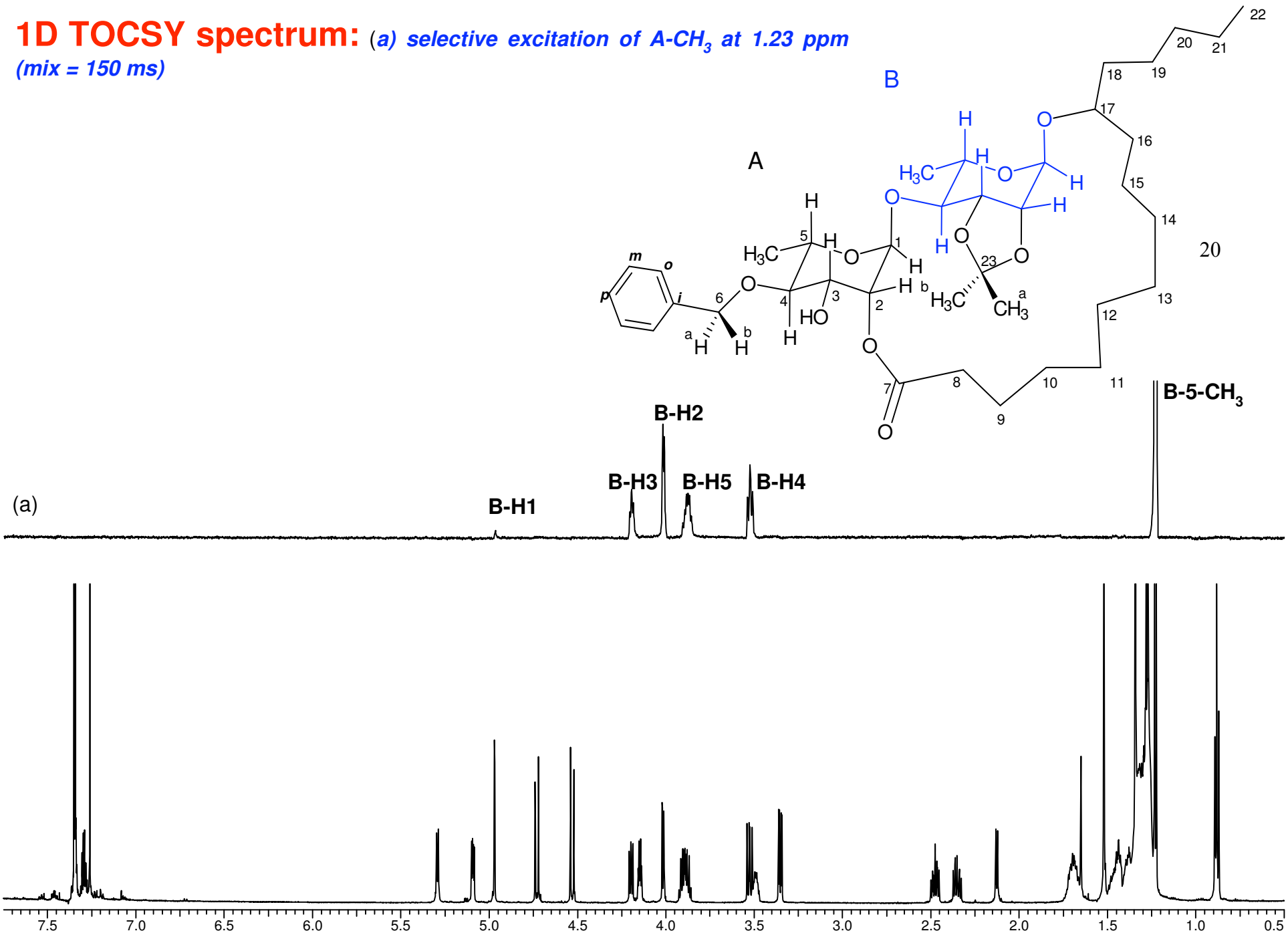


Complete assignments were performed in $CDCl_3$, 600 MHz



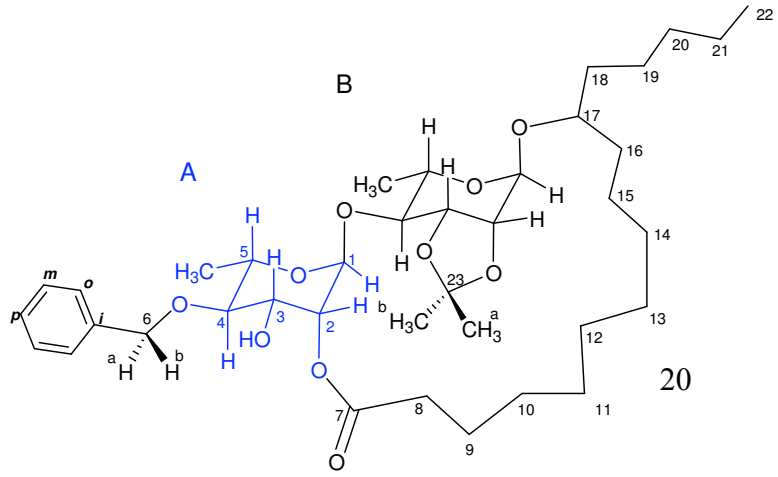
1D TOCSY spectrum: (*a) selective excitation of A-CH$_3$ at 1.23 ppm*

(mix = 150 ms)



1D TOCSY spectra: (*a) selective excitation of A-H2;*

(b)- selective excitation of A-CH_3 at 1.28 ppm (mix = 150 ms)



(a)

(b)

A-H1

A-H2

A-H3

A-H4

3-OH

OH*

5-CH_3

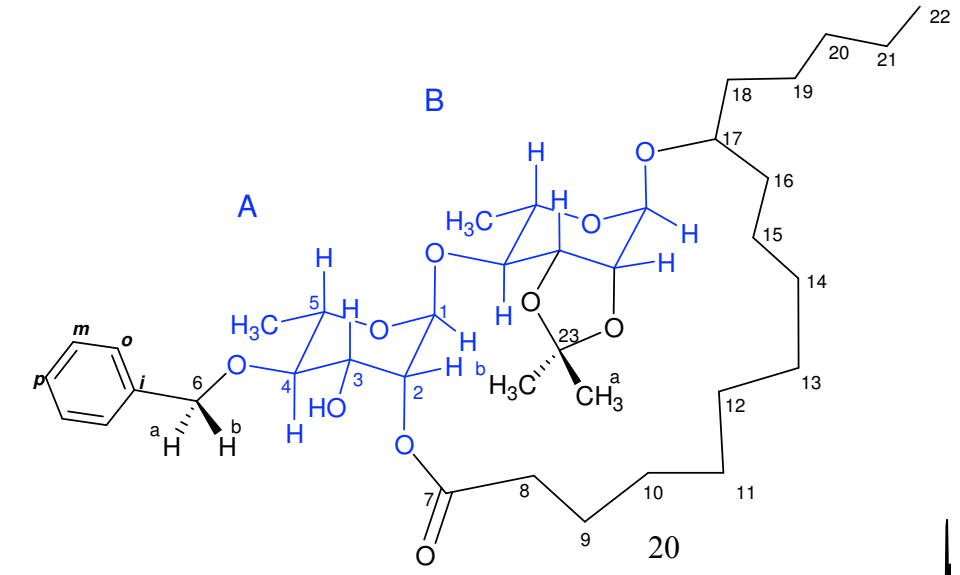
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5

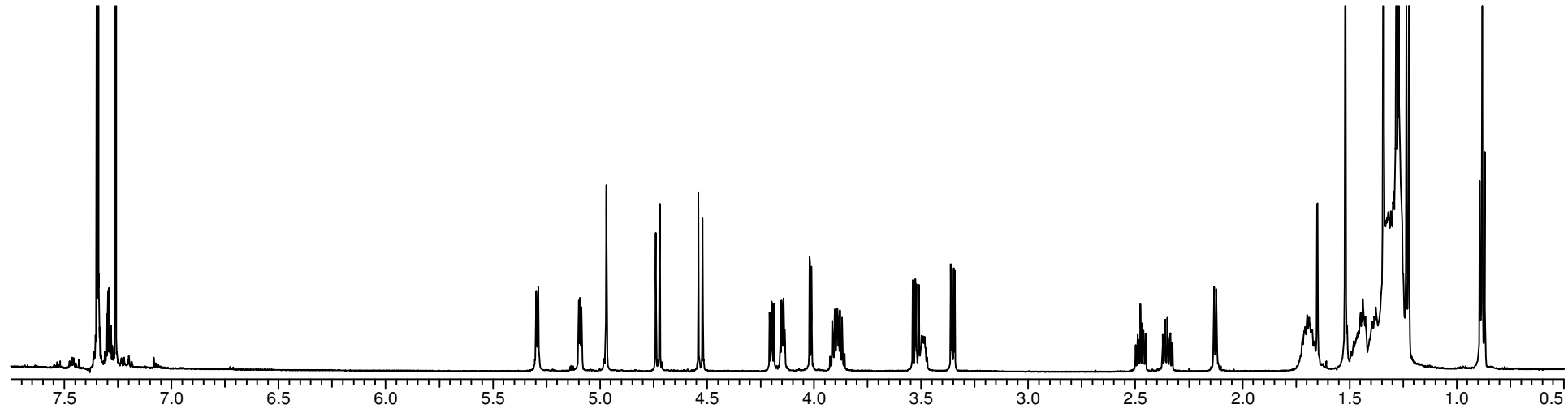
*-H_2O in $CDCl_3$

1D TOCSY spectrum

Spin system identification

Selective excitation of H5 at 3.90 ppm for both A and B-sugar moieties (mix = 150 ms)

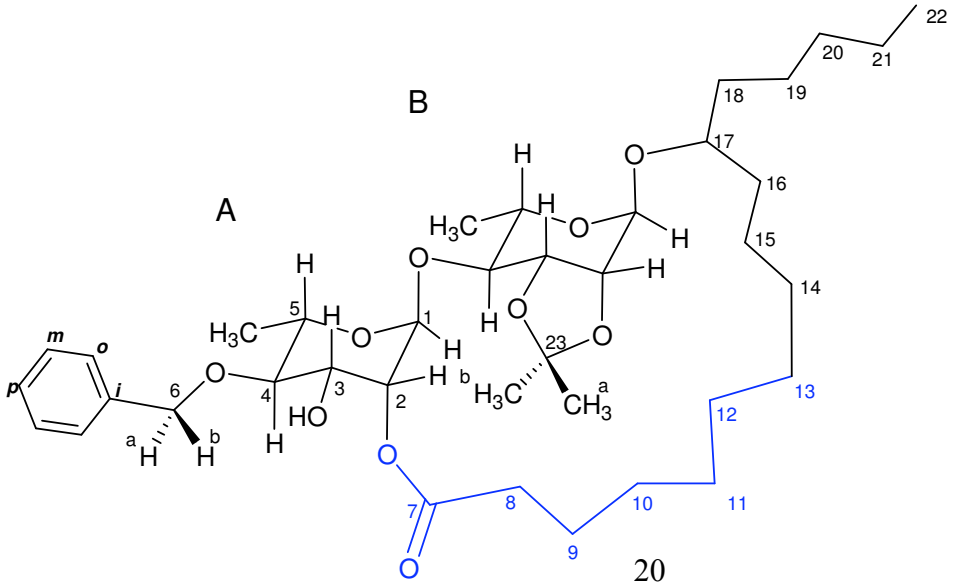




1D TOCSY spectrum

Spin system identification

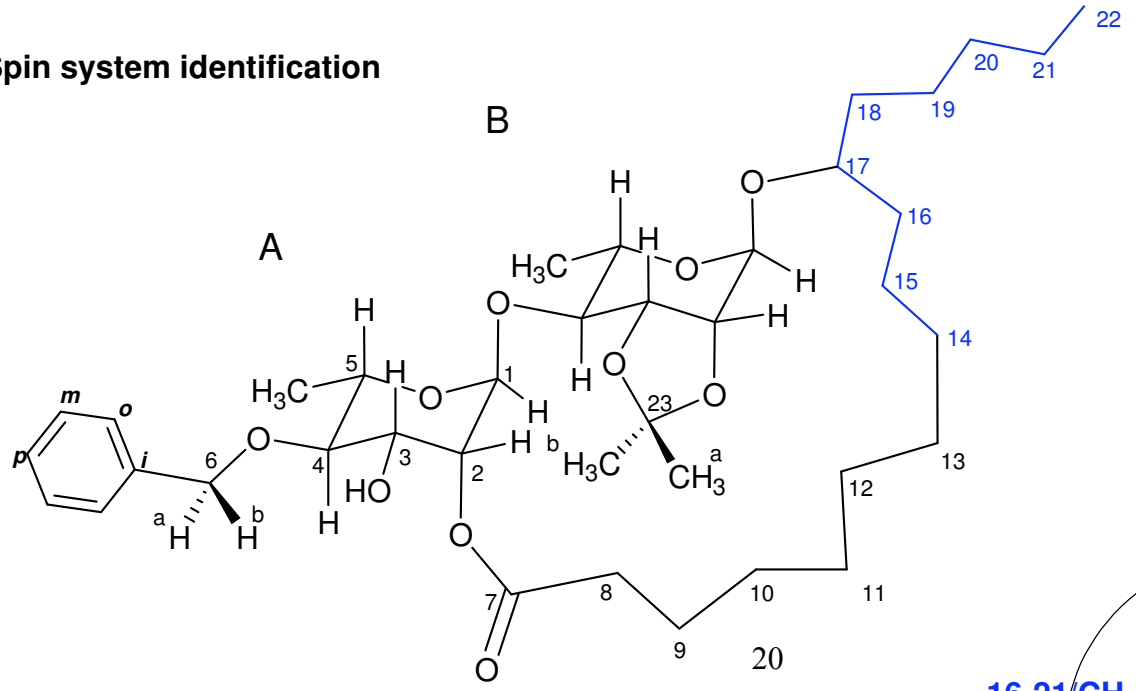
Selective excitation of H8a (mix = 150 ms)



1D TOCSY spectrum

Spin system identification

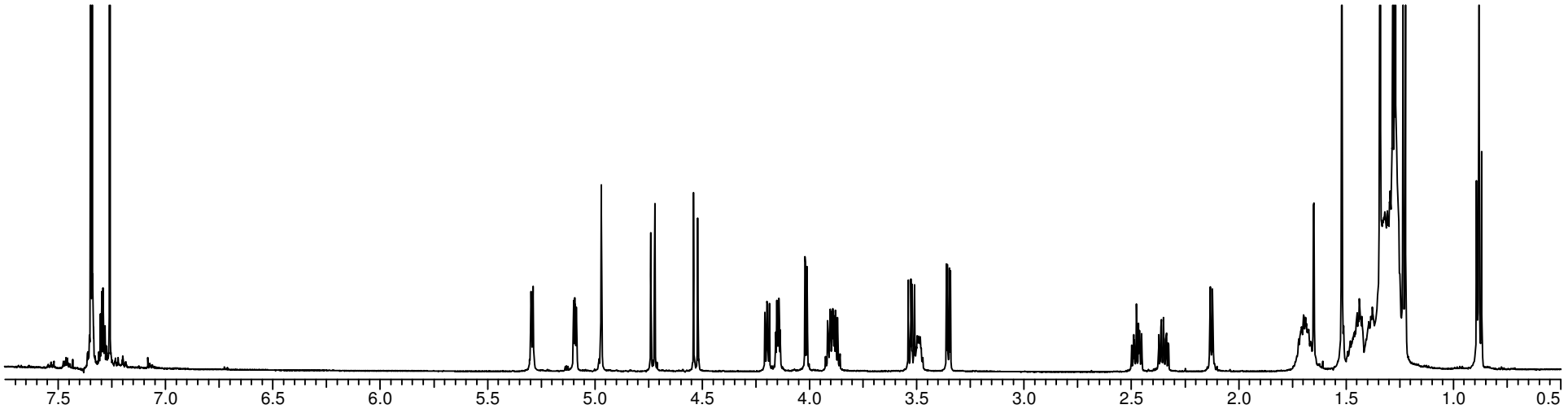
Selective excitation of H22 (mix = 150 ms)



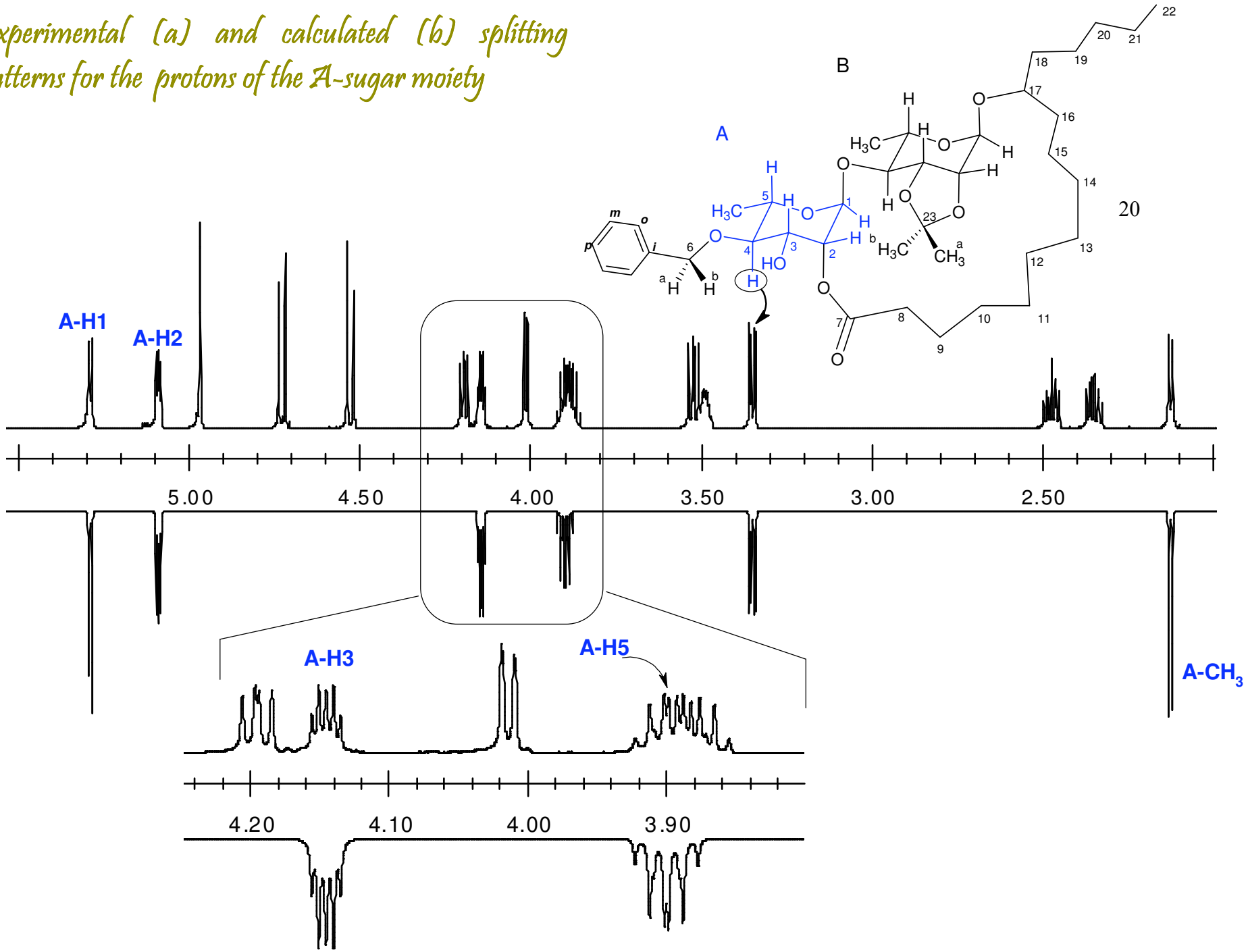
H22

16-21/CH_2's

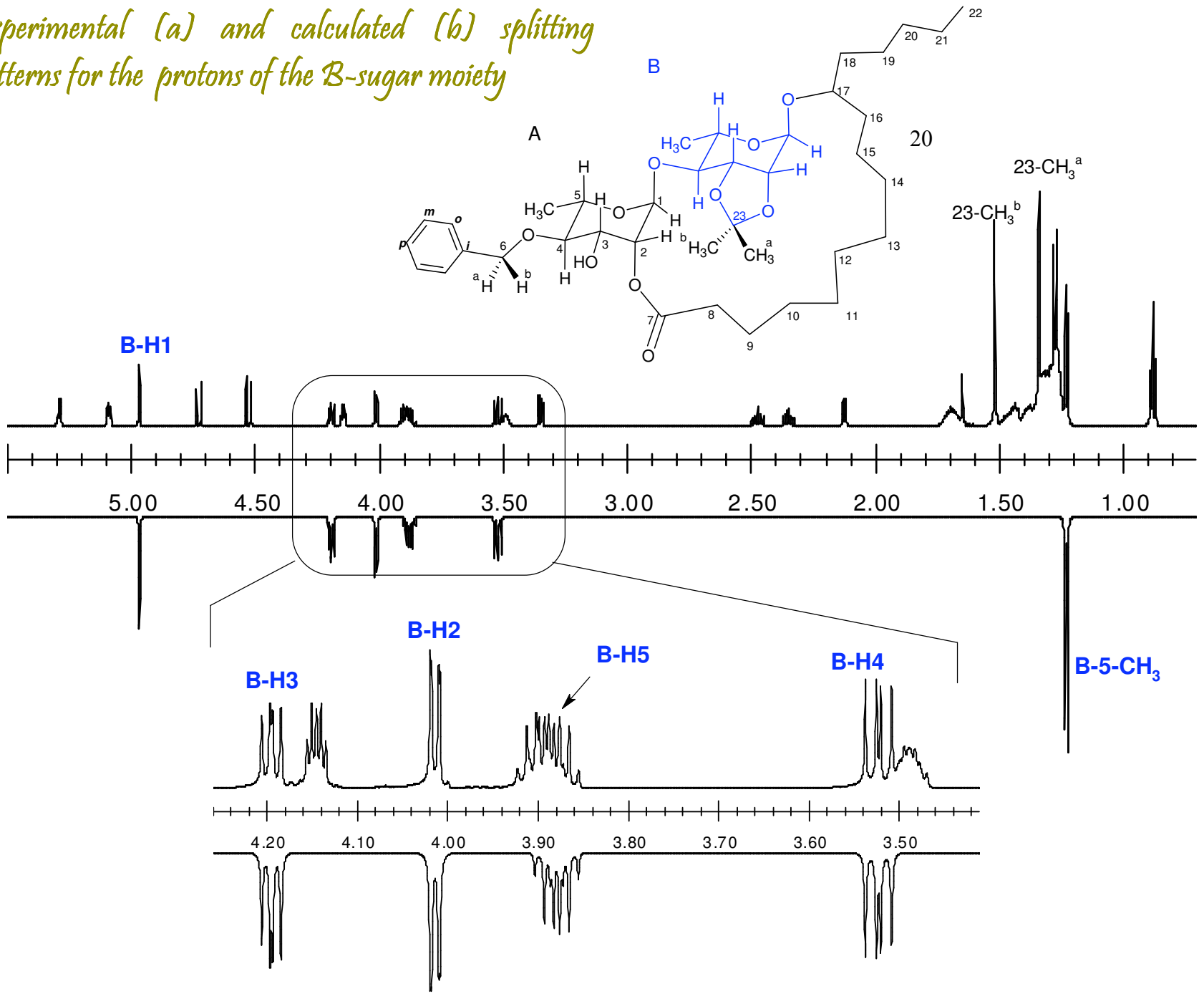
H17



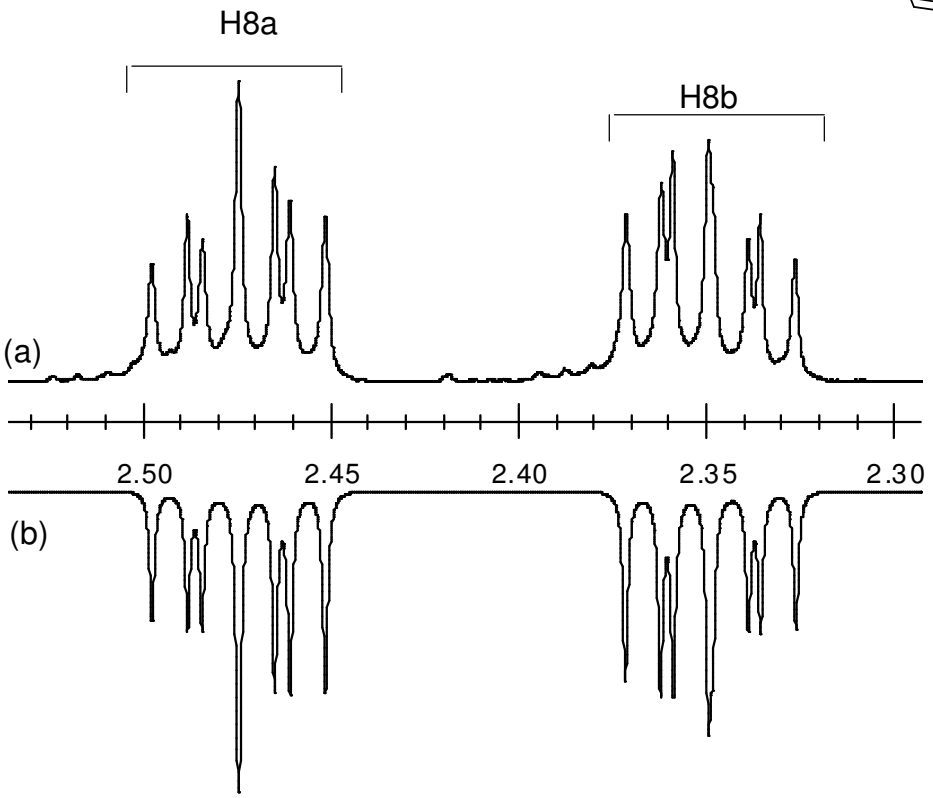
Experimental (a) and calculated (b) splitting patterns for the protons of the A-sugar moiety

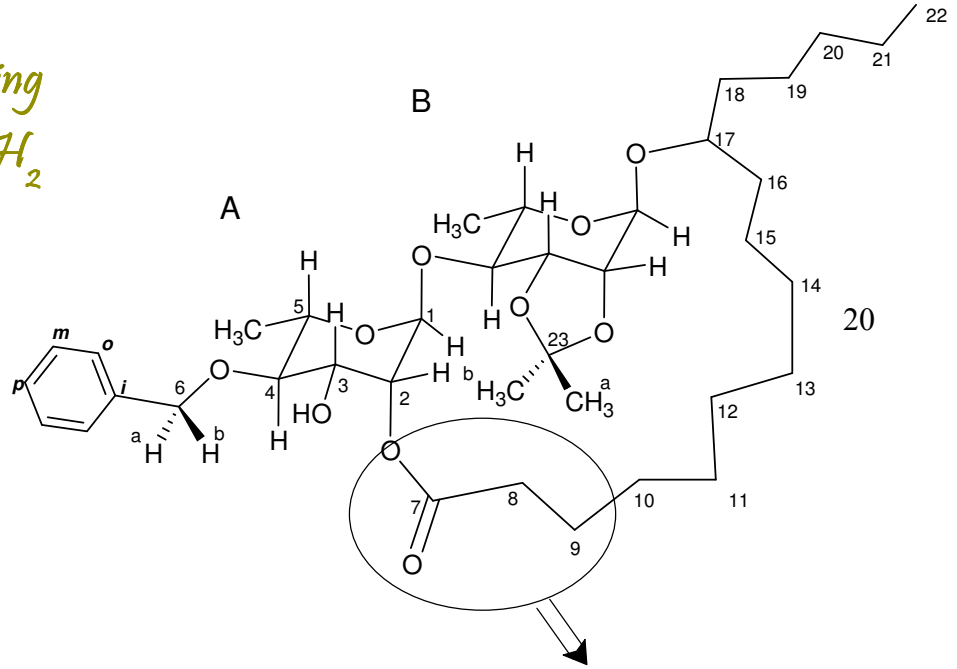


Experimental (a) and calculated (b) splitting patterns for the protons of the B-sugar moiety



Experimental (a) and calculated (b) splitting patterns for the methylene protons of the 8-CH_2 group





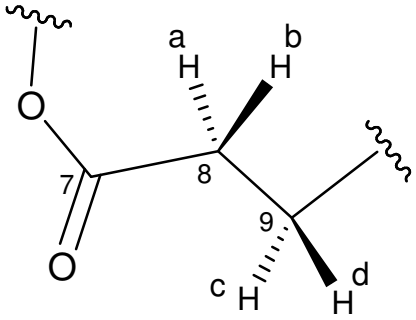
$^{2}J(H8a,H8b) = -13.98$ Hz

$^{3}J(H8a,H9d) = 8.3$ Hz

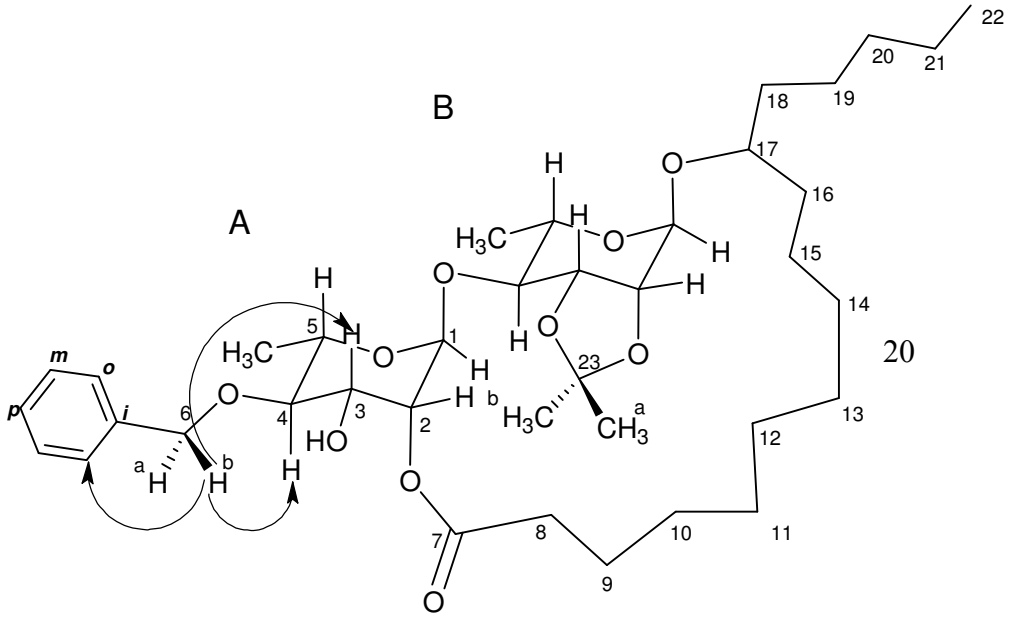
$^{3}J(H8a,H9c) = 5.4$ Hz

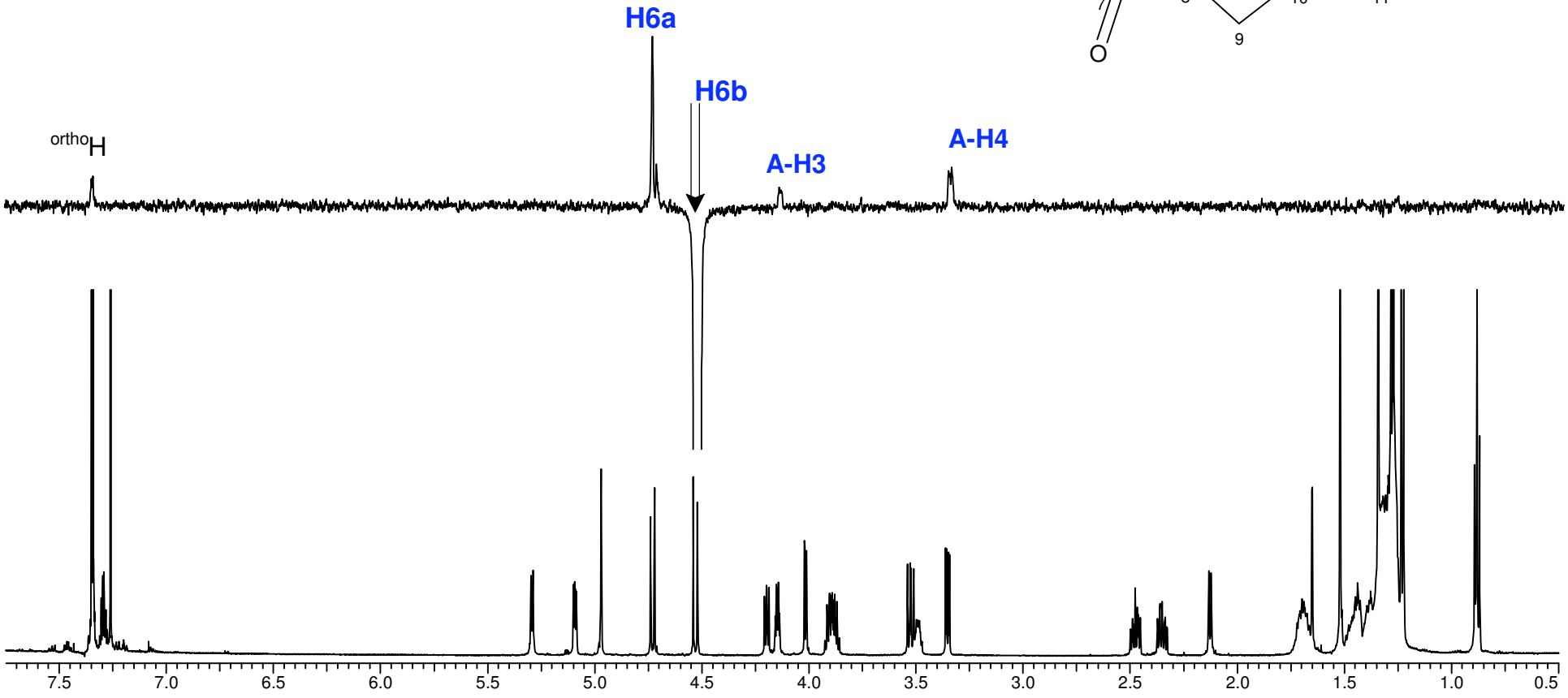
$^{3}J(H8b,H9c) = 7.95$ Hz

$^{3}j(H8b, H9d) = 5.35$ Hz

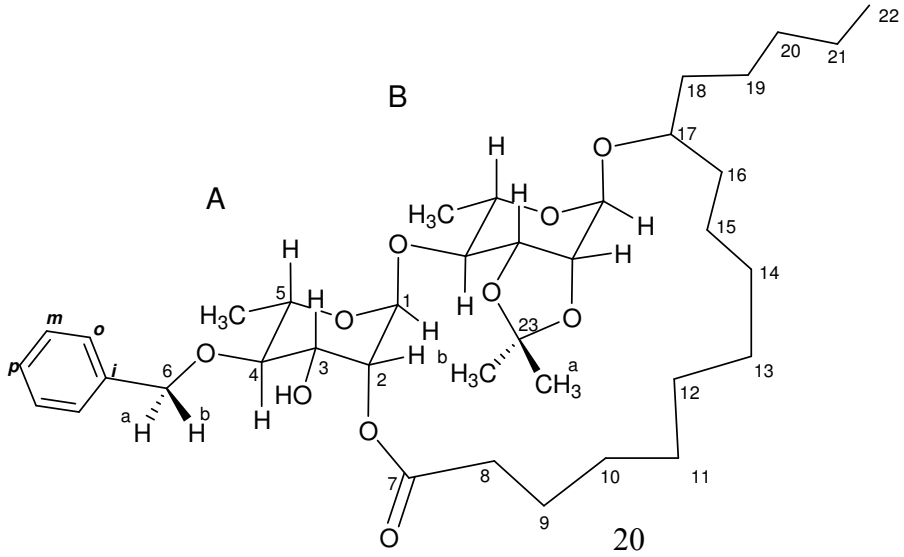


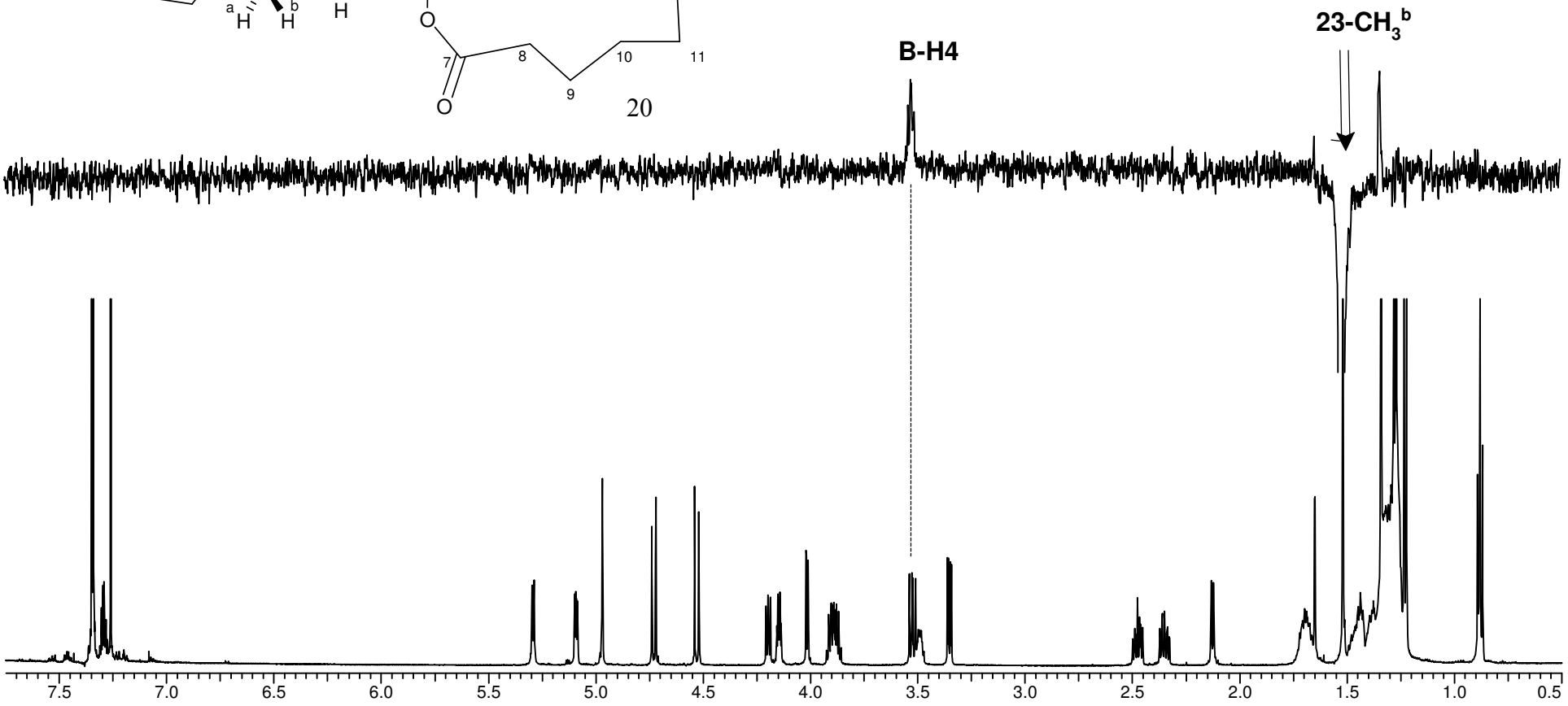
DPFGSENOE spectrum





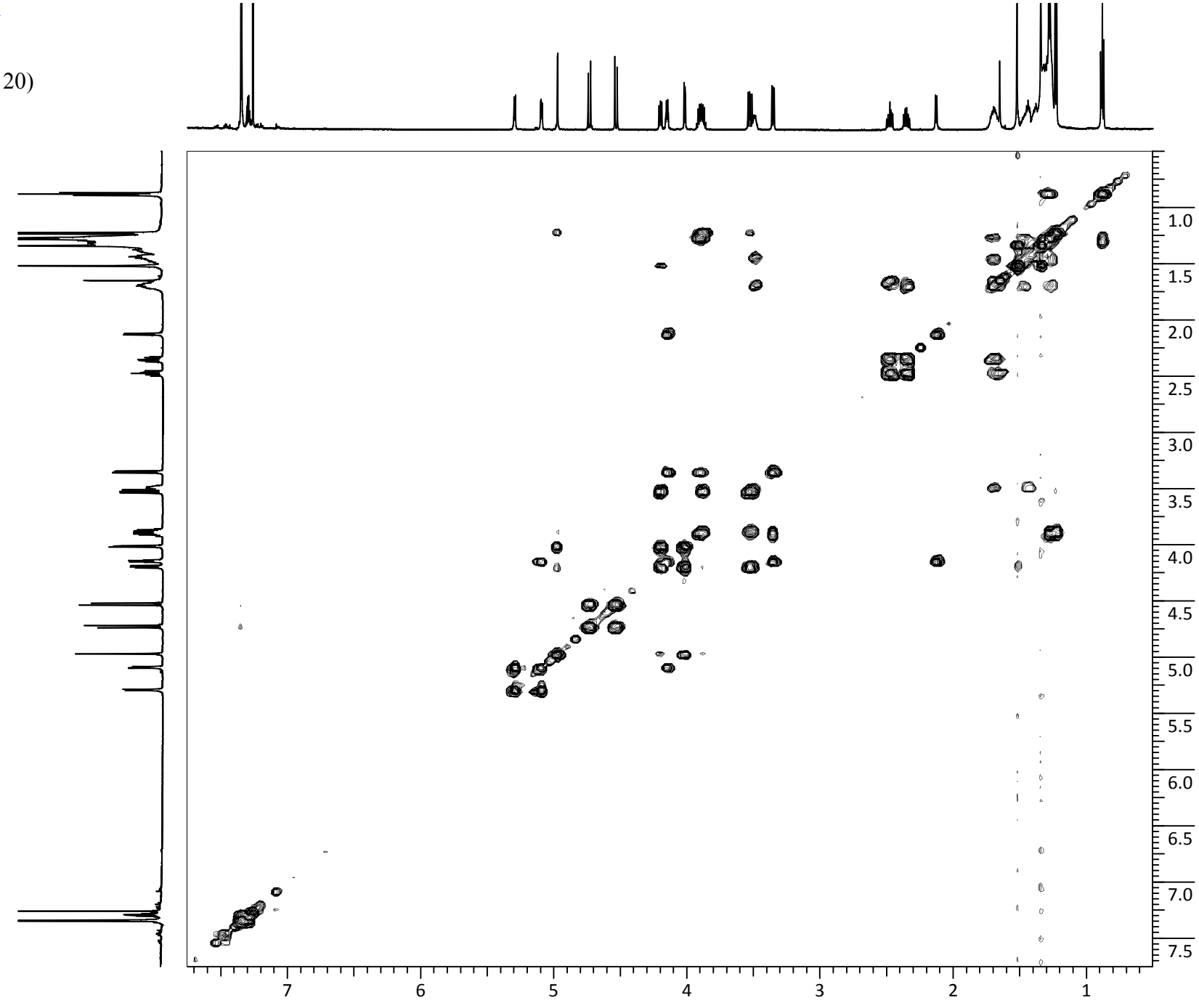
DPFGSENOE spectrum





gCOSY

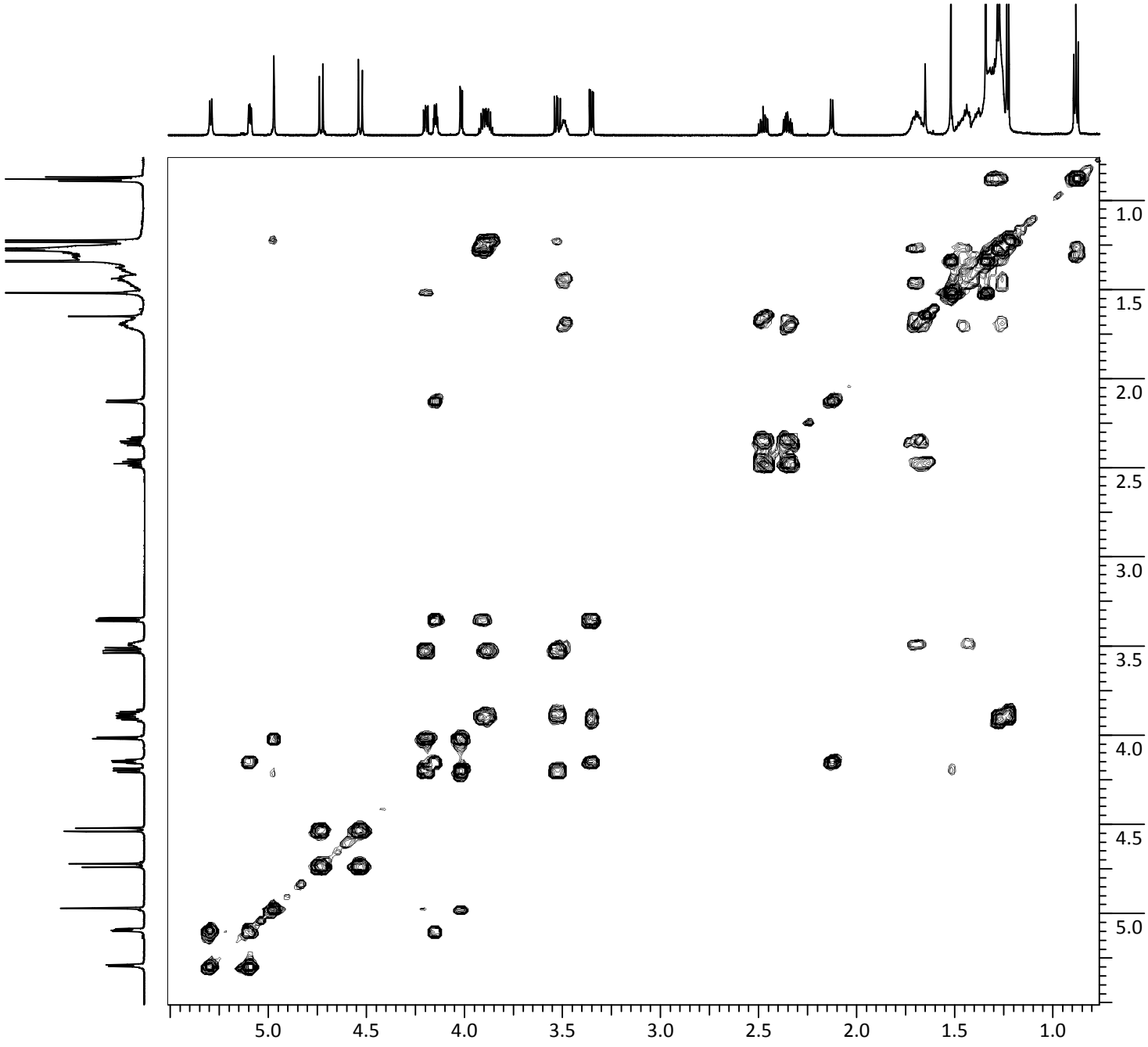
(for compd 20)



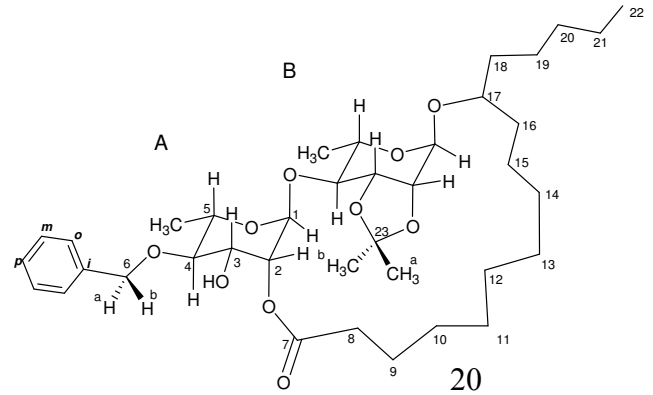
gCOSY

aliphatic region

(for compd 20)



