Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Total Synthesis of *cis*-Reticulatacin-10-ones A and B: Absolute Stereochemical Assignment

*Sherif B. Abdel Ghani, Lynda J. Brown, Bruno Figadère, and Richard C. D. Brown**

*Corresponding author rcb1@soton.ac.uk; FAX: +44 (0)23 80593781

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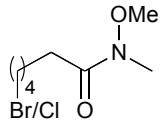
1.0 General methods

All reactions were carried out under an inert atmosphere in oven dried glassware. THF and Et_2O were distilled from sodium and benzophenone prior to use. Triethylamine and dichloromethane were dried by distillation from CaH_2. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solution using Bruker AC300, AV300 (300 and 75 MHz respectively) or Bruker DPX400 (400 and 100 MHz respectively) spectrometers. Chemical shifts are reported in δ units using $CHCl_3$ as an internal standard (δ 7.27 ppm ^{1}H, δ 77.15 ppm ^{13}C respectively). Infrared spectra were recorded on a Nicolet 380 spectrometer fitted with a Diamond platform, as solids or neat liquids. Melting points are uncorrected. Electron impact and chemical ionisation mass spectra were obtained using a Fisons VG platform single quadropole mass spectrometer. Electrospray mass spectra were obtained using a Micromass platform mass analyser with an electrospray ion source. Chiral HPLC separations were performed on a Agilent 1120 Compact LC using a Chiral CD-Ph column (4.6 x 250 mm) eluting with isopropanol:hexane (1:4, 1 mL/min), monitored by UV detection at 210 nm.

2.0 Preparation of Compounds

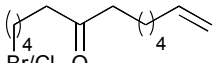
2.1 6-Bromo-*N*-methoxy-*N*-methyhexanamide (contains ~ 20% 6-chloro-*N*-methoxy-*N*-methy hexanamide)



To a stirred suspension of *O*,*N*-dimethylhydroxylamine hydrochloride (2.73 g, 27.98 mmol) in anhydrous CH_2Cl_2 (60 mL), 6-bromohexanoyl chloride (**8**, 5.00 g, 23.4 mmol) was added slowly, followed by dropwise addition of *i*-Pr_2NEt (9 mL, 51.6 mmol) at 0 °C. The solution was allowed to warm to rt, then stirred at rt for 4 h before dilution with CH_2Cl_2. The reaction mixture was washed with 1 N HCl (3 x 50 mL), brine (25 mL) and dried ($MgSO_4$) followed by concentration *in vacuo* affording the title Weinreb amide as a mixture (~4:1) with the corresponding alkyl chloride (5.30 g, 27.7 mmol, 99%).* IR ν_{max} (neat)/cm^{-1} 2937 (s), 2865 (s), 1658 (s), 1460 (s), 1415 (m), 997 (s); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.66 (3H, s, $NOCH_3$), 3.39 (2H, t, *J* = 6.7 Hz, CH_2Br), 3.15 (3H, s, NCH_3), 2.41 (2H, t, *J* = 7.4 Hz, CH_2CON-), 1.87 (2H, quintet, *J* = 7.0 Hz, CH_2), 1.64 (2H, quintet, *J* = 7.1 Hz, CH_2), 1.51-1.42 (2H, m, CH_2); [selected signals for the alkyl chloride: 3.52 (2H, t, *J* = 6.7 Hz, CH_2Cl), 1.83-1.77 (m, CH_2)]; ^{13}C-NMR (75 MHz, $CDCl_3$) δ 174.4 (C=O), 61.3 (OCH_3), 33.6 (CH_2), 32.6 (CH_2), 31.6 (CH_2), 27.9 (CH_2), 23.7 (NCH_3); [selected signals for the alkyl chloride: 44.9 (CH_2), 33.5 (CH_2), 32.5 (CH_2), 27.7 (CH_2), 23.9 (NCH_3)]; LRMS (EI^+) *m/z* 238 ($[M+H]^+$), 158 ($[M–halide]^+$); HRMS (ES^+) *m/z* $C_8H_{16}BrNNaO_2$ Calcd. 260.026, found 260.028.

*Yield calculated based on a 4:1 mixture of bromide and chloride

2.2 1-Bromotridec-12-en-6-one (9) (contains ~ 20% 1-chlorotridec-12-en-6-one)

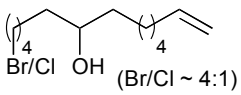


9 (Br/Cl ~ 4:1)

At –40 °C hept-7-enylmagnesium bromide in THF (30 mL of a 1.0 M solution, 30 mmol) was added dropwise to a solution of 6-bromo-*N*-methoxy-*N*-methyhexanamide* (2.10 g, 9.17 mmol)* in THF (25 mL). The mixture was left to stir at –35 ºC for 2 h. The reaction was quenched at –35 ºC by dropwise addition of cold water, then allowed to warm to rt. The mixture was extracted with ether (3 x 30 mL). The combined organic extract was washed with 1 N H_2SO_4 solution (20 mL) then water, brine, dried ($MgSO_4$) and concentrated *in vacuo* to give a colourless oil. Purification by silica gel column chromatography (Et_2O/hexane, 1:19→1:9) gave the haloketones as a colourless oil (1.452 g, 5.41 mmol, 59%).* IR ν_{max} (neat)/cm^{-1} 2931 (s), 2857 (s), 1712 (s), 1640 (s), 1460 (s), 1412 (m), 994 (s), 911 (s); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.77 (1H, tdd, *J* = 6.8, 10.2, 17.0 Hz, C<u>H</u>=CH_2), 5.02-4.87 (2H, m, CH=C<u>H</u>$_2$), 3.38 (2H, t, *J* = 6.7 Hz, CH_2Br), 2.39 (4H, q, *J* = 7.3 Hz, C<u>H</u>$_2$C=OC<u>H</u>$_2$), 2.03 (2H, q, *J* = 6.8 Hz, C<u>H</u>$_2$CH=CH_2), 1.90-1.80 (2H, m, C<u>H</u>$_2$$CH_2$Br), 1.65-1.49 (4H, m, CH_2), 1.41-1.20 (6H, m, CH_2); [selected signals for the alkyl chloride: 3.51 (2H, t, *J* = 6.6 Hz, CH_2Cl), 1.81-1.75 (2H, m, CH_2]; ^{13}C-NMR (75 MHz, $CDCl_3$) δ 210.8 (C=O), 138.8 (<u>C</u>H=CH_2), 114.4 (CH=<u>C</u>H_2), 42.8 (CH_2), 42.4 (CH_2), 33.6 (CH_2), 32.6 (CH_2), 28.7 (CH_2), 27.8 (CH_2), 23.7 (CH_2), 22.9 (CH_2) [selected signals for the alkyl chloride: 44.8 (CH_2Cl), 32.4 (CH_2), 26.5 (CH_2), 23.1 (CH_2)]; LRMS (CI^+) *m/z* 275 ([M+H]$^+$), 195 ([M–halide]$^+$); HRMS (ES^+) *m/z* $C_{13}H_{23}BrNaO$ Calcd. 297.083, found 297.083.

*Amounts and yields calculated based on a 4:1 mixture of bromide and chloride

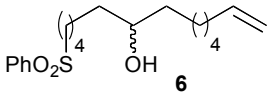
2.3 1-Bromotridec-12-en-6-ol (contains ~ 20% 1-chlorotridec-12-en-6-ol)



To a solution of the ketone (**9**, 30 mg, 0.112 mmol)* in EtOH (1 mL) was added $NaBH_4$ (12 mg, 0.33 mmol) at 0 °C. The reaction was left to warm to rt. After 30 min 1 N HCl was added dropwise to the reaction mixture [**CAUTION:** evolution of H_2 gas]. The mixture was extracted with ether (2 x 10 mL). The combined organic extract was washed with water, brine, then dried ($MgSO_4$) and concentrated *in vacuo*. Purification by silica gel column chromatography (EtOAc/hexane, 1:19→1:9) gave the title alcohol as a colourless oil (29.9 mg, 0.112 mmol, 100%).* IR ν_{max} (neat)/cm^{-1} 3347 (br), 2927 (s), 2855 (s), 1640 (s), 1460 (s), 994 (s), 909 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.81 (1H, tdd, *J* = 6.5, 10.3, 17.1 Hz, C<u>H</u>=CH_2), 5.00 (1H, d, *J* = 17.1 Hz, CH=C<u>H</u>H), 4.94 (1H, d, *J* = 10.3 Hz, CH=CH<u>H</u>), 3.59 (1H, m, C<u>H</u>OH), 3.41 (2H, t, *J* = 6.8 Hz, CH_2Br), 2.10-2.00 (2H, m, C<u>H$_2$</u>CH=CH_2), 1.90-1.80 (2H, m, C<u>H$_2$</u>CH_2Br), 1.55-1.25 (14H, m) [selected signals for the alkyl chloride: 3.56 (2H, t, *J* = 6.7 Hz, CH_2Cl), 1.83-1.77 (2H, m, CH_2)]; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 139.1 (<u>C</u>H=CH_2), 114.3 (CH=<u>C</u>H_2), 71.9 (CHOH), 37.6 (CH_2), 37.3 (CH_2), 33.8 (CH_2), 32.8 (CH_2), 29.2 (CH_2), 28.9 (CH_2), 28.3 (CH_2), 25.6 (CH_2), 24.9 (CH_2) [selected signals for the alkyl chloride: 45.2 (CH_2Br), 37.4 (CH_2), 32.7 (CH_2), 27.1 (CH_2), 25.1 (CH_2)]; LRMS (EI^+) *m/z* 277 ($[M+H]^+$).

*Amounts and yields calculated based on a 4:1 mixture of bromide and chloride

2.4 (±)-1-(Phenylsulfonyl)tridec-12-en-6-ol (6)



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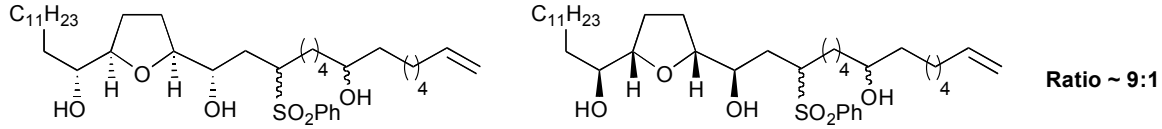
To a stirred solution of the 1-bromotridec-12-en-6-ol (120 mg, 0.45 mmol)* in dry DMF (2 mL) at rt, was added $PhSO_2Na$ (78 mg, 0.47 mmol). The reaction mixture was heated a 60 °C for 5 h. The cooled reaction mixture was partitioned between ether and water. The combined ether extract was washed with 1 N HCl (aq), water, brine, then dried ($MgSO_4$) and concentrated *in vacuo* to give a cloudy oil. Purification by silica gel column chromatography (EtOAc/hexane, 2:8→3:7) gave the title sulfone as a colourless oil (125 mg, 0.37 mmol, 82%). IR ν_{max} (neat)/cm^{-1} 3526 (br), 2927 (s), 2855 (s), 1639 (s), 1447 (s), 1303 (s), 1144 (s), 1086 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.90 (2H, d, *J* = 7.8 Hz), 7.65 (1H, t, *J* = 7.5 Hz), 7.56 (2H, t, *J* = 7.5 Hz), 5.80 (1H, m, tdd, *J* = 6.8, 10.0, 17.1 Hz, C<u>H</u>=CH_2), 4.98 (1H, d, *J* = 17.1 Hz, CH=C<u>H</u>H), 4.92 (1H, d, *J* = 10.0 Hz, CH=CH<u>H</u>), 3.53 (1H, m, C<u>H</u>OH), 3.07 (2H, m, CH_2SO_2), 2.03 (2H, q, *J* = 6.8 Hz, C<u>H$_2$</u>CH=CH_2), 1.77-1.67 (2H, m, C<u>H$_2$</u>CH_2S), 1.48-1.20 (14H, m); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 139.3 (CSO_2), 139.1 (<u>C</u>H=CH_2), 133.6 (CH), 129.3 (CH), 128.1 (CH), 114.3 (CH=<u>C</u>H_2), 71.6 (CHOH), 56.2 (CH_2), 37.5 (CH_2), 37.0 (CH_2), 33.7 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 28.3 (CH_2), 25.5 (CH_2), 25.1 (CH_2), 22.7 (CH_2); LRMS (CI^+) *m/z* 361.2 ($[M+Na]^+$).

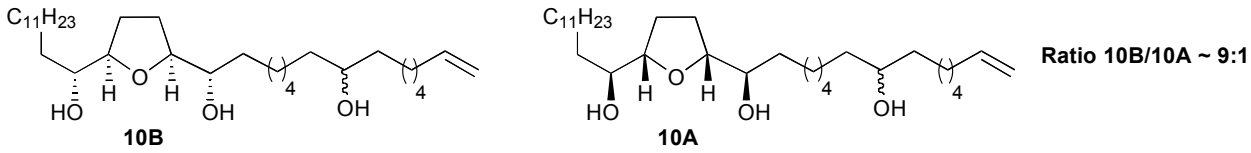
*Amounts calculated based on a 4:1 mixture of bromide and chloride

2.5 (1*S*,3*R*/*S*,8*R*/*S*)-1-[(2*S*,5*R*)-Tetrahydro-5-((1*R*)-1-hydroxytridecyl)furan-2-yl]-3-(phenylsulfonyl)pentadec-14-ene-1,8-diol (mixture of B/A isomers ~1:9)



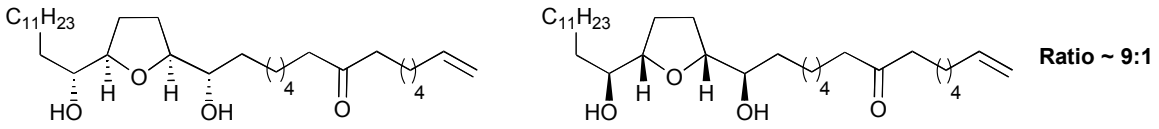
To a solution of the sulfone **6** (300 mg, 0.891 mmol) in dry THF (10 mL) at –78 °C, was added *n*-BuLi (730 µL of 2.45 M in hexane, 1.76 mmol) dropwise. The reaction mixture left to stir at –78 °C for 30 min before adding BF_3•Et_2O (225 µL, 1.76 mmol). The mixture was left to stir at –78 °C for 30 min, then a solution of enantiomeric epoxides (**5 B/A**, er ~ 9:1, 138.6 mg, 0.444 mmol) in THF (1 mL) was added dropwise. The mixture was left to stir at –78 °C for 1 h, then the cooling bath was removed and the reaction was allowed to warm to rt. Aqueous 1 N HCl (10 mL) was added dropwise, and the mixture was extracted with EtOAc (3 x 20 mL). The combined organic extract was washed with water, brine, then dried ($MgSO_4$) and concentrated *in vacuo*. Purification by silica gel column chromatography (EtOAc/hexane, 2:8→3:7) gave a mixture of diastereoisomeric sulfones as a colourless oil (160 mg, 0.246 mmol, 55%). IR ν_{max} (neat)/cm^{-1} 3381 (br), 2923 (s), 2853 (s), 1464 (s), 1447 (s), 1301 (s), 1143 (s), 1084 (s); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.89 (2H, d, *J* = 7.7 Hz), 7.64 (1H, t, *J* = 6.9 Hz), 7.55 (2H, t, *J* = 7.4 Hz), 5.80 (1H, m, C<u>H</u>=CH_2), 5.02-4.91 (2H, m, CH=C<u>H</u>$_2$), 3.90-3.70 (2H, m, CHO x 2), 3.60-3.48 (2H, m, C<u>H</u>OH x 2), 3.47-3.30 (2H, m), 2.10-1.70 (10H, m), 1.55-1.20 (39H, m), 0.92 (3H, t, *J* = 6.4 Hz, CH_3); ^{13}C-NMR (75 MHz, $CDCl_3$) [multiple signals observed due to the presence of diastereoisomers] δ 139.1 (C), 138.0 (CH), 133.6 (CH), 129.2 (2CH), 128.9 (2CH), 114.3 (CH_2), 82.6 (CH), 82.4 (CH), 82.3 (CH), 74.1 (CHOH), 72.0 (CHOH), 71.8 (CHOH), 71.6 (CHOH), 71.2 (CHOH), 60.9 ($CHSO_2$), 37.7 (CH_2), 37.6 (CH_2), 34.7 (CH_2), 33.8 (CH_2), 32.7 (CH_2), 32.0 (CH_2), 29.7 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 28.9 (CH_2), 28.9 (CH_2), 28.1 (CH_2), 26.6 (CH_2), 25.4 (CH_2), 25.3 (CH_2), 22.7 (CH_2), 14.2 (CH_3); LRMS (ES^+) *m/z* 651.5 ($[M+H]^+$), 673.5 ($[M+Na]^+$).

