

Supplementary Information

Efficient synthesis of glycosylamines in solventless conditions promoted by mechanical milling

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Experimental Section

General

Chemical reagents were purchased from Sigma-Aldrich or Acros (France) and solvents (analytical grade) such as methanol, diethyl ether, absolute ethanol and dichloromethane were provided by Prolabo. All reagent and solvents were used without any further purification. Reactions were conducted in a high speed vibrational ball-milling (Spex 8000M) into stainless steel jar (volume: 60 mL) with stainless steel balls (diameter: 13.0 mm). Syntheses were monitored by thin-layer chromatography (TLC) on silica gel 60 F₂₅₄ plates (Merck) and detection was conducted by charring with cerium molybdate reagent. **FTIR spectra were recorded on a Shimadzu FTIR-8400S spectrometer using ATR technique.** ¹H and ¹³C RMN spectra were recorded on a Bruker 300WB spectrometer at 300 and 75 MHz respectively. Assignments of ¹H and ¹³C signals were made using correlated spectroscopy (COSY) and heteronuclear single quantum correlation (HSQC). High-resolution electrospray mass spectra (HRMS) in the positive ion mode were obtained on a Q-ToF Ultima Global hybrid quadrupole/ time-of-flight instrument.

General procedure for the preparation of compounds **1a-1d**, **1g**, **1n-1p** and **1s-1u**

Liquid amine (6.0 mmol, 1.1 eq.) and SiO₂ (1 g) were mixed in a mortar with a pestle to obtain a powdery mixture. The as-obtained mixture was then introduced with the sugar (5.5 mmol, 1 eq.) into a stainless steel jar and 3 stainless steel balls were added. The jar was placed in a vibrational ball-milling and shaken at 30 Hz. After 1.5h milling, the reaction mixture was scratched off the vessel and dissolved in a minimum of methanol. The solution was filtered through a pad of silica gel and washed with methanol to remove the grinding auxiliary. After evaporation under vacuum, the resulting solid was subsequently triturated with diethyl ether and filtered to afford the corresponding glycosylamine.

General procedure for the preparation of compounds **1e-1f**, **2a**, **3a** and **4a**.

Amine (6.0 mmol, 1.1 eq.) and sugar (5.5 mmol, 1 eq.) were mixed in a mortar with a pestle and introduced with 3 stainless steel balls into a stainless steel jar. The jar was placed in a vibrational ball-milling and shaken at 30 Hz. After 1.5h milling, the reaction mixture was scratched off the vessel and triturated with diethyl ether and filtered to afford the corresponding glycosylamine.

General procedure for the preparation of compounds **1w**

p-Hydroxyaniline (6.0 mmol, 1.1 eq.) and L-rhamnose (5.5 mmol, 1 eq.) were mixed in a mortar with a pestle and introduced with 3 stainless steel balls into a stainless steel jar. The jar was placed in a vibrational ball-milling and shaken at 30 Hz. After 1.5h milling, the reaction mixture was directly purified by column chromatography on silica gel using CH₂Cl₂/MeOH to furnish the compound **1w**.

General procedure for the preparation of compounds **1h-1m, 1v and 1z**

Amine (5.5 mmol, 1 eq.) and sugar (5.5 mmol, 1 eq. for the synthesis of **1h-1j, 1v** or 11 mmol, 2 eq. for the synthesis of **1k-1m, 1z**) were mixed in a mortar with a pestle, then introduced with 3 stainless steel balls into a stainless steel jar. The jar was placed in a vibrational ball-milling and shaken at 30 Hz. After 1.5h to 3h milling, the reaction mixture was scratched off the vessel and dissolved in methanol. Finally, the solution was dried by evaporation under high vacuum to give the corresponding glycosylamine.

General procedure for the preparation of compounds **1q-1r**

Amino-ester hydrochloride (3.2 mmol, 1 eq.), potassium carbonate (3.2 mmol, 1 eq.) and SiO₂ (0.5 g) were mixed in a mortar with a pestle to obtain a powdery mixture. The as-obtained mixture was then introduced with 3 stainless steel balls into a stainless steel jar. The jar was placed in a vibrational ball-milling and shaken at 30 Hz for 2h. The sugar (3.2 mmol, 1.1 eq.) and SiO₂ (0.5 g) were then added in the jar and the mixture was continuously milled for 1.5h. The reaction mixture was directly purified by column chromatography on silica gel using CH₂Cl₂/MeOH to furnish the corresponding glycosylamine.

Characterization data

N-octyl-L-rhamnosylamine (**1a**)

White solid, yield: 94%. Ratio α/β : 93/7. IR (ATR) ν (cm⁻¹): 3380-3221, 2932, 2849, 1462-1430, 1112, 1095-1070, 1046, 762-722. α isomer: ¹H NMR (CD₃OD): δ 4.04 (d, 1H, *J*=1.1 Hz, H-1) ; 3.78 (dd, 1H, *J*=3.3, 1.1 Hz, H-2) ; 3.40 (dd, 1H, *J*=9.2, 3.3 Hz, H-3) ; 3.28 (t, 1H, *J*=9.2 Hz, H-4) ; 3.18 (dq, 1H, *J*=9.2, 6.0 Hz, H-5) ; 2.91 (ddd, 1H, *J*=11.6, 8.4, 6.4 Hz, -HN-CH₂-) ; 2.59 (ddd, 1H, *J*= 11.6, 8.4, 5.9 Hz, -HN-CH₂-) ; 1.61-1.41 (m, 2H, -NH₂-CH₂-CH₂-) ; 1.40-1.29 (m, 10H, -CH₂-CH₂-) ; 1.28 (d, 3H, *J*=5.9 Hz, H-6) ; 0.90 (t, 3H, *J*=6.8 Hz, CH₃-CH₂-). ¹³C NMR (CD₃OD): δ 88.4 (C-1), 76.0 (C-3), 74.6 (C-5), 74.1 (C-4), 73.1 (C-2), 46.3 (-HN-CH₂-), 33.0, 31.0, 30.6, 30.4, 28.4, 23.7 (-CH₂-CH₂-), 18.1 (C-6), 14.4 (CH₃-CH₂-). HRMS [M+H]⁺ calcd for C₁₄H₂₉NO₄: *m/z* 276.2175, found *m/z* 276.2182.

***N*-butyl-L-rhamnosylamine (1b)**

White solid, yield: 91%. Ratio α/β : 94/6. IR (ATR) ν (cm⁻¹): 3355-3221, 2964, 2858, 1454-1394, 1068, 1003, 897, 769-727. α isomer: ¹H NMR (CD₃OD): δ 4.04 (d, 1H, $J=1.1$ Hz, H-1) ; 3.78 (dd, 1H, $J=3.3, 1.1$ Hz, H-2) ; 3.40 (dd, 1H, $J=9.2, 3.3$ Hz, H-3) ; 3.28 (t, 1H, $J=9.2$ Hz, H-4) ; 3.17 (dq, $J=9.1, 6.0$ Hz, 1H, H-5) ; 2.93 (ddd, 1H, $J=11.6, 8.3, 6.5$ Hz, -HN-CH₂-) ; 2.59 (ddd, 1H, $J=11.6, 8.4, 5.9$ Hz, -HN-CH₂-) ; 1.58-1.30 (m, 4H, -CH₂-CH₂-) ; 1.27 (d, 3H, $J=6.0$ Hz, H-6) ; 0.94 (t, 3H, $J=7.2$ Hz, CH₃-CH₂). ¹³C NMR (CD₃OD): δ 88.4 (C-1), 76.0 (C-3), 74.7 (C-5), 74.1 (C-4), 73.1 (C-2), 46.0 (-HN-CH₂-), 33.2 (-HN-CH₂-CH₂-), 21.5 (-CH₂-CH₃), 18.1 (C-6), 14.3 (CH₃-CH₂). HRMS [M+H]⁺ calcd for C₁₀H₂₁NO₄: m/z 220.1549, found m/z 220.1546.

***N*-hexyl-L-rhamnosylamine (1c)**

White solid, yield: 89%. Ratio α/β : 91/9. IR (ATR) ν (cm⁻¹): 3306-3185, 2928, 2856, 1458-1419, 1092, 1055, 905, 771. α isomer: ¹H NMR (CD₃OD): δ 4.04 (d, 1H, $J=1.1$ Hz, H-1) ; 3.78 (dd, 1H, $J=3.3, 1.1$ Hz, H-2) ; 3.40 (dd, 1H, $J=9.2, 3.3$ Hz, H-3) ; 3.28 (t, 1H, $J=9.2$ Hz, H-4) ; 3.17 (dq, 1H, $J=9.1, 6.0$ Hz, H-5) ; 2.91 (ddd, 1H, $J=11.6, 8.5, 6.5$ Hz, -HN-CH₂-) ; 2.59 (ddd, 1H, $J=11.4, 8.4, 5.9$ Hz, -HN-CH₂-) ; 1.61-1.41 (m, 2H, -NH₂-CH₂-CH₂-) ; 1.41-1.29 (m, 6H, -CH₂-CH₂-) ; 1.27 (d, 3H, $J=5.9$ Hz, H-6) ; 0.91 (t, 3H, $J=6.8$ Hz, CH₃-CH₂-). ¹³C NMR (CD₃OD): δ 88.4 (C-1), 76.0 (C-3), 74.7 (C-5), 74.2 (C-4), 73.1 (C-2), 46.3 (-HN-CH₂-), 32.9, 31.0, 28.1, 23.7 (-CH₂-CH₂-), 18.1 (C-6), 14.4 (CH₃-CH₂-). HRMS [M+H]⁺ calcd for C₁₂H₂₅NO₄: m/z 248.1862, found m/z 248.1864.

***N*-decyl-L-rhamnosylamine (1d)**

White solid, yield: 95%. Ratio α/β : 82/18. IR (ATR) ν (cm⁻¹): 3443-3102, 2925, 2853, 1442-1416, 1089, 1066, 769, 620. α isomer: ¹H NMR (DMSO-*d*₆): δ 4.61 (d, 1H, $J=4.8$ Hz, OH-4) ; 4.52 (m, 2H, OH-2 + OH-3) ; 3.88 (s, 1H, H-1) ; 3.55-3.49 (m, 1H, H-2) ; 3.18 (m, 1H, H-3) ; 3.12-2.91 (m, 2H, H-4 + H-5) ; 2.86-2.71 (m, 1H, -HN-CH₂-) ; 2.56-2.35 (m, 1H, -HN-CH₂-) ; 2.08 (bs, 1H, -NH-) ; 1.44-1.16 (m, 18H, -CH₂-CH₂-) ; 1.12 (d, 3H, $J=5.8$ Hz, H-6) ; 0.85 (t, 3H, $J=6.4$ Hz, CH₃-CH₂-). ¹³C NMR (DMSO-*d*₆): δ 87.2 (C-1), 74.4 (C-3), 72.5, 72.4 (2s, C-4, C-5), 71.6 (C-2), 44.9 (-HN-CH₂-), 31.3, 30.0, 29.0, 28.7, 26.8, 22.1 (-CH₂-CH₂-), 18.1 (C-6), 13.9 (CH₃-CH₂-). HRMS [M+H]⁺ calcd for C₁₆H₃₃NO₄: m/z 304.2488, found m/z 304.2496.

***N*-dodecyl-L-rhamnosylamine (1e)**

White solid, yield: 98%. Ratio α/β : 91/9. IR (ATR) ν (cm⁻¹): 3450-3176, 2922, 2854, 1452, 1145, 1064, 873. α isomer: ¹H NMR (CD₃OD): δ 4.04 (d, 1H, $J=0.9$ Hz, H-1) ; 3.78 (dd, 1H, $J=3.3, 1.1$ Hz, H-2) ; 3.40 (dd, 1H, $J=9.2, 3.3$ Hz, H-3) ; 3.28 (t, 1H, $J=9.2$ Hz, H-4) ; 3.17 (dq, 1H, $J=9.1, 6.0$ Hz, H-5) ; 2.91 (ddd, 1H, $J=11.6, 8.4, 6.5$ Hz, -HN-CH₂-) ; 2.59 (ddd, 1H, $J=11.6, 8.4, 6.0$ Hz, -HN-CH₂-) ; 1.60-1.39 (m, 2H, -HN-CH₂-CH₂-) ; 1.39-1.19 (m, 18H, -

CH₂-CH₂-); 1.27 (d, 3H, *J*=6.1 Hz, H-6) ; 0.90 (t, 3H, *J*=6.8 Hz, **CH**₃-CH₂-). ¹³C NMR (CD₃OD): δ 88.4 (C-1), 76.0 (C-3), 74.6 (C-5), 74.2 (C-4), 73.1 (C-2), 46.3 (-HN-**CH**₂-), 33.0, 31.0, 30.7, 30.6, 30.4, 28.4, 23.7 (-CH₂-CH₂-), 18.1 (C-6), 14.4 (**CH**₃-CH₂-). HRMS [M+H]⁺ calcd for C₁₈H₃₇NO₄: *m/z* 332.2801, found *m/z* 332.2816.

***N*-hexadecyl-L-rhamnosylamine (1f)**

White solid, yield: 99%. Ratio α/β: 88/12. IR (ATR) ν (cm⁻¹): 3450-3100, 2945, 2827, 1442, 1090, 1062, 650. α isomer: ¹H NMR (CD₃OD) : δ 4.04 (d, 1H, *J*=0.9 Hz, H-1), 3.78 (dd, 1H, *J*=3.3, 1.1 Hz, H-2), 3.40 (dd, 1H, *J*=9.2, 3.4 Hz, H-3) ; 3.28 (t, 1H, *J*=9.2 Hz, H-4), 3.17 (dq, 1H, *J*=9.1, 6.0 Hz, H-5), 2.90 (ddd, 1H, *J*=11.6, 8.1, 6.6 Hz, -HN-**CH**₂-), 2.62 (ddd, 1H, *J*=11.6, 8.0, 6.5 Hz, -HN-**CH**₂-), 1.59-1.41 (m, 2H, -HN-CH₂-**CH**₂-), 1.39-1.22 (m, 29H, -CH₂-CH₂- + H-6), 0.89 (t, 3H, *J*=6.7 Hz, **CH**₃-CH₂-). ¹³C NMR (CD₃OD): δ 88.6(C-1), 76.1 (C-3), 74.6 (C-5), 74.3 (C-4), 73.2 (C-2), 46.4 (-HN-**CH**₂-), 33.0, 31.1, 30.7, 30.5, 30.3 28.3, 23.6 (-CH₂-CH₂-), 18.1 (C-6), 14.3 (**CH**₃-CH₂-). HRMS [M+H]⁺ calcd for C₂₂H₄₅NO₄: *m/z* 388.3427, found *m/z* 388.3428.

***N*-(L-rhamnosyl)-octyl-1,8-diamine (1h)**

White solid, yield: 96%. Ratio α/β: 87/13. IR (ATR) ν (cm⁻¹): 3531-3179, 2931, 2859, 1662, 1557, 1454-1416, 1139, 1073, 768, 662. α isomer: ¹H NMR (DMSO-*d*₆): δ 3.88 (s, 1H, H-1) ; 3.70-3.15 (bs, 6H, -OH (3)+-NH-+-NH₂) ; 3.54 (d, 1H, *J*=2.9 Hz, H-2) ; 3.20 (dd, 1H, *J*=8.8, 3.3 Hz, H-3) ; 3.16-2.92 (m, 2H, H-4+H-5) ; 2.85-2.71 (m, 1H, -HN-**CH**₂-) ; 2.51-2.41 (m, 3H, -HN-**CH**₂, -**CH**₂-NH₂) ; 1.45-1.20 (m, 12H, -CH₂-CH₂-) ; 1.12 (d, 3H, *J*=5.9 Hz, H-6). ¹³C NMR (DMSO-*d*₆): δ 87.2 (C-1), 74.5 (C-3), 72.6 (C-5), 72.4 (C-4), 71.6 (C-2), 44.9 (-HN-**CH**₂-), 41.7 (-**CH**₂-NH₂), 33.3, 30.0, 29.1, 26.9, 26.5 (-CH₂-CH₂-), 18.2 (C-6). HRMS [M+H]⁺ calcd for C₁₄H₃₁N₂O₄: *m/z* 291.2239, found *m/z* 291.2270

***N*-(L-rhamnosyl)-decyl-1,10-diamine (1i)**

White solid, yield: 95%. Ratio α/β: 91/9. IR (ATR) ν (cm⁻¹): 3501-3147, 2920, 2845, 1471, 1120, 1018, 784. α isomer: ¹H NMR (CD₃OD): δ 4.00 (s, 1H, H-1) ; 3.75 (d, 1H, *J*=2.6 Hz, H-2) ; 3.36 (dd, 1H, *J*=9.2, 3.1 Hz, H-3) ; 3.31-3.20 (m, 1H, H-4) ; 3.20-3.05 (m, 1H, H-5) ; 2.95-2.80 (m, 1H, -HN-**CH**₂-) ; 2.64-2.50 (m, 3H, -HN-**CH**₂- + -**CH**₂-NH₂) ; 1.55-1.36 (m, 4H, -**CH**₂-CH₂-NH- + -**CH**₂-CH₂-NH₂) ; 1.36-1.19 (m, 12H, -CH₂-CH₂-) ; 1.24 (d, 3H, *J*=6.1 Hz, H-6). ¹³C NMR (CD₃OD): δ 88.4 (C-1), 76.0 (C-3), 74.6 (C-5), 74.1 (C-4), 73.1 (C-2), 46.3 (-HN-**CH**₂-), 42.6 (-**CH**₂-NH₂), 33.9, 31.0, 30.6, 28.4, 28.0 (-CH₂-CH₂-), 18.2 (C-6). HRMS [M+H]⁺ calcd for C₁₆H₃₄N₂O₄: *m/z* 319.2552, found *m/z* 319.2581

***N*-(L-rhamnosyl)-dodecyl-1,12-diamine (1j)**

Pale yellow solid, yield: 96%. Ratio α/β: 93/7. IR (ATR) ν (cm⁻¹): 3389-3196, 2917, 2849, 1652, 1575, 1464, 1088, 1058, 859, 782-684. α isomer: ¹H NMR (CD₃OD): δ 4.04 (d, 1H,

$J=1.1$ Hz, H-1) ; 3.78 (dd, 1H, $J=3.3, 0.9$ Hz, H-2) ; 3.40 (dd, 1H, $J=9.2, 3.3$ Hz, H-3) ; 3.28 (t, 1H, $J=9.2$ Hz, H-4) ; 3.18 (dq, 1H, $J=9.2, 5.9$ Hz, H-5) ; 2.91 (ddd, 1H, $J=11.6, 8.4, 6.6$ Hz, -HN-**CH₂-**) ; 2.66-2.50 (m, 3H, -HN-**CH₂-** + -**CH₂-NH₂**) ; 1.57-1.40 (m, 4H, -**CH₂-CH₂-NH-** + -**CH₂-CH₂-NH₂**) ; 1.40-1.29 (m, 16H, -CH₂-CH₂-) ; 1.27 (d, 3H, $J=5.9$ Hz, H-6). ¹³C NMR (CD₃OD): δ 88.4 (C-1), 76.0 (C-3), 74.7 (C-5), 74.2 (C-4), 73.1 (C-2), 46.3 (-HN-**CH₂-**), 42.5 (-HN-**CH₂-**), 33.7, 31.0, 30.7, 30.6, 28.4, 28.0 (-CH₂-CH₂-), 18.1 (C-6). HRMS [M+H]⁺ calcd for C₁₈H₃₈N₂O₄: m/z 347.2910, found m/z 347.2903.

***N,N'*-bis-(L-rhamnosyl)-octyl-1,8-diamine (1k)**

White solid, yield: 95%. Ratio α,α / β,β : 82/18. IR (ATR) ν (cm⁻¹): 3419-3088, 2928, 2856, 1447, 1101, 1080, 901, 769-638. α,α isomer: ¹H NMR (DMSO-*d*₆): δ 4.61 (d, 2H, $J=4.9$ Hz, OH-4) ; 4.53 (d, 2H, $J=5.0$ Hz, OH-2), 4.50 (d, 2H, $J=5.7$ Hz, OH-3), 3.89 (s, 2H, H-1), 3.53 (t, 2H, $J=3.7$ Hz, H-2), 3.23-3.15 (m, 2H, H-3) ; 3.14-2.93 (m, 4H, H-4, H-5), 2.86-2.72 (m, 2H, -HN-**CH₂-**) ; 2.52-2.38 (m, 2H, -HN-**CH₂-**) ; 2.08 (s, 2H, -NH-) ; 1.45-1.30 (m, 4H, -**CH₂-CH₂-NH-**), 1.30-1.20 (m, 8H, -CH₂-CH₂-) ; 1.12 (d, 6H, $J=6.0$ Hz, H-6). ¹³C NMR (DMSO-*d*₆): δ 87.2 (C-1), 74.4 (C-3), 72.5 (C-5), 72.4 (C-4), 71.6 (C-2), 44.9 (-HN-**CH₂-**), 30.0, 29.0, 26.8 (-CH₂-CH₂-), 18.1 (C-6). HRMS [M+H]⁺ calcd for C₂₀H₄₀N₂O₈: m/z 437.2866, found m/z 437.2872.

***N,N'*-bis-(L-rhamnosyl)-decyl-1,10-diamine (1l)**

White solid, yield: 98%. Ratio α,α / β,β : 84/16. IR (ATR) ν (cm⁻¹): 3477-3203, 2920, 2849, 1462, 1142, 1111-1057, 860, 769-638. α,α isomer: ¹H NMR (DMSO-*d*₆): δ 4.61 (d, 2H, $J=4.6$ Hz, OH-4) ; 4.54-4.49 (m, 4H, OH-2 + OH-3) ; 3.88 (s, 2H, H-1), 3.60-3.49 (m, 2H, H-2), 3.18-3.14 (m, 2H, H-3) ; 3.10-2.93 (m, 4H, H-4, H-5), 2.84-2.70 (m, 2H, -HN-**CH₂-**) ; 2.51-2.36 (m, 2H, -HN-**CH₂-**) ; 2.08 (s, 2H, -NH-) ; 1.42-1.30 (m, 4H, -**CH₂-CH₂-NH-**), 1.29-1.19 (m, 12H, -CH₂-CH₂-), 1.12 (d, 6H, $J=5.8$ Hz, H-6). ¹³C NMR (DMSO-*d*₆): δ 87.2 (C-1), 74.4 (C-3), 72.5 (C-5), 72.4 (C-4), 71.6 (C-2), 44.9 (-HN-**CH₂-**), 30.0, 29.0, 26.8 (-CH₂-CH₂-), 18.1 (C-6). HRMS [M+H]⁺ calcd for C₂₂H₄₄N₂O₈: m/z 465.3179, found m/z 465.3176.

***N,N'*-bis-(L-rhamnosyl)-dodecyl-1,12-diamine (1m)**

White solid, yield: 98%. Ratio α,α / β,β : 89/11. IR (ATR) ν (cm⁻¹): 3512-3051, 2911, 2842, 1560, 1468, 1101, 1086, 1053, 852, 715. α,α isomer: ¹H NMR (CD₃OD): δ 4.04 (d, 2H, $J=1.1$ Hz, H-1) ; 3.78 (dd, 2H, $J=3.3, 1.1$ Hz, H-2) ; 3.40 (dd, 2H, $J=9.2, 3.5$ Hz, H-3) ; 3.28 (t, 2H, $J=9.0$ Hz, H-4) ; 3.17 (dq, 2H, $J=9.1, 6.0$ Hz, H-5) ; 2.91 (ddd, 2H, $J=11.6, 8.4, 6.5$ Hz, -HN-**CH₂-**) ; 2.59 (ddd, 2H, $J=11.6, 8.3, 5.9$ Hz, -HN-**CH₂-**) ; 1.60-1.42 (m, 4H, -**CH₂-CH₂-NH-**) ; 1.41-1.29 (m, 16H, -CH₂-CH₂-) 1.28 (d, 6H, $J=5.9$ Hz, H-6). ¹³C NMR (CD₃OD): δ 88.4 (C-1), 76.0 (C-3), 74.7 (C-5), 74.2 (C-4), 73.1 (C-2), 46.3 (-HN-**CH₂-**), 31.0, 30.7, 30.6, 28.4 (-CH₂-CH₂-), 18.1 (C-6). HRMS [M+H]⁺ calcd for C₂₄H₄₈N₂O₈: m/z 493.3513, found m/z 493.3492.

***N*-propargyl-*L*-rhamnosylamine (1n)**

Yellow solid, yield: 96%. Ratio α/β : 88/12. IR (ATR) ν (cm⁻¹): 3575-3104, 2976, 2833, 2125, 1448, 1141, 1055, 854, 707-628. α isomer: ¹H NMR (CD₃OD): δ 4.18 (d, 1H, $J=1.1$ Hz, H-1); 3.79 (dd, 1H, $J=3.4, 1.0$ Hz, H-2); 3.61 (dd, 1H, $J=16.4, 2.6$ Hz, -HN-CH₂-); 3.52 (dd, 1H, $J=16.4, 2.6$ Hz, -HN-CH₂-); 3.42 (dd, 1H, $J=9.2, 3.3$ Hz, H-3); 3.29 (t, 1H, $J=9.2$ Hz, H-4); 3.18 (dq, 1H $J=9.2, 6.0$ Hz, H-5); 2.57 (t, 1H, $J=2.5$ Hz, HC \equiv C-); 1.28 (d, 3H, $J=6.1$ Hz, H-6). ¹³C NMR (CD₃OD): δ 86.7 (C-1), 82.1 (HC \equiv C-); 75.8 (C-3), 74.6 (C-5), 74.0 (C-4), 72.8 (C-2 + HC \equiv C-), 34.6 (-HN-CH₂-), 18.1 (C-6). HRMS [M+H]⁺ calcd for C₉H₁₅NO₄: m/z 202.1035, found m/z 202.1070.

