DESIGN AND SYNTHESIS OF FONDAPARINUX AND ITS ANALOGS

A thesis submitted towards the partial fulfilment of the Master's degree program

By

Mohini Burnwal

Registration No. : 20212013

Under the guidance of

Prof. Raghavendra Kikkeri

Department of Chemistry

Indian Institute of Science Education and Research

Dr. Homi Bhabha Road, Pashan, Pune.

CERTIFICATE

This is to certify that this dissertation entitled "**Design and Synthesis of Fondaparinux and Its Analogs**" towards the partial fulfilment of the Master's degree programme at the Indian Institute of Science Education and Research, Pune represents the work carried out by Mohini Burnwal at the Indian Institute of Science Education and Research under the supervision of Prof. Raghavendra Kikkeri, Associate Professor, Department of Chemistry, during the academic year 2023-2024.

Prof. Raghavendra Kikkeri

Supervisor

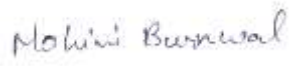
Professor

Department of Chemistry

IISER Pune

DECLARATION

I hereby declare that the matter embodied in the report entitled "**Design and Synthesis of Fondaparinux and Its Analogs**" are the results of the work carried out by me at the Department of Chemistry, Indian Institute of Science Education and Research, Pune, under the supervision of Prof. Raghavendra Kikkeri and the same has not been submitted elsewhere for any other degree. Wherever others contribute, every effort is made to indicate this clearly, with due reference to the literature and acknowledgement of collaborative research and discussions.



Mohini Burnwal

20212013

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CONTENTS

ABBREVIATIONS

Ac = Acetyl

AcOH = Acetic acid

Ac_2O = Acetic anhydride

AllOH = Allyl alcohol

AT = Antithrombin

BAIB = Bis(acetoxy)iodobenzene

$BF_3.Et_2O$ = Boron trifluoride diethyl etherate

BnBr = Benzyl bromide

BzCl = Benzoyl Chloride

CSA = Camphor sulfonic acid

$(ClAc)_2O$ = Chloroacetic anhydride

$CDCl_3$ = Deuterated chloroform

CH_3 = methyl

CH_3CN = Acetonitrile

$CHCl_3$ = Chloroform

CS = Chondroitin Sulfate

DCM = Dichloromethane

DCC = *N, N*-dicyclohexyl carbodiimide

DMF = *N, N*-Dimethylformamide

DMAP = 4-Dimethylaminopyridine

NEt_3 = Triethylamine

EtOAc = Ethyl acetate

GAGs =Glycosaminoglycans

GlcA = Glucuronic Acid

GlcNAc = *N*-acetylglucosamine

H = Hydrogen

HCl = Hydrochloric Acid

H_2SO_4 = Sulfuric Acid

HPLC = High-Performance Liquid Chromatography

HP = Heparin

HRMS = High-resolution mass spectroscopy

HS = Heparan Sulfate

J = Coupling constant

IdoA = Iduronic Acid

LevOH = Levulinic Acid

LMWH = Low Molecular Weight Heparin

m/z = Mass to charge ratio

MALDI = Matrix-Assisted Laser Desorption Ionization

MeOH = Methanol

MHz = Mega Hertz

mL = Mille Liter

mM = Millimolar

M.S. = Molecular Sives

Mw = Molecular weight

NAP-Br = Napthyl Bromide

NIS = *N*-Iodosuccinimide

NaOH = Sodium hydroxide

NaOMe = Sodium methoxide

NIS = *N*-Iodosuccinimide

nm = Nanometer

NMR = Nuclear magnetic resonance

ppm = parts per million

Py = Pyridine

P-TsOH = Para-tolunesulfonic acid

R.T = room temperature

NaCl = Sodium chloride

TBAI = Tetrabutylammonium iodide

^{t}BuOK = Tertiary butoxide

TBDPSCl = Tertiary-butyl-di-phenyl-silyl chloride

TLC = Thin Layer Chromatography

TMSOTf = Trimethylsilyltrifluoromethanesulfonate

TMSSPh = Trimethyl(thiophenol)silane

UFH = Unfractionated Heparin

ULMWH = Ultra-low molecular weight heparin

ZnI_2 = Zinc Iodide

ABSTRACT

Heparin is a linear polysaccharide comprised of alternating α (1,4)-D-glucosamine (GlcN) and β (1-4) glucuronic acid (GlcA) or α(1,4)-L-iduronic acid (IdoA) units. It is used as an anticoagulant to treat arterial thrombosis. There are three approved heparin-based anticoagulant drugs for clinical use: unfractionated heparin (UFH), low-molecular-weight heparin (LMWH), and pentasaccharide fondaparinux. UFH, which is derived from animal sources such as porcine intestine or bovine lung, has a rapid anticoagulant effect to treat acute thrombotic events but can cause heparin-induced thrombocytopenia and osteoporosis. LMWH, which is prepared by chemically or enzymatically degrading UFH, has a longer half-life and can be administered subcutaneously. However, its anticoagulant effect is only partially neutralized by protamine, which may result in bleeding risks. Fondaparinux, a pure synthetic pentasaccharide, has better antithrombotic efficacy and biosafety than UFH and LMWH but lacks an effective neutralizable agent, limiting its clinical use. Moreover, fondaparinux also possesses anti-inflammatory activity. Therefore, there is an immediate need to improve its bioavailability and reduce its anti-inflammatory activity and neutralization of the drug. To address this issue, we propose incorporating different protection/deprotection strategies to synthesize well-defined fondaparinux (FA) analogues with an amine linker. The synthetic FA will then be conjugated to different proteins through bioconjugation techniques, and the drug loading will be optimized. Finally, the chemically prepared fondaparinux conjugates will be tested for its anti-FXa, neutralizable, and anti-inflammatory activity.

1. INTRODUCTION:

Heparin is known for its anticoagulant or anti-thrombotic activity and is composed of alternative arrangements of α-1,4-D-glucosamine (GlcN) and α-1,4-D-glucuronic acid (GlcA) or β-1,4-L-iduronic acid (IdoA). There are three clinically approved heparin drugs available in the market, and they are unfractionated heparin (UFH), low molecular weight heparin (LMWH), and ultra-low molecular weight heparin (ULMWH). Heparin shows a quick anti-thrombotic action; however, it is associated with side effects, i.e., thrombocytopenia. Therefore, with heparin-based drugs, there must be some neutralizing agent to control its over anti-coagulation to improve its pharmacokinetics performance.

From the studies, it was observed that the LMWH, i.e., Enoxaparin, has the benefit of a long half-life over UFH and can also be neutralized. [5]For instance, in 2021, when COVID-19 was at its highest peak, clinical trial experiments were performed with COVID-19 patients from several Italian hospitals with their permission. Here, the patients were administrated with different drugs, including enoxaparin, for the anti-thrombotic action. While evaluating the experiments, they noticed that Enoxaparin was the drug that reached to 100% of patients. Additionally, after 3 weeks of administration, the fibrinogen level was decreased in the case of Enoxaparin and through this observation, it was concluded that Enoxaparin is able to exert the anti-coagulation action.

However, the LMWH is derived through chemical depolymerization of UFH, which is an animal-sourced heparin form, and this causes contamination and quality issues of the drug. Moreover, these are partially neutralized by protamine; therefore, due to a lack of neutralization, its clinical use is limited. This limitation has diverted people to find other alternative options, and with the studies, [1]it was found that heparins contain a unique pentasaccharide sequence of glucosamine, glucuronic acid and iduronic acid. It was observed that this specific unit efficiently binds with Factor Xa to show anti-coagulation action. The excellent discovery showed the way for its chemical synthesis, which later on in 2004, showed for the first time the chemically synthesized anticoagulant drug,

Fondaparinux, also known as Arixtra[3]. It comes under the ULMWH form of heparin. From the studies, it was shown that it is able to show a longer half-life and greater anti-coagulant action than the formal two drugs. It is an industrially obtained heparin-based drug through chemical synthesis. It shows anti-coagulant action by exhibiting antithrombin III-mediated exclusive factor Xa (FXa) inhibition activity.

For instance, [6]in 2022, the fondaparinux-based biotin conjugates were synthesised for the biological evaluation of the anti-coagulant activity through incorporation with protamine and avidin. Initially, the Fondaparinux was synthesised, which was further conjugated with biotin to make the analogues. These conjugates were further incorporated into avidin and protamine proteins for the evaluation of neutralization. From their biological studies, they found that the anti-thrombotic activity is efficiently neutralized by biotinylated fondaparinux with avidin.

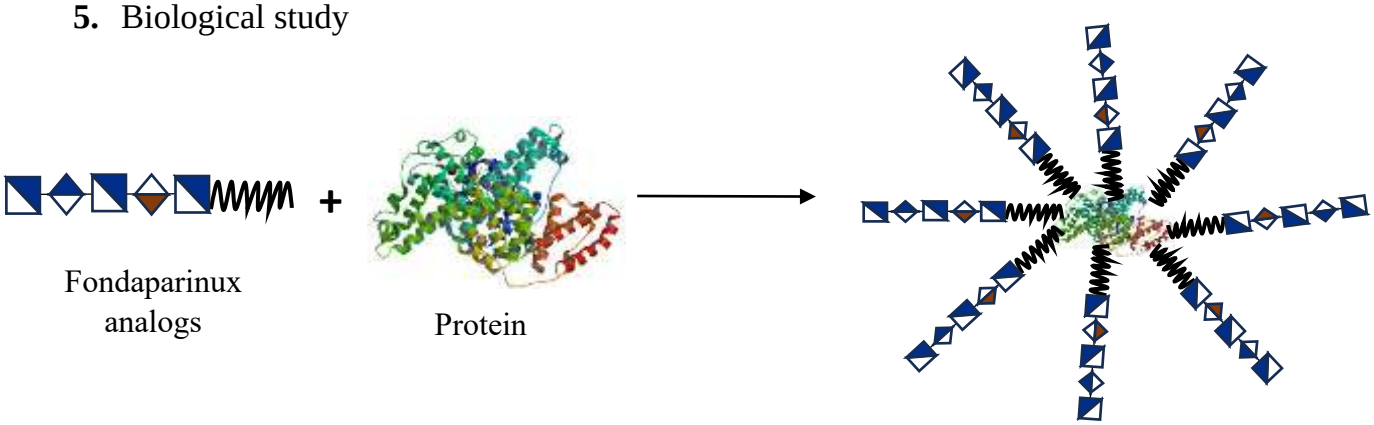
Therefore, inspired by them, we are also aiming to make fondaparinux conjugates to deal with the neutralization action. Although many glycosylation methods and synthetic strategies were published for its synthesis in the past few decades, most of these strategies are facing challenges of multi-step synthesis and cost effectivity. These are the motivations of our synthetic route. Moreover, heparin is known to show its anti-coagulation due to the 3-O sulfation pattern in glucosamine; still, the Fondaparinux contains only one glucosamine with 3-O sulfation and that intrigued us to investigate the specificity of 3-O sulfation pattern in Fondaparinux.

Therefore, we are initially aiming for the actual fondaparinux molecule, tackling its synthetic challenges. After optimization of the synthetic pattern, the same scheme will be followed for making the analogues, and these analogues will be conjugated to different proteins for biological studies.

The particular aims are:

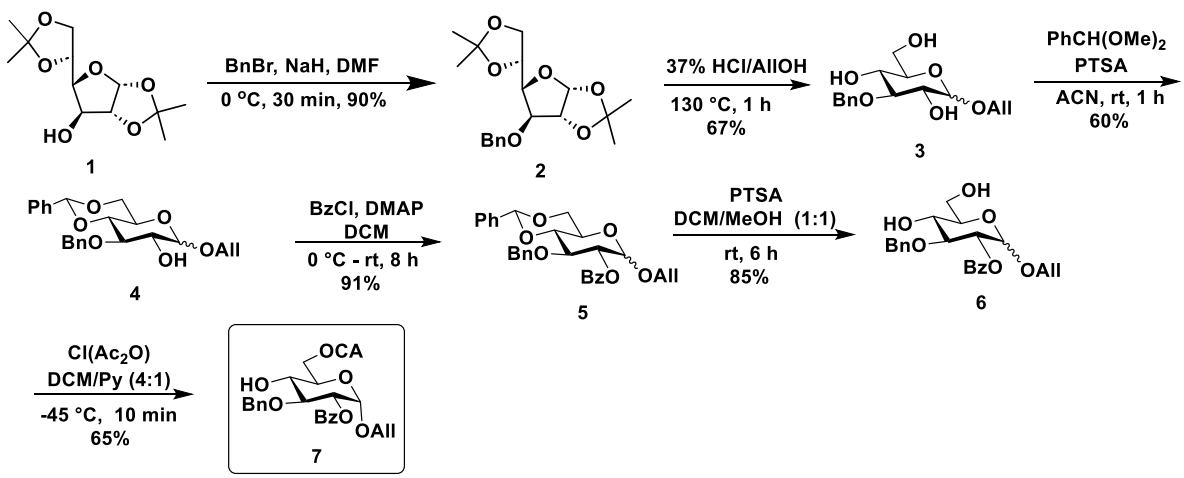
1. Synthesis of disaccharide donor
2. Synthesis of trisaccharide acceptor
3. 3+2 integration of disaccharide donor and trisaccharide acceptor
4. Synthesis of Fondaparinux analogues

5. Biological study



2. Result and Discussion:

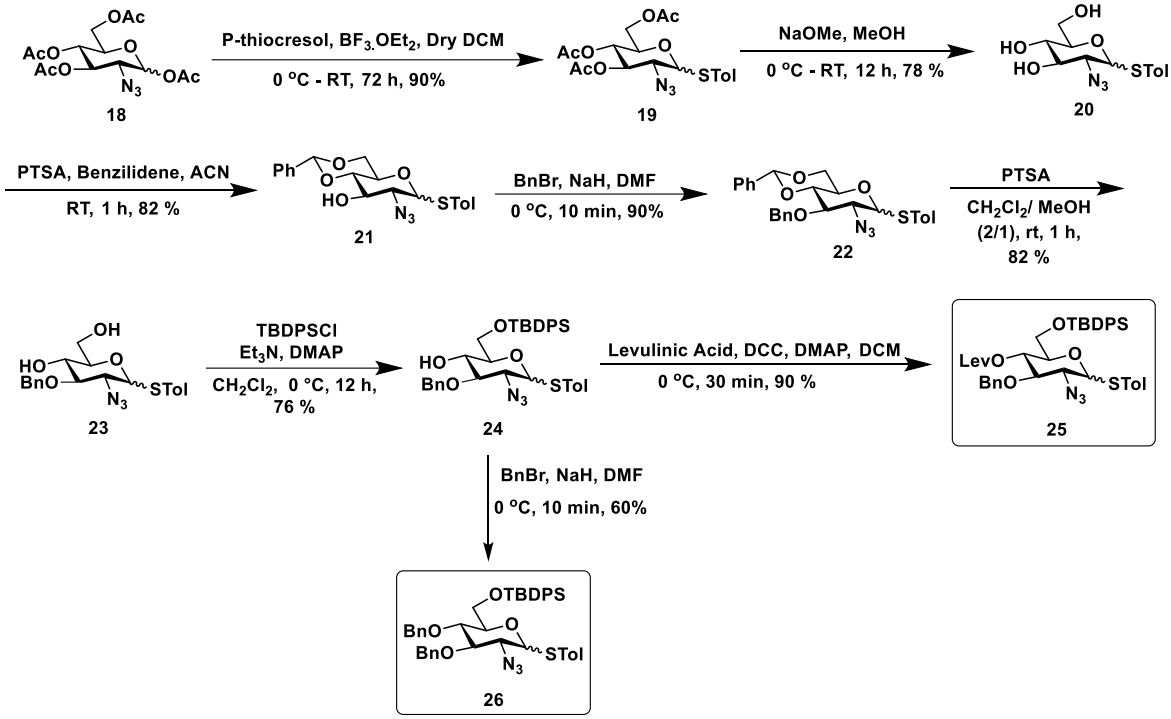
2.1 Synthesis of Glucose building block:



Scheme 1: Synthesis of Glucose Building Block

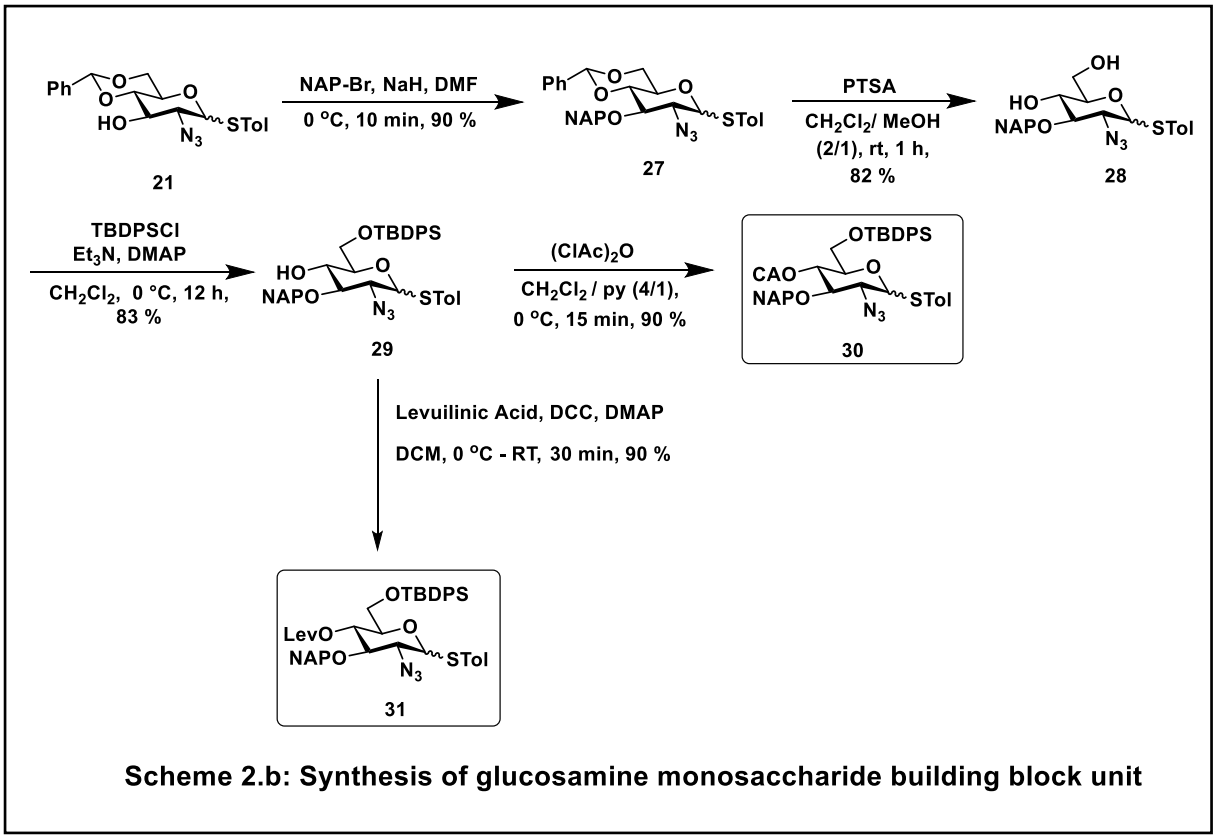
We are synthesising the disaccharide donor building block, for which glucose monosaccharide building block is required. We started from compound **1,** which was first benzylated. Then, compound **2** was taken for allyl glycosylation using 37% HCl in allyl alcohol. Compound **3** was taken further for benzylidene protection, followed by benzoylation using benzoyl chloride in DMAP. Then, compound **5** was subjected to benzylidene deprotection with 85% yield. Finally, compound **6** was subjected to chloroacetate protection using chloroacetic anhydride in pyridine to get the final glucose acceptor **7** with a 65% yield.

2.2 Synthesis of Glucosamine building block:



Scheme 2.a: Synthesis of glucosamine monosaccharide building block unit

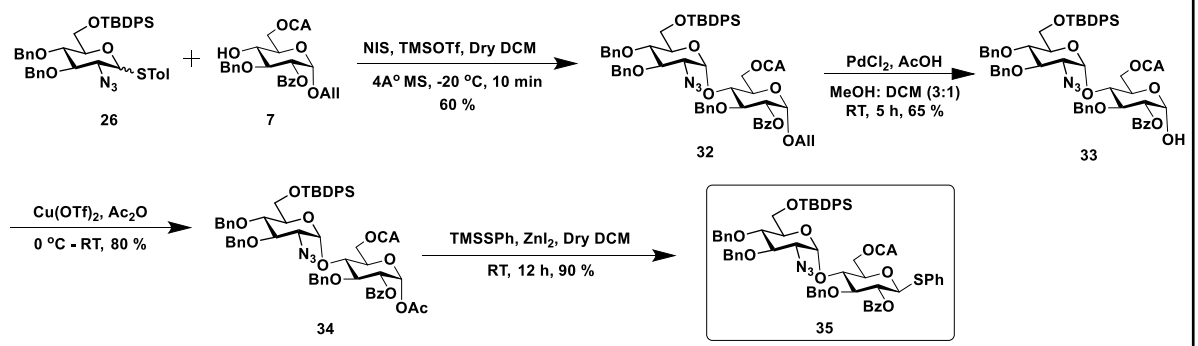
We require four different glucosamine building blocks for the fondaparinux pentasaccharide unit. We began with the per-acetylated form of glucosamine. Compound **1** was initially taken for thio-glycosylation using p-thiocresol and $BF_3.OEt_2$, followed by deacetylation using methanol and sodium methoxide with 78% yield. Compound **20** was subjected to benzylidene protection using pTSA and benzaldehyde dimethyl acetal in acetonitrile with 82% yield. Next, compound **21** was used for benzylation. Compound **22** was subjected to benzylidene ring opening using p TSA with an 82% yield. Compound **23** was taken for TBDPS protection using tert-butyl di-phenyl silane chloride (TBDPS-Cl) with 76% yield. Compound **24** was further divided into two batches; one batch was subject to Lev protection using levuilinic acid, DCC and DMAP with a 90% yield. Another batch of compound **24** was used for benzylation with a 60% yield.



Scheme 2.b: Synthesis of glucosamine monosaccharide building block unit

Next, compound **21** was taken for naphthyl protection using sodium hydride and naphthyl bromide, respectively. Compound **27** was subjected to benzylidene ring opening using pTSA with an 82% yield. Compound **28** was taken for TBDPS protection using tert-butyl di-phenyl silane chloride with 83% yield. Compound **29** was further divided into two batches; one batch was subject to Lev protection using levuilinic acid, DCC and DMAP with a 90% yield. Another batch was used for chloroacetate protection.