Determining multiplicity of carbon resonances



CH's

DEPT90

CH + CH_3

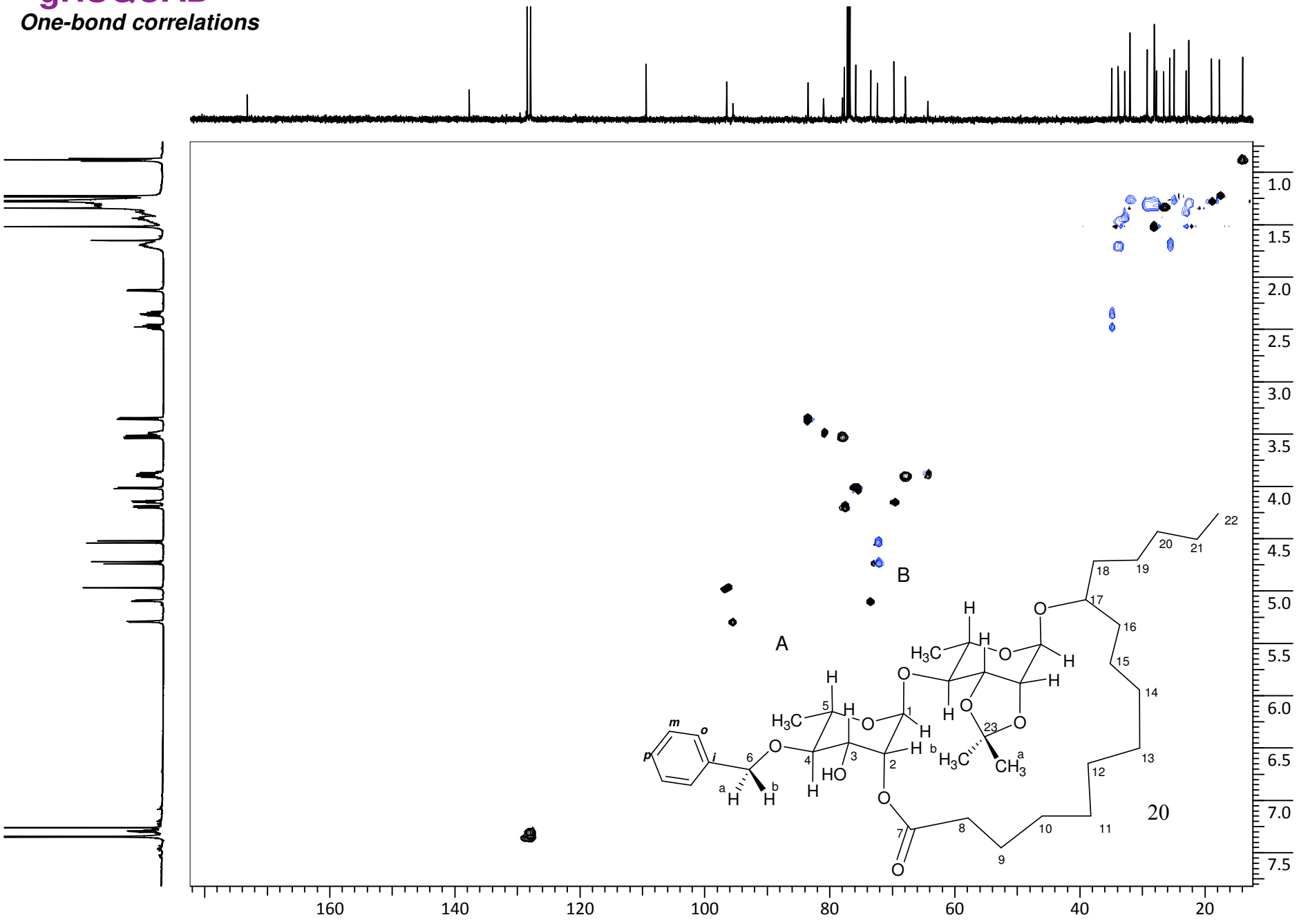
DEPT135

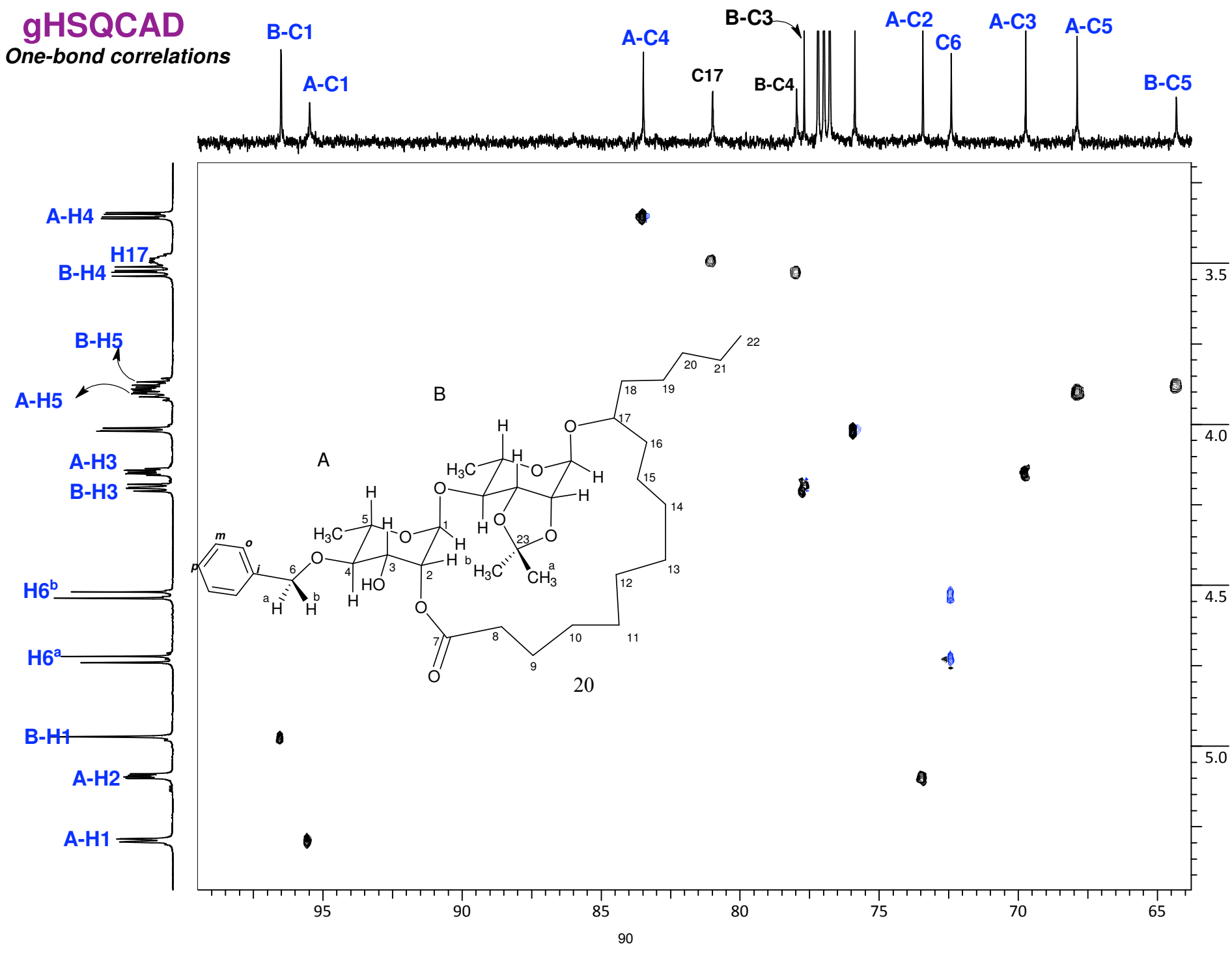
CH_2's

168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8

gHSQCAD

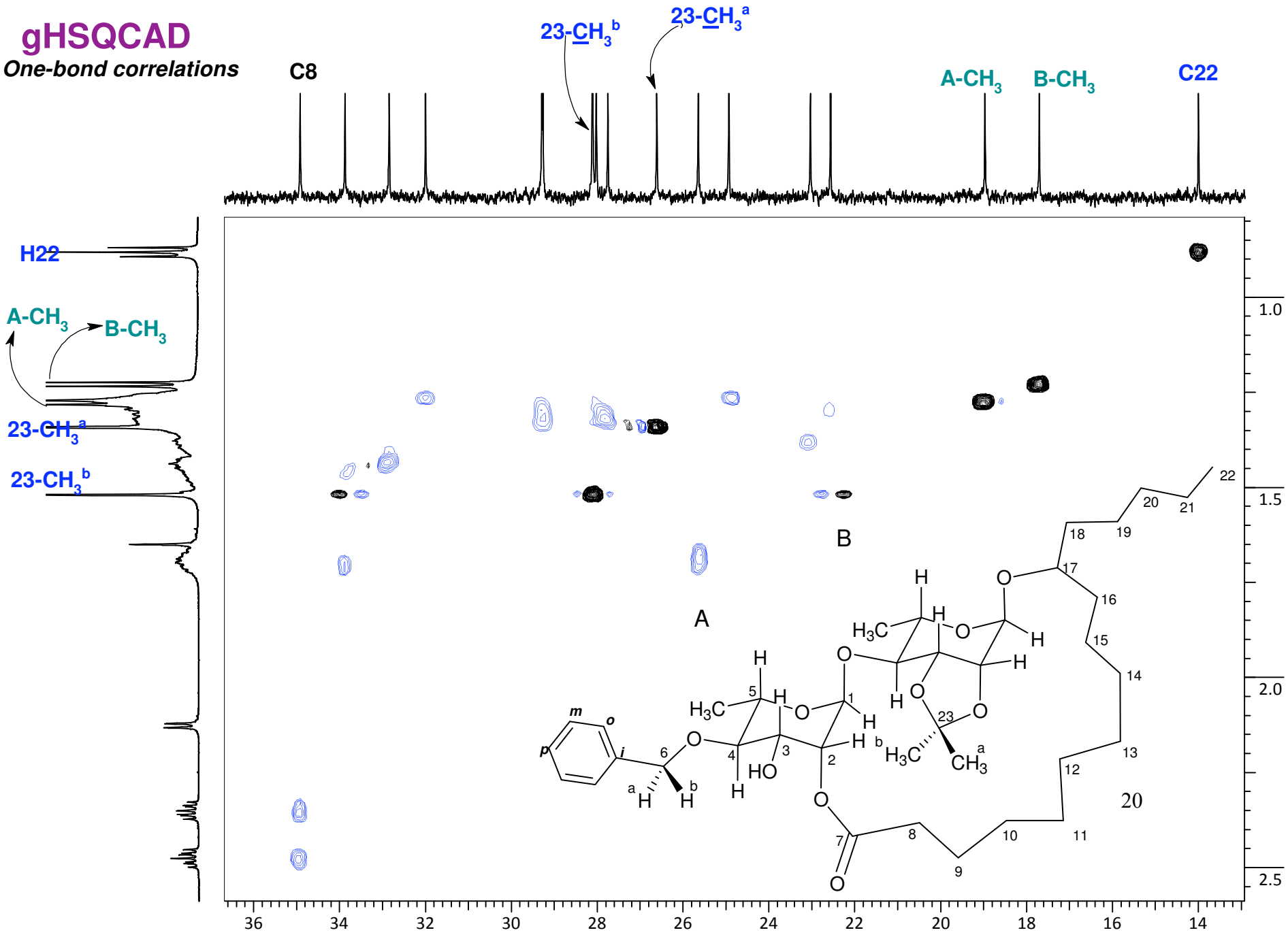
One-bond correlations




gHSQCAD
One-bond correlations
B-C1
A-C1
A-C4
C17
B-C3
B-C4
A-C2
C6
A-C3
A-C5
B-C5
A-H4
H17
B-H4
B-H5
A-H5
A-H3
B-H3
H6b
H6a
B-H1
A-H2
A-H1
A
B
20
3.5
4.0
4.5
5.0
95
90
85
80
75
70
65
90

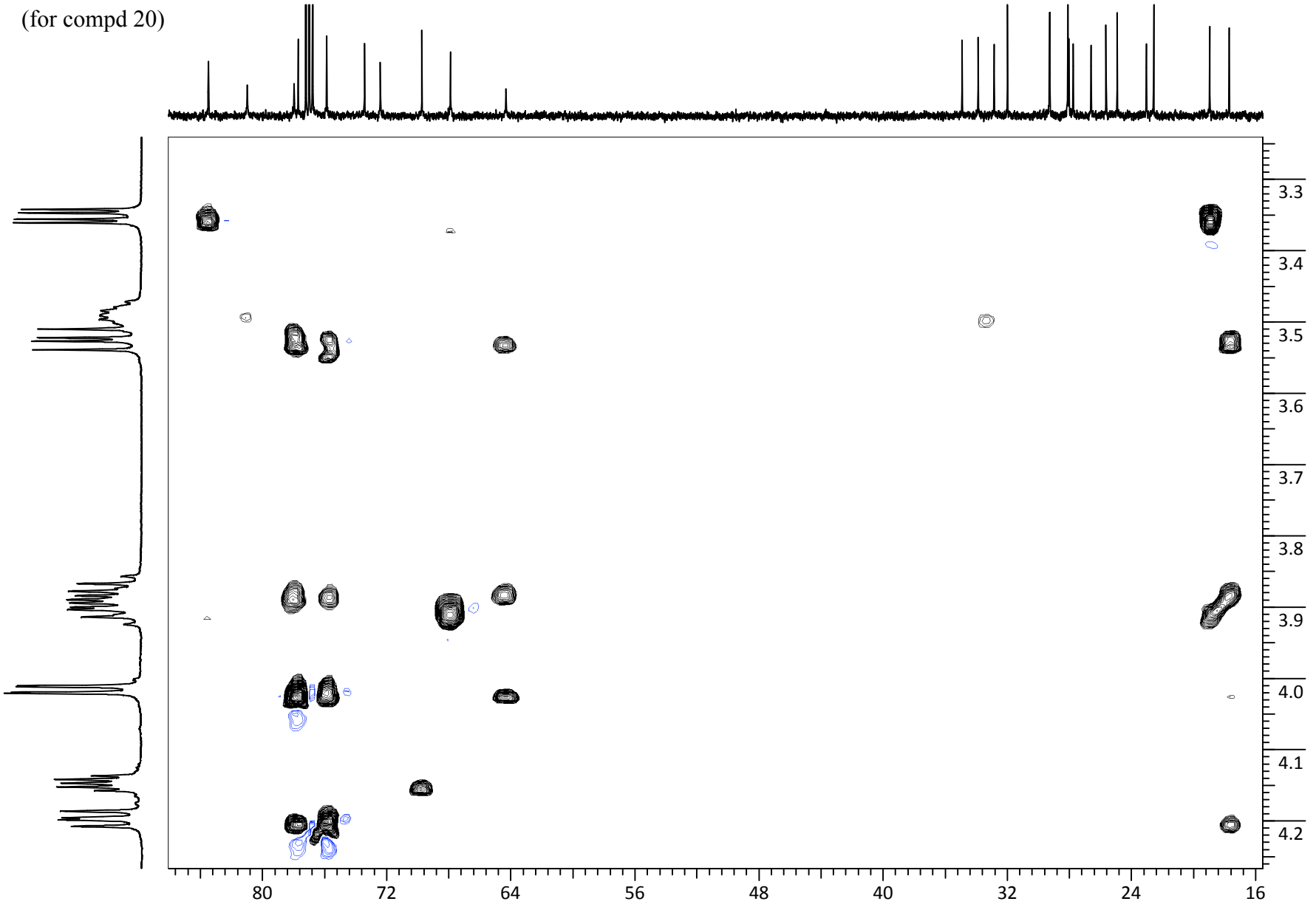
gHSQCAD

One-bond correlations



gHSQCTOCSY

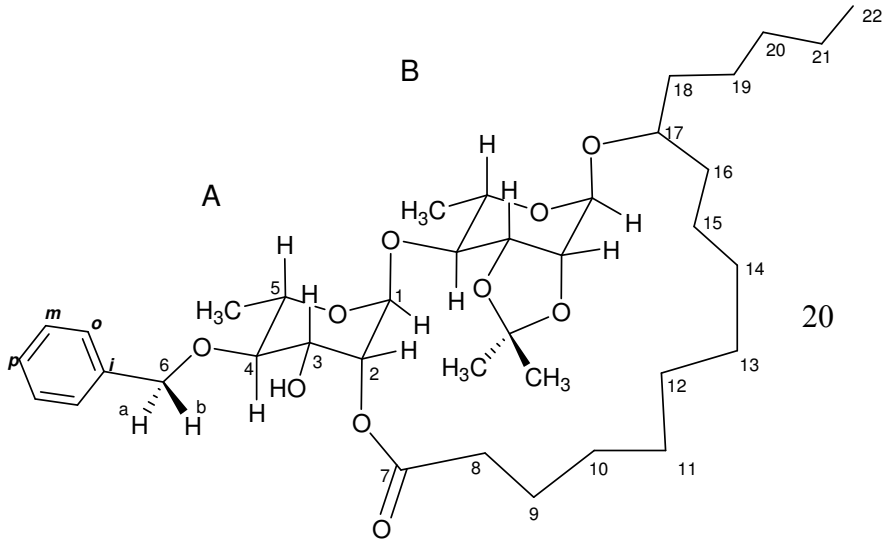
(for compd 20)

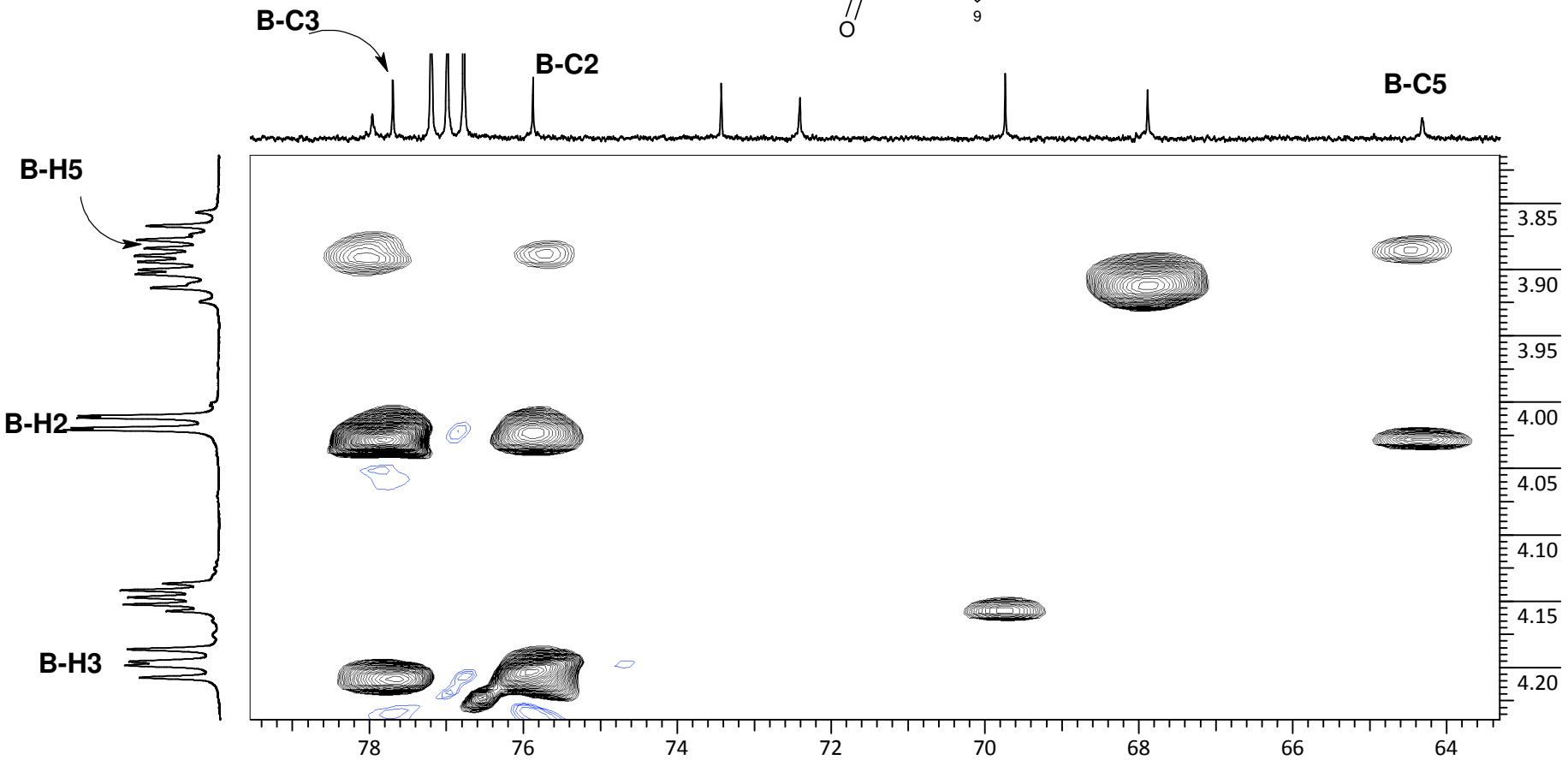


gHSQCTOCSY

spin system identification

(mix = 80 ms)

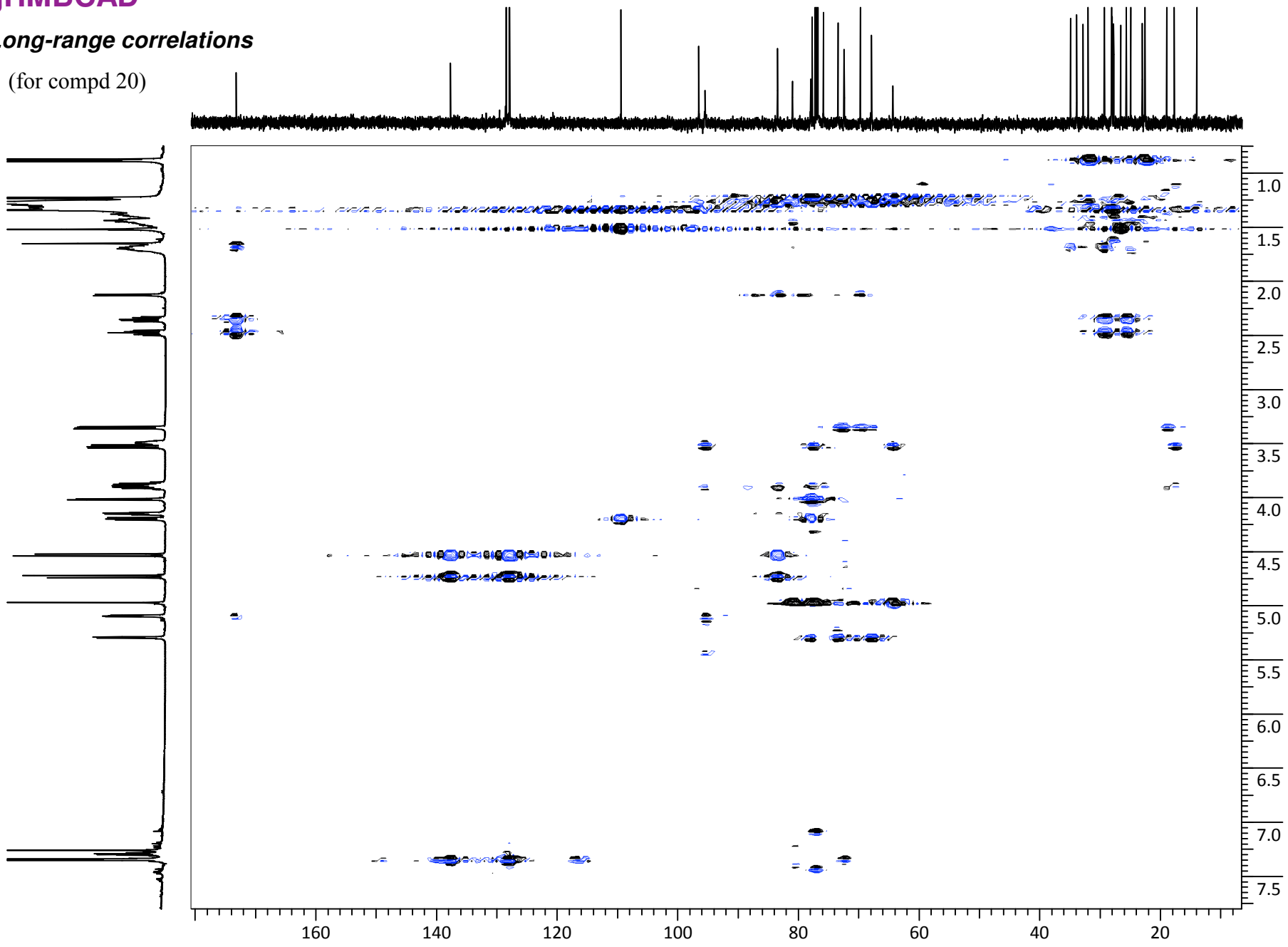




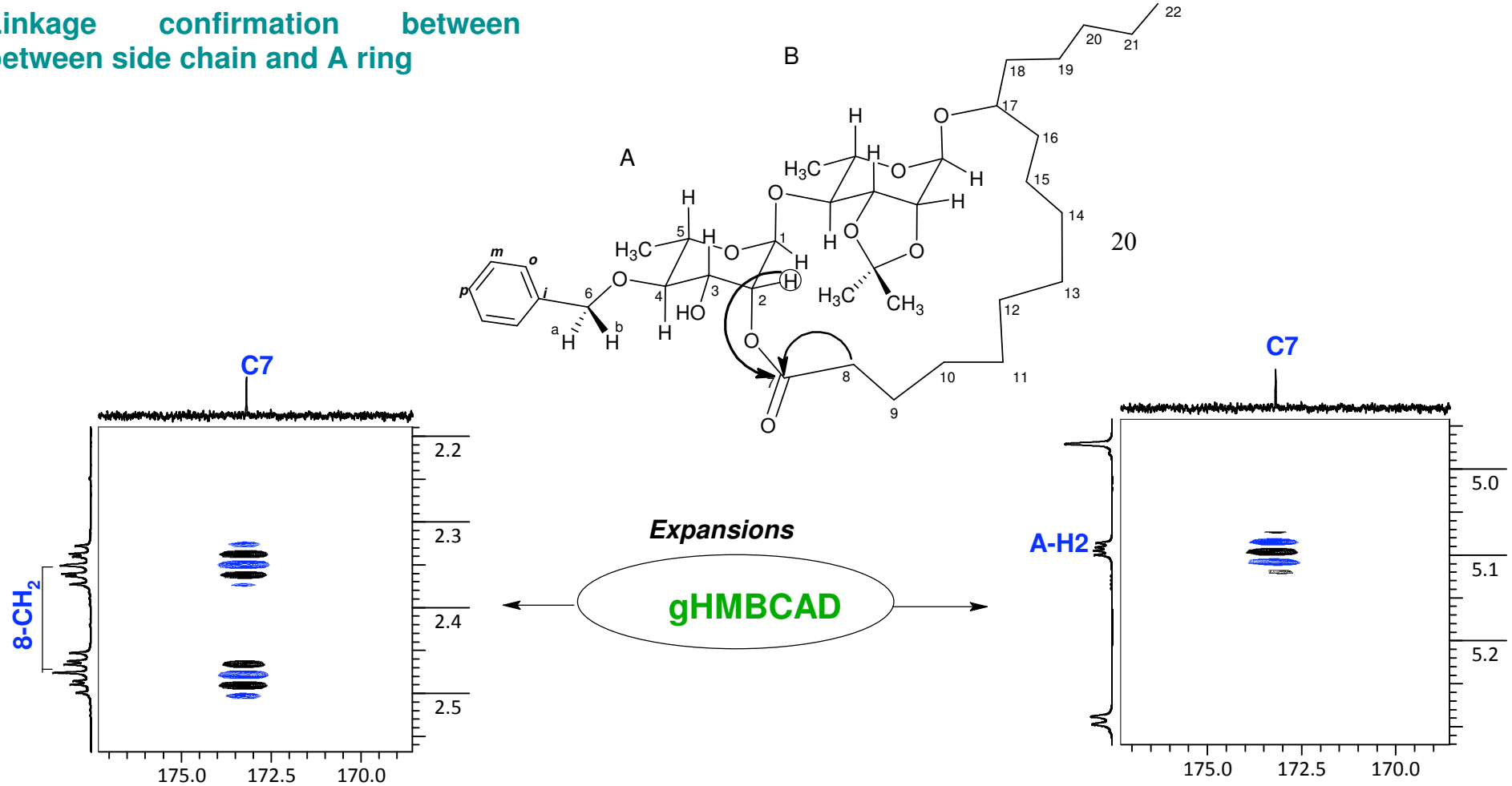
gHMBCAD

Long-range correlations

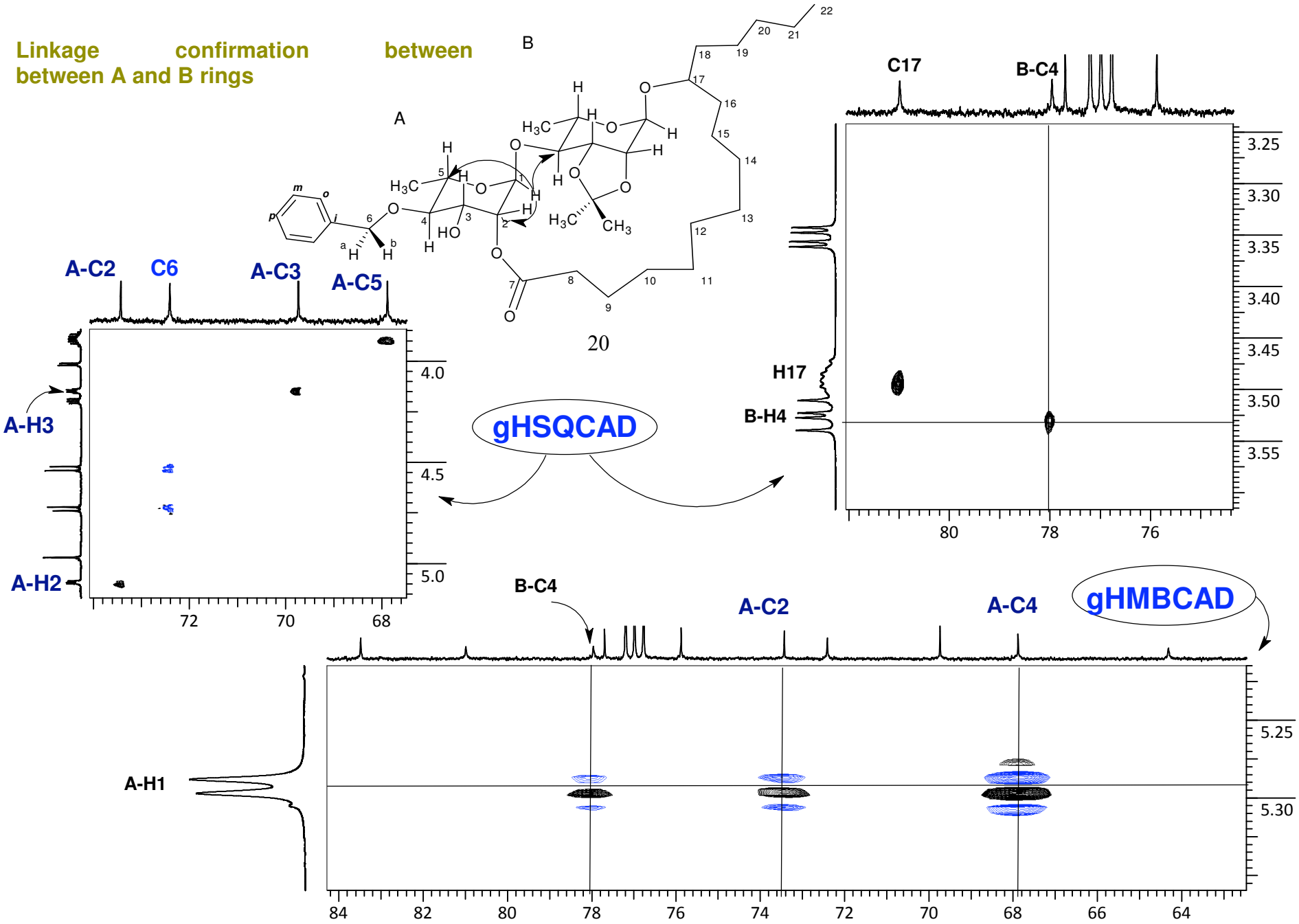
(for compd 20)



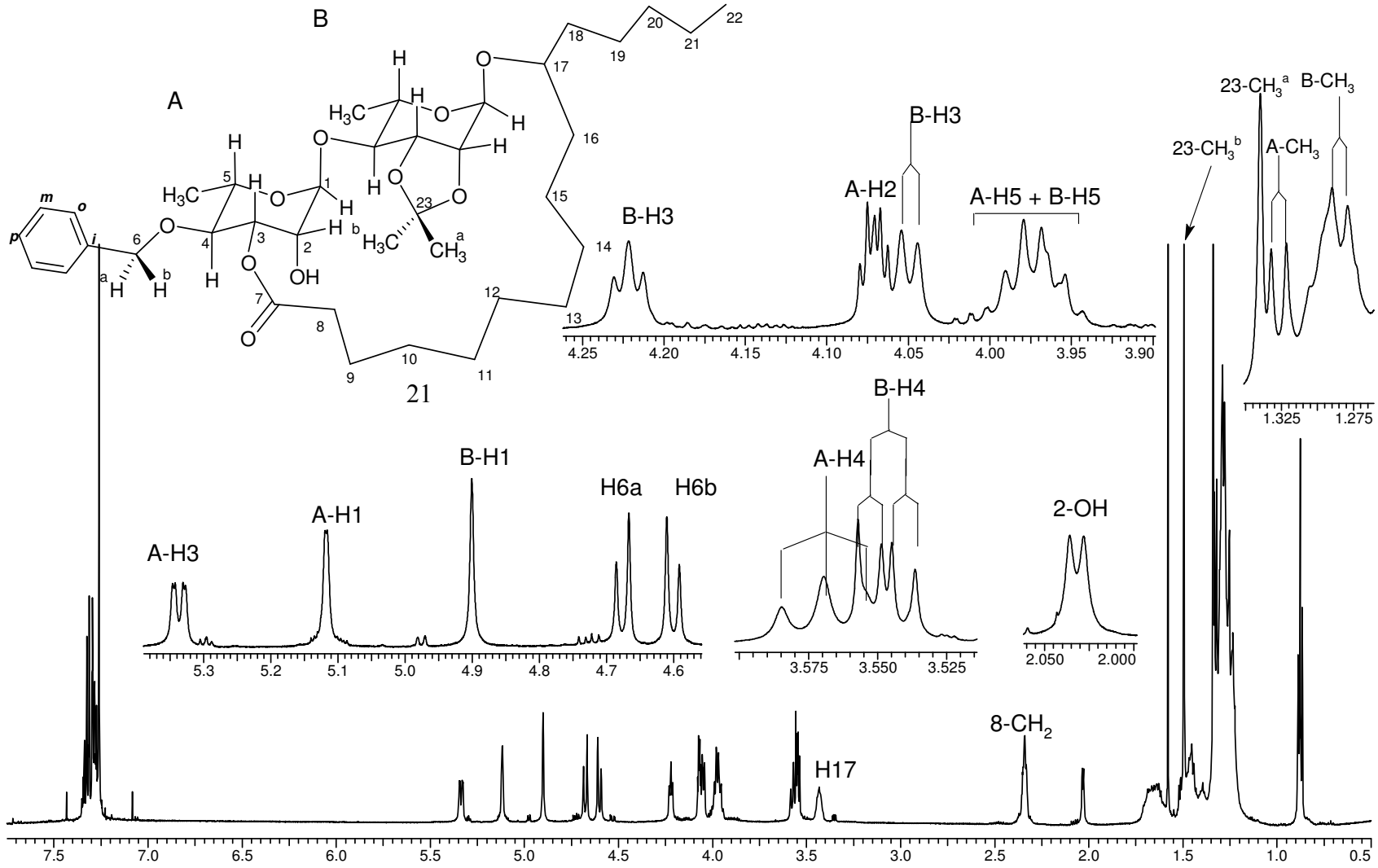
Linkage confirmation between between side chain and A ring



Linkage confirmation between A and B rings



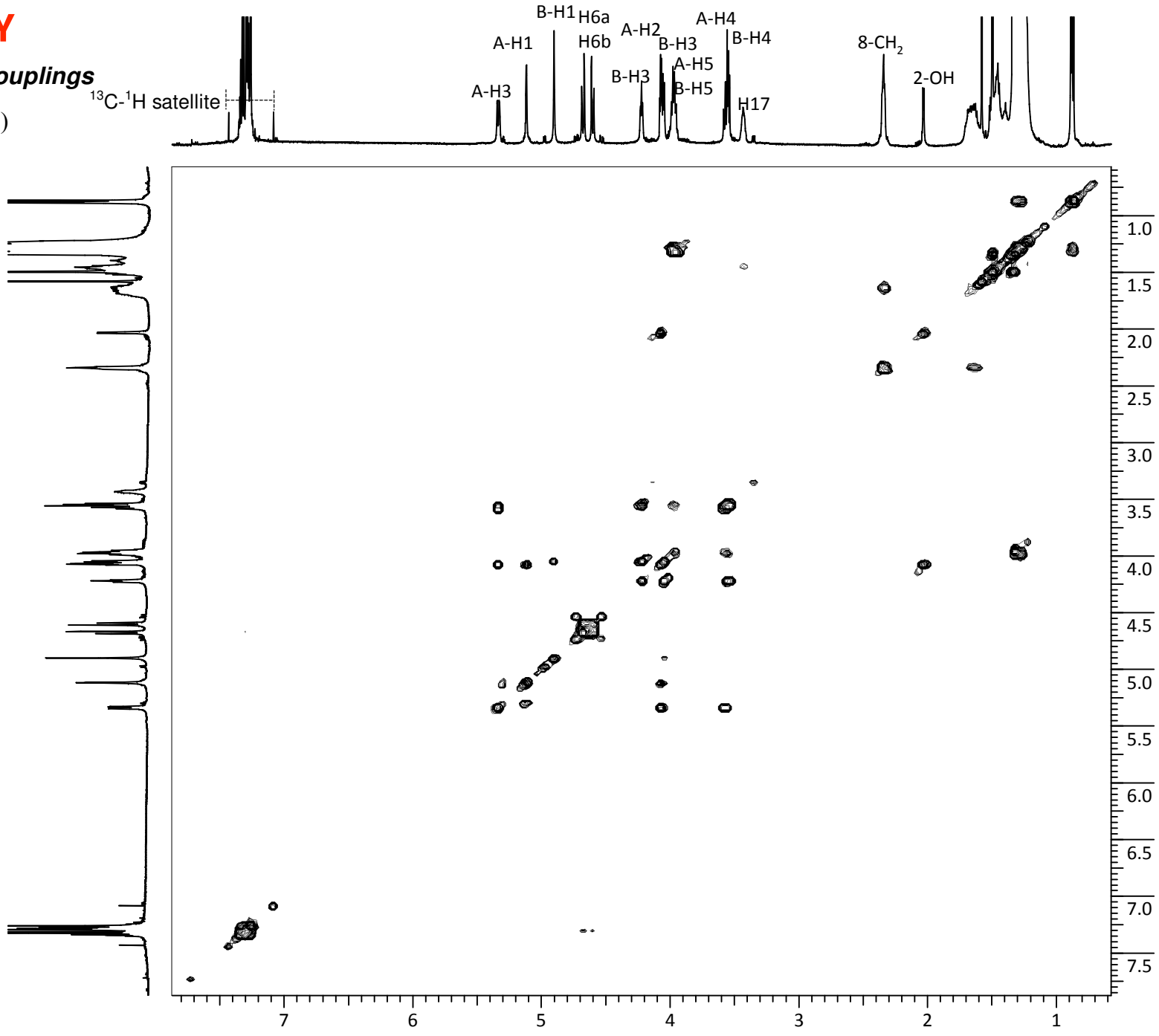
Complete assignments were performed in $CDCl_3$, 600 MHz



gCOSY

through ^{1}H-^{1}H couplings

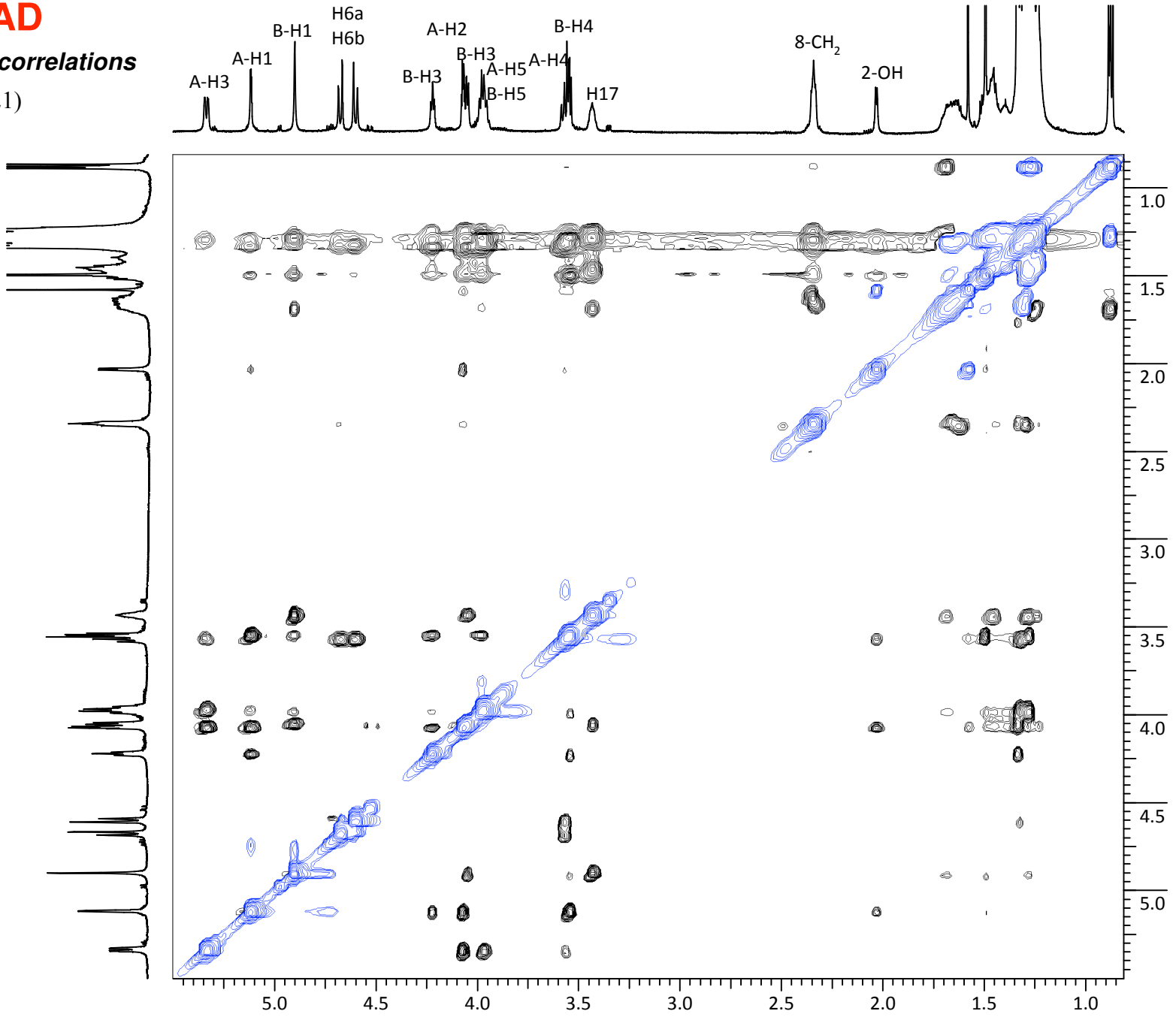
(for compd 21)



ROESYAD

through space correlations

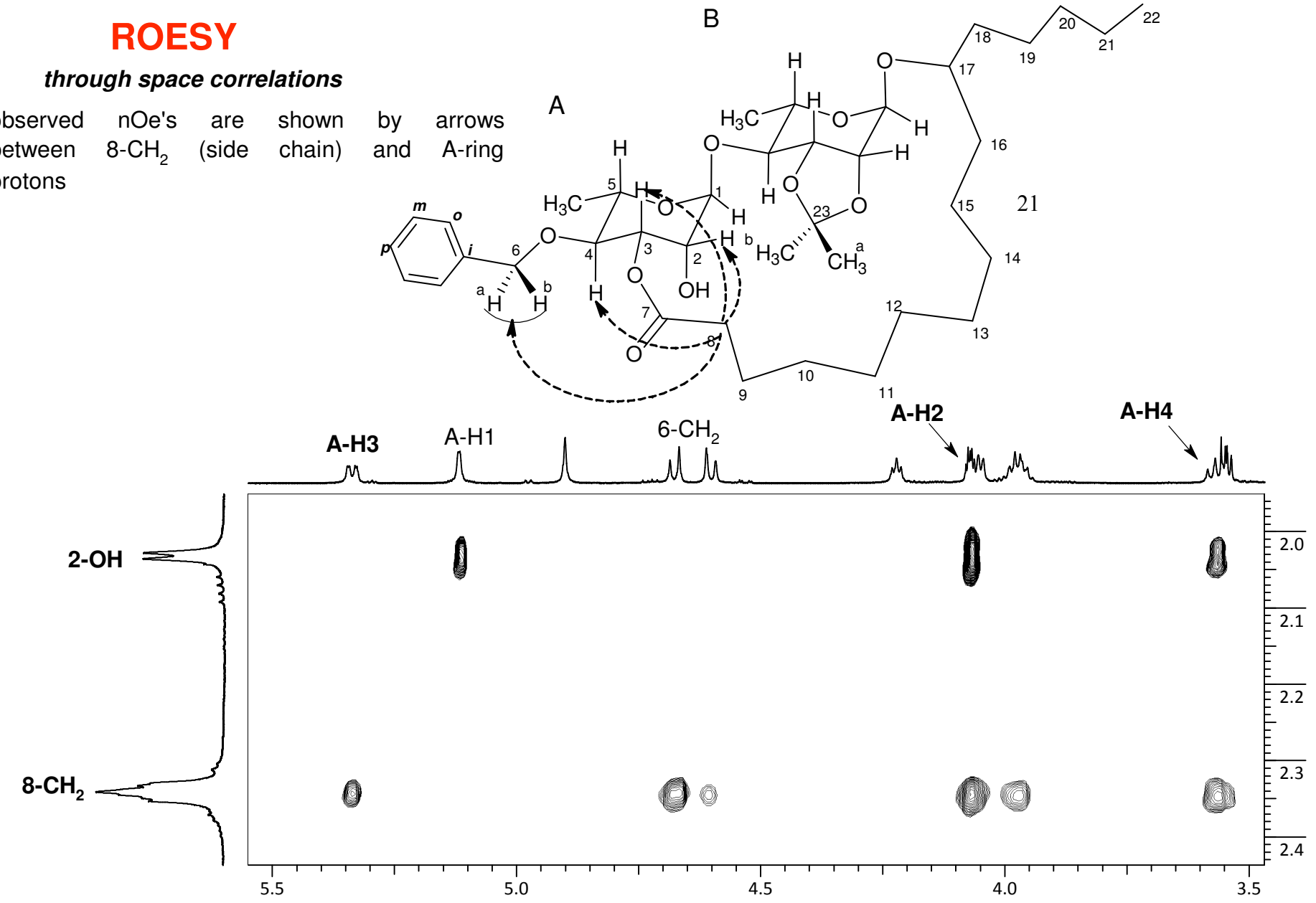
(for compd 21)



ROESY

through space correlations

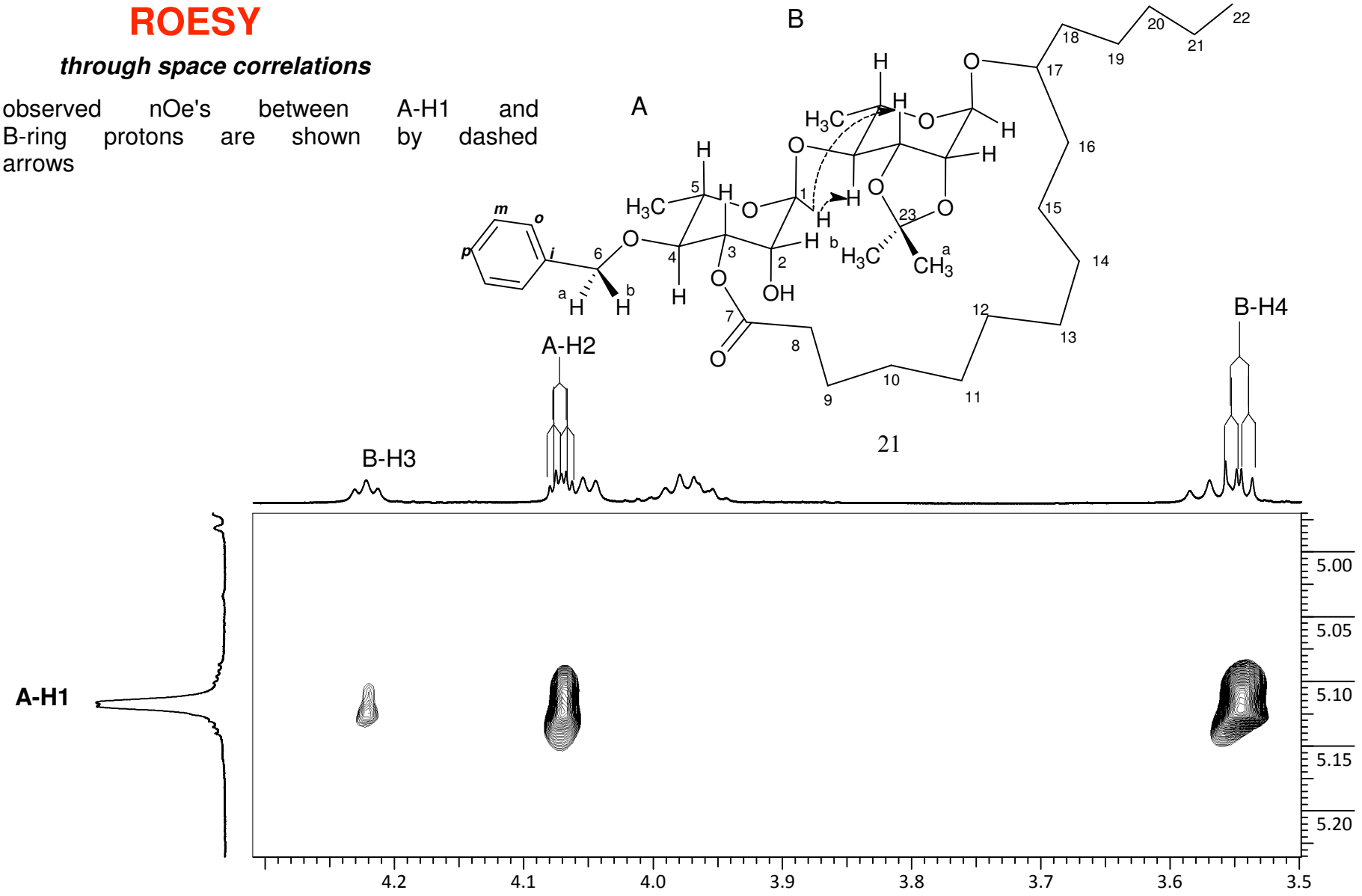
observed nOe's are shown by arrows between 8-CH_2 (side chain) and A-ring protons



