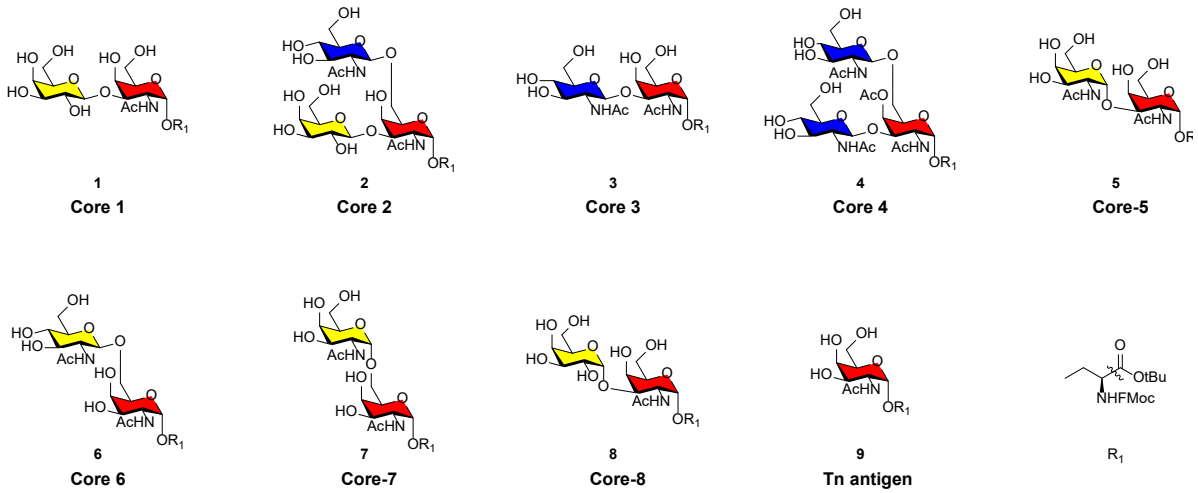
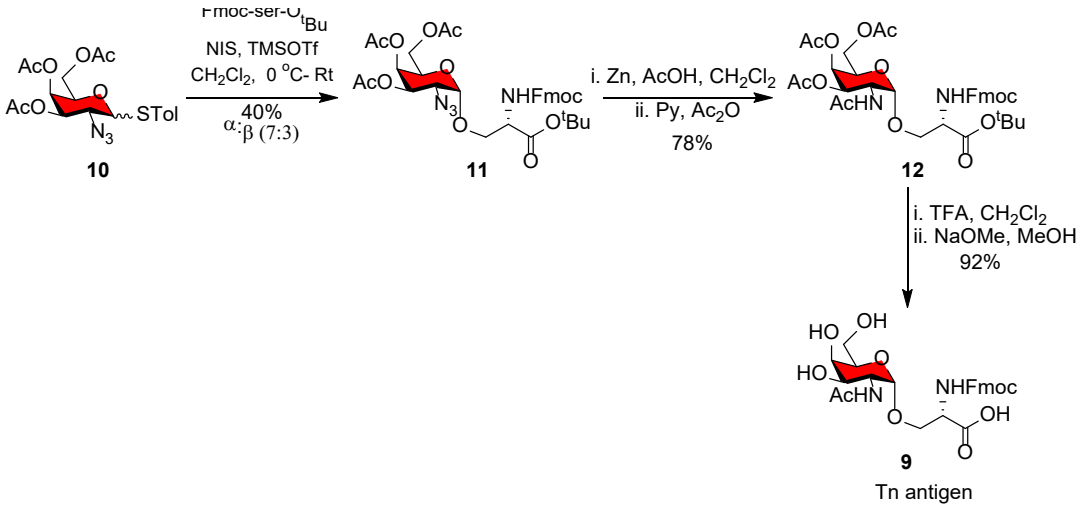


Figure 1: Structures of O-GalNAc mucin cores



Scheme 1: Synthesis of Tn antigen

Additional Materials:

NIS (N-Iodosuccinimide) (Sigma Aldrich,Cat No. 220051).

Fmoc-Ser-O^{t}Bu is commercially available and can also be synthesized using reported procedures.

TMSOTf (Trimethylsilyl trifluoromethanesulfonate) (Sigma Aldrich,Cat No. 225649) **! CAUTION** Fuming and Corrosive liquid.

TFA (Trifluoroacetic Acid) (Sigma Aldrich,Cat No. T6508) **! CAUTION** Highly Corrosive.

Sodium methoxide (Sigma Aldrich,Cat No. 164992) **! CAUTION** Reacts violently with water.

Procedure:

Synthesis of compound 9

1. In a 1 L round bottom flask, 20 g (50.5 mmol) of compound **10**[1] and 17.6 g of (45.9 mmol) Fmoc-Ser-O^{t}Bu[2] was dried under vacuum for 3 h. To the above mixture of donor and acceptor, 20 g of 4 Å molecular sieves powder was added followed by 250 mL of anhydrous dichloromethane. The mixture was allowed to stir at room temperature for 1 h under the argon atmosphere.

Δ Critical Step 4 Å molecular sieves must be freshly activated.

2. To the mixture from step 1, 15.4 g (68.8 mmol) of NIS was added at 0 °C and stirred for 5 min at the same temperature.

3. To the reaction mixture from step 3, 2.0 g (9.18 mmol) of TMSOTf was slowly added at 0 °C over 10 min. The reaction mixture was allowed to reach the room temperature over 2 h and stirred until completion.

4. The reaction mixture from step 3 was quenched with 1.5 mL of triethyl amine at room temperature. The solution was filtered through Celite® 545 and the solution was diluted to 400 mL using dichloromethane. The organic layer was washed with saturated aq. 400 mL of 1:1 hypo/$NaHCO_3$ solution followed by 400 mL of brine. The organic layer was dried over 50 g of anhydrous sodium sulphate, filtered and concentrated to dryness under reduced pressure.

5. The crude from step 4 was purified by flash column chromatography over 340 g of 60 Å silica gel using hexanes and ethyl acetate. The compound was eluted out at 40% ethyl acetate in hexanes. The solution was concentrated to obtain 12.8 g (40%) of compound **11** as a white solid.

Δ Critical Step The yield of the reaction was increased to 62% after two additional 60 Å silica gel purifications of the anomeric mixture.

6. In a 500 mL round bottom flask, 12 g (16.8 mmol) of compound **11** was dissolved in a 150 mL of 9:1 mixture of dichloromethane and glacial acetic acid under nitrogen atmosphere.

7. To the solution from step 6, 16.5 g (0.25 mol) of activated Zn was added in one portion at room temperature and stirred for 3h.

Δ Critical Step Zinc was activated using 1M HCl followed by washing with water, acetone and diethyl ether. If there is any heat evolution after the addition of Zn, cooling using ice-water mixture is recommended.

7. To the solution from step 6, 16.5 g (0.25 mol) of activated Zn was added in one portion at room temperature and stirred for 3h.

8. The reaction mixture from step 7 was filtered over Celite® 545 and concentrated to dryness under reduced pressure.

9. The crude product from step 8 was dissolved using 75 mL of anhydrous pyridine in a 500 mL round bottom flask under nitrogen atmosphere. 25 mL of acetic anhydride was slowly added using addition funnel over 20 min at room temperature. The reaction was allowed to stir at the same temperature for 1 h.

10. The reaction mixture from step 9 was concentrated to remove pyridine and acetic anhydride completely. The crude was dissolved in 300 mL of dichloromethane. The organic layer was washed with 200 ml of 1 M HCl, 200 mL of saturated NaHCO3 and water respectively. The organic layer was dried over 30 g of anhydrous sodium sulphate, filtered and concentrated to dryness.

11. The crude from step 10 was purified by flash column chromatography over 200 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out at 70% to 90% ethyl acetate in hexanes. The solution was concentrated to obtain 9.6 g of compound **12** as thick oil.

12. In a 250 mL round bottom flask, 9.5 g (12.6 mmol) of compound **12** from step 11 was dissolved in 50 mL of 9:1 mixture of TFA and anhydrous anisole under argon atmosphere. The reaction mixture was allowed to stir at room temperature for 1 h.

Δ Critical Step The reaction must be checked for completion every 15 min and increased time of stirring after completion leads to the decrease in yield.

13. The reaction mixture from step 12 was concentrated to dryness at 30 °C under reduced pressure. The crude was coevaporated with 50 mL of anhydrous toluene twice.

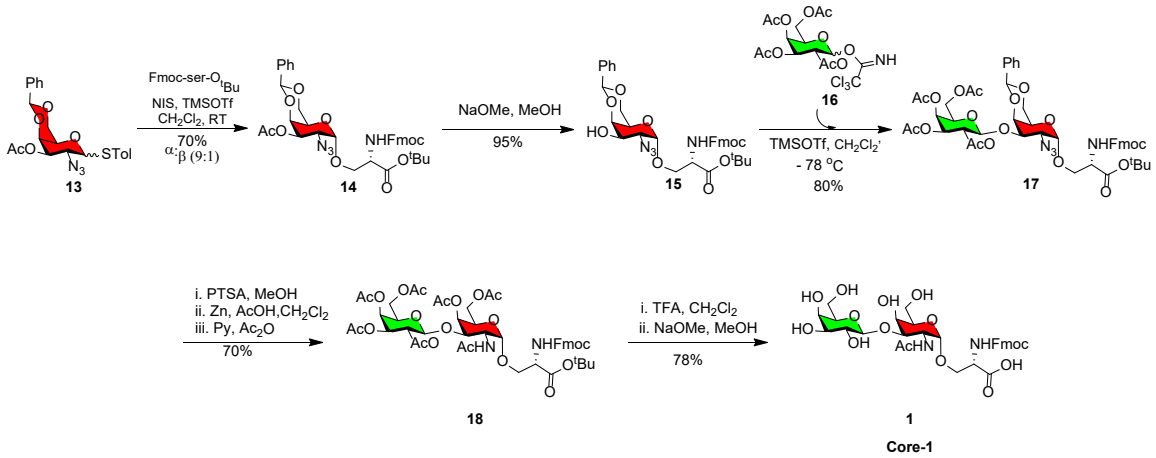
14. The crude from step 13 was dissolved in 150 mL of anhydrous methanol under argon atmosphere. Solid sodium methoxide was used to adjust the pH to 8.5 and stirred at room temperature until completion.

Δ Critical Step More than 0.2 eq of sodium methoxide was required due to use of TFA in the previous step. Exceeding the pH above 9 will increase the Fmoc deprotection. The reaction has to be constantly monitored for completeness as prolonged sitting leads to the Fmoc deprotection.

15. The reaction mixture from step 14 was neutralized using Dowex® 50WX8 to pH 7 and filtered over Celite® 545. The filtrate was concentrated and purified over 100g of C18 reverse phase gel using water and methanol. The product was eluted out in between 30% and 40% of MeOH in water. The solution was concentrated and lyophilized to obtain 6.5 g of compound **9** as a white powder.

Analytical Data:

Compound 9: ^{1}H NMR (400 MHz, MeOD) δ 7.81 (d, *J* = 7.5 Hz, 2H), 7.71 – 7.66 (m, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 2H), 4.80 (d, *J* = 3.2 Hz, 1H), 4.38 (d, *J* = 6.8 Hz, 2H), 4.31 – 4.19 (m, 3H), 3.97 – 3.89 (m, 2H), 3.75 (ddt, *J* = 20.3, 16.8, 5.5 Hz, 6H), 2.01 (s, 3H). ^{13}C NMR (101 MHz, MeOD) δ 175.57, 172.84, 156.70, 143.91, 141.19, 127.39, 126.79, 124.81, 119.53, 98.27, 71.06, 69.04, 68.90, 68.63, 66.57, 61.40, 56.27, 50.00, 21.51.



Scheme 2: Synthesis of Core-1 O-GalNAc glycan

Additional Materials:

NIS (N-Iodosuccinimide) (Sigma Aldrich,Cat No. 220051).

Fmoc-Ser-O^{t}Bu is commercially available and can also be synthesized using reported procedures.

TMSOTf (Trimethylsilyl trifluoromethanesulfonate) (Sigma Aldrich,Cat No. 225649) **! CAUTION** Fuming and Corrosive liquid.

TFA (Trifluoroacetic Acid) (Sigma Aldrich,Cat No. T6508) **! CAUTION** Highly Corrosive.

PTSA (*p*-toluenesulfonic acid) (Sigma Aldrich,Cat No. 402885)

Sodium methoxide (Sigma Aldrich,Cat No. 164992) **! CAUTION** Reacts violently with water.

Procedure:

Synthesis of compound 1

1. In a 1 L round bottom flask, 24.6 g (55.3 mmol) of compound **13**[3] and 16.4 g (48.3 mmol) of Fmoc-Ser-O^{t}Bu was coevaporated with 30 mL of anhydrous toluene twice and dried under high vacuum for a period of 3 h.

Δ Critical Step The compound should be well dried for a proper reaction and good yield.

2. The mixture from step 1 wad dissolved in 250 mL of anhydrous dichloromethane. 16.3 g (72.5 mmol) of NIS was added in one portion at room temperature and 2.2 g (9.6 mmol) of TMSOTf was added successively under argon atmosphere. The reaction mixture was stirred for 6 h or until completion.

Δ Critical Step Both the NIS and TMSOTf must be added at room temperature. Cooling the solution decreases the diastereomeric excess.

3. The reaction mixture from step 2 was slowly quenched with 5 mL of saturated aq $NaHCO_3$ solution at room temperature and diluted with 200 mL of dichloromethane. The organic layer was taken into a 1L separating funnel and washed with 400 mL of saturated aq solution of 1:1 $NaHCO_3$ and $Na_2S_2O_3$. The organic layer was further washed with 400 mL of brine and dried over 50 g of anhydrous sodium sulphate. The organic layer was filtered, concentrated and purified by flash column chromatography over 340 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out at 40% ethyl acetate in hexanes. The solution was concentrated to obtain 20.9 g (70%) of compound **14** as a white solid.

4. In a 500 mL of round bottom flask, 10 g (14.2 mmol) of compound **14** from step 3 was dissolved in 100 mL of anhydrous methanol under argon atmosphere.

5. To the solution from step 4, solid sodium methoxide was added until the pH reached 8.5 at 0 ^oC and stirred at room temperature until completion.

Δ Critical Step Sodium methoxide must be added very slowly such that the pH doesn't exceed 8.5. The reaction must be carefully monitored for completion. Prolonged stirring results in Fmoc deprotection.

6. The reaction mixture from step 5 was neutralized to pH 7 using Amberlite® IRC120 H acidic resin and filtered over Celite® 545. The filtrate was concentrated and purified by flash column chromatography over 200 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out at 45% ethyl acetate in hexanes. The solution was concentrated to obtain 8.9 g (95%) of compound **15** as a white solid.

7. In a 100 mL round bottom flask, 1.23 g (2.5 mmol) of compound **16**[4] and 1.5 g (2.3 mmol) of compound **15** was taken and coevaporated with 5 mL of toluene twice and dried under high vacuum over 6 h.

8. To the mixture from step 7, 30 mL of anhydrous dichloromethane and 2 g of powdered freshly dried 4 Å molecular sieves was added and stirred for 1 h under argon atmosphere.

9. The reaction mixture from step 8 was cooled to -78 ^{0}C using dry ice and ethyl acetate.

! CAUTION Proper clothing and gloves are must to get protected from cold burns.

10. To the reaction mixture from step 9, 50.4 mg (0.2 mmol) of TMSOTf was added slowly using a micro syringe and stirred at the same temperature for 1 h. The reaction was quenched with 50 uL of DIPEA and allowed the reaction temperature to reach room temperature over 30 min.

11. The reaction mixture from step 10 was filtered over Celite® 545 and concentrated under reduced pressure at 30 ºC.

12. The crude product from step 11 was purified by flash column chromatography over 50 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out at 45% ethyl acetate in hexanes. The solution was concentrated to obtain 1.8 g (80%) of compound **17** as a white solid.

13. In a 100 mL round bottom flask, 1.5 g (1.5 mmol) of compound **17** from step 12 was dissolved in 20 mL of anhydrous methanol under argon atmosphere.

Δ Critical Step If the compound is not completely soluble, adding 2 mL of anhydrous dichloromethane helps in dissolving the compound completely.

14. To the reaction mixture from step 13, 57.7 mg (0.3 mmol) of PTSA.H_2O was added at room temperature. The reaction mixture was stirred at 30 ºC for 3h.

Δ Critical Step Increasing the reaction temperature to 45 ºC increases the rate of the reaction.

15. 50 uL of DIPEA was added to the reaction mixture from step 14 to quench the reaction. The solution was concentrated to dryness under reduced pressure and dried under high vacuum over a period of 2 h.

16. The crude from step 15 was dissolved in a 10 mL (4:1) mixture of anhydrous dichloromethane and glacial acetic acid under nitrogen atmosphere and 0.9 g (15.0 mmol) of Zn dust was added and stirred at room temperature for 2 h.

Δ Critical Step 10 g of Zn dust was washed with 50 ml of 1 M HCl and successively with 50 mL of H_20, acetone and diethyl ether before using it for the reaction.

17. The reaction mixture from step 16 was filtered over Celite® 545 and concentrated to dryness under reduced pressure and dried under high vacuum for 2 h.

18. The crude product from step 17 was dissolved in 5 mL of pyridine under nitrogen atmosphere and 2 mL of acetic anhydride was added slowly at 0 ºC and stirred at room temperature for 2 h.

19. The reaction mixture from step 18 was concentrated to remove pyridine and acetic anhydride completely under reduced pressure at 50 °C. 150 mL of ethyl acetate was added and taken into a 500 mL separatory funnel. The organic layer was washed with 50 mL of saturated aq. $NaHCO_3$, 1N HCl and brine solution respectively. The separated organic layer was dried over 10 g of anhydrous sodium sulphate, filtered and concentrated under reduced pressure.

20. The crude product from step 19 was purified by flash column chromatography over 50 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out at 60% ethyl acetate in hexanes. The solution was concentrated to obtain 1.0 g (70%) of compound **18** as a white solid.

Δ Critical Step The intermediates in the three steps involving in the synthesis of compound **18** from **17** are stable and can be stored at 0 °C without moving forward.

21. 0.5 g (0.5 mmol) of compound **18** from step 20 was taken into a 25 mL round bottom flask.

22. To the mixture from step 21, a 5 mL (9:1) mixture of TFA and anhydrous anisole was added at 0 °C under argon atmosphere and stirred for 15 min at room temperature. The solvents were removed below 30 °C under reduced pressure. The crude mixture was coevaporated with 5 mL of anhydrous toluene twice and dried under high vacuum for 1 h.

Δ Critical Step The free acid can be stored only after purification.

23. The crude product from step 22 was dissolved in 5 mL of anhydrous methanol under argon atmosphere. Solid NaOMe was slowly added at 0 °C until the pH reaches 8.5 and stirred at room temperature until completion.

Δ Critical Step Sodium methoxide must be added very slowly such that the pH doesn't exceed 8.5. The reaction must be carefully monitored for completion. Prolonged stirring results in Fmoc deprotection.

24. The reaction mixture from step 23 was neutralized using Amberlite® IRC120 H acidic resin and filtered over Celite® 545. The solution was concentrated and purified by C_{18} (10 g) reverse phase flash column chromatography using H_20 and acetonitrile to obtain 0.27 g (78%) of compound **1** as a white solid.

Δ Critical Step Acetonitrile was evaporated and the remaining compound in water was lyophilized to obtain white solid.

Analytical Data:

Compound 14: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.5 Hz, 2H), 7.67 (t, J = 6.3 Hz, 2H), 7.54 (dd, J = 7.3, 1.7 Hz, 2H), 7.41 (td, J = 13.3, 7.5 Hz, 7H), 5.92 (d, J = 7.7 Hz, 1H), 5.53 (s, 1H), 5.31 (dd, J = 11.1, 2.9 Hz, 1H), 5.08 (d, J = 3.0 Hz, 1H), 4.51 – 4.38 (m, 4H), 4.31 – 4.21 (m, 2H), 4.15 (dd, J = 10.6, 2.7 Hz, 1H), 4.06 – 3.93 (m, 3H), 3.83 (s, 1H), 2.20 (s, 3H), 1.56 (s, 9H). ^{13}C NMR (101 MHz, CDCl3) δ 170.25, 168.61, 155.76, 143.66, 143.61, 141.14, 141.11, 137.30, 128.95, 128.06, 127.60, 127.00, 126.97, 125.95, 125.03, 124.97, 119.88, 100.49, 99.56, 82.91, 77.20, 73.09, 69.65, 69.06, 68.78, 67.12, 62.80, 57.05, 54.82, 46.89, 27.80, 20.81. ESI-MS calcd for **7** $C_{37}H_{40}N_4O_{10}$ [M + Na]+ m/z = 723.2642, found: 723.

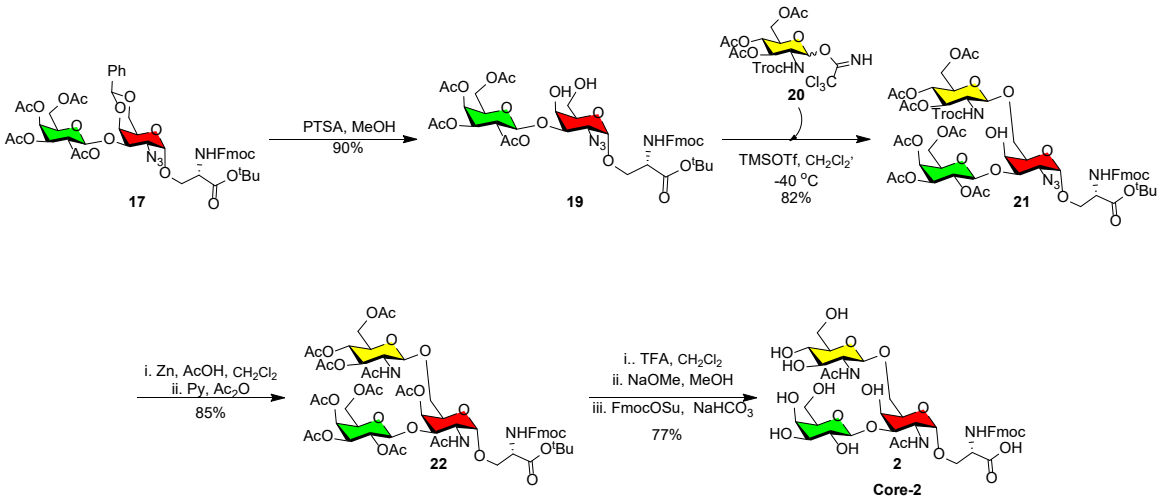
Compound 15: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.5 Hz, 2H), 7.60 (t, *J* = 7.0 Hz, 2H), 7.47 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.38 (dd, *J* = 12.7, 5.3 Hz, 3H), 7.36 – 7.29 (m, 4H), 5.86 (d, *J* = 7.8 Hz, 1H), 5.50 (s, 1H),

4.95 (d, *J* = 3.1 Hz, 1H), 4.42 (dd, *J* = 10.5, 7.1 Hz, 2H), 4.33 (dd, *J* = 10.4, 7.3 Hz, 1H), 4.21 (dd, *J* = 8.4, 5.1 Hz, 3H), 4.12 – 4.02 (m, 3H), 3.96 (dd, *J* = 10.7, 2.6 Hz, 1H), 3.90 (d, *J* = 12.5 Hz, 1H), 3.72 (s, 1H), 3.58 (dd, *J* = 10.6, 3.4 Hz, 1H), 1.50 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.82, 155.92, 143.86, 143.74, 141.33, 137.32, 129.37, 128.35, 127.82, 127.17, 127.14, 126.23, 125.18, 125.07, 120.10, 101.17, 99.88, 83.10, 77.35, 75.37, 69.68, 69.06, 67.22, 63.27, 60.61, 54.99, 47.09, 27.99.

Compound 17: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.63 – 7.57 (m, 2H), 7.52 – 7.47 (m, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.33 (dd, *J* = 16.6, 7.5 Hz, 5H), 5.78 (d, *J* = 7.8 Hz, 1H), 5.50 (s, 1H), 5.34 (d, *J* = 2.9 Hz, 1H), 5.25 (dd, *J* = 10.3, 8.0 Hz, 1H), 5.01 – 4.95 (m, 2H), 4.64 (d, *J* = 7.9 Hz, 1H), 4.45 – 4.38 (m, 2H), 4.35 (dd, *J* = 11.1, 5.1 Hz, 2H), 4.21 (dd, *J* = 13.5, 9.9 Hz, 2H), 4.14 – 4.03 (m, 3H), 4.02 – 3.91 (m, 3H), 3.84 – 3.73 (m, 2H), 3.71 (s, 1H), 2.13 (s, 3H), 2.03 (s, 3H), 1.99 (s, 3H), 1.97 (s, 3H), 1.50 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.27, 170.19, 170.11, 169.35, 168.72, 155.82, 143.65, 141.25, 137.51, 128.86, 128.10, 127.82, 127.12, 126.05, 125.07, 125.02, 120.09, 102.38, 100.55, 99.92, 83.04, 75.69, 75.53, 70.93, 70.81, 69.51, 68.97, 68.55, 67.16, 66.90, 63.47, 61.40, 58.70, 54.95, 47.03, 27.92, 20.65, 20.54.

