Design and Synthesis of Sulfate Oligo-Idose Analogs: Potential Heparan Sulfate Glycomimetics

A thesis

Submitted towards the partial fulfilment of the requirements for the

BS-MS Dual Degree Program

By

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CERTIFICATE

This is to certify that this dissertation entitled **Design and Synthesis of Sulfate Oligo-Idose Analogs: Potential Heparan Sulfate Glycomimetics** towards the partial fulfilment of the BS-MS dual degree programme at the Indian Institute of Science Education and Research, Pune represents the work carried out by **Dipti Chimnapure** at IISER Pune under the supervision of **Prof. Raghavendra Kikkeri**, Professor, Department of Chemistry during the academic year 2021-2022.

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Date- 20th Oct 2022

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DECLARATION

I hereby declare that the matter embodied in the report entitled **Design and Synthesis of Sulfate Oligo-Idose Analogs: Potential Heparan Sulfate Glycomimetics** 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.

Dipti Chimnapure

ID- 20171090

Date: 20-10-2022

Dedicated to

My Loving Parents

Acknowledgements

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Finally, I'm very thankful towards my parents and siblings for their constant encouragement and love. Their understanding and precious advice keeps me going despite all the challenges.

ABBREVIATIONS

°C: degree Celcius

Ac_2O: Acetic Anhydride

ACN: Acetonitrile

Bz-Cl- Benzoyl Chloride

CD_3OD- Methanol-d4

$CDCl_3$- Chloroform-d

CH_3- methyl

$CHCl_3$- Chloroform

CSA- Camphorsulfonic Acid

$Cu(OTf)_2$- Copper triflate

d- doublet

D2O- Deuterium hydroxide

DCM- Dichloromethane

Ddd- doublet of doublet of doublet

DDQ- 2,3- Dichloro-5,6-dicyano-1,4-benzoquinone

DMF- *N*,*N*-Dimethyl Formamide

Dt- doublet of triplet

Et_3N- Triethylamine

EtOAc- Ethyl acetate

GlcA- Glucuronic Acid

H^+- Hydrogen cation

H2O- water

H_2SO_4- Sulphuric Acid

HCl- Hydrochloric Acid

HRMS- High Resolution Mass Spectrometry

HS- Heparan Sulfate

J- Coupling Constant

L- litre

LiOH- Lithium Hydroxide

m/z- mass to charge ratio

MeOD- Methanol-d4

Mg- Milligram

MHz- Mega Hertz

ml- Millilitre

Mmol- Milli moles

Mol- moles

MS-Cl- Mesyl chloride

MW- Molecular weight

Na^+- Sodium ion

$Na_2S_2O_3$- Sodium thiosulfate

Na_2SO_4- Sodium sulfate

NaCl- Sodium Chloride

NaH- Sodium hydride

NapBr- (2-Bromomethyl)naphthalene

NIS- N-Iodosuccinimide

NMR- Nuclear Magnetic Resonance

PE- Pet Ether

Ppm- parts per million

*p*TSA- *p*- Toluenesulfonic Acid

Py- Pyridine

q- quartet

qd- quartet of doublet

RB- Round bottom

RM- Reaction mixture

RT- Room temperature

s- singlet

SO3.NMe3- Sulphur trioxide trimethylamine complex

t – triplet

tBuOH- tert-Butanol

$tBuO^{+}K^{-}$ - potassium tert-butoxide

THF- Tetrahydrofuran

TLC- Thin layer chromatography

TMSOTf- Trimethylsilyl trifluoromethanesulfonate

TMSSPh- Trimethyl(thiophenol) silane

ZnI_2- Zinc Iodide

δ- Chemical Shift

µl- Microlitre

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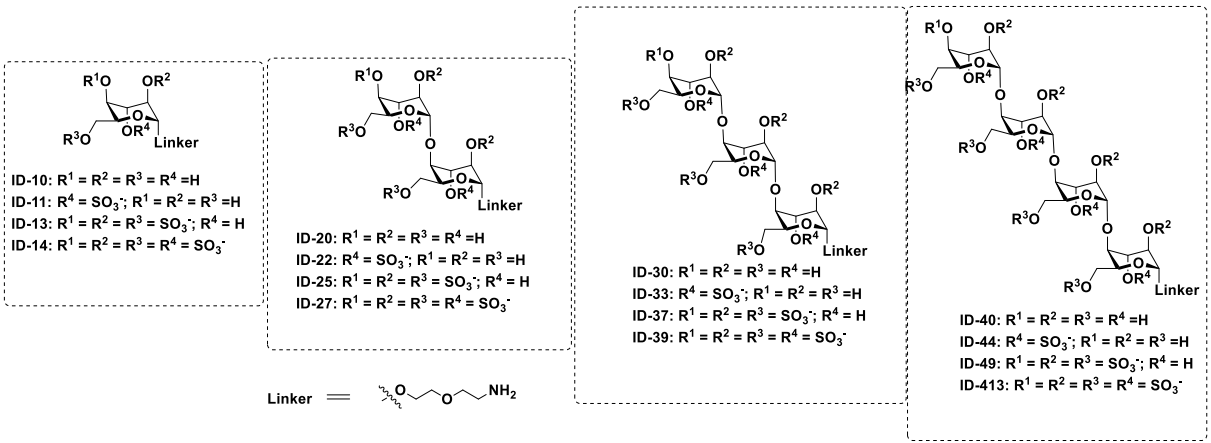
Abstract

The structural microheterogeneity of heparan sulfate (HS) is intrinsically governed by repeating disaccharide units, sulfation patterns, uronic acid composition and conformation plasticity of L-Iduronic acid. These factors synergistically promote HS-mediated biological activities. Despite rapid progress in synthesizing structurally defined HS oligosaccharides, how disaccharide heterogeneity directly contributes to HS biological functions is not well studied. Recently, we have shown that homo-oligosaccharides with different sulfation patterns can modulate the selectivity and specificity of growth factors and chemokines. Motivated by these results, we have synthesized L-idose-based homo-oligosaccharides with a wide range of sulfation patterns to fine-tune the specific HS-protein interactions. HS mimics were synthesized from L-idose thiophenol donor and β-L-idopyranosyl acceptor building block. We installed oligosaccharides using [2+2] glycosylation strategy. These mono, di and tetrasaccharides are subjected to divergent strategy, where selective protecting groups were removed and sulfated. So far, we successfully synthesized mono, disaccharides with partial and fully sulfated ligands and currently optimizing the synthesis of higher oligosaccharides. Once we have all 16 compounds in hand, we are planning to establish structure-activity relationships with heparin-binding proteins, particularly with growth factors and chemokines.



1. Introduction

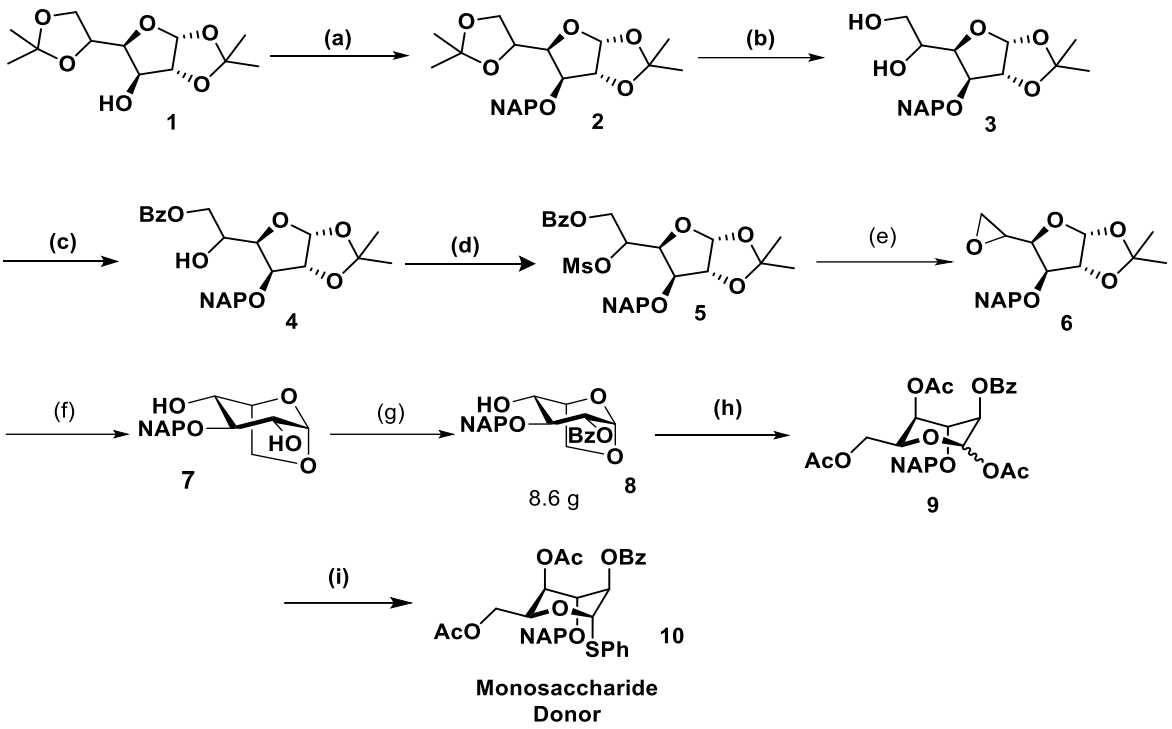
Glycans are the most abundant biomacromolecules on cell surfaces, in which various monosaccharide units are linked together regio and stereochemically to exert complex structure-functions [1]. Attempt to elucidate structural diversity of glycans led to the discovery of several subtle structures to fine-tune the biological activities. Hence, generating a broad library of a core glycans and its mimetics are important to identify specific sugar sequence essential to target protein of our interest. Among various cellular glycans, heparan sulfate (HS) is highly heterogenous and complex polysaccharide found both on the cell surface and in basement membrane (BM) [2]. They belong to the family of glycosaminoglycans (GAGs) covalently attached to a protein core of proteoglycan (PG). HS coordinates numerous cellular functions such as cell recognition, cell adhesion, cell migration and cell signaling through their binding with diverse proteins [3]. Identify HS core structures responsible for specific biological functions are attractive target for diagnostic and medicinal applications [4]. Structurally, HS composed of α-(1,4) linked disaccharide repeating units of D-glucosamine and hexuronic acid, which might be either 'D-glucuronic acid (GlcA) or L-iduronic acid (IdoA).' The structural diversity of HS comes from degree of *O*- and *N*-sulfation/acetylation on glucosamine and hexuronic acid ligands. Theoretically, HS tetrasaccharides can arrange themselves into 2,304 combinations. To elucidate the active ligand amount of these HS combinations, several research groups have synthesized broad HS libraries [5]. The pioneer works from the labs of Linhort, Hung, Boons, Seeberger, linda, Xuefei, Jian led to development of reliable synthetic and chemoenzymatic protocols to synthesize a broad HS libraries [67]. The majority of these HS libraries were able to decipher sulfation code, oligosaccharide chain length essential for specific protein binding. However, in nature HS usually occur as disaccharide heterogenous system, and thus elucidating the structural heterogeneity of HS in protein binding could result into functionally highly

active ligands[8]. To address this gap, we synthesized a new set of combinatorial HS libraries composed of homo HS oligosaccharides sequences with different sulfation code. The high-throughput screen of these glycans on microarray platform with various binding patterns with growth factors, and chemokines is expected to reveal the disaccharide heterogeneity in HS protein interactions[5].

2. Results and Discussion

2.1 Synthesis of Monosaccharide L- Idose Building block

Synthesis of sulfated oligo-idose is difficult as L-idose is not commercially available and stereoselective α-glycosylation between L-idose is challenging. Previously, we reported a linear approach to synthesizing oligo-iduronic acid building blocks and employed a divergent strategy to generate a library of sulfated iduronic acid oligosaccharides [9]. We also plan to utilize the same process here but slightly modify the protection group strategy to get a wide range of sulfation patterns. For example, we incorporated NAP protection at the 3rd position of L-Idose to synthesize 3-O sulfated derivatives [10]. Compound **8** was synthesized with a total yield of 17% from 1,2:5,6-di-*O*-isopropylidene-α- D -glucofuranose by a seven-step reaction. Briefly, we first converted compound **1** into 3-O-napthyl-protected D-glucofuranose building block by treating with 2-naphthyl methyl bromide (NapBr) “in the presence of sodium hydride in DMF solvent at 0 °C for 3 h.” The selective 2,3-diol deprotection followed by mesylation, epoxidation, and ring expansion yielded anhydrous-idose in overall good yield. A regioselective ring opening of **8** with Acetic Anhydride in the presence of $Cu(OTf)_2$ at 0 ˚C, led to **9** in 83% yield, which on reaction with trimethyl(phenylthio)silane in the presence of ZnI_2 at room temperature gives Monosaccharide donor **10** (**Scheme1**). Finally, we employed 3-*O*-Naphthyl-2-*O*-benzoyl-1,6-anhydro-β-L-idopyranoside (**8**) and an Idose-thiophenol donor (**10**) as important precursors to synthesize oligosaccharides [9]. All the reactions were done under inert atmosphere.



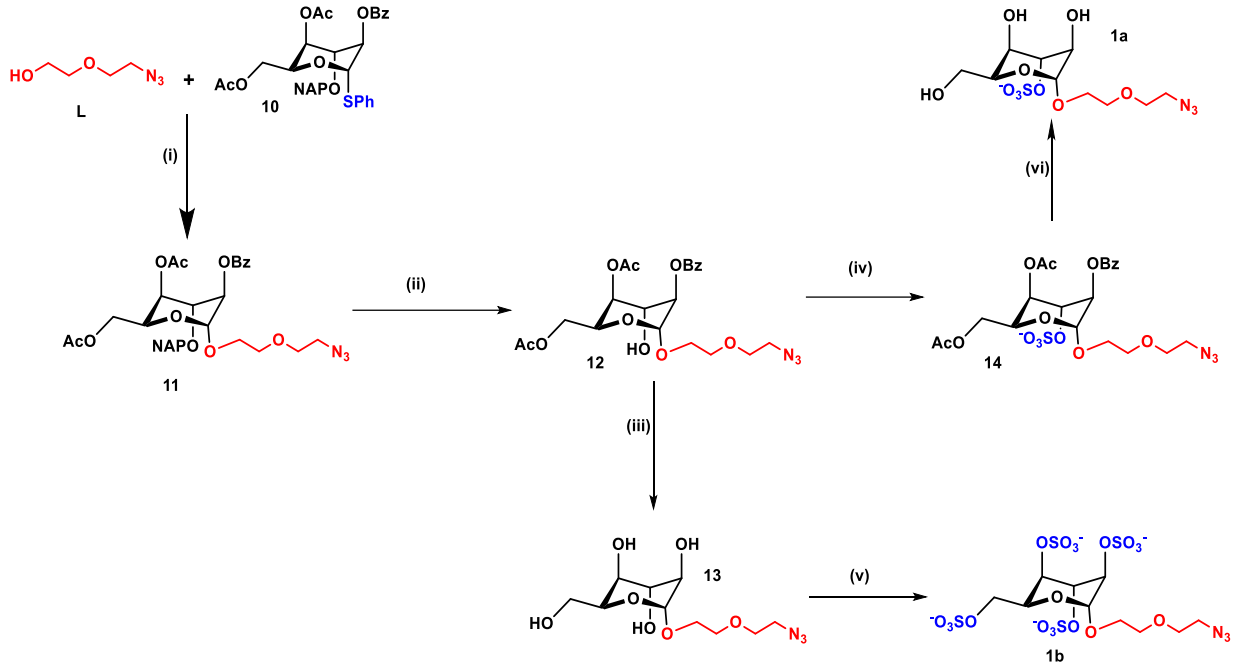
Scheme 1: Synthetic scheme for Idose building block and monosaccharide donor

(a) NaH, DMF, 0 °C, 3 h, 90%; (b) 64% AcOH, 40 °C, 12 h, 83%; (c) Bz-Cl, DCM/Py, 0 °C, 1 h, 73%; (d) Ms-Cl, Py 0 °C, 12h 76%; (e) tBuOK, tBuOH/DCM (1:1) 0 °C - RT, 12 h, 66%; (f) 2 N H_2SO_4, 1,4-Dioxane, 109 °C Reflux, 12 h, 63%; (g) Bz-Cl, DCM/Py, 0 °C, 30 min 76%; (h) $Cu(OTf)_2$, Ac_2O, 0 °C – RT, 12 h , 83%; (i) TMSSPh, ZnI_2, Dry DCM, 1 hr, 92%

2.2. Synthesis of Sulfated Monosaccharide Analogs

Once we had the L-idose donor in hand, we attempted to synthesize 3-O sulfated and fully sulfated monosaccharide analogs [5]. First, we glycosylated compound (**10**) with the azido-ethoxy-ethanol linker, using NIS, TMSOTf at -10°C to yield **11**. This is followed by NAP deprotection in the presence of DDQ, DCM:H_2O (18:1) (**12**). Then the 3-O sulphated molecule (**14**) was synthesized by treating 1**2** with $SO_3.NMe_3$ salt with DMF in microwave at 100°C (power 15 W). The significant shift in the NMR peak 4.54 ppm which corresponds to H-3 sulfation (non-sulfate compound showed H-3 peak between 3.9 to 4.0 ppm), confirming the regioselective sulfation. For full sulfation, we first deprotected acetate and benzoyl group using LiOH and THF:MeOH:H_2O (4:2:1) and then comp **13** was reacted with $SO_3.NMe_3$ salt with DMF in microwave at 100°C for 1 h to obtain fully sulfated L-idose. The compound was purified by first passing through Na^+ resin to remove trimethyl amine peaks, followed by LH-20, a size exclusion column to separate salts from the reaction

mixture. The final hydrogenolysis is pending for all these compounds and it will be done soon.



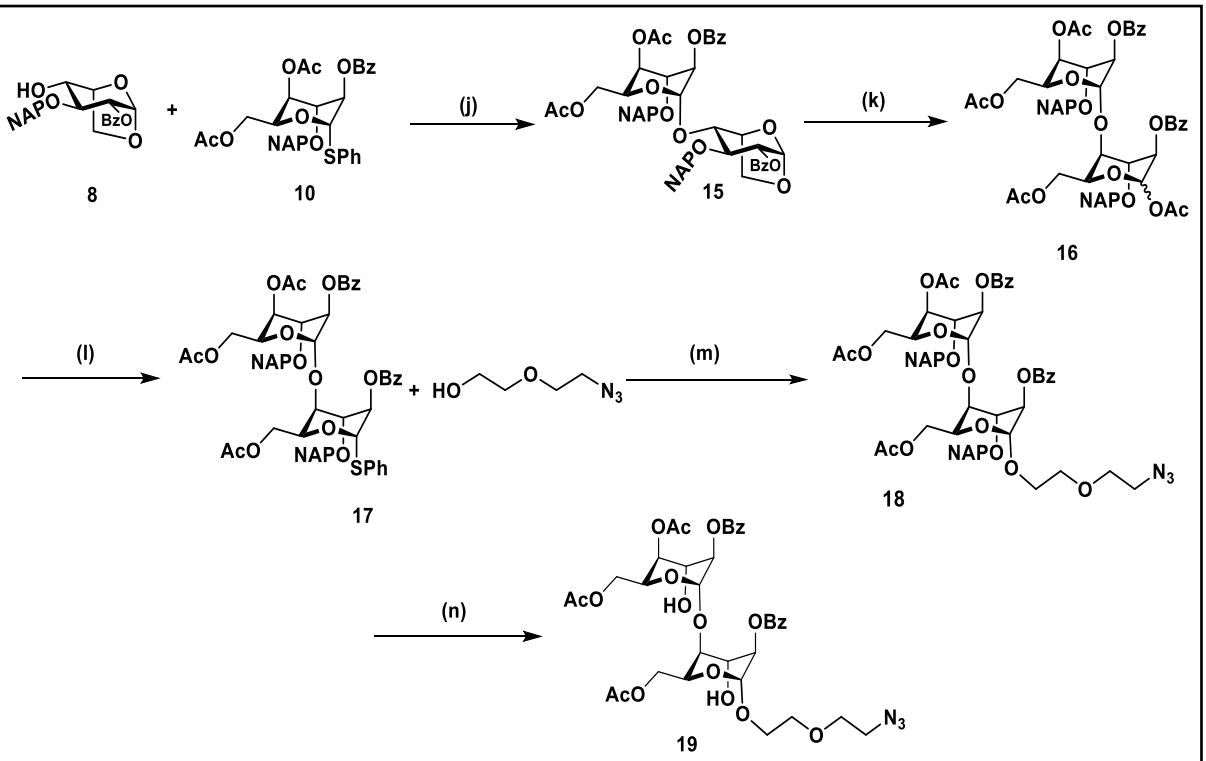
Scheme 2: Monosaccharide sulfation;

(i)TMSOTf, NIS, Dry DCM, -10C, 80%; (ii) DCM:H_2O (18:1), DDQ, RT, 3h, 82%; (iii) LiOH, THF:MeOH:H_2O (4:2:1), 0°C - RT, Overnight, 88%; (iv) $SO_3.NMe_3$, DMF, 60°C, 18h, 83%; (v) $SO_3.NMe_3$, DMF, 100°C,1/2h, 79%; (vi) LiOH, THF:MeOH:H_2O (4:2:1), 0°C to RT, 2 hr, 80%

2.3. Synthesis of Disaccharide L-Idose

After successfully synthesizing the monosaccharide analogs, we attempted to synthesize disaccharide by glycosylating **8** and **10 (Scheme 3)** in the presence of *N*-Iodosuccinimide (NIS) and a catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf) in DCM at -10˚C to get **15** of 68% yield. Disaccharide **15** was treated with a catalytic amount of Copper (II) trifluoromethanesulfonate ($Cu(OTf)_2$) in the presence of acetic anhydride at 0˚C to get **16** of 62%, in this case, both α and β products form, two anomeric peaks form. Then disaccharide derivative **16** was treated with trimethyl(phenylthio)silane in the presence of ZnI_2 in DCM at room temperature, leading to disaccharide thioglycoside donor **17** in a 96% yield, anomeric proton appears at 5.26 ppm as singlet indicating 1,4-α-glycosidic linkage. Using comp **19**, we attempted to synthesize partially and

fully sulfate analogs **(Scheme 3)**. Comp **19** was first glycosylated with azide linker (**L**) in the presence of NIS and TMSOTf to get 95% yield of **18**. Then naphthyl groups or global deprotected disaccharide was subjected to sulfation reaction as explained above. Unfortunately, we failed to obtain a fully sulfated compound after several attempts. We observed several partially sulfated disaccharide analogs in the compound, indicating that the sterically hindered 3-OH is not undergoing sulfation. Currently, we are planning to do step-by-step sulfation to achieve full sulfation.



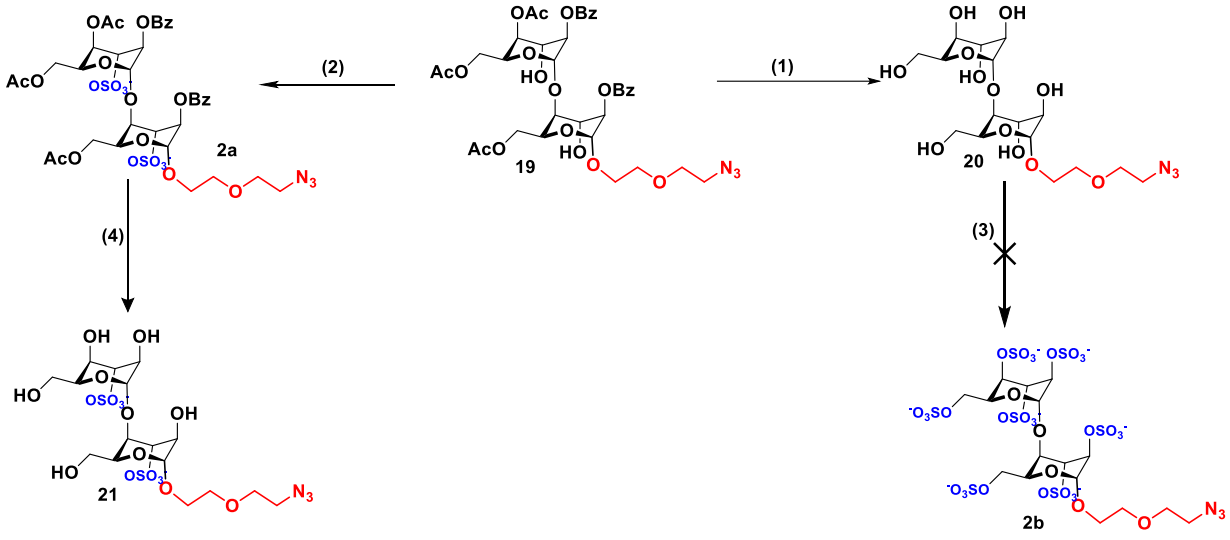
Scheme 3: Synthesis of Disaccharide Precursor

(j)TMSOTf, NIS, Dry DCM, -10°C, 68%; (k) $Cu(OTf)_2$, Ac_2O, 0 °C – RT, 12 h , 83%; (l) TMSSPh, ZnI_2, Dry DCM, 1 hr, 95% (m) TMSOTf, NIS, Dry DCM, -10°C, 85%; (n) DCM:H2O(18:1), DDQ, RT, 3h, 78%.

2.4. Synthesis of Sulfated Disaccharide Analogs

We attempted synthesizing 3-*O* sulphated and fully sulphated analogs of Disaccharide [5]. 3-*O* sulphated analog was synthesized from compound **19** using $SO_3.NMe_3$ salt with DMF in microwave at 100°C for half an hour (**2a**), the peak for proton at 3 position shifts downfield towards 4.5 ppm from non-sulfated 3rd position proton at 3.8 ppm. For fully sulphated molecule **19** was further deprotected completely using LiOH and THF:MeOH:H_2O (4:2:1) and then the resulting molecule (**20**) was treated in the presence of $SO_3.NMe_3$ salt with DMF for 40 minutes in the

microwave, this reaction did not go completely. The NMR of **2b** showed secondary peaks to the molecule peaks in 5.0 to 5.5 ppm region, indicating that sulfation reaction was partially pursued, it could be because of steric hindrance of 3-O-sulfation groups. We are now planning to keep this reaction for longer time to get fully sulfated analog.