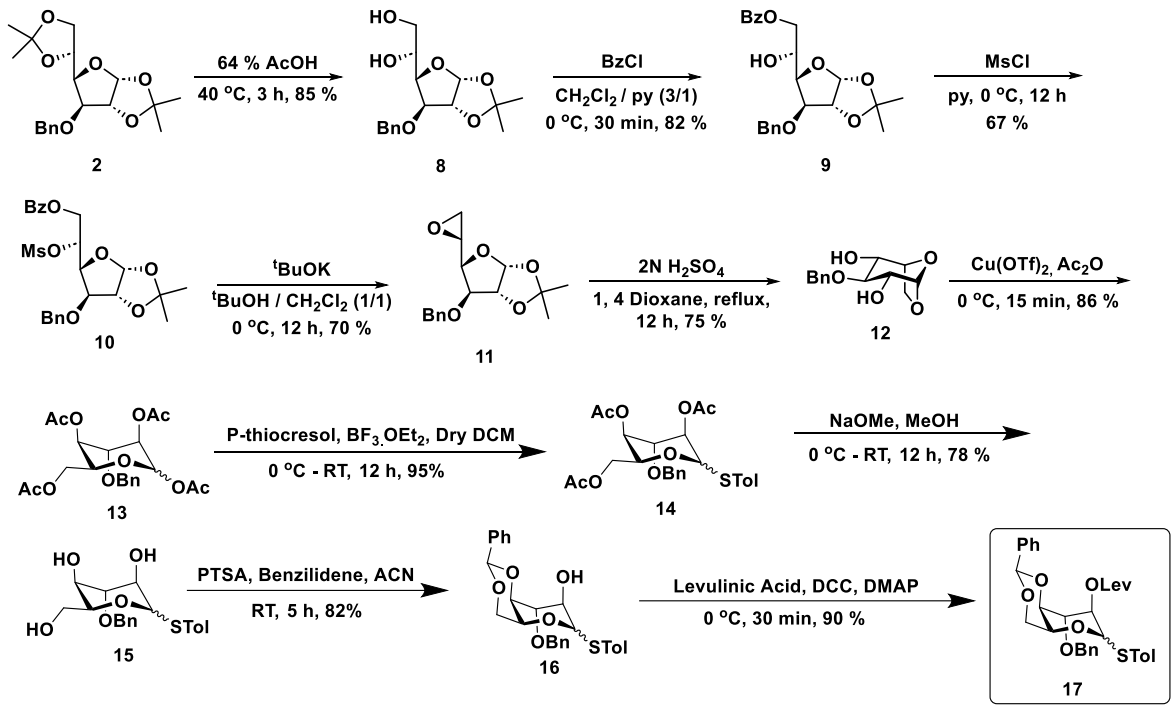
2.3 Synthesis of Disaccharide building block:



Scheme 3: synthesis of disaccharide donor building block

Once we synthesised the required monosaccharide building blocks compounds **26** and **7**, we proceeded for glycosylation using N-iodosuccsinamide and TMSOtf at -20 ºC with 60% yield. Compound **32** was subjected to allyl deprotection using palladium chloride in acetic acid, followed by acetylation using copper triflate in acetic anhydride with 80% yield. Finally, compound **34** was treated with TMSSPh and ZnI_2 in dry DCM to get the thio-phenyl disaccharide donor with a 90% yield.

2.4 Synthesis of Iduronic acid building block:



Scheme 4: Synthesis of Idose building block for tri-saccharide acceptor building block

For the tri-saccharide building block synthesis, we require an idose building block. We initiated from the di-acetal-protected glucofuranose sugar. The compound **2** was subjected to selective ketal deprotection using 64% acetic acid in water, followed by selective benzoylation at C6 by benzoyl chloride and pyridine. Compound **9** was taken for mesitylation using methane sulfonyl chloride. Then compound **10** was subjected to epoxidation, followed by ring expansion using 2 N H_2SO_4 with 75% yield. Compound **12** was further subjected to acetylation using copper triflate in acetic anhydride. Compound 13 was subjected to thio glycosylation, followed by deacetylation. Finally,

compound **16** was taken for benzylidene protection, followed by lev protection with a 90% yield.

3. Conclusion and Future Plans:

We have successfully synthesised the disaccharide donor building block and all the required monosaccharide building blocks of glucosamine, idose, and glucose. All the compounds were characterised by NMR, MALDI-TOF, and HRMS. Now, we are working on the tri-saccharide acceptor building block, which will be used for further integration with the disaccharide donor to get the pentasaccharide sequence. The successful methodology will be followed for making the fondaparinux analogs and they will be subjected to biological studies.

4. Experimental Section:

Materials:

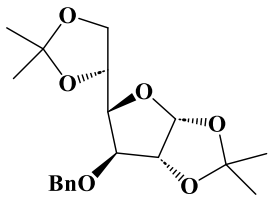
All chemicals were purchased from Sigma Aldrich, Spectrochemicals, Avra and Alfa Aeser. 1H, 13C, and DEPT were recorded on JEOL 400 MHz and Bruker 400 MHz with Tetramethyl silane (TMS) as the internal standard. Chemical shifts were expressed in ppm units, taking TMS as a reference. ESI HRMS data were recorded on Waters Synapt G2 spectrometer. All reactions were monitored by Thin Layer Chromatography (TLC) carried out on 0.25 mm E-Merck silica gel plates (60F-254) with UV-light, and for staining, CAM and $KMnO_4$ were used. All reactions were carried out under the nitrogen atmosphere with dry solvents purchased from a commercial supplier and used without purification. All solvent evaporations were carried out under reduced pressure on the Heidolph rotatory evaporator. Silica gel of 100 -200 mesh was used for column chromatography.

5. SYNTHETIC PROCEDURE:

5.1 Synthesis of Glucose building block:

Compound 2:

(3aR,5S,6S,6aR)-6-(benzyloxy)-5-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxole



2

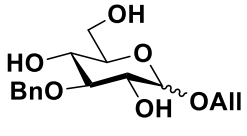
Commercially available compound **1** (50 g, 192.22 mmol) was dissolved in DMF and cooled to 0 °C. Then NaH (28 g, 182.22 mmol) was added at 0°C slowly, followed by the slow addition of BnBr (45.723 ml, 384.43 mmol) using the dropping funnel at 0°C. The reaction was kept for stirring for 12 h at 0 °C under the N_2 atmosphere and monitored using TLC. Reaction was completed and NaH was quenched by slow addition of MeOH, and then the reaction mixture was extracted by brine. Na_2SO_4 was used to dry the organic layer and evaporation of organic layer was done using the rotatory evaporator. Product purification was done by column chromatography. Compound 2 was obtained with a **90%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.37 – 7.27 (m, 5H), 5.90 (d, *J* = 3.7 Hz, 1H), 4.66 (q, *J* = 11.8 Hz, 2H), 4.59 (d, *J* = 3.7 Hz, 1H), 4.38 (dt, *J* = 7.6, 6.0 Hz, 1H), 4.14 (ddd, *J* = 14.7, 8.1, 4.6 Hz, 2H), 4.04 – 3.99 (m, 2H), 1.50 (s, 3H), 1.44 (s, 3H), 1.38 (s, 3H), 1.31 (s, 3H).

Compound 3:

(2R,3R,5R)-4-(benzyloxy)-2-(hydroxymethyl)-6-(((E)-prop-1-en-1-yl)oxy)tetrahydro-2H-pyran-3,5-diol



3

The vacuum-dried compound **2** (13 g, 37.14 mmol) was dissolved in allyl alcohol, and then 37% HCl in allyl alcohol was added to it. Then, the reaction was kept for reflux using a reflux condenser for 1 h at 120 °C under the N_2 atmosphere and monitored using TLC. Reaction was completed, and evaporation of reaction mixture was done using the

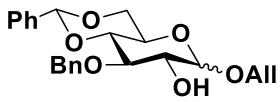
rotatory evaporator and product purification was done by column chromatography. The pure compound was obtained with a **67%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.40 – 7.29 (m, 5H), 5.99 – 5.85 (m, 1H), 5.35 – 5.21 (m, 2H), 4.90 (d, *J* = 3.5 Hz, 1H), 4.77 (dd, *J* = 11.5, 5.9 Hz, 1H), 4.25 – 4.18 (m, 1H), 4.03 (dd, *J* = 12.8, 6.3 Hz, 1H), 3.82 – 3.78 (m, 1H), 3.69 – 3.64 (m, 2H), 3.61 – 3.55 (m, 1H), 3.45 – 3.31 (m, 1H), 2.05 (d, *J* = 8.8 Hz, 3H).

Compound 4:

(2R,4aR,7R,8R,8aR)-8-(benzyloxy)-2-phenyl-6-(((E)-prop-1-en-1-yl)oxy)hexahydropyrano[3,2-d][1,3]dioxin-7-ol



4

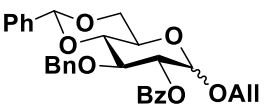
The vacuum-dried compound **3** (9.8 g, 31.89 mmol) was dissolved in CH_3CN. Then PTSA (606 mg, 3.1 mmol) and benzylidene (5.2 ml, 35.088 mmol) were added at RT, and the reaction was kept for stirring at rt for 30 min. The TLC was used to monitor the reaction. After completion of the response, PTSA was quenched by NEt_3, which made the reaction mixture's pH acidic to a little basic. Then, evaporation of reaction mixture was done by the rotatory evaporator. Product purification was done by column chromatography. The pure compound was obtained with a **60%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.51 – 7.46 (m, 2H), 7.40 – 7.23 (m, 8H), 5.98 – 5.87 (m, 1H), 5.55 (s, 1H), 5.32 (dt, *J* = 17.2, 3.1 Hz, 1H), 5.22 (dd, *J* = 10.4, 1.2 Hz, 1H), 4.94 (t, *J* = 7.5 Hz, 2H), 4.80 (d, *J* = 11.6 Hz, 1H), 4.29 – 4.18 (m, 2H), 4.08 – 4.01 (m, 1H), 3.87 (ddd, *J* = 18.5, 9.8, 5.2 Hz, 2H), 3.76 – 3.70 (m, 2H), 3.63 (t, *J* = 9.2 Hz, 1H).

Compound 5:

(2R,4aR,7R,8S,8aR)-8-(benzyloxy)-2-phenyl-6-(((E)-prop-1-en-1-yl)oxy)hexahydropyrano[3,2-d][1,3]dioxin-7-yl benzoate



5

The vacuum-dried compound **4** (41 g, 132 mmol) was dissolved in a solution of DCM and pyridine (1:4), and the reaction was cooled down to 0°C, followed by the catalytic addition of DMAP. Then, at 0 °C, benzoyl chloride (1.4 ml, 12.39 mmol) was added slowly. The reaction

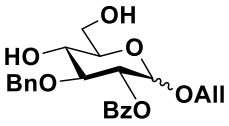
was kept for stirring for 1/2 h at 0 °C under the N_2 atmosphere and monitored using TLC. Reaction was completed and benzoyl chloride was quenched by MeOH at 0 °C, and evaporation of reaction mixture was done by the rotatory evaporator, followed by extraction using 10% HCl and $NaHCO_3$ solution. Na_2SO_4 was used to dry the organic layer, and product purification was done by column chromatography. Compound 5 was obtained with a **91%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 8.10 (dd, *J* = 5.1, 3.3 Hz, 2H), 7.60 – 7.56 (m, 1H), 7.49 (ddd, *J* = 7.8, 4.0, 1.7 Hz, 2H), 7.43 (d, *J* = 1.6 Hz, 1H), 7.41 – 7.34 (m, 5H), 7.32 – 7.25 (m, 3H), 5.98 – 5.87 (m, 1H), 5.56 (s, 1H), 5.36 – 5.28 (m, 1H), 5.22 (ddd, *J* = 10.4, 2.6, 1.4 Hz, 1H), 4.96 (dd, *J* = 7.9, 3.5 Hz, 2H), 4.81 (d, *J* = 11.6 Hz, 1H), 4.40 – 4.02 (m, 3H), 3.92 – 3.85 (m, 1H), 3.82 – 3.59 (m, 4H).

Compound 6:

(3R,5R,6R)-4-(benzyloxy)-5-hydroxy-6-(hydroxymethyl)-2-(((E)-prop-1-en-1-yl)oxy)tetrahydro-2H-pyran-3-yl benzoate



6

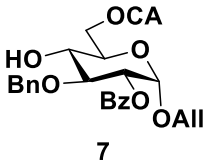
The vacuum-dried compound **5** (7 g, 13.9 mmol) was dissolved in a mixture of DCM and MeOH (2:1). Then PTSA (5.29 g, 27.88 mmol) was added at RT, and the reaction was kept for stirring at rt for 1 hr. The TLC was used to monitor the reaction. Reaction was completed and PTSA was quenched by NEt_3, which made the reaction mixture's pH acidic to a little basic. Then, evaporation of reaction mixture was done by the rotatory evaporator. Product purification was done by column chromatography. The pure product was obtained with an **85%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 8.09 – 8.02 (m, 2H), 7.61 – 7.56 (m, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.25 (dd, *J* = 5.8, 2.0 Hz, 2H), 7.23 – 7.17 (m, 3H), 5.86 – 5.76 (m, 1H), 5.29 – 5.22 (m, 1H), 5.18 (d, *J* = 3.7 Hz, 1H), 5.12 (dd, *J* = 10.4, 1.4 Hz, 1H), 5.07 (dd, *J* = 9.9, 3.7 Hz, 1H), 4.85 (d, *J* = 11.4 Hz, 1H), 4.76 – 4.72 (m, 1H), 4.18 (ddt, *J* = 13.3, 5.1, 1.5 Hz, 1H), 4.07 (dd, *J* = 7.4, 6.2 Hz, 1H), 3.99 (ddt, *J* = 13.3, 5.9, 1.3 Hz, 1H), 3.84 (d, *J* = 2.4 Hz, 2H), 3.81 – 3.75 (m, 2H).

Compound 7:

(2S,3R,4S,5R,6R)-4-(benzyloxy)-6-((2-chloroacetoxy)methyl)-5-hydroxy-2-(((E)-prop-1-en-1-yl)oxy)tetrahydro-2H-pyran-3-yl benzoate



7

The vacuum-dried compound **6** (4.1 g, 10.09 mmol) was dissolved in dry DCM and cooled to -45 ^{o}C. Then, at -45 ^{o}C, NEt_3 (1.7 ml, 12.11 mmol) and chloroacetic anhydride (2 g, 12.11 mmol) were added. The reaction was kept on stirring for 10 min under the N_2 atmosphere and monitored using TLC. Reaction was completed and it was quenched and extracted by 10% HCl solution. Product purification was done by column chromatography, and the pure product was obtained with a **65%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 8.11 – 8.06 (m, 2H), 7.64 – 7.58 (m, 1H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.27 – 7.24 (m, 5H), 5.89 – 5.78 (m, 1H), 5.31 – 5.24 (m, 1H), 5.20 – 5.13 (m, 2H), 5.09 (dd, *J* = 9.9, 3.7 Hz, 1H), 4.87 (d, *J* = 11.3 Hz, 1H), 4.73 (d, *J* = 11.4 Hz, 1H), 4.49 (qd, *J* = 11.9, 3.6 Hz, 2H), 4.19 (ddt, *J* = 13.2, 5.1, 1.4 Hz, 1H), 4.13 (s, 2H), 4.09 (t, *J* = 4.5 Hz, 1H), 4.06 – 3.94 (m, 2H), 3.64 (dd, *J* = 9.9, 9.0 Hz, 1H).

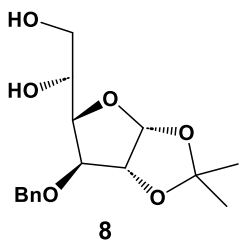
^{13}C NMR (101 MHz, $CDCl_3$)

δ 167.69 (s), 165.97 (s), 138.03 (s), 133.50 (d, *J* = 2.0 Hz), 129.89 (s), 128.67 (d, *J* = 3.3 Hz), 128.11 (d, *J* = 6.1 Hz), 117.88 (s), 95.59 (s), 79.70 (s), 75.49 (s), 73.75 (s), 70.11 (s), 69.40 (s), 68.73 (s), 64.83 (s), 40.84 (s).

5.2 Synthesis of Iduronic acid building block:

Compound 8:

(S)-1-((3aR,5S,6S,6aR)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)ethane-1,2-diol



8

The vacuum-dried compound **2** (59 g, 192.22 mmol) was taken, and 64% AcOH (230 ml) was added. The reaction was kept for reflux, using a reflux condenser for 12 h at 40 ^{o}C under the N_2 atmosphere and monitored using TLC. Reaction was completed and AcOH was quenched by slow addition of $NaHCO_3$, and then the reaction

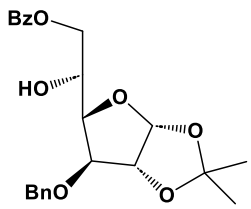
mixture was extracted by $NaHCO_3$ and brine. Na_2SO_4 was used to dry the organic layer, and evaporation of the organic layer was performed by the rotatory evaporator. Product purification was done by column chromatography. Compound 3 was obtained with an **85%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.39 – 7.28 (m, 15H), 5.93 (d, *J* = 3.8 Hz, 3H), 4.72 (d, *J* = 11.7 Hz, 3H), 4.62 (d, *J* = 3.8 Hz, 3H), 4.57 (d, *J* = 11.7 Hz, 3H), 4.14 – 4.09 (m, 6H), 4.05 – 4.00 (m, 3H), 3.80 (dd, *J* = 11.5, 3.4 Hz, 3H), 3.69 (dd, *J* = 11.5, 5.5 Hz, 3H), 2.04 (s, 1H), 1.48 (s, 9H), 1.31 (s, 9H).

Compound 9:

(S)-2-((3aR,5S,6S,6aR)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2,3 d][1,3]dioxol-5-yl)-2-hydroxyethyl benzoate



9

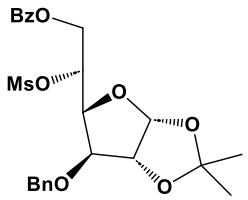
The vacuum-dried compound **8** (41 g, 132 mmol) was dissolved in DCM (100 ml). Then pyridine (10.692 ml, 79.1 mmol) was added, and the reaction was cooled down to 0 °C. BzCl (18.40 ml, 158 mmol) was added slowly by syringe at 0°C. The reaction was kept for stirring for 1/2 h at 0 °C under the N_2 atmosphere and monitored using TLC. Reaction was completed, and benzoyl chloride was quenched by MeOH at 0 °C. Then, evaporation of the reaction mixture was done by the rotatory evaporator and extracted by 10% HCl and $NaHCO_3$ solution. Na2SO4 was used to dry the organic layer, and product purification was done by column chromatography. Compound 4 was obtained with an **82%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 8.05 (dt, *J* = 3.2, 2.8 Hz, 2H), 7.58 – 7.52 (m, 1H), 7.45 – 7.28 (m, 7H), 5.97 (d, *J* = 3.7 Hz, 1H), 4.73 (d, *J* = 11.8 Hz, 1H), 4.67 – 4.57 (m, 3H), 4.44 (dd, *J* = 11.7, 6.0 Hz, 1H), 4.33 (ddd, *J* = 8.7, 6.0, 2.8 Hz, 1H), 4.25 (dd, *J* = 8.2, 3.2 Hz, 1H), 4.16 (d, *J* = 3.2 Hz, 1H), 1.48 (s, 3H), 1.33 (s, 3H).

Compound 10:

(S)-2-((3aR,5R,6S,6aR)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-2-((methylsulfonyl)oxy)ethyl benzoate



10

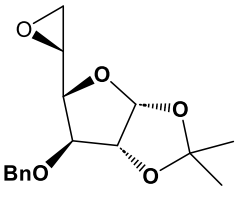
The vacuum-dried compound **9** (45 g, 108 mmol) was dissolved in pyridine. It was cooled to 0 ºC. Then MsCl (18.40 ml, 158 mmol) was added slowly by the dropping funnel at 0 ºC. The reaction was stirred for 12 h at 0 ºC under the N_2 atmosphere and monitored using TLC. Reaction was completed, and pyridine was quenched by the slow addition of MeOH at 0 ºC. Then, the pyridine was evaporated by the rotatory evaporator, followed by extraction using 10% HCl and brine. Na_2SO_4 was used to dry the organic layer, and product purification was done by column chromatography. Compound 10 was obtained with a **67%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 8.09 – 8.06 (m, 2H), 7.57 (ddd, *J* = 7.0, 2.5, 1.3 Hz, 1H), 7.47 – 7.29 (m, 7H), 5.92 (d, *J* = 3.6 Hz, 1H), 5.42 (ddd, *J* = 8.1, 6.2, 2.0 Hz, 1H), 4.92 (dd, *J* = 12.8, 2.0 Hz, 1H), 4.71 (d, *J* = 11.1 Hz, 1H), 4.64 – 4.60 (m, 2H), 4.53 – 4.46 (m, 2H), 4.15 (d, *J* = 3.1 Hz, 1H), 3.90 (s, 1H), 3.00 (s, 4H), 1.32 (s, 3H).

Compound 11:

(3aR,5S,6S,6aR)-6-(benzyloxy)-2,2-dimethyl-5-((R)-oxiran-2-yl)tetrahydrofuro[2,3-d][1,3]dioxole



11

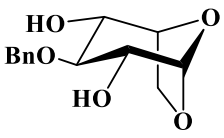
The vacuum-dried compound **10** (49.5 g, 100 mmol) was dissolved in a solution of DCM t-BuOH (1:1) and cooled to 0 ºC. Then, t-BuOK (24.82g, 158 mmol) was added at 0 ºC. The reaction was kept for stirring for 12 h at 0 ºC under the N_2 atmosphere and monitored using TLC. Reaction was completed, and t-BuOK was quenched by the addition of water, and the t-BuOH was evaporated by the rotatory evaporator. The reaction mixture was extracted by brine. Na_2SO_4 was used to dry the organic layer, and product purification was done by column chromatography. The pure compound was obtained with a **70%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.38 – 7.28 (m, 10H), 6.00 (d, *J* = 3.8 Hz, 2H), 4.74 (d, *J* = 12.2 Hz, 2H), 4.64 (d, *J* = 3.8 Hz, 2H), 4.52 (d, *J* = 12.2 Hz, 2H), 3.97 (d, *J* = 3.5 Hz, 2H), 3.81 (dd, *J* = 6.1, 3.5 Hz, 2H), 3.28 (ddd, *J* = 6.2, 4.3, 2.7 Hz, 2H), 2.77 (t, *J* = 4.6 Hz, 2H), 2.54 (dd, *J* = 4.9, 2.7 Hz, 2H), 1.66 (s, 1H), 1.45 (s, 6H), 1.32 (s, 6H).

