# Synthesis of MTX-Capped Octasaccharide & Metal-Free Activation of Carbonate Donor

**A Thesis submitted in partial fulfillment of the requirements of the degree of Doctor of Philosophy**

**By**

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**July 2023**

*Dedicated to ……*
*My Grandma (late Mrs. Gayatri Devi)*

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# CERTIFICATE

Certified that the work incorporated in the thesis entitled "***Synthesis of MTX-Capped Octasaccharide & Metal-Free Activation of Carbonate Donor***" submitted by **Mr. Kameshwar Prasad** 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**: August 8, 2023, Pune

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*Finally, I praise lord Vashudeva (lord Krishna), the almighty, for providing me with this opportunity and granting me the capability to proceed successfully. This piece of work will never be accomplished without his blessings.*

***Kameshwar Prasad***

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# *General remarks*

- ✓ $^{1}H$ NMR spectra were recorded on JEOL 400 MHz, Bruker 400 or 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 JEOL 100 MHz, Bruker 100MHz or Bruker 150 MHz spectrometer.
- ✓ High resolution mass spectroscopy (HRMS) was performed on Waters Synapt G2 or Applied Biosystems MALDI-ToF-ToF spectrometer.
- ✓ IR spectra were recorded on Perkin-Elmer 1310 or 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 and measured in degrees.
- ✓ All reactions were monitored by Thin-Layer Chromatography carried out on pre-coated Merck silica plates ($F_{254}$, 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 freshly prepared anhydrous solvents under anhydrous conditions and yields refer to chromatographically homogenous materials unless otherwise stated.
- ✓ All evaporations were carried out under reduced pressure on Büchi and Heidolph rotary evaporators 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.

# *Abbreviations*

Å – Angstrom

Ac – acetate

AcCl – Acyl chloride

AcOH – Acetic acid

ACN – Acetonitrile

$Ac_2O$ – Acetic anhydride

AG – Arabinogalactan

Arb*f* – Arabinofuranose

Bn – Benzyl

BnBr – Benzyl bromide

Bz – Benzoyl

BzBr – Benzoyl bromide

Boc – $^{tert}$Butyloxycarbonyl

$Boc_2O$ – $^{tert}$Butyloxycarbonyl anhydride

BSTFA – N, O-Bis(trimethylsilyl)trifluoroacetamide

$Bu_2SnO$ – Dibutyl-tin-oxide

Calcd – Calculated

$CH_2Cl_2$ – Dichloromethane

$CDCl_3$ – Chloroform-D

$CHCl_3$ – Chloroform

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

DCE – 1,2-Dichloroethane

DCM – Dichloromethane

DMAP – Dimethyl amino pyridine

DME – 1,2-Dimethoxyethane

DEPT - Distortionless Enhancement by Polarization Transfer

DMF – Dimethyl formamide

DIC - N,N'-Di(propan-2-yl)methanediimine

δ - Delta

Eq. – Equivalent

$Et_3N$ – Triethyl amine

EDC - 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide

EtOAc – Ethyl acetate

$Et_3SiH$ – Triethyl silane

g – Gram

Gal*f* – Galactofuranose

h – Hour

HRMS - High-Resolution Mass Spectrometry

Hz – Hertz

IR – Infrared

*J* – Coupling constant

LAM – Lipoarabinomannan

Lev - Levulinate

M – Molar

MTX – Methyl-thio-xylose

mg – Milligram

mL – millilitre

min. – minutes

MHz – Megahertz

mmol – millimolar

MS – Molecular sieves

Mtb – *Mycobacterium tuberculosis*

NaH – Sodium hydride

Nap – Naphthyl methyl

NaSMe – Sodium thio methoxide

NIS – N-Iodosuccinimide

PMP – p-Methoxy phenyl

Py – pyridine

p-TSA – p-toluene sulphonic acid

ppm – parts per million

Rib*f* – Ribofuranose

rt – Room temperature

Tb – tuberculosis

TBAI – Tetra butyl ammonium iodide

TBDPS – $^{tert}$butyl diphenyl silane

TBDPSCl - $^{tert}$butyl diphenyl silyl chloride

TFA – Triflouroacetic acid

THF – Tetrahydro furan

TLC – Thin layer chromatography

TMSOTf – Trimethyl silyl triflouromethanesulfonate

The thesis titled, "***Synthesis of MTX-Capped Octasaccharide and Metal-Free Activation of Carbonate Glycosyl Donor***" is divided into three chapters. Chapter one illustrates the introduction of carbohydrates, their classification, glycoconjugates and their biological significance, glycosylation, types of glycosylation, an account of donors and mode of activation, stereoselectivity and different approaches to achieve stereoselectivity. The second chapter starts with the introduction of *Mycobacterium tuberculosis (MTb)*, complex glycans present on the cell envelope of MTb and chemical synthesis of methyl thio-xylose containing octasaccharide motif exploiting silver-assisted gold-catalyzed glycosylation method. The third chapter of the thesis delineates development of a new method of activation of the ethynylcyclohexyl glycosyl carbonate donors for the synthesis of *O*-glycosides, *N*-glycosides, and its application in the synthesis of O-3 antigen from *Klebsiella pneumoniae*.

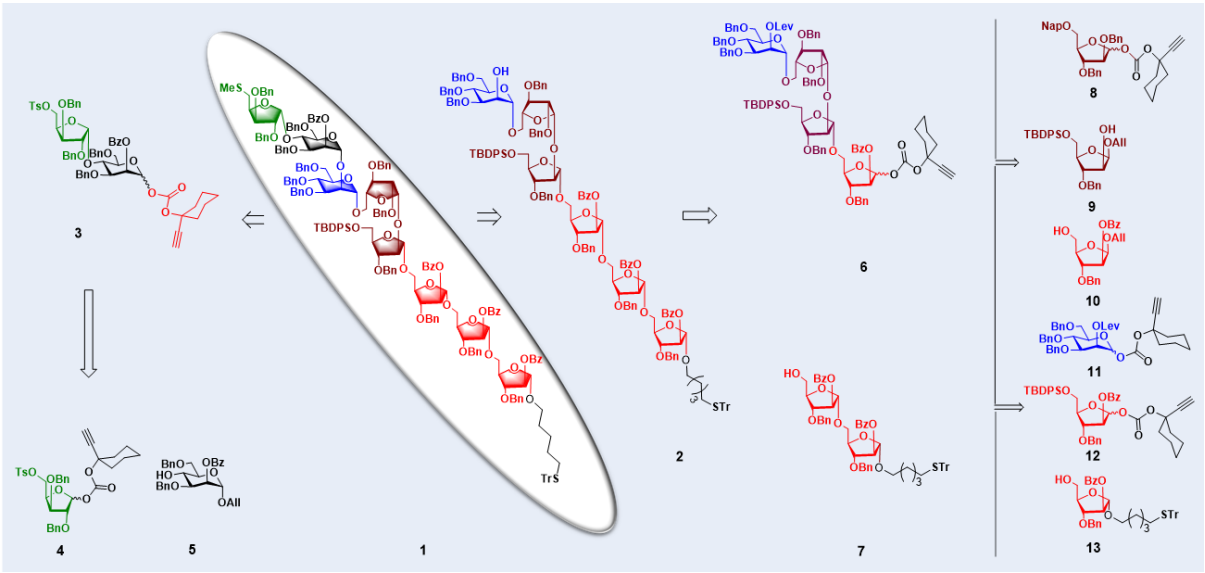
**Chapter 1**: **Introduction of glycosyl donors and stereoselective glycosylation**

Life on the earth contains four types of macromolecules: proteins, lipids, nucleic acids, and carbohydrates. Carbohydrates are further classified into three major classes: monosaccharides, disaccharides, and oligosaccharides. The word glycan is synonymous with an oligosaccharide - when it is conjugated to any aglycon the resulting molecule is known as glycoconjugate. Glycoconjugates are present in every form of life and mammals, are involved in a myriad of biological functions, broadly categorized into three categories mainly: (i) structural and modulatory functions, (ii) specific recognition by other molecules, glycan-binding proteins mainly, and (iii) molecular mimicry of host glycans. Quantification of homogenous glycoconjugates from Nature is a daunting task, due to their intrinsic heterogenous nature; thus, chemists came up with the alternate method termed as glycosylation. Glycosylation is one of the alternatives to obtain glycans and glycoconjugates. Broadly, glycosylations can be performed either by enzymatically or chemically. Glycosylation is a coupling reaction between a glycosyl donor and glycosyl acceptor in the presence of a suitable promoter to give a condensed product. Glycosyl donors often are sugar moieties with a leaving group at the anomeric position which can be activated in the presence of an activator (reagent) to form an oxocarbenium ion intermediate that can be attacked by a glycosyl acceptor (aglycon). The aglycon can be sugar, protein, lipid, or any other aglycon. In order to achieve glycosidic linkages, a plethora of glycosyl donors have been developed by glyco-chemists worldwide. Journey started more than a century ago with the first glycoside synthesis by Fischer using acidic media and later by Koenings and Knorr introduced halide donors in 1901 which could be activated by silver salts. Glycosyl halide donors are unstable and moister sensitive, which