2.6 (1*S*,8*R*/*S*)-1-[(2*S*,5*R*)-Tetrahydro-5-((1*R*)1-hydroxytridecyl)furan-2-yl]pentadec-14-ene-1,8-diol (10B) (+ 10A, ratio ~ 9:1)



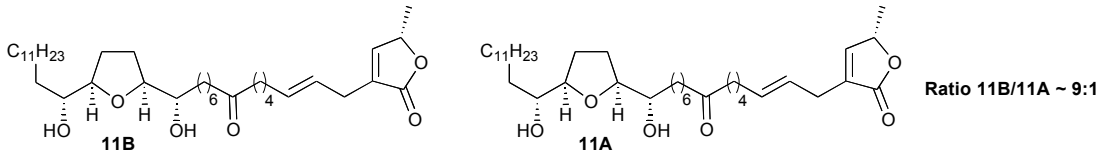
To a solution of 1-tetrahydro-5-(1-hydroxytridecyl)furan-2-yl)-3-(phenylsulfonyl)pentadec-14-ene-1,8-diol (A/B isomers, ratio ~ 1:9) (130 mg, 0.200 mmol) in dry MeOH (5 mL) at 0 °C, was added Na_2HPO_4 (80 mg, 0.56 mmol) and stirred for 2 min before the addition of Na/Hg amalgam 10% (600 mg). The reaction was allowed to warm to rt, left to stir for 3 h, then diluted with ether and dropwise addition of saturated NH_4Cl (aq). The mixture was extracted with EtOAc (4 x 10 mL) and the combined organic solution washed with water, brine, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by silica gel column chromatography (EtOAc-hexane, 1:4→1:1) gave the title isomeric triols as a white solid (83 mg, 0.162 mmol, 81%). $[\alpha]^{27}_D$ –0.07 ($CHCl_3$, *c* 1.00); Mp 55-58 °C; IR ν_{max} (neat)/cm^{-1} 3381 (br), 2917(s), 2849 (s), 1466 (s), 1308 (s), 1086 (s), 1026 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.81 (1H, tdd, *J* = 6.8, 10.0, 17.1 Hz, C<u>H</u>=CH_2), 4.99 (1H, qd, *J* = 1.8, 17.1 Hz, CH=C<u>H</u>H), 4.93 (1H, tdd, *J* = 1.3, 1.8, 10.0, CH=CH<u>H</u>), 3.85-3.78 (2H, m, CHO x 2), 3.62-3.54 (1H, m, C<u>H</u>OH), 3.45-3.38 (2H, m, C<u>H</u>OH x 2), 2.42 (3H, br, OH), 2.05 (2H, tq, *J* = 1.3, 6.8, C<u>H</u>$_2$CH=CH_2), 1.98-1.88 (2H, m, CH_2 THF), 1.80-1.71 (2H, m, CH_2 THF) 1.56-1.2 (42H, m), 0.88 (3H, t, *J* = 6.9 Hz, CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 139.2 (CH), 114.3 (CH_2), 82.8 (2 x CH), 74.5 (CH), 74.4 (CH), 72.1 (CH), 37.5 (CH), 34.2 (CH_2), 34.1 (CH_2), 33.8 (CH_2), 32.0 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.0 (CH_2), 28.3 (CH_2), 25.8 (CH_2), 25.7 (CH_2), 25.7 (CH_2), 25.6 (CH_2), 22.8 (CH_2), 14.2 (CH_3); LRMS (ES^+) *m/z* 511.5 ($[M+H]^+$), 533.5 ($[M+Na]^+$); HRMS (ES^+) *m/z* $C_{32}H_{62}NaO_4$ Calcd. 533.455, found 533.453.

2.7 (15*S*)-15-[(2*S*,5*R*)-Tetrahydro-5-((1*R*)1-hydroxytridecyl)furan-2-yl]-15-hydroxypentadec-1-en-8-one (+ A isomer, dr ~ 9:1)



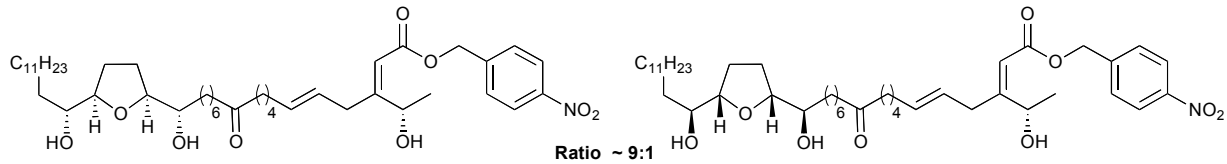
At 0 °C, Dess-Martin periodinane (51.1 mg, 0.117 mmol) was added in two batches to a solution of the triols (**10B/A** ratio ~ 9:1, 60 mg, 0.117 mmol) in dry CH_2Cl_2 (2 mL). After 5 h, the mixture was diluted with ether and filtered through a plug of silica eluting with 30% EtOAc in hexane and then concentrated *in vacuo*. Purification by silica gel column chromatography (EtOAc-hexane, 1:4→1:1) gave the title ketones as a white solid (33 mg, 0.064 mmol, 56%). The starting triols (10B/A ratio ~9:1, 20mg, 0.039mmol, 33%) were also recovered. $[\alpha]^{27}_D$ – 0.06 ($CHCl_3$, *c* 1.00); Mp 54-57 °C; IR ν_{max} (neat)/cm^{-1} 3441 (br), 2918 (s), 2849 (s), 1708 (s), 1640 (s), 1467 (s), 1414 (s), 1310 (s), 1079 (s), 1027 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.80 (1H, tdd, *J* = 6.5, 10.3, 16.8 Hz, C<u>H</u>=CH_2), 4.99 (1H, d, *J* = 16.8 Hz, CH=C<u>H</u>H), 4.94 (1H, d, *J* = 10.3, CH=CH<u>H</u>), 3.85-3.75 (2H, m, CHO x 2), 3.45-3.35 (2H, m, C<u>H</u>OH x 2), 2.43 (2H, br, OH), 2.38 (4H, t, *J* = 7.4 Hz, C<u>H_2</u>C=OC<u>H_2</u>), 2.08-2.01 (2H, m, C<u>H_2</u>CH=CH_2), 1.98-1.88 (2H, m, CH_2 THF), 1.80-1.71 (2H, m, CH_2 THF) 1.56-1.2 (40H, m), 0.88 (3H, t, *J* = 6.7 Hz, CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 211.6 (C=O), 139.0 (CH), 114.4 (CH_2), 82.8 (CH x 2), 74.5 (CH), 74.4 (CH), 42.9 (CH_2), 42.9 (CH_2), 34.2 (CH_2), 34.1 (CH_2), 33.7 (CH_2), 32.0 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 28.8 (CH_2), 28.8 (CH_2), 28.2 (CH_2), 25.8 (CH_2), 25.6 (CH_2), 23.9 (CH_2), 23.8 (CH_2), 22.8 (CH_2), 14.2 (CH_3); LRMS (ES^+) *m/z* 531.5 ($[M+Na]^+$); HRMS (ES^+) *m/z* $C_{32}H_{60}NaO_4$ Calcd. 531.439, found 531.438.

2.8 (4*E*)-4,5-Didehydro-*cis*-reticulatacin-10-one B/A (11B/A, dr ~ 9:1)



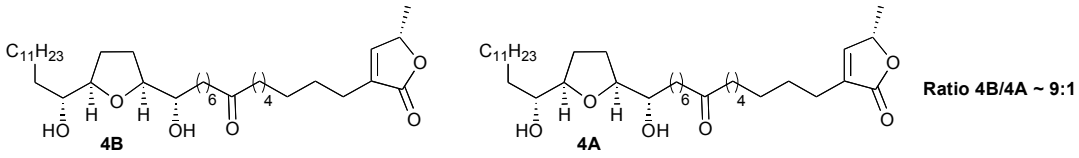
To a stirred solution of (15*S*)-15-[(2*S*,5*R*)-tetrahydro-5-((1*R*)1-hydroxytridecyl)furan-2-yl]-15-hydroxypentadec-1-en-8-one (+ A isomer, dr ~ 9:1) (26 mg, 0.051 mmol) and alkyne (**7**, 14.0 mg, 0.056 mmol) in DMF (3 mL) was added $CpRu(MeCN)_3PF_6$ (2.2 mg, 0.005 mmol, 10 mol %). The reaction was stirred at rt for 1 h, then diluted with ether and filtered through a plug of silica eluting with 40 % EtOAc in hexane. The solvents were removed *in vacuo*. Purification by silica gel column chromatography (EtOAc/hexane, 1:4→3:2) gave the title butenolide (21.8 mg, 0.036 mmol, 71 %) as a white solid, and the uncyclised nitrobenzyl ester byproduct (3 mg, 0.004 mmol, 8 %). **Data for 11B/A**: $[\alpha]^{26}_D$ +10.4 ($CHCl_3$, *c* 1.0); Mp 63-66 °C; IR ν_{max} (neat)/cm^{-1} 3431 (w), 3321 (s), 2918 (s), 2849 (s), 1737 (s), 1703 (s), 1469 (s), 1409 (s), 1377 (s), 1323 (s), 1086 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.00 (1H, q, *J* = 1.5 Hz, C<u>H</u>=C), 5.59-5.43 (2H, m, C<u>H</u>=C<u>H</u>CH_2C), 5.00 (1H, dq, *J* = 1.5, 6.9 Hz, C<u>H</u>CH_3), 3.85-3.77 (2H, m, CHO x 2), 3.45-3.34 (2H, m, C<u>H</u>OH x 2), 2.95 (2H, d, *J* = 6.5 Hz, =CHC<u>H_2</u>C), 2.44 (2H, br s, OH x 2), 2.40 (2H, t, *J* = 7.5 Hz, C<u>H_2</u>C=OCH_2), 2.38 (2H, t, *J* = 7.5 Hz, CH_2C=OC<u>H_2</u>), 2.07-1.99 (2H, m, C<u>H_2</u>CH=CH),1.98-1.89 (2H, m, CH_2 THF), 1.81-1.71 (2H, m, CH_2 THF), 1.54-1.20 (34H, m), 1.41 (3H, d, *J* = 6.9 Hz, C<u>H_3</u>CH), 0.89 (3H, t, *J* = 6.8 Hz, C<u>H_3</u>CH_2); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 211.4 (C), 173.6 (C), 149.6 (<u>C</u>H=C), 134.3 (<u>C</u>H=CH), 133.7 (CH=<u>C</u>), 124.4 (CH=<u>C</u>H), 82.8 (CH), 82.7 (CH), 77.7 (CH), 74.5 (CH), 74.4 (CH), 42.9 (<u>C</u>H_2C=O<u>C</u>H_2), 42.6 (CH), 34.2 (CH_2), 34.1 (CH_2), 32.3 (CH_2), 32.0 (CH_2), 30.5 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 28.9 (CH_2), 28.5 (CH_2), 28.2 (CH_2), 25.8 (CH_2), 25.6 (CH_2), 23.9 (CH_2), 23.4 (CH_2), 22.8 (CH_2), 19.2 (CH_3), 14.2 (CH_3); LRMS (ES^+) *m/z* 628 ($[M + Na]^+$).

Data for (*R*,2*Z*,5*E*)-4-nitrobenzyl 18-((2*R*,5*S*)-tetrahydro-5-((*S*)-1-hydroxyheptyl)furan-2-yl)-18-hydroxy-3-((*S*)-1-hydroxyethyl)-11-oxooctadeca-2,5-dienoate (+ A isomer, dr ~ 9:1)



IR ν_{max} (neat)/cm^{-1} 3384 (br), 2922 (s), 2852 (s), 1738 (s), 1719 (s), 1457 (s), 1346 (s), 1148 (s), 1071 (s); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.23 (2H, d, *J* = 8.7 Hz ArH), 7.54 (2H, d, *J* = 8.7 Hz ArH), 6.14 (1H, s, CH=C), 5.57-5.36 (2H, m, C<u>H</u>=C<u>H</u>CH$_2$C), 5.25 (2H, s, OCH$_2$Ar), 4.37 (1H, m, C<u>H</u>OHCH$_3$), 3.86-3.75 (2H, m, CHO x 2), 3.63 (1H, dd, *J* = 5.4, 13.4 Hz, =CHCH<u>H</u>C=), 3.45-3.35 (2H, m, CHOH x 2), 3.07 (1H, dd, *J* = 6.2, 13.4 Hz, =CHC<u>H</u>HC=), 2.46 (2H, br s, OH), 2.42-2.37 (4H, m, C<u>H$_2$</u>C=OC<u>H$_2$</u>), 2.02-1.88 (4H, m, CH$_2$), 1.82-1.65 (2H, m, CH$_2$), 1.52-1.17 (40H, m, CH$_2$), 1.34 (3H, d, *J* = 6.4 Hz, C<u>H$_3$</u>CHOH), 0.88 (3H, t, *J* = 6.6 Hz, <u>CH$_3$</u>CH$_2$); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 211.8 (C=O), 166.0 (C), 143.7 (CH), 132.5 (CH), 128.4 (CH), 126.9 (CH), 123.9 (CH), 112.9 (CH), 82.8 (CH), 82.7 (CH), 74.5 (CH), 74.4 (CH), 70.5 (CH), 64.3 (CH$_2$), 42.9 (<u>C</u>H$_2$C=OCH$_2$), 42.5 (CH$_2$C=O<u>C</u>H$_2$), 34.2 (CH$_2$), 34.1 (CH$_2$), 33.0 (CH$_2$), 32.1 (CH$_2$), 32.0 (CH$_2$), 28.2 (CH$_2$), 25.8 (CH$_2$), 25.5 (CH$_2$), 23.8 (CH$_2$), 23.1 (CH$_2$), 22.8 (CH$_2$), 22.4 (CH$_2$), 14.2 (CH$_3$); LRMS (ES$^+$) *m/z* 780 ([M+Na]$^+$).

2.9 *cis*-Reticulatacin-10-one B/A (4B/A, dr ~ 9:1)

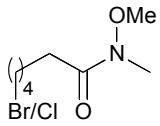


To a solution of (4*E*)-4,5-didehydro-*cis*-reticulatacin-10-one B/A (11B/A, dr ~ 9:1, 10 mg, 0.0165 mmol) and $NsNHNH_2$ (30.4 mg, 0.14 mmol) in THF (3 mL) was added a solution of NaOAc (11.5 mg, 0.14 mmol) in H_2O (1 mL). The mixture was stirred at rt for 36 h before EtOAc (10 mL) and brine (3 mL) were added. The organic phase was separated, re-extracting the aqueous solution with EtOAc (2 x 10 mL) and the combined organics was dried ($MgSO_4$), and concentrated *in vacuo*. ^{1}H NMR analysis of the crude product indicated that the reduction had not proceeded to completion, so the crude material was heated in THF (1 mL) containing $TsNHNH_2$ (6.0 mg, 0.032 mmol) and NaOAc (6.0 mg, 0.032 mmol) for 24 h. Following the same work-up procedure described above, the obtained residue was dissolved in ether and washed with 1 M HCl (aq), brine, saturated $KHCO_3$ (aq), then dried ($MgSO_4$). Purification by preparative normal phase HPLC (EtOAc/hexane, 35:65) gave *cis*-reticulatacin-10-ones B/A (**4B/A**, dr ~ 9:1) (7 mg, 0.0115 mmol, 69 %) as a white solid along with the hydrazone byproduct* (3.5 mg, 0.004 mmol, 25%). $[\alpha]^{26}_D$ +13.7 ($CHCl_3$, *c* 0.5); Mp 68-72 °C; IR ν_{max} (neat)/cm^{-1} 3449 (br), 2918 (s), 2849 (s), 1743 (s), 1703 (s), 1470 (s), 1458 (s), 1412 (s), 1321 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.98 (1H, q, *J* = 1.5 Hz, CH=C), 4.99 (1H, dq, *J* = 1.5, 6.8 Hz, $CHCH_3$), 3.85-3.77 (2H, m, CHO x 2), 3.45-3.38 (2H, m, CHOH x 2), 2.43 (2H, br, s, OH), 2.26 (4H, t, *J* = 7.4 Hz, $C\underline{H_2}C{=}OC\underline{H_2}$), 2.26 (2H, t, *J* = 7.8 Hz, $CH_2C{=}$), 1.98-1.89 (2H, m, CH_2 THF), 1.80-1.69 (2H, m, CH_2 THF), 1.62-1.20 (48H, m), 1.41 (3H, d, *J* = 6.8 Hz, CH_3CH), 0.87 (3H, t, *J* = 6.7 Hz, CH_3CH_2); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 211.6 (C), 174.0 (C) 149.0 (CH), 134.3 (C), 82.8 (CH), 82.7 (CH), 77.5 (CH), 74.5 (CH), 74.4 (CH), 42.9 ($\underline{C}H_2C{=}OCH_2$), 42.8 ($CH_2C{=}O\underline{C}H_2$), 34.2 ($CH_2$), 34.1 ($CH_2$), 32.0 ($CH_2$), 29.8 ($CH_2$), 29.8 ($CH_2$), 29.5 ($CH_2$), 29.4 ($CH_2$), 29.3 ($CH_2$), 29.2 ($CH_2$), 29.1 ($CH_2$), 28.2 ($2CH_2$), 27.4 ($CH_2$), 25.8 ($CH_2$), 25.6 ($CH_2$), 25.2 ($CH_2$), 23.9 ($CH_2$), 23.8 ($CH_2$), 22.8 ($CH_2$), 19.3 ($CH_3$), 14.2 ($CH_3$); LRMS ($ES^+$) *m/z* 630 ($[M+Na]^+$); HRMS ($ES^+$) *m/z* $C_{37}H_{66}NaO_6$ Calcd. 629.476, found 629.476.

