[Au]/[Ag]-Catalyzed Synthesis of Biologically Important Bacterial Oligosaccharides

विद्या वाचस्पति की
उपाधि की अपेक्षाओं की आंशिक पूर्ति में प्रस्तुत शोध प्रबंध

A Thesis submitted in partial fulfilment of the requirements of the degree of Doctor of Philosophy

द्वारा / By

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भारतीय विज्ञान शिक्षा एवं अनुसंधान संस्थान पुणे

INDIAN INSTITUTE OF SCIENCE EDUCATION AND RESEARCH PUNE

2024

Dedicated to….

My Parents

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CERTIFICATE

Certified that, the work incorporated in the thesis entitled, "***[Au]/[Ag]-Catalyzed Synthesis of Biologically Important Bacterial Oligosaccharides***" submitted by **Pratim Kumar Das** was carried out by the candidate, under my supervision. The work presented here or any part of it has not been included in any other thesis submitted previously for the award of any degree or diploma from any other University or institution.

Date: 18th Dec 2024

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Title of Thesis: [Au]/[Ag]-Catalyzed Synthesis of Biologically Important Bacterial Oligosaccharides

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Prof. Srinivas Hotha

Date: 18/12/2024

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General remarks

- ^{1}H NMR spectra were recorded on Bruker 400, JEOL 400, Bruker 600 MHz spectrometer using tetramethylsilane (TMS) as an internal standard. Chemical shifts are expressed in ppm units downfield to TMS.
- ^{13}C NMR spectra were recorded on Bruker 100, JEOL 100, Bruker 150 MHz spectrometer.
- High resolution mass spectroscopy (HRMS) was performed on Waters Synapt G2 and Applied Biosystems MALDI-TOF spectrometer.
- IR spectra were recorded on Perkin-Elmer 1310 and Perkin-Elmer 1600 FT-IR spectrometers with sodium chloride optics and are measured in cm^{-1}.
- Specific rotations were measured on a JASCO P-1020 or Rudolph polarimeter and measured in degree.
- All reactions were monitored by Thin-Layer Chromatography carried out on precoated Merck silica plates (F254, 0.25 mm thickness); compounds were visualized by UV light or by staining with anisaldehyde spray.
- All reactions were carried out under nitrogen or argon atmosphere with dry freshly prepared solvents under anhydrous conditions and yields refer to chromatographically homogenous materials unless otherwise stated.
- All evaporators were carried out under reduced pressure on Büchi and Heildoph rotary evaporator below 45 °C unless otherwise specified.
- Silica gel (100-200) and (230-400) mesh were used for column chromatography.
- All gold and transition metal salts were purchased from multinational commercial vendors.
- Materials were obtained from commercial suppliers and were used without further purification.
- Scheme, Figure and Compound numbers in abstract and individual chapters are different.

Abbreviation

Å – Angstrom
Ac – Acetate
AcBr – Acetyl bromide
AcCl – Acetyl chloride
AcOH – Acetic acid
Ac_2O – Acetic anhydride
AG – Arabinogalactan
Ara*f* – arabinofuranosyl / arabinofuranoside
Bn – Benzyl
BnBr – Benzyl bromide
Boc – t-butylcarbonyl
Bz – Benzoyl
BzCl – Benzoyl chloride
Calcd – Calculated
Cbz – Carbobenzoloxy
CAN – Cerric ammonium nitrate
cat. – catalytic
$CDCl_3$ – Chloroform-D
$CHCl_3$ – Chloroform
COSY– Homonuclear Correlation Spectroscopy
DDQ – 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DEPT – Distortionless Enhancement by Polarization Transfer
DMAP – N,N-Dimethylaminopyridine
DMF – N,N‟-Dimethyl formamide
D_2O – Deuterium oxide
δ – delta (in PPM)
EDC – 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide
eq. – equivalents
Et_3N – Triethyl amine
EtOH – Ethanol
EtOAc – Ethyl acetate
FE-SEM – Field Emission Scanning Electron Microscopy
g – gram
Gal*f* – galactofuranosyl / galactofuranoside
h – hour
HRMS – High-Resolution Mass Spectrometry
HSQC – Heteronuclear Single Quantum Coherence
Hz – Hertz
Im. – Imidazole
IR – Infrared
J – coupling constant
Kg – Kilogram
LAM – Lipoarabinomannan.
Man*p* – mannopyranosyl / mannopyranoside
MeOD – Methanol-D4
mg – milligram
MHz – Megahertz
mL – millilitre
mmol – millimolar
MS – Molecular sieves
Mtb – Mycobacterium tuberculosis
NAP – N-bromomethyl naphthalene
NGP – Neighbouring group participation
NIS – N-Iodosuccinimide
NMR – Nuclear Magnetic Resonance
PMB – p-Methoxy benzyl
Py – Pyridine
PTSA – *p*-Toluene sulfonic acid
ppm – parts per million
Rib*f* – ribofuranoside / ribofuranosyl
rt – room temperature
sat – saturated
TBAF – tetra-n-Butyl ammonium fluoride
TBAI – tetra-n-Butyl ammonium iodide
TBDMS – t-Butyldimethylsilyl
TBDMSCl – t-Butyldimethylchloride
TBDPS – t-Butyldiphenylsilyl
TBDPSCl – t-Butyldiphenylsilylchloride
TfOH – Triflouromethanesulfonic acid
THF – Tetrahydrofuran
TLC – Thin Layer Chromatography
TMSOTf – Trimethylsilyltrifluoromethanesulfonate
μmol – micromolar
μL – microliter

Synopsis

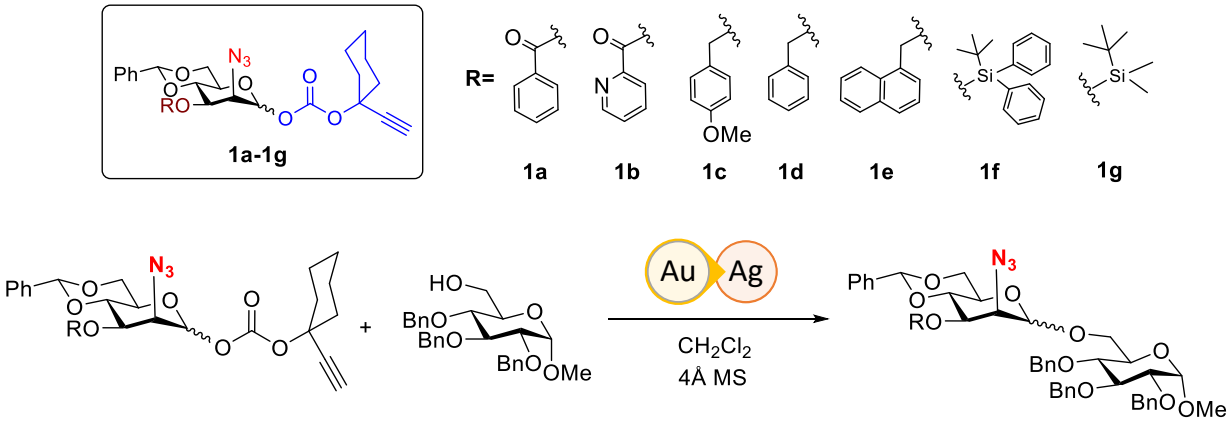
The thesis titled, "***[Au]/[Ag]-Catalyzed Synthesis of Biologically Important Bacterial Oligosaccharides***" is divided into four chapters. In chapter 1, a brief introduction about carbohydrates, methods for the synthesis of oligosaccharides and glycoconjugates and their biological significance is described. The chapter 2 deals with the stereoselective synthesis of 2-azido-2-*deoxy*-*β*-D-mannopyranosides using the novel [Au]/[Ag]-catalyzed glycosylation protocol. Chapter 3 delineates the first total synthesis of a hyperbranched complex pentasaccharide motif from the cell wall of *Clavibacter phaseoli* VKM-2641^{T} species. In chapter 4, a highly convergent and efficient synthetic route for the synthesis of giant linear 38-mer galactofuranan epitope of *Mycobacterium tuberculosis* cell wall is demonstrated.

Chapter 1: Introduction to Chemical Glycobiology.

Carbohydrates are essential biomolecules that play crucial role in the structure, function, and energy metabolism of living organisms. They are widely distributed in cell surfaces in the form of glycoconjugates e.g. oligosaccharides, glycoproteins and glycolipids. Glycoconjugates are responsible for many key biological processes including immune responses, cell-cell communication, hormonal controls and metabolism. The biomedical applications of glycoconjugates are widely acknowledged, and several carbohydrate-based drugs and vaccines are currently undergoing clinical trials. However, the inherent micro-heterogeneity of these naturally occurring glycoconjugates makes it challenging to obtain pure and structurally defined glycans. In this premise, chemical synthesis of oligosaccharides and glycoconjugates with defined structure and stereoselectivity is of high importance. In the last few decades, synthetic carbohydrate chemists have put numerous efforts to develop more efficient glycosyl donors with better glycosylation yields and stereoselectivity. In the early years, glycosylation required stoichiometric quantities of highly acidic promoters like BF_3•Et_2O and TfOH. Over the years, milder methods have been developed with catalytic activation, broader substrate scope and increased protecting group tolerance. The last decade has witnessed remarkable progress in glycoconjugate syntheses particularly with the emergence of gold-catalyzed glycosylation methodology. The novel protocol of silver-assisted gold-catalyzed activation of ethynylcyclohexyl carbonate donors has been widely utilized in the synthesis of complex oligosaccharides and glycoconjugates with excellent yield and selectivity. The following chapters delineates the extensive application of gold catalyzed glycosylation in the stereoselective synthesis of 1,2-*cis* mannopyranosides and complex cell wall oligosaccharides of bacterial origin.

Chapter 2: [Au]/[Ag]-catalyzed Direct Stereoselective Synthesis of 2-azido-2-*deoxy*-*β*-D-mannopyranosides

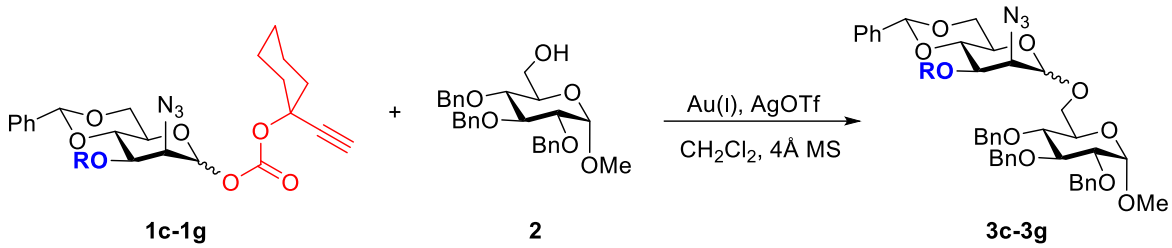
Synthesis of 1,2-*cis* glycosides remains a challenging task in carbohydrate chemistry. The *β*-ManNAc oligosaccharides are very important components in bacterial cell wall polysaccharides and are responsible for many key physiological functions. Synthesizing *β*-mannosides is even more tedious task due to the influence of anomeric effect and C2-axial substituent of mannose. According to the literature, Prof. Crich's procedure of conformationally constrained pyranosyl donor activation proved to be an efficient method for the synthesis of *β*-D-mannosides. However, the reports are primarily based on C2-ether type linkage as nonparticipating group and activating only thioglycoside donors majorly. As we target the synthesis of less explored *β*-ManNAc oligosaccharides, we set out to investigate our [Au]/[Ag]-catalyzed activation of mannosyl carbonate donors in the synthesis of 2-azido-2-*deoxy*-*β*-D-mannosides. A series of ethynyl cyclohexyl mannosyl carbonate donors **1a-1g** was synthesized in order to synthesize 2-azido-2-*deoxy*-*β*-D-mannosides directly utilizing silver-assisted gold catalysis. The C2-azido group was envisaged to serve for two purposes: (i) it can act as a non-participating group in glycosylation and (ii) it will serve as a precursor to the -NHAc group in the *β*-ManNAc glycoconjugate synthesis. Various protecting group was installed in the C3-position of the mannosyl carbonate donor to check the stereoelectronic effect of the C3-protecting group in the stereoselectivity outcome of the glycosylations.



Scheme 2.1. Proposed donor and model reaction for the stereoselective synthesis of 2-azido-2-*deoxy*-*β*-mannopyranosides

We aimed to explore the [Au]/[Ag]-catalyzed *β*-mannosylation methodology by activating mannosyl carbonate donors across a wide range of reaction temperatures, from -25 °C to +25 °C,

and varying the concentrations between 50 mM and 10 mM. The glycosylation with mannosyl carbonate donors **1c-1g** yielded disaccharides with high *β*-selectivity and excellent glycosylation yields. Surprisingly, the *β*-selectivity was not only dependent on temperature; it was found that the concentration of the glycosylation reaction has a profound effect on the selectivity outcome. The screening of the glycosylation showed that the C3-TBS equipped carbonate donor as the ideal donor furnishing the maximum *β*-selectivity.



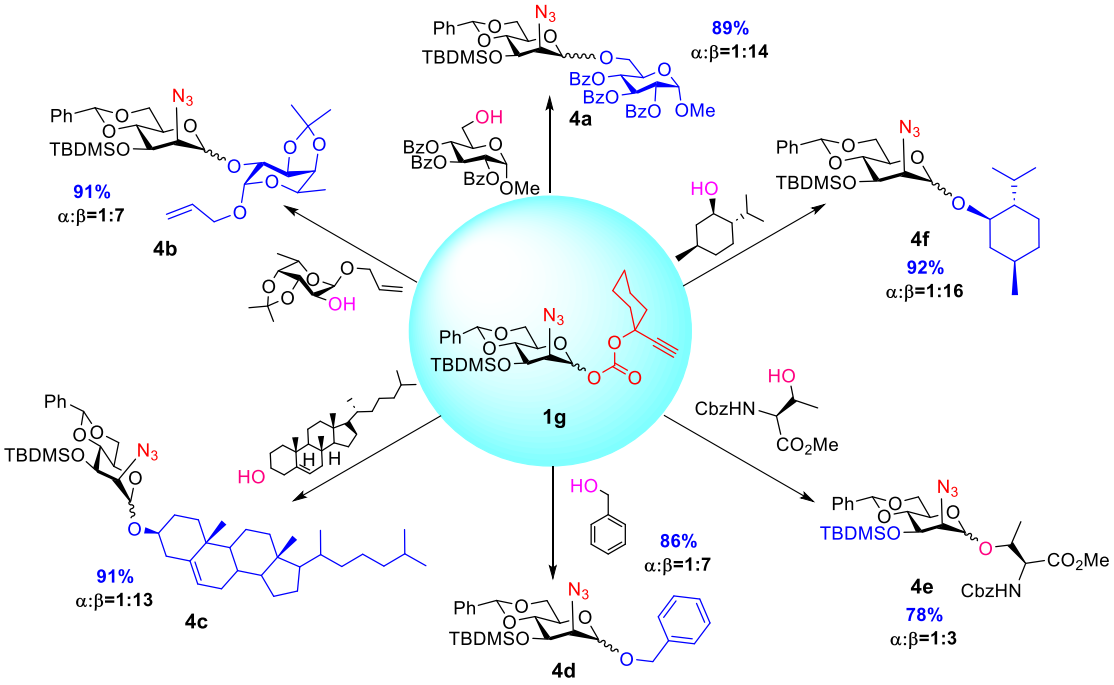
1c-1g **2** **3c-3g**

Entry	R =	Disaccharide	T= 25 °C (α:β)		T= 0 °C (α:β)		T= -25 °C (α:β)	
			50 mM	10 mM	50 mM	10 mM	50 mM	10 mM
1.	PMB	**3c**	1:6	1:10	1:8	1:13	1:6	1:15
2.	Bn	**3d**	1:5	1:10	1:6	1:12	1:5	1:11
3.	Nap	**3e**	1:6	1:8	1:7	1:14	1:5	1:14
4.	TBS	**3g**	1:7	1:11	1:9	1:18	1:8	1:19

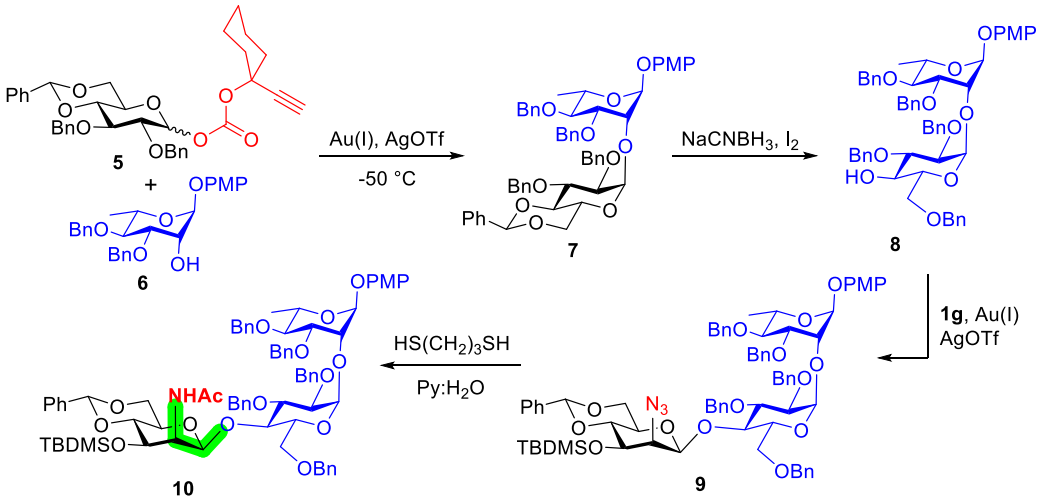
Table 2.1. Screening of all the carbonate donors in β-selectivity

The methodology proved to be extremely versatile in producing *β*-mannosides using variety of acceptors ranging from sugar acceptors, steroidal, aromatic alcohols and amino acid residues. The activation of optimized C3-TBS armed mannosyl donor **1g** in 0 °C/10 mM glycosylation conditions results into good to excellent *β*-selectivity furnishing *β*-mannoconjugates **4a-4f** with excellent glycosylation yields.

The mechanistic studies utilizing the VT-NMR reveals that the gold catalyzed activation of the carbonates lead to the generation of a highly reactive covalent *α*-triflate intermediate which is believed to be the key species responsible for the generation of *β*-mannosides. This novel protocol was successfully applied in the synthesis of a protected capsular trisaccharide motif of the *Streptococcus pneumoniae* 19F (**scheme 2.3**).



Scheme 2.2. Substrate scope of the methodology

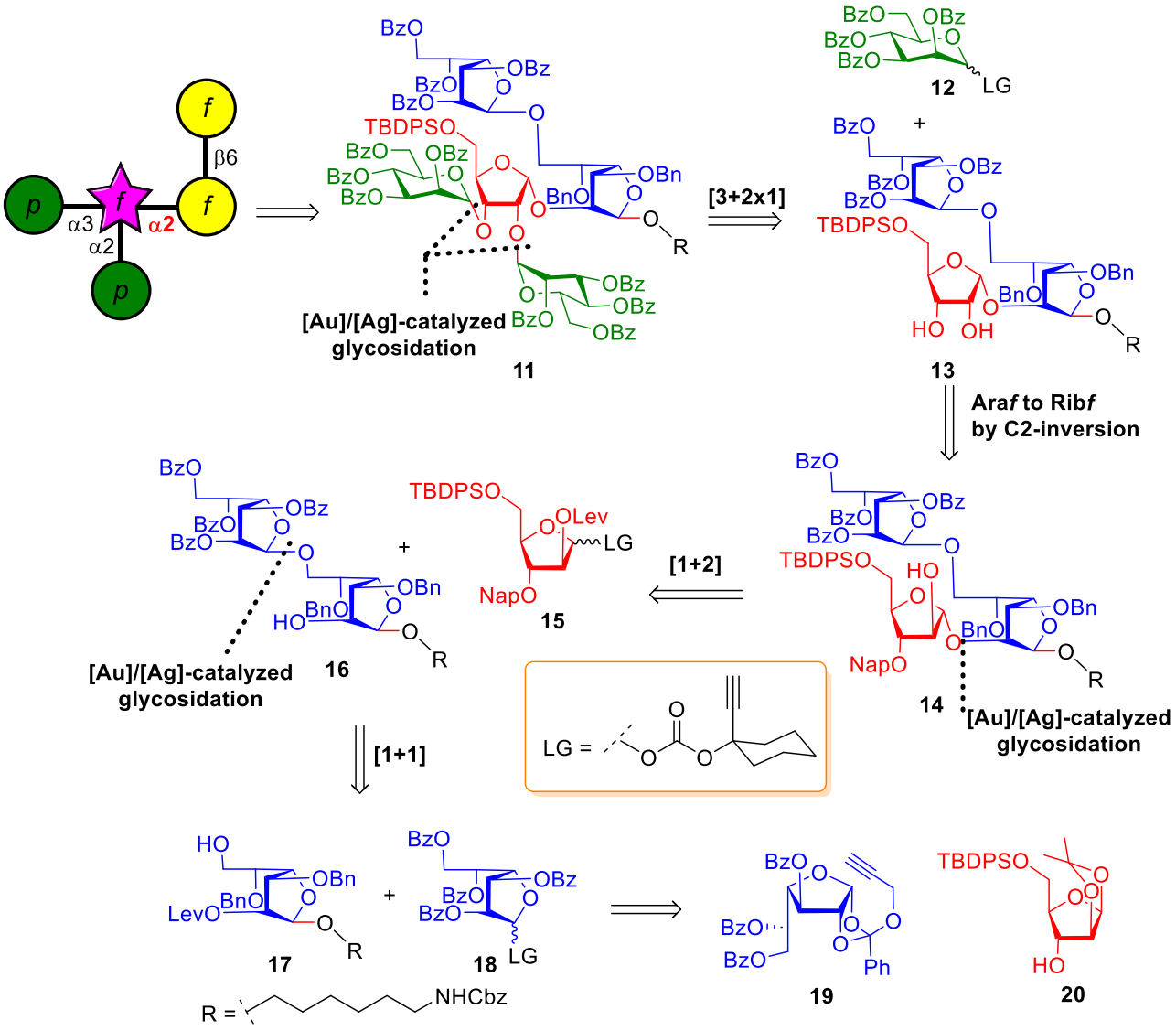


Scheme 2.3. Synthesis of the capsular trisaccharide of *S. pneumoniae* type 19F

Chapter 3: Total Synthesis of Conjugation-ready Hyperbranched Pentasaccharide of *Clavibacter phaseoli* VKM Ac-2641^{T}

Clavibacter is a genus of gram-positive bacteria which is responsible for various disease in many economically important plants. In the last decade, cell wall components of many Clavibacter species were structurally elucidated and chemical structures of the glycans were established. Among these, we targeted the total synthesis of a hyperbranched Pentasaccharide from the cell wall of *Clavibacter phaseoli* VKM-2641^{T} strain. The pentasaccharide features a highly branched

core 1,2-*cis* riboside motif attached to mannose and a di-galactofuranoside epitope. The conjugation ready pentasaccharide was envisaged from protected pentasaccharide motif **11**. Compound **11** can be synthesized by the coupling of the trisaccharide acceptor **13** and two units of mannosyl carbonate donor **12**. The *cis* riboside motif in **13** can be envisaged from the trisaccharide motif utilizing C2-inversion. Proceeding further into the retrosynthesis, trisaccharide **16** was envisaged from the easily accessible building blocks **17**, **18** and **20** (Scheme **3.1**).



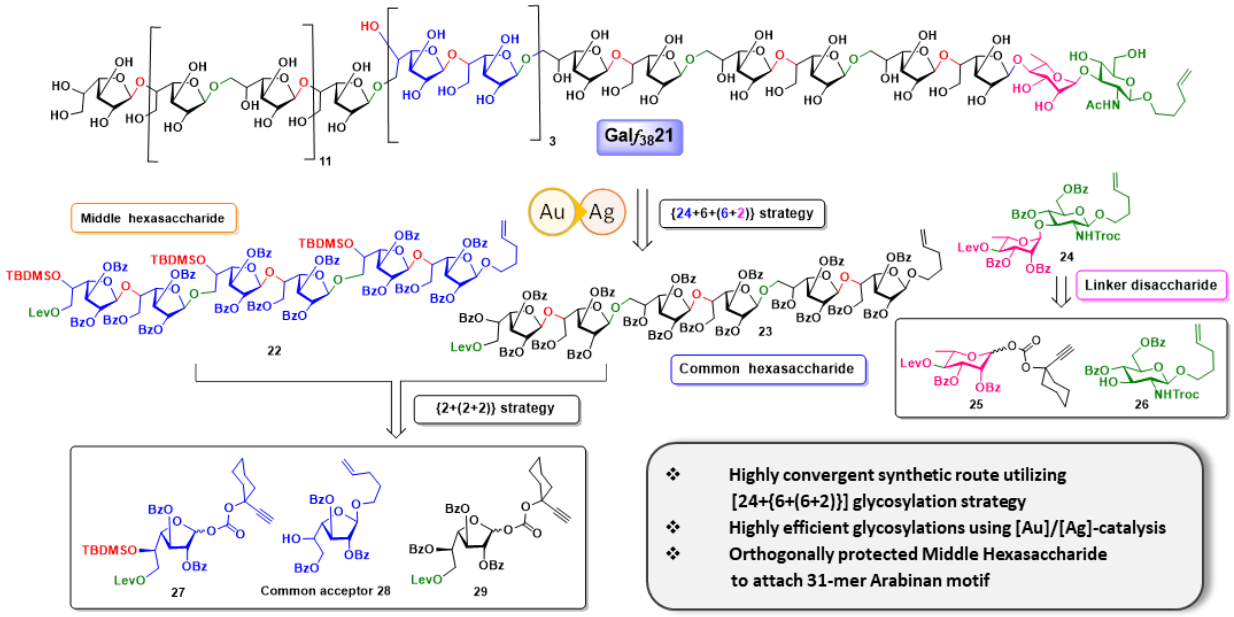
Scheme 3.1. Total Synthesis of Conjugation-ready Hyperbranched Pentasaccharide

The monosaccharide donors **15** and **18** were successfully synthesized from the commercially available D-galactose and D-arabinose. The aminohexyl linker at the reducing end of the Gal*f* residue was successfully attached using the Au(III)-catalyzed activation strategy of the Gal*f*

orthoester. [Au]/[Ag]-catalyzed glycosylation between Gal*f* donor **18** and acceptor **17** followed by Lev- deprotection successfully furnished the Gal*f* disaccharide acceptor **16**. Subsequent glycosylation between Ara*f* donor **15** acceptor **16** followed by deprotection yielded the trisaccharide **14**. PDC/Ac_2O mediated oxidation of **14** gave rise to the corresponding 2-ulose derivative which was subjected to reduction by $NaBH_4$ to successful furnish the α-Rib*f* containing trisaccharide. This nature inspired oxidation-reduction strategy proved to be extremely useful for the C2-inversions in oligosaccharide synthesis. Further Nap deprotection successfully yielded the di-ol acceptor **13**. Stepwise glycosylation with two mannosyl carbonate donors with trisaccharide **13** followed by global deprotection successfully furnished the Pentasaccharide. The total synthesis was accomplished using gold catalyzed glycosylation protocol with 9.6 % overall yield.

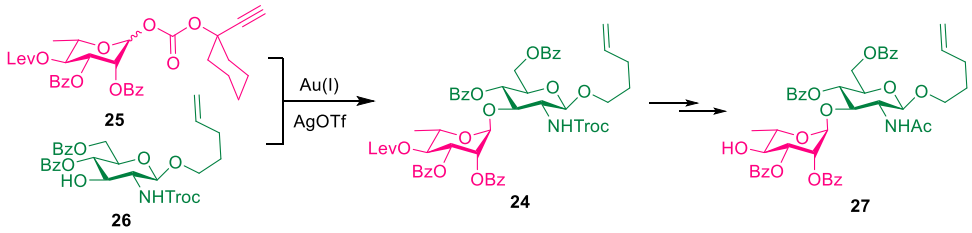
Chapter 4: Synthesis of tetradecasaccharide Reminiscent of Mycobacterial Cell wall

Tuberculosis is a severe infectious disease caused by *Mycobacterium tuberculosis*. The bacterium has a complex cell wall having diverse layers of heterogeneous glycans and lipids. We targeted the complex linear 38-mer Gal*f* residue which is an essential part of the giant 131-mer Arabinogalactan motif. The linear Gal*f* motif has a unique characteristic of possessing *β*-(1→5) and β-(1→6) linkages alternatively. To target this structure, a highly convergent synthetic strategy was developed using the [Au]/[Ag]-catalyzed glycosylation protocol. After retrosynthesis, the full length 38-mer Gal*f* **21** was envisaged from the middle hexasaccharide **22**, common hexasaccharide epitope **23** and the linker disaccharide motif **24** (Scheme **4.1**).



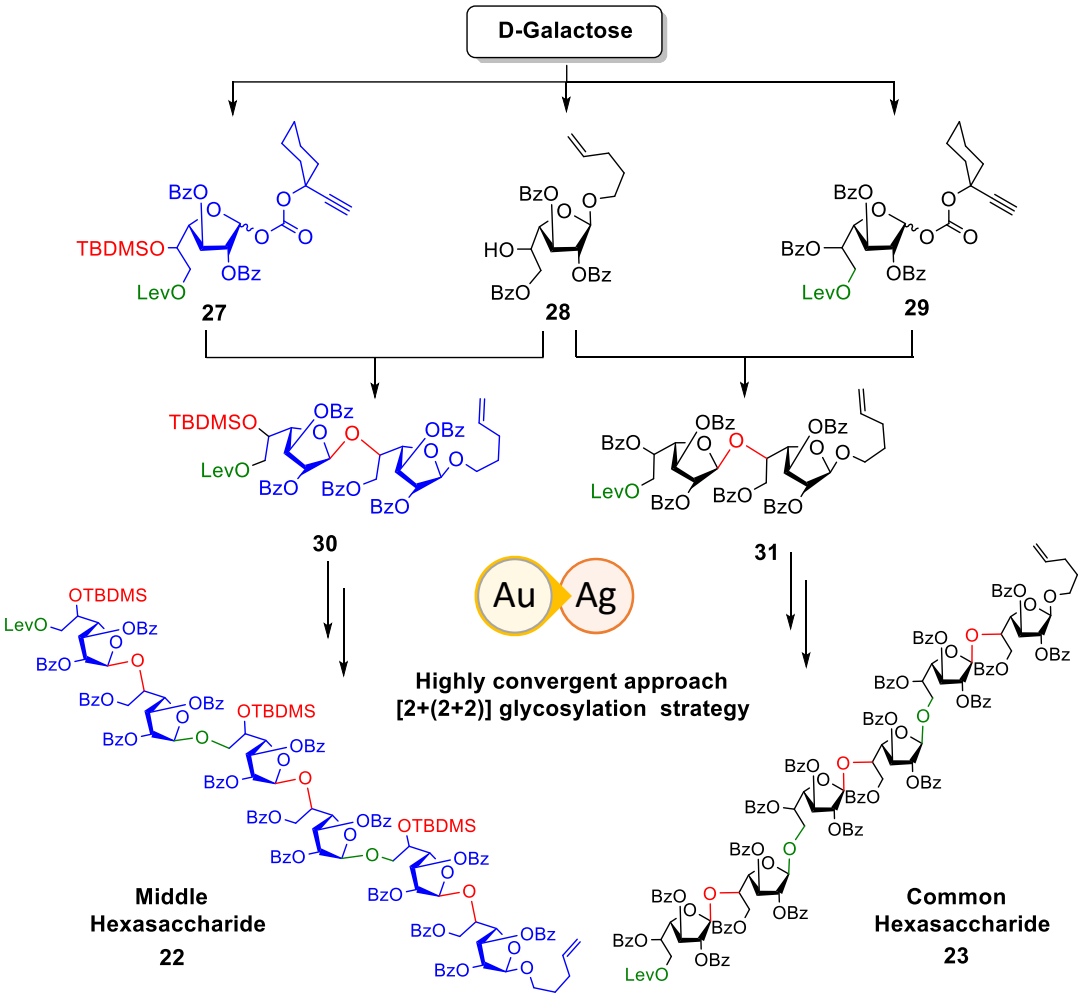
Scheme 4.1. Retrosynthesis of 38-mer Gal*f* residue of MTb cell wall

Our synthetic journey was started with the synthesis of the linker disaccharide at the reducing end. The rhamnosyl carbonate donor **25** and glucosamine acceptor **26** were synthesized from commercially available L-rhamnose and D-glucosamine. [Au]/[Ag]-catalyzed glycosylation between **25** and **26** followed by functional group interconversion successfully furnish the disaccharide acceptor **27** (Scheme **4.2**). The synthesis of the hexasaccharide motifs **22** and **23** started from the monosaccharide Gal*f* building block synthesis. Commercially available D-galactose was locked into an unfavorable furanose form and subsequent orthogonal protections and deprotections give rise to the galactofuranosyl carbonate donors **27**, **29** and a common acceptor **28**. The glycosylation between **27** and **28** gives rise to the disaccharide building block **30** for the synthesis of middle hexasaccharide. Similar glycosylation between donor **29** and acceptor **28** furnishes the disaccharide building block **31** for the common hexasaccharide synthesis. Subsequently, the disaccharides were divided into two parts: one part gives rise to disaccharide acceptors after lev deprotections; other part was subjected to pentenyl deprotections followed by treatment with carbonate reagent to successfully furnish the disaccharide donors. Following this synthetic strategy, both the middle and common hexasaccharide epitopes were synthesized utilizing [2+(2+2)] coupling strategy under the optimized [Au]/[Ag]-catalyzed glycosylation conditions with good to excellent yields (Scheme **4.3**).



Scheme 4.2. Synthesis of the linker disaccharide

We now begin the stitching of the large epitopes utilizing the silver assisted gold-catalyzed activation of carbonate donors. The glycosylation of the common hexasaccharide donor and disaccharide acceptor **27** followed by Lev-deprotection successfully yielded the octasaccharide acceptor **32**. The glycosylation between middle hexasaccharide carbonate donor and acceptor 32 gives rise to the fully protected 14-mer Gal*f* epitope **33** (Fig **4.1**). Currently, the final assembly of the repeating hexasaccharides with the 14-mer is underway in our group. Three TBDMS group in the middle hexasaccharide **22** are strategically placed to attach the branch 31-mer Arabinan epitope three times allowing the construction the giant 131-mer Arabinogalactan motif.



Scheme 4.3. Synthesis of the hexasaccharide epitopes

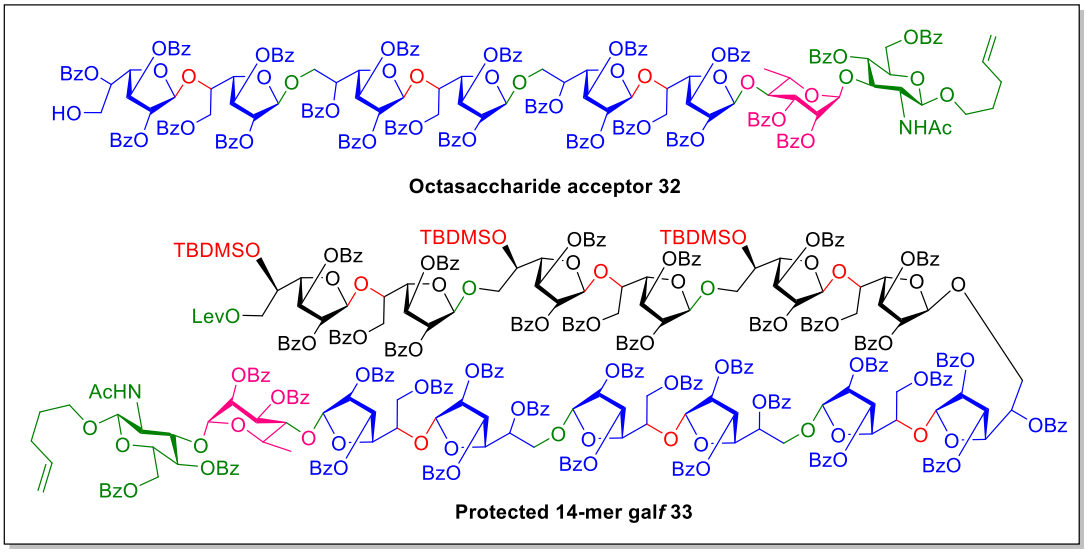


Fig 4.1. Synthesized large Gal*f* fragments.

Chapter 1

Introduction to Chemical Glycobiology

Chapter 1

1.1 Introduction of Carbohydrates: Source of life[1]

Within all lifeforms of earth, ranging from a tiny microorganism to a giant elephant, there are four major macromolecules named carbohydrates, proteins, lipids (fats) and nucleic acids. Among these, carbohydrates are one of the most abundant and extensively studied organic compounds on earth surface. Chemically carbohydrates are made up of carbon, hydrogen and oxygen atoms having a general formula of $(CH_2O)_n$ where 'n' represents the number of carbon atoms. Carbohydrates, the fundamental macronutrient essential for human health also serves as the major energy source for the human body fueling various biophysical processes and activities.

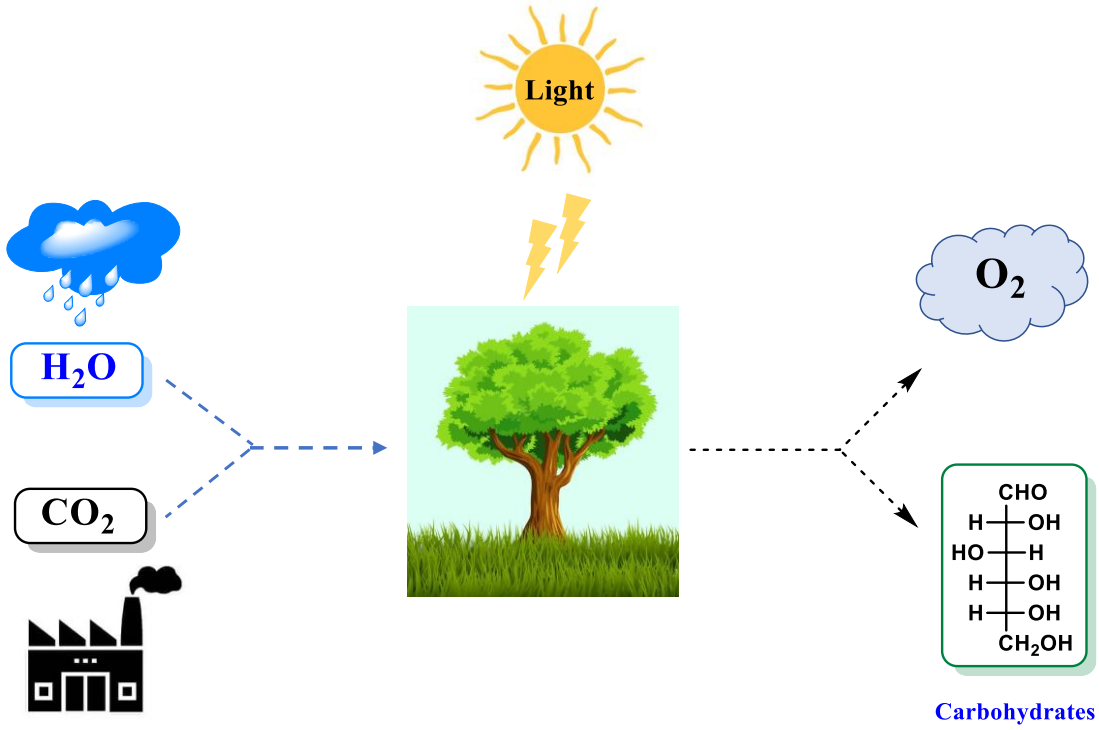


Fig 1.1 Process of Photosynthesis.

Carbohydrates draw the direct correlation between light energy and chemical energy. Naturally green plants, algae and some bacteria harvest the light energy from sun and convert it to chemical energy in the form of carbohydrates via a process called Photosynthesis.

$$6CO_2 + 6H_2O + \text{light energy} \rightarrow C_6H_{12}O_6 + 6O_2$$

In this process water (H_2O) gets reacted with atmospheric CO_2 in the presence of light energy to form O_2 and glucose ($C_6H_{12}O_6$). The monosaccharide glucose is further converted to complex oligosaccharides and glycoconjugates with the help of enzymes.

1.2 Structural diversity in carbohydrates[2a-c]:

Carbohydrates exhibit a distinctive diversity in nature, enabling the formation of complex oligomeric and polymeric structures beyond what is seen in proteins, nucleic acids, and lipids. Unlike amino acids and nucleic acids, which primarily offer head-to-tail polymerization, carbohydrates can undergo multiple ends for oligomerization because of the presence of different hydroxyl groups. Not only this, other unique features like anomeric stereochemistry, ring size, stereochemistry of the other centers, linkage position, branching and presence of other conjugates make the carbohydrates structurally far more diverse in the real world and at the same time very difficult to characterize. While for proteins, DNA and RNAs nature uses only few monomeric building blocks of amino and nucleic acids, but in the glycome world the database showcases an extensive array of carbohydrate structures due to its structural diversity (Table 1.1). The evolutionary reason behind nature's selection of such diverse carbohydrate library remains an intriguing question.

Oligomer size	Nucleotides	Peptides	Carbohydrates
1	4	20	20
2	16	400	1360
3	64	8000	126,080
4	256	160000	13,495,040

Table 1.1 Diversity space of macromolecule monomers[2c]

1.3 Early years of carbohydrate… Discovery and Nomenclature[1b,3]:

The discovery of carbohydrates as a distinct class of organic compounds began in the mid-1800s. In this era individual sugars were named ending with ‘-ose’. In 1838, Dumas coined the term ‘glucose’ (Greek ‘gleukos’ or sweet wine) for the sugar obtained from honey, grapes and starch. In 1855, Claude Bernard identified and named 'glycogen,' a substance similar to starch stored in mammalian livers[3b]. Glycogen is composed of glucose derived from the blood and can be converted back into glucose as needed by the body. In 1866, based on polarimetric studies German

chemist August Kekulé proposed the name dextrose for dextrorotatory glucose. The finest contribution to the carbohydrate world came from German scientist Emil Hermann Fischer. During the years 1880-1900, Fischer, utilizing his exceptional skills and brilliant intellect despite limited analytical methods and resources, worked on determining the relative configurations of the majority of known sugars. After a while Heinz and Heidi proposed the cyclic structure of glucose in aqueous solution, highlighting its existence in two distinct optical rotations (denoted as α and β). In 1926, Haworth proposed the carbohydrate ring preferably to be cyclic six membered pyranose rings that can adopt different conformational isomeric structures. In the early 1900s besides many of other organic chemist's belief, using electron diffraction studies Hassel and Barton demonstrated the non-planarity of pyranose ring. Later from the conformational study Edward observed that the free energy difference between the two conformers (α, β) is somewhat lesser than the expected value in favor of β (equatorial) isomer formation over axial isomer. This particular phenomenon is coined as "Anomeric effect" by Lemieux.

1.4 Biological significance of carbohydrates and glycoconjugates[4]

Initially in the early ages, carbohydrates were primarily recognized as a significant energy source and structural element for plants and living organisms, particularly forming cell walls in plants and exoskeletons in insects and arthropods. However, contemporary understanding reveals that carbohydrates play a far broader role in living systems, serving as a fundamental component of cellular organization and physiological functions across all domains of life. Carbohydrates are primarily found as conjugates covalently linked to various chemical substances like proteins,

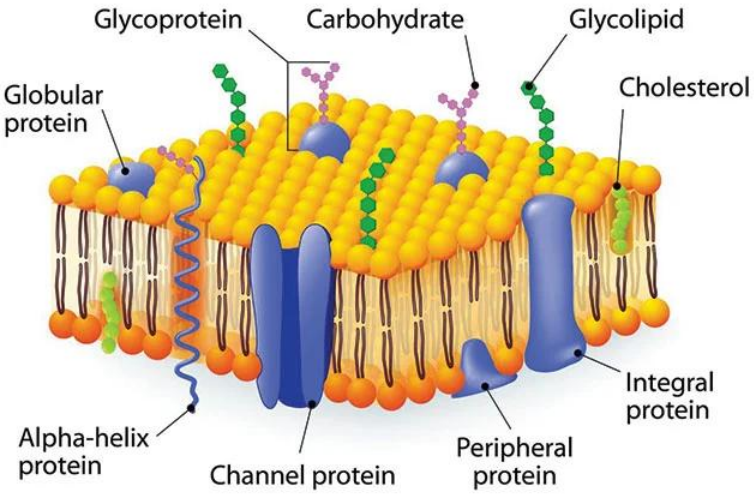
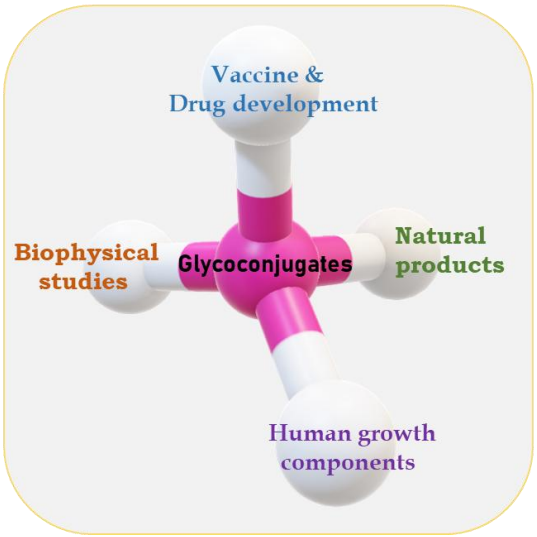


Fig 1.2 Natural abundance of glycoconjugates.

lipids, organic molecules, natural products, other sugar residues, and peptides through C-O, C-N, C-S, C-C and other heteroatom linkages as well. These are categorized into glycolipids, glycoproteins, oligosaccharides, polysaccharides, glycopeptides etc. The significance of cell surface glycoconjugates is multifaceted across various biological contexts. These complex molecules play essential roles in several key processes like intracellular trafficking and internalization, prokaryotic functions, extracellular communication, immune activation etc[4a]. These aspects and usefulness majorly draw the scientific world's attention to study the vast applications possible with glycoconjugates and paved the path of glycobiology. The term 'Glycobiology' was introduced in 1988 by Raymond Dwek[4b] to acknowledge the significance of carbohydrate chemistry and biochemistry in unraveling the cellular and molecular intricacies of glycans or glycoconjugates.

However, carbohydrates can also play a role in various adverse disease processes like inflammation, cancer metastasis, and bacterial or viral infections by taking part in vital host-guest interactions. In the recent worldwide deadly disaster of COVID-19 it has been identified that the virus known as SARS-COV-2, responsible for causing the COVID-19 illness, uses heparin sulfates found on the surface of cells to infect them[4c-e].



Furthermore, carbohydrates and their derivatives have been studied extensively as therapeutic agents for treating various diseases. In the last two decades, a total of 54 carbohydrate-based drugs containing carbohydrate moieties as the major structural units have been approved as drugs or diagnostic agents[4f]. Carbohydrates serve as a foundation in creating vaccine formulations, particularly those focused on combating microorganisms (antimicrobial vaccines) and cancer cells (anticancer vaccines) [4g]. Capsular polysaccharides and lipopolysaccharides are key components of microbial cell surfaces that can be recognized by the host immune system, making them potential targets for designing antibacterial vaccines [4h]. Besides, glycoconjugates are also routinely being used in nanomaterial development, genetic engineering, polymer industry etc.

1.5 Types of linkages in carbohydrates[5]

Going through the library of naturally available glycoconjugates, based on the relative position of C1 and C2 substituent, the linkages can be classified as two major classes 1,2-cis and 1,2-trans. Furthermore, according to the particular anomeric position, the linkage with axial C1 substituent is termed as α linkage and the linkage with equatorial C1 substituent is termed as β linkage. However, the moieties with no C2 substituents (2-deoxy sugars) can be termed as neither 1,2-cis nor 1,2-trans linkage but they can be defined as α or β based on the anomeric stereochemistry. Some of the representative glycosides with different type of linkages are shown in the Figure 1.3.

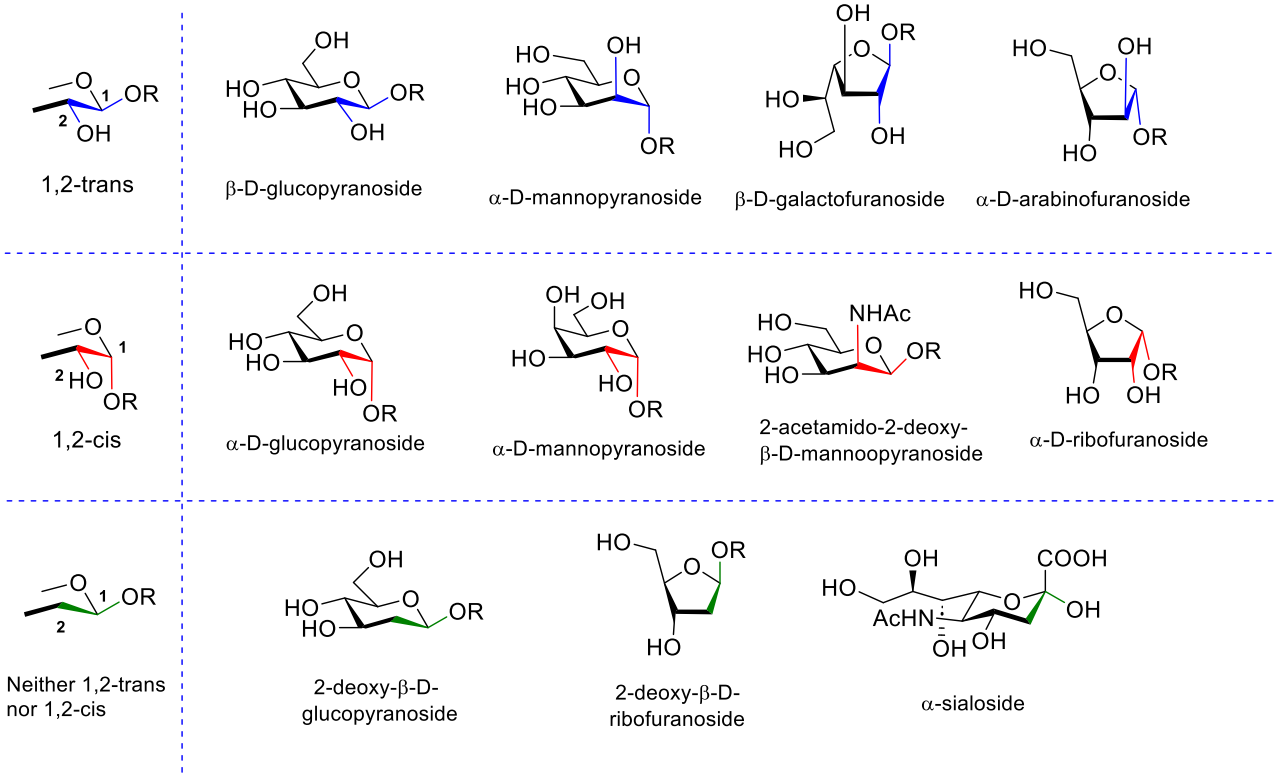


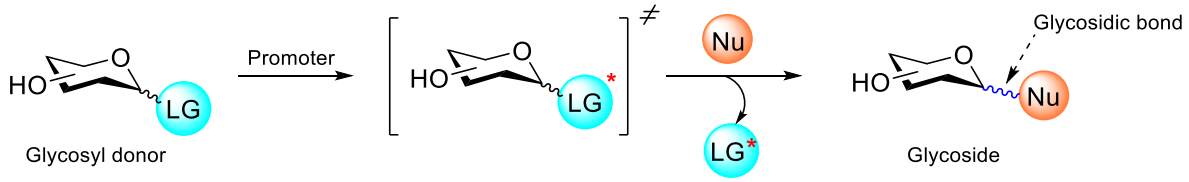
Fig 1.3. Types of glycosidic linkages

Anyway, it goes without saying that the occurrence of particular glycosidic bonds and linkages significantly impacts the physio-biological characteristics and functional roles within biological systems. Therefore, the synthesis of oligosaccharides and glycoconjugates featuring precise regio and stereochemical specificity within their linkages is highly significant in the field of carbohydrate chemistry.

1.6 Synthetic routes of glycoconjugates: Glycosylation[6]

As mentioned earlier, most of the naturally occurring glycans are not present in free form, rather they are linked with different kind of aglycones with different linkages. However, pure and well characterized glycoconjugates and oligosaccharides are indispensable research tools in glycobiology. But the glycans are present in heterogeneous forms and in very low concentrations in the natural resources. This makes the job of isolation and proper characterization of pure glycans way tougher. These inherent characteristics along with the structural diversity of the carbohydrates draw the scientific world's attention to chemically synthesize the required glycans in homogeneous forms and required amount.

Glycosylation is a coupling reaction in which a carbohydrate moiety gets covalently attached to another aglycone typically glycans, proteins, lipids containing at least one nucleophilic center. In this reaction, two participating moieties are there named glycosyl 'donor' and 'acceptor'.



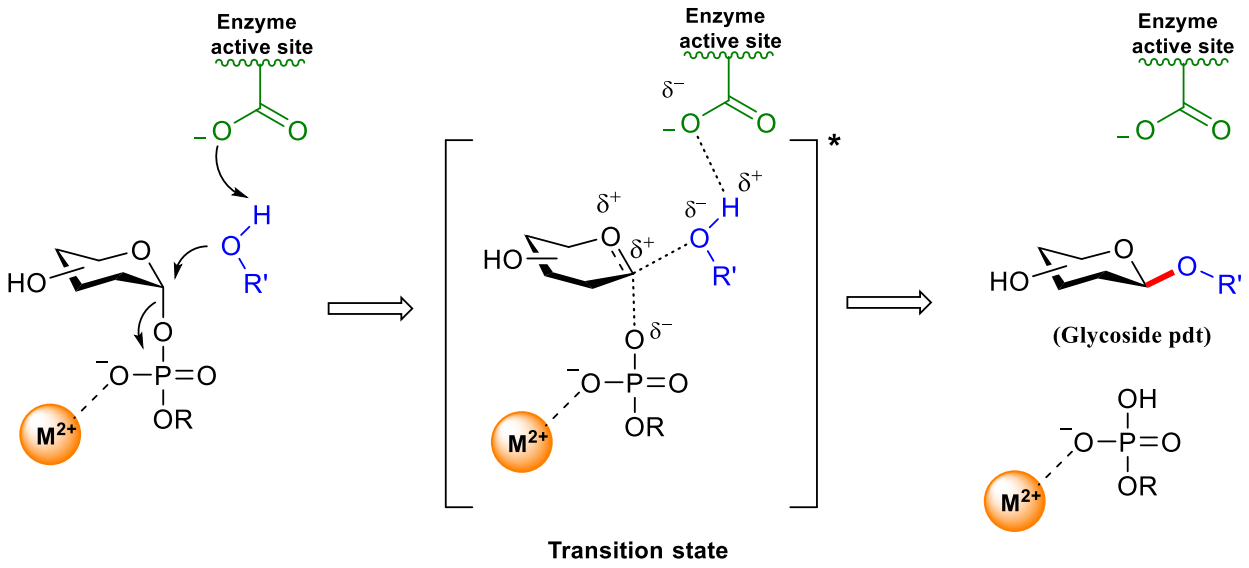
Scheme 1.1 General glycosylation mechanism

The glycosyl donor motif is invariably a carbohydrate moiety having a leaving group at the anomeric center which generates an electrophilic species by the activation by promoter or enzyme which later on gets attacked by acceptor nucleophile resulting in the formation of a new stereogenic center at the anomeric position. All the existing glycosylation methods can be broadly classified into two major categories: a) Enzymatic glycosylation, b) Chemical glycosylation.

1.6.1 Enzymatic glycosylation[6,7]

In natural systems, the glycoconjugates and oligosaccharides are synthesized with the assistance of various enzymes, including glycosyltransferases, glycosidases, and glycosynthases. The selectivity and regiospecificity of these enzymes play a crucial role in the synthesis of complex oligosaccharides and glycoconjugates. These enzymes can catalyze the formation of glycosidic bonds with precise regio- and stereochemical control, mild reaction conditions and catalytic conditions which indeed offer advantages over chemical synthesis in terms of flexibility and

efficiency. In this premise, in a Nobel winning work, Leloir and co-workers have identified a class of glycosyltransferases and their proper mode of action in biosynthesis of glycans. These transferases use nucleotide diphosphate sugar donors and are classified into retaining and inverting classes based on their stereochemistry at the anomeric position. A general enzymatic glycosylation process with inverting mechanism is shown in scheme 1.2.

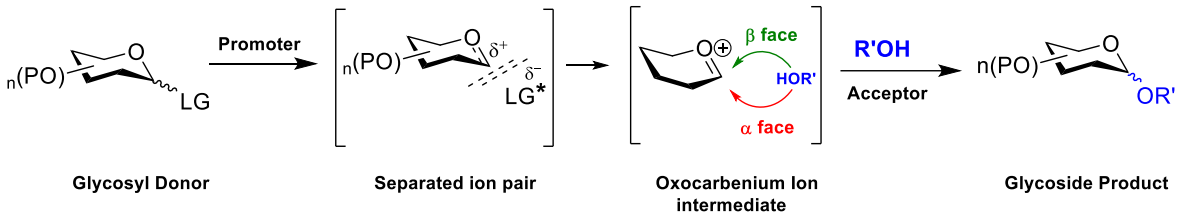


Scheme 1.2 General enzymatic glycosylation mechanism[7a]

However, the primary challenge in utilizing glycosyl transferase enzymes stems from factors such as the accessibility, cost of these enzymes, and the cost of sugar nucleotides. To overcome the challenges associated with glycosyltransferases, researchers have introduced glycosidases having cheaper substrate compatibility such as sugar halides and sugar *p*-nitrophenyl, to produce glycoconjugates in low yields. Later on, Withers group tackled these issues by developing glycosynthases, mutants of glycosidases created by replacing one catalytic aspartic or glutamic acid with another amino acid. These glycosynthases were then used to synthesize a range of glycoconjugates from fluoride glycosyl donors. Still the availability of limited number of enzymes and impracticality in large scale industrial synthesis remain as major drawbacks associated with enzymatic synthesis of the glycans. Therefore, utilizing chemical or hybrid chemo-enzymatic methods to obtain a wide range of glycoconjugates and oligosaccharides would be more beneficial in circumventing these restrictions.

1.6.2 Chemical Glycosylation[5]

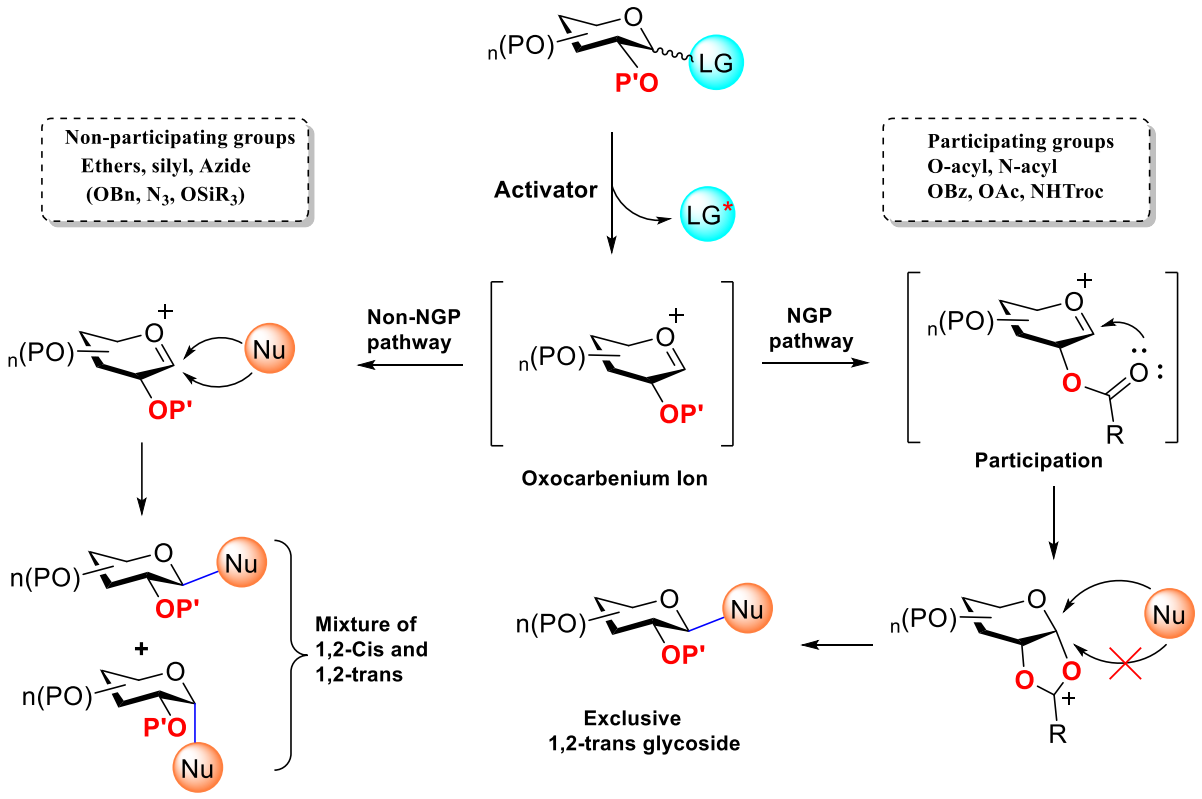
Chemical glycosylation method can produce homogeneous glycans in larger quantities than those available from most cellular production systems. This method involves one glycosyl donor motif equipped with a suitable leaving group and one glycosyl acceptor. Generally, upon treating with Lewis or Brønsted acids, the leaving group departs from the anomeric position generating a highly electrophilic oxocarbenium ion intermediate. Further the nucleophilic acceptor attacks the reactive intermediate to form a new glycosidic bond either in α- or β- fashion (Scheme 1.3).



Scheme 1.3 General representative chemical glycosylation.

The mechanism of chemical glycosylation is not completely understood till date but the exact mechanism and stereochemical outcome of the glycosylation depend on a number of structural and external factors such as nature of protecting groups, temperature, concentration, acceptor reactivity etc. However, the nature of the protecting group at C2 position of the donor moiety has a profound effect directly on the stereoselectivity of a particular glycosylation reaction.

The concept of neighboring group participation (NGP) is widely used in the syntheses of oligosaccharides. When an ester type protecting group is installed at C2 position of the glycosyl donor, it stabilizes the generated oxocarbenium ion through anchimeric assistance by forming a cyclic acyloxy type intermediate (Scheme 1.4). Due to this covalent participation the incoming nucleophile is bound to attack from one particular face resulting into exclusive 1,2-trans glycoside product. On the contrary when there is no participation from C2-subtituent, the generated oxocarbenium ion can be trapped from both faces by the nucleophile which results in generation of mixture of glycosides (1,2-cis and 1,2-trans). However, in this situation, the ratio of the cis- and trans- products depends on the other external factors especially the anomeric effect and temperature.



Scheme 1.4 Common C2-participation mechanism in chemical glycosylation

1.7 Factors effecting the glycosylation mechanism and outcome

1.7.1 Anomeric effect[8]

The C1 carbon of any cyclic carbohydrate which is called the 'anomeric center' serves as the central point for any chemical reaction. Now in this particular center many unconventional things happen w.r.t structure and reactivity of the carbohydrates. In 1955, Edward first observed that there is an unusual preference for the formation of sterically more demanding α-glucoside over β-glucoside. Later on, this effect was further studied in detail by Lemieux and the term 'anomeric effect' was coined by him.

The anomeric effect can be understood through two primary factors: (i) electrostatic interaction and (ii) stereo electronic effects. From the electrostatic point of view, if we take a closure look on the equatorial conformer **1a**, the two dipoles generated by the lone pair electrons of endocyclic oxygen and the anomeric polar heteroatomic C-O bond are aligned in the almost same direction.

This alignment generates electrostatic repulsion between the two dipoles and makes the equatorial conformer less favored (fig 1.4).

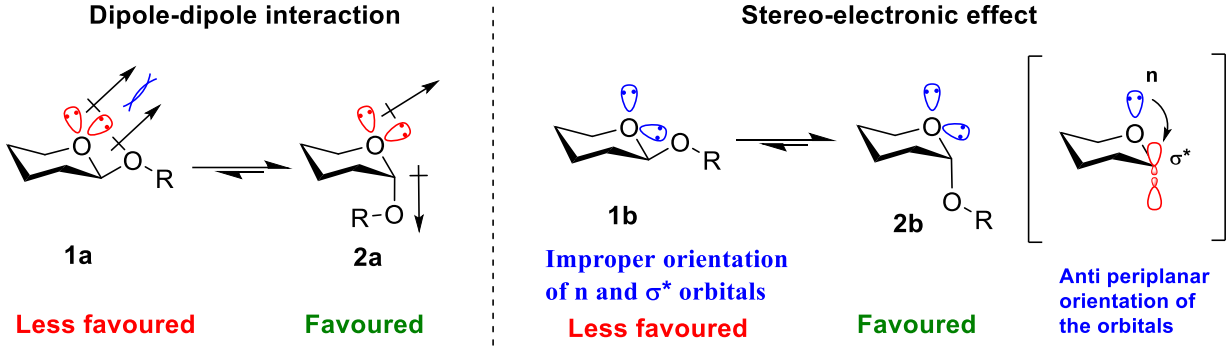


Fig 1.4 Illustration of the origin of Anomeric effect.

Another major factor generates from the molecular orbital point of view. In the axial conformer the unshared electrons of the endocyclic oxygen aligns in the antiperiplanar manner with the σ* orbital of the C-O bond. This perfect alignment facilitates the n→σ* electron donation and formation of a lower energy molecular orbital according to molecular orbital theory. This hyperconjugative effect make the axial anomer more favourable than the equatorial anomer where there is no particular alignment of the orbitals for such electron donation (fig 1.4).

1.7.2 Structural aspects of the glycosyl donors

The structural constituents of the glycosyl donor have a profound effect on the reactivity of the glycosyl donor in any glycosylation reaction.

1.7.2.1 Nature of the protecting groups[9]:

During any glycan synthesis, both the glycosyl donor and acceptor are equipped with different protecting groups according to the targeted linkage. Now these protecting groups have profound stereo-electronic participation during glycosylation. So far, it's already been discussed that the direct participation from C2- substituent (NGP) greatly contributes to the stereochemical outcome of the reaction. Not only the direct participation, the steric bulkiness of the C2 protecting group also effects the ratio of the formed glycosides. Now the reactivity of the glycosyl donor greatly depends on the electron withdrawing or donating tendency of the protecting groups. This rationalization was first drawn by Fraser-Reid *et al* in 1988. It was observed that the introduction of ester-type protecting groups was found to significantly diminish the reactivity of *n*-pentenyl

glycosyl donors in comparison to other protective groups. This decrease in reactivity is attributed to the heightened electron-withdrawing influence of the ester groups, which reduces the electron density and consequently, the nucleophilicity of the leaving group, resulting in a less reactive glycosyl donor. Furthermore, the electron-deficient nature of the ester groups can destabilize the formed oxocarbenium ion which can prevent the departure of the leaving group. These donors are referred to as "disarmed donors." Conversely, glycosyl donors equipped with ether protecting groups, termed "armed donors," enhance the reactivity of the donor (Fig 1.5).

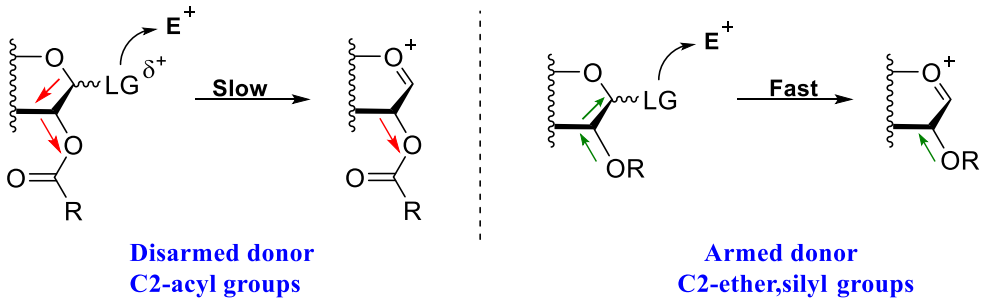


Fig 1.5 Armed-disarmed effect

Later on, another class of donors called 'Super armed' donor was introduced by Demchenko *et al*. Installation of ester type protecting group at C2 and ether type groups at rest of the position serve both for the enhanced reactivity of the donor as well as the stereoselective synthesis of 1,2-trans glycoside.

However, not only C2 substituent of the donor, the other remote protecting groups like C4 or C6 positions also have direct or indirect influence on the stereochemical outcome of the glycosylation. An ester or ether substituent at the C-6 position plays a crucial role in controlling the stereochemical outcome of glycosylation reactions. Although there is no proper experimental evidence to fully support this, but it's a hypothesized principle of long-range 6-O-ester or carbonate group assistance resulting towards the preferential formation of α-glucosides. Besides, the presence of strong electron-withdrawing or sterically bulky substituents at the C-6 position is advantageous for the formation of 1,2-cis glucosides. This effect may be attributed to shielding the equatorial face of the anomeric center, either through spatial hindrance or stereo electronic factors that favor the acceptor approach from the axial face. There is a notable remote participation effect observed from the C-4 position for D-galacto, aialic acid series and the C-3 position for L-fucose, L-rhamnose, D-mannose, and D-glucose series also.

1.7.2.2 Nature of leaving group

In many instances, glycosylation reactions typically follow a unimolecular S_N1 mechanism, where the orientation of the leaving group at the anomeric center is not crucial. However, there are cases where glycosylation reactions occur through a bimolecular S_N2 mechanism, resulting in the inversion of the anomeric configuration. In such scenarios, glycosyl donors with a 1,2-cis orientation yield 1,2-trans glycosides, particularly when utilizing glycosyl halides with insoluble catalysts. One of the profound examples of such bimolecular reaction pathway is the use of highly reactive glucosyl bromides as donors by Lemieux *et al*.[10]

1.7.3 Reactivity of glycosyl acceptor[11]

Not only the glycosyl donor, the chemical reactivity of the acceptor also has a vital role in the stereochemical outcome of a glycosylation. Usually in carbohydrate chemistry the equatorial hydroxyl groups are more reactive than the axial ones. Besides the steric congestion around the particular nucleophilic oxygen center also lowers the reactivity of the hydroxyl groups. Thus, the C6-primary OH group (in case of pyranosides) and (C5-OH in case of furanosides) are more nucleophilic in nature than the other ring hydroxyls of C2, C3, C4 etc. Also, the presence of electron-withdrawing groups (e.g., -OAc, -OBz) in an acceptor, especially in the sugar aglycon, typically reduces the reactivity of the alcohol.

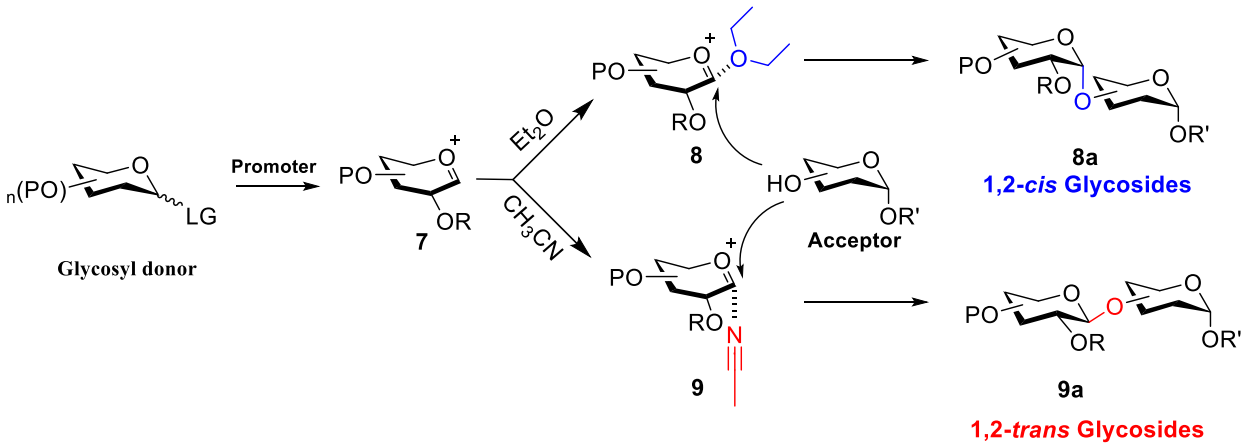
When the reaction is following more S_N1 like pathway, the reactivity of alcohols typically shows an inverse relationship with 1,2-cis stereoselectivity. More reactive hydroxyl groups tend to produce lower selectivity, as stronger nucleophiles lead to faster reactions, making control more challenging. When it comes to sugar or aliphatic glycosyl acceptors, the general guideline suggests that glycosylation of highly reactive primary hydroxyl groups results in poorer stereoselectivity compared to reactions involving secondary hydroxyl groups.

However, the reactivity vs selectivity trend is completely different when the reaction is undergoing through more S_N2 like mechanism. In these circumstances, the higher reactivity of the acceptors results into enhanced selectivity.

1.7.4 Reaction conditions

1.7.4.1 Solvent effect[12]

To this day, the majority of glycosylation reactions adhere to a common reaction mechanism possessing different kind of ionic intermediates. Now stability of these charged species largely depends on several solvent parameters like polarity, dielectric constant, Lewis basicity, molecular dipole etc. The influence of non-participating solvents on achieving selectivity in glycosylation reactions is relatively insignificant. However, the solvent-coordinated hypothesis suggests that a solvent molecule aligns preferentially with the oxocarbenium ion, favoring one side of the ring for nucleophilic attack. Alternatively, the conformation and counterion distribution hypothesis, based on quantum mechanical calculations and solvent dynamic simulations by Hunenberger and Sato, proposes that the oxocarbenium ion adopts various conformations influenced by solvent properties, thus impacting the stereochemical result.



Scheme 1.5 Solvent participation in glycosylation

However, use of participating solvents like acetonitrile, diethyl ether, tetrahydrofuran, dioxane has an adverse effect on the stereochemical outcome of the glycosylation. Solvent like acetonitrile traps the oxocarbenium ion intermediate **7** from the axial face forming an exclusive axial nitrilium ion intermediate **9** thus facilitating the attack of the incoming nucleophile from the opposite face resulting in equatorial glycoside **9a** (**scheme 1.5**). On the contrary, ether type solvents participate from the equatorial face of the oxocarbenium ion leading to the formation of axial glycosides **8a** (**scheme 1.5**).

1.7.4.2 Effect of promoters and additives[13]

As discussed earlier, reaction rate has a profound effect on the stereoselectivity of the glycosylation. Faster the reaction, harder to control the selectivity. Thus, gentler activation

conditions typically yield better results for 1,2-*cis* glycosylation. Thioglycosides, exhibit better outcomes when activated by mild promoters like iodonium dicollidine perchlorate (IDCP) or molecular bromine. Trichloroacetimidates are most effectively activated by strongly acidic catalysts such as trimethylsilyl trifluoromethanesulfonate (TMS-triflate, TMSOTf) or trifluoromethanesulfonic acid (triflic acid, TfOH). On the other hand, halide-ion-catalyzed reactions demonstrate optimal performance in glycosylation involving glycosyl halides.

Besides, modifications to these promoter systems like addition of extra agents (additives) often influence the stereochemical outcome of glycosylation. Use of perchlorate ion and diphenyltin sulfide additives are particularly notable in this occasion for their significant impact on 1,2-cis glycosylations.

1.7.4.3 Temperature and pressure[14]

Thermodynamic and kinetic control have an important contribution in the selectivity of every organic reaction. Glycosylation is not an exception to that. Lower temperature favors the kinetically controlled glycosylation resulting in equatorial glycosides although adverse examples are there. Besides, increasing pressure in reactions involving glycosyl donors improves 1,2-trans selectivity. For glycosylations with nonparticipating glycosyl donors, applying high-pressure conditions significantly boosts reaction yield with minimal alterations in stereoselectivity.

1.8 Evolution of glycosyl donors[15-22]

As depicted earlier, because of the structural diversity of carbohydrates, synthesis of glycoconjugates and oligosaccharides with defined linkage and stereoselectivity is a herculean task for synthetic chemists. Since the very initial contributions on developing glycosylation methods by Michael, Koenigs, Knorr and Fischer, several glycosyl donors have been developed in the last 100 years. However, each methodology has its own advantages and disadvantages. That's why even today, there remains no widely accepted method for glycosylation in oligosaccharide synthesis, and determining the appropriate glycosylation technique for a particular glycosidic bond is still a considerable challenge.

The story of glycosylation begins at 1879 when for the first time American organic chemist Arthur Michael used glycosyl halides as donors for glycosylation[15a]. Later on, in 1893, Emil Fischer developed first acid catalyzed glycosylation utilizing hemiacetal as donor and strong Brønsted

acid[15b]. Taking cue from these early milestones several potential glycosyl donors have been developed (Fig. 1.6).

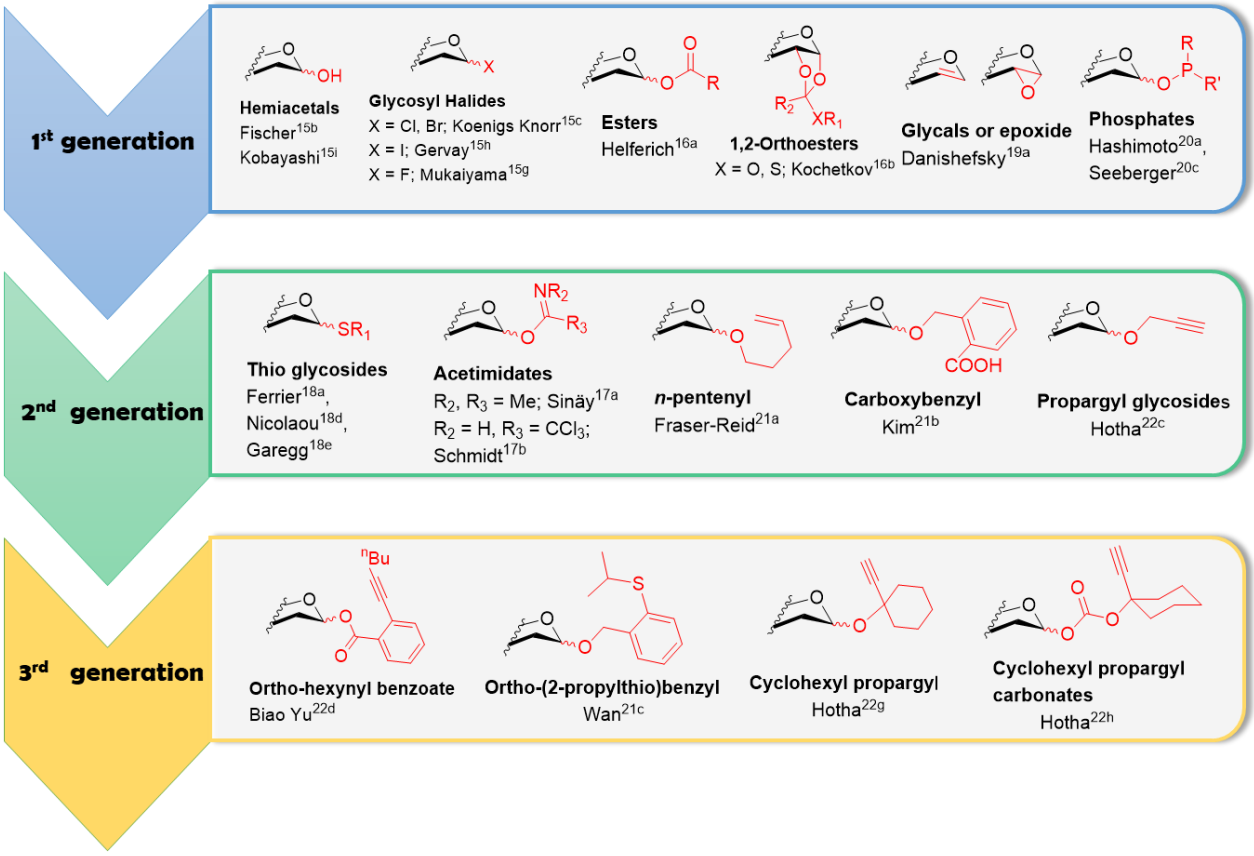


Fig 1.6 Three generations of donor development.

1.8.1 Glycosyl halides[15]

In 1901, first practical glycosylation was done by Koenigs and Knorr using glycosyl chloride and bromide as donor and insoluble silver salts like Ag_2O, $AgCO_3$ as promoter[15c]. This approach was recognized as the earliest method for synthesizing 1,2-trans glycosidic linkages. But The challenge with utilizing heavy metal salts lay in their limited solubility in organic solvents, necessitating excessive amounts beyond stoichiometric proportions. Later on, Helferich and colleagues improved the glycosylation process by introducing organic solvent-soluble metal salts like $HgBr_2$, $Hg(CN)_2$, HgO, $HgCl_2$, and HgI_2. Besides, Lewis acid-based catalyst such as $SnCl_4$, BF_3•OEt_2, $Sn(OTf)_3$-TMU, $Sn(OTf)_3$-collidine, I_2, $LiClO_4$, DDQ etc were used to improve the yields[15d-f]. However, the highly unstable nature of glycosyl bromides warrants exploration of alternative donors. Mukaiyama *et al* introduced more stable glycosyl fluoride donors in 1981[15g]. Later on, in

1998, Gervay-Hague utilized glycosyl iodides[15h] while synthesizing glycoconjugates. Although glycosyl iodides exhibit lower stability compared to glycosyl chlorides and bromides, they offer superior advantages in terms of efficiency, reaction speed, and stereoselectivity. Despite the significant benefits of glycosyl halides as donors, they are not commonly practical in large-scale glycoside synthesis due to the use of highly toxic promoter systems in stoichiometric quantity.

1.8.2 Glycosyl esters and orthoesters[16]

In 1933, Helferich[16a] introduced glycosyl esters as donors. A good thermal stability and effortless preparation from the corresponding hemiacetals made the anomeric esters widely accessible in glycosyl donor community. Anomeric esters can be activated by using variety of Lewis as well as Brønsted acids viz. $SnCl_4$, BF_3•Et_2O, $FeCl_3$, TMSOTf, TfOH etc. However harsher conditions are needed during glycosylation owing to the lesser reactivity of the esters specially in pyranosides. Thus, the application of ester donors in large glycan syntheses is not well explored.

Later on, another special type of esters called glycosyl 1,2-orthoesters was introduced as glycosyl donors by Kochetkov[16b]. These types of donors can be prepared from the corresponding per-*O*-acylated derivative of the sugar and alcohol of anyone's choice via glycosyl halide under strong basic condition. Although milder and catalytic activation condition is required in case of orthoesters, however the drawbacks like the unstable nature of the orthoesters under acidic condition and formation of undesired direct glycoside during glycosylation make the orthoester donors less significant in the complex glycoconjugate synthesis.

1.8.3 Glycosyl imidates[17]

Glycosyl imidates stand out as exceptionally adaptable and commonly employed donors in carbohydrate synthesis. Originating from Sinäy's pioneering work developing dimethyl imidiates in 1976, this class of donors has been extensively modified to trichloro and trifluoroacetamidates and utilized by Schmidt and colleagues[17a-b]. Imidate donors can be easily constructed starting from the corresponding hemiacetal and commercially available trichloroacetonitrile using bases like K_2CO_3, Cs_2CO_3, DBU etc. Strong Lewis acid promoters like BF_3•Et_2O, TMSOTf, $ZnBr_2$ can be used to activate imidates towards glycosylation. However, later on the brilliant structural modification of TCA and TFA donors into *N*-phenyl trifluoro derivative makes the donor highly reactive and efficient in glycosylations giving the ability of getting activated by mild salts like

$Bi(OTf)_3$ or $Yb(OTf)_3$[17c]. For many years the trichloro and trifluoroacetamidate donors had excellent contribution in synthetic carbohydrate chemistry. However, the drawbacks associated with these donors like the poor stability of the armed donors and the generation of acetamide byproduct during glycosylation reduced the range of applications of glycosyl imidates

1.8.4 Thioglycosides[18]

Undoubtedly, thioglycosides are one of the major class of donors that has been extensively utilized across various domains within synthetic carbohydrate chemistry. In 1973, R J Ferrier pioneered their use by employing $HgSO_4$ or $Hg(OAc)_2$ for activation, showcasing their effectiveness in glycoside synthesis[18a]. Since the introduction, in the last few decades, a wide library of activators like DMTST, IDCP, MeOTf were applied to enhance the reactivity and applicability of thio donors. However, the major contributions came in 1990 from van Boom and Fraser-Reid where they have implemented NIS and TfOH/AgOTf as the promoter, and till date it remains the best activation condition of thioglycosides towards oligosaccharide synthesis[18b-c]. Thioglycosides offer several notable advantages over other glycosyl donors: (i) the ability to withstand a wide array of chemical modifications and remain inert during various glycosylation conditions. (ii) readily synthesizable from per-*O*-acylated derivatives and hemiacetals, (iii) a wide range of activation temperatures, from 50°C to -80°C. Owing to these advantages, thioglycosides have been widely used in the areas of one pot glycosylation and orthogonal activation approaches. Nevertheless, the necessity for stoichiometric use of promoters continues to pose a significant drawback in the application of thioglycoside donors.

1.8.5 Glycals and anhydro sugars[19]

The use of glycals as glycosyl donors presents an intriguing aspect and finds application in a broad spectrum of glycoside synthesis specially in the syntheses of an important class of 2-*deoxy* or 2,6-*dideoxy* glycosides. Glycals can be easily prepared from the corresponding sugar halides and hemiacetals and some substituted glycals are commercially available also. Furthermore, the glycals serve as the direct precursors of 1,2-anhydro sugars, another class of glycosyl donors. Although Lemieux introduced 1,2-anhydro sugars as glycosyl donors for the first time for synthesizing sucrose, significant recognition also goes to Danishefsky for his extensive research on employing 1,2-anhydro sugars in complex glycoconjugate syntheses. Danishefsky and his team developed

an efficient method for preparing 1,2-anhydro sugars from glycals using dimethyldioxirane (DMDO) as an oxidant, which can be activated to obtain exclusive 1,2-*trans* glycosides[19a-b].

1.8.6 Glycosyl phosphates[20]

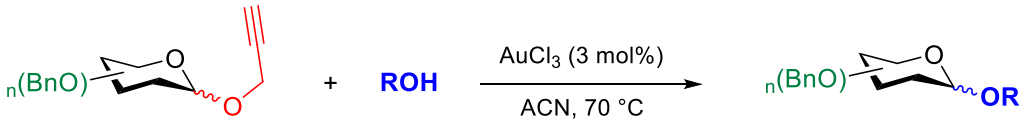
Glycosyl phosphates are recognized for their versatility as donors in the synthesis of complex oligosaccharides, utilizing both chemical and enzymatic methods. Introduced by Hashimoto and Ikegami in 1989, the phosphate donor has undergone several structural modifications towards glycosyl diphenyl phosphate, glycosyl diphenylphosphineimidates and glycosyl phosphoramidites by the same group later on[20a-b]. Due to the thermal stability and effective leaving group properties of the donor when activated by promoters, glycosyl phosphates are also employed in solid-phase oligosaccharide syntheses by Seeberger group[20c-d], demonstrating their potential as valuable building blocks. However, activation of these donors with a stoichiometric quantity of TMSOTf remains as the major drawback of glycosyl phosphates.

1.8.7 Other glycosyl donors[21]

Among the other developed notable glycosyl donors, Fraser-Reid's *n*-pentenyl glycosides[21a], Kim's carboxybenzyl glycosides[21b], and Wan's ortho-(2-propylthio)benzyl donor[21c] have made notable contributions to carbohydrate synthesis.

1.9 Modern era of alkynyl glycosyl donors: harvesting Gold's alkynophilicity since 2006[22]

The utilization of transition metal catalysis in glycosylation reactions is a relatively recent development in carbohydrate chemistry, gaining significant popularity over the past two decades. A substantial amount of literature reports of activation of glycosyl donors by transition metals catalysts has emerged in recent years including Ni(II), Pd(II), Ti(II), Cu(II), Rh(II) etc. However, Gold catalyzed glycosylation was completely unknown. Initially, utilization of Au(III) as homogeneous catalyst in organic syntheses introduced by Fukuda and Ukimoto[22a], subsequently, the Hashmi group[22b] made pioneering advancements in the synthesis of arenes through gold catalysis. Taking cue from these reports, Hotha and Kashyap reported the activation of propargyl glycosyl donor by catalytic $AuCl_3$ in 2006[22c]. This advent of gold catalysis in the realm of synthetic carbohydrates marked a notable milestone.



Scheme 1.6 1st report of Gold catalyzed glycosylation by Hotha group

In this method, armed glycosyl propargyl donors were activated by $AuCl_3$ at 70 °C to furnish the mixture of 1,2-cis and 1,2-trans glycosides. However, this method was limited to armed glycosyl donors, and there was a lack of stereochemical control, as only ether-type linkages could be utilized. Besides elevated temperature was needed to activate the glycosyl donors. Despite of these drawbacks, this pioneering discovery by Hotha group paved the pathway of exploring gold catalysis further in carbohydrate chemistry. Later on, Yu group's discovery of activation of anomeric *ortho*-alkynylbenzoates[22d] by $Ph_3PAuOTf$ and Zhu group's findings on the $AuCl_3$ catalyzed activation of alkyne-functionalized 2,2-dimethylbut-3-ynyl thioglycosides[22e] are regarded as notable progressions in the field of glycoside synthesis.

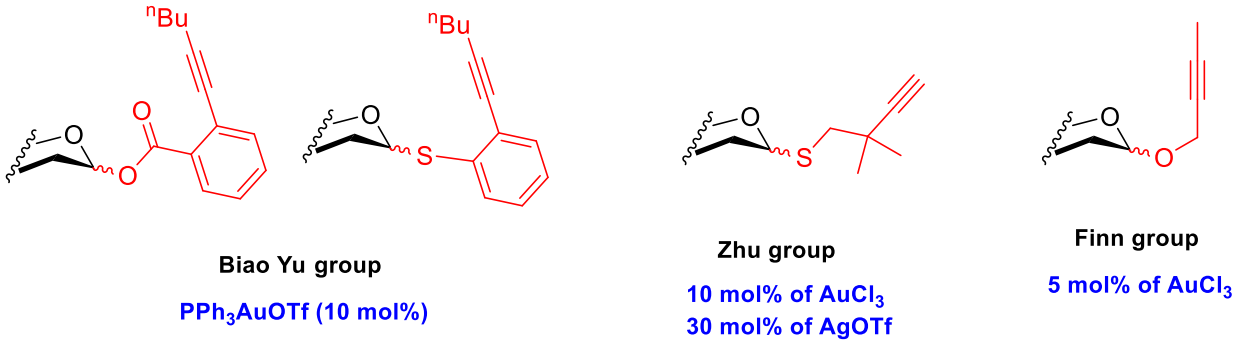


Fig 1.7 Worldwide Development of gold catalyzed alkynyl donors

Nevertheless, Hotha and coworkers gave tireless efforts to overcome the drawbacks associated with the propargyl donors. Soon after the initial discovery, propargyl 1,2-orthoesters[22f] were identified as glycosyl donors by Hotha group which can be activated by $AuBr_3$. The higher reactivity of the orthoesters allows the activation possible at lower temperature (25 °C) and for the disarmed sugar moieties also. Later, in 2012 ethynylcyclohexyl glycoside donors[22g] was introduced which can be activated by using 10 mol% $AuCl_3$ and $AgSbF_6$ as co-catalyst at 25 °C. The enhanced reactivity of the substituted propargyl donors is attributed to the *gem*-dialkyl effect during cyclization named 'Thorpe-Ingold effect'. Still this donor was ineffective in case of disarmed donor.

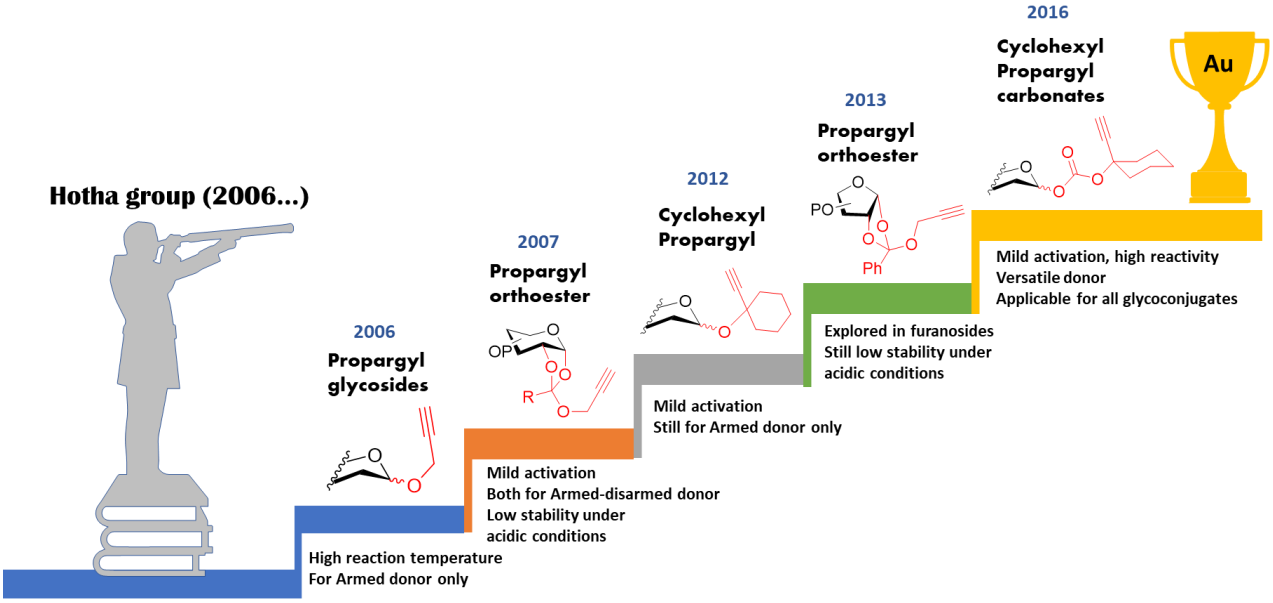
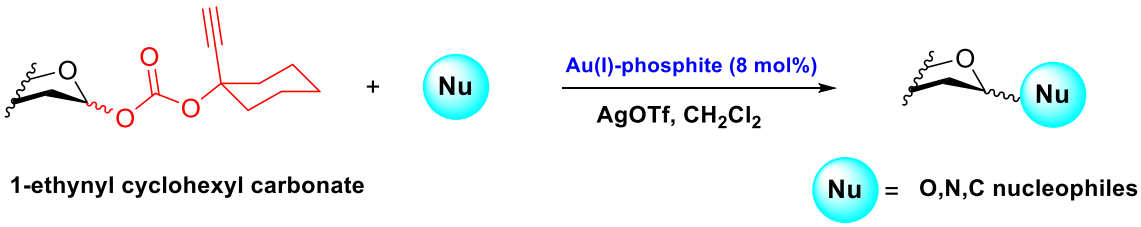


Fig 1.8 Contribution to the Gold catalyzed glycosylation by Hotha and coworkers.

Then in 2016, another breakthrough came from Hotha group when Mishra *et al* introduced the versatile 1-ethynylcyclohexyl glycosyl carbonate donor[22h] into the world of synthetic carbohydrate chemistry. The effective activation of the donor was facilitated by strategically utilizing an alkyne functionality in conjunction with a highly alkynophilic gold complex, along with AgOTf as promoters. Ultimately, this donor was discovered to surpass all the constraints linked with previously developed donors by Hotha group. Later on, the donor has been extensively studied for the synthesis of many captivating glycosides and has proven to be a highly effective and promising option for synthesis of *O*-glycosides as well as *N*- and *C*-glycosides.



Scheme 1.7 Glycosylation using alkynyl glycosyl carbonate donor.

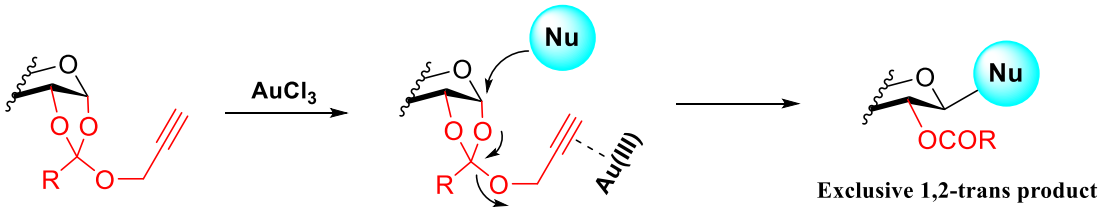
In recent years, Hotha group has extensively utilized the alkynyl glycosyl carbonate donor in large oligosaccharide synthesis area. Several large fragments of the *Mycobacterium tuberculosis* cell wall have been successfully synthesized employing the carbonate donor which includes

nonadecaarabinofuranoside (**19 Ara*f*s**) [22i] (Arabinogalactan), a heneicosaccharide (**15 Ara*f*s+ 6 Man*p*s**) [22j] from lipoarabinomannan motif and a pentacosasaccharide (**23 Ara*f*s+2 Gal*f*s**) [22k] moiety of arabinogalactan. In 2021, we utilized this donor chemistry to synthesize Fondaparinux, an anticoagulant that is clinically approved and poses major synthetic challenges[22l]. These syntheses proved the versatility and effectiveness of the alkynyl glycosyl carbonate donor in synthetic carbohydrate chemistry.

1.10 Approaches towards syntheses of different glycoside linkages[5,22f,23-27]

1.10.1 Synthesis of 1,2-trans linkages[5,22f]

As discussed earlier, 1,2-trans glycosides can be easily achieved through neighboring group participation (NGP) when the glycosyl donor is equipped with an ester protecting group at C2-position. The benzoyl group is the most commonly employed protective group in NGP due to its ease of application and the stabilizing effect of the aromatic ring on the tertiary carbocation. However, an indirect application of the NGP motif can be seen in the glycosylation of propargyl orthoester[22f] type donor developed by Hotha group where the glycosyl donor is conformationally locked at C1 and C2 position in such a way that the incoming nucleophile is bound to attack from the opposite face of the orthoester ring furnishing exclusive 1,2-*trans* glycosides.



Scheme 1.8- 1,2-trans glycosylation using propargyl orthoester glycosyl donors

1.10.2 Synthesis of 1,2-*cis* linkages[23-25]

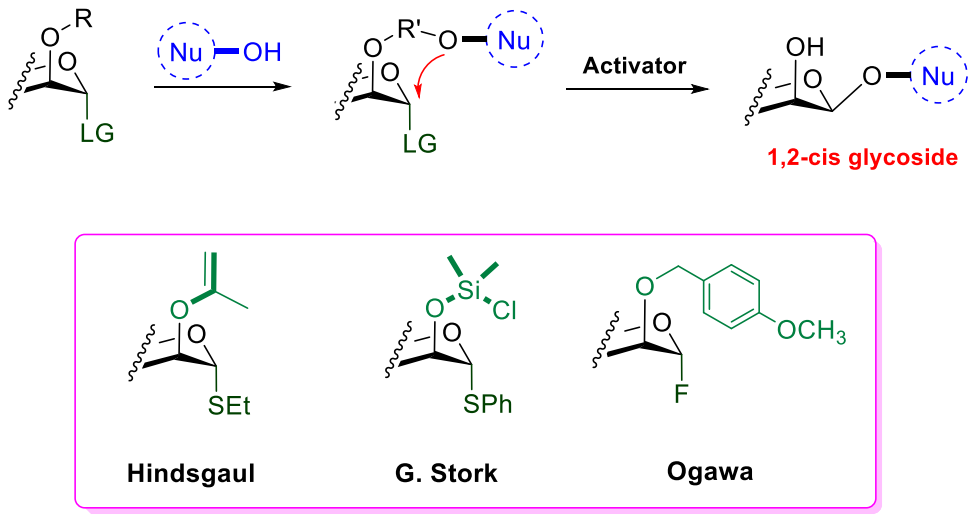
Numerous oligosaccharides featuring 1,2-*cis* O-glycosidic bonds hold significant value owing to their biological functions and potential therapeutic applications. Synthesis of 1,2-*cis* glycosides is a herculean task in carbohydrate chemistry. While numerous literature reports demonstrate exceptional cis-selective glycosylation for specific carbohydrate structures, there is presently no universally applicable method for exclusively producing 1,2-*cis* stereoisomers. Nevertheless,

many approaches were utilized towards the synthesis of cis-linked glycoconjugates including modification of structural elements and changing reaction conditions.

The first and foremost requirement for the synthesis of cis glycosides is the presence of a non-participating group at C-2 position of the glycosyl donor. Although the existence of non-participating group does not necessarily guarantee the generation of exclusive cis-glycosides as there are other important participating factors like anomeric effect, reaction temperature, protecting group influence etc. Anomeric effect intrinsically favors the formation of axial glycosides which in particular is advantageous in the cis-glycosylation of glucose, galactose series but on the contrary, for mannose series, it facilitates the trans glycoside formation. Besides, for mannose the cis-glycosylation is more challenging owing to the electrostatic repulsion between the C2 axial substituent and incoming nucleophile.

Developing efficient methods for synthesis of cis- as well as trans- glycosides in 2-deoxy sugar series remains a challenging endeavor in carbohydrate chemistry. The lack of C-2 substituents reduces neighboring participation and stereo electronic effects, thereby making the synthesis of both α- and β-2-deoxy glycosides significantly difficult. Some of the approaches taken by the scientific community towards the synthesis of 1,2-*cis* glycosides are discussed here.

1.10.2.1 Intramolecular approaches[23]

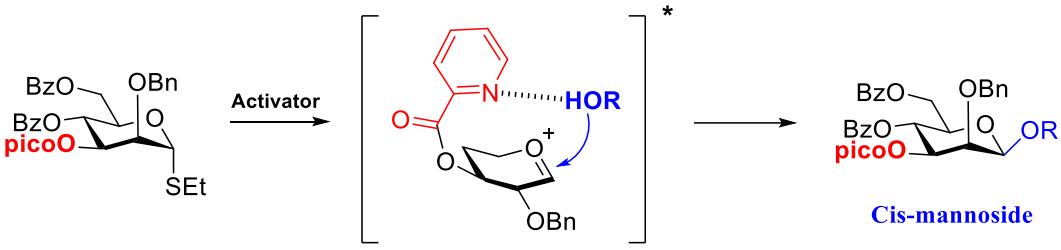


Scheme 1.9 Intramolecular aglycone delivery approaches.

In 1991, a brilliant approach of Intramolecular Aglycon Delivery (IAD) was introduced by Ole Hindsgaul[23a] towards the synthesis of β-mannopyranosides. In this approach, typically the glycosyl donor is equipped with an anchoring group at C2 position which makes a covalent attachment with the desired aglycone first (**scheme 1.9**). Then upon activation of the leaving group, the aglycone is delivered to the anomeric center from the same face intramolecularly resulting in 1,2-*cis* glycosides. Starting from isopropylene linker by Hindsgaul, later on Stork[23b] and Ogawa[23c] contributed to this excellent concept using Silyl and PMB linkers.

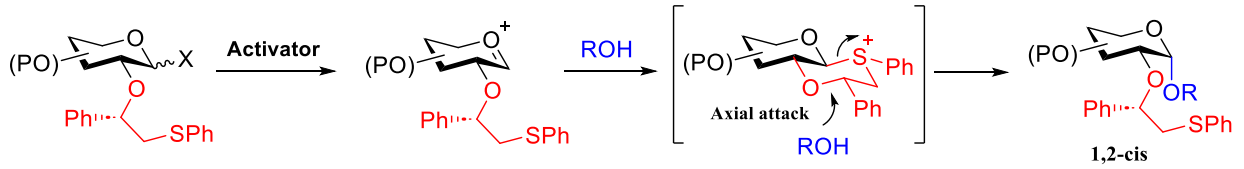
1.10.2.2 Intermolecular approaches[24]

Another excellent approach was introduced by Demchenko group[24a] named Hydrogen bond mediated aglycone delivery (HAD). In various instances, picoloyl groups were introduced at various positions of the glycosyl donor to serve as "H-bond acceptors" facilitating hydrogen bond-mediated delivery of nucleophiles to the aglycon, with the aim of achieving cis glycosylation. For example, C-3 equipped picoloyl group of mannose facilitates the formation of β-manno pyranosides (**scheme 1.10**).



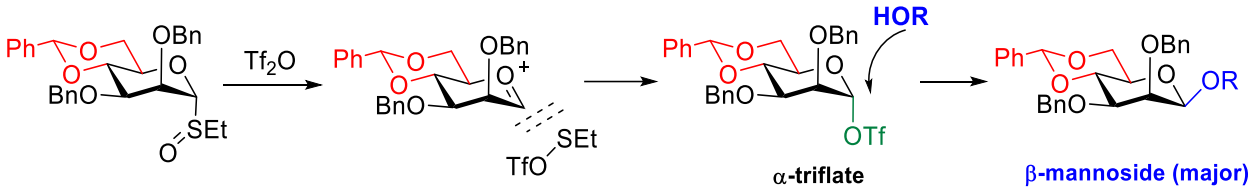
Scheme 1.10 Hydrogen bond mediated aglycon delivery.

Until now, neighboring group participation has primarily been associated with the synthesis of 1,2-*trans* glycosides. However, in 2005 G.J. Boons[24b] demonstrated in 2005 that the anchimeric assistance provided by a C-2 protecting group can also facilitate the formation of 1,2-cis glycosides. A chiral auxiliary consisting of a (1*S*)-Phenyl-2-(phenyl sulfonyl) ether moiety was incorporated at the C-2 position of the sugar moiety which during glycosylation traps the oxocarbenium ion intermediate by forming a *trans*-decalin type sulfonium ion intermediate. Due to this equatorial trapping, the inbound nucleophile is set to attack from the axial side resulting in the 1,2-cis glycoside (**scheme 1.11**).



Scheme 1.11 Chiral auxiliary mediated cis glycosylation

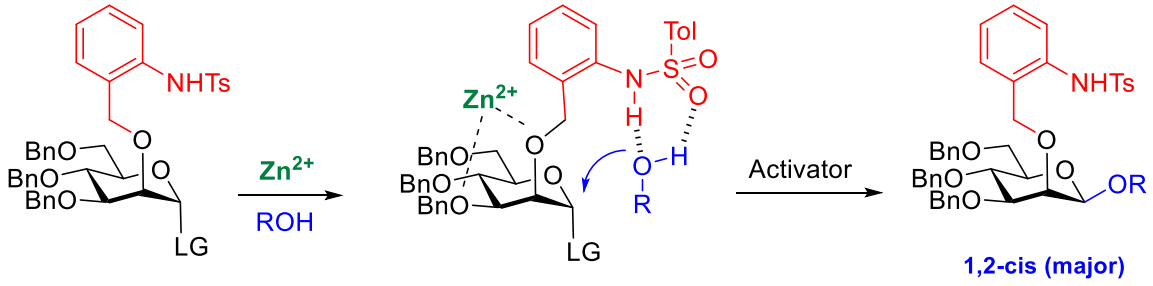
One of the most important contribution in the field of β-mannosylation came from Crich group in 1996. Introduction of 4,6-*O*-benzylidine locked glycosyl donors into the pre-activation-based glycosylation in presence of a triflate source led to a predominantly covalent α-triflate intermediate which further undergo S_N2 type displacement by the incoming nucleophile to furnish the 1,2-*cis* mannoside as the major product (**scheme 1.12**)[24c].



Scheme 1.12 4,6-benzylidine equipped cis-mannosylation by Crich group

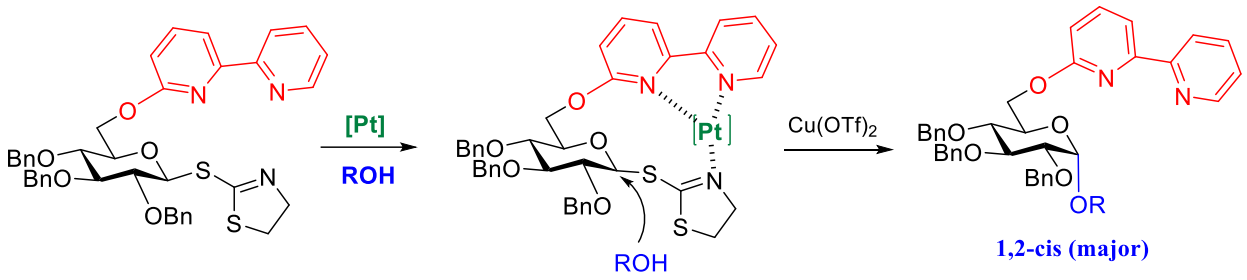
1.10.2.3 Chelation based strategies[25]

In recent years, chelation-assisted directing glycosylation has gained significant attention within the scientific community. A beautiful example of bimodal chelation with C2-*O*-TsNHbenzyl ether (TAB) as a protecting group was introduced by Ding *et al.* wherein the chelation between the ring oxygens and Zn^{2+} ion and hydrogen bonding between the incoming acceptor and NHTs linker direct the aglycone to attack from the same face furnishing the cis glycoside as major product (**scheme 1.13**)[25a].



Scheme 1.13 TAB based chelation directing cis mannosylation by Ding *et al*.

The Demchenko group made another significant contribution to glycosylation through the utilization of metal chelation techniques. The use of multi-dentate metal coordination with a protecting group at O-6 and/or O-5 significantly influences the stereoselectivity of chemical glycosylation. Their research demonstrated that Platinum(IV) complexation with 6-*O*-bipyridyl to the leaving group, such as thiazolinyl, notably blocks one face of the glycosyl donor forcing the acceptor to attack from the opposite face preferentially which indeed results into 1,2-*cis* glycoside as major product (**scheme 1.14**)[25b].

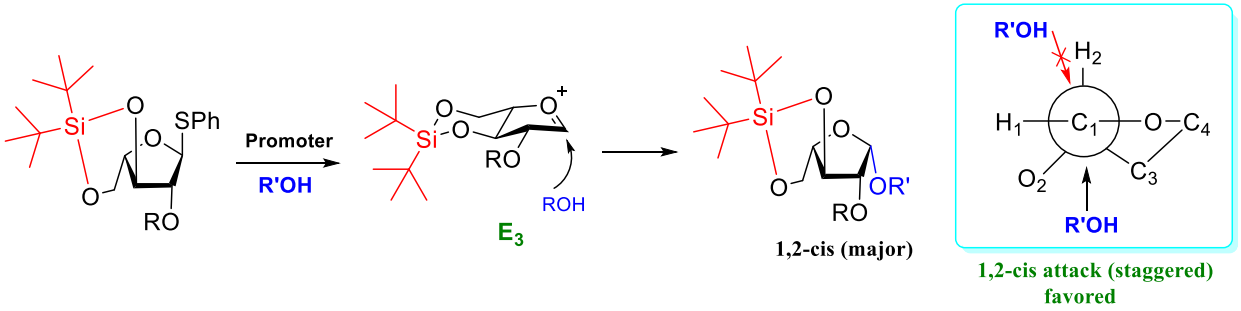


Scheme 1.14 Platinum chelation in stereoselective glycosylation by Demchenko group.

1.10.3 1,2-cis glycosylation in furanosides[26,27]

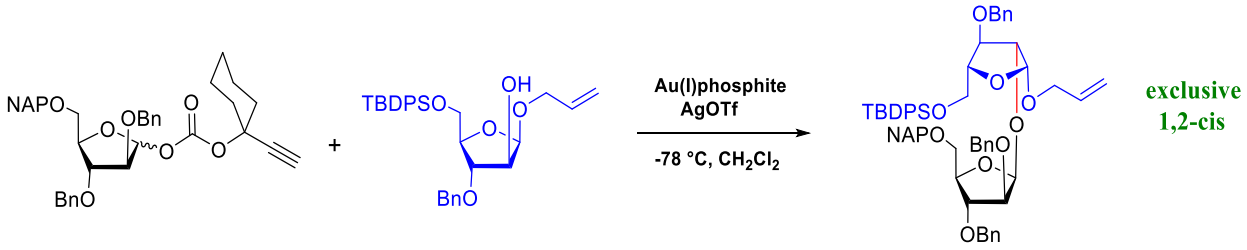
1.10.3.1 Direct approaches[26]

Achieving 1,2-*cis* selectivity in furanosides poses greater difficulty than pyranosides due to the weak anomeric effect in furanosides and the inherent flexibility of furanose rings, allowing them to adopt various twisted and enveloped conformations. The rapid conformational change of furanosides is attributed to the low energy difference between the conformers. So, in order to achieve stereoselectivity in glycosylations the best way is to restrict the flexibility of furanose rings by immobilizing or stabilizing the intermediate formed during the glycosylation reaction into a fixed conformation. One major contribution in restricting the conformation of furanosides came from Boons group[26a] in 2006 where they have utilized fused ring silyl protecting groups to achieve β-selectivity in arabinofuranosides. The introduction of di-^{t}butyl silane group at C3 and C5 restricts the oxocarbenium ion generated during the glycosylation in one particular conformation. Furthermore, DFT calculations showed existence of the E_3 conformer of oxocarbenium ion predominantly over ^3E conformer owing to the internal ring strain which undergoes nucleophilic attack of the acceptor from *syn*-face resulting into 1,2-*cis* arabinfuranosides (Scheme 1.15).



Scheme 1.15 Conformation restriction directed glycosylation by Boons group.

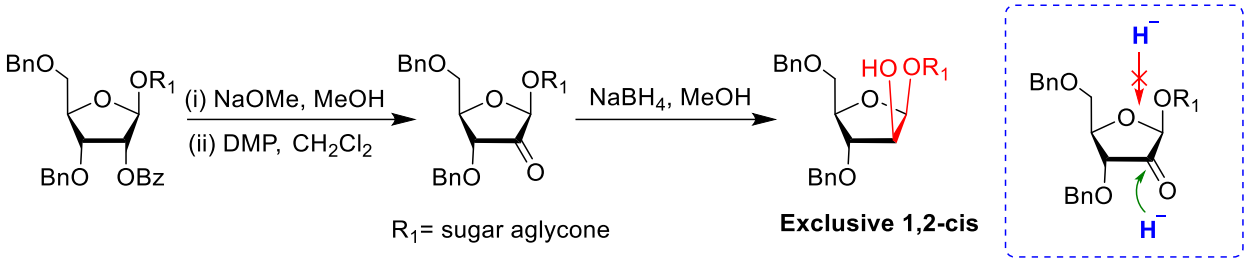
Based on protecting group influence in stereochemical outcome of glycosylation, another excellent approach named Reciprocal-Donor-Acceptor-Selectivity (RDAS) was successfully demonstrated in furanosides by Hotha group. Wherein, the sterically more demanding and less reactive acceptors result into β-selective arabinofuranosylation in low temperature activation. Molecular modelling data indicates the preferential approach of the donor from the face with less steric demands furnishing into 1,2-*cis* arabinofuranosides (Scheme 1.16) [26b].



Scheme 1.16 RDAS approach towards the synthesis of 1,2-*cis* arabinofuranosides

1.10.3.2 Indirect approaches[27]

In recent years, Hotha group has developed a novel bioinspired approach based on oxidation-reduction technique to achieve challenging 1,2-*cis*-arabinofuranosylation under catalytic conditions, drawing inspiration from the biochemistry of Mtb. In this method, a previously synthesized 1,2-*trans* ribofuranoside with C2-OBz group is taken as starting material. After deprotection of the C2-OBz group, resulting secondary alcohol was oxidized to the corresponding ketone which further undergoes reduction to give 1,2-cis arabinofuranoside exclusively. The selective reduction can be illustrated based on the steric crowding around the ring carbonyl group. The C1 and C3 substituent blocks the *exo*-face of the carbonyl forcing the incoming hydride to attack from the *exo*-face resulting into 1,2-*cis* arabinofuranoside (Scheme 1.17) [27].



Scheme 1.17 Oxidation-reduction method to synthesize 1,2-*cis* arabinofuranosides

Later on, this novel oxidation-reduction methodology was used in the synthetic route of pentacosafuranoside subunit of MTb. Cell wall by Hotha and coworkers[22k].

Numerous alternative methods for achieving stereoselectivity exist beyond the ones mentioned here. Nevertheless, achieving complete stereocontrol of *cis*-selectivity remains the primary hurdle in carbohydrate chemistry. Strategies employed are often tailored for particular cases and rely heavily on specific protecting groups, thereby constraining their applicability to a limited range of substrates.

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Chapter 2

[Au]/[Ag]-catalyzed Direct Stereoselective Synthesis of 2-azido-2-*deoxy*-β-D-mannopyranosides

Chapter 2

2.1 Introduction

2.1.1. Naturally occurring β-ManNAc containing oligosaccharides

N-Acetylmannosamine, also known as 2-acetamido-2-*deoxy*-mannopyranose (ManNAc), is a prevalent element in bacterial polysaccharides[1]. Additionally, ManNAc serves as a crucial intermediate in the biosynthesis of N-acetylneuraminic acid[2]. N-Acetyl-*β*-D-mannosamine units are less prevalent in nature than their β-linked mannose counterparts; however, they play a crucial role in serving as key constituents in the repeating units of several cell wall lipopolysaccharides, such as opportunistic pathogens like *Pseudomonas aeruginosa*[3], *Aeromonas salmonicida*[4] and *E. coli* serotype 01[5]. The repeating units with *β*-D-ManNAc components found in the capsular polysaccharides of *Streptococcus pneumoniae* appear to be significantly more important for their infectiousness and molecular complexity, most notably displayed in the serotypes 19F, 19B, 9L etc[6-8] (Fig **2.1**).

Also noteworthy is the relatively rare but important presence of N-acetyl-*β*-D-mannosaminuronic acid as a prominent component of capsular polysaccharides in serious pathogenic bacteria[9-11], particularly in *Streptococcus aureus*[12], which is a leading cause of hospital-associated infections (Fig **2.2**).

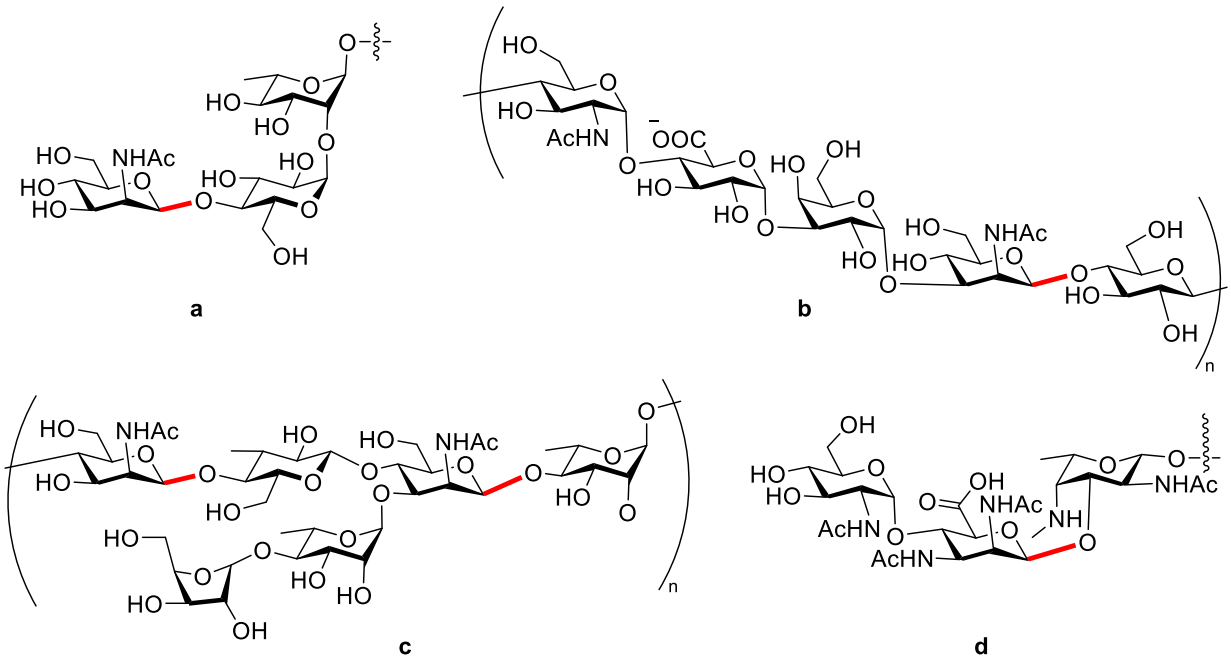


Fig. 2.1. Naturally occurring 1,2-*cis* mannosamine glycosides: a) *S. pneumonie* 19F, b) *S. pneumonie* 9L, c) *S. pneumonie* 19B, d) *P. aeruginosa*

The key feature of these aforementioned molecules is the presence of *β*-D-ManNAc linkage which poses a significant challenge to synthesize. Nevertheless, the notable biological significance of these polysaccharides has prompted the synthetic research community to put considerable efforts in development of new synthetic methodologies towards the synthesis of *β*-D-ManNAc containing oligosaccharides.

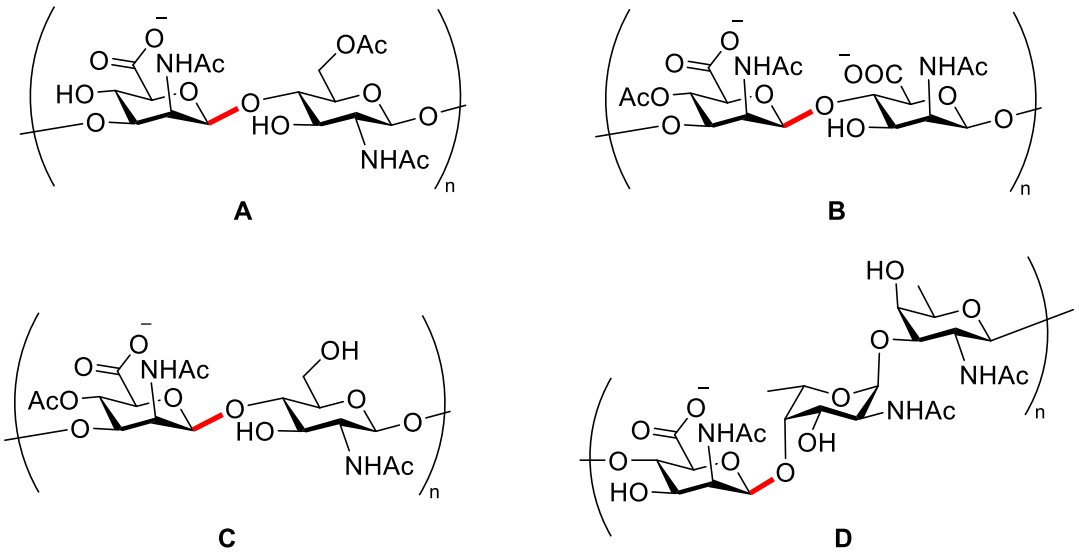


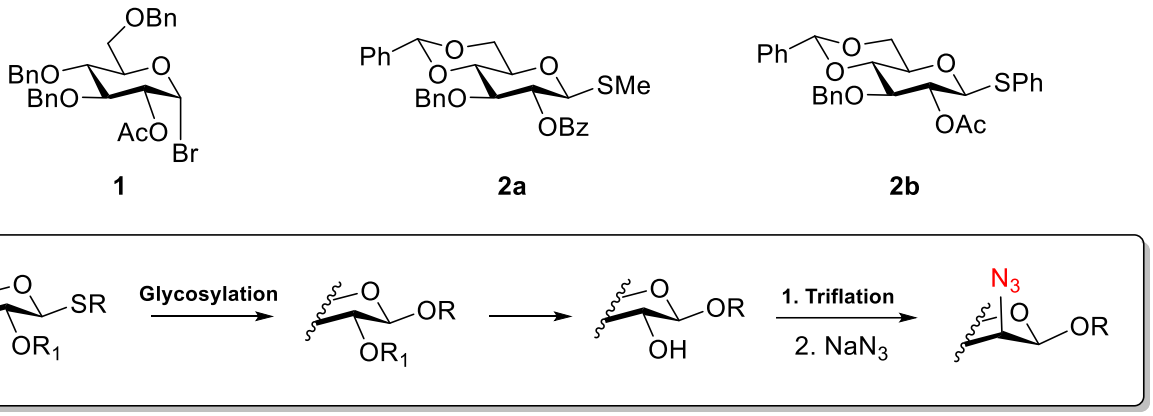
Fig 2.2. Naturally occurring 1,2-*cis* mannosamine glycosides: A) E. coli K7[7], B) Haemophilus influenza[8], Neisseria meningitidis[9], D) Streptococcus aureus[10].

2.1.2. Literature reports on the synthesis of β-ManNAc glycosides

Mannose possesses a strong tendency to create 1,2-*trans* or α-linkages because the anomeric effect is particularly pronounced in this group of sugars[13]. Besides, the presence of C2-axial substituent also emphasizes the formation of *α*-mannoside during glycosylation. However, some uncontrolled glycosylations can result in anomeric mixtures depending on the protecting groups and reaction conditions. It is needless to mention that, to synthesize 1,2-*cis* linkage during glycosylation, the glycosyl donor should be equipped with C2 non-participating type protecting group. However, in the synthesis of *β*-D-ManNAc linkages, 2-azido mannosyl motifs are used which can be reduced and acetylated to furnish the desired *β*-D-ManNAc glycans.

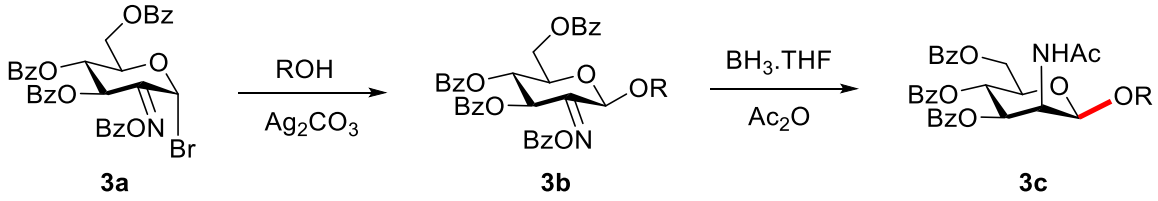
Initially, over the years the indirect glucoside donors were used in glycosylation followed by C2-inversion to produce *β*-D-Mannosyl linkage. The *α*-D-glucosyl bromide **1** and benzylidene equipped thioglucosyl donors **2a** and **2b** were used to construct the *β*-glucoside linkages which

were transformed to *β*-mannoside linkages by diacylation at C2 and inversion of configuration through S_N2 displacement with azide (scheme **2.1**)[14-16].



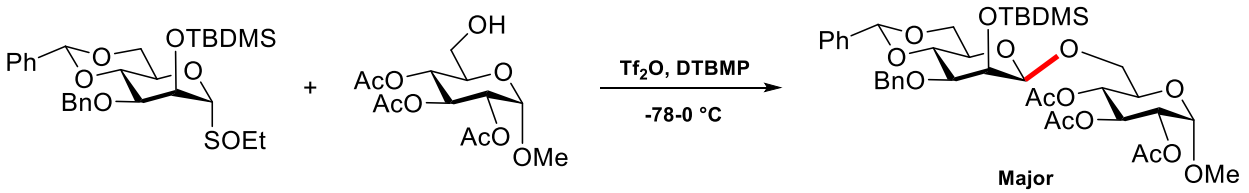
Scheme 2.1. Indirect synthesis of β-mannoside from glucoside donors.

Another notable indirect approach of synthesizing 1,2-*cis* ManNAc linkages involves the glycosylation of oximinoglycosyl donors[17]. Initially, silver promoted glycosylation of the oximinoglycosyl bromide **3a** generates the *β*-D-glycosidulose oxime **3b** which is further subjected to reduction followed by acetylation to furnish the *β*-ManNAc glycosides (scheme **2.2**).



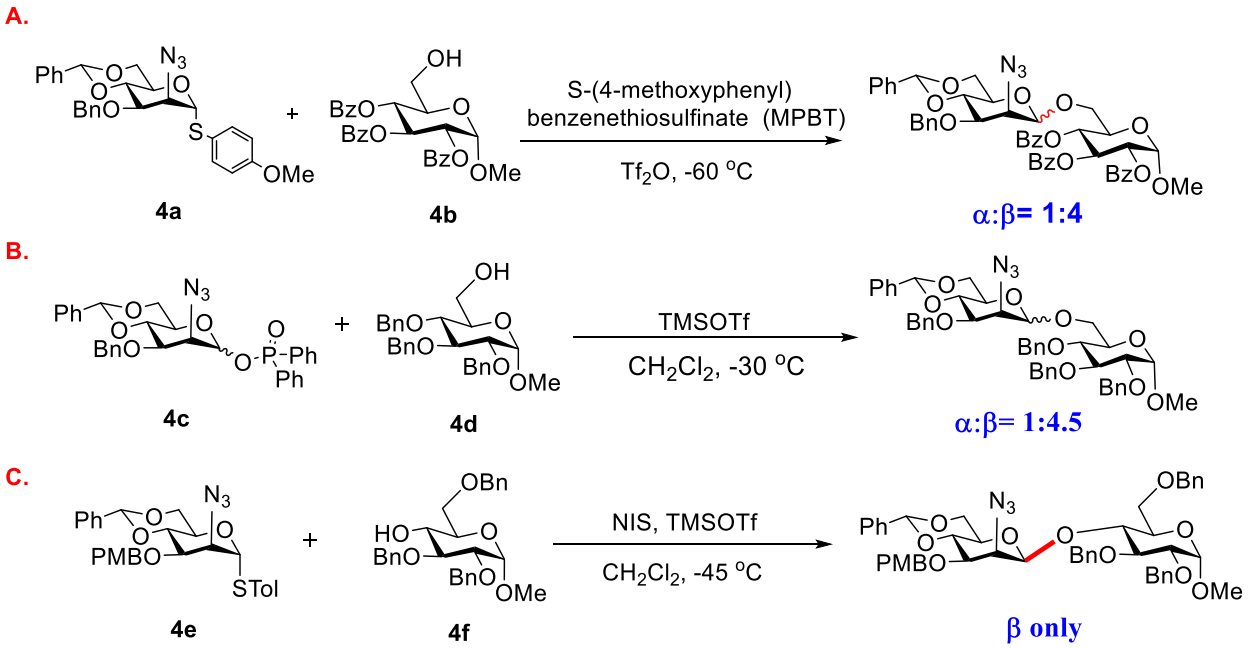
Scheme 2.2. Indirect synthesis of *β*-ManNAc glycosides via oximinoglycosyl donors

The most significant advancement in the field of β-mannosidic linkages was made by Prof. David Crich's group in 1996. Their study demonstrated that glycosylation using the conformationally restricted 4,6-*O*-benzylidine-locked mannopyranosyl sulfoxide donor predominantly produces *β*-mannopyranoside as the main product[18]. Spectroscopic investigations using a phenyl sulfoxide mannosyl donor suggested the formation of a reactive *α*-triflate intermediate which undergoes S_N2 type attack from the incoming nucleophile leading to the production of β-mannoside predominantly (scheme **2.3**)[19].



Scheme 2.3. Crich's benzylidene equipped donor in the synthesis of *β*-mannosides.

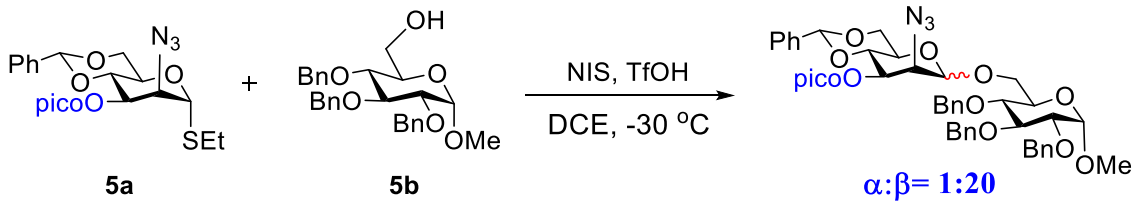
Although, the conformationally constrained benzylidene concept has been effectively demonstrated over the years towards the synthesis of *β*-mannosides using C2-ethers as a non-participating group at the donor's end; however, studies showed that this methodology gives relaxed *β*-selectivity in the glycosylations of 2-azido-mannosyl donors. Only a handful of reports are there in the synthesis of *β*-ManNAc containing oligosaccharides. In 2001, Van boom group showed that glycosylation of the benzylidene equipped 2-azio-thiomannosyl donor **4a** with MPBT as promoter effectively furnished 2-azido-2-*deoxy*-*β*-D-mannoside as a major product (scheme **2.4**)[20].



Scheme 2.4. Reports on the synthesis of 2-azido-2-*deoxy*-β-D-mannosides

Also reported by Hashimoto group and Mishra group, glycosylations with 2-azido-mannnosyl phosphate donor **4c** and mannosyl thiotolyl donor **4e** yielded *β*-D-mannoside as predominant products (Scheme **2.4**)[21,22].

Recently, Demchenko group has demonstrated the utilization of C3-picoloyl group in the glycosylation of benzylidene locked 2-azido-mannosyl thioethyl donors which indeed furnish the *β*-D-mannosides as a major product[23]. Hydrogen bond mediated aglycone delivery is anticipated to play a pivotal role in this *β*-selective mannosylation (scheme **2.5**).



Scheme 2.5. Synthesis of 22-azido-2-*deoxy*-*β*-D-mannosides using HAD.

2.2. Present work

Current literature on the synthesis of 2-azido-2-*deoxy*-*β*-D-mannopyranosides primarily focuses on glycosylation reactions utilizing older generation thio- or phosphate- donors. These traditional donors have been the subject of study; however, there is a notable gap in understanding how the stereo-electronic effects of various protecting groups influence the selectivity of the resulting reactions. The impact of these protective groups on the outcome of glycosylation reactions has not yet been thoroughly explored or demonstrated in the existing reports. In 2016, Hotha group unveiled the ethynyl cyclohexyl glycosyl carbonate donors for the synthesis of oligosaccharides and glycoconjugates[24]. The modern generation glycosyl donors offer milder catalytic activation and enhanced protecting group tolerance. Therefore, it's worthwhile to explore the new generation of gold catalyzed glycosylation along with the influence of protecting groups in *β*-mannosylation.

In this premise, we set out to explore the silver assisted gold catalyzed activation of ethynyl glycosyl carbonate donors using a range of temperatures and concentrations. A set of 2-azidomannosyl carbonate donors **6a**-**6g** having different protecting groups including ethers, esters and silyl ethers were proposed to synthesize the 2-azido-2-*deoxy*-*β*-D-mannosides. This work also aims to examine the stereo-electronic influence of the C3-protecting group on the selectivity outcomes of the glycosylation reactions. The C2-azide group will serve two purposes: (i) serving as non-participating group in 1,2-*cis*-glycosylations and (ii) it can be converted to NHAc post glycan synthesis.

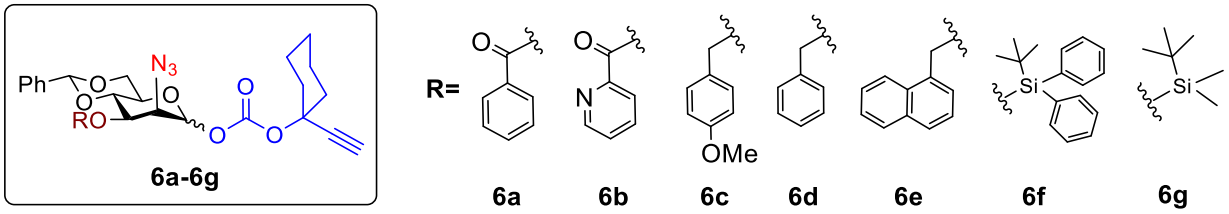
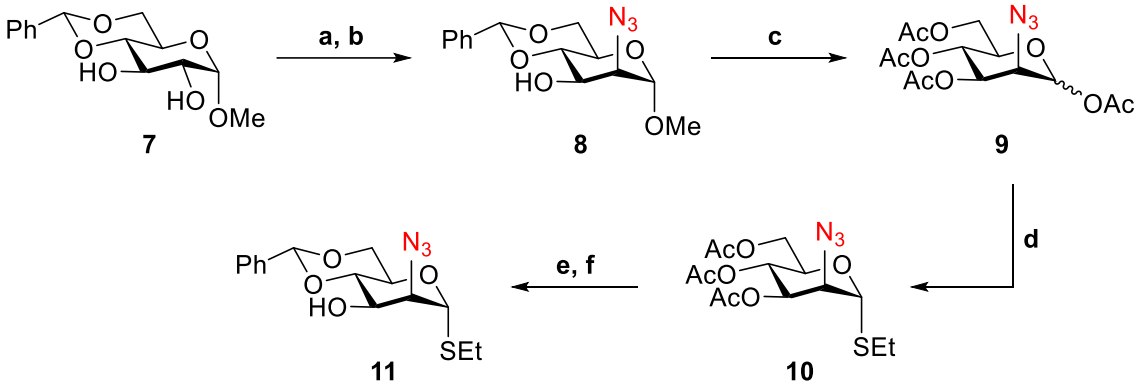


Fig. 2.3. Proposed 2-azidomannosyl carbonate donors for β-mannosylation

2.2.1 Synthesis of benzylidene equipped mannoside derivative 11

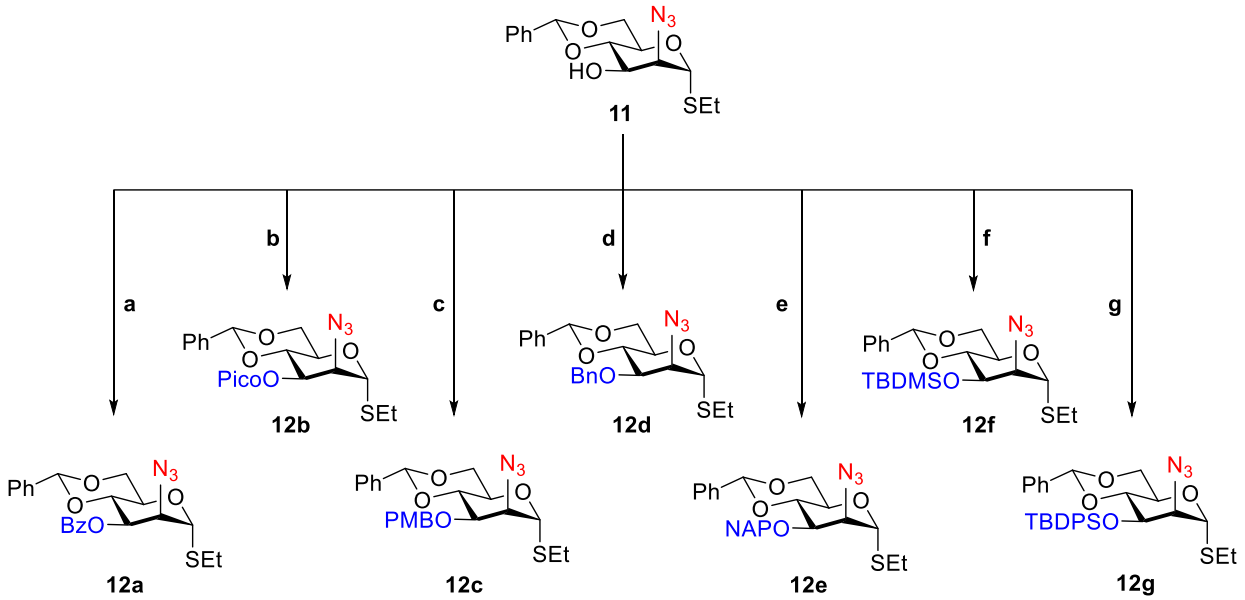
Our synthetic journey begun with the synthesis of C3-OH free mannoside **7**[25]. The C2-OH group of the easily accessible building block **7** was selectively protected using Tf_2O in pyridine/CH_2Cl_2 conditions to make it a good leaving group which was directly treated with NaN_3/DMF in 70 ºC to successfully obtain the C2-azido mannoside **8** in 64 % yield over two steps[25]. Compound **8** was treated with H_2SO_4 in Ac_2O to furnish the tetra-acetate derivative **9**. The acetate derivative was glycosylated using BF_3.Et_2O and EtSH to obtain the thioglycoside **10** in 74% yield. Further, all acetates of thioglycosides **10** were deprotected under Zemplén deacetylation conditions to obtain a tri-OH derivative which was subsequently treated with $PhCH(OMe)_2$ in CSA/acetonitrile to furnish the 4,6-*O*-benzilidine protected thioglycoside **11** in 83 % yield over two steps (Scheme **2.6**). The formation of building block **11** was confirmed by NMR and MALDI-ToF studies which were in good agreement with the data reported earlier by Demchenko group[23].



Scheme 2.6. Synthesis of mannoside **11**. Reagents: a) Tf_2O, pyridine, CH_2Cl_2, 0-25 ºC, 1 h, b) NaN_3, DMF, 70 ºC, 8 h, 64 % over two steps; c) 2% H_2SO_4, Ac_2O, 0-25 ºC, 4 h, 88 %; d) EtSH, BF_3.Et_2O, CH_2Cl_2, 25 ºC, 4 h, 74 %; e) NaOMe, CH_2Cl_2: MeOH, 25 ºC, 2 h, f) $PhCH(OMe)_2$, CSA, Acetonitrile, 25 ºC, 4 h, 83 % over two steps.

2.2.2. Synthesis of different C3-protected mannoside derivatives

Now having the C3-OH free mannoside derivative **11** in our hand, we started masking the C3-position with different protecting groups. First, we treated the compound **11** with BzCl in pyridine to obtain benzoate **12a** in 91 % yield[23]. Coupling of compound **11** with commercially available 2-piconilic acid using EDCI furnished the picolyl-protected mannoside **12b**[23]. Further, treatment of compound **11** with PMBCl, BnBr and NapBr in NaH/DMF/TBAI conditions successfully furnished the C3-ether protected building blocks **12c**, **12d** and **12e** respectively with 91, 90 and 90 % yields (Scheme **2.7**).

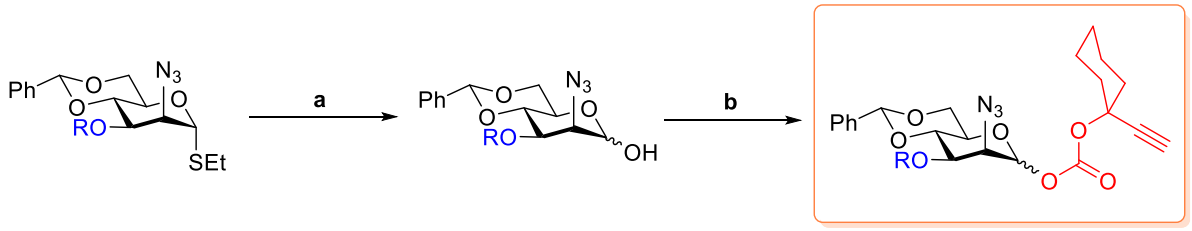


Scheme 2.7. Synthesis of the different C3-protected mannosides. Reagents: a) BzCl, pyridine, DMAP, 0-25 ºC, 2 h, 91 %, b) 2-picolinic acid, EDC, DMAP, 25 ºC, 2 h, 92 %. c) NaH, 4-methoxybenzyl chloride, TBAI, DMF, 0-25 ºC, 2 h, 91 % d) NaH, BnBr, TBAI, DMF, 0-25 ºC, 2 h, 90 %; e) NaH, NAPBr, TBAI, DMF, 0-25 ºC, 2 h, 90 %; f) TBDMSOTf, lutidine, CH_2Cl_2, 0-25 ºC, 2 h, 90 %; g) TBDPSCl, DMF, DMAP, 60 ºC, 2 h, 62 %;

Subsequently, we moved our forward synthesis towards the protection of silyl ethers. Compound **11** smoothly underwent secondary TBS protection when treated with TBDMSOTf in 2,6-lutidine/CH_2Cl_2 to obtain the TBS protected compound **12f** in 90 % yield. As the C3-OH of compound **11** was a secondary one, the TBDPS protection required elevated temperature of 60 ºC using TBDPSCl/DMF to furnish compound **12g** in 62 % yield (Scheme **2.7**).

2.2.3. Synthesis of 2-azido-mannosyl carbonate donors

With the different C3-protected thioglycosides in our hand we advanced our synthesis towards the transformation of thioglycosides into desired mannosyl carbonate donors. Initially, we tried the conventional NIS/TfOH mediated hydrolysis of the thiosugars **12a-12g** to generate the corresponding hemiacetals which resulted in poor yields due to the simultaneous deprotection of the acid labile benzylidene group. However, the treatment of thioglycosides **12a-12g** with NBS and $CaCO_3$ in acetone: H_2O[26] successfully generated the corresponding hemiacetals **13a-13g** with good to excellent yields. Subsequent treatment of the hemiacetals **13a-13g** with carbonate reagent **13h** in CH_2Cl_2/ DMAP condition[24] furnishes the corresponding mannosyl carbonate donors **15a-15g** with excellent yields (**scheme 2.8**).



R = -Bz (**12a**), -Picoloyl (**12b**), -PMB (**12c**), -Bn (**12d**), -Nap (**12e**), -TBDMS (**12f**), -TBDPS (**12g**),

R = -Bz (**13a**), -Picoloyl (**13b**), -PMB (**13c**), -Bn (**13d**), -Nap (**13e**), -TBDMS (**13f**), -TBDPS (**13g**),

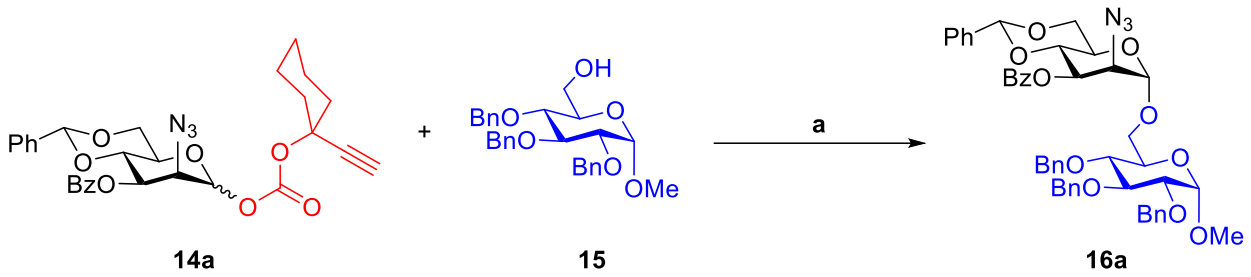
R = -Bz (**14a**), -Picoloyl (**14b**), -PMB (**14c**), -Bn (**14d**), -Nap (**14e**), -TBDMS (**14f**), -TBDPS (**14g**).

Scheme 2.8. Synthesis of the mannosyl carbonate donors. Reagents: a) NBS, $CaCO_3$, Acetone: H_2O, 0-25 ºC, 30 min, 81 % (13a**)**, 79 % (13b**),** 76 % (13c**)**, 79 % (13d**),** 73 % (13e**),** 76 % (13f**),** 72 % (13g**)**; b) 1- ethynylcyclohexyl (4-nitrophenyl) carbonate (**13h**), CH_2Cl_2, DMAP, 0-25 ºC, 8 h, 89 % (14a**)**, 91 % (14b**)**, 90 % (14c**)**, 91 % (14d**)**, 92 % (14e**)**, 86 % (14f**)**, 81 % (14g**)**.

2.2.4 Initial trial glycosylations with carbonate donors 14a and 14c

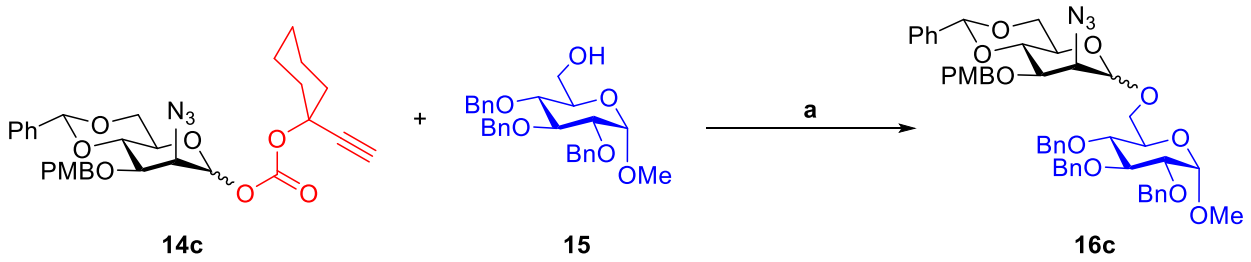
We started the journey of β-selective glycosylation with C3-Bz protected mannosyl donor **14a**. Glycosylation of **14a** with the very popular primary acceptor **15** by the catalytic activation with chloro[2,4-di-*tert*-butylphenyl) phosphite]gold **17** and AgOTf[24] in 50 mM reaction concentration w.r.t the donor at 25 ºC successfully yielded the disaccharide **16a** in 86 % yield. However, the 2D-NMR analysis of disaccharide **16a** showed that the $J_{C1\text{-}H1}$ value is 177 Hz at the anomeric position which indeed confirms that the formed disaccharide **16a** is the undesired α-mannoside (Scheme **2.9**). The probable explanation for the formation of the *α*-product is due to the distal C3-

participation of the benzoyl group thus blocking the *β*-face of the donor and facilitating the attack of the nucleophile from the *α*-face as depicted by Demchenko group[23].



Scheme 2.9. Glycosylation with C3-Bz equipped mannosyl carbonate donor: Reagents: a) chloro[2,4-di-*tert*-butylphenyl) phosphite]gold (**17**), AgOTf, CH_2Cl_2, 4Å MS powder, **50 mM**, 25 ºC, 15 min, 86% (only α).

Well, after seeing the adverse effect of the C3-acylates in the glycosylation, we moved on to study the influence of C3-ethers towards glycosylation. The C3-*O*-PMB armed mannosyl donor **14c** was subjected to glycosylation with the same acceptor **15** under identical conditions (*c* 50 mM, T = 25 ºC) which successfully resulted in a mixture of disaccharides **16c** with a *α*:*β* ratio of 1:6 in 84 % yield (Scheme **2.10**). The 2D-NMR analysis of the disaccharide mixture showed that the $J_{C1\text{-}H1}$ value of the major isomer at the anomeric position is 162.4 Hz which indeed confirms that the major disaccharide product is the desired *β*-mannoside.

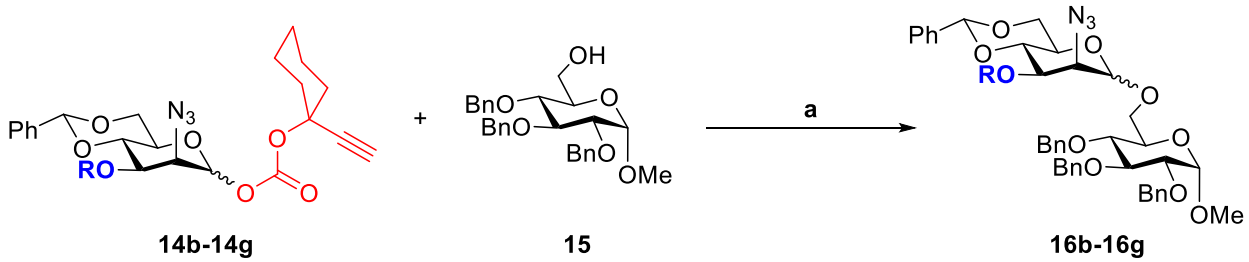


Scheme 2.10. Glycosylation with C3-PMB equipped mannosyl carbonate donor: Reagents: a) Chloro[2,4-di-tert-butylphenyl) phosphite]gold (**17**), AgOTf, CH_2Cl_2, 4Å MS powder, *c*50 mM, 25 ºC, 15 min, 84 % (α:β = 1:6).

2.2.5 C3-protecting group influence on β-selectivity

After exploring the silver assisted gold catalyzed *β*-selective mannosylation strategy, we subjected other C3-protected mannosyl donors **14b-14g** for glycosylation with the same primary acceptor **15** under identical conditions (*c* 50 mM, T = 25 ºC). The C3-benzyl ether donor **14d** and Nap-armed

donor **14e** yielded almost identical *β*-selectivity of 1:5 and 1:6 respectively to produce the corresponding disaccharides **16d** and **16e** with excellent overall yields of 86 % and 88 %. The best *β*-selectivity of 1:7 in 50 mM concentration was noticed from the C3-*O*-TBDMS mannosyl carbonate donor **14f** with 89 % yield (Table **2.11**).



14b-14g **15** **16b-16g**

Entry	C3-protecting group (R)	Disaccharide	Selectivity (α:β)	Yield
1	PMB	16c	**1:6**	84 %
2	Bn	16d	**1:5**	86 %
3	NAP	16e	**1:6**	88 %
4	TBDMS	16f	**1:7**	89 %
5	TBDPS	16g	**1:2.5**	81 %
6	Pico[x]	16b	**1:1.6**	74 %

[x]Required 90 mol% of Au (I) and AgOTf catalysts due to the quenching of gold-chloride

Scheme 2.11. Screening glycosylations of different C3-proected mannosyl donor. Reagents: a) Chloro[2,4-di-tert-butylphenyl) phosphite]gold (**17**), AgOTf, CH_2Cl_2, 4Å MS powder, 50 mM, 25 ^oC, 15 min.

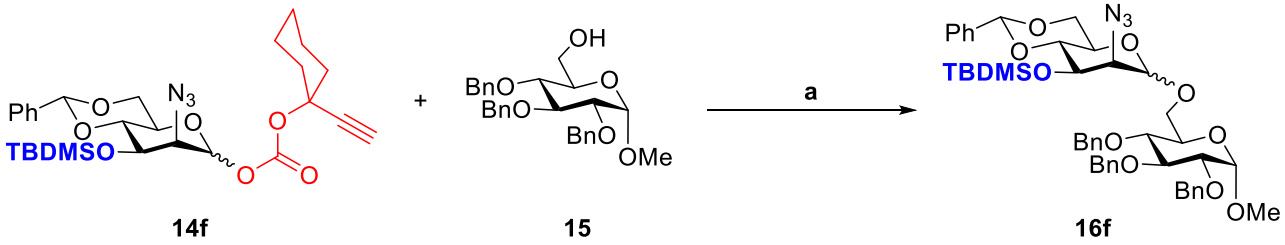
The significant stereo-electronic influence of the C3-protecting groups on *β*-selectivity is evident when the C3-TBDPS ether protected carbonate donor **14g** is subjected to glycosylation under analogous reaction conditions. Donor **14g** produced the corresponding disaccharide **16g** with an impressive yield of 81%; however, it exhibited reduced β-selectivity of 1:2.5 (Scheme **2.11**). The stereochemical outcome of this glycosylation is probably attributed to the spatial orientation of TBDPS group. Between the two silyl groups, TBDPS- having two phenyl rings might have imparted greater steric buttressing on the *β*-face of the formed oxocarbenium ion, consequently diminishing *β*-selectivity compared to the C3-TBDMS carbonate donor variant.

While all other protecting groups worked fine with the *β*-mannosylation in gold-catalyzed glycosylation conditions, the C3-piconyl carbonate donor **14b** needed a higher catalyst loading of 0.9 equivalents due to the quenching of the gold catalyst by pyridinyl moiety. Subsequently, the

C3-piconyl-protected carbonate donor **14b** exhibited an unusual β-selectivity of 1:1.6 yielding the disaccharide **16b**, attributed to the alteration in reaction conditions (Scheme **2.11**).

2.2.6. Dilution effect on β-selective mannosylation

It is well established in organic chemistry that reaction concentration significantly influences both the mechanism and the outcome of some reactions. For instance, depending on the degree of dilution, a reaction can be intramolecular or intermolecular in nature. According to the literature, the concentration of the glycosylation has notable effect on the selectivity of the reaction when the glycosylation is going via hydrogen bond mediated aglycone delivery (HAD) as reported by Demchenko group[23] wherein they showed the glycosylation of C3-pico equipped thioethyl mannosides produced fivefold increase in the *β*-selectivity when the reaction concentration was changed from 50 mM to 5 mM. Although there is no apparent possibility of the intermolecular hydrogen bonding in gold-catalyzed glycosidations, we sought to investigate whether there is any concentration effect in the *β*-selectivity of the gold catalyzed glycosylation conditions.



14f **15** **16f**

Entry	Concentration	Yield	Selectivity (α:β)
1.	**50 mM**	89 %	**1:7**
2.	**10 mM**	82 %	**1:11**
3.	**5 mM**	66 %	**1:11**

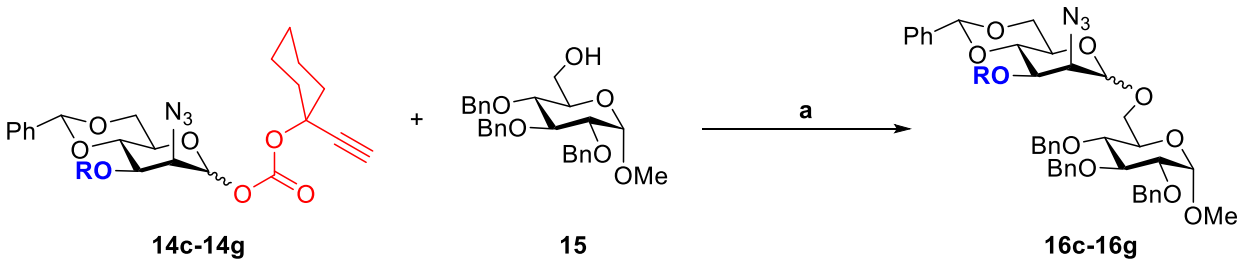
Table 2.1. Dilution effect on β-mannosylation

Earlier, the C3-*O*-TBS equipped carbonate donor **14f** resulted in *β*-selectivity of 1:7 at 50 mM reaction concentration. Keeping all other reaction parameters identical, the donor **14f** was subjected to glycosylation with acceptor **15** at 10 mM concentration to a surprising enhancement of β-selectivity to 1:11 with 82 % yield. Further increasing the reaction dilution to 5 mM did not show any improvement in β-selectivity; however, the extremely high dilution of 5 mM significantly reduced the yield of the glycosylation due to the lesser reactivity of the acceptor in

dilute conditions and increased yield of undesired hemiacetal formation (Table **2.1**). The data clearly shows that the concentration indeed influences the *β*-stereoselectivity.

2.2.7 Screening of all the carbonate donors towards β-selective mannosylation

Having the dilution effect on selectivity in our hand, we set out to screen all the differently C3-protected carbonate donors under gold catalyzed glycosylation to examine how the β-selectivity is influenced by the reaction temperature and concentration. We conducted the glycosylation at +25 ºC, 0 ºC and -25 ºC and at each temperature we sought to carry out the glycosylation at two different reaction concentrations 50 mM and 10 mM. This study aims to provide a comprehensive understanding of the optimization of the ideal combination of temperature and concentration to achieve the highest possible *β*-selectivity.



14c-14g **15** **16c-16g**

Entry	Donor	Disaccharide	T= 25 °C (α:β)		T= 0 °C (α:β)		T= -25 °C (α:β)	
			50 mM	10 mM	50 mM	10 mM	50 mM	10 mM
1.	PMB	16c	1:6	1:10	1:8	1:13	1:6	1:15
2.	Bn	16d	1:5	1:10	1:6	1:12	1:5	1:11
3.	NAP	16e	1:6	1:8	1:7	1:14	1:5	1:14
4.	TBS	16f	1:7	1:11	1:9	1:18	1:8	1:19

Table 2.2. Screening of all the carbonate donors in β-selectivity

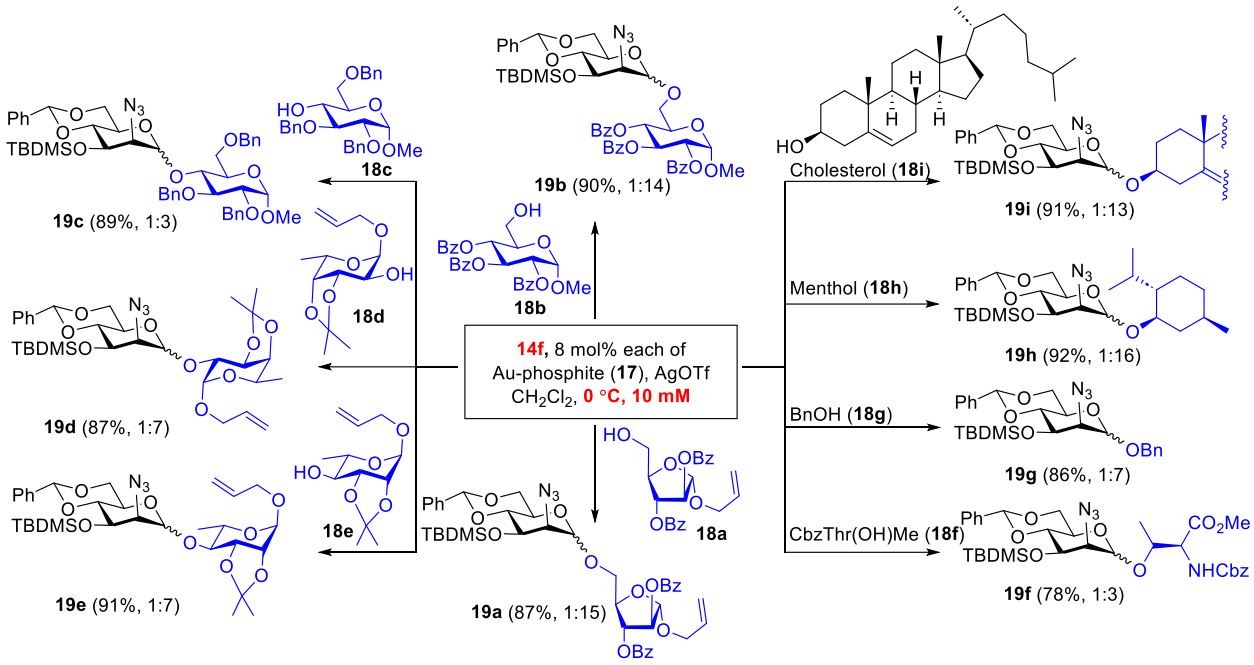
Glycosylation with C3-PMB carbonate donor **14c** with the acceptor **15** in 10 mM also resulted in increased *β*-selectivity of 1:10. Lowering the reaction temperature to 0 °C while maintaining the 10mM concentration improved the selectivity a bit to 1:8. Further lowering the glycosylation temperature to -25 °C didn't notably improve the *β*-selectivity as shown in Table **2.2**. However, for the glycosylation of donor **14c**, changing both the temperature and dilution to 0 °C and 10 mM respectively significantly enhanced the *β*-selectivity to 1:13. Maintaining the dilution of 10 mM while further lowering the temperature to -25 °C yielded the *β*-selectivity of 1:15 (Table **2.2**).

For the glycosylation outcome with C3-Bn carbonate donor **14d** and C3-Nap donor **14e**, the trend was similar to that of C3-PMB protected donor. The selectivity numbers indicated in Table **2.2** suggests improvement in *β*-selectivity with the simultaneous change in concentration and temperature. In the screening glycosylations of both the carbonate donors **14d** and **14e** at 0 °C successfully yielding the disaccharides **16d** and **16e**; increasing the dilution from 50 mM to 10 mM doubles the *β*-selectivity from 1:6 and 1:7 to 1:12 and 1:14 respectively (Table **2.2**, entry 2 and 3). In case of C3-TBS equipped donor **14f**, the β-selectivity was more promising than the other derivatives. When **14f** was subjected to glycosylation at 0 °C, changing the concentration from 50 to 10 mM resulted into substantial improvement of *β*-selectivity to 1:18 (Table **2.2**, entry 4). Furthermore, decreasing the reaction temperature to -25 °C at 10 mM had a minimal effect on selectivity in case of donor **14f**. Owing to the fact that reactions at subzero temperatures need special care and additional infrastructure, we have opted to conduct the glycosylations at 0 °C and 10 mM.

The data presented in Table **2.2** clearly indicates that variations in temperature alone exert a limited impact on the selectivity outcome of the glycosylation reaction. However, the combined use of temperature and dilution can significantly enhance *β*-selectivity in the gold-catalyzed mannosylation strategy.

2.2.8 Substrate scope of the methodology

Having good *β*-selectivity with primary armed sugar acceptor **15** in our hand, we moved on to explore the versatility of this methodology with diverse range of acceptors. Donor **14f** was subjected to glycosylation with disarmed primary acceptor **18b** at 0 °C/10 mM conditions which successfully furnished the disaccharide **19b** with 90 % yield and a selectivity of 1:14 (α:β). The glycosylation with furanosyl acceptor **18a** exhibited a high β-selectivity of 1:15, successfully yielding disaccharide **19a** with an 87% yield. Not only primary acceptors, this diastereoselective synthesis works effectively with secondary sugar acceptors also. For example, glycosylation of carbonate donor **14f** with fucosyl acceptor **18d** and rhamnosyl acceptor **18e** yielded the disaccharide **19d** and **19f** respectively with 87 % and 91 % yield furnishing β-selectivity of 1:7 in both the cases (Scheme **2.12**).



Scheme 2.12. Substrate scope of the synthesis of 2-azido-2-*deoxy*-*β*-D-mannosides

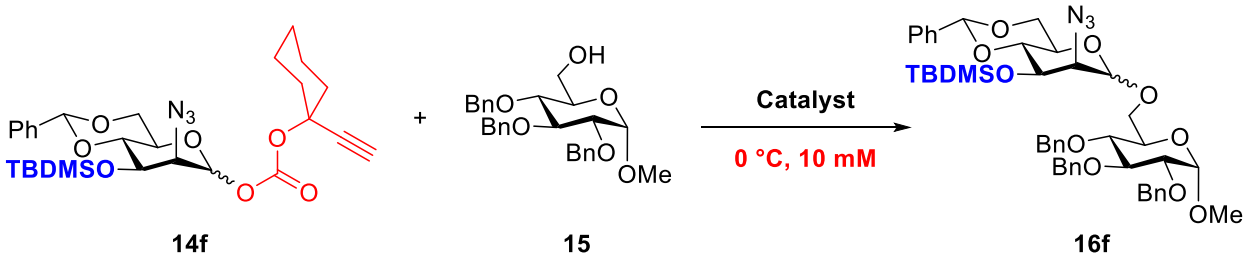
More sterically demanding acceptors compromised the *β*-selectivity. Glycosylation of donor **14f** with acceptor **18c** yielded the disaccharide **19c** in 89 % yield with a selectivity of 1:3 (α:β). The current protocol proved very promising for non-sugar acceptors also. Glycosylations of donor **14f** with commercially available cholesterol **18i** and menthol **18h** exhibited high *β*-selectivity of 1:13 and 1:16 with 91% and 92% yield respectively furnishing the corresponding glycoconjugates **19i** and **19h**. Furthermore, the methodology was tested with acceptors such as benzyl alcohol **18g** and threonine residue **18f** to successfully furnish the corresponding conjugates **19g** and **19f** with *β*-selectivities of 1:7 and 1:3, along with commendable glycosylation yields of 86% and 78%, respectively (Scheme **2.12**).

2.3. The mechanism of the glycosylation

2.3.1. Counter anion effect on selectivity:

The alkynyl glycosyl carbonate can be activated using the optimized combination of Au(I) **17** and AgOTf, or an alternative combination of Au(I) **17** and $AgNTf_2$. Under the same glycosylation conditions of 0 °C and 10 mM, employing the identical acceptor **15** and donor **14f**, the selectivity outcome varied significantly depending on the catalyst combination used. It has already been observed that the activation of donor **14f** with standard Au(I)+AgOTf exhibited high selectivity outcome of 1:18. However, when donor **14f** was activated using Au(I)+$AgNTf_2$ combination, the

β-selectivity drastically reduced to 1:3 under identical conditions (Table **2.3**). This clearly indicates that there is a significant participation of the catalyst counter anion in the reaction mechanism.



14f **15** **16f**

Entry	Catalyst combination	Selectivity (α:β)	Yield
1.	**Au(I) + AgOTf**	**1:18**	**89 %**
2.	**Au(I) + $AgNTf_2$**	**1:3**	**81 %**

Table 2.3. Counter anion effect on selectivity

2.3.2 Acceptor screening on β-selectivity

Literature studies indicate that the mechanism of glycosylation can transition between S_N1 and S_N2 depending on the specific conditions and substrates involved[27]. Principles of organic chemistry suggest that a highly nucleophilic nucleophile is likely to favor the S_N2 pathway, whereas lower nucleophilicity tends to promote a dissociative mechanism, consistent with the S_N1 pathway.

The previously obtained *β*-selectivity for various substrates is summarized in a streamlined format in Table **2.4**. When the nucleophilicity is very high in case of primary sugar acceptors **15**, **18a** and **18b**, the selectivity numbers are excellent like 1:18, 1:15 and 1:14 at 0 °C/ 10 mM (entry 1, table **2.4**). The obtained *β*-selectivity of 1:16 and 1:13 are very promising in case of highly nucleophilic steroidal acceptors also e.g. cholesterol **18h** and menthol **18i** (entry 2). However, decrease in nucleophilicity, as seen with secondary sugar acceptors **18d** and **18e**, led to the reduction of *β*-selectivity to 1:7 (entry 3) under the same reaction conditions. The *β*-selectivity further reduced to 1:3 when the secondary C4-glucoside acceptors **18c** and **18j** are subjected to glycosylation with donor **14f**. From this comparison, it is evident that the alteration in the *β*-selectivity must have a direct correlation with the acceptor's nucleophilicity.

It is conceivable that the diminished nucleophilicity of the acceptors may prompt the reaction mechanism to adopt a dissociative pathway, potentially leading to a loss of diastereoselectivity. However, these proposed mechanisms remain speculative and require further validation.

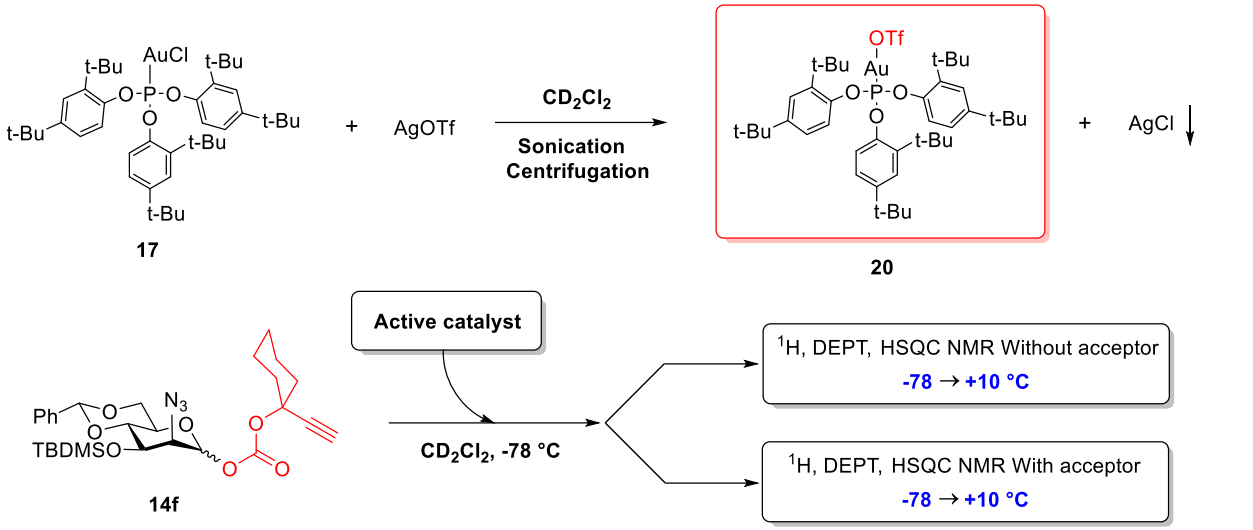
Entry	Acceptor	Nature	Product (yield)	Selectivity (α:β)
1	**15, 18a, 18b**	Primary sugar acceptors Highly nucleophilic	**16f** (86%) **19a** (87%) **19b** (90%)	1:18 (for **16f**) 1:15 (for **19a**) 1:14 (for **19b**)
2	**18h, 18i**	Aliphatic acceptors Highly nucleophilic	**19h** (92%) **19i** (91%)	1:16 (for **19h**) 1:13 (for **19i**)
3	**18d, 18e**	Secondary sugar acceptors Moderately nucleophilic	**19d** (87%) **19e** (91%)	1:7 (for **19d**) 1:7 (for **19e**)
4	**18c, 18j**	Secondary glucoside acceptors Poor nucleophiles	**19c** (89%) **19j** (85%)	1:3 (for **19c**) 1:3 (for **19j**)

Table 2.4. Comparison of acceptor nucleophilicity vs β-selectivity

2.4. VT-NMR studies using mannosyl carbonate donor 14f

To investigate the mechanism of gold-catalyzed *β*-mannosylation, we planned VT-NMR experiments in collaboration with Prof. David Crich at the University of Georgia at Athens, USA.

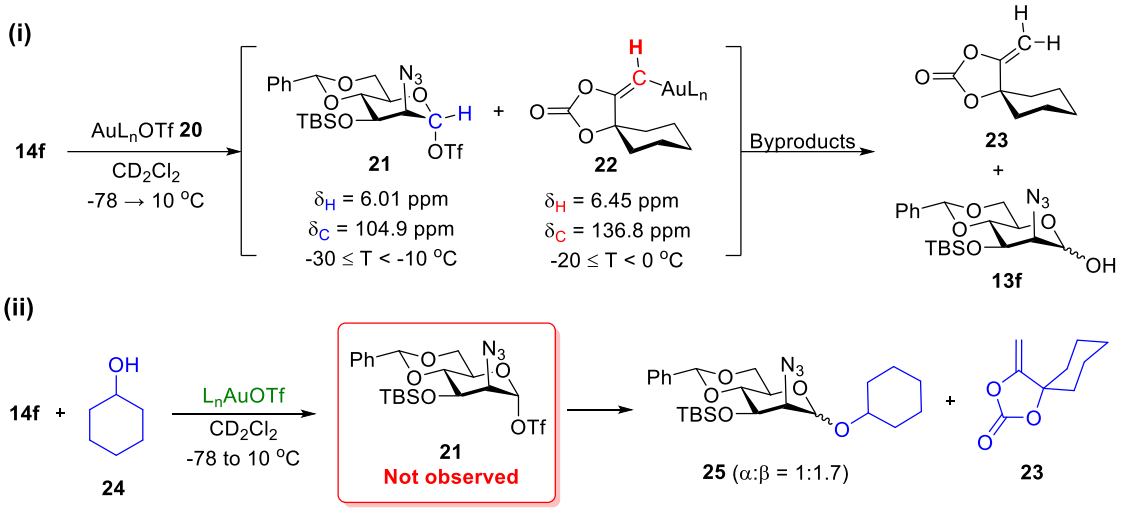
At first, chloro[2,4-di-*tert*-butylphenyl)phosphite]gold (**17**) and AgOTf were mixed, sonicated and centrifuged to generate the active catalytic species [tris(2,4-di-*tert*-butylphenyl)phosphite]gold trifluoromethanesulfonate **20**. When the active catalyst was infused into the solution of the carbonate donor **14f** at -78 °C, no activation of the glycosyl donor was observed. The NMR probe temperature was then raised in 10 °C increments with ^{1}H, ^{19}F and DEPT-135 NMR spectra recorded at each step until decomposition was observed. At -30 °C, the presence of likely *α*-triflate species **21** and cyclic carbonate side product **22** was observed. The *α*-triflate was characterized by resonance at δ_H = 6.01 ppm at ^{1}H NMR and 104.9 ppm in the DEPT-135 NMR corresponding to the anomeric H_1 and C_1 atoms (Fig**. 2.5**). Further, the low temperature HSQC experiment at –25 °C revealed a contour corresponding to the δ_H = 6.01 ppm and δ_C =104.9 ppm confirming



Scheme 2.13. Proposed set of experiments for VT-NMR studies

the presence of the reactive covalent *α*-triflate intermediate **21** (Fig **2.5**). Interestingly, at –20 °C, a new singlet appeared at δ_H = 6.45 ppm, which displayed an HSQC correlation with the DEPT-135 NMR signal at δ_C = 136.8 ppm (Fig **2.5**). This resonance is tentatively attributed to the vinylidene gold complex **22**, which, in the presence of moisture may decompose to form the cyclic carbonate **23** (Scheme **2.14**). The presence of *α*-triflate was most prominent in the temperature range –30 °C to –10 °C. Above –10 °C, there was no characteristic peak corresponding to the triflate species indicating the instability and decomposition of the intermediate above –10 °C (**fig 2.4**).

Significantly, there was minimal to no change in the anomeric ratio of the unreacted donor **14f** throughout the VT NMR experiments, indicating that both anomers were consumed at roughly the same rate. When the same VT-NMR experiment was carried out in presence of cyclohexanol acceptor, at –30 °C the formation of cyclohexyl glycosides **25** was observed. The formation of the glycoside products is confirmed by the two DEPT peaks at δ_c = 97.7 and 97.0 ppm corresponding to the anomeric carbons. The resulting glycoside ratio was found to be α:β = 1:1.17 which was characterized by coupled HSQC experiment. Notably, in this time mannosyl triflate **21** was not observed indicating the immediate conversion of any reactive intermediate to the product at relatively higher temperature (Fig **2.6**).



Scheme 2.14. VT-NMR experiment (i) without the acceptor (ii) with acceptor cyclohexanol

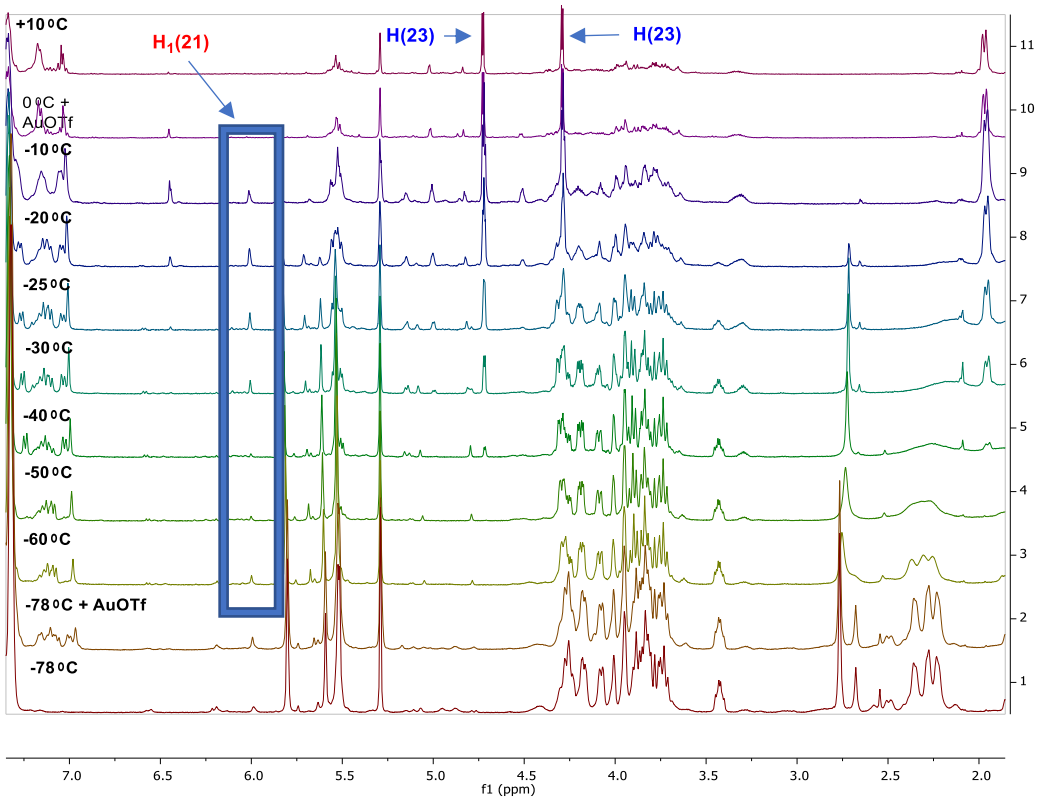


Fig 2.4. Activation of donor **14f** and Stacked VT-^{1}H NMR without acceptor.

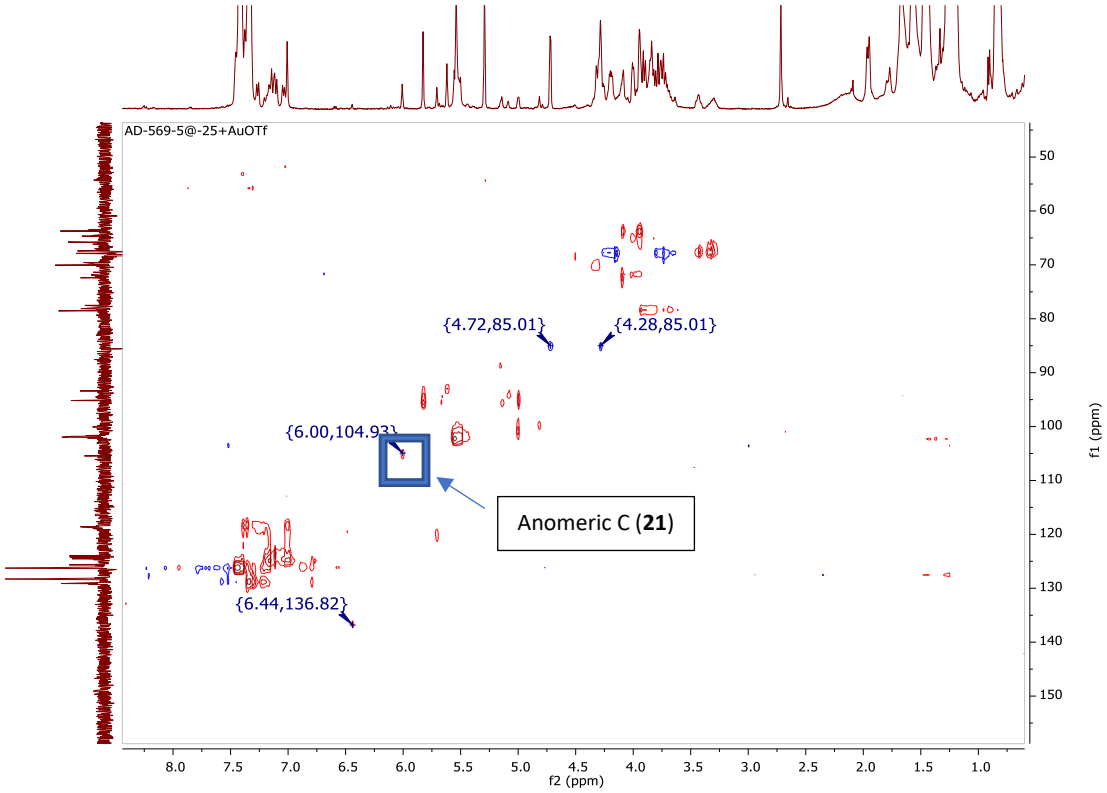


Fig. 2.5. Low temperature HSQC experiment with donor **14f** without acceptor

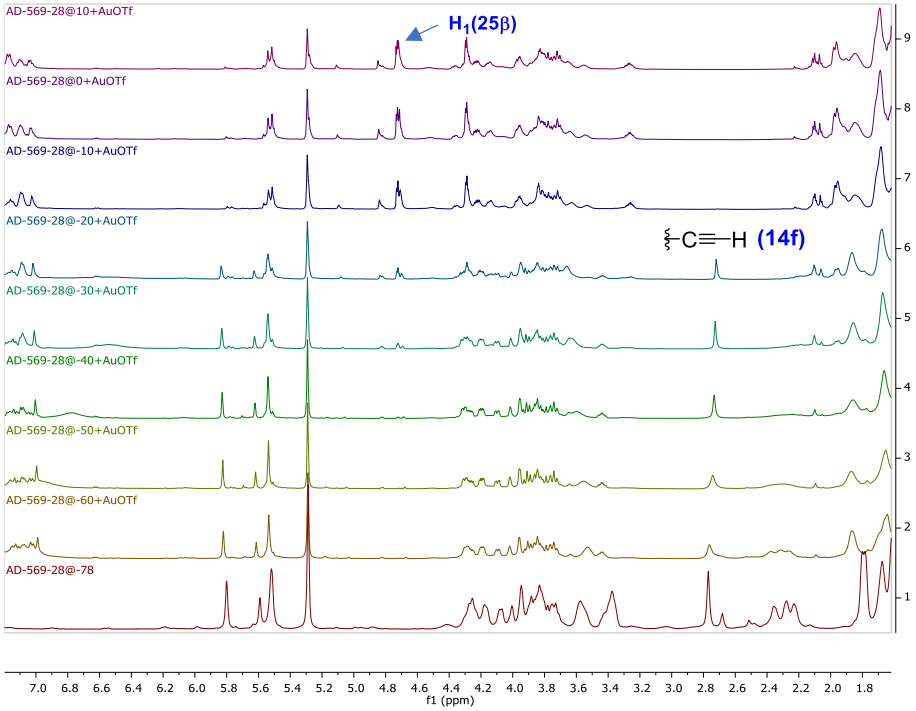
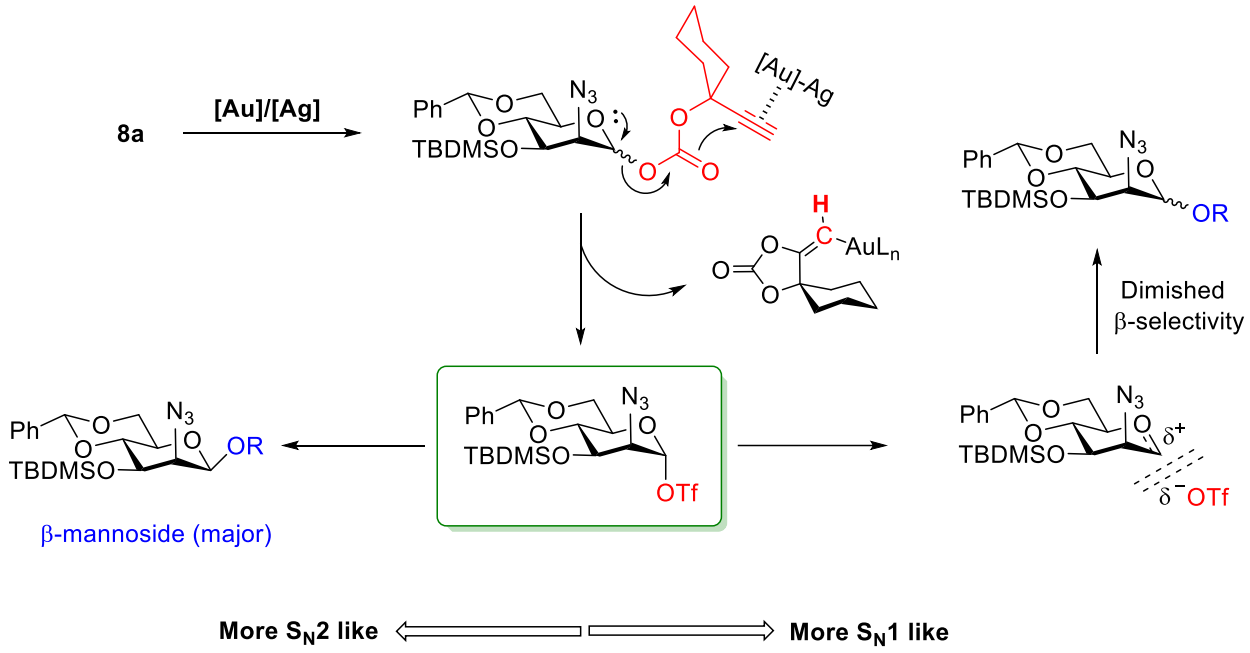


Fig 2.6. Activation of donor **14f** and Stacked VT-^{1}H NMR with cyclohexanol.

2.5. Mechanistic pathway of the gold catalyzed β-mannosylation

The VT-NMR studies in hand, the mechanism of the [Au]/[Ag]-catalyzed *β*-mannosylation can be outlined. Upon activation of the 2-azidomannosyl carbonate donors with the Au-phosphite **17** and AgOTf, the triple bond in the carbonate motif gets activated by the gold's alkynophilicity. This activation facilitates the departure of the leaving group, leading to the formation of a gold-alkylidine complex **22**. Subsequently, the participating triflate captures the electrophilic species generated from the donor and furnish the covalent *α*-triflate species. When the acceptor nucleophilicity is high, then it can attack the *α*-triflate species via an S_N2 type mechanism resulting in the formation of the 2-azido-2-*deoxy*-*β*-D-mannosides as major product (Scheme **2.15**). When the acceptor nucleophilicity is not promising enough then the chances of S_N2 type attack diminishes and the reaction goes via more dissociative type mechanism and thus resulting into diminished diasterioselectivity. Besides, the *β*-selectivity enhancements in the diluted reaction media is in good agreement with the mechanism. When the concentration of the reaction mixture is more (50 mM), the equilibria favors more dissociative type mechanism leading to the diminished diasterioselectivity. However, when the concentration of the reaction mixture is less (10 mM), the equilibria enhanced stability of triflate thereby enhancing the diasterioselectivity.

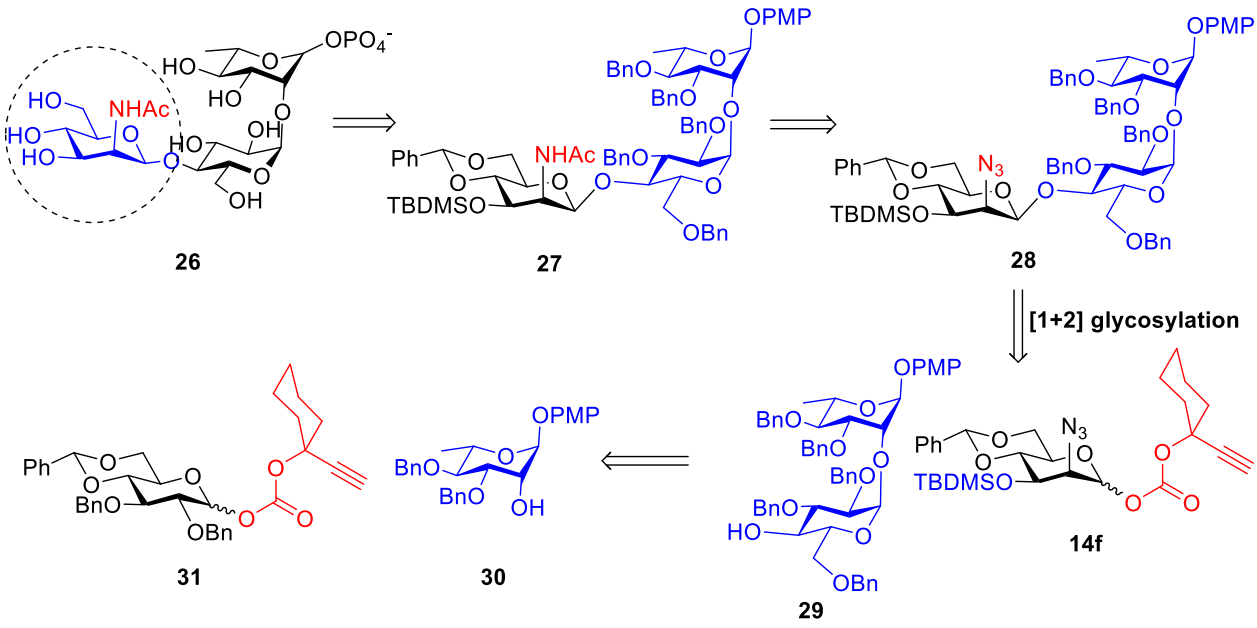


Scheme 2.15. Plausible reaction mechanism of [Au]/[Ag]-catalyzed *β*-mannosylation

2.6 Synthesis of the trisaccharide of *S. pneumonie*

To demonstrate the applicability of the developed methodology, we targeted a synthesis of trisaccharide motif from the cell wall of *Streptococcus pneumonie* 19F. Streptococcus pneumoniae (SP) is a prevalent human pathogen linked to a wide range of diseases and continues to be a leading cause of morbidity and mortality globally, particularly among children[28].

The trisaccharide present in the *S. pneumonie* 19F variant consisting of ManNAc, glucose and rhamnose residue, has a notable feature of two 1,2-*cis* linkages which makes it very challenging for its synthesis[29]. From the non-reducing end, it has one 1,2-*cis* ManNAc linkage and 1,2-*cis* glucopyranoside linkage (Scheme **2.16**). Nevertheless, the trisaccharide motif was targeted in a convergent synthetic pathway using just developed silver-assisted gold catalyzed mannosylation methodology.