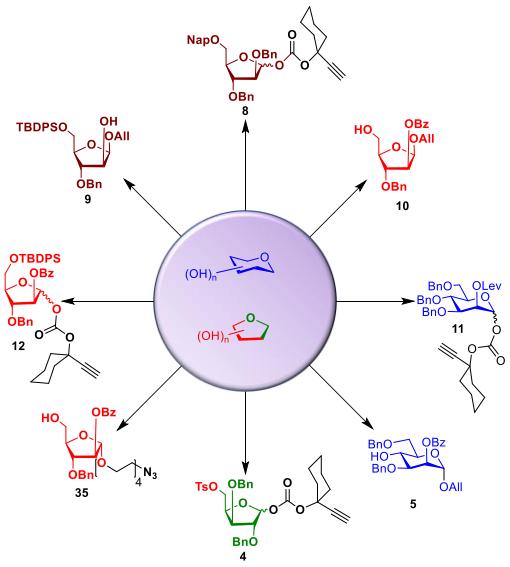
prompted chemists to look for other donors. Later different donors e.g., thio-donors, imidate donors, phosphate or phosphite donors, glycals, and hemiacetals were developed and activated under different activators. In field of glycosylation, Hotha and Kashyap introduced gold-catalyzed glycosylation using propargyl glycosides in 2006. In order to improve the efficacy of their method, Hotha and Mishra came up with 1-ethynylcyclohexyl glycosyl carbonate donor chemistry which was indeed a remarkable discovery in the field of donor chemistry. This donor is readily accessible, highly shelf stable, and activated by 8 mol% each of of Au(I)-phosphite and AgOTf. This glycosyl donor was exploited to synthesize oligosaccharides, e.g., a tridecasaccharide, a heneicosasaccharyl mannose capped arabinomannan, a pentacosafuranoside of arabinogalactan, a linear nonadecaarabinofuranoside, and branched heneicosafuranosyl arabinogalactan motif of *Mycobacterium tuberculosis* cell wall. Furthermore, a highly useful Fondaparinux pentasaccharide and *N*-glycosides were also synthesised utilizing the same donor chemistry.

**Chapter 2: Chemical synthesis of MTX-capped octasaccharide from *Mtb* cell envelope**

Tuberculosis (TB) is one of the deadly diseases that mainly affects human lungs. *Mycobacterium tuberculosis* (MTb) is the causative agent of TB. Cell envelope of MTb contains three major glycans: arabinogalactan (AG), lipomannan (LM), and Lipoarabinomannan (LAM). Lipoarabinomannan contains three major domains: MPI anchor, mannose polysaccharide backbone, and arabinan domain. When these LAM motifs are connected to the mannose residue

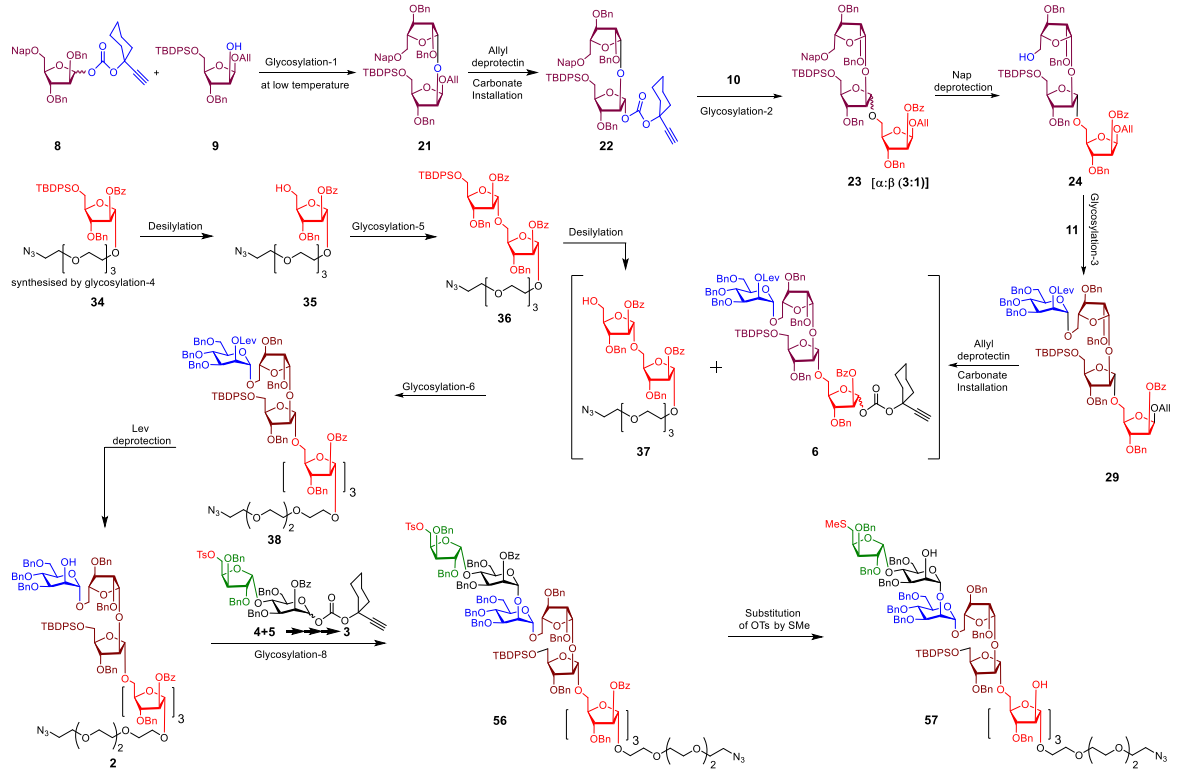


***Scheme 2.1:*** *Retrosynthesis of MTX-capped ManLAM octasaccharide motif*




Scheme 2.2: Synthesis of building blocks

at the non-reducing end, the resulting glycoconjugate is termed as ManLAM which is further capped by thio-methyl-xylose motif and the full conjugate is abbreviated as "MTX-capped LAM." Currently, MTX-capped LAM is explored as a vaccine candidate and as a biomarker for the detection of MTb as well. Interesting biological roles interested us to develope a chemical route to synthesize the MTX-capped-octasaccharide using our inhouse methods. Accordingly, the synthesis of octasaccharides is visualized from eight simple building blocks which in turn can be synthesized from commercially available arabinose and mannose in eight to ten steps. Once all the building blocks in hand, we moved forward to the synthesis of chemically challenging 1,2-*cis* linkages. The glycosylation reaction (Mishra et al. *Angew. Chem., Int. Ed.* **2016**, *55*, 7786–7791) between the glycosyl donor **8** and glycosyl acceptor **9** using [Au]/[Ag]-catalysts at room temperature afforded a α:β mixture of compounds **21** within 15 min; however, only *β*-isomer was observed at lower temperature (-78 ºC).