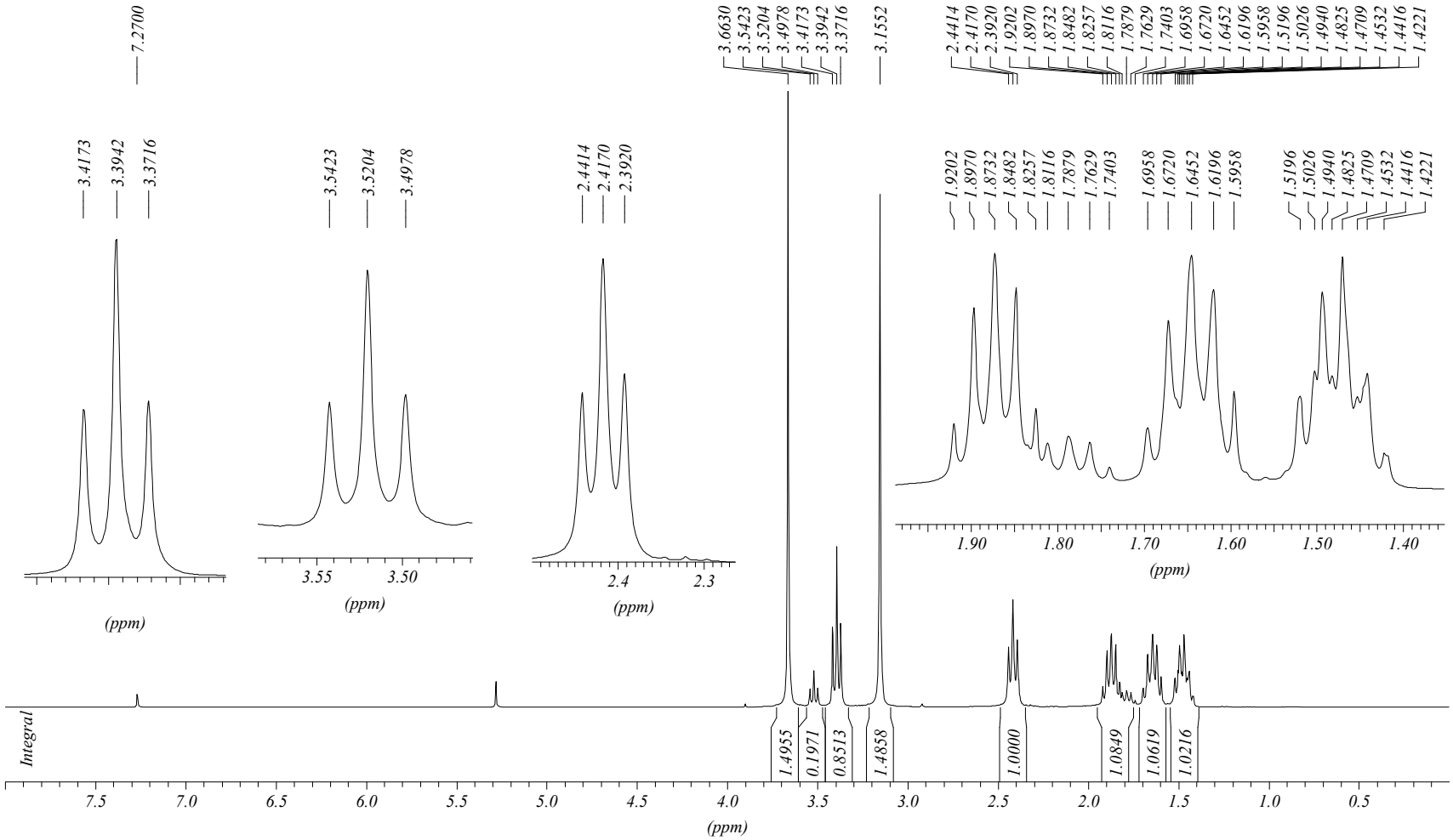
*The hydrazone byproduct (12 mg, 0.014 mmol) was converted to the mixture of *cis*-reticulaticin-10-ones B/A (dr ~ 9:1) by dissolving in THF (1 mL), water (0.2 mL) and AcOH (0.2 mL). The reaction mixture was left to stir at rt for 3 days. The mixture was neutralised with saturated $NaHCO_3$ (aq) and extracted with EtOAc (3 x 10 mL), dried ($MgSO_4$) and purified by silica gel column chromatography (20 % to 50 % EtOAc/hexane, 1:41:1) to give the diastereomeric mixture of acetogenins **4B/A** (7 mg, 0.011 mmol, 78%).

3.0 NMR Spectra

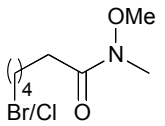
3.1 ^{1}H NMR 6-Bromo-*N*-methoxy-*N*-methyhexanamide (contains ~ 20% 6-chloro-*N*-methoxy-*N*-methyhexanamide)



shbf4719/2 big scale crude amide



3.2 ^{13}C NMR 6-Bromo-*N*-methoxy-*N*-methyhexanamide (contains ~ 20% 6-chloro-*N*-methoxy-*N*-methyhexanamide)



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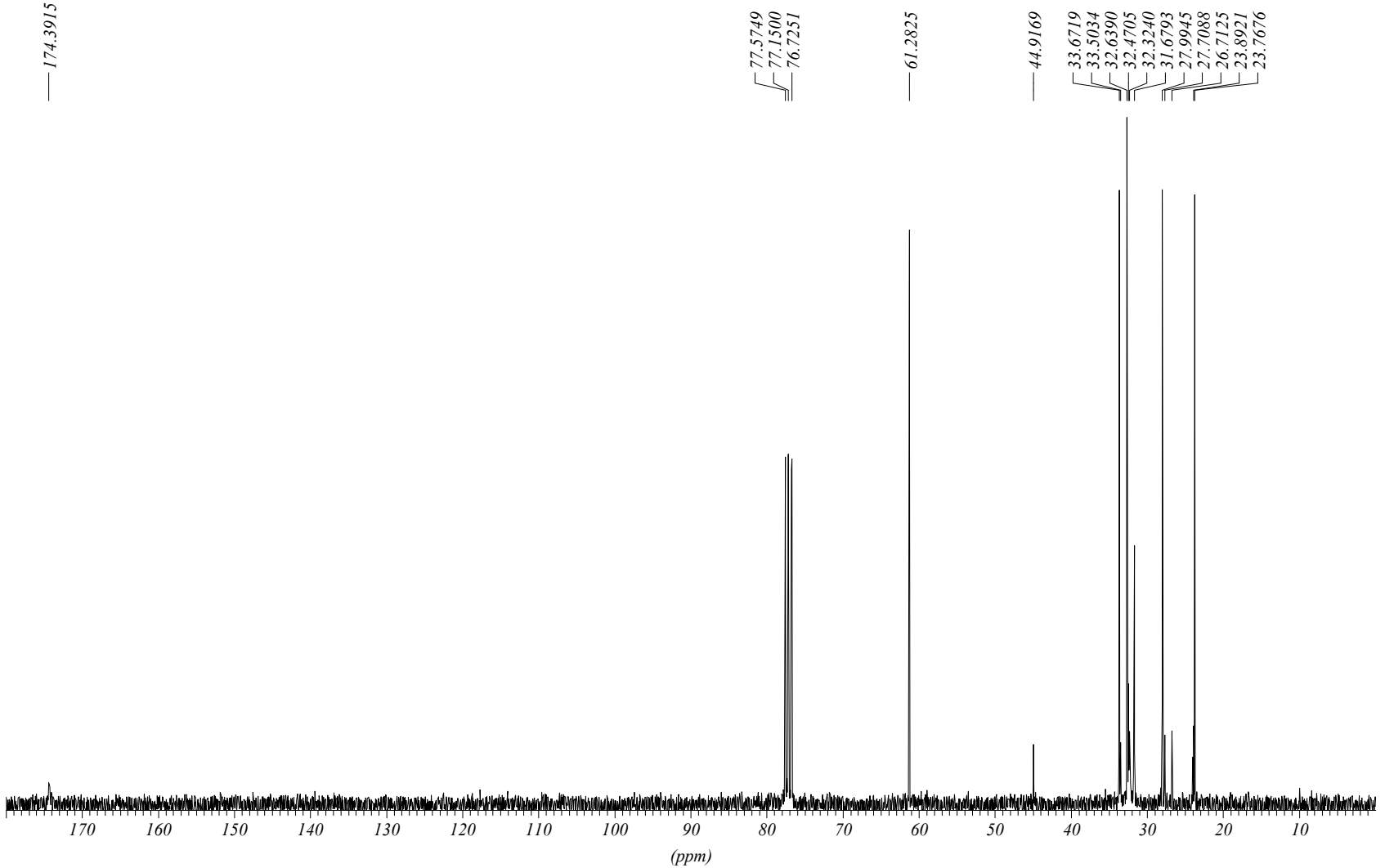
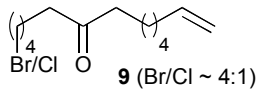
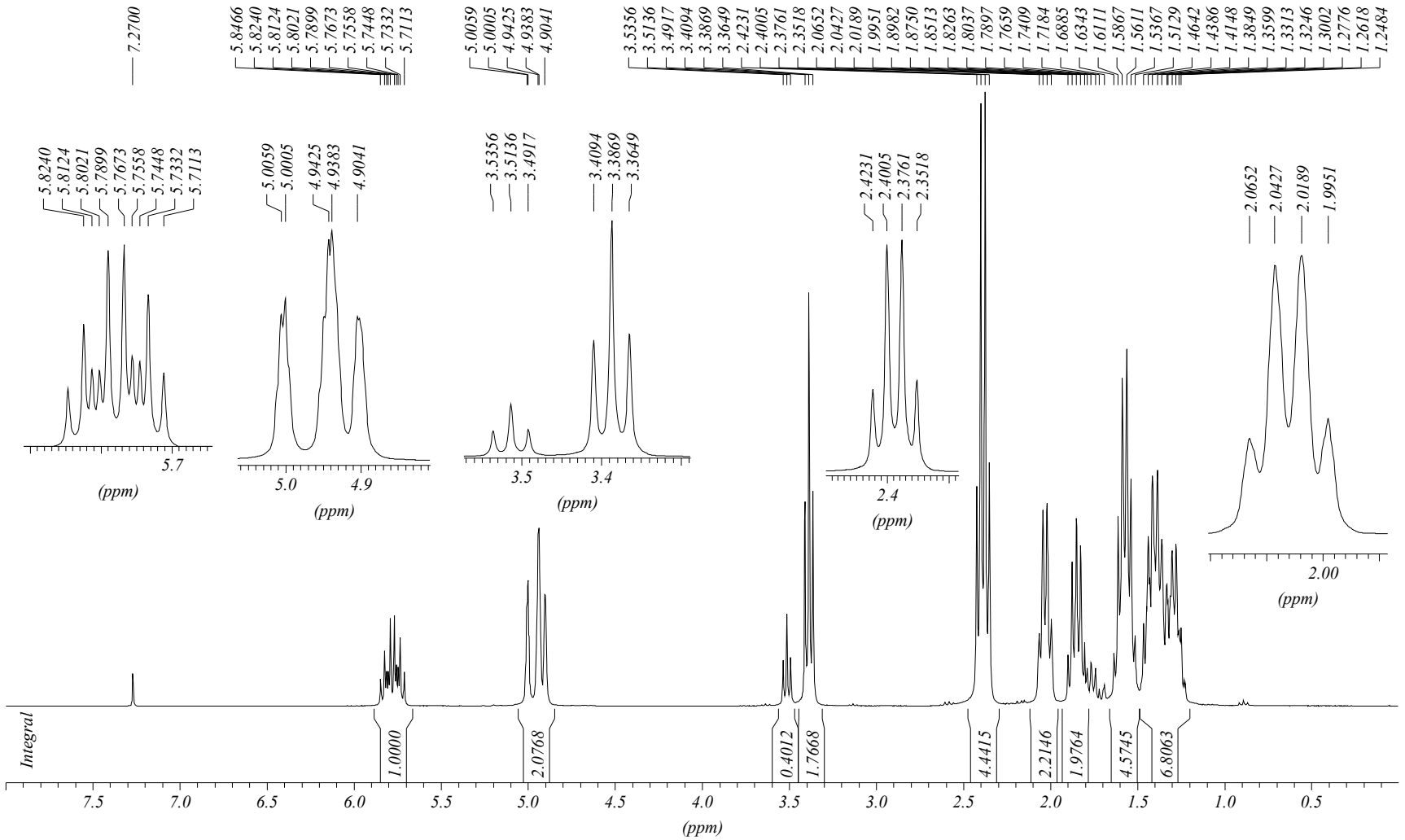


3.3 ^{1}H NMR 1-Bromotridec-12-en-6-one (9) (contains ~ 20% 1-chlorotridec-12-en-6-one)

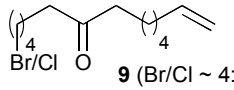


9 (Br/Cl ~ 4:1)

shbf4719/9 Ketone

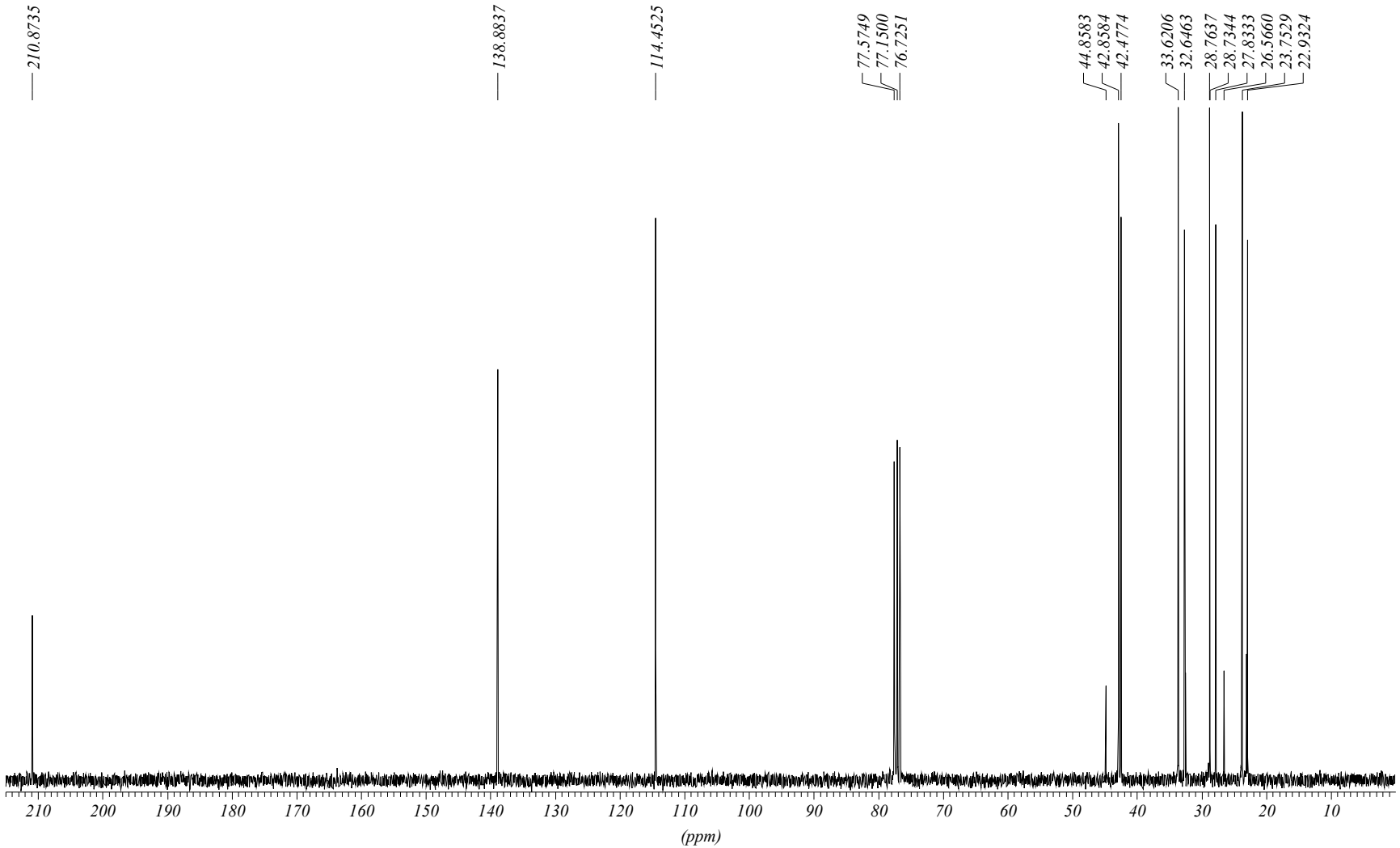


3.4 ^{13}C NMR 1-Bromotridec-12-en-6-one (9) (contains ~ 20% 1-chlorotridec-12-en-6-one)