Scheme 2.16. Retrosynthetic synthesis of the target trisaccharide

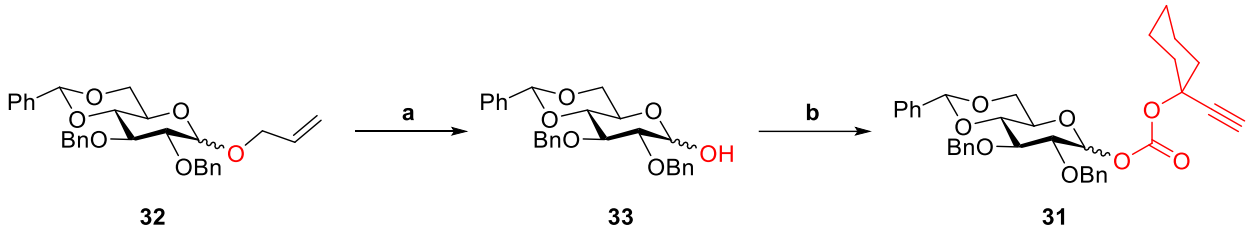
2.6.1. Retrosynthesis

The naturally occurring trisaccharide can be envisaged from the protected trisaccharide **27**. The NHAc containing **27** can be synthesized from the azide containing trisaccharide **28** by reductive acylation. Compound **28** can be envisaged from the 2-azido mannosyl carbonate donor **14f** and

disaccharide acceptor **29**. The Glu*p*-Rha*p* disaccharide **29** can be synthesized from the benzylidene equipped glucoside carbonate donor **31** and the rhamnosyl acceptor **30**.

2.6.2. Synthesis of the glucoside carbonate donor 31

The easily accessible building block **32** was prepared from commercially available D-glucose. The anomeric allyl group of benzylidene **32** was deprotected using $PdCl_2$ and a ternary solvent system of 1,2-DME:CH_2Cl_2:MeOH to successfully yield the hemiacetal **33** in 66 % yield. Subsequently, the C1-OH of compound **33** was masked using carbonate reagent **13h** using CH_2Cl_2/DMAP to successfully furnish the carbonate donor **31** in 91 % yield (Scheme **2.17**).



Scheme 2.17. Synthesis of the carbonate donor **31**. Reagents: a) $PdCl_2$, 1,2-DME: CH_2Cl_2: MeOH (3:1:1), 0-25 °C, 4 h, 66 %; b) 1- ethynylcyclohexyl (4-nitrophenyl) carbonate (**13h**), CH_2Cl_2, DMAP, 0-25 ºC, 8 h, 91 %.

2.6.3. Synthesis of the trisaccharide 27

Literature reported rhamnosyl acceptor **30**[30] was prepared from the commercially available L-rhamnose. The donor **31** and acceptor **30** were glycosylated at -50 °C under [Au]/[Ag]-catalyzed glycosylation conditions to successfully obtain the disaccharide **34** in 86 % yield. The 2D-NMR studies of thus formed disaccharide **34** clearly showed the glucoside anomeric $J_{C1\text{-}H1}$ value of 176 Hz in coupled HSQC experiment, which proved that thus formed disaccharide **34** features the pure 1,2-*cis* linkage. The benzylidene group of **34** was reductively cleaved using $NaCNBH_3/I_2$ mediated to furnish the disaccharide acceptor **29** in 76 % yield (Scheme **2.18**).

Subsequently, the disaccharide acceptor **29** and the mannosyl carbonate **14f** prepared *vide supra* were glycosylated using the optimized glycosylation condition of 0 ºC/10 mM to successfully synthesize the trisaccharide **28** in 92 % yield with *β*-selectivity of 1:3 which could be separated easily by silica gel column chromatography. The structural integrity of the formed trisaccharide was confirmed by MALDI-ToF and NMR studies. In the ^{13}C NMR of compound **28**, three peaks

of 100.0, 97.4 and 96.7 ppm in the anomeric region confirmed the formation of the desired trisaccharide. Besides, in the HRMS (ESI-TOF) studies, the observed mass for $C_{73}H_{85}N_3O_{15}SiNa$: 1294.5646 was in good agreement with the calculated m/z: 1294.5647. In the ^{1}H-^{13}C Coupled HSQC NMR of compound **34**, the $J_{C1\text{-}H1}$ value of 163 Hz strongly supported the formation of *β*-mannosidic linkage in the major product.

To transform the azide to amine group, several reduction strategies were deployed including the most popular Zn/AcOH mediated condition. But none of these worked smoothly in our case. Ultimately, the azide of **28** was successfully reduced by utilizing 1,3-propanedithiol under pyridine:H_2O solvent system to generate the corresponding NH_2 derivative which was readily blocked using Ac_2O/pyridine to successfully provide the desired trisaccharide **27** in 89 % yield over two steps (Scheme **2.18**). The structural integrity was confirmed by the HRMS (ESI-ToF) and NMR studies (Table **2.5**). In the ^{13}C NMR of compound **27**, the three anomeric peaks of 100.0, 97.5 and 96.9 ppm confirmed the identity of the trisaccharide, while the carbonyl peak at 170.1 ppm confirmed the presence of NHAc motif in the trisaccharide **27**. Further, in the HRMS spectra of compound **27**, the observed mass of *m/z* 1310.5875 closely aligned with the calculated *m/z* for $C_{75}H_{89}NO_{16}SiNa$: 1310.5848.

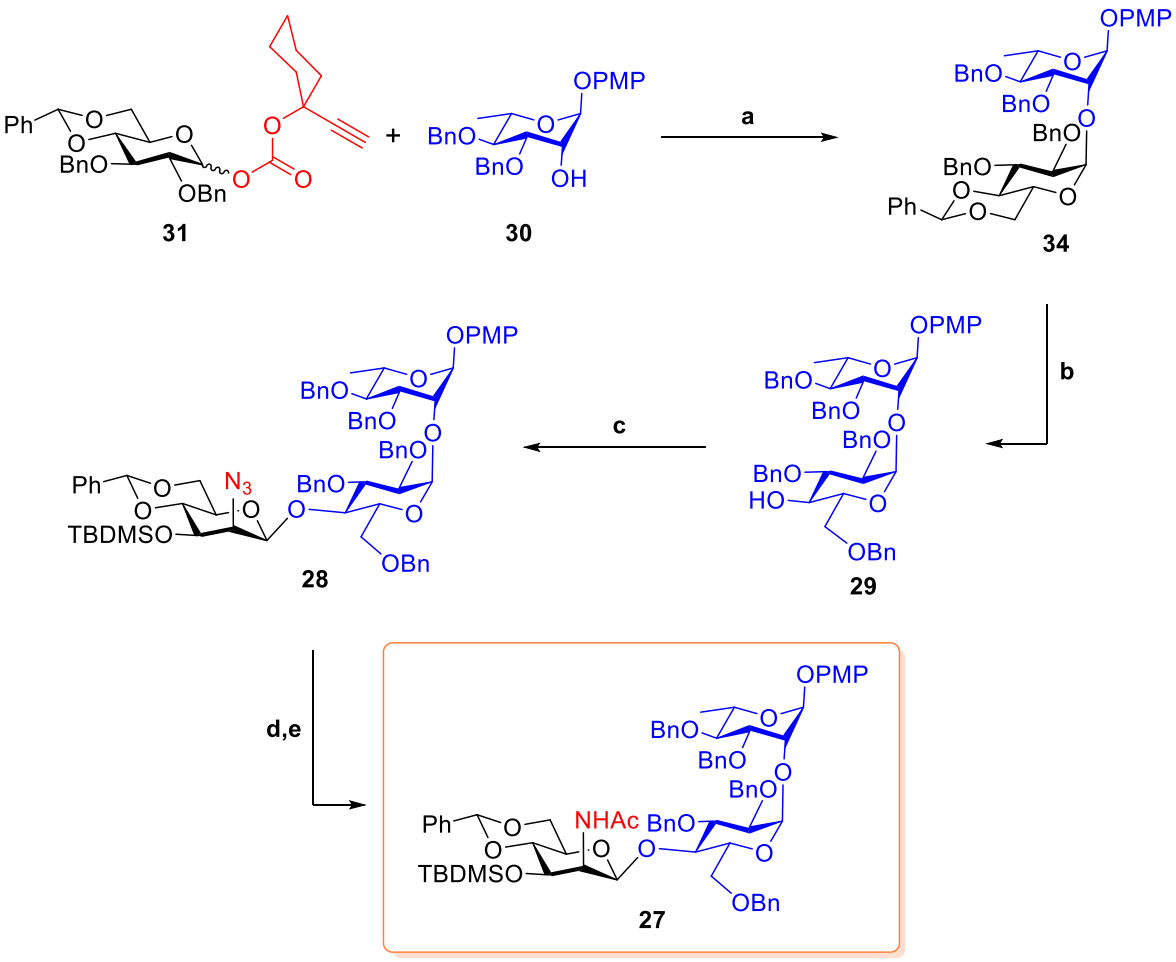
Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
Anomeric	5.37 (d, *J* = 1.9 Hz, 1H), 4.87 (d, *J* = 11.6 Hz, 1H), 4.52 (s, 1H)	100.0, 97.5 and 96.9
PMP	6.94 – 6.89 (m, 2H), 6.83 – 6.78 (m, 2H)	155.0, 150.5, 117.8, 117.8, 114.7, 114.7
TBDMS	0.85 (s, 9H)	25.7, 25.7, 25.7, 18.2, -4.8, -4.8
NHAc	1.79 (s, 3H)	170.1, 23.4

Table 2.5. NMR characterization of trisaccharide **27**

2.7. Summary

In summary, the present study shows the novelty of the silver assisted gold catalyzed activation of ethynyl cyclohexyl mannosyl carbonate donors towards the synthesis of *β*-mannosamine glycosides. The C2-azido group in the donor serves perfectly as a non-participating group as well as a precursor to the amine functionality. The utility of this methodology was successfully demonstrated by synthesizing a library of 2-azido-2-*deoxy*-*β*-D-mannosides using variety of acceptors. The high *β*-mannoselectivity is dependent on temperature and concentration of the

reaction; the VT-NMR studies successfully demonstrated the mechanism and the presence of highly reactive covalent *α*-triflate intermediate. The versatility of the methodology was successfully demonstrated by the synthesis of a protected capsular trisaccharide motif of *Streptococcus pneumoniae type* 19F. Further applications of this methodology for the synthesis of more complex *β*-ManNAc oligosaccharides is currently underway.



Scheme 2.18. Synthesis of the protected trisaccharide **27**. Reagents: a) chloro[2,4-di-*tert*-butylphenyl)phosphite]gold (**17**), AgOTf, CH_2Cl_2, 4Å MS powder, -50 ºC, 1 h, 86%; b) $NaCNBH_3$, I_2, ACN, 25 ºC, 1.5 h, 76 %; c) chloro[2,4-di-*tert*-butylphenyl)phosphite]gold (**17**), AgOTf, CH_2Cl_2, 4Å MS powder, 0 ºC, 10 mM, 1 h, 92 % (α:β=1:3), only β was isolated; d) 1,3-propanedithiol, pyridine:H_2O (5:1), 25 ºC , 8 h; e) Ac_2O, pyridine, 25 ºC, 2 h, 89 % over two steps.

2.8. General experimental procedures

Method A: General Procedure for the [Au]/[Ag]-catalyzed Glycosidation at 25 ºC

To a solution of glycosyl carbonate donor (0.1 mmol) and acceptor (0.1 mmol) in anhydrous CH_2Cl_2 (2 mL for 50 mM and 10 ml for 10 mM) freshly activated 4Å MS powder (30 mg/mL) was added and stirred for 20 min under nitrogen atmosphere. AgOTf (10 mol%) and Au-phosphite (**17**) (10 mol%) were added to the solution and stirred for 30mins at 25 ºC. After the completion the reaction was quenched by Et_3N and the reaction mixture was filtered through a bed of Celite. The filtrate was concentrated in vacuo, and resulting residue was purified by column chromatography (ethyl acetate/hexane as mobile phase) to afford the corresponding disaccharides.

α:β ratios were determined by comparison of the integral intensities of the relevant signals in ^1H NMR spectra.

Method B : General Procedure for the [Au]/[Ag]-catalyzed Glycosidation at 0 ºC

To a solution of glycosyl carbonate donor (0.1 mmol) and acceptor (0.1 mmol) in anhydrous CH_2Cl_2 (2 mL for 50 mM and 10 ml for 10 mM) freshly activated 4Å MS powder (30 mg/mL) was added and stirred for 20 min under nitrogen atmosphere. The solution was then cooled to 0 ºC, AgOTf (10 mol%) and Au-phosphite (**17**) (10 mol%) were added to the solution and stirred for 1hour at 0 ºC. After the completion the reaction was quenched by Et_3N and the reaction mixture was filtered through a bed of Celite. The filtrate was concentrated in vacuo, and resulting residue was purified by column chromatography (ethyl acetate/hexane as mobile phase) to afford the corresponding disaccharides.

Method C: General Procedure for the [Au]/[Ag]-catalyzed Glycosidation at -25 ºC

To a solution of glycosyl carbonate donor (0.1 mmol) and acceptor (0.1 mmol) in anhydrous CH_2Cl_2 (2 mL for 50 mM and 10 ml for 10 mM) freshly activated 4Å MS powder (30 mg/mL) was added and stirred for 20 min under nitrogen atmosphere. The solution was then cooled to -25 ºC, AgOTf (10 mol%) and Au-phosphite (**17**) (10 mol%) were added to the solution and stirred for 2 hours at -25 ºC. After the completion the reaction was quenched by Et_3N and the reaction mixture was filtered through a bed of Celite. The filtrate was concentrated in vacuo, and resulting residue was purified by column chromatography (ethyl acetate/hexane as mobile phase) to afford the corresponding disaccharides.

Procedure D: General procedure for the synthesis of hemiacetals from ethyl thioglycosides

To a vigorously stirred suspension of ethyl thioglycoside (1 mmol) and calcium carbonate (5 mmol) in acetone/water (9:1) was added N-bromosuccinimide (2 mmol). After the disappearance of the starting material (15mins) the suspension was filtered and treated with satd. aq. $NaHCO_3$ solution and washed with ethyl acetate. The oraganic layer was concentrated in vacuo and purified by silica gel column chromatography (ethyl acetate/hexane as mobile phase) to obtain the corresponding hemiacetals.

Procedure E: Synthesis of Ethynylcyclohexyl Glycosyl Carbonate Donors

To a solution of corresponding hemiacetal (1.0 mmol) in anhydrous CH_2Cl_2 (10 mL/1 g of hemiacetal), ethynylcyclohexyl (4-nitrophenyl) carbonate (1.2 mmol) and DMAP (1.1 mmol) were added and the reaction mixture was stirred at 25 °C for 3 h. After complete consumption of the starting hemiacetal, the reaction mixture was concentrated in vacuo and purified by silica gel column chromatography (ethyl acetate/hexane as mobile phase) to obtain the ethynylcyclohexyl glycosyl carbonate donors.

2.9. Characterization data

Ethyl 2-azido-4,6-*O*-benzylidene-2-*deoxy*-3-*O*-*p*-methoxybenzyl-1-thio-α-D mannopyranoside (12c): Compound **11** (*Org. Biomol. Chem.* **2020**, *18*, 6682-6695) (1 g, 2.96 mmol) was dissolved in anhydrous DMF (5 ml) and cooled to 0 ºC. NaH (60% oil dispersion, 142.25 mg, 3.56 mmol) was added and stirred for 10 minutes at 0 ºC. *p*-methoxybenzyl chloride (482.26 µL, 3.56 mmol) was added dropwise and stirred for 2 h at 25 ºC. After the completion the reaction mixture was poured into cold water with vigorous shaking, extracted with ethyl acetate (3x25 mL) and combined organic layers was washed with cold water (2x25 mL), brine solution (3x25 mL), and dried over Na_2SO_4. The organic layer was then evaporated in vacuo and purified by column chromatography (ethyl acetate/hexanes) to obtain compound **12c** (1.15 g, 85 % yield). $[\alpha]_D^{25}$ = +48.7 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2927, 2102, 1512, 1374, 1247,1091, 908, 821; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (dd, *J* = 7.6, 2.1 Hz, 2H), 7.43 – 7.36 (m, 3H), 7.33 – 7.28 (m, 2H), 6.90 – 6.86 (m, 2H), 5.63 (s, 1H), 5.24 (d, *J* = 1.2 Hz, 1H), 4.81 (d, *J* = 11.7 Hz, 1H), 4.65 (d, *J* = 11.7 Hz, 1H), 4.26 – 4.19 (m, 2H), 4.15 – 4.09 (m, 1H), 4.09 – 4.04 (m, 1H), 3.99 (dd, *J* = 3.5, 1.2 Hz, 1H), 3.86 (t, *J* = 11.5 Hz, 1H), 3.81 (s, 3H), 2.71 – 2.53 (m, 2H), 1.31 – 1.27 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.5, 137.5, 129.9, 129.5, 129.5, 129.1, 128.3, 128.3, 126.2, 126.2, 114.0, 114.0, 101.7, 83.6, 79.3, 75.6, 73.1, 68.6, 64.5, 64.2, 55.3, 25.5, 14.9; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{27}N_3O_5SNa$ 480.1568; Found: 480.1566.

Ethyl 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-*deoxy*-1-thio-α-D-mannopyranoside (12d): Compound **11** (1 g, 2.96 mmol) was dissolved in anhydrous DMF (5 ml) and cooled to 0 ºC. NaH (60% oil dispersion, 142.25 mg, 3.56 mmol) was added and stirred for 10 minutes at 0 ºC. Benzyl bromide (422.45 µL, 3.56 mmol) was added dropwise and stirred for 2 h at 25 ºC. After the completion the reaction mixture was poured into cold water with vigorous shaking, extracted with ethyl acetate (3x25 mL) and combined organic layers was washed with cold water (2x25 mL), brine solution (3x25 mL), and dried over Na_2SO_4. The organic layer was then evaporated in vacuo and purified by column chromatography (ethyl acetate/hexane as mobile phase) to obtain compound **12d** (1.10 g, 87 % yield). $[\alpha]_D^{25}$ = +65.7 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3045, 2969, 2870 , 2102, 1455, 1375; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (dq, *J* = 6.8, 2.5 Hz, 2H), 7.39 – 7.28 (m, 8H), 5.61 (s, 1H), 5.23 (d, *J* = 1.1 Hz, 1H), 4.88 (d, *J* = 12.0 Hz, 1H), 4.70 (d, *J* = 12.1 Hz, 1H), 4.24 – 4.17 (m, 2H), 4.13 (t, *J* = 9.0 Hz, 1H), 4.07 (dd, *J* = 9.4, 3.6 Hz, 1H), 4.01 (dd, *J* = 3.6, 1.3 Hz, 1H), 3.85 (t, *J* = 11.5 Hz, 1H), 2.69 – 2.51 (m, 2H), 1.27 (t, *J* = 7.4 Hz, 3H); ^{13}C

NMR (101 MHz, $CDCl_3$): δ 137.9, 137.5, 129.1, 128.6, 128.6, 128.4, 128.4, 128.0, 127.8, 127.8, 126.2, 126.2, 101.7, 83.6, 79.4, 76.0, 73.5, 68.6, 64.5, 64.3, 25.5, 15.0; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{25}N_3O_4SNa$ 450.1463; Found: 450.1462.

Ethyl 2-azido-4,6-*O*-benzylidene-3-*O*-(naphthalen-1-yl methyl)-2-*deoxy*-1-thio-α-D-mannopyranoside (12e): To a solution of compound **11** (1 g, 2.96 mmol) in anhydrous DMF (5 mL) was cooled to 0 °C under nitrogen atmosphere and NaH (60% oil dispersion, 154.11 mg, 3.85 mmol) was added and stirred for 10 minutes at 0 ºC, 2-bromomethyl naphthalene (786.37 mg, 3.56 mmol) was added and stirred for 2 h at 25 ºC. After the completion of the reaction it was quenched by ice cold water, extracted with ethyl acetate (3x25 mL) and combined oraganic layers was washed with cold water (2x25 mL), brine solution (2x 25 mL), and dried over Na_2SO_4. The organic layer was evaporated in vacuo and purified by column chromatography (ethyl acetate/hexanes as mobile phase) to obtain compound **12e** as a sticky gum (1.19 g, 84 %). $[\alpha]_D^{25}$ = +52.4 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2925, 2101, 1374, 1265, 1091, 856; ^1H NMR (400 MHz, $CDCl_3$): δ 7.84 (m, 3H), 7.75 (m, 1H), 7.56 – 7.52 (m, 2H), 7.48 (m, 3H), 7.44 – 7.39 (m, 3H), 5.67 (s, 1H), 5.27 (d, *J* = 1.3 Hz, 1H), 5.04 (d, *J* = 12.4 Hz, 1H), 4.90 (d, *J* = 12.4 Hz, 1H), 4.28 – 4.19 (m, 3H), 4.18 – 4.14 (m, 1H), 4.10 (dd, *J* = 3.4, 1.3 Hz, 1H), 3.93 – 3.85 (m, 1H), 2.70 – 2.52 (m, 2H), 1.28 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.5, 135.4, 133.4, 133.1, 129.1, 128.4, 128.4, 128.3, 128.1, 127.8, 126.4, 126.2, 126.2, 126.2, 126.0, 125.6, 101.8, 83.6, 79.4, 76.1, 73.4, 68.6, 64.5, 64.3, 25.5, 14.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{26}H_{28}N_3O_4S$ 478.1800 ; Found: 478.1801.

Ethyl 2-azido-4,6-*O*-benzylidene-3-*O*-(*tert*-butyldimethylsilyl)-2-*deoxy*-1-thio-α-D-mannopyranoside (12f): To a solution of alcohol **11** (1 g, 2.96 mmol) in anhydrous CH_2Cl_2 (5 mL) was added 2,6-lutidine (1.72 mL, 14.82 mmol) and cooled to 0 °C. TBDMSOTf (816.81 µL, 3.56 mmol) was added dropwise at 0 °C under nitrogen atmosphere and the resulting reaction mixture was stirred at 25 °C for 1 h. After completion, ice-cold water (10 mL) was added and extracted with CH_2Cl_2 (2 x 25 mL). The combined organic phases were washed with brine (2 x 25 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo, crude residue was purified by silica gel column chromatography using ethyl acetate in n-hexane as a mobile phase to obtain compound **12f** (1.22 g, 91 % yield). $[\alpha]_D^{25}$ = +62.6 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2929, 2857, 2103, 1461, 1257, 1095, 843; ^1H NMR (400 MHz, $CDCl_3$): δ 7.51 – 7.47 (m, 2H), 7.36 (dd, *J* = 5.1, 2.1 Hz, 3H), 5.58 (s, 1H), 5.23 (d, *J* = 1.2 Hz, 1H), 4.28 (dd, *J* = 9.5, 3.8 Hz, 1H), 4.22 – 4.15 (m, 2H),

3.97 – 3.92 (m, 2H), 3.87 – 3.80 (m, 1H), 2.72 – 2.56 (m, 2H), 1.30 (t, *J* = 7.4 Hz, 3H), 0.89 (s, 9H), 0.11 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.4, 129.1, 128.2, 128.2, 126.3, 126.3, 102.1, 83.7, 79.5, 70.9, 68.6, 66.7, 64.6, 25.9, 25.9, 25.9, 25.6, 18.4, 15.0, -4.4, -4.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{33}N_3O_4SSiNa$ 474.1858 ; Found: 474.1852.

Ethyl 2-azido-3-*O*-(*tert*-butyldiphenylsilyl)-4,6-*O*-benzylidene-2-*deoxy*-1-thio-α-D-mannopyranoside (12g): Compound **11** (500mg, 1.48 mmol) was dissolved in anhydrous DMF (4 ml). Imidazole (302.67 mg, 4.45 mmol), DMAP (90.53 mg, 740.97 µmol) were added to the solution followed by dropwise addition of TBDPSCl (499.56 µL, 1.93 mmol). The reaction mixture was heated on a heating mantle and stirred at 60 °C for 2 h. After completion the reaction mixture was extracted with ethyl acetate (3x25 mL). The combined organic layer was washed with cold water (2x25 mL) and brine solution (2x25mL). Organic layer was dried over anhydrous Na_2SO_4, the organic layer was concentrated in vacuo and the residue was purified by silica gel column chromatography (ethyl acetate/hexanes) to furnish compound **12g** (600 mg, 70% yield). $[\alpha]_D^{25}$ = +53.6 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2937, 2861, 2109, 1379, 1095, 847 ; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 – 7.64 (m, 4H), 7.47 – 7.29 (m, 8H), 7.27 (d, *J* = 2.0 Hz, 2H), 7.24 (s, 1H), 5.45 (s, 1H), 5.15 (s, 1H), 4.38 – 4.31 (m, 1H), 4.14 (dd, *J* = 10.1, 3.6 Hz, 1H), 4.07 – 3.99 (m, 2H), 3.79 (t, *J* = 9.7 Hz, 1H), 3.56 (dt, *J* = 3.6, 1.5 Hz, 1H), 2.61 – 2.44 (m, 2H), 1.22 (t, *J* = 7.4 Hz, 3H), 1.07 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.4, 136.1, 136.1, 136.1, 136.1, 133.2, 133.2, 130.1, 129.7, 128.9, 128.1, 128.1, 128.0, 128.0, 127.5, 127.5, 126.4, 126.4, 102.1, 83.7, 79.2, 70.8, 68.5, 66.2, 64.6, 27.0, 27.0, 27.0, 25.5, 19.3, 14.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{31}H_{38}N_3O_4SSi$ 576.2352 ; Found: 576.2357.

2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-*deoxy*-D-mannopyranose (13a) {α:β = 1:1.7}: Compound **13a** was prepared according to the general procedure **D** (*Org. Biomol. Chem.* **2020**, *18*, 6682-6695); pale yellow sticky gum (291 mg, 81%); $[\alpha]_D^{25}$ = +6.7 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2934, 2863, 1725, 1236, 1090, 908; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (dt, *J* = 8.6, 1.5 Hz, 2H), 7.63 – 7.56 (m, 1H), 7.51 – 7.42 (m, 4H), 7.38 – 7.29 (m, 3H), 5.86 – 5.80 (m, 1H), 5.62 (s, 1H), 5.19 (t, *J* = 2.1 Hz, 1H), 4.40 – 4.28 (m, 1H), 4.28 – 4.22 (m, 2H), 4.17 (t, *J* = 9.8 Hz, 1H), 3.93 – 3.51 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.9, 165.9, 137.1, 136.9, 133.8, 133.6, 130.1, 130.1, 130.1, 130.1, 129.3, 129.2, 129.2, 128.9, 128.7, 128.7, 128.6, 128.6, 128.4, 128.4, 128.3, 128.3, 126.2, 126.2, 126.2, 126.2, 102.0, 101.9, 93.8, 93.5, 76.6, 75.6, 72.2, 70.3, 68.8, 68.4,

67.4, 64.5, 64.0, 62.9.; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{20}N_3O_6$ 398.1352; Found: 398.1356.

2-azido-4,6-*O*-benzylidene-3-*O*-picoloyl -2-*deoxy*-D-mannopyranose (13b) {α:β = 2.4:1}: Compound **13b** was prepared according to the general procedure **D** (214 mg, 79 % yield); pale yellow sticky foam; $[\alpha]_D^{25}$ = +10.3 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2925, 2855, 2105, 1729, 1306, 1288, 1092, 916; ^1H NMR (400 MHz, $CDCl_3$): δ 8.79 – 8.74 (m, 1H), 8.18 (m, 1H), 7.84 (td, *J* = 7.8, 1.8 Hz, 1H), 7.54 – 7.40 (m, 3H), 7.34 – 7.27 (m, 3H), 5.90 (dd, *J* = 9.7, 3.9 Hz, 1H), 5.61 (s, 1H), 5.56 – 5.49 (m, 1H), 5.30 (s, 1H), 4.42 – 4.31 (m, 1H), 4.31 – 4.20 (m, 3H), 3.92 – 3.82 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.0, 163.9, 150.0, 149.9, 146.9, 146.6, 137.6, 137.5, 137.2, 136.9, 129.2, 129.2, 128.3, 128.3, 128.3, 128.3, 127.7, 127.5, 126.3, 126.3, 126.2, 126.2, 125.9, 125.8, 102.0, 101.9, 94.0, 93.7, 76.4, 75.4, 73.0, 71.4, 68.9, 68.5, 67.3, 64.1, 63.9, 63.0.; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{19}N_4O_6$ 399.1304; Found: 399.1301.

2-azido-4,6-*O*-benzylidene-2-*deoxy*-3-*O*-*p*-methoxybenzyl-D-mannopyranose (13c) {α:β = 1:1.4}: Compound **13c** was prepared from **12c** (1.0 g, 2.19 mmol) according to procedure **D** (715 mg, 79 %); pale yellow sticky syrup; $[\alpha]_D^{25}$ = +9.0 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3407, 2925, 2108, 1511, 1241,1091, 1029, 825; ^1H NMR (400 MHz, $CDCl_3$): δ 7.51 – 7.46 (m, 2H), 7.41 – 7.35 (m, 3H), 7.32 – 7.27 (m, 2H), 6.90 – 6.84 (m, 2H), 5.60 (d, *J* = 8.2 Hz, 1H), 5.09 (s, 1H), 4.81 (t, *J* = 12.3 Hz, 1H), 4.67 (dd, *J* = 11.7, 7.4 Hz, 1H), 4.33 – 4.18 (m, 1H), 4.15 (dd, *J* = 9.5, 3.6 Hz, 1H), 4.08 (t, *J* = 9.3 Hz, 1H), 4.01 (td, *J* = 9.6, 5.1 Hz, 1H), 3.94 (ddq, *J* = 9.9, 3.4, 1.7 Hz, 1H), 3.81 – 3.77 (m, 4H), 3.33 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.5, 159.4, 137.5, 137.3, 130.1, 129.7, 129.5, 129.5, 129.4, 129.4, 129.2, 129.1, 128.4, 128.4, 128.3, 128.3, 126.2, 126.2, 126.1, 126.1, 114.0, 114.0, 113.9, 113.9, 101.7, 101.6, 94.0, 93.3, 79.1, 78.5, 77.1, 74.9, 73.1, 73.0, 68.8, 68.5, 67.2, 65.0, 64.0, 63.0, 55.4, 55.4; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{23}N_3O_6Na$ 436.1484; Found: 436.1486.

2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-*deoxy*-D-mannopyranose (13d) {α:β = 1:1.4}: Compound **13d** was prepared from compound **12d** (1g, 2.34 mmol) according to the general procedure **D** (702 mg, 78 %): pale yellow sticky syrup; $[\alpha]_D^{25}$ = +8.4 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3413, 2872, 2107, 1378, 1274, 1091, 911; ^1H NMR (400 MHz, $CDCl_3$): δ 7.50 (dt, *J* = 6.9, 2.1 Hz, 2H), 7.43 – 7.29 (m, 8H), 5.62 (d, *J* = 9.1 Hz, 1H), 5.12 (dd, *J* = 3.6, 1.5 Hz, 1H), 4.92 (t, *J* = 11.7 Hz, 1H), 4.79 – 4.73 (m, 1H), 4.26 – 4.09 (m, 2H), 4.07 – 3.98 (m, 2H), 3.88 – 3.70 (m, 2H), 3.09 (t, *J* = 2.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.1, 137.7, 137.4, 137.3,

129.2, 129.1, 128.7, 128.7, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.1, 127.9, 127.8, 127.8, 127.7, 127.7, 126.2, 126.2, 126.1, 126.1, 101.8, 101.7, 94.1, 93.3, 79.3, 78.6, 77.5, 75.3, 73.4, 73.4, 68.8, 68.5, 67.1, 65.0, 64.0, 63.0; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{21}N_3O_5Na$ 406.1378; Found: 406.1388.

2-azido-4,6-*O*-benzylidene-3-*O*-(naphthalen-1-yl methyl)-2-*deoxy*-D-mannopyranose (13e) {α:β = 1:1.6}: The title compound was prepared from **12e** (1.0 g, 2.09 mmol) according to procedure **D** (690 mg, 76 %); pale yellow gum; $[\alpha]_D^{25}$ = +4.7 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3437, 2926, 2109, 1699, 1269, 1090, 903; ^1H NMR (400 MHz, $CDCl_3$): δ 7.84 (qd, *J* = 6.6, 5.7, 3.0 Hz, 3H), 7.79 – 7.73 (m, 1H), 7.55 – 7.46 (m, 5H), 7.45 – 7.38 (m, 3H), 5.64 (s, 1H), 5.11 – 5.07 (m, 1H), 5.03 (s, 1H), 4.91 (dd, *J* = 12.5, 6.9 Hz, 1H), 4.24 (m, 1H), 4.20 – 4.09 (m, 1H), 4.08 – 3.98 (m, 2H), 3.92 – 3.72 (m, 2H), 3.34 (dt, *J* = 9.5, 4.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.4, 137.3, 135.5, 135.1, 133.3, 133.3, 133.2, 133.1, 129.2, 129.2, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.1, 128.0, 127.8, 127.8, 126.6, 126.4, 126.4, 126.2, 126.2, 126.2, 126.2, 126.2, 126.2, 126.0, 125.6, 125.6, 101.8, 101.7, 94.0, 93.3, 79.2, 78.5, 77.3, 75.3, 73.2, 73.2, 68.8, 68.4, 67.1, 65.0, 63.9, 63.0; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{24}H_{23}N_3O_5Na$ 456.1535; Found: 456.1539.

2-azido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-*deoxy*-D-mannopyranose (13f) {α:β = 1:1.4}: Compound **13f** was prepared from **12f** (1.0 g, 2.21 mmol) according to procedure **D** (760 mg, 84 %); colorless sticky gum; $[\alpha]_D^{25}$ = +10.2 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3433, 2936, 2110, 1380, 1260, 1095, 846; ^1H NMR (400 MHz, $CDCl_3$): δ 7.48 (m, 2H), 7.40 – 7.33 (m, 3H), 5.56 (s, 1H), 5.14 (d, *J* = 1.6 Hz, 1H), 4.42 – 4.28 (m, 1H), 4.23 – 4.06 (m, 1H), 4.04 – 3.95 (m, 1H), 3.95 – 3.89 (m, 1H), 3.89 – 3.76 (m, 2H), 3.09 (s, 1H), 0.90 (s, 9H), 0.12 (d, *J* = 2.3 Hz, 3H), 0.07 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.4, 137.2, 129.2, 129.1, 128.3, 128.3, 128.3, 128.3, 126.3, 126.3, 126.3, 126.3, 102.2, 102.1, 94.2, 93.2, 79.4, 78.6, 73.0, 70.0, 68.8, 68.5, 67.5, 67.2, 65.4, 64.1, 25.9, 25.9, 25.9, 25.8, 25.8, 25.8, 18.4, 18.3, -4.3, -4.4, -4.7, -4.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{30}N_3O_5Si$ 408.1954; Found: 408.1950.

2-azido-4,6-*O*-benzylidene-3-*O*-*tert*-butyldiphenylsilyl-2-*deoxy*-D-mannopyranose (13g) {α:β = 1:1.1}: Compound **13g** was prepared from **12g** (500mg, 0.87 mmol) according to procedure **D** (356mg, 77 %); light brown sticky gum; $[\alpha]_D^{25}$ = +12.7 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2938, 2861,2111, 1436, 1093, 1024, 846 ; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.61 (m, 4H), 7.46 – 7.37 (m, 2H), 7.35 – 7.26 (m, 7H), 7.15 (ddt, J = 20.8, 6.9, 1.6 Hz, 2H), 5.38 (d, J = 12.1 Hz, 1H), 5.04 (dd, J = 3.6, 1.7 Hz, 1H), 4.44 (dd, J = 9.5, 3.8 Hz, 1H), 4.10 (ddd, J = 21.5, 9.7, 4.1 Hz, 1H),

3.96 (dt, J = 33.3, 9.4 Hz, 1H), 3.88 – 3.74 (m, 1H), 3.74 – 3.68 (m, 1H), 3.65 – 3.59 (m, 1H), 2.83 (d, J = 3.6 Hz, 1H), 1.07 (d, J = 1.6 Hz, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.3, 137.0, 136.3, 136.3, 136.3, 136.3, 136.1, 136.1, 136.0, 136.0, 133.5, 133.2, 133.2, 132.7, 130.2, 130.0, 129.8, 129.6, 129.0, 128.9, 128.1, 128.1, 128.1, 128.1, 127.9, 127.9, 127.8, 127.8, 127.5, 127.5, 127.4, 127.4, 126.4, 126.4, 126.4, 126.4, 102.1, 102.0, 94.2, 93.2, 79.1, 78.3, 73.0, 70.0, 68.7, 68.3, 67.1, 67.1, 64.9, 64.1, 27.0, 27.0, 27.0, 27.0, 27.0, 27.0, 19.3, 19.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{34}N_3O_5Si$ 532.2268; Found: 532.2274.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)- 2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-*deoxy*--D-mannopyranose (14a) {α:β = 1:1.1}: Compound **14a** was prepared from compound **13a** (250 mg, 0.6 mmol) according to the procedure **E**; (306 mg, 89 %); pale yellow sticky syrup; $[\alpha]_D^{25}$ = +25.6 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3293, 2934, 2110, 1762, 1726, 1237, 1089, 844; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (m, 2H), 7.63 – 7.56 (m, 1H), 7.50 – 7.40 (m, 4H), 7.33 (dt, *J* = 4.6, 2.9 Hz, 3H), 6.04 (d, *J* = 1.7 Hz, 1H), 5.88 – 5.79 (m, 1H), 5.61 (d, *J* = 5.6 Hz, 1H), 4.48 – 4.39 (m, 1H), 4.38 – 4.32 (m, 1H), 4.31 – 4.18 (m, 1H), 4.18 – 4.10 (m, 1H), 3.94 – 3.83 (m, 1H), 2.70 (dd, *J* = 3.0, 1.1 Hz, 1H), 2.29 – 2.13 (m, 2H), 1.98 – 1.86 (m, 2H), 1.77 – 1.50 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.7, 165.7, 150.5, 150.5, 137.0, 136.8, 133.8, 133.7, 130.2, 130.1, 130.1, 130.1, 129.3, 129.2, 129.0, 129.0, 128.6, 128.6, 128.6, 128.6, 128.4, 128.4, 128.3, 128.3, 126.2, 126.2, 126.2, 126.2, 102.0, 102.0, 95.0, 94.2, 82.4, 82.3, 79.4, 79.2, 75.8, 75.7, 75.7, 75.3, 71.6, 70.0, 68.5, 68.3, 68.3, 66.2, 62.1, 61.5, 37.0, 36.9, 36.7, 36.6, 25.0, 24.9, 22.6, 22.6, 22.6, 22.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{30}N_3O_8$ 548.2033; Found: 548.2040.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)- 2-azido-3-*O*-picoloyl-4,6-*O*-benzylidene-2-deoxy-D-mannopyranose (14b) {α:β = 1:1.7}: Compound **14b** was prepared from compound **13b** (200 mg, 0.5 mmol) according to the procedure **E** (251 mg, 91 %); pale yellow sticky gum; $[\alpha]_D^{25}$ = +4.7 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2939, 2110, 1757, 1728, 1235, 1095, 901; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.80 – 8.74 (m, 1H), 8.17 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.85 (td, *J* = 7.7, 1.7 Hz, 1H), 7.53 – 7.46 (m, 1H), 7.40 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.30 (tt, *J* = 3.0, 1.7 Hz, 3H), 6.03 (d, *J* = 1.6 Hz, 1H), 5.87 – 5.82 (m, 1H), 5.56 (d, *J* = 4.6 Hz, 1H), 4.42 – 4.35 (m, 1H), 4.35 – 4.22 (m, 2H), 4.13 (td, *J* = 9.9, 4.8 Hz, 1H), 3.91 – 3.79 (m, 1H), 2.69 (d, *J* = 4.8 Hz, 1H), 2.26 – 2.11 (m, 2H), 1.97 – 1.85 (m, 2H), 1.74 – 1.51 (m, 5H), 1.41 – 1.30 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.0, 163.9, 150.4, 150.4, 150.2, 150.1, 146.8, 146.7, 137.3, 137.3, 136.8, 136.7, 129.3, 129.2, 128.3, 128.3, 128.3, 128.3, 127.6, 127.5, 126.2, 126.2, 126.2, 126.2, 125.9, 125.8, 102.1, 102.0, 95.0, 94.2, 82.3, 82.2, 79.4, 79.3, 77.4, 75.7, 75.7, 75.5, 75.0, 72.3, 70.8, 68.4, 68.2, 66.2, 61.8,

61.2, 36.9, 36.8, 36.7, 36.6, 24.9, 24.9, 22.6, 22.6, 22.5, 22.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{28}H_{29}N_4O_8$ 549.1985; Found: 549.1987.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)- 2-azido-4,6-*O*-benzylidene-2-*deoxy*-3-*O*-*p*-methoxybenzyl-D-mannopyranose (14c) {α:β = 1:1.5}: Compound **14c** was prepared from **13c** (700 mg, 1.69 mmol) according to procedure **E** (860 mg, 90 %); pale yellow sticky gum; $[\alpha]_D^{25}$ = +11.7 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3288, 2936, 21110, 1761, 1512, 1238, 1091, 909 ; ^1H NMR (400 MHz, $CDCl_3$): δ 7.48 (dt, *J* = 7.6, 1.8 Hz, 2H), 7.41 – 7.35 (m, 3H), 7.31 – 7.26 (m, 2H), 6.90 – 6.83 (m, 2H), 5.90 (d, *J* = 1.6 Hz, 1H), 5.60 (d, *J* = 8.8 Hz, 1H), 4.82 (dd, *J* = 11.7, 6.1 Hz, 1H), 4.67 (d, *J* = 11.7 Hz, 1H), 4.37 – 4.25 (m, 1H), 4.15 (dd, *J* = 5.4, 2.0 Hz, 1H), 4.10 – 3.89 (m, 2H), 3.88 – 3.81 (m, 1H), 3.79 (s, 3H), 2.66 (dd, *J* = 1.7, 0.7 Hz, 1H), 2.25 – 2.10 (m, 2H), 1.95 – 1.83 (m, 2H), 1.73 – 1.49 (m, 6H), 1.39 – 1.29 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.6, 159.5, 150.8, 150.4, 137.3, 137.2, 130.0, 130.0, 129.6, 129.6, 129.3, 129.3, 129.2, 129.1, 128.4, 128.4, 128.3, 128.3, 126.2, 126.1, 126.1, 126.1, 114.1, 114.1, 114.0, 114.0, 101.8, 101.8, 95.5, 94.2, 82.4, 82.4, 79.2, 79.0, 78.5, 78.2, 76.3, 75.6, 75.6, 75.0, 73.3, 73.0, 68.4, 68.3, 68.1, 66.0, 62.6, 61.7, 55.4, 55.4, 37.0, 37.0, 36.6, 36.5, 25.0, 24.9, 22.6, 22.6, 22.5, 22.5; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{30}H_{33}N_3O_8Na$ 586.2165; Found: 586.2164.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)- 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-*deoxy*-D-mannopyranose (14d) {α:β = 1.1:1}: Compound **14d** was prepared from compound **13d** (600 mg, 1.56 mmol) according to the procedure **E** (760 mg, 91 %); pale yellow sticky gum; $[\alpha]_D^{25}$ = +7.2 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2930, 2111, 1762, 1368, 1238, 1090, 910; ^1H NMR (400 MHz, $CDCl_3$): δ 7.49 (dt, *J* = 7.0, 2.2 Hz, 2H), 7.41 – 7.30 (m, 8H), 5.62 (d, *J* = 8.4 Hz, 1H), 5.60 (d, *J* = 1.6 Hz, 1H), 4.92 (dd, *J* = 12.2, 9.8 Hz, 1H), 4.76 (d, *J* = 12.2 Hz, 1H), 4.39 – 4.26 (m, 1H), 4.18 (dd, *J* = 5.3, 1.7 Hz, 1H), 4.08 (dt, *J* = 6.0, 2.2 Hz, 1H), 3.97 – 3.78 (m, 2H), 3.45 (d, *J* = 4.8 Hz, 1H), 2.66 (s, 1H), 2.26 – 2.10 (m, 2H), 1.96 – 1.83 (m, 2H), 1.74 – 1.55 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 150.8, 150.5, 138.0, 137.6, 137.3, 137.2, 129.2, 129.2, 128.7, 128.7, 128.6, 128.6, 128.4, 128.4, 128.4, 128.4, 128.2, 127.9, 127.9, 127.9, 127.6, 127.6, 126.2, 126.2, 126.2, 126.2, 101.8, 101.8, 95.5, 94.3, 82.4, 79.3, 79.1, 78.7, 78.3, 76.8, 76.8, 75.6, 75.6, 75.4, 73.7, 73.4, 68.5, 68.3, 68.1, 66.0, 62.6, 61.8, 37.0, 37.0, 36.7, 36.6, 25.0, 25.0, 22.7, 22.7, 22.6, 22.6; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{29}H_{31}N_3O_7Na$ 556.2059; Found: 556.2070.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)- 2-azido-3-*O*-naphthalen-1-yl methyl-4,6-*O*-benzylidene-2-deoxy-D-mannopyranose (14e) {α:β = 1:1.6}: The title compound was prepared

from **13e** (600 mg, 1.38 mmol) according to procedure **E** (704 mg, 87 %); pale yellow sticky foam; $[\alpha]_D^{25}$ = +8.7 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2936, 2110, 1762, 1237, 1090, 907; ^1H NMR (400 MHz, $CDCl_3$): δ 7.84 (dt, *J* = 8.1, 3.8 Hz, 3H), 7.79 – 7.72 (m, 1H), 7.56 – 7.46 (m, 5H), 7.45 – 7.38 (m, 3H), 5.95 (d, *J* = 1.8 Hz, 1H), 5.65 (d, *J* = 10.0 Hz, 1H), 5.07 (dd, *J* = 12.5, 10.5 Hz, 1H), 4.93 (dd, *J* = 12.5, 1.8 Hz, 1H), 4.40 – 4.28 (m, 1H), 4.24 (d, *J* = 7.4 Hz, 1H), 4.22 – 4.07 (m, 2H), 4.02 – 3.80 (m, 2H), 2.69 – 2.64 (m, 1H), 2.26 – 2.11 (m, 2H), 1.98 – 1.80 (m, 2H), 1.76 – 1.50 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 150.7, 150.4, 137.3, 137.2, 135.4, 135.0, 133.3, 133.3, 133.2, 133.1, 129.2, 129.2, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.1, 128.1, 127.8, 127.8, 126.7, 126.3, 126.3, 126.2, 126.2, 126.2, 126.2, 126.2, 126.0, 125.6, 125.4, 101.8, 101.8, 95.4, 94.2, 82.4, 82.4, 79.2, 79.0, 78.6, 78.2, 76.7, 75.6, 75.6, 75.3, 73.5, 73.2, 68.4, 68.3, 68.1, 66.0, 62.5, 61.8, 37.0, 36.9, 36.6, 36.5, 24.9, 24.9, 22.6, 22.6, 22.5, 22.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{33}H_{34}N_3O_7$ 584.2497; Found: 584.2495.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)- 2-azido-3-*O*- *tert*-butyldimethylsilyl -4,6-*O*-benzylidene-2-*deoxy*-D-mannopyranose (14f) {α:β = 1:3}: Compound **14f** was prepared from **13f** (1.0 g, 2.45 mmol) according to procedure **E** (1.22 g, 89 %); pale yellow sticky gum; $[\alpha]_D^{25}$ = +15.7 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2933, 2859, 2109, 1761, 1236, 1106, 1007, 841; ^1H NMR (400 MHz, $CDCl_3$): δ 7.47 (qd, *J* = 3.6, 1.7 Hz, 2H), 7.39 – 7.32 (m, 3H), 5.91 (d, *J* = 1.6 Hz, 1H), 5.56 (d, *J* = 6.5 Hz, 1H), 4.35 (dt, *J* = 10.5, 5.3 Hz, 1H), 4.26 (dd, *J* = 10.2, 4.4 Hz, 1H), 4.03 – 3.85 (m, 3H), 3.79 (q, *J* = 10.8, 9.9 Hz, 1H), 2.67 (d, *J* = 1.6 Hz, 1H), 2.28 – 2.13 (m, 2H), 1.97 – 1.85 (m, 2H), 1.76 – 1.53 (m, 6H), 0.90 (s, 9H), 0.12 (d, *J* = 2.1 Hz, 3H), 0.07 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 150.9, 150.6, 137.3, 137.2, 129.2, 129.2, 129.2, 128.3, 128.3, 128.3, 126.3, 126.3, 126.3, 126.3, 102.3, 102.2, 95.7, 93.9, 82.5, 82.4, 79.2, 79.1, 78.8, 78.4, 75.6, 75.6, 72.6, 70.1, 68.5, 68.3, 68.2, 66.1, 65.0, 64.0, 37.1, 37.1, 36.6, 36.6, 25.9, 25.9, 25.9, 25.8, 25.8, 25.8, 25.0, 25.0, 22.7, 22.7, 22.6, 22.6, 18.4, 18.3, -4.3, -4.3, -4.7, -4.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{28}H_{40}N_3O_7Si$ 558.2635; Found: 558.2635.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)- 2-azido-3-*O*- *tert*-butyldiphenylsilyl -4,6-*O*-benzylidene-2-*deoxy*-D-mannopyranose (14g) {α:β = 1:1.2}: Compound **14g** was prepared from **13g** (400 mg, 0.75 mmol) according to procedure **E** (450 mg, 88 %); pale yellow thick syrup; $[\alpha]_D^{25}$ = +9.3 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2933, 2859, 2109, 1761, 1382, 1236, 1106, 841; ^1H NMR (400 MHz, $CDCl_3$): δ 7.71 – 7.62 (m, 4H), 7.46 – 7.26 (m, 9H), 7.23 – 7.13 (m, 2H), 5.84 (d, *J* = 1.8 Hz, 1H), 5.39 (s, 1H), 4.41 (dd, *J* = 9.6, 3.9 Hz, 1H), 4.23 – 4.17 (m, 1H), 4.10 – 4.02 (m, 1H), 3.83 – 3.69 (m, 2H), 3.55 (dd, *J* = 3.9, 1.8 Hz, 1H), 2.67 – 2.57 (m, 1H), 2.25

– 2.07 (m, 2H), 1.88 (dt, *J* = 8.2, 4.2 Hz, 2H), 1.74 – 1.50 (m, 6H), 1.07 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 150.7, 150.4, 137.1, 137.0, 136.2, 136.2, 136.2, 136.2, 136.1, 136.1, 136.0, 136.0, 133.2, 133.1, 133.1, 132.7, 130.2, 130.1, 129.8, 129.7, 129.0, 129.0, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.6, 127.6, 127.5, 127.5, 126.4, 126.4, 126.3, 126.3, 102.1, 102.0, 95.6, 94.1, 82.5, 82.4, 79.1, 78.9, 78.3, 78.0, 75.5, 75.5, 72.4, 70.0, 68.3, 68.1, 68.0, 66.2, 64.7, 63.7, 37.0, 37.0, 36.7, 36.5, 27.0, 27.0, 27.0, 26.9, 26.9, 26.9, 25.0, 24.9, 22.6, 22.6, 22.5, 22.5, 19.3, 19.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{38}H_{44}N_3O_7Si$ 682.2948; Found: 682.2961.

Methyl 6-*O*-(2-azido-4,6-*O*-benzylidene-3-*O*-picoloyl-2-*deoxy*-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (16b) {α:β = 1:2}: Compound **16b** was synthesized from donor **14b** (55 mg, 0.1 mmol) and acceptor **15** (47 mg, 0.1 mmol) according to the general procedure **A** (68 mg, 80 % yield); pale yellow sticky gum; $[\alpha]_D^{25}$ = +12.6 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): ; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.84 – 8.78 (m, 1H), 8.17 (ddt, *J* = 7.9, 2.3, 1.1 Hz, 1H), 7.84 (tdd, *J* = 7.8, 4.6, 1.8 Hz, 1H), 7.48 (tdd, *J* = 7.1, 4.8, 1.3 Hz, 1H), 7.44 – 7.35 (m, 9H), 7.35 – 7.29 (m, 11H), 5.57 (s, 1H), 5.28 (dd, *J* = 10.2, 3.9 Hz, 1H), 5.05 – 4.99 (m, 1H), 4.98 – 4.91 (m, 1H), 4.90 – 4.85 (m, 1H), 4.83 – 4.77 (m, 1H), 4.72 – 4.66 (m, 1H), 4.65 – 4.58 (m, 2H), 4.41 (d, *J* = 1.3 Hz, 1H), 4.33 – 4.28 (m, 1H), 4.18 – 4.09 (m, 2H), 4.08 – 3.95 (m, 2H), 3.93 – 3.85 (m, 1H), 3.84 – 3.68 (m, 2H), 3.61 – 3.54 (m, 1H), 3.54 – 3.48 (m, 1H), 3.45 (dd, *J* = 10.7, 1.9 Hz, 1H), 3.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.2, 164.0, 150.3, 150.2, 147.1, 138.7, 138.7, 138.4, 138.2, 138.1, 137.2, 137.1, 136.9, 129.2, 129.1, 128.7, 128.7, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 128.0, 128.0, 127.9, 127.7, 127.7, 127.4, 127.3, 126.3, 126.3, 126.2, 126.2, 125.7, 125.6, 102.0, 101.9, 100.4, 99.3, 98.0, 98.0, 82.2, 80.2, 79.9, 77.6, 77.4, 77.0, 76.1, 75.8, 75.3, 75.2, 74.8, 73.5, 73.5, 71.8, 71.3, 69.9, 69.6, 68.7, 68.6, 68.4, 67.5, 66.6, 64.2, 62.4, 62.2, 60.5, 55.4, 55.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{47}H_{48}N_4O_{11}Na$ 867.3217, Found: 867.3259.

Methyl 6-*O*-(2-azido-4,6-*O*-benzylidene-2-*deoxy*-3-*O*- *p*-methoxybenzyl-D-mannopyranosyl) -2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (16c): Compound **16c** was synthesized from donor **14c** (55 mg, 0.1 mmol) and acceptor15 (46 mg, 0.1 mmol) according to the general procedure **A** (77 mg, 90 % for 50 mM; 75 mg, 88 % for 10 mM), **B** (76 mg, 89 % for 50 mM; 72 mg, 84 % for 10 mM) and **C** (76 mg, 89 % for 50 mM; 68 mg, 80 % for 10 mM); light yellow sticky gum; $[\alpha]_D^{25}$ = -9.0 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2925, 2106, 1512, 1249, 1087, 912 ; ^{1}H NMR (400

MHz, $CDCl_3$): δ 7.49 (dq, *J* = 6.6, 2.4 Hz, 2H), 7.45 – 7.26 (m, 18H), 7.26 – 7.12 (m, 2H), 6.91 – 6.86 (m, 2H), 5.56 (s, 1H), 5.00 (d, *J* = 10.9 Hz, 1H), 4.88 (d, *J* = 11.6 Hz, 1H), 4.84 – 4.79 (m, 2H), 4.78 (s, 1H), 4.66 (dd, *J* = 12.1, 10.3 Hz, 2H), 4.60 – 4.55 (m, 2H), 4.25 (dd, *J* = 10.5, 4.9 Hz, 1H), 4.21 (d, *J* = 1.3 Hz, 1H), 4.06 – 4.02 (m, 1H), 4.02 – 3.98 (m, 1H), 3.95 (t, *J* = 9.5 Hz, 1H), 3.85 (t, *J* = 10.3 Hz, 1H), 3.79 (s, 3H), 3.77 (dd, *J* = 5.4, 2.0 Hz, 1H), 3.69 (dd, *J* = 3.9, 1.3 Hz, 1H), 3.59 (dd, *J* = 9.6, 3.8 Hz, 1H), 3.50 (ddd, *J* = 10.4, 4.4, 2.3 Hz, 2H), 3.43 (dd, *J* = 10.1, 8.8 Hz, 1H), 3.35 (s, 3H), 3.20 (td, *J* = 9.7, 4.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.6, 138.8, 138.5, 138.2, 137.4, 129.9, 129.6, 129.6, 129.1, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 128.0, 127.8, 127.8, 126.1, 126.1, 114.0, 114.0, 101.6, 100.4, 98.0, 82.2, 79.9, 78.5, 77.3, 75.9, 75.3, 74.7, 73.5, 72.6, 69.6, 68.5, 68.4, 67.4, 63.6, 55.4, 55.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{49}H_{53}N_3O_{11}$ 882.3577, Found: 882.3579.

Methyl 6-*O*-(2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-*deoxy*-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (16d): Compound **16d** was synthesized from donor **13d** (55 mg, 0.1 mmol) and acceptor **15** (48 mg, 0.1 mmol) according to the general procedure **A** (75 mg, 88 % for 50 mM; 73 mg, 85 % for 10 mM), **B** (76 mg, 89 % for 50 mM; 70 mg, 82 % for 10 mM) and **C** (75 mg, 88 % for 50 mM; 70 mg, 82 % for 10 mM); pale yellow gum; $[\alpha]_D^{25}$ = +1.2 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2920, 2108, 1595, 1456, 1368, 1093, 911; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (dt, *J* = 7.0, 2.7 Hz, 2H), 7.41 – 7.31 (m, 19H), 7.27 (d, *J* = 4.4 Hz, 4H), 5.58 (s, 1H), 5.02 (d, *J* = 10.9 Hz, 1H), 4.89 (dd, *J* = 12.1, 4.6 Hz, 2H), 4.85 – 4.78 (m, 2H), 4.75 (d, *J* = 12.5 Hz, 1H), 4.66 (d, *J* = 12.0 Hz, 1H), 4.61 – 4.56 (m, 2H), 4.26 (dd, *J* = 10.5, 4.9 Hz, 1H), 4.21 (d, *J* = 1.3 Hz, 1H), 4.08 – 4.03 (m, 1H), 4.03 – 3.95 (m, 2H), 3.86 (t, *J* = 10.3 Hz, 1H), 3.79 (ddd, *J* = 10.0, 5.2, 1.9 Hz, 1H), 3.73 (dd, *J* = 3.8, 1.2 Hz, 1H), 3.61 (dd, *J* = 9.6, 3.7 Hz, 1H), 3.54 – 3.49 (m, 2H), 3.44 (t, *J* = 9.4 Hz, 1H), 3.36 (s, 3H), 3.21 (q, *J* = 4.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.8, 138.6, 138.2, 137.9, 137.4, 129.1, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 126.1, 126.1, 101.6, 100.4, 98.0, 82.2, 79.9, 78.6, 77.3, 75.9, 75.8, 74.7, 73.5, 73.0, 69.6, 68.5, 68.4, 67.3, 63.6, 55.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{48}H_{51}N_3O_{10}Na$: 852.3471, Found: 852.3484.

Methyl 6-*O*-((2-azido-3-*O*-(naphthalen-1-yl methyl)-4,6-*O*-benzylidene-2-*deoxy*-D-mannopyranosyl))-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (16e): Compound **7c** was synthesized from donor **16e** (55 mg, 0.1 mmol) and acceptor **15** (44 mg, 0.1 mmol) according to

the general procedure **A** (77 mg, 91 % for 50 mM; 72 mg, 85 % for 10 mM), **B** (76 mg, 90 % for 50 mM; 75 mg, 89 % for 10 mM) and **C** (75 mg, 89 % for 50 mM; 70 mg, 83 % for 10 mM); colorless sticky syrup; $[\alpha]_D^{25}$ = +17.6 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2924, 2106, 1497, 1362, 1088, 910, 819; ^1H NMR (400 MHz, $CDCl_3$): δ 7.88 – 7.83 (m, 3H), 7.79 – 7.76 (m, 1H), 7.56 – 7.47 (m, 6H), 7.44 – 7.41 (m, 3H), 7.39 – 7.31 (m, 10H), 7.25 – 7.22 (m, 3H), 7.18 – 7.13 (m, 1H), 5.61 (s, 1H), 5.05 – 5.00 (m, 2H), 4.93 (d, *J* = 12.7 Hz, 1H), 4.88 (d, *J* = 11.7 Hz, 1H), 4.82 (dd, *J* = 11.5, 9.3 Hz, 2H), 4.66 (d, *J* = 12.1 Hz, 1H), 4.59 – 4.54 (m, 2H), 4.27 (dd, *J* = 10.5, 4.9 Hz, 1H), 4.21 (d, *J* = 1.4 Hz, 1H), 4.05 (dd, *J* = 5.4, 1.5 Hz, 1H), 4.04 – 3.99 (m, 2H), 3.88 (t, *J* = 10.3 Hz, 1H), 3.79 (dt, *J* = 6.7, 1.8 Hz, 1H), 3.77 – 3.75 (m, 1H), 3.66 (dd, *J* = 9.6, 3.7 Hz, 1H), 3.54 – 3.48 (m, 2H), 3.43 (dd, *J* = 10.1, 8.8 Hz, 1H), 3.33 (s, 3H), 3.25 – 3.18 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.7, 138.5, 138.1, 137.4, 135.2, 133.3, 133.2, 129.2, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 127.8, 127.8, 127.8, 126.9, 126.4, 126.2, 126.2, 126.2, 125.8, 101.7, 100.3, 98.0, 82.2, 79.9, 78.5, 77.3, 75.9, 75.6, 74.7, 73.5, 72.9, 69.6, 68.5, 68.4, 67.3, 63.6, 55.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{52}H_{53}N_3O_{10}Na$ 902.3628, Found: 902.3623.

Methyl 6-*O*-((2-azido-4,6-*O*-benzylidene-3-*O*-(*tert*-butyldimethylsilyl)-2-*deoxy*-D-mannopyranosyl))-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (16f): Compound **16f** was synthesized from donor **14f** (56 mg, 0.1 mmol) and acceptor **15** (47 mg, 0.1 mmol) according to the general procedure **A** (78 mg, 91 % for 50 mM; 74 mg, 86 % for 10 mM), **B** (76 mg, 89 % for 50 mM; 75 mg, 88 % for 10 mM) and **C** (76 mg, 89 % for 50 mM; 70 mg, 82 % for 10 mM); pale yellow sticky gum; $[\alpha]_D^{25}$ = +2.4 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2926, 2861, 2108, 1728, 1459, 1370, 1091, 846; ^1H NMR (400 MHz, $CDCl_3$): δ 7.49 – 7.46 (m, 2H), 7.38 – 7.30 (m, 18H), 5.52 (s, 1H), 5.02 (d, *J* = 10.9 Hz, 1H), 4.92 (d, *J* = 11.6 Hz, 1H), 4.85 – 4.79 (m, 2H), 4.67 (d, *J* = 12.1 Hz, 1H), 4.63 – 4.58 (m, 2H), 4.36 (d, *J* = 1.3 Hz, 1H), 4.26 (dd, *J* = 10.4, 4.9 Hz, 1H), 4.10 (dd, *J* = 10.5, 2.0 Hz, 1H), 4.04 (t, *J* = 9.2 Hz, 1H), 3.92 – 3.85 (m, 2H), 3.84 (s, 1H), 3.82 – 3.78 (m, 1H), 3.77 – 3.73 (m, 1H), 3.55 (dt, *J* = 9.4, 4.8 Hz, 2H), 3.44 (dd, *J* = 10.1, 8.8 Hz, 1H), 3.40 (s, 3H), 3.22 (td, *J* = 9.7, 4.9 Hz, 1H), 0.91 (s, 9H), 0.12 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.8, 138.5, 138.2, 137.3, 129.0, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 128.0, 127.8, 127.8, 126.2, 126.2, 102.0, 100.1, 98.0, 82.2, 80.0, 78.6, 77.7, 75.9, 74.8, 73.5, 72.0, 69.7, 68.9, 68.4, 67.5, 66.2, 55.3, 25.8, 25.8, 25.8,

18.3, -4.2, -4.9; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{47}H_{59}N_3O_{10}SiNa$ 876.3867, Found: 876.3848.

Methyl 6-*O*-((2-azido-3-*O*-(*tert*-butyldiphenylsilyl)-4,6-*O*-benzylidene-2-*deoxy*-D-mannopyranosyl))-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (16g) {α:β = 1:3}: Compound **16g** was synthesized from donor **14g** (70 mg, 0.1 mmol) and acceptor **15** (48 mg, 0.1 mmol) according to the general procedure **A** (81 mg, 81 %); pale yellow sticky gum; $[\alpha]_D^{25}$ = +3.6 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2928, 2861, 2110, 1728, 1459, 1370, 1093, 847 ; ^1H NMR (400 MHz, $CDCl_3$): δ 7.73 – 7.63 (m, 4H), 7.41 – 7.27 (m, 18H), 7.26 – 7.18 (m, 8H), 5.37 (s, 1H), 5.03 (dd, *J* = 16.3, 10.9 Hz, 1H), 4.86 – 4.79 (m, 2H), 4.75 – 4.64 (m, 1H), 4.62 – 4.54 (m, 1H), 4.47 (d, *J* = 11.5 Hz, 1H), 4.32 – 4.23 (m, 1H), 4.18 (dd, *J* = 10.4, 4.9 Hz, 1H), 4.15 – 4.10 (m, 1H), 4.00 (dd, *J* = 10.4, 8.3 Hz, 2H), 3.91 – 3.80 (m, 2H), 3.80 – 3.67 (m, 3H), 3.53 – 3.39 (m, 3H), 3.28 (s, 3H), 3.07 (dt, *J* = 9.6, 4.8 Hz, 1H), 1.06 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.9, 138.8, 138.4, 138.2, 138.2, 138.1, 137.3, 136.3, 136.3, 136.2, 136.1, 136.1, 136.1, 136.0, 136.0, 136.0, 136.0, 133.4, 133.3, 133.1, 132.9, 130.1, 130.0, 129.7, 129.6, 128.9, 128.8, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.1, 128.1, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.5, 127.5, 127.5, 127.5, 127.4, 127.4, 126.4, 126.4, 126.3, 126.3, 102.0, 101.8, 100.2, 99.6, 98.0, 97.9, 82.2, 82.2, 80.0, 79.9, 79.0, 78.3, 77.5, 75.9, 75.8, 75.2, 74.9, 73.6, 73.3, 71.7, 70.7, 70.6, 69.7, 68.5, 68.4, 68.3, 67.3, 66.0, 65.8, 64.5, 64.1, 63.4, 55.2, 55.2, 27.0, 27.0, 27.0, 26.9, 26.9, 26.9, 19.3, 19.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{57}H_{63}N_3O_{10}SiNa$ 1000.4180; Found: 1000.4157.

Allyl 5-*O*-((2-azido-4,6-*O*-benzylidene-3-*O*-(*tert*-butyldimethylsilyl)-2-*deoxy*-D-mannopyranosyl))-2,3-di-*O*-benzoyl-α-D-arabinofuranoside (19a): Compound **19a** was synthesized from donor **14f** (56 mg, 0.1 mmol) and acceptor **18a** (40 mg, 0.1 mmol) according to the general procedure **B** (69 mg, 87 %); pale yellow sticky syrup; $[\alpha]_D^{25}$ = -25.9 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2930, 2858, 2108, 1724, 1259, 1096, 842; ^1H NMR (400 MHz, $CDCl_3$): δ 8.07 (ddd, *J* = 8.5, 3.5, 1.4 Hz, 4H), 7.62 – 7.57 (m, 2H), 7.49 – 7.45 (m, 6H), 7.35 (dd, *J* = 5.1, 2.1 Hz, 3H), 6.02 – 5.91 (m, 1H), 5.54 (d, *J* = 1.5 Hz, 2H), 5.41 – 5.35 (m, 2H), 5.32 (s, 1H), 5.23 (dq, *J* = 10.5, 1.5 Hz, 1H), 4.77 (d, *J* = 1.2 Hz, 1H), 4.53 (ddd, *J* = 7.2, 5.4, 3.0 Hz, 1H), 4.37 (dd, *J* = 11.0, 3.1 Hz, 1H), 4.33 – 4.27 (m, 2H), 4.16 – 4.11 (m, 1H), 4.03 – 3.98 (m, 2H), 3.92 – 3.86 (m, 2H), 3.85 (s, 1H), 3.34 (td, *J* = 9.7, 4.9 Hz, 1H), 0.89 (s, 9H), 0.10 (s, 3H), 0.06 (s, 3H); ^{13}C NMR

(101 MHz, $CDCl_3$): δ 166.0, 165.5, 137.3, 133.9, 133.7, 133.7, 130.1, 130.1, 130.0, 130.0, 129.2, 129.2, 129.1, 128.7, 128.7, 128.6, 128.6, 128.3, 128.3, 126.2, 126.2, 117.6, 105.1, 102.1, 100.1, 82.1, 81.7, 78.7, 77.7, 72.3, 69.7, 68.5, 68.2, 67.7, 65.9, 25.8, 25.8, 25.8, 18.3, -4.3, -4.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{41}H_{49}N_3O_{11}SiNa$ 810.3033; Found: 810.3032.

Methyl 6-*O*-((2-azido-4,6-*O*-benzylidene-3-*O*-(*tert*-butyldimethylsilyl)-2-*deoxy*-D-mannopyranosyl))-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (19b): Compound **19b** was synthesized from donor **14f** (56 mg, 0.1 mmol) and acceptor **18b** (51 mg, 0.1 mmol) according to the general procedure **B** (81 mg, 90 %); pale yellow sticky gum; $[\alpha]_D^{25}$ = +1.8 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2928, 2856, 2108, 1727, 1255, 1091, 842; ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.97 – 7.94 (m, 2H), 7.89 – 7.85 (m, 2H), 7.53 – 7.45 (m, 4H), 7.41 – 7.34 (m, 8H), 7.31 – 7.27 (m, 2H), 6.19 (t, *J* = 9.6 Hz, 1H), 5.55 – 5.49 (m, 2H), 5.32 – 5.26 (m, 2H), 4.64 (d, *J* = 1.3 Hz, 1H), 4.34 (ddd, *J* = 10.3, 7.0, 2.0 Hz, 1H), 4.20 (dd, *J* = 10.5, 4.9 Hz, 1H), 4.15 (dd, *J* = 11.0, 2.0 Hz, 1H), 4.03 (dd, *J* = 3.7, 1.3 Hz, 1H), 3.98 (dd, *J* = 9.3, 3.7 Hz, 1H), 3.81 (t, *J* = 9.6 Hz, 2H), 3.76 – 3.70 (m, 1H), 3.50 (d, *J* = 4.2 Hz, 3H), 3.28 (td, *J* = 9.7, 4.9 Hz, 1H), 0.92 (s, 9H), 0.13 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.9, 165.8, 165.7, 137.3, 133.7, 133.5, 133.2, 130.0, 130.0, 129.9, 129.9, 129.8, 129.8, 129.3, 129.1, 129.1, 128.8, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.2, 128.2, 126.2, 126.2, 102.0, 100.5, 96.9, 78.6, 72.2, 72.0, 70.5, 69.6, 69.0, 68.8, 68.4, 67.5, 66.1, 55.6, 25.8, 25.8, 25.8, 18.3, -4.3, -4.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{47}H_{53}N_3O_{13}SiNa$ 896.3426; Found: 896.3416.

Methyl 4-*O*-((2-azido-3-*O*-(*tert*-butyldimethylsilyl)-4,6-*O*-benzylidene-2-*deoxy*-D-mannopyranosyl))-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (19c) {α:β = 1:3}: Compound **19c** was synthesized from donor **14f** (56 mg, 0.1 mmol) and acceptor **18c** (47 mg, 0.1 mmol) according to the general procedure **B** (76 mg, 89 %); pale yellow sticky gum; $[\alpha]_D^{25}$ = -0.6 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2929, 2858, 2107, 1253, 1095, 1046, 841; ^1H NMR (400 MHz, $CDCl_3$): δ 7.49 – 7.43 (m, 2H), 7.41 (dt, *J* = 8.2, 1.9 Hz, 2H), 7.38 – 7.29 (m, 16H), 5.49 (s, 1H), 5.19 – 4.99 (m, 1H), 4.98 – 4.87 (m, 1H), 4.79 (t, *J* = 10.6 Hz, 1H), 4.72 (d, *J* = 11.9 Hz, 1H), 4.69 – 4.61 (m, 3H), 4.55 – 4.47 (m, 1H), 4.04 – 3.90 (m, 3H), 3.82 – 3.76 (m, 2H), 3.74 – 3.65 (m, 4H), 3.62 – 3.56 (m, 1H), 3.54 (dd, *J* = 9.7, 3.8 Hz, 1H), 3.40 (s, 3H), 3.09 – 2.92 (m, 1H), 0.87 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 139.3, 138.3, 138.2, 138.0, 137.9, 137.8, 137.5, 137.4, 129.1, 129.0, 128.7, 128.7, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.3,

128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.7, 127.7, 127.7, 127.7, 127.5, 127.3, 126.3, 126.3, 126.3, 126.3, 102.1, 102.0, 101.4, 99.9, 98.4, 97.9, 81.7, 80.5, 80.4, 79.5, 79.2, 78.6, 77.3, 77.2, 75.5, 75.4, 73.8, 73.8, 73.6, 73.2, 72.2, 70.4, 70.0, 69.6, 69.5, 69.1, 68.6, 68.5, 67.4, 66.6, 65.3, 64.9, 55.5, 55.4, 25.9, 25.9, 25.9, 25.8, 25.8, 25.8, 18.3, 18.3, -4.3, -4.4, -4.8, -4.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{47}H_{59}N_3O_{10}SiNa$ 876.3867; Found: 876.3873.

Allyl 2-*O*-((2-azido-3-*O*-(*tert*-butyldimethylsilyl)-4,6-*O*-benzylidene-2-*deoxy*-D-mannopyranosyl))-3,4-*O*-isopropylidene-α-L-fucopyranoside (19d) {α:β = 1:7}: Compound **19d** was synthesized from donor **14f** (56 mg, 0.1 mmol) and acceptor **18d** (25 mg, 0.1 mmol) according to the general procedure **B** (55 mg, 87 %); pale yellow sticky gum; $[\alpha]_D^{25}$ = +61.5 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2927, 2861, 2108, 1376, 1083, 1045, 845; ^1H NMR (400 MHz, $CDCl_3$): δ 7.49 – 7.44 (m, 2H), 7.35 (dd, *J* = 5.2, 2.0 Hz, 3H), 5.99 – 5.87 (m, 1H), 5.54 (s, 1H), 5.30 (q, *J* =1.7 Hz, 1H), 5.21 (q, *J* =1.4 Hz, 1H), 4.93 (d, *J* = 3.5 Hz, 1H), 4.81 (d, *J* = 1.3 Hz, 1H), 4.47 (dd, *J* = 6.6, 5.4 Hz, 1H), 4.35 – 4.24 (m, 2H), 4.20 (dd, *J* = 6.6, 2.1 Hz, 1H), 4.11 (dd, *J* = 6.6, 2.1 Hz, 1H), 4.09 – 4.01 (m, 2H), 3.97 (dd, *J* = 3.8, 1.3 Hz, 1H), 3.94 (dd, *J* = 9.2, 3.7 Hz, 1H), 3.88 – 3.83 (m, 1H), 3.83 – 3.78 (m, 1H), 3.34 – 3.24 (m, 1H), 1.51 (s, 3H), 1.35 (s, 3H), 1.29 (d, *J* = 6.5 Hz, 3H), 0.89 (s, 9H), 0.10 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.5, 137.4, 134.3, 133.5, 129.0, 129.0, 128.2, 128.2, 128.2, 128.2, 126.3, 126.3, 126.2, 126.2, 118.1, 117.1, 109.5, 109.2, 102.2, 102.0, 100.4, 99.9, 97.2, 95.3, 79.3, 78.6, 76.5, 76.4, 75.7, 75.6, 74.6, 74.1, 72.2, 70.3, 68.7, 68.6, 68.5, 68.5, 67.7, 66.0, 65.4, 65.2, 64.3, 63.3, 28.5, 27.2, 26.6, 25.9, 25.9, 25.9, 25.8, 25.8, 25.8, 25.6, 18.3, 18.3, 16.4, 16.3, -4.3, -4.3, -4.8, -4.9; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{31}H_{47}N_3O_9SiNa$ 656.2979; Found: 656.2977.

Allyl 4-*O*-((2-azido-3-*O*-(*tert*-butyldimethylsilyl)-4,6-*O*-benzylidene-2-*deoxy*-D-mannopyranosyl))-2,3-*O*-isopropylidine-α-L-rhamnopyranoside (19e) {α:β = 1:7}: Compound **19e** was synthesized from donor **14f** (56 mg, 0.1 mmol) and acceptor **18e** (25 mg, 0.1 mmol) according to the general procedure **B** (58 mg, 91 %); pale yellow sticky syrup; $[\alpha]_D^{25}$ = +18.7 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2924, 2854, 2108, 1837, 1379, 1253, 1083, 842; ^1H NMR (400 MHz, $CDCl_3$): δ 7.53 – 7.45 (m, 2H), 7.35 (dd, *J* = 5.1, 2.1 Hz, 3H), 5.96 – 5.85 (m, 1H), 5.55 (d, *J* = 12.8 Hz, 1H), 5.31 (dt, *J* = 17.2, 1.7 Hz, 1H), 5.22 (dq, *J* = 10.4, 1.4 Hz, 1H), 5.13 (d, *J* = 1.3 Hz, 1H), 5.02 (d, *J* = 6.3 Hz, 1H), 4.75 (d, *J* = 3.9 Hz, 1H), 4.28 – 4.23 (m, 2H), 4.20 – 4.13 (m, 2H), 4.03 – 3.97 (m, 2H), 3.93 – 3.79 (m, 3H), 3.72 – 3.67 (m, 1H), 3.31 (dd, *J* =

9.8, 4.9 Hz, 1H), 1.51 (s, 3H), 1.33 (s, 3H), 1.31 (d, *J* = 5.8 Hz, 3H), 0.90 (s, 9H), 0.11 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.6, 137.4, 133.7, 133.7, 129.1, 129.0, 128.2, 128.2, 128.2, 128.2, 126.4, 126.4, 126.2, 126.2, 119.2, 118.0, 109.6, 109.3, 102.1, 102.0, 100.0, 98.1, 96.2, 96.0, 81.2, 79.3, 79.0, 78.3, 78.0, 76.7, 76.4, 76.2, 72.2, 70.5, 68.8, 68.5, 68.2, 68.1, 67.6, 66.3, 65.2, 64.8, 64.3, 64.1, 28.2, 28.0, 26.6, 26.5, 25.9, 25.9, 25.9, 25.8, 25.8, 25.8, 18.4, 18.3, 17.6, 17.5, -4.3, -4.3, -4.7, -4.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{31}H_{48}N_3O_9Si$ 634.3160; Found: 634.3159.

Benzyl *N*-((benzyloxy)carbonyl)-L-allothreoninate 2-azido-4,6-*O*-benzylidene-3-*O*-(*tert*-butyldimethylsilyl)-2-*deoxy*-D-mannopyranoside (19f) {α:β = 1:3}: Compound **19f** was synthesized from donor **14f** (56 mg, 0.1 mmol) and acceptor **18f** (35 mg, 0.1 mmol) according to the general procedure **B** (57 mg, 78 %); light brown sticky gum; $[\alpha]_D^{25}$ = +22.7 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2927, 2855, 2107, 1726, 1508, 1255, 1086, 840; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 – 7.44 (m, 2H), 7.43 – 7.28 (m, 14H), 5.67 – 5.54 (m, 1H), 5.51 (s, 1H), 5.19 (d, *J* = 2.0 Hz, 1H), 5.18 – 5.08 (m, 3H), 4.60 – 4.55 (m, 1H), 4.50 – 4.44 (m, 1H), 4.14 (dt, *J* = 10.4, 5.1 Hz, 1H), 3.90 – 3.84 (m, 1H), 3.78 (dd, *J* = 3.8, 1.3 Hz, 1H), 3.75 – 3.65 (m, 2H), 3.10 (dt, *J* = 9.6, 4.9 Hz, 1H), 1.30 (d, *J* = 6.4 Hz, 3H), 0.89 (s, 9H), 0.11 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.2, 170.0, 157.0, 156.7, 137.3, 137.3, 137.3, 136.4, 135.5, 135.1, 129.1, 129.1, 129.0, 128.9, 128.9, 128.8, 128.8, 128.8, 128.8, 128.8, 128.7, 128.7, 128.7, 128.5, 128.5, 128.5, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 126.3, 126.3, 126.2, 126.2, 102.1, 102.0, 100.7, 97.6, 79.2, 78.5, 74.2, 72.0, 70.3, 68.9, 68.4, 68.3, 67.6, 67.6, 67.5, 67.4, 67.3, 66.3, 64.7, 64.4, 58.7, 58.6, 25.9, 25.9, 25.9, 25.8, 25.8, 25.8, 18.5, 18.4, 18.3, 17.4, -4.3, -4.3, -4.7, -4.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{38}H_{49}N_4O_9Si$ 733.3269; Found: 733.3279.

Benzyl 2-azido-4,6-*O*-benzylidene-3-*O*-(*tert*-butyldimethylsilyl)-2-*deoxy*-D-mannopyranoside (19g) {α:β = 1:7}: Compound **19g** was synthesized from donor **14f** (56 mg, 0.1 mmol) and acceptor **18g** (11µL, 0.1 mmol) according to the general procedure **B** (43 mg, 86 %); pale yellow sticky syrup; $[\alpha]_D^{25}$ = -22.9 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2928, 2856, 2107, 1460, 1254, 1086, 838; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (dt, *J* = 7.2, 2.5 Hz, 2H), 7.28 – 7.22 (m, 8H), 5.45 (s, 1H), 4.85 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 12.1 Hz, 1H), 4.50 (d, *J* = 1.4 Hz, 1H), 4.22 (dd, *J* = 10.4, 4.9 Hz, 1H), 3.85 (dd, *J* = 9.4, 3.6 Hz, 1H), 3.81 – 3.71 (m, 3H), 3.23 – 3.15 (m, 1H), 0.78 (s, 9H), -0.01 (s, 3H), -0.05 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.4, 137.3, 136.6, 136.5, 129.0, 129.0, 128.7, 128.7, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2,

128.2, 128.2, 128.2, 128.2, 128.2, 126.3, 126.3, 126.2, 126.2, 102.1, 102.0, 98.4, 98.1, 79.4, 78.8, 72.4, 70.9, 70.4, 69.4, 68.7, 68.5, 67.5, 66.2, 65.3, 64.2, 25.8, 25.8, 25.8, 25.8, 25.8, 25.8, 18.3, 18.3, -4.3, -4.4, -4.9, -4.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{26}H_{36}N_3O_5Si$ 498.2424; Found: 498.2427.

Menthyl 2-azido-4,6-*O*-benzylidene-3-*O*-(*tert*-butyldimethylsilyl)-2-*deoxy*-β-D-mannopyranoside (19h): Compound **19h** was synthesized from donor **14f** (56 mg, 0.1 mmol) and acceptor **18h** (16 mg, 0.1 mmol) according to the general procedure **B** (50 mg, 92 %); pale yellow sticky gum; $[\alpha]_D^{25}$ = -40.4 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2954, 2926, 2106, 1379, 1119, 1084, 965, 840; ^1H NMR (400 MHz, $CDCl_3$): δ 7.50 – 7.46 (m, 2H), 7.38 – 7.34 (m, 3H), 5.54 (s, 1H), 4.71 (d, *J* = 1.4 Hz, 1H), 4.26 (dd, *J* = 10.4, 4.9 Hz, 1H), 3.99 (dd, *J* = 9.4, 3.8 Hz, 1H), 3.87 – 3.83 (m, 1H), 3.83 – 3.79 (m, 2H), 3.52 (d, *J* = 4.3 Hz, 1H), 3.34 – 3.25 (m, 1H), 2.30 (d, *J* = 2.6 Hz, 1H), 2.07 – 1.99 (m, 1H), 1.71 – 1.60 (m, 3H), 1.30 – 1.29 (m, 4H), 0.95 (d, *J* = 6.6 Hz, 3H), 0.92 (d, *J* = 1.6 Hz, 3H), 0.90 (s, 9H), 0.77 (d, *J* = 6.9 Hz, 3H), 0.11 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.5, 129.0, 128.2, 128.2, 126.3, 126.3, 102.0, 96.8, 79.0, 77.4, 72.6, 68.6, 67.5, 67.0, 47.9, 40.5, 34.4, 31.6, 25.8, 25.8, 25.8, 25.3, 23.2, 22.4, 21.1, 18.3, 15.8, -4.2, -4.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{29}H_{47}N_3O_5SiNa$ 568.3183; Found: 568.3134.

Cholesteryl 2-azido-4,6-*O*-benzylidene-3-*O*-(*tert*-butyldimethylsilyl)-2-*deoxy*-β-D-mannopyranoside (19i): Compound **19i** was synthesized from donor **14f** (56 mg, 0.1 mmol) and acceptor **18i** (39 mg, 0.1 mmol) according to the general procedure **B** (71 mg, 91 %); pale yellow sticky foam; $[\alpha]_D^{25}$ = -18.7 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2933, 2860, 2107, 1838, 1815, 1258, 1083, 840; ^1H NMR (400 MHz, $CDCl_3$): δ 7.49 – 7.44 (m, 2H), 7.35 (dd, *J* = 5.1, 2.0 Hz, 3H), 5.53 (s, 1H), 5.37 (dt, *J* = 4.2, 1.9 Hz, 1H), 4.74 (d, *J* = 1.4 Hz, 1H), 4.28 (d, *J* = 3.8 Hz, 1H), 4.00 (dd, *J* = 9.4, 3.7 Hz, 1H), 3.88 – 3.84 (m, 2H), 3.83 – 3.80 (m, 1H), 3.60 (tq, *J* = 9.8, 4.9 Hz, 1H), 3.31 (d, *J* = 4.7 Hz, 1H), 2.38 – 2.29 (m, 2H), 2.05 – 1.94 (m, 5H), 1.73 – 1.57 (m, 10H), 1.45 (d, *J* = 1.9 Hz, 3H), 1.33 (d, *J* = 2.8 Hz, 3H), 1.26 (s, 3H), 1.15 – 1.08 (m, 5H), 1.02 (s, 3H), 0.90 (s, 9H), 0.87 (d, *J* = 1.8 Hz, 3H), 0.86 (d, *J* = 1.8 Hz, 3H), 0.68 (s, 3H), 0.11 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 140.5, 137.4, 129.0, 128.2, 128.2, 126.2, 126.2, 122.3, 102.0, 97.9, 78.9, 78.8, 72.6, 68.6, 67.5, 66.8, 56.9, 56.2, 50.3, 42.4, 39.9, 39.6, 38.7, 37.3, 36.6, 36.3, 35.9, 32.1, 32.0, 30.6, 28.3, 28.1, 25.8, 25.8, 25.8, 24.5, 23.9, 22.9, 22.7, 21.1, 19.5, 18.8, 18.3, 12.0, -4.3, -4.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{46}H_{73}N_3O_5SiNa$ 798.5216; Found: 798.5217.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3-di-*O*-benzyl-4,6-*O*-benzylidene--D-mannopyranose (31) {α:β = 1:2}: Prepared according to the literature reported procedure (*Beilstein Journal of Organic Chemistry*, **2007**, *3*, No. 26; *Angew Chem Int*. *Ed*. **2016**, *55*,7786–7791); 823 mg, 67 % (pale yellow sticky gum); $[\alpha]_D^{25}$ = +9.7 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2927, 1504, 1454, 1100, 1023, 829; ^1H NMR (400 MHz, $CDCl_3$): δ 7.53 (dd, *J* = 7.4, 2.2 Hz, 2H), 7.43 – 7.30 (m, 13H), 5.66 (d, *J* = 8.0 Hz, 1H), 5.60 (d, *J* = 5.1 Hz, 1H), 4.97 (dd, *J* = 11.3, 2.2 Hz, 1H), 4.90 – 4.83 (m, 2H), 4.80 (d, *J* = 13.9 Hz, 1H), 4.46 – 4.32 (m, 1H), 4.09 (d, *J* = 9.3 Hz, 1H), 3.91 – 3.79 (m, 1H), 3.79 – 3.67 (m, 2H), 3.66 – 3.56 (m, 1H), 2.67 (d, *J* = 6.8 Hz, 1H), 2.21 (td, *J* = 12.5, 6.3 Hz, 2H), 2.02 – 1.88 (m, 2H), 1.75 – 1.57 (m, 5H), 1.43 – 1.33 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 151.5, 151.2, 138.7, 138.3, 138.0, 137.7, 137.3, 137.2, 129.1, 129.1, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 126.1, 126.1, 126.1, 126.1, 101.4, 101.3, 97.6, 94.0, 82.8, 82.5, 81.5, 81.3, 81.0, 80.8, 78.7, 78.3, 78.3, 78.3, 75.6, 75.4, 75.3, 75.2, 75.2, 73.8, 68.8, 68.6, 66.8, 64.9, 36.9, 36.8, 36.8, 36.7, 25.0, 25.0, 22.6, 22.6, 22.6, 22.5.

***p*-methoxyphenyl 2-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-3,4-di-*O*-benzyl-α-D-rhamnopyranoside (34):** To a solution of glycosyl carbonate donor **31** (400 mg, 668.12 µmol) and acceptor **30** (*Tetrahedron Assym.* **2019**, *20*, 1791-1797) (301.01 mg, 668.12 µmol) in anhydrous CH_2Cl_2 (4 mL) freshly activated 4Å MS powder (0.100 g) was added and stirred for 20 min under nitrogen atmosphere. The solution was then cooled to -50 ºC, AgOTf (17.17 mg, 66.81 µmol) and Au-phosphite (**3**) (58.75 mg, 66.81 µmol) were added to the solution and stirred at -50 ºC for 2 h. After the completion the reaction was quenched by Et_3N (100 µ L) and filtered off through a bed of Celite. The filtrate was concentrated in vacuo, and resulting residue was purified by column chromatography (ethyl acetate/hexane as mobile phase) to afford the disaccharide **34** as a pale yellow sticky gum (495 mg, 84 % yield). $[\alpha]_D^{25}$ = +9.0 (*c* = 0.17, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2928, 2864, 1503, 1367, 1081, 1029, 828; ^1H NMR (400 MHz, $CDCl_3$): δ 7.54 (dt, *J* = 6.6, 2.6 Hz, 2H), 7.47 – 7.40 (m, 9H), 7.36 – 7.29 (m, 14H), 6.97 – 6.93 (m, 2H), 6.86 – 6.82 (m, 2H), 5.59 (s, 1H), 5.44 (d, *J* = 2.0 Hz, 1H), 5.00 (d, *J* = 11.3 Hz, 1H), 4.97 (dd, *J* = 7.4, 3.6 Hz, 2H), 4.91 (d, *J* = 2.8 Hz, 1H), 4.88 (d, *J* = 2.4 Hz, 1H), 4.85 (d, *J* = 11.8 Hz, 1H), 4.75 (d, *J* = 11.8 Hz, 1H), 4.70 (dd, *J* = 11.3, 3.2 Hz, 2H), 4.29 (td, *J* = 9.9, 4.9 Hz, 1H), 4.21 – 4.15 (m, 2H), 4.09 (dd, *J* = 9.1, 3.1 Hz, 1H), 4.04 (dd, *J* = 10.2, 4.9 Hz, 1H), 3.88 (dd, *J* = 9.4, 6.2

Hz, 1H), 3.80 (s, 3H), 3.69 – 3.62 (m, 4H), 1.34 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 154.9, 150.5, 139.0, 138.6, 138.5, 138.4, 137.7, 129.0, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 126.2, 126.2, 117.7, 117.7, 114.7, 114.7, 101.3, 98.5, 96.7, 82.5, 80.1, 79.6, 78.8, 78.4, 75.5, 75.3, 75.2, 73.3, 72.4, 69.1, 69.0, 63.0, 55.8, 18.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{54}H_{56}O_{11}Na$ 903.3720; Found: 903.3719.

***p*-methoxyphenyl 2-*O*-(2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl)-3,4-di-*O*-benzyl-α-D-rhamnopyranoside (29):** Benzylidene compound **34** (500 mg, 567.52 µmol) was dissolved in MeCN (5 mL). Freshly activated 4Å MS powder (0.100 g) was added and stirred for 20 min under nitrogen atmosphere. $NaBH_3CN$ (178.32 mg, 2.84 mmol) was added at 25 ºC and stirred for 5 mins. I_2 (504.14 mg, 1.99 mmol) was added portion wise to the reaction mixture and it was stirred at 25 ºC for 1 h. After completion indicated by TLC, the reaction mixture was filtered through a bed of Celite. The filtrate was diluted with CH_2Cl_2 (25 mL) and washed with satd. $NaHCO_3$ solution (2x25 mL), brine solution (2x25 mL), dried over Na_2SO_4 and concentrated in vacuo. The resultant crude was purified by silica gel column chromatography (ethyl acetate/hexane as mobile phase) to afford the disaccharide acceptor **29** as a colorless sticky gum (402 mg, 80 % yield). $[\alpha]_D^{25}$ = +7.0 (*c* = 0.1, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3436, 2927, 1504, 1368, 1176, 1081, 986, 826; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.36 (m, 8H), 7.36 – 7.28 (m, 17H), 6.95 (d, *J* = 9.0 Hz, 2H), 6.83 (d, *J* = 9.0 Hz, 2H), 5.41 (d, *J* = 2.1 Hz, 1H), 5.02 (dd, *J* = 7.5, 3.9 Hz, 2H), 4.95 (d, *J* = 10.9 Hz, 1H), 4.87 – 4.80 (m, 2H), 4.79 – 4.71 (m, 2H), 4.68 (dd, *J* = 11.3, 5.1 Hz, 2H), 4.51 (d, *J* = 12.2 Hz, 1H), 4.41 (d, *J* = 12.1 Hz, 1H), 4.24 (t, *J* = 2.6 Hz, 1H), 4.18 – 4.12 (m, 1H), 4.09 (dd, *J* = 9.1, 3.1 Hz, 1H), 3.97 – 3.86 (m, 2H), 3.80 (s, 3H), 3.77 – 3.65 (m, 2H), 3.65 – 3.59 (m, 1H), 3.52 – 3.47 (m, 1H), 3.45 – 3.39 (m, 1H), 2.43 (s, 1H), 1.36 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 155.0, 150.5, 139.0, 138.6, 138.5, 138.4, 138.1, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.1, 128.1, 128.1, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.5, 127.5, 127.5, 117.8, 117.8, 114.7, 114.7, 96.9, 96.6, 80.9, 80.3, 79.8, 78.7, 75.3, 75.2, 74.4, 73.6, 72.7, 72.1, 70.9, 70.5, 69.3, 68.9, 55.8, 18.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{54}H_{58}O_{11}Na$ 905.3877; Found: 905.3857.

***p*-methoxyphenyl-(2-azido-3-*O*-(*tert*-butyldimethylsilyl)-4,6-*O*-benzylidene-2-*deoxy*-β-D-mannopyranosyl)-(1 → 4)-*O*-(2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl)-(1 → 2)-3,4-di-*O*-benzyl-α-D-rhamnopyranoside (28):** Compound **28** was synthesized according to the general

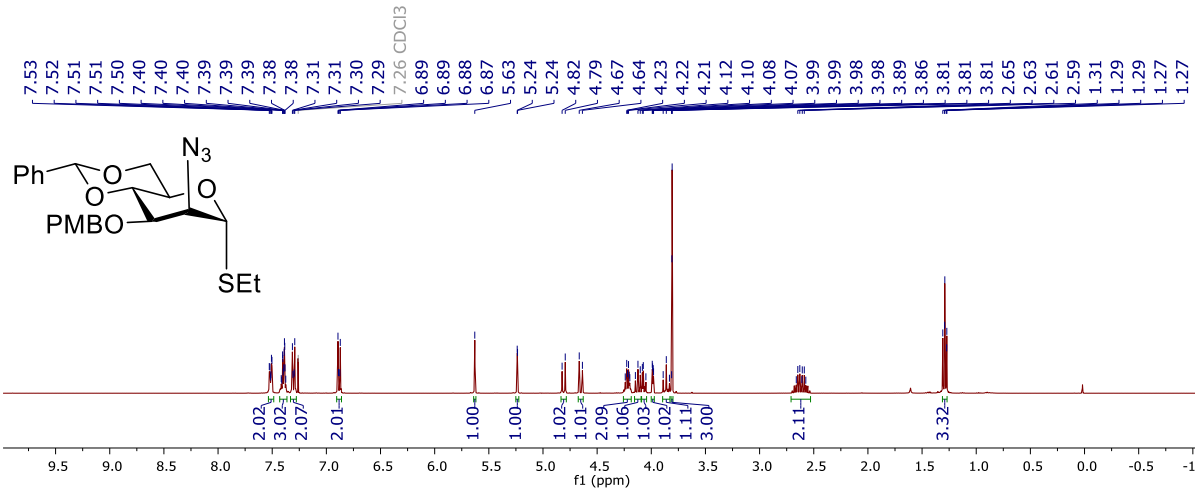
procedure B. $[\alpha]_D^{25}$ = +10.0 (*c* = 0.02, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2933, 2859, 2109, 1264, 1081, 1029, 828; ^1H NMR (400 MHz, $CDCl_3$): δ 7.48 – 7.44 (m, 2H), 7.43 – 7.27 (m, 28H), 6.96 – 6.92 (m, 2H), 6.85 – 6.81 (m, 2H), 5.47 (s, 1H), 5.36 (d, *J* = 1.9 Hz, 1H), 5.04 (d, *J* = 10.8 Hz, 1H), 5.00 (d, *J* = 10.8 Hz, 1H), 4.91 – 4.87 (m, 2H), 4.82 – 4.77 (m, 3H), 4.74 (d, *J* = 10.7 Hz, 1H), 4.62 (d, *J* = 11.8 Hz, 1H), 4.60 – 4.54 (m, 2H), 4.26 (d, *J* = 12.1 Hz, 1H), 4.20 (dt, *J* = 6.1, 2.3 Hz, 2H), 4.07 (dd, *J* = 9.3, 3.1 Hz, 1H), 4.05 – 3.99 (m, 2H), 3.97 (d, *J* = 9.5 Hz, 1H), 3.86 (d, *J* = 6.2 Hz, 1H), 3.79 (s, 3H), 3.71 (d, *J* = 9.1 Hz, 1H), 3.68 (d, *J* = 3.6 Hz, 1H), 3.66 – 3.59 (m, 2H), 3.57 (d, *J* = 3.7 Hz, 1H), 3.55 (d, *J* = 4.1 Hz, 1H), 3.21 (dd, *J* = 12.3, 2.1 Hz, 2H), 3.02 – 2.95 (m, 1H), 1.36 (d, *J* = 6.2 Hz, 3H), 0.90 (s, 9H), 0.07 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 155.0, 150.5, 139.4, 138.7, 138.6, 138.6, 137.8, 137.4, 129.1, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.5, 127.5, 127.3, 127.3, 126.3, 126.3, 117.8, 117.8, 114.7, 114.7, 102.0, 100.0, 97.4, 96.7, 80.3, 80.1, 79.5, 79.0, 78.7, 77.2, 75.5, 75.2, 75.0, 73.7, 73.1, 72.3, 72.1, 69.9, 69.0, 68.5, 68.1, 67.3, 66.5, 55.8, 25.8, 25.8, 25.8, 18.3, 18.1, -4.2, -4.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{73}H_{85}N_3O_{15}SiNa$ 1294.5647; Found: 1294.5646.

***p*-methoxyphenyl-(2-acetamido-3-*O*-(*tert*-butyldimethylsilyl)-4,6-*O*-benzylidene-2-*deoxy*-β-D-mannopyranosyl)-(1 → 4)-*O*-(2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl)-(1 → 2)-3,4-di-*O*-benzyl-α-D-rhamnopyranoside (27):** To a solution of trisaccharide **28** (50 mg, 39.29 μmol) in pyridine: H_2O (10:1) (1 mL) at 25 °C was added Et_3N (164.29 μL, 1.18 mmol) and 1,3-propanedithiol (137.79 μL, 1.38 mmol) sequentially. The reaction was stirred for 6h at 25 °C. After completion indicated by TLC analysis, Azeotropic removal of the solvents with PhMe (3 x10 mL) gave the corresponding free amine compound as a pale-yellow residue. The isolated amine compound was used immediately in the next step of the reaction without further purification. The residue was dissolved in anhydrous pyridine (800 μl) and Ac_2O (6.67 μL, 70.59 μmol) was added dropwise and stirred at 25 °C for 2 h. After completion of the starting material he reaction mixture was diluted with ethyl acetate (25 mL). The organic layer was successively washed with 1N HCl solution (2x20 mL), saturated $NaHCO_3$ solution (2x20 mL) and brine solution (20 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified with silica gel column chromatography (Ethyl acetate/hexane as mobile phase) to furnish the desired trisaccharide **27** as a pale yellow sticky gum (41 mg, 81 % over two steps). $[\alpha]_D^{25}$ = +16.7 (*c* = 0.03, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2924, 2859, 1663, 1457, 1239, 1096, 1034, 841; ^1H NMR

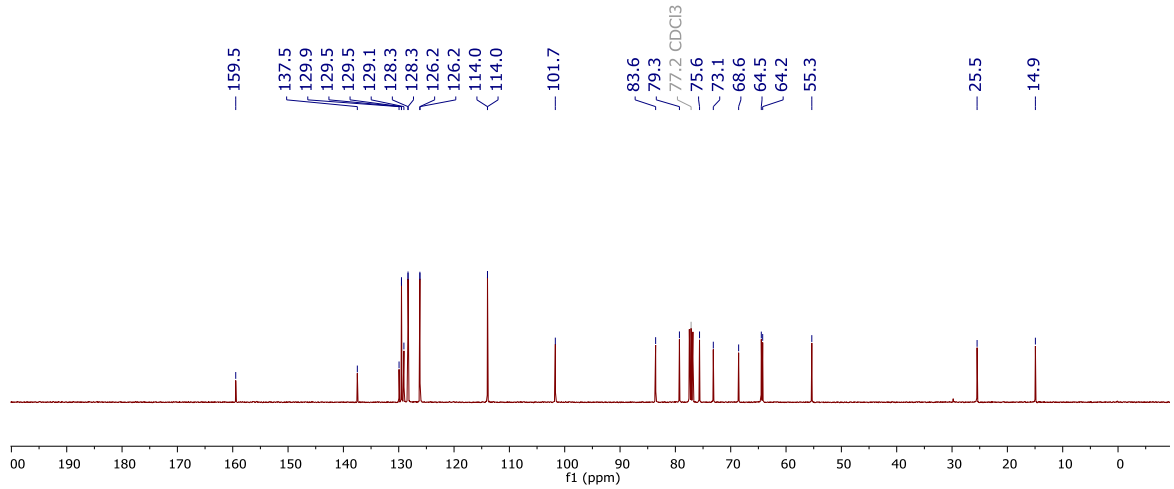
(400 MHz, $CDCl_3$): δ 7.48 – 7.41 (m, 4H), 7.40 – 7.27 (m, 24H), 7.25 – 7.21 (m, 3H), 6.94 – 6.89 (m, 2H), 6.83 – 6.78 (m, 2H), 5.45 (s, 1H), 5.37 (d, *J* = 1.9 Hz, 1H), 4.98 (d, *J* = 11.3 Hz, 2H), 4.93 (d, *J* = 3.8 Hz, 1H), 4.87 (d, *J* = 11.6 Hz, 1H), 4.76 (s, 2H), 4.73 (d, *J* = 2.5 Hz, 1H), 4.70 (d, *J* = 3.3 Hz, 1H), 4.63 – 4.55 (m, 3H), 4.44 (ddd, *J* = 9.9, 4.7, 1.7 Hz, 1H), 4.33 (d, *J* = 12.0 Hz, 1H), 4.16 (dd, *J* = 3.3, 2.0 Hz, 1H), 4.13 – 4.00 (m, 4H), 3.94 – 3.83 (m, 2H), 3.78 (s, 3H), 3.68 – 3.60 (m, 3H), 3.58 (dd, *J* = 9.5, 3.7 Hz, 1H), 3.43 – 3.33 (m, 2H), 3.22 (dd, *J* = 11.1, 1.7 Hz, 1H), 3.09 (dt, *J* = 9.8, 4.8 Hz, 1H), 1.79 (s, 3H), 1.34 (d, *J* = 6.2 Hz, 3H), 0.85 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.1, 155.0, 150.5, 139.7, 138.6, 138.6, 138.5, 138.0, 137.4, 129.0, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.1, 127.9, 127.9, 127.8, 127.7, 127.6, 127.4, 127.4, 127.4, 126.6, 126.6, 126.2, 126.2, 117.8, 117.8, 114.7, 114.7, 102.0, 100.0, 97.5, 96.9, 80.4, 80.2, 80.1, 79.8, 78.8, 75.9, 75.4, 75.3, 74.8, 73.6, 73.1, 72.3, 70.6, 70.1, 68.9, 68.8, 68.1, 67.1, 55.8, 53.8, 25.7, 25.7, 25.7, 23.4, 18.4, 18.2, -4.8, -4.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{75}H_{89}NO_{16}SiNa$ 1310.5848; Found: 1310.5875.

2.10. NMR Spectral charts

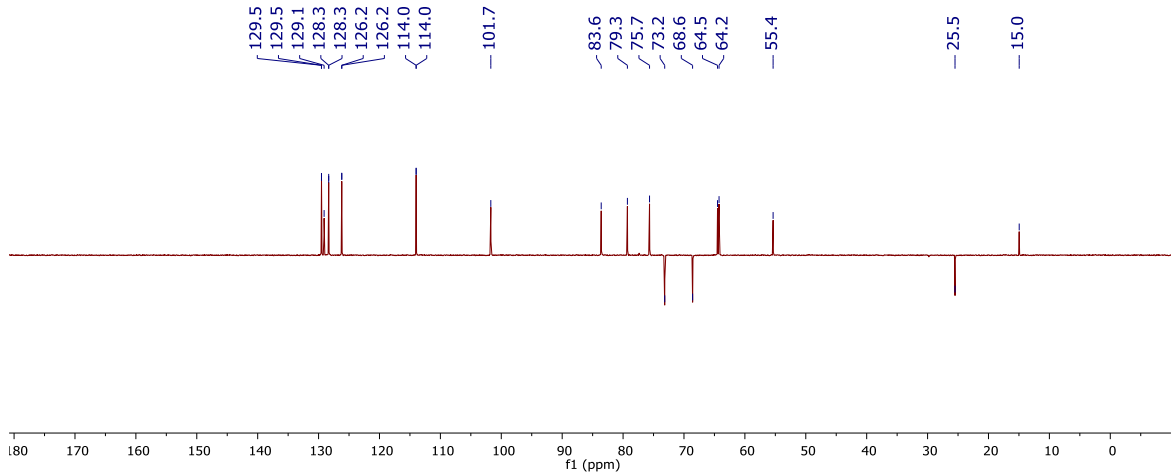
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **12c**



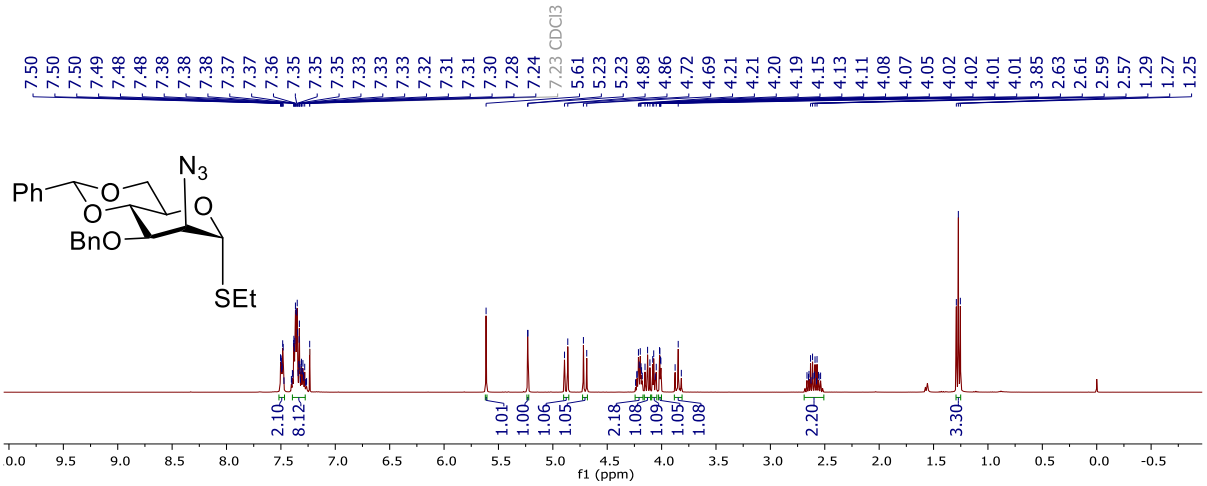
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **12c**



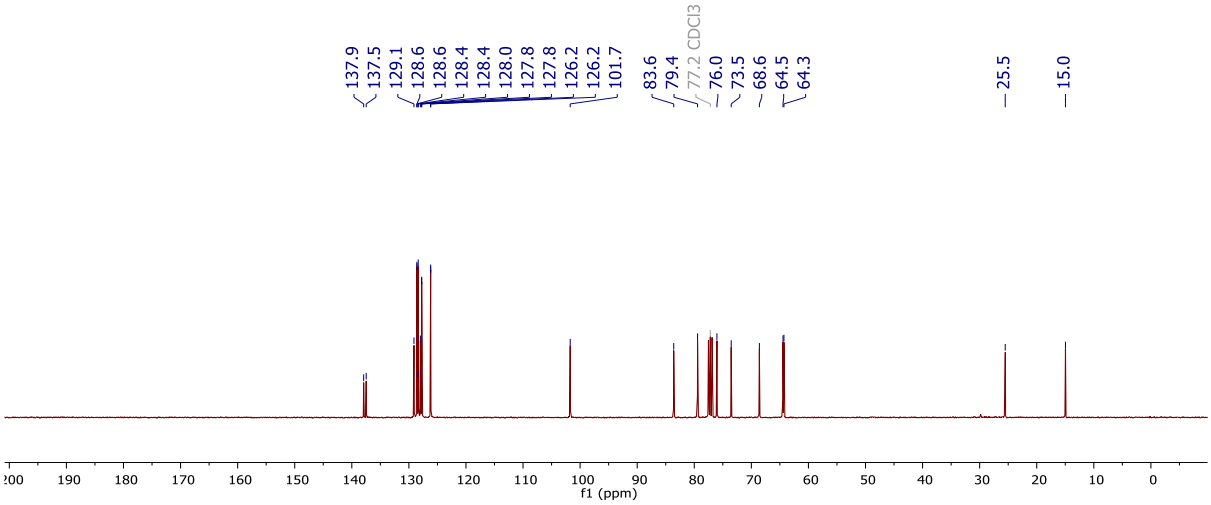
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **12c**



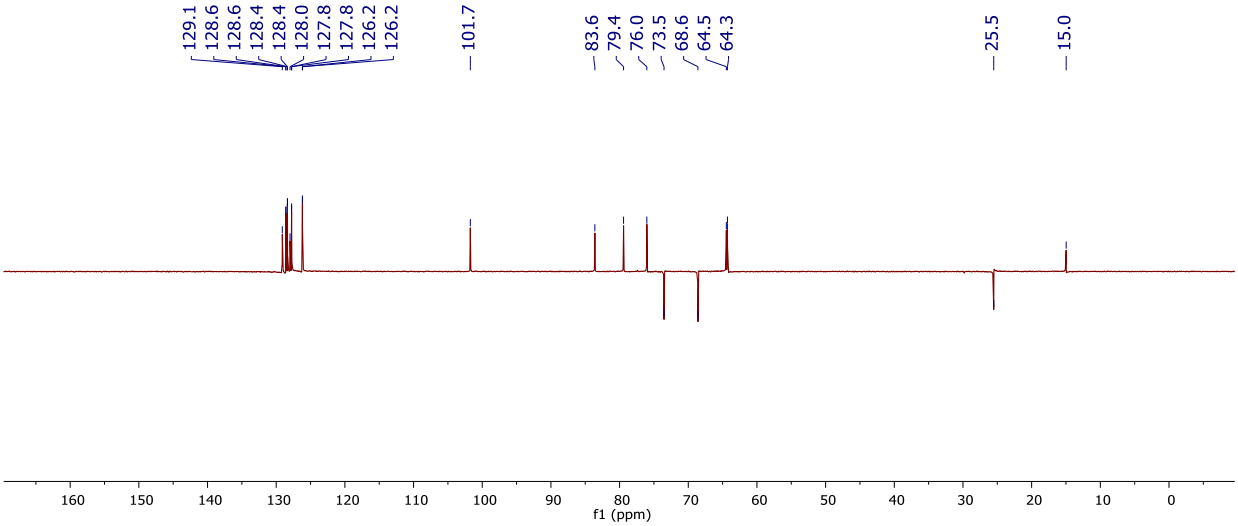
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **12d**



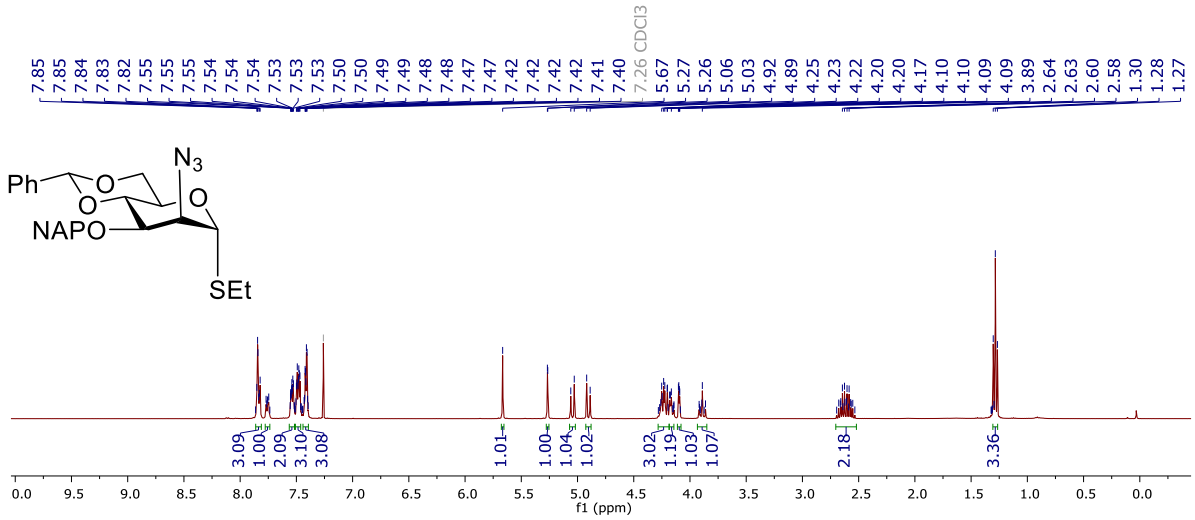
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **12d**



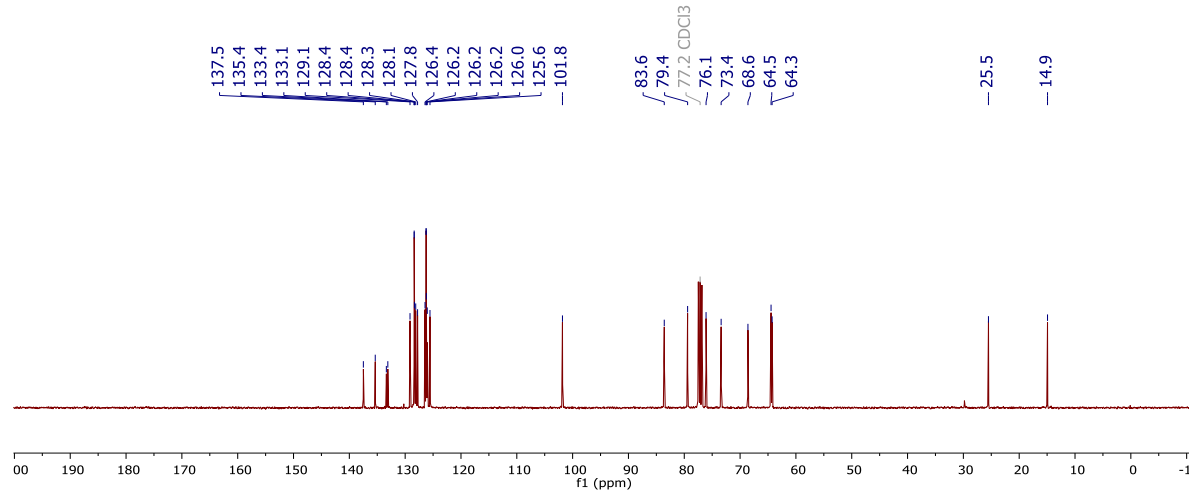
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **12d**



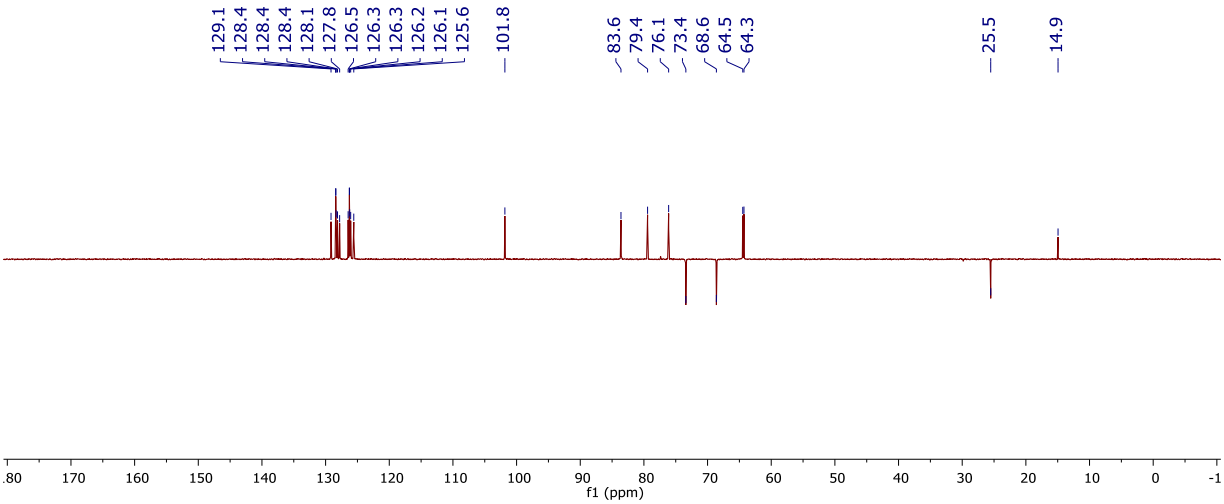
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **12e**



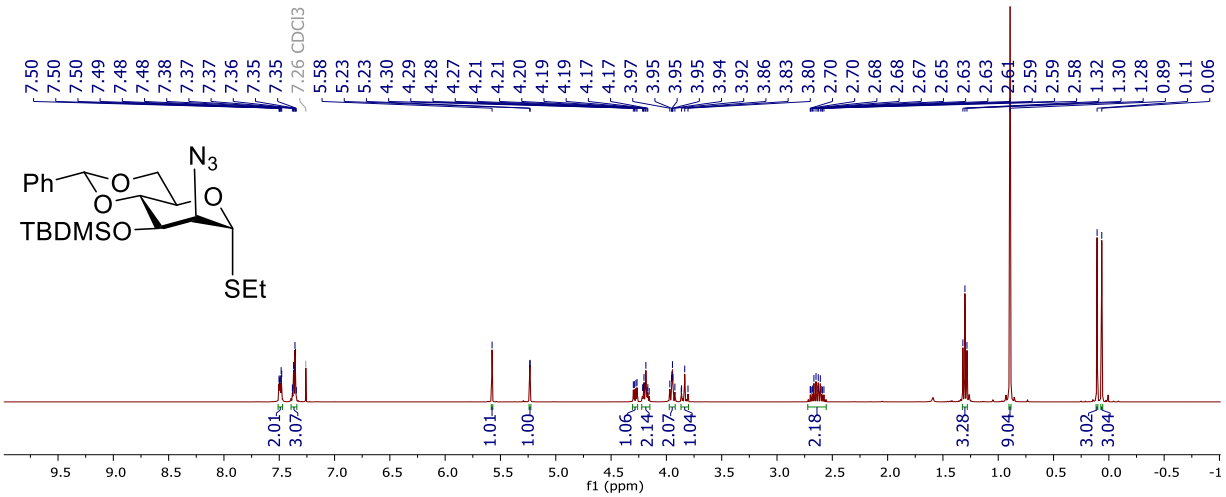
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **12e**



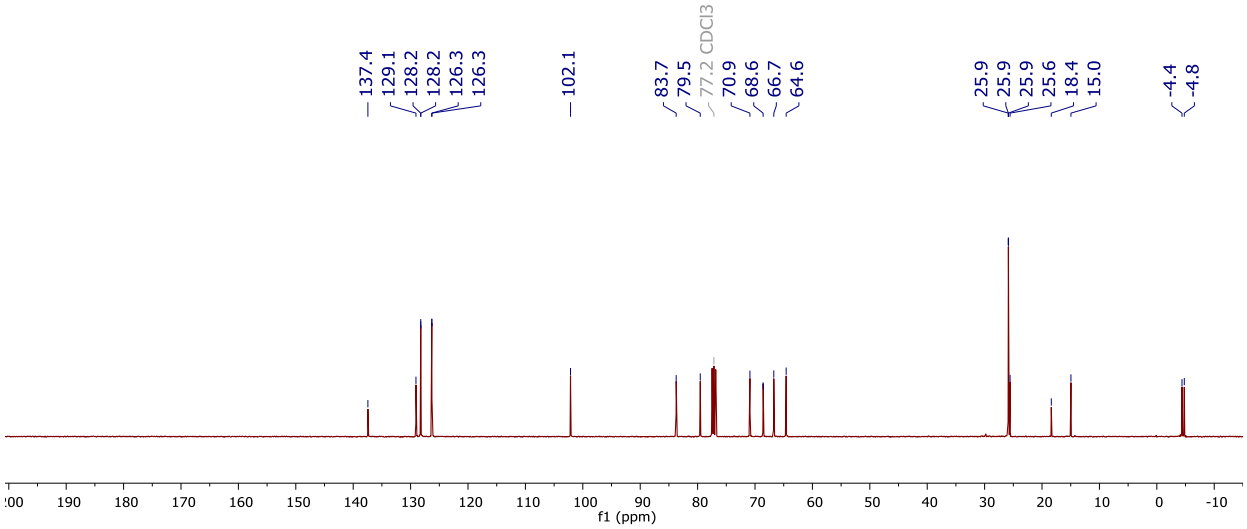
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **12e**



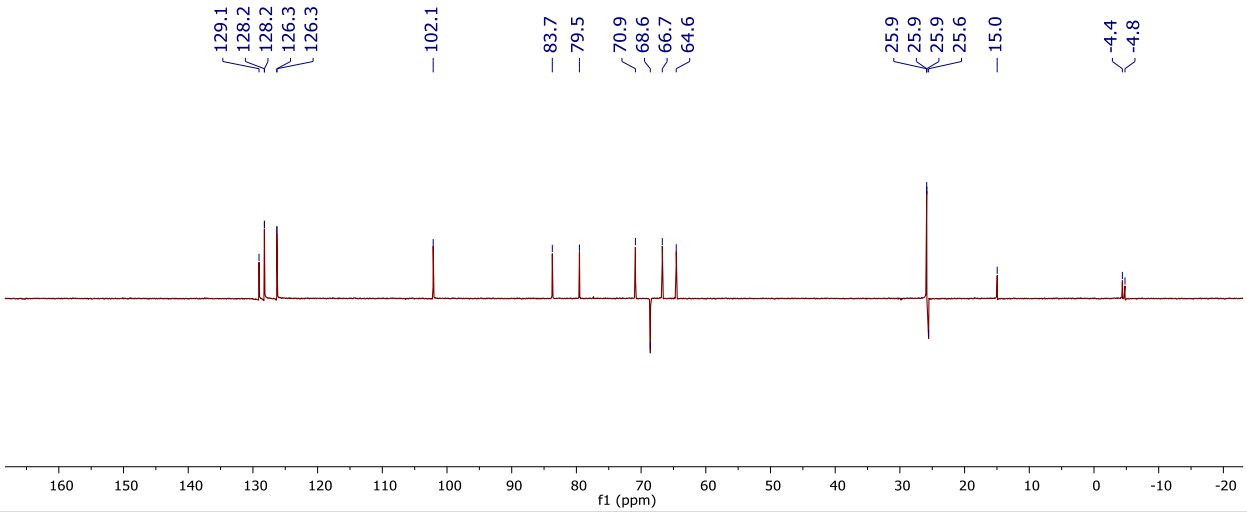
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **12f**



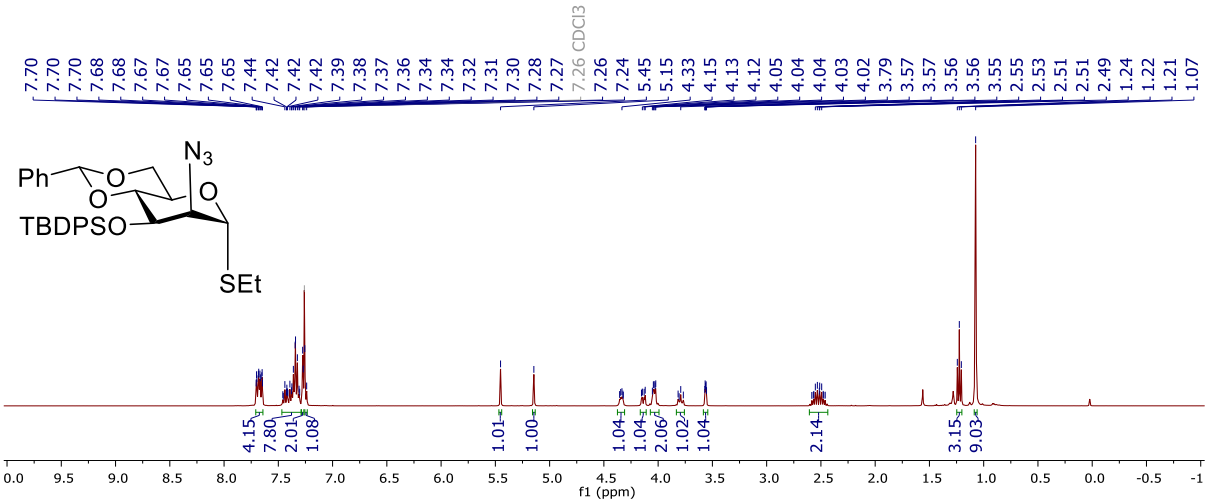
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **12f**



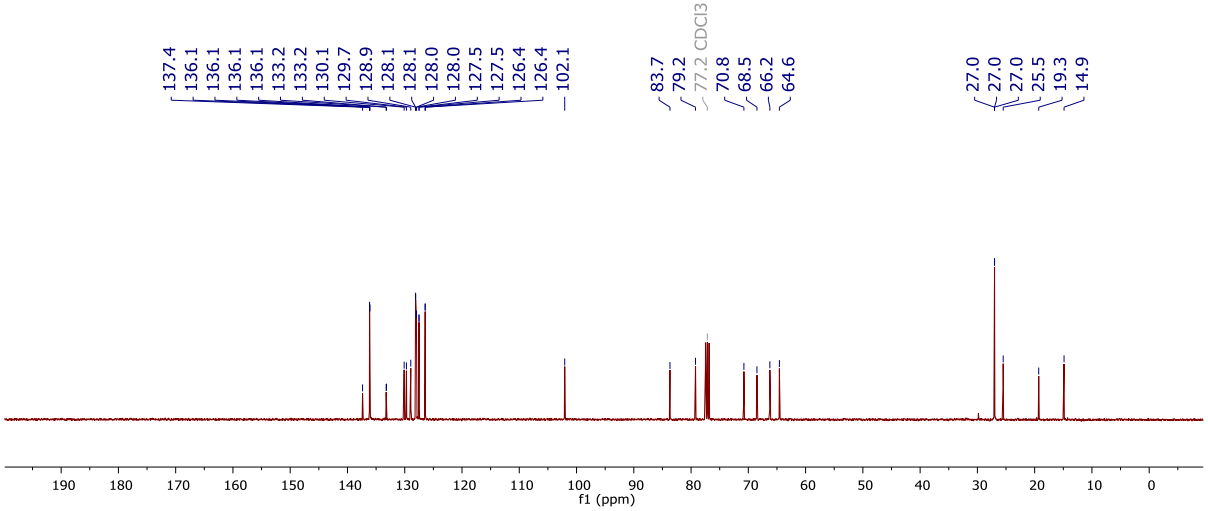
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **12f**



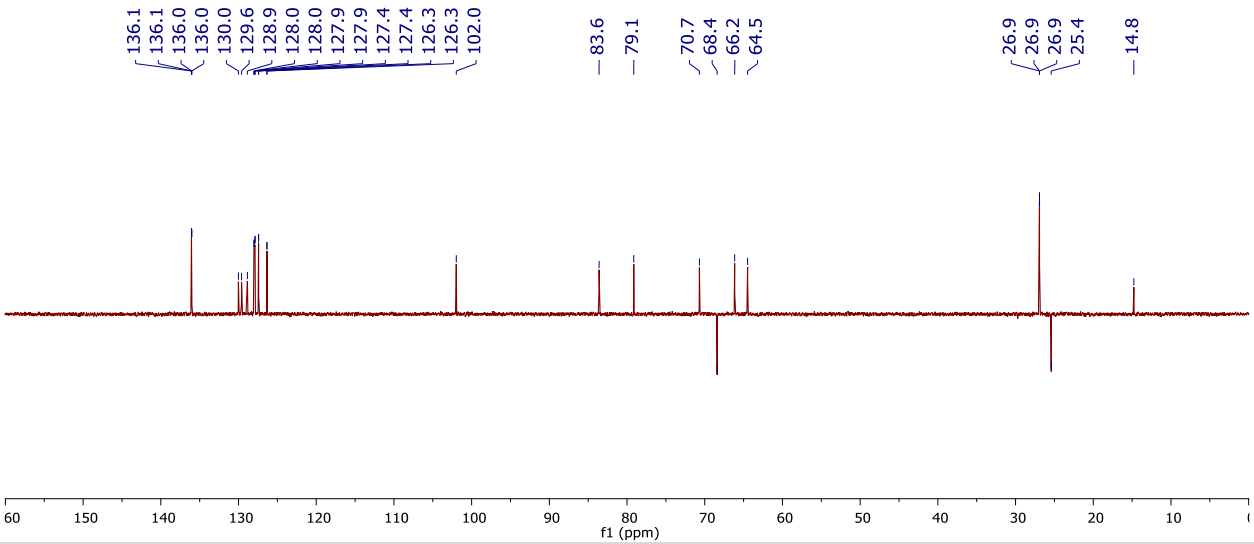
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **12g**



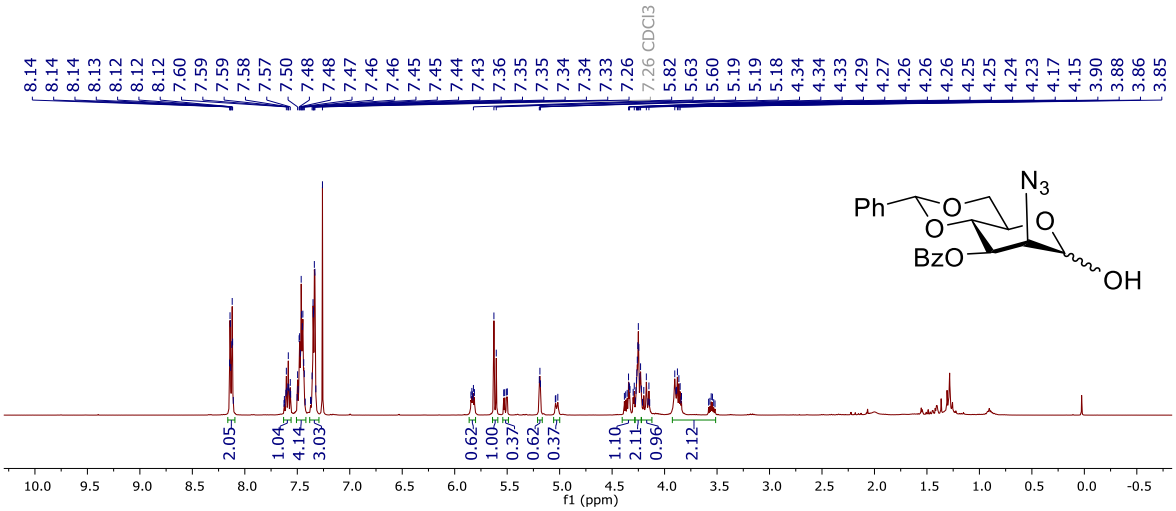
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **12g**



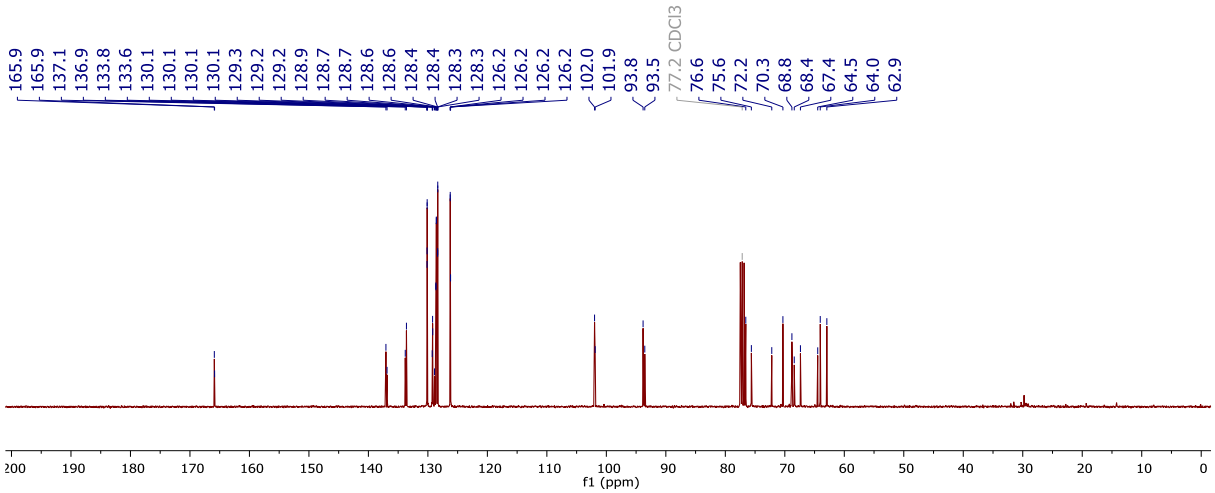
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **12g**



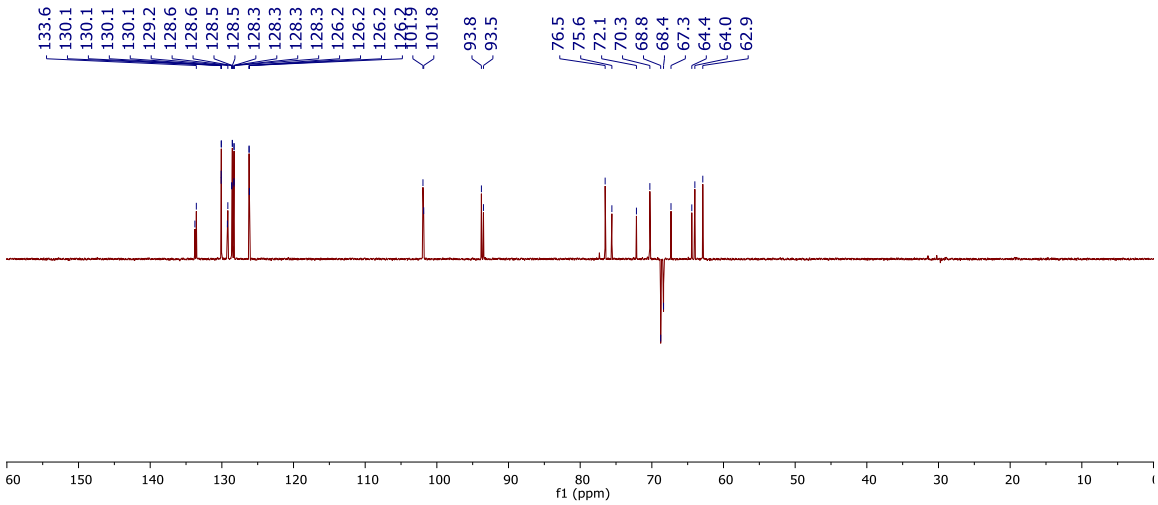
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **13a**



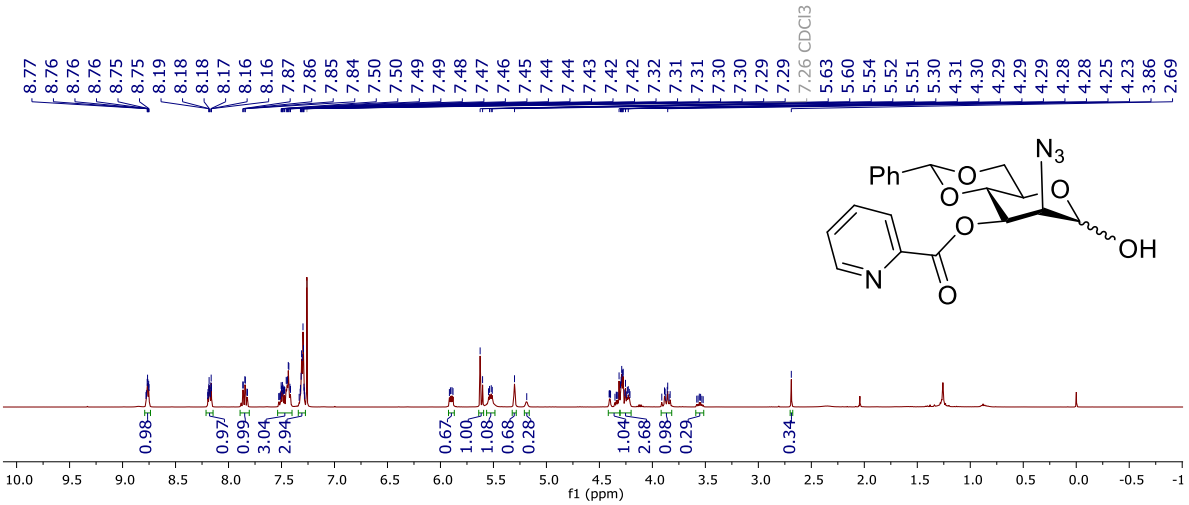
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **13a**



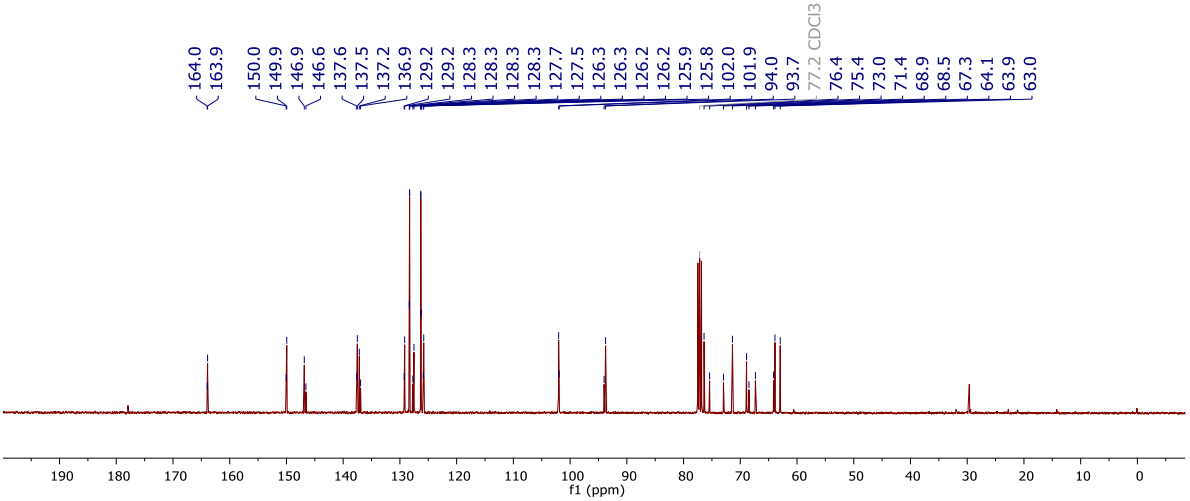
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **13a**



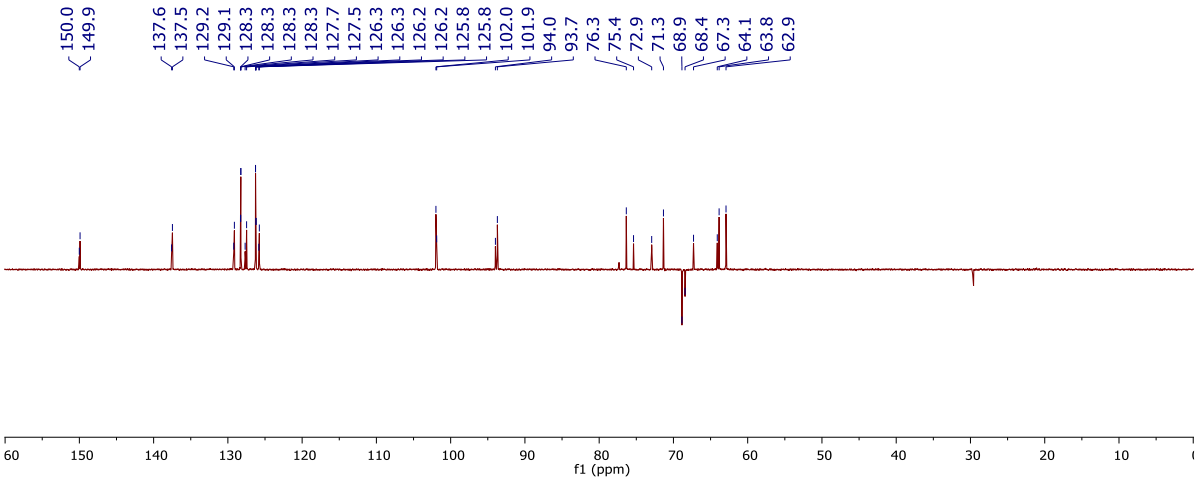
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **13b**



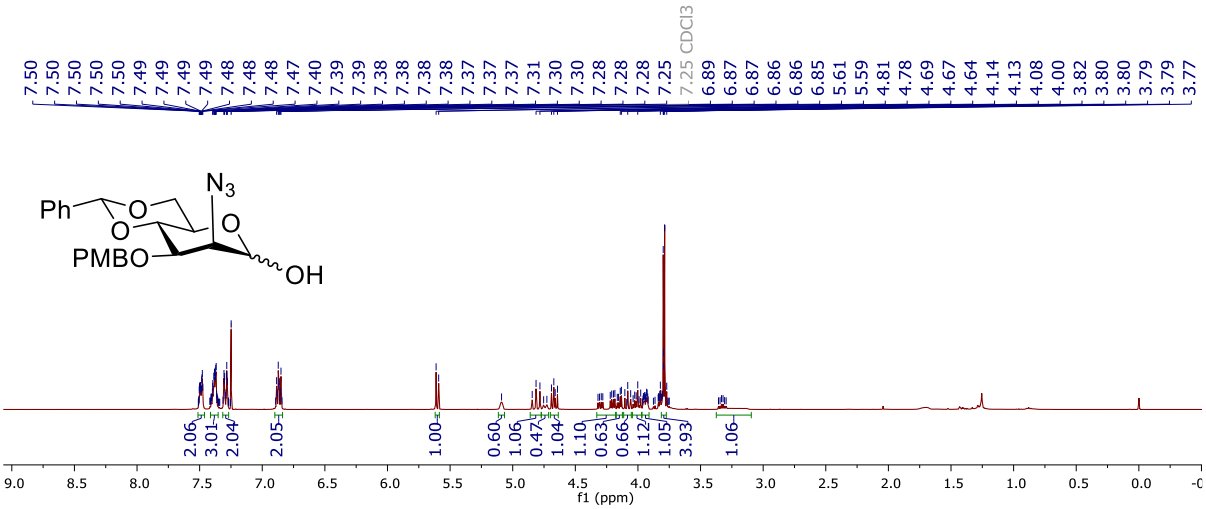
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **13b**



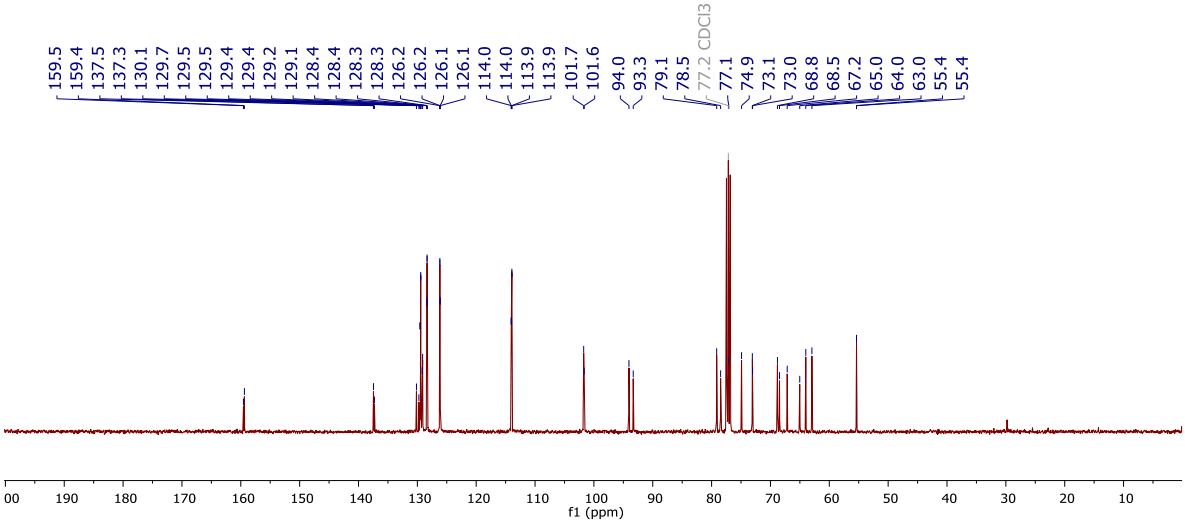
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **13b**



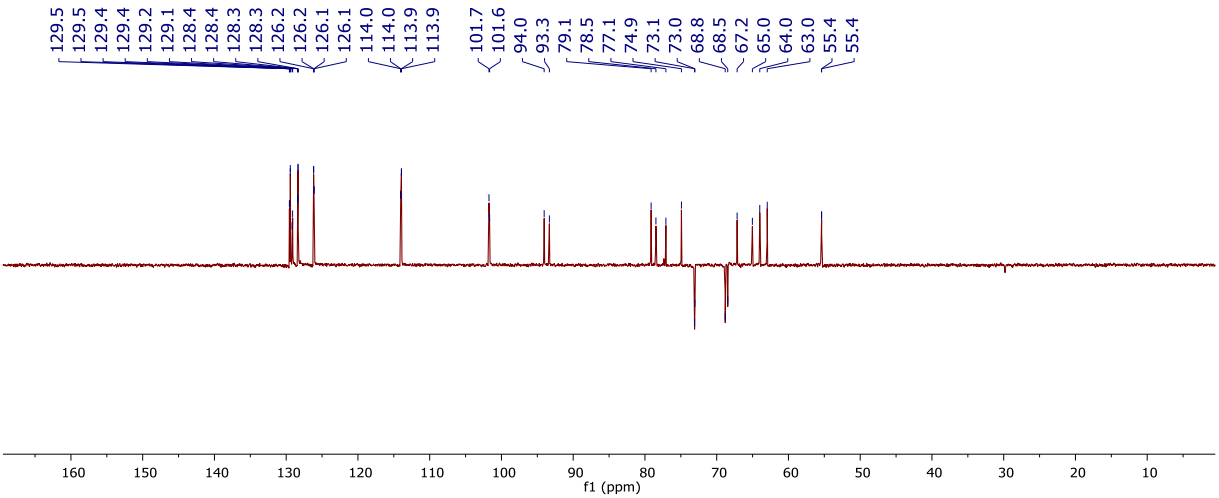
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **13c**



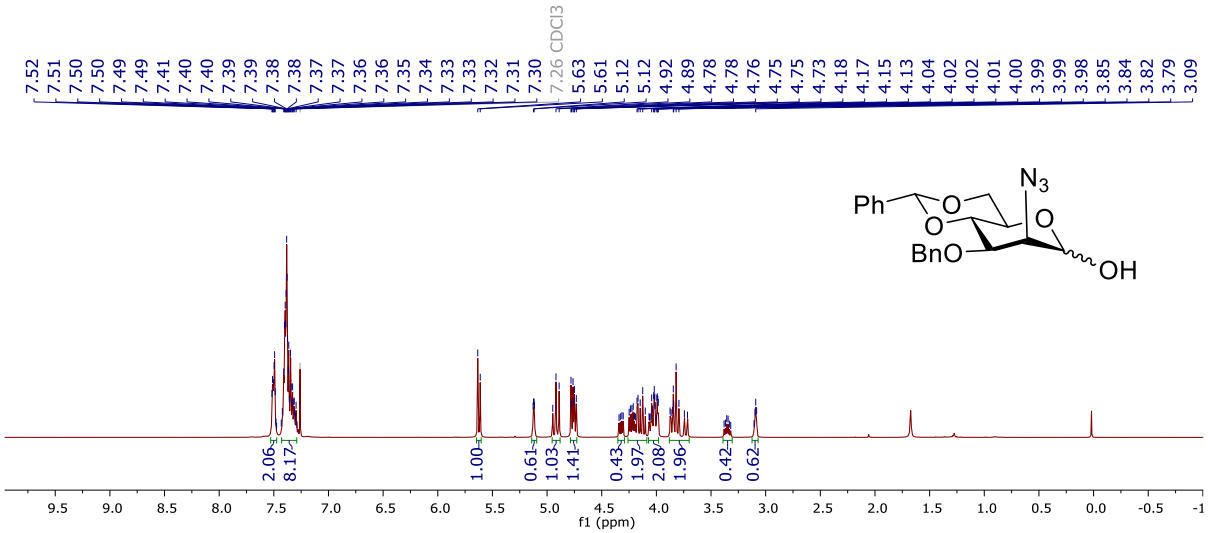
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **13c**



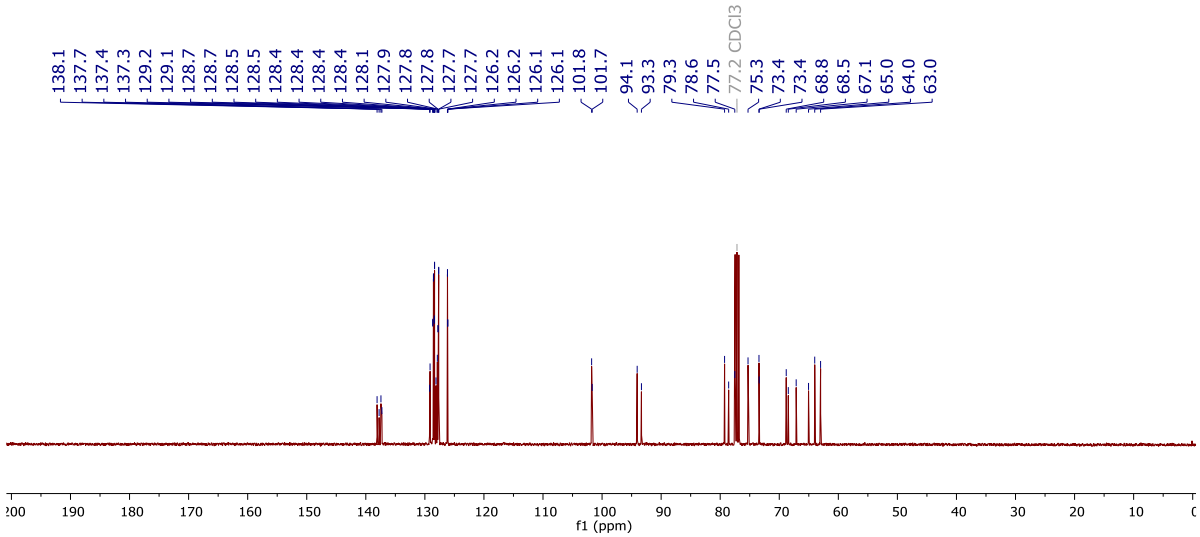
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **13c**



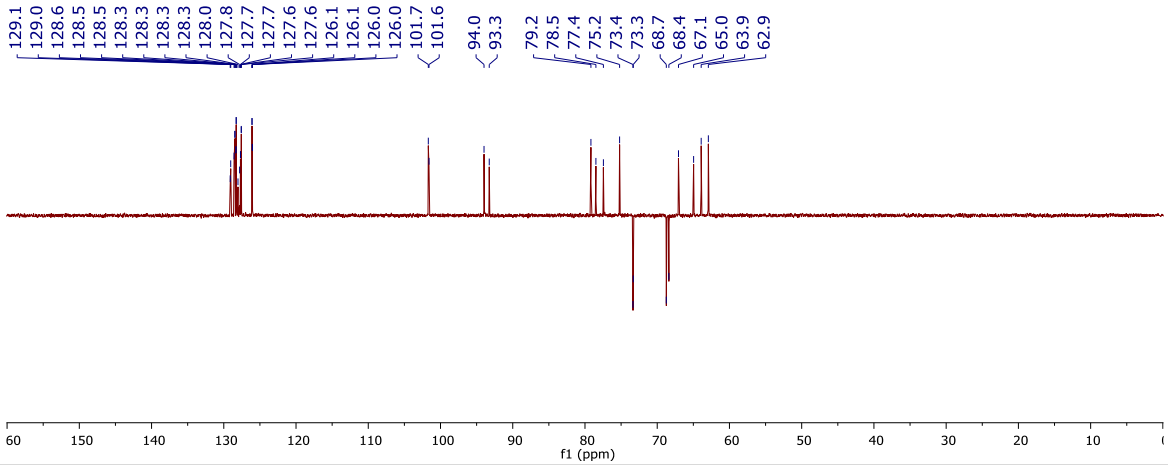
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **13d**



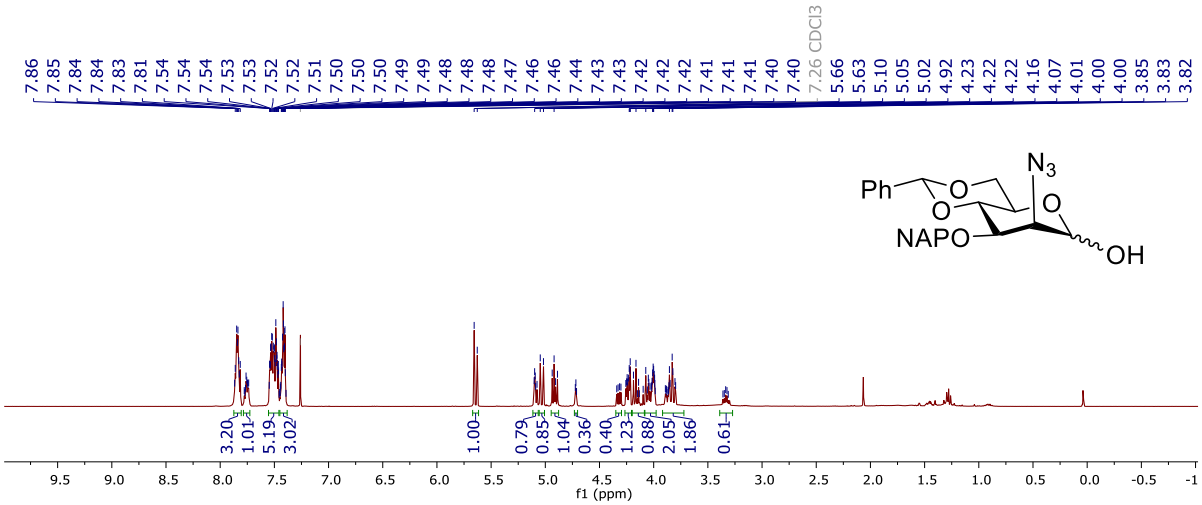
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **13d**



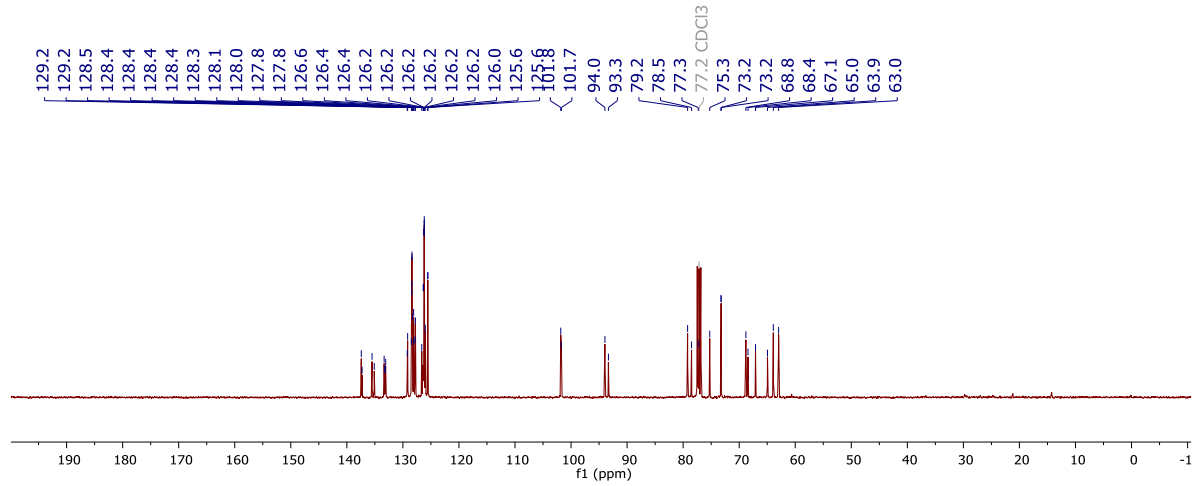
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **13d**



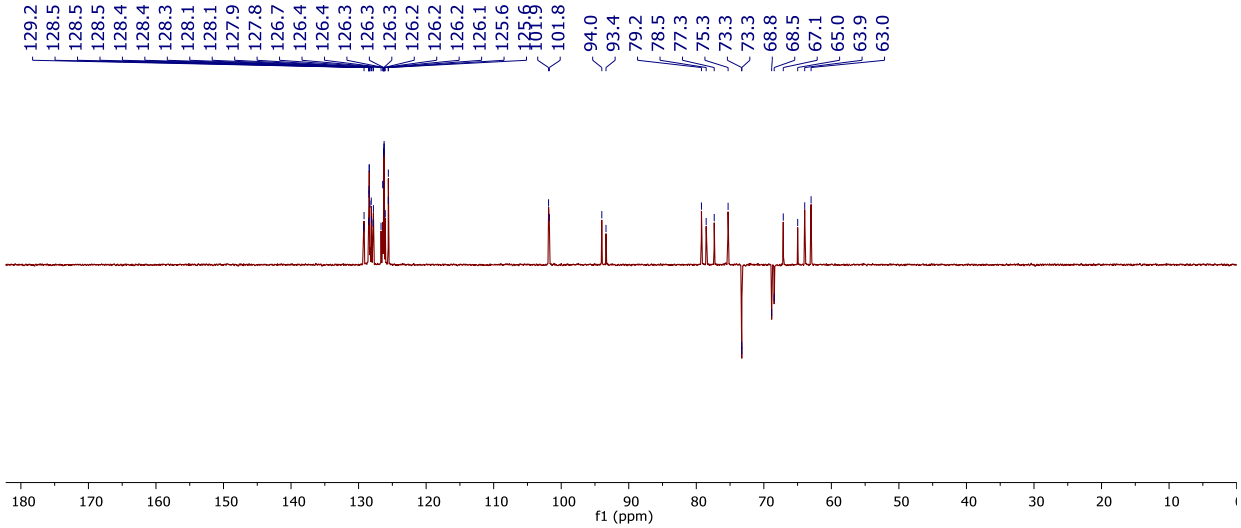
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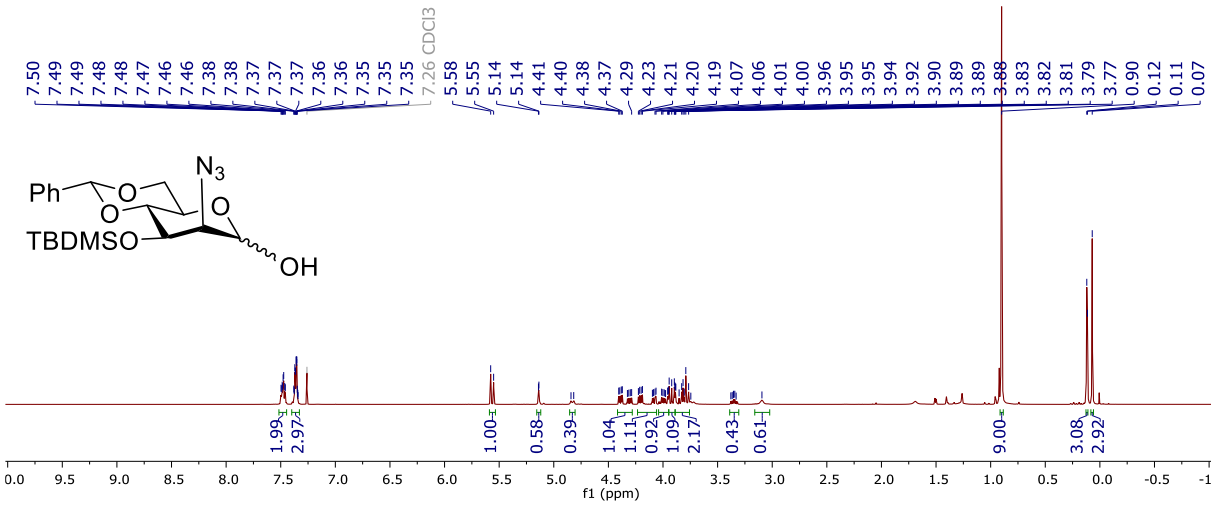
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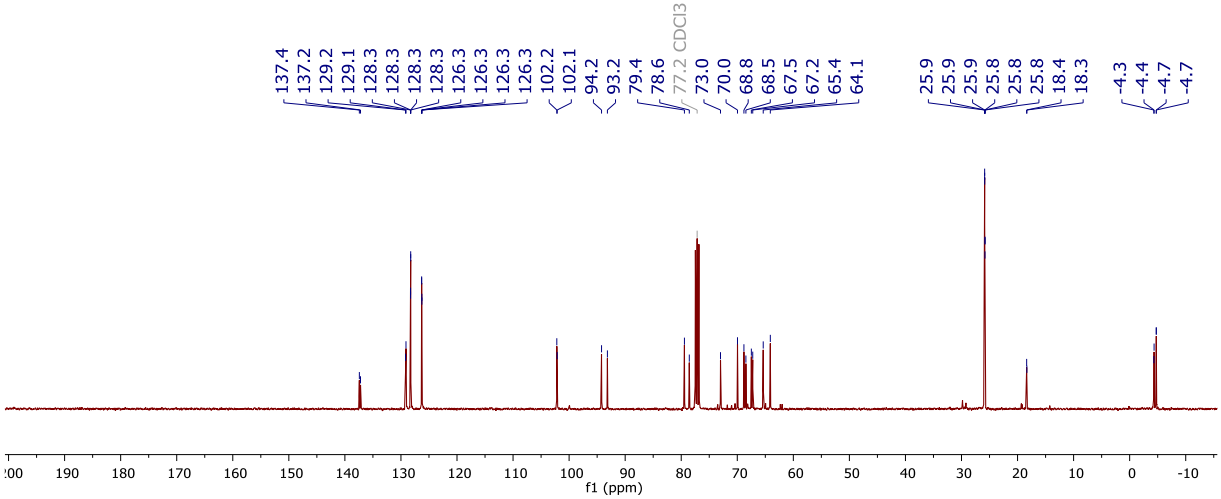
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **13e**



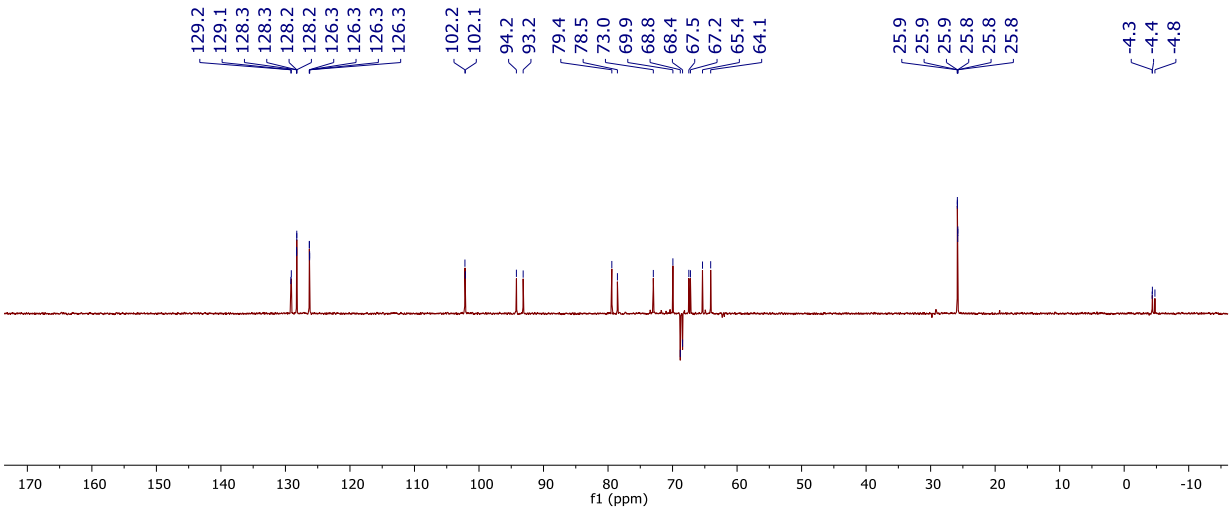
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **13f**



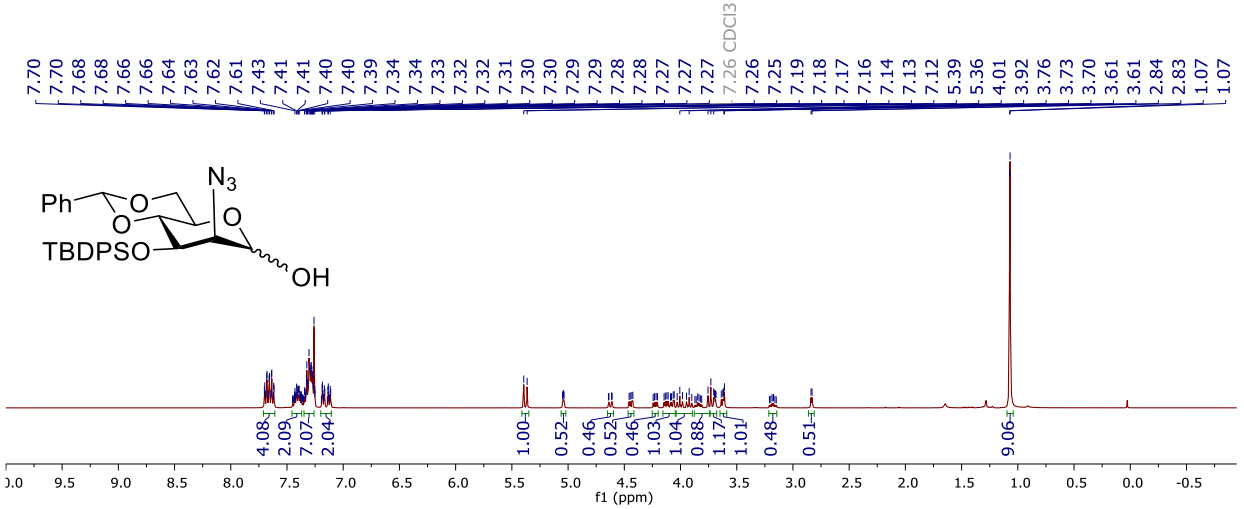
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **13f**



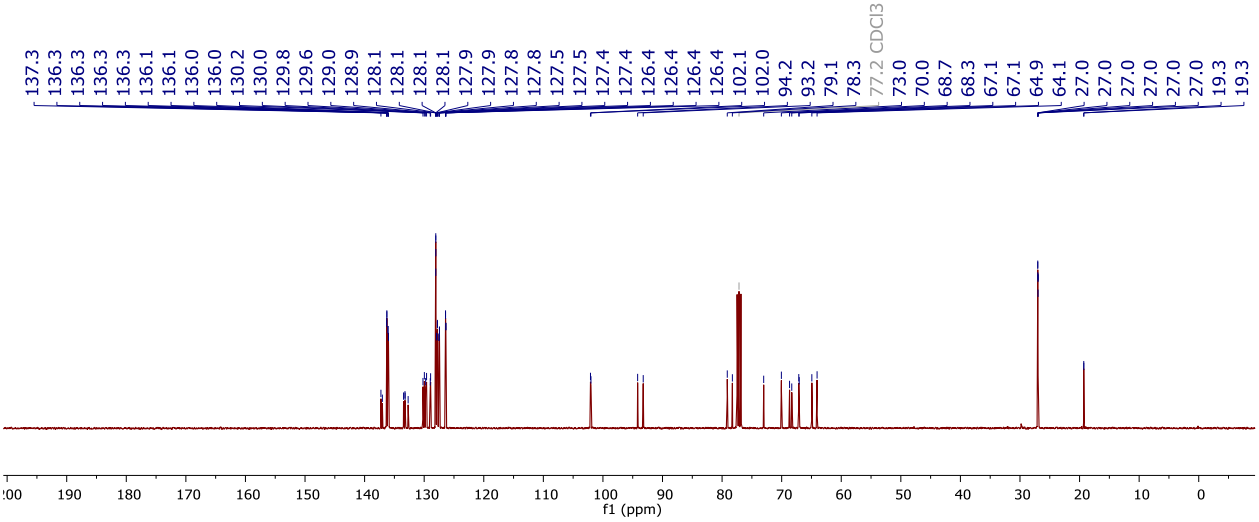
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **13f**



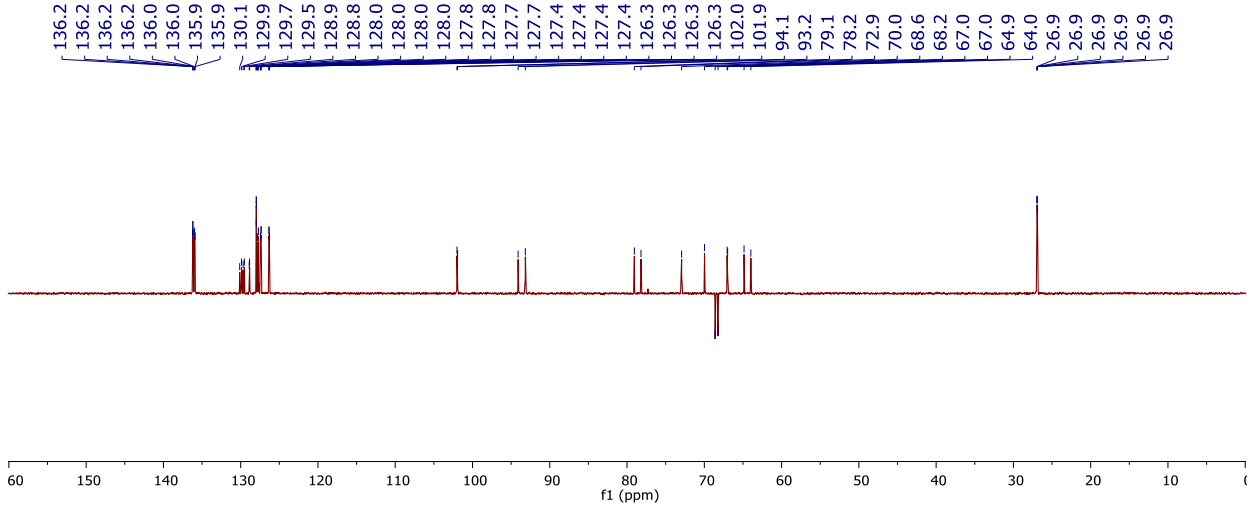
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **13g**



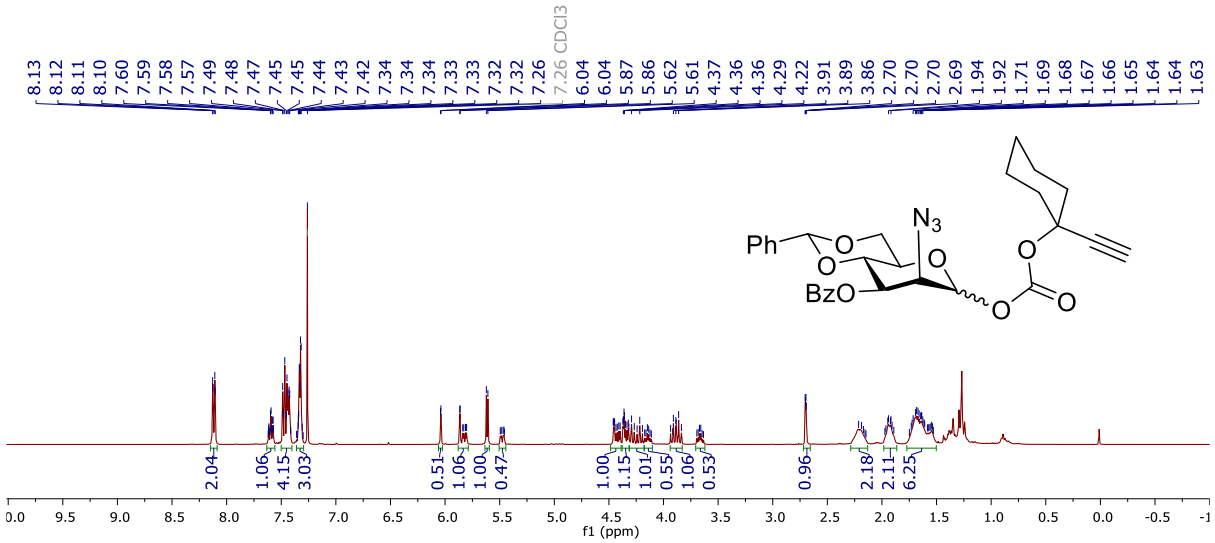
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **13g**



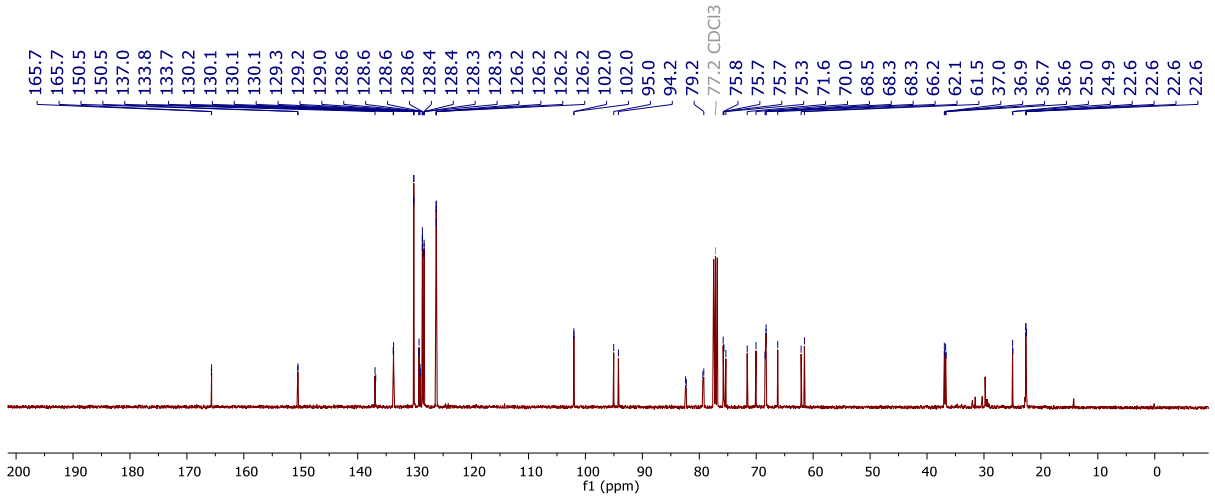
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **13g**



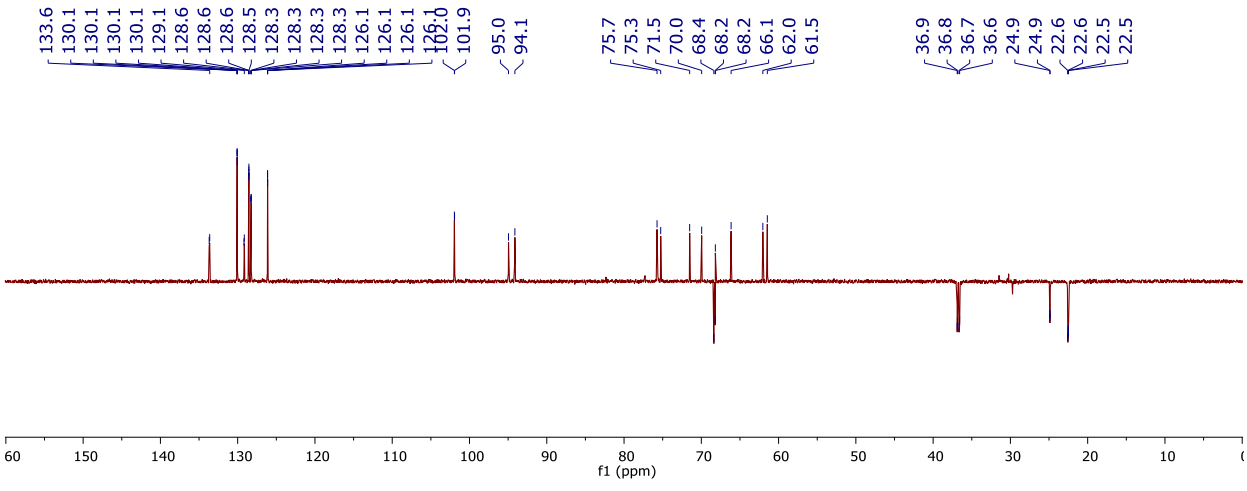
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **14a**



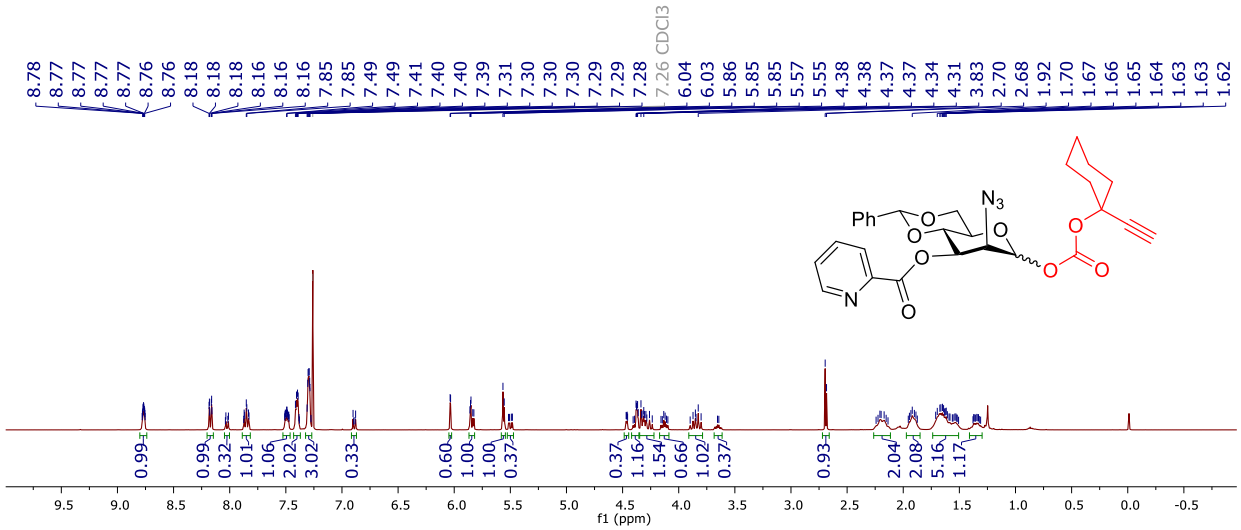
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **14a**



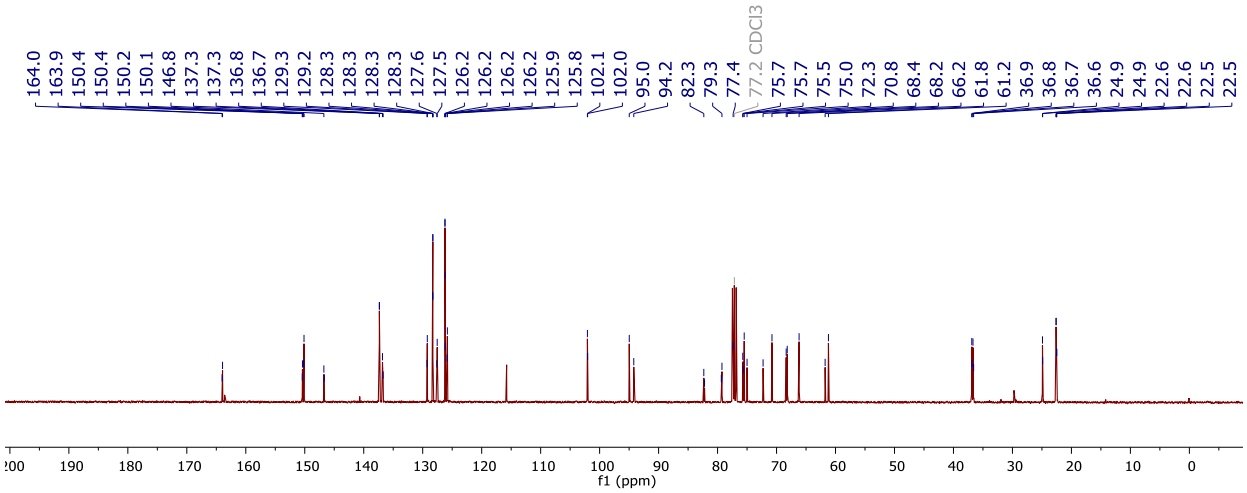
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **14a**



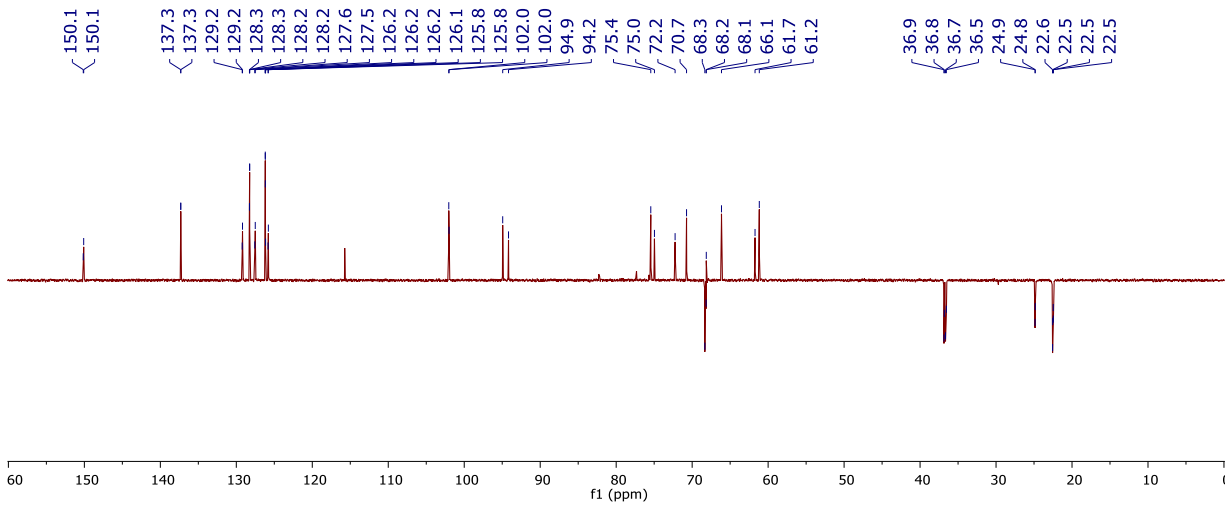
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **14b**



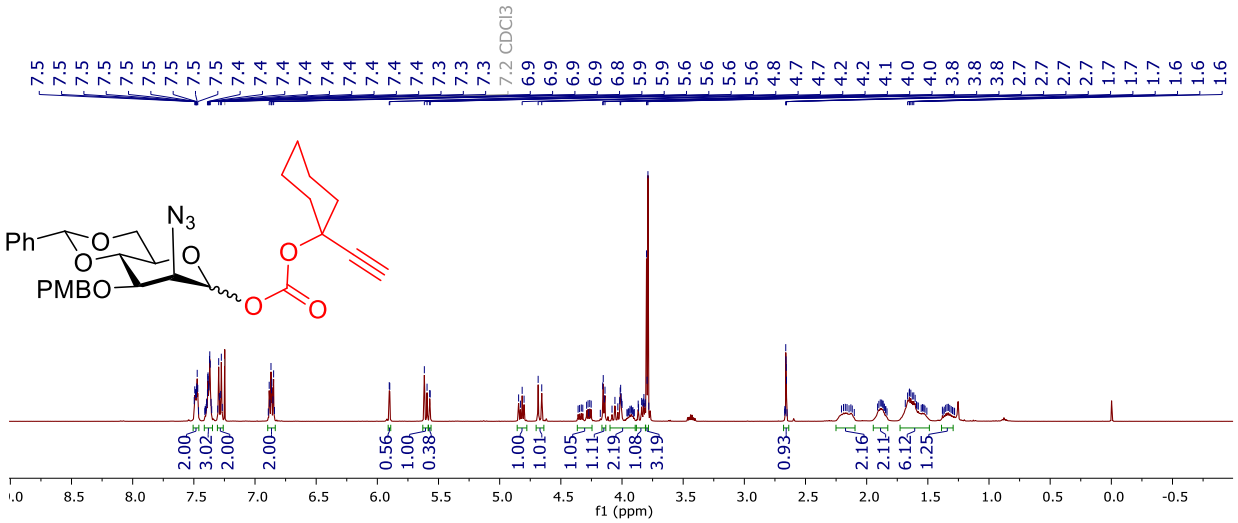
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **14b**



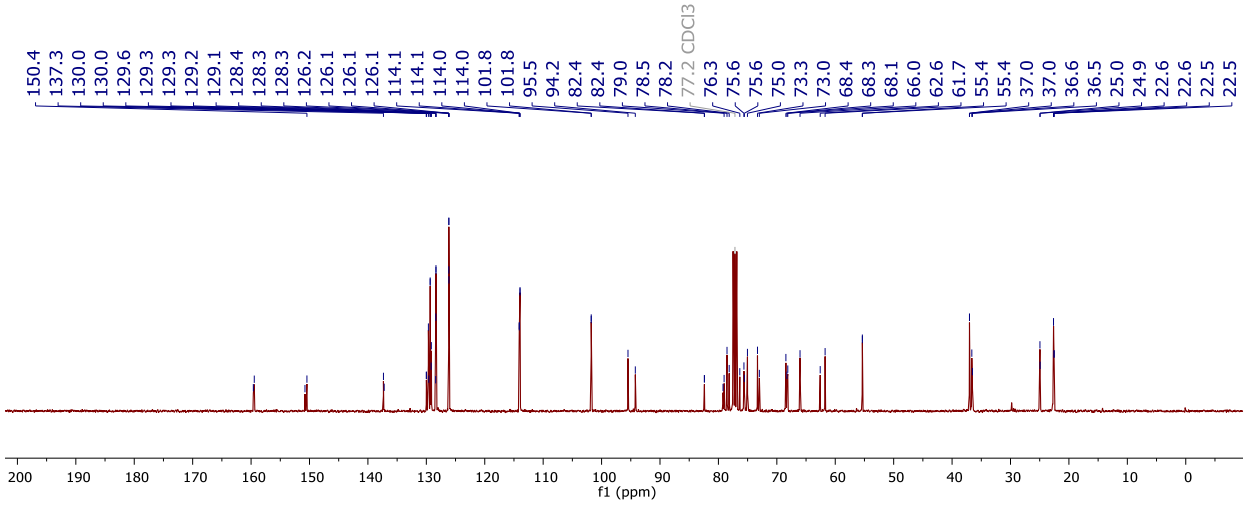
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **14b**



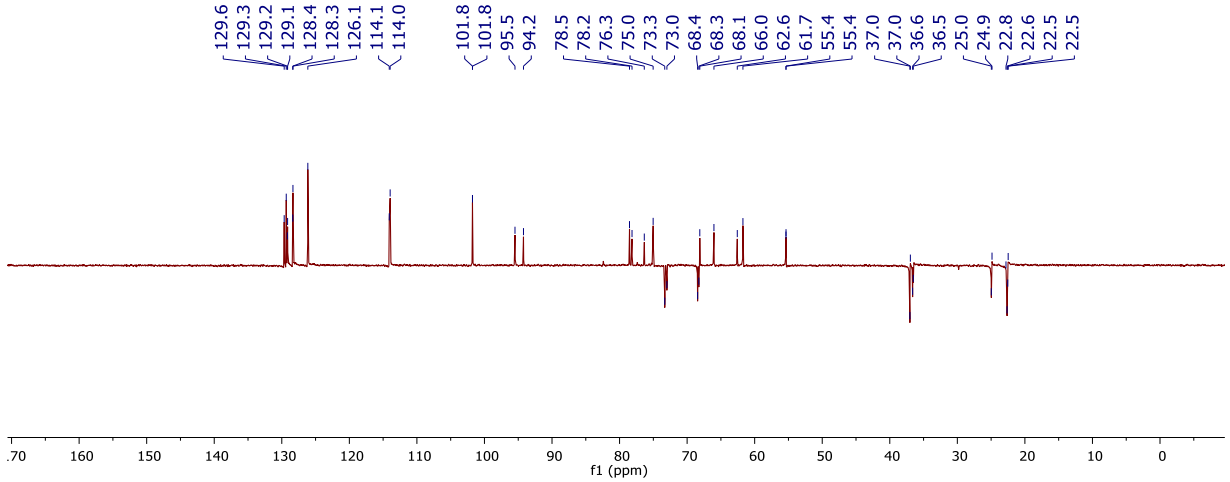
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **14c**



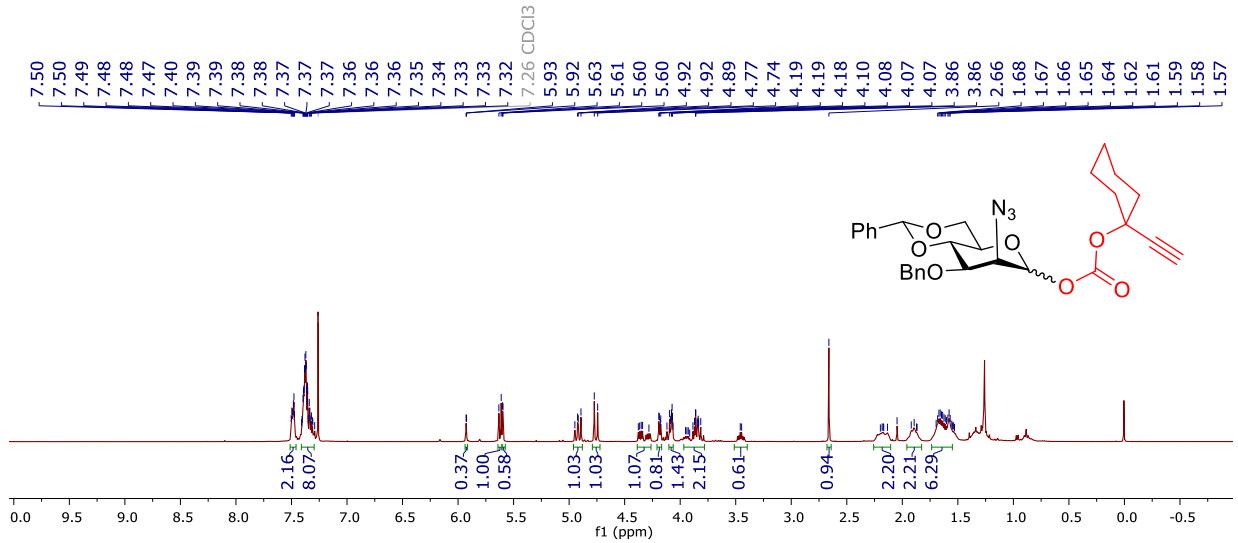
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **14c**