***Scheme 2.3:*** *Forward chemical synthesis of MTX-capped-octasaccharide*

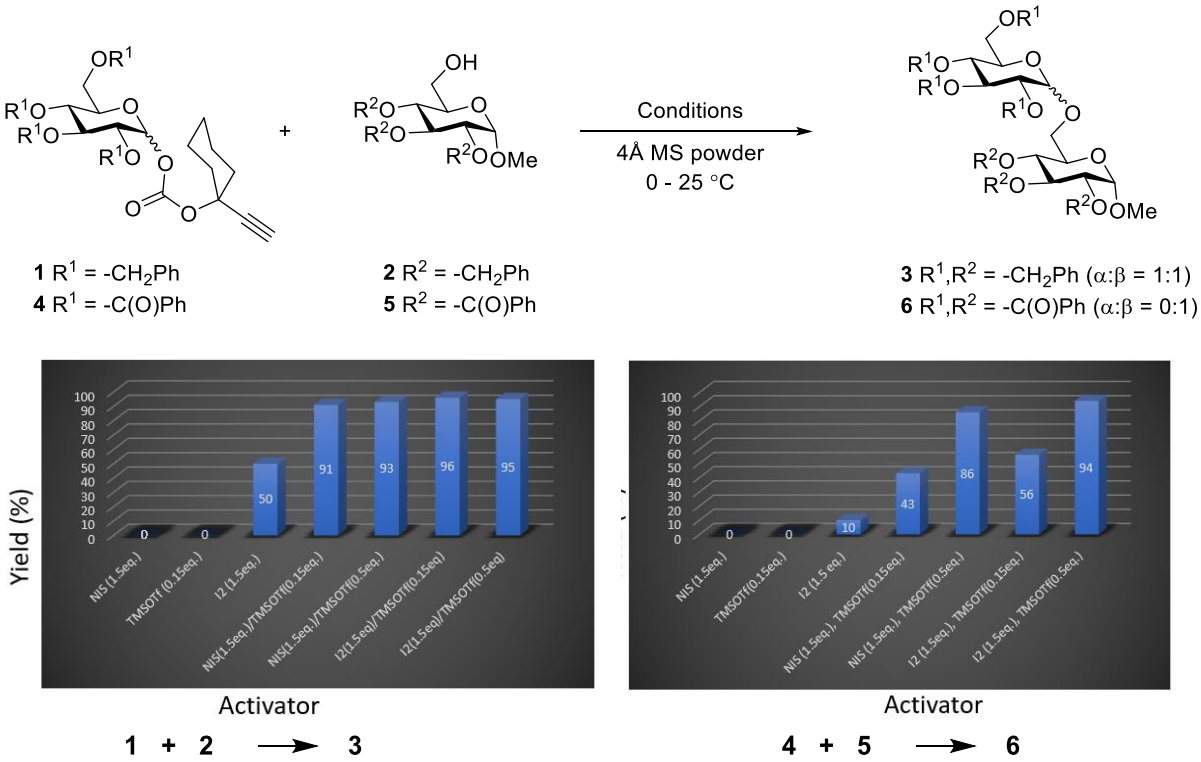
Moving forward, disaccharide **21** was treated with $PdCl_2$ to convert into hemiacetal, which was further reacted with carbonate reagent to achieve disaccharide carbonate donor **22**. Disaccharide donor **22** was further glycosylated with acceptor **10** under gold-silver glycosylation conditions at lower temperature to afford the trisaccharide **23** to obtain desired isomer as major product; mixture of isomers was carried forward and desired isomer of **24** was separated and glycosylated with donor **11** again to furnish tetrasaccharide **29**, which was exposed to the $PdCl_2$ conditions to convert into hemiacetal, subsequently, converted into tetrasaccharide carbonate donor **6**. TEG-$N_3$ linker containing disaccharide **37** was synthesized after two glycosylation and desilylation reaction sequence, which was glycosylated with tetrasaccharide carbonate donor **6** to furnish hexasaccharide **38**. Subsequently, hexasaccharide **38** was treated with hydrazine acetate to convert it into hexasaccharide acceptor **2**. Disaccharide donor **3** was synthesized in three steps - first step was glycosylation of building blocks **4** and **5**, second allyl deprotection, and third step was carbonate donor preparation. Once the disaccharide donor **3** and hexasaccharide acceptor **2** are in hand, we glycosylated them to accomplish the octasaccharide **56**. Substitution by thio-methyl at nonreducing end lead to the the methyl-thio-xylose containing octasaccharide motif **57**. All the compounds after each step were well characterized by HRMS, NMR spectroscopy. Synthesized octasaccharide has a azide linker at the nonreducing end which can be exploited for the bioconjugation for further biological studies.

**Chapter 3: Metal-free activation of alkyne glycosyl carbonate donors**

The coordination of Lewis acid with different functional groups, such as imine, carbonyl, alkene, and alkyne, is an important method for activating these functional groups that facilitate many organic transformations. Recently, gold and platinum complexes with alkyne have been of keen interest to several organic chemists. Besides a plethora of transition metal catalysts, electrophilic iodonium source has become popular in cyclization and other organic transformations. Apart from those organic transformations, Lewis-acids are well explored by glycochemists for glycosylation reactions. In transition metal catalysis, Gold catalysed glycosylation was discovered by Hotha and Kashyap in 2006 wherein, 5 mol% of $AuCl_3$-activated per-*O*-benzylated propargyl glycosyl donor thereby producing several glycosides. Later, several modifications were reported by Hotha's and other groups using gold as the main activator for the glycosylation reaction.

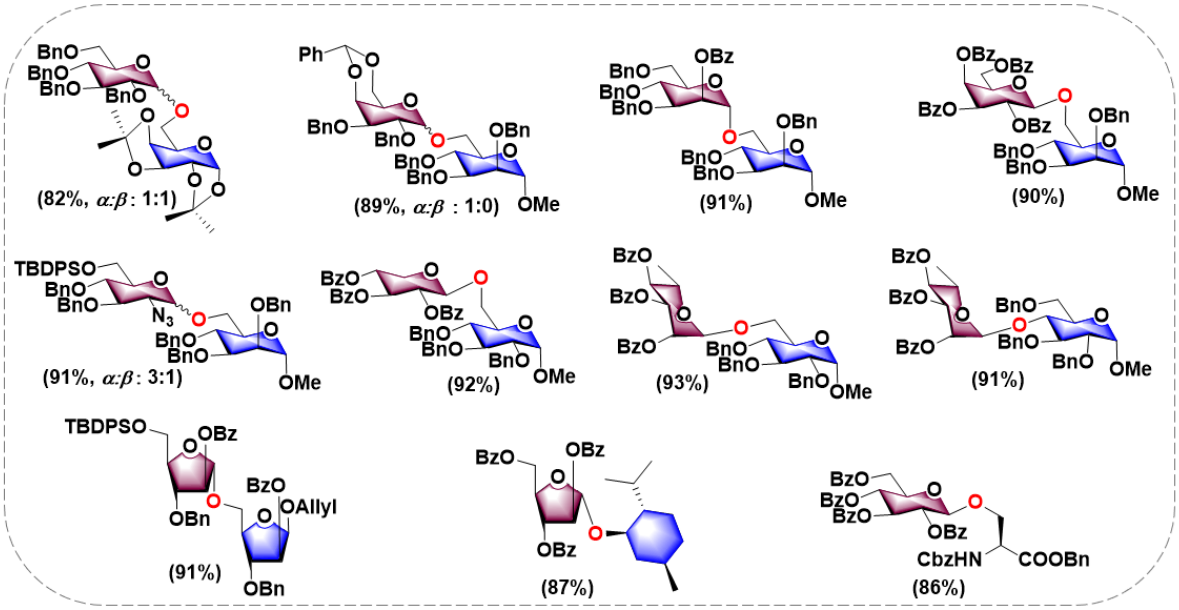
To overcome the limitation of the first gold catalysed glycosyl donor (propargyl glycosyl donors), a stable, versatile, and easily accessible carbonate donor (ethynyl cyclohexyl

carbonate) was discovered exactly after ten years in 2016, which was catalysed by gold {chloro[tris(2,4-di-*tert*-butylphenyl)phosphite]gold} and silver {silver triflate} salts to give higher yields in glycosylation. Alkyne carbonate donor was exploited for synthesizing several oligosaccharides synthesis and N-glycoside, including amide glycosides.



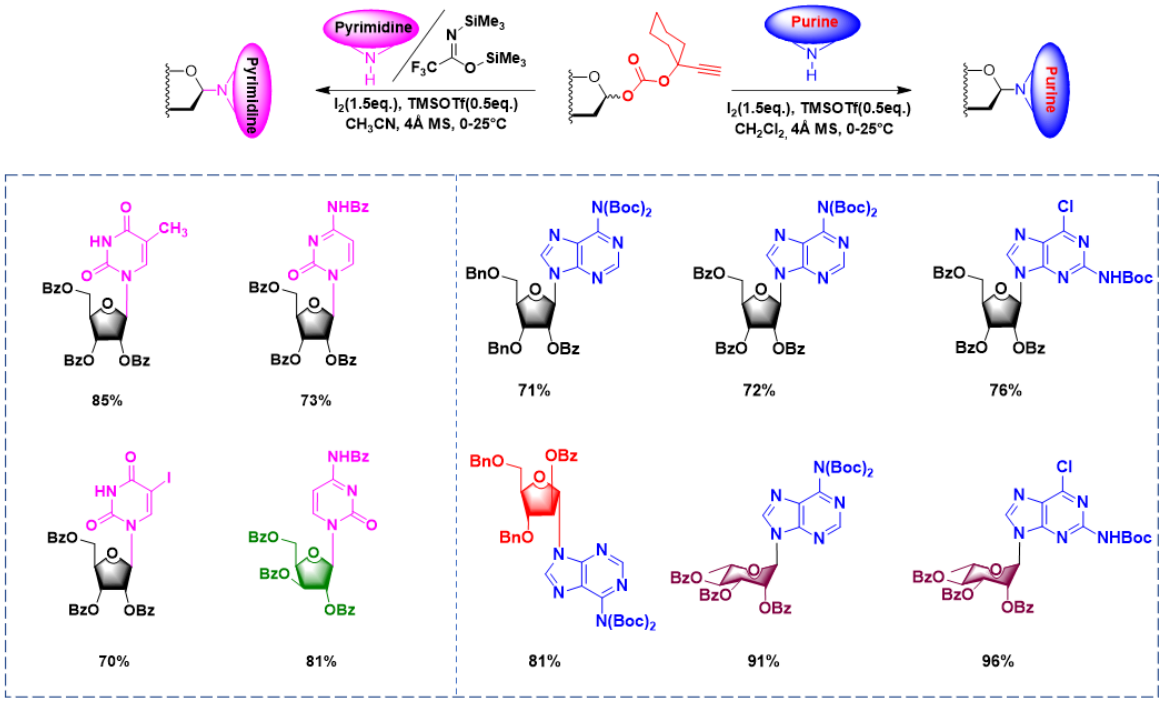

***Scheme 3.1:*** *Screening of reaction conditions for the model glycosylation reaction*

To make the reported donor metal activation free and reduce the overall per glycosylation reaction cost, we envisioned a metal-free and cost-effective activator for the activation of ethynylcyclohexyl glycosyl carbonate donor. So, in this regard, we commenced with the ethynyl carbonate donor as a model substrate for our exploration. The alkynophilicity of iodonium reagents drew our attention to the metal-free activation of ethynyl cyclohexyl carbonate donor. A combination of NIS (1.5 eq.) and TMSOTf (0.15 eq.) afforded excellent yield (91%) when glycosyl donor **1** was glycosylated with glycosyl acceptor **2**, but the yield of the reaction was poor for disarmed donors (those with C2-esters). However, when NIS was replaced by iodine the yield of the reaction increased and further addition of TMSOTf (0.15 - 0.50 eq.) drastically improved the reaction yield to 96% (**1**+**2**→**3**) and (**4**+**5**→**6**) 94%. After optimization of the reaction conditions, we moved forward towards the substrate scope for the generalization of the method.