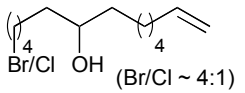


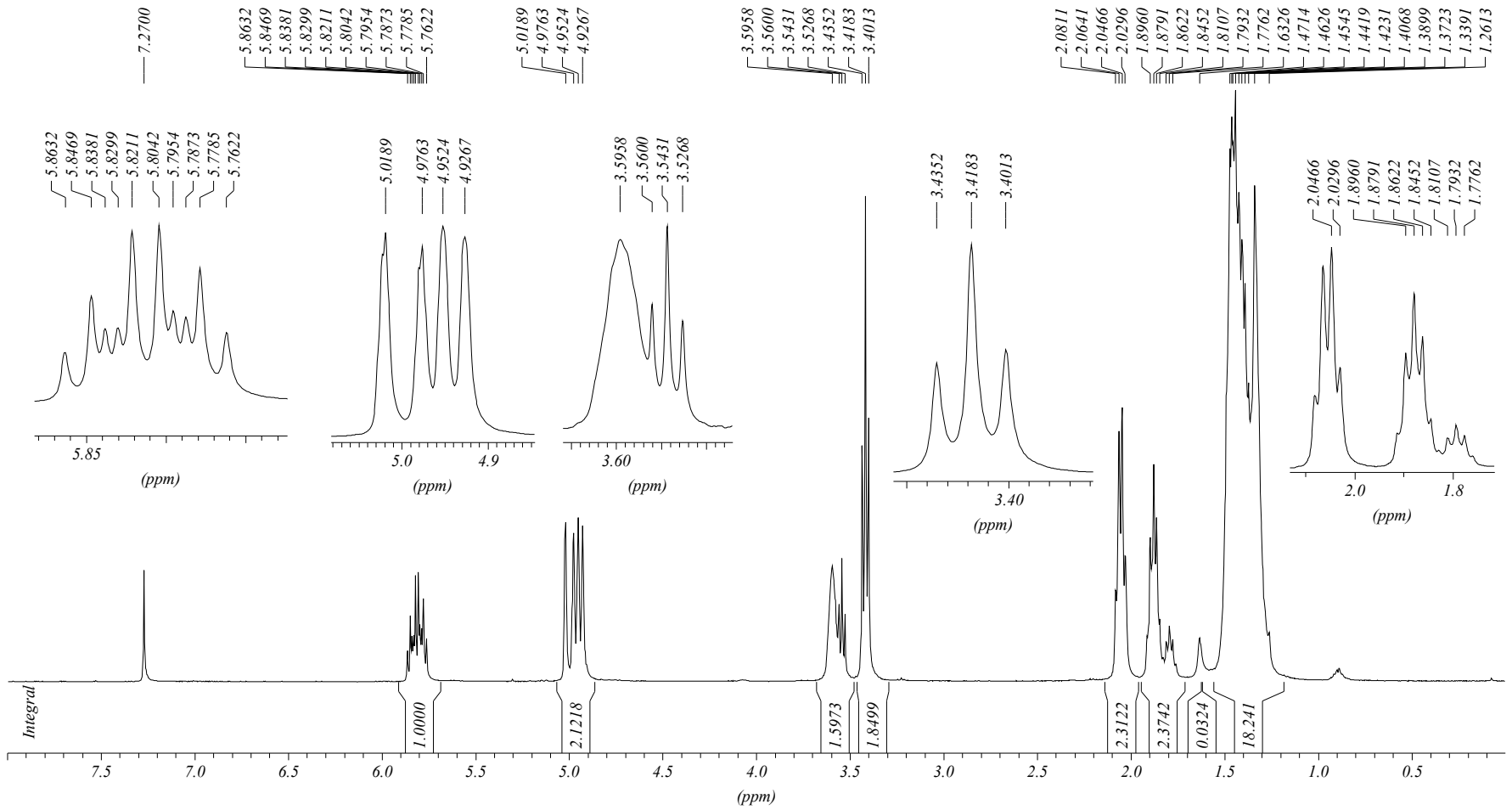
9 (Br/Cl ~ 4:1)

shbf4719/9 Ketone

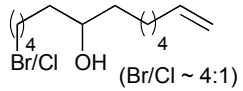


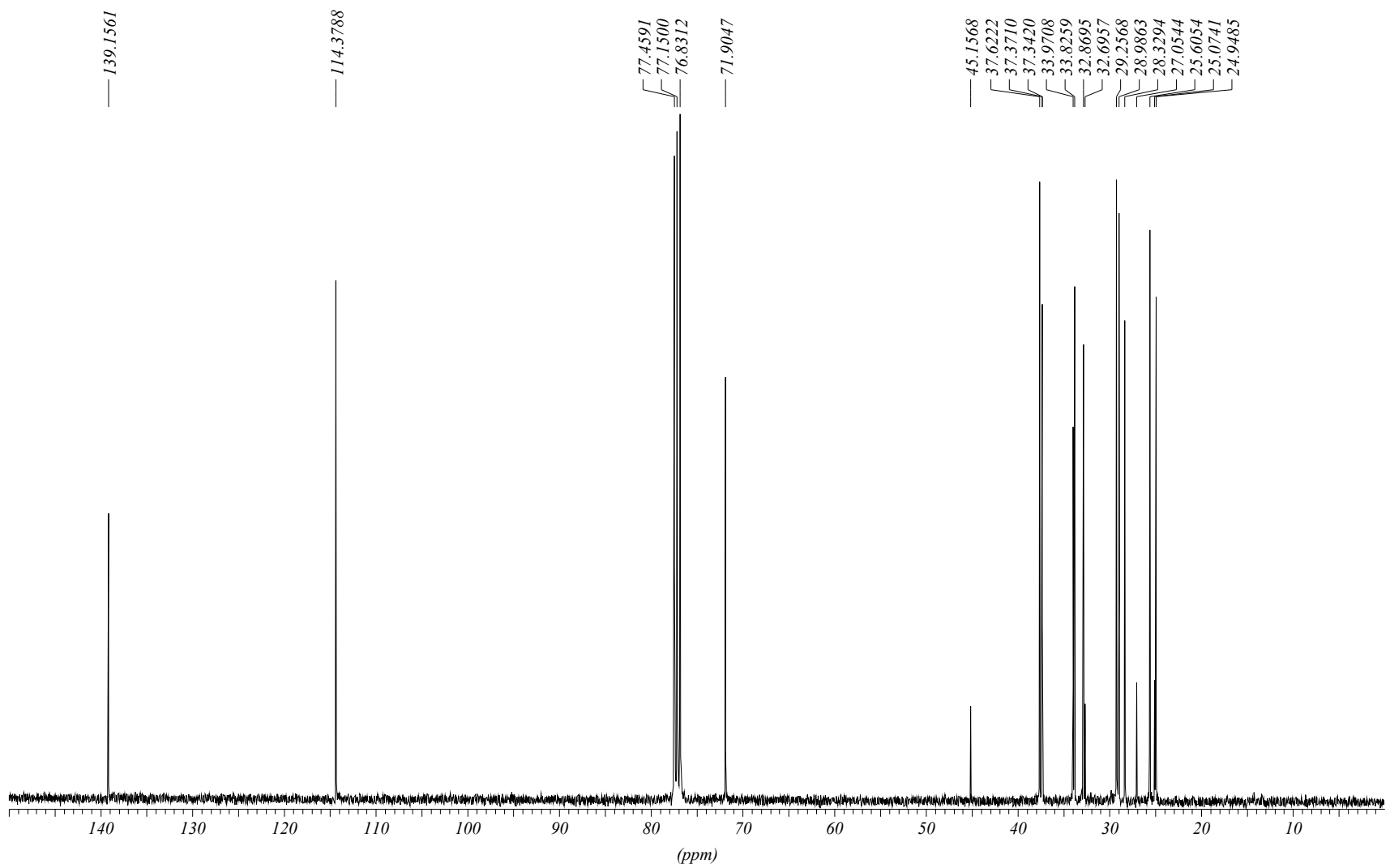
3.5 ^{1}H NMR 1-Bromotridec-12-en-6-ol (contains ~ 20% 1-chlorotridec-12-en-6-ol)



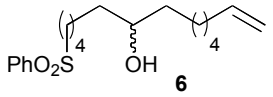


3.6 ^{13}C NMR 1-Bromotridec-12-en-6-ol (contains ~ 20% 1-chlorotridec-12-en-6-ol)

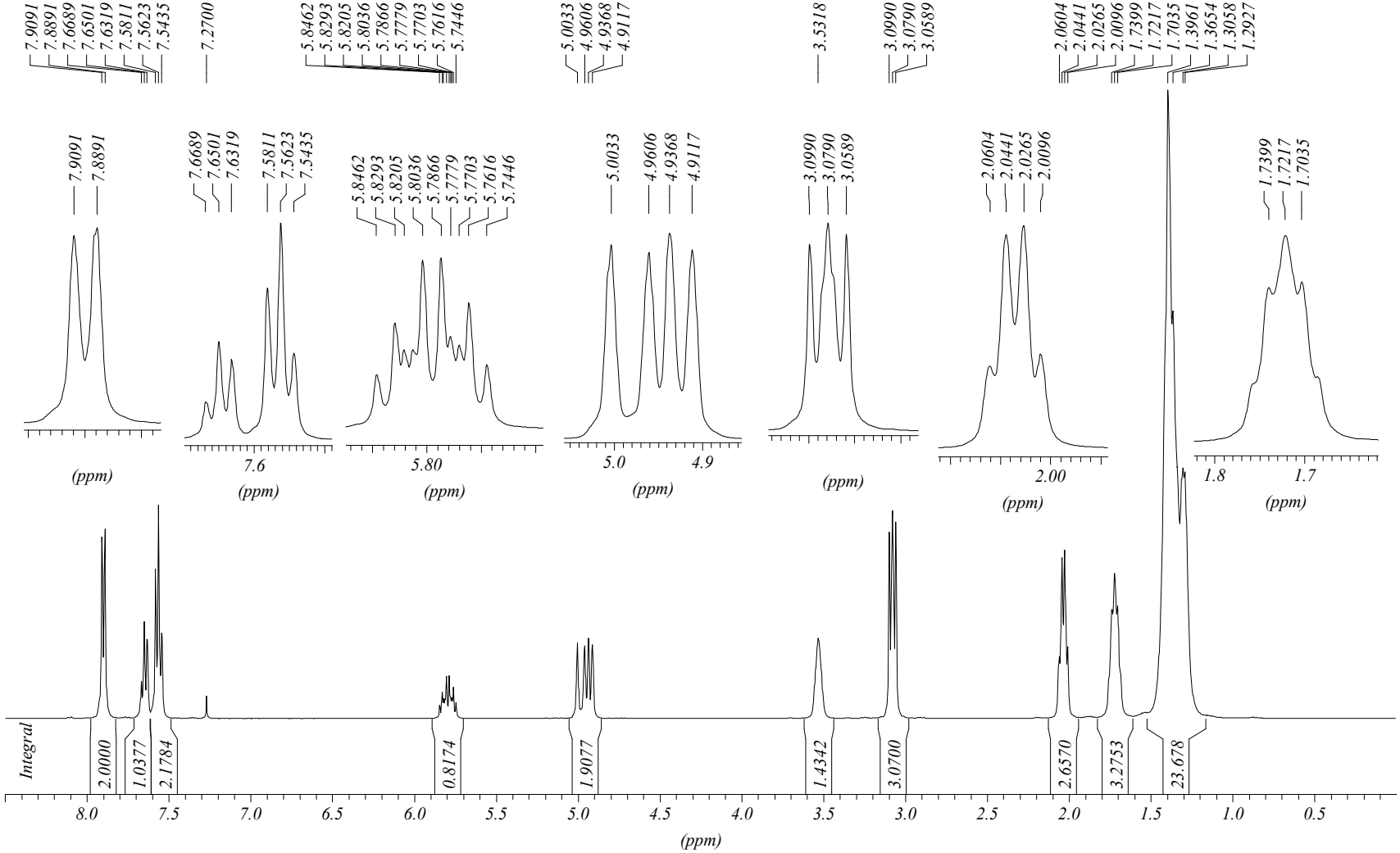




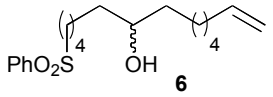
3.7 ^{1}H NMR (±)-1-(Phenylsulfonyl)tridec-12-en-6-ol (6)



4719/66.1-sulphone-6-OH-tride-13-ene

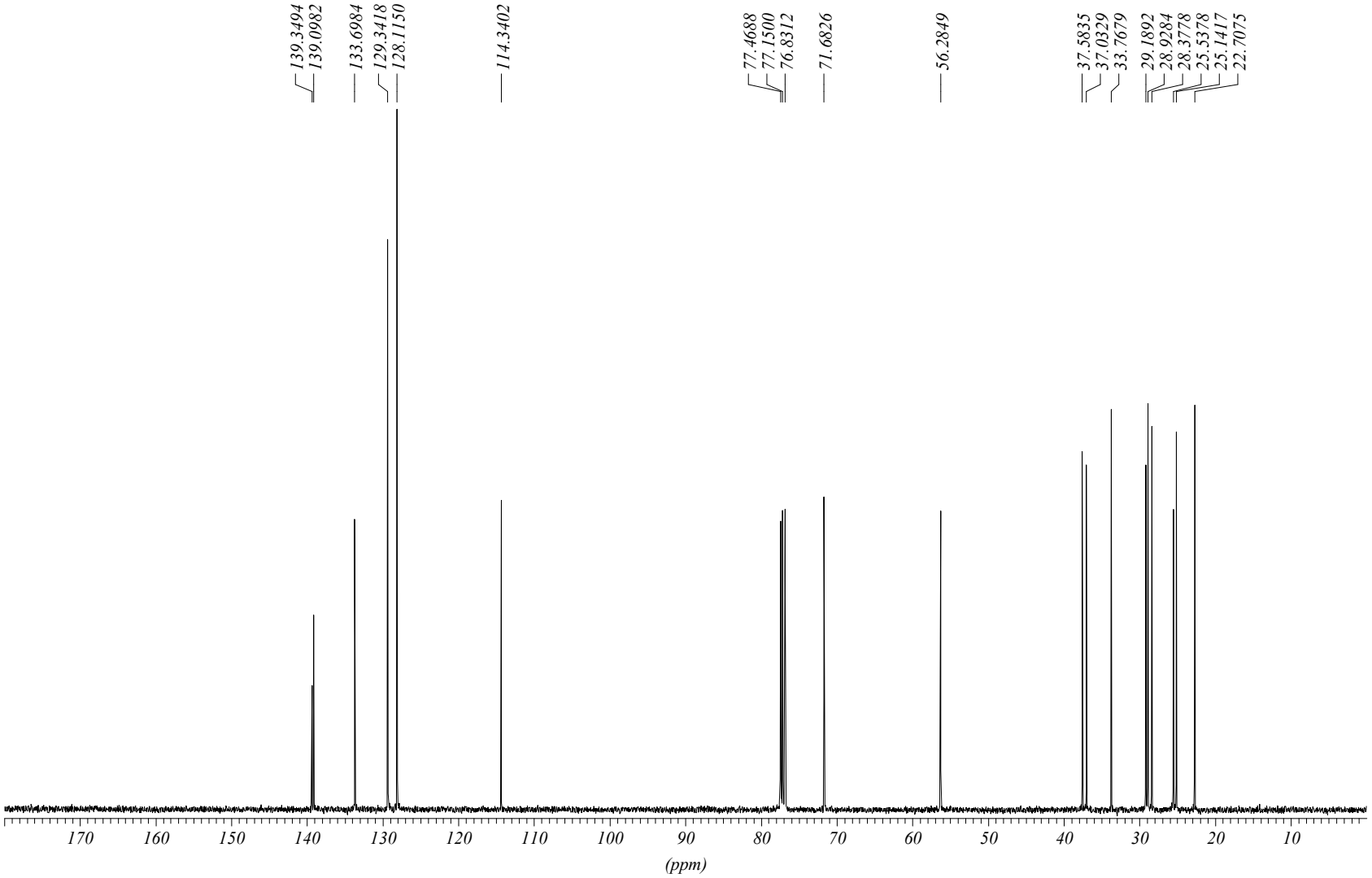


3.8 ^{13}C NMR (±)-1-(Phenylsulfonyl)tridec-12-en-6-ol (6)

