Supporting Information for: Exploration of a Novel, Enamine-Solid-Base Catalyzed Aldol Condensation with C-glycosidic Pyranoses and Furanoses

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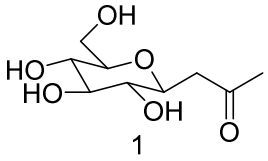
General Information. Proton and carbon nuclear magnetic resonance (^{1}H NMR and ^{13}C NMR, respectively) spectra were acquired using Agilent DD2 400 MHz. Chemical shifts (δ) are reported in parts per million (ppm) and are referenced to the residual solvent peak. Coupling constants (J) are reported in Hz. Liquid chromatography coupled with mass spectrometry (LC-MS) analysis were recorded on a Varian 500-MS using electrospray ionization (ESI) and an Atlantis T3 column (3 μm, 2.1x150 mm). Chemicals and solvents were purchased from Fisher Chemicals, Sigma-Aldrich, Alfa-Aesar, JT Baker or TCI and used as received unless otherwise noted. All reactions were performed under ambient atmosphere unless otherwise noted. Analytical thin layer chromatography was performed on pre-coated 250 μm layer thickness silica gel 60 F254 Plates (EMD Chemicals Inc.). Visualization was performed by ultraviolet light and/or by staining with acidic ceric ammonium nitrate solution (CAM). Purifications by column chromatography or by plugs were performed using SilicaFlash F60 silica gel (40-63 μm, 230-400 mesh, Silicycle). Procedures in the following experimental are the optimized procedures. Room temperature (RT) was 20 °C ± 2 °C.

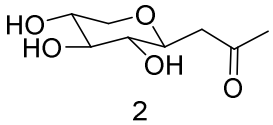
Representative synthesis of C-glycosidic Ketones, 1. Following the general procedure reported by Cavezza *et al.*[1] with minor changes a solution of sodium hydroxide (NaOH) (3.33 g, 83.2 mmol, 1.5 equivalents), in methanol (MeOH) (20 mL, 4.2 M) was slowly added to a solution containing D-glucose (10 g, 55.5 mmol) and pentane-2,4-dione (6.70 g, 66.9 mmol, 1.2 eq.) in MeOH (23 mL, 2.41 M). The reaction was stirred at 50 °C for 2 hours. After complete conversion (shown by TLC), the reaction was cooled using an ice-bath, followed by acidification to pH 3 with hydrochloric acid (HCl) (6.8 mL, 83.2 mol, 37% wt/Nt). The product was concentrated by rotatory evaporation, followed by desalination using ethanol (EtOH). When

needed (determined by proton nuclear magnetic resonance, ^{1}H NMR), the product was purified by column chromatography on silica gel using the appropriate eluent system (either 15:4:1 EtOAc:MeOH:H_2O or 9:1 DCM:MeOH). The product yield of nonulose, **1**, was near quantitative.



1

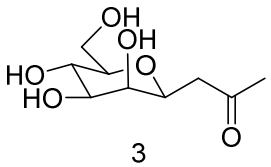
1-((2S,3R,4R,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)propan-2-one (1). The reaction was performed following the general procedure described above. Compound **1** was obtained in a 99% isolated yield as a brown caramel-like solid; Rf = 0.37 (15:4:1 EtOAc:MeOH:H_2O). ^{1}H NMR (400 MHz, MeOD): δ 3.79 (dd, J= 11.9, 2.2 Hz, 1H), 3.66 (td, J= 9.2, 2.9 Hz, 1H) overlapping with 3.61 (dd, J= 11.9, 5.1 Hz, 1H), 3.36-3.31 (m, 1H, overlapping with MeOD), 3.27-3.21 (m, 2H), 3.07 (t, J= 9.2 Hz, 1H), 2.89 (dd, J= 15.9, 3 Hz, 1H), 2.60 (dd, J= 15.9, 9.1 Hz, 1H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, MeOD): δ 210.31, 81.68, 79.62, 77.27, 75.12, 71.74, 62.81, 47.19, 30.62. Matched literature.[2]



2

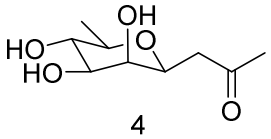
1-((2S,3R,4S,5R)-3,4,5-trihydroxytetrahydro-2H-pyran-2-yl)propan-2-one (2). The reaction was performed following the general procedure described above. Compound **2** was obtained in a 79% isolated yield as a dark brown crystalline solid; Rf = 0.21 (9:1 DCM:MeOH). ^{1}H NMR (400 MHz, MeOD): δ 3.81 (dd, J= 11.1, 5.4 Hz, 1H), 3.57 (td, J= 9.4, 2.8 Hz, 1H), 3.47-3.41 (m, 1H),

3.27 (t, J= 8.9 Hz, 1H), 3.14 (t, J= 10.9, 1H), 3.05 (t, J= 9.2 Hz, 1H), 2.88 (dd, J= 15.9 Hz, 2.8 Hz), 2.54 (dd, J= 16, 9.4 Hz, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, MeOD): δ 210.07, 79.85, 78.32, 75.24, 71.60, 71.13, 47.31, 30.78. Matched literature.[1,3]



3

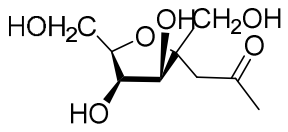
1-((2S,3S,4R,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)propan-2-one (3). The reaction was performed following the general procedure described above. Compound **3** was obtained in a 67% isolated yield as a brownish white caramel-like solid; Rf = 0.47 (15:4:1 EtOAc:MeOH:H_2O). ^{1}H NMR (400 MHz, MeOD): δ 3.92 (dd, J= 7.7, 5.4 Hz, 1H), 3.81 (dd, J= 11.8, 2.4 Hz, 1H), 3.74 (d, J= 3.1 Hz, 1H), 3.66 (dd, J=11.7, 5.7 Hz, 1H), 3.57-3.48 (m, 2H), 3.22-3.18 (m, 1H), 2.89 (dd, J= 17, 7.8 Hz, 1H), 2.72 (dd, J= 17, 5.3 Hz, 1H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, MeOD): δ 209.83, 82.18, 76.48, 75.71, 72.57, 68.71, 63.04, 45.82, 30.65. Matched literature.[4]



4

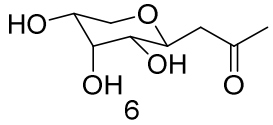
1-((2S,3S,4S,5S,6R)-3,4,5-trihydroxy-6-methyltetrahydro-2H-pyran-2-yl)propan-2-one (4). The reaction was performed following the general procedure described above. Compound **4** was obtained in a55 % isolated yield as a yellowish white powder; Rf = 0.23 (9:1 DCM:MeOH). ^{1}H NMR (400 MHz, MeOD): δ 3.89-3.86 (m, 1H), 3.72 (dd, J= 3.4, 0.9 Hz, 1H), 3.43 (dd, J= 9.2, 3.5 Hz, 1H), 3.35-3.26 (m,1H), 3.23-3.18 (m, 1H), 2.86 (dd, J=16.8, 8 Hz, 1H), 2.65 (dd, J=

16.8, 5.1 Hz, 1H), 2.17 (s, 3H), 1.24 (d, J= 6.1 Hz, 3H); ^{13}C NMR (100 MHz, MeOD): δ 209.73, 77.76, 76.25, 75.69, 74.16, 72.65, 45.91, 30.69, 18.39. m/z (LC-MS) found ($C9H16O5Na^{+}$): 227.1, Calcd $[M+H]^{+}$: 227.09.



5

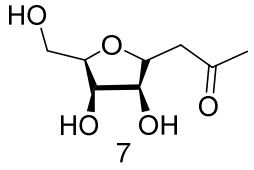
1-((3S,4S,5R)-3,4-dihydroxy-2,5-bis(hydroxymethyl)tetrahydrofuran-2-yl)propan-2-one (5). The reaction was performed following the general procedure described above. Compound 5 was obtained in a 38% isolated yield as a brownish orange caramel-like solid; Rf = 0.15 (17:2:1 EtOAc:MeOH:H2O). 1H NMR (400 MHz, MeOD): δ 3.79 (dd, J= 12, 2.1 Hz, 1H), 3.69-3.59 (m, 3H), 3.36-3.21 (m, 2H), 3.07 (t, J= 9.1 Hz, 1H), 2.88 (dd, J= 15.8, 2.9 Hz, 1H), 2.60 (dd, J= 16, 9.2 Hz, 1H), 2.20 (s, 3H); 13C NMR (100 MHz, MeOD): δ 210.43, 81.83, 79.78, 77.43, 75.28, 71.88, 62.96, 47.34, 30.76. m/z (LC-MS) found (C9O6H16): 221.2, Calcd $[M+H]^{+}$: 221.20.



6

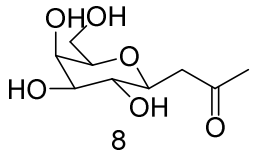
1-((2S,3R,4R,5R)-3,4,5-trihydroxytetrahydro-2H-pyran-2-yl)propan-2-one (6). The reaction was performed following the general procedure described above. The following product was 1 of 2 isomers (**6** & **7**) produced in the Knoevenagel condensation reaction with D-ribose. Compound **6** was obtained in an 81% isolated yield (7:3 mixture of **6**:**7**, respectively) as a clear yellow caramel; Rf = 0.38 (17:2:1 EtOAc:MeOH:H_2O). ^{1}H NMR (400 MHz, MeOD) isolated isomer: δ

4.03-4.01 (m, 1H), 3.91 (td, J= 9.4, 2.8 Hz, 1H), 3.63-3.59 (m, 1H), 3.56-3.47 (m, 2H), 3.21 (dd, J= 9.7, 2.4 Hz, 1H), 2.83 (dd, J= 15.7, 2.7 Hz, 1H), 2.47 (dd, J= 15.7, 9.5 Hz, 1H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, MeOD): δ 210.49, 72.86, 72.45, 72.18, 68.78, 66.44, 47.30, 30.51. m/z (LC-MS) found ($C_8O_5H_{14}Na^+$): 213.2, Calcd [M^+]: 213.07. Matched literature.[3,5]



7

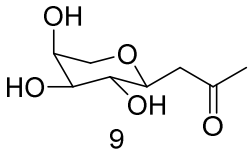
1-((2R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)propan-2-one (7). The reaction was performed following the general procedure above. The following product was 2 of 2 isomers (**6** & **7**) produced in the Knoevenagel condensation reaction with D-ribose. Compound **7** was obtained in an 81% isolated yield (7:3 mixture of **6**:**7**, respectively) as a clear yellow caramel; Rf = 0.21 (17:2:1 EtOAc:MeOH:H2O). ^{1}H NMR (400 MHz, MeOD) isolated isomer: δ 3.91 (dd, J= 12.4, 2.2 Hz, 1H), 3.81-3.78 (m, 2H), 3.67-3.66 (m, 1H), 3.61 (t, J= 3.3 Hz, 1H), 3.54 (dd, J= 12.5, 1 Hz, 1H), 2.92 (dd, J= 16.9, 7.9 Hz, 1H), 2.68 (dd, J= 17.0, 5.1 Hz, 1H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, MeOD): δ 209.44, 76.62, 73.22, 72.21, 71.08, 70.23, 46.00, 30.57. m/z (LC-MS) found ($C_8O_5H_{14}$ Na^+): 213.2, Calcd [M^+]: 213.07. Matched literature.[3,5]



8

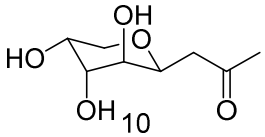
1-((2S,3R,4R,5R,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)propan-2-one (8). The reaction was performed following the general procedure described above. Compound **8** was obtained in a 79% isolated yield as a whitish yellow solid; Rf = 0.32

(15:4:1 EtOAc:MeOH:H_2O). ^{1}H NMR (400 MHz, MeOD): δ 3.87 (dd, J= 2.93, 0.78 Hz, 1H), 3.66-64 (m, 2H) overlapping with 3.62 (td, J= 9.0, 2.93 Hz, 1H), 3.49-3.37 (m, 3H), 2.88 (dd, J= 15.85, 2.93 Hz, 1H), 2.64 (dd, J= 16.04, 9.19 Hz, 1H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, MeOD): δ 210.34, 80.26, 77.87, 76.23, 72.27, 70.88, 62.63, 47.24, 30.60. m/z (LC-MS) found ($C9O6H16Na^+$): 243.2, Calcd [M^+]: 243.08. Matched literature.[6,7]



9

1-((2S,3R,4S,5S)-3,4,5-trihydroxytetrahydro-2H-pyran-2-yl)propan-2-one (9). The reaction was performed following the general procedure described above. Compound **9** was obtained in a 66% isolated yield as a brown caramel solid; Rf = 0.43 (15:4:1 EtOAc:MeOH:H_2O). ^{1}H NMR (400 MHz, MeOD): δ 3.83-3.80 (m, 2H), 3.57-3.52 (m, 2H), 3.47-3.35 (m, 1H), 2.89 (dd, J= 15.8, 2.0 Hz, 1H), 2.63 (dd, J= 15.2, 10.1 Hz, 1H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, MeOD): δ 210.17, 78.30, 75.58, 72.20, 71.42, 70.93, 47.12, 30.65. m/z (LC-MS) found ($C8O5H14Na^+$): 213.2, Calcd [M^+]: 213.07.

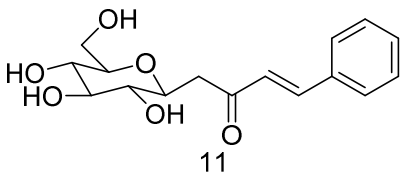


10

1-((2S,3S,4R,5R)-3,4,5-trihydroxytetrahydro-2H-pyran-2-yl)propan-2-one (10). The reaction was performed following the general procedure described above. Compound **10** was obtained in a 56% isolated yield as a brown wet crystalline solid; Rf = 0.43 (15:4:1 EtOAc:MeOH:H_2O). ^{1}H NMR (400 MHz, MeOD): δ 3.83-3.80 (m, 2H), 3.57-3.52 (m, 2H) 3.48-

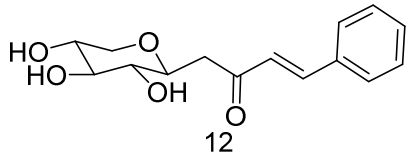
3.35 (m, 2H), 2.89 (dd, J= 15.9, 2.6 Hz, 1H), 2.63 (dd, J= 15.9, 9.3 Hz, 1H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, MeOD): δ 210.19, 78.28, 75.56, 72.18, 71.41, 70.92, 47.11, 30.65. m/z (LC-MS) found ($C8O5H14Na^{+}$): 213.2, Calcd [M^{+}]: 213.07.

Representative procedure for the synthesis of (E)-α,β-unsaturated glycosidic ketones 11-20. Following the procedure previous reported by our lab,[8] one of the C-glycosidic ketones, **1-10**, (nonulose, **1**, 0.5 g, 2.27 mmol), L-proline (0.2614 g, 2.27 mmol, 1 equiv.), magnesium oxide (MgO) (0.05 g, 10 wt%) and an internal standard, biphenyl, (17.5 mg, 0.113 mmol, 0.05 equiv.) were added to a 4 dram vial equipped with a Teflon© coated magnetic stir bar. Methanol (5 mL) was added and the resulting solution was stirred rapidly until dissolution. Once, dissolved a small aliquot was taken for quantitative ^{1}H NMR analysis. Subsequently, benzaldehyde (2.71 mmol, 1.2 equiv.) was added to the reaction mixture, the reaction was heated to 50 °C and monitored by liquid chromatography coupled with a refractive index detector (LC-RI) until completion. Upon completion, the reaction was stopped and the mixture was filtered using a glass fritted funnel to remove the solid base catalyst MgO. The catalyst was rinsed with methanol in triplicate, the filtrate collected and concentrated by rotatory evaporation. The crude reaction mixture was analyzed by ^{1}H NMR to confirm the conversion of the C-glycosidic ketone. The resulting mixture was purified by a silica gel plug by first washing with 100% DCM, followed by 9:1 DCM:MeOH to elute the product. . Concentration of the eluate provided a 91% isolated yield of product.



11

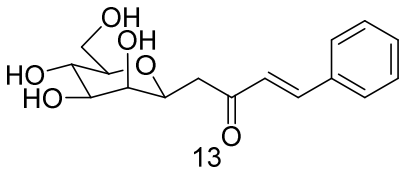
(E)-4-phenyl-1-((2S,3R,4R,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)but-3-en-2-one (11). The reaction was performed following the general procedure described above. Compound **11** was obtained in a 91 & 92% yields; beige-white powder; R_f = 0.18 (1:9 MeOH:DCM); ^{1}H NMR (400 MHz, CD_3OD): δ 7.64 (d, *J* = 16.2 Hz, 1H), 7.62 (m, 2H), 7.39 (t, *J* = 3.1 Hz, 3H), 6.90 (d, *J* = 16.2 Hz, 1H), 3.77-3.72 (m, 2H), 3.60 (dd, *J* = 11.9, 5.1 Hz, 1H), 3.37-3.31 (m, 2H), 3.24-3.19 (m, 1H), 3.16-3.08 (m, 2H), 2.89 (dd, *J* = 15.8, 9 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD): δ 201.01, 144.84, 136.02, 131.69, 130.04, 129.55, 127.49, 81.64, 79.74, 77.49, 75.15, 71.70, 62.77, 44.38. *m/z* (LC-MS) (C16O6H20) found: 309.3, Calcd $[M+H]^+$ 309.133. For spectroscopic data refer to de Winter *et al.*[8]



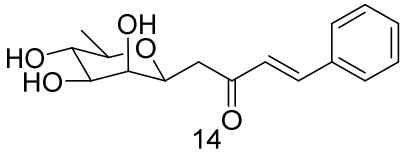
12

(E)-4-phenyl-1-((2S,3R,4S,5R)-3,4,5-trihydroxytetrahydro-2H-pyran-2-yl)but-3-en-2-one (12). The reaction was performed following the general procedure described above. Compound **12** was obtained in a quantitative yield as a light orangey yellow powder; R_f = 0.38 (9:1 DCM:MeOH). ^{1}H NMR (400 MHz, MeOD): δ 7.62 (d, *J*= 16.2 Hz, 1H) overlapping with 7.61 (m, 2H), 7.39 (t, *J*= 3.1 Hz, 3H), 6.85 (d, *J*= 16.2 Hz, 1H), 3.81 (dd, *J*= 11.2, 5.3 Hz, 1H), 3.71-3.66 (m, 1H), 3.50-3.44 (m, 1H), 3.35-3.29 (m, 1H), 3.18-3.13 (m, 2H), 3.10 (dd, *J*= 15.8, 2.5 Hz, 1H), 2.87 (dd, *J*= 15.8, 9.2 Hz, 1H); ^{13}C NMR (100 MHz, MeOD): δ 201.00, 144.98, 136.10,

131.85, 130.19, 129.67, 127.67, 79.96, 78.65, 75.31, 71.67, 71.18, 44.37. m/z (LC-MS) (C15O5H18) found: 279.2, Calcd $[M+H]^+$: 279.12.