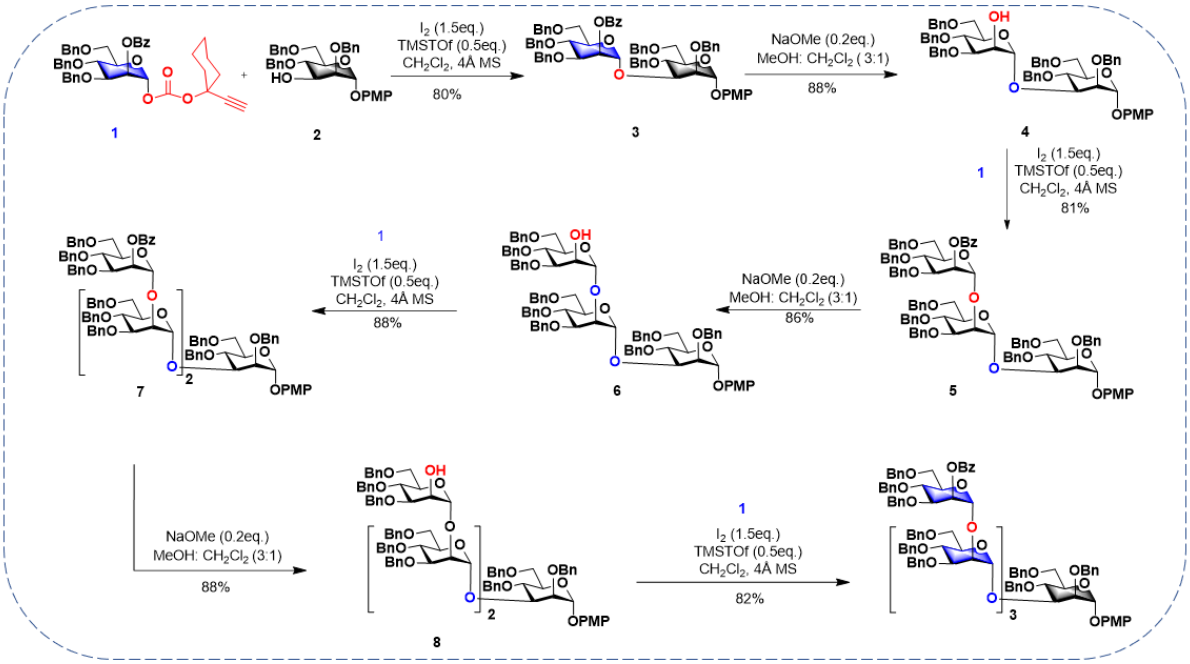

***Scheme 3.2:*** *Synthesis of different O-glycosides*

A plethora of donors (pyranosyl, furanosyl, pentose, hexose) were explored with different acceptors to produce a broad range of *O*-glycosides. Interestingly, different functional groups, i.e., benzylidene, silyl-ether, iso-propylidene, Cbz, and allyl, tolerated well during the glycosylation reaction. All the donors having C2-benzyl protection afforded a mixture of 1,2-*cis* and 1,2-*trans* glycosides whereas those embedded with C2-benzoates produced 1,2-*trans* glycosides in a stereoselective fashion. Further, this methodology was utilized for the synthesis




***Scheme 3.2:*** *Synthesis of different N-glycosides*

of *N*-glycosides (purines and pyrimidines). All the nucleosides were obtained in good to excellent yield (71 to 96% yield). It was interesting that unnatural nucleosides were obtained in higher yield than natural nucleosides. Purines were made soluble to give improved regioselectivity by introducing bis-Boc-protecting group. Pyrimidines were first silylated with BSTFA to make them soluble in acetonitrile and then reacted with glycosyl donors.




***Scheme 3.3:*** *Synthesis of O-3 antigen (repeating unit) of Klebsiella Pneumoniae*

Experience and successful syntheses of above glycosides, disaccharide and nucleosides encouraged us to apply metal free activation of alkynyl glycosyl carbonate donor chemistry to the synthesis of a pentasaccharide motif reminiscent of *Klebsiella pneumoniae* (O-3 antigen). *Klebsiella pneumoniae* is responsible for the wide range of infections, including pneumonia, urinary tract infections, bacteremias, and liver abscesses. So, vaccine development is an alternative initiative to combat this challenge, here we targeted the synthesis of the pentasaccharide repeating unit of O-3-antigen of *K. pneumoniae,* which can be a vaccine candidate for the treatment of the disease caused by *Klebsiella Pneumoniae*.

In summary, stable easily accessible and versatile alkynyl glycosyl donors were activated under metal-free conditions using stoichiometric quantity of readily available molecular iodine and TMSOTf. The extrusion product resulting from the carbonate moiety was characterised by the SCXRD. Apart from the use of stoichiometric quantities, glycosylations happen in a smooth manner producing glycosides, disaccharide, and nucleoside in a very simple fashion.

# *Chapter 1*

## *Introduction to*

## *Glycosyl Donors &*

## *Stereoselective-Glycosylation*

## 1.1 - Introduction[1–3]

Kingdom of life on the earth contains four major types of macromolecules: proteins, lipids, nucleic acid, and carbohydrates. The term carbohydrate was coined initially for the glucose-like monosaccharide with an empirical composition of $C_n(H_2O)_n$, but later on, panoramically used for all the 'kingdom of carbohydrates'. August Kekulé, a German chemist in 1866, introduced the concept of chirality to carbohydrates and named it as dextrose. Another German chemist Emil Fischer started his work on the relative conformation of carbohydrates. Alcohols, aldehydes, and ketones resemble carbohydrates molecules. So, *carbohydrates* are molecules containing polyhydroxy, aldehydes, or ketones.

## 1.2 - Classification of carbohydrates[1,2,3]

Carbohydrates are broadly categorized into monosaccharides, disaccharides, and trisaccharides. The monosaccharide contains one sugar unit, such as glucose (derived from an ancient Greek word gleukos which meant "**sweet, delightful wine"**), galactose (Greek word for milk, "galact" one of the components of lactose in milk), fructose (from Latin "Fructus" meant fruit), and ribose (the sugar present in DNA and RNA). Monosaccharides can be further classified based on the number of carbons, functional group, the stereochemistry of anomeric carbon, ring size, and type of bonding. Disaccharides contain two monosaccharide units, such as sucrose (a French word for sugar "sucre" present in cane sugar, containing glucose and fructose), lactose (the Latin word for milk "lact" present in milk containing glucose and galactose), and maltose (a French word for "malt" which is a disaccharide of two glucose units and present in germinating grains). Polysaccharides are a long chain of monosaccharides, e.g., starch (polysaccharide of glucose unit stored in cereal grains and potato), cellulose (a major component of the plats cell wall and repeating linear polysaccharide of glucose monosaccharide unit), and glycogen (one form of glucose stored in muscles and liver). Polysaccharides are higher molecular weight carbohydrates that yield monosaccharides upon hydrolysis. Hydrolysis classifies polysaccharides into homopolysaccharides and heteropolysaccharides. Homopolysaccharide yields a single monosaccharide upon hydrolysis, e.g., starch and cellulose. On the other hand, heteropolysaccharides yield more than one monosaccharide upon hydrolysis, e.g., pectins. Further classification is based on the molecular weight of the polymer, the type of chain (linear or branded) formed, the type of linkages ($\alpha$ or $\beta$), and the position of linkages between two units.

### 1.3 - Conformational analysis of carbohydrates[4,5]

osaccharides exist mainly in six-membered pyranose and five-membered furanose forms; both conformations adopt puckered shapes to minimize eclipsing interactions.

