Supporting Information

Effects of Linker and Liposome Anchoring on Lactose-functionalized Glycomacromolecules as Multivalent Ligands for Binding Galectin-3

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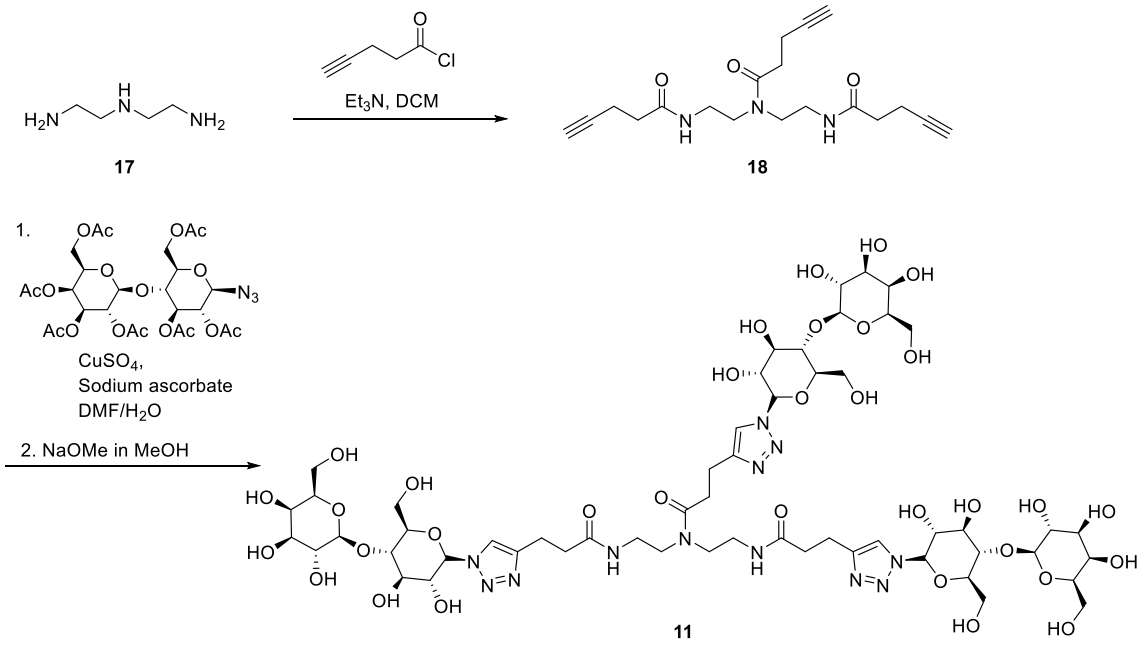
Contents

1. Additional information on synthesis of glycomacromolecules and liposome formulation



Scheme S 1: Scheme of the synthesis of compound **11**.

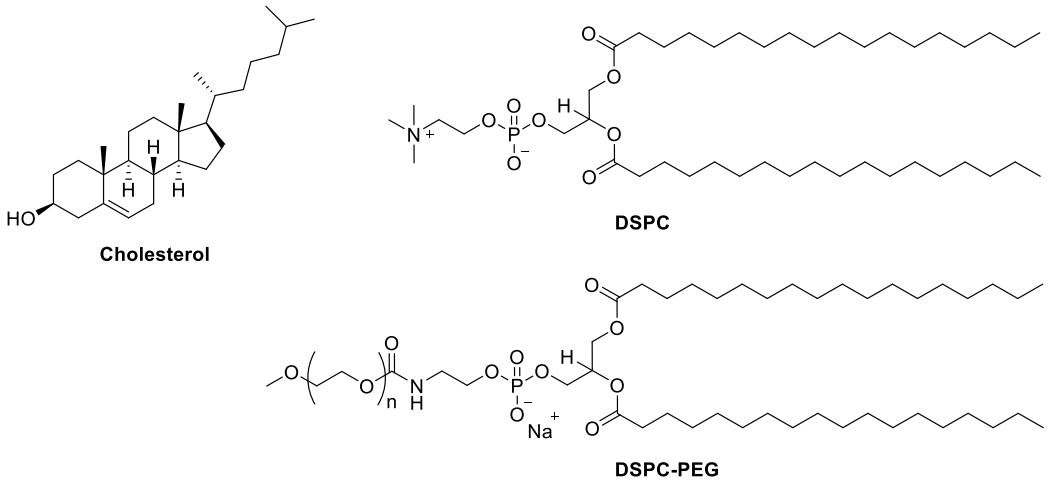


Figure S 1: Components used for the liposome formulation.

1.1. Additional information on the characterization of the functionalization degree of the liposomes

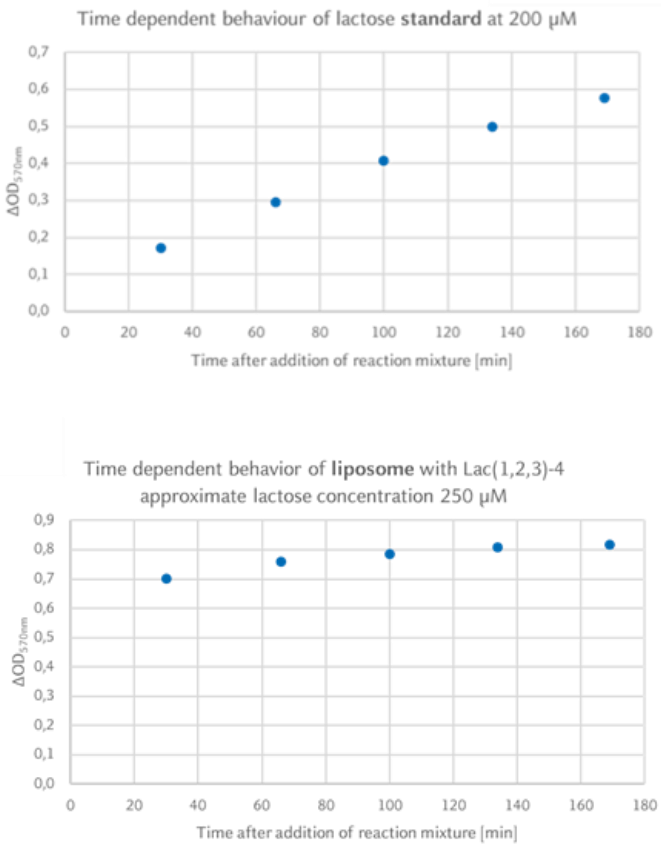
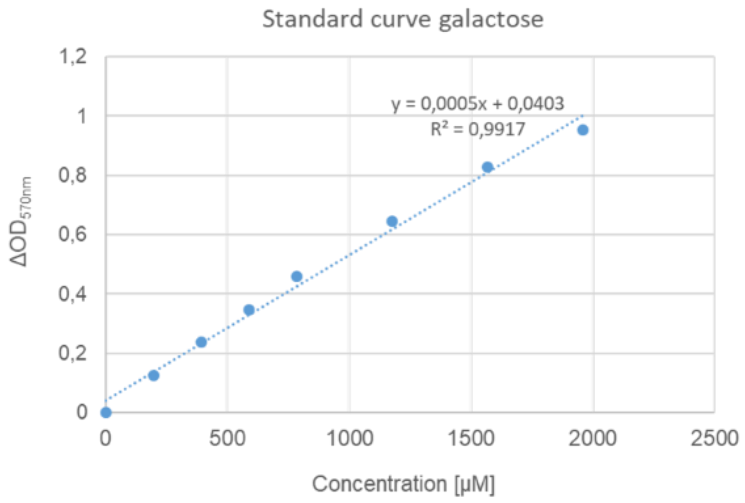


Figure S 2: Results of the Lactose-Assay Kit measuring the time dependent behavior of the absorbent resulting from the conversion of the lactose standard provided by the kit (top) and of the liposome **L10 (bottom)**.

A



B

Sample	Measured conc. [µM]	Theoretical conc.* [µM]
Liposome L4	143±19	149
Liposome L9	389±53	376
Liposome L10	320±54	447

Figure S 3: Results of the lactose-assay kit: Resulting lactose concentration (B) using the galactose standard curve (A).*calculated from total amount of weighted lipids in consideration of coupling efficiency and for 100 % of lactose-oligomer on outer surface of liposome.

2. Additional information on binding studies of glycomacromolecules

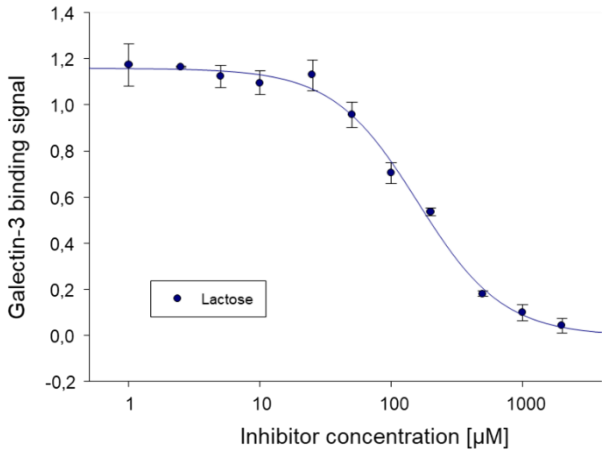


Figure S 4: ELISA inhibition curve of Gal-3 with lactose.

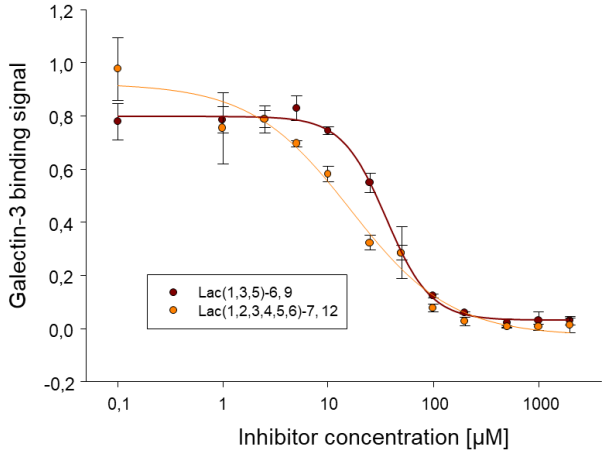


Figure S 5: ELISA inhibition curve of Gal-3 with glycomacromolecules **9** and **12**.

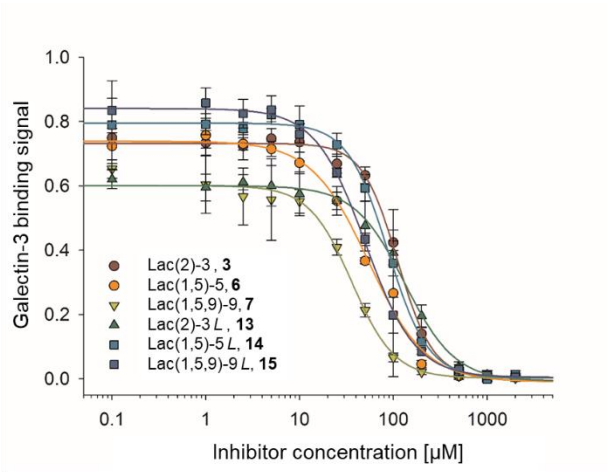


Figure S 6: ELISA inhibition curve of Gal-3 with glycomacromolecules **3,6,7** and **13-15.**

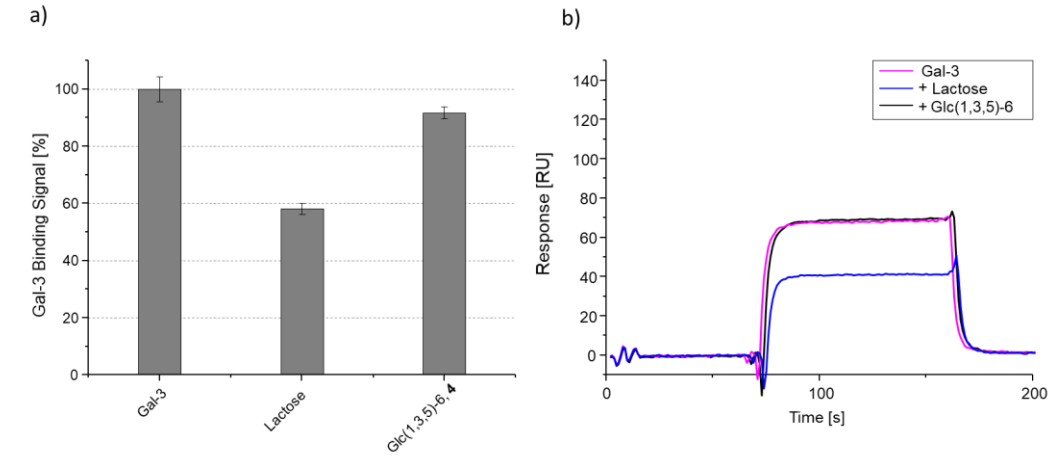


Figure S 7: Results from the SPR inhibition studies of Gal-3 with the controls lactose and Glc(1,3,5)-6, **16**.

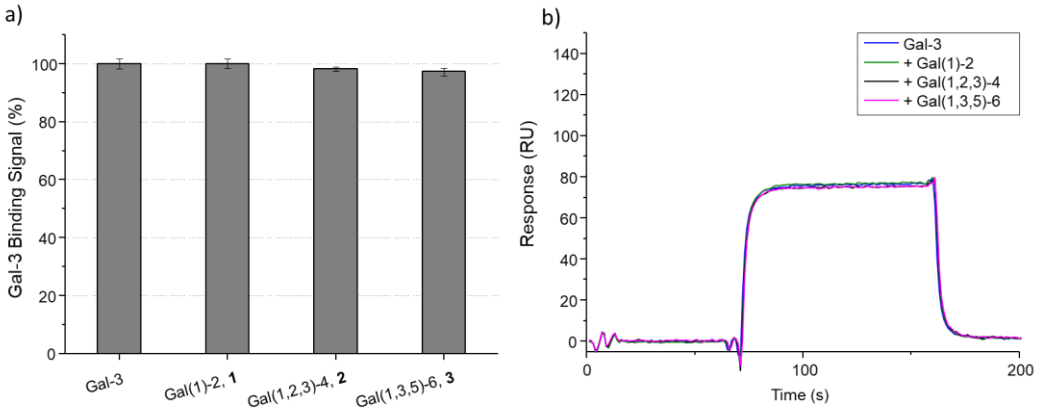


Figure S 8: Results from the SPR inhibition studies of Gal-3 with galactose samples **1, 2** and **3.**

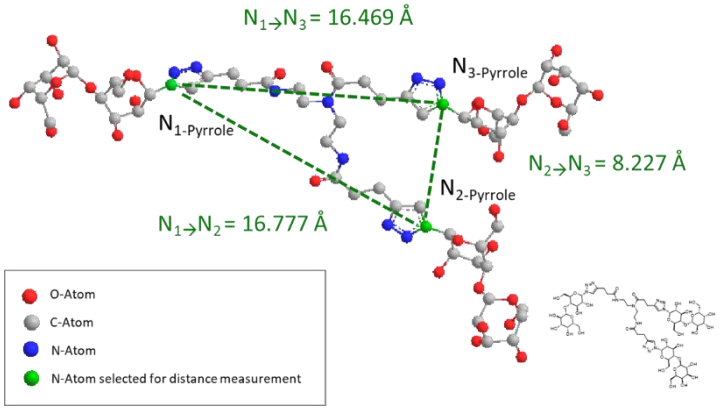


Figure S 9: Chem3D-simulation and measurement of the distances between the three nitrogen-atoms of the triazoles (marked in green) of Lac$_3$TPD **11** after MM2 conformational minimization**.**

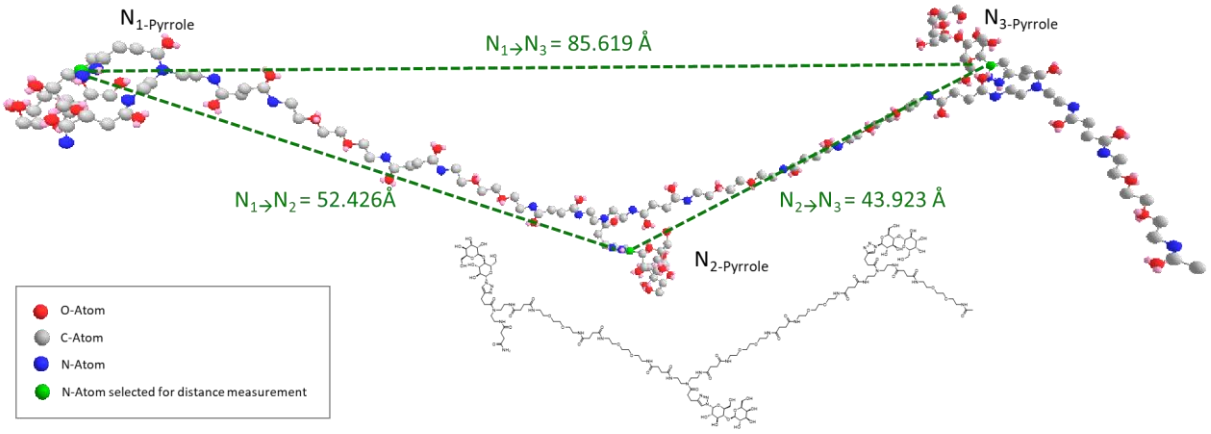


Figure S 10: Chem3D-simulation and measurement of the distances between the three nitrogen-atoms of the triazoles (marked in green) of Lac_3TPD **8** after MM2 conformational minimization**.**

3. Analytical data of glycomacromolecules

3.1. Gal(1)-2, **1**

^{1}H-NMR (300 MHz, Deuterium Oxide) δ [ppm]: 7.90 (s, 1 H, triazole-C*H*), 4.65 (t, J = 5.1 Hz, 2 H, -N-N-C*H*$_2$-), 4.37 (d, J = 7.8 Hz, 1 H, C*H*$_{anomer}$Gal), 4.29 (dt, J = 11.6, 4.8 Hz, 1 H, -C*H*$_{pyranose}$), 4.09 (dt, J = 11.1, 5.2 Hz, 1 H, C*H*$_{pyranose}$), 3.91 (dd, J = 3.4, 1.0 Hz, 1 H, --C*H*$_{pyranose}$), 3.78 – 3.72 (m, 2 H, C*H*$_{pyranose}$), 3.70 – 3.58 (m, 10 H, C*H*$_{pyranose}$, O-C*H*$_2$-), 3.54 – 3.29 (m, 13 H, C*H*$_{pyranose,}$ C=ONH-C*H*$_2$), 3.01 (t, J = 7.1 Hz, 2 H, CH=C-C*H*$_2$), 2.79 (t, J = 7.2 Hz, 2 H, CH=C-CH$_2$-C*H*$_2$), 2.56 – 2.41 (m, 8 H, , NHC=O-C*H*$_2$), 2.00 (s, 3H, -C*H*$_3$). HR-MS (ESI) calc. for $C_{33}H_{59}N_9O_{14}$ $[M+2H]^{2+}$ 402.7085; found 402.7084. Yield: 51 mg (63 %).

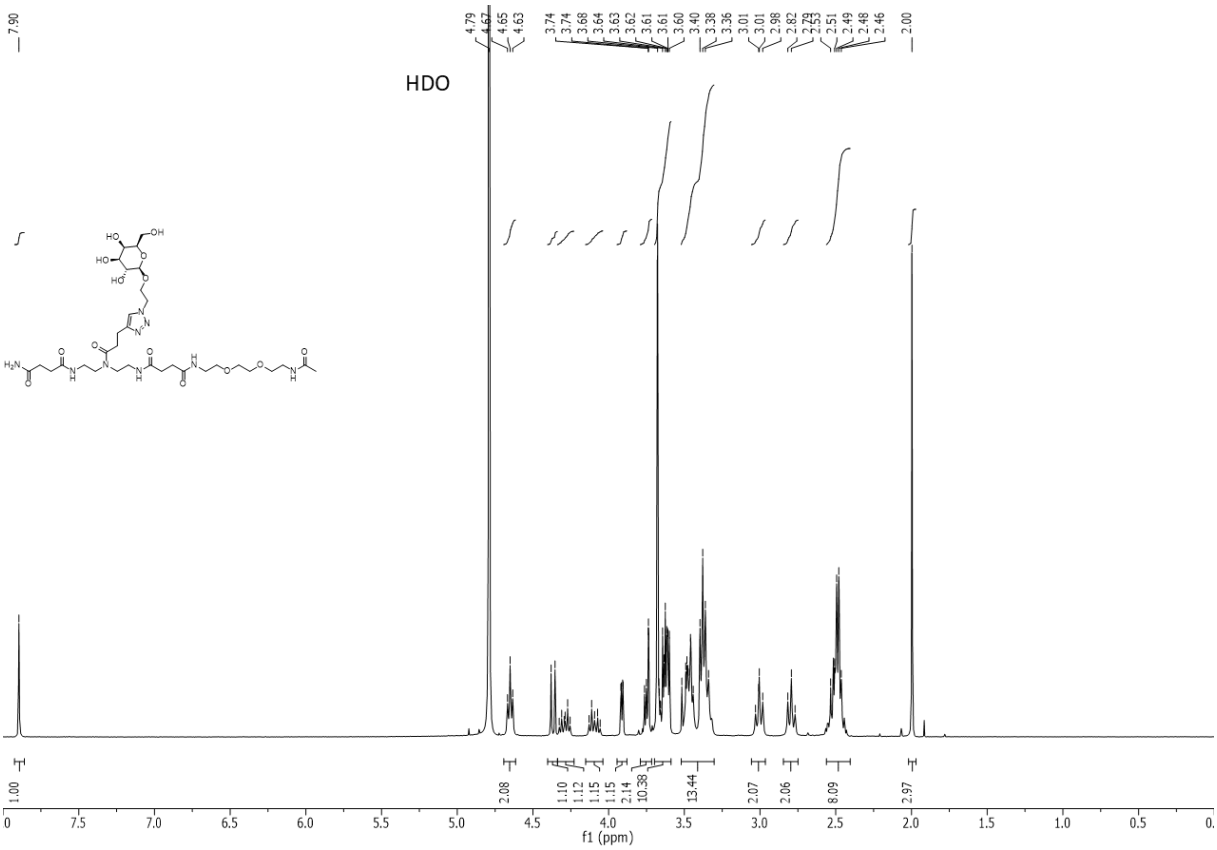


Figure S 11: ^{1}H-NMR spectrum of compound **1.**

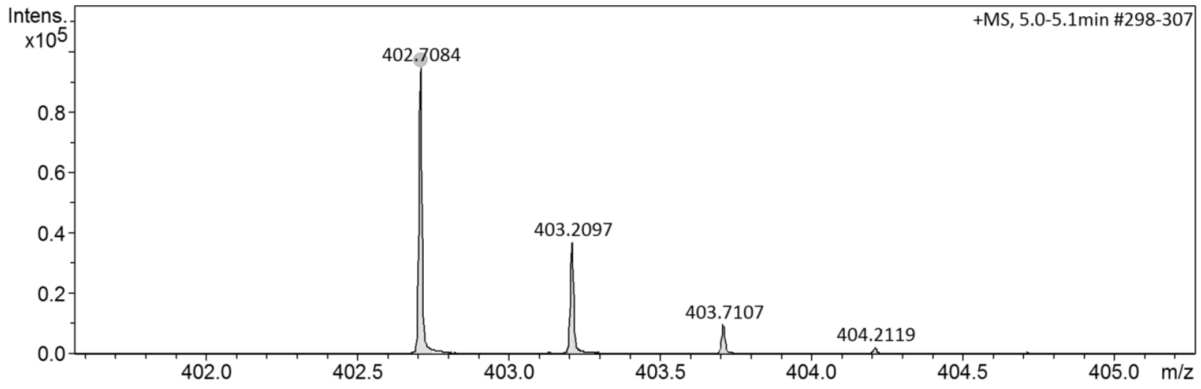


Figure S 12: HR-MS spectrum of compound **1**.

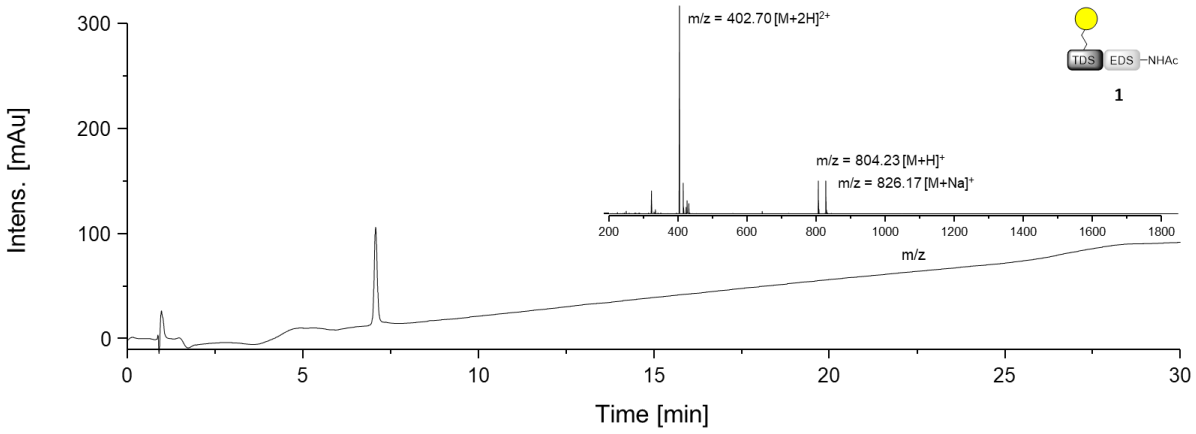


Figure S 13: RP-HPLC and ESI-MS spectrum of compound **1**.