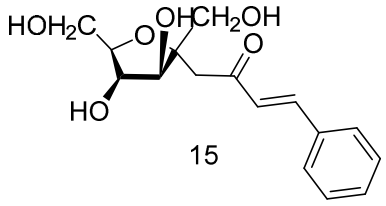


(E)-4-phenyl-1-((2S,3S,4R,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)but-3-en-2-one (13). The reaction was performed following the general procedure described above. Compound **13** was obtained in a quantitative yield as yellowish white crystals; R_f = 0.24 (9:1 DCM:MeOH). ^{1}H NMR (400 MHz, MeOD): δ 7.67 (d, *J*= 16.2 Hz, 1H) overlapping with 7.66-7.64 (m, 2H), 7.42 (t, *J*= 3.1 Hz, 3H), 6.89 (d, *J*= 16.2 Hz, 1H), 4.02 (t, *J*= 6 Hz, 1H), 3.83-3.80 (m, 2H), 3.68 (dd, *J*= 11.7, 5.5 Hz, 1H), 3.57 (d, *J*= 9.4 Hz, 1H), 3.52 (dd, *J*= 9.4, 3.3 Hz, 1H), 3.35-3.26 (m, 1H), 3.25-3.20 (m, 1H), 3.16 (dd, *J*=16.6, 7 Hz, 1H), 2.98 (dd, *J*= 16.6, 5.7 Hz, 1H); ^{13}C NMR (100 MHz, MeOD): δ 200.59, 144.99, 136.12, 131.86, 130.20, 129.69, 127.60, 82.24, 76.60, 76.06, 72.74, 68.76, 63.13, 43.10. m/z (LC-MS) (C16O6H20) found: 309.3, Calcd $[M+H]^+$: 309.13.



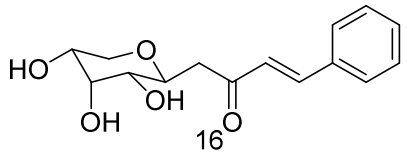
(E)-4-phenyl-1-((2S,3S,4S,5S,6R)-3,4,5-trihydroxy-6-methyltetrahydro-2H-pyran-2-yl)but-3-en-2-one (14). The reaction was performed following the general procedure described above. Compound **14** was obtained in a quantitative yield as a clear yellow thick oil; R_f = 0.28 (9:1 DCM:MeOH). ^{1}H NMR (400 MHz, MeOD): δ 7.66 (d, *J*= 16.2 Hz, 1H) overlapping with 7.63

(m, 2H), 7.41 (t, *J*= 3.1 Hz, 3H), 6.86 (d, *J*= 16.2 Hz, 1H), 3.99 (t, *J*=5.8 Hz, 1H), 3.8 (d, *J*= 2.9 Hz, 1H), 3.47 (dd, *J*= 9.3, 3.4 Hz, 1H), 3.32-3.30 (m, 1H), 3.26-3.19 (m, 1H), 3.15 (dd, *J*= 16.5, 7.5 Hz, 1H), 2.90 (dd, *J*=16.5, 5.4 Hz, 1H), 1.24 (d, *J*= 5.9, 3H); ^{13}C NMR (100 MHz, MeOD): δ 200.65, 144. 95, 136.10, 131.85, 130.20, 129.65, 127.69, 77.80, 76.33, 76.01, 74.22, 72.82, 43.11, 18.42. m/z (LC-MS) (C16O5H20) found: 293.3, Calcd $[M+H]^+$: 293.12.

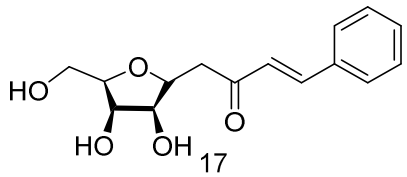


15

(E)-1-((3S,4S,5R)-3,4-dihydroxy-2,5-bis(hydroxymethyl)tetrahydrofuran-2-yl)-4-phenylbut-3-en-2-one (15). The reaction was performed following the general procedure described above. Compound **15** was obtained in a quantitative yield as a yellow crystalline solid; R_f = 0.21 (9:1 DCM:MeOH). ^{1}H NMR (400 MHz, MeOD): δ 7.66 (d, *J*= 16.2 Hz, 1H) overlapping with 7.66-7.64 (m, 2H), 7.41 (t, *J*= 3.3 Hz, 3H), 6.91 (d, *J*= 16.2 Hz, 1H), 3.80-3.74 (m, 2H), 3.63 (dd, *J*= 11.9, 5.1 Hz, 1H), 3.45-3.36 (m, 1H), 3.32-3.30 (m, 1H), 3.26-3.22 (m, 1H), 3.17 (t, *J*= 9 Hz, 1H) overlapping with 3.13 (dd, *J*= 15.9, 2.7 Hz, 1H), 2.91 (dd, *J*= 15.9.8.9 Hz, 1H); ^{13}C NMR (100 MHz, MeOD): δ 201.17, 145.00, 136.15, 131.84, 130.19, 129.70, 127.63, 81.78, 79.88, 77.62, 75.29, 71.82, 62.91, 44.52. m/z (LC-MS) (C16O6H20) found: 309.2, Calcd $[M+H]^+$: 309.13.

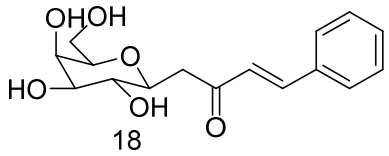


(E)-4-phenyl-1-((2R,3S,5S)-3,4,5-trihydroxytetrahydro-2H-pyran-2-yl)but-3-en-2-one (16). The reaction was performed following the general procedure described above using the 7:3 isomeric mixture of **6** & **7**. Compound **16** was obtained in a quantitative yield as a clear yellow caramel in a 7:3 pyranose:furanose ratio; R_f = 0.5 & 0.45 (9:1 DCM:MeOH), the products were isolated as a mixture of **16** & **17** and the following spectral characterization describes only the pyranose **16**. ^{1}H NMR (400 MHz, MeOD): δ 7.64 (d, *J*= 16.4 Hz, 1H) within 7.66-7.63 (m, 2H, overlapping with furanose **17**), 7.42 (br. t, *J*= 3.5 Hz, 3H, overlapping with furanose **17**), 6.89 (d, *J*= 16.4 Hz, 1H, overlapping with furanose **17**), 4.05 (t, *J*= 2.6 Hz, 1H), 4.02 (td, *J*= 9.5, 2.6 Hz, 1H), 3.64-3.62 (m, 1H, overlapping with furanose **17**), 3.59-3.49 (m, 2H, overlapping with furanose **17**), 3.30-3.29 (m, 1H, overlapping with MeOD), 3.06 (dd, *J*= 15.6, 2.6 Hz, 1H), 2.78 (dd, *J*= 15.3, 9.4 Hz, 1H); ^{13}C NMR (100 MHz, MeOD): δ 201.36, 144.72, 136.01, 131.68, 130.05, 129.52, 127.48, 73.20, 72.50, 72.25, 68.85, 66.49, 44.38. m/z (LC-MS) (C15O5H18) found: 279.2, Calcd $[M+H]^+$: 279.12.



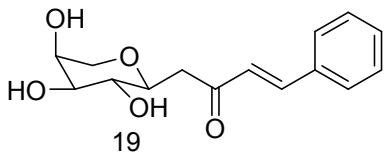
(E)-1-((2R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-4-phenylbut-3-en-2-one (17). The reaction was performed following the general procedure described above using the 7:3 isomeric mixture of **6** & **7**. Compound **17** was obtained in a quantitative yield as a clear yellow caramel in a 7:3 pyranose:furanose ratio; R_f = 0.5 & 0.45 (9:1 DCM:MeOH), the

products were isolated as a mixture of **16** & **17** and the following spectral characterization describes only the furanose **17**. ^{1}H NMR (400 MHz, MeOD): δ 7.67 (d, *J*= 15.8 Hz, 1H) overlapping with 7.66-7.63 (m, 2H, overlapping with pyranose **16**), 7.42 (br. t, *J*= 3.5 Hz, 3H, overlapping with pyranose **16**), 6.88 (d, *J*= 15.8 Hz, 1H, overlapping with pyranose **16**), 3.94-3.90 (m, 2H), 3.80-3.79 (m, 1H), 3.74 (m, 1H), 3.65 (t, *J*= 3.5 Hz, 1H overlapping with pyranose **16**), 3.59-3.49 (m, 1H, overlapping with pyranose **16**), 3.20 (dd, *J*= 16.4, 7.6 Hz, 1H), 2.94 (dd, *J*= 16.4, 5.3 Hz, 1H); ^{13}C NMR (100 MHz, MeOD): δ 200.42, 144.83, 135.96, 131.72, 130.06, 129.54, 127.53, 76.98, 73.38, 72.28, 71.12, 70.28, 43.20. m/z (LC-MS) (C16O6H20) found: 279.2, Calcd $[M+H]^{+}$: 279.12.



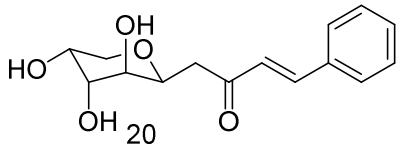
18

(E)-4-phenyl-1-((2S,3R,4R,5R,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)but-3-en-2-one (18). The reaction was performed following the general procedure described above. Compound 1**8** was obtained in a quantitative yield as a white solid; Rf = 0.26 (9:1 DCM:MeOH). ^{1}H NMR (400 MHz, MeOD): δ 7.66 (d, *J*= 16.2 Hz, 1H) overlapping with 7.66-7.64 (m, 2H), 7.41 (t, *J*= 2.7 Hz, 3H), 6.92 (d, *J*= 16.2 Hz, 1H), 3.90-3.89 (m, 1H), 3.72 (t, 1H), 3.65 (d, *J*= 5.9 Hz, 2H), 3.52-3.48 (m, 3H), 3.11 (dd, *J*= 15.8, 2.5 Hz, 1H), 2.97 (dd, *J*= 15.8, 8.8 Hz, 1H); ^{13}C NMR (100 MHz, MeOD): δ 201.16, 144.82, 136.04, 131.66, 130.04, 129.53, 127.55, 80.19, 78.06, 76.32, 72.31, 70.88, 62.57, 44.36. m/z (LC-MS) found (C16O6H20): 309.3, Calcd $[M+H]^{+}$: 309.13.



19

(E)-4-phenyl-1-((2S,3R,4S,5S)-3,4,5-trihydroxytetrahydro-2H-pyran-2-yl)but-3-en-2-one (19). The reaction was performed following the general procedure described above. Compound **19** was obtained in a 98% isolated yield as a whitish yellow solid; Rf = 0.35 (9:1 DCM:MeOH). ^{1}H NMR (400 MHz, MeOD): δ 7.66 (d, *J*= 16.2 Hz, 1H) overlapping with 7.66-7.63 (m, 2H), 7.41 (t, *J*= 3.5 Hz, 3H), 6.8 (d, *J*= 16.2 Hz, 1H), 3.84-3.80 (m, 2H), 3.65 (td, *J*= 9.2, 2.5 Hz, 1H), 3.55-3.49 (m, 3H), 3.1 (dd, *J*= 15.8, 2.5 Hz, 1H), 2.96 (dd, *J*= 15.8, 9.2 Hz, 1H); ^{13}C NMR (100 MHz, MeOD): δ 201.15, 144.84, 136.01, 131.68, 130.04, 129.52, 127.62, 78.65, 75.68, 72.31, 71.44, 70.99, 44.15. m/z (LC-MS) (C15O5H18) found: 279.3, Calcd [M+H] $^{+}$: 229.12.



20

(E)-4-phenyl-1-((2S,3S,4R,5R)-3,4,5-trihydroxytetrahydro-2H-pyran-2-yl)but-3-en-2-one (20). The reaction was performed following the general procedure described above. Compound **20** was obtained in a quantitative yield as a yellowish white solid; Rf = 0.35 (9:1 DCM:MeOH). ^{1}H NMR (400 MHz, MeOD): δ 7.66 (d, *J*= 16.2 Hz, 1H) overlapping with 7.66-7.63 (m, 2H), 7.42 (t, *J*= 3.3 Hz, 3H), 6.89 (d, *J*= 16.2 Hz, 1H), 3.81 (m, 2H), 3.65 (td, J= 9.2, 2.5 Hz, 1H), 3.655-3.49 (m, 3H), 3.10 (dd, *J*= 15.7, 2.5 Hz, 1H), 2.98 (dd, *J*= 15.7, 9.2 Hz, 1H); ^{13}C NMR (100 MHz, MeOD): δ 201.15, 144.84, 136.02, 131.68, 130.04, 129.52, 127.62, 78.66, 75.68, 72.31, 71.45, 70.99, 44.16. m/z (LC-MS) (C15O5H18) found: 279.3, Calcd [M+H] $^{+}$: 279.12.

References

(1) Cavezza, A.; Boulle, C.; Guéguiniat, A.; Pichaud, P.; Trouille, S.; Ricard, L.; Dalko-Csiba, M. Synthesis of Pro-XylaneTM: A New Biologically Active C-Glycoside in Aqueous Media. *Bioorg. Med. Chem. Lett.* **2009**, *19* (3), 845–849, DOI 10.1016/j.bmcl.2008.12.037.

(2) Howard, S.; Withers, S. G. Bromoketone C-Glycosides, a New Class of β-Glucanase Inactivators. *J. Am. Chem. Soc.* **1998**, *120* (40), 10326–10331, DOI 10.1021/ja981580r.

(3) Wang, J.; Li, Q.; Ge, Z.; Li, R. A Versatile and Convenient Route to Ketone C-Pyranosides and Ketone C-Furanosides from Unprotected Sugars. *Tetrahedron* **2012**, *68* (4), 1315–1320, DOI 10.1016/j.tet.2011.11.029.

(4) Rodrigues, F.; Canac, Y.; Lubineau, A. A Convenient, One-Step, Synthesis of β-C-Glycosidic Ketones in Aqueous Media. *Chem. Commun.* **2000**, No. 20, 2049–2050, DOI 10.1039/b006642g.

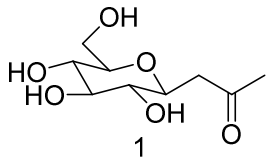
(5) Riemann, I.; Papadopoulos, M. A.; Knorst, M.; Fessner, W.-D. C-Glycosides by Aqueous Condensation of B-Dicarbonyl Compounds with Unprotected Sugars. *Aust. J. Chem.* **2002**, *55* (2), 147, DOI 10.1071/CH02012.

(6) Richter, C.; Krumrey, M.; Klaue, K.; Mahrwald, R. Cascade Reactions of Unprotected Ketoses with Ketones - A Stereoselective Access to C-Glycosides. *European J. Org. Chem.* **2016**, *2016* (31), 5309–5320, DOI 10.1002/ejoc.201601058.

(7) Ranoux, A.; Lemiègre, L.; Benoit, M.; Guégan, J.-P.; Benvegnu, T. Horner-Wadsworth-Emmons Reaction of Unprotected Sugars in Water or in the Absence of Any Solvent: One-Step Access to C -Glycoside Amphiphiles. *European J. Org. Chem.* **2010**, *2010* (7), 1314–1323, DOI 10.1002/ejoc.200901286.

(8) de Winter, T. M.; Petitjean, L.; Erythropel, H. C.; Moreau, M.; Hitce, J.; Coish, P.; Zimmerman, J. B.; Anastas, P. T. Greener Methodology: An Aldol Condensation of an Unprotected C-Glycoside with Solid Base Catalysts. *ACS Sustain. Chem. Eng.* **2018**, *6* (6), 7810–7817, DOI 10.1021/acssuschemeng.8b00816.

Spectroscopic Data



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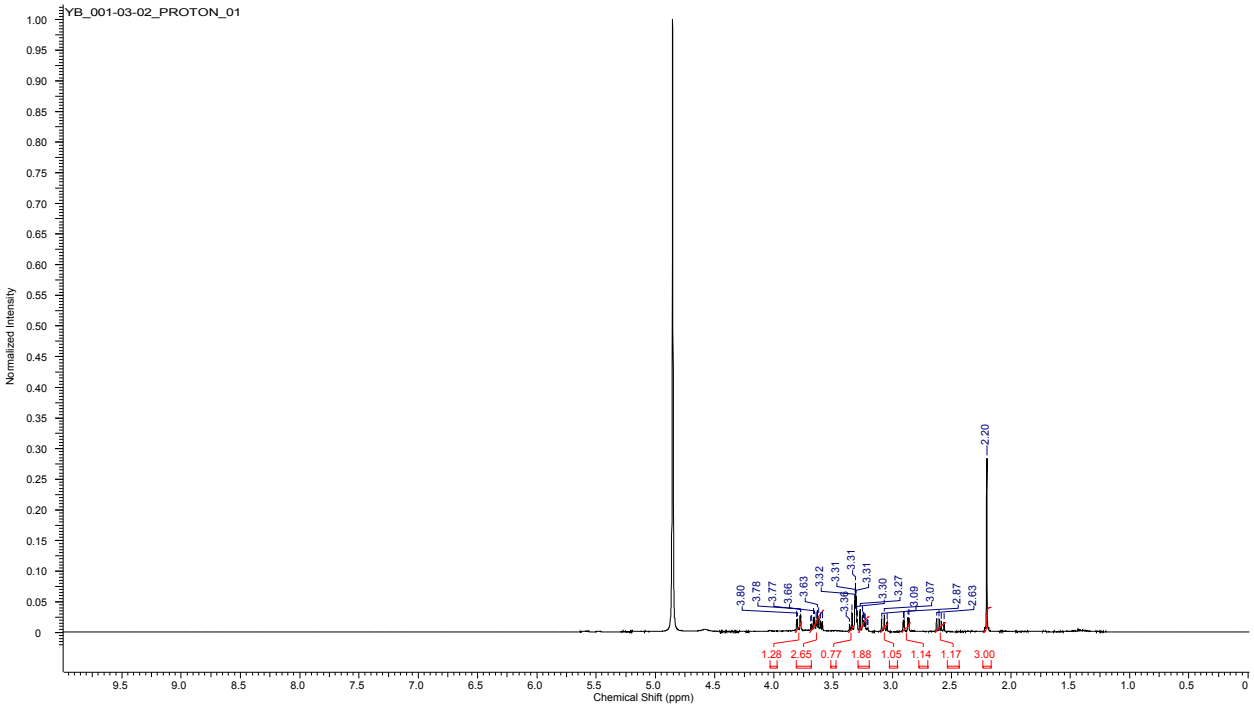