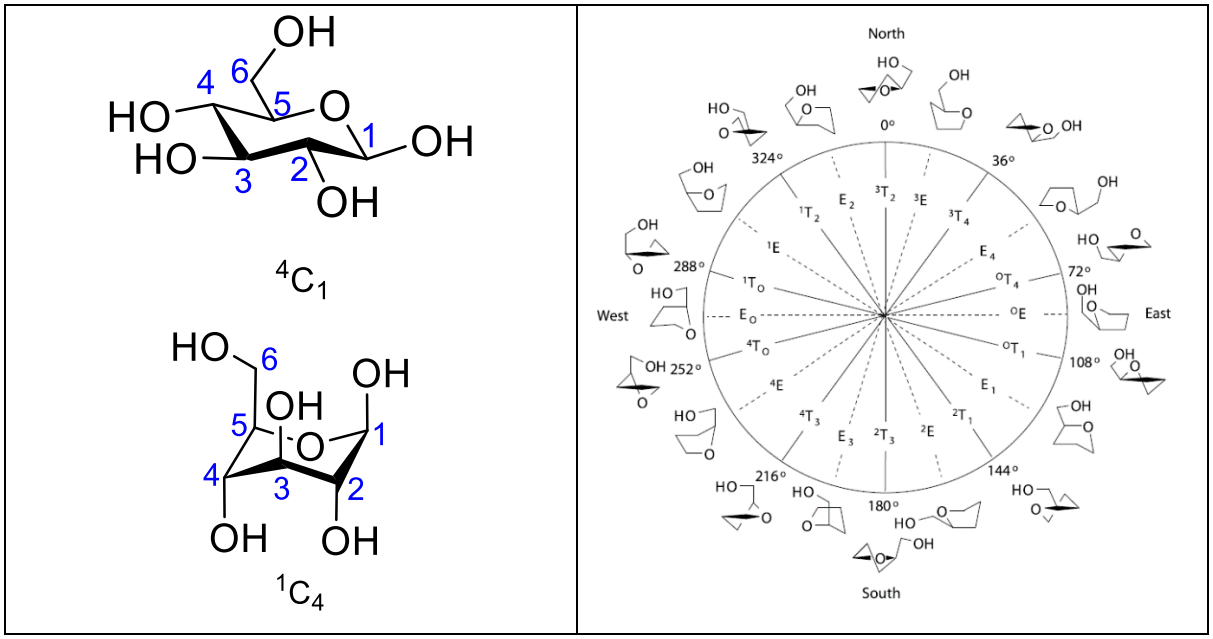



***Figure 1.1:*** *$^4C_1$: More stable chair conformation of the lowest number carbon C-1 is projecting below the reference plane, and C-4 is above the plane; $^1C_4$: the lowest number carbon C-1 is projecting above the reference plane, and C-4 is below the plane; in right (in left), Pseudo rotational itinerary for furanose (in right)* [4,5]

Pyranose conformation adopts chair conformation unless any destabilizing factor is present within the ring. Pyranose conformation can exist in two chair conformation, i.e., $^4C_1$ & $^1C_4$ (**Figure 1.1**). The chair is abbreviated as "C" and the position of the first and fourth atoms in the ring above and below the plane is given as superscripts and a subscript, respectively.

Other conformations for pyranose ring are boat, skew or twist-boat, and half-chair conformations abbreviated as B, S, and H, respectively. Furanose is present in envelope and twist conformations, but this description is skimpy for intermediate conformations. To explain these conformations, a pseudo-rotational itinerary which can be simplified using two formalisms: (i) Altona-Sundaralingam (AS) system and Cremer-pople (CP) system (**Figure 1.1**).

### 1.4 - Biological significance of glycans

The word glycan is synonymous with oligosaccharide.[6] Glycans can be homo or hetero-polymers of monosaccharide residue and can polymerize linearly or in a branched manner.

However, when it is conjugated to any aglycone residue, it is known as a glycoconjugate. Glycoproteins, proteoglycans, and glycolipids are the three primary classes of glycoconjugates. Further can be classified based on attachment to the glycan. Glycolipids and proteoglycans are attached via oxygen atoms; however, glycoproteins can be attached via *O*, *N*, *and S*- atoms.[7] Recently, it was found that glycans are also attached to the RNA and classified as RNA-glycan conjugate (**Figure 1.3**).[8]

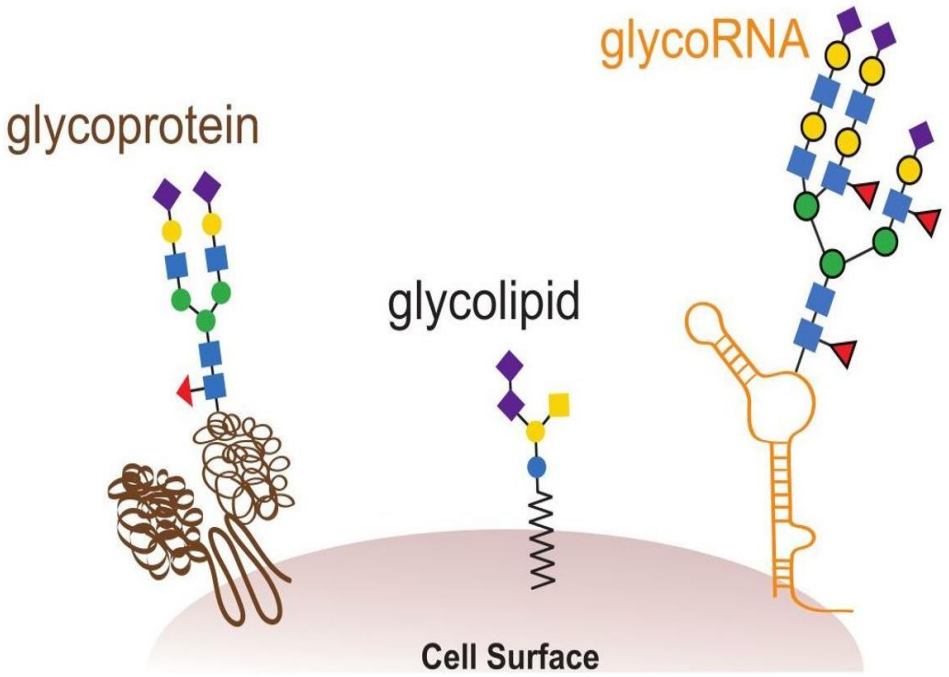



***Figure 1.3:*** *Cell surface glycoconjugates*[8]

Glycans are present in every cell of the kingdom of life including mammals, involved in a myriad of biological functions, broadly categorized into three categories mainly: (i) structural and modulatory functions, (ii) molecular mimicry of host glycans, and (iii) specific recognition by other molecules, glycan-binding proteins mainly. Glycan-binding proteins (GBPs) are of two types: Intrinsic GBPs and extrinsic GBPs.

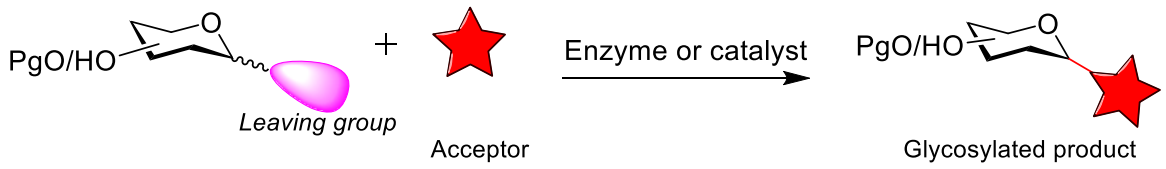
Structural and modulatory functions of glycans in eukaryotic are organizing, stabilizing, and protecting cells. Moreover, proteins folding, intracellular purposeful trafficking, lysosomal degradation, endocytosis, cell adhesion, and cell repulsion are other vital roles. Glycans are also involved in tuning protein functions, organization and modulation of growth factors, sink, and depot for biologically important molecules. Cell-cell and cell-pathogen interactions fall under specific recognition by other molecular functions of glycans.[9] Glycans immunomodulatory functions on the Fc region of IgG antibodies are crucial for antibodies-based development of therapeutics.[10] Carbohydrates are also present in several FDA-approved

carbohydrate-based drugs, typically removing carbohydrate moiety from the drug, abolishing its therapeutic value. These drugs can be categorized based on the number of carbohydrate residues present, e.g., monosaccharide based: Doxorubicin, Daunorubicin, Epirubicin, Epirubicin, Idarubicin (Anthracycline antibiotics and agents), Fludarabine phosphate, Stavudine, Adenosine, Gemcitabine, Ribavirin, Acadesine (Nucleotides and nucleoside and their analogs), Amphotericin B (Polyenes), Etoposide, Lincomycin, Clindamycin, pentostatin; disaccharide based: Sucralfate, Lactulose, Vancomycin; trisaccharide based: Tobramycin, Digoxin; and Oligosaccharides based: Heparin and heparin-like saccharides, streptomycin, Neomycin, Acarbose.[11,12]

Furthermore, Bacterial cell surface glycans are involved in pathogenesis, protection from environmental stress, and others. These glycans are highly conserved and accessible and, thus, crucial immunological targets for developing antibacterial vaccines.[13] Carbohydrate functions are now being elucidated in detail but have been slow compared with the pace of revelations in protein and nucleic acid chemistry. There are some technical challenges: determining the oligosaccharide sequence in a specific glycoconjugate is still challenging. Other than this, microheterogeneity in the product formed in the endoplasmic reticulum and Golgi apparatus. Thus, it is not easy to obtain a homogeneous and chemically well-defined glycoconjugate from biological sources.[14] With such material in hand, it is not easier to reveal other biological functions. In order to achieve pure and homogenous glycans or glycoconjugates, the synthetic root is one of the most preferred solutions.