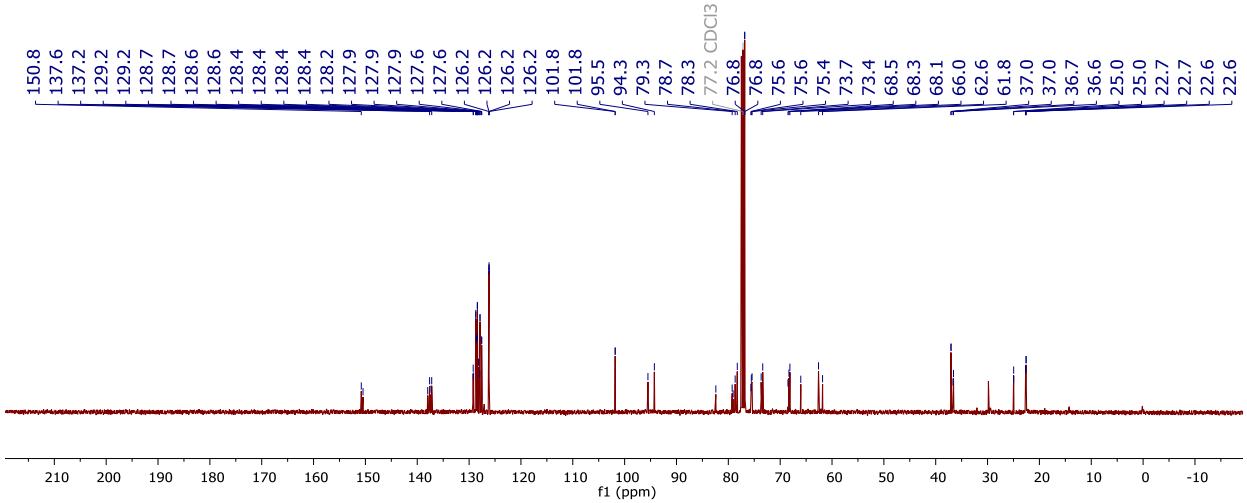
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **14c**



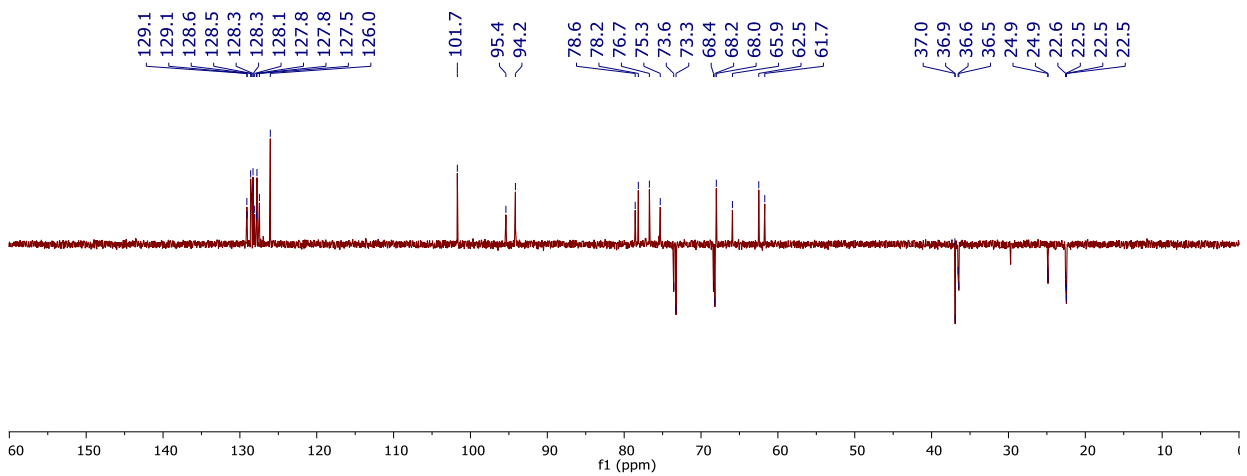
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **14d**



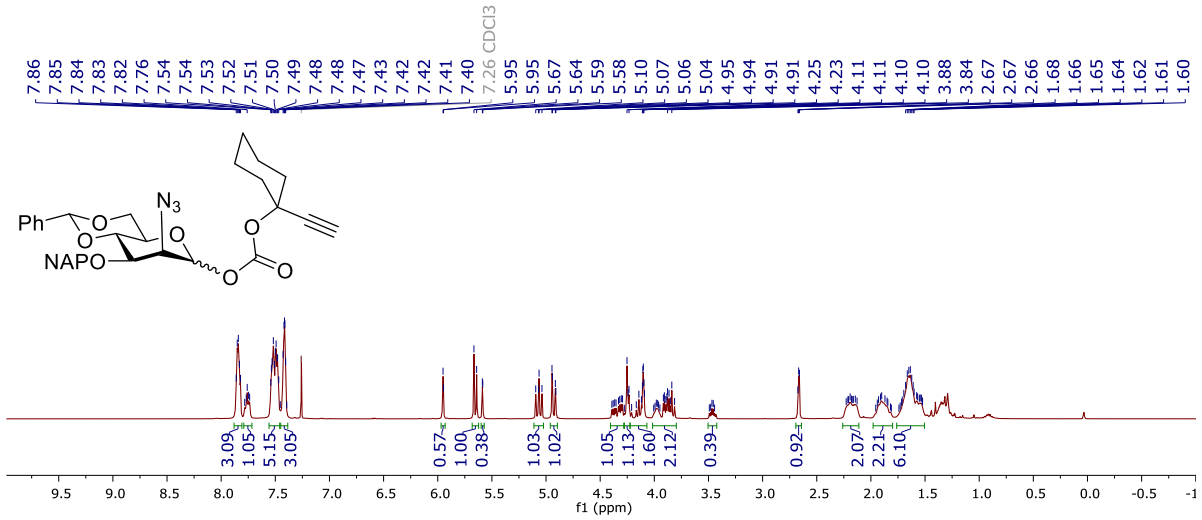
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **14d**



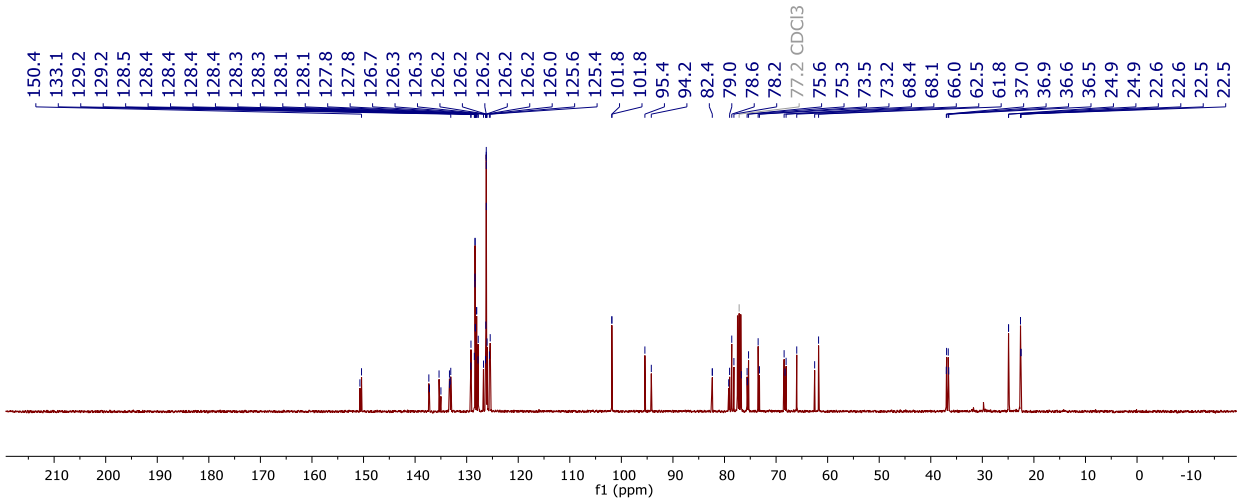
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **14d**



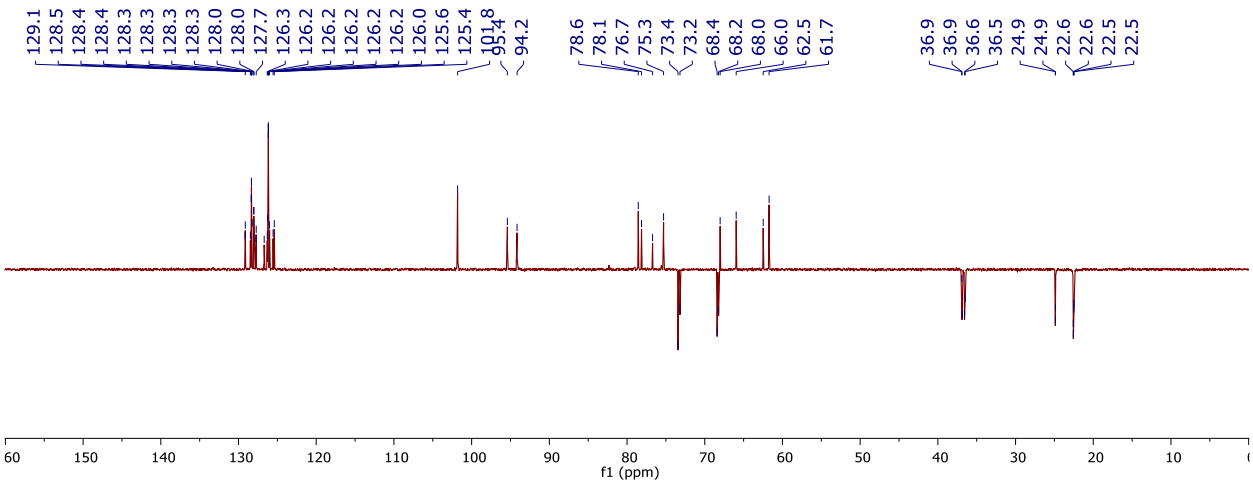
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **14e**



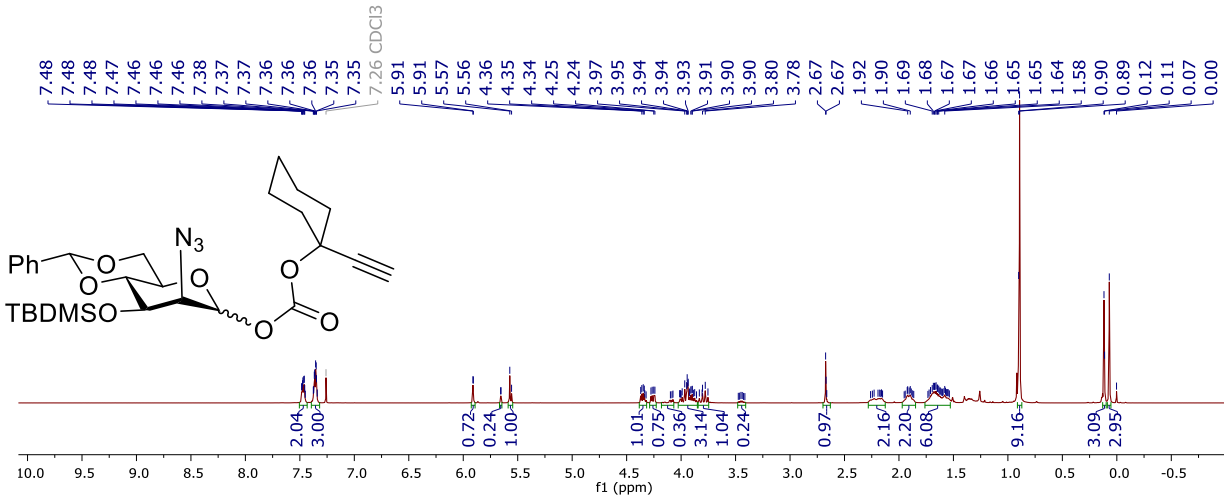
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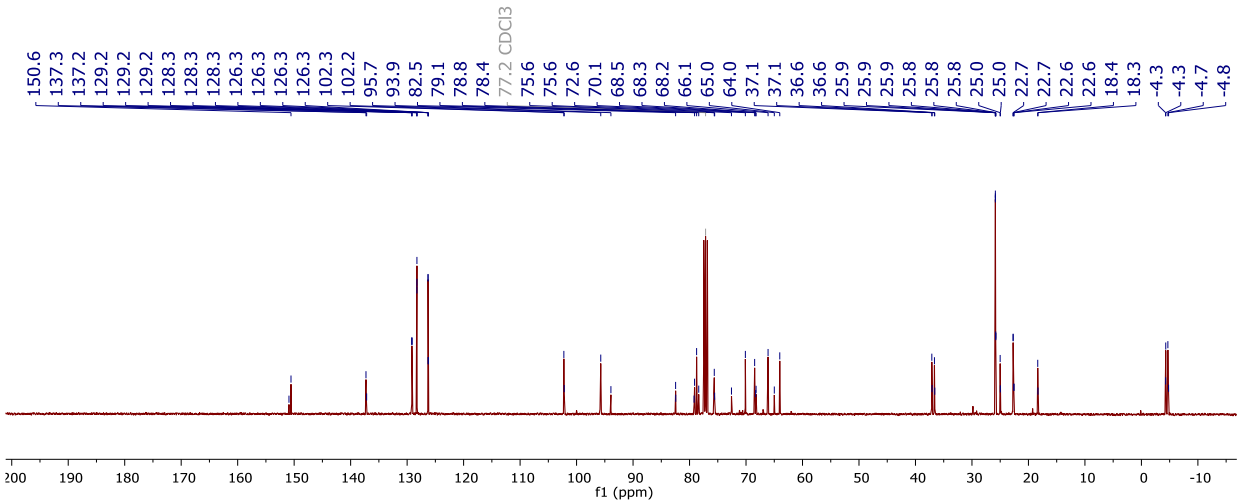
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **14e**



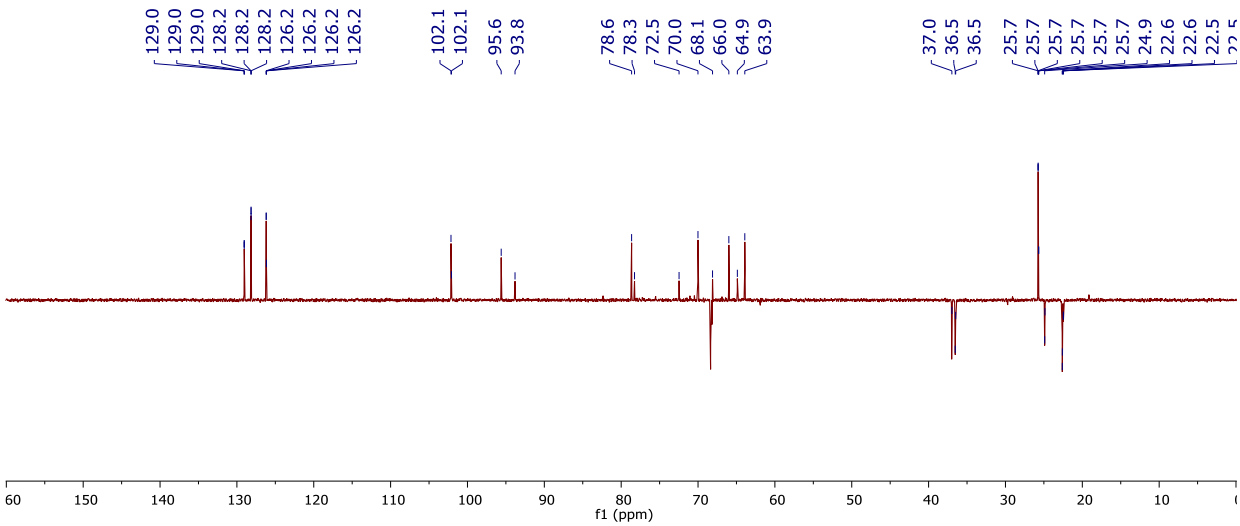
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **14f**



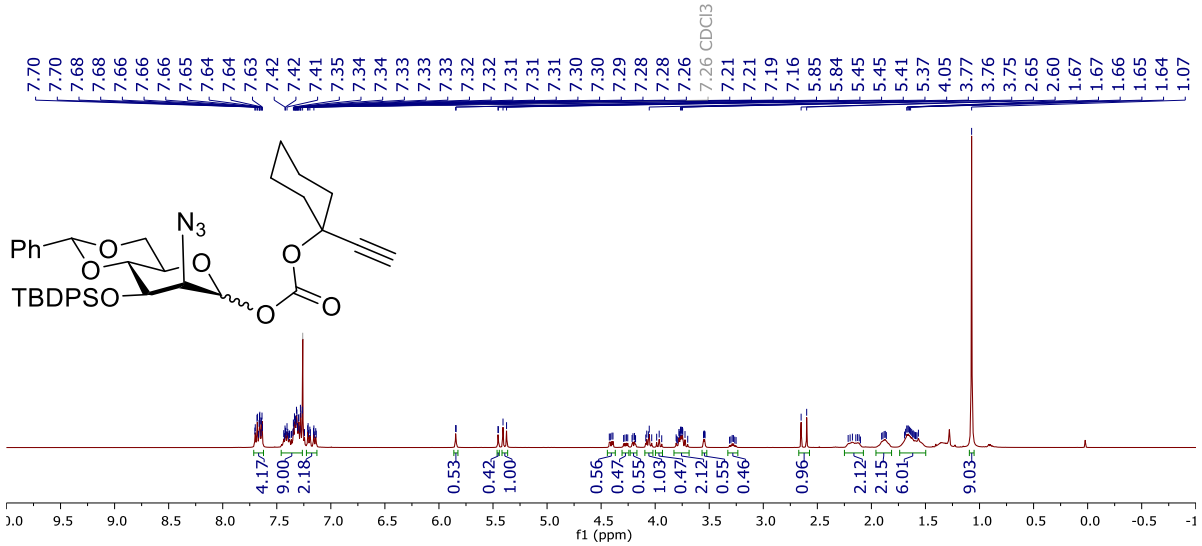
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **14f**



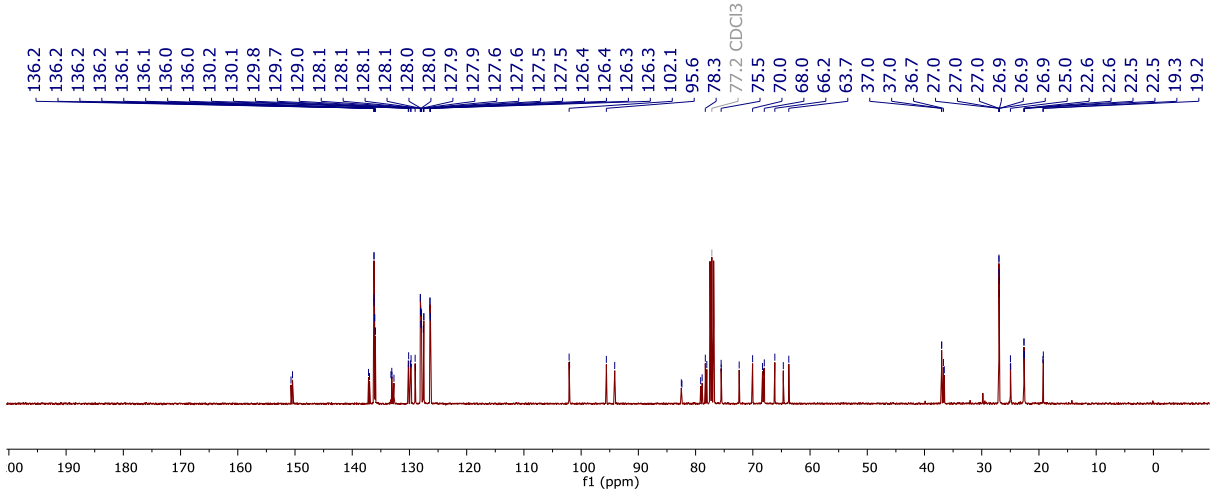
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **14f**



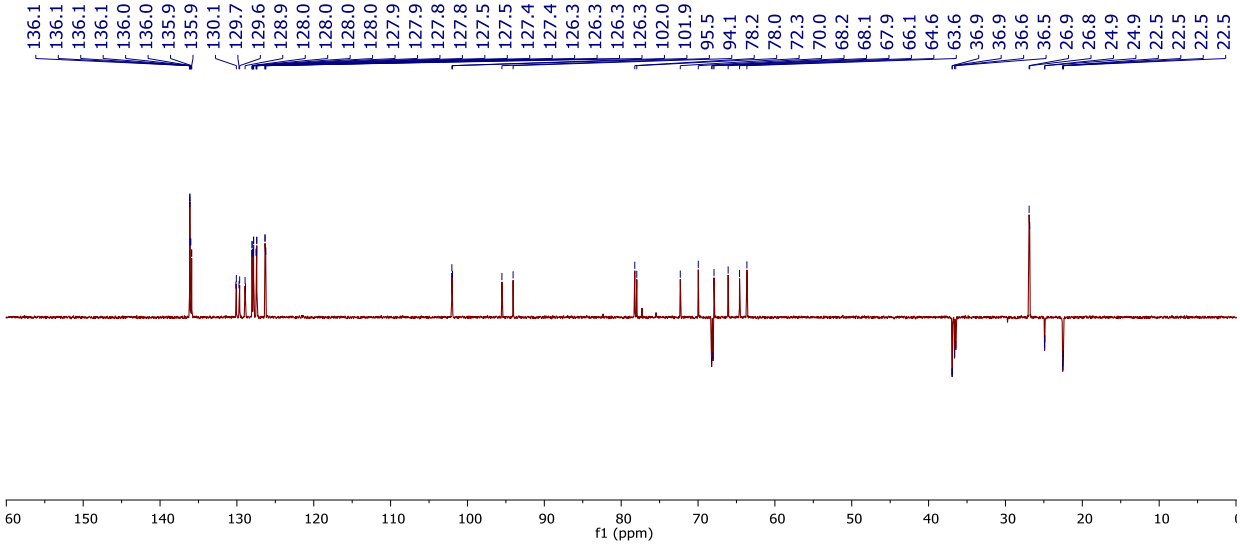
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **14g**



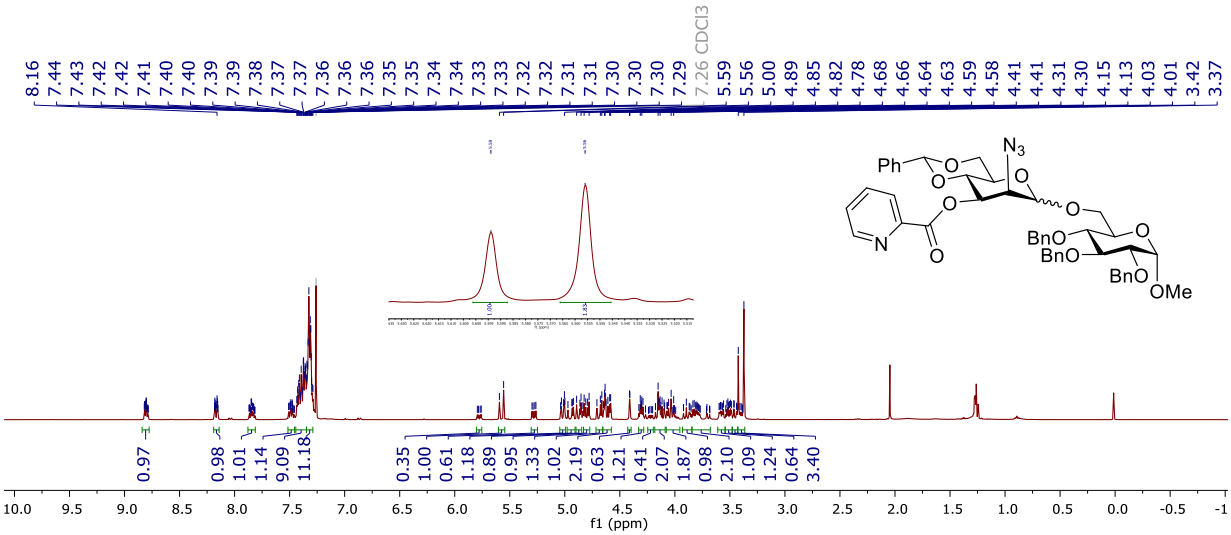
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **14g**



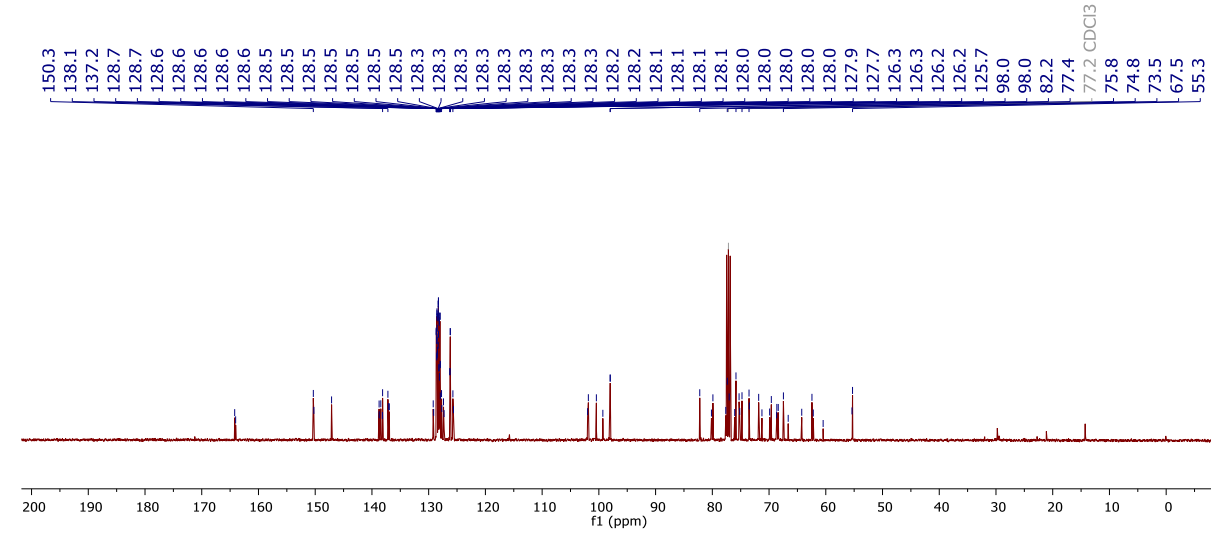
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **14g**



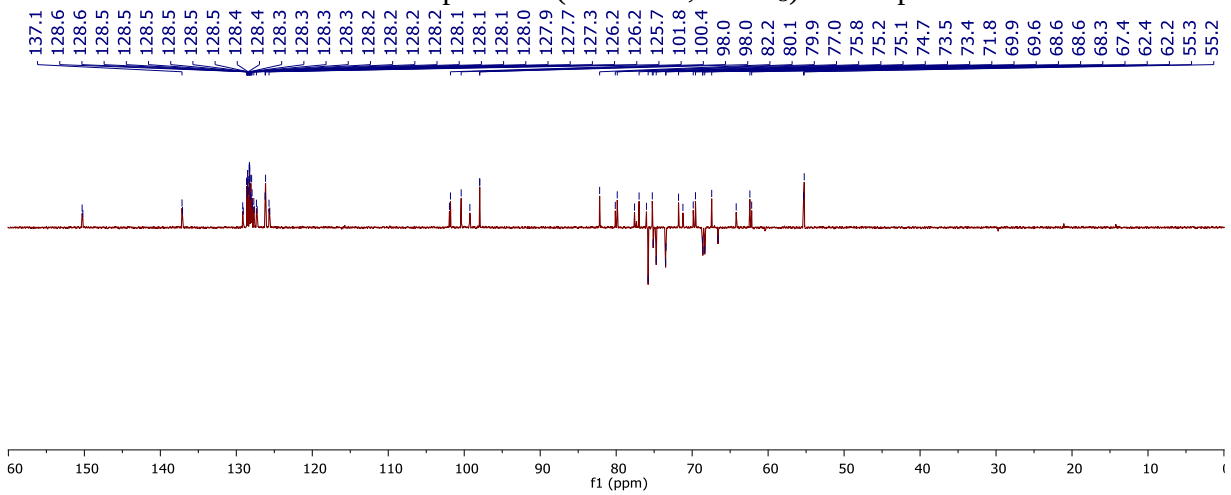
1H NMR Spectrum (400 MHz, $CDCl_3$) of compound **16b**



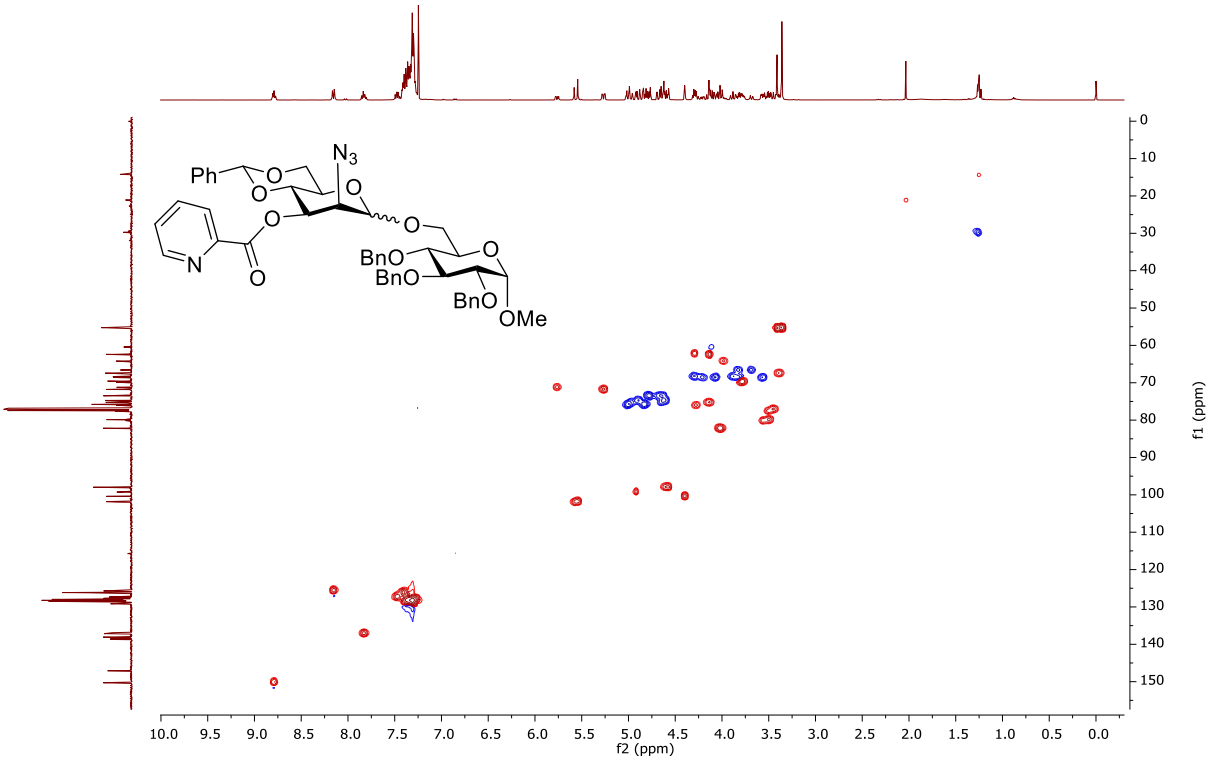
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **16b**



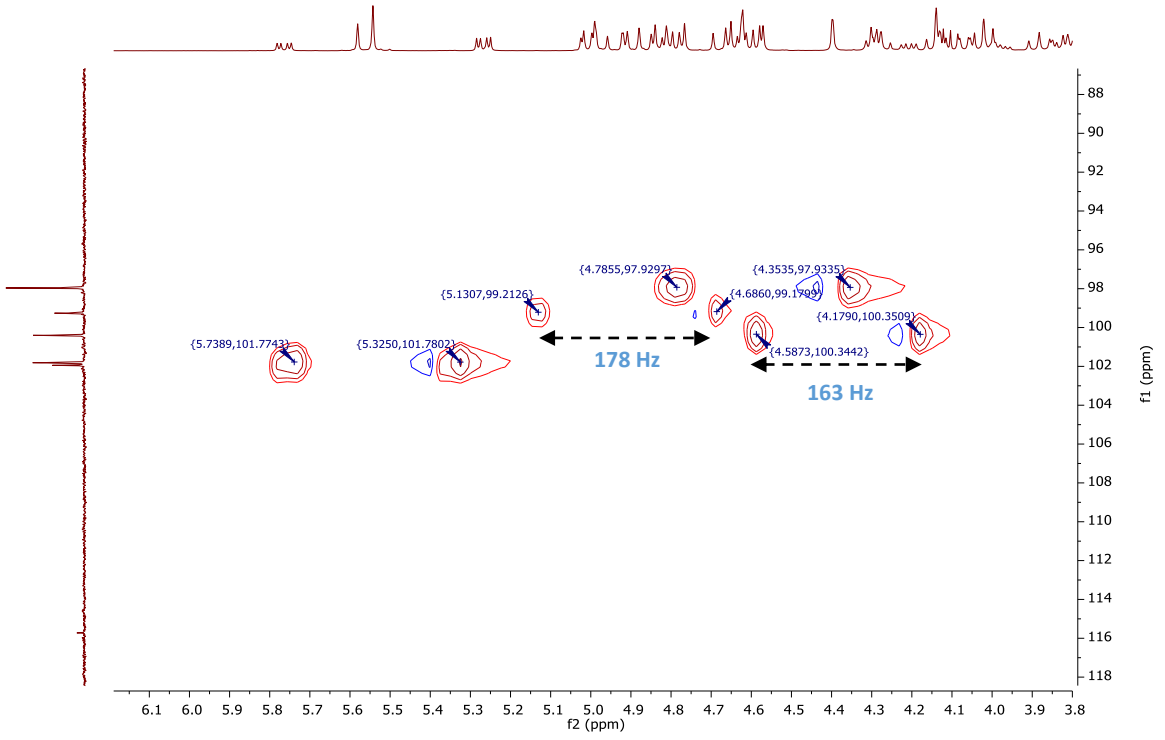
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **16b**



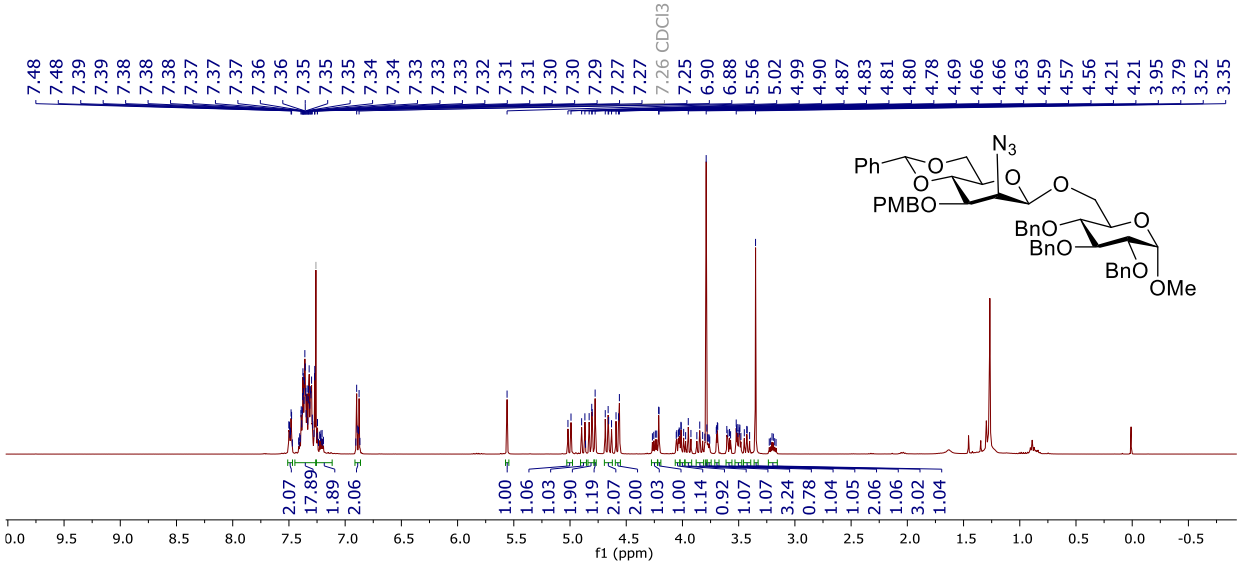
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **16b**



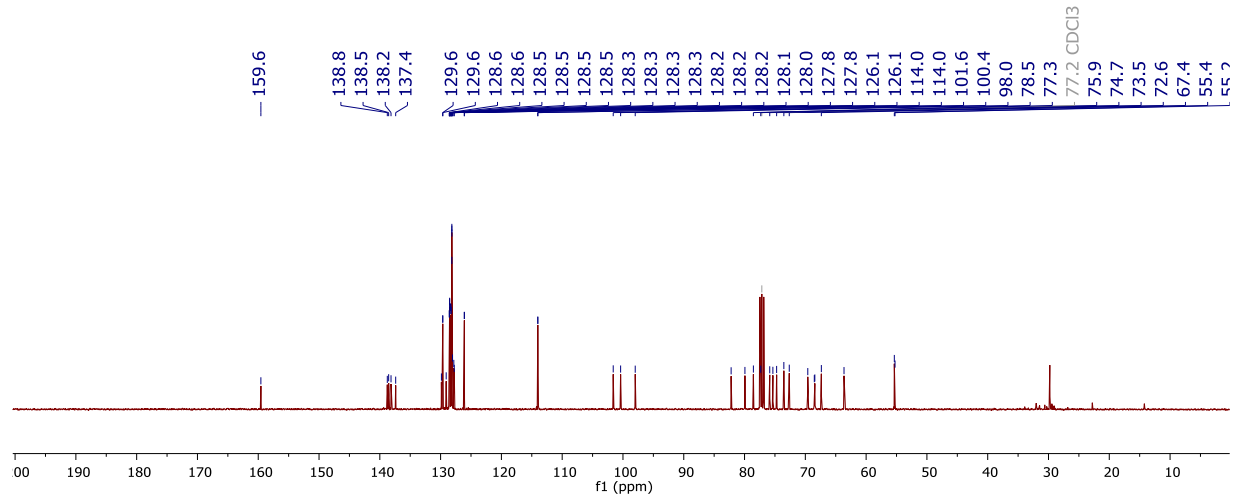
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **16b**



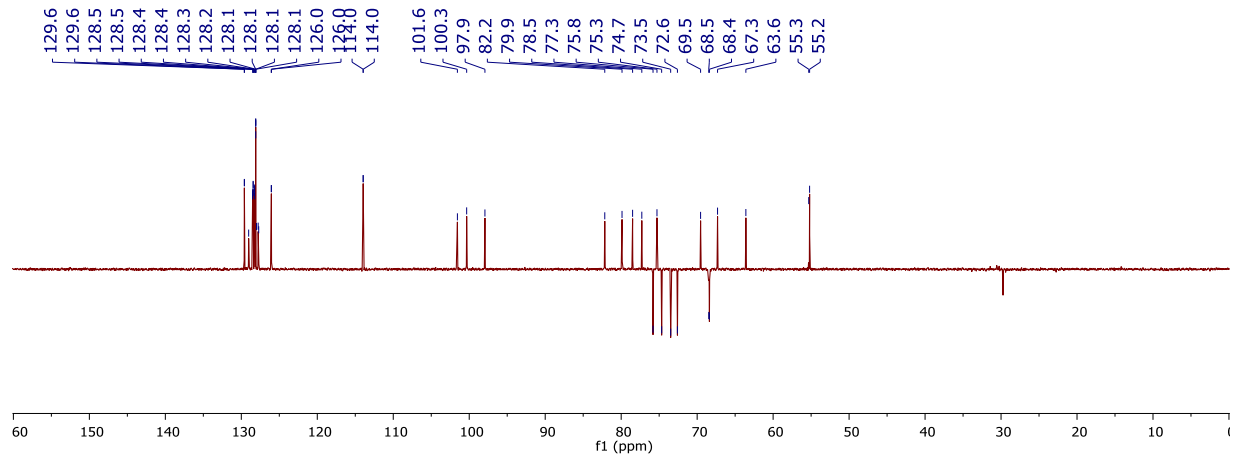
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **16c**



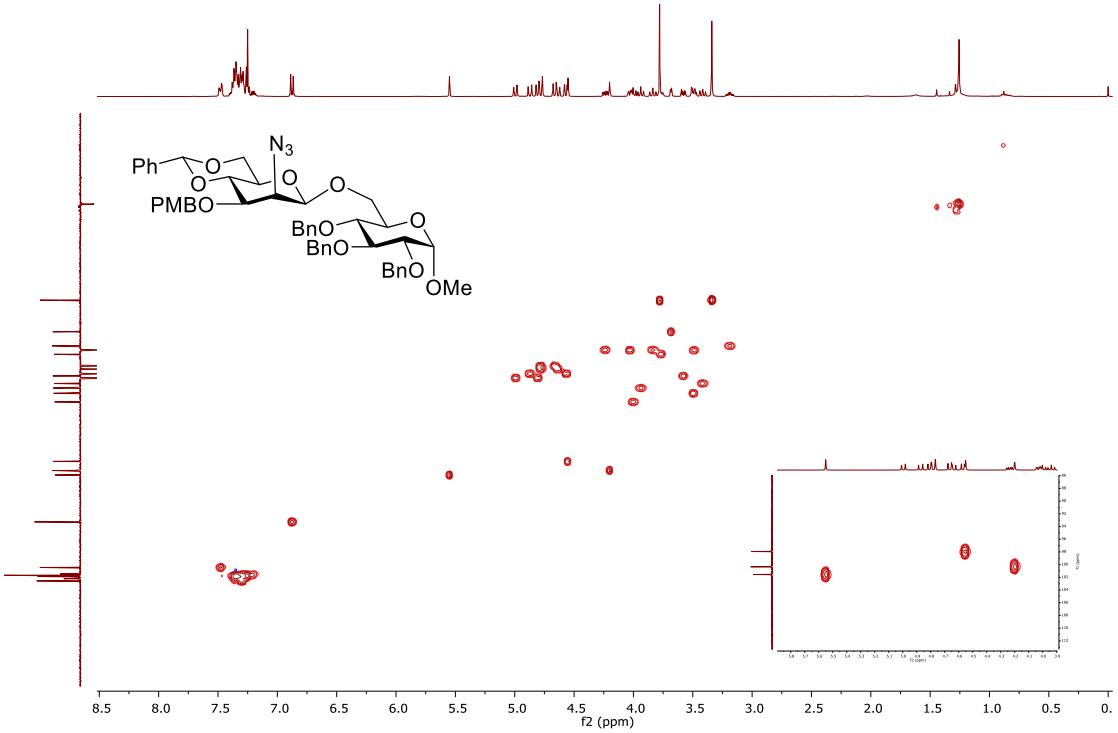
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of compound **16c**



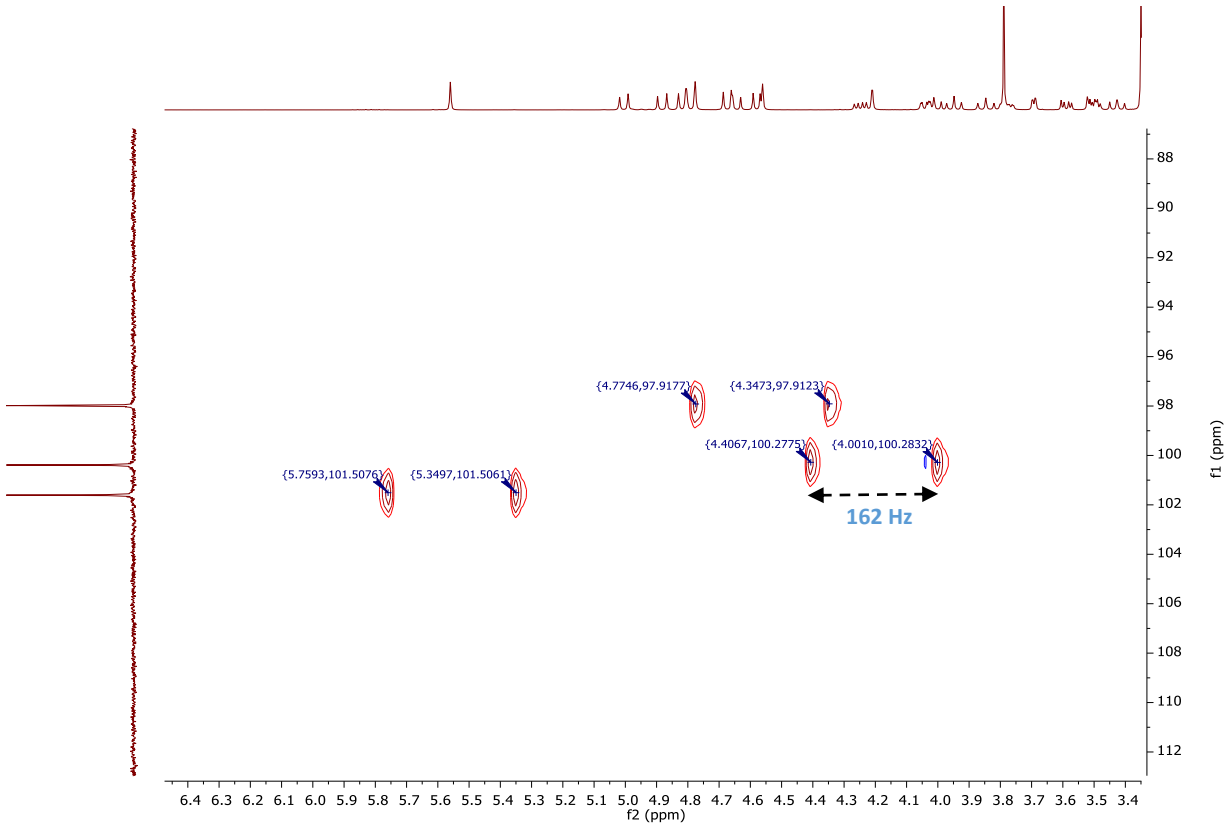
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **16c**



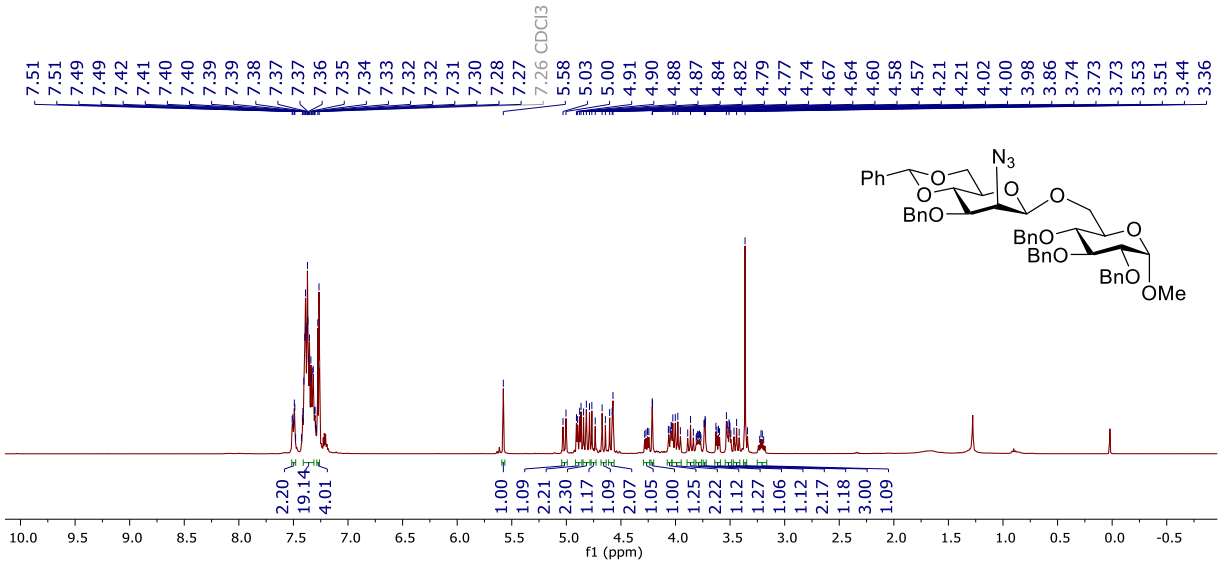
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **16c**



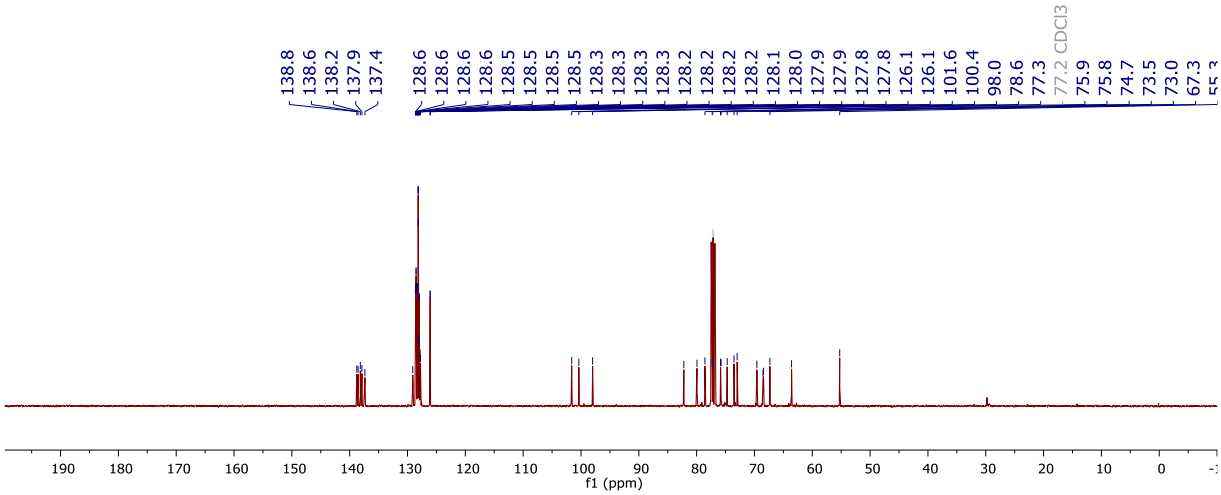
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **16c**



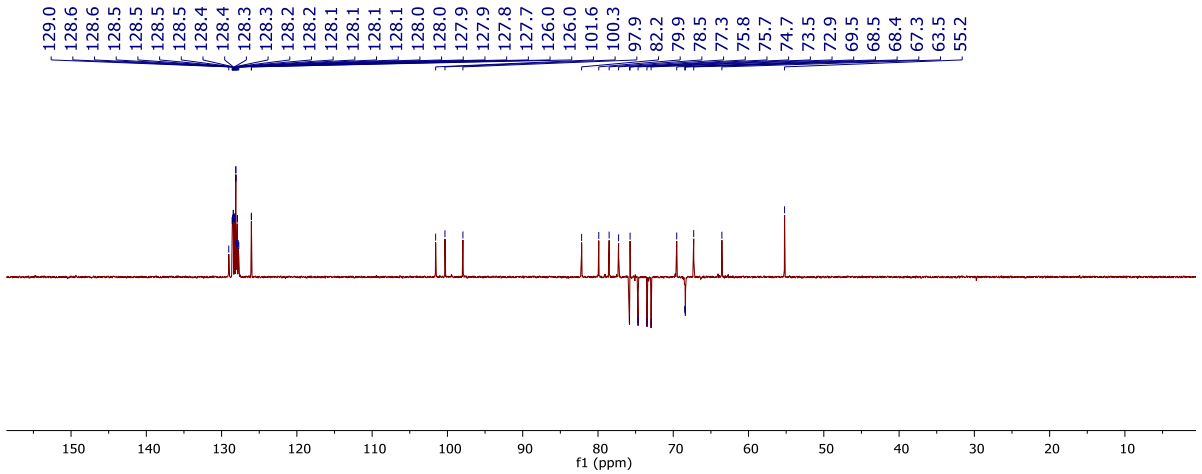
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **16d**



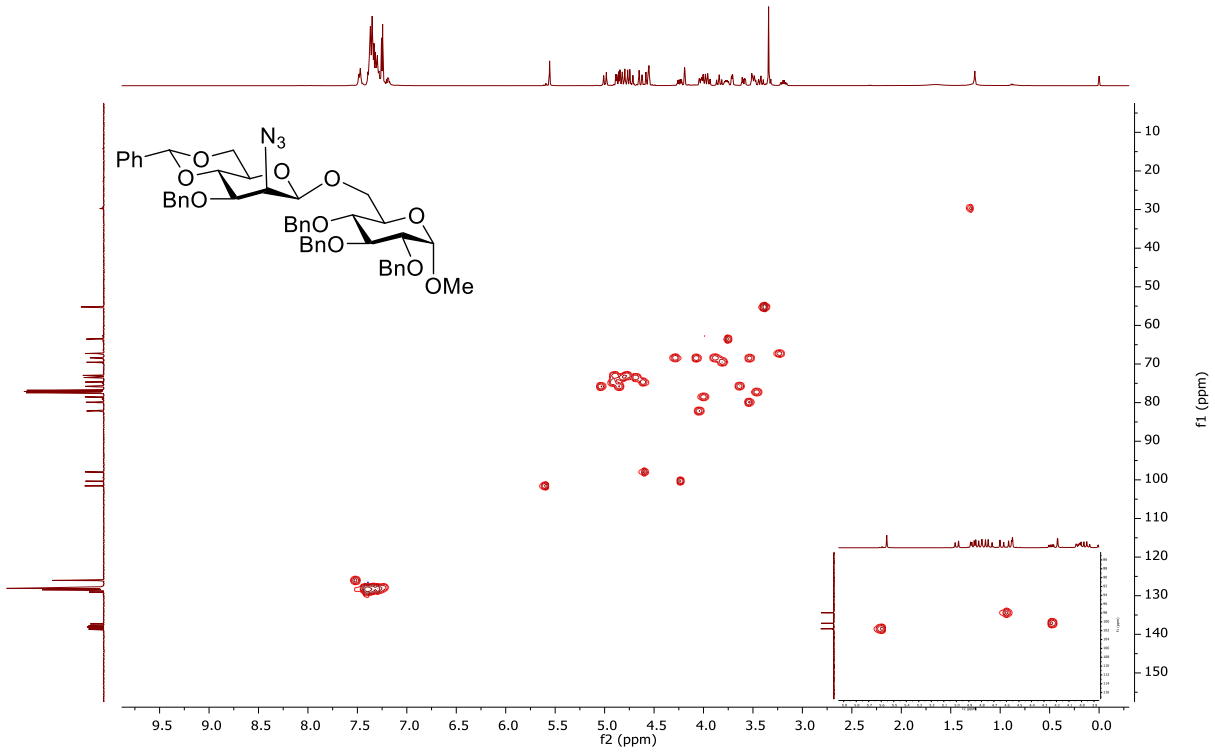
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **16d**



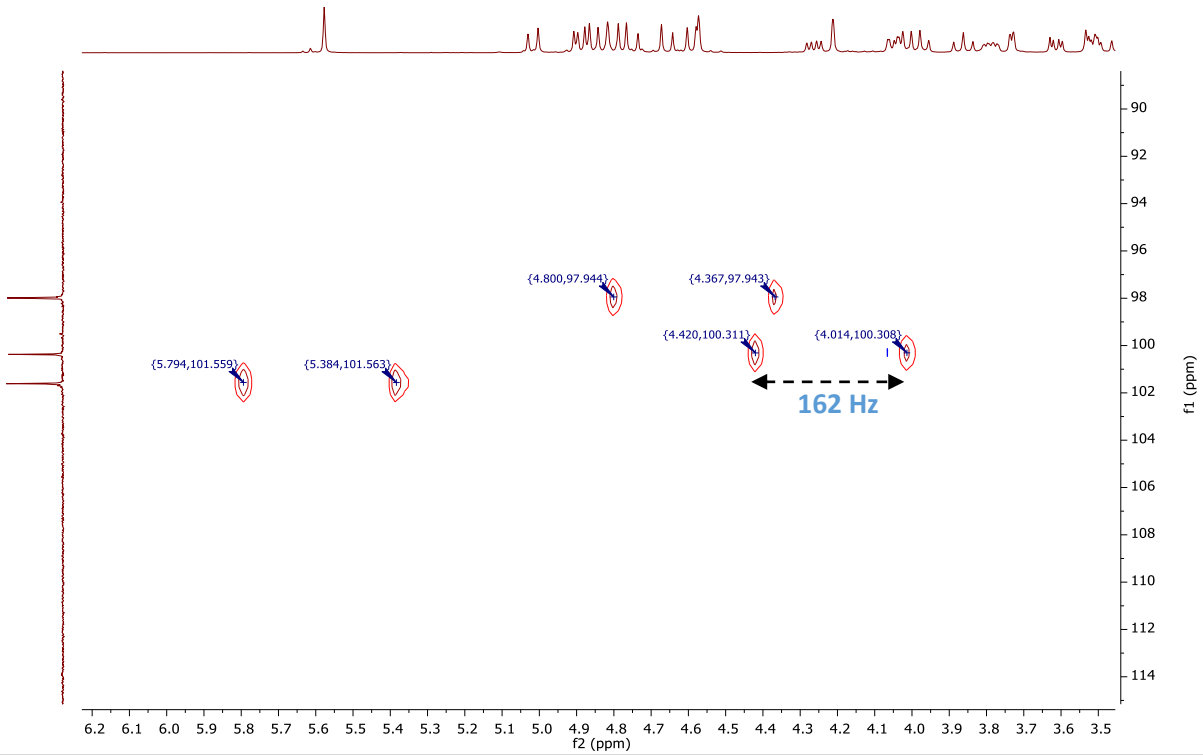
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **16d**



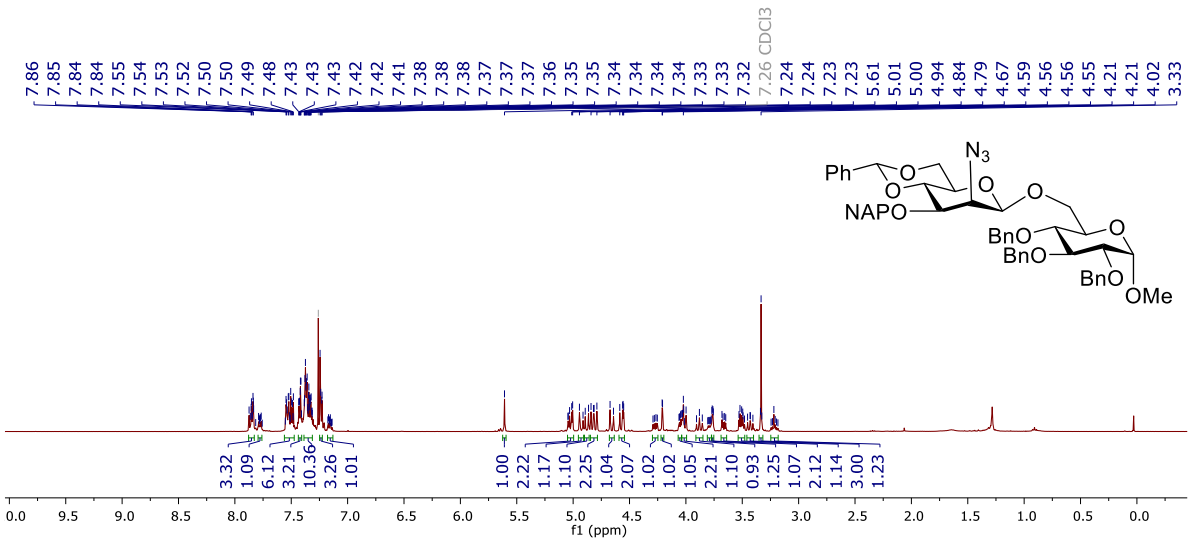
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **16d**



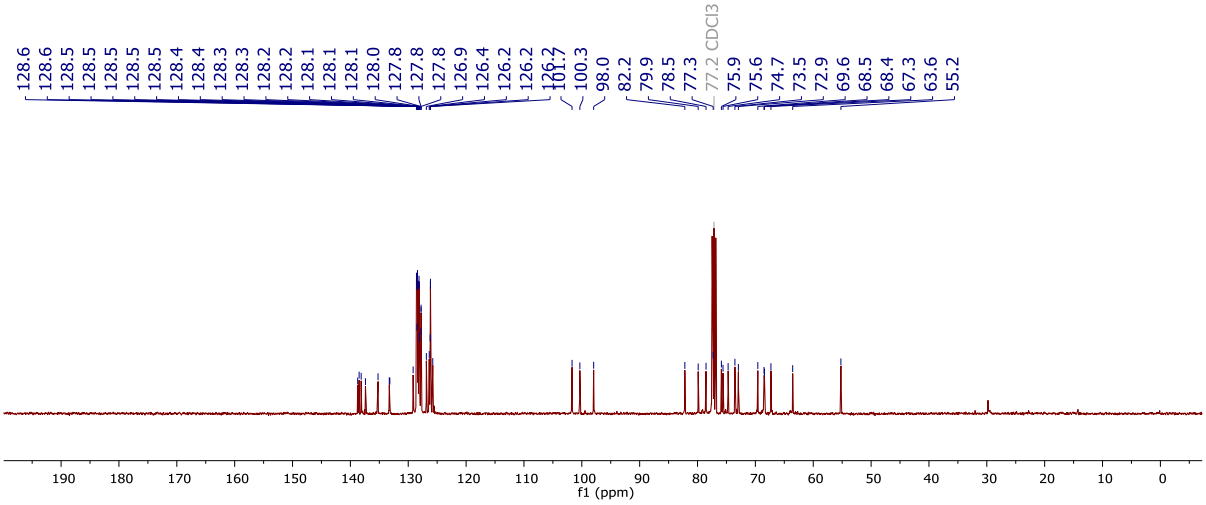
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **16d**



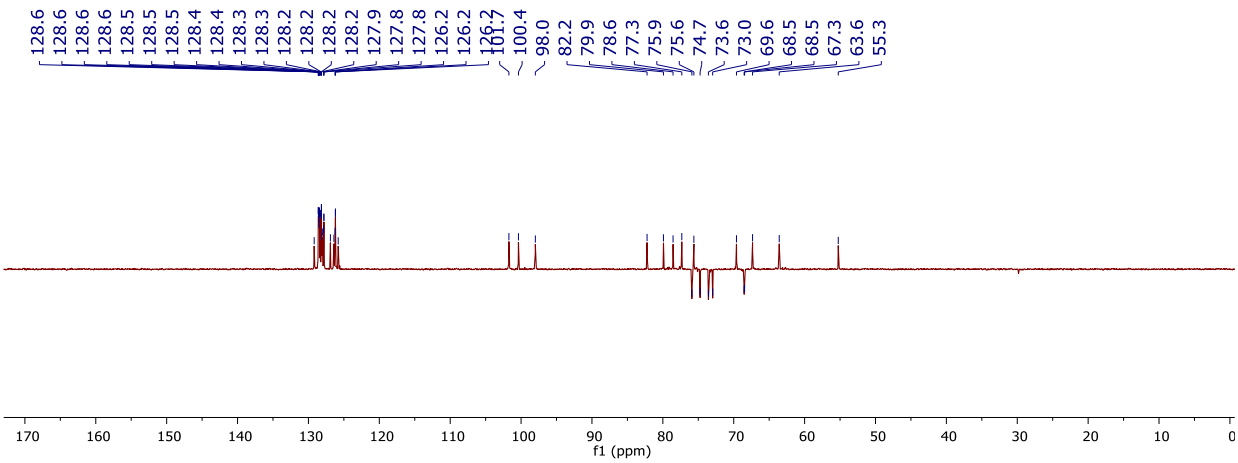
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **16e**



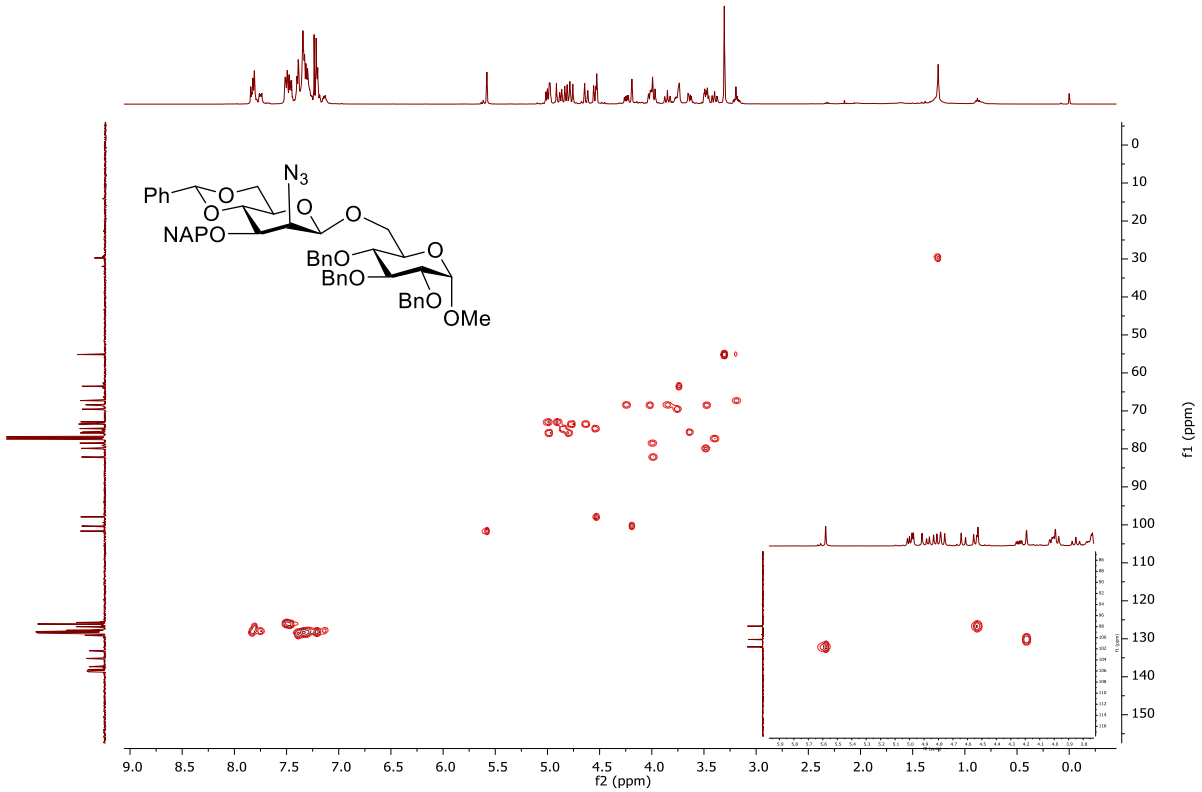
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **16e**



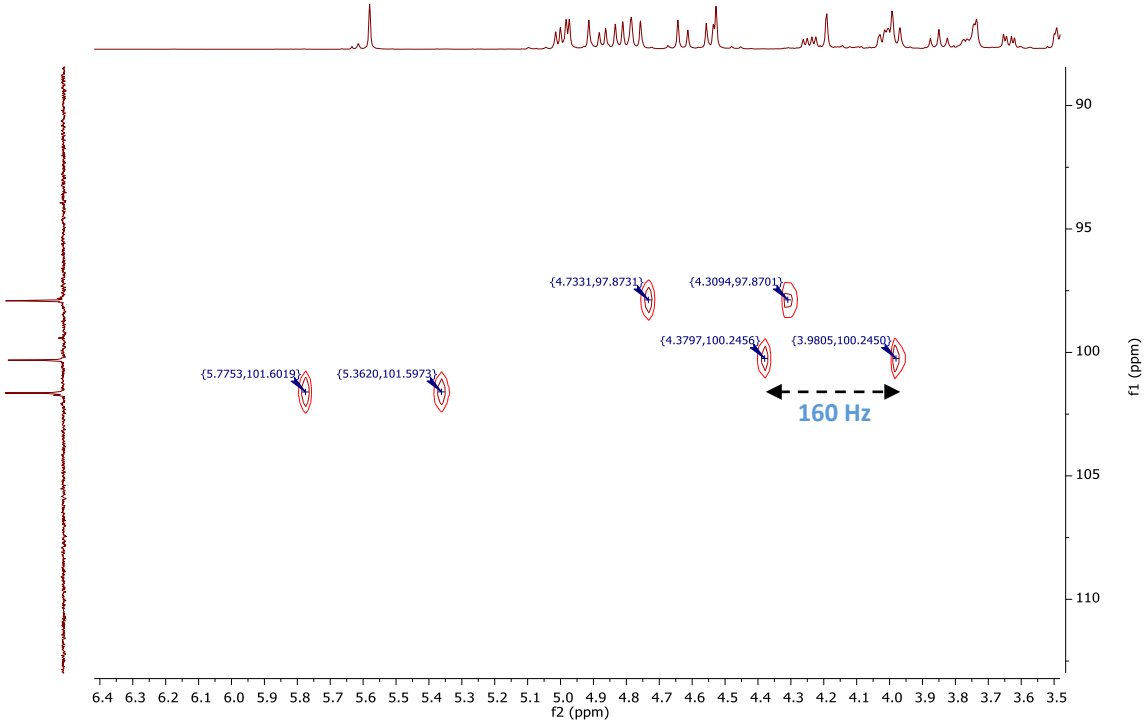
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **16e**



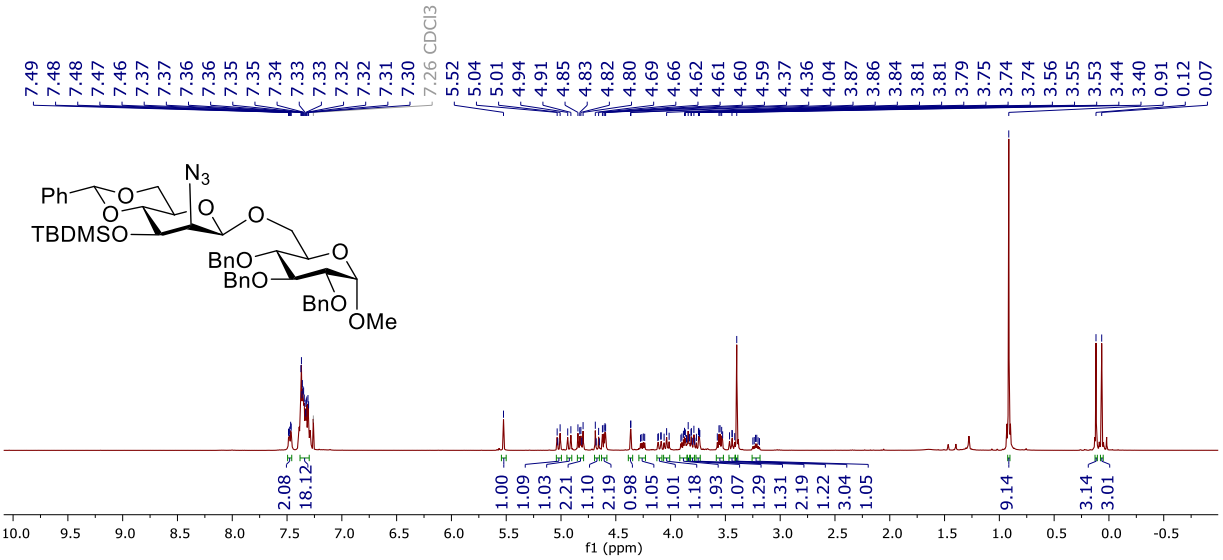
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **16e**



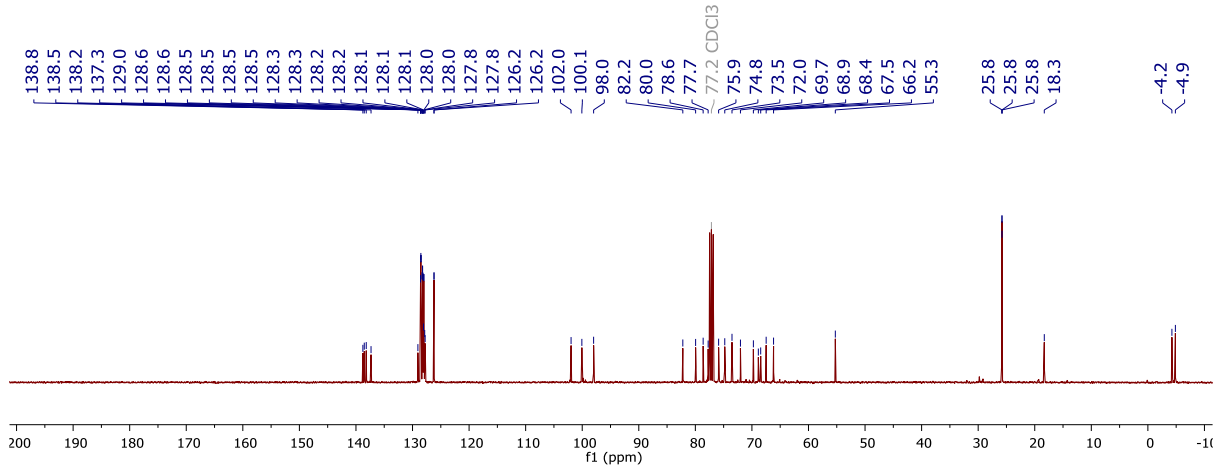
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz $CDCl_3$) of compound **16e**



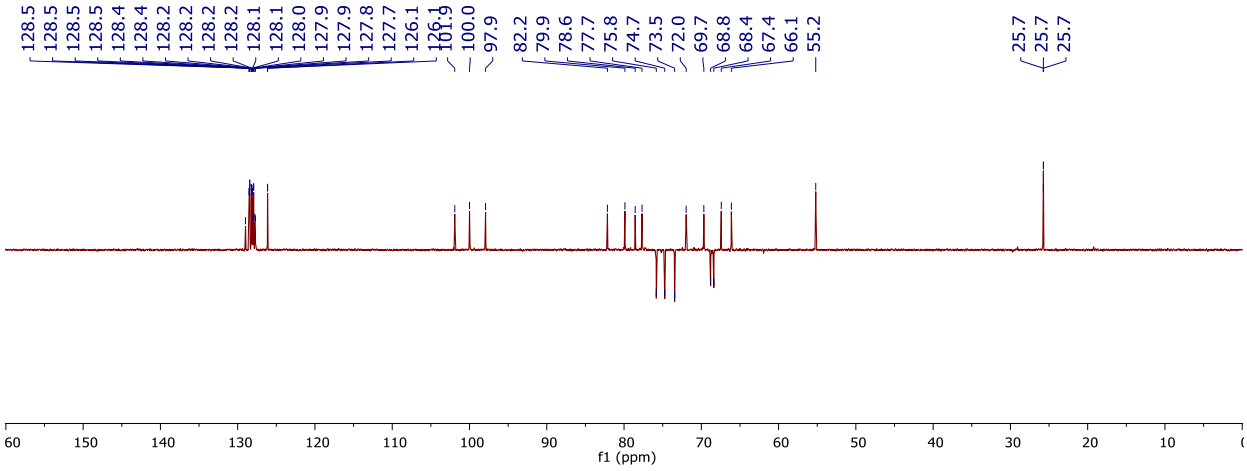
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **16f**



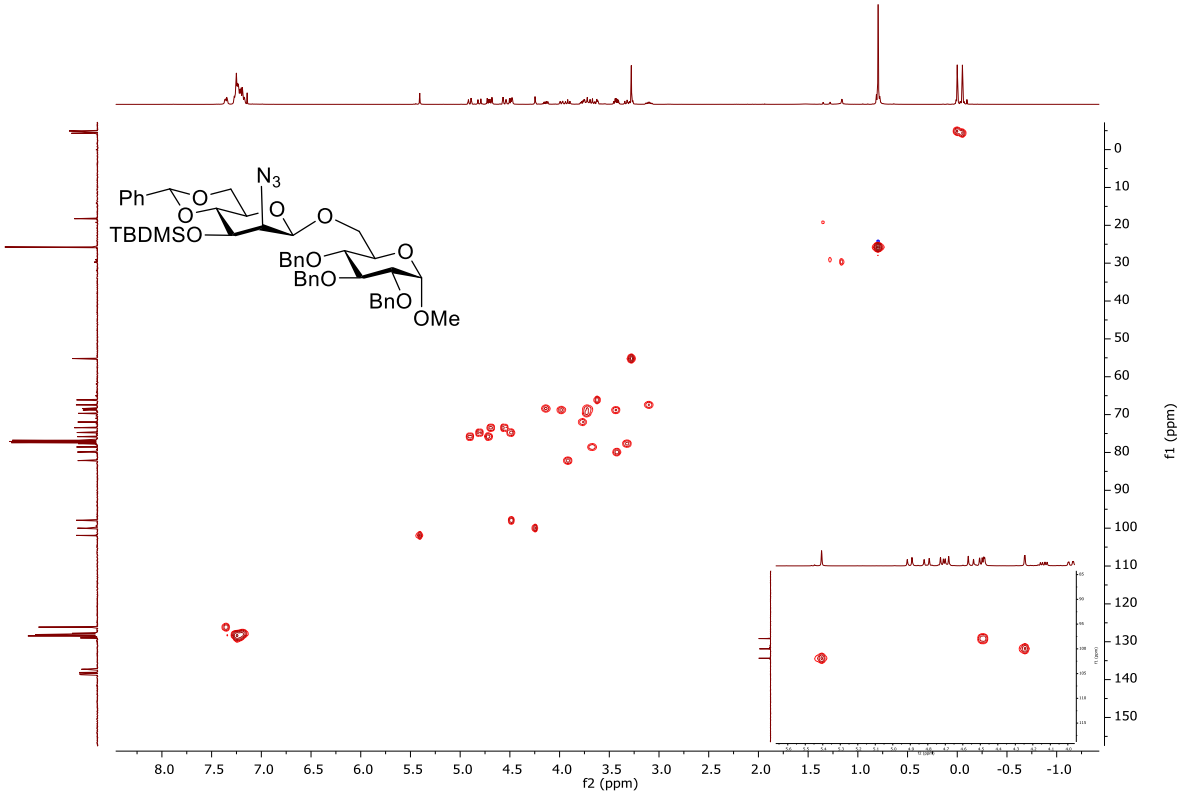
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **16f**



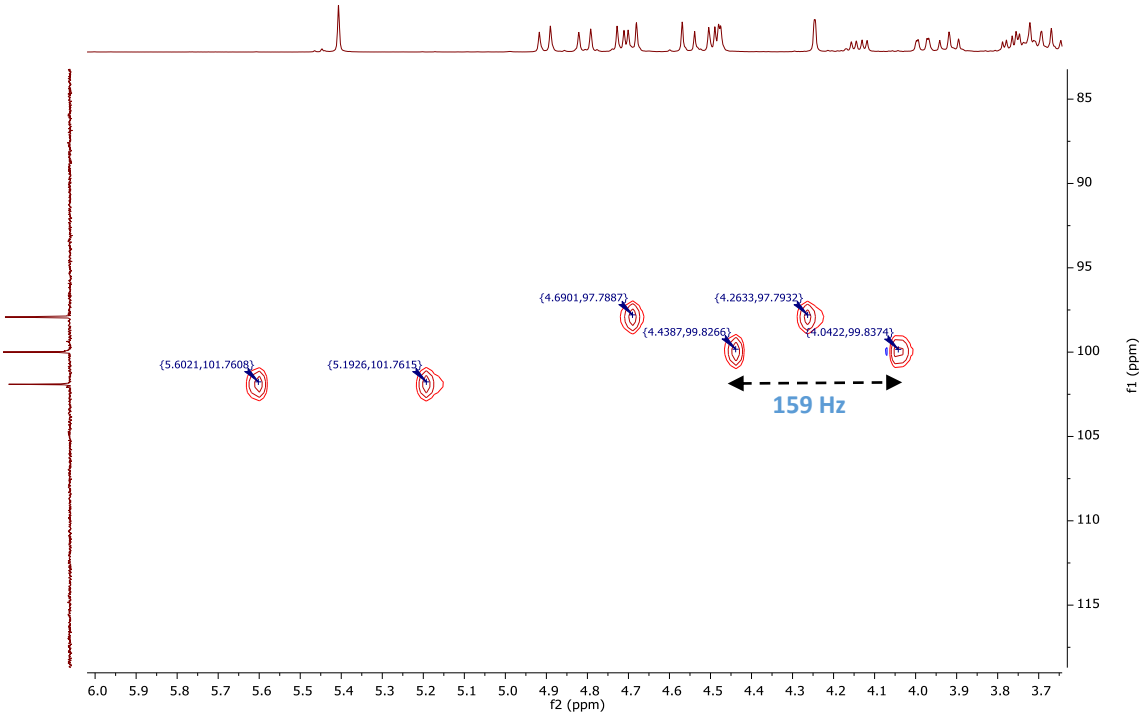
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **16f**



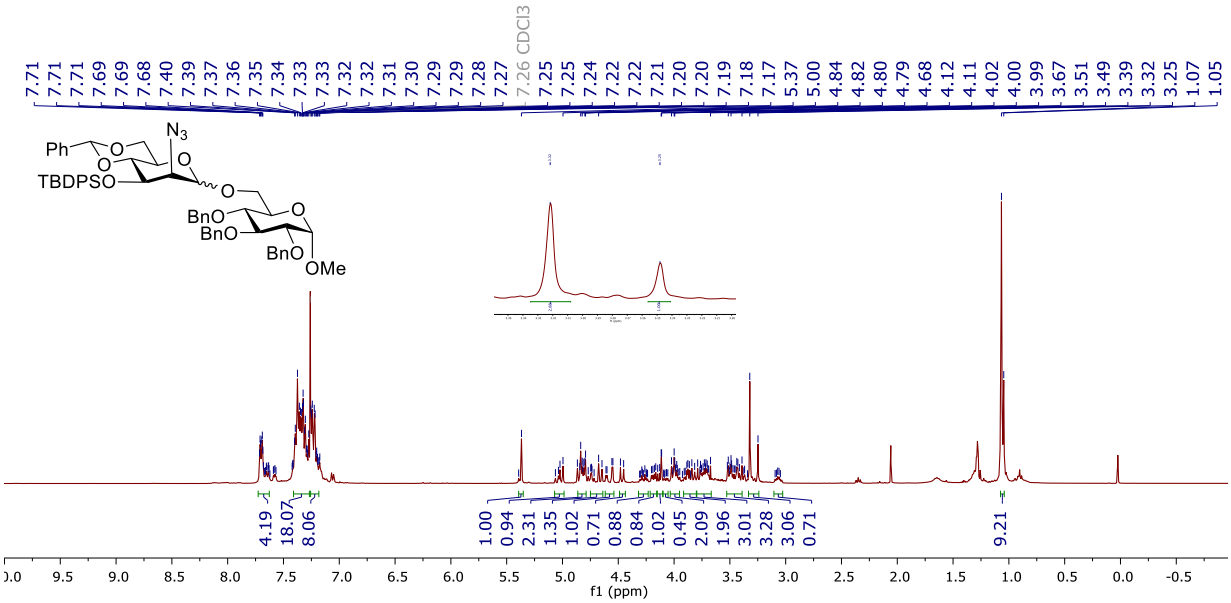
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **16f**



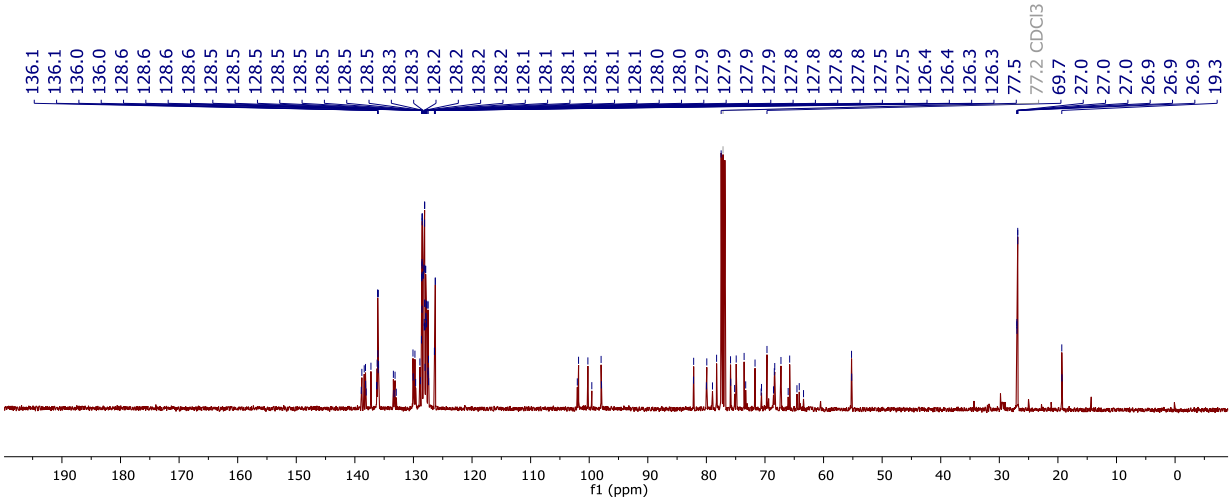
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **16f**



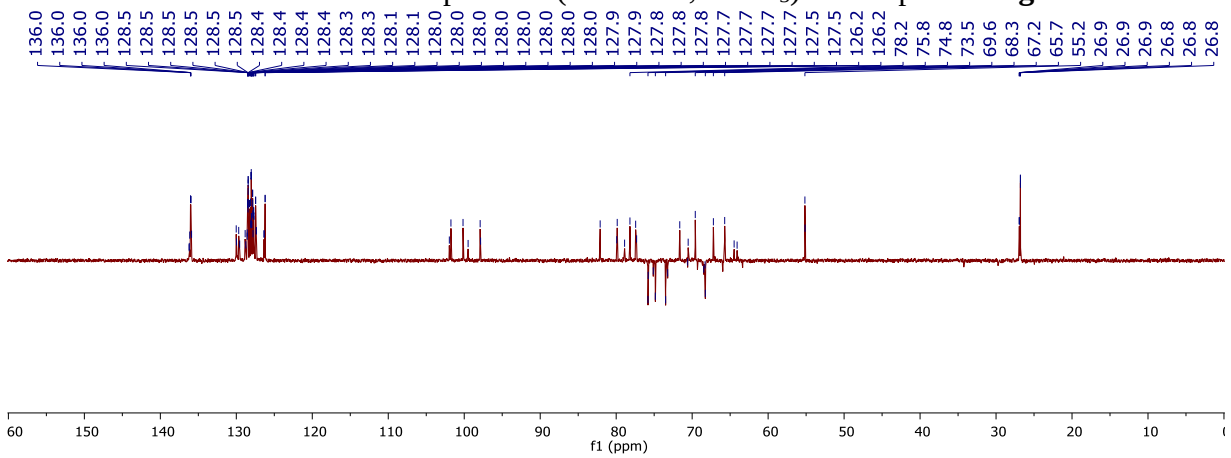
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **16g**



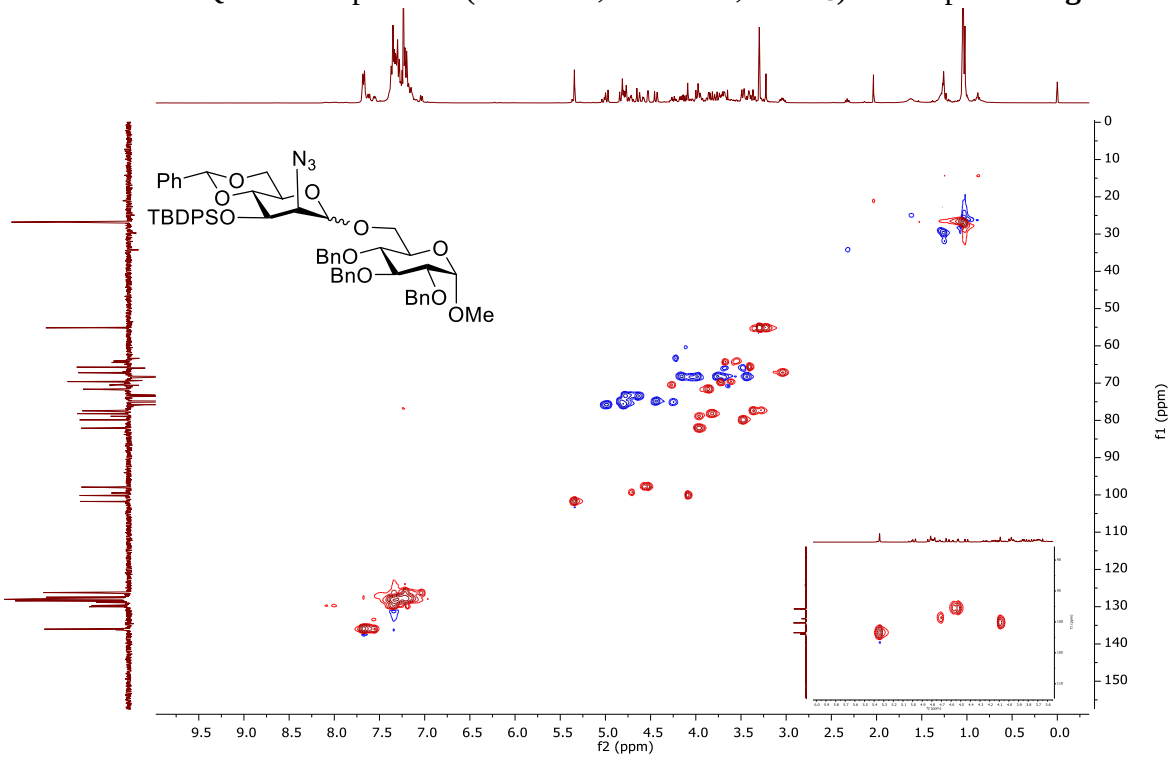
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **16g**



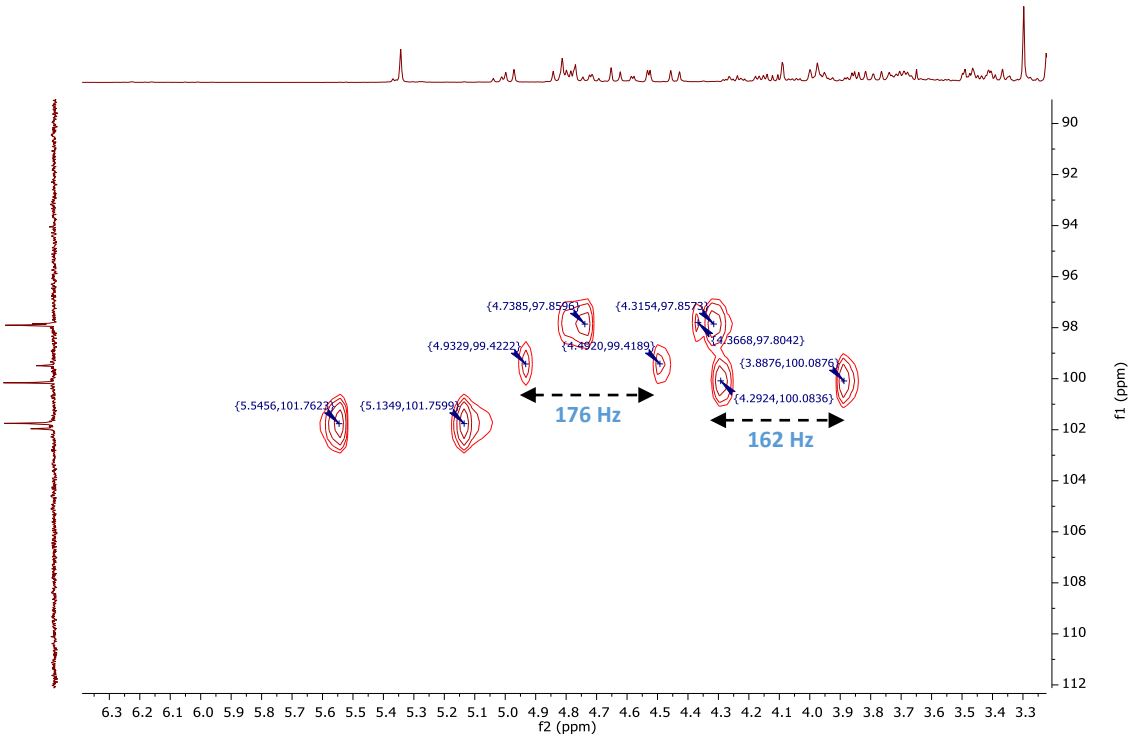
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **16g**



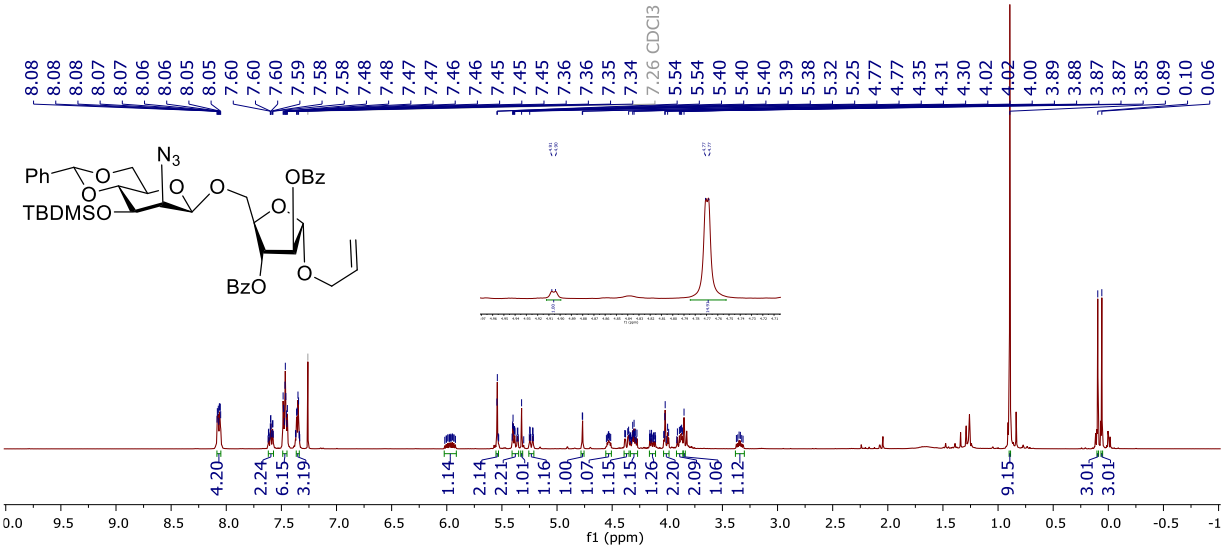
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **16g**



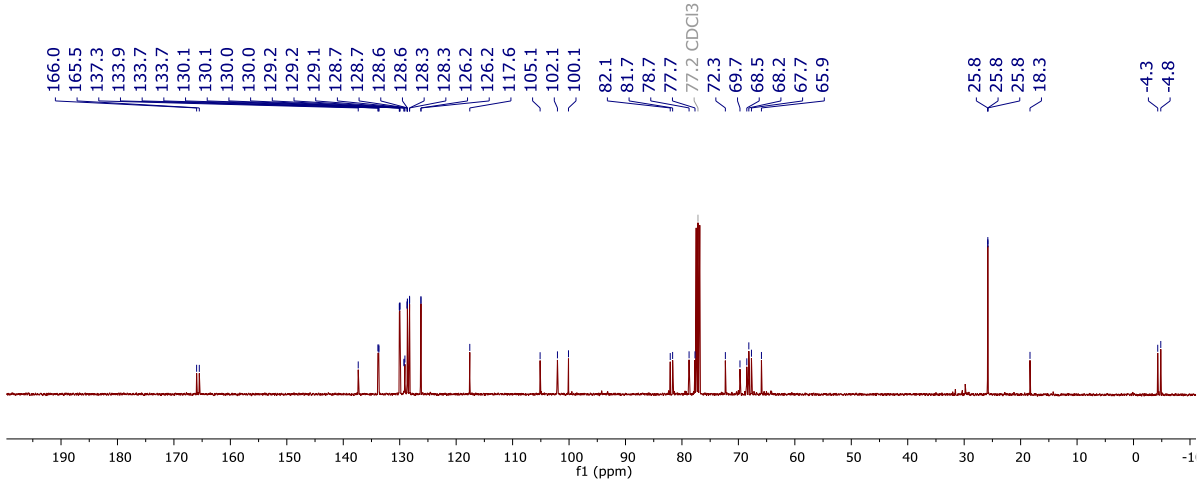
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz,101 MHz, $CDCl_3$) of compound **16g**



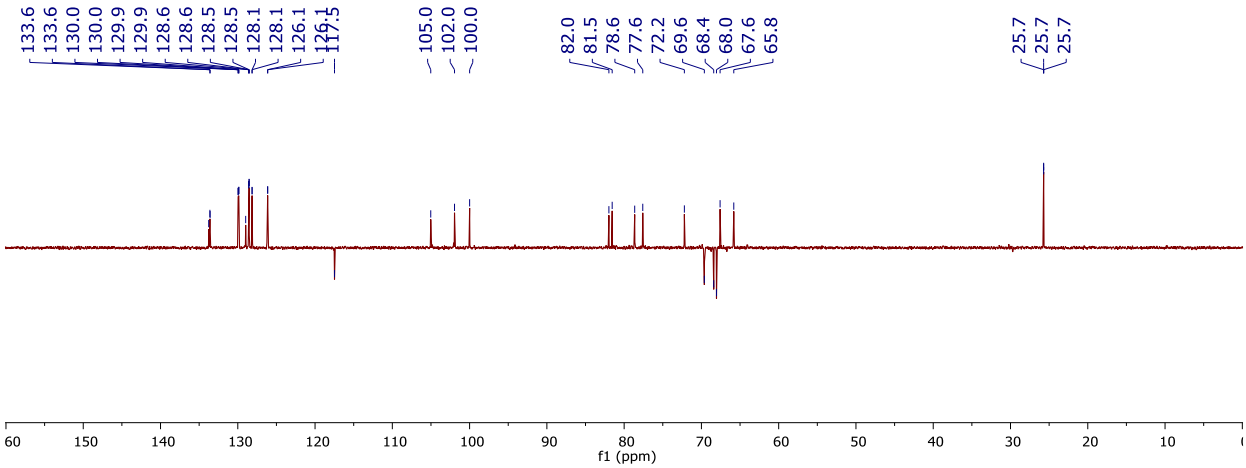
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **19a**



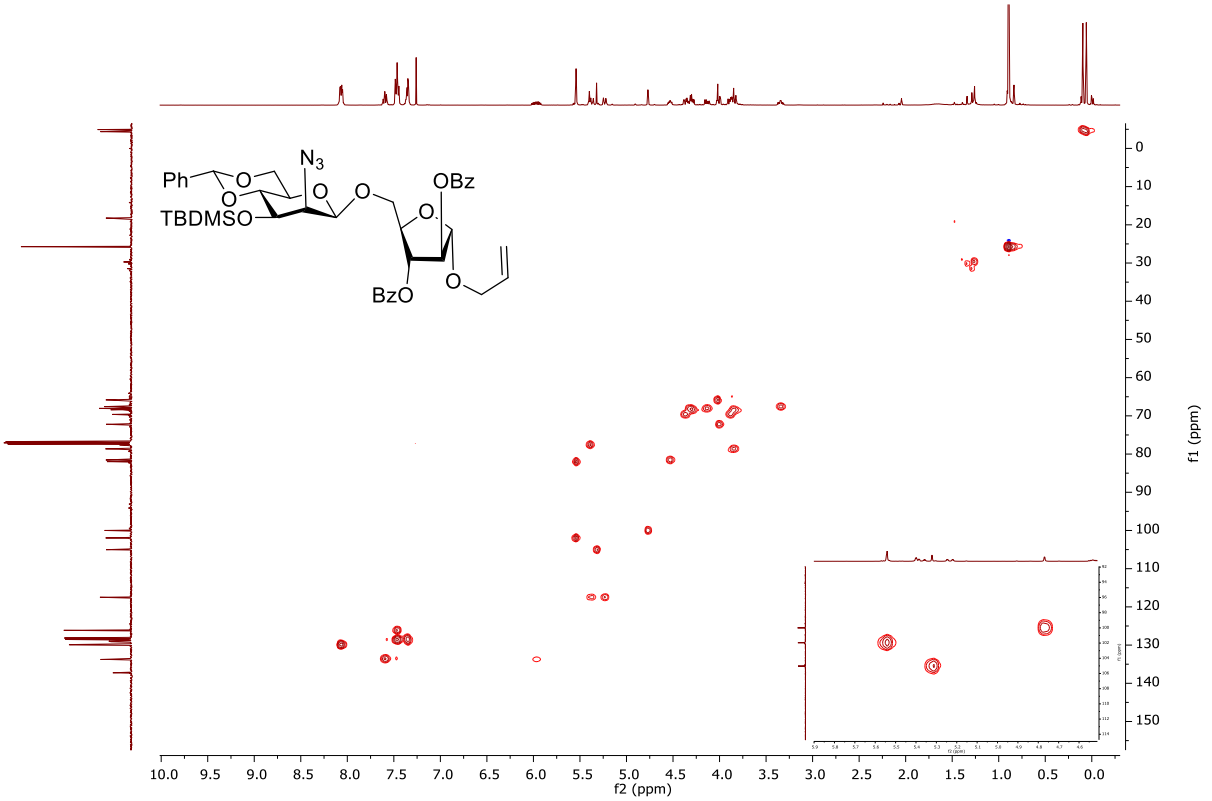
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **19a**



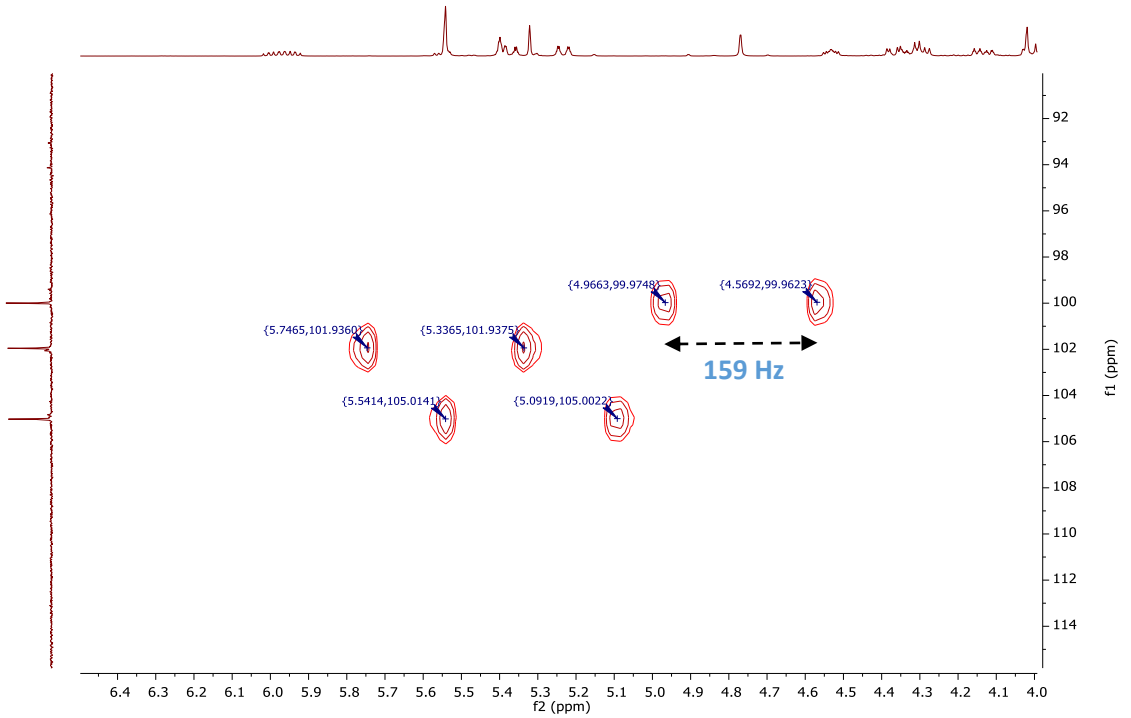
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **19a**



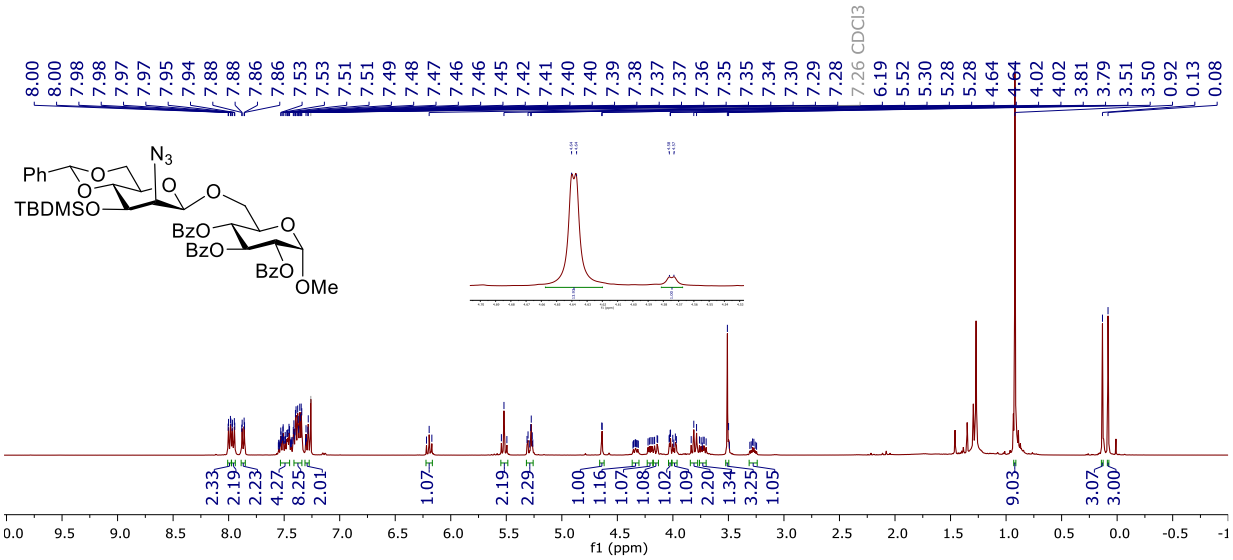
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **19a**



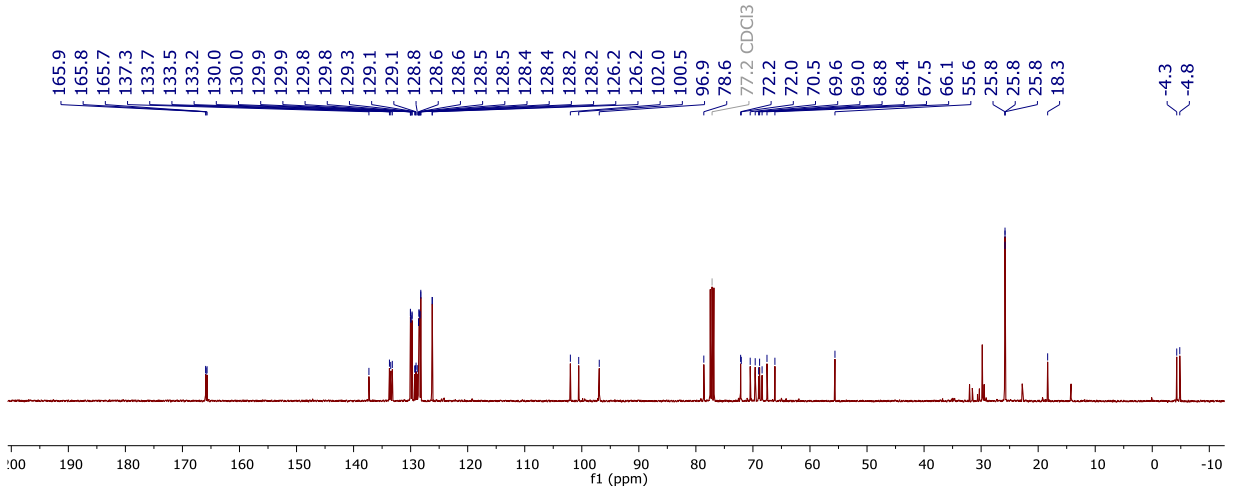
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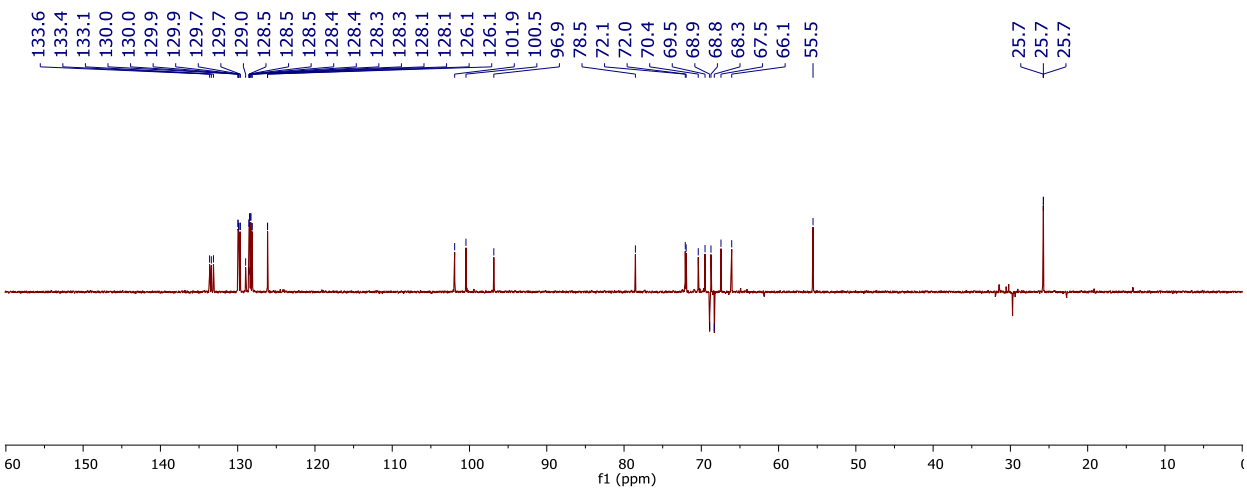
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **19b**



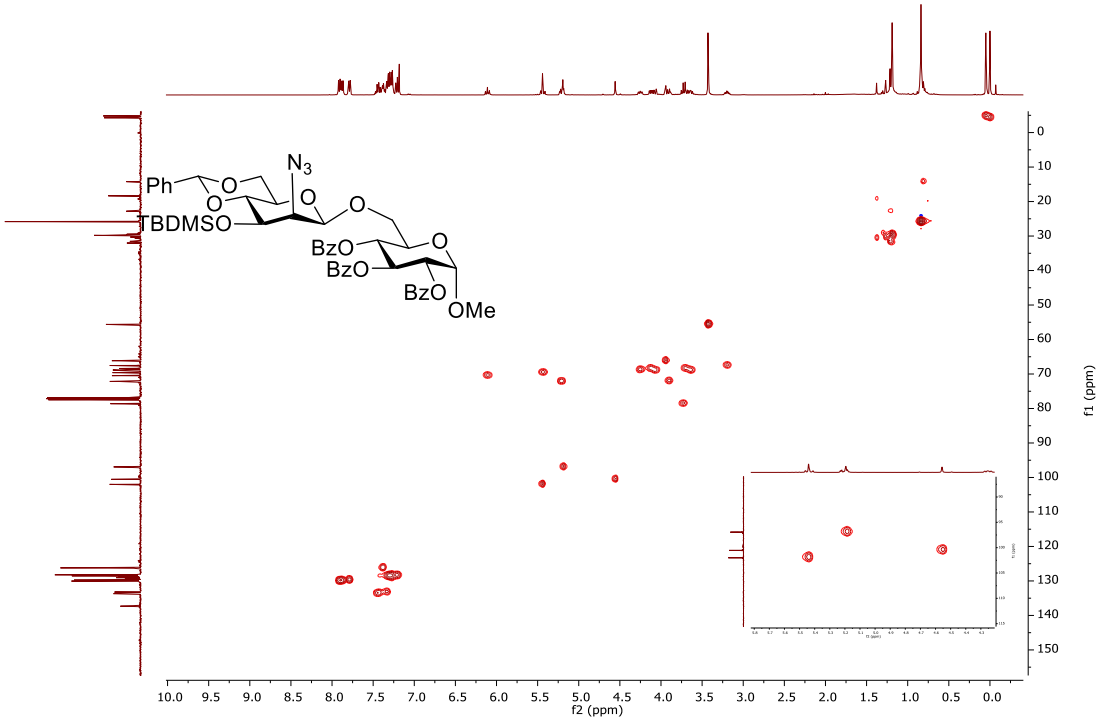
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **19b**



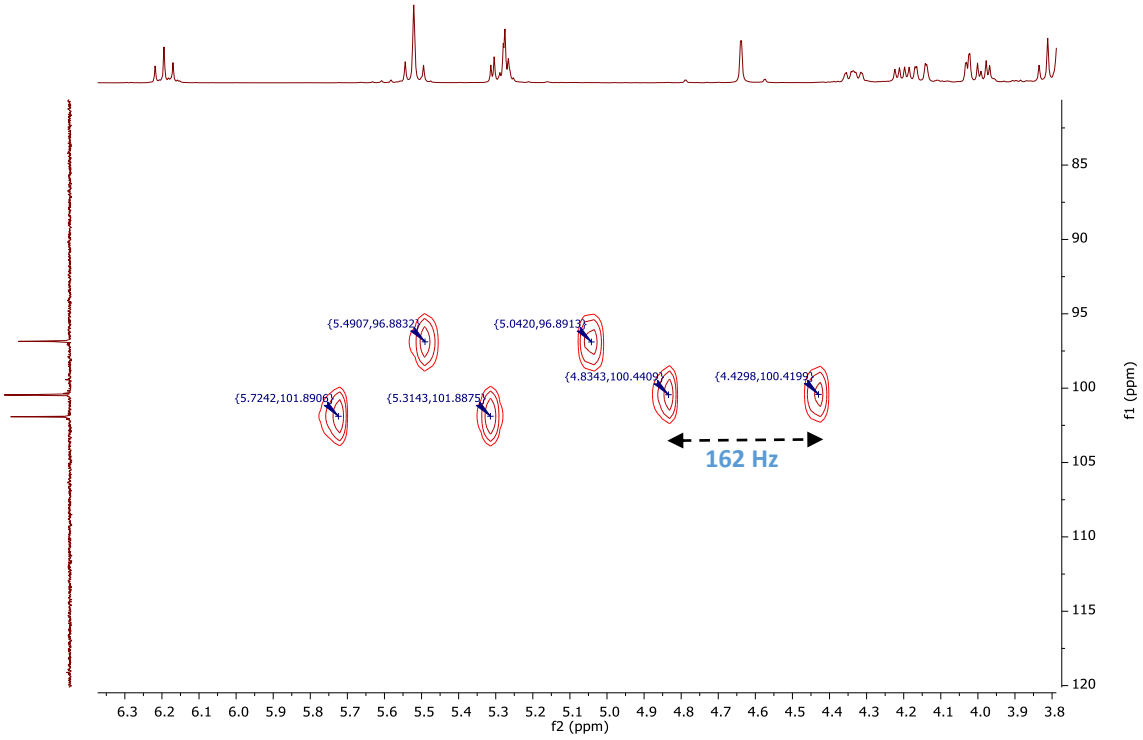
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **19b**



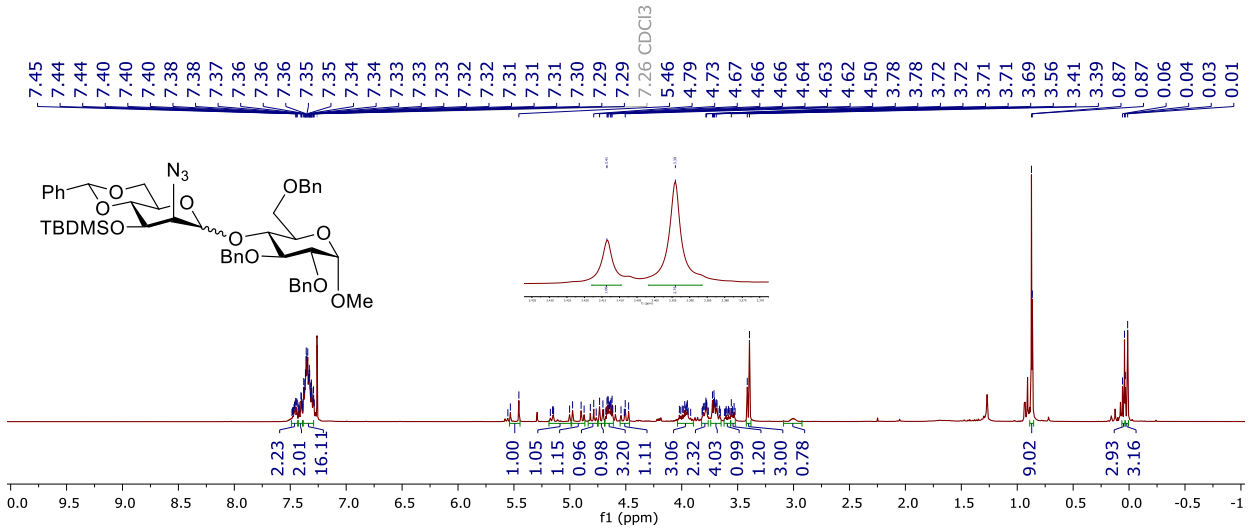
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **19b**



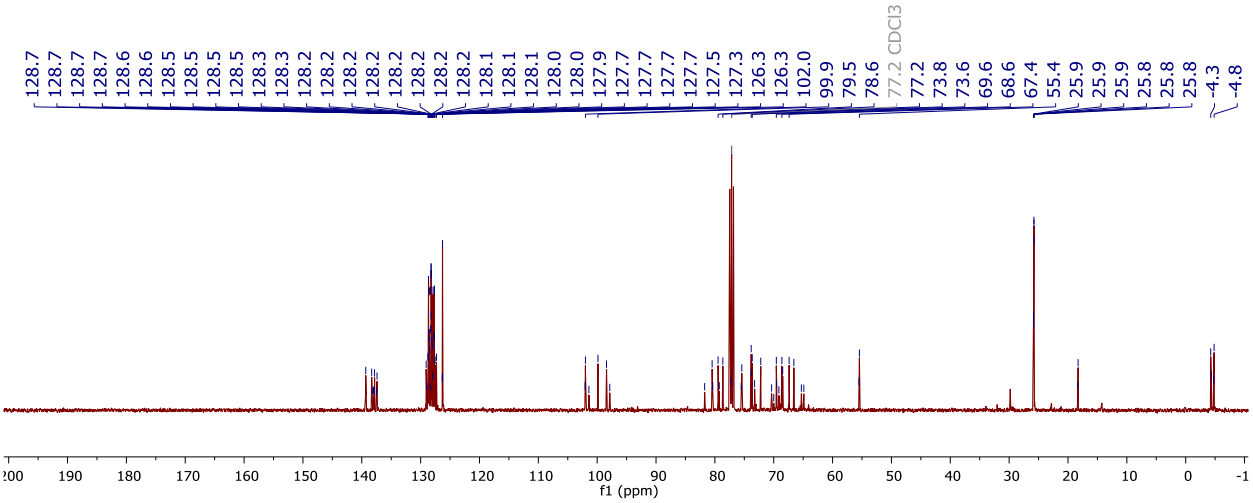
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **19b**



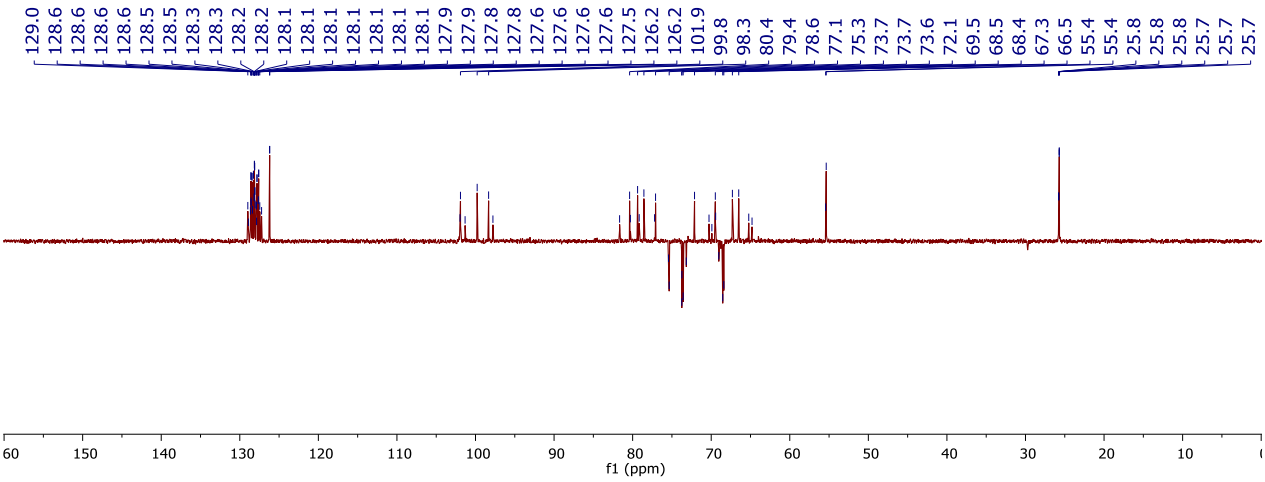
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **19c**



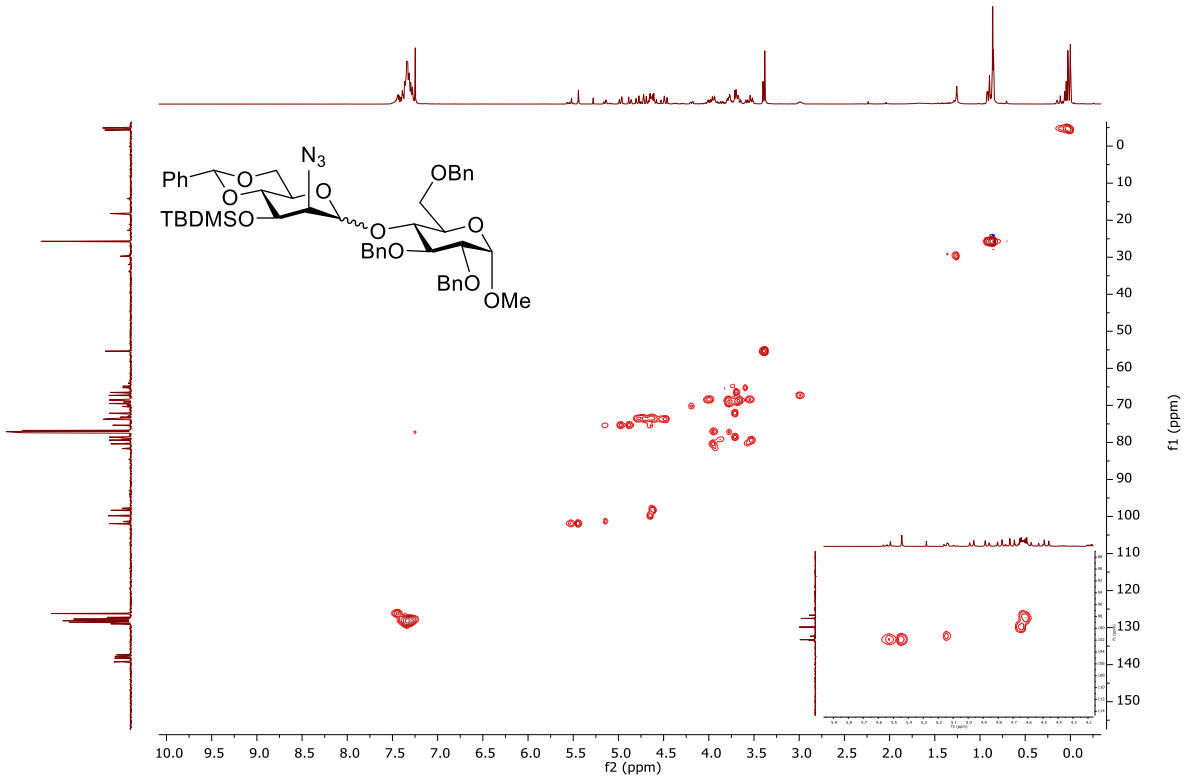
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **19c**



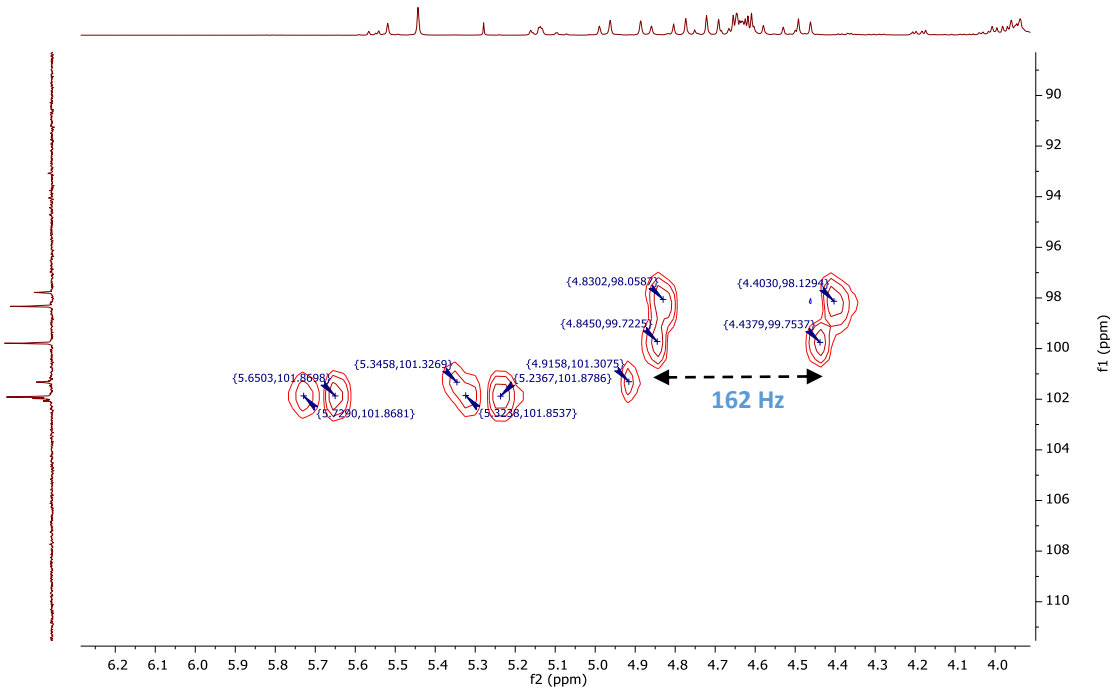
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **19c**



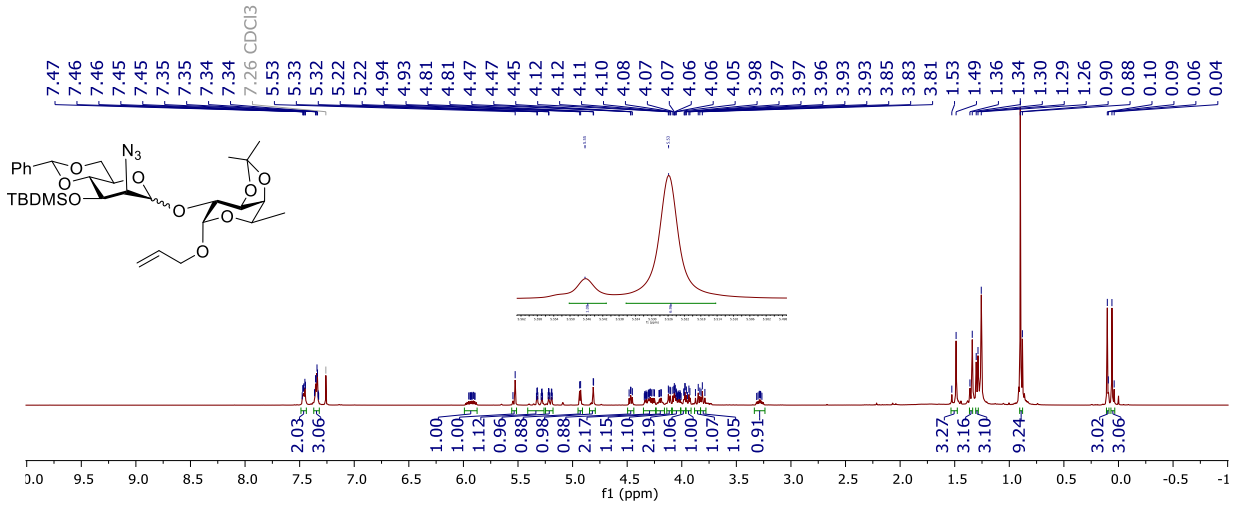
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, $CDCl_3$) of compound **19c**



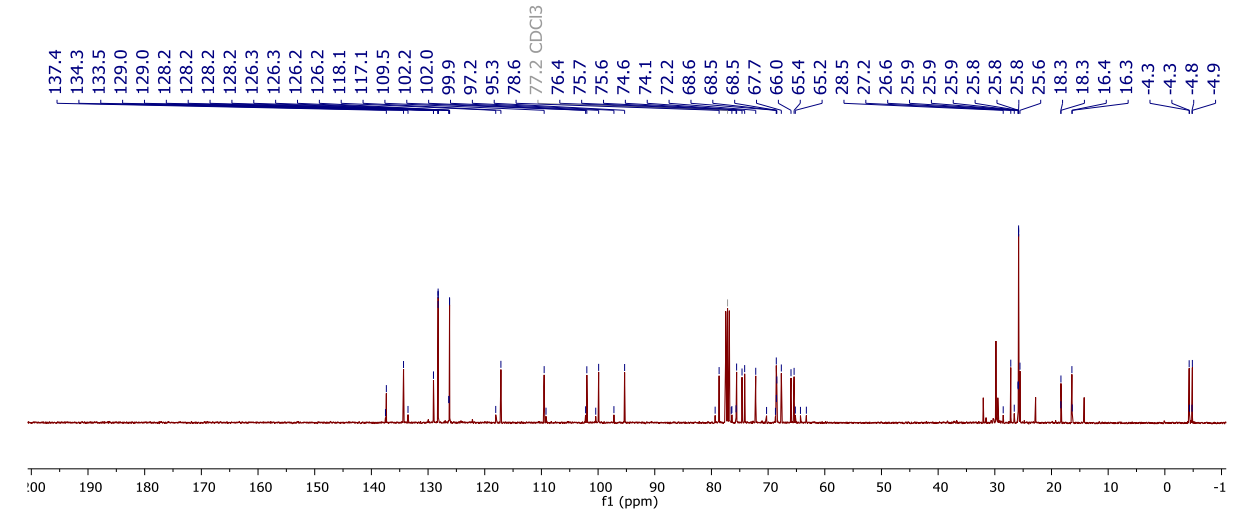
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **19c**



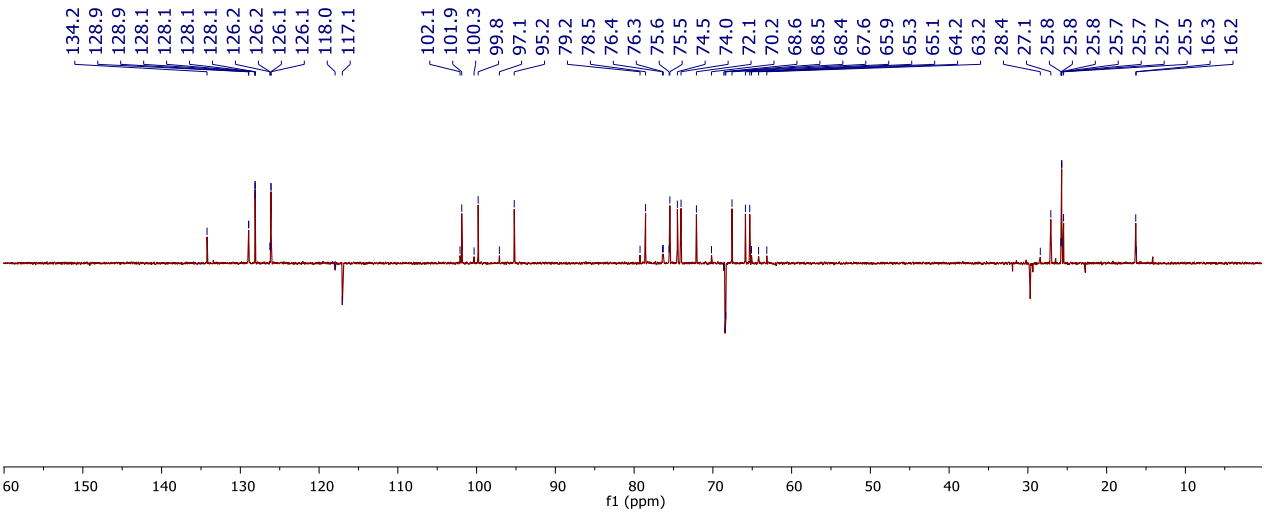
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **19d**



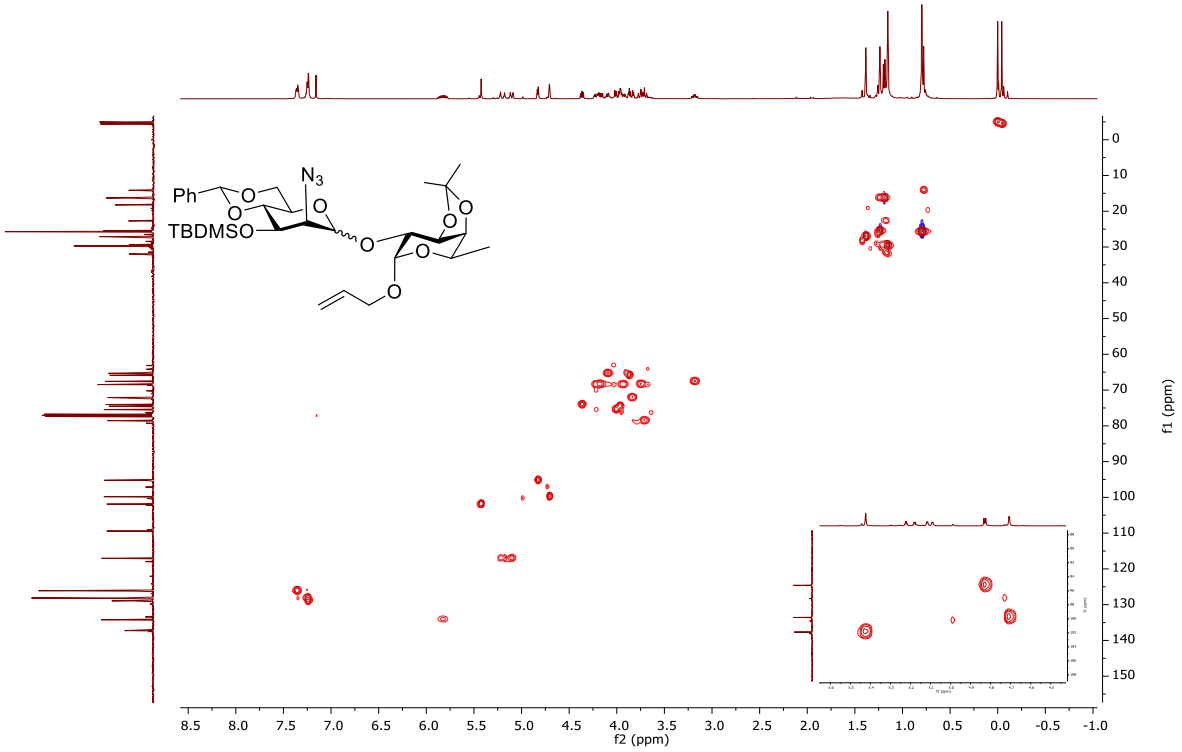
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **19d**



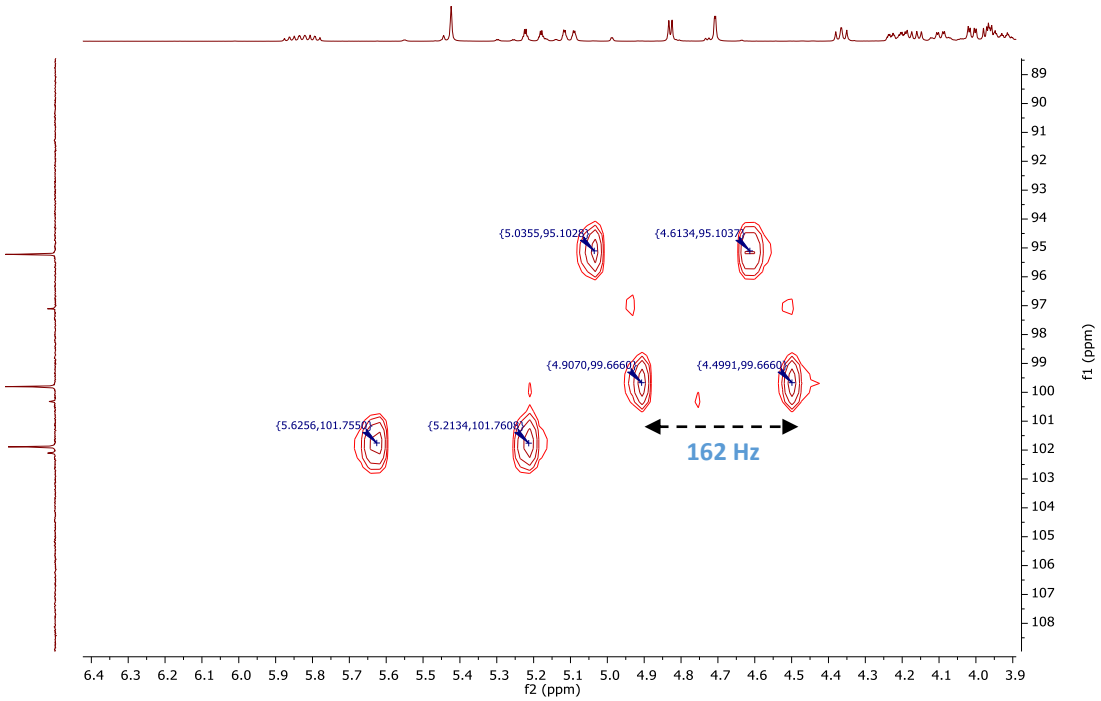
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **19d**



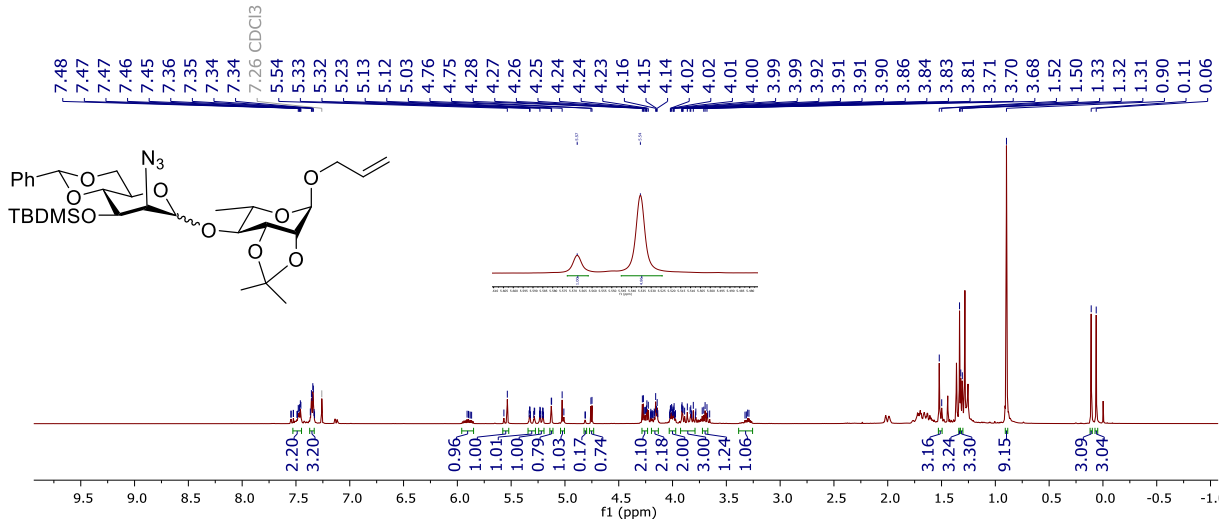
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **19d**



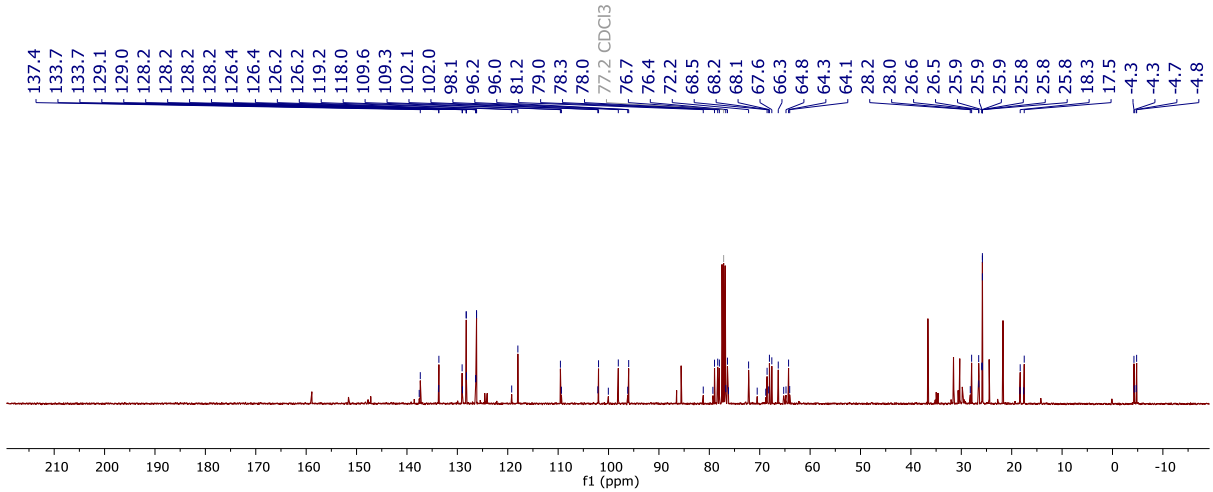
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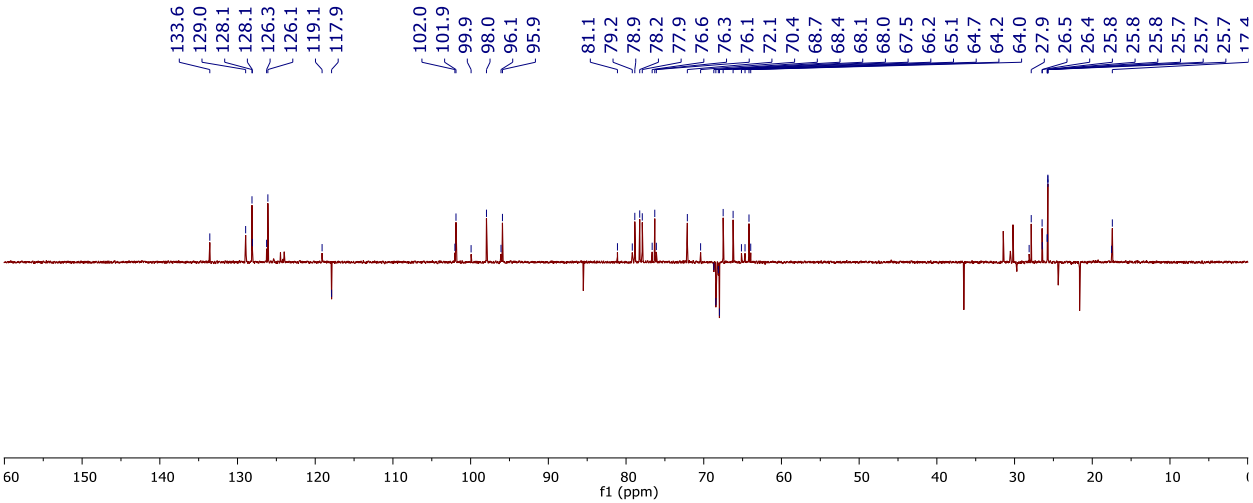
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **19e**



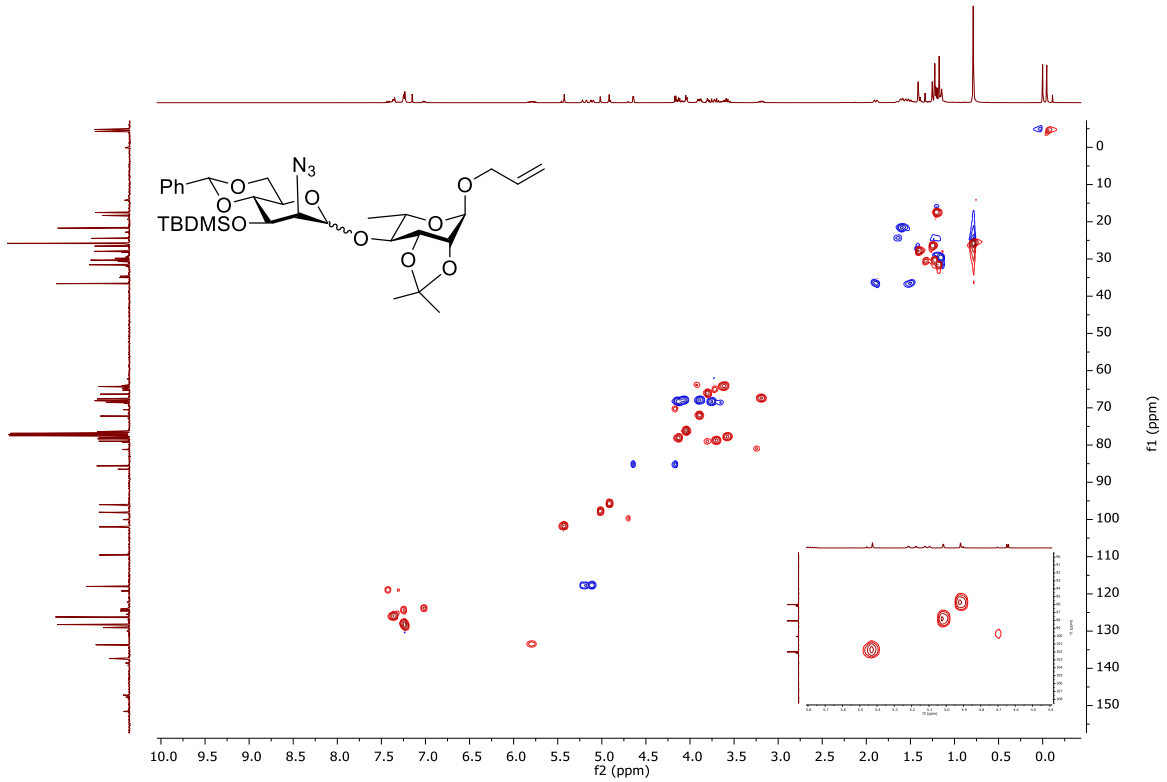
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **19e**



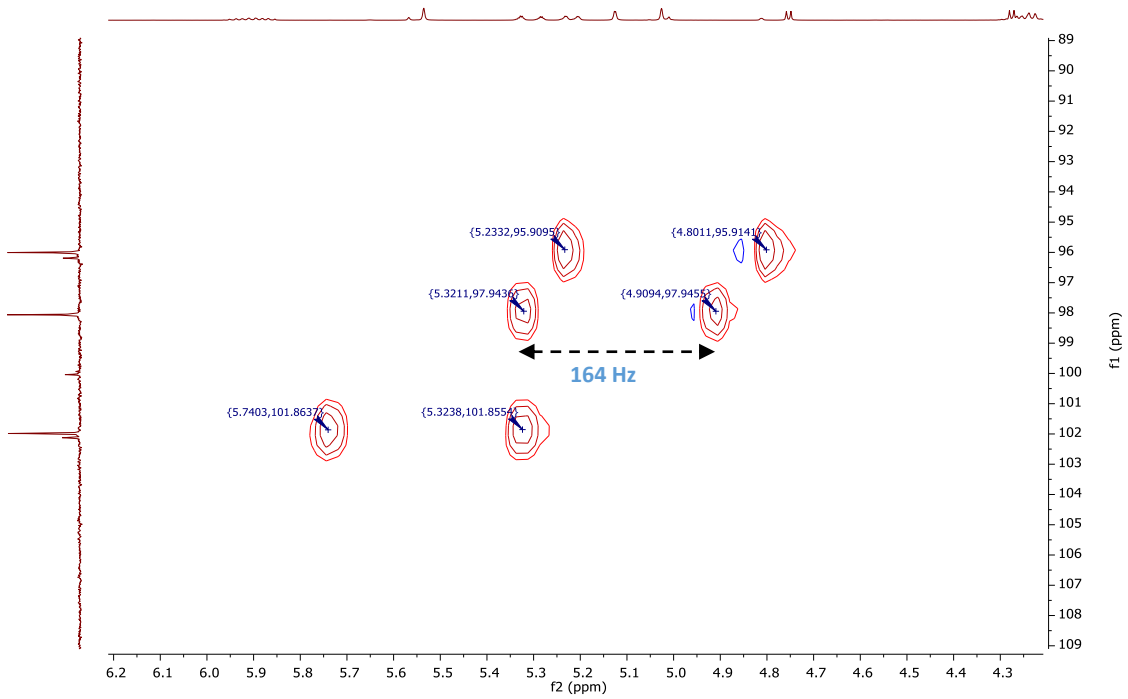
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **19e**



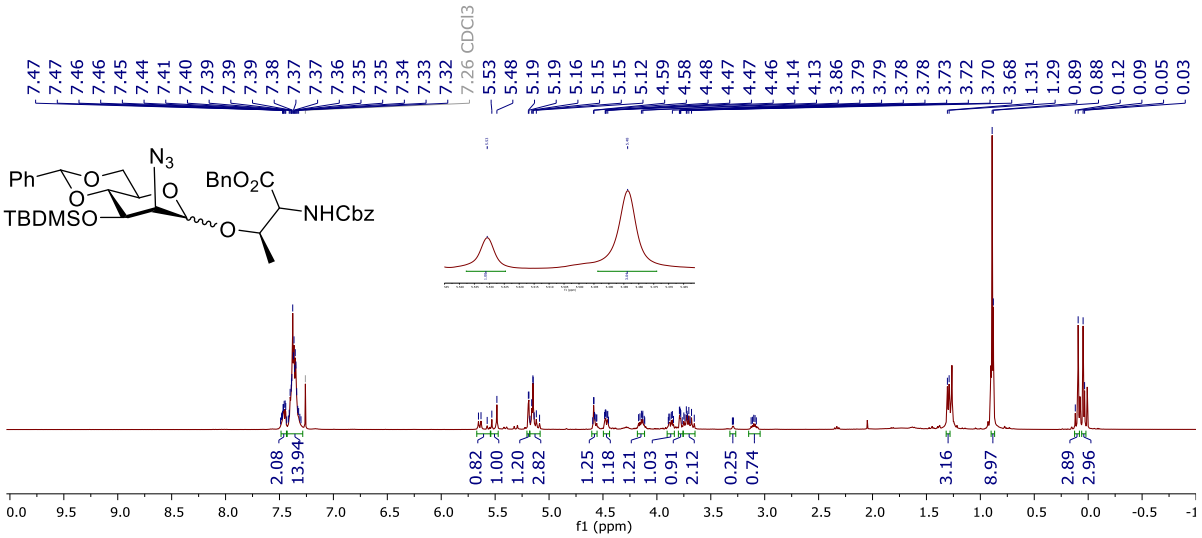
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **19e**



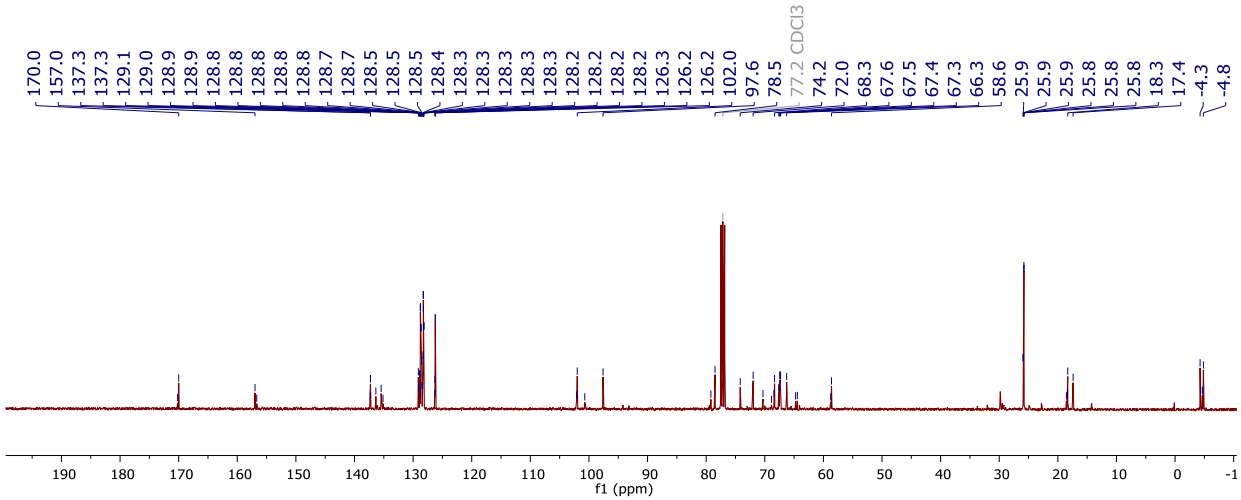
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **19e**



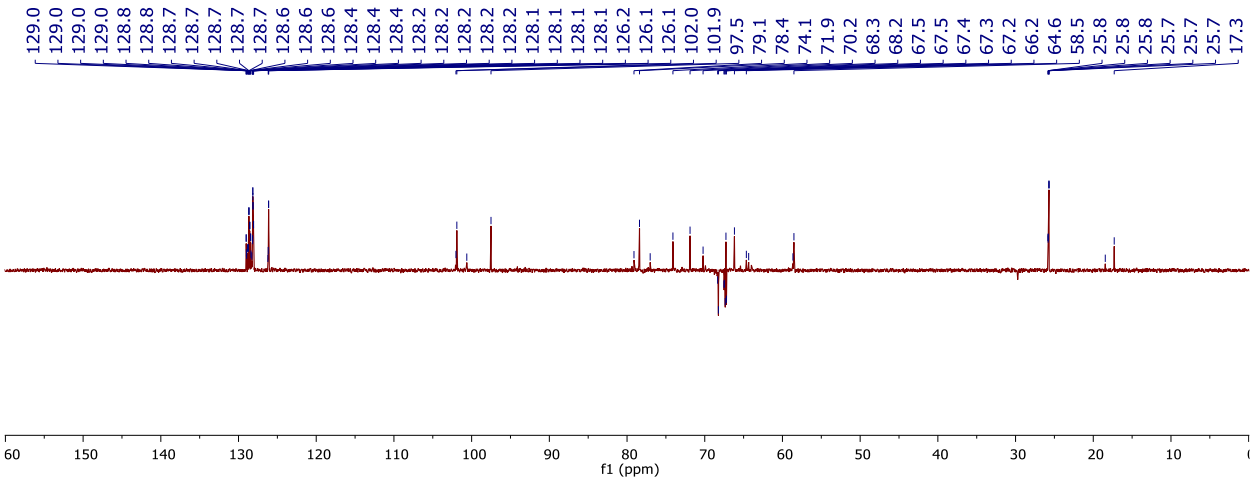
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **19f**



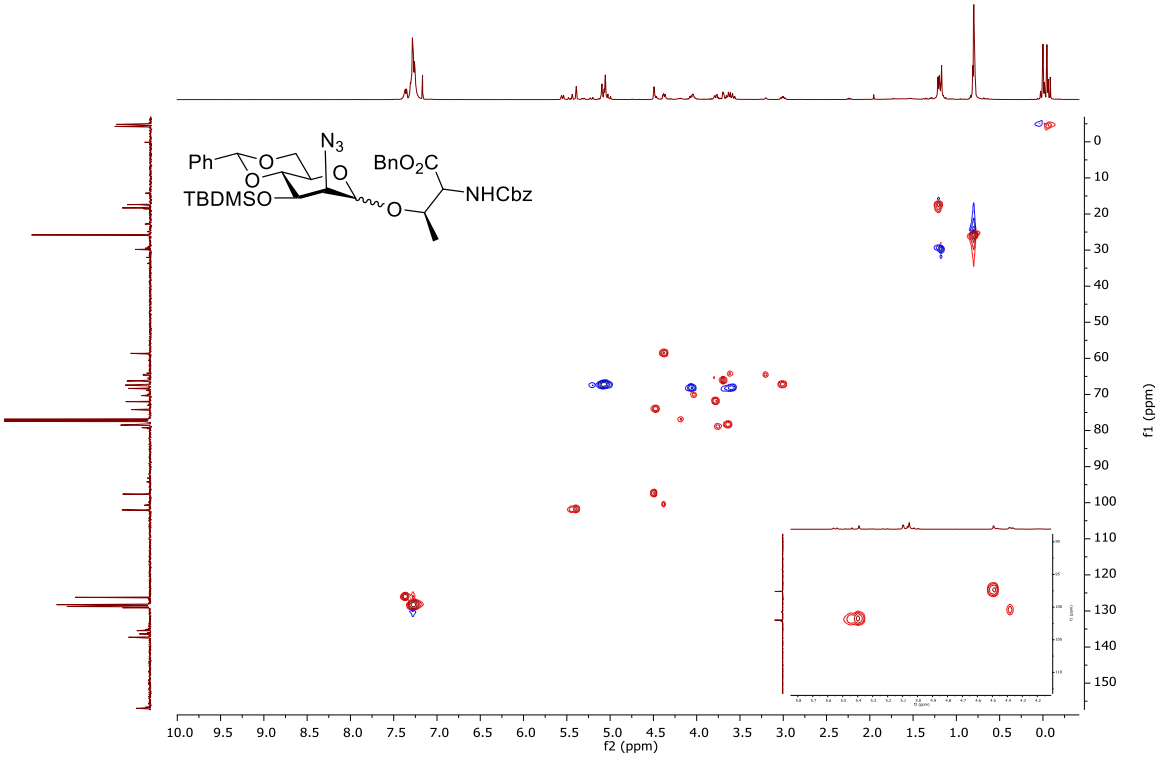
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **19f**



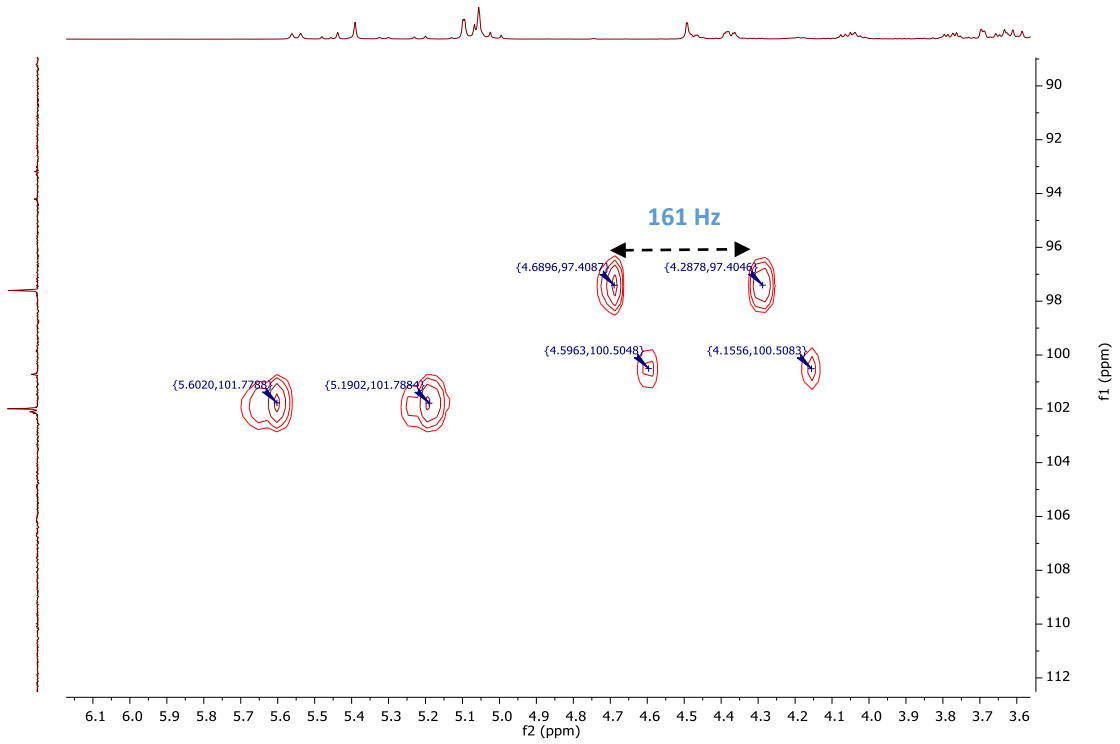
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **19f**



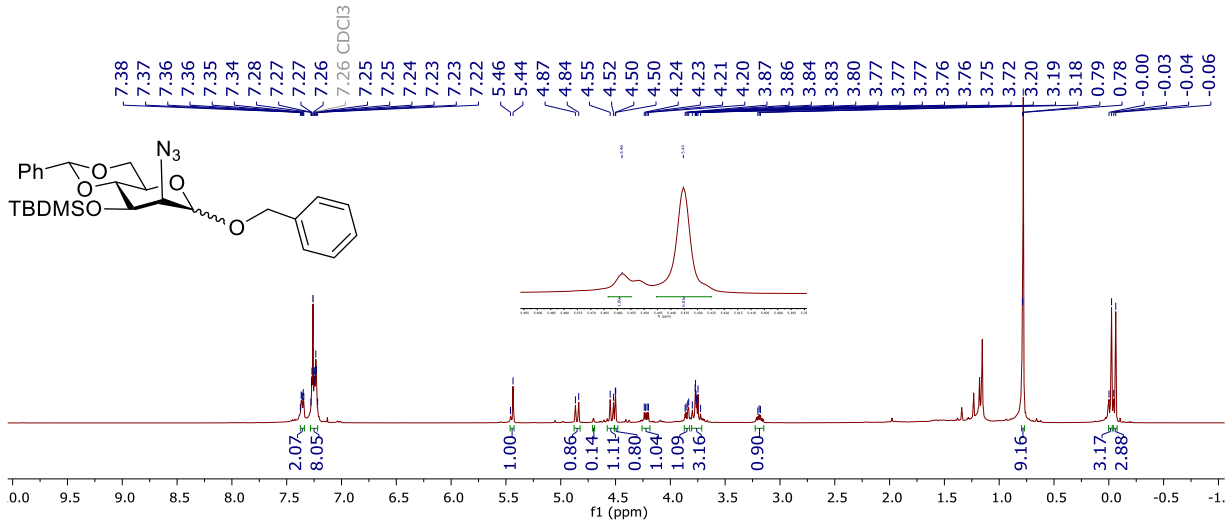
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **19f**



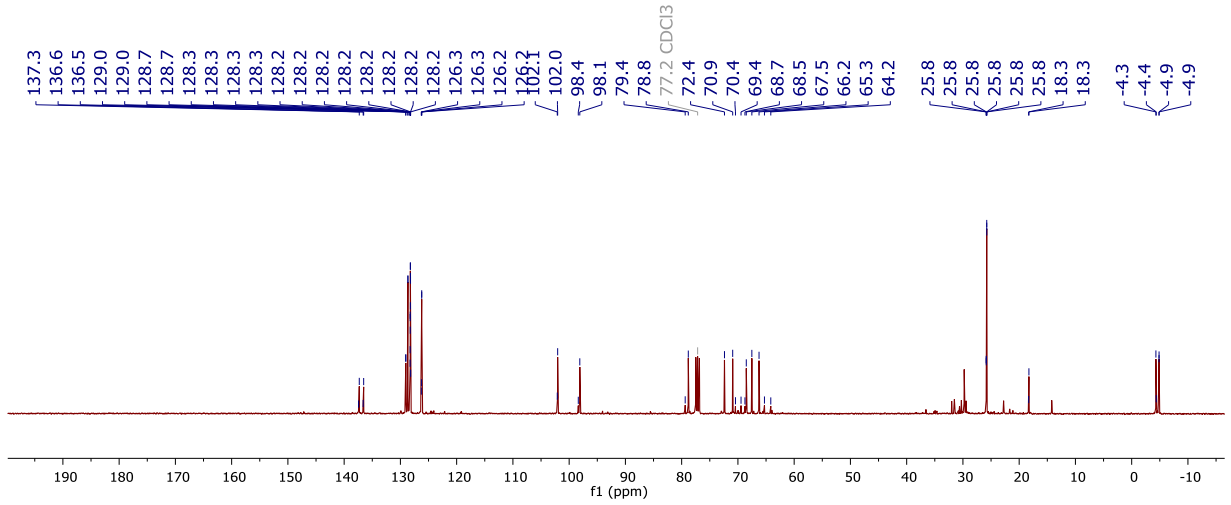
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **19f**



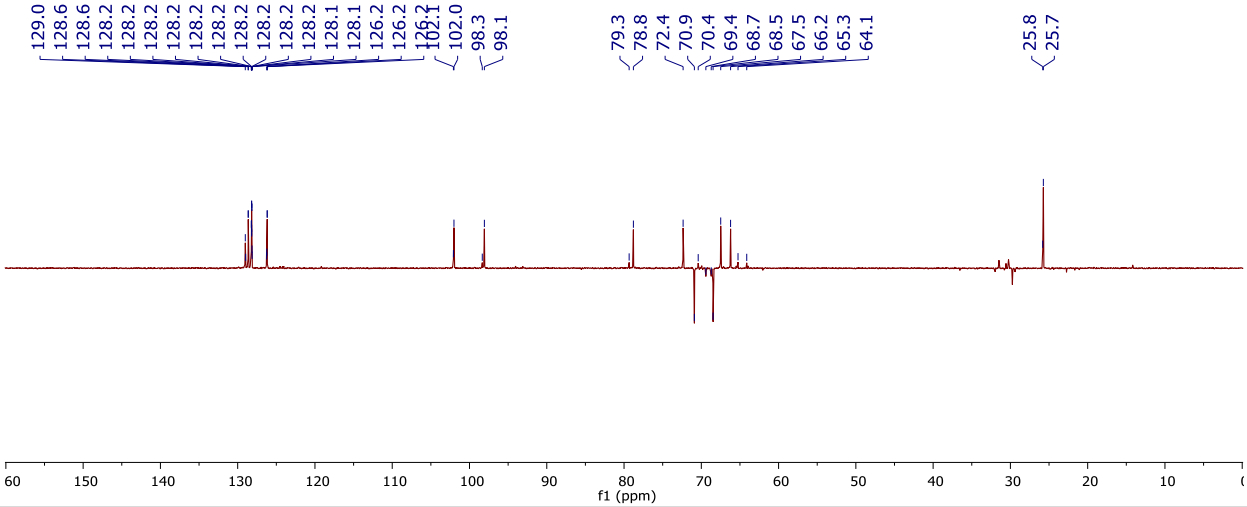
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **19g**



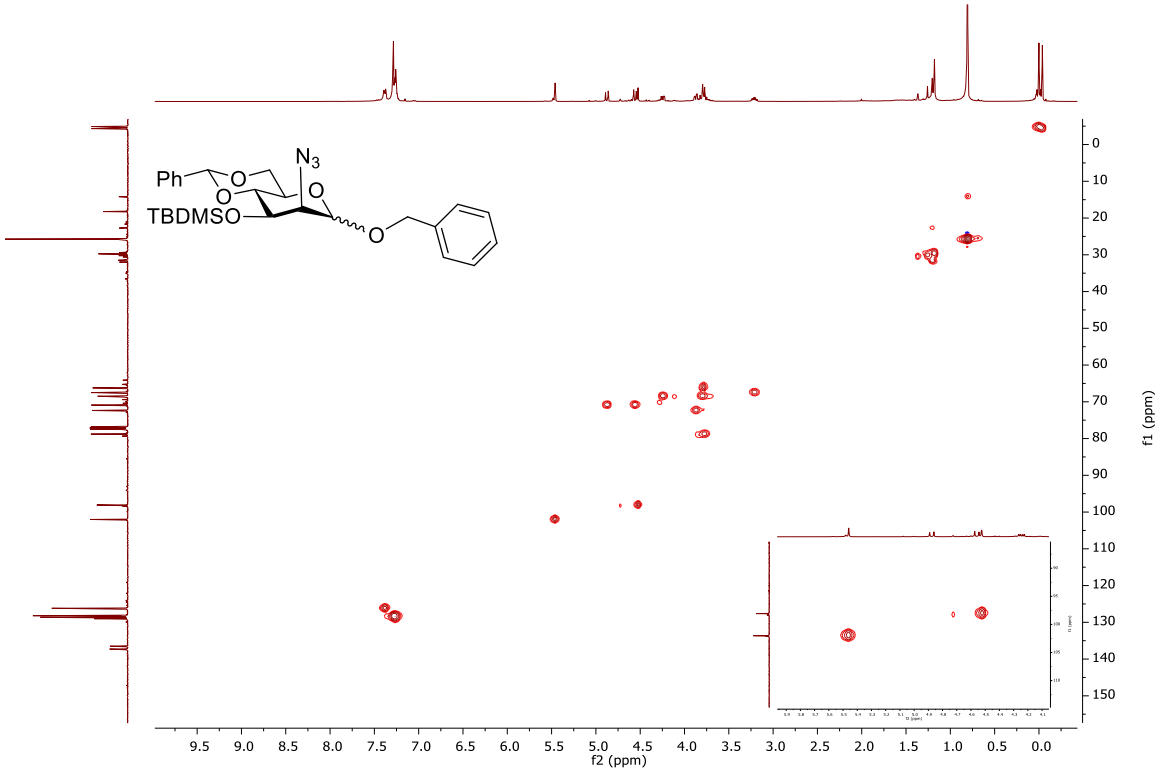
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **19g**



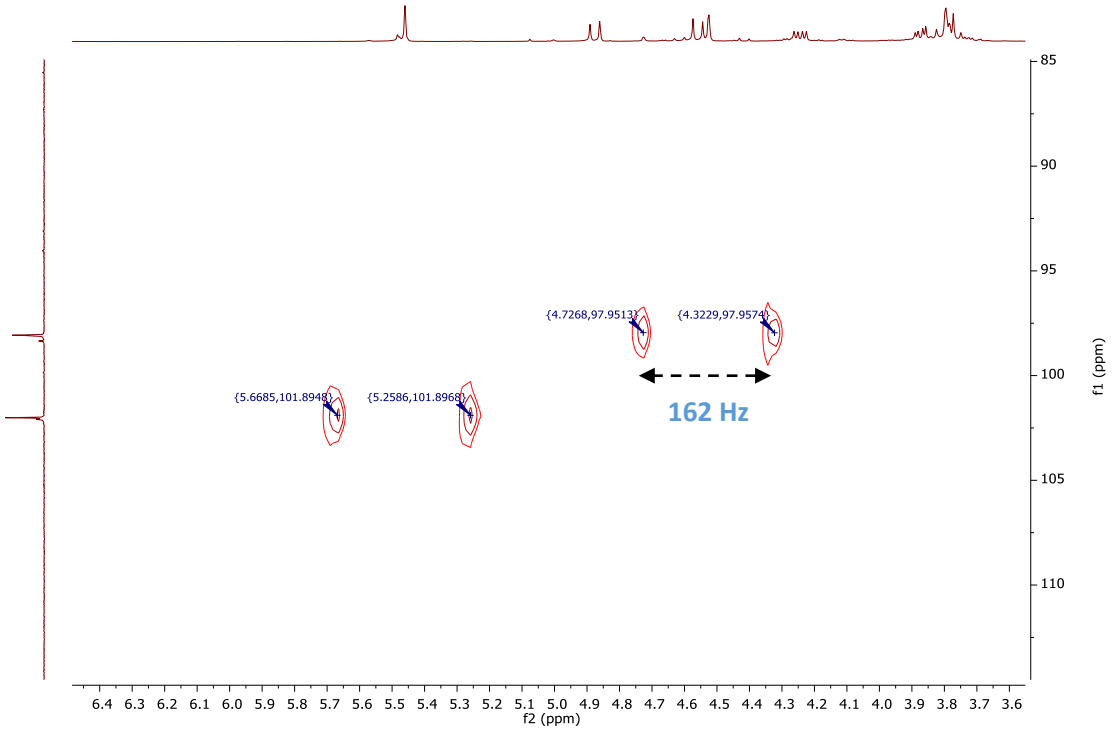
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **19g**



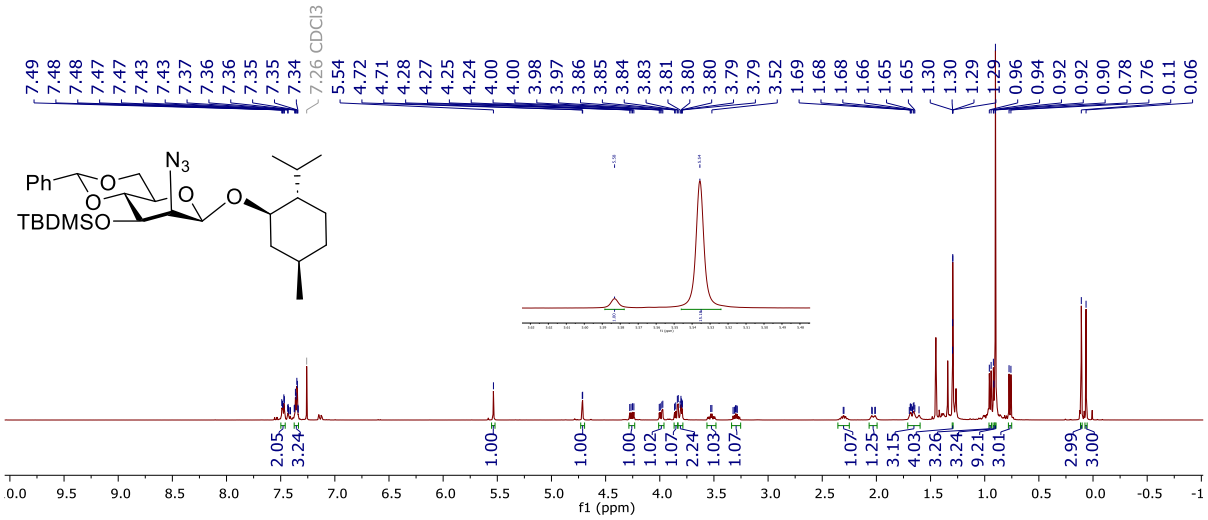
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **19g**



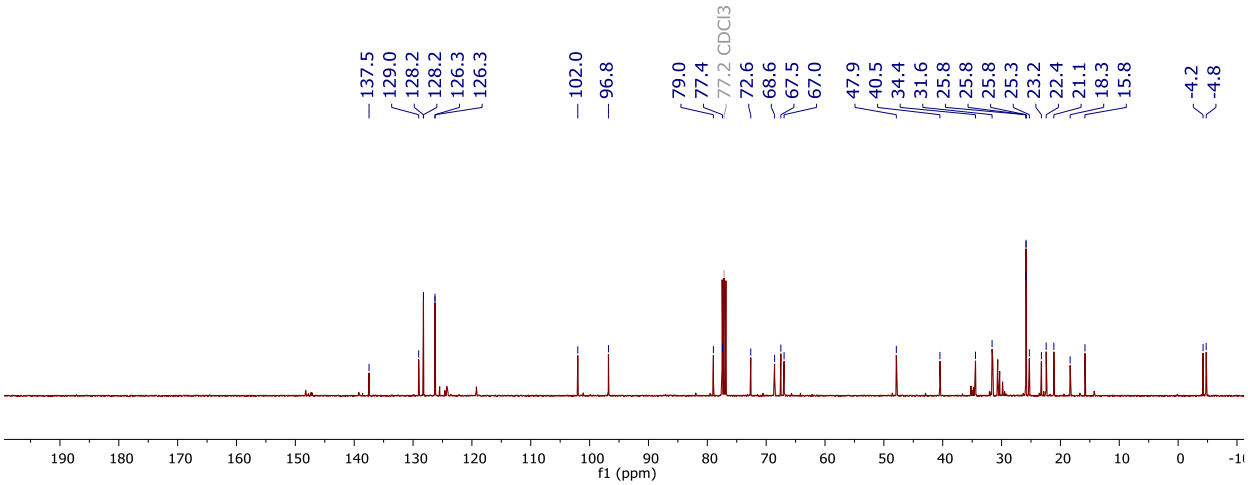
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **19g**



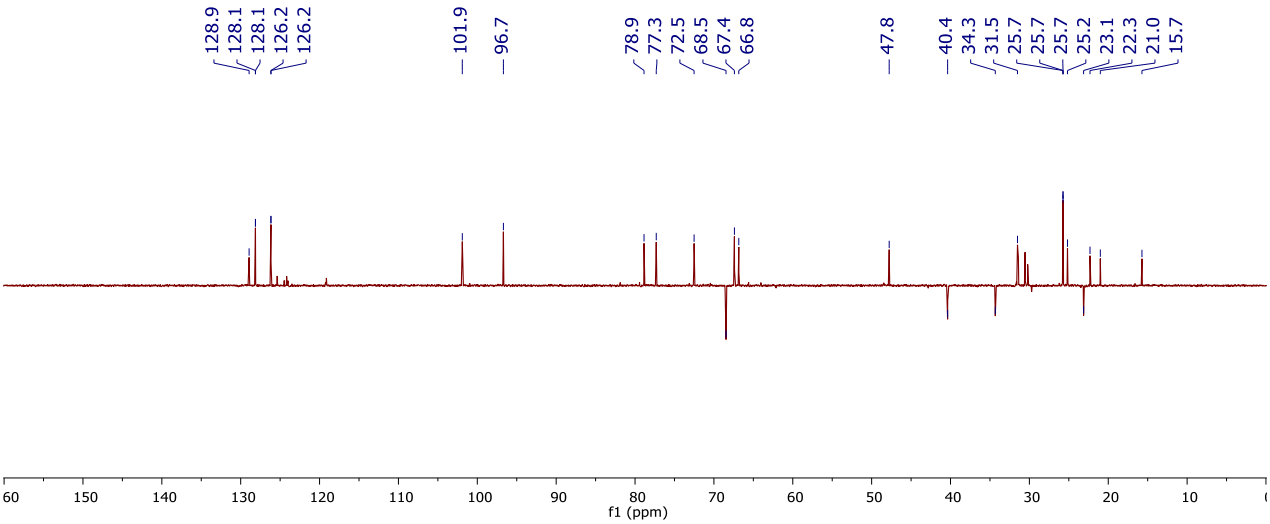
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **19h**



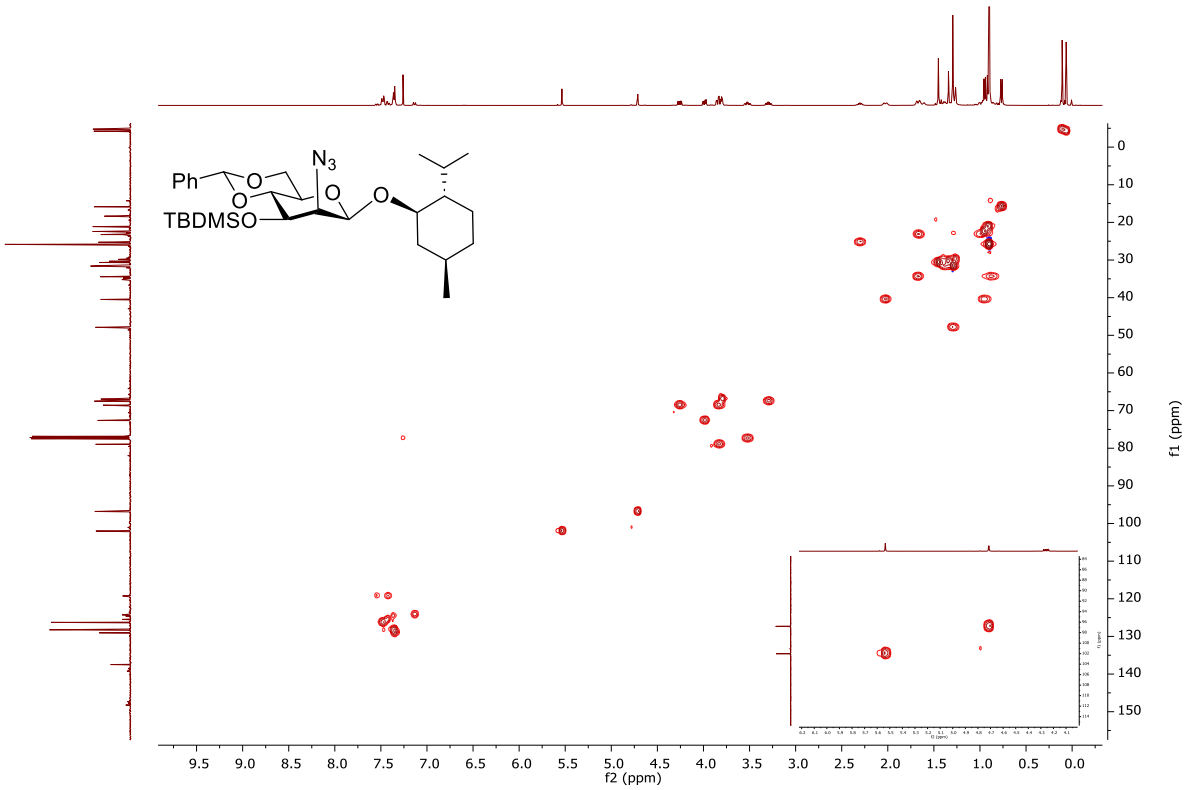
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **19h**



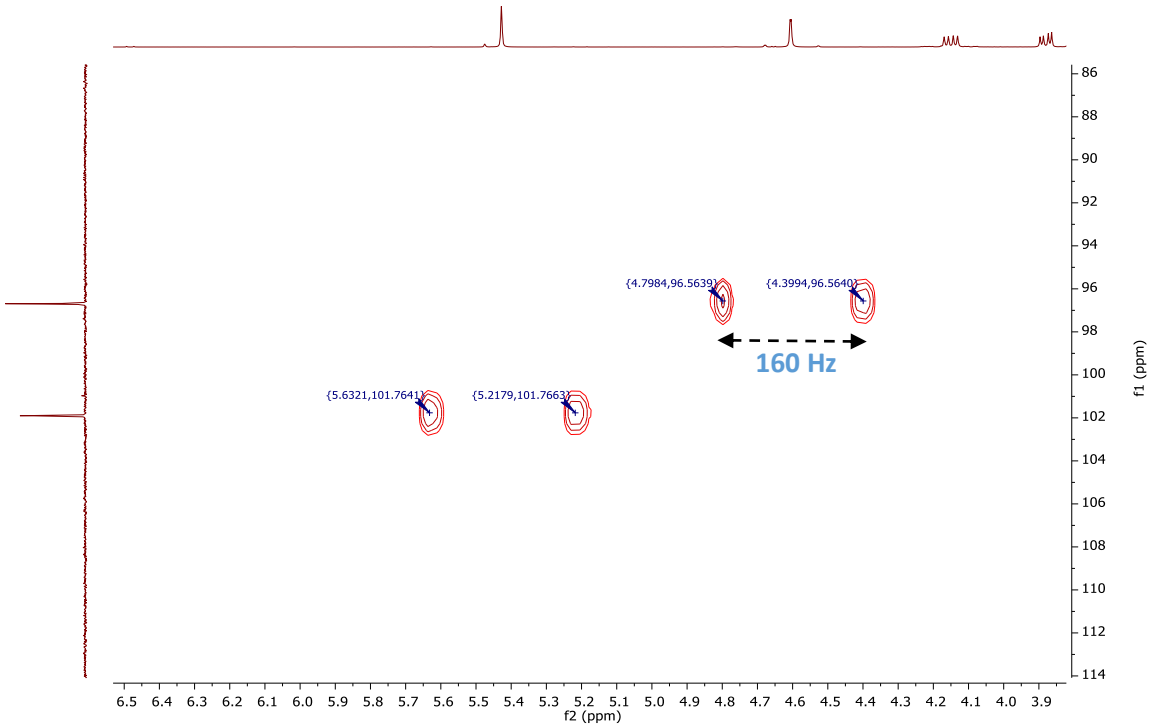
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **19h**



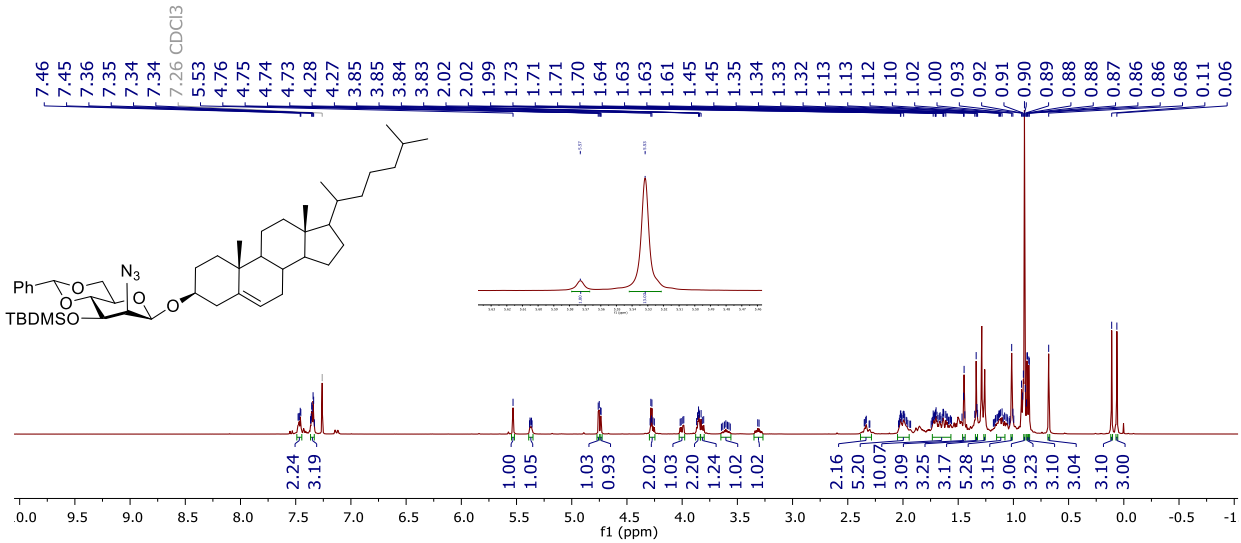
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **19h**



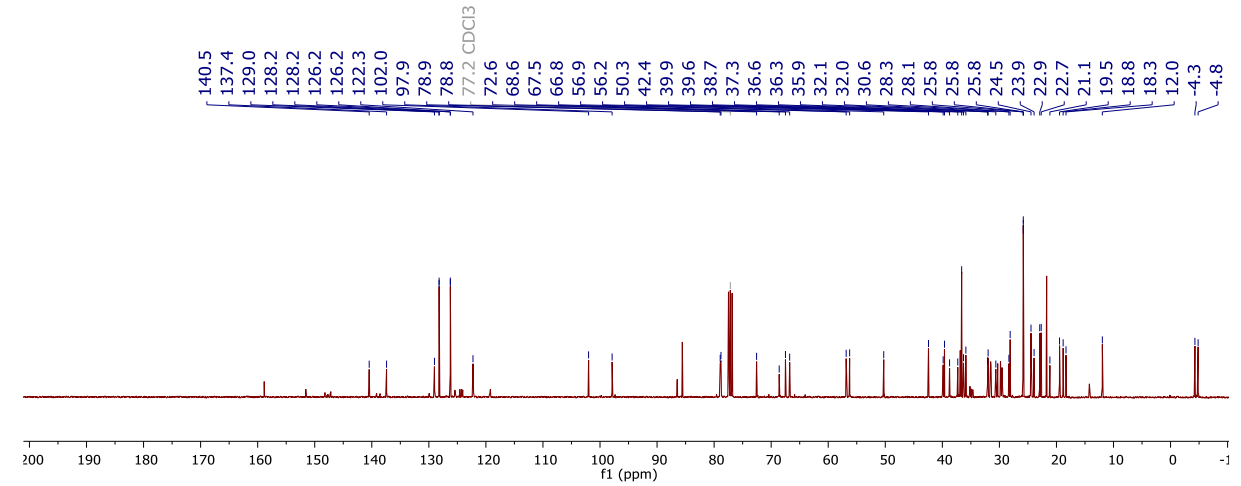
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **19h**



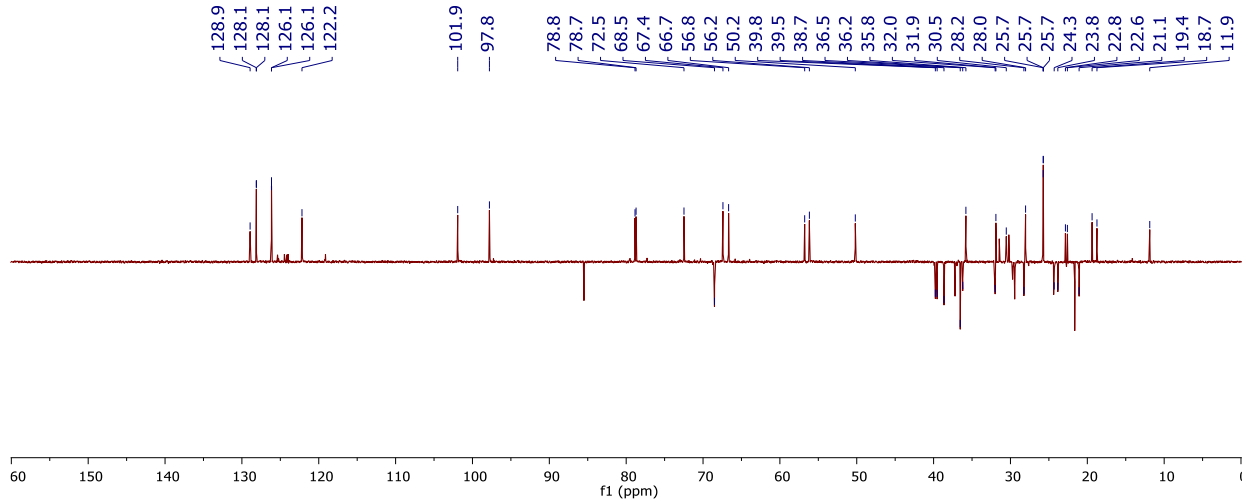
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **19i**