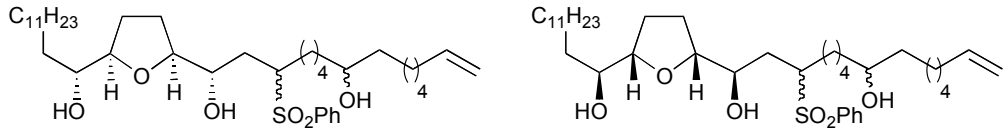


6

4719/66

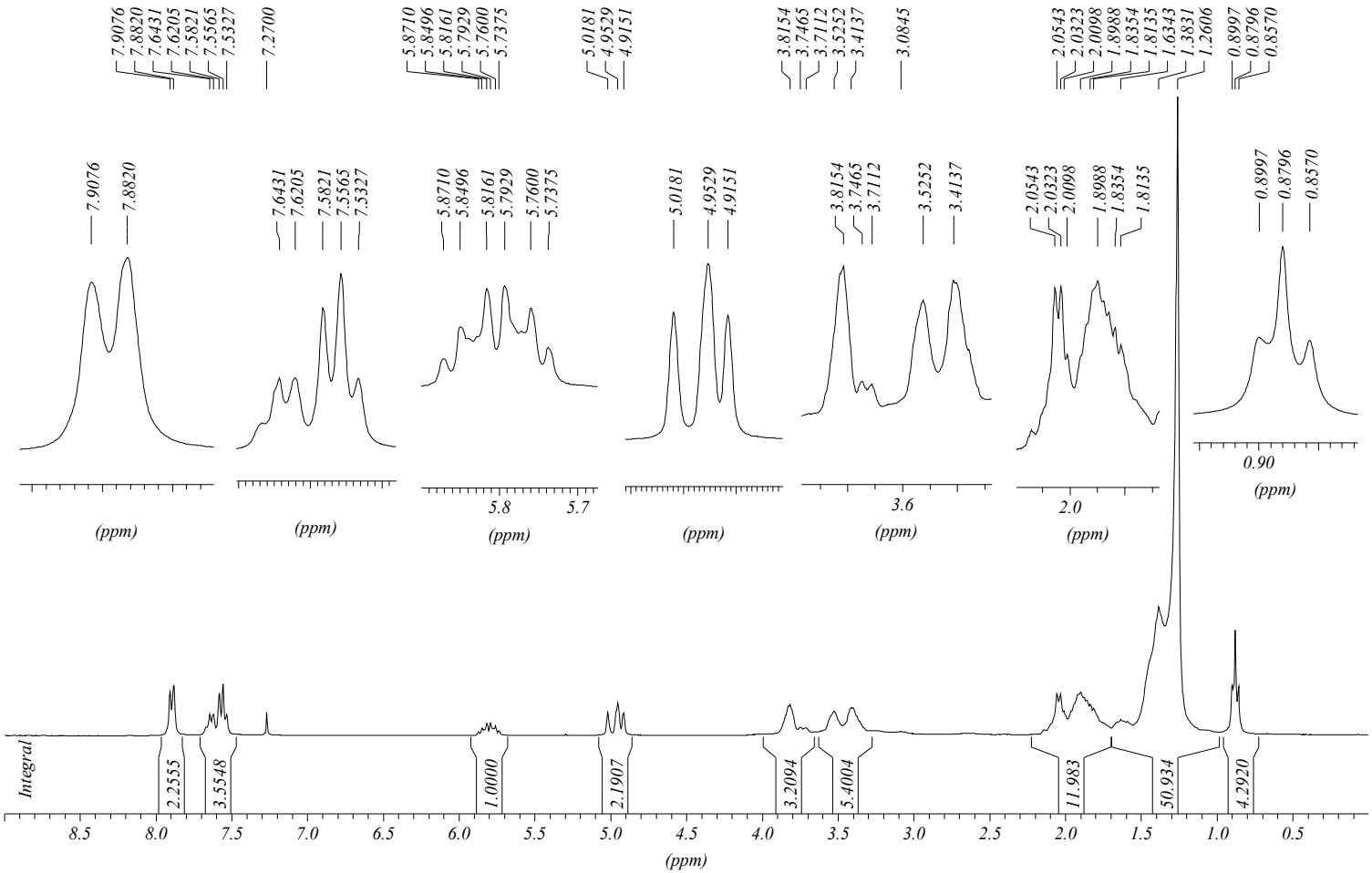


3.9 ^{1}H NMR (1*S*,3*R*/*S*,8*R*/*S*)-1-[(2*S*,5*R*)-Tetrahydro-5-((1*R*)-1-hydroxytridecyl)furan-2-yl]-3-(phenylsulfonyl)pentadec-14-ene-1,8-diol (mixture of A and B isomers in a ratio of 1:9)

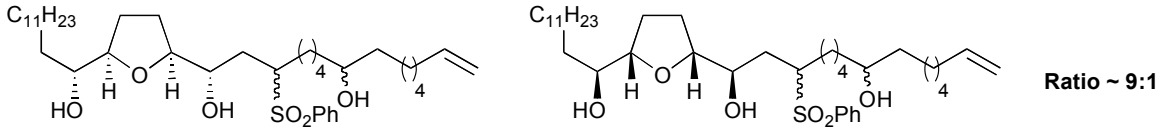


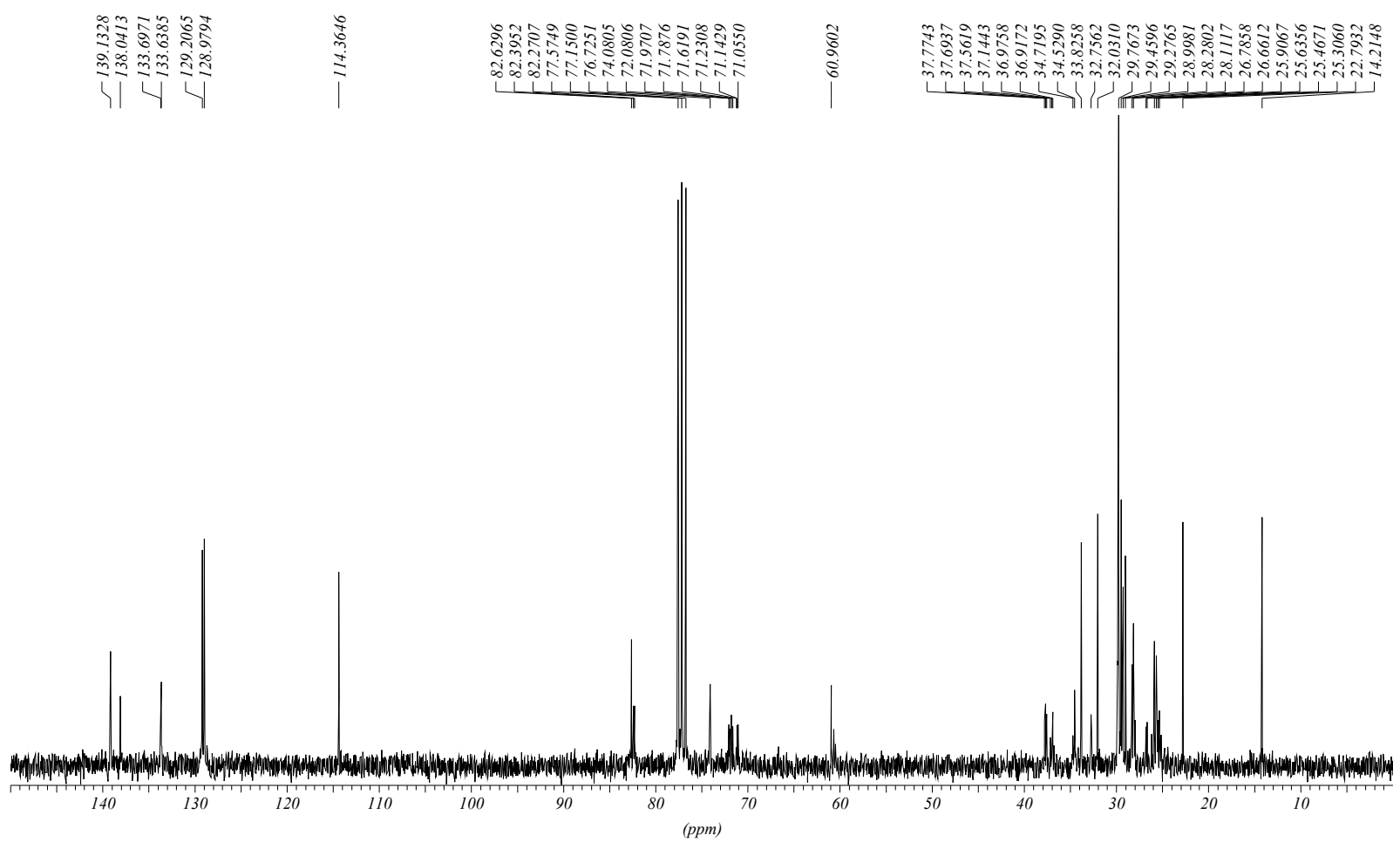
Ratio ~ 9:1

shbf4719/100 pure reticulata thf sulfon 6OL 13 ene

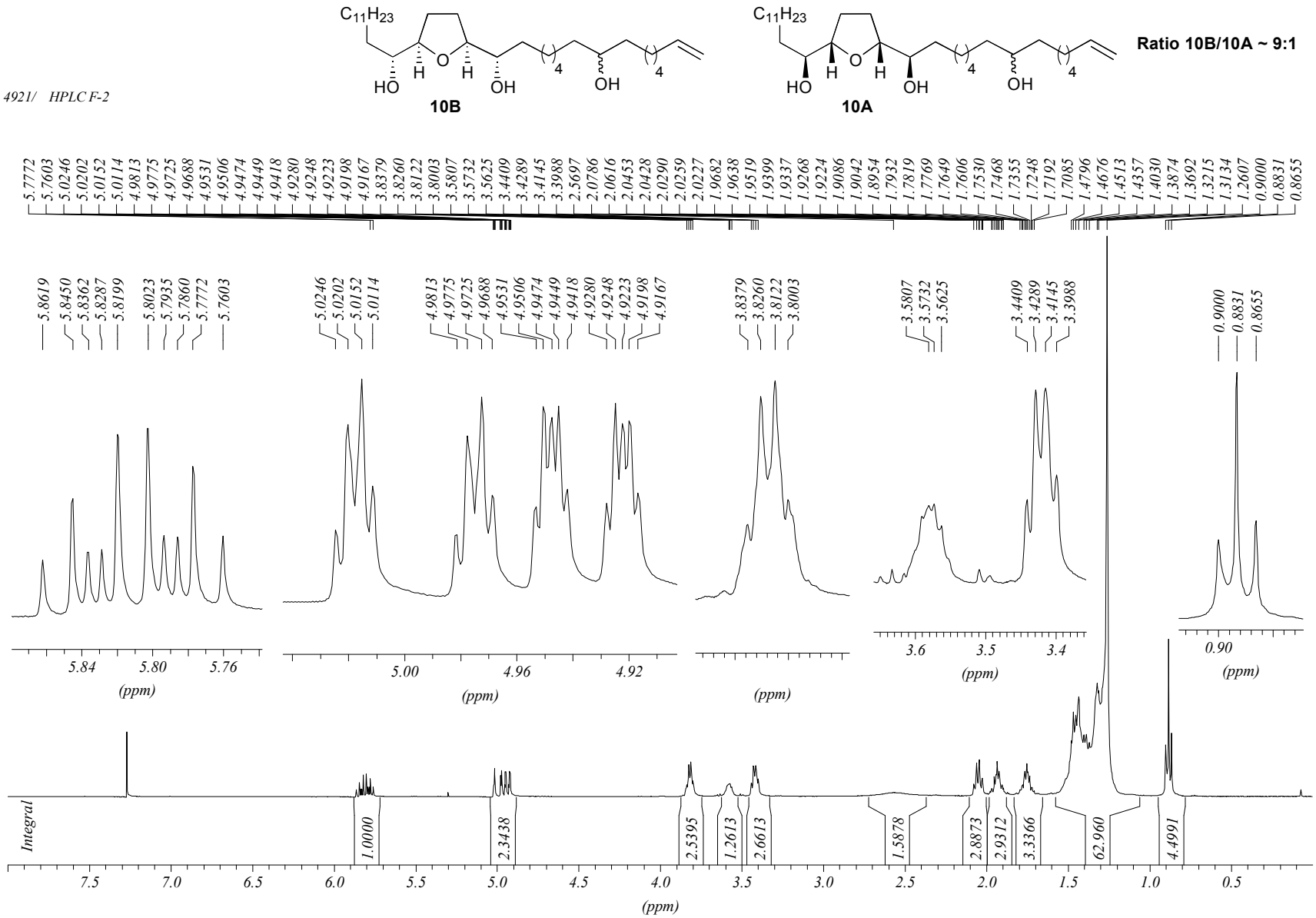


3.10 ^{13}C NMR (1*S*,3*R*/*S*,8*R*/*S*)-1-[(2*S*,5*R*)-Tetrahydro-5-((1*R*)-1-hydroxytridecyl)furan-2-yl]-3-(phenylsulfonyl)pentadec-14-ene-1,8-diol (mixture of A and B isomers in a ratio of 1:9)

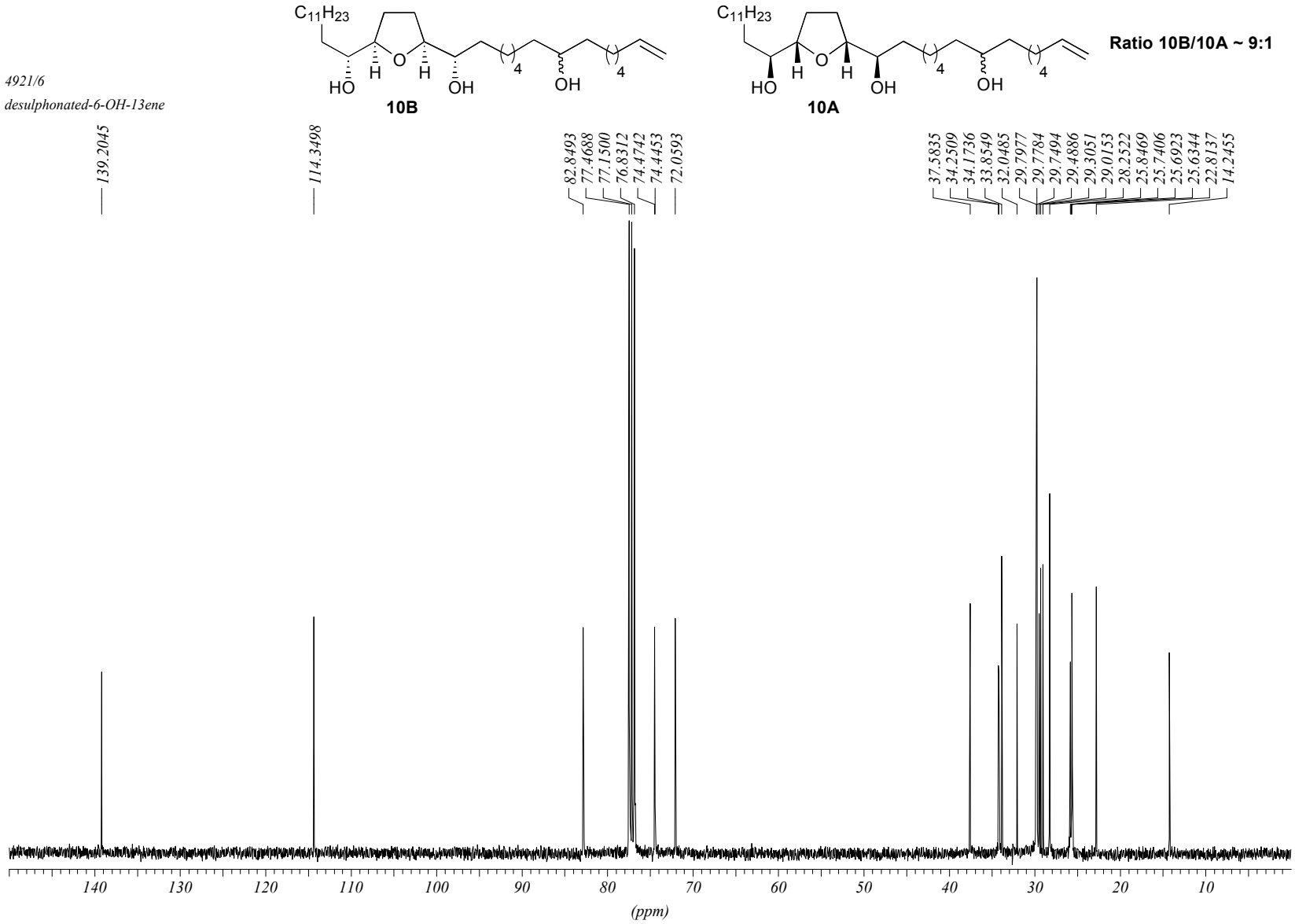




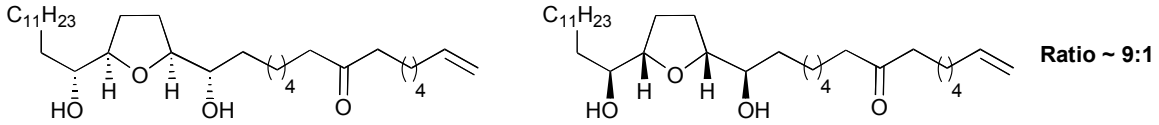
3.11 ^{1}H NMR (1*S*,8*R*/*S*)-1-[(2*S*,5*R*)-Tetrahydro-5-((1*R*)1-hydroxytridecyl)furan-2-yl]pentadec-14-ene-1,8-diol (10A/B, ratio ~ 1:9)