**1.5 - Glycosylation**

Extraction of homogenous glycans and glycoconjugates from nature is a daunting task. Owing to their broad range of functions in biological processes, chemists started looking into alternate methods.



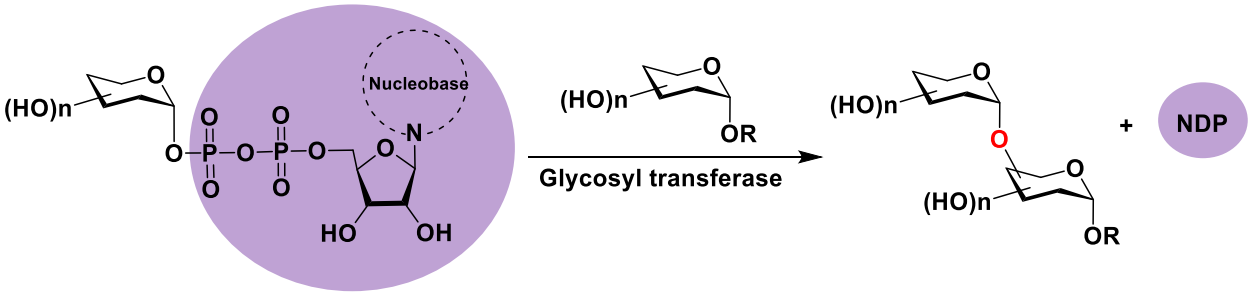

***Scheme 1.1:*** *Representation of glycosylation reaction*

Glycosylation is one of the alternatives to obtain glycans and glycoconjugates. Chemists came up with two types of glycosylations: (i) Enzymatic glycosylation and (ii) Chemical glycosylation. Glycosylation is a coupling reaction between a glycosyl donor and glycosyl

acceptor in the presence of a suitable promoter to give a condensation product. A Glycosyl donor is a sugar moiety with a leaving group at the anomeric position, and the glycosyl acceptor can be sugar, protein, lipid, or any other aglycon (**Scheme 1.1**).

### 1.5.1 - Enzymatic glycosylation[15–17]

Transferring sugar nucleotide donor substrate to the specific hydroxy group acceptor substrate by the enzyme (glycosyl transferase, exo-glycosidase, endo-glycosidase, and others) in stereospecific and regiospecific manner is known as enzyme-catalyzed glycosylation. Uridine diphosphate glycosyl donors are activated donors employed by glycosyl transferases in glycosylation. However, fucosyl- and mannosyl-transferases utilize guanosine diphosphate (β-GDP-Fuc, α-GDP-Man), and sialyltransferases utilize cytidine monophosphate (β-CMP-NeuAc) activated donors for glycosylation.




***Scheme 1.2:*** *Enzyme (glycosyl transferase) catalysed glycosylation*

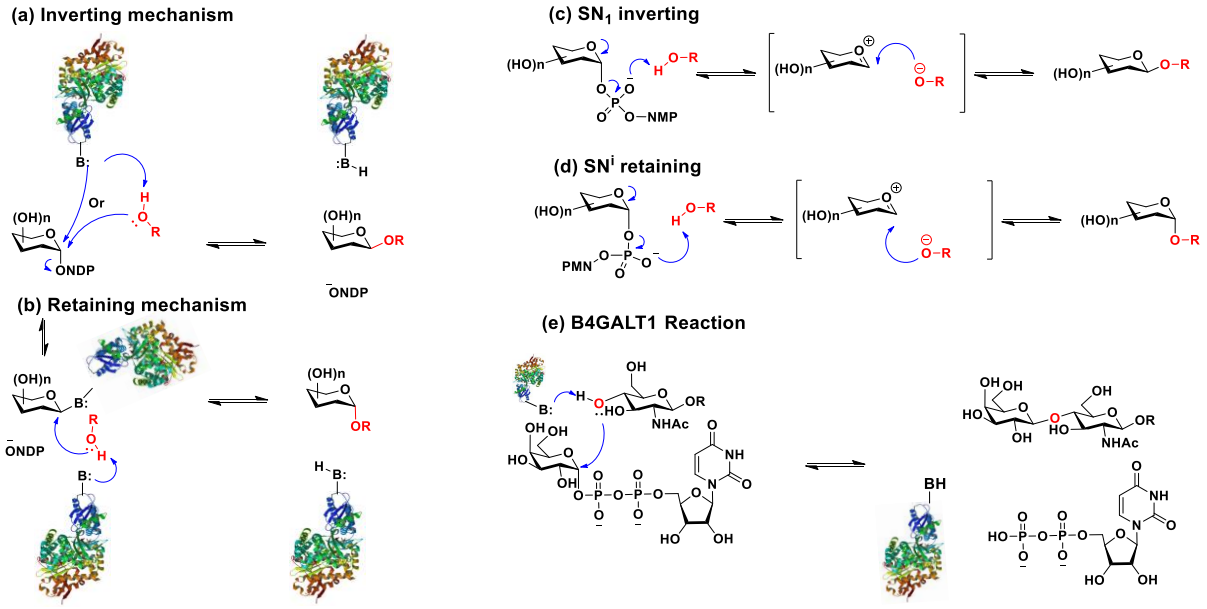
The carbohydrate-Active enzymes (CAZy) database (http://www.cazy.org) annotates nearly 500,000 GT sequences across all kingdoms of life and organize them into 106 different families (**Scheme 1.2**).

#### 1.5.1.1 - Mechanistic insights of enzyme catalysed glycosylation[15-17]

Glycosyl transferases use a restricted number of glycosyl-sugar-donors for the synthesis of different glycosidic linkages by transferring them into different position of glycosyl acceptors, either to invert or retain stereochemistry of the anomeric position.

The mechanistic path of the enzyme still needs to be clarified, and there are different proposed mechanisms. Inverting enzymes mostly follow the $S_N1$ inversion path, wherein the donor is transferred to the hydroxyl group of an acceptor from opposite phase to the leaving group of the donor, and displacement of leaving group from the opposite side yields inverted glycosylated product. Some enzymes attack the donor from opposite side of the leaving group and utilize basic groups for deprotection of the acceptor hydroxyl group. Further, enzyme-bound sugar transferred to the acceptor moiety from the opposite side leads to the retention of

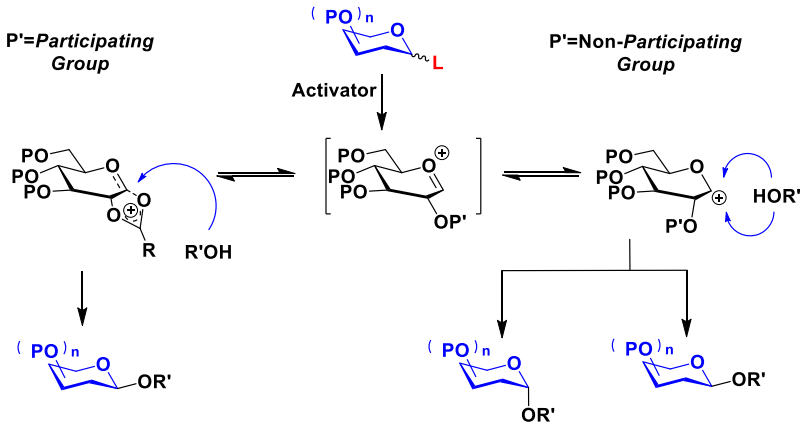
stereoselectivity at the anomeric position. A few inverting enzymes, without any catalytic base, have also been reported, following $S_N1$ inverting mechanism; wherein, the oxygen atom of *β*-phosphate assists in the deprotection of the hydroxyl group of the acceptor. The $S_Ni$ mechanism was recently proposed. In this mechanism, *β*-phosphate participates in the deprotonation of the acceptor hydroxyl group, and attack from the same side resulting in the retention of anomeric conformation (**Scheme 1.3**).




***Scheme 1.3:*** *Glycosyl transferase reaction mechanism. (a) $SN_2$ inverting mechanism (b) double displacement retaining mechanism (c) $SN_1$ inverting mechanism (d) $SN^i$ retaining mechanism (e) B4GALT1 reaction*

### 1.5.2 - Chemical glycosylation[18]

Glycosyl donor carrying a leaving group is activated by an activator in the presence of any water sequesters (molecular sieves) to generate an intermediate oxocarbenium ion after the departure of leaving group, which remains in equilibrium with ring carbocation, when there is no participating group present (generally at C-2 position). If any ester-type participating group is present at C-2, the cyclic acyltrioxolenium ion remains in equilibrium with the oxocarbenium ion. In the former case, the incoming acceptor carrying a free hydroxyl group or any other nucleophilic centre possibly attacks from both sides, yielding a mixture of products (1,2-*trans* and 1,2-*cis*). However, in the latter case, the cyclic acyltrioxolenium ion blocks one face, enabling the attack of the incoming nucleophiles from the opposite side to furnish a stereoselective (1,2-*trans*) product (**Scheme: 1.4**).