3.2. Gal(1,3,5)-6, **2**

^{1}H-NMR (300 MHz, Deuterium Oxide) δ [ppm]: 7.90 (s, 3 H, triazole-CH), 4.65 (t, J = 5.0 Hz, 6 H, -N-N-C*H*$_2$-), 4.37 (d, J = 7.8 Hz, 3 H, C*H*$_{anomer}$Gal), 4.29 (dt, J = 9.9, 4.8 Hz, 3 H, C*H*$_{pyranose}$), 4.09 (dt, J = 11.0, 5.1 Hz, 3H, C*H*$_{pyranose}$), 3.91 (d, J = 3.3 Hz, 3H, C*H*$_{pyranose}$), 3.78 – 3.71 (m, 6 H, C*H*$_{pyranose}$), 3.70 – 3.56 (m, 30 H, C*H*$_{pyranose}$, O-C*H*$_2$-), 3.53 – 3.30 (m, 39H, C*H*$_{pyranose,}$ C=ONH-C*H*$_2$), 3.00 (t, J = 7.1 Hz, 6 H, CH=C-C*H*$_2$), 2.79 (t, J = 7.2 Hz, 6 H CH=C-CH$_2$-C*H*$_2$), 2.53-2.44 (m, 24 H, NH-C=O-C*H*$_2$-), 2.00 (s, 3H, -C*H*$_3$). HR-MS (ESI) calc. for $C_{95}H_{164}N_{25}O_{40}$ $[M+3H]^{3+}$ 765.0517; found 765.0522. Yield: 119 mg (52 %).

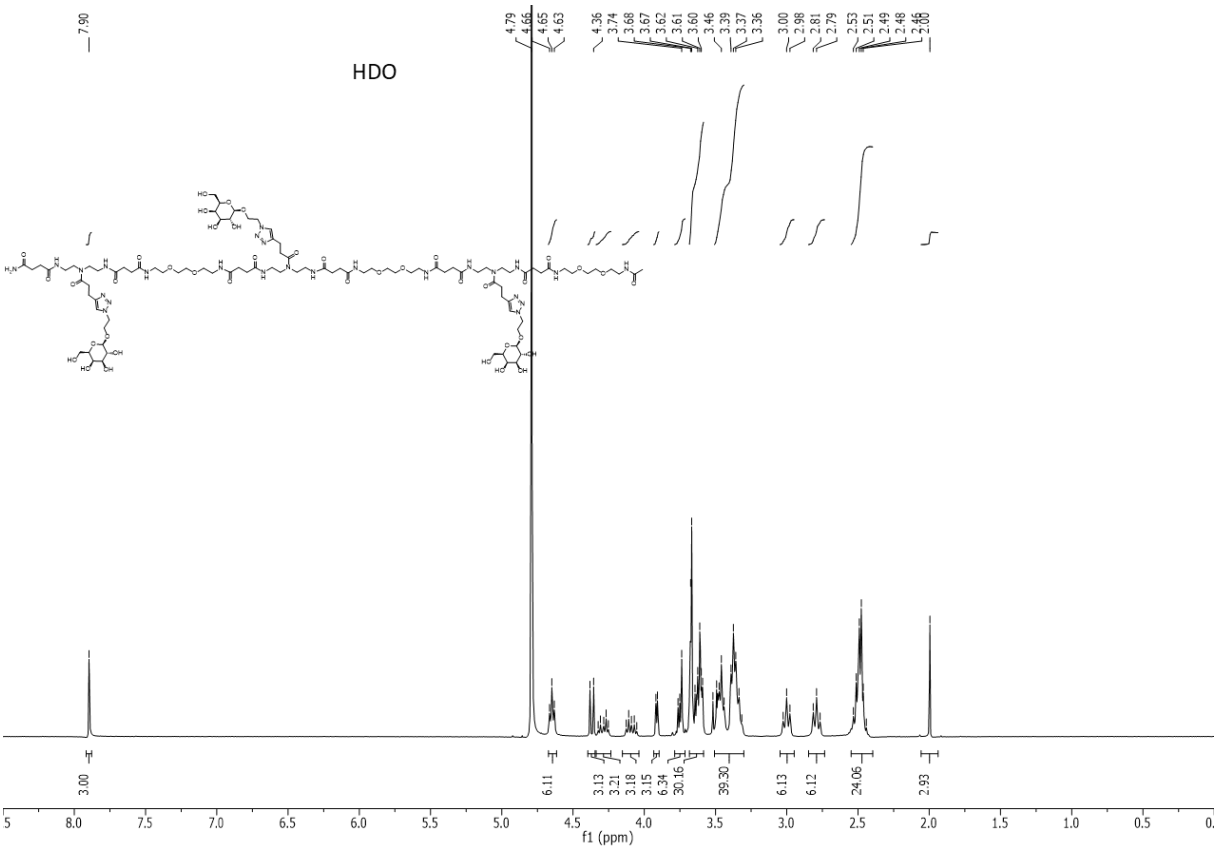


Figure S 14: ^{1}H-NMR spectrum of compound **2.**

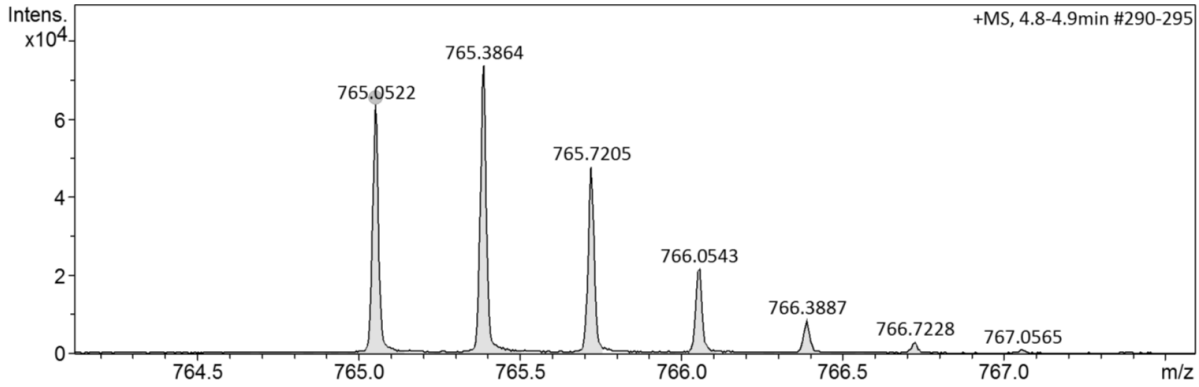


Figure S 15: HR-MS spectrum of compound **2**.

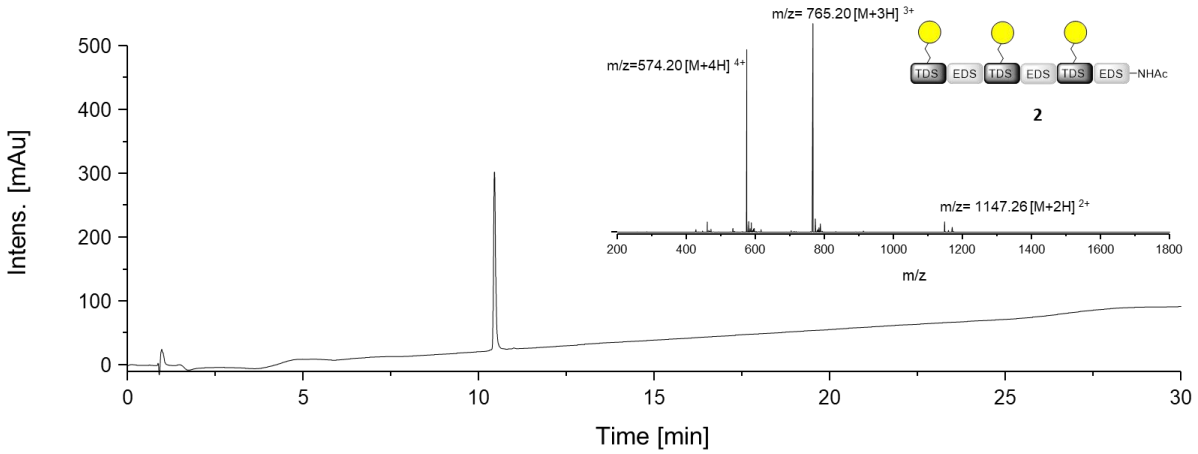


Figure S 16: RP-HPLC and ESI-MS spectrum of compound **2**.

3.3 Gal(1,2,3)-4, **3**

^{1}H-NMR (300 MHz, D_2O) δ [ppm] 7.89 (s, 3H, triazole-C*H*), 4.64 (t, J = 4.7 Hz, 6H, -N-N-CH_2-), 4.37 (d, J = 7.8 Hz, 3H, CH_{anomer}Gal), 4.28 (dt, J = 9.9, 4.7 Hz, 3H, -C$H_{pyranose}$), 4.09 (dt, J = 10.8, 5.0 Hz, 3H, -C$H_{pyranose}$), 3.91 (d, J = 3.0 Hz, 3H, -C$H_{pyranose}$), 3.81 – 3.71 (m, 6H, -C$H_{pyranose}$), 3.70 – 3.58 (m, 15H, C$H_{pyranose}$, O-CH_2-), 3.53 – 3.29 (m, 30H, C$H_{pyranose,}$ C=ONH-CH_2), 3.04 – 2.92 (m, 6H, CH=C-CH_2), 2.78 (t, J = 7.0 Hz, 6H, CH=C-CH$_2$-CH_2), 2.53-2.42 (m, 16H, -N-C=O-CH_2-), 1.99 (s, 3H, -CH_3). HR-MS (ESI) calc. for $C_{75}H_{128}N_{21}O_{32}$ $[M+3H]^{3+}$ 611.6339; found 611.6340. Yield: 90 mg (49 %).

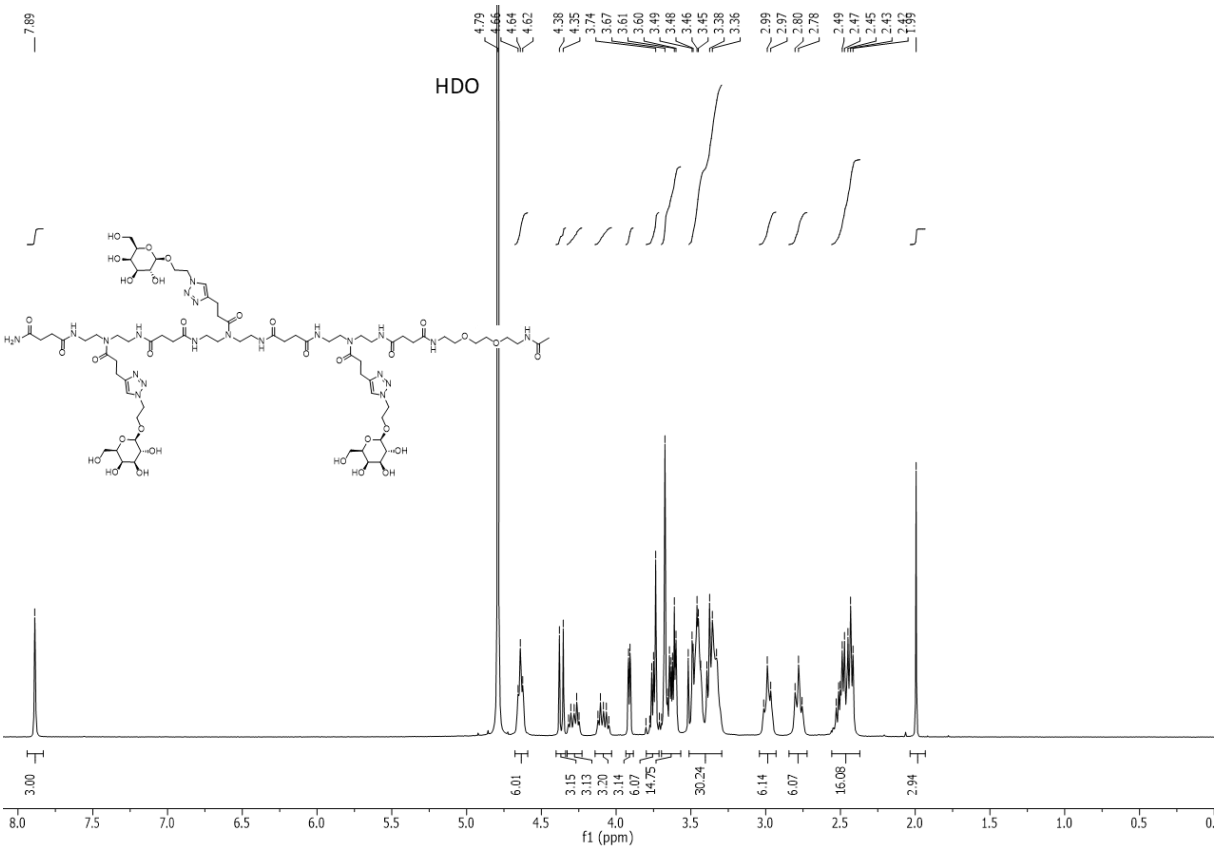


Figure S 17: ^{1}H-NMR spectrum of compound **3.**

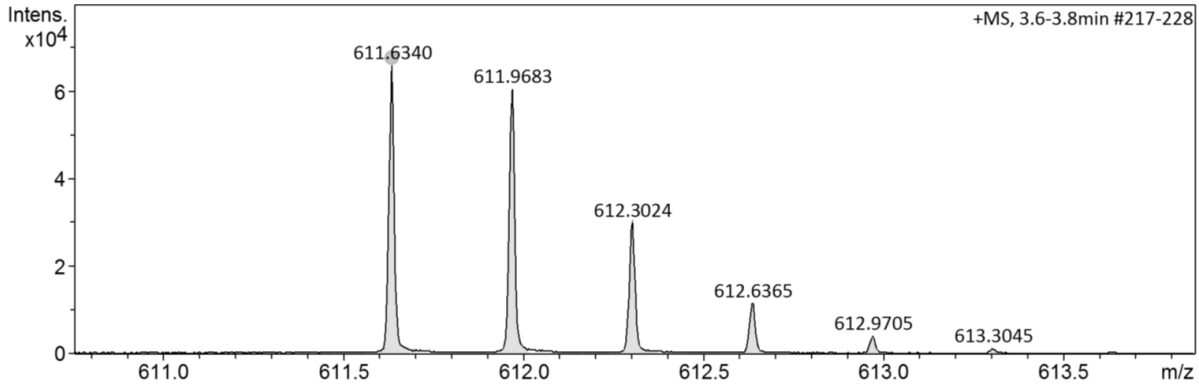


Figure S 18: HR-MS spectrum of compound **3**.

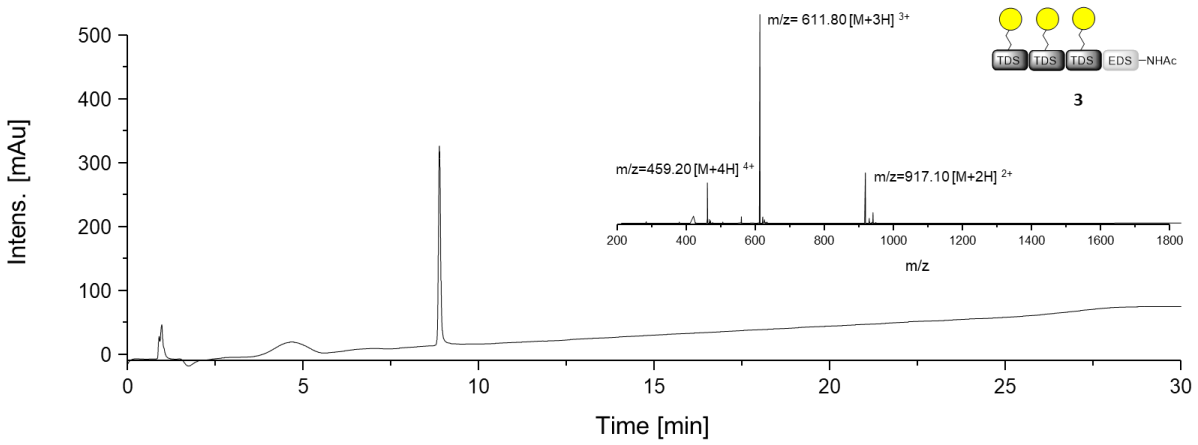


Figure S 19: RP-HPLC and ESI-MS spectrum of compound **3**.

3.4 Lac(1)-2, **4**

^{1}H NMR (300 MHz, Deuterium Oxide) δ [ppm]: 8.05 (s, 1 H, triazole-C*H*), 5.75 (d, J = 9.2 Hz, 1H, C*H*$_{anomer}$Glc), 4.52 (d, J = 7.7 Hz, 1H, C*H*$_{pyranose}$, O-C*H*$_2$-), 4.10 – 3.73 (m, 10H, C*H*$_{pyranose}$, O-C*H*$_2$-), 3.72 – 3.57 (m, 10H,), 3.47-3.31 (m 12 H, C=ONH-C*H*$_2$), 3.05 (t, J = 7.1 Hz, 2 H, CH=CH-C*H*$_2$), 2.82 (t, J = 7.0 Hz, 2 H, CH=CH-CH$_2$-C*H*$_2$), 2.58 – 2.43 (m, 8 H, NHC=O-C*H*$_2$) , 2.00 (s, 3 H, -C*H*$_3$). HR-MS (ESI) calc. for $C_{37}H_{65}N_9O_{18}$ $[M+2H]^{2+}$ 461.7218; found 461.7217. Yield: 51 mg (55 %).

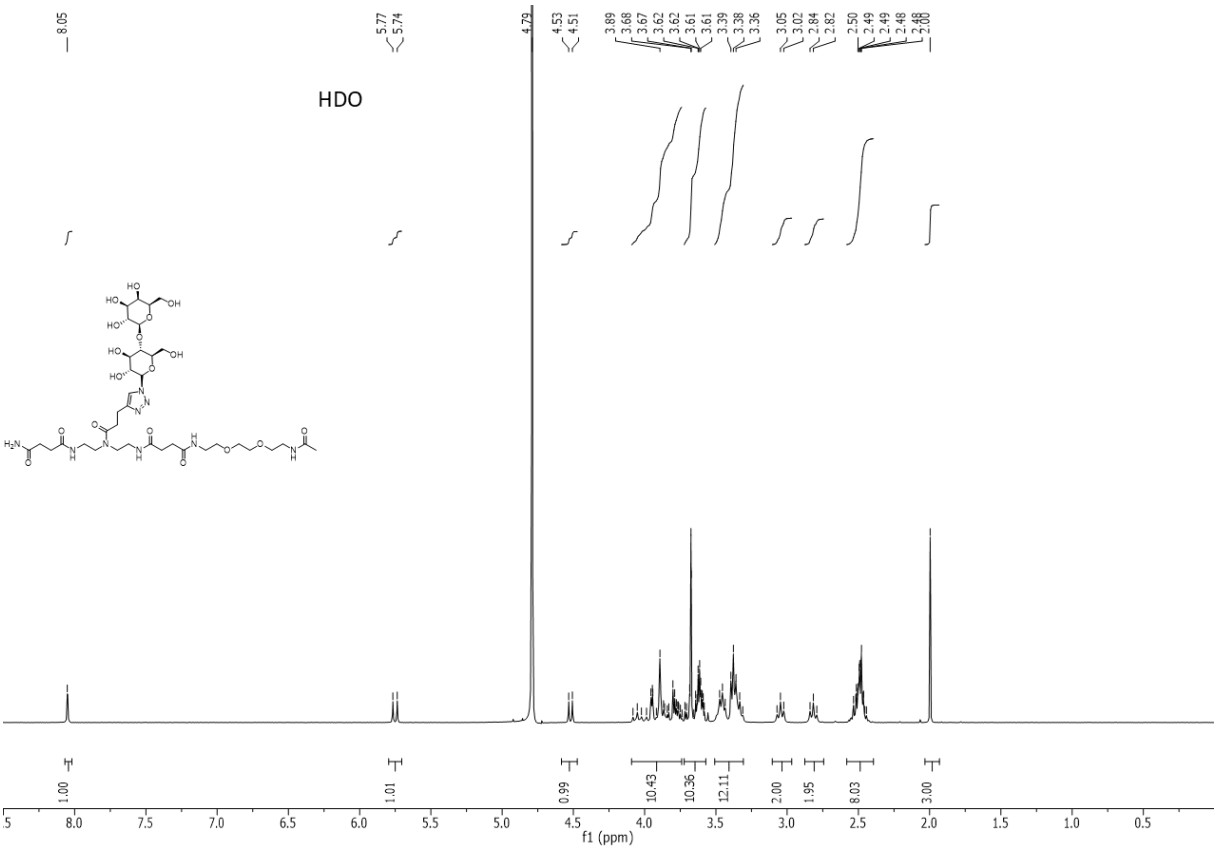


Figure S 20: ^{1}H-NMR spectrum of compound **4.**

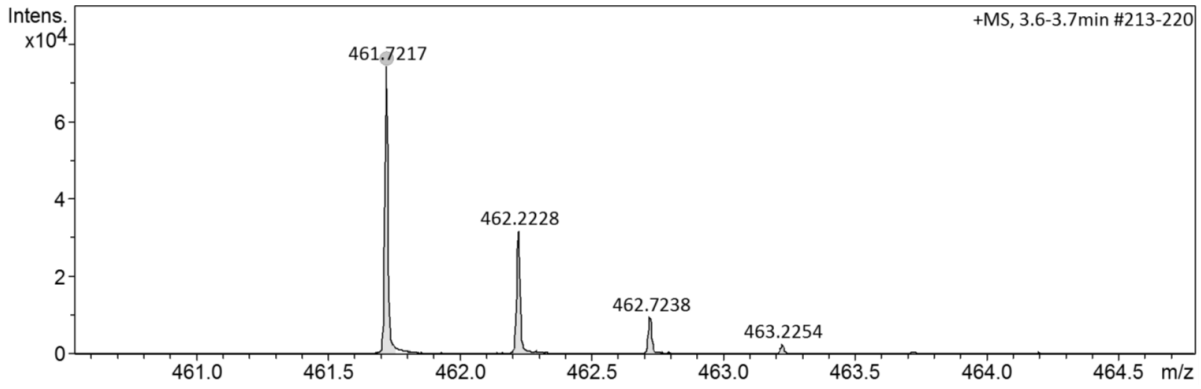


Figure S 21: HR-MS spectrum of compound **4**.

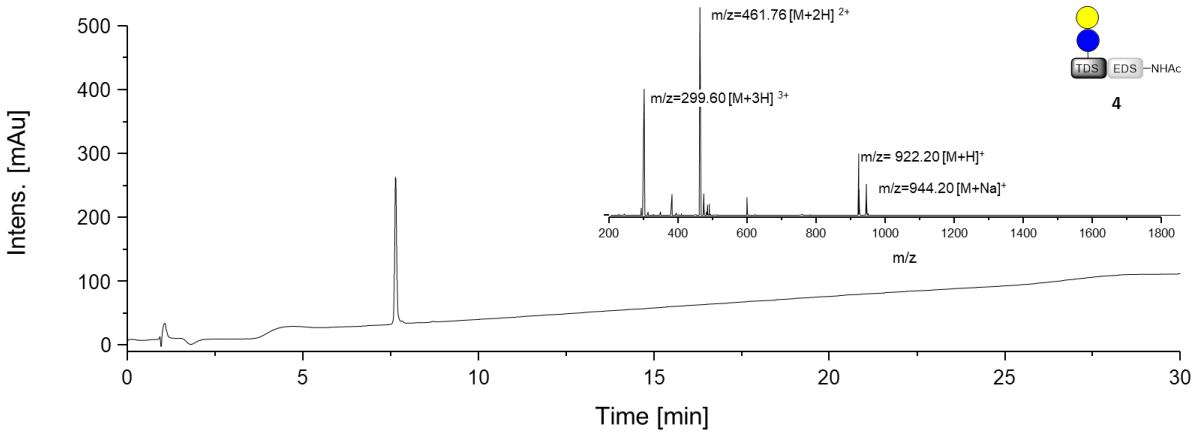


Figure S 22: RP-HPLC and ESI-MS spectrum of compound **4**.

3.5 Lac(1)-2, **4***

^{1}H-NMR (600 MHz, Deuterium Oxide) δ [ppm]: 8.44 (br s, 1H, NH), 8.03 (m, 1H, triazole-C*H*), 5.74 (d, ^{3}J = 9.3 Hz,1H, CH_{anomer}Glc), 4.50 (d, ^{3}J = 7.8 Hz, 1H, CH_{anomer}-Gal), 4.03 (t, ^{3}J = 9.0 Hz, 1H, CH_{pyranose}), 3.97 – 3.55 (m, 19H, O-CH_2-, CH_{pyranose}), 3.45 (m, 4H, C=ONH-CH_2), 3.36 (m, 4H, C=ONH-CH_2), 3.32 (t, 3J = 6.1 Hz, 2H, C=ONH-CH_2), 3.20 (m, 2H, CH_2-NH_2), 3.03 (t, ^{3}J = 7.1 Hz, 2H, CH=CH-CH_2), 2.80 (t, ^{3}J = 7.2 Hz, 2H, CH=CH-CH_2-CH_2), 2.47 (m, 8H, NHC=O-CH_2). HR-MS (ESI) calc. for $C_{35}H_{63}N_9O_{17}$ $[M+2H]^{2+}$ 440.72; found 440.72. Yield: 48 mg (54 %).