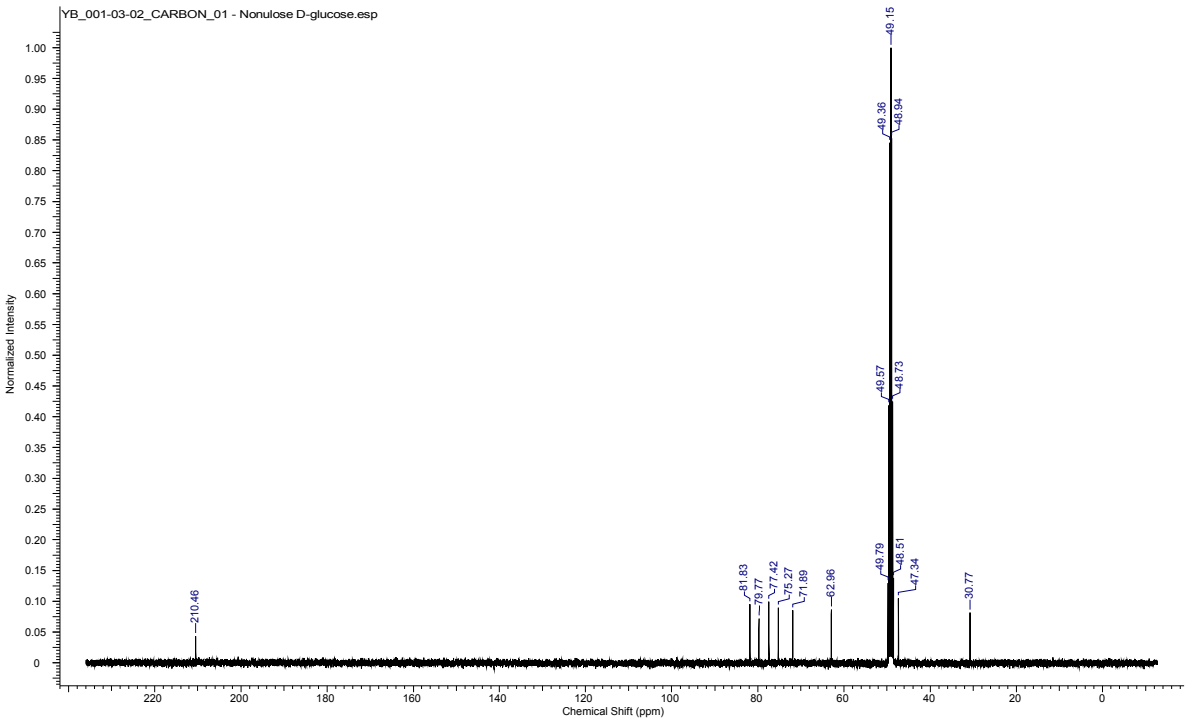

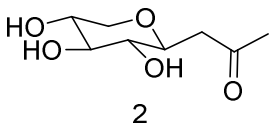
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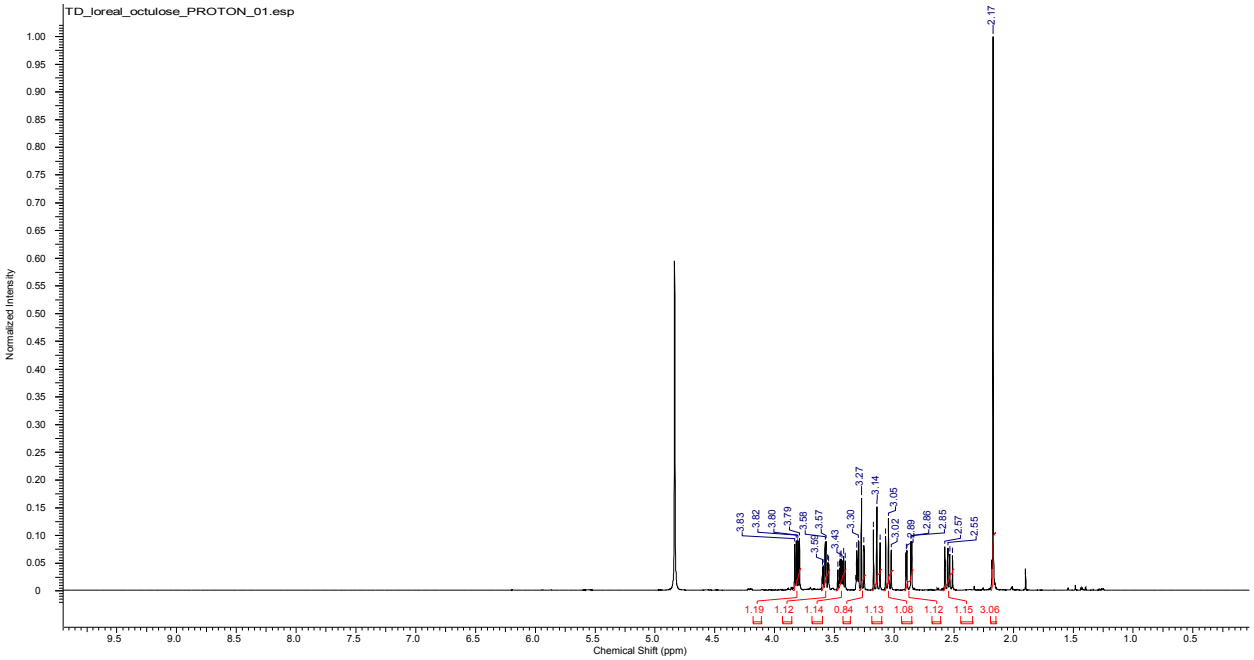
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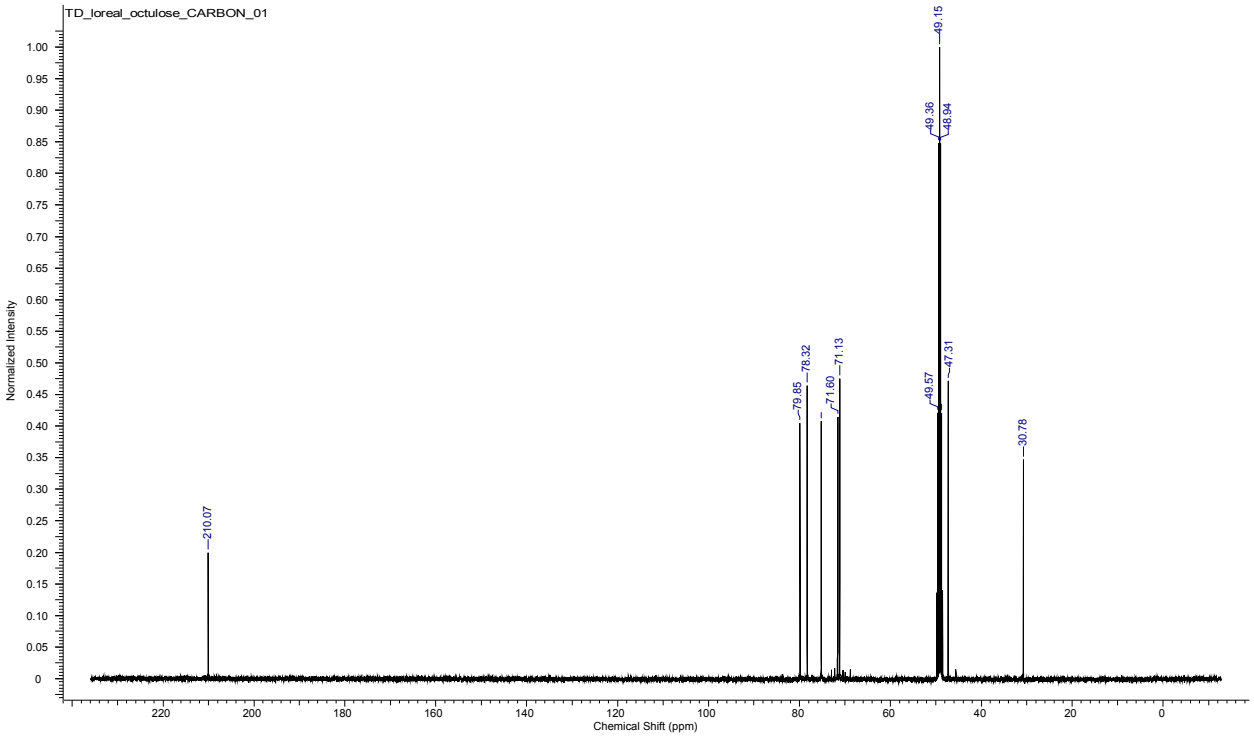
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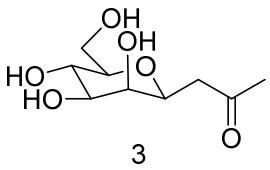
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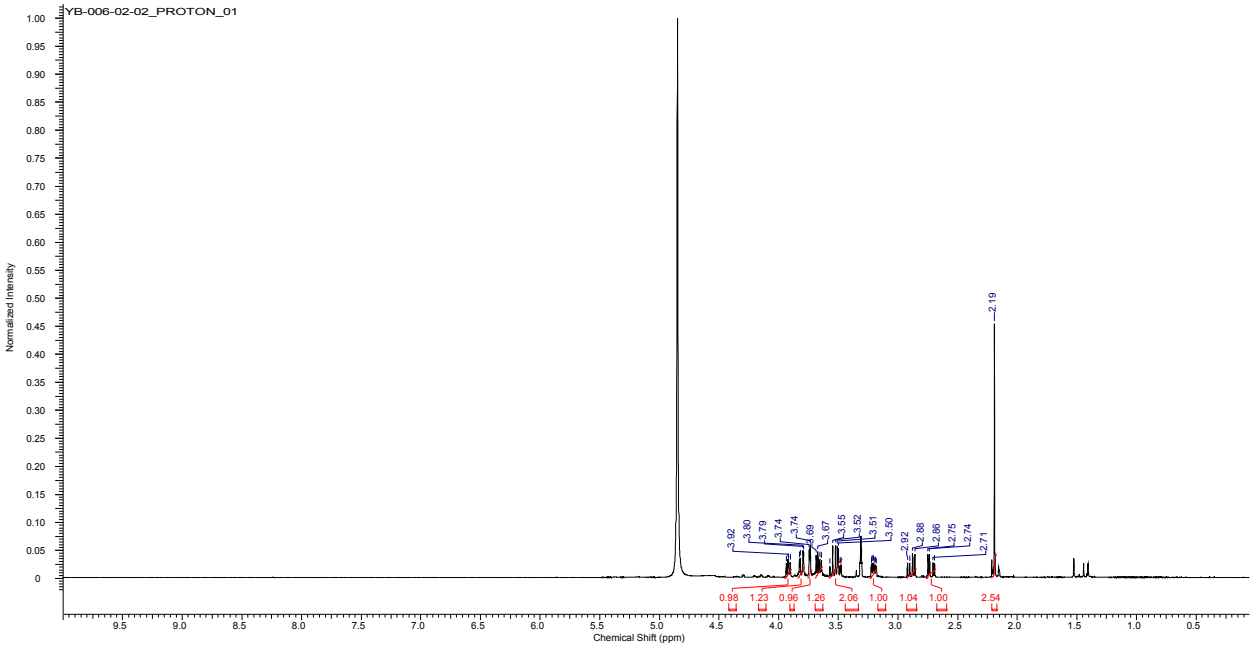
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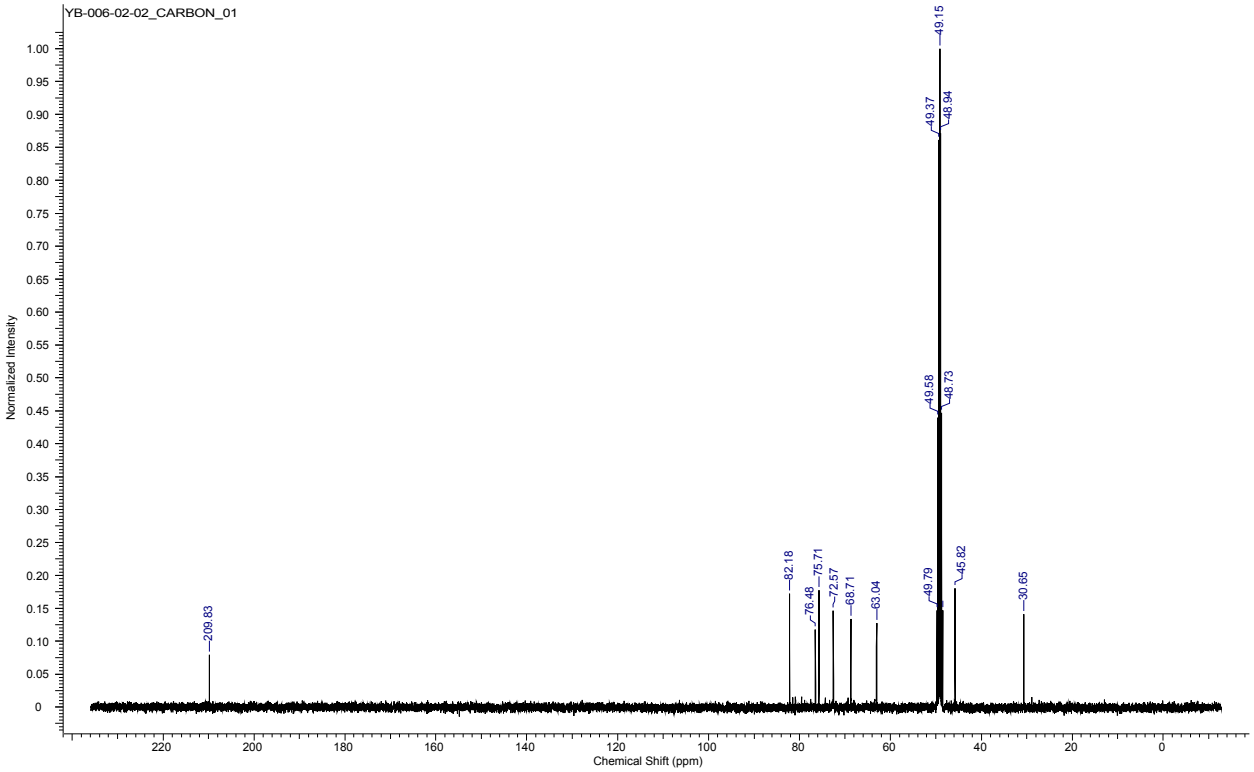
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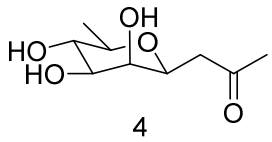
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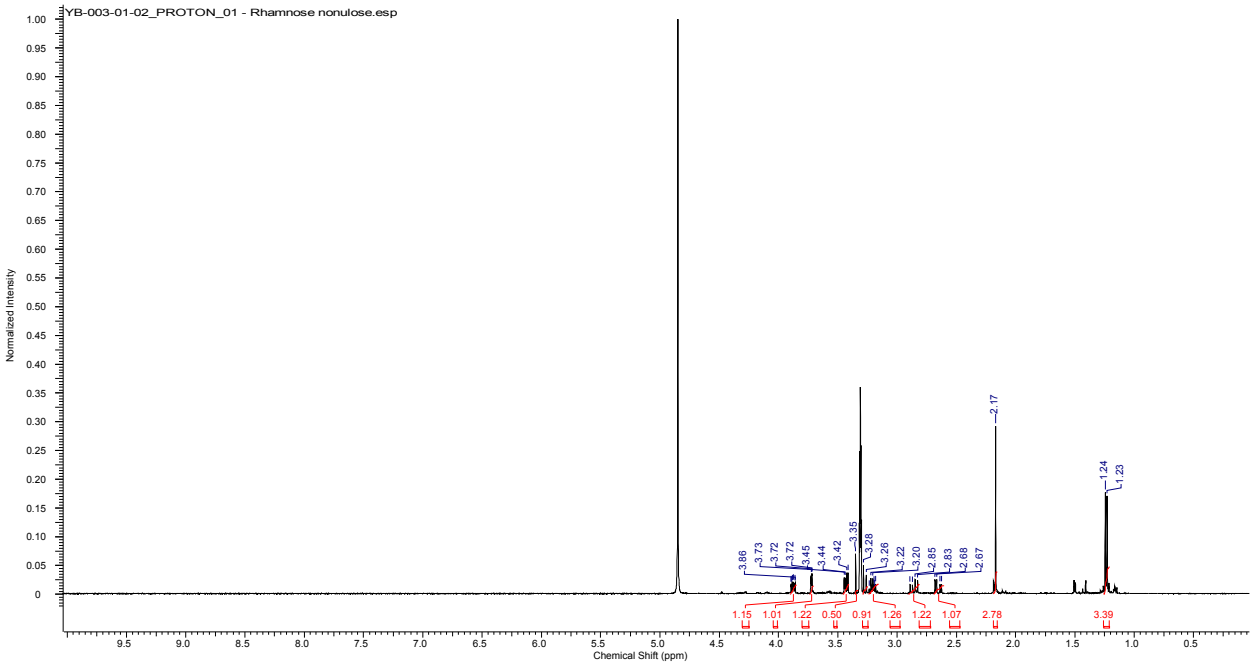
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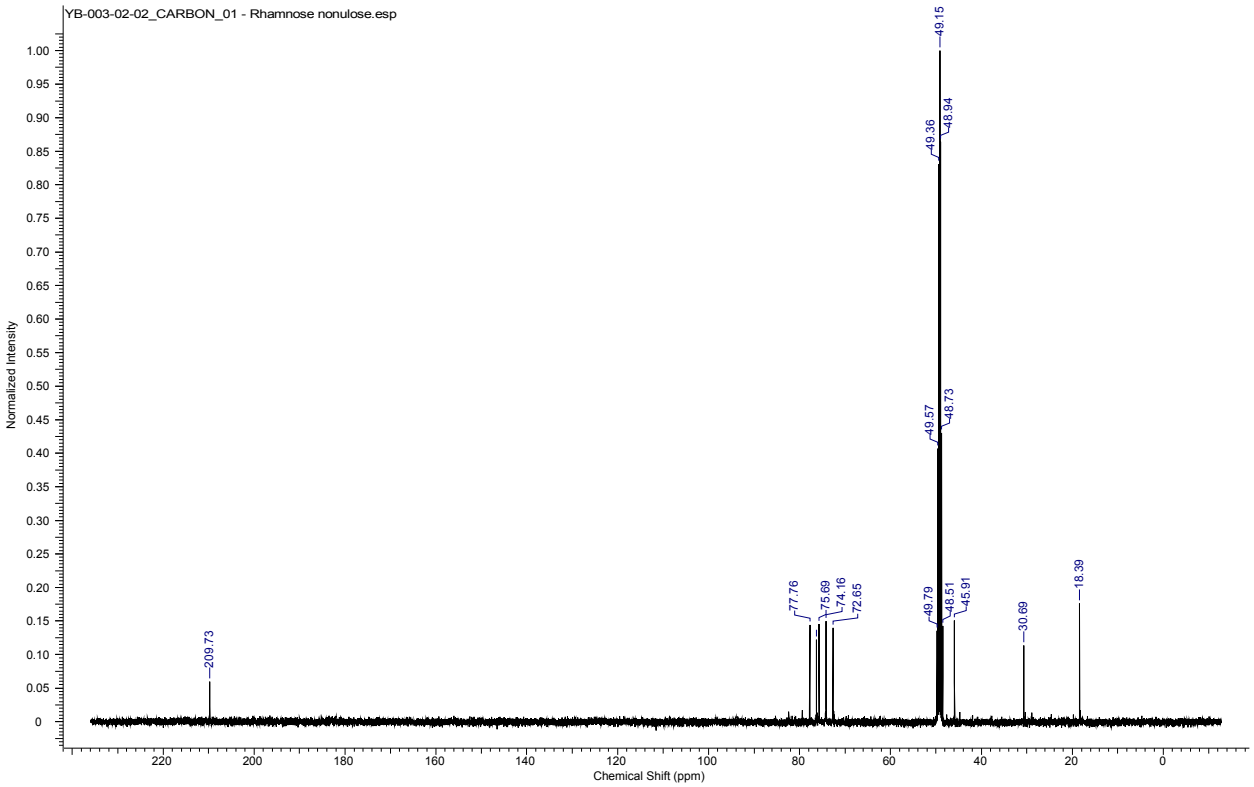