Compound 12:

(1S,2R,3S,4R,5S)-3-(benzyloxy)-6,8-dioxabicyclo[3.2.1]octane-2,4-diol



12

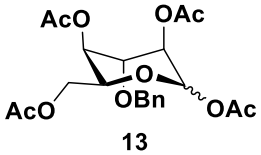
The vacuum-dried compound **11** (49.5 g, 100 mmol) was dissolved in dioxane, and 2N H_2SO_4 was added. The reaction was kept for reflux at 105 °C using the reflux condenser for 12 h under the N_2 atmosphere and monitored using TLC. Reaction was completed and 2N H_2SO_4 was quenched by the slow addition of 3N NaOH, and then the reaction mixture was extracted by brine. Na_2SO_4 was used to dry the organic layer and evaporation of organic layer was performed by the rotatory evaporator. Product purification was done by column chromatography. The pure compound was obtained with a **75%** yield.

^{1}H NMR (400 MHz, CDCL3)

δ 7.38 (d, *J* = 4.4 Hz, 4H), 7.34 – 7.29 (m, 1H), 5.29 (d, *J* = 1.7 Hz, 1H), 4.95 (d, *J* = 11.6 Hz, 1H), 4.74 (d, *J* = 11.6 Hz, 1H), 4.43 (t, *J* = 4.6 Hz, 1H), 4.03 (d, *J* = 7.9 Hz, 1H), 3.89 – 3.84 (m, 1H), 3.72 (dd, *J* = 7.7, 5.2 Hz, 1H), 3.68 – 3.62 (m, 1H), 3.39 (t, *J* = 7.9 Hz,1H), 2.22 (d, *J* = 3.2 Hz, 1H), 2.01 (d, *J* = 8.9 Hz, 1H).

Compound 13:

(3R,4S,5R,6S)-6-(acetoxymethyl)-4-(benzyloxy)tetrahydro-2H-pyran-2,3,5-triyl triacetate



13

The vacuum-dried compound **12** (600 mg, 0.5 mmol) was dissolved in acetic anhydride and cooled to 0 °C. Then, at 0 °C, the copper triflate (20 mg, 0.05 mmol) was added. The reaction was kept on stirring for 15 min and monitored using TLC. Reaction was completed, and the reaction mixture was quenched by slow addition of $NaHCO_3$ solution and extracted by $NaHCO_3$ solution. Na_2SO_4 was used to dry the organic layer

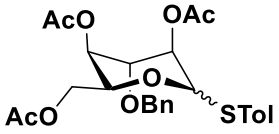
and evaporation of organic layer was performed by the rotatory evaporator. Product purification was done by column chromatography. The pure compound was obtained with an **86%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.52 (dd, *J* = 6.5, 3.0 Hz, 2H), 7.34 – 7.29 (m, 3H), 5.42 (d, *J* = 3.2 Hz, 2H), 5.24 (t, *J* = 10.0 Hz, 2H), 5.06 (dd, *J* = 9.9, 3.3 Hz, 1H), 4.75 – 4.70 (m, 1H), 4.16 (ddd, *J* = 17.5, 11.4, 6.6 Hz, 2H), 3.94 (dd, *J* = 12.0, 5.6 Hz, 1H), 2.12 (s, 3H), 2.09 (d, *J* = 5.1 Hz, 3H), 2.04 (s, 3H), 1.98 (s, 3H).

Compound 14:

(2S,3R,4S,5R)-2-(acetoxymethyl)-4-(benzyloxy)-6-(p-tolylthio)tetrahydro-2H-pyran-3,5-diyl diacetate

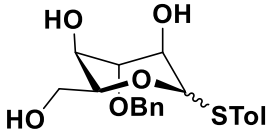


14

The vacuum-dried compound **13** (6 g, 13.69 mmol) was dissolved in dry DCM and cooled to 0 °C. Then P-thiocresol (3.4 g, 27.38 mmol) was added at 0 °C and $BF_3.OEt_2$ (17.49 g, 123 mmol) was added slowly by the dropping funnel at 0 °C. The reaction was kept on stirring for 72 h under the N_2 atmosphere and monitored using TLC. After the completion of the reaction $BF_3.OEt_2$ was quenched by slow addition of NaHCO3, and then the reaction mixture was extracted by $NaHCO_3$ and brine. Na_2SO_4 was used to dry the organic layer, and evaporation of organic layer was performed by the rotatory evaporator. The compound was dried using the high vacuum and proceeded to the next step.

Compound: 15

(2S,3R,4S,5R)-4-(benzyloxy)-2-(hydroxymethyl)-6-(p-tolylthio)tetrahydro-2H-pyran-3,5-diol



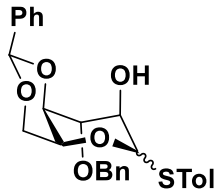
15

The vacuum-dried compound **19** (41 g, 93.8 mmol) was dissolved in MeOH (200 ml). Then, it was cooled down to 0°C. Then NaOMe (20.26 g, 375 mmol) was added slowly, and the reaction was kept on stirring at 0°C for 12 h under the N_2 atmosphere. The TLC was used to monitor the reaction. Reaction was completed and NaOMe was quenched by amberlite acidic resin to neutralise the solution. Then, the reaction mixture

was filtered and evaporated by the rotatory evaporator. Product purification was done by column chromatography. Pure compound was obtained with a **78%** yield.

Compound 16:

(2R,4aS,7R,8R,8aR)-8-(benzyloxy)-2-phenyl-6-(p-tolylthio)hexahydropyrano[3,2-d][1,3]dioxin-7-ol



16

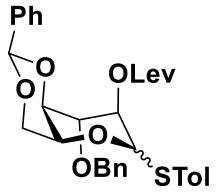
The vacuum-dried compound **20** (19.25 g, 61.90 mmol) was taken and dissolved in CH_3CN. Then PTSA (1.1 g, 6.19 mmol) and Benzilidine (10.22 ml, 68.09 mmol) were added at RT, and the reaction was kept for stirring at rt for 30 min. The TLC was used to monitor the reaction. Reaction was completed and PTSA was quenched by NEt_3, which made the reaction mixture's pH acidic to a little basic. Then, evaporation of reaction mixture was done by the rotatory evaporator. Product purification was done by column chromatography. The pure product was obtained with an **82%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.48 – 7.29 (m, 12H), 7.09 (d, *J* = 8.0 Hz, 2H), 5.56 (d, *J* = 32.0 Hz, 2H), 4.83 (d, *J* = 11.8 Hz, 1H), 4.59 (d, *J* = 11.8 Hz, 1H), 4.45 (s, 1H), 4.31 (dd, *J* = 12.6, 1.3 Hz, 1H), 4.13 – 4.07 (m, 3H), 3.84 – 3.78 (m, 2H), 2.31 (s, 3H).

Compound 17:

(2R,4aS,7R,8S,8aR)-8-(benzyloxy)-2-phenyl-6-(p-tolylthio)hexahydropyrano[3,2-d][1,3]dioxin-7-yl 4-oxopentanoate



17

The vacuum-dried compound **24** (266 mg, 0.5 mmol) was dissolved in DCM and cooled to 0 ºC. Then at 0 ºC, DCC (236 mg, 1.14 mmol) and DMAP (7 mg, 0.05 mmol) were added, followed by the slow addition of levulinic acid. The reaction was kept on stirring for 30 min and monitored by TLC. Reaction was completed and the reaction mixture was filtered by celite filtration to remove urea. Then, the product was evaporated by the rotatory evaporator and purification was done by column chromatography. The pure product was obtained with a **90%** yield.

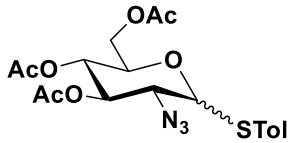
^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.51 (dd, *J* = 7.2, 2.3 Hz, 2H), 7.42 (dd, *J* = 7.8, 4.8 Hz, 3H), 7.40 – 7.37 (m, 2H), 7.36 (d, *J* = 1.6 Hz, 1H), 7.35 – 7.32 (m, 2H), 7.31 (dd, *J* = 4.2, 1.9 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 5.60 (s, 1H), 5.50 (s, 1H), 5.24 (d, *J* = 15.0 Hz, 2H), 4.89 (d, *J* = 11.8 Hz, 1H), 4.62 (d, *J* = 11.8 Hz, 1H), 4.41 (s, 1H), 4.28 (d, *J* = 12.7 Hz, 1H), 4.13 – 4.08 (m, 1H), 4.01 (s, 1H), 2.60 – 2.51 (m, 4H), 2.29 (s, 3H), 1.95 (s, 3H).

5.3 Synthesis of Glucosamine building block:

Compound 19:

(2R,3S,4R,5R)-2-(acetoxymethyl)-5-azido-6-(p-tolylthio)tetrahydro-2H-pyran-3,4-diyl diacetate

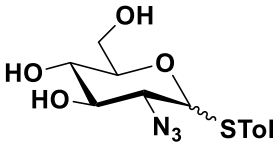


19

Commercially available compound **18** (35 g, 91.125 mmol each) was dissolved in dry DCM. Then P-thiocresol (28 g, 182.22 mmol each) was added at rt and cooled to 0 °C. Then, at 0 °C, the $BF_3.OEt_2$ (32.33 g, 227.81 mmol) was added slowly by the dropping funnel. The reaction was kept on stirring for 72 h under the N_2 atmosphere and monitored using TLC. Reaction was completed and $BF_3.OEt_2$ was quenched by slow addition of NaHCO3, and then, the reaction mixture was extracted by $NaHCO_3$ and brine. Na_2SO_4 was used to dry the organic layer and evaporation of organic layer was performed by the rotatory evaporator. The compound was dried using the high vacuum and proceeded to the next step.

Compound: 20

(2R,3S,4R,5R)-5-azido-2-(hydroxymethyl)-6-(p-tolylthio)tetrahydro-2H-pyran-3,4-diol



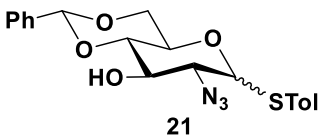
20

The vacuum-dried compound **19** (41 g, 93.8 mmol) was dissolved in MeOH (200 ml). Then, it was cooled down to 0°C. Then NaOMe (20.26 g, 375 mmol) was added slowly and the reaction was kept for stirring at 0°C for 12 h under the N_2 atmosphere. The TLC was used to monitor the reaction. Reaction was completed and NaOMe was quenched by amber lite acidic resin to neutralise the solution. Then, the reaction mixture

was filtered and evaporated by the rotatory evaporator. Product purification was done by column chromatography, and the pure compound was obtained with a **78%** yield.

Compound 21:

(2R,4aR,7R,8R,8aS)-7-azido-2-phenyl-6-(p-tolylthio)hexahydropyrano[3,2-d][1,3]dioxin-8-ol



21

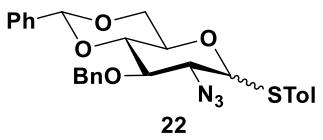
The vacuum-dried compound **20** (19.25 g, 61.90 mmol) was taken and dissolved in CH_3CN. Then PTSA (1.1 g, 6.19 mmol) and Benzilidine (10.22 ml, 68.09 mmol) were added at RT, and the reaction was kept for stirring at rt for 30 min. The TLC was used to monitor the reaction. Reaction was completed and PTSA was quenched by NEt_3, which made the reaction mixture's pH acidic to a little basic. Then, evaporation of reaction mixture was done by the rotatory evaporator. Product purification was done by column chromatography. The pure product was obtained with an **82%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.52 – 7.50 (m, 6H), 7.45 (t, *J* = 2.7 Hz, 5H), 7.39 (d, *J* = 1.5 Hz, 6H), 7.37 (dd, *J* = 6.7, 1.8 Hz, 13H), 7.15 (t, *J* = 9.1 Hz, 12H), 5.54 (s, 4H), 5.51 – 5.46 (m, 6H), 4.45 – 4.35 (m, 7H), 4.22 (dd, *J* = 10.3, 5.0 Hz, 4H), 4.03 (t, *J* = 9.5 Hz, 4H), 3.87 (dd, *J* = 10.0, 5.6 Hz, 4H), 3.73 (t, *J* = 10.3 Hz, 6H), 3.54 (t, *J* = 9.4 Hz, 4H), 3.45 – 3.38 (m, 4H), 2.98 (s, 6H), 2.34 (s, 12H), 1.65 (s, 3H).

Compound 22:

(2R,4aR,7R,8R,8aS)-7-azido-8-(benzyloxy)-2-phenyl-6-(p-tolylthio)hexahydropyrano[3,2-d][1,3]dioxine



22

The vacuum-dried compound **21** (15 g, 37.58 mmol) was dissolved in DMF and cooled to 0^{o}C. Then NaH (2.94 g, 122.57 mmol) was added at 0^{o}C. After some time, benzyl bromide (4.9 ml, 41.3 mmol) was added, and the reaction was kept on stirring at 0 C for 10 min under the N_2 atmosphere. The TLC was used to monitor the reaction. Reaction was completed and NaH was quenched by MeOH. Then, evaporation of reaction

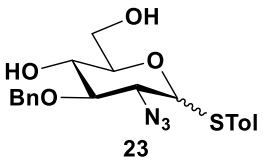
mixture was done by the rotatory evaporator. Product purification was done by column chromatography, and the pure compound was obtained with a **90%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.52 (dd, *J* = 7.2, 1.9 Hz, 2H), 7.43 – 7.38 (m, 7H), 7.37 – 7.28 (m, 3H), 7.15 (d, *J* = 8.1 Hz, 2H), 5.61 (s, 1H), 5.50 (d, *J* = 4.8 Hz, 1H), 4.99 (d, *J* = 10.9 Hz, 1H), 4.84 (d, *J* = 10.9 Hz, 1H), 4.46 (td, *J* = 9.9, 4.9 Hz, 1H), 4.24 (dd, *J* = 10.4, 4.9 Hz, 1H), 4.02 – 3.93 (m, 2H), 3.81 – 3.73 (m, 2H), 2.35 (s, 3H).

Compound 23:

(2R,3S,4R,5R)-5-azido-4-(benzyloxy)-2-(hydroxymethyl)-6-(p-tolylthio)tetrahydro-2H-pyran-3-ol



23

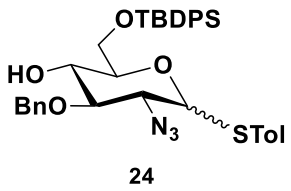
The vacuum-dried compound **22** (8 g, 15.6 mmol) was dissolved in a mixture of DCM and MeOH (2:1). Then PTSA (5.9 g, 31.36 mmol) was added at RT, and the reaction was kept for stirring at rt for 1 hr. The TLC was used to monitor the reaction. Reaction was completed and PTSA was quenched by NEt_3, which made the reaction mixture's pH acidic to a little basic. Then, evaporation of reaction mixture was done by the rotatory evaporator. Product purification was done by column chromatography. The pure product was obtained with an **82%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.37 (dd, *J* = 6.1, 4.5 Hz, 2H), 7.32 (dd, *J* = 4.8, 2.0 Hz, 3H), 7.29 – 7.25 (m, 1H), 7.07 (d, *J* = 8.1 Hz, 3H), 5.36 (d, *J* = 5.4 Hz, 1H), 4.89 – 4.80 (m, 2H), 4.15 – 4.10 (m, 1H), 3.80 – 3.72 (m, 2H), 3.69 – 3.60 (m, 4H), 3.28 – 3.15 (m, 1H), 2.85 (t, *J* = 6.0 Hz, 1H), 2.28 (s, 4H).

Compound 24:

(2R,3S,4R,5R)-5-azido-4-(benzyloxy)-2-(((tert-butyldiphenylsilyl)oxy)methyl)-6-(p-tolylthio)tetrahydro-2H-pyran-3-ol



24

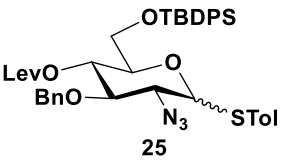
The vacuum-dried compound **22** (2.9 g, 7.3 mmol) was dissolved in dry DCM and cooled to 0 ºC. Then, at 0 oC NEt3 (3 ml, 22 mmol), Imidazole (998 mg, 14.67 mmol) and DMAP (448 mg, 3.6 mmol) were added, followed by slow addition of TBDPSCl (2.2 ml, 8.8 mmol). The reaction was kept for stirring at 0 ºC under an N_2 atmosphere for 12 h. The TLC was used to monitor the reaction. Reaction was completed and the reaction mixture was extracted by brine. Product purification was done by column chromatography. The pure product was obtained with a **76%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.72 – 7.66 (m, 4H), 7.47 – 7.33 (m, 13H), 7.05 (d, *J* = 8.0 Hz, 2H), 5.48 (d, *J* = 5.4 Hz, 1H), 4.92 (q, *J* = 11.0 Hz, 2H), 4.31 – 4.25 (m, 1H), 3.86 (dddd, *J* = 18.2, 12.0, 10.2, 3.5 Hz, 4H), 3.70 (dd, *J* = 10.1, 8.7 Hz, 1H), 2.65 (d, *J* = 2.8 Hz, 1H), 2.32 (s, 3H), 1.08 (s, 9H).

Compound 25:

(2R,3S,4R,5R)-5-azido-4-(benzyloxy)-2-(((tert-butyldiphenylsilyl)oxy)methyl)-6-(p-tolylthio)tetrahydro-2H-pyran-3-yl 4-oxopentanoate



25

The vacuum-dried compound 24 was dissolved in DCM and cooled to 0 ºC. Then, at 0 C, DCC and DMAP were added, followed by the slow addition of levulinic acid. The reaction was kept on stirring for 30 min and monitored by TLC. Reaction was completed and the reaction mixture was filtered by celite filtration to remove urea. Then, product was evaporated by the rotatory evaporator and purification was done by column chromatography. The pure product was obtained with a **90%** yield.

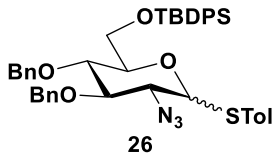
^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.73 – 7.68 (m, 4H), 7.48 – 7.32 (m, 13H), 7.07 (d, *J* = 8.2 Hz, 2H), 5.60 (d, *J* = 5.4 Hz, 1H), 5.23 (t, *J* = 9.6 Hz, 1H), 4.88 (d, *J* = 11.1 Hz, 1H), 4.73 (d, *J* = 11.1 Hz, 1H),

4.47 – 4.40 (m, 1H), 3.99 (dd, *J* = 10.3, 5.4 Hz, 1H), 3.89 – 3.69 (m, 3H), 2.61 (t, *J* = 6.7 Hz, 2H), 2.38 (dd, *J* = 10.3, 4.1 Hz, 2H), 2.34 (s, 3H), 2.16 (s, 3H), 1.08 (s, 9H).

Compound 26:

(((2R,3S,4R,5R)-5-azido-3,4-bis(benzyloxy)-6-(p-tolylthio)tetrahydro-2H-pyran-2-yl)methoxy)(tert-butyl)diphenyl silane



26

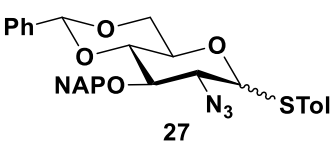
The vacuum-dried compound **21** (15 g, 37.58 mmol) was dissolved in DMF and cooled to 0°C. Then NaH (2.94 g, 122.57 mmol) was added at 0°C. After some time, benzyl bromide (4.9 ml, 41.3 mmol) was added, and the reaction was kept on stirring at 0 °C for 10 min under the N_2 atmosphere. The TLC was used to monitor the reaction, and reaction was completed and NaH was quenched by MeOH. Then, evaporation of reaction mixture was done by the rotatory evaporator. Product purification was done by column chromatography. Pure compound was obtained with a **60%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.80 (dd, *J* = 7.9, 1.5 Hz, 3H), 7.72 – 7.68 (m, 7H), 7.67 – 7.64 (m, 14H), 7.43 – 7.38 (m, 26H), 7.35 – 7.32 (m, 25H), 7.30 – 7.28 (m, 19H), 7.21 (dd, *J* = 6.6, 2.5 Hz, 7H), 7.05 – 7.02 (m, 9H), 5.56 (d, *J* = 5.3 Hz, 4H), 4.91 (t, *J* = 5.4 Hz, 12H), 4.87 – 4.84 (m, 5H), 4.72 (dd, *J* = 20.6, 10.8 Hz, 6H), 4.27 (d, *J* = 7.7 Hz, 4H), 4.03 – 3.88 (m, 12H), 3.87 – 3.82 (m, 12H), 2.31 (s, 16H), 1.05 (d, *J* = 6.3 Hz, 37H).

Compound 27:

(2R,4aR,7R,8R,8aS)-7-azido-8-(naphthalen-2-ylmethoxy)-2-phenyl-6-(p-tolylthio)hexahydropyrano[3,2-d][1,3]dioxine



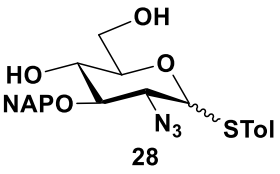
27

The vacuum-dried compound **21** (5.2 g, 13.02 mmol) was dissolved in DMF and cooled to 0°C. Then NaH (625 mg, 399.13 mmol) was added at 0°C. After some time, naphthyl bromide (3.456 g, 15.63 mmol) was added and the reaction was kept on stirring at 0°C for 10 min under the N_2 atmosphere. The TLC was used to monitor the reaction. Reaction was completed and NaH was quenched by MeOH. Then, evaporation of

reaction mixture was done by the rotatory evaporator. Product purification was done by column chromatography. Pure compound was obtained with a **90%** yield.

Compound 28:

(2R,3S,4R,5R)-5-azido-2-(hydroxymethyl)-4-(naphthalen-2-ylmethoxy)-6-(p-tolylthio)tetrahydro-2H-pyran-3-ol

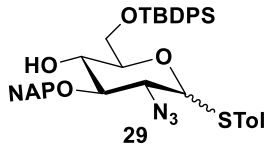


28

The vacuum-dried compound **27** (13 g, 24.256 mmol) was dissolved in a mixture of DCM and MeOH (2:1). Then CSA (11.26 g, 48.512 mmol) was added at RT, and the reaction was kept for stirring at rt for 1 hr. The TLC was used to monitor the reaction. Reaction was completed and CSA was quenched by NEt_3, which made the reaction mixture's pH acidic to a little basic. Then, evaporation of reaction mixture was done by the rotatory evaporator. Product purification was done by column chromatography. The pure product was obtained with an **82%** yield.