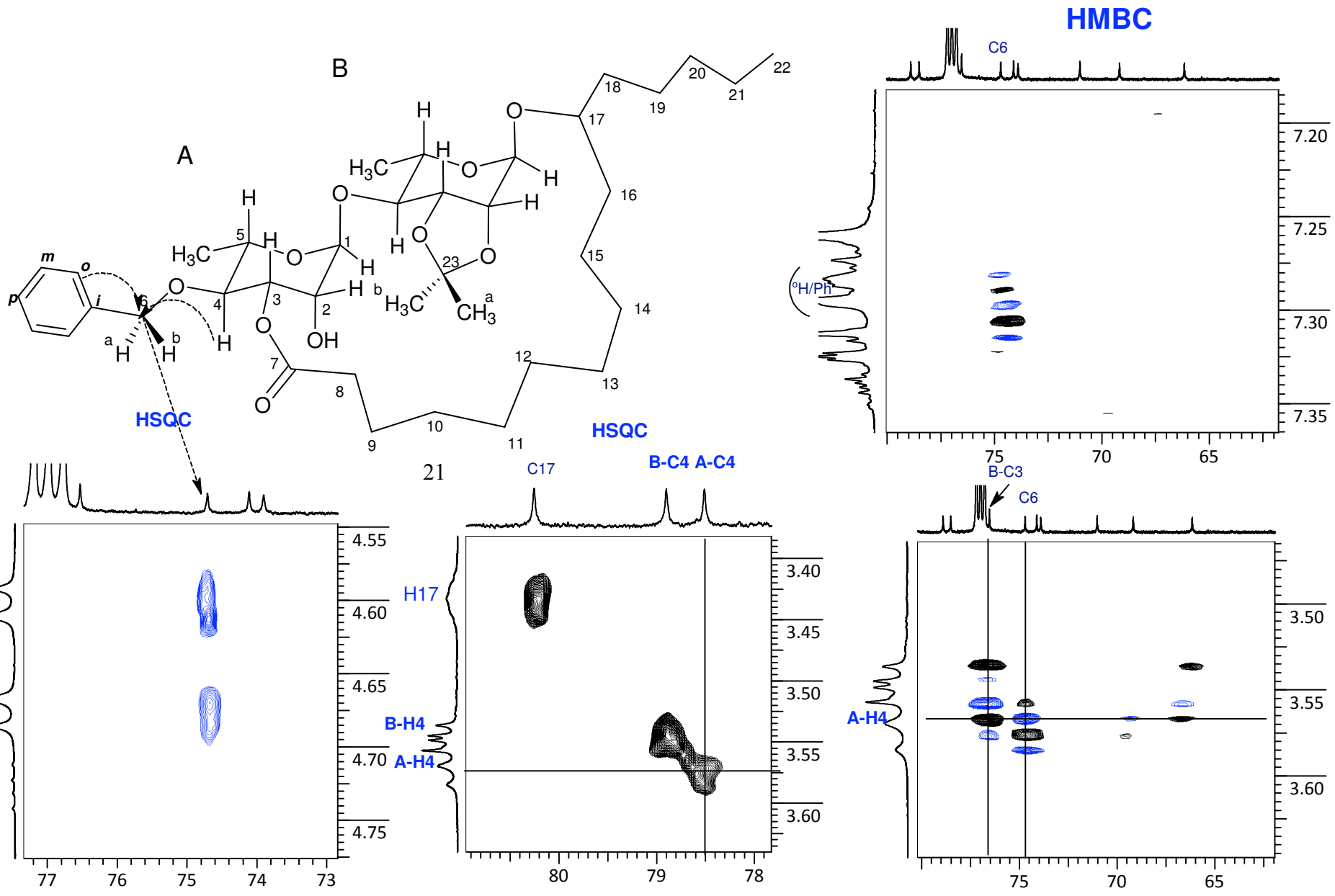
ROESY

through space correlations

observed nOe's between A-H1 and B-ring protons are shown by dashed arrows

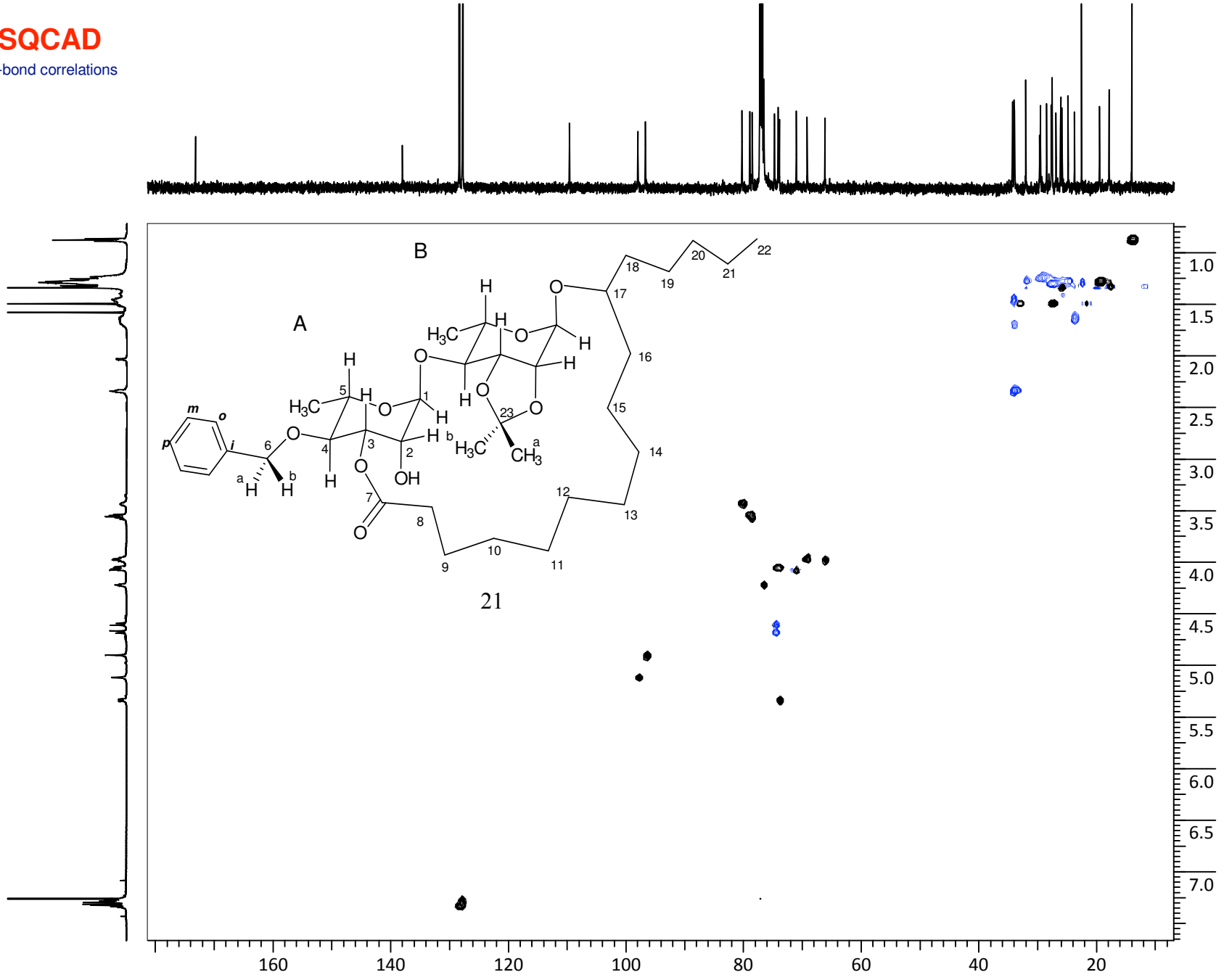


Assigment of A-H4/A-C4



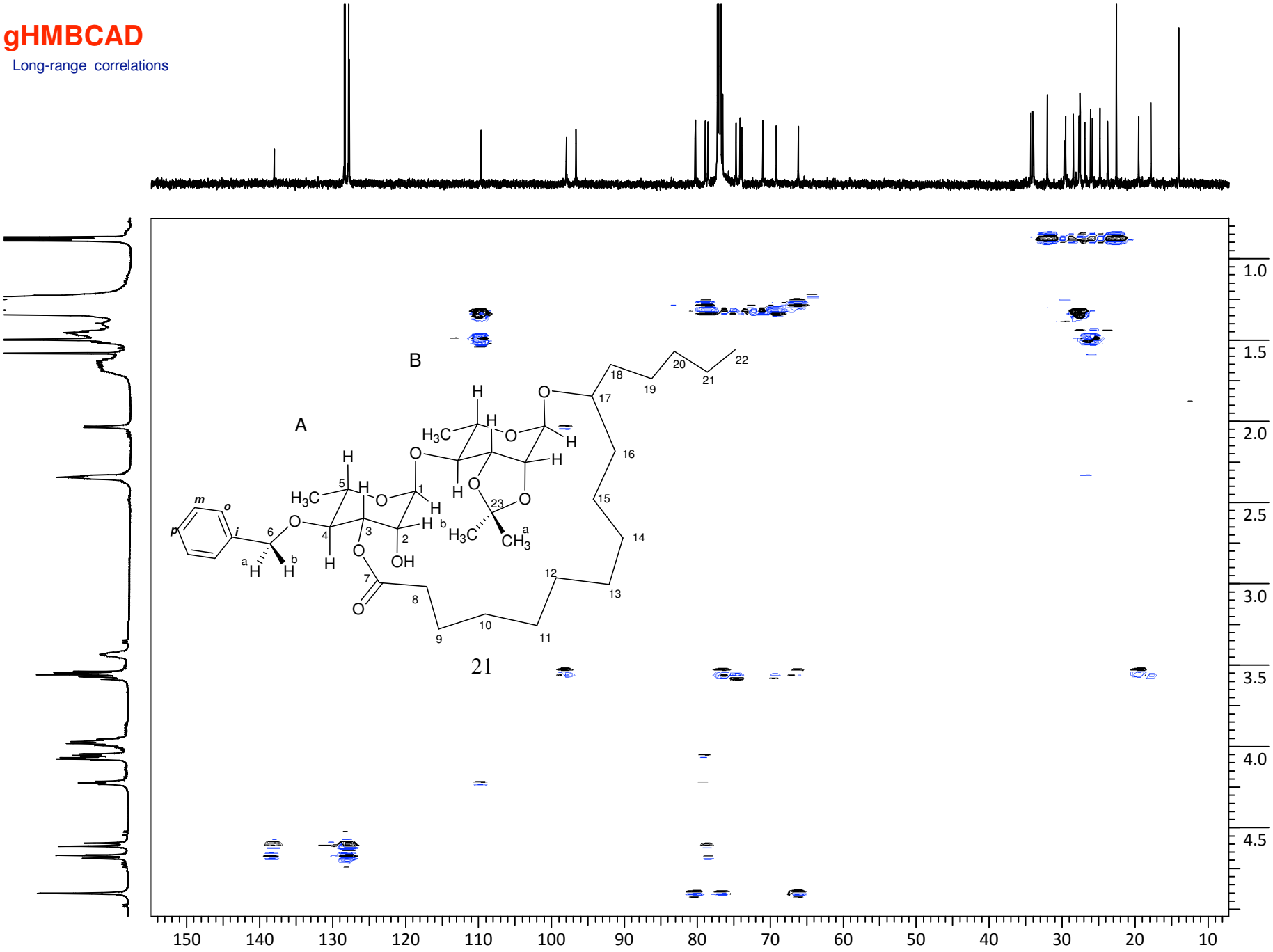
gHSQCAD

One-bond correlations

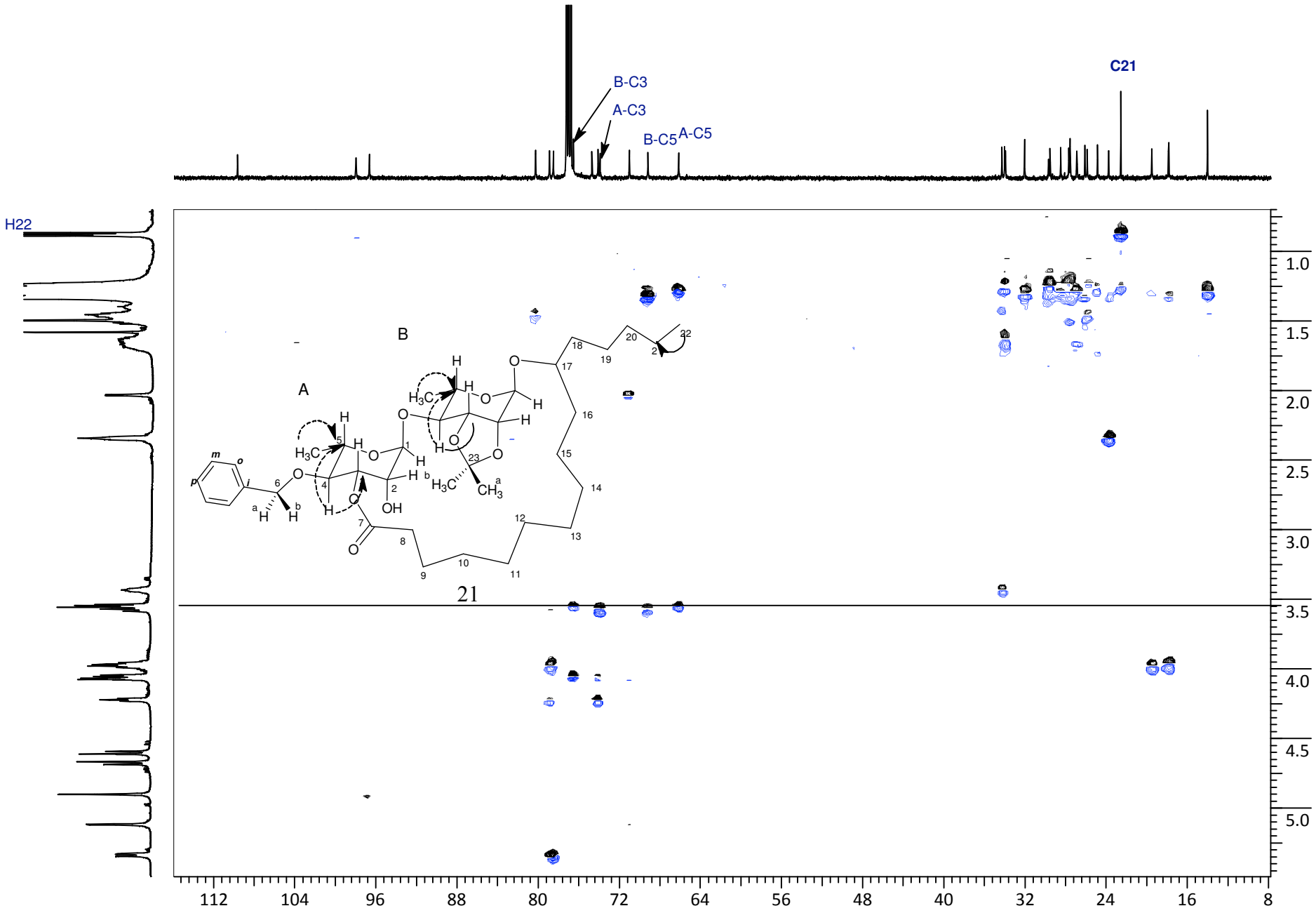


gHMBCAD

Long-range correlations



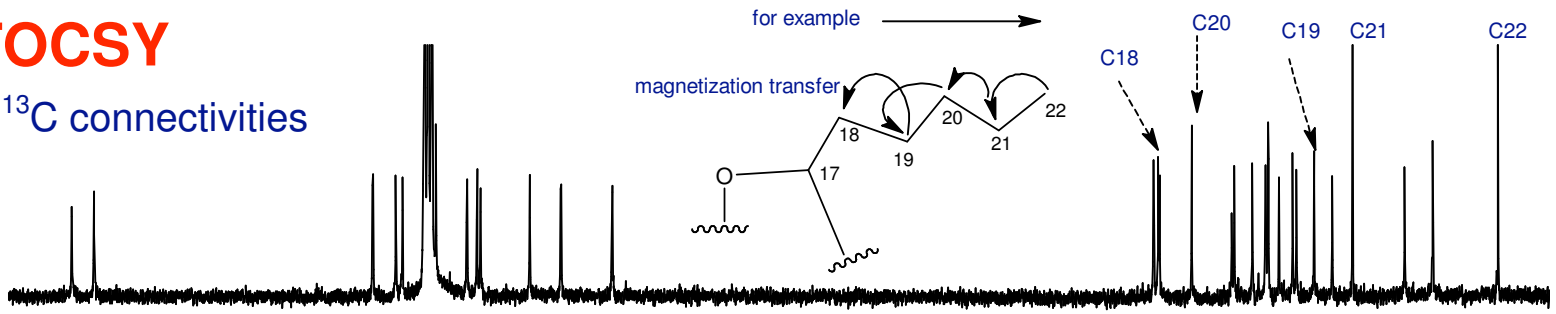
gH2BCD two bond correlations between proton and carbon

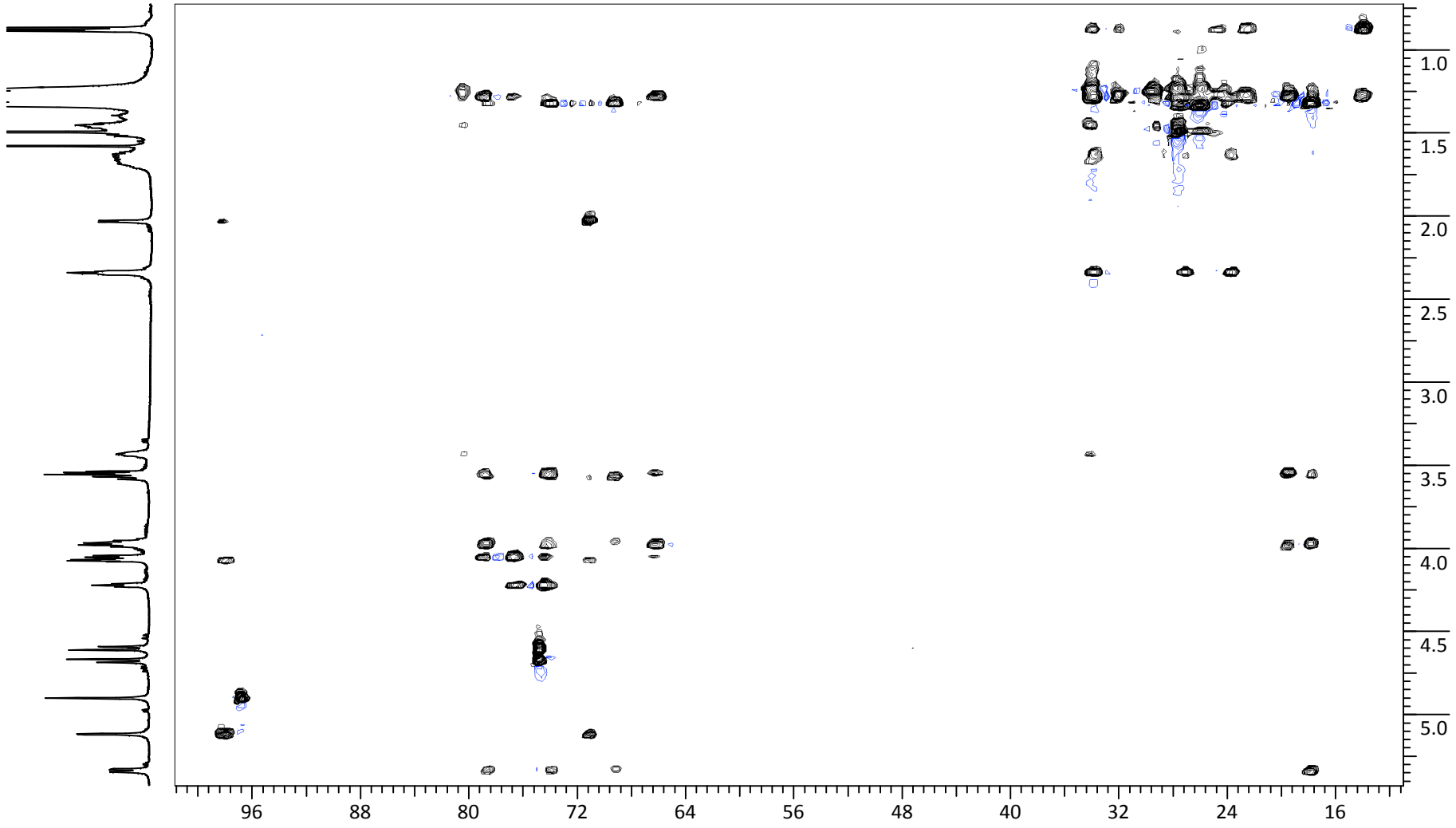


gHSQCTOCSY

^{1}H-^{1}H and ^{13}C-^{13}C connectivities

(for compd 21)

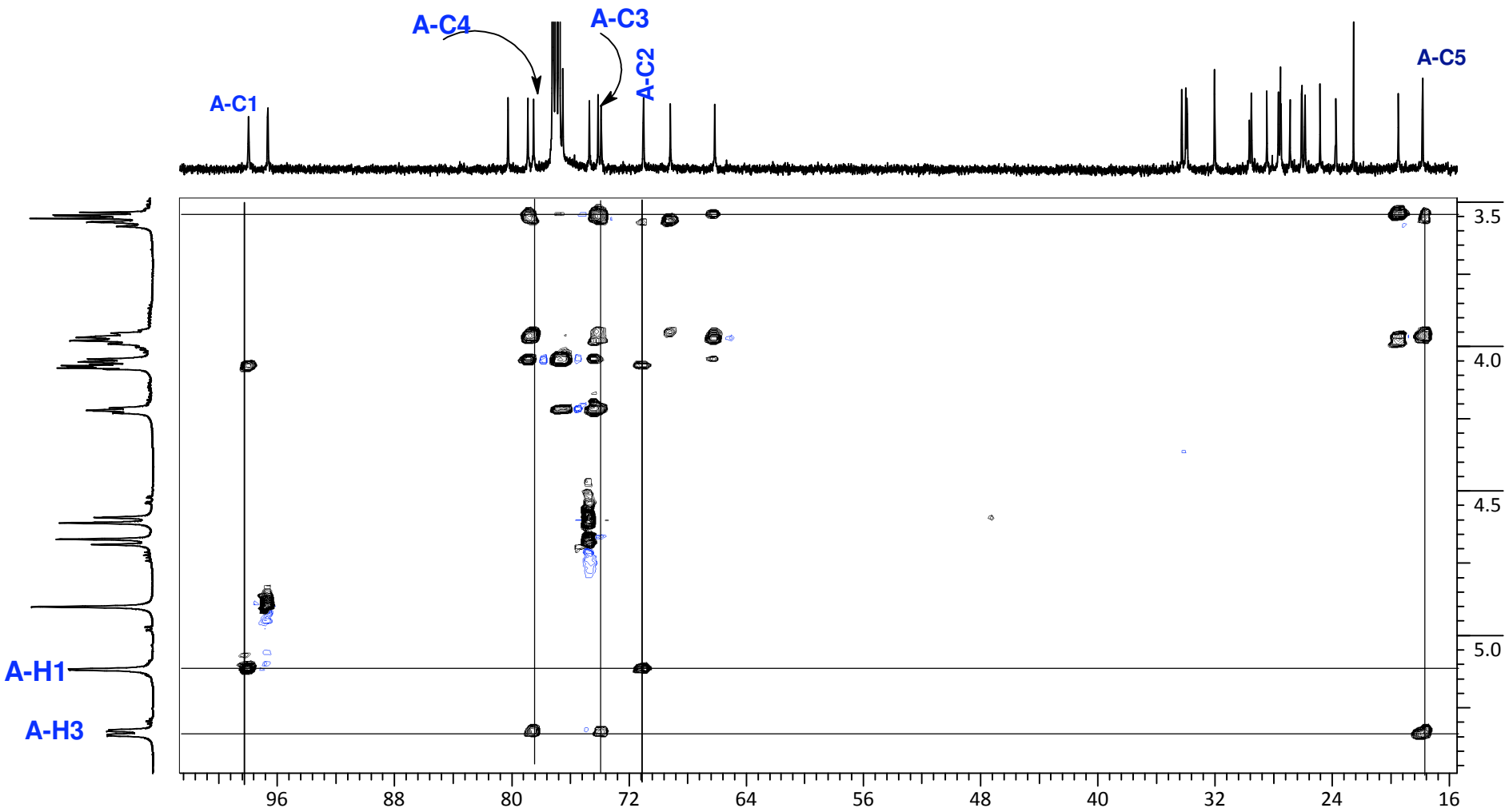


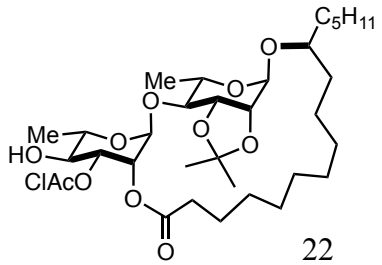


gHSQCTOCSY

^{1}H-^{1}H and ^{13}C-^{13}C connectivities

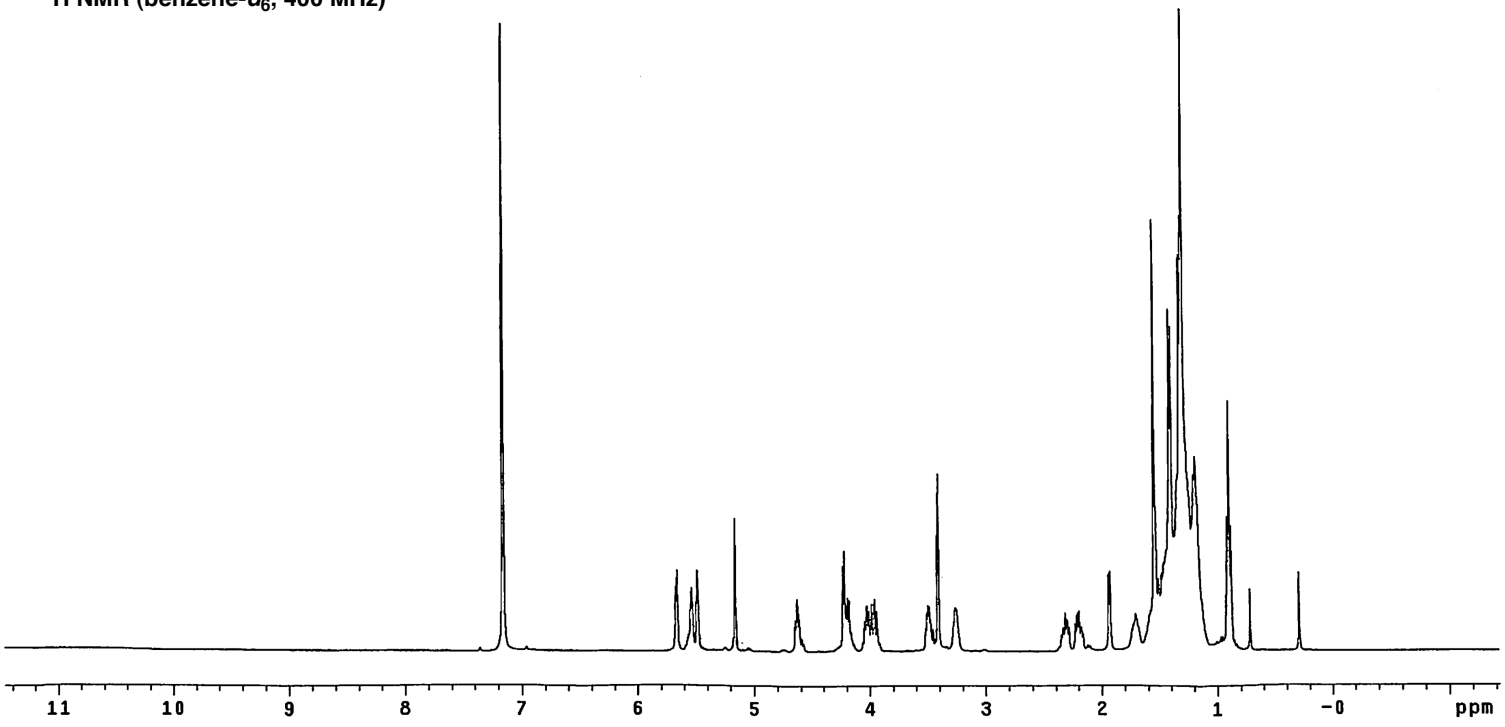
(for compd 21)

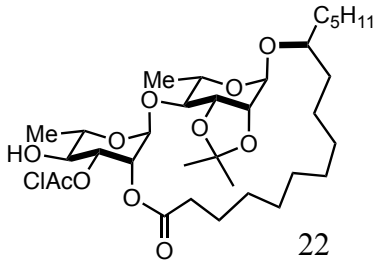




22

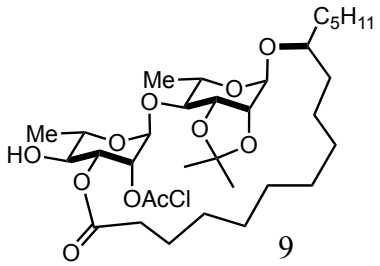
^{1}H NMR (benzene-d_6, 400 MHz)





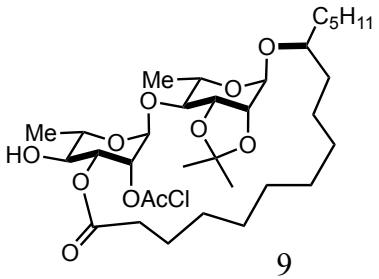
22

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



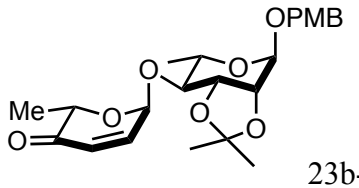
9

^{1}H NMR (benzene-d_6, 400 MHz)



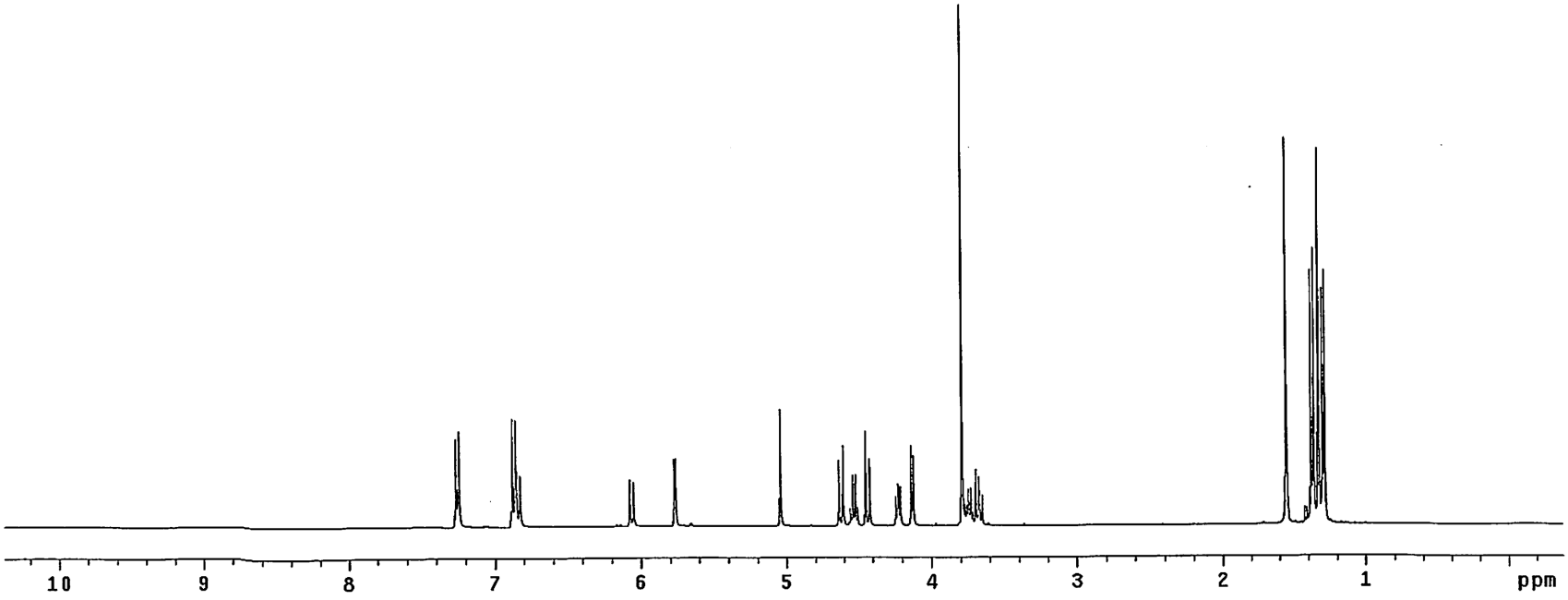
9

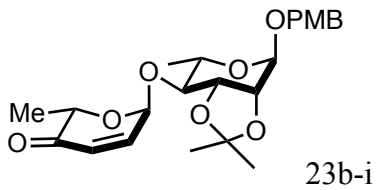
^{13}C NMR ($CDCl_3$, 100 MHz)



23b-i

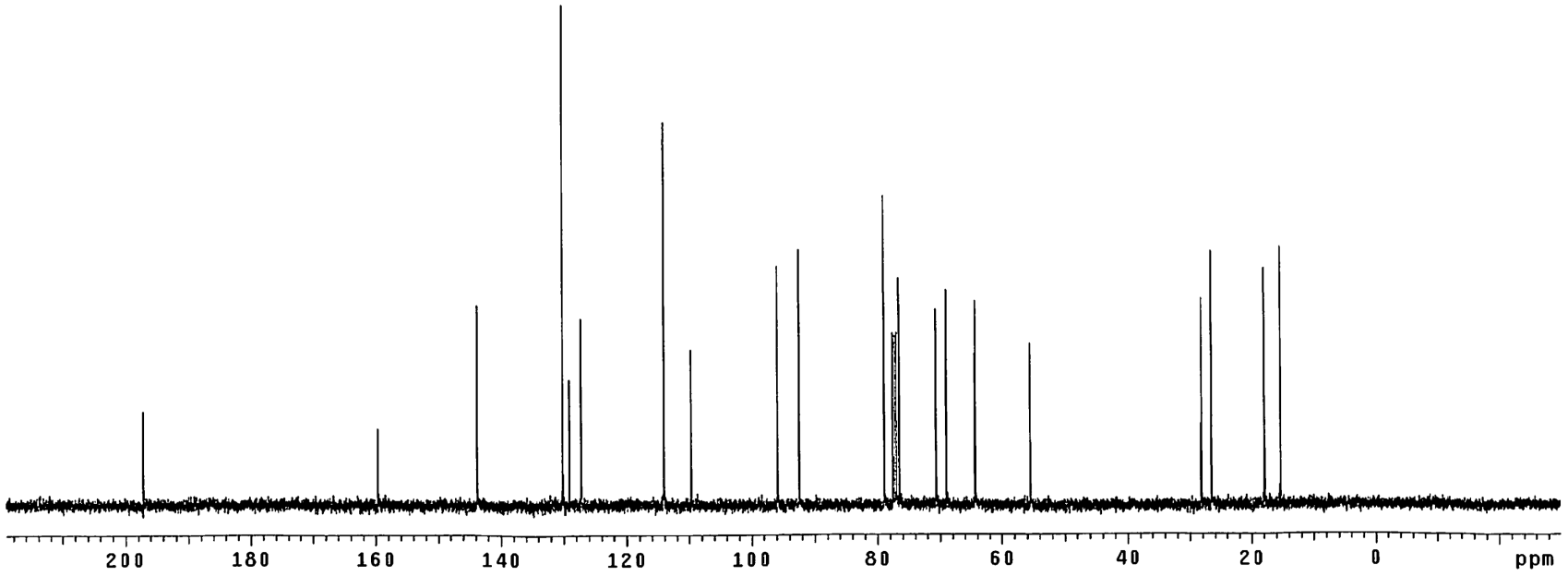
^{1}H NMR ($CDCl_3$, 400 MHz)

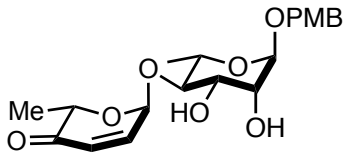




23b-i

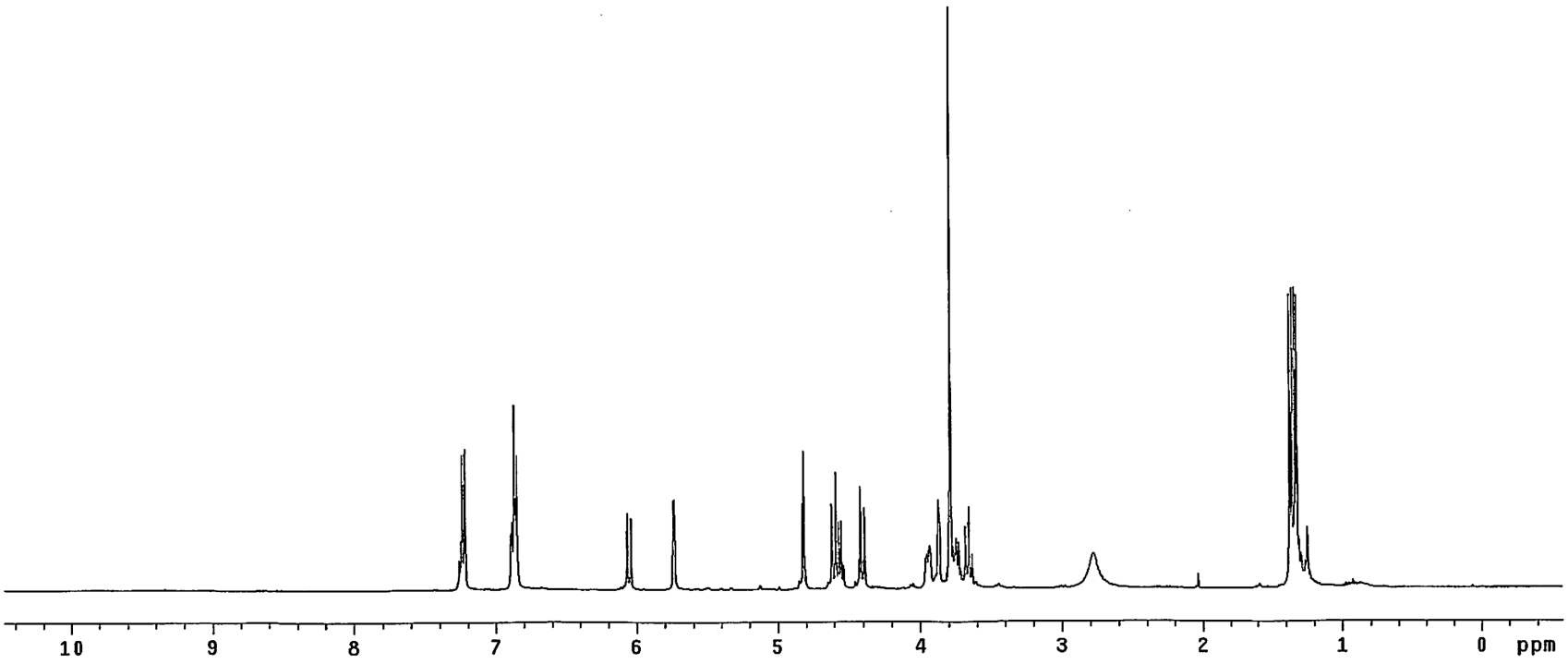
^{13}C NMR ($CDCl_3$, 100 MHz)

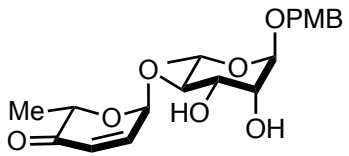




24

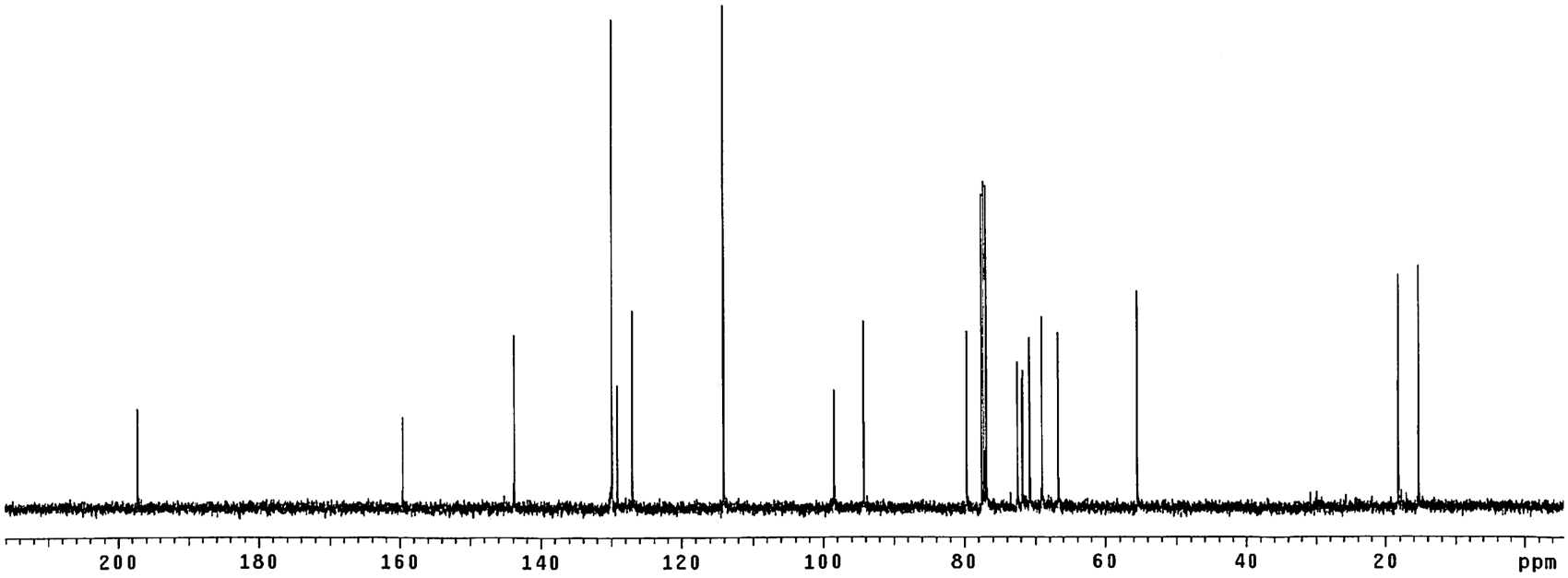
^{1}H NMR ($CDCl_3$, 400 MHz)

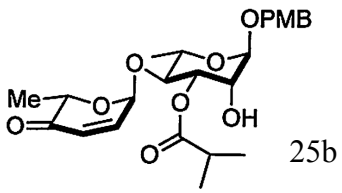




24

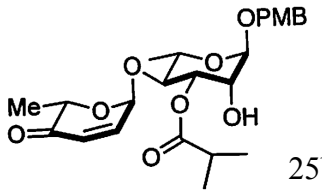
^{13}C NMR ($CDCl_3$, 100 MHz)





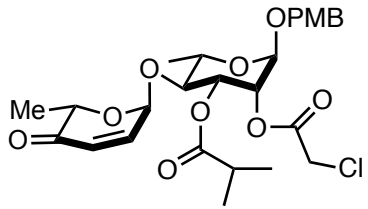
25b

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



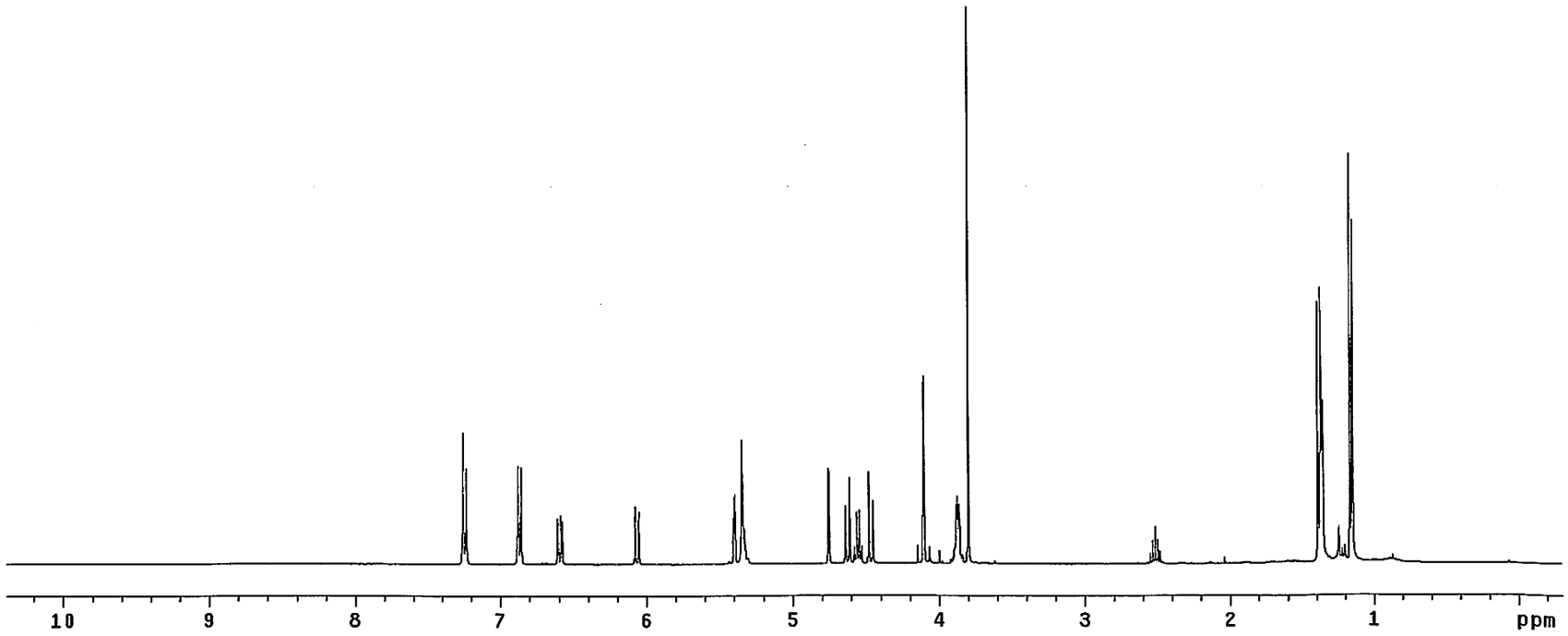
25b

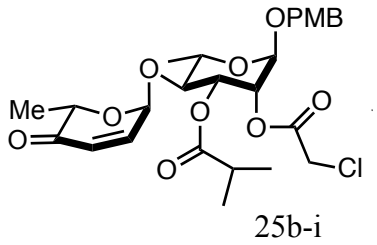
^{13}C NMR ($CDCl_3$, 100 MHz)



25b-i

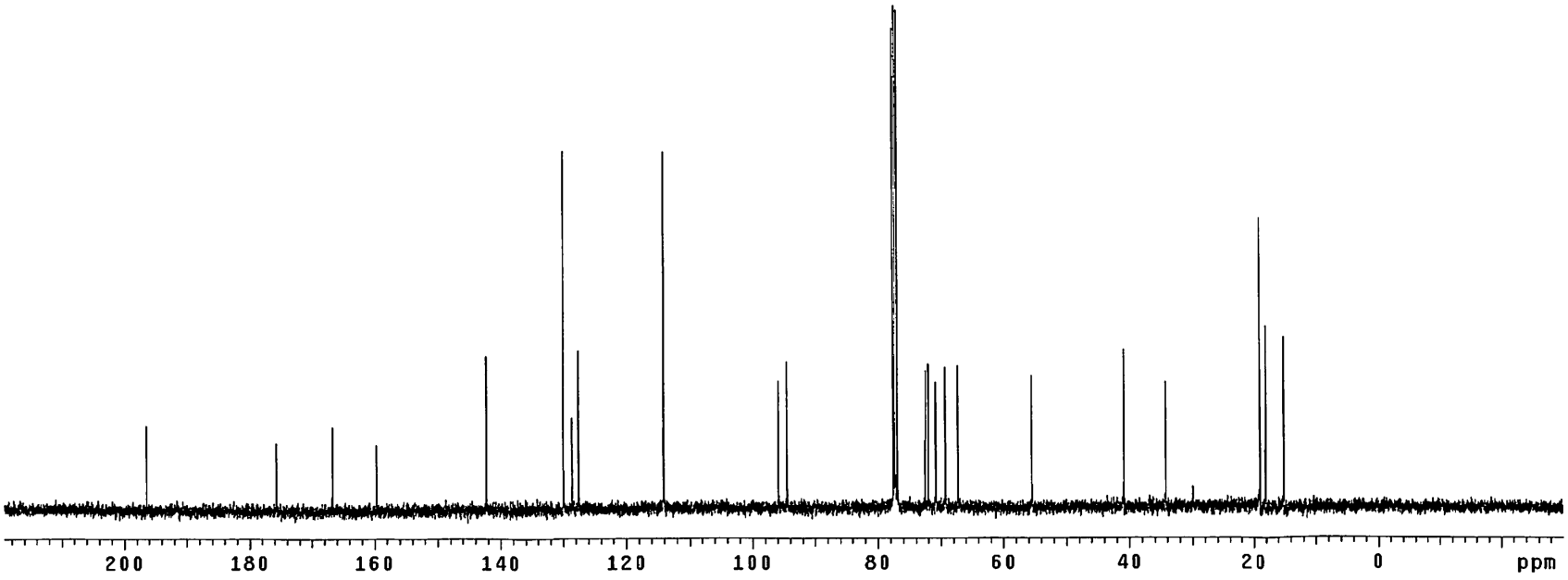
^{1}H NMR ($CDCl_3$, 400 MHz)