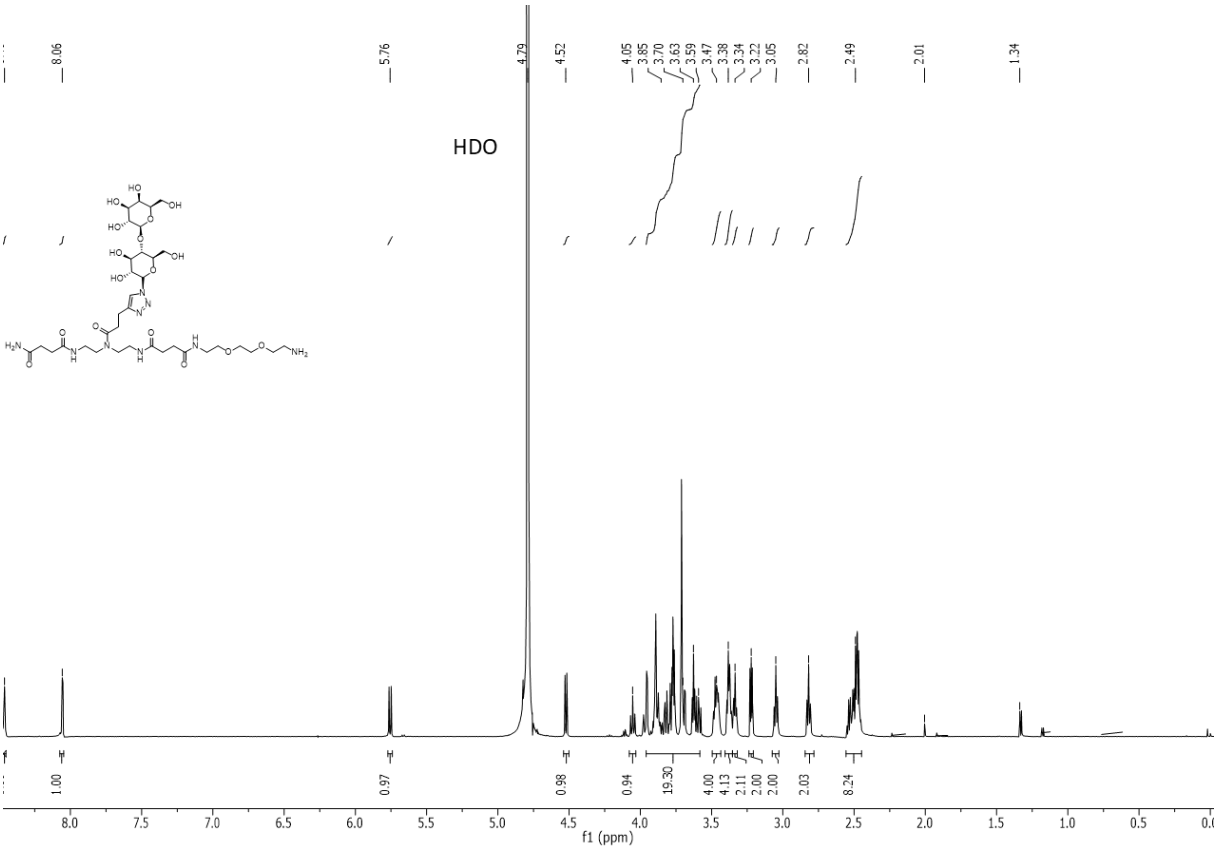


Figure S 23: ^{1}H-NMR spectrum of compound **4*.**

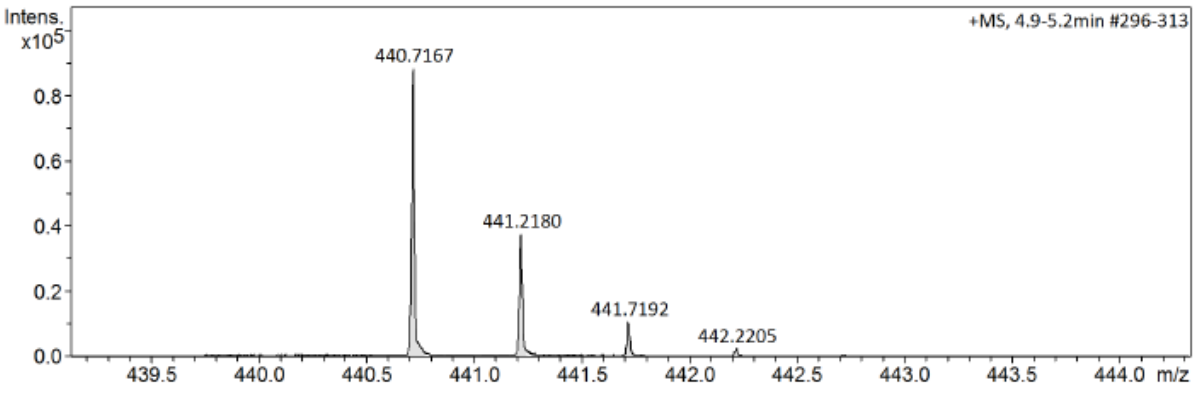


Figure S 24: HR-MS spectrum of compound **4***.

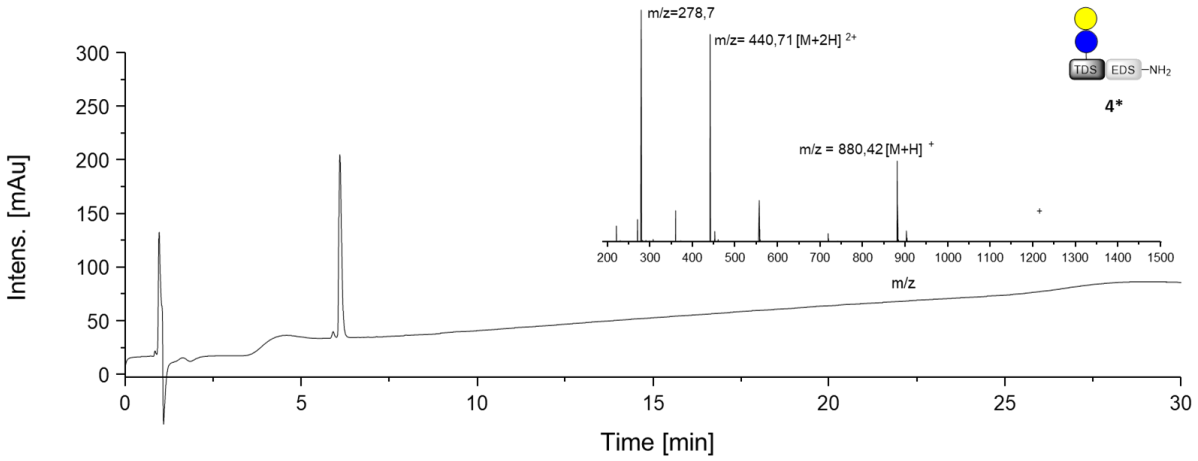


Figure S 25:RP-HPLC and ESI-MS spectrum of compound **4***.

3.6 Lac(2)-3, **5**

^{1}H-NMR (300 MHz, Deuterium Oxide) δ [ppm]: 8.05 (s, 1H, triazole-C*H*); 5.75 (d, ^{3}J = 9.2 Hz, 1H, C*H*$_{anomer}$Glc), 4.52 (d, ^{3}J = 7.7 Hz, 1H, C*H*$_{anomer}$-Gal), 4.09-3.92 (m, 3H, C*H*$_{pyranose}$), 3.93-3.82 (m, 4H, C*H*$_{pyranose}$), 3.81-3.73 (m, 3H, C*H*$_{pyranose}$), 3.72-3.54 (m, 18H, C*H*$_{pyranose}$, C*H*$_{2\ pyranose}$, O-C*H*$_2$-), 3.51-3.28 (m, 16H, C*H*$_{pyranose}$, C=ONH-C*H*$_2$), 3.04 (t, ^{3}J = 7.1 Hz, 2H, CH=CH-C*H*$_2$), 2.81 (t, ^{3}J = 7.1 Hz, 2H, CH=CH-CH$_2$-C*H*$_2$), 2.57-2.45 (m, 12H, NHC=O-C*H*$_2$), 1.99 (s, 3H, C*H*$_3$). HR-MS (ESI): m/z calc. for $C_{47}H_{83}N_{11}O_{22}$ $[M+2H]^{2+}$ 576.7852; found 576.7847. Yield: 267.1 mg (66 %).

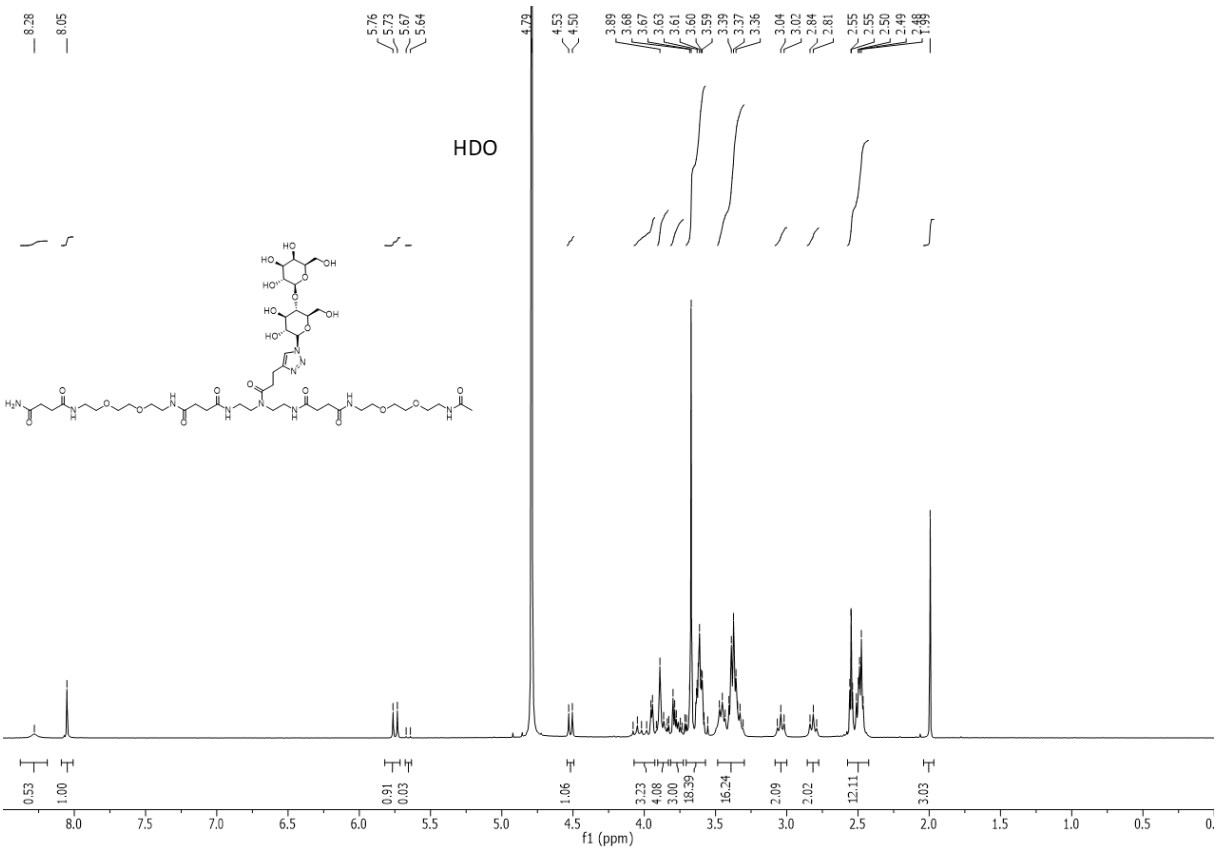


Figure S 26: ^{1}H-NMR spectrum of compound **5**.

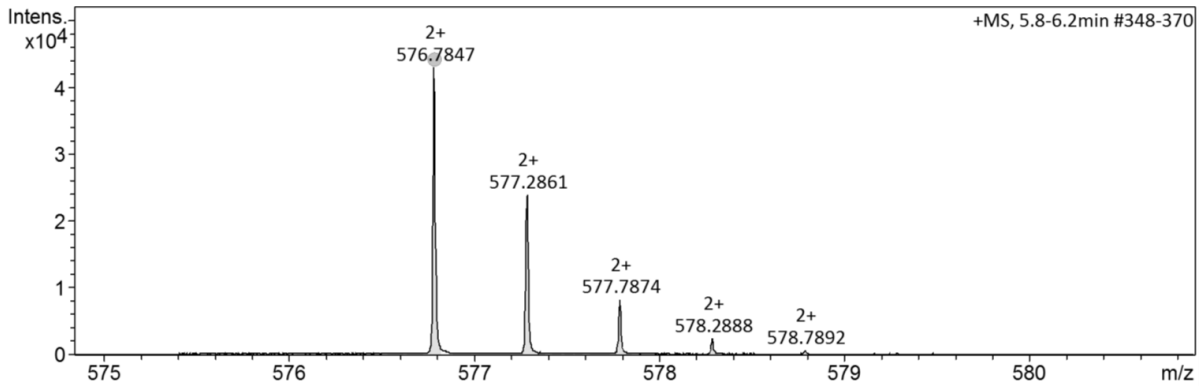


Figure S 27: HR-MS spectrum of compound **5**.

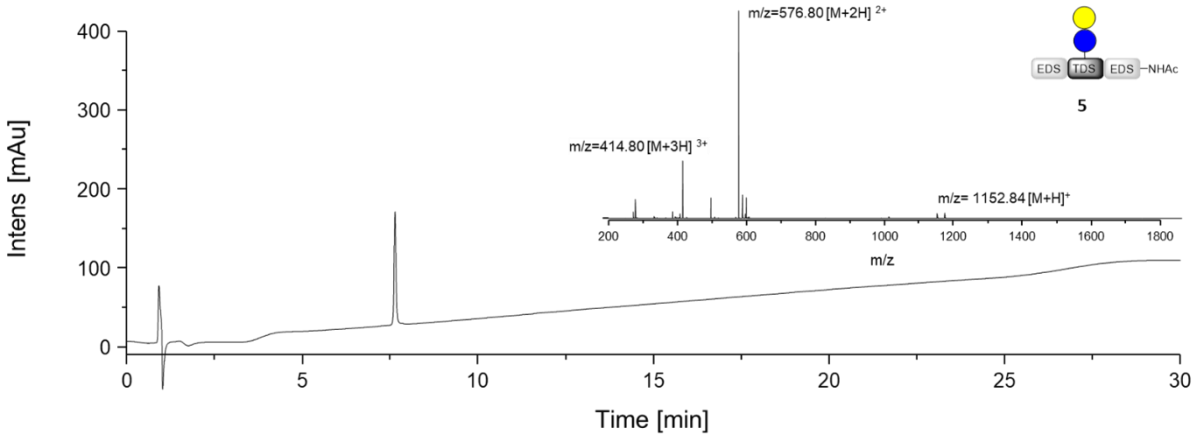


Figure S 28: RP-HPLC and ESI-MS spectrum of compound **5**.

3.7 Lac(1,5)-5, **6**

^{1}H-NMR (300 MHz, Deuterium Oxide) δ [ppm]: 8.05 (s, 2H, triazole-C*H*), 5.75 (d, 2H, ^{3}J = 9.1 Hz, C*H*$_{anomer}$Glc), 4.52 (d, ^{3}J = 7.7 Hz, 2H, C*H*$_{anomer}$-Gal), 4.10-3.73 (m, 18H, C*H*$_{pyranose}$), 3.72-3.54 (m, 30H, C*H*$_{pyranose}$, C*H*$_{2\ pyranose,}$ O-C*H*$_{2}$-), 3.51-3.29 (m, 28H, C*H*$_{pyranose}$ C=ONH-C*H*$_{2}$), 3.04 (t, ^{3}J = 7.1 Hz, 4H, CH=CH-C*H*$_{2}$), 2.81 (t, ^{3}J = 6.5 Hz, 4H, CH=CH-CH$_{2}$-C*H*$_{2}$), 2.56-2.44 (m, 20H, NHC=O-C*H*$_{2}$), 1.94 (s, 1,5H, C*H*$_{3}$), 1.92 (s, 1,5H, C*H*$_{3}$). HR-MS (ESI): m/z calc. for $C_{82}H_{142}N_{19}O_{39}$ $[M+3H]^{3+}$ 672.3232; found: 672.3225. Yield: 145.0 mg (28 %).

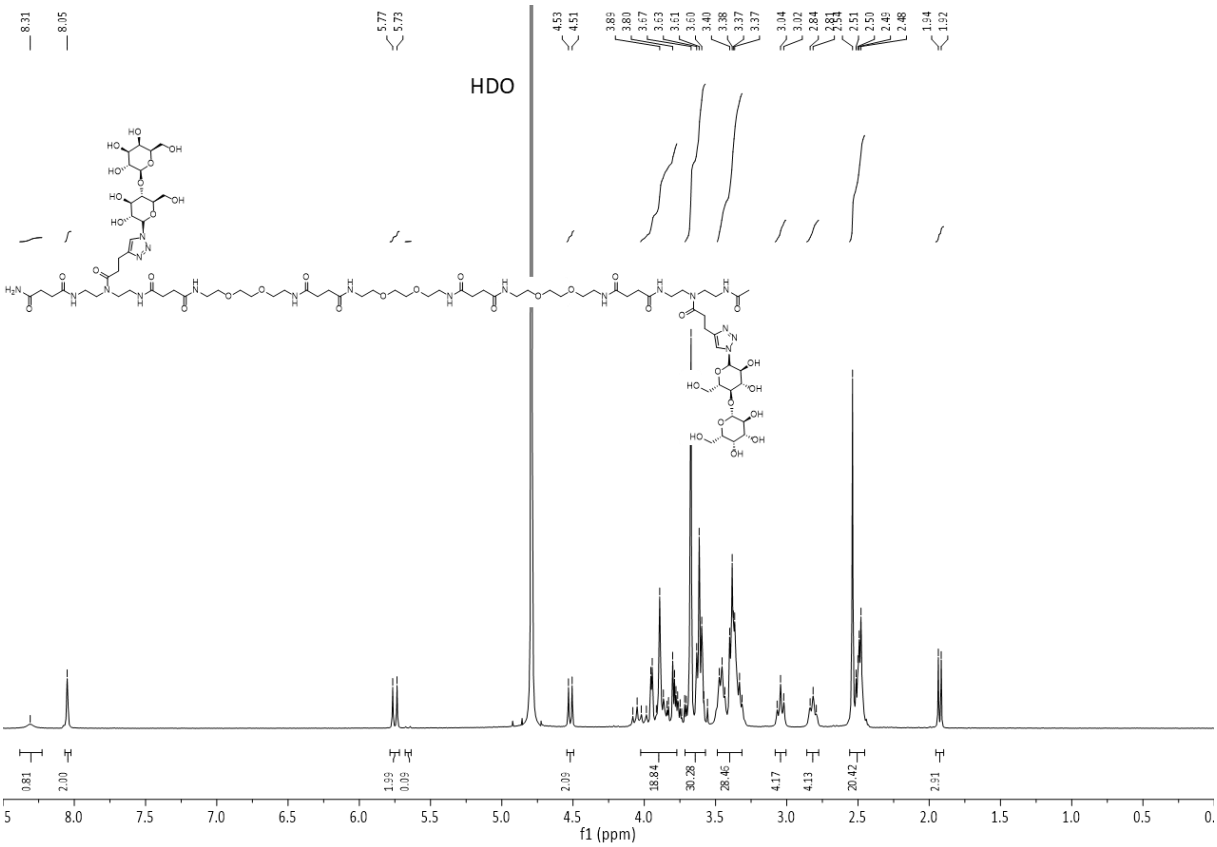


Figure S 29: ^{1}H-NMR spectrum of compound **6**.

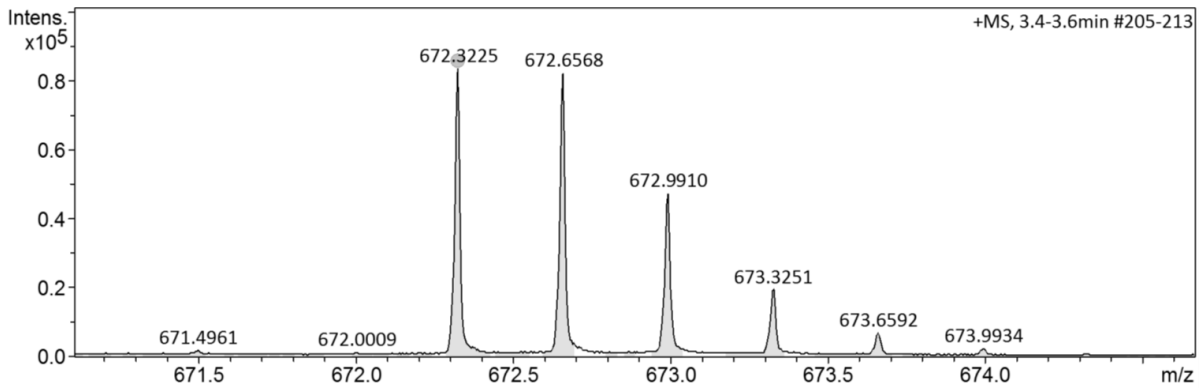


Figure S 30: HR-MS spectrum of compound **6**.

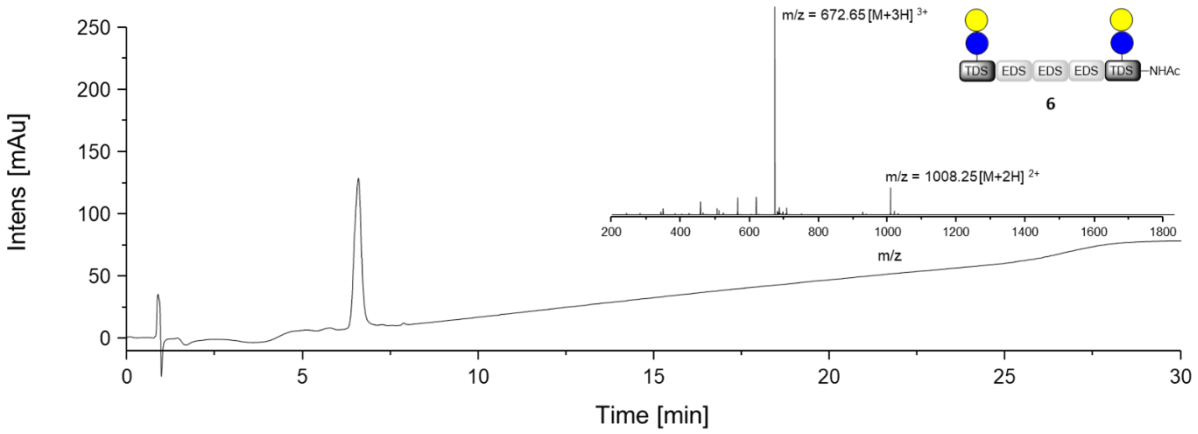


Figure S 31: RP-HPLC and ESI-MS spectrum of compound **6**.

3.8 Lac(1,5,9)-9, **7**

^{1}H-NMR (300 MHz, Deuterium Oxide) δ [ppm]: 8.05 (s, 3H, triazole-C*H*), 5.75 (d, ^{3}J = 9.2 Hz, 3H, C*H*$_{anomer}$Glc), 4.52 (d, 3H, 3J = 7.7 Hz, C*H*$_{anomer}$-Gal), 4.10-3.92 (m, 8H, C*H*$_{pyranose}$), 3.92-3.82 (m, 14 H, C*H*$_{pyranose}$), 3.82-3.73 (m, 6H, C*H*$_{pyranose}$), 3.72-3.55 (m, 54H, C*H*$_{pyranose}$, C*H*$_{2\ pyranose,}$ O-C*H*$_2$-), 3.51-3.28 (m, 50H, C*H*$_{pyranose,}$ C=ONH-C*H*$_2$), 3.04 (t, ^{3}J = 7.0 Hz, 6H, CH=CH-C*H*$_2$), 2.81 (t, ^{3}J = 7.0 Hz, 6H, CH=CH-CH$_2$-C*H*$_2$), 2.57-2.42 (m, 36H, NHC=O-C*H*$_2$), 1.94 (s, 1,5H, C*H*$_3$), 1.92 (s, 1,5H, C*H*$_3$). HR-MS (ESI): m/z calc. for $C_{137}H_{237}N_{31}O_{64}$ $[M+4H]^{4+}$ 835.1555; found 835.1562. Yield: 76 mg (32 %).