***Scheme: 1.4:*** *Chemical approach of glycosylation, intermediates during the reaction, and after-effect of protecting groups on output, L = leaving group, P = protecting group, R'OH = nucleophile or acceptor*

In other words, glycosylation is the genesis of glycosidic linkages, and these linkages can be *O-, N-, S-, and C*-linkages between acceptor and sugar residue from donor moiety. These linkages are termed *O-glycoside, N-glycoside, S-glycoside, and C-glycoside.* To synthesize these glycosides using chemical approach, a plethora of glycosyl donors have been developed by glyco-chemists worldwide.

No single donor enables the synthesis of all types of glycosidic linkages in a stereoselective manner. Owing to complexity of glycosylation, different glycosyl donors were developed in this direction. The highlights of developing donor chemistry are the activation of glycosyl donors using suitable promoters, the nature of protecting groups leading to the stereoselective outcome, and the orthogonal activation of glycosyl donors.

### 1.6 – Glycosyl donors and activators in chemical glycosylation[18,19]

Each of the glycosyl donors and activator(s) has its advantages and disadvantages. A plethora of glycosyl donors and activators for glycosylation reactions has been discovered since the beginning of glycosylation. Halide donors, imidate donors, thio donors, and alkyne-based donors are few examples of glycosyl donors (**Figure 1.4**). These donors can be activated using different activators, e.g., BrØnsted acids, Lewis-acids, metal salts, photo-catalysts, and organo-catalysts. These activators activate the leaving group of glycosyl donors in the following ways: (i) direct activation: wherein activation of leaving group takes place directly at the anomeric heteroatom, (ii) remote activation: wherein activation of the leaving group takes place in a remote atom or functional group and (iii) bidentate activation: wherein activation of leaving

group takes place from direct or remote activation mode, it depends on the activator used in the glycosylation reaction.

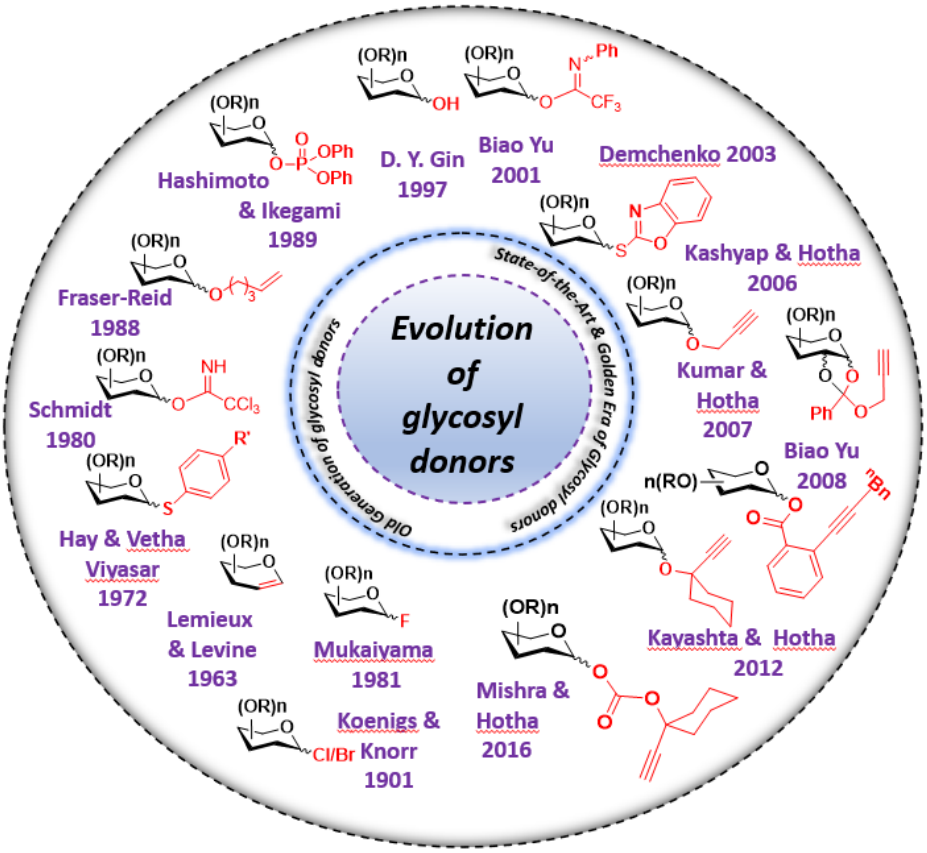



***Figure 1.4:*** *Different glycosyl donors and names of their pioneers with years of origin*

### 1.6.1 - Glycosyl halide donors[20]

Donor chemistry is more than a century old. Koenings|Knorr and Fischer|Armstrong introduced halide donors in 1901, activated using $Ag_2O$ and $Ag_2CO_3$ to synthesize glycosidic bonds, later different halide sources, e.g., AcBr, $BiBr_3$-$Me_3SiBr$, $PPh_3$/N-halo succinimide, and $PBr_3$ were employed for halide donor activation; and recently, different silver salts were also exploited. These glycosyl halides were very unstable and moister sensitive, which prompted chemists to look for other donors. Although glycosyl fluoride was known from the earlier days of glycosylation but exploited for glycosylation late in 1981 by the Mukaiyama group, this fluoride donor was thermally and chemically more stable than other halide donors. DAST, HF-py, $Ph_3P$/DEAD/$Et_3O$-$BF_4$, hexafluoropropane, 2-fluoro-1-methyl-pyridinum tosylate, etc. reagents can produce fluoride donors from lactol and different flourophilic reagents such as metal salts, Lewis acids activation produce the glycosidic product. Fluoride donor was also exploited for the stereoselective glycosylation of 2-*deoxy* sugars.

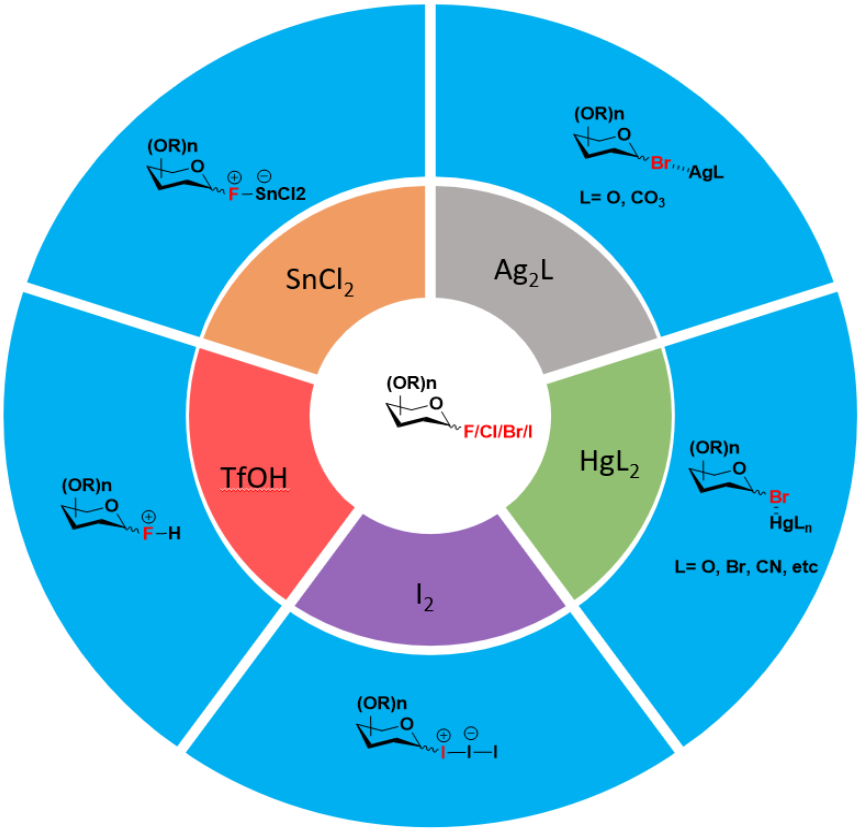



***Figure 1.5:*** *Different activators and their mode of activation. Inner circle showing halide donors, middle circular sections showing different activators, outer circular sections showing mode of activation of glycosyl donors*

### 1.6.2 – Thioglycosyl donors[21]

In 1972, Ferrier, Hay, and Vethavidyasar reported the thioglycoside donor and activated it with $HgSO_4$. For around two decades, different research groups discovered different thiophilic promoters, concluded that bromonium or iodonium ions are more thiophilic than other promoters reported earlier. Thioglycosides were found to be very stable under different reagents and uprise as a versatile glycosyl donor. In 1990, NIS/TfOH activation of thioglycosides was a pathbreaking discovery, and made it a versatile glycosyl donor. Thioglycosyl donor is associated with several advantages and disadvantages; advantages are: (i) activation under mild conditions, (ii) tolerance of routinely employed protecting groups, functional group transformation, and glycosylation conditions, (iii) easy to prepare from per-*O*-acetylated sugars under $BF_3$.$Et_2O$ conditions, and (iv) amenable for latent activation. The thioglycosyl donors are activated selectively under AgOTf/TolSCl at -78 ºC and cautiously raised in temperature, followed by repeating the promoter and acceptor, leading to the one-pot

synthesis of oligosaccharides are some of the advantages. The nasty odour of the starting thiols compounds and stoichiometric activation are among the significant disadvantages.