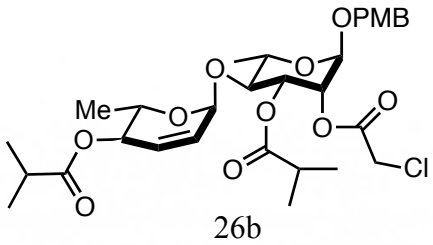




25b-i

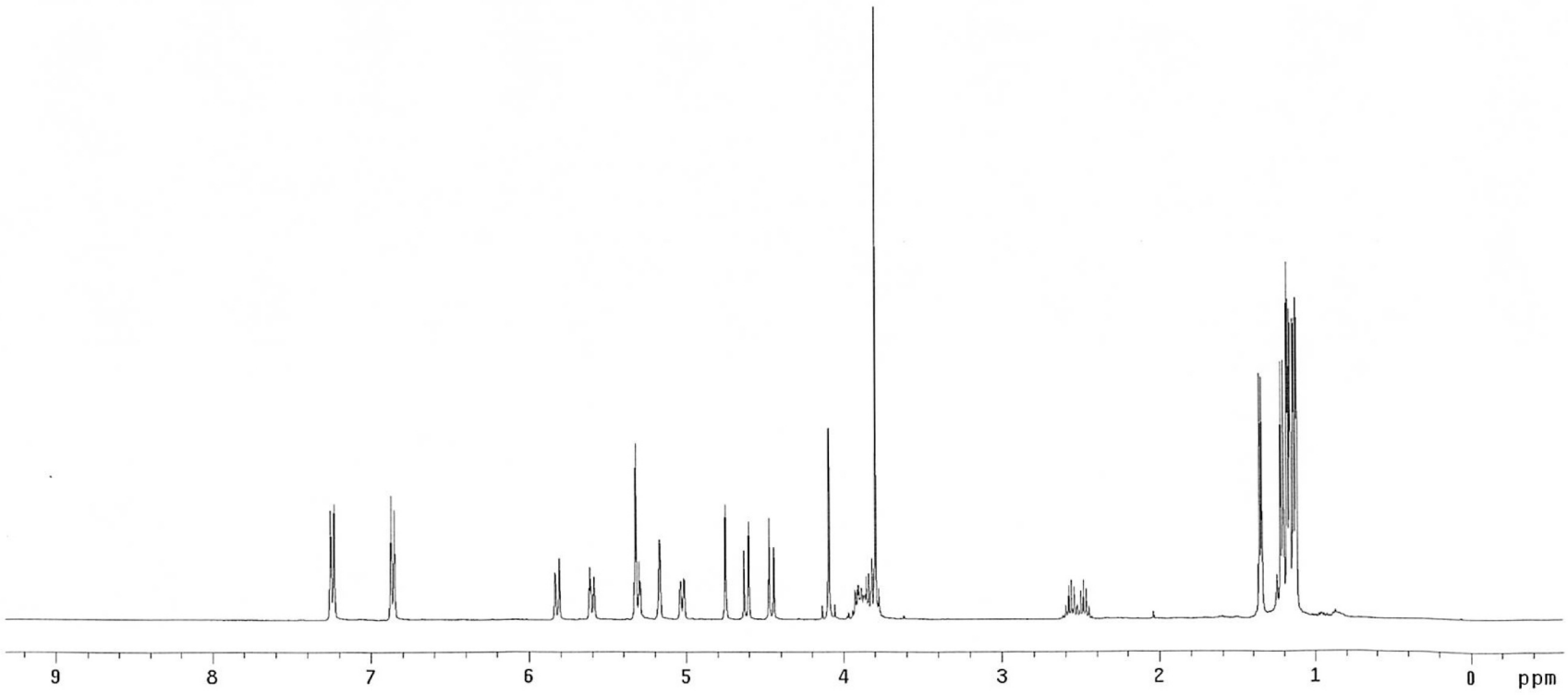
^{13}C NMR ($CDCl_3$, 100 MHz)

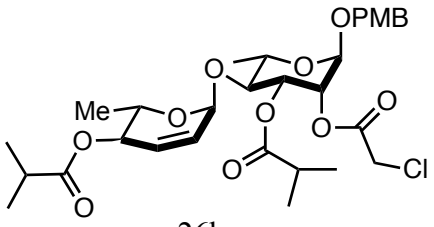




26b

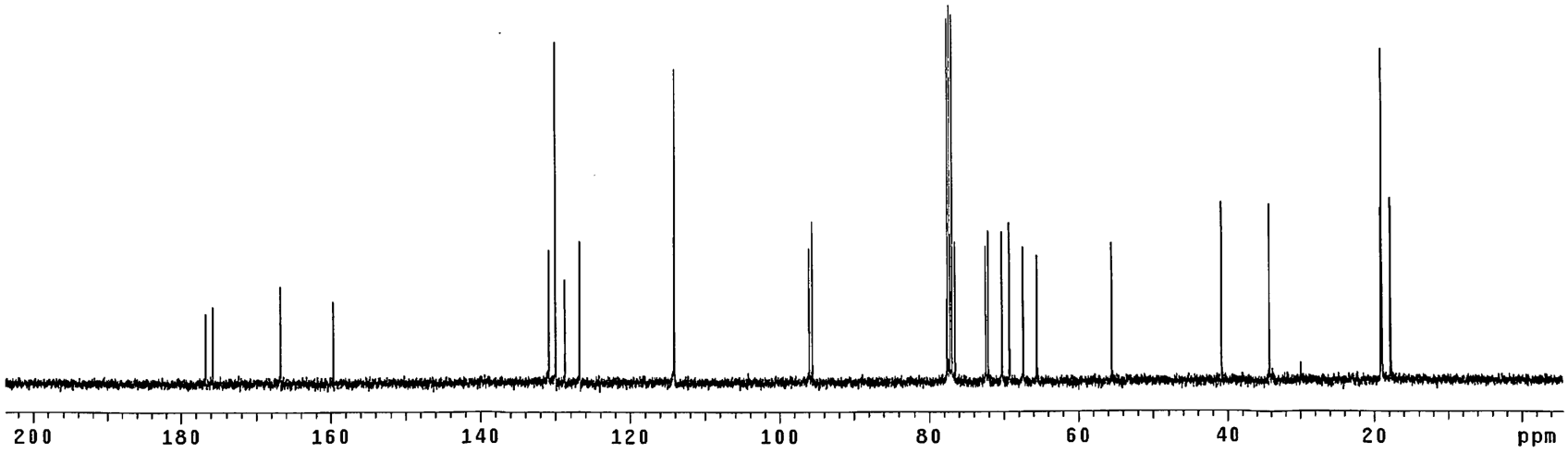
^{1}H NMR ($CDCl_3$, 400 MHz)

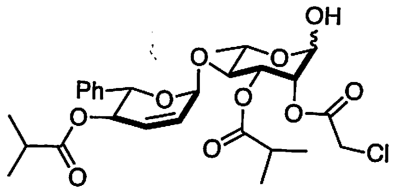




26b

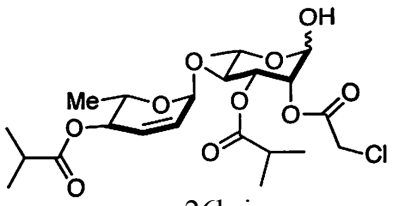
^{13}C NMR ($CDCl_3$, 100 MHz)





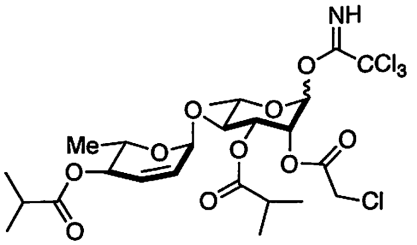
26b-i

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



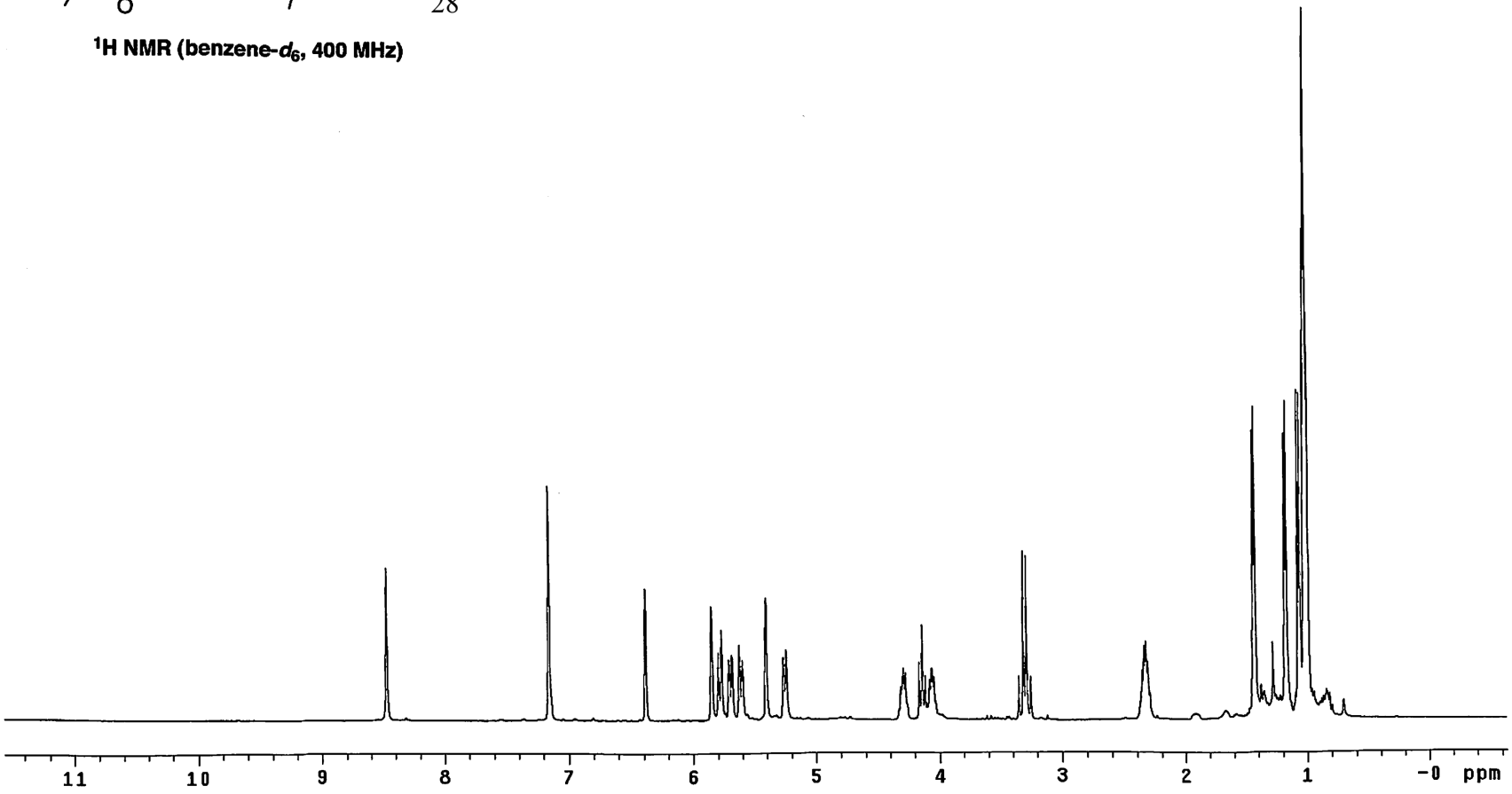
26b-i

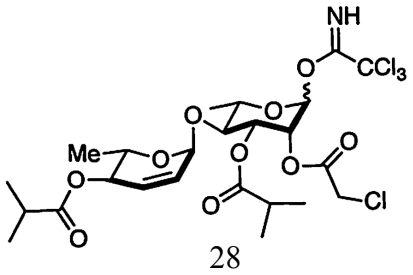
^{13}C NMR ($CDCl_3$, 100 MHz)



28

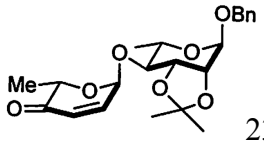
^{1}H NMR (benzene-d_6, 400 MHz)





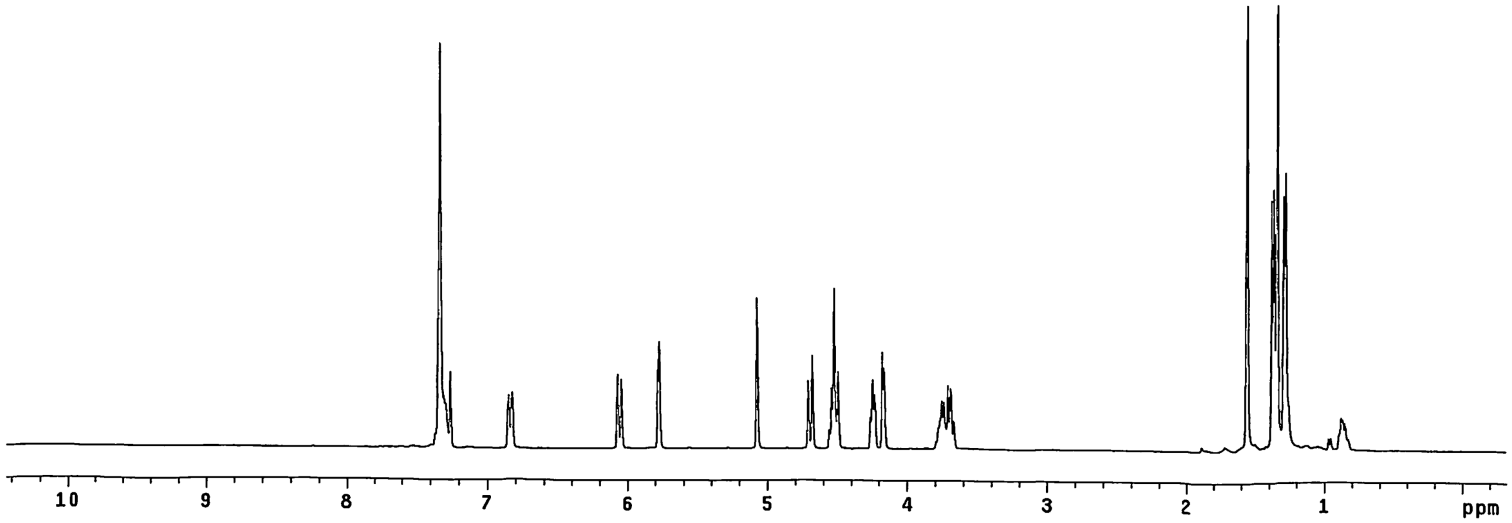
28

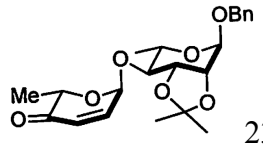
^{13}C NMR (benzene-d_6, 100 MHz)



23a-i

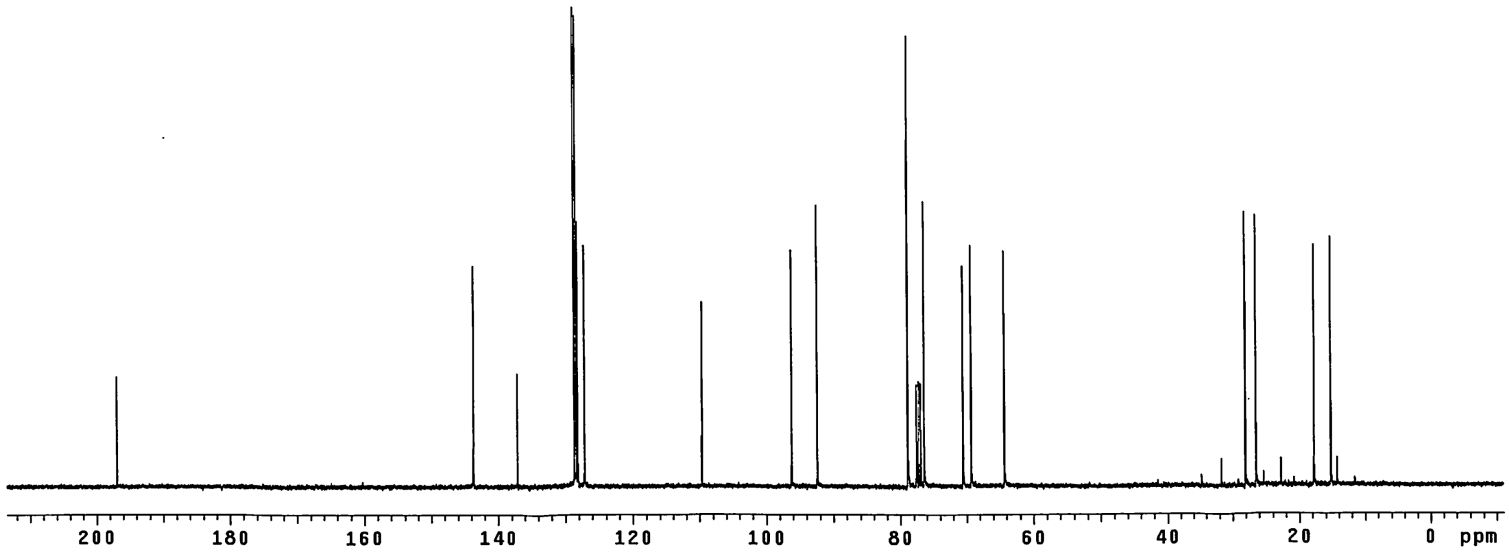
^{1}H NMR ($CDCl_3$, 400 MHz)

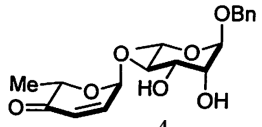




23a-i

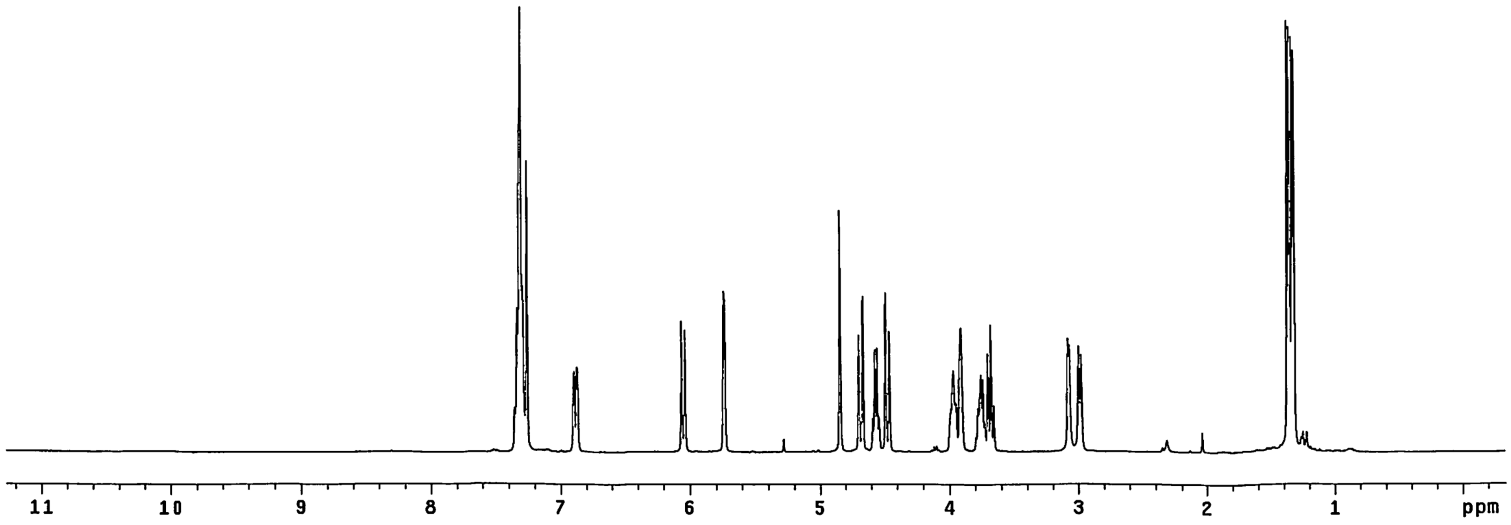
^{13}C NMR ($CDCl_3$, 100 MHz)

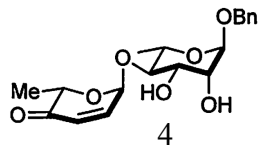




4

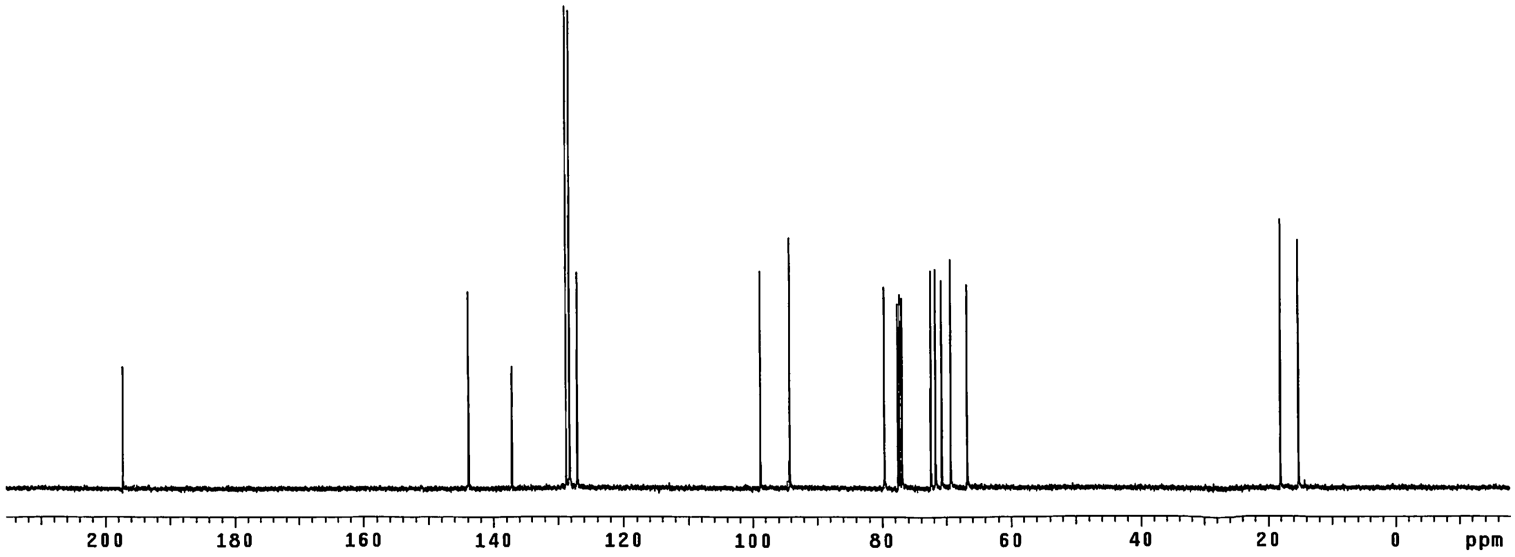
^{1}H NMR ($CDCl_3$, 400 MHz)

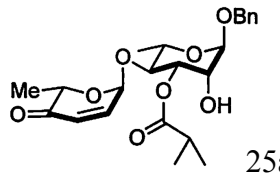




4

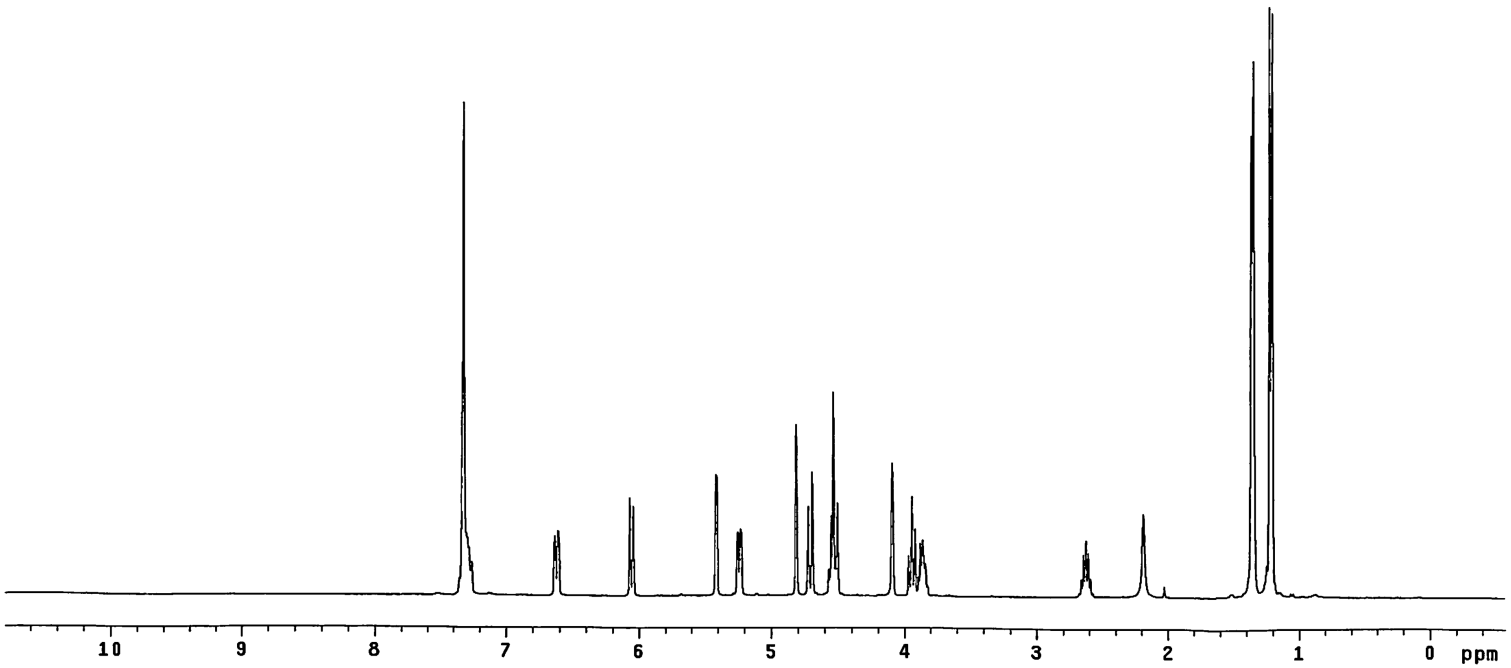
^{13}C NMR ($CDCl_3$, 100 MHz)

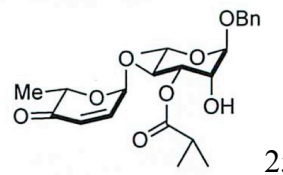




25a

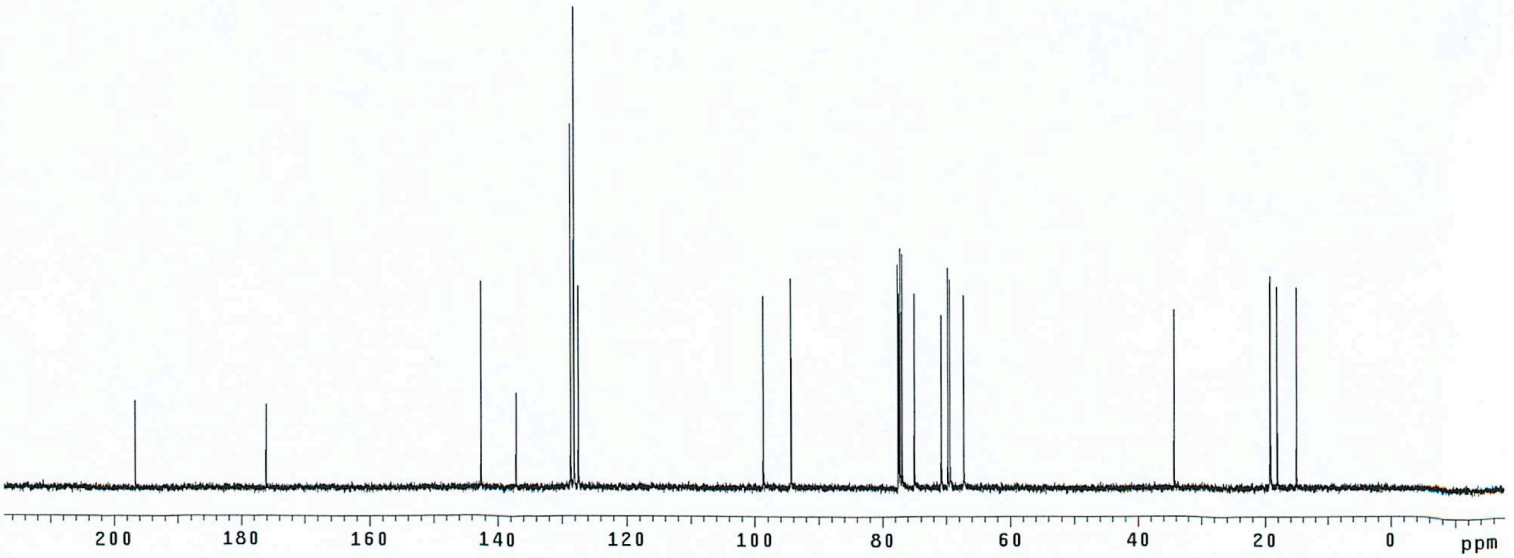
^{1}H NMR ($CDCl_3$, 400 MHz)

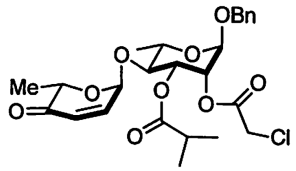




25a

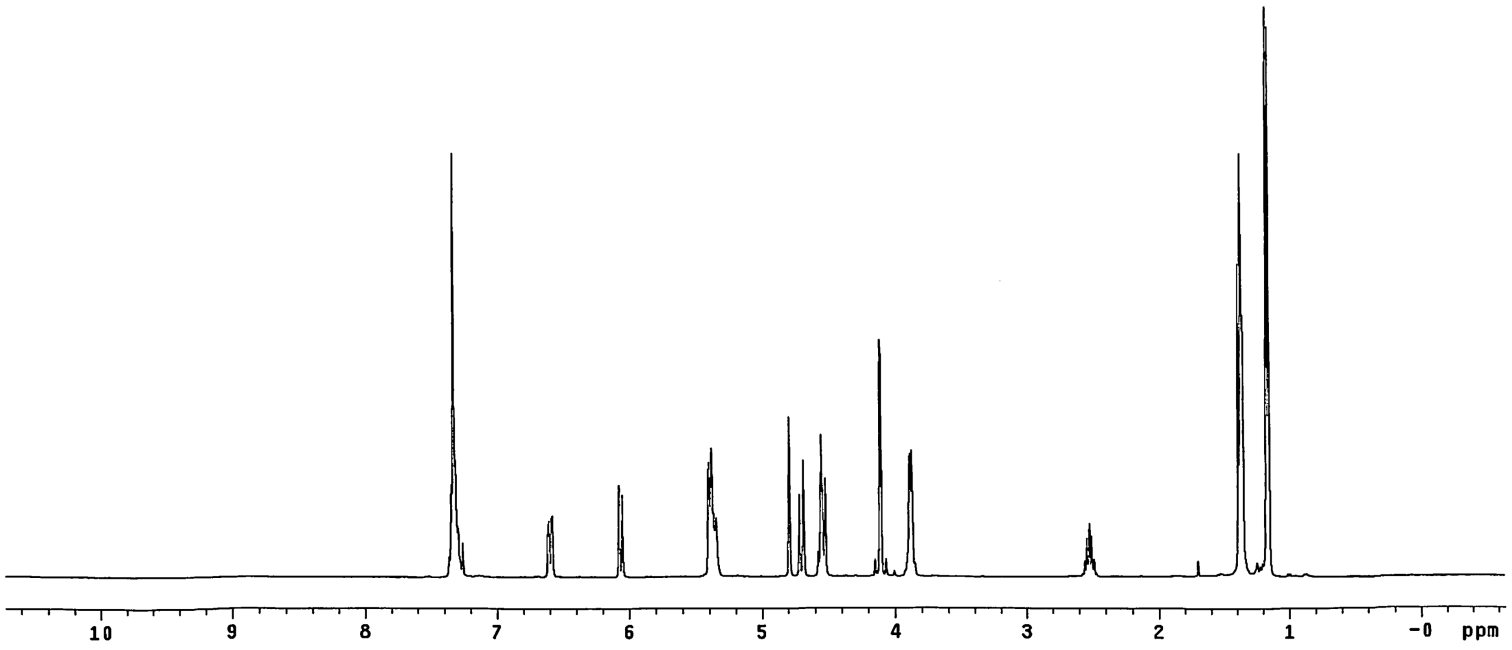
^{13}C NMR ($CDCl_3$, 100 MHz)

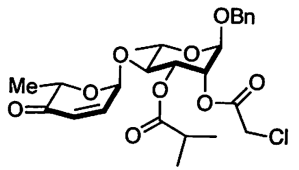




25a-i

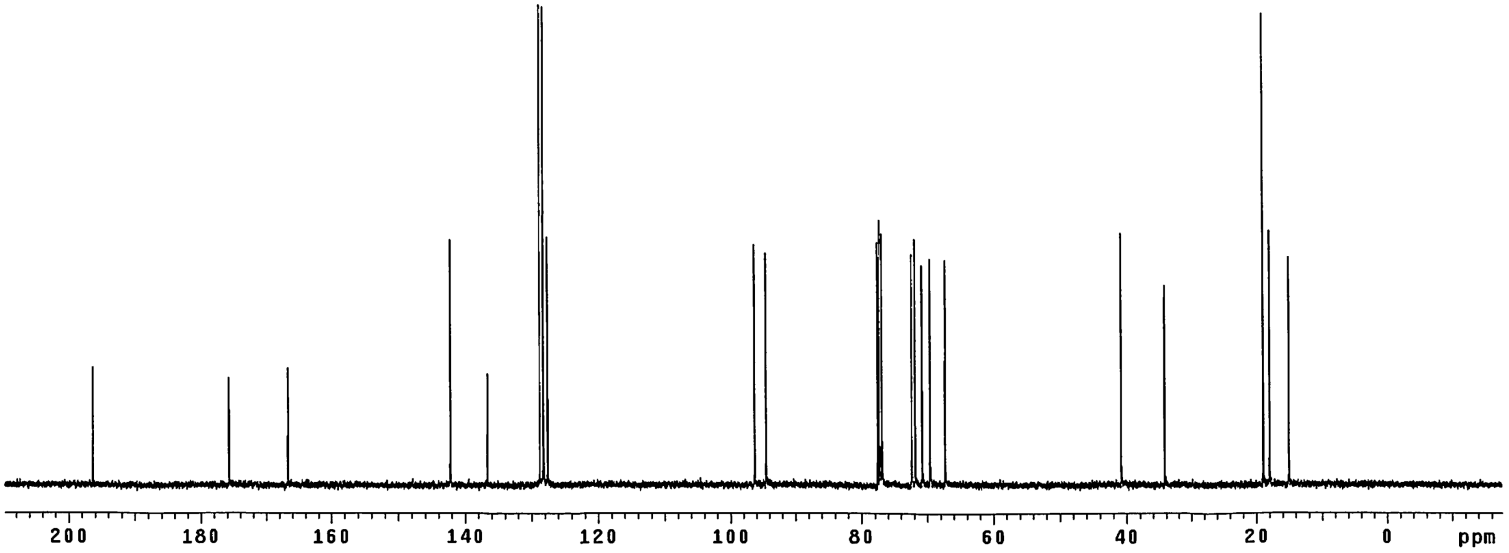
^{1}H NMR ($CDCl_3$, 400 MHz)

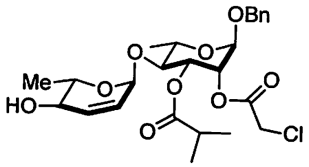




25a-i

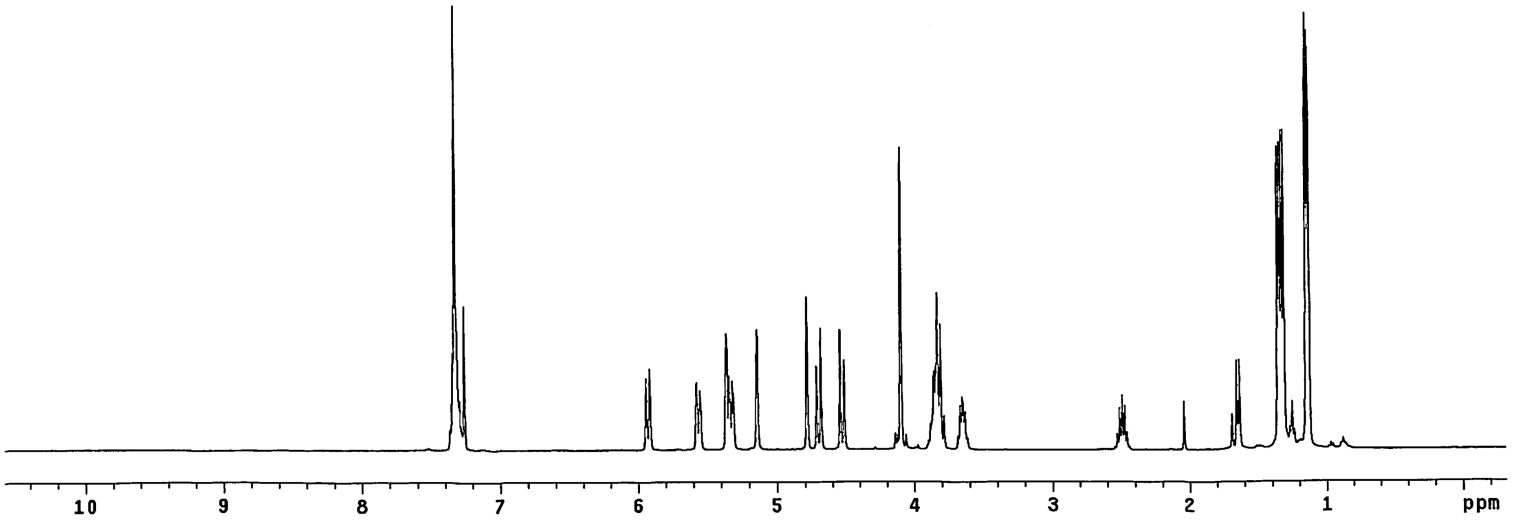
^{13}C NMR ($CDCl_3$, 100 MHz)

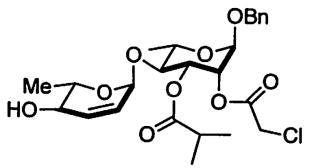




25a-ii

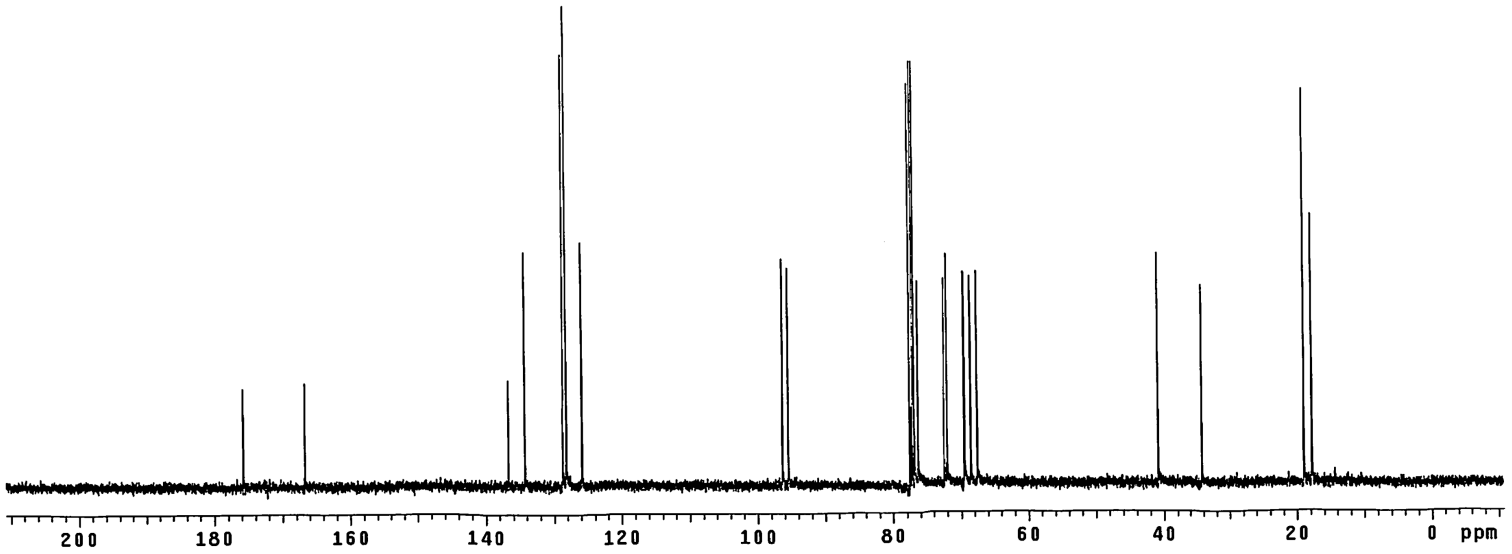
^{1}H NMR ($CDCl_3$, 400 MHz)

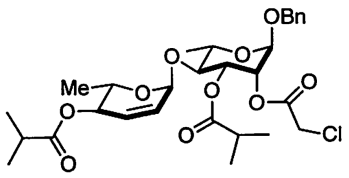




25a-ii

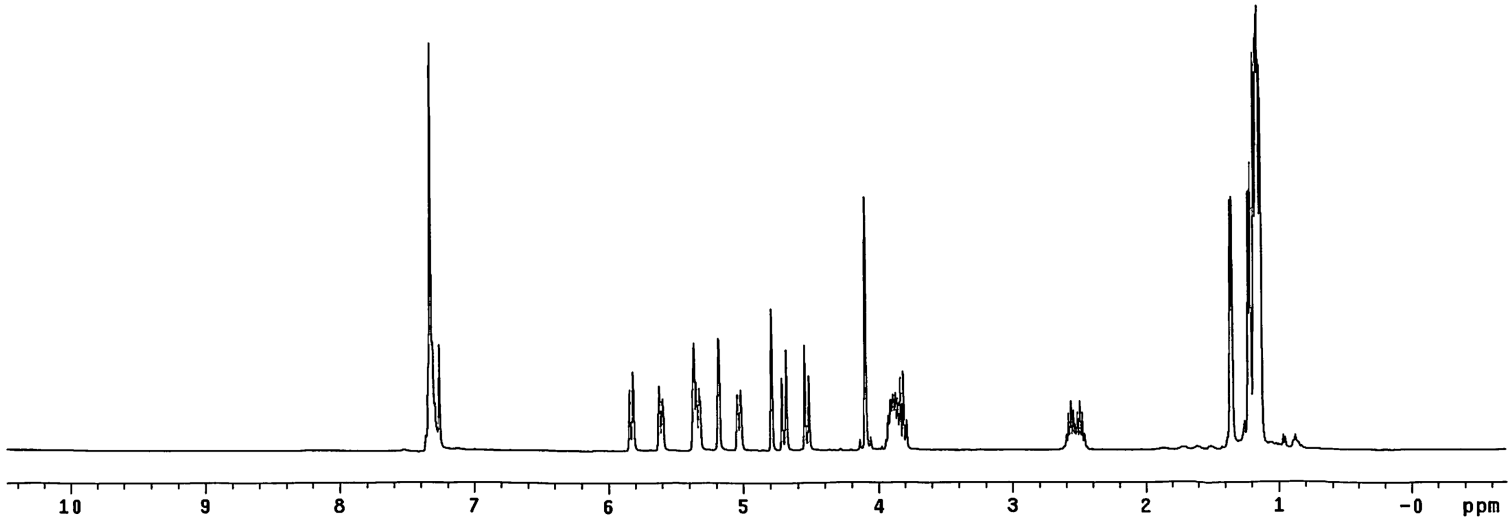
^{13}C NMR ($CDCl_3$, 100 MHz)

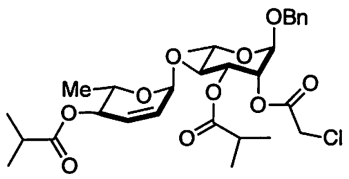




26a

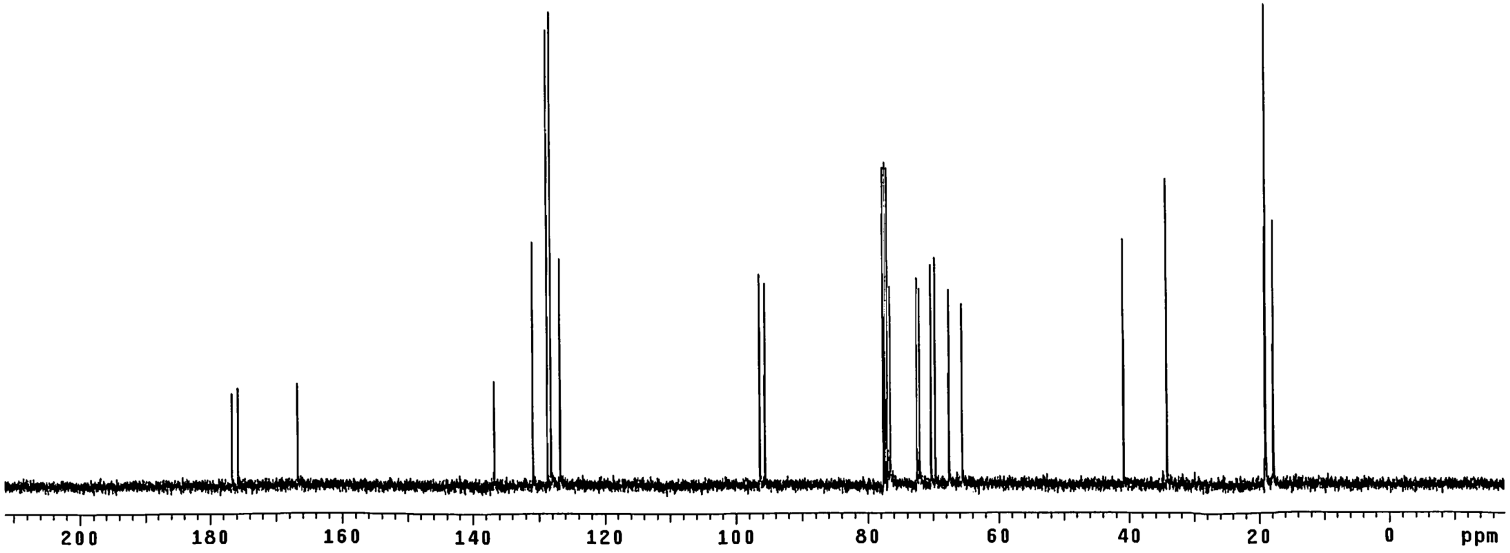
^{1}H NMR ($CDCl_3$, 400 MHz)

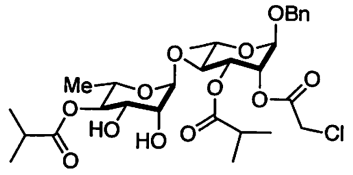




26a

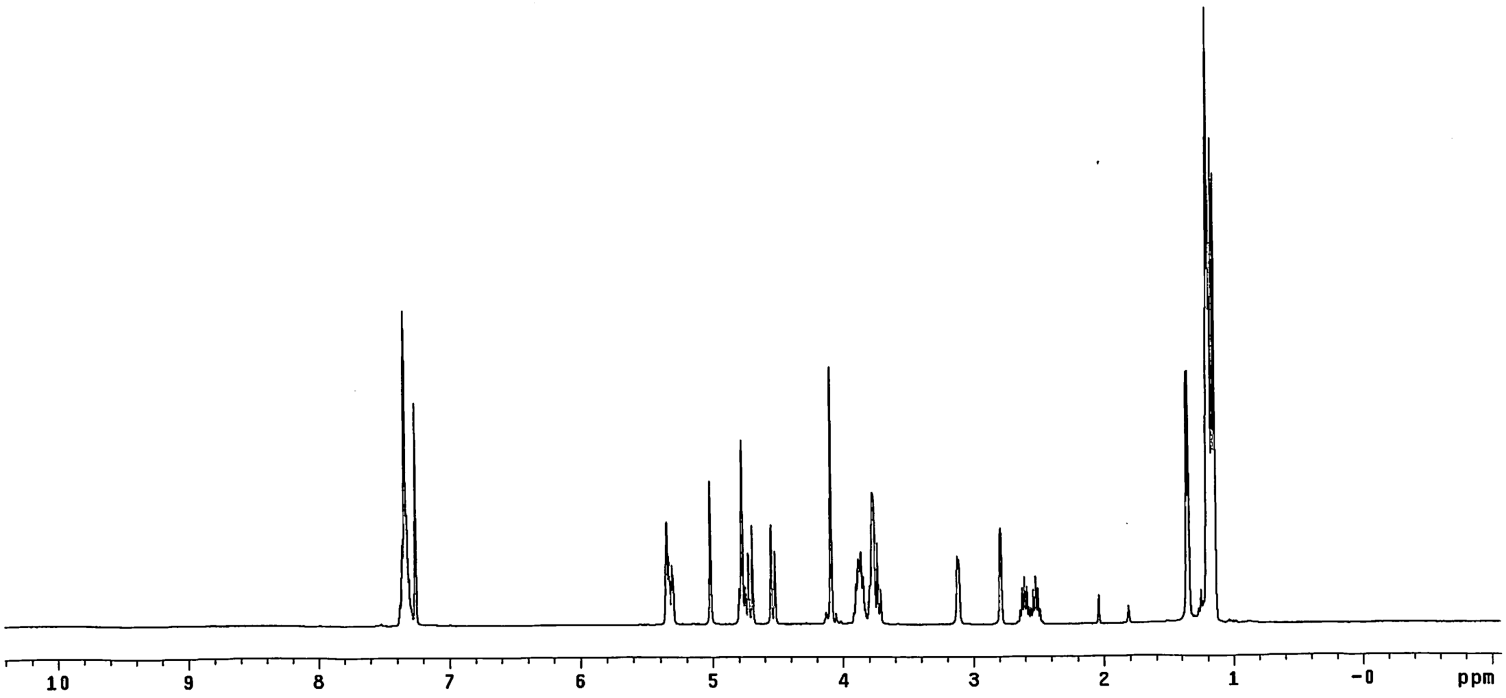
^{13}C NMR ($CDCl_3$, 100 MHz)