Compound 18: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.57 (d, *J* = 7.4 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 2H), 5.76 (d, *J* = 8.8 Hz, 1H), 5.69 (s, 1H), 5.33 (s, 2H), 5.13 – 5.05 (m, 1H), 4.93 (d, *J* = 10.8 Hz, 1H), 4.84 (s, 1H), 4.58 – 4.33 (m, 5H), 4.22 (t, *J* = 6.6 Hz, 1H), 4.14 – 4.08 (m, 3H), 4.02 (d, *J* = 7.3 Hz, 1H), 3.98 – 3.90 (m, 2H), 3.84 (d, *J* = 6.0 Hz, 2H), 3.73 (s, 1H), 2.14 (s, 3H), 2.11 (s, 3H), 2.04 (s, 3H), 2.00 (s, 6H), 1.95 (s, 3H), 1.92 (s, 3H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.49, 170.40, 170.35, 170.13, 170.09, 169.68, 169.05, 155.81, 143.65, 141.32, 141.29, 127.87, 127.10, 124.86, 120.11, 100.54, 98.53, 83.13, 77.20, 73.04, 70.86, 70.71, 68.65, 68.57, 67.81, 67.16, 66.72, 62.65, 61.06, 54.82, 48.65, 47.08, 28.00, 23.24, 20.70, 20.66, 20.54.

Compound 1: ^{1}H NMR (400 MHz, D_2O) δ 7.76 (d, *J* = 7.3 Hz, 2H), 7.60 (dd, *J* = 14.3, 7.3 Hz, 2H), 7.36 (dt, *J* = 15.3, 7.3 Hz, 4H), 4.44 (dd, *J* = 9.9, 5.9 Hz, 2H), 4.31 (d, *J* = 7.4 Hz, 1H), 4.25 (dd, *J* = 11.0, 3.6 Hz, 1H), 4.10 (d, *J* = 17.3 Hz, 3H), 3.85 (dt, *J* = 20.1, 12.7 Hz, 4H), 3.75 – 3.39 (m, 9H), 1.93 (s, 3H). ^{13}C NMR (101 MHz, D_2O) δ 176.24, 174.53, 157.47, 143.75, 140.86, 127.92, 127.41, 127.37, 124.91, 120.08, 104.62, 97.88, 77.25, 74.73, 72.45, 70.61, 70.53, 68.85, 68.60, 68.49, 66.26, 60.99, 60.78, 56.23, 48.39, 46.76, 22.07.



Scheme 3: Synthesis of Core-2 O-GalNAc glycan

Additional Materials:

TMSOTf (Trimethylsilyl trifluoromethanesulfonate) (Sigma Aldrich,Cat No. 225649) **! CAUTION** Fuming and Corrosive liquid.

TFA (Trifluoroacetic Acid) (Sigma Aldrich,Cat No. T6508) **! CAUTION** Highly Corrosive.

PTSA (*p*-toluenesulfonic acid) (Sigma Aldrich,Cat No. 402885)

Sodium methoxide (Sigma Aldrich,Cat No. 164992) **! CAUTION** Reacts violently with water.

FmocOSu (N-(9-Fluorenylmethoxycarbonyloxy)succinimide) (Sigma Aldrich,Cat No. 8510140)

Procedure:

Synthesis of compound 2

1. In a 100 mL round bottom flask, 1.5 g (1.5 mmol) of compound **17** was dissolved in 20 mL of anhydrous methanol under argon atmosphere.

2. To the reaction mixture from step 2, 57.7 mg (0.3 mmol) of PTSA.H_2O was added at room temperature. The reaction mixture was stirred at 30 ºC for 3h.

Δ Critical Step Increasing the reaction temperature to 45 ºC increases the rate of the reaction.

3. 50 uL of DIPEA was added to the reaction mixture from step 2 to quench the reaction. The solution was concentrated to dryness under reduced pressure and purified by flash column chromatography over 50 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out from 60% - 80% ethyl acetate in hexanes. The solution was concentrated to obtain 1.2 g (90%) of compound **19** as a white solid.

4. In a 100 mL round bottom flask, 1.1 g (1.8 mmol) of compound **20**[5] and 1.5 g (1.6 mmol) of compound **19** was coevaporated with 5 mL of anhydrous toluene twice and dried under high vacuum for a period of 3 h.

Δ Critical Step The compound should be well dried for a proper reaction and good yield.

5. The mixture from step 4 wad dissolved in 30 mL of anhydrous dichloromethane and 2 g of 4 Å freshly dried molecular sieves powder was added. The mixture was stirred at room temperature under argon atmosphere for 1 h. The solution was cooled to -40 ºC using dry ice and acetonitrile.

! CAUTION Proper clothing and gloves are must to get protected from cold burns.

6. 53.3 mg (0.2 mmol) of TMSOTf was added slowly to the reaction mixture from step 5 using a micro syringe. The reaction mixture was stirred for 1 h or until completion at the same temperature. The reaction was quenched with 50 uL of DIPEA and allowed the reaction temperature to reach room temperature over 30 min.

7. The reaction mixture from step 6 was filtered over Celite® 545 and concentrated under reduced pressure at 30 ºC.

8. The crude product from step 7 was purified by flash column chromatography over 50 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out at 45% ethyl acetate in hexanes. The solution was concentrated to obtain 1.8 g (82%) of compound **21** as a white solid.

9. In a 100 mL round bottom flask, 1 g (0.7 mmol) compound **21** from step 8 was dissolved in a mixture of 15 mL anhydrous dichloromethane and 5 mL of glacial acetic acid under nitrogen atmosphere and 0.72 g (11.0 mmol) of Zn dust was added and stirred at 40 ºC for 12 h.

Δ Critical Step 10 g of Zn dust was washed with 50 ml of 1 M HCl and successively with 50 mL of H_20, acetone and diethyl ether before using it for the reaction.

10. The reaction mixture from step 9 was filtered over Celite® 545 and concentrated to dryness under reduced pressure and dried under high vacuum for 2 h.

11. The crude product from step 10 was dissolved in 10 mL of pyridine under nitrogen atmosphere and 5 mL of acetic anhydride was added slowly at 0 ºC and stirred at room temperature for 2 h.

12. The reaction mixture from step 11 was concentrated to remove pyridine and acetic anhydride completely under reduced pressure at 50 ºC. 150 mL of ethyl acetate was added and taken into a 500 mL separatory funnel. The organic layer was washed with 50 mL of saturated aq. $NaHCO_3$, 1N HCl and brine solution respectively. The separated organic layer was dried over 10 g of anhydrous sodium sulphate, filtered and concentrated under reduced pressure.

13. The crude product from step 12 was purified over 50 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out at 80% ethyl acetate in hexanes. The solution was concentrated to obtain 0.8 g (85%) of compound **22** as a white solid.

14. 0.7 g (0.5 mmol) of compound **22** from step 13 was taken into a 25 mL round bottom flask.

15. To the mixture from step 14, a 7 mL (9:1) mixture of TFA and anhydrous anisole was added at 0 ºC under argon atmosphere and stirred for 15 min at room temperature. The solvents were removed below 30 ºC under reduced pressure. The crude mixture was coevaporated with 5 mL of anhydrous toluene twice and dried under high vacuum for 1 h.

Δ Critical Step The free acid can be stored only after purification.

16. The crude product from step 15 was dissolved in 5 mL of anhydrous methanol under argon atmosphere. Solid NaOMe was slowly added at 0 ºC until the pH reaches 8.5 and stirred at room temperature until completion.

Δ Critical Step Sodium methoxide must be added very slowly such that the pH doesn't exceed 8.5. The reaction must be carefully monitored for completion. 50% of Fmoc was deprotected even after maintaining the pH.

17. The reaction mixture from step 16 was neutralized using Amberlite® IRC120 H acidic resin and filtered over Celite® 545. The solution was concentrated and dried and high vacuum for 1 h.

18. The crude product from step 17 was dissolved in a mixture of acetone (6 mL) and H_2O (3 mL) under nitrogen atmosphere. To the vigorously stirred solution under nitrogen atmosphere was added 63 mg (0.75 mmol) of $NaHCO_3$ and 168 mg (0.5 mmol) of FmocOSu. The reaction mixture was stirred at room temperature for 2 h.

19. The reaction mixture from step 18 was concentrated and purified by C_{18} (10 g) reverse phase flash column chromatography using H_20 and acetonitrile to obtain 0.37 g (77%) of compound **2** as a white solid.

Δ Critical Step Acetonitrile was evaporated and the remaining compound in water was lyophilized to obtain white solid.

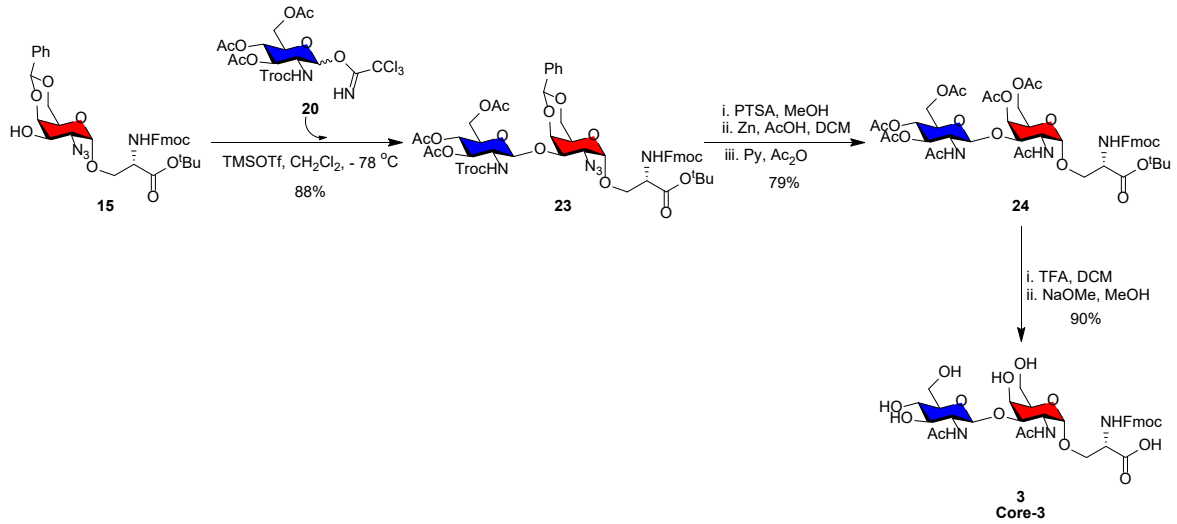
Analytical Data:

Compound 19: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.61 (d, *J* = 7.4 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 2H), 5.95 (d, *J* = 7.9 Hz, 1H), 5.35 (s, 1H), 5.24 (dd, *J* = 10.3, 8.0 Hz, 1H), 4.98 (dd, *J* = 10.5, 3.3 Hz, 1H), 4.88 (d, *J* = 3.2 Hz, 1H), 4.58 (d, *J* = 8.0 Hz, 1H), 4.48 – 4.32 (m, 3H), 4.20 (t, *J* = 6.8 Hz, 1H), 4.13 – 4.00 (m, 4H), 3.93 (dd, *J* = 24.1, 10.8 Hz, 2H), 3.87 – 3.78 (m, 3H), 3.73 (dd, *J* = 14.2, 7.5 Hz, 1H), 3.60 (dd, *J* = 10.5, 3.4 Hz, 1H), 2.14 (s, 3H), 2.05 (s, 3H), 1.98 (d, *J* = 5.8 Hz, 6H), 1.49 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.40, 170.10, 170.05, 169.54, 168.87, 155.86, 143.81, 143.68, 141.33, 127.78, 127.12, 125.16, 120.07, 101.78, 99.67, 83.06, 78.08, 77.20, 71.28, 70.61, 70.05, 69.91, 69.03, 68.28, 66.93, 62.66, 61.55, 58.41, 55.02, 47.17, 27.93, 20.62, 20.53

Compound 21: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (t, *J* = 7.4 Hz, 2H), 7.68 – 7.60 (m, 2H), 7.58 – 7.51 (m, 2H), 7.48 – 7.32 (m, 7H), 5.83 (d, *J* = 7.8 Hz, 1H), 5.38 (d, *J* = 2.8 Hz, 1H), 5.29 (dd, *J* = 10.3, 7.9 Hz, 1H), 5.06 – 4.97 (m, 2H), 4.69 (d, *J* = 7.9 Hz, 1H), 4.51 – 4.42 (m, 2H), 4.39 (dd, *J* = 12.2, 5.0 Hz, 2H), 4.25 (dd, *J* = 14.2, 9.5 Hz, 2H), 4.13 (ddd, *J* = 23.9, 10.6, 5.4 Hz, 3H), 3.99 (dd, *J* = 16.6, 7.5 Hz, 2H), 3.82 (ddd, *J* = 23.7, 14.1, 7.2 Hz, 3H), 2.17 (s, 3H), 2.07 (s, 3H), 2.03 (s, 2H), 2.00 (d, *J* = 6.9 Hz, 3H), 1.54 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.32, 170.25, 170.17, 169.42, 155.90, 143.73, 141.32, 137.60, 128.93, 128.17, 127.88, 127.20, 127.14, 126.12, 125.08, 120.15, 102.44, 100.63, 99.97, 83.10, 77.28, 75.74, 75.62, 71.00, 70.90, 69.03, 68.65, 67.23, 67.00, 63.55, 61.48, 58.79, 55.03, 47.11, 27.99, 20.72, 20.69, 20.59. MS (MALDI-TOF, dhb, positive ion mode):m/z: found: 1384.35 [M+Na]+; C57H70Cl3N5O27 Na calcd 1384.32.

Compound 22: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.2 Hz, 2H), 7.60 (d, *J* = 4.9 Hz, 2H), 7.39 (t, *J* = 7.1 Hz, 2H), 7.31 (t, *J* = 6.7 Hz, 2H), 6.11 (d, *J* = 6.5 Hz, 1H), 6.00 (d, *J* = 7.1 Hz, 1H), 5.81 (d, *J* = 8.4 Hz, 1H), 5.44 (t, *J* = 9.3 Hz, 1H), 5.32 (d, *J* = 2.6 Hz, 1H), 5.24 (s, 1H), 5.06 (dd, *J* = 10.0, 8.2 Hz, 1H), 5.01 – 4.88 (m, 2H), 4.84 – 4.69 (m, 2H), 4.53 (d, *J* = 7.8 Hz, 1H), 4.47 (s, 2H), 4.36 (d, *J* = 4.2 Hz, 2H), 4.23 (d, *J* = 6.6 Hz, 2H), 4.12 – 4.00 (m, 3H), 3.93 (s, 2H), 3.88 – 3.78 (m, 3H), 3.62 (dd, *J* = 44.9, 9.1 Hz, 3H), 3.43 – 3.35 (m, 1H), 2.13 (s, 3H), 2.09 (s, 3H), 2.03 (s, 3H), 2.02 – 1.97 (m, 12H), 1.94 (d, *J* = 10.7 Hz, 6H), 1.88 (s, 3H), 1.47 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.64, 170.46, 170.39, 170.29, 170.23, 170.11, 169.69, 169.48, 169.27, 156.00, 143.67, 141.29, 127.80, 127.14, 124.95, 120.06, 100.65, 100.15, 97.85, 82.90, 77.21, 77.00, 76.79, 73.24, 71.63, 70.81, 70.68, 69.09, 68.79, 68.69, 67.07, 66.70, 61.97, 61.00, 55.58, 54.73, 48.69, 47.05, 28.00, 23.27, 20.74, 20.69, 20.65, 20.62, 20.51.

Compound 2: ^{1}H NMR (600 MHz, D_2O) δ 7.86 (t, *J* = 7.7 Hz, 2H), 7.73 – 7.61 (m, 2H), 7.48 (dt, *J* = 14.7, 7.4 Hz, 2H), 7.45 – 7.36 (m, 2H), 4.77 (d, *J* = 2.9 Hz, 3H), 4.58 (dd, *J* = 10.7, 5.6 Hz, 1H), 4.49 (d, *J* = 8.3 Hz, 2H), 4.37 (d, *J* = 7.8 Hz, 1H), 4.30 – 4.20 (m, 2H), 4.12 (d, *J* = 9.1 Hz, 2H), 3.91 (dd, *J* = 22.9, 12.6 Hz, 4H), 3.83 – 3.70 (m, 5H), 3.57 (dddd, *J* = 30.7, 25.5, 21.8, 10.6 Hz, 7H), 3.36 (d, *J* = 3.8 Hz, 2H), 1.97 (s, 6H). ^{13}C NMR (151 MHz, D_2O) δ 176.26, 174.57, 174.27, 157.45, 143.88, 140.93, 128.02, 127.52, 125.02, 120.18, 120.13, 104.63, 101.23, 97.89, 76.87, 75.80, 74.82, 73.81, 72.49, 70.57, 69.93, 69.37, 69.03, 68.79, 68.53, 66.31, 60.84, 60.69, 56.13, 55.66, 48.37, 46.90, 22.21, 22.11.



Scheme 4: Synthesis of Core-3 O-GalNAc glycan

Additional Materials:

TMSOTf (Trimethylsilyl trifluoromethanesulfonate) (Sigma Aldrich,Cat No. 225649) **! CAUTION** Fuming and Corrosive liquid.

TFA (Trifluoroacetic Acid) (Sigma Aldrich,Cat No. T6508) **! CAUTION** Highly Corrosive.

PTSA (*p*-toluenesulfonic acid) (Sigma Aldrich,Cat No. 402885)

Sodium methoxide (Sigma Aldrich,Cat No. 164992) **! CAUTION** Reacts violently with water.

Procedure:

Synthesis of compound 3

1. In a 100 mL round bottom flask, 1.6 g (2.6 mmol) of compound **20**[5] and 1.4 g (2.1 mmol) of compound **15** was taken and coevaporated with 5 mL of toluene twice and dried under high vacuum over 6 h.

2. To the mixture from step 2, 30 mL of anhydrous dichloromethane and 2 g of powdered freshly dried 4 Å molecular sieves was added and stirred for 1 h under argon atmosphere.

3. The reaction mixture from step 2 was cooled to -78 ^{0}C using dry ice and ethyl acetate.

! CAUTION Proper clothing and gloves are must to get protected from cold burns.

4. To the reaction mixture from step 3, 94 mg (0.4 mmol) of TMSOTf was added slowly using a micro syringe and stirred at the same temperature for 1 h. The reaction was quenched with 100 uL of DIPEA and allowed the reaction temperature to reach room temperature over 30 min.

5. The reaction mixture from step 4 was filtered over Celite® 545 and concentrated under reduced pressure at 30 °C.

6. The crude product from step 5 was purified by flash column chromatography over 50 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out at 40% ethyl

acetate in hexanes. The solution was concentrated to obtain 2.1 g (88%) of compound **23** as a white solid.

7. In a 100 mL round bottom flask, 2.0 g (1.7 mmol) of compound **23** from step 6 was dissolved in 20 mL of anhydrous methanol under argon atmosphere.

Δ Critical Step If the compound is not completely soluble, adding 2 mL of anhydrous dichloromethane helps in dissolving the compound completely.

8. To the reaction mixture from step 7, 68 mg (0.3 mmol) of PTSA.H_2O was added at room temperature. The reaction mixture was stirred at 30 ºC for 3h.

Δ Critical Step Increasing the reaction temperature to 45 ºC increases the rate of the reaction.

9. 60 uL of DIPEA was added to the reaction mixture from step 8 to quench the reaction. The solution was concentrated to dryness under reduced pressure and dried under high vacuum over a period of 2 h.

10. The crude from step 9 was dissolved in a mixture of 10 mL anhydrous dichloromethane and 5 mL of glacial acetic acid under nitrogen atmosphere and 1.6 g (25.5 mmol) of Zn dust was added and stirred at room temperature for 40 ºC for 12 h.

Δ Critical Step 10 g of Zn dust was washed with 50 ml of 1 M HCl and successively with 50 mL of H_20, acetone and diethyl ether before using it for the reaction.

11. The reaction mixture from step 10 was filtered over Celite® 545 and concentrated to dryness under reduced pressure and dried under high vacuum for 2 h.

12. The crude product from step 11 was dissolved in 10 mL of pyridine under nitrogen atmosphere and 5 mL of acetic anhydride was added slowly at 0 ºC and stirred at room temperature for 2 h.

13. The reaction mixture from step 12 was concentrated to remove pyridine and acetic anhydride completely under reduced pressure at 50 ºC. 150 mL of ethyl acetate was added and taken into a 500 mL separatory funnel. The organic layer was washed with 50 mL of saturated aq. $NaHCO_3$, 1N HCl and brine solution respectively. The separated organic layer was dried over 10 g of anhydrous sodium sulphate, filtered and concentrated under reduced pressure.

14. The crude product from step 13 was purified by flash column chromatography over 50 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out at 65% ethyl acetate in hexanes. The solution was concentrated to obtain 1.4 g (79%) of compound **24** as a white solid.

Δ Critical Step The intermediates in the three steps involving in the synthesis of compound **18** from **17** are stable and can be stored at 0 ºC without moving forward.

15. 1.0 g (1.0 mmol) of compound **24** from step 14 was taken into a 25 mL round bottom flask.

16. To the mixture from step 15, a 10 mL (9:1) mixture of TFA and anhydrous anisole was added at 0 ºC under argon atmosphere and stirred for 15 min at room temperature. The

solvents were removed below 30 °C under reduced pressure. The crude mixture was coevaporated with 5 mL of anhydrous toluene twice and dried under high vacuum for 1 h.

Δ Critical Step The free acid can be stored only after purification.

17. The crude product from step 16 was dissolved in 5 mL of anhydrous methanol under argon atmosphere. Solid NaOMe was slowly added at 0 °C until the pH reaches 8.5 and stirred at room temperature until completion.

Δ Critical Step Sodium methoxide must be added very slowly such that the pH doesn't exceed 8.5. The reaction must be carefully monitored for completion. Prolonged stirring results in Fmoc deprotection. If there is a Fmoc deprotection, FmocOSu can be used in reinstalling the deprotected Fmoc (See step 18 in core-2 synthesis)

18. The reaction mixture from step 17 was neutralized using Amberlite® IRC120 H acidic resin and filtered over Celite® 545. The solution was concentrated and purified by C_{18} (10 g) reverse phase flash column chromatography using H_20 and acetonitrile to obtain 0.6 g (90%) of compound **3** as a white solid.

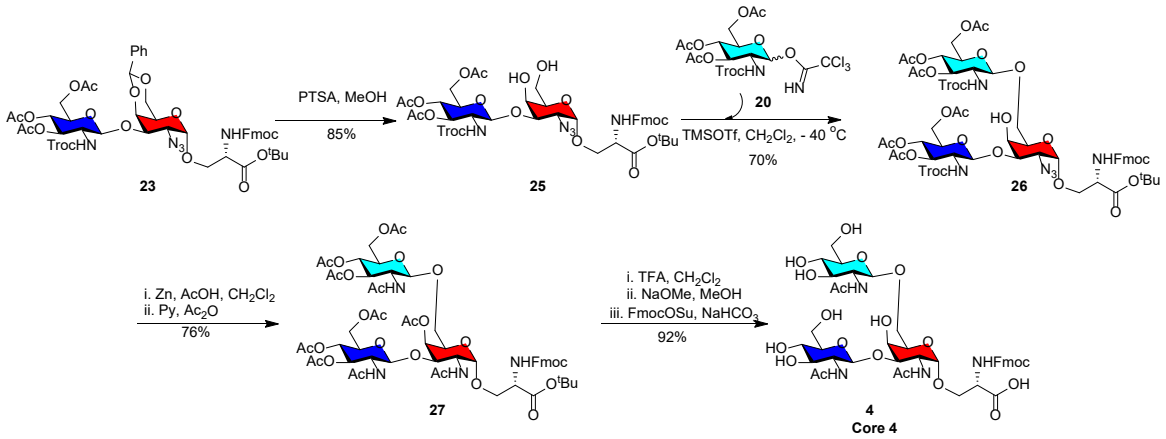
Δ Critical Step Acetonitrile was evaporated and the remaining compound in water was lyophilized to obtain white solid.