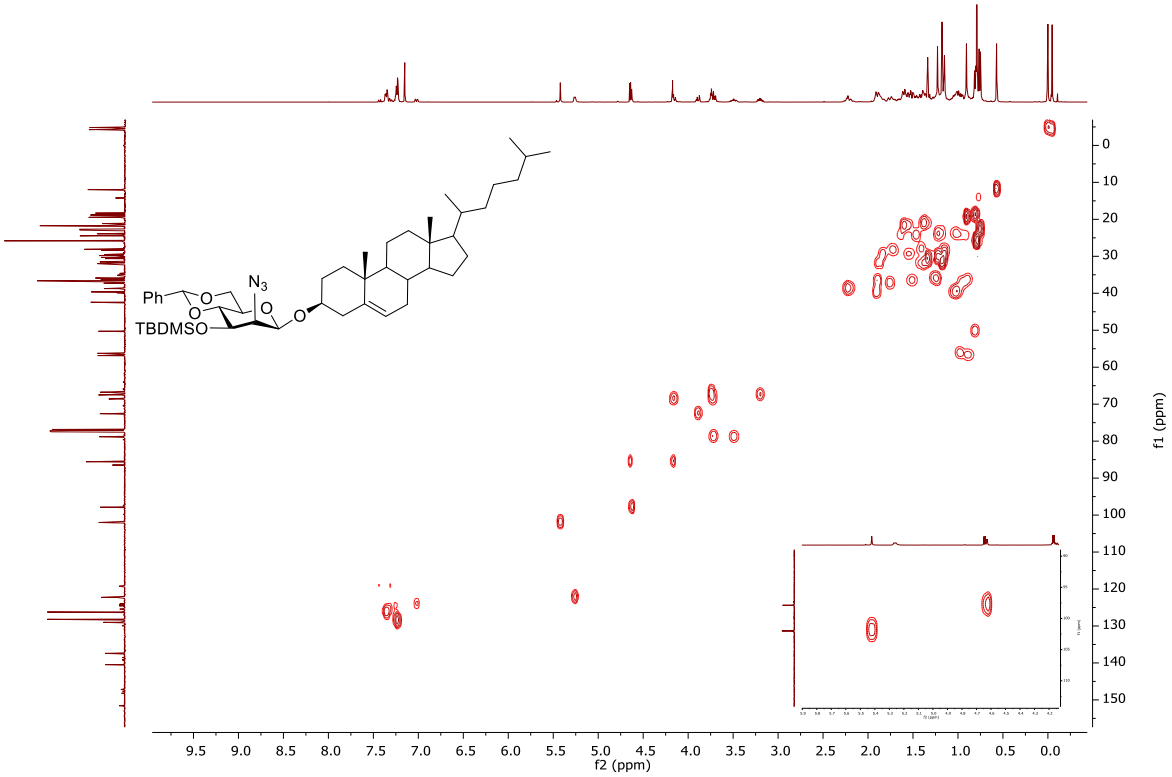
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **19i**



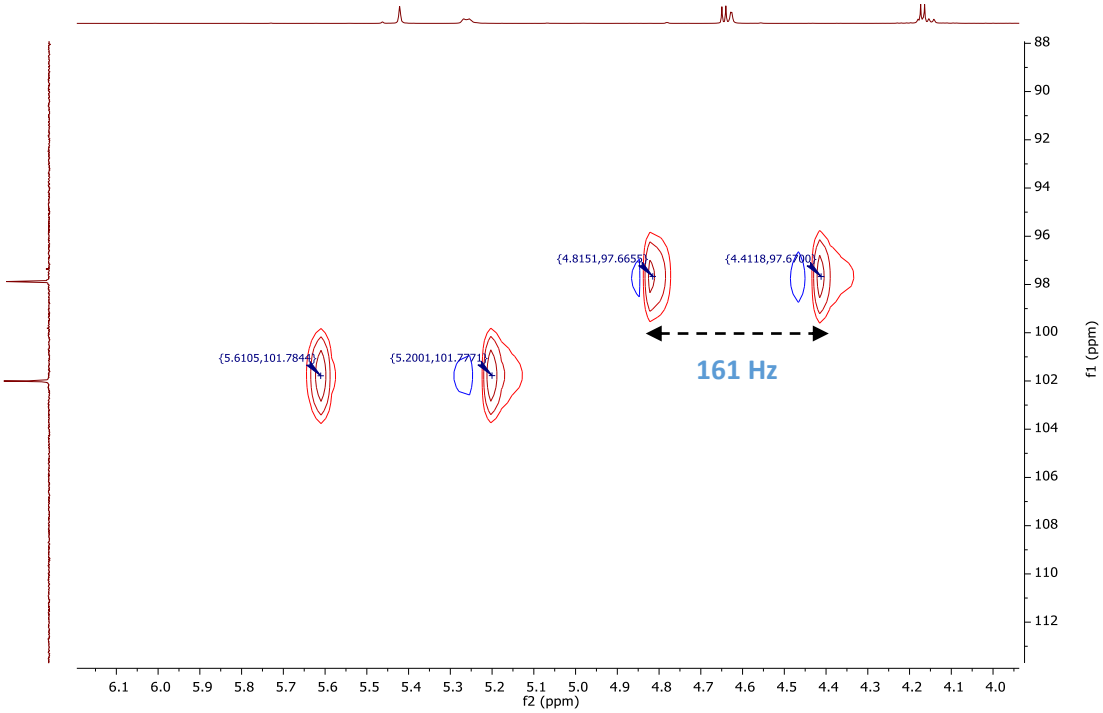
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **19i**



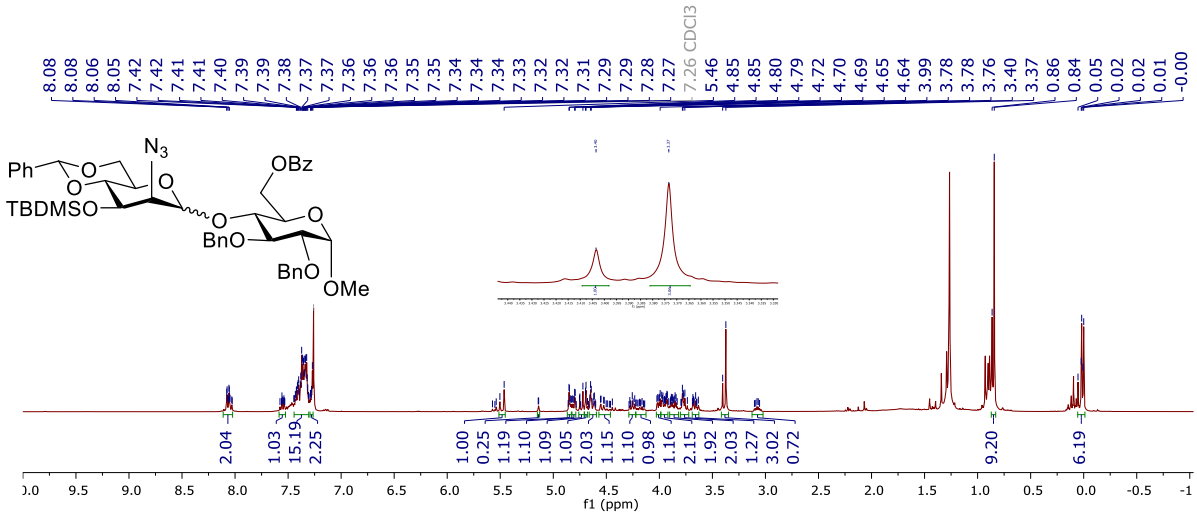
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **19i**



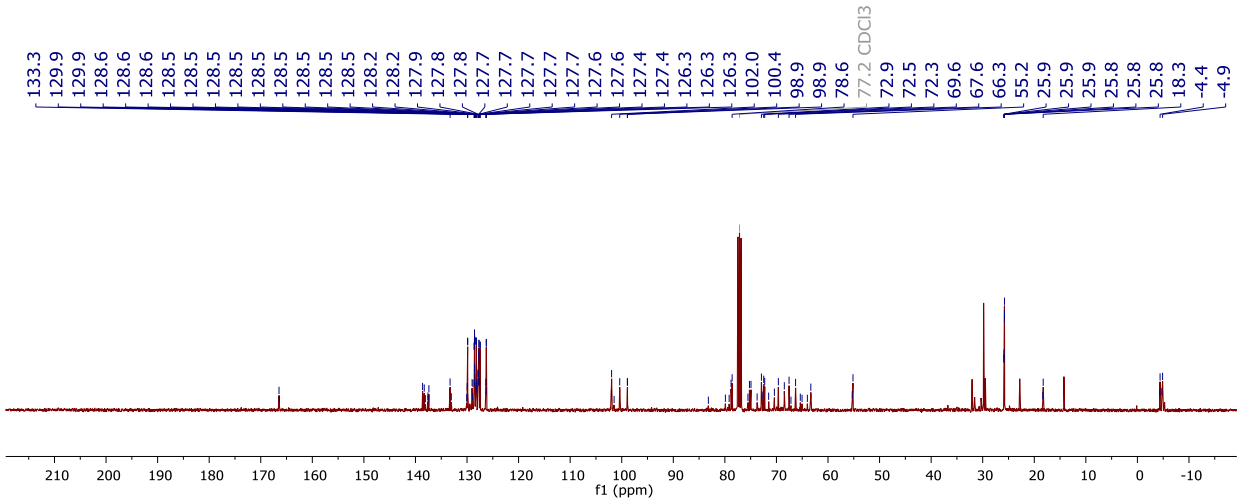
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **19i**



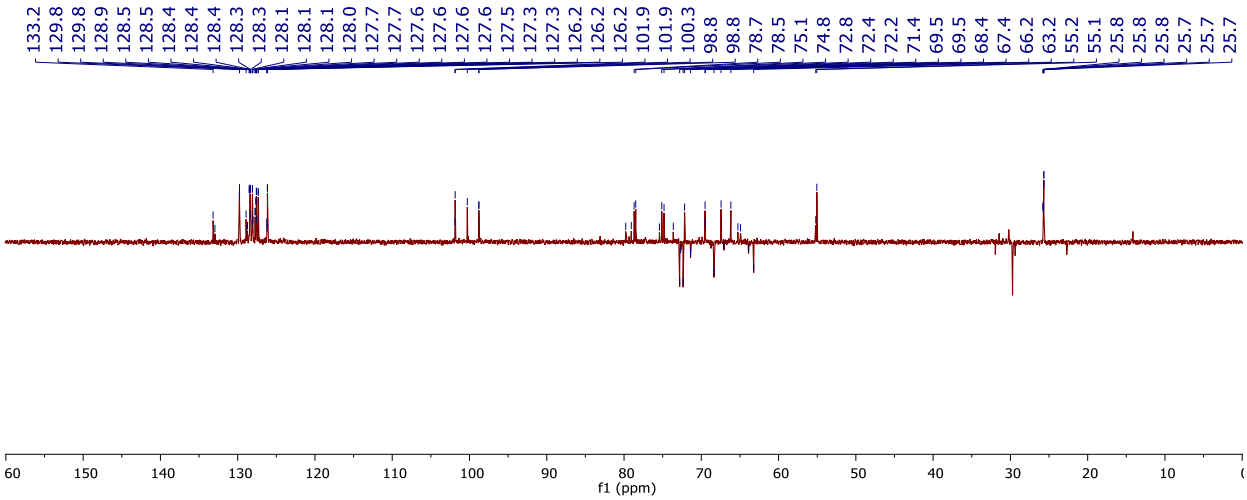
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **19j**



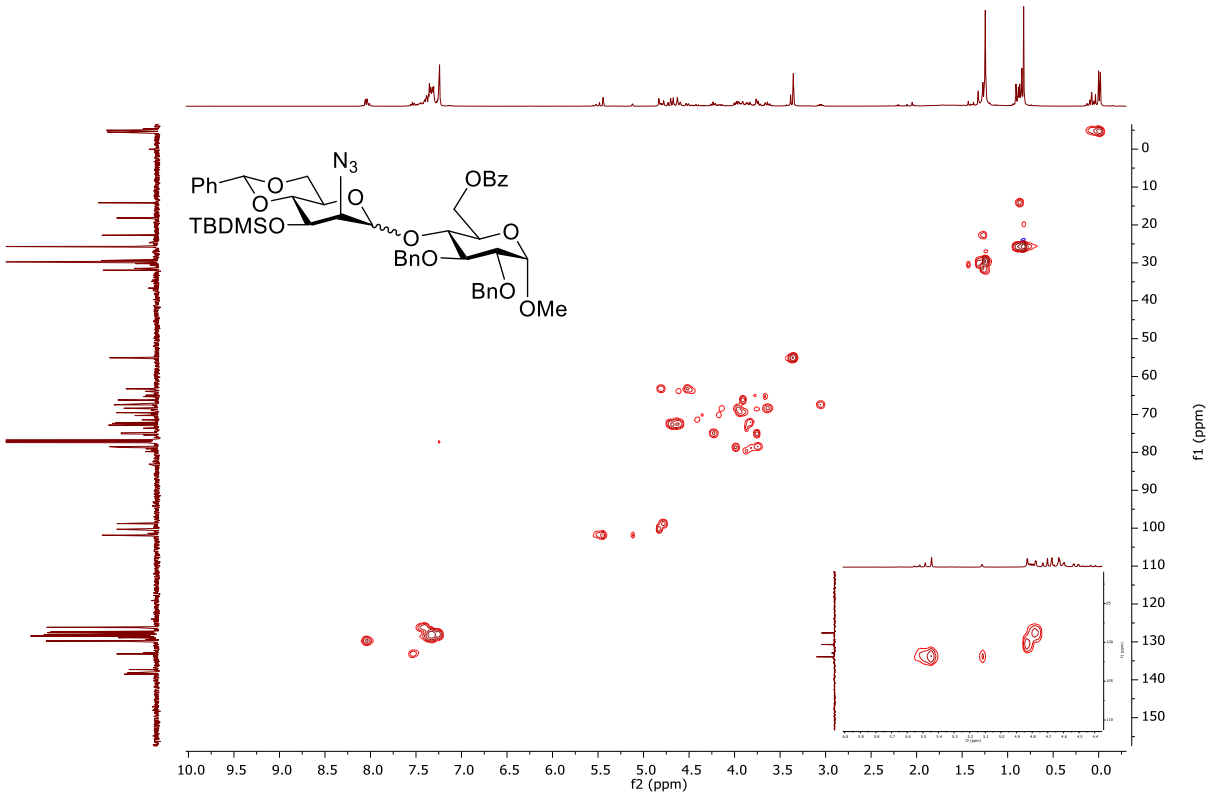
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **19j**



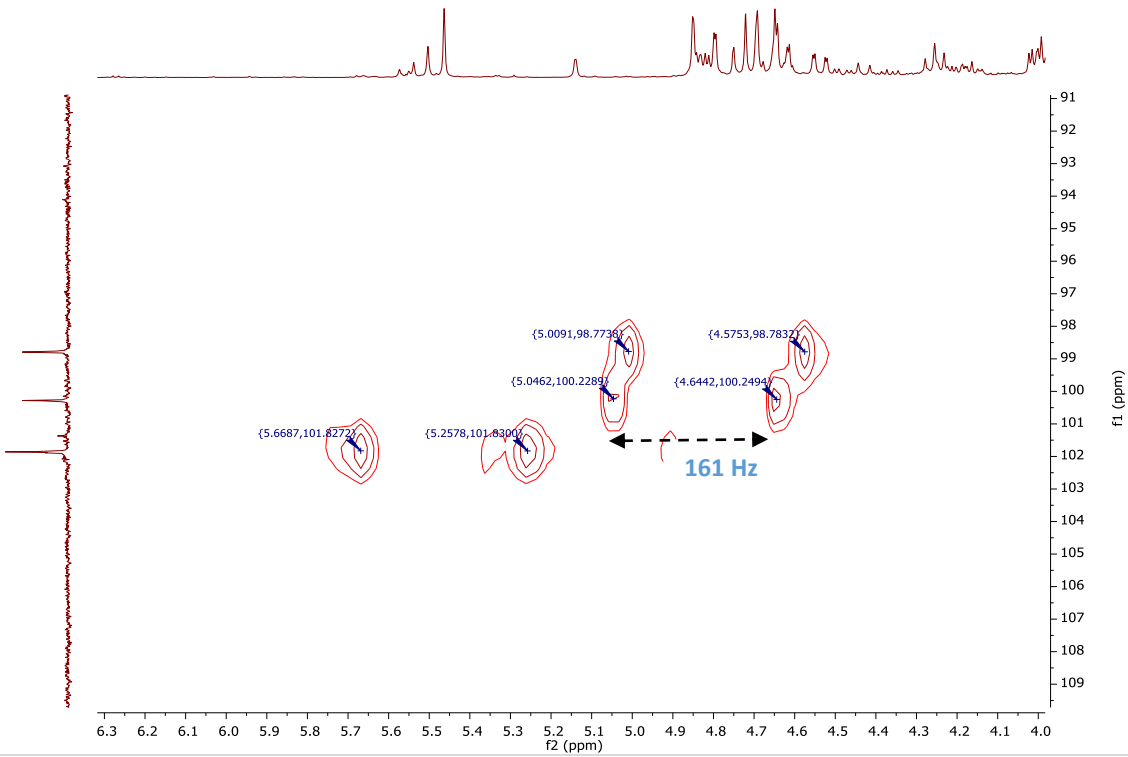
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **19j**



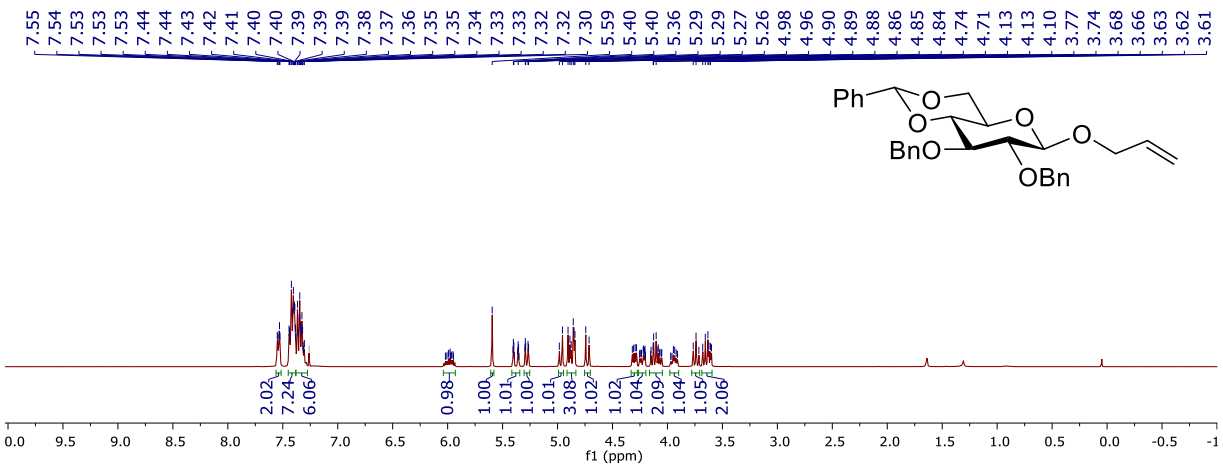
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **19j**



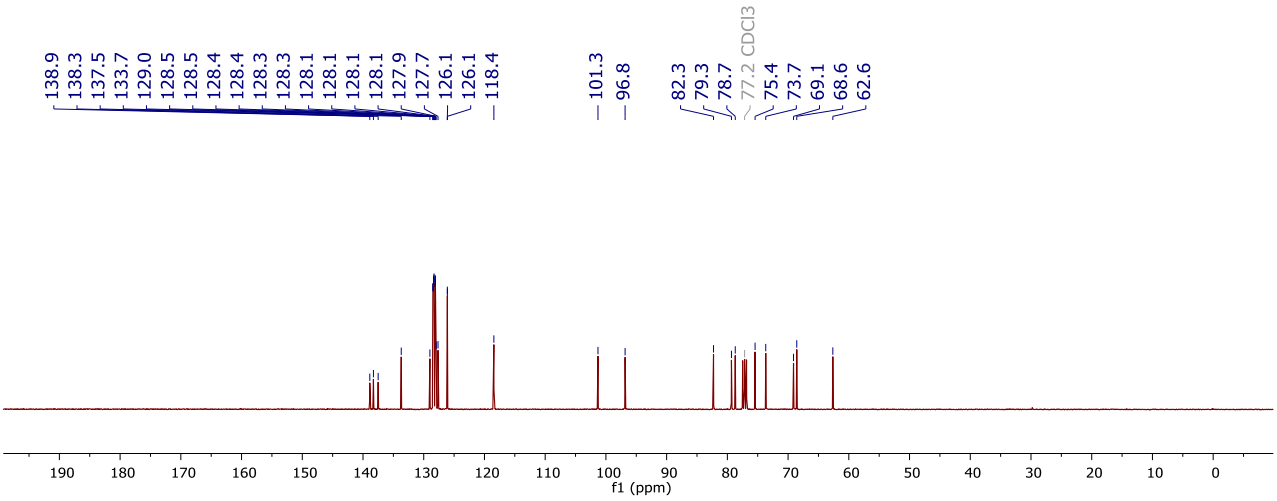
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **19j**



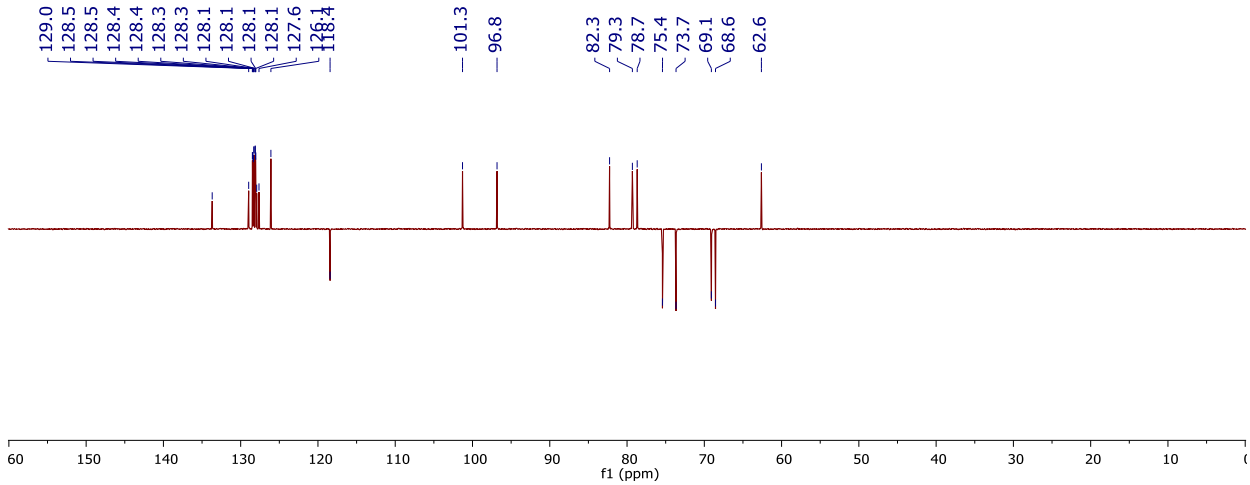
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **32**



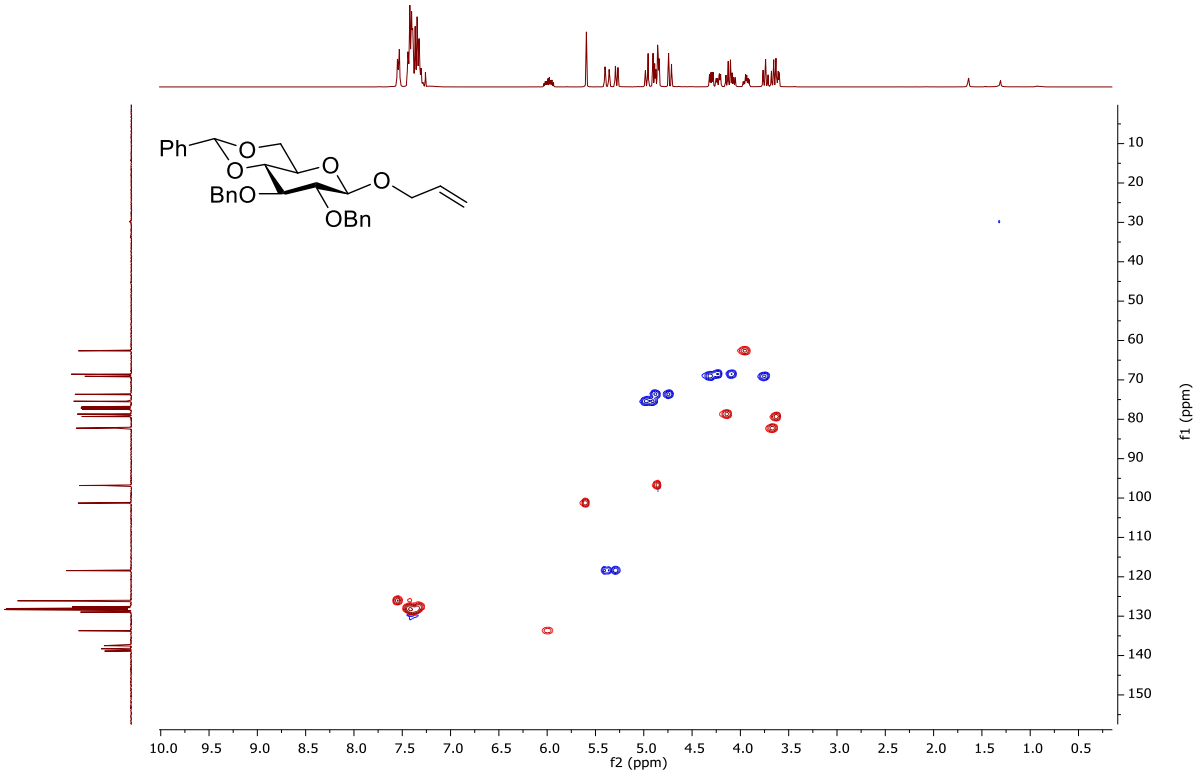
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **32**



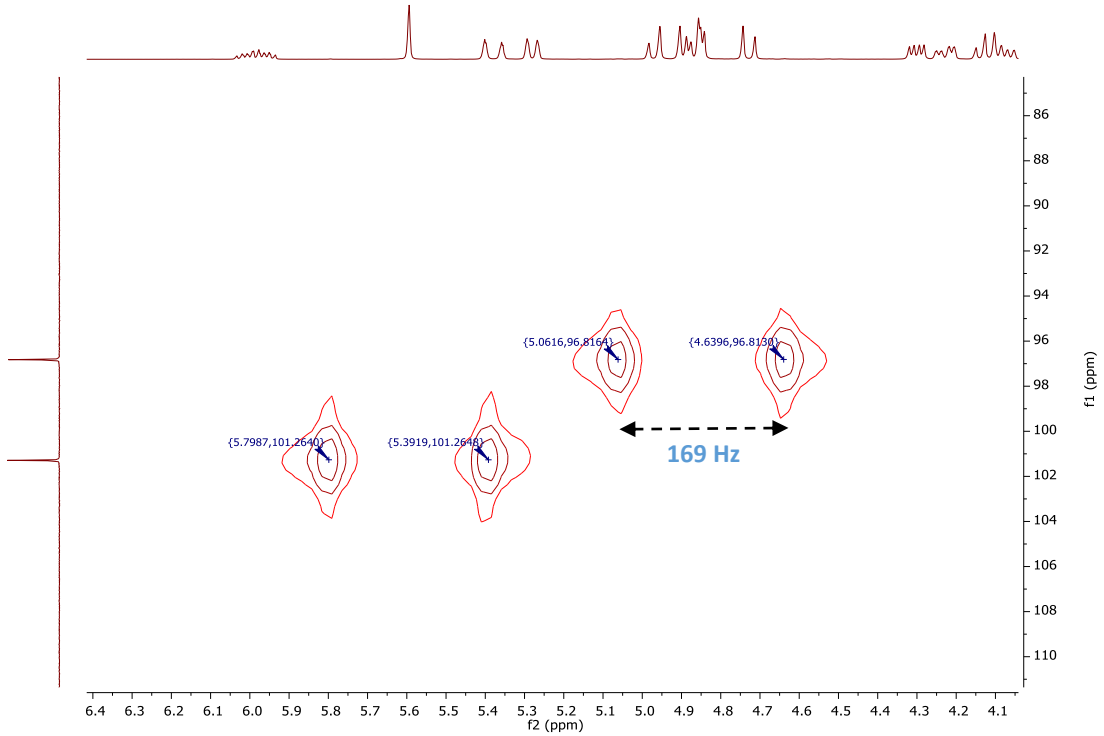
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **32**



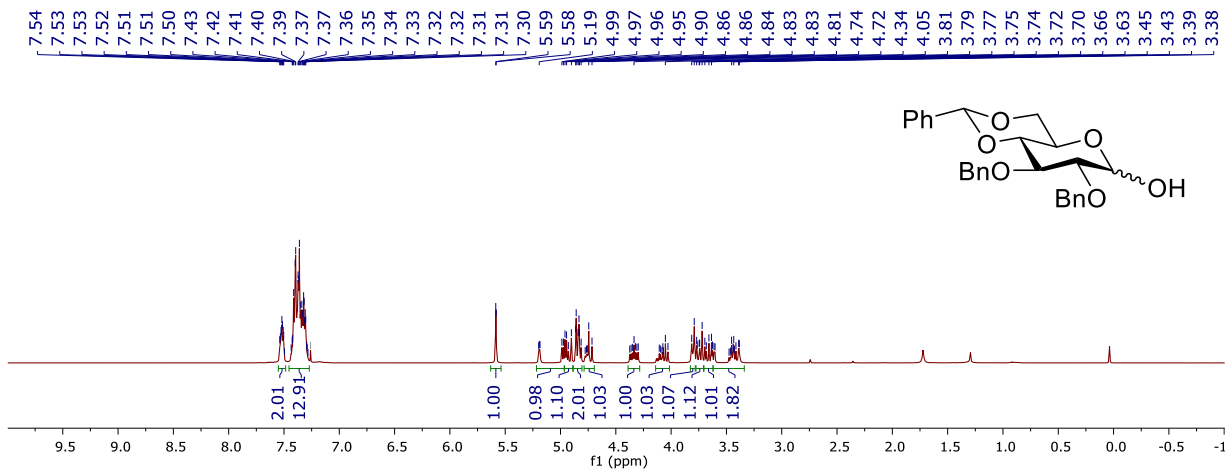
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **32**



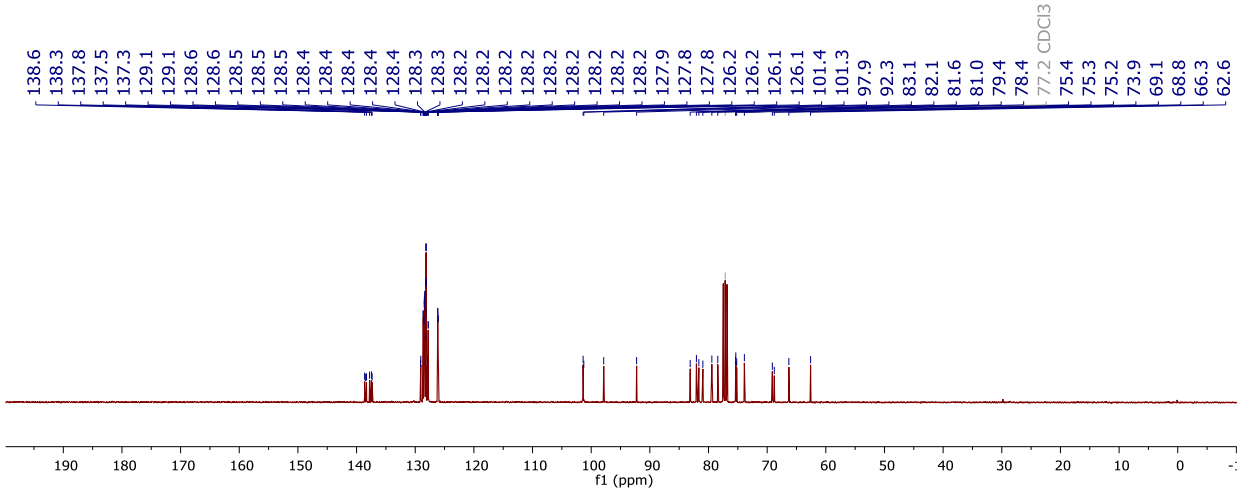
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **32**



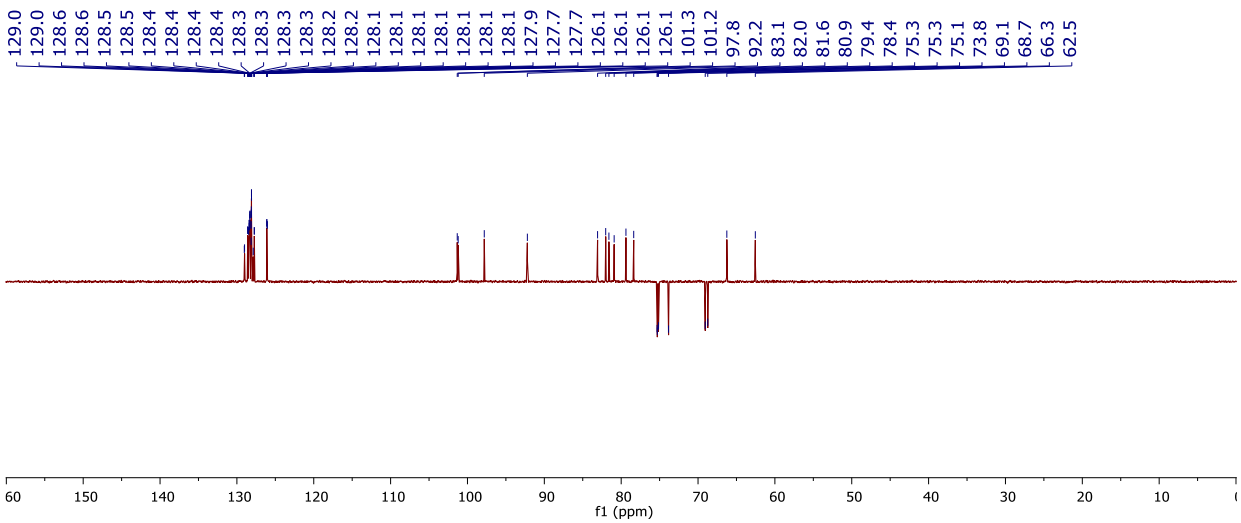
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **33**



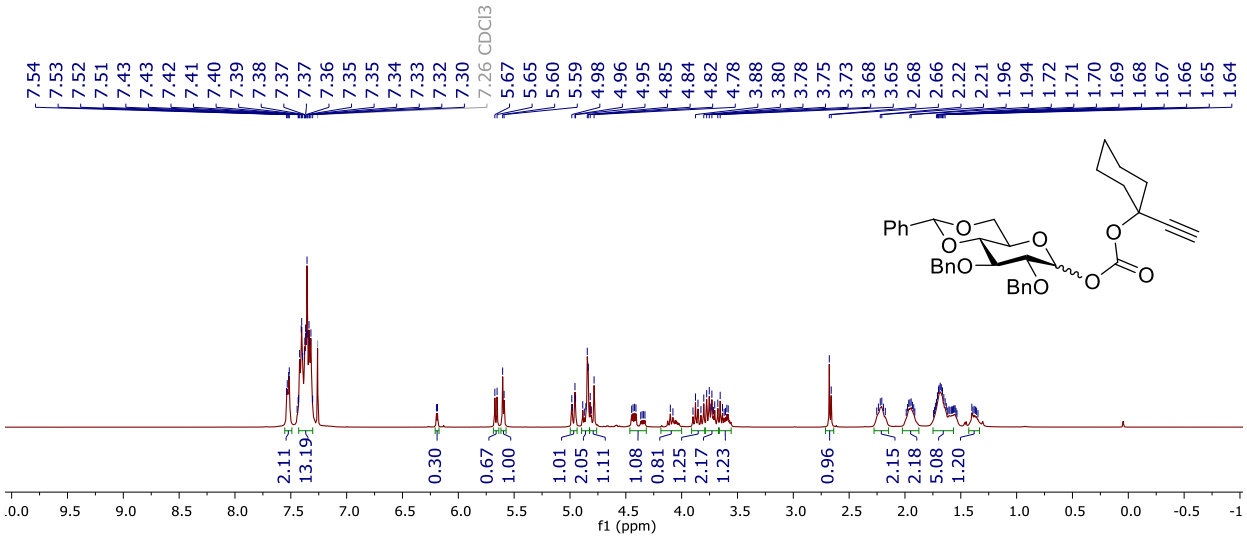
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **33**



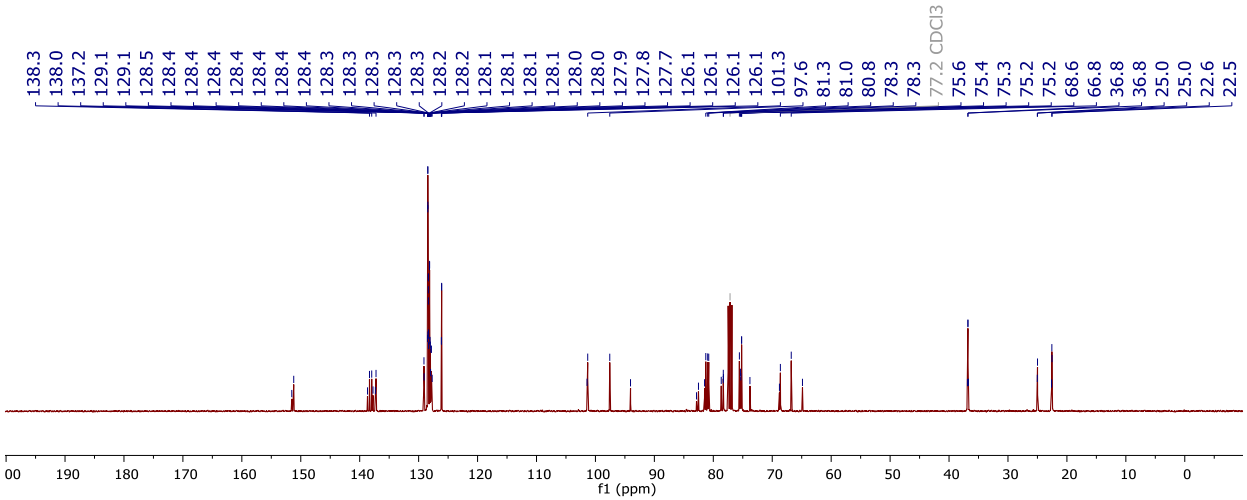
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **33**



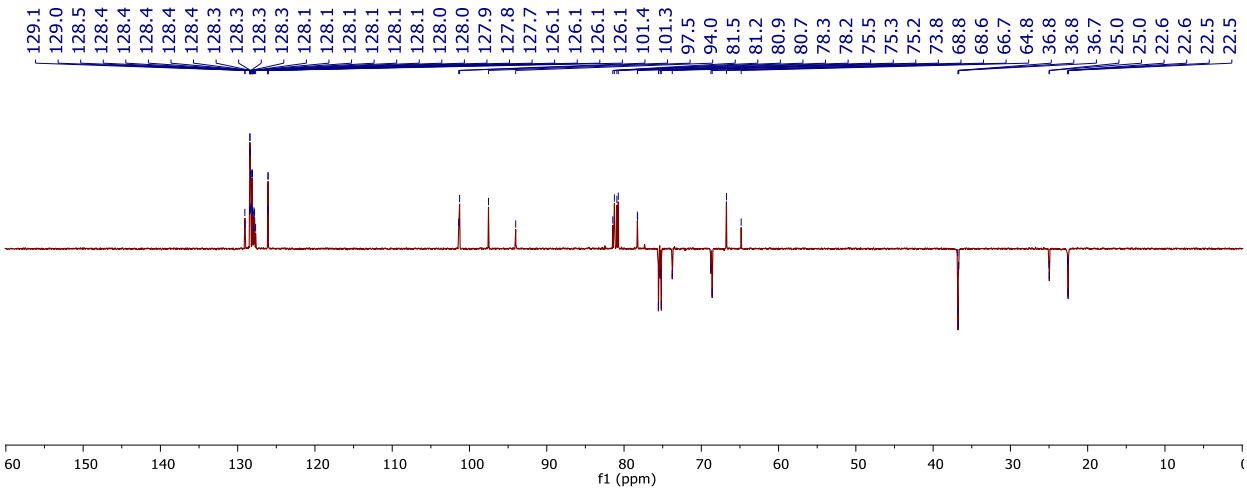
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **31**



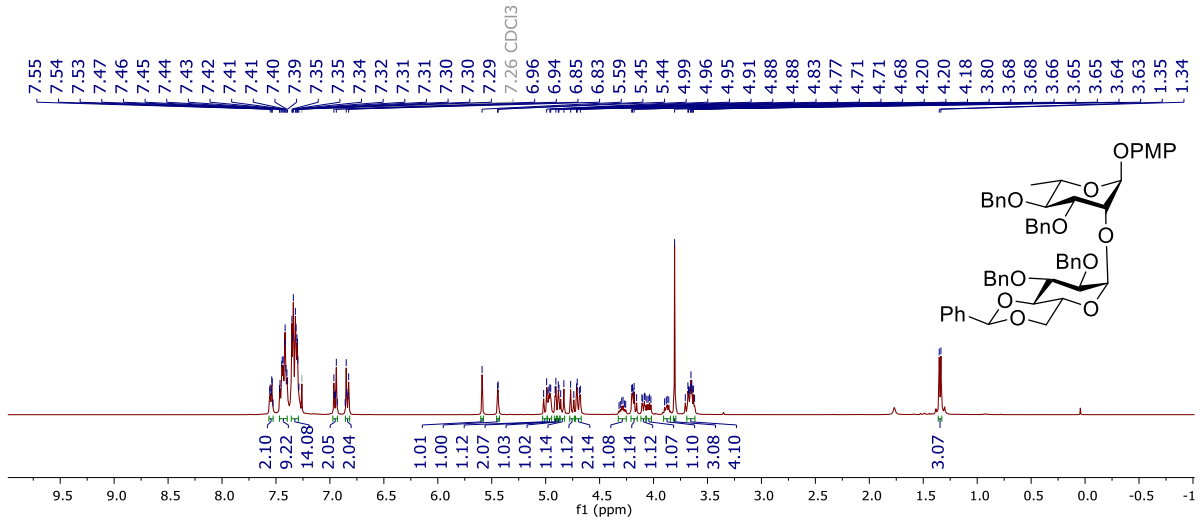
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **31**



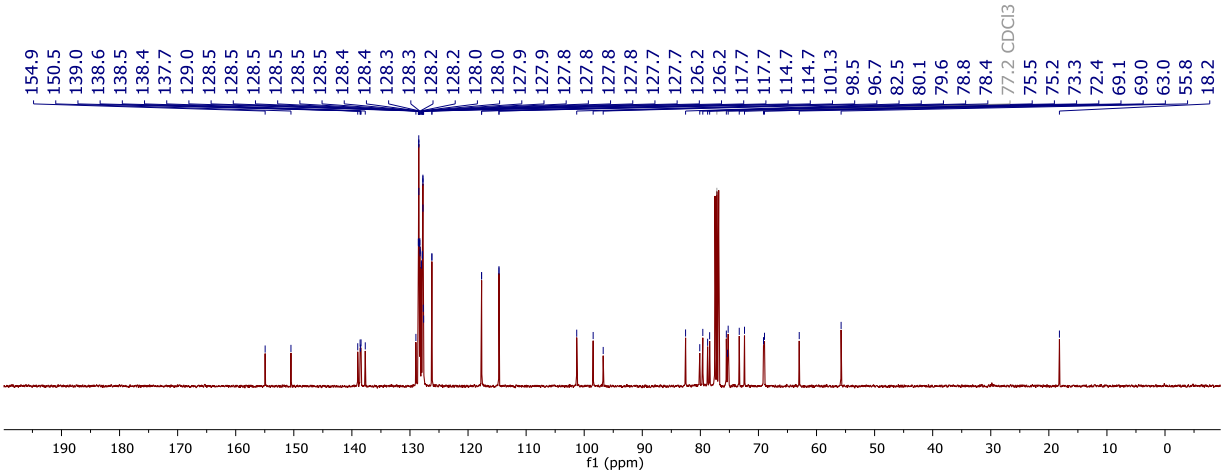
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **31**



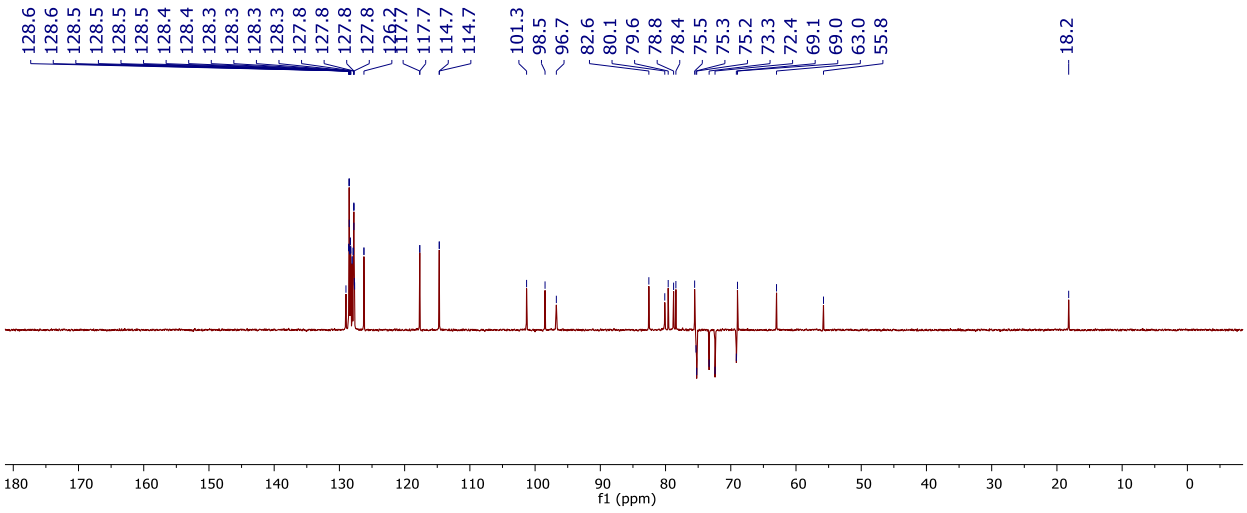
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **34**



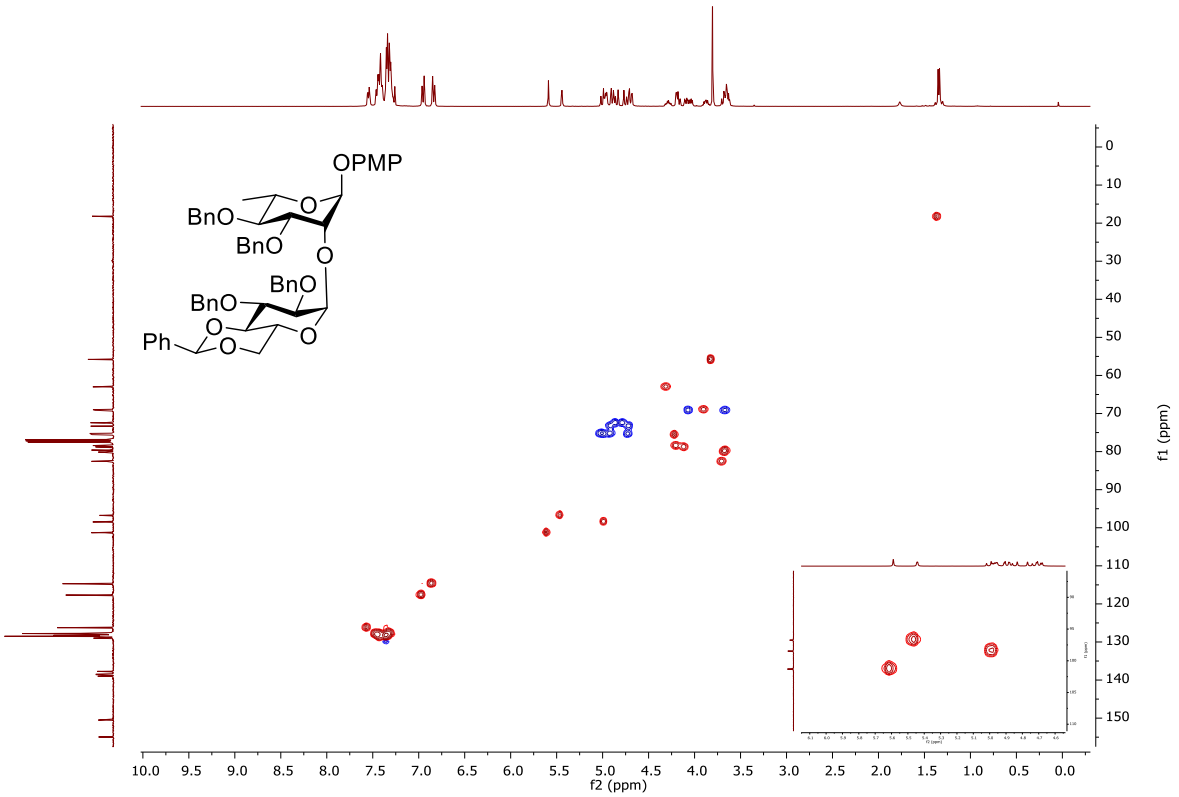
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **34**



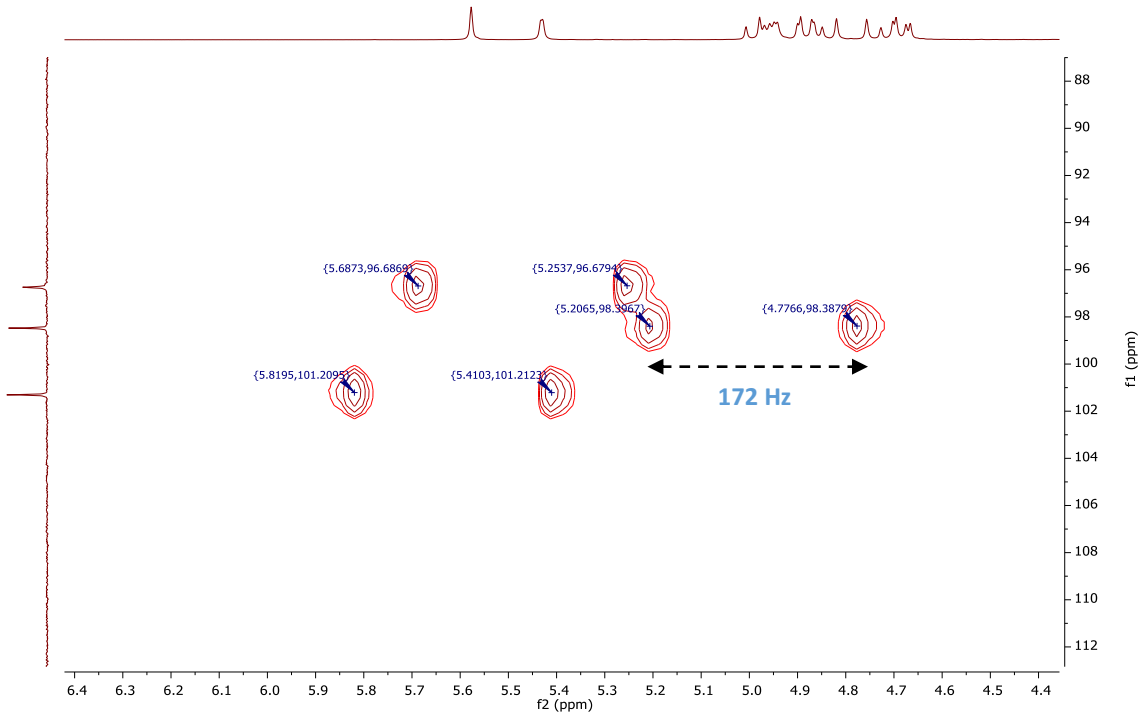
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **34**



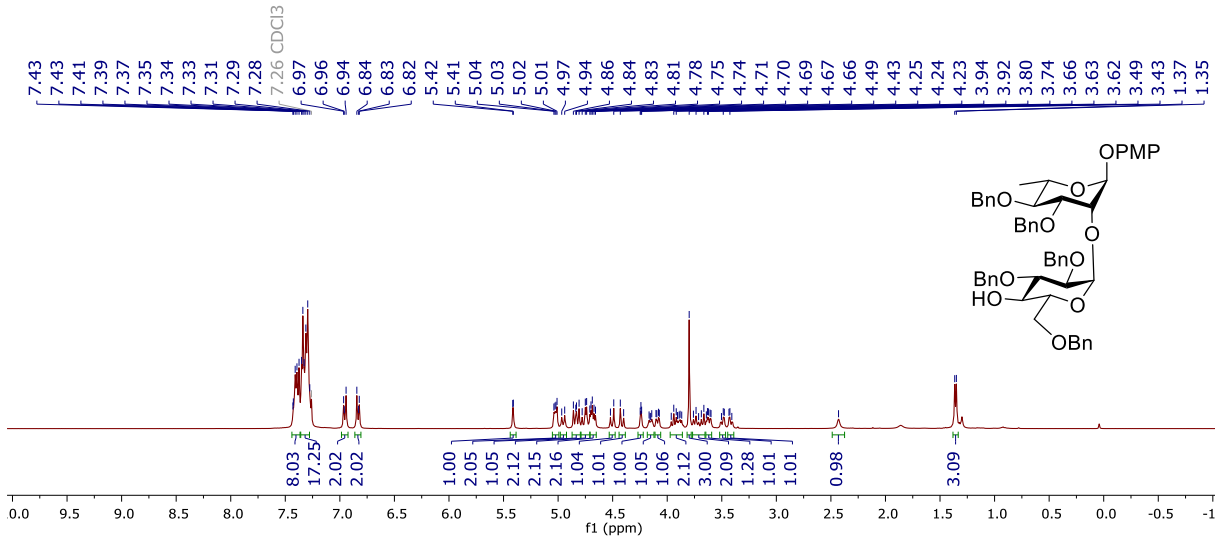
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **34**



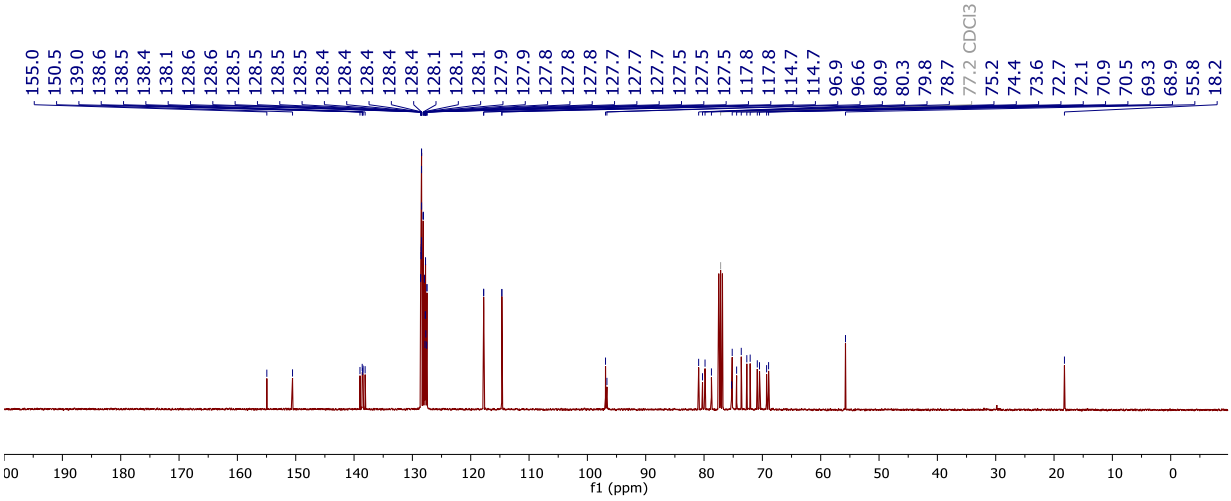
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **34**



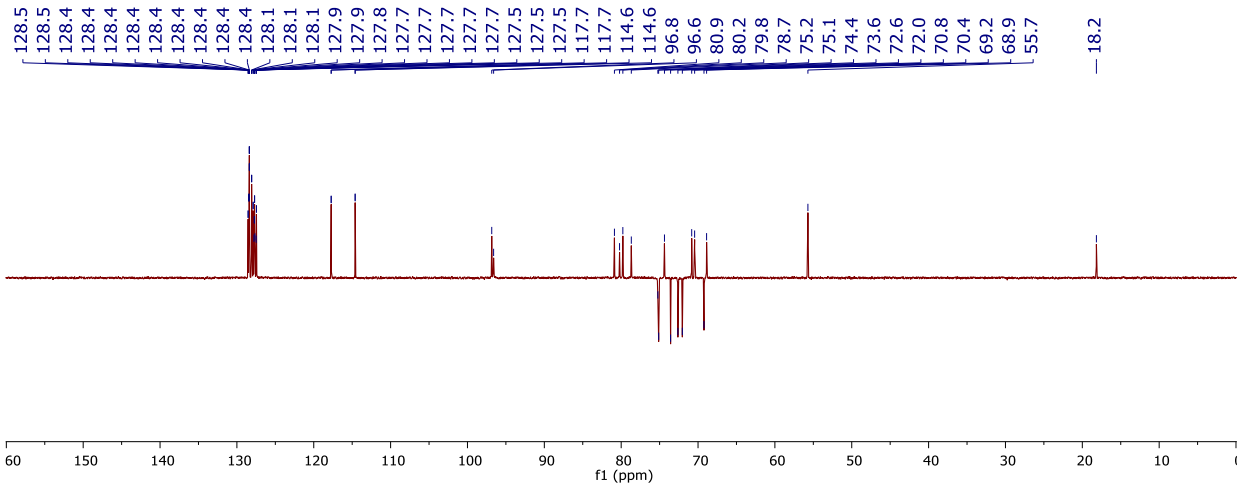
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **29**



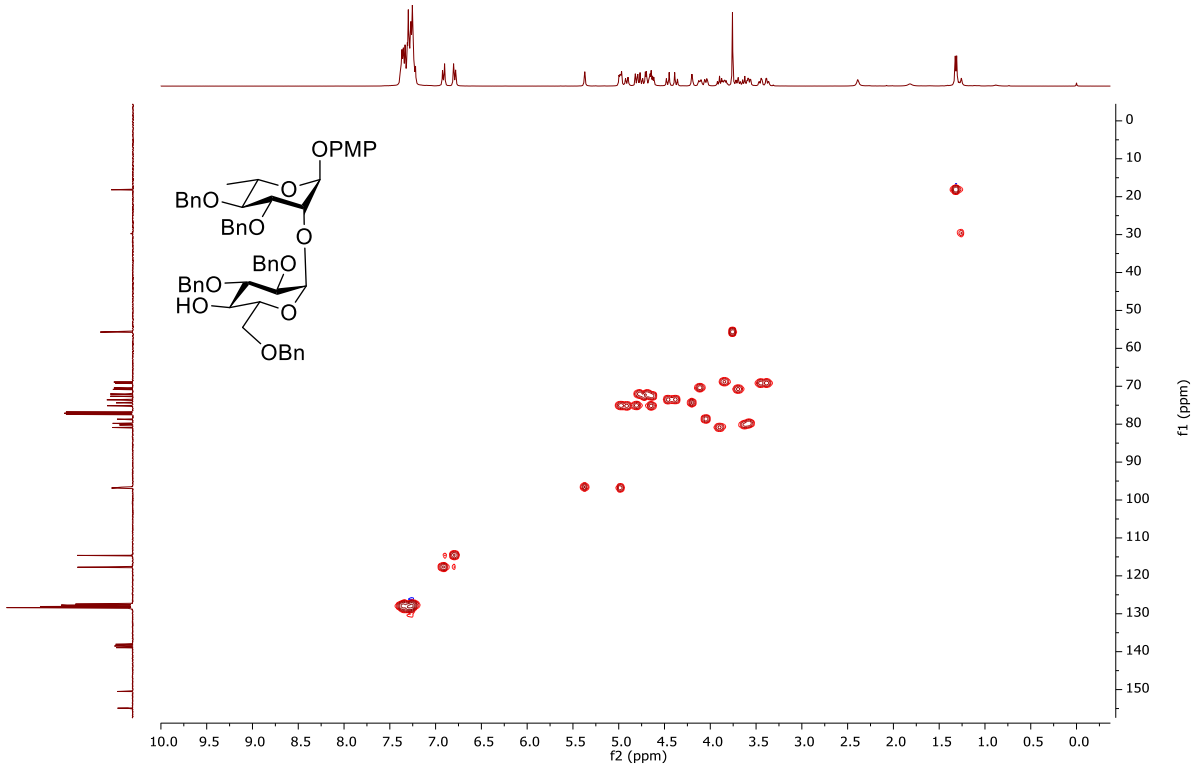
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **29**



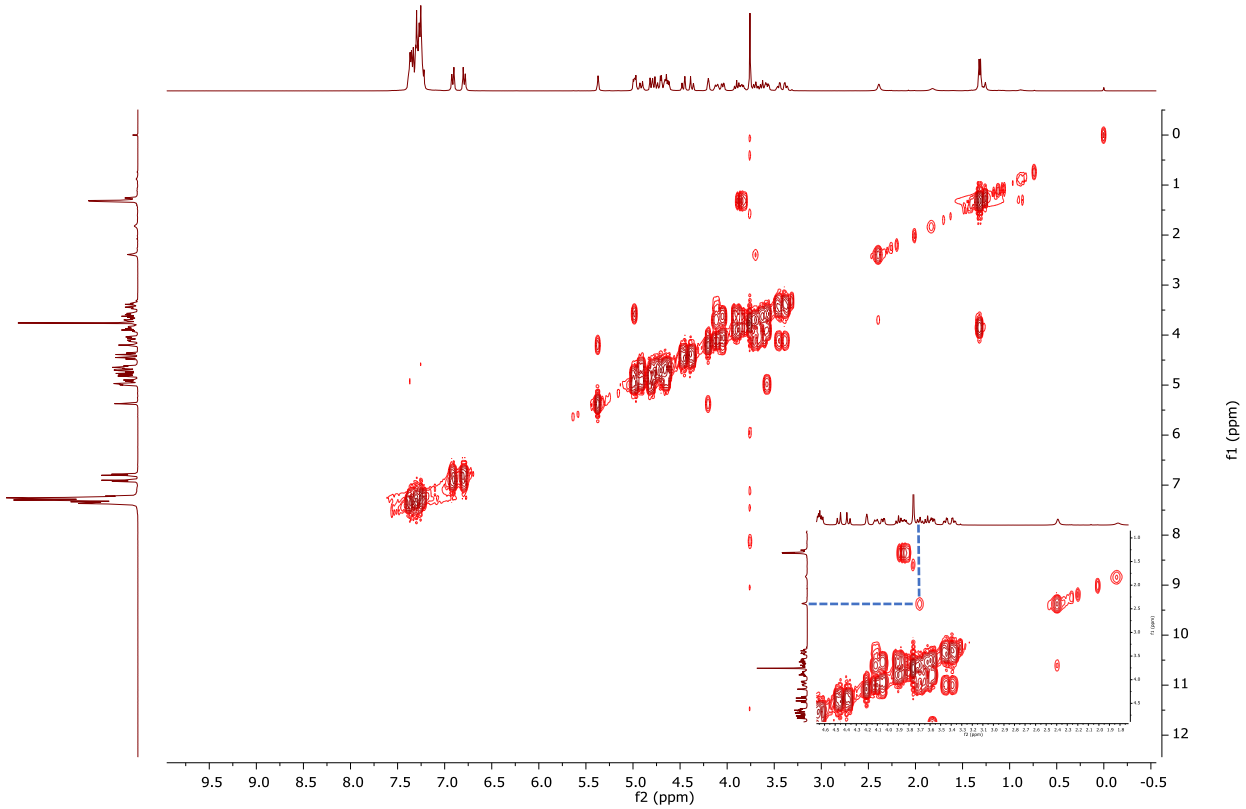
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **29**



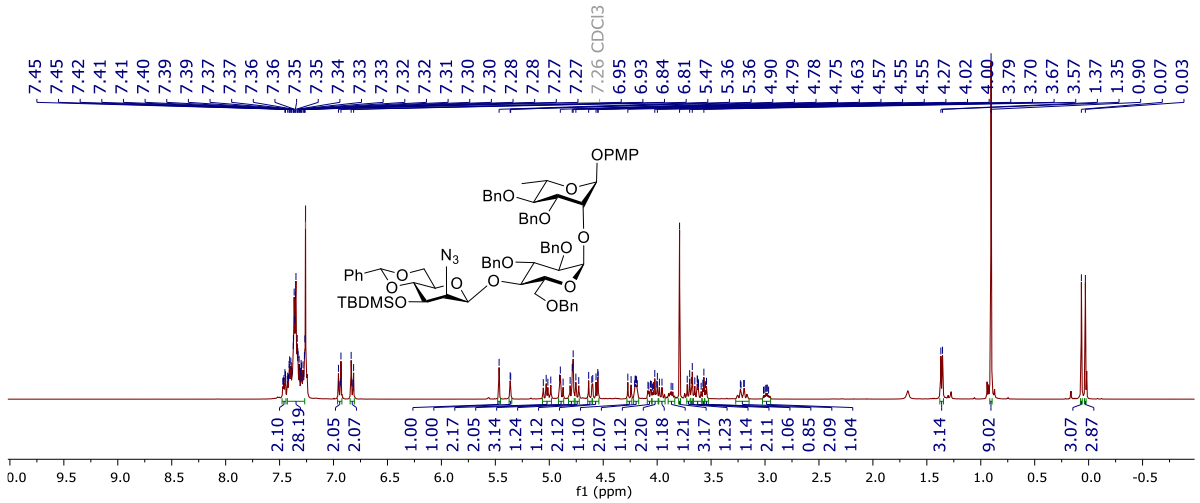
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, $CDCl_3$) of compound **29**



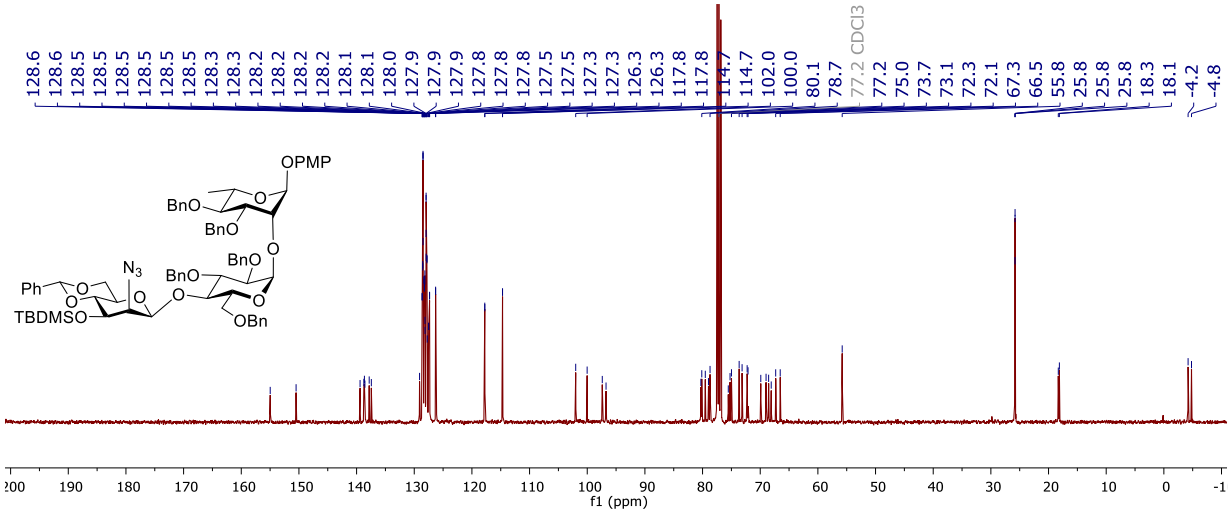
^{1}H-^{1}H COSY NMR Spectrum (400 MHz, $CDCl_3$) of compound **29**



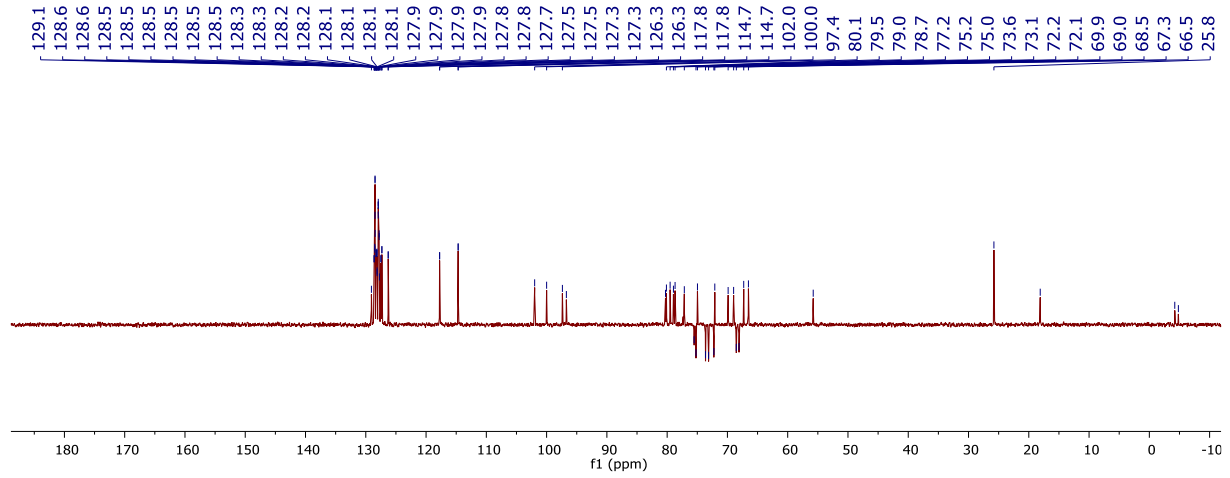
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **28**



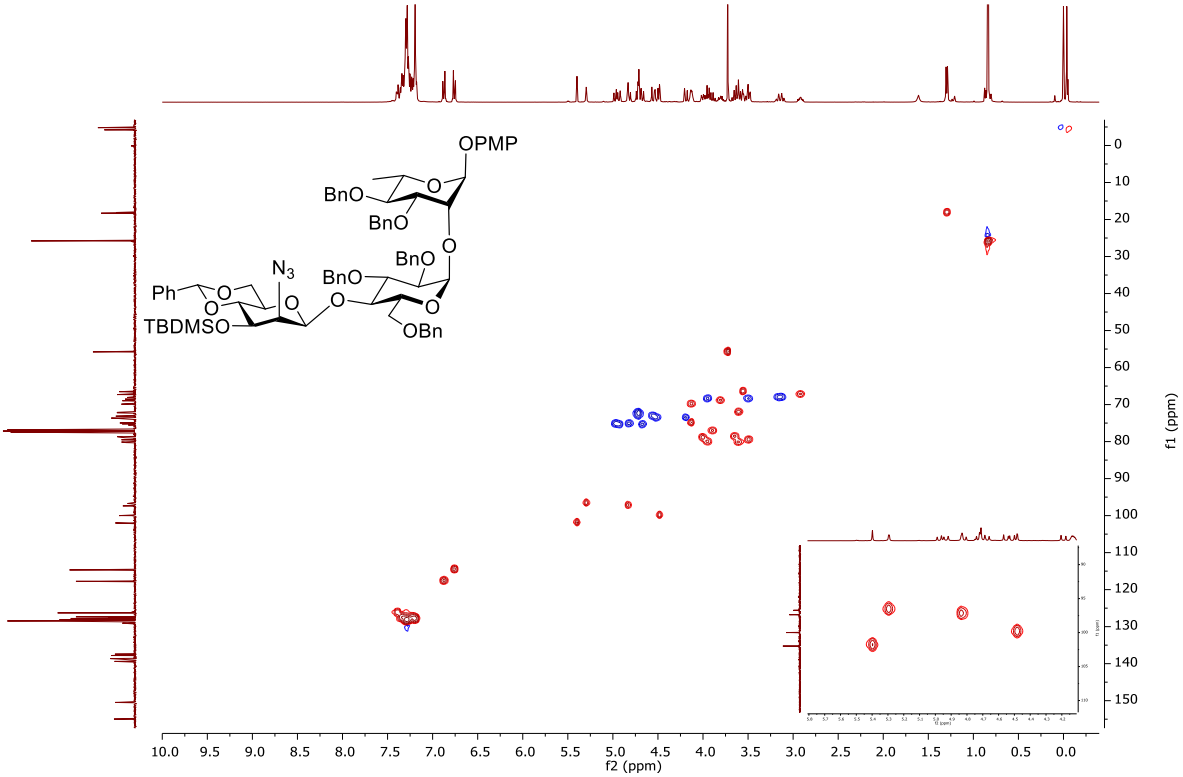
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **28**



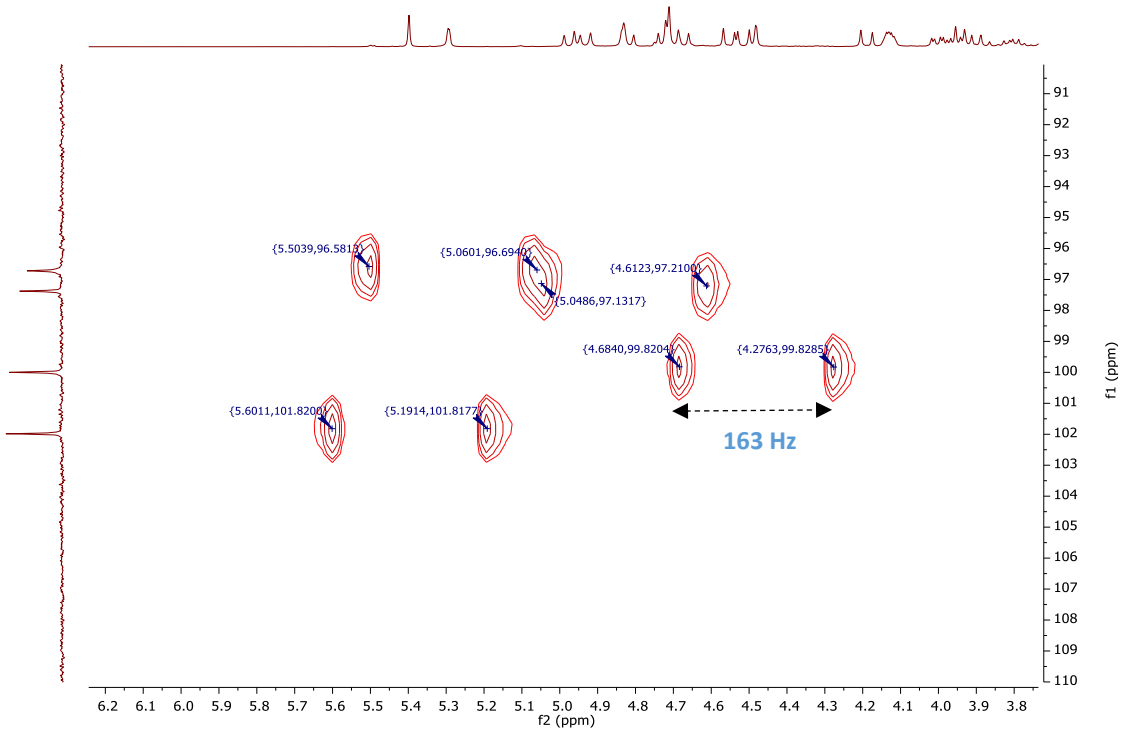
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **28**



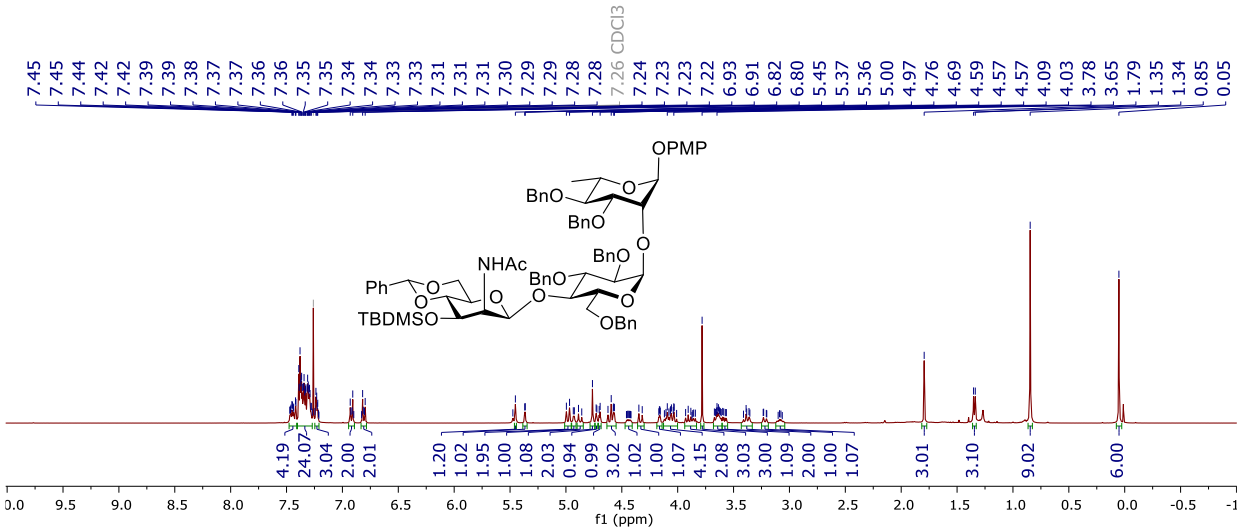
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **28**



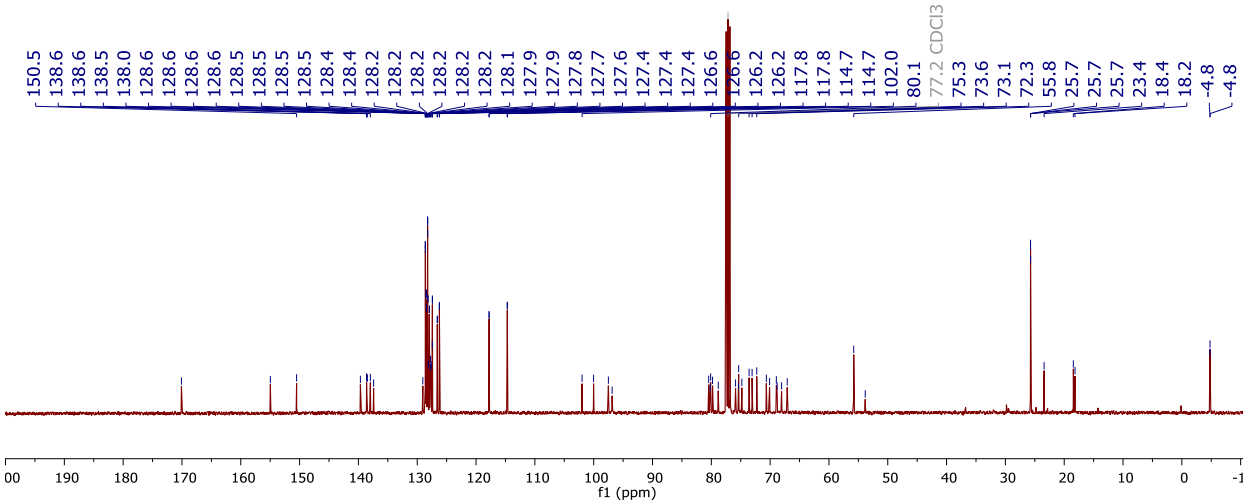
^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **28**



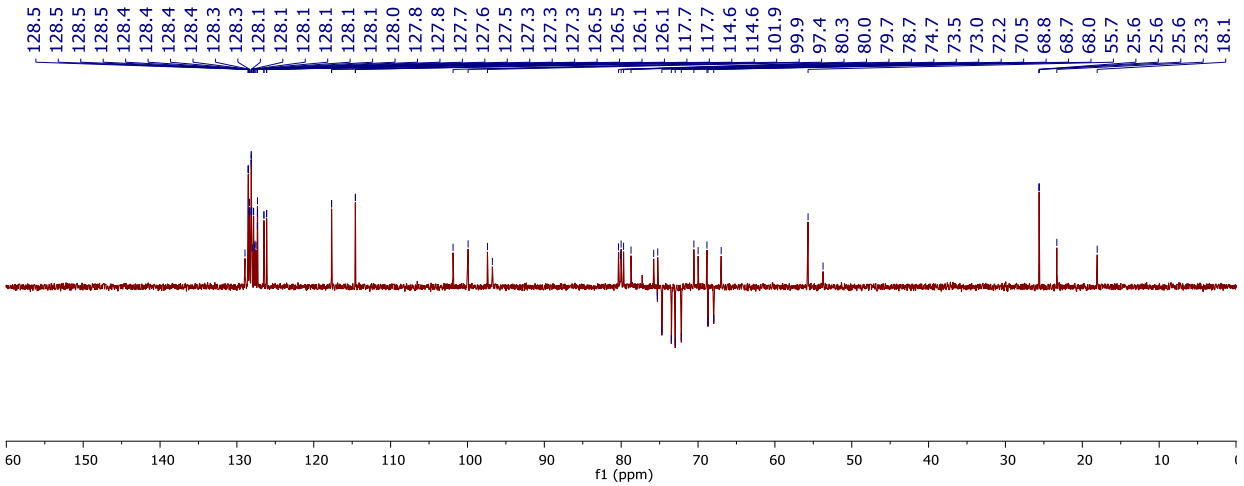
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **27**



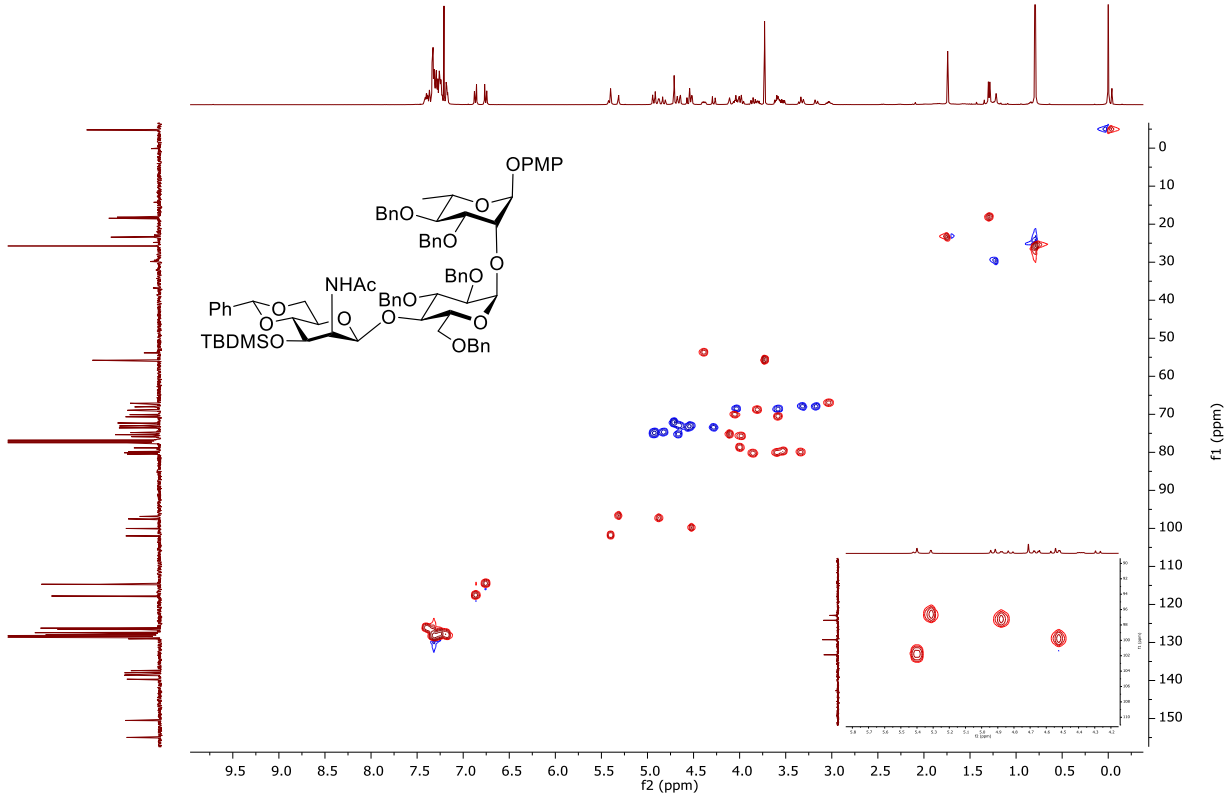
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **27**



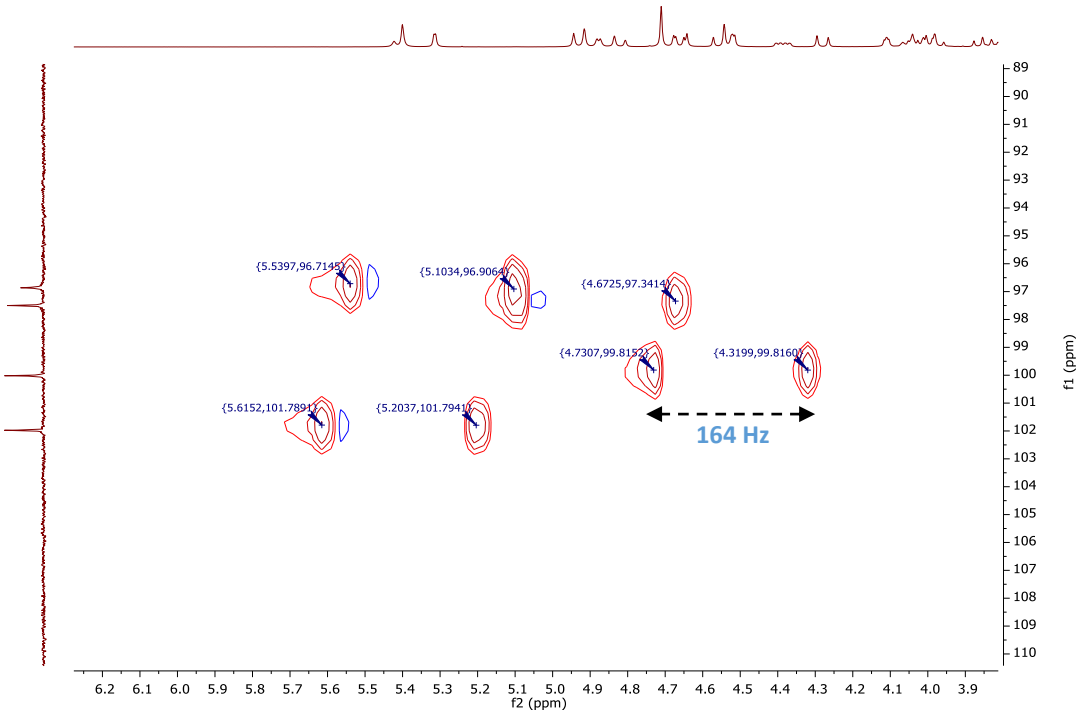
DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **27**



^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **27**



^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (400 MHz, 101 MHz, $CDCl_3$) of compound **27**



2.11. General Procedure for the VT NMR studies

VT NMR studies of glycosyl ethynylcyclohexyl carbonate 14f:

An oven-dried vial was charged with glycosyl donor **14f** (35 mg, 0.063 mmol) and kept overnight under a high vacuum. After that CD_2Cl_2 (0.75 mL) was added under an Ar atmosphere and the resulting solution was placed into a vacuum dried NMR tube and sealed with the septum cap under an Ar atmosphere. The active catalyst [tris(2,4-di-*tert*-butylphenyl)phosphite]gold trifluoromethanesulfonate solution was prepared as follows: an oven-dried vial was charged with [tris(2,4-di-*tert*-butylphenyl)phosphite]gold chloride **17** (61 mg, 0.069 mmol, 1.1 equiv) and AgOTf (20 mg, 0.077 mmol, 1.2 equiv) under an Ar atmosphere, and CD_2Cl_2 (0.2 mL) was added. The resulting cloudy solution was sonicated for 4 minutes before formation of white precipitate of AgCl was observed. The resulting suspension was filtered through a syringe filter and the filtrate was collected into an oven-dried vial under an Ar atmosphere and cooled down to –78 °C using dry ice. The NMR tube containing the glycosyl donor solution then was placed into the NMR probe and cooled down to –78 °C. The first ^{1}H, ^{13}C, and DEPT-135 spectra were collected, then the sample was quickly removed from the probe and the solution of active gold catalyst precooled to –78 °C was quickly added. The sample was returned to the cold NMR probe and ^{1}H, DEPT-135 and ^{19}F spectra were recorded shortly after. The temperature then was increased to –60 °C and ^{1}H, DEPT-135, and ^{19}F spectra were acquired after 5 minutes. After that the temperature was increased by 10 °C increments and ^{1}H, ^{19}F, and DEPT-135 spectra were acquired at each temperature after 5 minutes. In the temperature range from 0 °C to +10 °C only ^{1}H, ^{19}F spectra were recorded. After termination of the VT experiment, the sample was collected, and distributed between EtOAc (30 mL) and saturated aq. $NaHCO_3$ (30 mL). The organic layer was collected, washed with brine (30 mL), dried over $MgSO_4$ and concentrated to dryness. The residue was purified by a flash column chromatography on a silica gel eluting with hexanes:EtOAc (0→50%, EtOAc) to give tris(2,4-di-*tert*-butylphenyl)phosphite admixed with hydrolysis products (40 mg).

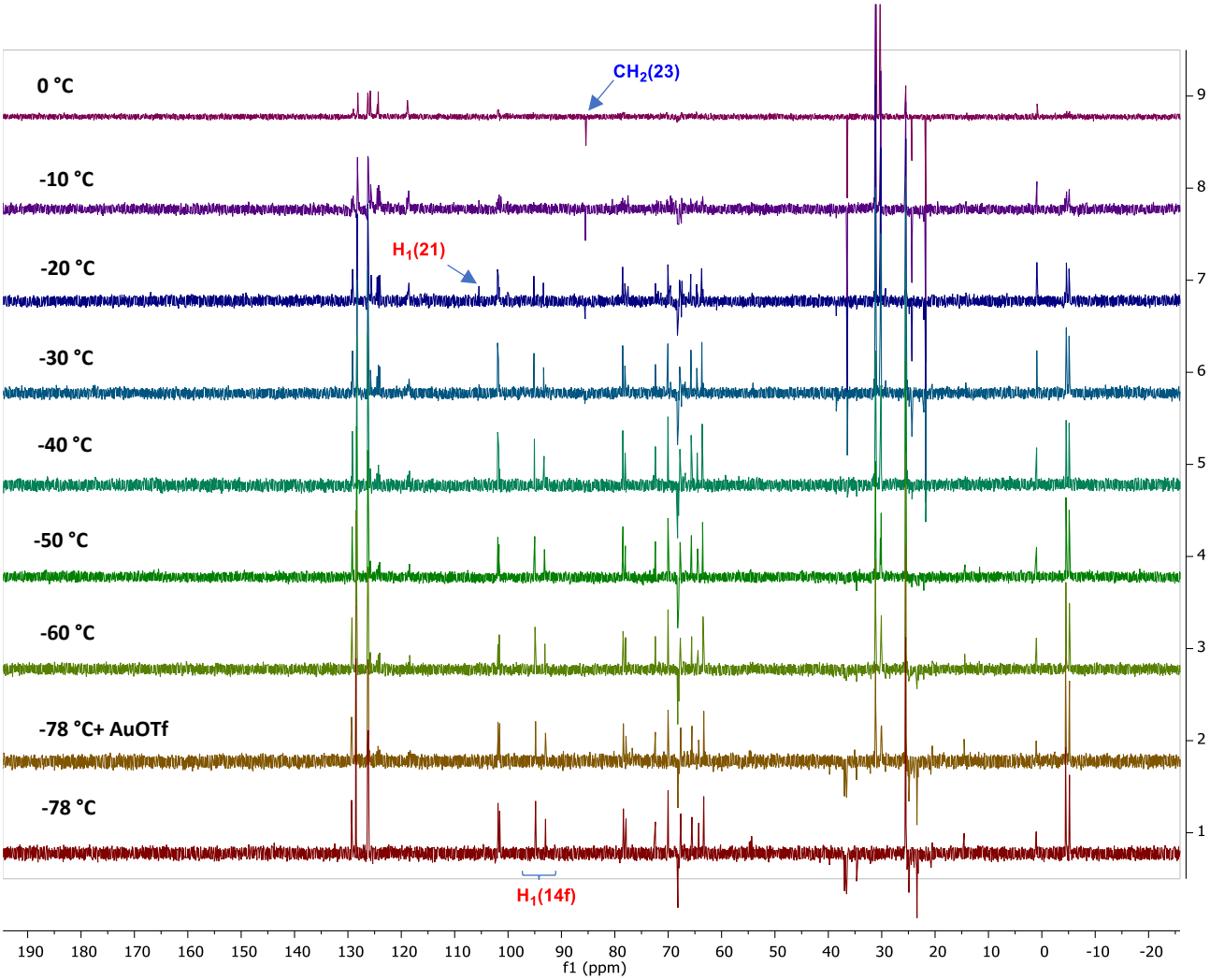
VT NMR studies of glycosylation reaction between glycosyl donor 14f and cyclohexanol:

An oven-dried vial was charged with glycosyl donor **14f** (41 mg, 0.074 mmol) and kept overnight under a high vacuum. After that CD_2Cl_2 (0.75 mL) was added followed by addition of cyclohexanol (8 µL, 0.076 mmol, 1.03 equiv) under an Ar atmosphere and the resulting solution was placed into a vacuum dried NMR tube and sealed with the septum cap under an Ar atmosphere.

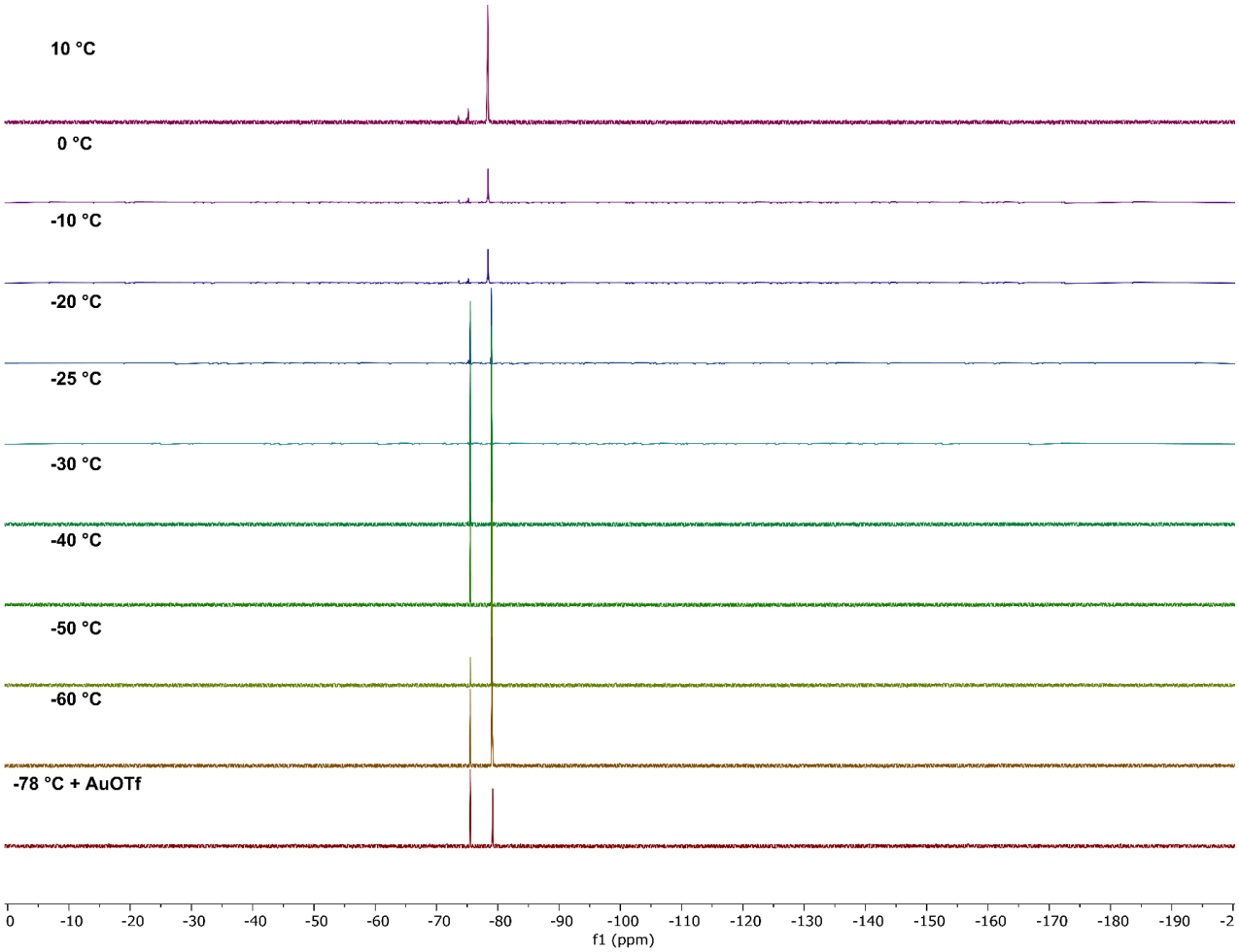
The active catalyst [tris(2,4-di-*tert*-butylphenyl)phosphite]gold trifluoromethanesulfonate solution was prepared as follows: an oven-dried vial was charged with [tris(2,4-di-*tert*-butylphenyl)phosphite]gold chloride **17** (71 mg, 0.081 mmol, 1.1 equiv) and AgOTf (20.8 mg, 0.081 mmol, 1.1 equiv) under an Ar atmosphere, and CD_2Cl_2 (0.17 mL) was added. The resulting cloudy solution was sonicated for 4 minutes before formation of white precipitate of AgCl was observed. The resulting suspension was filtered through a syringe filter and the filtrate was collected into an oven-dried vial under an Ar atmosphere and cooled down to –78 °C using dry ice. The NMR tube containing the glycosyl donor solution then was placed into the NMR probe and cooled down to –78 °C. The first ^{1}H, ^{13}C, and DEPT-135 spectra were collected, then the sample was quickly removed from the probe and the solution of active gold catalyst precooled to –78 °C was quickly added. The sample was returned to the cold NMR probe and ^{1}H, DEPT-135 and ^{19}F spectra were recorded shortly after. The temperature then was increased to –60 °C and ^{1}H, DEPT-135, and ^{19}F spectra were acquired after 5 minutes. After that the temperature was increased by 10 °C increments and ^{1}H, ^{19}F, and DEPT-135 spectra were acquired at each temperature after 5 minutes. In the temperature range from 0 °C to +10 °C only ^{1}H, ^{19}F spectra were recorded. After termination of the VT experiment, the sample was collected and distributed between EtOAc (30 mL) and saturated aq. $NaHCO_3$ (30 mL). The organic layer was collected, washed with brine (30 mL), dried over $MgSO_4$ and concentrated to dryness. The residue was purified by a flash column chromatography on a silica gel eluting with hexanes:EtOAc (0→30%, EtOAc) to give tris(2,4-di-*tert*-butylphenyl)phosphite admixed with hydrolysis products (30 mg) and cyclohexyl glycoside **25** (6 mg) as a mixture of anomers (α:β = 1:1.7).

2.12. VT-NMR Spectral Charts

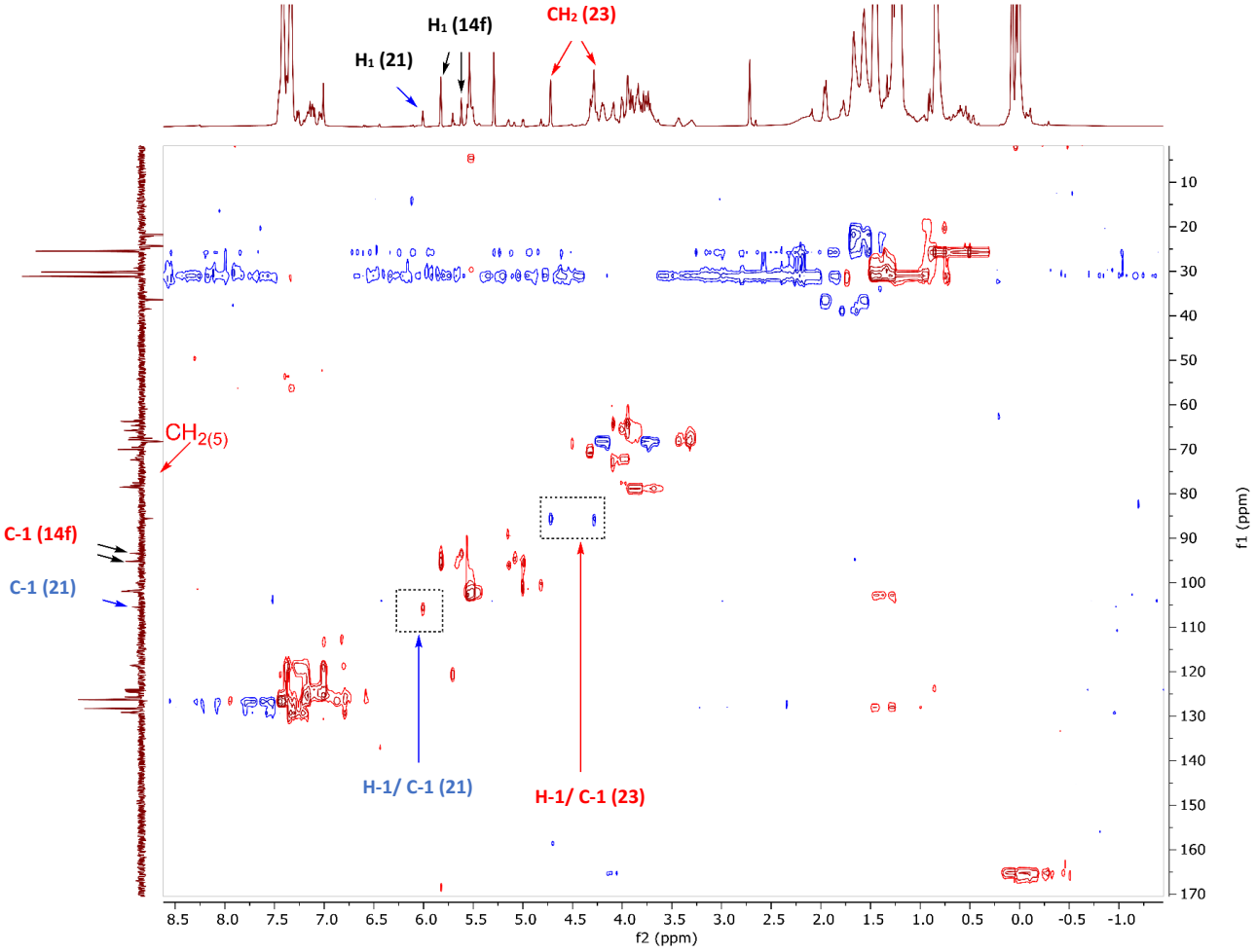
Stacked DEPT-135 (125 MHz, CD_2Cl_2) spectra from VT NMR experiment with glycosyl donor **14f**



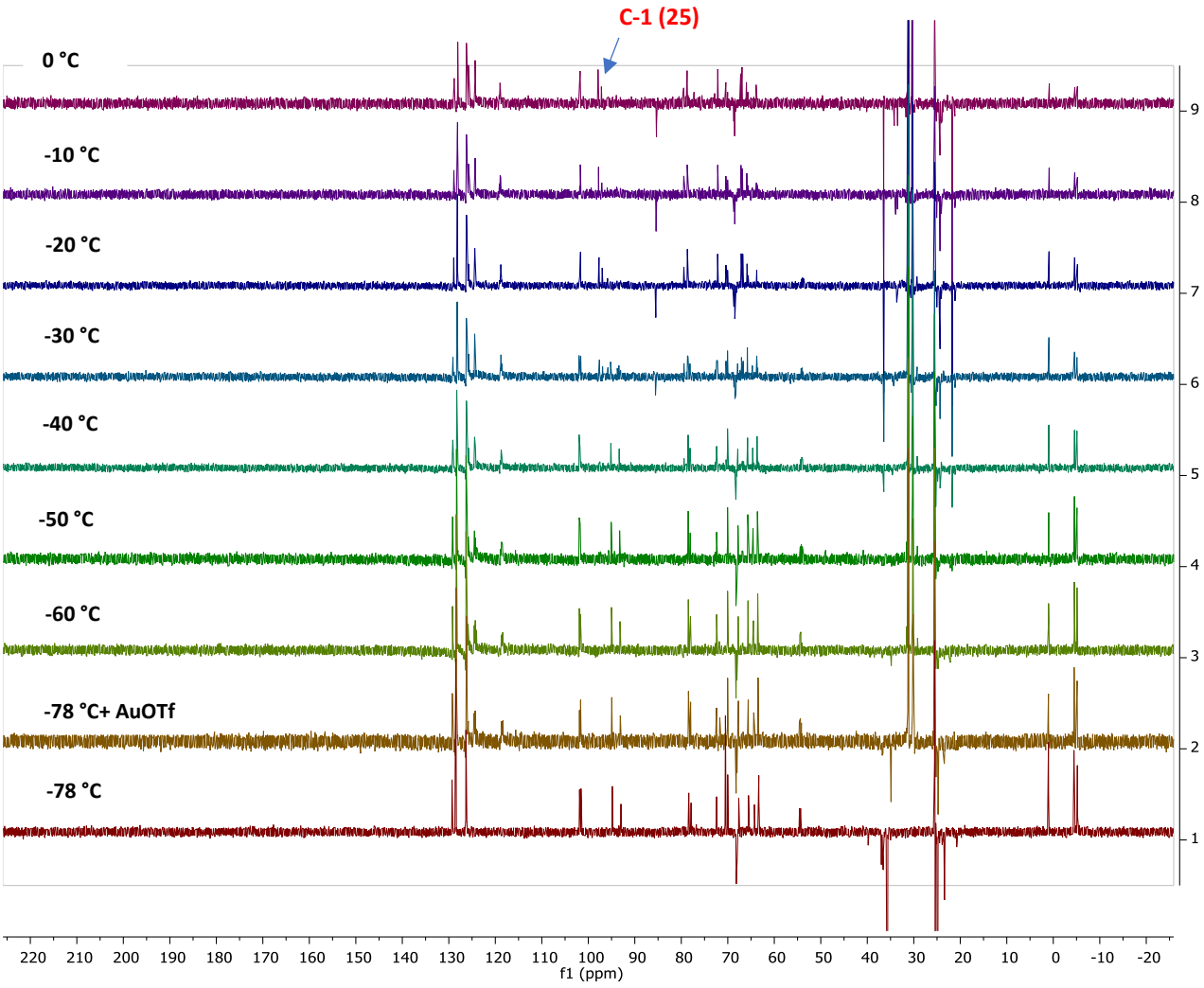
Stacked ^{19}F NMR (470 MHz, CD_2Cl_2) spectra from VT NMR experiment with donor **14f**



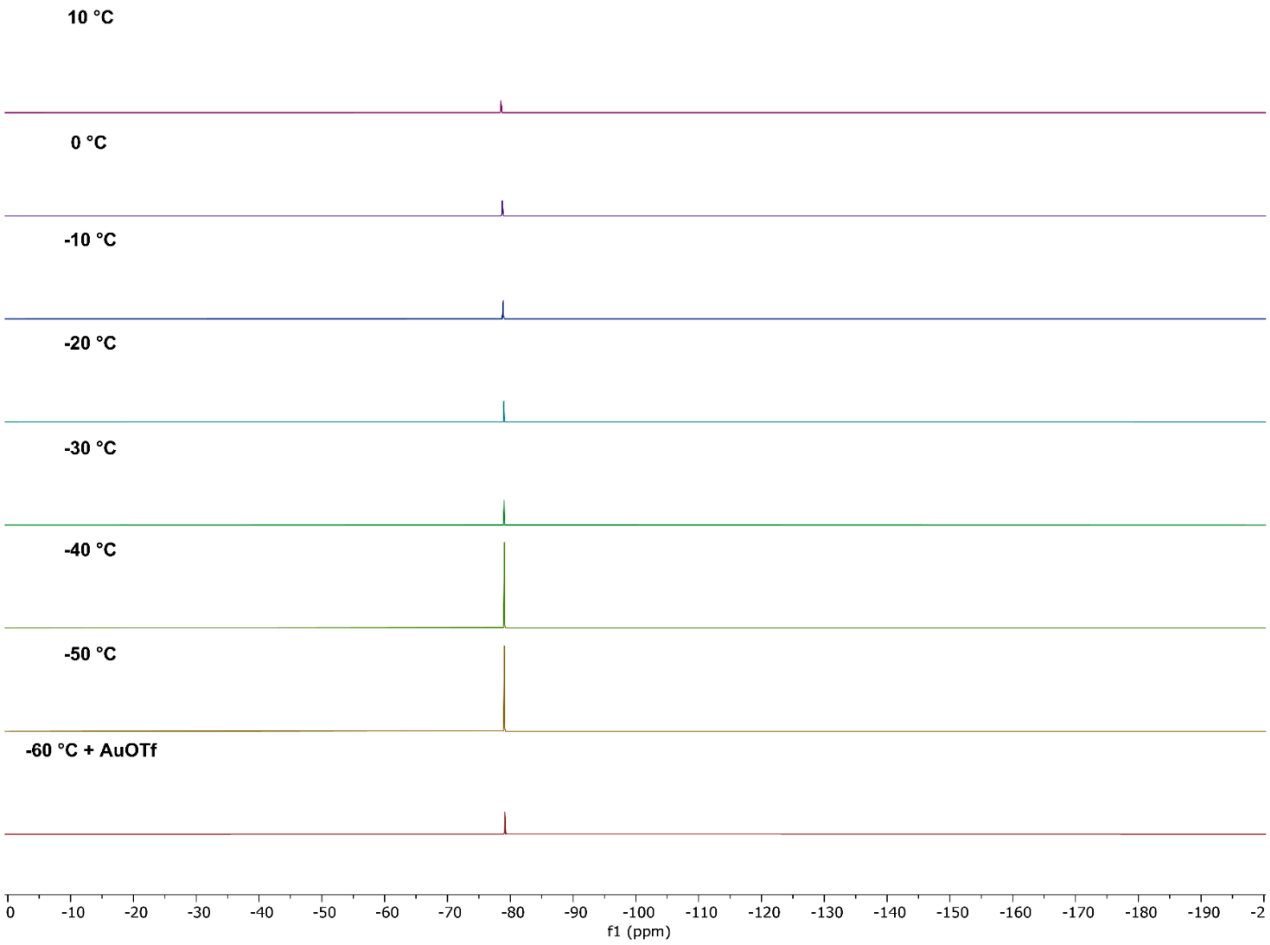
HSQC (500 MHz, CD_2Cl_2) spectrum at -25 °C from VT NMR experiment with glycosyl donor **14f**



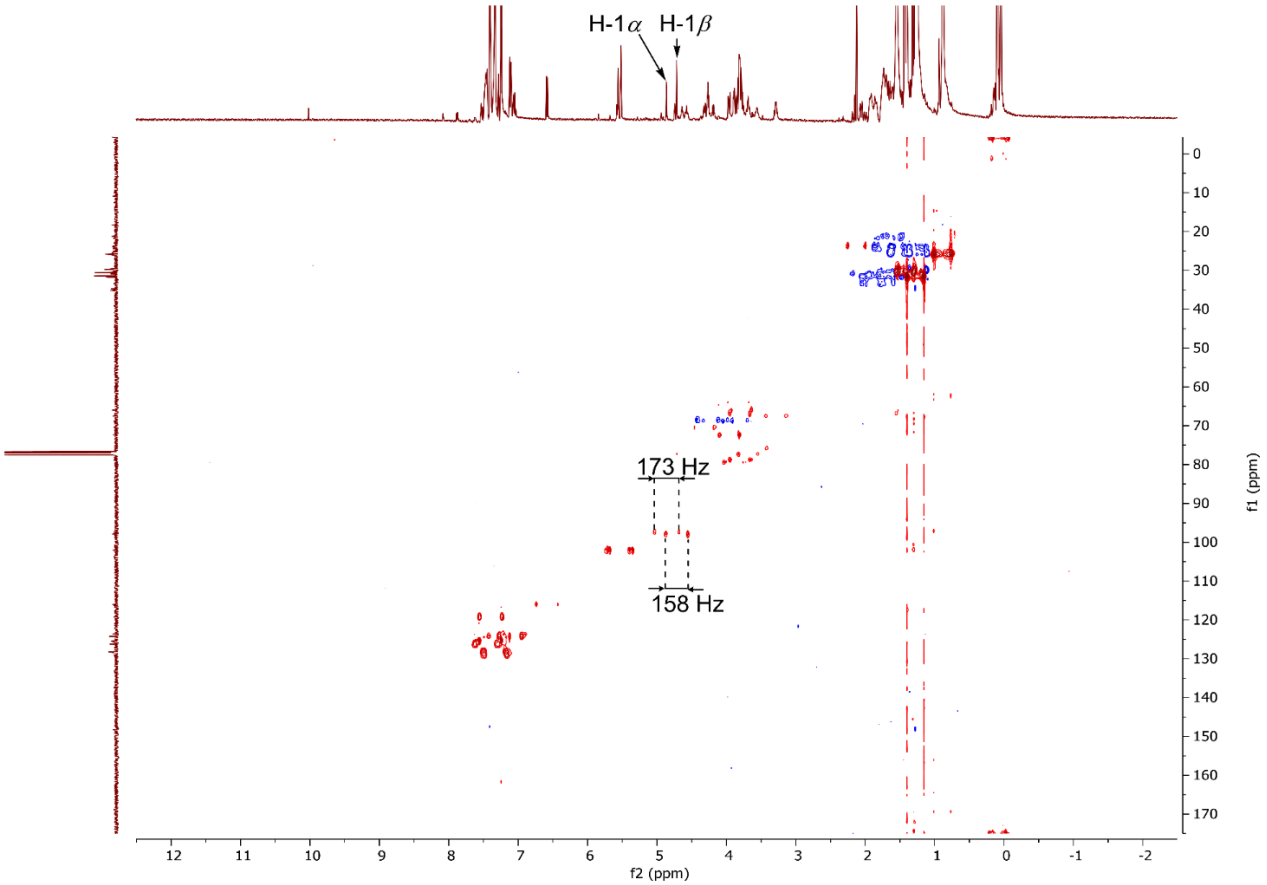
Stacked DEPT-135 (125 MHz, CD_2Cl_2) spectra from VT NMR experiment with glycosyl donor **14f** and cyclohexanol



Stacked ^{19}F NMR (470 MHz, CD_2Cl_2) spectra from VT NMR experiment with glycosyl donor **14f** and cyclohexanol



Coupled gHSQCAD (500 MHz, CD_2Cl_2) spectrum of cyclohexyl glycoside **25**



2.13. References

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Chapter 3

Total Synthesis of Conjugation-ready Hyperbranched Pentasaccharide of *Clavibacter phaseoli* VKM Ac-2641^{T}

Chapter 3

3.1 Introduction

Clavibacter belong to a genus of Gram-positive bacteria known for its significance as plant pathogens, particularly affecting crops of agricultural importance[1]. The genus Clavibacter, which belongs to the family Microbacteriaceae and the class Actinobacteria, currently includes six officially recognized species among which *Clavibacter michiganensis* stands out as a prominent pathogen responsible for serious bacterial diseases in a wide variety of plants including potato and tomato leading to major economic losses across the farmer community worldwide[2,3,4]. This plant pathogen contains four sub-species including *michiganensis*, *chilensis*, *californiensis* and *phaseoli* and mainly resides in the xylem vessels of the plants[2]. The pathogen can enter into the plants via lesions, hydathodes or contaminated seeds. Once inside the plant, the bacteria can reach the xylem and develop systemic infections like potato ring rot (by subsp. *sepedonicus*), alfalfa's stunting and wilting (by subsp. *insidiosus*), cankers in tomato (by subsp. *michiganesis*), Goss's wilting and stunting (by subsp. *nebraskensis*), bacterial mosaic (by subsp. *tessellarius*) etc. (**Figure 1**)[5].

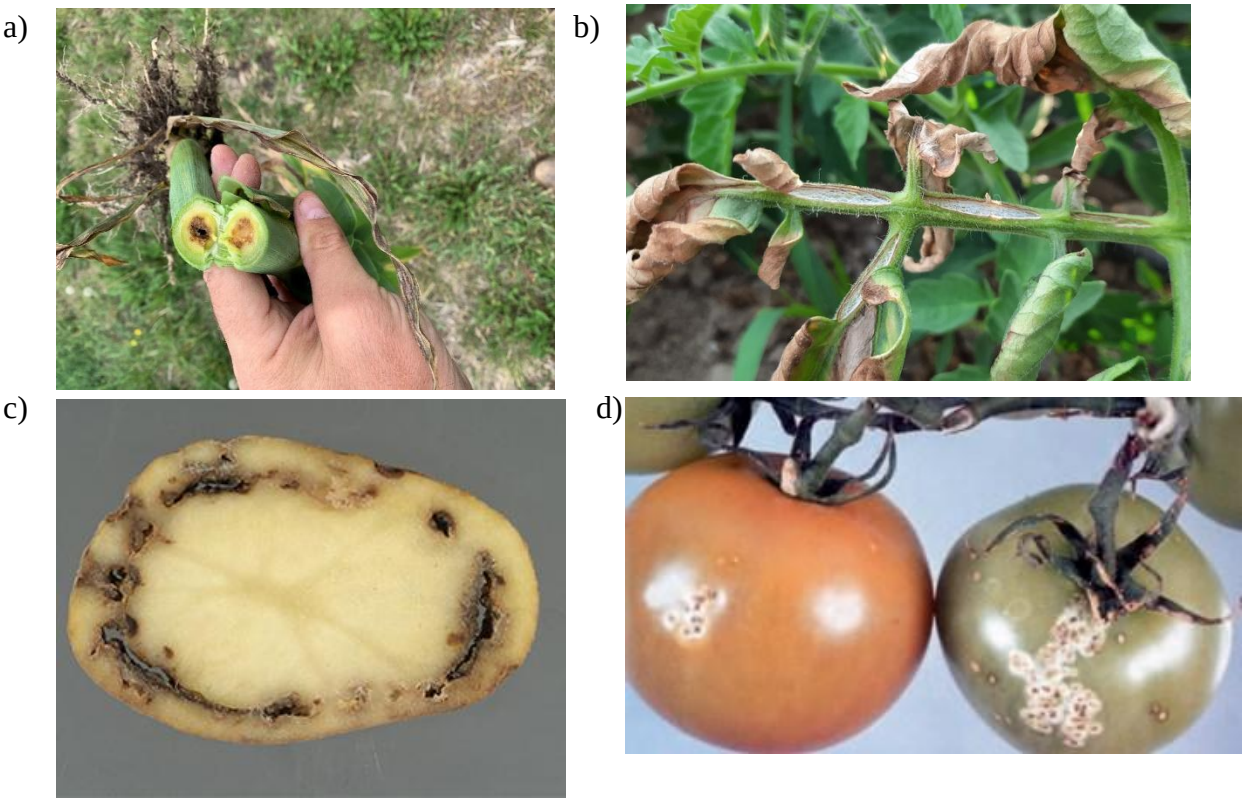


Fig 1. Bacterial diseases in plants by Clavibacter: a) Goss's wilt and blight in corn[6], b) Tomato leaves wilting[7], c) Potato ring rot[8], d) Tomato canker[7].

3.2 Biological importance of cell wall in pathogenicity

The cell wall is a very crucial component of any pathogen. The cell wall is not only crucial for maintaining structural integrity, it also plays a pivotal role in infection and pathogenesis[9]. That's why the relationship between bacterial infections and the structure of bacterial cell walls is a critical area of study in microbiology, particularly due to the implications for antibiotic development and understanding bacterial pathogenicity. Here are some key points regarding the role of cell wall in any bacterial infection:

A. Target for the antibiotics: The unique glycan structure in bacterial cell walls makes it a prime target for antibiotics. These antibiotics work by disrupting the glycan synthesis, weakening the cell wall and causing cell lysis, which is especially effective against Gram-positive bacteria[9,10].

B. Virulence factors: Components such as lipopolysaccharides (LPS) in Gram-negative bacteria play a role in pathogenicity by triggering strong immune responses[9].

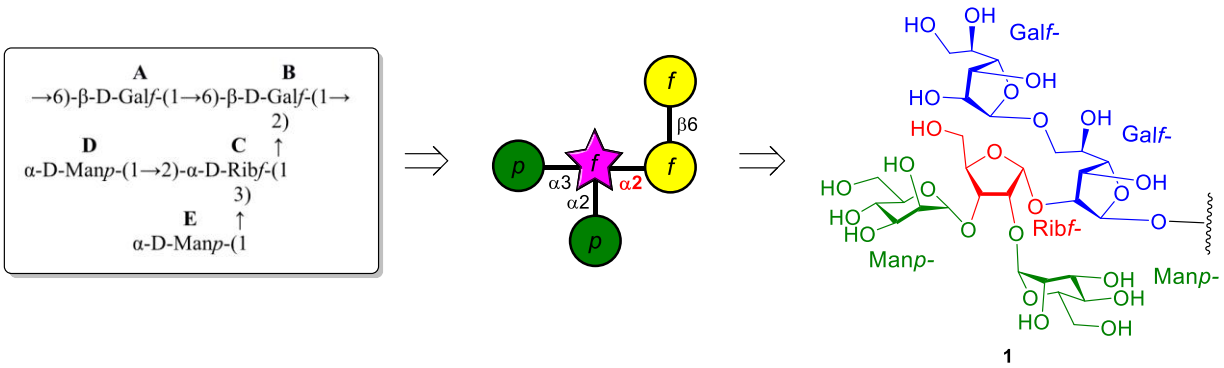
C. Immune evasion: The complex structure of the cell wall, especially in Gram-negative bacteria, can help them avoid detection and attack by the host immune system. The outer membrane acts as a barrier to antibiotics and immune molecules, making infections harder to treat[9].

Clearly understanding the structure and biosynthesis of the cell wall is crucial for developing new antimicrobial therapies[11]. However, getting pure and uniform glycans of interest from natural resources is a herculean task because of the heterogeneous nature. Thus, for preparation of homogeneous glycans, chemical or biosynthetic pathways of the synthesis of oligosaccharides and glycoconjugates are crucial[12].

3.3 Novel galactofuranans in cell walls of plant pathogens

Since the last decade, numerous new galactofuranans and galactomanans have been isolated from the cell walls of plant pathogens, particularly Clavibacter species and subspecies like *C. michiganensis* VKM Ac-1403^T, *C. tesselarius* VKM Ac-1406^T, *C. insidiosus* VKM Ac-1402^T etc. and their structures have been elucidated[13,14,15]. Each of them presents its own unique synthetic challenges, but particularly one galactofuranan glycopolymer molecule garnered our major attention that was isolated recently by Alexandar Shaskov group[16] from the cell wall of *Clavibacter phaseoli* VKM-2641^T. The structure was established as a pentasaccharide repeating unit

possessing galactose, ribose and mannose units[16]. Chemically, the pentasaccharide was having a (1→6)-linked *β*-D-galactofuranan chain with a side branched trisaccharide attached to every second galactofuranose residue. The trisaccharide features a distinctive and unique glycan linkage that consists of a core hyperbranched 1,2-*cis* Rib*f* motif attached to two (*α*-D-Man*p*) residues on C2 and C3 simultaneously[16] (**scheme 3.1**).

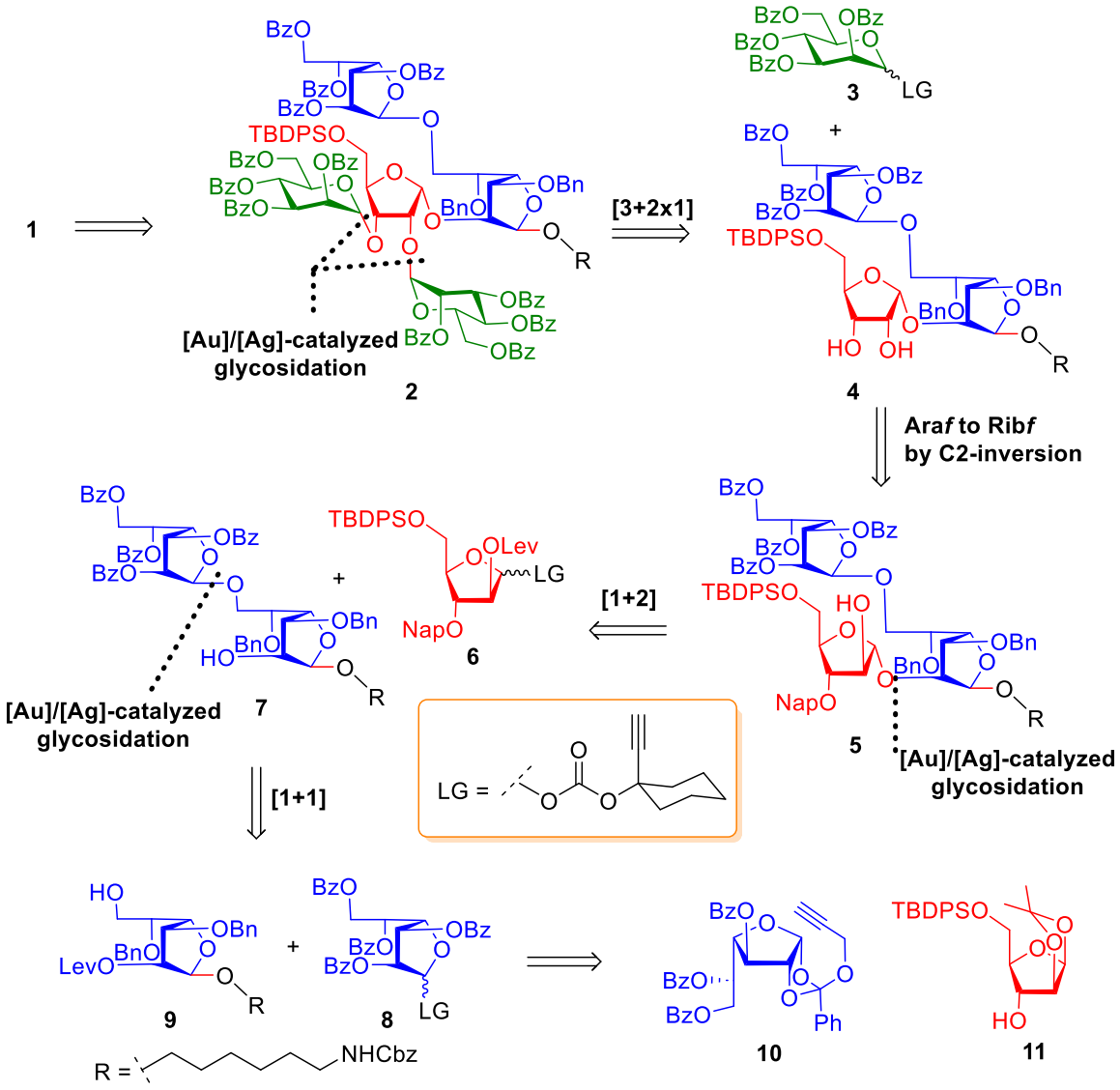


Scheme 3.1. Targeted Hyperbranched Pentasaccharide of *Clavibacter phaseoli* VKM-2641^T

To the best of our knowledge, there are no existing reports in the literature on the chemical synthesis or biosynthesis of novel cell wall galactofuranans from Clavibacter species. So, this hyperbranched pentasaccharide of *Clavibacter phaseoli* VKM-2641^T would be very challenging synthetic target. We planned to synthesize the molecule using our [Au]/[Ag]-catalyzed activation of alkynyl glycosyl carbonate donors[17].

3.4 Retrosynthetic analysis of the target Pentasaccharide

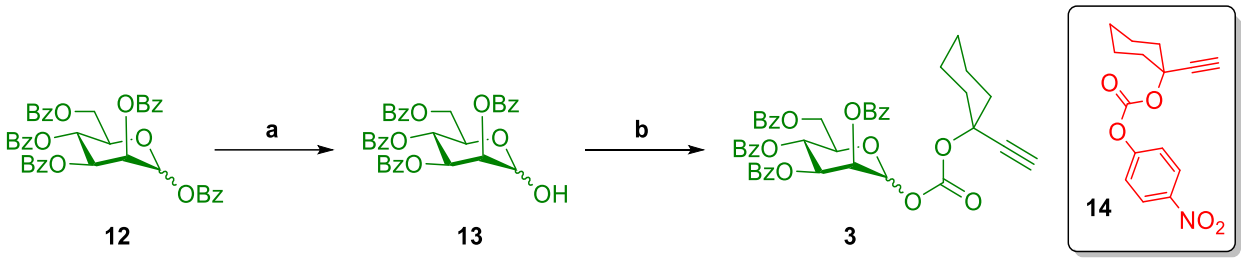
The target naturally occurring pentasaccharide **1** can be envisaged from the protected pentasaccharide **2** having an aminohexyl linker at the reducing end for further immunological studies. Compound **2** can be synthesized from simultaneous glycosylation of two mannosyl carbonate donor **3** in a {3+(2x1)} fashion at the C2 and C3 positions of the Rib*f* motif of the trisaccharide aglycone **4**. The trisaccharide **4** can be synthesized from trisaccharide **5** with a conversion of *α*-Ara*f* to *α*-Rib*f* by implementing C2-inversion of the core motif. Trisaccharide 5 can be synthesized via a [1+2] glycosylation strategy from Ara*f* donor **6** and digalactofuranosyl aglycone **7**. The Gal*f* disaccharide **7** can be envisaged from the carbonate donor **8** and the linker attached acceptor **9**. The Ara*f* and Gal*f* carbonate donors can be synthesized from easily accessible monosaccharide building blocks **10** and **11 (**Scheme **3.2)**. Strategically placed benzoyl and levulinate groups at the C2 position of carbonate donor ensures the 1,2-*trans* glycoside.



Scheme 3.2. Retrosynthetic analysis of the target Pentasaccharide

3.5 Synthesis of the Man*p* carbonate donor 3

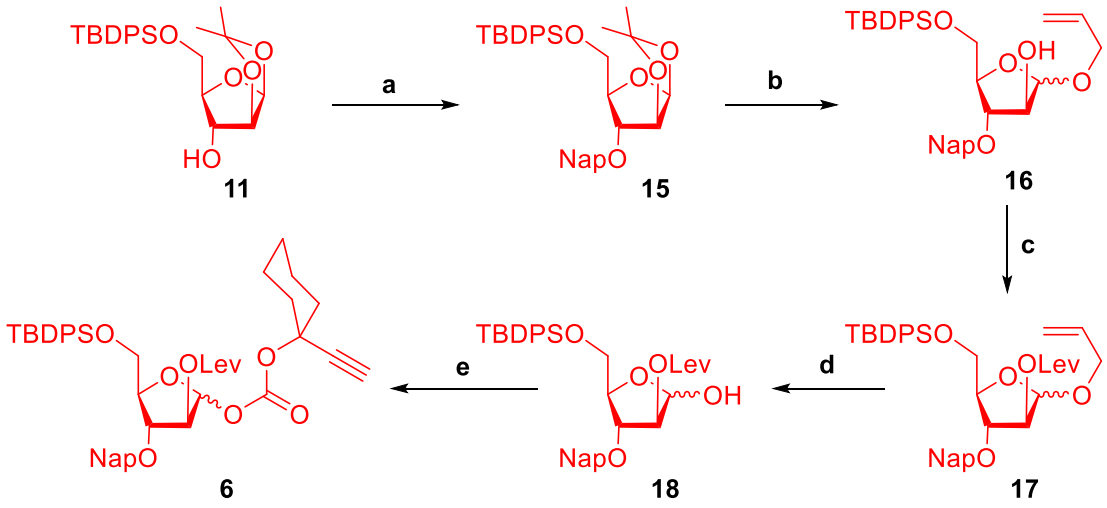
Our synthetic journey started from the synthesis of the mannosyl carbonate donor **3**. Per-*O*-benzoylated mannose **12** was subjected to selective anomeric deprotection of anomeric benzoate by hydrazine acetate in DMF[18] to furnish the hemiacetals **13** in 74 % yield. The hemiacetal **13** was further masked with carbonate reagent **14**[17] in CH_2Cl_2, DMAP conditions to furnish the mannosyl carbonate donor **3** in 92 % yield (Scheme **3.3**).



Scheme 3.3. Synthesis of carbonate donor 3. Reagents: a) H_2NNH_2•AcOH, DMF, 25 °C, 5 h, 74%; b) 1- ethynylcyclohexyl (4-nitrophenyl) carbonate (**14**), CH_2Cl_2, DMAP, 25 ºC, 8 h, 92 %.

3.6 Synthesis of the Ara*f* carbonate donor 6

Synthesis of the Ara*f*- carbonate donor was started from the easily accessible monosaccharide building block **11**[19]. The C3-OH of **11** was protected as Nap-ether by using NapBr in NaH/DMF to obtain the Nap-protected compound **15** in 90 % yield. The acetonide group of compound **15** was subjected to acidic cleavage under *p*TSA and allyl alcohol at 55 °C to furnish the allyl glycoside **16** in 80 % yield. Further, the C2-OH of compound **16** was blocked using Lev-acid in DIC/DMAP coupling conditions to obtain Lev-protected compound **17**. The allyl group of **17** was successfully cleaved using $PdCl_2$ and a specially optimized ternary solvent system of DME:CH_2Cl_2:MeOH (to prevent the C2-C1 Lev migration[19]) to obtain the hemiacetal **18** in 78% yield which was further masked using the carbonate reagent **14** under CH_2Cl_2/DMAP condition to successfully provide the Ara*f*- carbonate donor **6** in 85 % yield (Scheme **3.4**).

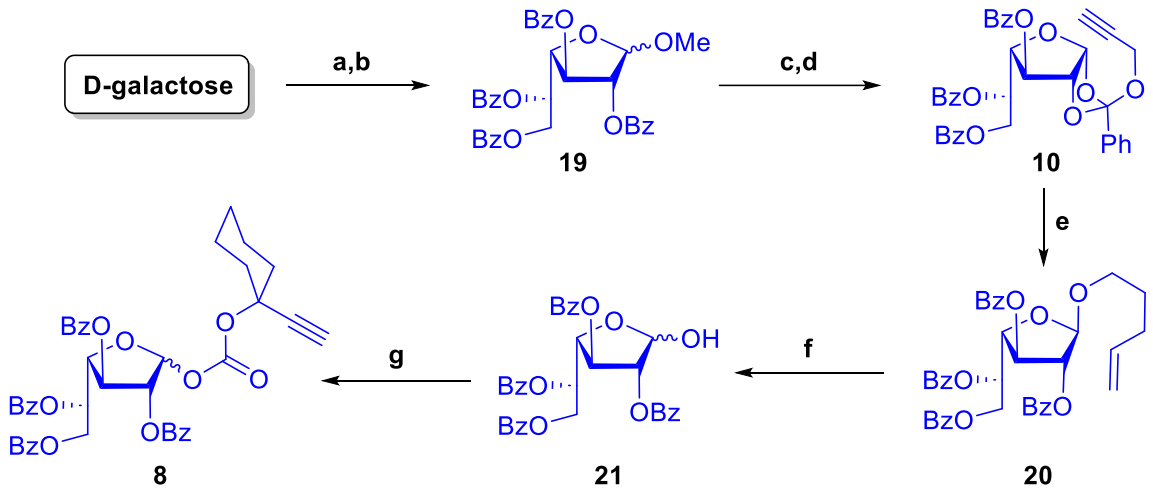


Scheme 3.4: Synthesis of the Ara*f* carbonate donor 6: Reagents: a) NaH, NAPBr, TBAI, DMF, 0-25 ºC, 2 h, 90%; b) *p*TSA, allyl alcohol, CH_2Cl_2, 55 °C, 3 h, 80 %; c) Lev-acid, DIC, DMAP,

CH_2Cl_2, 0-25 ºC, 2 h, 95%; d) $PdCl_2$, DME: CH_2Cl_2: MeOH (3:1:1), 25 °C, 4h, 78%; e) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate (**14**), CH_2Cl_2, DMAP, 0-25 ºC, 3 h, 85%.

3.7 Synthesis of Gal*f* carbonate donor 8

It is well known that the hexose sugars always tend to cyclize in pyranoside form as the furanose form is thermodynamically less stable[20]. Nevertheless, commercially available D-galactose was forcefully locked in a furanoside form by treating with $FeCl_3$ and MeOH in 80 ºC and subsequent treatment of the methyl galactofuranoside with benzoyl chloride and pyridine to give the per-*O*-benzoyl galactofuranoside derivative **19** in a compromised yield of 43 % over two steps.[21] Now compound **19** was treated with acetyl bromide and MeOH to generate the corresponding bromoside which was directly subjected to the treatment of propargyl alcohol and lutidine under TBAI/ CH_2Cl_2 conditions to successfully give the galactofuranose orthoester derivative **10** in 61 % yield over two steps (Scheme **3.5**).



Scheme 3.5: Synthesis of Gal*f* carbonate donor 8. Reagents: a) $FeCl_3$, CH_3OH, 80 ºC, 2 d, b) BzCl, pyridine, DMAP, 0-25 ºC, 5 h, 43 % over two steps; c) AcBr, CH_3OH, CH_2Cl_2, 0 ºC, 4h, d) Propargyl alcohol, 2,6- lutidine, TBAI, CH_2Cl_2, 25 ºC, 8 h, 61% over two steps; e) $AuBr_3$, 4-pentene-1-ol, CH_2Cl_2, 4Å MS powder, 25 ºC, 20 min, 84 %; f) NIS, TfOH, CH_3CN: CH_2Cl_2: H_2O (3:5:0.5), -20 -0 ºC, 2 h; 89%; g) 1- ethynylcyclohexyl (4-nitrophenyl) carbonate (**14**), CH_2Cl_2, DMAP, 0-25 ºC, 3 h, 92 %.

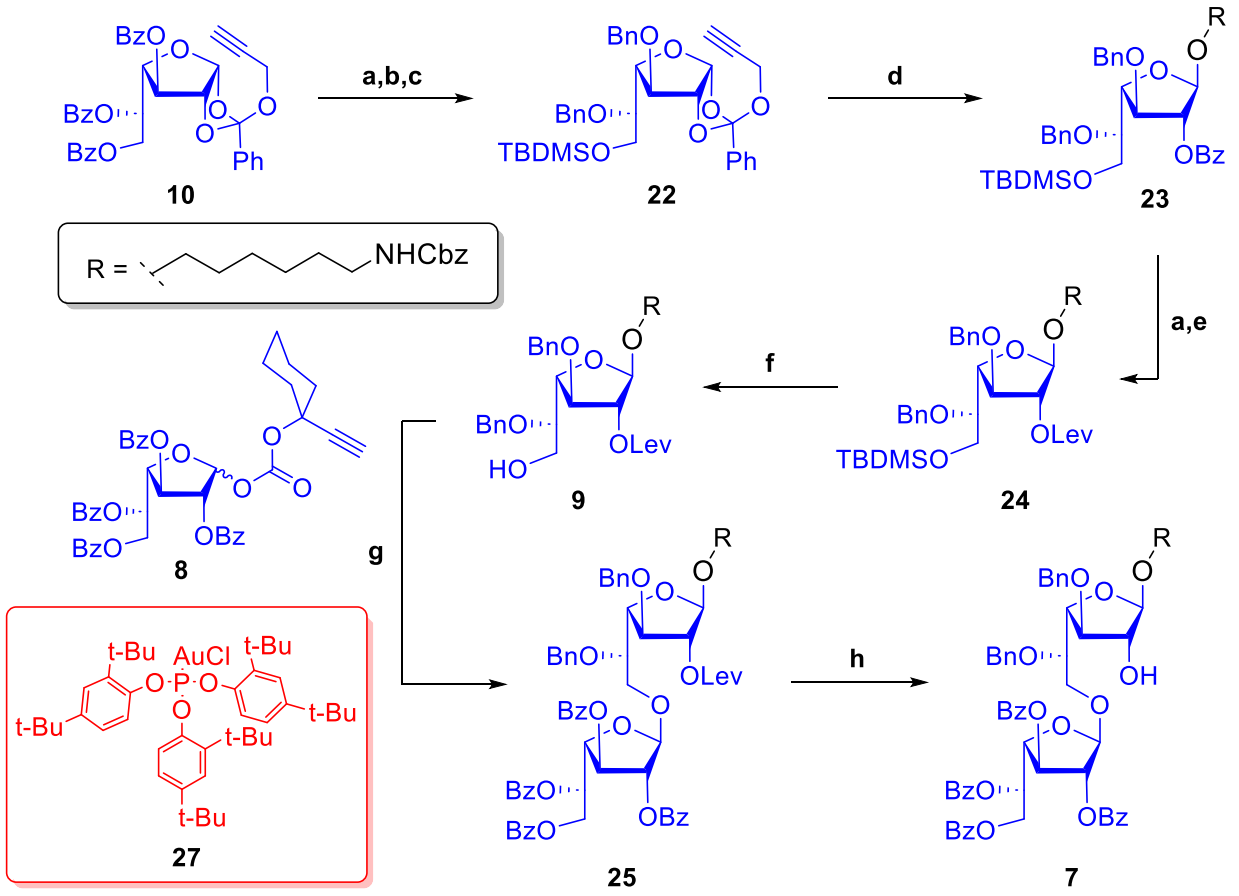
Further, the orthoester **10** was glycosylated by gold catalyzed opening of orthoesters[22] using catalytic $AuBr_3$ and 4-pentene-1-ol to obtain the pentenyl Gal*f* 20. In order to generate our desired

carbonate donor, first the pentenyl group was subjected to an acid mediated hydrolysis involving NIS/TfOH conditions to generate the hemiacetals **21** which was subsequently masked with the carbonate reagent **14** under CH_2Cl_2/DMAP condition to successfully obtain the gal*f* carbonate donor **8** in 92 % yield (Scheme **3.5**).

3.8 Synthesis of the digalactofuranosyl acceptor 7

The synthesis of the digalactofuranoside started from the per-*O*-benzoyl orthoester motif **10** prepared *vide supra*. The orthoester motif needs to be orthogonally protected in order to elongate the side chain coupling at both C2 and C6 position. With that perspective, compound **10** was subjected to Zemplén deacetylation using NaOMe in methanol to obtain the tri-OH which was immediately treated with TBDMSCl under Et_3N/ CH_2Cl_2 conditions to obtain the C6-silyl protected compound. The C3 and C5-OH were protected using BnBr under NaH/DMF conditions to successfully furnish the orthoester motif **22** in 74 % yield over three steps. The orthoester **22** was subjected to the glycosylation with the commercially available benzyl (6-hydroxyhexyl) carbamate **26** under catalytic $AuBr_3$ activation conditions to successfully attach the linker at the reducing end yielding the orthogonally protected Gal*f* motif **23**. In the ^{13}C NMR, the carbonyl peak at 156.5 ppm originating from the -NHCbz moiety confirms the successful attachment of the desired linker at the reducing end of Gal*f* **23** (**scheme 3.6**).

The C2-Bz group of **23** was deprotected using NaOMe/MeOH to obtain the C2-OH free compound which was directly protected using Lev-acid/DIC/DMAP condition to obtain compound **24** in 87% yield over two steps. The C6-TBDMS ether of compound **24** was deprotected with the treatment of HF•py yielding the Gal*f* acceptor **9** in 90 % yield. Acceptor **9** was glycosylated with Gal*f* carbonate donor **8** prepared *vide supra* using Au-phosphite **27** and AgOTf to successfully obtain the Gal*f* disaccharide **25** in 86 % yield. In the anomeric region of the ^{13}C NMR spectrum, two peaks at 106.0 and 105.9 ppm confirmed the structural integrity of the formed digalactofuranoside **25**. Also, in the HRMS (ESI-MS) studies, the observed *m/z* value of 1292.4827 for $C_{73}H_{75}NO_{19}Na$ is in good agreement with the calculated *m/z* 1292.4831. Subsequent deprotection of the levulinate of compound **25** by hydrazine hydrate in AcOH/pyridine buffer medium furnished the desired digalactofuranoside acceptor **7** in 89 % yield.

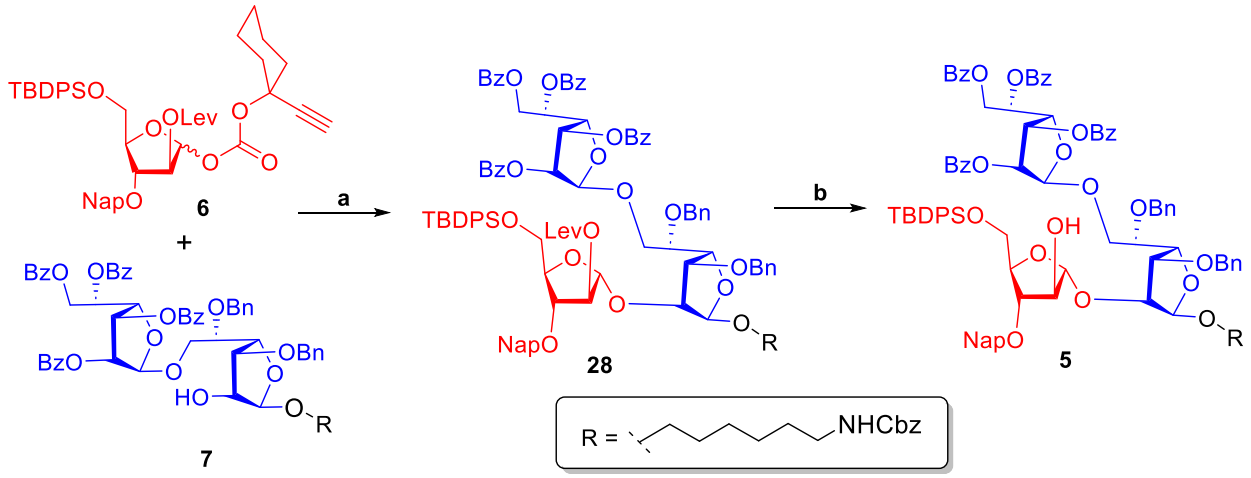


Scheme 3.6: Synthesis of the di-galactofuranosyl acceptor 7. Reagents: a) NaOMe, MeOH: CH_2Cl_2 (1:1), 25 ºC, 2 h, b) TBDMSCl, Et_3N, CH_2Cl_2, 0-25 ºC, 2 h, c) NaH, BnBr, TBAI, DMF, 0-25 ºC, 2 h, 74 % over three steps; d) ROH **(26)**, $AuBr_3$, CH_2Cl_2, 4Å MS powder, 25 ºC, 30 min, 86%; e) Lev-acid, DIC, DMAP, CH_2Cl_2, 0-25 ºC, 2 h, 87% over two steps; f) HF·py, pyridine, 0-25 ºC, 2 h, 90 %; g) chloro[2,4-di-*tert*-butylphenyl)phosphite]gold (**27**), AgOTf, CH_2Cl_2, 4Å MS powder, 25 ºC, 15 min, 86%; h) H_2NNH_2•H_2O, AcOH: Pyridine (22:27 eq), CH_2Cl_2, 30 min, 89%.

3.9 Synthesis of the core trisaccharide 5

Having the Ara*f* carbonate donor **6** and digalactofuranoside acceptor **7** in our hand, we proceeded for the synthesis of the core trisaccharide of the molecule. Donor **6** and acceptor **7** were coupled using the standard [Au]/[Ag]-catalyzed glycosylation condition to furnish the trisaccharide **28** in 87 % yield (Scheme **3.7**). The successful formation of the core trisaccharide **28** was confirmed by HRMS(ESI-MS) and NMR studies. The three peaks of 105.9, 105.9 and 105.1 ppm at the anomeric region of ^{13}C NMR confirmed the structural integrity of thus formed trisaccharide **28** (Table **3.1**).

Also, the observed *m/z* value in the HRMS spectral chart for $C_{105}H_{110}NO_{23}Si$: 1780.7283 is in good agreement with the calculated *m/z* 1780.7238 for compound **28**.



Scheme 3.7: Synthesis of the Core trisaccharide motif 5. Reagents: a) Chloro[2,4-di-tert-butylphenyl) phosphite] gold (**27**), AgOTf, CH_2Cl_2, 4Å MS powder, 25 ºC, 1h, 87%; b) H_2NNH_2•H_2O, AcOH: Pyridine (22:27 eq), CH_2Cl_2, 30 min, 89%.

Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
Anomeric	5.32 (d, 1H), 5.19 (s, 1H), 5.09 (s,1H)	105.9, 105.9 and 105.1
Benzoates	7.11 – 8.06 (Total 20H)	166.2, 165.8, 165.8, 165.4
Levulinoate	2.67 (td, 2H), 2.14 (s, 3H), 1.56 – 1.49 (m, 2H)	206.2, 171.8, 37.8, 29.8, 29.8
NHCbz	1.56 – 1.49 (m, 2H), 1.45 – 1.39 (m, 2H), 1.29 – 1.20 (m, 4H)	156.5, 41.1, 29.4, 27.9, 26.5, 25.9

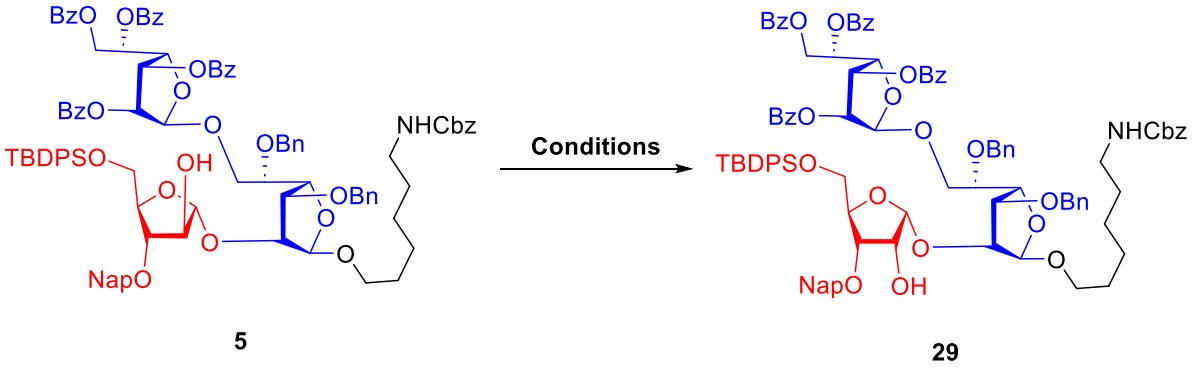
Table 3.1. Characterization of the core trisaccharide **28**

Further, the C2-Lev of trisaccharide **28** was deprotected using hydrazine hydrate to obtain the core trisaccharide aglycone **5** in 89 % yield (Scheme **3.7**). As confirmed from the ^{13}C NMR and ^{1}H-^{13}C HSQC studies, the two peaks at 106.2 and 105.8 ppm in the anomeric region were identified to be from the di-galactofuranose residue while the peak at 107.7 ppm corresponds to the 1,2-*trans* Ara*f* linkage.

3.10 Conversion of Ara*f* to Rib*f* in trisaccharide

Now the major challenge was to convert the 1,2-*trans* Ara*f* to 1,2-*cis* Rib*f* at the trisaccharide level. We started with the conventional S_N2 type approach for the inversion of the configuration[23,24]. In

the initial approach, the C2-OH of compound **5** was protected with Tf_2O/pyridine to make it a good leaving group and both $TBANO_2$ and KNO_2 were deployed as nitrite sources for the epimerization. In both the cases, despite the triflation being effective the inversions were not successful even at elevated temperature as the outcome was either no reaction or unidentified inseparable mixture of products noticed in the TLC (**table 3.2**).



5 **29**

Entry	Conditions	Outcome
1	Tf_2O, Pyridine then $TBANO_2$, DMF, 25 °C	**No reaction**
2	Tf_2O, Pyridine then KNO_2, DMF, 60 °C, 3 h	**Inseparable mixture**
3	Dess Martin Periodinane, CH_2Cl_2, 25 °C, 8 h then $NaBH_4$, EtOAc:EtOH, 0- 25 °C, 2 h.	**No reaction**
4	PDC, Ac_2O, CH_2Cl_2, 25 °C, 8 h then $NaBH_4$, EtOAc:EtOH, 0- 25 °C, 2 h.	**No reaction**
5	**PDC, Ac_2O, CH_2Cl_2, 60 °C, 3 h then $NaBH_4$, EtOAc:EtOH, 0- 25 °C, 2 h.**	**72 % yield**

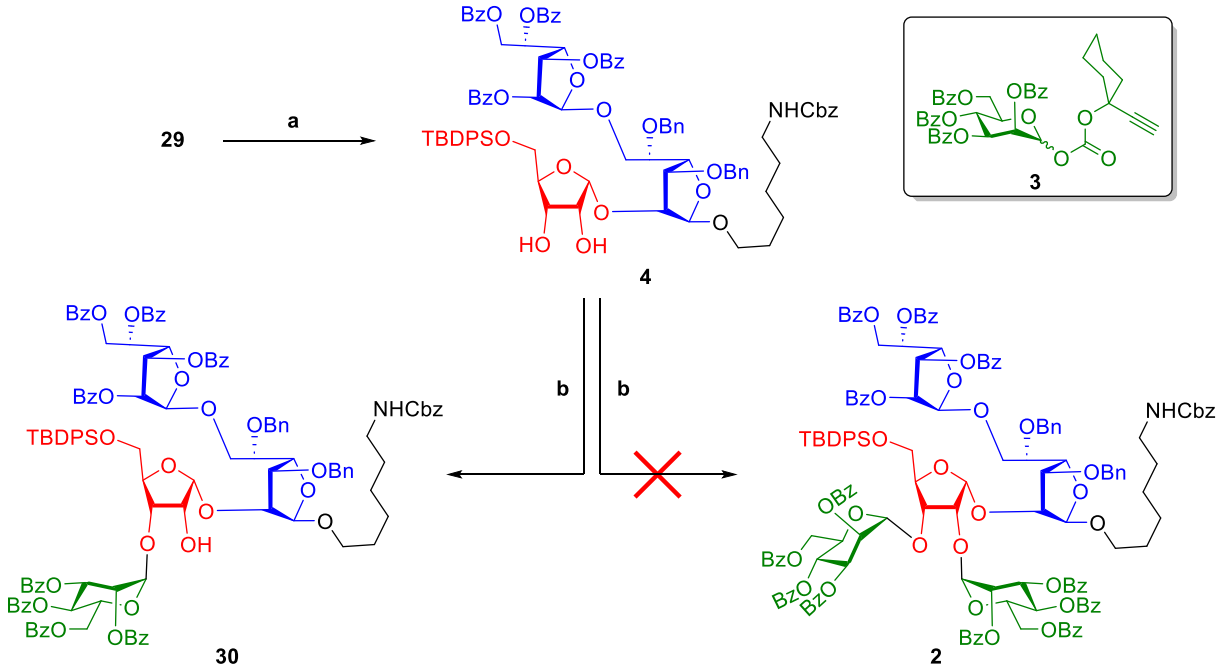
Table 3.2. Optimization table for the epimerization in trisaccharide

Then we shifted our attention to a special nature inspired oxidation-reduction procedure for the epimerization of sugars which was a long-known strategy and was first successfully utilized in furanosides by Hotha group[22]. However, the oxidation by Dess-Martin Periodinane and Pyridinium dichromate (PDC) were not successful at room temperature. Nevertheless, after much experimentation, it was observed that PDC/Ac_2O oxidation at 60 °C for 3 h followed by reduction by $NaBH_4$ in EtOAc/EtOH solvent system successfully furnished the epimerized trisaccharide **29** in 72 % yield (Table **3.2**). The C2-epimerization in the trisaccharide motif was confirmed by ^{13}C

NMR analysis wherein the upfield shift of the anomeric peak of 107.7 ppm to 101.0 ppm was noticed confirming the conversion of 1,2-*trans* Ara*f* linkage to desired 1,2-*cis* Rib*f*.

3.11 Attempt to synthesize the desired Pentasaccharide 2

The attempt to synthesize our desired protected pentasaccharide **2** was started from the deprotection of the C3-Nap group of trisaccharide **29** by DDQ in CH_2Cl_2:MeOH which yielded the trisaccharide di-ol acceptor **4** in 76 % yield. Now based on our outlined strategy of {3+(2x1)} coupling, the glycosylation of **4** with two units of mannosyl carbonate donor **3** shall furnish the desired pentasaccharide **2**. However, in practice, when the glycosylation of **4** was carried out at room temperature with even an increased stoichiometric amount of 4 equivalents of donor **3**, there was no formation of the pentasaccharide. Further, carrying out the glycosylation even at 40 °C with reverse addition of the carbonate donor still failed to furnish the pentasaccharide **2** which was evident from NMR and mass analysis.



Scheme 3.8: Attempt to synthesize Pentasaccharide. Reagents: a) DDQ, CH_2Cl_2: MeOH (1:2), 25 °C, 4 h, 76%; b) **3**, Chloro[2,4-di-tert-butylphenyl) phosphite] gold (**27**), AgOTf, CH_2Cl_2, 4Å MS powder, 25 ºC, 1h, 80 % for **30**.

In the aforementioned attempts of glycosylations in [3+(2x1)] fashion, the only product was established as a tetrasaccharide according to the HRMS (ESI-MS) analysis. The observed mass of 2142.7695 implies the formation of a tetrasaccharide (calcd. mass for $C_{123}H_{121}NO_{30}SiNa$: 2142.7640) as a result of monoglycosylation of donor **3** with di-ol acceptor **4**. In the ^{13}C NMR spectrum, the existence of four peaks of δ 106.5, 106.0, 102.2 and 101.0 ppm in the anomeric region confirmed the formation of a tetrasaccharide. Further the detailed 2D NMR analysis including the ^{1}H-^{13}C HSQC, ^{1}H-^{1}H COSY, and ^{1}H-^{13}C HMBC of the formed tetrasaccharide compound reveals that the mannose unite is attached to the C3-position of the central Rib*f* core motif (Scheme **3.8**). It actually suggests that the C3-sugar unit and the C1 galactan unit (both aligned in *syn* orientation relative to the C2-OH) creating steric problems for the glycosylation of the C2-OH. This factor could be responsible for the unsuccessful addition of one more mannose unit **3** during glycosylation, leading to the formation of a tetrasaccharide **30** instead.

3.12 Final synthesis of the target Pentasaccharide 1a

Now, we decided to revise our synthetic strategy to couple one mannose unit at a time instead of glycosylating two units simultaneously. In order to achieve that, we started the glycosylation from trisaccharide acceptor **29**. Compound **29** was glycosylated with mannosyl carbonate donor **3** using the [Au]/[Ag]-catalyzed glycosylation which indeed successfully furnished the tetrasaccharide **31** in 83 % yield (Scheme **3.9**). Four peaks at δ 106.4, 106.0, 101.8 and 101.4 ppm in the anomeric region of ^{13}C NMR spectrum confirmed the formation of the tetrasaccharide. Further, the observed mass for $C_{134}H_{129}NO_{30}Si$ $[M+H]^+$: 2260.8540 is indeed matching with the calculated *m/z* 2260.8447 of compound **31**. Now as we can see in this revised strategy, the C2-OH of the core Rib*f* unit was successfully glycosylated which provides an insight about the spatial difference between a Nap-protecting group and a whole sugar unit at C3-position of Rib*f*.

Further, the C3-Nap moiety of tetrasaccharide **31** was deprotected using DDQ in CH_2Cl_2/MeOH to obtain the tetrasaccharide acceptor **32** in 72% yield. Subsequently, the glycosylation of acceptor **32** with one more unit of mannosyl carbonate donor **3** using catalytic Au-phosphite **27** and AgOTf successfully furnished the desired protected pentasaccaride **2** in 81 % yield (Scheme **3.9**). The successful formation of pentasaccharide **2** was confirmed by thorough NMR spectra analysis (Table **3.3**) and HRMS(ESI-MS) analysis. In the ^{13}C NMR spectrum, five peaks at δ 106.4, 106.2, 101.3, 101.1 and 99.4 ppm in the anomeric region confirmed the structural integrity of

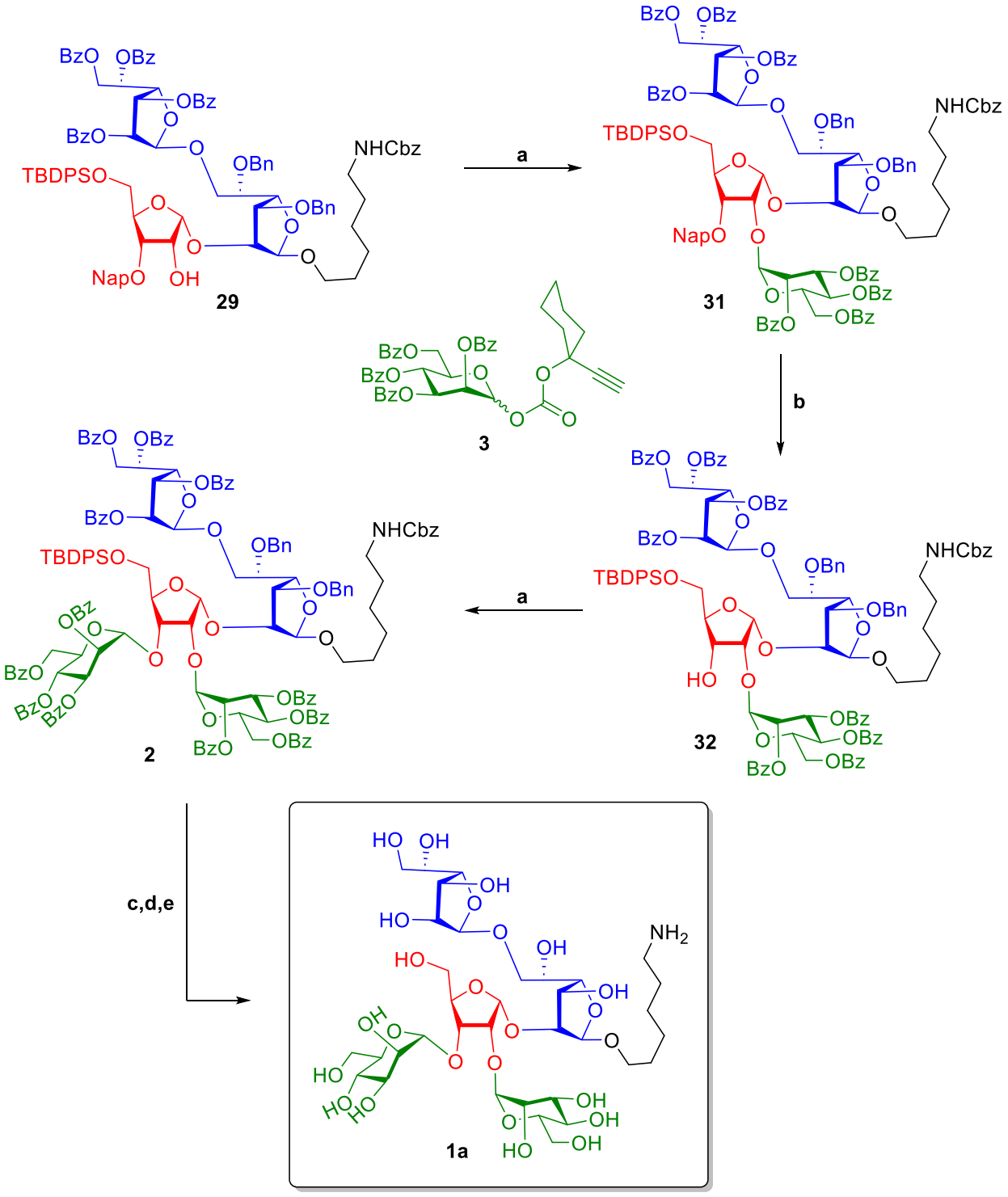
pentasaccharide **2**. Besides in the HRMS analysis, the observed *m/z* value for $C_{157}H_{147}NO_{39}SiNa$: 2720.9744 is in good agreement with the calculated m/z: 2720.9217 for pentasaccharide **2**.

Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
Anomeric	5.33 (s, 1H), 5.28 (d, 1H), 5.17 (d, 1H), 5.05 (1H), 4.85 (d, 1H)	106.4, 106.2, 101.3, 101.1 and 99.4
Benzoates	7.14 – 8.08 (Total 60H)	166.2, 166.2, 166.1, 165.9, 165.8, 165.8, 165.8, 165.4, 165.4, 165.4, 165.2, 164.4
TBDPS	1.05 (s, 9H)	27.1, 27.1, 27.0 and 19.5
NHCbz	1.48 (t, *J* = 7.3 Hz, 2H), 1.39 – 1.34 (m, 2H), 1.24 – 1.17 (m, 4H)	156.5, 41.2, 29.7, 29.5, 26.7, 26.0

Table 3.3. NMR characterization of the Pentasaccharide **2**

Thereafter, pentasaccharide **2** was subjected to global deprotection. First, the TBDPS group of **2** was deprotected using HF in pyridine to generate the mono-ol Pentasaccharide which was directly taken forward for the debenzoylation by Zemplén conditions using NaOMe/MeOH to obtain the poly-ol pentasaccharide. Subsequently, it was subjected to the hydrogenolysis using $Pd(OH)_2/C$ and H_2 to remove the benzyl and carboxybenzyl groups which successfully furnished the desired fully deprotected conjugation ready pentasaccharide **1a** in 66 % yield over three steps. The successful formation of pentasaccharide **1a** was confirmed by NMR and HRMS (ESI-MS) spectral analysis. In the ^{13}C spectrum, five resonances at δ 107.8, 105.4, 102.7, 101.5 and 92.6 ppm in the anomeric region confirmed the structural integrity of the pentasaccharide **1a**. Additionally in the ESI-MS analysis, the observed *m/z* value for $C_{35}H_{63}NO_{25}$ $[M+H]^+$: 898.3787 (calcd. m/z: 898.3767) established the successful formation of the desired pentasaccharide **1a**.

In summary, an efficient and convergent strategy was developed for the synthesis of the hyperbranched pentasaccharide **1a** of the cell wall of *Clavibacter phaseoli* VKM-2641^T. The alkynyl glycosyl carbonate donor was employed as a versatile donor in both mono and oligosaccharide synthesis. By utilizing silver-assisted gold-catalyzed glycosylation method, we accomplished significant benefits including catalytic efficiency, mild activation conditions, high yields, and reduced reaction times. The attachment of aminohexyl linker at the reducing end facilitates further immunological studies.



Scheme 3.9. Final synthesis of target Pentasaccharide. Reagents: a) **3**, Chloro[2,4-di-tert-butylphenyl) phosphite] gold (**27**), AgOTf, CH_2Cl_2, 4Å MS powder, 25 ºC, 1h, 83 % for **29**, 81 % for **2**; b) DDQ, CH_2Cl_2: MeOH (1:2), 25 °C, 4 h, 72%; c) HF·py, pyridine, 0-25 ºC, 4 h, d) NaOMe, MeOH, 25 °C, 3 h, e) H_2, $Pd(OH)_2/C$, H_2O, 18 h, 66 % over three steps.

3.13 Characterization data and Experimental procedures

2,3,4,6-tetra-*O*-benzoyl-D-mannopyranose (9): To a solution of per-benzoyl compound **12** (1.0 g, 1.43 mmol) in anhydrous DMF was added Hydrazine-acetate (566 µL, 7.14 mmol) and stirred at 25 ºC for 6 h. After completion of the reaction, excess hydrazine was quenched using acetone. The reaction mixture was diluted with EtOAc and washed with brine solution, dried over Na_2SO_4 and concentrated in vacuo. The resultant crude was purified by silica gel column chromatography (EtOAc/hexane as mobile phase) to obtain the hemiacetal **13** as a colorless foam (634 mg, 74 %); $[\alpha]_D^{25}$ = +9.7 (*c* = 1.0, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): IR (cm^{-1}, $CHCl_3$): 2955, 1729, 1451, 1261, 1176, 1018, 904; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 7.85 (m, 8H), 7.58 – 7.46 (m, 3H), 7.44 – 7.27 (m, 9H), 6.29 (t, *J* = 9.9 Hz, 1H), 5.82 – 5.71 (m, 2H), 5.34 (ddd, *J* = 10.2, 3.6, 1.2 Hz, 1H), 4.72 – 4.61 (m, 2H), 4.54 – 4.15 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 166.4, 166.4, 166.1, 166.0, 166.0, 165.4, 165.4, 133.7, 133.6, 133.6, 133.5, 133.5, 133.3, 133.3, 133.3, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.7, 129.7, 129.5, 129.2, 129.2, 129.0, 129.0, 129.0, 129.0, 128.9, 128.8, 128.8, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 96.1, 90.5, 74.2, 72.6, 72.5, 72.4, 70.4, 69.6, 69.6, 67.8, 63.2, 63.0; HRMS (ESI-MS): m/z calcd. For $C_{34}H_{28}O_{10}$ $[M+Na]^+$: 619.1579; Found: 619.1580.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,4,6-tetra-*O*-benzoyl-D-mannopyranoside (3)

The hemiacetal **9** (1.5g, 2.51 mmol) was dissolved in anhydrous CH_2Cl_2 (8 mL) at 25 ºC. DMAP (460.76 mg, 3.77 mmol) was added to a stirring solution at 25 ºC. After 10 min, ethynyl cyclohexyl (4-nitrophenyl) carbonate **10** (872.82 mg, 3.02 mmol) was added and stirred at 25 ºC for 3 h. After completion of the hemiacetal as indicated by TLC, the reaction mixture was concentrated *in vacuo* and the oily residue was partially purified by silica gel column chromatography (*n*-hexane/EtOAc) to obtain the glycosyl carbonate donor **3** as colorless foam (1.73 g, 92% yield). $[\alpha]_D^{25}$ = +48.3 (c = 0.15, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2940, 1729, 1596, 1451, 1261, 1188, 1019, 904; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (ddd, *J* = 8.4, 6.0, 1.4 Hz, 2H), 7.98 – 7.92 (m, 3H), 7.92 – 7.84 (m, 3H), 7.57 – 7.47 (m, 3H), 7.43 (dd, *J* = 8.1, 6.8 Hz, 3H), 7.39 – 7.33 (m, 4H), 7.30 (dd, *J* = 8.1, 1.8 Hz, 2H), 6.04 (d, *J* = 8.0 Hz, 1H), 5.96 (t, *J* = 9.5 Hz, 1H), 5.83 – 5.72 (m, 1H), 5.71 – 5.55 (m, 1H), 4.70 – 4.50 (m, 2H), 4.49 – 4.29 (m, 1H), 2.44 (s, 1H), 2.21 – 1.96 (m, 2H), 1.91 – 1.73 (m, 2H), 1.70 – 1.40 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 166.2, 165.9, 165.8, 165.4, 165.2, 165.2, 165.0, 150.9, 150.7, 133.6, 133.6, 133.5, 133.5, 133.4, 133.4, 133.3, 133.2, 130.2, 130.2, 130.1,

130.1, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.7, 129.6, 129.0, 129.0, 128.8, 128.8, 128.7, 128.7, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 95.2, 92.6, 82.3, 82.3, 79.0, 79.0, 75.4, 75.3, 73.3, 72.9, 70.9, 70.6, 70.5, 70.2, 69.1, 68.8, 62.8, 62.5, 36.8, 36.6, 36.6, 36.6, 25.0, 24.9, 22.6, 22.6, 22.4, 22.4; HRMS (ESI-MS): m/z calcd. For $C_{43}H_{38}O_{12}$ $[M+Na]^+$: 769.2260; Found: 769.2253.

3-*O*-(naphthalen-1-yl methyl)-1,2-*O*-isopropylidene-5-*O*-tert-butyldiphenylsilyl-β-D-arabinofuranoside (15): Compound **11**[19] (2.0 g, 4.67 mmol) was dissolved in anhydrous DMF (10 mL) and cooled to 0 °C under nitrogen atmosphere. NaH (60% oil dispersion, 223.96 mg, 5.60 mmol) was added and stirred for 10 minutes at 0 ºC, 2-bromomethyl naphthalene (1.24g, 5.60 mmol) was added and stirred for 2 h at 25 ºC. After the completion of the reaction it was quenched by ice cold water with vigorous shaking, extracted with ethyl acetate (3x25 mL) and combined oraganic layers was washed with cold water (2x25 mL), brine solution (3x25 mL), and dried over Na_2SO_4. The organic layer was evaporated in vacuo and purified by column chromatography (ethyl acetate/hexanes as mobile phase) to obtain compound **15** (2.36 g, 89% yield). $[\alpha]_D^{25}$ = -9.0 (c = 0.30, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3059, 2938, 2862, 1465, 1376, 1099, 1017, 858; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.78 (m, 4H), 7.65 (dt, *J* = 7.8, 1.5 Hz, 4H), 7.50 – 7.44 (m, 3H), 7.42 – 7.39 (m, 2H), 7.35 (dd, *J* = 7.8, 6.3 Hz, 4H), 5.92 (d, *J* = 4.0 Hz, 1H), 4.78 (d, *J* = 2.6 Hz, 2H), 4.72 (d, *J* = 4.1 Hz, 1H), 4.28 (d, *J* = 3.5 Hz, 2H), 3.82 (dd, *J* = 6.4, 3.7 Hz, 2H), 1.35 (s, 3H), 1.31 (s, 3H), 1.02 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7, 135.7, 135.7, 135.7, 135.1, 134.9, 133.4, 133.4, 133.2, 133.2, 129.9, 129.8, 128.5, 128.1, 127.9, 127.9, 127.8, 127.8, 126.7, 126.3, 126.1, 125.8, 112.6, 105.9, 85.4, 85.3, 83.0, 71.9, 63.6, 27.1, 26.9, 26.9, 26.9, 26.3, 19.3; HRMS (ESI-MS): m/z calcd. For $C_{35}H_{40}O_5Si$ $[M+Na]^+$: 591.2542; Found: 591.2542.

Allyl 3-*O*-(naphthalen-1-yl methyl)-5-*O*-tert-butyldiphenylsilyl-D-arabinofuranoside (16):

To a solution of the acetonide **15** (1.50 g, 2.64 mmol) in anhydrous CH_2Cl_2 (10 mL), allyl alcohol (1.08 mL, 15.82 mmol) and PTSA (90.82 mg, 527.44 µmol) were added and the reaction mixture was refluxed at 55 °C for 3 h. Then the reaction mixture was quenched with Et_3N (1 mL) and the volatile components were removed under vacuum. The crude product was purified by silica gel column chromatography (EtOAc/hexane as mobile phase) to obtain the desired allyl glycoside **16** (1.20 g, 80% yield). $[\alpha]_D^{25}$ = +12.5 (c = 0.08, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3052, 2929, 2857, 1427, 1111, 856, 821 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.77 (m, 4H), 7.74 – 7.63 (m, 3H), 7.57 –

7.35 (m, 9H), 7.29 (d, *J* = 7.5 Hz, 1H), 6.06 – 5.78 (m, 1H), 5.42 – 5.35 (m, 1H), 5.24 (ddt, *J* = 7.0, 3.5, 1.5 Hz, 1H), 5.21 – 5.14 (m, 1H), 4.97 – 4.88 (m, 1H), 4.84 – 4.71 (m, 1H), 4.39 – 4.26 (m, 2H), 4.25 – 4.14 (m, 1H), 4.13 – 3.99 (m, 2H), 3.86 – 3.57 (m, 2H), 3.31 (d, *J* = 10.4 Hz, 1H), 1.05 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7, 135.7, 135.7, 135.7, 135.7, 135.6, 135.6, 135.6, 135.4, 134.5, 133.8, 133.5, 133.4, 133.4, 133.4, 133.2, 133.1, 132.4, 132.4, 130.0, 130.0, 129.9, 129.8, 128.4, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 126.9, 126.5, 126.3, 126.1, 126.1, 125.9, 125.9, 125.8, 117.8, 117.3, 108.0, 100.7, 84.7, 84.7, 84.4, 82.6, 78.3, 78.1, 72.2, 72.1, 68.8, 68.3, 65.6, 64.2, 26.9, 26.9, 26.9, 26.8, 26.8, 26.8, 19.4, 19.2; HRMS (ESI-MS): m/z calcd. For $C_{35}H_{40}O_5Si$ $[M+Na]^+$: 591.2542; Found: 591.2546.

Allyl 2-*O*-(4-oxopentanoyl)-3-*O*-(naphthalen-1-yl methyl)-5-*O*-tert-butyldiphenylsilyl-D-arabinofuranoside (17): Compound **16** (1.2 g, 2.11 mmol) was dissolved in anhydrous CH_2Cl_2 (8 mL). DMAP (128.88 mg, 1.05 mmol) and levulinic acid (318.47 mg, 2.74 mmol) and N,N'-Diisopropylcarbodiimide (429.45 µL, 2.74 mmol) were added at 25 ºC under nitrogen atmosphere. The reaction mixture stirred for 2 h. After completion of the reaction CH_2Cl_2 was evaporated in vacuo and the residue was purified by silica gel column chromatography (ethyl acetate/hexanes as mobile phase) to furnish the C2-Lev derivative **14** (1.28 g, 91 % yield). $[\alpha]_D^{25}$ = +11.2 (c = 0.08, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3053, 2930, 2857, 1742, 1719, 1361, 1112, 821; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.74 (m, 4H), 7.72 – 7.65 (m, 3H), 7.65 – 7.61 (m, 1H), 7.48 (dt, *J* = 6.7, 2.8 Hz, 2H), 7.45 – 7.33 (m, 7H), 6.02 – 5.70 (m, 1H), 5.39 – 5.22 (m, 2H), 5.21 – 5.05 (m, 2H), 4.89 – 4.70 (m, 2H), 4.38 – 4.26 (m, 1H), 4.26 – 4.15 (m, 1H), 4.14 – 3.86 (m, 2H), 3.86 – 3.77 (m, 2H), 2.72 – 2.64 (m, 2H), 2.59 (td, *J* = 6.5, 1.1 Hz, 1H), 2.48 (dt, *J* = 9.9, 6.4 Hz, 1H), 2.16 (s, 3H), 1.05 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.2, 206.2, 172.2, 171.8, 135.8, 135.8, 135.7, 135.7, 135.7, 135.7, 135.7, 135.4, 135.3, 134.2, 134.2, 134.0, 133.5, 133.5, 133.4, 133.4, 133.3, 133.3, 133.1, 133.1, 129.9, 129.8, 129.8, 129.8, 128.3, 128.2, 128.0, 128.0, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.0, 126.5, 126.2, 126.1, 126.0, 126.0, 125.7, 117.5, 117.2, 105.1, 99.4, 83.6, 82.9, 82.2, 82.0, 81.6, 79.4, 72.5, 72.4, 68.7, 67.9, 65.8, 63.4, 37.9, 37.9, 29.9, 29.9, 27.9, 27.9, 27.0, 27.0, 27.0, 26.8, 26.8, 26.8, 19.4, 19.4; HRMS (ESI-MS): m/z calcd. For $C_{40}H_{46}O_7Si$ $[M+Na]^+$: 689.2910; Found: 689.2924.

2-*O*-(4-oxopentanoyl)-3-*O*-(naphthalen-1-yl methyl)-5-*O*-tert-butyldiphenylsilyl-D-arabinofuranose (18): Allyl glycoside **17** (1.0 g, 1.50 mmol) was dissolved in 10 mL of anhydrous 1,2-DME/CH_2Cl_2/MeOH (3:1:1) and cooled to 0 ºC. A suspension of $PdCl_2$ (53.18 mg, 299.90 µmol) in MeOH (1 mL) was added to the reaction mixture at 0 °C and the reaction mixture was allowed to stir at 25 °C for 4h. Then the reaction mixture was quenched with Et_3N (1 mL) and it was passed through a bed of Celite. The filtrate was concentrated in vacuo and the crude residue was purified by silica gel column chromatography (ethyl acetate and hexane as mobile phase) to obtain the desired hemiacetal **15** (734 mg, 78% yield). $[\alpha]_D^{25}$ = +12.3 (c = 0.13, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3053, 2930, 1740, 1718, 1361, 1112, 857, 821; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.74 (m, 4H), 7.66 – 7.59 (m, 4H), 7.48 (ddd, *J* = 5.8, 4.8, 3.4 Hz, 2H), 7.45 – 7.37 (m, 4H), 7.37 – 7.33 (m, 3H), 5.53 – 5.30 (m, 1H), 5.21 – 5.11 (m, 1H), 4.89 – 4.79 (m, 1H), 4.78 – 4.63 (m, 1H), 4.49 – 4.38 (m, 1H), 4.16 – 4.09 (m, 1H), 3.86 – 3.60 (m, 3H), 3.37 – 3.21 (m, 1H), 2.67 – 2.58 (m, 2H), 2.41 (dt, *J* = 15.1, 6.5 Hz, 1H), 2.16 (s, 3H), 1.02 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.7, 206.2, 172.1, 171.8, 135.8, 135.8, 135.7, 135.7, 135.7, 135.7, 135.7, 135.7, 135.0, 134.7, 133.4, 133.3, 133.3, 133.2, 133.2, 133.2, 132.4, 132.3, 130.2, 130.1, 129.9, 129.9, 128.5, 128.4, 128.1, 128.1, 128.0, 128.0, 128.0, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.1, 127.1, 126.9, 126.3, 126.3, 126.2, 126.2, 125.9, 125.8, 101.1, 95.6, 84.4, 82.3, 82.1, 80.8, 80.4, 80.1, 72.4, 72.3, 64.8, 63.6, 38.1, 37.8, 29.9, 29.9, 27.9, 27.9, 26.9, 26.9, 26.9, 26.9, 26.9, 26.9, 19.3, 19.3; HRMS (ESI-MS): m/z calcd. For $C_{37}H_{42}O_7Si$ $[M+Na]^+$: 649.2597; Found: 649.2608.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2-*O*-(4-oxopentanoyl)-3-*O*-(naphthalen-1-yl methyl)-5-*O*-tert-butyldiphenylsilyl-D-arabinofuranoside (6): The hemiacetal **18** (800 mg, 1.28 mmol) was dissolved in anhydrous CH_2Cl_2 (5 mL) at 25 ºC. DMAP (187.11 mg, 1.53 mmol) was added to a stirring solution at 25 ºC. After 10 min, ethynyl cyclohexyl (4-nitrophenyl) carbonate **14** (443.05 mg, 1.53 mmol) was added and stirred at 25 ºC for 8 h. After completion of the hemiacetal as indicated by TLC, the reaction mixture was concentrated *in vacuo* and the oily residue was partially purified by silica gel column chromatography (*n*-hexane/EtOAc) to obtain the glycosyl carbonate donor **5** (904 mg, 90 % yield). $[\alpha]_D^{25}$ = +52.0 (c = 0.05, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3287, 2936, 1752, 1239, 1109, 954, 904; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 – 7.77 (m, 4H), 7.68 (t, *J* = 1.2 Hz, 1H), 7.65 – 7.56 (m, 3H), 7.50 – 7.43 (m, 3H), 7.43 – 7.31 (m, 6H), 6.25 – 6.10 (m, 1H), 5.42 – 5.35 (m, 1H), 4.90 (d, *J* = 12.2 Hz, 1H), 4.79 – 4.72 (m, 1H), 4.49 – 4.38 (m, 1H), 4.19 (dt, *J* = 5.1, 1.1 Hz, 1H), 3.85 – 3.77 (m, 2H), 2.70 – 2.57 (m, 3H), 2.48 (t, *J* = 6.3

Hz, 2H), 2.26 – 2.19 (m, 1H), 2.16 (s, 3H), 2.10 (s, 1H), 1.89 (td, *J* = 9.7, 4.8 Hz, 2H), 1.74 – 1.51 (m, 6H), 1.02 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.3, 206.1, 171.9, 171.6, 151.4, 151.2, 135.8, 135.7, 135.7, 135.7, 135.7, 135.7, 135.7, 135.3, 135.1, 133.4, 133.3, 133.3, 133.2, 133.2, 133.2, 133.2, 133.1, 129.9, 129.8, 129.8, 129.8, 129.8, 128.3, 128.3, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.0, 127.0, 126.5, 126.2, 126.2, 126.1, 126.0, 125.9, 125.7, 103.0, 96.9, 85.8, 85.8, 82.8, 82.7, 82.4, 81.3, 79.7, 78.3, 77.9, 77.6, 75.3, 75.2, 72.8, 72.4, 64.3, 62.8, 37.9, 37.8, 37.1, 37.0, 36.8, 36.5, 29.9, 29.8, 27.9, 27.8, 27.0, 27.0, 27.0, 26.8, 26.8, 26.8, 25.1, 25.0, 22.7, 22.7, 22.6, 22.6, 19.4, 19.4; HRMS (ESI-MS): m/z calcd. For $C_{46}H_{52}O_9Si$ $[M+Na]^+$: 799.3278; Found: 799.3365.

3,5,6-tri-*O*-benzoyl-α-D-galactofuranoside-prop-2-ynyl-1,2-orthobenzoate (10): Per-*O*-benzoyl methyl galacto-furanosides **19** (1.0 mmol) were dissolved in anhydrous CH_2Cl_2 and cooled to 0 °C. Acetyl bromide (6.5 mmol) was added to the reaction mixture followed by the drop-wise addition of MeOH (4.5 mmol) and stirred at 0 °C for 2 h. After complete conversion of the starting material, the reaction mixture was diluted with CH_2Cl_2 and poured over ice-water mixture and was extracted with CH_2Cl_2 (3x50 mL). The organic layer was washed with ice-cold saturated $NaHCO_3$ (1x25 mL), brine solution (1x25 mL), dried over Na_2SO_4 and concentrated *in vacuo* to afford corresponding furanosyl bromide as a white foam which was immediately carried forward to the next step without any further purification. To a solution of the crude furanosyl bromide prepared *vide supra* in anhydrous CH_2Cl_2, propargyl alcohol (2.0 mmol), 2,6-lutidine (2.2 mmol) and tetra *n*-butyl ammonium iodide (0.5 mmol) were added and the reaction mixture was allowed to stir at 25 °C. After 15 h, the reaction mixture was diluted with CH_2Cl_2 and water, extracted with saturated aqueous oxalic acid solution (3x25 mL), saturated $NaHCO_3$ (1x25 mL), brine solution (1x25 mL), dried over Na_2SO_4 and concentrated *in vacuo* to obtain a crude product that was purified by silica gel column chromatography using EtOAc and hexane as mobile phase to obtain the corresponding orthoester **10** (61 % yield over two steps). $[\alpha]_D^{25}$ = +45.6 (c = 0.10, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3068, 2924, 1724, 1452, 1261, 1102, 1034, 984; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.97 (m, 2H), 7.96 – 7.93 (m, 2H), 7.92 – 7.88 (m, 2H), 7.75 – 7.71 (m, 2H), 7.52 – 7.47 (m, 2H), 7.45 – 7.38 (m, 6H), 7.36 – 7.30 (m, 4H), 6.35 (d, *J* = 4.3 Hz, 1H), 5.64 (d, *J* = 2.8 Hz, 1H), 5.51 – 5.45 (m, 1H), 5.24 (d, *J* = 4.3 Hz, 1H), 4.74 (dd, *J* = 8.0, 2.9 Hz, 1H), 4.69 (dd, *J* = 12.4, 4.0 Hz, 1H), 4.50 (dd, *J* = 12.4, 5.0 Hz, 1H), 4.02 (dd, *J* = 5.5, 2.5 Hz, 2H), 2.40 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.86, 165.37, 165.37, 134.35, 133.80, 133.14, 133.11,

130.12, 129.94, 129.94, 129.92, 129.92, 129.78, 129.78, 129.72, 129.63, 128.87, 128.63, 128.63, 128.56, 128.56, 128.40, 128.40, 128.38, 128.38, 126.77, 126.77, 123.49, 105.91, 85.56, 85.03, 79.43, 76.75, 73.94, 71.53, 63.25, 52.12; HRMS (ESI-MS): m/z calcd. For $C_{37}H_{30}O_{10}$ $[M+Na]^+$: 657.1737; Found: 657.1735.

Pent-4-enyl 2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranoside (20): To a solution of propargyl-1,2-orthoester **10** (2.0g, 3.15 mmol) in anhydrous CH_2Cl_2 (10 mL), 4-penten-1-ol (1.0 mL, 9.45 mmol) and freshly activated 4Å MS powder were added under nitrogen atmosphere and stirred for 15 min at 25 °C. $AuBr_3$ (206.4 mg, 472.71 µmol) was added and the reaction mixture was allowed to stir for 1 h. After completion, the reaction was neutralized by the addition of Et_3N (1 ml) and passed through a bed of Celite. The filtrate was concentrated *in vacuo* and purified by silica gel column chromatography using ethyl acetate and hexane as mobile phase to obtain corresponding pentenyl glycoside **20** (1.76 g, 84% yield); $[\alpha]_D^{25}$ = -8.3 (c = 0.18, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3071, 2932, 1724, 1451, 1259, 1104, 969; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 8.04 (m, 4H), 7.97 (d, *J* = 1.3 Hz, 2H), 7.91 (dd, *J* = 8.1, 1.0 Hz, 2H), 7.57 – 7.48 (m, 4H), 7.43 – 7.27 (m, 8H), 6.10 (dt, *J* = 8.1, 4.4 Hz, 1H), 5.86 – 5.76 (m, 1H), 5.66 (s, 1H), 5.49 (s, 1H), 5.32 (s, 1H), 5.05 – 4.93 (m, 2H), 4.78 (d, *J* = 7.0 Hz, 2H), 4.68 (d, *J* = 5.1 Hz, 1H), 3.83 – 3.76 (m, 1H), 3.59 – 3.52 (m, 1H), 2.23 – 2.12 (m, 2H), 1.80 – 1.69 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 165.8, 165.7, 165.5, 138.0, 133.5, 133.4, 133.3, 133.1, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.7, 129.7, 129.6, 129.5, 129.1, 129.0, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 115.1, 105.7, 82.1, 81.3, 77.6, 70.4, 66.9, 63.5, 30.3, 28.7; HRMS (ESI-MS): m/z calcd. For $C_{39}H_{36}O_{10}$ $[M+Na]^+$: 687.2205; Found: 687.2200.

2,3,5,6-tetra-*O*-benzoyl-D-galactofuranose (21): The pent-4-enyl glycoside **20** (1.5 g, 2.26 mmol) was dissolved in a mixture of solvents CH_2Cl_2/CH_3CN/H_2O (5.0:3.0:0.5) (10 mL) and the reaction mixture was cooled to 0 °C. After 15 min, NIS (1.02 g, 4.51 mmol) and TfOH (39.84 µL, 451.33 µmol) were added to the reaction mixture simultaneously and the reaction was allowed to stir at 0 °C for another 1 h. After completion, the reaction mixture was quenched with $NaHCO_3$ solution (1 mL) and diluted with CH_2Cl_2 (50 mL). The organic layer was successively washed with satd. $Na_2S_2O_3$ solution (2x25 mL), brine solution (50 mL), dried over Na_2SO_4 and concentrated in *vacuo* to obtain crude hemiacetal which was purified by silica gel column chromatography (*n*-hexane/EtOAc) to obtain the hemiacetal **21** (1.2 g, 89 % yield). $[\alpha]_D^{25}$ = +86.6 (c = 0.10, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3443, 3069, 1722, 1451, 1261, 1100, 1032, 859; ^{1}H NMR

(400 MHz, $CDCl_3$) δ 8.12 – 8.02 (m, 4H), 8.01 – 7.88 (m, 4H), 7.56 – 7.46 (m, 4H), 7.42 – 7.27 (m, 8H), 6.18 – 6.06 (m, 1H), 5.90 – 5.71 (m, 1H), 5.69 – 5.64 (m, 1H), 5.59 – 5.51 (m, 1H), 4.91 – 4.84 (m, 1H), 4.83 – 4.70 (m, 2H), 4.20 – 3.96 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 166.3, 166.2, 165.9, 165.9, 165.8, 165.7, 165.6, 133.6, 133.6, 133.6, 133.5, 133.5, 133.3, 133.2, 133.2, 130.1, 130.1, 130.1, 130.1, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.6, 129.5, 129.5, 129.0, 129.0, 128.9, 128.9, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 101.1, 96.0, 82.8, 81.8, 79.2, 77.8, 77.8, 75.8, 72.3, 70.7, 63.7, 63.3; HRMS (ESI-MS): m/z calcd. For $C_{34}H_{28}O_{10}$ $[M+Na]^+$: 619.1579; Found: 619.1580.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,5,6-tetra-*O*-benzoyl-D-galactofuranoside (8):

The hemiacetal **21** (1.5 g, 2.51 mmol) was dissolved in anhydrous CH_2Cl_2 (8 mL) at 25 ºC. DMAP (460.76 mg, 3.77 mmol) was added to a stirring solution at 25 ºC. After 10 min, ethynyl cyclohexyl (4-nitrophenyl) carbonate **14** (872.83 mg, 3.02 mmol) was added and stirred at 25 ºC for 8 h. After completion of the hemiacetal as indicated by TLC, the reaction mixture was concentrated *in vacuo* and the oily residue was purified by silica gel column chromatography (*n*-hexane/EtOAc) to obtain the glycosyl carbonate donor **8** (1.73 g, 92% yield). $[\alpha]_D^{25}$ = -6.4 (c = 0.39, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3293, 2939, 1723, 1451, 1238, 1101, 946, 853; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (td, *J* = 8.5, 1.3 Hz, 4H), 7.99 – 7.87 (m, 4H), 7.61 – 7.48 (m, 4H), 7.46 – 7.32 (m, 5H), 7.32 – 7.27 (m, 3H), 6.42 (s, 1H), 6.21 – 6.05 (m, 1H), 5.77 – 5.67 (m, 2H), 4.87 (t, *J* = 4.4 Hz, 1H), 4.76 (qd, *J* = 11.9, 5.6 Hz, 2H), 2.66 (d, *J* = 0.7 Hz, 1H), 2.27 – 2.13 (m, 2H), 1.99 – 1.86 (m, 2H), 1.77 – 1.49 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 166.0, 165.8, 165.7, 165.6, 165.6, 165.5, 165.2, 151.1, 150.8, 133.7, 133.7, 133.6, 133.6, 133.4, 133.3, 133.2, 133.1, 130.4, 130.4, 130.2, 130.2, 130.1, 130.1, 130.1, 130.1, 130.1, 130.0, 130.0, 130.0, 129.9, 129.8, 129.8, 129.8, 129.8, 129.7, 129.6, 129.6, 129.6, 129.4, 129.4, 128.9, 128.9, 128.8, 128.7, 128.7, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 102.3, 96.5, 83.8, 82.5, 81.3, 80.2, 78.7, 78.5, 77.3, 76.1, 75.5, 75.2, 74.1, 70.7, 70.2, 69.7, 63.6, 62.9, 36.9, 36.8, 36.7, 36.6, 25.0, 25.0, 22.6, 22.6, 22.6, 22.6; HRMS (ESI-MS): m/z calcd. For $C_{43}H_{38}O_{12}$ $[M+Na]^+$: 769.2260; Found: 769.2253.