Compound 29:

(2R,3S,4R,5R)-5-azido-2-(((tert-butyldiphenylsilyl)oxy)methyl)-4-(naphthalen-2-ylmethoxy)-6-(p-tolylthio)tetrahydro-2H-pyran-3-ol



29

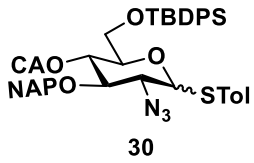
The vacuum-dried compound **28** (10.87 g, 24.109 mmol) was dissolved in dry DCM and cooled to 0 °C. Then, at 0 °C NEt_3 (10.16 ml, 72.329 mmol), Imidazole (6.56 g, 96.43 mmol) and DMAP (1.47 g, 12.05 mmol) were added, followed by slow addition of TBDPSCl (7.5 ml, 28.931 mmol). The reaction was kept on stirring at 0 °C under the N_2 atmosphere for 12 h and monitored by TLC. Reaction was completed and the reaction mixture was extracted by brine, and product purification was done by column chromatography. The pure product was obtained with an **83%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.82 (ddd, *J* = 9.4, 7.6, 3.6 Hz, 36H), 7.74 – 7.64 (m, 55H), 7.54 – 7.44 (m, 29H), 7.36 – 7.31 (m, 52H), 7.02 (t, *J* = 8.5 Hz, 15H), 5.45 (d, *J* = 5.3 Hz, 4H), 5.04 (t, *J* = 3.8 Hz, 8H), 4.37 – 4.24 (m, 8H), 3.92 (t, *J* = 3.9 Hz, 7H), 3.73 (ddd, *J* = 18.3, 13.8, 9.2 Hz, 12H), 2.27 (s, 13H), 1.05 (s, 37H).

Compound 30:

(2R,3S,5R)-5-azido-2-(((tert-butyldiphenylsilyl)oxy)methyl)-4-(naphthalen-2-ylmethyl)-6-(p-tolylthio)tetrahydro-2H-pyran-3-yl 2-chloroacetate

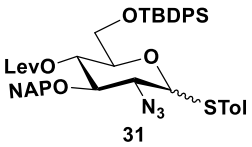


30

The vacuum-dried compound **29** () was dissolved in the solution DCM and pyridine (4:1) and cooled to 0 °C. Then, at 0 °C, NEt_3 was added, followed by the slow addition of chloroacetic anhydride. The reaction was kept on stirring under the N_2 atmosphere for 15 min and monitored by TLC. Reaction was completed and the reaction mixture was quenched and extracted by 10% HCl solution, and product purification was done by column chromatography. The pure product was obtained with a **90%** yield.

Compound 31:

1-((2S,3S,5R)-5-azido-2-(((tert-butyldiphenylsilyl)oxy)methyl)-4-(naphthalen-2-ylmethoxy)-6-(p-tolylthio)tetrahydro-2H-pyran-3-yl)pentane-1,4-dione



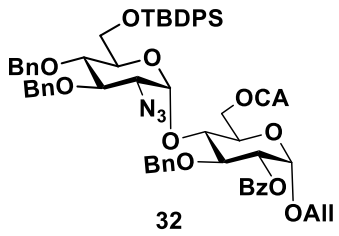
31

The vacuum-dried compound 29 (12.137 g, 17.607 mmol) was dissolved in DCM and cooled to 0 °C. Then at 0 °C, DCC (7.262 g, 35.215 mmol) and DMAP (215 mg, 122.17 mmol) were added, followed by the slow addition of levulinic acid. The reaction was kept on stirring for 30 min and monitored by TLC. The reaction was completed, and the reaction mixture was filtered by celite filtration to remove urea. Then, the product was evaporated by the rotatory evaporator and purification was done by column chromatography. The pure product was obtained with a **90%** yield.

5.4 Synthesis of Di-saccharide building block:

Compound 32:

(2S,3R,4S,5R,6R)-2-(allyloxy)-5-(((2R,3R,5S,6R)-3-azido-4,5-bis(benzyloxy)-6-(((tert-butyldiphenylsilyl)oxy)methyl)tetrahydro-2H-pyran-2-yl)oxy)-4-(benzyloxy)-6-((2-chloroacetoxy)methyl)tetrahydro-2H-pyran-3-yl benzoate



32

Compound **26** (3.6 g, 4.9 mmol) and Compound **7** (1.93 g, 3.9 mmol) were dissolved in dry DCM, and freshly dried 4 Å molecular sieves were added under anhydrous conditions. After stirring for 1 hr at RT, the reaction mixture was cooled to -78 ^{o}C. Then, at -78 ^{o}C, TMSOTf (178 µL, 0.9 mmol) was added, and the reaction was monitored using TLC. After the completion of the reaction, the reaction mixture was quenched with triethylamine, and the molecular sieve was filtered using celite filtration, followed by the extraction using $NaHCO_3$. Na_2SO_4 was used to dry the organic layer and evaporated by the rotatory evaporator. Product purification was done by column chromatography, and the pure compound was obtained with a **60%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

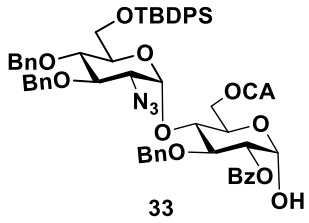
δ 7.96 (d, *J* = 8.0 Hz, 2H), 7.54 (td, *J* = 6.6, 1.1 Hz, 4H), 7.48 – 7.43 (m, 1H), 7.36 – 7.27 (m, 6H), 7.24 – 7.17 (m, 10H), 7.10 (s, 7H), 5.76 – 5.63 (m, 1H), 5.48 (d, *J* = 3.4 Hz, 1H), 5.19 – 5.12 (m, 1H), 5.06 – 4.99 (m, 3H), 4.80 (ddd, *J* = 13.3, 10.6, 2.7 Hz, 5H), 4.64 (d, *J* = 10.5 Hz, 1H), 4.37 (d, *J* = 11.9 Hz, 1H), 4.22 (dd, *J* = 12.7, 5.4 Hz, 1H), 4.14 – 4.01 (m, 2H), 3.90 – 3.82 (m, 4H), 3.79 – 3.71 (m, 2H), 3.65 (dd, *J* = 18.9, 6.5 Hz, 2H), 3.58 – 3.48 (m, 2H), 3.22 (dd, *J* = 7.2, 2.4 Hz, 1H), 0.93 (d, *J* = 1.9 Hz, 9H).

^{13}C NMR (101 MHz, $CDCl_3$)

δ 166.99, 165.88, 138.03, 136.33 – 135.77, 135.72, 133.48, 133.00, 129.87, 129.57, 128.80 – 127.46, 117.89, 98.20, 95.19, 92.22, 80.24, 78.33, 78.03, 77.48, 77.16, 76.84, 75.77, 75.28, 75.03, 74.29, 73.09, 68.72, 68.19, 64.62, 63.56, 62.59, 62.18, 53.54, 40.56, 29.80, 27.00, 19.43.

Compound 33:

(2S,3R,4S,5R,6R)-5-(((2R,3R,4R,5S,6R)-3-azido-4,5-bis(benzyloxy)-6-(((tert-butyldiphenylsilyl)oxy)methyl)tetrahydro-2H-pyran-2-yl)oxy)-4-(benzyloxy)-6-((2-chloroacetoxy)methyl)-2-hydroxytetrahydro-2H-pyran-3-yl benzoate



33

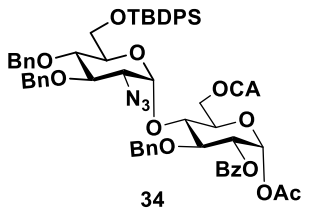
The vacuum-dried compound **32** (1.4 g, 1.2 mmol) was dissolved in a solution of MeOH and DCM (3:1). Then, at RT, $PdCl_2$ (45 mg, 0.2 mmol) was added with the catalytic amount of acetic acid into the reaction mixture and the reaction mixture was kept on stirring for 5 h. After the completion of the reaction, the palladium chloride was filtered using celite filtration, followed by evaporation using the rotatory evaporator. Product purification was done by column chromatography, and the pure compound was obtained with a **65%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 8.05 (dd, *J* = 10.9, 4.7 Hz, 2H), 7.68 – 7.62 (m, 4H), 7.54 (t, *J* = 6.9 Hz, 1H), 7.40 (dd, *J* = 12.1, 4.2 Hz, 6H), 7.34 – 7.29 (m, 7H), 7.18 (dd, *J* = 18.0, 5.2 Hz, 9H), 7.02 (d, *J* = 7.9 Hz, 1H), 5.59 (s, 1H), 5.43 (d, *J* = 3.4 Hz, 1H), 5.24 (s, 1H), 5.11 (dd, *J* = 9.7, 3.1 Hz, 1H), 4.95 – 4.87 (m, 4H), 4.77 (d, *J* = 10.1 Hz, 1H), 4.50 (d, *J* = 11.3 Hz, 1H), 4.36 (t, *J* = 9.1 Hz, 1H), 4.17 (t, *J* = 9.8 Hz, 2H), 4.03 – 3.92 (m, 2H), 3.89 – 3.83 (m, 2H), 3.78 – 3.71 (m, 2H), 3.65 – 3.59 (m, 1H), 3.37 – 3.30 (m, 1H), 2.27 (s, 2H), 1.04 (s, 9H).

Compound 34:

(2R,3R,4S,5R,6R)-2-acetoxy-5-(((1R,2R,4R,5R,6R)-5-azido-7,8-dibenzyl-2-(((tert-butyldiphenylsilyl)oxy)methyl)-3,7l4,8l4-trioxabicyclo[4.2.0]oct-7-en-4-yl)oxy)-4-(benzyloxy)-6-((2-chloroacetoxy)methyl)tetrahydro-2H-pyran-3-yl benzoate



34

The vacuum-dried compound **33** (600 mg, 0.5 mmol) was dissolved in acetic anhydride and cooled to 0 °C. Then, at 0 °C, the copper triflate (20 mg, 0.05 mmol) was added. The reaction was kept on stirring for 15 min and monitored using TLC. Reaction was completed and the reaction mixture was quenched by slow addition of $NaHCO_3$ solution and extracted by $NaHCO_3$ solution. Na_2SO_4 was used to dry the organic layer and evaporation of the organic layer was done by the rotatory evaporator.

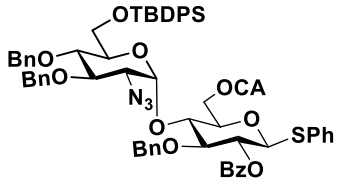
Product purification was done by column chromatography. The pure compound was obtained with an **80%** yield.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 8.05 – 7.98 (m, 2H), 7.65 (ddd, *J* = 5.9, 3.8, 1.4 Hz, 5H), 7.58 (dd, *J* = 8.3, 6.5 Hz, 1H), 7.42 (ddd, *J* = 12.8, 9.4, 4.1 Hz, 7H), 7.37 – 7.29 (m, 11H), 7.22 – 7.20 (m, 4H), 6.37 (t, *J* = 4.2 Hz, 1H), 5.58 (d, *J* = 3.9 Hz, 1H), 5.35 – 5.30 (m, 1H), 4.97 – 4.90 (m, 2H), 4.85 (ddd, *J* = 21.9, 12.7, 4.5 Hz, 4H), 4.78 – 4.72 (m, 1H), 4.48 – 4.43 (m, 1H), 4.31 – 4.25 (m, 1H), 4.23 – 4.17 (m, 1H), 4.07 – 3.98 (m, 2H), 3.97 – 3.94 (m, 1H), 3.93 – 3.89 (m, 1H), 3.86 (d, *J* = 9.8 Hz, 1H), 3.82 – 3.77 (m, 1H), 3.73 (d, *J* = 12.4 Hz, 1H), 3.66 (d, *J* = 15.1 Hz, 1H), 3.59 (d, *J* = 9.4 Hz, 1H), 3.35 (dd, *J* = 10.2, 4.0 Hz, 1H), 2.14 (s, 2H), 1.04 (s, 9H).

Compound 35:

(2S,3R,4S,5R,6R)-5-(((2R,3R,4R,5S,6R)-3-azido-4,5-bis(benzyloxy)-6-(((tert-butyldiphenylsilyl)oxy)methyl)tetrahydro-2H-pyran-2-yl)oxy)-4-(benzyloxy)-6-((2-chloroacetoxy)methyl)-2-(phenylthio)tetrahydro-2H-pyran-3-yl benzoate



35

The vacuum-dried compound **34** (366 mg, 0.3 mmol) was mixed with ZnI_2 (223 mg, 0.7 mmol), and the mixture was dried under high vacuum pressure for 2 h. Then, after 2 hr under the N_2 atmosphere, DCM and TMSSPh (10 ml, 52.8 mmol) were added to the reaction mixture. The reaction was kept for stirring at rt for 12 h and monitored using TLC. Reaction was completed and ZnI_2 was filtered by celite bed. The reaction mixture was extracted by the brine water solution and evaporated by the rotatory evaporator. Product purification was done by column chromatography, and the pure compound was obtained with a **90%** yield.

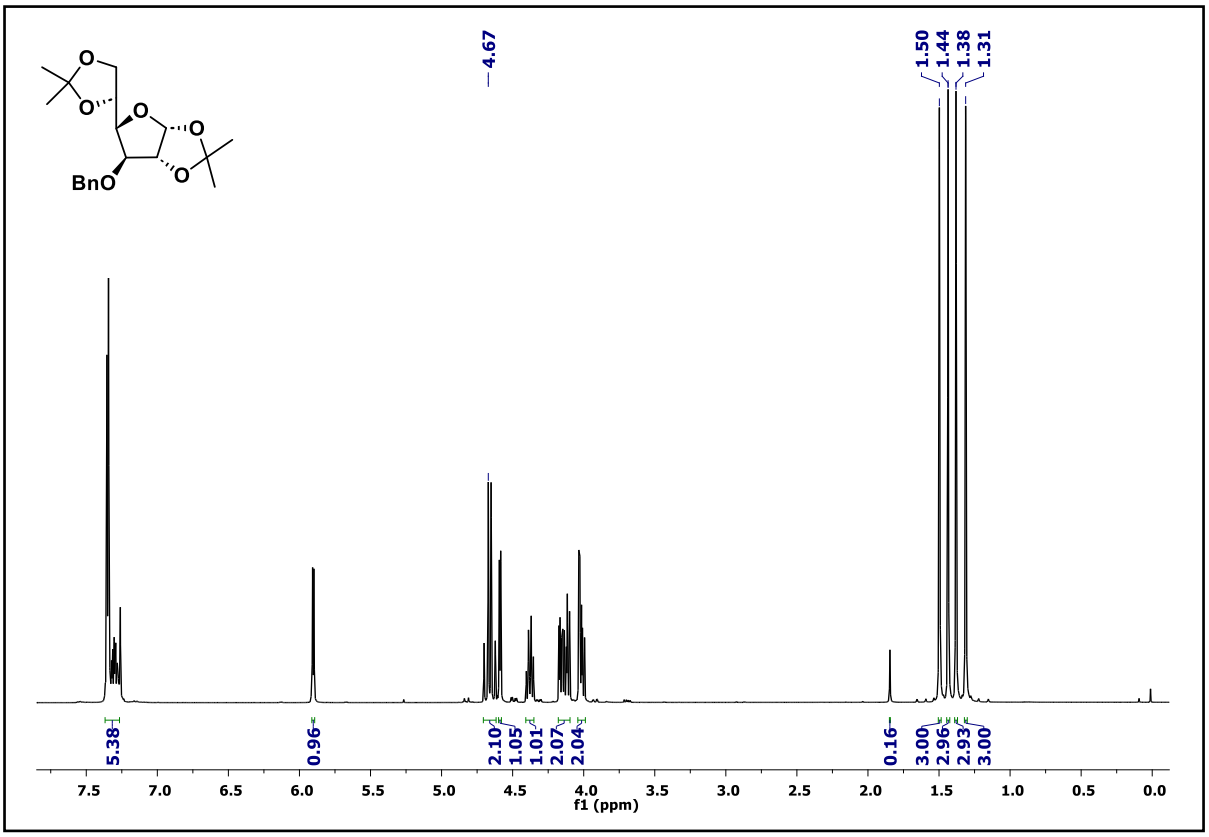
^{1}H NMR (400 MHz, $CDCl_3$)

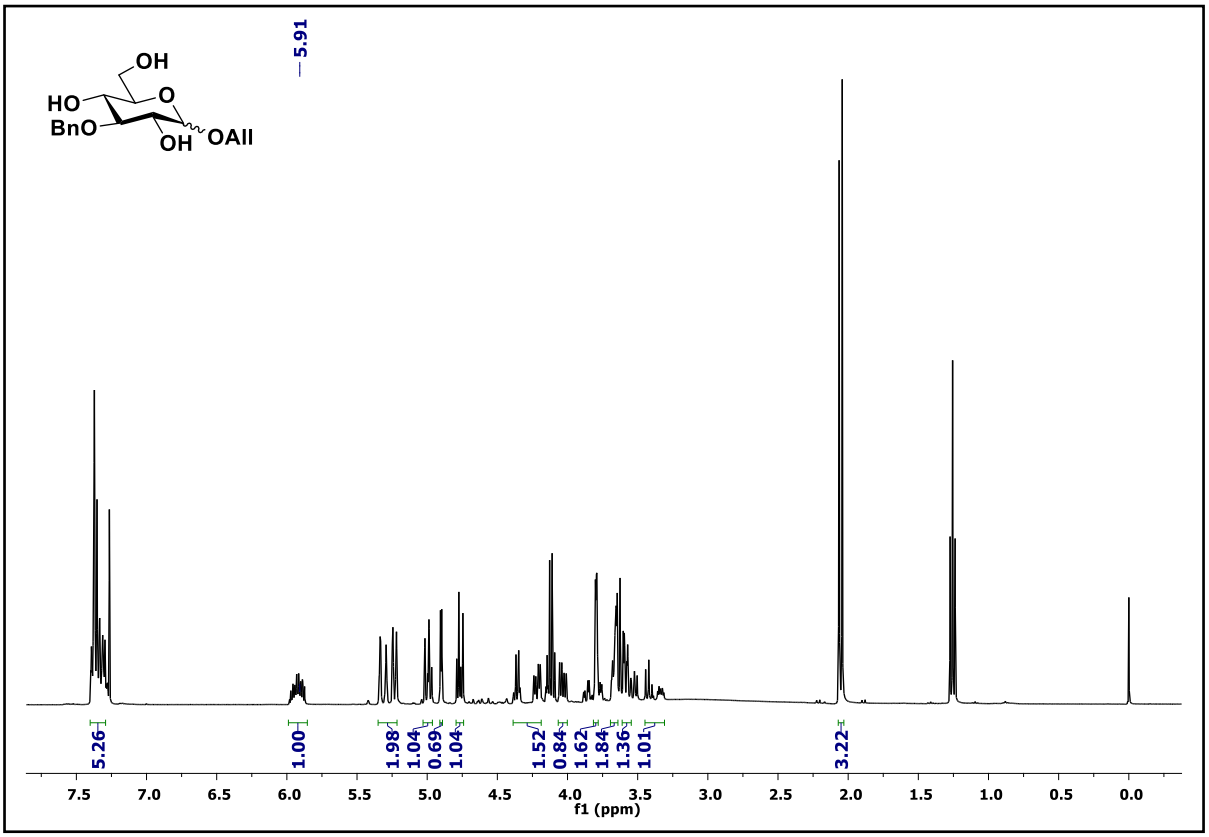
δ 8.10 (d, *J* = 7.8 Hz, 2H), 7.64 (d, *J* = 7.0 Hz, 4H), 7.49 – 7.37 (m, 10H), 7.35 – 7.26 (m, 13H), 7.23 – 7.17 (m, 6H), 5.52 (d, *J* = 3.6 Hz, 1H), 5.31 (t, *J* = 9.2 Hz, 1H), 4.90 (dd, *J* = 18.2, 7.5 Hz, 2H), 4.86 – 4.79 (m, 3H), 4.74 (dd, *J* = 23.1, 12.0 Hz, 2H), 4.58 (d, *J* = 11.8 Hz, 1H), 4.18 (dd, *J* = 11.7, 4.8 Hz, 1H), 4.04 – 3.89 (m, 3H), 3.83 (dd, *J* = 17.6, 8.9 Hz, 3H), 3.76 (s, 1H), 3.69 (dd, *J* = 21.0, 8.1 Hz, 2H), 3.59 (d, *J* = 9.2 Hz, 1H), 3.29 (dd, *J* = 10.0, 3.5 Hz, 1H), 1.04 (s, 9H).

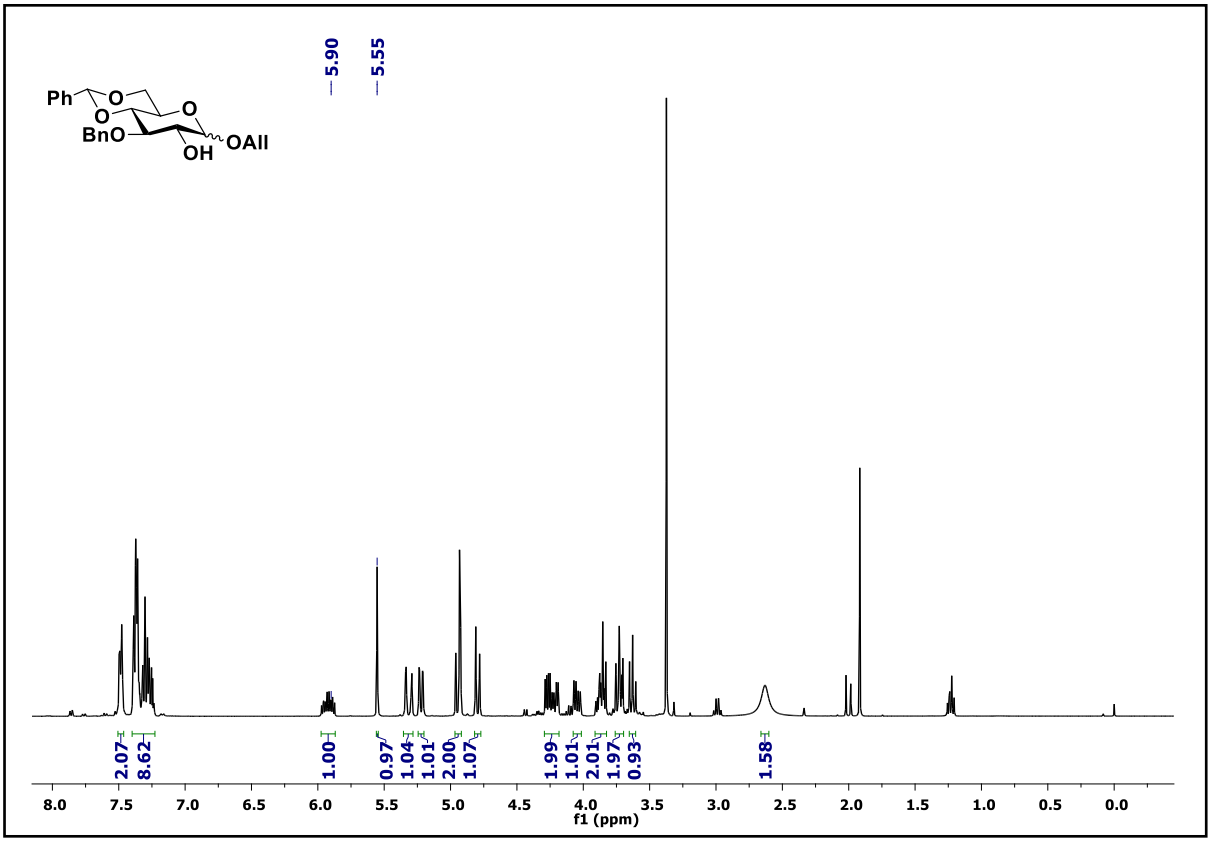
^{13}C NMR (101 MHz, $CDCl_3$)

δ 166.79, 165.23, 137.79, 137.35, 135.94, 135.67, 133.96 – 133.64, 133.64 – 133.15, 132.87, 131.95, 130.25 – 129.83, 129.62, 128.87, 128.79 – 127.45, 98.06, 85.78, 84.58, 79.93, 77.92, 77.42, 77.10, 76.78, 76.29, 75.67, 75.26, 74.77, 73.75, 73.12, 72.63, 64.57, 63.34, 62.07, 40.52, 26.95, 19.36.