Analytical Data:

Compound 23: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.4 Hz, 2H), 7.62 (dd, *J* = 7.1, 4.2 Hz, 2H), 7.47 (d, *J* = 6.4 Hz, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.37 – 7.30 (m, 5H), 5.74 (d, *J* = 8.0 Hz, 1H), 5.50 (s, 1H), 5.21 (t, *J* = 9.9 Hz, 1H), 5.02 – 4.91 (m, 3H), 4.70 (d, *J* = 12.0 Hz, 1H), 4.59 (dd, *J* = 23.4, 10.1 Hz, 2H), 4.48 – 4.40 (m, 2H), 4.37 (d, *J* = 2.2 Hz, 1H), 4.34 – 4.16 (m, 4H), 4.05 – 3.96 (m, 3H), 3.95 – 3.91 (m, 1H), 3.86 (dd, *J* = 10.7, 3.2 Hz, 1H), 3.74 (s, 1H), 3.59 (dd, *J* = 18.5, 8.8 Hz, 1H), 3.36 (d, *J* = 8.3 Hz, 1H), 2.01 (s, 3H), 1.98 (d, *J* = 4.9 Hz, 6H), 1.49 (s, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.42, 170.31, 169.40, 168.63, 155.89, 153.86, 143.75, 143.48, 141.24, 137.57, 128.87, 128.10, 127.89, 127.27, 127.18, 126.05, 125.34, 125.10, 120.28, 101.64, 100.55, 99.51, 95.28, 83.09, 76.34, 75.39, 74.50, 71.67, 71.58, 69.44, 68.99, 68.28, 67.21, 63.46, 61.40, 58.69, 56.09, 54.90, 47.06, 27.94, 20.71, 20.62, 20.59.

Compound 24: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.2 Hz, 2H), 7.57 (s, 2H), 7.36 (t, *J* = 7.3 Hz, 2H), 7.28 (t, *J* = 7.3 Hz, 2H), 6.18 (d, *J* = 7.7 Hz, 1H), 6.02 (d, *J* = 5.5 Hz, 1H), 5.85 (d, *J* = 8.0 Hz, 1H), 5.31 (dd, *J* = 21.6, 6.4 Hz, 2H), 5.00 (t, *J* = 9.7 Hz, 1H), 4.89 (dd, *J* = 11.6, 5.7 Hz, 2H), 4.48 – 4.41 (m, 1H), 4.37 (d, *J* = 4.2 Hz, 3H), 4.26 – 4.16 (m, 2H), 4.11 – 4.05 (m, 2H), 4.03 – 3.98 (m, 1H), 3.95 – 3.83 (m, 3H), 3.77 (d, *J* = 9.0 Hz, 1H), 3.63 (d, *J* = 9.5 Hz, 1H), 3.51 (d, *J* = 8.8 Hz, 1H), 2.06 (s, 3H), 2.03 (s, 3H), 1.99 – 1.97 (m, 9H), 1.92 (s, 3H), 1.90 (s, 3H), 1.44 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.11, 170.73, 170.62, 170.41, 169.89, 169.23, 168.94, 155.85, 143.63, 141.17, 127.73, 127.02, 124.85, 119.98, 99.25, 98.34, 82.88, 72.88, 71.87, 68.87, 68.55, 68.32, 67.57, 66.95, 62.50, 61.35, 55.31, 54.79, 48.81, 47.01, 27.90, 23.22, 23.12, 20.60, 20.55, 20.51.

Compound 3: ^{1}H NMR (400 MHz, D_2O) δ 7.31 – 7.12 (m, 4H), 7.08 – 6.89 (m, 4H), 4.65 (s, 1H), 4.38 (d, *J* = 8.1 Hz, 1H), 4.06 (dd, *J* = 41.3, 11.9 Hz, 4H), 3.83 – 3.33 (m, 13H), 3.17 (s, 1H), 1.91 (d, *J* = 7.6 Hz, 6H). ^{13}C NMR (101 MHz, D_2O) δ 176.18, 174.33, 173.60, 157.18, 143.45, 140.69, 127.66, 127.16, 124.76, 119.85, 102.41, 97.84, 76.84, 75.43, 73.54, 70.42, 69.31, 68.59, 61.04, 60.10, 56.18, 55.49, 48.89, 48.20, 46.55, 22.28, 22.22.



Scheme 5: Synthesis of Core-4 O-GalNAc glycan

Additional Materials:

TMSOTf (Trimethylsilyl trifluoromethanesulfonate) (Sigma Aldrich,Cat No. 225649) **! CAUTION** Fuming and Corrosive liquid.

TFA (Trifluoroacetic Acid) (Sigma Aldrich,Cat No. T6508) **! CAUTION** Highly Corrosive.

PTSA (*p*-toluenesulfonic acid) (Sigma Aldrich,Cat No. 402885)

Sodium methoxide (Sigma Aldrich,Cat No. 164992) **! CAUTION** Reacts violently with water.

FmocOSu (N-(9-Fluorenylmethoxycarbonyloxy)succinimide) (Sigma Aldrich,Cat No. 8510140)

Procedure:

Synthesis of compound 4

1. In a 100 mL round bottom flask, 3.0 g (2.6 mmol) of compound **23** was dissolved in 30 mL of anhydrous methanol under argon atmosphere.

2. To the reaction mixture from step 2, 101 mg (0.5 mmol) of PTSA.H_2O was added at room temperature. The reaction mixture was stirred at 30 ºC for 3h.

Δ Critical Step Increasing the reaction temperature to 45 ºC increases the rate of the reaction.

3. 100 uL of DIPEA was added to the reaction mixture from step 2 to quench the reaction. The solution was concentrated to dryness under reduced pressure and purified by flash column chromatography over 50 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out from 60% - 80% ethyl acetate in hexanes. The solution was concentrated to obtain 2.3 g (85%) of compound **25** as a white foamy solid.

4. In a 100 mL round bottom flask, 0.6 g (1.0 mmol) of compound **20**[5] and 1.0 g (0.97 mmol) of compound **25** was coevaporated with 5 mL of anhydrous toluene twice and dried under high vacuum for a period of 3 h.

Δ Critical Step The compound should be well dried for a proper reaction and good yield.

5. The mixture from step 4 wad dissolved in 20 mL of anhydrous dichloromethane and 1.5 g of 4 Å freshly dried molecular sieves powder was added. The mixture was stirred at room temperature under argon atmosphere for 1 h. The solution was cooled to -78 ºC using dry ice and ethyl acetate.

! CAUTION Proper clothing and gloves are must to get protected from cold burns.

6. 43 mg (0.19 mmol) of TMSOTf was added slowly to the reaction mixture from step 5 using a micro syringe. The reaction mixture was stirred for 1 h or until completion at the same temperature. The reaction was quenched with 40 uL of DIPEA and allowed the reaction temperature to reach room temperature over 30 min.

7. The reaction mixture from step 6 was filtered over Celite® 545 and concentrated under reduced pressure at 30 ºC.

8. The crude product from step 7 was purified by flash column chromatography over 50 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out at 50% ethyl acetate in hexanes. The solution was concentrated to obtain 1.0 g (70%) of compound **26** as a white solid.

9. In a 100 mL round bottom flask, 1 g (0.67 mmol) compound **26** from step 8 was dissolved in a mixture of 15 mL anhydrous dichloromethane and 5 mL of glacial acetic acid under nitrogen atmosphere and 0.7 g (10.0 mmol) of Zn dust was added and stirred at 40 ºC for 12 h.

Δ Critical Step 10 g of Zn dust was washed with 50 ml of 1 M HCl and successively with 50 mL of H_20, acetone and diethyl ether before using it for the reaction.

10. The reaction mixture from step 9 was filtered over Celite® 545 and concentrated to dryness under reduced pressure and dried under high vacuum for 2 h.

11. The crude product from step 10 was dissolved in 10 mL of pyridine under nitrogen atmosphere and 5 mL of acetic anhydride was added slowly at 0 ºC and stirred at room temperature for 2 h.

12. The reaction mixture from step 11 was concentrated to remove pyridine and acetic anhydride completely under reduced pressure at 50 ºC. 150 mL of ethyl acetate was added and taken into a 500 mL separatory funnel. The organic layer was washed with 50 mL of saturated aq. $NaHCO_3$, 1N HCl and brine solution respectively. The separated organic layer was dried over 10 g of anhydrous sodium sulphate, filtered and concentrated under reduced pressure.

13. The crude product from step 12 was purified over 50 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out from 70-80% ethyl acetate in hexanes. The solution was concentrated to obtain 0.6 g (76%) of compound **27** as a white solid.

14. 0.5 g (0.39 mmol) of compound **27** from step 13 was taken into a 25 mL round bottom flask.

15. To the mixture from step 14, a 5 mL (9:1) mixture of TFA and anhydrous anisole was added at 0 ºC under argon atmosphere and stirred for 15 min at room temperature. The

solvents were removed below 30 °C under reduced pressure. The crude mixture was coevaporated with 5 mL of anhydrous toluene twice and dried under high vacuum for 1 h.

Δ Critical Step The free acid can be stored only after purification.

16. The crude product from step 15 was dissolved in 5 mL of anhydrous methanol under argon atmosphere. Solid NaOMe was slowly added at 0 °C until the pH reaches 8.5 and stirred at room temperature until completion. until completion.

Δ Critical Step Sodium methoxide must be added very slowly such that the pH doesn't exceed 8.5. The reaction must be carefully monitored for completion. 70% of Fmoc was deprotected even after maintaining the pH.

17. The reaction mixture from step 16 was neutralized using Amberlite® IRC120 H acidic resin and filtered over Celite® 545. The solution was concentrated and dried and high vacuum for 1 h.

18. The crude product from step 17 was dissolved in a mixture of acetone (3 mL) and H_2O (1.5 mL) under nitrogen atmosphere. To the vigorously stirred solution under nitrogen atmosphere was added 49 mg (0.58 mmol) of $NaHCO_3$ and 131 mg (0.39 mmol) of FmocOSu. The reaction mixture was stirred at room temperature for 2 h.

19. The reaction mixture from step 18 was concentrated and purified by C_{18} (10 g) reverse phase flash column chromatography using H_20 and acetonitrile to obtain 0.33 g (92%) of compound **4** as a white solid.

Δ Critical Step Acetonitrile was evaporated and the remaining compound in water was lyophilized to obtain white solid.

Analytical Data:

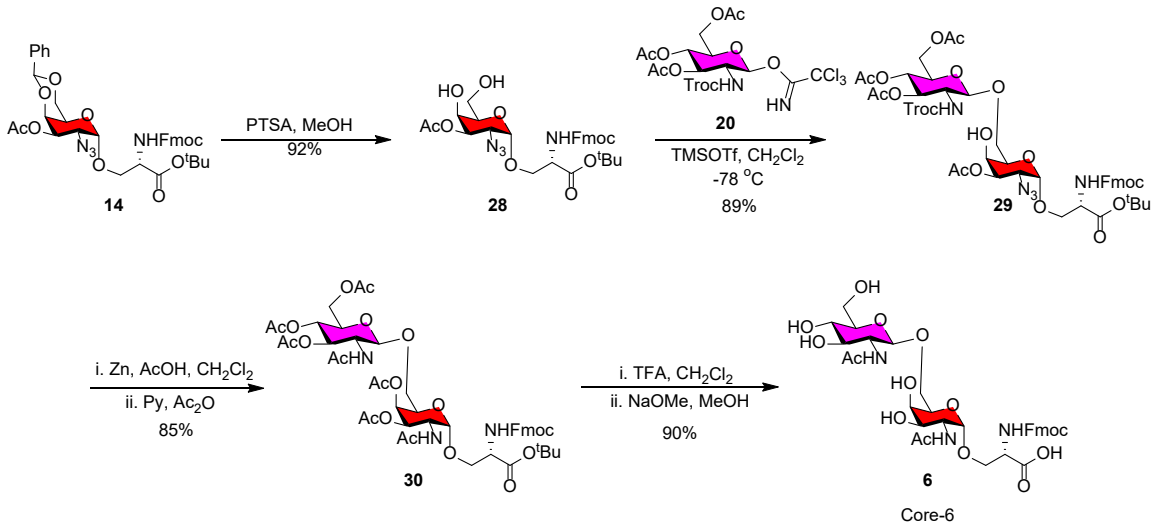
Compound 25: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.4 Hz, 2H), 7.61 (t, *J* = 7.9 Hz, 2H), 7.39 (dd, *J* = 13.8, 6.9 Hz, 2H), 7.31 (dt, *J* = 11.6, 5.9 Hz, 2H), 5.97 (d, *J* = 8.2 Hz, 1H), 5.32 (d, *J* = 8.6 Hz, 1H), 5.24 (t, *J* = 10.0 Hz, 1H), 4.97 – 4.85 (m, 2H), 4.71 (d, *J* = 11.5 Hz, 2H), 4.58 (d, *J* = 12.0 Hz, 1H), 4.49 – 4.40 (m, 2H), 4.35 – 4.27 (m, 1H), 4.21 (t, *J* = 7.0 Hz, 1H), 4.10 (t, *J* = 9.0 Hz, 3H), 4.02 (dd, *J* = 11.0, 4.0 Hz, 1H), 3.95 – 3.82 (m, 4H), 3.77 – 3.71 (m, 1H), 3.69 – 3.59 (m, 2H), 3.54 – 3.47 (m, 1H), 3.07 (s, 1H), 2.02 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.63, 170.33, 169.42, 168.79, 155.88, 154.13, 143.82, 143.52, 141.18, 127.75, 127.14, 125.31, 125.08, 120.09, 100.85, 99.36, 95.23, 82.95, 77.94, 74.46, 71.93, 71.21, 69.91, 68.75, 68.47, 67.00, 62.41, 61.82, 58.47, 56.04, 54.93, 47.08, 27.88, 20.55.

Compound 26: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.4 Hz, 2H), 7.69 – 7.58 (m, 2H), 7.44 – 7.29 (m, 4H), 6.34 (d, *J* = 7.0 Hz, 1H), 5.91 (d, *J* = 7.0 Hz, 1H), 5.69 (t, *J* = 9.7 Hz, 1H), 5.32 (s, 1H), 5.22 (d, *J* = 8.9 Hz, 1H), 5.18 – 5.10 (m, 1H), 4.99 (ddd, *J* = 23.7, 14.5, 7.0 Hz, 2H), 4.92 – 4.78 (m, 3H), 4.73 (d, *J* = 12.1 Hz, 1H), 4.64 – 4.54 (m, 2H), 4.51 – 4.40 (m, 2H), 4.35 (dd, *J* = 17.6, 7.1 Hz, 1H), 4.23 (ddd, *J* = 22.3, 19.5, 7.5 Hz, 3H), 4.16 – 4.06 (m, 2H), 4.06 – 3.97 (m, 3H), 3.91 (dd, *J* = 30.1, 10.3 Hz, 3H), 3.71 – 3.54 (m, 3H), 3.49 (d, *J* = 8.9 Hz, 1H), 3.30 (dd, *J* = 18.6, 9.2 Hz, 1H), 3.23 (dd, *J* = 17.9, 8.2 Hz, 1H), 2.06 (s, 4H), 2.04 (s, 3H), 2.00 (d, *J* = 5.0 Hz, 9H), 1.96 (s, 3H), 1.49 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.74, 170.61, 170.56, 170.11, 169.61, 169.35, 155.87, 154.07, 153.76, 143.81, 143.51, 141.28, 127.85, 127.25, 125.18, 125.00, 120.22, 101.14, 97.73, 95.64, 95.44, 83.24, 77.47, 77.35, 77.15, 76.83, 75.02, 74.90, 74.49, 74.20, 71.74, 71.39, 70.67, 69.75, 69.18, 68.19, 67.25, 61.99, 61.42, 59.41, 56.95, 56.16, 54.47, 53.50, 47.03, 27.95, 20.68, 20.60. MS (MALDI-TOF, dhb, positive ion mode):m/z: found: 1515.23 [M+Na]+; C58H70Cl6N6O27Na calcd 1515.23.

Compound 27: ^{1}H NMR (400 MHz, MeOD) δ 7.81 (d, *J* = 7.6 Hz, 2H), 7.74 – 7.65 (m, 2H), 7.41 (t, *J* = 7.1 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 2H), 5.49 (dd, *J* = 12.9, 6.8 Hz, 1H), 5.25 (t, *J* = 9.9 Hz, 1H), 5.10 – 4.92 (m, 3H), 4.71 (dd, *J* = 13.1, 5.8 Hz, 2H), 4.55 – 4.36 (m, 3H), 4.36 – 4.27 (m, 2H), 4.27 – 4.19 (m, 3H), 4.19 – 4.06 (m,

3H), 3.98 – 3.83 (m, 4H), 3.78 (dd, *J* = 17.7, 6.4 Hz, 4H), 3.63 – 3.48 (m, 2H), 2.01 (dt, *J* = 12.2, 5.7 Hz, 24H), 1.90 (d, *J* = 11.3 Hz, 6H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, MeOD) δ 171.86, 171.75, 171.62, 170.81, 170.74, 170.44, 170.38, 169.86, 157.07, 149.85, 148.76, 143.89, 141.26, 137.08, 127.55, 126.95, 124.83, 124.25, 119.76, 101.33, 100.94, 98.37, 82.12, 76.37, 72.68, 71.67, 71.52, 71.37, 71.16, 70.28, 69.62, 68.90, 66.91, 66.54, 62.05, 61.44, 55.47, 55.23, 54.20, 47.07, 29.51, 27.10, 22.14, 21.78, 19.67, 19.53, 19.40, 19.37, 19.34.

Compound 4: ^{1}H NMR (600 MHz, D_2O) δ 8.23 (d, *J* = 7.0 Hz, 2H), 8.04 (s, 2H), 7.82 (d, *J* = 7.8 Hz, 2H), 7.79 – 7.71 (m, 2H), 4.66 (d, *J* = 4.5 Hz, 2H), 4.50 (d, *J* = 7.8 Hz, 2H), 4.44 (s, 1H), 4.32 – 4.06 (m, 7H), 4.03 – 3.91 (m, 4H), 3.85 (t, *J* = 8.8 Hz, 2H), 3.83 – 3.76 (m, 1H), 3.70 (s, 3H), 2.32 (s, 3H), 2.29 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, D_2O) δ 174.32, 174.11, 173.63, 173.59, 157.23, 143.55, 140.75, 127.82, 127.30, 124.79, 120.00, 102.38, 101.23, 97.77, 75.76, 75.44, 73.78, 73.47, 69.90, 69.37, 69.13, 69.08, 68.73, 66.25, 61.20, 60.66, 60.18, 55.47, 48.09, 46.62, 22.23.



Scheme 6: Synthesis of Core-6 O-GalNAc glycan

Additional Materials:

TMSOTf (Trimethylsilyl trifluoromethanesulfonate) (Sigma Aldrich,Cat No. 225649) **! CAUTION** Fuming and Corrosive liquid.

TFA (Trifluoroacetic Acid) (Sigma Aldrich,Cat No. T6508) **! CAUTION** Highly Corrosive.

PTSA (*p*-toluenesulfonic acid) (Sigma Aldrich,Cat No. 402885)

Sodium methoxide (Sigma Aldrich,Cat No. 164992) **! CAUTION** Reacts violently with water.

Procedure:

Synthesis of compound 6

1. In a 100 mL round bottom flask, 2.0 g (3.0 mmol) of compound **14** was dissolved in 20 mL of anhydrous methanol under argon atmosphere.

2. To the reaction mixture from step 2, 115 mg (0.6 mmol) of PTSA.H_2O was added at room temperature. The reaction mixture was stirred at 30 °C for 3h.

Δ Critical Step Increasing the reaction temperature to 45 °C increases the rate of the reaction.

3. 100 uL of DIPEA was added to the reaction mixture from step 2 to quench the reaction. The solution was concentrated to dryness under reduced pressure and purified by flash column chromatography over 50 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out from 60% - 80% ethyl acetate in hexanes. The solution was concentrated to obtain 1.71 g (92%) of compound **28** as a white solid.

4. In a 100 mL round bottom flask, 0.71 g (1.1 mmol) of compound **20**[5] and 0.64 g (1.0 mmol) of compound **28** was coevaporated with 5 mL of anhydrous toluene twice and dried under high vacuum for a period of 3 h.

Δ Critical Step The compound should be well dried for a proper reaction and good yield.

5. The mixture from step 4 wad dissolved in 20 mL of anhydrous dichloromethane and 1.5 g of 4 Å freshly dried molecular sieves powder was added. The mixture was stirred at room temperature under argon atmosphere for 1 h. The solution was cooled to -78 °C using dry ice and ethyl acetate.

! CAUTION Proper clothing and gloves are must to get protected from cold burns.

6. 44.2 mg (0.2 mmol) of TMSOTf was added slowly to the reaction mixture from step 5 using a micro syringe. The reaction mixture was stirred for 1 h or until completion at the same temperature. The reaction was quenched with 50 uL of DIPEA and allowed the reaction temperature to reach room temperature over 30 min.

7. The reaction mixture from step 6 was filtered over Celite® 545 and concentrated under reduced pressure at 30 °C.

8. The crude product from step 7 was purified by flash column chromatography over 50 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out at 45% ethyl acetate in hexanes. The solution was concentrated to obtain 1.0 g (89%) of compound **29** as a white solid.

9. In a 100 mL round bottom flask, 0.85 g (0.79 mmol) compound **29** from step 8 was dissolved in a mixture of 15 mL anhydrous dichloromethane and 5 mL of glacial acetic acid under nitrogen atmosphere and 0.77 g (11.8 mmol) of Zn dust was added and stirred at 40 °C for 12 h.

Δ Critical Step 10 g of Zn dust was washed with 50 ml of 1 M HCl and successively with 50 mL of H_20, acetone and diethyl ether before using it for the reaction.

10. The reaction mixture from step 9 was filtered over Celite® 545 and concentrated to dryness under reduced pressure and dried under high vacuum for 2 h.

11. The crude product from step 10 was dissolved in 10 mL of pyridine under nitrogen atmosphere and 5 mL of acetic anhydride was added slowly at 0 °C and stirred at room temperature for 2 h.

12. The reaction mixture from step 11 was concentrated to remove pyridine and acetic anhydride completely under reduced pressure at 50 °C. 150 mL of ethyl acetate was added and taken into a 500 mL separatory funnel. The organic layer was washed with 50 mL of saturated aq. $NaHCO_3$, 1N HCl and brine solution respectively. The separated organic layer was dried over 10 g of anhydrous sodium sulphate, filtered and concentrated under reduced pressure.

13. The crude product from step 12 was purified over 50 g of 60 Å silica gel using hexanes and ethyl acetate. The product was eluted out at 70% ethyl acetate in hexanes. The solution was concentrated to obtain 0.67 g (85%) of compound **30** as a white solid.

14. 0.5 g (0.5 mmol) of compound **30** from step 13 was taken into a 25 mL round bottom flask.

15. To the mixture from step 14, a 5 mL (9:1) mixture of TFA and anhydrous anisole was added at 0 °C under argon atmosphere and stirred for 15 min at room temperature. The solvents were removed below 30 °C under reduced pressure. The crude mixture was coevaporated with 5 mL of anhydrous toluene twice and dried under high vacuum for 1 h.

Δ Critical Step The free acid can be stored only after purification.

16. The crude product from step 15 was dissolved in 5 mL of anhydrous methanol under argon atmosphere. Solid NaOMe was slowly added at 0 °C until the pH reaches 8.5 and stirred at room temperature until completion.

Δ Critical Step Sodium methoxide must be added very slowly such that the pH doesn't exceed 8.5. The reaction must be carefully monitored for completion.

17. The reaction mixture from step 16 was neutralized using Amberlite® IRC120 H acidic resin and filtered over Celite® 545.

18. The reaction mixture from step 17 was concentrated and purified by C_{18} (10 g) reverse phase flash column chromatography using H_20 and acetonitrile to obtain 0.33 g (90%) of compound **6** as a white solid.

Δ Critical Step Acetonitrile was evaporated and the remaining compound in water was lyophilized to obtain white solid.

Analytical Data:

Compound 28: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.5 Hz, 2H), 7.61 (d, *J* = 7.4 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.34 – 7.29 (m, 2H), 6.02 (d, *J* = 8.1 Hz, 1H), 5.15 (dd, *J* = 11.0, 2.8 Hz, 1H), 4.90 (d, *J* = 3.5 Hz, 1H), 4.40 (ddd, *J* = 8.1, 6.1, 2.7 Hz, 3H), 4.23 – 4.18 (m, 2H), 4.16 (dd, *J* = 11.1, 3.0 Hz, 1H), 3.88 (dd, *J* = 10.7, 3.1 Hz, 2H), 3.80 – 3.73 (m, 3H), 2.15 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.92, 168.84, 155.92, 143.77, 141.31, 127.69, 127.12, 125.15, 125.10, 119.97, 99.96, 83.15, 70.78, 70.43, 69.80, 68.95, 66.92, 63.24, 57.27, 55.09, 47.13, 27.91, 20.93.