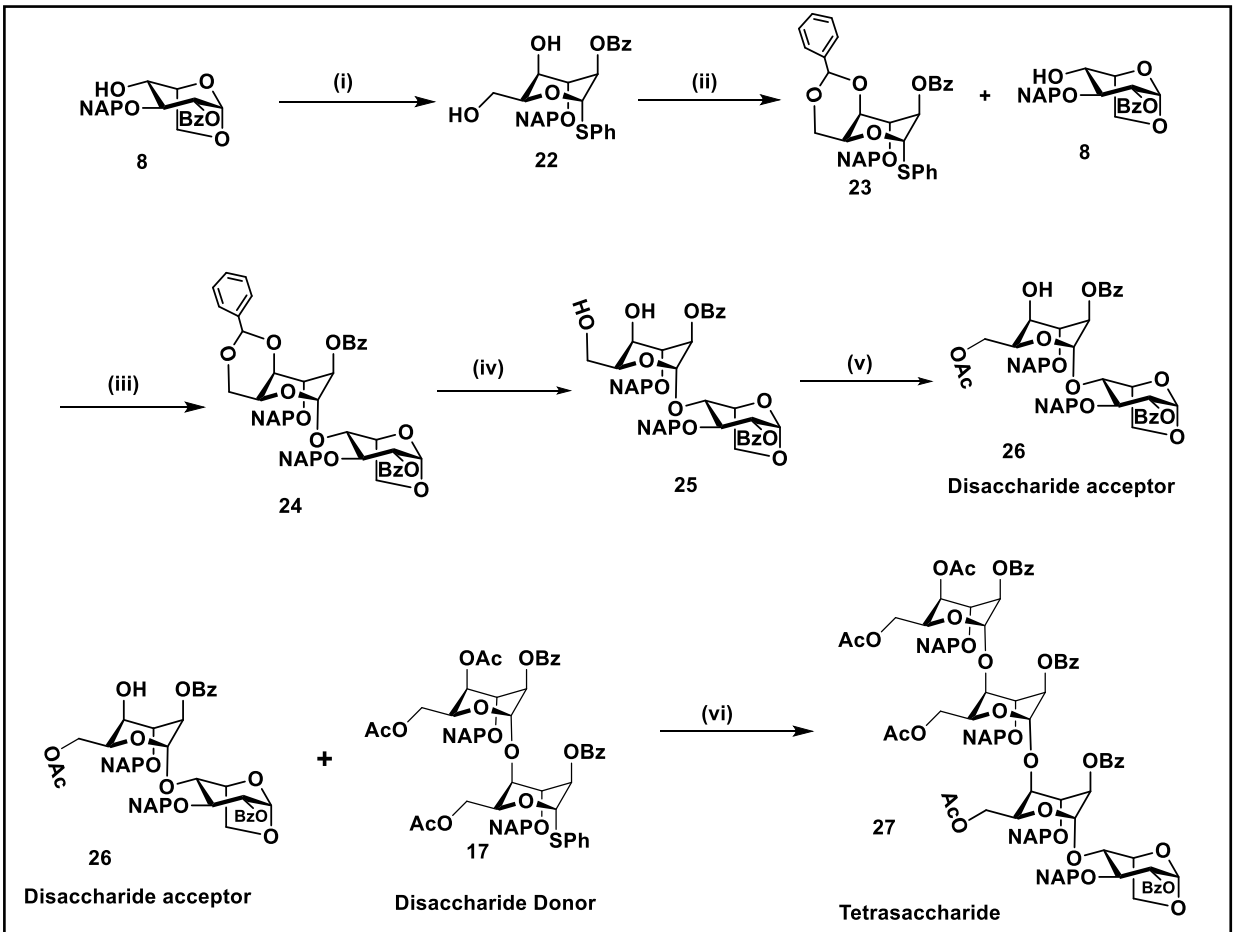
Scheme 4: Sulfation of Disaccharide

1) LiOH, THF:MeOH:H_2O, (4:2:1), Overnight, 88% 2) $SO_3.NMe_3$, DMF, 100°C, Microwave, 68% 3) $SO_3.NMe_3$, DMF, 100°C, Microwave; 4) LiOH, THF:MeOH:H_2O (4:2:1), 2hr, 70%

2.5. Synthesis of Tetrasaccharide Idose Precursor

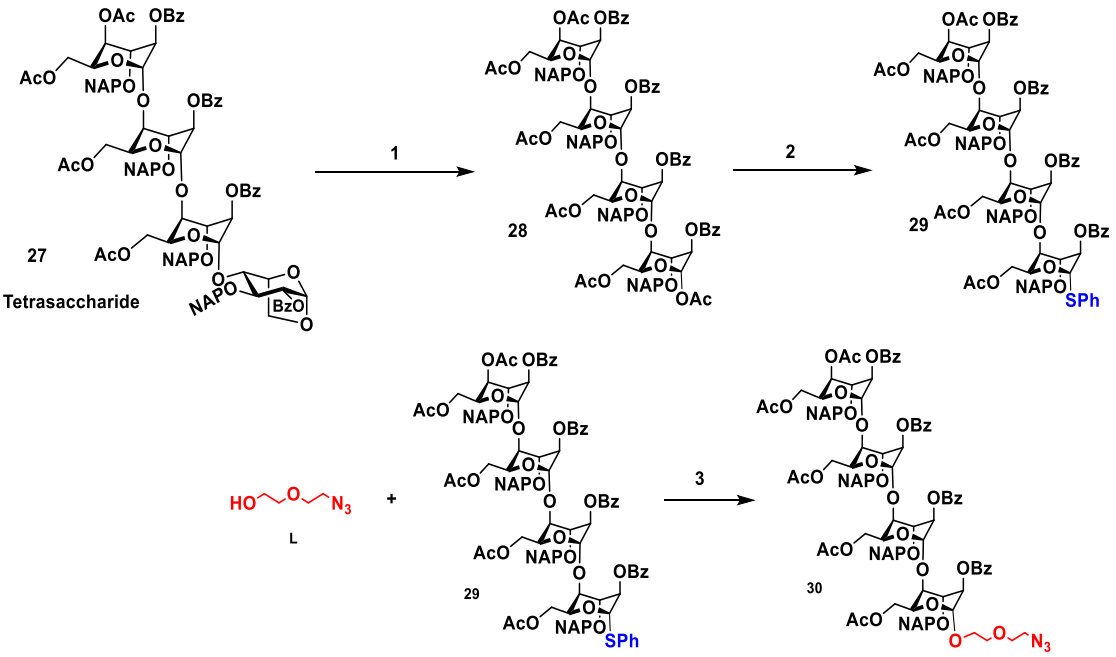
Finally, we attempted to synthesize tetrasaccharide analog using disaccharide acceptor (**26**) and thiophenol donor **22**. The donor **22** was synthesized by ring opening of β-L-idose **8** in the presence of trimethyl(phenylthio)silane and ZnI_2, then after filtering the reaction mixture, it was kept stirring with 3:3:2 ratio of H_2O:1,4-dioxane:10%HCl respectively. Finally, comp **22** was treated with p-toluenesulfonic acid (p-TSA) in the presence of MeOH/DCM (2/1) ratio at room temperature to get **23** of 77% yield. **23** and **8** were glycosylated in the presence of *N*-Iodosuccinimide (NIS) and a catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf) in DCM at -10°C to get 70% of **24**. Then the benzylidene deprotected disaccharide **25** was treated with required amount of acetic anhydride (Ac_2O) and triethyl amine (TEA)) in the presence of DCM at room temperature to get disaccharide acceptor **26**. Compound **17** and **26** were

glycosylated at -10°C in presence of NIS and TMSOTf in DCM to get tetrasaccharide (**27**) (**Scheme 5)**. TLC and NMR studies showed that product and free-OH donor were coming to the same Rf. We tried different solvent systems to separate; however, all attempts failed. Then we decided to proceed further and purify the impurities in the following steps. The tetrasaccharide was converted into donor (**29**) for linker glycosylation by first doing acetylation (**28**) using $Cu(OTf)_2$ in the presence of Ac_2O followed by thiophenol substitution (**29**) using TMSSPh in the presence of DCM at the anomeric position of the fourth ring. It was then glycosylated with the linker **L** to get tetrasaccharide linker (**30**) (**Scheme 6**). Unfortunately, we failed to separate the impurities in all these steps.



Scheme 5: Synthesis of Tetrasaccharide

i) ZnI_2, TMSSPh, H_2O:1,4-dioxane:10% HCl (3:3:2), RT, overnight, 82% ii) benzaldehyde, PTSA, ACN, RT, 2-4 hr, 73%; iii) TMSOTf, NIS, DCM, -10°C, 78%; iv) CSA, DCM:Methanol (1:2), RT, 8 h, 79%; v) Ac_2O, TEA, DCM, 83%; vi) TMSOTf, NIS, DCM, -10°C, 62%.



Scheme 6: Tetrasaccharide precursor

(1) Cu(OTf)2, Ac2O, 0°C to RT, 12 h, 80%; (2). TMSSPh, ZnI2, Dry DCM, 1 h, 85%; (3). TMSOTf, NIS, Dry DCM, -10°C, 75%

3.Conclusion

In conclusion, we have optimized the conditions to synthesize the protected form of L-idose donor in bulk quantity. We have successfully synthesized selective 3-O and fully sulfated L-idose monosaccharides. In the case of disaccharide, we synthesized a partially sulfated analog; however, the fully sulfated analog was a mixture of more than one disaccharide. Unfortunately, these polar compounds were difficult to separate in C18 and size exclusion column chromatography. Therefore, we plan to do step-by-step sulfation to achieve a fully sulfated disaccharide analog. Finally, we attempted to synthesize tetrasaccharide analog using [2+2] glycosylation. The purification of the glycosylated product was challenging as both product and free OH donor came at the same Rf. We proceeded further till linker glycosylation with the impure fraction. However, we failed to separate the mixture again. Now we are planning to synthesize the tetrasaccharide using [2+1+1] strategy [9].

4. Experimental Section

4.1. General Materials and Methods:

The reagents used for synthesis during the project duration were ordered from Sigma-Aldrich, spectrochem, Avra Chemicals. The solvents used for reactions and purification were from Finar sol.

Purification of the molecules was done using column chromatography. For most molecules 100-200 mesh silica was used with solvent system of EtOAc/ pet ether or DCM/ MeOH and a few times EA-PE-DCM system was used. For sulphated molecules size exclusion chromatography LH-20 and G-10 cyclodextrin beads and reverse phase chromatography (Bond elut) were used. Na+, H+ resin was used for neutralization of bases in deprotection reactions of pre-final molecules.

Thin layer chromatography (TLC) was used as primary detector of the reaction process. UV (Ultraviolet) light or CAM charring was used for visibility of spots.

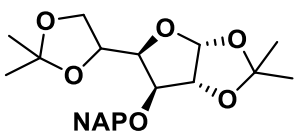
For sulfation Monowave 300 was used from Dr. Shabana Khan's lab.

Jeol 400MHz and Bruker 400MHz spectrometers were used to generate and record all the 1H(400MHz), 13C(101MHz), and 2D NMR spectra. The chemical shifts(δ) for the residual peak of the deuterated solvents in ppm are (1H: $CDCl_3$- 7.26 ppm, MeOH-d4- 3.31 ppm, 4.74ppm, ^{13}C: $CDCl_3$- 77.16 ppm, MeOH-d4 – 49.00 ppm). For NMR analysis MNova software was used. For drawing the structures of molecules ChemDraw Scifinder was used.

5. Synthetic Procedure

5.1. Synthesis of Idose Monosaccharide building block

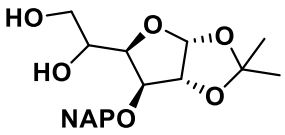
Synthesis of Compound 2-



In a 1L RB flask compound **1** (43 g, 0.167 mol**)** was dissolved in 100ml DMF, the solution cooled down to 0°C. Further, NaH (8.34 g, 0.334 mol) was added to it in portions, followed by slow addition of (2-Bromomethyl)naphthalene (55.6 g, 0.2508 mol), resulting into precipitate formation, so more DMF (approx. 100 ml) was added slowly to dissolve it.

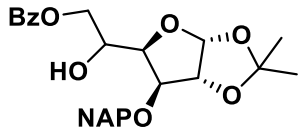
The RM was kept stirring overnight under inert atmosphere. After completion the DMF was evaporated, the RM in fluid form was dissolved in DCM and washed with H_2O and brine alternatively 2-3 times. The DCM layer was dried over Na_2SO_4. DCM was evaporated under reduced pressure. The crude was purified further using column chromatography in DCM/PE solvent system (**90%** yield). **1H NMR:** (400 MHz, $CDCl_3$) δ 7.86 – 7.78 (m, 4H), 7.51 – 7.43 (m, 3H), 5.93 “(d, *J* = 3.7 Hz, 1H), 5.93 (d, *J* = 3.7 Hz, 1H), 4.82 (q, *J* = 12.0 Hz, 2H), 4.82 (q, *J* = 12.0 Hz, 2H), 4.63 (d, *J* = 3.7 Hz, 1H), 4.63 (d, *J* = 3.7 Hz, 1H), 4.42 (dt, *J* = 7.7, 6.0 Hz, 1H), 4.42 (dt, *J* = 7.7, 6.0 Hz, 1H)”, 4.18 – 4.11 (m, 2H), 4.08 (d, *J* = 3.1 Hz, 1H), 4.03 (dd, *J* = 8.6, 5.8 Hz, 1H), 1.46 (d, *J* = 23.7 Hz, 6H), 1.35 (d, *J* = 33.8 Hz, 6H). **^{13}C NMR:** (101 MHz, CHLOROFORM-D) δ 135.15 (s), 133.23 (d, *J* = 17.8 Hz), 128.31 (s), 127.88 (d, *J* = 17.2 Hz), 126.56 (s), 126.19 (d, *J* = 17.5 Hz), 125.74 (s), 111.92 (s), 109.13 (s), 105.41 (s), 82.76 (s), 81.56 (d, *J* = 25.5 Hz), 77.75 – 76.60 (m), 72.57 (d, *J* = 11.2 Hz), 67.52 (s), 26.93 (s), 26.35 (s), 25.57 (s). HRMS (ESI-TOF) m/z [M+Na]+ calculated for $C_{20}H_{24}NaO_6^+$: 423.1778; found: 423.1783.

Synthesis of compound 3-



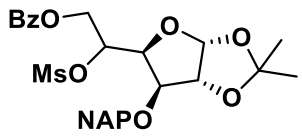
In a 1L RB flask compound **2** (48 g, 0.1218 mol) was partially dissolved in 64% glacial acetic acid (400 ml). The solution was kept in an oil bath that was heat up to 40°C. A reflux condenser was attached to the RB flask. RM was left overnight at 40°C. Once completed the reaction was quenched at ice cold temperature using ice cold $NaHCO_3$. The quenched RM was washed with DCM 3-4 times, the DCM layer was then washed with saturated $NaHCO_3$ 3 times. Further purification was done by column chromatography using EtOAc and DCM system (**83%** yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 – 7.76 (m, 36H), 7.52 – 7.42 (m, 27H), 5.96 (d, *J* = 3.8 Hz, 9H), 5.29 (s, 3H), 4.88 (d, *J* = 11.9 Hz, 9H), 4.69 (dd, *J* = 17.6, 7.9 Hz, 18H), 4.14 (q, *J* = 3.0 Hz, 18H), 4.10 – 4.04 (m, 9H), 3.82 (dd, *J* = 11.5, 3.4 Hz, 9H), 3.71 (dd, *J* = 11.5, 5.4 Hz, 9H), 3.46 (s, 2H), 2.03 (s, 2H), 1.48 (s, 28H), 1.32 (s, 28H). **^{13}C NMR** (101 MHz, CHLOROFORM-D) δ 134.59 (s), 133.23 (d, *J* = 9.2 Hz), 128.75 (s), 127.94 (d, *J* = 18.1 Hz), 126.99 (s), 126.42 (d, *J* = 15.2 Hz), 125.59 (s), 111.95 (s), 105.25 (s), 82.11 (d, *J* = 25.8 Hz), 80.04 (s), 78.13 – 76.44 (m), 72.33 (s), 69.32 (s), 64.44 (s), 26.56 (d, *J* = 49.8 Hz). HRMS(ESI-TOF) m/z [M+Na]+ calculated for $C_{20}H_{24}NaO_6^+$: 383.1465; found: 383.1470

Synthesis of compound 4-



In a 1L RB flask compound **3** (48 g, 0.1331 mol**)** was dissolved in Dry DCM (400 ml) and AR dry Pyridine (100 ml), under inert atmosphere. The solution was cooled down to 0˚C. Then Benzoyl Chloride (18.5 ml, 0.1598 mol) was added dropwise using dropping funnel. After half to one hour at 0˚C the reaction was completed, and was quenched using MeOH, solvent was evaporated. The fluid was dissolved in DCM, and the solution was given 10% HCl wash 3 times, followed by 3 times wash of Sat. $NaHCO_3$. For further purification column chromatography was done using EA/PE solvent system (**73%** yield). **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 8.05 (d, *J* = 1.2 Hz, 3H), “8.03 (d, *J* = 1.4 Hz, 3H), 7.85 (d, *J* = 2.8 Hz, 1H), 7.84 – 7.80 (m, 7H), 7.79 (s, 3H), 7.56 (t, *J* = 1.3 Hz, 1H), 7.54 (t, *J* = 1.8 Hz, 1H),” 7.52 (t, *J* = 1.3 Hz, 1H), 7.49 – 7.46 (m, 6H), 7.45 (d, *J* = 1.6 Hz, 2H), 7.43 (t, *J* = 1.5 Hz, 2H), 7.41 (s, 3H), 7.39 (d, *J* = 1.5 Hz, 1H), 5.99 (d, *J* = 3.7 Hz, 3H), 5.28 (s, 1H), 4.90 (s, 1H), 4.87 (s, 2H), 4.76 (s, 2H), 4.72 (d, *J* = 5.4 Hz, 1H), 4.68 (d, *J* = 3.7 Hz, 4H), 4.65 (d, *J* = 2.8 Hz, 2H), 4.45 (dd, *J* = 11.7, 6.1 Hz, 3H), 4.36 (d, *J* = 6.0 Hz, 3H), 4.25 (d, *J* = 3.2 Hz, 2H), 4.23 (d, *J* = 3.2 Hz, 1H), 4.20 (d, *J* = 3.2 Hz, 3H), 2.15 (s, 4H), 1.46 (s, 9H), 1.32 (s, 9H), -0.01 (d, *J* = 3.2 Hz, 1H). **^{13}C NMR** (101 MHz, CHLOROFORM-D) δ 134.71 – 134.52 (m), 133.25 (s), 129.82 (s), 128.74 (s), 128.47 (s), 128.03 (s), 127.84 (s), 127.01 (s), 126.32 (s), 125.61 (s), 112.40 – 111.53 (m), 105.38 (s), 82.28 (s), 81.77 (s), 79.62 (s), 77.75 – 76.29 (m), 72.46 (s), 68.13 (s), 67.30 (s), 26.66 (d, *J* = 46.2 Hz). HRMS (ESI-TOF) m/z [M+H]+ calculated for $C_{27}H_{29}O^+$: 465.1908; found: 465.1913

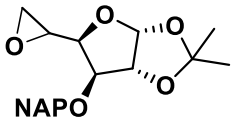
Synthesis of Compound 5-



Compound **4** (35 g, 0.0754 mol) was dissolved in AR Dry Pyridine (100 ml), the solution was then kept in an ice bath while stirring, Methane sulfonyl Chloride (14.5 ml, 0.1884 mol) was added using syringe under inert atmosphere. The reaction was left overnight from 0˚C to RT. “Once completed pyridine was evaporated under reduced pressure. The RM was dissolved in DCM and washed with 10% HCl 2-3 times, the extracted organic layer was again washed with Saturated $NaHCO_3$ and dried over Na_2SO_4”. The formed product was once passed through silica column to ensure purity, using EA/PE solvent system (**76%** yield). **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 8.10 – 8.08 (m, 1H), 8.07 – 8.05 (m, 1H), 7.85 (dd, *J* = 5.5, 1.7 Hz, 2H), 7.83 – 7.79 (m, 2H), 7.59 (dd, *J* = 2.9, 1.6 Hz, 1H), 7.57 (t, *J* = 1.9 Hz, 1H), 7.55 (t, *J* = 1.3 Hz, 1H), 7.53 (d, *J* = 1.7 Hz, 1H),

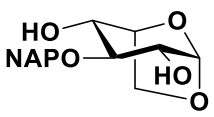
7.51 (d, *J* = 1.7 Hz, 1H), 7.47 (s, 1H), 7.46 (dd, *J* = 2.8, 1.0 Hz, 2H), 7.44 (s, 1H), 7.42 (d, *J* = 1.6 Hz, 1H), 5.95 (d, *J* = 3.6 Hz, 1H), 5.46 (ddd, *J* = 8.1, 6.3, 2.0 Hz, 1H), 4.96 (d, *J* = 2.0 Hz, 1H), 4.93 (d, *J* = 2.0 Hz, 1H), 4.86 (d, *J* = 11.3 Hz, 1H), 4.81 – 4.75 (m, 1H), 4.68 (t, *J* = 7.7 Hz, 1H), 4.53 (d, *J* = 6.3 Hz, 1H), 4.52 – 4.47 (m, 2H), 4.21 (d, *J* = 3.1 Hz, 1H), 2.98 (s, 3H), 1.50 (s, 3H), 1.34 – 1.30 (m, 3H). **^{13}C NMR** (101 MHz, CHLOROFORM-D) δ 167.47 – 165.32 (m), 134.68 (d, *J* = 0.5 Hz), 133.35 (t, *J* = 4.5 Hz), 133.22 – 133.16 (m), 129.99 – 129.80 (m), 129.76 – 129.63 (m), 128.78 – 128.52 (m), 128.41 (d, *J* = 1.4 Hz), 128.20 – 128.14 (m), 127.86 – 127.73 (m), 127.02 (d, *J* = 1.4 Hz), 112.45 – 112.40 (m), 105.48 (d, *J* = 2.3 Hz), 81.67 (s), 78.44 (s), 77.19 (dd, *J* = 42.1, 21.8 Hz), 75.48 (s), 72.60 (s), 64.19 (s), 39.58 – 39.01 (m), 27.74 – 26.09 (m). HRMS (ESI-TOF) m/z [M+NH_4]+ calculated for formula $C_{28}H_{34}NO_9S^+$: 560.1949; found: 560.1957

Synthesis of compound 6 –



The SM (compound **5**) (34 g, 0.0632 mol) was dissolved in DCM (170 ml), then tBuOH (170 ml) was added. $tBuO^-K^+$ (15.5 g, 0.139 mol) was added at 0°C. Precipitate was formed more DCM was added to dissolve it. Reaction was kept overnight under inert atmosphere. RM was dark brown which was an indicator of reaction going well. On completion Solvent was evaporated, the residue was dissolved in DCM. Organic layer was washed with brine and dried over Na_2SO_4, and evaporated under reduced pressure. The column chromatography was done in three solvents (**64%** yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 – 7.70 (m, 12H), 7.57 – 7.39 (m, 9H), 6.03 (d, *J* = 3.8 Hz, 3H), 5.29 (s, 1H), 4.89 (t, *J* = 12.2 Hz, 3H), 4.68 (t, *J* = 7.9 Hz, 6H), 4.01 (d, *J* = 3.5 Hz, 3H), 3.81 (dd, *J* = 6.1, 3.5 Hz, 3H), 3.32 (ddd, *J* = 6.2, 4.3, 2.7 Hz, 3H), 2.82 – 2.72 (m, 3H), 2.53 (dd, *J* = 4.9, 2.7 Hz, 3H), 1.44 (s, 9H), 1.33 (s, 9H). **^{13}C NMR** (101 MHz, CHLOROFORM-D) δ 134.71 (s), 133.51 – 132.89 (m), 128.68 – 128.34 (m), 127.98 – 127.82 (m), 127.07 – 126.67 (m), 126.51 – 126.47 (m), 126.33 – 126.28 (m), 125.57 (s), 112.06 (s), 105.56 (d, *J* = 2.2 Hz), 82.57 (dd, *J* = 6.3, 5.0 Hz), 82.13 (s), 77.48 (d, *J* = 6.2 Hz), 77.13 (s), 76.81 (s), 50.61 – 49.92 (m), 43.33 (s), 26.67 (d, *J* = 50.9 Hz).

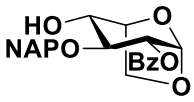
Synthesis of compound 7 –



Compound **6** (14.3 g, 0.04187 mol) was dissolved in 1,4-Dioxane (90 ml), 2N H_2SO_4 (90 ml) was added to it. The RB flask was kept on reflux at 105˚C overnight. After completion the solvent was evaporated. The RM was dissolved in EtOAc, the organic layer was washed with brine and dried over Na_2SO_4. Column chromatography was done for further

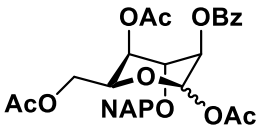
purification, EtOAc and DCM were used for column (**63%** yield)." "**^{1}H NMR** (400 MHz, MeOD) δ 7.80 – 7.68 (m, 1H), 7.47 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.40 – 7.31 (m, 1H), 5.15 (d, *J* = 1.8 Hz, 1H), 4.95 (t, *J* = 8.1 Hz, 1H), 4.29 (t, *J* = 4.6 Hz, 1H)", 4.21 (s, 1H), 4.01 (d, *J* = 7.7 Hz, 1H), 3.78 (dd, *J* = 7.8, 4.1 Hz, 1H), 3.62 (dd, *J* = 7.1, 5.4 Hz, 1H), 3.51 (dd, *J* = 7.9, 1.7 Hz, 1H), 3.46 (t, *J* = 8.0 Hz, 1H), 3.27 – 3.22 (m, 1H). **^{13}C NMR** (101 MHz, MeOD) δ 136.24 (s), 133.16 (d, *J* = 33.2 Hz), 128.21 – 127.08 (m), 126.34 (s), 126.00 – 125.42 (m), 102.15 (s), 83.48 (s), 77.57 (dd, *J* = 42.1, 22.8 Hz), 75.75 (s), 74.83 (d, *J* = 6.2 Hz), 71.13 (s), 64.72 (s), 49.26 – 47.45 (m). HRMS m/z calculated for [M+Na]+ $C_{17}H_{18}NaO_5^+$: 325.1046; found: 325.1048

Synthesis of compound 8-



Compound **7** (8 g, 0.0278 mol) was dissolved in DCM: Pyridine (4:1), the solution was taken to 0°C, benzoyl chloride (3.86 ml, 0.03336 mol) was then added dropwise using dropping funnel. Kept for half an hour under inert atmosphere, once completed reaction was quenched with MeOH. Solvent was evaporated. Work up was done using DCM, 10% HCl and later organic layer was washed with $NaHCO_3$ and dried over Na_2SO_4. Further purification was done by column chromatography using solvent system EtOAc and pet ether (**79%** yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 – 8.00 (m, 2H), 7.78 – 7.74 (m, 1H), 7.71 (dt, *J* = 9.4, 5.2 Hz, 3H), 7.59 – 7.53 (m, 1H), 7.46 – 7.41 (m, 3H), 7.39 (d, *J* = 7.6 Hz, 2H), 7.36 (d, *J* = 1.6 Hz, 1H), 5.53 (d, *J* = 1.7 Hz, 1H), 5.10 (dd, *J* = 8.2, 1.7 Hz, 1H), 4.93 (d, *J* = 11.9 Hz, 1H), 4.83 (d, *J* = 11.9 Hz, 1H), 4.47 (t, *J* = 4.6 Hz, 1H), 4.14 (d, *J* = 7.8 Hz, 1H), 3.91 (t, *J* = 8.2 Hz, 1H), 3.72 (dt, *J* = 16.3, 8.1 Hz, 1H). **^{13}C NMR** (101 MHz, CHLOROFORM-D) δ 165.91 (s), 135.46 (s), 133.52 (s), 133.17 (d, *J* = 15.8 Hz), 129.92 (s), 129.45 (s), 128.58 (d, *J* = 4.2 Hz), 127.88 (d, *J* = 16.3 Hz), 126.86 (s), 126.24 (d, *J* = 17.3 Hz), 125.75 (s), 99.57 (s), 80.31 (s), 77.59 – 76.63 (m), 75.02 (d, *J* = 39.4 Hz), 71.60 (s), 65.41 (s). HRMS m/z [M+Na]+ calculated for $C_{24}H_{22}NaO_6^+$: 429.1309; found: 429.1313

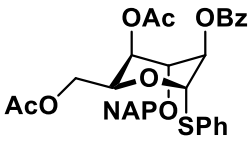
Synthesis of compound 9 –



Compound **8** (4.6 g, 8.85 mmol) was dissolved in Ac2O (20 ml), $Cu(OTf)_2$ (0.335 g, 0.885 mmol) was added to the solution at 0˚C. Reaction was allowed to stir overnight at RT. Once completed Ac2O was evaporated. RM was dissolved in EtOAc. The organic layer was extracted in EtOAc, washed using $NaHCO_3$, and dried over Na_2SO_4. Column chromatography for further purification (**83%** yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 0.8 Hz, 1H), 8.10 (d, *J* = 1.4 Hz, 1H), 8.09 (d, *J* = 1.1 Hz, 1H), 8.07 (t, *J* = 1.5 Hz, 1H),

7.89 – 7.81 (m, 1H), 7.63 – 7.55 (m, 1H), 7.52 – 7.42 (m, 2H), 7.26 (s, 1H), 6.24 (d, *J* = 1.6 Hz, 1H), 5.38 – 5.33 (m, 1H), 5.28 (dd, *J* = 4.3, 3.1 Hz, 1H), 5.05 (s, 1H), 5.01 – 4.97 (m, 1H), 4.95 – 4.93 (m, 1H), 4.90 (d, *J* = 1.9 Hz, 1H), 4.64 (td, *J* = 6.5, 1.6 Hz, 1H), 4.50 (ddd, *J* = 7.4, 5.6, 2.0 Hz, 1H), 4.33 (d, *J* = 4.9 Hz, 1H), 4.31 – 4.25 (m, 1H), 4.23 (d, *J* = 6.1 Hz, 1H), 4.06 (t, *J* = 3.1 Hz, 1H), 3.96 (td, *J* = 2.8, 1.3 Hz, 1H), 2.12 – 2.01 (m, 2H), 1.96 – 1.90 (m, 1H), 1.61 (d, *J* = 12.1 Hz, 1H).