6. SPECTRAL DATA




OH
HO
O
BnO
OH
OAll
5.91
5.26
1.00
1.98
1.04
0.69
1.04
1.52
0.84
1.62
1.84
1.36
1.01
3.22
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)


Ph
O
O
O
BnO
OH
OAll
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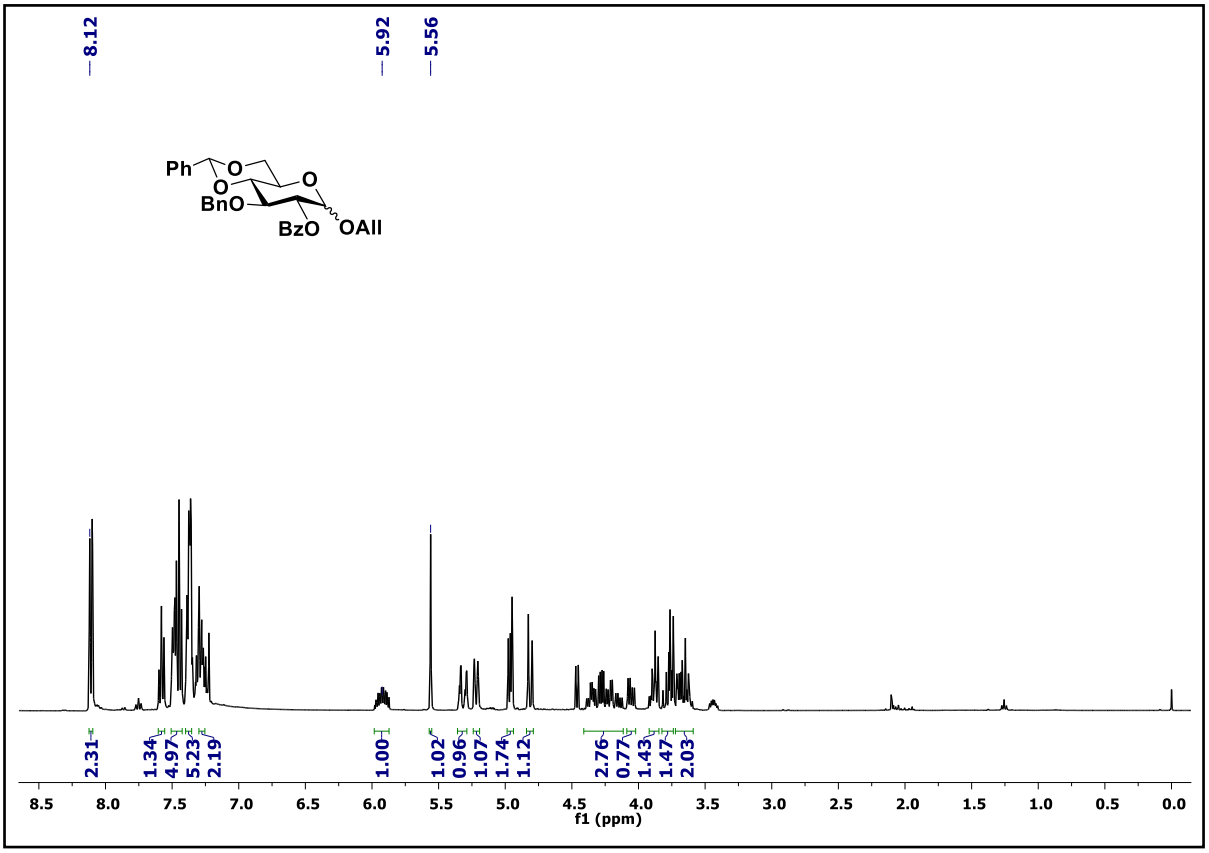
2.07
8.62
1.00
0.97
1.04
1.01
2.00
1.07
1.99
1.01
2.01
1.97
0.93
1.58
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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5.92
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Ph
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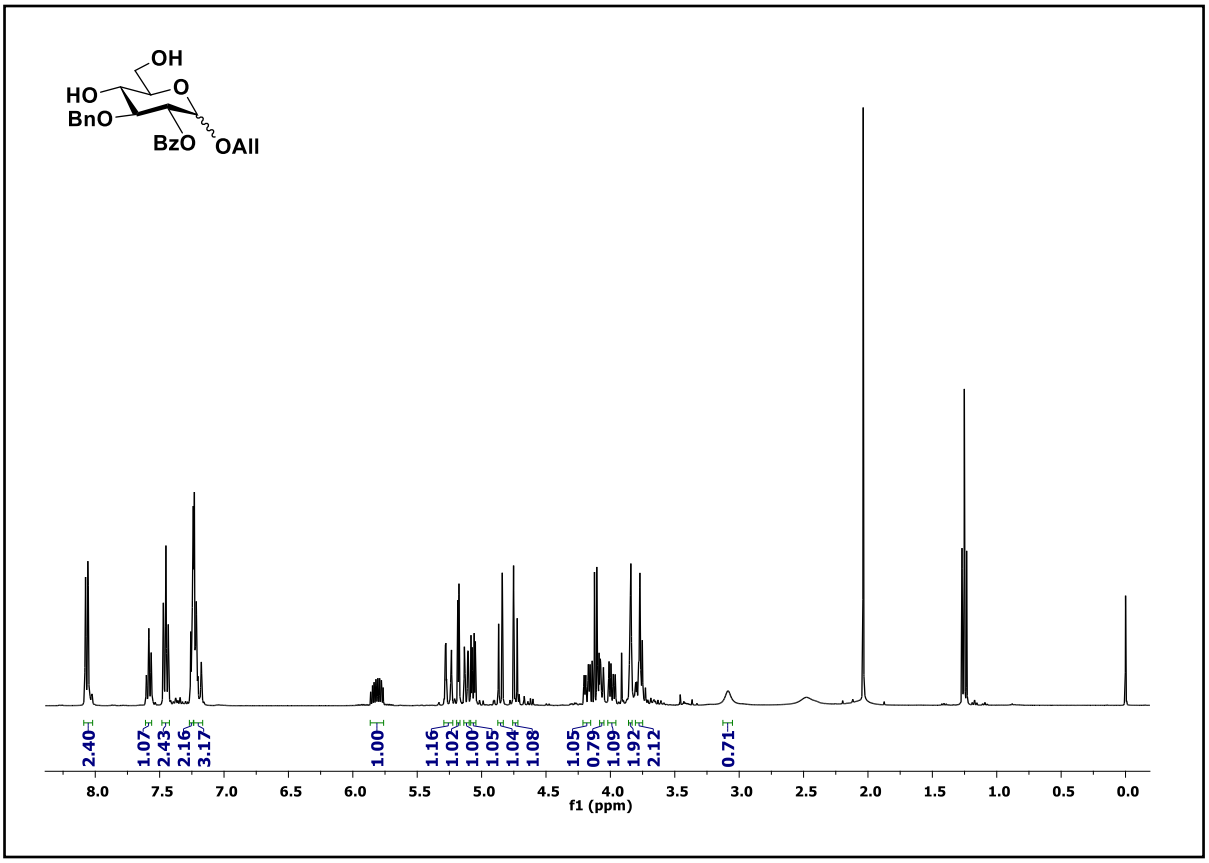
O
O
BnO
BzO
OAll
2.31
1.34
4.97
5.23
2.19
1.00
1.02
0.96
1.07
1.74
1.12
2.76
0.77
1.43
1.47
2.03
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


OH
HO
O
BnO
BzO
OAll
2.40
1.07
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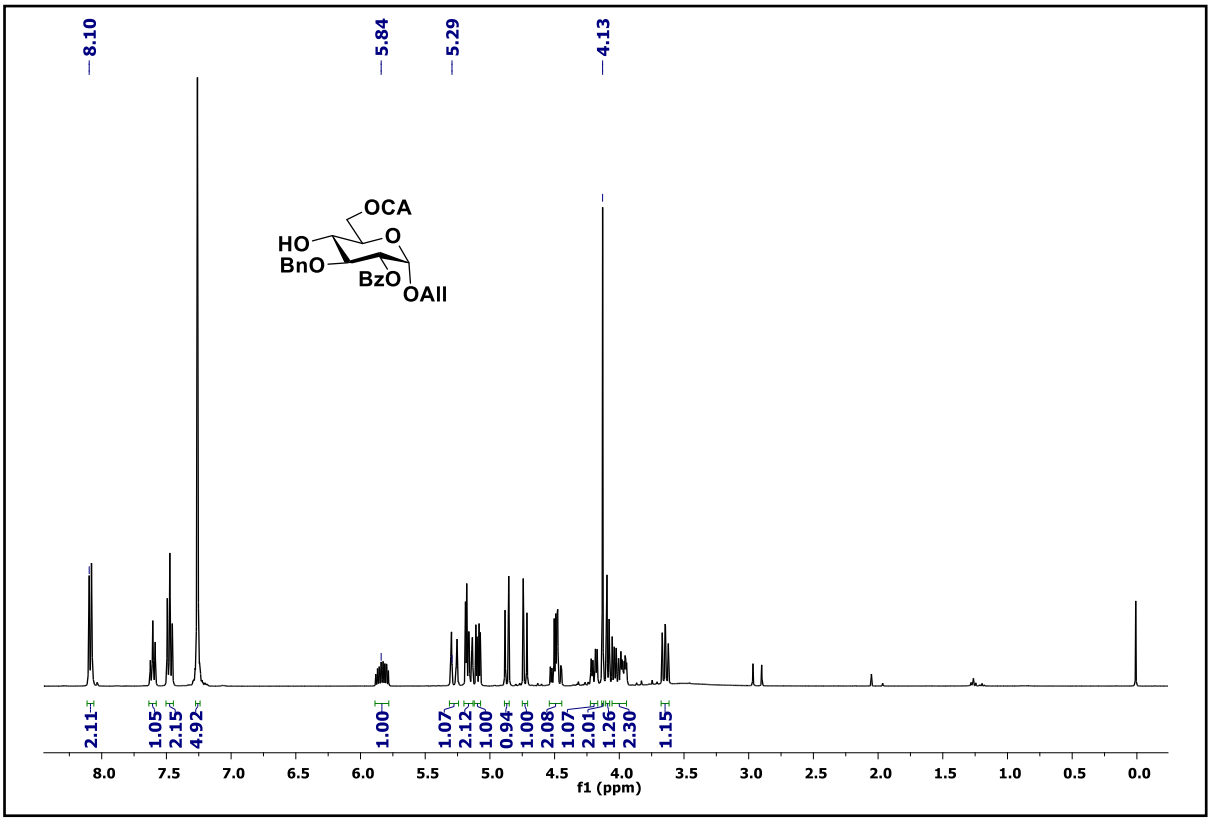
2.16
3.17
1.00
1.16
1.02
1.00
1.05
1.04
1.08
1.05
0.79
1.09
1.92
2.12
0.71
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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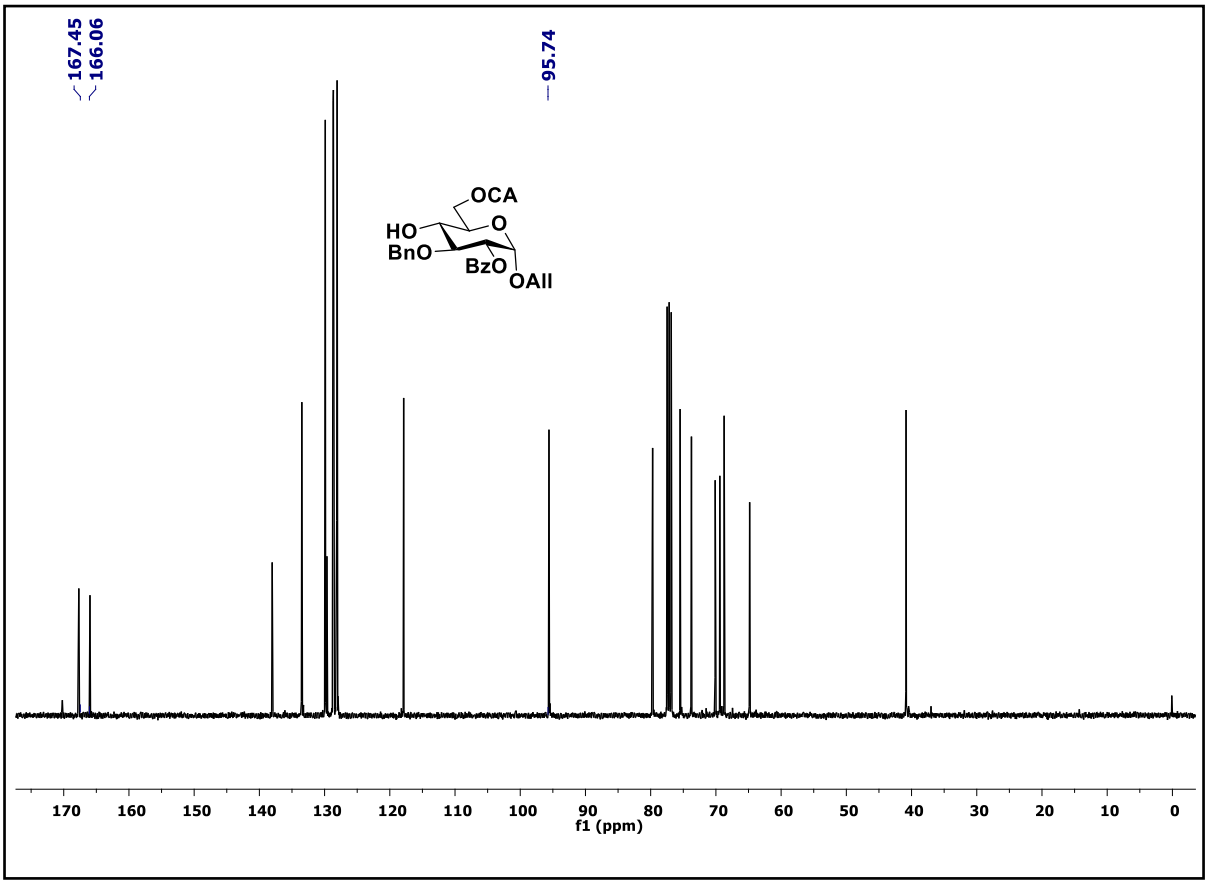
5.84
5.29
4.13
OCA
O
HO
BnO
BzO
OAll
2.11
1.05
2.15
4.92
1.00
1.07
2.12
1.00
0.94
1.00
2.08
1.07
2.01
1.26
2.30
1.15
f1 (ppm)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166.06
95.74
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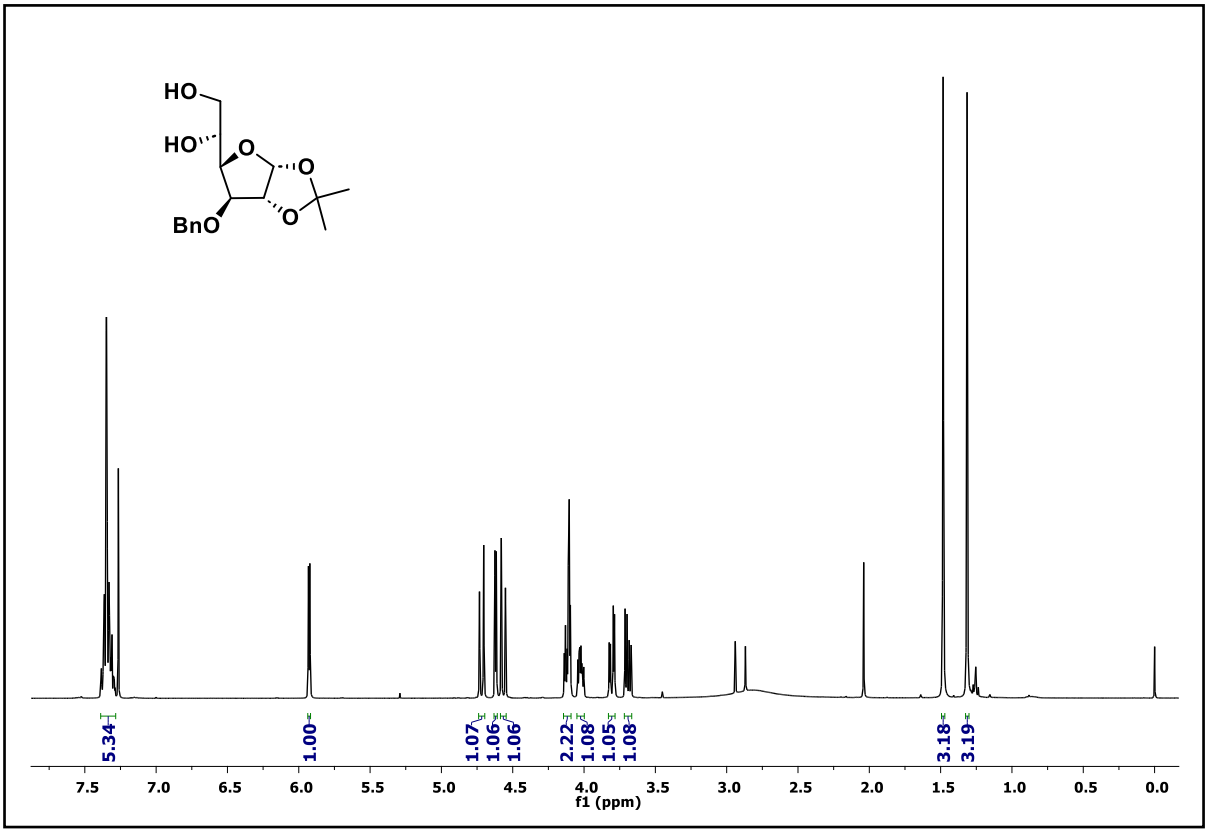
O
HO
BnO
BzO
OAll
f1 (ppm)


HO
HO
O
O
O
BnO
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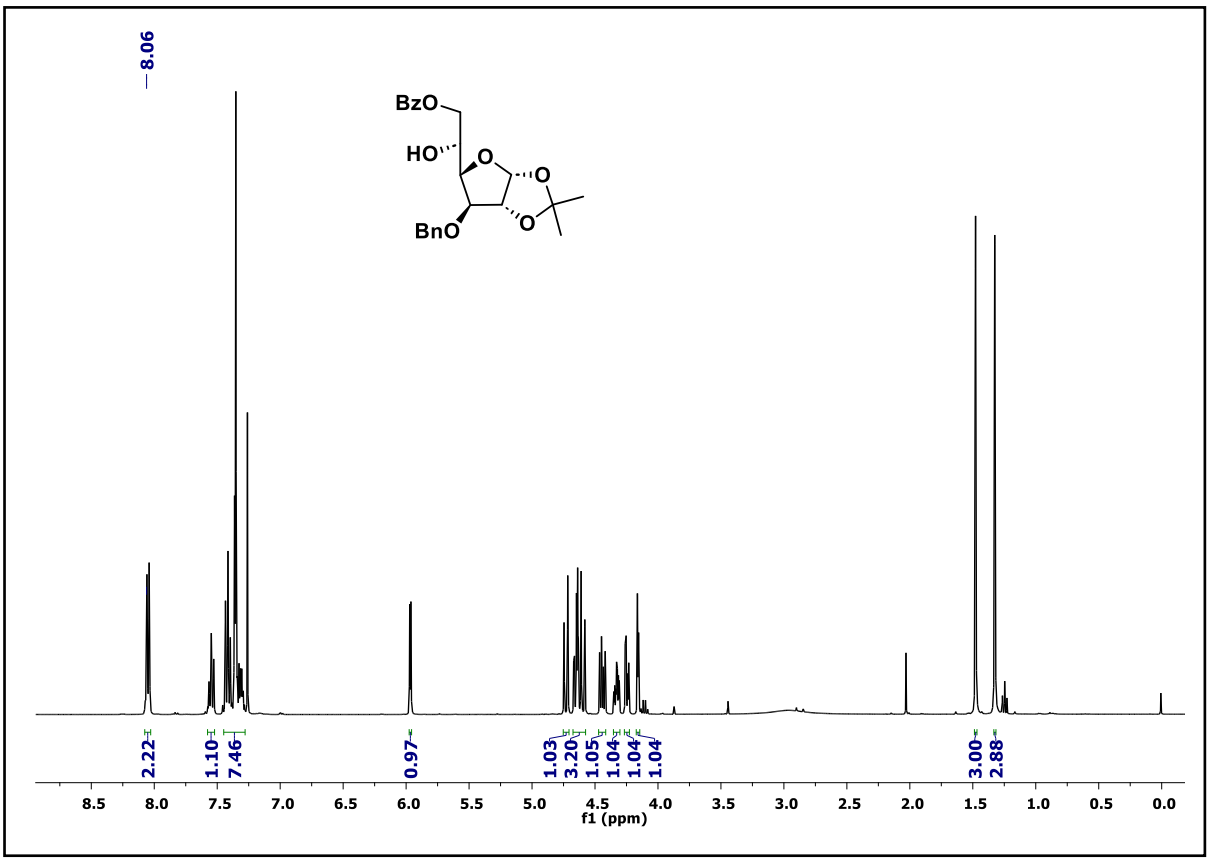
1.00
1.07
1.06
1.06
2.22
1.08
1.05
1.08
3.18
3.19
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