Compound 29: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.62 (dd, *J* = 13.1, 7.4 Hz, 2H), 7.39 (td, *J* = 7.3, 3.6 Hz, 2H), 7.33 (dd, *J* = 13.7, 6.9 Hz, 2H), 5.89 (d, *J* = 7.2 Hz, 1H), 5.49 (d, *J* = 7.8 Hz, 1H), 5.39 (t, *J* = 9.8 Hz, 1H), 5.16 (dd, *J* = 11.0, 2.7 Hz, 1H), 4.97 – 4.87 (m, 2H), 4.70 (dd, *J* = 23.3, 10.1 Hz, 2H), 4.58 (d, *J* = 12.1 Hz, 1H), 4.46 – 4.38 (m, 2H), 4.34 – 4.29 (m, 1H), 4.25 (t, *J* = 7.3 Hz, 1H), 4.14 (d, *J* = 12.2 Hz, 1H), 4.08 (s, 1H), 4.05 – 3.99 (m, 2H), 3.96 (d, *J* = 8.4 Hz, 1H), 3.92 (t, *J* = 5.6 Hz, 1H), 3.90 – 3.85 (m, 1H), 3.74 (d, *J* = 10.9 Hz, 1H), 3.66 (dd, *J* = 9.8, 5.7 Hz, 1H), 3.61 – 3.56 (m, 1H), 3.25 (dd, *J* = 18.2, 8.4 Hz, 1H), 2.16 (s, 3H), 2.01 (s, 3H), 1.99 (s, 3H), 1.98 (s, 3H), 1.49 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.76,

170.31, 169.88, 169.46, 168.58, 155.82, 153.92, 143.93, 143.69, 141.23, 141.16, 127.79, 127.25, 125.27, 120.02, 100.21, 98.67, 95.44, 83.20, 74.30, 71.69, 71.06, 70.52, 68.91, 68.68, 68.36, 67.27, 66.69, 61.79, 57.27, 56.26, 54.69, 47.07, 27.93, 20.98, 20.60.

Compound 30: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.5 Hz, 2H), 7.61 (t, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.31 (dd, *J* = 13.5, 6.7 Hz, 2H), 6.07 (d, *J* = 7.5 Hz, 1H), 5.92 (d, *J* = 7.6 Hz, 1H), 5.72 (d, *J* = 9.6 Hz, 1H), 5.48 (t, *J* = 9.8 Hz, 1H), 5.29 (d, *J* = 2.9 Hz, 1H), 5.05 (d, *J* = 11.2 Hz, 1H), 4.93 (t, *J* = 9.5 Hz, 1H), 4.89 – 4.76 (m, 2H), 4.54 (t, *J* = 8.8 Hz, 1H), 4.45 – 4.41 (m, 1H), 4.38 (d, *J* = 5.9 Hz, 2H), 4.26 – 4.19 (m, 2H), 4.04 (s, 1H), 4.00 (d, *J* = 12.0 Hz, 1H), 3.95 (d, *J* = 7.1 Hz, 1H), 3.74 (dd, *J* = 10.1, 5.0 Hz, 2H), 3.63 (d, *J* = 6.4 Hz, 1H), 3.52 (dd, *J* = 10.4, 7.4 Hz, 1H), 3.42 (d, *J* = 9.4 Hz, 1H), 2.11 (s, 3H), 1.99 (s, 3H), 1.97 (d, *J* = 3.1 Hz, 9H), 1.91 (s, 5H), 1.87 (s, 3H), 1.47 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.84, 170.64, 170.55, 170.41, 170.23, 170.00, 169.47, 169.01, 155.98, 143.70, 141.26, 127.79, 127.16, 127.14, 125.06, 120.02, 99.70, 98.21, 82.98, 77.21, 77.00, 76.79, 71.64, 71.42, 68.82, 68.62, 68.36, 68.17, 67.67, 67.23, 62.00, 55.79, 54.69, 47.53, 47.03, 28.01, 23.22, 20.72, 20.69, 20.63, 20.59.

Compound 6: ^{1}H NMR (600 MHz, D_2O) δ 8.19 (s, 2H), 7.99 (s, 2H), 7.85 – 7.63 (m, 4H), 4.98 (s, 3H), 4.62 (s, 1H), 4.37 (s, 1H), 4.26 (s, 1H), 4.24 – 3.87 (m, 9H), 3.85 (s, 1H), 3.73 (s, 2H), 2.26 (s, 6H). ^{13}C DEPT 135 NMR (101 MHz, $CDCl_3$) δ 127.79, 127.26, 124.98, 124.82, 119.96, 101.20, 97.79, 75.80, 73.36, 69.91, 69.90, 69.31, 69.28, 68.66, 68.50, 68.40, 67.68, 67.63, 66.47, 60.65, 56.11, 55.60, 49.65, 46.65, 22.28, 22.13.

Reference:

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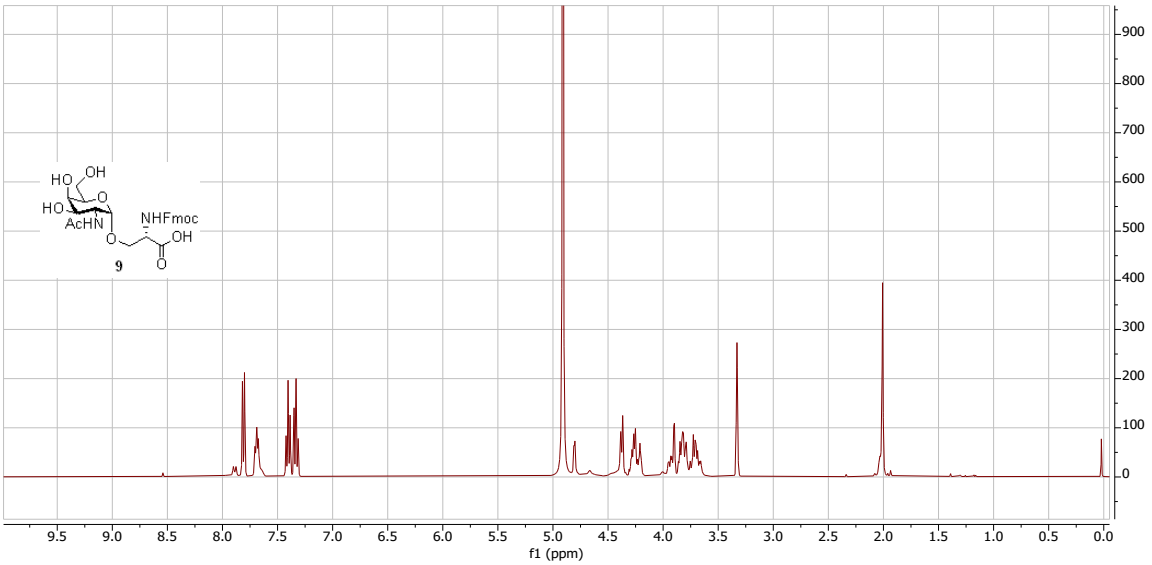
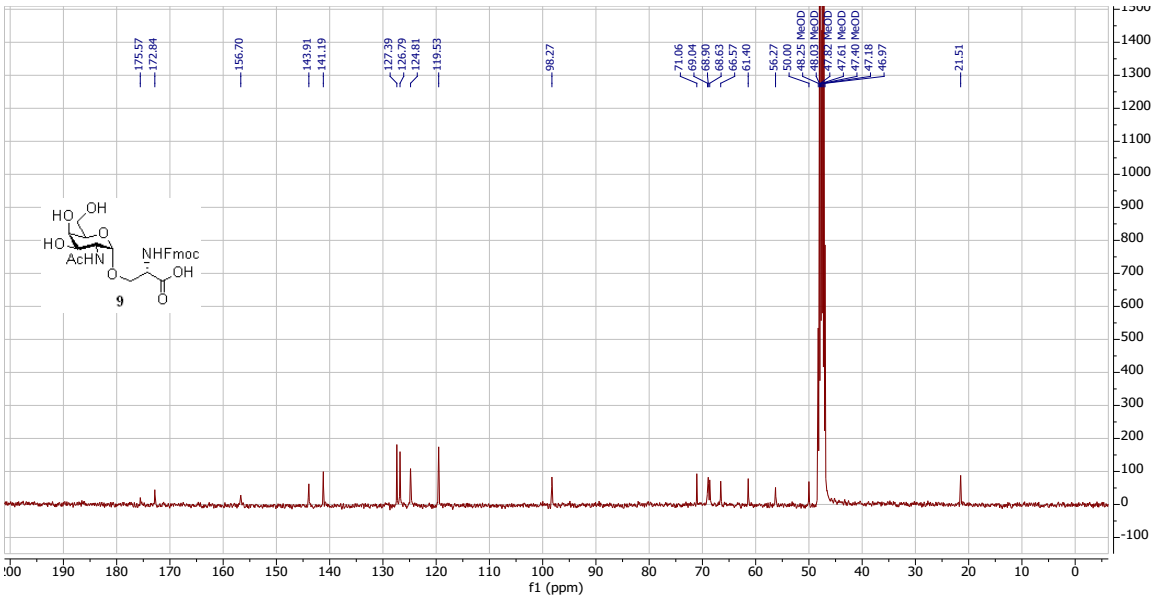
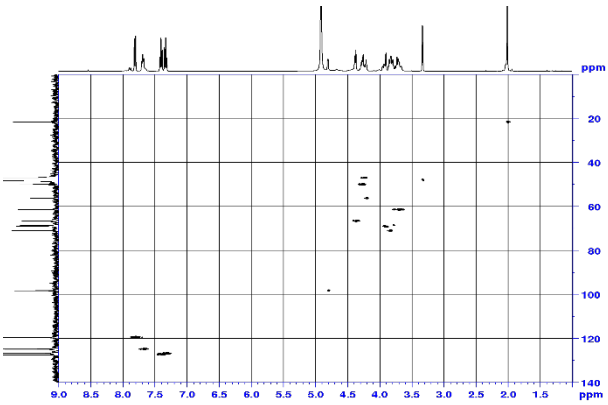
NMR Spectra







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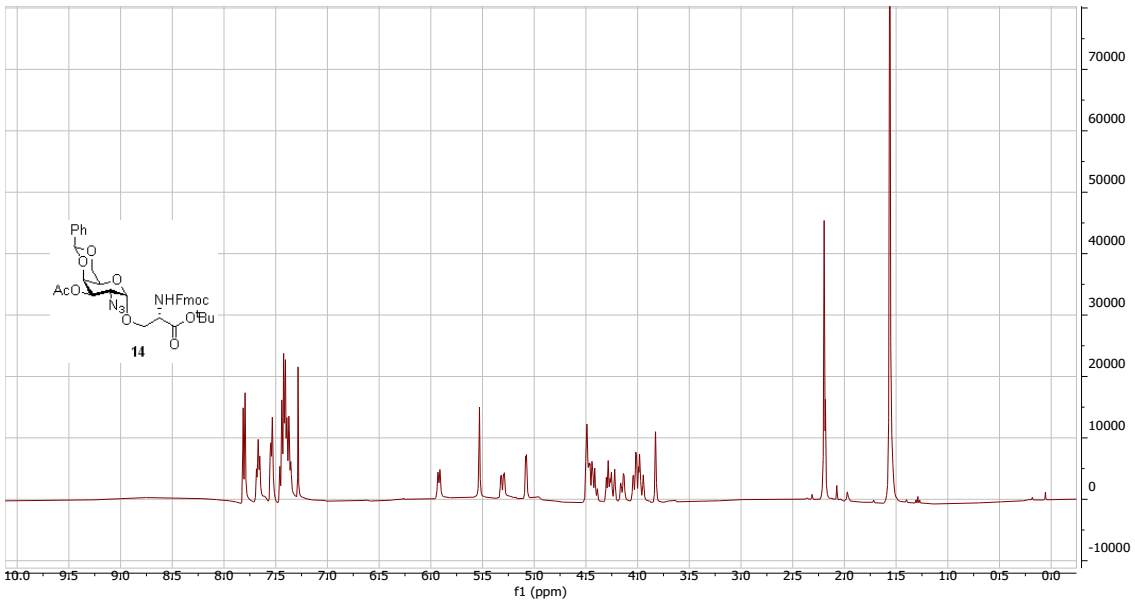

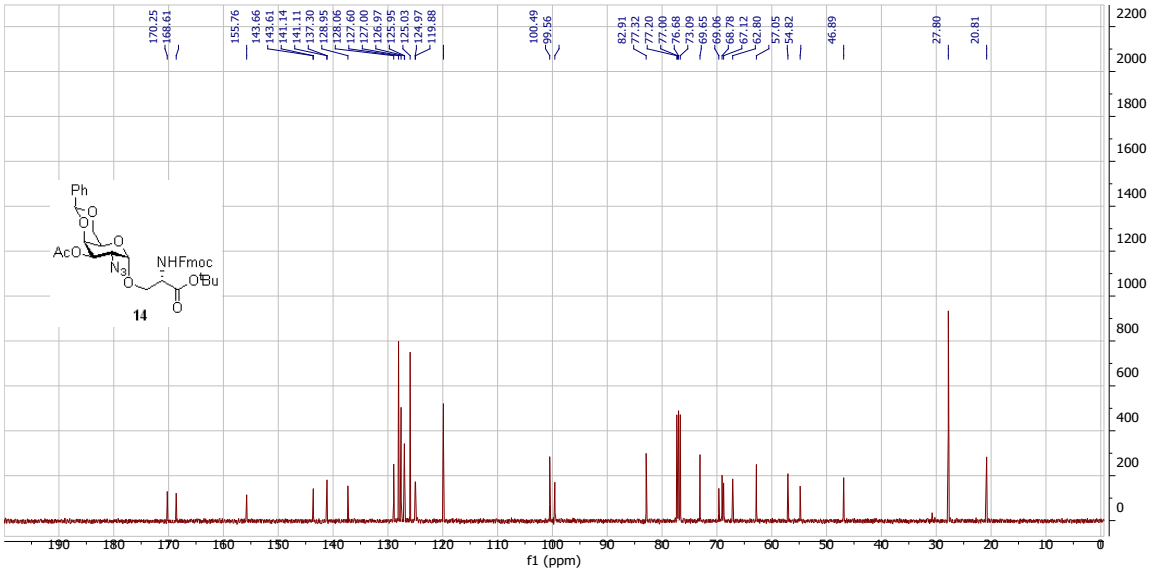

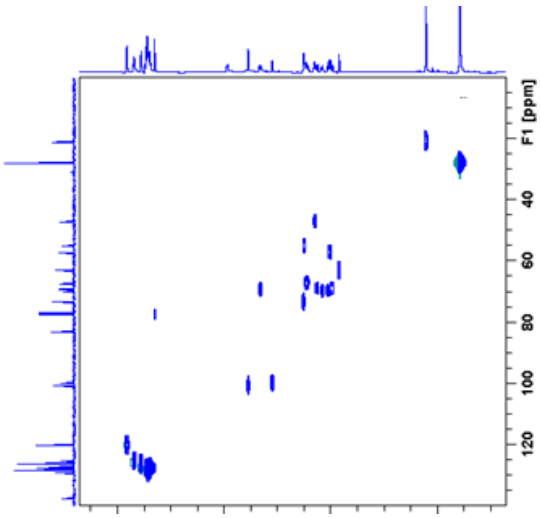

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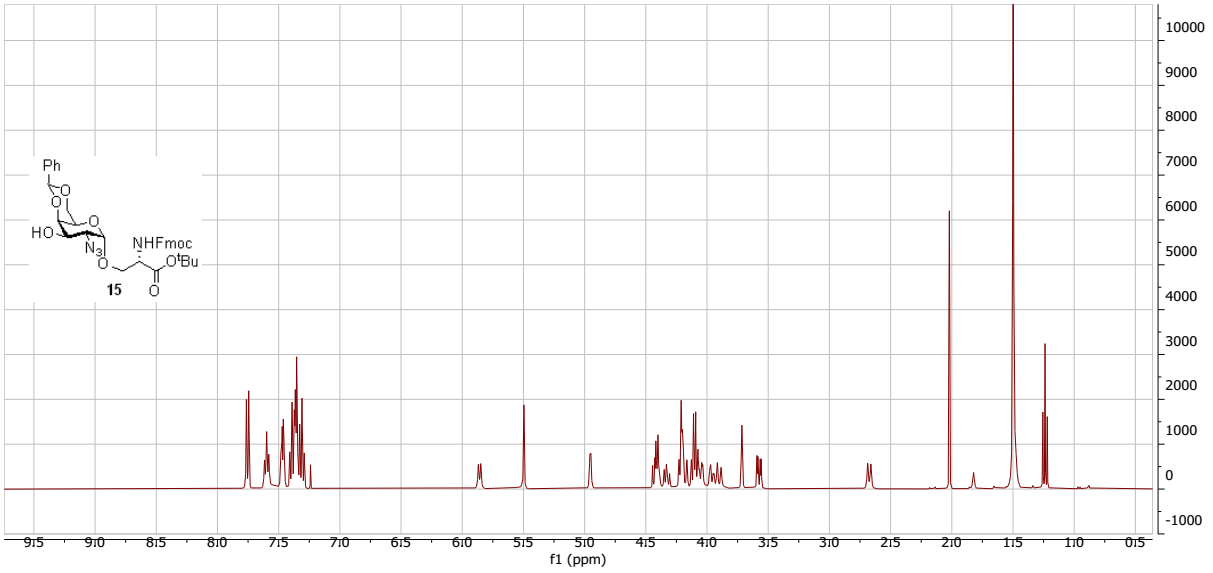
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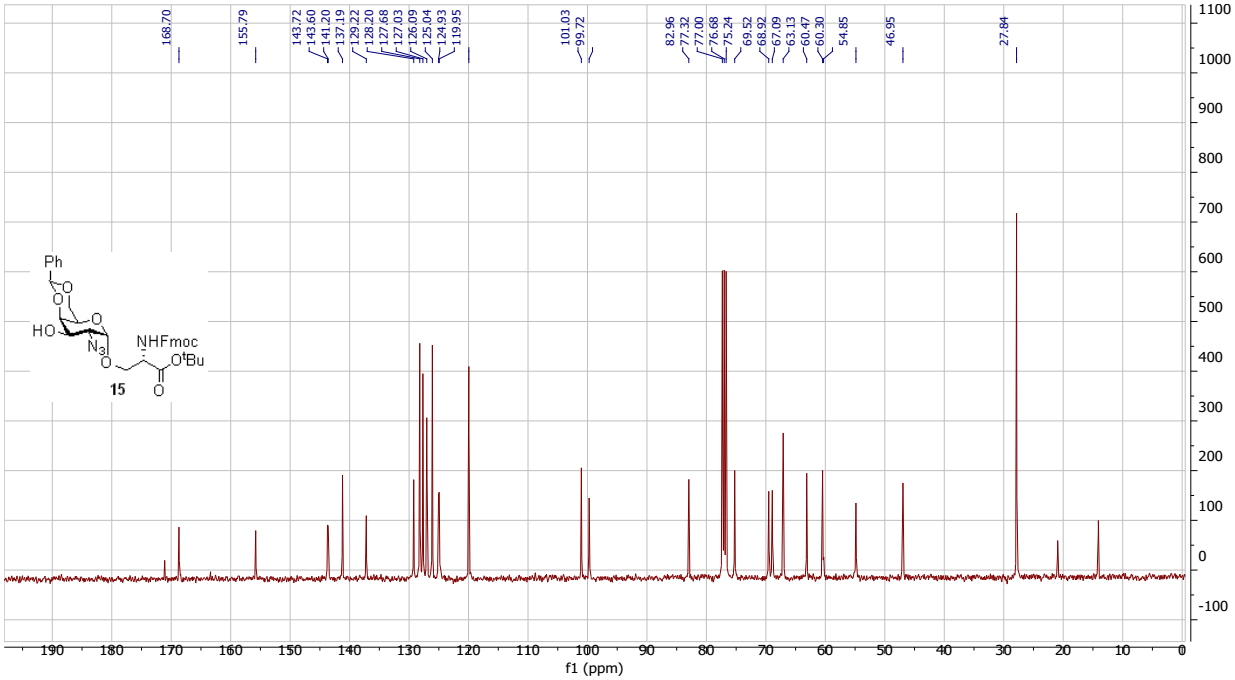
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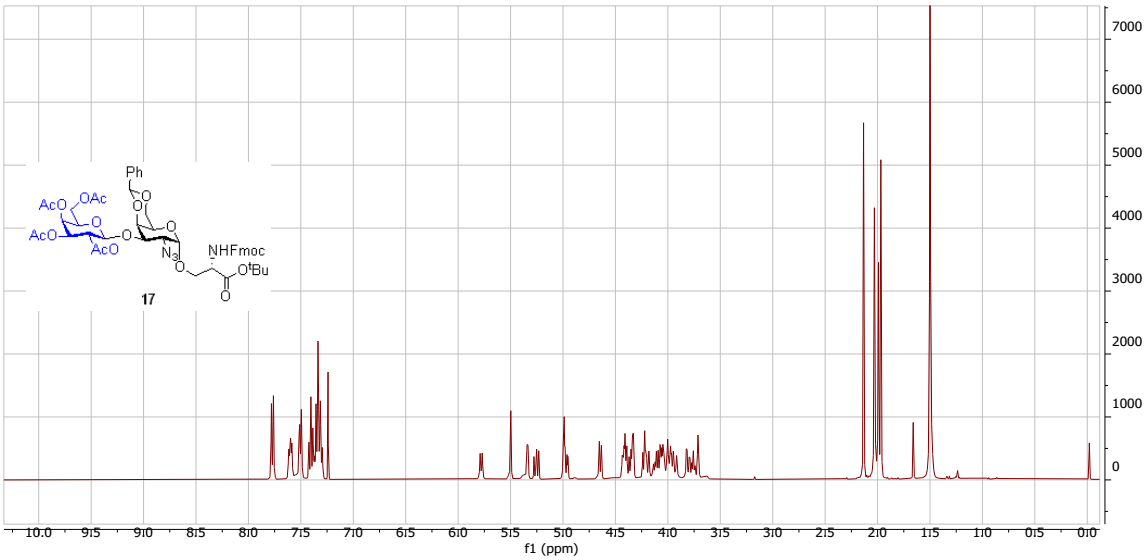