6-O-(*tert*-butyldimethylsilyl)-3,5-di-*O*-benzyl-α-D-galactofuranoside-prop-2-ynyl-1,2-orthobenzoate (19): To a solution of orthoester **10** (3 g, 4.73 mmol) in CH_2Cl_2: MeOH (1:1) (15 mL), NaOMe (153.23 mg, 2.84 mmol) was added and stirred for 2 h at 25 ºC. After the completion of the benzoate orthoester, the reaction mixture was concentrated in vacuo to obtain a residue that was stirred in presence of pet ether (for removal of methyl benzoate) the pet ether was decanted to afford triol orthoester. The resultant orthoester was dissolved in anhydrous CH_2Cl_2 (10 mL) and cooled to 0 ºC. Et_3N (3.03 mL, 21.72 mmol) and DMAP (106.13 mg, 868.72 µmol) were added. TBDMSCl (785.61 mg, 5.21 mmol) was added portion wise at 0 ºC and continued stirring for 2h at 25 ºC. After the completion of the reaction, ice-cold water was added and extracted with CH_2Cl_2 (50 mL), organic layer was washed with brine (2x50 mL), dried over Na_2SO_4 and concentrated in vacuo. The resultant crude was dissolved in dry DMF (15 mL) and cooled to 0 ºC. Sodium hydride (60% dispersion in mineral oil) (389.36 mg, 9.73 mmol) was added portion-wise and the reaction mixture became cake like solid. Benzyl bromide (1.16 mL, 9.73 mmol) and catalytic amount of TBAI were added and stirred for 2h at 25 ºC. After the completion the reaction was quenched with ice, EtOAc (50 mL) was added. The organic layer was washed with brine solution (2x50 mL), dried over Na_2SO_4 and concentrated in vacuo. The resultant crude was purified by silica gel column chromatography (EtOAc/hexane as mobile phase) to obtain the desired fully protected orthoester **22** (2.16g, 74% yield over 3 steps). $[\alpha]_D^{25}$ = -17.6 (c = 0.09, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3046, 2937, 2862, 1724, 1458, 1081, 983, 840; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 8.3, 1.5 Hz, 2H), 7.37 – 7.28 (m, 9H), 7.25 – 7.23 (m, 2H), 7.17 – 7.12 (m, 2H), 6.24 (d, *J* = 4.4 Hz, 1H), 5.03 (dd, *J* = 4.4, 1.1 Hz, 1H), 4.60 (d, *J* = 11.6 Hz, 1H), 4.51 (d, *J* = 11.7 Hz, 1H), 4.45 (d, *J* = 11.8 Hz, 1H), 4.33 – 4.26 (m, 2H), 4.23 (dd, *J* = 3.1, 1.2 Hz, 1H), 4.01 (dd, *J* = 5.4, 2.5 Hz, 2H), 3.56 (dd, *J* = 5.0, 1.6 Hz, 2H), 3.30 (dd, *J* = 7.6, 5.0 Hz, 1H), 2.38 (t, *J* = 2.4 Hz, 1H), 0.85 (s, 9H), -0.05 (d, *J* = 1.5 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 137.4, 135.6, 129.7, 128.6, 128.6, 128.3, 128.3, 128.3, 128.3, 128.1, 128.0, 128.0, 127.9, 127.9, 127.5, 126.7, 126.7, 122.9, 105.9, 87.3, 85.6, 81.9, 79.6, 79.1, 73.7, 73.3, 71.9, 63.5, 51.8, 26.0, 26.0, 26.0, 18.3, -5.3, -5.4; HRMS (ESI-MS): m/z calcd. For $C_{36}H_{44}O_7Si$ $[M+Na]^+$: 639.2753; Found: 639.2753.

***N*-benzyloxycarbonyl-6-aminohexanyl 6-O-*tert*-butyldimethylsilyl-2-*O*-benzoyl-3,5-di-*O*-benzyl-β-D-galactofuranoside (23):** Compound **22** (1.0 g, 1.62 mmol) and Benzyl (6-hydroxyhexyl) carbamate **26** (1.02 g, 4.05 mmol) were dissolved in anhydrous CH_2Cl_2 (8 mL). Freshly activated 4 Å molecular sieves powder was added to the solution and stirred. After 15mins,

$AuBr_3$ (106.19 mg, 243.18 µmol) was added and the reaction mixture was stirred at 25 ºC for 30 mins. After the completion of the starting material, reaction was quenched with Et_3N (1 mL) and passed through a bed of Celite. The filtrate was concentrated *in vacuo* and purified by silica gel column chromatography using ethyl acetate and hexane as mobile phase to obtain corresponding linker attached glycoside **23** (1.13 g, 86% yield). $[\alpha]_D^{25}$ = -45.8 (c = 0.12, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.69 – 7.63 (m, 1H), 7.52 – 7.43 (m, 6H), 7.42 – 7.26 (m, 9H), 7.25 (d, *J* = 2.5 Hz, 2H), 5.41 (d, *J* = 1.5 Hz, 1H), 5.21 (d, *J* = 17.5 Hz, 3H), 4.93 (s, 1H), 4.79 (dd, *J* = 17.4, 11.7 Hz, 2H), 4.49 (d, *J* = 12.0 Hz, 1H), 4.39 (d, *J* = 11.5 Hz, 1H), 4.33 (dd, *J* = 6.3, 2.4 Hz, 1H), 4.14 (dt, *J* = 6.4, 1.2 Hz, 1H), 3.92 (qd, *J* = 10.3, 6.4 Hz, 2H), 3.80 (dt, *J* = 9.8, 6.6 Hz, 1H), 3.69 (td, *J* = 6.4, 2.4 Hz, 1H), 3.54 (dt, *J* = 9.7, 6.4 Hz, 1H), 3.27 (q, *J* = 6.7 Hz, 2H), 1.70 (t, *J* = 6.7 Hz, 2H), 1.59 (q, *J* = 7.0 Hz, 2H), 1.51 – 1.41 (m, 4H), 1.01 (s, 9H), 0.17 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 156.5, 138.4, 137.8, 136.8, 133.4, 129.9, 129.9, 129.7, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 127.9, 127.7, 106.0, 83.0, 82.6, 81.7, 78.2, 73.9, 72.3, 67.4, 66.6, 63.2, 41.1, 30.0, 29.3, 26.6, 26.0, 26.0, 26.0, 25.9, 18.4, -5.2, -5.3; HRMS (ESI-MS): m/z calcd. For $C_{47}H_{61}NO_9Si$ $[M+Na]^+$: 834.4013; Found: 834.4008.

***N*-benzyloxycarbonyl-6-aminohexanyl 6-O-*tert*-butyldimethylsilyl-2-*O*-(4-oxopentanoyl)-3,5-di-*O*-benzyl-β-D-galactofuranoside (24):** To a solution of compound **23** (1.5 g, 1.85 mmol) in CH_2Cl_2: MeOH (1:1) (8 mL), NaOMe (29.94 mg, 554.13 µmol) was added and stirred for 1 h at 25 ºC. After the completion of the benzoate, the excess NaOMe was quenched by Amberlite IR 120H resin. The resin was filtered off and the filtrate was concentrated in vacuo to obtain a residue that was stirred in presence of pet ether (for removal of methyl benzoate) the pet ether was decanted to afford C2-OH compound which was dissolved in anhydrous CH_2Cl_2 (8 mL). DMAP (103.54 mg, 847.48 µmol) and levulinic acid (255.86 mg, 2.20 mmol) and *N*,*N*′-Diisopropylcarbodiimide (345.02 µL, 2.20 mmol) were added at 25 ºC under nitrogen atmosphere. The reaction mixture stirred for 2 h. After completion of the reaction CH_2Cl_2 was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate/hexanes as mobile phase) to furnish the C2-Lev ester **24** (1.29 g, 87 % yield over two steps). $[\alpha]_D^{25}$ = -73.0 (c = 0.10, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3357, 2929, 2857, 1719, 1360, 1251, 1104, 837; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 4.4 Hz, 3H), 7.33 – 7.19 (m, 12H), 5.09 (s, 2H), 5.05 (d, *J* = 1.5 Hz, 1H), 4.98 (s, 1H), 4.85 (s, 1H), 4.63 (dd, *J* = 11.8, 4.0 Hz, 2H), 4.36 (d, *J* = 12.0 Hz, 1H), 4.29 (d, *J* =

11.4 Hz, 1H), 4.15 (dd, *J* = 6.2, 2.5 Hz, 1H), 3.89 (dt, *J* = 6.2, 1.2 Hz, 1H), 3.84 – 3.72 (m, 2H), 3.64 (dt, *J* = 9.7, 6.6 Hz, 1H), 3.53 (td, *J* = 6.3, 2.5 Hz, 1H), 3.39 (dt, *J* = 9.7, 6.4 Hz, 1H), 3.15 (q, *J* = 6.7 Hz, 2H), 2.69 – 2.59 (m, 2H), 2.53 – 2.38 (m, 2H), 2.14 (s, 3H), 1.56 (t, *J* = 6.7 Hz, 2H), 1.47 (q, *J* = 7.0 Hz, 2H), 1.33 (p, *J* = 5.2 Hz, 4H), 0.90 (s, 9H), 0.06 (d, *J* = 1.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.3, 172.0, 156.5, 138.5, 137.9, 136.8, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.2, 128.1, 127.9, 127.8, 105.7, 82.6, 82.2, 81.6, 78.2, 73.9, 72.1, 67.2, 66.6, 63.1, 41.1, 37.8, 29.9, 29.9, 29.2, 27.9, 26.5, 26.0, 26.0, 26.0, 25.9, 18.3, -5.3, -5.3; HRMS (ESI-MS): m/z calcd. For $C_{45}H_{63}NO_{10}Si$ $[M+Na]^+$: 828.4118; Found: 828.4084.

***N*-benzyloxycarbonyl-6-aminohexanyl 2-*O*-(4-oxopentanoyl)-3,5-di-*O*-benzyl-β-D-galactofuranoside (9):** Compound **24** (1.20 g, 1.49 mmol) was dissolved in anhydrous pyridine (6 mL), HF•py (531.06 µL, 5.95 mmol) was added at 0 °C and the reaction mixture was stirred at 25 °C for another 3 h. Upon completion of the reaction, the reaction mixture was diluted with ethyl acetate (50 mL). The organic layer was successively washed with 1N HCl solution (2x50 mL), saturated $NaHCO_3$ solution (2x50 mL) and brine solution (50 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified with silica gel column chromatography (ethyl acetate/hexane) to furnish the compound **9** (927 mg, 90% yield)**.** $[\alpha]_D^{25}$ = -58.2 (c = 0.11, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3373, 2929, 2866, 1712, 1529, 1239, 1065; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 4.4 Hz, 4H), 7.32 – 7.27 (m, 9H), 7.26 (d, *J* = 1.6 Hz, 2H), 5.13 – 5.06 (m, 3H), 4.99 (s, 1H), 4.89 (s, 1H), 4.68 (d, *J* = 11.9 Hz, 1H), 4.60 (d, *J* = 11.6 Hz, 1H), 4.51 (d, *J* = 11.6 Hz, 1H), 4.42 (d, *J* = 11.9 Hz, 1H), 4.22 (dd, *J* = 6.3, 4.4 Hz, 1H), 3.92 (dt, *J* = 6.4, 1.2 Hz, 1H), 3.77 – 3.62 (m, 3H), 3.60 (q, *J* = 4.9 Hz, 1H), 3.43 (dt, *J* = 9.8, 6.2 Hz, 1H), 3.15 (q, *J* = 6.7 Hz, 2H), 2.70 (dt, *J* = 6.0, 2.8 Hz, 2H), 2.51 (dd, *J* = 6.7, 5.0 Hz, 2H), 2.32 (s, 1H), 2.16 (s, 3H), 1.63 – 1.53 (m, 2H), 1.51 – 1.43 (m, 2H), 1.38 – 1.29 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.4, 171.9, 156.5, 138.2, 137.5, 136.8, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.2, 128.2, 128.2, 128.1, 128.0, 127.9, 105.9, 83.0, 82.9, 81.7, 78.0, 73.0, 72.3, 67.3, 66.6, 62.3, 41.0, 37.8, 29.9, 29.9, 29.2, 27.9, 26.4, 25.7; HRMS (ESI-MS): m/z calcd. For $C_{39}H_{49}NO_{10}$ $[M+Na]^+$: 714.3253; Found: 714.3254.

***N*-benzyloxycarbonyl-6-aminohexanyl 2-*O*-(4-oxopentanoyl)-3,5-di-*O*-benzyl-6-*O*-(2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranoside (25)**: To a solution of acceptor **9** (463.21 mg, 669.55 µmol) and glycosyl carbonate donor **8** (500 mg, 669.55 µmol) in anhydrous

CH_2Cl_2 (4 mL) was added freshly activated 4Å MS powder (0.100 g) at 25 ºC under nitrogen atmosphere. After 15 min of vigorous stirring at 25 ºC, chloro[tris(2,4-di-tertbutylphenyl) phosphite] gold(I) (**27**) (47.10 mg, 53.56 µmol) and AgOTf (13.76 mg, 53.56 µmol) were added simultaneously to the reaction mixture and stirred for 15 minutes. After completion the reaction mixture was quenched by adding Et_3N (200 µL) and filtered off through a bed of Celite® and the filtrate was concentrated in vacuo, the obtained crude was purified by silica gel column chromatography using EtOAc and Hexane as mobile phase to furnish desired disaccharide **25** (730 mg, 86% yield). $[\alpha]_D^{25}$ = -18.9 (c = 0.36, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3064, 2930, 1721, 1452, 1262, 1108, 1026; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 8.02 (m, 4H), 7.98 – 7.94 (m, 2H), 7.91 – 7.87 (m, 2H), 7.54 – 7.46 (m, 4H), 7.37 – 7.27 (m, 18H), 7.24 (d, *J* = 3.2 Hz, 5H), 6.08 (dt, *J* = 7.7, 3.9 Hz, 1H), 5.67 (d, *J* = 5.0 Hz, 1H), 5.49 (s, 1H), 5.36 (s, 1H), 5.08 (s, 3H), 5.00 (s, 1H), 4.94 (s, 1H), 4.79 – 4.73 (m, 2H), 4.72 – 4.63 (m, 3H), 4.39 (dd, *J* = 11.7, 5.2 Hz, 2H), 4.24 (dd, *J* = 6.1, 2.1 Hz, 1H), 4.03 – 3.93 (m, 2H), 3.79 (d, *J* = 6.2 Hz, 2H), 3.61 (dd, *J* = 11.4, 4.9 Hz, 1H), 3.39 (dd, *J* = 11.2, 4.9 Hz, 1H), 3.11 (q, *J* = 6.8 Hz, 2H), 2.67 (td, *J* = 6.5, 3.9 Hz, 2H), 2.53 – 2.43 (m, 2H), 2.15 (s, 3H), 1.48 – 1.38 (m, 4H), 1.30 (d, *J* = 2.7 Hz, 1H), 1.25 – 1.17 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.4, 172.0, 166.2, 165.8, 165.8, 165.5, 156.5, 138.2, 137.8, 136.9, 133.6, 133.5, 133.4, 133.2, 130.1, 130.1, 130.1, 130.1, 129.9, 129.9, 129.8, 129.8, 129.6, 129.5, 129.0, 128.9, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.2, 128.2, 128.1, 127.9, 127.8, 106.0, 105.9, 82.6, 82.2, 82.0, 81.9, 81.6, 77.5, 76.2, 73.9, 72.2, 70.3, 67.6, 67.4, 66.5, 63.8, 41.0, 37.8, 29.9, 29.8, 29.2, 27.9, 26.4, 25.8; HRMS (ESI-MS): m/z calcd. For $C_{73}H_{75}NO_{19}$ $[M+Na]^+$: 1292.4831; Found: 1292.4827.

***N*-benzyloxycarbonyl-6-aminohexanyl 3,5-di-*O*-benzyl-6-*O*-(2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranoside (7):** To a solution of C2-Lev compound **25** (500 mg, 393.58 µmol) in CH_2Cl_2 (4 mL), a buffer solution of py/AcOH (27:22) (1.5 mL) and 70% hydrazine hydrate (95.65 µL, 1.97 mmol) were added and the reaction mixture was stirred at 25 °C for 1 h. After completion, the reaction was quenched by the addition of acetone (200 µL) and the reaction mixture was extracted with CH_2Cl_2 (30 mL). The organic layer was washed with 1N HCl (2x25 mL), saturated $NaHCO_3$ solution (2x25 mL) and brine (25 mL), dried over Na_2SO_4 and concentrated in vacuo and the crude residue was purified by silica gel column chromatography to achieve the desired product **7** (411 mg, 89% yield). $[\alpha]_D^{25}$ = -45.3 (c = 0.34, $CHCl_3$); IR (cm^{-1},

$CHCl_3$): 3401, 2932, 1720, 1602, 1452, 1259, 1095, 1025; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 8.06 (m, 2H), 8.03 – 8.00 (m, 2H), 7.99 – 7.95 (m, 2H), 7.92 – 7.87 (m, 2H), 7.54 – 7.44 (m, 4H), 7.36 – 7.26 (m, 23H), 6.08 (dt, *J* = 7.5, 3.9 Hz, 1H), 5.68 (d, *J* = 5.1 Hz, 1H), 5.45 (d, *J* = 1.2 Hz, 1H), 5.34 (s, 1H), 5.08 (s, 2H), 4.93 (s, 1H), 4.77 (dt, *J* = 7.1, 3.1 Hz, 4H), 4.72 (dd, *J* = 5.2, 3.3 Hz, 1H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.49 (d, *J* = 11.2 Hz, 1H), 4.41 (d, *J* = 12.0 Hz, 1H), 4.33 (dd, *J* = 3.2, 2.0 Hz, 1H), 4.11 – 4.02 (m, 2H), 3.82 – 3.76 (m, 2H), 3.73 (td, *J* = 6.2, 2.0 Hz, 1H), 3.58 (dt, *J* = 9.6, 6.6 Hz, 1H), 3.38 – 3.26 (m, 2H), 3.08 (q, *J* = 6.8 Hz, 2H), 1.42 – 1.33 (m, 4H), 1.23 – 1.14 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 165.9, 165.8, 165.6, 156.5, 138.0, 136.9, 136.8, 133.6, 133.6, 133.4, 133.3, 130.1, 130.1, 130.0, 130.0, 130.0, 130.0, 129.8, 129.8, 129.6, 129.5, 128.9, 128.9, 128.9, 128.9, 128.7, 128.7, 128.7, 128.7, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.2, 128.1, 128.1, 128.1, 127.9, 109.0, 105.6, 85.5, 83.7, 82.1, 81.6, 77.9, 77.5, 76.6, 73.9, 72.1, 70.2, 67.6, 66.6, 66.6, 63.8, 41.0, 29.8, 29.3, 26.5, 25.8; HRMS (ESI-MS): m/z calcd. For $C_{68}H_{69}NO_{17}$ $[M+Na]^+$: 1194.4463; Found: 1194.4459.

***N*-benzyloxycarbonyl-6-aminohexanyl 2-*O*-(2-*O*-(4-oxopentanoyl)-3-*O*-(naphthalen-1-yl methyl)-5-*O*-tert-butyldiphenylsilyl-α-D-arabinofuranosyl)-3,5-di-*O*-benzyl-6-*O*-(2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranoside (28)**: To a solution of acceptor **7** (754.37 mg, 643.50 µmol) and glycosyl carbonate donor **6** (500.0 mg, 643.50 µmol) in anhydrous CH_2Cl_2 (5 mL) was added freshly activated 4Å MS powder (0.200 g) at 25 ºC under nitrogen atmosphere. After 15 min of vigorous stirring at 25 ºC, chloro[tris(2,4-di-tertbutylphenyl) phosphite] gold(I) (**23**) (45.27 mg, 51.48 µmol) and AgOTf (13.23 mg, 51.48 µmol) were added simultaneously to the reaction mixture and stirred for 30 minutes. After completion the reaction mixture was quenched by adding Et_3N (200 µL) and filtered off through a bed of Celite® and the filtrate was concentrated in vacuo, the obtained crude was purified by silica gel column chromatography using EtOAc and Hexane as mobile phase to afford desired trisaccharide **28** (996 mg, 87% yield). $[\alpha]_D^{25}$ = -5.6 (c = 0.16, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3403, 2931, 1723, 1597, 1457, 1361, 1260, 1103; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 7.9, 5.0 Hz, 4H), 7.97 (d, *J* = 7.9 Hz, 2H), 7.89 (d, *J* = 7.9 Hz, 2H), 7.81 – 7.71 (m, 4H), 7.65 (dd, *J* = 16.8, 7.2 Hz, 4H), 7.53 – 7.40 (m, 9H), 7.37 – 7.27 (m, 19H), 7.21 (t, *J* = 7.2 Hz, 4H), 7.17 – 7.11 (m, 4H), 6.09 (s, 1H), 5.64 (d, *J* = 4.9 Hz, 1H), 5.48 (s, 1H), 5.32 (d, *J* = 14.0 Hz, 2H), 5.19 (s, 1H), 5.09 (s, 3H), 4.98 – 4.87 (m, 2H), 4.78 – 4.70 (m, 3H), 4.69 – 4.61 (m, 3H), 4.48 (d, *J* = 11.9 Hz, 1H), 4.37 – 4.27 (m, 3H), 4.19

(dd, *J* = 7.6, 2.8 Hz, 1H), 4.14 – 4.06 (m, 2H), 3.99 (dd, *J* = 10.1, 4.6 Hz, 1H), 3.80 (t, *J* = 6.6 Hz, 3H), 3.76 – 3.65 (m, 2H), 3.46 – 3.37 (m, 1H), 3.17 – 3.06 (m, 2H), 2.67 (td, *J* = 6.4, 3.0 Hz, 2H), 2.48 (dt, *J* = 12.9, 6.4 Hz, 2H), 2.14 (s, 3H), 1.56 – 1.49 (m, 2H), 1.45 – 1.39 (m, 2H), 1.29 – 1.20 (m, 4H), 1.01 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.2, 171.8, 166.2, 165.8, 165.8, 165.4, 156.5, 138.3, 137.9, 136.9, 135.7, 135.7, 135.7, 135.7, 135.2, 133.5, 133.4, 133.4, 133.3, 133.3, 133.3, 133.1, 133.1, 130.1, 130.1, 130.0, 130.0, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.6, 129.5, 129.0, 129.0, 129.0, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 126.9, 126.1, 126.0, 126.0, 105.9, 105.9, 105.1, 84.5, 84.5, 83.2, 82.0, 82.0, 81.9, 81.7, 80.3, 77.6, 76.0, 73.6, 72.4, 71.9, 70.4, 67.7, 67.5, 66.5, 63.9, 63.4, 41.1, 37.8, 29.8, 29.8, 29.4, 27.9, 26.8, 26.8, 26.8, 26.5, 25.9, 19.4; HRMS (ESI-MS): m/z calcd. For $C_{105}H_{109}NO_{23}Si$ $[M+H]^+$: 1780.7238; Found: 1780.7283.

***N*-benzyloxycarbonyl-6-aminohexanyl 2-*O*-(3-*O*-(naphthalen-1-yl methyl)-5-*O*-tert-butyldiphenylsilyl-α-D-arabinofuranosyl)-3,5-di-*O*-benzyl-6-*O*-(2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranoside (5):** Compound **28** (500 mg, 280.73 µmol) was dissolved in anhydrous CH_2Cl_2 (4 mL). A buffer solution of py/AcOH (27:22 mmol) (1 mL) and 70% hydrazine hydrate (97.46 µL, 1.40 mmol) were added and the reaction mixture was stirred at 25 °C for 1 h. After completion, the reaction was quenched by the addition of acetone (500 µL) and the reaction mixture was extracted with CH_2Cl_2 (25 mL). The organic layer was washed with 1N HCl (2x25 mL), saturated $NaHCO_3$ solution (2x25 mL) and brine (25 mL), dried over Na_2SO_4 and concentrated in vacuo and the crude residue was purified by silica gel column chromatography to achieve the desired product **5** (421 mg, 89% yield)**.** $[\alpha]_D^{25}$ = -12.4 (c = 0.11, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3408, 2929, 1723, 1453, 1262, 1107, 1069, 822; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 8.04 (m, 4H), 8.02 – 7.96 (m, 2H), 7.93 – 7.87 (m, 2H), 7.82 – 7.77 (m, 1H), 7.76 – 7.68 (m, 5H), 7.63 – 7.58 (m, 2H), 7.52 – 7.34 (m, 19H), 7.33 – 7.28 (m, 9H), 7.23 – 7.14 (m, 8H), 6.12 (td, *J* = 6.2, 5.7, 3.3 Hz, 1H), 5.64 (d, *J* = 5.0 Hz, 1H), 5.49 (d, *J* = 1.1 Hz, 1H), 5.33 (s, 1H), 5.24 (s, 1H), 5.16 – 5.07 (m, 3H), 4.96 (s, 1H), 4.91 – 4.86 (m, 1H), 4.79 – 4.74 (m, 2H), 4.73 – 4.66 (m, 3H), 4.64 (d, *J* = 11.8 Hz, 1H), 4.50 (d, *J* = 11.8 Hz, 1H), 4.42 – 4.36 (m, 2H), 4.34 (d, *J* = 11.8 Hz, 1H), 4.28 (q, *J* = 2.8 Hz, 1H), 4.22 (dd, *J* = 7.5, 2.9 Hz, 1H), 4.12 (dd, *J* = 7.4, 3.9 Hz, 2H), 4.00 (dd, *J* = 10.0, 4.8 Hz, 1H), 3.87 (dd, *J* = 11.2, 2.7 Hz, 1H), 3.82 (ddd, *J* = 7.7, 4.7, 2.9 Hz, 1H), 3.76 – 3.64 (m, 4H), 3.44 (dt, *J* = 9.7, 6.5 Hz, 1H), 3.14 (q, *J* = 6.7 Hz, 2H), 1.56 (q, *J* = 7.0 Hz,

2H), 1.48 – 1.41 (m, 2H), 1.37 – 1.33 (m, 2H), 1.25 (d, *J* = 7.1 Hz, 2H), 1.04 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 165.8, 165.7, 165.4, 156.5, 138.3, 138.0, 136.8, 135.7, 135.7, 135.6, 135.6, 135.3, 133.5, 133.4, 133.3, 133.3, 133.2, 133.1, 132.4, 132.4, 130.1, 130.1, 130.1, 130.1, 130.0, 130.0, 130.0, 129.9, 129.9, 129.8, 129.8, 129.6, 129.5, 129.0, 129.0, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.7, 127.7, 127.6, 126.6, 126.2, 126.0, 125.8, 107.7, 106.2, 105.8, 85.0, 84.9, 84.5, 81.9, 81.7, 81.6, 80.2, 78.1, 77.6, 76.0, 73.5, 72.2, 71.8, 70.3, 67.8, 67.5, 66.6, 64.3, 63.9, 41.0, 29.8, 29.3, 26.8, 26.8, 26.8, 26.4, 25.8, 19.2; HRMS (ESI-MS): m/z calcd. For $C_{100}H_{103}NO_{21}Si$ $[M+Na]^+$: 1704.6690; Found: 1704.6630.

***N*-benzyloxycarbonyl-6-aminohexanyl 2-*O*-(3-*O*-(naphthalen-1-yl methyl)-5-*O*-tert-butyldiphenylsilyl-α-D-ribofuranosyl)-3,5-di-*O*-benzyl-6-*O*-(2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranoside (29)**: To a solution of alcohol **5** (500 mg, 297.09 µmol) in anhydrous CH_2Cl_2 (5 mL), pyridiniumdichromoate (78.24 mg, 207.96 µmol) and Ac_2O (98.29 µL, 1.04 mmol) were added, the reaction was heated at 55 °C for 3 h under nitrogen atmosphere. After completion of the starting material indicated by TLC, the reaction mixture was quickly passed through a bed of silica gel using ethyl acetate as the mobile phase, the organic solvent was evaporated in vacuo to obtain corresponding crude 2-ulose derivative which was directly carried forward to the next step without purification. The crude product was dissolved in a mixture of solvents EtOH/EtOAc (2:1) [5 mL] and the mixture was cooled to 0 °C. $NaBH_4$ (14.63 mg, 386.68 µmol) was added portion-wise to the reaction mixture at 0 °C and was stirred at 25 °C for 2 h. After completion of the reaction, it was quenched with Acetone (200 µL) and the solvents were evaporated in vacuo. The crude residue was purified by silica gel column chromatography using ethyl acetate and hexane as mobile phase to obtain the epimerized compound **29** (366 mg, 73% yield). $[\alpha]_D^{25}$ = +3.1 (c = 0.13, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3407, 2927, 1724, 1456, 1261, 1189, 1104, 823; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (td, *J* = 8.4, 1.4 Hz, 4H), 7.98 – 7.94 (m, 2H), 7.87 – 7.83 (m, 2H), 7.77 – 7.67 (m, 4H), 7.65 – 7.59 (m, 2H), 7.57 – 7.53 (m, 2H), 7.51 – 7.27 (m, 26H), 7.25 – 7.12 (m, 10H), 6.07 (td, *J* = 5.7, 3.4 Hz, 1H), 5.61 (d, *J* = 5.1 Hz, 1H), 5.44 (d, *J* = 1.2 Hz, 1H), 5.25 (d, *J* = 12.0 Hz, 1H), 5.15 (d, *J* = 4.6 Hz, 1H), 5.08 (s, 2H), 5.04 (d, *J* = 1.9 Hz, 1H), 4.90 – 4.78 (m, 2H), 4.73 (d, *J* = 5.7 Hz, 2H), 4.71 – 4.65 (m, 2H), 4.65 – 4.58 (m, 2H), 4.44 (d, *J* = 11.8 Hz, 1H), 4.38 – 4.31 (m, 2H), 4.26 – 4.21 (m, 1H), 4.18 (dd, *J* = 7.4, 2.9 Hz, 2H), 4.09 (dd, *J* = 7.3, 3.9 Hz, 1H), 4.04 (dd, *J* = 6.9, 2.3 Hz, 1H), 3.96 (dd, *J* = 10.0, 4.7 Hz, 1H), 3.77 (tt,

J = 4.6, 2.7 Hz, 1H), 3.71 – 3.55 (m, 4H), 3.43 – 3.36 (m, 1H), 3.20 – 3.06 (m, 3H), 1.55 – 1.48 (m, 2H), 1.44 – 1.39 (m, 2H), 1.33 – 1.29 (m, 2H), 1.26 – 1.21 (m, 2H), 1.00 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 165.9, 165.8, 165.4, 156.5, 138.3, 138.0, 136.9, 135.7, 135.7, 135.6, 135.6, 135.4, 133.5, 133.4, 133.3, 133.3, 133.2, 133.1, 133.1, 133.1, 130.1, 130.1, 130.1, 130.1, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.7, 129.6, 129.1, 129.0, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 126.7, 126.3, 126.1, 125.8, 106.4, 105.9, 101.0, 85.3, 84.4, 82.0, 81.8, 81.7, 80.5, 77.6, 76.9, 76.1, 73.5, 73.3, 72.6, 71.9, 70.4, 67.9, 67.6, 66.6, 64.2, 63.8, 41.1, 29.8, 29.5, 26.9, 26.9, 26.9, 26.6, 25.9, 19.3; HRMS (ESI-MS): m/z calcd. For $C_{100}H_{103}NO_{21}Si$ $[M+Na]^+$: 1704.6690; Found: 1704.6669.

***N*-benzyloxycarbonyl-6-aminohexanyl 2-*O*-(5-*O*-tert-butyldiphenylsilyl-α-D-ribofuranosyl)-3,5-di-*O*-benzyl-6-*O*-(2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranoside (4)**: Compound **29** (200 mg, 118.84 µmol) was dissolved in a mixture of solvents of CH_2Cl_2/ MeOH (1:3) (2 mL). DDQ (53.95 mg, 237.67 µmol) was added to the reaction mixture and it was stirred for 4 h at 25 °C. After the completion of the reaction as indicated by TLC, the reaction was quenched by Et_3N (200 µL) and the solvent was evaporated under reduced pressure. The crude residue was purified by silica gel column chromatography using ethyl acetate and hexane as mobile phase to obtain desired acceptor **4** (140mg, 76% yield). $[\alpha]_D^{25}$ = +18.7 (c = 0.12, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3404, 2930, 1724, 1456, 1262, 1109, 823; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 – 8.05 (m, 2H), 8.03 – 8.00 (m, 2H), 7.98 – 7.94 (m, 2H), 7.88 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.66 (ddd, *J* = 7.6, 5.6, 1.6 Hz, 4H), 7.53 – 7.47 (m, 4H), 7.42 – 7.27 (m, 21H), 7.25 – 7.19 (m, 8H), 6.07 (dt, *J* = 7.6, 3.9 Hz, 1H), 5.64 (d, *J* = 5.0 Hz, 1H), 5.47 (d, *J* = 1.2 Hz, 1H), 5.32 (s, 1H), 5.18 (d, *J* = 4.4 Hz, 1H), 5.07 (s, 2H), 5.00 (s, 1H), 4.84 (s, 1H), 4.76 – 4.70 (m, 2H), 4.69 – 4.62 (m, 3H), 4.48 (d, *J* = 11.7 Hz, 1H), 4.39 (d, *J* = 11.9 Hz, 1H), 4.32 – 4.29 (m, 1H), 4.19 (td, *J* = 6.6, 3.6 Hz, 2H), 4.13 (dd, *J* = 6.3, 2.9 Hz, 1H), 4.04 (td, *J* = 5.7, 2.6 Hz, 2H), 3.98 (dd, *J* = 10.0, 4.6 Hz, 1H), 3.83 – 3.79 (m, 1H), 3.76 – 3.71 (m, 3H), 3.66 – 3.61 (m, 1H), 3.37 (dt, *J* = 10.7, 6.6 Hz, 1H), 3.11 (q, *J* = 6.7 Hz, 3H), 2.57 (s, 1H), 1.49 (t, *J* = 7.1 Hz, 2H), 1.43 – 1.38 (m, 2H), 1.30 (d, *J* = 8.4 Hz, 2H), 1.24 – 1.20 (m, 2H), 1.04 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 165.8, 165.7, 165.4, 156.4, 138.0, 137.9, 136.7, 135.6, 135.6, 135.5, 135.5, 133.5, 133.4, 133.3, 133.1, 133.1, 133.0, 130.0, 130.0, 130.0, 130.0, 129.8, 129.8, 129.8, 129.7, 129.7, 129.5, 129.4, 128.9, 128.9, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3,

128.3, 128.3, 128.3, 128.1, 128.0, 128.0, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 106.3, 105.9, 102.1, 86.1, 85.9, 82.8, 81.9, 81.5, 81.5, 77.5, 76.1, 73.5, 72.3, 71.8, 71.0, 70.2, 67.6, 67.5, 66.5, 64.0, 63.8, 41.0, 29.8, 29.3, 26.8, 26.8, 26.8, 26.4, 25.8, 19.2; HRMS (ESI-MS): m/z calcd. For $C_{89}H_{95}NO_{21}Si$ $[M+Na]^+$: 1564.6063; Found: 1564.6078.

***N*-benzyloxycarbonyl-6-aminohexanyl 2-*O*-(3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-5-*O*-tert-butyldiphenylsilyl-α-D-ribofuranosyl)-3,5-di-*O*-benzyl-6-*O*-(2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranoside (30)**: Acceptor **4** (66mg, 42.78 µmol) was dissolved in anhydrous CH_2Cl_2 (400 µL). Freshly activated 4Å MS powder (30 mg) was added to the solution and stirred for 20 min under nitrogen atmosphere. AgOTf (2.64 mg, 10.27 µmol) and chloro[tris(2,4-di-tertbutylphenyl) phosphite] gold(I) (**27**) (9.03 mg, 10.27 µmol) were added to the solution at 25 °C. Donor **3** (95.84 mg, 128.34 µmol) was dissolved in anhydrous CH_2Cl_2 (400 µL) and added dropwise to the reaction mixture and it was further stirred for 1 h at 25 °C. After the completion of the donor as indicated by the TLC, the reaction was quenched by Et_3N (50 µL), MS powder was filtered off using a bed of celite. The filtrate was concentrated in vacuo and the resultant crude mixture was purified by silica gel column chromatography using ethyl acetate and hexane as mobile phase to furnish tetratasaccharide **30** (71 mg, 78% yield). $[\alpha]_D^{25}$ = +1.8 (c = 0.06, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3067, 2926, 1725, 1452, 1264, 1108, 1069, 1027; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 – 8.01 (m, 6H), 7.99 – 7.97 (m, 2H), 7.95 – 7.94 (m, 2H), 7.91 – 7.86 (m, 5H), 7.80 – 7.75 (m, 4H), 7.59 (ddd, *J* = 8.2, 5.4, 1.5 Hz, 4H), 7.49 – 7.46 (m, 5H), 7.43 – 7.36 (m, 10H), 7.34 – 7.30 (m, 17H), 7.23 – 7.16 (m, 10H), 6.07 (q, *J* = 2.3 Hz, 1H), 5.84 (t, *J* = 9.6 Hz, 1H), 5.61 (d, *J* = 5.2 Hz, 1H), 5.56 (t, *J* = 9.7 Hz, 1H), 5.49 – 5.45 (m, 2H), 5.33 (s, 1H), 5.06 (d, *J* = 5.1 Hz, 3H), 4.95 (d, *J* = 2.2 Hz, 1H), 4.82 (d, *J* = 8.0 Hz, 1H), 4.72 (d, *J* = 5.8 Hz, 2H), 4.65 – 4.62 (m, 2H), 4.61 (d, *J* = 4.8 Hz, 1H), 4.59 (d, *J* = 3.3 Hz, 1H), 4.55 (d, *J* = 1.9 Hz, 1H), 4.53 (d, *J* = 2.0 Hz, 1H), 4.42 – 4.39 (m, 1H), 4.28 (d, *J* = 11.6 Hz, 1H), 4.25 (dd, *J* = 4.2, 2.0 Hz, 1H), 4.22 (dd, *J* = 6.7, 2.7 Hz, 1H), 4.13 – 4.11 (m, 2H), 4.07 (dt, *J* = 7.8, 3.5 Hz, 2H), 4.00 (q, *J* = 2.9 Hz, 1H), 3.93 (dd, *J* = 10.3, 5.0 Hz, 1H), 3.78 (ddd, *J* = 7.9, 4.9, 3.2 Hz, 1H), 3.72 – 3.69 (m, 1H), 3.61 (dq, *J* = 9.8, 6.6, 6.1 Hz, 2H), 3.54 (dd, *J* = 11.3, 3.8 Hz, 1H), 3.43 (dd, *J* = 11.3, 2.8 Hz, 1H), 3.32 (td, *J* = 6.5, 2.3 Hz, 1H), 3.08 (d, *J* = 6.7 Hz, 2H), 1.47 – 1.45 (m, 2H), 1.39 – 1.36 (m, 2H), 1.23 – 1.19 (m, 4H), 1.03 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.3, 166.2, 165.9, 165.9, 165.8, 165.5, 165.3, 164.8, 156.5, 138.5, 138.2, 136.9, 135.7, 135.7, 135.7, 135.7, 133.6, 133.5, 133.4, 133.4, 133.4, 133.3, 133.2, 133.2, 133.0, 130.2, 130.1,

130.1, 130.1, 130.1, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.7, 129.7, 129.6, 129.6, 129.1, 129.1, 129.0, 128.9, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 106.5, 106.0, 102.2, 101.0, 86.2, 84.2, 82.0, 81.8, 80.1, 80.1, 77.7, 76.4, 73.7, 72.9, 72.8, 72.2, 71.9, 71.8, 70.4, 69.8, 67.8, 67.5, 66.6, 63.9, 63.6, 63.3, 60.6, 41.1, 29.8, 29.5, 27.0, 27.0, 27.0, 26.6, 25.9, 19.4; HRMS (ESI-MS): m/z calcd. For $C_{123}H_{121}NO_{30}Si$ $[M+Na]^+$: 2142.7640; Found: 2142.7903.

***N*-benzyloxycarbonyl-6-aminohexanyl 2-*O*-(2-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-3-*O*-(naphthalen-1-yl methyl)-5-*O*-tert-butyldiphenylsilyl-α-D-ribofuranosyl)-3,5-di-*O*-benzyl-6-*O*-(2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranoside (31)**: Acceptor **29** (100 mg, 59.42 µmol) was dissolved in anhydrous CH_2Cl_2 (600 µL). Freshly activated 4Å MS powder (30 mg) was added to the solution and stirred for 20 min under nitrogen atmosphere. AgOTf (3.05 mg, 11.88 µmol) and chloro[tris(2,4-di-tertbutylphenyl) phosphite] gold(I) (**27**) (10.45 mg, 11.88 µmol) were added to the solution at 25 °C. Donor **3** (88.74 mg, 118.84 µmol) was dissolved in anhydrous CH_2Cl_2 (300 µL) and added dropwise to the reaction mixture and it was further stirred for 1 h at 25 °C. After the completion of the donor as indicated by the TLC, the reaction was quenched by Et_3N (50 µL), MS powder was filtered off using a bed of celite. The filtrate was concentrated in vacuo and the resultant crude mixture was purified by silica gel column chromatography using ethyl acetate and hexane as mobile phase to furnish the tetrasaccharide **31** (112 mg, 83% yield). $[\alpha]_D^{25}$ = +3.8 (c = 0.08, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2926, 2856, 1723, 1452, 1263, 1107, 1026, 823; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 – 8.03 (m, 4H), 7.97 (t, *J* = 1.6 Hz, 2H), 7.95 – 7.94 (m, 2H), 7.93 – 7.89 (m, 4H), 7.88 – 7.84 (m, 4H), 7.63 – 7.60 (m, 2H), 7.55 (d, *J* = 5.7 Hz, 2H), 7.51 (d, *J* = 6.4 Hz, 4H), 7.49 – 7.44 (m, 7H), 7.43 – 7.38 (m, 8H), 7.35 – 7.27 (m, 27H), 7.19 – 7.16 (m, 6H), 6.05 (dt, *J* = 7.4, 3.8 Hz, 1H), 5.97 (t, *J* = 9.7 Hz, 1H), 5.81 – 5.75 (m, 1H), 5.68 (t, *J* = 9.7 Hz, 1H), 5.61 (d, *J* = 5.1 Hz, 1H), 5.46 (d, *J* = 1.1 Hz, 1H), 5.34 – 5.29 (m, 2H), 5.14 (d, *J* = 1.7 Hz, 1H), 5.11 – 5.03 (m, 4H), 4.97 (d, *J* = 6.1 Hz, 1H), 4.76 (d, *J* = 12.7 Hz, 2H), 4.71 (dd, *J* = 7.2, 3.2 Hz, 2H), 4.67 (d, *J* = 5.5 Hz, 1H), 4.63 – 4.59 (m, 4H), 4.51 (d, *J* = 6.2 Hz, 1H), 4.40 (q, *J* = 1.9 Hz, 1H), 4.38 – 4.36 (m, 1H), 4.34 (d, *J* = 2.4 Hz, 1H), 4.22 – 4.20 (m, 1H), 4.17 – 4.14 (m, 2H), 4.07 – 4.05 (m, 1H), 3.92 (dd, *J* = 10.5, 4.0 Hz, 1H), 3.80 (q, *J* = 3.9 Hz, 1H), 3.70 – 3.67 (m, 1H), 3.65 (d, *J* = 5.6 Hz,

1H), 3.63 – 3.60 (m, 1H), 3.57 (dd, *J* = 11.2, 3.0 Hz, 1H), 3.39 – 3.33 (m, 1H), 3.09 (d, *J* = 6.3 Hz, 2H), 1.53 – 1.48 (m, 2H), 1.41 – 1.37 (m, 2H), 1.26 – 1.20 (m, 4H), 1.00 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 166.1, 166.0, 165.8, 165.8, 165.3, 165.3, 165.0, 156.5, 138.7, 138.2, 138.0, 136.9, 135.9, 135.7, 135.7, 135.6, 135.5, 135.5, 133.6, 133.5, 133.4, 133.3, 133.3, 133.2, 133.1, 133.1, 133.1, 133.0, 132.9, 130.1, 130.1, 130.1, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.7, 129.6, 129.3, 129.3, 129.1, 129.1, 128.9, 128.8, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.9, 127.9, 127.8, 127.7, 127.5, 127.5, 126.2, 126.0, 125.9, 125.7, 106.4, 106.0, 101.8, 101.4, 86.0, 84.3, 82.4, 82.0, 81.6, 80.4, 80.0, 77.7, 77.4, 75.9, 73.5, 73.1, 73.1, 72.9, 71.8, 71.7, 70.4, 69.9, 67.9, 67.4, 66.5, 64.2, 63.9, 63.6, 41.1, 29.8, 29.7, 26.9, 26.9, 26.9, 26.6, 25.9, 19.3; HRMS (ESI-MS): m/z calcd. For $C_{134}H_{129}NO_{30}Si$ $[M+H]^+$: 2260.8447 ; Found: 2260.8540.

***N*-benzyloxycarbonyl-6-aminohexanyl 2-*O*-(2-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-5-*O*-tert-butyldiphenylsilyl-α-D-ribofuranosyl)-3,5-di-*O*-benzyl-6-*O*-(2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranoside (32)**: Compound **31** (100 mg, 44.22 µmol) was dissolved in a mixture of solvents of CH_2Cl_2/ MeOH (1:3) (1 mL). DDQ (20.07 mg, 88.43 µmol) was added to the reaction mixture and it was stirred for 4 h at 25 °C. After the completion of the reaction as indicated by TLC, the reaction was quenched by Et_3N (200 µL) and the solvent was evaporated under reduced pressure. The crude residue was purified by silica gel column chromatography using ethyl acetate and hexane as mobile phase to furnish the tetrasaccharide acceptor **32** (71 mg, 76% yield). $[\alpha]_D^{25}$ = +2.9 (c = 0.10, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 3064, 2926, 2861, 1725, 1456, 1261, 1103, 824; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.99 (m, 6H), 7.98 – 7.94 (m, 5H), 7.90 – 7.87 (m, 3H), 7.86 (d, *J* = 1.5 Hz, 1H), 7.84 – 7.82 (m, 2H), 7.65 (ddd, *J* = 8.0, 5.2, 1.6 Hz, 4H), 7.52 – 7.44 (m, 8H), 7.42 – 7.37 (m, 7H), 7.35 – 7.29 (m, 18H), 7.28 – 7.27 (m, 3H), 7.25 – 7.24 (m, 2H), 7.20 – 7.13 (m, 8H), 6.07 (td, *J* = 5.7, 3.4 Hz, 1H), 5.96 (t, *J* = 9.7 Hz, 1H), 5.72 (t, *J* = 9.7 Hz, 1H), 5.66 – 5.59 (m, 2H), 5.45 (d, *J* = 1.2 Hz, 1H), 5.31 – 5.26 (m, 2H), 5.10 (d, *J* = 7.9 Hz, 1H), 5.06 (s, 2H), 4.96 (s, 1H), 4.72 (d, *J* = 5.7 Hz, 2H), 4.63 – 4.62 (m, 1H), 4.61 (d, *J* = 2.4 Hz, 1H), 4.57 (d, *J* = 2.9 Hz, 1H), 4.54 (s, 1H), 4.50 (d, *J* = 5.0 Hz, 1H), 4.42 (dd, *J* = 5.8, 4.1 Hz, 1H), 4.24 (s, 1H), 4.23 – 4.14 (m, 3H), 4.10 (q, *J* = 3.8 Hz, 2H), 3.92 (dd, *J* = 7.0, 3.0 Hz, 1H), 3.83 (dd, *J* = 10.3, 4.2 Hz, 1H), 3.72 (dq, *J* = 13.1, 3.5, 3.1

Hz, 3H), 3.65 – 3.57 (m, 2H), 3.33 (q, *J* = 7.3, 6.8 Hz, 1H), 3.12 – 3.06 (m, 2H), 2.79 (s, 1H), 1.51 – 1.45 (m, 2H), 1.41 – 1.37 (m, 2H), 1.25 – 1.18 (m, 4H), 1.05 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 166.2, 165.9, 165.9, 165.8, 165.4, 165.3, 165.3, 156.5, 138.5, 138.1, 136.9, 135.7, 135.7, 135.7, 135.7, 133.6, 133.5, 133.4, 133.4, 133.4, 133.3, 133.3, 133.2, 133.1, 132.9, 130.1, 130.1, 130.1, 130.1, 130.1, 130.0, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.7, 129.6, 129.5, 129.3, 129.1, 129.1, 128.9, 128.9, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 128.0, 128.0, 127.9, 127.9, 127.7, 127.7, 106.5, 106.1, 102.8, 100.4, 87.4, 87.3, 83.2, 82.0, 81.7, 81.1, 77.7, 77.2, 76.7, 73.4, 72.8, 72.7, 72.0, 71.7, 70.4, 69.8, 69.7, 67.8, 67.5, 66.6, 64.2, 64.0, 63.1, 41.1, 29.8, 29.6, 26.9, 26.9, 26.9, 26.6, 26.0, 19.4; HRMS (ESI-MS): m/z calcd. For $C_{123}H_{121}NO_{30}Si$ $[M+H]^+$: 2120.7821; Found: 2120.7908.

***N*-benzyloxycarbonyl-6-aminohexanyl 2-*O*-(2,3-di-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-5-*O*-tert-butyldiphenylsilyl-α-D-ribofuranosyl)-3,5-di-*O*-benzyl-6-*O*-(2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranoside (2)**: Acceptor **32** (100 mg, 47.14 µmol) was dissolved in anhydrous CH_2Cl_2 (600 µL). Freshly activated 4Å MS powder (30 mg) was added to the solution and stirred for 20 min under nitrogen atmosphere. AgOTf (2.42 mg, 9.43 µmol) and chloro[tris(2,4-di-tertbutylphenyl) phosphite] gold(I) (**27**) (8.29 mg, 9.43 µmol) were added to the solution at 25 °C. Donor **3** (70.40 mg, 94.28 µmol) was dissolved in anhydrous CH_2Cl_2 (300 µL) and added dropwise to the reaction mixture and it was further stirred for 1 h at 25 °C. After the completion of the donor as indicated by the TLC, the reaction was quenched by Et_3N (50 µL), MS powder was filtered off using a bed of celite. The filtrate was concentrated in vacuo and the resultant crude mixture was purified by silica gel column chromatography using ethyl acetate and hexane as mobile phase to furnish pentasaccharide **2** (103 mg, 81% yield). $[\alpha]_D^{25}$ = +2.3 (c = 0.04, $CHCl_3$); IR (cm^{-1}, $CHCl_3$): 2928, 1725, 1601, 1451, 1264, 1094, 1026, 824; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 – 8.04 (m, 2H), 8.01 (ddt, *J* = 6.0, 2.9, 1.7 Hz, 6H), 7.95 – 7.91 (m, 8H), 7.88 – 7.83 (m, 5H), 7.81 – 7.77 (m, 2H), 7.73 – 7.70 (m, 2H), 7.63 (ddd, *J* = 7.7, 3.0, 1.5 Hz, 4H), 7.49 – 7.37 (m, 21H), 7.35 – 7.26 (m, 27H), 7.14 – 7.09 (m, 8H), 6.04 (dt, *J* = 7.4, 3.9 Hz, 1H), 5.97 (t, *J* = 9.2 Hz, 1H), 5.72 (td, *J* = 9.6, 5.7 Hz, 2H), 5.60 – 5.55 (m, 2H), 5.44 (q, *J* = 6.2, 5.5 Hz, 2H), 5.33 (s, 1H), 5.28 (d, *J* = 1.6 Hz, 1H), 5.17 (d, *J* = 3.8 Hz, 1H), 5.05 (q, *J* = 2.2 Hz, 3H), 4.90 (s, 1H), 4.85 (d, *J* = 7.9 Hz, 1H), 4.72 (d, *J* = 6.8 Hz, 1H), 4.70

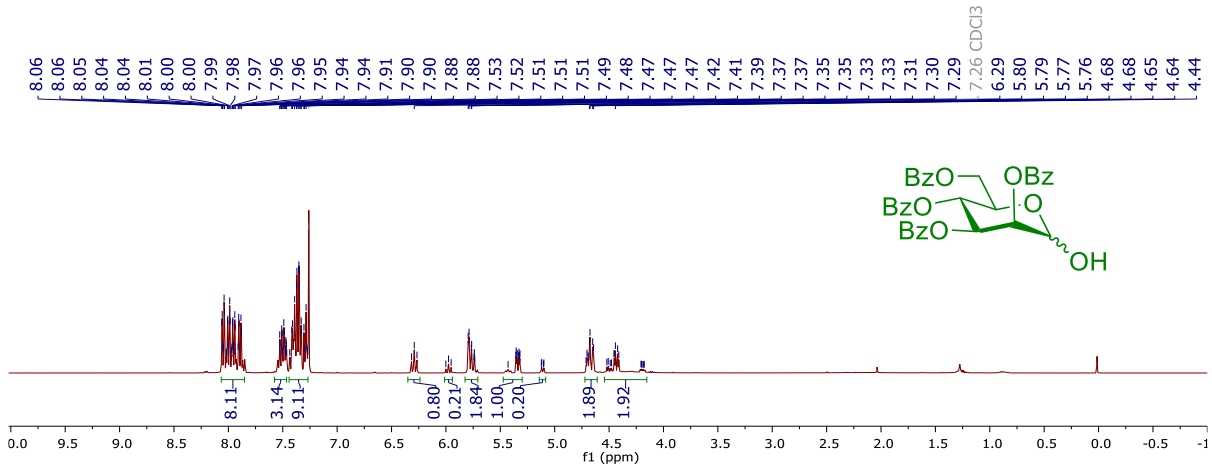
– 4.67 (m, 2H), 4.64 (d, *J* = 5.6 Hz, 1H), 4.61 – 4.58 (m, 2H), 4.55 (d, *J* = 3.3 Hz, 1H), 4.49 – 4.45 (m, 2H), 4.35 (q, *J* = 4.5, 3.4 Hz, 2H), 4.21 – 4.15 (m, 2H), 4.15 – 4.06 (m, 2H), 4.05 (t, *J* = 4.6 Hz, 1H), 4.00 (dt, *J* = 7.9, 3.8 Hz, 2H), 3.94 (dd, *J* = 7.7, 3.8 Hz, 1H), 3.87 (d, *J* = 3.6 Hz, 1H), 3.75 (q, *J* = 5.2, 4.1 Hz, 1H), 3.69 – 3.58 (m, 3H), 3.56 (d, *J* = 3.6 Hz, 2H), 3.42 – 3.34 (m, 1H), 3.06 (d, *J* = 8.3 Hz, 2H), 1.48 (t, *J* = 7.3 Hz, 2H), 1.39 – 1.34 (m, 2H), 1.24 – 1.17 (m, 4H), 1.05 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.2, 166.2, 166.1, 165.9, 165.8, 165.8, 165.8, 165.4, 165.4, 165.4, 165.2, 164.4, 156.5, 139.5, 139.0, 138.3, 137.0, 135.8, 135.8, 135.7, 135.7, 135.7, 133.6, 133.5, 133.5, 133.4, 133.3, 133.3, 133.2, 133.2, 133.2, 133.2, 133.1, 133.0, 130.2, 130.1, 130.1, 130.1, 130.1, 130.1, 130.1, 130.1, 130.1, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.7, 129.7, 129.7, 129.7, 129.6, 129.6, 129.2, 129.2, 129.2, 129.2, 129.1, 129.1, 129.1, 129.1, 129.1, 128.7, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 127.9, 127.5, 127.5, 106.4, 106.2, 101.3, 101.1, 99.4, 87.2, 83.1, 83.0, 82.0, 81.7, 80.5, 77.8, 77.4, 76.6, 74.6, 73.5, 73.1, 73.0, 72.7, 72.2, 72.1, 71.8, 71.8, 70.5, 70.1, 69.9, 67.7, 67.6, 66.5, 64.0, 64.0, 63.5, 63.1, 41.2, 29.7, 29.5, 27.1, 27.1, 27.0, 26.7, 26.0, 19.5; HRMS (ESI-MS): m/z calcd. For $C_{157}H_{147}NO_{39}Si$ $[M+H]^+$: 2698.9398; Found: 2698.9900.

6-aminohexanyl 2-*O*-((2,3-di-*O*-α-D-mannopyranosyl)-α-D-ribofuranosyl)-6-*O*-(β-D-galactofuranosyl)-β-D-galactofuranoside (1a): The protected pentasaccharide **2** (25mg, 9.26 µmol) was dissolved in anhydrous pyridine (1 mL). HF•py (3.30 µL, 37.04 µmol) was added at 0 °C and the reaction mixture was stirred at 25 °C for another 4 h. Upon completion of the reaction, the reaction mixture was diluted with ethyl acetate (20 mL). The organic layer was successively washed with 1N HCl solution (2x15 mL), saturated $NaHCO_3$ solution (2x15 mL) and brine solution (20 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was dissolved in MeOH (1 mL), NaOMe (1.45 mg, 26.81 µmol) was added and the reaction mixture was stirred at 25 °C for 3 h. After completion of the starting material as indicated by TLC, the reaction was quenched with Amberlite IR-120H resin. The solid resin was filtered off and the filtrate was concentrated in vacuo and dried in high vacuum. The crude was washed thoroughly with n-pentane to remove methyl benzoate formed during the benzoyl deprotection. The pentane layer was decanted off and the crude mixture was again dried and directly subjected to the next

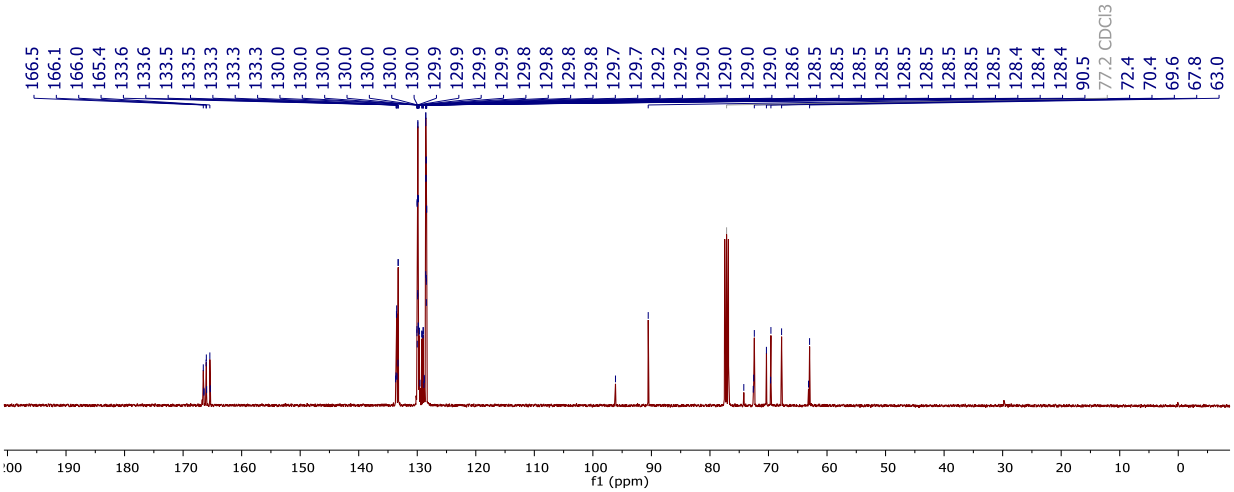
step without purification. The crude residue was dissolved in H_2O (1 mL), $Pd(OH)_2$ (on carbon) (15%) was added under H_2 atmosphere (balloon pressure) and stirred for 18 hours at 25 °C. filtered through a pad of Celite® and concentrated under reduced pressure. The crude residue was purified using bond elute C18-prepacked column using acetonitrile and deionized water as mobile phase. The collected fractions were lyophilized to obtain the desired deprotected pentasaccharide **1a** (5.47 mg, 66% yield over three steps). $[\alpha]_D^{25}$ = +12.7 (c = 0.04, H_2O); IR (cm^{-1}, MeOH): 3446, 2935, 1259, 1109, 946, 837; ^1H NMR (600 MHz, D_2O) δ 5.85 (d, *J* = 3.7 Hz, 1H), 5.21 (d, *J* = 4.3 Hz, 1H), 5.08 (d, *J* = 1.9 Hz, 1H), 4.94 (d, *J* = 1.8 Hz, 1H), 4.50 (d, *J* = 7.9 Hz, 1H), 4.18 – 4.14 (m, 2H), 4.11 (dt, *J* = 7.0, 3.8 Hz, 2H), 4.03 (ddd, *J* = 13.4, 3.8, 1.8 Hz, 2H), 3.97 (dd, *J* = 6.3, 3.6 Hz, 1H), 3.90 (dt, *J* = 6.4, 4.2 Hz, 3H), 3.84 (dd, *J* = 12.3, 2.1 Hz, 1H), 3.81 – 3.71 (m, 4H), 3.70 – 3.58 (m, 11H), 3.57 – 3.51 (m, 3H), 3.48 (dt, *J* = 9.6, 6.5 Hz, 2H), 3.43 – 3.36 (m, 3H), 3.35 – 3.30 (m, 2H), 3.07 (dd, *J* = 13.6, 6.8 Hz, 2H), 1.55 – 1.50 (m, 3H), 1.47 – 1.40 (m, 2H), 1.32 – 1.24 (m, 5H); ^{13}C NMR (151 MHz, D_2O) δ 107.8, 105.4, 102.7, 101.5, 92.6, 87.1, 85.1, 82.9, 82.0, 81.0, 78.3, 76.7, 76.1, 75.5, 75.3, 73.5, 73.0, 72.8, 70.8, 70.1, 69.5, 69.1, 69.1, 68.9, 68.4, 68.1, 62.7, 61.5, 60.8, 60.2, 40.3, 28.6, 28.5, 25.6, 24.9; HRMS (ESI-MS): m/z calcd. For $C_{35}H_{63}NO_{25}$ $[M+H]^+$: 898.3767; Found: 898.3787.

3.14. NMR Spectral Charts

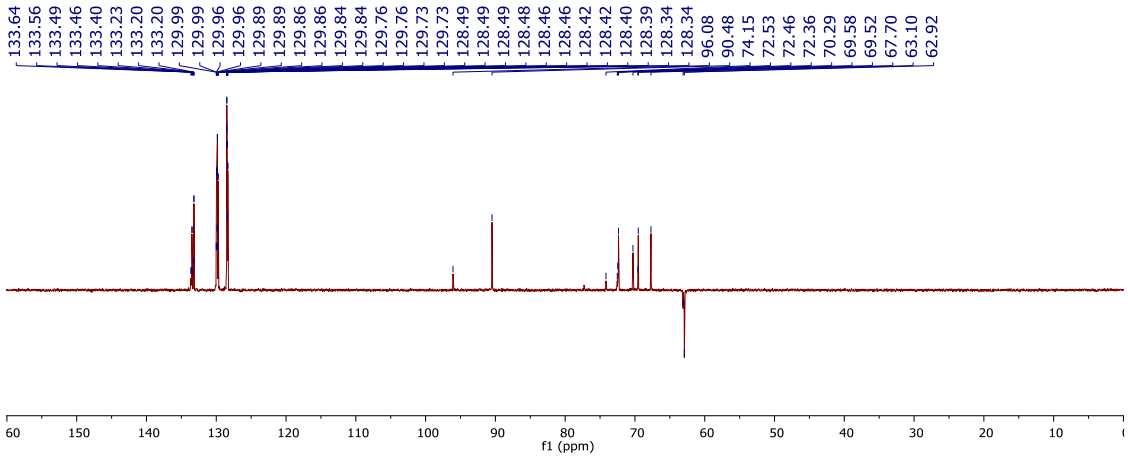
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **13**



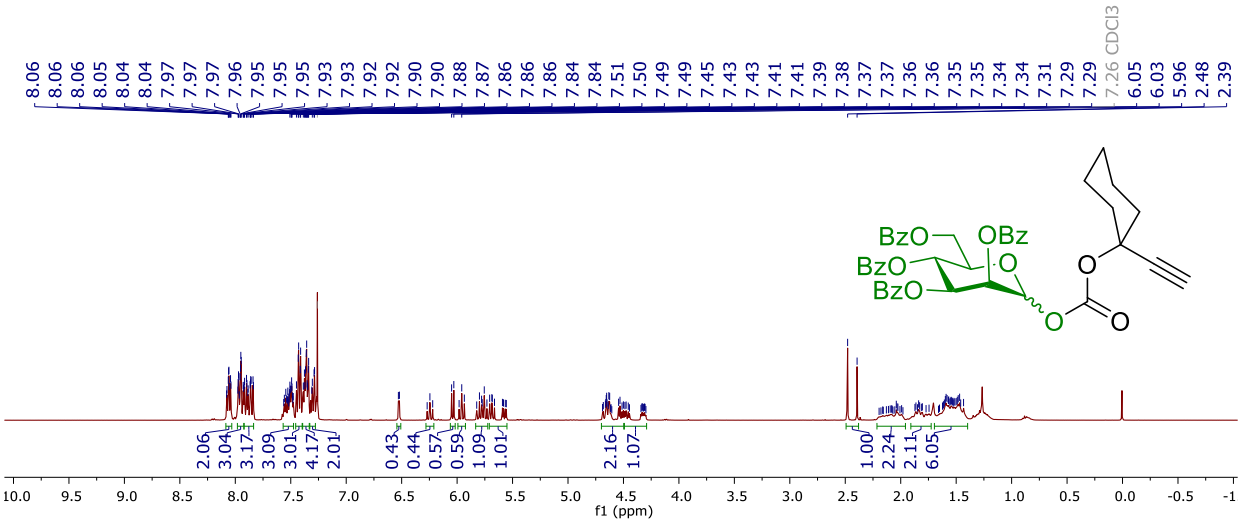
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **13**



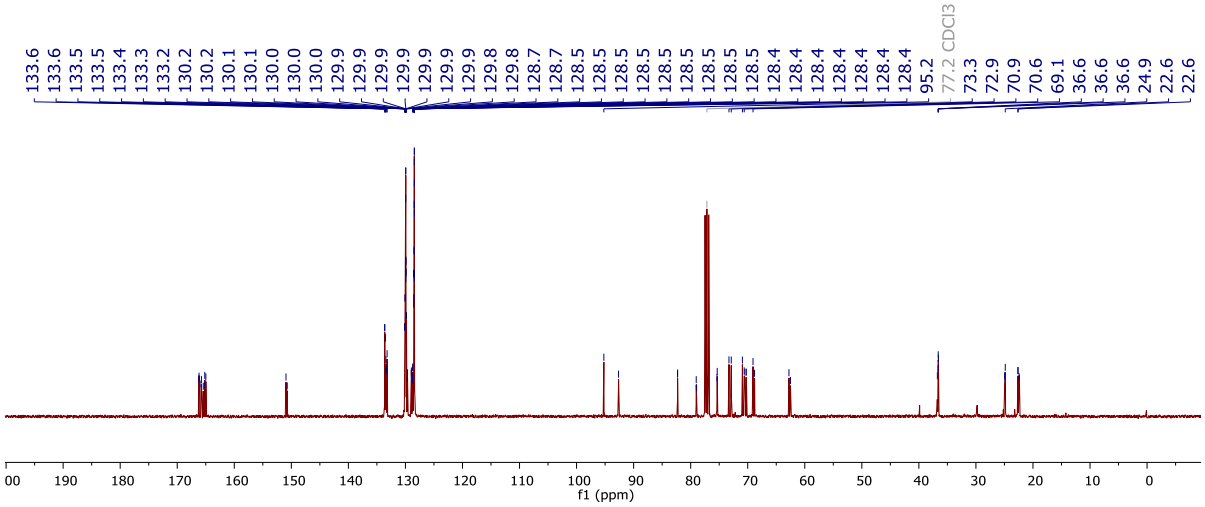
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **13**



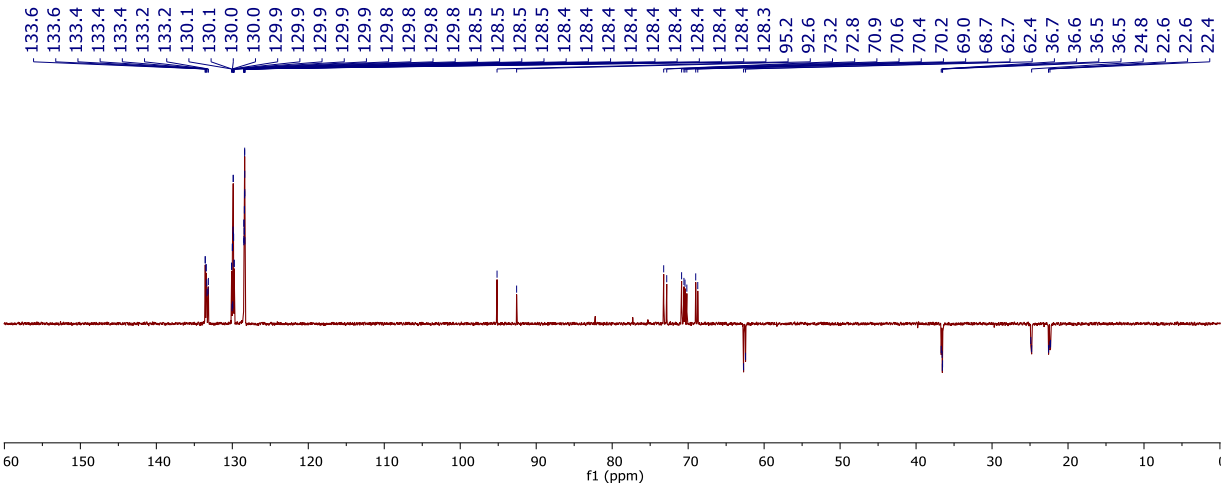
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **3**



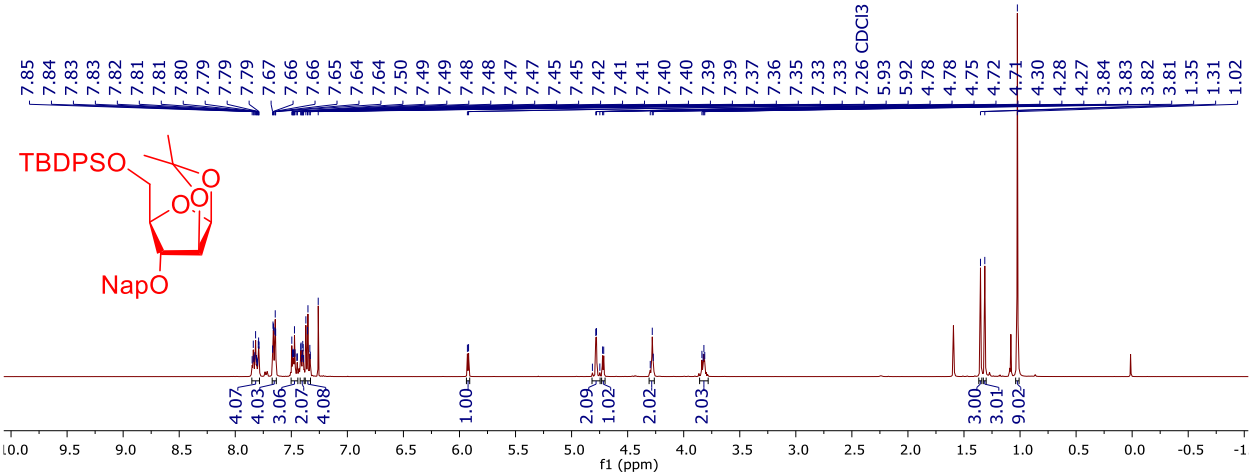
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **3**



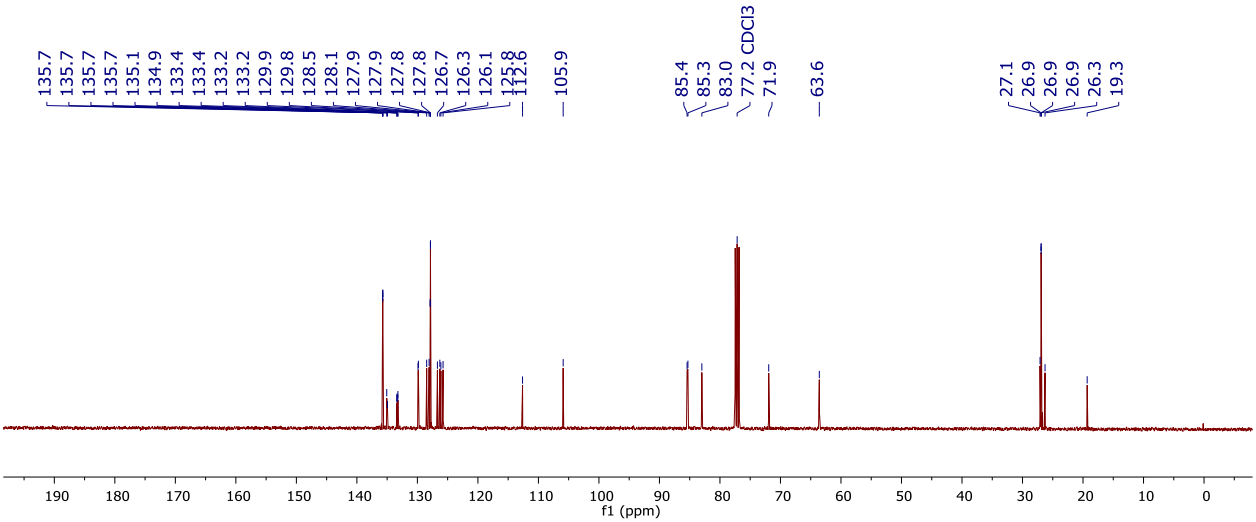
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **3**



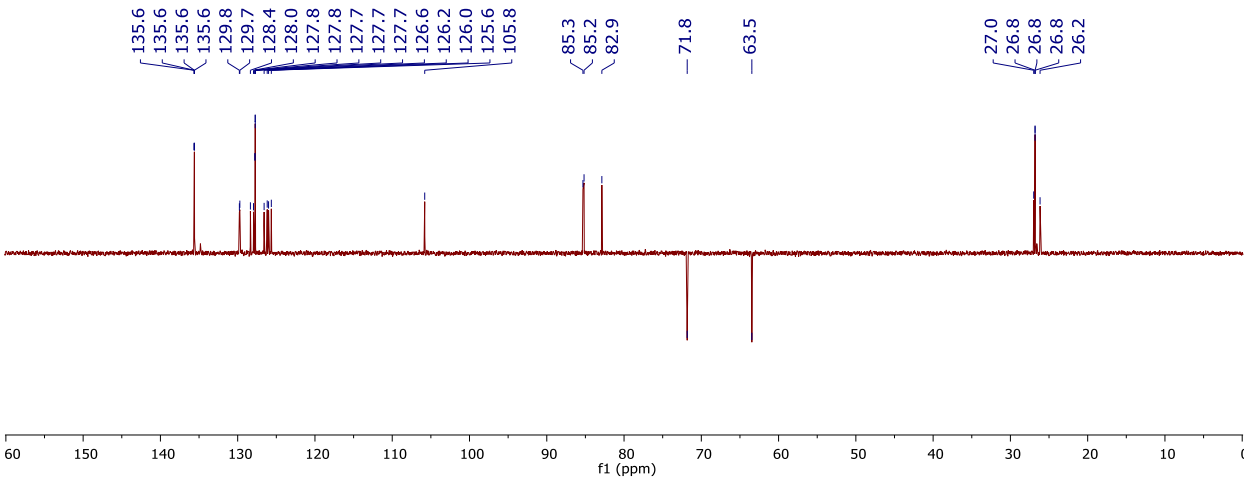
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **15**



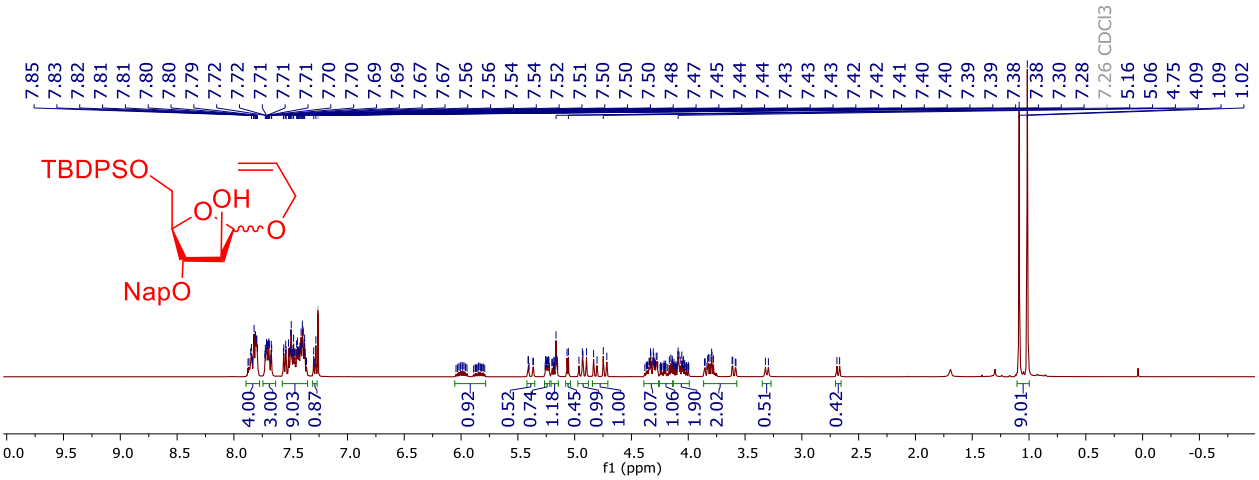
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **15**



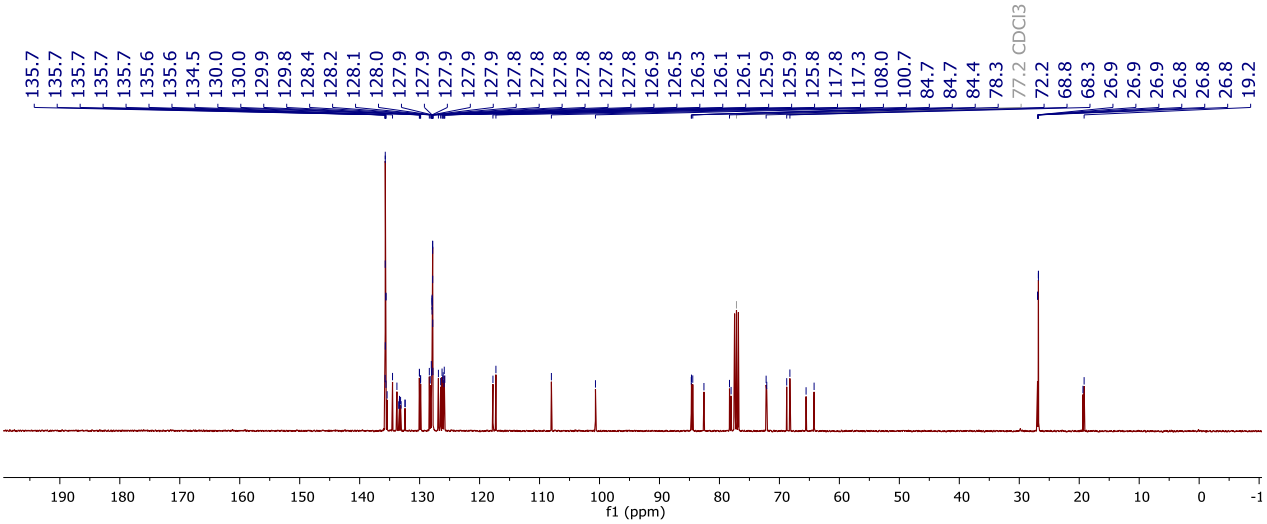
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **15**



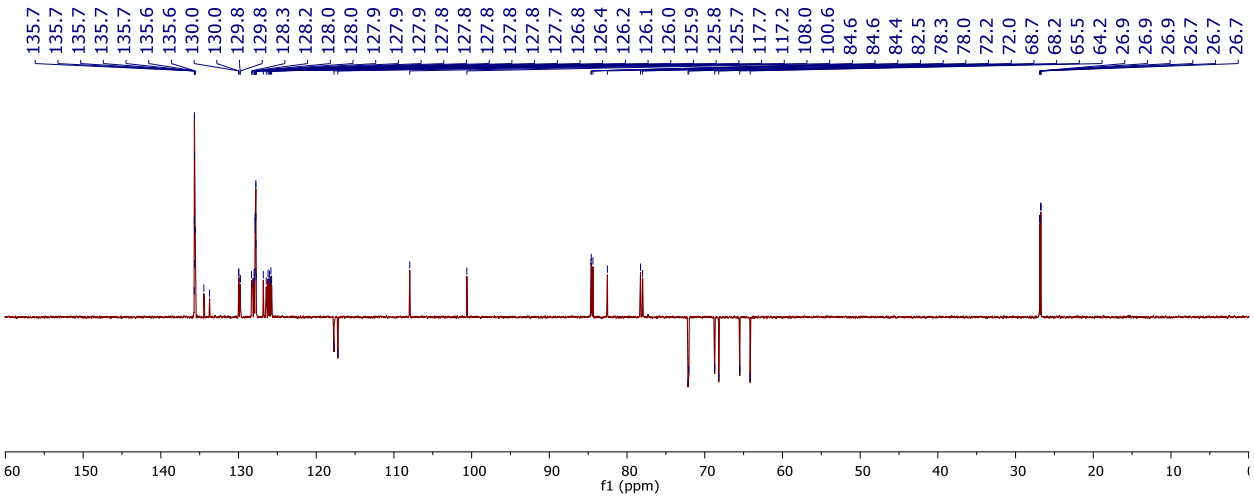
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **16**



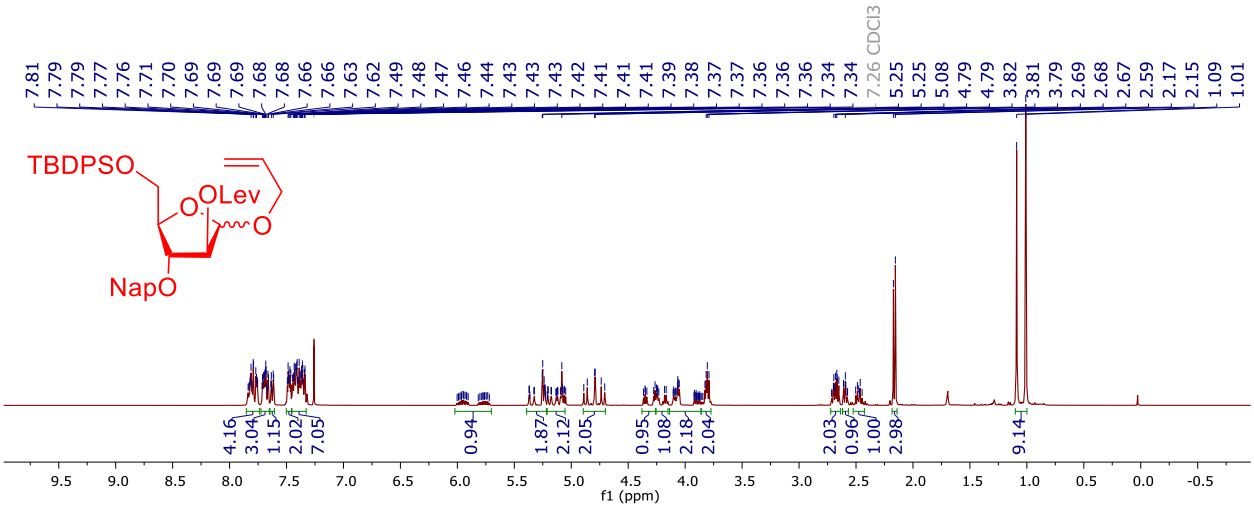
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **16**



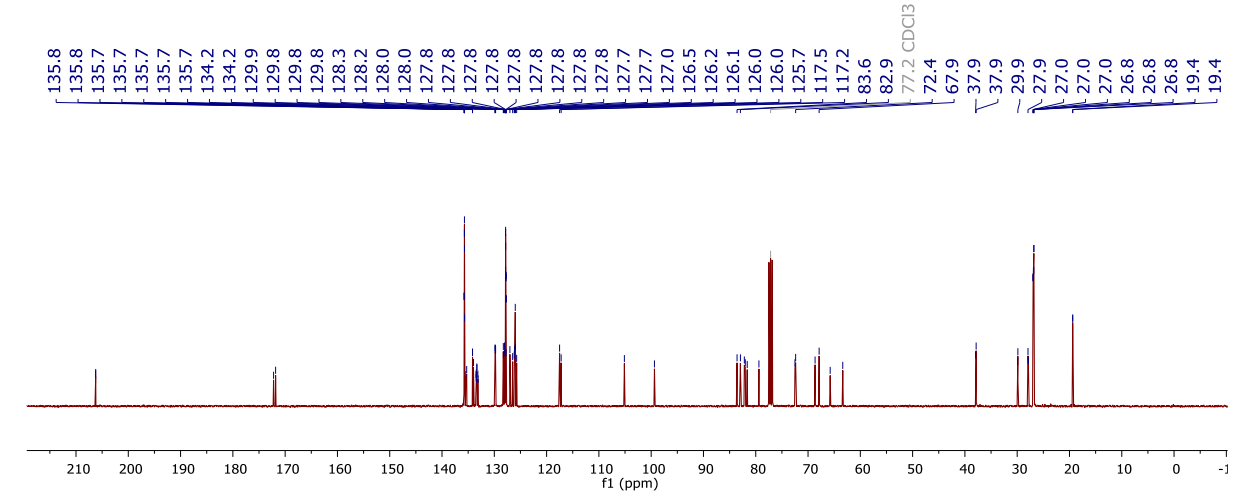
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **16**



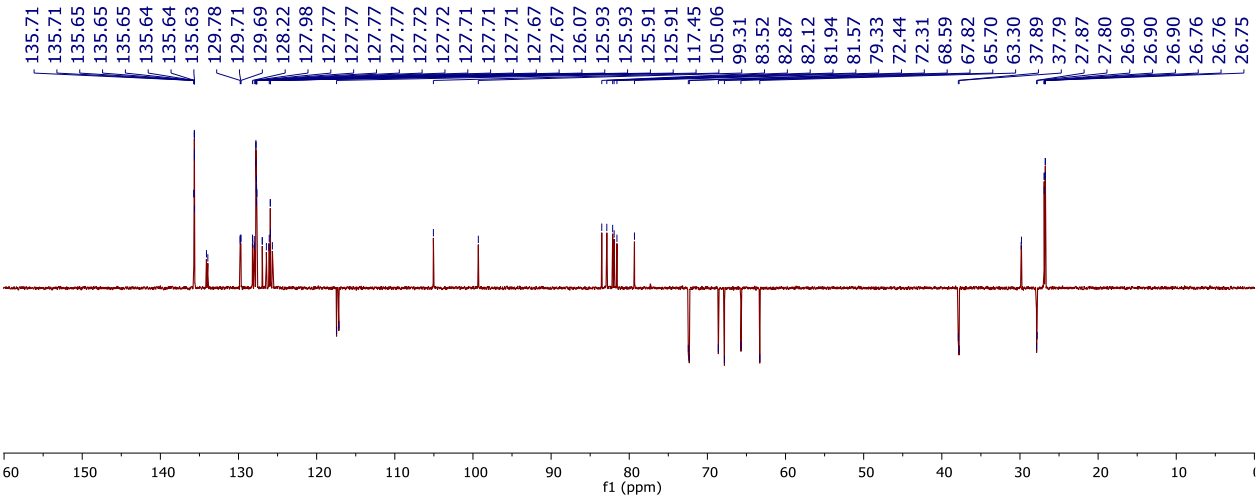
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **17**



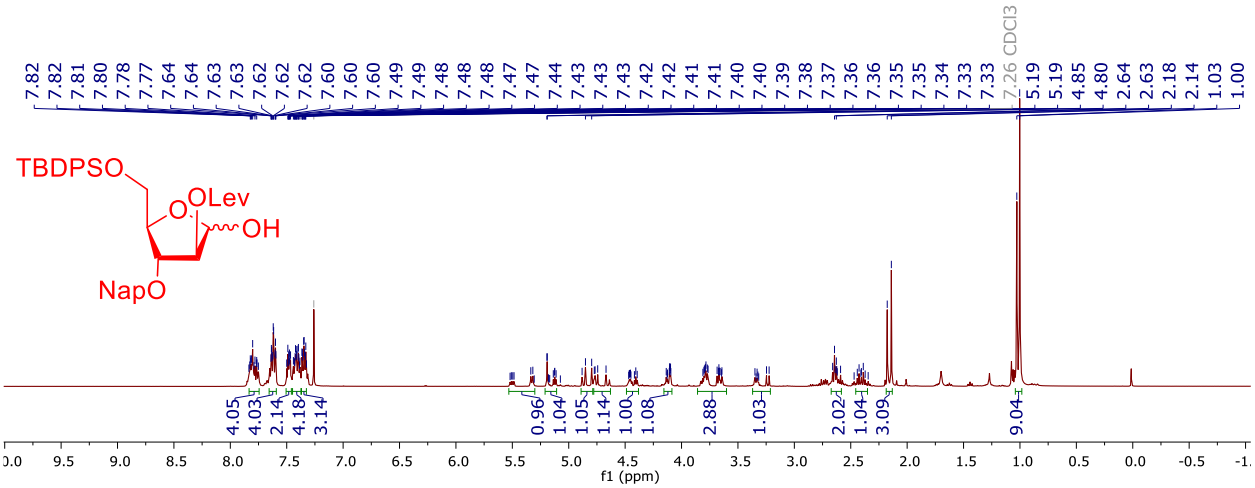
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **17**



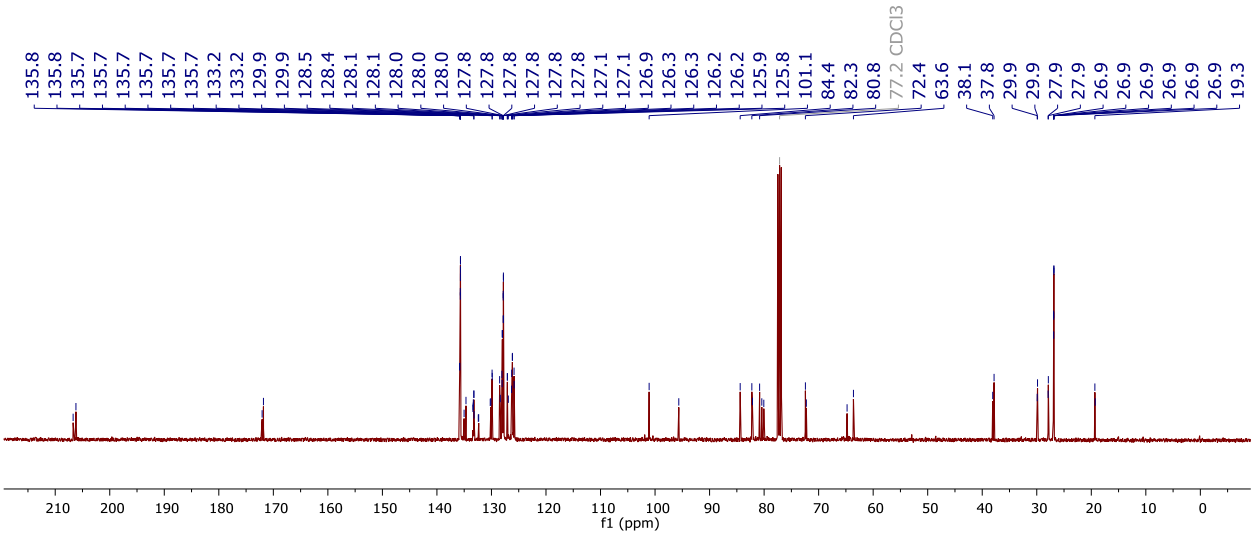
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **17**



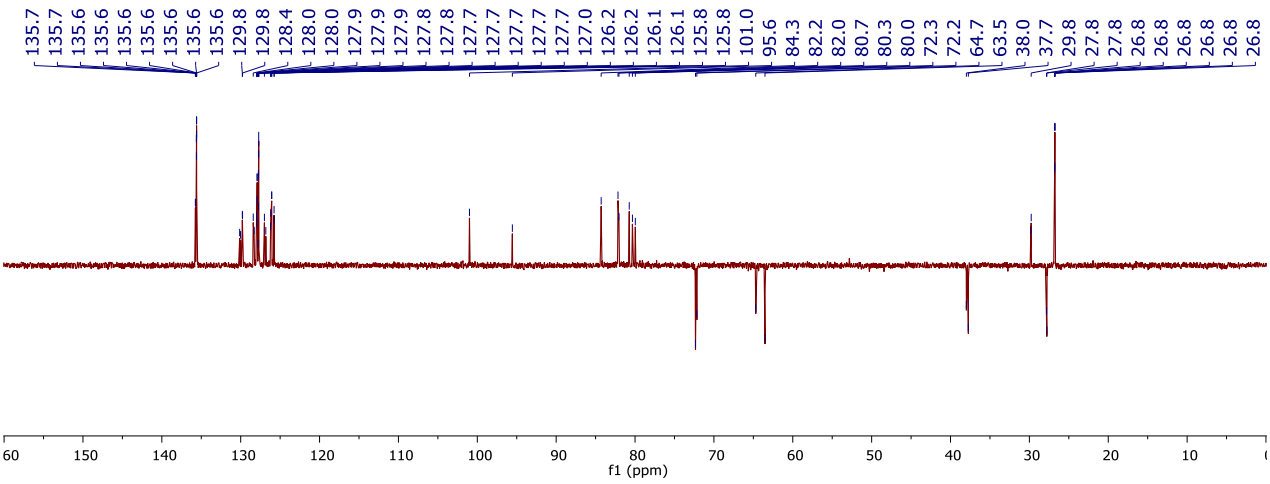
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **18**



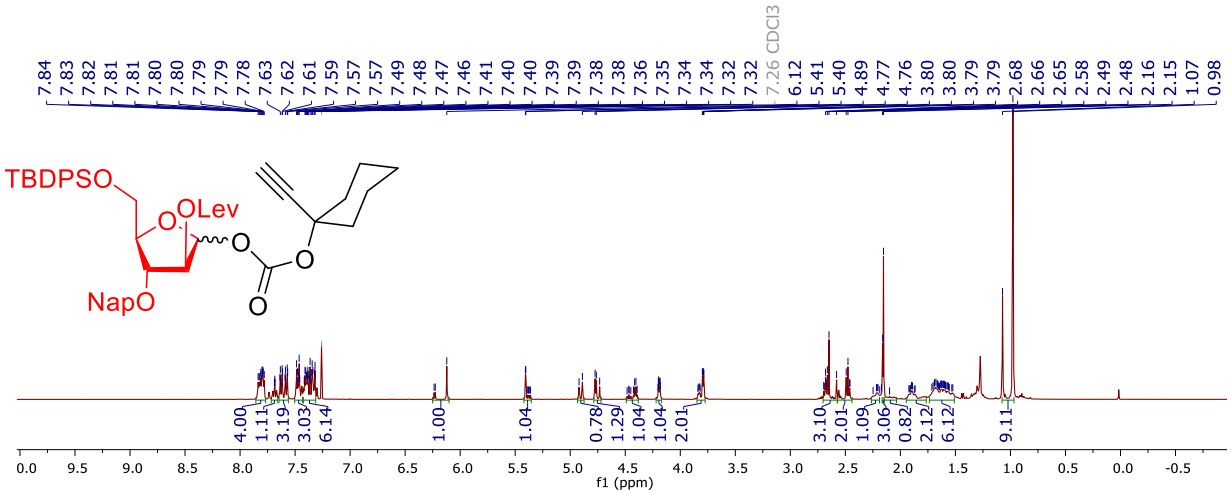
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **18**



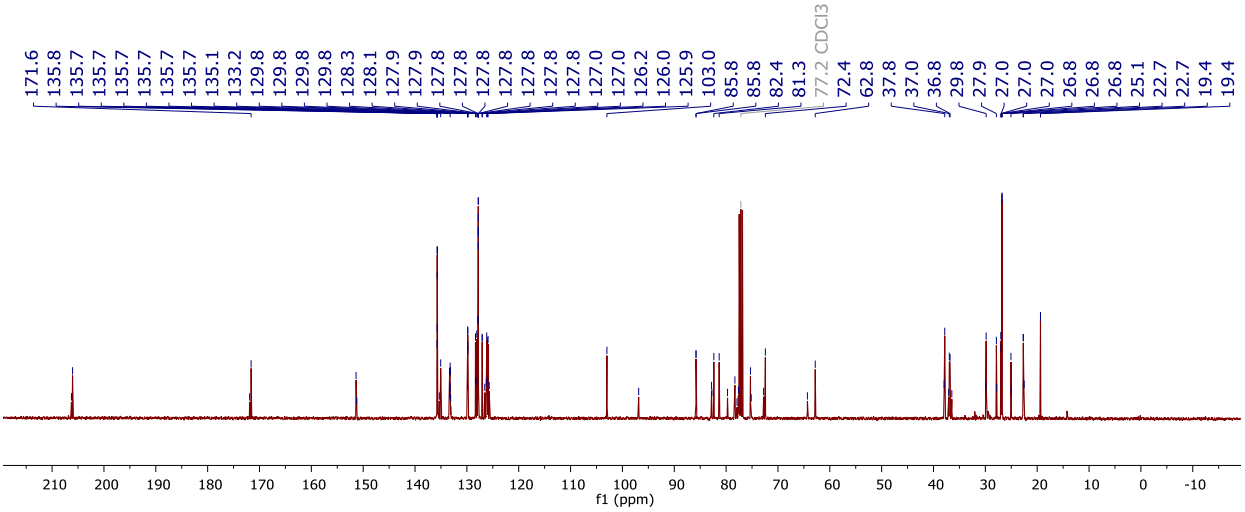
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **18**



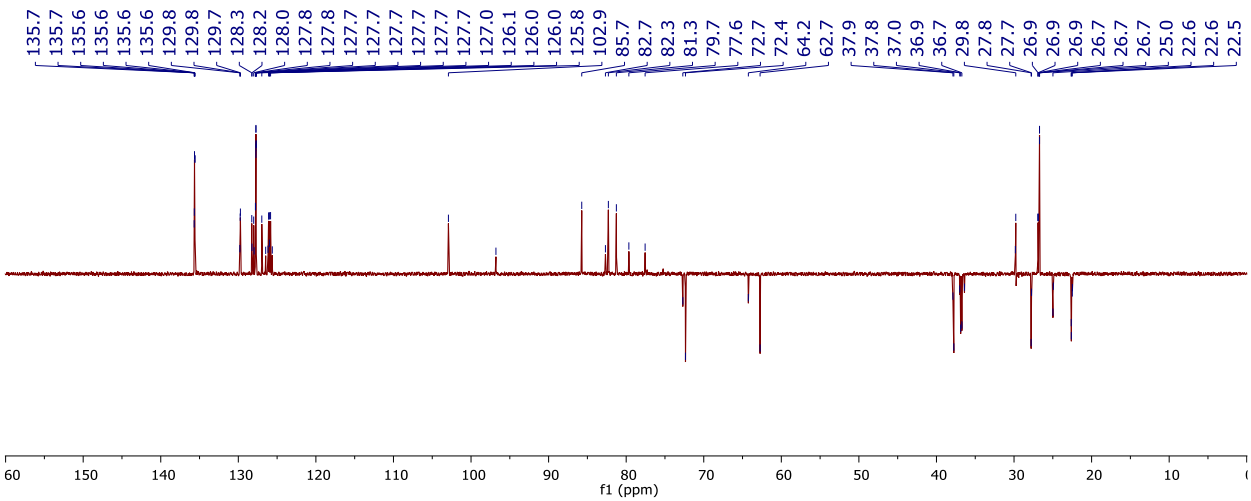
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **6**



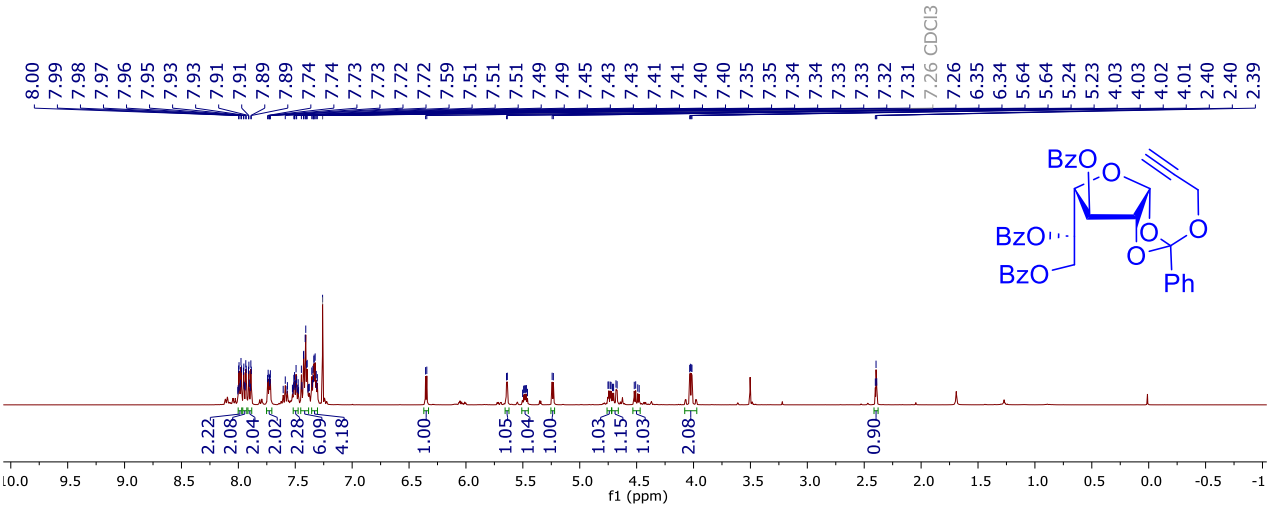
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **6**



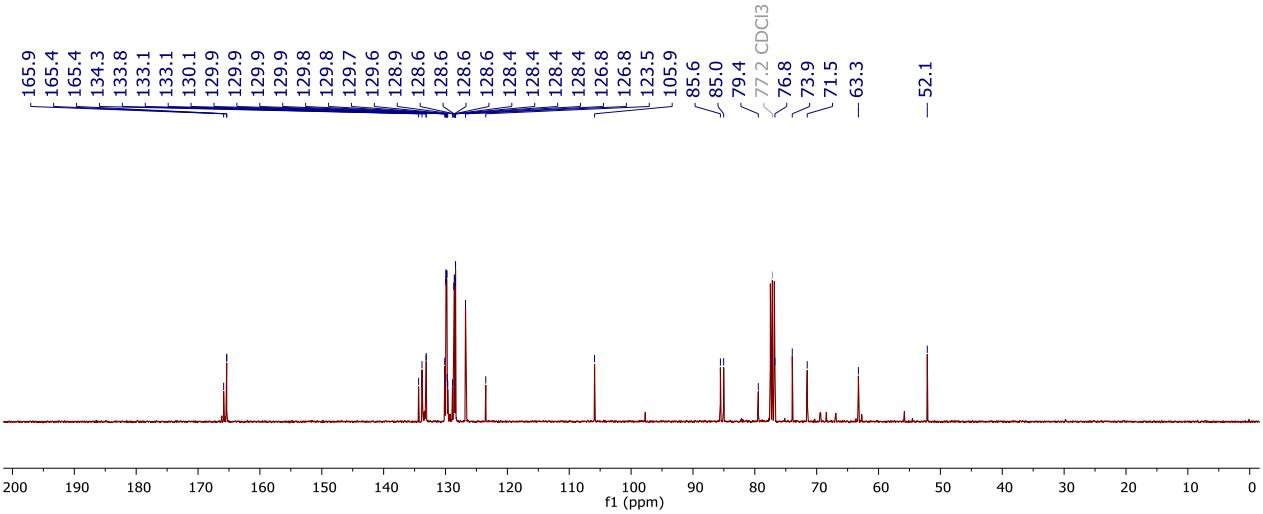
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **6**



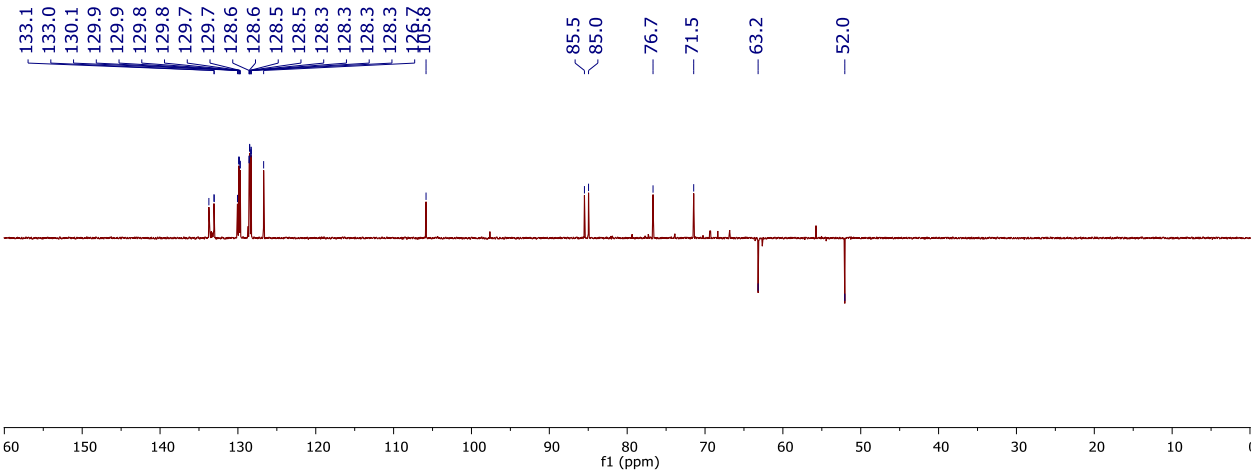
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **10**



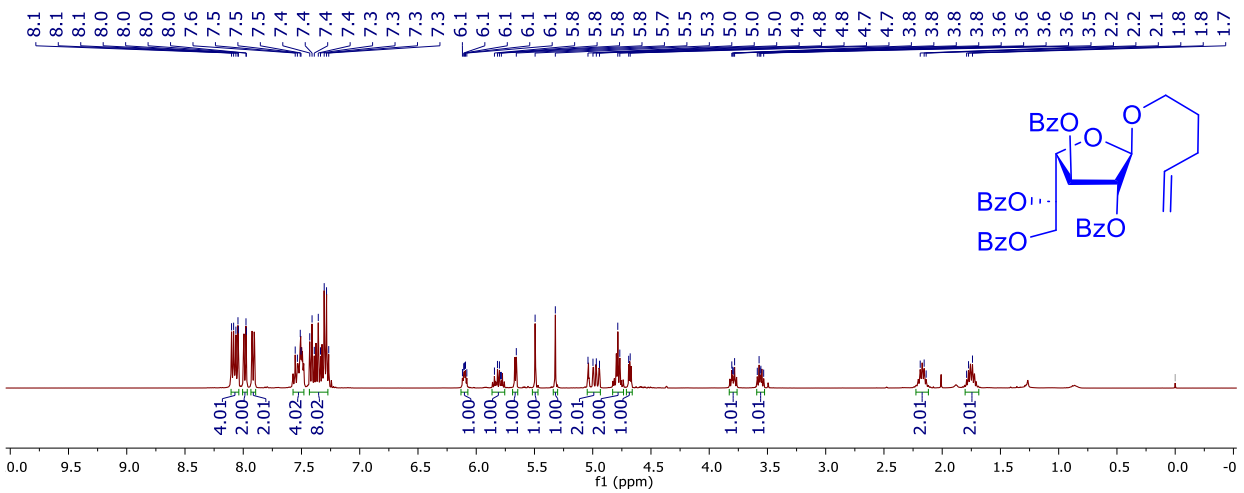
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **10**



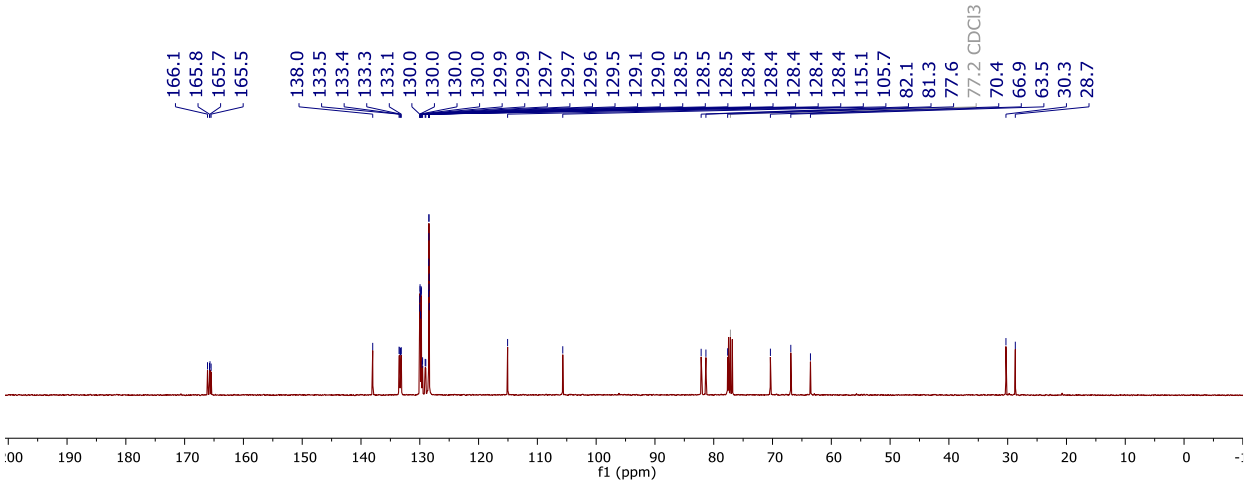
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **10**



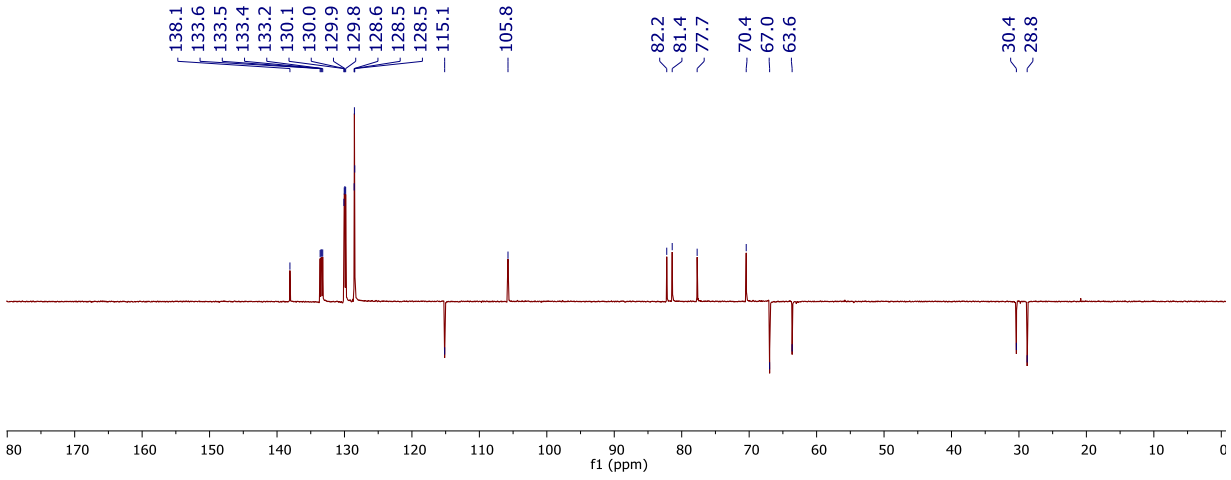
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **20**



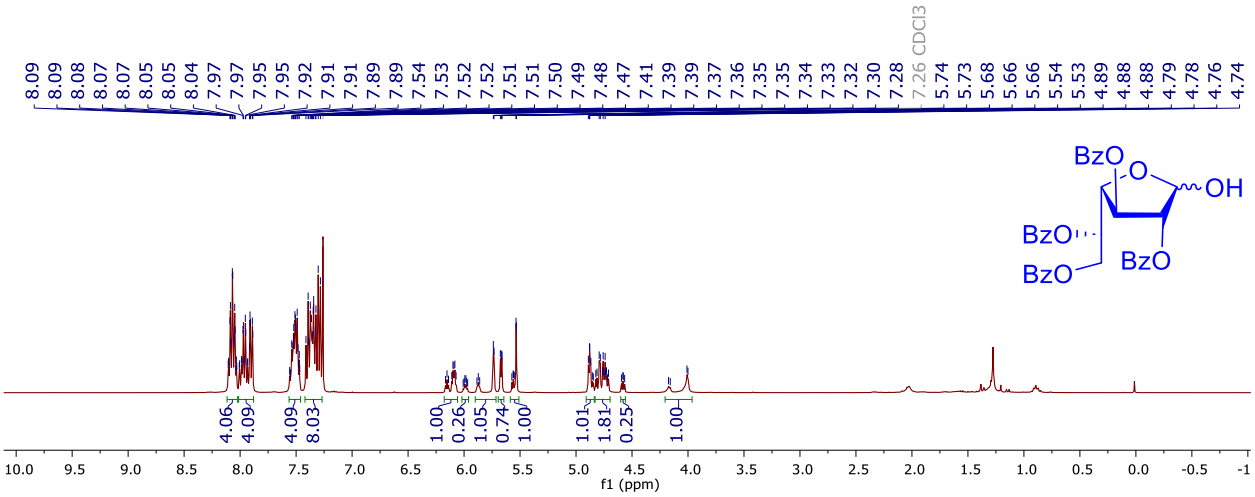
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **20**



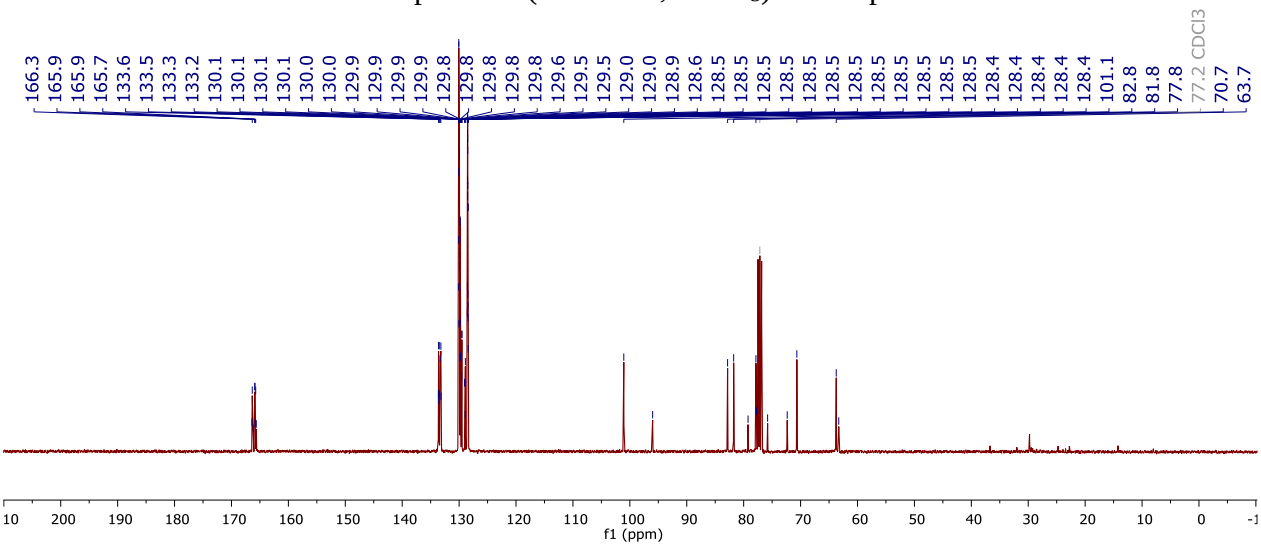
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **20**



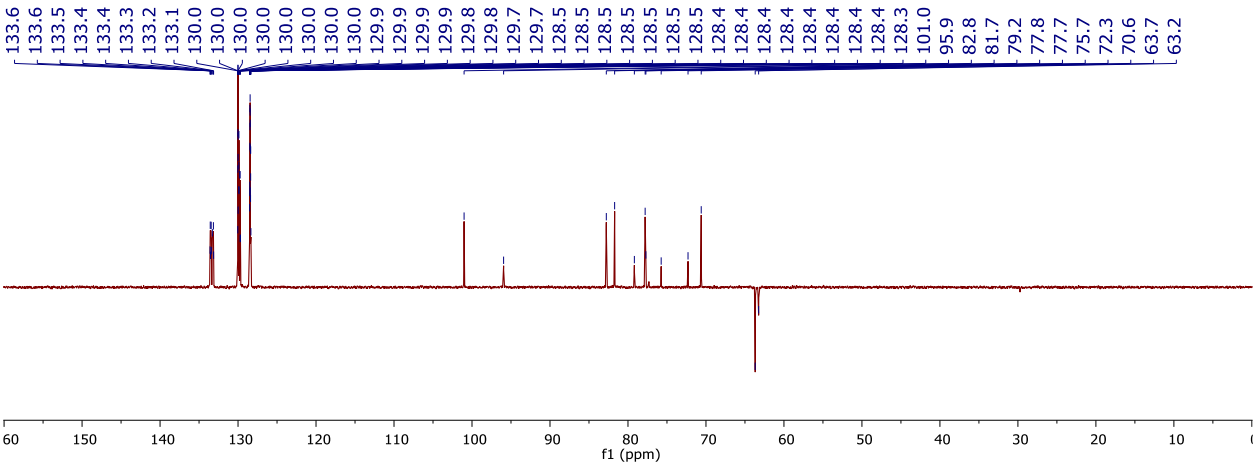
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **21**



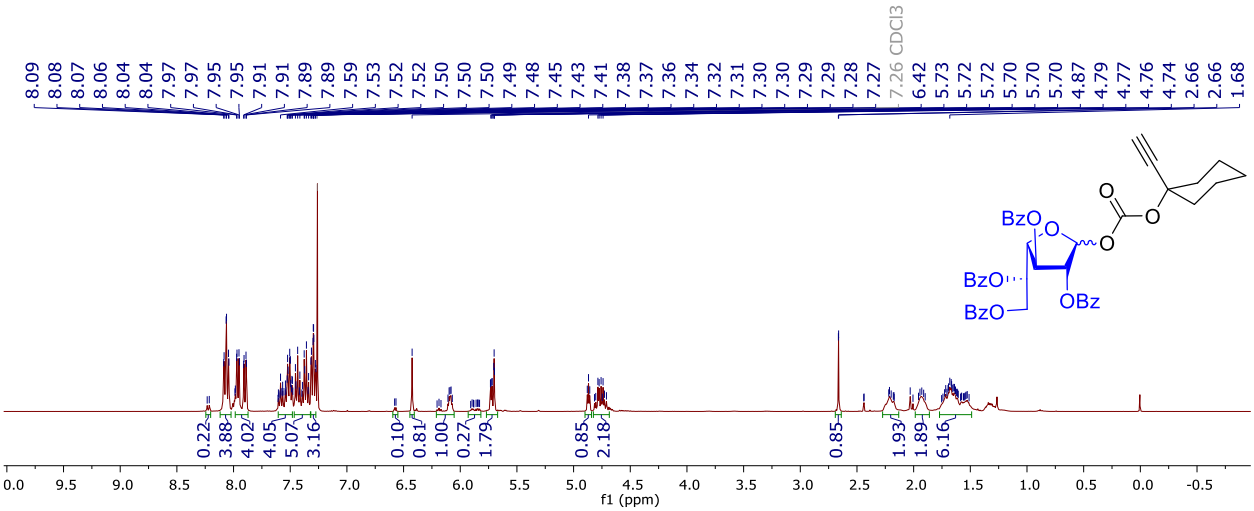
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **21**



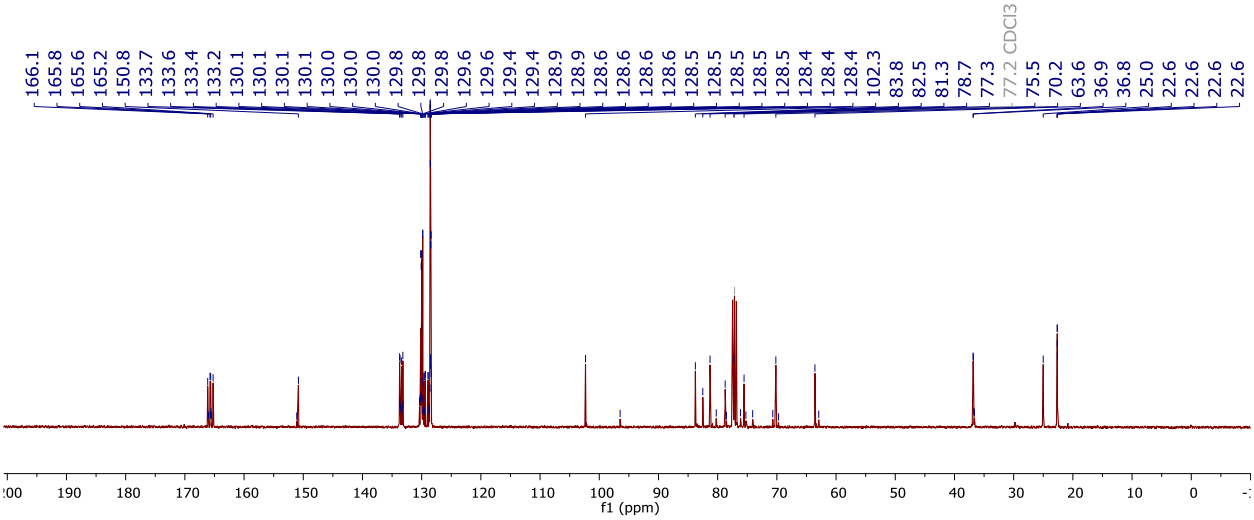
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **21**



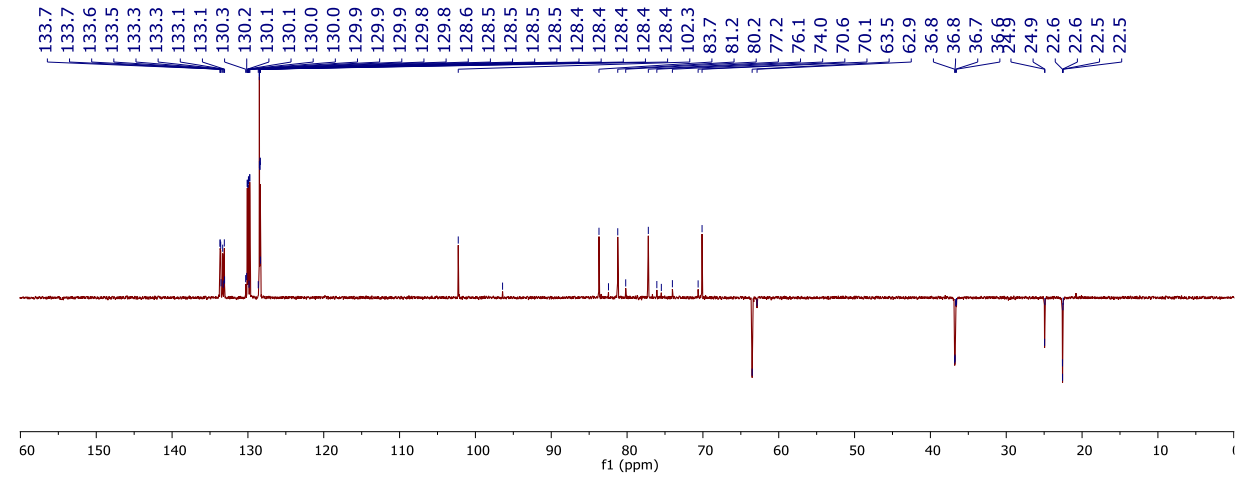
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **8**



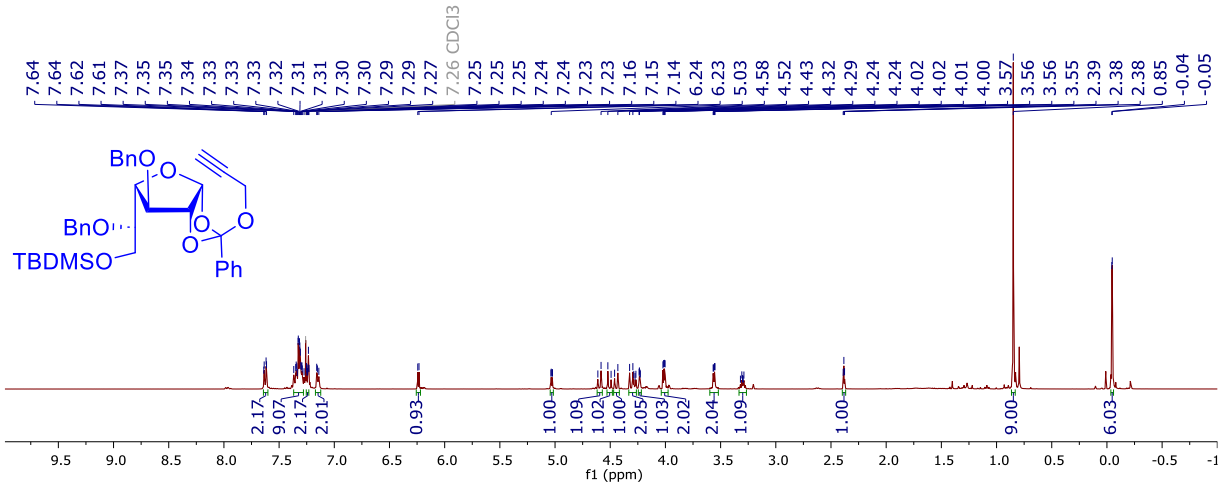
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **8**



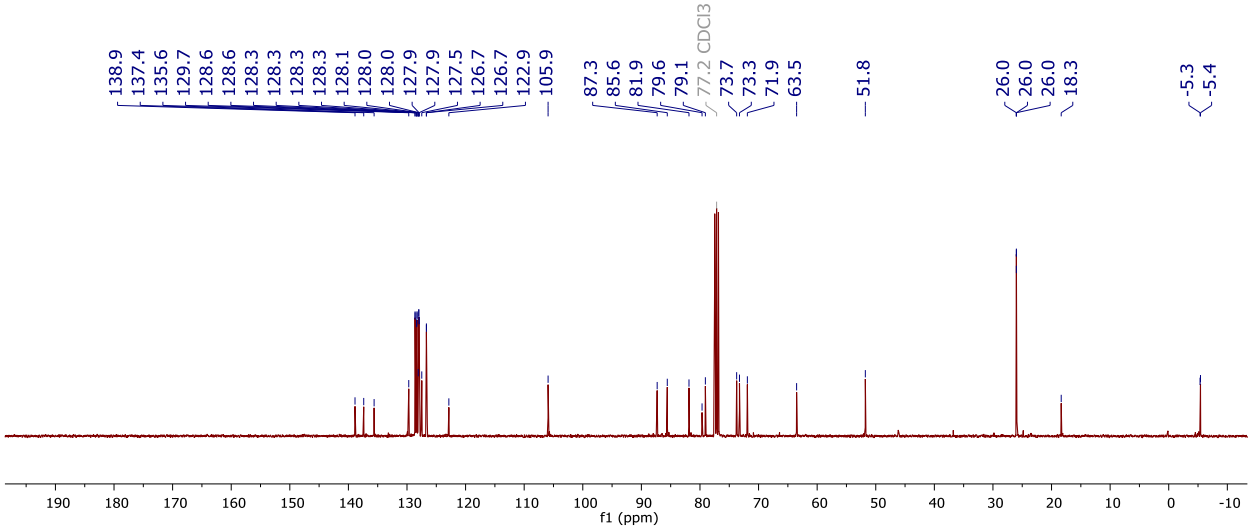
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **8**



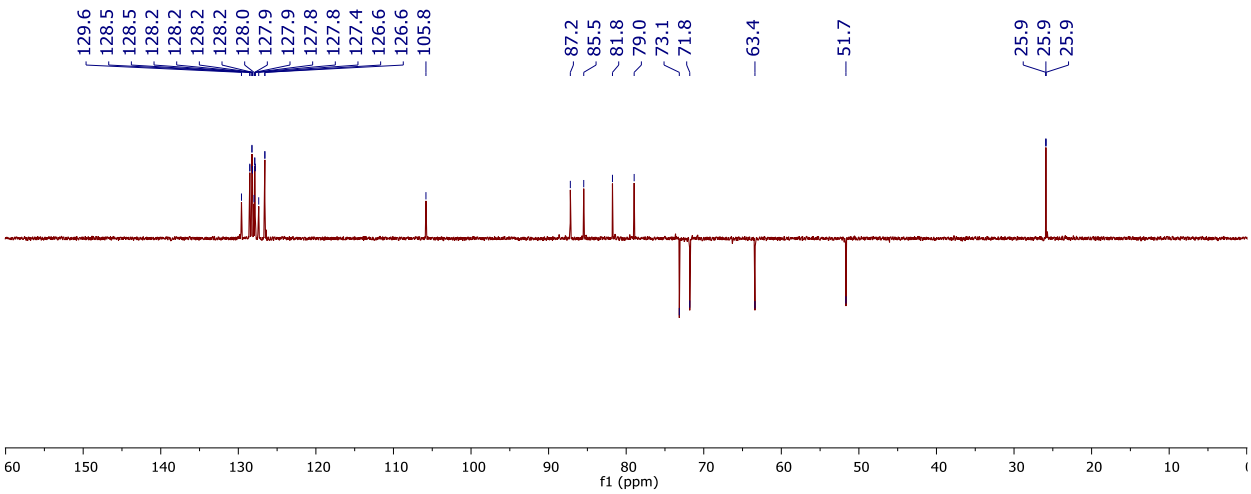
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **22**



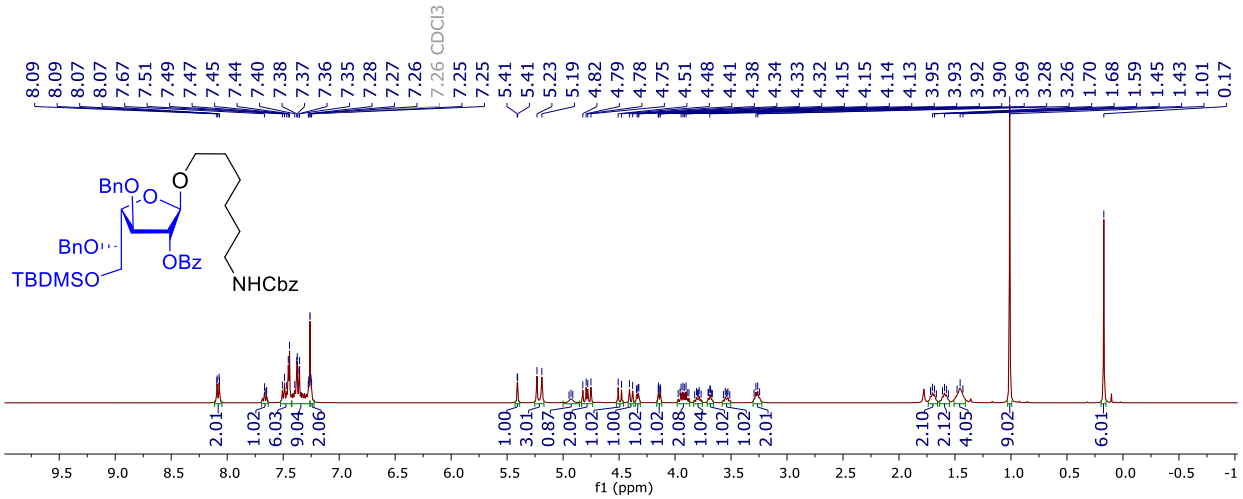
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **22**



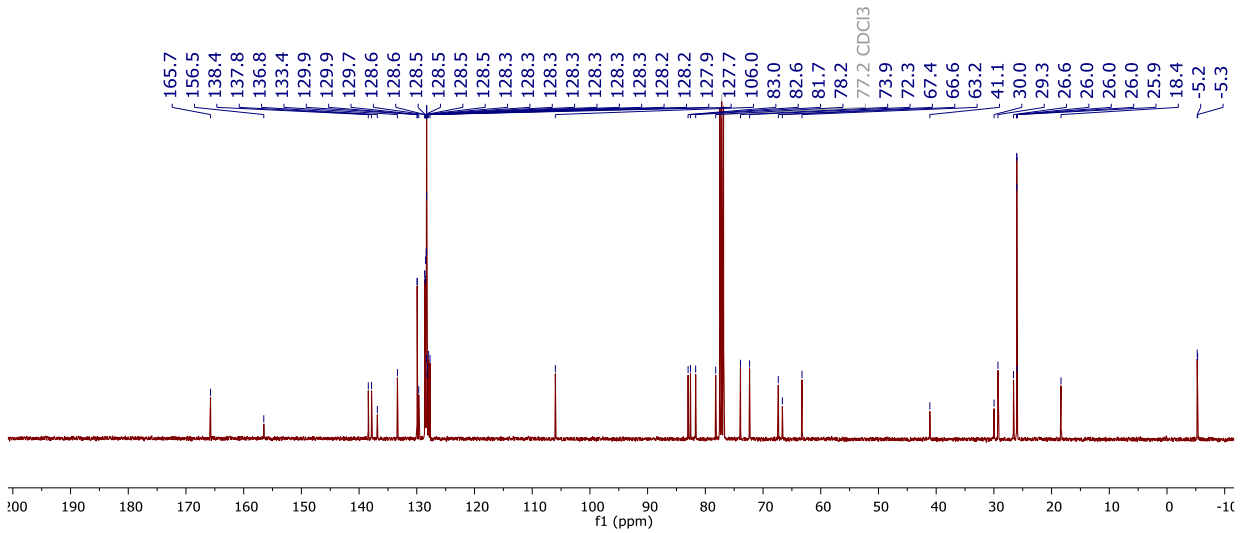
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **22**



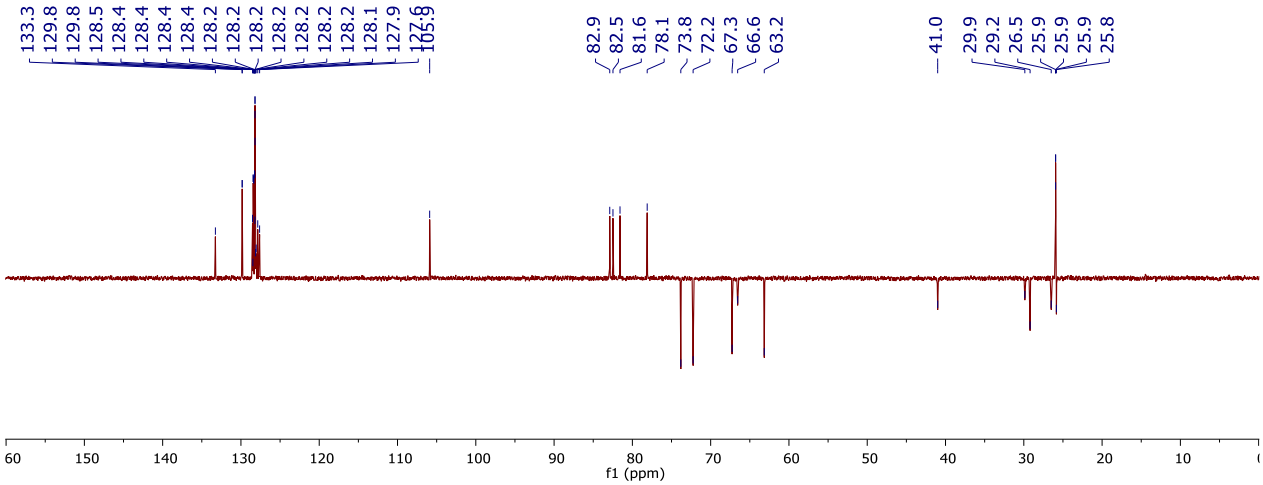
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **23**



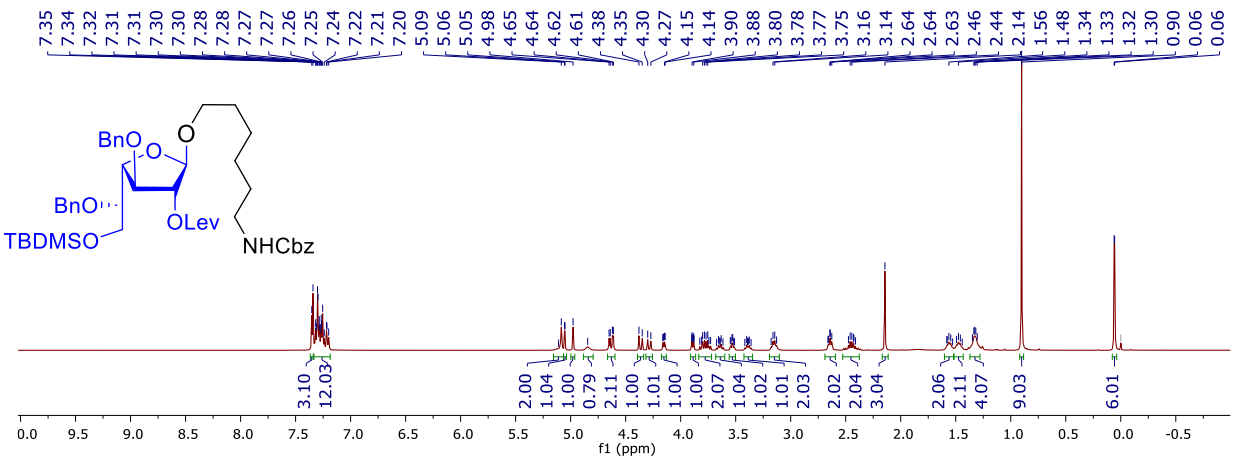
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **23**



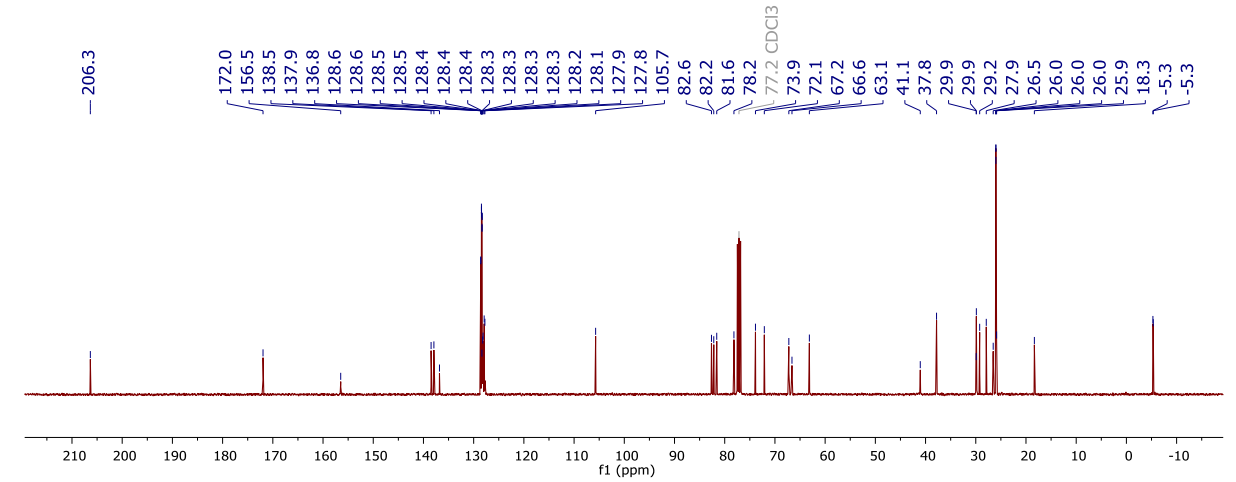
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **23**



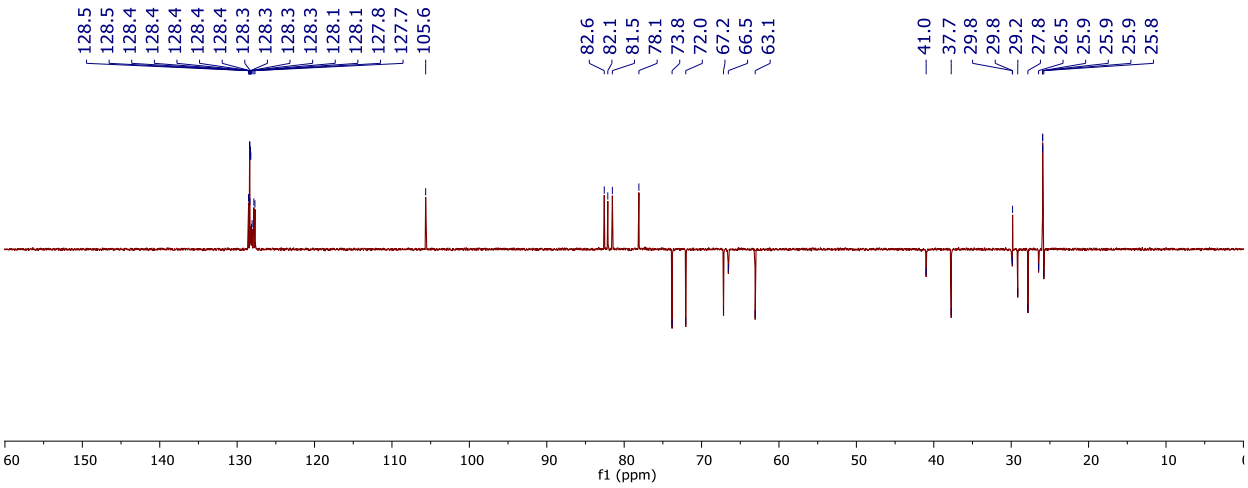
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **24**



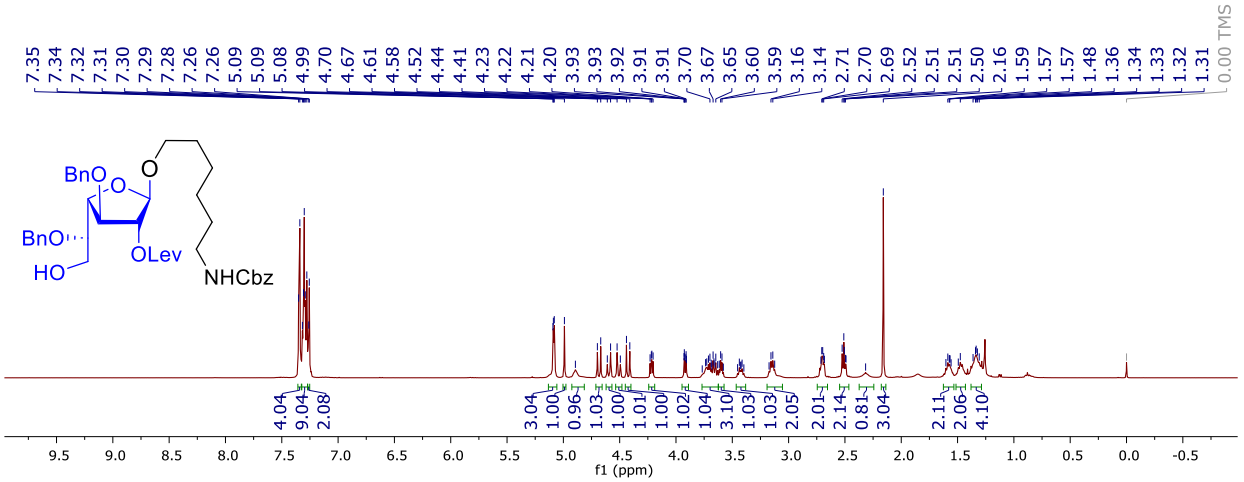
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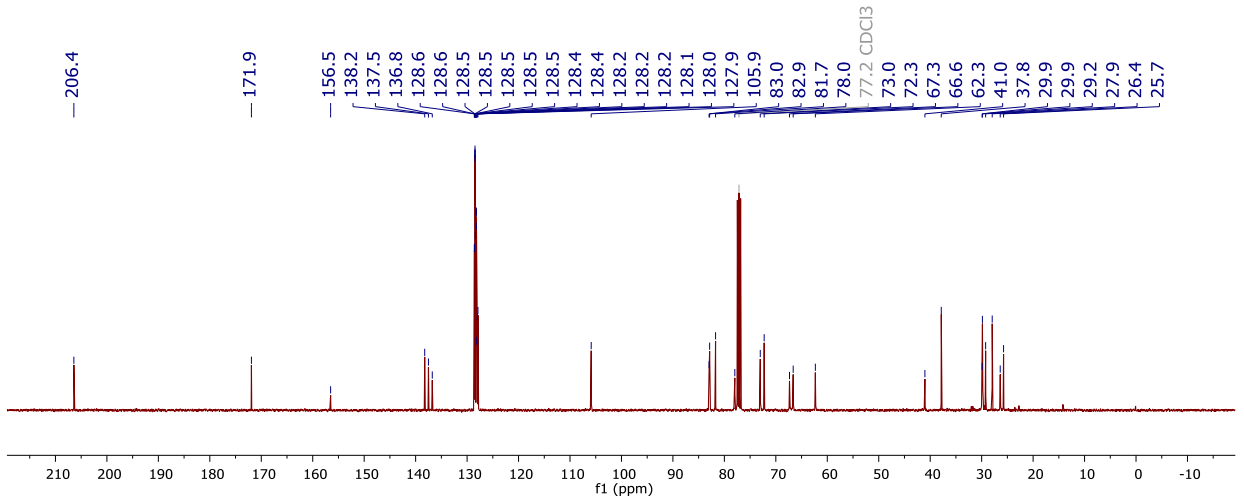
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **24**



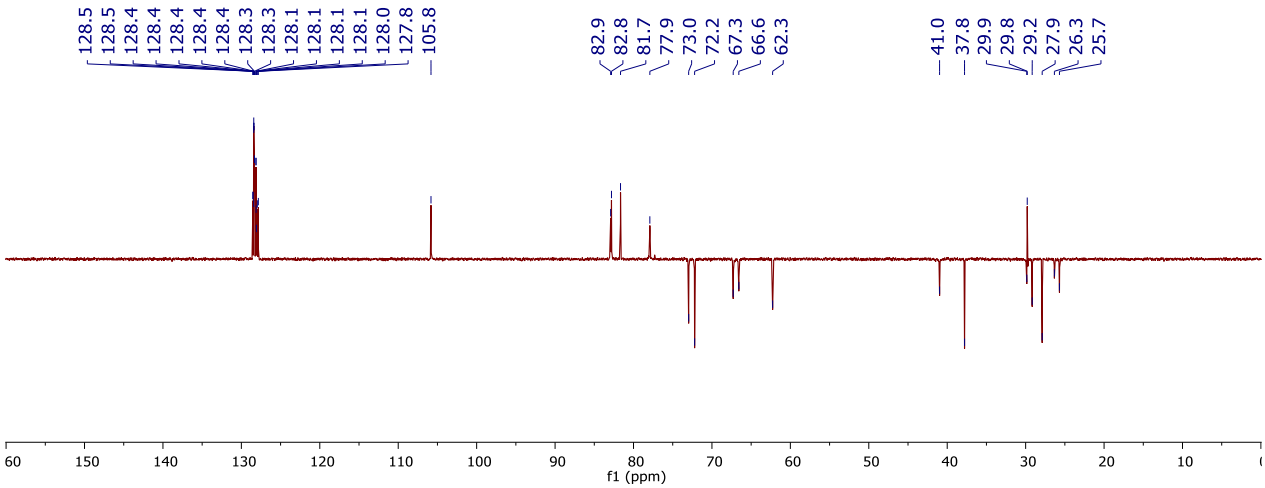
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **9**



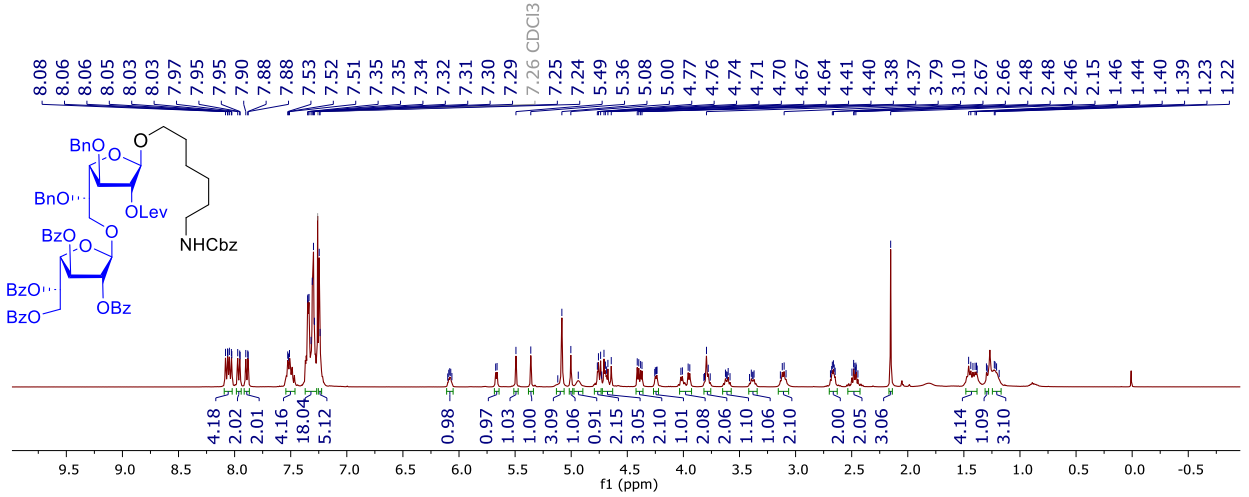
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **9**



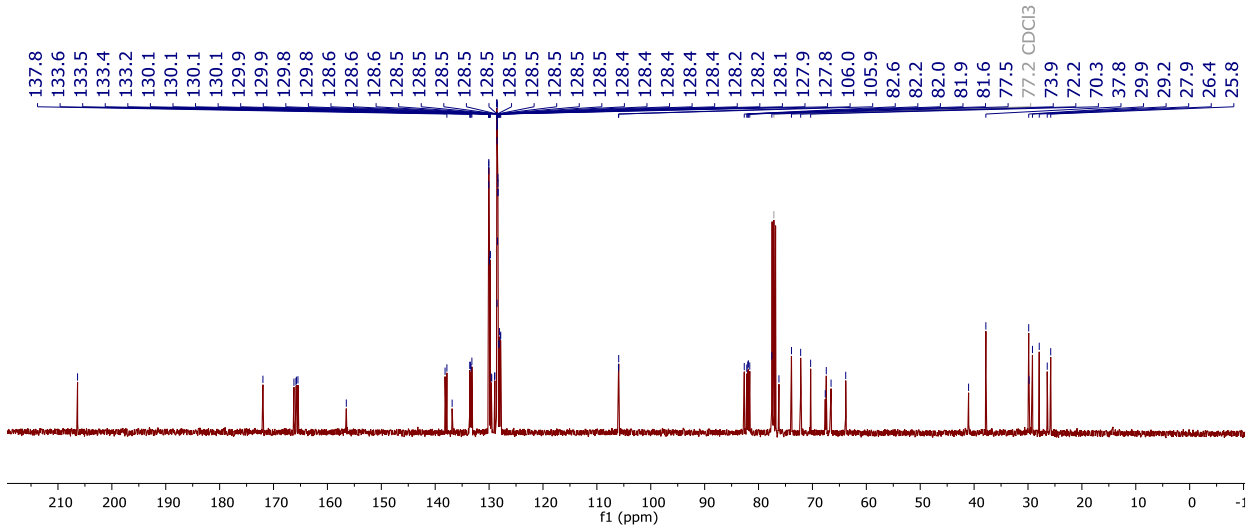
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **9**



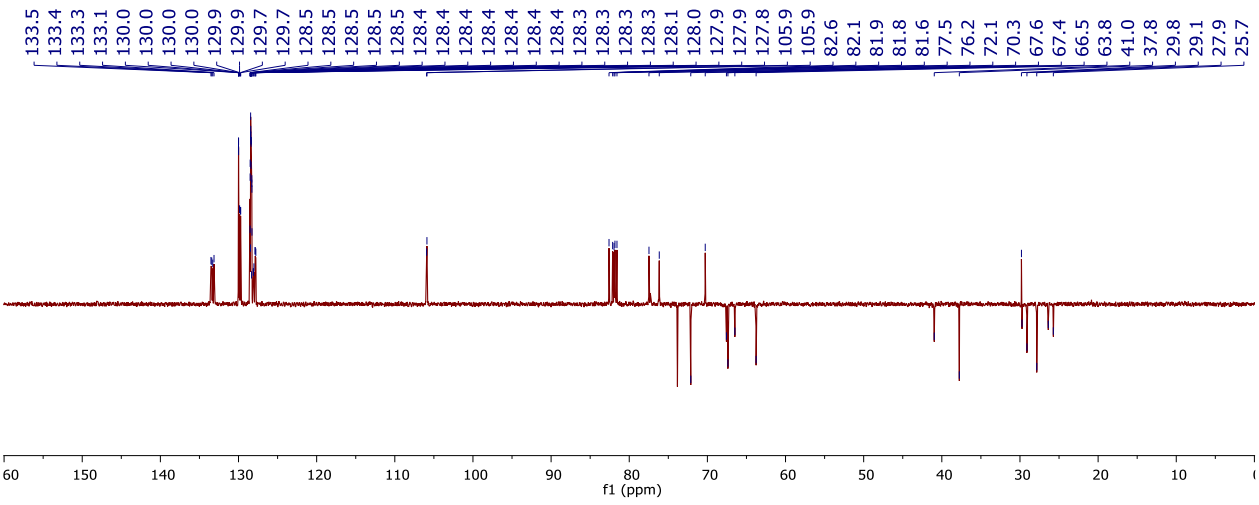
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **25**



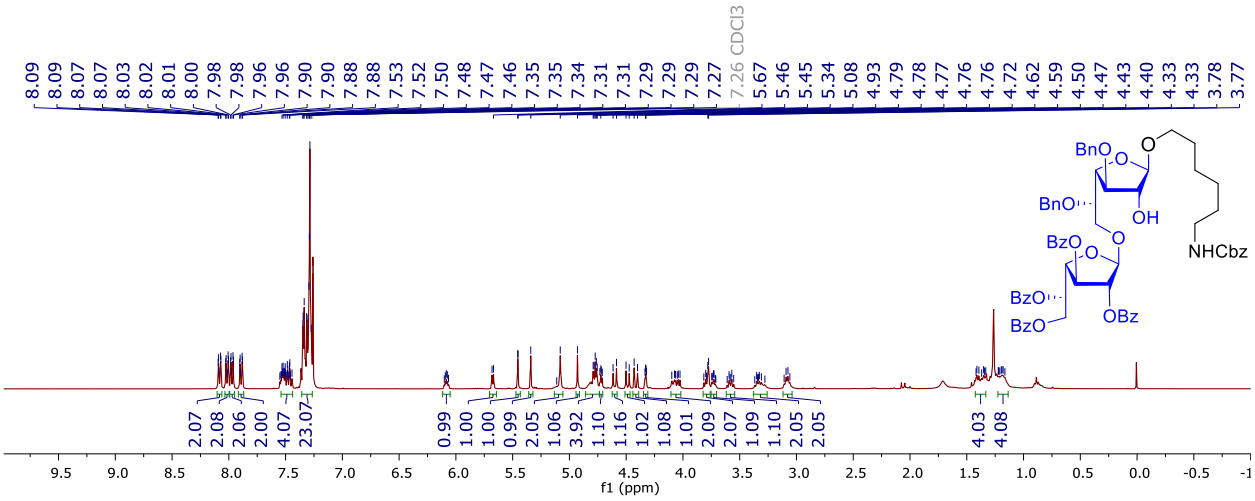
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **25**



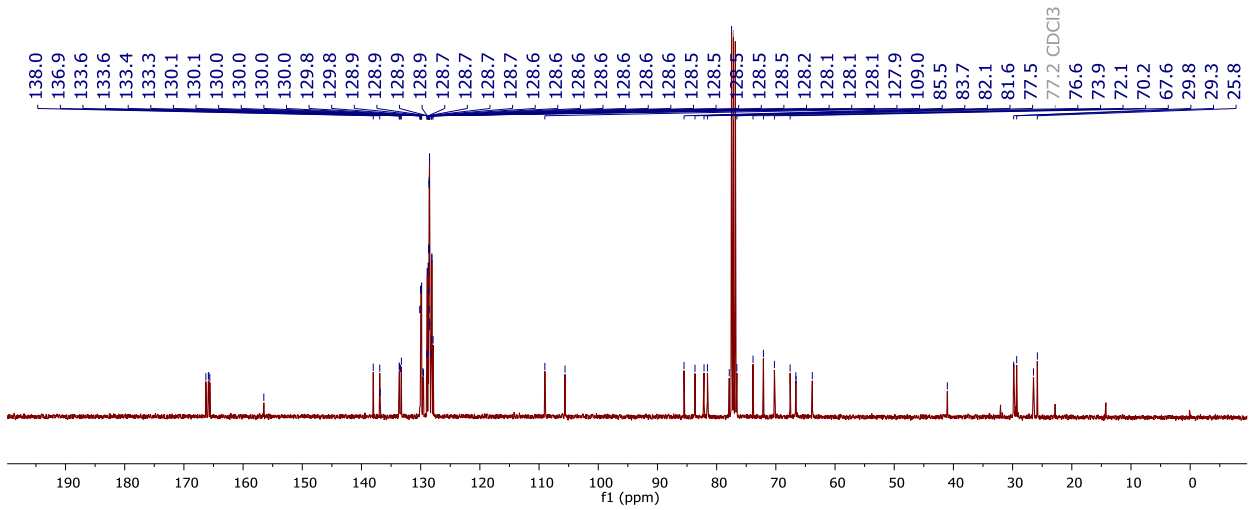
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **25**



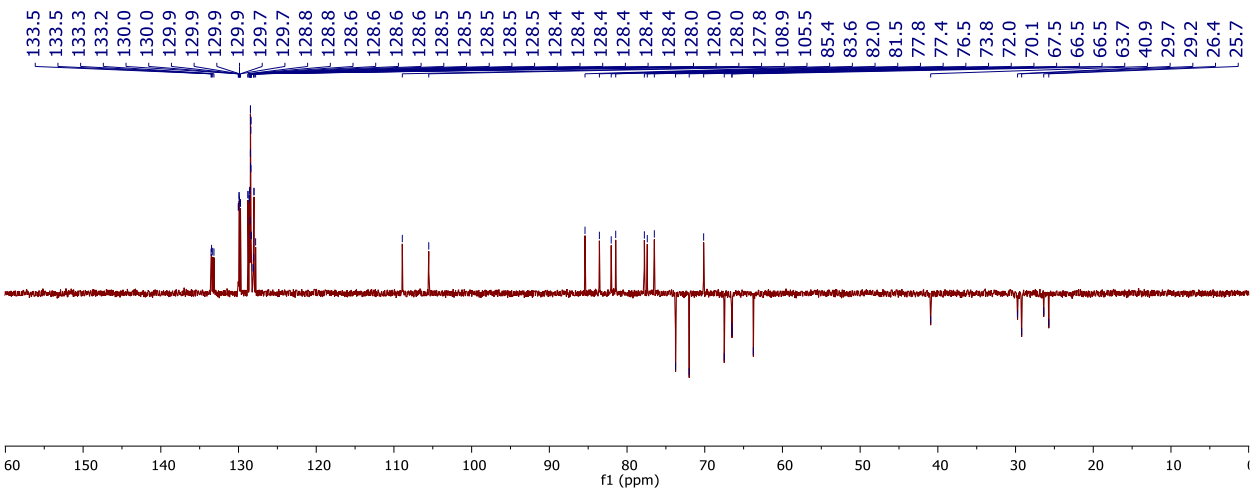
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **7**



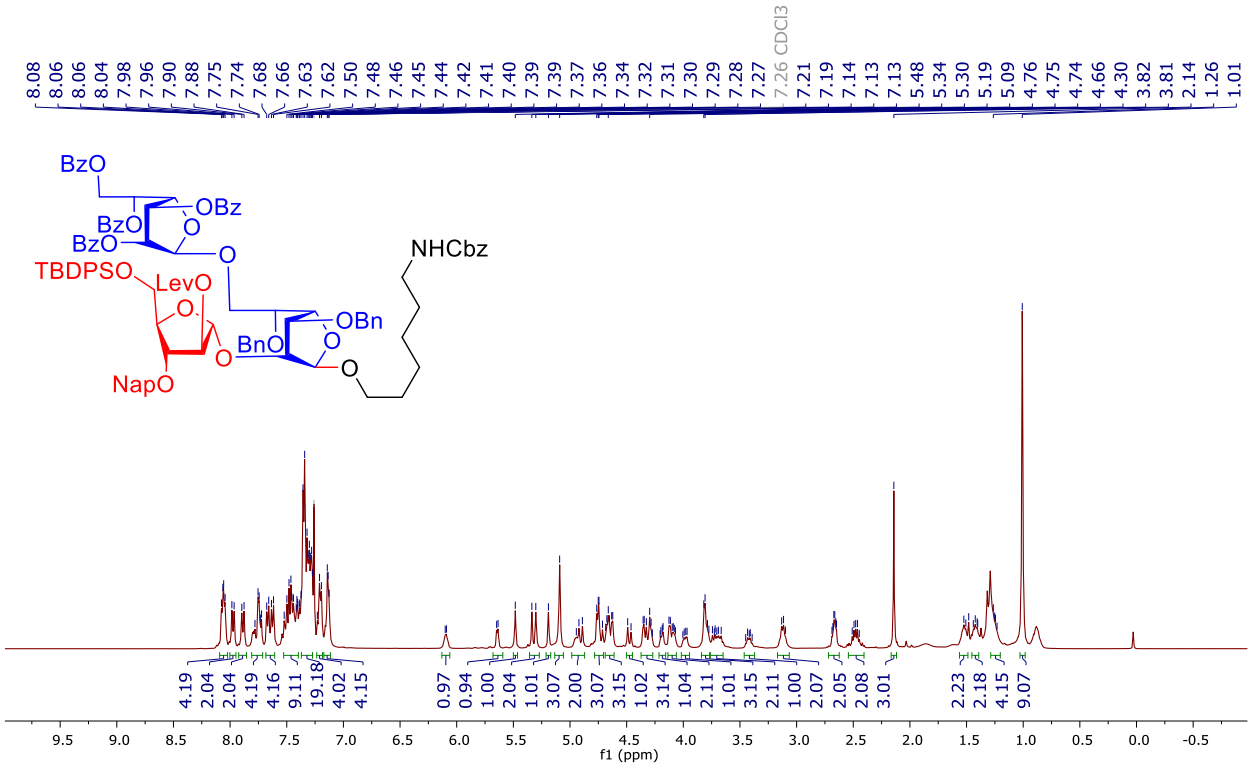
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **7**



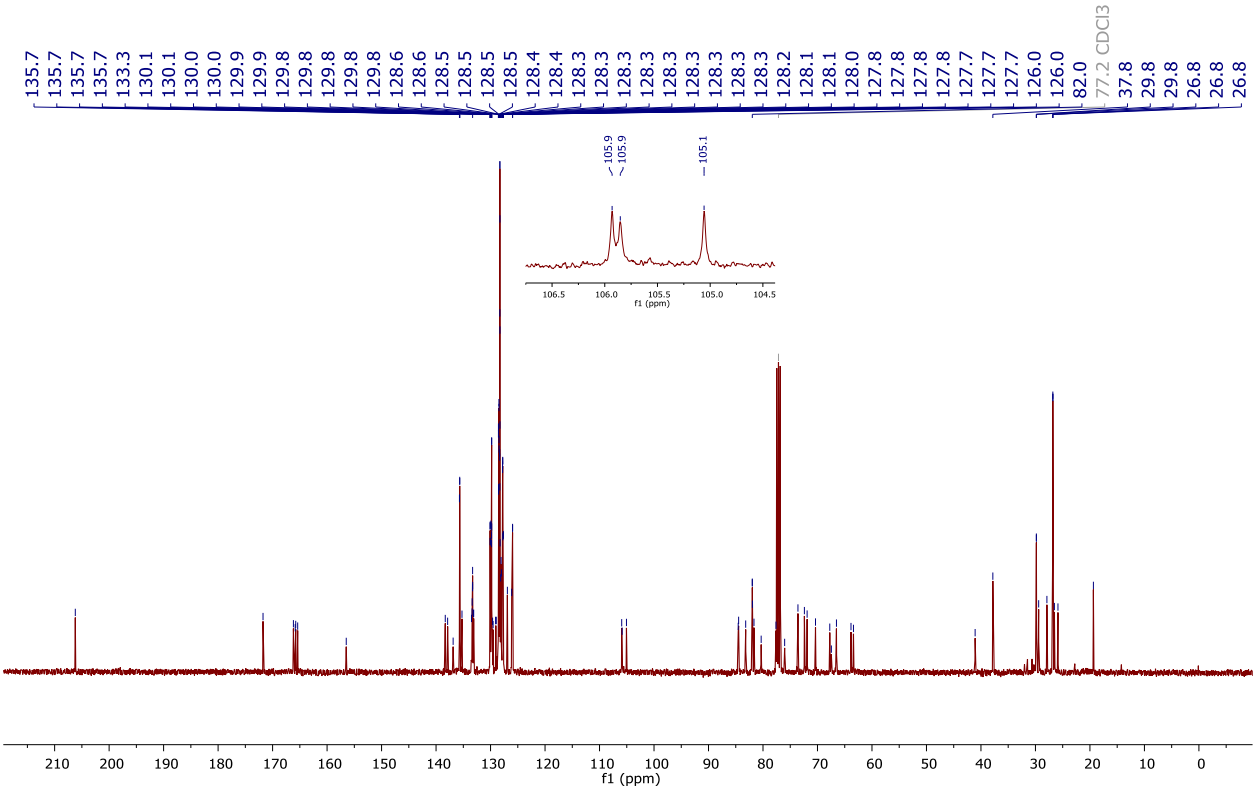
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **7**



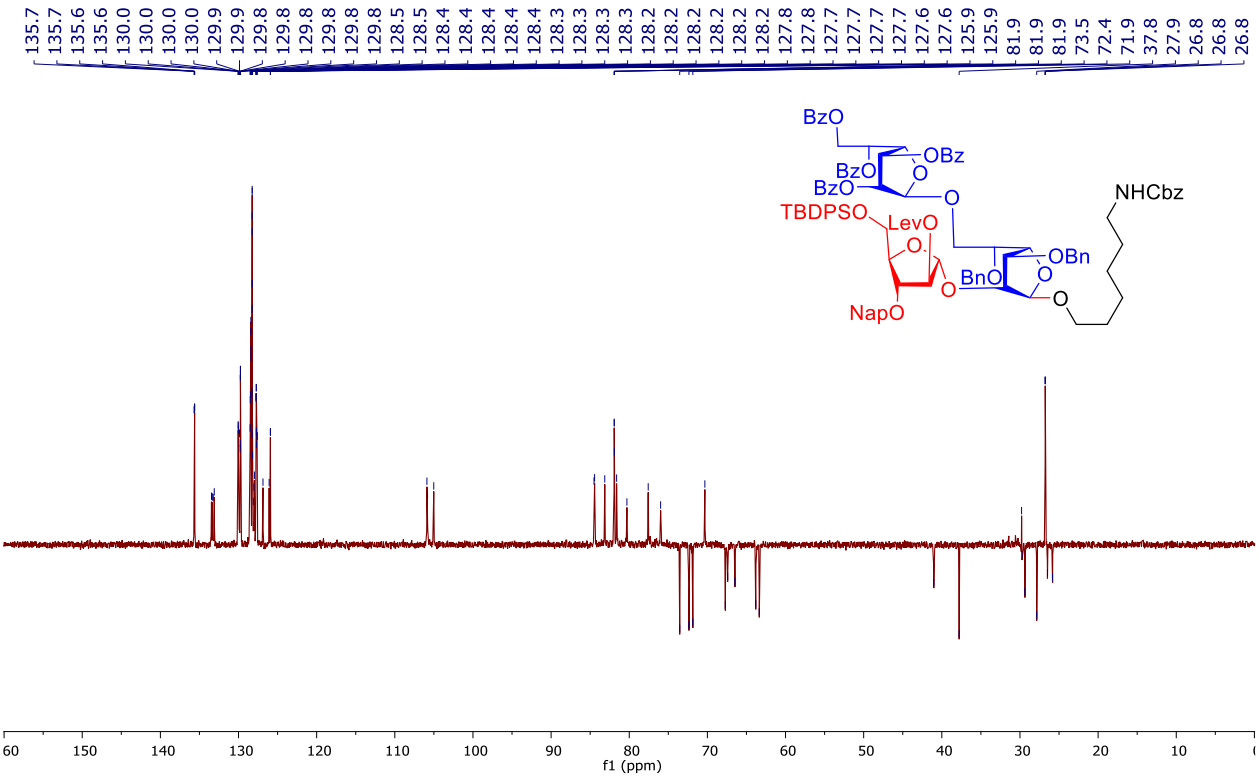
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **28**



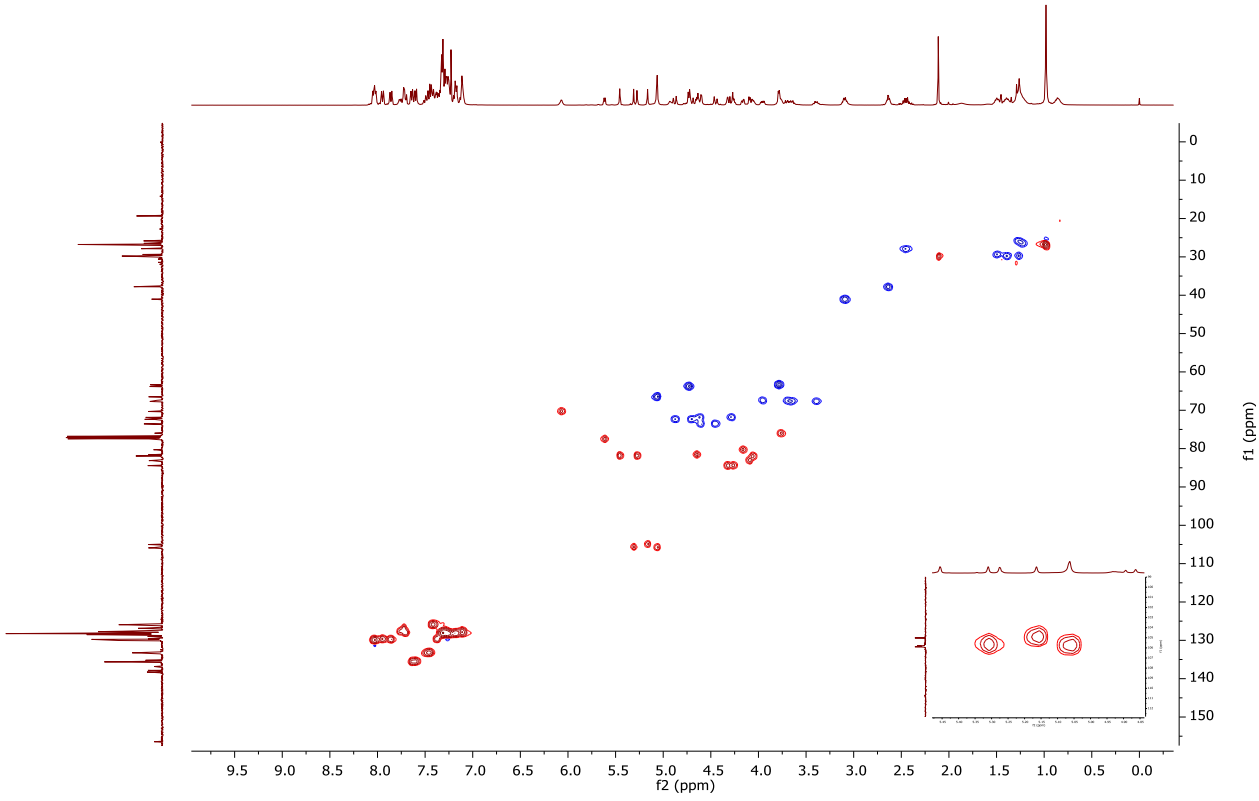
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **28**



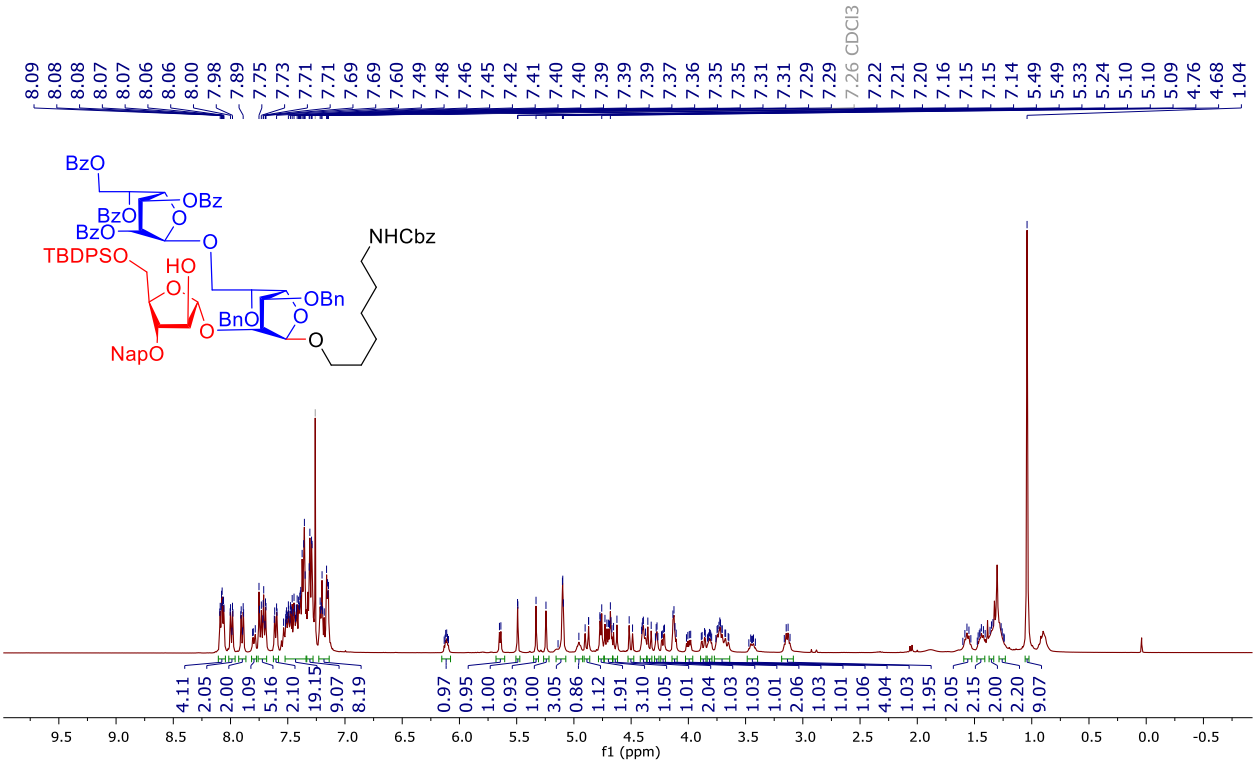
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **28**



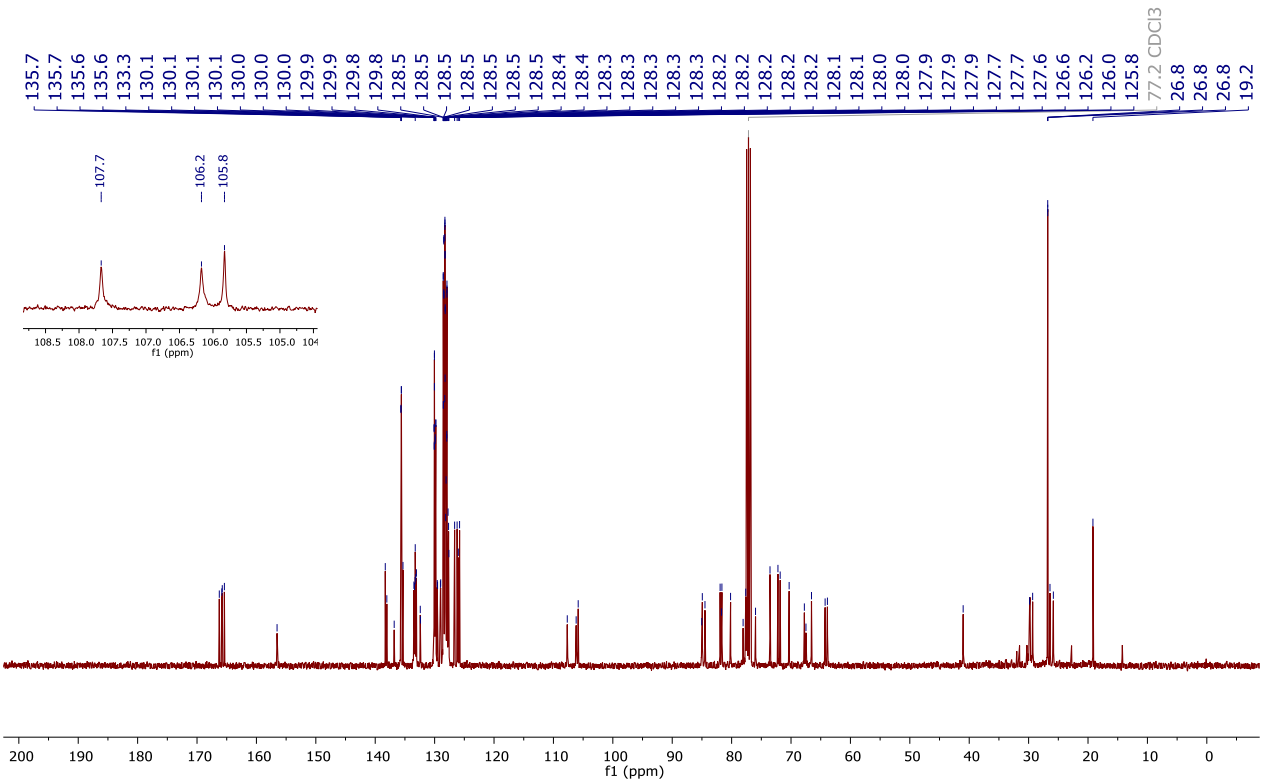
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **28**



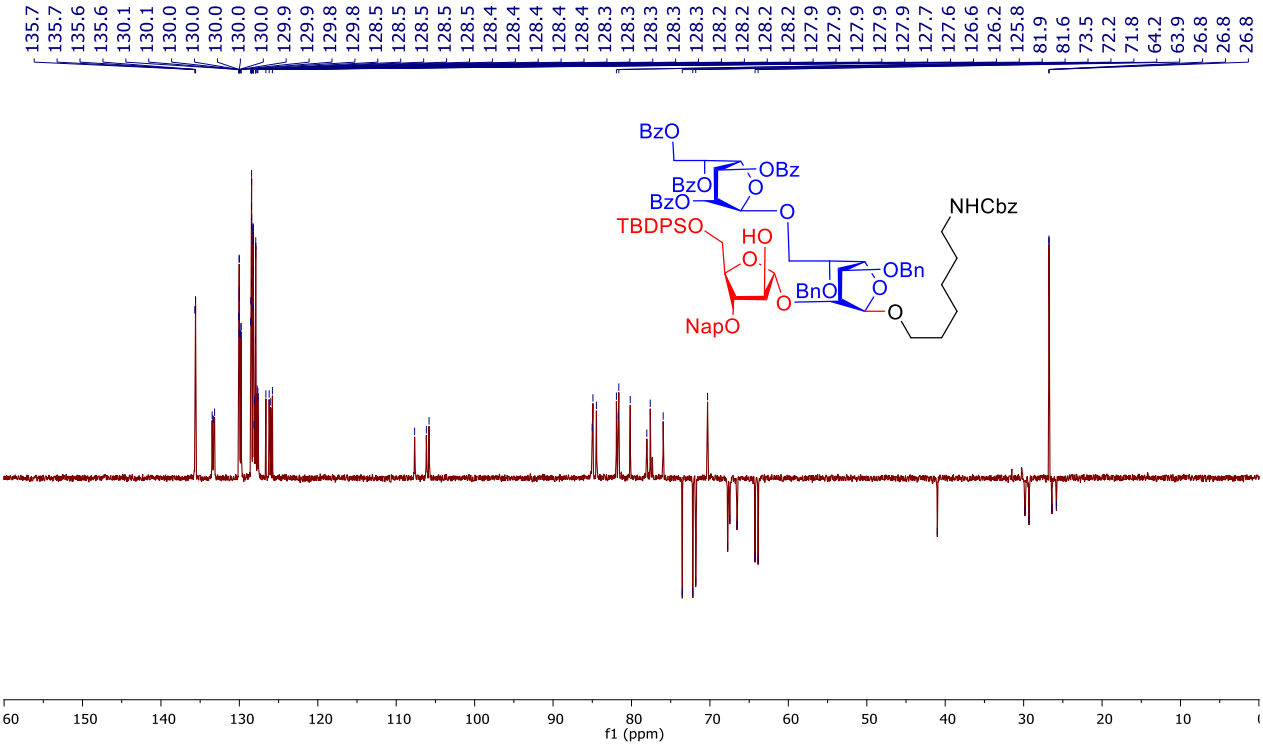
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **5**



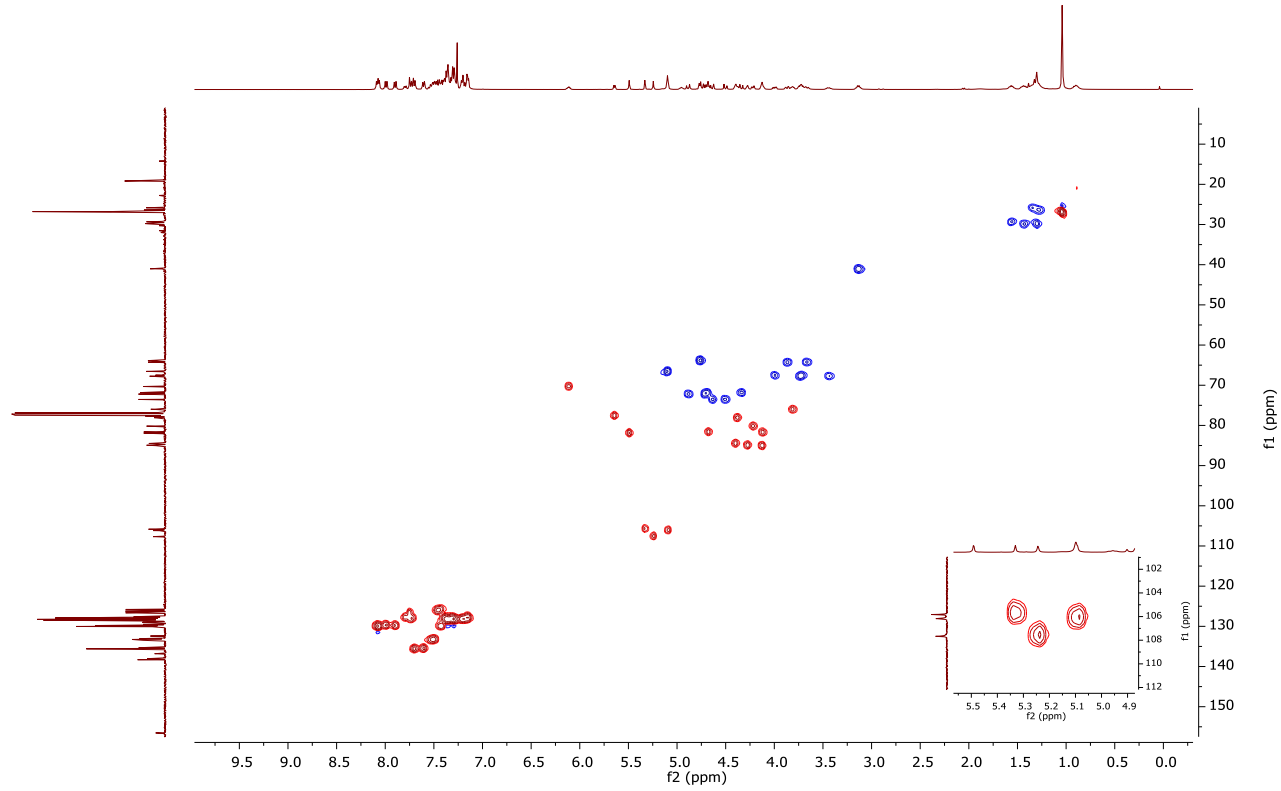
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **5**



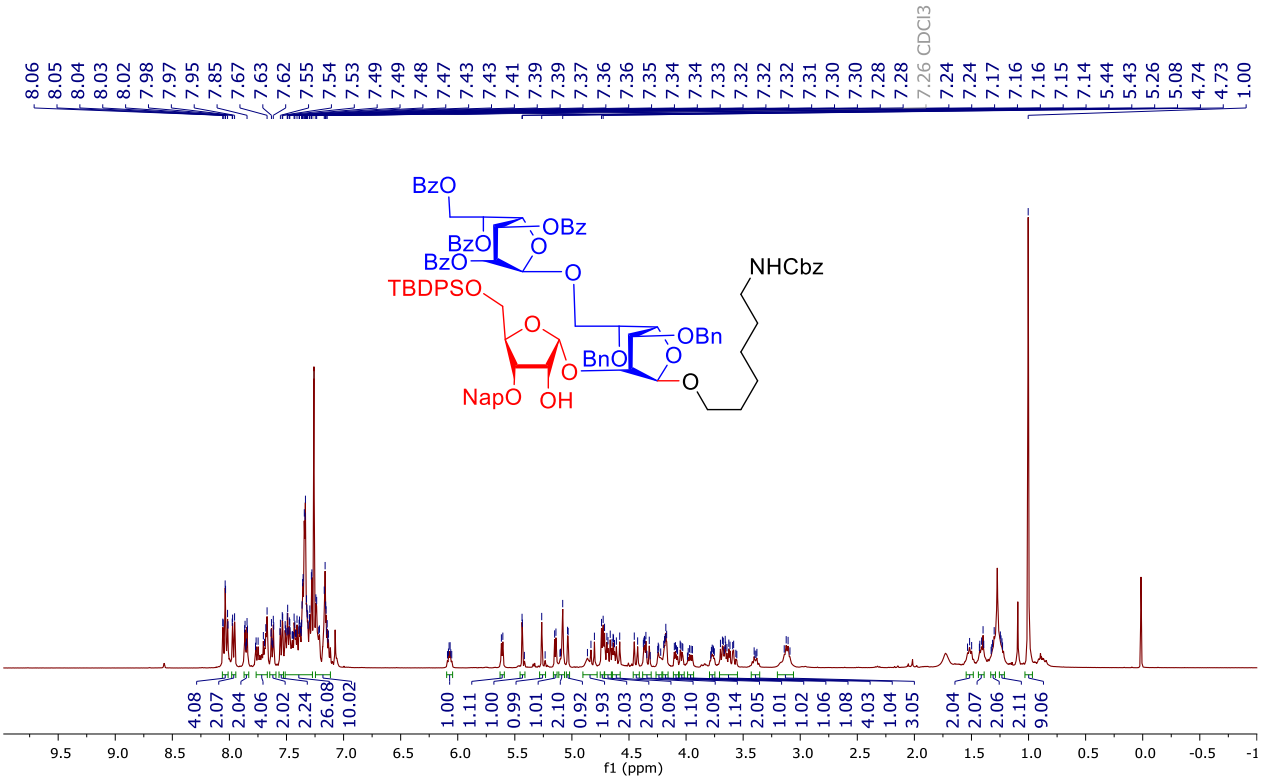
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **5**



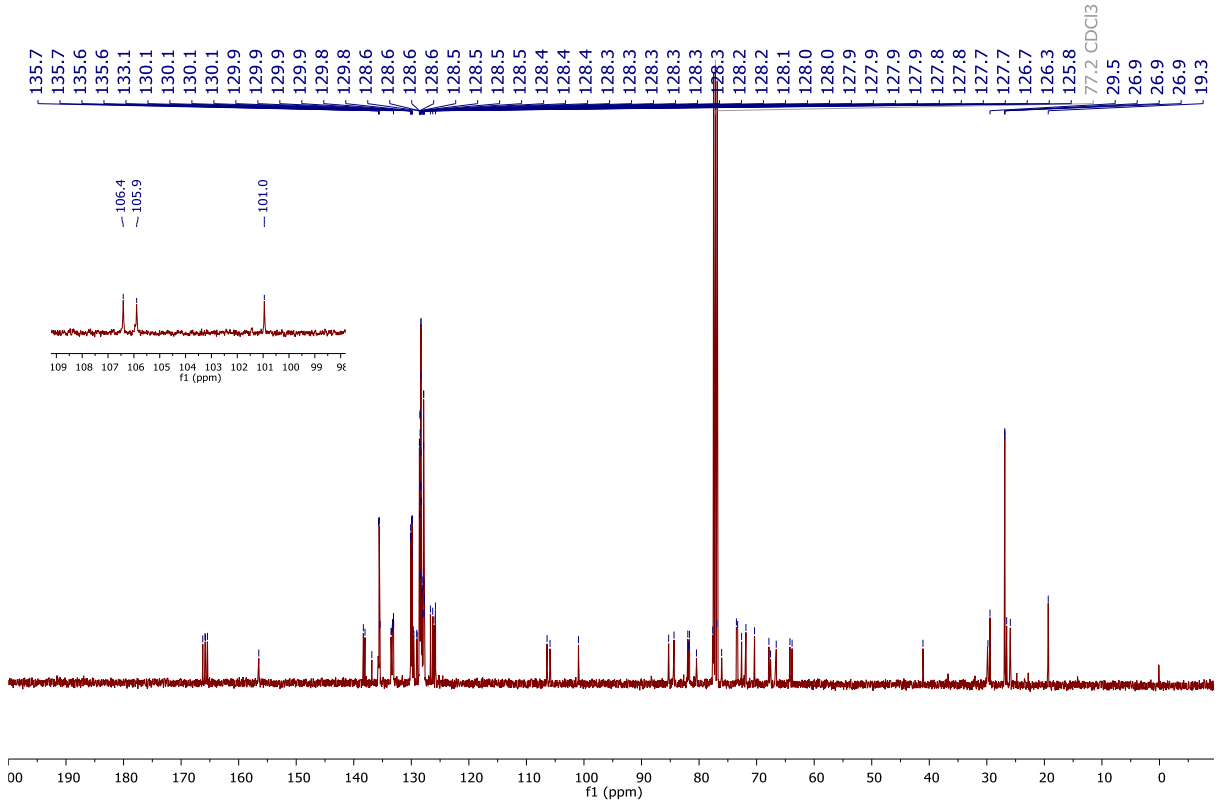
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **5**