8.06
BzO
HO
O
O
O
BnO
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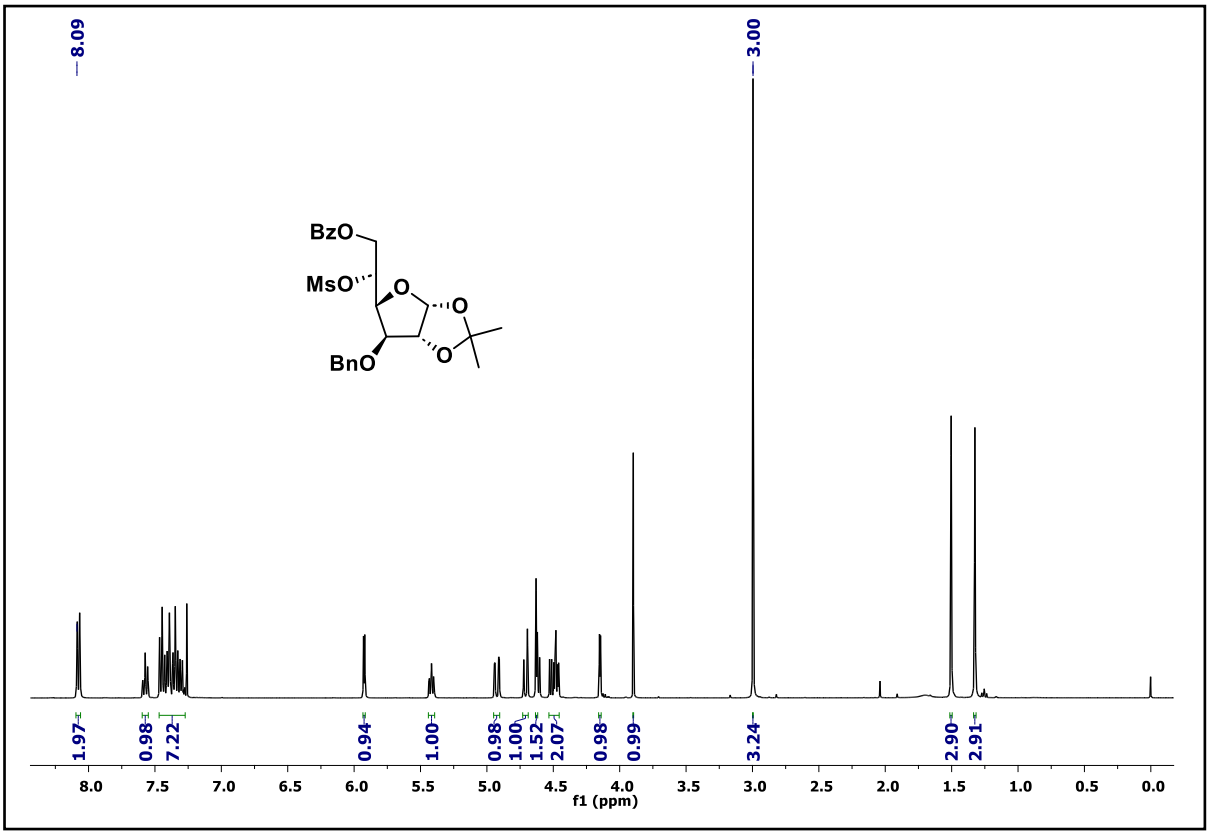
7.46
0.97
1.03
3.20
1.05
1.04
1.04
1.04
3.00
2.88
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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BzO
MsO
BnO
O
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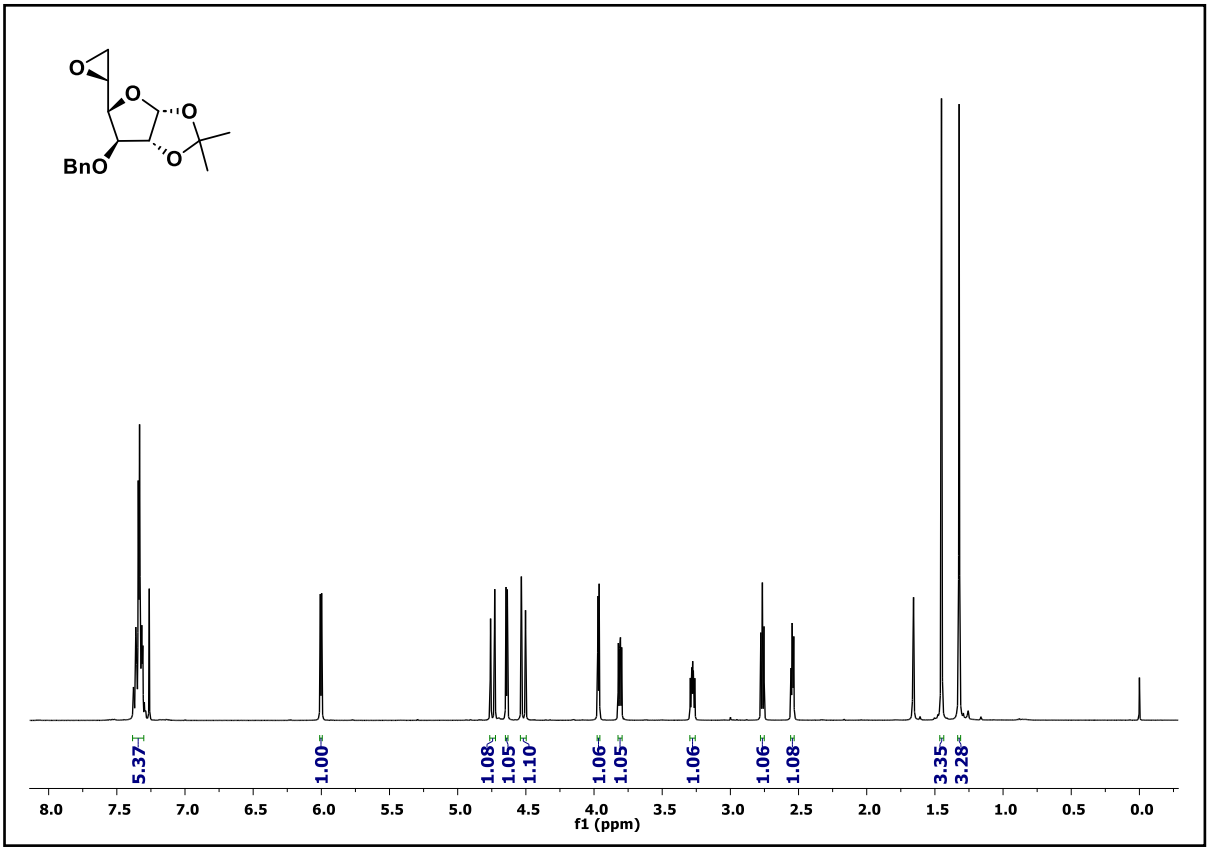
0.98
7.22
0.94
1.00
0.98
1.00
1.52
2.07
0.98
0.99
3.24
2.90
2.91
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


O
BnO
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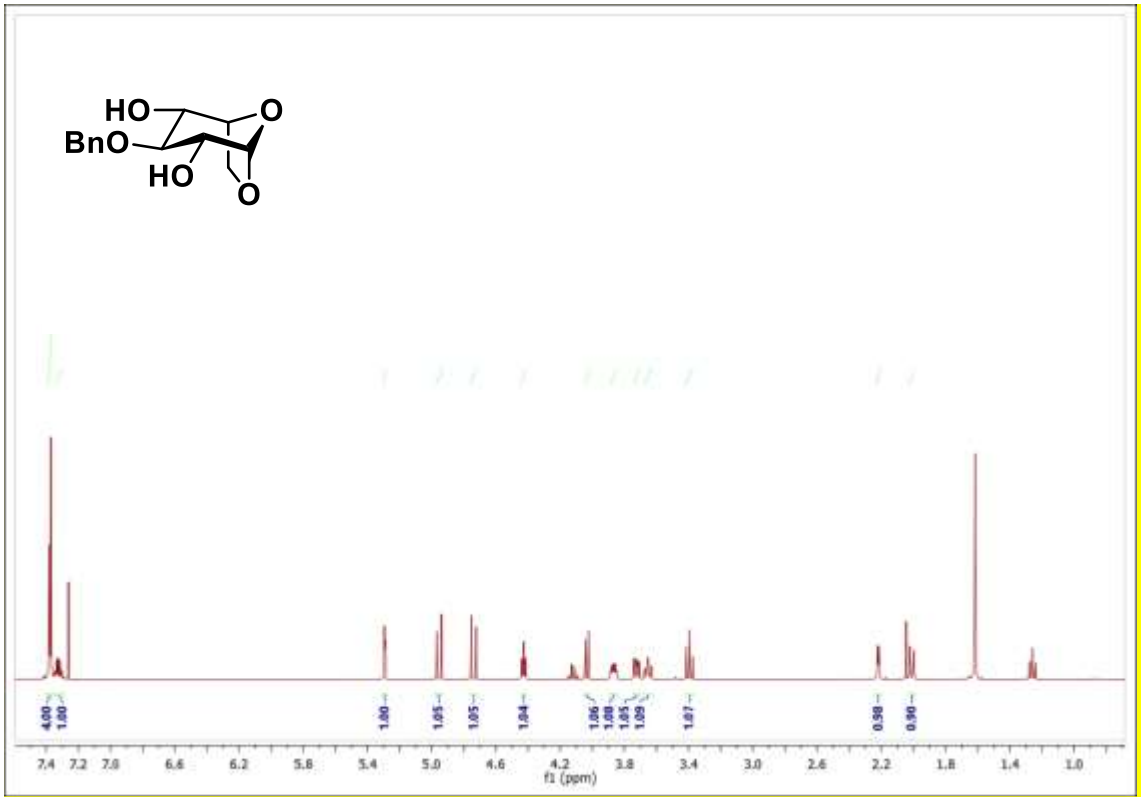
1.08
1.05
1.10
1.06
1.05
1.06
1.06
1.08
3.35
3.28
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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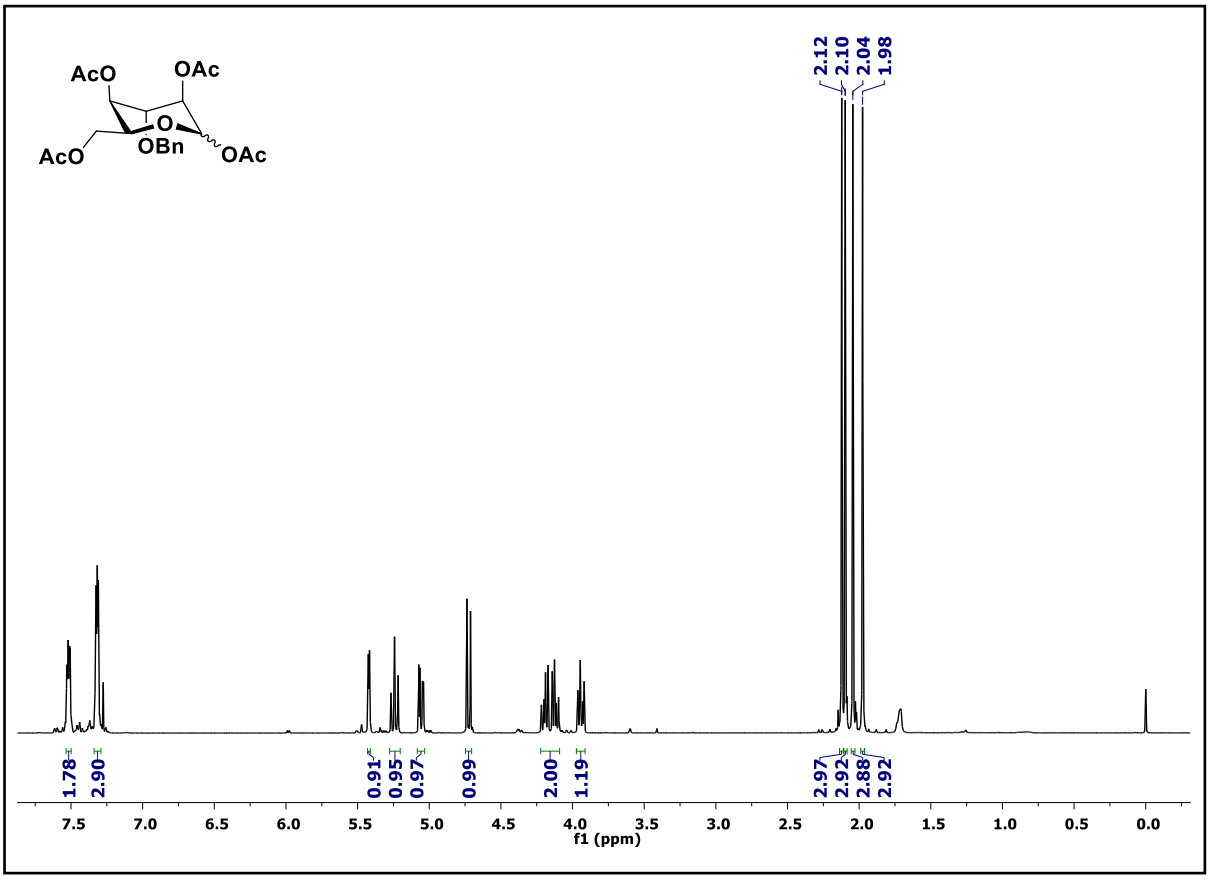
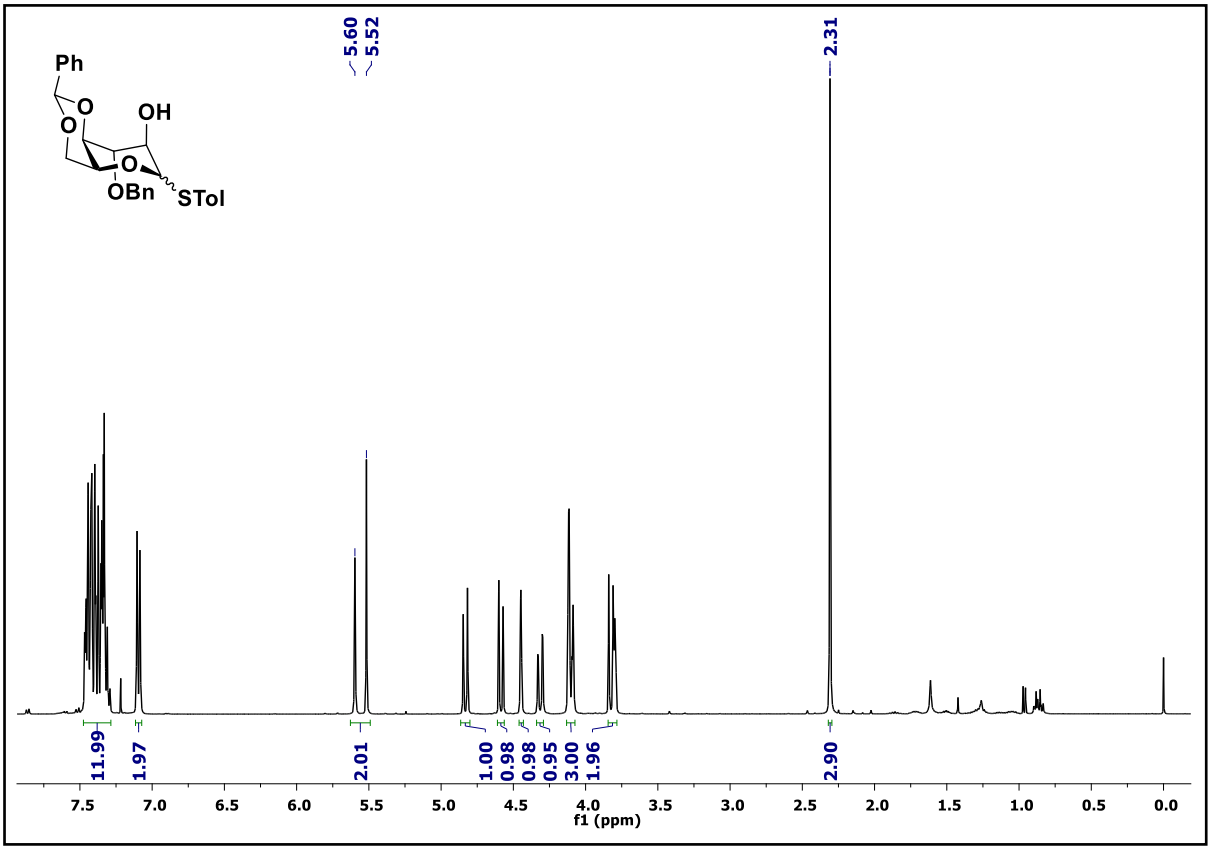
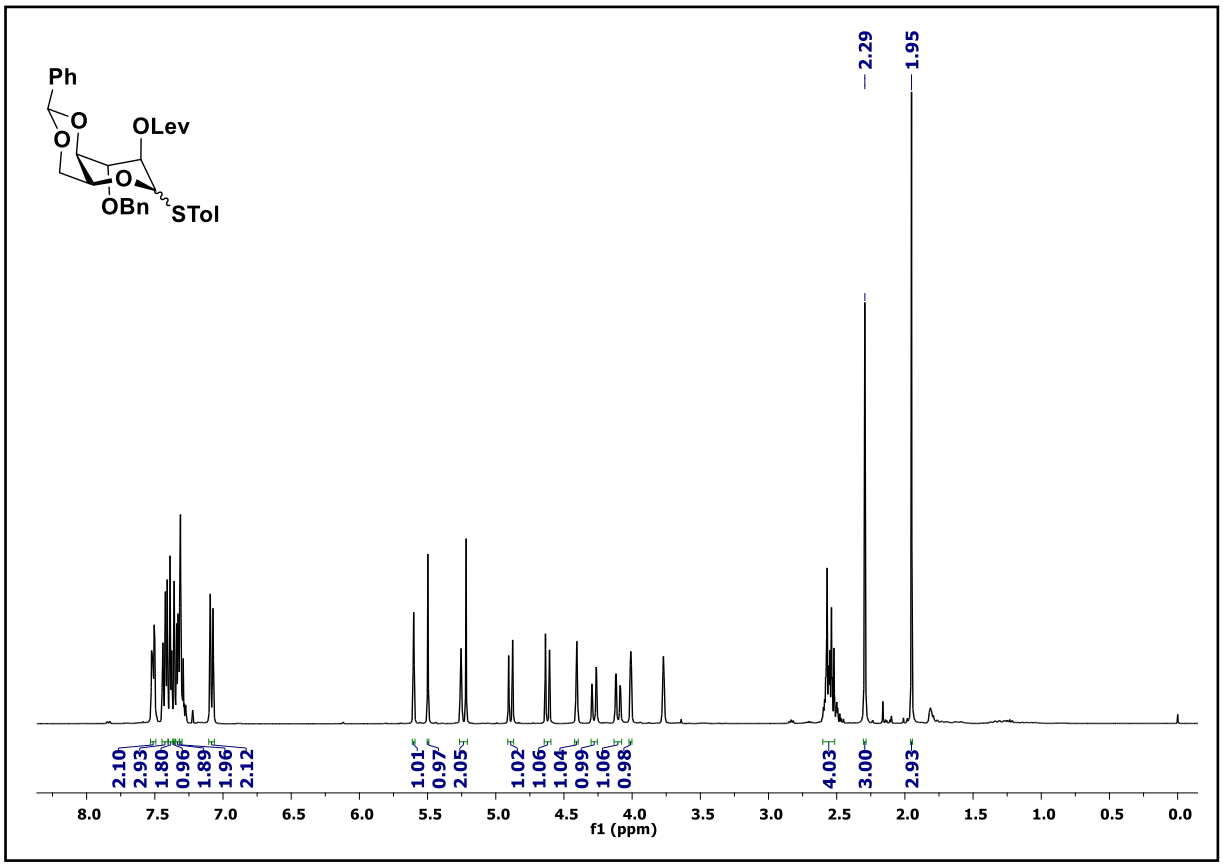
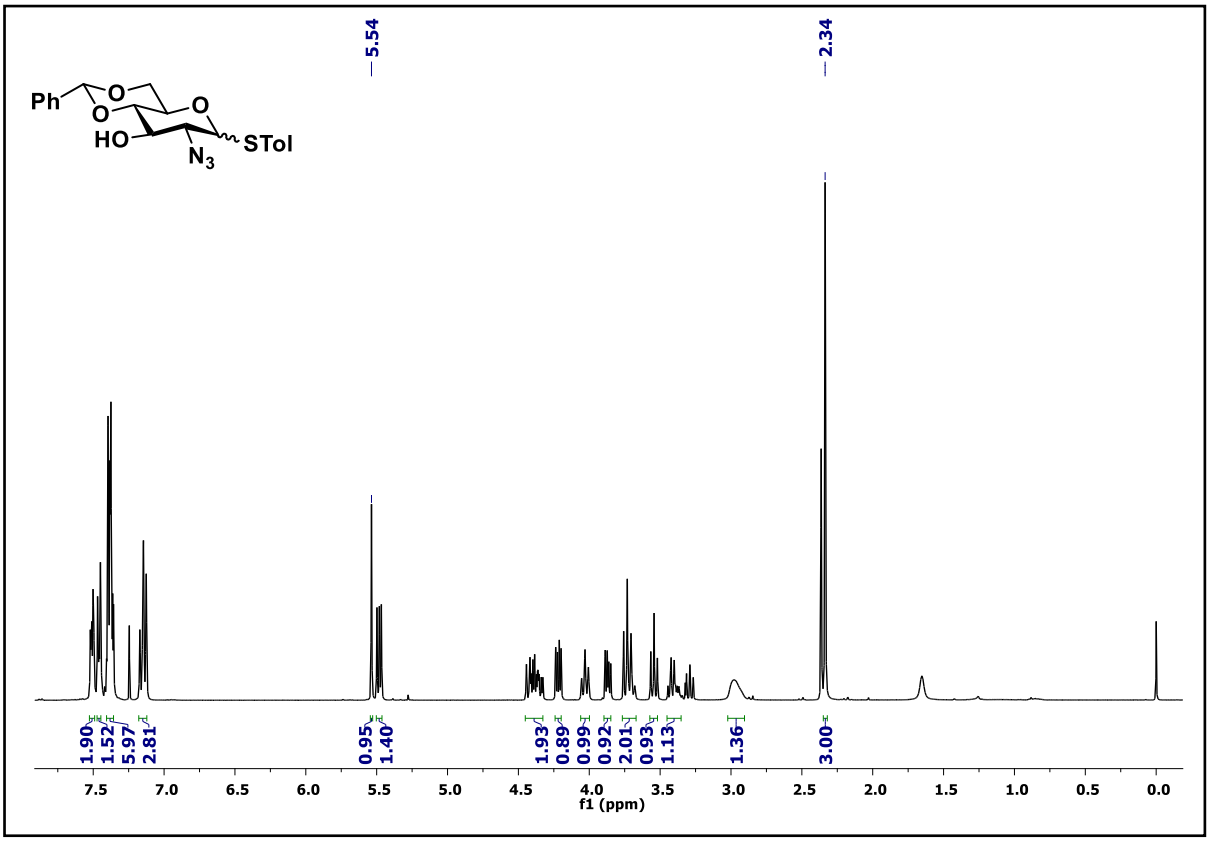
O
BnO
HO
O
4.00
1.00
1.00
1.01
1.05
1.04
1.06
1.08
1.05
1.09
1.07
0.98
0.90
7.4 7.2 7.0 6.6 6.2 5.8 5.4 5.0 4.6 4.2 3.8 3.4 3.0 2.6 2.2 1.8 1.4 1.0
f1 (ppm)