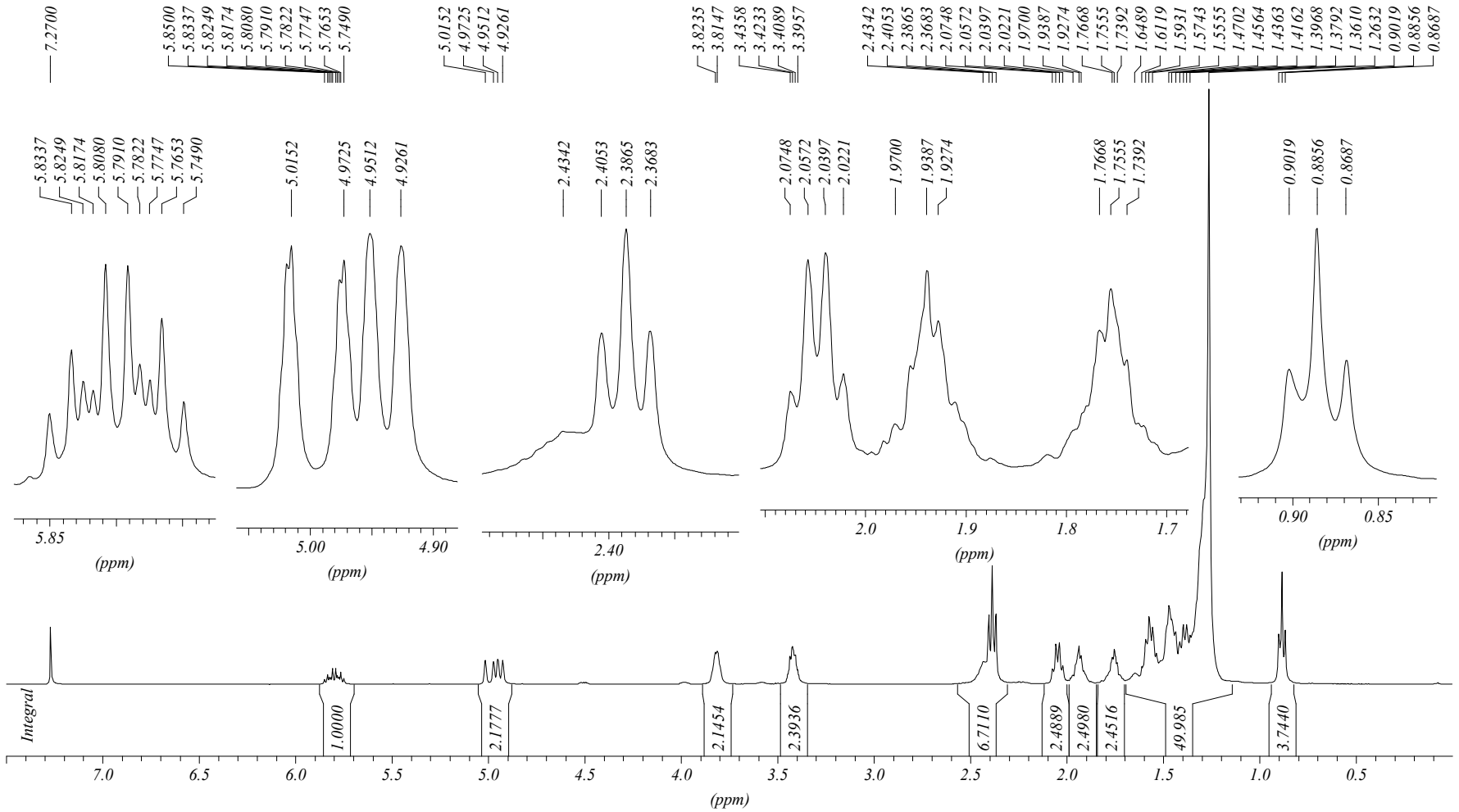
3.12 ^{13}C NMR (1*S*,8*R*/*S*)-1-[(2*S*,5*R*)-Tetrahydro-5-((1*R*)1-hydroxytridecyl)furan-2-yl]pentadec-14-ene-1,8-diol (10A/B, ratio ~ 1:9)



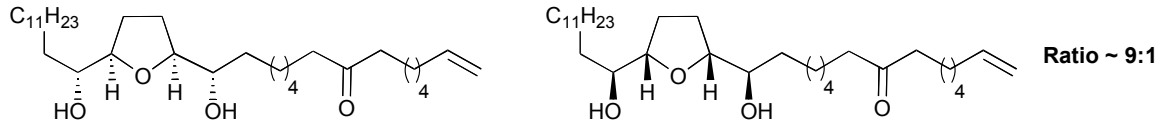
3.13 ^{1}H NMR (15*S*)-15-[(2*S*,5*R*)-Tetrahydro-5-((1*R*)1-hydroxytridecyl)furan-2-yl]-15-hydroxypentadec-1-en-8-one (mixture of A and B isomers in a ratio of 1:9)

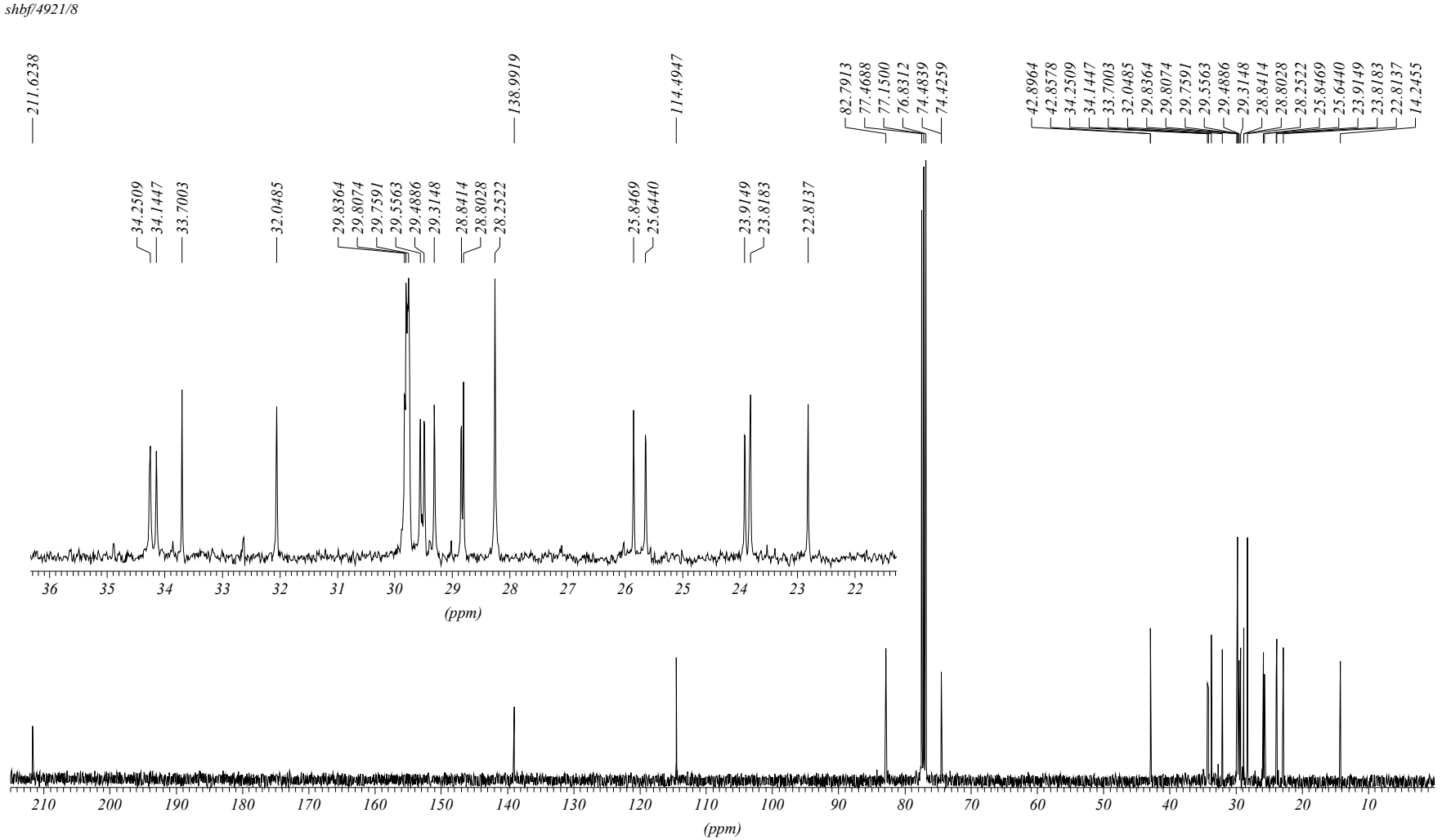


shbf/4921/8

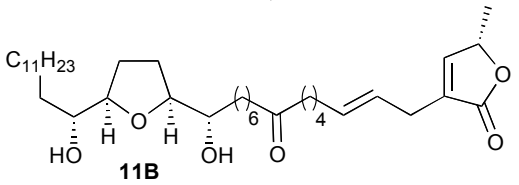


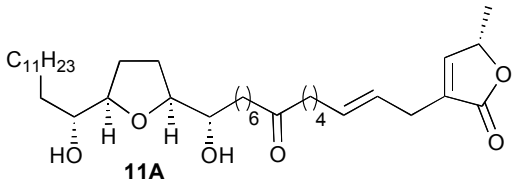
3.14 ^{13}C NMR (15*S*)-15-[(2*S*,5*R*)-Tetrahydro-5-((1*R*)1-hydroxytridecyl)furan-2-yl]-15-hydroxypentadec-1-en-8-one (mixture of A and B isomers in a ratio of 1:9





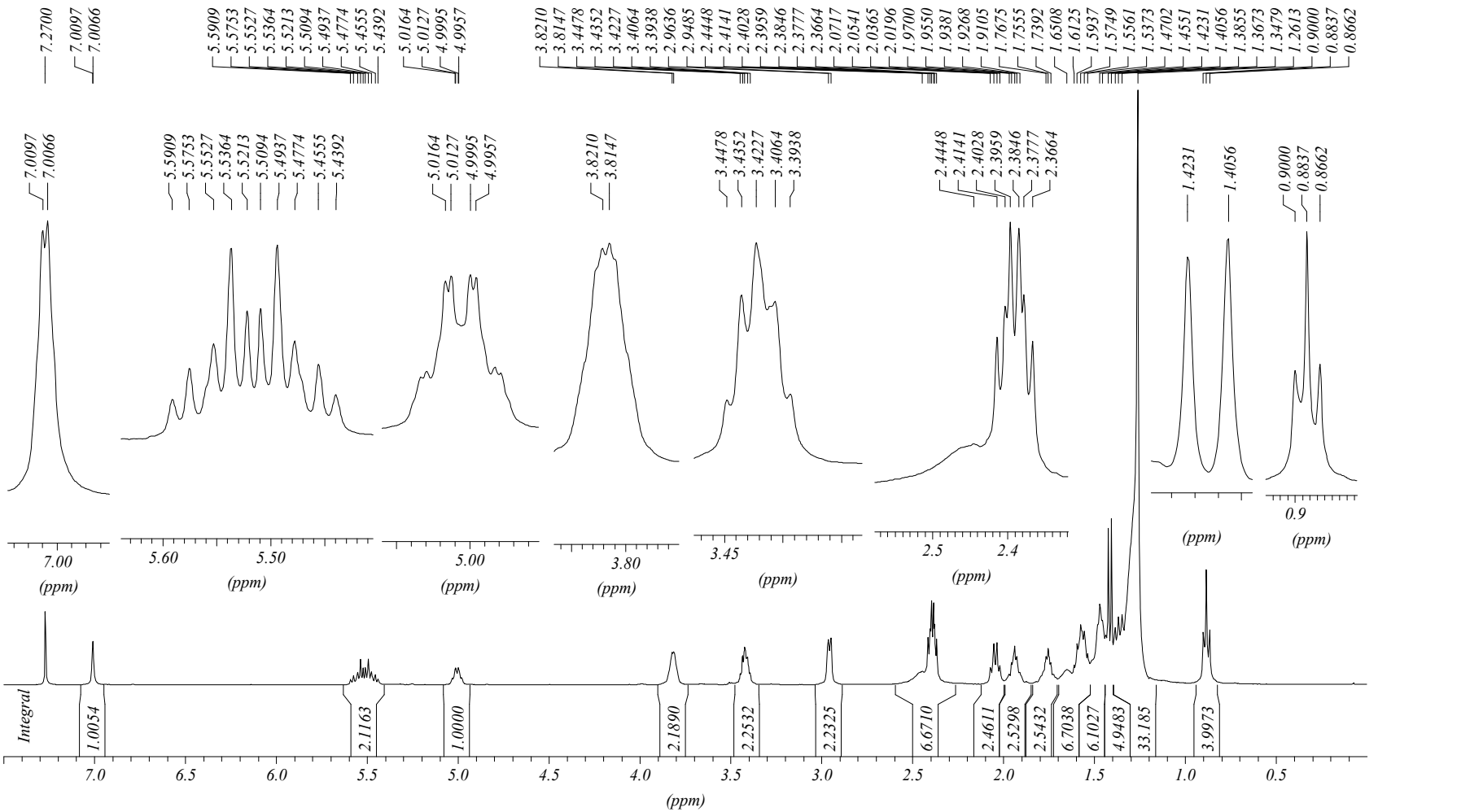
3.15 ^{1}H NMR (4*E*)-4,5-Didehydro-*cis*-reticulatacin-10-one A/B (11A/B, dr ~ 1:9)



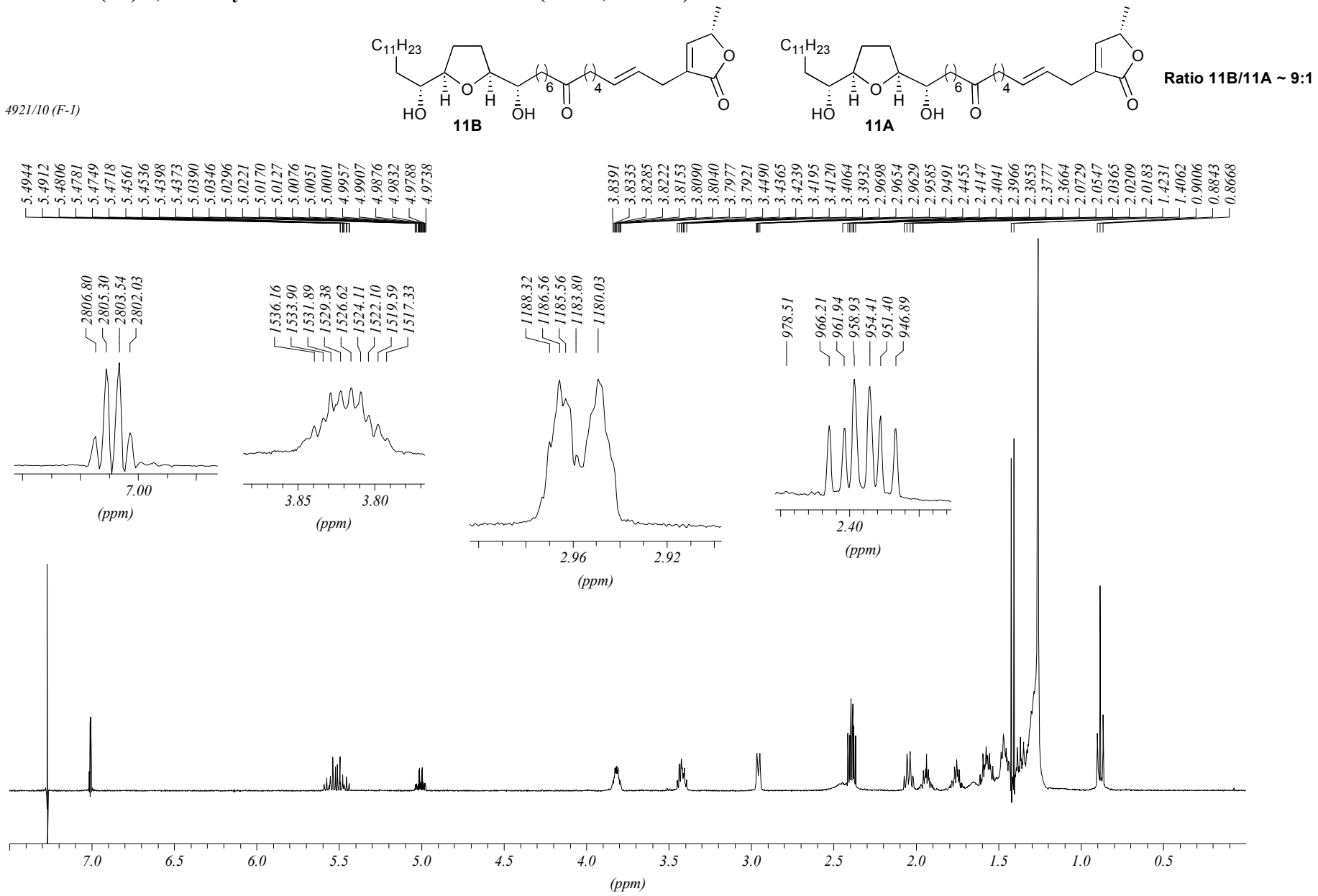


Ratio 11B/11A ~ 9:1

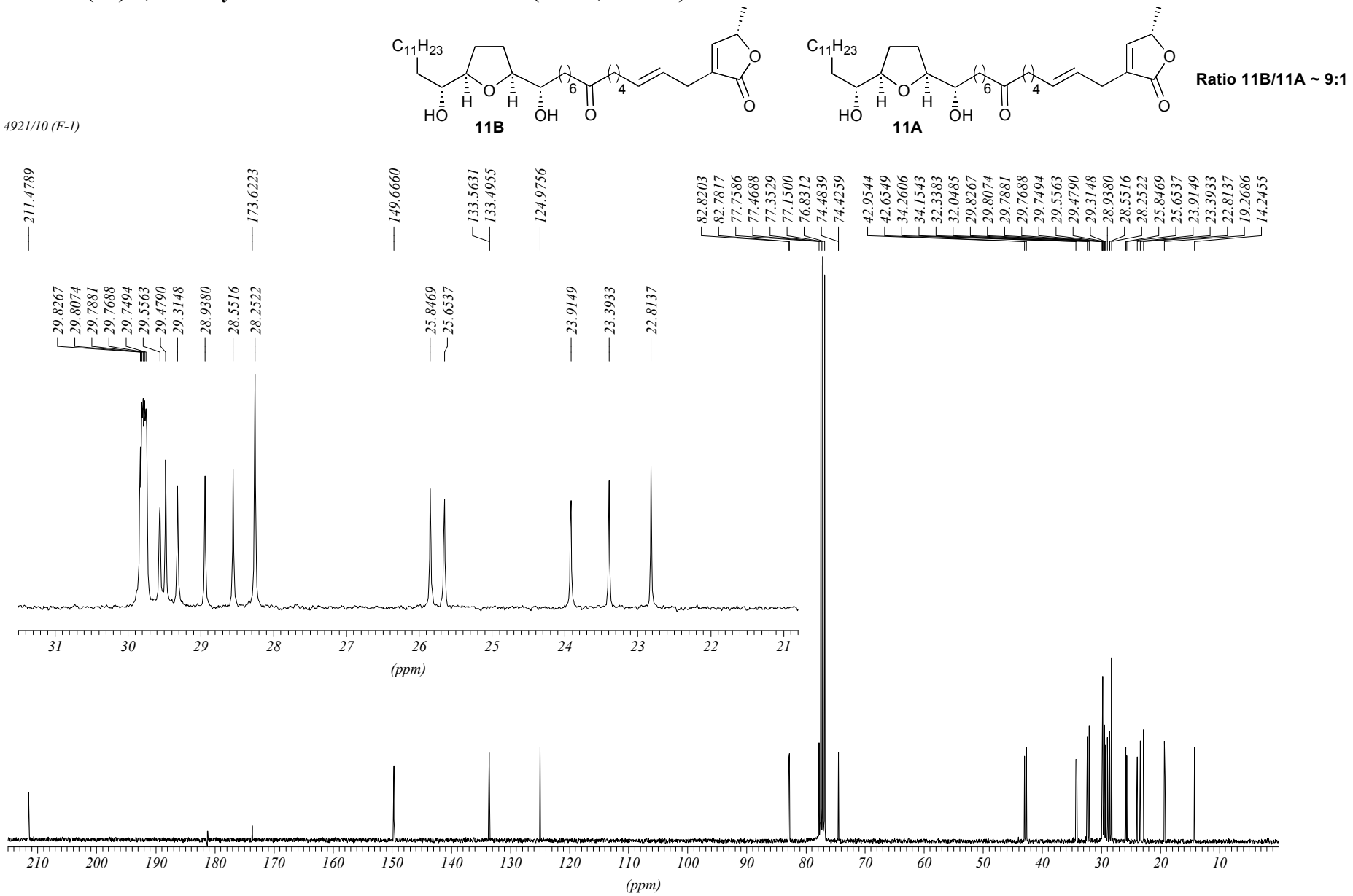
4921/10 (F-1)didehydro reticulatacin-10-one