***N*-allyl-*L*-rhamnosylamine (1o)**

Light yellow solid, yield: 91%. Ratio α/β : 90/10. IR (ATR) ν (cm⁻¹): 3468-3085, 2971, 2864, 1651, 1453, 1061, 1035, 860, 772. α isomer: ¹H NMR (CD₃OD): δ 6.01-5.80 (m, 1H, -HC=CH₂); 5.24-5.04 (m, 2H, -HC=CH₂); 4.05 (d, 1H, $J=1.1$ Hz, H-1); 3.78 (dd, 1H, $J=3.4, 1.1$ Hz, H-2); 3.54-3.45 (m, 1H, -HN-CH₂-); 3.39 (dd, 1H, $J=9.2, 3.3$ Hz, H-3); 3.36-3.24 (m, 2H, H-4 + -HN-CH₂-); 3.16 (dq, 1H, $J=9.1, 6.1$ Hz, H-5); 1.28 (d, 3H, $J=5.9$ Hz, H-6). ¹³C NMR (CD₃OD): δ 137.5 (-HC=CH₂), 116.8 (-HC=CH₂), 87.6 (C-1), 76.0 (C-3), 74.6 (C-5), 74.1 (C-4), 73.1 (C-2), 48.7 (-HN-CH₂-), 18.1 (C-6). HRMS [M+H]⁺ calcd for C₉H₁₇NO₄: m/z 204.1223, found m/z 204.1230

***N*-(3-hydroxypropyl)-*L*-rhamnosylamine (1p)**

Yellow solid, yield: 92%. Ratio α/β : 92/8. IR (ATR) ν (cm⁻¹): 3381-3281, 2955, 2901, 1492, 1145, 1087-1028, 856, 711. α isomer: ¹H NMR (CD₃OD): δ 4.04 (d, 1H, $J=0.9$ Hz, H-1); 3.77 (dd, 1H, $J=3.3, 1.1$ Hz, H-2); 3.62 (t, 2H, $J=6.2$ Hz, -CH₂-OH); 3.40 (dd, 1H, $J=9.2, 3.3$ Hz, H-3); 3.27 (t, 1H, $J=9.0$ Hz, H-4); 3.17 (dq, 1H, $J=9.1, 6.0$ Hz, H-5); 3.02 (dt, 1H, $J=12.0; 7.3$ Hz, -HN-CH₂-); 2.70 (dt, 1H, $J=11.8, 7.1$ Hz, -HN-CH₂-); 1.77-1.62 (m, 2H, -CH₂-CH₂-OH); 1.27 (d, 3H, $J=5.9$ Hz, H-6). ¹³C NMR (CD₃OD): δ 88.5 (C-1), 75.9 (C-3), 74.6 (C-5), 74.1 (C-4), 73.1 (C-2), 61.4 (-CH₂-OH), 43.6 (-HN-CH₂-), 33.7 (-CH₂-CH₂-OH), 18.1 (C-6). HRMS [M+H]⁺ calcd for C₉H₁₉NO₅: m/z 222.1328, found m/z 222.1336.

***N*-(alanine methyl ester)-*L*-rhamnosylamine (1q)**

Yellow oil, yield: 68%. Ratio α/β : 89/11. IR (ATR) ν (cm⁻¹): 3430-3029, 2950, 2753, 1736, 1589, 1452, 1222, 1041, 842, 670. α isomer: ¹H NMR (CD₃OD): δ 4.10 (d, 1H, $J=1.1$ Hz, H-1); 3.78 (dd, 1H, $J=3.3, 1.1$ Hz, H-2); 3.69 (s, 3H, -CO-OCH₃); 3.55 (q, 1H, $J=7.0$ Hz, -HN-CH-); 3.39 (dd, 1H, $J=9.3, 3.4$ Hz, H-3); 3.25 (t, 1H, $J=9.2$ Hz, H-4); 3.13 (dq, 1H, $J=9.2; 6.0$ Hz, H-5); 1.26 (d, 3H, $J=7.0$ Hz, CH₃-CH-); 1.21 (d, 3H, $J=5.9$ Hz, H-6). ¹³C NMR (CD₃OD): δ 178.0 (-CO-OCH₃), 87.4 (C-1), 75.9 (C-3), 74.5 (C-5), 74.0 (C-4), 72.9 (C-2), 54.4 (-HN-CH-), 52.3 (-CO-OCH₃), 18.8 (CH₃-CH-), 18.0 (C-6).). HRMS [M+Na]⁺ calcd for C₁₀H₁₉NO₆: m/z 272.1099, found m/z 272.1104.

***N*-(leucine methyl ester)-L-rhamnosylamine (1r)**

Pale yellow oil, yield: 70%. Ratio α/β : 90/10. IR (ATR) ν (cm⁻¹): 3555-3200, 2924, 2854, 1747, 1525, 1446, 1228, 1080, 744. α isomer: ¹H NMR (CD₃OD): δ 4.05 (s, 1H, H-1) ; 3.79 (dd, 1H, $J=3.3, 0.9$ Hz, H-2) ; 3.66 (s, 3H, -CO-OCH₃) ; 3.41-3.33 (m, 2H, H-3, -HN-CH-) ; 3.24 (t, 1H, $J=9.2$ Hz, H-4) ; 3.11 (dq, 1H, $J=9.1, 6.0$ Hz, H-5) ; 1.78-1.56 (m, 1H, (CH₃)₂CH-) ; 1.43 (t, 2H, $J=7.4$ Hz, (CH₃)₂CH-CH₂-) ; 1.18 (d, 3H, $J=6.0$ Hz, H-6) ; 0.93-0.89 (2d, 6H, $J=6.6$ Hz, (CH₃)₂CH-). ¹³C NMR (CD₃OD) : δ 178.6 (-CO-OCH₃), 88.9 (C-1), 75.9 (C-3), 74.3 (C-5), 74.0 (C-4), 72.9 (C-2), 58.8 (-HN-CH-), 52.1 (-CO-OCH₃-), 44.1 (-CH-CH₂-), 25.9 ((CH₃)₂CH-), 23.0, 22.8 ((CH₃)₂CH-), 18.0 (C-6). HRMS [M+H]⁺ calcd for C₁₃H₂₅NO₆: m/z 292.17510, found m/z 292.17546.

***N*-benzyl-L-rhamnosylamine (1s)**

Yellow solid, yield: 94%. Ratio α/β : 90/10. IR (ATR) ν (cm⁻¹): 3356-3090, 2975, 2860, 1606, 1570, 1452, 1101-1022, 754-669. α isomer: ¹H NMR (CD₃OD): δ 7.39-7.26 (m, 5H, H_{ar}), 4.07 (d, 1H, $J=12.7$ Hz, -HN-CH₂-), 4.04 (d, 1H, $J=0.6$ Hz H-1), 3.85 (d, 1H, $J=12.9$ Hz, -HN-CH₂-), 3.82 (m, 1H, H-2), 3.46-3.35 (m, 2H, H-3 + H-4) ; 3.18 (dq, 1H, $J=8.8, 6.1$ Hz, H-5), 1.35 (d, 3H, $J=6.1$ Hz, H-6). ¹³C NMR (CD₃OD): δ 140.9 (-CH₂-C_{ar}), 129.6, 129.4, 128.1 (CH_{ar}), 87.5 (C-1), 76.0 (C-3), 74.6 (C-5), 74.2 (C-4), 73.1 (C-2), 49.9 (-HN-CH₂-), 18.1 (C-6). HRMS [M+H]⁺ calcd for C₁₃H₁₉NO₄: m/z 254.1378, found m/z 254.1386.

***N*-(2,4-dimethoxybenzyl)-L-rhamnosylamine (1t)**

Yellow solid, yield: 94%. IR (ATR) ν (cm⁻¹): 3482-3098, 2925, 2847, 1597, 1513, 1454, 1262, 1141. α isomer (major isomer): ¹H NMR (CDCl₃): δ 6.87-6.73 (m, 3H, H_{ar}), 4.28 (bs, 4H, -OH (3) + -NH-), 3.95 (d, 1H, $J=12.5$ Hz, -HN-CH₂-), 3.93 (s, 1H, H-1), 3.87-3.83 (m, 1H, H-2), 3.82-3.81 (2s, 6H, -OCH₃), 3.71 (d, 1H, $J=12.7$ Hz, -HN-CH₂-), 3.36-3.29 (m, 2H, H-3 and H-4) ; 3.15-3.03 (m, 1H, H-5), 1.26 (d, 3H, $J=6.1$ Hz, H-6). ¹³C NMR (CDCl₃): δ 149.0, 148.4, (CO_{ar}), 131.8 (-CH₂-C_{ar}), 121.2, 112.3, 111.2 (CH_{ar}), 86.2 (C-1), 74.9 (C-3), 73.2 (C-5), 72.8 (C-4), 71.9 (C-2), 56.0 (-OCH₃), 49.1 (-HN-CH₂-), 17.9 (C-6). HRMS [M+H]⁺ calcd for C₁₅H₂₃NO₆: m/z 314.1559, found m/z 314.1598

***N*-phenyl-L-rhamnosylamine (1u)**

Brown solid, yield: 99%. IR (ATR) ν (cm⁻¹): 3473-3354, 2989, 2850, 1600, 1504, 1112, 1070, 885, 746, 692. α isomer (major isomer): ¹H NMR (CD₃OD): δ 7.16-6.67 (m, 5H, H_{ar}), 4.83 (m, 1H, H-1) ; 3.91 (dd, 1H, $J=3.4, 1.0$ Hz, H-2), 3.54-3.49 (m, 1H, H-3) ; 3.37-3.30 (m, 2H, H-4 + H-5), 1.27 (d, 3H, $J=5.9$ Hz, H-6). ¹³C NMR (CD₃OD): δ 147.1 (CN_{ar}), 130.0, 119.5, 115.1 (CH_{ar}), 83.4 (C-1), 75.9 (C-3), 74.1 (C-5), 74.0 (C-4), 73.0 (C-2), 18.0 (C-6). HRMS [M+H]⁺ calcd for C₁₂H₁₇NO₄: m/z 240.1191, found m/z 240.1230

***N*-(4-aminophenyl)-L-rhamnosylamine (1v)**

Brown solid, yield: 90%. IR (ATR) ν (cm⁻¹): 3600-3034, 2906-2764, 1616, 1506, 1448-1363, 1046, 823, 684. Ratio α/β : 85/15. α isomer : ¹H NMR (CD₃OD): δ 6.68-6.59 (m, 4H, H_{ar}) ; 4.72 (m, 1H, H-1) ; 3.90-3.88 (m, 1H, H-2) ; 3.50-3.47 (m, 1H, H-3) ; 3.33-3.30 (m, 2H, H-4 and H-5) ; 1.26-1.20 (m, 3H, H-6). ¹³C NMR (CD₃OD): δ 140.2 (CN_{ar}), 118.5 (CH_{ar}), 84.6 (C-1), 76.0 (C-3), 74.2 (C-5), 74.1 (C-4), 73.2 (C-2), 18.0 (C-6). LRMS [M+H]⁺ calcd for C₁₂H₁₈N₂O₄: m/z 255.3, found m/z 255.2.

***N*-(4-hydroxyphenyl)-L-rhamnosylamine (1w)**

Pale yellow solid, yield: 59%. IR (ATR) ν (cm⁻¹): 3506-3288, 2920, 2855, 1595, 1511, 1455, 1260, 1083, 995, 883, 697. α isomer (major isomer): ¹H NMR (CD₃OD): δ 6.76-6.42 (m, 4H, H_{ar}), 4.74 (m, 1H, H-1),), 3.95 (m, 1H, H-2), 3.56-3.52 (m, 1H, H-3) ; 3.37-3.31 (m, 2H, H-4 and H-5), 1.30 (m, 3H, H-6). ¹³C NMR (CD₃OD): δ 151.0 (CO_{ar}), 139.9 (CN_{ar}), 116.8, 116.7 (CH_{ar}), 84.5 (C-1), 75.9 (C-3), 74.1 (C-5), 74.0 (C-4), 73.1 (C-2), 18.0 (C-6). HRMS [M+H]⁺ calcd for C₁₂H₁₇NO₅: m/z 256.1172, found m/z 256.1179.

***N,N'*-bis-(L-rhamnosyl)-phenyl-1,4-diamine (1z)**

Brown solid, yield: 95%. IR (ATR) ν (cm⁻¹): 3600-3035, 2976-2850, 1625, 1518, 1442, 1078, 891, 688. α,α (major isomer) :¹H NMR (DMSO-*d*₆): δ 6.55 (s, 4H, H_{ar}) ; 5.01 (d, 2H, *J*=10.7 Hz, -NH-) ; 4.77 (d, 2H, *J*=5.1 Hz, OH-2) ; 4.70 (d, 2H, *J*=4.6 Hz, OH-4) ; 4.65 (s, 2H, H-1) ; 4.62 (d, 2H, *J*=4.6 Hz, OH-3) ; 3.72-3.62 (m, 2H, H-2) ; 3.32-3.17 (m, 2H, H-3) ; 3.23-3.05 (m, 4H, H-4 and H-5), 1.09 (d, 6H, *J*=5.3 Hz, H-6). ¹³C NMR (DMSO-*d*₆): δ 138.1 (CN_{ar}), 114.9 (CH_{ar}), 82.1 (C-1), 74.3 (C-3), 72.4-72.2 (2s, C-5 and C-4), 71.4 (C-2), 18.1 (C-6). LRMS [M+Na]⁺ calcd for C₁₈H₂₈N₂O₈: m/z 423.4, found m/z 423.1.

***N*-dodecyl-D-glucosylamine (2a)**

White solid, yield: 97%. IR (ATR) ν (cm⁻¹): 3371-3136, 2914, 2847, 1514, 1467, 1078, 1014, 895, 719-607. β (major isomer): ¹H NMR (DMSO-*d*₆): δ 4.81 (d, 1H, *J*=4.5 Hz, OH-3); 4.77 (d, 1H, *J*=4.8 Hz, OH-4); 4.42 (d, 1H, *J*=4.2 Hz, OH-2); 4.32 (t, 1H, *J*=5.8 Hz, OH-6); 3.67-3.61 (m, 2H, H-1 + H-6a) ; 3.44-3.36 (m, 1H, H-6b) ; 3.11 (dt, 1H, *J*=8.7, 4.4 Hz, H-3); 3.02-2.98 (m, 2H, H-4 + H-5) ; 2.95 (td, 1H, *J*=8.6; 4.1 Hz, H-2) ; 2.80-2.70 (m, 1H, -HN-**CH**₂-) ; 2.52-2.44 (m, 1H, -HN-**CH**₂-) ; 2.14 (bs, 1H, NH) ; 1.42-1.32 (m, 2H, + -**CH**₂-CH₂-NH-) ; 1.29-1.17 (m, 18H, -CH₂-CH₂-) ; 0.85 (t, 3H, *J*=6.5 Hz, **CH**₃-CH₂-). ¹³C NMR (DMSO-*d*₆): δ 90.8 (C-1), 77.6 (C-3), 77.4 (C-5), 73.5 (C-2), 70.6 (C-4), 61.4 (C-6), 45.5 (-HN-**CH**₂-), 31.3, 30.0, 29.0, 28.7, 26.8, 22.1 (-CH₂-CH₂-), 13.9 (**CH**₃-CH₂-). HRMS [M+H]⁺ calcd for C₁₈H₃₇NO₅ : m/z 348.2750, found m/z 348.2758.

***N*-dodecyl-D-galactosylamine (3a)**

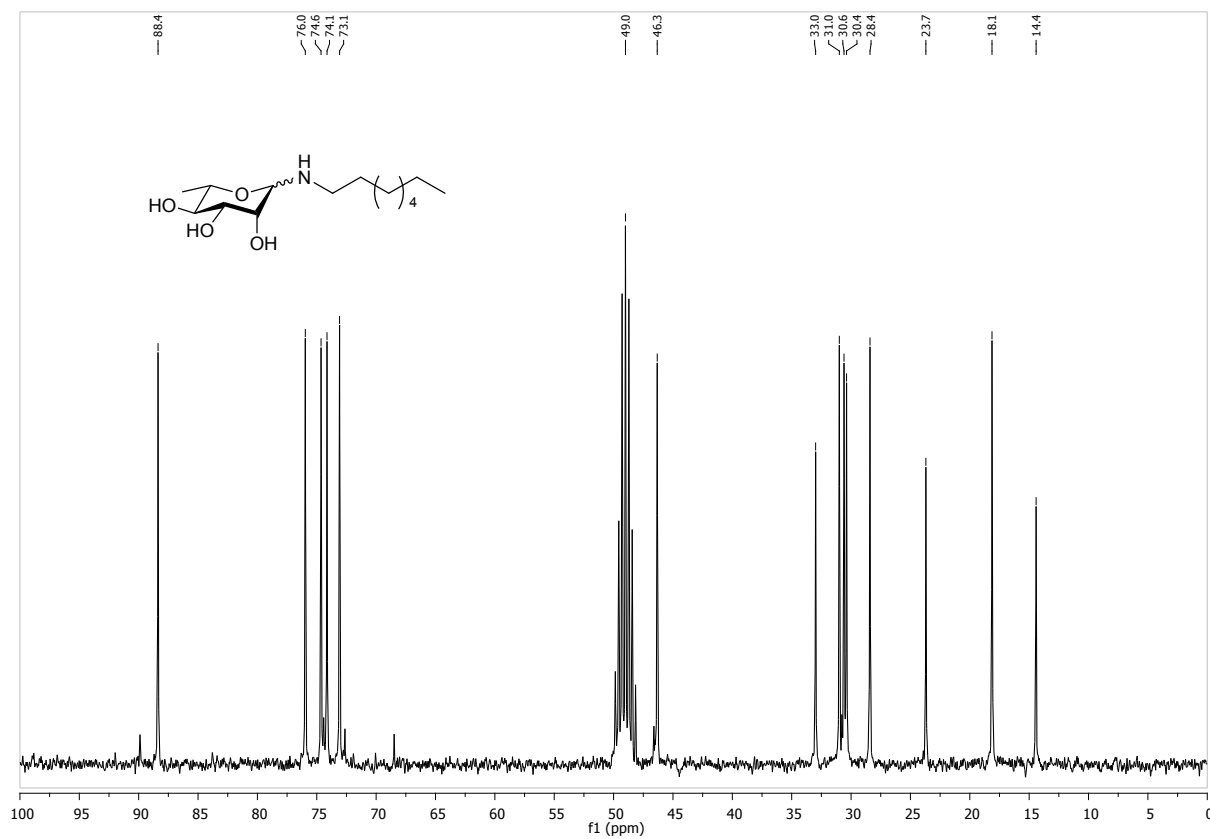
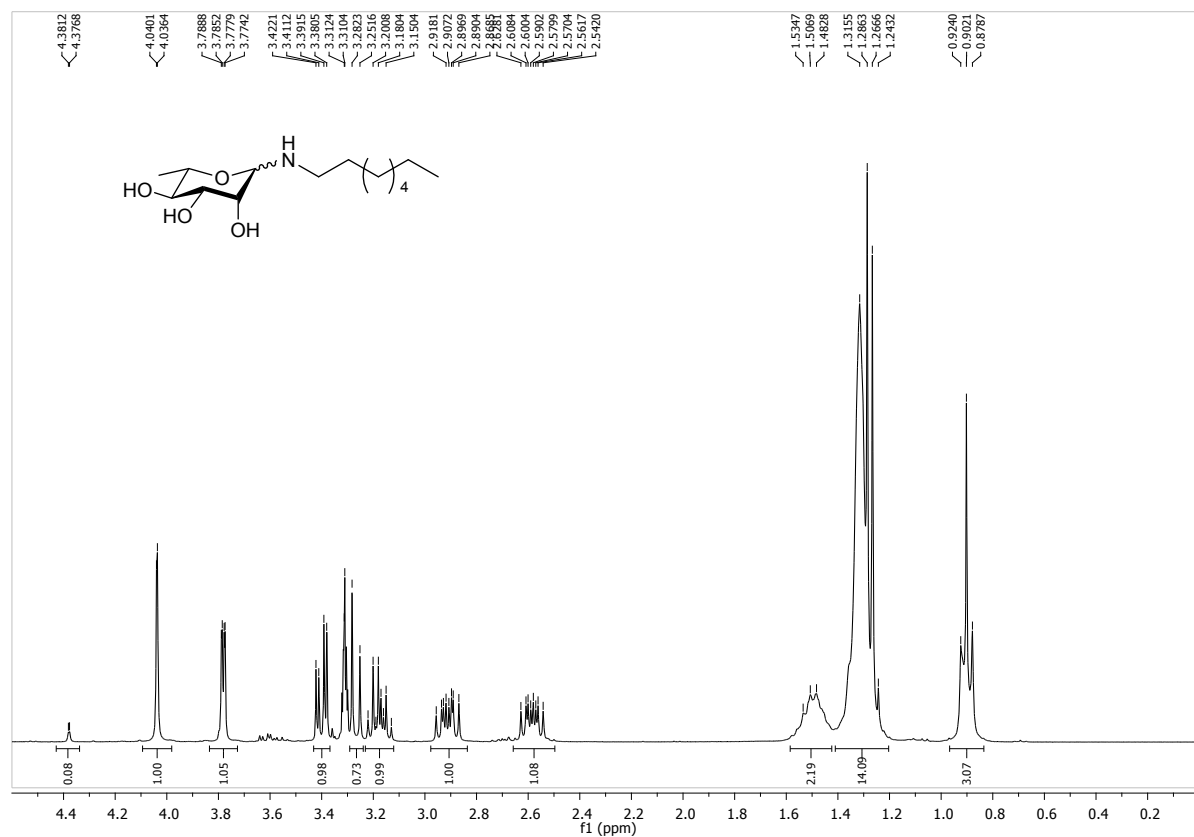
White solid, yield: 94%. IR (ATR) ν (cm⁻¹): 3439-3246, 2914, 2847, 1460, 1122, 1050, 866, 673. β (major isomer): ¹H NMR (CD₃OD): δ 3.85 (dd, 1H, $J=9.7, 3.6$ Hz, H-4), 3.78 (d, 1H, $J=8.4$ Hz, H-1) 3.73-3.65 (m, 2H, H-6a, H-6b), 3.49-3.31 (m, 3H, H-2, H-3, H-5), 2.97-2.79 (m, 1H, -HN-CH₂-), 2.68-2.52 (m, 1H, -HN-CH₂-), 1.58-1.41 (m, 2H, -CH₂-CH₂-NH-); 1.39-1.17 (m, 18H, -CH₂-CH₂-), 0.90 (t, 3H, $J=6.6$ Hz, CH₃-CH₂-). ¹³C NMR (CD₃OD): δ 92.5 (C-1), 77.5-75.8 (2s, C-3, C-5), 72.5 (C-2), 70.7 (C-4), 62.7 (C-6), 47.2 (-HN-CH₂-), 33.1, 31.2, 30.8, 30.5, 28.4, 23.7 (-CH₂-CH₂-), 14.4 (CH₃-CH₂-). HRMS [M+H]⁺ calcd for C₁₈H₃₇NO₅: m/z 348.2750, found m/z 348.2757.