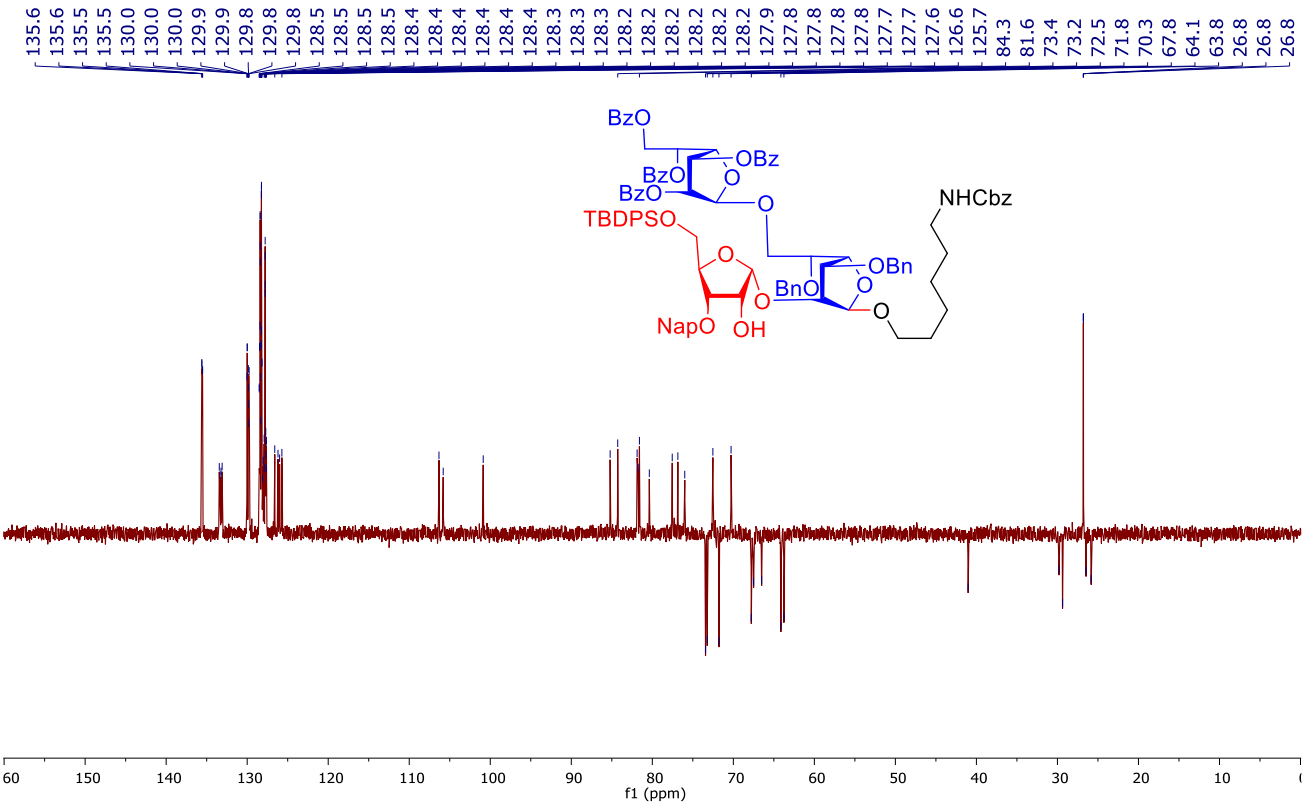
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **29**



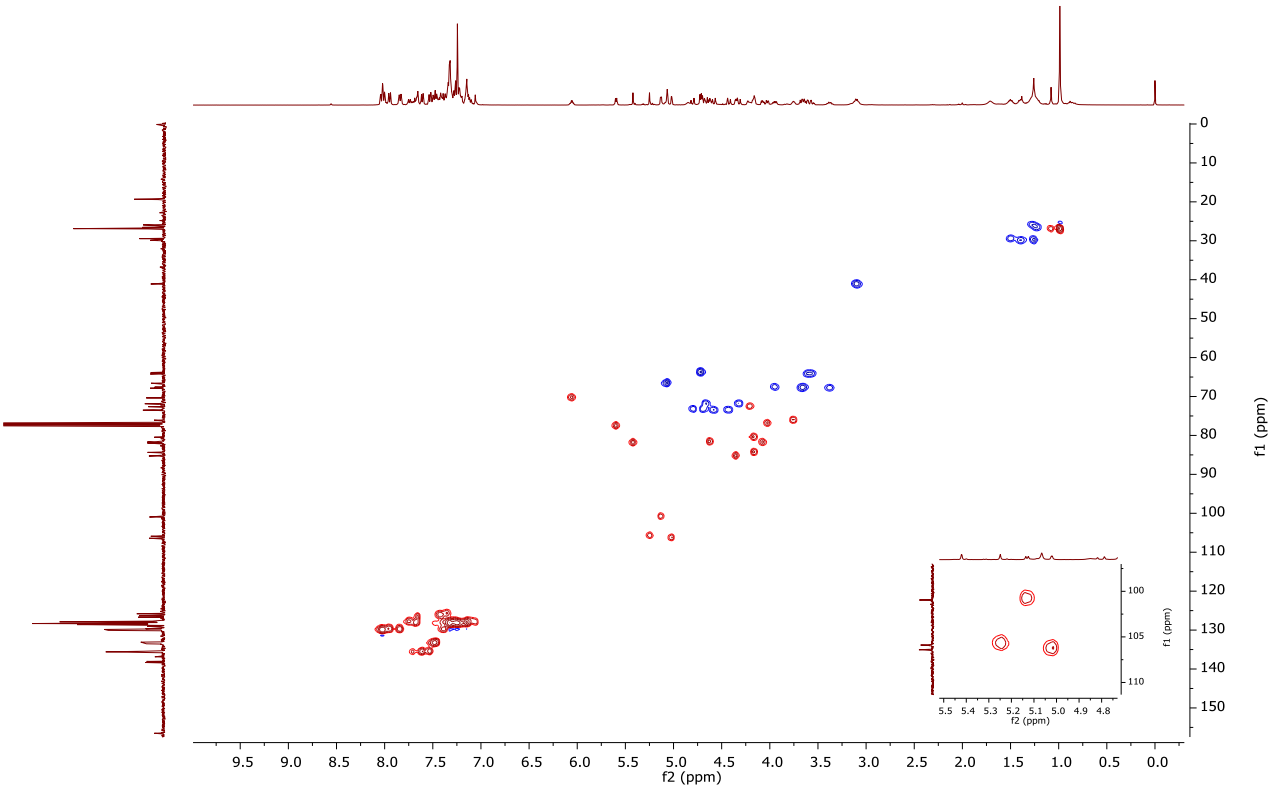
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **29**



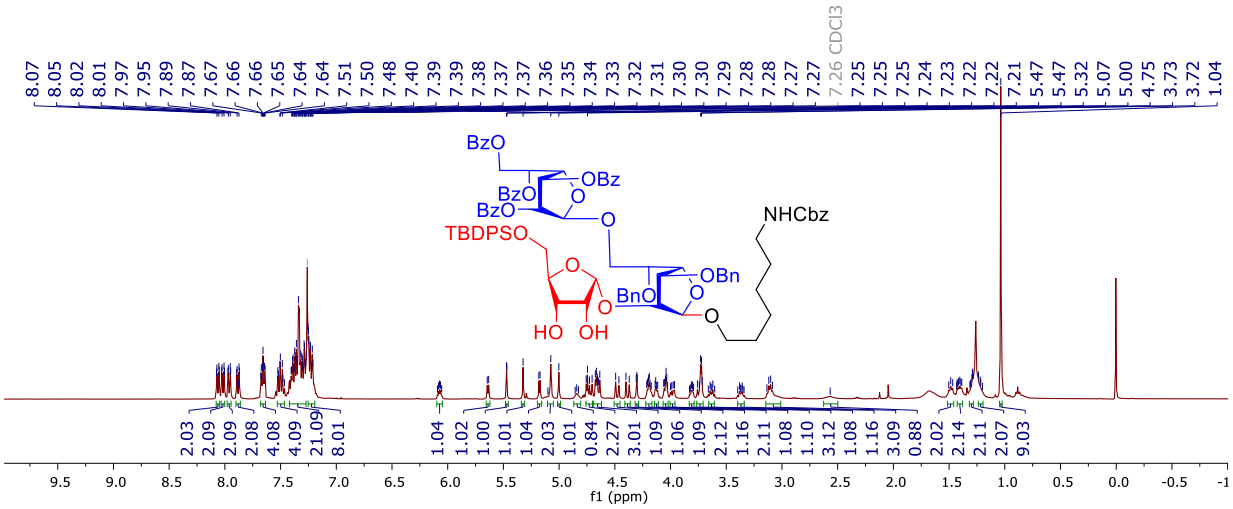
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **29**



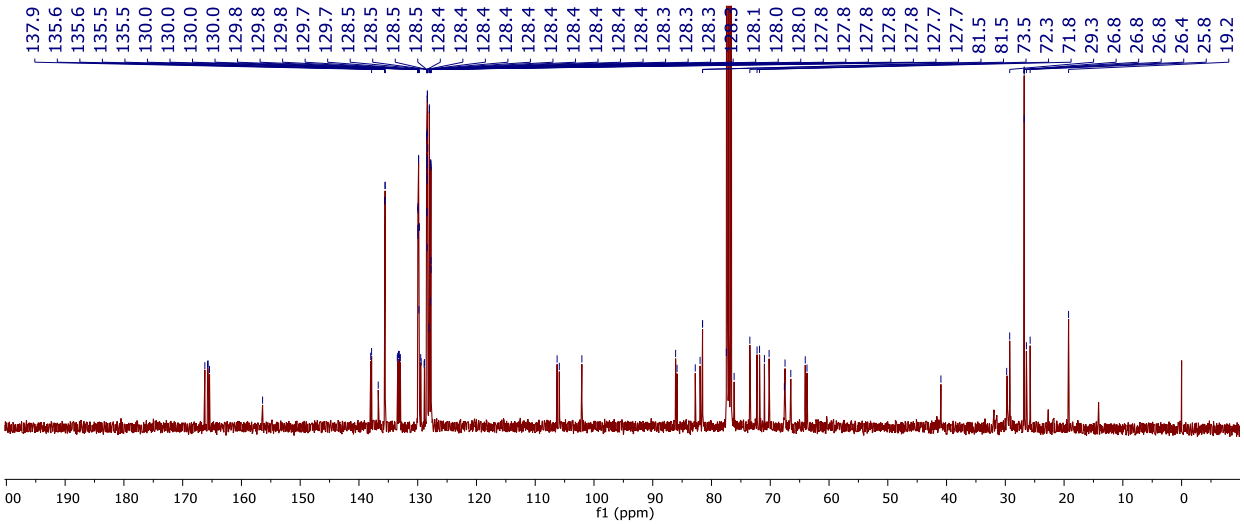
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **29**



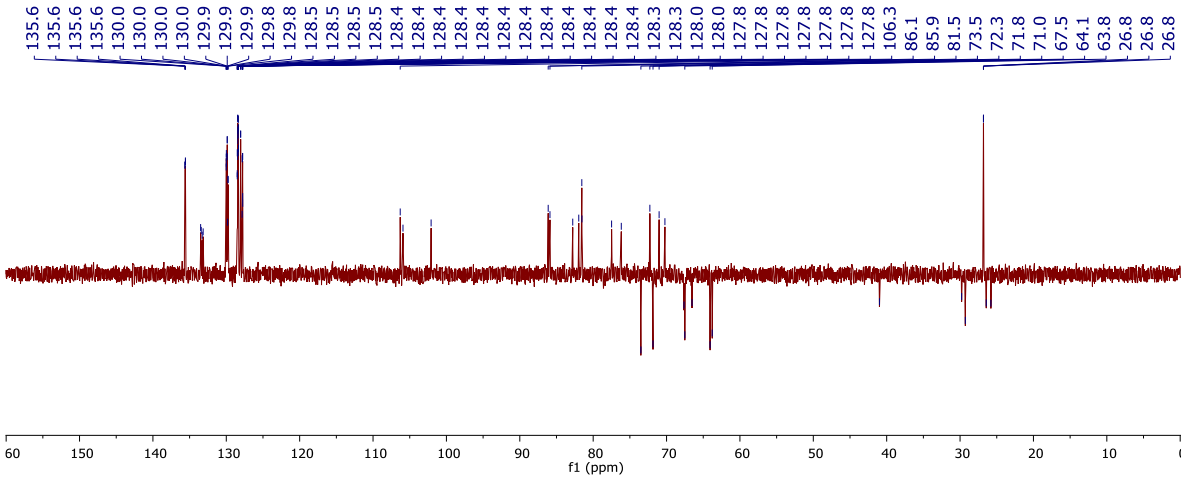
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **4**



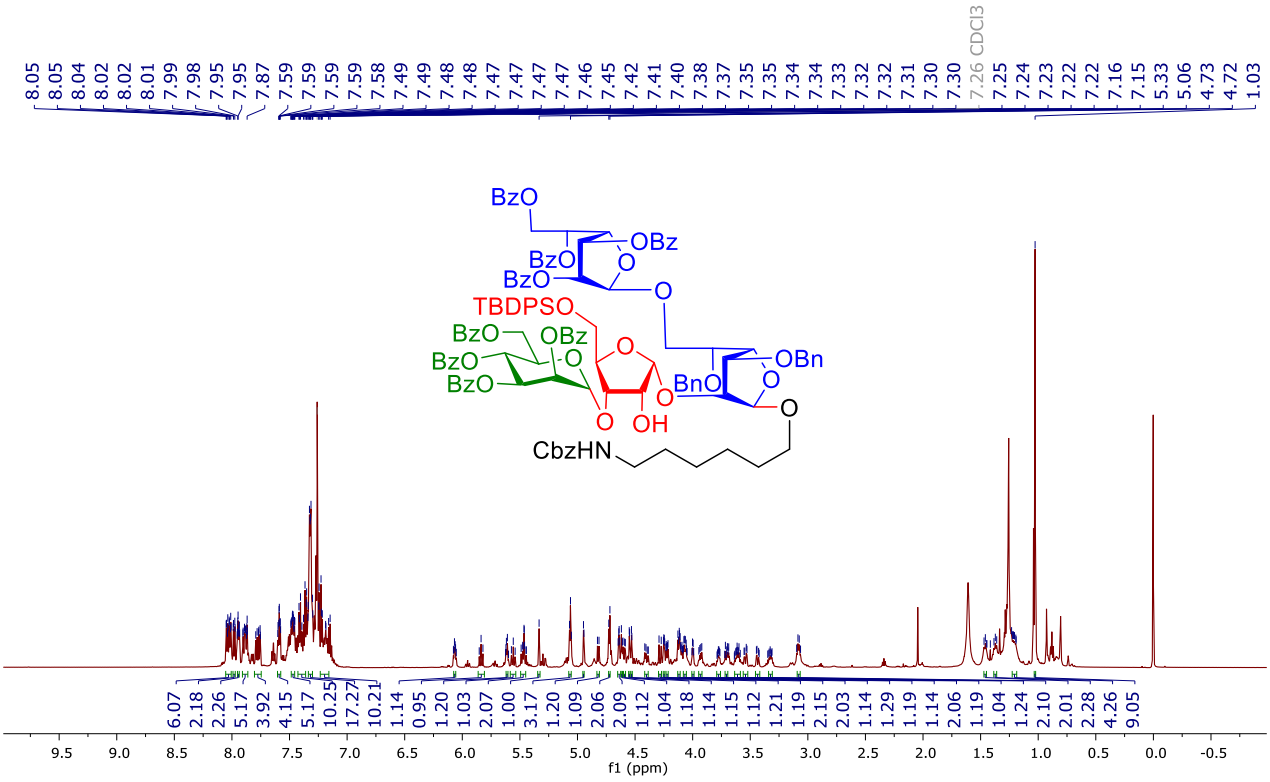
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **4**



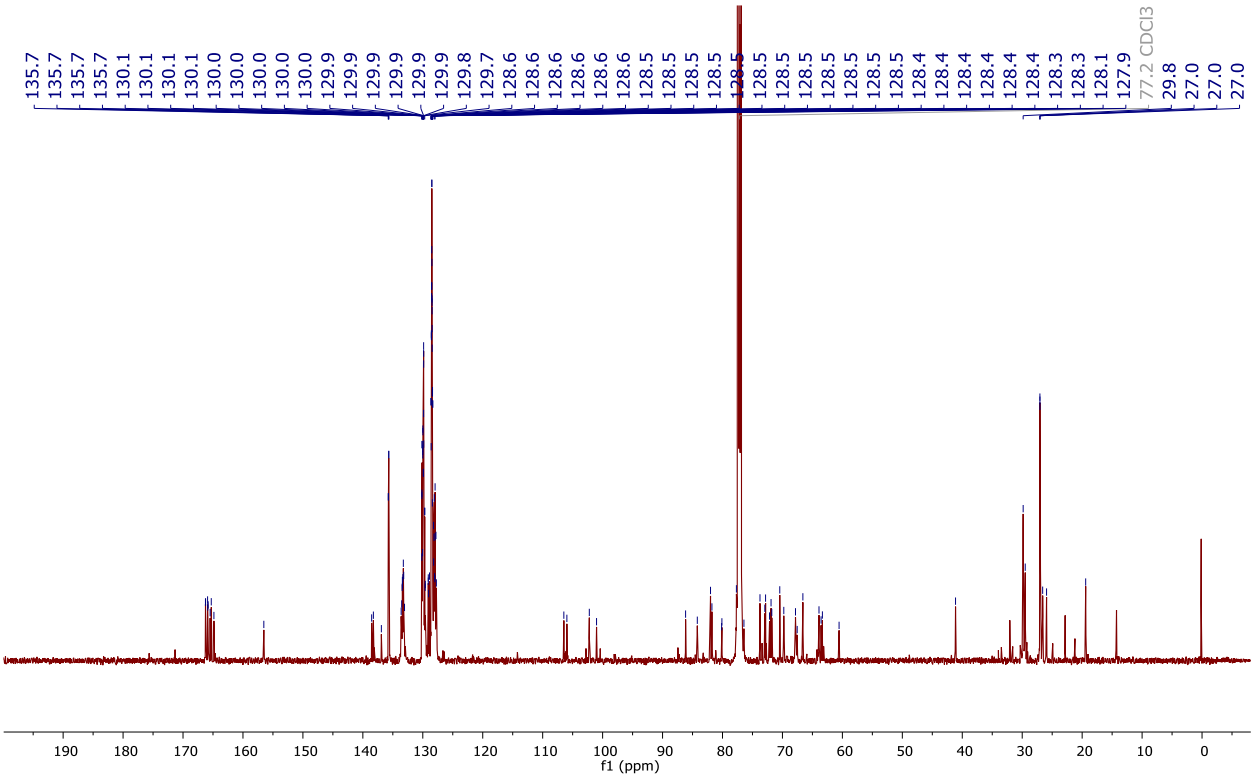
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **4**



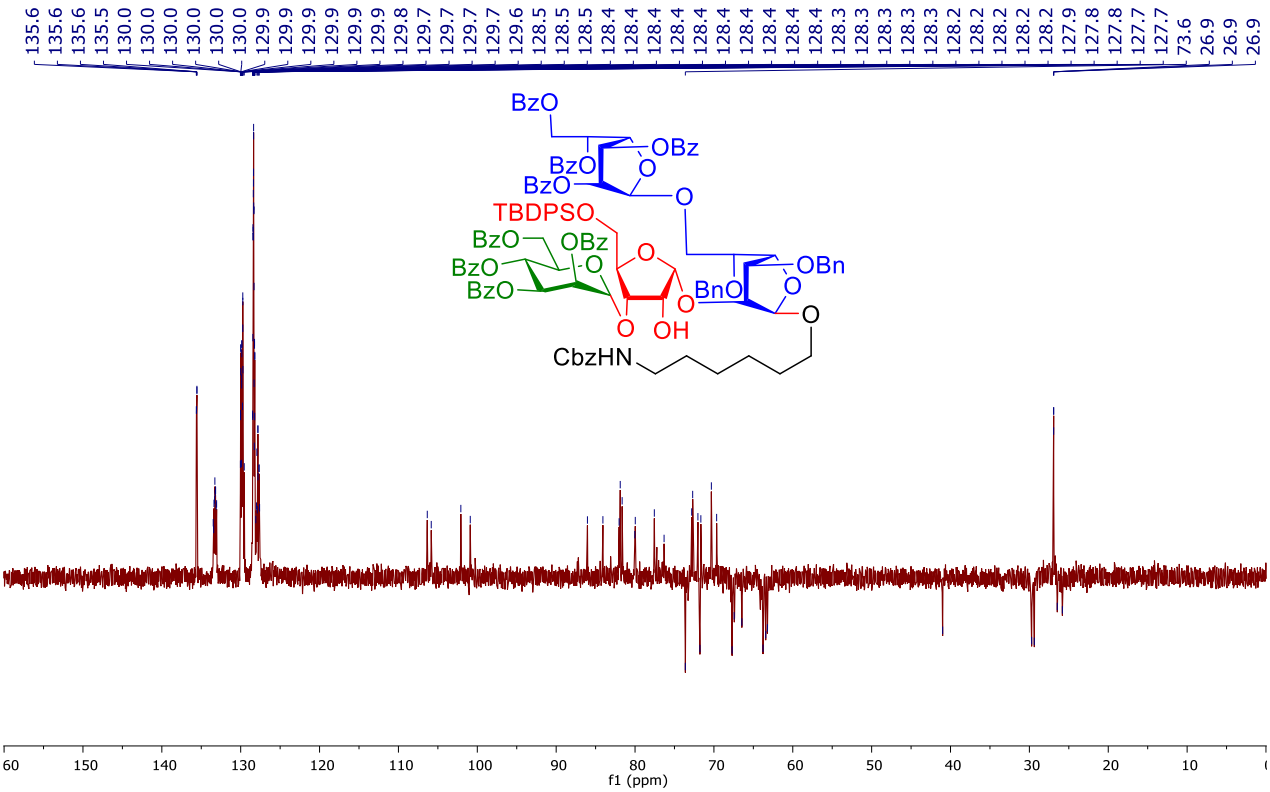
^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of compound **30**



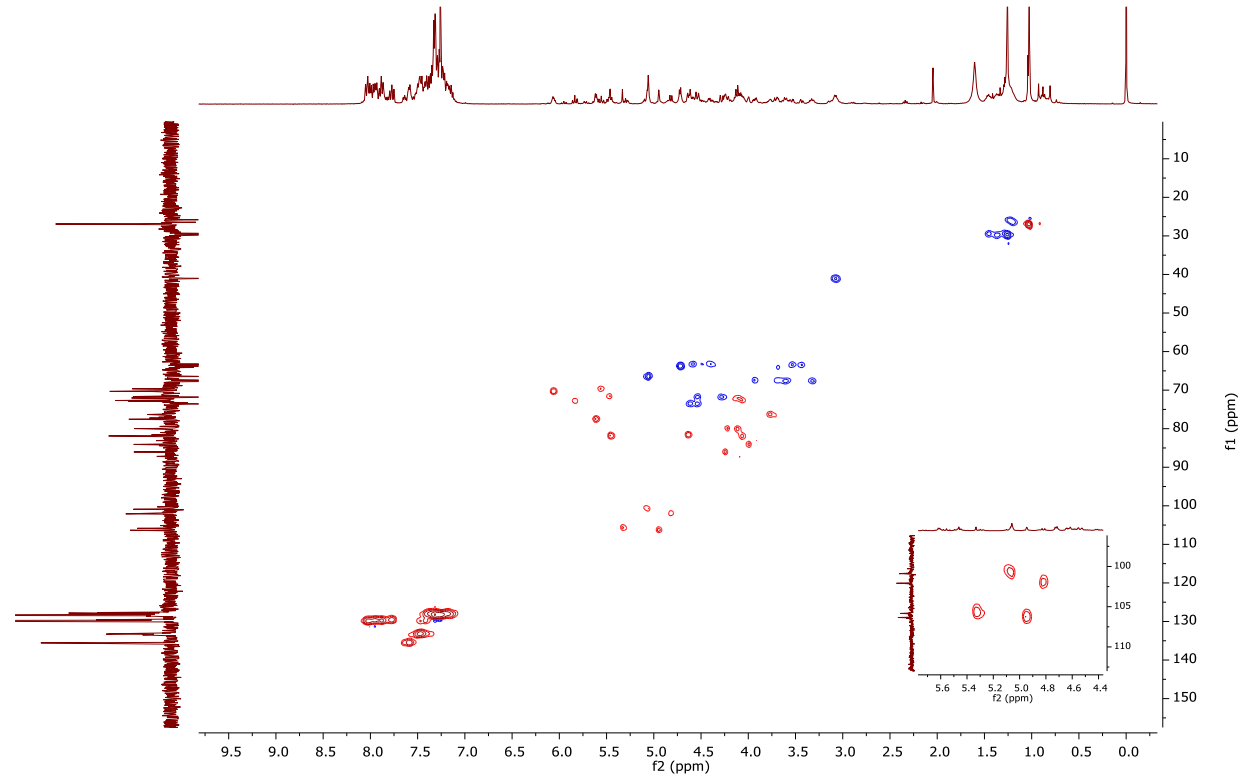
^{13}C NMR Spectrum (151 MHz, $CDCl_3$) of compound **30**



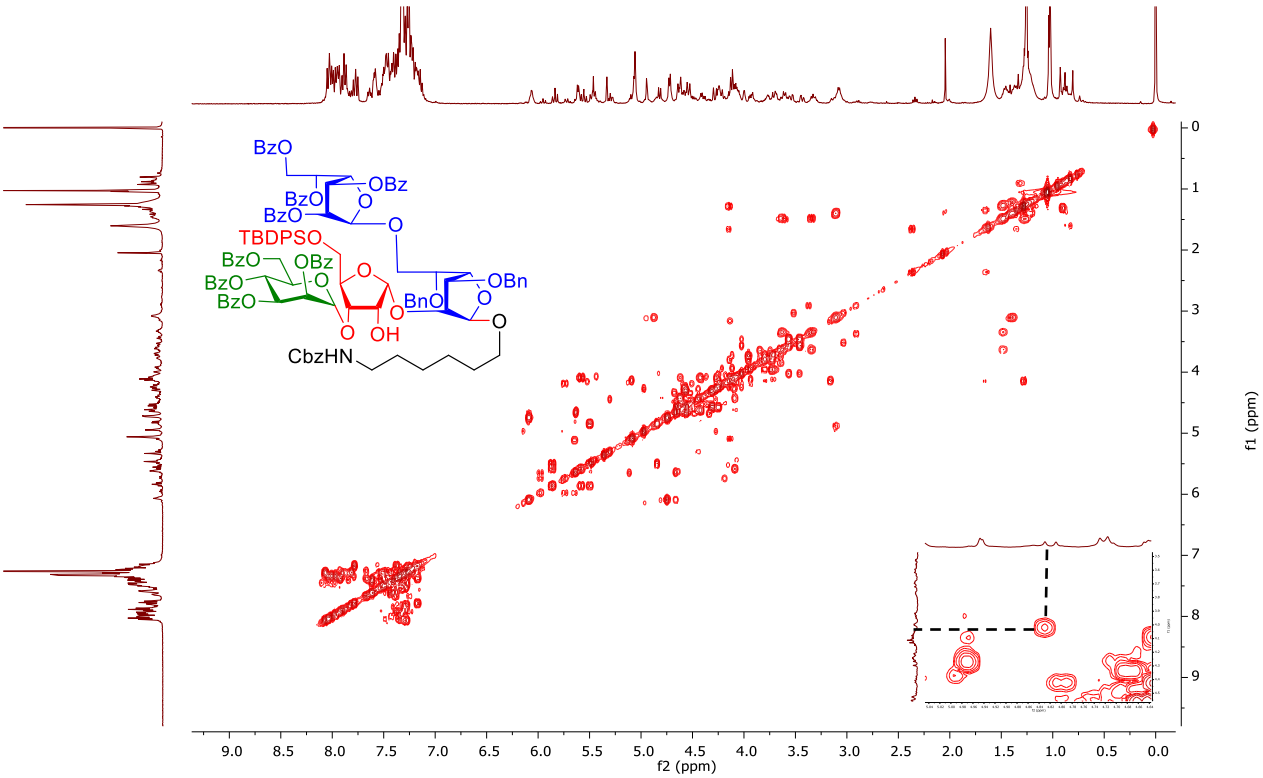
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **30**



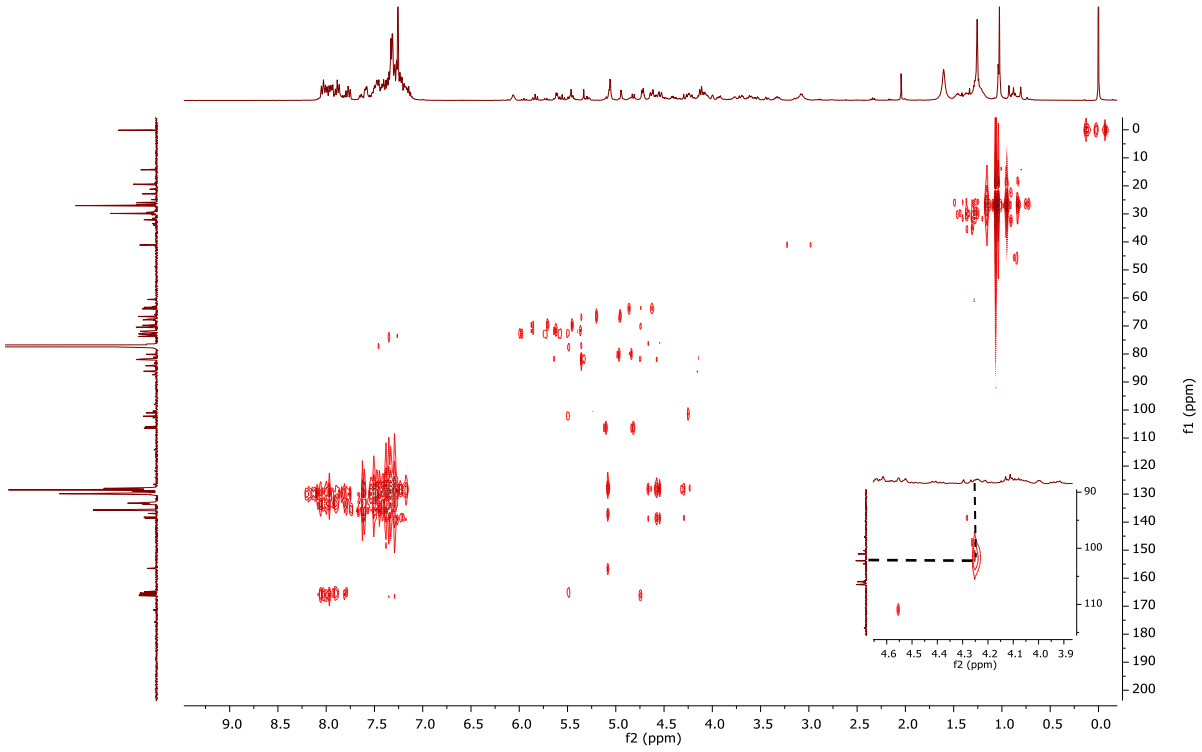
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **30**



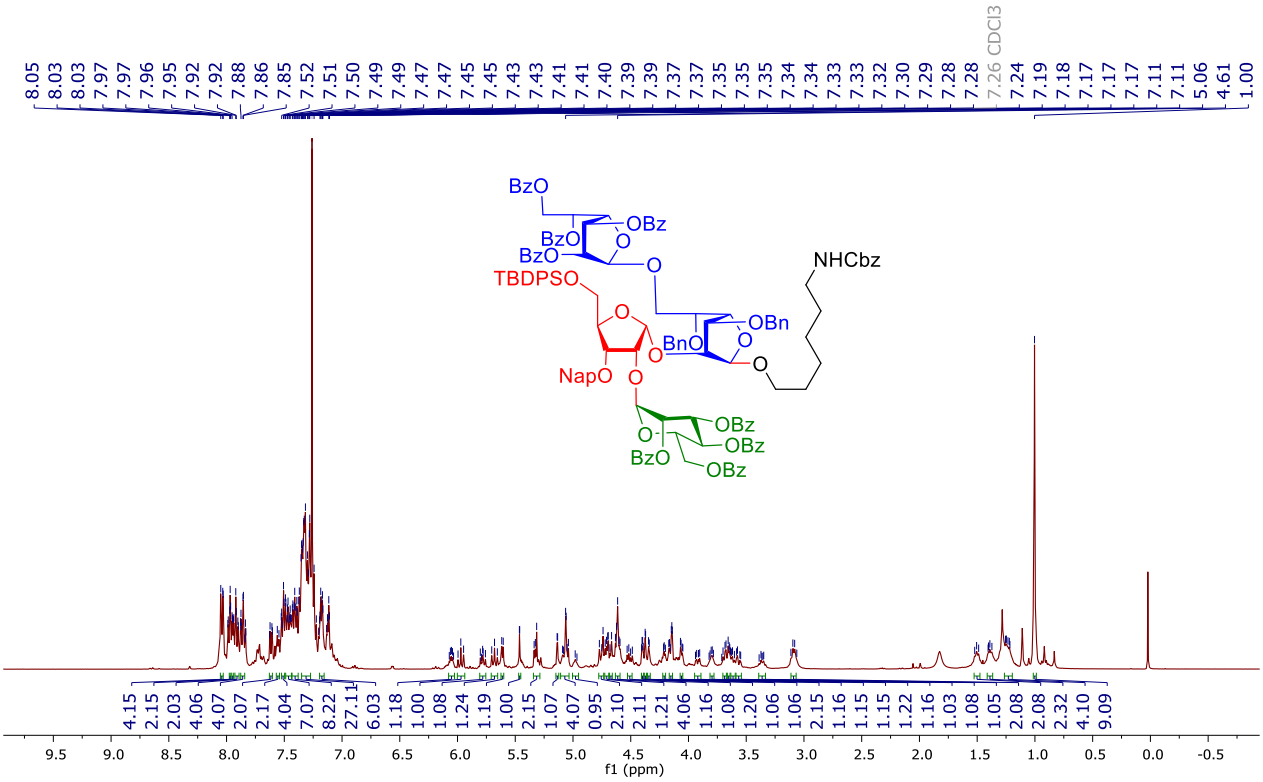
^{1}H-^{1}H COSY NMR Spectrum (600 MHz, $CDCl_3$) of compound **30**



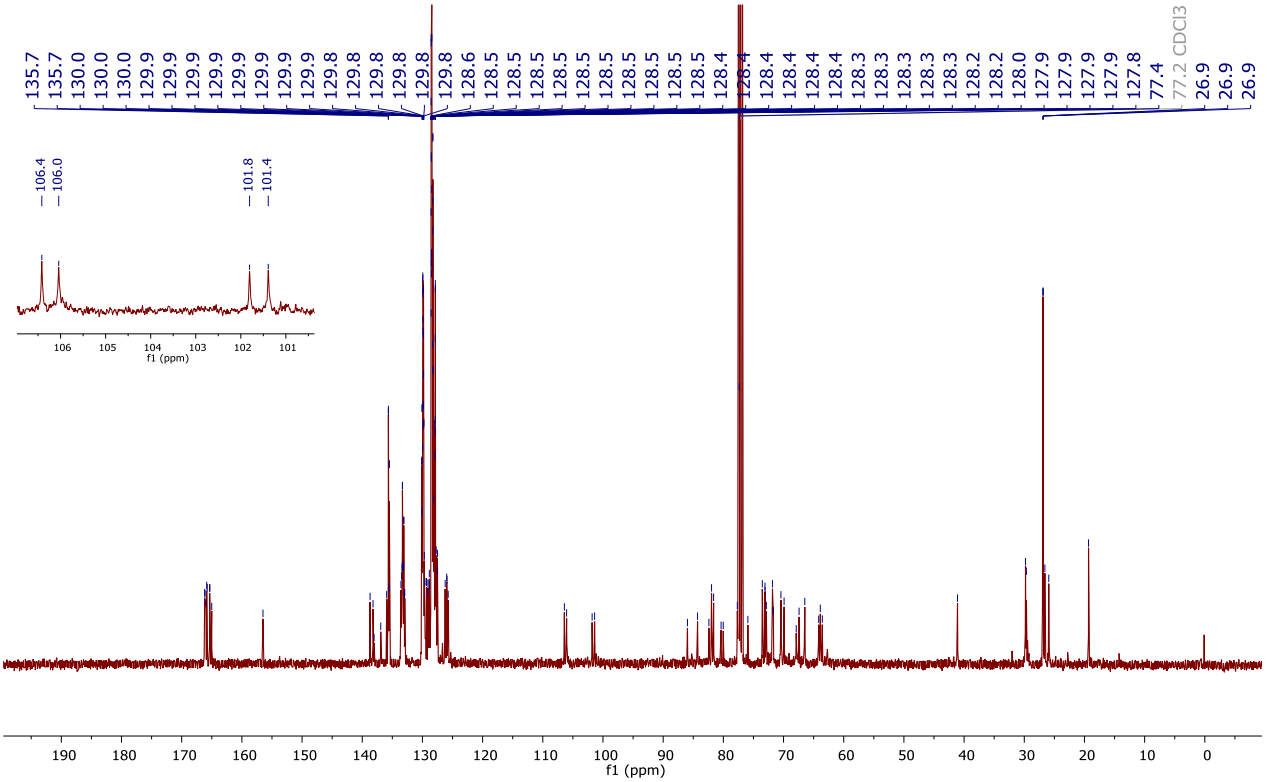
^{1}H-^{13}C HMBC NMR Spectrum (600 MHz, 151 MHz, $CDCl_3$) of compound **30**



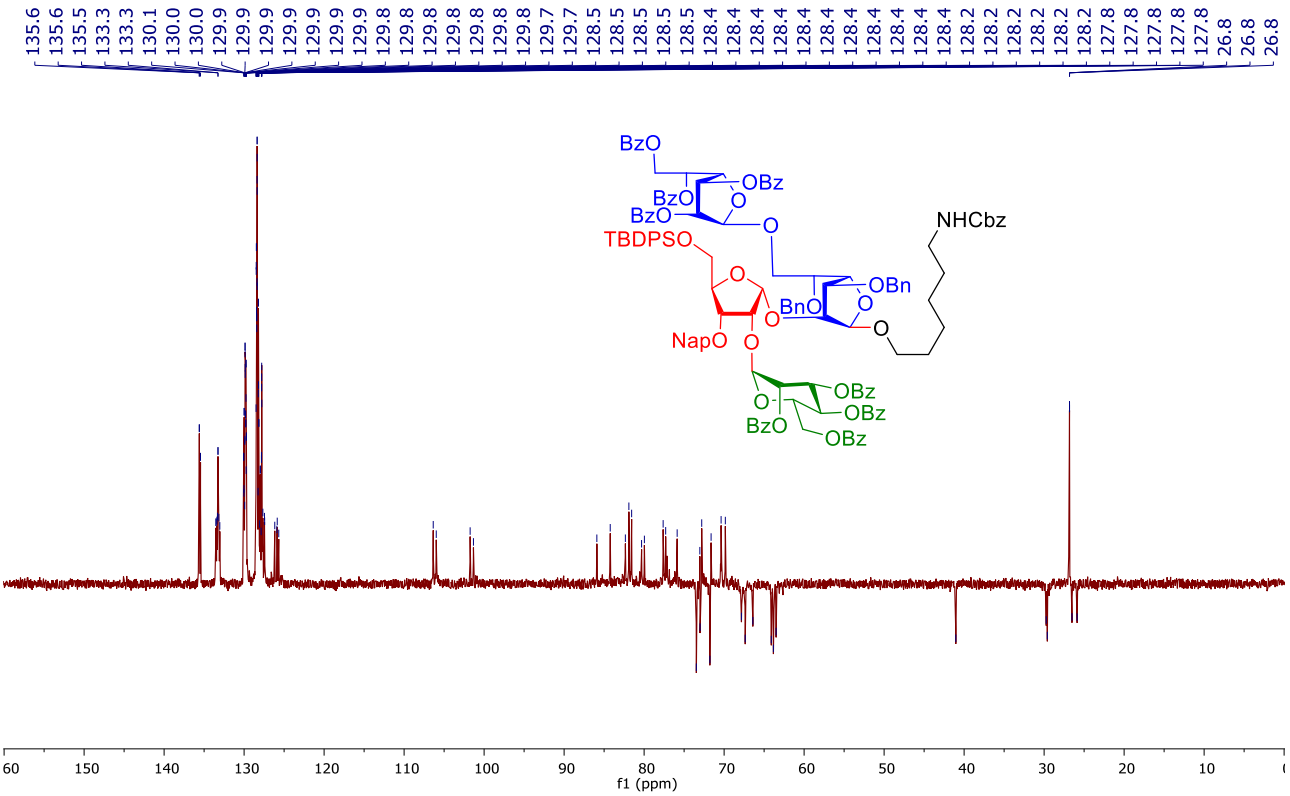
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **31**



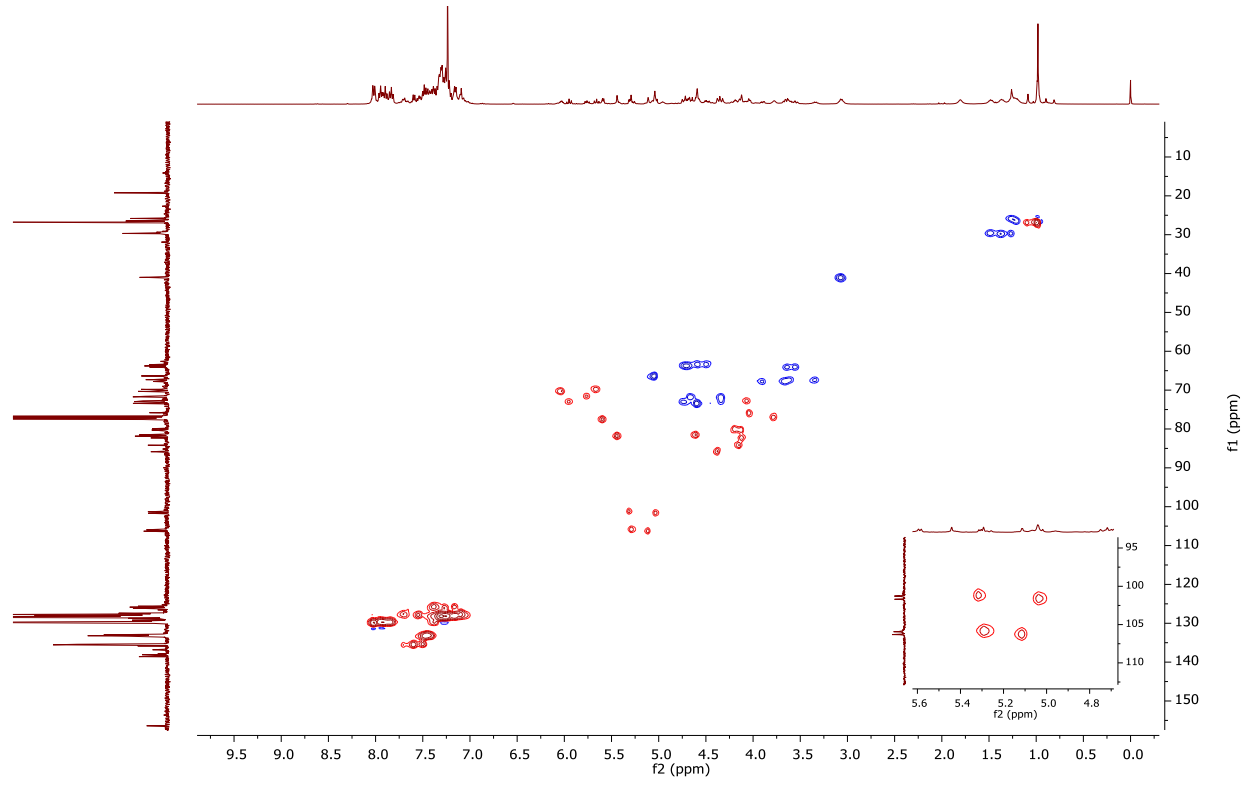
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **31**



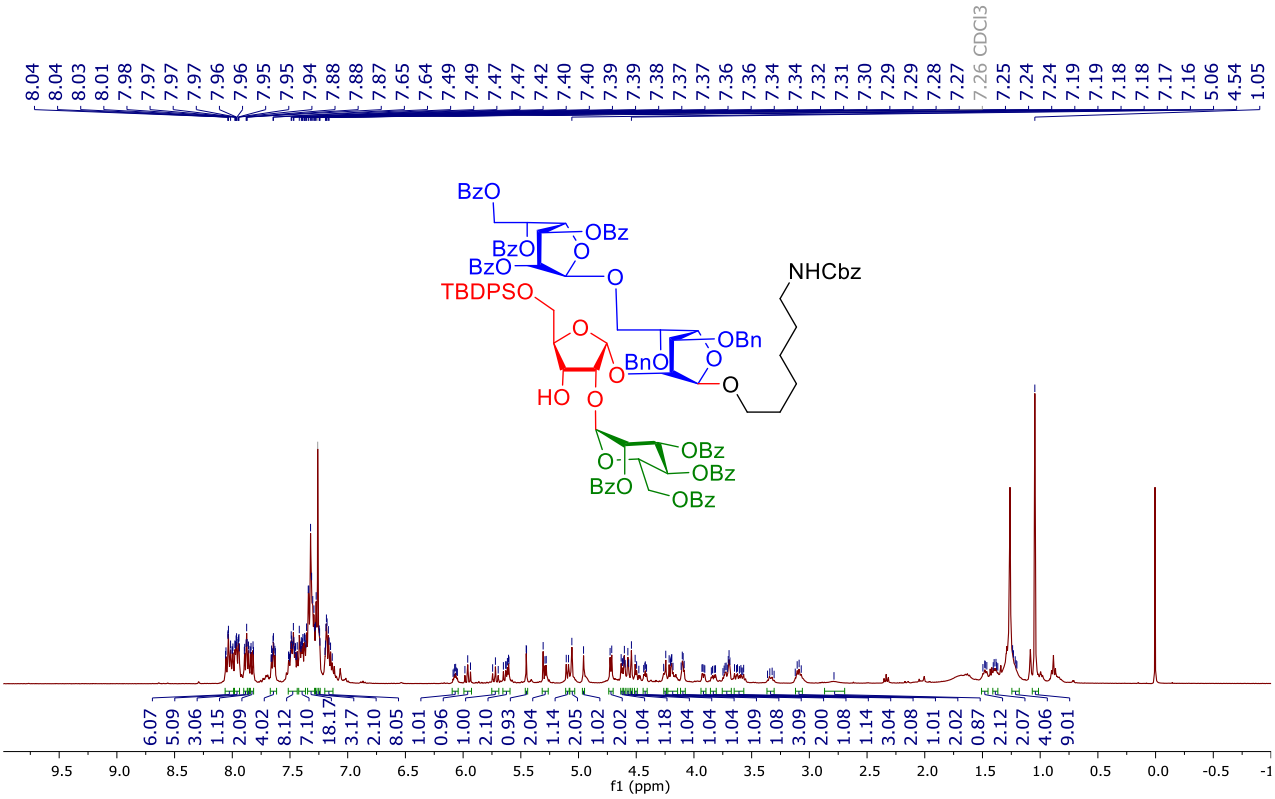
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **31**



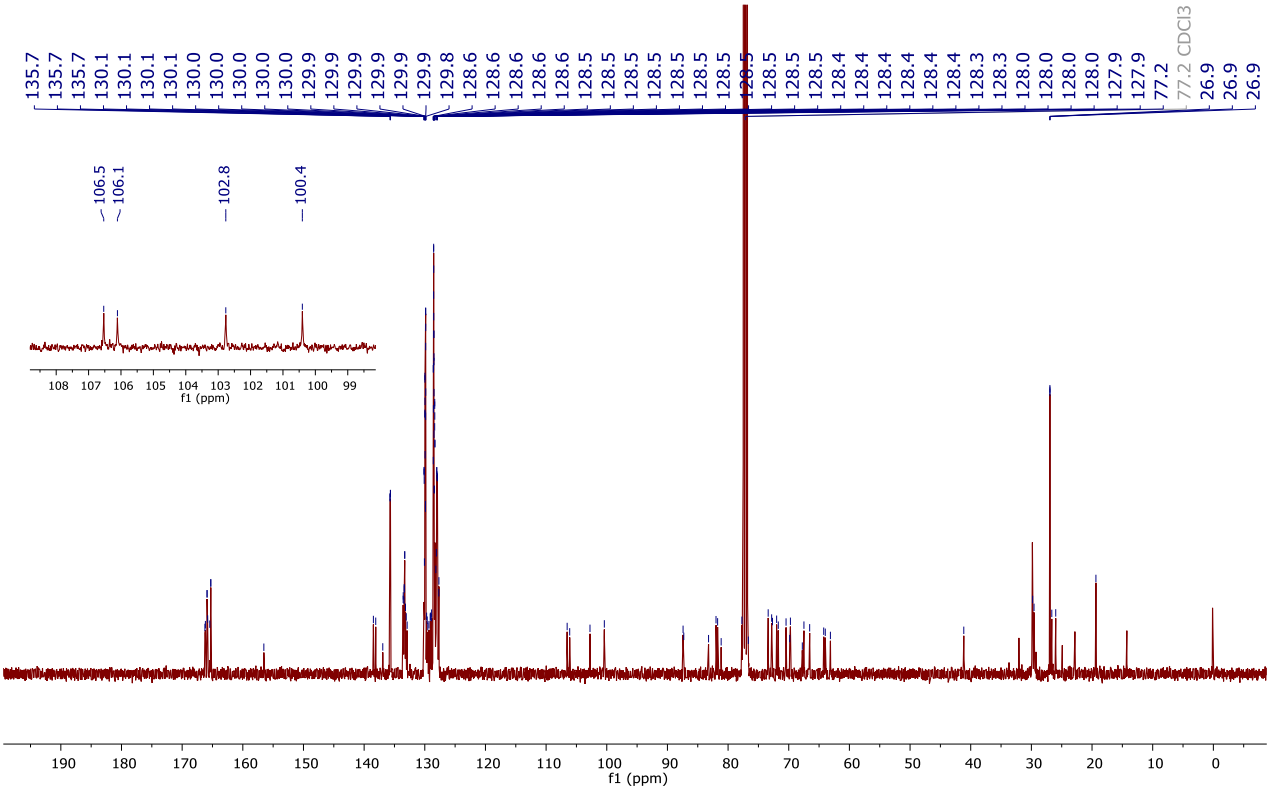
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **31**



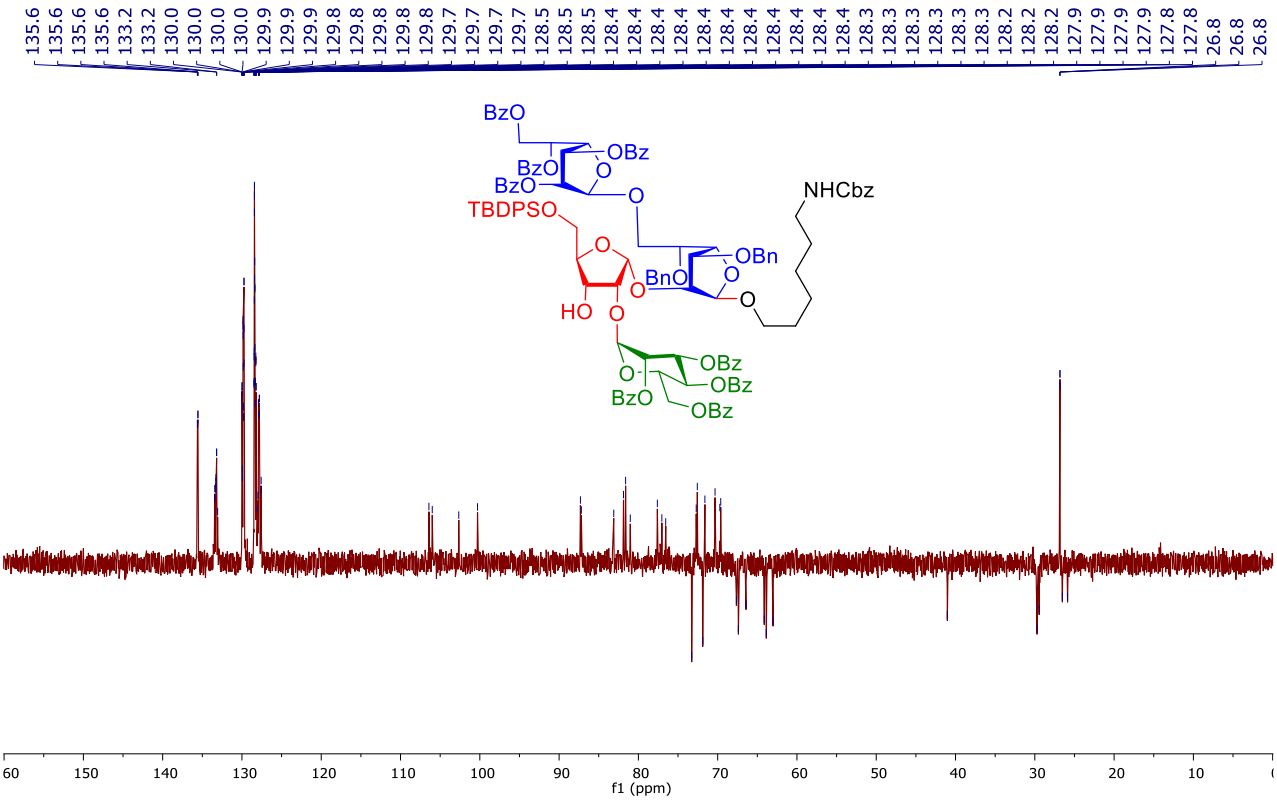
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **32**



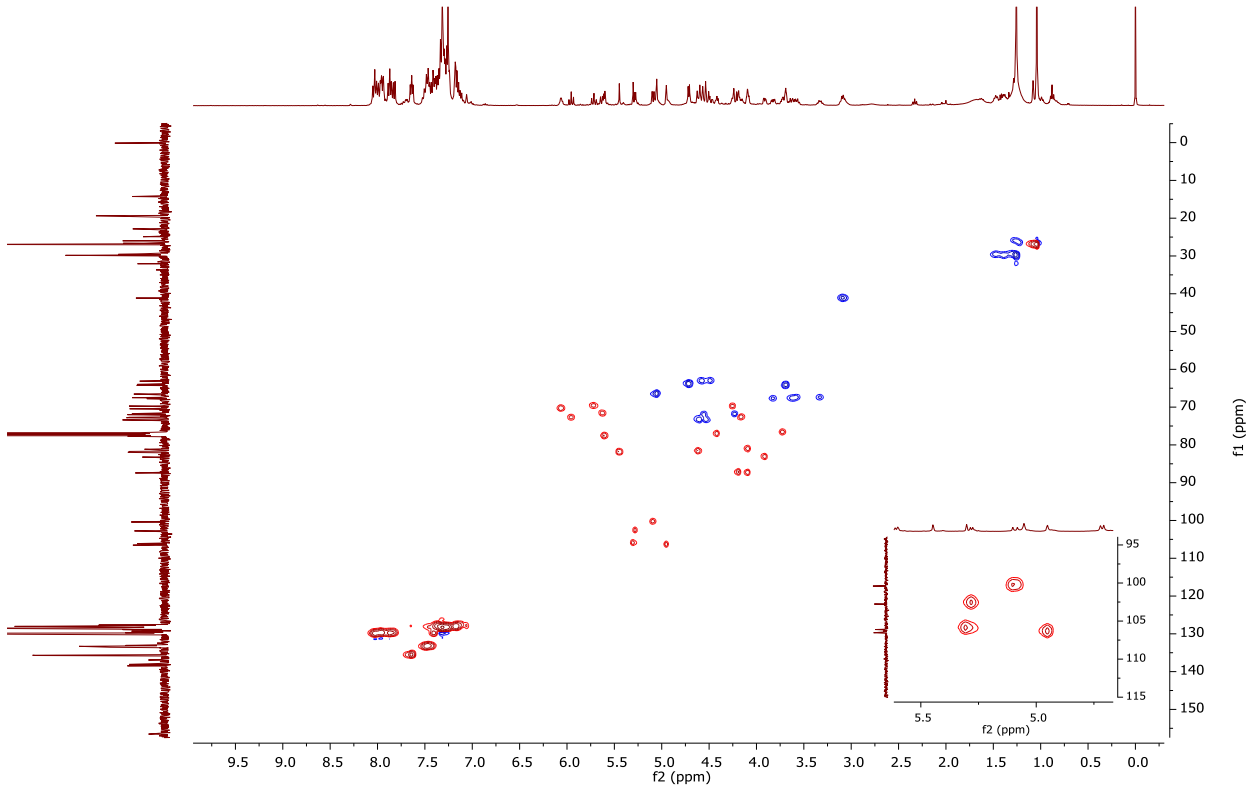
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **32**



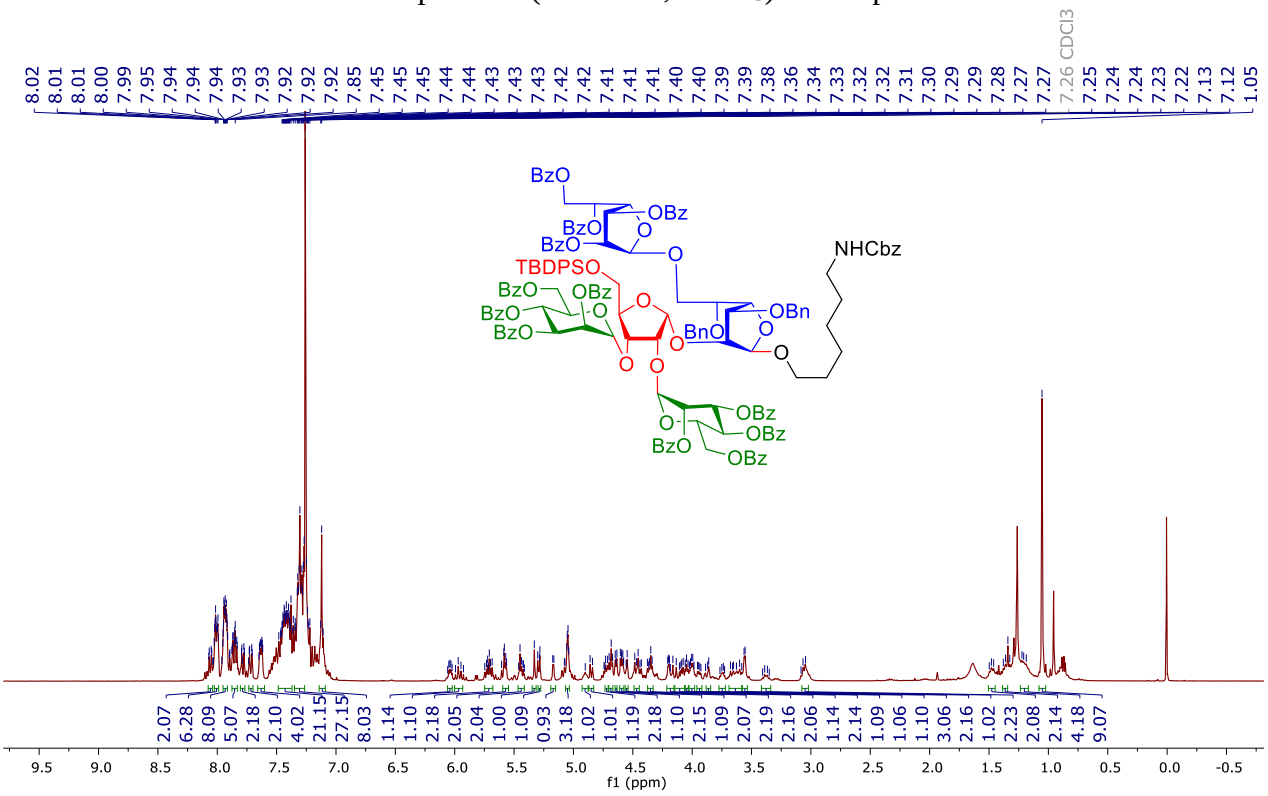
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **32**



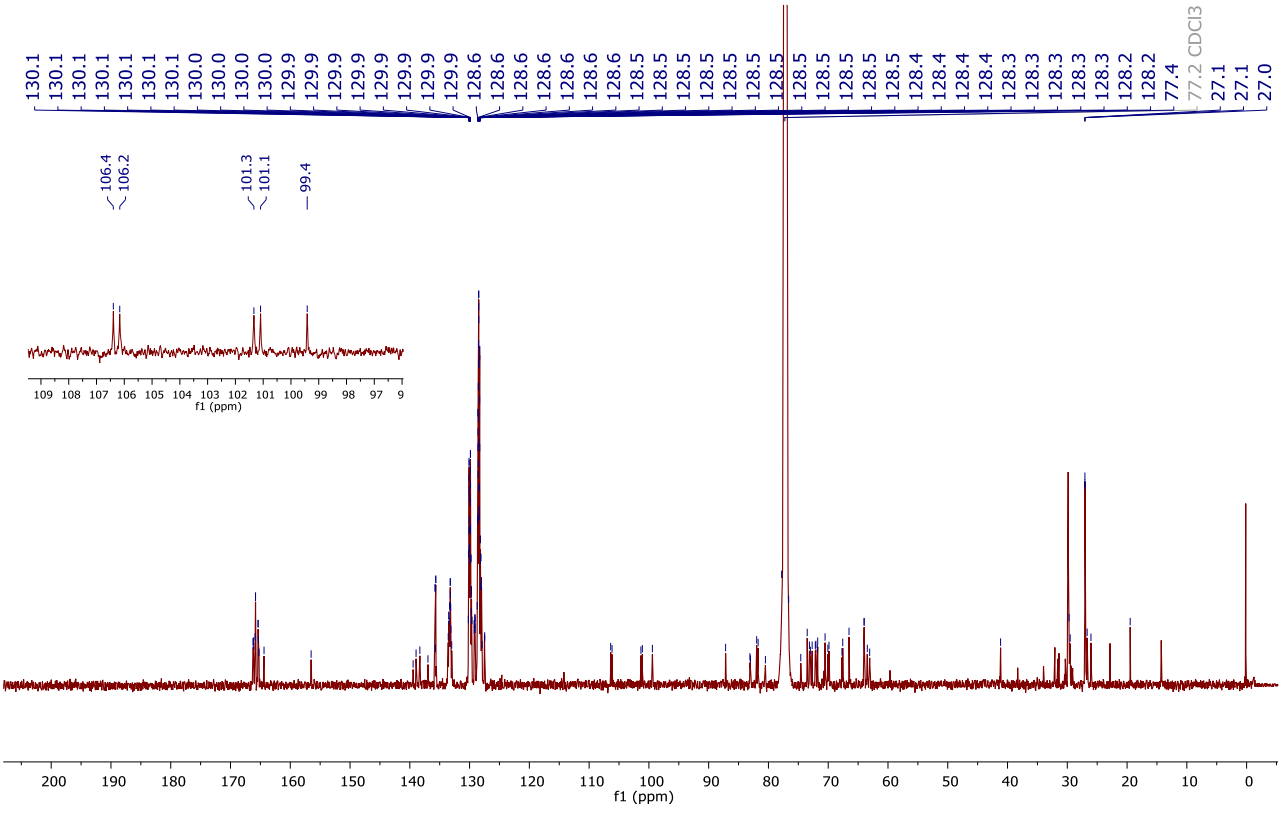
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **32**



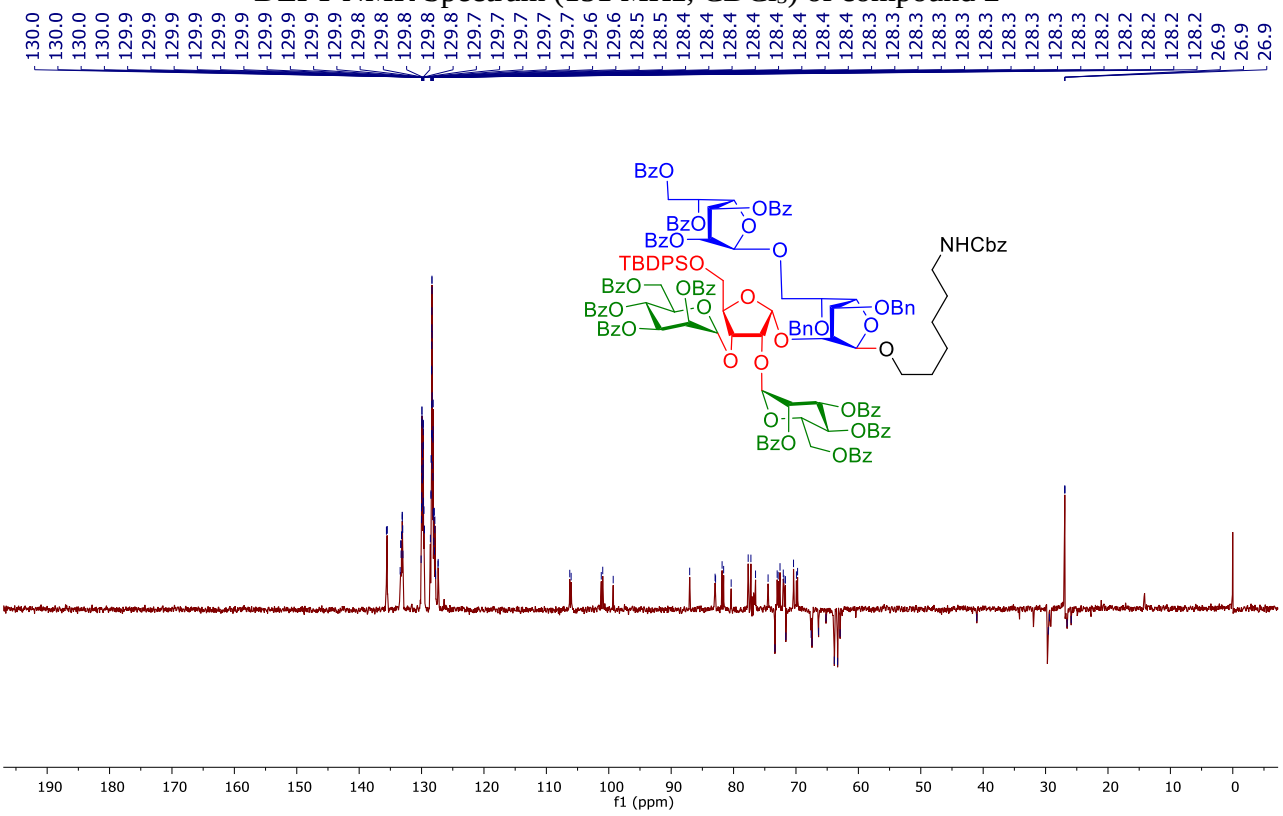
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **2**



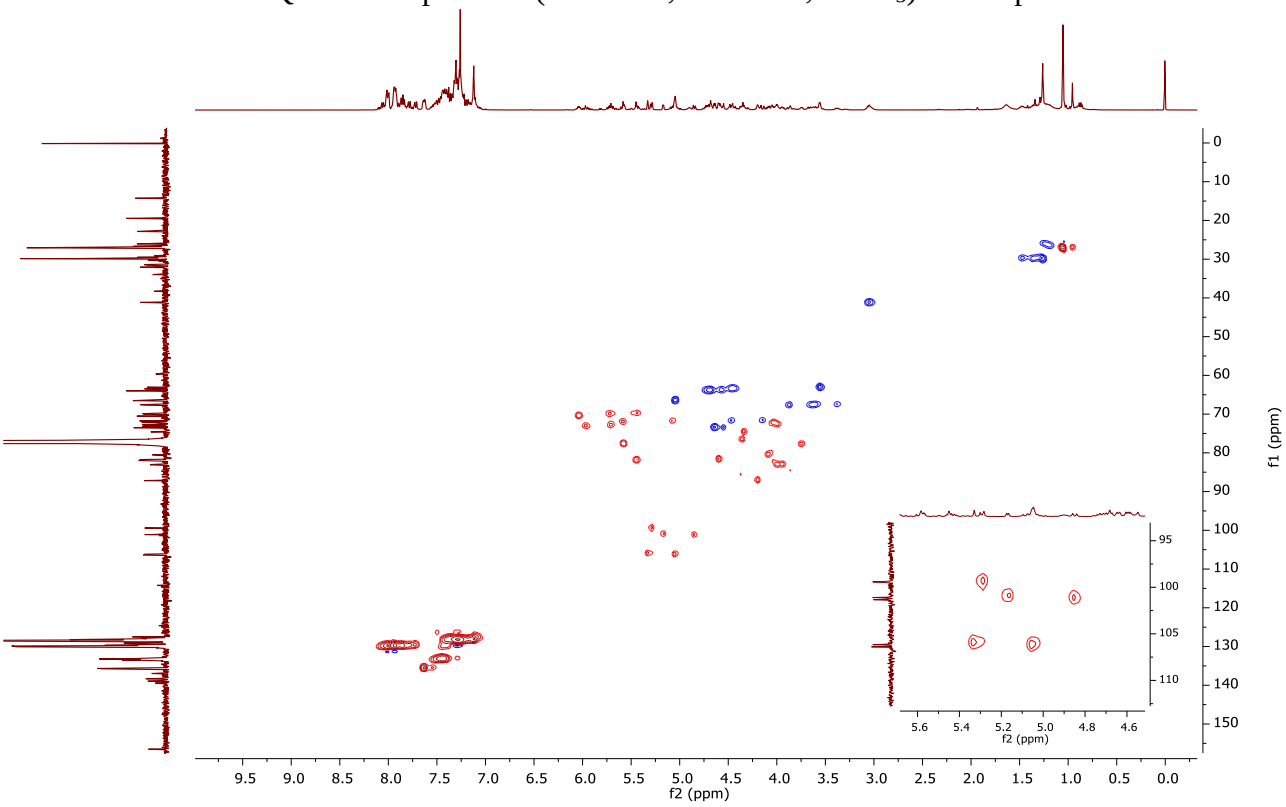
^{13}C NMR Spectrum (151 MHz, $CDCl_3$) of compound **2**



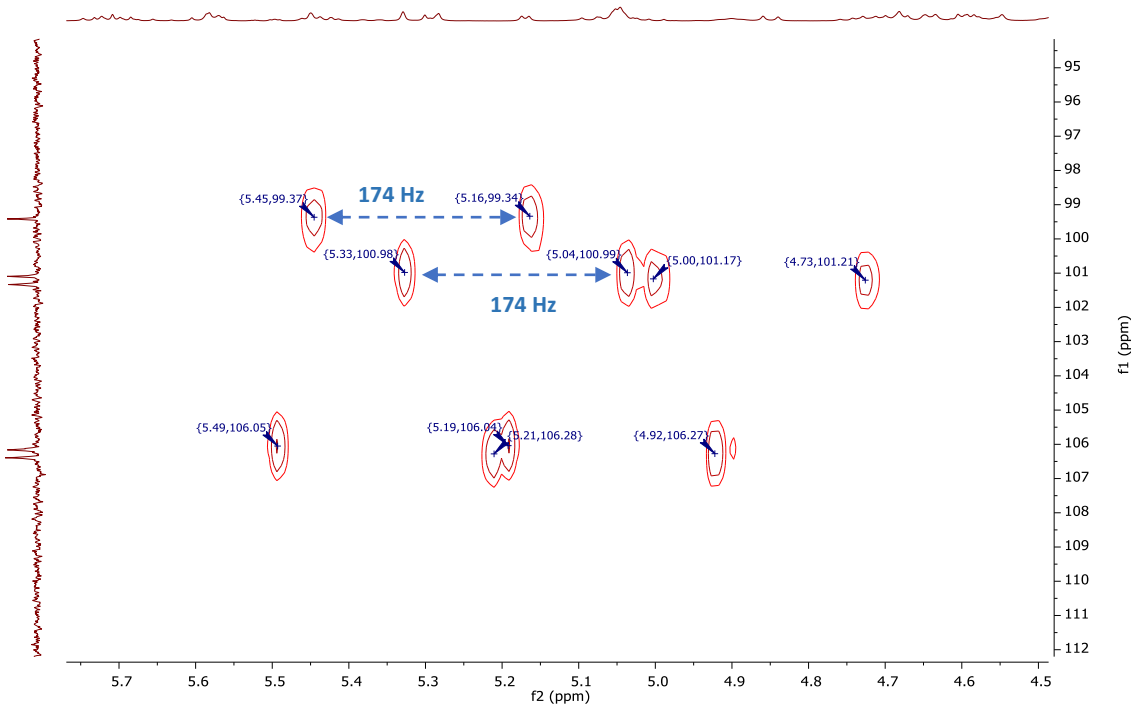
DEPT NMR Spectrum (151 MHz, $CDCl_3$) of compound **2**



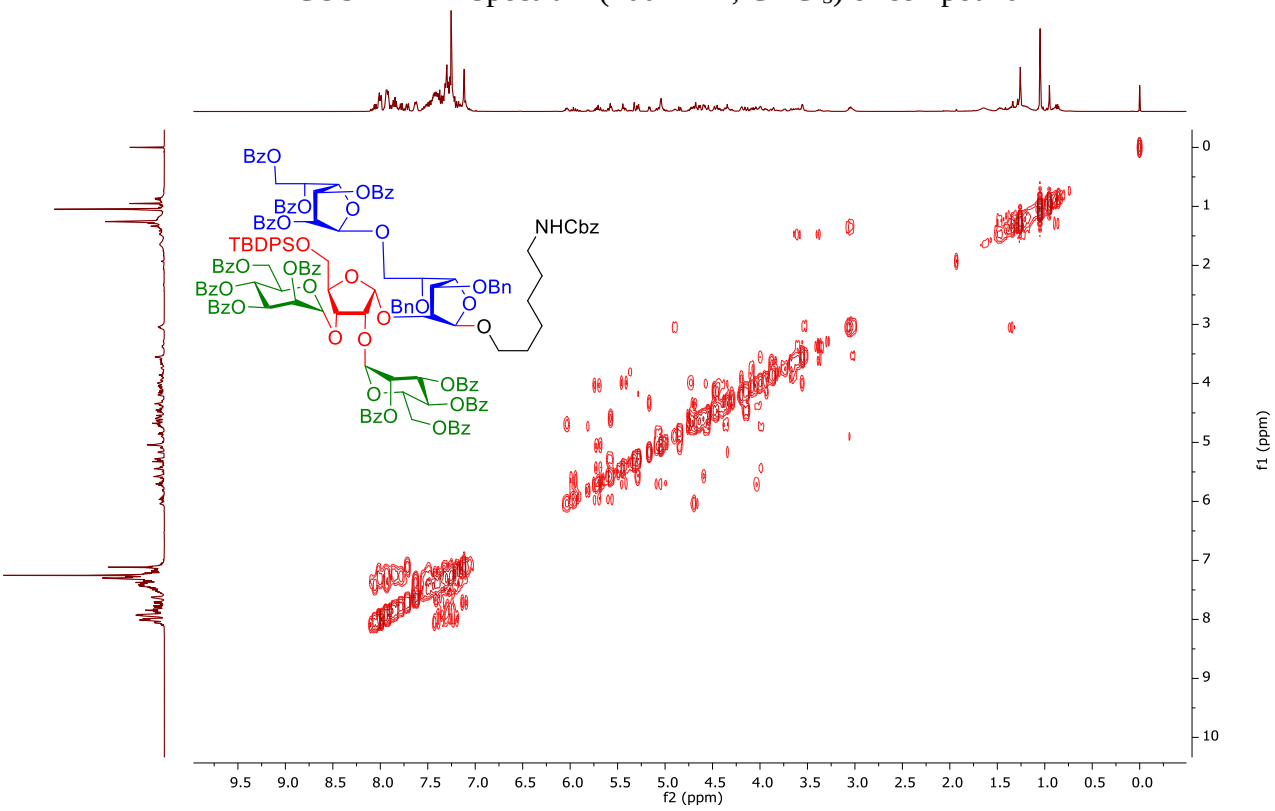
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **2**



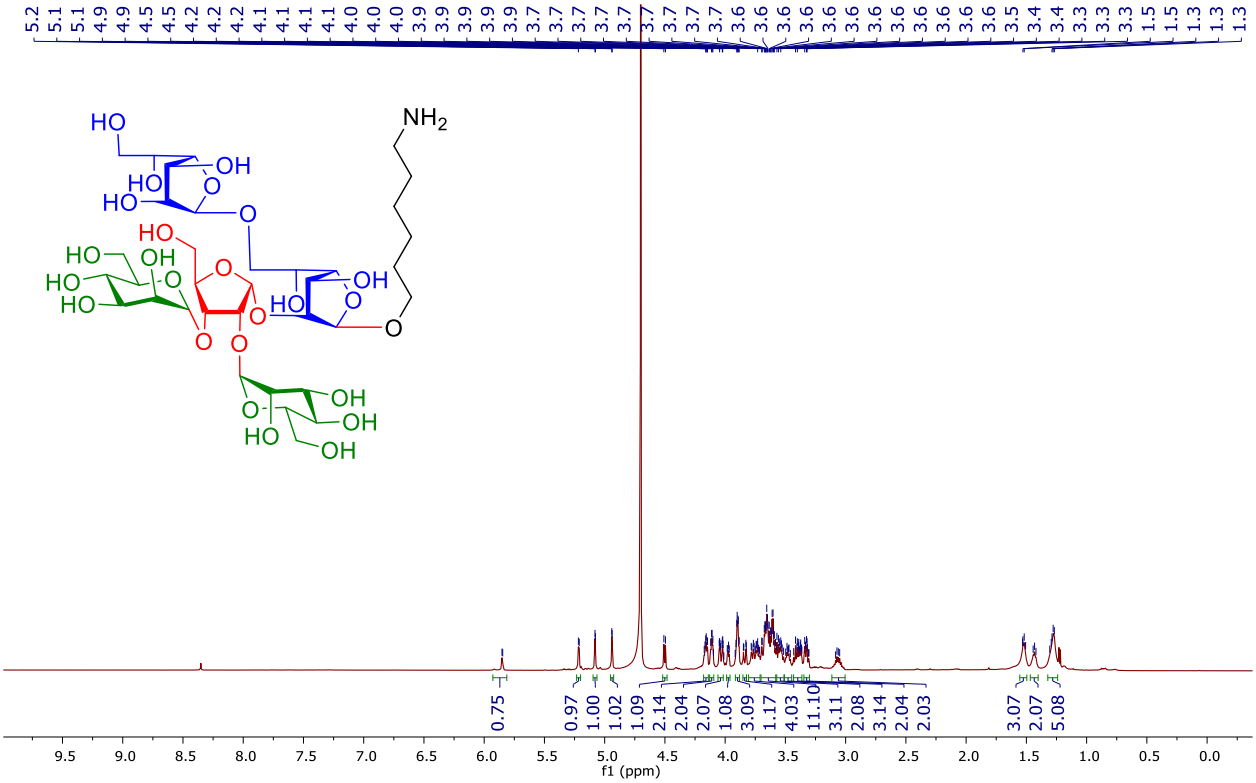
^{1}H-^{13}C Coupled HSQC NMR (Anomeric expansion) (600 MHz, 151 MHz, $CDCl_3$) of compound **2**



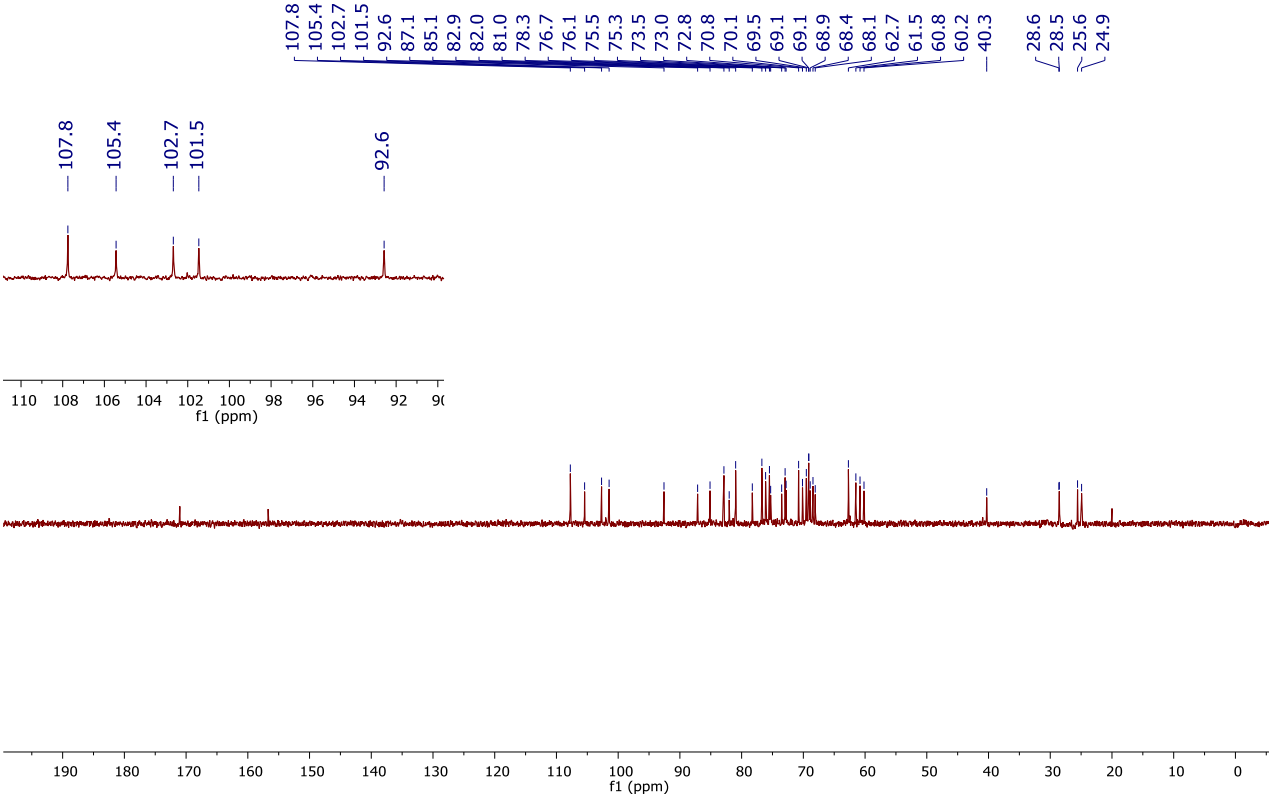
^{1}H-^{1}H COSY NMR Spectrum (400 MHz, $CDCl_3$) of compound **2**



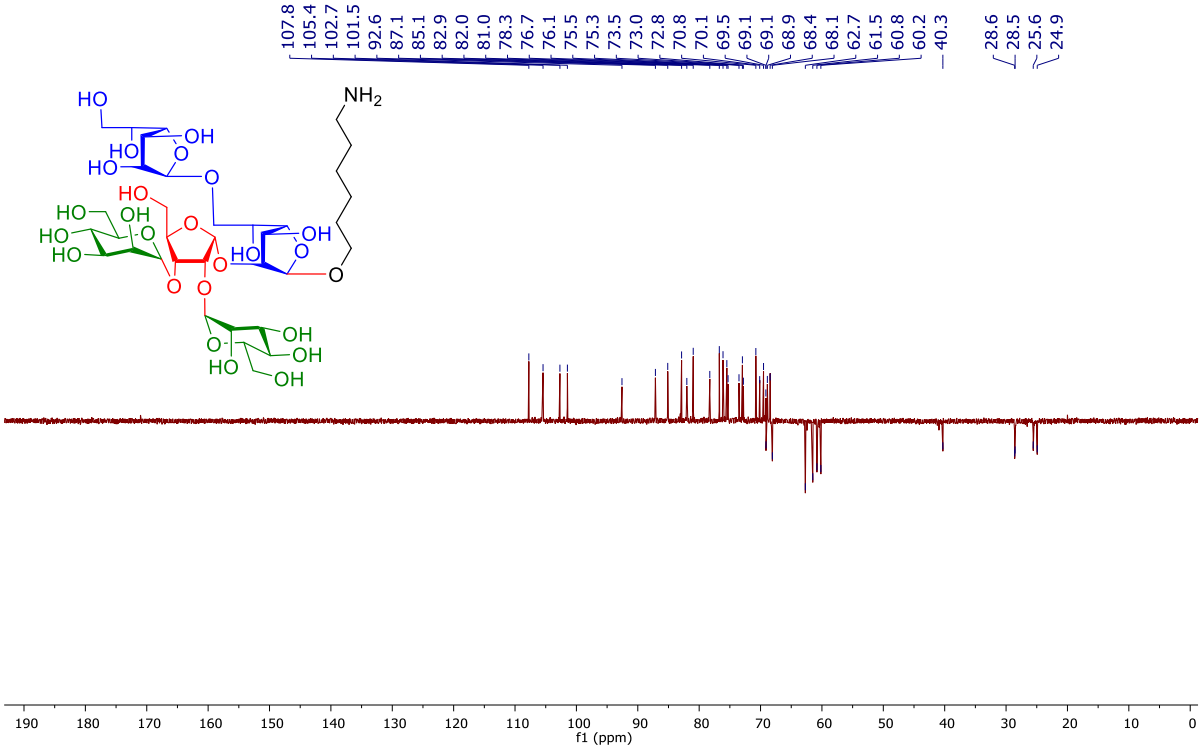
^{1}H NMR Spectrum (600 MHz, D_2O) of compound **1a**



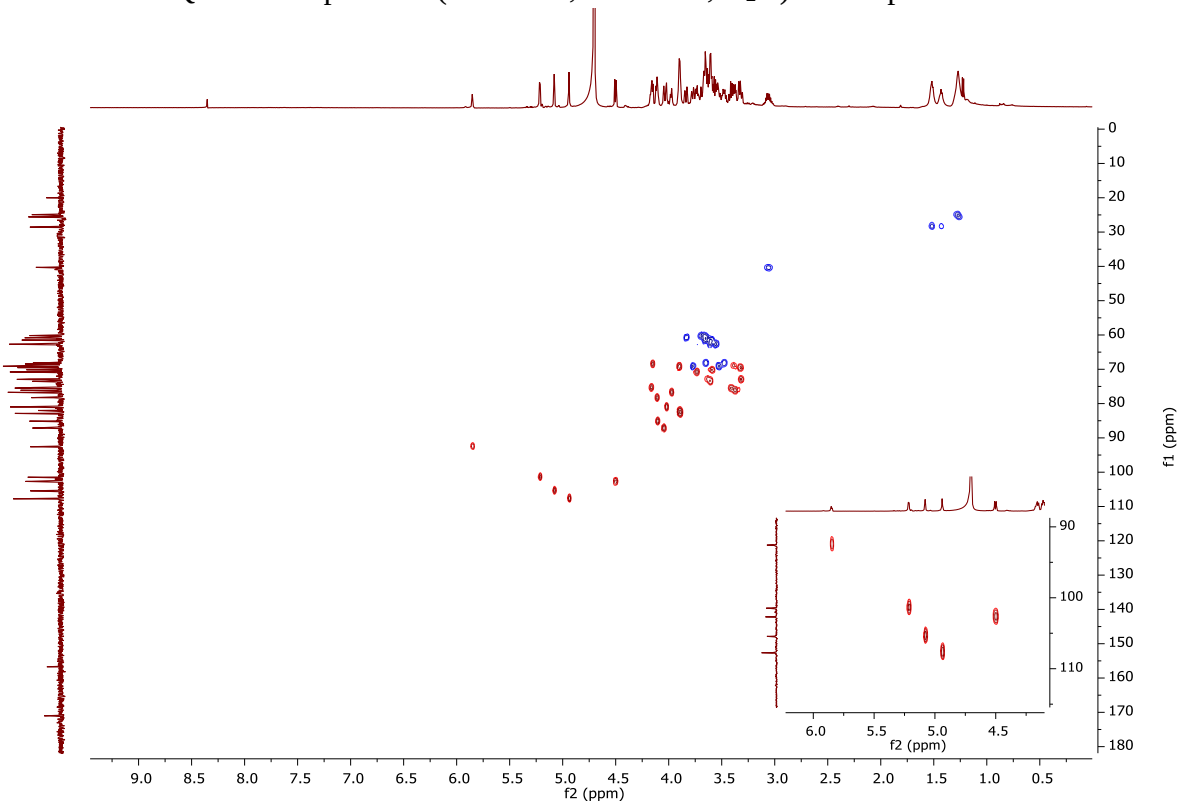
^{13}C NMR Spectrum (151 MHz, D_2O) of compound **1a**



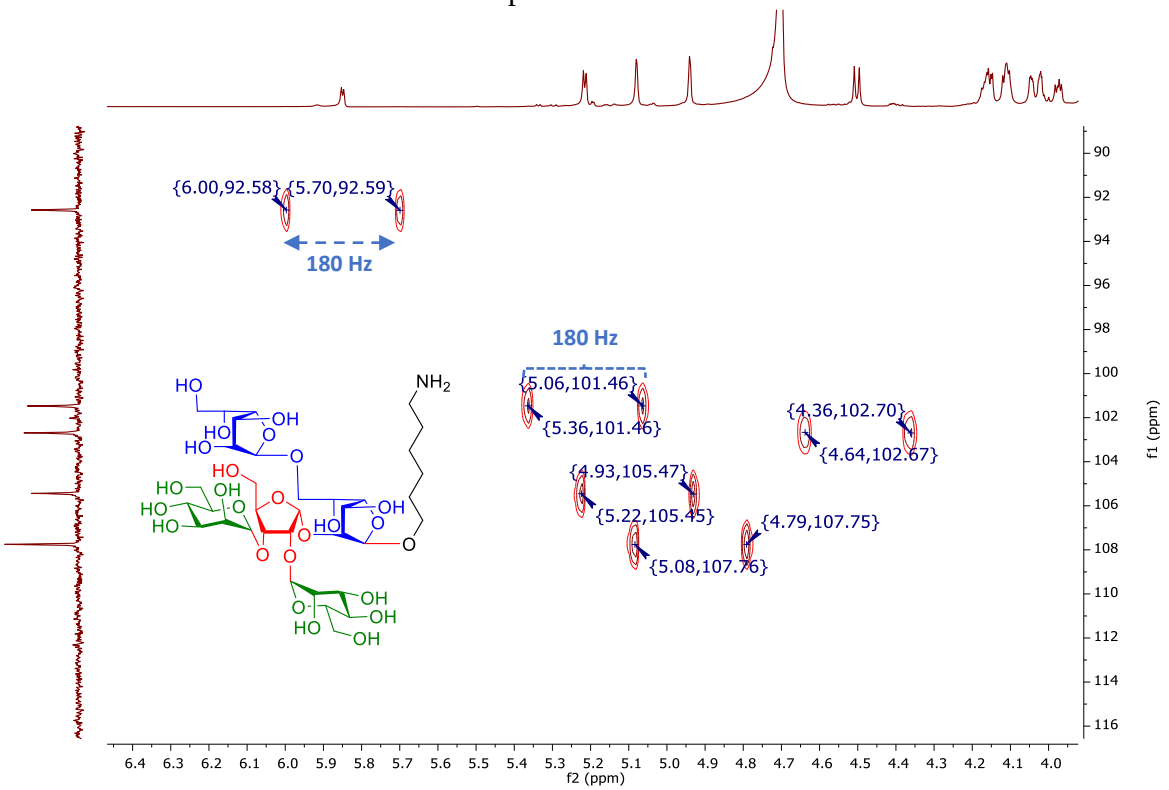
DEPT NMR Spectrum (151 MHz, D_2O) of compound **1a**



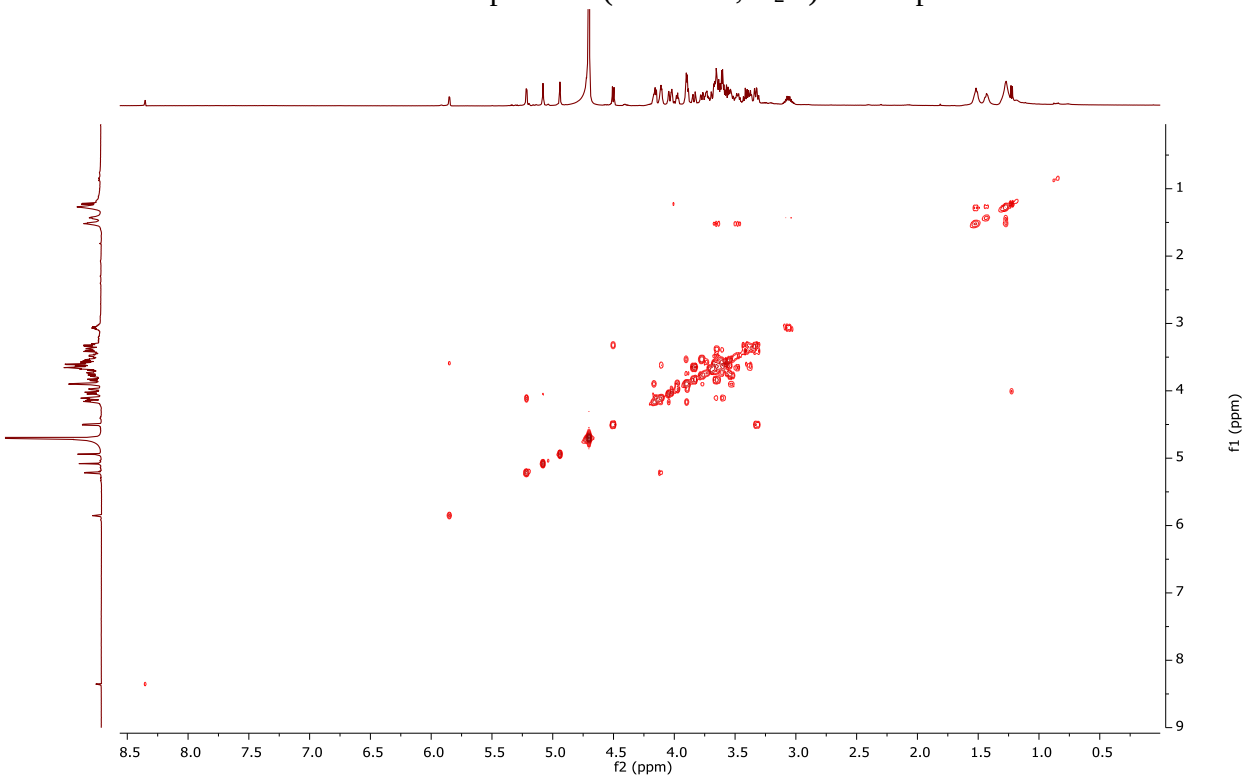
^{1}H-^{13}C HSQC NMR Spectrum (600 MHz, 151 MHz, D_2O) of compound **1a**



^{1}H-^{13}C Coupled HSQC NMR Spectrum (Anomeric expansion) (600 MHz, 151 MHz, D_2O) of compound **1a**



^{1}H-^{1}H COSY NMR Spectrum (600 MHz, D_2O) of compound **1a**



3.15. References

1. Francis, I.; Holsters, M.; Vereecke, D. *Environ. Microbiol*, **2010**, *12*, 1–12.
2. Li, X.; Tambong, J.; Yuan, K.; Chen, W.; Xu, H.; Levesque, A.; Solke, H. *Int. J. Syst. Evol. Microbiol.* **2018**, *68*, 234–240.
3. Eichenlaub, R.; Gartemann. K. H. *Annu. Rev. Phytopathol*. **2011**, *49*, 445–464.
4. Oh, E. J.; Bae, C.; Lee, H. B.; Hwang, I. S.; Lee, H. I.; Yea, M. C.; Oh, C. S. *Int. J. Syst. Evol. Microbiol*. **2016**, *66*, 4065–4070.
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Chapter 4

Synthesis of Tetradecasaccharide Reminiscent of Mycobacterial Cell wall

Chapter- 4

4.1 Introduction

Tuberculosis (TB) is a long-lasting infectious disease caused by the bacterium *Mycobacterium tuberculosis* (Mtb). While it can affect various organs, TB predominantly impacts the lungs, resulting in symptoms such as a persistent cough, chest pain, and coughing up blood. Although TB is both preventable and treatable, in 2022, it was the second leading cause of death from a single infectious agent globally, following COVID-19. In 2022, the official death toll from tuberculosis was approximately 1.13 million, nearly twice as high as the 0.63 million deaths attributed to HIV/AIDS. The impact of the COVID-19 pandemic on tuberculosis mortality has been significantly greater compared to its effect on HIV/AIDS[1].

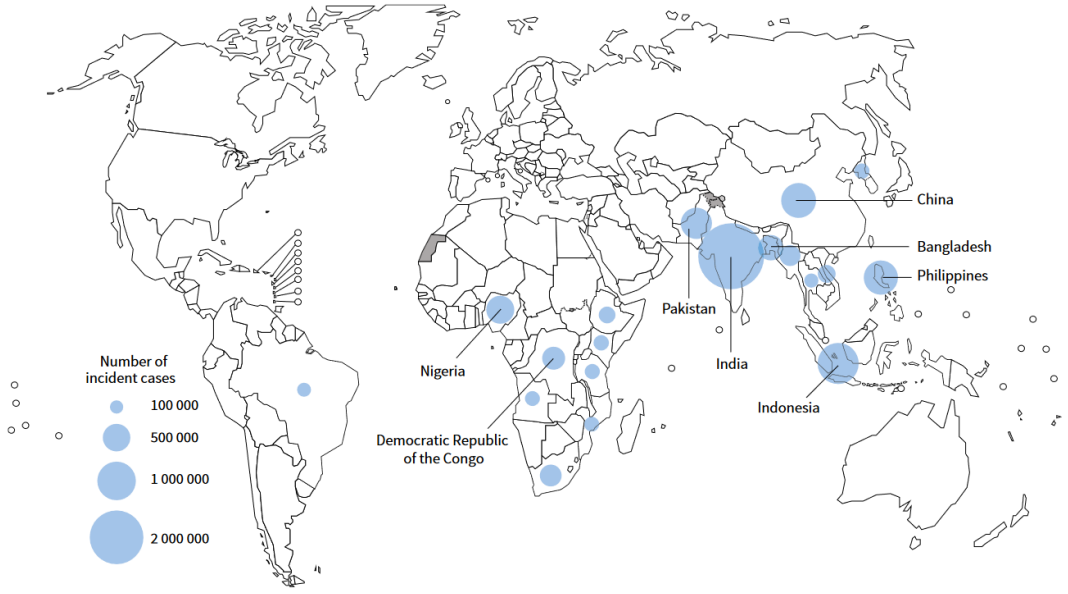


Fig 4.1: Estimated number of TB incidents in 2022, for countries having at least 100000 cases (Global Tuberculosis Report by WHO, 2023)

In 2022, the majority of tuberculosis cases were reported in the WHO regions of South-East Asia (46%), Africa (23%), and the Western Pacific (18%). Smaller percentages were seen in the Eastern Mediterranean (8.1%), the Americas (3.1%), and Europe (2.2%). The 30 countries with the highest TB burden accounted for 87% of all estimated new TB cases globally. Among these, eight countries—India (27%), Indonesia (10%), China (7.1%), the Philippines (7.0%), Pakistan (5.7%), Nigeria (4.5%), Bangladesh (3.6%), and the Democratic Republic of the Congo (3.0%)—were responsible for more than two-thirds of the global total. Tuberculosis can impact individuals of

any age or gender. However, the highest prevalence is observed among adult men (aged 15 years and older), who accounted for an estimated 5.8 million cases in 2022, representing 55% of the total estimated cases[1].

Drug-resistant tuberculosis remains a significant public health issue, with resistance to rifampicin—considered the most effective first-line treatment—being particularly alarming. Tuberculosis that is resistant to both rifampicin and isoniazid is classified as multidrug-resistant TB (MDR-TB). Both MDR-TB and rifampicin-resistant TB (RR-TB) necessitate treatment with second-line medications[1]. For patients with drug-susceptible tuberculosis, the World Health Organization currently recommends a 6-month course which consists the four first-line medications: rifampicin, isoniazid, ethambutol, and pyrazinamide[2a]. As we all know, the most effective treatment during any pandemic caused by a fatal disease is the vaccination. Till date, Bacillus Calmette-Guérin (BCG), developed back in 1918 is the only certified and licensed vaccine available for the treatment of TB[2b] and continues to be widely used. However, its effectiveness in preventing severe forms of TB in infants is limited. At present, there is no vaccine available to prevent or treat TB in adults, either before or after exposure to the Mtb. There are currently twelve vaccines undergoing various stages of clinical trials to combat Tuberculosis.

4.2 *Mycobacterium tuberculosis*

In 1882, Robert Koch identified the tubercle bacillus, *Mycobacterium tuberculosis* (Mtb), as the bacterium responsible for causing tuberculosis (TB) in humans[3]. There are nine known species in the group of Mycobacterium species out of which the three most important species are *M. tuberculosis*, *M. bovis* and *M. africanum*[4a,4b]. These species are primarily responsible for TB in human. *Mycobacterium tuberculosis* is a rod-shaped, weakly Gram-positive bacterium that measures between 0.3 to 0.6 micrometers in width and 1 to 4 micrometers in length. Now the cell wall structure of any pathogen draws a major attention to the scientific world to understand the host-pathogen interactions and immune responses. It is essential to thoroughly understand and study the intricate components of the cell wall of *Mycobacterium tuberculosis* to effectively develop a vaccine against TB.

4.3 Structural components of the cell wall of *Mycobacterium tuberculosis*

In the mid-20th century, researchers began to elucidate the unique features of the cell wall of M. tuberculosis. In modern era, the application of advanced techniques like electron microscopy and mass spectrometry has provided a more detailed view of the cell wall's architecture, uncovering complex layers and components that play a role in the bacterium's pathogenicity. Notably, microbiologist Patrick J. Brennan made a groundbreaking contribution by revealing the chemical structure of the cell wall of *M. tuberculosis*[5a]. The lipid rich waxy cell wall of Mtb consisting of three major structural components: a) a thick long chain mycolic acid layer which helps the bacterium in the resistance of antibiotics and harsh chemicals, b) hyperbranched arabinogalactan (AG) and lipoarabinomannan (LAM) layers which contribute in further enhancing the bacterium's resistance to chemical and physical stress, and c) a peptidoglycan layer which provides structural support and rigidity (Fig. **4.2**)[5b-d]. This central structure of the cell wall is referred to as the mycolyl arabinogalactan-peptidoglycan (mAGP) complex.

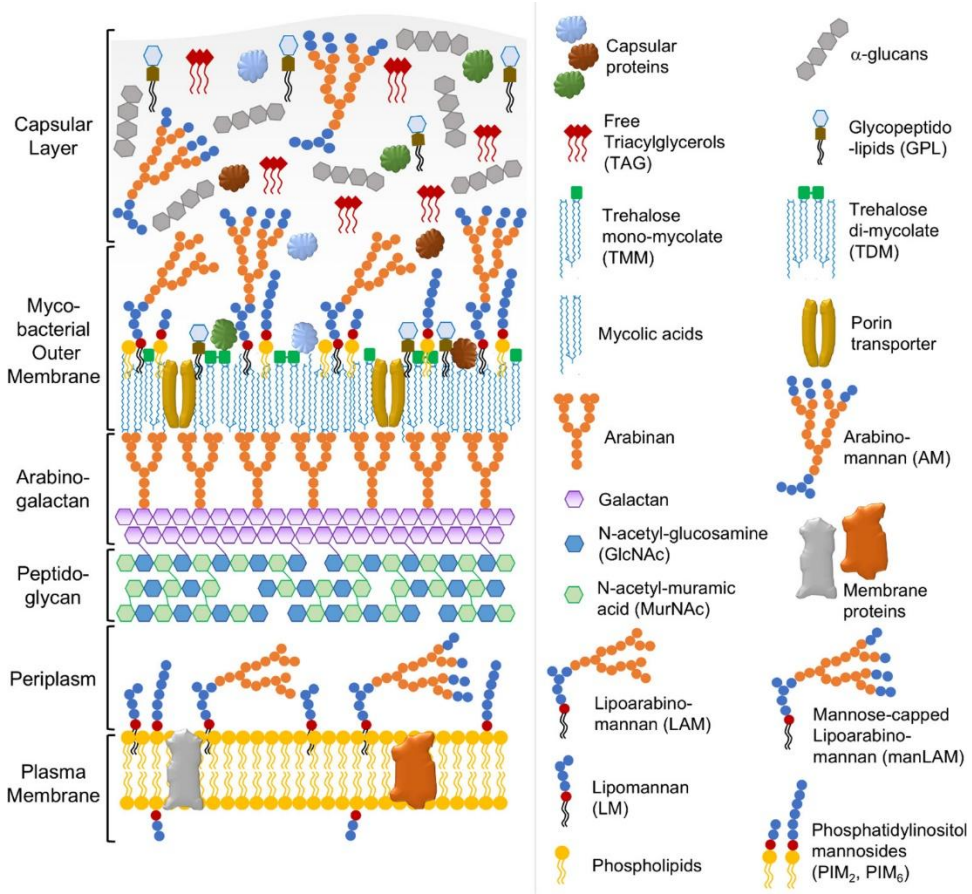


Fig 4.2. Representation of typical cell wall components of *M. tuberculosis*[5d]

4.4 Arabinogalactan

Arabinogalactan (AG) is a complex hyperbranched polysaccharide featuring a backbone predominantly composed of galactose and arabinose sugars in furanosyl form[7a]. This backbone consists of a linear chain of galactose units, with branching segments of arabinose. The linear galactofuranose chain which consists 36-Gal*f* residues in an alternating *β*-(1→5)-linked and *β*-(1→6)-linked D-galactofuranose residues[7b]. This galactan core is covalently attached to three highly branched arabinan chains in an alternative 8th, 10th and 12th residues from the reducing end. Each Ara*f* chain is composed of 31 arabinofuranose residues which is covalently linked to the mycolic acid layer at the non-reducing end[7c]. At the reducing end the galactan chain is linked with the peptidoglycan layer via a linker disaccharide motif containing rhamnose and glucosamine residues. The highly branched Arabinan chain has some unique characteristics. It majorly possesses repeating *α*-D-Ara*f* residue with a terminal capping of 1,2-*cis* linkage of *β*-D-Ara*f*-(1→2) residues (**Fig 4.3**).

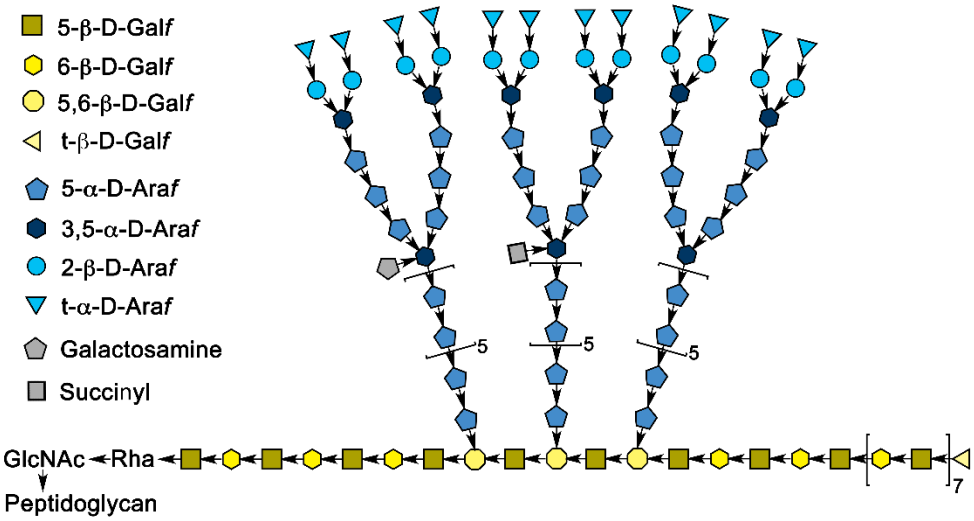


Fig 4.3. Cartoon representation of Arabinogalactan of M. tuberculosis[6]

Besides Arabinogalactan (AG), *Mycobacterium tuberculosis* also contains another significant class of immunologically active polysaccharides, namely lipoarabinomannan (LAM) and lipomannan (LM). LAM and LM both possess structural resemblance having a backbone of high mannan epitopes. The mannan polysaccharide chain typically contains linearly linked α-(1→6)-Man*p* sugar residues with branching of α-(1→2)-Man*p* linkages[7d-f]. Our research mainly focuses on the AG domain of the *M. tuberculosis* cell wall.

4.5 Significance of the Capsular polysaccharides in TB treatment

As discussed earlier, the mycobacterial cell wall features a distinctive glycosylated polysaccharide epitopes that are responsible for the cell wall integrity and durability and also enhances resistance to lysozyme and antibiotics[8]. Understanding and regulating the glycosylation patterns is crucial for designing drugs that can effectively target and penetrate the mycobacterial cell wall. Besides, enzymes that play a role in glycan biosynthesis, degradation, remodeling, and recycling present promising targets for drug development. Ensuring consistent glycan substrates is crucial for investigating the kinetics and inhibition of these enzymes, which can aid in the creation of new antimycobacterial treatments[8a]. Glycans derived from mycobacteria can be incorporated into glycoconjugate vaccines, where they are covalently attached to a carrier protein. Homogenous glycans are essential to maintain consistent vaccine composition and ensure reliable immunogenicity. Although less prevalent than glycoprotein-based drugs, glycans can also be developed as therapeutic agents. Thus, homogeneous glycan preparations are crucial for determining structure-activity relationships and enhancing pharmacokinetics[8b-d].

Recently, cases of multi-drug resistant (MDR) tuberculosis have been rising rapidly, along with an increase in extensively drug-resistant (XDR) tuberculosis cases[1]. By now, it's clearly understood that the cell wall glycopolymer of *M. tuberculosis* is very essential to investigate the host-pathogen interactions and immunological responses. Availability of pure and homogeneous glycans will direct us to focus on the development of the new drug candidates against TB. Now isolation of glycans from the natural resources is a herculean task as they were present in a heterogeneous manner. So, for getting the pure glycans in hand we have to mimic the naturally occurring oligosaccharides either by biosynthetic pathways or chemical syntheses of glycosides. Having several limitations of enzymatic syntheses including narrow substrate scope, high cost, handling difficulties etc., chemical syntheses remains as the most dependable method for obtaining pure oligosaccharides.

4.6 Chemical syntheses of Cell wall reminiscent of *M. tuberculosis*

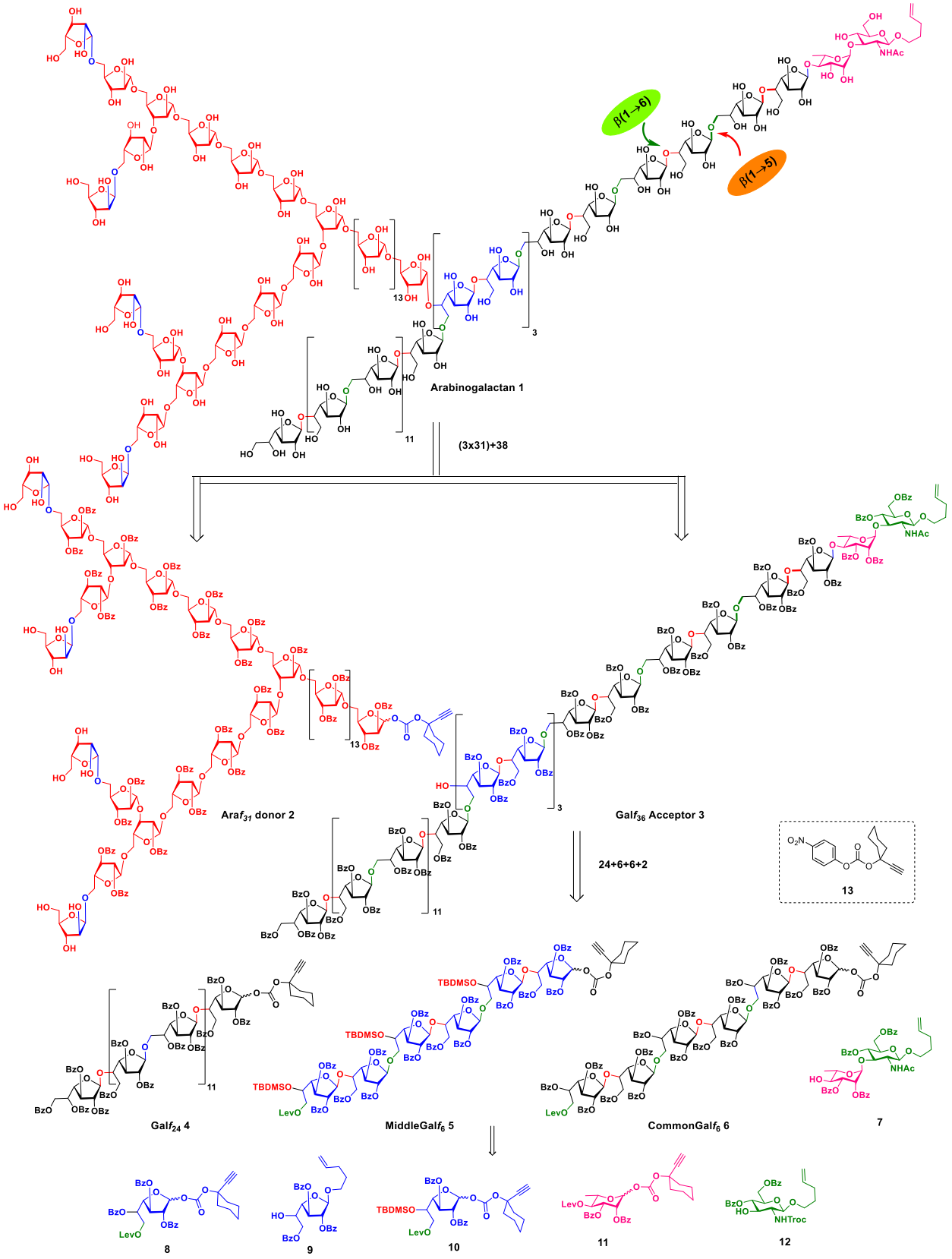
With advancements in the glycosyl donor development, very efficient glycosylation methods over the years, the chemical synthesis of complex oligosaccharides captured the attention of synthetic carbohydrate chemists. The first major contribution in the synthesis of AG fragment of Mtb came from Gurjar group in 1998 where they have synthesized a pentaarabinofuranosyl motif A using *n*-pentenyl and thiopyridyl arabinofuranoside donors.[9a] Next, Lowary group synthesized a docosanasaccharide arabinan motif using highly convergent [(2x5) +7+5] glycosylation protocol via thiotolyl and trichloroacetimidate donors.[9b] Another important contribution towards the synthesis of large arabinan fragment comes from Ito group in 2011 where they have synthesized a docosanaccharide epitope via a convergent [(2x7)+8] coupling strategy using thiotolyl glycosyl donors.[9c] One of the most interesting feature of this work is the synthesis of 1,2-*cis* arabinan linkage via stereo controlled tethering of 3,5-O-tetra-*i*-propyldisiloxanylidene-armed donors and intramolecular aglycone delivery (IAD). More recently, Seeberger group contributed significantly in the syntheses of oligoarabinofuranosides using the automated solid phase glycan synthesis.[9d,9e] The Hotha group has greatly advanced the field of oligosaccharide syntheses by pioneering the use of [Au]-catalyzed mild activation techniques for propargyl glycosyl donors[10a] and propargyl 1,2-orthoesters[10b]. They utilized this strategy to synthesize the common branched hexaarabinofuranoside epitope of AG and LAM.[10c] They later expanded their approach to synthesize a complete 21-mer arabinogalactan residue using a highly convergent [(2x4)+7+6] strategy with a notable innovation of the incorporation of digalactofuranoside motif into the arabinan residue for the first time.[10d] Subsequently, the Hotha group developed an even milder activation strategy of alkynyl carbonate glycosyl donors.[10e] They have extensively utilized the alkynyl glycosyl carbonate donor in the syntheses of branched tridecasaccharide[10e], a linear nonadecaarabinofuanoside motif[10f] and subsequently pentacosafuranoside subunit[10g] of mycobacterial AG by their silver-assisted gold catalyzed protocol. The Xin-Shan Ye group set a world record in 2017 by synthesizing the longest well-defined carbohydrate chain of mycobacterial arabinogalactan, consisting of 92 monosaccharide units, using a pre-activation-based glycosylation strategy.[11] These reports strongly motivate us to aim for the full-length synthesis of the arabinogalactan motif using our innovative [Au]/[Ag]-catalyzed mild activation of alkynyl glycosyl carbonate donors.

4.7 Present work

As discussed earlier, the target arabinogalactan **1** has some unique features which makes it very challenging to synthesize: a) highly branched arabinan (Ara*f*) at the *C*-5 of β(1→6) Gal*f* residues selectively at 8th, 10th and 12th positions of the galactan chain, b) the linear galactofuranan chain containing 36 Gal*f* residues via alternating β(1→5) and β(1→6) linkages, c) linker disaccharide consisting of rhamnopyranose and glucosamine residue that serve as linker unit. Now the first and foremost challenge of this synthesis is the bulk production of galactofuranose building blocks as locking the galactose sugar in furanose form is a thermodynamically unfavorable process making it a herculean task for the synthetic chemists. Well, to begin with the synthesis of our target arabinogalactan **1**, we first started the retrosynthesis and cut the giant molecule into two relatively smaller fragments: (i) Araf_{31}**2** donor and (ii) the linear Galf_{38}**3** acceptor. My colleague Dr Sumit Sen focused on the synthesis of the branched Araf_{31}**2** donor while this chapter covers the synthesis of linear Galf_{38} acceptor **3**.

4.7.1 Retrosynthesis of linear Galf_{38} acceptor 3

In the synthesis of the linear Galf_{38} acceptor **3**, a highly convergent synthetic strategy was envisioned via [24+6+6+2] coupling protocol. It was envisaged that the linear acceptor **3** can be synthesized from the middle hexasaccharide motif **5**, the repeating common hexasaccharide motif **6** and the linker disaccharide epitope **7** (Scheme **4.1**). The hexasaccharide motifs can be further synthesized from the galactosyl carbonate donor motifs **8** and **10** and a common aglycon **9**. The linker disaccharide can be synthesized from the rhamnosyl carbonate donor **11** and glucosamine acceptor motif **12**. In the envisioned common hexasaccharide **6** motif, Lev group is strategically kept at C6-OH position to further deprotect it and elongate the oligosaccharide chain. To attach three arabinan chains at the branching points, the middle hexasaccharide epitope **5** was designed with orthogonal -OTBDMS and -OLev protecting groups. All the building blocks are armed with *n*-pentenyl group at the reducing group so that it can be transformed to corresponding alkynyl glycosyl carbonate donor via the deprotection into hemiacetal and masking the hemiacetal with the carbonate reagent **13**. Benzoate group is installed in the C2-OH of each glycosyl donor moiety to assure formation of 1,2-*trans* glycoside during the glycosylation (Scheme **4.1**).

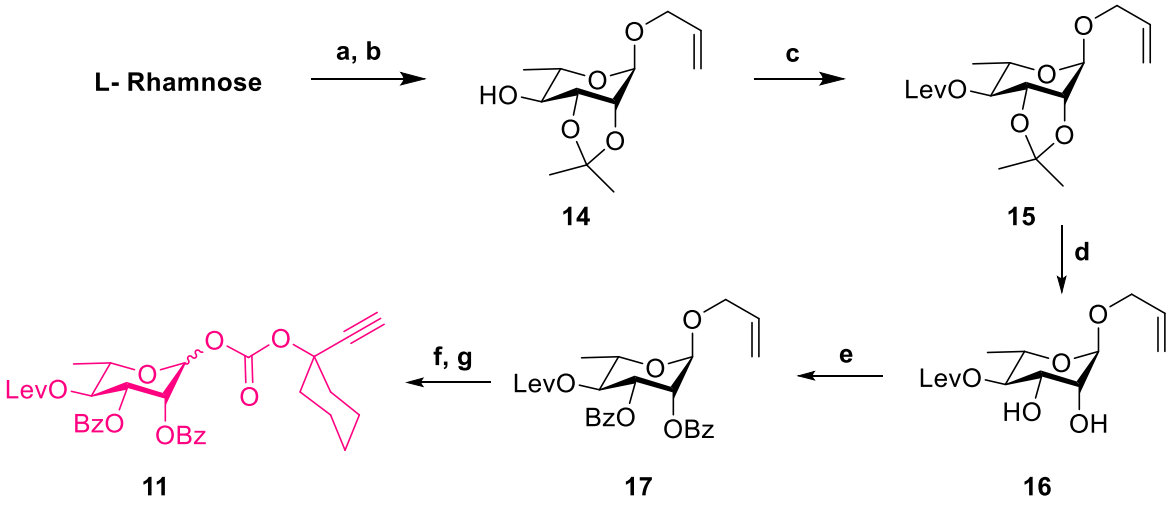


Scheme 4.1. Retrosynthetic Analysis of Arabinogalactan **1**

4.7.2 Synthesis of building blocks 11 and 12

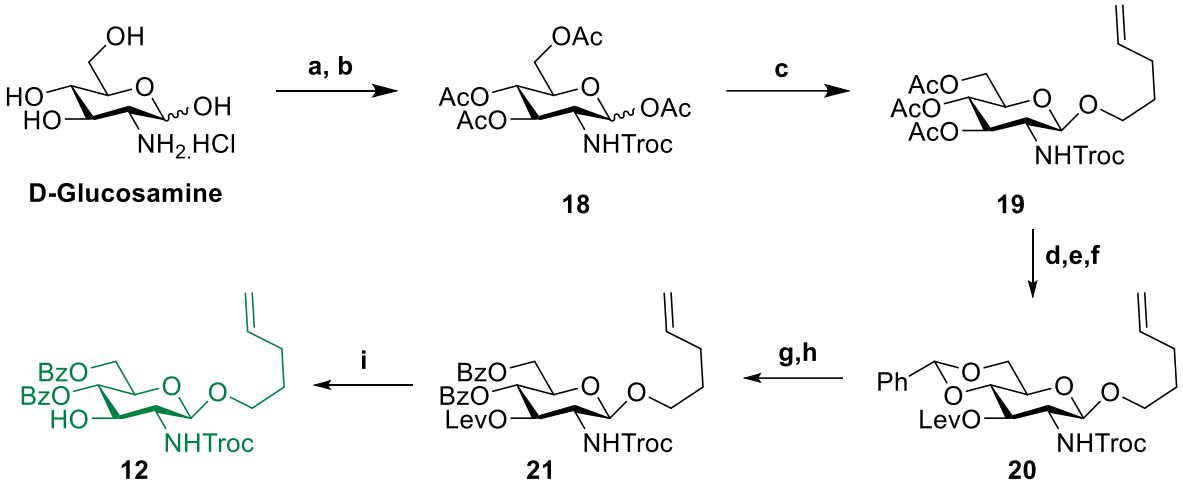
We commenced our synthesis of the fragment epitopes from the reducing end of the linear Gal*f* molecule. In order to synthesize the linker disaccharide, the rhamnopyranosyl carbonate donor **11** and the glucosamine acceptor **12** were the primary targets.

The synthesis of the donor **11** started with commercially available L-rhamnose by locking it in the pyranosyl form by the treatment of acetyl chloride and allyl alcohol at 80 °C for 5 h followed by the acetonide protection using 2,2-DMP and catalytic amount of PTSA in anhydrous acetone at 25 °C for 2 h which lead to the compound **14**. The C3-OH of compound **14** was protected levulinoate using levulinic acid, DIC and DMAP at 25 °C to produce compound **15** in 91% yield. The acetonide moiety of compound **15** was deprotected using catalytic PTSA resulting in the diol **16** which was subjected to further protection using benzoyl chloride in pyridine giving the di-OBz rhamnopyranoside **17**. The allyl group was cleaved off using $PdCl_2$ to obtain the corresponding hemiacetal which was directly treated with 1-ethynylcyclohexyl (4-nitrophenyl) carbonate **13** in the presence of DMAP to afford rhamnopyranosyl carbonate donor **11** in 81% yield over two steps (Scheme **4.2**).



Scheme 4.2. Synthesis of Building Block 11. Reagents: a) AcCl, allyl alcohol, 80 ºC, 5 h; b) 2,2-dimethoxypropane, PTSA, dry acetone, 25 ºC, 2 h, 76% over two steps; c) Lev-acid, DIC, DMAP, CH_2Cl_2, 0-25 ºC, 1 h, 91%; d) PTSA, CH_3OH:CH_2Cl_2 (1:1), 25 ºC, 4 h, 74%; e) BzCl, pyridine, DMAP, 0-25 ºC, 5 h, 92%; f) $PdCl_2$, CH_3OH:CH_2Cl_2 (1:1), 0 to 25 ºC, 4 h; g) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate (**13**),CH_2Cl_2, DMAP, 25 ºC, 8 h, over two steps 81%.

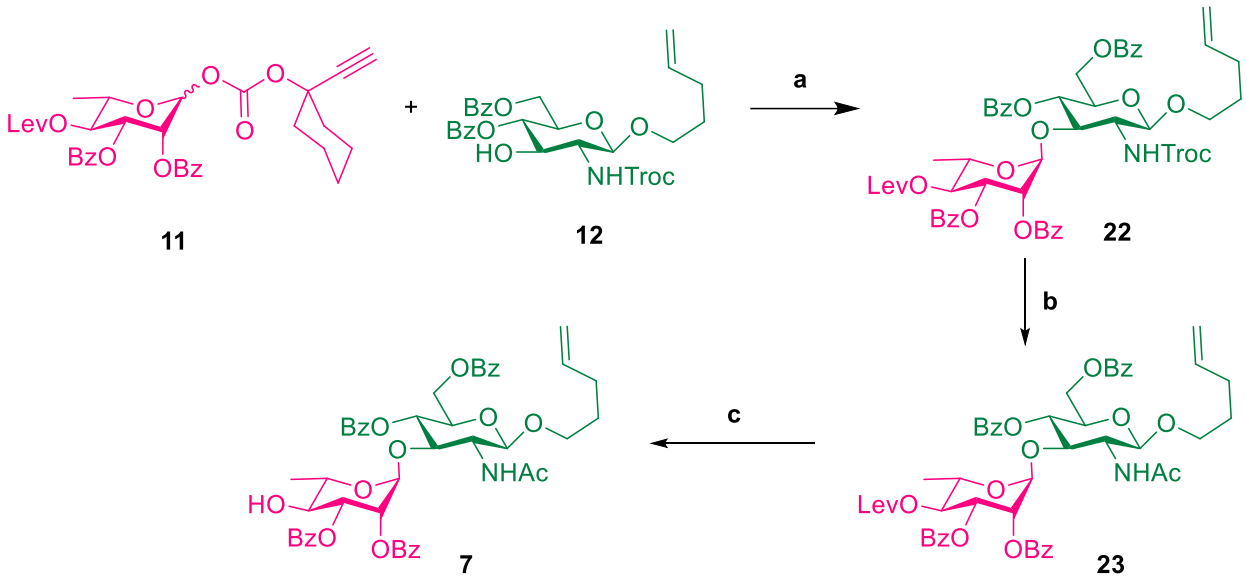
The synthesis of aglycon **12** started with the protection of amine group of commercially available D-glucosamine using TrocCl in presence of $NaHCO_3$, subsequently it was treated with Ac_2O in pyridine to give the tetra-acetate glucosamine derivative **18** in 78% yield over two steps. Compound **18** was refluxed at 60 ºC for 4 h in presence of 4-pentene-1-ol and BF_3•Et_2O furnishing the pentenyl glycoside **19**. The acetates of glycoside **19** were deprotected using NaOMe followed by the protection of 4,6-*O*-benzylidine using $PhCH(OMe)_2$ and catalytic CSA produced the benzylidene protected compound which was further subjected to Lev protection using levulinic acid, DIC and DMAP at 25 °C to furnish the fully protected glycoside **20**. Now the benzylidene group was deprotected using catalytic PTSA to give the diol compound which was protected using benzoyl chloride and pyridine to obtain compound **21** in 78% yield over two steps. Further, C-3 Lev deprotection of compound **21** using hydrazine hydrate in buffer solution of acetic acid and pyridine for 30 min gave us the desired aglycon **12** in 89 % yield (Scheme **4.3**).



Scheme 4.3. Synthesis of Building Block 12. Reagents: a) TrocCl, $NaHCO_3$, H_2O, 5 h, 0 ºC; b) Ac_2O, Pyridine, 0-25 ºC, 5 h, 78% over two steps; c) 4-pentene-1-ol, $BF_3.Et_2O$, CH_2Cl_2, 60 ºC, 4 h, 83%; d) NaOMe, CH_3OH: CH_2Cl_2 (1:1), 0 ºC, 1 h; e) $PhCH(OMe)_2$, CSA, Acetonitrile, 25 ºC, 4 h; f) Lev-Acid, DIC, DMAP, CH_2Cl_2, 0-25 ºC, 1 h, 76% over three steps; g) PTSA, CH_3OH: CH_2Cl_2 (1:1), 25 ºC, 4 h; f) BzCl, pyridine, DMAP, 0-25 ºC, 5 h, 78 % over two steps; i) $NH_2NH_2.H_2O$, AcOH: Pyridine (22:27 eq.), CH_2Cl_2, 30 min, 89%.

4.7.3 Synthesis of Disaccharide Acceptor 7:

The rhamnosyl carbonate donor **11** and the glucosamine aglycon **12** were coupled using the [Au]/[Ag]-catalyzed glycosylation conditions to give the disaccharide **22** in 85% yield. As naturally it was present as NHAc derivative, the NHTroc of disaccharide **22** was transformed to NHAc utilizing Zn dust, AcOH and Ac_2O to obtain the desired disaccharide **23** in 88 % yield. The successful formation of the disaccharide **23** was characterized by both NMR and MALDI-ToF spectroscopic techniques (Table **4.1**). Subsequently, the Lev group of **23** was deprotected using standard hydrazine hydrate in buffer solution of acetic acid and pyridine to obtain the desired linker disaccharide acceptor **7** in 91 % yield.



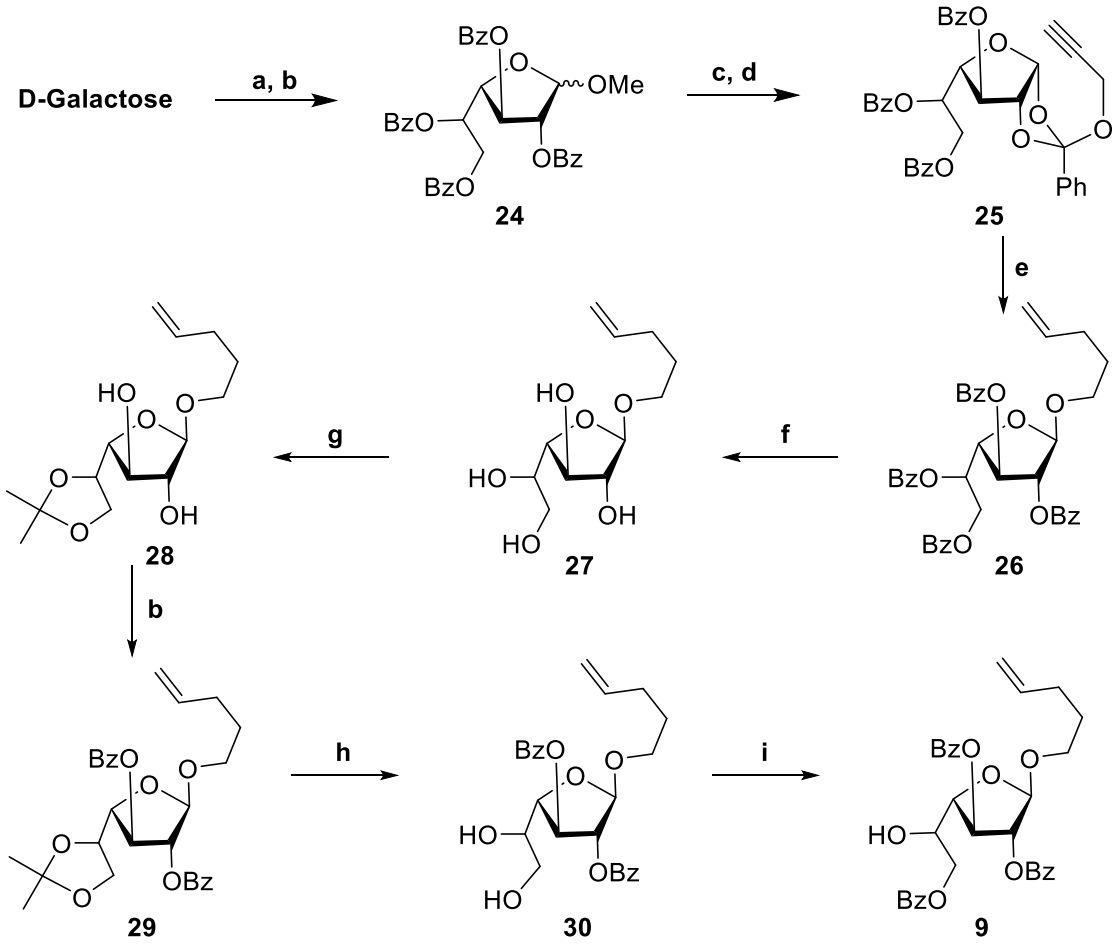
Scheme 4.4. Synthesis of Disaccharide 7. Reagents: a) 8mol% chloro[2,4-di-*tert*-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ºC, 20 min, 85%; b) Zn dust, AcOH, Ac_2O, 25 ºC, 6 h, 88%; c) $NH_2NH_2.H_2O$, AcOH: Pyridine (22:27 eq.), CH_2Cl_2, 30 min, 91%.

Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
Anomeric	5.14 (s, 1H), 4.88 (d, *J* = 3.6 Hz, 1H)	99.7 and 97.7
Acetamide	2.17 (s, 3H)	170.9 and 23.6
Levulinoate	2.62 – 2.30 (m, 2H) and 2.06 (s, 3H) and 1.76 (t, *J* = 6.9 Hz, 2H)	206.1, 172.0, 37.9, 30.5 and 29.7

Table 4.1. Characteristic ^{1}H and ^{13}C NMR Signals for linker disaccharide **23**

4.7.4 Synthesis of Building Block 9:

The journey of the synthesis of common Gal*f*-hexasaccharide commenced with the synthesis of common monosaccharide acceptor **9**. Commercially available D-galactose was locked in the furanose form by refluxing in MeOH and $FeCl_3$ for 48 h. Then the free hydroxyl groups were protected using benzoyl chloride and pyridine in 45 % yield over two steps. The methyl per-*O*-Bz galactofuranoside **24** was transformed to its corresponding furanosyl bromoside by treating with AcBr and Methanol in anhydrous CH_2Cl_2 at 0 ºC for 2 h which was subsequently exposed to propargyl alcohol, 2,6-lutidine and TBAI to furnish the propargyl galactofuranoside orthoester motif **25** in 74 % yield over two steps (Scheme **4.5**).



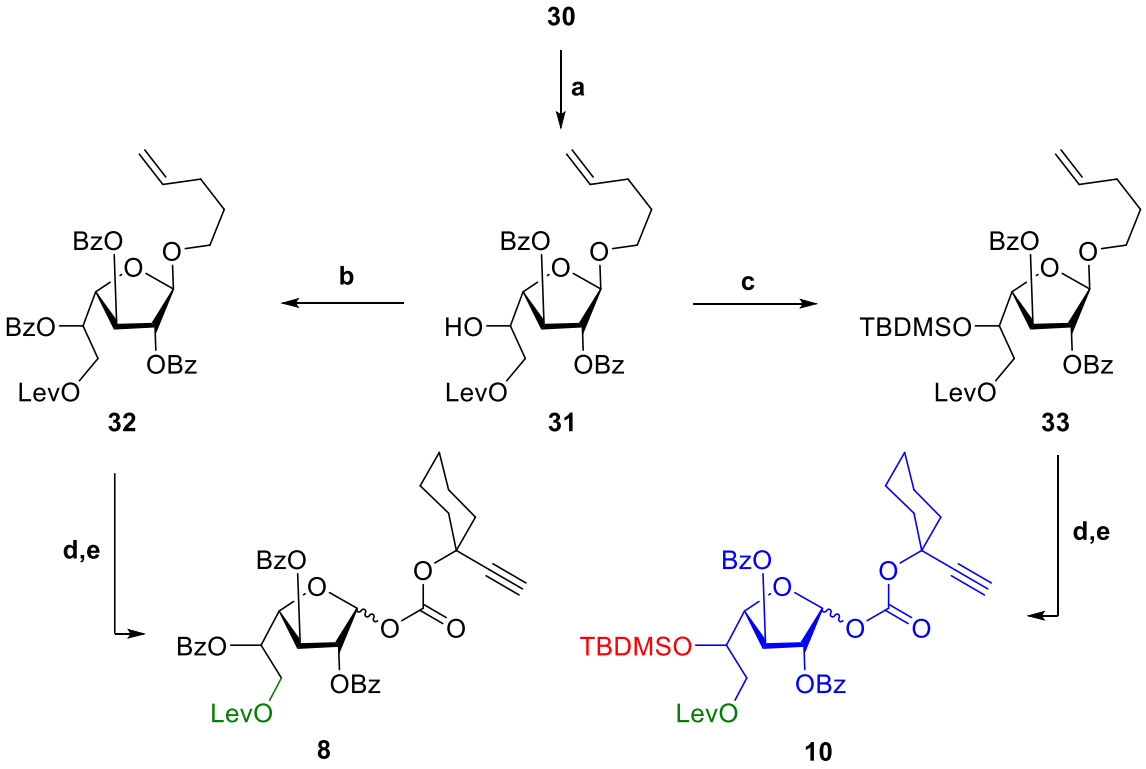
Scheme 4.5. Synthesis of Building Block 10. Reagents: a) $FeCl_3$, CH_3OH, 80 ºC, 2 d; b) BzCl, pyridine, DMAP, 0-25 ºC, 5 h, 45 % over two steps; c) AcBr, CH_3OH, 0 ºC, 4 h; d) Propargyl alcohol, 2,6- lutidine, TBAI, CH_2Cl_2, 25 ºC, 8 h, over two steps 64%; e) 10 mol% $AuBr_3$, 4-

pentene-1-ol, CH_2Cl_2, 4Å MS powder, 25 ºC, 20 min, 89 %; f) NaOMe, CH_2Cl_2: CH_3OH (1:1), 25 ºC, 2 h, 92%; g) 2,2-dimethoxypropane, *p*TSA, acetone, 25 ºC, 5 h, 80%; h) *p*TSA, CH_3OH:CH_2Cl_2 (1:1), 25 ºC, 6 h, 76%; i) Benzoic Anhydride, Et_3N, CH_2Cl_2, 0 ºC, 5 h, 72%.

Orthoester **25** was glycosylated using the Au(III) catalyzed glycosylation strategy with 4-pentene-1-ol in anhydrous CH_2Cl_2 to afford the corresponding pentenyl galactofuranoside **26** in 84 % yield. The benzoyl groups of **26** were deprotected under Zemplén conditions (NaOMe/MeOH) to furnish tetraol **27** in 92% yield which was subjected to acetonide protection employing 2,2-dimethoxy propane (DMP) and PTSA (cat.) in anhydrous acetone to give compound **28**. The C-2 and C-3 hydroxyl groups were again protected as benzoates using benzoyl chloride and pyridine producing the compound **29** in 92 % yield. Further, the acid mediated cleavage of the acetonide group of compound **29** by catalytic PTSA gave the diol **30** in 76% yield which will be used further as a common building block for the synthesis of monosaccharide acceptors and carbonate donors in our total synthesis. The diol **30** was converted to aglycon **9** by the selective benzoylation of C-6 OH using benzoic anhydride in presence of Et_3N in CH_2Cl_2 in 72 % yield (Scheme **4.5**).

4.7.5 Synthesis of the Carbonate donor building blocks 8 and 10:

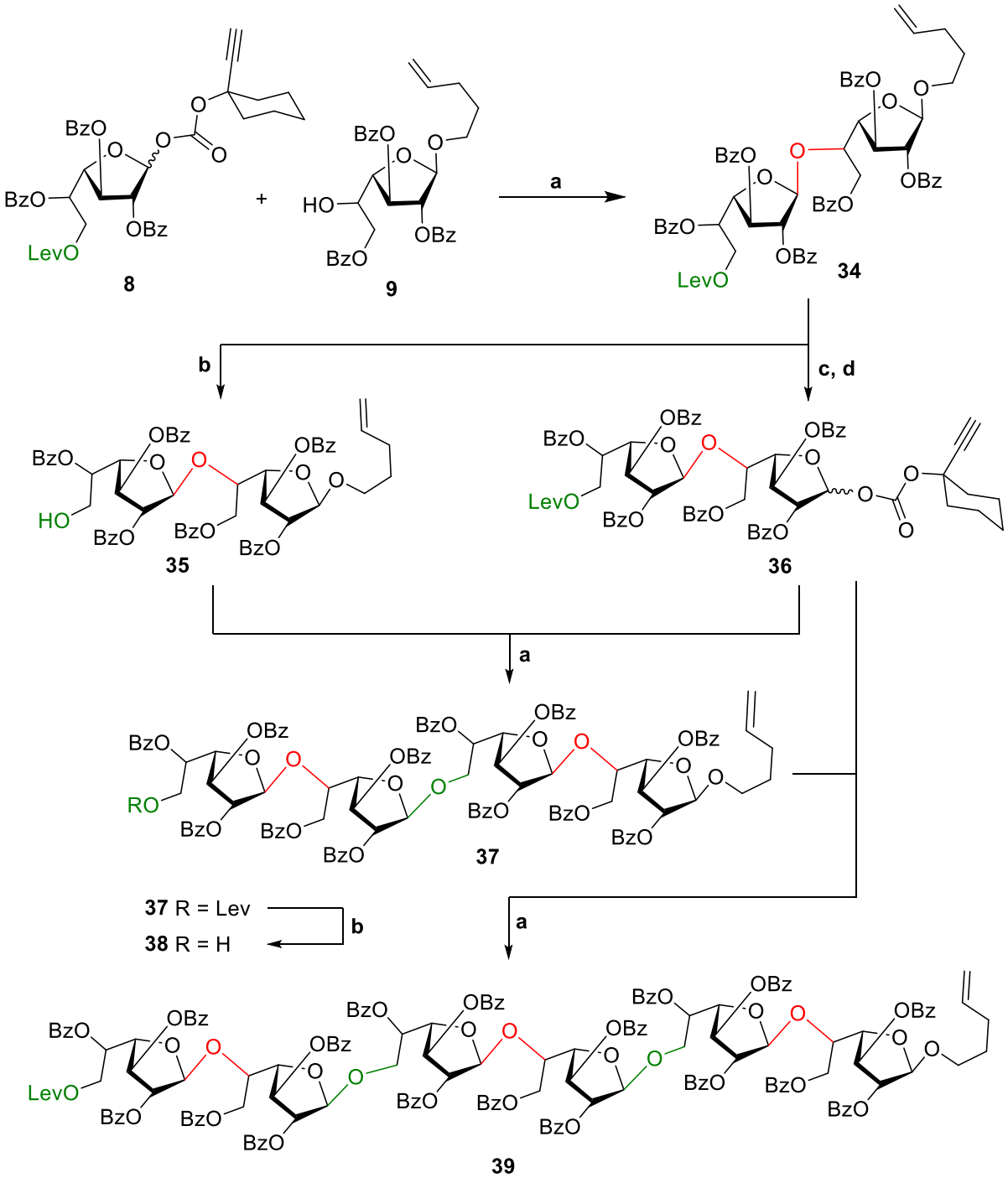
The synthesis of the monosaccharide galactofuranosyl carbonate donors started from diol compound **30** prepared *vide supra*. The primary C6-OH of **30** was selectively protected using Lev-anhydride and Et_3N in CH_2Cl_2 resulting in compound **31** which was divided into two parts for the orthogonal protection of the C5-OH. First, **31** was treated with benzoyl chloride and pyridine to obtain compound **32** in 92% yield. In parallel, the C5-OH was protected as silyl ether using TBDMSOTf and 2,6-lutidine in CH_2Cl_2 to furnish the silyl protected galactofuranoside **33** in 76% yield. The pentenyl glycosides **32** and **33** were independently converted to the corresponding hemiacetals via a common reaction protocol using NIS and catalytic TfOH which further transformed to the corresponding galactofuranosyl carbonate donors **8** and **10** using the carbonate reagent **13** in the presence of DMAP in CH_2Cl_2 in 84% and 76% yield respectively (Scheme **4.6**).



Scheme 4.6. Synthesis of Carbonate donors 8 and 10. Reagents: a) Lev-anhydride, Et_3N, DMAP, CH_2Cl_2, 0 ºC, 4 h, 62%; b) BzCl, pyridine, DMAP, 0-25 ºC, 5 h, 92%; c) TBDMSOTf, 2,6- lutidine, CH_2Cl_2, 0 ºC, 1 h, 76%; d) NIS, TfOH, CH_3CN:CH_2Cl_2:H_2O (3:5:0.5), -20 - 0 ºC, 2 h; e) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate **(13),** CH_2Cl_2, DMAP, 25 ºC, 8 h, 84% for **8** and 76 % for **10** over two steps.

4.7.6 Synthesis of Common Hexasaccharide motif 39

After synthesizing glycosyl donor **8** and glycosyl acceptor **9**, a glycosylation reaction was conducted using [Au]/[Ag] catalysis yielding a disaccharide **34** in 86 % yield. Disaccharide **34** was then split into two parts: First, the C6-primary Lev group was deprotected using standard protocol of $NH_2NH_2.H_2O$ in AcOH and pyridine buffer medium to obtain the aglycon **35** in 91 % yield for further elongation of the galactofuranosyl chain. The remaining part of the disaccharide **34** was converted to the corresponding alkynyl galactofuranosyl carbonate donor **36** using the standard two step protocol that involves the deprotection of the pentenyl group at the reducing end and masking the hemiacetal with easily available carbonate reagent **13** in the presence of DMAP in CH_2Cl_2 in 81 % yield over two steps.



Scheme 4.7. Synthesis of Common Hexasaccharide Motif 39. Reagents: a) 8mol% chloro[2,4-di-*tert*-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ºC, 20 min, 86% for **34**, 81 % for **37**, 76% for **39**; b) NH_2NH_2, AcOH: Pyridine (22:27 eq.), CH_2Cl_2, 30 min, 80% for **35**, 78% for **38**. c) NIS, TfOH, CH_3CN:CH_2Cl_2:H_2O (3:5:0.5), 0- 25 ºC, 2 h; d) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate **(13),** CH_2Cl_2, DMAP, 25 ºC, 8 h, over two steps 81%.

With access to disaccharide donor **35** and acceptor **36**, we initiated the synthesis of the common hexasaccharide motif **39**. To begin with, [Au]/[Ag]-catalyzed glycosylation between **35** and **36** was successfully performed to obatin the tetrasaccharide **37** in 81 % yield. The Lev group at the non-reducing end of the tetrasaccharide was deprotected using $NH_2NH_2.H_2O$ in AcOH and pyridine buffer medium to obtain the tetrasacchride acceptor **38**. Then ultimately, the [Au]/[Ag]-catalyzed coupling between the donor **35** prepared *vide supra* and acceptor **38** was carried in a [2+4] fashion out to furnish the desired common hexasaccharide **39** in 76 % yield (Scheme **4.8**). The successful synthesis of the desired common hexasaccharide epitope **39** was verified using NMR (Table **4.2**) and MALDI-TOF spectral analysis. Primarily, six resonances at δ 106.8, 106.8, 106.0, 105.6, 105.6 and 105.5 ppm in the anomeric region of the ^{13}C NMR spectrum confirmed the structural integrity of Gal_6f **39**. Besides, the observed *m/z* value for $C_{172}H_{148}O_{51}Na$: 3053.394 was in good agreement with the calculated m/z: 3053.895 for the compound **39**.

Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
Anomeric	5.78 (m, 3H), 5.21 (s, 1H) and 5.18 (d, 2H)	106.8, 106.8, 106.0, 105.6, 105.6 and 105.5
Benzoates	7.10 – 8.02 (Total 90H)	166.2, 166.0, 166.0, 165.9, 165.9, 165.8, 165.7, 165.7, 165.7, 165.6, 165.5, 165.5, 165.5, 165.3, 165.2, 165.2, 165.2 and 165.1
Levulinoate	1.72 – 1.63 (m, 2H), 2.60 – 2.50 (m, 2H) and 1.99 (s, 3H)	206.3, 172.1, 37.8, 30.3 and 29.7

Table 4.2. Characteristic ^{1}H and ^{13}C NMR Signals for Common hexasaccharide epitope **39**

4.7.7 Synthesis of Middle Gal*f*$_6$ Hexasaccharide epitope 45:

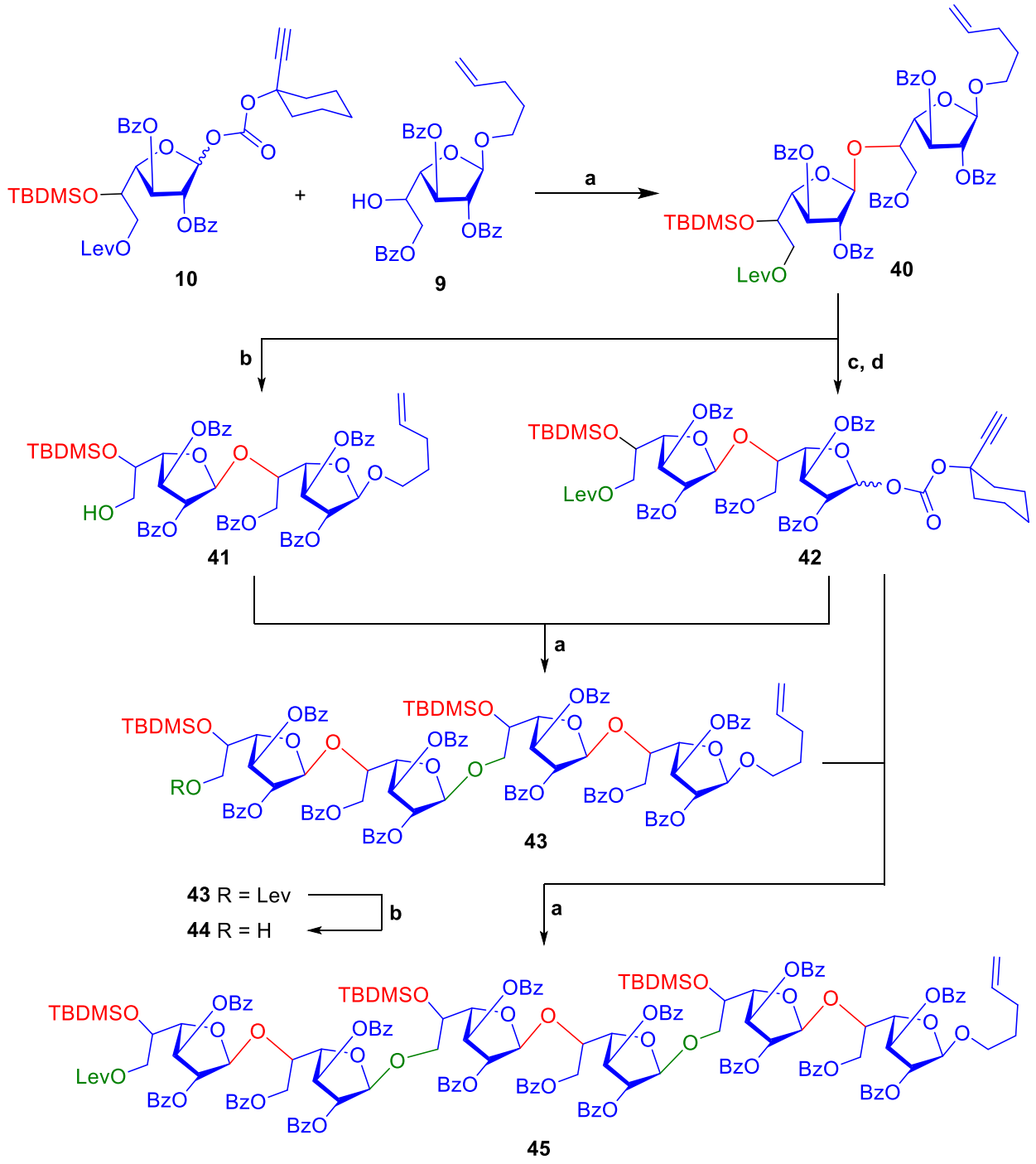
The synthesis of the middle repeating hexasaccharide **45** commenced with highly convergent protocol similar to that of the common hexasaccharide. It began with the synthesis of disaccharide **40** using galactofuranosyl donor **10** and common monosaccharide acceptor **9** prepared *vide supra* via the [Au]/[Ag]-catalysed glycosylation conditions in 87 % yield. Disaccharide **40** was divided into two portions: initially, the C6-primary Lev group was deprotected using $NH_2NH_2{\cdot}H_2O$ in AcOH and pyridine buffer, yielding aglycon **41** in 91% yield, which was required for further extension of the galactofuranosyl chain. Simultaneously, the transformation of another portion of disaccharide **40** into the corresponding alkynyl galactofuranosyl carbonate donor **42** was successfully made using the aforementioned standard two-step process involving deprotection of

the pentenyl group at the reducing end and then masking thus resulting hemiacetals with carbonate reagent **13**. However, during the acid mediated cleavage of the pentenyl group using TfOH, the cleavage of the TBDMS group was noticed thus resulting in the lowering of the yield during the hemiacetal formation step. However, we optimized the reaction and it was noticed that using a acid free cleavage of the *n*-pentenyl group using *N*-Bromosuccinimide (NBS) in moist acetonitrile yields hemiacetals in very good yields which was later transformed into the corresponding alkynyl galactofuranosyl donor **42** using easily available carbonate reagent **13** in the presence of DMAP in CH_2Cl_2 in 78 % yield over two steps (Scheme **4.8**).

In continuation, the disaccharide donor **41** and acceptor **42** were coupled in a [2+2] fashion under standard [Au]/[Ag]-catalysis conditions to smoothly afford the tetrasaccharide **43** in 80 % yield. Thereafter, the primary Lev group of **43** was deprotected using $NH_2NH_2{\bullet}H_2O$ in AcOH and pyridine buffer conditions to obtain the tetrasaccharide aglycon **44** which was directly glycosylated with the previously prepared digalactofuranosyl carbonate donor **42** in a [2+4] manner *via* the gold catalyzed glycosylation strategy to successfully obtain the desired middle hexasaccharide epitope **45** in 73 % yield (**scheme 4.8**). Of course, it goes without saying that the successful formation of the middle hexasaccharide was confirmed by the NMR (Table **4.3**) and MALDI-TOF techniques. The six resonances at δ 106.5, 106.5, 105.7, 105.6, 105.4 and 105.3 ppm in the anomeric region of the ^{13}C NMR confirmed the structural integrity of **45** as a hexasaccharide. Further in the MS analysis, the observed *m/z* value for $C_{169}H_{178}O_{48}Si_3Na$: 3084.7112 is in good agreement with the calculated *m/z* 3084.4792 for compound **45**.

Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
Anomeric	5.6 (m, 3H), 5.1 (s, 1H) and 5.0 (d, 2H)	106.5, 106.5, 105.7, 105.6, 105.4 and 105.3
Benzoates	7.2 – 8.1 (Total 75H)	166.2, 166.0, 166.0, 165.8, 165.8, 165.7, 165.5, 165.5, 165.5, 165.4, 165.3, 165.3, 165.2, 165.2 and 165.1
Levulinoate	1.70 (td, *J* = 7.3, 3.9 Hz, 2H), 2.50 (t, *J* = 6.1 Hz, 2H) and 2.11 (s, 3H)	29.9, 30.3, 37.9, 172.5 and 206.4
-OTBDMS	0.81 – 0.74 (m, 27H)	18.2, 18.2, 18.1, 25.9, 25.9, 25.9, 25.8, 25.8, 25.8, 25.7, 25.7, 25.7, -4.1, -4.2, -4.6, -4.7, -4.7 and -4.7

Table 4.3. Characteristic ^{1}H and ^{13}C NMR Signals for middle hexasaccharide epitope **45**



Scheme 4.8. Synthesis of Middle Hexasaccharide Motif 45. Reagents: a) 8mol% chloro[2,4-di-*tert*-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ºC, 20 min, 87% for **40**, 80% for **43**, 73% for **45**; b) NH_2NH_2, AcOH: Pyridine (22:27 eq.), CH_2Cl_2, 30 min, 80% for **41,** 78% for **44;** c) NBS, CH_3CN:H_2O (10:1), 0- 25 ºC, 2 h; d) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate **(17),** CH_2Cl_2, DMAP, 25 ºC, 8 h, over two steps 78%.

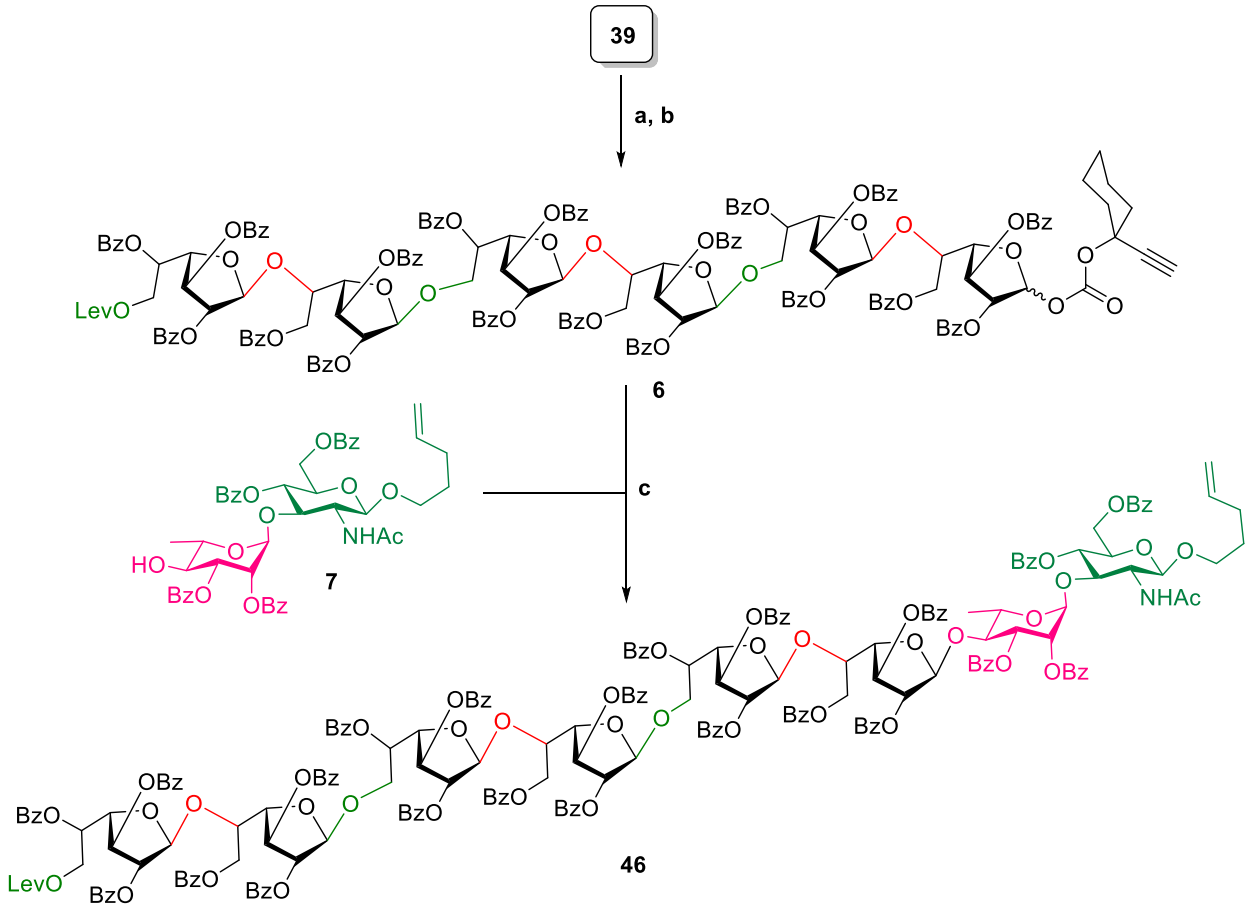
4.7.8 Synthesis of Terminal Gal*f*$_8$ Octasaccharide epitope 46:

Now having all the repeating hexasaccharide and linker disaccharide epitopes in our hand, we commence the stitching of the large epitopes utilizing our standard [Au]/[Ag]-catalysed glycosylation conditions. The *n*-pentenyl group at the reducing end of the common hexasaccharide **39** was cleaved using the standard NIS/TfOH mediated reaction to obtain the hemiacetals which was directly transformed into the corresponding hexasaccharide carbonate donor **6** using carbonate reagent **13** in the presence of DMAP in CH_2Cl_2 in 76% yield over two steps (Scheme **4.9**). The new carbonyl peak at δ 150.9 ppm in the ^{13}C NMR spectrum of compound **6** confirmed the successful formation of the carbonate donor motif.

Now the hexasaccharide donor **6** was glycosylated with the linker disaccharide acceptor **7** prepared *vide supra* in a [6+2] fashion using the [Au]/[Ag]-catalyzed glycosylation conditions in anhydrous CH_2Cl_2 in 25 °C to successfully afforded the terminal octasaccharide **46** in 72% yield in just 20 min. The structural integrity of the octasaccharide was further verified using NMR spectral analysis which revealed eight distinct peaks in the anomeric region of the ^{13}C NMR (Table **4.4**). Among the eight peaks, the closely spaced resonances at δ 107.5-105.6 ppm belong to the galactan motif, and the isolated two peaks of δ 100.0 and 97.7 ppm confirms the Rha*p*-GlcN motif attachment. Also, the observed *m/z* value of 3818.605 amu is in good correlation with the calcd. *m/z* of 3818.134 in the MALDI-ToF studies confirmed the successful formation of the terminal octasaccharide **46**.

Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
Anomeric	5.77-5.74 (m, 3H), 5.51 (s, 1H), 5.17-5.15 (d, 2H), 5.09 (s, 1H) and 4.95 (d, 1H)	107.5, 106.8, 106.8, 106.0, 105.7, 105.6, 100.0 and 97.7
Benzoates	7.03 – 8.09 (Total 110H)	166.4, 166.2 (2C), 166.1 (2C), 166.0, 165.9 (2C), 165.8 (3C), 165.6 (3C), 165.3 (3C), 165.2 (2C), 165.1, 164.9 and 164.6
Levulinoate	2.52-2.55 (m, 2H) and 1.99 (s, 3H), 1.76 (m, 2H)	206.5, 172.2, 37.9, 30.5 and 29.8
Acetamide	2.20 (s, 3H)	171.0 and 23.5

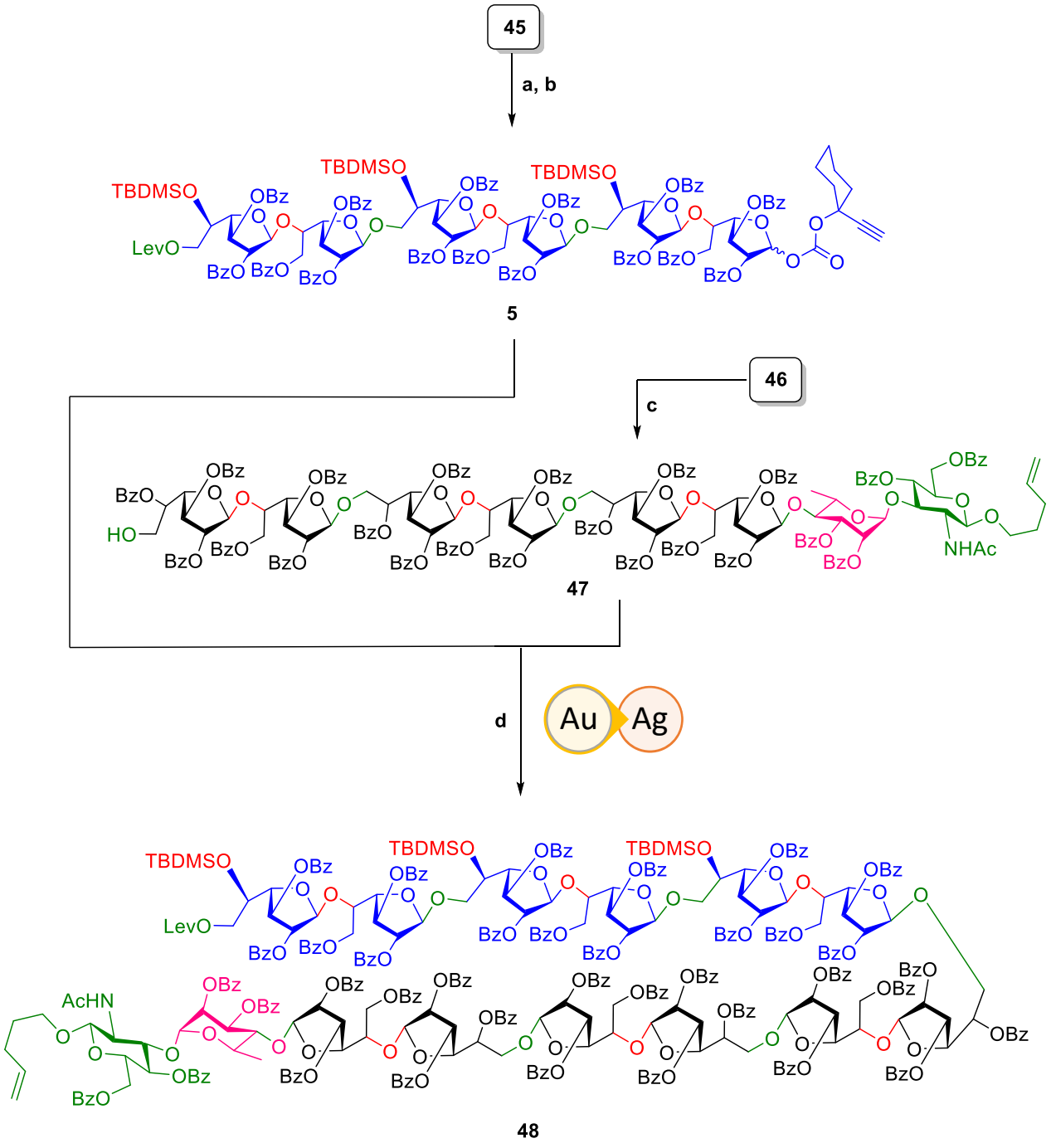
Table 4.4. Characteristic ^{1}H and ^{13}C NMR Signals for octasaccharide epitope **46**



Scheme 4.9. Synthesis of Terminal Octasaccharide Motif 46. Reagents: a) NIS, TfOH, CH_3CN:CH_2Cl_2:H_2O (3:5:0.5), 0- 25 ºC, 2 h; b) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate **(17),** CH_2Cl_2, DMAP, 25 ºC, 8 h, over two steps 76%. c) 8mol% chloro[2,4-di-*tert*-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ºC, 30 min, 72%.

4.7.9 Synthesis of linear Gal*f*$_{14}$ epitope 48:

The synthetic elongation of the linear galactan chain was continued further utilizing the gold catalyzed glycosylation protocol. The *n*-pentenyl group at the reducing end of the middle hexasaccharide motif **45** was successfully deprotected using NBS in moist CH_3CN to obtain the corresponding hexasacchairde hemiacetal which was immediately treated with carbonate reagent **17** under CH_2Cl_2/DMAP condition to successfully furnish the desired middle hexasaccharide carbonate donor **5** in 78 % yield over two steps (Scheme **4.10**). In the ^{13}C NMR spectrum of compound **5**, the appearance of a new carbonyl peak at δ 150.9 ppm confirms the successful formation of the carbonate donor motif. Besides, in the MALDI-ToF spectra, the observed *m/z* value of 3165.1538 is in good agreement with the calcd. *m/z* of compound **5**: 3165.0781 amu.



Scheme 4.10. Synthesis of Gal*f*$_{14}$ Motif 48. Reagents: a) NBS, CH_3CN:H_2O (10:1), 0- 25 ºC, 30 min; b) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate **(17),** CH_2Cl_2, DMAP, 25 ºC, 8 h, over two steps 78%. c) NH_2NH_2, AcOH: Pyridine (22:27 eq.), CH_2Cl_2, 30 min, 81%; d) 8mol% chloro[2,4-di-*tert*-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ºC, 20 min, 87%.

Moving on to the synthesis of the acceptor, the Lev group at the non-reducing end of the octasaccharide **46** was deprotected using hydrazine hydrate to afford the octasaccharide acceptor **47** (Scheme **4.10**). In the MALDI-ToF spectra, the observed *m/z* value of 3720.7358 (calcd. 3720.0972) confirms the formation of the acceptor **47**.

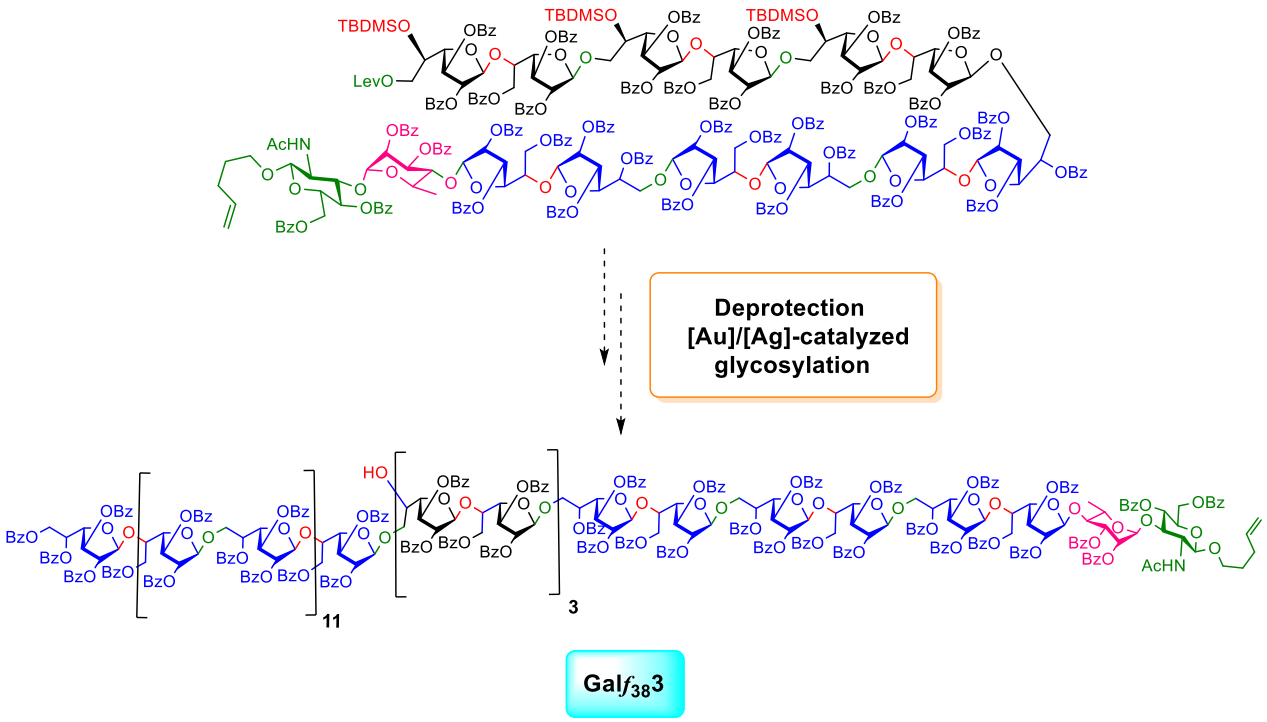
Now the middle hexasaccharide donor **5** and acceptor **47** were glycosylated using the standard [Au]/[Ag]-catalyzed activation protocol to furnish the 14-mer linear Gal*f* motif **48** in 77% yield. The structural integrity of the formed 14-mer was assessed using NMR spectral studies (Table **4.5**) and MALDI-ToF studies. In the anomeric region of the ^{13}C NMR, fourteen resonances confirmed the formation of Gal$_{14}$*f*. In the MALDI-ToF spectra, the observed *m/z* value of 6699.6313 amu is in good correlation with the calcd. *m/z* of compound **48**: 6697.0378 which confirmed the successful formation of the epitope Gal$_{14}$*f* **48**.

Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
Anomeric	5.76-5.68 (m, 6H), 5.50 (s, 1H), 5.15-5.11 (m, 5H), 5.10 (s, 1H) and 4.95 (d, 1H)	107.5, 106.9, 106.9, 106.8, 106.5, 106.5, 106.0, 106.0, 105.7, 105.7, 105.5, 105.4, 100.0, 97.7
Benzoates	7.03 – 8.05 (Total 185H)	166.4, 166.2 (2C), 166.1, 166.0 (5C), 165.9 (5C), 165.8 (3C), 165.7 (2C), 165.6, 165.5 (3C), 165.4 (2C), 165.3 (2C), 165.2 (6C), 165.1 (2C), 164.9, 164.6
Levulinoate	2.47 (m, 2H) and 2.10 (s, 3H), 1.78-1.75 (m, 2H)	206.5, 172.5, 37.9, 30.3 and 29.8
Acetamide	2.18 (s, 3H)	170.9 and 23.5

Table 4.5. Characteristic ^{1}H and ^{13}C NMR Signals for 14-mer epitope **48.**

4.7.10 Synthesis of linear Gal*f*$_{38}$ epitope 3:

The final assembly of all the hexasaccharide motifs to furnish the Gal*f*$_{38}$ acceptor **3** is currently under progress. So far, adequate quantities of Gal*f*$_{14}$ epitope **48** and common hexasaccharide carbonate donor **6** are successfully synthesized. After the formation of the acceptor **3** and the branch arabinan portion, we need to perform the glycosylation to couple the large Gal*f* and Ara*f* motifs followed by careful global deprotection to reach our goal of the synthesis of the 131-mer arabinogalactan residue.



Scheme 4.11. Synthesis of linear Galf_{38} epitope **3**

In summary, a highly convergent and efficient synthetic strategy was identified for the synthesis of the highly branched and complex arabinogalactan motif of *Mycobacterium tuberculosis*. Efficient cyclohexyl propargyl carbonate donors was employed as versatile donor in the synthesis of monosaccharides as well as large fragments such as hexasaccharides and octasaccharides. The catalytic mild activation of the donors by [Au]/[Ag]-dual catalysis, high yields and shorter reaction time of the glycosylations make the current methodology highly efficient for the oligosaccharide synthesis. The final assembly of 131-mer of arabinogalactan is currently underway in our group.

4.8 General Experimental Procedures

a) General Procedure for allyl glycosides synthesis (for 14)

A suspension of commercially available sugar (1 mmol) in solvent allyl alcohol (5 mL) was cooled down to 0 °C. Acetyl chloride (2.5 mmol) was added dropwise to the reaction mixture. Then the reaction mixture was refluxed at 80 °C for 5 h. After completion, the excess acetyl chloride was quenched by adding excess Et_3N in 0 °C and the reaction mixture was concentrated under reduced pressure and purified through silica gel column chromatography (CH_2Cl_2/ CH_3OH) to obtain the corresponding allyl glycoside as a pale-yellow sticky liquid.

b) General procedure for acetonide protection (for 14 and 28)

The corresponding sugar (1 mmol) having free OH group was dissolved in anhydrous acetone (4 mL). 2,2-dimethoxy propane (1.2 mmol) and PTSA (0.2 mmol) was added to the reaction mixture and it was allowed to stir at 25 °C for 2 h. After the completion of the starting material indicated by TLC, excess Et_3N was added for quenching and concentrated under reduced pressure to obtain a light brown residue which was purified using column chromatography (EtOAc/ n-hexane as mobile phase) to obtain the desired acetonide protected product as yellow sticky gum.

c) General procedure of Levulinoate protection (for 14 and 20)

To the solution of deprotected sugar (1 mmol) in anhydrous CH_2Cl_2, levulinic acid (1.5 mmol) and *N*,*N*′-Diisopropylcarbodiimide (1.5 mmol) and DMAP (1.0 mmol) were added under nitrogen atmosphere and the reaction mixture was stirred for 2 h at 25 °C. After the cosumption of the starting alcohol, the reaction mixture was concentrated under reduced pressure and purified on silica gel column chromatography (*n*-hexane/ EtOAc) to furnish the Lev-ester protected glycoside as a pale-yellow gum.

d) General procedure for deprotection of Isopropylidene group (for 15 and 30)

The acetonide protected sugar compound (1 mmol) was dissolved in anhydrous solvent mixture of CH_3OH/CH_2Cl_2 (1:1) (5 mL). pTSA (0.2 mmol) was added to the reaction mixture and it was stirred for 4 h at 25 °C. After the completion of the reaction, it was quenched by adding excess Et_3N and concentrated under reduced pressure to obtain a light brown residue which was purified using column chromatography (EtOAc/ *n*-hexane as mobile phase) to obtain the deprotected glycoside as a sticky liquid.

e) General procedure for acetate/benzoate ester protection of sugar alcohols (for 17, 18, 21, 29, 32)

Hydroxyl free sugar compound (1 mmol) was dissolved in anhydrous pyridine (5 mL) and cooled to 0 °C. Benzoyl chloride/acetic anhydride (1.2 mmol per OH) was added slowly dropwise to the reaction mixture at 0°C under a nitrogen atmosphere. The mixture was then allowed to gradually warm to 25°C and stirred for 5-8 hours.After the completion of the starting material as indicated by TLC, the reaction mixture was diluted with CH_2Cl_2 (50 mL). The combined organic layer was subsequently washed with 1*N* HCl solution (2x50 mL), saturated aqueous $NaHCO_3$ solution (2x 50 mL) and brine solution (50 mL). The organic layer was dried over Na_2SO_4, evaporated *in vacuo* and the crude mixture was purified using silica gel column chromatography (EtOAc and hexane as mobile phase) to obtain the corresponding ester protected compounds.

f) General procedure for deprotection of allyl glycosides (for 11)

Allyl glycoside (1 mmol) was dissolved in a mixture of solvents CH_3OH/CH_2Cl_2 (1:1) (10 mL) and it was cooled to 0 ºC under nitrogen atmosphere. A suspension of $PdCl_2$ (0.2 eqv) in MeOH (1 mL) was added dropwise to the reaction mixture and it was gradually warmed 25 ºC and stirred further for 4 h. After the completion, excess Et_3N was added to the reaction mixture for quenching and the excess palladium was filtered off using a bed of celite. The filtrate was concentrated *in vacuo* and the resultant residue was purified using silica gel column chromatography (EtOAc/ hexane) to obtain the corresponding hemiacetal compounds.

g) General procedure for synthesis of ethynylcyclohexyl glycosyl carbonate donors (for 6, 8, 10, 11, 36, 42)

To a stirring solution of hemiacetal (1 mmol) in anhydrous CH_2Cl_2 (5 mL), DMAP (1 mmol) was added at 25 ºC and stirred for 15 min. Carbonate reagent **13** (1.2 mmol) was added portion wise to the reaction mixture and further stirred for 8 h under nitrogen atmosphere. After the completion of the starting hemiacetal, the reaction mixture was concentrated under reduced pressure and the crude mixture was put into purification using column chromatography (EtOAc/ hexane) to yield the corresponding alkynyl glycosyl carbonate donors as sticky foams.

h) General Procedure for Troc- protection of amine (for 18)

To an ice-cold solution of glucosamine hydrochloride (1 mmol) in water, a 2.0 N solution of $NaHCO_3$ was added and the mixture was stirred for 1 h. After that, TrocCl (1 mmol) was added dropwise to the same solution and further stirred for 2 h. The resulting solid precipitate was then filtered and dried to obtain the NHtroc sugar and it was directly subjected to the next reaction without further purification.

i) General procedure of synthesis of *n*-pentenyl glycosides from per-acetate ester compound (for 19)

The per-acetate sugar motif (1 mmol) and 4-pentene-1-ol (2 mmol) were dissolved in anhydrous CH_2Cl_2 (5 mL). Freshly activated 4Å MS powder was added to the reaction mixture and it was stirred for 15 min under nitrogen atmosphere. $BF_3.Et_2O$ (3 mmol) was added dropwise and the reaction mixture was refluxed at 60 ºC for 4 h. After the completion the reaction mixture was cooled to 25 ºC and the excess BF_3 was quenched by adding Et_3N. The reaction mixture was filtered through celite bed and the resultant filtrate was concentrated under reduced pressure. The resultant crude residue was purified using silica gel column chromatography (*n*-hexane/EtOAc) to furnish the corresponding pentenyl glycoside as a sticky gum.

j) General procedure of saponification of benzoate/acetate esters (for 20 and 27)

To a solution of ester protected sugar (1 mmol) in CH_3OH: CH_2Cl_2 (2:1) (5 mL) was added NaOMe (0.2 mmol per ester group) and it was stirred for 1-2 h at 25 ºC. After the completion of the starting material, the reaction mixture was neutralized with Amberlite IR-120H resin. Subsequently, the solid resin was filtered off through a Celite® bed and the filtrate was concentrated under reduced pressure. The resultant crude was purified using silica gel column chromatography (*n*-hexane/EtOAc as mobile phase) to obtain the deprotected glycoside as a sticky liquid.

k) General procedure for benzylidine protection (for 20)

To a suspension of sugar (1 mmol) in anhydrous acetonitrile was added benzaldehyde dimethylacetal (1.5 mmol) and 10-camphorsulfonic acid (CSA) (0.1 mmol) at 25 ºC and the reaction mixture was stirred for 4 h under nitrogen atmosphere. After completion, the reaction was quenched by adding excess Et_3N and concentrated *in vacuo*. The resultant crude was purified using

silica gel column chromatography (*n*-hexane/EtOAc as mobile phase) to obtain the benzylidene protected glycoside as an amorphous solid.

l) General procedure for benzylidine deprotection (for 21)

*p*TSA (0.2 mmol) was to a solution of benzylidine protected derivative (1 mmol) CH_3OH: CH_2Cl_2 (2:1) (5 mL) and stirred for 4 h at 25 °C. After the completion of the starting material it was quenched by adding excess Et_3N and concentrated under reduced pressure to obtain a light brown residue which was purified using column chromatography (*n*-hexane and EtOAc as mobile phase) to obtain the deprotected glycoside as a pale-yellow gum.

m) General procedure of Levulinoate deprotection (for 7, 12, 35, 38, 41, 44)

To a solution of glycoside (1 mmol) in anhydrous CH_2Cl_2 were added acetic acid (22 mmol) and pyridine (27 mmol) and stirred for 5 min at 25 ºC. Hydrazine hydrate (5 mmol) was added dropwise to the reaction mixture and it was further stirred for 30 min at 25 ºC. After the completion of the starting material, excess hydrazine was quenched by adding acetone. Then the reaction mixture was diluted with CH_2Cl_2 (50 mL), the organic layer was washed with 1*N* HCl solution (2x50 mL), saturated aqueous $NaHCO_3$ solution (2x 50 mL) and brine solution (50 mL) successively. The combined organic layer was dried over anhydrous Na_2SO_4, concentrated *in vacuo* and the resulting crude was purified using silica gel column chromatography (EtOAc/ hexane) to furnish the corresponding deprotected compound.

n) General Procedure for Glycosylation (for 22, 34, 37, 39, 40, 43, 45, 46, 48)

Alkynyl glycosyl carbonate donor (1 mmol) and acceptor (1 mmol) were dissolved in anhydrous CH_2Cl_2 (5 mL). Freshly activated 4Å MS powder was added to the reaction mixture and it was stirred for 15 min under nitrogen atmosphere. Subsequently, Au-phosphite catalyst (0.08 mmol) and AgOTf (0.08 mmol) were added and it was further stirred for 20-30 min at 25 ^{0}C. After the completion indicated by TLC, the reaction was quenched by adding Et3N and the MS powder was filtered off using a Celite® bed. The filtrate was concentrated *in vacuo* and the resulting crude was purified using silica gel column chromatography (hexane/ EtOAc) to furnish the desired glycoside.

o) Procedure for the synthesis of galactofuranoside (for 24)

A suspension of commercially available D-galactose (1 mmol) in anhydrous methanol (10 mL) with ferric chloride (8 mmol) was heated to 60 °C for 48 hours under nitrogen atmosphere. Then it was cooled to 25 °C, Celite (1.0 g) and a saturated aqueous solution of $NaHCO_3$ (30 mL) were added. The mixture was stirred for further 1 h at 25 °C. The formed white precipitate was filtered through a Celite® bed, washed thoroughly with methanol, and resultant filtrate was concentrated *in vacuo*. The resulting solid was extracted with boiling ethyl acetate-ethanol (2:1, v/v, 3 x 50 mL), and the combined organic extracts were concentrated *in vacuo* and the crude residue was then washed with THF, filtered, and evaporated to yield methyl galactofuranoside which was carried forward to the next step without further purification.

p) General procedure for the synthesis of propargyl 1,2-orthoesters (for 25)

Per-*O*-acyl methyl galactofuranoside (1.0 mmol) was dissolved in anhydrous CH_2Cl_2 (5 mL) and cooled to 0 °C. Acetyl bromide (6.5 mmol) was added dropwise to the reaction mixture followed by the drop-wise addition of MeOH (4.5 mmol) and further stirred at 25 °C for 4 h under nitrogen atmosphere. After completion, the reaction mixture was diluted with CH_2Cl_2 (50 mL). The organic layer was washed with ice water (2x 25 mL), ice-cold saturated $NaHCO_3$ (2x50 mL), brine solution (50 mL) subsequently. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to afford corresponding furanosyl bromide as a white foam which was immediately taken to the next step without any further purification. To a solution of the crude furanosyl bromide prepared *vide supra* in dry CH_2Cl_2, propargyl alcohol (2.0 mmol), 2,6-lutidine (2.2 mmol) and tetra *n*-butyl ammonium iodide (0.5 mmol) were added and the reaction mixture was allowed to stir at 25 °C. After 8 h. After completion, the reaction mixture was diluted with CH_2Cl_2 (50 mL), extracted with saturated aqueous oxalic acid solution (3x25 mL), saturated $NaHCO_3$ solution (2x25 mL), brine solution (25 mL), dried over Na_2SO_4 and concentrated *in vacuo* to obtain a resultant residue that was subjected to purification through column chromatography (Hexane/ EtOAc) to obtain the furanosyl orthoester as a pale-yellow foam.

q) General procedure of $AuBr_3$ mediated orthoester opening (for 26)

Freshly activated 4Å MS powder was added to a solution of propargyl orthoester (1 mmol) and 4-pentene-1-ol (3 mmol) in anhydrous CH_2Cl_2 (5 mL) and stirred for 15 min. $AuBr_3$ (0.1 mmol) was added at 25 °C and the reaction was further stirred for 20 min under nitrogen atmosphere. After completion of the starting orthoester, excess Et_3N was added to the the reaction for quenching and

passed through Celite® bed. The filtrate was concentrated *in vacuo* and the resultant residue was subjected to purification by silica gel column chromatography (Hexane/ EtOAc) to obtain the furanosyl orthoester as a pale-yellow sticky gum.

r) General procedure for NIS mediated pentenyl deprotection (for 8, 10, 36)

Pentenyl glycoside (1 mmol) was dissolved in a trinary solvent mixture of CH_3CN:CH_2Cl_2:H_2O (3:5:0.5) (10 mL) and the reaction mixture was cooled to -20 °C. NIS (2 mmol) and TfOH (0.2 mmol) were added to the reaction mixture and it was allowed to stir at 0 °C for further 2 h. After completion indicated by TLC, the mixture was quenched with satd. $NaHCO_3$ solution (2 mL) and diluted with CH_2Cl_2 (50 mL). The organic layer was washed with saturated $Na_2S_2O_3$ solution (50 mL), saturated $NaHCO_3$ solution (2x 50 mL) and brine solution (50 mL) successively. The organic phase was dried over Na_2SO_4 and evaporated in *vacuo* to obtain crude that was purified by column chromatography (ethyl acetate/ hexane) to obtain the corresponding hemiacetal as light brown sticky gum.

s) General procedure for selective Lev protection of alcohols (for 31)

Deprotected sugar compound (1 mmol) was dissolved in anhydrous CH_2Cl_2 (5 mL) and cooled to 0 °C. Et_3N (5 mmol) was added followed by a dropwise addition of freshly prepared Lev-anhydride (1.1 mmol) and the reaction mixture was stirred for 4 h at 0 °C. After the completion, the reaction mixture was diluted with CH_2Cl_2 (50 mL) and it was washed with cold water (2x 25 mL). The organic fraction was dried over Na_2SO_4 and concentrated in *vacuo* and the resultant crude was purified by silica gel column chromatography (ethyl acetate and hexane as mobile phase) to furnish the corresponding Lev-protected compound as light-yellow sticky gum.

t) General procedure for the selective benzoyl protection of alcohols (for 9)

Benzoic anhydride (1.2 mmol) was added portion wise into a solution contaning sugar alcohol (1 mmol) and Et_3N (5 mmol) in dry CH_2Cl_2 (10 mL), at 0 ^{0}C under nitrogen atmosphere. The reaction mixture was continued to stir for another 5 h at 25 ^{0}C. Then the reaction mixture was diluted with CH_2Cl_2 (25 mL) and washed with 1*N* HCl (2x25 mL), saturated aq. $NaHCO_3$ solution (2x25 mL) and brine. The organic fraction was dried over anhydrous Na_2SO_4, concentrated *in vacuo* and the resultant crude subjected to purification through column chromatography (hexane/EtOAc as mobile phase) to obtain the desired primary benzoyl protected compound.

u) General procedure for TBDMS protection of alcohols (for 33)

To a solution of sugar alcohol (1 mmol) in anhydrous CH_2Cl_2 (10 mL) was added 2,6-lutidine (5 mmol) and it was cooled to 0 ºC. TBDMSOTf (1.5 mmol) was added dropwise to the reaction mixture and it was further stirred for 1 h at 0 ºC under nitrogen atmosphere. Upon completion of the starting material, the reaction was diluted with CH_2Cl_2 (50 mL) and washed with 1*N* HCl (2x25 mL), saturated aq. $NaHCO_3$ solution (2x25 mL) and brine solution (25 mL). The organic fraction was dried over Na_2SO_4, concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography (*n*-hexane and EtOAc) to obtain the desired silyl protected compound.

r) General procedure for NBS mediated pentenyl deprotection (for 42)

Pentenyl glycoside (1 mmol) was dissolved in a solvent mixture of acetone: H_2O (10:1) (10 mL) and the reaction mixture was cooled to 0 °C. $CaCO_3$ (5 mmol) was added to the reaction mixture and stirred for 10 mins. NBS (2 mmol) added to the reaction mixture and it was allowed to stir at 25 °C for 30 min. After completion indicated by TLC, the excess $CaCO_3$ was filtered off. The filtrate was diluted with CH_2Cl_2 (50 mL), washed with saturated $Na_2S_2O_3$ solution (2x50 mL), and brine solution (50 mL) successively. The organic phase was dried over Na_2SO_4 and evaporated in *vacuo* to obtain crude that was purified by column chromatography (ethyl acetate/ hexane) to obtain the corresponding hemiacetal as light brown sticky gum.

4.9. Characterization data

Allyl 2,3-*O*-isopropylidine-α-L-rhamnopyranoside (14): Yield: 76 % over two steps; Pale yellow syrup; $[\alpha]_D^{25}$ = +27.5 (*c* = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.96 – 5.82 (m, 1H), 5.32 – 5.25 (m, 1H), 5.20 (dq, J = 10.4, 1.3 Hz, 1H), 4.99 (s, 1H), 4.20 – 4.14 (m, 2H), 4.08 (dd, J = 7.2, 5.7 Hz, 1H), 3.99 (ddt, J = 12.8, 6.2, 1.3 Hz, 1H), 3.67 (dq, J = 9.3, 6.3 Hz, 1H), 3.37 (dd, J = 9.3, 7.2 Hz, 1H), 2.85 (s, 1H), 1.51 (s, 3H), 1.34 (s, 3H), 1.28 (d, J = 6.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.7, 117.9, 109.6, 96.3, 78.6, 76.0, 74.6, 68.1, 66.0, 28.1, 26.2, 17.6; HRMS (ESI-MS): m/z calcd. For $C_{12}H_{20}O_5$ $[M+Na]^+$: 267.1208; Found: 267.1216.