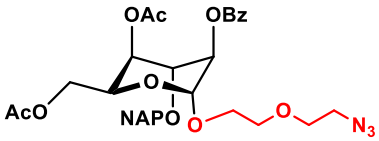
Synthesis of Compound 10 –



Compound **9** (3.6 g, 6.56 mmol) was dried properly. The RB flask was covered with aluminium foil, ZnI_2 (4.4 g, 13.76 mmol) was weighed and added to it. The RB flask was kept on high vacuum for 3 hr. After removing inert atmosphere was maintained. Dry DCM was added under Nitrogen gas and the RM was kept stirring, TMSSPh (3.7 g, 20.33 mmol) was added to it at RT. Rection was completed in an hour. RM was Celite filtered. Column chromatography was done for further purification (**92%**). **^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 8.06 (ddd, *J* = 4.0, 3.3, 2.8 Hz, 1H), 7.92 (s, 1H), 7.88 (d, *J* = 8.5 Hz, 1H), 7.85 – 7.82 (m, 1H), 7.60 (t, *J* = 1.9 Hz, 1H), 7.58 (t, *J* = 1.5 Hz, 1H), 7.56 (d, *J* = 1.3 Hz, 1H), 7.55 (t, *J* = 1.3 Hz, 1H), 7.50 – 7.46 (m, 1H), 7.45 – 7.39 (m, 1H), 5.65 (s, 1H), 5.53 – 5.48 (m, 1H), 5.13 (dt, *J* = 4.5, 1.9 Hz, 1H), 5.10 – 5.04 (m, 1H), 4.94 (t, *J* = 8.8 Hz, 1H), 4.36 – 4.22 (m, 1H), 3.96 (dd, *J* = 2.5, 1.1 Hz, 1H), 2.03 (s, *J* = 3.8 Hz, 1H), 1.95 (s, *J* = 2.9 Hz, 1H). HRMS m/z calculated for $C_{34}H_{32}NaO_8S^+$: 623.1710; found: 623.1713

5.2. Synthesis of Sulphated Monosaccharide Analogs

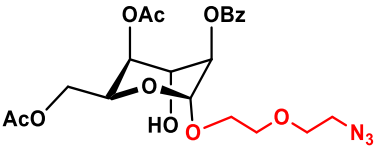
Synthesis of Compound 11-



Compound **10** (560 mg, 0.932 mmol) and linker **L** (183.3 mg, 1.398 mmol) were glycosylated at -10˚C in the presence of TMSOTf (33.74 µl, 0.186 mmol), NIS (272.6 mg, 1.212 mmol) and 4 Å molecular sieves in DCM for 1hr. After completion, triethylamine was used to quench the reaction. $Na_2S_2O_3$ work up was done. Silica column was done for purification (**78%**). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.13 – 8.02 (m, 2H), 7.84 (dd, *J* = 12.7, 5.6 Hz, 4H), 7.63 – 7.56 (m, 1H), 7.51 (dd, *J* = 8.6, 1.3 Hz, 1H), 7.49 – 7.41 (m, 4H), 5.32 – 5.26 (m, 1H), 5.01 (dd, *J* = 16.6, 9.9 Hz, 3H), 4.87 (d, *J* = 11.8 Hz, 1H), 4.61 (td, *J* = 6.4, 1.5 Hz, 1H), 4.23 (t, *J* = 5.9 Hz, 2H), 3.98 – 3.92 (m, 1H), 3.89 (dd, *J* = 3.4, 1.7 Hz, 1H), 3.76 – 3.67 (m, 3H), 3.64 (dt, *J* = 9.9, 4.8 Hz, 1H), 3.56 (dd, *J* = 10.5, 5.0

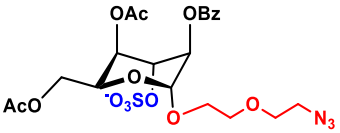
Hz, 1H), 3.19 – 3.12 (m, 2H), 2.02 (d, *J* = 26.9 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.42 (d, *J* = 52.6 Hz), 165.16 (s), 135.06 (s), 133.55 (s), 133.13 (d, *J* = 17.4 Hz), 129.82 (s), 129.47 (s), 128.45 (s), 128.24 – 127.41 (m), 126.53 (s), 126.09 (d, *J* = 16.9 Hz), 125.69 (s), 98.22 (s), 77.80 – 76.22 (m), 72.55 (d, *J* = 43.4 Hz), 70.23 (d, *J* = 12.4 Hz), 67.96 – 66.85 (m), 63.31 (d, *J* = 84.5 Hz), 50.71 (s), 20.80 (d, *J* = 4.1 Hz). HRMS m/z [M+Na]+ calculated for $C_{32}H_{35}N_3NaO_{10}^+$: 644.2215; found: 644.2212

Synthesis of Compound 12-



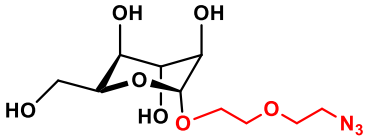
Compound **11** (440 mg, 0.707 mmol) was dissolved in DCM and water was added maintaining solvent ratio (18:1). DDQ (481.8 mg, 2.122 mmol) was added to the solution at RT. The reaction was kept overnight. After completion quenched and washed with sat. $NaHCO_3$. Column was done for more purification (**71%**). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 15.4, 8.4 Hz, 1H), 7.63 – 7.54 (m, 1H), 7.45 (t, *J* = 7.7 Hz, 1H), 7.27 (s, 1H), 5.14 – 5.06 (m, 1H), 4.98 (s, 1H), 4.58 (td, *J* = 6.5, 1.8 Hz, 1H), 4.27 (dd, *J* = 7.1, 4.3 Hz, 1H), 4.06 (s, 1H), 4.01 – 3.93 (m, 1H), 3.77 – 3.66 (m, 3H), 3.58 – 3.47 (m, 1H), 3.44 – 3.37 (m, 1H), 2.09 (s, 1H), 2.00 (s, 1H). HRMS m/z calculated for $C_{21}H_{27}N_3NaO_{10}^+$: 504.1589; found: 504.1589

Synthesis of Compound 13-



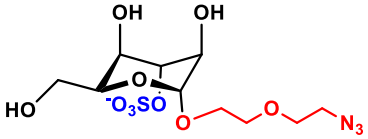
Compound **12** (100 mg, 0.207 mmol) was dried over high vacuum in a G-10 sulfation tube and salt $SO_3.NMe_3$ (289 mg, 2.077 mmol) was added to it and kept under high vacuum for 2 more hours then DMF (2 ml) was added to the tube, the sulfation was carried out in microwave at 100°C and power of 800W for ½ hr, DMF was evaporated under reduced pressure. Silica column was done for purification (**90%**). **^{1}H NMR** (400 MHz, MeOD) δ 7.98 (dd, *J* = 5.1, 3.3 Hz, 1H), 7.57 – 7.51 (m, 1H), 7.40 (dd, *J* = 10.7, 4.8 Hz, 1H), 5.17 – 5.12 (m, 1H), 5.09 (d, *J* = 1.4 Hz, 1H), 4.92 (s, 1H), 4.67 (s, 2H), 4.54 (td, *J* = 3.0, 1.0 Hz, 1H), 4.48 (ddd, *J* = 7.0, 5.2, 1.4 Hz, 1H), 4.12 (qd, *J* = 11.4, 6.3 Hz, 1H), 3.81 (ddd, *J* = 10.6, 5.7, 3.3 Hz, 1H), 3.77 – 3.71 (m, 1H), 3.67 – 3.60 (m, 2H), 3.29 (t, *J* = 4.9 Hz, 1H), 3.25 (d, *J* = 5.4 Hz, 1H), 3.21 (dt, *J* = 3.2, 1.6 Hz, 1H), 2.83 (s, 1H), 1.96 (d, *J* = 4.9 Hz, 3H). HRMS m/z [M-H]- calculated for $C_{21}H_{26}N_3O_{13}S^-$: 559.1108; found: 559.1102

Synthesis of Compound 14-



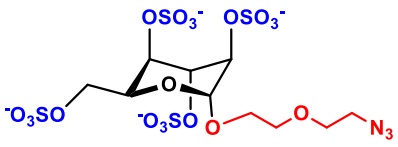
After dissolving SM **12** (138 mg, 0.2907 mmol) in THF, MeOH and water were added, solvent ratio (4:2:1). Lithium Hydroxide Monohydrate (183 mg, 4.369 mmol) was added at 0˚C. Reaction kept overnight. Once completed the RM was neutralized using Amberlite H^+ resin. Solvent evaporated under reduced pressure. Silica column was done for further purification (**70%**). **^{1}H NMR** (400 MHz, MeOD) δ 4.71 (d, *J* = 2.6 Hz, 1H), 3.99 (ddd, *J* = 7.2, 4.9, 2.4 Hz, 1H), 3.88 – 3.79 (m, 1H), 3.72 – 3.67 (m, 1H), 3.61 (dddd, *J* = 9.1, 6.4, 4.9, 3.3 Hz, 6H), 3.54 (d, *J* = 5.3 Hz, 1H), 3.48 – 3.44 (m, 1H), 3.32 – 3.26 (m, 2H), 3.21 (dt, *J* = 3.2, 1.6 Hz, 1H). **^{13}C NMR** (101 MHz, MeOD) δ 101.01 (s), 70.54 (s), 69.74 (dd, *J* = 13.9, 2.8 Hz), 68.88 (s), 66.83 (s), 61.17 (s), 50.39 (s), 48.25 (s), 48.14 – 47.51 (m), 47.40 (s), 47.19 (s), 46.98 (s). HRMS m/z [M+Na]+ calculated for $C_{10}H_{26}N_3NaO7^+$: 316.1115; found: 316.1118

Synthetic procedure of 1a-



The SM **13** (41 mg, 0.0732 mmol) was dissolved in THF, MeOH and H_2O were added maintaining solvent ratio 4:2:1 respectively. Lithium Hydroxide monohydrate (11.05 mg, 0.2633 mmol) was added at 0˚C. After completion in 1hr, the RM was quenched using Amberlite H^+ resin till the pH becomes neutral and filtered. The solvent was evaporated. Silica column and LH-20 resin column chromatography were used for further purification. **^{1}H NMR** (400 MHz, MeOD) δ 4.71 (s, 1H), 4.35 (dd, *J* = 5.2, 2.2 Hz, 1H), 4.02 (ddd, *J* = 6.8, 5.2, 1.6 Hz, 1H), 3.85 – 3.79 (m, 2H), 3.76 – 3.69 (m, 2H), 3.68 – 3.60 (m, 5H), 3.55 – 3.49 (m, 1H), 3.29 (t, *J* = 4.9 Hz, 2H), 3.25 (s, 1H), 3.21 (dt, *J* = 3.1, 1.5 Hz, 1H**). ^{13}C NMR** (101 MHz, MeOD) δ 100.86 (s), 75.09 (s), 69.97 (d, *J* = 53.3 Hz), 67.59 (dd, *J* = 63.5, 30.2 Hz), 61.45 (s), 50.56 (s), 47.65 (dp, *J* = 64.3, 21.4 Hz). HRMS m/z [M-H]- calculated for $C_{10}H_{18}N_3O_{10}S^-$: 371.0634; found: 371.0629

Synthetic procedure of 1b-

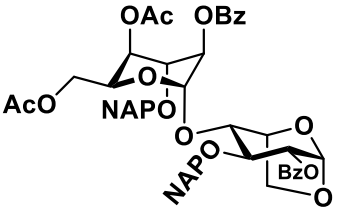


Compound **14** (54 mg, 0.184 mmol) was dried and sulphated in the presence of $SO_3.NMe_3$ (717.5 mg, 5.155 mmol) and DMF (2 ml) at 100°C, 800W for 40 minutes. DMF was evaporated under reduced pressure. G-10 a size exclusion column chromatography and Na^+ resin (ion-exchange) columns were done for further purification (**30%**). **^{1}H NMR** (400 MHz, D_2O) δ 5.09 (s, 1H), 4.98 (d, *J* = 2.7 Hz, 1H), 4.54 (t,

J = 2.8 Hz, 2H), 4.51 – 4.47 (m, 1H), 4.25 (dd, *J* = 11.2, 3.2 Hz, 1H), 4.19 (dd, *J* = 11.2, 8.3 Hz, 1H), 3.97 – 3.90 (m, 1H), 3.78 (dd, *J* = 6.7, 3.2 Hz, 4H), 3.75 – 3.69 (m, 1H), 3.47 (dd, *J* = 5.5, 4.2 Hz, 2H). HRMS m/z calculated for $C_{10}H_{15}N_3O_{19}S_4^{4-}$: 607.9121; found: 607.9118

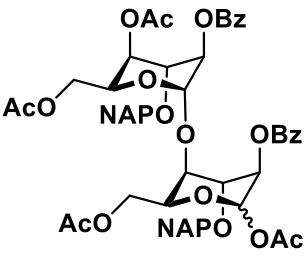
5.3. Synthesis of Idose Disaccharide Precursor

Synthesis of Compound 15 (Glycosylation) –



Monosaccharide donor **10** (1 g, 1.664 mmol) and acceptor **8** (0.733 g, 1.82 mmol) were weighed in an RB flask, and along with magnetic bead the RB was kept on high vacuum for 2 hr. 4 Å molecular sieves were heated for 15 minutes on hot gun, kept on high vacuum after that and when it reached RT the molecular sieves were added to the flask, inert atmosphere was maintained. After keeping the RB flask on high vacuum for 10 minutes after adding the sieves, Dry DCM was added to that and kept for stirring for 2 hr under nitrogen. TMSOTf (62 µl, 0.336 mmol) and NIS (0.486 g, 2.164 mmol) were added at -10˚C. The glycosylation was done in ½ to 1 hr. Celite filtration and $Na_2S_2O_3$ work up was done. Column chromatography was done for further purification. Mixture was eluted which is evident from NMR data, many multiplets are present. In spectra many base peaks are also present (**84%). ^{1}H NMR** (400 MHz, CHLOROFORM-D) δ 8.05 (dt, *J* = 4.6, 2.1 Hz, 2H), 7.89 (s, 1H), 7.84 – 7.81 (m, 1H), 7.78 (dd, *J* = 5.8, 3.8 Hz, 1H), 7.72 – 7.69 (m, 2H), 7.61 (t, *J* = 1.3 Hz, 1H), 7.59 (d, *J* = 1.7 Hz, 1H), 7.58 – 7.55 (m, 2H), 7.54 (d, *J* = 1.6 Hz, 1H), 7.48 – 7.42 (m, 5H), 7.40 (dd, *J* = 4.9, 2.6 Hz, 2H), 7.37 (s, 1H), 7.34 (d, *J* = 1.4 Hz, 1H), 7.33 – 7.31 (m, 1H), 7.25 (s, 3H), 7.20 (ddd, *J* = 8.0, 3.7, 2.1 Hz, 3H), 7.02 (dd, *J* = 8.4, 1.6 Hz, 1H), 5.51 (t, *J* = 2.5 Hz, 1H), 5.26 – 5.25 (m, 1H), 5.15 (s, 1H), 5.03 – 4.98 (m, 2H), 4.94 (t, *J* = 7.4 Hz, 2H), 4.68 – 4.68 (m, *J* = 4.3 Hz, 1H), 4.49 (d, *J* = 11.7 Hz, 1H), 4.29 – 4.24 (m, 2H), 4.05 (td, *J* = 11.4, 5.0 Hz, 2H), 3.93 (dd, *J* = 9.6, 7.2 Hz, 2H), 3.82 (dd, *J* = 10.7, 5.6 Hz, 1H), 1.98 (s, 2H), 1.81 (s, 2H), 1.57 (s, 2H), 1.24 (s, 2H).

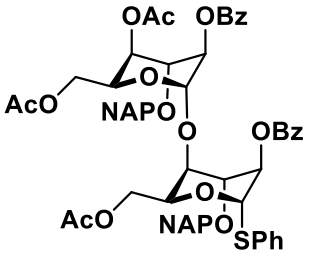
Synthesis of Compound 16 –



Compound **15** (730 mg, 0.813 mmol) was dissolved in Ac_2O (5 ml), $Cu(OTf)_2$ (29.5 mg, 0.0813 mmol) was added to it at 0˚C. Reaction kept overnight at RT. Once completed solvent was evaporated. RM was dissolved in EtOAc, organic layer extracted in EtOAc, washed using $NaHCO_3$, and dried over

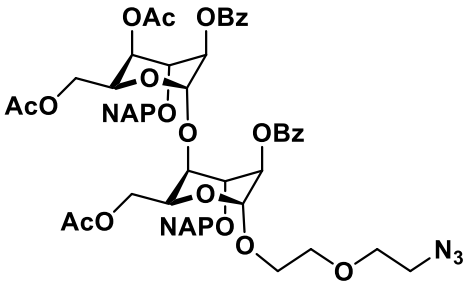
Na_2SO_4. Column chromatography was done for further purification (**91%**). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 – 7.99 (m, 2H), 7.90 (ddd, *J* = 20.1, 13.7, 8.7 Hz, 4H), 7.81 – 7.72 (m, 6H), 7.68 – 7.65 (m, 1H), 7.59 (ddd, *J* = 7.6, 3.1, 1.7 Hz, 2H), 7.51 – 7.36 (m, 8H), 7.13 (dd, *J* = 15.4, 7.4 Hz, 2H), 6.31 – 6.24 (m, 1H), 5.51 (dd, *J* = 4.5, 2.3 Hz, 1H), 5.44 (t, *J* = 1.9 Hz, 1H), 5.28 (s, 1H), 5.21 (s, 1H), 5.08 – 4.95 (m, 3H), 4.86 (dd, *J* = 10.8, 4.5 Hz, 2H), 4.63 – 4.59 (m, 1H), 4.54 – 4.41 (m, 4H), 4.36 (t, *J* = 4.5 Hz, 1H), 4.23 (d, *J* = 2.5 Hz, 1H), 3.93 – 3.81 (m, 3H), 3.36 (dd, *J* = 11.7, 3.9 Hz, 1H), 2.12 (s, 1H), 2.05 (s, 1H), 2.03 (d, *J* = 2.7 Hz, 3H), 1.95 (d, *J* = 2.9 Hz, 3H), 1.84 (s, 1H).

Synthesis of compound 17 –



Compound **16** (1.69 g, 1.693 mmol) was dried properly. The RB flask was covered with aluminium foil, ZnI_2 (1.137 g, 3.56 mmol) was weighed and added to it. The RB flask was kept on high vacuum for 3 hr. After removing inert atmosphere was maintained. Dry DCM was added under Nitrogen gas and the RM was kept stirring, TMSSPh (0.962 g, 5.26 mmol) was added to it at RT. Rection was completed in an hour. RM was Celite filtered. No work up. Column chromatography was done for purification (**96%**). "**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 8.0, 6.6 Hz, 1H), 7.86 (s, 1H), 7.84 – 7.81 (m, 1H), 7.77 – 7.72 (m, 1H), 7.71 (s, 1H)", 7.71 (s, 1H), 7.67 – 7.64 (m, 1H), 7.60 (d, *J* = 7.4 Hz, 1H), 7.57 – 7.55 (m, 1H), 7.54 (d, *J* = 1.6 Hz, 1H), 7.47 – 7.41 (m, 1H), 7.39 – 7.35 (m, 1H), 7.25 (d, *J* = 2.1 Hz, 1H), 7.12 (t, *J* = 7.8 Hz, 1H), 5.70 (s, 1H), 5.62 (s, 1H), 5.26 (s, 1H), 5.14 – 5.05 (m, 1H), 4.99 (d, *J* = 12.1 Hz, 1H), 4.84 (t, *J* = 11.1 Hz, 1H), 4.52 (dt, *J* = 6.2, 3.1 Hz, 1H), 4.46 (ddd, *J* = 6.5, 5.9, 2.3 Hz, 1H), 4.25 (s, 1H), 3.87 – 3.79 (m, 1H), 3.36 (dd, *J* = 11.7, 4.1 Hz, 1H), 2.01 (s, 1H), 1.94 (s, 1H), 1.89 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.62 (d, *J* = 5.5 Hz), 165.29 (d, *J* = 44.1 Hz), 135.62 (s), 134.71 (d, *J* = 13.6 Hz), 133.61 (s), 133.29 (d, *J* = 12.4 Hz), 133.06 (d, *J* = 4.9 Hz), 132.20 (s), 129.89 (d, *J* = 19.3 Hz), 129.34 (s), 129.02 (s), 128.31 (dd, *J* = 18.7, 8.4 Hz), 128.00 (d, *J* = 5.9 Hz), 127.68 (t, *J* = 6.3 Hz), 126.78 (d, *J* = 7.3 Hz), 126.25 – 126.01 (m), 125.86 – 125.59 (m), 101.72 (s), 86.20 (s), 77.42 (d, *J* = 11.0 Hz), 77.05 (s), 76.73 (s), 74.50 (s), 73.23 (s), 72.53 (d, *J* = 8.8 Hz), 68.73 (s), 67.40 (s), 66.90 (s), 65.97 (s), 64.14 (s), 62.84 (d, *J* = 18.1 Hz), 20.66 (d, *J* = 25.3 Hz).

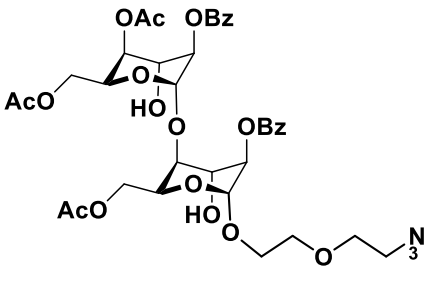
Synthesis of Compound 18 -



Compound **17** (0.953 g, 0.909 mmol) was glycosylated with azide linker (**L**) (178.74 mg, 0.934 mmol) in the presence of TMSOTf, NIS and DCM. Celite filtration was done followed by $Na_2S_2O_3$ work up. Column chromatography was done for further purification (**93%**). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 – 8.00 (m, 1H), 7.96 (s, 1H), 7.90 – 7.86 (m, 1H), 7.82 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.80 – 7.71 (m, 3H), 7.65 (dd, *J* = 8.4, 1.6 'Hz, 1H), 7.62 – 7.56 (m, 1H), 7.26 (s, 1H), 7.15 (t, *J* = 7.9 Hz, 1H), 5.43 (t, *J* = 2.2 Hz, 1H), 5.28 (d, *J* = 5.1 Hz, 1H)', 5.02 (dd, *J* = 13.6, 8.2 Hz, 2H), 4.83 (dd, *J* = 19.7, 11.5 Hz, 1H), 4.58 – 4.43 (m, 3H), '4.16 (t, *J* = 3.0 Hz, 1H), 4.01 – 3.95 (m, 1H), 3.86 (dt, *J* = 13.4, 5.3 Hz, 1H), 3.74 – 3.68 (m, 2H), 3.62 (ddd, *J* = 10.2, 6.0, 4.1 Hz, 1H)', 3.56 (ddd, *J* = 10.4, 5.8, 4.2 Hz, 1H), "3.42 (dd, *J* = 11.6, 4.1 Hz, 1H), 3.17 – 3.12 (m, 1H), 2.03 (s, 1H), 1.95 (s, 1H), 1.92 (s, 1H)". **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.90 – 169.82 (m), 165.27 (d, *J* = 37.6 Hz), 134.99 (d, *J* = 55.8 Hz), 133.60 (s), 133.29 (d, *J* = 4.8 Hz), 133.13 (d, *J* = 2.1 Hz), 132.96 (s), 129.84 (d, *J* = 10.7 Hz), 129.25 (d, *J* = 22.3 Hz), 128.45 (s), 128.25 (d, *J* = 2.3 Hz), 128.11 (s), 127.92 (d, *J* = 11.4 Hz), 127.67 (d, *J* = 4.6 Hz), 126.92 (s), 126.54 (s), 126.08 (d, *J* = 5.8 Hz), 125.95 (s), 125.79 (s), 101.09 (s), 98.44 (s), 77.36 (s), 77.04 (s), 76.72 (s), 75.24 (s), 72.75 (d, *J* = 36.7 Hz), 70.22 (d, *J* = 7.9 Hz), 67.90 (d, *J* = 27.2 Hz), 67.35 (s), 66.79 (s), 65.29 (s), 64.21 – 64.07 (m), 62.81 (d, *J* = 37.3 Hz), 50.68 (s), 20.79 (d, *J* = 3.5 Hz). HRMS m/z [M+Na]+ calculated for $C_{58}H_{59}N_3NaO_{17}$: 1087.4183; found: 1087.4215

5.4. Synthesis of Sulfated Disaccharide Analogs

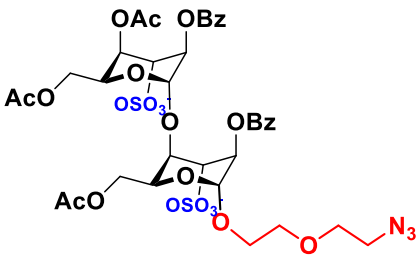
Synthesis of compound 19 –



The SM **18** (1.017 g, 0.95 mmol) was dried properly and dissolved in DCM:H2O (18:1), DDQ(1.16 g, 5.11 mmol) was added to the RM. Reaction was kept overnight at RT. Once completed $NaHCO_3$ was used to quench the reaction and work up. Column chromatography was done for further purification (**69%**). **1H NMR** (400 MHz, CDCl3) δ 8.17 – 8.09 (m, 1H), 8.07 – 7.99 (m, 1H), 7.59 (ddd, J

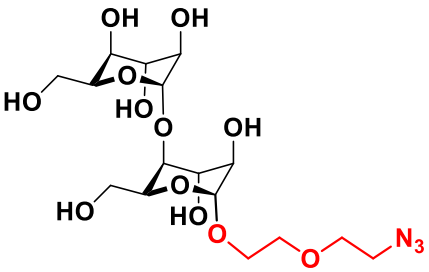
= 13.2, 11.1, 7.4 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.43 (t, J = 7.8 Hz, 1H), 5.28 (d, J = 13.7 Hz, 1H), 5.23 (dd, J = 4.1, 2.4 Hz, 1H), 5.12 – 5.03 (m, 2H), 4.56 – 4.51 (m, 1H), 4.47 (td, J = 6.4, 2.7 Hz, 1H), 4.44 – 4.37 (m, 1H), 4.31 (dd, J = 11.2, 6.1 Hz, 1H), 4.17 – 4.08 (m, 1H), 4.00 – 3.94 (m, 1H), 3.91 (dd, J = 7.7, 3.4 Hz, 1H), 3.87 – 3.83 (m, 1H), 3.75 (dd, J = 11.7, 3.4 Hz, 1H), 3.72 – 3.66 (m, 1H), 3.64 (dd, J = 7.6, 3.0 Hz, 1H), 3.58 (t, J = 8.0 Hz, 1H), 3.45 (s, 1H), 3.37 – 3.29 (m, 1H), 2.10 – 1.97 (m, 5H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.90 – 169.59 (m), 165.40 (d, *J* = 26.2 Hz), 133.63 (d, *J* = 7.2 Hz), 129.90 (d, *J* = 17.9 Hz), 129.24 (d, *J* = 7.5 Hz), 128.55 (d, *J* = 18.9 Hz), 100.95 (s), 98.28 (s), 78.58 (s), 77.15 (dd, *J* = 42.1, 21.9 Hz), 70.43 – 69.89 (m), 69.30 (d, *J* = 24.5 Hz), 68.21 (s), 67.16 (d, *J* = 14.6 Hz), 64.87 (d, *J* = 8.6 Hz), 62.45 (d, *J* = 55.7 Hz), 50.69 (s), 22.15 – 19.63 (m). HRMS m/z calculated for $C_{36}H_{43}N_3NaO_{17}^+$: 812.2485; found: 812.2491

Synthesis of Compound 2a-



Compound **19** (53 mg, 0.067 mmol) was dried in a G-10 sulfation tube, and sulphated in the presence of $SO_3.NMe_3$ (186.79 mg, 1.34 mmol) and DMF (2 ml) at 100°C, 800W for 1/2hr in a microwave. Solvent was evaporated under reduced pressure. Molecule is quite labile due to which we had to take precautions towards its external temperature. Passed through silica column then LH-20 was done as salt was still present (**66%**). **^{1}H NMR** (400 MHz, MeOD) δ 8.17 – 8.08 (m, 1H), 8.04 – 7.94 (m, 1H), 7.58 – 7.48 (m, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 5.35 – 5.25 (m, 1H), 5.06 (s, 1H), 4.92 (d, *J* = 9.9 Hz, 1H), 4.86 (s, 1H), 4.67 (d, *J* = 2.6 Hz, 1H), 4.57 (t, *J* = 3.6 Hz, 1H), 4.51 – 4.39 (m, 1H), 4.30 (d, *J* = 6.7 Hz, 1H), 4.06 – 3.99 (m, 1H), 3.84 – 3.77 (m, 1H), 3.76 – 3.70 (m, 1H), 3.64 (t, *J* = 4.8 Hz, 1H), 3.28 (t, *J* = 5.0 Hz, 1H), 3.23 – 3.19 (m, 1H), 2.00 – 1.84 (m, 1H). HRMS m/z [M-H]- calculated for $C_{36}H_{41}N_3O_{23}S_2^{2-}$: 946.1499; found 946.1501

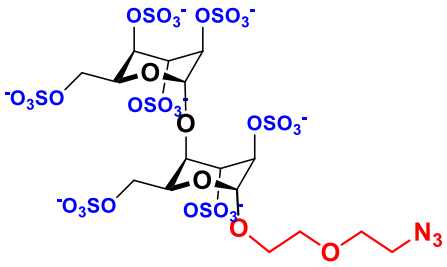
Synthesis of Compound 20-



Compound **19** (71 mg, 0.0899 mmol) was dissolved in THF with MeOH and Water in the solvent ratio (4:2:1) respectively. LiOH (94.30 mg, 2.25 mmol) was added at 0°C. RM was allowed to stir for 3 hr. Once completed the RM was neutralized using H^+ resin, solvent was evaporated under reduced pressure and silica column chromatography was done for purification (**60%**). **^{1}H NMR** (400 MHz, MeOD) δ 4.80 (d,

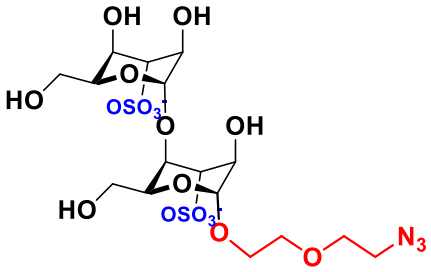
J = 2.4 Hz, 1H), 4.31 (ddd, *J* = 7.1, 4.7, 2.3 Hz, 1H), 4.20 (td, *J* = 6.4, 2.2 Hz, 1H), 4.05 (t, *J* = 4.4 Hz, 1H), 3.95 – 3.88 (m, 1H), 3.84 – 3.78 (m, 3H), 3.78 – 3.74 (m, 2H), 3.74 – 3.69 (m, 4H), 3.68 – 3.62 (m, 2H), 3.60 – 3.54 (m, 1H), 3.44 – 3.39 (m, 2H), 3.33 (dt, *J* = 3.2, 1.6 Hz, 1H**). ^{13}C NMR** (101 MHz, MeOD) δ 102.33 (s), 101.28 (s), 76.80 (s), 69.66 (dd, *J* = 14.4, 12.9 Hz), 69.24 (d, *J* = 12.2 Hz), 67.29 (d, *J* = 82.8 Hz), 61.22 (s, *J* = 87.6 Hz), 60.35 (s), 50.38 (s), 47.63 (dp, *J* = 42.8, 21.4 Hz). HRMS m/z calculated for $C_{16}H_{29}N_3NaO_{12}^+$: 478.1643; found: 478.1642

Synthesis of Compound 2b-



Compound **20** (35 mg, 0.077 mmol) was dried and sulphated in the presence of DMF (2 ml) and $SO_3.NMe_3$ (748 mg, 5.3 mmol). DMF was evaporated under reduced pressure. G-10 size exclusion chromatography was done for purification**. ^{1}H NMR** (400 MHz, D_2O) δ 5.17 (d, *J* = 7.2 Hz, 1H), 5.10 (d, *J* = 8.4 Hz, 1H), 5.07 (s, 1H), 4.80 (s, 1H), 4.58 (d, *J* = 7.0 Hz, 1H), 4.51 – 4.45 (m, 3H), 4.29 – 4.24 (m, 2H), 4.23 – 4.16 (m, 2H), 3.99 (s, 1H), 3.92 (dt, *J* = 8.3, 3.8 Hz, 1H), 3.77 (dd, *J* = 6.4, 3.5 Hz, 4H), 3.73 (d, *J* = 4.0 Hz, 1H), 3.49 – 3.43 (m, 2H).

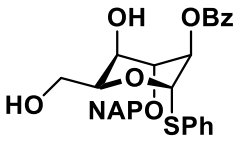
Synthesis of Compound 21-



Compound **2a** (32 mg, 0.03376 mmol) was dissolved in THF with MeOH, H_2O in the solvent ratio (4:2:1). LiOH (8.6 mg, 0.2026 mmol) was added at 0°C. once the reaction is completed the RM was neutralized using Amberlite H^+ resin. LH-20 size exclusion chromatography was done for the purification. NMR data not been obtained yet. **^{1}H NMR** (400 MHz, D_2O) δ 4.82 – 4.76 (m, 1H), 4.54 (t, *J* = 2.3 Hz, 1H), 4.28 (t, *J* = 4.0 Hz, 1H), 4.11 (ddd, *J* = 17.1, 9.9, 4.3 Hz, 1H), 3.91 (d, *J* = 1.4 Hz, 1H), 3.85 (d, *J* = 2.5 Hz, 1H), 3.82 – 3.79 (m, 1H), 3.78 – 3.74 (m, 1H), 3.72 (dd, *J* = 3.3, 2.1 Hz, 1H), 3.69 – 3.61 (m, 4H), 3.34 (t, *J* = 4.9 Hz, 1H).