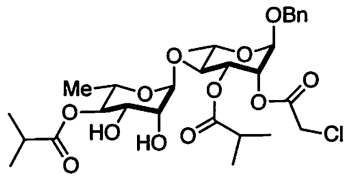




26a-i

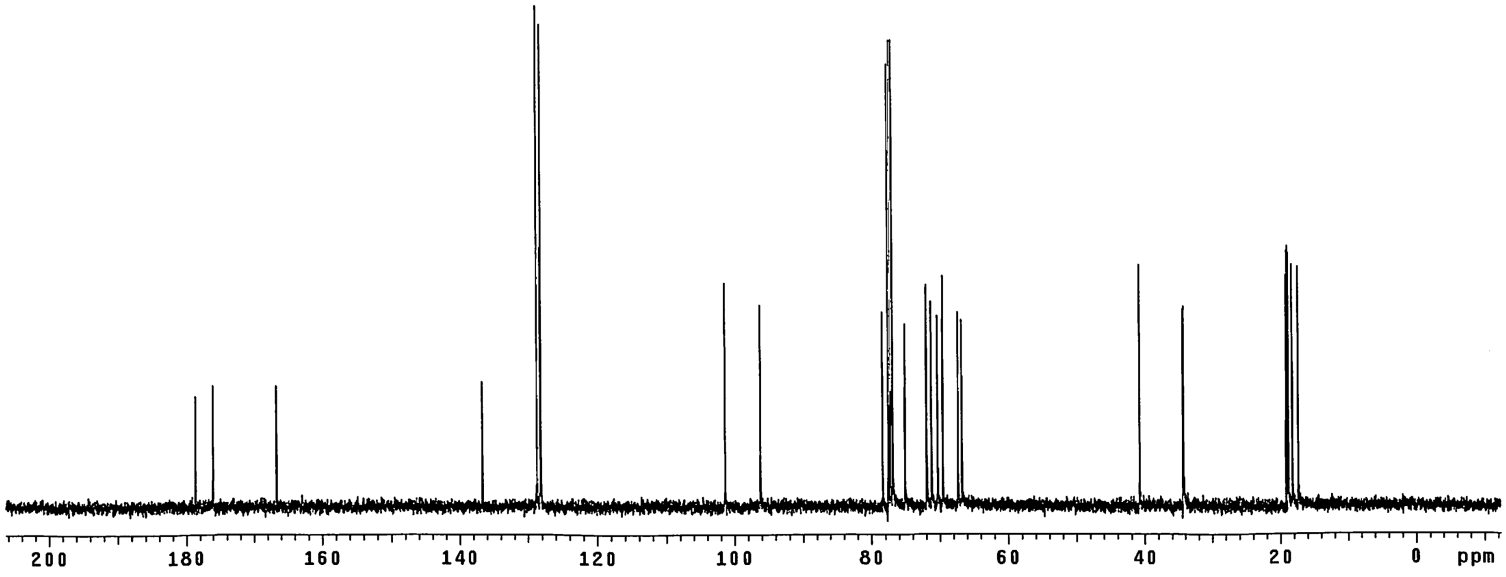
^{1}H NMR ($CDCl_3$, 400 MHz)

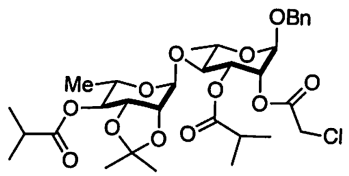




26a-i

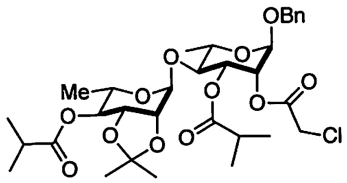
^{13}C NMR ($CDCl_3$, 100 MHz)





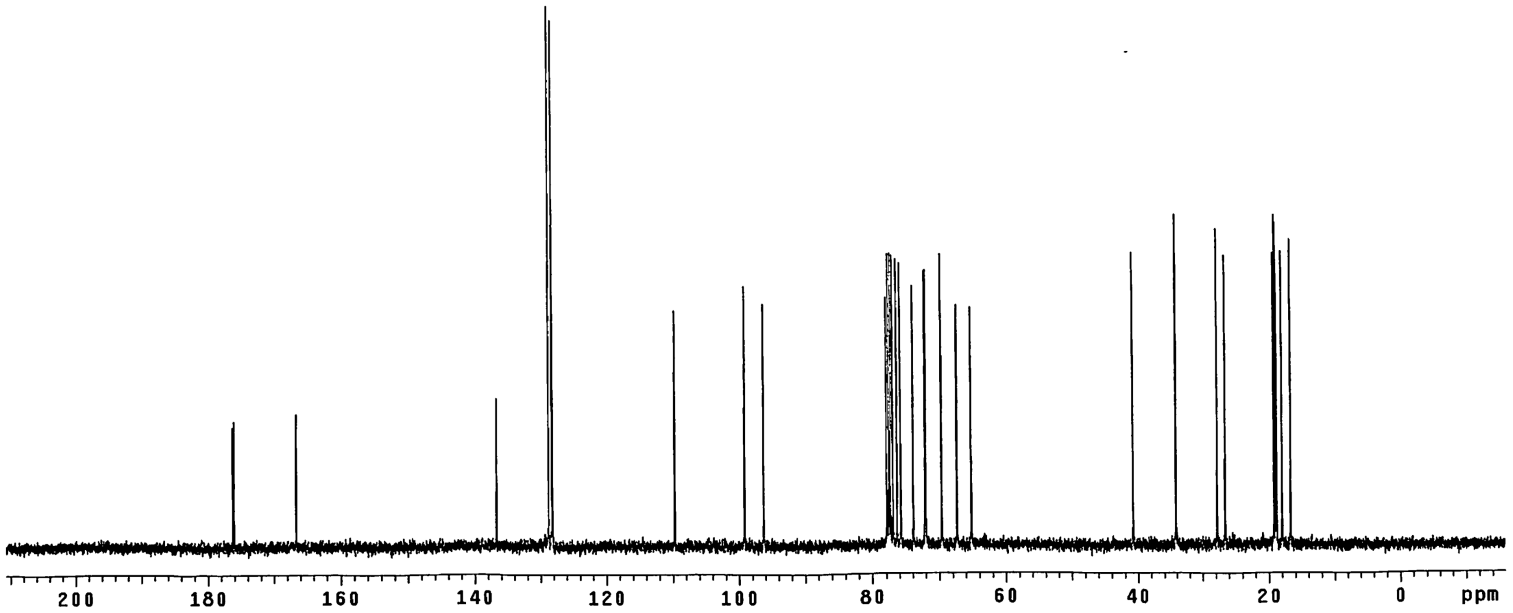
27

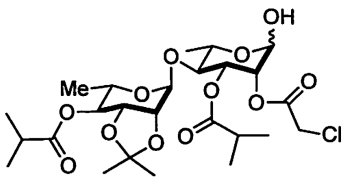
^{1}H NMR ($CDCl_3$, 500 MHz)



27

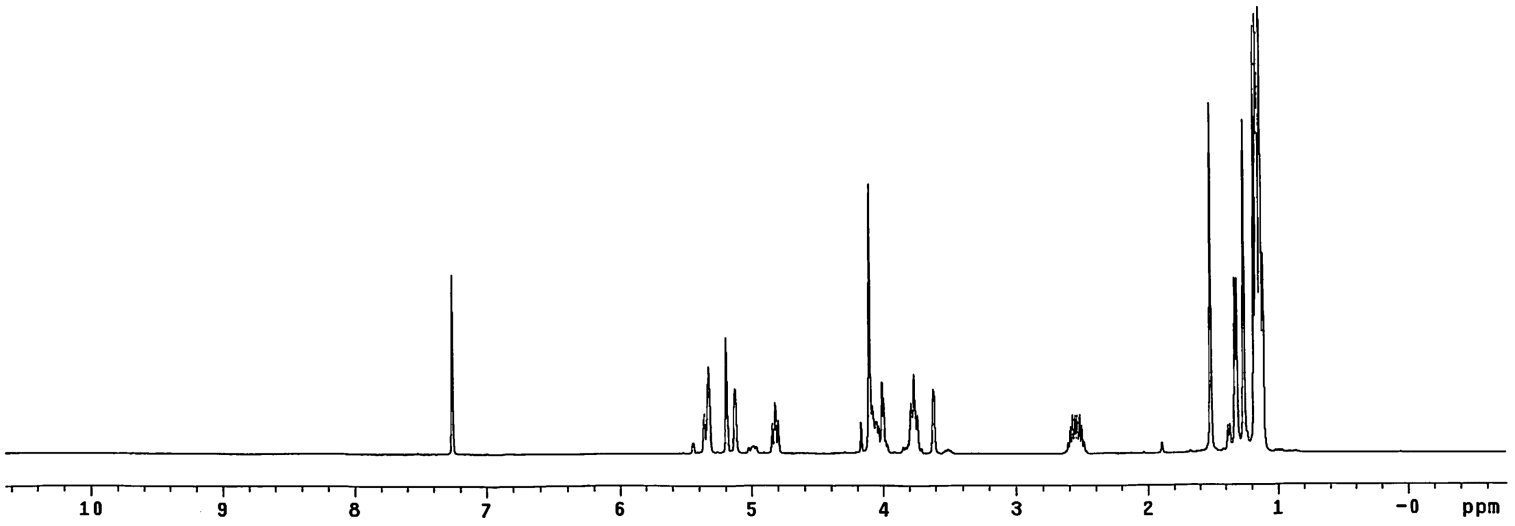
^{13}C NMR ($CDCl_3$, 100 MHz)

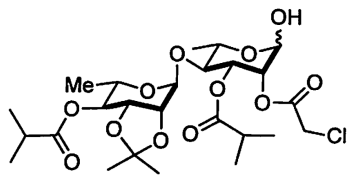




27a

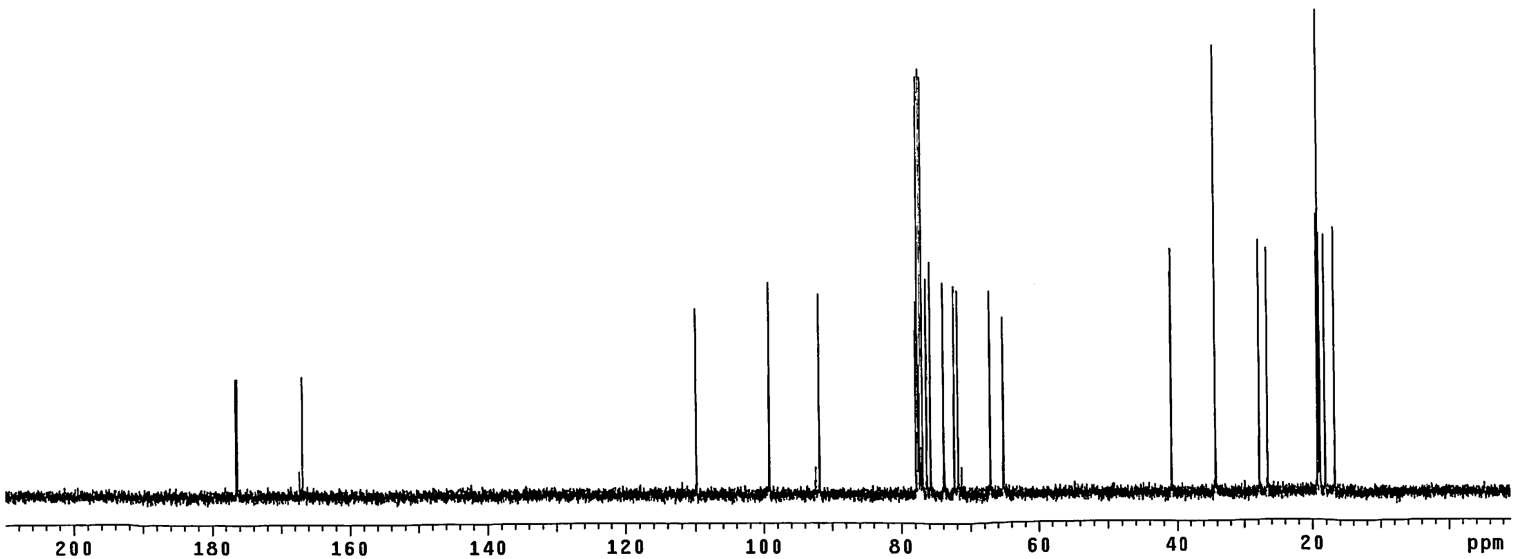
^{1}H NMR ($CDCl_3$, 400 MHz)

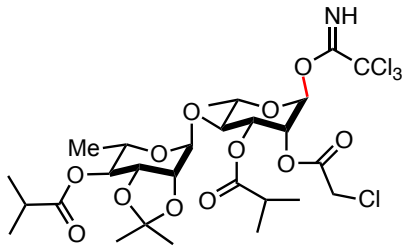




27a

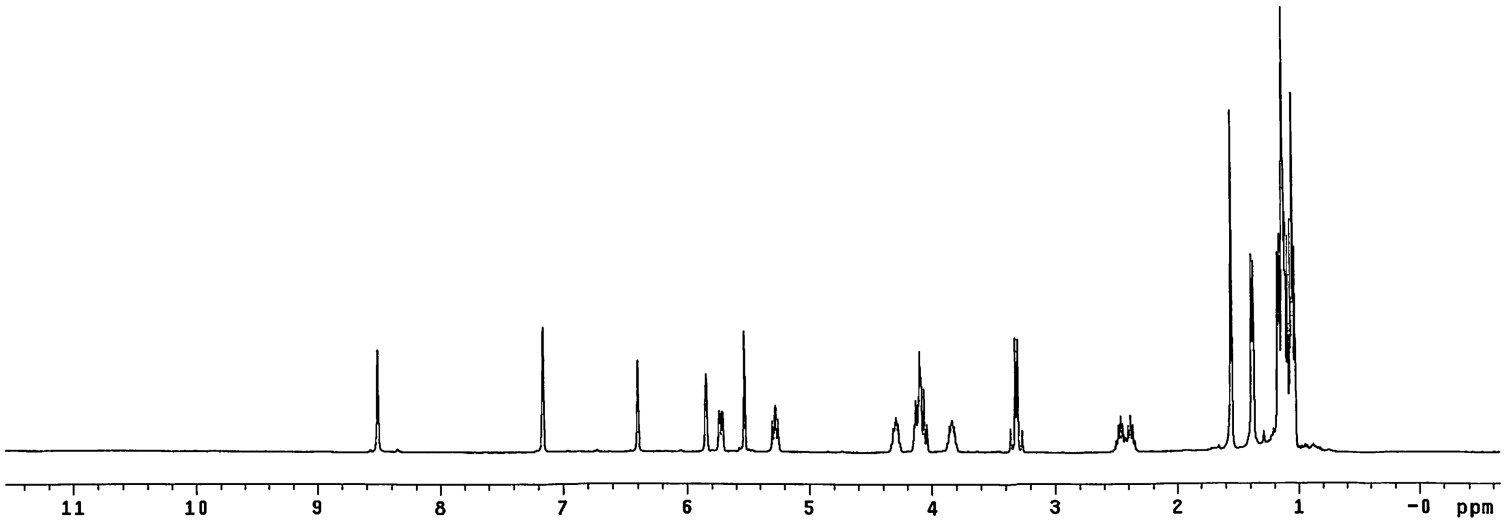
^{13}C NMR ($CDCl_3$, 100 MHz)

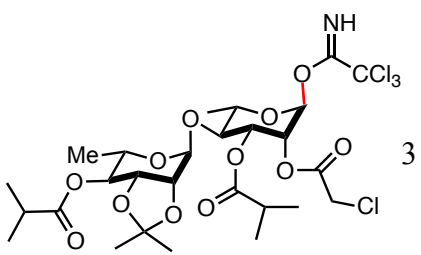




3

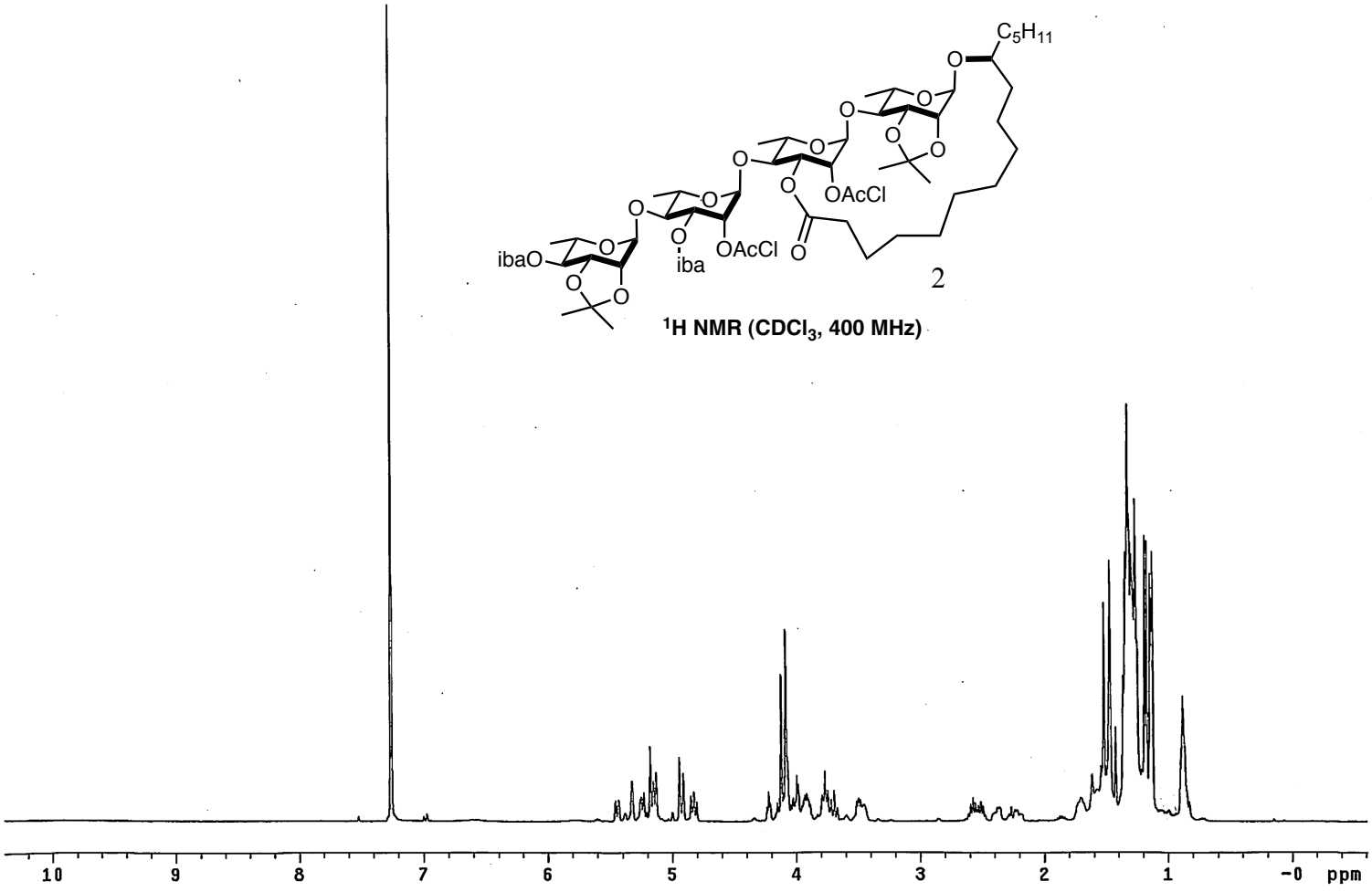
^{1}H NMR (benzene-d_6, 400 MHz)

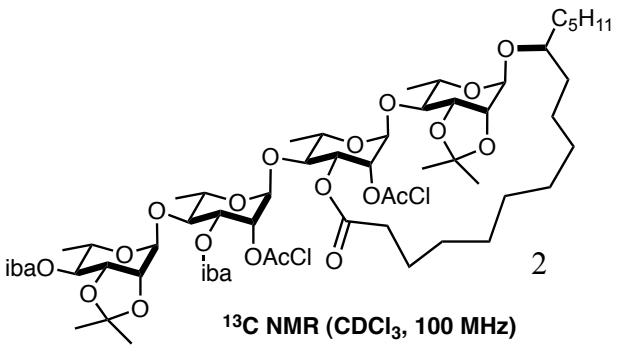




3

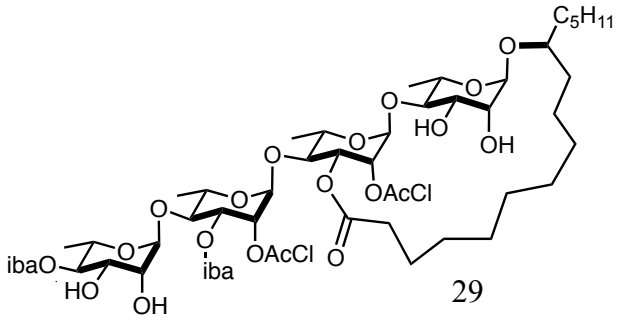
^{13}C NMR (benzene-d_6, 100 MHz)


C5H11
OAcCl
OAcCl
ibaO
iba
2
1H NMR (CDCl3, 400 MHz)
10
9
8
7
6
5
4
3
2
1
-0
ppm



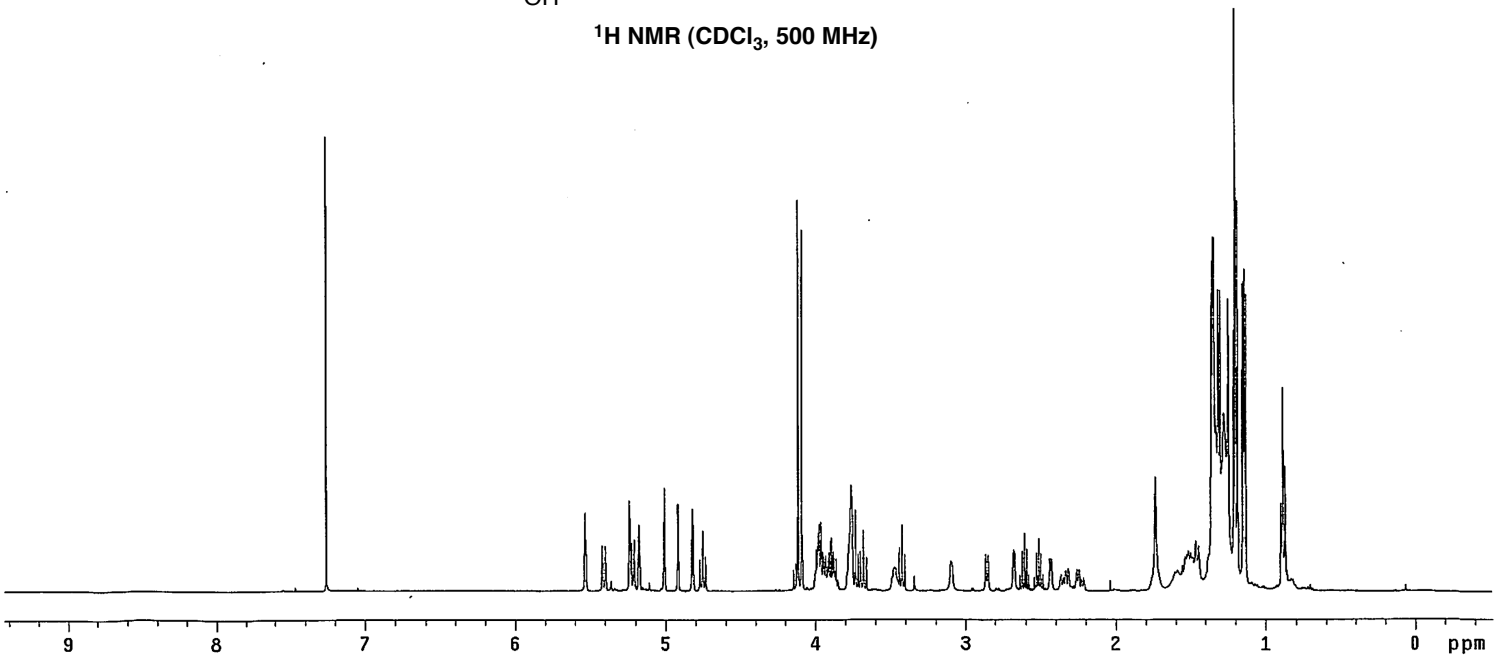
2

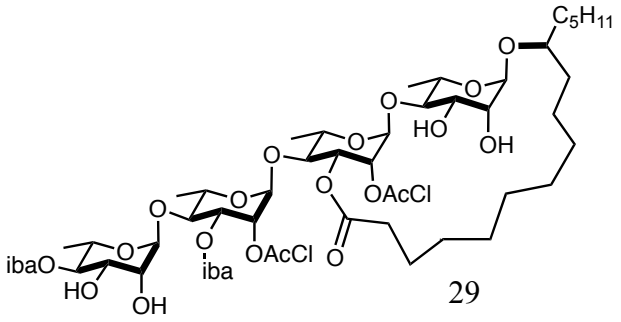
^{13}C NMR ($CDCl_3$, 100 MHz)



29

^{1}H NMR ($CDCl_3$, 500 MHz)

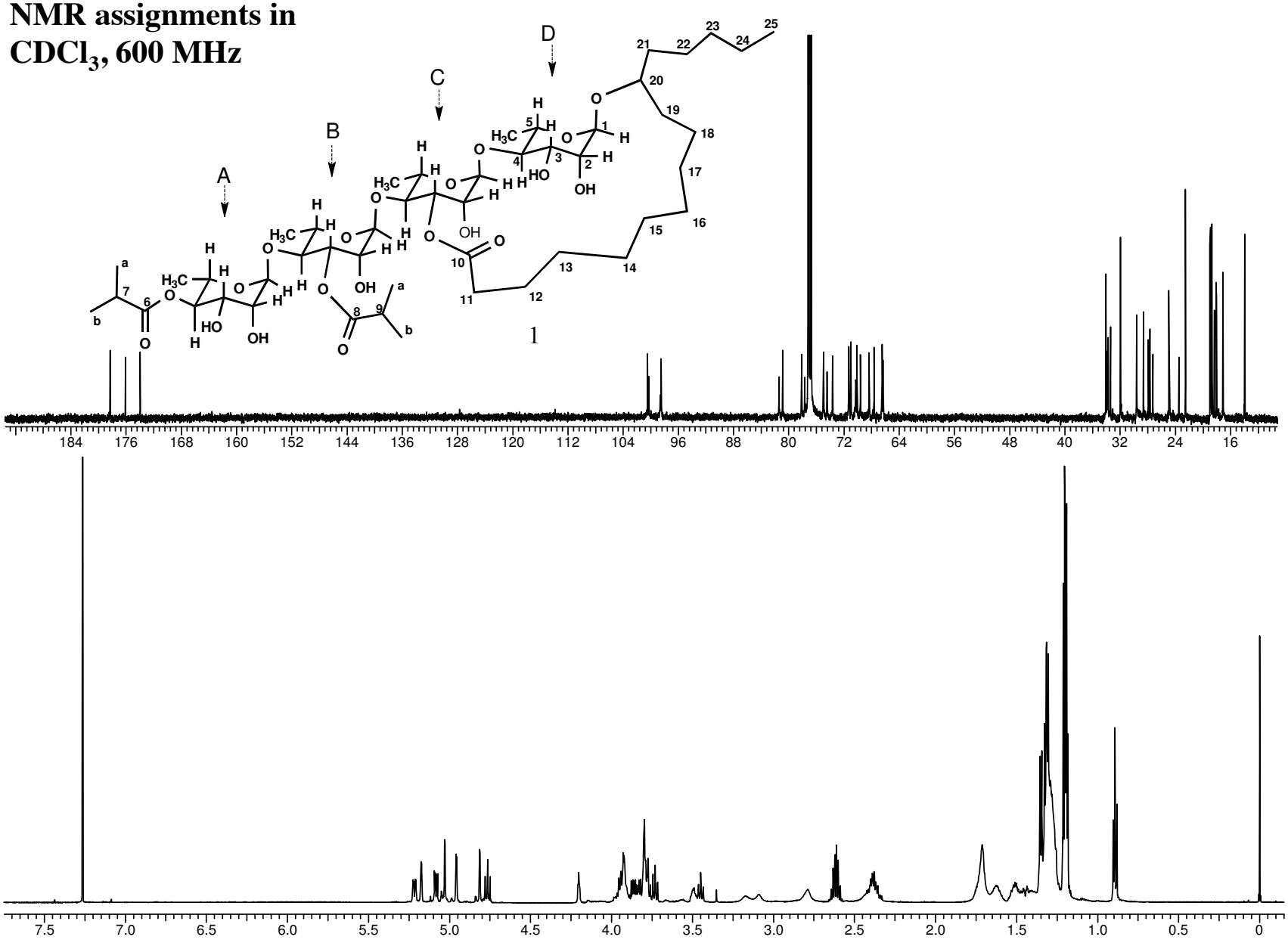




29

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

NMR assignments in $CDCl_3$, 600 MHz

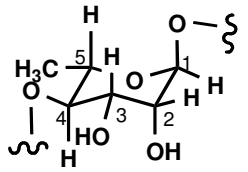


Spin system identification for each sugar moiety (A-D) (for synthetic 1)

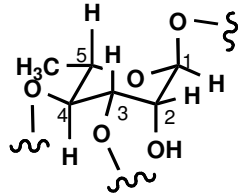
zTOCSY1D experimental subspectra (b-e); Control ^{1}H NMR spectrum - (a)

Sugar moiety

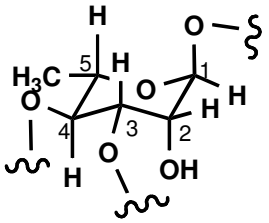
D



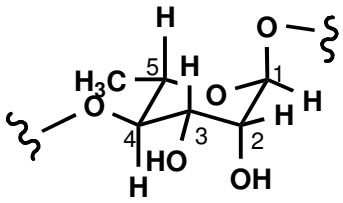
C



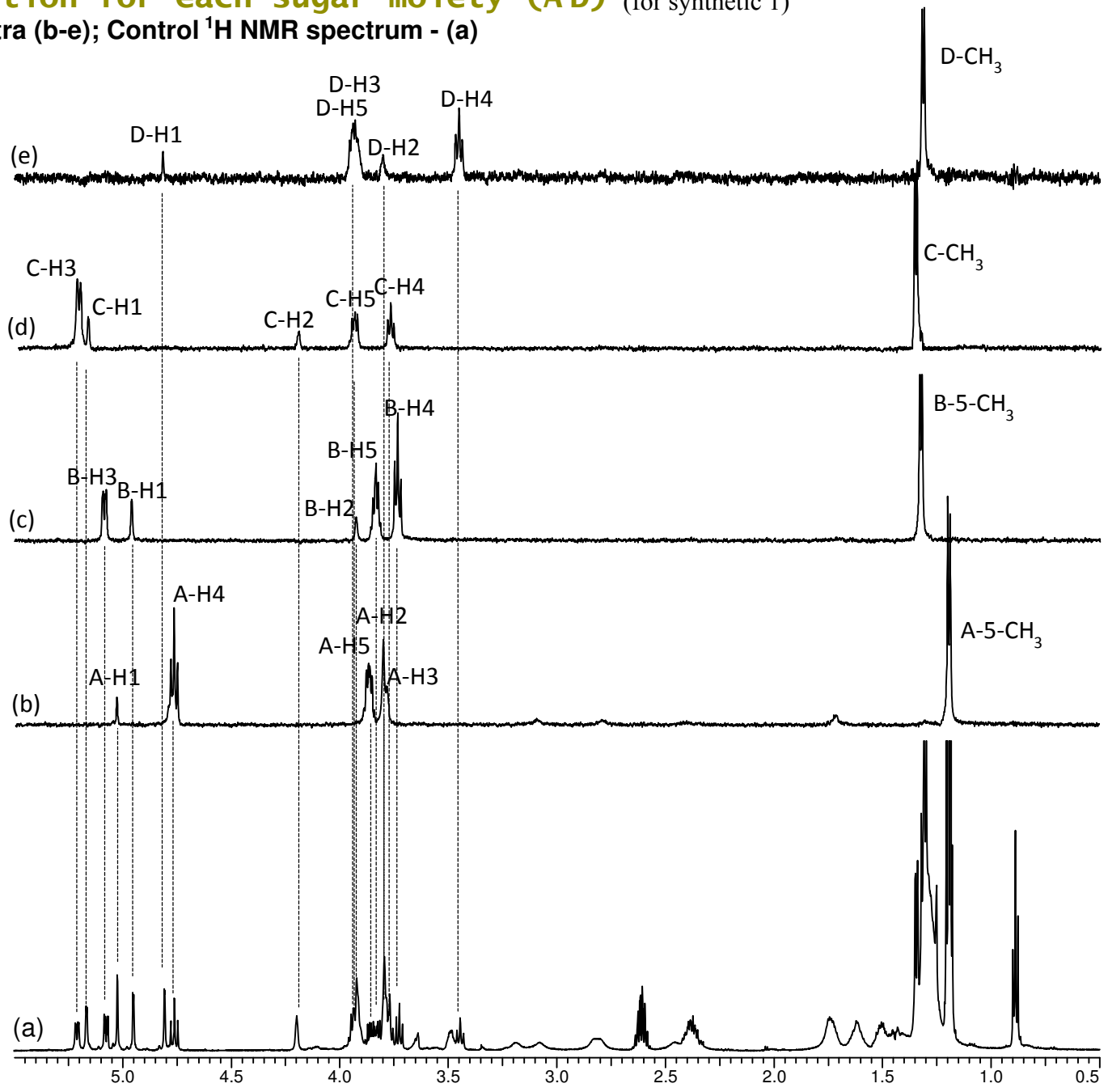
B



A

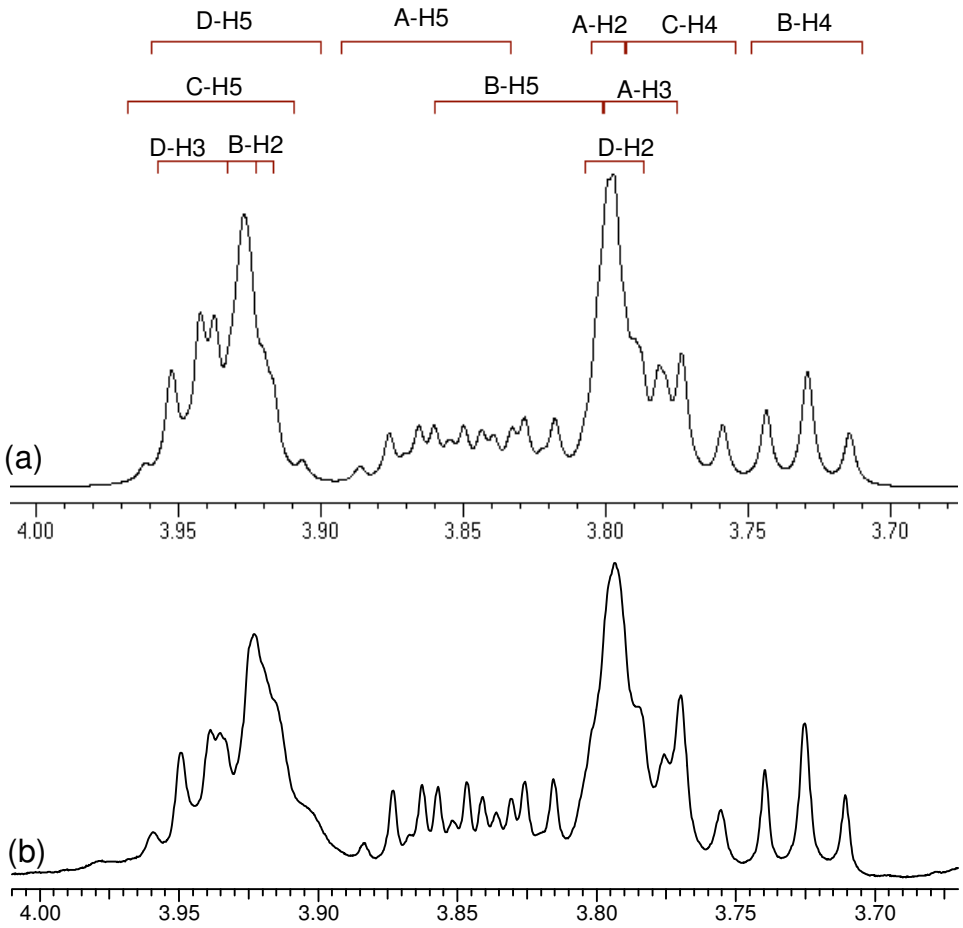


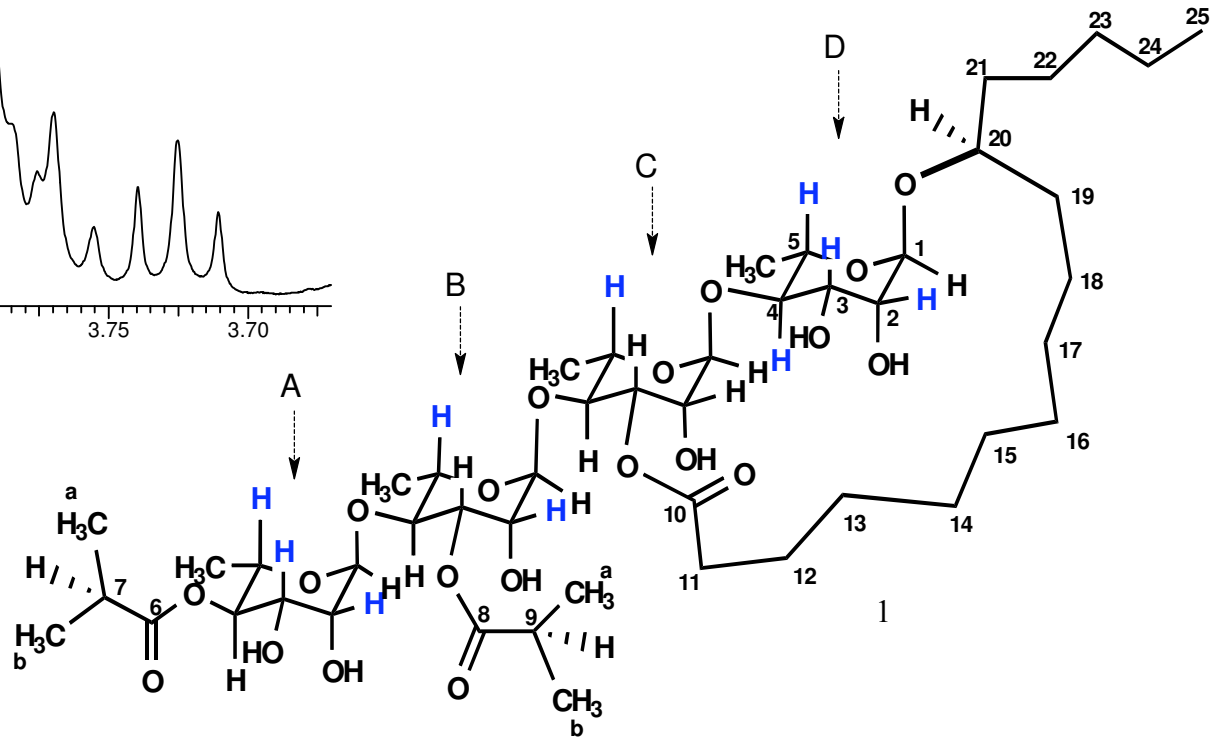
Control ^{1}H NMR



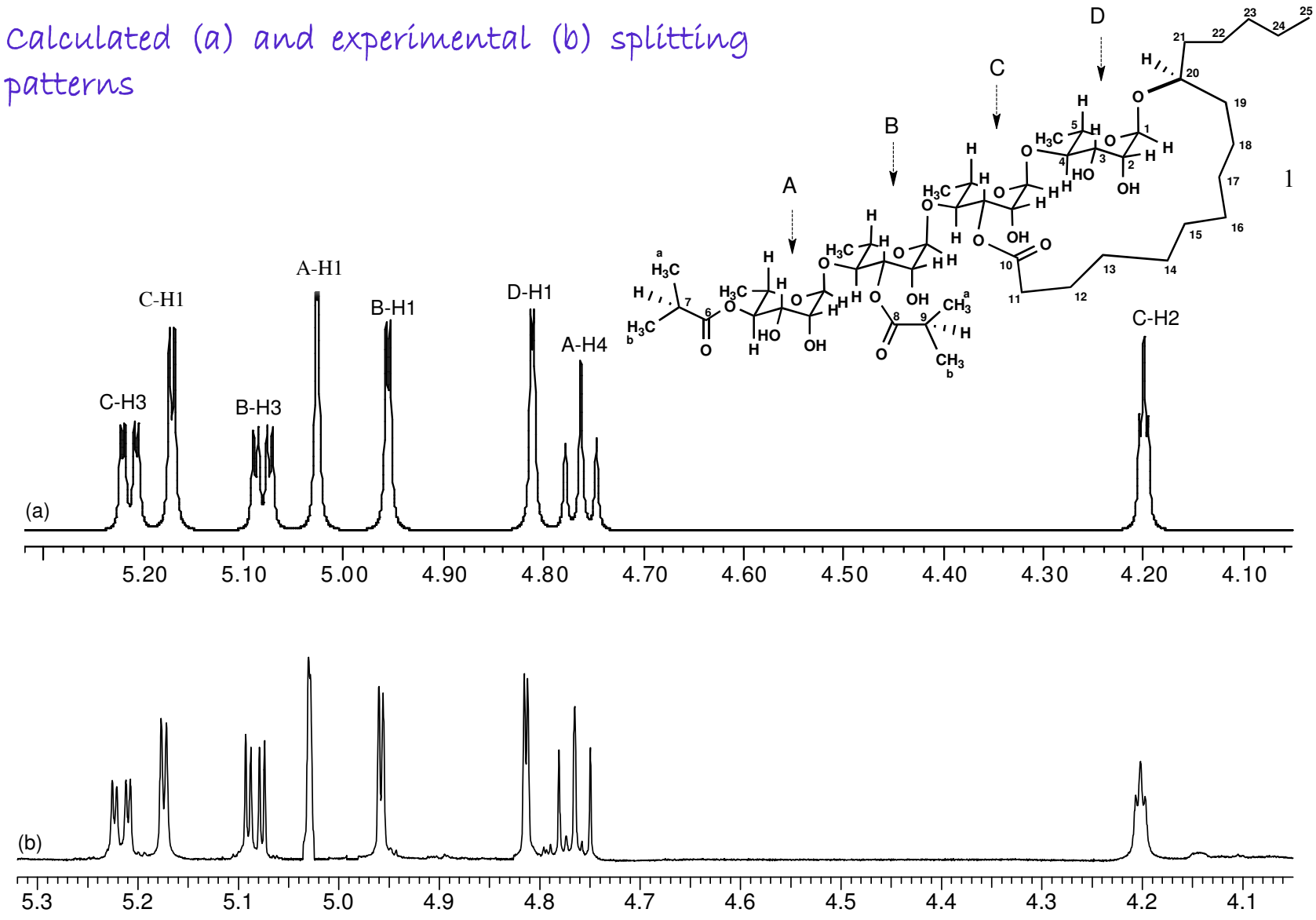
Calculated (a) and experimental (b) splitting patterns

*Chemical shifts and coupling constants of the overlapped proton peaks **B-H2, D-H3, C-H5, D-H5, A-H5, B-H5, D-H2, A-H2, A-H3, C-H4** were identified using high-resolution 1D zTOCSY experiments

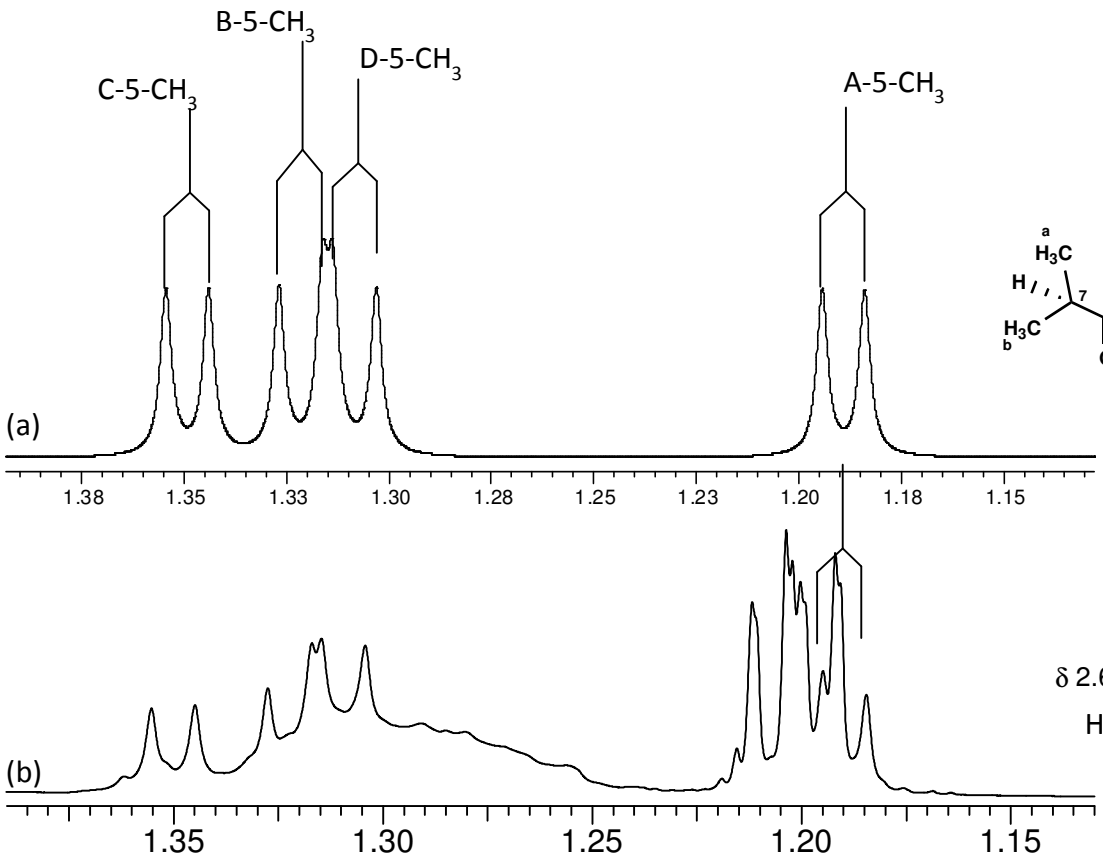


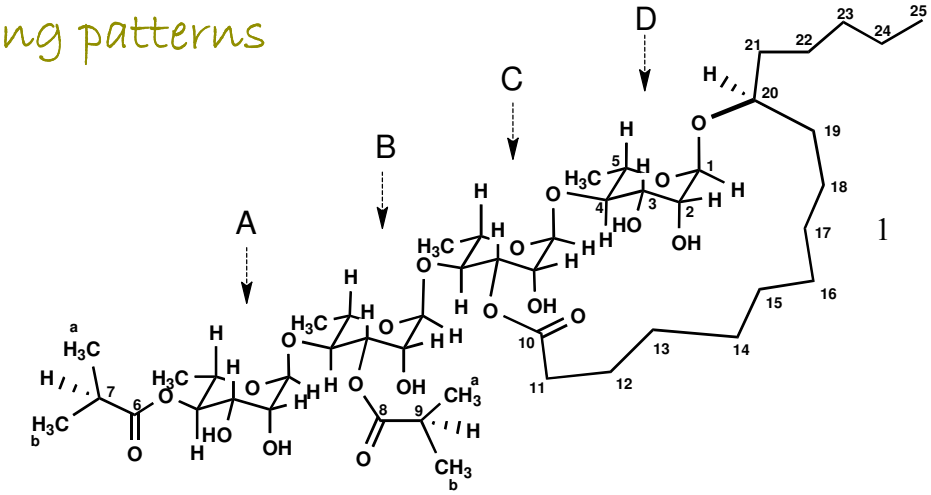


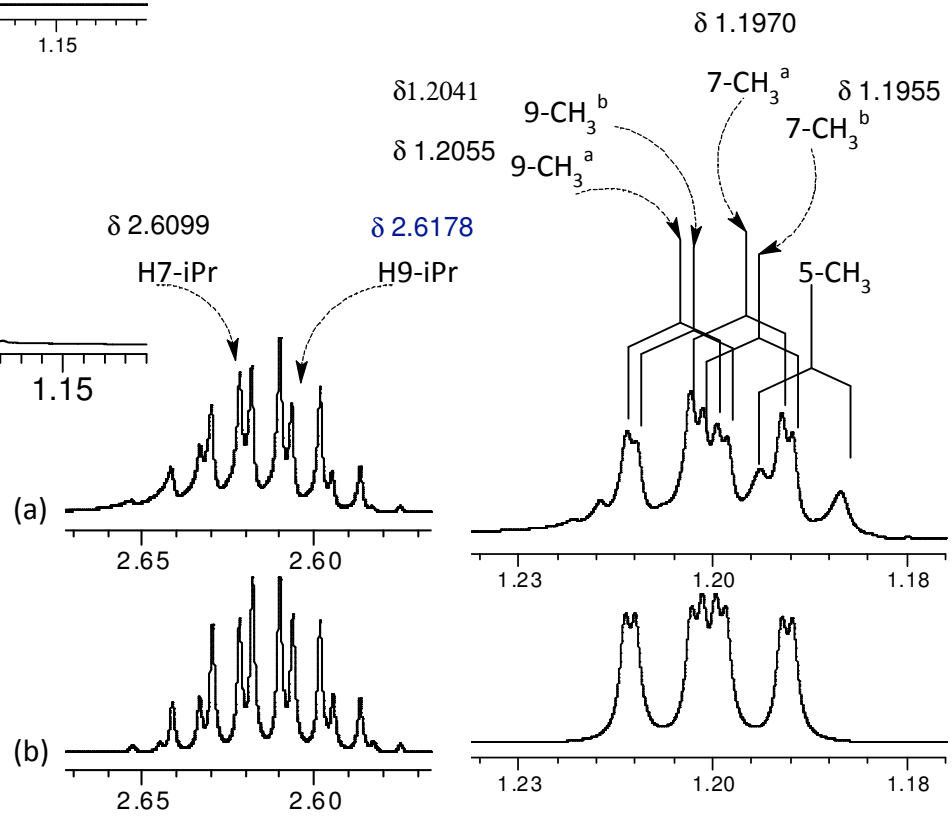
Calculated (a) and experimental (b) splitting patterns



Calculated (a) and experimental (b) splitting patterns



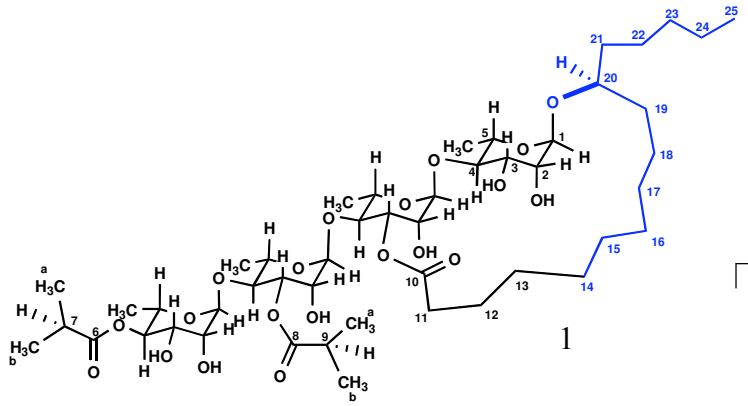




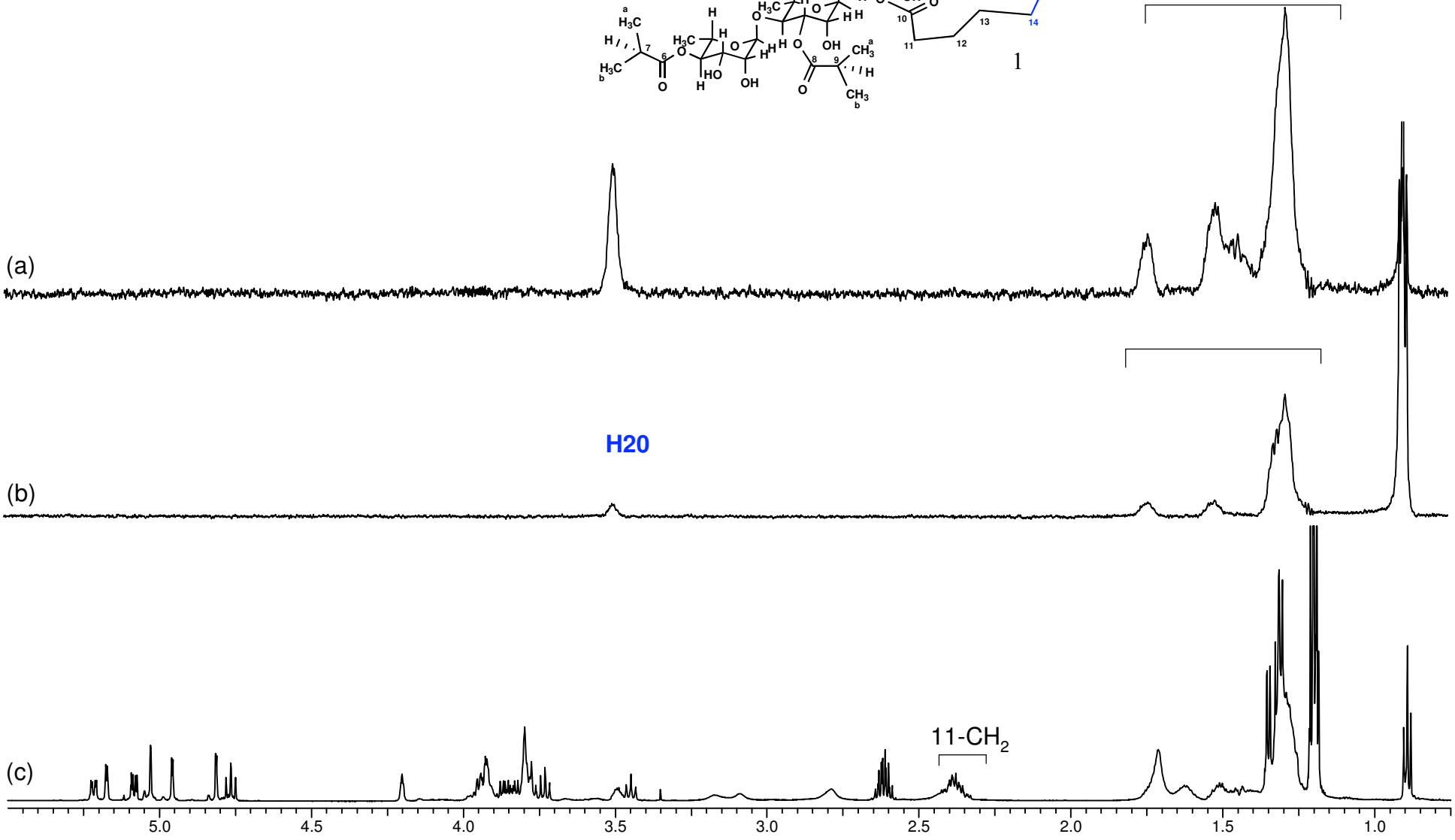
Selective excitation of H20 at 3.50 ppm (*a*);

Selective excitation of H25 (CH_3) at 0.89 ppm (*b*);

Control ^{1}H NMR spectrum (*c*).