***N*-dodecyl-D-(4-*O*- α -D-glucopyranosyl)-glucosylamine (4a)**

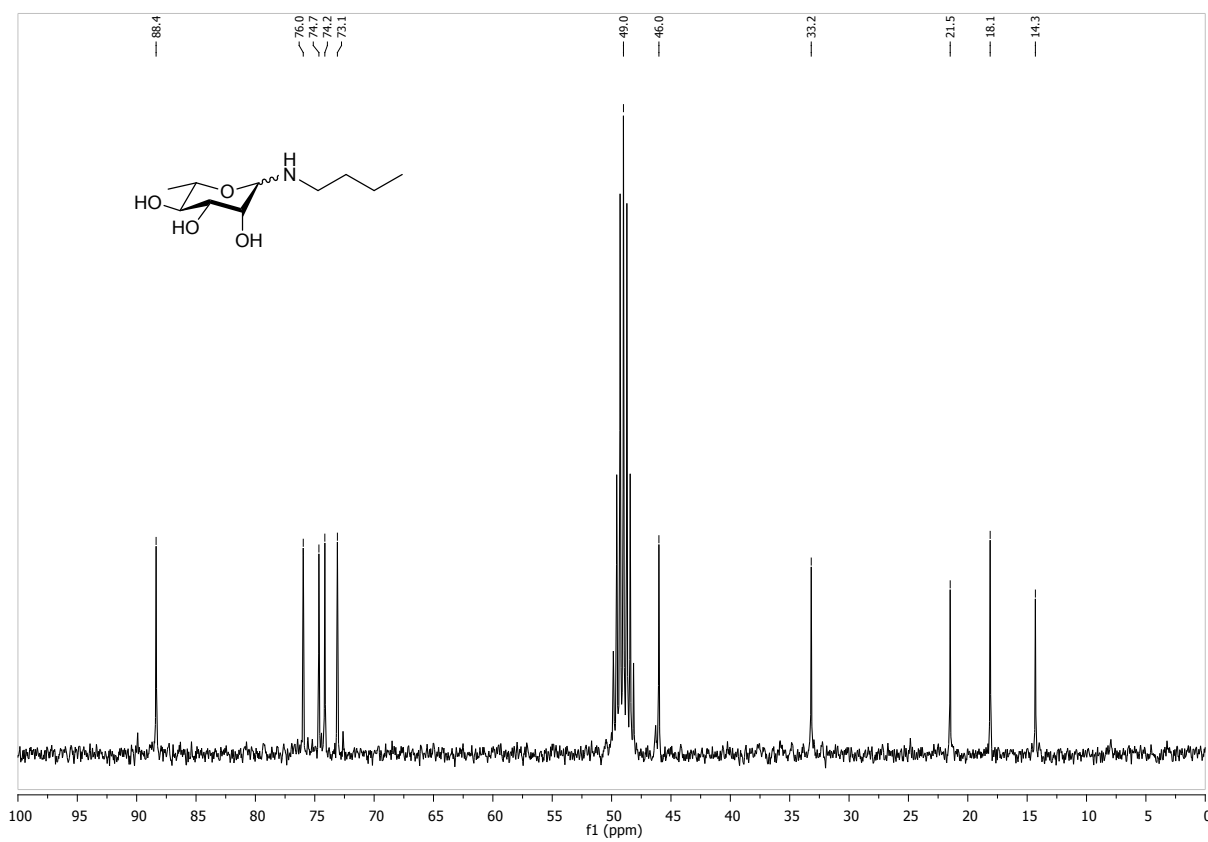
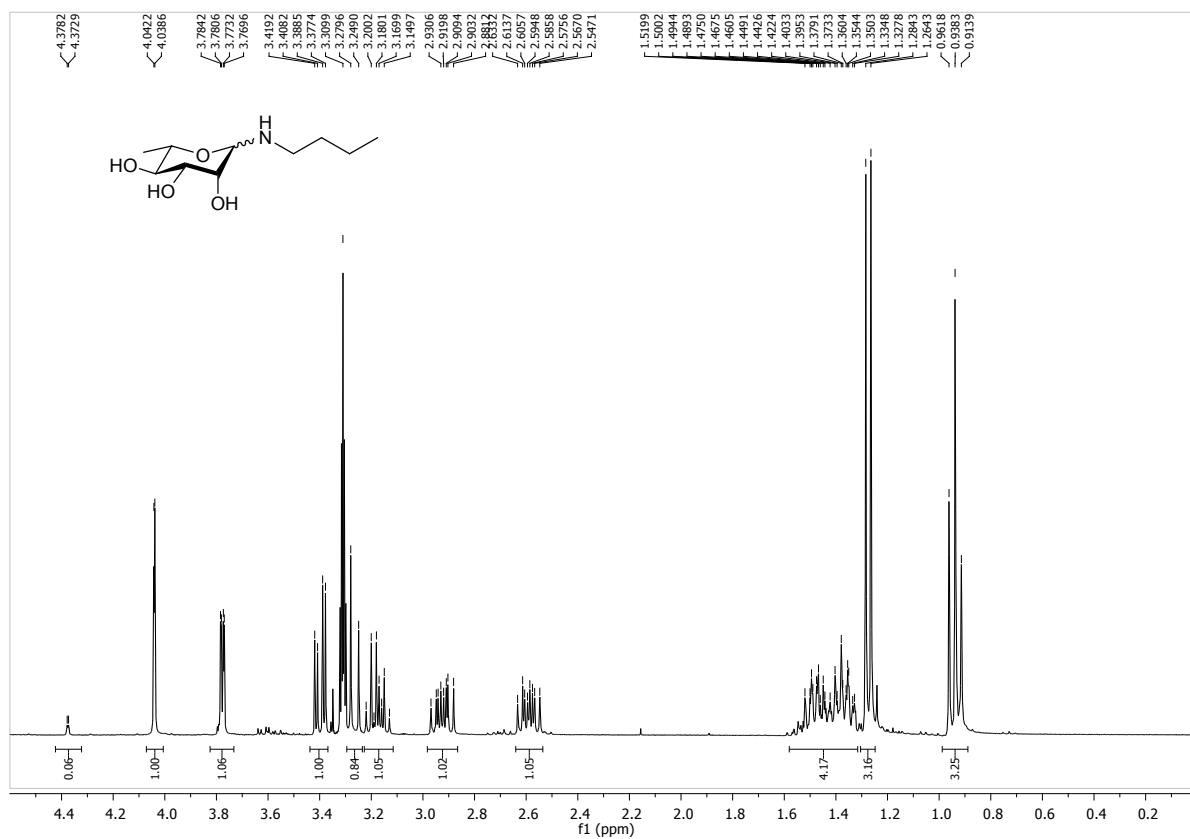
White solid, yield: 99%. Ratio α/β : 20/80. IR (ATR) ν (cm⁻¹): 3573-3084, 2925, 2856, 1558, 1448, 1122-1004, 862, 717. β isomer: ¹H NMR (CD₃OD): δ 5.15 (d, 1H, $J=3.1$ Hz, H-1'); 3.97-3.74 (m, 4H, H-1 + H-6 or H-6' (3)); 3.66-3.47 (m, 5H, H-3, H-3', H-4, H-5', H-6 (or H-6')); 3.44 (dd, 1H, $J=9.6, 3.6$ Hz, H-2'); 3.38-3.17 (m, 2H, H-4', H-5); 3.12 (t, 1H, $J=8.8$ Hz, H-2); 2.96-2.84 (m, 1H, -HN-CH₂-); 2.72-2.55 (m, 1H, -HN-CH₂-); 1.59-1.42 (m, 2H, -CH₂-CH₂-NH-); 1.41-1.21 (m, 18H, -CH₂-CH₂-); 0.90 (t, 3H, $J=6.5$ Hz, CH₃-CH₂-). ¹³C NMR (CD₃OD): δ 102.9 (C-1'), 91.8 (C-1), 81.6 (C-4), 78.7 (C-3 or C-3'), 77.6 (C-5), 75.1 (C-3 or C-3'), 74.7 (C-5'), 74.6 (C-2), 74.2 (C-2'), 71.5 (C-4'), 62.7-62.4 (2s, C-6, C-6'), 47.2 (-HN-CH₂-), 33.1, 31.1, 30.7, 30.4, 28.1, 23.7 (-CH₂-CH₂-), 14.4 (CH₃-CH₂-). HRMS [M+H]⁺ calcd for C₂₄H₄₇NO₁₀: m/z 510.3249, found m/z 510.3257

^1H and ^{13}C spectra

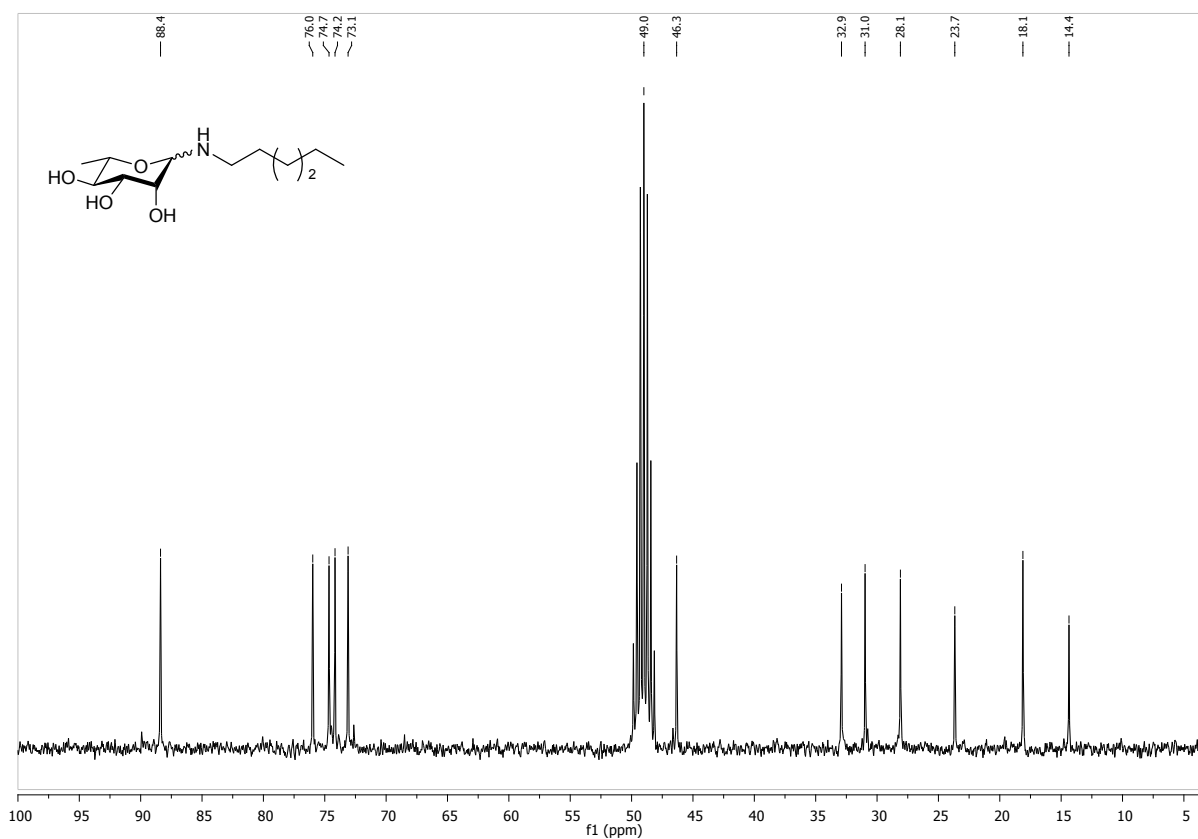
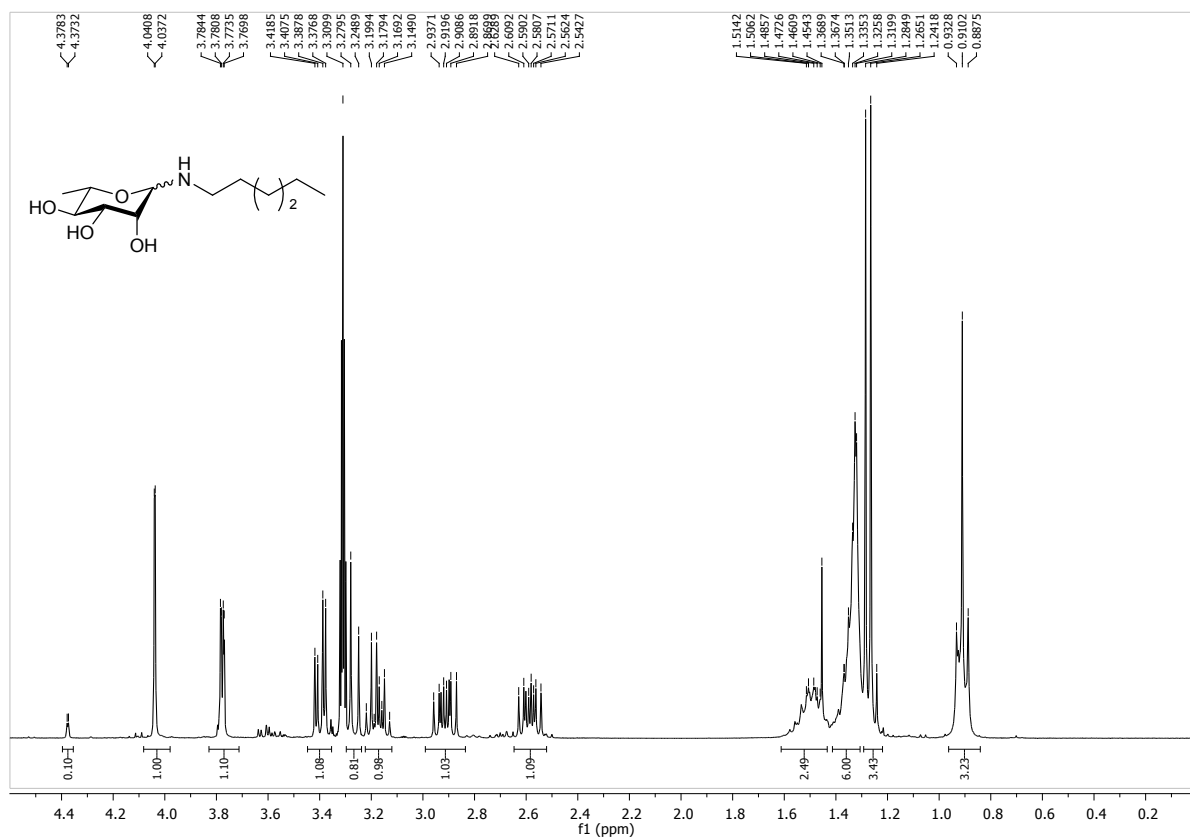
N-octyl-L-rhamnosylamine (1a)



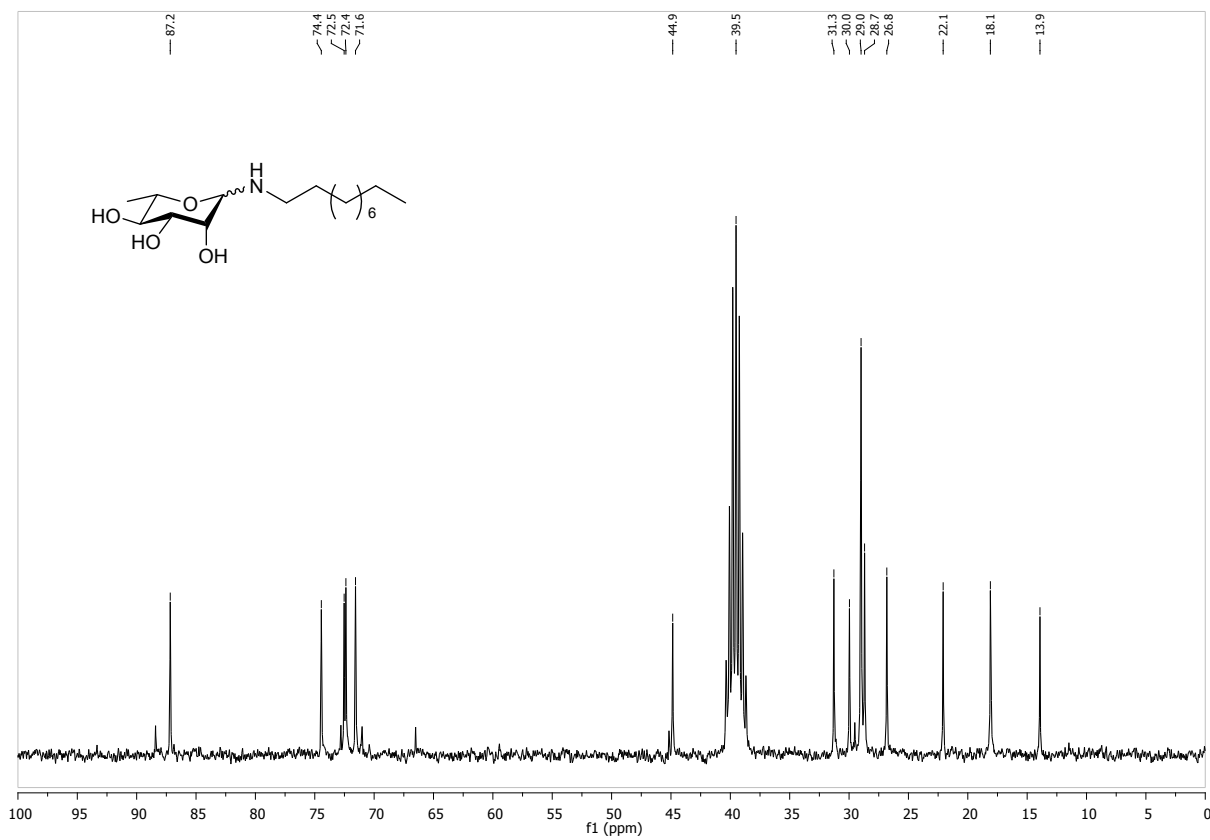
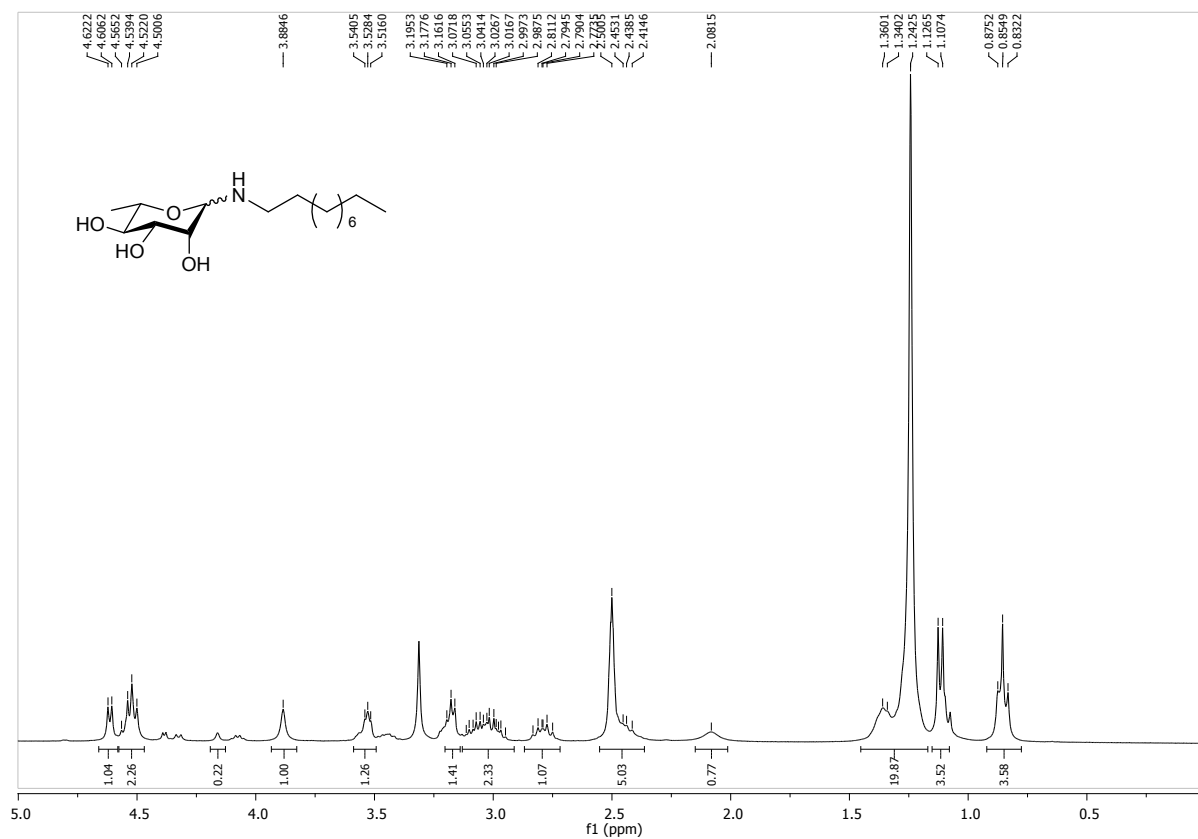
N-butyl-L-rhamnosylamine (1b)



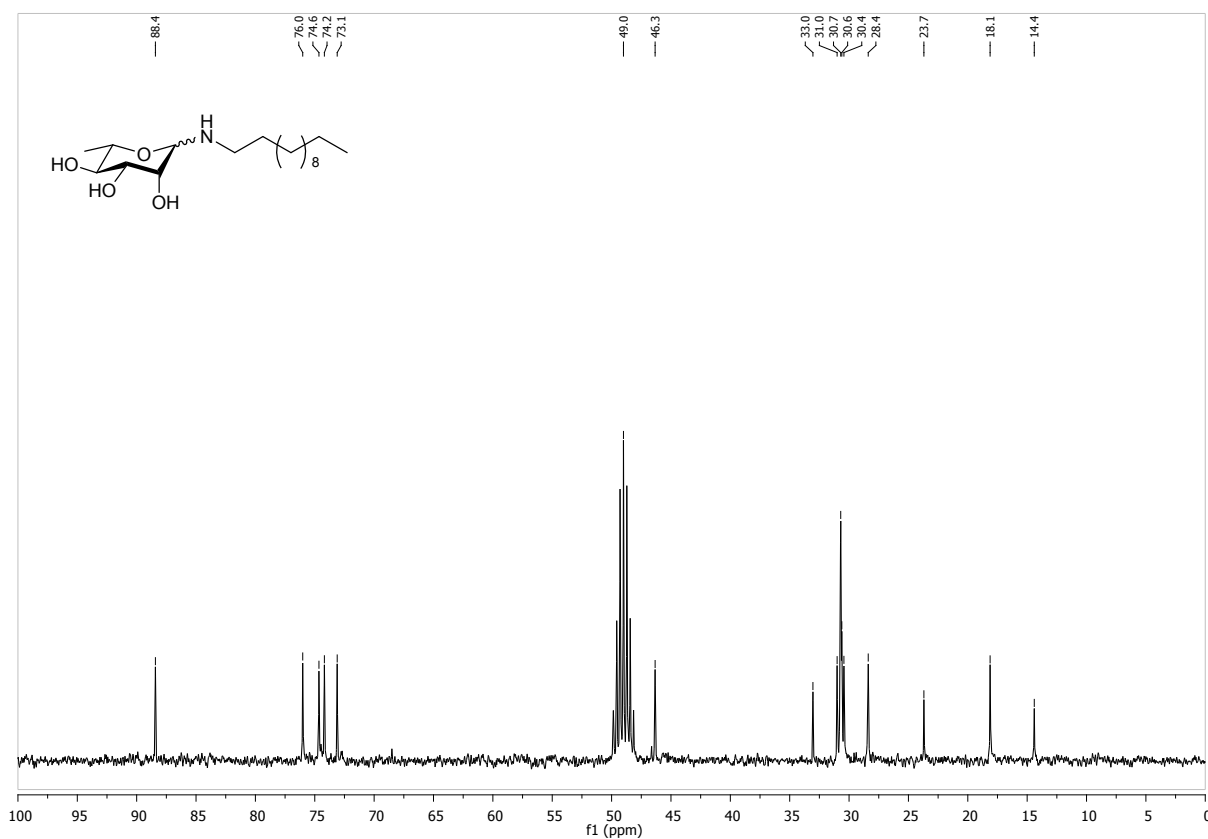
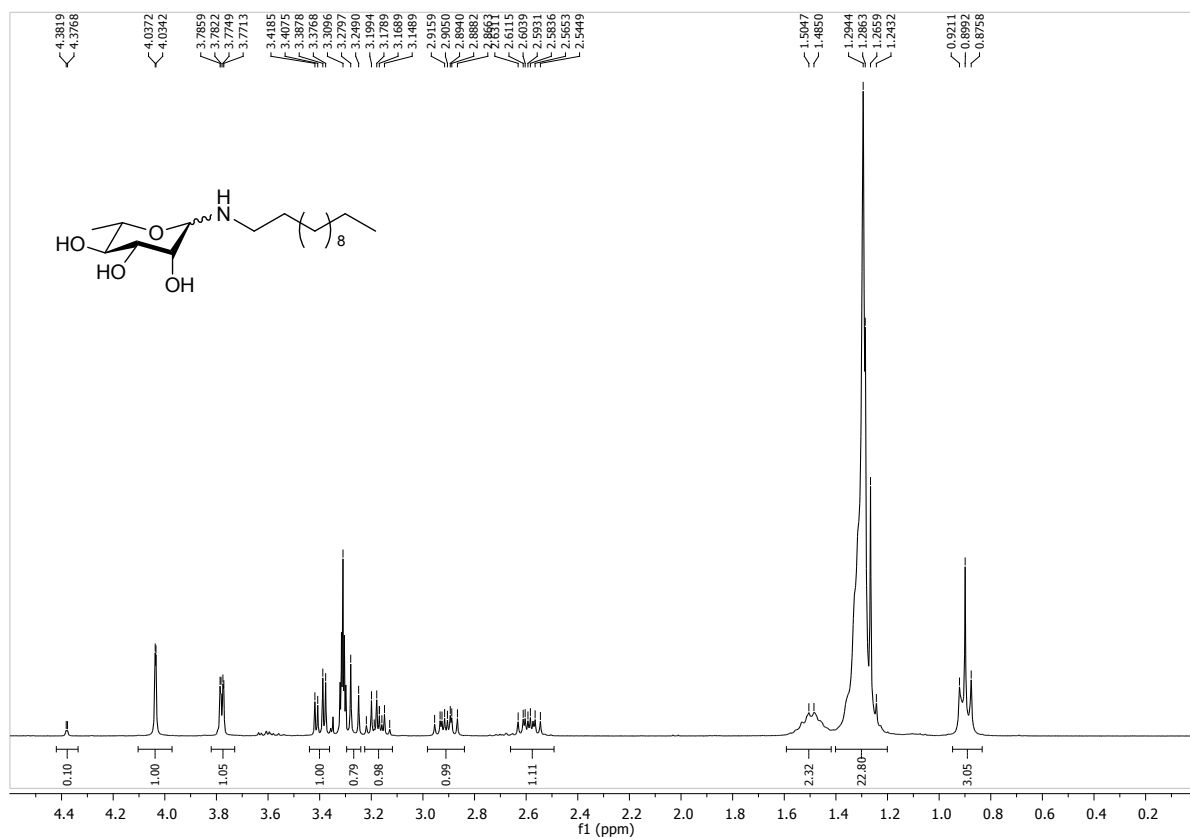
N-hexyl-L-rhamnosylamine (1c)