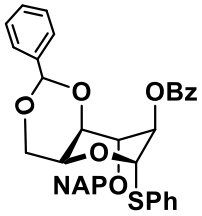
5.5. Synthesis of Idose Tetrasaccharide Precursor

Synthesis of Compound 22-



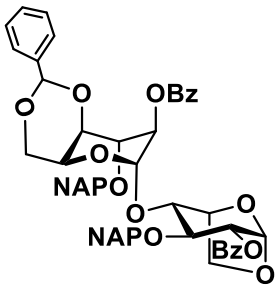
Compound **8** (1.2 g, 2.95 mmol) was taken with ZnI_2 (1.979 g, 6.21 mml) in an RB flask covered with aluminium foil. After drying the compound for 3 hr, it was dissolved in DCM and TMSSPh (1.667 g, 9.15 mmol) was added at RT. The RM was kept for overnight stirring. We got the intermediate from this process, to make product the RM was taken in a conical flask and 10% HCl:H_2O:Dioxane(10:15:15) were added and kept stirring, 1 ml HCl was added at the intervals of ½ hr till the completion of the reaction (**85%**). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 – 7.98 (m, 1H), 7.88 (d, *J* = 6.8 Hz, 1H), 7.86 – 7.82 (m, 1H), 7.59 – 7.55 (m, 2H), 7.50 – 7.46 (m, 1H), 7.43 (dd, *J* = 10.7, 4.8 Hz, 1H), 7.35 – 7.31 (m, 1H), 7.31 – 7.27 (m, 1H), 5.66 (s, 1H), 5.60 – 5.56 (m, 1H), 5.07 (d, *J* = 11.9 Hz, 1H), 4.84 (dd, *J* = 12.8, 6.5 Hz, 1H), 4.06 – 3.96 (m, 1H), 3.93 – 3.87 (m, 1H).

Synthesis of Compound 23-



Compound **22** (1.282 g, 2.481mmol) was dissolved in ACN (12 ml), benzaldehyde (0.755 g, 4.963 mmol) and *p*-TSA (0.0944 g, 0.496 mmol) were added to it. The Reaction was completed in 3 hr. Confirmed using TLC. ACN was evaporated, the residue was dissolved in DCM and given $NaHCO_3$ wash. The organic layer was dried over Na_2SO_4. Column chromatography was done for further purification (**77%**). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.92 (s, 1H), 7.85 (ddd, *J* = 10.6, 7.9, 3.6 Hz, 1H), 7.60 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.58 – 7.54 (m, 1H), 7.52 – 7.44 (m, 2H), 7.33 – 7.26 (m, 2H), 7.23 – 7.17 (m, 1H), 5.84 (s, 1H), "5.59 (d, *J* = 2.9 Hz, 1H), 5.14 (d, *J* = 11.9 Hz, 1H), 4.87 (d, *J* = 11.9 Hz, 1H), 4.55 (s, 1H), 4.40 (d, *J* = 8.1 Hz, 1H), 4.21 (dd, *J* = 12.7, 1.8 Hz, 1H)", 4.14 (s, 1H), 3.98 (s, 1H).

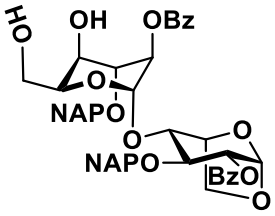
Synthesis of Compound 24-



Compound **8** (1.155 g, 1.91 mmol) and compound **23** (0.621 g, 1.528 mmol) with molecular sieves were dissolved in DCM and glycosylated by adding TMSOTf (0.085 g, 0.382 mmol) and NIS (0.558 g, 25 mmol) at -10˚C. RM was celite filtered and $Na_2S_2O_3$ was used for washing the DCM layer. Organic layer

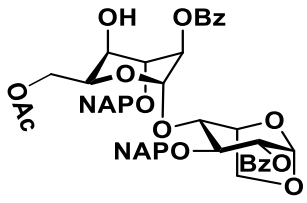
dried over Na_2SO_3. Column chromatography was used for further purification (**72%**). "**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 8.2, 1.1 Hz, 3H)", 7.87 (ddd, *J* = 12.6, 7.2, 3.6 Hz, 5H), 7.70 (dd, *J* = 8.6, 4.3 Hz, 1H), 7.60 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.58 – 7.54 (m, 2H), 7.53 – 7.48 (m, 4H), 7.44 (dd, *J* = 9.4, 2.6 Hz, 3H), 7.42 – 7.37 (m, 3H), 7.31 (ddd, *J* = 7.1, 6.4, 2.9 Hz, 5H), "7.10 (dd, *J* = 8.4, 1.5 Hz, 1H), 5.57 (d, *J* = 1.7 Hz, 1H), 5.29 (dd, *J* = 17.1, 14.3 Hz, 3H), 5.12 – 5.05 (m, 2H), 4.91 (d, *J* = 11.4 Hz, 1H), 4.68 (t, *J* = 4.5 Hz, 1H)", 4.65 – 4.54 (m, 2H), 4.33 (d, *J* = 7.7 Hz, 1H), 4.28 (dd, *J* = 8.3, 3.8 Hz, 1H), 4.10 (s, 1H), 4.08 – 4.03 (m, 1H), 4.00 (t, *J* = 8.4 Hz, 1H), 3.91 (d, *J* = 10.4 Hz, 2H), 3.87 – 3.83 (m, 1H), 3.32 (dd, *J* = 12.7, 1.3 Hz, 1H), 1.56 (s, 3H), 1.27 (d, *J* = 11.7 Hz, 2H). **^{13}C NMR** (101 MHz, CHLOROFORM-D) δ 165.89 (d, *J* = 19.5 Hz), 137.91 (s), 135.90 – 134.76 (m), 133.62 – 132.62 (m), 130.15 (s), 129.82 (s), 129.38 (t, *J* = 1.6 Hz), 128.96 (s), 128.40 (d, *J* = 3.2 Hz), 128.21 – 128.10 (m), 128.00 (s), 127.91 (d, *J* = 4.4 Hz), 127.82 (s), 127.70 (s), 127.21 (s), 126.52 (d, *J* = 3.8 Hz), 126.36 (dd, *J* = 1.7, 0.8 Hz), 126.29 – 126.07 (m), 125.90 (d, *J* = 1.5 Hz), 100.89 (s), 99.50 (s), 95.39 (s), 78.69 (s), 77.43 (s), 77.11 (s), 76.82 (d, *J* = 6.5 Hz), 75.27 (s), 74.35 (s), 73.26 (d, *J* = 52.6 Hz), 72.24 (d, *J* = 48.5 Hz), 65.84 (d, *J* = 21.2 Hz), 59.69 (s).

Synthesis of Compound 25-



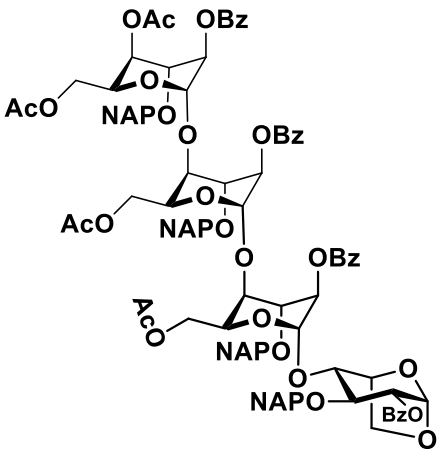
Compound **24** (1.143 g, 1.27 mmol) was dissolved in DCM (5 ml), same volume of MeOH was added to the solution. CSA (0.590 g, 2.54 mmol) was added. After 5 hr the reaction will be completed. Solvent was evaporated, the residue was dissolved in DCM and washed with $NaHCO_3$, and dried over Na_2SO_4. Column chromatography was done for further purification. The product gets precipitated in column (**80%**). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 7.6, 6.3 Hz, 1H), 7.87 (s, 1H), 7.83 – 7.74 (m, 2H), 7.58 (dd, *J* = 5.8, 3.5 Hz, 1H), 7.53 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.46 – 7.39 (m, 2H), 7.35 (dd, *J* = 10.8, 4.8 Hz, 1H), "7.32 – 7.28 (m, 1H), 7.23 (t, *J* = 7.8 Hz, 1H), 7.18 (s, 1H), 7.03 (dd, *J* = 8.4, 1.6 Hz, 1H), 5.41 (d, *J* = 1.6 Hz, 1H), 5.25 – 5.22 (m, 1H), 5.08 (dd, *J* = 9.2, 2.6 Hz, 1H), 4.97 (d, *J* = 11.4 Hz, 1H), 4.85 – 4.80 (m, 1H)", 4.60 (t, *J* = 4.5 Hz, 1H), 4.52 (s, 1H), 4.35 (t, *J* = 4.6 Hz, 1H), 4.24 (dd, *J* = 8.2, 3.3 Hz, 1H), 3.93 (t, *J* = 8.4 Hz, 1H), 3.84 (d, *J* = 2.2 Hz, 1H), 3.77 (dd, *J* = 7.2, 5.2 Hz, 1H), 3.63 (s, 1H), 3.40 (dt, *J* = 12.1, 4.4 Hz, 1H), 3.22 (dd, *J* = 12.1, 3.8 Hz, 1H). HRMS m/z calculated for $C_{48}H_{44}NaO_{12}^+$: 835.2725; found: 835.2730

Synthesis of Compound 26-



Compound **25** (0.83 g, 1.02 mmol) was dissolved in DCM, Ac_2O (1.9 ml, 10.14 mmol) and Triethylamine (0.143 ml,1.02 mmol) was added to it at 0˚C. Once completed the reaction was quenched with triethylamine. The solvent was evaporated and the fluid was dissolved in DCM. The solution was given sat. $NaHCO_3$ wash. The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. Further purification was done using column chromatography (**87%**). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 – 7.99 (m, 1H), 7.86 (s, 1H), 7.83 – 7.76 (m, 2H), 7.71 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.63 – 7.56 (m, 1H), 7.52 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.49 – 7.40 (m, 3H), 7.38 (s, 1H), 7.37 – 7.30 (m, 1H), 7.28 (s, 1H), 7.19 (dd, *J* = 8.1, 7.6 Hz, 1H), 7.07 (dd, *J* = 8.4, 1.6 Hz, 1H), 5.51 (d, *J* = 1.7 Hz, 1H), 5.30 – 5.28 (m, 1H), 5.16 (s, 1H), 5.03 – 4.99 (m, 1H), 4.98 (s, 1H), 4.87 (d, *J* = 11.5 Hz, 1H), 4.76 (d, *J* = 11.8 Hz, 1H), 4.71 – 4.63 (m, 1H), 4.53 (d, *J* = 11.8 Hz, 1H), 4.27 (dd, *J* = 8.2, 2.9 Hz, 1H), 4.19 (dd, *J* = 9.2, 3.6 Hz, 1H), 3.98 – 3.92 (m, 1H), 3.83 – 3.73 (m, 1H), 2.54 (d, *J* = 10.6 Hz, 1H), 1.91 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.92 (s), 165.51 (d, *J* = 48.7 Hz), 135.16 (d, *J* = 78.3 Hz), 133.91 (s), 133.51 – 132.61 (m), 129.70 (d, *J* = 15.7 Hz), 129.03 (d, *J* = 22.6 Hz), 128.77 (s), 128.18 (t, *J* = 28.2 Hz), 127.76 (d, *J* = 1.9 Hz), 127.36 (d, *J* = 40.9 Hz), 126.44 – 126.19 (m), 126.06 – 125.56 (m), 99.41 (s), 95.23 (s), 77.99 (s), 77.38 (s), 77.06 (s), 76.75 (s), 75.21 (d, *J* = 8.8 Hz), 74.17 (s), 72.24 (d, *J* = 102.4 Hz), 67.53 (d, *J* = 123.7 Hz), 65.84 (d, *J* = 57.4 Hz), 63.21 (s), 20.73 (s). HRMS m/z calculated for $C_{50}H_{46}NaO_{13}^+$: 877.2831; found: 877.2839

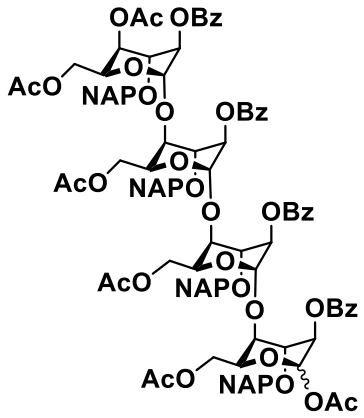
Synthesis of Compound 27-



Compound **17** (donor) (1.02 g, 1.007 mmol) was glycosylated with Compound **26** (acceptor) (0.606 g, 0.708 mmol) (1,4-glycosidic linkage), to form tetrasaccharide. RM was Celite filtered and $Na_2S_2O_3$ work up was done. Organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. For further purification column chromatography was used. Mixture with free OH

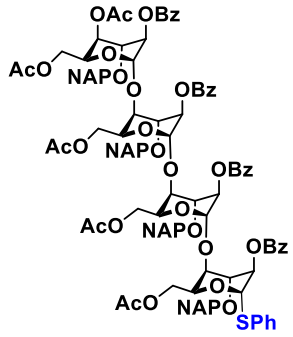
was eluted (**78%**). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 – 7.98 (m, 1H), 7.89 (dd, *J* = 17.1, 6.2 Hz, 1H), 7.83 (dd, *J* = 6.5, 5.3 Hz, 1H), 7.79 (dd, *J* = 6.0, 2.0 Hz, 1H), 7.76 – 7.71 (m, 2H), "7.71 – 7.68 (m, 1H), 7.67 – 7.63 (m, 1H), 7.62 – 7.52 (m, 2H), 7.49 – 7.39 (m, 4H), 7.39 – 7.34 (m, 2H), 7.32 – 7.30 (m, 1H), 7.28 (d, *J* = 4.8 Hz, 1H), 7.22 – 7.13 (m, 2H), 7.08 (dd, *J* = 8.4, 1.5 Hz, 1H), 5.48 (d, *J* = 1.7 Hz, 1H)", 5.40 – 5.33 (m, 1H), 5.20 (d, *J* = 13.6 Hz, 1H), 5.08 (d, *J* = 1.9 Hz, 1H), 5.02 – 4.96 (m, 1H), 4.95 – 4.89 (m, 1H), 4.87 – 4.77 (m, 1H), 4.62 (dd, *J* = 10.2, 5.4 Hz, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.52 – 4.47 (m, 1H), 4.38 (dd, *J* = 6.6, 4.3 Hz, 1H), 4.34 – 4.29 (m, 1H), 4.26 (d, *J* = 5.5 Hz, 1H), 4.23 – 4.16 (m, 1H), 4.15 – 4.11 (m, 1H), 4.10 – 4.07 (m, 1H), 4.01 (dd, *J* = 11.6, 5.0 Hz, 1H), 3.92 (dd, *J* = 9.9, 2.7 Hz, 1H), 3.90 – 3.85 (m, 1H), 3.84 – 3.79 (m, 1H), 3.64 – 3.60 (m, 1H), 3.57 (dd, *J* = 11.4, 4.6 Hz, 1H), 3.51 – 3.43 (m, 1H), 2.02 (d, *J* = 1.4 Hz, 1H), 1.94 (d, *J* = 1.4 Hz, 1H), 1.90 – 1.85 (m, 2H), 1.71 (s, 1H).

Synthesis of Compound 28-



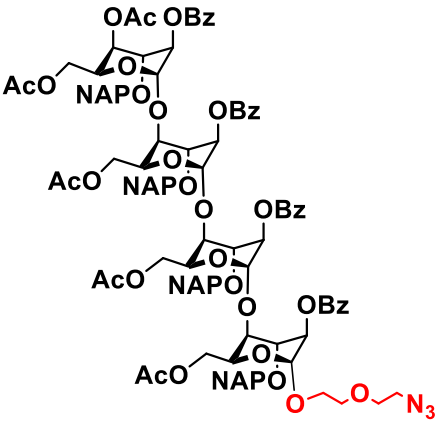
Compound **27** (530 mg, 0.298 mmol) was dissolved in Ac_2O (3 ml), $Cu(OTf)_2$ (11 mg, 0.0298 mmol) was added to it at 0˚C. Reaction kept overnight at RT. Once completed, solvent was evaporated. RM was dissolved in EtOAc, organic layer extracted in EtOAc, washed using NaHCO3, and dried over Na_2SO_4. Column chromatography was done for purification (**66%**). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.2 Hz, 1H), 7.93 (d, *J* = 7.4 Hz, 1H), 7.87 (dd, *J* = 8.0, 6.6 Hz, 1H), 7.82 (dd, *J* = 4.9, 3.5 Hz, 1H), 7.77 – 7.70 (m, 2H), 7.68 – 7.61 (m, 3H), 7.60 – 7.53 (m, 2H), 7.46 (dd, *J* = 7.3, 4.0 Hz, 1H), 7.43 – 7.37 (m, 3H), 7.36 – 7.33 (m, 2H), 7.23 – 7.19 (m, 1H), 7.15 (dd, *J* = 14.6, 6.7 Hz, 1H), 6.27 – 6.20 (m, 1H), 5.42 (dd, *J* = 4.7, 2.3 Hz, 1H), 5.37 – 5.26 (m, 1H), 5.18 (s, 1H), 4.95 (dd, *J* = 7.7, 3.5 Hz, 1H), 4.88 (ddd, *J* = 14.9, 9.5, 6.9 Hz, 2H), 4.81 – 4.75 (m, 1H), 4.65 (s, 1H), 4.55 – 4.46 (m, 1H), 4.40 – 4.32 (m, 1H), 4.26 – 4.21 (m, 1H), 4.15 – 4.02 (m, 2H), 3.87 (d, *J* = 14.0 Hz, 1H), 3.64 – 3.54 (m, 1H), 2.09 (s, 1H), 2.04 (d, *J* = 2.0 Hz, 1H), 1.97 – 1.93 (m, 2H), 1.91 (s, 1H), 1.88 (s, 1H), 1.86 (d, *J* = 2.0 Hz, 1H), 1.84 (s, 1H), 1.81 (s, 1H), 1.79 (s, 1H), 1.73 (d, *J* = 5.1 Hz, 1H).

General synthetic procedure of 29-



Compound **28** (370 mg, 0.197 mmol) was dried properly. The RB flask was covered with aluminium foil, ZnI_2 (132 mg, 0.413 mmol) was weighed and added to it. The RB flask was kept on high vacuum for 3 hr. After removing inert atmosphere was maintained. Dry DCM was added under Nitrogen gas and the RM was kept stirring, TMSSPh (116 µl, 0.610 mmol) was added to it at RT. Rection was completed in an 2hr. RM was Celite filtered. No work up is required. Column chromatography was done for purification (**76%**).

General synthetic procedure of 30-



Compound **29** (0.953 g, 0.909 mmol) was glycosylated with azide linker (**L**) (178.74 mg, 0.934 mmol) in the presence of TMSOTf, NIS and DCM. Celite filtration was done followed by Na2S2O3 work up. Column chromatography was done for further purification (approx**. 50%**). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 – 7.90 (m, 1H), 7.79 (dd, *J* = 11.2, 4.1 Hz, 1H), 7.75 (d, *J* = 7.0 Hz, 1H), 7.71 – 7.61 (m, 2H), 7.61 – 7.54 (m, 2H), 7.53 – 7.46 (m, 2H), 7.42 – 7.34 (m, 2H), 7.33 – 7.24 (m, 4H), 7.16 – 7.06 (m, 2H), 5.31 – 5.20 (m, 1H), 5.14 – 5.09 (m, 1H), 4.89 (dd, *J* = 11.2, 6.4 Hz, 1H), 4.85 – 4.78 (m, 1H), 4.73 (dd, *J* = 9.1, 6.3 Hz, 1H), 4.68 (s, 1H), 4.57 (s, 1H), 4.43 – 4.36 (m, 1H), 4.31 – 4.26 (m, 1H), 4.23 – 4.18 (m, 1H), 4.17 – 4.06 (m, 1H), 4.05 – 3.95 (m, 1H), 3.76 (dd, *J* = 9.9, 4.5 Hz, 1H), 3.64 – 3.57 (m, 1H), 3.56 – 3.44 (m, 2H), 3.05 (dt, *J* = 5.9, 3.9 Hz, 1H), 1.87 (s, 1H), 1.83 (s, 1H), 1.79 (s, 1H), 1.76 (s, 1H), 1.68 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.15 – 169.63 (m), 165.29 (dd, *J* = 32.1, 21.0 Hz), 135.43 – 135.31 (m), 135.05 – 134.48 (m), 133.63 (s), 133.10 (t, *J* = 15.5 Hz), 129.90 (dd, *J* = 15.2, 6.5 Hz), 129.30 (s), 128.48 (s), 128.31 – 128.03 (m), 127.93 – 127.56 (m), 127.00 (s), 126.55 (s), 126.19 – 125.75 (m), 100.43 (d, *J* = 25.5 Hz), 98.32 (s), 77.36 (s), 77.04 (s), 76.72 (s), 76.52 – 75.41 (m), 74.78 (s), 72.98 (dd, *J* = 60.4, 16.3 Hz), 70.21 (s), 68.52 (s), 67.91 (d, *J* = 26.2 Hz), 66.97 (s), 66.27 (s), 65.37 (s), 62.53 (s), 50.67 (s), 29.78 – 29.62 (m), 20.65 (dd, *J* = 14.5, 8.2 Hz).

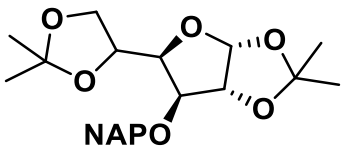
5. References

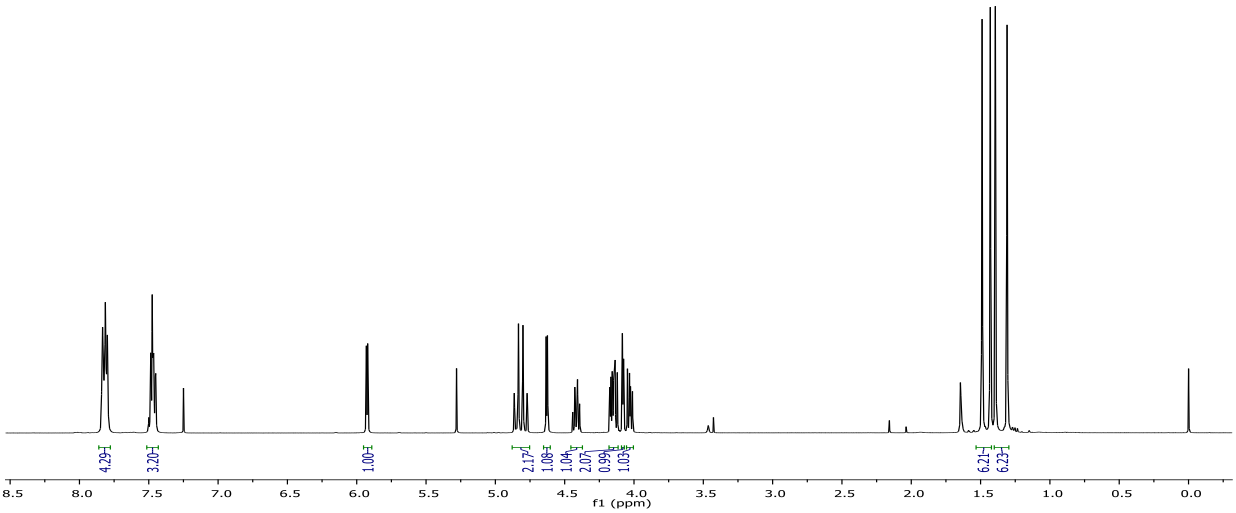
1. Whitelock JM, Iozzo R V. Heparan sulfate: a complex polymer charged with biological activity. *Chem Rev*. 2005;105(7):2745-2764.
2. Sarrazin S, Lamanna WC, Esko JD. Heparan sulfate proteoglycans. *Cold Spring Harb Perspect Biol*. 2011;3(7):a004952.
3. Gallagher JT. Heparan sulfate: growth control with a restricted sequence menu. *J Clin Invest*. 2001;108(3):357-361. doi:10.1172/JCI13713
4. Varki A. Biological roles of glycans. *Glycobiology*. 2017;27(1):3-49.
5. Shanthamurthy CD, Gimeno A, Leviatan Ben-Arye S, et al. Sulfation Code and Conformational Plasticity of l-Iduronic Acid Homo-Oligosaccharides Mimic the Biological Functions of Heparan Sulfate. *ACS Chem Biol*. 2021;16(11):2481-2489. doi:10.1021/acschembio.1c00582
6. Schell P, Orgueira HA, Roehrig S, Seeberger PH. Synthesis and transformations of D-glucuronic and L-iduronic acid glycals. *Tetrahedron Lett*. 2001;42(23):3811-3814.
7. Esko JD, Lindahl U, others. Molecular diversity of heparan sulfate. *J Clin Invest*. 2001;108(2):169-173.
8. Shanthamurthy CD, Leviatan Ben-Arye S, Kumar NV, et al. Heparan Sulfate Mimetics Differentially Affect Homologous Chemokines and Attenuate Cancer Development. *J Med Chem*. 2021;64(6):3367-3380. doi:10.1021/acs.jmedchem.0c01800
9. Shanthamurthy CD, Kikkeri R. Linear Synthesis of De novo Oligo-Iduronic Acid. *European J Org Chem*. 2019;2019(18):2950-2953. doi:https://doi.org/10.1002/ejoc.201900540
10. Gerdy B, Kurup S, van de Westerlo EMA, et al. 3-O-sulfated oligosaccharide structures are recognized by anti-heparan sulfate antibody HS4C3. *J Biol Chem*. 2006;281(8):4654-4662.
11. Lindahl U, Kjellén L. Heparin or heparan sulfate-what is the difference? *Thromb Haemost*. 1991;66(07):44-48.
12. Tumova S, Woods A, Couchman JR. Heparan sulfate proteoglycans on the cell surface: versatile coordinators of cellular functions. *Int J Biochem \& cell Biol*. 2000;32(3):269-288.