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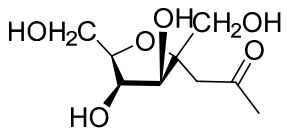
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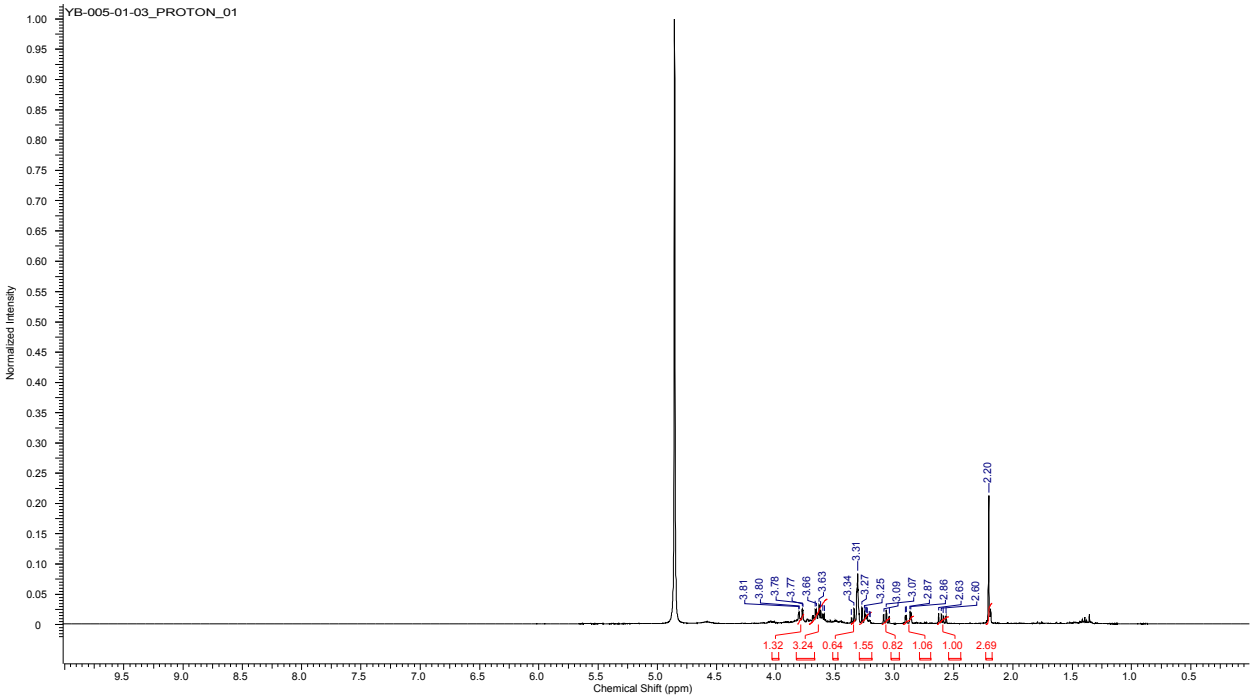
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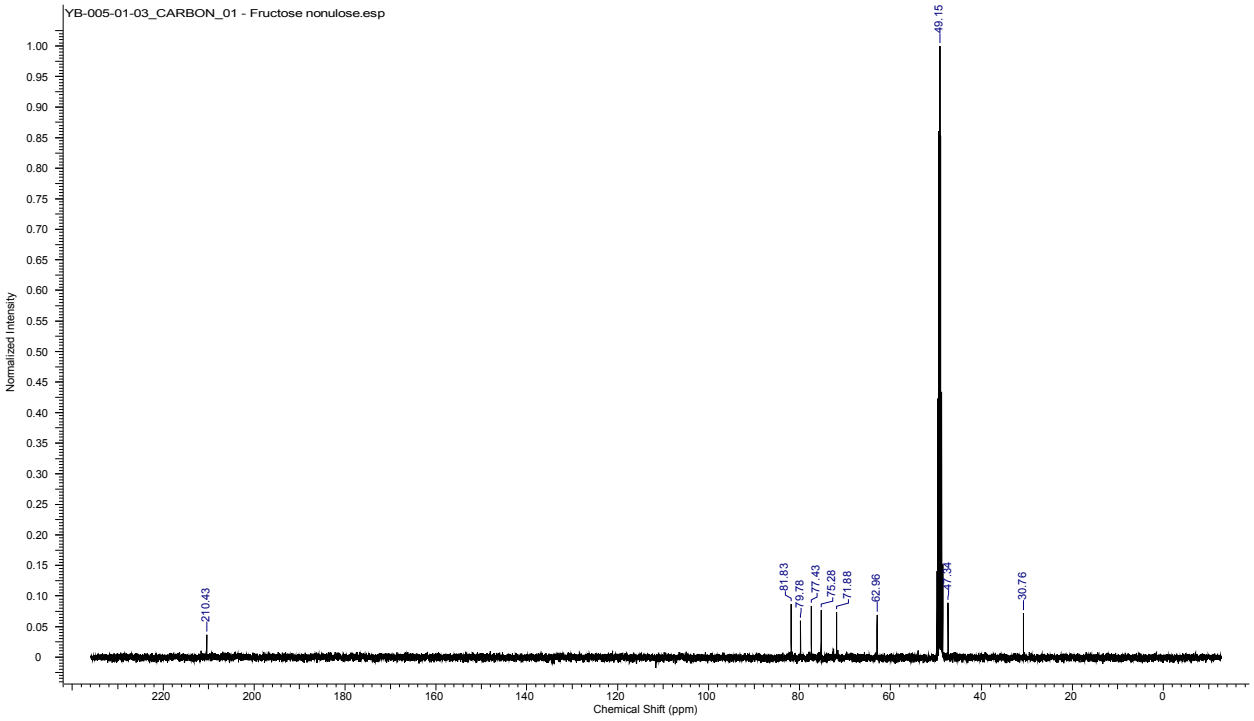
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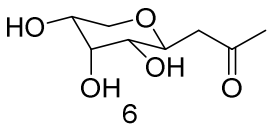
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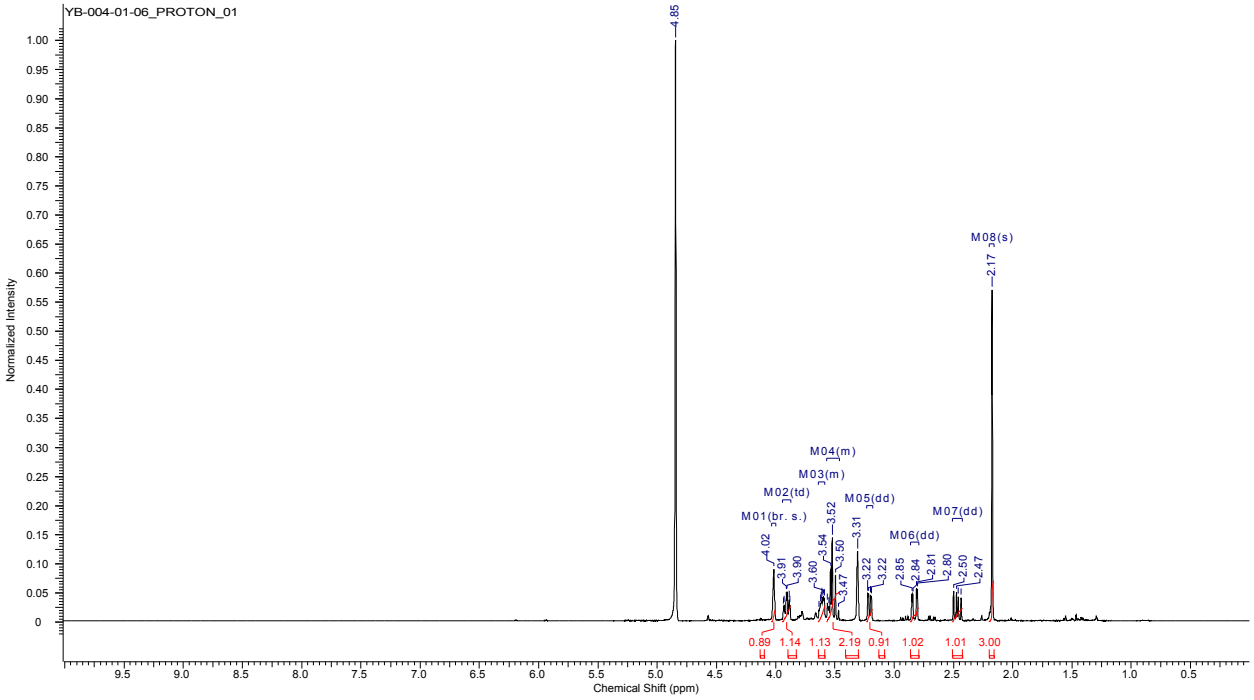
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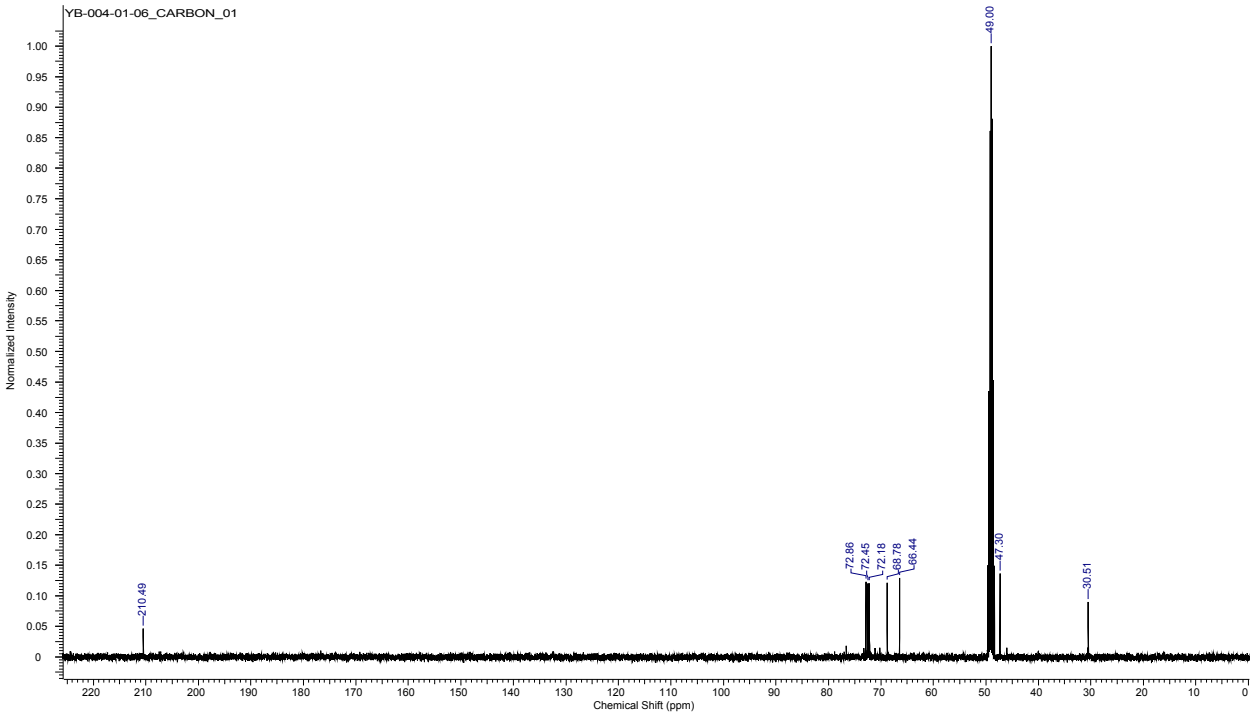
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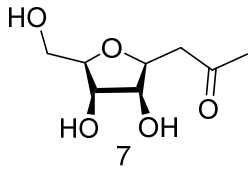
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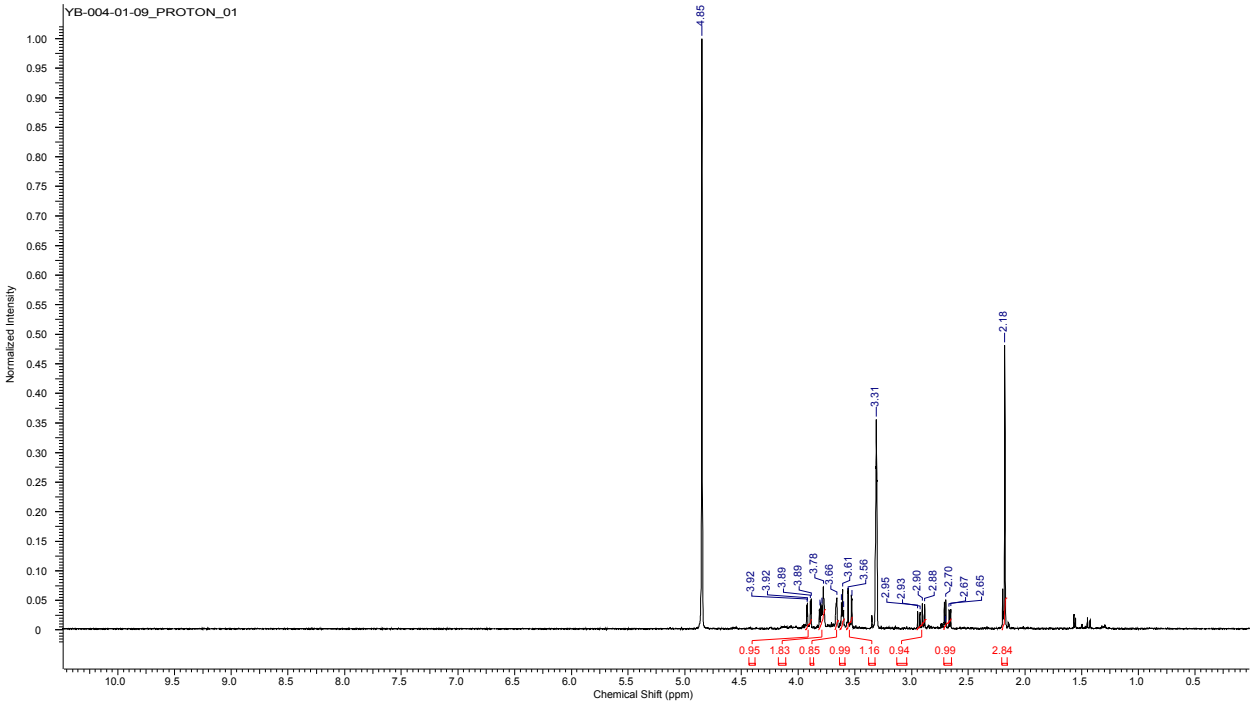
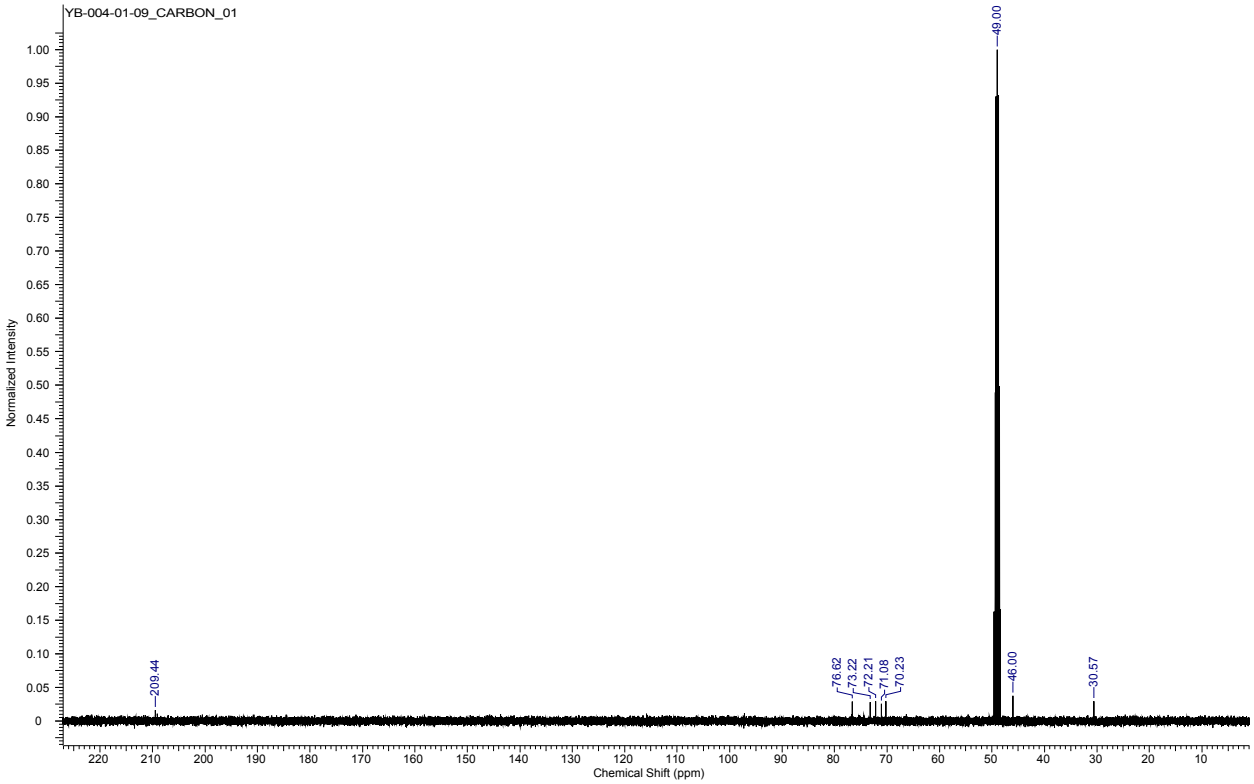
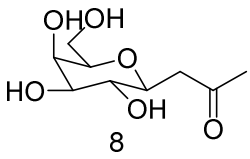
O