Allyl 2,3-*O*-isopropylidine-4-*O*-(4-oxopentanoyl)-α-L-rhamnopyranoside (15): Yield: 91 %; Pale yellow syrup; $[\alpha]_D^{25}$ = +12.5 (*c* = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.95 – 5.83 (m, 1H), 5.29 (dq, J = 17.2, 1.5 Hz, 1H), 5.20 (dt, J = 10.3, 1.4 Hz, 1H), 5.03 (s, 1H), 4.83 (dd, J = 10.1, 7.1 Hz, 1H), 4.19 – 4.13 (m, 3H), 3.99 (ddt, J = 12.8, 6.2, 1.3 Hz, 1H), 3.74 (dq, J = 10.2, 6.3 Hz, 1H), 2.90 – 2.80 (m, 1H), 2.71 – 2.60 (m, 2H), 2.58 – 2.50 (m, 1H), 2.16 (s, 3H), 1.53 (s, 3H), 1.32 (s, 3H), 1.16 (d, J = 6.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.5, 172.1, 133.6, 118.0, 109.8, 96.2, 76.1, 75.8, 74.9, 68.2, 64.2, 38.0, 29.9, 28.1, 27.8, 26.5, 17.0; HRMS (ESI-MS): m/z calcd. For $C_{17}H_{26}O_7$ $[M+Na]^+$: 365.1576; Found: 365.1543.

Allyl 2,3-di-*O*-benzoyl-4-*O*-(4-oxopentanoyl)-α-L-rhamnopyranoside (17): Yield: 92 %; Colorless gum; $[\alpha]_D^{25}$ = +28.6 (*c* = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 – 8.03 (m, 2H), 7.90 – 7.85 (m, 2H), 7.61 – 7.55 (m, 1H), 7.51 – 7.43 (m, 3H), 7.36 – 7.31 (m, 2H), 6.01 – 5.89 (m, 1H), 5.69 (dd, *J* = 10.1, 3.4 Hz, 1H), 5.61 (dd, *J* = 3.5, 1.8 Hz, 1H), 5.44 – 5.33 (m, 2H), 5.26 (dq, *J* = 10.4, 1.4 Hz, 1H), 5.00 (d, *J* = 1.7 Hz, 1H), 4.26 (ddt, *J* = 12.9, 5.2, 1.5 Hz, 1H), 4.13 – 4.03 (m, 2H), 2.72 – 2.62 (m, 1H), 2.58 (q, *J* = 4.9, 4.2 Hz, 1H), 2.55 – 2.49 (m, 1H), 2.43 – 2.34 (m, 1H), 2.06 (s, 3H), 1.34 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.1, 172.1, 165.6, 165.5, 133.5, 133.4, 133.3, 130.0, 130.0, 129.9, 129.9, 129.5, 129.4, 128.6, 128.6, 128.5, 128.5, 118.1, 96.6, 71.7, 70.9, 70.1, 68.6, 66.7, 37.9, 29.7, 28.1, 17.6; HRMS (ESI-MS): m/z calcd. For $C_{28}H_{30}O_9$ $[M+Na]^+$: 533.1788; Found: 533.1754.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3-di-*O*-benzoyl-4-*O*-(4-oxopentanoyl)-α-L-rhamnopyranoside (11): Yield: 81 % over two steps from **17**; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +9.6 (*c* = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 1.35 (d, J = 6.2 Hz, 6H), 1.56 – 1.83 (m, 10H), 1.84 – 2.00 (m, 4H), 2.07 (d, J = 2.1 Hz, 6H), 2.15 – 2.28 (m, 4H), 2.31 – 2.47 (m, 2H), 2.51 – 2.63 (m, 4H), 2.66 – 2.74 (m, 4H), 3.41 (qd, J = 10.6, 5.4 Hz, 1H), 3.55 (ddd, J = 15.6, 8.9, 6.2

Hz, 1H), 3.73 – 3.85 (m, 1H), 4.13 (ddd, J = 62.8, 9.8, 6.2 Hz, 2H), 4.63 – 4.80 (m, 1H), 4.96 (d, J = 1.4 Hz, 2H), 5.38 – 5.50 (m, 1H), 5.60 (dd, J = 3.4, 1.7 Hz, 1H), 5.65 – 5.68 (m, 1H), 5.69 – 5.76 (m, 1H), 7.35 (t, J = 7.8 Hz, 4H), 7.43 – 7.55 (m, 6H), 7.56 – 7.64 (m, 2H), 7.89 (dt, J = 8.5, 2.0 Hz, 4H), 7.98 – 8.13 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 14.1, 17.6, 22.4, 22.6, 25.0, 25.2, 25.2, 28.0, 28.0, 29.7, 30.8, 30.8, 36.7, 36.8, 37.0, 37.0, 37.9, 37.9, 66.6, 67.5, 67.6, 68.9, 70.1, 70.8, 71.6, 75.1, 75.6, 76.0, 76.0, 78.0, 78.9, 82.9, 93.7, 97.5, 128.4, 128.4, 128.4, 128.5, 128.6, 128.6, 128.6, 128.7, 129.1, 129.2, 129.4, 129.5, 129.8, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 130.0, 133.3, 133.4, 133.5, 133.7, 150.4, 152.3, 165.2, 165.5, 165.5, 165.6, 172.0, 172.1, 206.0, 206.1.; HRMS (ESI-MS): m/z calcd for $C_{34}H_{36}O_{11}$ $[M+Na]^+$: 643.2155; Found: 643.2143.

Acetyl 2-deoxy-2-(((2,2,2-trichloroethoxy)carbonyl)amino)-3,4,6-tri-*O*-acetyl-β-D-glucopyranoside (18): Yield: 78 % over two steps; Amorphous solid; $[\alpha]_D^{25}$ = +19.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.21 (q, J = 3.5 Hz, 1H), 5.32 – 5.12 (m, 3H), 4.80 (dt, J = 12.0, 2.7 Hz, 1H), 4.72 – 4.57 (m, 1H), 4.30 – 4.14 (m, 2H), 4.09 – 3.97 (m, 2H), 2.18 (dd, J = 4.5, 2.3 Hz, 3H), 2.08 – 2.06 (m, 3H), 2.02 (dt, J = 5.4, 2.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.3, 171.3, 170.8, 170.8, 169.3, 169.3, 168.7, 168.7, 154.2, 154.2, 95.3, 95.3, 92.4, 90.5, 75.0, 74.7, 70.5, 70.4, 69.8, 69.7, 67.8, 67.6, 61.7, 61.6, 53.9, 53.3, 21.0, 20.9, 20.8, 20.8, 20.8, 20.8, 20.7, 20.7; HRMS (ESI-MS): m/z calcd for $C_{17}H_{22}Cl_3NO_{11}$ $[M+Na]^+$: 544.0516; Found: 544.0538.

Pent-4-enyl 2-deoxy-2-(((2,2,2-trichloroethoxy)carbonyl)amino)-3,4,6-tri-*O*-acetyl-β-D-glucopyranoside (19): Yield: 83%; Pale yellow sticky foam; $[\alpha]_D^{25}$ = +32.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 – 5.74 (m, 1H), 5.27 – 5.20 (m, 2H), 5.11 – 4.98 (m, 3H), 4.86 (d, J = 3.7 Hz, 1H), 4.78 (d, J = 12.0 Hz, 1H), 4.64 (d, J = 12.1 Hz, 1H), 4.24 (dd, J = 12.3, 4.6 Hz, 1H), 4.10 – 4.00 (m, 2H), 3.96 (ddd, J = 10.2, 4.6, 2.3 Hz, 1H), 3.72 (dt, J = 9.8, 6.5 Hz, 1H), 3.45 (dt, J = 9.7, 6.4 Hz, 1H), 2.18 – 2.11 (m, 2H), 2.08 (s, 3H), 2.02 (s, 3H), 1.99 (s, 3H), 1.73 (t, J = 6.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 170.8, 169.5, 154.3, 137.8, 115.5, 97.4, 95.5, 74.7, 71.3, 68.4, 68.2, 67.9, 62.1, 54.1, 30.5, 28.5, 20.8, 20.8, 20.7; HRMS (ESI-MS): m/z calcd for $C_{20}H_{28}Cl_3NO_{10}$ $[M+Na]^+$: 570.0676, Found: 570.0643.

Pent-4-enyl 2-deoxy-2-(((2,2,2-trichloroethoxy)carbonyl)amino)-3-*O*-(4-oxopentanoyl)-4,6-*O*-benzylidine-β-D-glucopyranoside (20): Yield: 76 % over three steps from **19**; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +16.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.74 (p, *J* = 6.9 Hz, 2H), 2.13 (s, 3H), 2.14 – 2.25 (m, 2H), 2.50 – 2.80 (m, 4H), 3.43 (dt, *J* = 9.7, 6.5 Hz, 1H), 3.64 – 3.83 (m, 3H), 3.90 (td, *J* = 9.9, 4.7 Hz, 1H), 4.05 (td, *J* = 10.2, 3.7 Hz, 1H), 4.28 (dd, *J* = 10.2, 4.7

Hz, 1H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.79 – 4.91 (m, 2H), 4.97 – 5.11 (m, 2H), 5.35 (dt, *J* = 10.0, 5.0 Hz, 2H), 5.52 (s, 1H), 5.80 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 7.30 – 7.42 (m, 3H), 7.46 (dd, *J* = 6.6, 3.0 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 28.1, 28.5, 29.9, 30.5, 38.0, 54.7, 63.0, 68.0, 68.9, 70.5, 74.8, 79.2, 95.6, 98.2, 101.6, 115.5, 126.3, 126.3, 128.3, 128.3, 129.2, 137.0, 137.9, 154.5, 172.8, 206.1; HRMS (ESI-MS): m/z calcd for $C_{26}H_{32}Cl_3NO_9$ $[M+Na]^+$: 630.1040; Found: 630.1033.

Pent-4-enyl 2-deoxy-2-(((2,2,2-trichloroethoxy)carbonyl)amino)-3-*O*-(4-oxopentanoyl)-4,6-di-*O*-benzoyl-β-D-glucopyranoside (21): Yield: 78 % over two steps; Light brown sticky gum; $[\alpha]_D^{25}$ = +21.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 (ddd, *J* = 11.6, 8.3, 1.5 Hz, 4H), 7.59 – 7.51 (m, 2H), 7.41 (q, *J* = 8.1 Hz, 4H), 5.86 – 5.72 (m, 1H), 5.52 – 5.41 (m, 2H), 5.32 (d, *J* = 9.8 Hz, 1H), 5.07 – 4.97 (m, 2H), 4.93 (d, *J* = 3.7 Hz, 1H), 4.81 (d, *J* = 12.1 Hz, 1H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.53 (dd, *J* = 12.2, 2.9 Hz, 1H), 4.38 (dd, *J* = 12.2, 5.2 Hz, 1H), 4.25 (ddd, *J* = 8.6, 5.1, 2.8 Hz, 1H), 4.15 (td, *J* = 10.0, 3.7 Hz, 1H), 3.77 (dt, *J* = 9.8, 6.5 Hz, 1H), 3.49 (dt, *J* = 9.8, 6.5 Hz, 1H), 2.55 (q, *J* = 6.2, 5.6 Hz, 2H), 2.47 – 2.30 (m, 2H), 2.18 – 2.10 (m, 2H), 2.01 (s, 3H), 1.79 – 1.74 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.7, 172.7, 166.2, 165.3, 154.3, 137.8, 133.7, 133.2, 130.0, 130.0, 129.8, 129.8, 129.7, 129.0, 128.6, 128.6, 128.5, 128.5, 115.5, 97.4, 95.6, 74.8, 71.3, 69.5, 68.1, 68.1, 63.1, 54.2, 37.8, 30.5, 29.6, 28.5, 28.1; HRMS (ESI-MS): m/z calcd for $C_{33}H_{36}Cl_3NO_{11}$ $[M+Na]^+$: 750.1252; Found: 750.1265.

Pent-4-enyl 2-deoxy-2-(((2,2,2-trichloroethoxy)carbonyl)amino)-4,6-di-*O*-benzoyl-β-D-glucopyranoside (12): Yield: 89 %; Colorless gum; $[\alpha]^{25}{}_D$= +25.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.78 (q, *J* = 6.9 Hz, 2H), 2.16 (dt, *J* = 13.4, 7.0 Hz, 2H), 3.49 (dt, *J* = 9.7, 6.5 Hz, 1H), 4.04 (ddd, *J* = 9.9, 4.2, 2.2 Hz, 2H), 4.20 (td, *J* = 10.4, 3.7 Hz, 1H), 4.49 (s, 1H), 4.57 (dd, *J* = 12.2, 2.2 Hz, 1H), 4.71 (s, 1H), 4.74 – 4.82 (m, 1H), 4.92 (d, *J* = 3.7 Hz, 1H), 4.94 – 5.13 (m, 2H), 5.31 – 5.47 (m, 2H), 5.81 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 7.44 (dt, *J* = 20.8, 7.7 Hz, 4H), 7.52 – 7.68 (m, 2H), 7.90 – 8.18 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 28.6, 30.6, 53.9, 63.5, 68.0, 69.5, 70.7, 74.5, 75.0, 95.3, 97.6, 115.5, 128.5, 128.6, 128.6, 128.6, 129.2, 129.7, 129.9, 130.0, 130.2, 130.2, 133.5, 133.7, 137.9, 154.4, 167.1, 167.8; HRMS (ESI-MS): m/z calcd for $C_{28}H_{30}Cl_3NO_9$ $[M+Na]^+$: 652.0884; Found: 652.4462.

Pent-4-enyl 2-deoxy-2-(((2,2,2-trichloroethoxy)carbonyl)amino)-4,6-di-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-4-*O*-(4-oxopentanoyl)-α-L-rhamnopyranosyl)-β-D-glucopyranoside (22): Yield: 85 %; Pale yellow sticky gum; $[\alpha]^{25}{}_D$= +10.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$)

δ 8.05 (ddd, *J* = 9.8, 8.1, 1.4 Hz, 4H), 7.99 – 7.95 (m, 2H), 7.88 – 7.85 (m, 2H), 7.58 – 7.52 (m, 3H), 7.47 – 7.39 (m, 7H), 7.32 (t, *J* = 7.8 Hz, 2H), 5.86 – 5.74 (m, 1H), 5.58 – 5.50 (m, 2H), 5.49 – 5.42 (m, 2H), 5.25 – 5.19 (m, 2H), 5.10 – 4.95 (m, 3H), 4.92 (d, *J* = 3.7 Hz, 1H), 4.80 (d, *J* = 12.1 Hz, 1H), 4.53 (dd, *J* = 12.2, 2.8 Hz, 1H), 4.40 – 4.27 (m, 2H), 4.20 (ddd, *J* = 10.0, 5.0, 2.8 Hz, 1H), 4.14 (t, *J* = 9.6 Hz, 1H), 3.88 (dq, *J* = 12.1, 6.1 Hz, 1H), 3.77 (dt, *J* = 9.9, 6.5 Hz, 1H), 3.51 (dt, *J* = 10.0, 6.5 Hz, 1H), 2.62 – 2.47 (m, 2H), 2.43 – 2.35 (m, 1H), 2.33 – 2.25 (m, 1H), 2.20 – 2.12 (m, 2H), 2.05 (s, 3H), 1.78 (t, *J* = 6.9 Hz, 2H), 0.75 (d, *J* = 6.2 Hz, 3H);^{13}C NMR (101 MHz, $CDCl_3$) δ 206.0, 172.0, 166.3, 165.7, 165.2, 165.2, 154.4, 137.8, 133.6, 133.6, 133.2, 133.2, 130.1, 130.1, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.7, 129.5, 129.4, 129.4, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 115.5, 99.4, 97.7, 95.5, 80.0, 75.4, 71.4, 71.2, 70.5, 69.6, 68.3, 68.0, 67.3, 63.1, 55.3, 37.8, 30.5, 29.7, 28.5, 28.0, 17.0; HRMS (ESI-MS): m/z calcd for $C_{53}H_{54}Cl_3NO_{17}$ $[M+Na]^+$: 1104.2355; Found: 1104.2376.

Pent-4-enyl 2-deoxy-2-acetamido-4,6-di-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-4-*O*-(4-oxopentanoyl)-β-L-rhamnopyranosyl)-β-D-glucopyranoside (23): Yield: 88 %; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +22.5 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 7.96 (m, 6H), 7.89 (d, *J* = 7.8 Hz, 2H), 7.60 – 7.51 (m, 3H), 7.49 – 7.37 (m, 7H), 7.33 (t, *J* = 7.7 Hz, 2H), 5.94 – 5.74 (m, 2H), 5.59 – 5.46 (m, 2H), 5.45 – 5.39 (m, 1H), 5.23 (t, *J* = 10.0 Hz, 1H), 5.17 – 5.11 (m, 1H), 5.02 (dd, *J* = 18.6, 13.6 Hz, 2H), 4.88 (d, *J* = 3.6 Hz, 1H), 4.62 (td, *J* = 10.1, 3.6 Hz, 1H), 4.52 (dd, *J* = 12.1, 2.8 Hz, 1H), 4.34 (dd, *J* = 12.1, 4.9 Hz, 1H), 4.18 (dt, *J* = 7.5, 3.4 Hz, 1H), 4.10 (t, *J* = 9.8 Hz, 1H), 3.87 (dd, *J* = 10.1, 5.9 Hz, 1H), 3.75 (dt, *J* = 9.9, 6.7 Hz, 1H), 3.48 (dt, *J* = 10.0, 6.6 Hz, 1H), 2.62 – 2.30 (m, 4H), 2.17 (s, 3H), 2.14 (q, *J* = 6.2 Hz, 2H), 2.06 (s, 3H), 1.76 (t, *J* = 6.9 Hz, 2H), 0.69 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.1, 172.0, 170.9, 166.4, 166.1, 165.2, 165.1, 137.8, 133.7, 133.5, 133.2, 133.2, 130.1, 130.1, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.6, 129.5, 129.4, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 115.5, 99.7, 97.7, 80.6, 71.6, 71.3, 70.7, 69.6, 68.3, 67.9, 67.4, 63.2, 52.9, 37.9, 30.5, 29.7, 28.6, 28.1, 23.6, 17.0; HRMS (ESI-MS): m/z calcd. For $C_{52}H_{55}NO_{16}$ $[M+Na]^+$: 972.3419; Found: 972.3465.

Pent-4-enyl 2-deoxy-2-acetamido-4,6-di-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-β-L-rhamnopyranosyl)-β-D-glucopyranoside (7): Yield: 91 %; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +18.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 7.99 (m, 6H), 7.91 (d, *J* = 7.7 Hz, 2H), 7.61 – 7.52 (m, 3H), 7.44 (tt, *J* = 9.0, 5.2 Hz, 7H), 7.33 (t, *J* = 7.7 Hz, 2H), 5.93 – 5.74 (m,

2H), 5.54 (t, *J* = 9.6 Hz, 1H), 5.43 – 5.32 (m, 2H), 5.16 – 5.12 (m, 1H), 5.09 – 4.96 (m, 2H), 4.85 (d, *J* = 3.7 Hz, 1H), 4.62 – 4.50 (m, 2H), 4.34 (dd, *J* = 12.1, 4.9 Hz, 1H), 4.22 – 4.16 (m, 1H), 4.11 (t, *J* = 9.7 Hz, 1H), 3.79 – 3.65 (m, 3H), 3.47 (dt, *J* = 10.0, 6.5 Hz, 1H), 2.46 (s, 1H), 2.14 (s, 3H), 2.14 – 2.10 (m, 2H), 1.75 (p, *J* = 7.0 Hz, 2H), 0.77 (d, *J* = 5.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 166.9, 166.4, 166.0, 165.3, 137.8, 133.7, 133.6, 133.4, 133.2, 130.1, 130.1, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.8, 129.6, 129.5, 129.5, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 115.4, 99.5, 97.7, 79.9, 72.5, 72.2, 72.1, 70.5, 69.9, 68.3, 67.8, 63.2, 53.1, 30.5, 28.6, 23.6, 17.2; HRMS (ESI-MS): m/z calcd. For $C_{47}H_{49}NO_{14}$ $[M+Na]^+$: 874.3051; Found: 874.3087.

3,5,6-tri-*O*-benzoyl-α-D-galactofuranoside-prop-2-ynyl-1,2-orthobenzoate (25): Yield: 64 % over two steps; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +45.6 (c = 0.10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.97 (m, 2H), 7.96 – 7.93 (m, 2H), 7.92 – 7.88 (m, 2H), 7.75 – 7.71 (m, 2H), 7.52 – 7.47 (m, 2H), 7.45 – 7.38 (m, 6H), 7.36 – 7.30 (m, 4H), 6.35 (d, *J* = 4.3 Hz, 1H), 5.64 (d, *J* = 2.8 Hz, 1H), 5.51 – 5.45 (m, 1H), 5.24 (d, *J* = 4.3 Hz, 1H), 4.74 (dd, *J* = 8.0, 2.9 Hz, 1H), 4.69 (dd, *J* = 12.4, 4.0 Hz, 1H), 4.50 (dd, *J* = 12.4, 5.0 Hz, 1H), 4.02 (dd, *J* = 5.5, 2.5 Hz, 2H), 2.40 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.86, 165.37, 165.37, 134.35, 133.80, 133.14, 133.11, 130.12, 129.94, 129.94, 129.92, 129.92, 129.78, 129.78, 129.72, 129.63, 128.87, 128.63, 128.63, 128.56, 128.56, 128.40, 128.40, 128.38, 128.38, 126.77, 126.77, 123.49, 105.91, 85.56, 85.03, 79.43, 76.75, 73.94, 71.53, 63.25, 52.12; HRMS (ESI-MS): m/z calcd. For $C_{37}H_{30}O_{10}$ $[M+Na]^+$: 657.1737; Found: 657.1735.

Pent-4-enyl 2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranoside (26): Yield: 89 %; Pale yellow sticky foam; $[\alpha]_D^{25}$ = -8.3 (c = 0.18, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 8.04 (m, 4H), 7.97 (d, *J* = 1.3 Hz, 2H), 7.91 (dd, *J* = 8.1, 1.0 Hz, 2H), 7.57 – 7.48 (m, 4H), 7.43 – 7.27 (m, 8H), 6.10 (dt, *J* = 8.1, 4.4 Hz, 1H), 5.86 – 5.76 (m, 1H), 5.66 (s, 1H), 5.49 (s, 1H), 5.32 (s, 1H), 5.05 – 4.93 (m, 2H), 4.78 (d, *J* = 7.0 Hz, 2H), 4.68 (d, *J* = 5.1 Hz, 1H), 3.83 – 3.76 (m, 1H), 3.59 – 3.52 (m, 1H), 2.23 – 2.12 (m, 2H), 1.80 – 1.69 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 165.8, 165.7, 165.5, 138.0, 133.5, 133.4, 133.3, 133.1, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.7, 129.7, 129.6, 129.5, 129.1, 129.0, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 115.1, 105.7, 82.1, 81.3, 77.6, 70.4, 66.9, 63.5, 30.3, 28.7; HRMS (ESI-MS): m/z calcd. For $C_{39}H_{36}O_{10}$ $[M+Na]^+$: 687.2205; Found: 687.2200.

Pent-4-enyl β-D-galactofuranoside (27): Yield: 92 %; Colorless syrup; $[\alpha]^{25}_{D}$ = +42.6 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $MeOD_4$) δ 1.4 – 1.9 (m, 2H), 1.7 – 2.4 (m, 2H), 3.4 (dt, *J* = 9.7, 6.5 Hz, 1H), 3.5 – 3.6 (m, 2H), 3.6 – 3.7 (m, 2H), 3.8 – 3.9 (m, 2H), 4.0 (dd, *J* = 6.7, 4.0 Hz, 1H), 4.8 (d, *J* = 1.9 Hz, 1H), 4.9 – 5.0 (m, 2H), 5.8 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H); ^{13}C NMR (101 MHz, $MeOD_4$) δ 28.7, 30.1, 63.2, 66.9, 71.0, 77.3, 82.1, 82.7, 108.1, 113.9, 138.1; HRMS (ESI-MS): m/z calcd for $[C_{11}H_{20}O_6Na^+]$: 271.1158; Found: 271.1197.

Pent-4-enyl 5,6-*O*-isopropylidene-β-D-galactofuranoside (28): Yield: 80 %; Colorless syrup; $[\alpha]^{25}_{D}$= +22.6 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39 (s, 3H), 1.42 (s, 3H), 1.68 (p, *J* = 7.1 Hz, 2H), 2.04 – 2.15 (m, 2H), 3.07 (d, *J* = 11.6 Hz, 1H), 3.47 (dt, *J* = 9.8, 6.4 Hz, 1H), 3.76 (dt, *J* = 9.7, 6.7 Hz, 1H), 3.90 – 4.16 (m, 6H), 4.35 (td, *J* = 7.8, 1.7 Hz, 1H), 4.91 – 5.12 (m, 3H), 5.79 (ddt, *J* = 16.9, 10.1, 6.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 25.7, 25.7, 28.7, 30.4, 65.8, 67.3, 75.8, 78.2, 78.7, 85.7, 108.6, 110.3, 115.3, 137.9; HRMS (ESI-MS): m/z calcd for $[C_{14}H_{24}O_6Na^+]$: 311.1471; Found: 311.1478.

Pent-4-enyl 2,3-di-*O*-benzoyl-5,6-*O*-isopropylidene-β-D-galactofuranoside (29): Yield: 88 %; Pale yellow sticky gum; $[\alpha]^{25}_{D}$= +18.1 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (s, 3H), 1.47 (s, 3H), 1.68 – 1.84 (m, 2H), 2.12 – 2.27 (m, 2H), 3.56 (dt, *J* = 9.6, 6.2 Hz, 1H), 3.84 (dt, *J* = 9.5, 6.6 Hz, 1H), 4.02 (dd, *J* = 8.6, 6.3 Hz, 1H), 4.17 (dd, *J* = 8.6, 6.8 Hz, 1H), 4.33 (dd, *J* = 5.4, 4.6 Hz, 1H), 4.54 (q, *J* = 6.3 Hz, 1H), 4.92 – 5.09 (m, 2H), 5.29 (s, 1H), 5.46 (d, *J* = 1.0 Hz, 1H), 5.49 (d, *J* = 4.5 Hz, 1H), 5.83 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 4H), 7.54 – 7.61 (m, 2H), 7.98 – 8.16 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 25.3, 26.4, 28.8, 30.3, 65.7, 66.8, 75.7, 77.6, 81.7, 83.3, 105.7, 110.0, 115.0, 128.4, 128.5, 128.5, 128.5, 129.2, 129.2, 129.9, 129.9, 129.9, 130.1, 133.5, 133.5, 138.0, 165.3, 165.6; HRMS (ESI-MS): m/z calcd for $[C_{28}H_{32}O_8Na^+]$: 519.1995; Found: 519.1993.

Pent-4-enyl 2,3-di-*O*-benzoyl-β-D-galactofuranoside (30): Yield: 76 %; Colourless syrup**;** $[\alpha]^{25}_{D}$= +24.9 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.72 (dq, *J* = 13.0, 6.6 Hz, 2H), 1.99 – 2.32 (m, 2H), 2.92 (s, 1H), 3.25 (s, 1H), 3.52 (dt, *J* = 9.5, 6.1 Hz, 1H), 3.68 – 3.91 (m, 3H), 4.14 (s, 1H), 4.31 (dd, *J* = 4.5, 3.4 Hz, 1H), 4.90 – 5.10 (m, 2H), 5.24 (s, 1H), 5.49 (d, *J* = 1.2 Hz, 1H), 5.60 (d, *J* = 4.4 Hz, 1H), 5.80 (ddt, *J* = 16.9, 10.1, 6.6 Hz, 1H), 7.35 – 7.49 (m, 4H), 7.50 – 7.63 (m, 2H), 8.05 (d, *J* = 8.2 Hz, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 28.7, 30.3, 64.3, 66.9, 71.0, 78.0, 81.5, 83.9, 105.8, 115.0, 128.5, 128.6, 128.6, 128.6, 129.1, 129.1, 129.9, 129.9, 129.9, 130.0,

133.6, 133.6, 138.0, 165.5, 166.1; HRMS (ESI-MS): m/z calcd for [$C_{25}H_{28}O_8Na^+$]: 489.1682; Found: 489.1683

Pent-4-enyl 2,3,6-tri-*O*-benzoyl-β-D-galactofuranoside (9): Yield: 72 %; Pale yellow sticky foam; $[\alpha]^{25}_D$ = +24.9 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.55 – 1.90 (m, 2H), 2.14 (qd, *J* = 7.4, 6.9, 3.9 Hz, 2H), 2.79 (s, 1H), 3.51 (dt, *J* = 9.6, 6.2 Hz, 1H), 3.75 (dt, *J* = 9.5, 6.6 Hz, 1H), 4.38 (dd, *J* = 4.8, 2.2 Hz, 1H), 4.49 (dd, *J* = 8.2, 4.6 Hz, 2H), 4.55 – 4.65 (m, 1H), 4.87 – 5.05 (m, 2H), 5.26 (s, 1H), 5.52 (d, *J* = 1.3 Hz, 1H), 5.65 (d, *J* = 4.8 Hz, 1H), 5.79 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 7.35 – 7.50 (m, 6H), 7.49 – 7.65 (m, 3H), 7.91 – 8.15 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 28.8, 30.3, 66.2, 67.0, 69.2, 78.2, 81.6, 83.2, 105.8, 115.1, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 129.1, 129.2, 129.8, 129.8, 129.9, 130.0, 130.0, 130.0, 130.0, 133.2, 133.7, 133.7, 138.1, 165.5, 166.2, 166.6; HRMS (ESI-MS): m/z calcd for [$C_{32}H_{32}O_9Na^+$]: 583.1944; Found: 583.5387

Pent-4-enyl 2,3-di-*O*-benzoyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranoside (31): Yield: 62 %; Pale yellow sticky gum; $[\alpha]^{25}_D$ = +12.7 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.79 (m, 2H), 2.15 (s, 3H), 2.20 (m, 2H), 2.59 (t, *J* = 6.4 Hz, 2H), 2.74 (t, *J* = 6.6 Hz, 2H), 2.84 – 2.91 (m, 1H), 3.54 (dt, *J* = 9.5, 6.1 Hz, 1H), 3.77 (dt, *J* = 9.4, 6.6 Hz, 1H), 4.20 – 4.39 (m, 4H), 4.92 – 5.06 (m, 2H), 5.25 (s, 1H), 5.50 (s, 1H), 5.61 (d, *J* = 4.5 Hz, 1H), 5.74 – 5.89 (m, 1H), 7.45 (q, *J* = 7.4 Hz, 4H), 7.59 (q, *J* = 7.3 Hz, 2H), 8.07 (t, *J* = 6.6 Hz, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 27.9, 28.7, 29.8, 30.3, 38.0, 65.8, 66.8, 68.8, 77.9, 81.5, 82.9, 105.7, 115.0, 128.5, 128.5, 128.6, 128.6, 129.1, 129.2, 129.9, 129.9, 129.9, 129.9, 133.6, 133.6, 138.1, 165.4, 166.0, 172.7, 206.7; HRMS (ESI-MS): m/z calcd for [$C_{30}H_{34}O_{10}Na^+$]: 577.2050; Found: 577.2040.

Pent-4-enyl 2,3,5-tri-*O*-benzoyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranoside (32): Yield: 92 %; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +29.6 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (ddd, *J* = 8.6, 5.3, 1.4 Hz, 4H), 7.92 – 7.88 (m, 2H), 7.60 – 7.51 (m, 3H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.35 – 7.31 (m, 2H), 7.31 – 7.27 (m, 2H), 5.92 – 5.78 (m, 2H), 5.54 (dt, *J* = 5.2, 1.0 Hz, 1H), 5.44 (d, *J* = 1.2 Hz, 1H), 5.28 (s, 1H), 5.04 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.98 (ddt, *J* = 10.2, 2.2, 1.3 Hz, 1H), 4.58 – 4.54 (m, 2H), 4.48 (dd, *J* = 11.7, 7.5 Hz, 1H), 3.79 (dt, *J* = 9.6, 6.6 Hz, 1H), 3.56 (dt, *J* = 9.6, 6.2 Hz, 1H), 2.70 – 2.65 (m, 2H), 2.53 (dd, *J* = 6.9, 5.9 Hz, 2H), 2.23 – 2.16 (m, 2H), 2.09 (s, 3H), 1.81 – 1.73 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.4, 172.4, 165.9, 165.7, 165.6, 138.1, 133.6, 133.5, 133.4, 130.1, 130.1, 130.0, 130.0, 129.9, 129.9, 129.6, 129.2, 129.1, 128.6,

128.6, 128.5, 128.5, 128.5, 128.5, 115.1, 105.7, 82.2, 81.3, 77.6, 70.3, 67.0, 63.2, 37.9, 30.4, 29.8, 28.8, 27.9; HRMS (ESI-MS): m/z calcd. For $C_{37}H_{38}O_{11}$ $[M+Na]^+$: 566.1917; Found: 566.1967.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,5-tri-*O*-benzoyl-6-*O*-(4-oxopentanoyl)-D-galactofuranoside (8): Yield: 84 % over two steps from **32**; Colorless foam; $[\alpha]_D^{25}$ = +12.7 (c = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 8.3, 1.4 Hz, 1H), 8.09 – 8.05 (m, 2H), 8.05 – 8.00 (m, 2H), 8.00 – 7.96 (m, 1H), 7.90 – 7.86 (m, 1H), 7.61 – 7.49 (m, 3H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.30 (ddd, *J* = 5.5, 4.2, 2.7 Hz, 2H), 6.90 – 6.84 (m, 1H), 6.38 (s, 1H), 5.90 (dt, *J* = 7.7, 4.1 Hz, 1H), 5.65 (d, *J* = 1.4 Hz, 1H), 5.61 (dt, *J* = 4.8, 1.0 Hz, 1H), 4.76 (dd, *J* = 4.8, 3.6 Hz, 1H), 4.63 – 4.53 (m, 1H), 4.53 – 4.45 (m, 1H), 2.68 (q, *J* = 3.5 Hz, 2H), 2.56 – 2.50 (m, 2H), 2.25 – 2.17 (m, 1H), 2.10 (d, *J* = 5.1 Hz, 3H), 1.94 (td, *J* = 9.3, 4.8 Hz, 2H), 1.79 – 1.46 (m, 6H), 1.34 (dt, *J* = 8.9, 4.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.8, 206.8, 172.4, 172.3, 165.8, 165.8, 165.7, 165.7, 165.6, 165.3, 151.1, 150.8, 133.8, 133.8, 133.7, 133.6, 133.5, 133.4, 130.4, 130.4, 130.2, 130.2, 130.1, 130.1, 130.1, 130.1, 130.0, 130.0, 130.0, 130.0, 129.4, 129.3, 129.3, 128.9, 128.7, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 102.3, 96.4, 83.7, 82.5, 82.4, 81.2, 80.1, 78.8, 78.6, 77.2, 76.0, 75.6, 75.3, 74.0, 70.3, 70.0, 63.1, 62.5, 37.9, 37.9, 36.8, 36.8, 36.8, 36.6, 29.8, 29.8, 27.9, 27.9, 25.0, 24.9, 22.6, 22.6, 22.6, 22.5; HRMS (ESI-MS): m/z calcd. For $C_{41}H_{40}O_{13}$ $[M+Na]^+$: 648.1971; Found: 648.1920.

Pent-4-enyl 2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranoside (33): Yield: 76 %; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +28.9 (c = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 – 8.05 (m, 4H), 7.57 (td, *J* = 7.3, 1.6 Hz, 2H), 7.44 (td, *J* = 7.7, 3.2 Hz, 4H), 5.89 – 5.78 (m, 1H), 5.64 – 5.61 (m, 1H), 5.42 (d, *J* = 1.5 Hz, 1H), 5.19 (s, 1H), 5.07 – 4.94 (m, 2H), 4.36 – 4.31 (m, 2H), 4.31 – 4.26 (m, 1H), 4.22 (dd, *J* = 10.3, 6.2 Hz, 1H), 3.77 (dt, *J* = 9.6, 6.6 Hz, 1H), 3.52 (dt, *J* = 9.6, 6.2 Hz, 1H), 2.72 (dd, *J* = 7.6, 6.4 Hz, 2H), 2.57 (t, *J* = 6.9 Hz, 2H), 2.23 – 2.16 (m, 2H), 2.15 (s, 3H), 1.74 (td, *J* = 6.7, 4.8 Hz, 2H), 0.86 (s, 9H), 0.13 (d, *J* = 10.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.4, 172.6, 165.6, 165.6, 138.2, 133.5, 133.4, 130.1, 130.1, 130.0, 130.0, 129.5, 129.3, 128.5, 128.5, 128.5, 128.5, 115.1, 105.6, 82.8, 82.3, 76.9, 69.7, 66.8, 65.9, 38.0, 30.4, 29.9, 28.8, 27.9, 25.8, 25.8, 25.8, 18.2, -4.5, -4.7; HRMS (ESI-MS): m/z calcd. For $C_{36}H_{48}O_{10}Si$ $[M+Na]^+$: 691.2914; Found: 691.2934.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(4-oxopentanoyl)-D-galactofuranoside (10): Yield: 76 % over two steps from **33**; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +9.7 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 8.01 (m, 4H), 7.62 – 7.55 (m, 2H), 7.45 (td, *J* = 7.7, 4.0 Hz, 4H), 6.28 (s, 1H), 5.75 – 5.68 (m, 1H), 5.63 (d, *J* = 1.7 Hz, 1H), 4.51 (dd, *J* = 5.2, 4.3 Hz, 1H), 4.35 – 4.24 (m, 2H), 4.21 (dd, *J* = 10.0, 5.7 Hz, 1H), 2.74 – 2.64 (m, 3H), 2.55 (dd, *J* = 6.8, 5.9 Hz, 2H), 2.28 – 2.15 (m, 2H), 2.14 (s, 3H), 1.91 (ddd, *J* = 12.5, 8.4, 5.0 Hz, 2H), 1.79 – 1.45 (m, 6H), 0.83 (s, 9H), 0.11 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.4, 206.4, 172.5, 172.4, 165.6, 165.5, 165.5, 165.2, 151.2, 150.9, 133.8, 133.6, 133.6, 133.5, 130.2, 130.2, 130.2, 130.2, 130.1, 130.1, 130.0, 130.0, 129.2, 129.2, 129.0, 128.9, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 102.3, 96.4, 85.2, 85.2, 82.6, 82.3, 81.5, 78.5, 78.0, 76.6, 76.3, 75.5, 75.0, 73.8, 70.4, 69.5, 65.6, 65.1, 37.9, 36.9, 36.8, 36.8, 36.8, 36.5, 29.9, 29.8, 27.9, 27.9, 26.0, 26.0, 26.0, 25.8, 25.8, 25.8, 25.0, 25.0, 22.7, 22.7, 22.5, 22.5, 18.3, 18.2, -4.5, -4.6, -4.6, -4.7; HRMS (ESI-MS): m/z calcd. For $C_{40}H_{50}O_{12}Si$ $[M+Na]^+$: 773.2969; Found: 773.2956.

Pent-4-enyl 2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (34): Yield: 86 %; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +21.6 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (td, *J* = 7.5, 6.9, 1.5 Hz, 8H), 7.83 (ddd, *J* = 7.7, 6.1, 1.4 Hz, 4H), 7.58 – 7.50 (m, 2H), 7.50 – 7.34 (m, 9H), 7.30 (dd, *J* = 15.4, 7.8 Hz, 4H), 7.23 (dd, *J* = 8.9, 6.7 Hz, 3H), 5.92 – 5.86 (m, 1H), 5.84 – 5.76 (m, 3H), 5.66 (d, *J* = 1.5 Hz, 1H), 5.54 (dd, *J* = 5.3, 1.4 Hz, 1H), 5.50 (d, *J* = 1.4 Hz, 1H), 5.22 (s, 1H), 5.03 – 4.97 (m, 1H), 4.97 – 4.91 (m, 2H), 4.77 (t, *J* = 7.3 Hz, 1H), 4.73 – 4.67 (m, 2H), 4.59 – 4.52 (m, 2H), 4.42 (dd, *J* = 11.9, 7.9 Hz, 1H), 3.74 (dt, *J* = 9.6, 6.6 Hz, 1H), 3.51 (dt, *J* = 9.6, 6.2 Hz, 1H), 2.64 – 2.55 (m, 2H), 2.47 (t, *J* = 6.4 Hz, 2H), 2.19 – 2.10 (m, 2H), 2.04 (s, 3H), 1.75 – 1.66 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.3, 172.2, 166.2, 165.8, 165.7, 165.6, 165.5, 165.3, 138.1, 133.5, 133.5, 133.4, 133.4, 133.3, 133.1, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.6, 129.1, 129.1, 129.0, 128.9, 128.7, 128.7, 128.6, 128.6, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 115.0, 105.6, 105.3, 82.5, 82.2, 82.0, 81.8, 77.9, 77.2, 73.1, 70.4, 66.9, 64.6, 63.4, 37.9, 30.3, 29.7, 28.8, 27.9; HRMS (ESI-MS): m/z calcd. For $C_{64}H_{60}O_{19}$ $[M+Na]^+$: 1155.3626; Found: 1155.3687.

Pent-4-enyl 2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranoside (35): Yield: 80 %; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +22.3 (c = 1.0, $CHCl_3$);

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 8.03 (m, 3H), 8.03 – 8.00 (m, 4H), 7.99 (d, *J* = 1.5 Hz, 1H), 7.85 (ddd, *J* = 8.5, 4.0, 1.4 Hz, 4H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.55 – 7.46 (m, 3H), 7.46 – 7.43 (m, 3H), 7.42 (s, 1H), 7.35 (dd, *J* = 8.3, 6.9 Hz, 2H), 7.32 – 7.23 (m, 8H), 5.86 – 5.76 (m, 3H), 5.70 (d, *J* = 1.8 Hz, 1H), 5.58 (dd, *J* = 5.7, 1.9 Hz, 2H), 5.51 (d, *J* = 1.5 Hz, 1H), 5.25 (s, 1H), 5.05 – 4.98 (m, 2H), 4.97 – 4.93 (m, 1H), 4.80 – 4.73 (m, 2H), 4.71 – 4.67 (m, 1H), 4.54 (dd, *J* = 5.3, 3.3 Hz, 1H), 4.02 (dd, *J* = 11.6, 6.8 Hz, 1H), 3.94 (dd, *J* = 11.7, 5.2 Hz, 1H), 3.76 (dt, *J* = 9.6, 6.6 Hz, 1H), 3.53 (dt, *J* = 9.6, 6.2 Hz, 1H), 3.15 (s, 1H), 2.20 – 2.09 (m, 2H), 1.76 – 1.68 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 166.3, 166.1, 165.7, 165.7, 165.4, 138.1, 133.9, 133.6, 133.4, 133.4, 133.3, 133.2, 130.1, 130.1, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.7, 129.7, 129.7, 129.7, 129.0, 128.9, 128.7, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 115.1, 105.7, 105.7, 82.4, 82.2, 81.9, 81.8, 77.8, 77.5, 73.5, 73.0, 67.0, 64.8, 61.5, 30.3, 28.8; HRMS (ESI-MS): m/z calcd. For $C_{59}H_{54}O_{17}$ $[M+Na]^+$: 1057.3259; Found: 1057.3247.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-D-galactofuranoside (36): Yield: 81 % over two steps; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +12.4 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (t, *J* = 1.2 Hz, 1H), 8.01 (dq, *J* = 5.9, 1.3 Hz, 4H), 7.98 (dt, *J* = 2.6, 1.4 Hz, 2H), 7.96 (d, *J* = 1.5 Hz, 1H), 7.87 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.82 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.59 – 7.54 (m, 1H), 7.53 – 7.45 (m, 5H), 7.44 – 7.35 (m, 5H), 7.32 – 7.27 (m, 6H), 7.26 – 7.25 (m, 1H), 6.34 (s, 1H), 5.89 (ddd, *J* = 5.0, 1.8, 0.7 Hz, 1H), 5.84 (dt, *J* = 7.8, 4.0 Hz, 1H), 5.75 (s, 1H), 5.73 – 5.71 (m, 1H), 5.60 (d, *J* = 1.4 Hz, 1H), 5.54 (dd, *J* = 5.1, 1.5 Hz, 1H), 4.84 (dd, *J* = 5.0, 3.6 Hz, 1H), 4.79 – 4.72 (m, 2H), 4.71 – 4.65 (m, 2H), 4.52 (dd, *J* = 11.8, 4.1 Hz, 1H), 4.39 (dd, *J* = 11.8, 7.7 Hz, 1H), 2.65 (s, 1H), 2.62 – 2.56 (m, 2H), 2.50 – 2.45 (m, 2H), 2.24 – 2.15 (m, 2H), 2.04 (s, 3H), 1.95 – 1.84 (m, 2H), 1.73 – 1.50 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.4, 172.3, 166.2, 165.8, 165.6, 165.6, 165.3, 165.2, 150.9, 133.8, 133.7, 133.4, 133.4, 133.3, 133.1, 130.1, 130.1, 130.1, 130.1, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.7, 129.6, 128.9, 128.9, 128.7, 128.7, 128.6, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 105.6, 102.2, 84.6, 82.5, 82.1, 82.0, 81.0, 78.7, 77.6, 76.6, 75.6, 73.2, 70.4, 64.6, 63.2, 37.9, 36.8, 36.8, 29.8, 27.9, 25.0, 22.7, 22.7; HRMS (ESI-MS): m/z calcd. For $C_{68}H_{62}O_{21}$ $[M+Na]^+$: 1237.3681; Found: 1237.3655.

Pent-4-enyl 2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (37): Yield: 81 %; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +16.7 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.95 (m, 12H), 7.91 (d, *J* = 1.2 Hz, 1H), 7.89 (d, *J* = 1.5 Hz, 1H), 7.83 (ddd, *J* = 8.5, 4.0, 1.4 Hz, 4H), 7.80 (d, *J* = 1.3 Hz, 2H), 7.78 (d, *J* = 1.4 Hz, 2H), 7.77 – 7.74 (m, 2H), 7.44 (ddt, *J* = 7.3, 4.8, 1.2 Hz, 7H), 7.42 – 7.37 (m, 4H), 7.36 – 7.30 (m, 8H), 7.30 – 7.25 (m, 7H), 7.24 – 7.20 (m, 4H), 7.18 (dd, *J* = 6.8, 3.3 Hz, 5H), 7.15 (d, *J* = 2.6 Hz, 1H), 5.95 (dt, *J* = 7.8, 3.9 Hz, 1H), 5.83 (dd, *J* = 4.9, 3.0 Hz, 2H), 5.78 – 5.73 (m, 4H), 5.65 (d, *J* = 1.6 Hz, 1H), 5.62 (d, *J* = 1.6 Hz, 1H), 5.60 (dd, *J* = 4.9, 1.6 Hz, 1H), 5.50 (dd, *J* = 5.1, 1.6 Hz, 1H), 5.48 (d, *J* = 1.5 Hz, 1H), 5.37 (d, *J* = 1.5 Hz, 1H), 5.19 (d, *J* = 10.4 Hz, 2H), 5.00 – 4.94 (m, 1H), 4.94 – 4.90 (m, 2H), 4.85 (dd, *J* = 5.2, 3.4 Hz, 1H), 4.77 – 4.72 (m, 1H), 4.70 – 4.67 (m, 2H), 4.65 (q, *J* = 4.2, 3.0 Hz, 3H), 4.59 (d, *J* = 5.3 Hz, 1H), 4.54 – 4.50 (m, 2H), 4.36 (dd, *J* = 11.9, 7.8 Hz, 1H), 4.10 (dd, *J* = 11.4, 4.0 Hz, 1H), 3.98 (dd, *J* = 11.4, 7.7 Hz, 1H), 3.72 (dt, *J* = 9.7, 6.6 Hz, 1H), 3.48 (dt, *J* = 9.6, 6.2 Hz, 1H), 2.55 (q, *J* = 7.2 Hz, 2H), 2.43 (t, *J* = 6.3 Hz, 2H), 2.14 – 2.07 (m, 2H), 2.00 (s, 3H), 1.67 (dt, *J* = 8.6, 5.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.4, 172.2, 166.3, 166.1, 166.0, 165.8, 165.8, 165.7, 165.6, 165.6, 165.6, 165.3, 165.2, 165.2, 138.2, 133.6, 133.5, 133.4, 133.4, 133.3, 133.3, 133.3, 133.3, 133.2, 133.2, 133.1, 133.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.6, 129.2, 129.1, 129.0, 129.0, 129.0, 129.0, 129.0, 129.0, 128.9, 128.9, 128.8, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 115.0, 106.8, 105.6, 105.6, 105.6, 82.9, 82.5, 82.5, 82.1, 82.0, 81.9, 81.9, 81.9, 77.9, 77.8, 77.2, 77.1, 73.2, 72.9, 71.9, 70.4, 67.6, 66.9, 65.4, 64.8, 63.3, 37.9, 30.4, 29.7, 28.8, 27.9; HRMS (ESI-MS): m/z calcd. For $C_{118}H_{104}O_{35}$ $[M+Na]^+$: 2103.6256; Found: 2103.6289.

Pent-4-enyl 2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (38): Yield: 78 %; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +23.5 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 8.03 (m, 3H), 8.00 (ddd, *J* = 8.3, 4.1, 2.4 Hz, 10H), 7.95 – 7.92 (m, 2H), 7.91 – 7.88 (m, 2H), 7.88 – 7.84 (m, 2H), 7.84 – 7.81 (m, 2H), 7.81 – 7.78 (m, 2H), 7.78 – 7.74 (m, 2H), 7.52 – 7.42 (m, 9H), 7.41 – 7.28 (m, 16H), 7.24 – 7.17 (m, 10H), 5.99 (dt, *J*

= 7.6, 3.8 Hz, 1H), 5.84 (dd, *J* = 5.1, 1.6 Hz, 1H), 5.82 – 5.76 (m, 3H), 5.75 (s, 1H), 5.67 (dd, *J* = 8.1, 1.8 Hz, 2H), 5.61 (dd, *J* = 4.9, 1.6 Hz, 1H), 5.54 (dt, *J* = 6.3, 3.2 Hz, 2H), 5.50 (d, *J* = 1.5 Hz, 1H), 5.38 (d, *J* = 1.5 Hz, 1H), 5.22 (d, *J* = 7.1 Hz, 2H), 5.02 – 4.96 (m, 2H), 4.96 – 4.90 (m, 2H), 4.79 – 4.68 (m, 6H), 4.65 (dd, *J* = 6.3, 3.1 Hz, 1H), 4.54 (dd, *J* = 5.2, 3.2 Hz, 1H), 4.12 (dd, *J* = 11.4, 4.0 Hz, 1H), 4.01 (dt, *J* = 10.6, 7.1 Hz, 2H), 3.93 (q, *J* = 6.5, 5.4 Hz, 1H), 3.73 (dt, *J* = 9.6, 6.6 Hz, 1H), 3.50 (dt, *J* = 9.6, 6.1 Hz, 1H), 3.35 (d, *J* = 7.8 Hz, 1H), 2.17 – 2.07 (m, 2H), 1.73 – 1.65 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 166.2, 166.1, 166.1, 166.0, 165.8, 165.7, 165.6, 165.6, 165.3, 165.3, 165.3, 138.1, 133.6, 133.6, 133.5, 133.5, 133.4, 133.3, 133.3, 133.3, 133.2, 133.1, 133.0, 133.0, 130.1, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.7, 129.7, 129.2, 129.1, 129.1, 129.0, 128.9, 128.9, 128.8, 128.7, 128.7, 128.7, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 115.0, 106.7, 106.2, 105.6, 105.6, 82.5, 82.5, 82.5, 82.4, 82.0, 81.9, 81.9, 81.4, 78.0, 77.6, 77.4, 77.2, 73.9, 73.3, 72.8, 71.9, 67.6, 66.9, 65.4, 64.8, 61.2, 30.3, 28.8; HRMS (ESI-MS): m/z calcd. For $C_{113}H_{98}O_{33}$ $[M+Na]^+$: 2005.5888; Found: 2005.5885.

Pent-4-enyl 2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (39): Yield: 76 %; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +19.7 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.92 (m, 17H), 7.90 – 7.85 (m, 5H), 7.84 – 7.75 (m, 14H), 7.49 – 7.40 (m, 10H), 7.35 (ddd, *J* = 14.4, 7.5, 3.1 Hz, 12H), 7.31 – 7.24 (m, 11H), 7.24 – 7.20 (m, 7H), 7.19 – 7.10 (m, 14H), 5.98 – 5.87 (m, 2H), 5.83 (t, *J* = 3.8 Hz, 2H), 5.80 – 5.73 (m, 6H), 5.62 (dt, *J* = 17.3, 6.0 Hz, 5H), 5.53 – 5.47 (m, 2H), 5.37 (d, *J* = 9.4 Hz, 2H), 5.23 – 5.15 (m, 3H), 5.01 – 4.89 (m, 3H), 4.83 (dt, *J* = 12.4, 4.4 Hz, 2H), 4.78 – 4.63 (m, 9H), 4.59 (t, *J* = 6.8 Hz, 2H), 4.55 – 4.48 (m, 2H), 4.36 (dd, *J* = 11.9, 7.8 Hz, 1H), 4.09 (td, *J* = 11.0, 3.8 Hz, 2H), 4.04 – 3.88 (m, 2H), 3.72 (dt, *J* = 9.7, 6.6 Hz, 1H), 3.48 (dt, *J* = 9.7, 6.2 Hz, 1H), 2.60 – 2.50 (m, 2H), 2.43 (t, *J* = 6.6 Hz, 2H), 2.11 (p, *J* = 7.1 Hz, 2H), 1.99 (s, 3H), 1.72 – 1.63 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.3, 172.1, 166.2, 166.0, 166.0, 165.9, 165.9, 165.8, 165.7, 165.7, 165.7, 165.6, 165.5, 165.5, 165.5, 165.3, 165.2, 165.2, 165.2, 165.1, 138.1, 133.5, 133.5, 133.4, 133.4, 133.3, 133.3, 133.3, 133.3, 133.3, 133.2, 133.2, 133.2, 133.2, 133.1,

132.9, 132.9, 132.9, 132.9, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.6, 129.1, 129.1, 129.0, 129.0, 129.0, 129.0, 128.9, 128.9, 128.8, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 115.0, 106.8, 106.8, 106.0, 105.6, 105.6, 105.5, 82.9, 82.8, 82.6, 82.5, 82.5, 82.1, 82.0, 81.9, 81.9, 81.9, 81.9, 81.8, 77.9, 77.8, 77.7, 77.2, 77.1, 77.1, 73.2, 73.2, 73.0, 72.1, 71.8, 70.4, 67.8, 67.6, 66.8, 65.5, 65.3, 64.7, 63.2, 37.8, 30.3, 29.7, 28.8, 27.8; HRMS (MALDI-ToF): m/z calcd. For $C_{172}H_{148}O_{51}$ $[M+Na]^+$: 3053.8952; Found: 3053.3940.

Pent-4-enyl 2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (40): Yield: 87 %; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +18.9 (c = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (dt, *J* = 8.4, 1.5 Hz, 4H), 8.01 – 7.97 (m, 4H), 7.83 – 7.78 (m, 2H), 7.57 (dd, *J* = 6.9, 1.9 Hz, 2H), 7.50 – 7.39 (m, 8H), 7.39 – 7.30 (m, 3H), 7.26 – 7.20 (m, 2H), 5.86 – 5.74 (m, 2H), 5.69 (s, 1H), 5.64 (d, *J* = 3.9 Hz, 2H), 5.48 (d, *J* = 1.4 Hz, 1H), 5.19 (s, 1H), 5.03 – 4.90 (m, 2H), 4.79 – 4.72 (m, 1H), 4.71 – 4.63 (m, 3H), 4.55 (dd, *J* = 4.9, 3.4 Hz, 1H), 4.36 – 4.24 (m, 2H), 4.16 (dd, *J* = 10.7, 6.7 Hz, 1H), 3.79 – 3.71 (m, 1H), 3.54 – 3.46 (m, 1H), 2.66 (t, *J* = 6.9 Hz, 2H), 2.51 (dd, *J* = 6.9, 5.3 Hz, 2H), 2.18 – 2.14 (m, 1H), 2.12 (s, 3H), 2.11 (d, *J* = 1.5 Hz, 1H), 1.75 – 1.66 (m, 2H), 0.80 (s, 9H), 0.11 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.6, 172.6, 166.3, 165.8, 165.6, 165.6, 165.4, 138.2, 133.6, 133.6, 133.6, 133.3, 133.2, 130.1, 130.1, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.3, 129.2, 129.2, 129.1, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.3, 128.3, 126.2, 115.1, 105.7, 105.1, 83.4, 82.6, 82.2, 81.7, 77.3, 77.1, 72.6, 69.6, 66.9, 66.0, 64.7, 37.9, 30.4, 29.9, 28.8, 27.9, 25.8, 25.8, 25.8, 18.1, -4.6, -4.6; HRMS (ESI-MS): m/z calcd. For $C_{63}H_{70}O_{18}Si$ $[M+Na]^+$: 1165.4229; Found: 1165.4270.

Pent-4-enyl 2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-β-D-galactofuranosyl)-β-D-galactofuranoside (41): Yield: 80 %; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +23.4 (c = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 – 8.04 (m, 2H), 8.03 – 7.97 (m, 6H), 7.85 – 7.81 (m, 2H), 7.62 – 7.54 (m, 2H), 7.47 – 7.38 (m, 7H), 7.37 – 7.27 (m, 5H), 7.25 (d, *J* =

7.9 Hz, 1H), 5.86 – 5.84 (m, 1H), 5.84 – 5.75 (m, 1H), 5.71 – 5.67 (m, 3H), 5.49 (d, *J* = 1.4 Hz, 1H), 5.22 (s, 1H), 5.00 (dt, *J* = 17.1, 1.8 Hz, 1H), 4.95 (ddd, *J* = 10.2, 2.2, 1.2 Hz, 1H), 4.77 – 4.71 (m, 2H), 4.71 – 4.63 (m, 2H), 4.53 (dd, *J* = 5.2, 2.9 Hz, 1H), 4.06 (ddd, *J* = 7.9, 4.8, 3.3 Hz, 1H), 3.83 – 3.73 (m, 2H), 3.69 – 3.62 (m, 1H), 3.52 (dt, *J* = 9.6, 6.1 Hz, 1H), 2.95 (s, 1H), 2.21 – 2.10 (m, 2H), 1.76 – 1.69 (m, 2H), 0.85 (s, 9H), 0.10 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 166.3, 165.8, 165.6, 165.4, 138.2, 133.8, 133.5, 133.5, 133.3, 133.2, 130.1, 130.1, 130.1, 130.1, 130.0, 130.0, 129.9, 129.9, 129.8, 129.8, 129.8, 129.4, 129.3, 129.1, 129.1, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.3, 128.3, 115.1, 105.7, 105.6, 82.7, 82.6, 82.5, 81.9, 77.6, 77.0, 73.3, 71.3, 67.0, 65.0, 63.4, 30.4, 28.8, 25.9, 25.9, 25.9, 18.2, -4.4, -4.7; HRMS (ESI-MS): m/z calcd. For $C_{58}H_{64}O_{16}Si$ $[M+Na]^+$: 1067.3861; Found: 1067.3861.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-D-galactofuranoside (42): Yield: 78 % over two steps; Colorless sticky foam; $[\alpha]_D^{25}$ = +17.8 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 8.02 (m, 4H), 8.01 – 7.92 (m, 4H), 7.90 – 7.79 (m, 2H), 7.58 (ddd, *J* = 7.5, 4.5, 1.7 Hz, 2H), 7.52 – 7.35 (m, 9H), 7.33 – 7.26 (m, 4H), 6.31 (s, 1H), 5.92 (dt, *J* = 4.7, 1.0 Hz, 1H), 5.78 – 5.65 (m, 2H), 5.64 – 5.56 (m, 2H), 4.83 – 4.71 (m, 2H), 4.70 – 4.52 (m, 3H), 4.24 (dq, *J* = 8.6, 4.4 Hz, 2H), 4.17 – 4.09 (m, 1H), 2.65 (d, *J* = 7.5 Hz, 3H), 2.55 – 2.46 (m, 2H), 2.26 – 2.14 (m, 2H), 2.12 (s, 3H), 1.96 – 1.85 (m, 2H), 1.72 – 1.49 (m, 6H), 0.81 (s, 9H), 0.11 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.5, 206.5, 172.6, 172.6, 166.2, 166.1, 165.8, 165.7, 165.6, 165.5, 165.5, 165.3, 165.1, 165.1, 151.3, 150.8, 133.8, 133.7, 133.7, 133.7, 133.5, 133.5, 133.3, 133.3, 133.1, 133.1, 130.2, 130.2, 130.1, 130.1, 130.1, 130.1, 130.1, 130.1, 130.0, 130.0, 130.0, 130.0, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.7, 129.7, 129.4, 129.3, 129.2, 129.2, 129.1, 129.1, 128.9, 128.7, 128.7, 128.7, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 105.4, 104.9, 102.3, 96.0, 84.9, 83.9, 83.4, 83.1, 82.5, 82.5, 82.1, 82.1, 81.1, 80.8, 78.7, 78.6, 77.0, 76.8, 76.7, 76.5, 75.5, 75.2, 72.9, 72.8, 69.6, 69.6, 66.2, 65.7, 64.6, 64.6, 37.9, 37.9, 36.9, 36.8, 36.8, 36.7, 29.9, 29.5, 27.9, 27.9, 25.8, 25.8, 25.8, 25.8, 25.8, 25.8, 25.0, 24.8, 22.8, 22.7, 22.7, 22.7, 18.2, 18.1, -4.6, -4.6, -4.7, -4.7; HRMS (ESI-MS): m/z calcd. For $C_{67}H_{72}O_{20}Si$ $[M+Na]^+$: 1247.4284; Found: 1247.4283.

Pent-4-enyl 2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (43): Yield: 80 %; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +15.4 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 8.01 (m, 8H), 8.00 – 7.91 (m, 9H), 7.85 – 7.81 (m, 2H), 7.77 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.59 – 7.51 (m, 3H), 7.46 – 7.34 (m, 19H), 7.28 (dd, *J* = 8.0, 2.2 Hz, 3H), 7.21 (td, *J* = 7.9, 1.5 Hz, 4H), 5.85 (td, *J* = 5.3, 1.4 Hz, 2H), 5.82 – 5.73 (m, 1H), 5.71 (dd, *J* = 5.2, 1.7 Hz, 2H), 5.69 – 5.65 (m, 2H), 5.65 – 5.62 (m, 2H), 5.55 (d, *J* = 1.5 Hz, 1H), 5.48 (d, *J* = 1.4 Hz, 1H), 5.19 (s, 1H), 5.11 (s, 1H), 5.01 – 4.90 (m, 2H), 4.73 – 4.61 (m, 7H), 4.55 (ddd, *J* = 13.0, 5.0, 2.8 Hz, 3H), 4.31 – 4.20 (m, 3H), 4.11 (dd, *J* = 10.6, 6.6 Hz, 1H), 4.03 (dd, *J* = 10.2, 3.1 Hz, 1H), 3.74 (dt, *J* = 9.6, 6.6 Hz, 1H), 3.58 – 3.46 (m, 2H), 2.63 (t, *J* = 6.7 Hz, 2H), 2.49 (td, *J* = 6.5, 1.8 Hz, 2H), 2.17 – 2.11 (m, 2H), 2.11 (s, 3H), 1.73 – 1.69 (m, 2H), 0.79 (s, 9H), 0.76 (s, 9H), 0.13 (s, 3H), 0.08 (s, 6H), 0.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.4, 172.5, 166.2, 166.1, 165.8, 165.7, 165.5, 165.5, 165.5, 165.3, 165.3, 165.2, 138.2, 133.5, 133.5, 133.5, 133.5, 133.5, 133.4, 133.2, 133.1, 133.1, 133.0, 130.1, 130.1, 130.1, 130.1, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.3, 129.3, 129.3, 129.3, 129.3, 129.3, 129.1, 129.1, 129.1, 129.1, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.2, 128.2, 128.2, 128.2, 115.0, 106.4, 105.7, 105.4, 105.3, 84.1, 83.4, 83.0, 82.5, 82.0, 82.0, 81.8, 81.3, 77.4, 77.2, 77.0, 76.8, 73.0, 72.5, 71.1, 70.1, 69.6, 66.9, 65.8, 65.4, 64.5, 37.9, 30.4, 29.9, 28.8, 27.9, 25.9, 25.9, 25.9, 25.8, 25.8, 25.8, 18.2, 18.1, -4.1, -4.6, -4.7, -4.7; HRMS (ESI-MS): m/z calcd. For $C_{116}H_{124}O_{33}Si_2$ $[M+Na]^+$: 2123.7461; Found: 2123.7505.

Pent-4-enyl 2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (44): Yield: 78 %; Colorless gum; $[\alpha]_D^{25}$ = +20.3 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 7.97 (m, 14H), 7.96 – 7.93 (m, 2H), 7.86 – 7.82 (m, 2H), 7.80 – 7.75 (m, 2H), 7.54 (dd, *J* = 9.3, 7.3 Hz, 3H), 7.45 – 7.32 (m, 20H), 7.26 – 7.21 (m, 7H), 5.85 (dd, *J* = 7.7, 5.5 Hz, 2H), 5.81 – 5.74 (m, 1H), 5.73 – 5.65 (m, 6H), 5.50 (dd, *J* = 12.6, 1.3 Hz, 2H), 5.20 (s, 1H), 5.14 (s, 1H), 5.01 – 4.90 (m, 2H), 4.75 – 4.67 (m, 4H), 4.66 – 4.60 (m, 3H), 4.59 – 4.52 (m, 3H), 4.31 (dt, *J* = 7.8, 3.6 Hz, 1H), 4.02 (dq, *J* = 7.6, 5.1, 4.3 Hz, 2H), 3.81 – 3.71 (m, 2H), 3.65 – 3.47 (m, 3H), 3.06 (s, 1H),

2.13 (p, *J* = 7.0 Hz, 2H), 1.73 – 1.66 (m, 2H), 0.83 (s, 9H), 0.79 (s, 9H), 0.13 (s, 3H), 0.07 (s, 6H), 0.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 166.2, 166.1, 165.7, 165.6, 165.6, 165.5, 165.4, 165.4, 165.3, 138.1, 133.7, 133.5, 133.5, 133.5, 133.4, 133.4, 133.2, 133.2, 133.1, 133.0, 130.1, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.7, 129.7, 129.4, 129.3, 129.3, 129.3, 129.3, 129.1, 129.1, 129.1, 129.1, 128.9, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 115.0, 106.3, 105.9, 105.7, 105.3, 84.1, 82.7, 82.6, 82.5, 82.4, 82.0, 81.8, 81.5, 77.7, 77.2, 77.1, 77.0, 73.4, 73.1, 71.2, 71.2, 69.9, 66.9, 65.6, 64.5, 63.2, 30.4, 28.8, 25.9, 25.9, 25.9, 25.9, 25.9, 25.9, 18.2, 18.1, -4.2, -4.4, -4.6, -4.8; HRMS (ESI-MS): m/z calcd. For $C_{111}H_{118}O_{31}Si_2$ $[M+Na]^+$: 2025.7093; Found: 2025.7146.

Pent-4-enyl 2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (45): Yield: 73 %; Colorless gum; $[\alpha]_D^{25}$ = +23.4 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.93 (m, 24H), 7.81 (dt, *J* = 16.3, 8.0 Hz, 6H), 7.50 – 7.28 (m, 37H), 7.24 – 7.17 (m, 8H), 5.90 – 5.83 (m, 3H), 5.73 – 5.63 (m, 9H), 5.56 (s, 2H), 5.49 (s, 1H), 5.20 (s, 1H), 5.14 (d, *J* = 10.6 Hz, 2H), 5.02 – 4.90 (m, 2H), 4.74 – 4.62 (m, 9H), 4.61 – 4.51 (m, 7H), 4.32 – 4.21 (m, 4H), 4.15 – 4.04 (m, 2H), 3.99 (dd, *J* = 10.3, 3.0 Hz, 1H), 3.75 (dt, *J* = 9.6, 6.5 Hz, 1H), 3.59 – 3.45 (m, 3H), 2.64 (t, *J* = 6.6 Hz, 2H), 2.50 (t, *J* = 6.1 Hz, 2H), 2.14 (d, *J* = 7.0 Hz, 2H), 2.11 (s, 3H), 1.70 (td, *J* = 7.3, 3.9 Hz, 2H), 0.81 – 0.74 (m, 27H), 0.10 (dd, *J* = 14.5, 6.4 Hz, 12H), 0.03 (d, *J* = 8.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.4, 172.5, 166.2, 166.0, 166.0, 165.8, 165.8, 165.7, 165.5, 165.5, 165.5, 165.4, 165.3, 165.3, 165.2, 165.2, 165.1, 138.1, 133.5, 133.5, 133.5, 133.4, 133.4, 133.4, 133.4, 133.2, 133.2, 133.1, 133.1, 133.1, 133.0, 133.0, 133.0, 130.1, 130.1, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.7, 129.7, 129.7, 129.3, 129.3, 129.3, 129.3, 129.3, 129.3, 129.3, 129.2, 129.2, 129.2, 129.2, 129.2, 129.1, 129.1, 129.1, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.2, 115.0, 106.5, 106.5, 105.7, 105.6, 105.4, 105.3, 84.2, 84.1, 83.4, 82.9, 82.8, 82.5, 82.0, 82.0, 81.8, 81.7, 81.5, 81.3, 77.4, 77.4, 77.1,

76.9, 76.9, 76.8, 73.0, 72.9, 72.5, 71.2, 71.0, 70.1, 70.1, 69.5, 66.9, 65.8, 65.4, 65.2, 64.4, 37.9, 30.3, 29.9, 28.8, 27.8, 25.9, 25.9, 25.9, 25.8, 25.8, 25.8, 25.7, 25.7, 25.7, 18.2, 18.2, 18.1, -4.1, -4.2, -4.6, -4.7, -4.7, -4.7; HRMS (MALDI-TOF): m/z calcd. For $C_{169}H_{178}O_{48}Si_3$ $[M+Na]^+$: 3084.4798; Found: 3084.7112.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (6): Yield: 76 % over two steps; Colorless gum; $[\alpha]_D^{25}$ = +11.2 (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 – 7.92 (m, 16H), 7.86 (dd, *J* = 8.8, 2.9 Hz, 4H), 7.84 – 7.78 (m, 8H), 7.75 (dd, *J* = 7.7, 4.7 Hz, 6H), 7.45 – 7.27 (m, 29H), 7.25 – 7.12 (m, 27H), 6.33 (s, 1H), 5.88 (dd, *J* = 8.3, 4.6 Hz, 3H), 5.81 – 5.79 (m, 1H), 5.76 – 5.72 (m, 5H), 5.71 (s, 1H), 5.61 (dd, *J* = 11.1, 6.6 Hz, 3H), 5.57 (d, *J* = 4.5 Hz, 2H), 5.49 (d, *J* = 5.2 Hz, 1H), 5.39 – 5.31 (m, 2H), 5.16 (d, *J* = 14.5 Hz, 2H), 4.83 – 4.78 (m, 3H), 4.74 – 4.69 (m, 2H), 4.64 (d, *J* = 4.6 Hz, 8H), 4.57 (d, *J* = 5.2 Hz, 2H), 4.50 (dd, *J* = 12.0, 4.0 Hz, 1H), 4.34 (dd, *J* = 11.9, 7.8 Hz, 1H), 4.10 – 4.04 (m, 2H), 3.91 (ddd, *J* = 11.8, 7.7, 3.9 Hz, 2H), 2.64 – 2.51 (m, 3H), 2.42 (t, *J* = 6.8 Hz, 2H), 2.18 – 2.12 (m, 2H), 2.00 (s, 3H), 1.89 – 1.82 (m, 2H), 1.68 – 1.60 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 206.5, 172.2, 166.2, 166.1, 166.1, 166.0, 166.0, 165.8, 165.8, 165.8, 165.6, 165.6, 165.6, 165.6, 165.3, 165.3, 165.3, 165.2, 165.2, 165.2, 150.9, 133.8, 133.7, 133.4, 133.4, 133.3, 133.3, 133.3, 133.3, 133.3, 133.2, 133.2, 133.2, 133.2, 133.1, 133.0, 133.0, 133.0, 132.9, 130.9, 130.1, 130.1, 130.1, 130.1, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.7, 129.6, 129.1, 129.1, 129.0, 129.0, 129.0, 129.0, 129.0, 129.0, 129.0, 129.0, 128.9, 128.9, 128.8, 128.7, 128.7, 128.7, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.4, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 106.8, 106.7, 106.0, 105.8, 105.6, 102.3, 84.6, 82.9, 82.8, 82.7, 82.6, 82.5, 82.1, 81.9, 81.9, 81.9, 81.8, 81.1, 78.6, 77.9, 77.8, 77.6, 77.4, 77.1, 76.9, 76.7, 75.6, 73.4, 73.3, 73.0, 72.1, 71.9, 70.5, 67.8, 67.5, 65.6, 65.4, 64.7, 63.3, 37.9, 36.8, 36.8, 29.7, 27.9, 25.0, 22.7, 22.6.

Pent-4-enyl 2-deoxy-2-acetamido-4,6-di-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-4-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-

(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-L-rhamnopyranosyl)-β-D-glucopyranoside (46): Yield: 72 %; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +9.7 (*c* = 0.1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 – 7.72 (m, 42H), 7.54 – 7.07 (m, 73H), 6.02 – 5.90 (m, 1H), 5.90 – 5.82 (m, 2H), 5.81 – 5.71 (m, 7H), 5.67 – 5.59 (m, 4H), 5.56 (d, *J* = 8.8 Hz, 2H), 5.50 – 5.44 (m, 2H), 5.43 – 5.28 (m, 3H), 5.15 (s, 1H), 5.13 (s, 1H), 5.09 – 4.98 (m, 1H), 4.94 – 4.85 (m, 1H), 4.84 – 4.75 (m, 3H), 4.73 – 4.59 (m, 11H), 4.57 – 4.47 (m, 5H), 4.39 – 4.32 (m, 2H), 4.18 – 3.99 (m, 4H), 3.94 – 3.84 (m, 3H), 3.78 – 3.65 (m, 1H), 3.55 – 3.43 (m, 1H), 2.56 – 2.49 (m, 2H), 2.42 (t, *J* = 6.5 Hz, 2H), 2.18 (s, 3H), 1.99 (s, 3H), 1.79 – 1.74 (m, 2H), 1.64 – 1.58 (m, 2H), 0.77 (d, *J* = 5.7 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 206.5, 172.2, 171.0, 166.4, 166.2, 166.2, 166.1, 166.1, 166.0, 165.9, 165.9, 165.8, 165.8, 165.8, 165.6, 165.6, 165.6, 165.3, 165.3, 165.3, 165.2, 165.2, 165.1, 164.9, 164.6, 137.9, 133.7, 133.7, 133.4, 133.4, 133.4, 133.4, 133.3, 133.3, 133.3, 133.3, 133.3, 133.2, 133.2, 133.2, 133.2, 133.2, 133.1, 133.0, 133.0, 132.9, 132.9, 132.7, 130.1, 130.1, 130.1, 130.1, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.7, 129.7, 129.7, 129.7, 129.6, 129.5, 129.4, 129.4, 129.0, 129.0, 129.0, 129.0, 129.0, 129.0, 129.0, 129.0, 129.0, 128.9, 128.8, 128.8, 128.7, 128.7, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 115.4, 107.5, 106.8, 106.8, 106.0, 105.7, 105.6, 100.0, 97.7, 83.4, 82.9, 82.8, 82.6, 82.4, 82.1, 82.0, 82.0, 81.9, 81.9, 81.8, 80.7, 77.9, 77.8, 77.8, 77.4, 77.2, 77.0, 76.9, 76.4, 73.2, 73.0, 72.5, 72.2, 72.1, 72.0, 71.6, 70.9, 70.5, 68.3, 68.1, 67.9, 67.8, 67.6, 65.5, 65.4, 64.8, 63.3, 63.2, 52.8, 37.9, 30.5, 29.8, 28.6, 27.9, 23.5, 17.6; HRMS (MALDI-TOF): m/z calcd. For $C_{214}H_{187}NO_{64}$ $[M+Na]^+$: 3819.7828; Found: 3820.4250.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (5):

Yield: 78 % over two steps; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +5.6 (c = 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 8.00 (m, 12H), 7.97 – 7.92 (m, 12H), 7.84 (d, *J* = 7.8 Hz, 2H), 7.77 (dd, *J* = 7.7, 4.5 Hz, 4H), 7.46 – 7.29 (m, 37H), 7.23 – 7.17 (m, 8H), 6.33 (s, 1H), 5.92 (d, *J* = 5.0 Hz, 1H), 5.84 (dd, *J* = 9.8, 5.0 Hz, 2H), 5.72 – 5.65 (m, 8H), 5.63 (d, *J* = 4.8 Hz, 1H), 5.55 (d, *J* = 6.4 Hz, 3H), 5.10 (d, *J* = 4.7 Hz, 2H), 4.77 (t, *J* = 4.4 Hz, 1H), 4.69 – 4.60 (m, 8H), 4.57 – 4.51 (m, 6H), 4.26 – 4.20 (m, 4H), 4.13 – 4.08 (m, 1H), 3.99 (ddd, *J* = 10.2, 7.1, 3.0 Hz, 2H), 3.48 (t, *J* = 9.0 Hz, 2H), 2.62 (dd, *J* = 12.8, 6.2 Hz, 3H), 2.49 (d, *J* = 6.6 Hz, 2H), 2.15 (d, *J* = 6.3 Hz, 2H), 2.11 (s, 3H), 1.85 (d, *J* = 11.7 Hz, 2H), 1.63 – 1.51 (m, 6H), 0.79 (s, 9H), 0.75 (d, *J* = 4.0 Hz, 18H), 0.12 (s, 3H), 0.10 (s, 3H), 0.07 (d, *J* = 4.8 Hz, 6H), 0.03 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.5, 172.5, 166.2, 166.0, 166.0, 165.8, 165.8, 165.6, 165.5, 165.4, 165.4, 165.3, 165.3, 165.2, 165.2, 165.1, 165.1, 150.9, 133.6, 133.6, 133.5, 133.5, 133.5, 133.4, 133.4, 133.4, 133.4, 133.2, 133.2, 133.2, 133.1, 133.0, 133.0, 130.1, 130.1, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.7, 129.7, 129.7, 129.7, 129.3, 129.3, 129.3, 129.3, 129.3, 129.3, 129.2, 129.2, 129.2, 129.2, 129.1, 129.1, 129.1, 129.1, 128.7, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.2, 106.5, 106.4, 105.7, 105.6, 105.4, 102.3, 84.6, 84.3, 84.2, 83.4, 82.9, 82.9, 82.5, 82.0, 82.0, 81.8, 81.5, 81.3, 81.0, 78.5, 77.5, 76.9, 76.9, 76.7, 76.6, 75.5, 73.5, 73.0, 72.5, 71.2, 71.2, 70.2, 70.1, 69.6, 65.8, 65.5, 65.4, 65.4, 64.4, 37.9, 36.8, 36.8, 29.9, 27.9, 25.9, 25.9, 25.9, 25.9, 25.9, 25.9, 25.7, 25.7, 25.7, 25.0, 22.8, 22.6, 18.3, 18.2, 18.1, -4.1, -4.2, -4.6, -4.7, -4.7, -4.7; HRMS (ESI-MS): m/z calcd. For $C_{173}H_{180}O_{50}Si_3$ $[M+Na]^+$: 3064.0746; Found: 3064.1558.

Pent-4-enyl 2-deoxy-2-acetamido-4,6-di-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-4-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-L-rhamnopyranosyl)-β-D-glucopyranoside (47): Yield: 81 %; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +6.7 (*c* = 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 7.86 (m, 30H), 7.82 – 7.73 (m, 16H), 7.48 – 7.28 (m, 34H), 7.25 – 7.10 (m, 30H), 5.99 (d, J = 9.6 Hz, 1H), 5.93 – 5.86 (m, 2H), 5.76 (ddd, J = 14.3, 8.5, 4.1 Hz, 7H), 5.68 – 5.63 (m, 4H), 5.61 – 5.55 (m, 3H), 5.53 – 5.47 (m, 4H), 5.40 (d, J = 1.7 Hz, 1H), 5.34 (d, J = 1.6 Hz, 2H), 5.17 (d, J = 15.2 Hz, 2H), 5.10 – 4.98 (m,

3H), 4.95 (t, J = 3.5 Hz, 2H), 4.83 – 4.77 (m, 2H), 4.74 – 4.72 (m, 1H), 4.71 – 4.61 (m, 9H), 4.59 – 4.50 (m, 3H), 4.41 – 4.33 (m, 2H), 4.20 – 4.12 (m, 2H), 4.11 – 4.00 (m, 3H), 4.00 – 3.87 (m, 6H), 3.76 (dt, J = 10.0, 6.6 Hz, 1H), 3.50 (dt, J = 10.0, 6.6 Hz, 1H), 2.19 (s, 3H), 2.18 – 2.13 (m, 2H), 1.80 – 1.74 (m, 2H), 0.80 (d, J = 5.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 166.5, 166.4, 166.2, 166.2, 166.1, 166.1, 166.0, 166.0, 165.9, 165.9, 165.8, 165.6, 165.6, 165.5, 165.3, 165.3, 165.3, 165.2, 165.2, 165.1, 164.9, 164.6, 137.8, 133.7, 133.7, 133.6, 133.5, 133.4, 133.4, 133.3, 133.3, 133.3, 133.3, 133.2, 133.2, 133.2, 133.2, 133.2, 133.2, 133.1, 133.0, 133.0, 133.0, 132.9, 132.7, 130.1, 130.1, 130.1, 130.1, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.6, 129.6, 129.6, 129.5, 129.5, 129.4, 129.4, 129.3, 129.1, 129.0, 129.0, 129.0, 128.9, 128.9, 128.9, 128.9, 128.9, 128.8, 128.7, 128.7, 128.7, 128.7, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.1, 128.1, 115.4, 107.5, 106.8, 106.7, 106.2, 106.0, 105.7, 100.0, 97.7, 83.4, 82.7, 82.6, 82.5, 82.4, 82.4, 82.0, 82.0, 81.9, 81.9, 81.8, 81.4, 80.6, 77.9, 77.9, 77.6, 77.5, 77.2, 76.8, 76.4, 73.9, 73.3, 72.8, 72.5, 72.2, 72.0, 71.5, 70.9, 68.3, 68.0, 67.9, 67.7, 67.6, 65.5, 65.5, 65.4, 64.8, 63.2, 61.1, 52.8, 30.4, 28.6, 23.5, 17.6; HRMS (MALDI-TOF): m/z calcd. For $C_{209}H_{181}NO_{62}$ $[M+Na]^+$: 3721.6818; Found: 3722.6636.

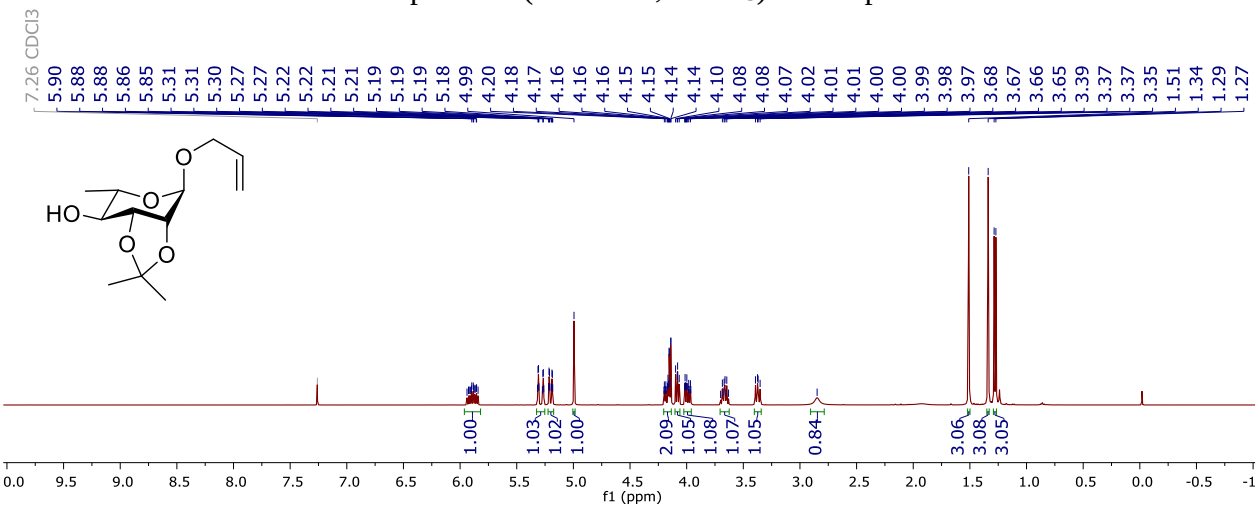
Pent-4-enyl 2-deoxy-2-acetamido-4,6-di-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-4-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldimethylsilyl-6-*O*-(4-oxopentanoyl)- β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-L-rhamnopyranosyl)-β-D-glucopyranoside (48): Yield: 66 %; Pale yellow sticky gum; $[\alpha]_D^{25}$ = +14.7 (c = 0.1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 (t, *J* = 7.8 Hz, 4H), 8.02 – 7.87 (m, 38H), 7.83 (dd, *J* = 13.0, 7.7 Hz, 4H), 7.79 – 7.71 (m,

22H), 7.59 – 7.48 (m, 8H), 7.47 – 7.28 (m, 54H), 7.25 – 7.02 (m, 55H), 5.83 (dq, *J* = 17.3, 6.6 Hz, 6H), 5.79 – 5.76 (m, 2H), 5.72 (dd, *J* = 13.2, 6.5 Hz, 5H), 5.68 – 5.63 (m, 9H), 5.61 (s, 4H), 5.56 (d, *J* = 8.7 Hz, 3H), 5.52 (s, 2H), 5.47 (d, *J* = 9.6 Hz, 2H), 5.38 (s, 1H), 5.32 (d, *J* = 6.0 Hz, 2H), 5.14 – 5.06 (m, 6H), 5.05 – 4.99 (m, 1H), 4.93 (d, *J* = 3.4 Hz, 1H), 4.81 – 4.75 (m, 3H), 4.73 – 4.67 (m, 3H), 4.62 (t, *J* = 7.5 Hz, 13H), 4.58 – 4.48 (m, 14H), 4.38 (d, *J* = 4.4 Hz, 1H), 4.34 (dd, *J* = 12.2, 4.8 Hz, 1H), 4.26 – 4.17 (m, 5H), 4.13 – 4.08 (m, 3H), 4.01 (d, *J* = 7.6 Hz, 4H), 3.96 – 3.93 (m, 1H), 3.92 – 3.85 (m, 5H), 3.77 – 3.73 (m, 1H), 3.65 (s, 1H), 3.52 – 3.42 (m, 3H), 2.62 (t, *J* = 6.6 Hz, 2H), 2.47 (dt, *J* = 6.9, 3.7 Hz, 2H), 2.18 (s, 3H), 2.17 – 2.13 (m, 2H), 2.10 (s, 3H), 1.78 – 1.75 (m, 2H), 0.78 (d, *J* = 5.7 Hz, 3H), 0.75 (s, 9H), 0.72 (s, 9H), 0.69 (s, 9H), 0.08 – 0.04 (m, 9H), -0.00 (dd, *J* = 6.4, 2.8 Hz, 9H): ^{13}C NMR (151 MHz, $CDCl_3$) δ 206.5, 172.5, 170.9, 166.4, 166.2, 166.2, 166.1, 166.0, 166.0, 166.0, 166.0, 166.0, 165.9, 165.9, 165.9, 165.9, 165.9, 165.8, 165.8, 165.8, 165.7, 165.7, 165.6, 165.5, 165.5, 165.5, 165.4, 165.4, 165.3, 165.3, 165.2, 165.2, 165.2, 165.2, 165.2, 165.2, 165.1, 165.1, 164.9, 164.6, 137.9, 133.7, 133.6, 133.5, 133.5, 133.5, 133.5, 133.4, 133.4, 133.4, 133.4, 133.4, 133.3, 133.3, 133.3, 133.3, 133.2, 133.2, 133.2, 133.2, 133.2, 133.2, 133.2, 133.2, 133.2, 133.2, 133.2, 133.1, 133.1, 133.1, 133.0, 133.0, 133.0, 132.9, 132.9, 132.9, 132.8, 132.7, 130.1, 130.1, 130.1, 130.1, 130.0, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.6, 129.5, 129.4, 129.4, 129.4, 129.4, 129.3, 129.3, 129.3, 129.3, 129.3, 129.3, 129.3, 129.2, 129.2, 129.2, 129.1, 129.1, 129.1, 129.1, 129.0, 129.0, 129.0, 129.0, 129.0, 129.0, 129.0, 128.9, 128.9, 128.9, 128.9, 128.8, 128.8, 128.7, 128.7, 128.7, 128.7, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.1, 128.1, 115.4, 107.5, 106.9, 106.9, 106.8, 106.5, 106.5, 106.0, 106.0, 105.7, 105.7, 105.5, 105.4, 100.0, 97.7, 84.3, 84.1, 83.4, 83.4, 82.9, 82.9, 82.8, 82.7, 82.7, 82.6, 82.4, 82.0, 82.0, 82.0, 82.0, 81.9, 81.9, 81.9, 81.9, 81.8, 81.7, 81.6, 81.5, 81.3, 80.6,

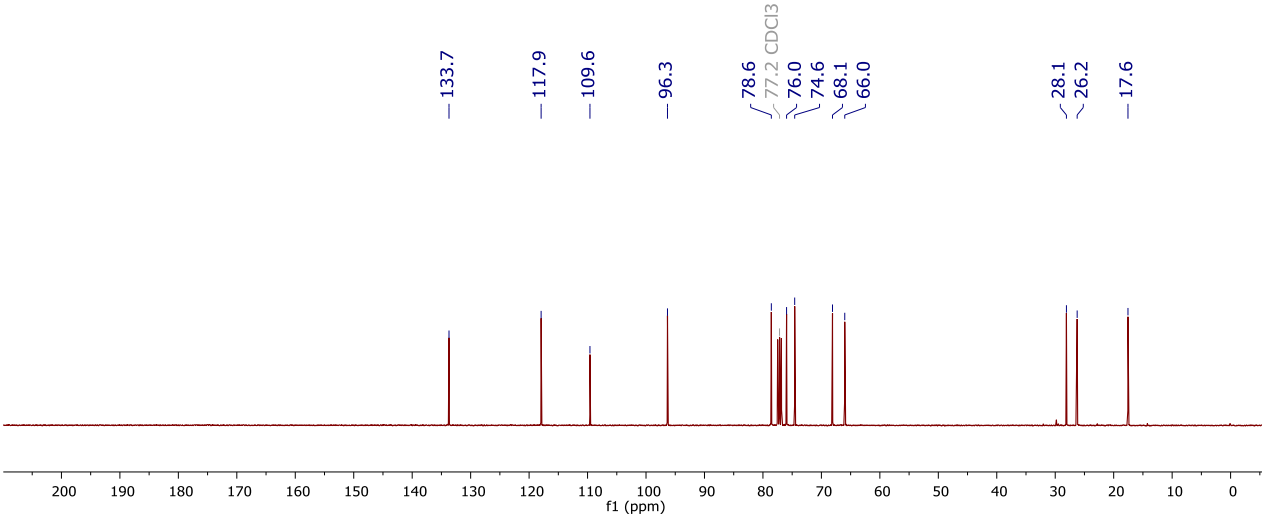
77.9, 77.8, 77.4, 77.4, 77.4, 77.4, 77.2, 77.2, 77.2, 77.1, 77.0, 76.9, 76.8, 76.4, 73.2, 73.0, 72.8, 72.5, 72.5, 72.2, 72.2, 72.1, 72.1, 72.0, 71.5, 71.2, 71.1, 70.9, 70.2, 70.1, 69.6, 68.3, 68.1, 67.9, 67.8, 67.6, 65.8, 65.5, 65.5, 65.5, 65.2, 65.1, 64.8, 63.2, 52.8, 37.9, 30.3, 29.8, 28.6, 27.9, 25.8, 25.8, 25.8, 25.8, 25.8, 25.8, 25.8, 25.8, 25.7, 23.5, 18.2, 18.1, 18.1, 17.6, -4.2, -4.2, -4.6, -4.7, -4.7, -4.7; HRMS (MALDI-TOF): m/z calcd. For $C_{209}H_{181}NO_{62}$ $[M+Na]^+$: 6697.0738; Found: 6699.6313.

4.10. NMR Spectral charts

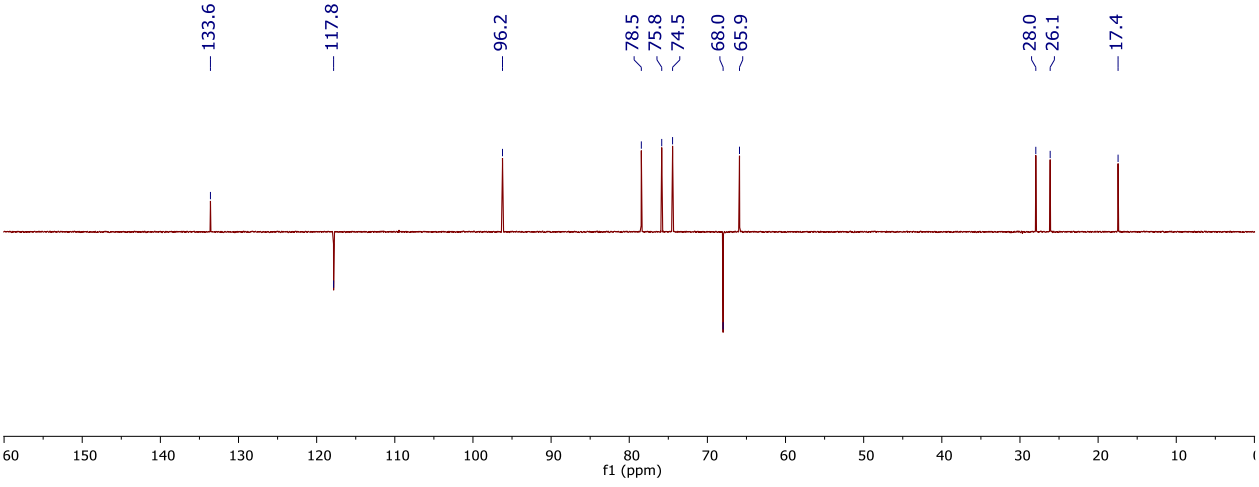
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **14**



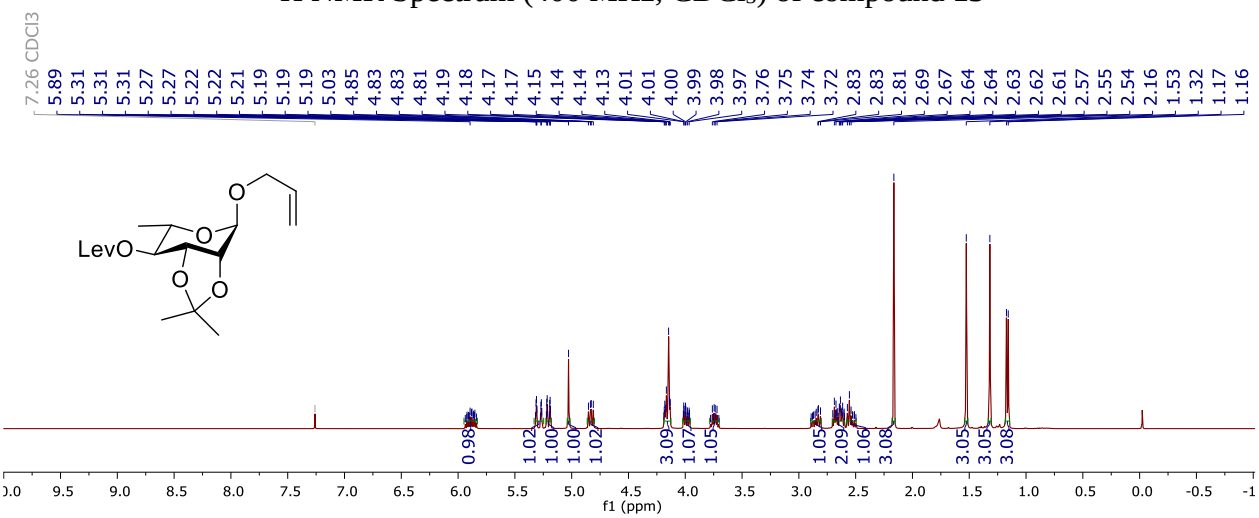
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **14**



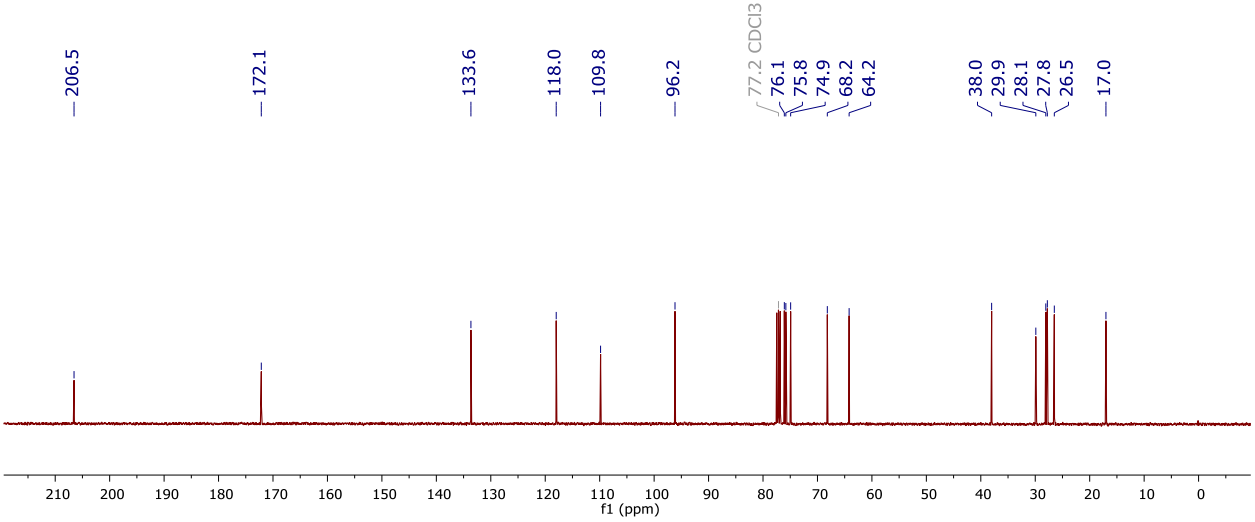
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **14**



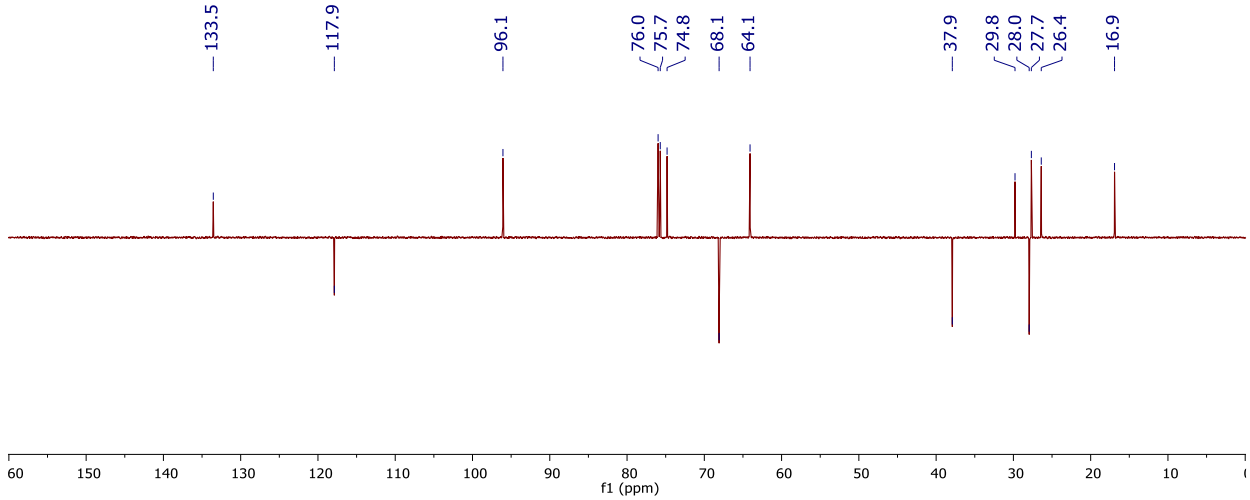
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **15**



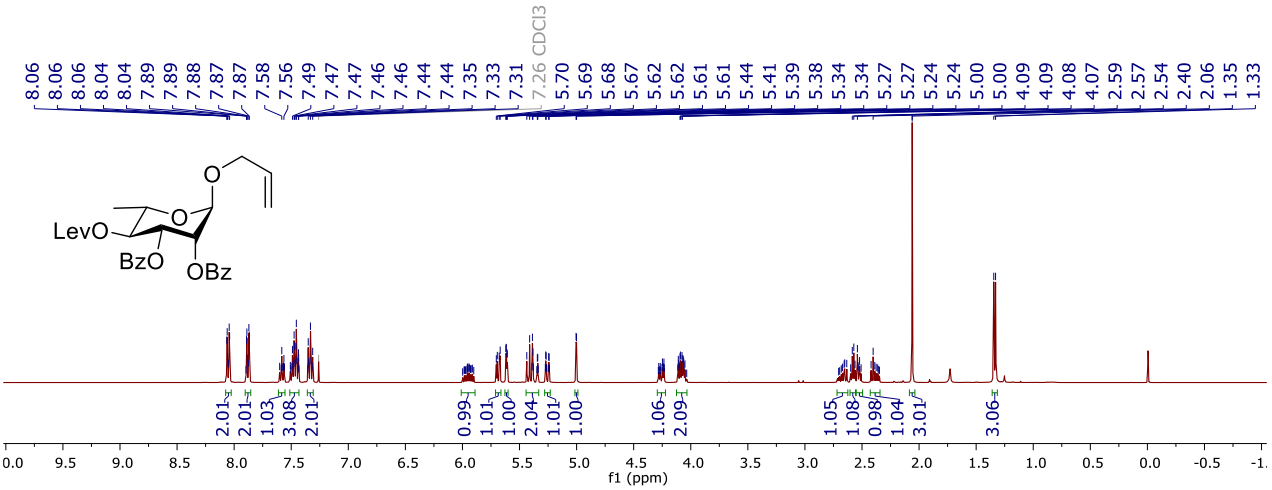
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **15**



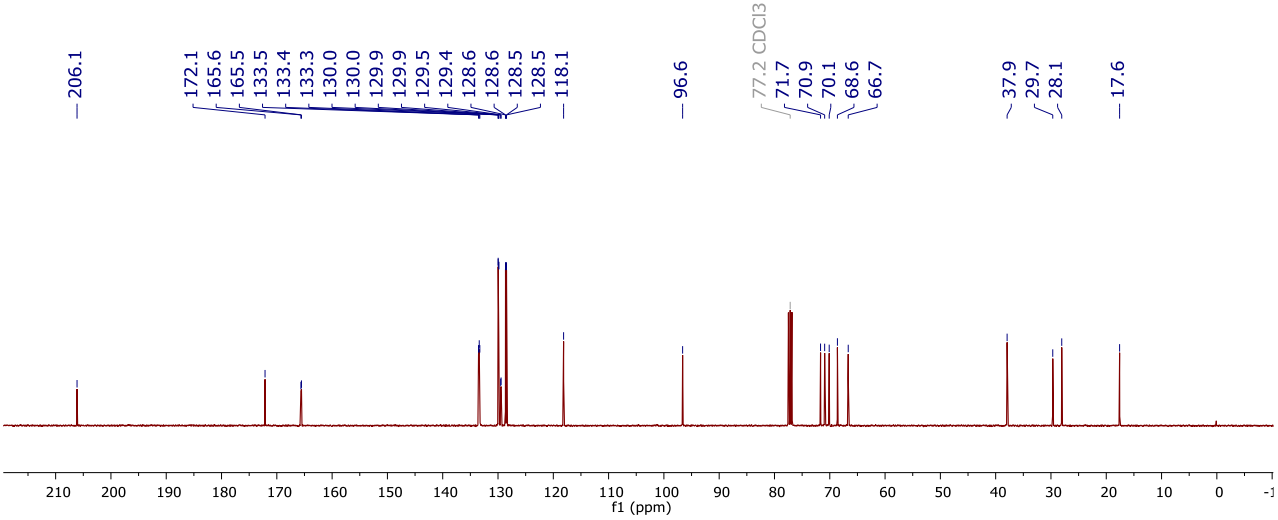
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **15**



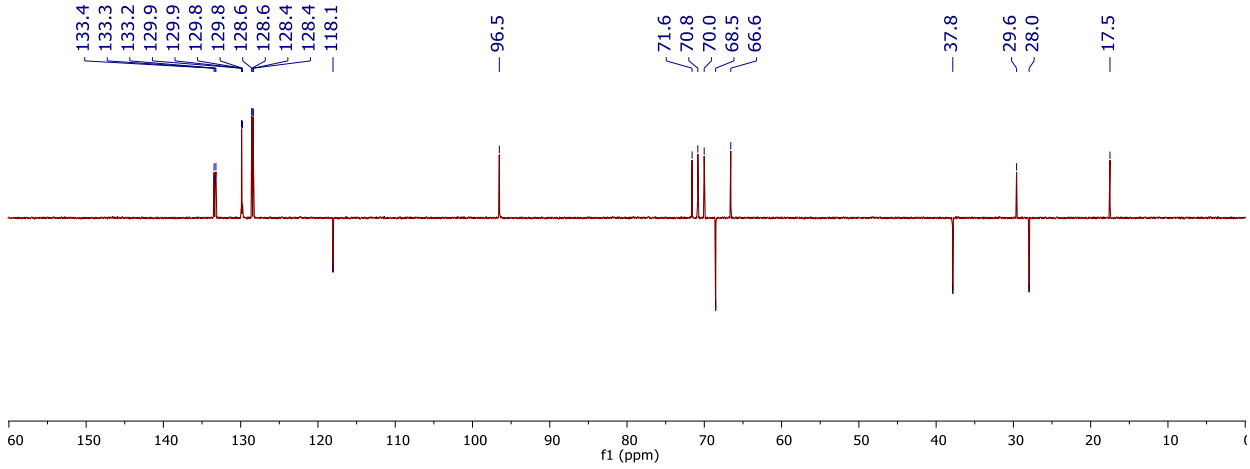
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **17**



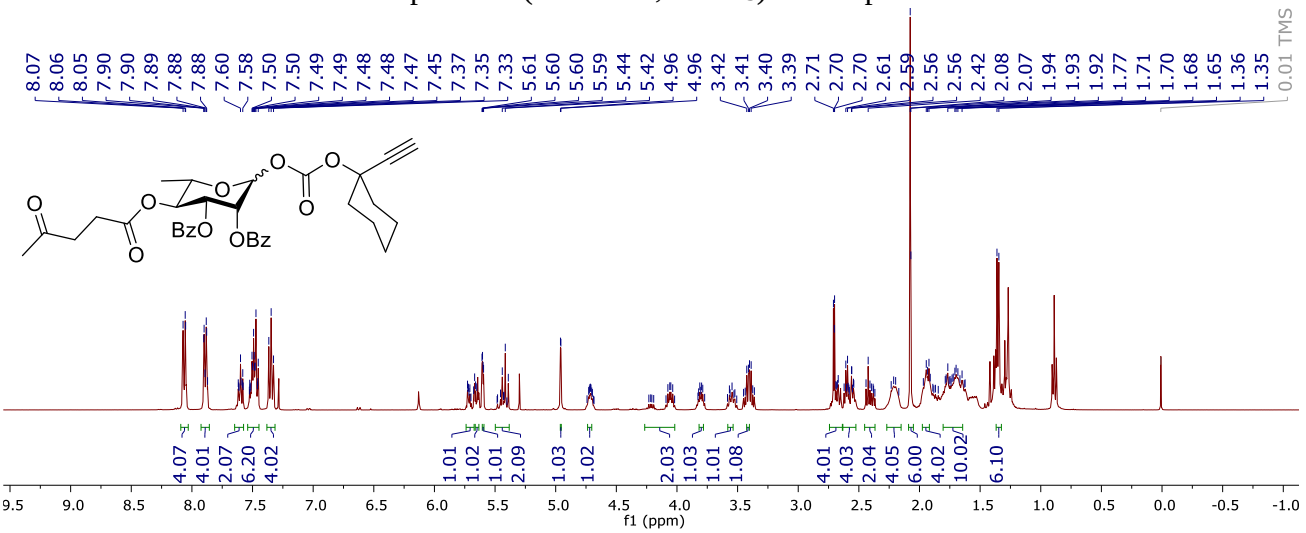
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **17**



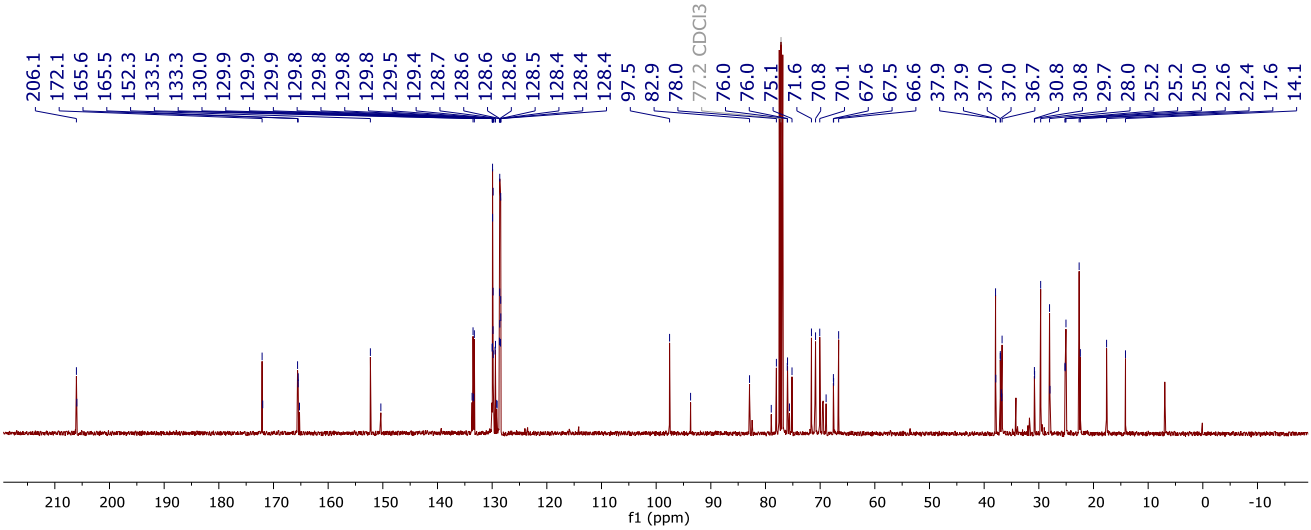
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **17**



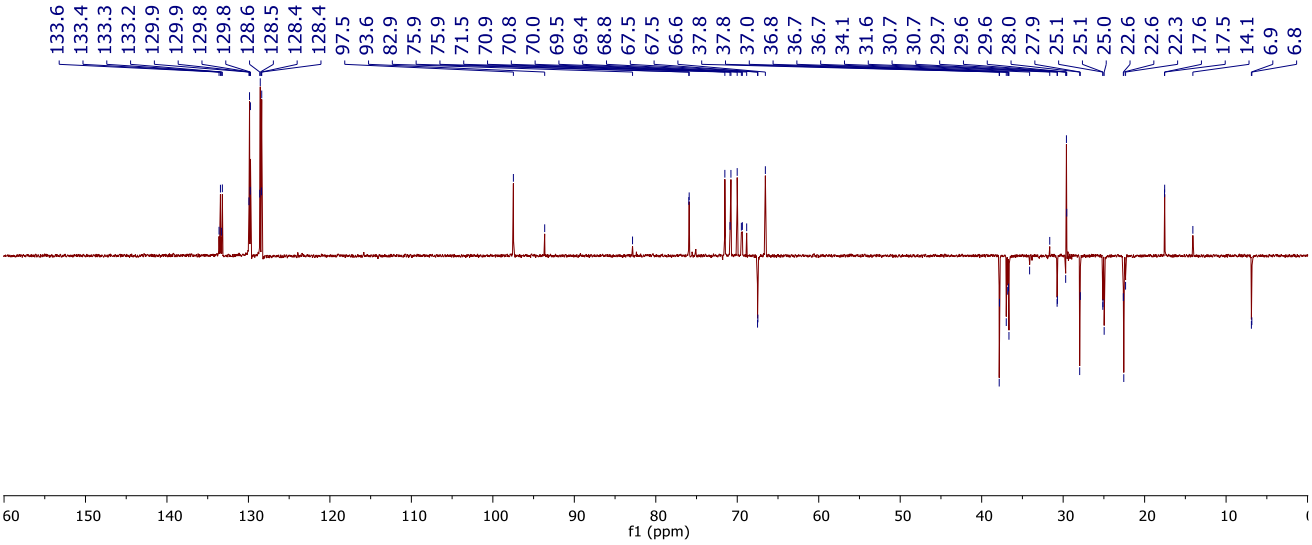
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **11**



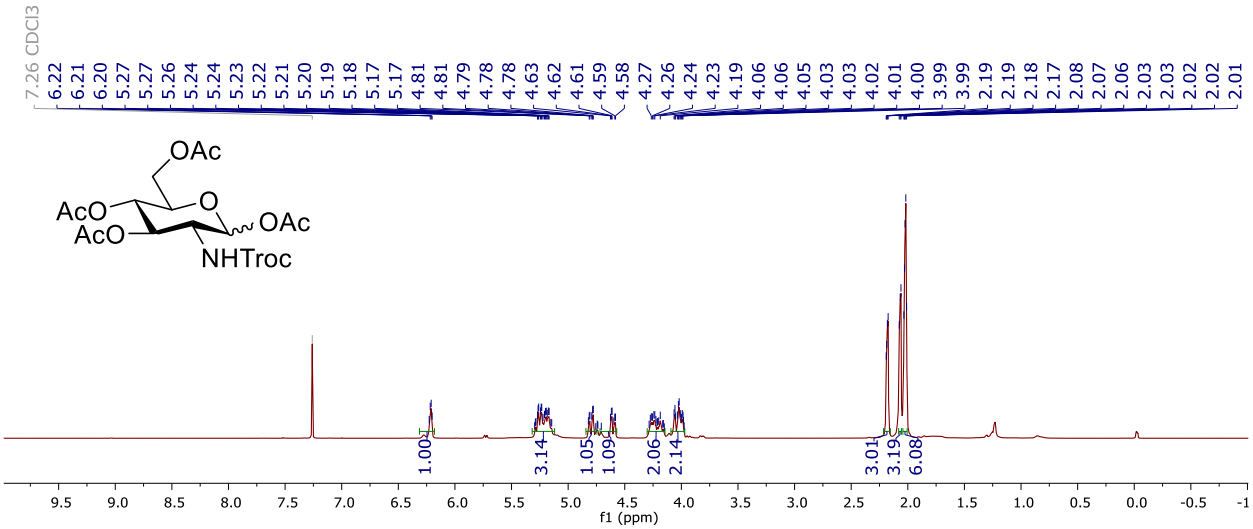
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **11**



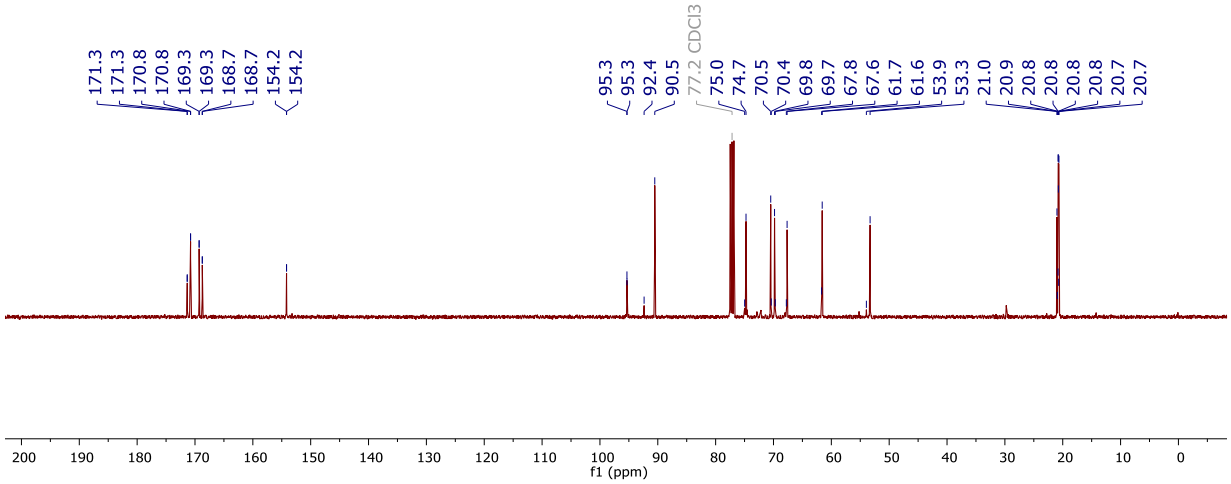
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **11**



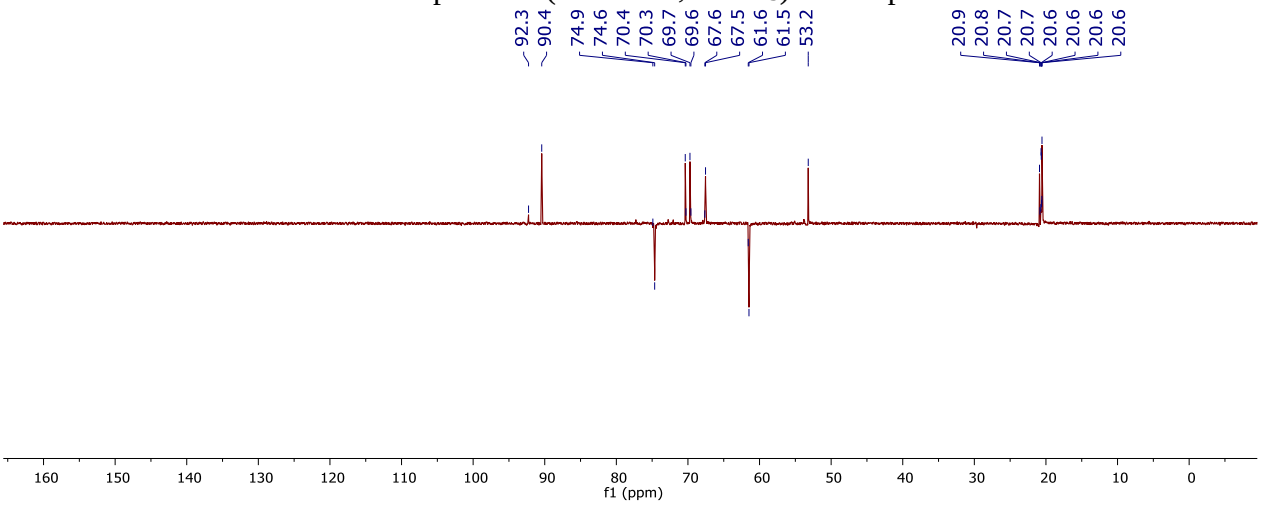
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **18**



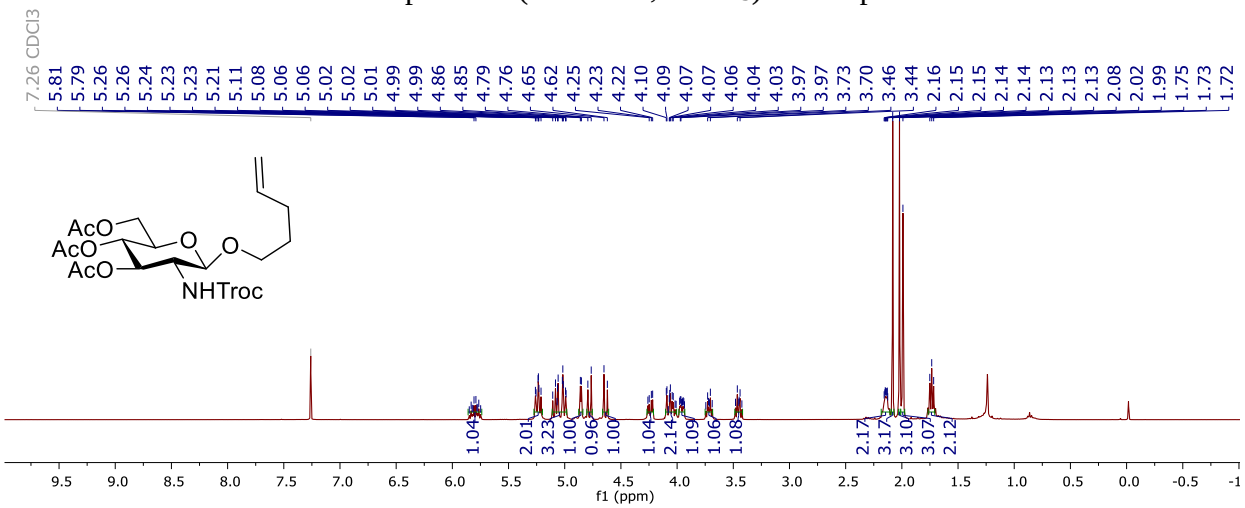
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **18**



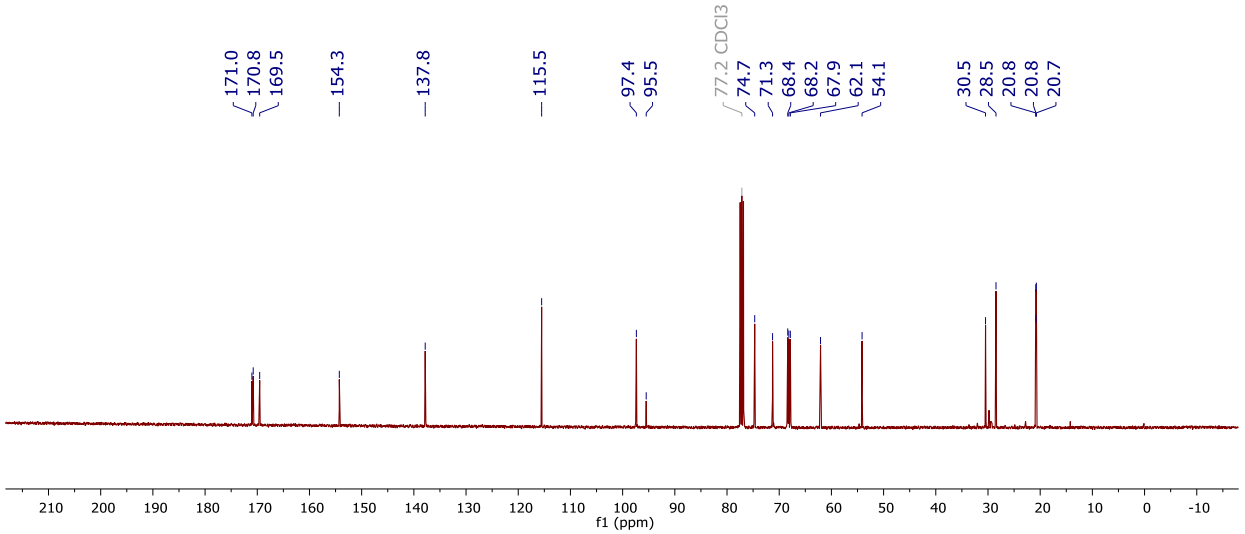
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **18**



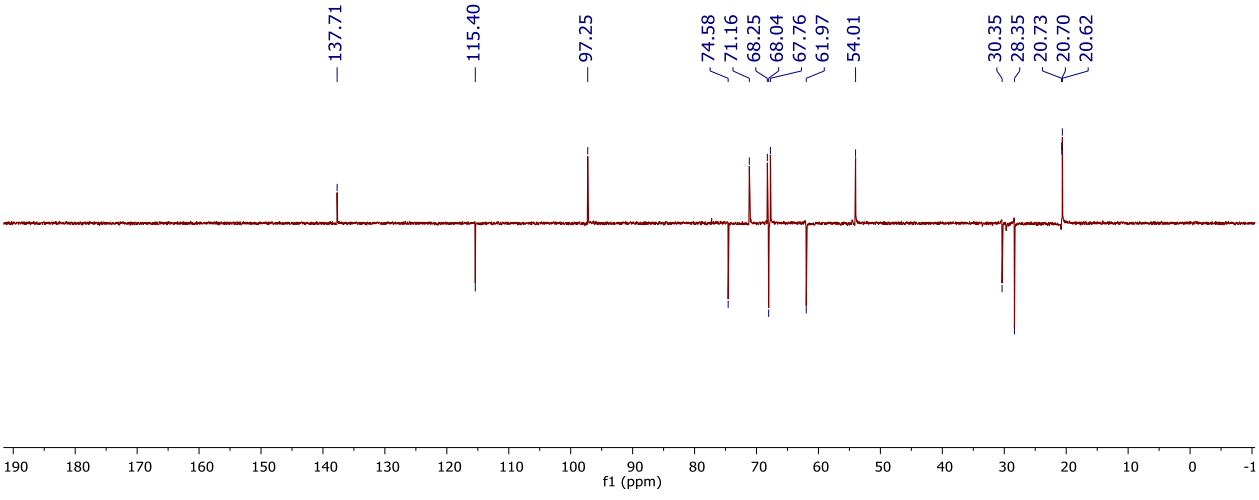
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **19**



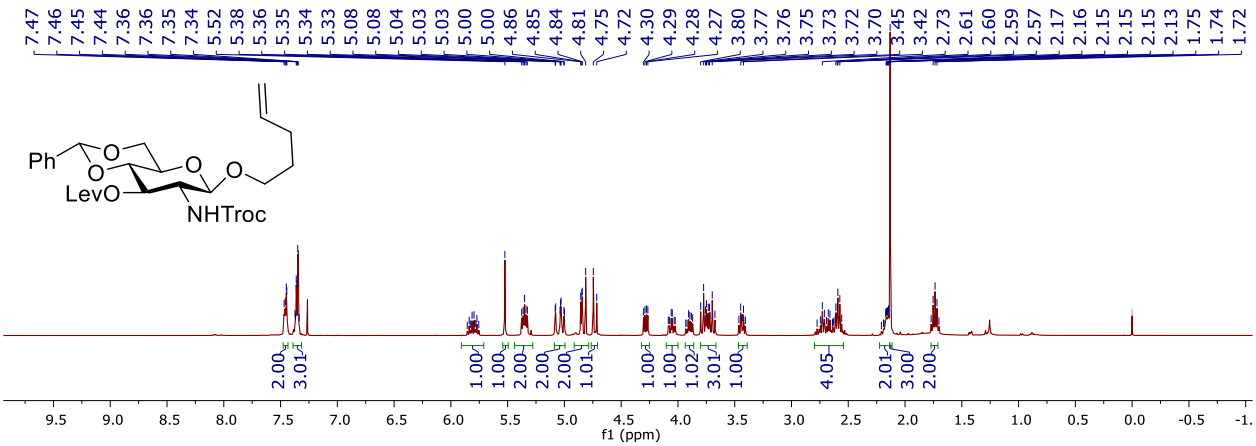
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **19**



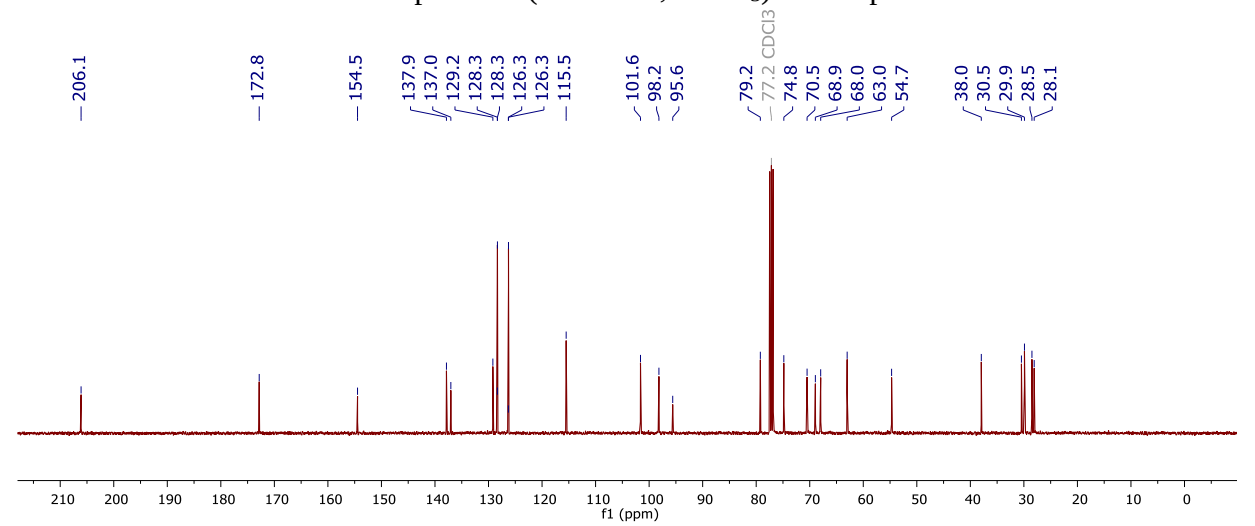
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **19**



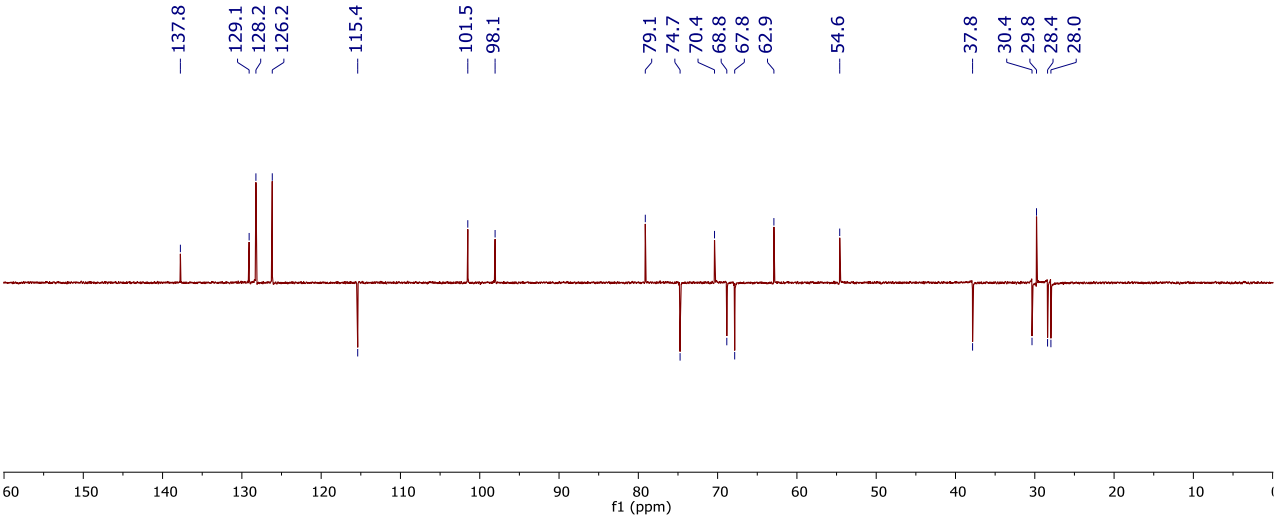
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **20**



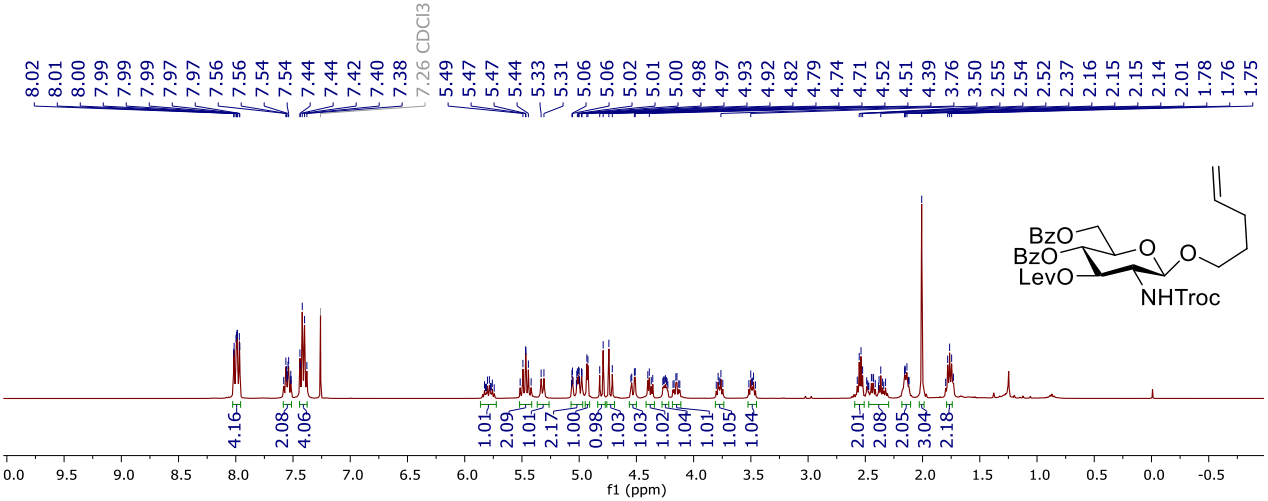
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **20**



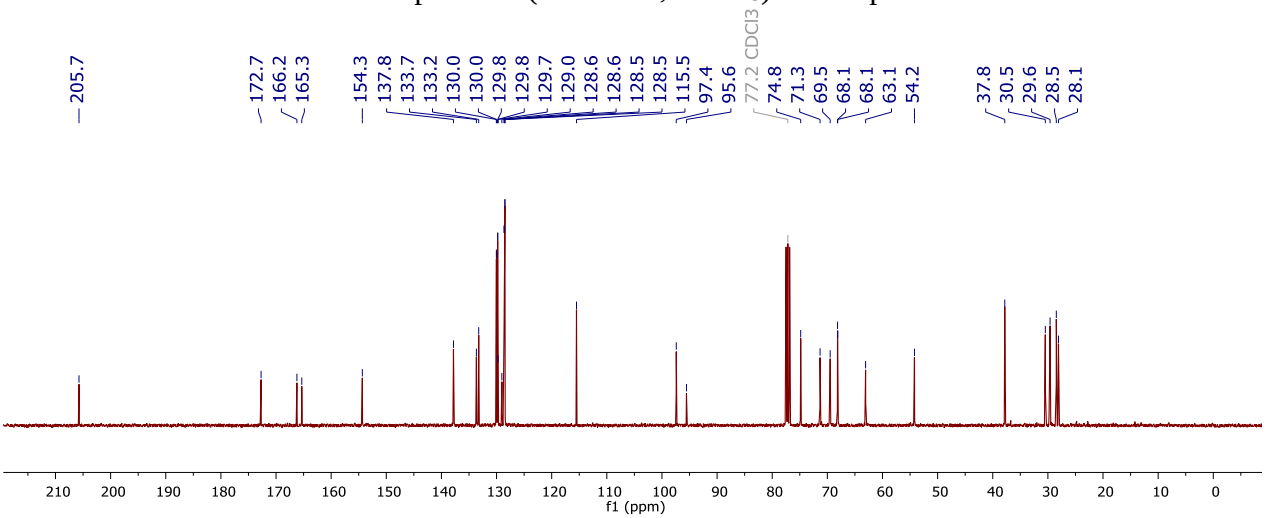
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **20**



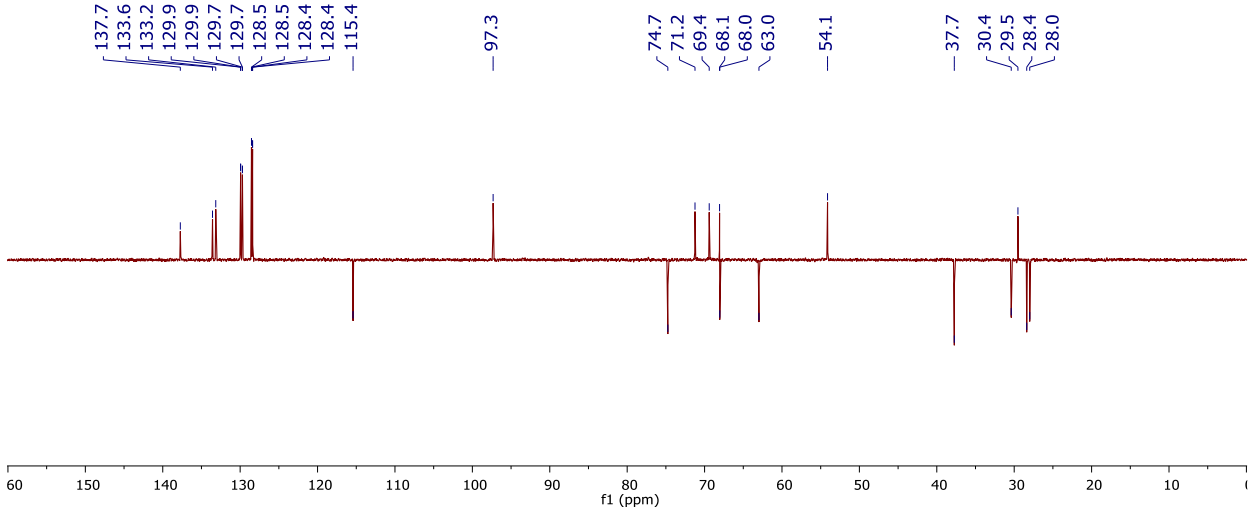
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **21**



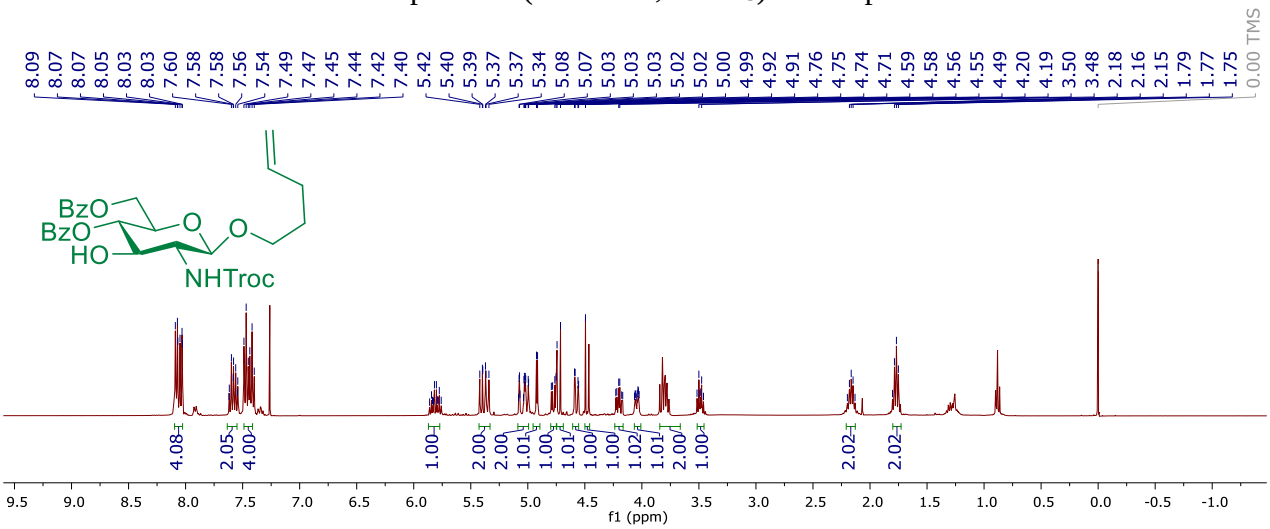
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **21**



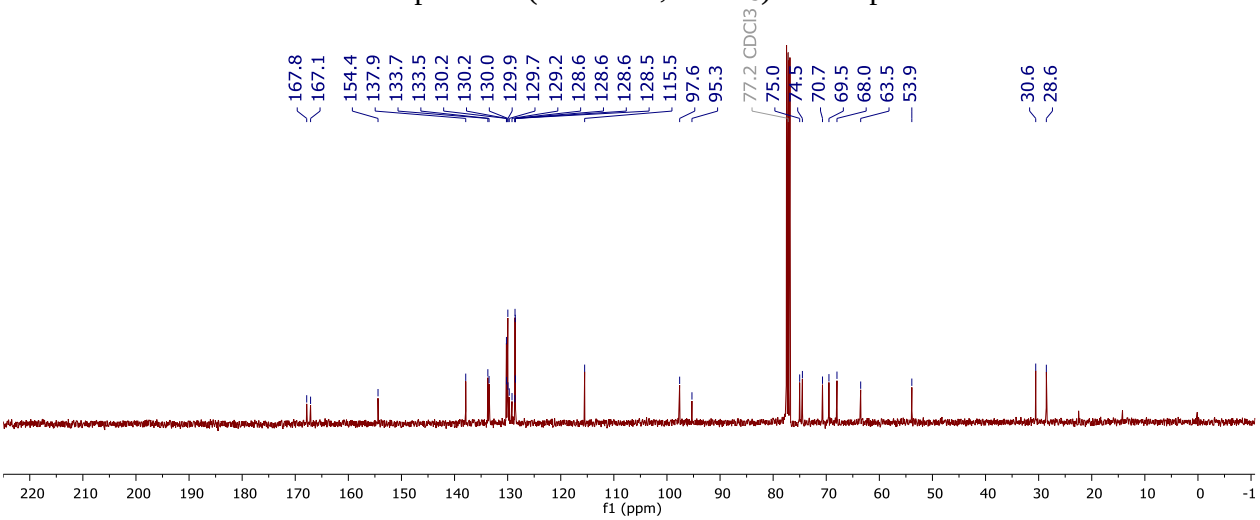
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **21**



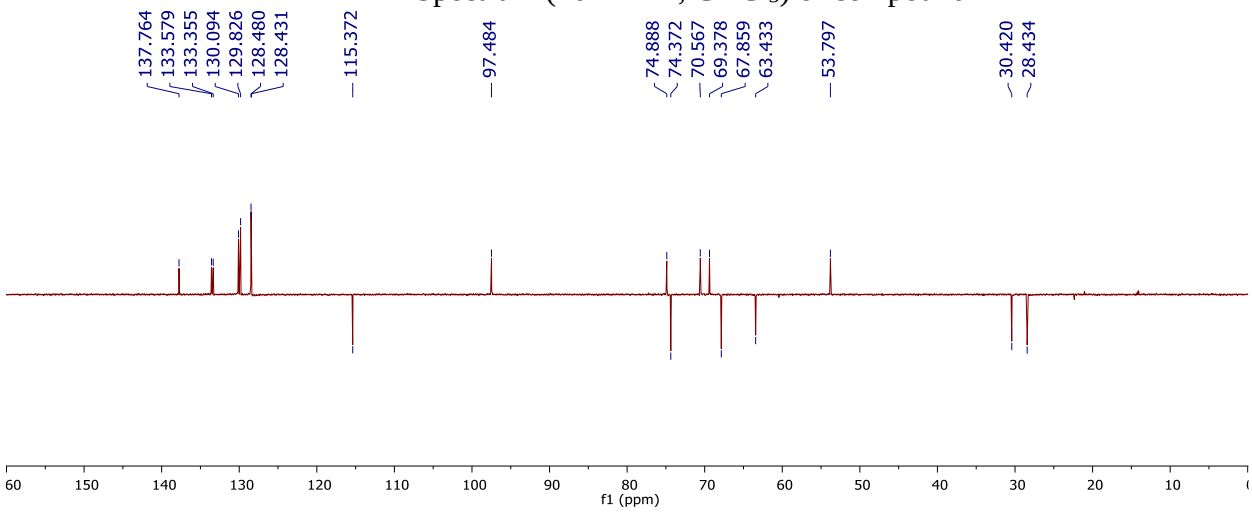
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **12**



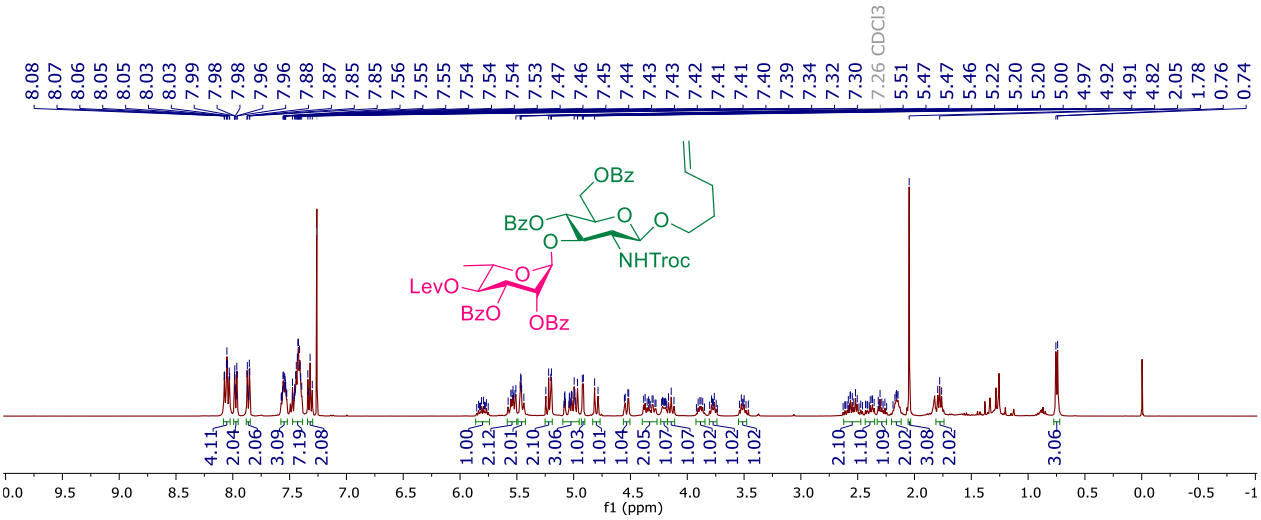
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **12**



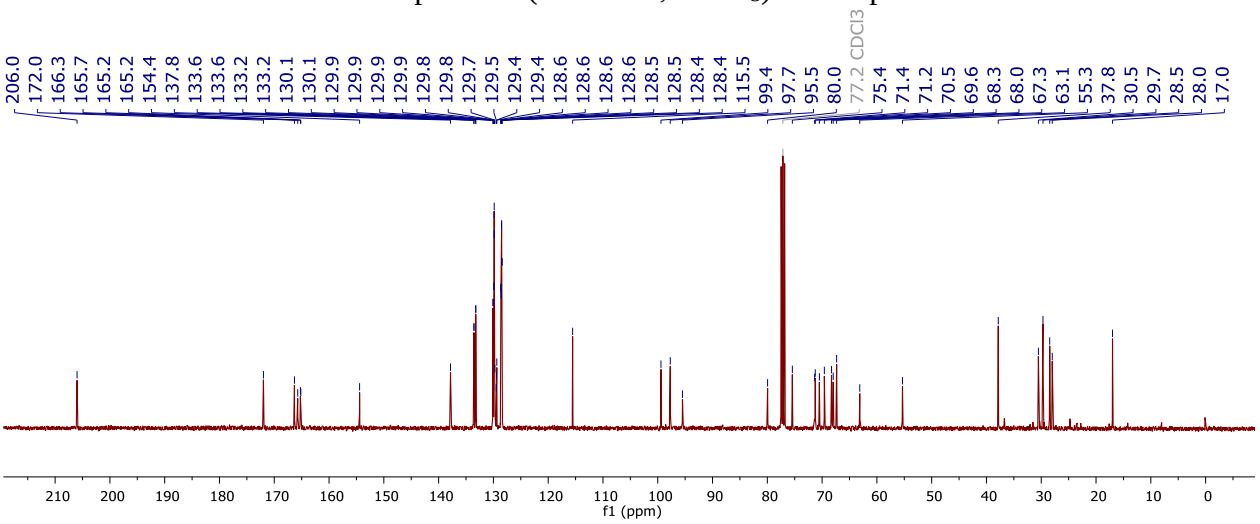
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **12**



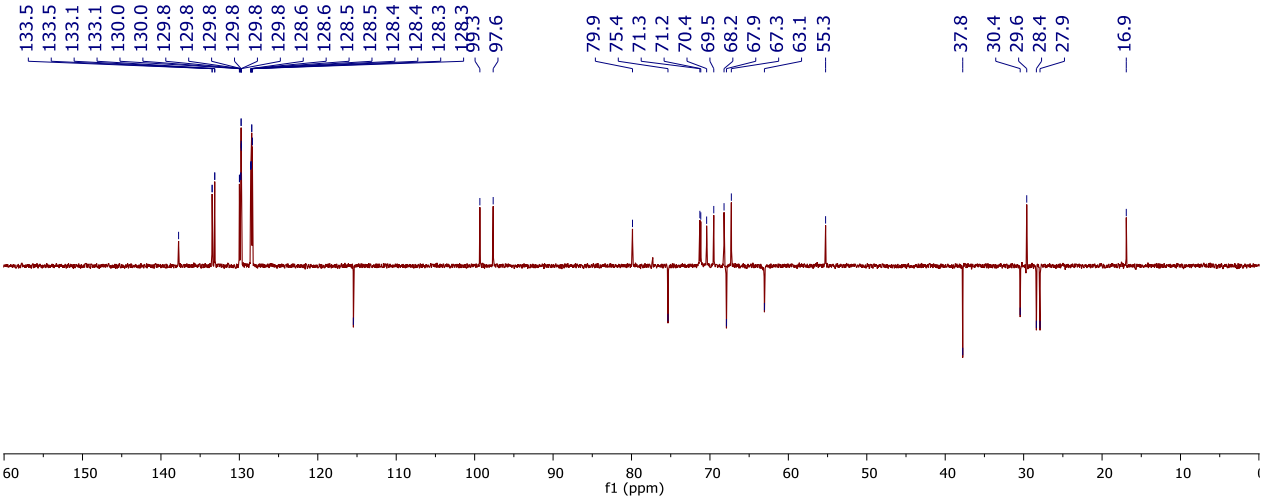
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **22**



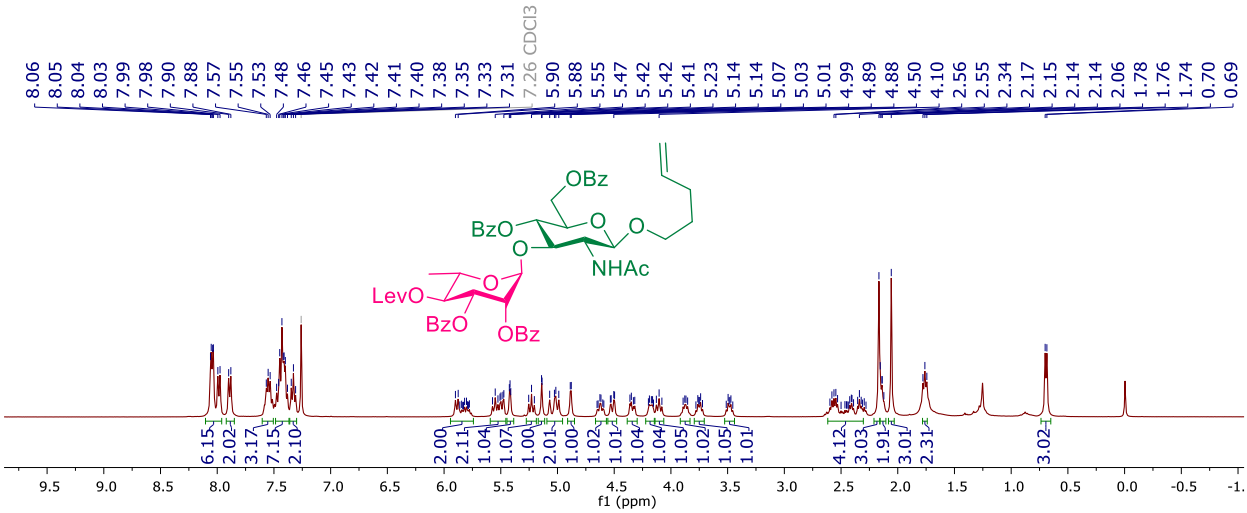
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **22**



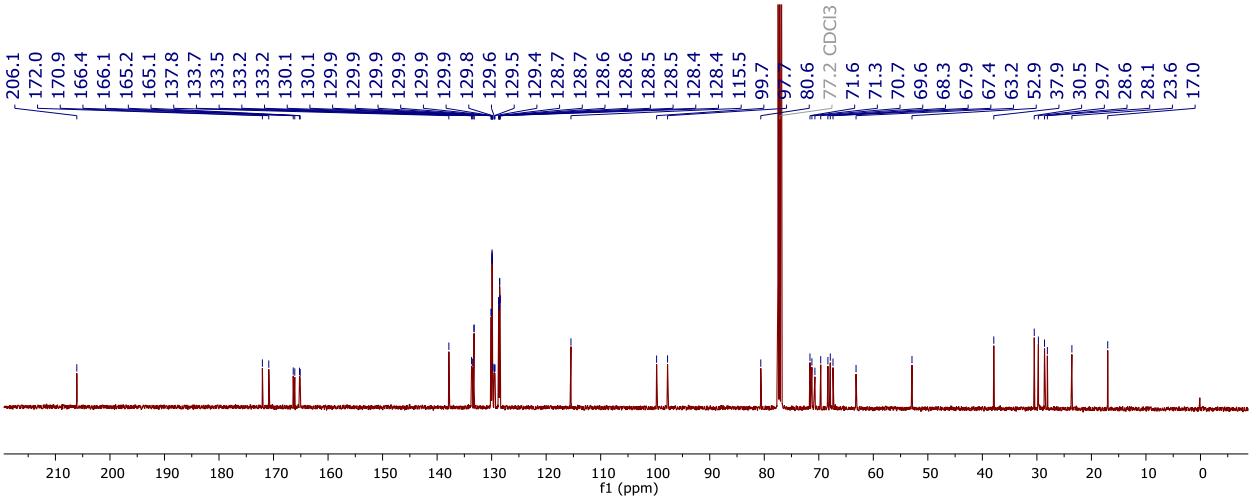
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **22**



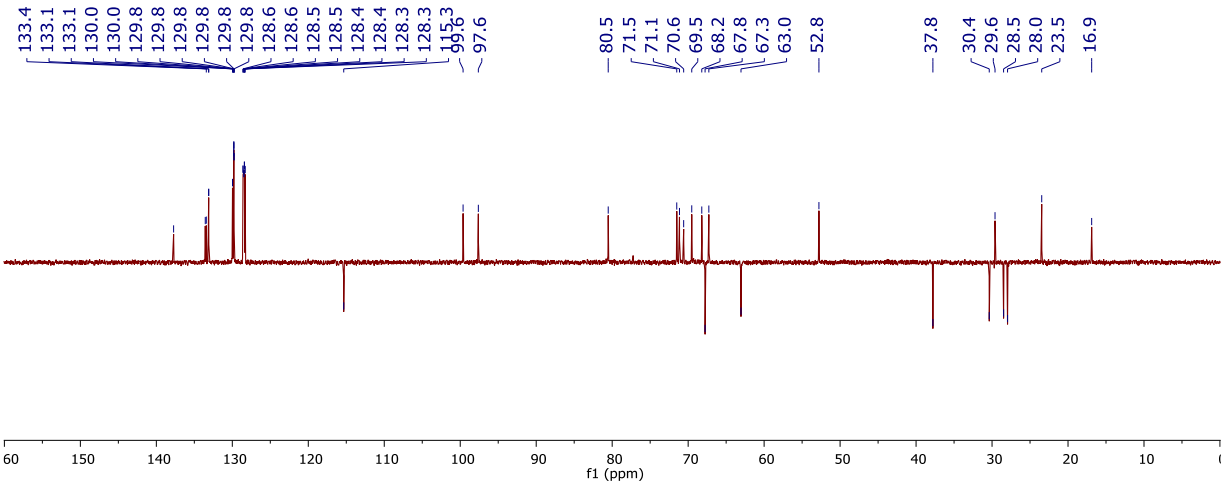
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **23**



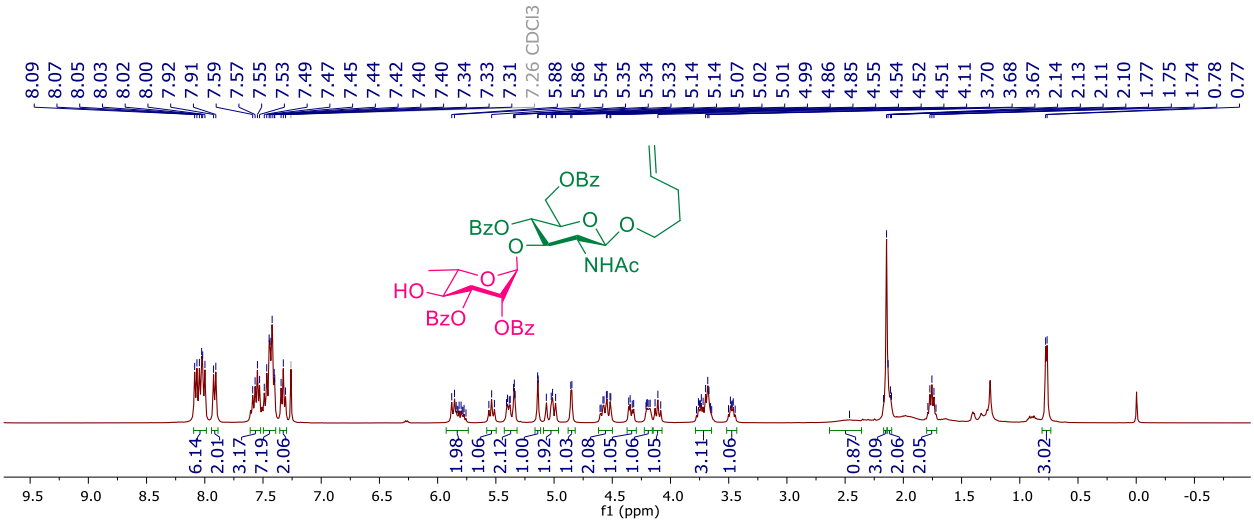
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **23**



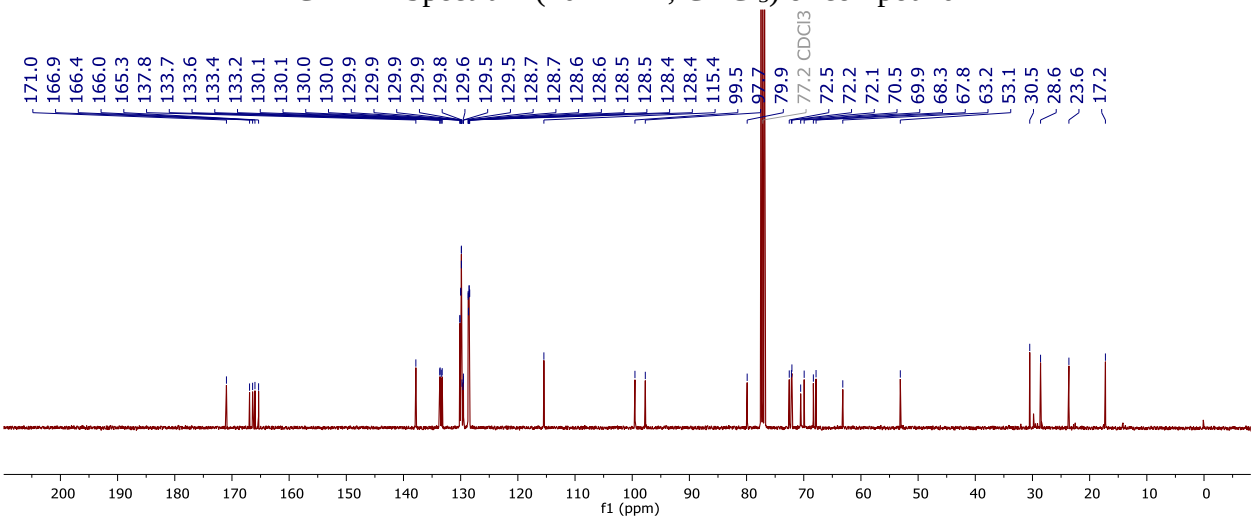
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **23**



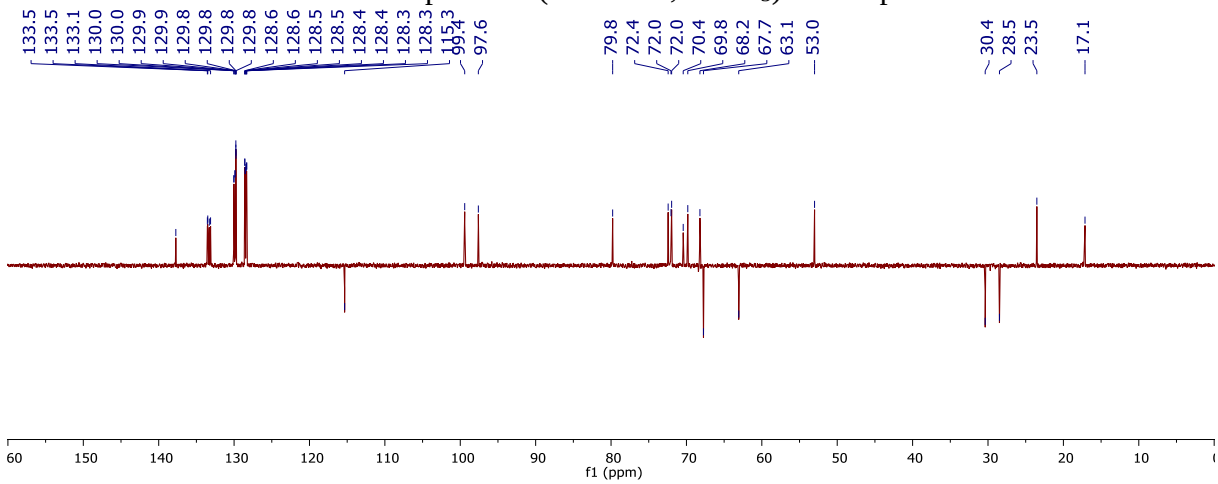
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **7**



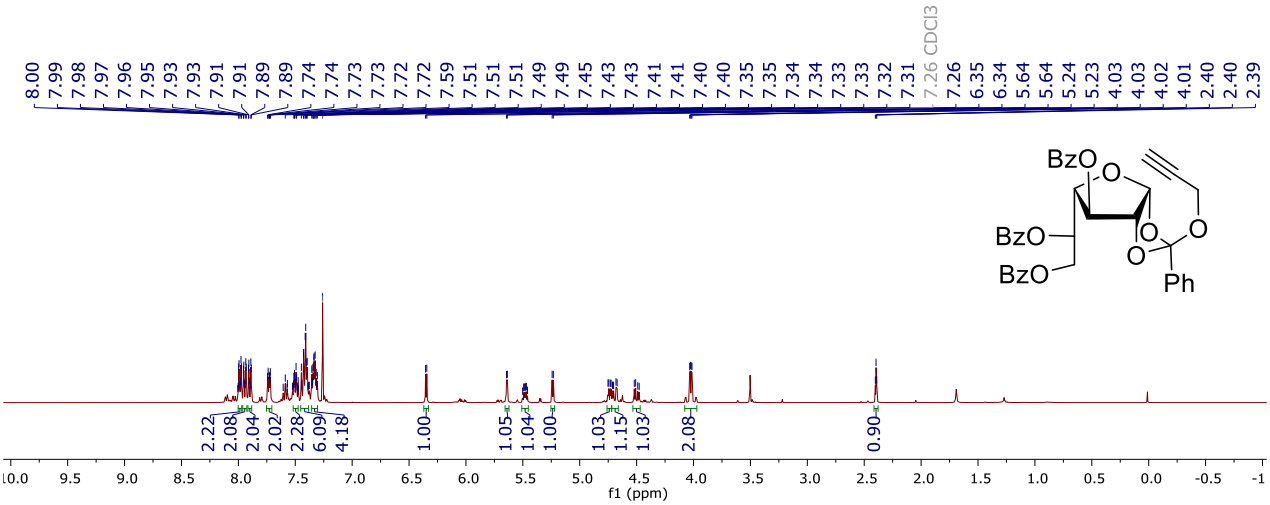
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **7**



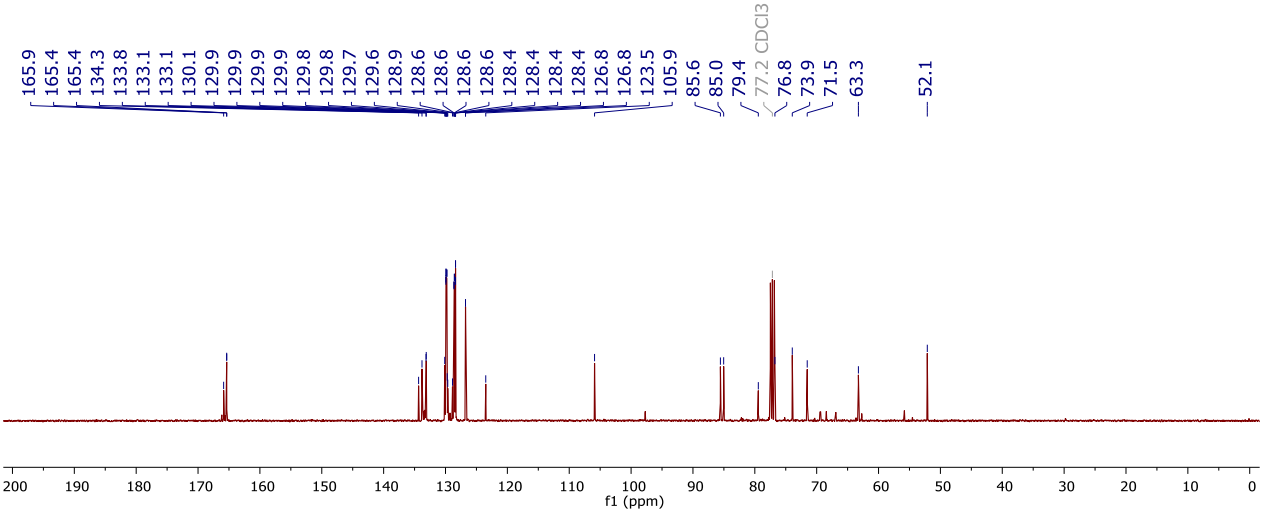
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **7**



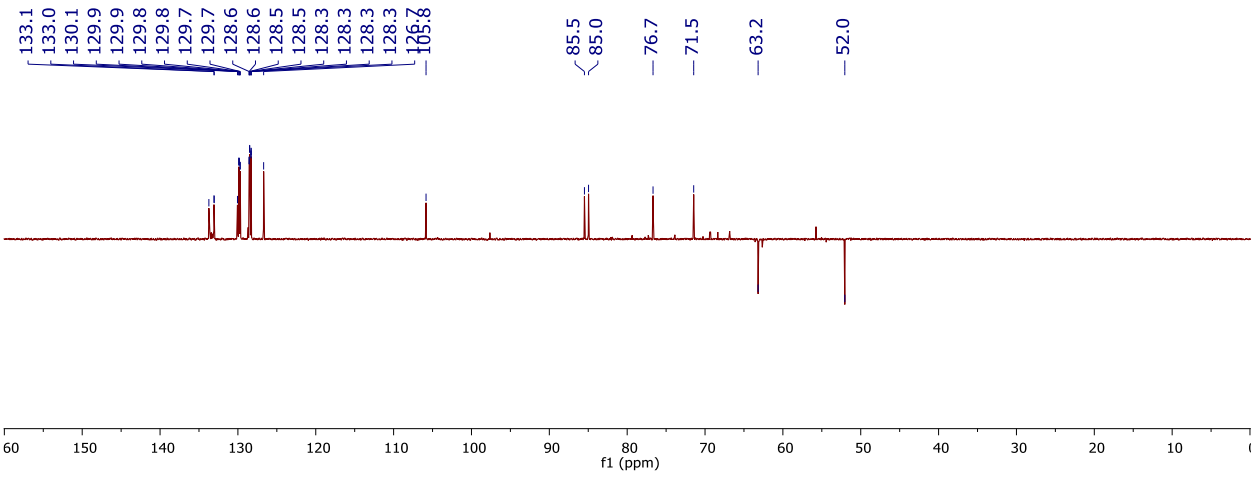
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **25**



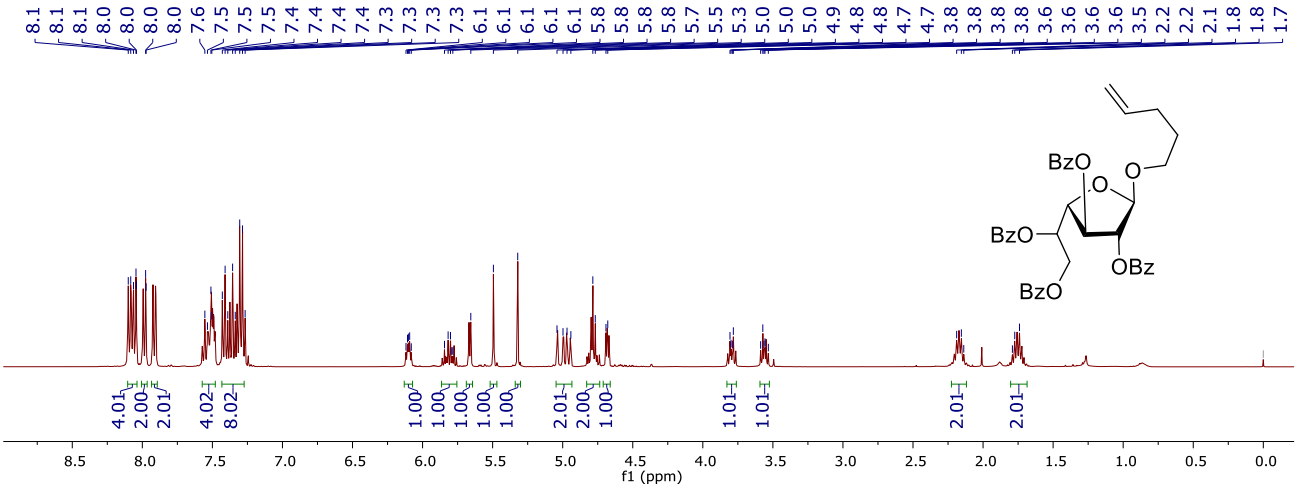
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **25**



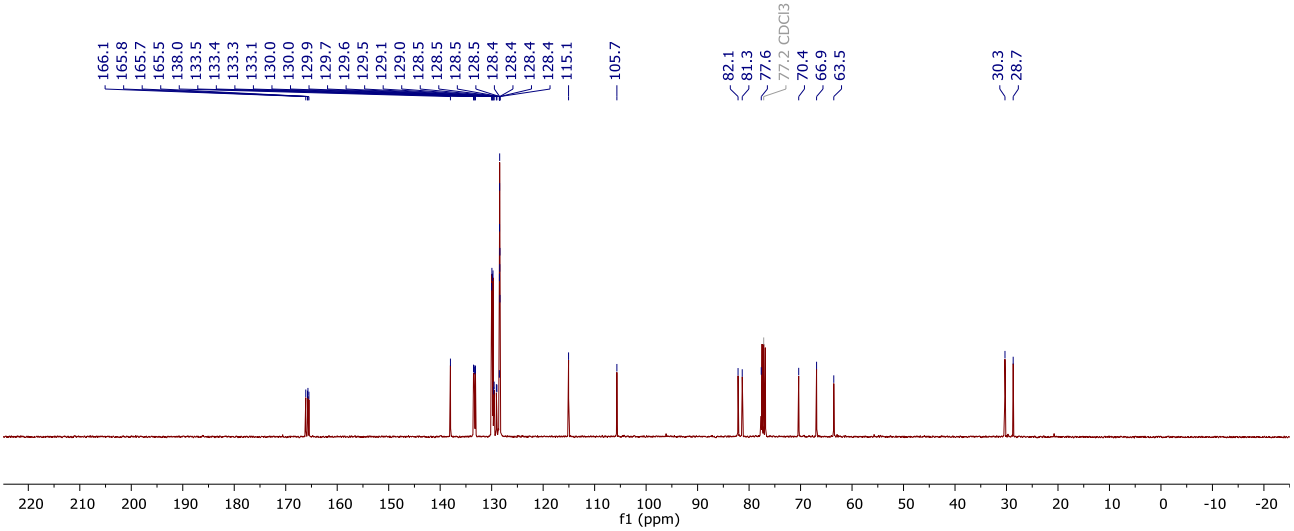
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **25**



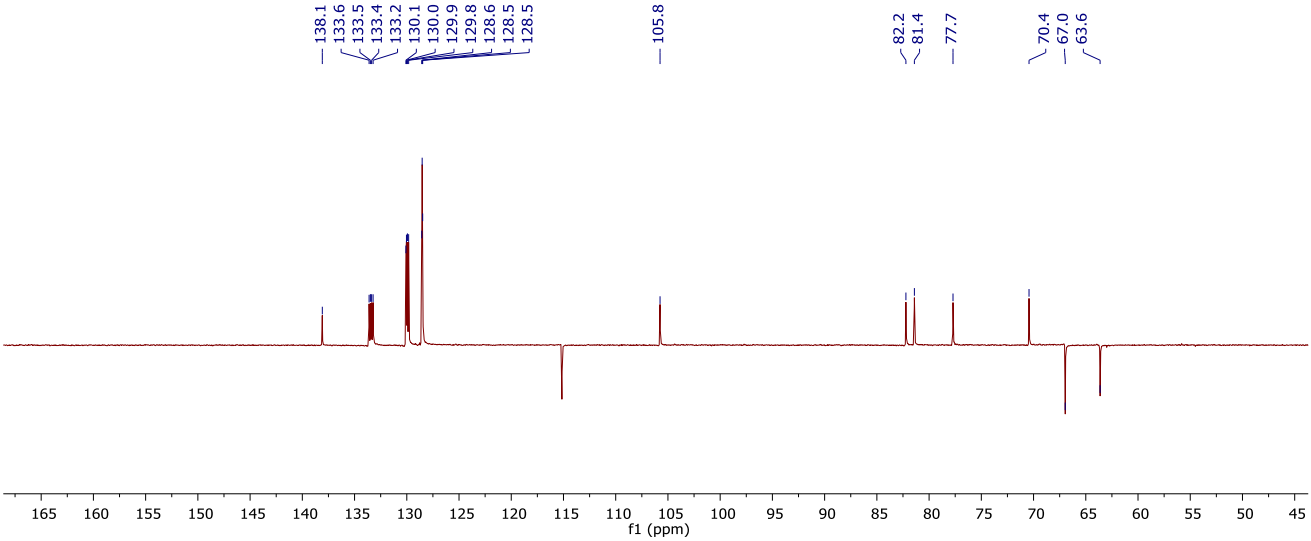
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **26**



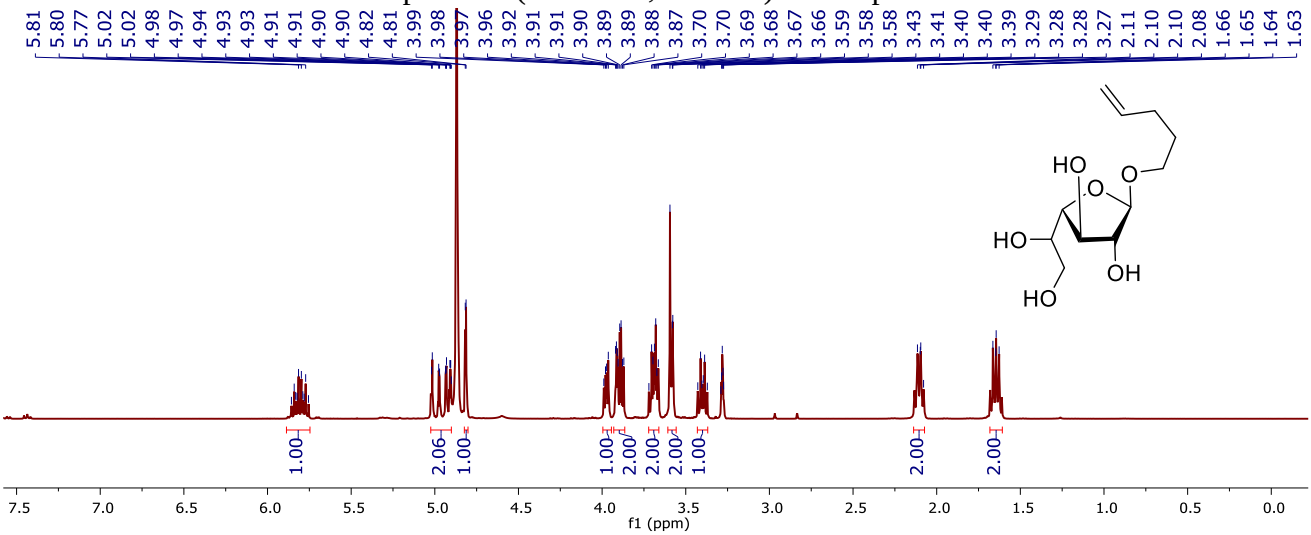
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **26**



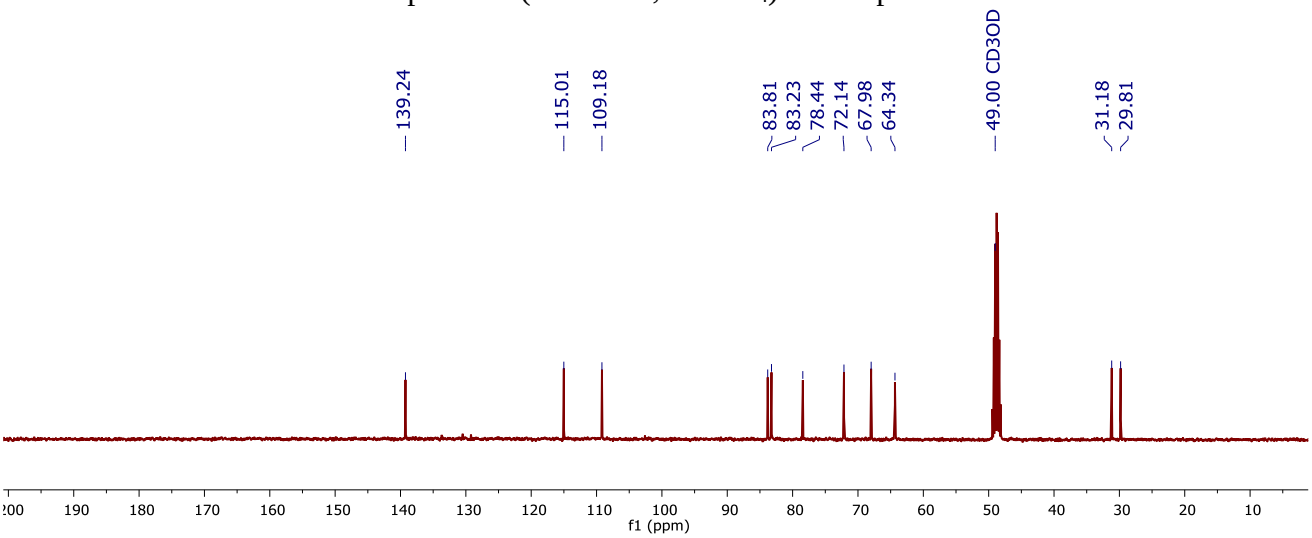
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **26**



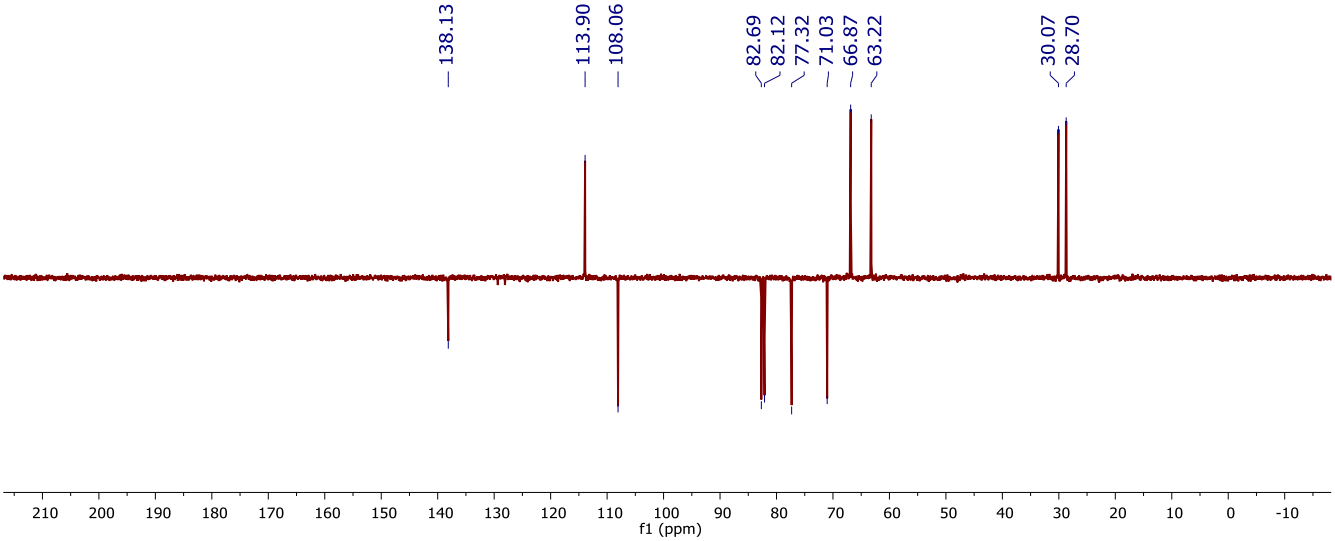
^{1}H NMR Spectrum (400 MHz, $MeOD_4$) of compound **27**



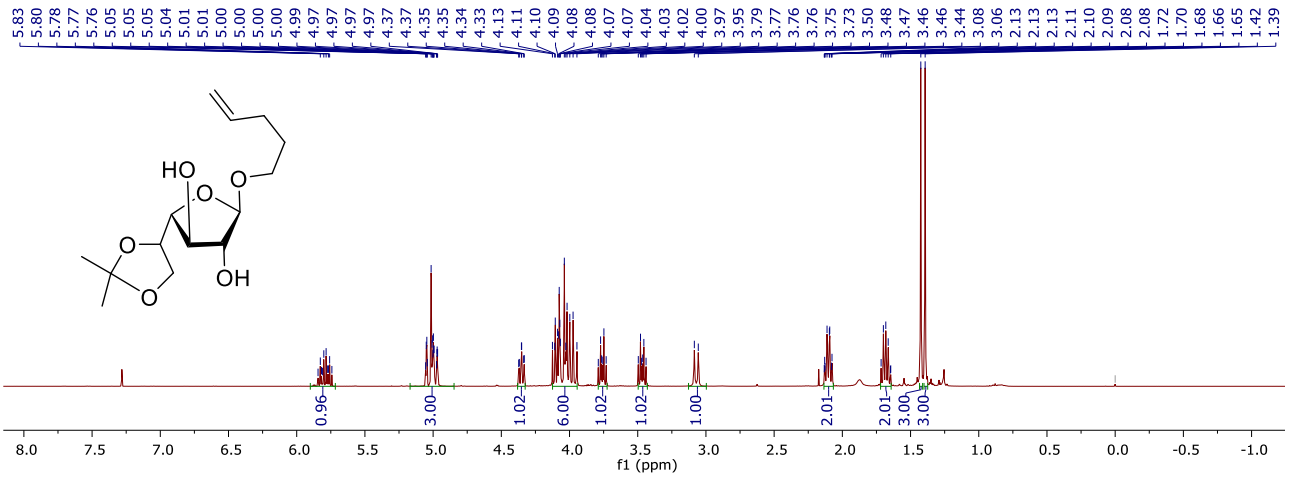
^{13}C NMR Spectrum (101 MHz, $MeOD_4$) of compound **27**



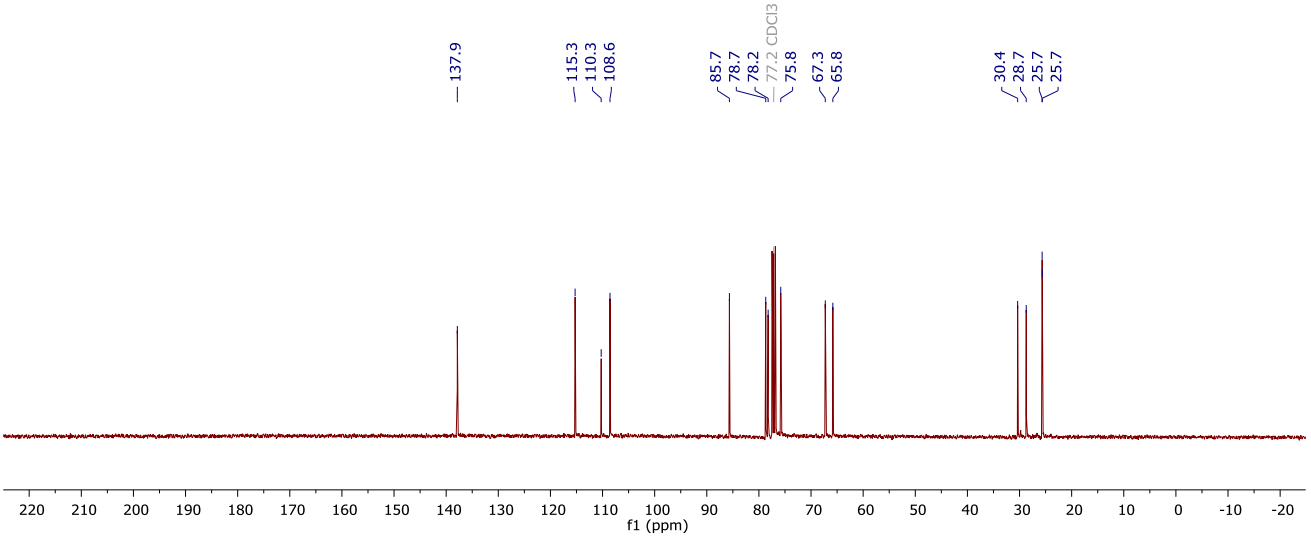
DEPT NMR Spectrum (101 MHz, $MeOD_4$) of compound **27**



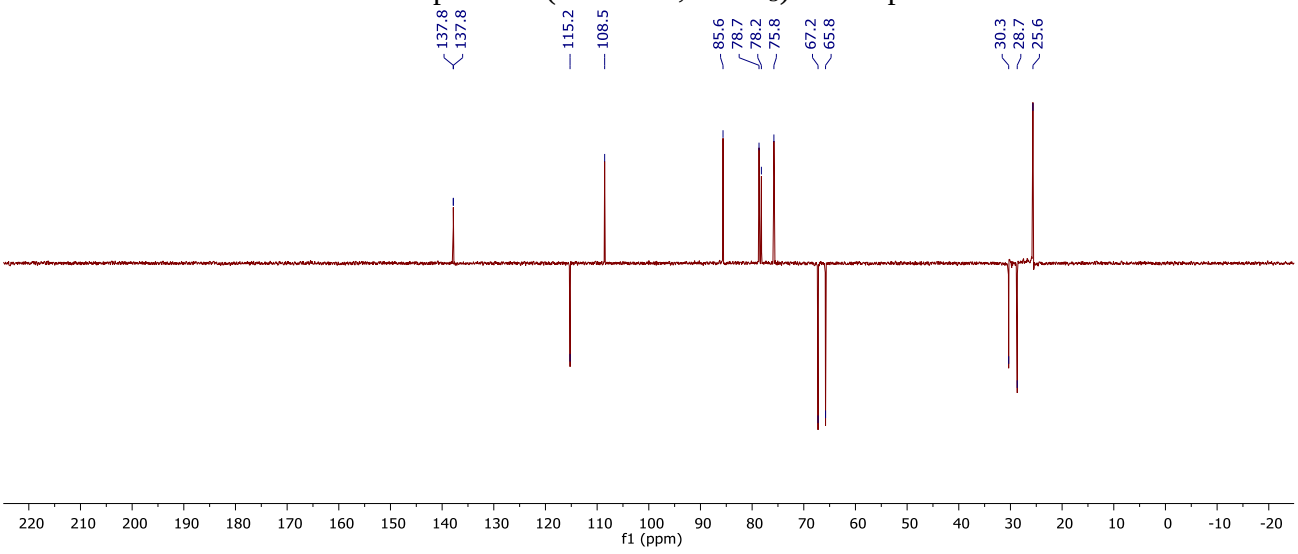
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **28**



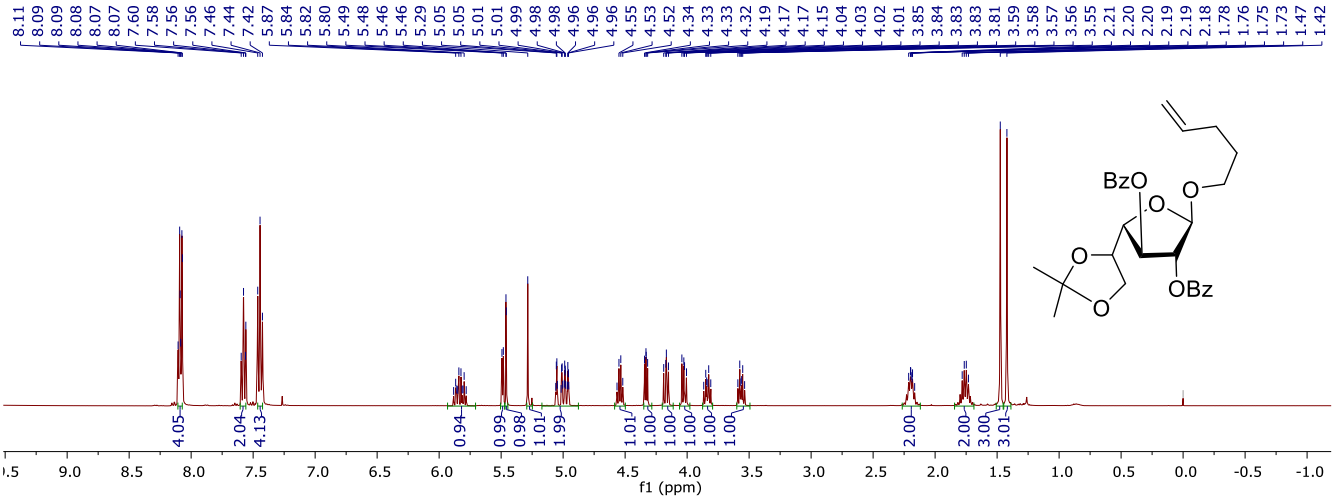
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **28**



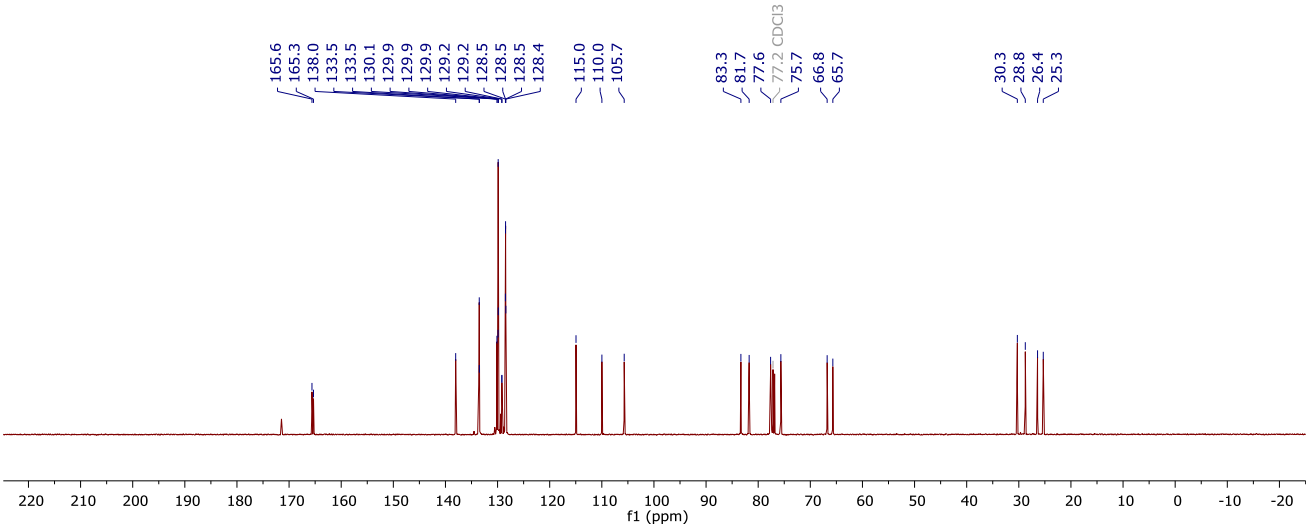
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **28**