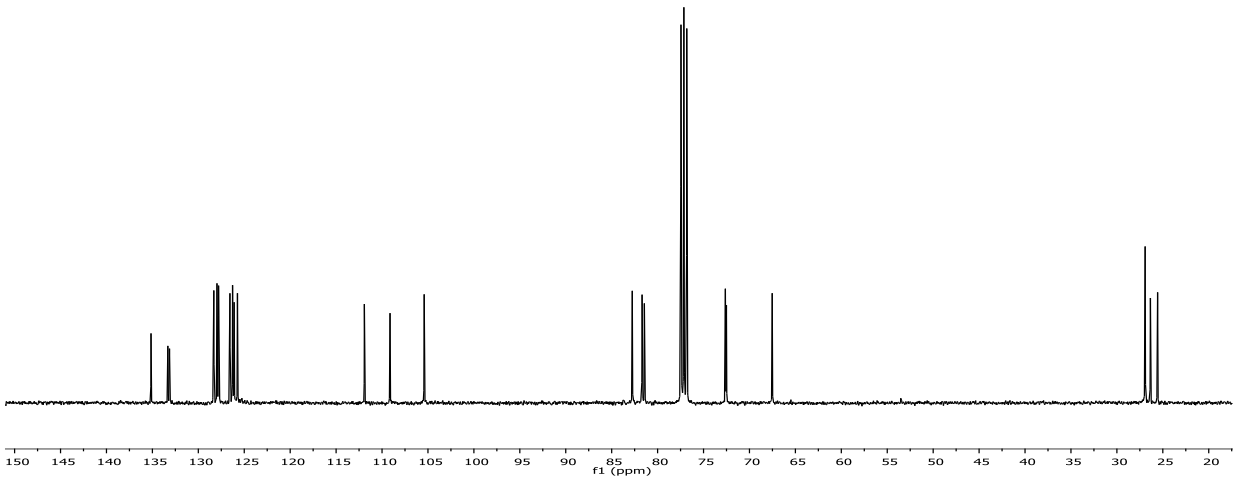
6. Spectral Data

1. Monosaccharide L-Idose NMR

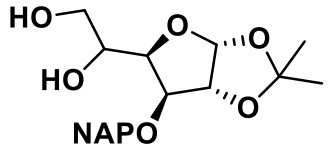
1. 1H and 13C NMR of Compound 2

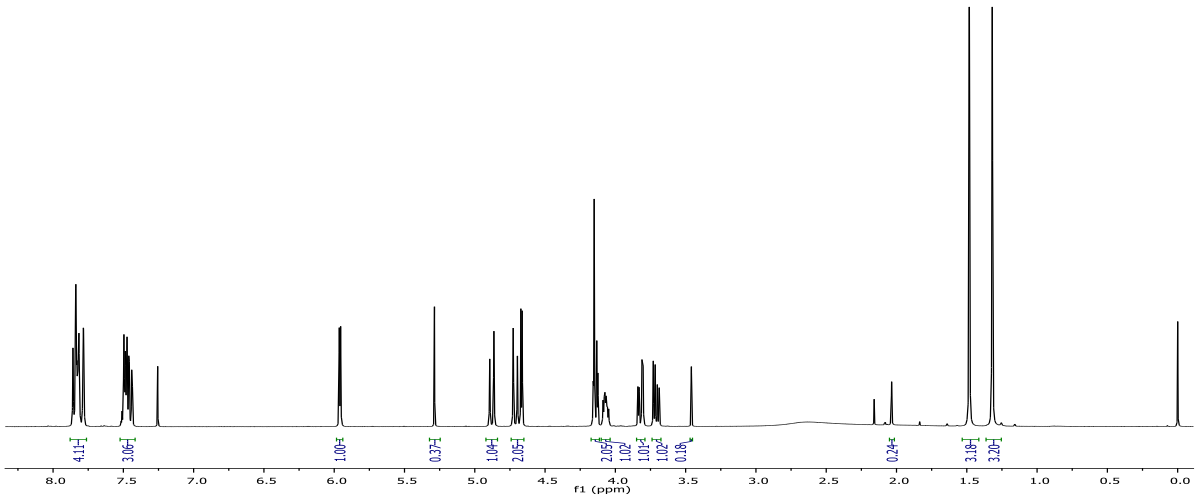


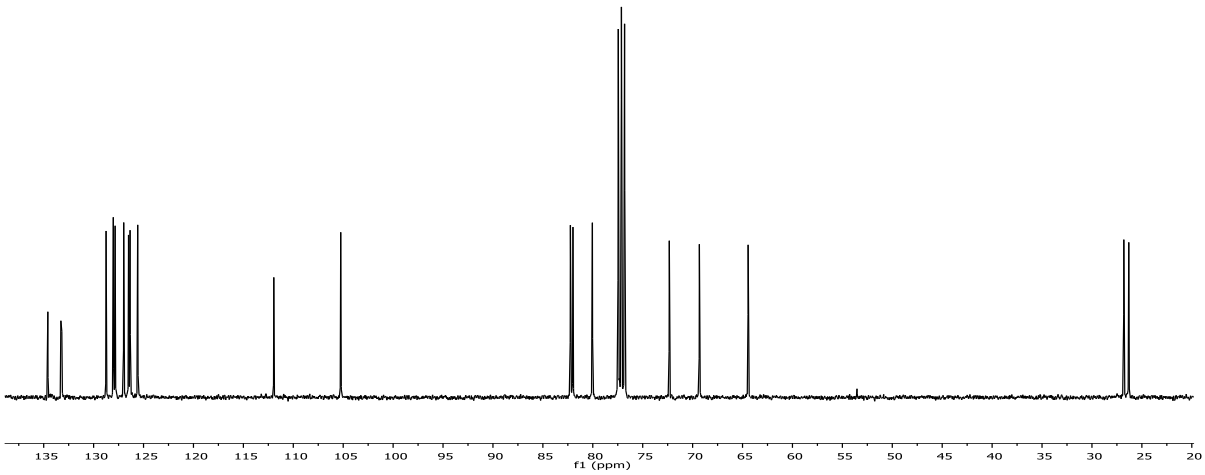


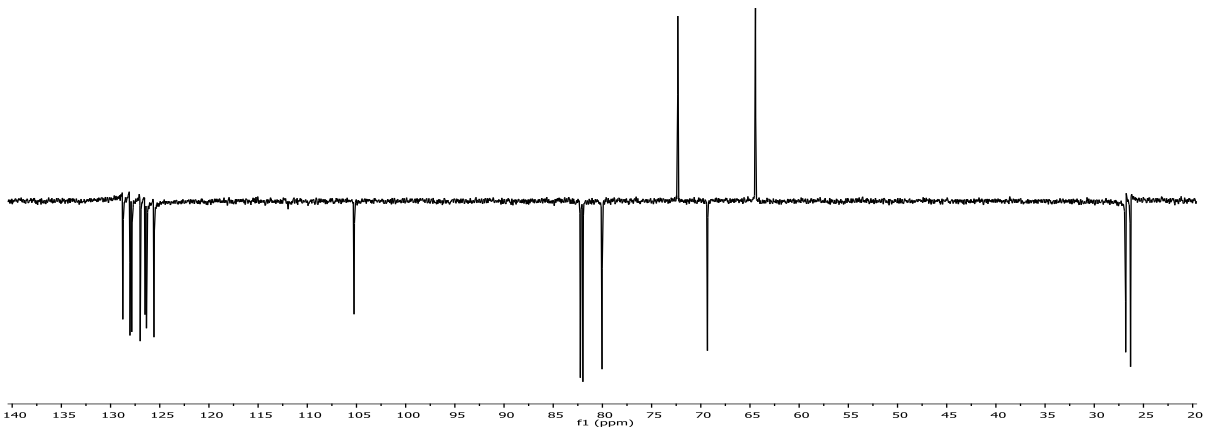


2. 1H, 13C and DEPT-135 NMR of Compound 3

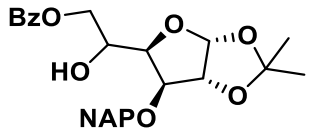


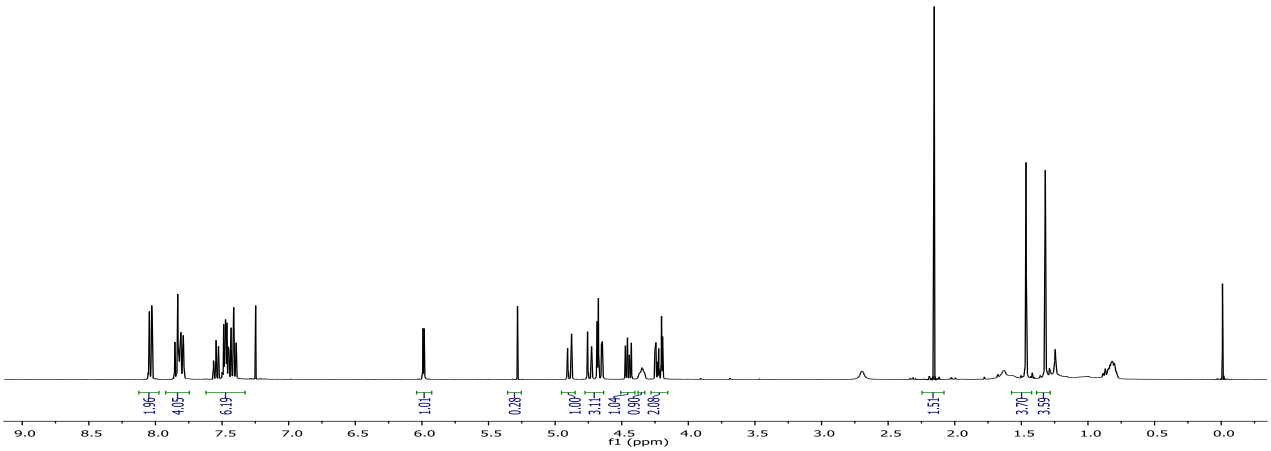


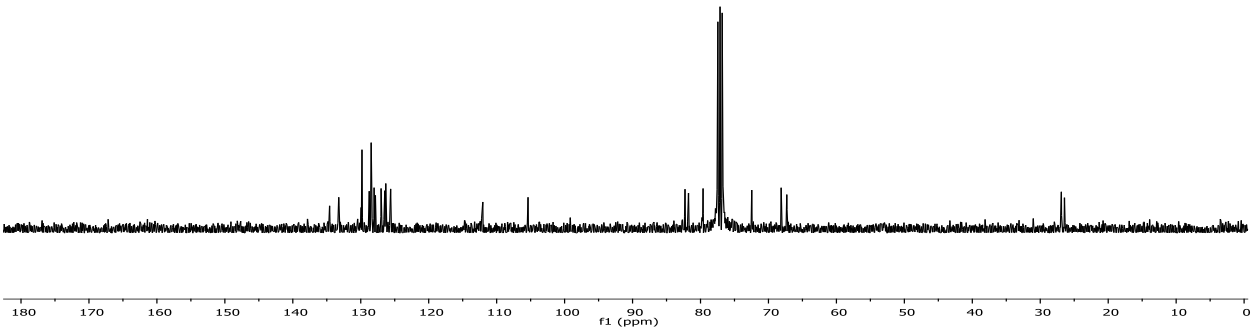


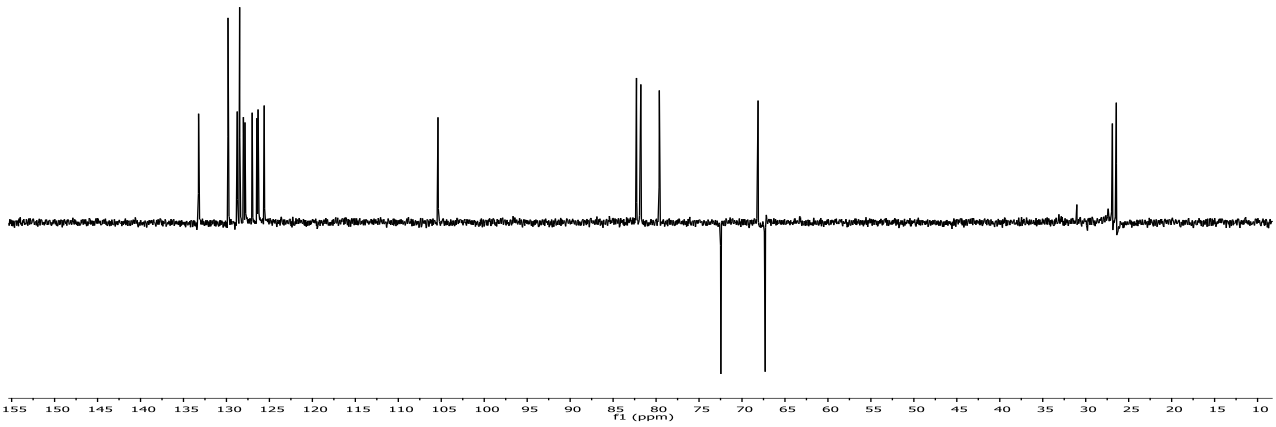


3. 1H, 13C and DEPT-135 NMR of compound 4

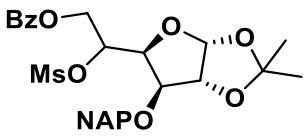


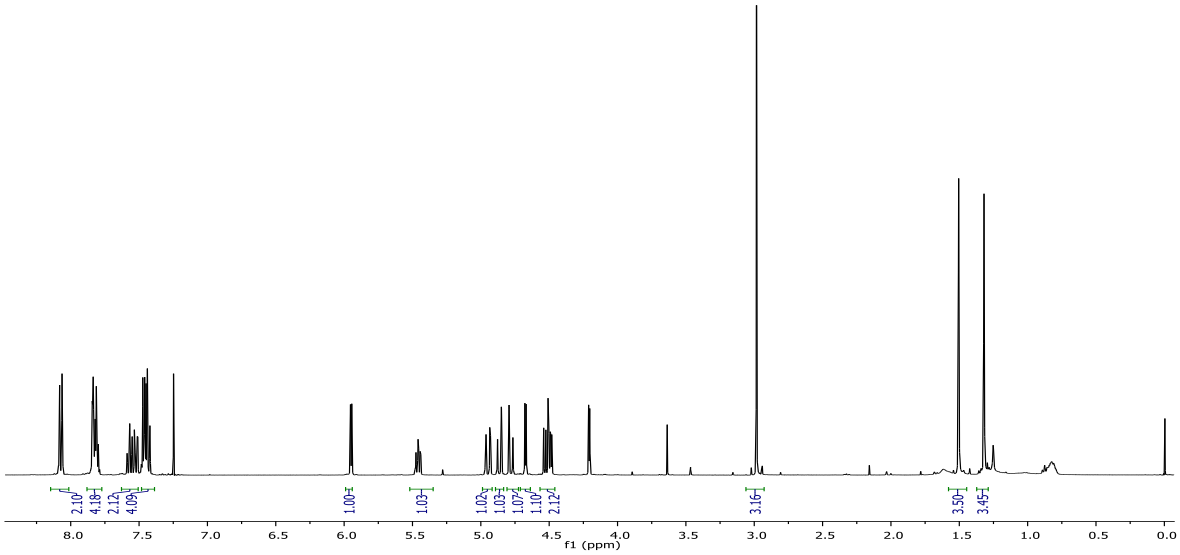


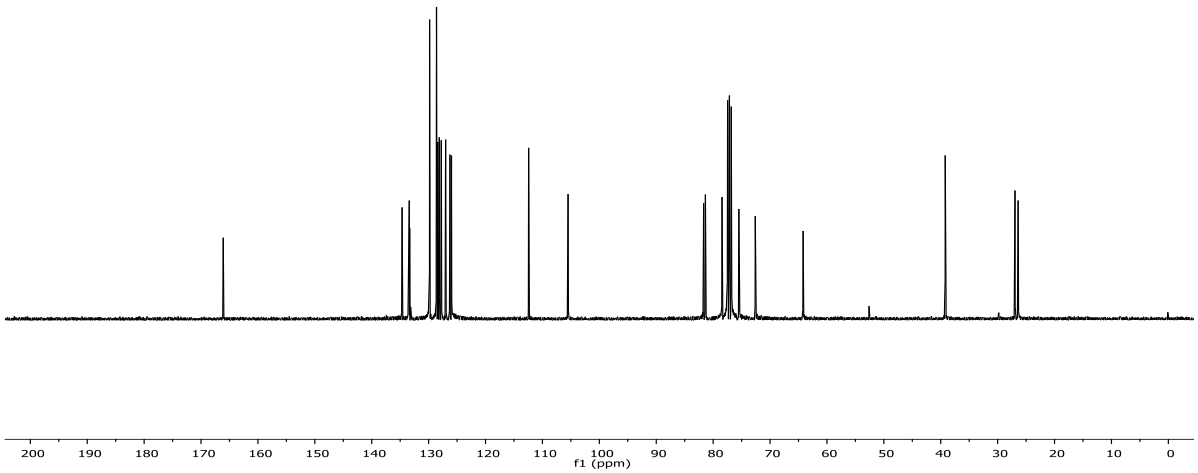




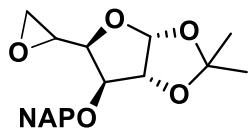
4. 1H and 13C NMR of compound 5

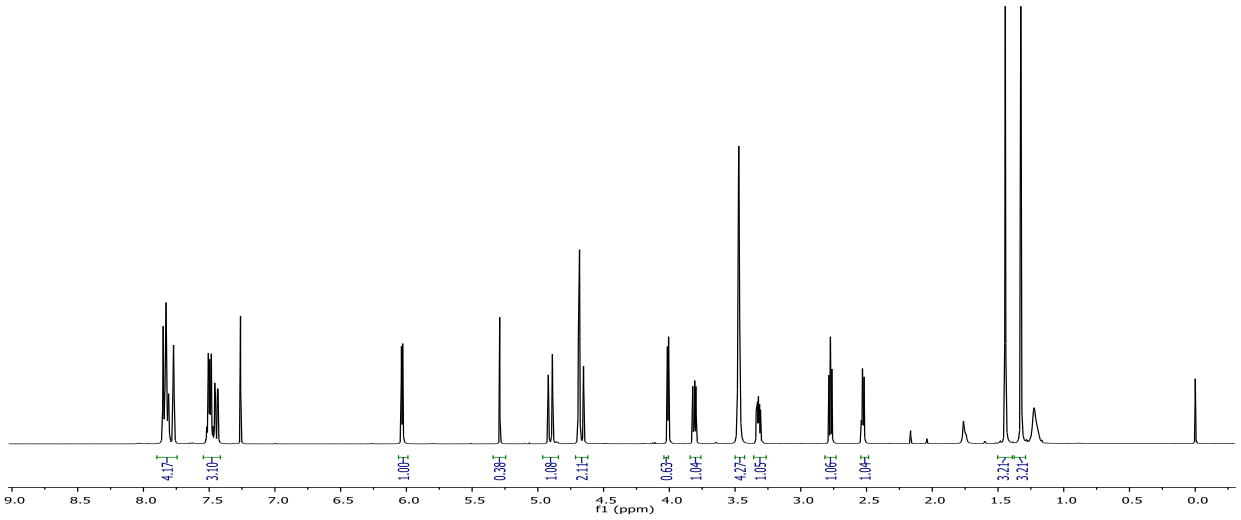


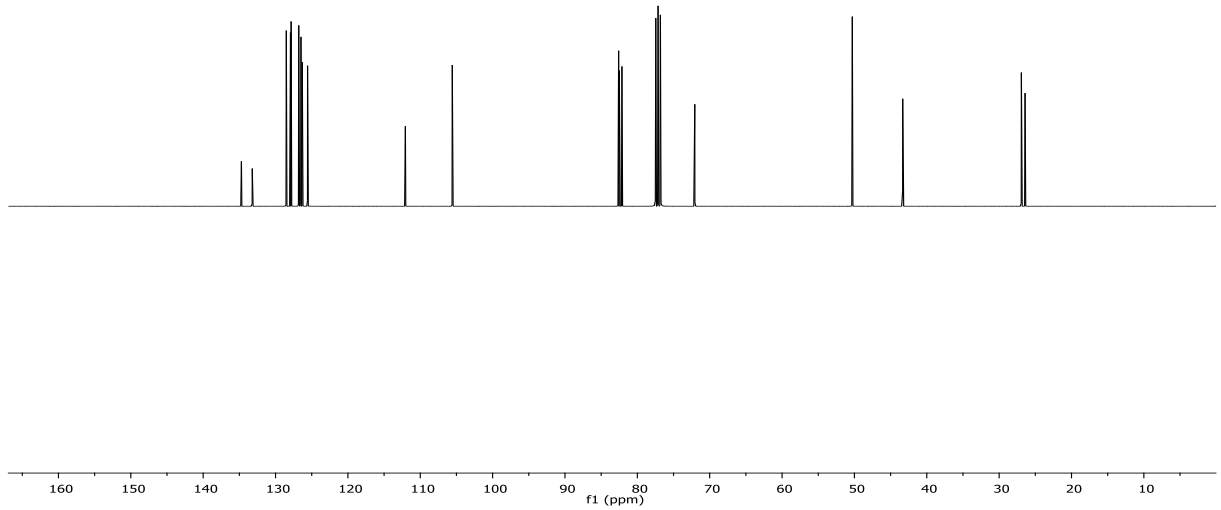




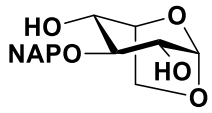
5. 1H and 13C NMR of compound 6

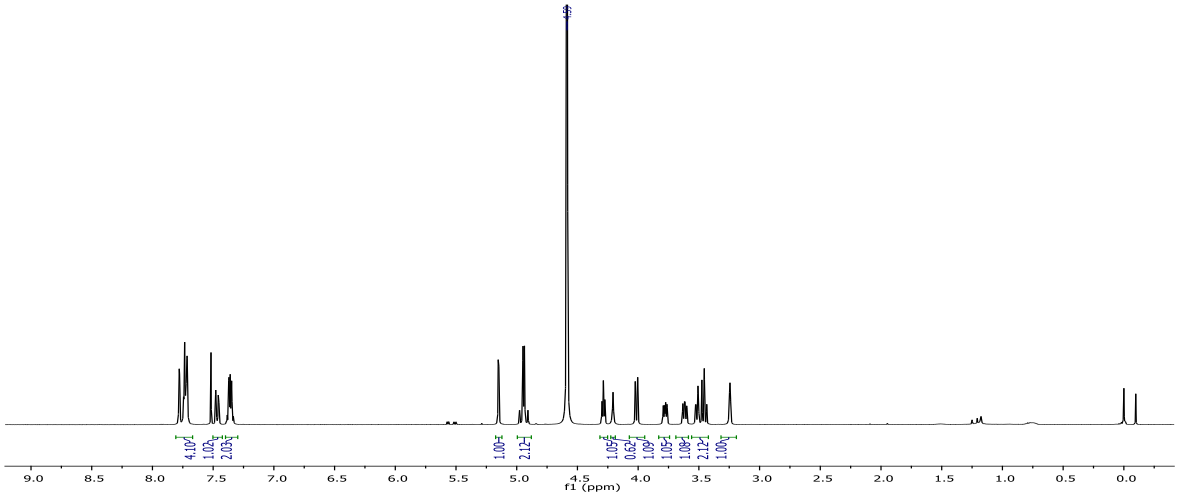


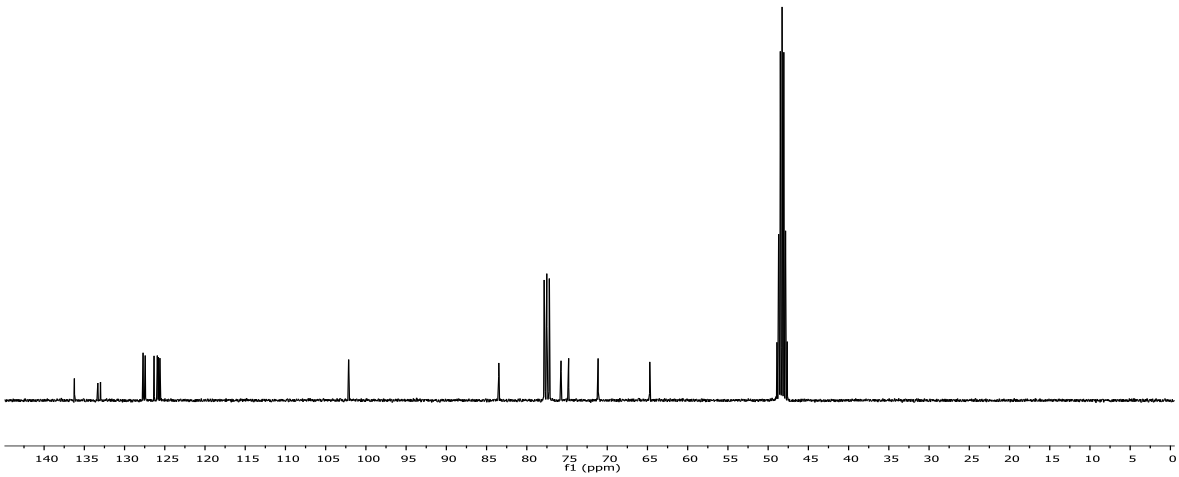


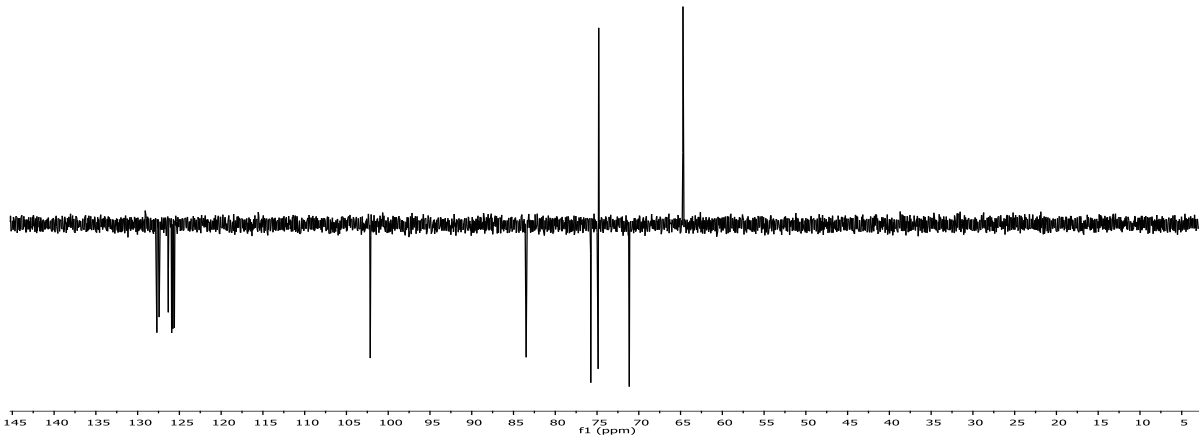