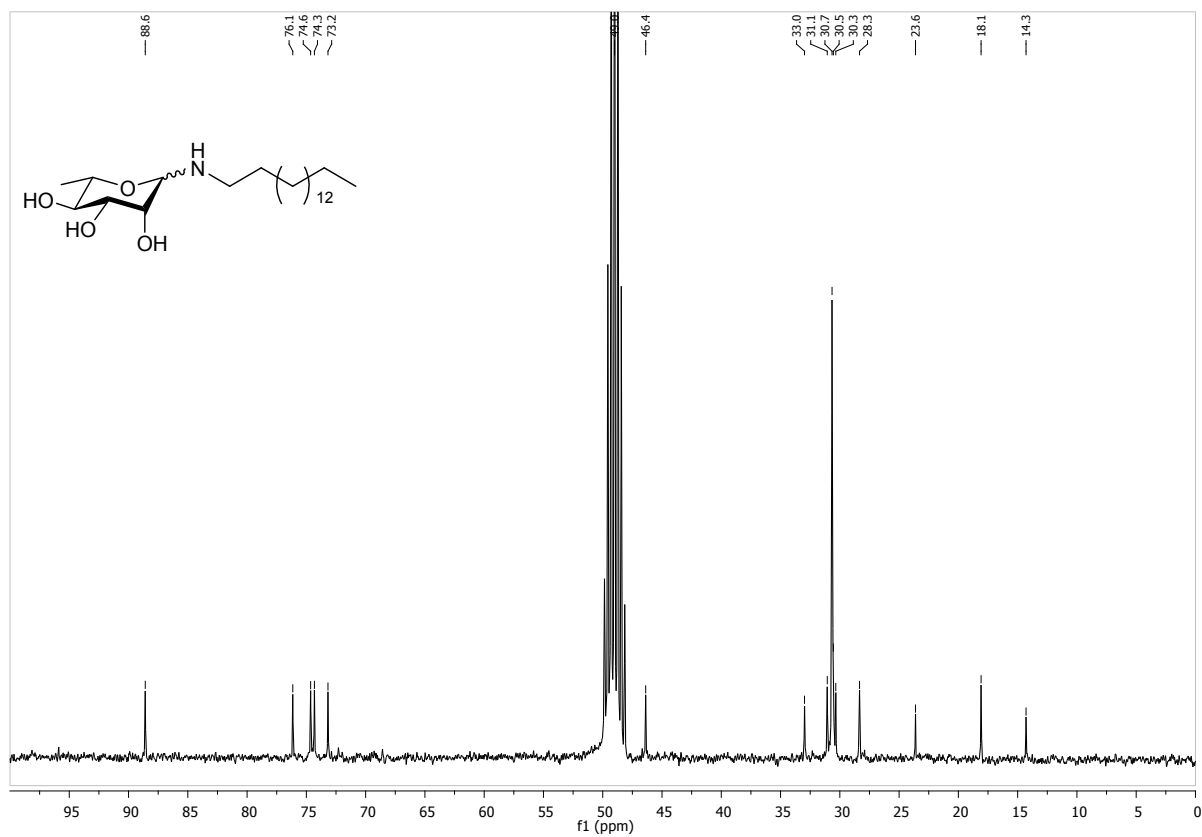
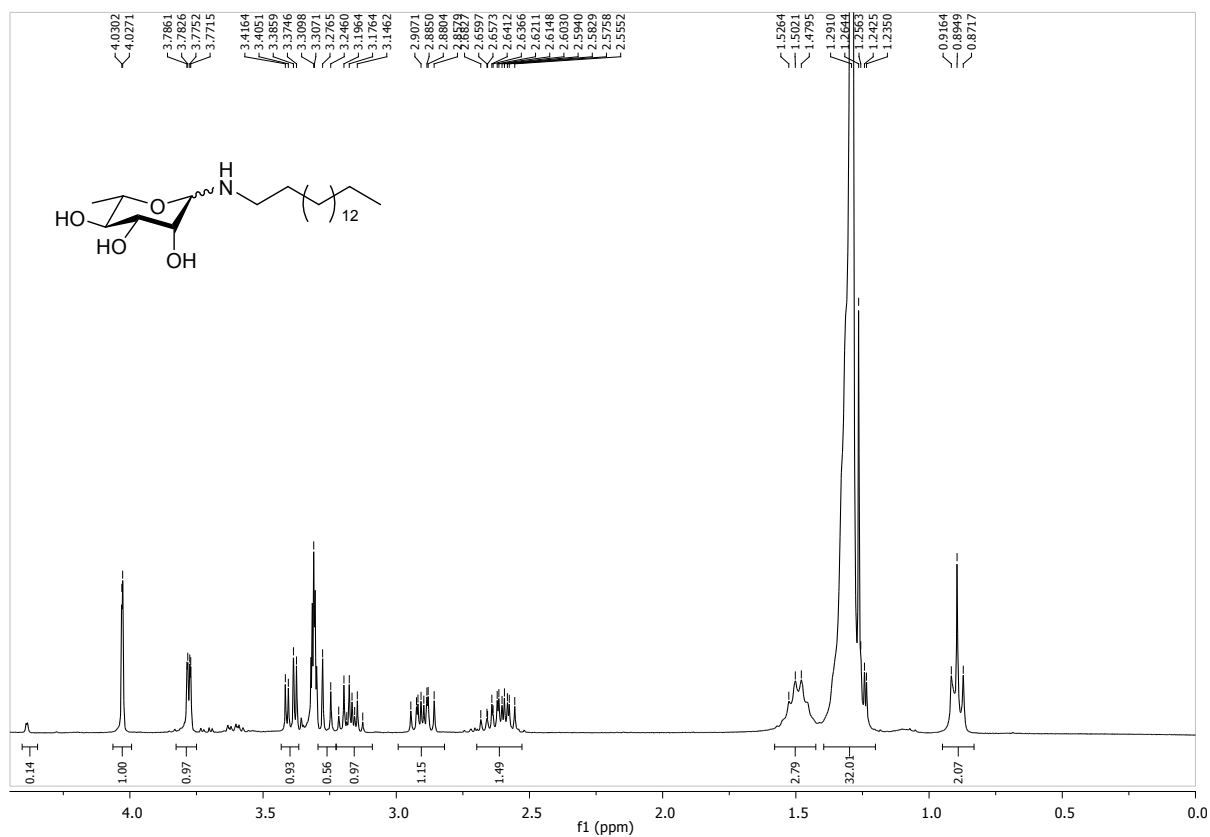
N-decyl-L-rhamnosylamine (1d)



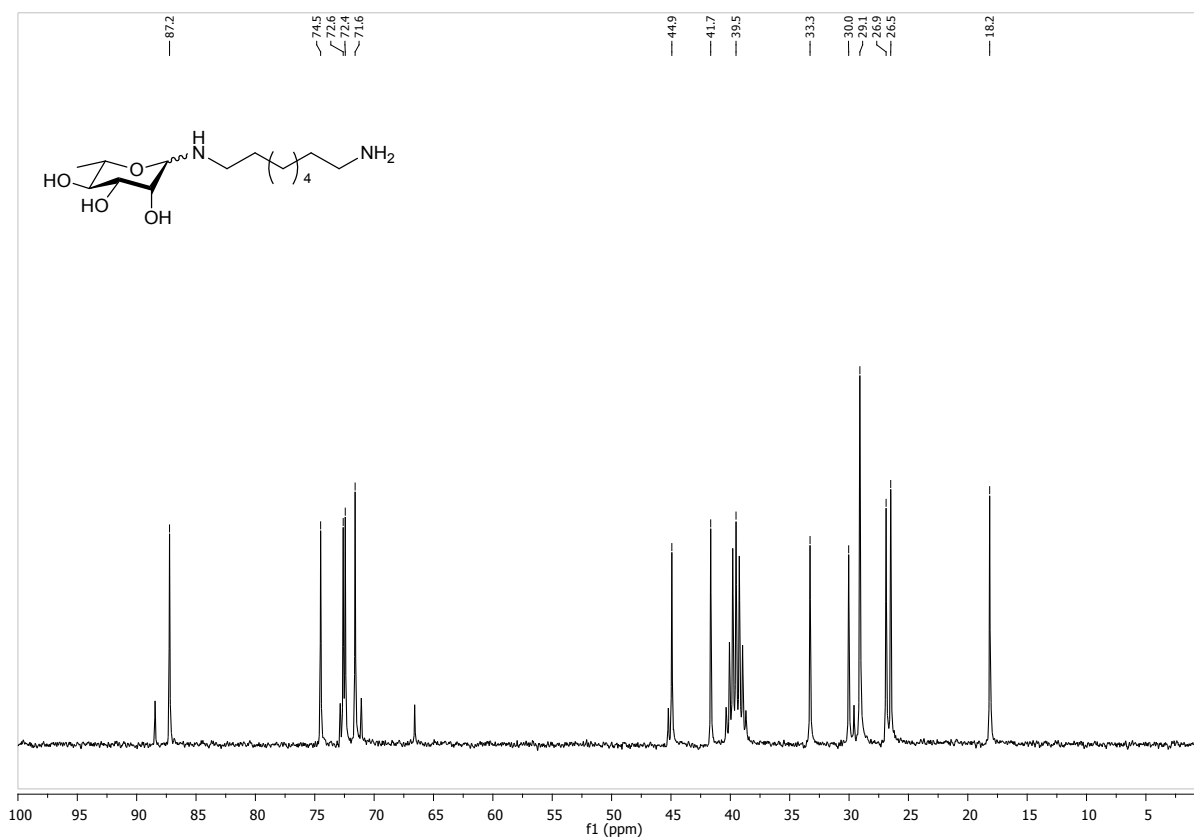
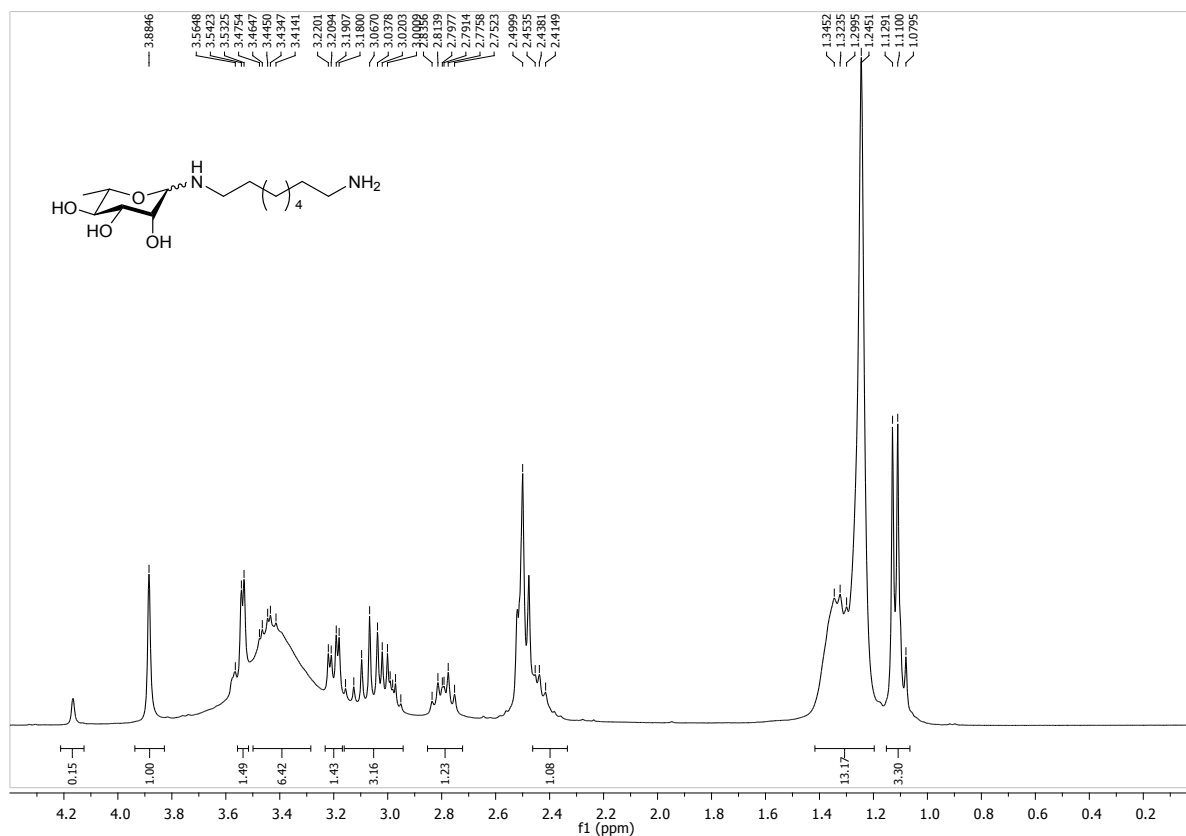
N-dodecyl-L-rhamnosylamine (1e)



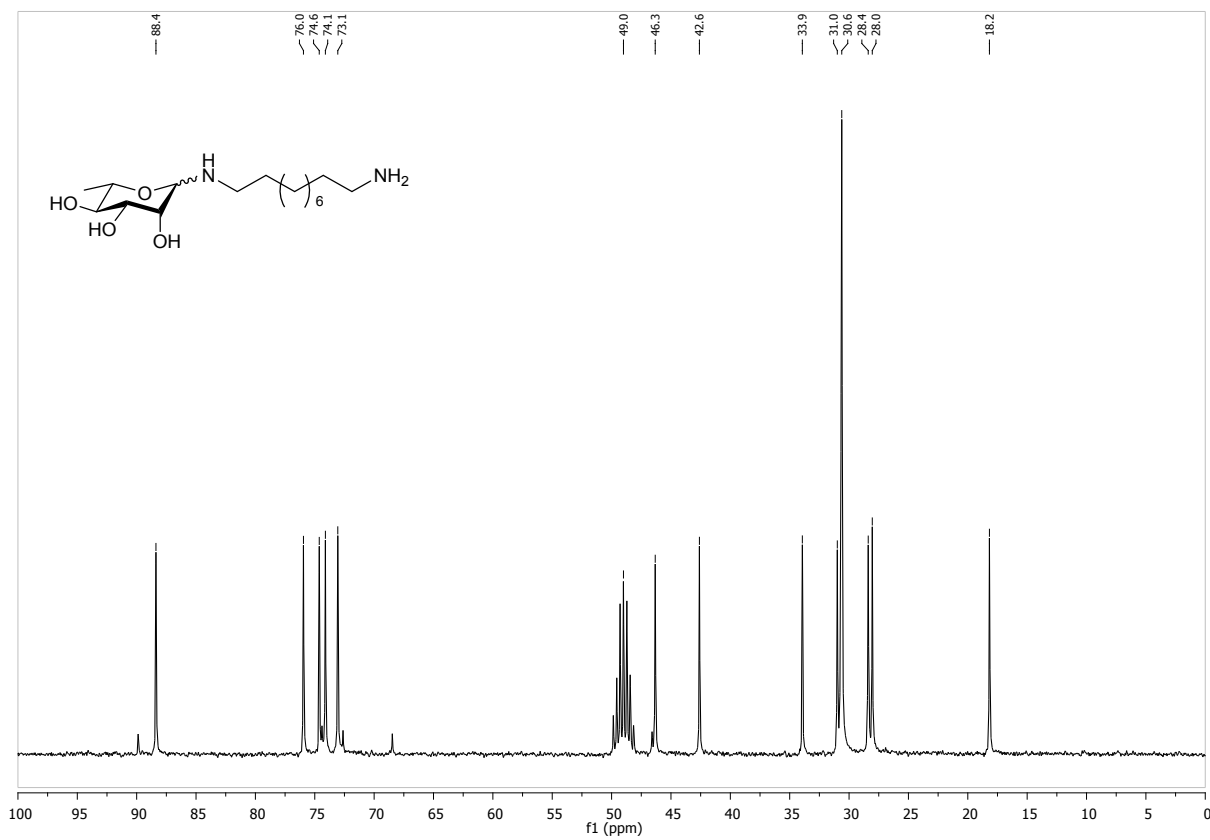
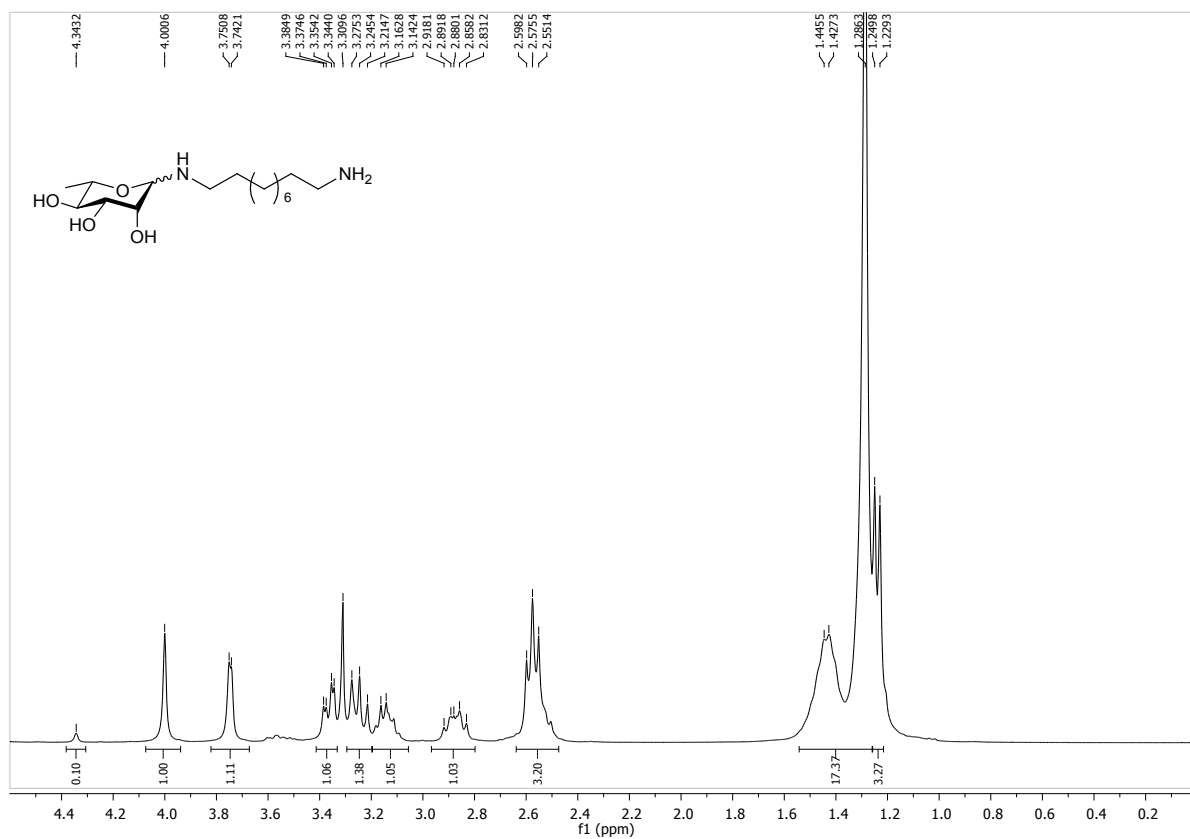
N-hexadecyl-L-rhamnosylamine (1f)



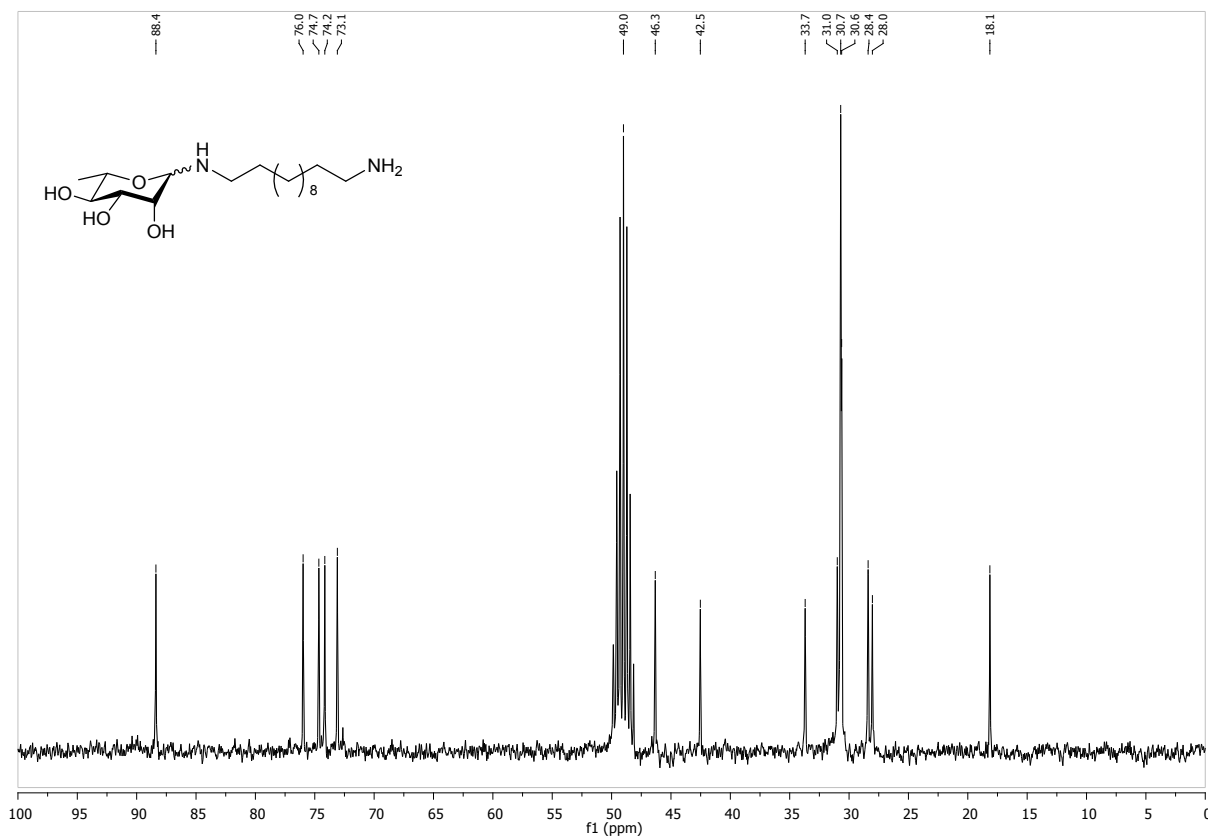
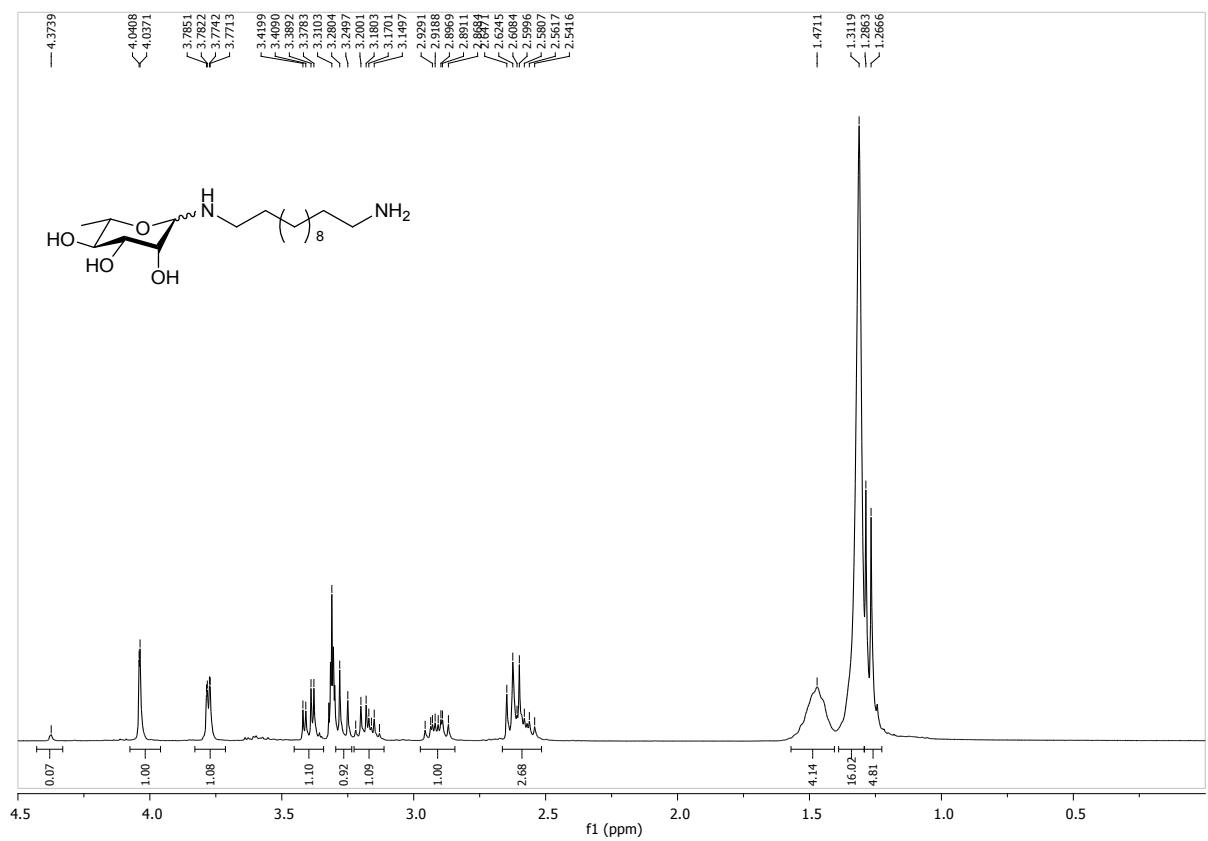
N-(L-rhamnosyl)-octyl-1,8-diamine (**1h**)