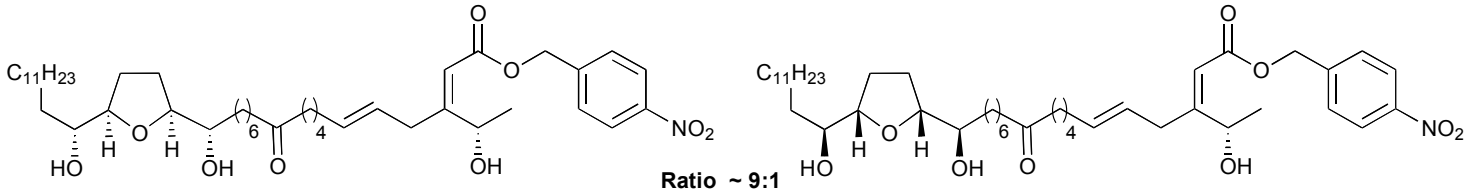
3.16 ^{1}H NMR (4*E*)-4,5-Didehydro-*cis*-reticulatacin-10-one A/B (11A/B, dr ~ 1:9)



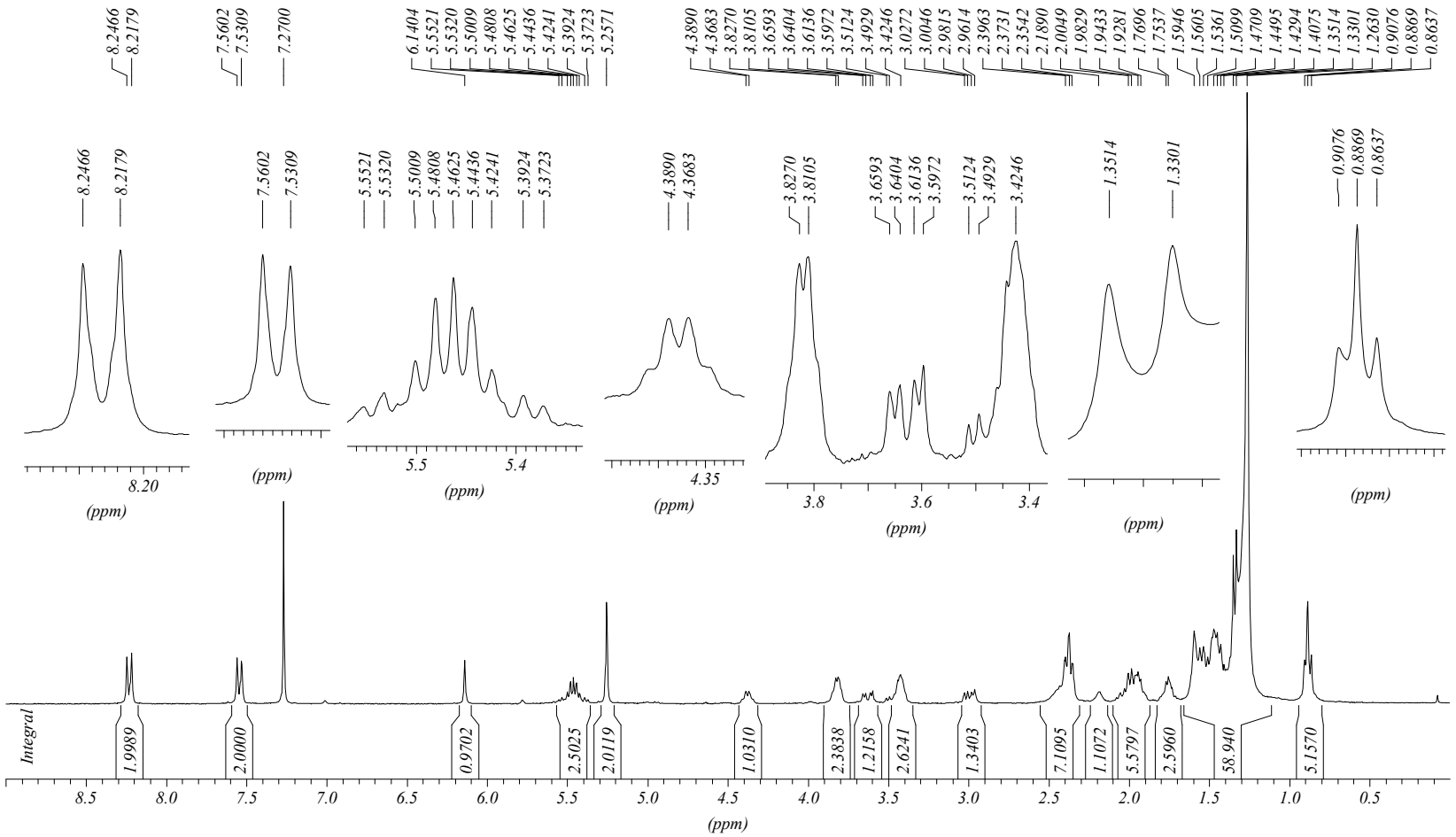
3.17 ^{13}C NMR (4*E*)-4,5-Didehydro-*cis*-reticulatacin-10-one A/B (11A/B, dr ~ 1:9)



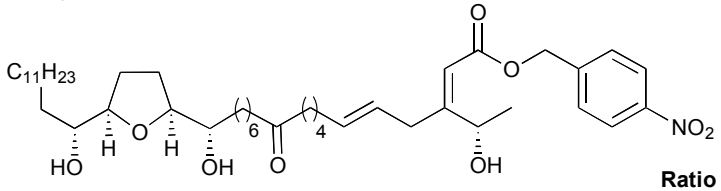
3.18 ^{1}H NMR (*R*,2*Z*,5*E*)-4-Nitrobenzyl 18-((2*R*,5*S*)-tetrahydro-5-((*S*)-1-hydroxyheptyl)furan-2-yl)-18-hydroxy-3-((*S*)-1-hydroxyethyl)-11-oxooctadeca-2,5-dienoate (dr ~ 1:9)



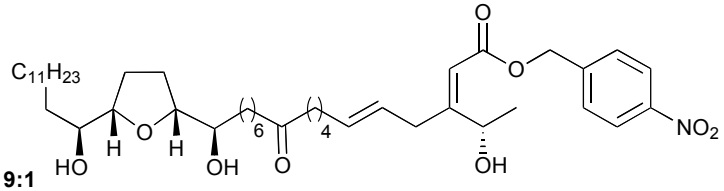
shbf4921/10 F2 the opend product

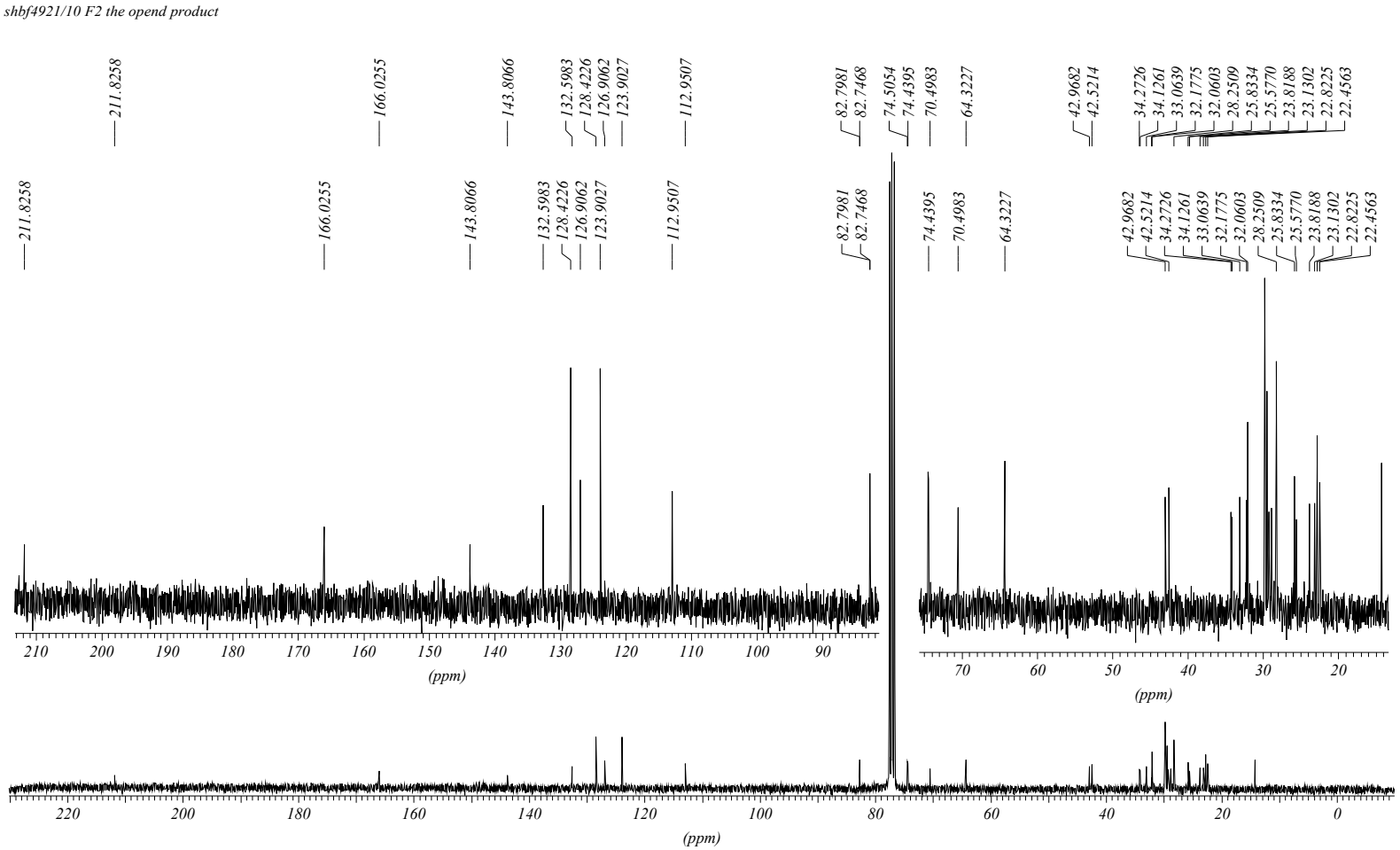


3.19 ^{13}C NMR (*R*,2*Z*,5*E*)-4-Nitrobenzyl 18-((2*R*,5*S*)-tetrahydro-5-((*S*)-1-hydroxyheptyl)furan-2-yl)-18-hydroxy-3-((*S*)-1-hydroxyethyl)-11-oxooctadeca-2,5-dienoate (dr ~ 1:9)

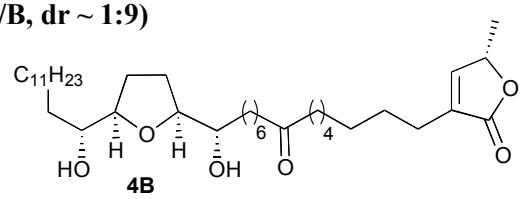


Ratio ~ 9:1

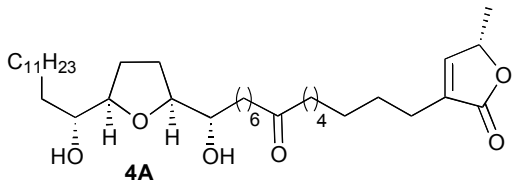




3.20 ^{1}H NMR *cis*-Reticulatacin-10-one A/B (4A/B, dr ~ 1:9)