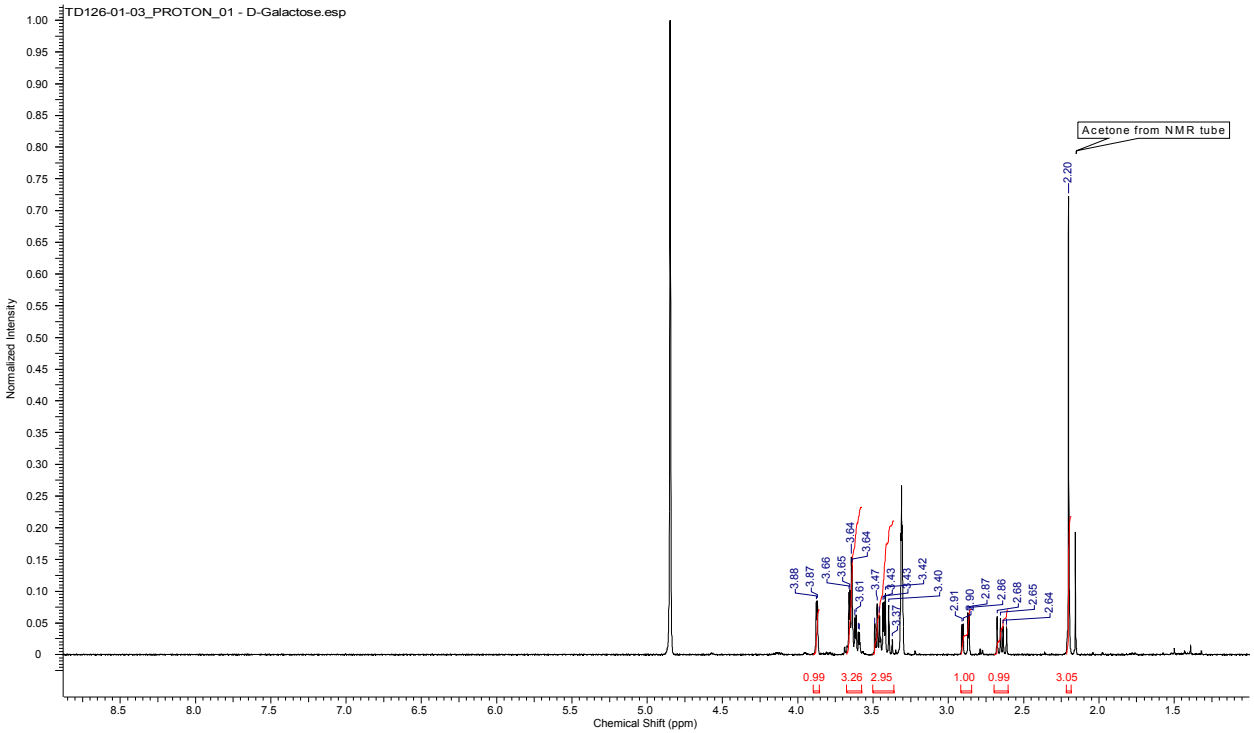
7

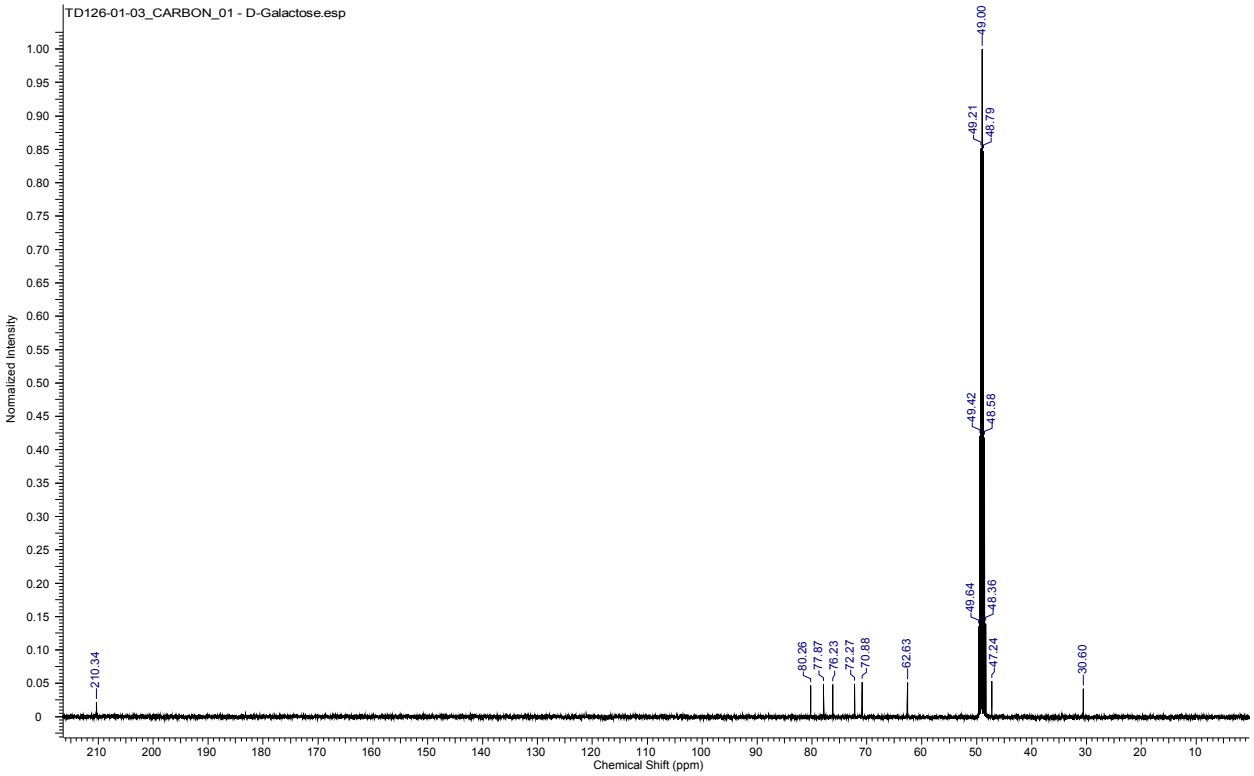

YB-004-01-09_PROTON_01
Normalized Intensity
Chemical Shift (ppm)
4.85
3.31
2.18
3.92
3.92
3.89
3.89
3.78
3.66
3.61
3.56
2.95
2.93
2.90
2.88
2.70
2.67
2.65
0.95
1.83
0.85
0.99
1.16
0.94
0.99
2.84

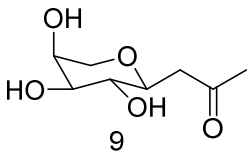

YB-004-01-09_CARBON_01
Normalized Intensity
Chemical Shift (ppm)
49.00
209.44
76.62
73.22
72.21
71.08
70.23
46.00
30.57


OH
OH
O
HO
OH
O

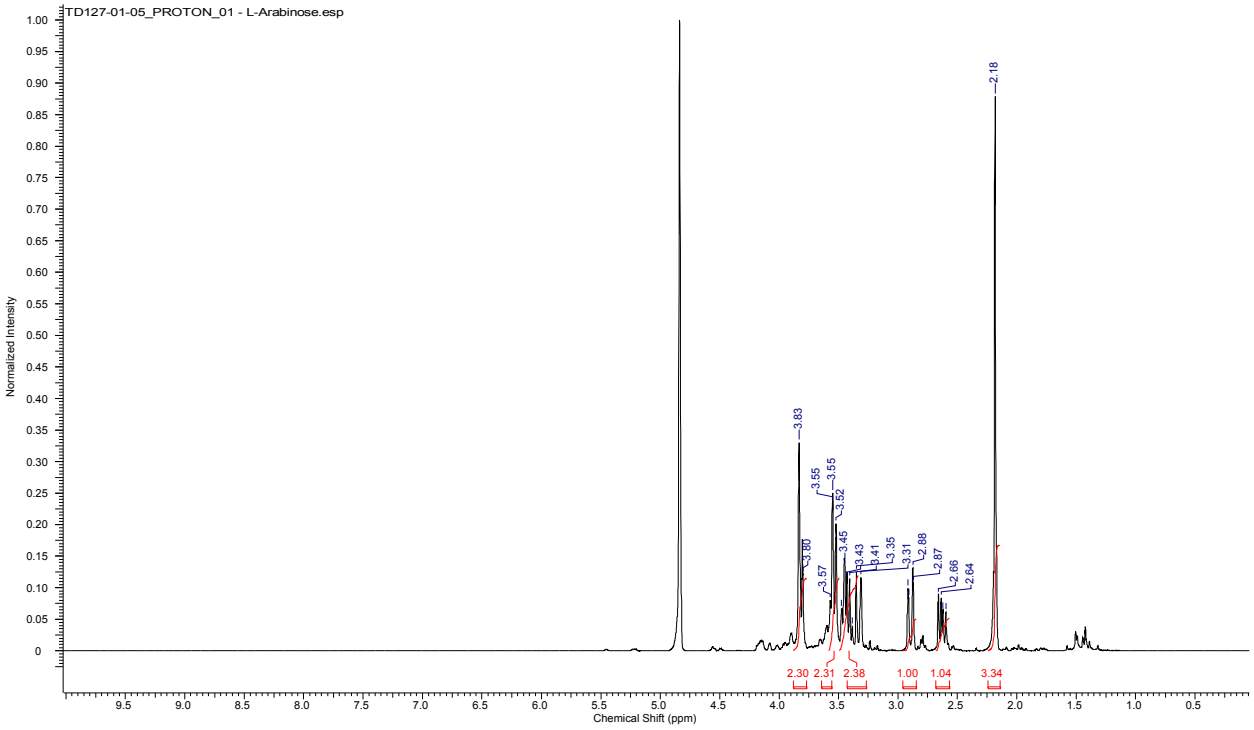
8

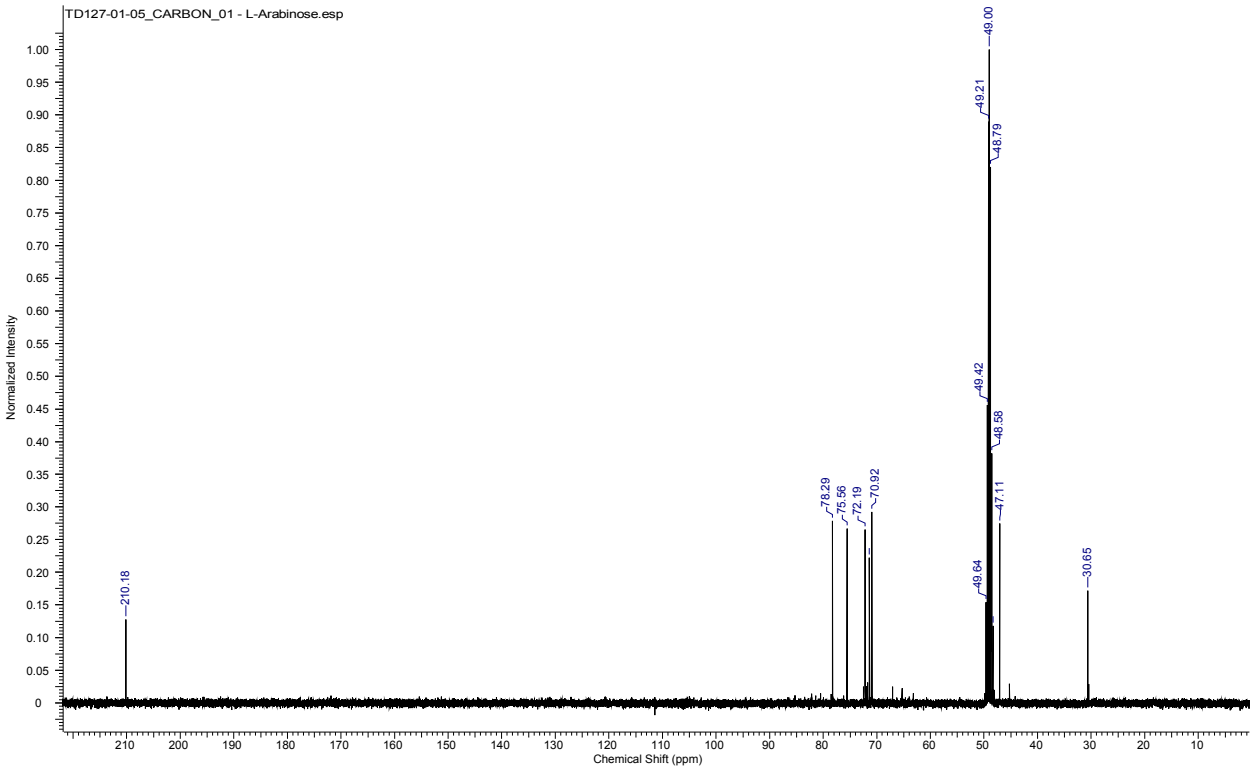

TD126-01-03_PROTON_01 - D-Galactose.esp
Normalized Intensity
Chemical Shift (ppm)
Acetone from NMR tube
2.20
3.88
3.87
3.66
3.65
3.64
3.64
3.61
3.47
3.43
3.43
3.42
3.40
3.37
2.91
2.90
2.87
2.86
2.68
2.65
2.64
0.99
3.26
2.95
1.00
0.99
3.05

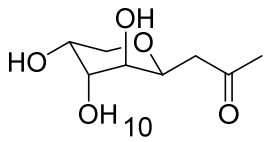

TD126-01-03_CARBON_01 - D-Galactose.esp
Normalized Intensity
Chemical Shift (ppm)
49.00
49.21
48.79
49.42
48.58
49.64
48.36
210.34
80.26
77.87
76.23
72.27
70.88
62.63
47.24
30.60

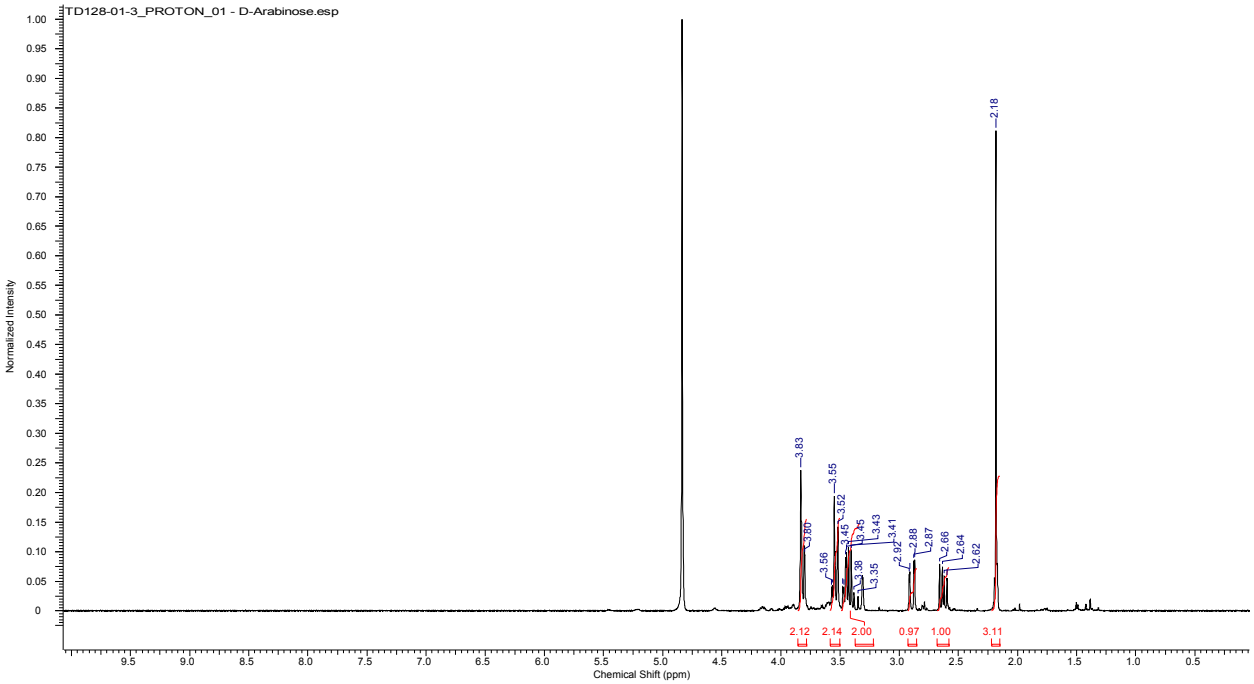

OH
O
HO
OH
O

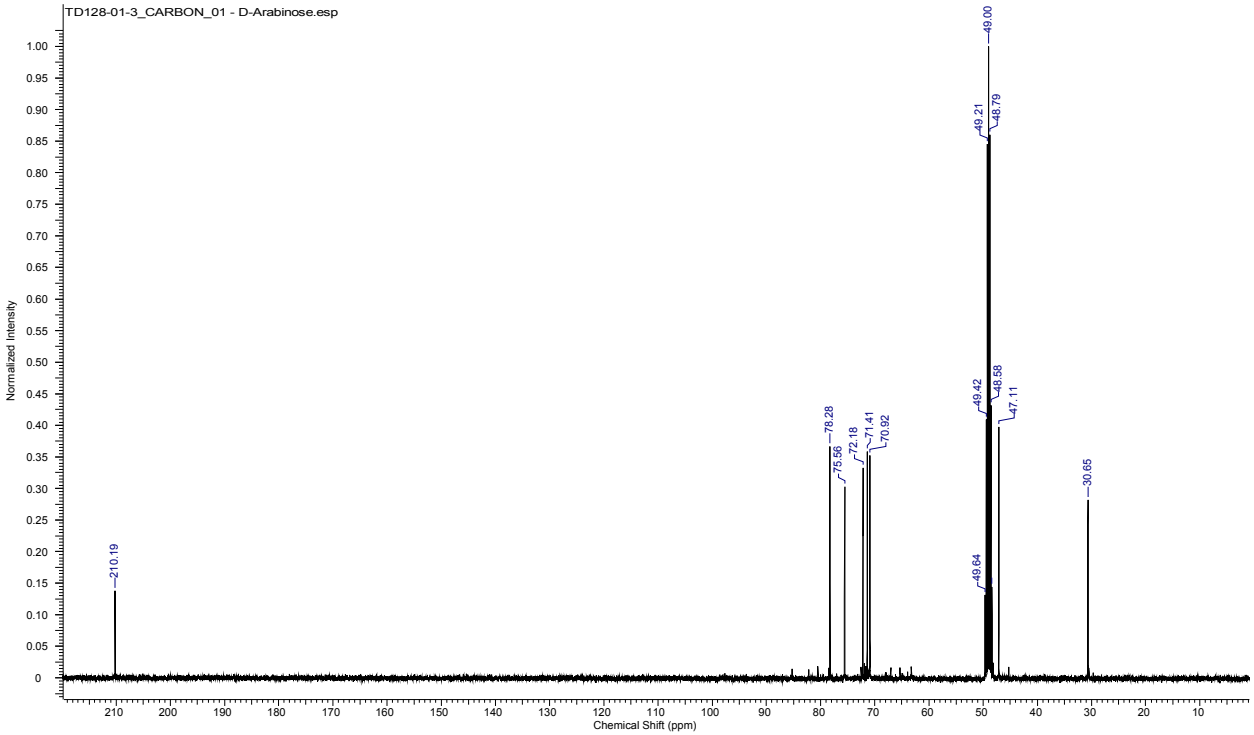
9

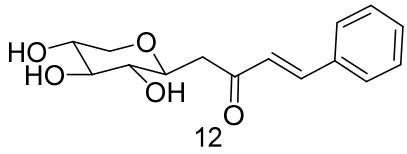

TD127-01-05_PROTON_01 - L-Arabinose.esp
Normalized Intensity
Chemical Shift (ppm)
3.83
3.55
3.55
3.52
3.80
3.57
3.45
3.43
3.41
3.35
3.31
2.88
2.87
2.66
2.64
2.18
2.30
2.31
2.38
1.00
1.04
3.34