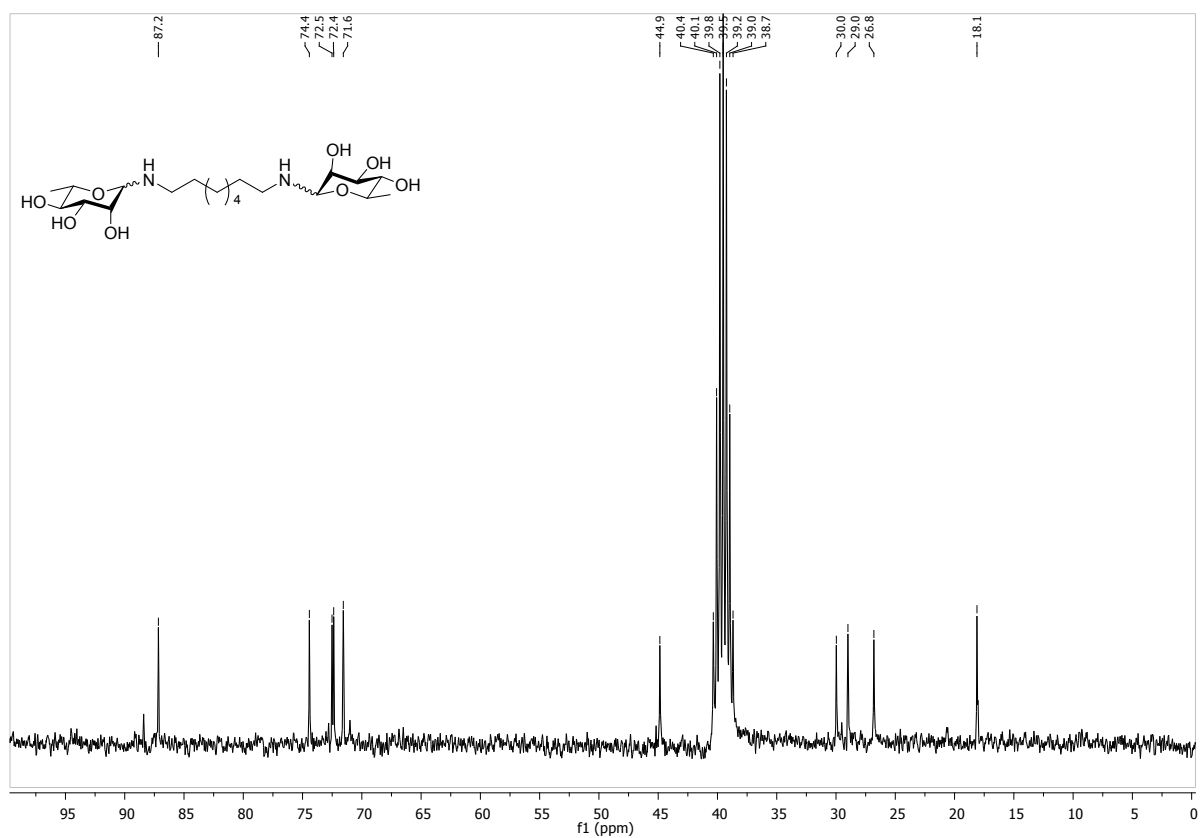
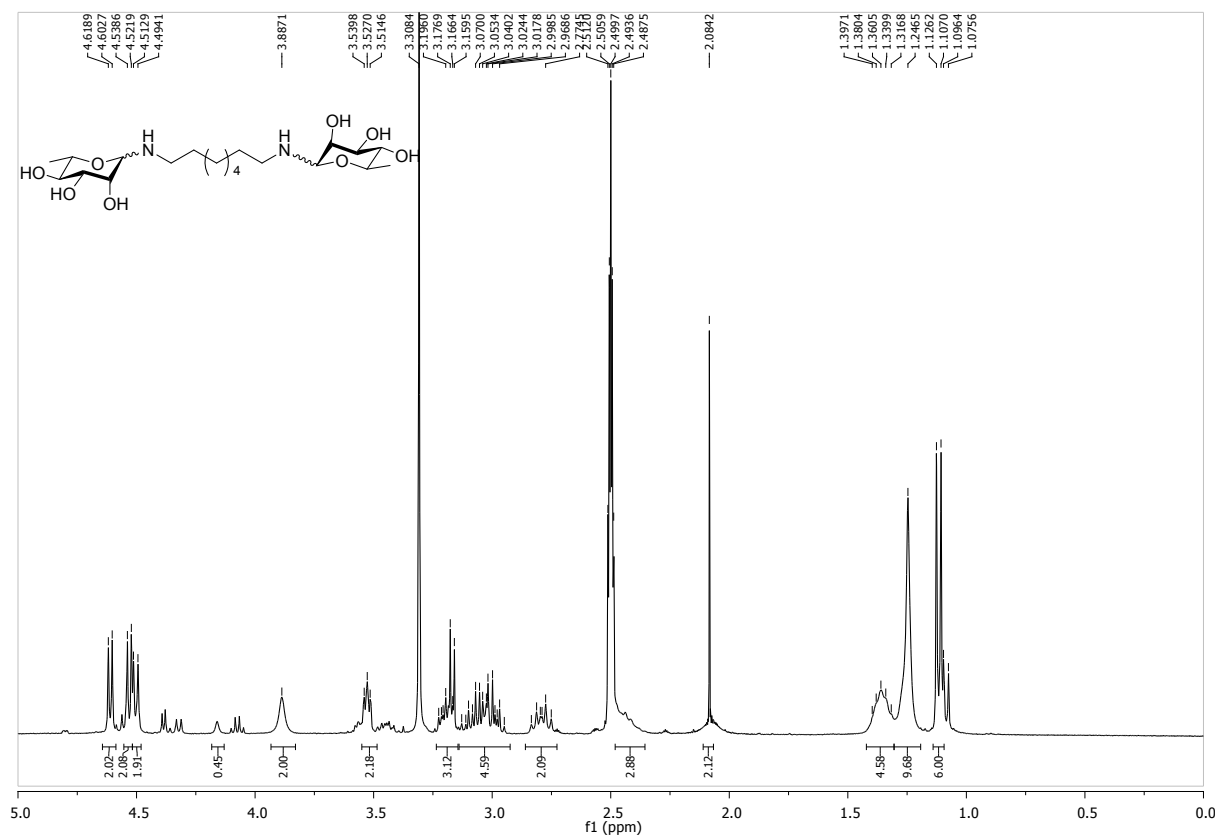
N-(L-rhamnosyl)-decyl-1,10-diamine (**1i**)



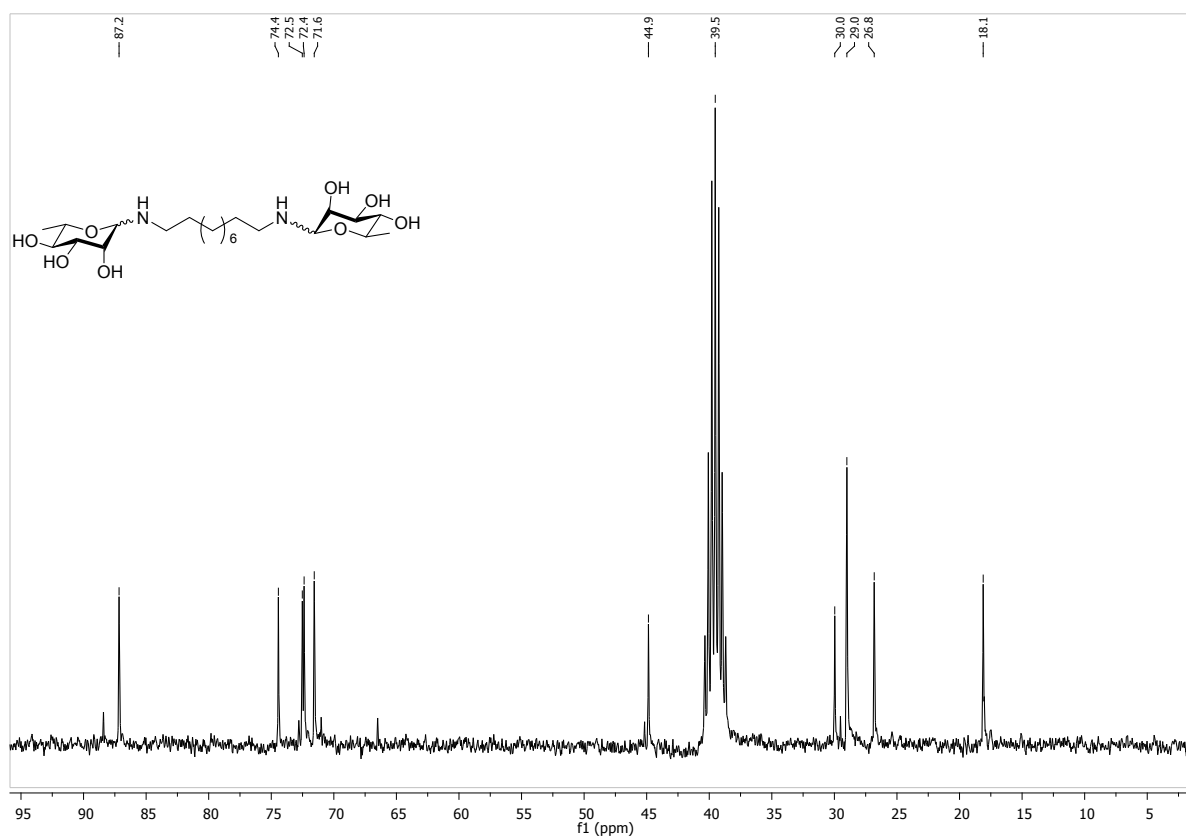
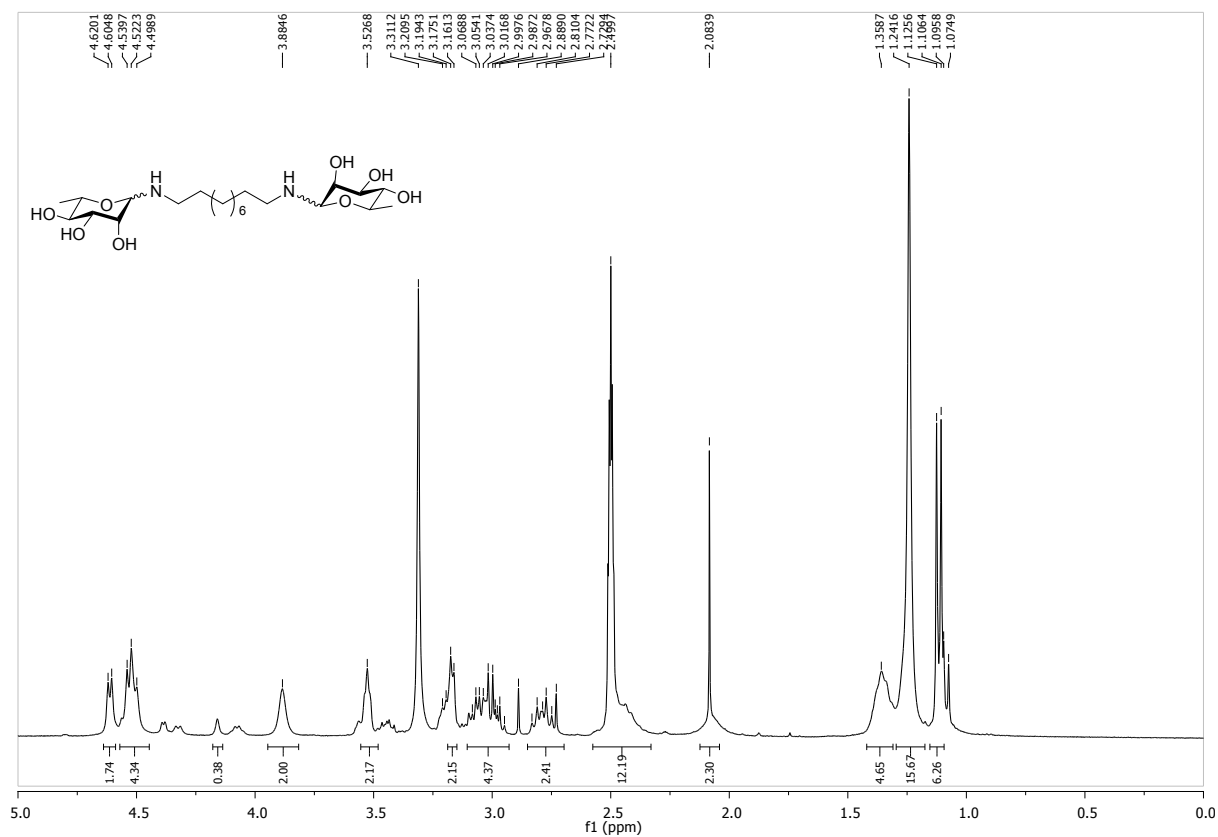
N-(L-rhamnosyl)-dodecyl-1,12-diamine (**1j**)



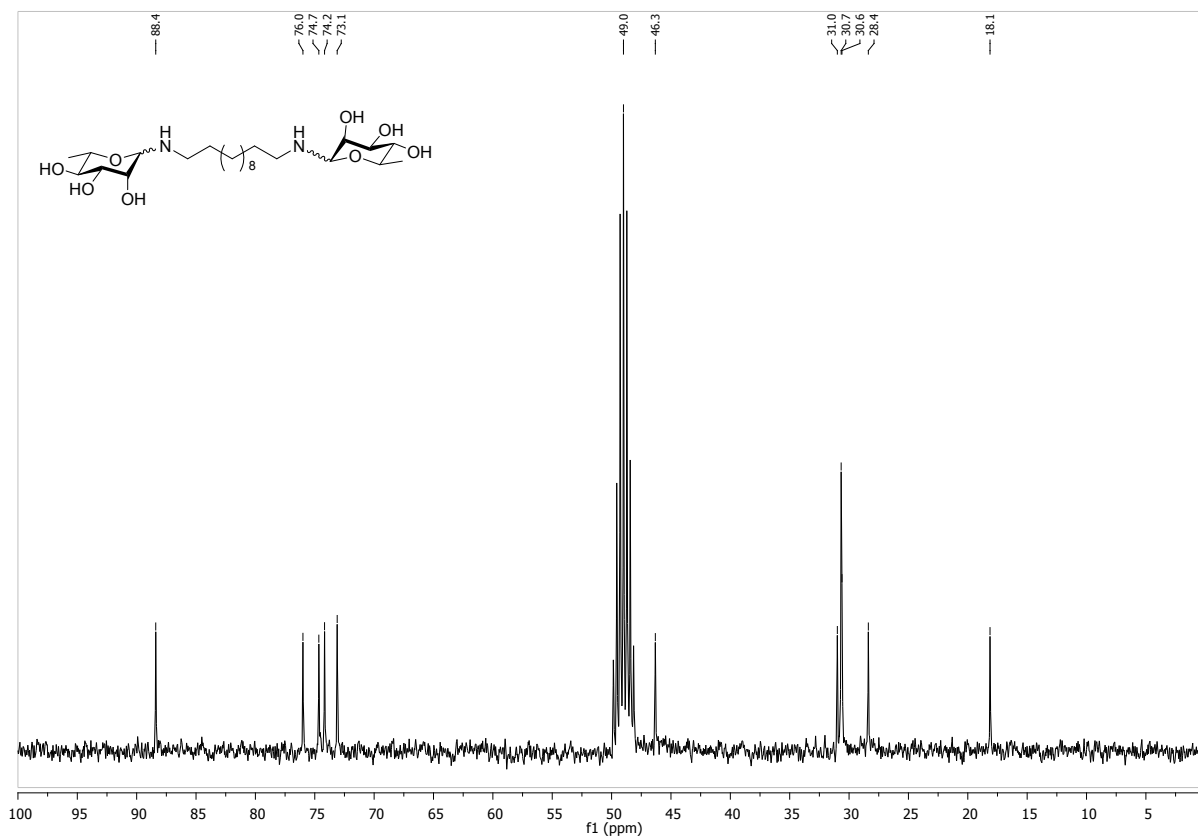
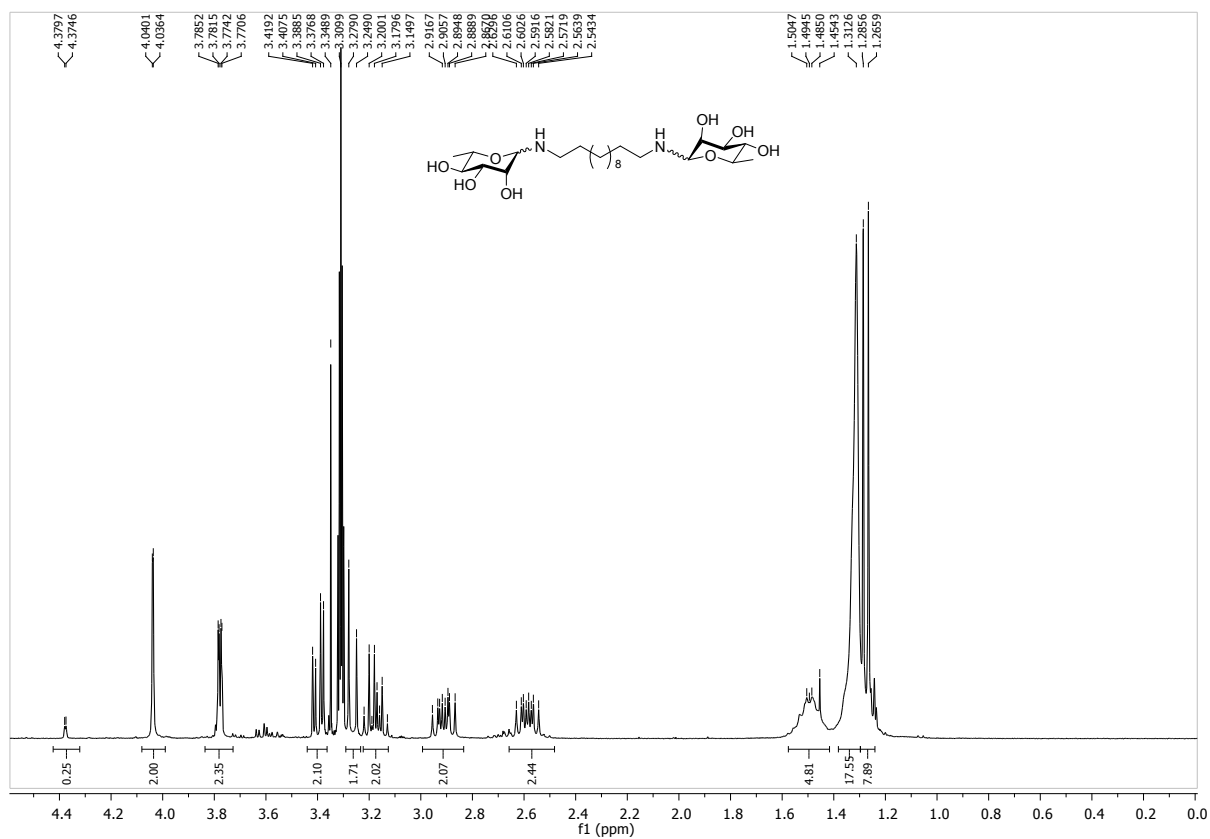
N,N'-bis-(L-rhamnosyl)-octyl-1,8-diamine (**1k**)



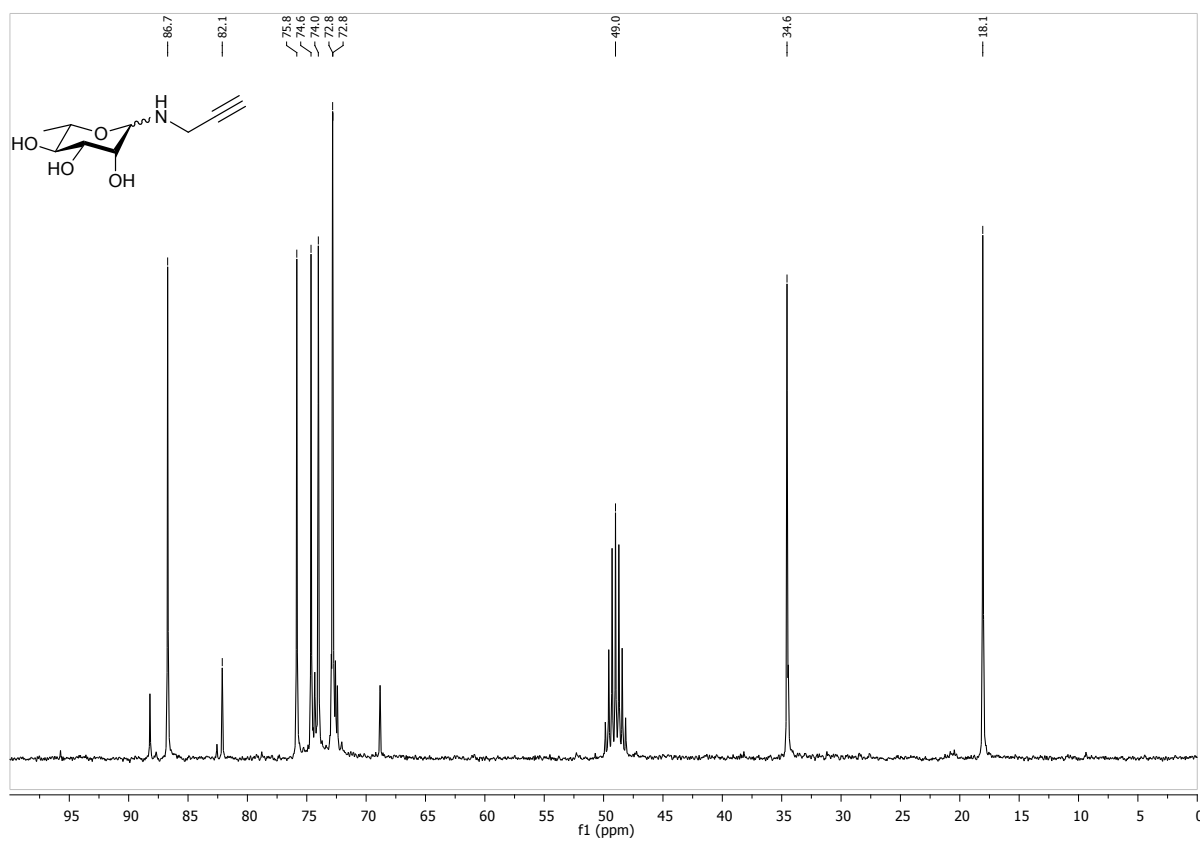
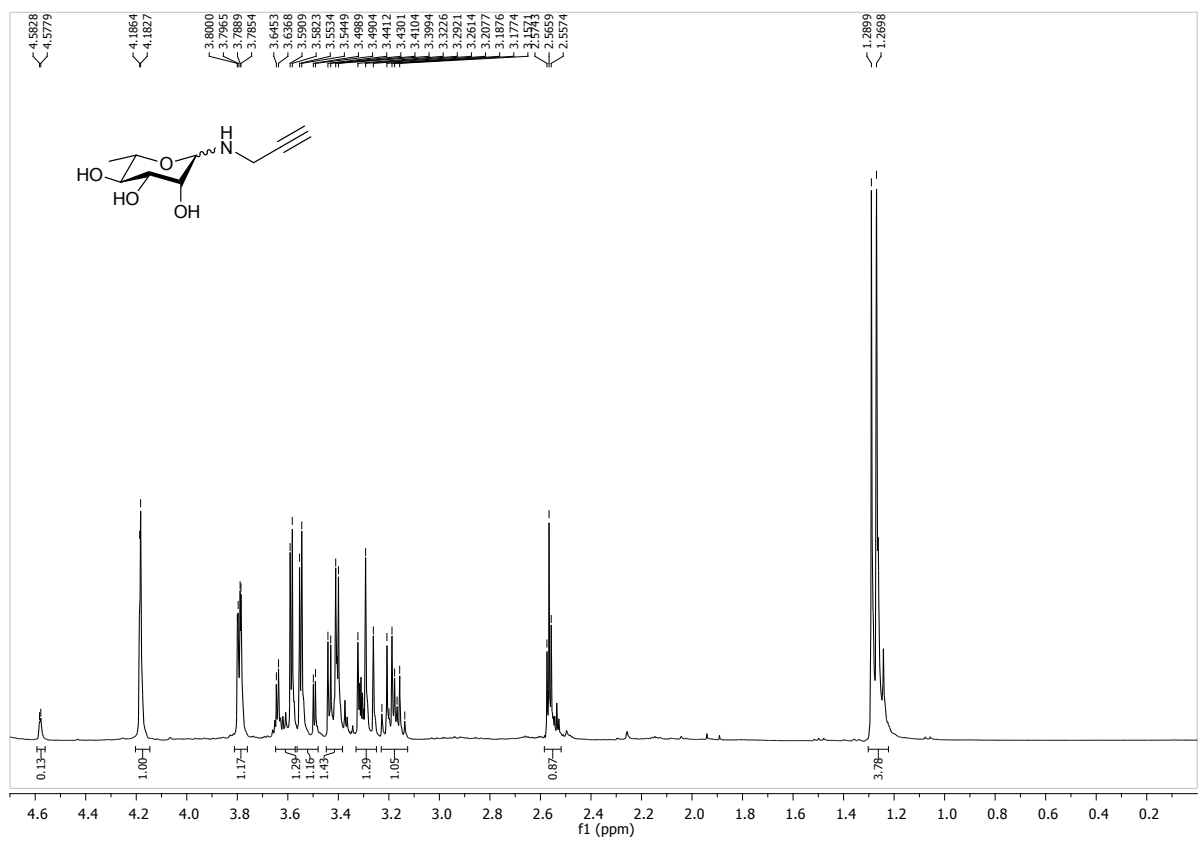
N,N'-bis-(L-rhamnosyl)-decyl-1,10-diamine (**1**)