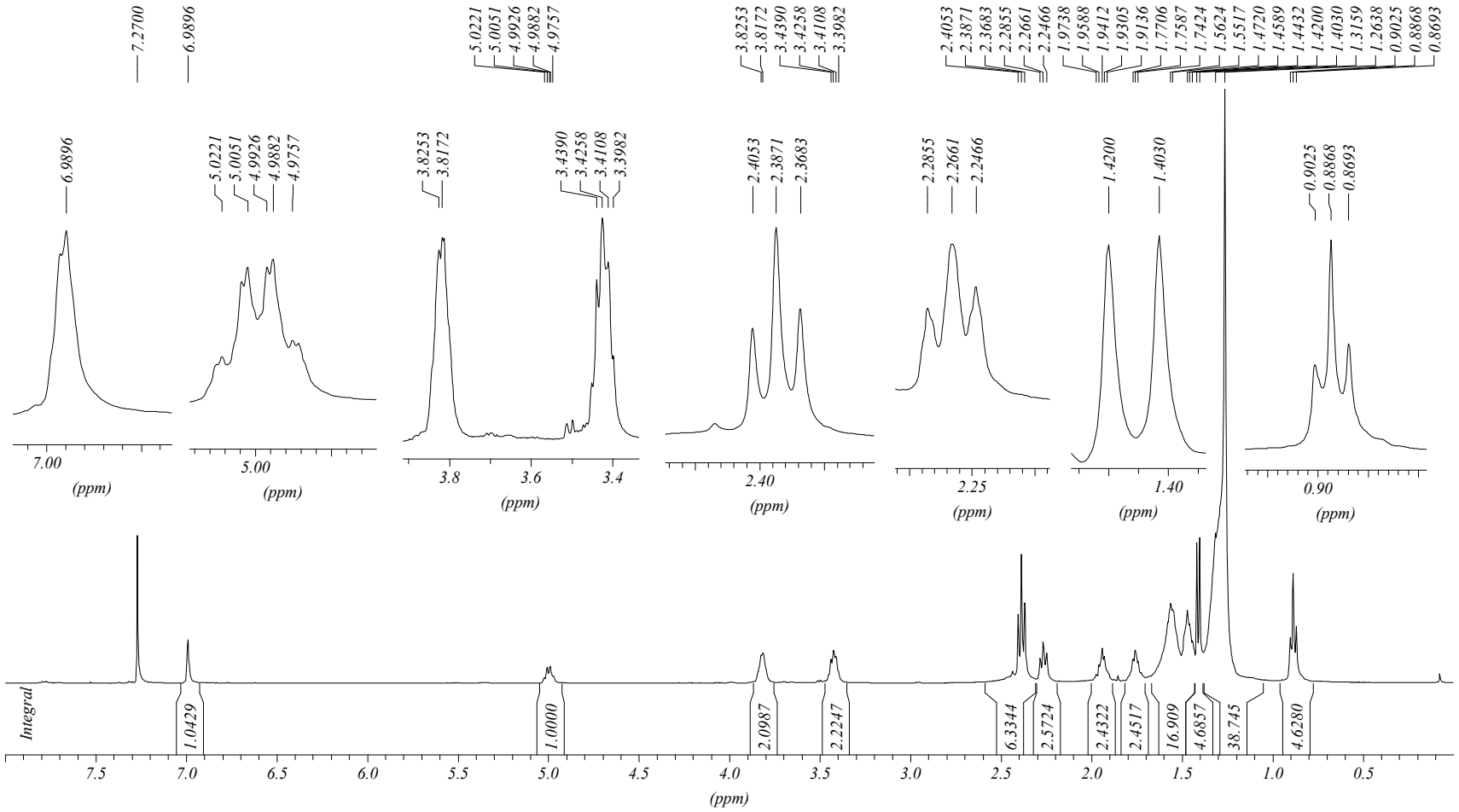
4B



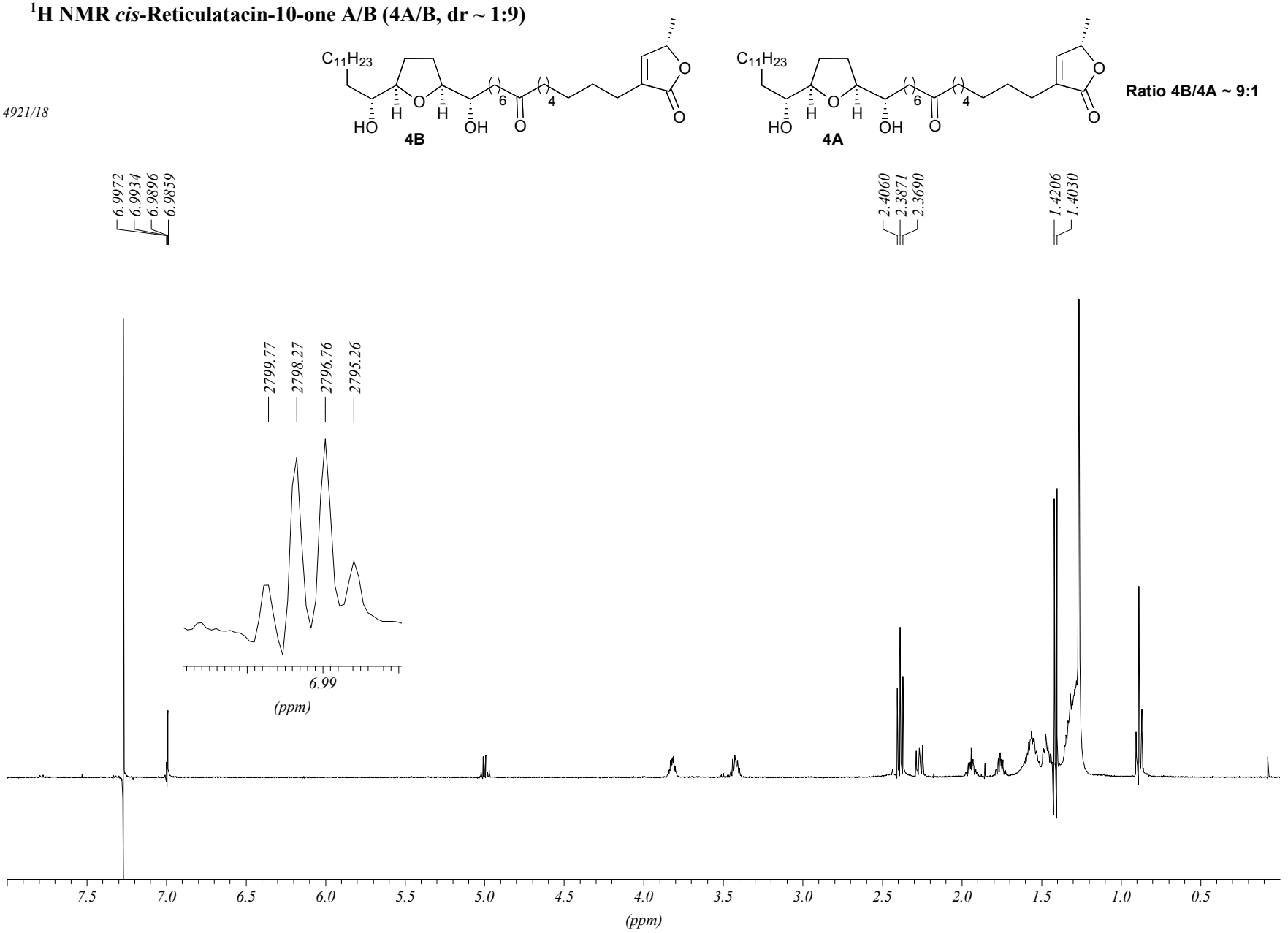
4A

Ratio 4B/4A ~ 9:1

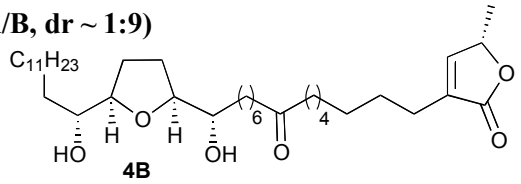
4921/18Reticulatacin-10-one

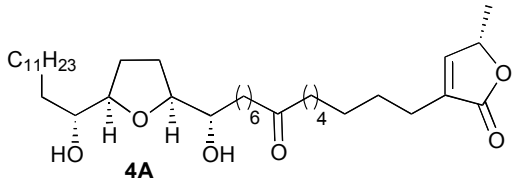


3.21 ^{1}H NMR *cis*-Reticulatacin-10-one A/B (4A/B, dr ~ 1:9)



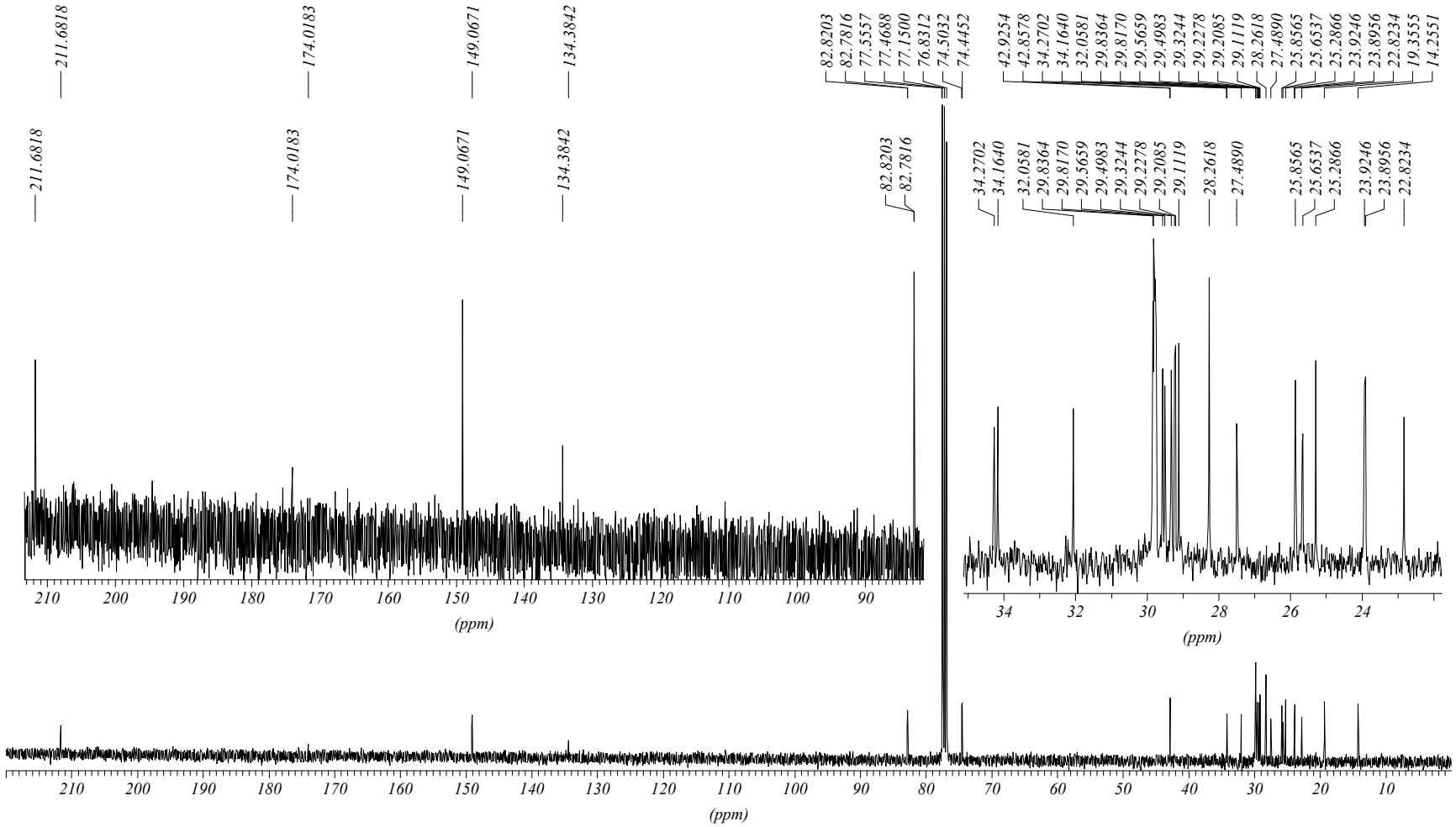
3.22 ^{13}C NMR *cis*-Reticulatacin-10-one A/B (4A/B, dr ~ 1:9)



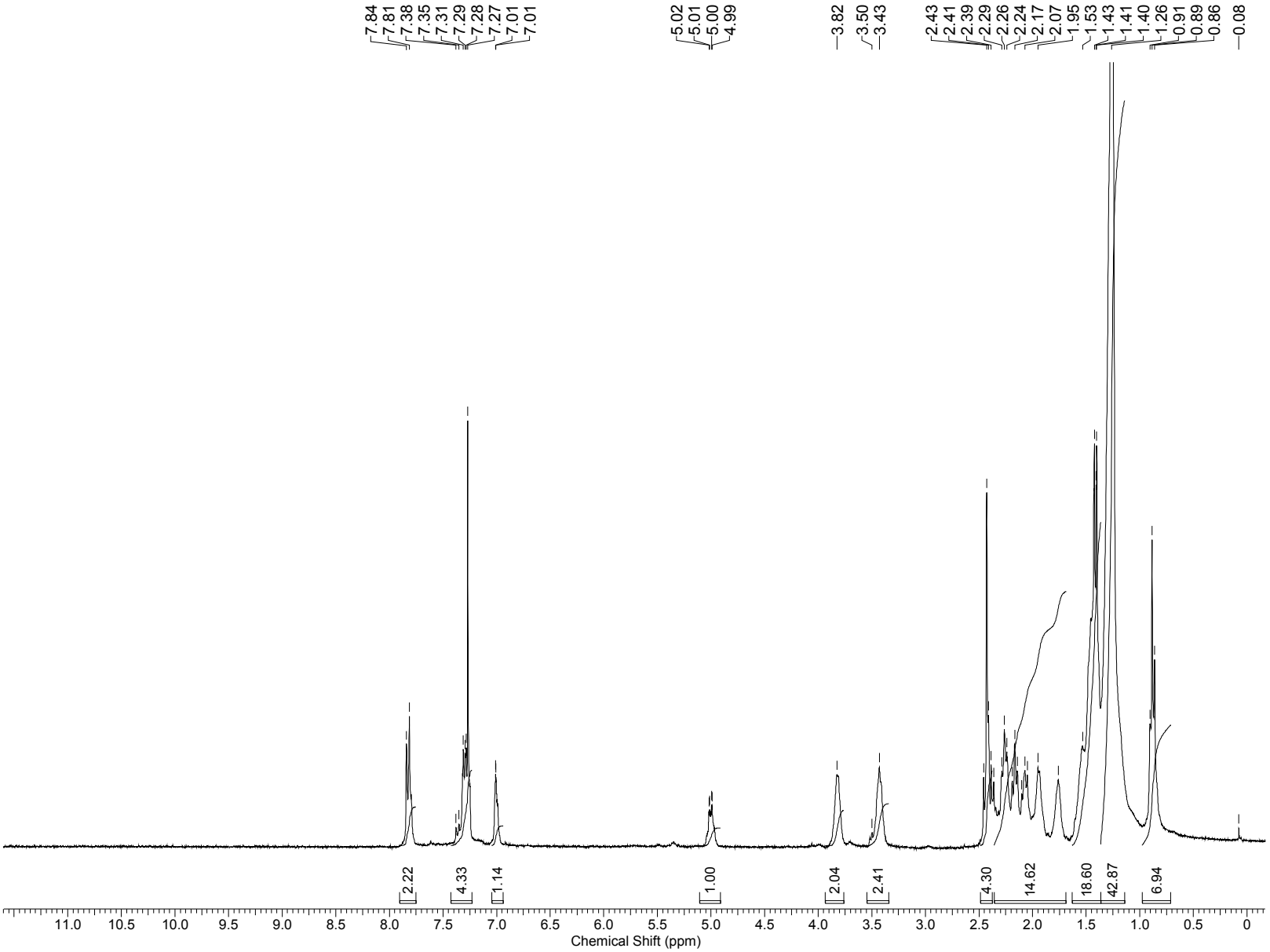


Ratio 4B/4A ~ 9:1

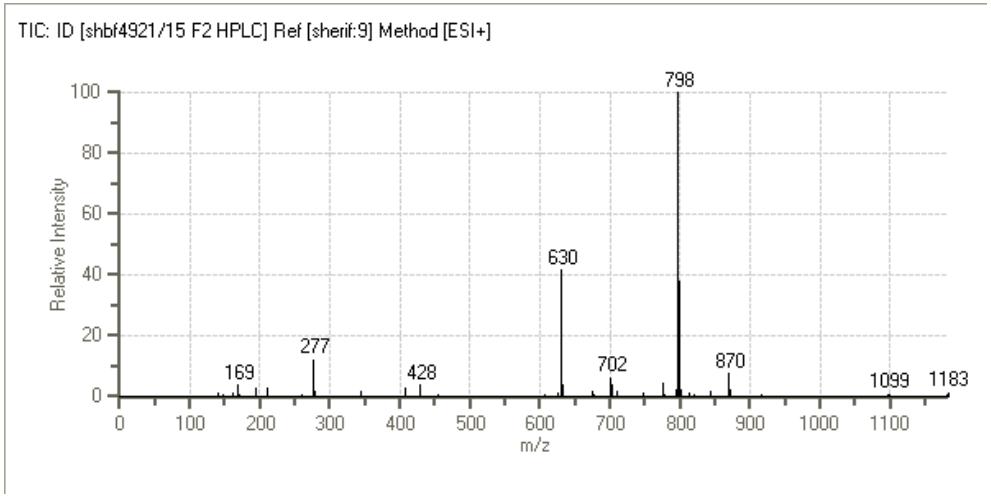
4921/18



3.23 ^{1}H NMR Hydrazone byproduct

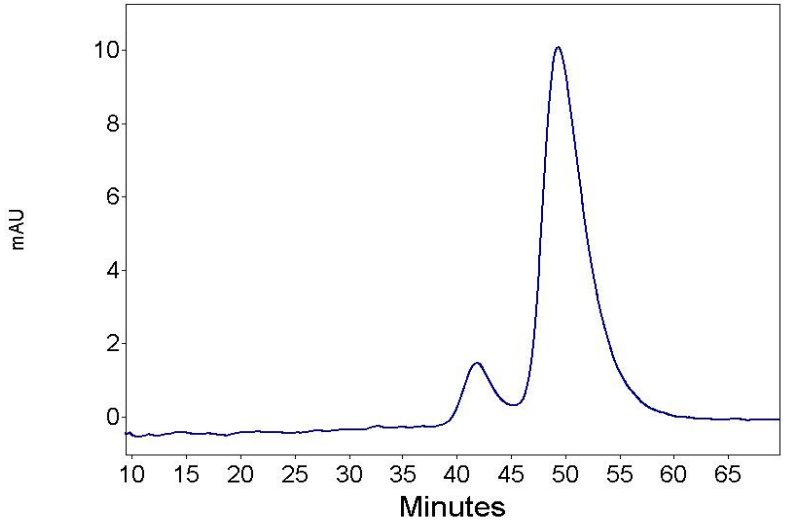


3.24 Mass spectrum Hydrazone byproduct

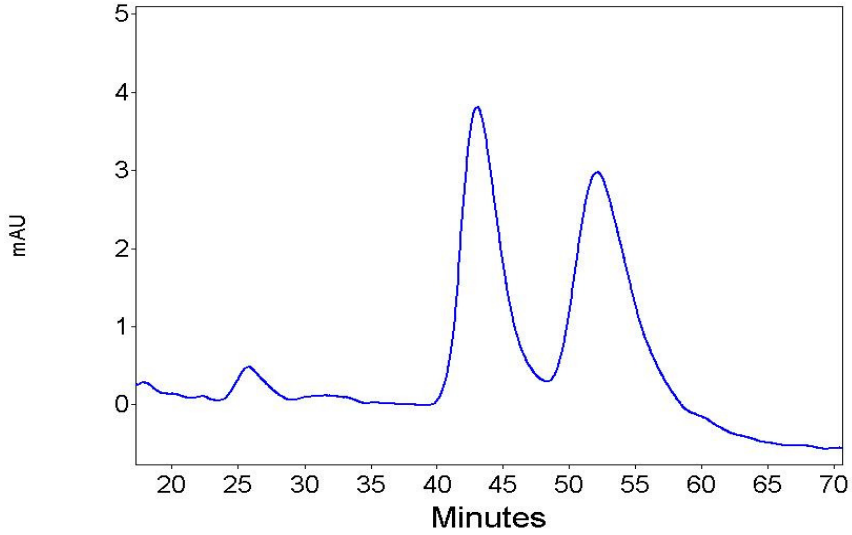


4.0 Chromatograms

4.1 Chiral HPLC chromatogram of synthetic *cis*-reticulatacin-10-one A/B (4A/B, dr ~ 1:9)



4.2 Chiral HPLC chromatogram of natural *cis*-reticulatacin-10-one A/B (4A/B)



4.3 Overlay of chiral HPLC chromatograms of — natural *cis*-reticulatacin-10-one A/B (4A/B)

— synthetic *cis*-reticulatacin-10-one A/B (4A/B, dr ~ 1:9)