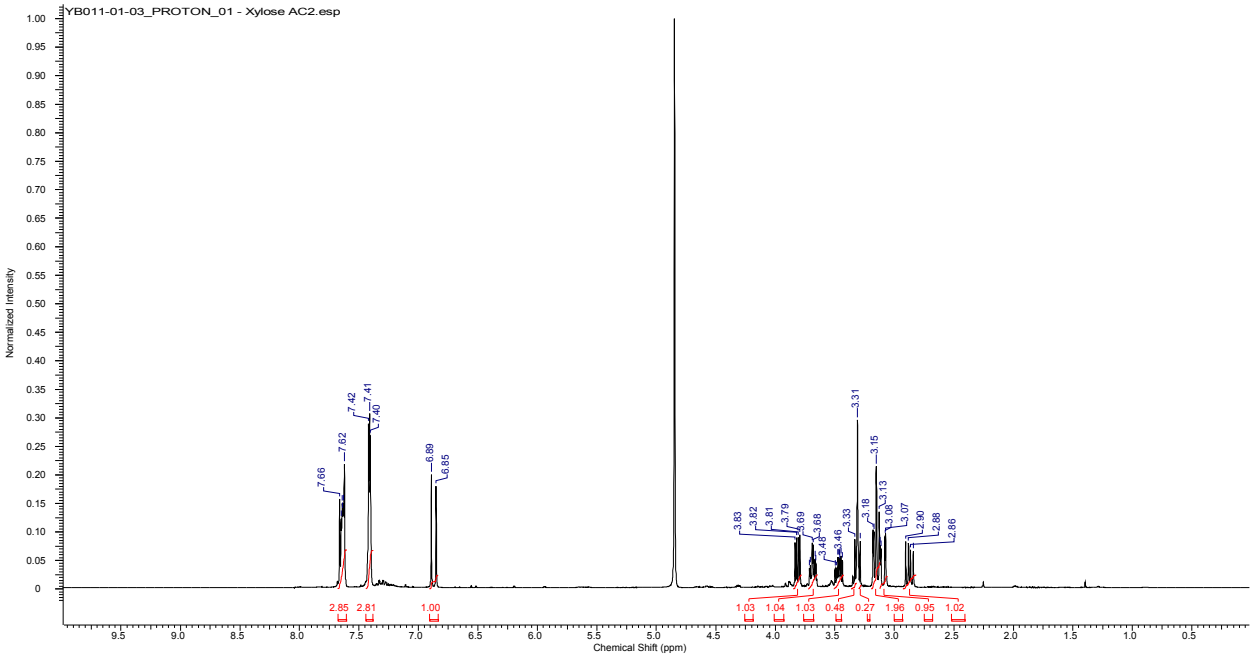

TD127-01-05_CARBON_01 - L-Arabinose.esp
Normalized Intensity
Chemical Shift (ppm)
49.00
49.21
48.79
49.42
48.58
78.29
75.56
72.19
70.92
47.11
49.64
30.65
210.18

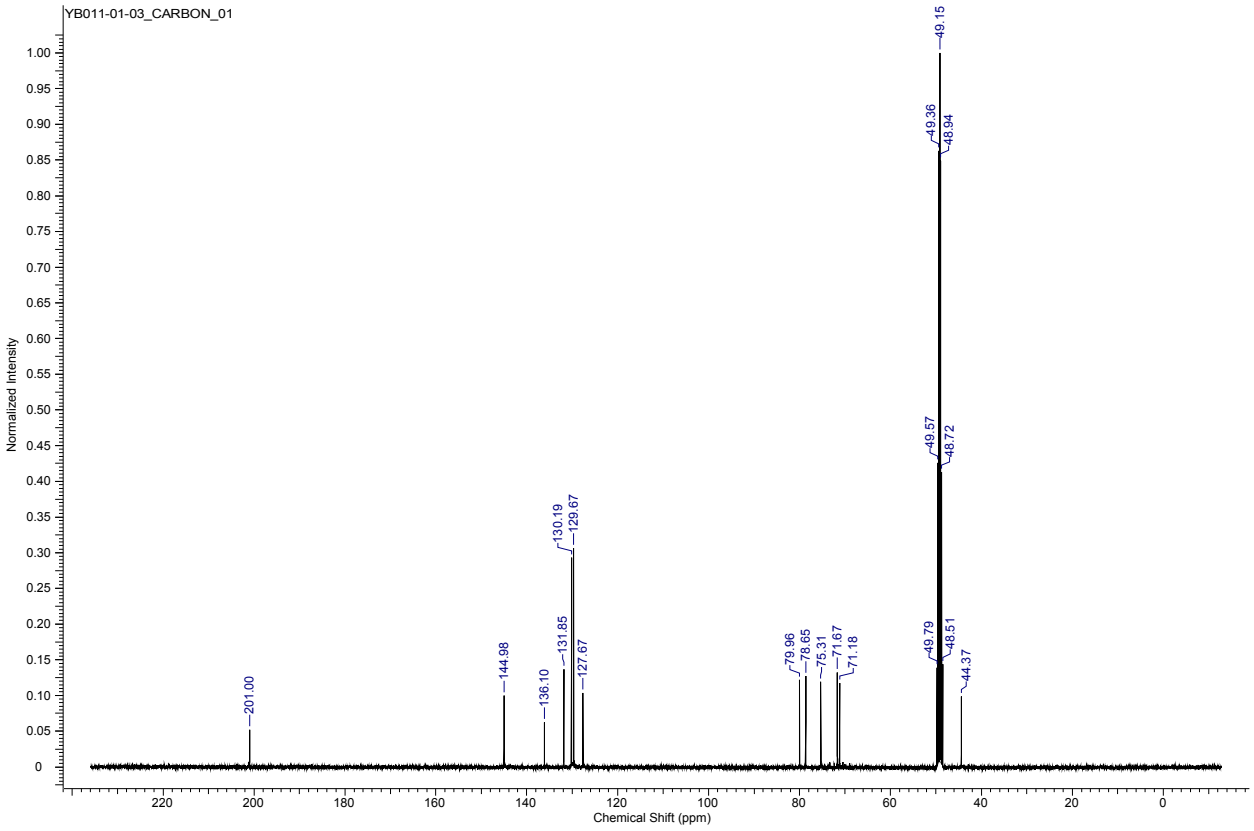

OH
HO
O
OH
10
O

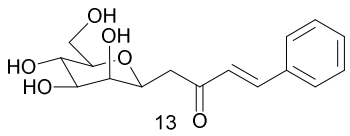

TD128-01-3_PROTON_01 - D-Arabinose.esp
Normalized Intensity
Chemical Shift (ppm)
3.83
3.55
3.52
3.56
3.43
3.41
2.92
2.88
2.87
2.66
2.64
2.62
2.18
3.35
2.12
2.14
2.00
0.97
1.00
3.11

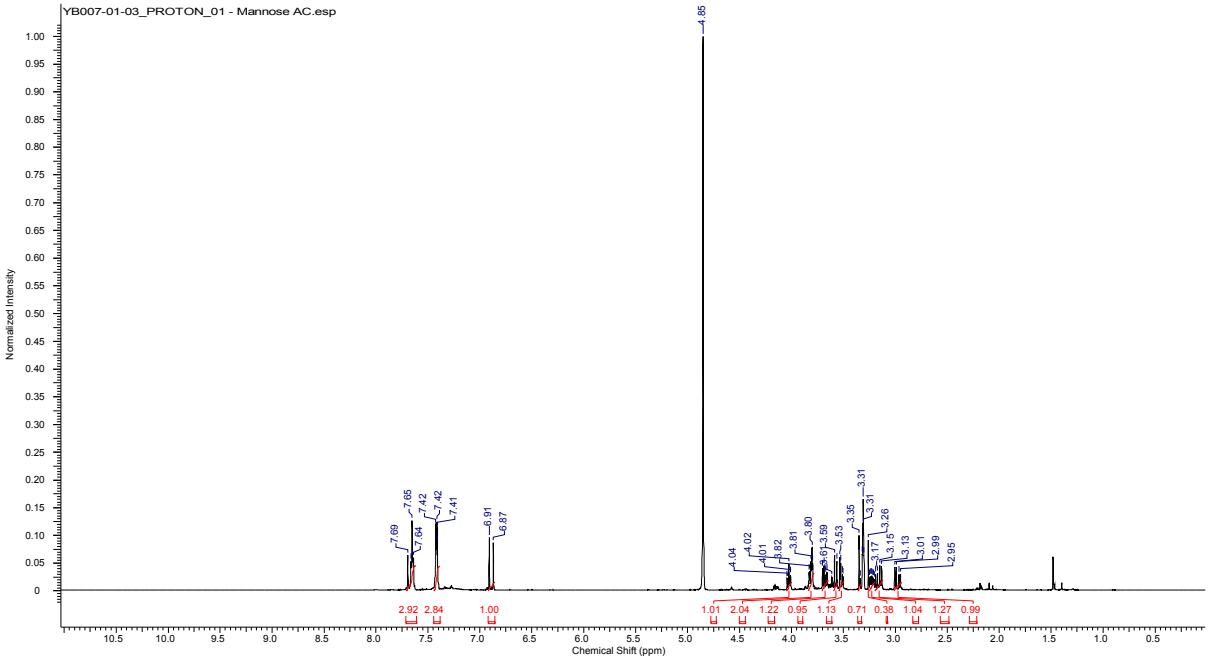

TD128-01-3_CARBON_01 - D-Arabinose.esp
Normalized Intensity
Chemical Shift (ppm)
49.00
49.21
48.79
49.42
48.58
47.11
78.28
75.56
72.18
71.41
70.92
30.65
210.19
49.64

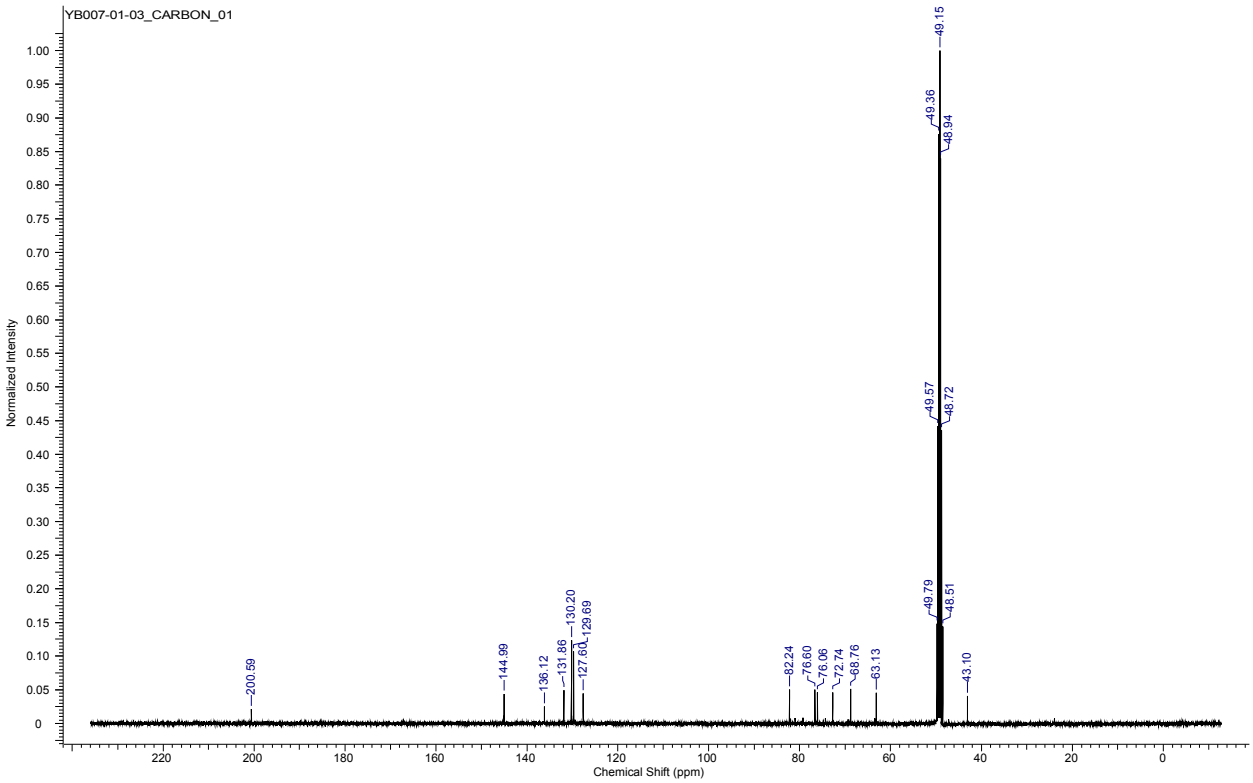

HO
HO
O
OH
O
12

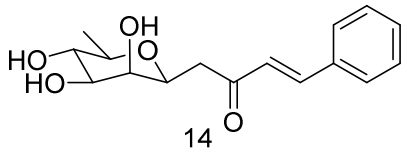

YB011-01-03_PROTON_01 - Xylose AC2.esp
Normalized Intensity
Chemical Shift (ppm)
7.66
7.62
7.42
7.41
7.40
6.89
6.85
3.83
3.82
3.81
3.79
3.69
3.68
3.48
3.46
3.33
3.31
3.18
3.15
3.13
3.08
3.07
2.90
2.88
2.86
2.85
2.81
1.00
1.03
1.04
1.03
0.48
0.27
1.96
0.95
1.02

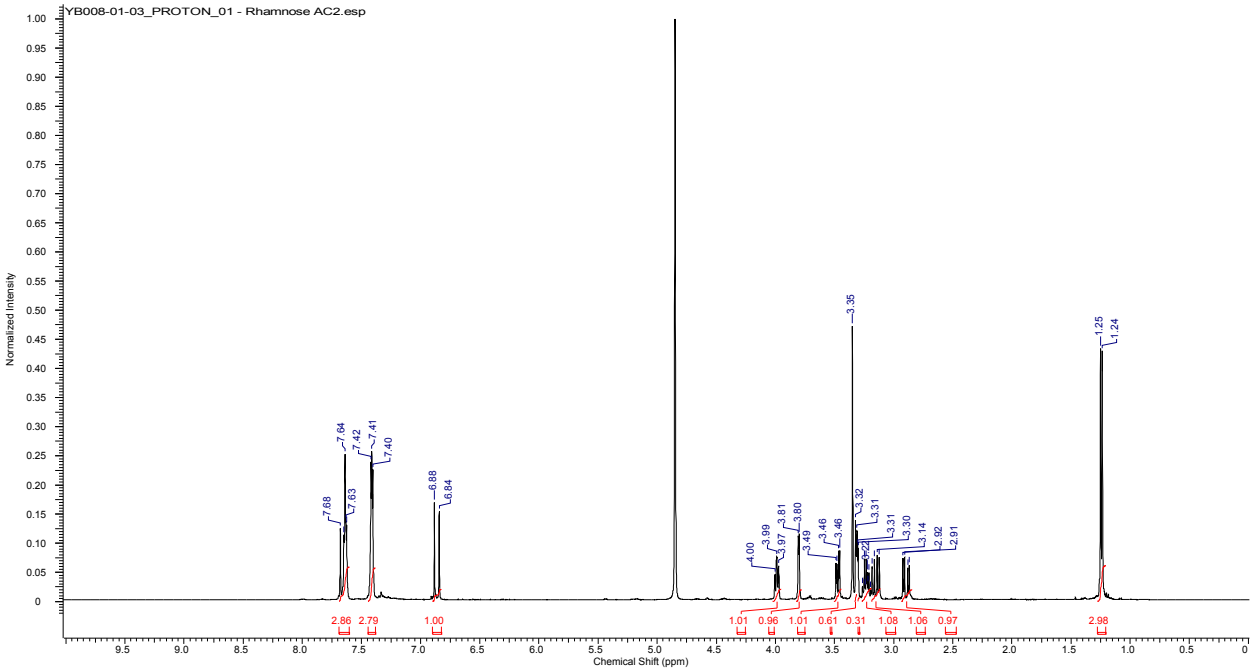

YB011-01-03_CARBON_01
Normalized Intensity
Chemical Shift (ppm)
201.00
144.98
136.10
131.85
130.19
129.67
127.67
79.96
78.65
75.31
71.67
71.18
49.79
49.57
49.36
49.15
48.94
48.72
48.51
44.37