6. 1H, 13C and DEPT-135 NMR of compound 7

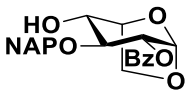


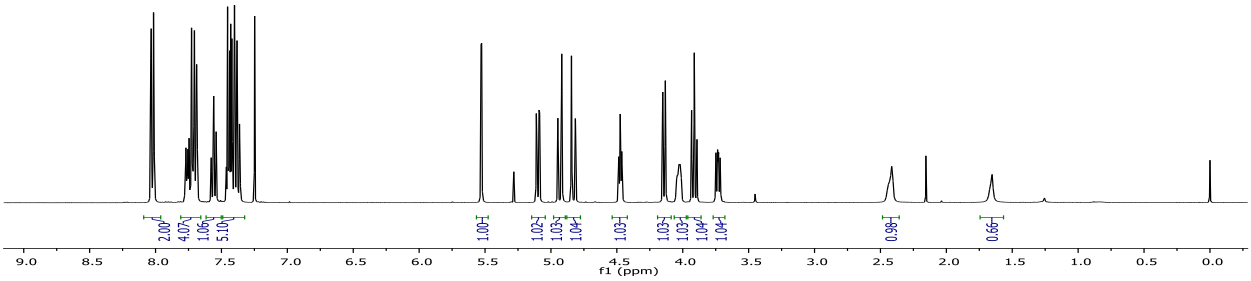


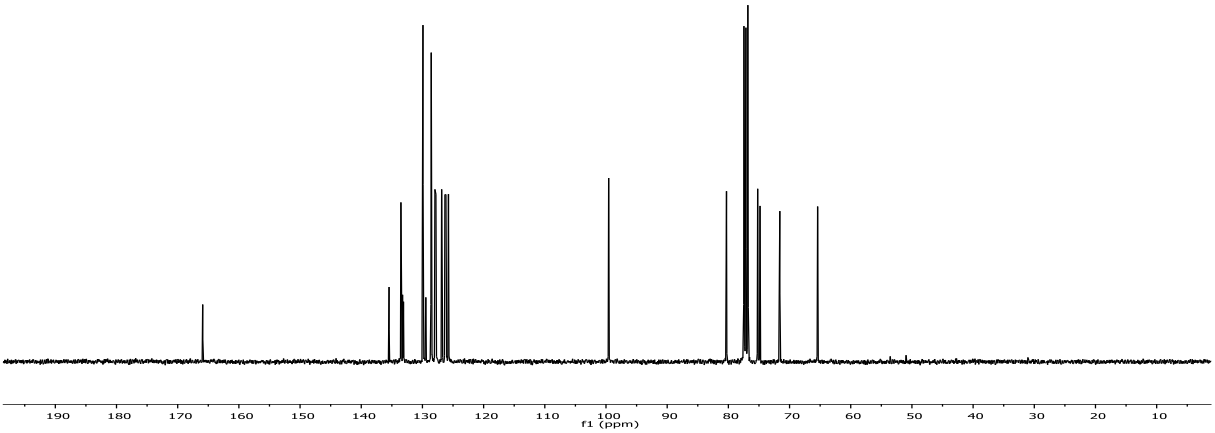


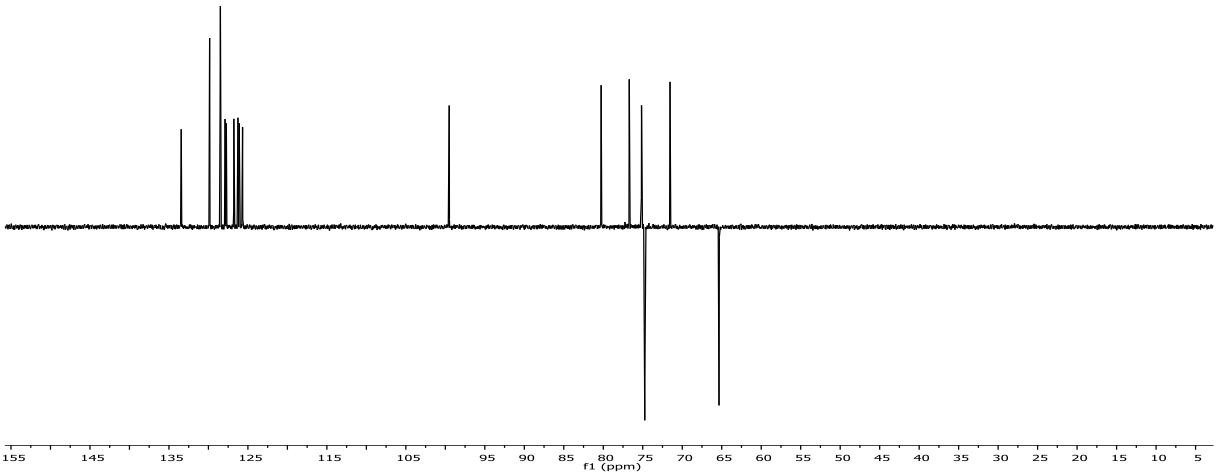


7. 1H, 13C and DEPT-135 NMR of compound 8

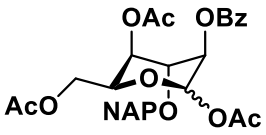


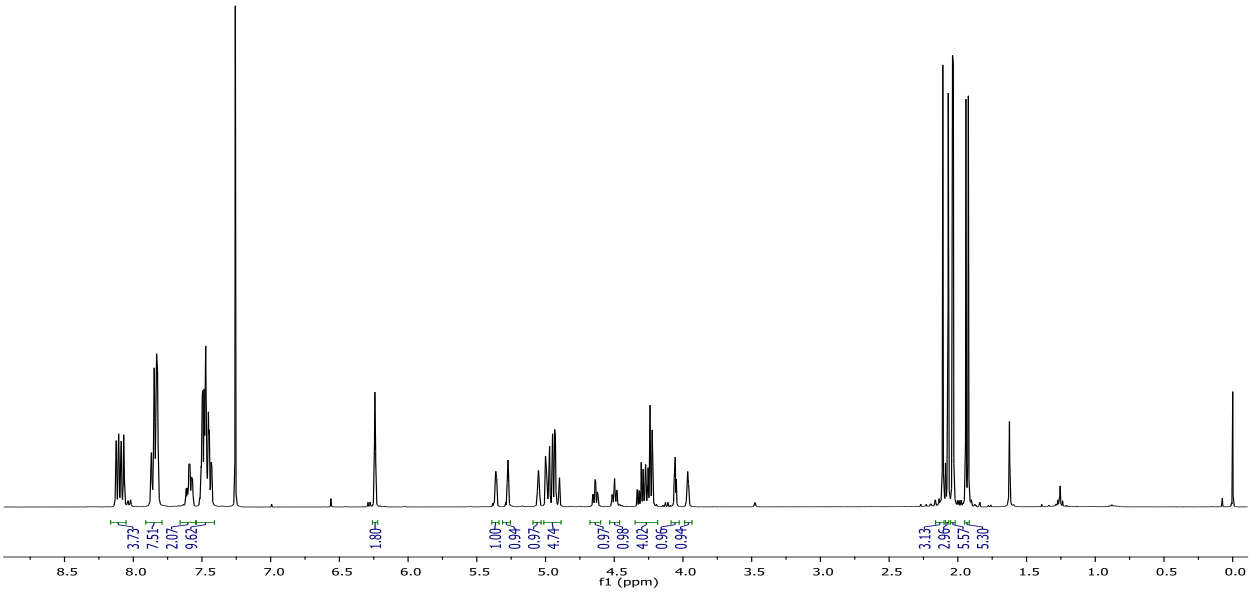




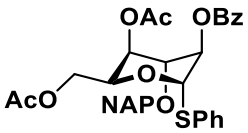


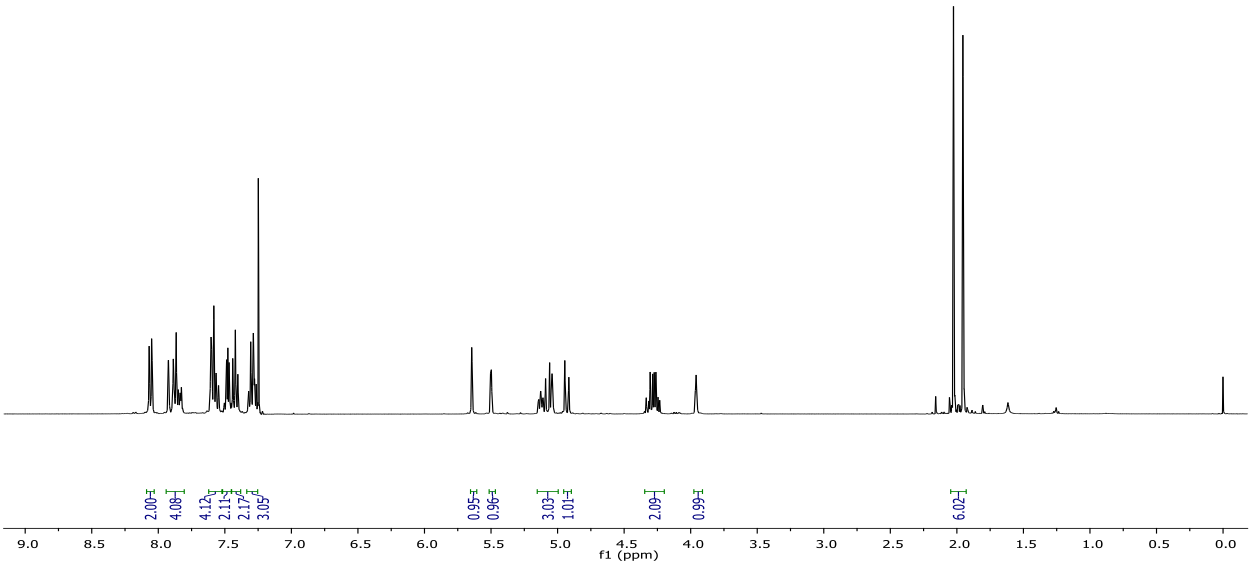
8. 1H NMR of compound 9



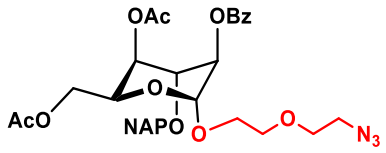


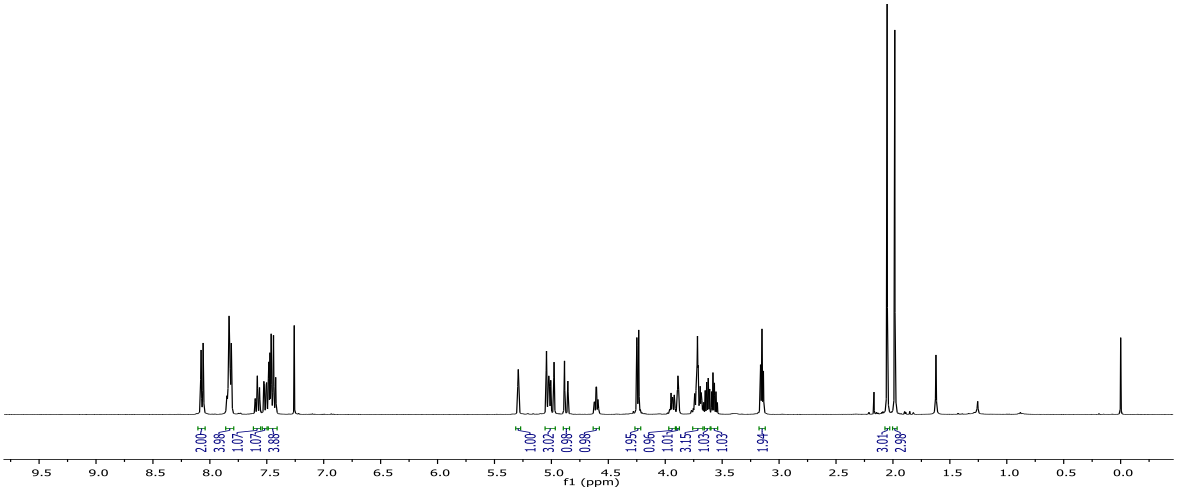
9. 1H NMR of Compound 10

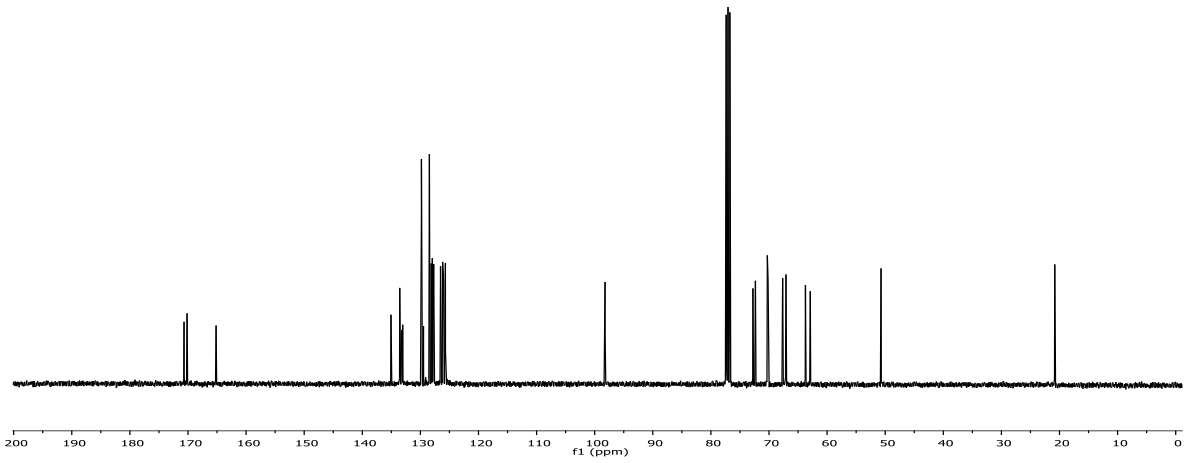


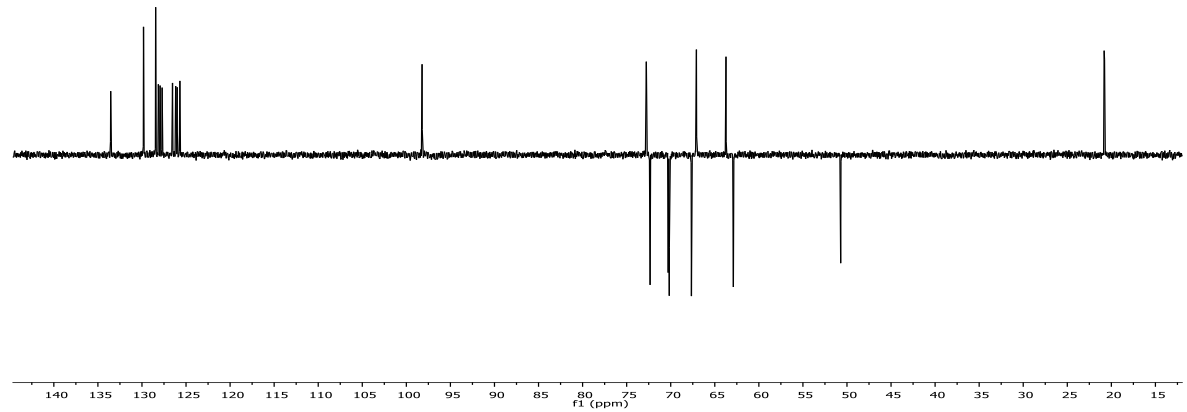


10. 1H, 13C and DEPT-135 NMR of compound 11

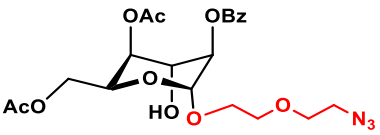


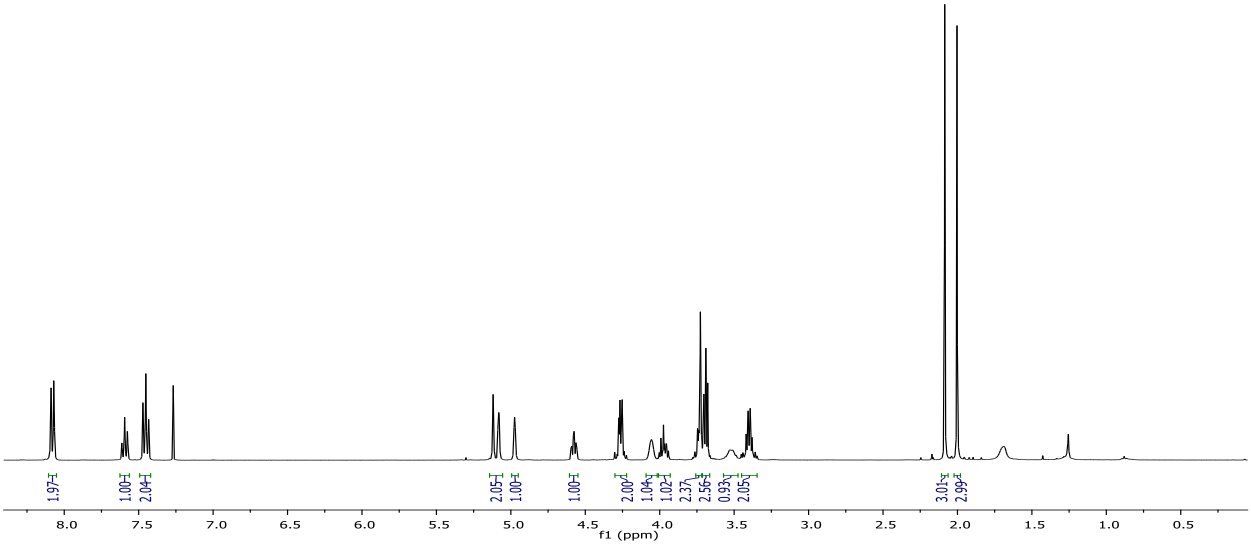




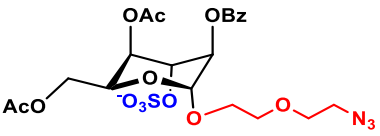


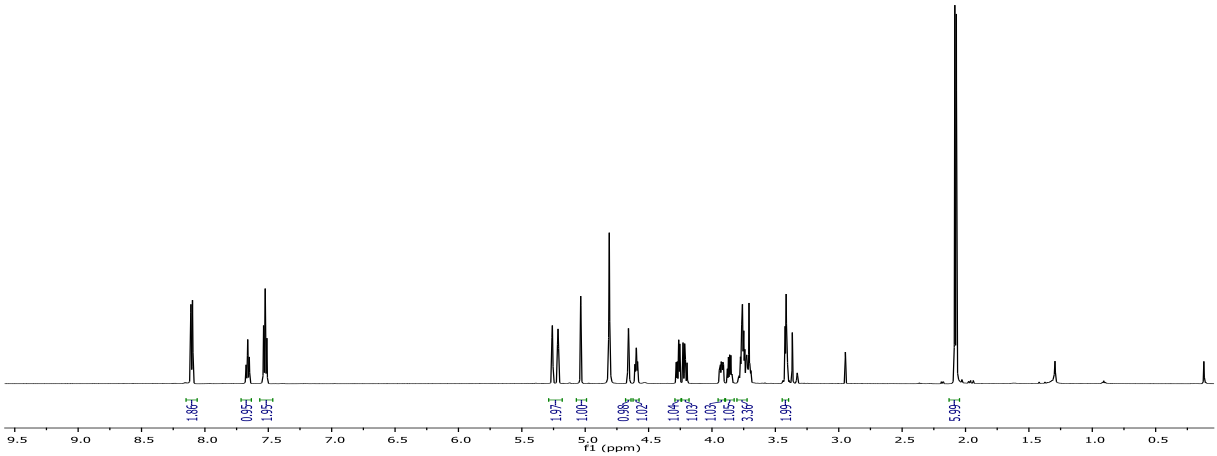
11. 1H NMR of compound 12

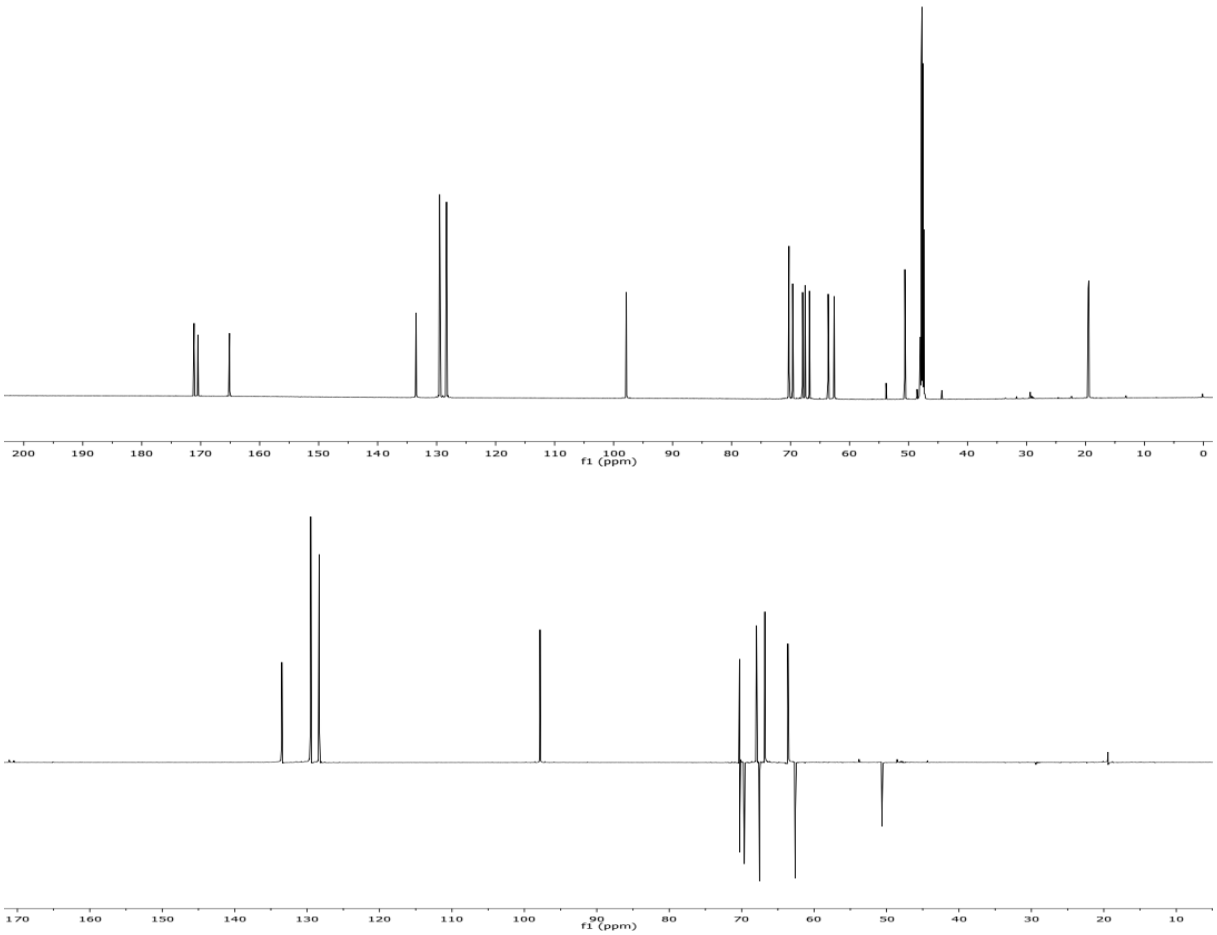




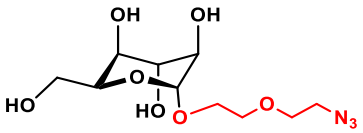
12. 1H, 13C and DEPT-135 NMR of compound 13