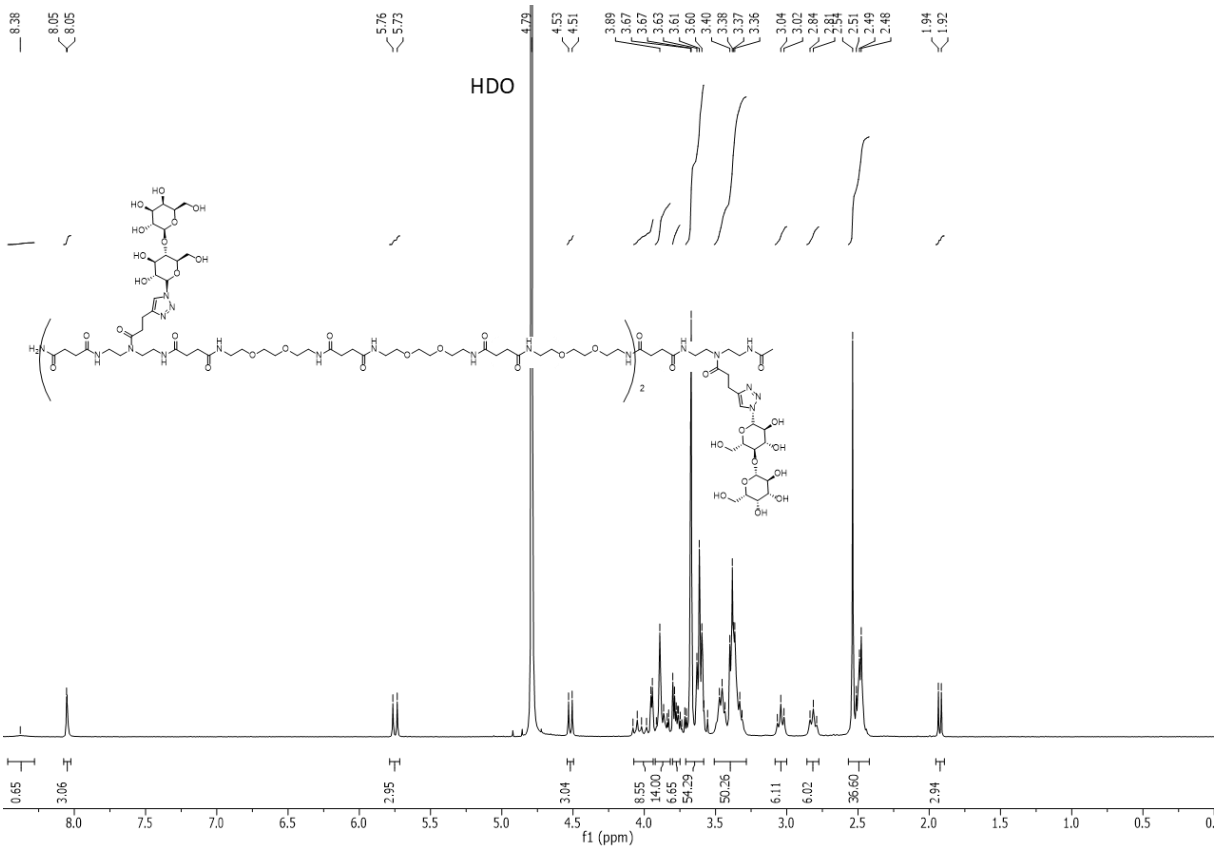


Figure S 32: ^{1}H-NMR spectrum of compound **7.**

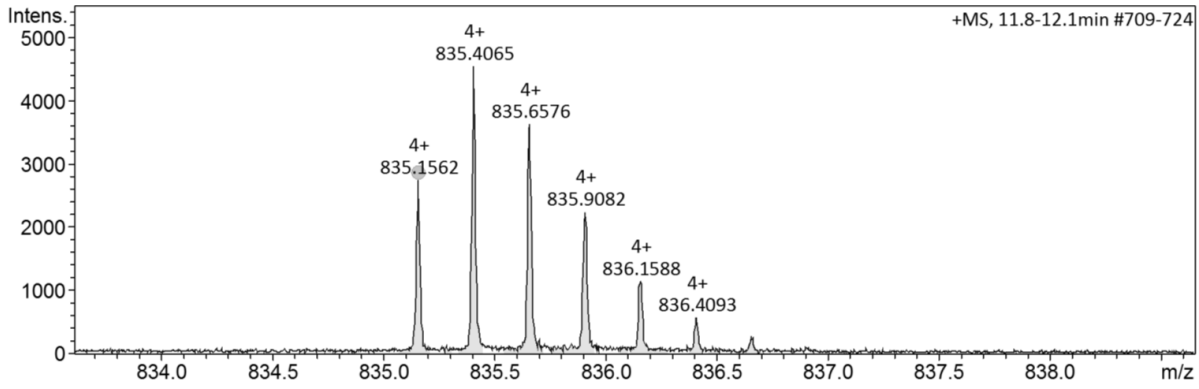


Figure S 33: HR-MS spectrum of compound **7**.

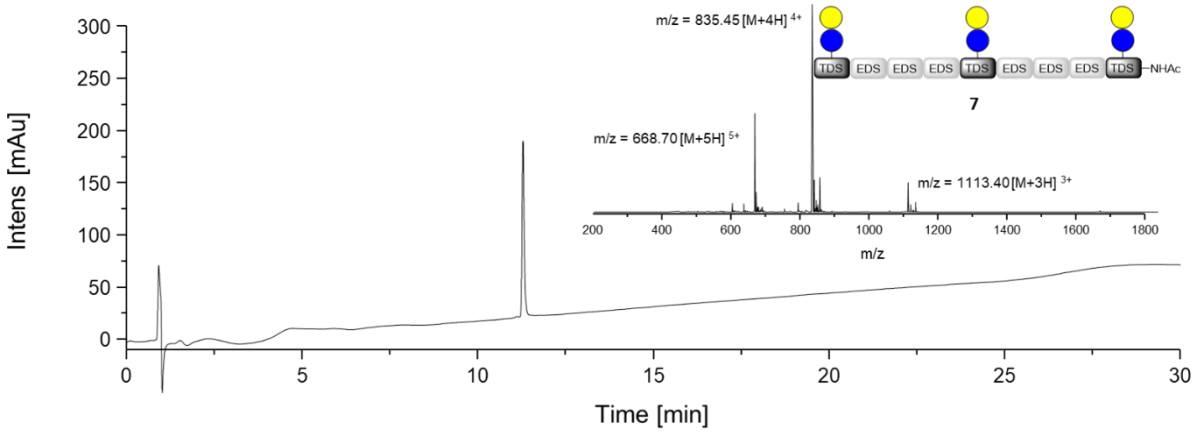


Figure S 34: RP-HPLC and ESI-MS spectrum of compound **7**.

3.9 Lac(1,4,7)-8, **8**

^{1}H-NMR (300 MHz Deuterium Oxide) δ [ppm]: 8.05 (s, 3H, triazole-C*H*), 5.75 (d, ^{3}J = 9.2 Hz, 3H, C*H*$_{anomer}$Glc), 4.52 (d, ^{3}J = 7.6 Hz, 3H, C*H*$_{anomer}$-Gal), 4.11 – 3.53 (m, 77H, C*H*$_{pyranose}$, C*H*$_{2\ pyranose,}$ O-C*H*$_{2}$-), 3.53 – 3.24 (m, 43H, C*H*$_{pyranose}$, C*H*$_{2\ pyranose,}$ C=ONH-C*H*$_{2}$), 3.04 (t, ^{3}J = 7.1 Hz, 6H, CH=CH-C*H*$_{2}$), 2.81 (t, ^{3}J = 7.1 Hz, 6H, CH=CH-CH$_{2}$-C*H*$_{2}$), 2.59 – 2.38 (m, 32H, NHC=O-C*H*$_{2}$), 1.99 (s, 3H, C*H*$_{3}$). HR-MS (ESI) calc. for $C_{127}H_{219}N_{29}O_{60}$ $[M+4H]^{4+}$ 777.6239; found 777.6229. Yield: 107 mg (35 %).

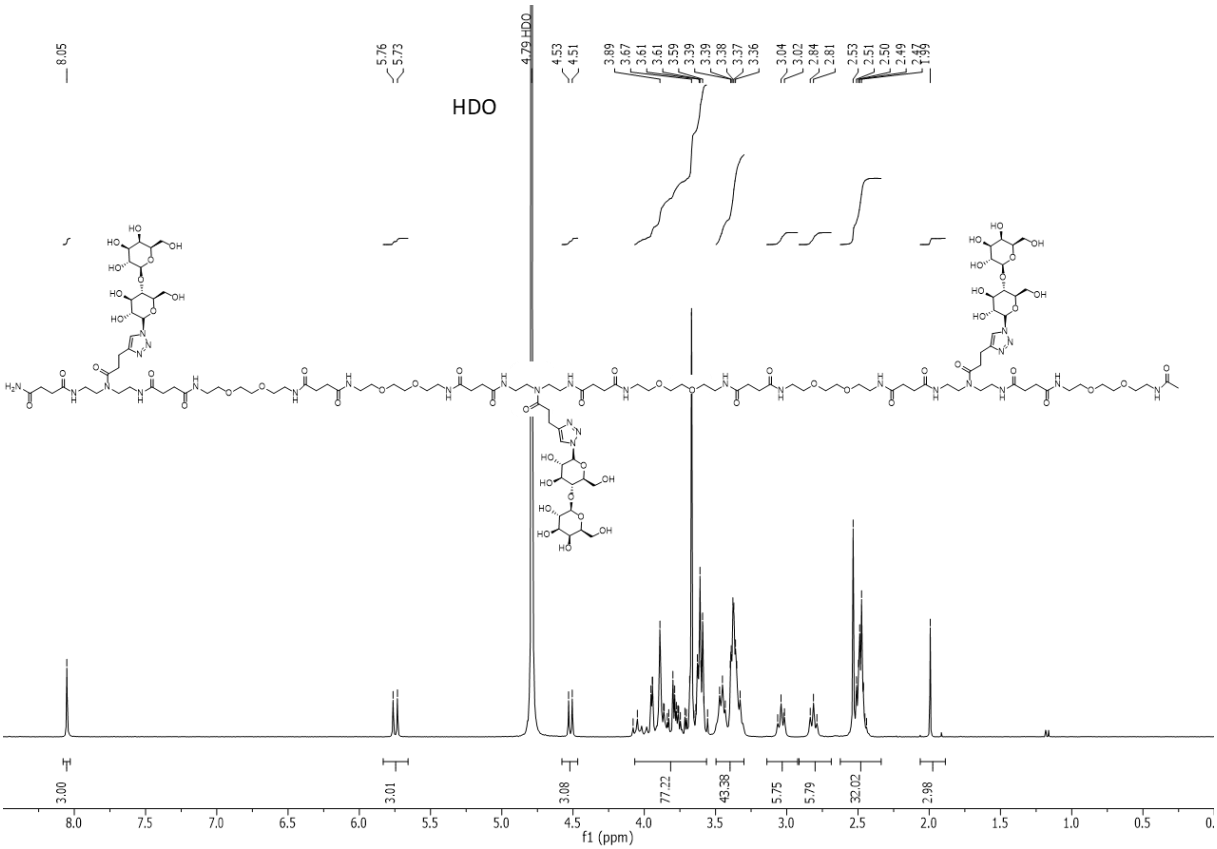


Figure S 35: ^{1}H-NMR spectrum of compound **8.**

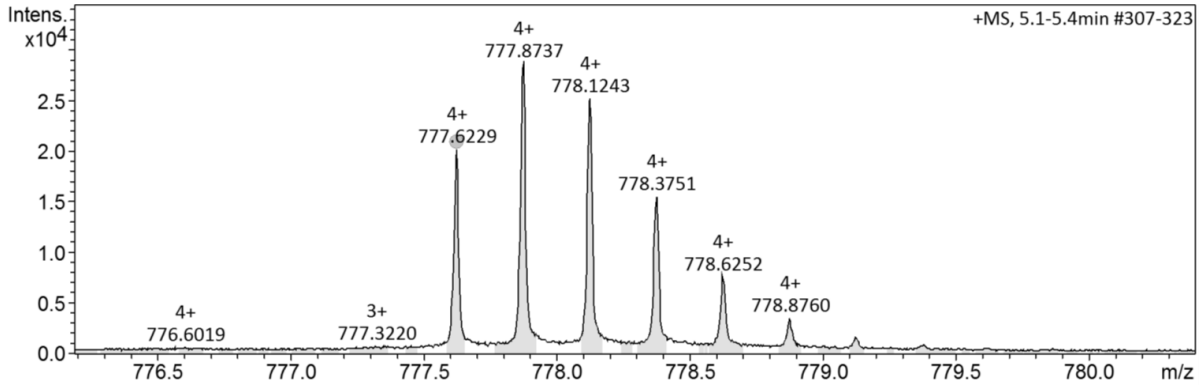


Figure S 36: HR-MS spectrum of compound **8**.

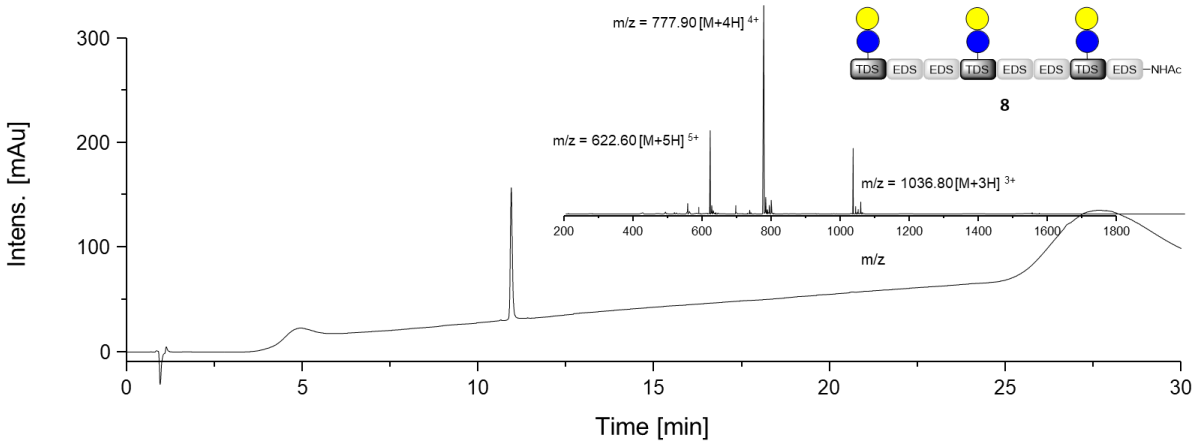


Figure S 37: RP-HPLC and ESI-MS spectrum of compound **8**.

3.10 Lac(1,3,5)-6, **9**

^{1}H-NMR (300 MHz, Deuterium Oxide) δ [ppm]: 8.05 (s, 3H, triazole-C*H*), 5.75 (d, ^{3}J = 9.2 Hz, 3H, C*H*$_{anomer}$Glc), 4.52 (d, ^{3}J = 7.7 Hz, 3H, C*H*$_{anomer}$-Gal), 4.09 – 3.73 (m, 30H, C*H*$_{pyranose}$, C*H*$_{2\ pyranose,}$ O-C*H*$_{2}$-), 3.73 – 3.55 (m, 30H, C*H*$_{pyranose}$, C*H*$_{2\ pyranose,}$ O-C*H*$_{2}$-), 3.53 – 3.26 (m, 36H, C*H*$_{pyranose}$, C=ONH-C*H*$_{2}$), 3.04 (t, ^{3}J = 7.1 Hz, 6H, CH=CH-C*H*$_{2}$), 2.81 (t, ^{3}J = 7.1 Hz, 6H, CH=CH-CH$_{2}$-C*H*$_{2}$), 2.60 – 2.38 (m, 24H, NHC=O-C*H*$_{2}$), 1.99 (s, 3H, C*H*$_{3}$). HR-MS (ESI) calc. for $C_{107}H_{182}N_{25}O_{52}$ $[M+3H]^{3+}$ 883.0783; found: 883.0787. Yield: 109 mg (41 %).

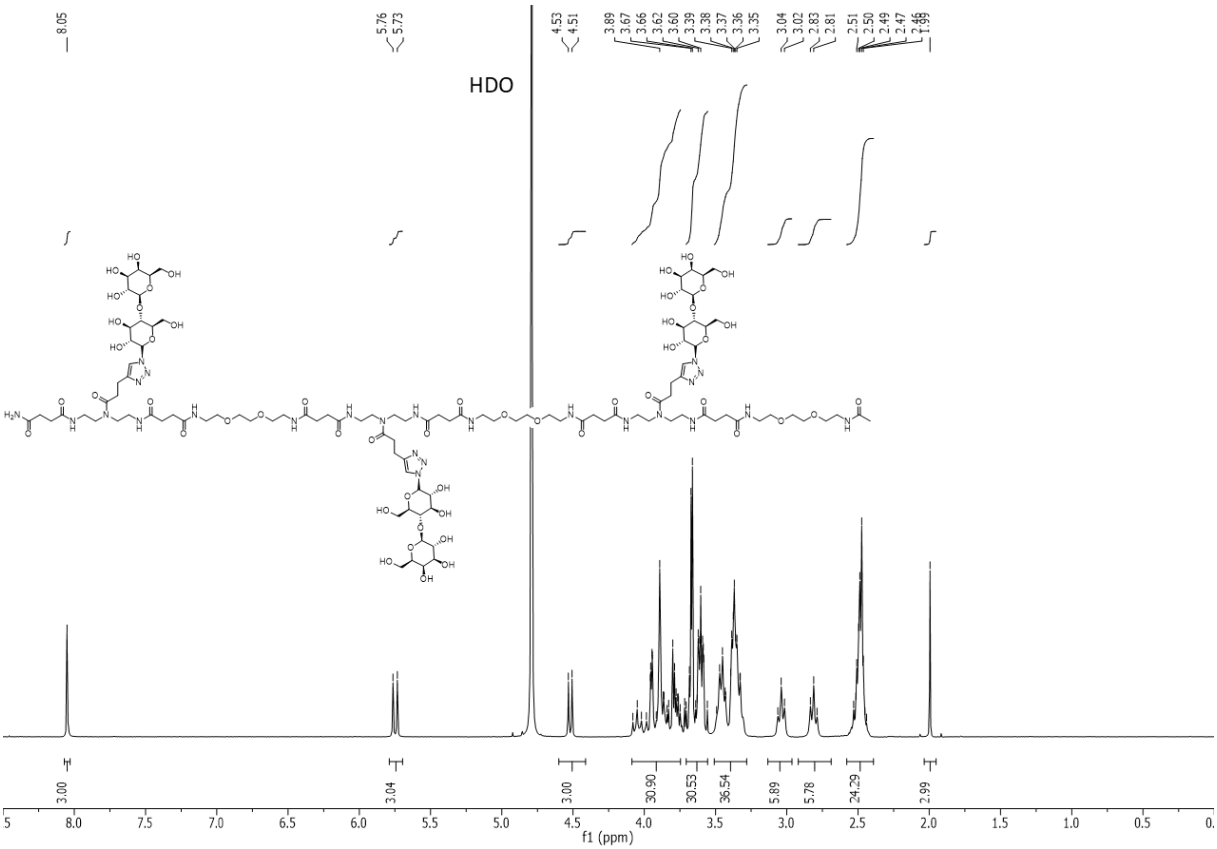


Figure S 38: ^{1}H-NMR spectrum of compound **9.**

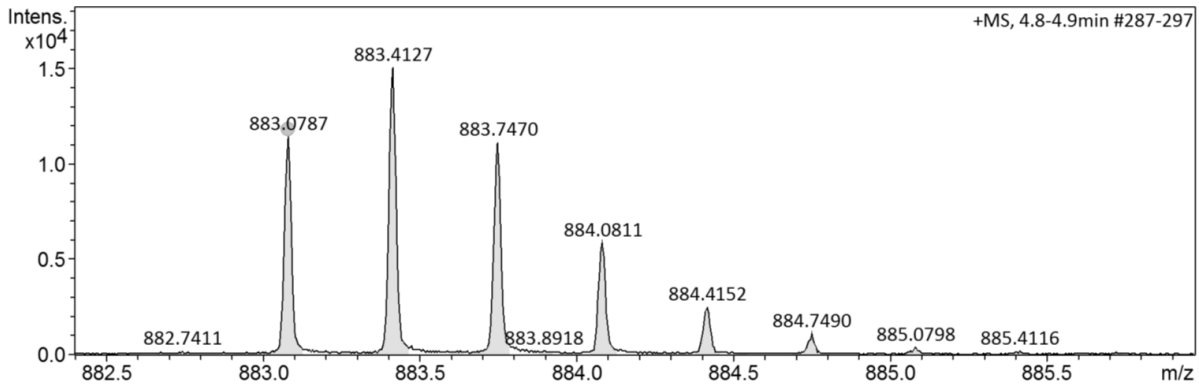


Figure S 39: HR-MS spectrum of compound **9**.

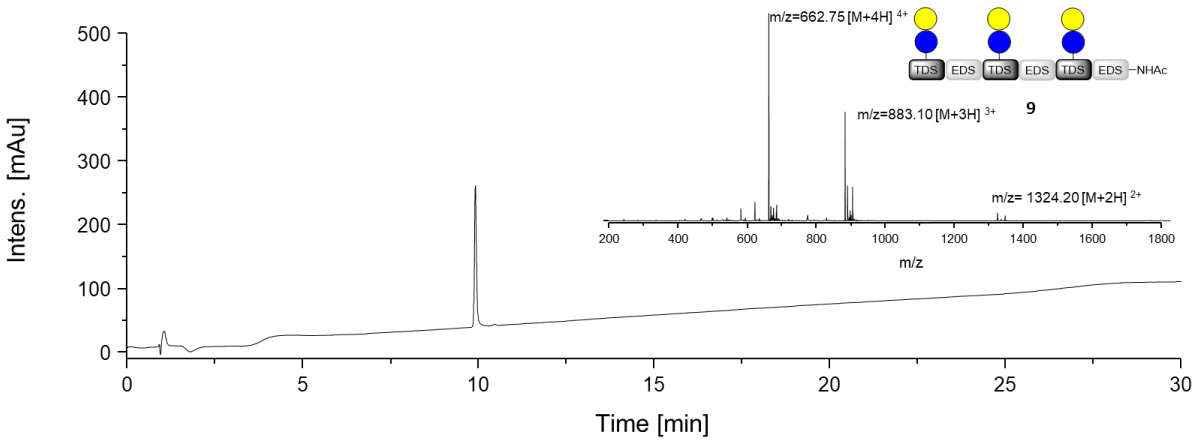


Figure S 40: RP-HPLC and ESI-MS spectrum of compound **9**.

3.11 Lac(1,3,5)-6, **9***

^{1}H-NMR (600 MHz, Deuterium Oxide) δ [ppm]: 8.43 (br s, 2 H, NH), 8.03 (m, 3H, triazole-C*H*), 5.73 (m, 3H, C*H*$_{anomer}$Glc), 4.50 (d, ^{3}J = 7.8 Hz, 3H, C*H*$_{anomer}$-Gal), 4.03 (t, ^{3}J = 9.1 Hz, 3H, C*H*$_{pyranose}$), 3.99 – 3.55 (m, 57H, C*H*$_{pyranose}$, C*H*$_{2\ pyranose,}$ O-C*H*$_2$-), 3.44 (m, 12 H, C=ONH-C*H*$_2$), 3.33 (m, 22H, C*H*$_{pyranose,}$ C=ONH-C*H*$_2$), 3.20 (t, ^{3}J = 5.1 Hz, 2 H, C*H*$_2$-NH$_2$), 3.02 (m, 6H, CH=CH-C*H*$_2$), 2.79 (m, 6H, CH=CH-CH$_2$-C*H*$_2$), 2.47 (m, 24 H, NHC=O-C*H*$_2$). HR-MS (ESI) calc. for $C_{105}H_{180}N_{25}O_{51}$ $[M+3H]^{3+}$ 869.07; found: 869.08. Yield: 103 mg (40 %).

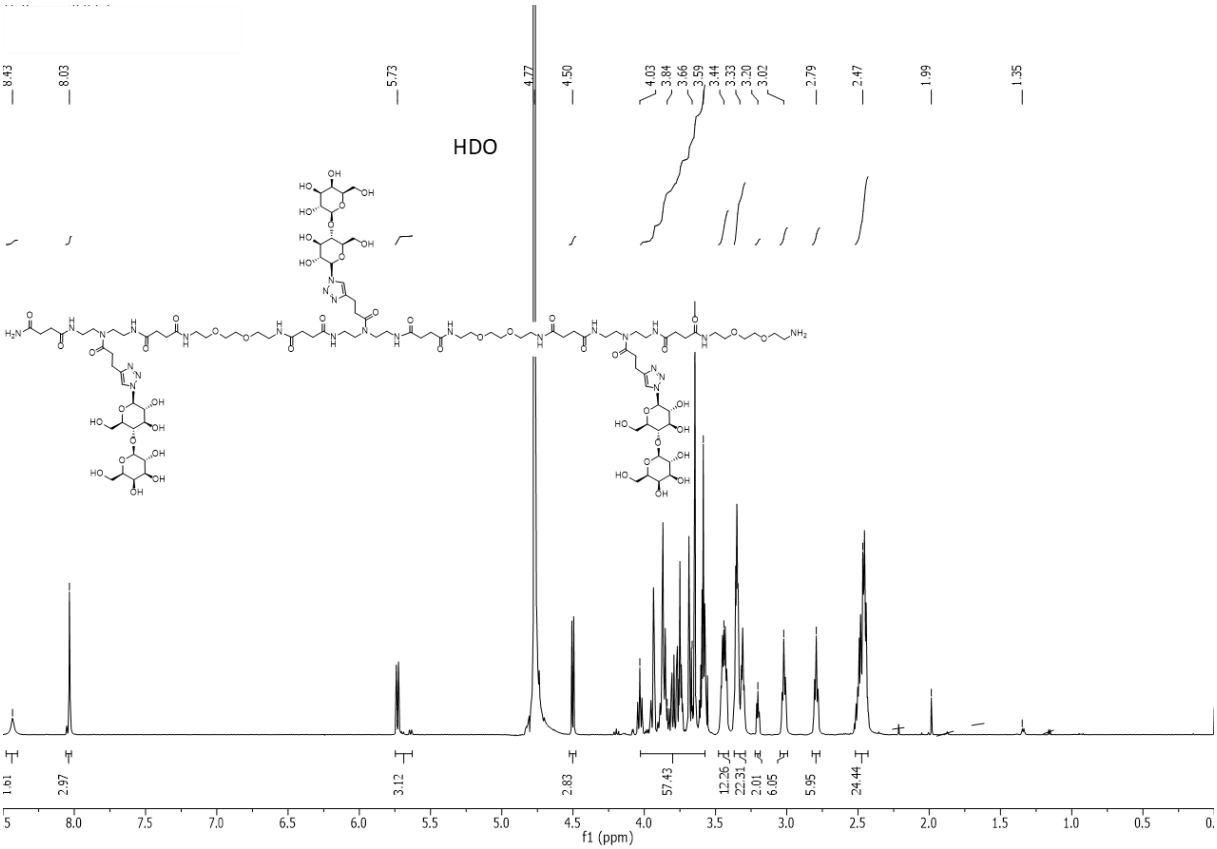


Figure S 41: ^{1}H-NMR spectrum of compound Lac(1,3,5)-6, **9*.**

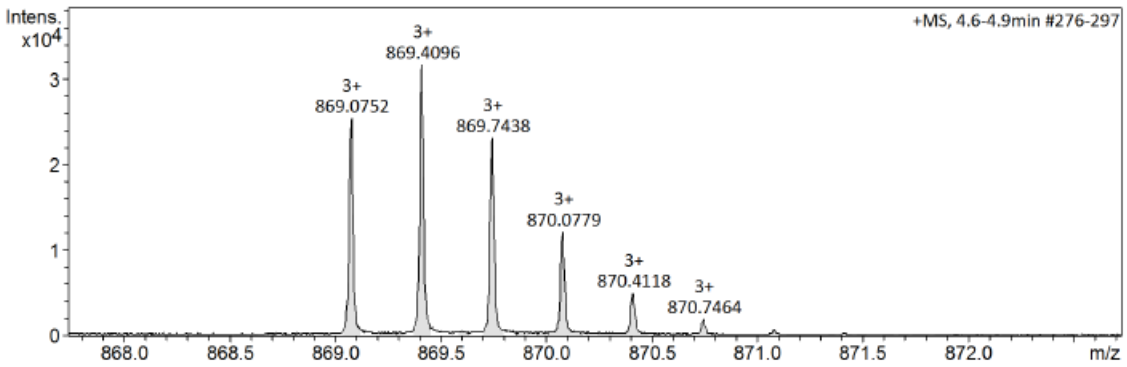


Figure S 42: HR-MS spectrum of compound **9***.