AcO
OAc
O
OBn
AcO
OAc
2.12
2.10
2.04
1.98
1.78
2.90
0.91
0.95
0.97
0.99
2.00
1.19
2.97
2.92
2.88
2.92
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)


Ph
O
O
OH
O
OBn
STol
5.60
5.52
2.31
11.99
1.97
2.01
1.00
0.98
0.98
0.95
3.00
1.96
2.90
f1 (ppm)


Ph
O
O
OLev
O
OBn
STol
2.29
1.95
2.10
2.93
1.80
0.96
1.89
1.96
2.12
1.01
0.97
2.05
1.02
1.06
1.04
0.99
1.06
0.98
4.03
3.00
2.93
f1 (ppm)


Ph
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O
O
HO
N3
STol
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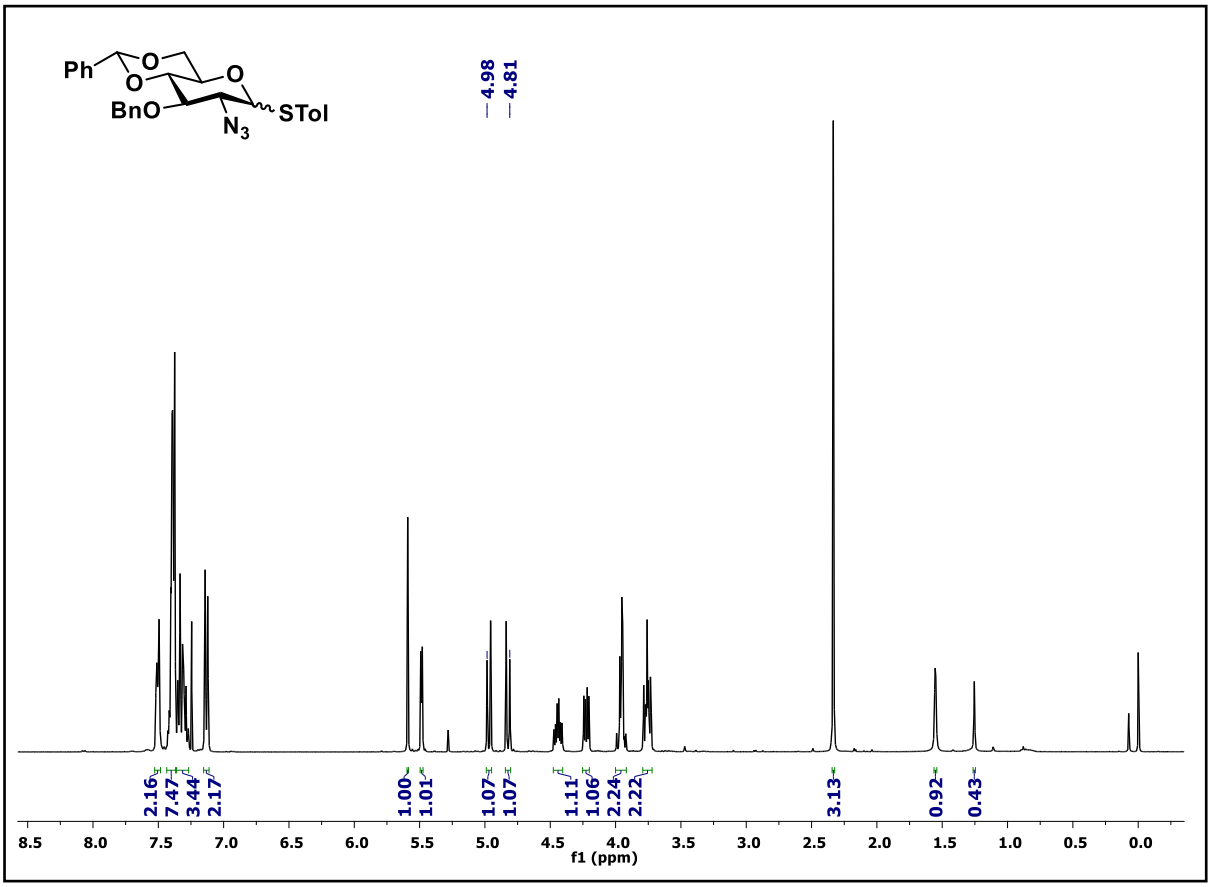
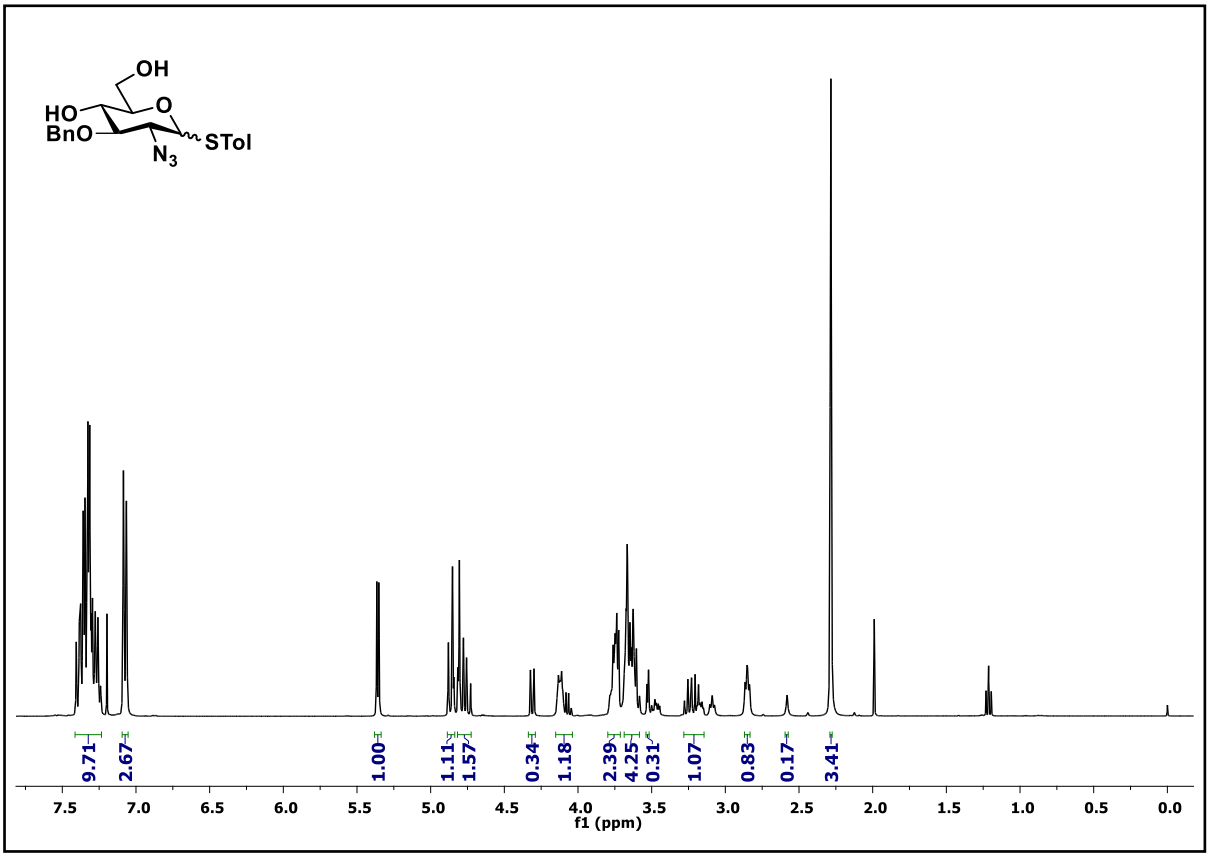
2.34
1.90
1.52
5.97
2.81
0.95
1.40
1.93
0.89
0.99
0.92
2.01
0.93
1.13
1.36
3.00
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


Ph
O
O
O
BnO
N3
STol
4.98
4.81
2.16
7.47
3.44
2.17
1.00
1.01
1.07
1.07
1.11
1.06
2.24
2.22
3.13
0.92
0.43
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)


OH
HO
O
BnO
STol
N3
9.71
2.67
1.00
1.11
1.57
0.34
1.18
2.39
4.25
0.31
1.07
0.83
0.17
3.41
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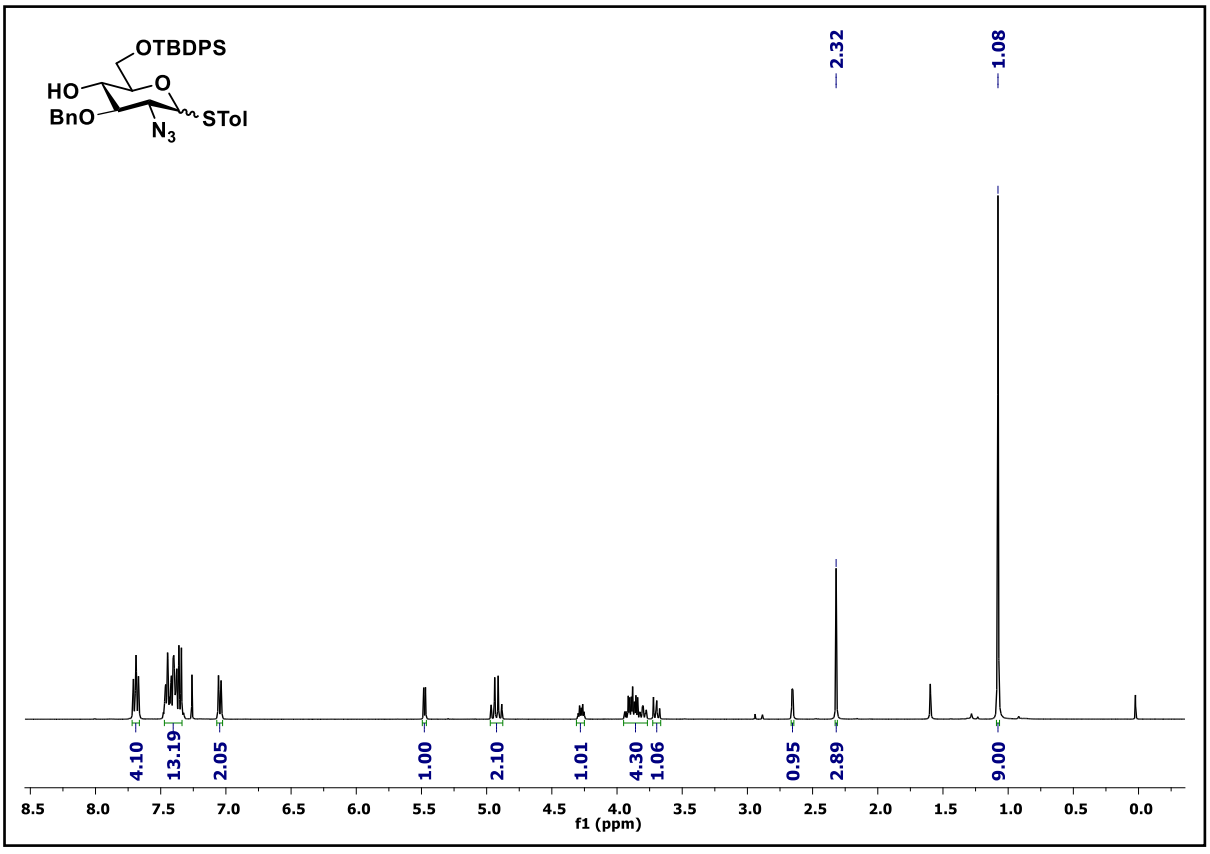
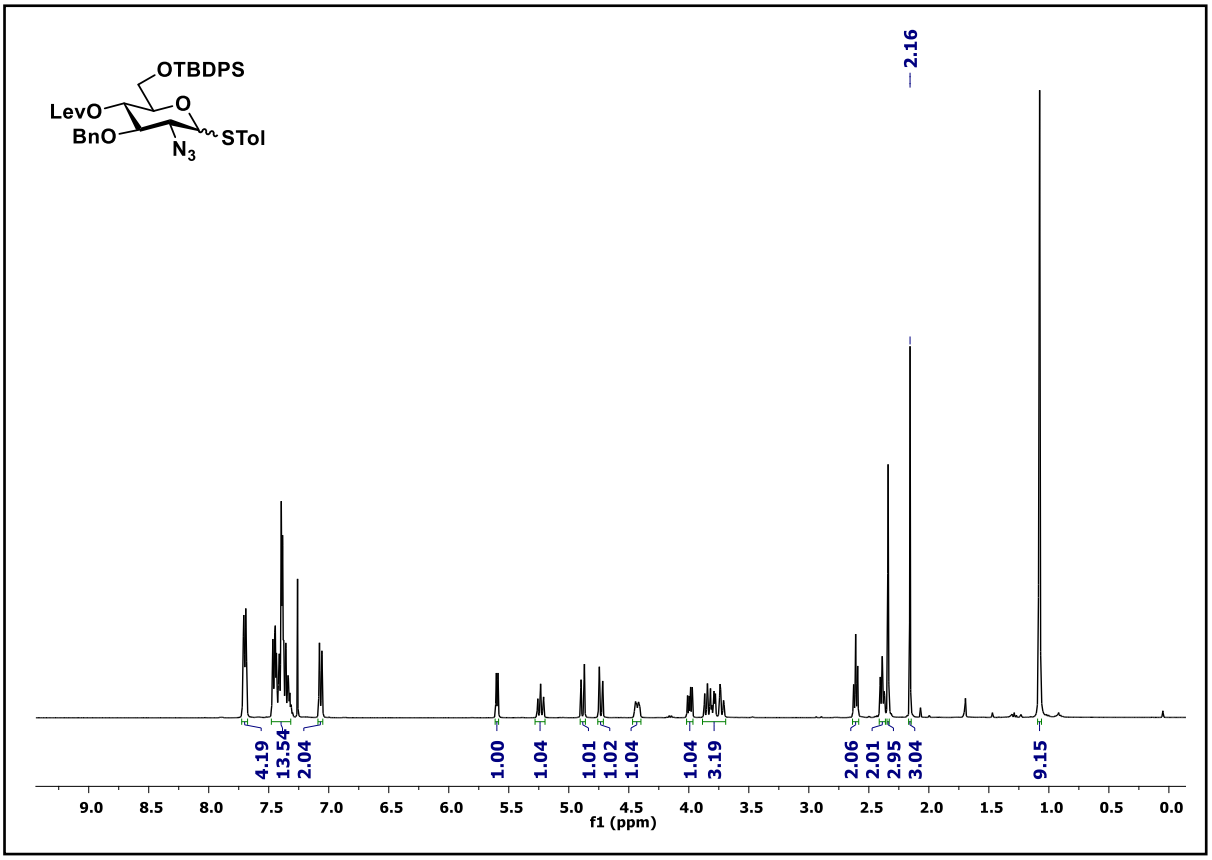
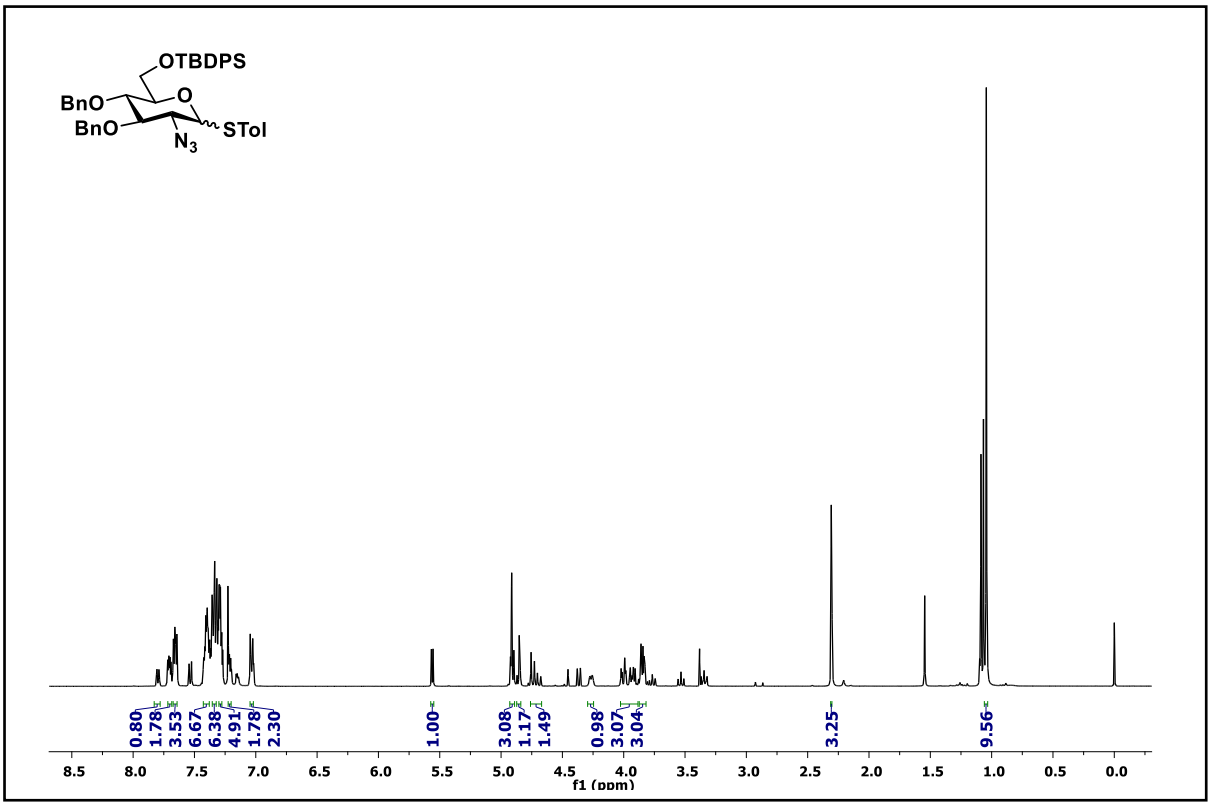
f1 (ppm)


OTBDPS
HO
O
BnO
STol
N3
2.32
1.08
4.10
13.19
2.05
1.00
2.10
1.01
4.30
1.06
0.95
2.89
9.00
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)


OTBDPS
LevO
O
BnO
N3
STol
2.16
4.19
13.54
2.04
1.00
1.04
1.01
1.02
1.04
1.04
3.19
2.06
2.01
2.95
3.04
9.15
f1 (ppm)


OTBDPS
BnO
O
BnO
N3
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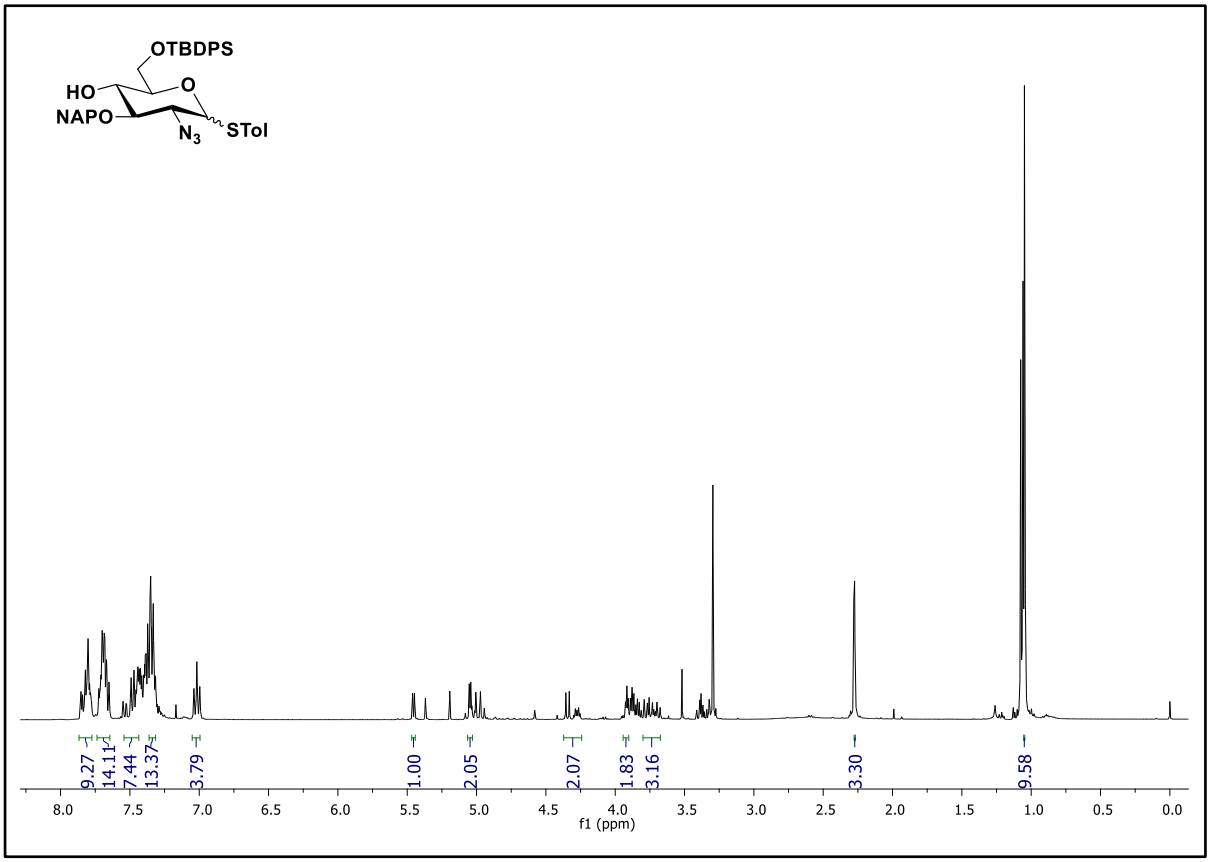
3.53
6.67
6.38
4.91
1.78
2.30
1.00
3.08
1.17
1.49
0.98
3.07
3.04
3.25
9.56
f1 (ppm)