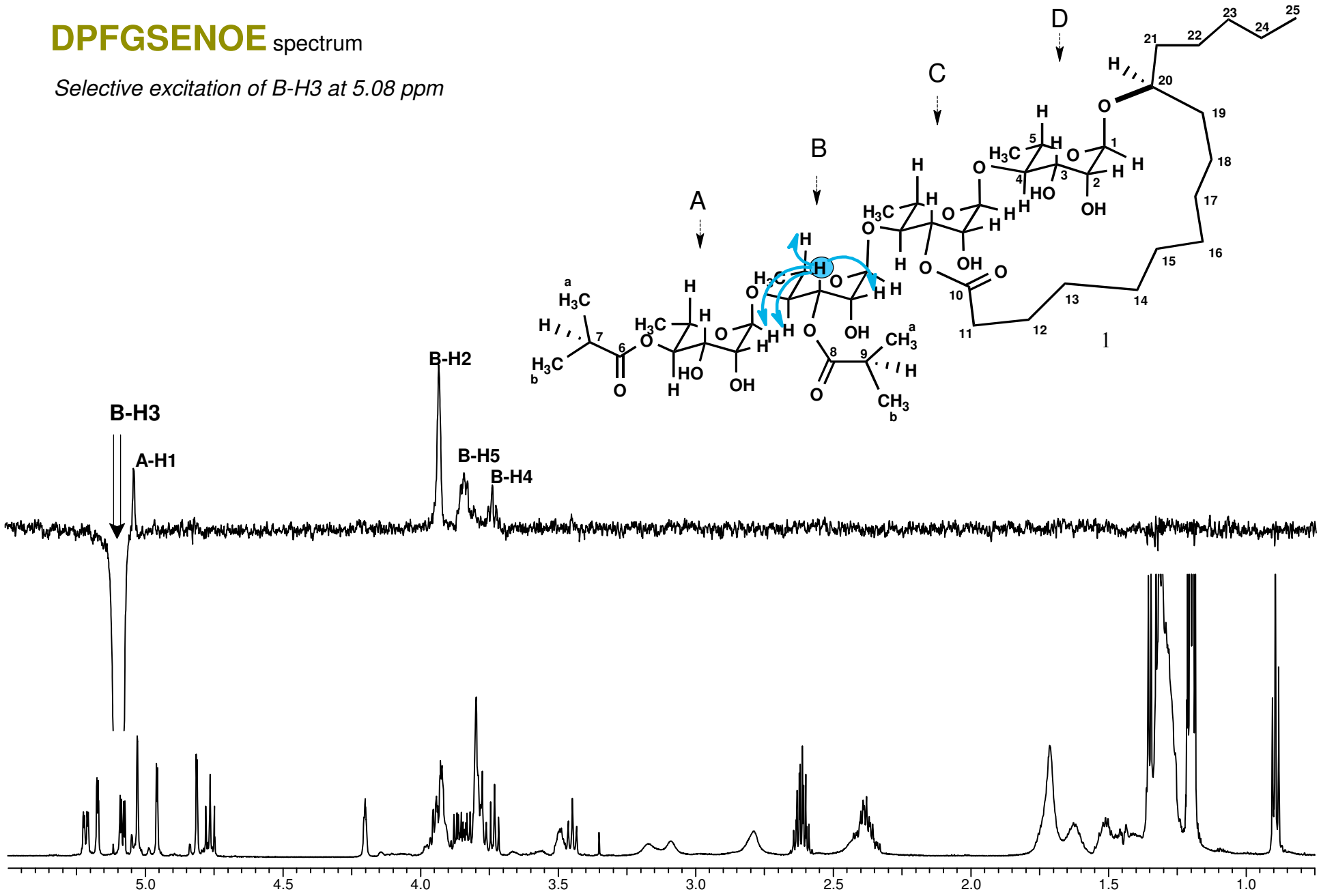


1



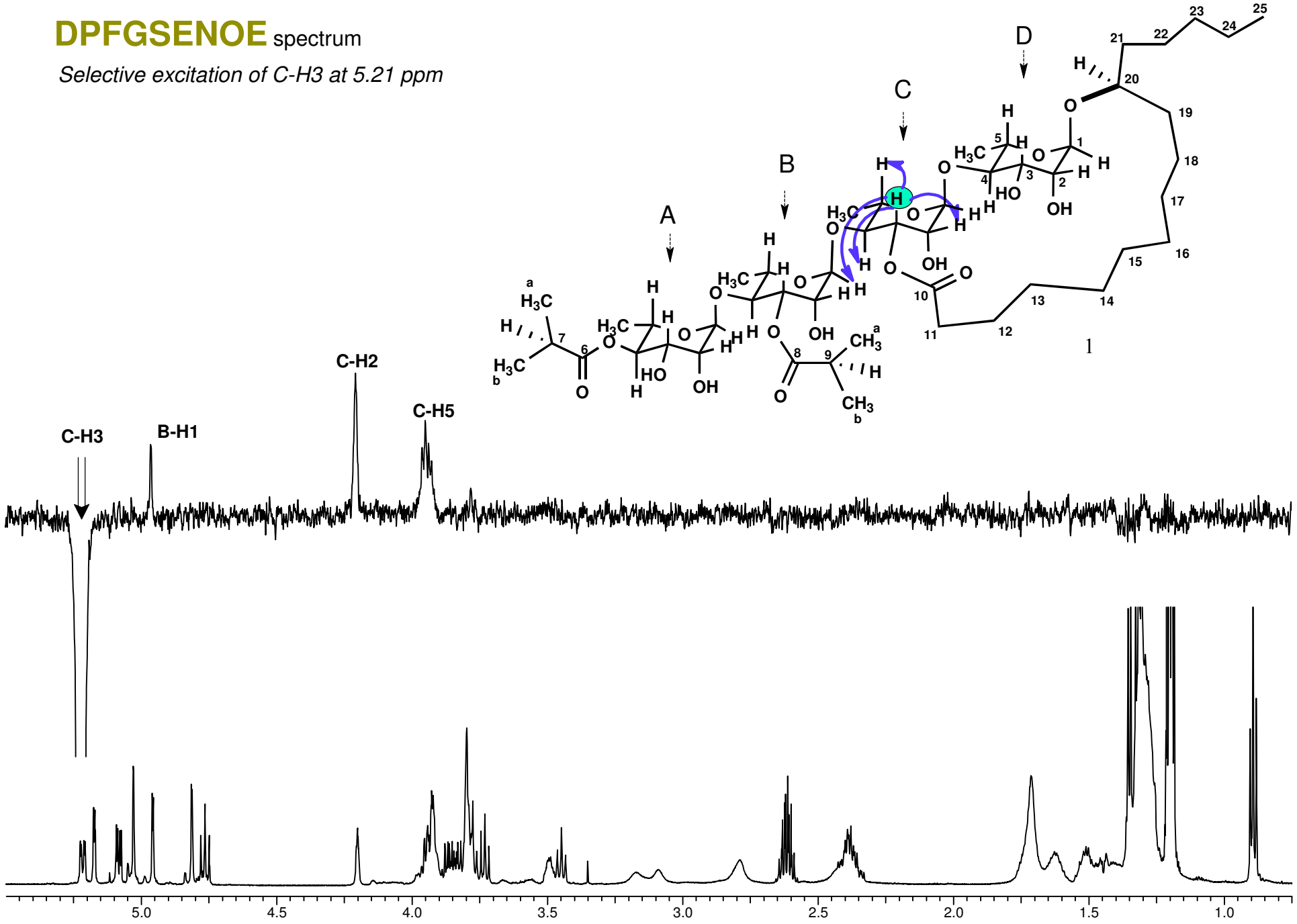
DPFGSENOE spectrum

Selective excitation of B-H3 at 5.08 ppm



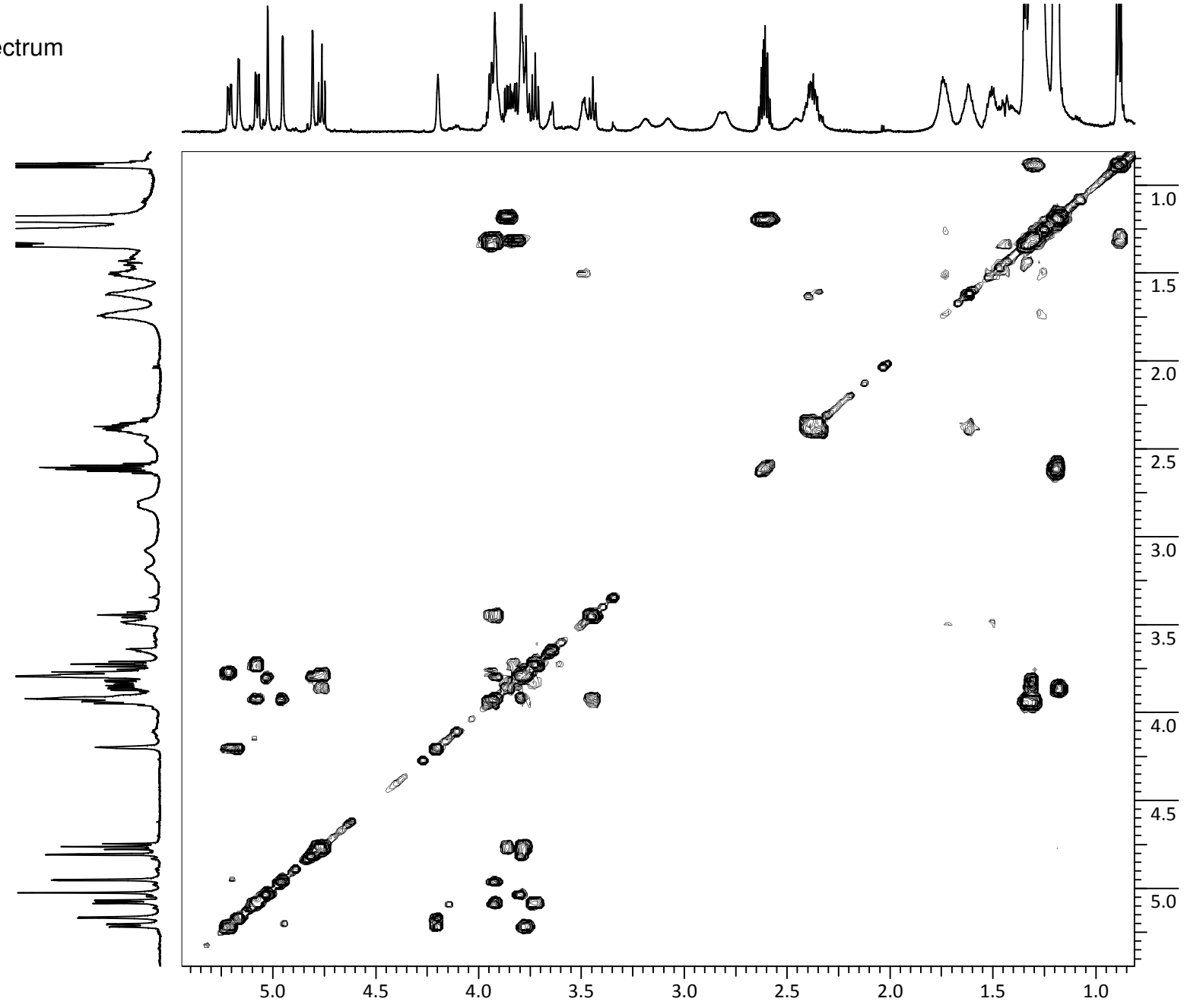
DPFGSENOE spectrum

Selective excitation of C-H3 at 5.21 ppm



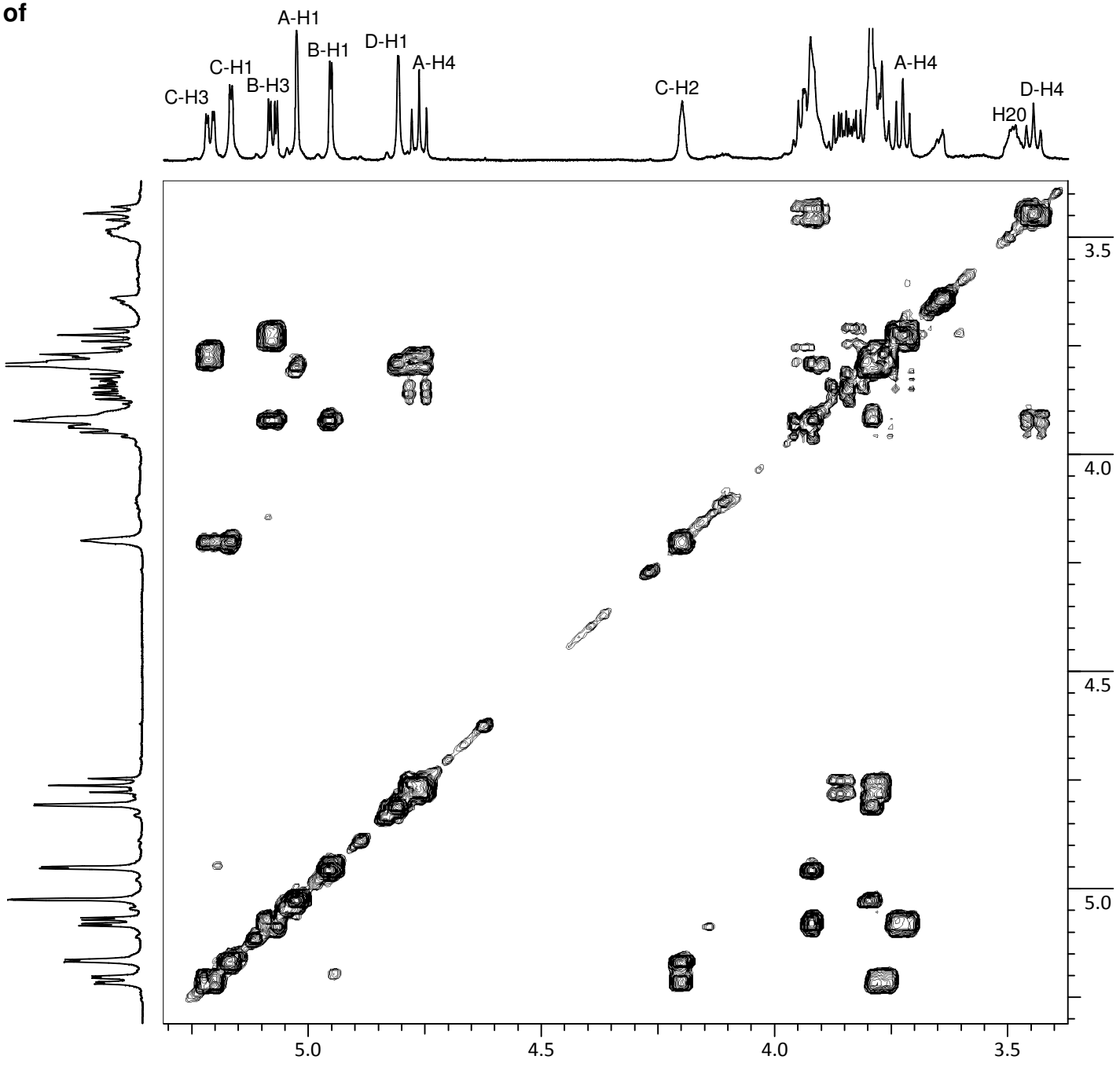
gCOSY spectrum

(for synthetic 1)



Expanded portion of the gCOSY spectrum

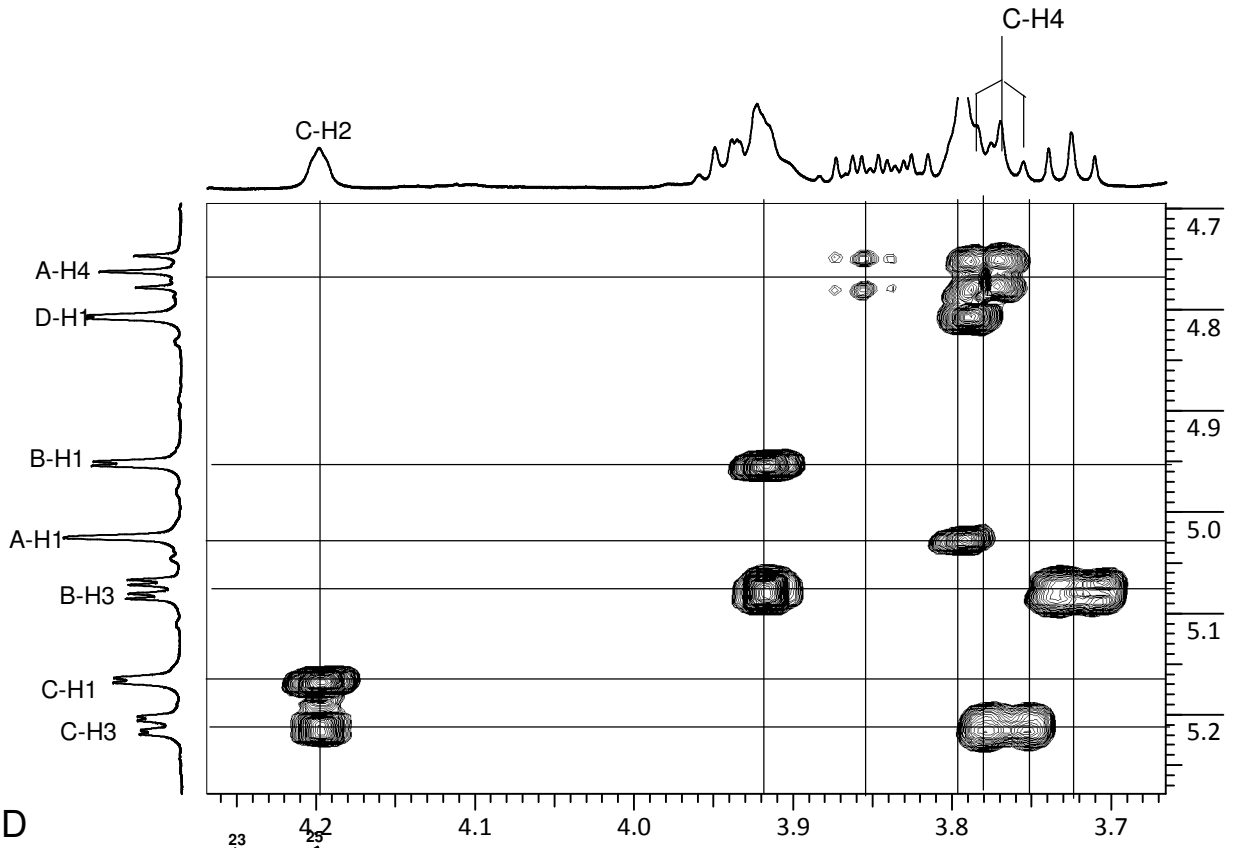
(for synthetic 1)

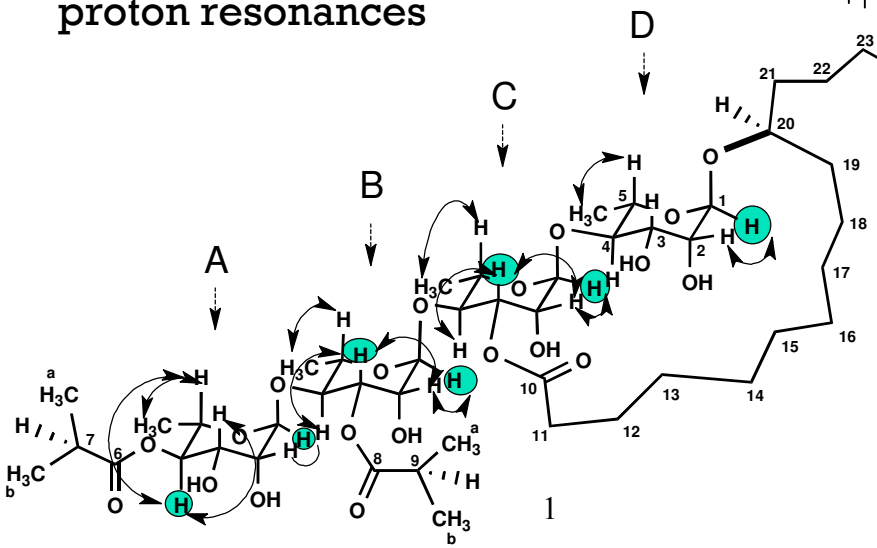


Expanded portions of the gCOSY spectrum

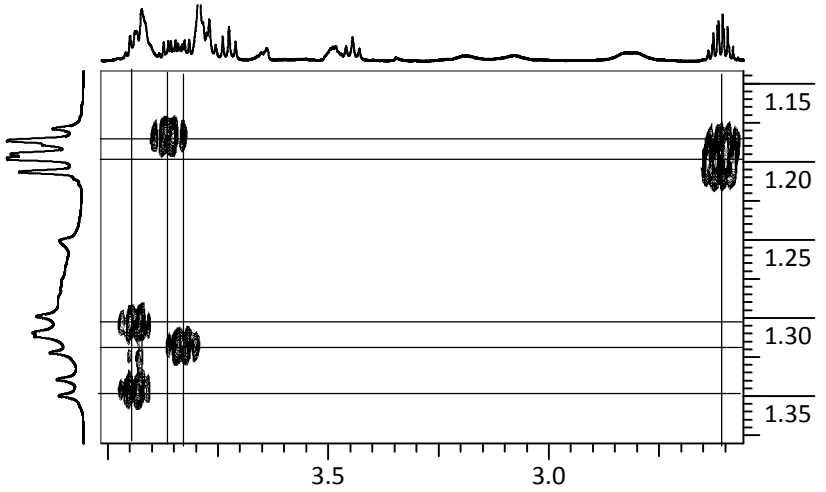
^{1}H-^{1}H connectivities

identification of overlapped A-H5, B-H5, C-5 and D-H5 proton resonances

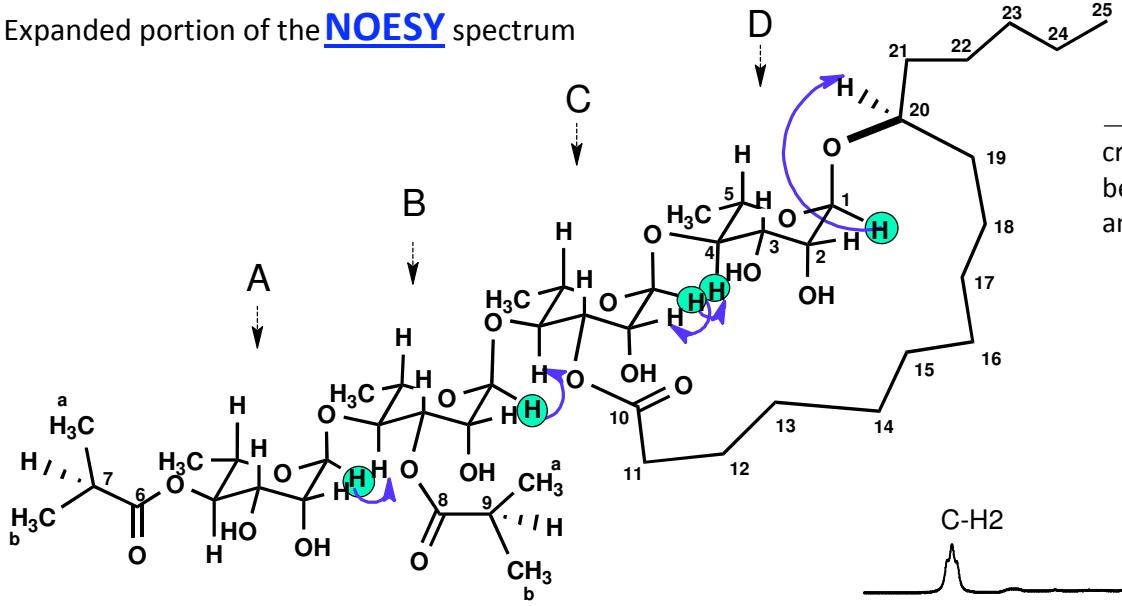




1



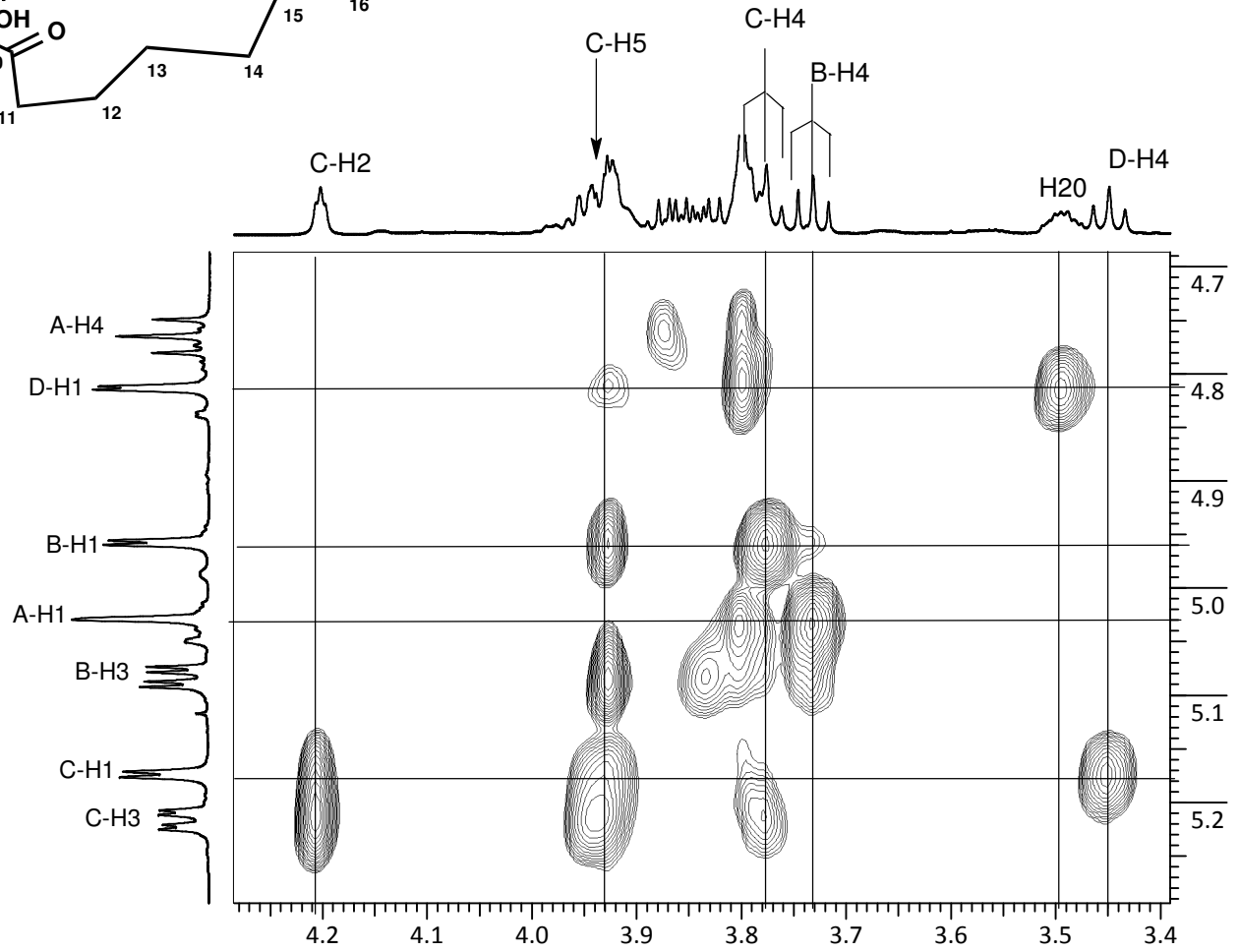
Expanded portion of the **NOESY** spectrum



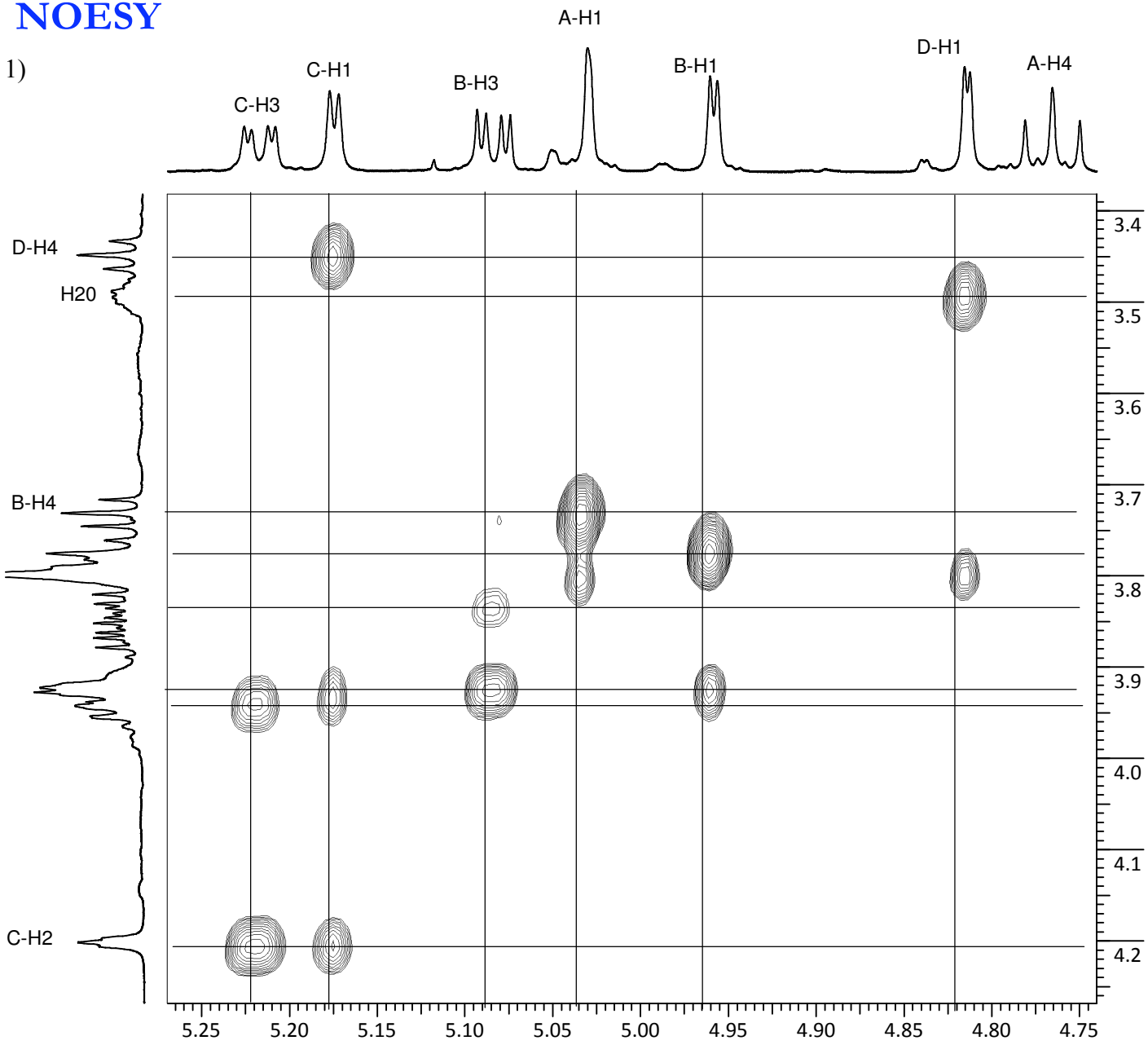
1

Linkage confirmation between sugar moieties

cross peaks observed on the contour plot of the NOESY spectrum between A-H1 and B-H4; between B-H1 and C-H4; between C-H1 and D-H4 are shown by curved arrows

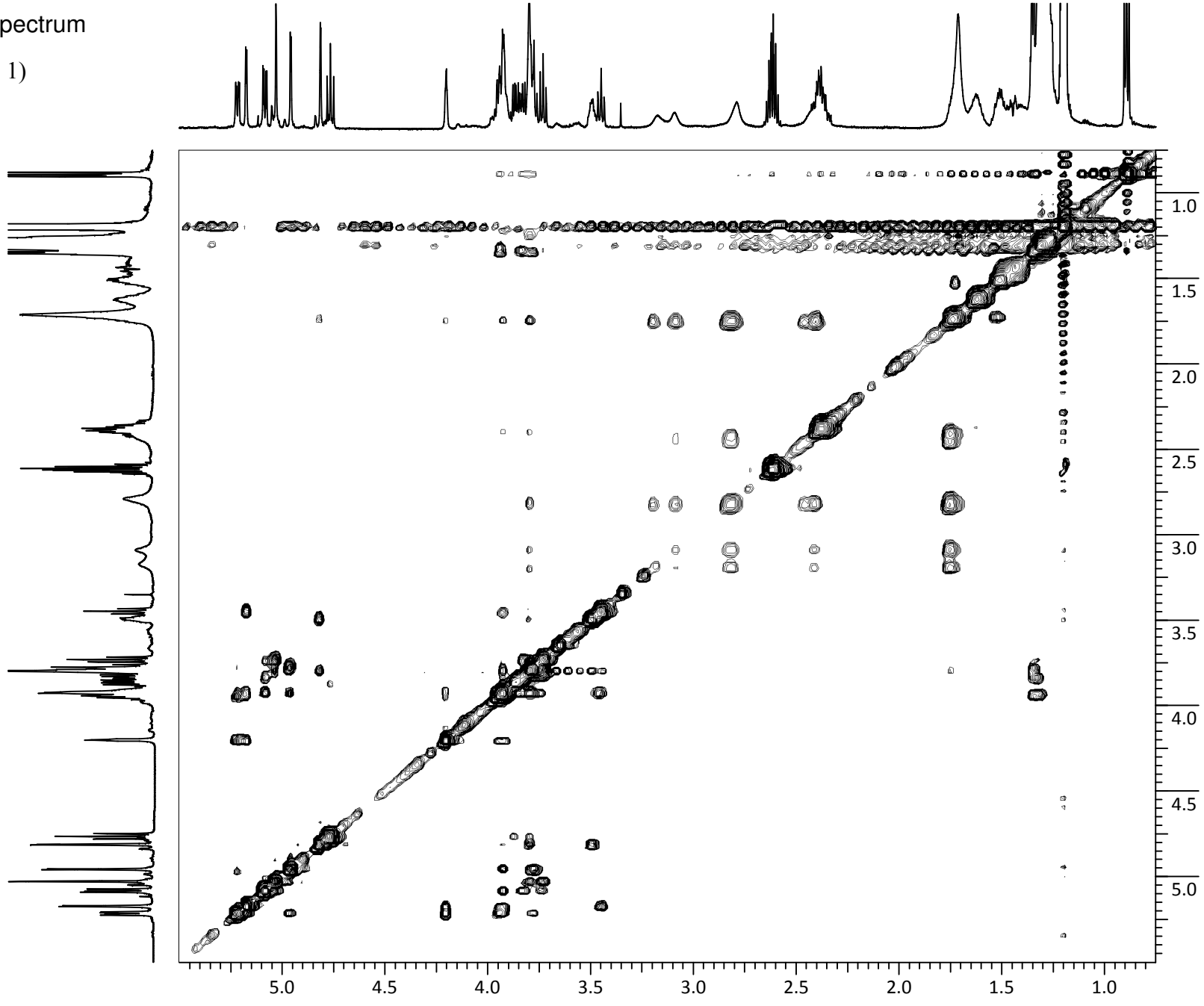


Linkage confirmation between sugar moieties by NOESY correlations (for synthetic 1)



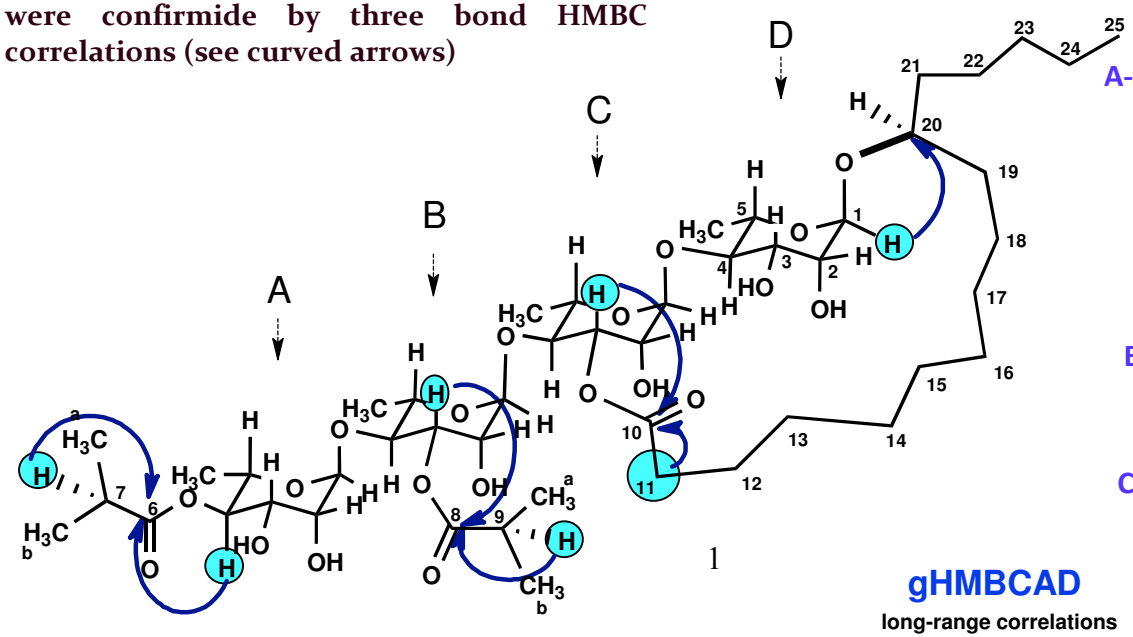
NOESY spectrum

(for synthetic 1)



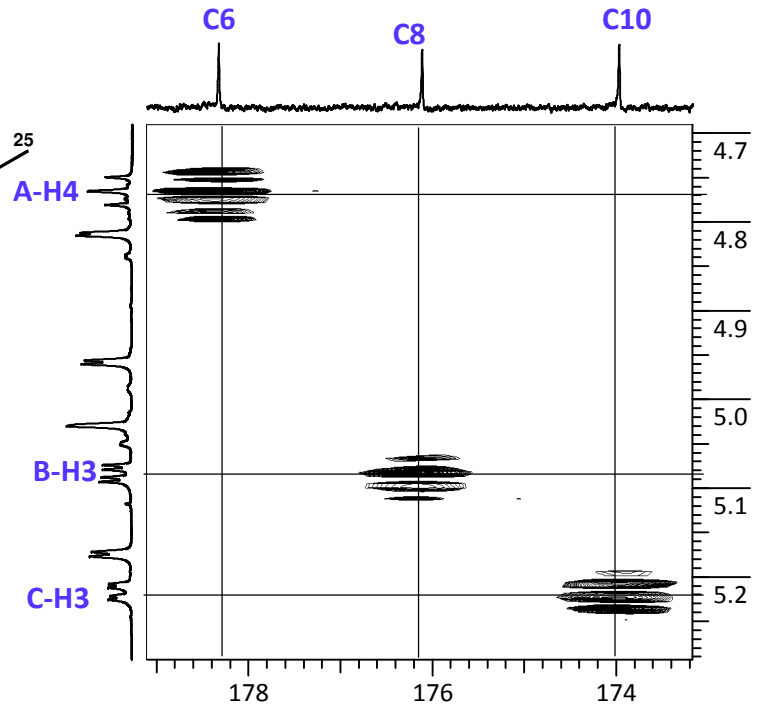
The linkage positions of the side chain ($C_{16}H_{31}O_3$) and the substituents $(CH_3)_2CHC(O)$

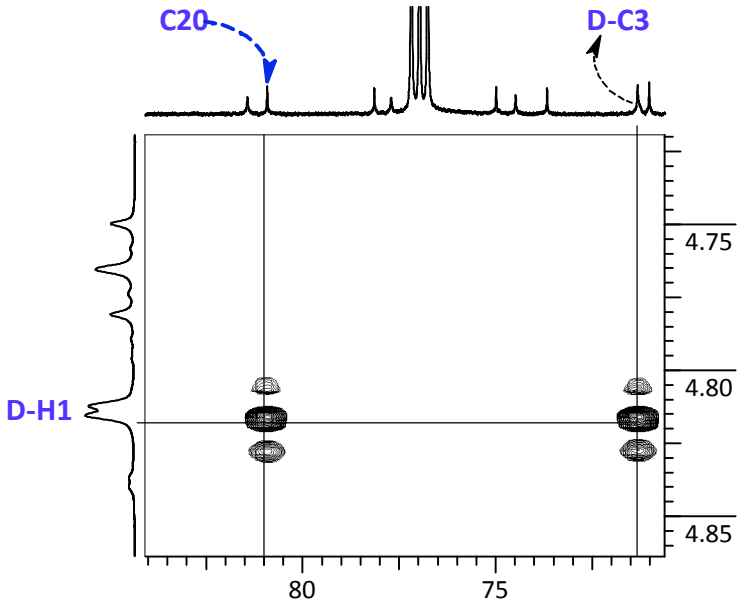
were confirmide by three bond HMBC correlations (see curved arrows)