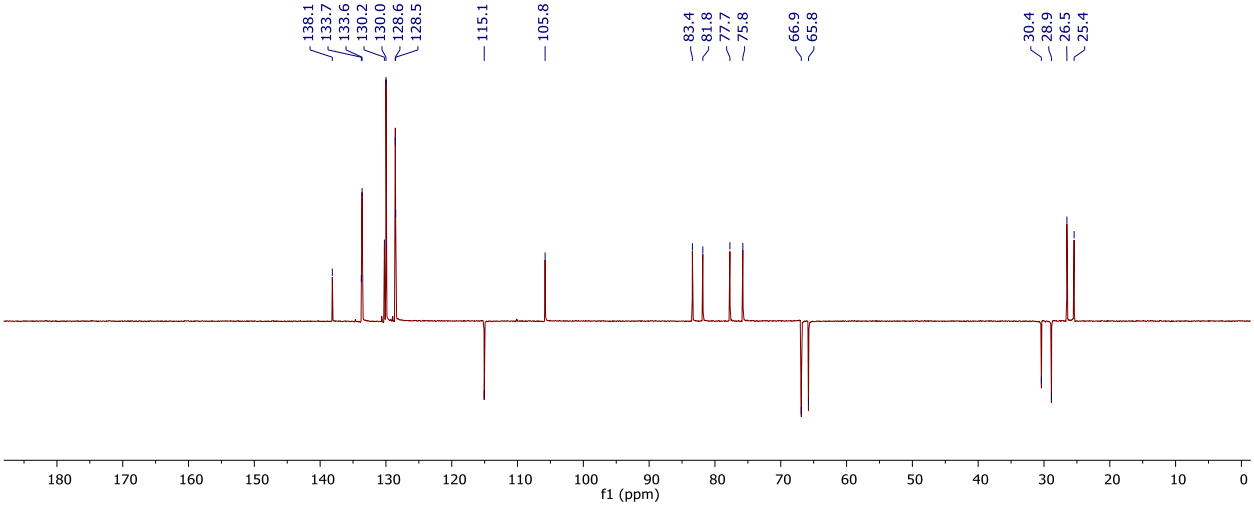
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **29**



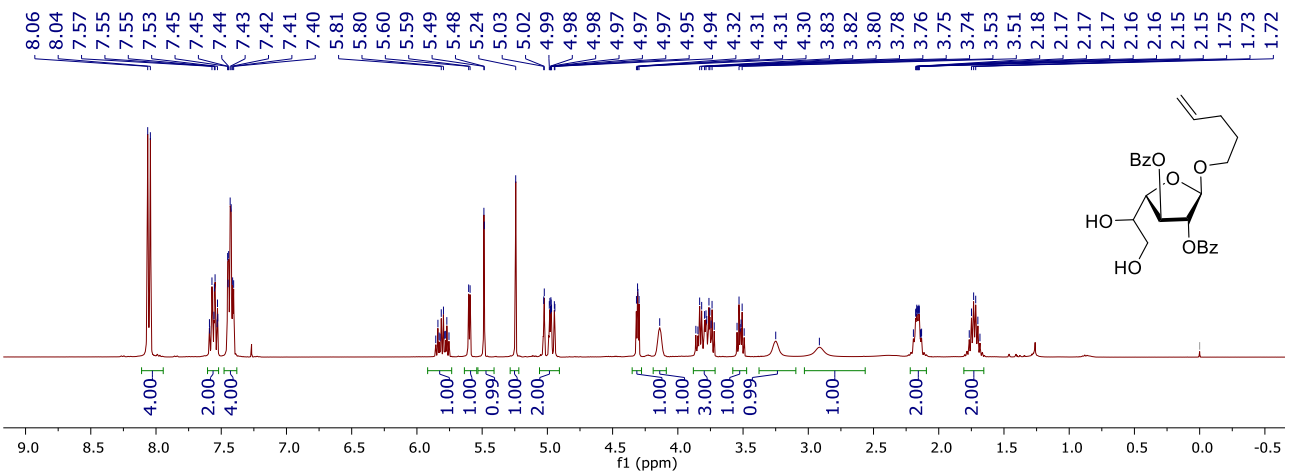
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **29**



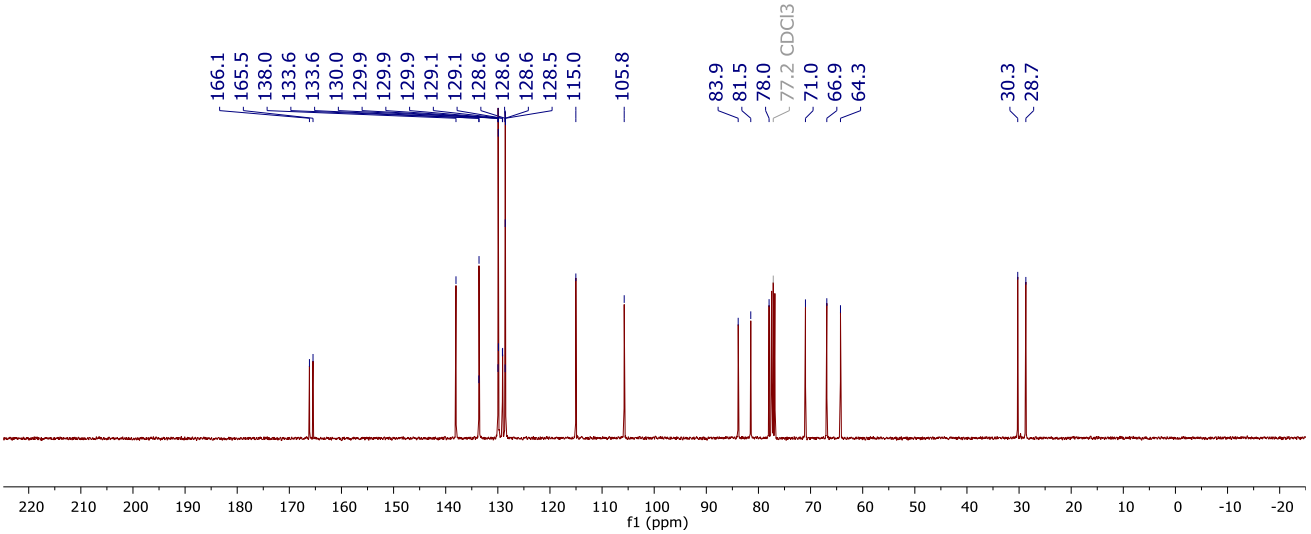
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **29**



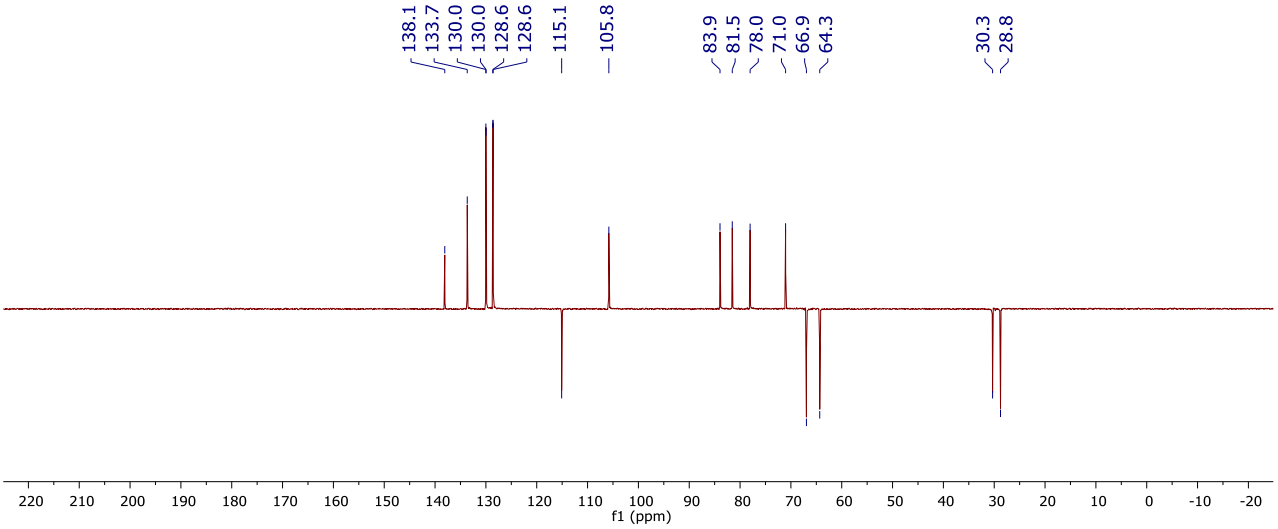
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **30**



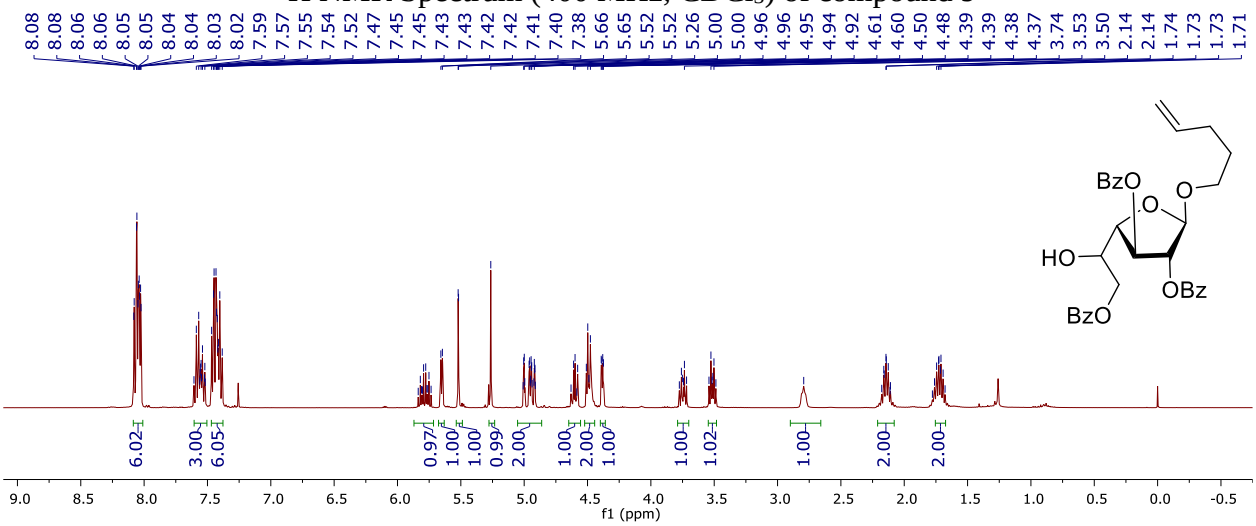
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **30**



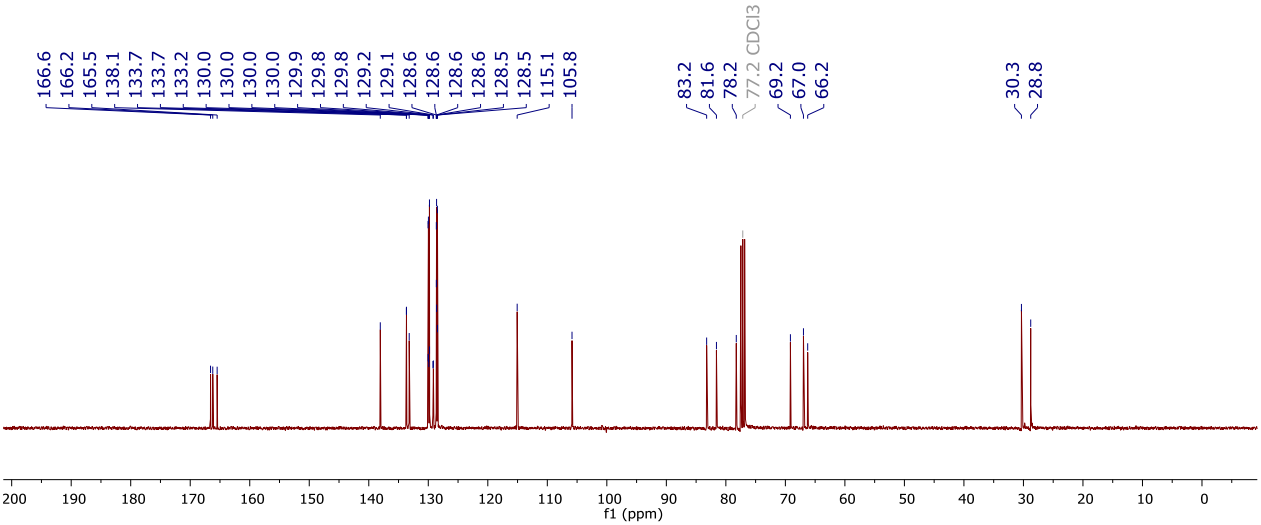
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **30**



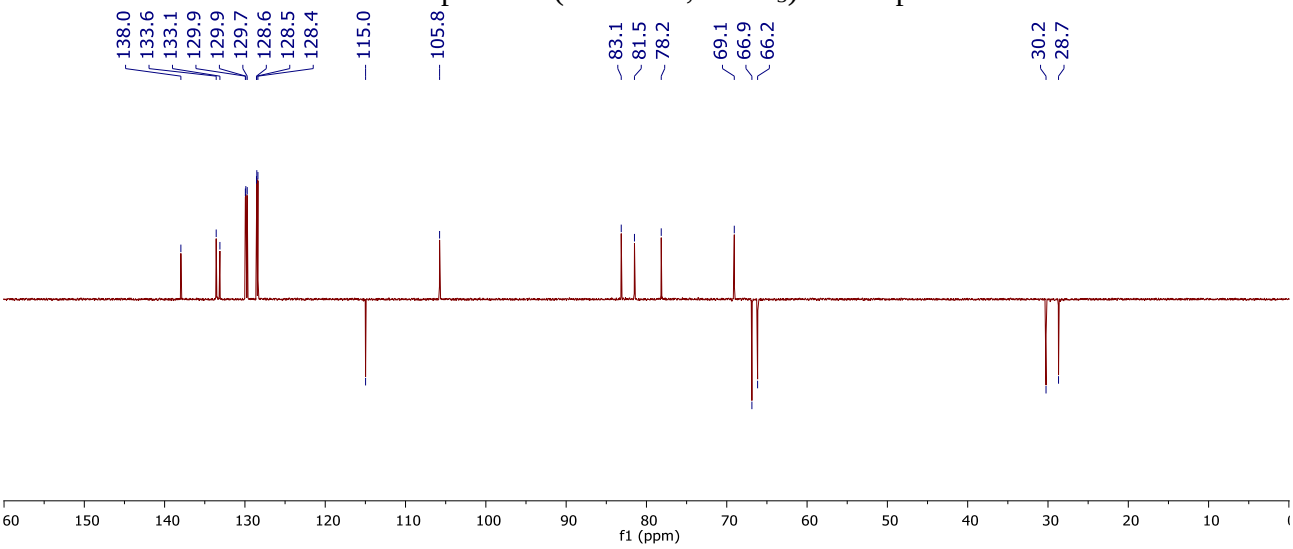
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **9**



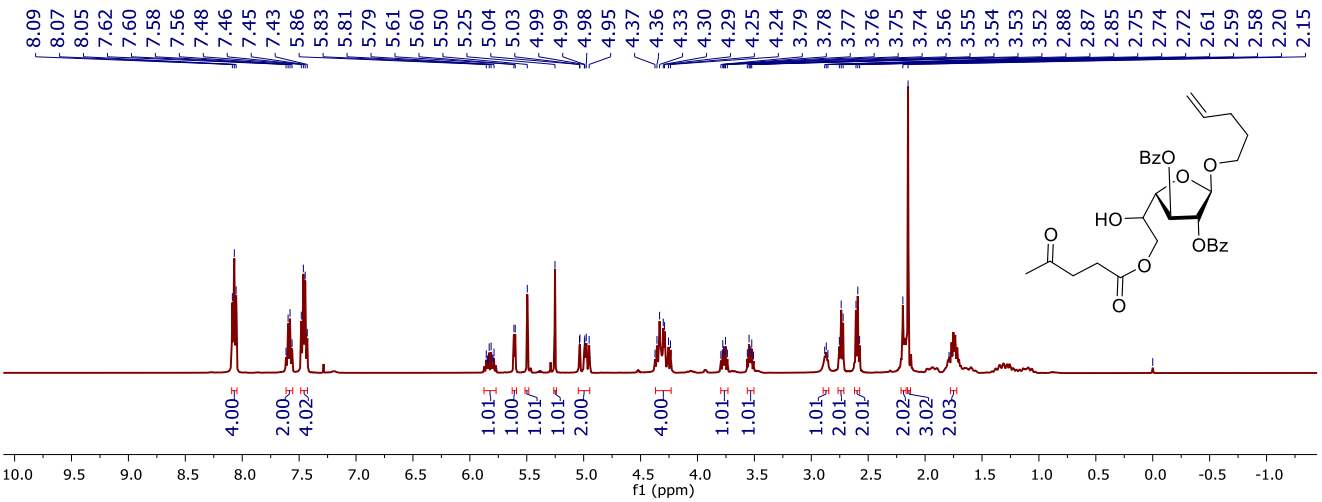
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **9**



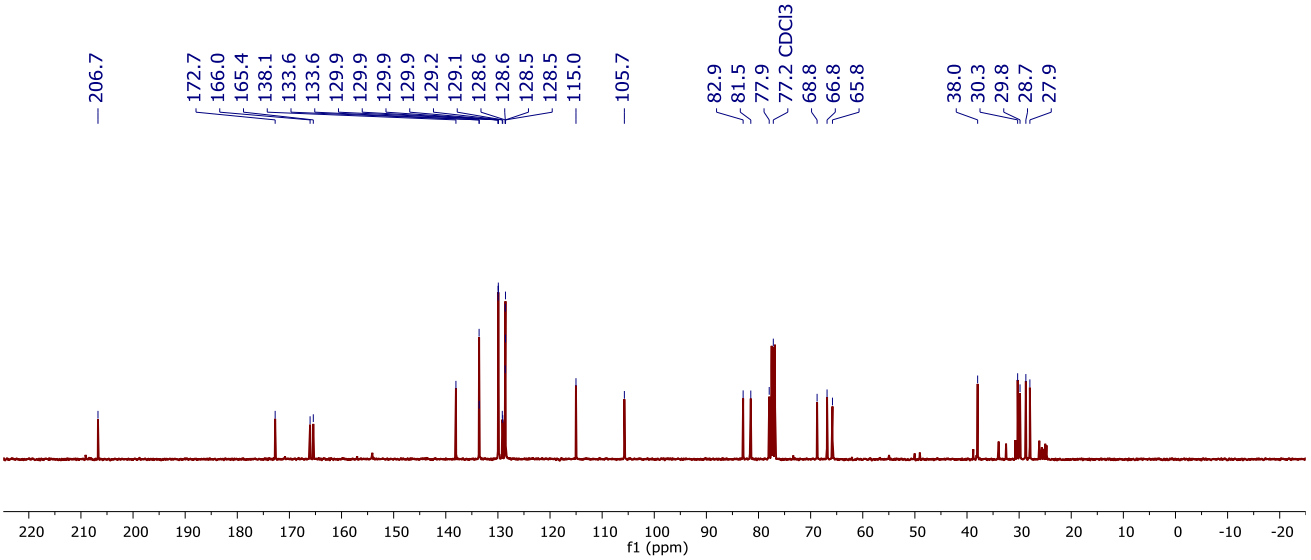
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **9**



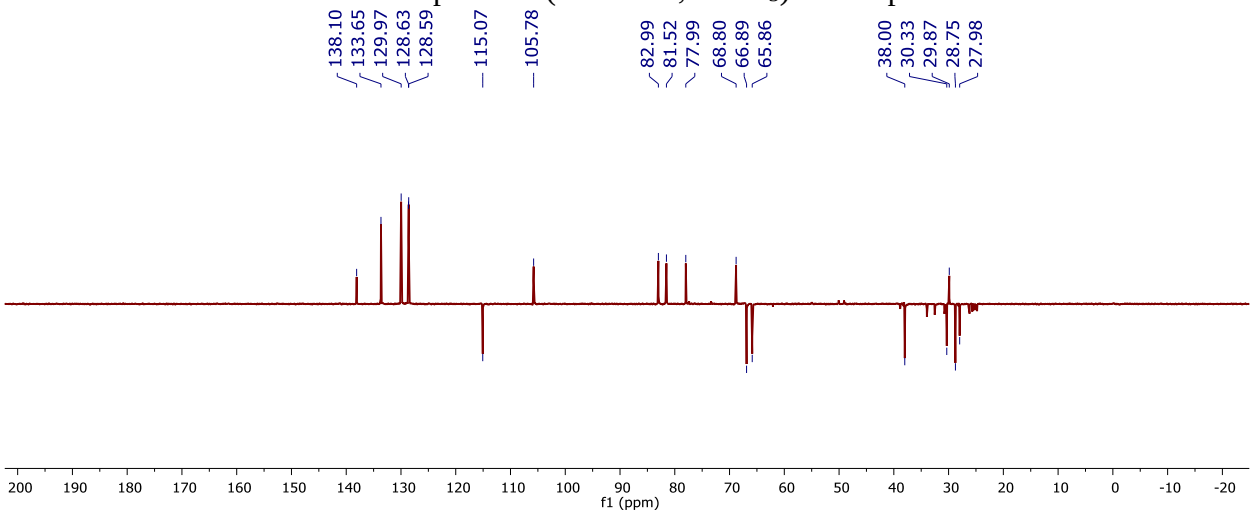
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **31**



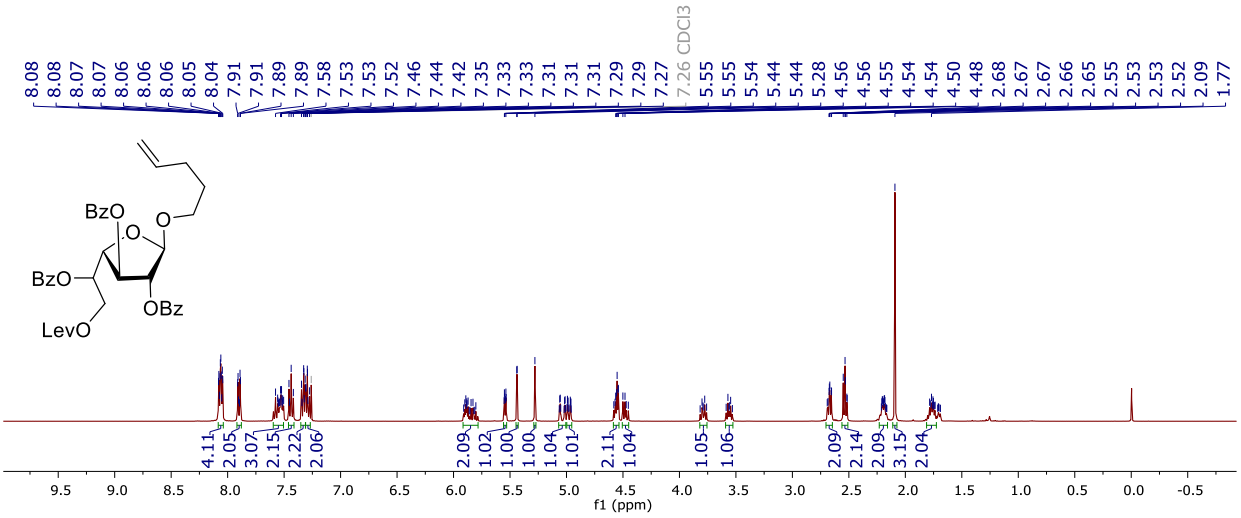
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **31**



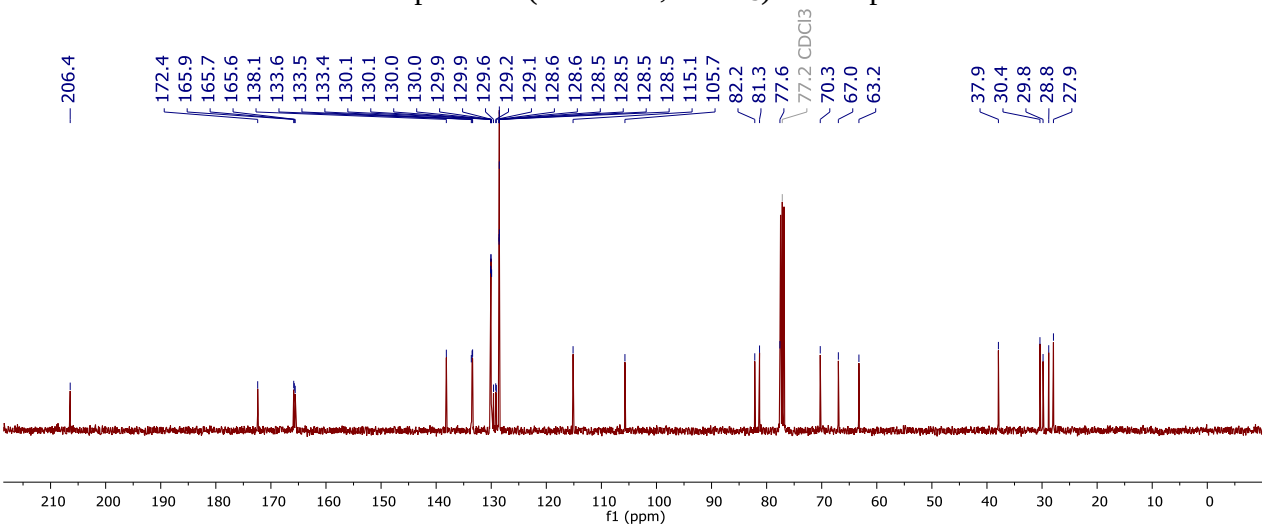
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **31**



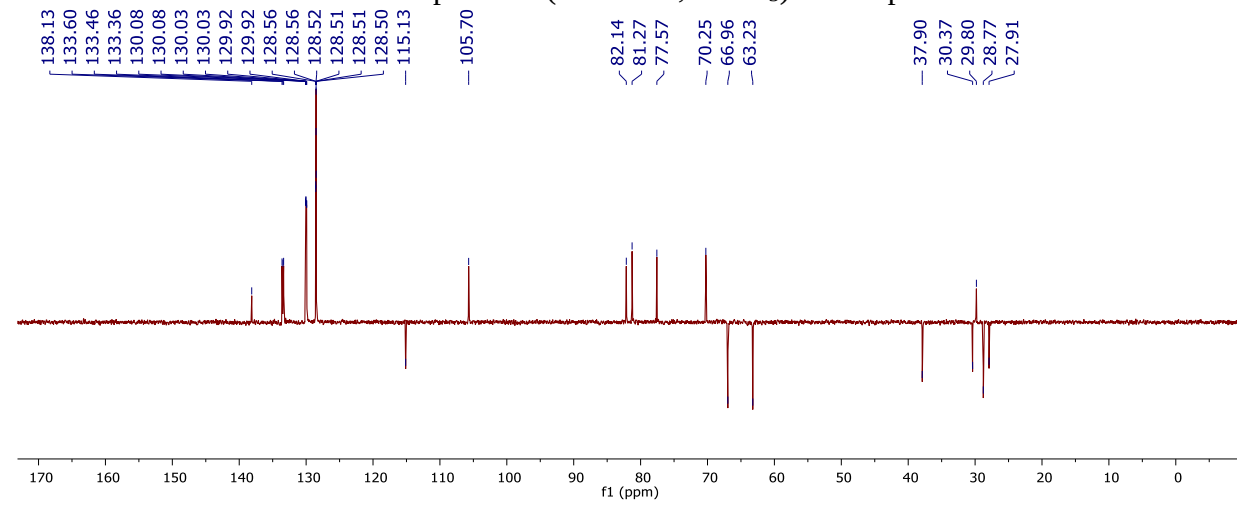
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **32**



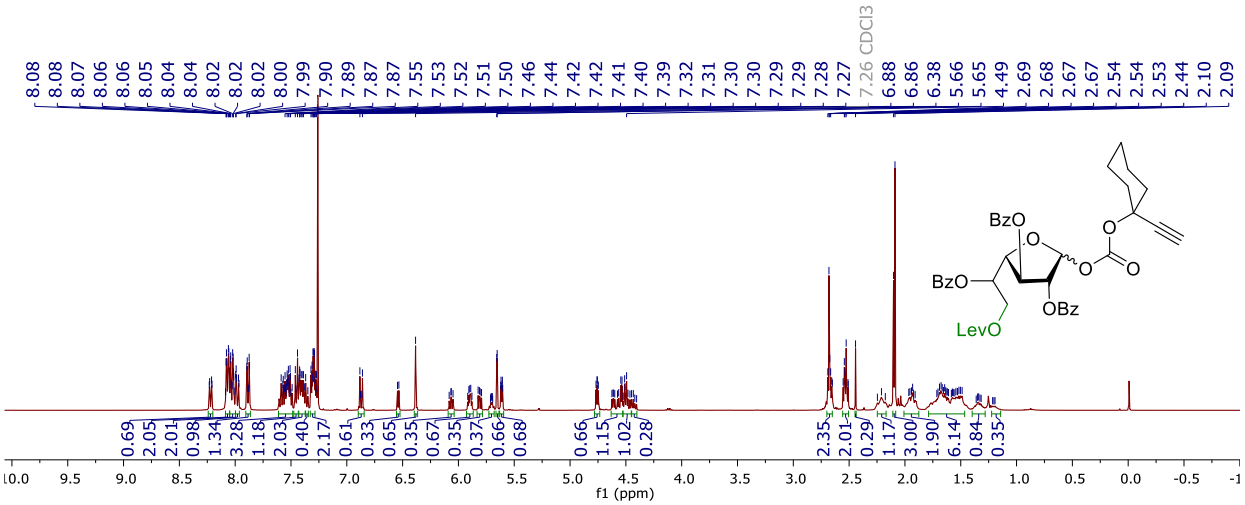
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **32**



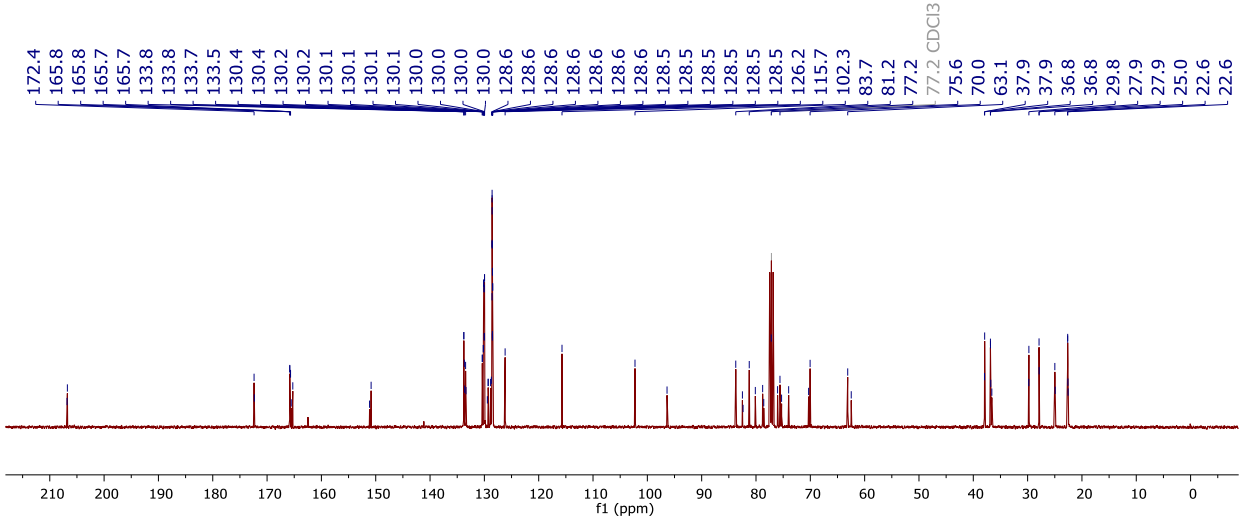
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **32**



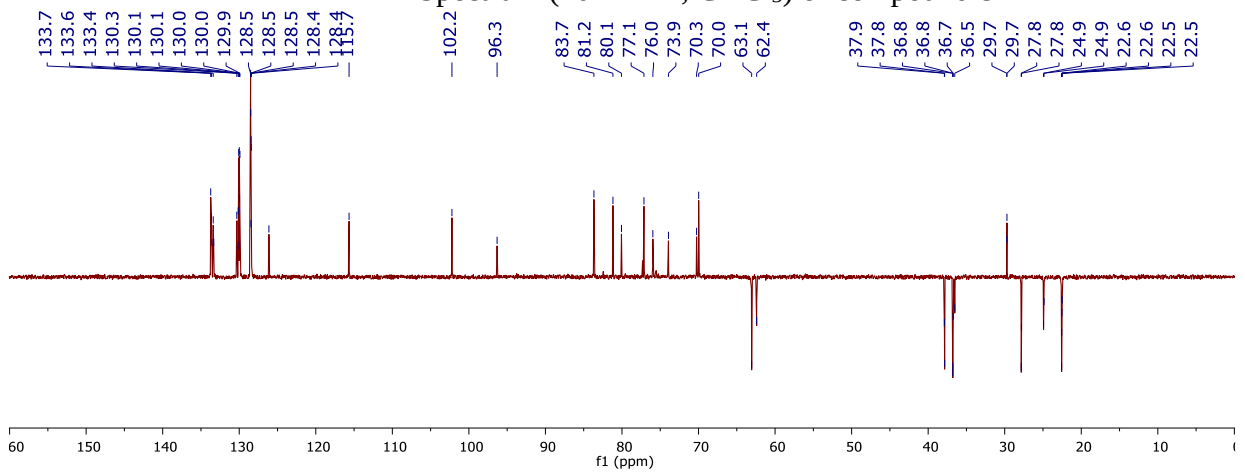
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **8**



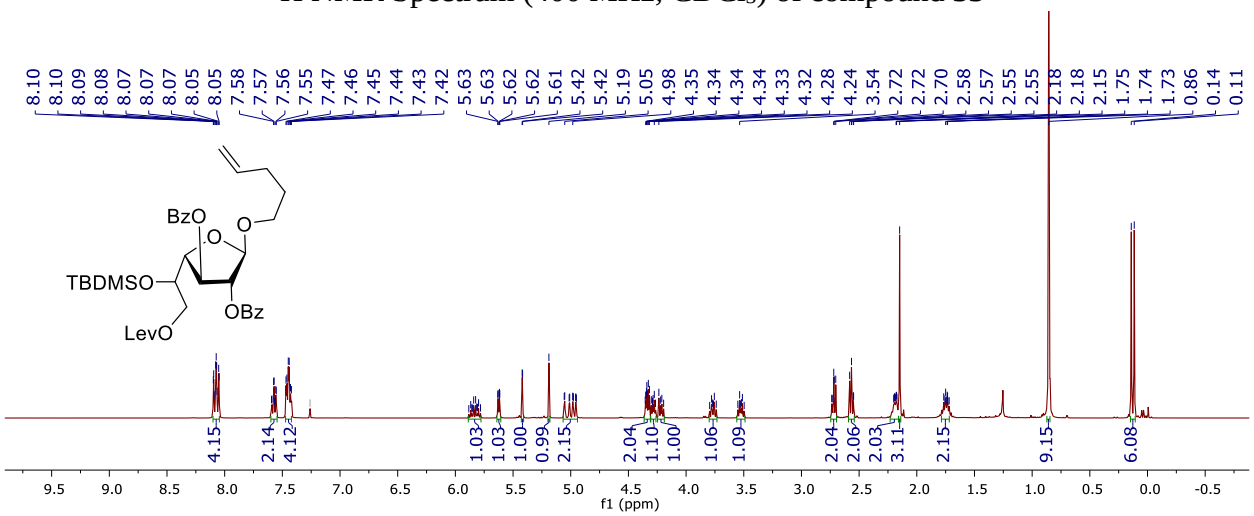
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **8**



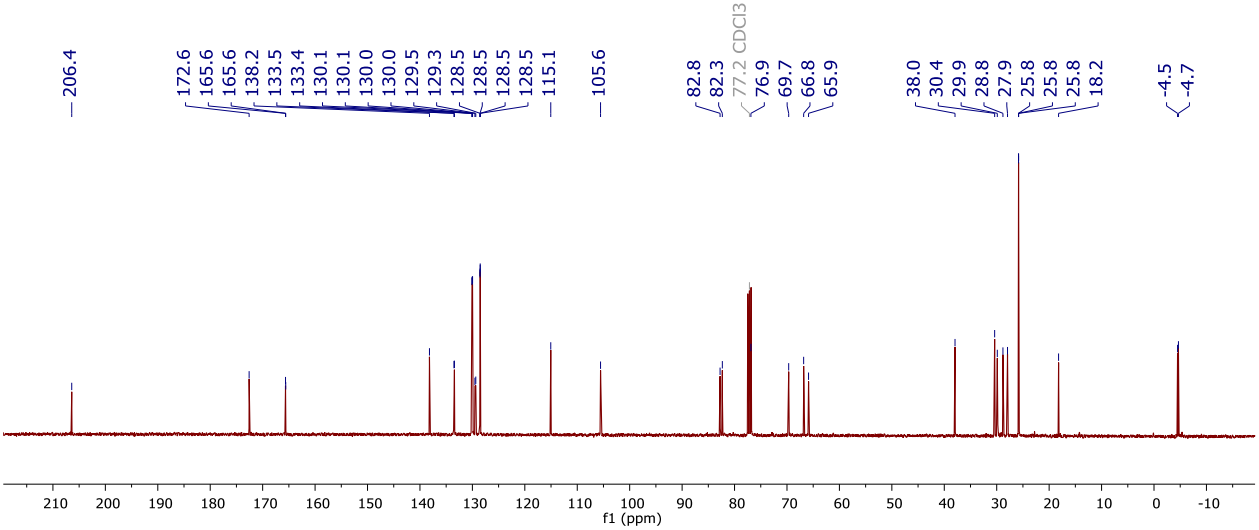
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **8**



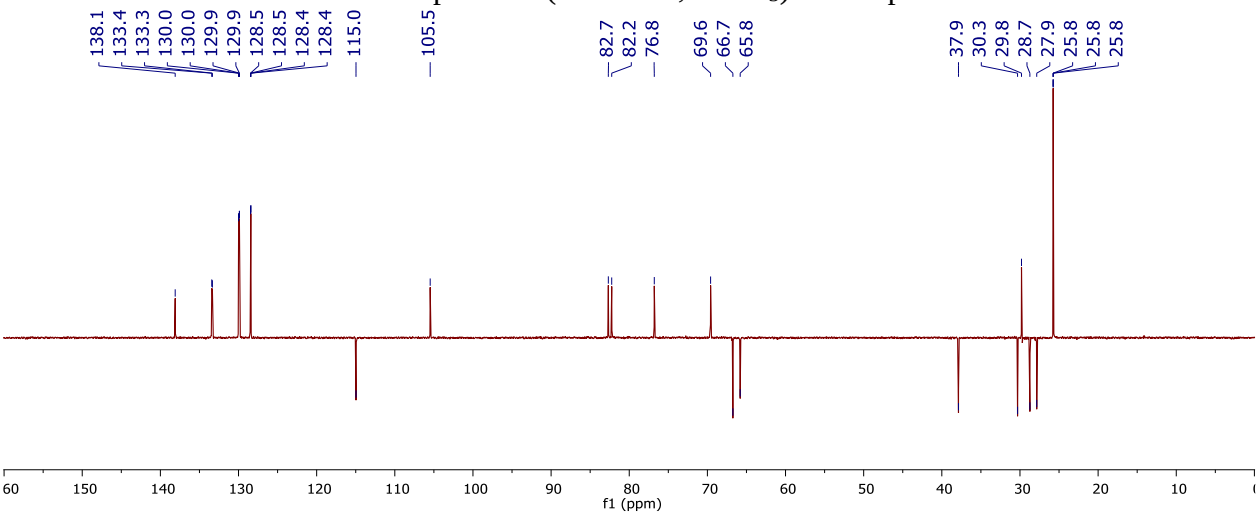
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **33**



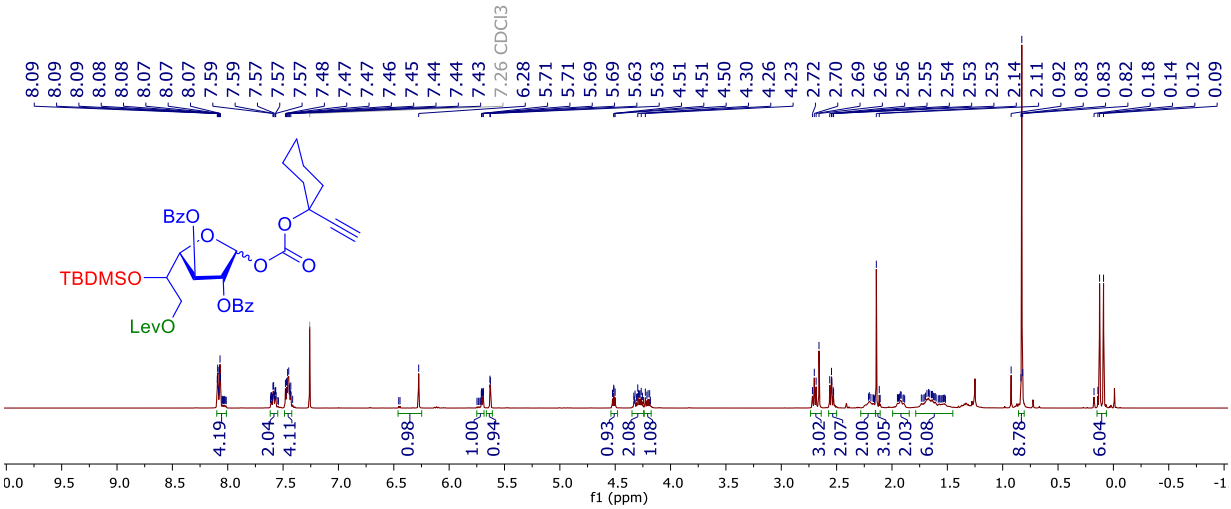
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **33**



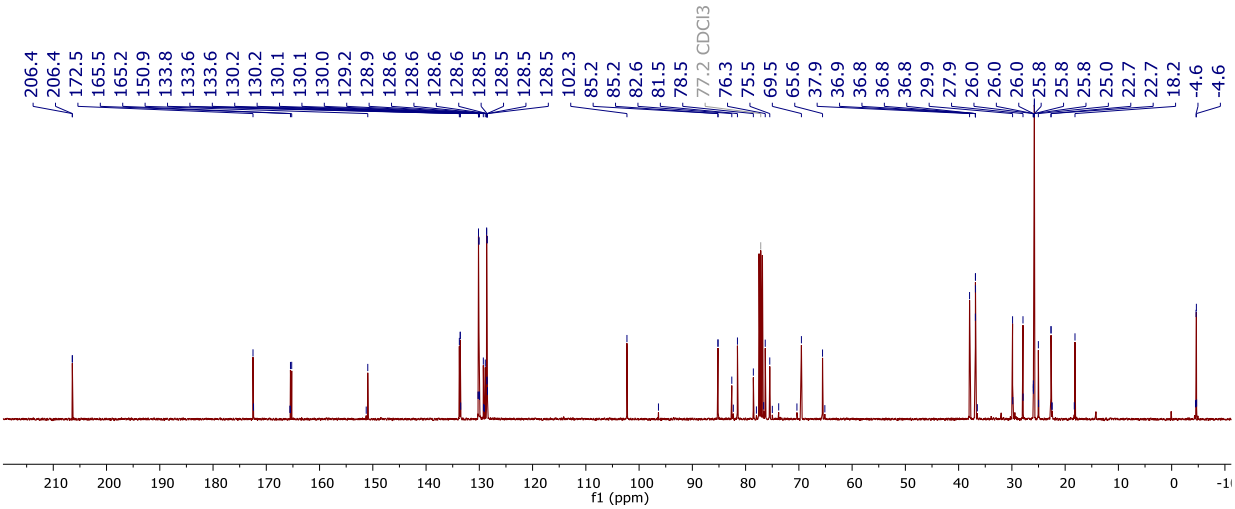
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **33**



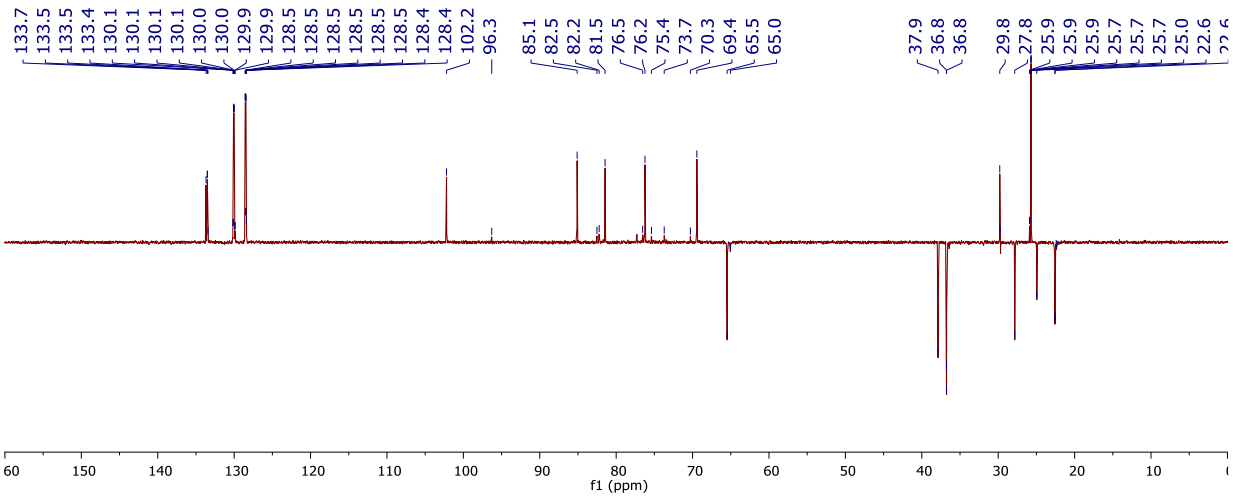
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **10**



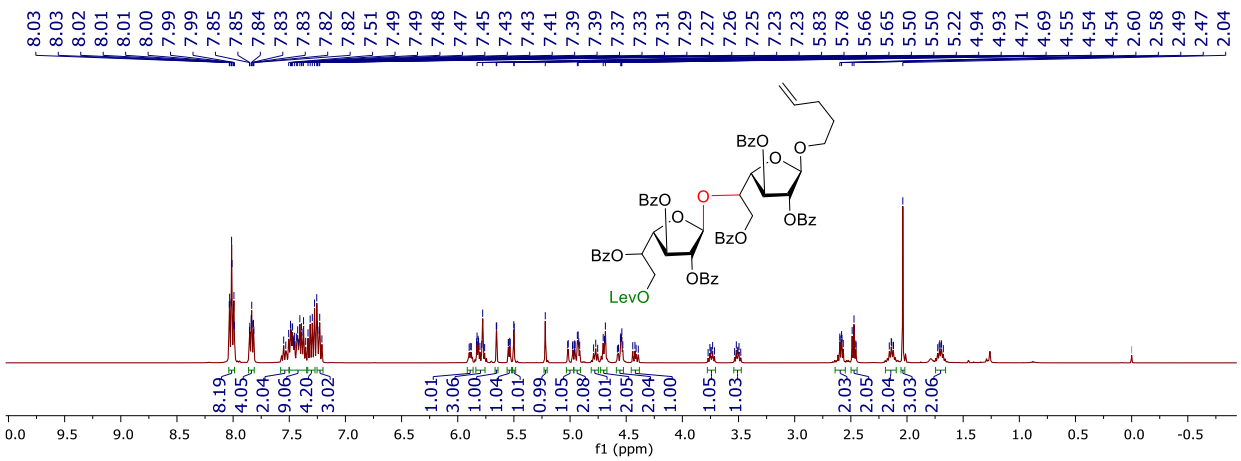
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **10**



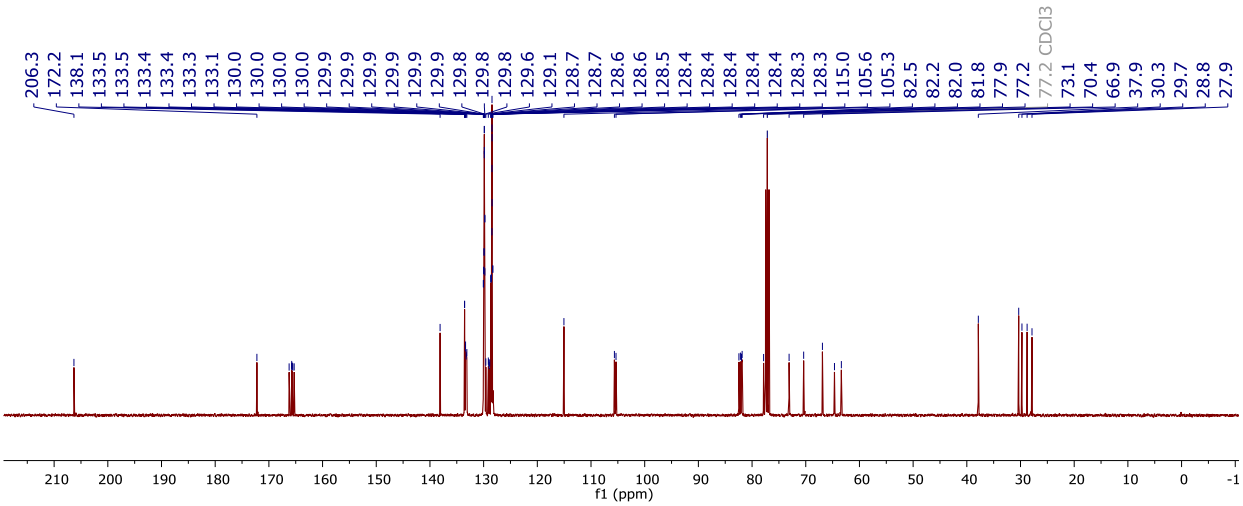
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **10**



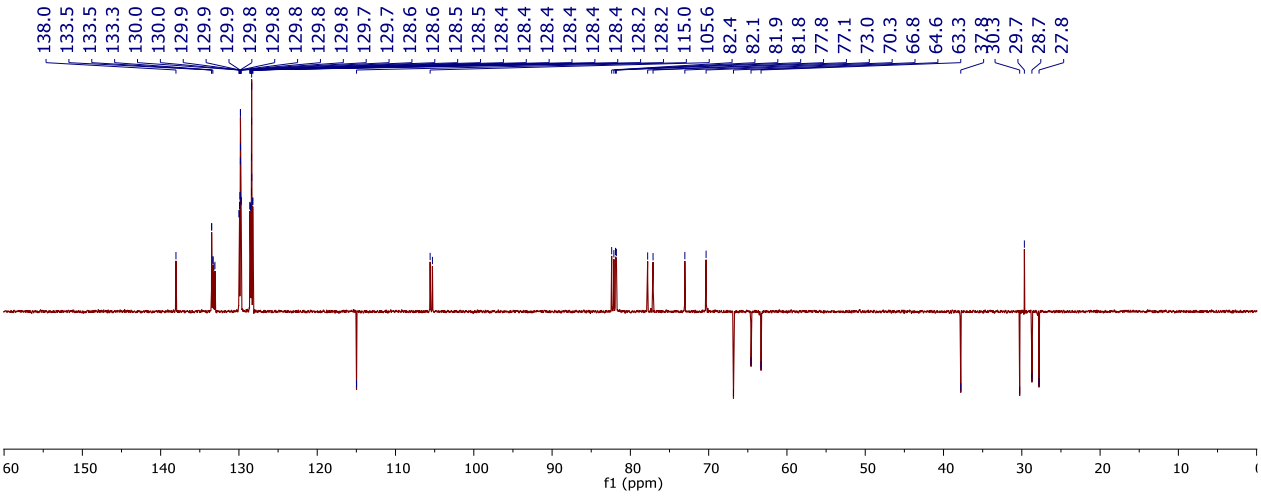
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **34**



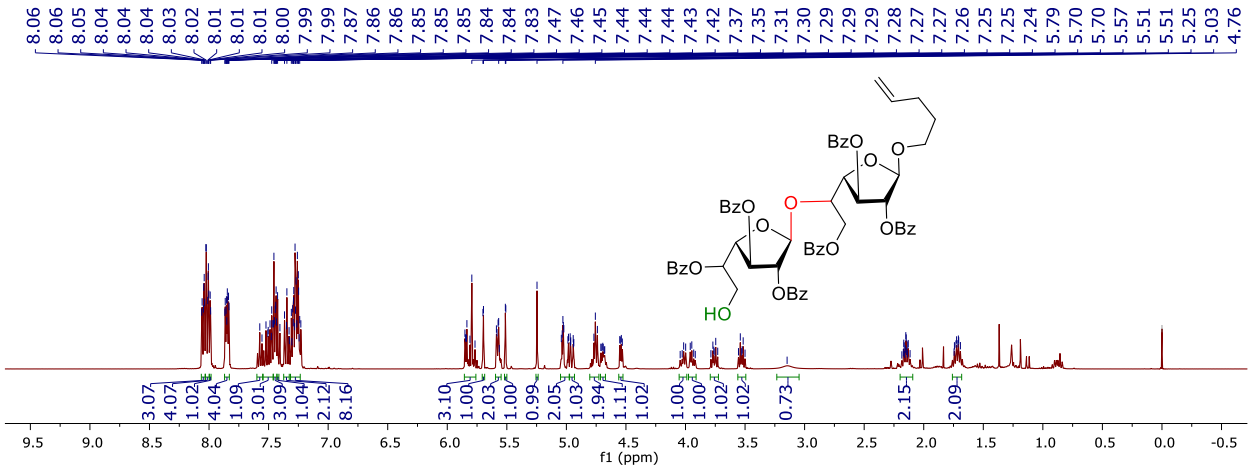
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **34**



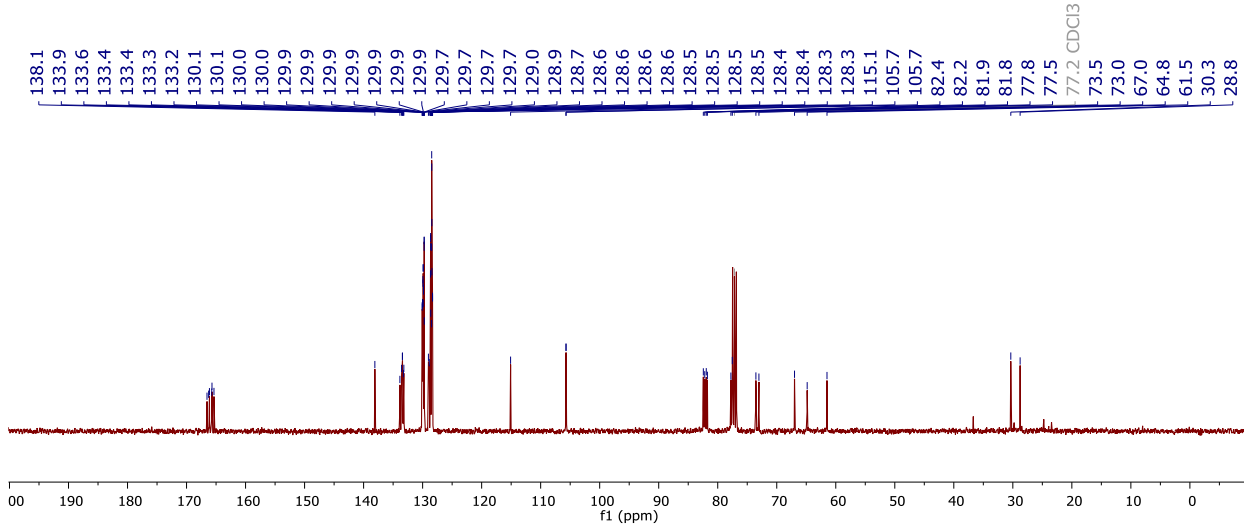
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **34**



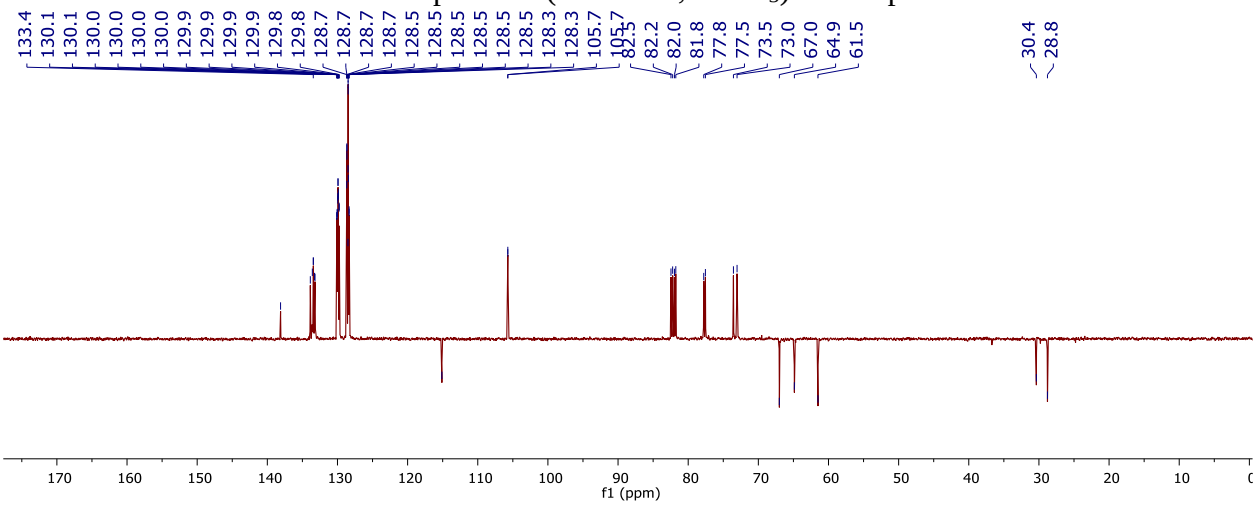
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **35**



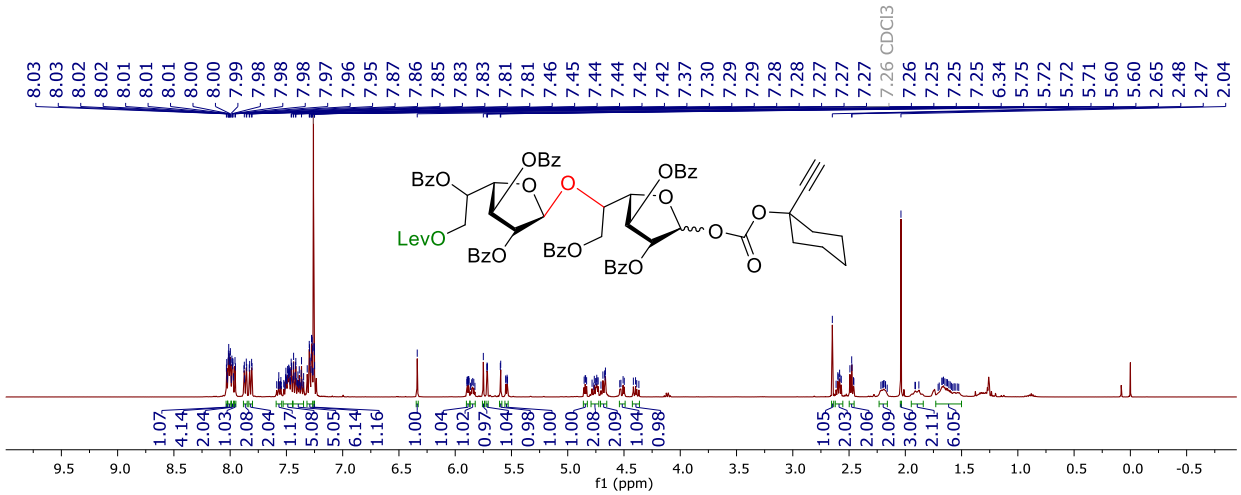
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **35**



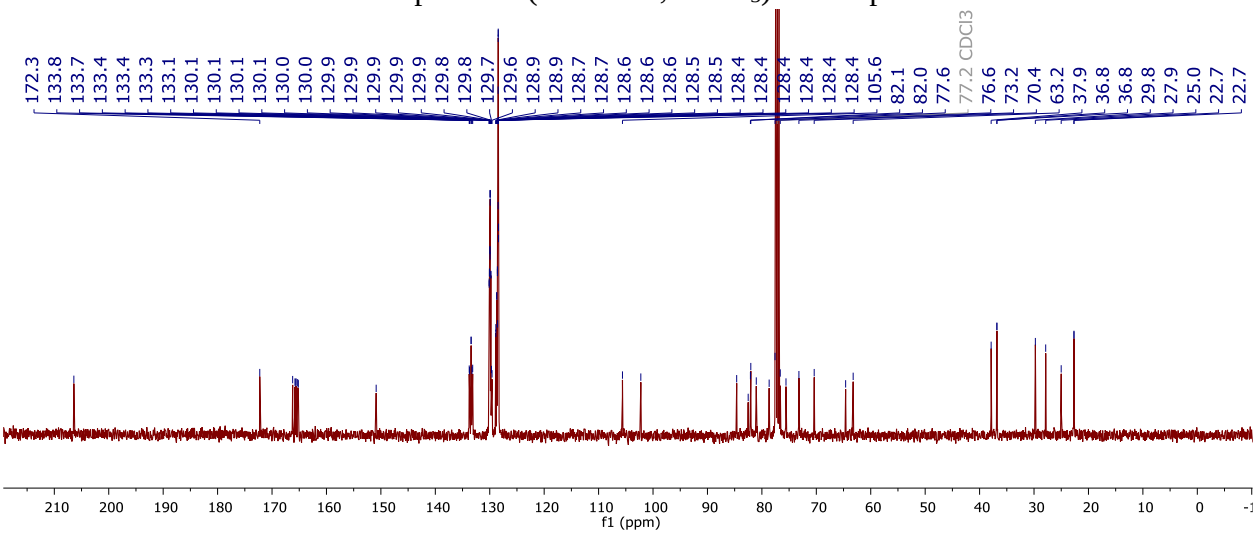
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **35**



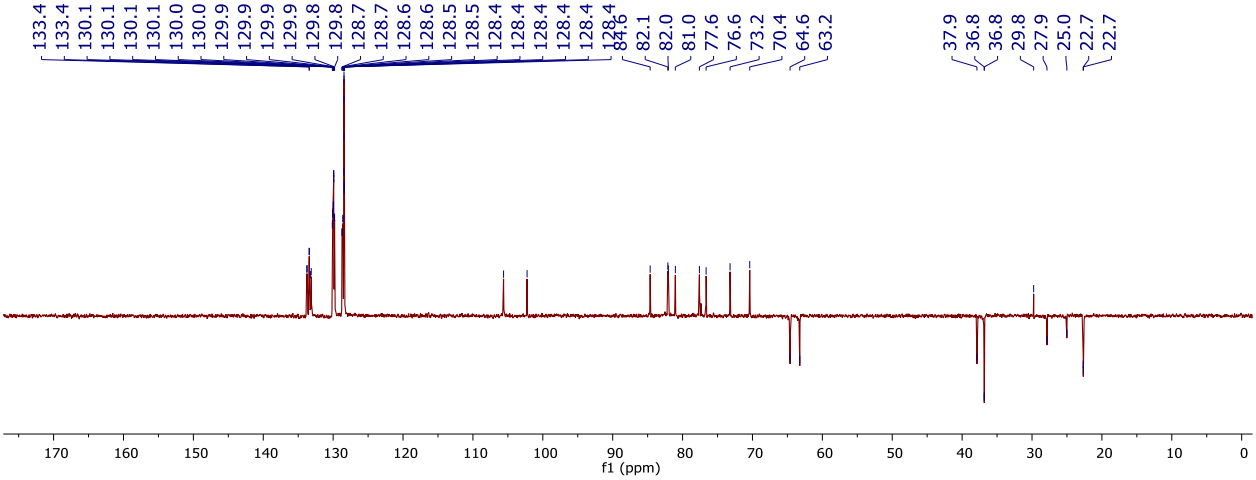
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **36**



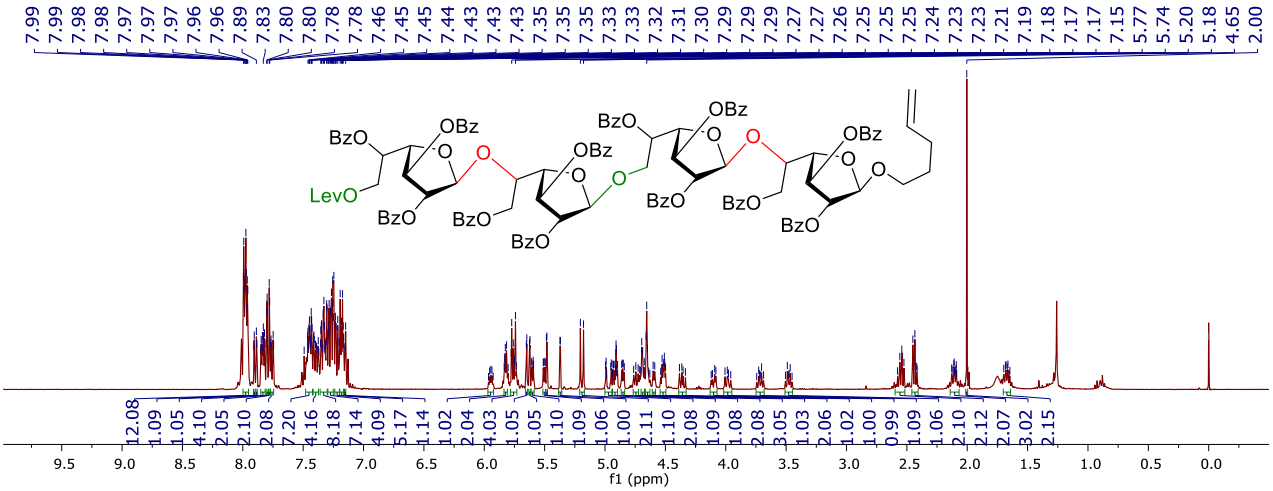
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **36**



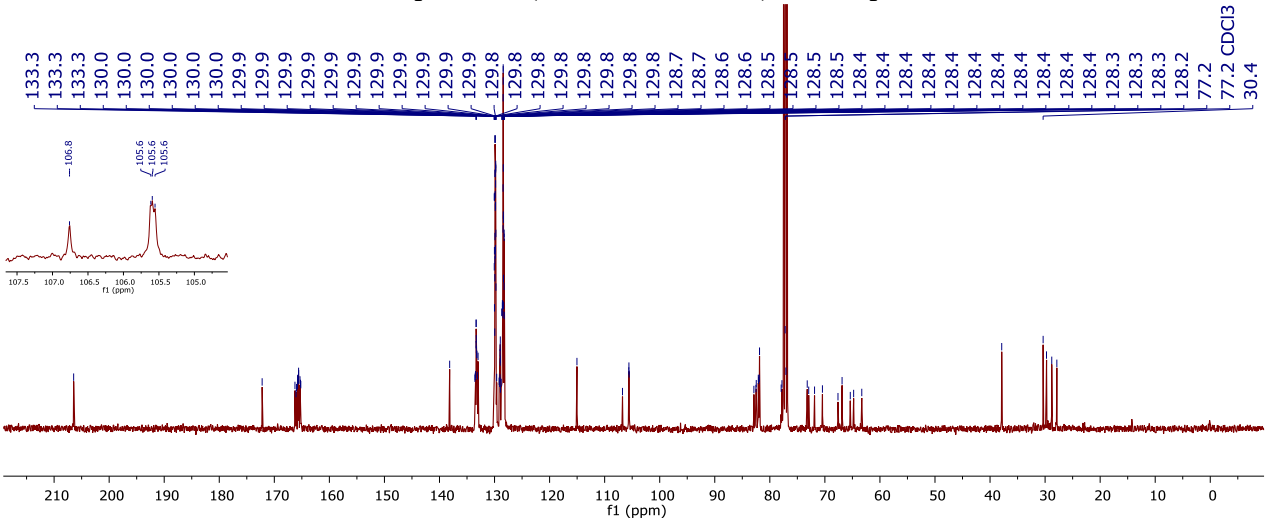
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **36**



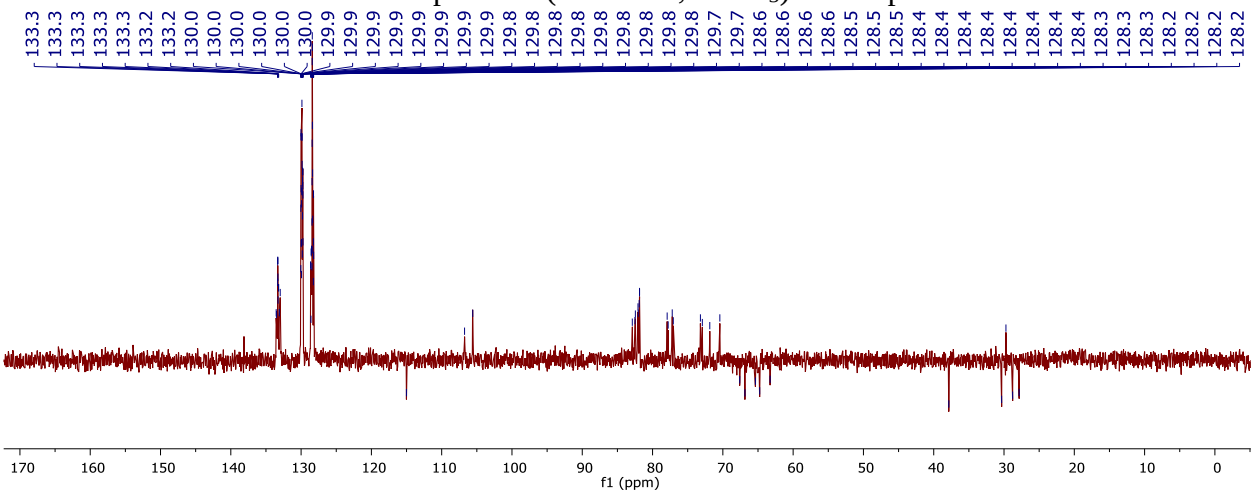
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **37**



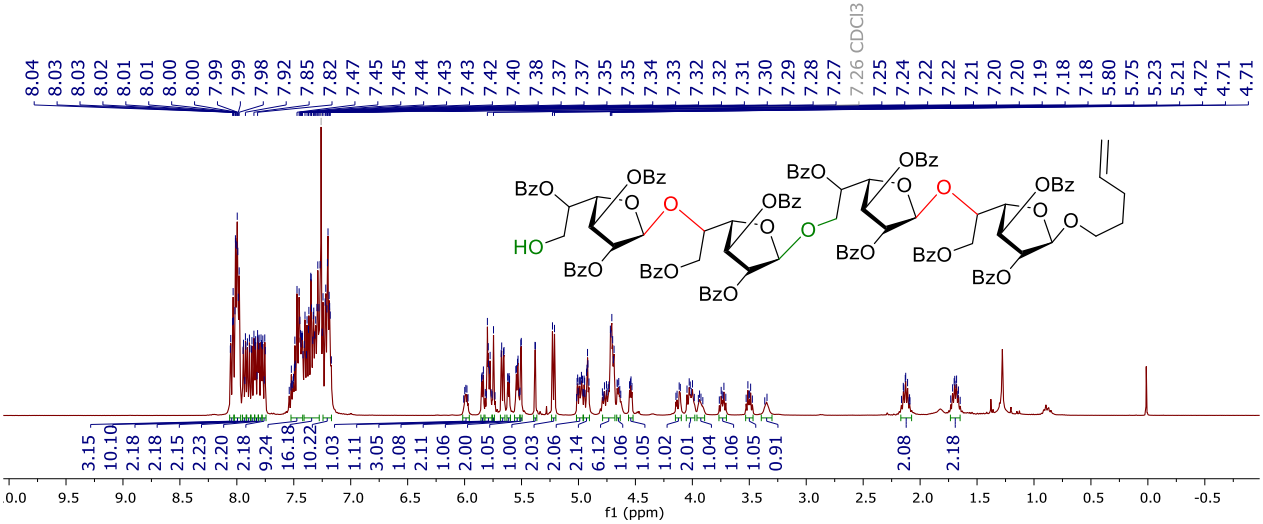
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **37**



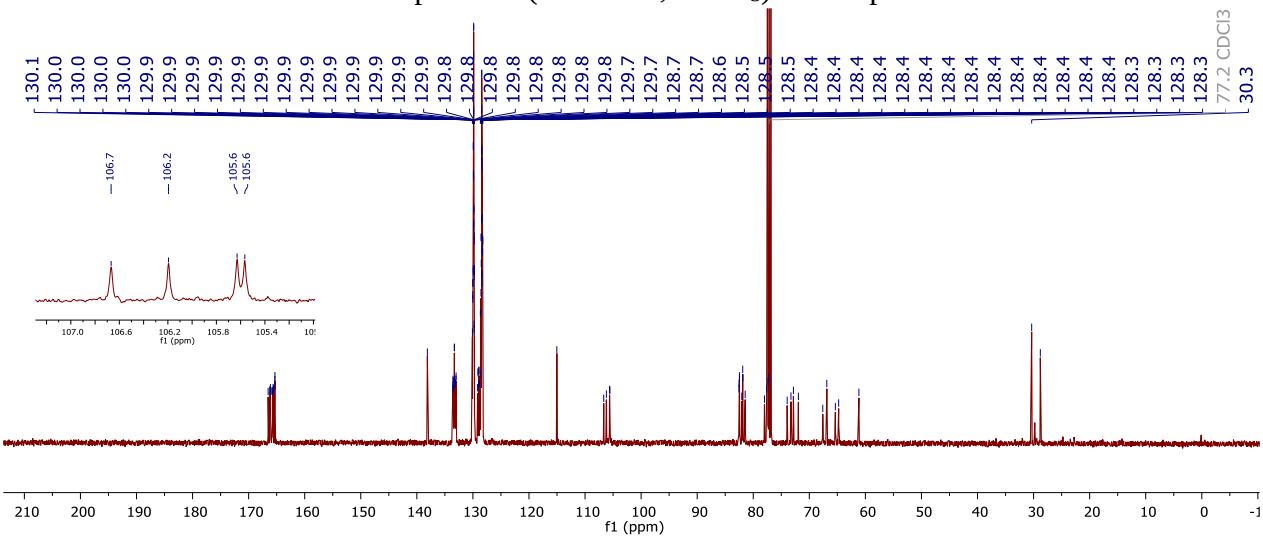
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **37**



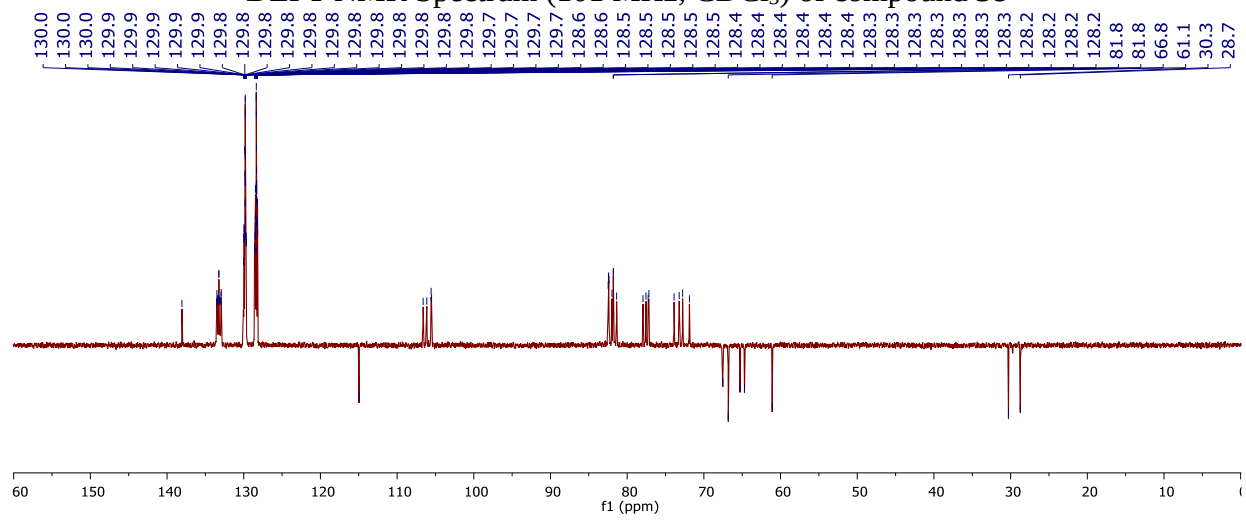
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **38**



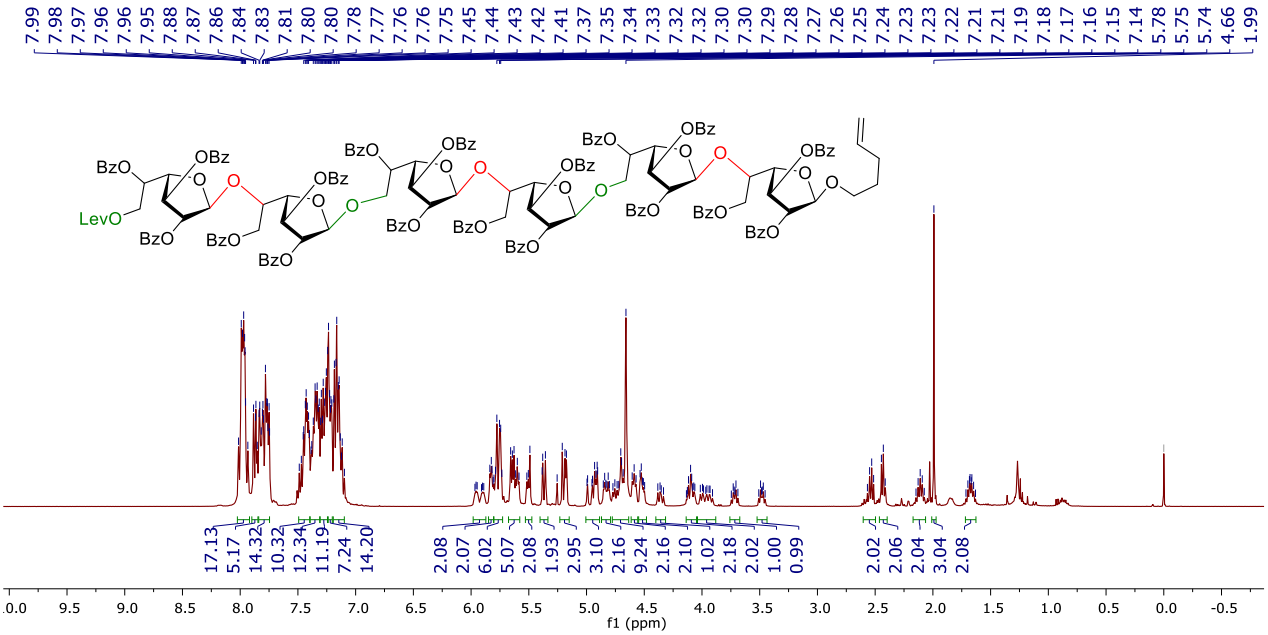
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **38**



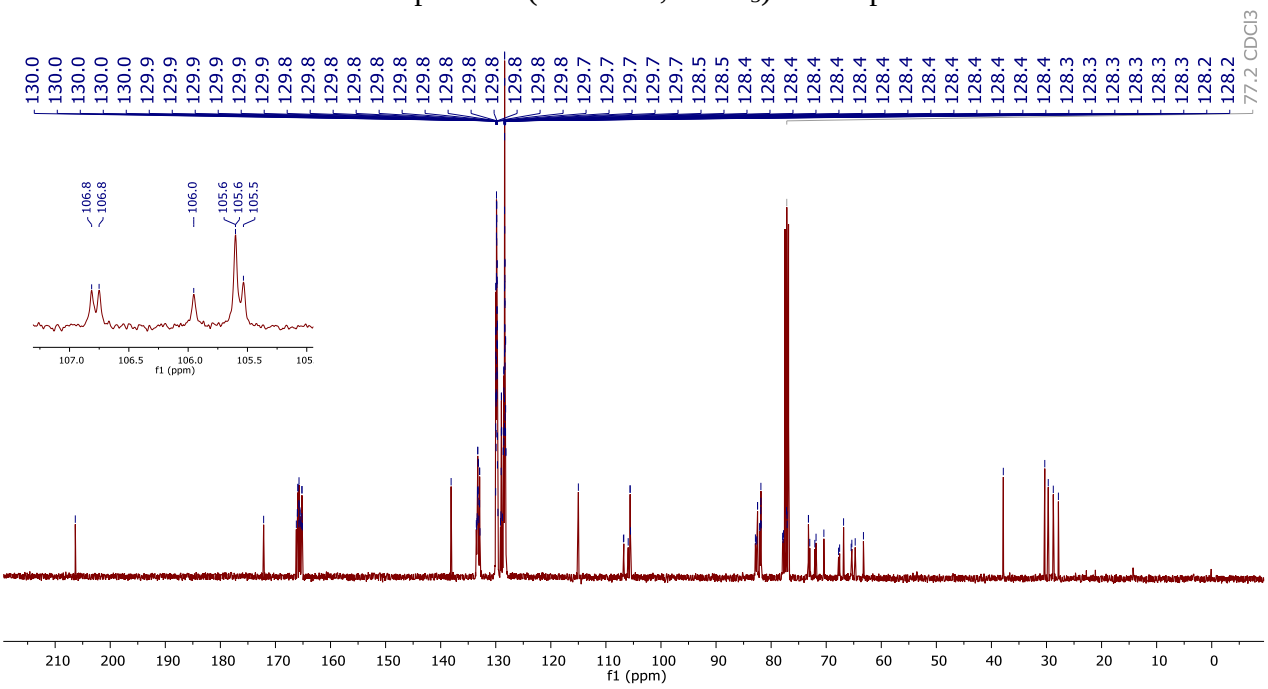
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **38**



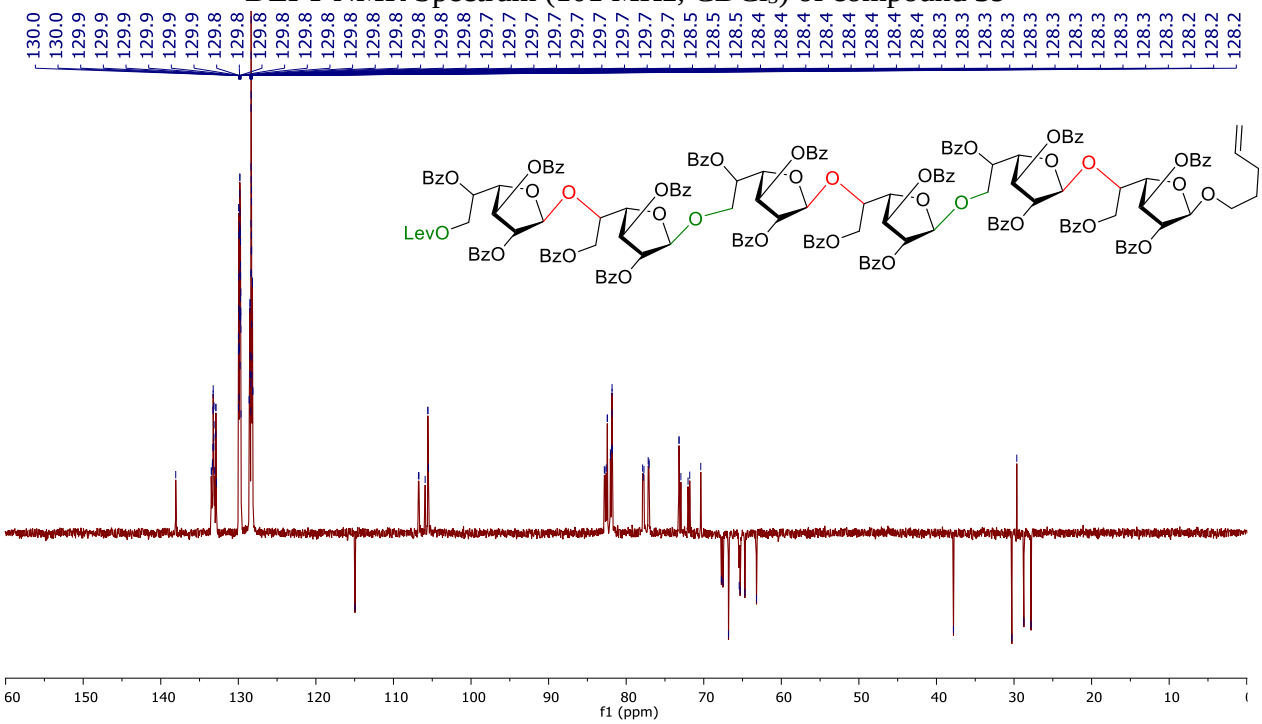
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **39**



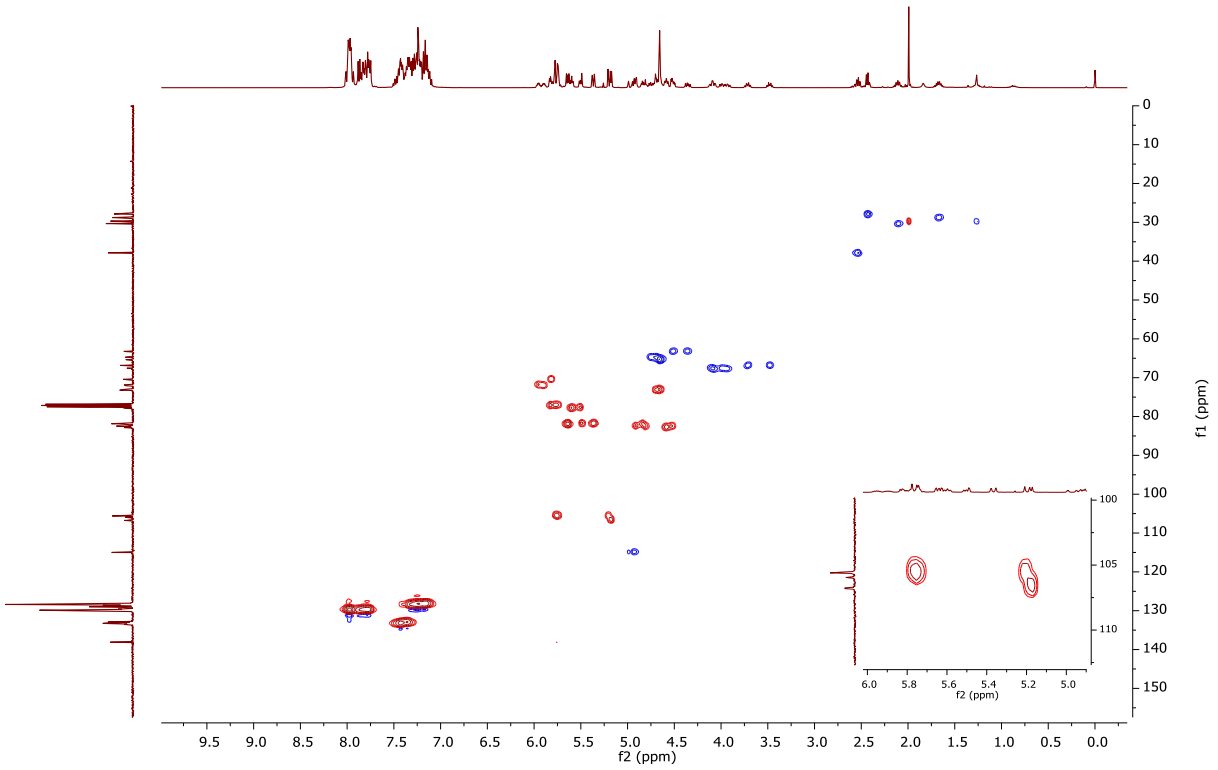
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **39**



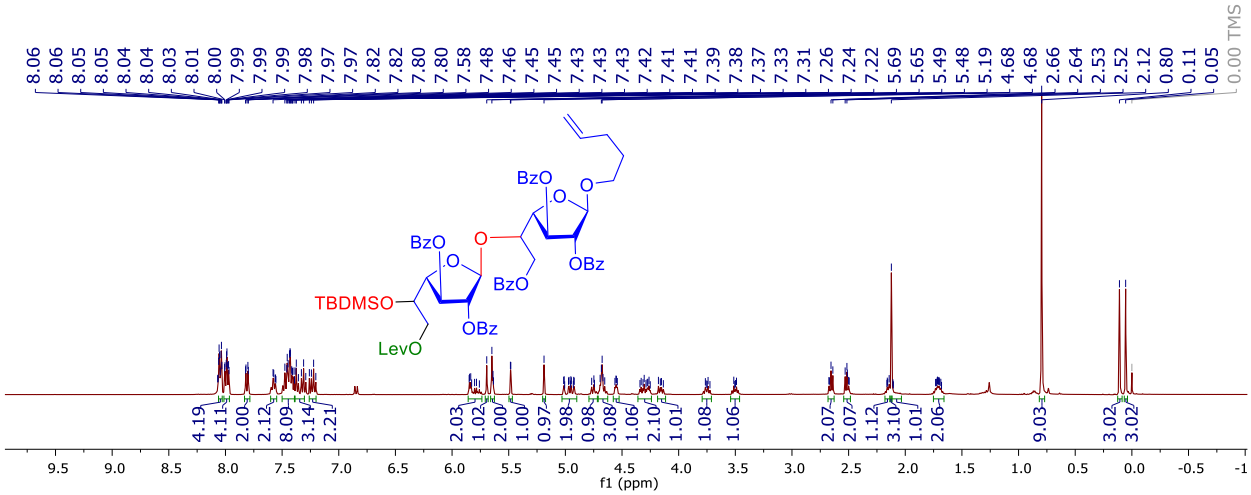
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **39**



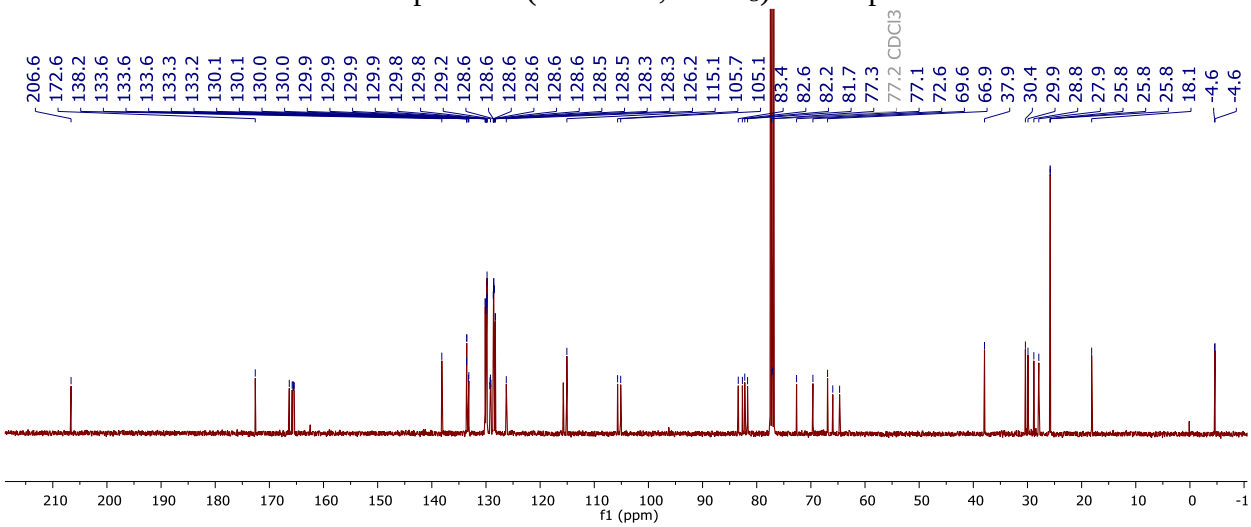
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **39**



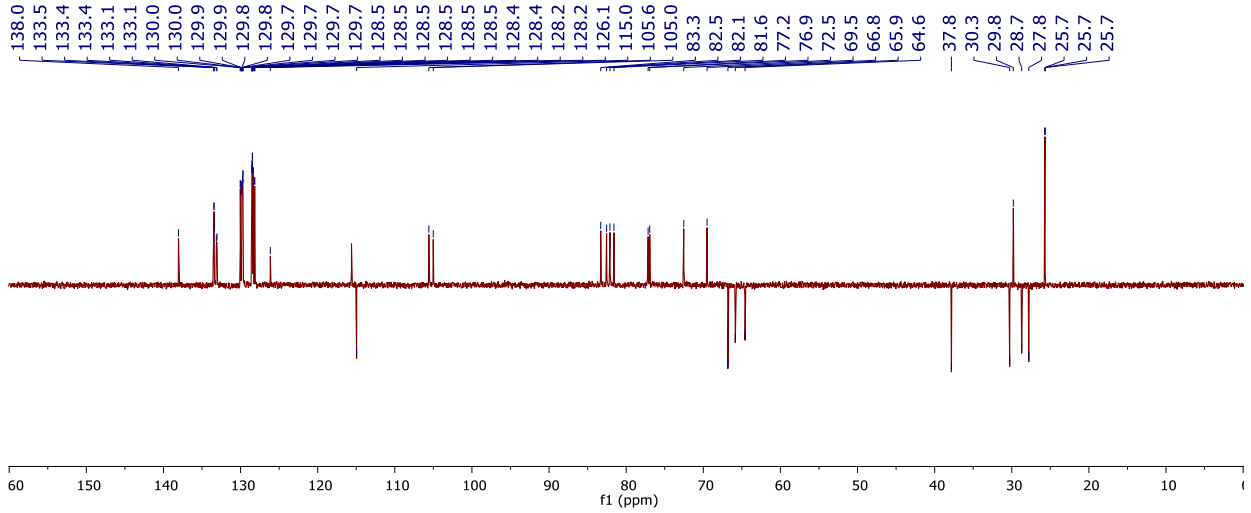
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **40**



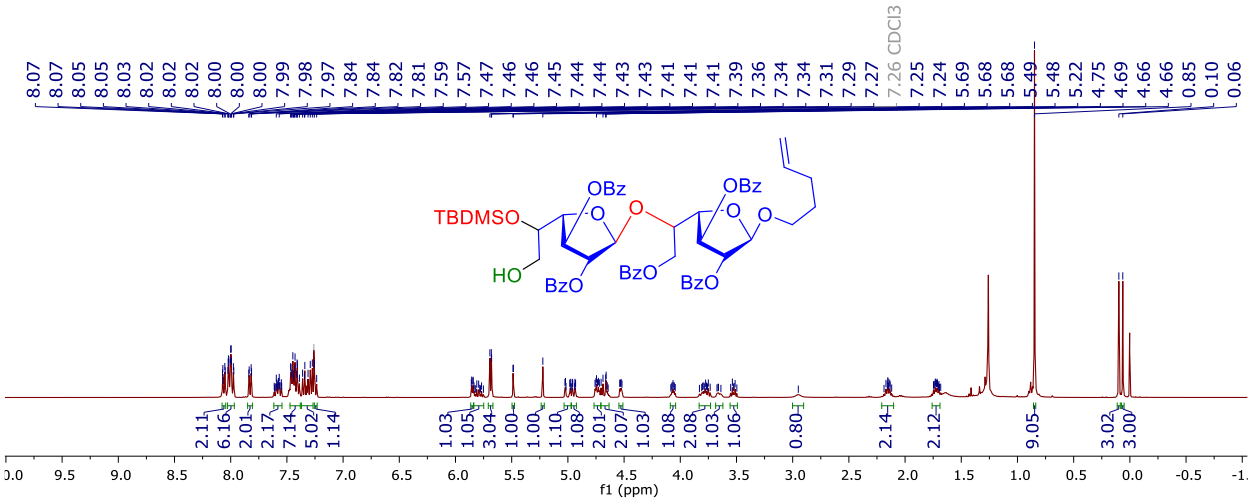
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **40**



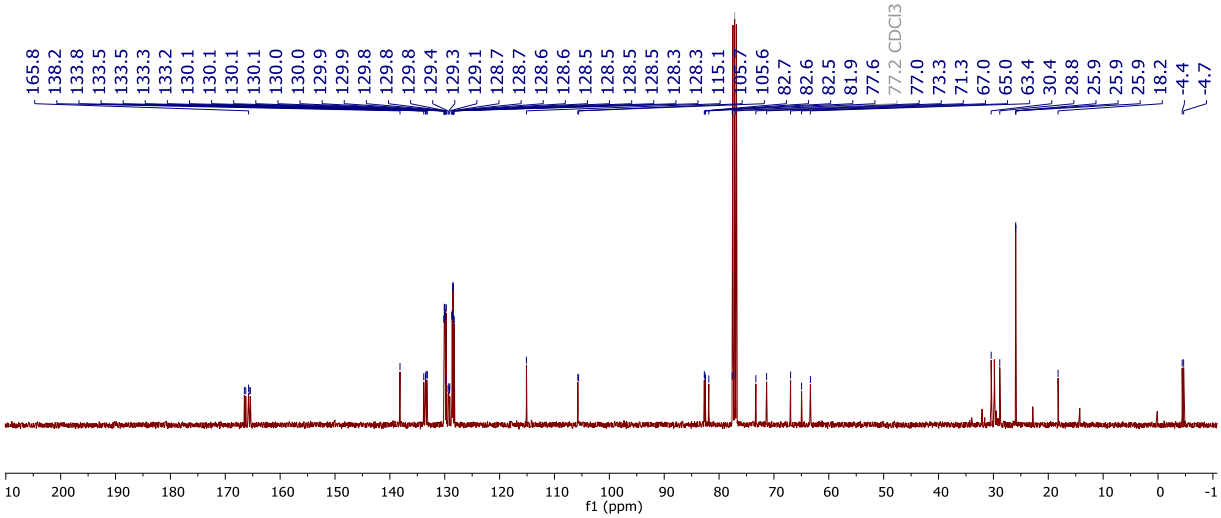
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **40**



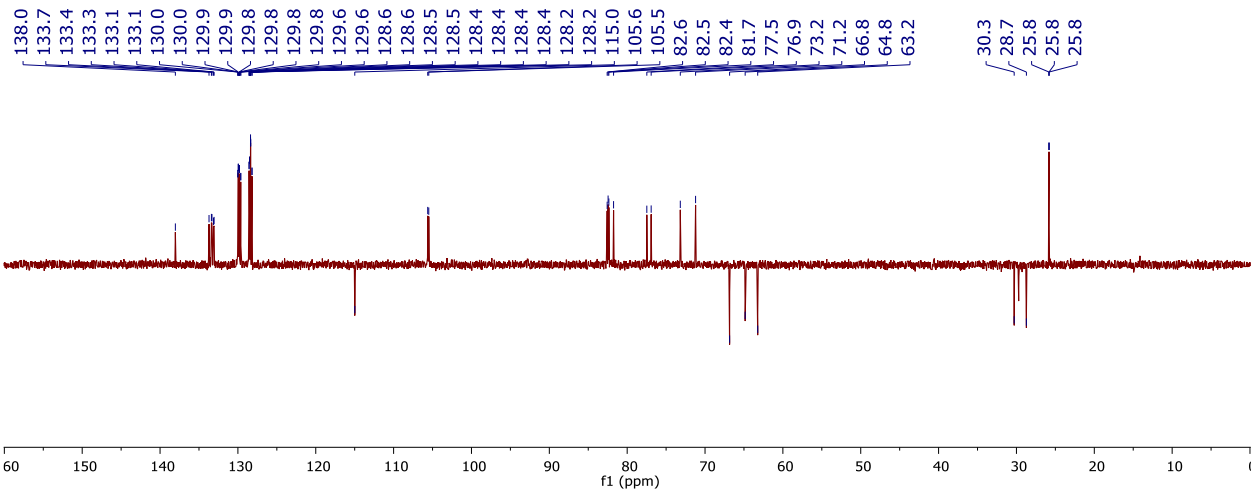
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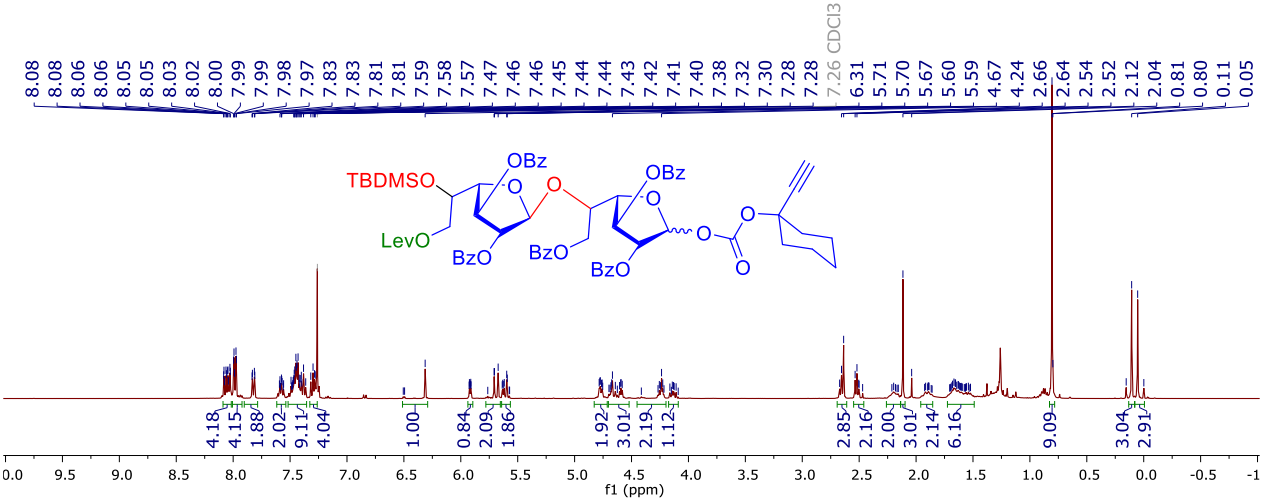
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **41**



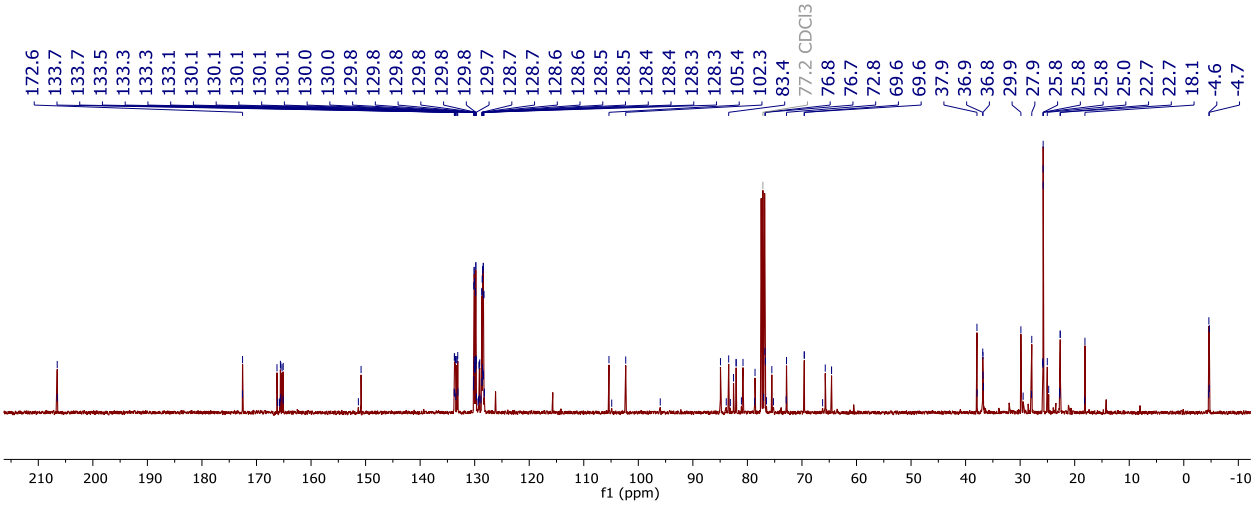
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **41**



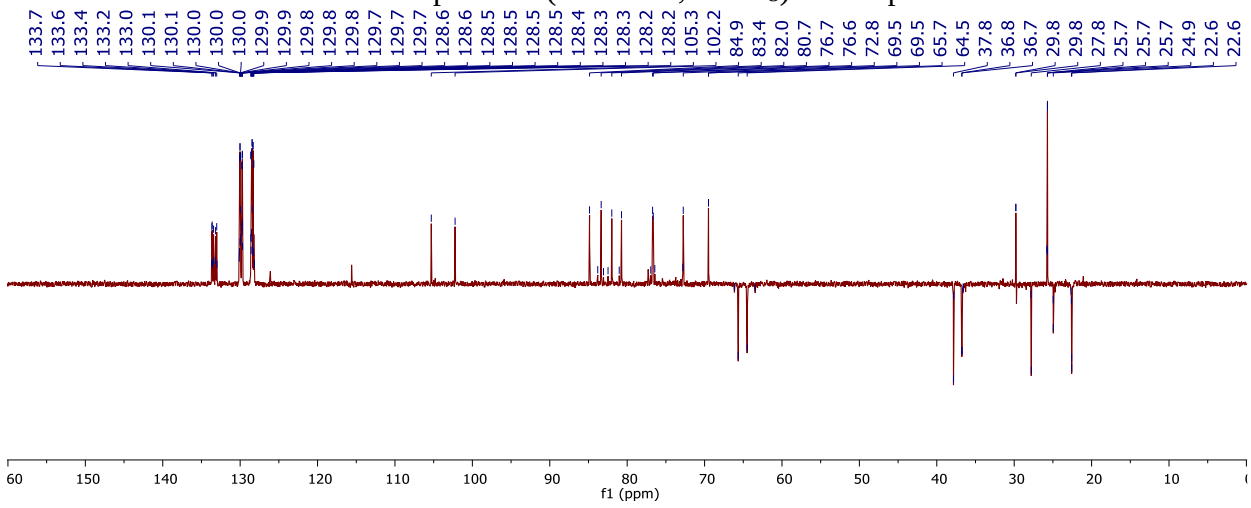
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **42**



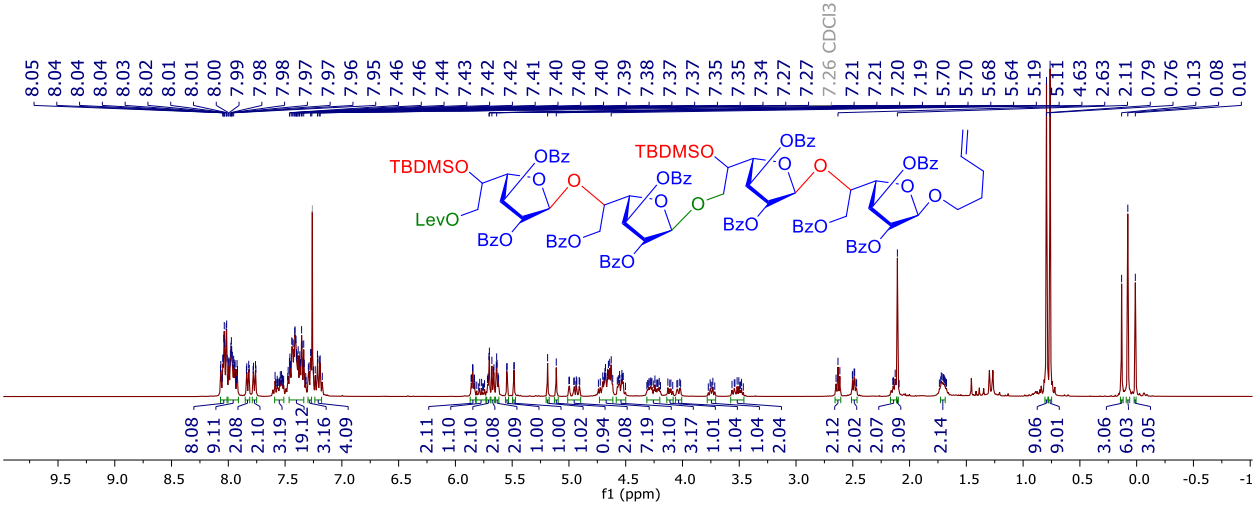
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **42**



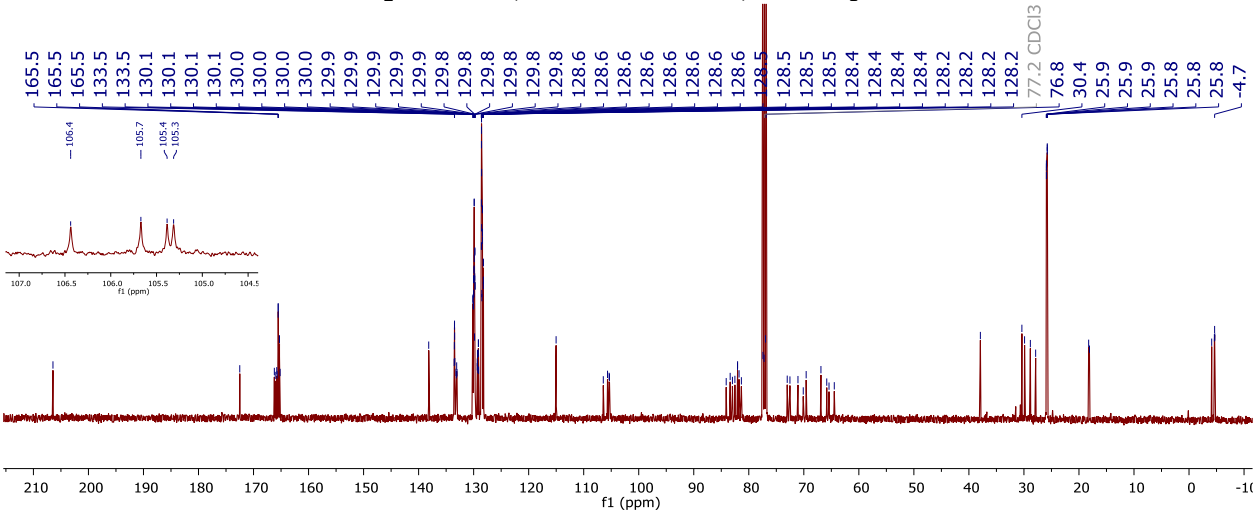
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **42**



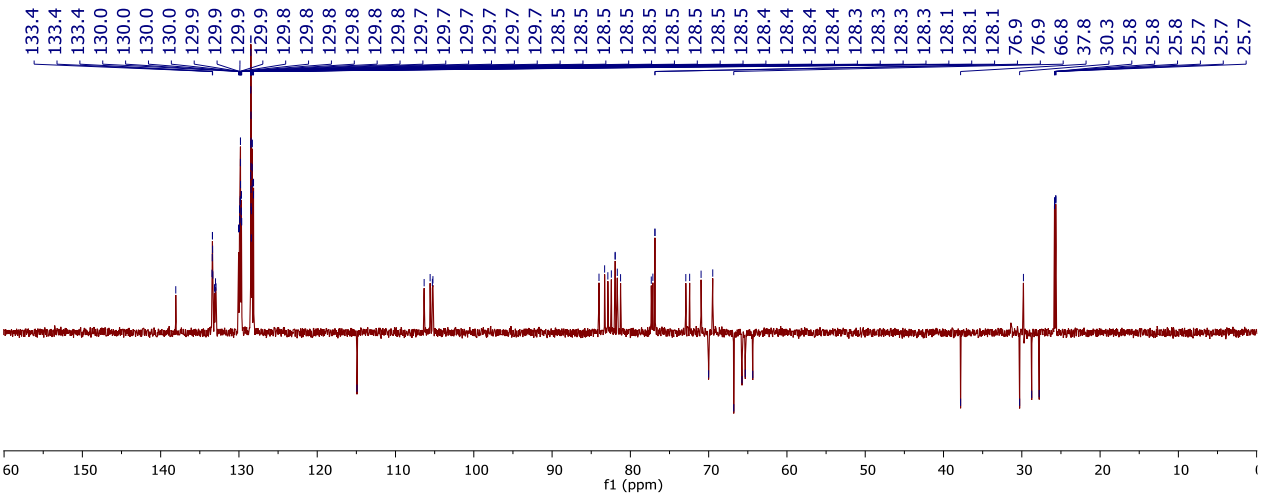
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **43**



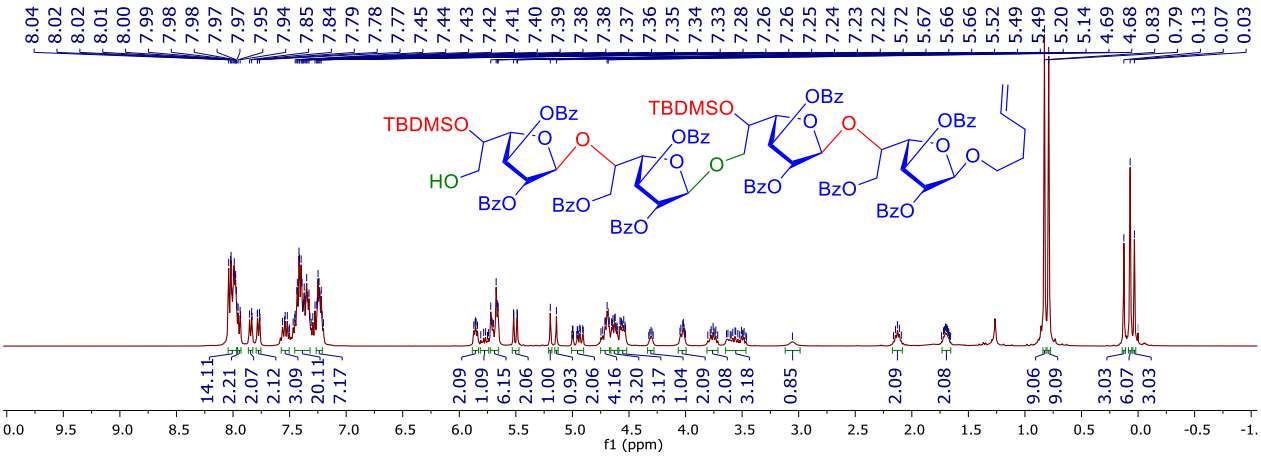
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **GF-47**



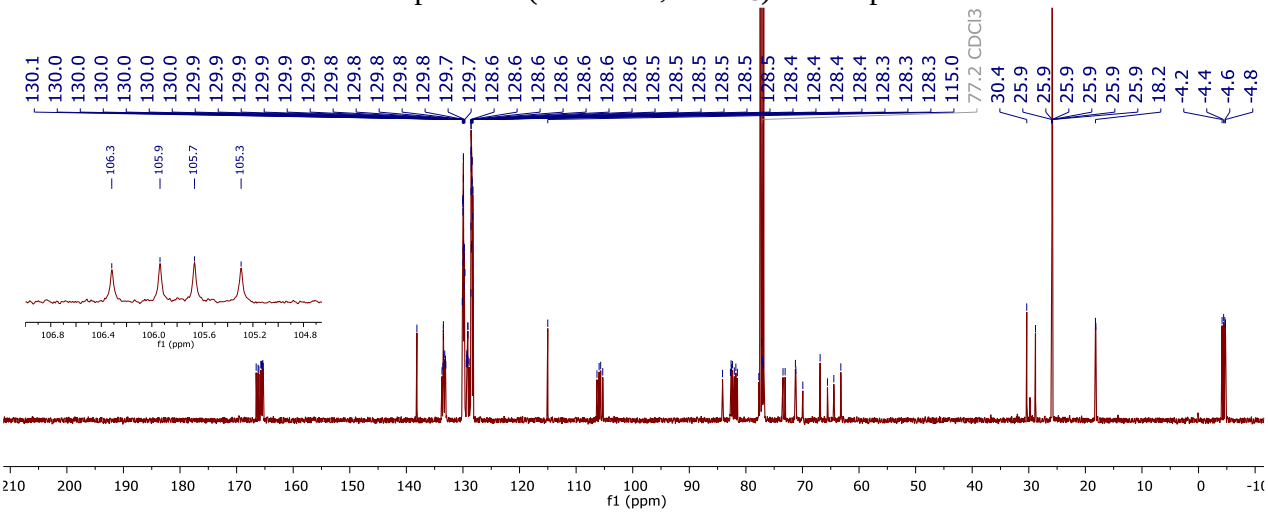
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **GF-47**



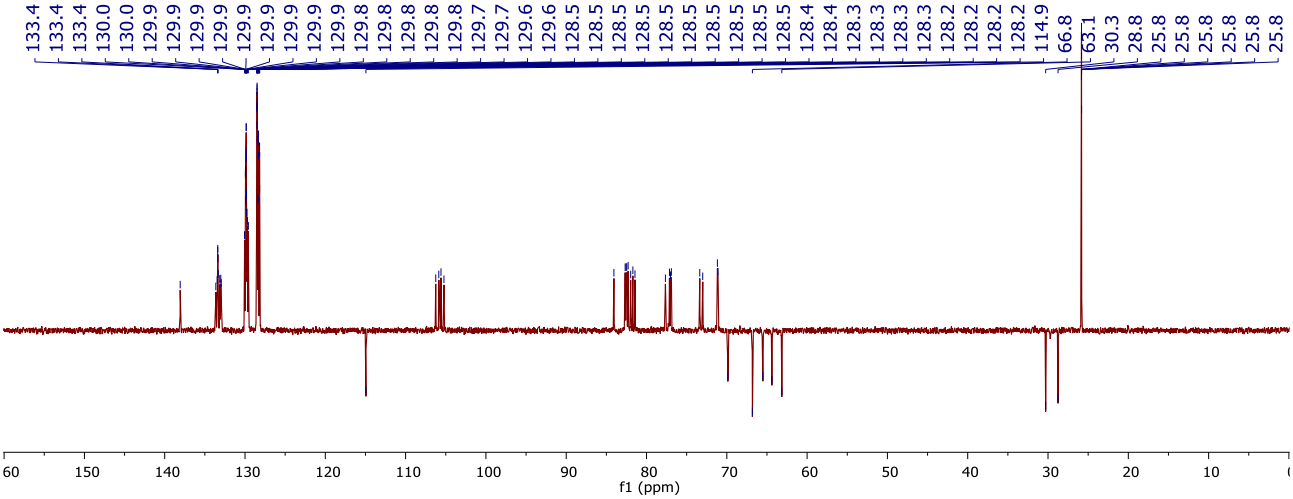
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **44**



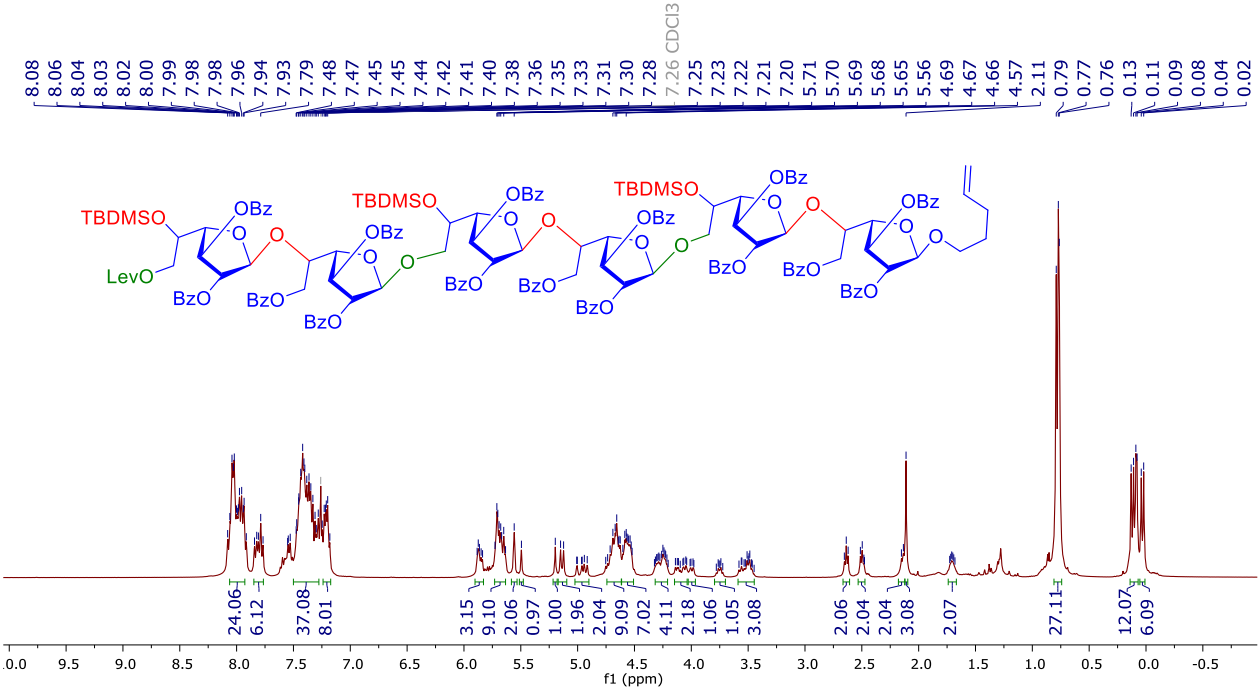
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **44**



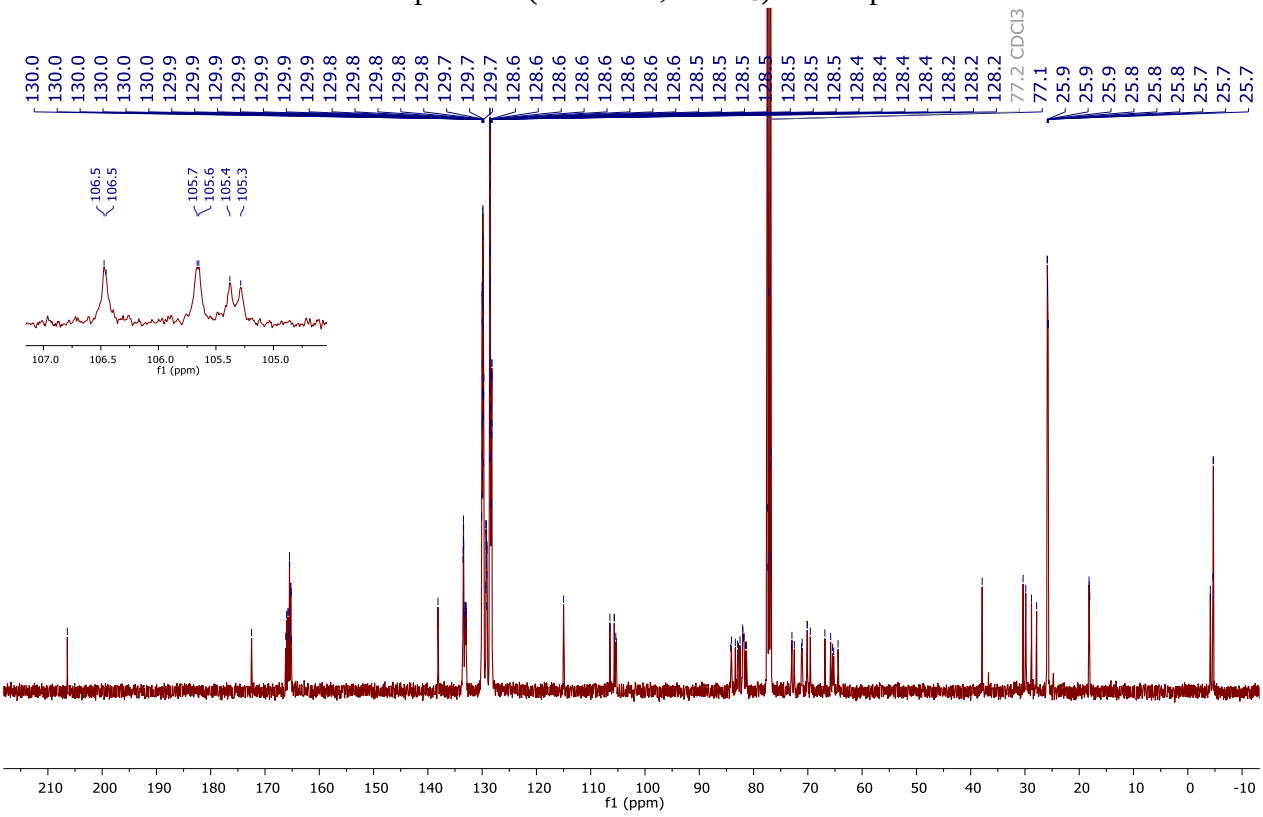
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **44**



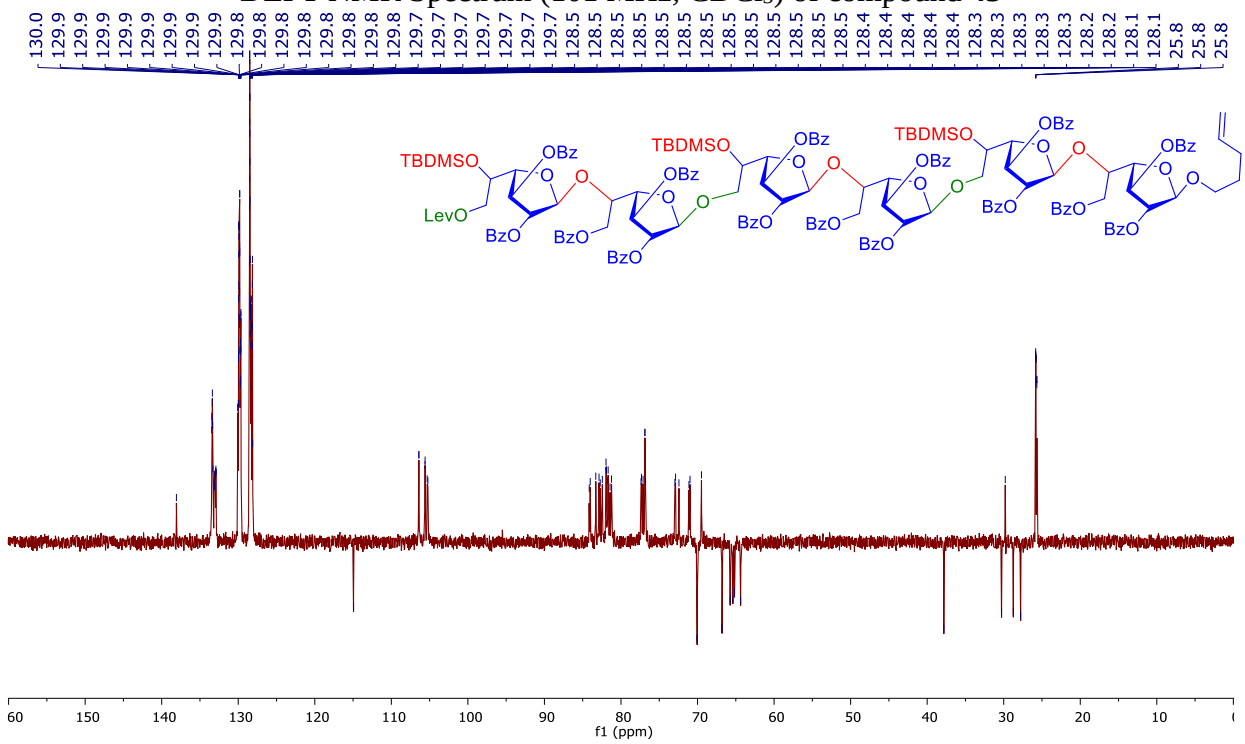
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **45**



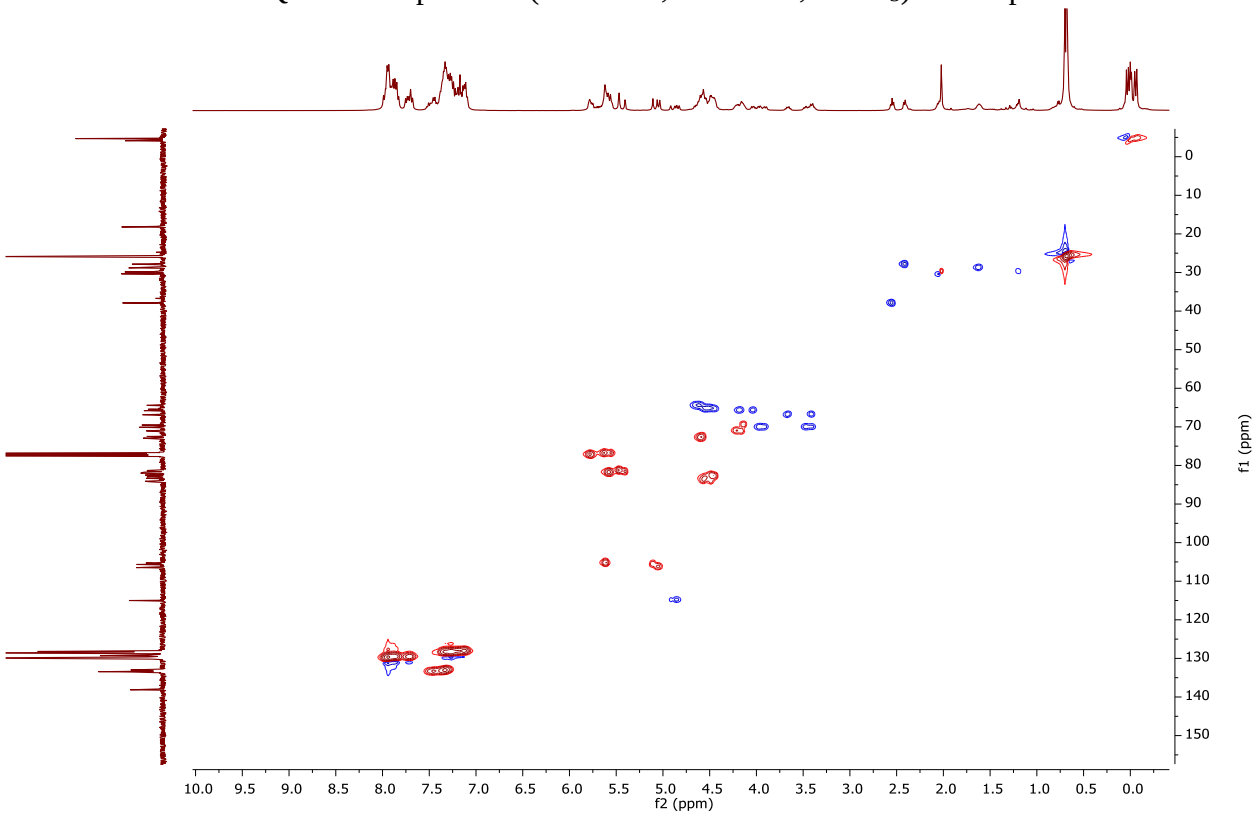
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **45**



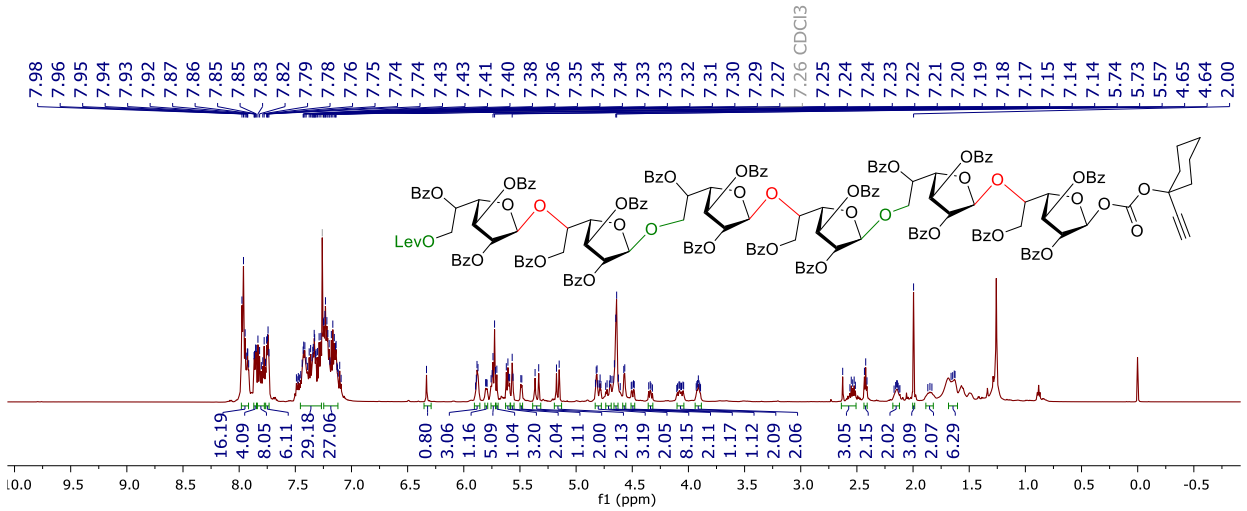
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **45**



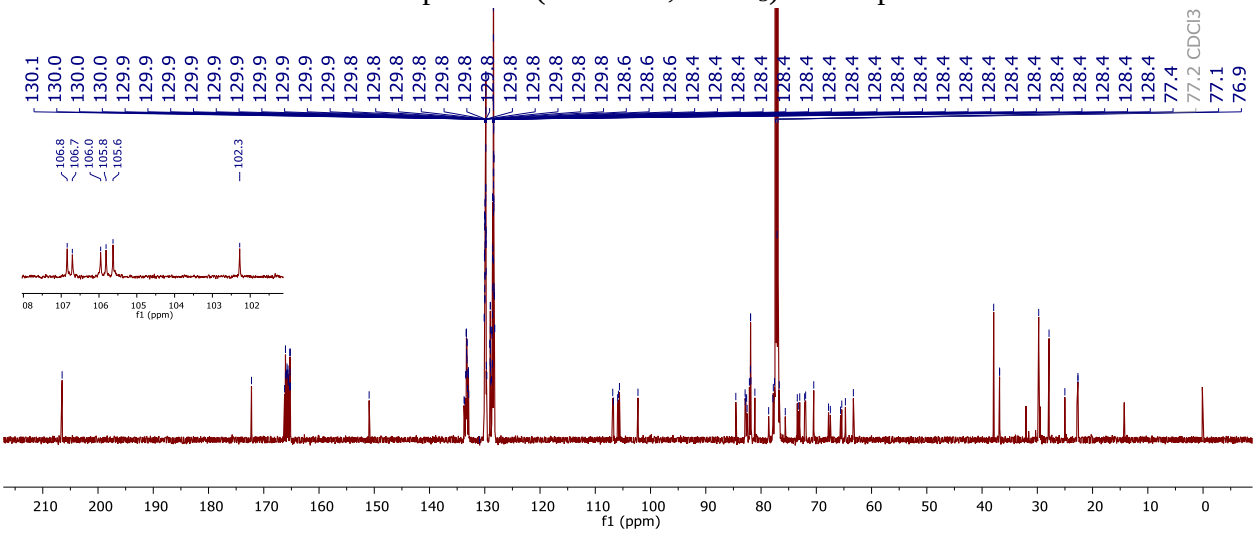
^{1}H-^{13}C HSQC NMR Spectrum (400 MHz, 101 MHz, $CDCl_3$) of compound **45**



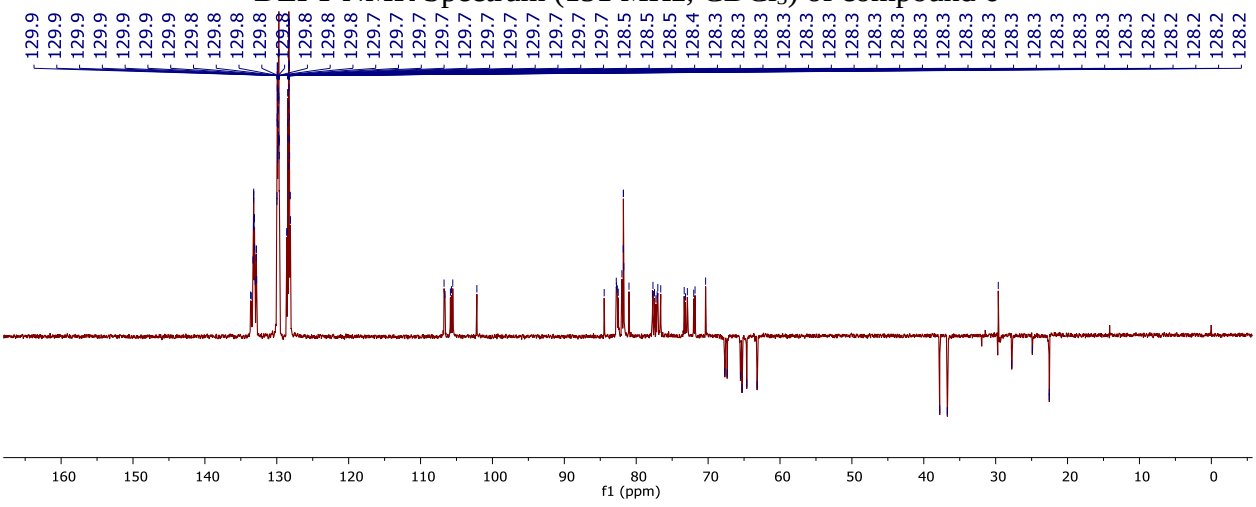
^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of compound **6**



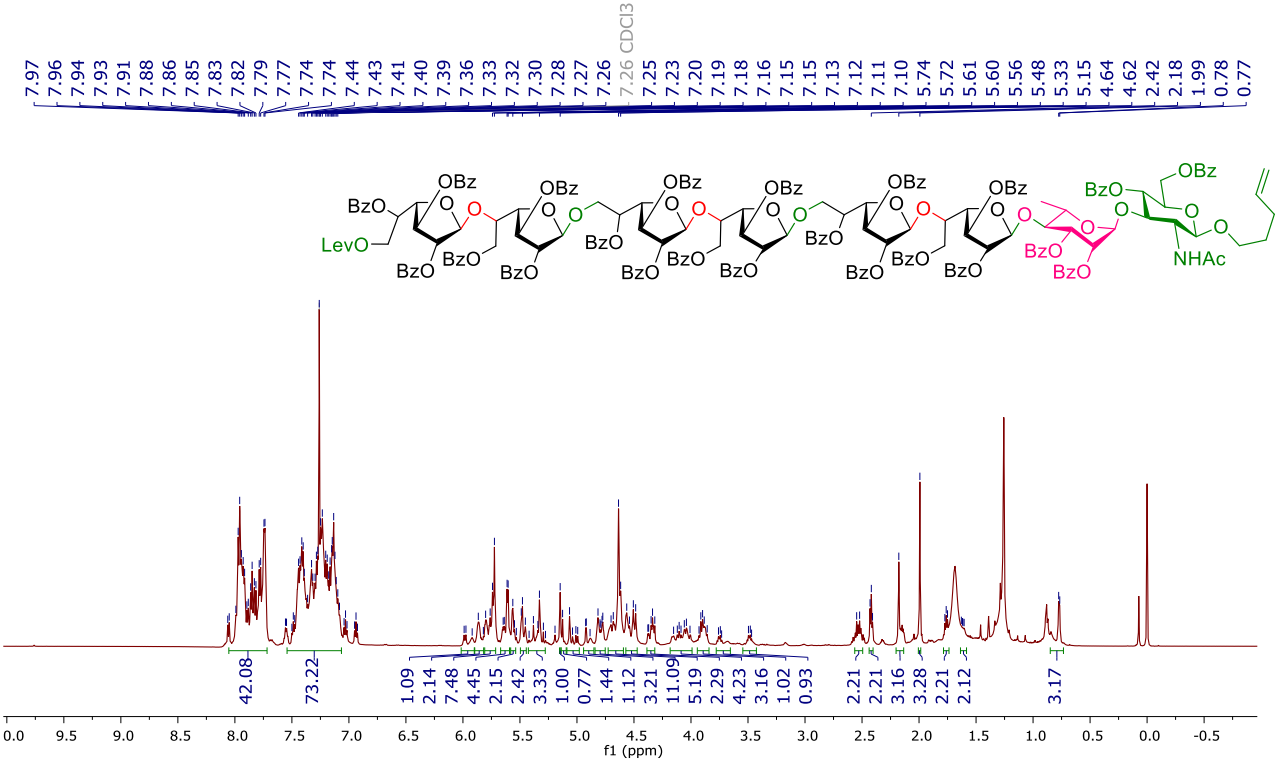
^{13}C NMR Spectrum (151 MHz, $CDCl_3$) of compound **6**



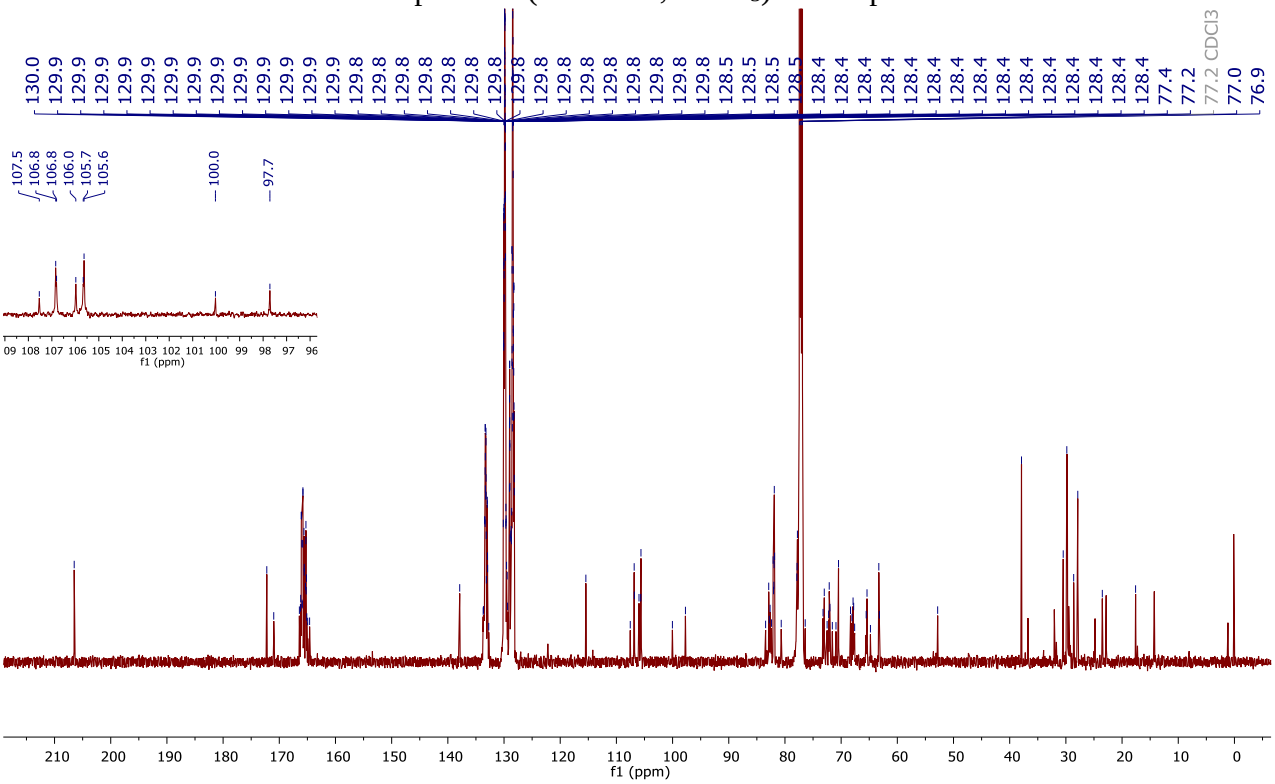
DEPT NMR Spectrum (151 MHz, $CDCl_3$) of compound **6**



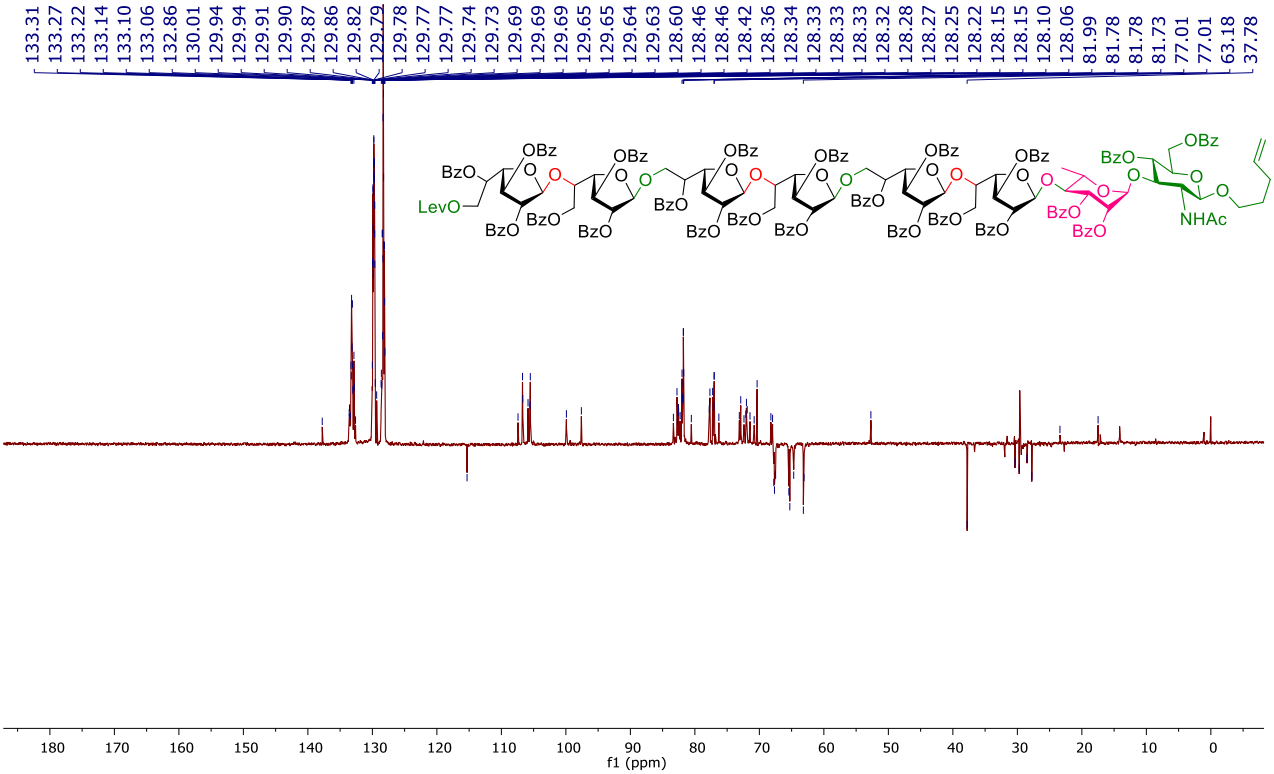
^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of compound **46**



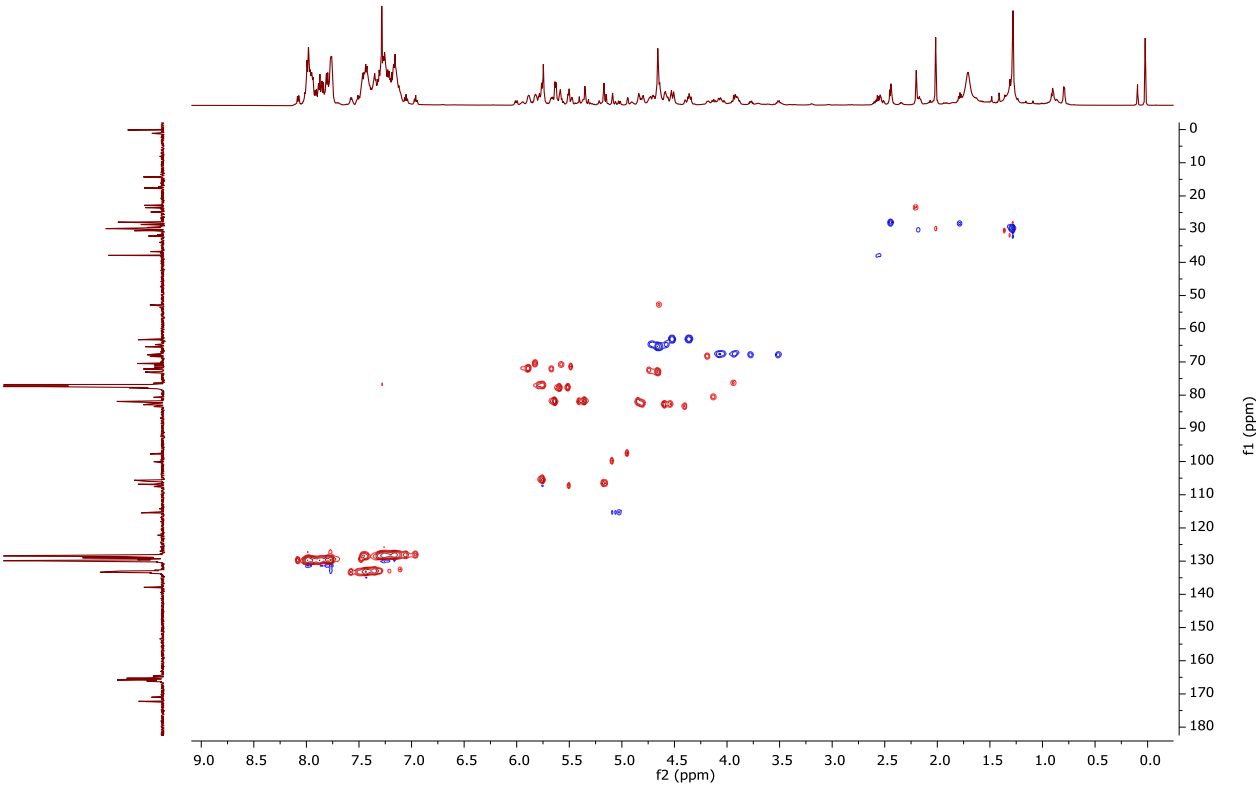
^{13}C NMR Spectrum (151 MHz, $CDCl_3$) of compound **46**



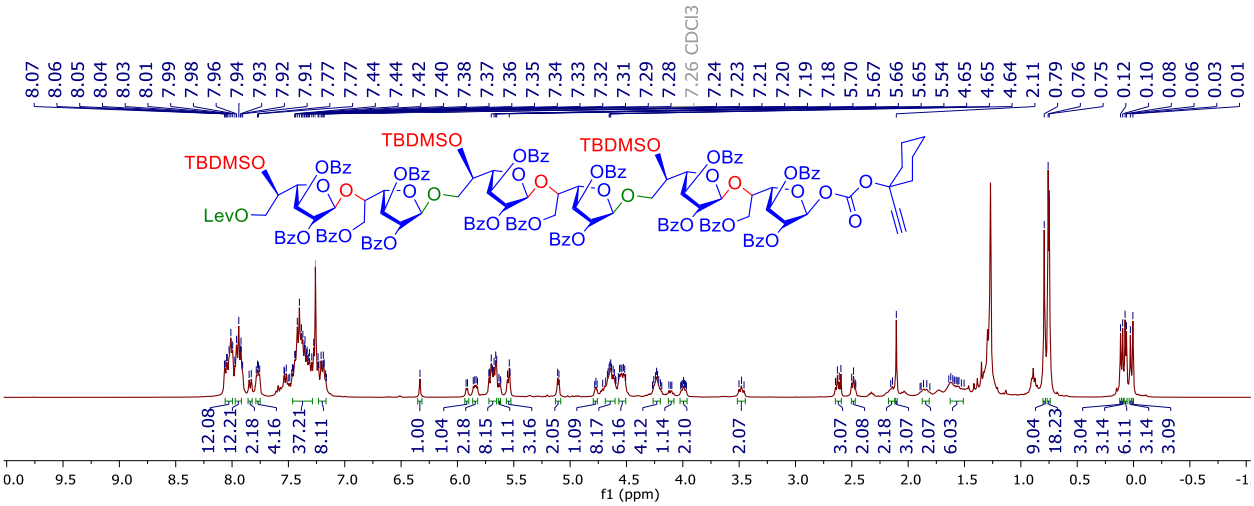
DEPT NMR Spectrum (151 MHz, $CDCl_3$) of compound **46**



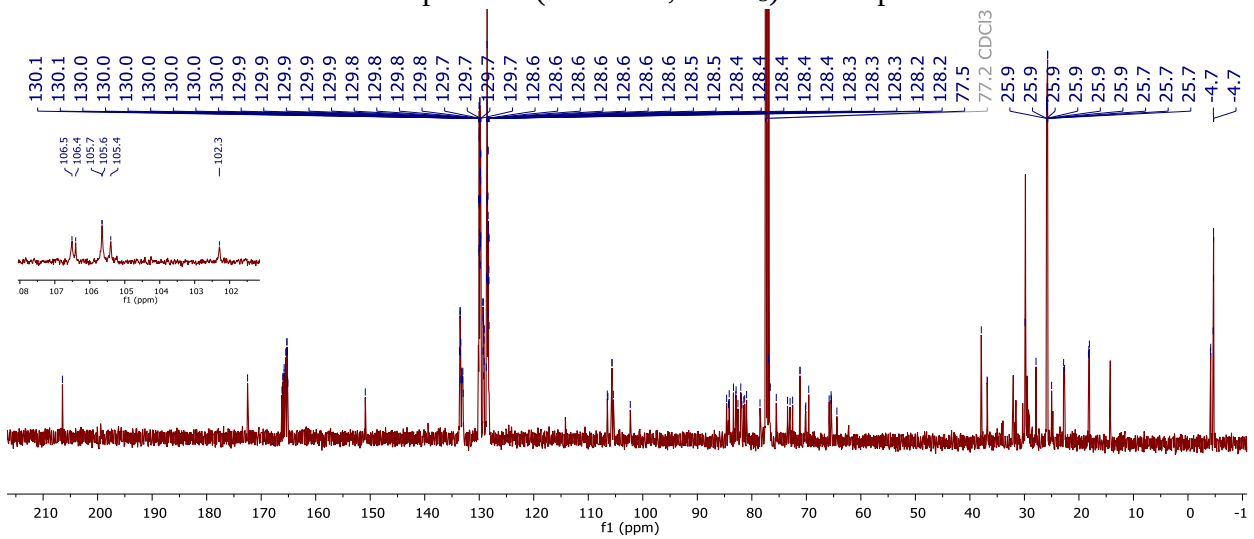
^{1}H-^{13}C HSQC NMR Spectrum (600 MHz, 151 MHz, $CDCl_3$) of compound **46**



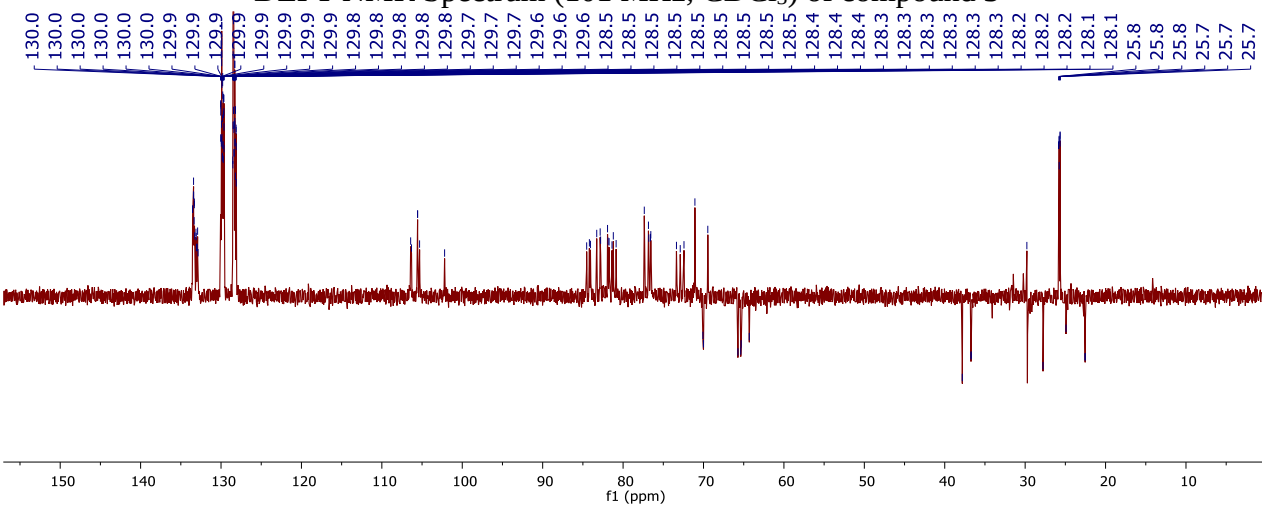
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **5**



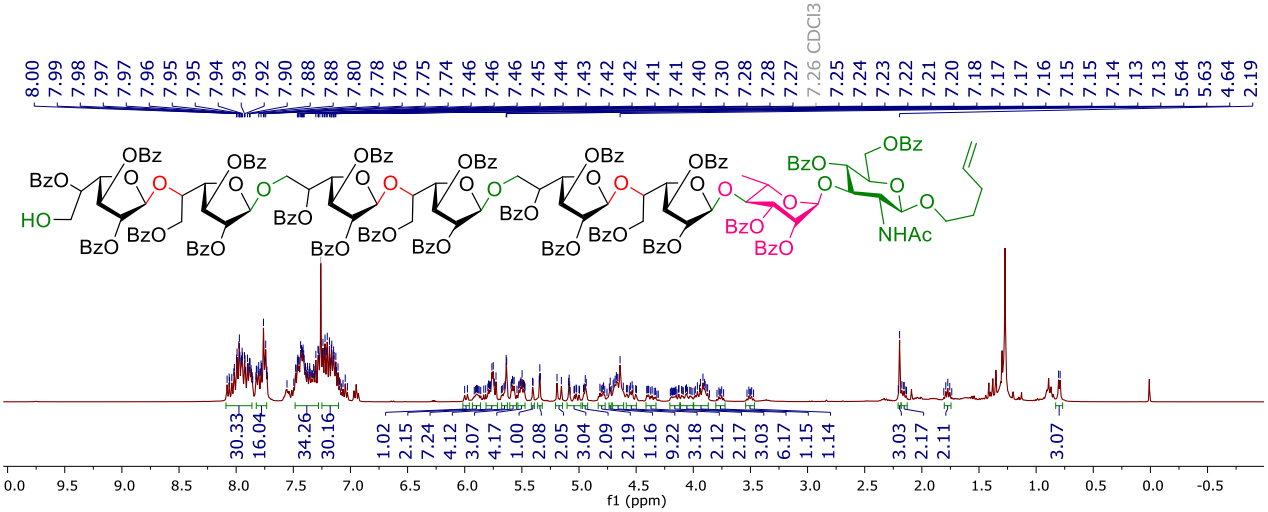
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **5**



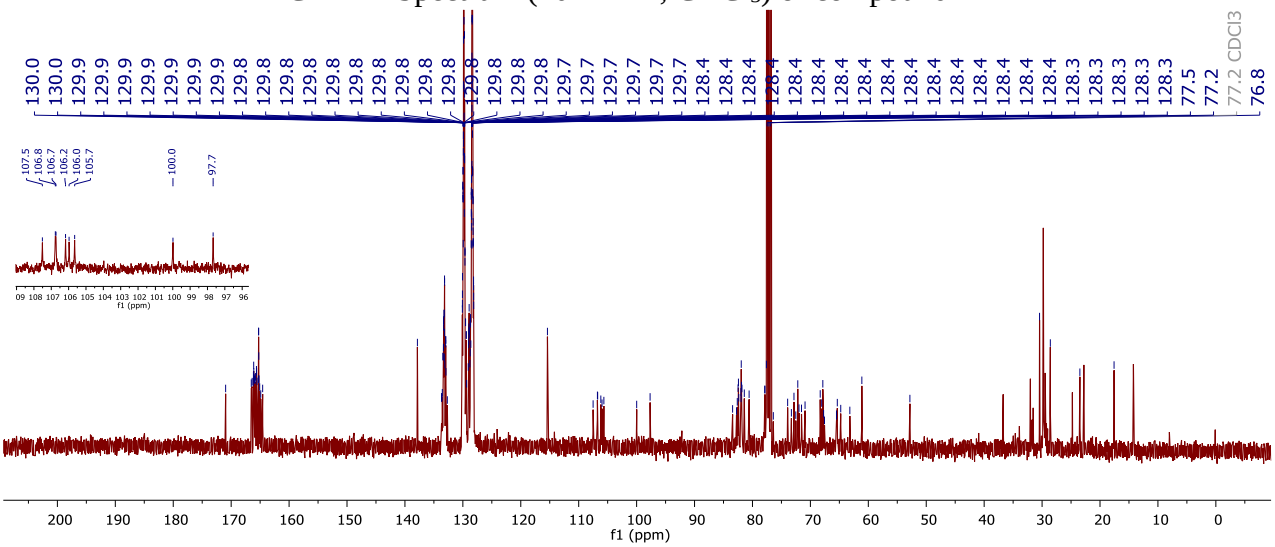
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **5**



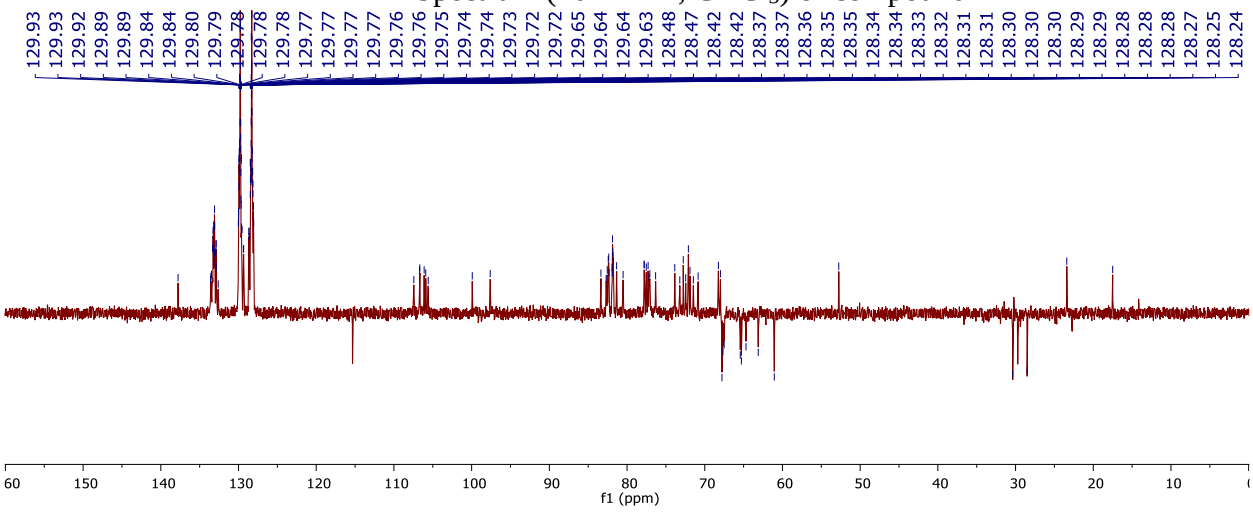
^{1}H NMR Spectrum (400 MHz, $CDCl_3$) of compound **47**



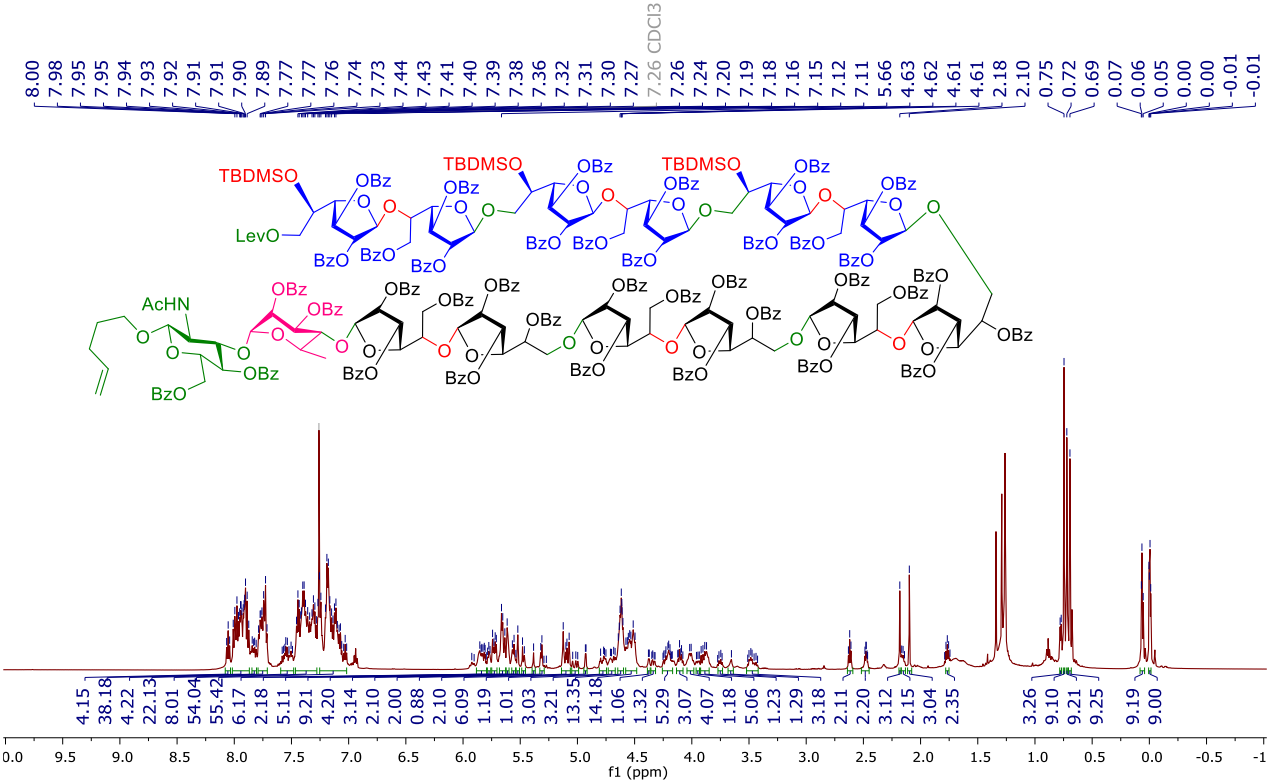
^{13}C NMR Spectrum (101 MHz, $CDCl_3$) of compound **47**



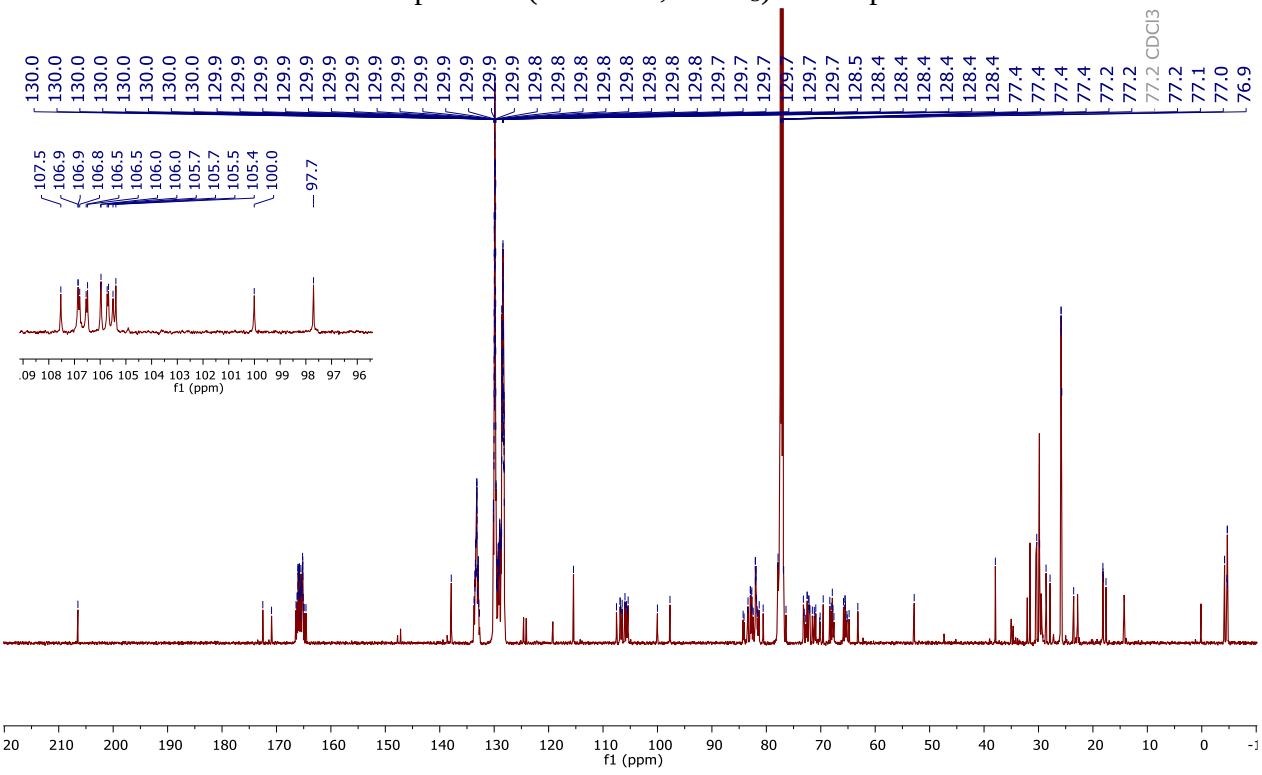
DEPT NMR Spectrum (101 MHz, $CDCl_3$) of compound **47**



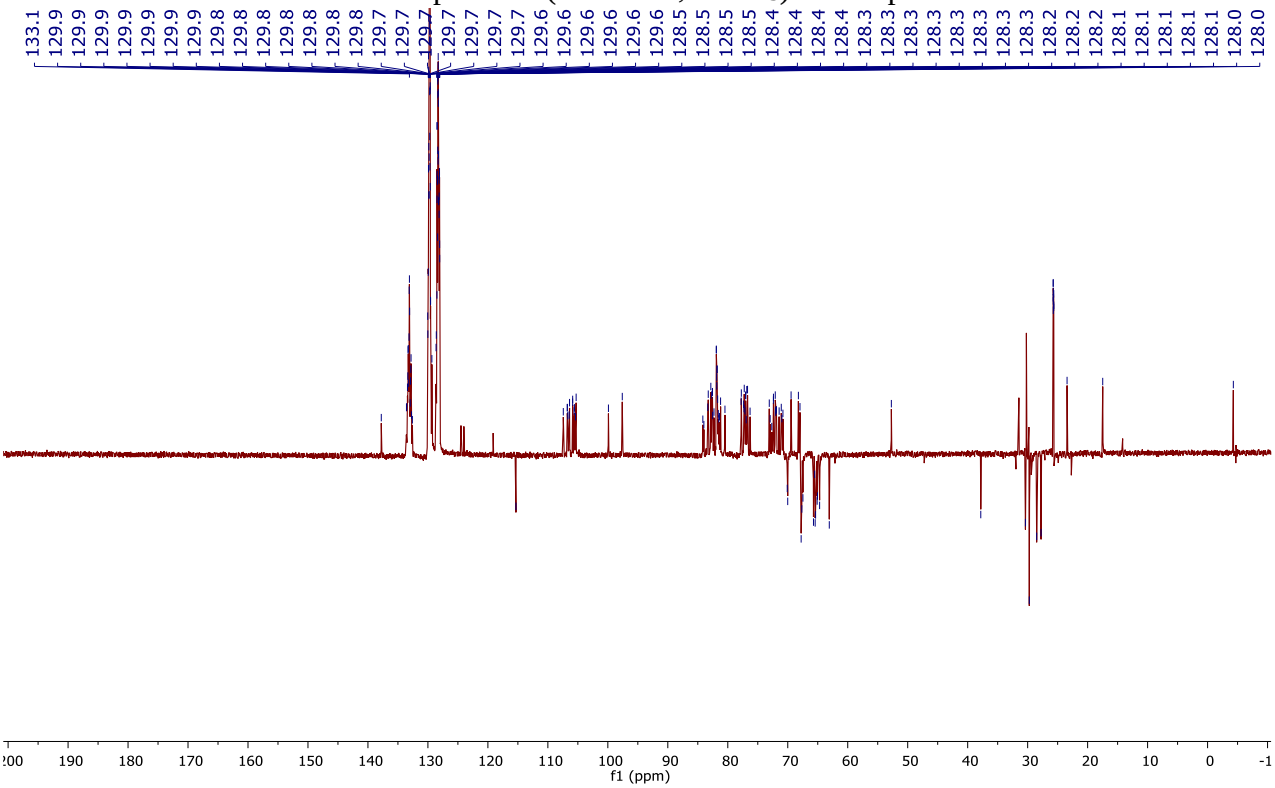
^{1}H NMR Spectrum (600 MHz, $CDCl_3$) of compound **48**



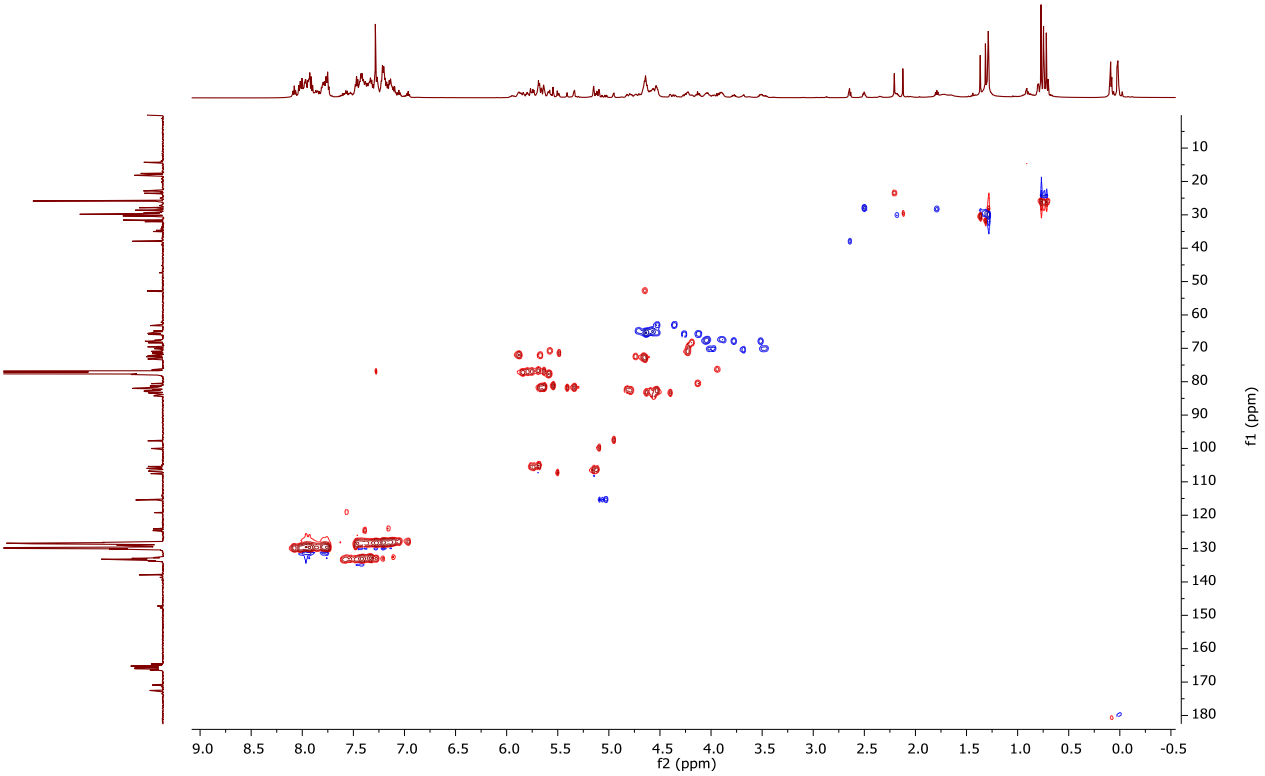
^{13}C NMR Spectrum (151 MHz, $CDCl_3$) of compound **48**



DEPT NMR Spectrum (151 MHz, $CDCl_3$) of compound **48**



^{1}H-^{13}C HSQC NMR Spectrum (600 MHz, 151 MHz, $CDCl_3$) of compound **48**



4.11. References

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List of publications

1. Synthesis of N-Glycosides by Silver-Assisted Gold Catalysis. Saptashwa Chakraborty, Bijoyananda Mishra, **Pratim Kumar Das**, Sandip Pasari, and Srinivas Hotha* *Angew. Chem. Int. Ed.* **2023**, *62*, e202214167.
2. Total Synthesis of Conjugation-Ready Hyperbranched Pentasaccharide of Clavibacter phaseoli VKM Ac-2641^{T} by [Au]/[Ag] Catalysis. **Pratim Kumar Das**, and Srinivas Hotha*. *Org. Lett.* **2024**, *26*, 6709−6713.
3. [Au]/[Ag]-Catalyzed Glycosidation of Ethynylcyclohexyl Glycosyl Carbonates Enables Direct Stereoselective Synthesis of 2-Azido-2-*deoxy*-β-mannopyranosides **Pratim Kumar Das**, Daniil A. Ahiadorme, Niteshlal Kasdekar, Jayashree Rajput, Madhuri Vangala,* David Crich,* and Srinivas Hotha*. *Org. Lett.* (Just accepted) (https://doi.org/10.1021/acs.orglett.4c04208)
4. [Au]/[Ag]-catalyzed expedient synthesis of tetradecasaccharide reminiscent of arabinogalactan motif of Mycobacterium tuberculosis cell wall. **Pratim Kumar Das**, Mahesh Neralkar, Sumit Sen and Srinivas Hotha*. (**Manuscript under preparation**)
5. Silver assisted gold catalysed synthesis of tripodal hyperbranched oligosaccharides and their immunological studies. **Pratim Kumar Das**, Ganesh P. Shinde, Rohith C. S., Pooja Joshi and Srinivas Hotha*. (**Manuscript under preparation**)

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Cell Envelope Proteomics of Mycobacteria

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Glycosylation

Synthesis of *N*-Glycosides by Silver-Assisted Gold Catalysis

*Saptashwa Chakraborty, Bijoyananda Mishra, Pratim Kumar Das, Sandip Pasari, and Srinivas Hotha**

Abstract: The synthesis of *N*-glycosides from stable glycosyl donors in a catalytic fashion is still challenging, though they exist ubiquitously in DNA, RNA, glycoproteins, and other biological molecules. Herein, silver-assisted gold-catalyzed activation of alkynyl glycosyl carbonate donors is shown to be a versatile approach for the synthesis of purine and pyrimidine nucleosides, asparagine glycosides and quinolin-2-one *N*-glycosides. Thus synthesized nucleosides were subjected to the oxidation–reduction sequence for the conversion of Rib*f*- into Ara*f*- nucleosides, giving access to nucleosides that are otherwise difficult to synthesize. Furthermore, the protocol is demonstrated to be suitable for the synthesis of 2'-modified nucleosides in a facile manner. Direct attachment of an asparagine-containing dipeptide to the glucopyranose and subsequent extrapolation to afford the dipeptide disaccharide unit of chloroviruses is yet another facet of this endeavor.

Bourgeoning advancements in glycobiology demonstrated the role played by ubiquitously present glycoconjugates in a myriad of biological processes, including protein folding, signal transduction, fertilization, embryogenesis, neuronal development, and proliferation of cells.[1] Glycoconjugates can be visualized as glycan moieties attached to a protein as in glycoproteins, and lipids as in glycolipids, through a glycosidic linkage.[2] Glycans can be attached to the aglycons through an *O*-, *N*-, *S*- or *C*-glycosidic bond, and they are usually referred to as *O*-glycosides, *N*-glycosides, thioglycosides and *C*-glycosides, respectively.[3] Among these, *N*-glycosides occupy a special position as they are present in DNA/RNA, wherein a nucleobase (purine or pyrimidine) is glycosylated to a ribofuranose through the ring nitrogen atom.[4] Besides, many proteins are post-translationally glycosylated through asparagine amides, and some N-linked glycosides are explored as small molecule inhibitors (Figure 1). Several decades of research culminated in the development of facile glycosylation protocols for the synthesis of *O*- and *C*- glycosides.[5] Although similar, the synthesis of *N*-glycosides is far more challenging owing to complex compatibility issues between the basicity of *N*-nucleophiles and the acidic reaction conditions used in most glycosylation protocols.[6]

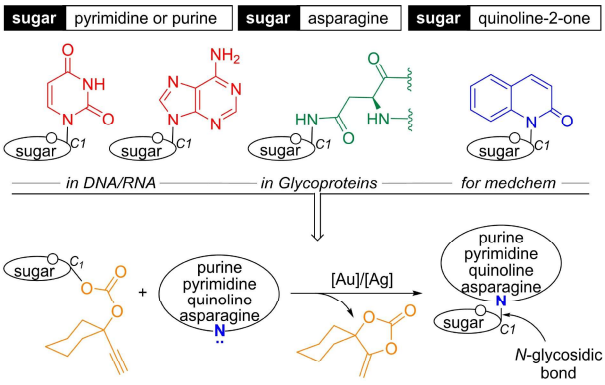


Figure 1. Synthesis of *N*-glycosides.

The Vorbrüggen modified silyl version of the Hilbert–Johnson nucleosidation from anomeric 1-*O*-acyl glycosyl donors is one of the most popular methods for the synthesis of pyrimidine nucleosides;[7] however, it is not always applicable to the synthesis of purine and asparagine glycosides. The use of strong Lewis acids while performing this nucleosidation often limits the choice of protecting groups while synthesizing purine *N*-glycosides. Catalytic activation of *o*-alkynyl benzoates with $[Ph_3PAuNTf_2]$,[6] *o*-(1-phenylvinyl) benzoates[8a] with NIS/TMSOTf or propargyl orthoesters[8b] with $AuBr_3$ are recent improvements for the original Vorbrüggen conditions. The synthesis of amide glycosides is routinely performed by chemical functionalization of N_3, NH_2 or glycals.[8c] Apart from these methods, the synthesis of asparagine glycosides by nucleophilic displacement of the anomeric –OH group is challenging and rarely investigated; the direct glycosidation of asparagine is cumbersome.[9] Quinolin-2-one glycosides were reported to be accessible through intramolecular N-arylation using Pd-catalysis, albeit with the fomation of other possible isomers.[10] A unified and direct method for the synthesis of *N*-glycosides under catalytic, mild conditions and in high yields from shelf-stable molecules will augment the development of novel therapeutics and, diagnostics and also enhance our current understanding of their biological roles.

We envisioned that the recently discovered ethynylcyclohexyl glycosyl carbonate donors[11] might offer a unique solution towards the synthesis of all these *N*-glycosides under catalytic and mild conditions from shelf-stable donors (Figure 1). Accordingly, the journey commenced with the

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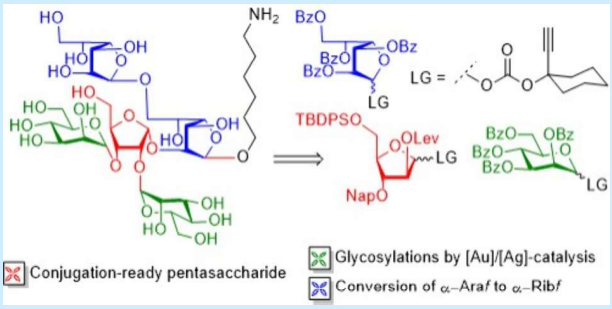
Total Synthesis of Conjugation-Ready Hyperbranched Pentasaccharide of *Clavibacter phaseoli* VKM Ac-2641^T by [Au]/[Ag] Catalysis

Pratim Kumar Das and Srinivas Hotha*

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ABSTRACT: Infections by *Clavibacter* spp. cause an economic burden to farmers. The components present in the cell wall glycopolymers (CWGs) are important for studying the host−pathogen interactions, colonization, and infection. A pentasaccharide containing a hyperbranched Rib*f*-, Gal*f*-, and Man*p*- has recently been identified. Herein, we describe the first total synthesis of the conjugation-ready hyperbranched pentasaccharide of *C. phaseoli* VKM Ac-2641^T using the [Au]/[Ag]-catalyzed glycosidation chemistry of ethynylcyclohexyl carbonate glycosyl donors. The pentasaccharide was synthesized in a highly convergent fashion from readily accessible monosaccharide building blocks.



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Bacterial diseases in agriculturally important plants cause severe economic losses to farmers.[1] Many vascular pathogens cause systemic infections after entering the host through lesions.[2] The tomato canker, potato ring rot, wilting and stunting in alfalfa, wilt and leaf blight in corn, and bacterial mosaic in wheat are caused by five subspecies belonging to the *Clavibacter* spp.[3] For example, *Clavibacter michiganensis* subsp. *michiganensis* induces tomato canker,[4a] *C. michiganensis* subsp. *insidiosus* causes potato ring rot,[4b] and *C. michiganensis* subsp. *tessellarius* causes bacterial mosaic in wheat.[4c] Presence of three of the five subspecies of *C. michiganensis* are quarantined worldwide and, therefore, subjected to international quarantine regulations that affect farmers financially.[5] In contrast to other plant bacterial pathogenic species in the Actinobacteria genera, *Clavibacter* spp. are host-specific at the species level and they are known to colonize in the xylem.[6] Mitigating the host−pathogen interactions is one of the strategies envisioned to deal with these bacterial infections. Earlier studies have shown that bacterial or microbial colonization and infection of microbial host plant cells and host−pathogen communication are governed by the cell wall glycopolymers.[7] The composition and structure of cell wall glycopolymers (CWGs) of some of the *Clavibacter* strains has gained a lot of attention for studying their role in the host colonization and infection.[8] Recently, the CWG structure of *Clavibacter phaseoli* VKM Ac-2641^T, a plant pathogen responsible for the newly identified bacterial leaf-yellowing disease suffered by bean leaves, was reported (Figure 1).[9] The glycopolymer was established as (1 → 6)-linked *β*-D-Gal*f* with branching trisaccharide *α*-D-Man*p*-(1 → 2)-[*α*-D-Man*p*(1 → 3)]-*α*-D-Rib*f*-(1→ at O-2 on every second galactofuranose residue by 2D-NMR spectral studies.[9] In

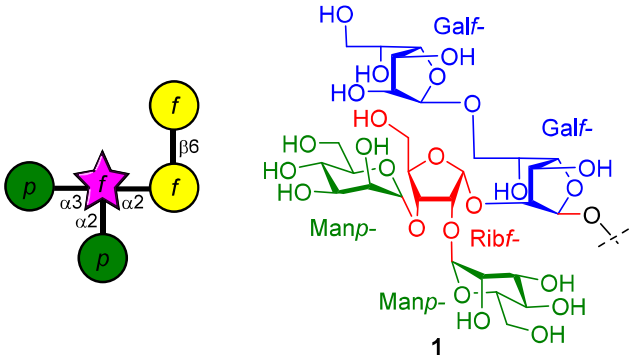


Figure 1. Monomer of the cell wall glycopolymer of *Clavibacter phaseoli* VKM Ac-2641^T

other words, the monomer (**1**) can be visualized as a hyperbranched ribofuranose unit attached to two mannopyranosides at the C2 and C3 positions, and the C1 position is glycosylated to a digalactofuranoside. As part of our interest in the application of our silver-assisted gold-catalyzed glycosidations using glycosyl ethynylcyclohexyl carbonate donors for the synthesis of sterically demanding and highly branched

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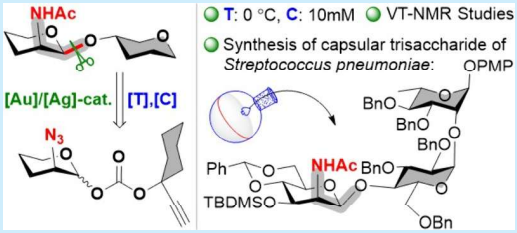
[Au]/[Ag]-Catalyzed Glycosidation of Ethynylcyclohexyl Glycosyl Carbonates Enables Direct Stereoselective Synthesis of 2-Azido-2-deoxy-β-mannopyranosides

Pratim Kumar Das, Daniil A. Ahiadorme,‡ Niteshlal Kasdekar,‡ Jayashree Rajput, Madhuri Vangala,* David Crich,* and Srinivas Hotha*

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ABSTRACT: We describe the [Au]/[Ag]-catalyzed activation of ethynylcyclohexyl 2-azido-4,6-*O*-benzylidene mannosyl carbonates for β-mannosamine linkage preparation in high yield and selectivity in a temperature- and concentration-dependent manner. VT-NMR studies reveal an anomeric triflate intermediate generated in the absence of an acceptor alcohol that is stable up to −10 °C. The generality of the protocol was illustrated by successful application to a series of acceptors and by synthesis of a fully protected *Streptococcus pneumoniae* type 19F capsular trisaccharide.



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Glycosylation is one of the most important reactions that is employed to synthesize complex glycan targets.[1] It can be visualized as the conjugation between a glycan and another molecule termed the aglycon.[1b] In glycosylation, the glycan portion usually contains a leaving group that gets activated in the presence of promoters, resulting in the formation of a highly electrophilic intermediate; glycans possessing the leaving group are referred to as glycosyl donors.[1] Many pioneering efforts over the past century have culminated in the development of various glycosyl donors for the formation of diverse glycosidic bonds. Often the highest 1,2-*trans* stereoselectivities were accomplished by furnishing the glycosyl donor with a participating group such as an ester at the C2 position so that it can impart neighboring group participation to afford 1,2-*trans* glycosides in a facile manner.[1] Alternatively, participation through thioether auxiliaries[1c] and picolinyl groups[1d] from C2 or other remote positions has been explored. However, the stereoselective synthesis of 1,2-*cis* glycosides is still a difficult task. These challenging 1,2-*cis* glycosides can be synthesized by either intramolecular aglycon delivery (IAD),[2a−c] reactions at low temperatures,[2d] H-bond-mediated aglycon delivery (HAD),[2e] steric buttressing,[2f] or conversion of a 1,2-*trans* to a 1,2-*cis* glycoside by inversion of configuration at C2.[2g−i]

Of the many sugars, mannose occupies a special position, as many bacterial, mammalian, and microbial species contain high-molecular-weight mannans differentiated by 1,2-*trans* (α-) and 1,2-*cis* (β-) mannosidic linkages.[3] The C2 position of the mannopyranosyl sugar is disposed axially; therefore, the synthesis of 1,2-*trans* mannosides becomes relatively easier due to the strong anomeric effect as well as the favorable steric hindrance of the axial substituent. The synthesis of 1,2-*cis* mannosides was reported by intramolecular aglycon delivery,[2a] stereochemical editing,[2h] Crich β-mannosylation equipping the glycosyl donor with 4,6-benzylidene acetals,[2d] or HAD.[2e] ManNAc (also called *N*-acetylmannosamine or 2-acetamido-2-deoxy-mannopyranose) has emerged as a common component in capsular polysaccharides of bacteria and prokaryotes and is a key precursor for the biosynthesis of *N*-acetylneuraminic acid in mammals.[3] Additionally, the occurrence of ManNAc residues in biologically important glycans,[3] asparagine-linked glycopeptides,[4] and vaccine candidates warrants the development of novel glycosylation methods for the β-stereoselective synthesis of mannosamine derivatives (Scheme 1A). The synthesis of 1,2-*trans* (α-) mannopyranosides can be accomplished through neighboring group participation, whereas the stereoselective synthesis of 1,2-*cis* (β-) glycosides of ManNAc is cumbersome. Earlier studies showed that glycosyl donors that produced excellent β-mannosylation met with limited success when applied for the synthesis of glycosides of β-mannosamine.[5a] As a result, a vast majority of literature reports resorted to indirect methods of converting glucose to mannose after the glycosylation event. The stereochemical editing of βGlc*p*→βMan*p*NAc demands careful planning of other functional groups (Scheme 1B). In this context, the direct stereoselective synthesis of β-glycosides of mannosamines is of paramount significance. Notably, complete β-manno selectivity was noticed while synthesizing a trisacchar-

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