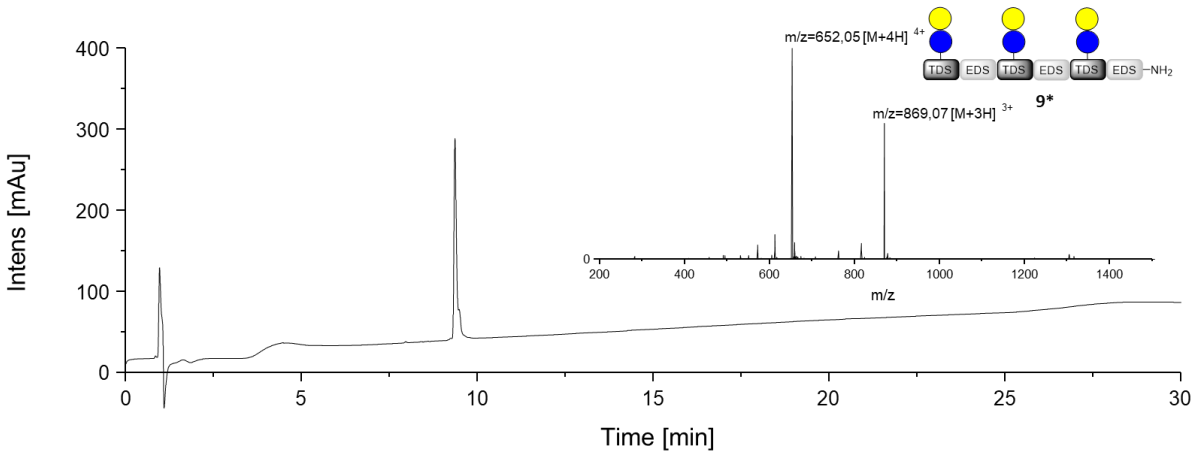


Figure S 43: RP-HPLC and ESI-MS spectrum of compound **9*.**

3.12 Lac(1,2,3)-4, **10**

^{1}H-NMR (300 MHz, Deuterium Oxide) δ [ppm]:8.12 – 7.97 (m, 3H, triazole-C*H*), 5.74 (d, ^{3}J = 9.2 Hz, 3H, C*H*$_{anomer}$Glc), 4.52 (d, ^{3}J = 7.6 Hz, 3H, C*H*$_{anomer}$-Gal), 4.10 – 3.53 (m, 44H, C*H*$_{pyranose}$, C*H*$_{2\ pyranose,}$ O-C*H*$_{2}$-), 3.53 – 3.25 (m, 28H, C*H*$_{pyranose,}$ C=ONH-C*H*$_{2}$), 3.12 – 2.93 (m, 6H, CH=CH-C*H*$_{2}$), 2.88 – 2.70 (m, 6H, CH=CH-CH$_{2}$-C*H*$_{2}$), 2.57 – 2.35 (m, 16H, NHC=O-C*H*$_{2}$), 1.99 (s, 3H, C*H*$_{3}$). HR-MS (ESI) calc. for $C_{87}H_{146}N_{21}O_{44}$ $[M+3H]^{3+}$ 729.6605; found 729.6606. Yield: 121 mg (55 %).

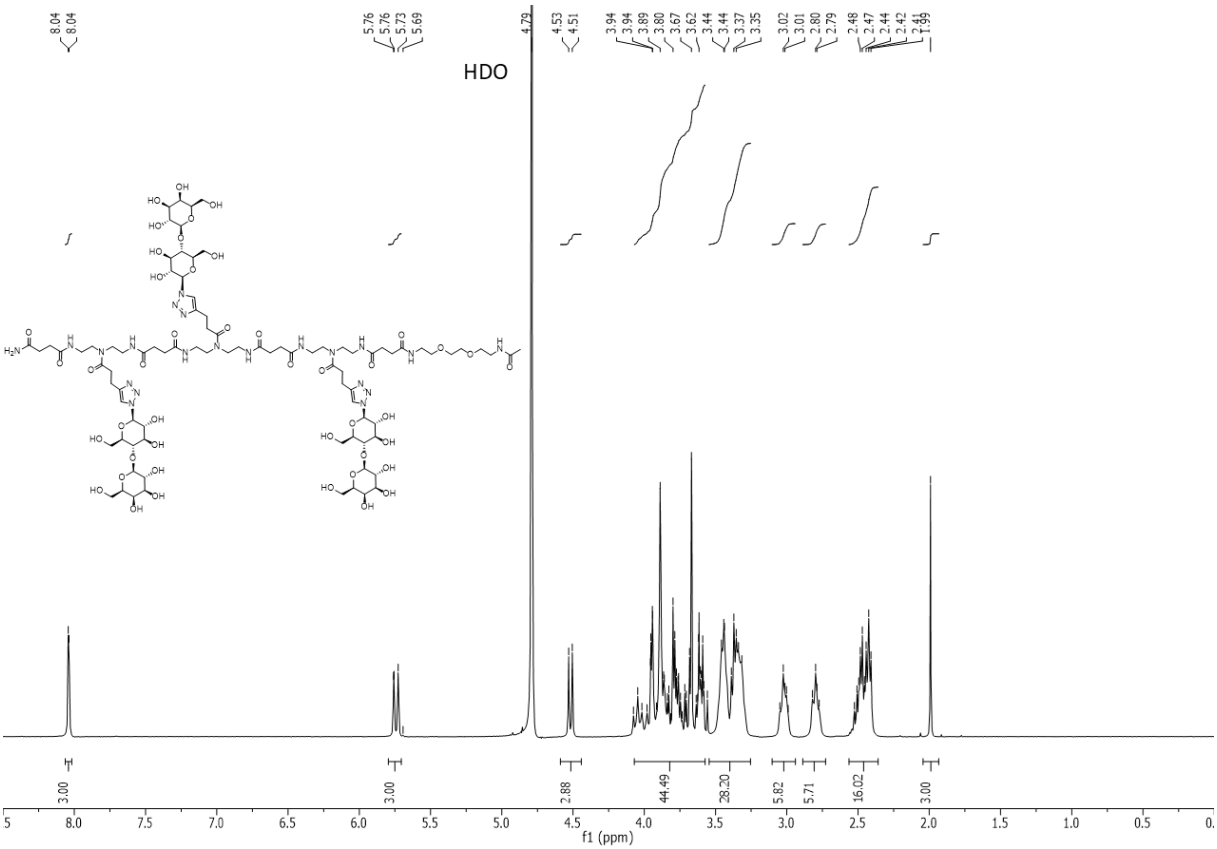


Figure S 44: ^{1}H-NMR spectrum of compound **10.**

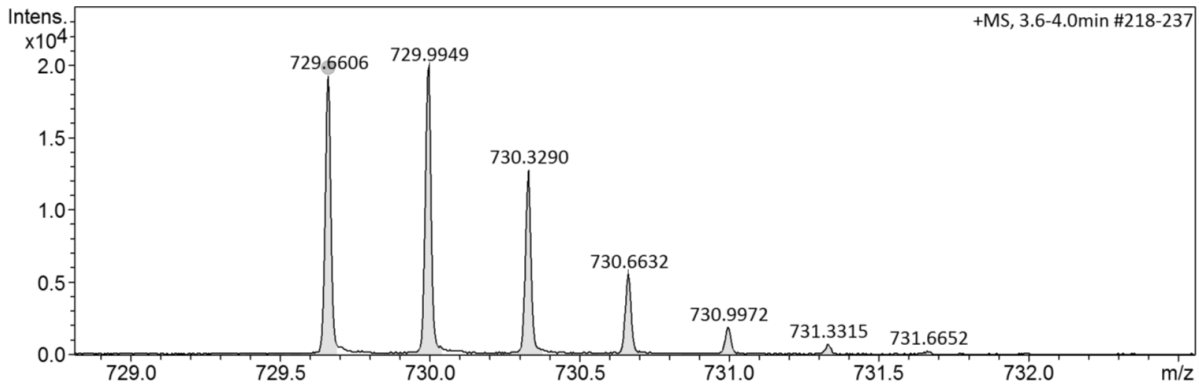


Figure S 45: HR-MS spectrum of compound **10**.

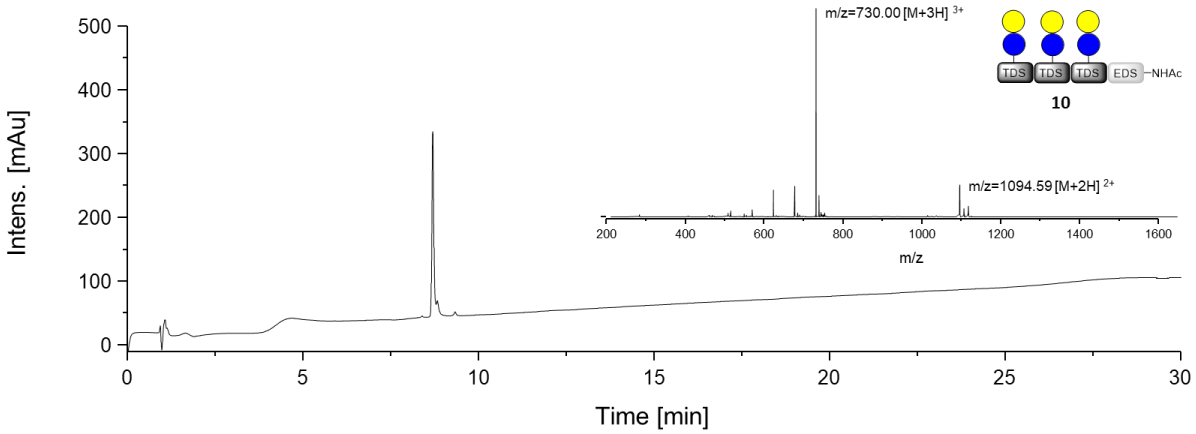


Figure S 46: RP-HPLC and ESI-MS spectrum of compound **10**.

3.13 Lac(1,2,3)-4, **10***

^{1}H-NMR (600 MHz, Deuterium Oxide) δ [ppm]: 8.45 (br s, 1H, NH), 8.02 (m, 3H, triazole-C*H*), 5.74 (m, 3H, C*H*$_{\text{anomer}}$Glc), 4.50 (d, ^{3}J = 7.8 Hz, 3H, C*H*$_{anomer}$-Gal), 4.03 (m, 3 H, C*H*$_{\text{pyranose}}$), 3.96 – 3.55 (m, 41H, C*H*$_{\text{pyranose}}$, C*H*$_{2\ \text{pyranose,}}$ O-C*H*$_2$-), 3.43 (m, 12H, C=ONH-C*H*$_2$), 3.33 (m, 14H, C=ONH-C*H*$_2$), 3.20 (m, 2H, C*H*$_2$-NH$_2$), 3.01 (m, 6H, CH=CH-C*H*$_2$), 2.78 (m, 6H, CH=CH-CH$_2$-C*H*$_2$), 2.45 (m, 16H, NHC=O-C*H*$_2$). HR-MS calc. for $C_{85}H_{144}N_{21}O_{43}$ $[M+3H]^{3+}$ 715.66; found: 715.66. Yield: 97 mg (45 %).

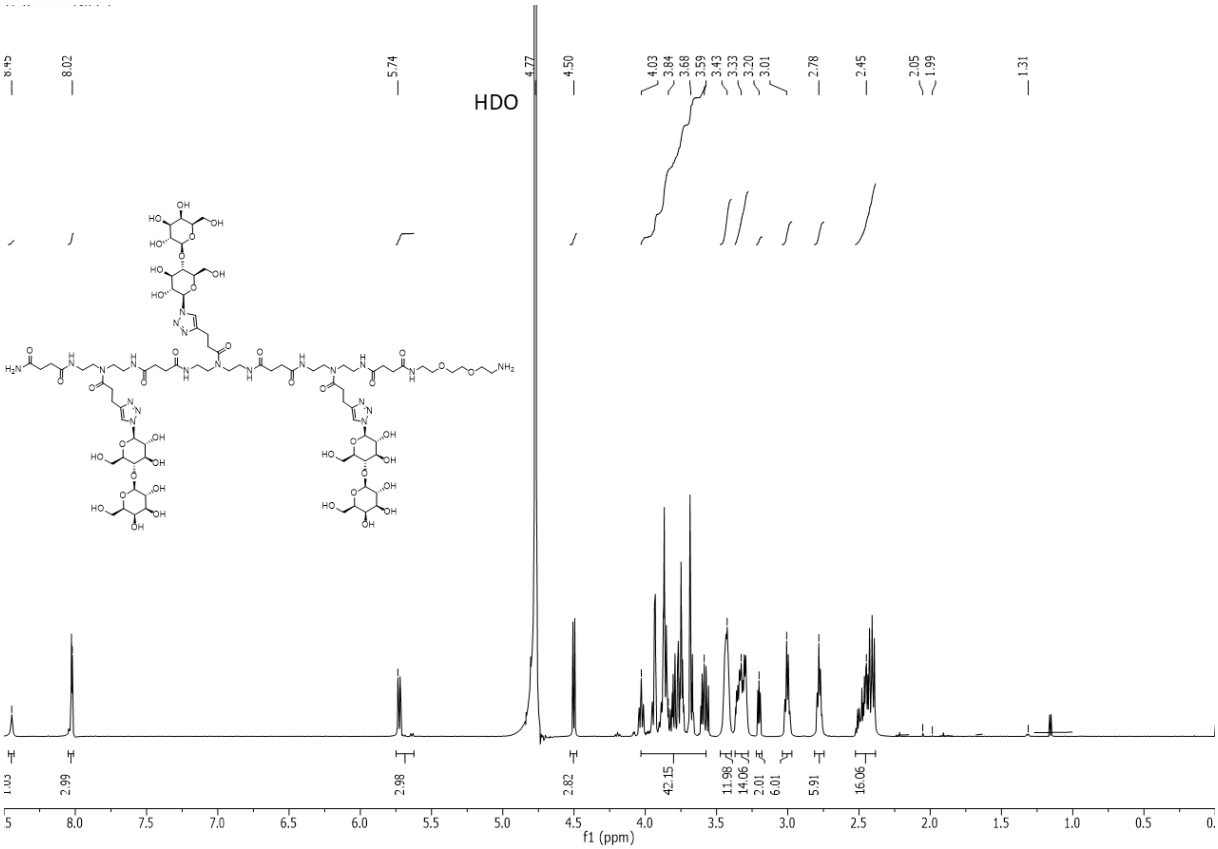


Figure S 47: ^{1}H-NMR spectrum of compound **10*.**

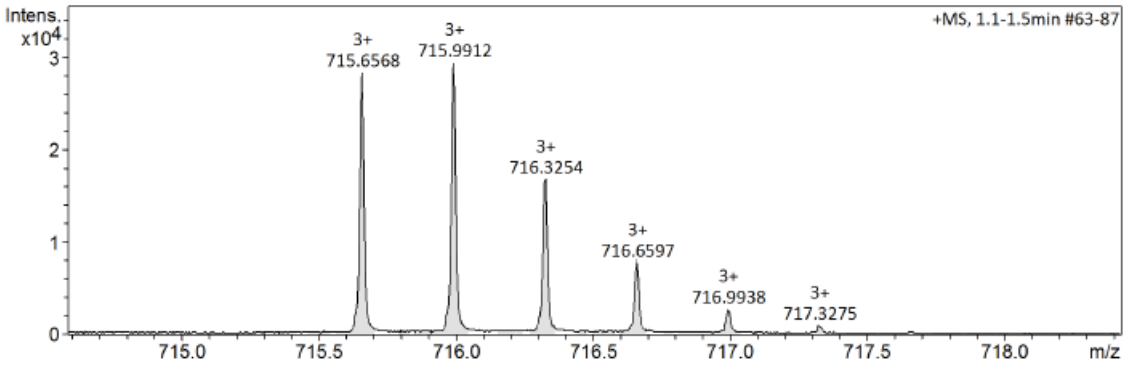


Figure S 48: HR-MS spectrum of compound **10***.

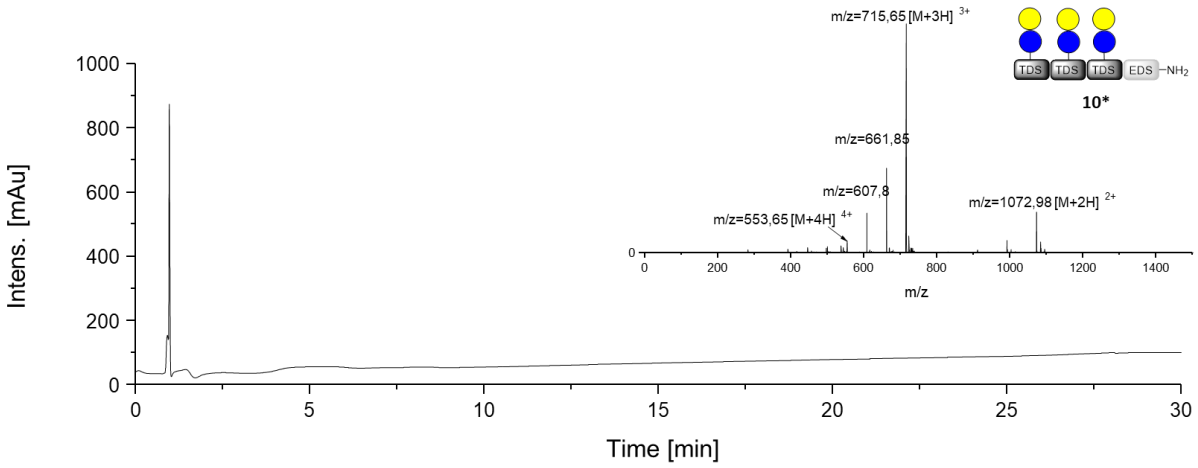


Figure S 49: RP-HPLC and ESI-MS spectrum of compound **10***.

3.14 Lac_3TPD, **11**

^{1}H NMR (300 MHz, Deuterium Oxide) δ [ppm]: 8.03 (s, 2H, triazole-C*H*), 8.00 (s, 1H, triazole-C*H*), 5.77 – 5.68 (m, 3H, CH_{anomer}Glc), 4.52 (d, ^{3}J = 7.7 Hz, 3H, CH_{anomer}-Gal), 4.04 (t, ^{3}J = 8.6 Hz, 3H, C$H_{pyranose}$), 3.99 – 3.73 (m, 27H), 3.69 (dd, ^{3}J = 10.0, 3.3 Hz, 3H, C$H_{pyranose}$), 3.59 (dd, ^{3}J = 10.0, 7.6 Hz, 3H, C$H_{pyranose}$), 3.38 – 3.21 (m, 8H, C=ONH-CH_2), 3.07 – 2.92 (m, 6H, CH=CH-CH_2), 2.71 (t, ^{3}J = 7.1 Hz, 2H, CH=CH-CH_2-CH_2), 2.65 – 2.51 (m, 4H, CH=CH-CH_2-CH_2). HR-MS (ESI) calc. for $C_{55}H_{90}N_{12}O_{33}$ $[M+2H]^{2+}$ 723.2861; found 723.2859. Yield: 73 mg (50 %).

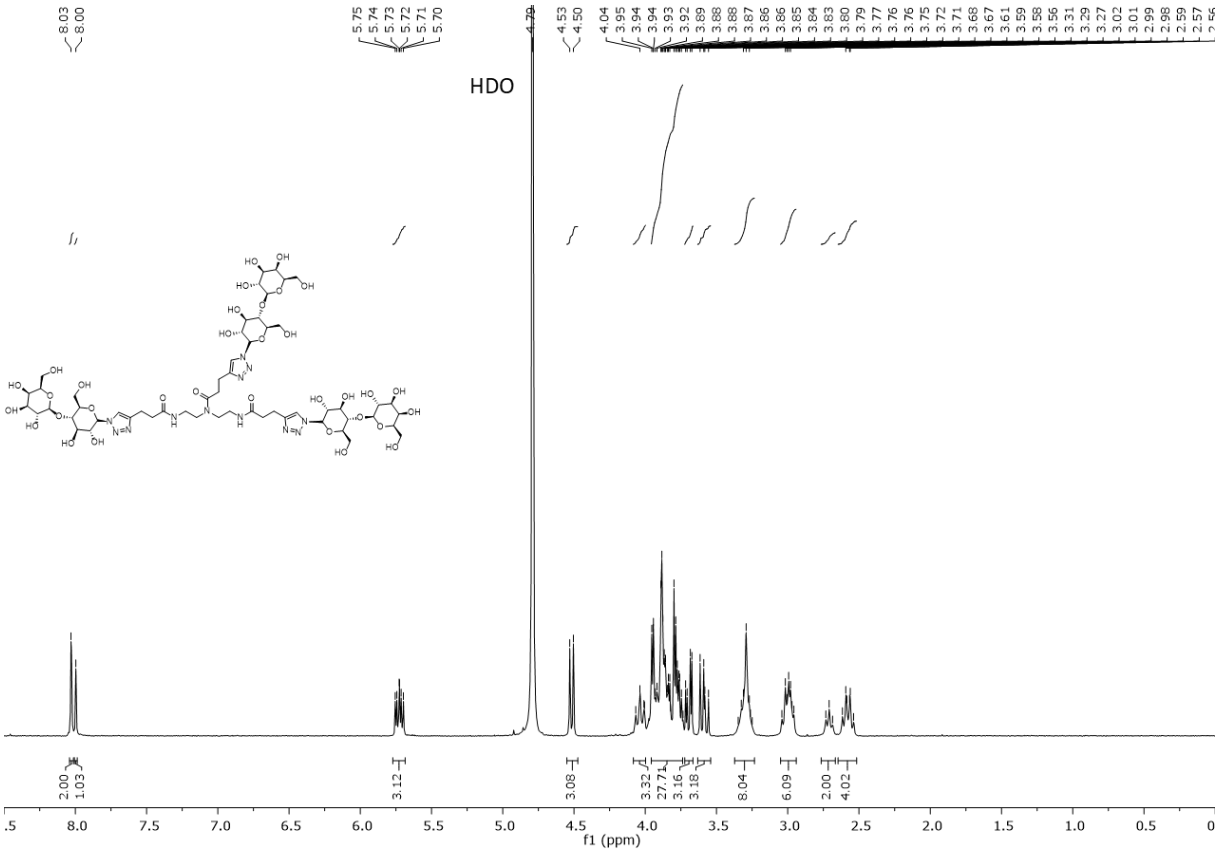


Figure S 50: ^{1}H-NMR spectrum of compound **11.**

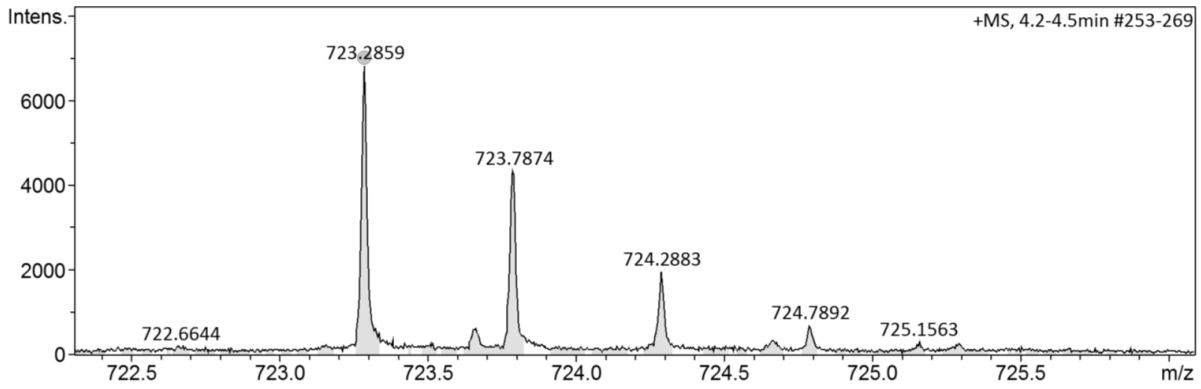


Figure S 51: HR-MS spectrum of compound **11**.