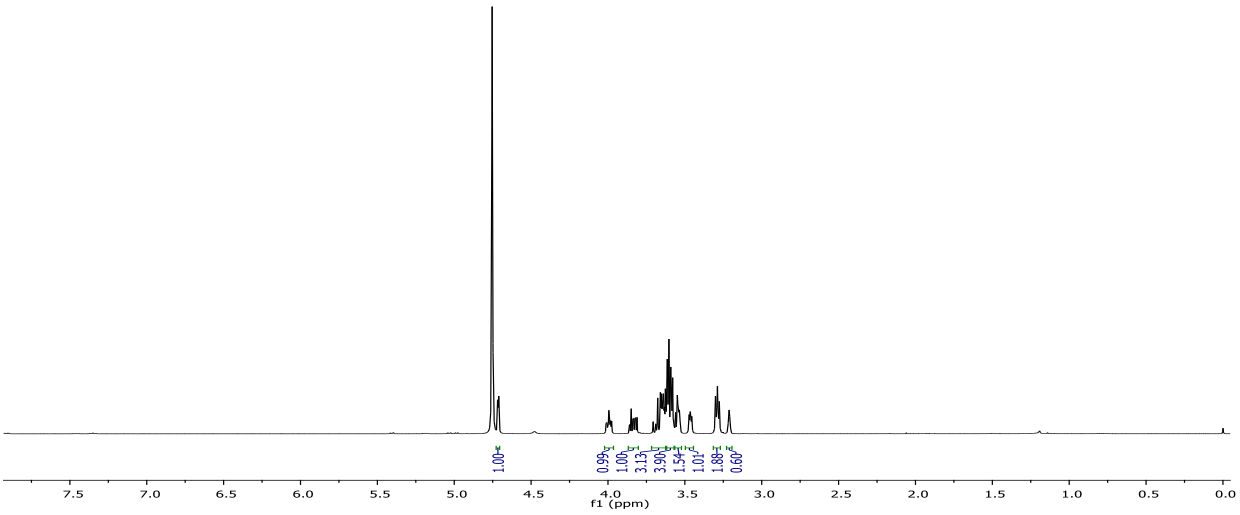


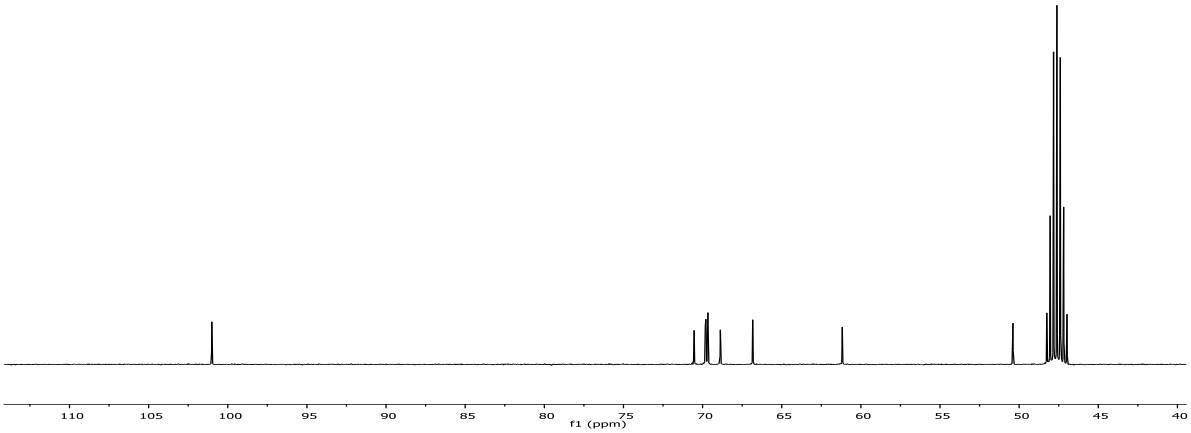




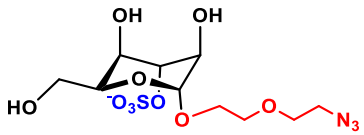
13. 1H and 13C NMR of compound 14

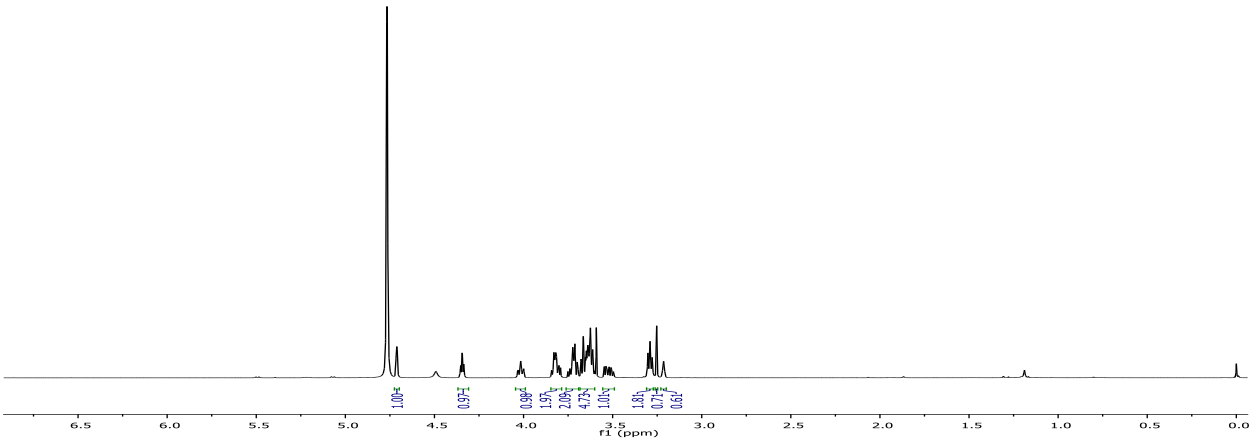


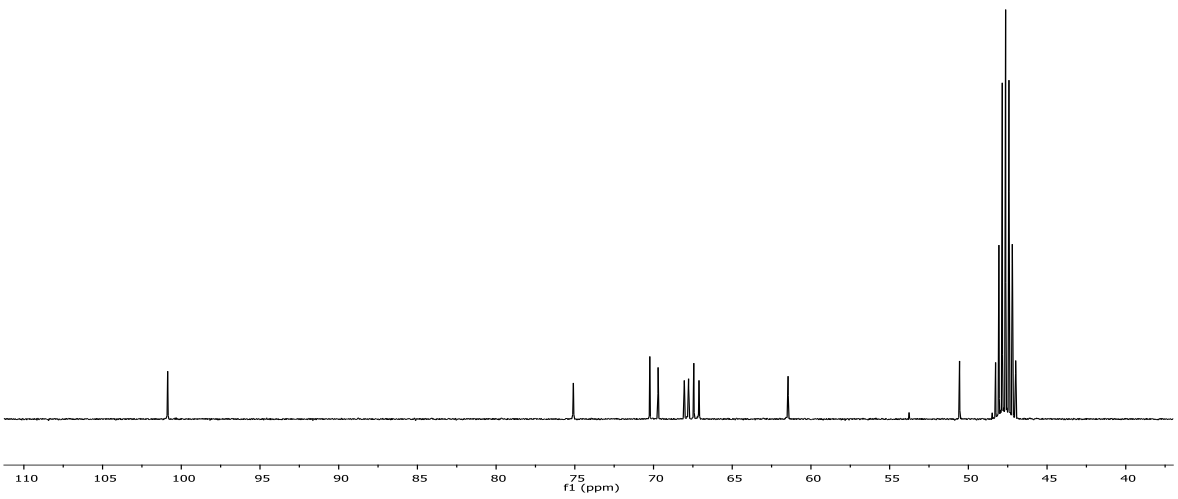


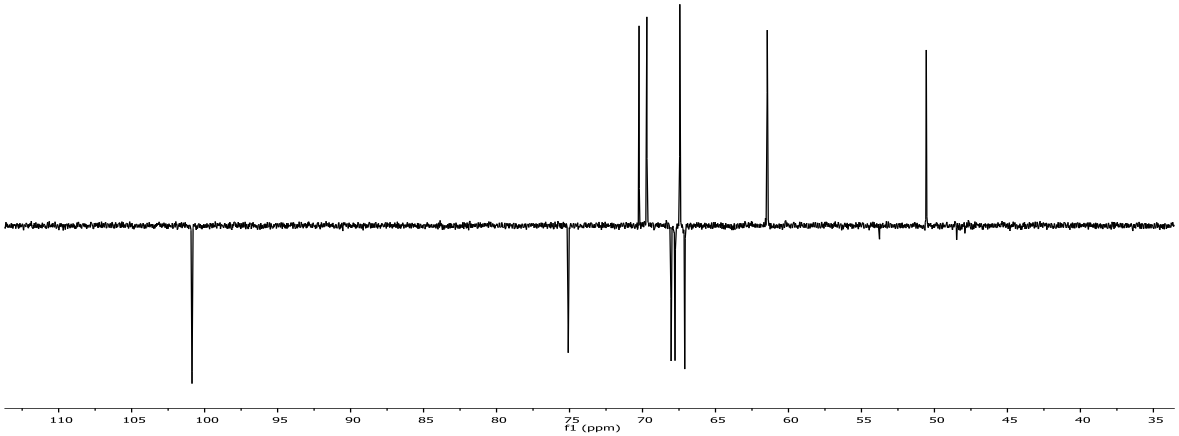


14. 1H, 13C and DEPT-135 NMR of compound 1a

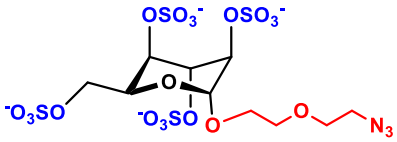


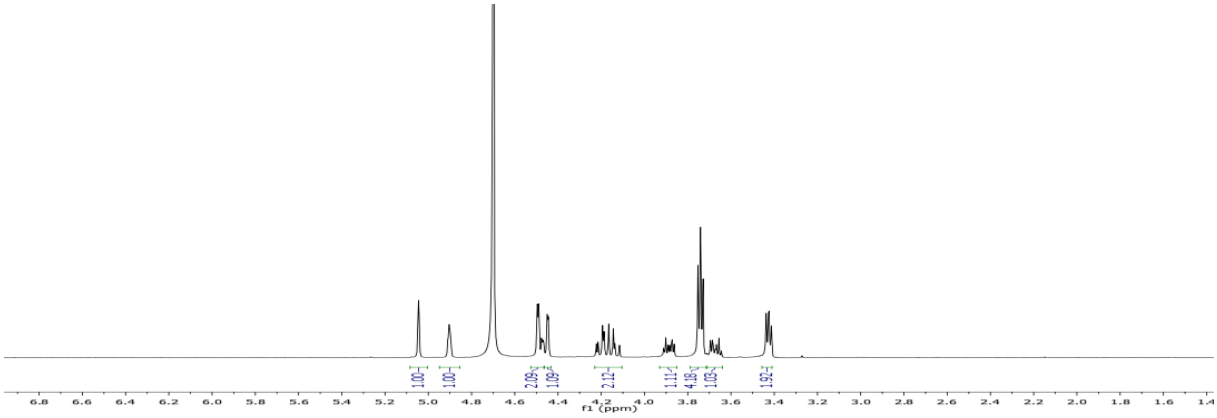


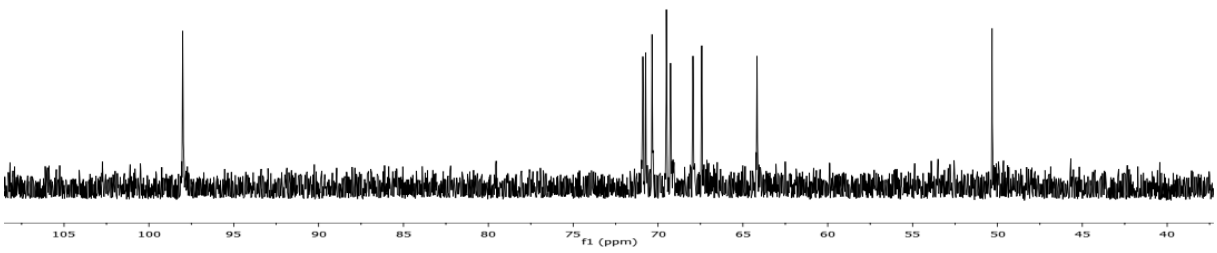


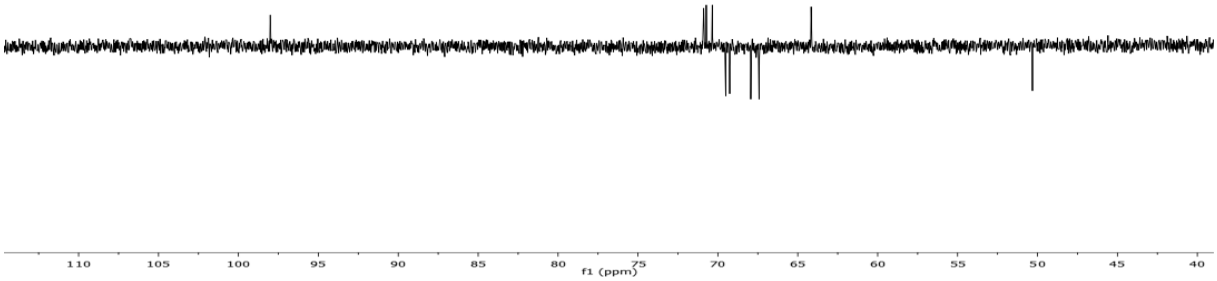


15. 1H, 13C and DEPT-135 NMR of compound 1b



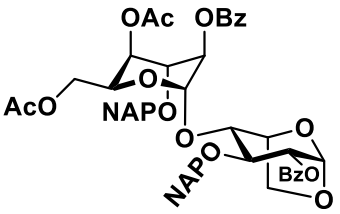


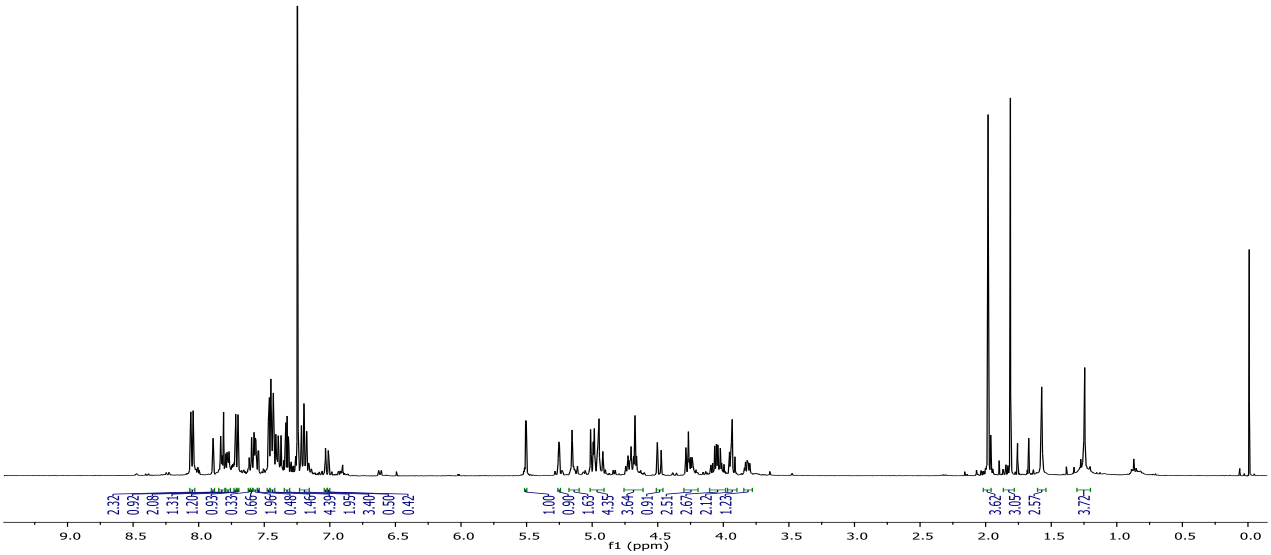




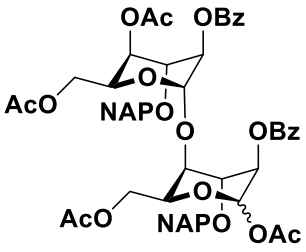
2. Disaccharide L- idose NMR

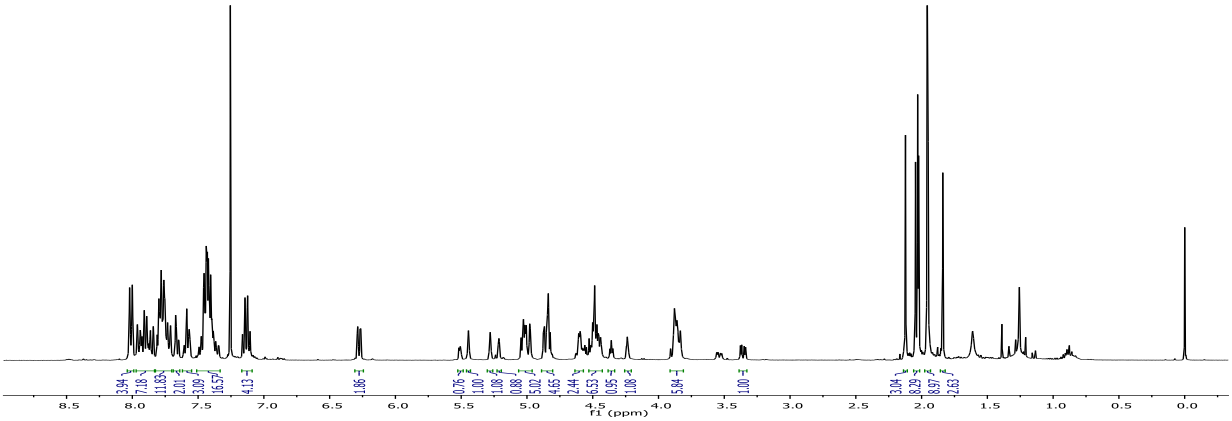
16. 1H NMR of compound 15



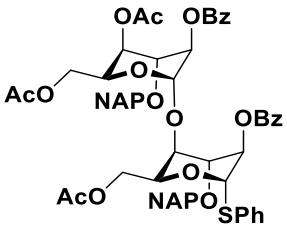


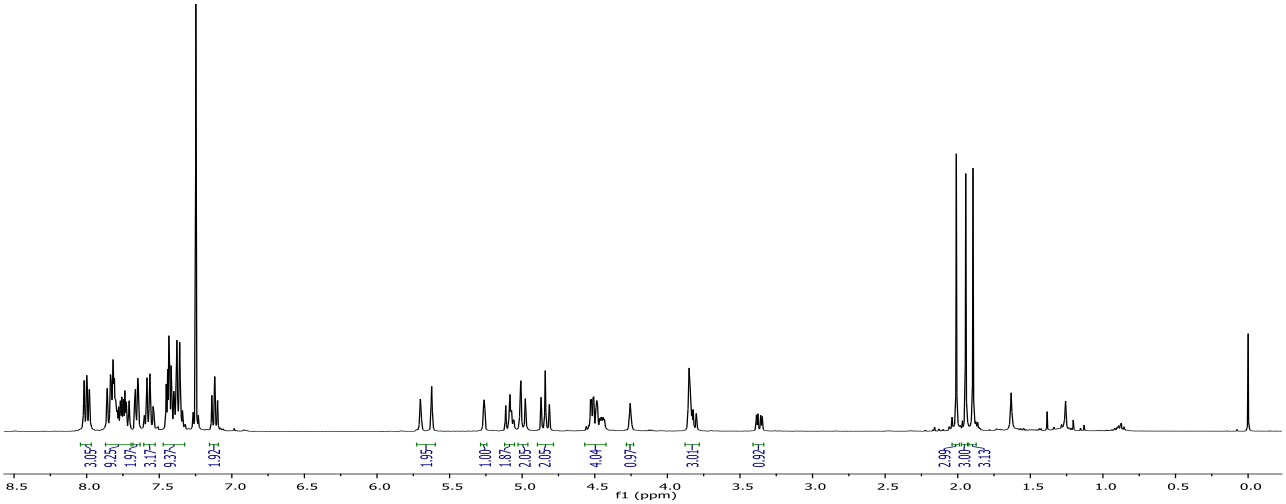
17. 1H NMR of compound 16

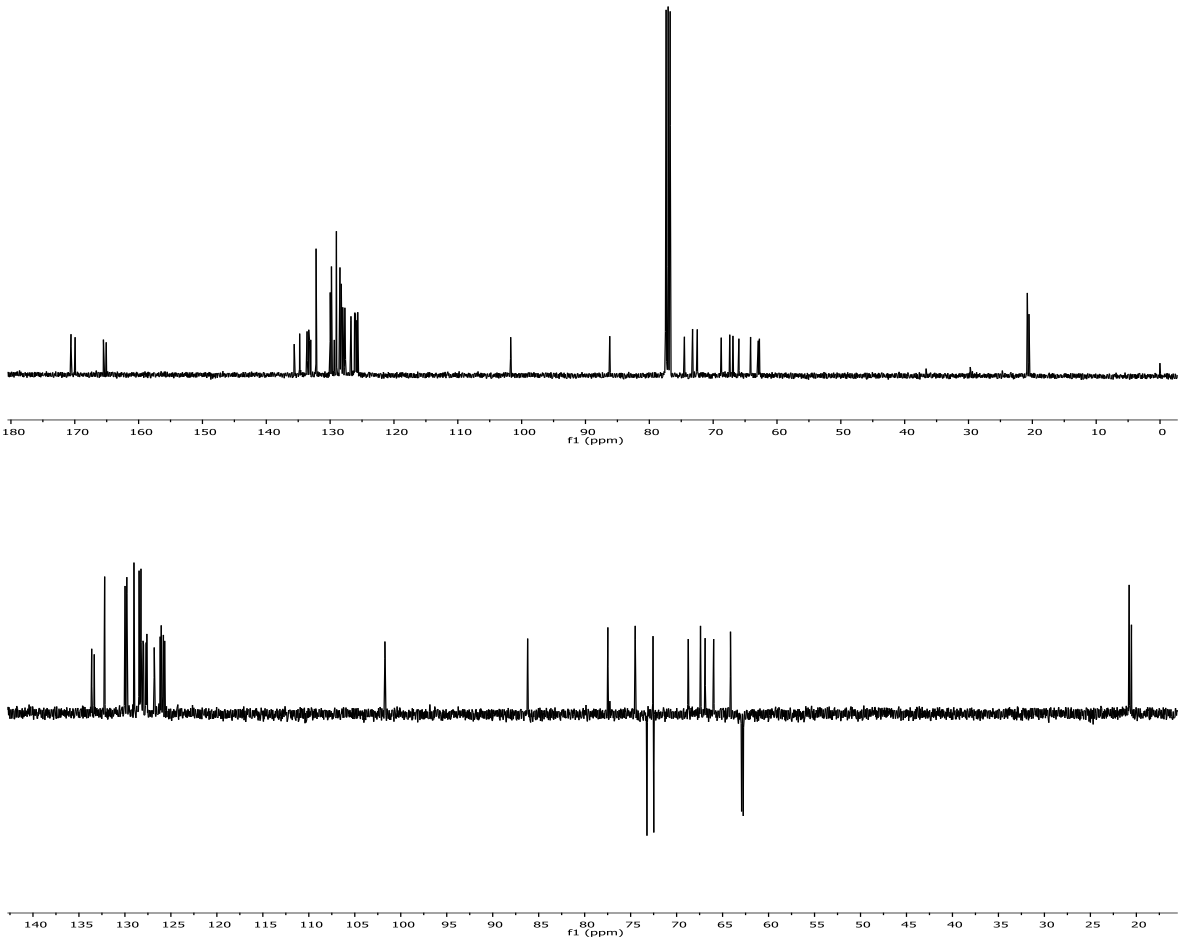




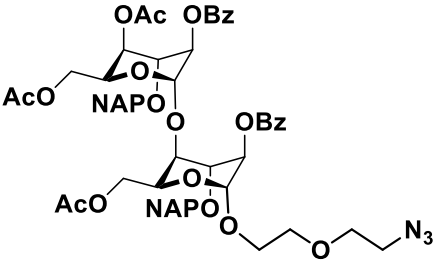
18. 1H, 13C and DEPT-135 NMR of compound 17

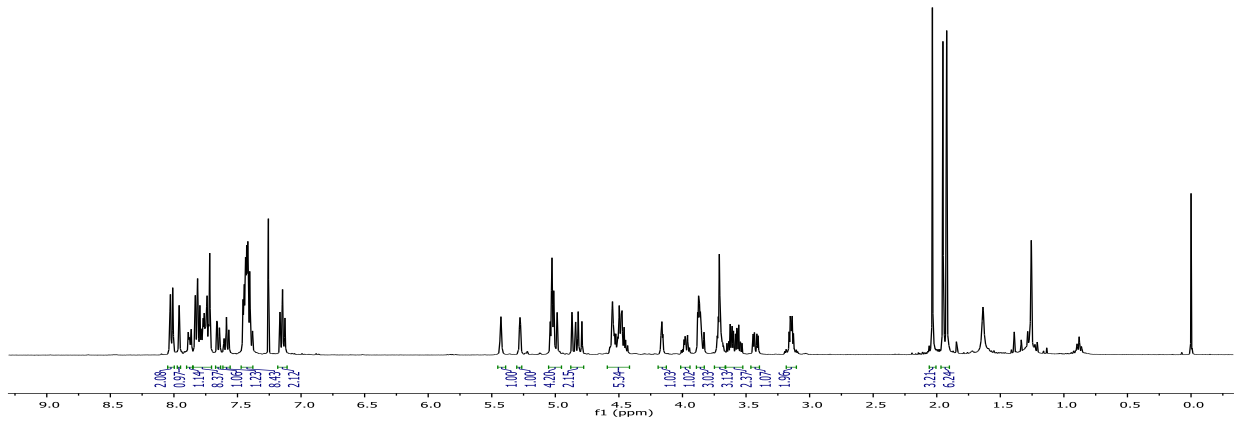


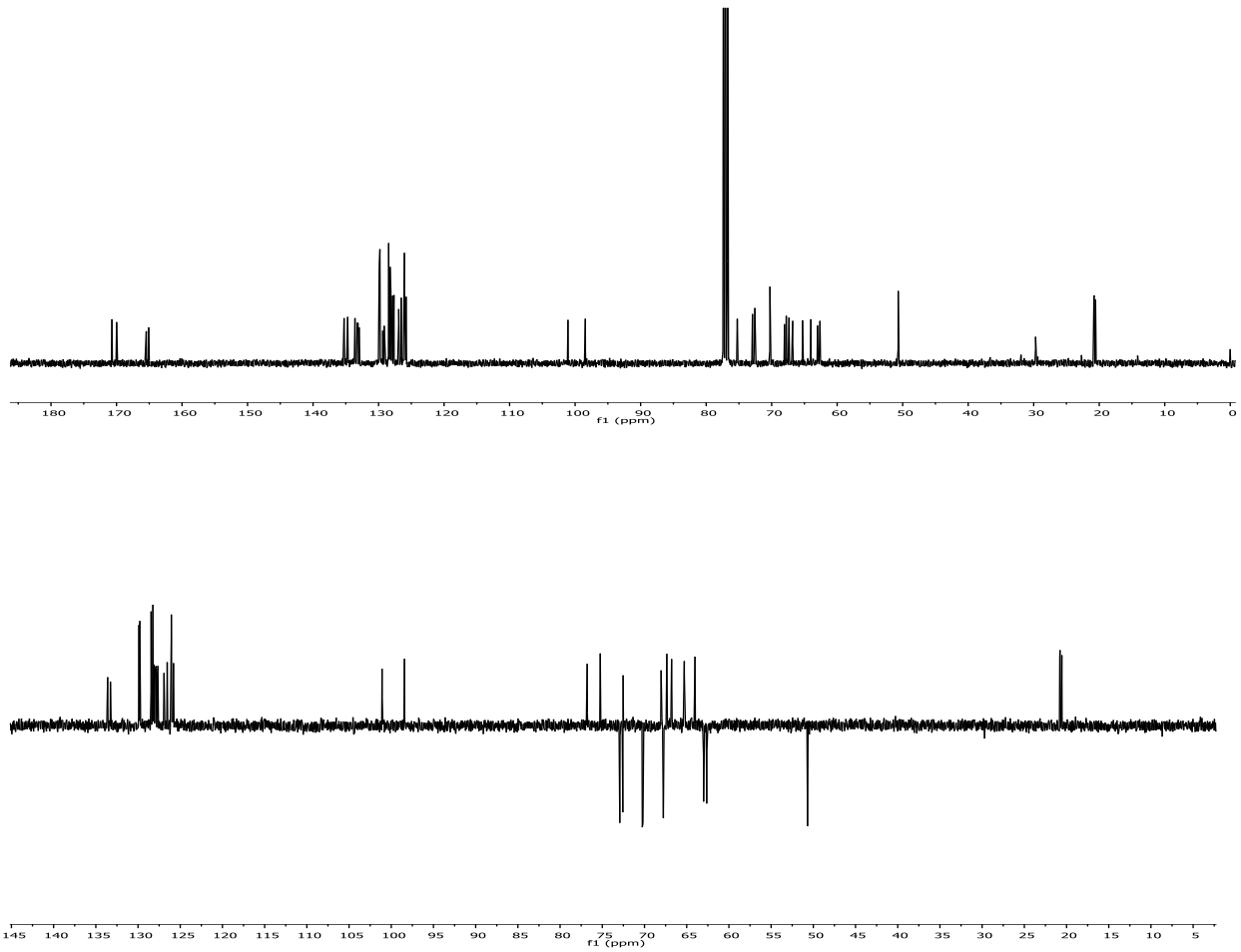




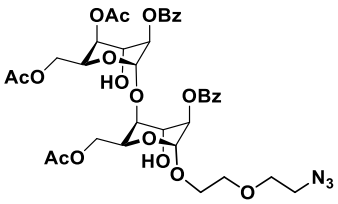
19. 1H, 13C and DEPT-135 NMR of compound 18

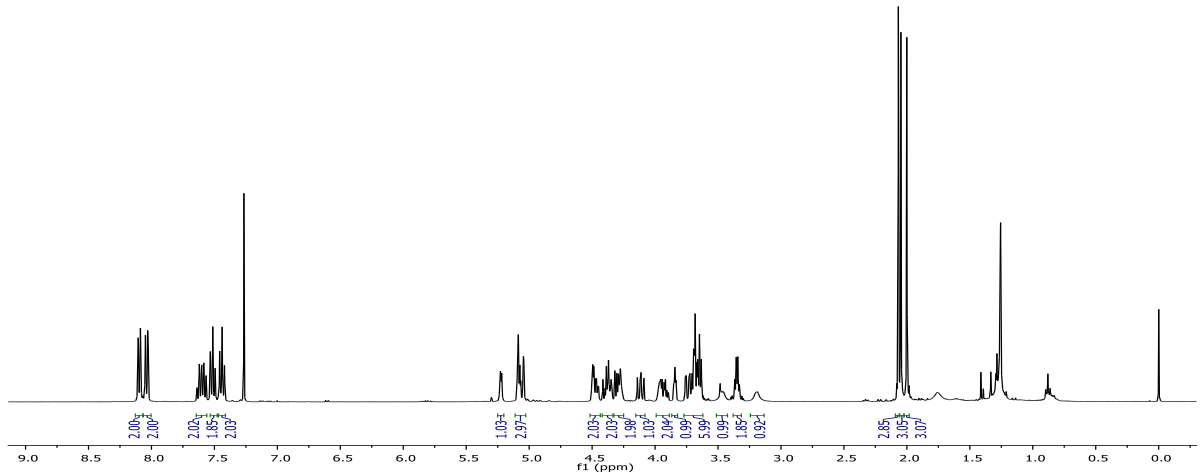


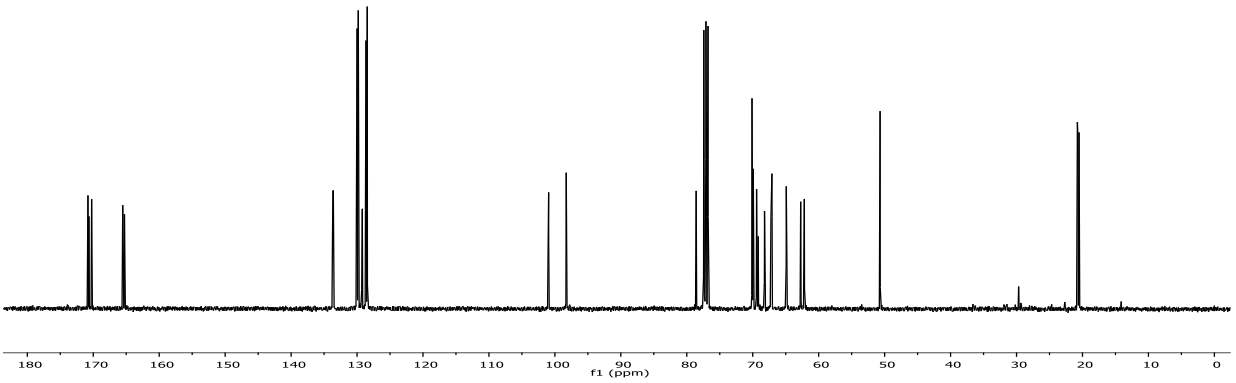


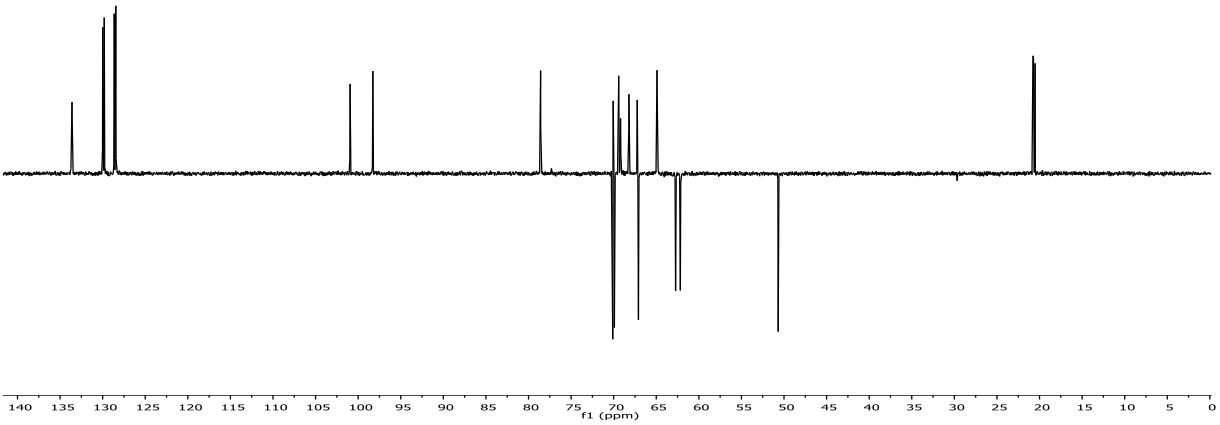


20. 1H, 13C and DEPT-135 NMR of compound 19

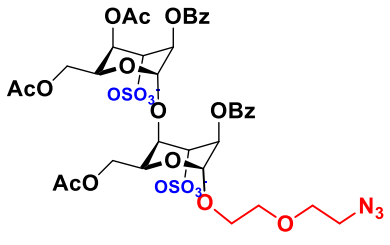


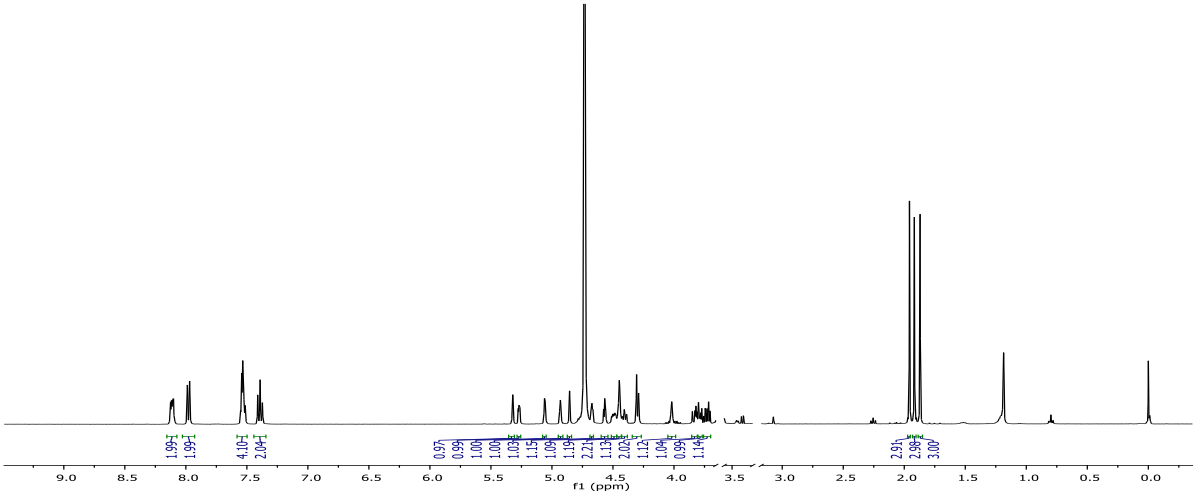



180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

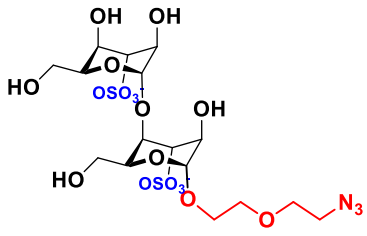

140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)