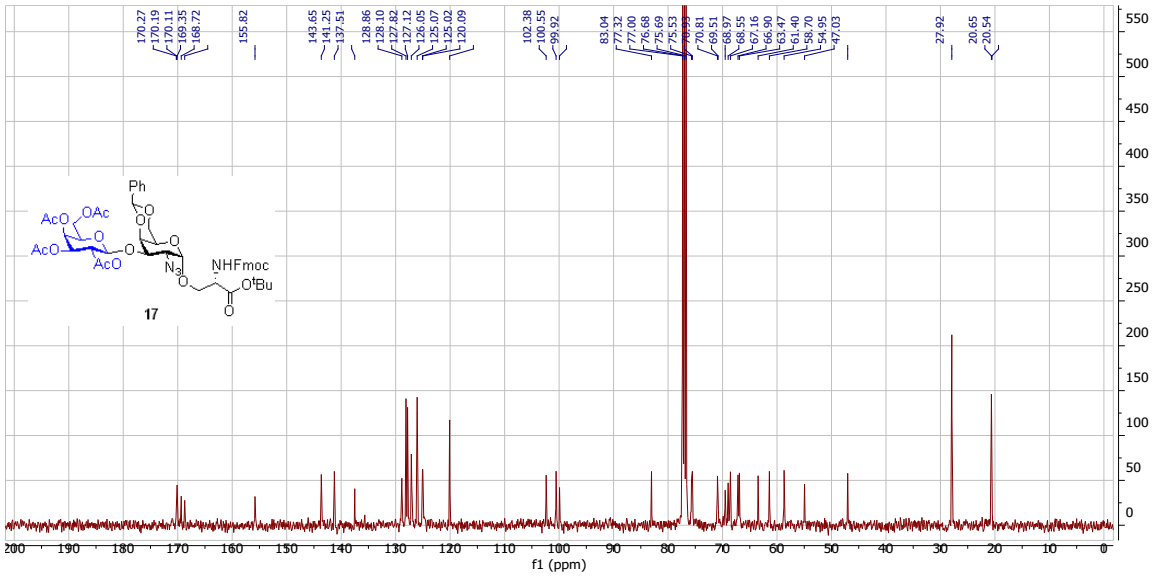

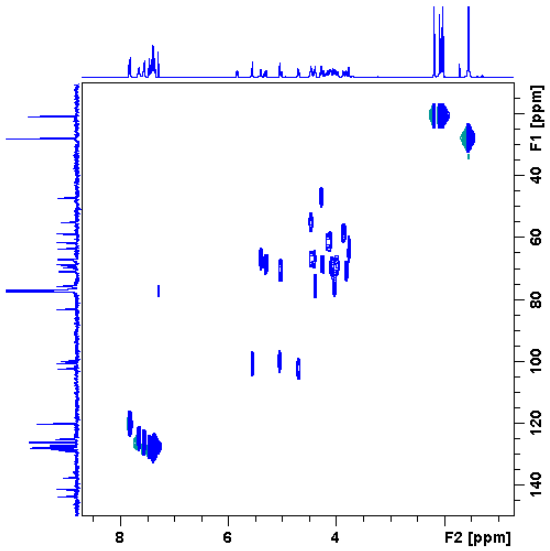

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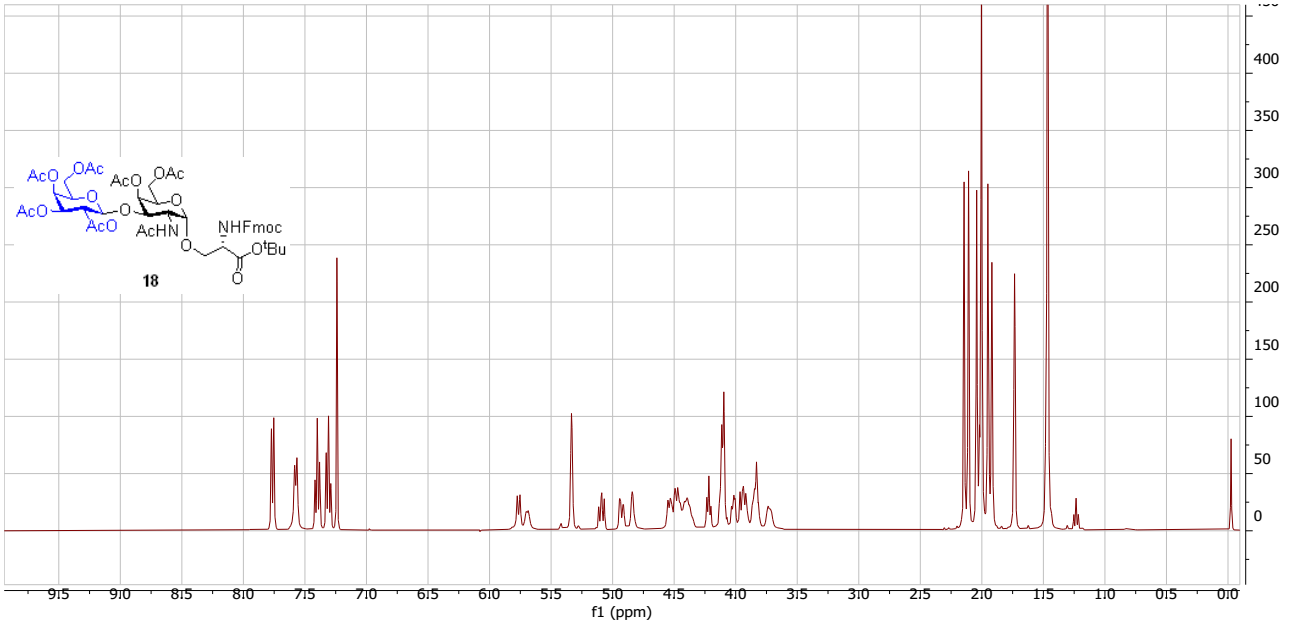
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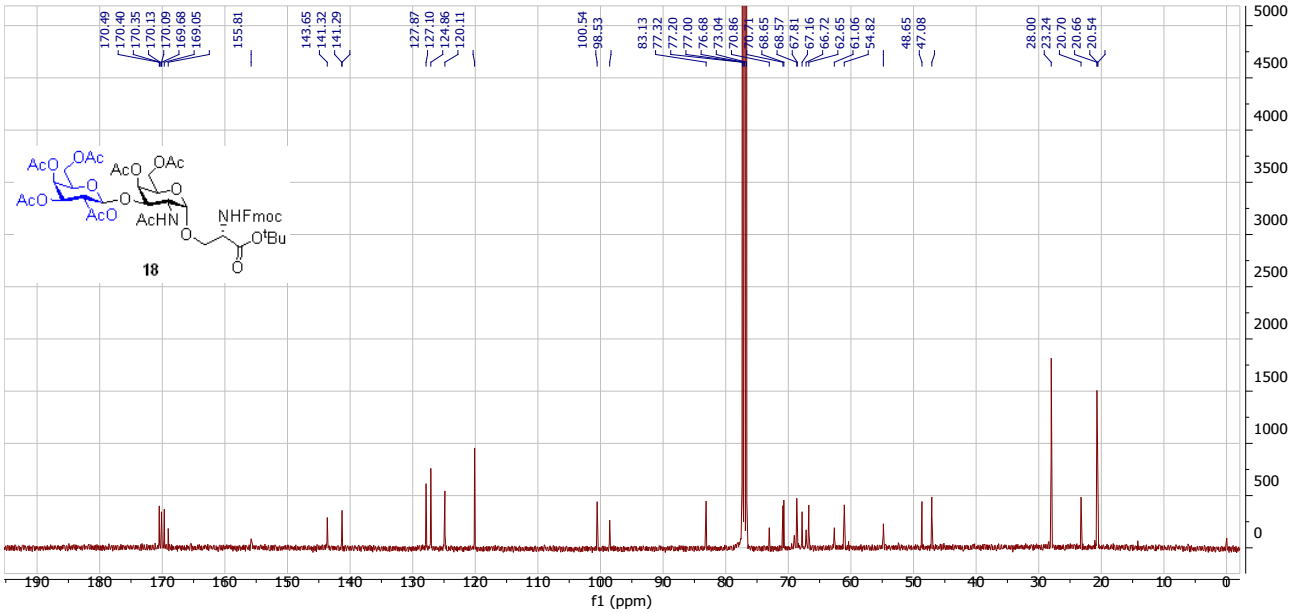
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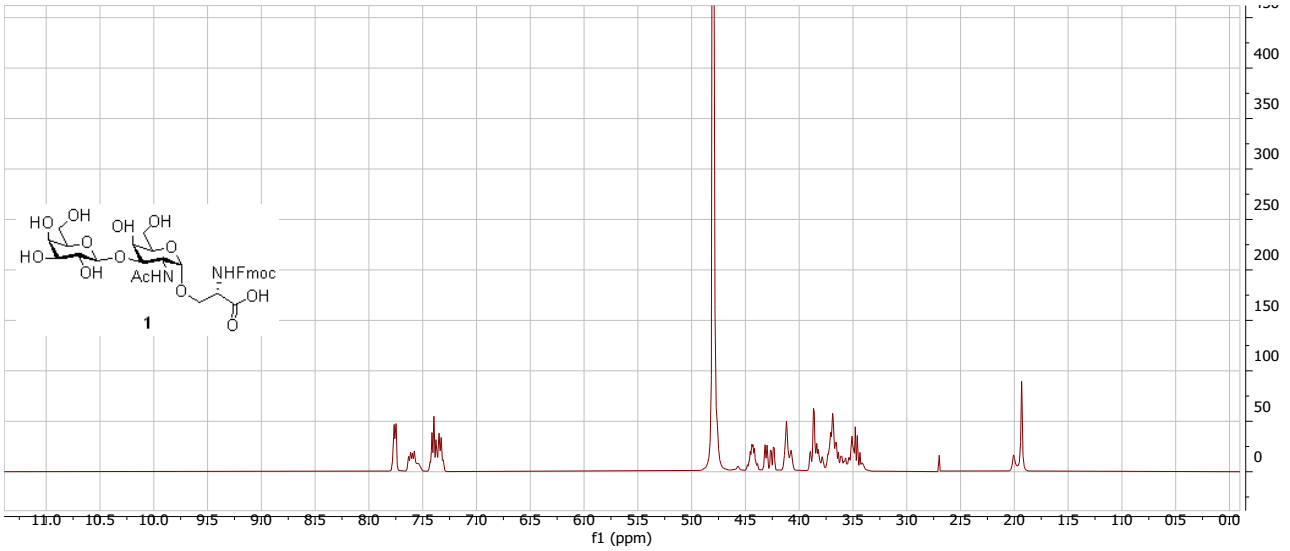
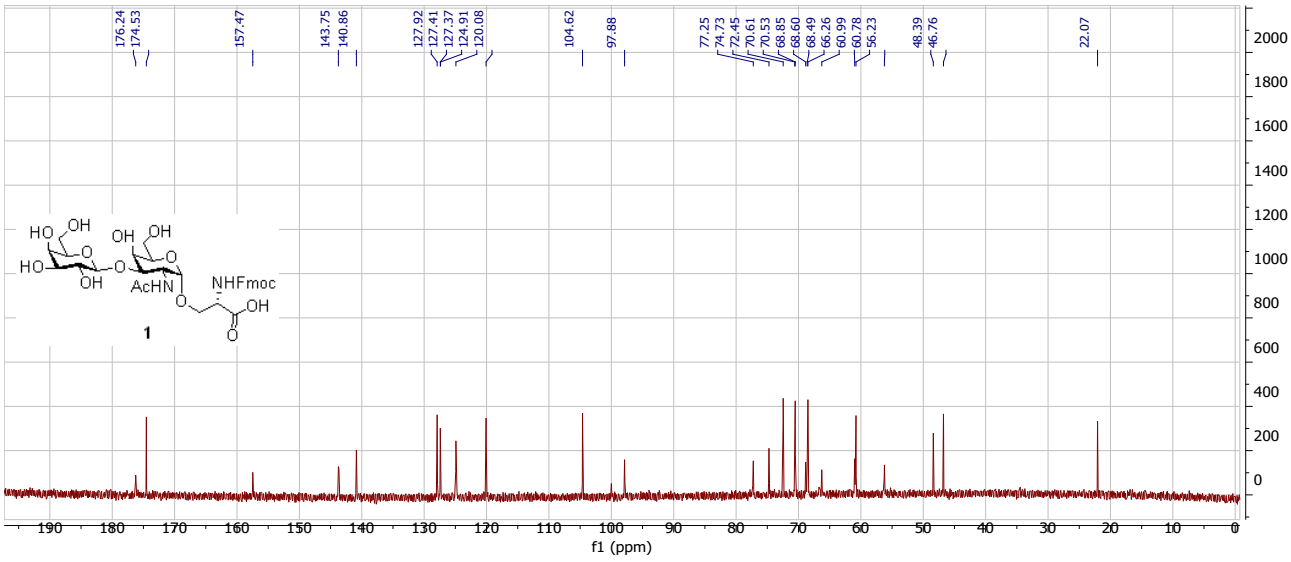
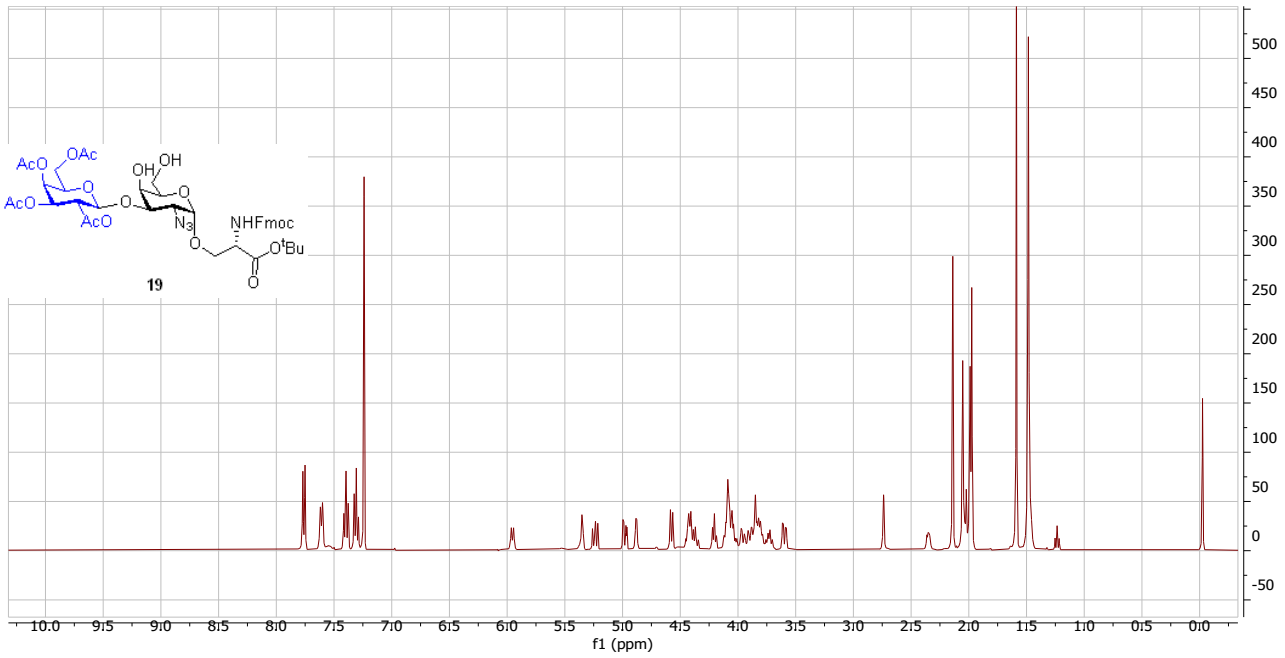
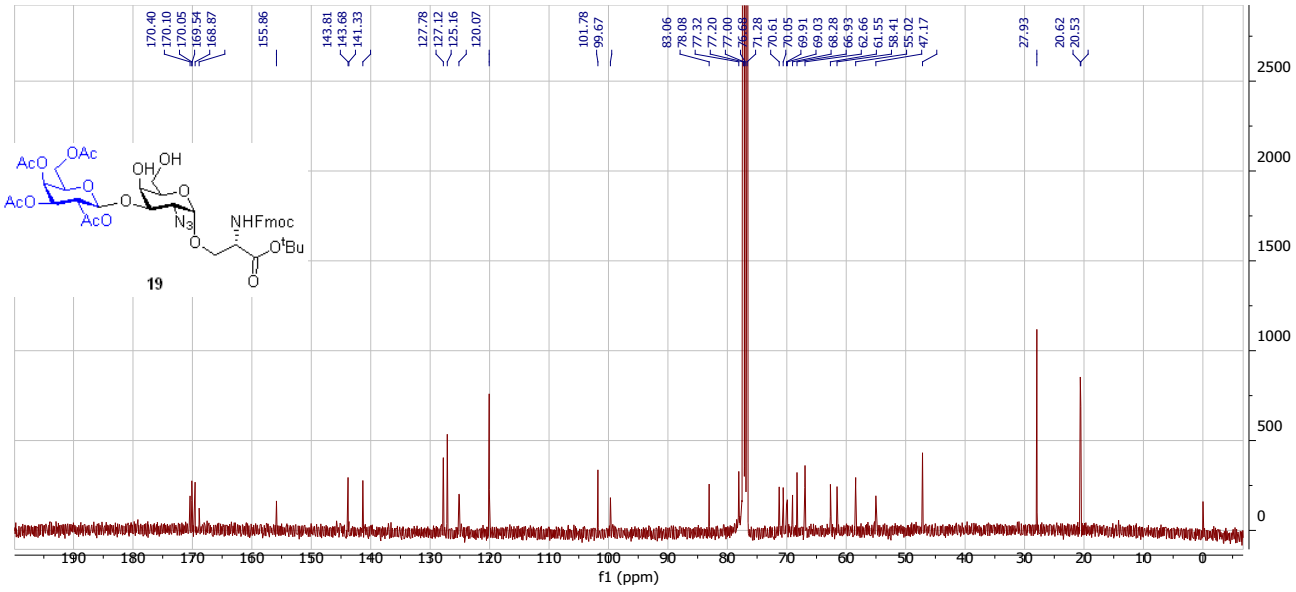
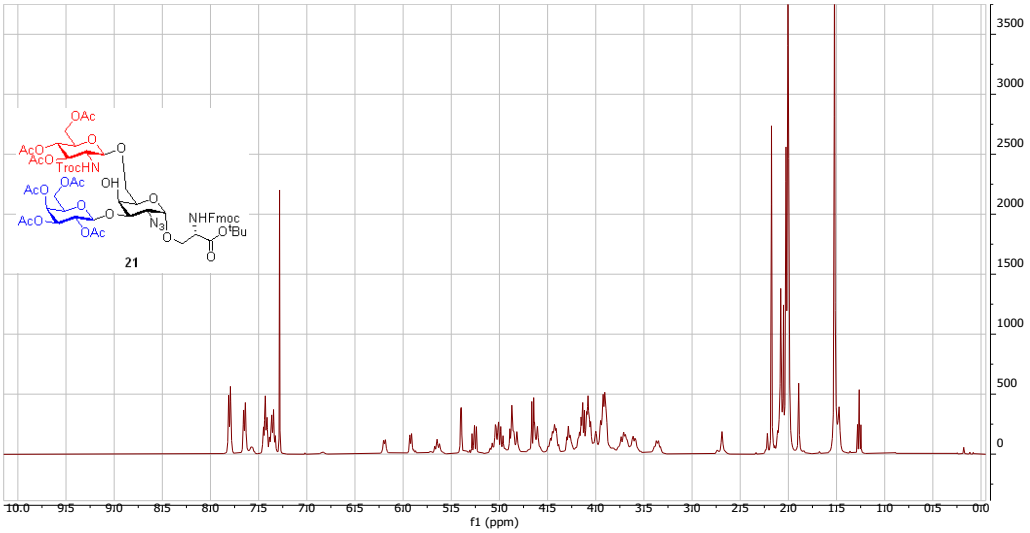
169.05
155.81
143.65
141.32
141.29
127.87
127.10
124.86
120.11
100.54
98.53
83.13
77.32
77.20
77.00
76.68
73.04
70.86
70.71
68.65
68.57
67.81
67.16
66.72
62.65
61.06
54.82
48.65
47.08
28.00
23.24
20.70
20.66
20.54
AcO
OAc
AcO
O
AcO
AcO
OAc
AcHN
O
NHFmoc
O
O
O
tBu
18
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

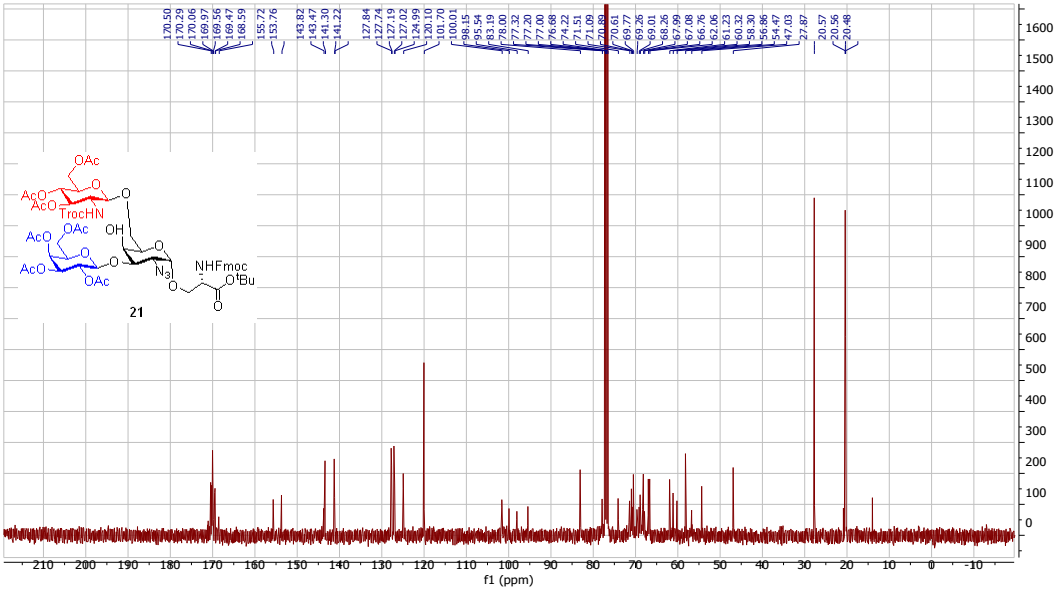

HO
OH
OH
OH
HO
O
O
OH
AcHN
NHFmoc
O
OH
O
1
400
350
300
250
200
150
100
50
0
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

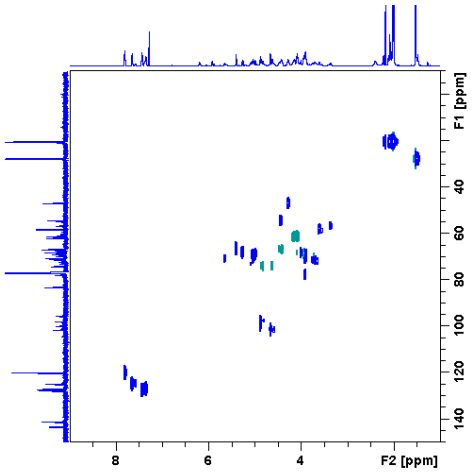

176.24
174.53
157.47
143.75
140.86
127.92
127.41
127.37
124.91
120.08
104.62
97.88
77.25
74.73
72.45
70.61
70.53
68.85
68.60
68.49
66.26
60.99
60.78
56.23
48.39
46.76
22.07
HO
OH
OH
OH
HO
O
O
OH
AcHN
NHFmoc
O
OH
O
1
2000
1800
1600
1400
1200
1000
800
600
400
200
0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


AcO
OAc
AcO
AcO
OH
OH
O
O
N3
NHFmoc
O
OtBu
O
19
500
450
400
350
300
250
200
150
100
50
0
-50
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

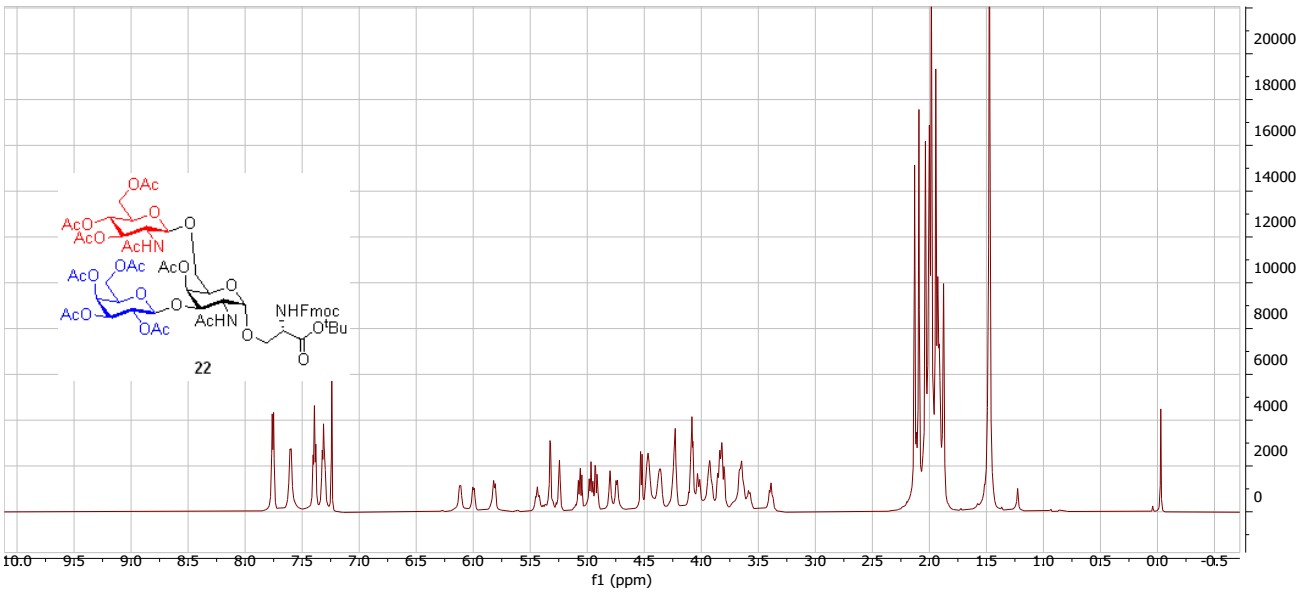

170.40
170.10
170.05
169.54
168.87
155.86
143.81
143.68
141.33
127.78
127.12
125.16
120.07
101.78
99.67
83.06
78.08
77.32
77.20
77.00
76.68
71.28
70.61
70.05
69.91
69.03
68.28
66.93
62.66
61.55
58.41
55.02
47.17
27.93
20.62
20.53
AcO
OAc
AcO
AcO
OH
OH
O
O
N3
NHFmoc
O
OtBu
O
19
2500
2000
1500
1000
500
0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