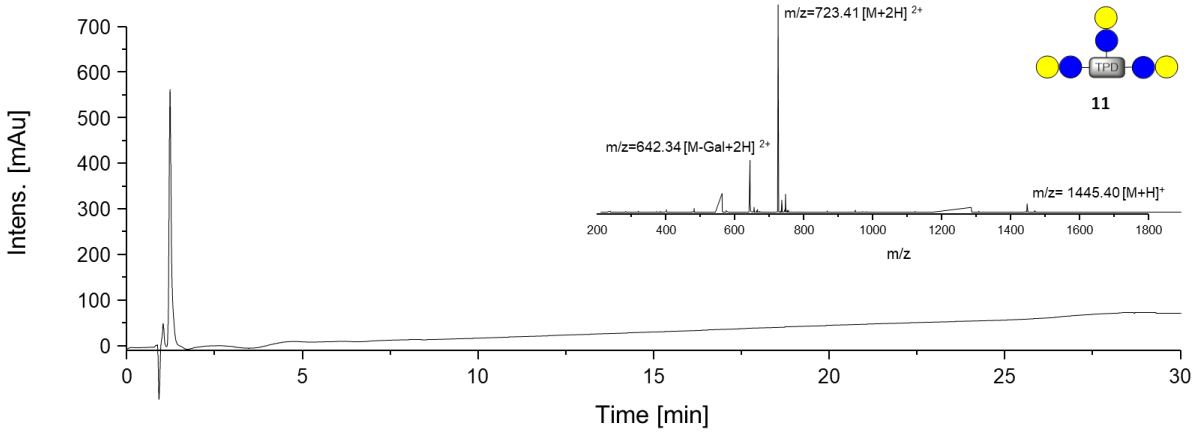


Figure S 52: RP-HPLC and ESI spectrum of compound **11.**

3.15 Lac(1,2,3,4,5,6)-7, **12**

^{1}H-NMR (300 MHz, Deuterium Oxide) δ [ppm]: 8.04 (m, 6H, triazole-CH), 5.74 (d, J = 9.2 Hz, 6H, C*H*$_{anomer}$Glc), 4.52 (d, J = 7.6 Hz, 6H, C*H*$_{anomer}$-Gal), 4.10 – 3.74 (m, 62H, C*H*$_{pyranose}$, O-C*H*$_2$-), 3.72 – 3.54 (m, 20H, C*H*$_{\text{pyranose}}$, C*H*$_2$ $_{\text{pyranose,}}$ O-C*H*$_2$-), 3.50 – 3.27 (m, 50H, C=ONH-C*H*$_2$), 3.04-2.98 (m, 12H, CH=CH-C*H*$_2$), 2.85 – 2.72 (m, 12H, CH=CH-CH$_2$-C*H*$_2$), 2.52-2.41 (m, 28H, NHC=O-C*H*$_2$), 1.99 (s, 3H, C*H*$_3$). HR-MS (ESI+) m/z calc. for $C_{162}H_{267}N_{39}O_{83}$ $[M+4H]^{4+}$ 1021.6962; found 1021.6962. Yield: 235.1 mg (55 %).

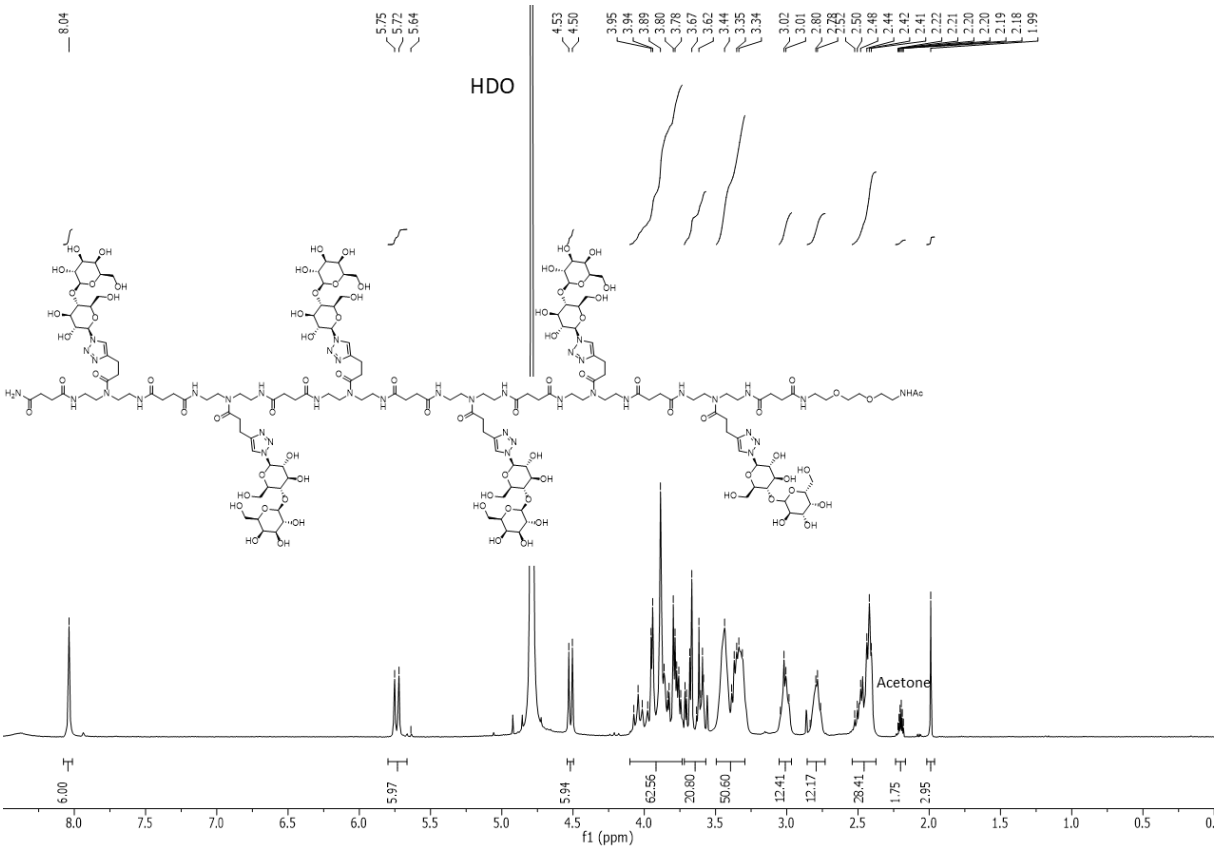


Figure S 53: ^{1}H-NMR spectrum of compound **12.**

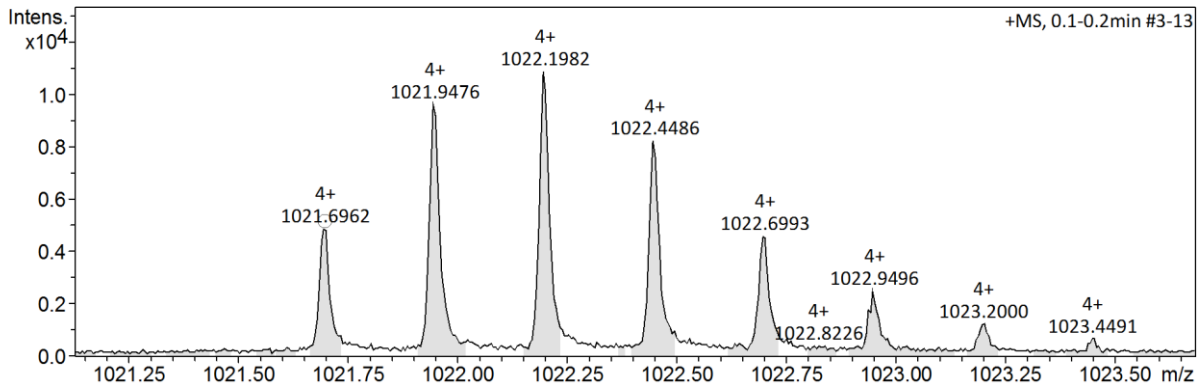


Figure S 54: HR-MS spectrum of compound **12**.

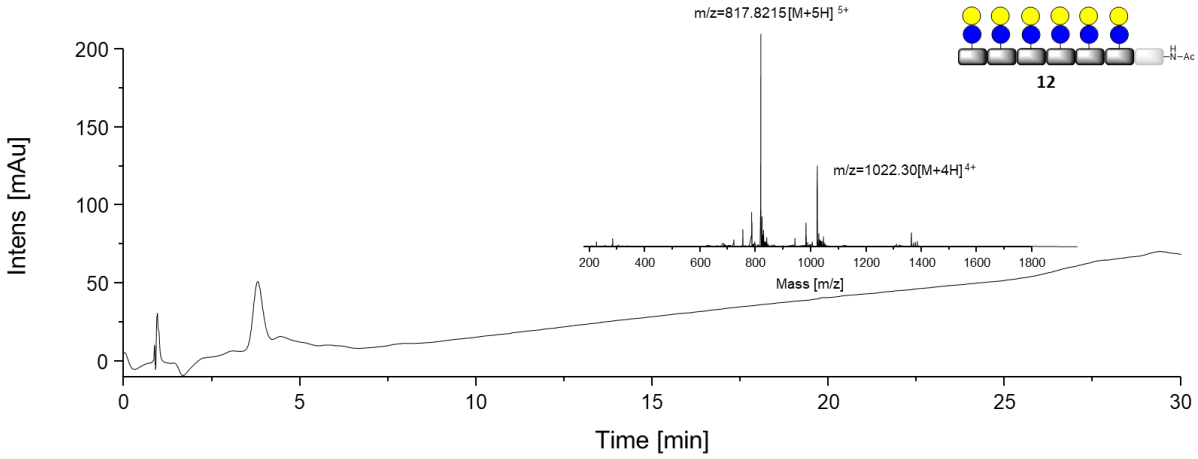


Figure S 55: RP-HPLC and ESI spectrum of compound **12.**

3.16 Lac(2)-3 L, **13**

^{1}H-NMR (300 MHz, Deuterium Oxide) δ [ppm]:7.84 (s, 1H, triazole-C*H*), 4.53 (t, 2H, ^{3}J = 6.8 Hz, , O-C*H*$_2$-), 4.46 (2x d, 2H, ^{3}J ≈ 7.7 Hz , ^{3}J ≈ 7.7 Hz, C*H*$_{anomer}$Glc, C*H*$_{anomer}$-Gal), 4.01-3.70 (m, 7H, C*H*$_{pyranose}$), 3.70-3.51 (m, 22H, O-C*H*$_2$- , C*H*$_{pyranose,}$ -N-N-C*H*$_2$-), 3.50-3.29 (m, 17, C=ONH-C*H*$_{2,}$ C*H*$_{pyranose}$), 3.00 (t, ^{3}J = 7.0 Hz, 2H, CH=CH-C*H*$_2$), 2.79 (t, ^{3}J = 7.1 Hz, 2H, CH=CH-CH$_2$-C*H*$_2$), 2.57-2.43 (m, 12H, NHC=O-C*H*$_2$), 2.21 (p, 2H, ^{3}J = 6.6 Hz, CH$_2$-C*H*$_2$-CH$_2$), 1.99 (s, 3H, C*H*$_3$). HR-MS (ESI): m/z calc. for $C_{50}H_{89}N_{11}O_{23}$ $[M+2H]^{2+}$ 605.8061; found 605.8072. Yield: 235.1 mg (55 %).

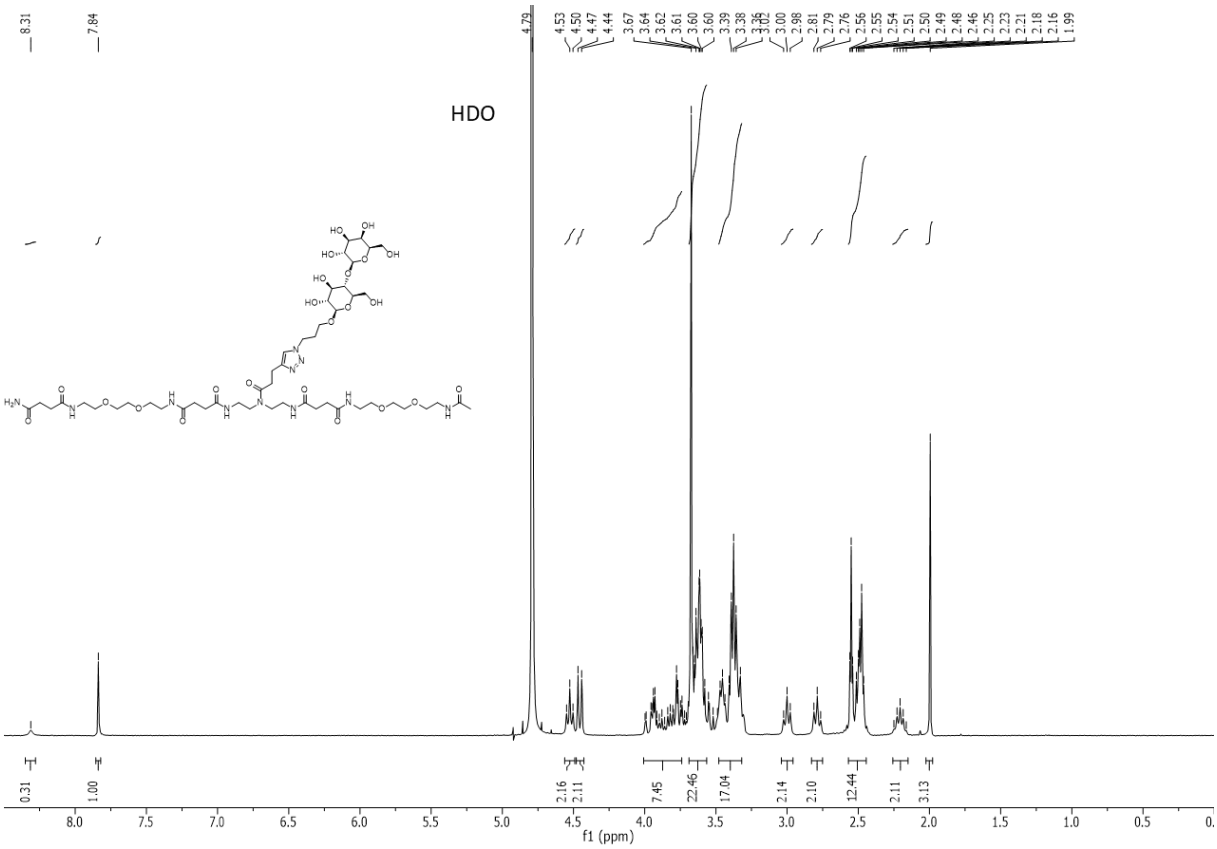


Figure S 56: ^{1}H-NMR spectrum of compound **13.**

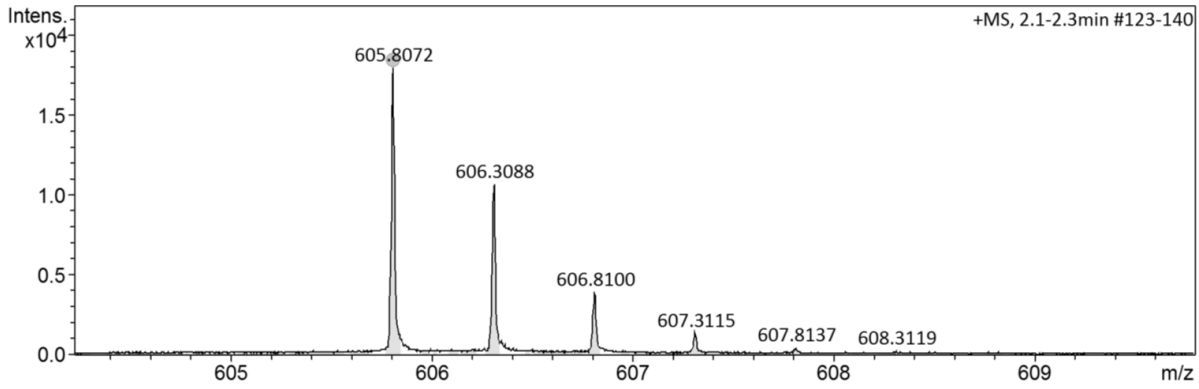


Figure S 57: HR-MS spectrum of compound **13**.

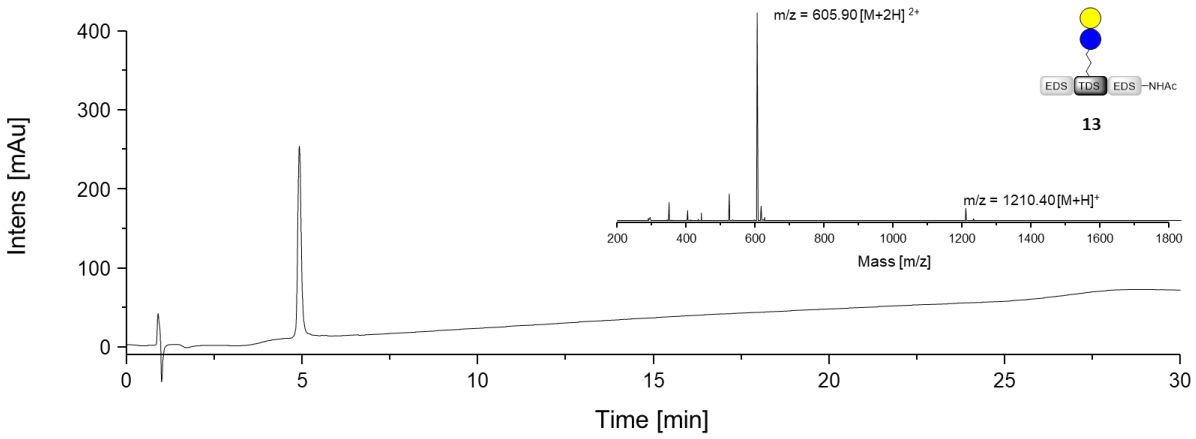


Figure S 58: RP-HPLC and ESI spectrum of compound **13**.

3.17 Lac(1,5)-5 L, **14**

^{1}H-NMR (300 MHz, Deuterium Oxide) δ [ppm]:7.84 (s, 2H, triazole-C*H*), 4.53 (t, ^{3}J = 6.8 Hz, 4H, O-C$H_{2propyl}$), 4.46 (m, 4 H, CH_{anomer}Glc, CH_{anomer}-Gal), 4.01-3.70 (m, 13H, C$H_{pyranose}$), 3.70-3.51 (m, 37H, O-CH_2-, C$H_{pyranose,}$ -N-N-CH_2-), 3.50-3.29 (m, 30H, C=ONH-C$H_{2,}$ C$H_{pyranose}$), 3.00 (t, ^{3}J = 7.0 Hz, 4H, CH=CH-CH_2), 2.79 (t, 4H, CH=CH-CH$_2$-CH_2), 2.56-2.45 (m, 20H, NHC=O-CH_2), 2.21 (m, 4H, CH$_2$-CH_2-CH$_2$), 1.94 (s, 1.5H, CH_3), 1.91 (s, 1.5H, CH_3). HR-MS (ESI): m/z calc. for $C_{88}H_{154}N_{19}O_{41}$ $[M+3H]^{3+}$ 711.0178; found 711.0183. Yield: 120.7 mg (23 %).

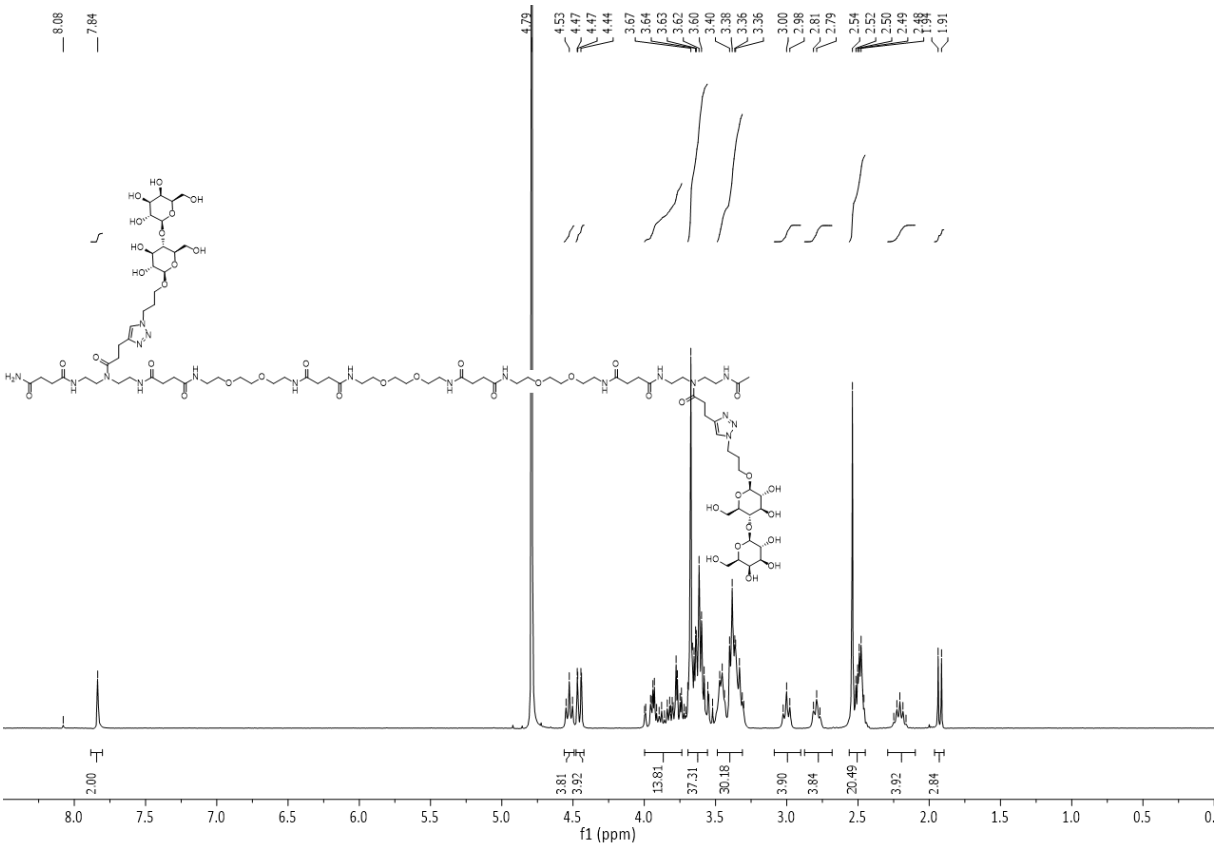


Figure S 59: ^{1}H-NMR spectrum of compound **14.**

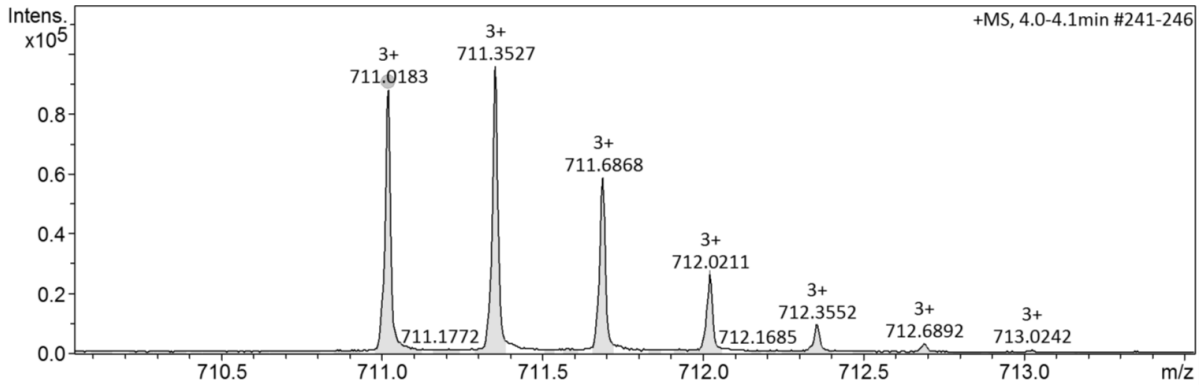


Figure S 60: HR-MS spectrum of compound **14**.

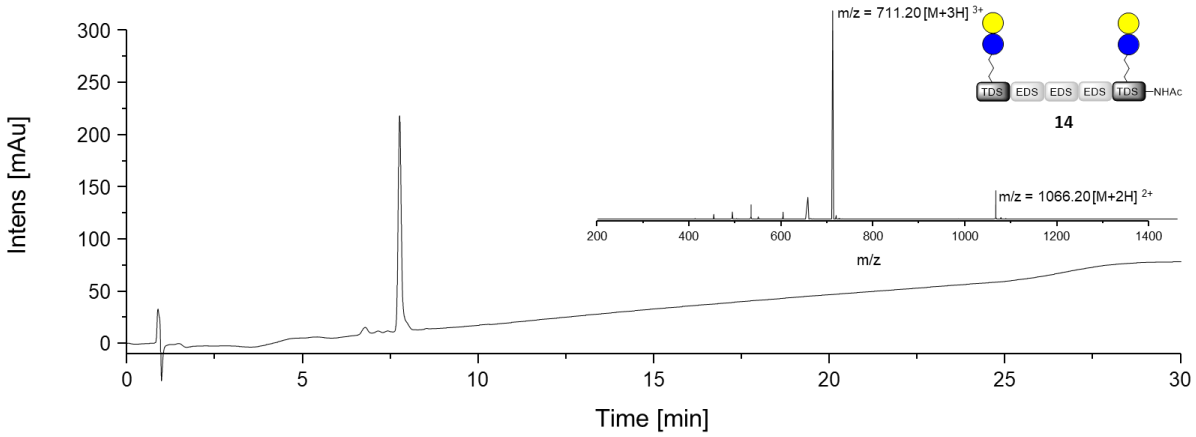


Figure S 61: RP-HPLC and ESI-MS spectrum of compound **14**.