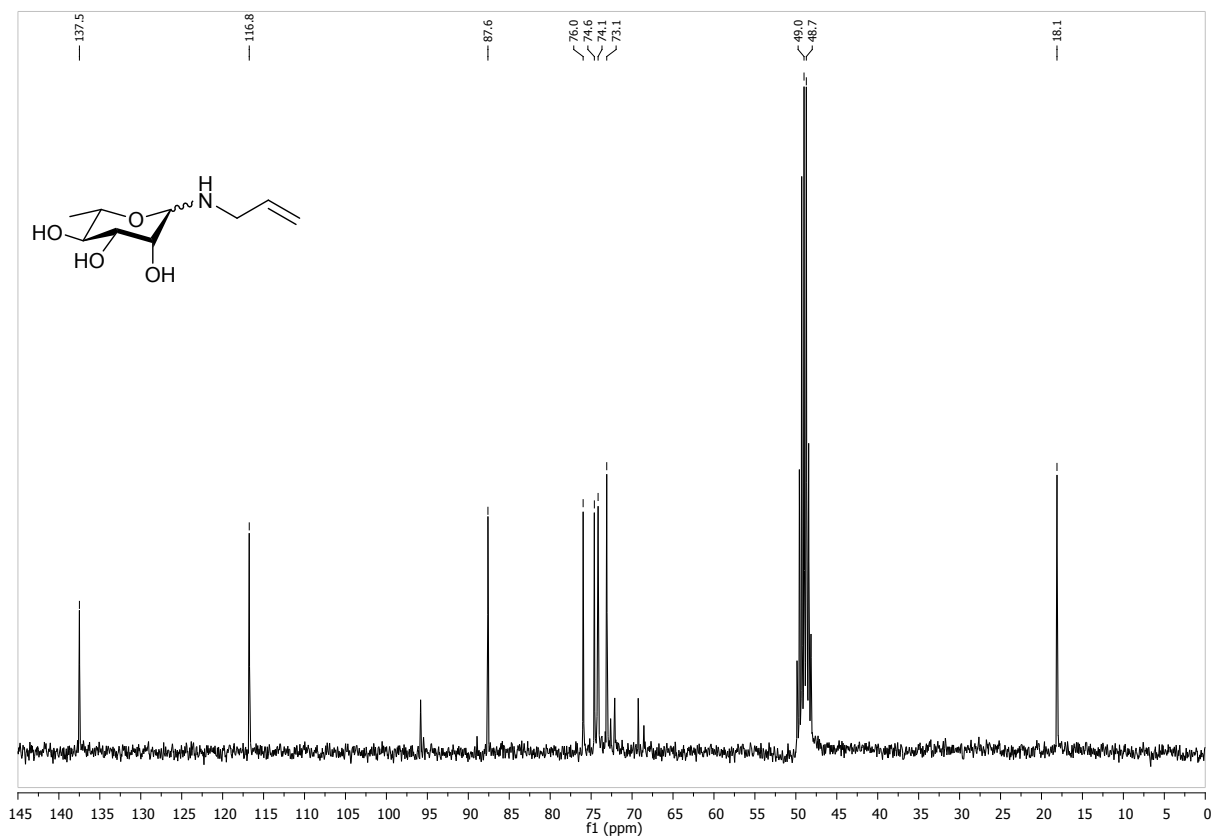
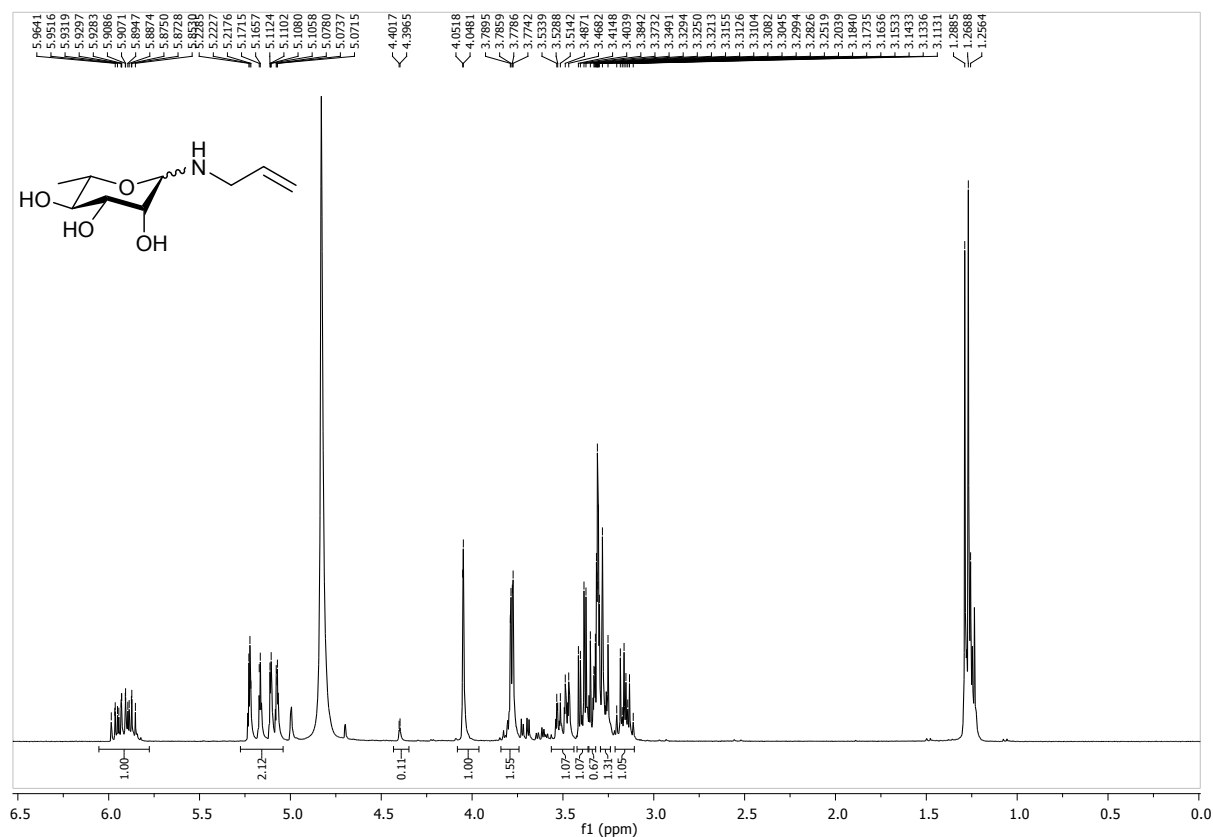
N,N'-bis-(L-rhamnosyl)-dodecyl-1,12-diamine (**1m**)



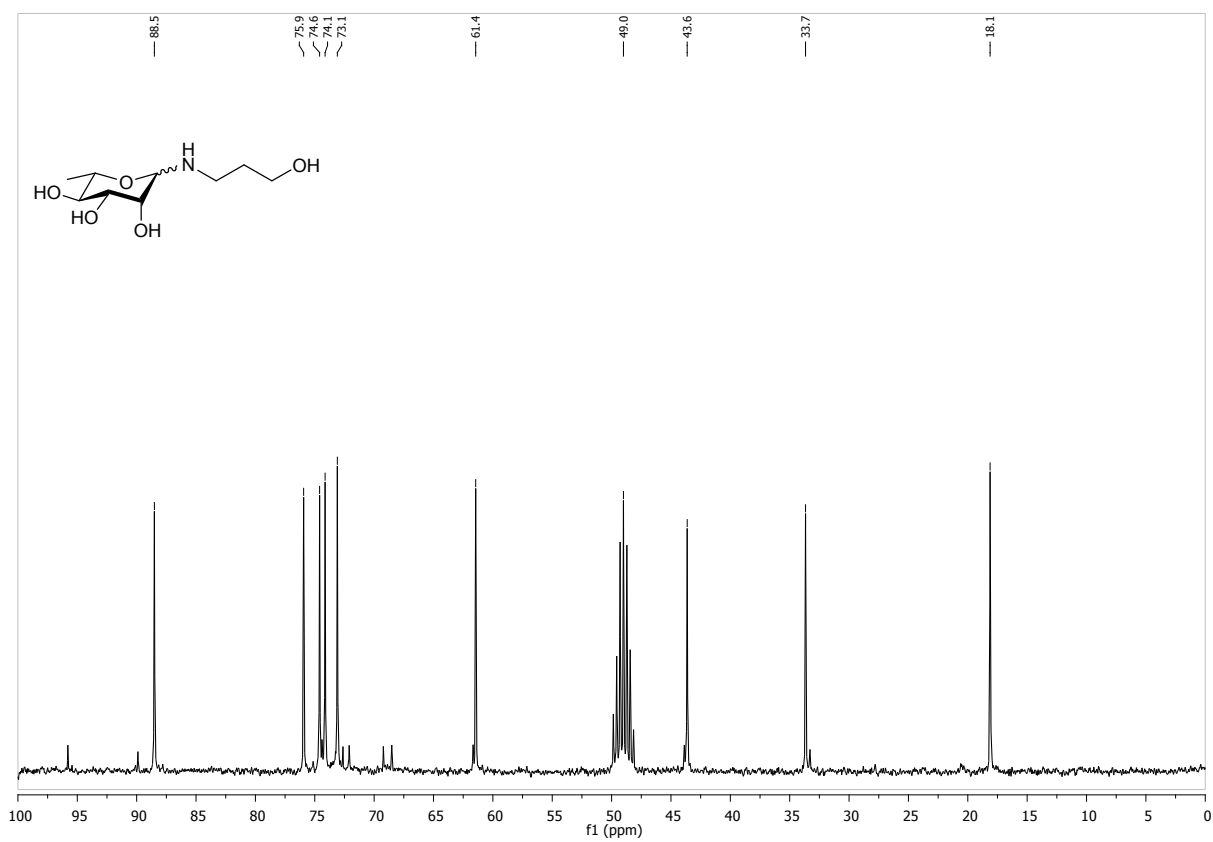
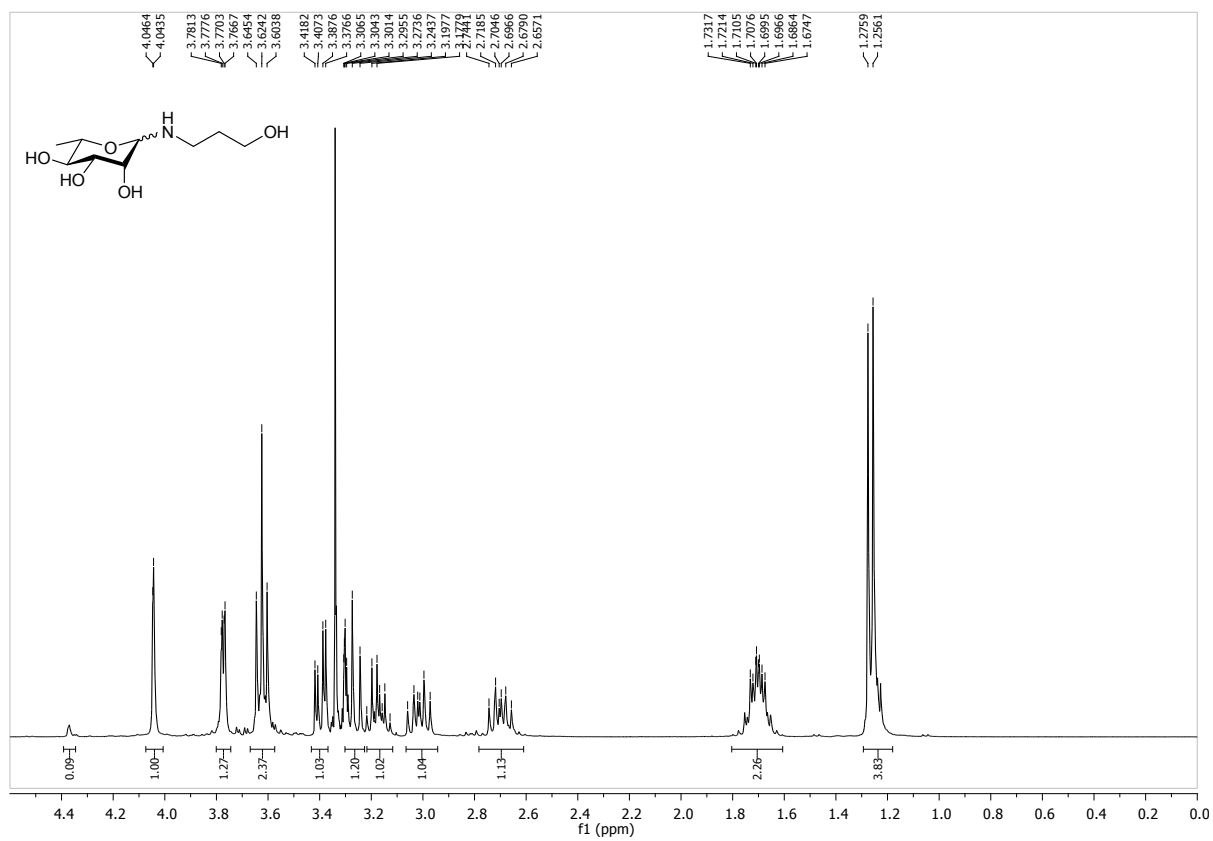
N-propargyl-L-rhamnosylamine (1n)



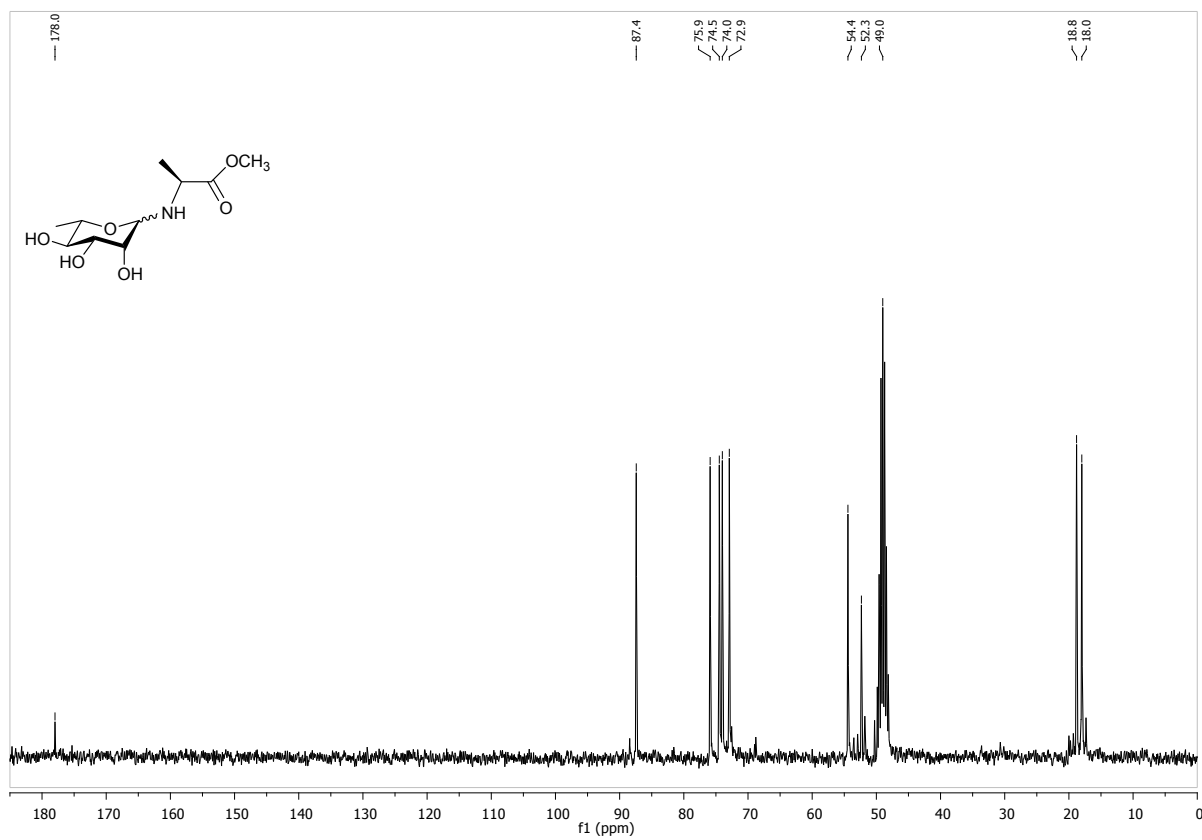
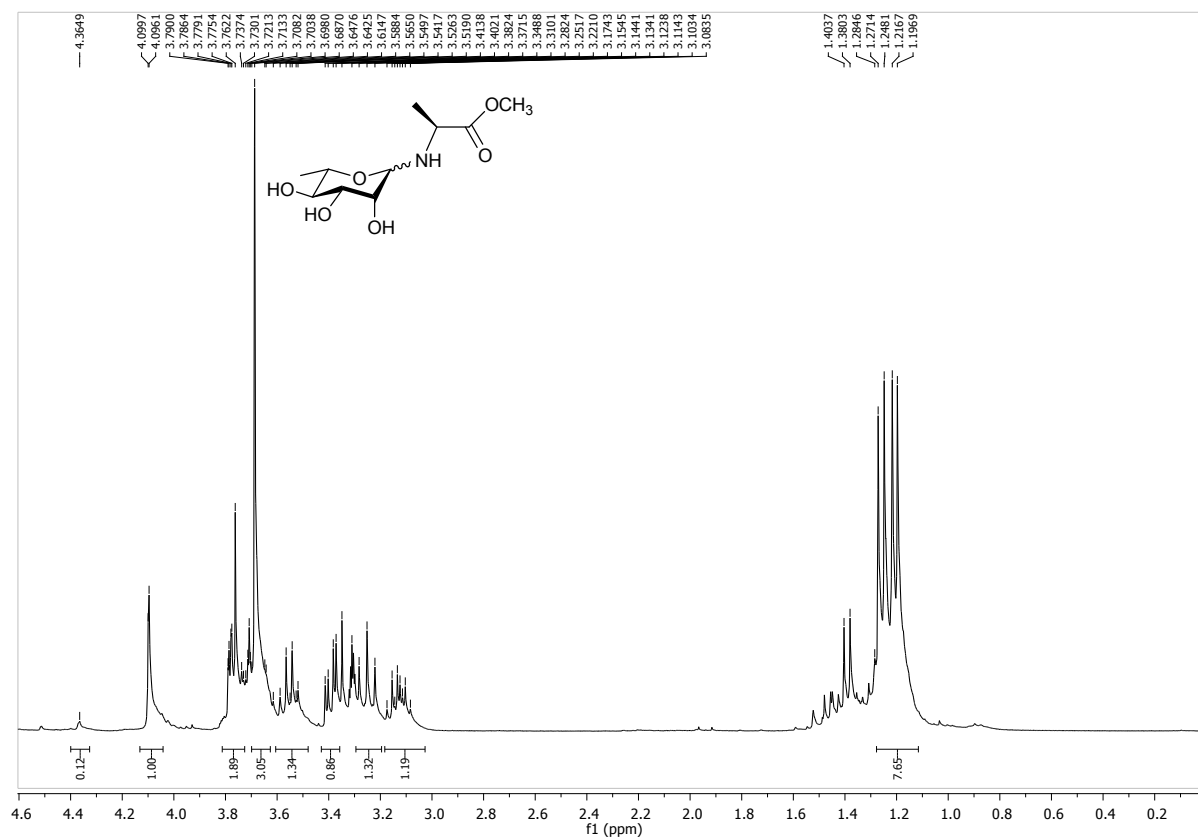
N-allyl-L-rhamnosylamine (**1o**)



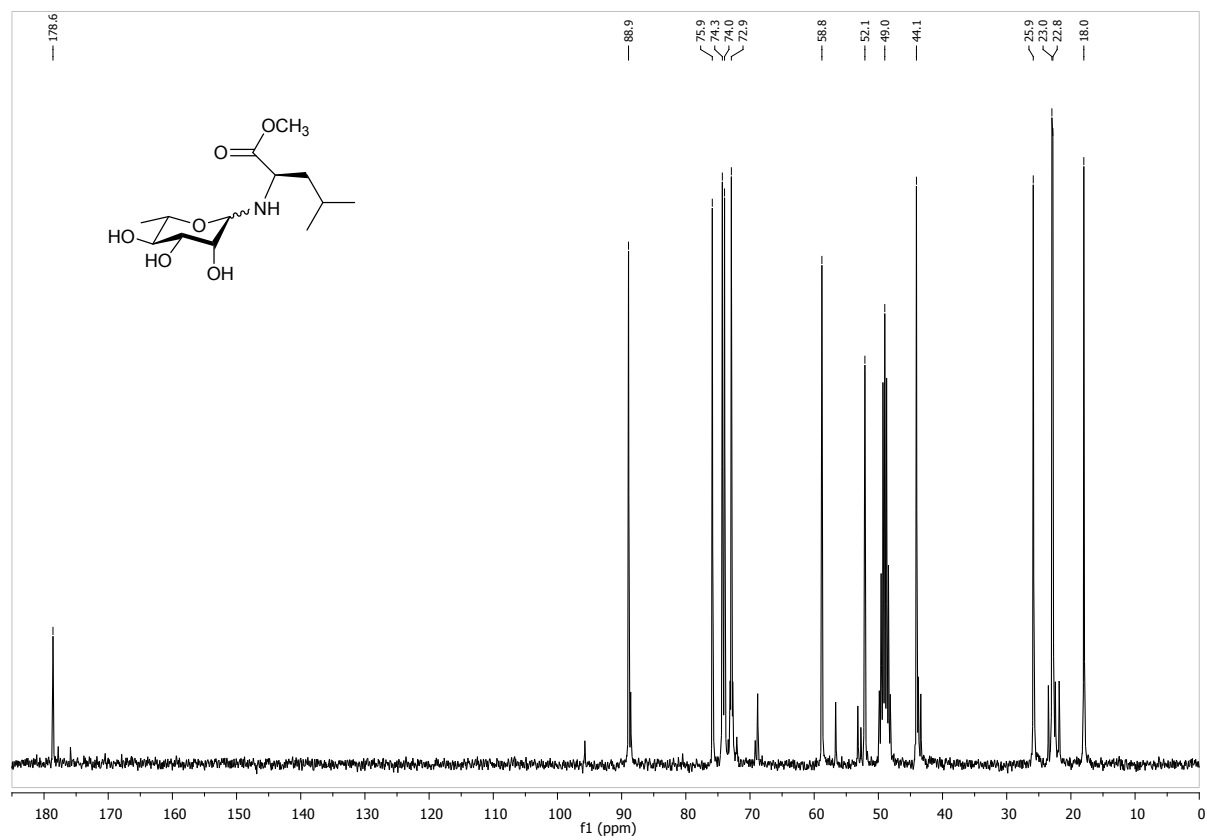
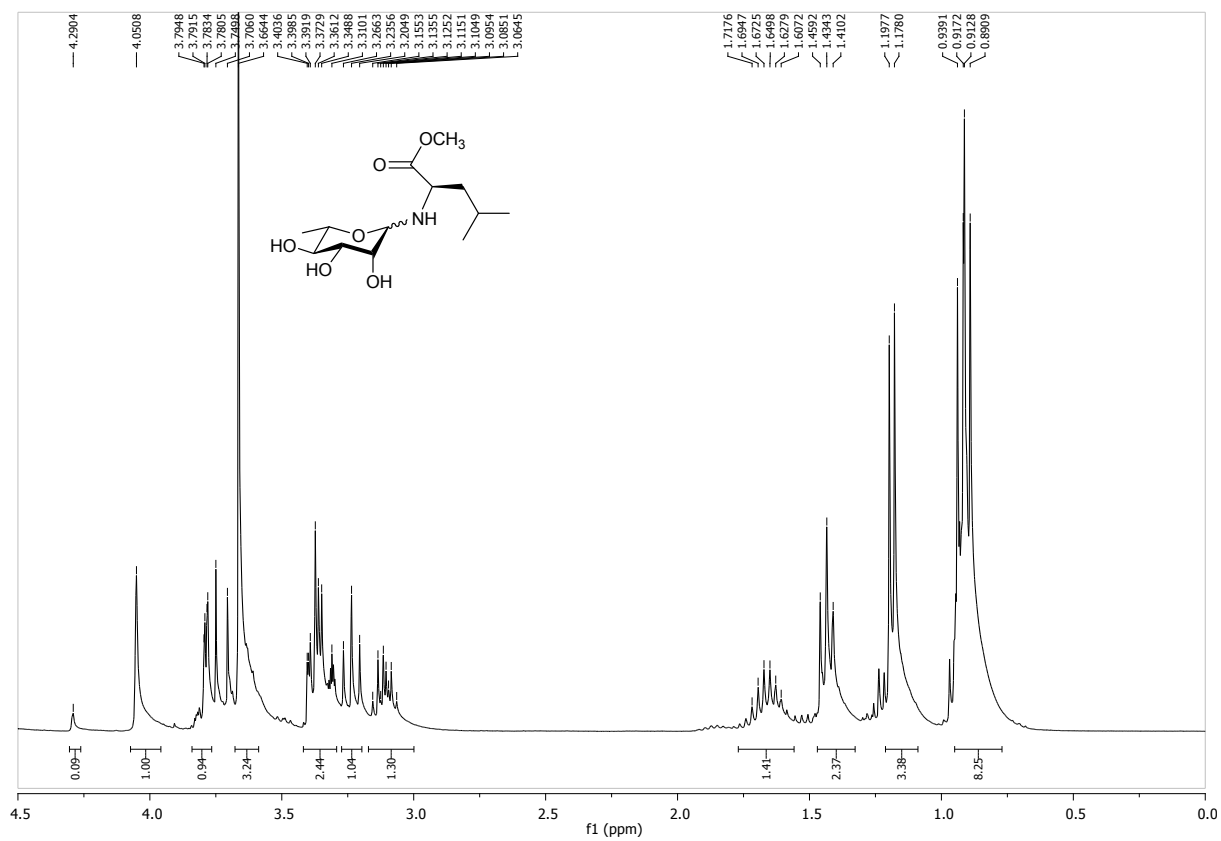
N-(3-hydroxypropyl)-*L*-rhamnosylamine (**1p**)