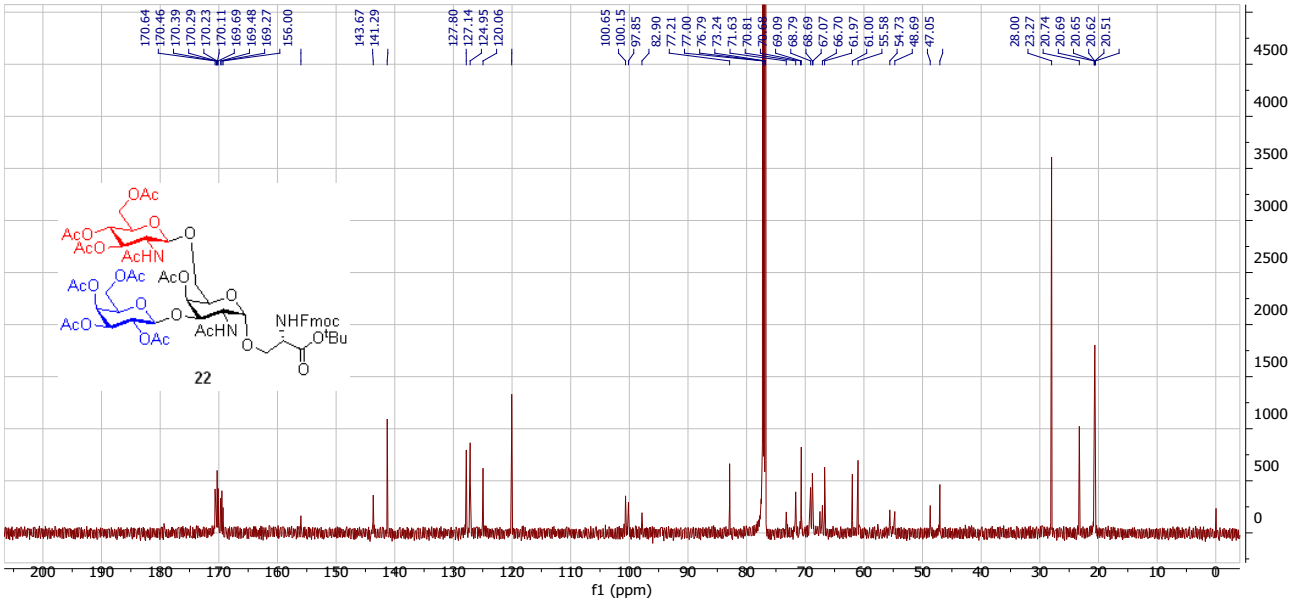


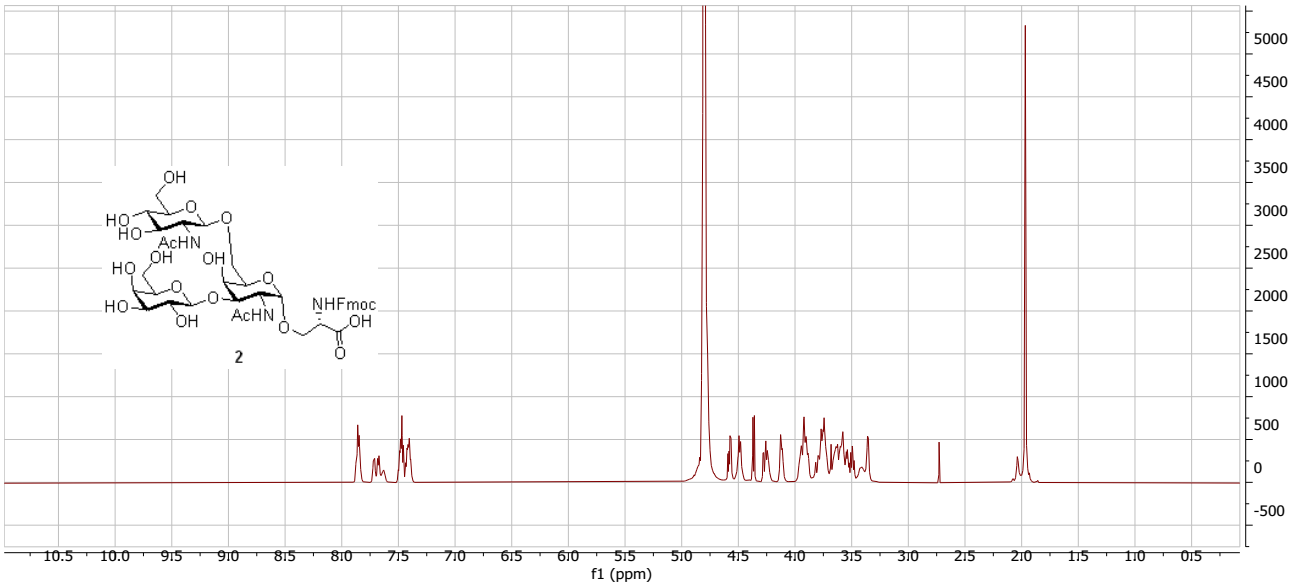


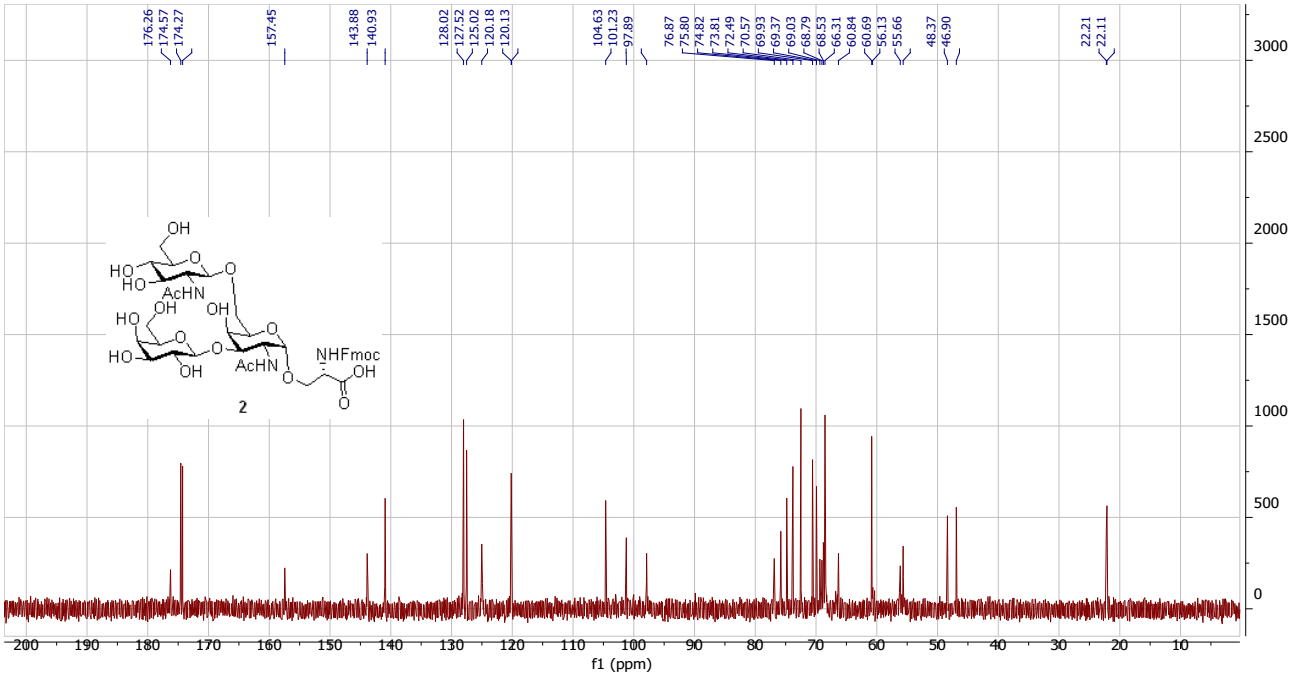


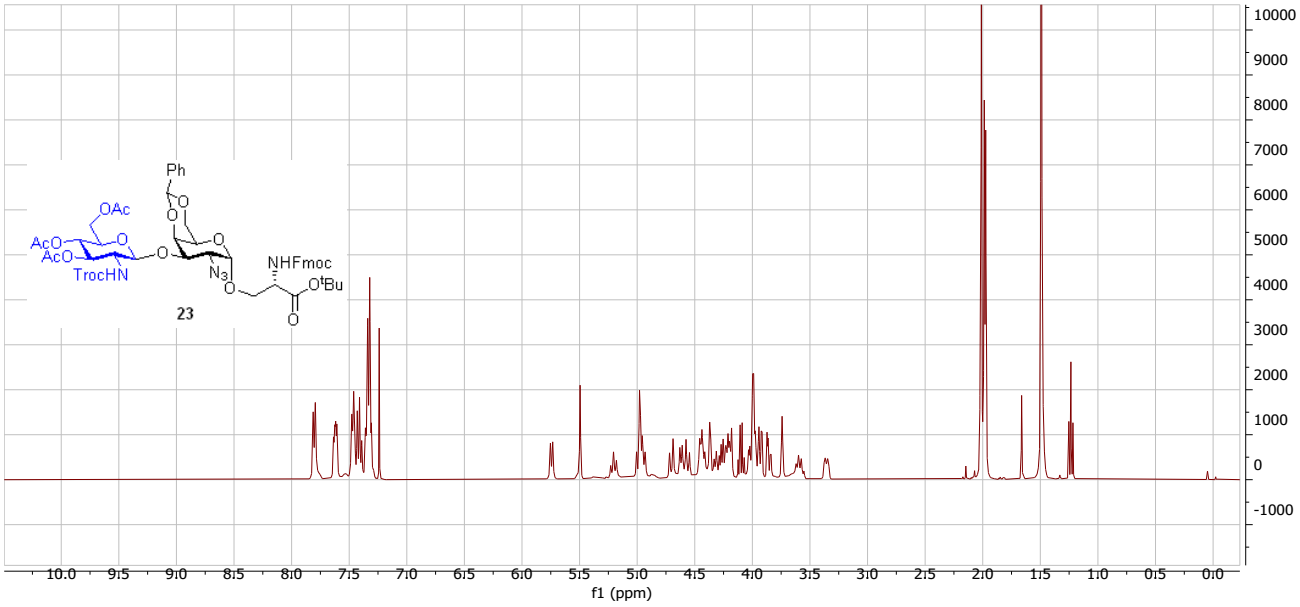
2D HSQC 600 MHz

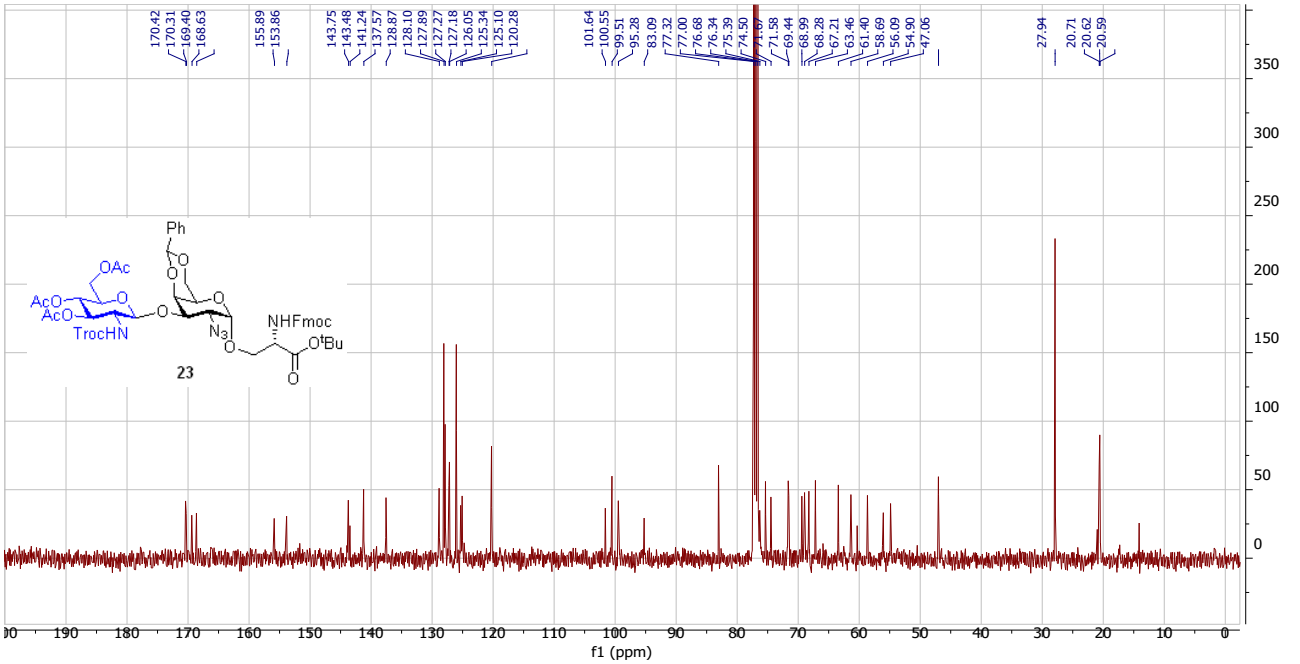

OAc
AcO
AcO
AcHN
O
AcO
OAc
AcO
AcO
OAc
AcHN
AcO
O
O
NHFmoc
O
O
tBu
22
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

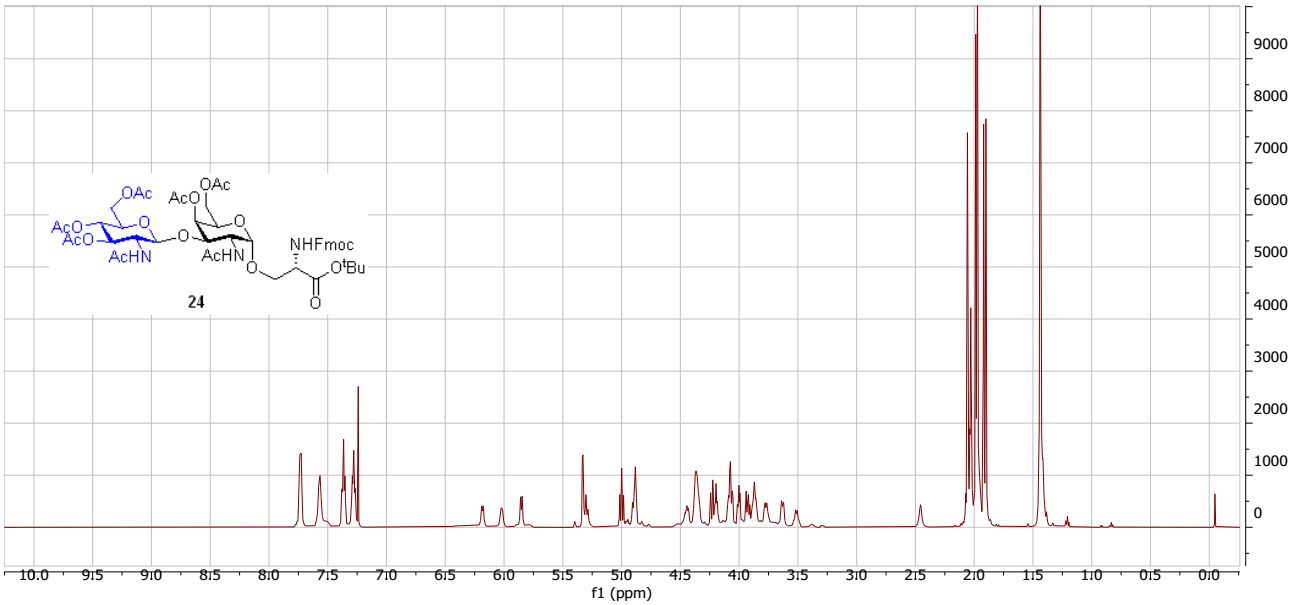

170.64
170.46
170.39
170.29
170.23
170.11
169.69
169.48
169.27
156.00
143.67
141.29
127.80
127.14
124.95
120.06
100.65
100.15
97.85
82.90
77.21
77.00
76.79
73.24
71.63
70.81
69.09
68.79
68.69
67.07
66.70
61.97
61.00
55.58
54.73
48.69
47.05
28.00
23.27
20.74
20.69
20.65
20.62
20.51
OAc
AcO
AcO
AcHN
O
AcO
OAc
AcO
AcO
OAc
AcHN
AcO
O
O
NHFmoc
O
O
tBu
22
4500
4000
3500
3000
2500
2000
1500
1000
500
0
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

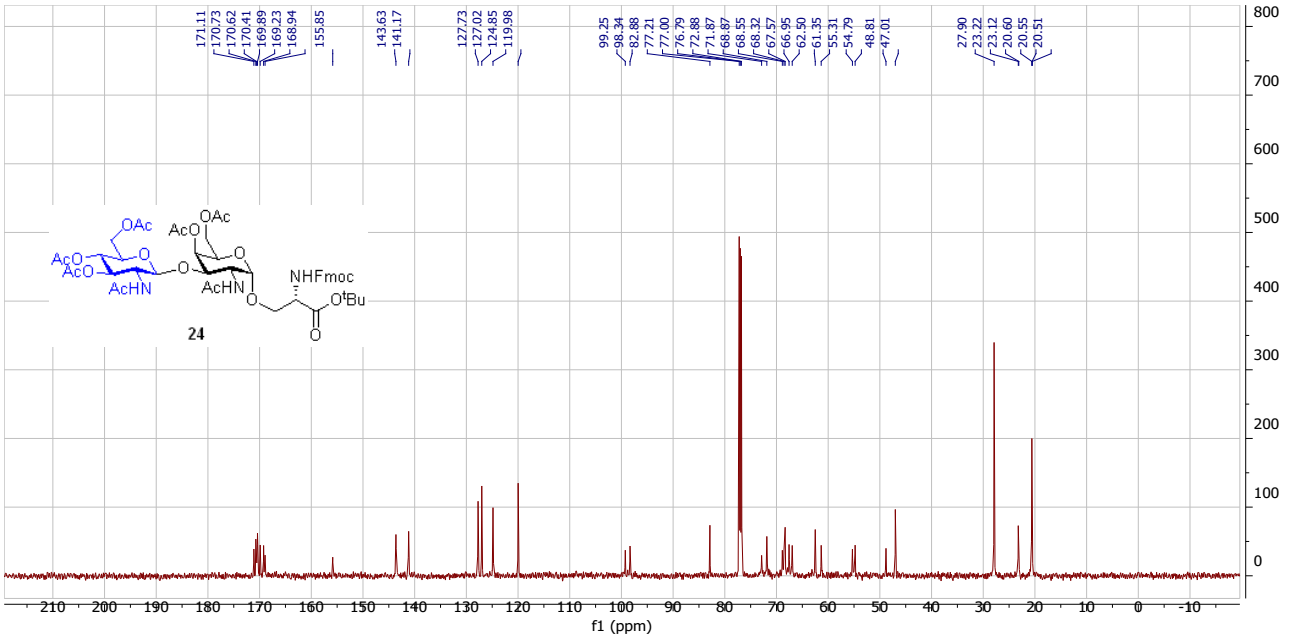

OH
HO
HO
AcHN
OH
HO
OH
HO
AcHN
NHFmoc
OH
O
2
f1 (ppm)

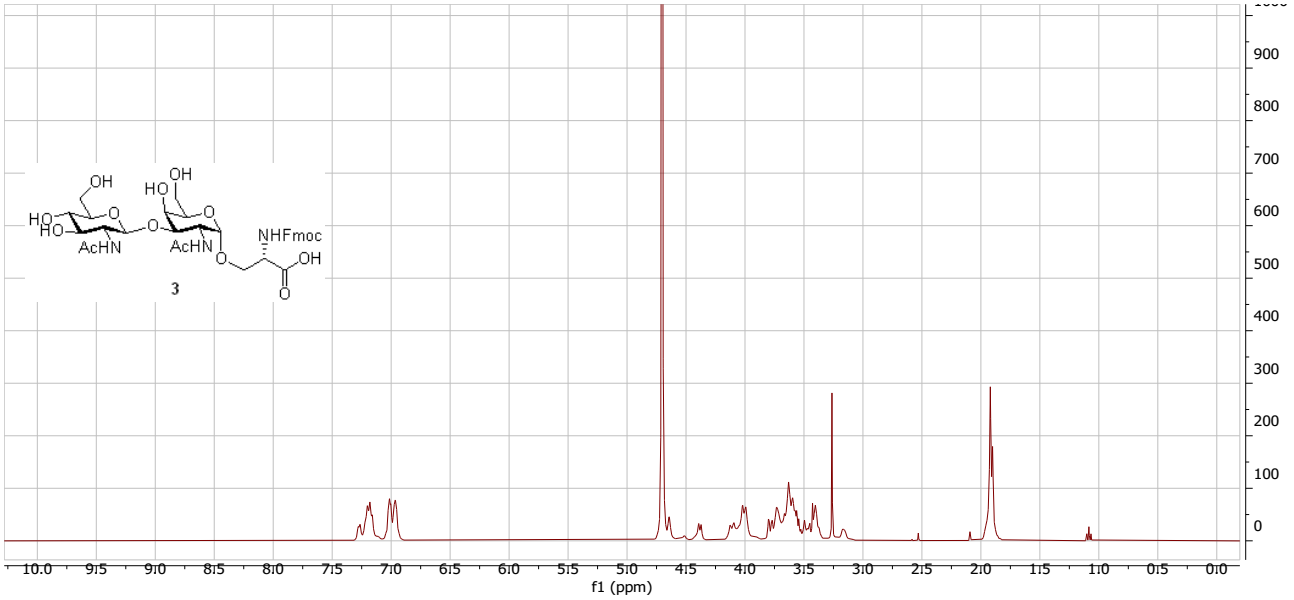

176.26
174.57
174.27
157.45
143.88
140.93
128.02
127.52
125.02
120.18
120.13
104.63
101.23
97.89
76.87
75.80
74.82
73.81
72.49
70.57
69.93
69.37
69.03
68.79
68.53
66.31
60.84
60.69
56.13
55.66
48.37
46.90
22.21
22.11
OH
HO
HO
AcHN
OH
HO
OH
HO
AcHN
NHFmoc
OH
O
2
f1 (ppm)

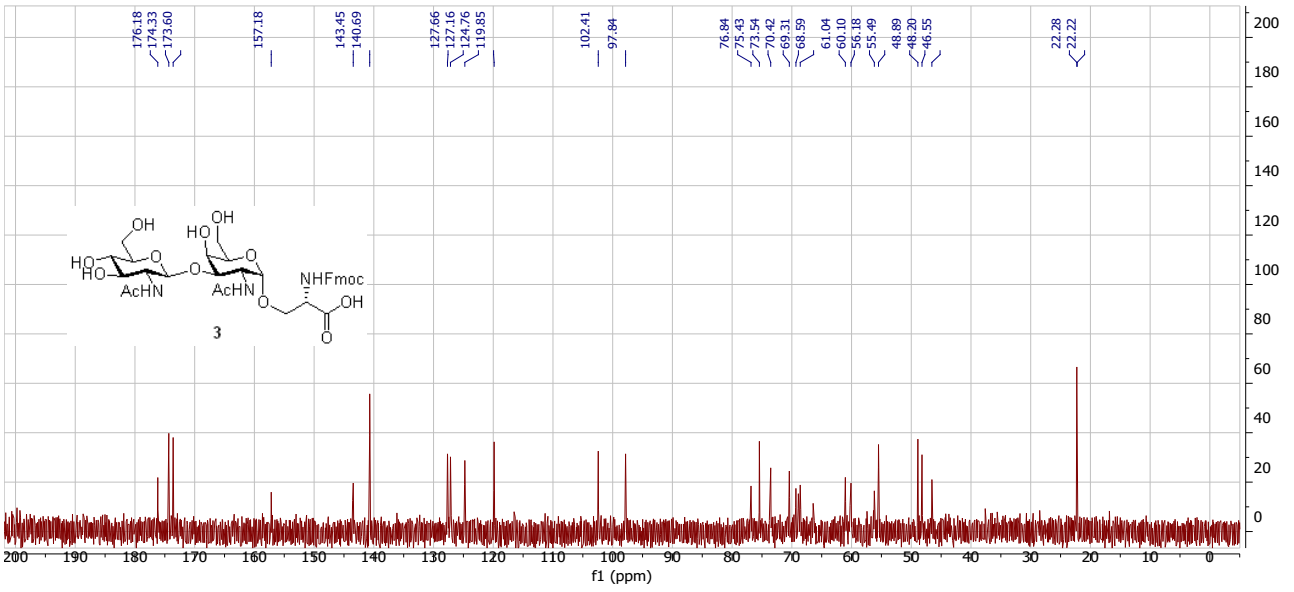

Ph
OAc
AcO
AcO
TrocHN
N3
NHFmoc
OtBu
23
f1 (ppm)