3.18 Lac(1,5,9)-9 L, **15**

^{1}H-NMR (300 MHz, Deuterium Oxide) δ [ppm]:7.84 (s, 3H, triazole-C*H*), 4.53 (t, ^{3}J = 6.8 Hz, 6H, O-C$H_{2\text{propyl}}$-), 4.46 (m, 6H, CH_{anomer}Glc, CH_{anomer}-Gal), 4.01-3.70 (m, 20H, CH_{pyranose}), 3.70-3.51 (m, 66H, O-CH_2-, CH_{pyranose}, -N-N-CH_2-), 3.50-3.30 (m, 52H, CH_{pyranose}, C=ONH-CH_2), 3.00 (t, ^{3}J = 6.9 Hz, 6H, CH=CH-CH_2), 2.79 (t, ^{3}J = 7.0 Hz, 6H, CH=CH-CH_2-CH_2), 2.56-2.45 (m, 36H, NHC=O-CH_2), 2.21 (m, 6H, CH_2-CH_2-CH_2), 1.94 (s, 1.5H, CH_3), 1.91 (s, 1.5H, CH_3). HR-MS (ESI): m/z calc. for $C_{146}H_{255}N_{31}O_{67}$ $[M+4H]^{4+}$ 878.6869; found 878.6877. Yield: 69.9 mg (22 %).

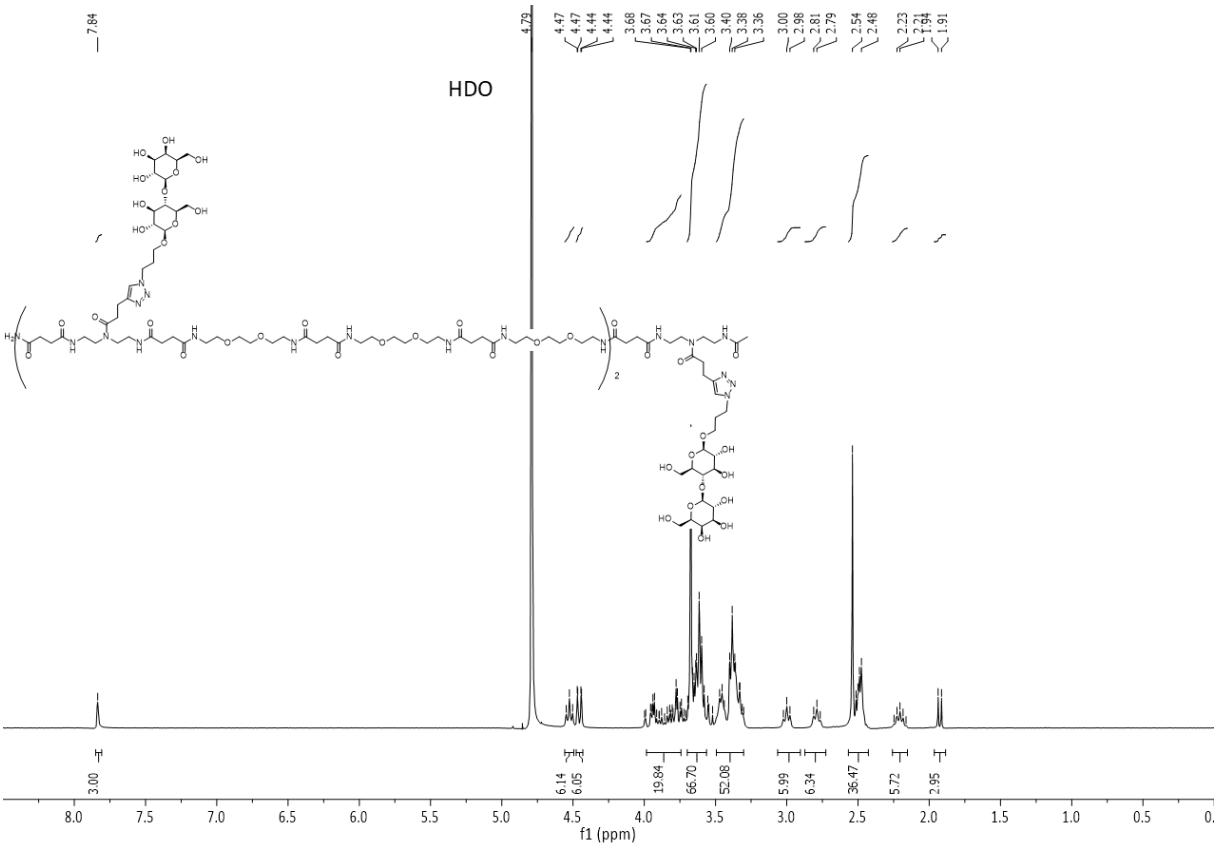


Figure S 62: ^{1}H-NMR spectrum of compound **15.**

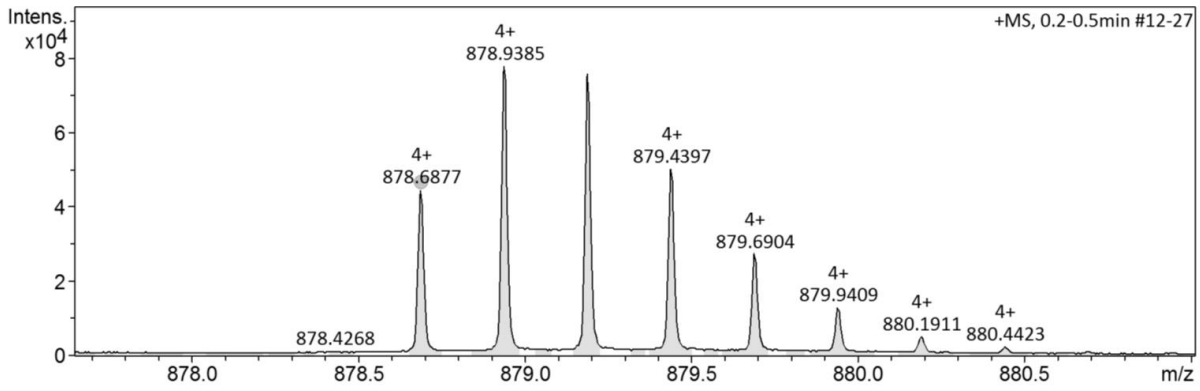


Figure S 63: HR-MS spectrum of compound **15**.

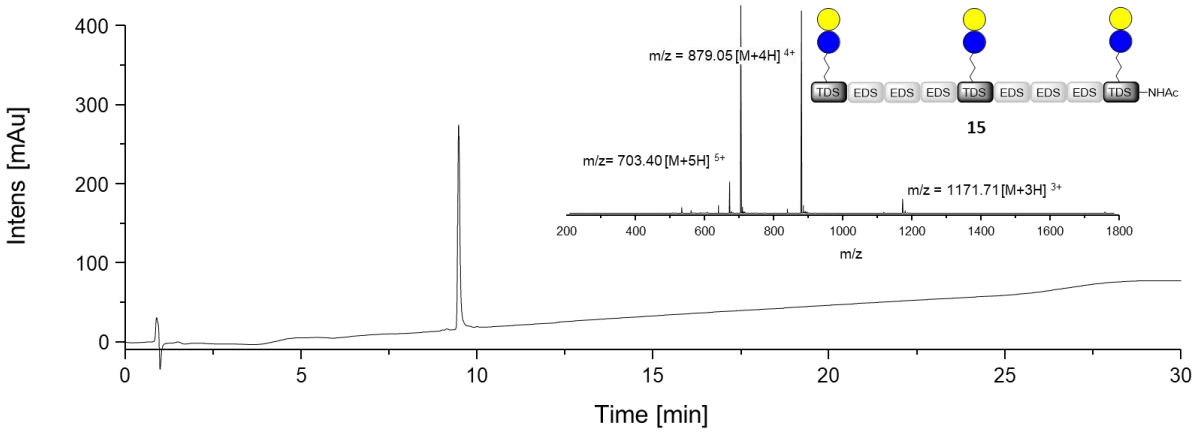


Figure S 64: RP-HPLC and ESI-MS spectrum of compound **15**.

3.19 Glc(1,3,5)-6, **16**

^{1}H-NMR (300 MHz, D_2O) δ [ppm]7.93 – 7.87 (m, 3H, triazole-C*H*), 4.88 (d, J = 3.4 Hz, 2.7H, C*H*$_{anomer}$Glc), 4.72 –4.59 (m, 6H, -N-N-C*H*$_2$), 4.43 (d, J = 7.9 Hz, 0.3H, C*H*$_{anomer}$Glc), 4.16 – 4.02 (m, 3H, O-C*H*$_2$-), 4.00 – 3.86 (m, 3H, O-C*H*$_2$-), 3.73 – 3.56 (m, 33H, O-C*H*$_2$-, C=ONH-C*H*$_2$, C*H*$_{pyranose}$), 3.55 – 3.43 (m, 17H, O-C*H*$_2$-), 3.42 – 3.30 (m, 27H, C*H*$_2$-NH_2), 3.00 (t, J = 7.3 Hz, 6H, CH=C-C*H*$_2$), 2.92 – 2.74 (m, 9H, CH=C-CH_2-C*H*$_2$), 2.58 – 2.42 (m, 24H, NHC=O-C*H*$_2$), 2.00 (s, 3H, -C*H*$_3$). HR-MS (ESI) calc. for $C_{95}H_{164}N_{25}O_{40}$ $[M+3H]^{3+}$ 765.0517; found 765.0527. Yield: 110 mg (48 %).

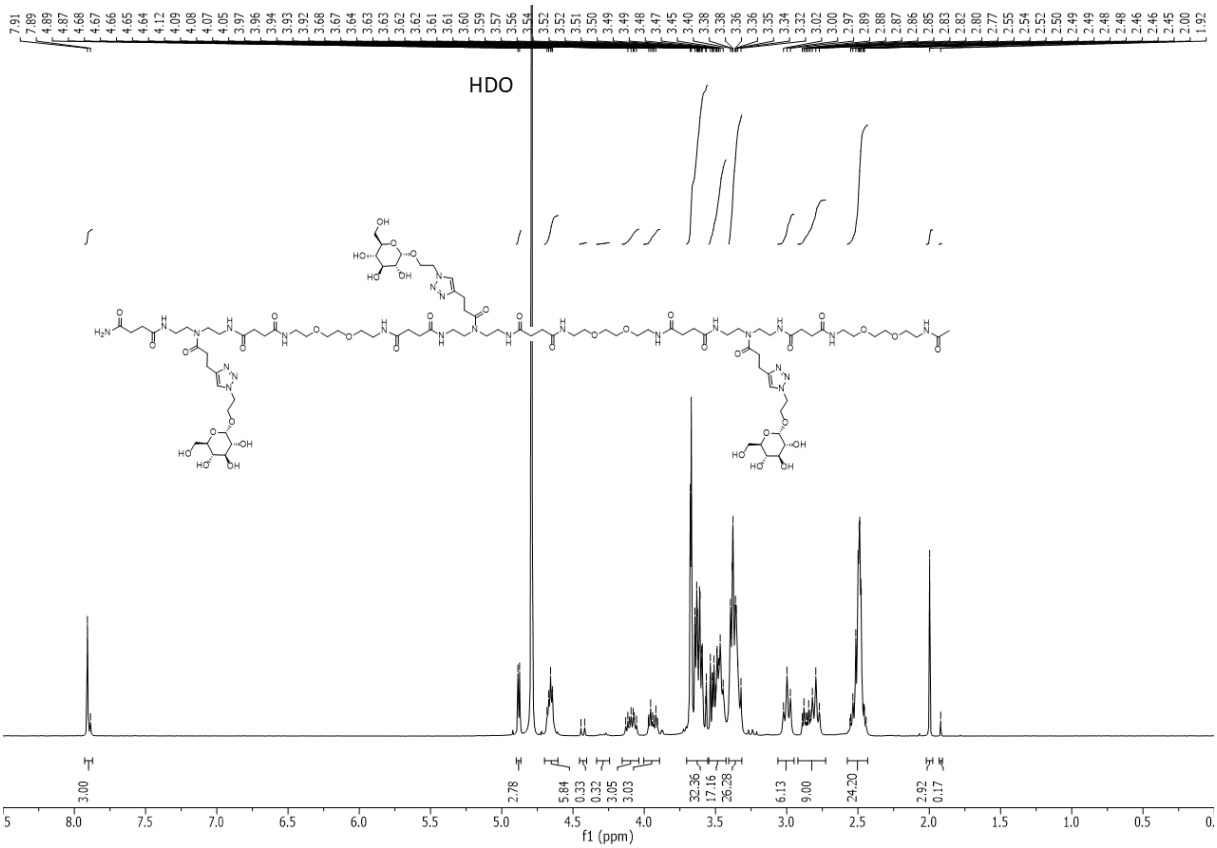


Figure S 65: ^{1}H-NMR spectrum of compound **16.**

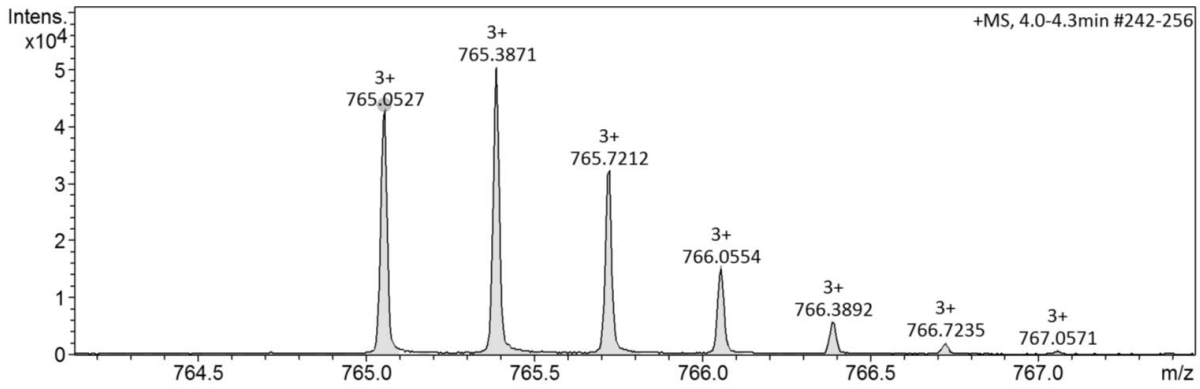


Figure S 66: HR-MS spectrum of compound **16**.

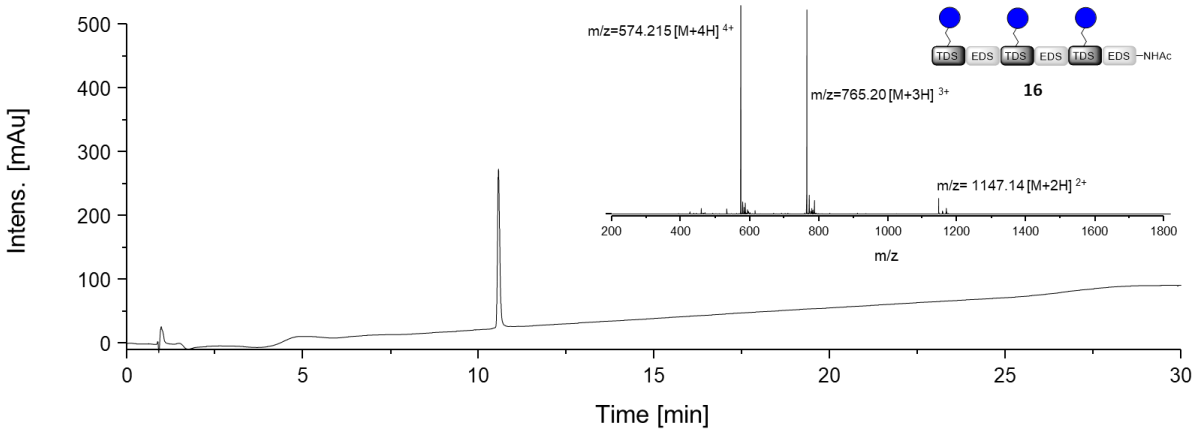


Figure S 67*:* RP-HPLC and ESI-MS spectrum of compound **16**.

3.20 Glc(1,3,5)-6, **16***

^{1}H-NMR (600 MHz, Deuterium Oxide) δ [ppm]: 8.46 (br s. 1 H. NH). 7.88 (m, 3H, triazole-C*H*), 4.80 (m, 3H, CH_{anomer}Glc), 4.64 (m, 6H, -N-N-CH_2-), 4.41 (d, $^{3}J_{HH}$ = 7.9 Hz, 0.6H, CH_{anomer}Glc), 4.07 (m, 3H, O-CH_2-), 3.91 (m, 3H, O-CH_2-), 3.75 (dd, $^{3}J_{HH}$ = 5.6; 4.6 Hz, 2H, O-CH_2-), 3.69 (s, 4H, O-CH_2-), 3.65 (s, 8H, O-CH_2-), 3.63 – 3.28 (m, 59H, O-CH_2-, C=ONH-CH_2, C$H_{pyranose}$), 3.21 (m, 2H, CH_2-NH_2), 2.98 (m, 6H, CH=C-CH_2), 2.87– 2.75 (m, 9H, CH=C-CH_2-CH_2), 2.48 (m, 24H, NHC=O-CH_2). ESI-MS m/z calc. for $C_{93}H_{162}N_{25}O_{39}$ $[M+3H]^{3+}$ 751.04. found: 751.25. Yield: 86 mg (38 %).

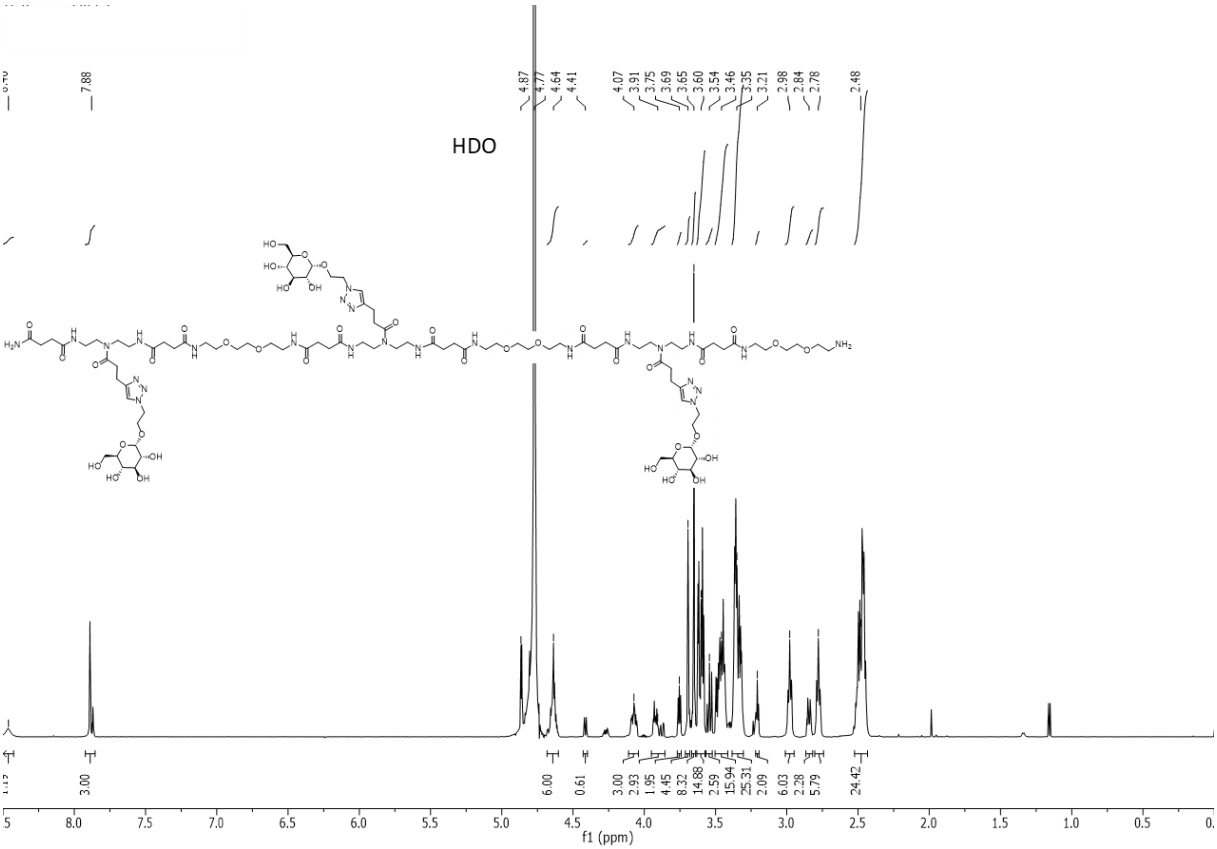


Figure S 68: ^{1}H-NMR spectrum of compound 1**6*.**

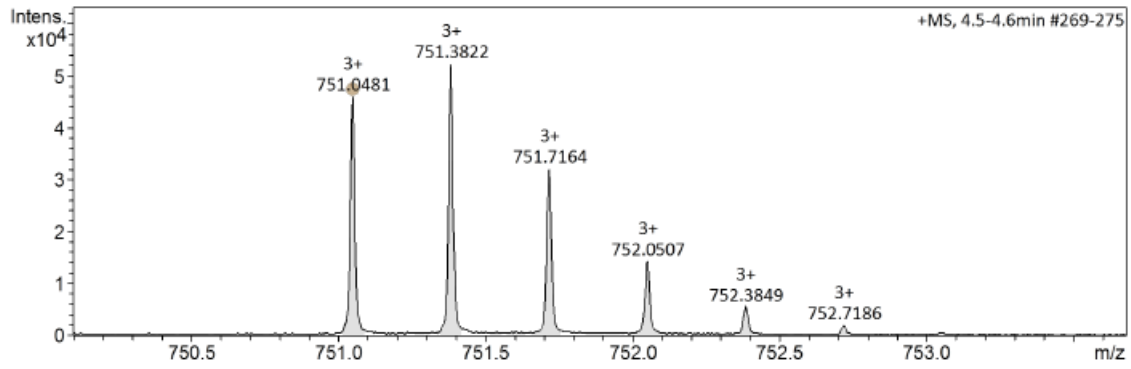


Figure S 69: HR-MS spectrum of compound **16***.

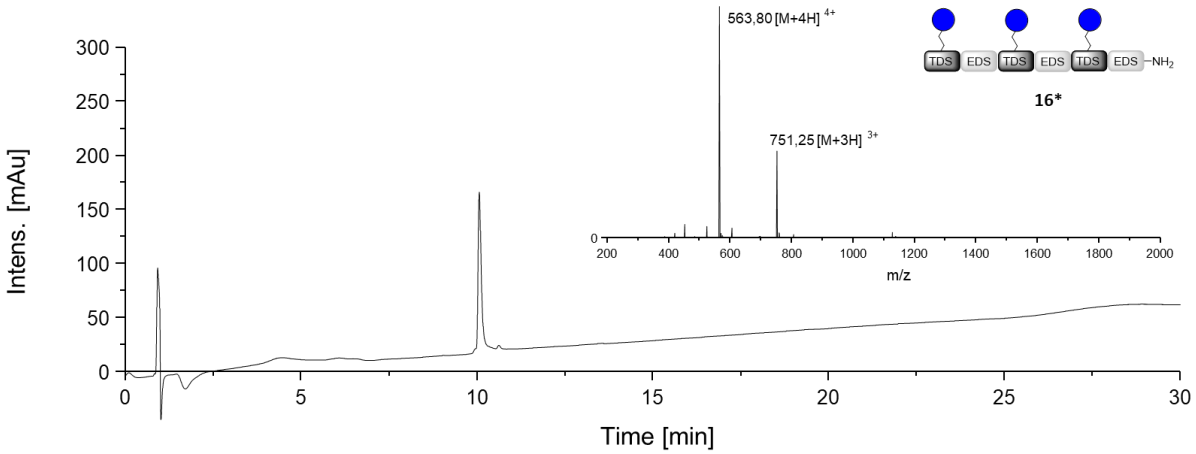


Figure S 70*:* RP-HPLC and ESI-MS spectrum of compound **16***.

4. Analytical data for glycomacromolecule-lipid conjugates

4.1. Lac(1)-2-PEG-DSPE-conjugate, **L4**

Yield: 2.01 mg (58 %). Conversion: 66 %. MALDI-TOF-MS calc. for $C_{173}H_{330}N_{11}O_{73}PNa$ $[M+Na]^+$ 3786.5; found: 3787.8.