OTBDPS
HO
O
NAPO
N3
STol
9.27
14.11
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13.37
3.79
1.00
2.05
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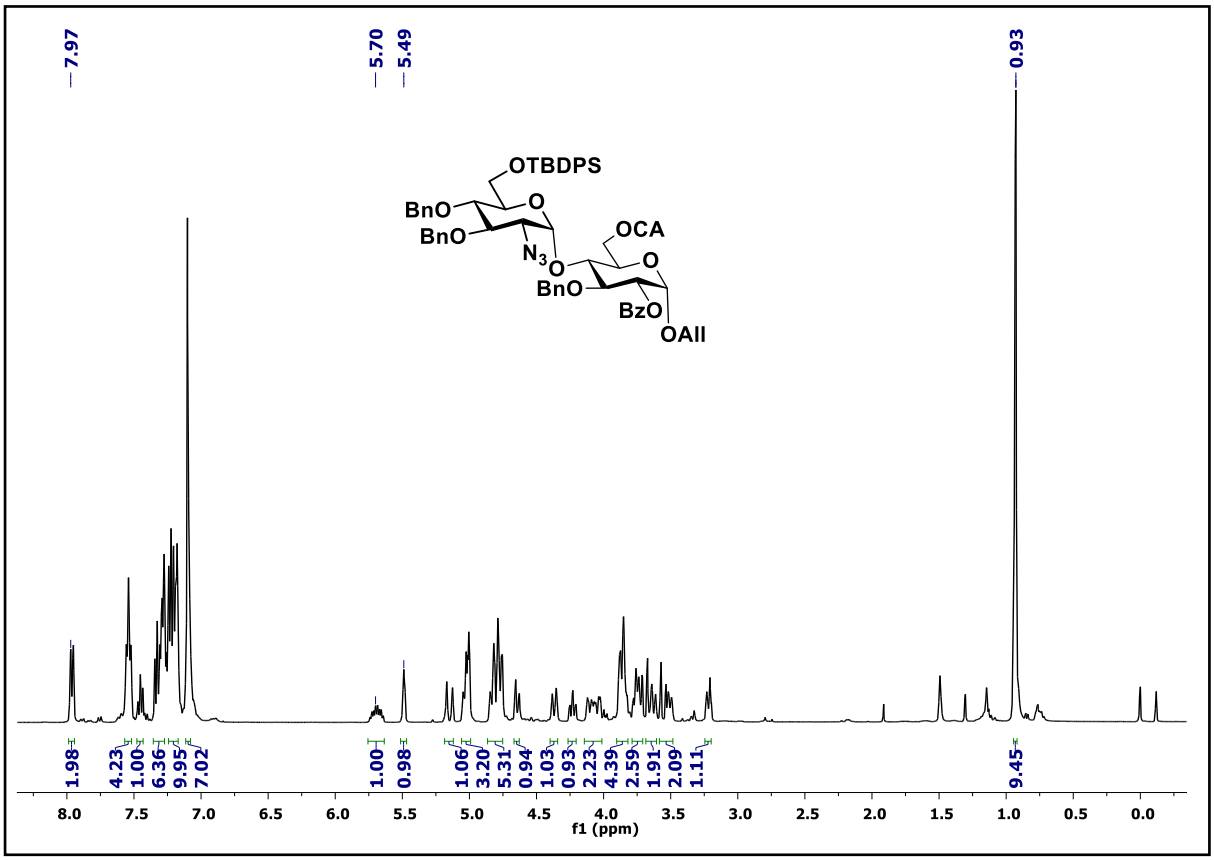
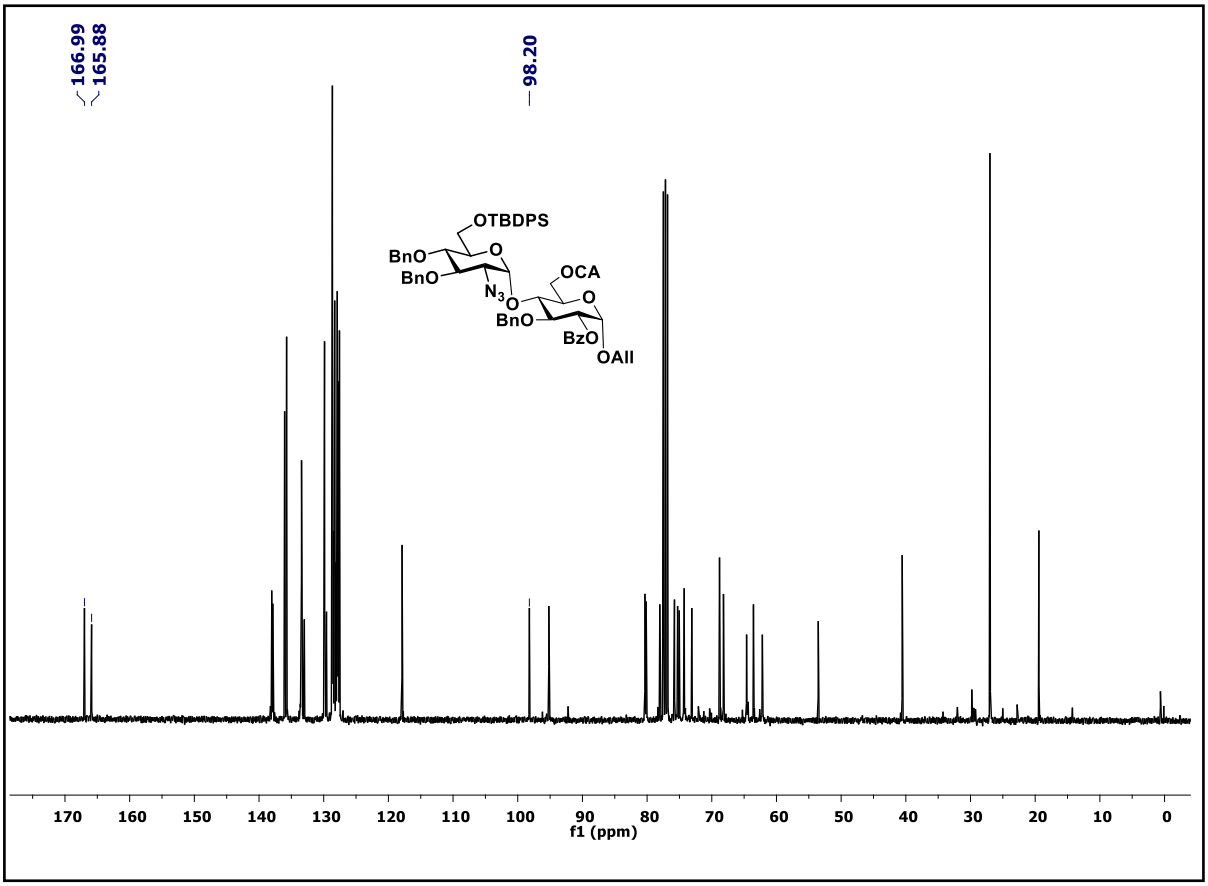
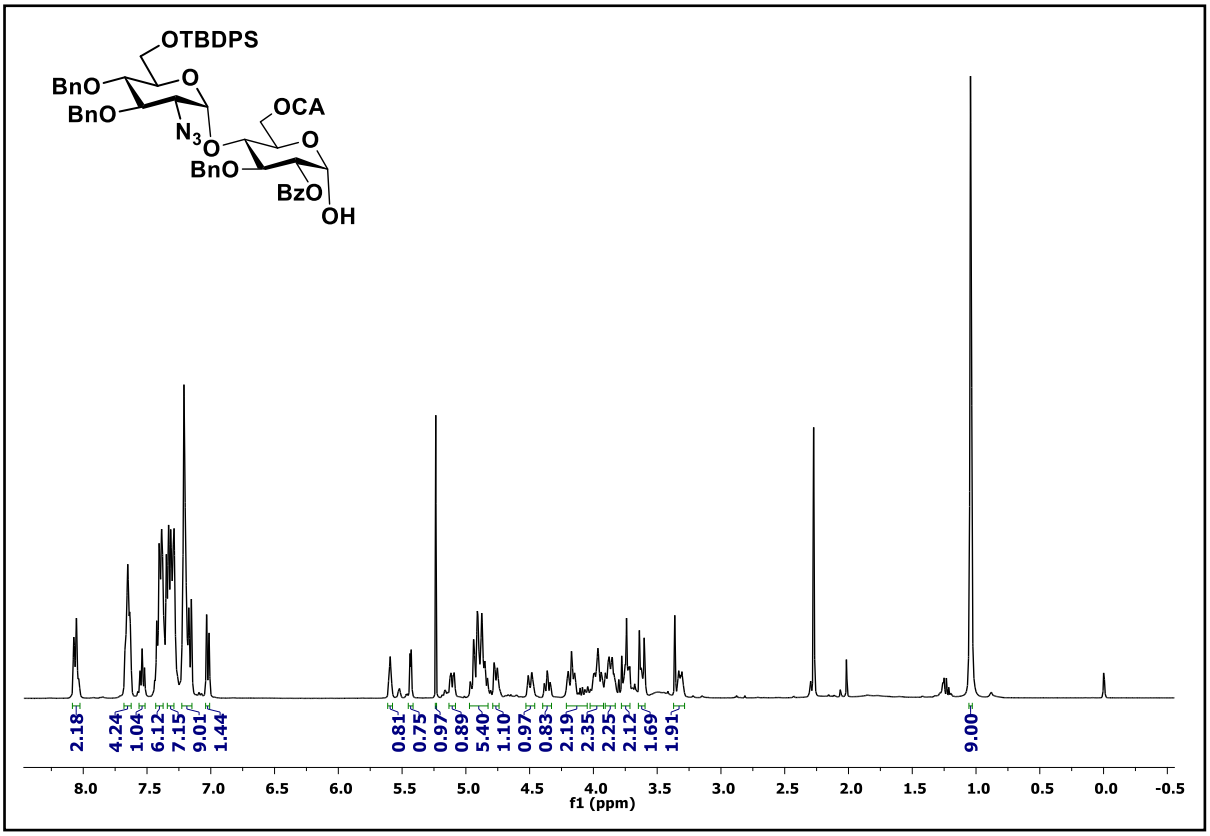
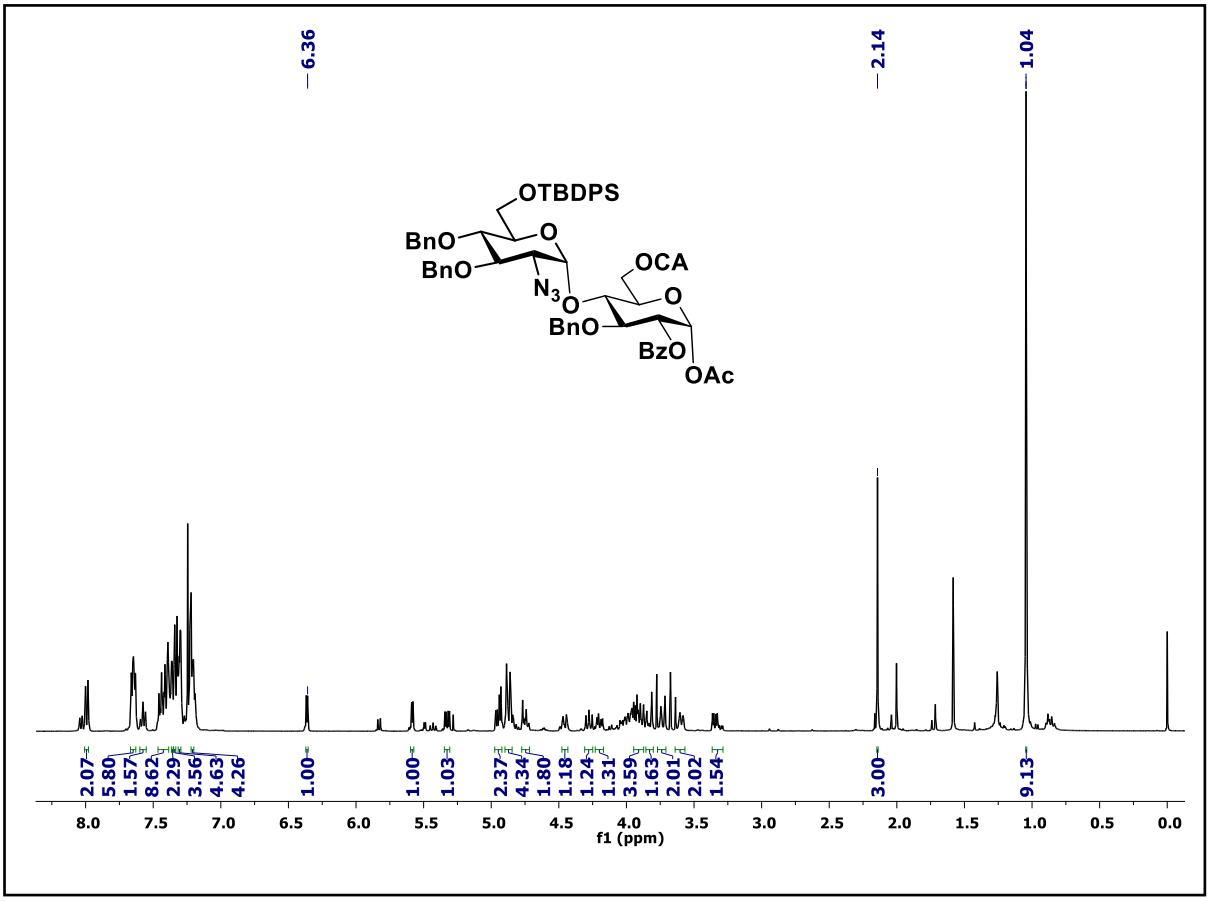
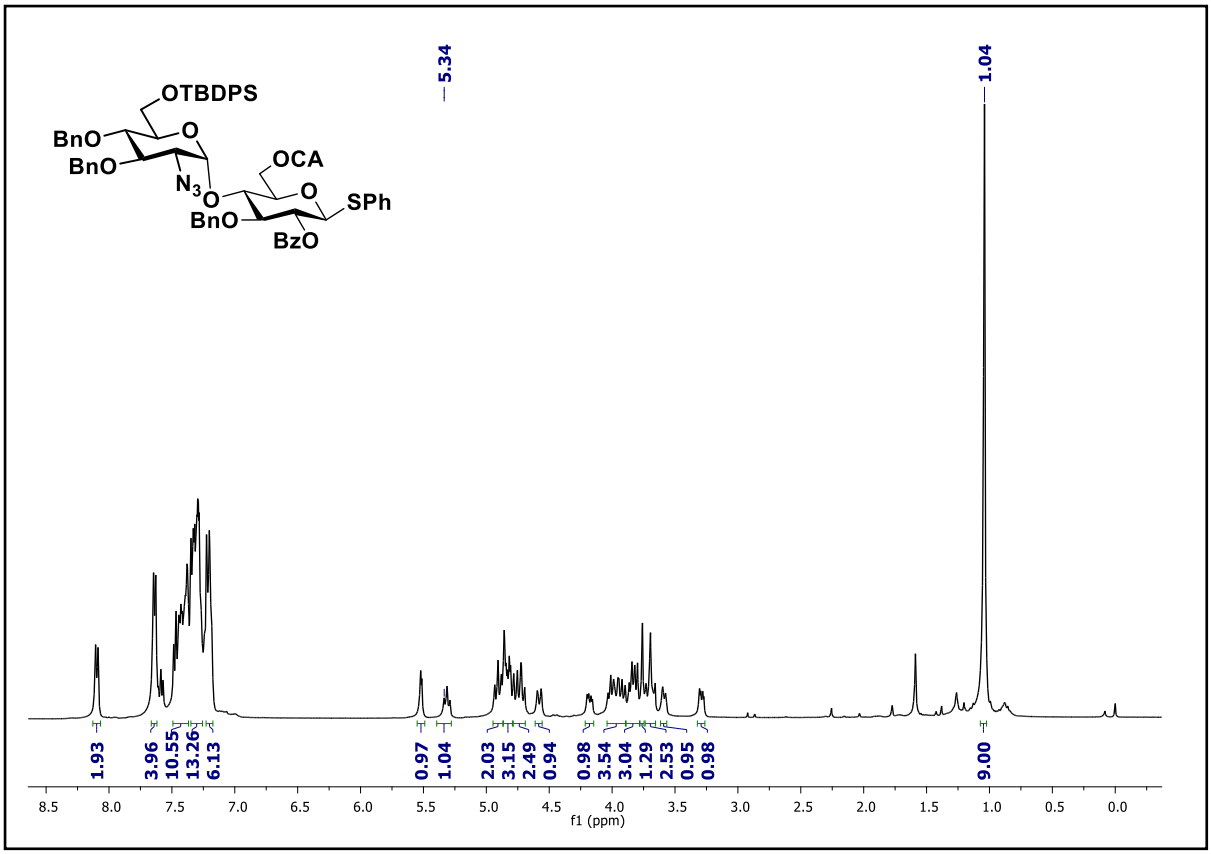
1.83
3.16
3.30
9.58
f1 (ppm)

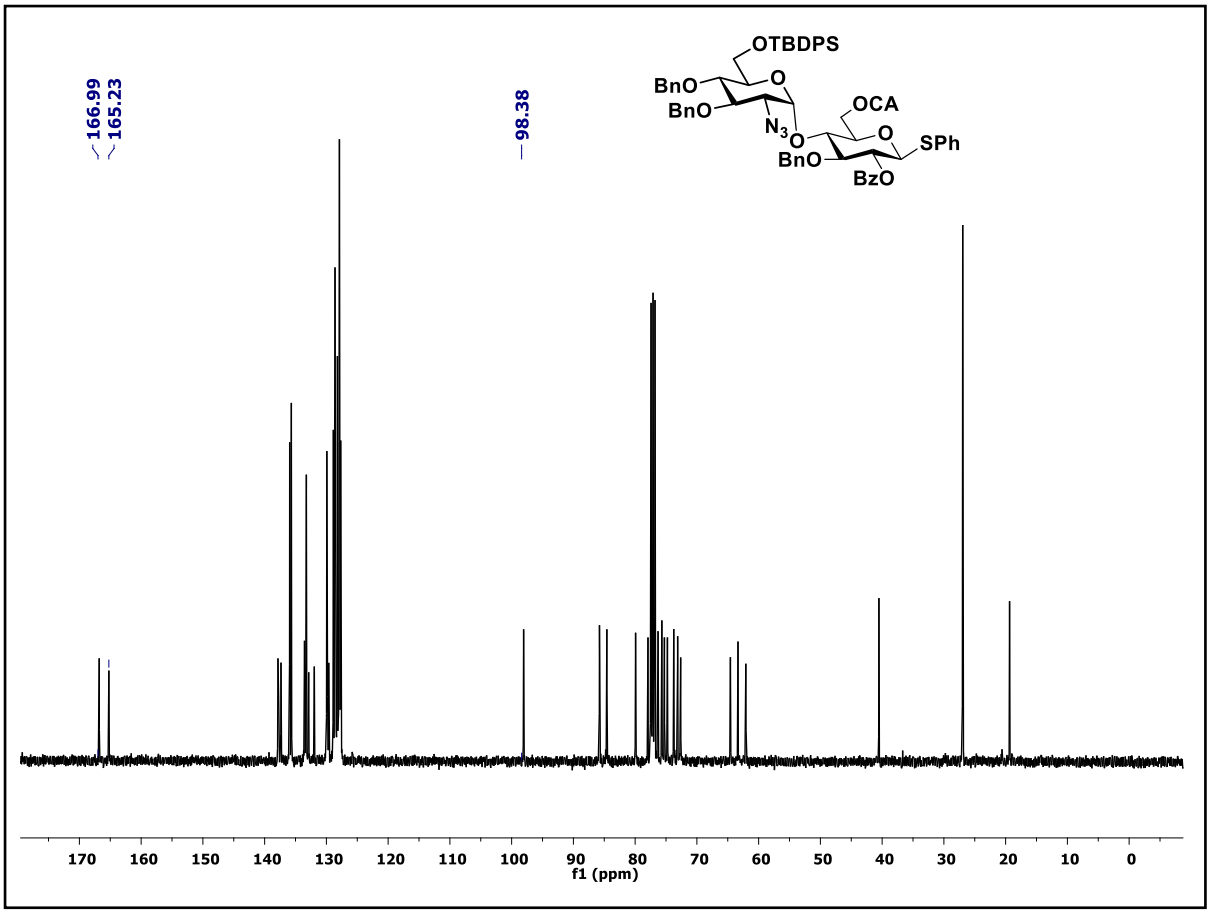

7.97
5.70
5.49
0.93
OTBDPS
BnO
O
BnO
N3
OCA
O
O
BnO
BzO
OAll
1.98
4.23
1.00
6.36
9.95
7.02
1.00
0.98
1.06
3.20
5.31
0.94
1.03
0.93
2.23
4.39
2.59
1.91
2.09
1.11
9.45
f1 (ppm)


166.99
165.88
98.20
OTBDPS
BnO
BnO
O
N3
O
OCA
O
BnO
BzO
OAll
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


OTBDPS
BnO
BnO
O
N3
O
OCA
O
BnO
BzO
OH
2.18 4.24 1.04 6.12 7.15 9.01 1.44 0.81 0.75 0.97 0.89 5.40 1.10 0.97 0.83 2.19 2.35 2.25 2.12 1.69 1.91 9.00
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)


6.36
2.14
1.04
OTBDPS
BnO
BnO
O
N3
O
OCA
O
BnO
BzO
OAc
2.07
5.80
1.57
8.62
2.29
3.56
4.63
4.26
1.00
1.00
1.03
2.37
4.34
1.80
1.18
1.24
1.31
3.59
1.63
2.01
2.02
1.54
3.00
9.13
f1 (ppm)


5.34
1.04
OTBDPS
BnO
BnO
O
N3
O
OCA
O
SPh
BnO
BzO
1.93
3.96
10.55
13.26
6.13
0.97
1.04
2.03
3.15
2.49
0.94
0.98
3.54
3.04
1.29
2.53
0.95
0.98
9.00
f1 (ppm)



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