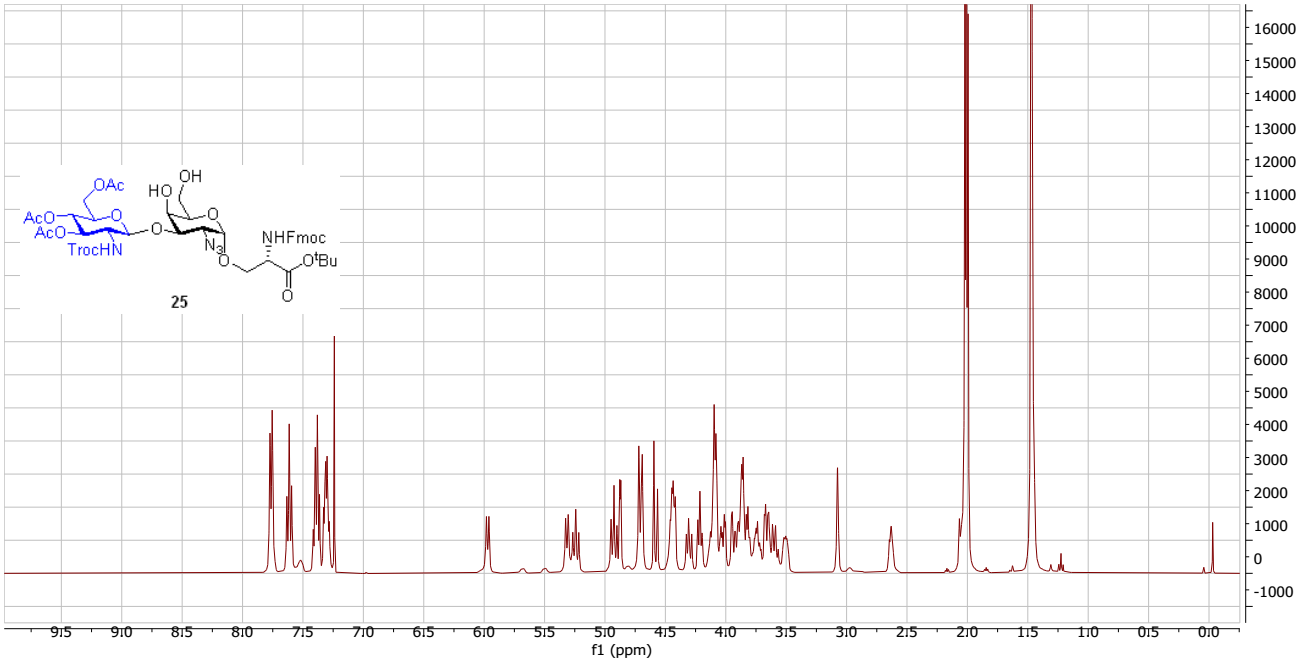

170.42
170.31
169.40
168.63
155.89
153.86
143.75
143.48
141.24
137.57
128.87
128.10
127.89
127.27
127.18
126.05
125.34
125.10
120.28
101.64
100.55
99.51
95.28
83.09
77.32
77.00
76.68
76.34
75.39
74.50
71.67
71.58
69.44
68.99
68.28
67.21
63.46
61.40
58.69
56.09
54.90
47.06
27.94
20.71
20.62
20.59
Ph
OAc
AcO
AcO
TrocHN
N3
NHFmoc
OtBu
23
f1 (ppm)

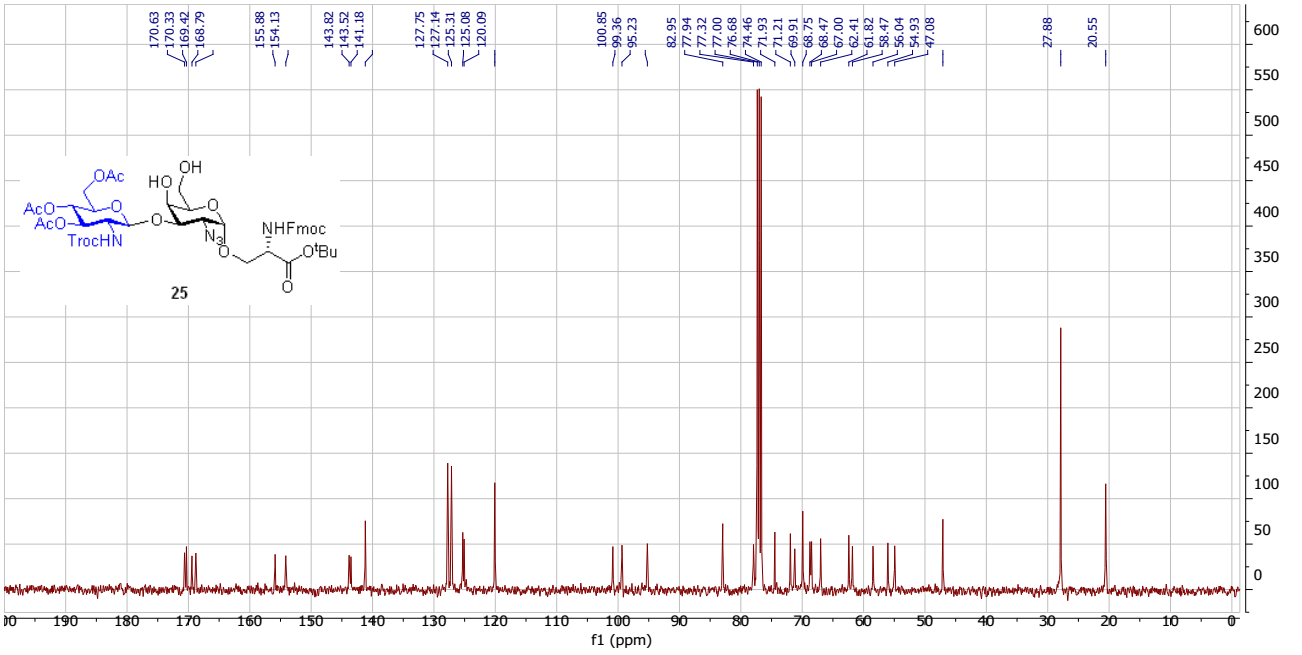

OAc
AcO
AcO
AcHN
O
OAc
AcO
O
AcHN
O
NHFmoc
O
O
OtBu
24
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

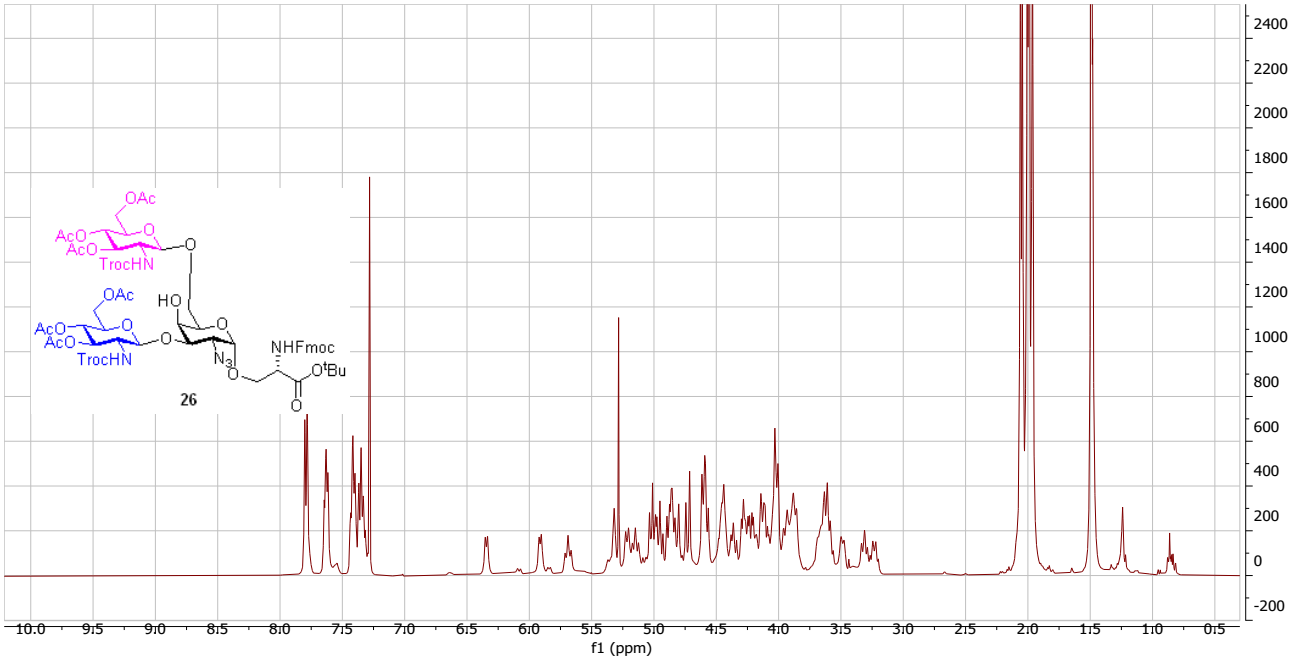

171.11
170.73
170.62
170.41
169.89
169.23
168.94
155.85
143.63
141.17
127.73
127.02
124.85
119.98
99.25
98.34
82.88
77.21
77.00
76.79
72.88
71.87
68.87
68.55
68.32
67.57
66.95
62.50
61.35
55.31
54.79
48.81
47.01
27.90
23.22
23.12
20.60
20.55
20.51
OAc
AcO
AcO
AcHN
O
OAc
AcO
O
AcHN
O
NHFmoc
O
O
OtBu
24
800
700
600
500
400
300
200
100
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

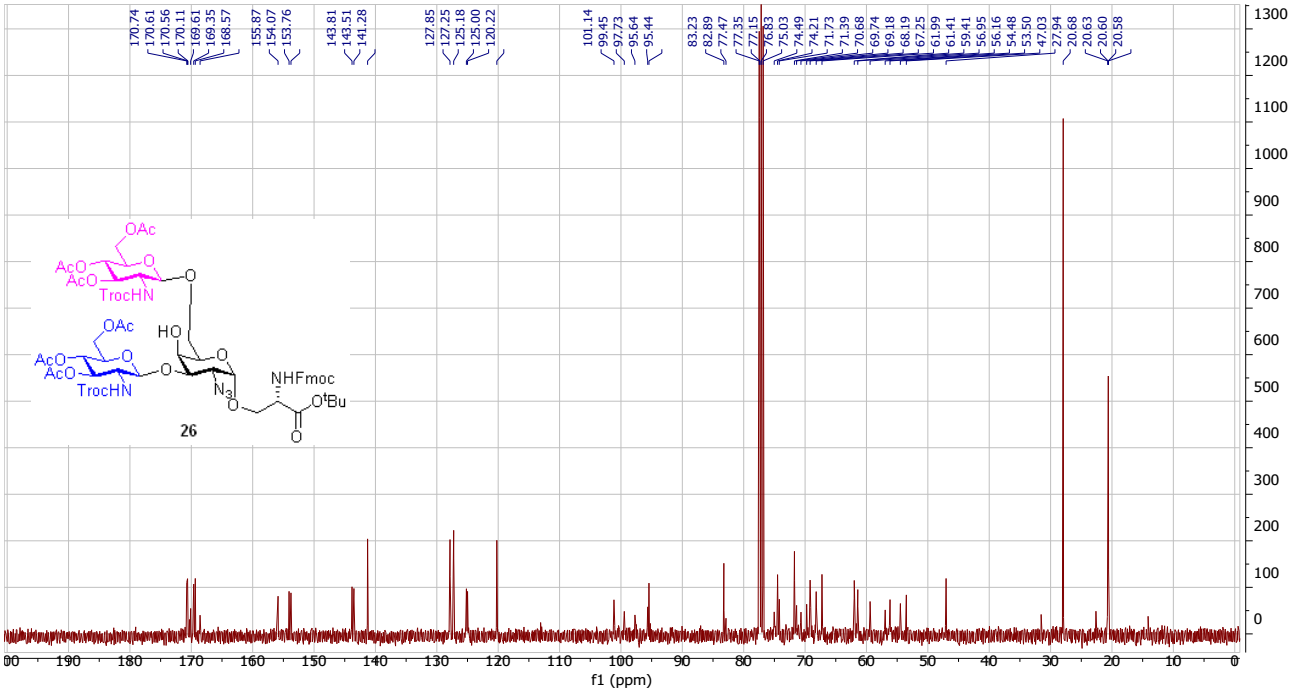

OH
HO
HO
O
AcHN
OH
HO
O
AcHN
O
NHFmoc
OH
O
3
f1 (ppm)

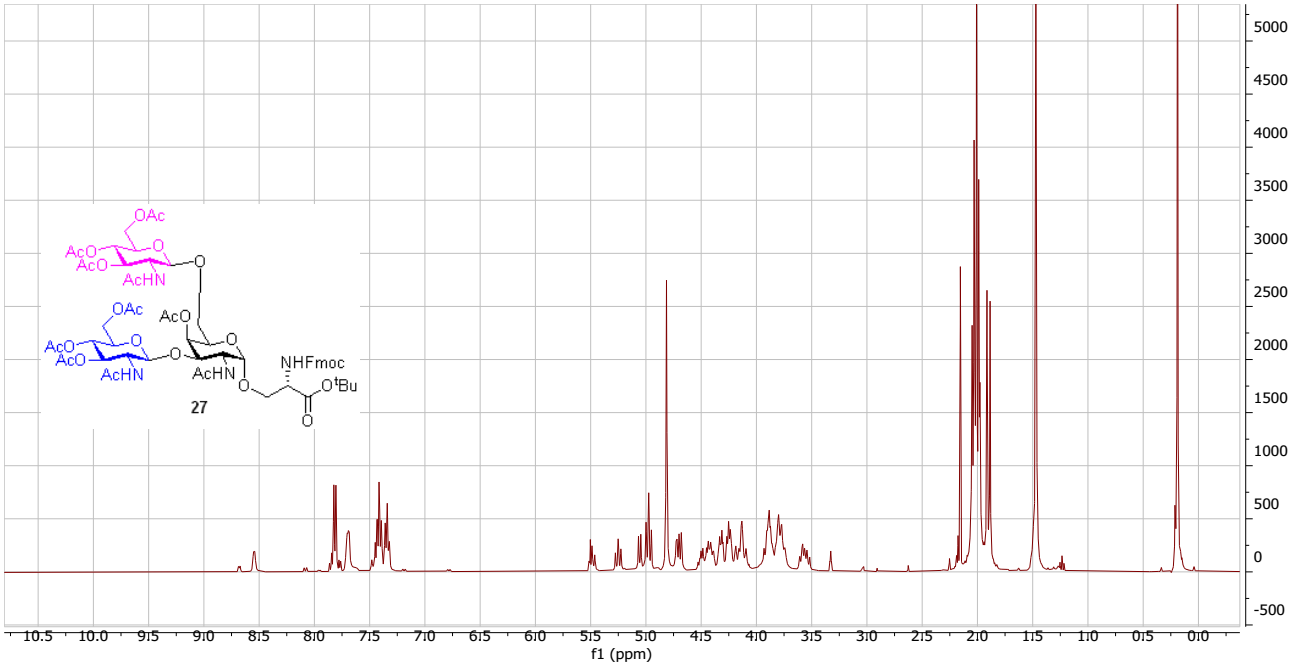

176.18
174.33
173.60
157.18
143.45
140.69
127.66
127.16
124.76
119.85
102.41
97.84
76.84
75.43
73.54
70.42
69.31
68.59
61.04
60.10
56.18
55.49
48.89
48.20
46.55
22.28
22.22
OH
HO
HO
O
AcHN
OH
HO
O
AcHN
O
NHFmoc
OH
O
3
f1 (ppm)

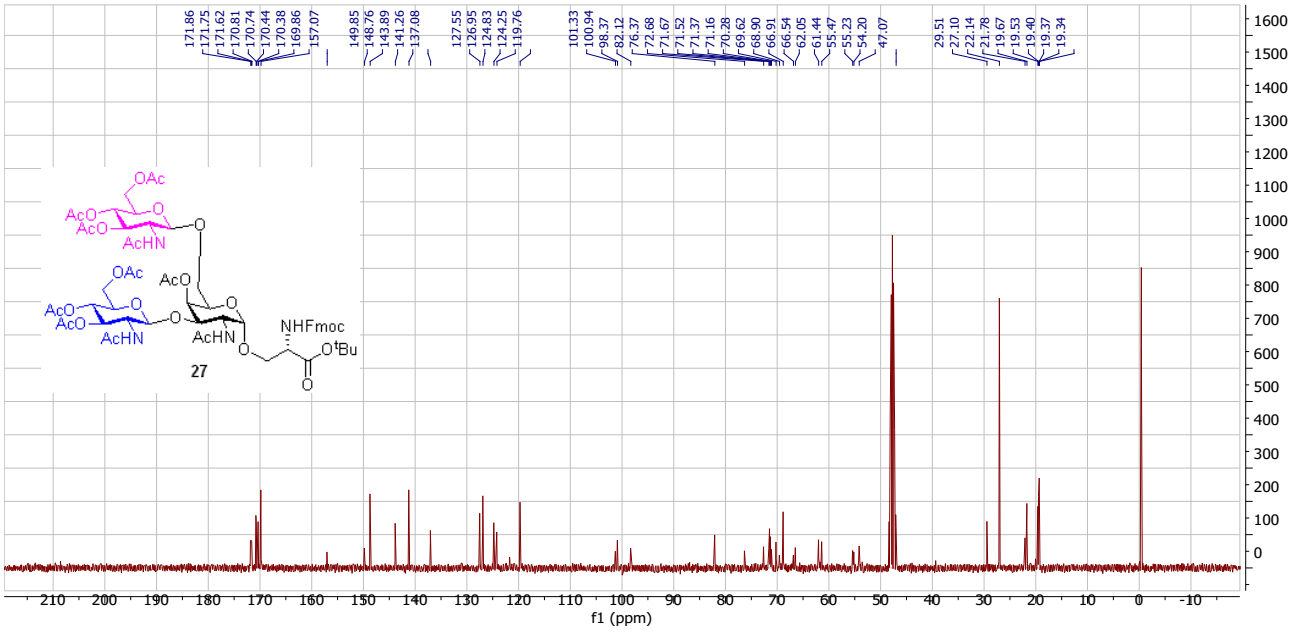

OAc
AcO
AcO
TrocHN
HO
OH
O
N3
NHFmoc
OtBu
25
f1 (ppm)

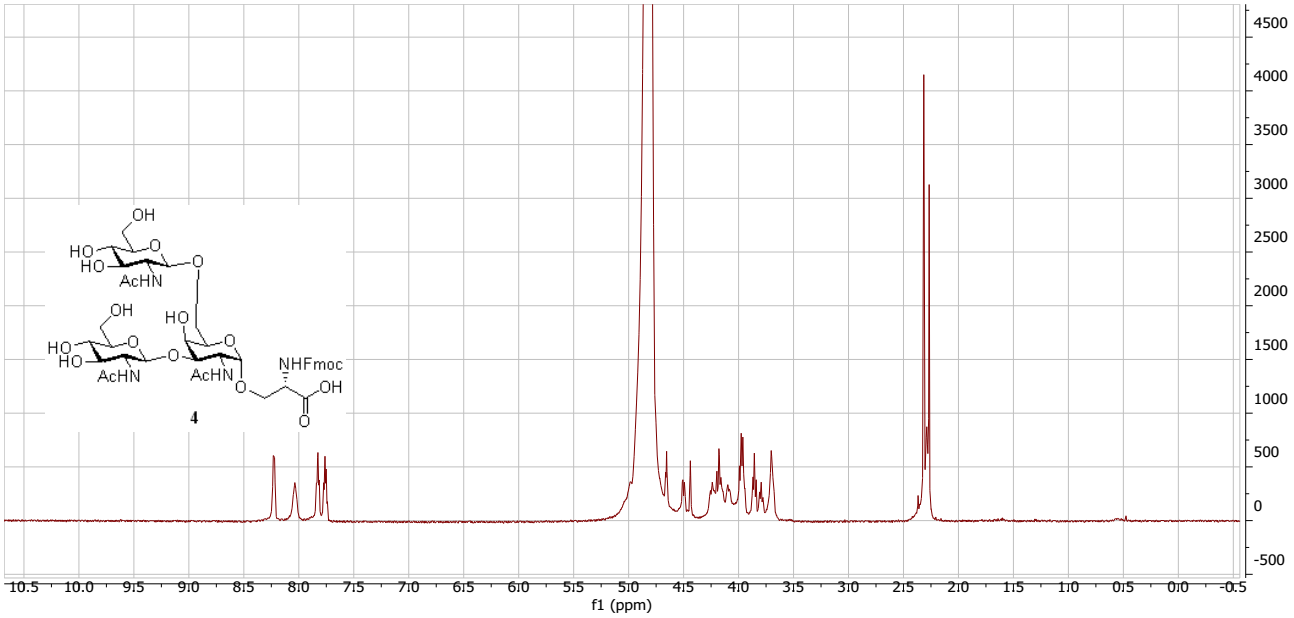

170.63
170.33
169.42
168.79
155.88
154.13
143.82
143.52
141.18
127.75
127.14
125.31
125.08
120.09
100.85
99.36
95.23
82.95
77.94
77.32
77.00
76.68
74.46
71.93
71.21
69.91
68.75
68.47
67.00
62.41
61.82
58.47
56.04
54.93
47.08
27.88
20.55
OAc
AcO
AcO
TrocHN
HO
OH
O
N3
NHFmoc
OtBu
25
f1 (ppm)

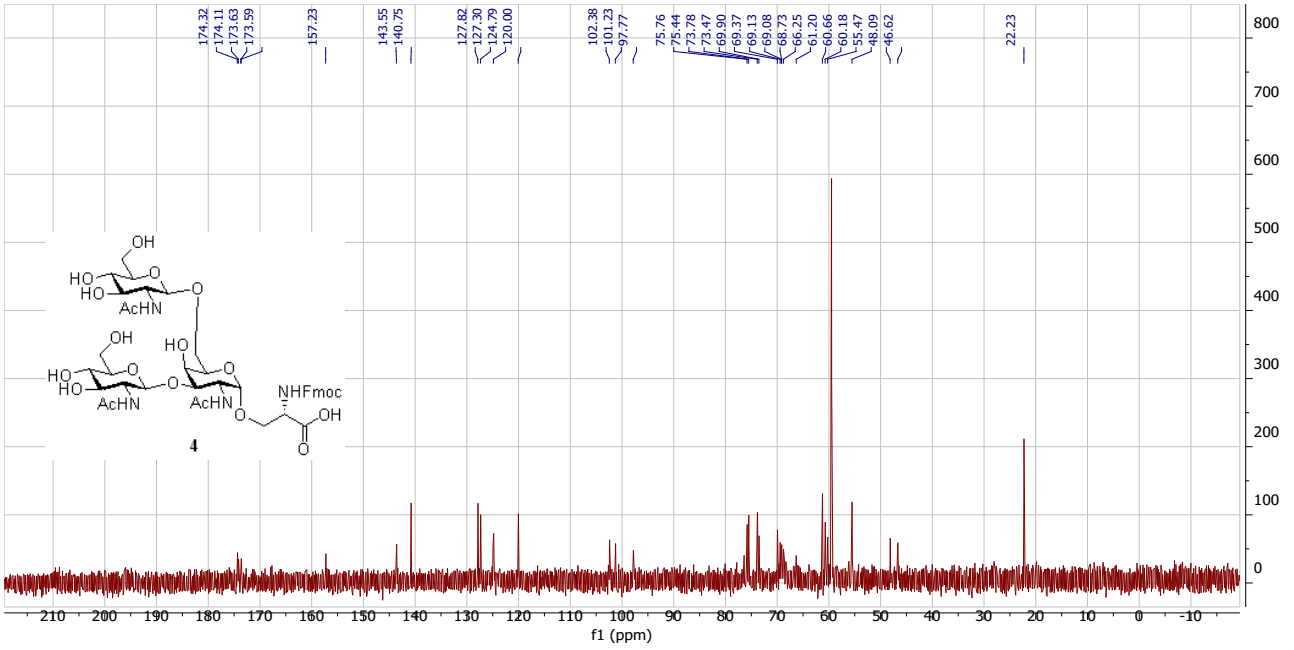

OAc
AcO
AcO
TrocHN
HO
NHFmoc
O^{t}Bu
26
f1 (ppm)