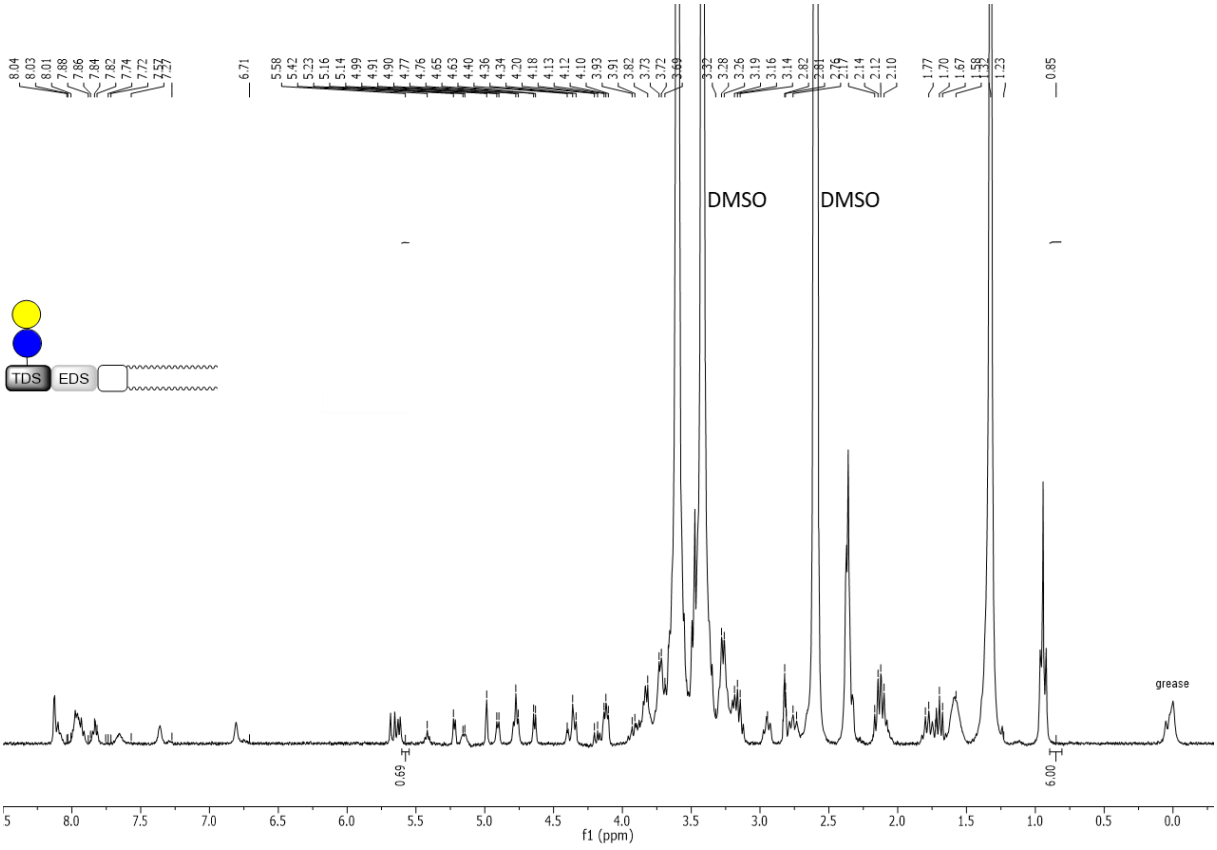


Figure S 71:[1]H-NMR spectrum of compound **L4**.

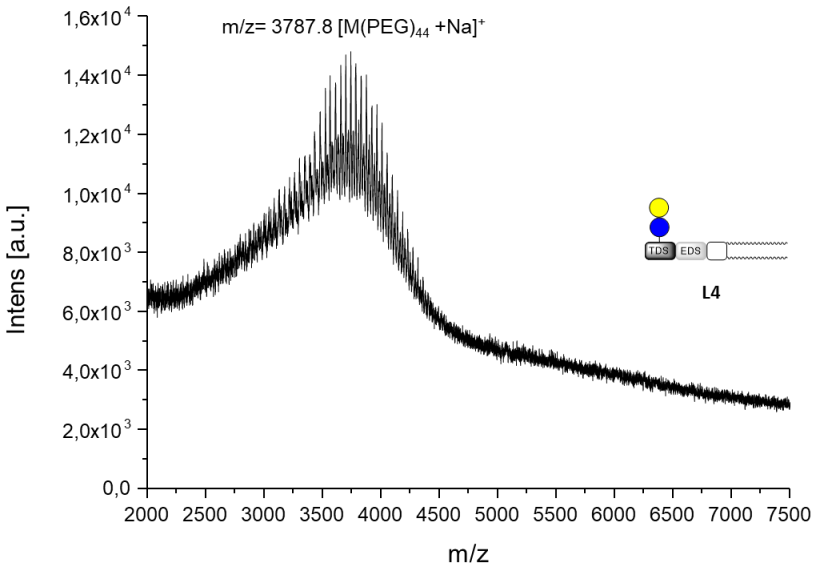


Figure S 72: MALDI-TOF-MS-spectrum of compound **L4**.

4.2. Lac(1,3,5)-6-PEG-DSPE-conjugate, **L9**

Yield: 2.26 mg (44 %). Conversion: 56 %. MALDI-TOF-MS calc. für $C_{243}H_{446}N_{27}O_{107}PNa$ $[M+Na]^+$ 5511.3; found: 5511.6.

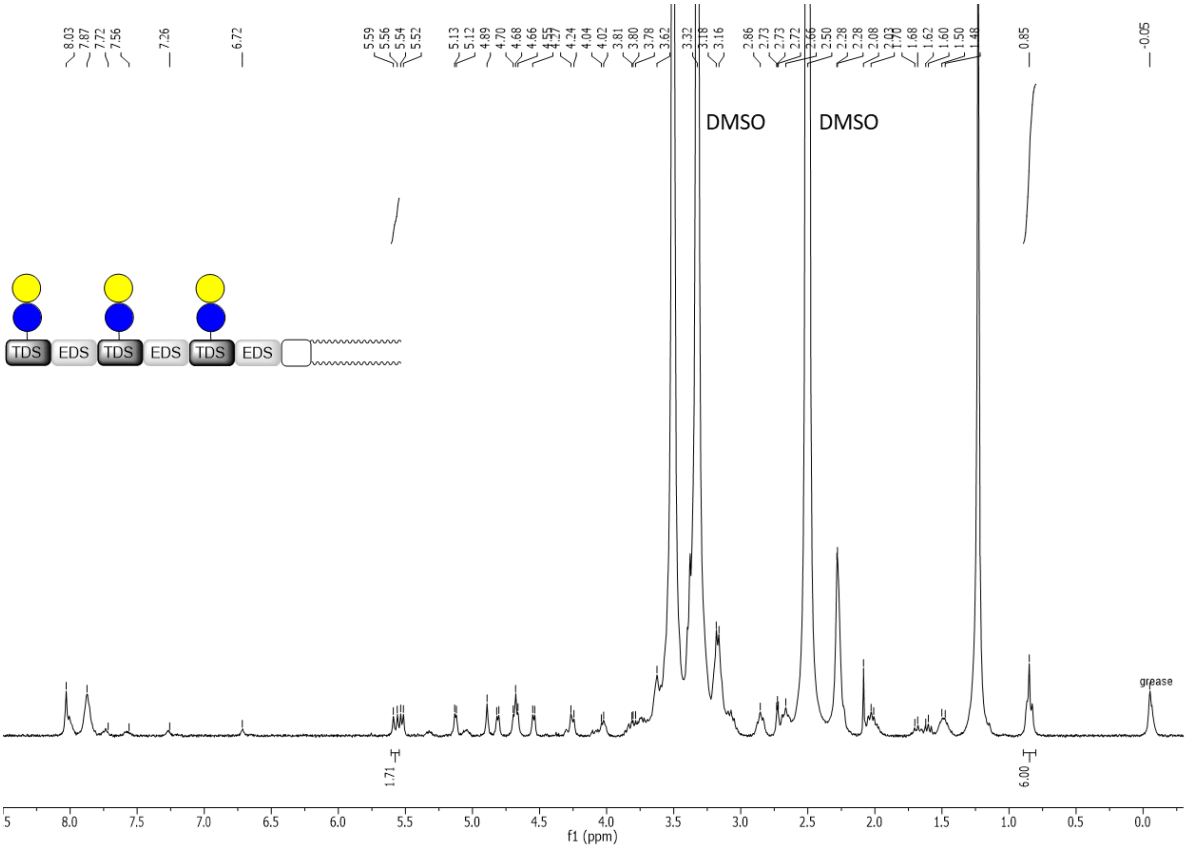


Figure S 73: ^{1}H-NMR spectrum of compound **L9.**

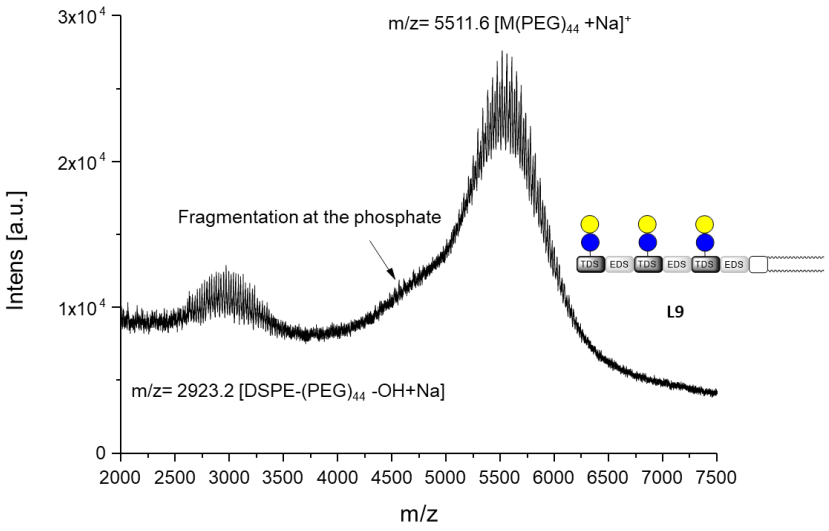


Figure S 74: MALDI-TOF-MS-spectrum of compound **L9**.

4.3. Lac(1,2,3)-4-PEG-DSPE-conjugate, **L10**

Yield: 3.00 mg (69 %). Conversion: 66 %. MALDI-TOF-MS calc. for $C_{223}H_{410}N_{23}O_{99}PNa$ $[M+Na]^+$ 5051.8; found 5052.5.

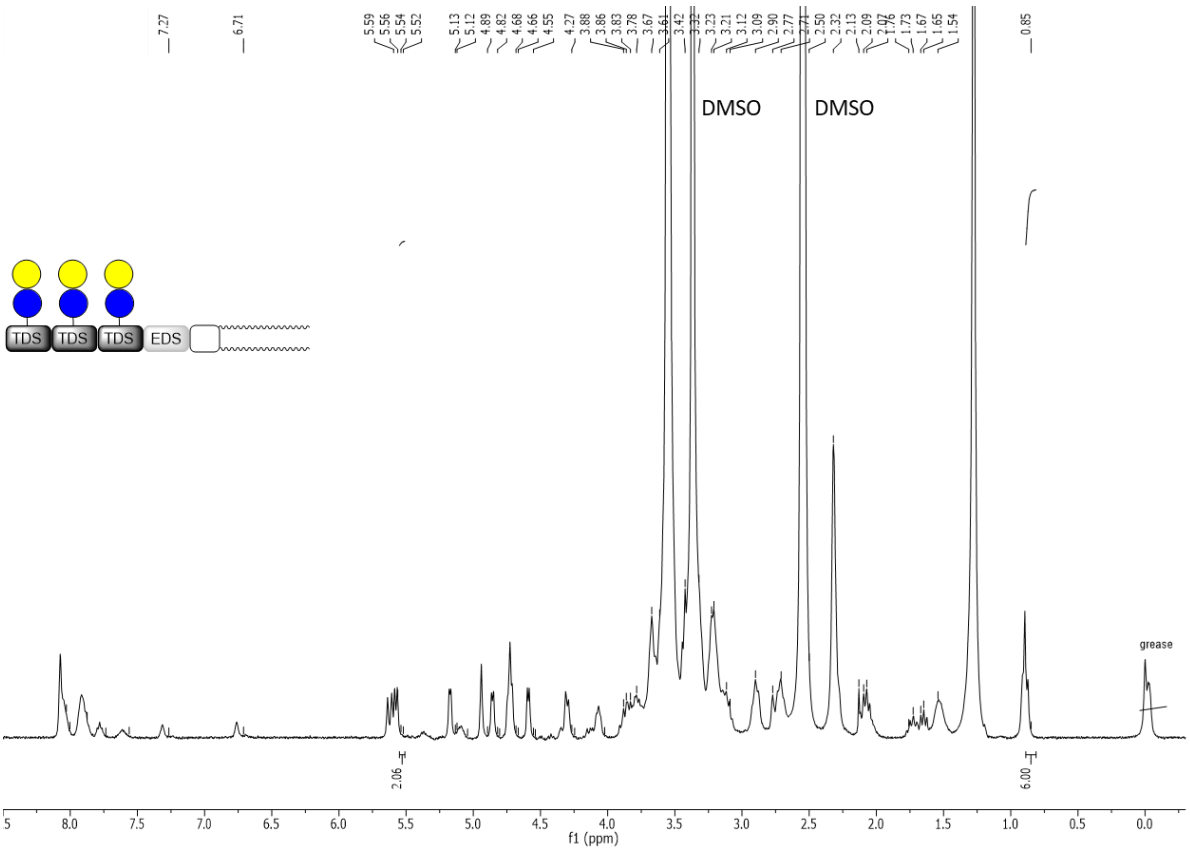


Figure S 75: ^{1}H-NMR spectrum of compound **L10.**

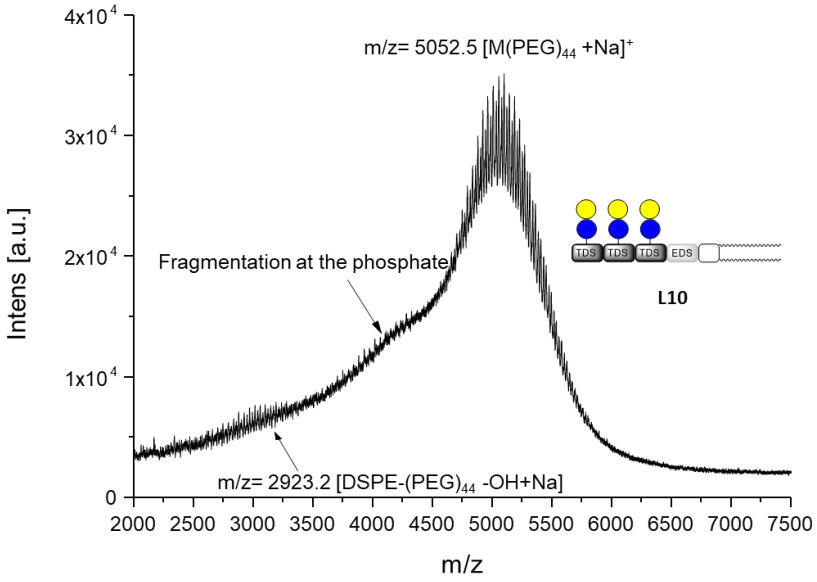


Figure S 76: MALDI-TOF-MS-spectrum of compound **L10**.

4.4. Glc(1,3,5)-6-PEG-DSPE-conjugate**, L16**

Yield: 1.54 mg (35 %). Conversion: 62 % (as determined by ^{1}H-NMR). MALDI-TOF-MS calc. for $C_{231}H_{428}N_{27}O_{95}PNa$ $[M+Na]^+$ 5158.0; found: 5158.7.

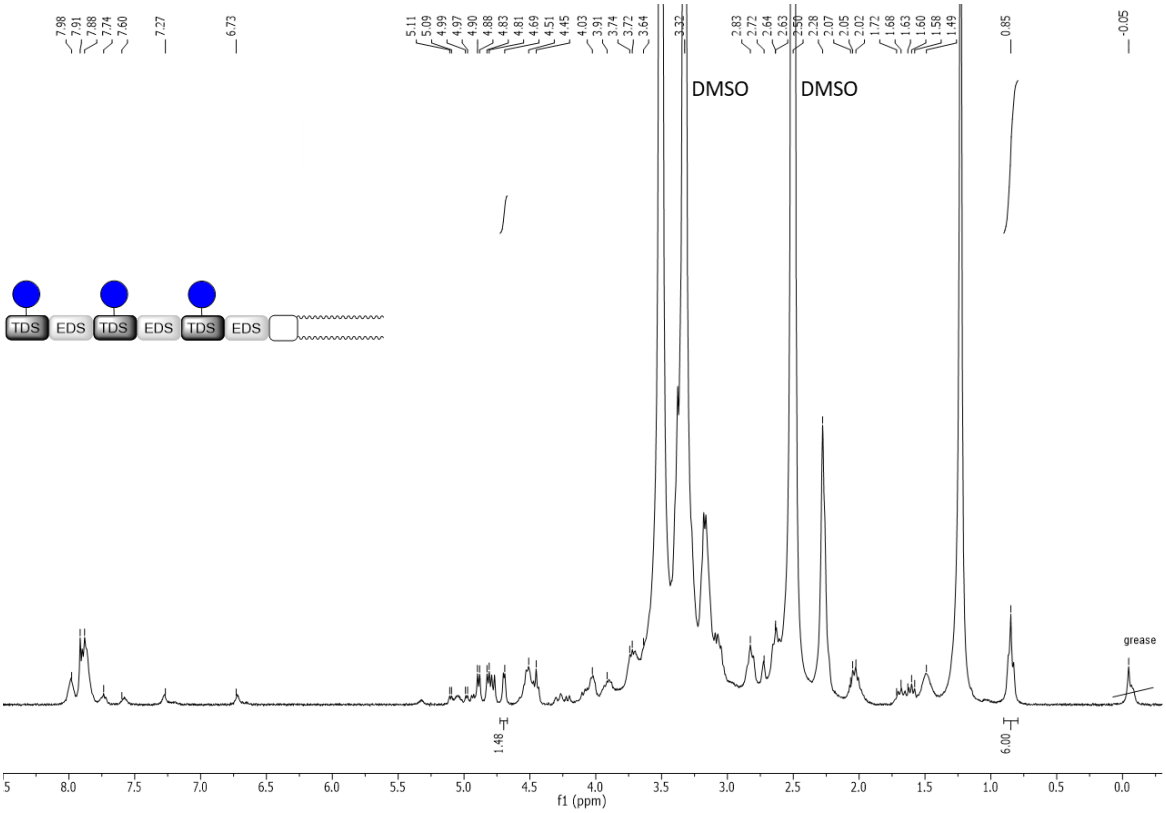


Figure S 77: ^{1}H-NMR spectrum of compound **L16.**

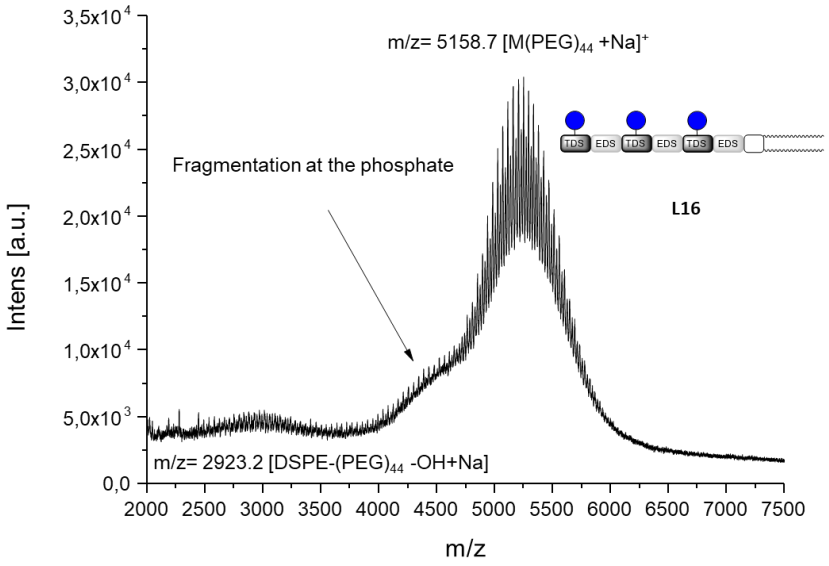


Figure S 78: MALDI-TOF-MS-spectrum of compound **L16.**

5. Analytical data of liposomes

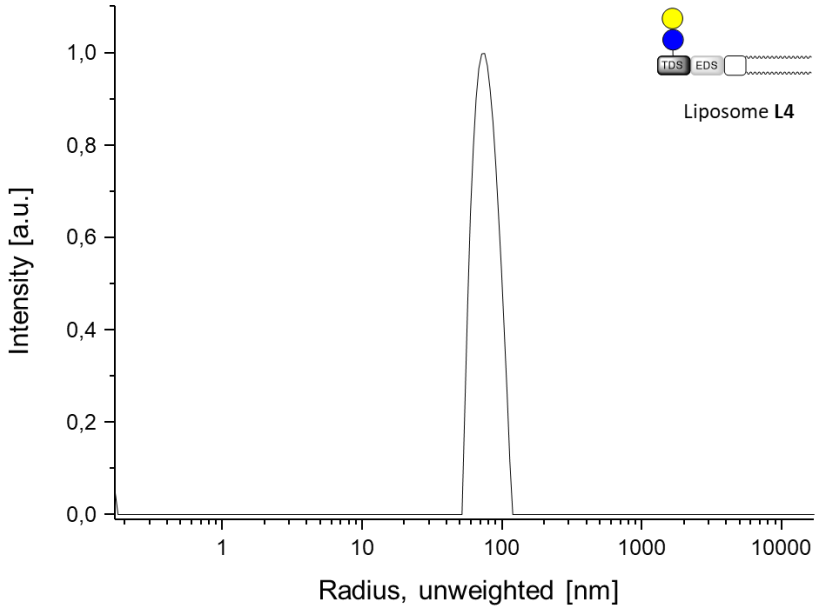


Figure S 79: Exemplary DLS spectrum of **liposome L4.**

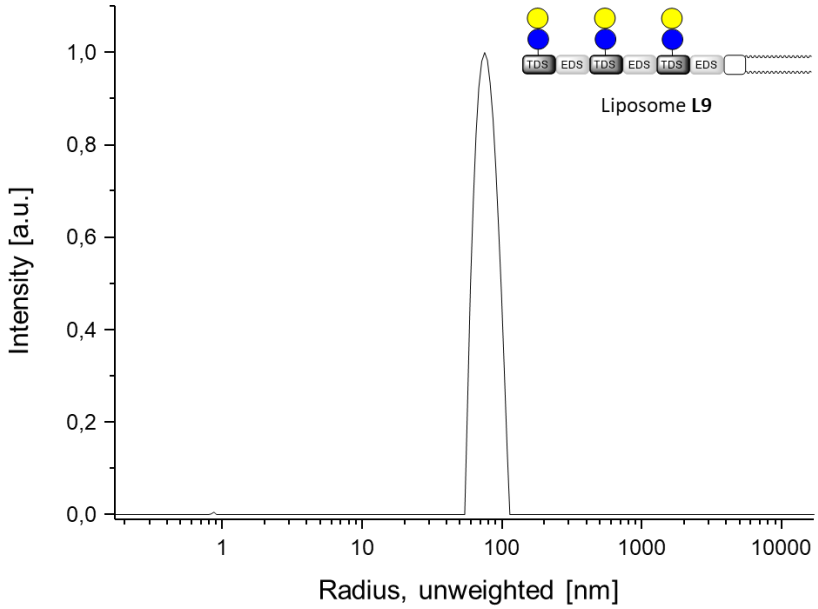


Figure S 80: Exemplary DLS spectrum of **liposome L9.**

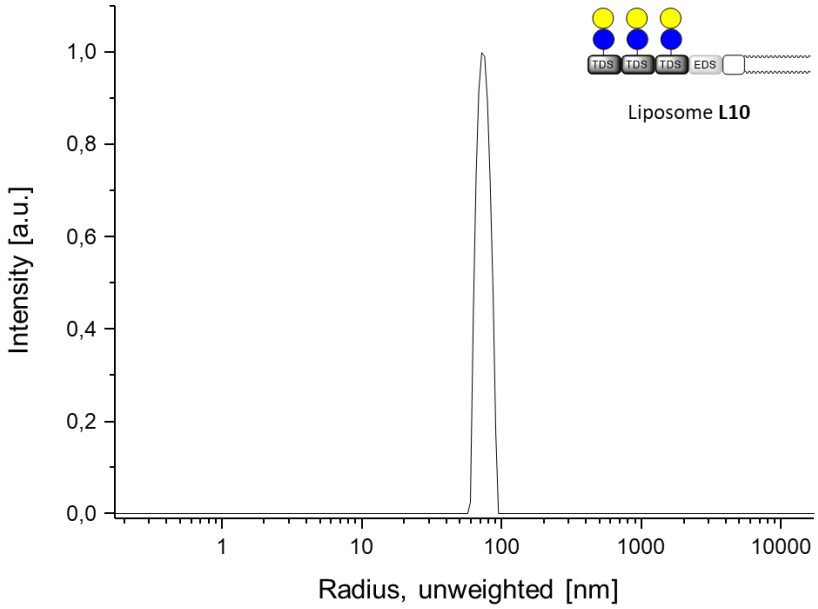


Figure S 81: Exemplary DLS spectrum of **liposome L10.**

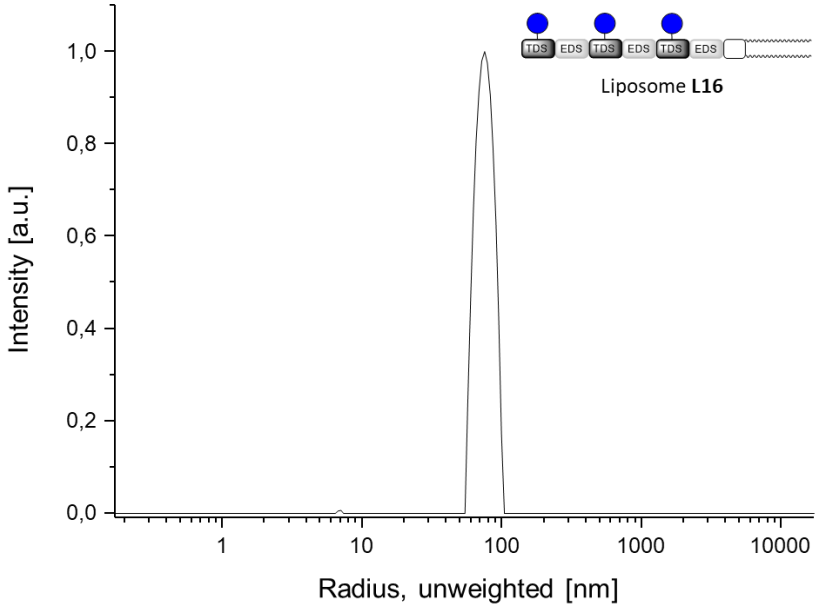


Figure S 82: Exemplary DLS spectrum of **liposome L16.**