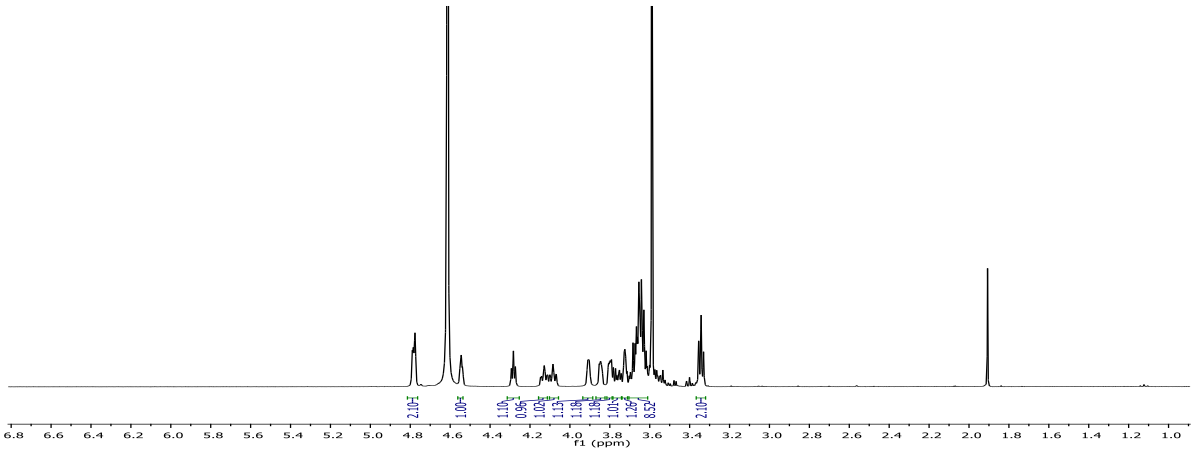
21. 1H NMR of compound 2a



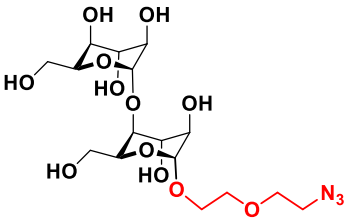


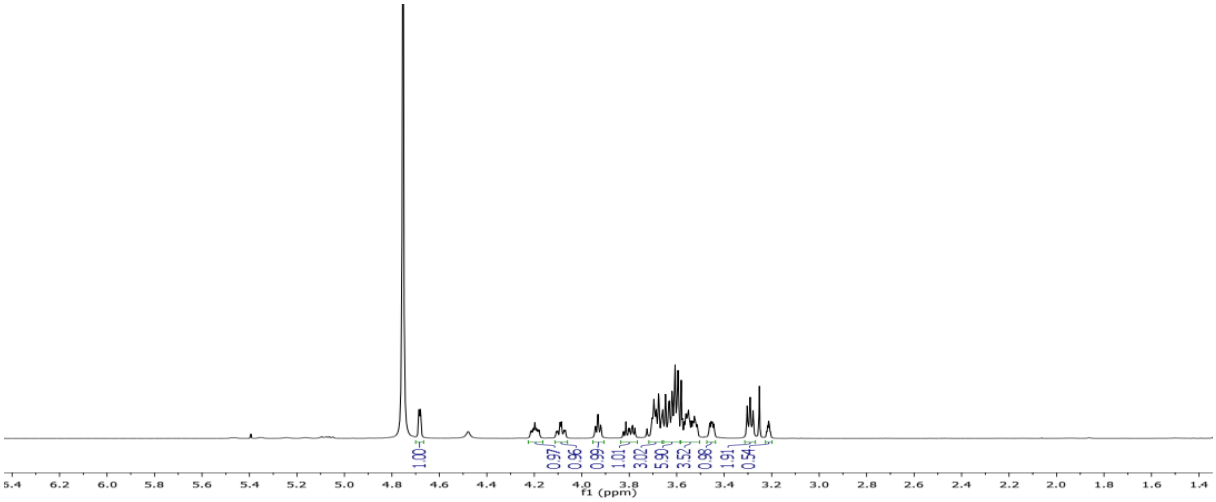
21. 1H NMR of Compound 21

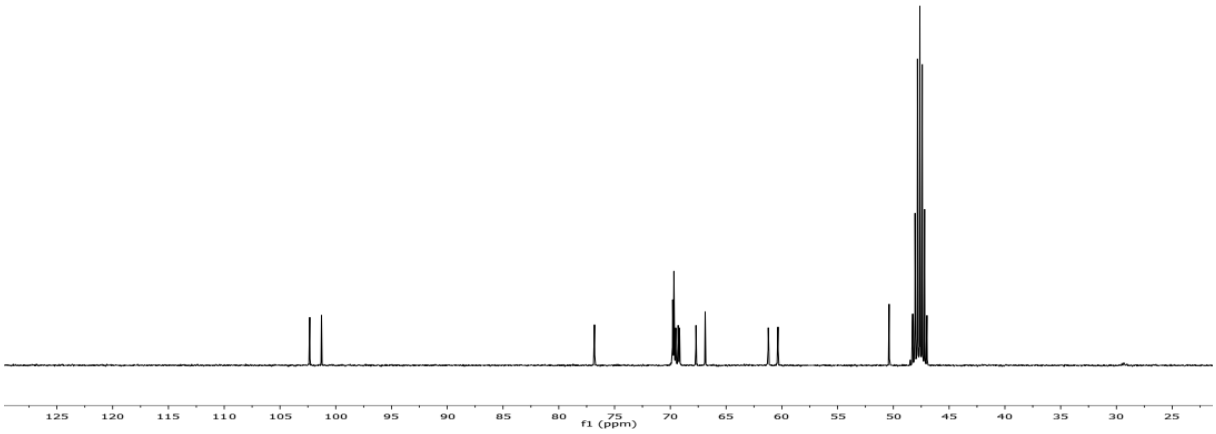


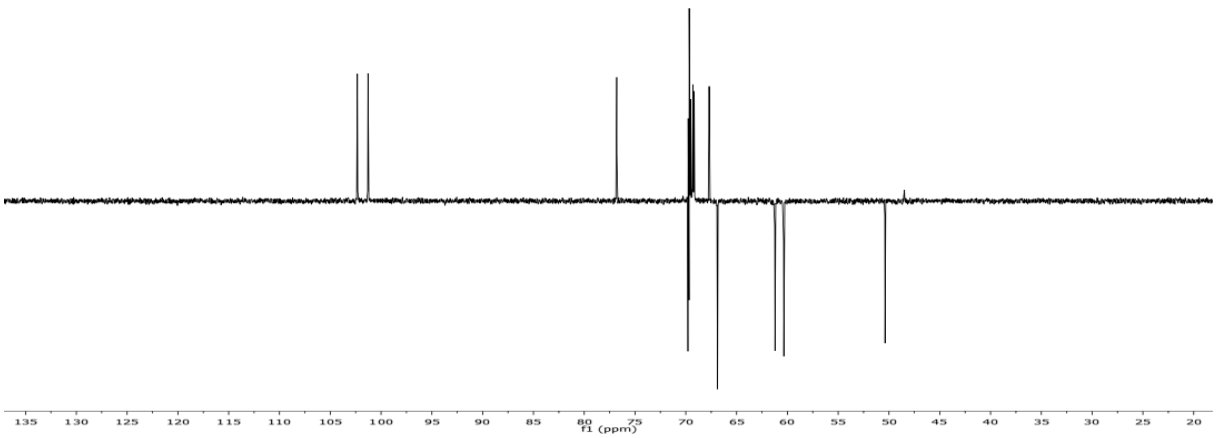


22. 1H, 13C and DEPT-135 NMR of compound 20

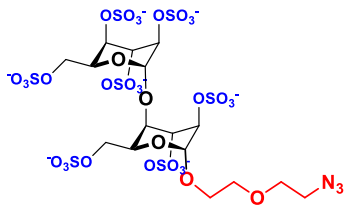


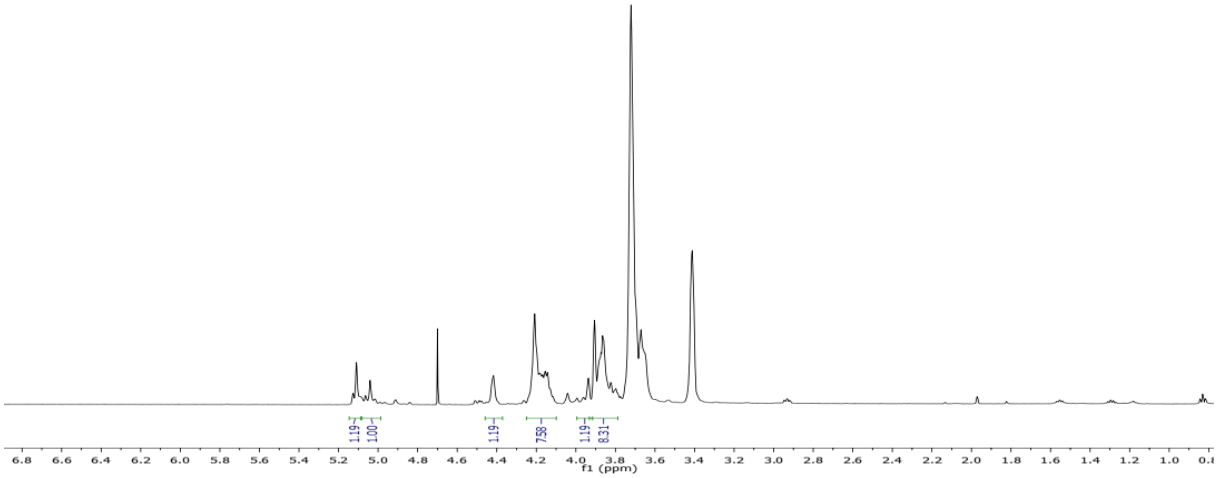


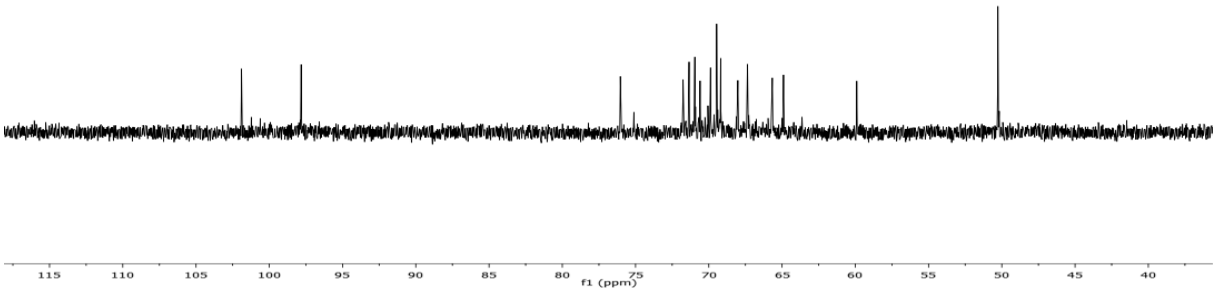


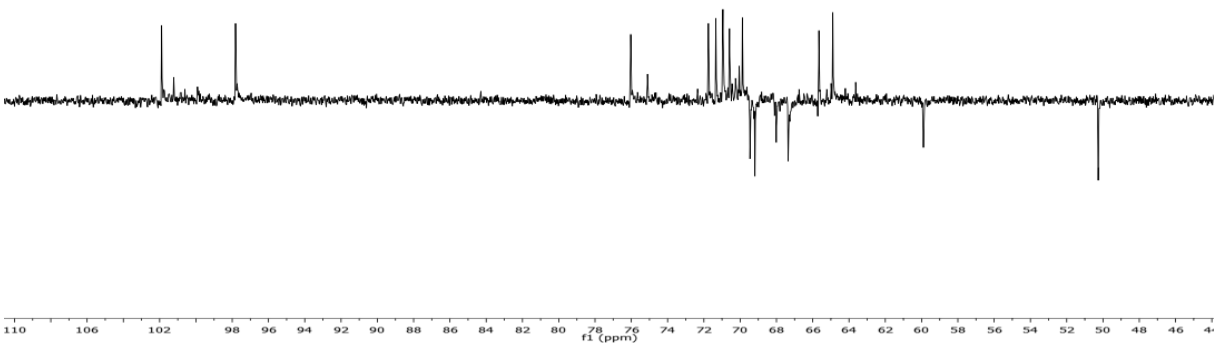


23. 1H, 13C and DEPT-135 NMR of compound 2b



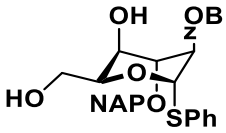


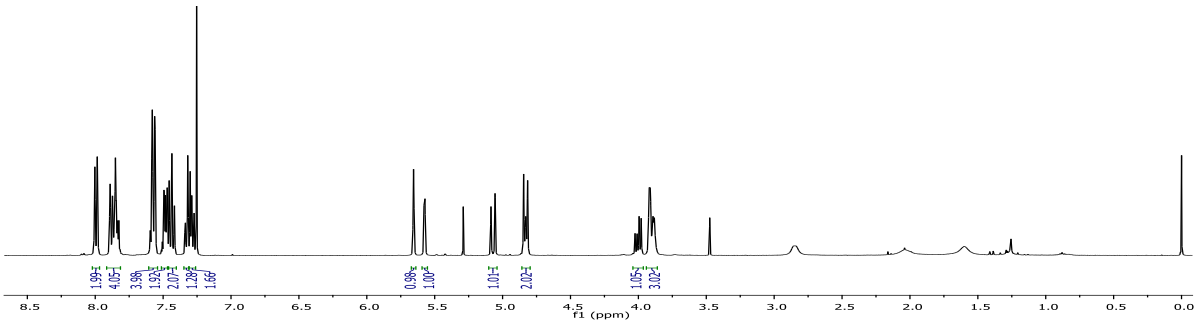




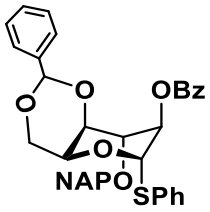
3. Tetrasaccharide L-idose NMR

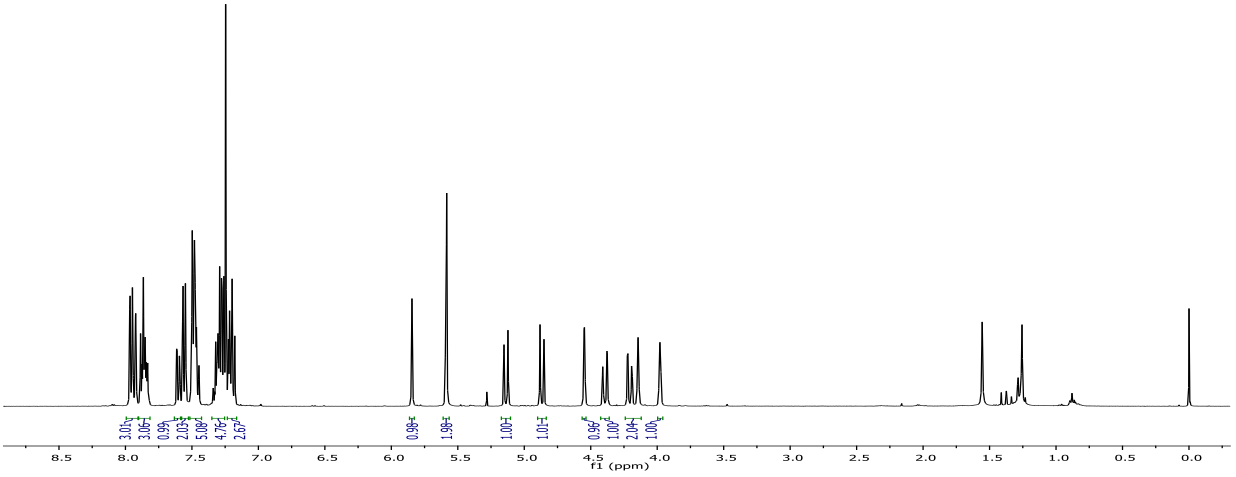
24. 1H NMR of compound 22



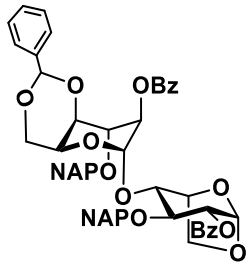


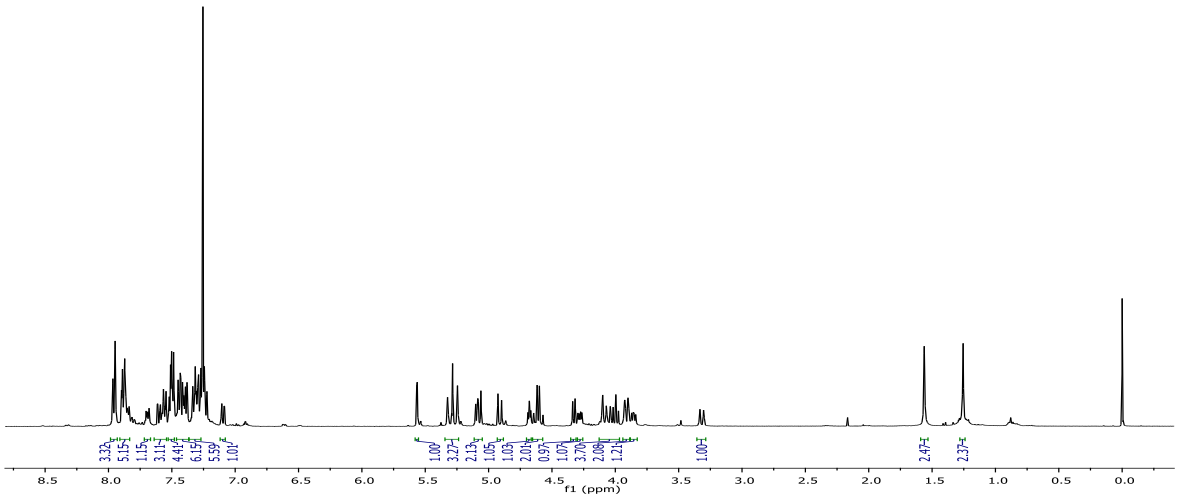
25. 1H NMR of compound 23

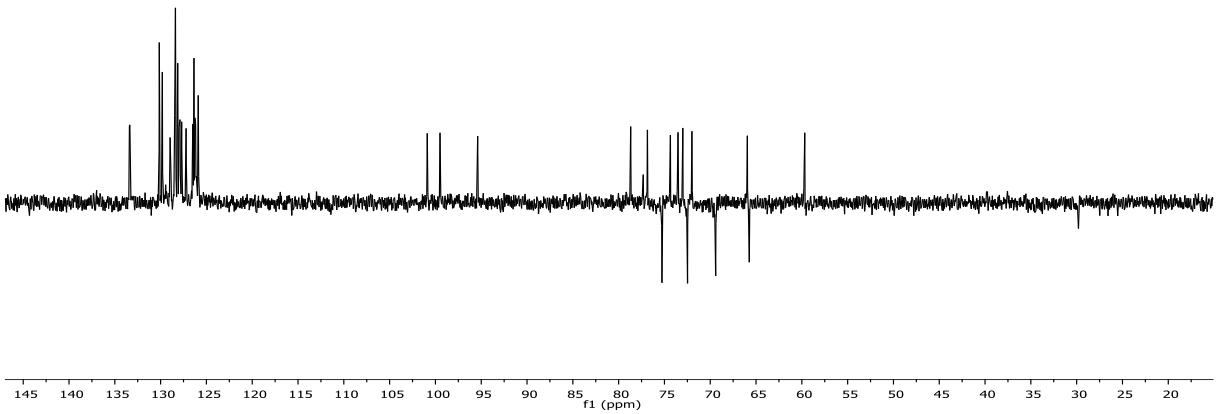




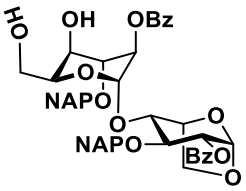
26. 1H and 13C NMR of compound 24

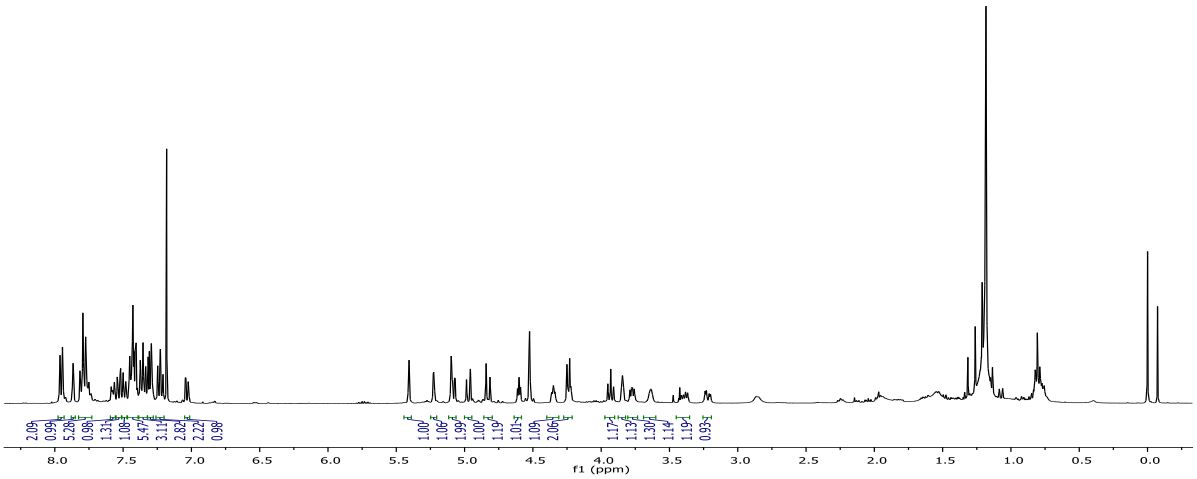




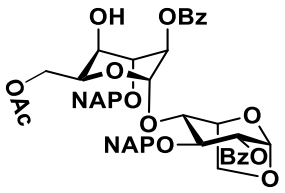


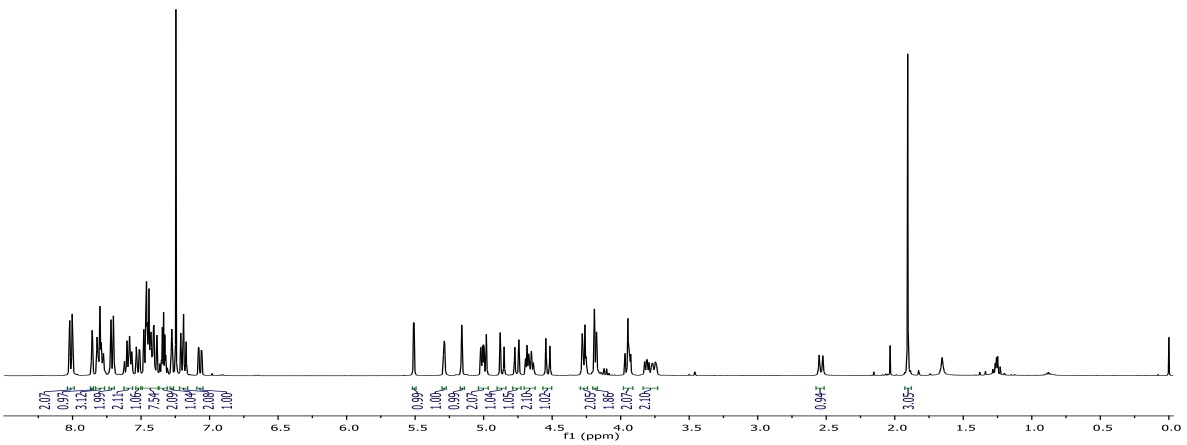
27. 1H NMR of compound 25

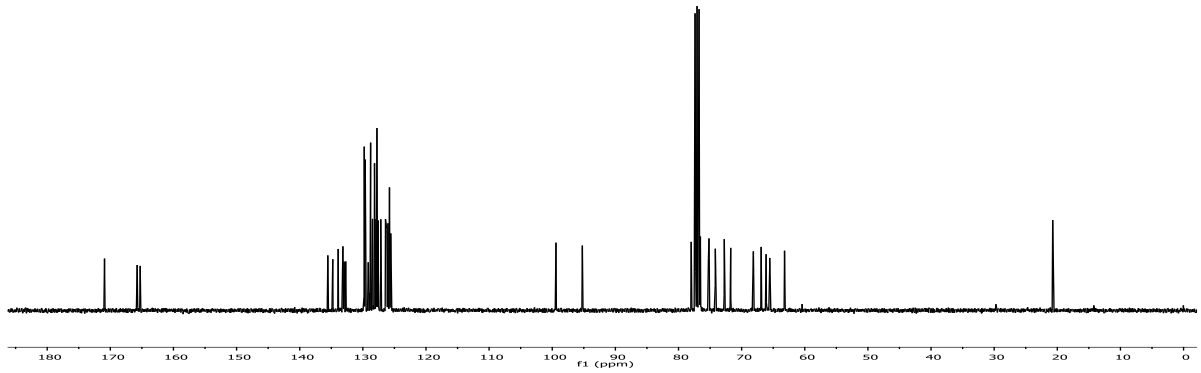


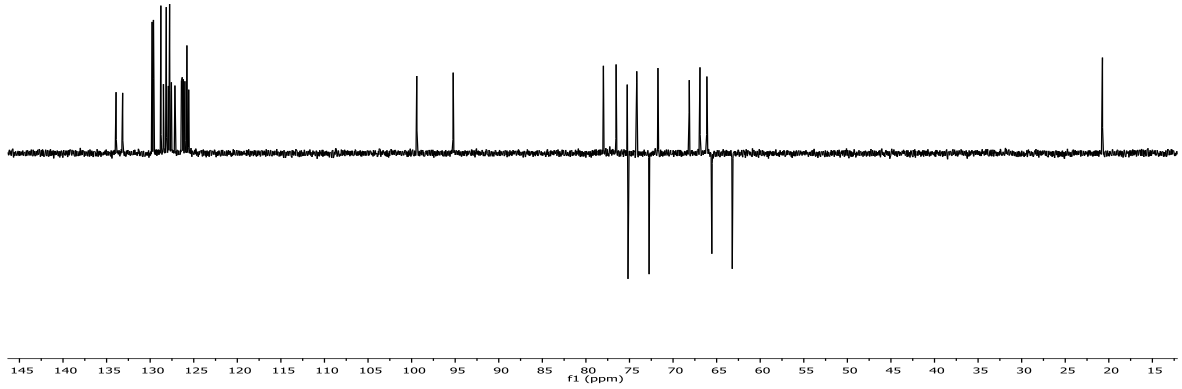


28. 1H, 13C and DEPT-135 NMR of compound 26

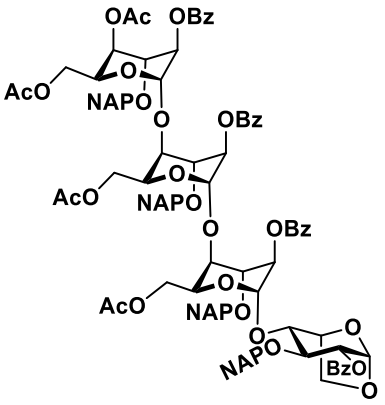


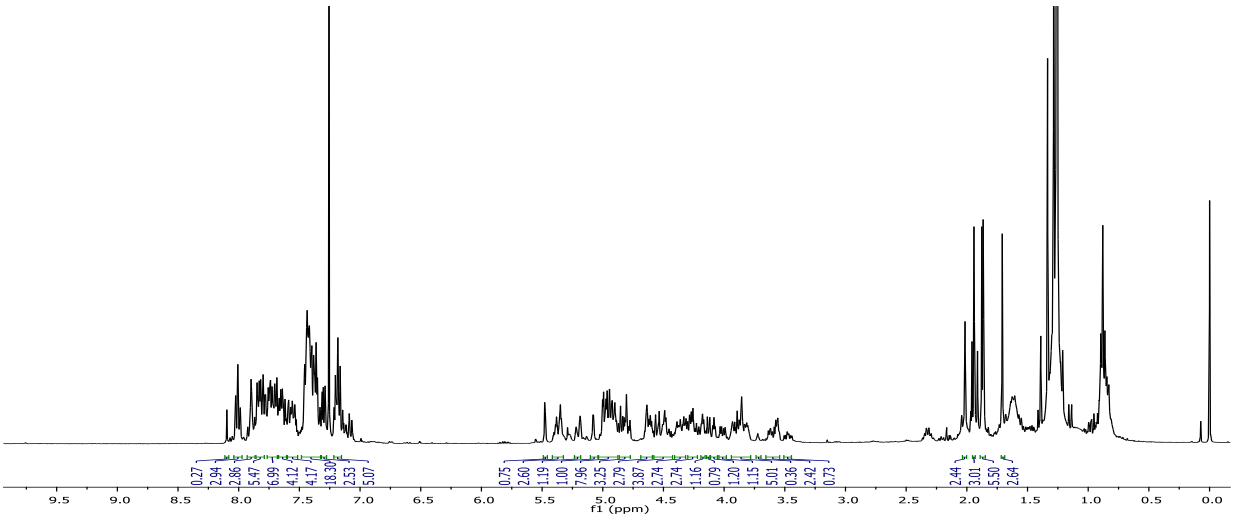




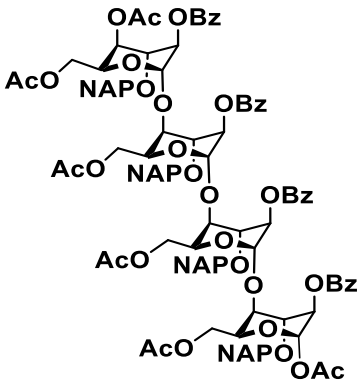


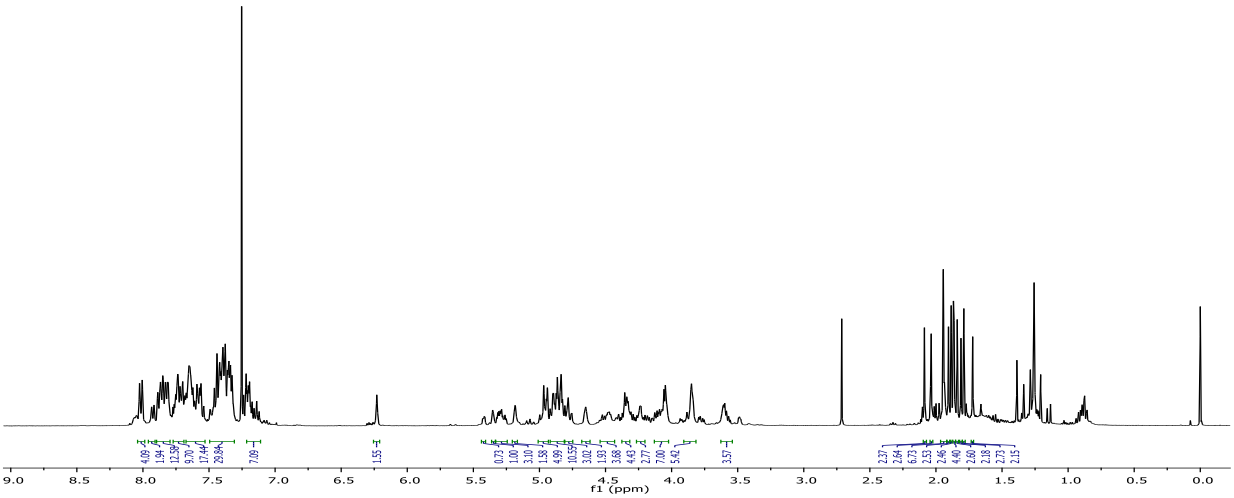
29. 1H NMR of compound 27



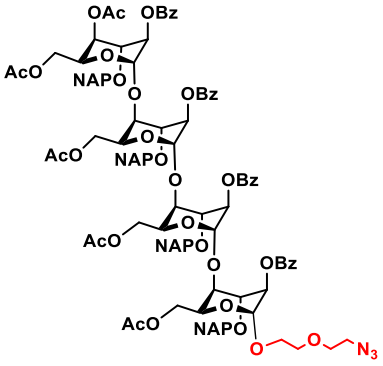


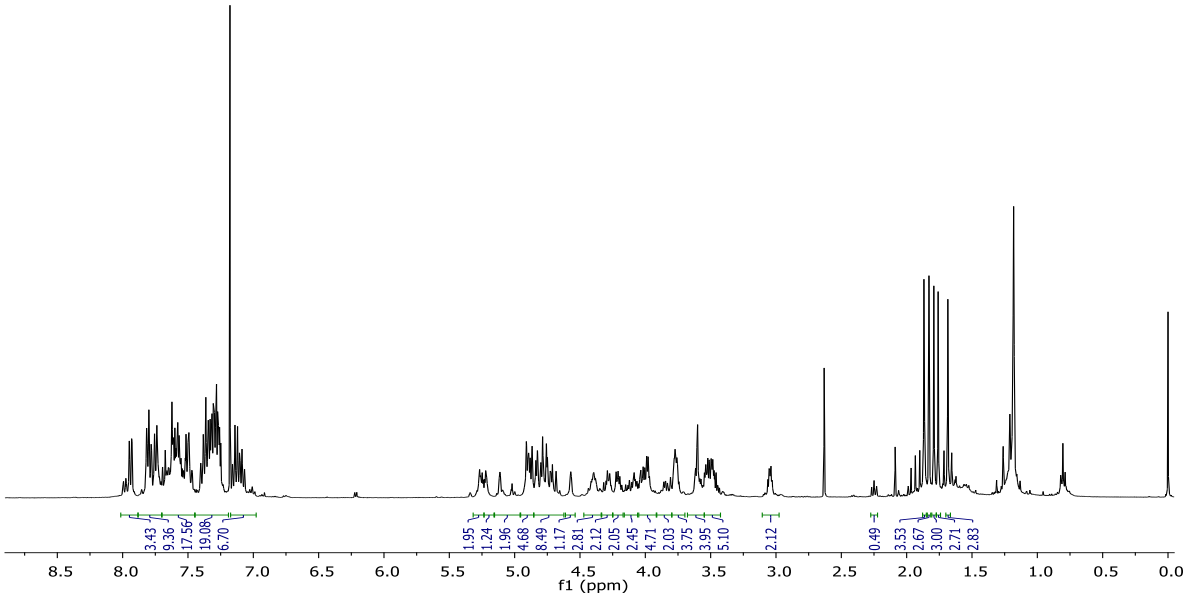
30. 1H NMR of compound 28

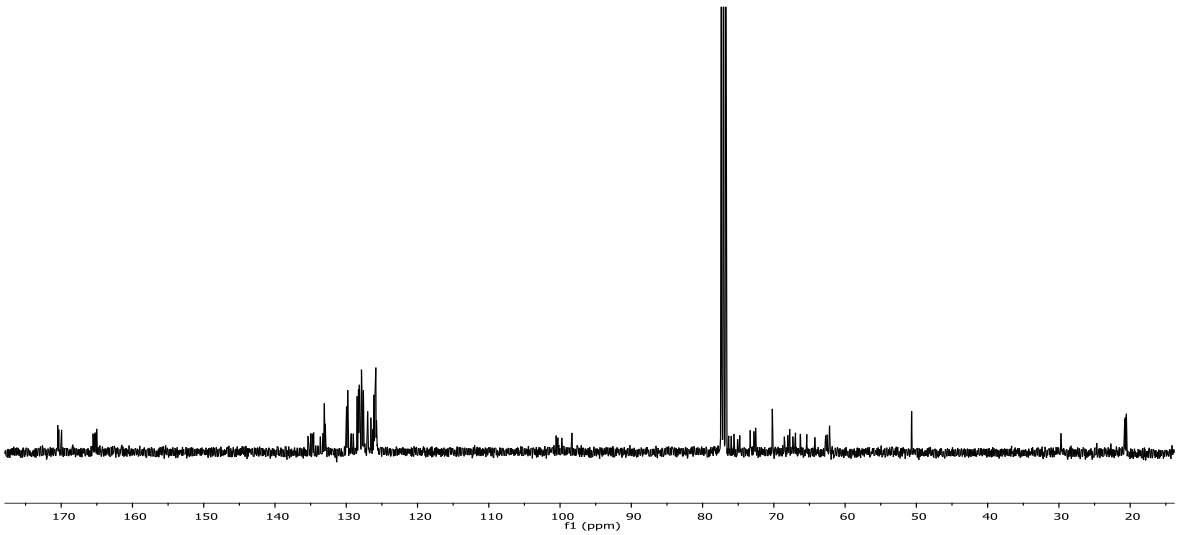




31. 1H and 13C NMR of compound 30


OAc
OBz
AcO
NAPO
O
OBz
AcO
NAPO
O
OBz
AcO
NAPO
O
OBz
AcO
NAPO
O
O
N3


3.43
9.36
17.56
19.08
6.70
1.95
1.24
1.96
4.68
8.49
1.17
2.81
2.12
2.05
2.45
4.71
2.03
3.75
3.95
5.10
2.12
0.49
3.53
2.67
3.00
2.71
2.83
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
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)