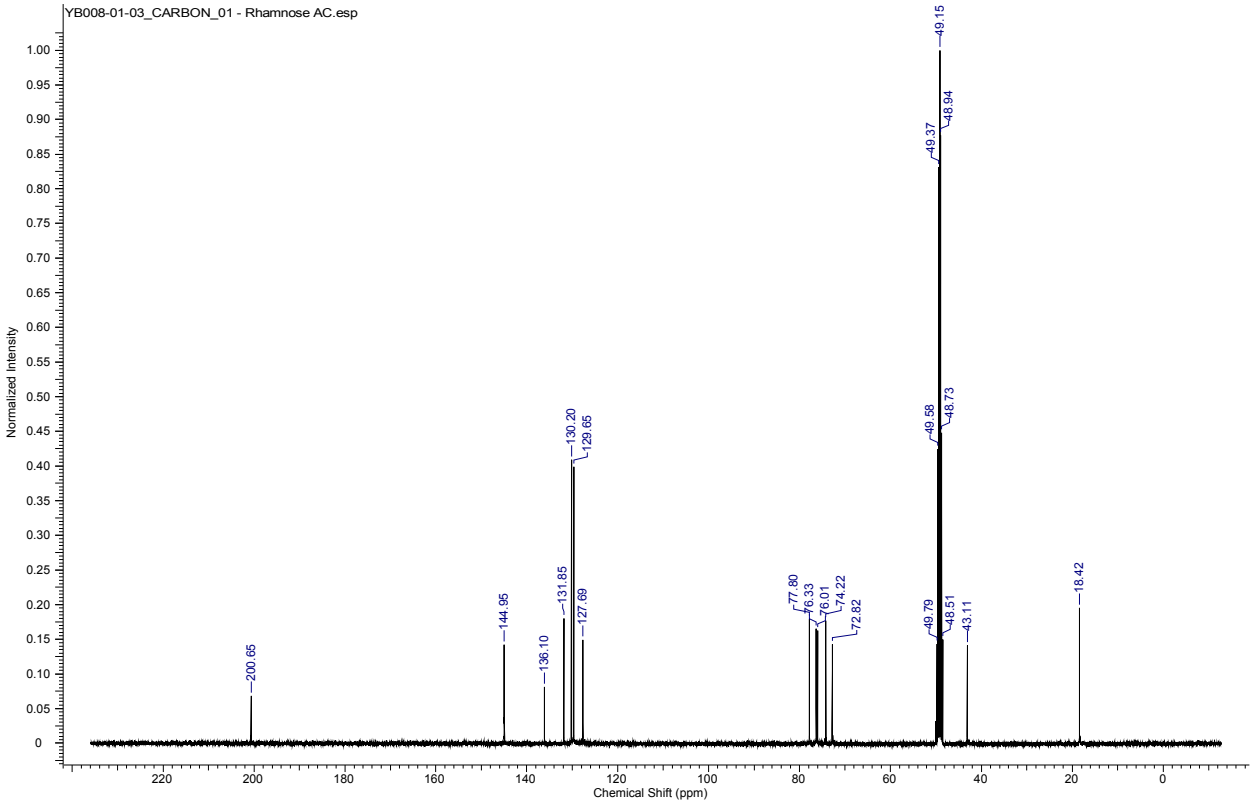

OH
OH
HO
HO
O
13
O

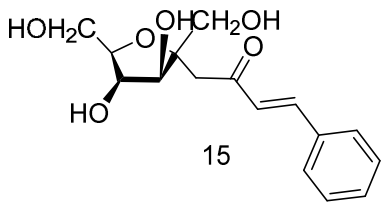

YB007-01-03_PROTON_01 - Mannose AC.esp
Normalized Intensity
Chemical Shift (ppm)
4.85
7.69
7.65
7.64
7.42
7.42
7.41
6.91
6.87
4.04
4.02
4.01
3.82
3.81
3.80
3.61
3.59
3.53
3.35
3.31
3.31
3.26
3.17
3.15
3.13
3.01
2.99
2.95
2.92
2.84
1.00
1.01
2.04
1.22
0.95
1.13
0.71
0.38
1.04
1.27
0.99


YB007-01-03_CARBON_01
Normalized Intensity
Chemical Shift (ppm)
200.59
144.99
136.12
131.86
130.20
129.69
127.60
82.24
76.60
76.06
72.74
68.76
63.13
49.79
49.57
49.36
49.15
48.94
48.72
48.51
43.10

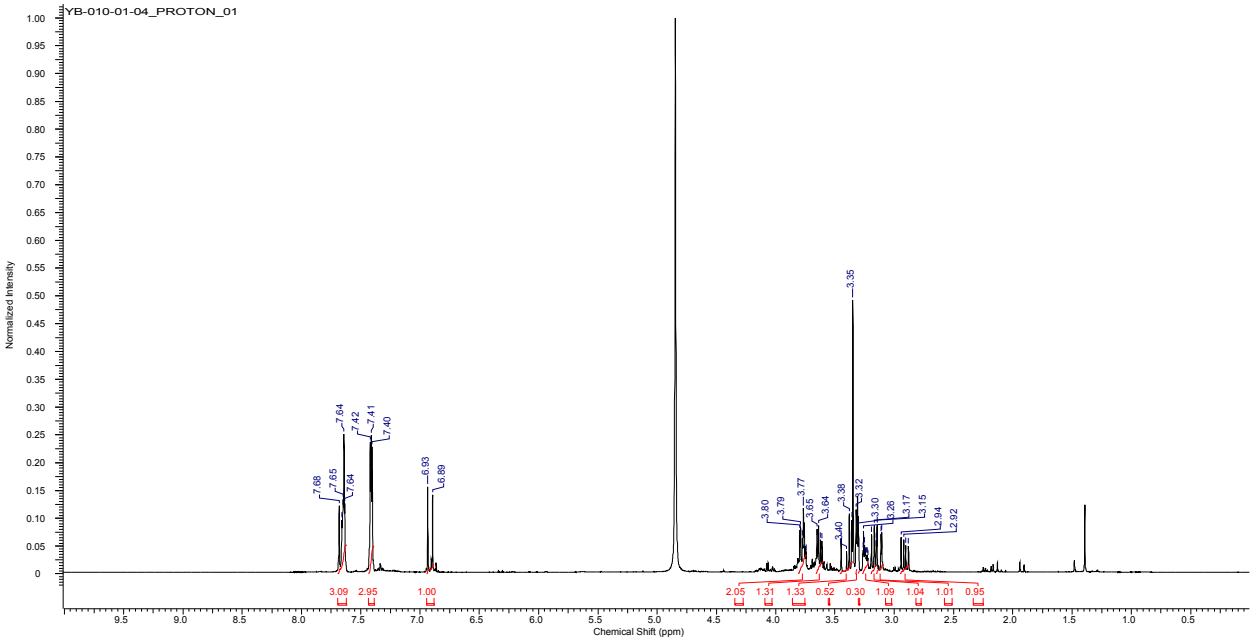

OH
O
HO
HO
O
14

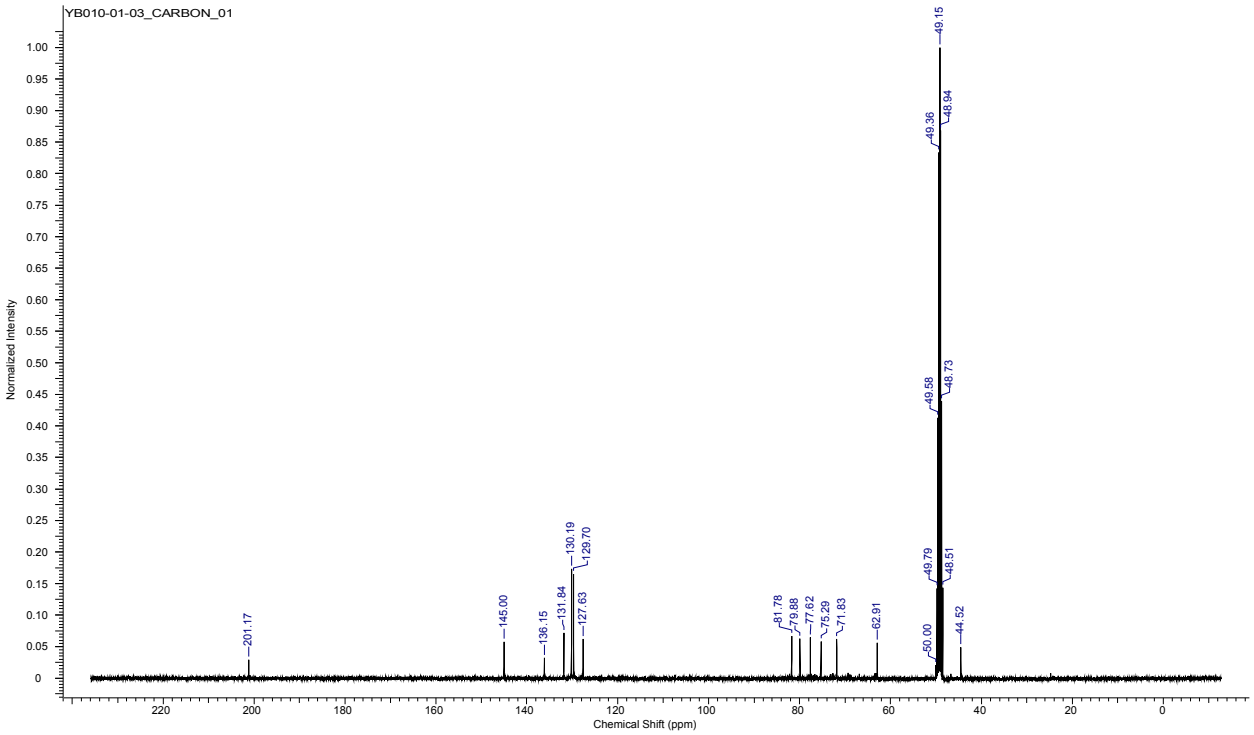

YB008-01-03_PROTON_01 - Rhamnose AC2.esp
Normalized Intensity
Chemical Shift (ppm)
7.68
7.64
7.63
7.42
7.41
7.40
6.88
6.84
4.00
3.99
3.97
3.81
3.80
3.49
3.46
3.46
3.35
3.32
3.31
3.31
3.30
3.14
2.92
2.91
1.25
1.24
2.86
2.79
1.00
1.01
0.96
1.01
0.61
0.31
1.08
1.06
0.97
2.98

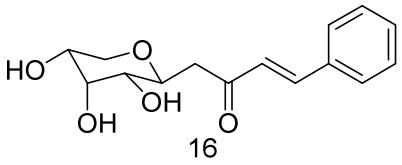

YB008-01-03_CARBON_01 - Rhamnose AC.esp
Normalized Intensity
Chemical Shift (ppm)
200.65
144.95
136.10
131.85
130.20
129.65
127.69
77.80
76.33
76.01
74.22
72.82
49.79
49.58
49.37
49.15
48.94
48.73
48.51
43.11
18.42


HOH2C
OH
CH2OH
O
O
HO

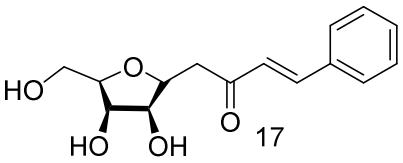
15


YB-010-01-04_PROTON_01
Normalized Intensity
Chemical Shift (ppm)
7.68
7.65
7.64
7.64
7.42
7.41
7.40
6.93
6.88
3.80
3.79
3.77
3.65
3.64
3.40
3.38
3.35
3.32
3.30
3.26
3.17
3.15
2.94
2.92
3.09
2.95
1.00
2.05
1.31
1.33
0.52
0.30
1.09
1.04
1.01
0.95

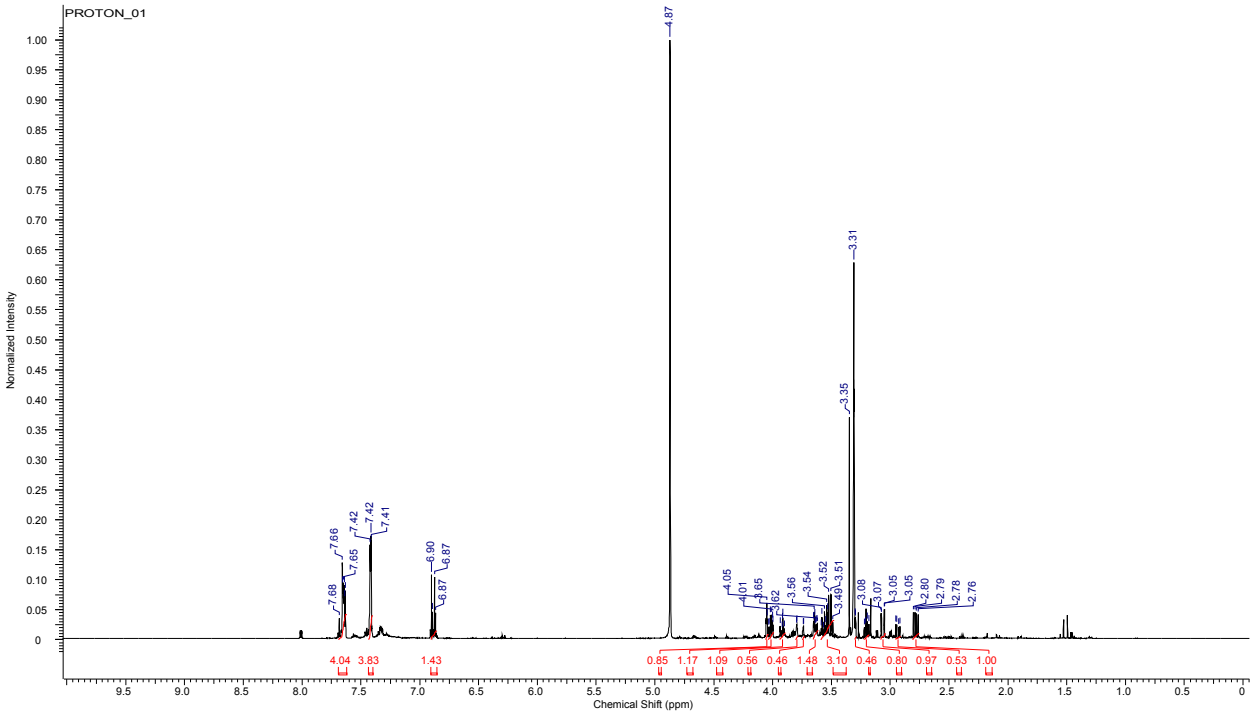

YB010-01-03_CARBON_01
Normalized Intensity
Chemical Shift (ppm)
201.17
145.00
136.15
131.84
130.19
129.70
127.63
81.78
79.88
77.62
75.29
71.83
62.91
50.00
49.79
49.58
49.36
49.15
48.94
48.73
48.51
44.52

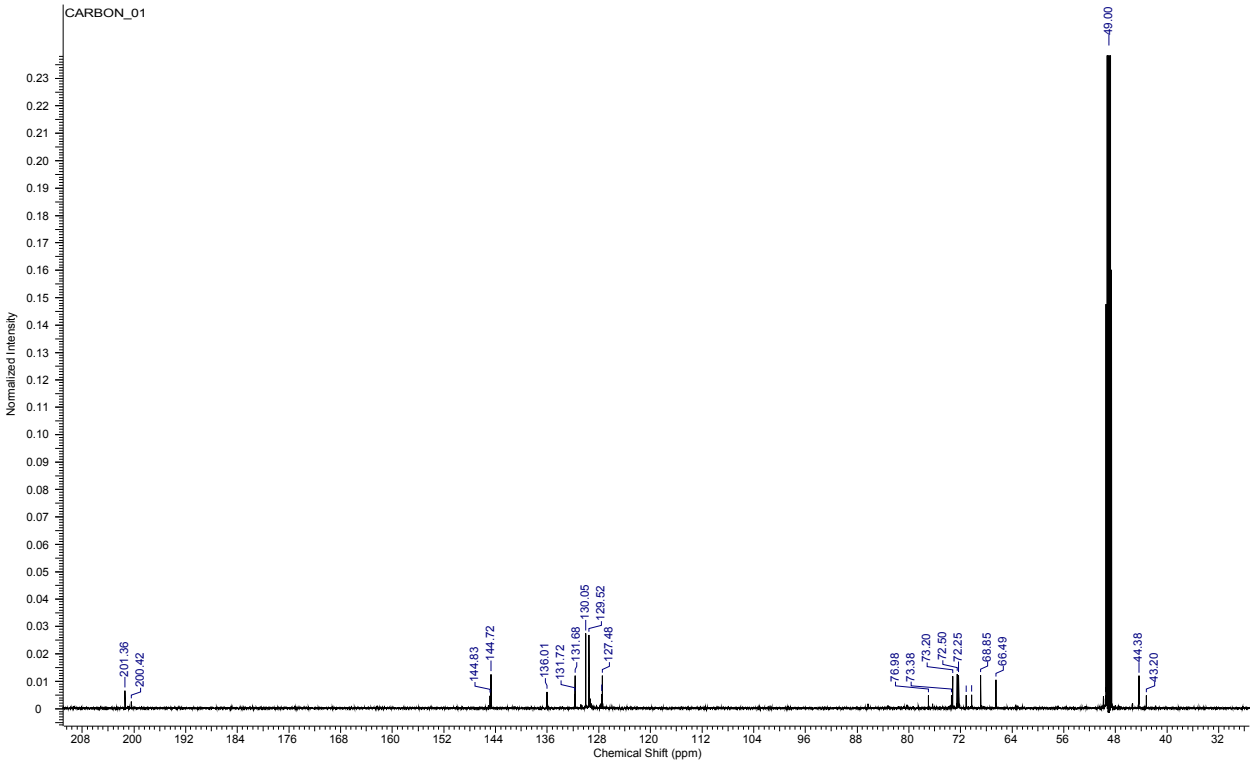

HO
O
OH
OH
O
16

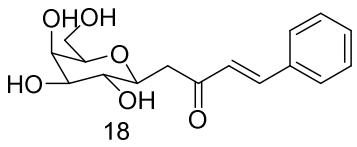
&


HO
O
HO
OH
O
17

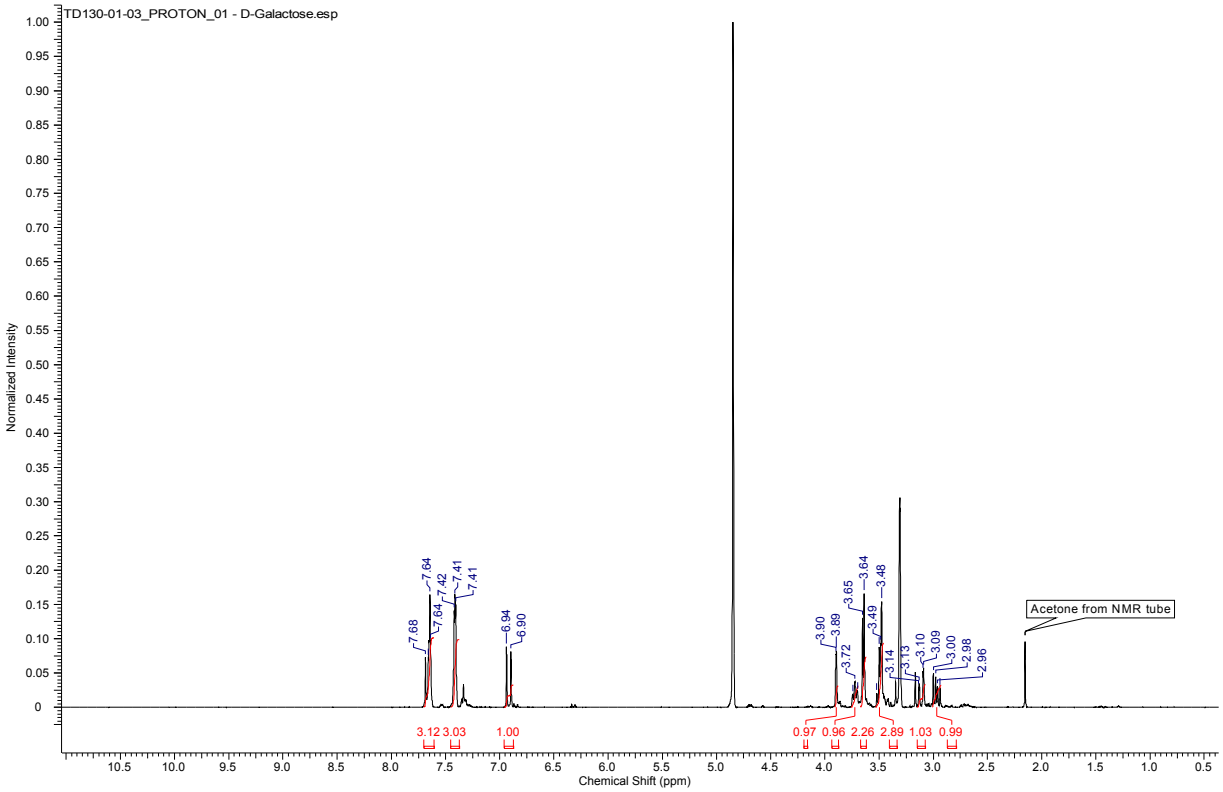
(7:3 ratio)