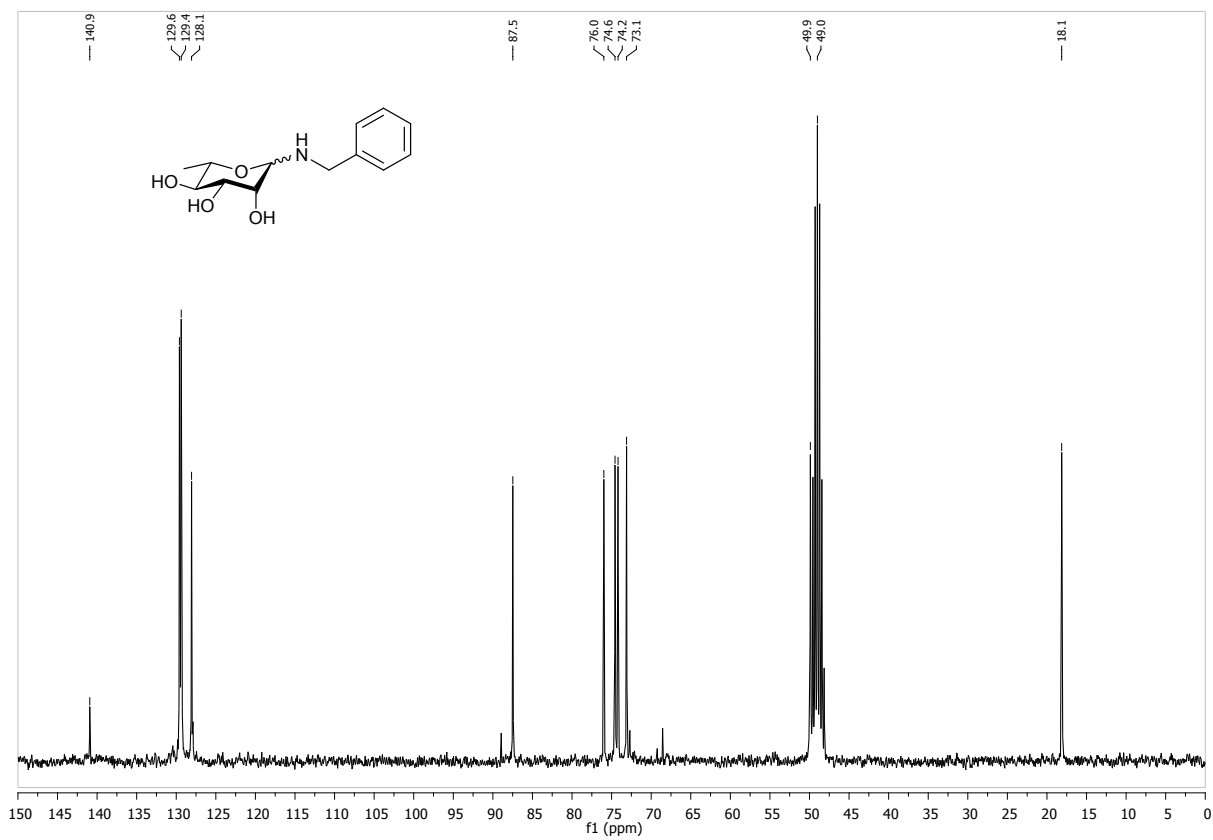
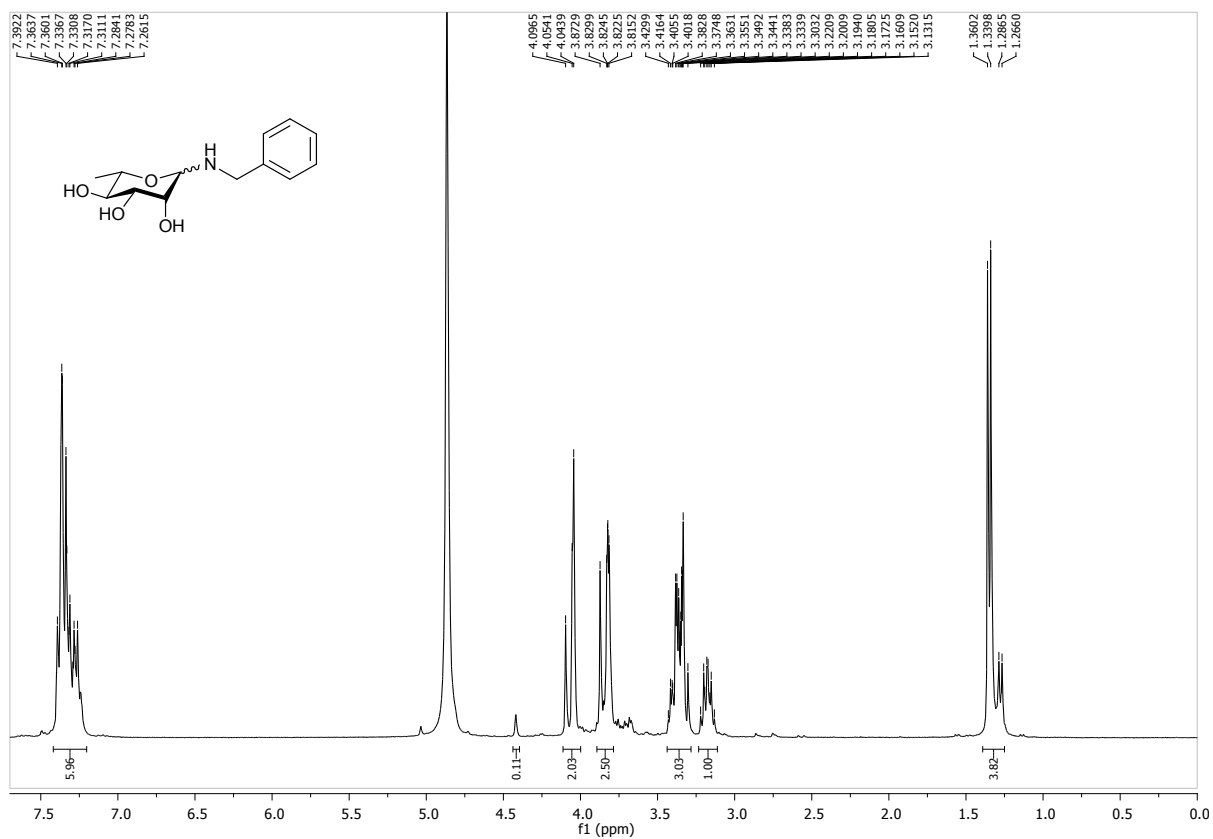
N-(alanine methyl ester)-*L*-rhamnosylamine (**1q**)



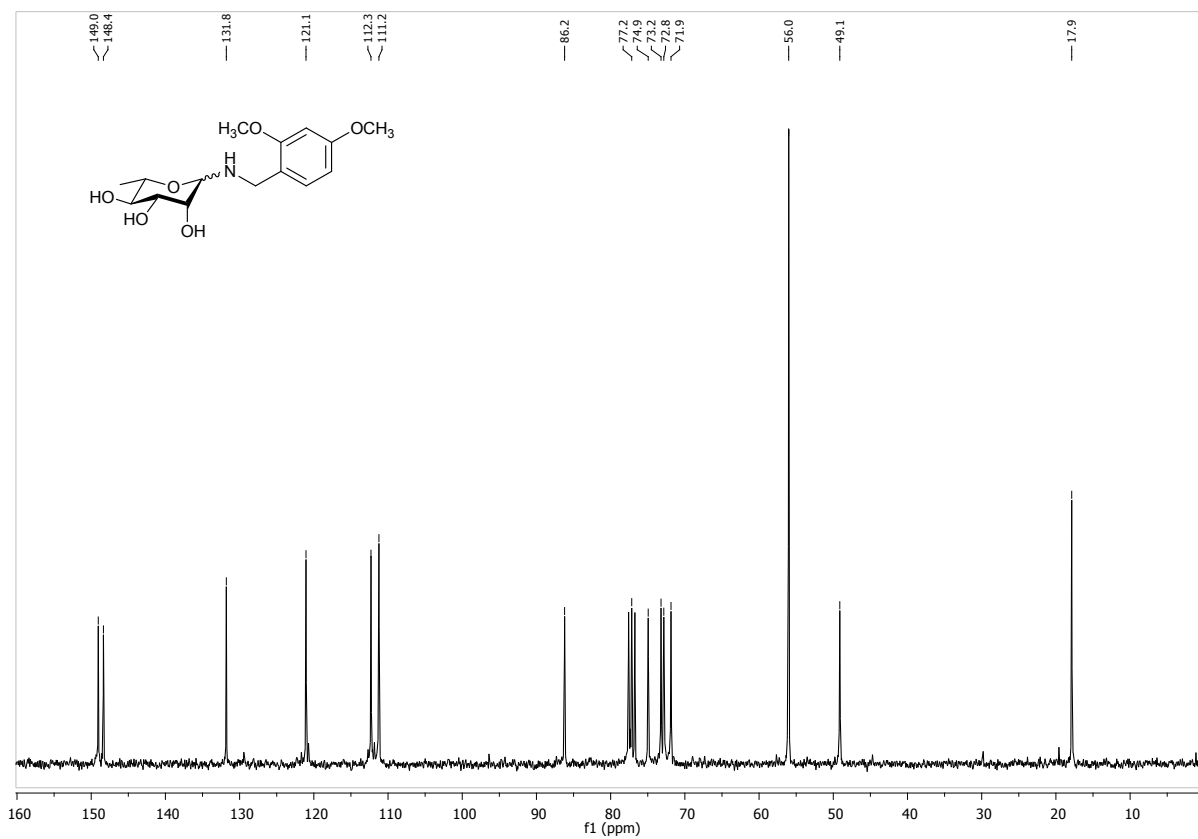
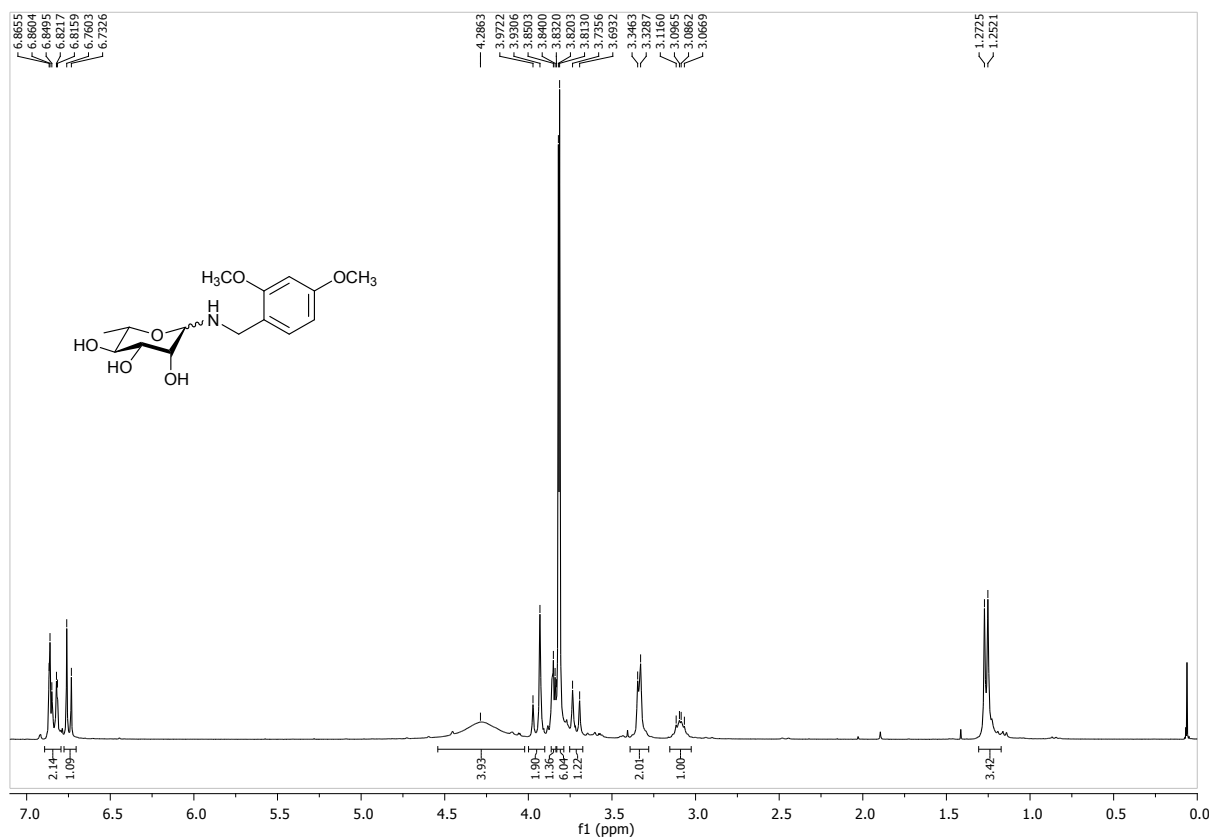
N-(leucine methyl ester)-L-rhamnosylamine (**1r**)



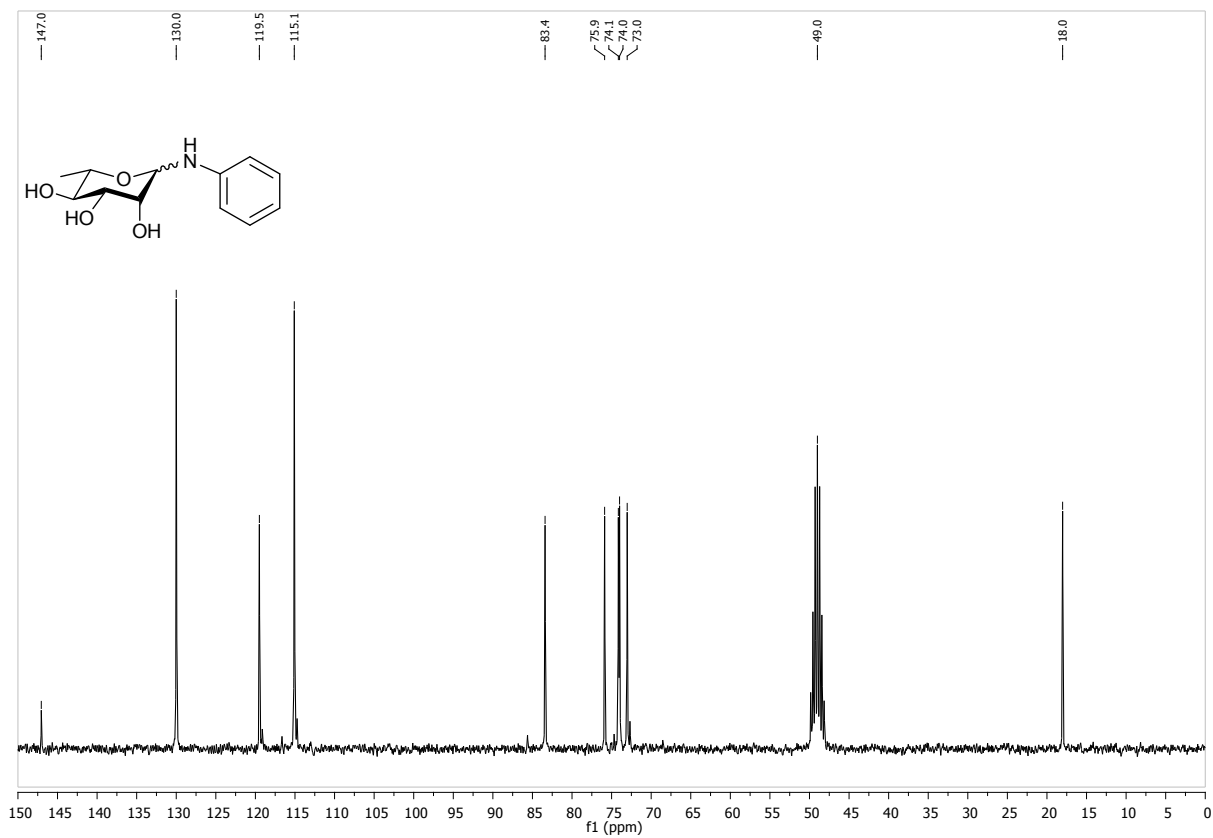
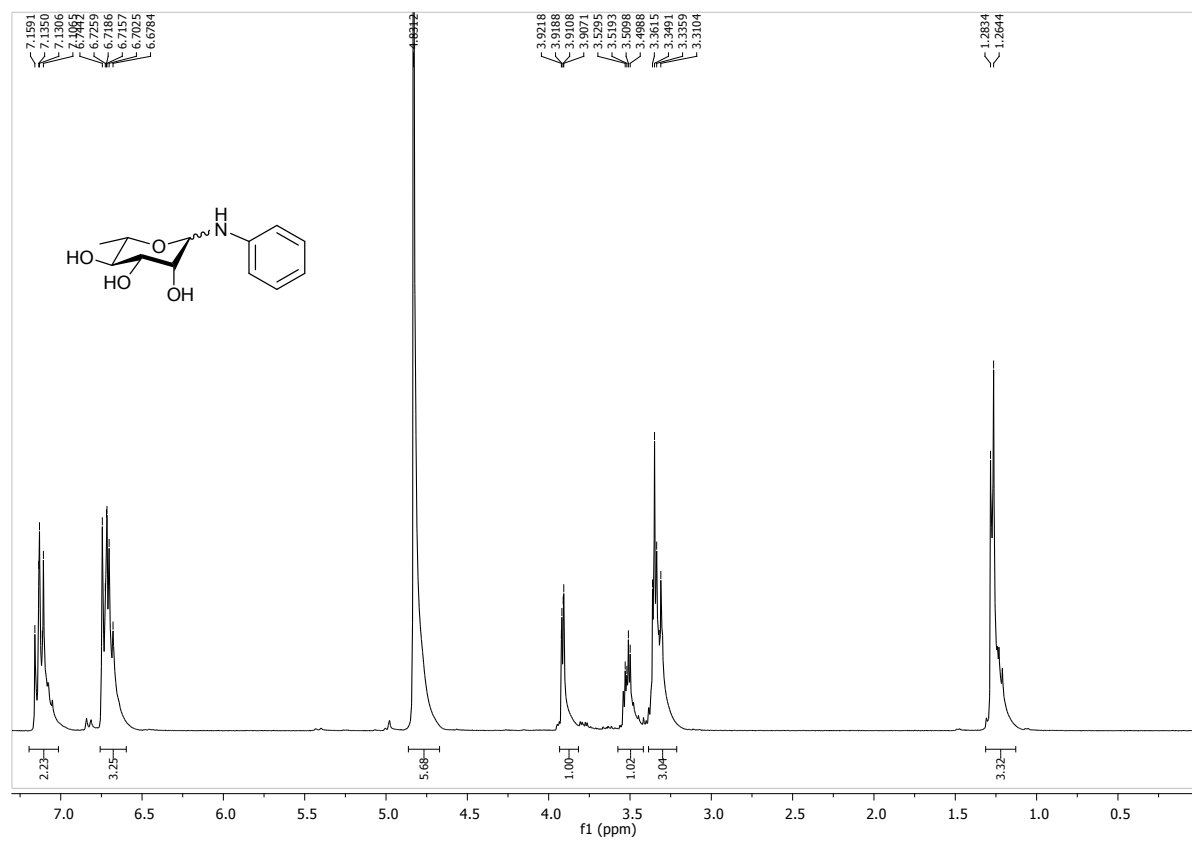
N-benzyl-L-rhamnosylamine (**1s**)



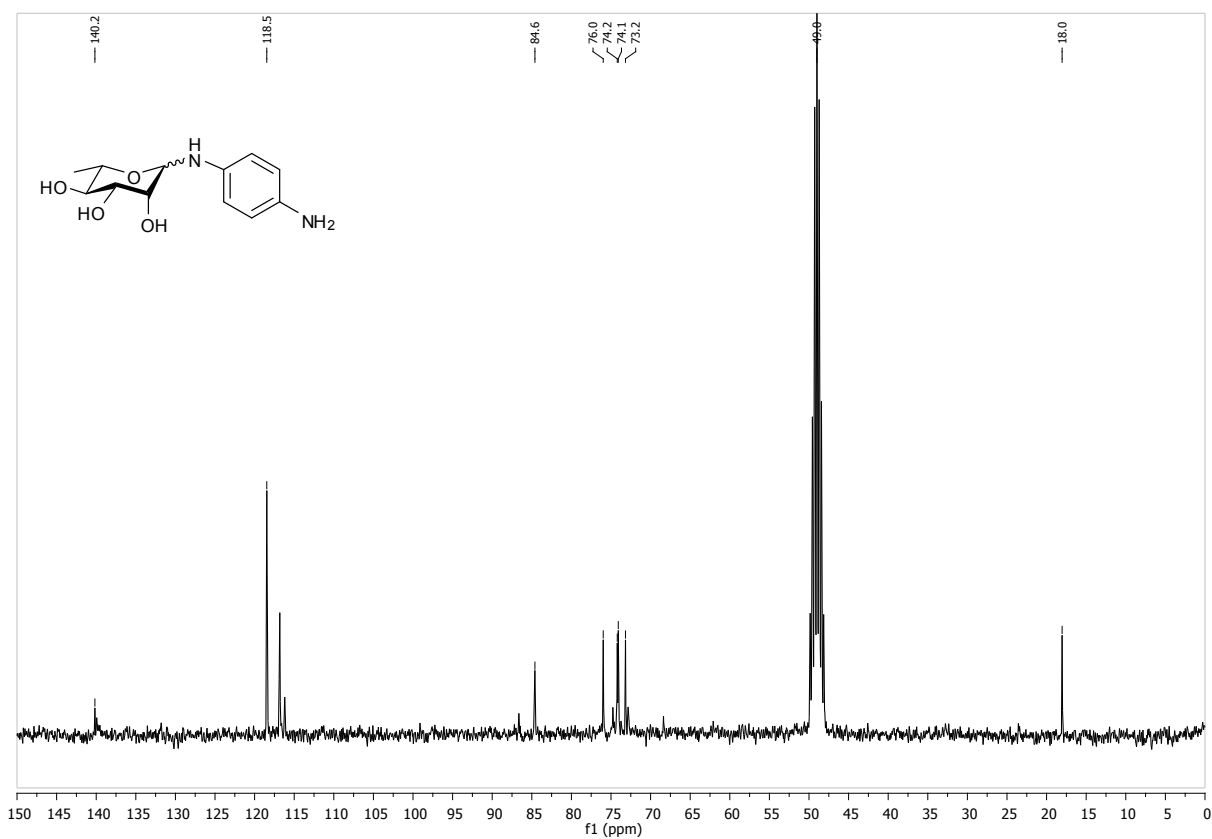
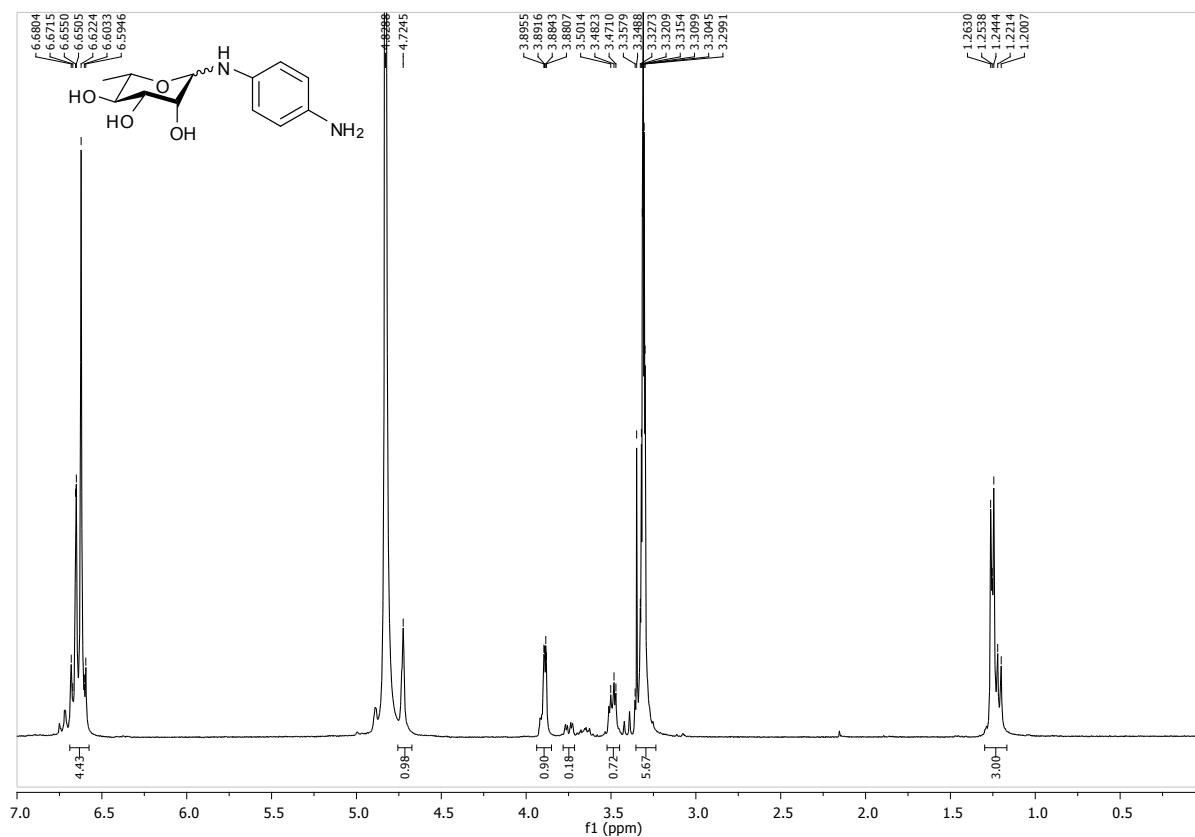
N-(2,4-dimethoxybenzyl)-L-rhamnosylamine (**1t**)