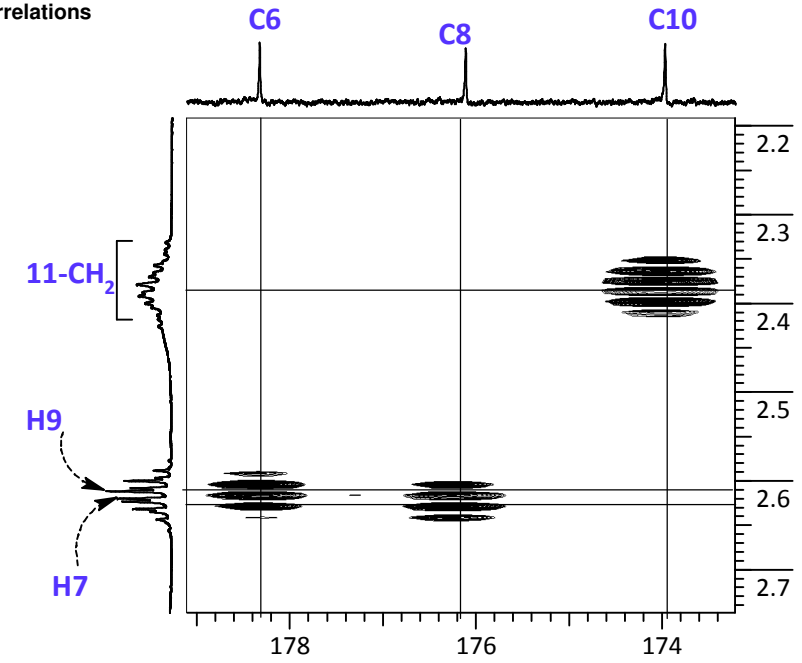


gHMBCAD

long-range correlations

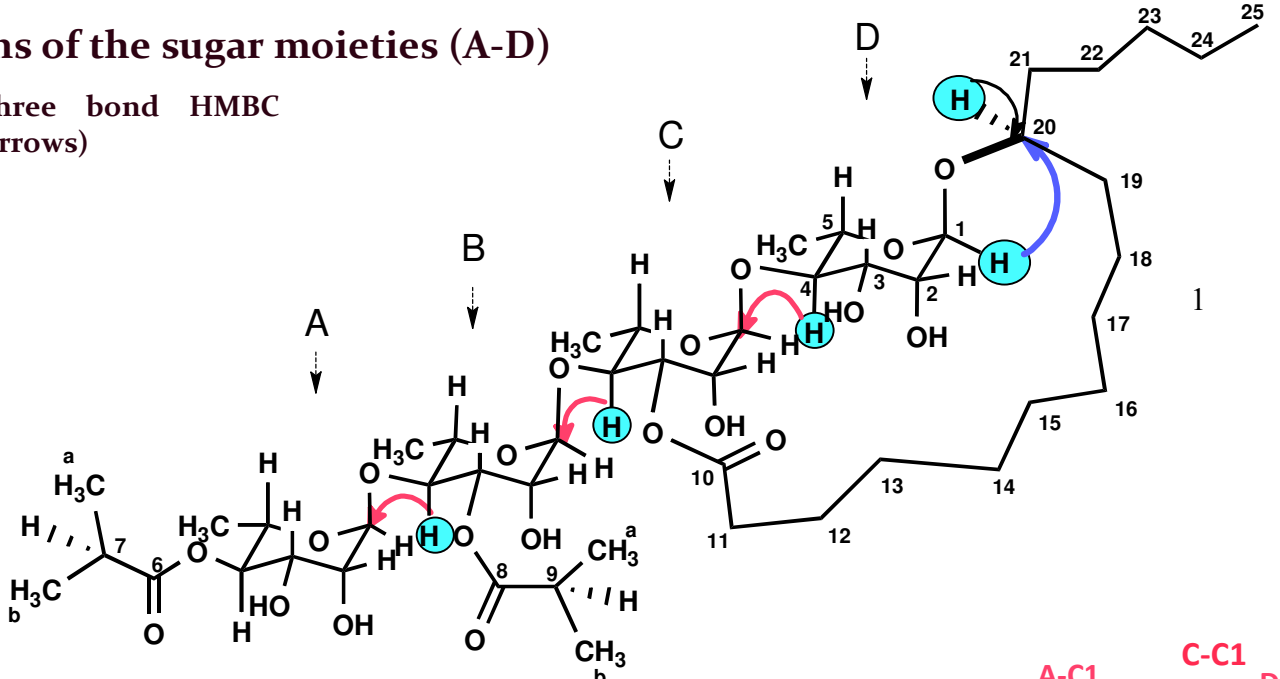




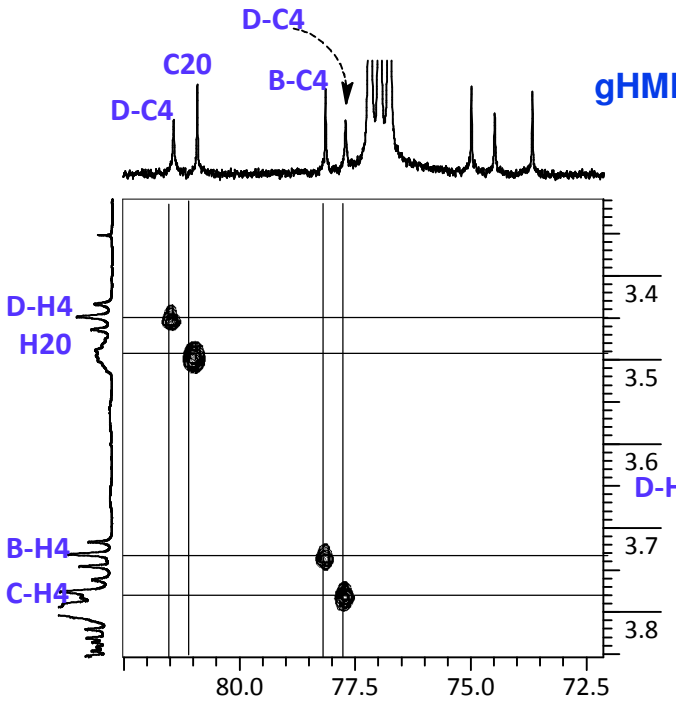


The linkage positions of the sugar moieties (A-D)

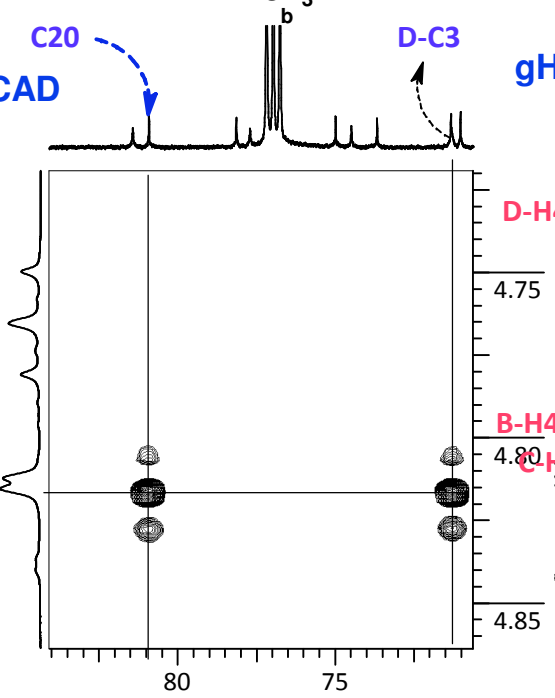
were confirmide by three bond HMBC correlations (see curved arrows)



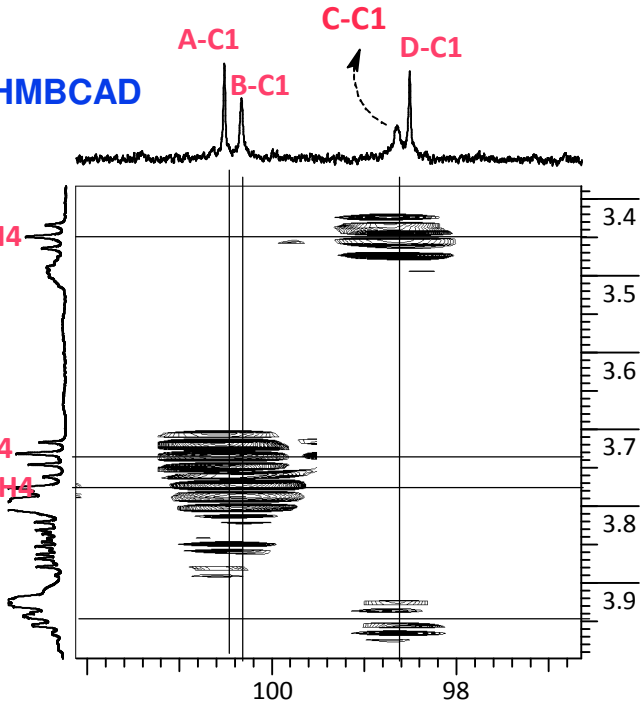
gHSQCAD
one-bond correlations



gHMBCAD



gHMBCAD



The linkage positions of the sugar moieties (A-D)

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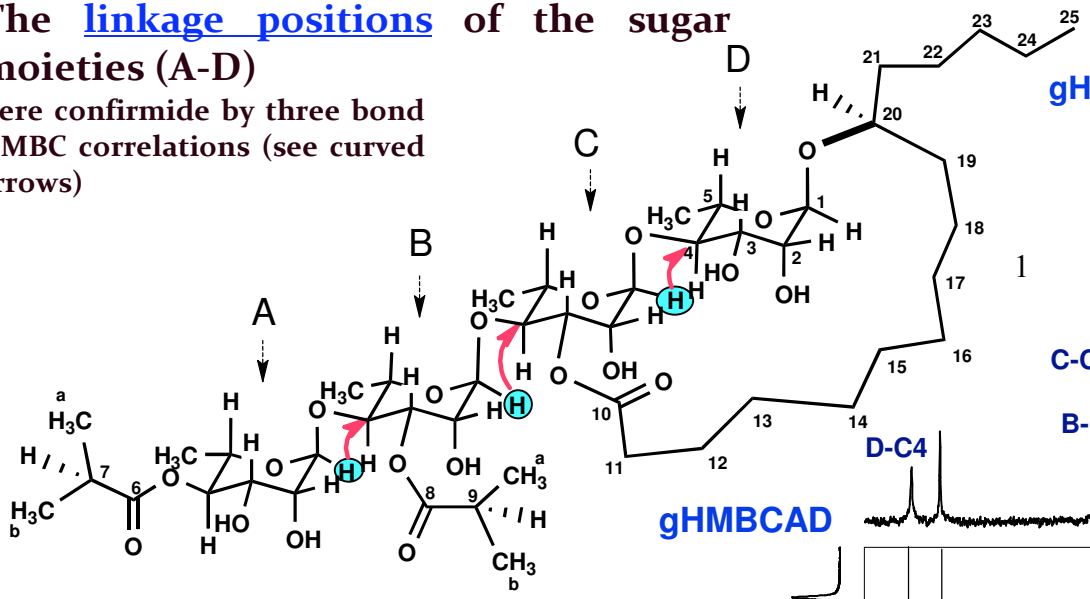
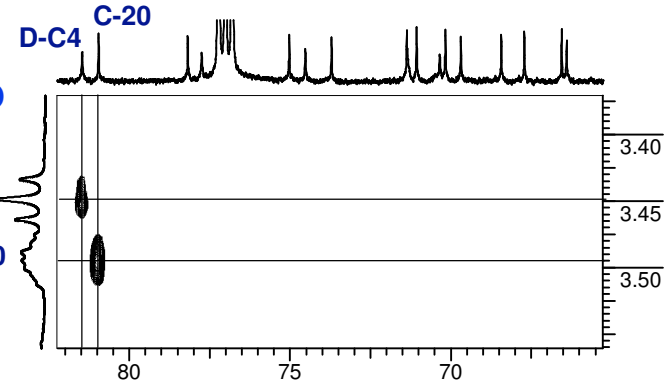
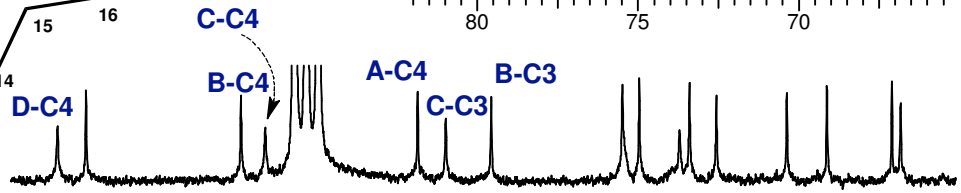
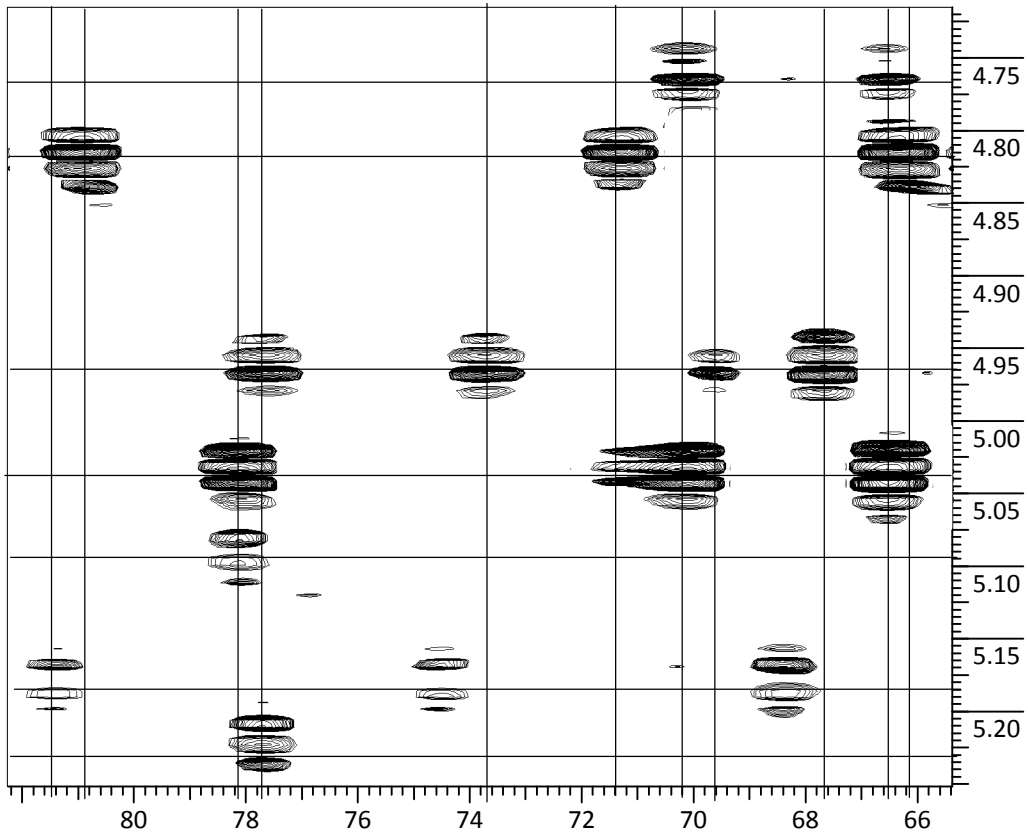


gHSQCAD



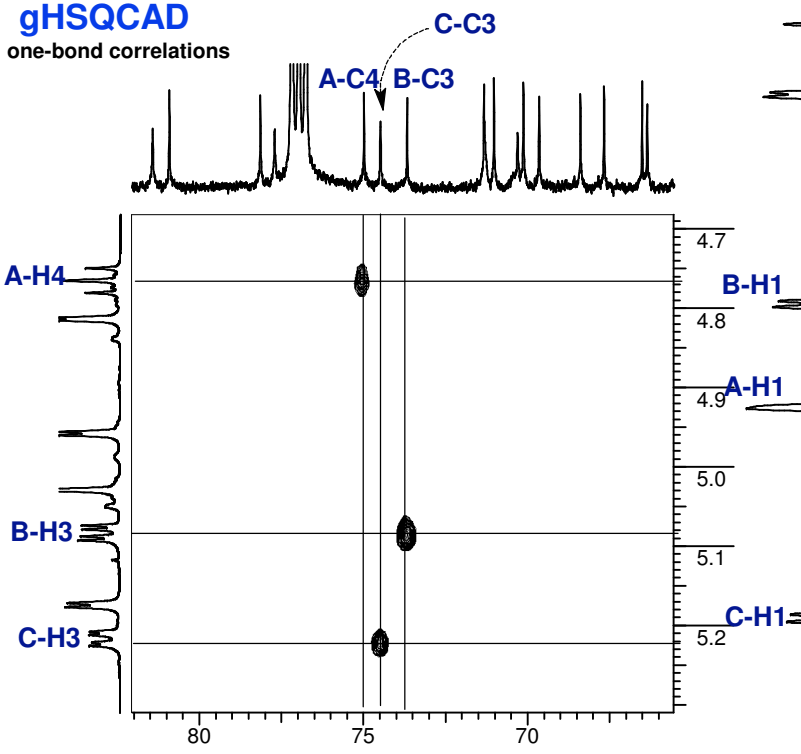


gHMBCAD



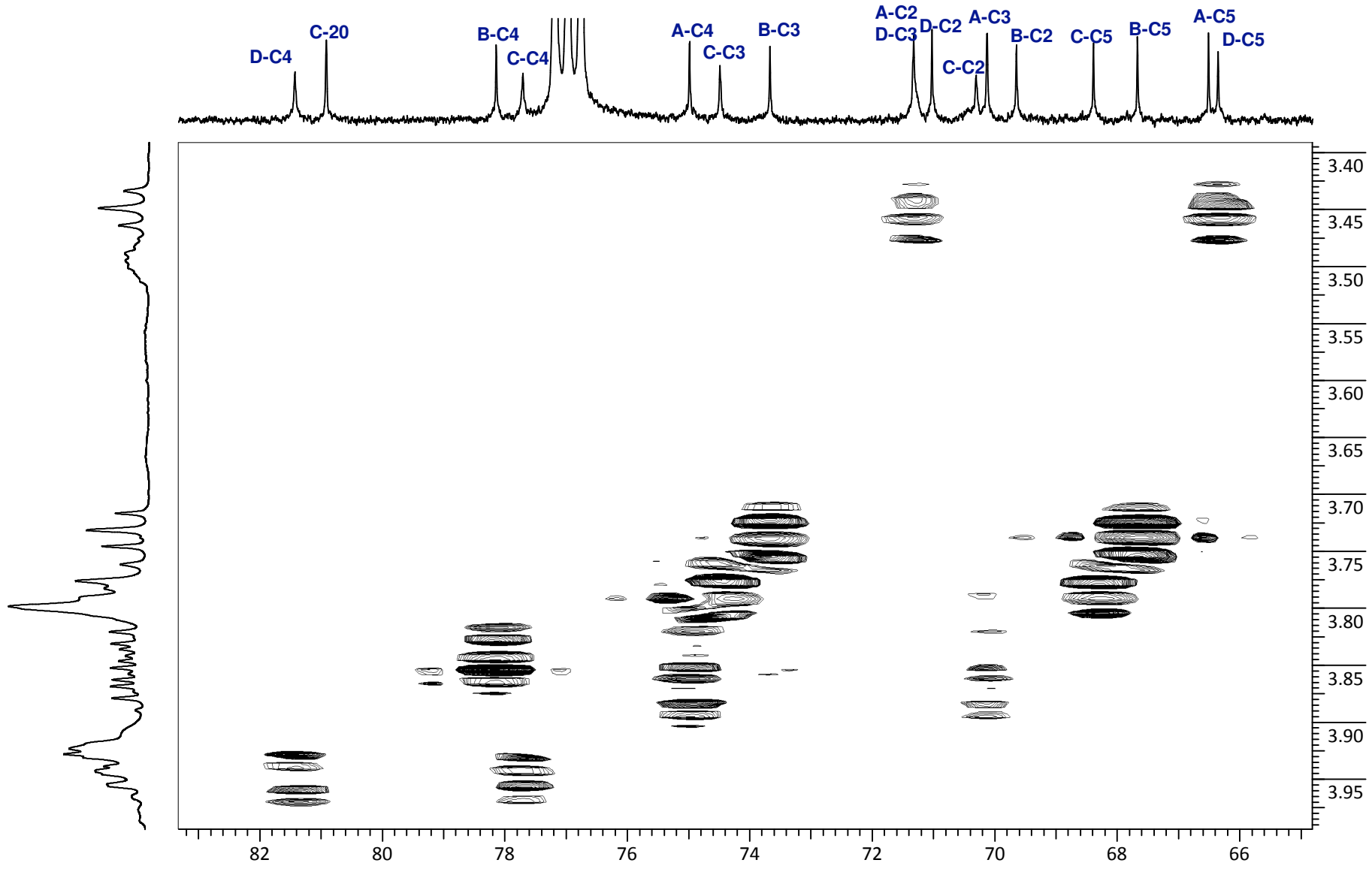
gHSQCAD

one-bond correlations

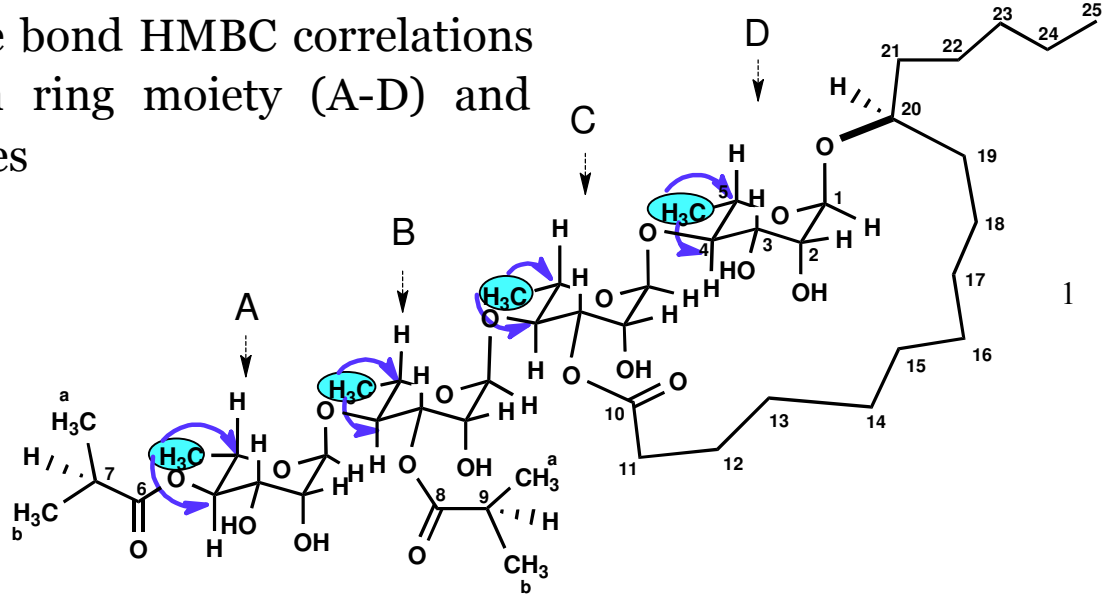


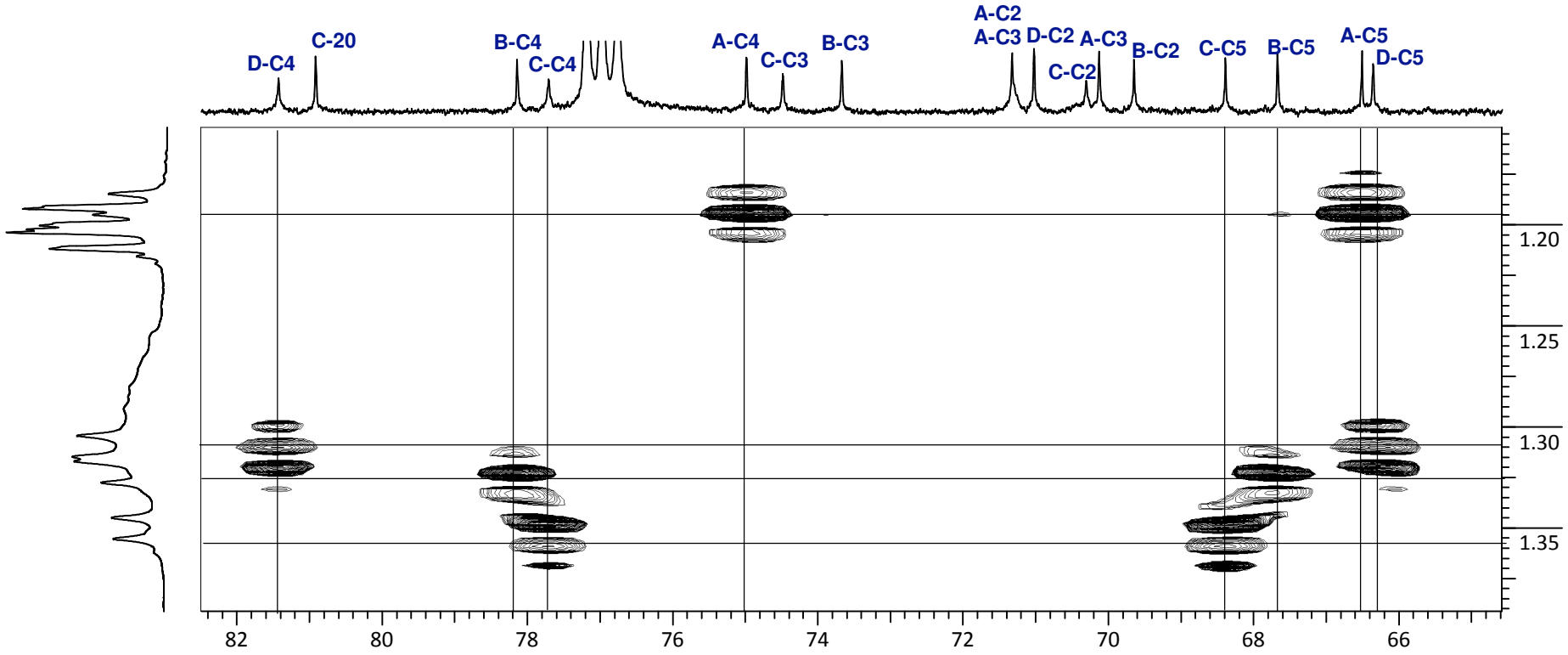
Expanded portion of the gHMBCAD spectrum

(for synthetic 1)

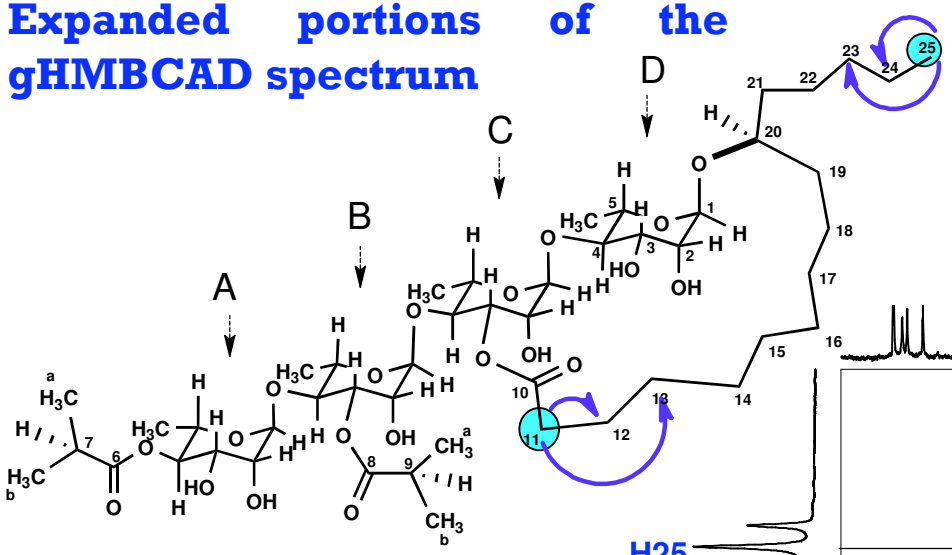


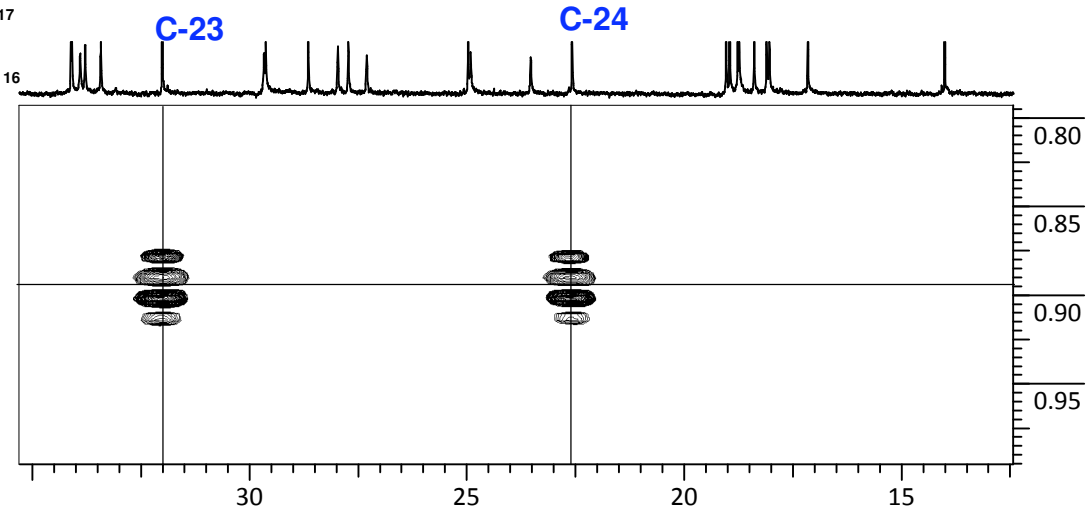
Observed two and three bond HMBC correlations between CH_3's of each ring moiety (A-D) and C4/C5 carbon resonances



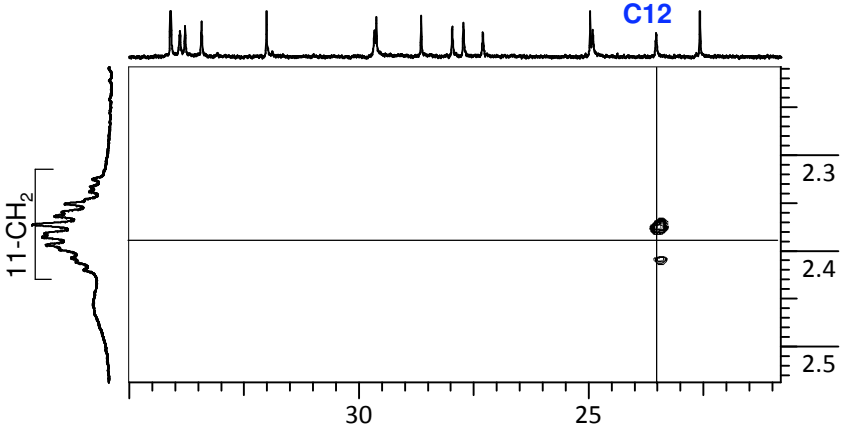


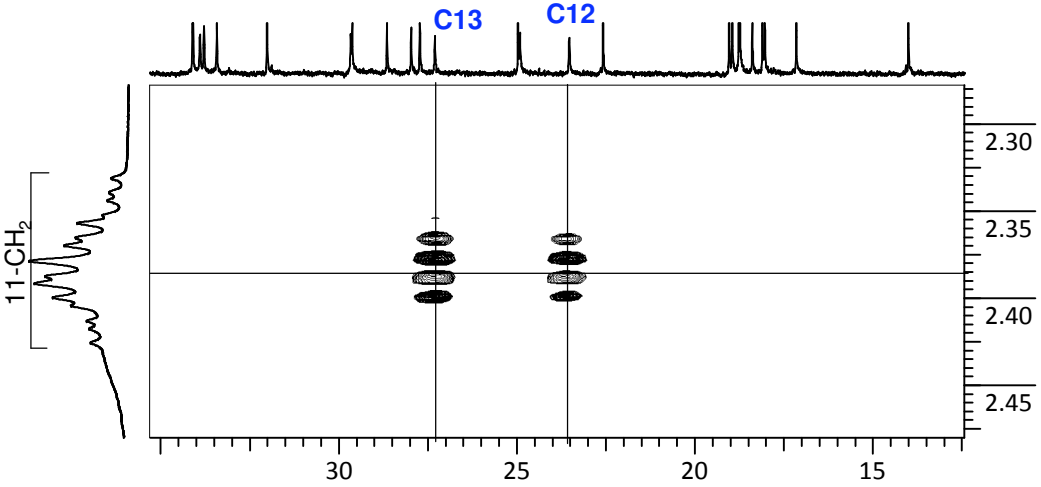
Expanded portions of the gHMBCAD spectrum





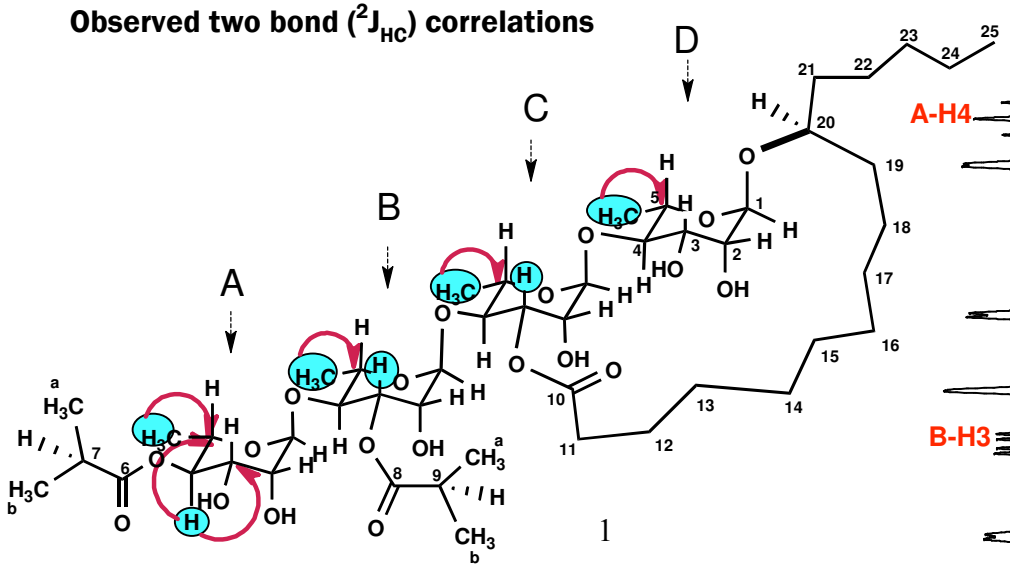
gH$_2$BCAD

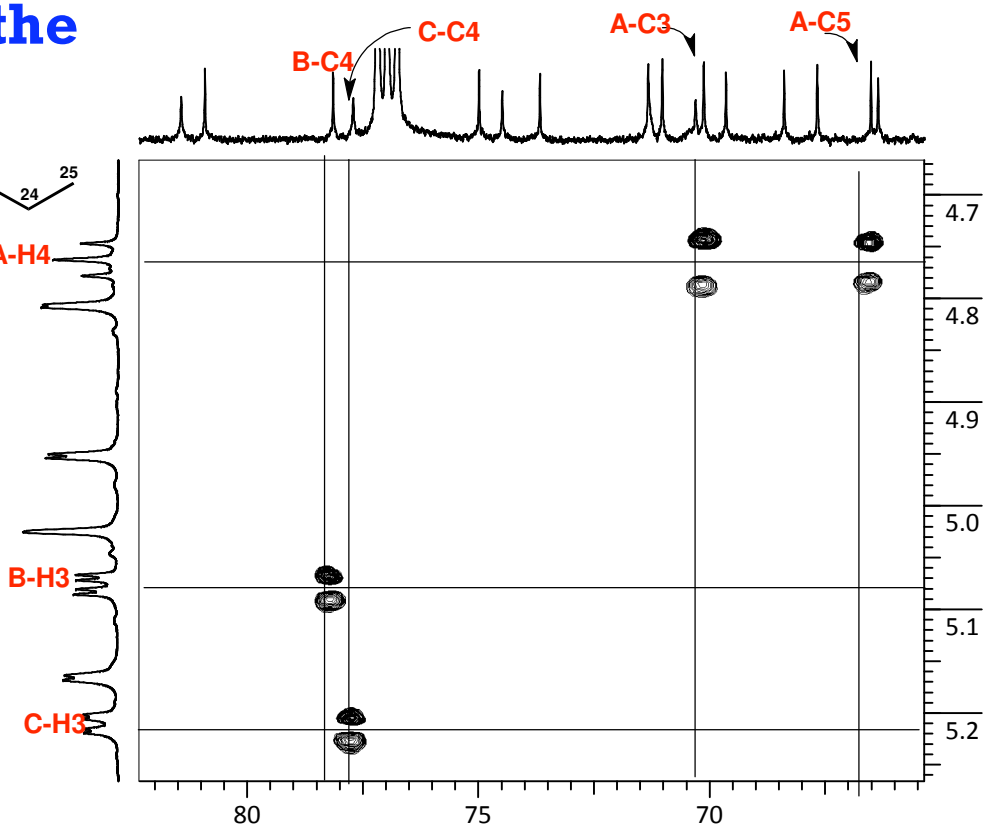


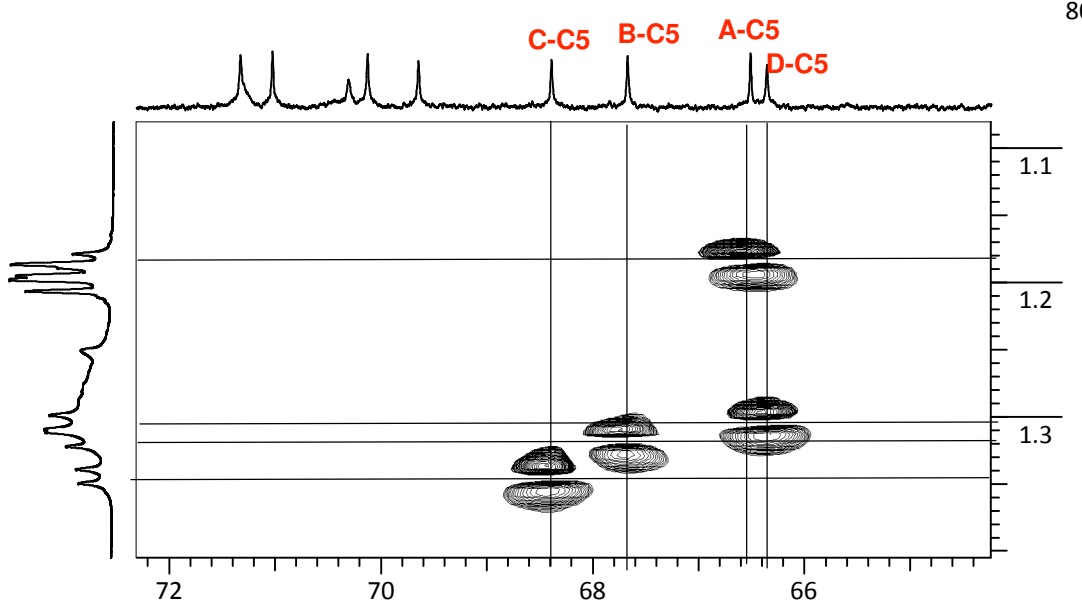


Expanded portions of the gH2BCAD spectrum

Observed two bond ($^2J_{HC}$) correlations



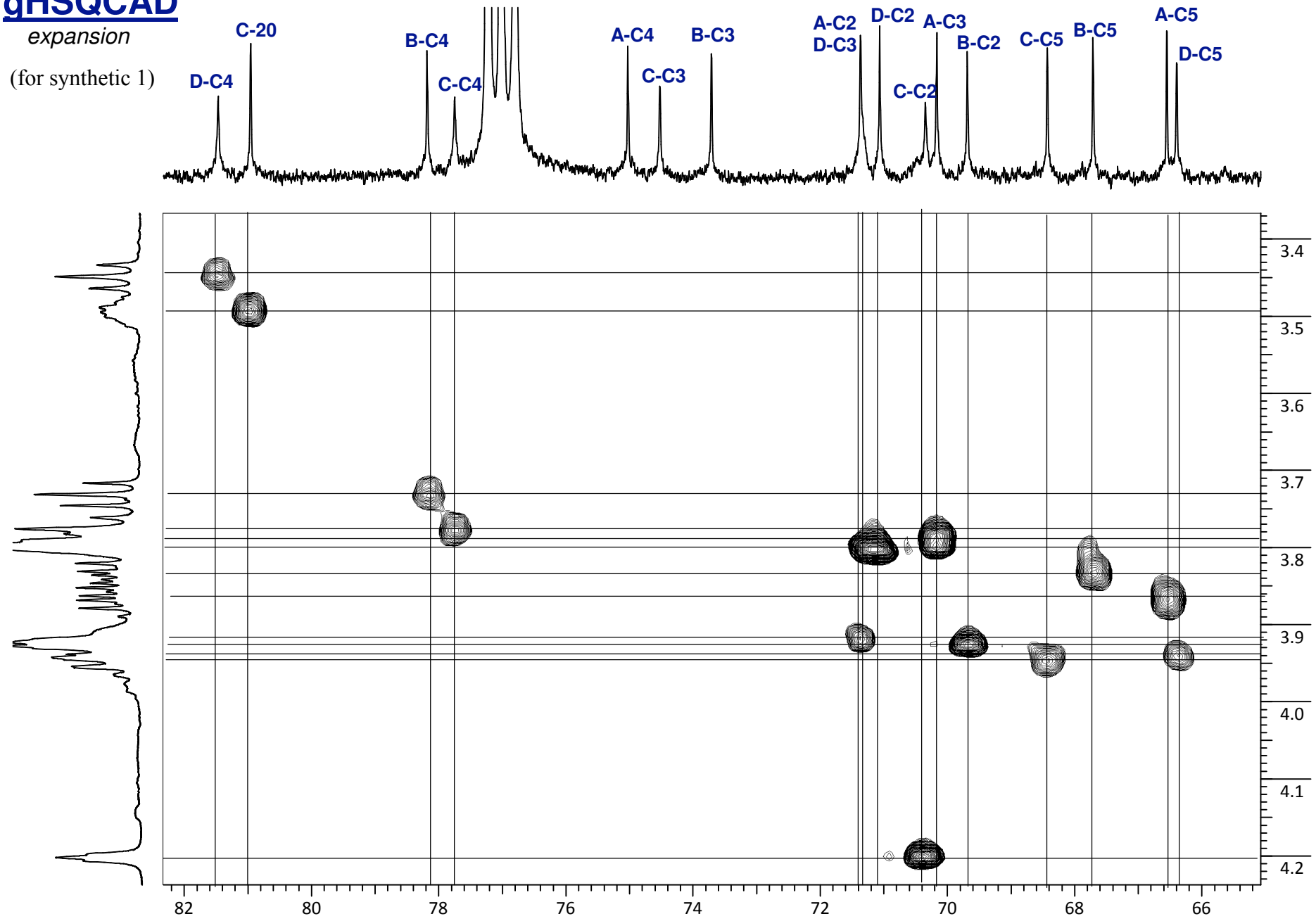




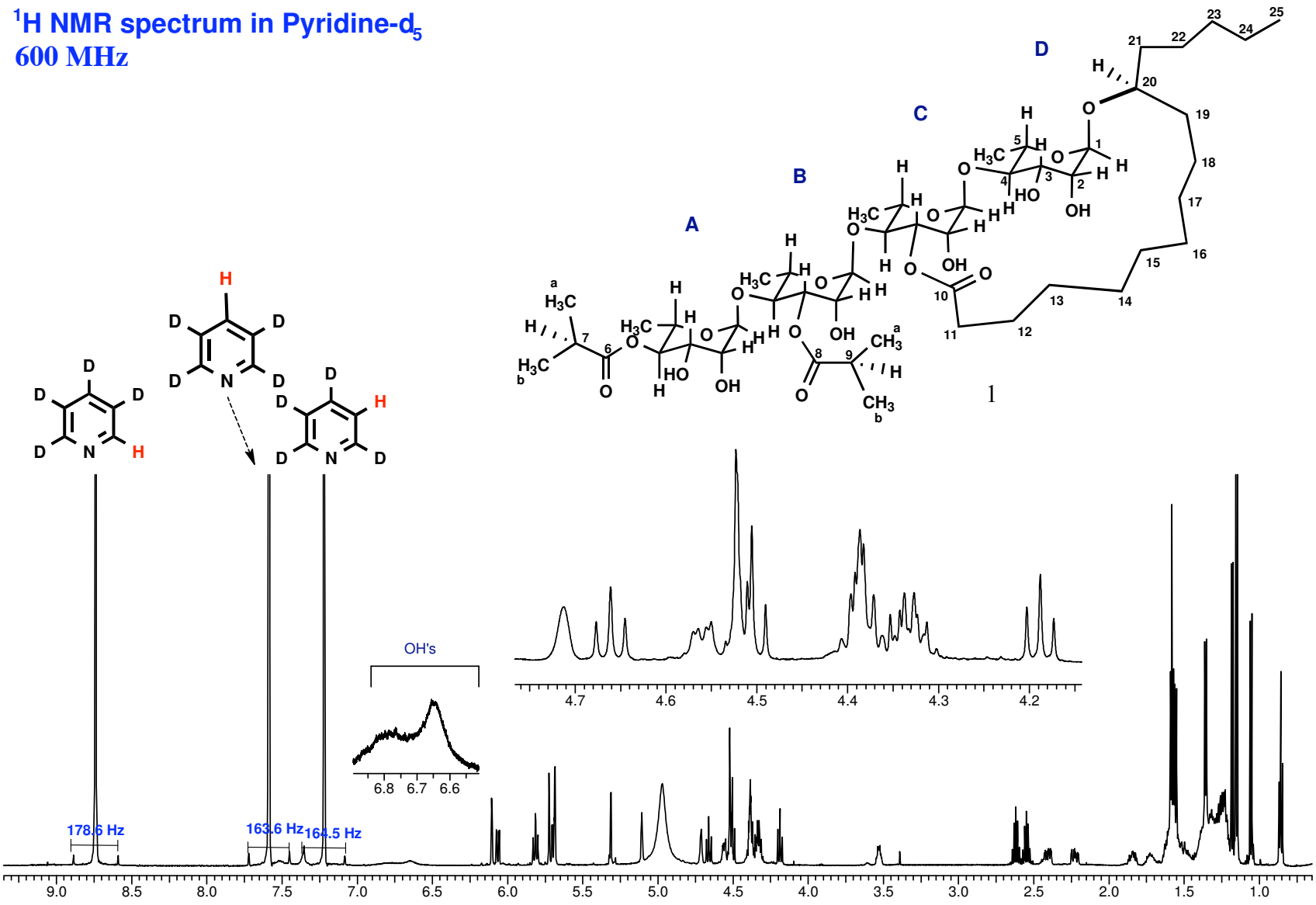
gHSQCAD

expansion

(for synthetic 1)



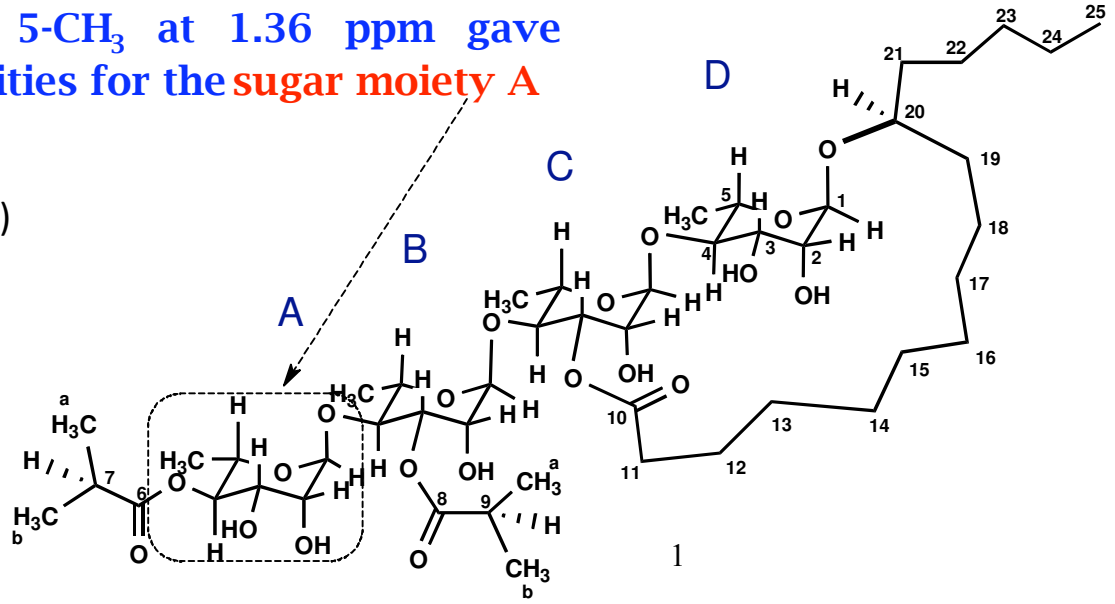
^{1}H NMR spectrum in Pyridine-d_5
600 MHz



Selective excitation of 5-CH_3 at 1.36 ppm gave proton-proton connectivities for the sugar moiety A

1D TOCSY subspectrum (b);

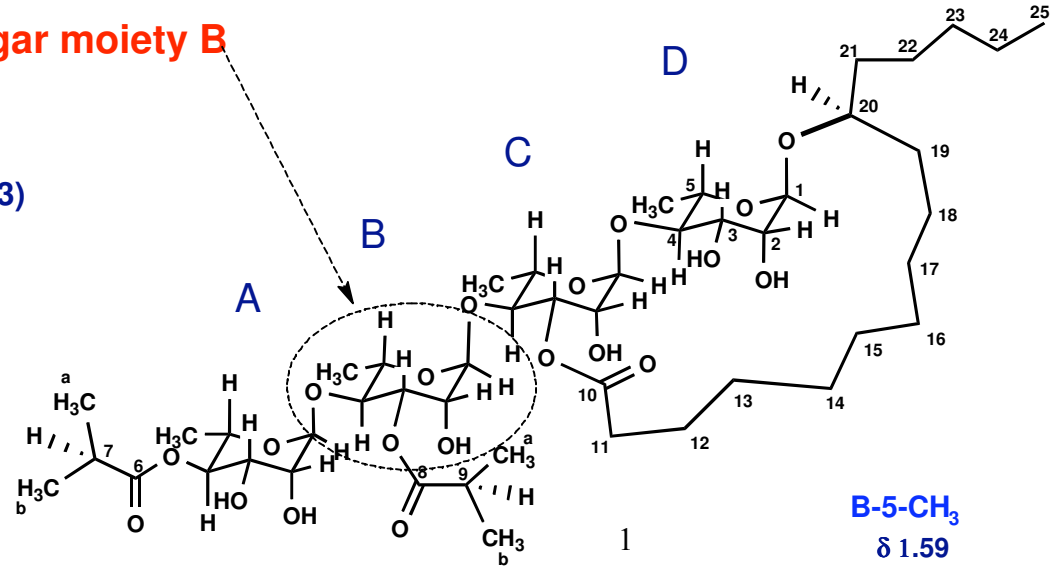
Control ^{1}H NMR spectrum (a)