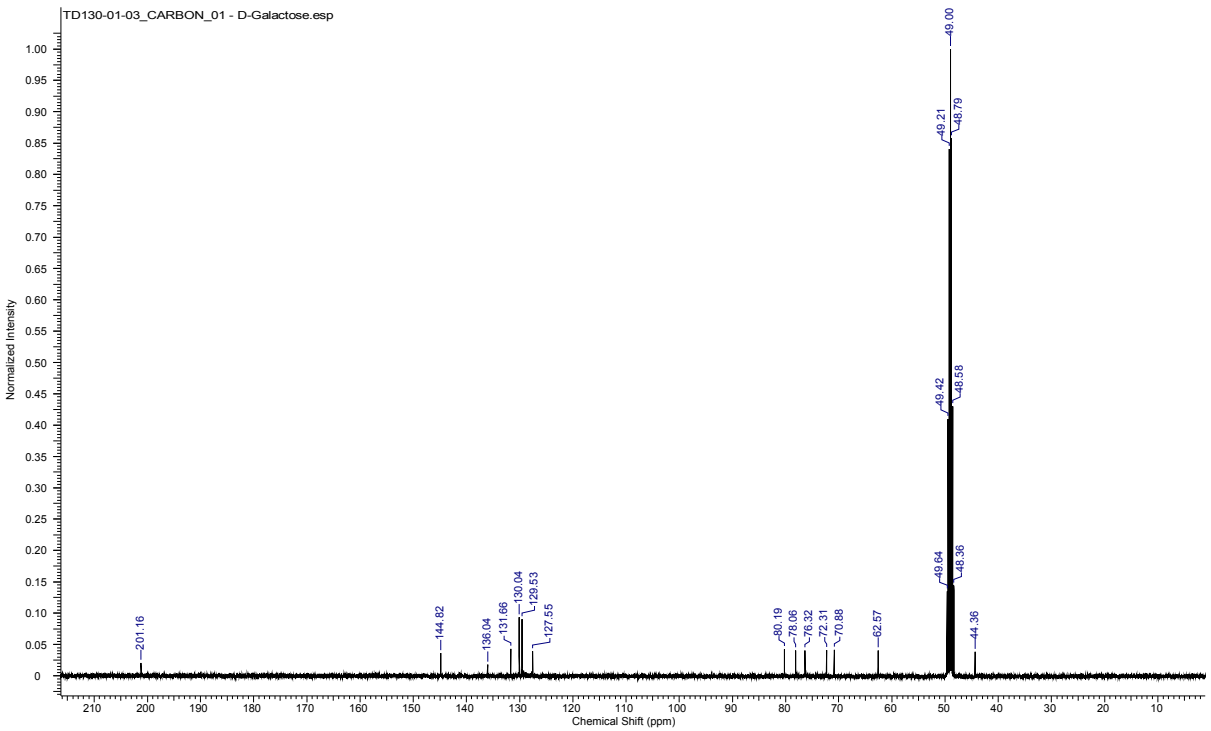

PROTON_01
Normalized Intensity
Chemical Shift (ppm)
4.87
3.31
3.35
7.66
7.65
7.42
7.42
7.41
7.68
6.90
6.87
6.87
4.05
4.01
3.65
3.62
3.56
3.54
3.52
3.51
3.49
3.08
3.07
3.05
3.05
2.80
2.79
2.78
2.76
4.04
3.83
1.43
0.85
1.17
1.09
0.56
0.46
1.48
3.10
0.46
0.80
0.97
0.53
1.00

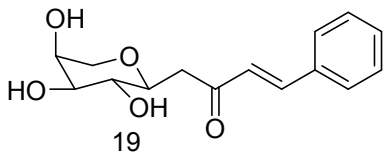

CARBON_01
Normalized Intensity
Chemical Shift (ppm)
49.00
201.36
200.42
144.83
144.72
136.01
131.72
131.68
130.05
129.52
127.48
76.98
73.38
73.20
72.50
72.25
68.85
66.49
44.38
43.20


OH
OH
O
HO
OH
O

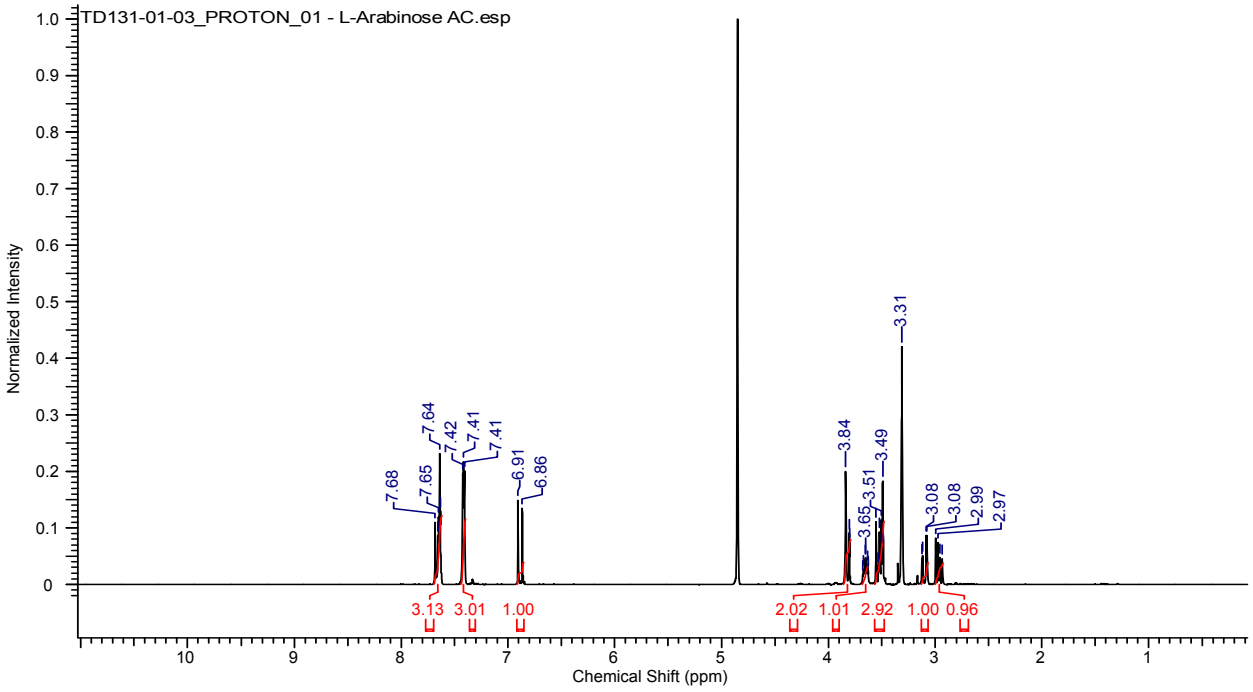
18

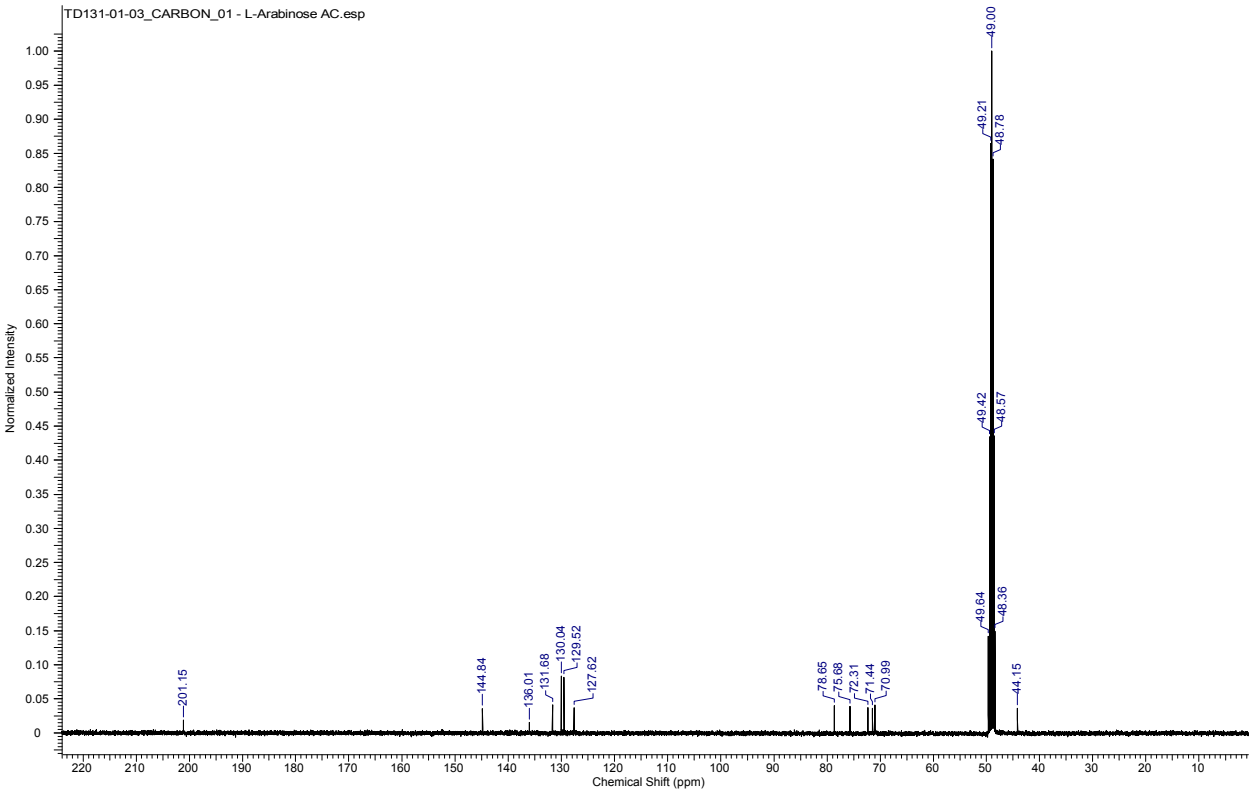

TD130-01-03_PROTON_01 - D-Galactose.esp
Normalized Intensity
Chemical Shift (ppm)
7.68
7.64
7.64
7.42
7.41
7.41
6.94
6.90
3.90
3.89
3.72
3.65
3.64
3.49
3.48
3.14
3.13
3.10
3.09
3.00
2.98
2.96
Acetone from NMR tube
3.12
3.03
1.00
0.97
0.96
2.26
2.89
1.03
0.99

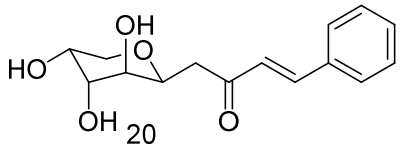

TD130-01-03_CARBON_01 - D-Galactose.esp
Normalized Intensity
Chemical Shift (ppm)
201.16
144.82
136.04
131.66
130.04
129.53
127.55
80.19
78.06
76.32
72.31
70.88
62.57
49.64
49.42
49.21
49.00
48.79
48.58
48.36
44.36

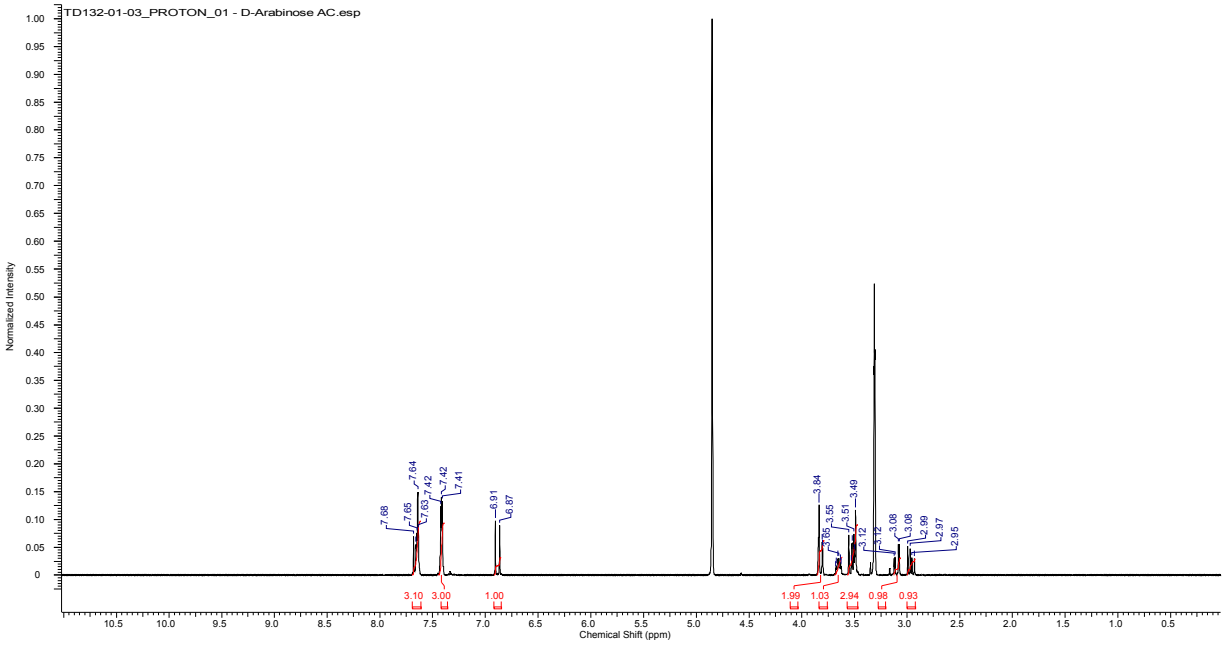

OH
O
HO
OH
O

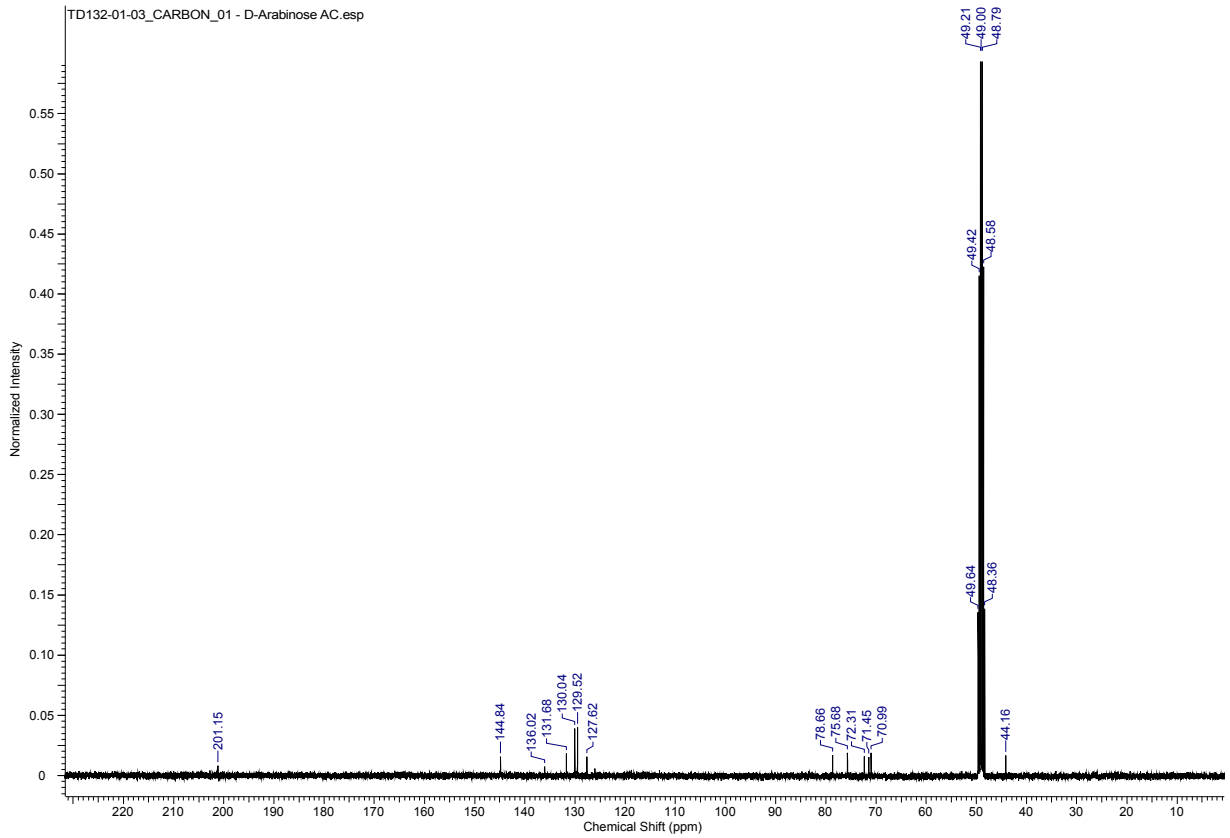
19


TD131-01-03_PROTON_01 - L-Arabinose AC.esp
Normalized Intensity
Chemical Shift (ppm)
7.68
7.65
7.64
7.42
7.41
7.41
6.91
6.86
3.84
3.65
3.51
3.49
3.31
3.08
3.08
2.99
2.97
3.13
3.01
1.00
2.02
1.01
2.92
1.00
0.96


TD131-01-03_CARBON_01 - L-Arabinose AC.esp
Normalized Intensity
Chemical Shift (ppm)
201.15
144.84
136.01
131.68
130.04
129.52
127.62
78.65
75.68
72.31
71.44
70.99
49.64
49.42
49.21
49.00
48.78
48.57
48.36
44.15


OH
HO
O
OH
O
20


TD132-01-03_PROTON_01 - D-Arabinose AC.esp
Normalized Intensity
Chemical Shift (ppm)
7.68
7.65
7.64
7.63
7.42
7.42
7.41
6.91
6.67
3.84
3.55
3.51
3.49
3.12
3.08
3.08
2.99
2.97
2.95
3.10
3.00
1.00
1.99
1.03
2.94
0.98
0.93


TD132-01-03_CARBON_01 - D-Arabinose AC.esp
Normalized Intensity
Chemical Shift (ppm)
49.21
49.00
48.79
49.42
48.58
49.64
48.36
201.15
144.84
136.02
131.68
130.04
129.52
127.62
78.66
75.68
72.31
71.45
70.99
44.16