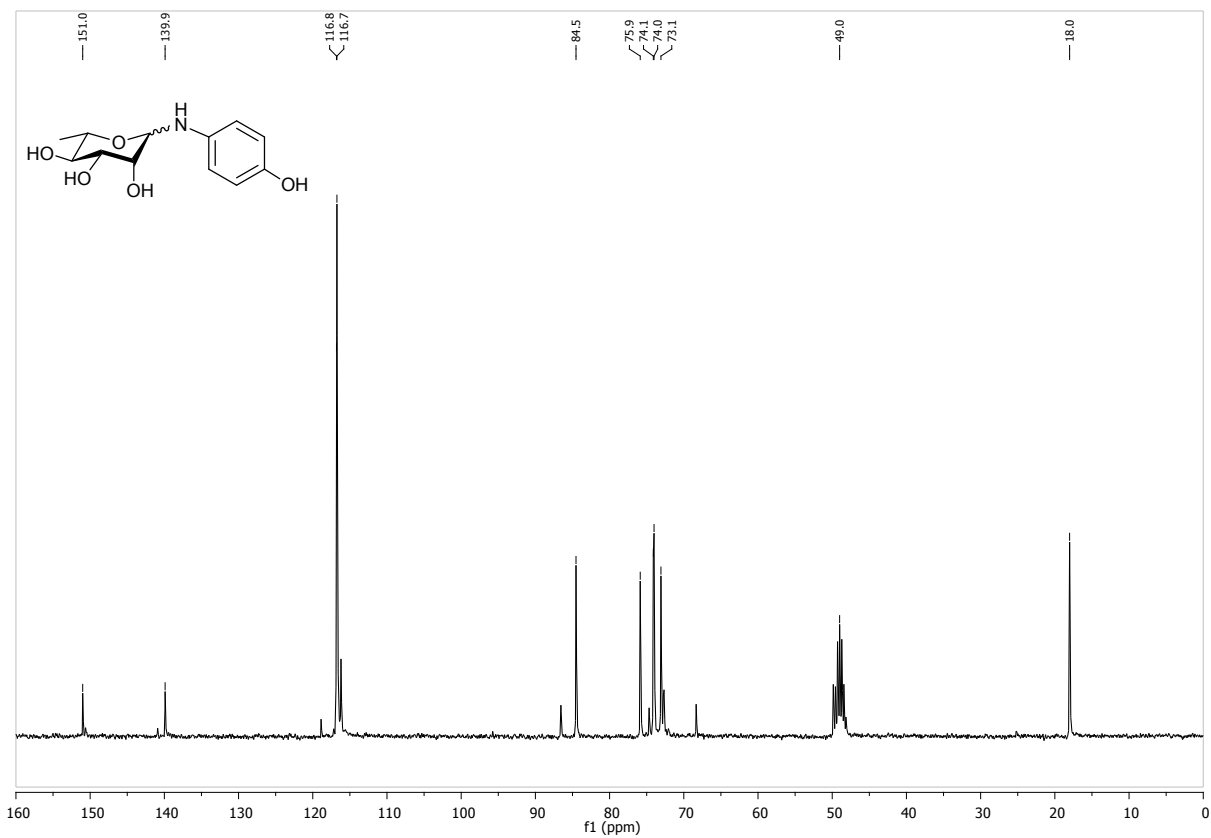
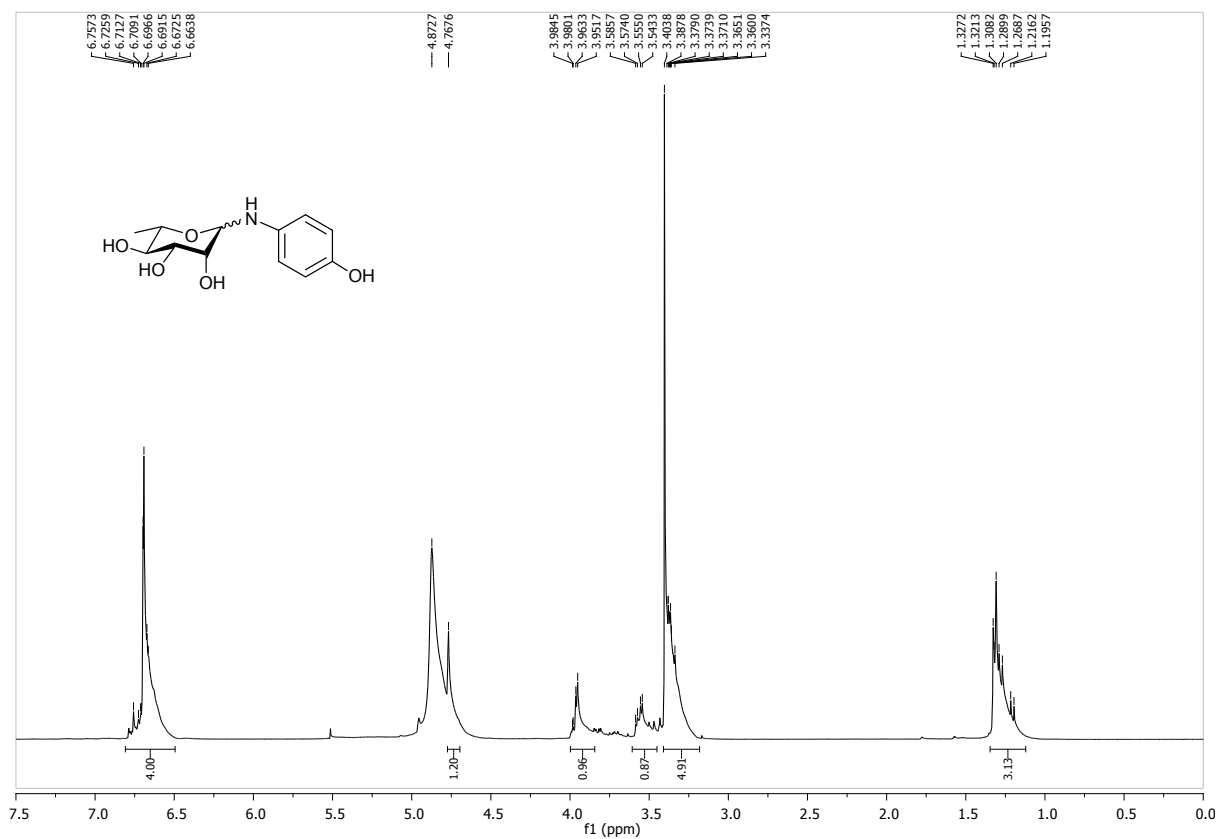
N-phenyl-L-rhamnosylamine (**1u**)



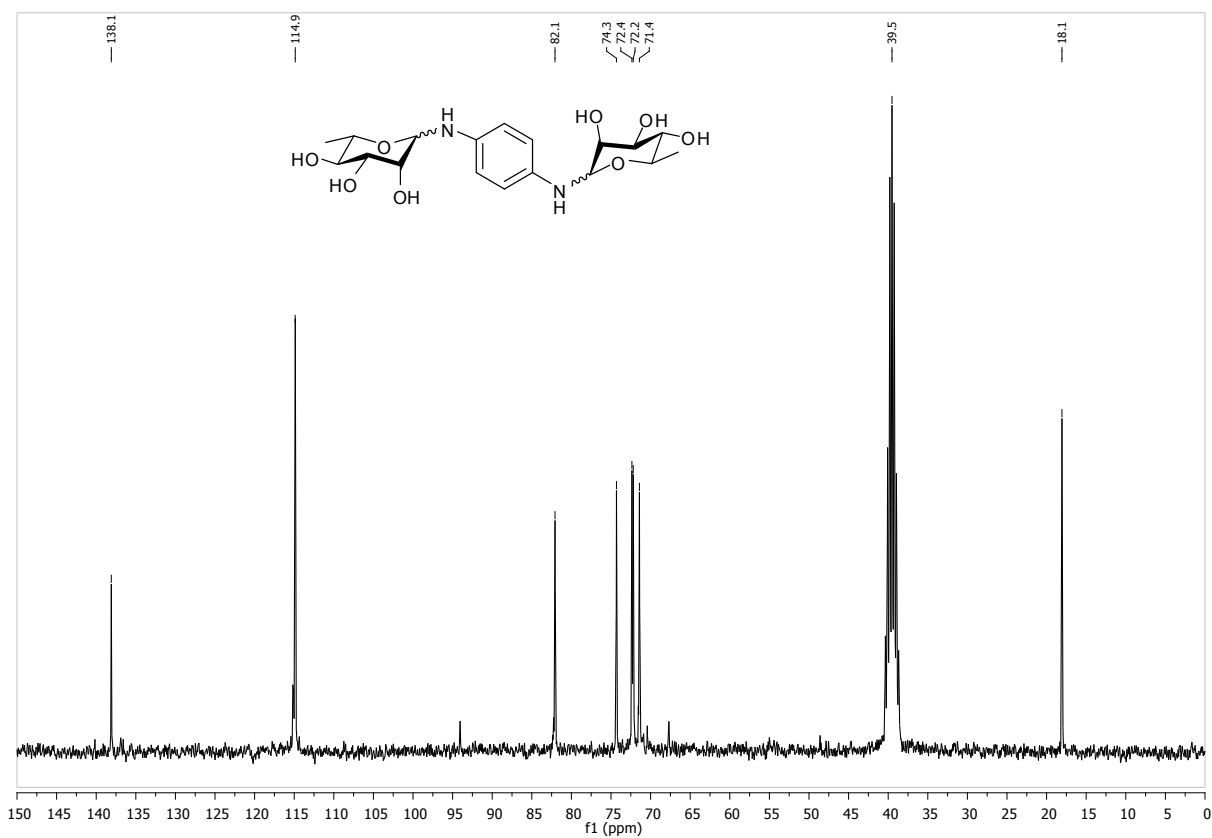
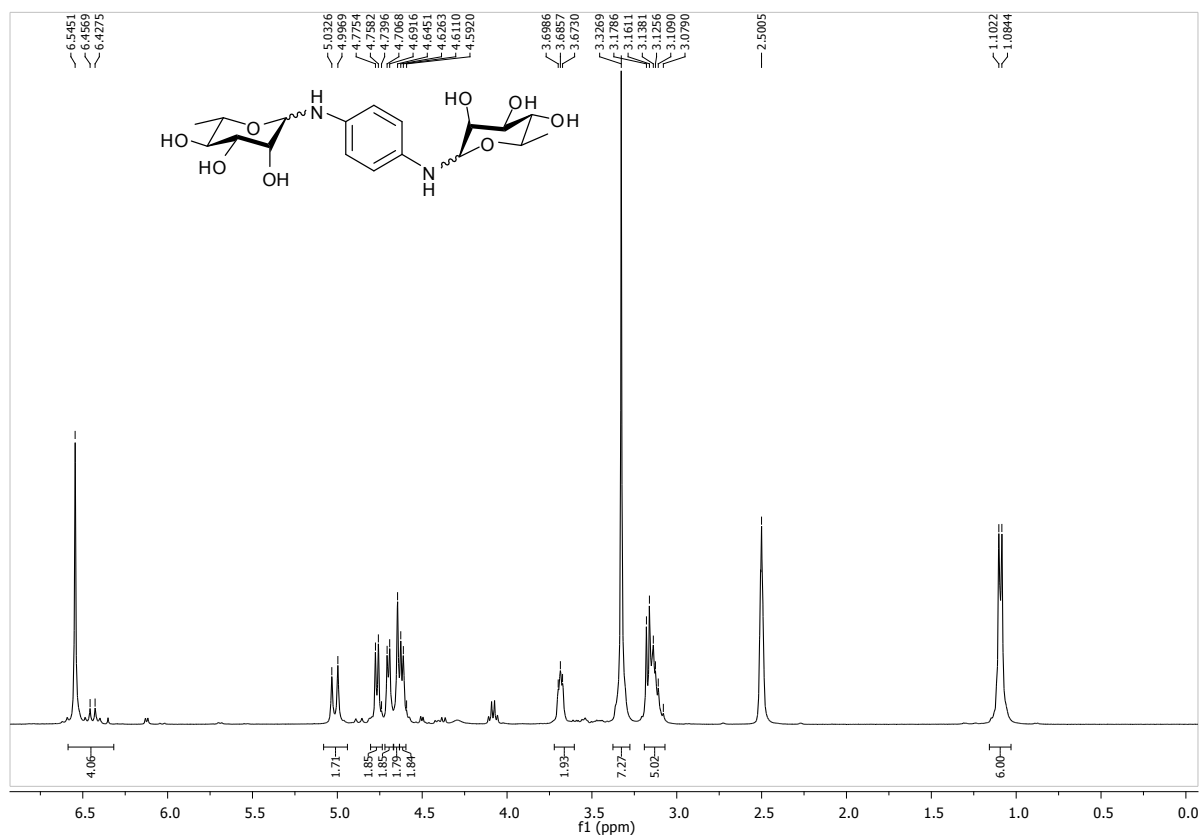
***N*-(4-aminophenyl)-L-rhamnosylamine (1v)**



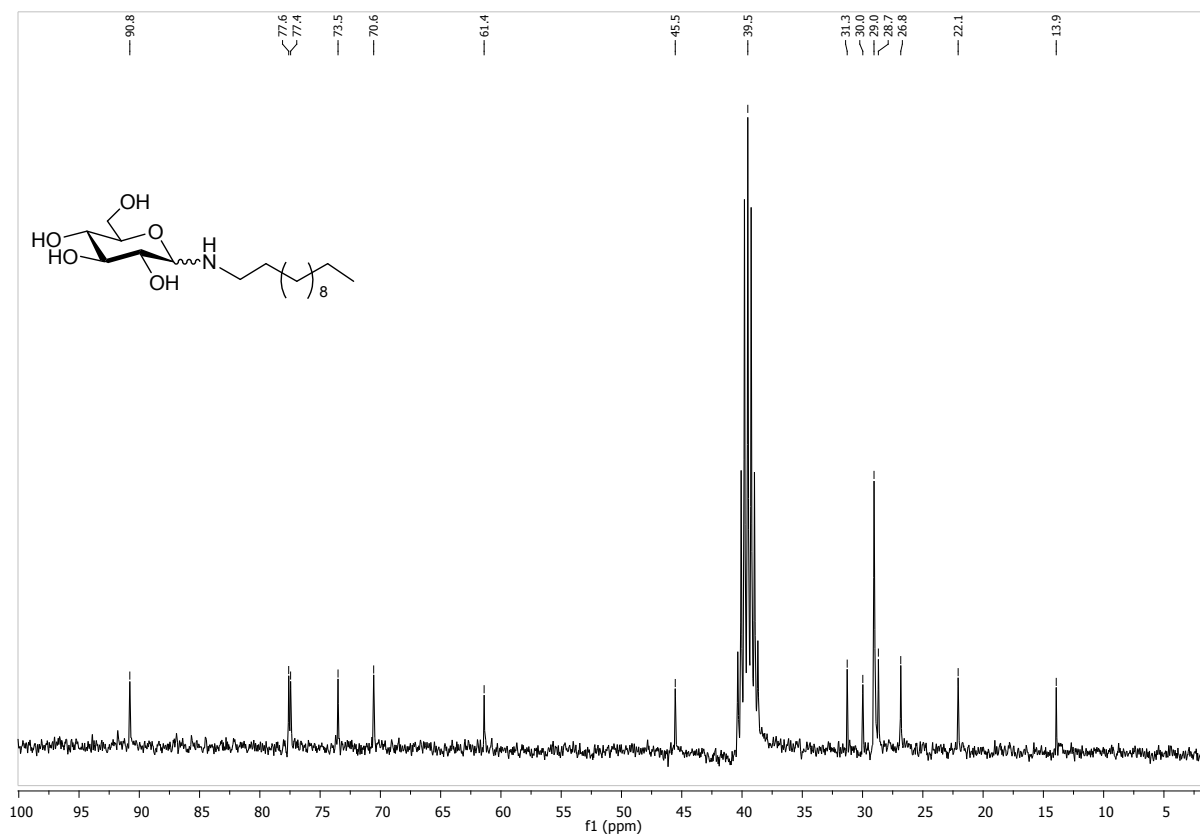
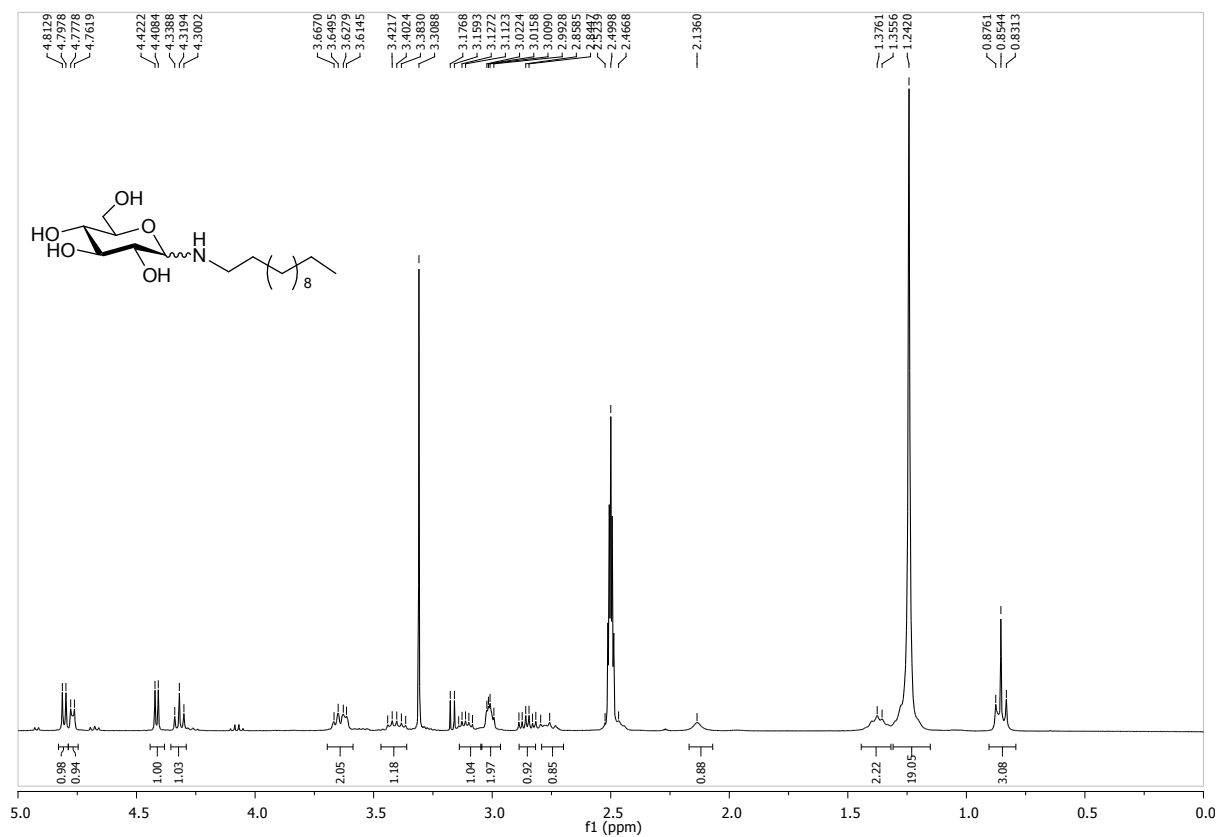
***N*-(4-hydroxyphenyl)-L-rhamnosylamine (1w)**



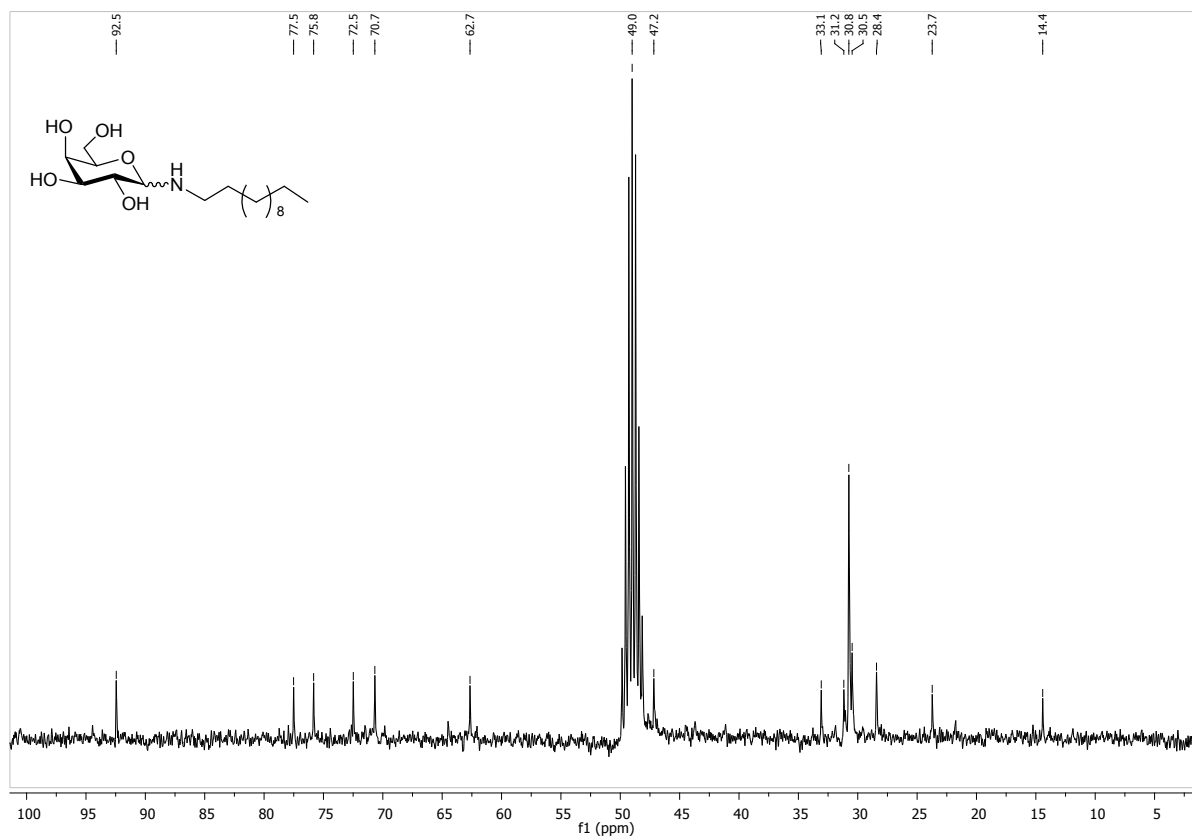
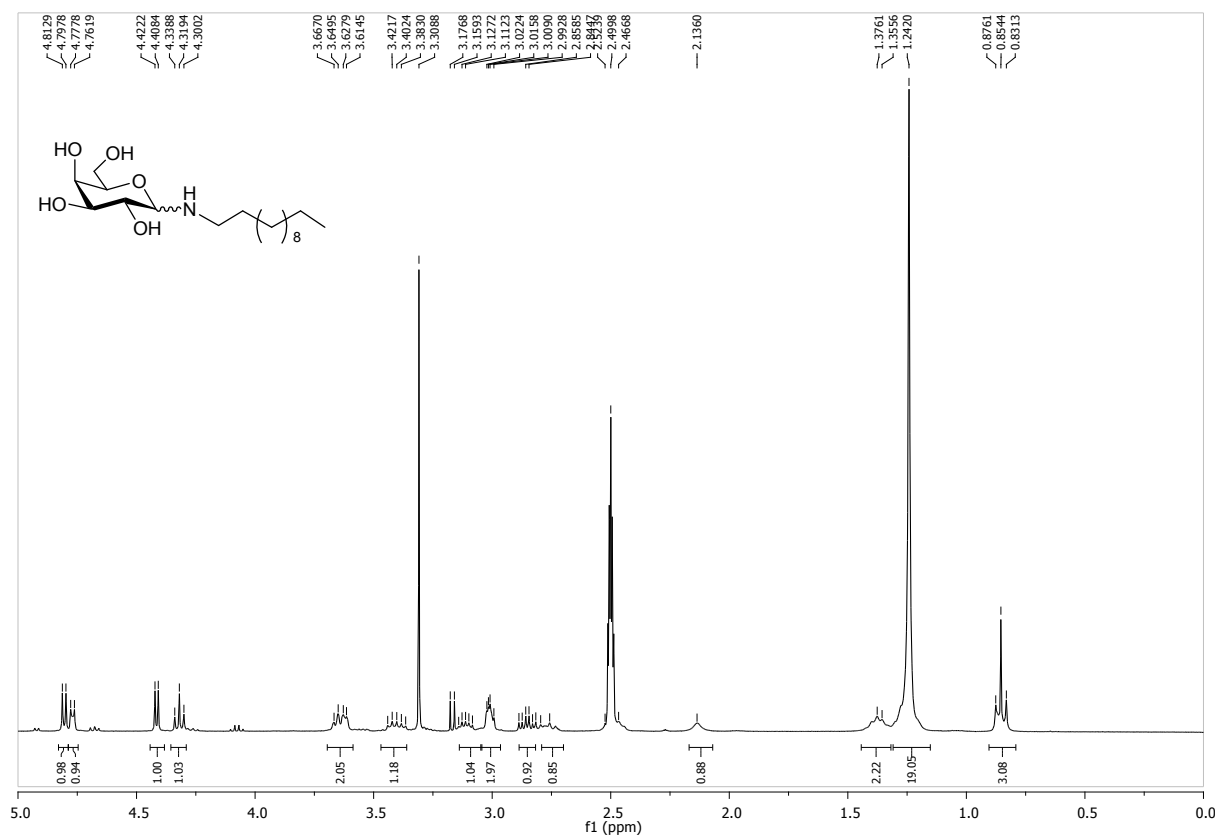
***N,N'*-bis-(L-rhamnosyl)-phenyl-1,4-diamine (1z)**



N-dodecyl-D-glucosylamine (2a)



N-dodecyl-D-galactosylamine (3a)



N-dodecyl-D-(4-*O*- α -D-glucopyranosyl)-glucosylamine (4a)