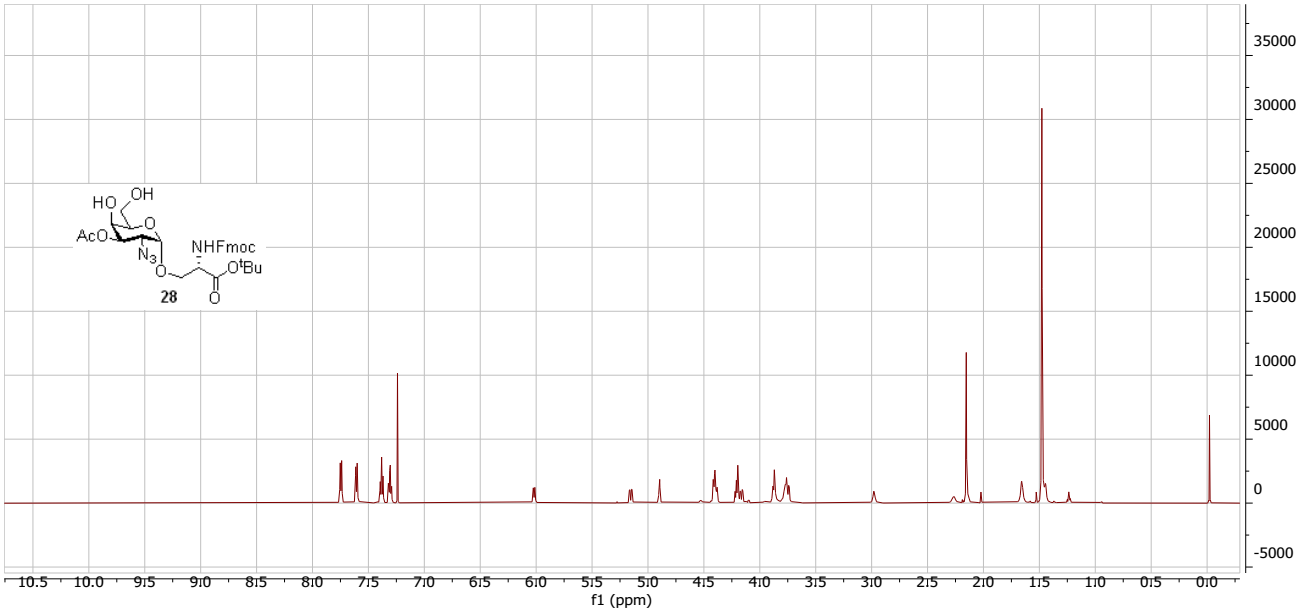

170.74
170.61
170.56
170.11
169.61
169.35
168.57
155.87
154.07
153.76
143.81
143.51
141.28
127.85
127.25
125.18
125.00
120.22
101.14
99.45
97.73
95.64
95.44
83.23
82.89
77.47
77.35
77.15
76.83
75.03
74.49
74.21
71.73
71.39
70.68
69.74
69.18
68.19
67.25
61.99
61.41
59.41
56.95
56.16
54.48
53.50
47.03
27.94
20.68
20.63
20.60
20.58
OAc
AcO
AcO
TrocHN
HO
NHFmoc
O^{t}Bu
26
f1 (ppm)

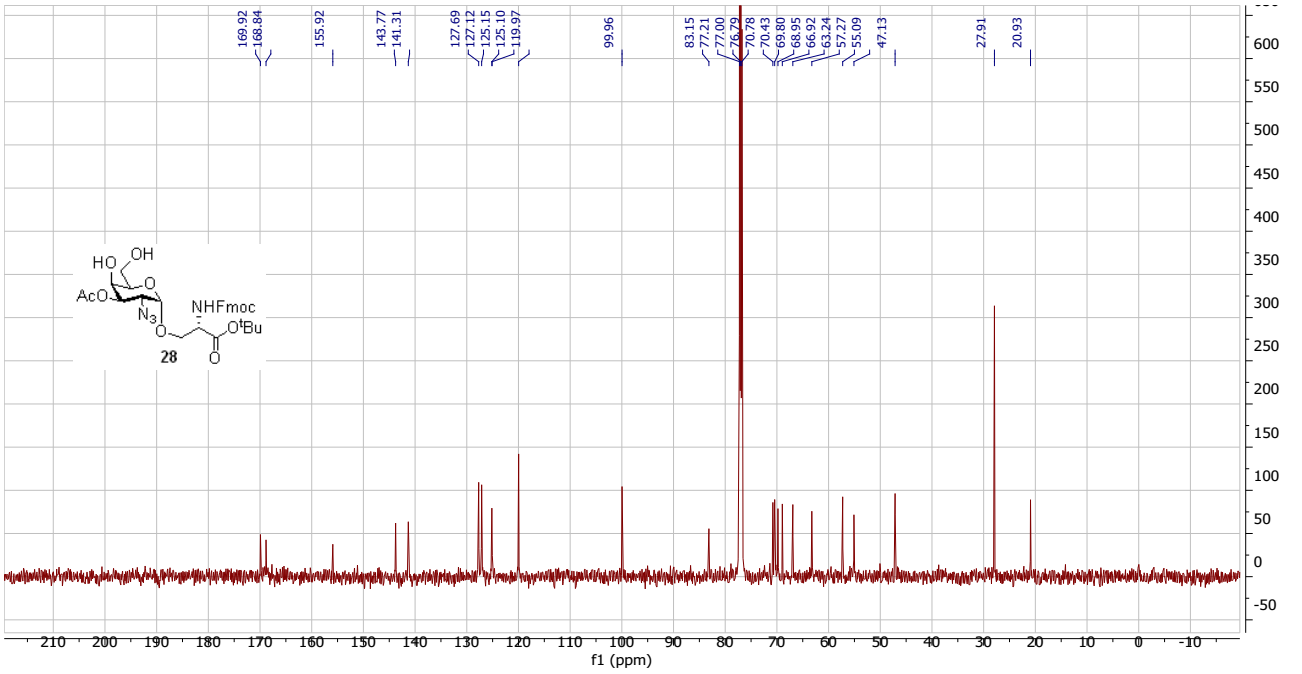

OAc
AcO
AcO
AcHN
AcO
NHFmoc
O^{t}Bu
27
f1 (ppm)

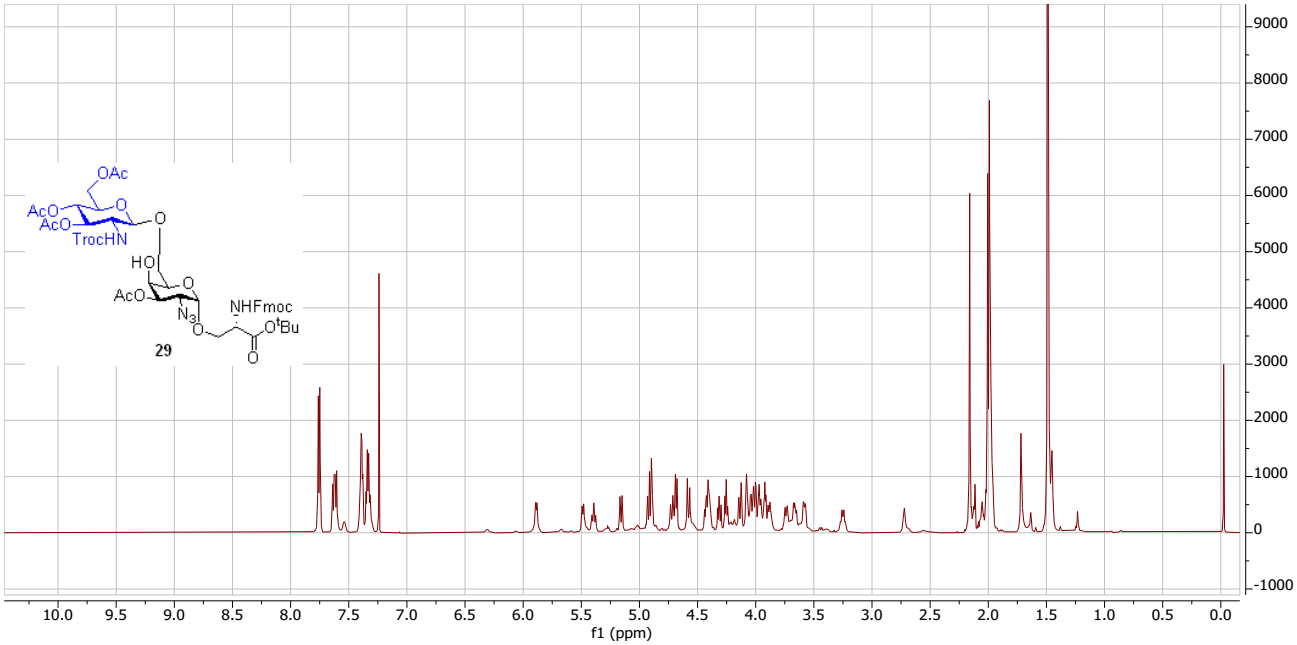

171.86
171.75
171.62
170.81
170.74
170.44
170.38
169.86
157.07
149.85
148.76
143.89
141.26
137.08
127.55
126.95
124.83
124.25
119.76
101.33
100.94
98.37
82.12
76.37
72.68
71.67
71.52
71.37
71.16
70.28
69.62
68.90
66.91
66.54
62.05
61.44
55.47
55.23
54.20
47.07
29.51
27.10
22.14
21.78
19.67
19.53
19.40
19.37
19.34
OAc
AcO
AcO
AcHN
AcO
NHFmoc
O^{t}Bu
27
f1 (ppm)

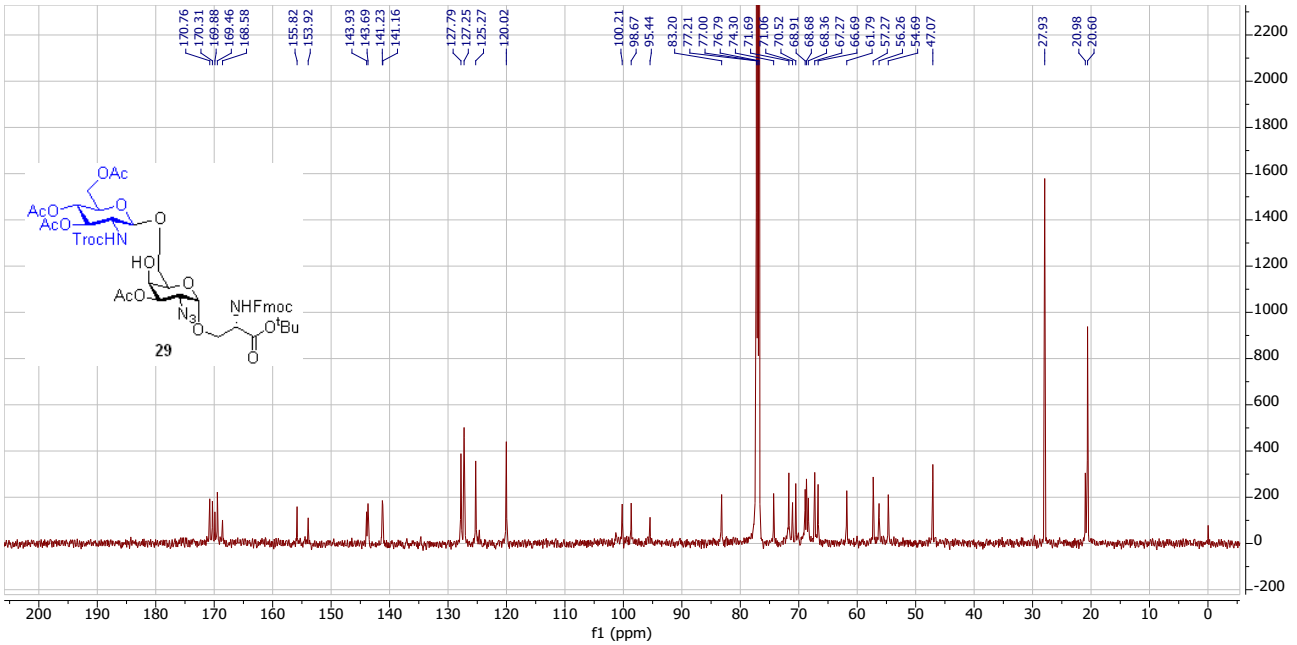

OH
HO
HO
AcHN
O
HO
NHFmoc
OH
4
f1 (ppm)

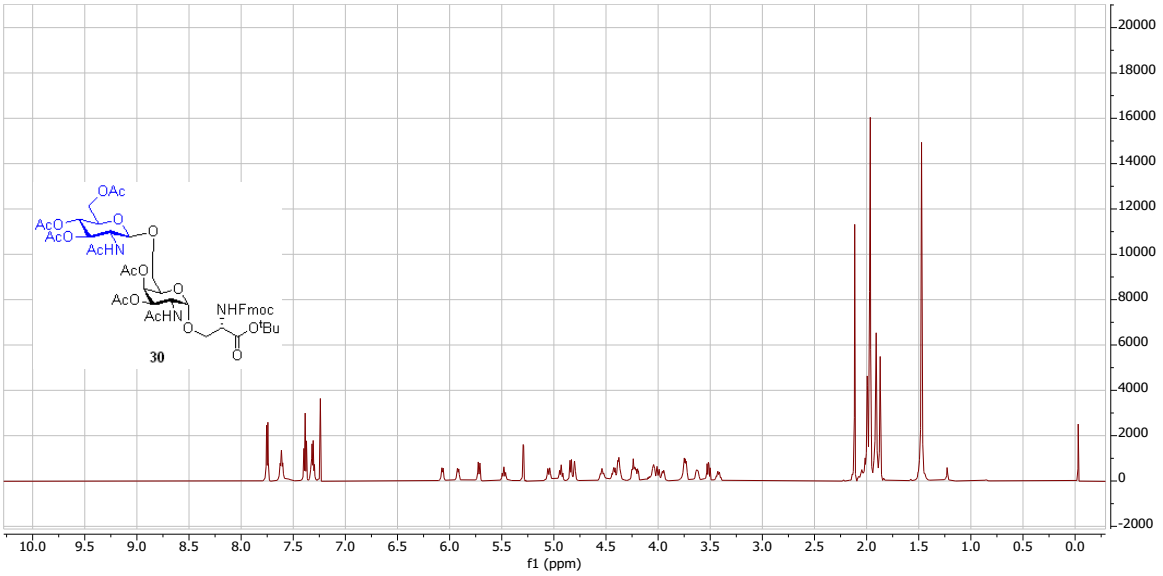

174.32
174.11
173.63
173.59
157.23
143.55
140.75
127.82
127.30
124.79
120.00
102.38
101.23
97.77
75.76
75.44
73.78
73.47
69.90
69.37
69.13
69.08
68.73
66.25
61.20
60.66
60.18
55.47
48.09
46.62
22.23
4
f1 (ppm)

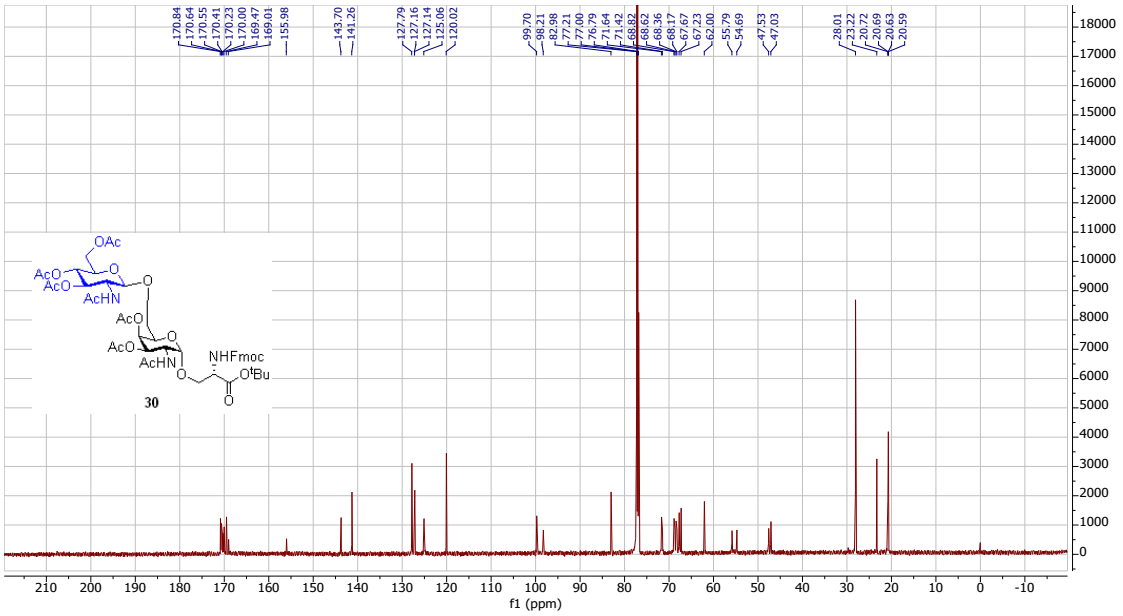

HO
OH
AcO
O
N3
O
NHFmoc
OtBu
O
28
35000
30000
25000
20000
15000
10000
5000
0
-5000
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

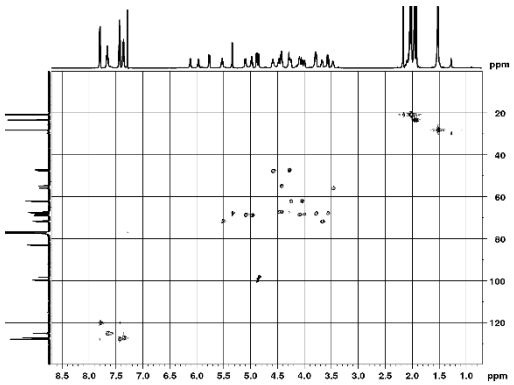

169.92
168.84
155.92
143.77
141.31
127.69
127.12
125.15
125.10
119.97
99.96
83.15
77.21
77.00
76.79
70.78
70.43
69.80
68.95
66.92
63.24
57.27
55.09
47.13
27.91
20.93
HO
OH
AcO
O
N3
O
NHFmoc
OtBu
O
28
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OAc
AcO
AcO
TrocHN
HO
AcO
N3
NHFmoc
O
O
O
tBu
29
f1 (ppm)

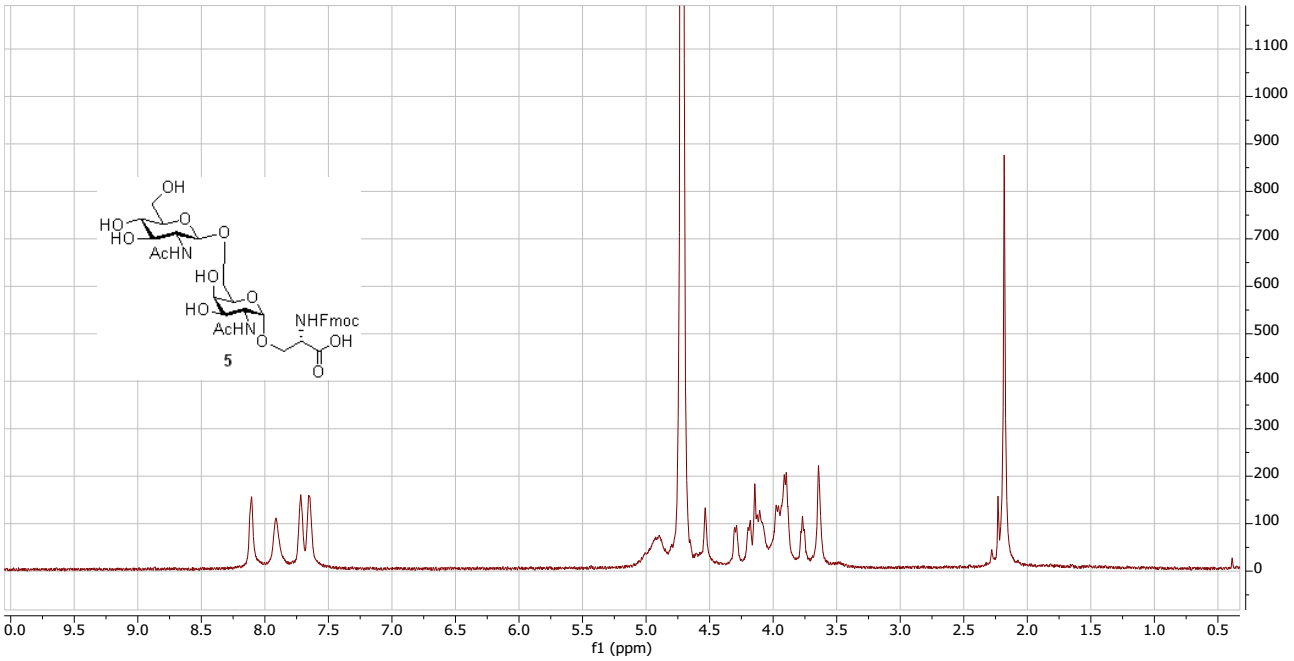

170.76
170.31
169.88
169.46
168.58
155.82
153.92
143.93
143.69
141.23
141.16
127.79
127.25
125.27
120.02
100.21
98.67
95.44
83.20
77.21
77.00
76.79
74.30
71.69
71.06
70.52
68.91
68.68
68.36
67.27
66.69
61.79
57.27
56.26
54.69
47.07
27.93
20.98
20.60
OAc
AcO
AcO
TrocHN
HO
AcO
N3
NHFmoc
O
O
O
tBu
29
f1 (ppm)

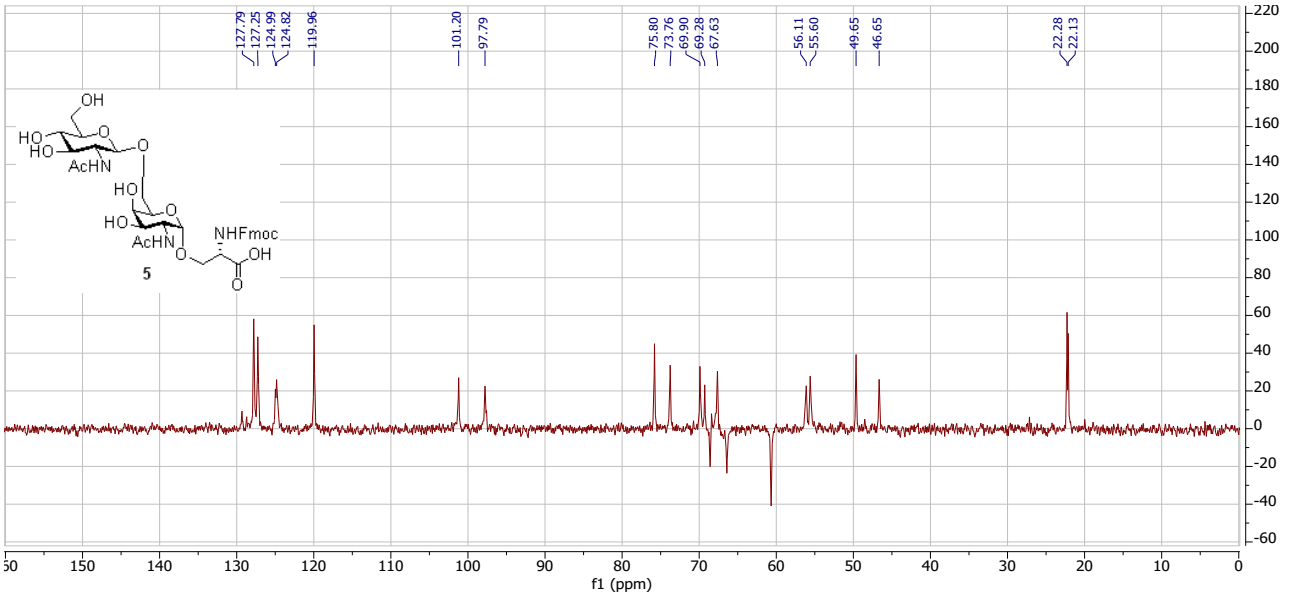






2D HSQC 600 MHz


OH
HO
HO
O
O
AcHN
HO
HO
O
AcHN
O
NHFmoc
OH
O
5
f1 (ppm)


127.79
127.25
124.99
124.82
119.96
101.20
97.79
75.80
73.76
69.90
69.28
67.63
56.11
55.60
49.65
46.65
22.28
22.13
OH
HO
HO
O
O
AcHN
HO
HO
O
AcHN
O
NHFmoc
OH
O
5
f1 (ppm)