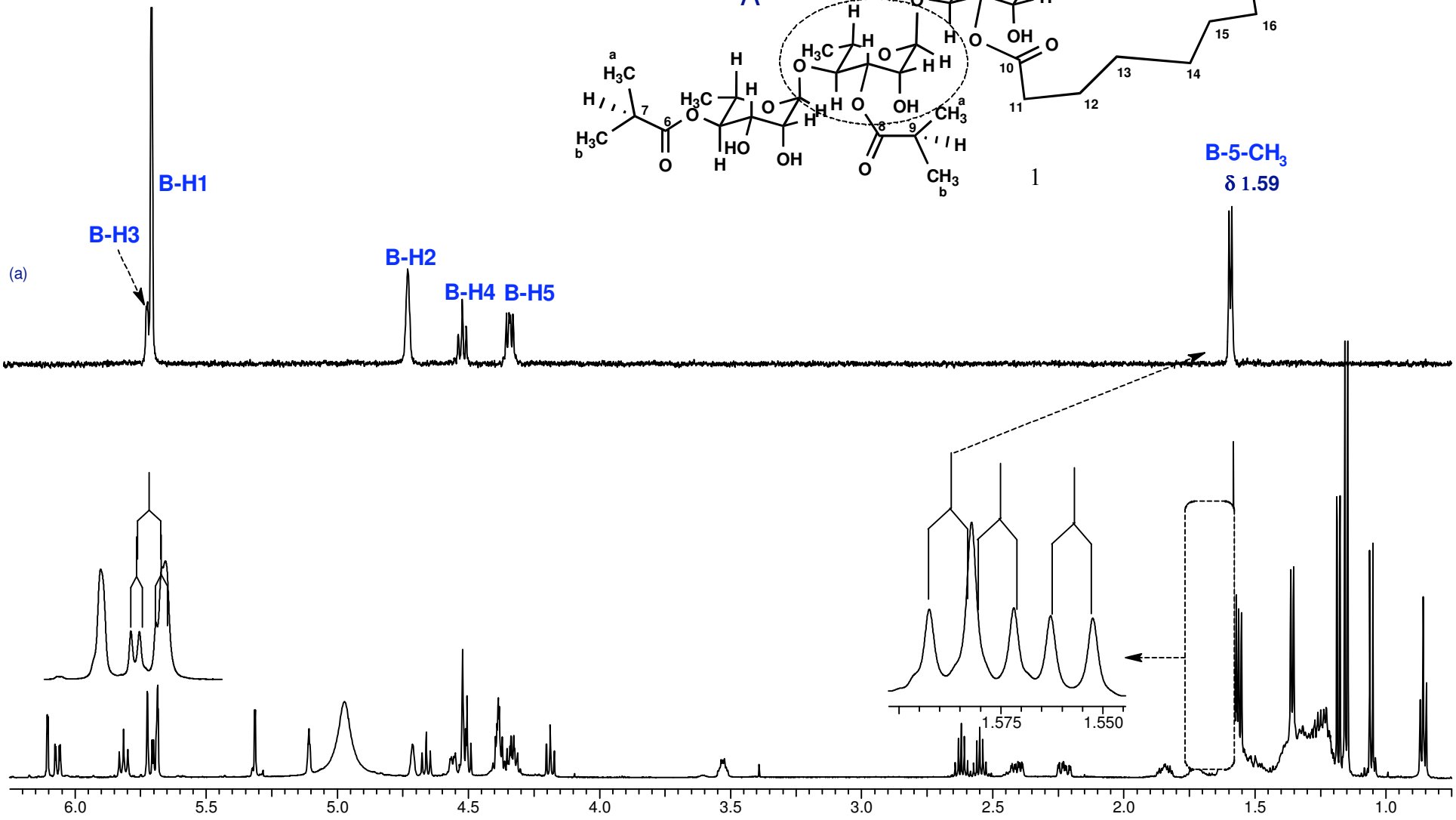


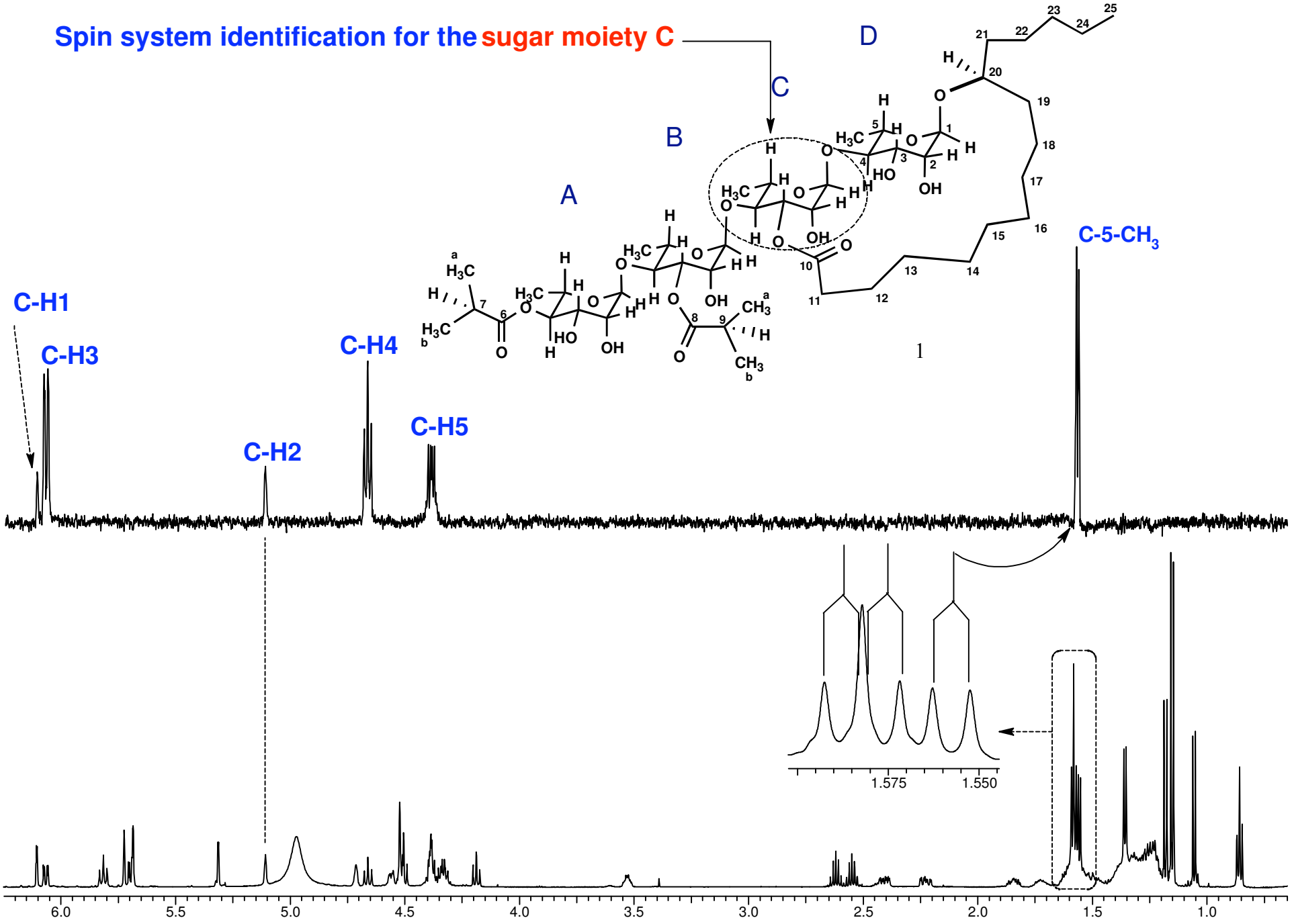
Spin system identification for the sugar moiety B

1D TOCSY subspectrum (a)

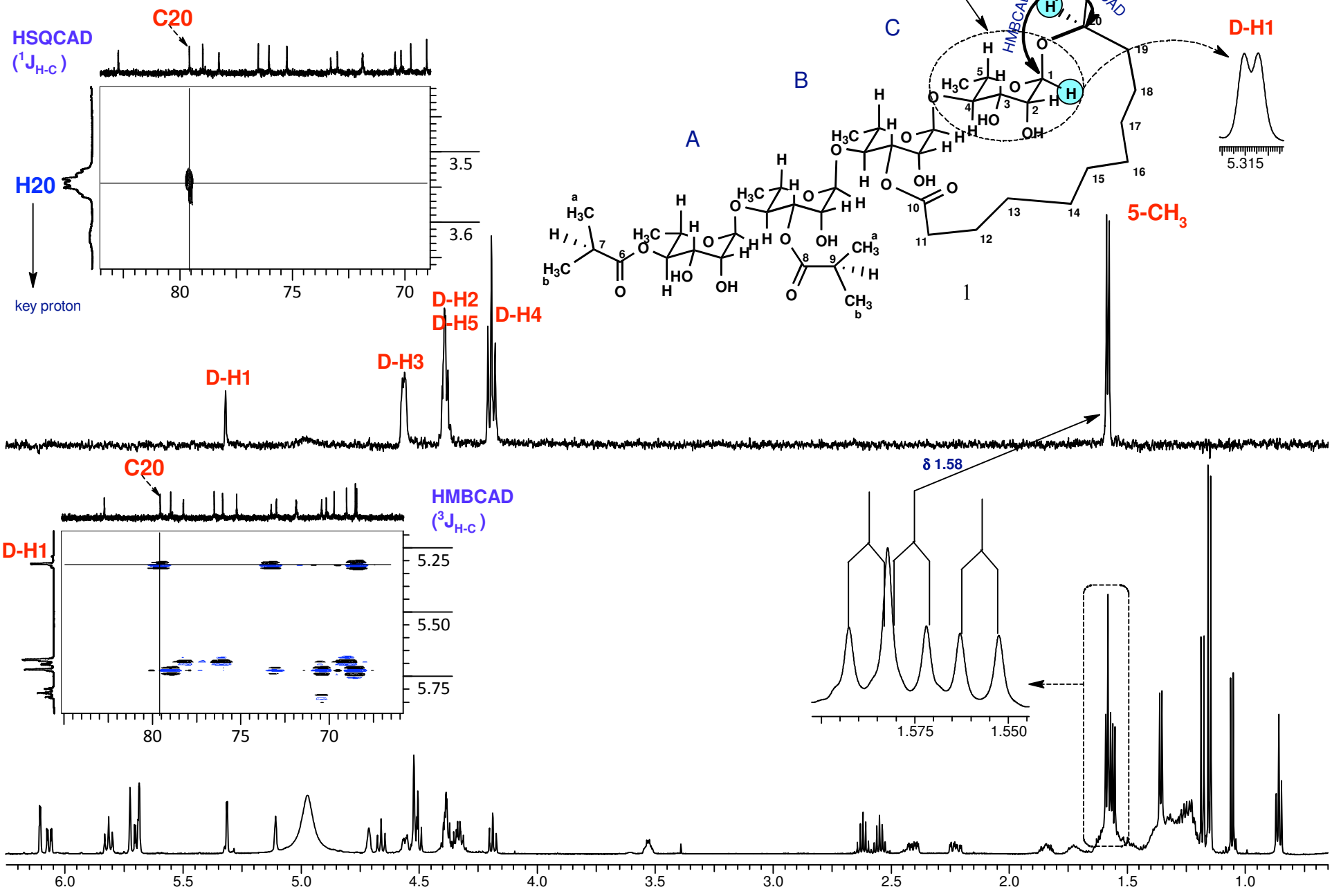
Selective excitation of signals (B-H1 and B-H3)



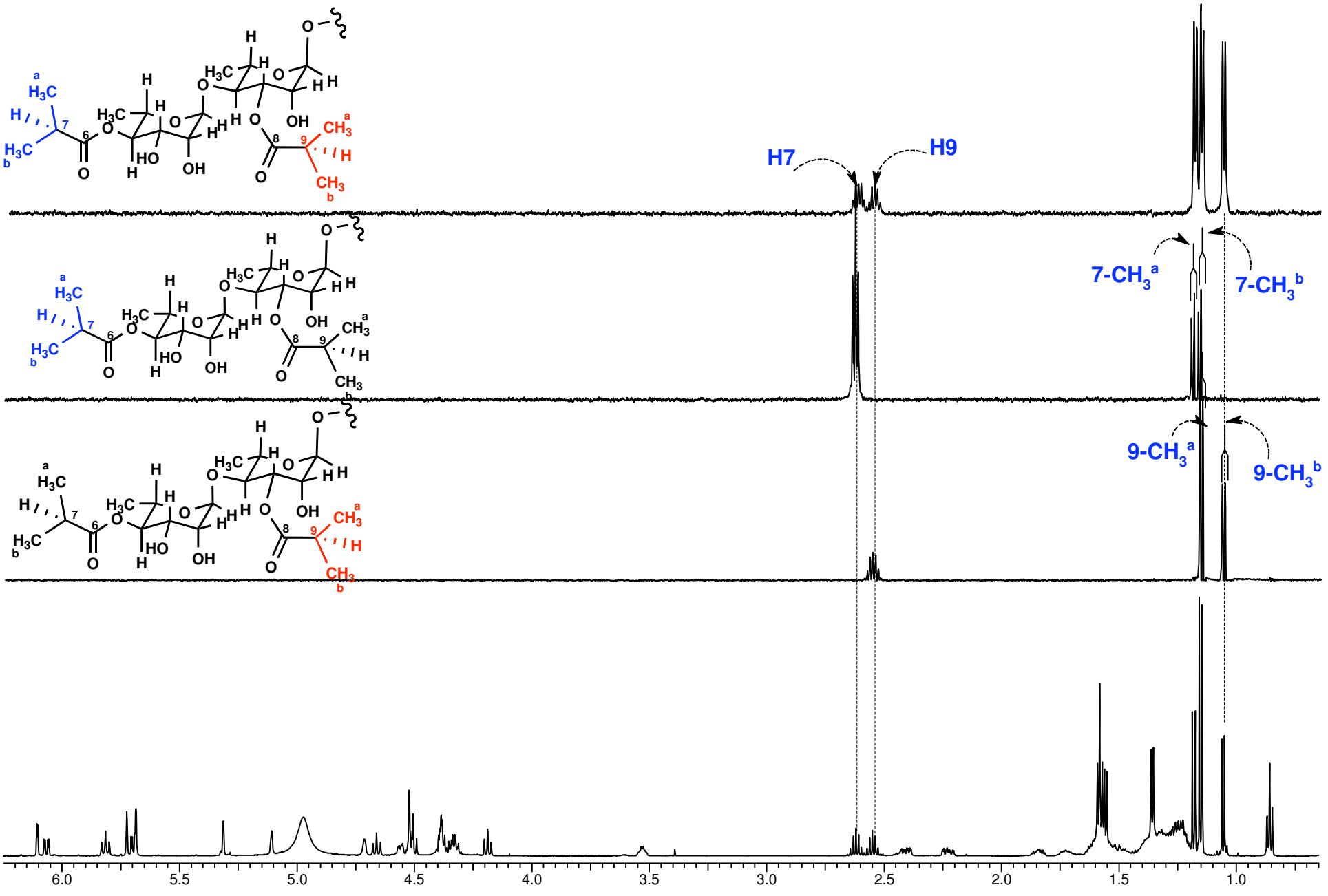



Spin system identification for the sugar moiety C
A
B
C
D
C-H1
C-H3
C-H2
C-H4
C-H5
C-5-CH3
1
1.575
1.550
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

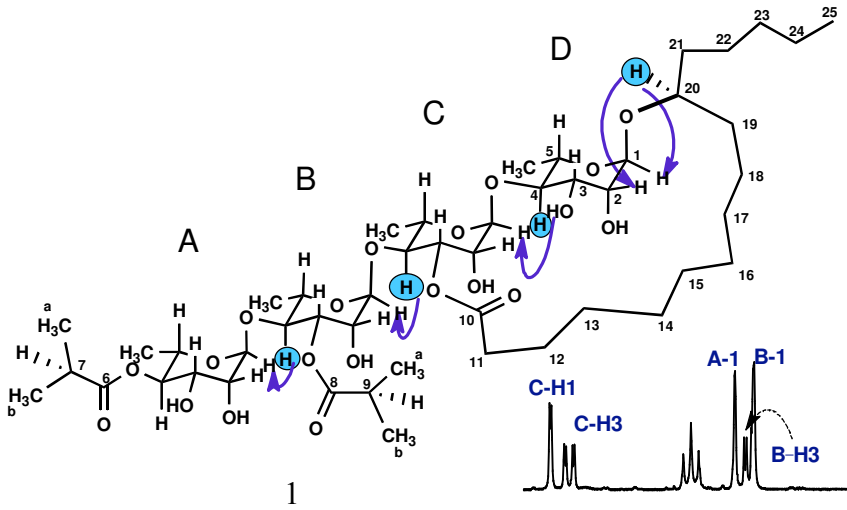
Diffrentiation and Spin system identification for the sugar moiety D



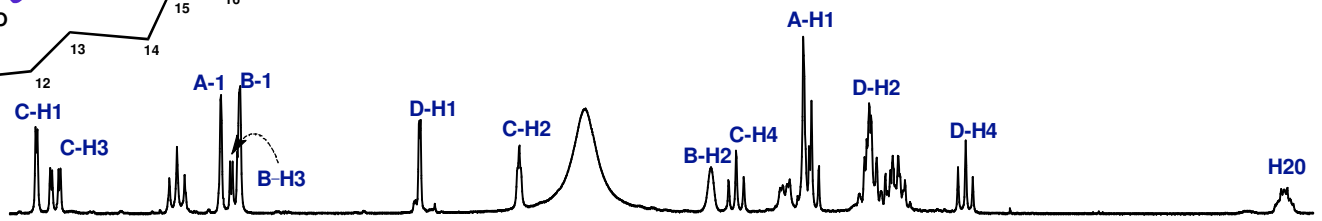
Spn system identification for the isopropyl groups (for synthetic 1)

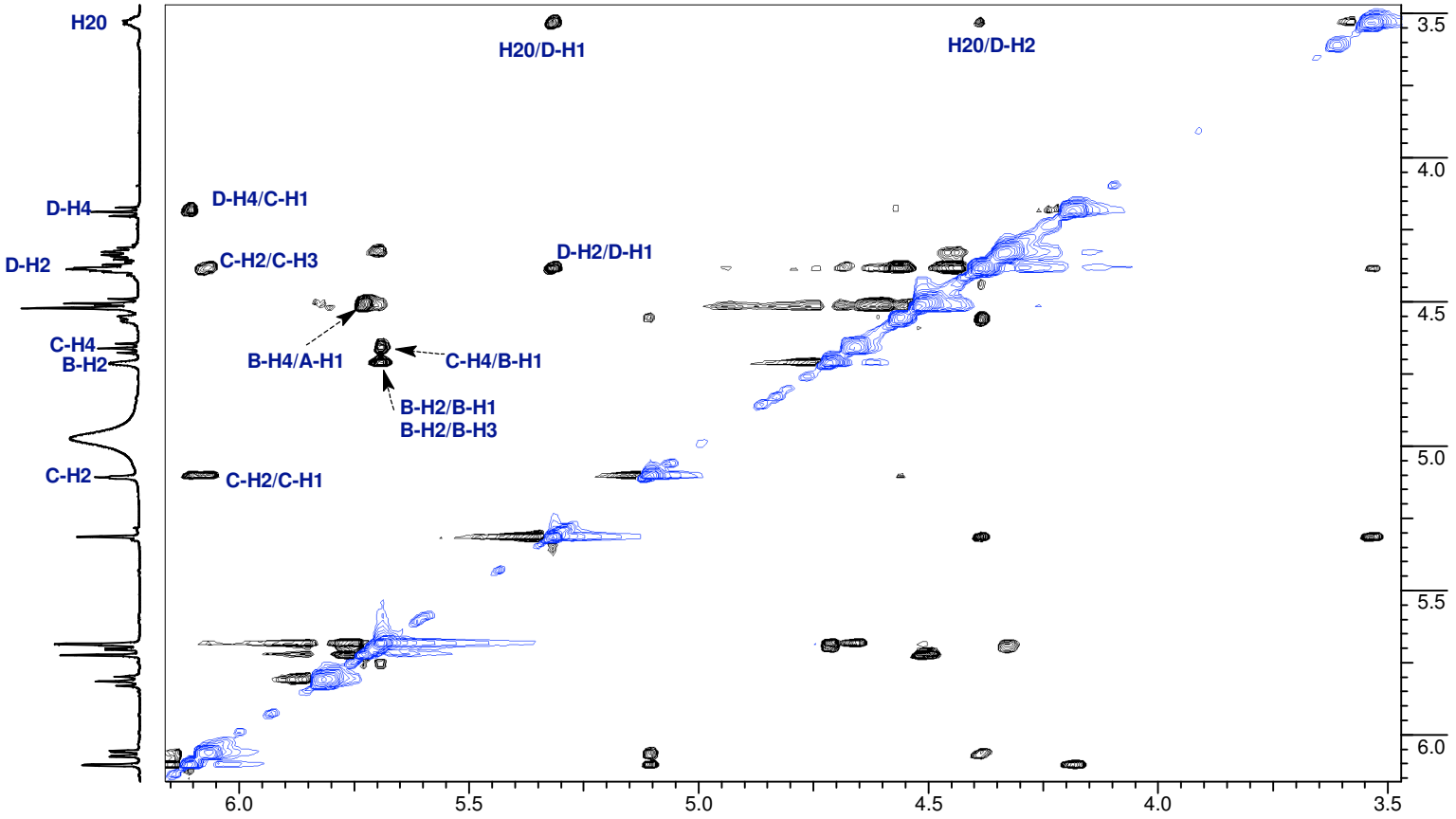


ROESYAD correlations (through space) confirm the linkage position between sugar moieties (A-D)



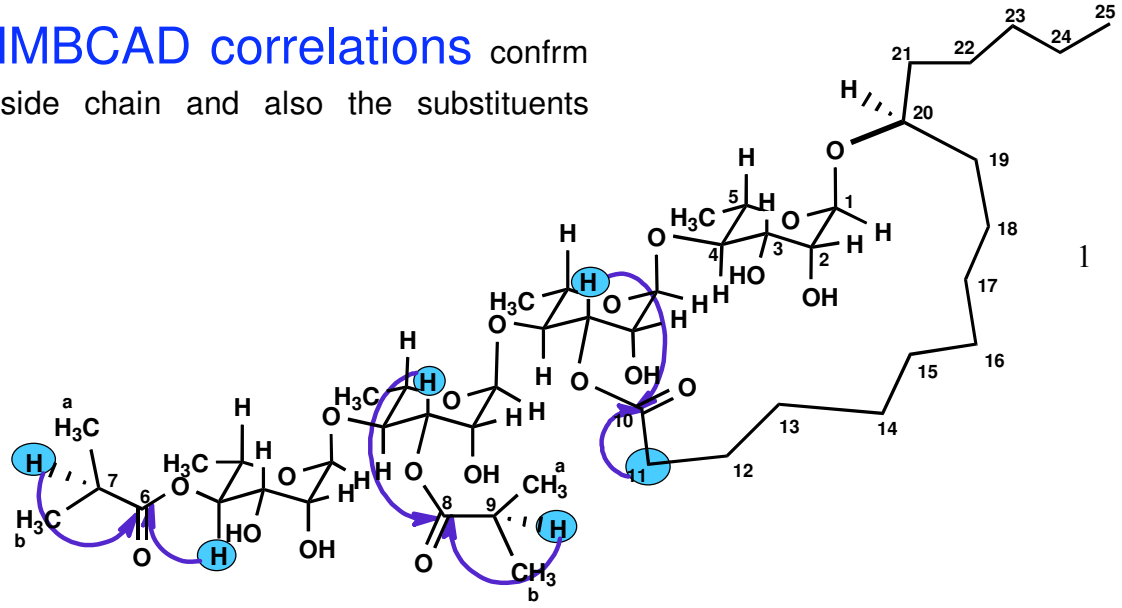
1

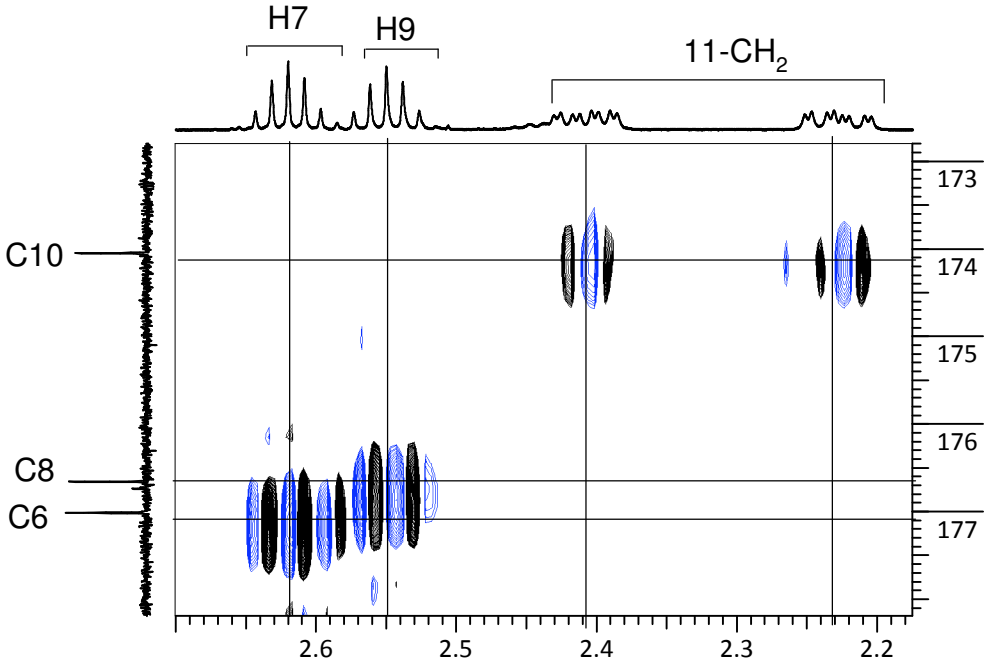


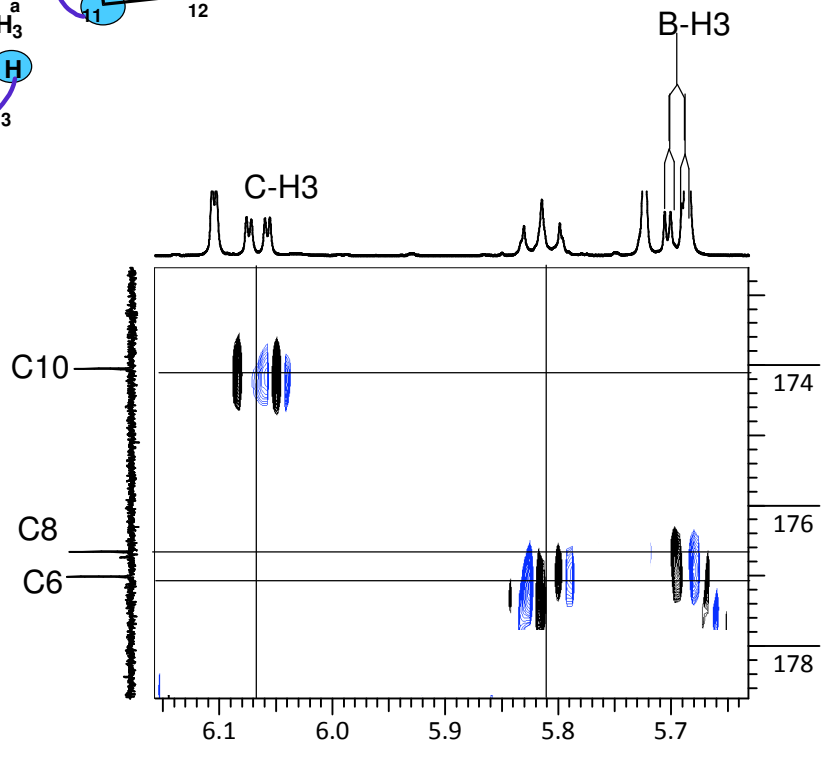


Three bond ($^3J_{HC}$) HMBCAD correlations confrm

the linkage position of the side chain and also the substituents $(CH_3)_2CH$-C(O)



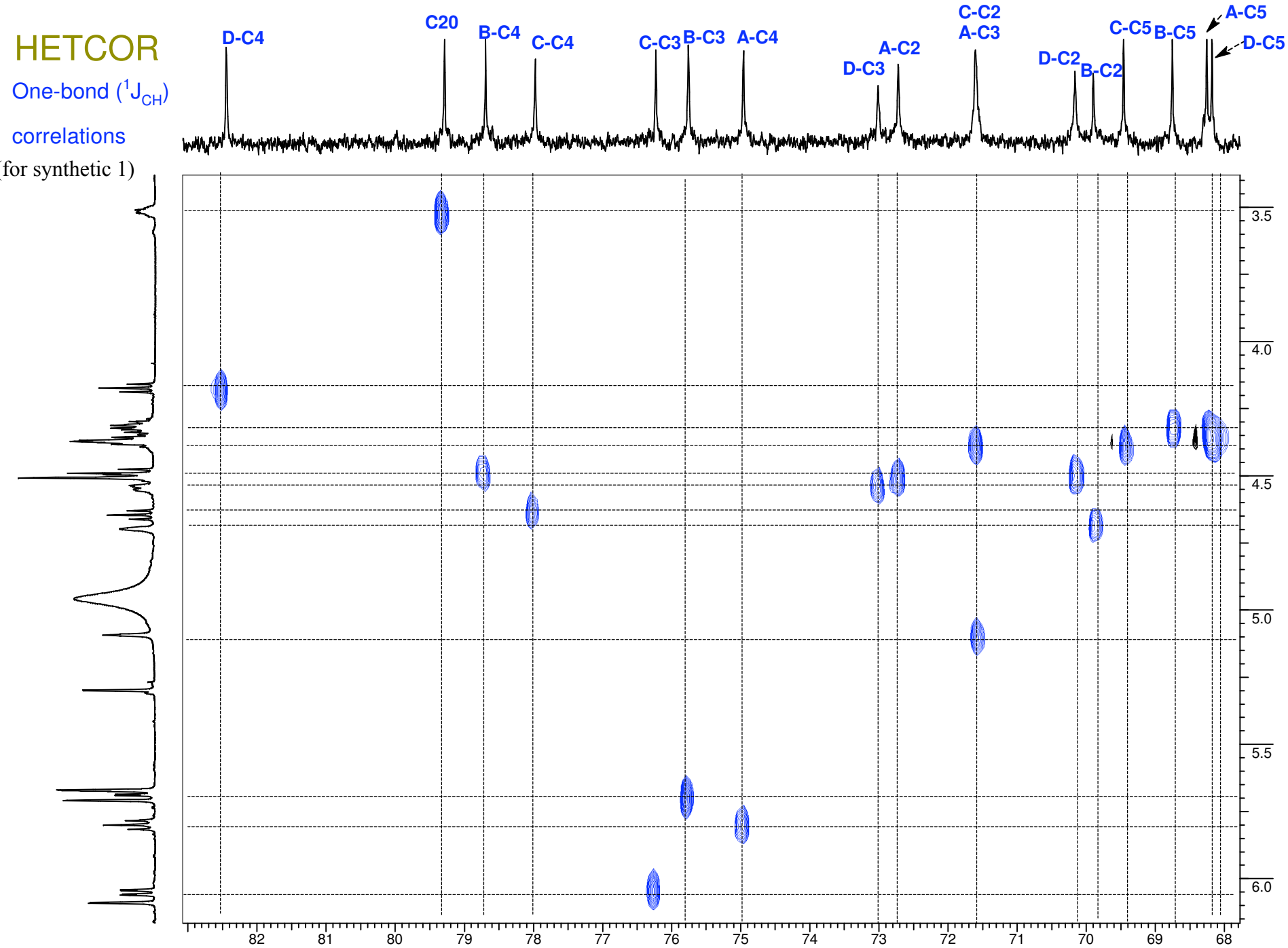




HETCOR

One-bond ($^1J_{CH}$) correlations

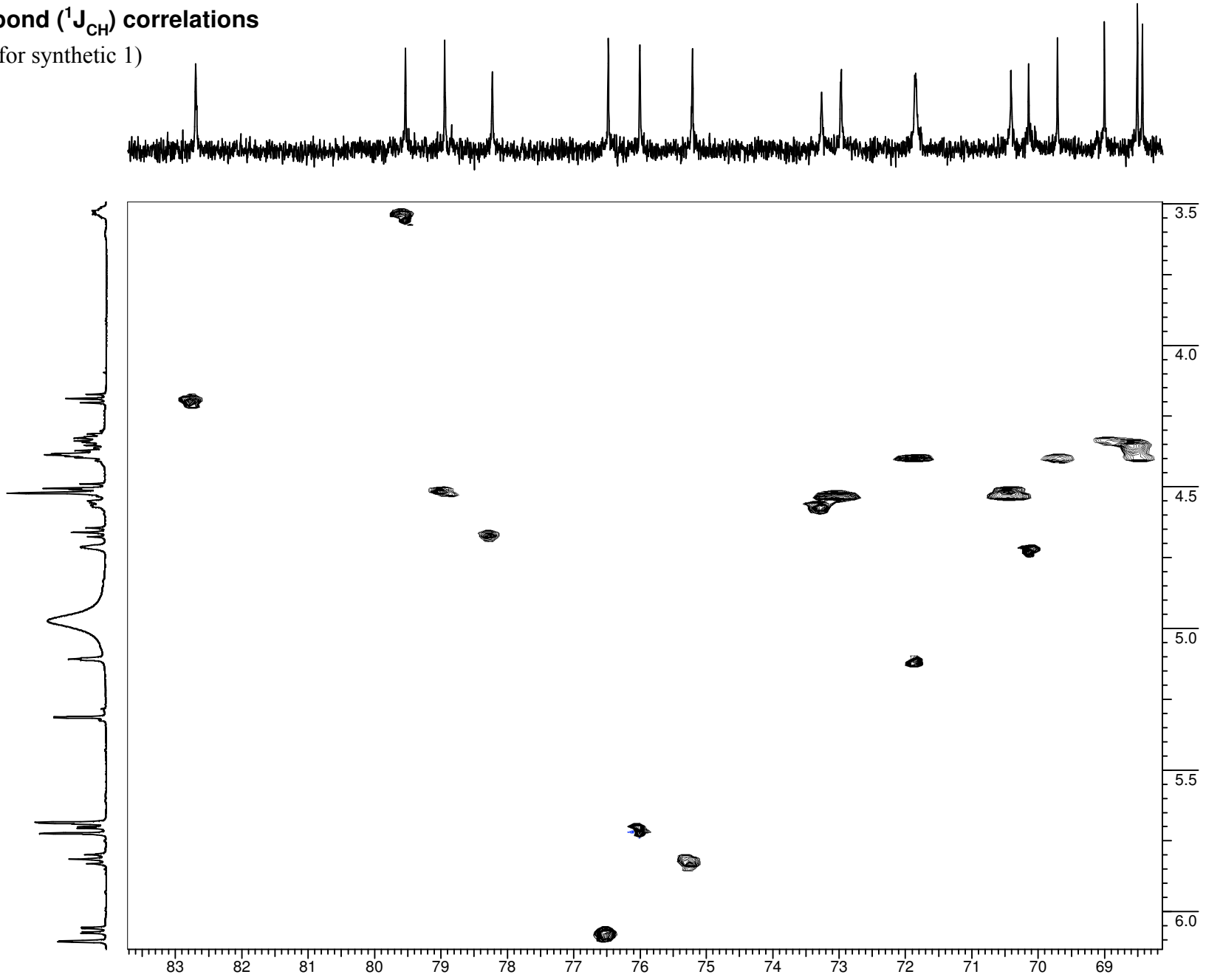
(for synthetic 1)



HSQCAD

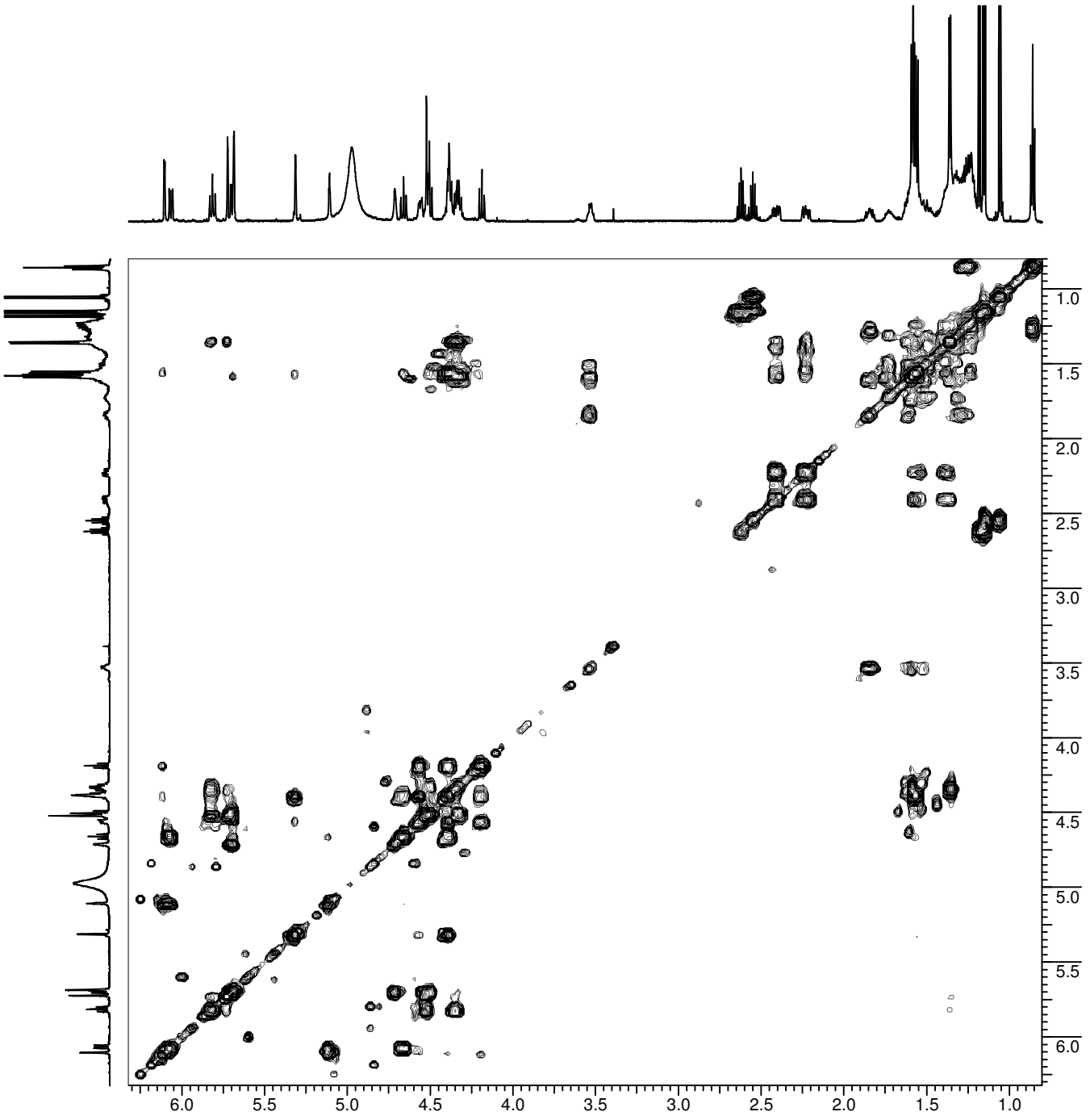
One-bond ($^1J_{CH}$) correlations

(for synthetic 1)

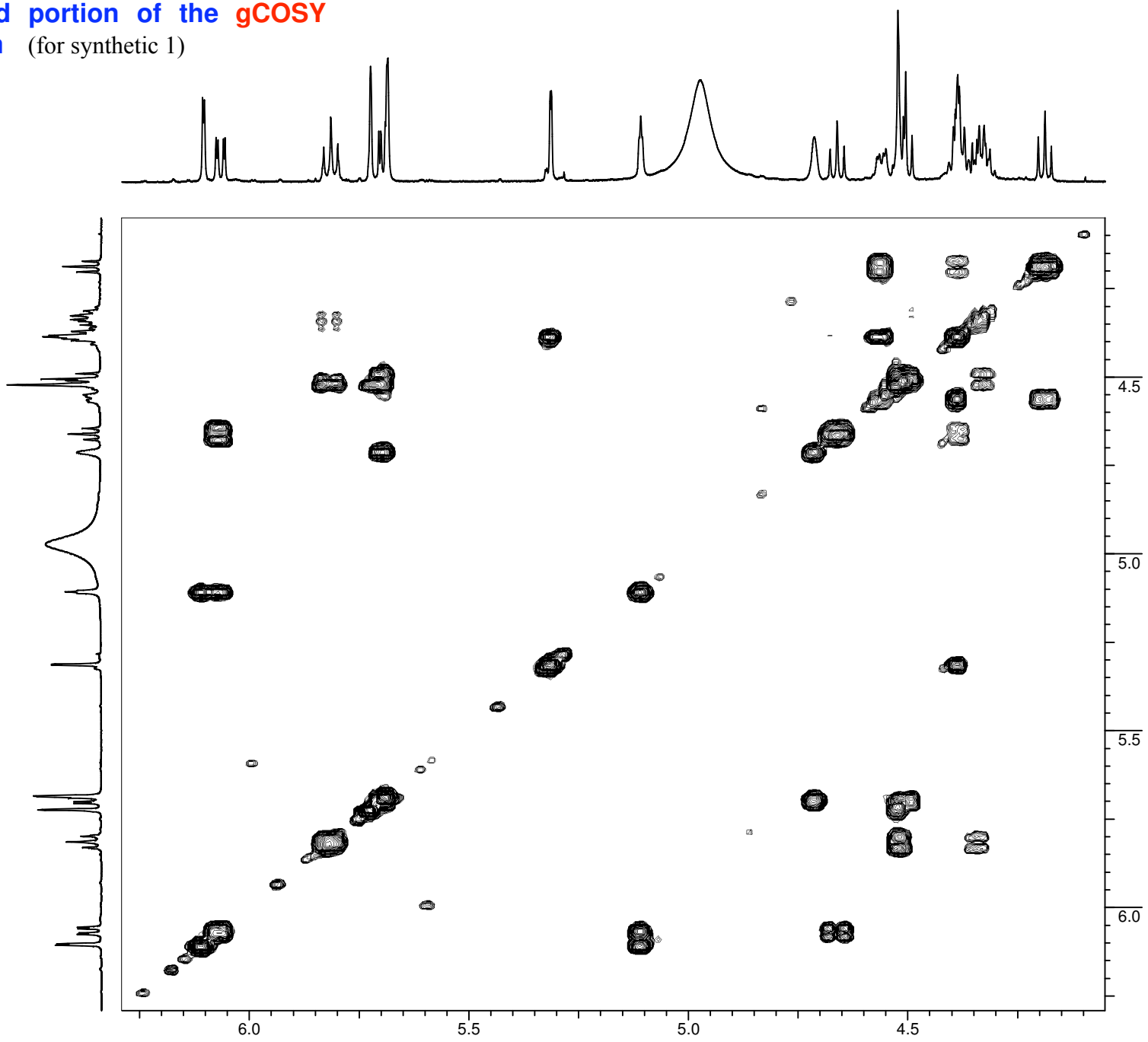


gCOSY

(for synthetic 1)

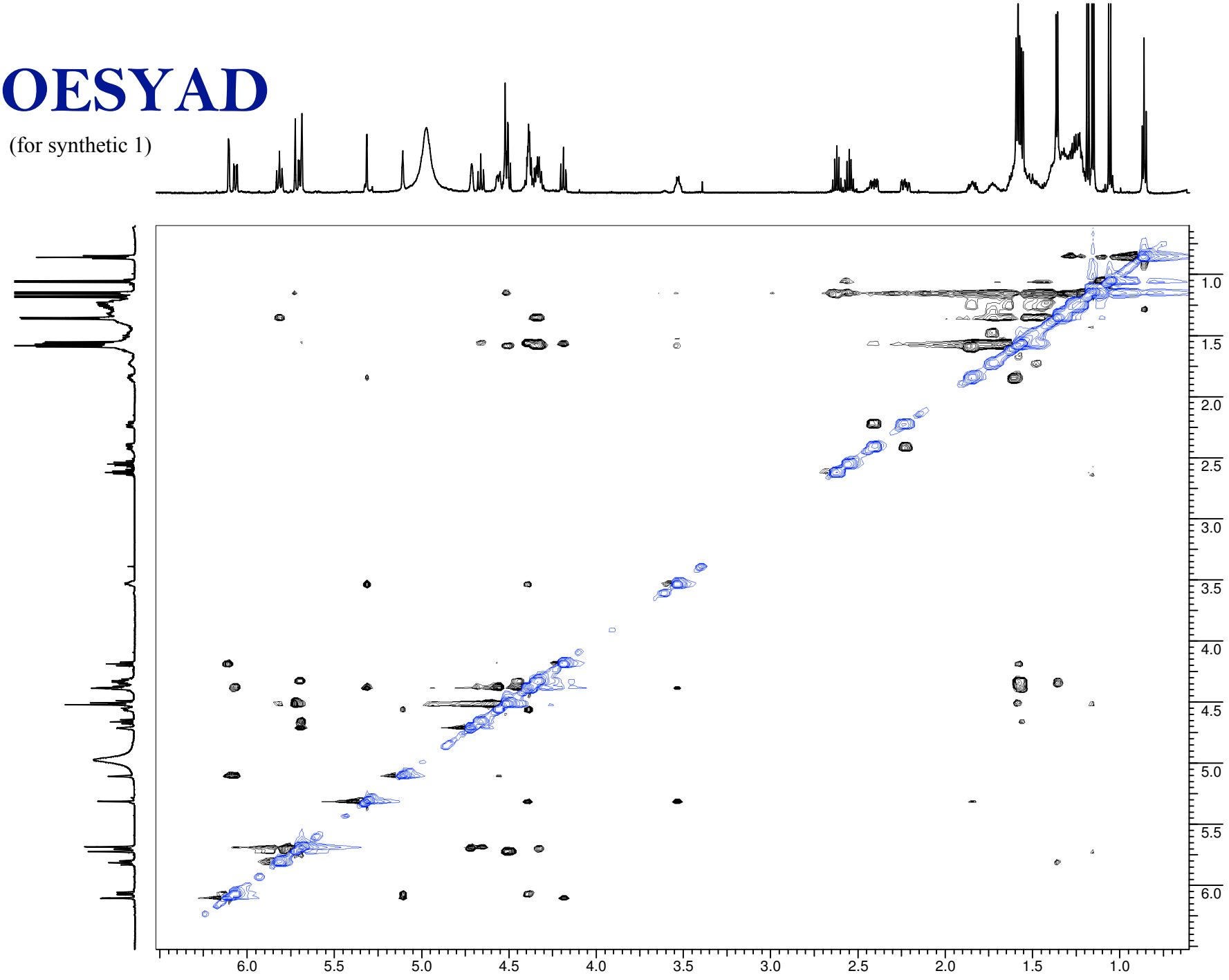


Expanded portion of the gCOSY spectrum (for synthetic 1)

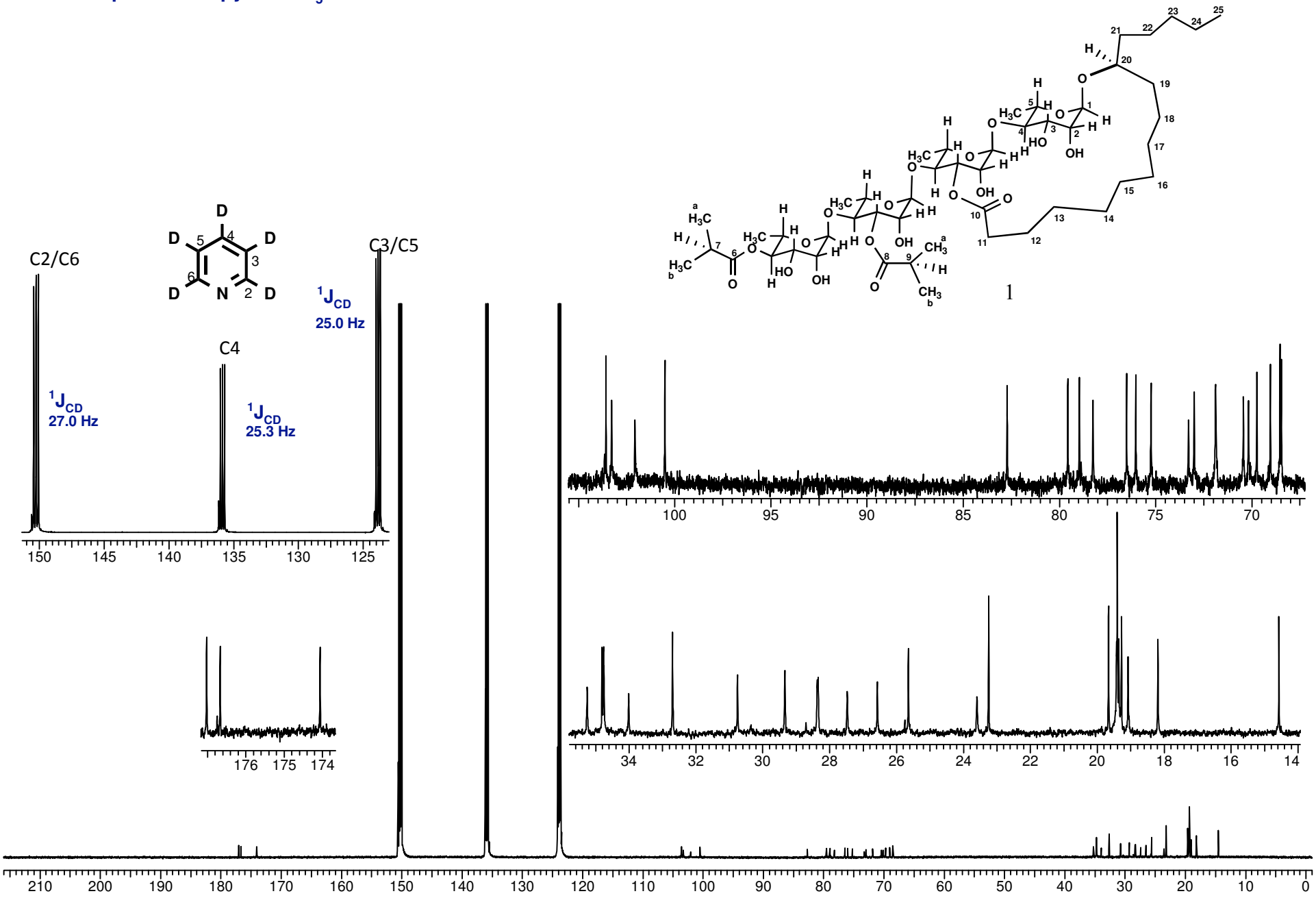


ROESYAD

(for synthetic 1)



^{13}C NMR spectrum in pyridine-d_5



Comparison of 1H NMR in different solvents