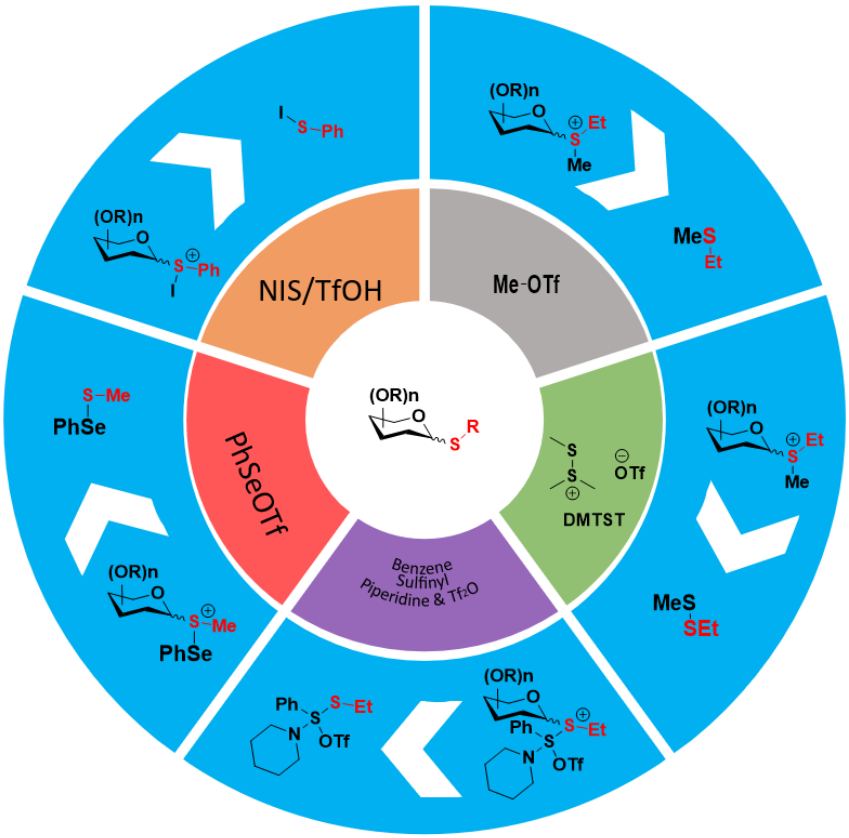



***Figure 1.6:*** *Different activators and their mode of activation. Inner circle showing thio donors, middle circular sections showing different activators, outer circular sections showing mode of activation of glycosyl donors and their extruded products*

### 1.6.3 – Imidate glycosyl donors[22,23]

Trichloroacetimidate donor was discovered by R. R. Schimdt in 1980; it is one of the most widely used glycosyl donor known to date. The donor can be easily synthesised using trichloroacetonitrile in the presence of any organic (e.g., DBU, DMAP) or inorganic base (e.g., $K_2CO_3$, $Cs_2CO_3$). Initially, strong Lewis acids, e.g., $BF_3{\cdot}Et_2O$, TMSOTf, $Tf_2O$, AgOTf, etc., were used to activate this donor. However, later scientists came up with different promotors like Lanthanum salts and Lanthanum triflates to overcome the toxicity of salts. $Bi(OTf)_3$ was introduced; molecular $I_2$ with $Et_3SiH$ was also employed to generate HI in an *in situ* to initiate the reaction. More recently, Pd- and Au- catalysts were found to be catalyse the glycosylation through promoter-acceptor-adduct and donor-enabled self-organized transition state leading to the stereoselective products. One of the drawbacks of an imidate donor is that this donor is

highly unstable and cannot be stored for a long time. A similar type of donor, N-phenyltrifluoroacetimidate, was advanced by Yu et al. in 2001. The aforementioned basic conditions for preparing trichloroacetimidate donor and *N*-phenyl trifluoro imidoyl chloride enable the synthesis of *N*-phenyltrifluoroacetimidate donor. The mode of activation is similar to the trichloroacetimidate activation. The leaving group of N-phenyltrifluroacetimidate donor is less competitive with the acceptor than the leaving group of trichloroacetimidate donor.

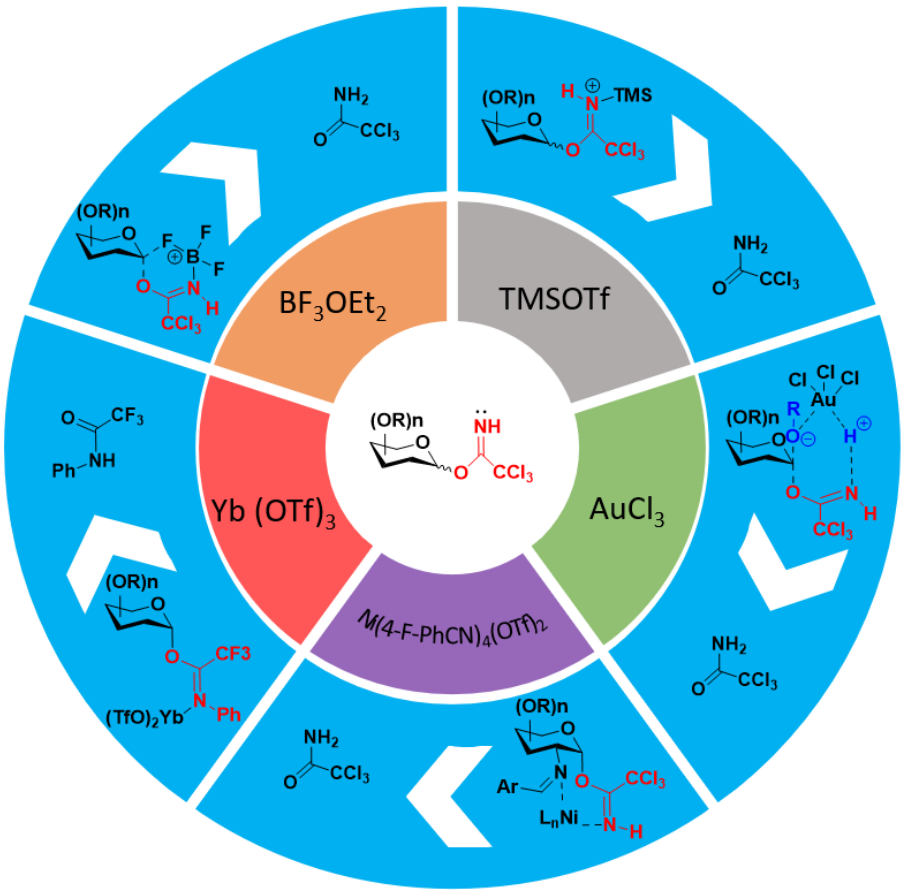



***Figure 1.7:*** *Different activators and their mode of activation. Inner circle showing imidate donors, middle circular sections showing different activators, outer circular sections showing mode of activation of glycosyl donors and their extruded products*

### 1.6.4 - Phosphate or phosphite donors[24]

Ikegami and Hashimoto discovered the phosphate donor chemistry and later, different groups introduced phosphite and other phosphate-based donors. These donors can be activated with a stoichiometric amount of TMSOTf, which is accountable for the limited substrate scope for glycosylation.

### 1.6.5 - Glycal donors[25,26]

Glycals were employed by the Ferrier group in glycosylation reaction and designated as Ferrier reaction. Different metal salts (e.g., $FeCl_3$, $ZnCl_2$, Ceric ammonium nitrate, etc.), Lewis acids, and metal triflates were exploited to activate glycals. Ferric triflate and per-*O*-acetyl glycals with alcohol in $CH_2Cl_2$ yielded *α*-isomer as a major product. In 2014, Hotha group incorporated hypervalent iodine in the reaction mixture to activate glycals and accomplished 2-*deoxy*-amino acid glycoconjugates. These donors are extremely useful for synthesizing 2,3-unsaturated glycosides, 2-*deoxy*-glycosides, and 2-*deoxy*-glycoconjugates.

### 1.6.6 - Alkyne donors and golden era of glycosyl donors

In the transition metal-catalyzed glycosylation series, the inception of gold (III) catalyzed glycosylation was discovered by Hotha and Kashyap in 2006. The innate alkynophilic nature of the gold catalyst was the propulsion of the reaction. Per-*O*-benzylated propargyl glycosides were activated using $AuCl_3$. However, this method was not suitable for activation of per-*O*-benzoylated donors. Moreover, high reaction temperature, prolonged reaction time, and stereoselectivity were other concerns.[27] To overcome these limitations associated with propargyl glycosyl donor, Hotha and Kayastha introduced 1-ethynylcyclohexanyl glycosyl donors, invoking the "Thorpe-Ingold-effect" and found attachment of cyclohexyl moiety in the donor improved the reaction reactivity. Addition of silver salt with Au (III) catalyst in reaction mixture solvated by acetonitrile and dichloromethane reduced the reaction temperature to room temperature and improved the yield of the glycosylation reaction. However, the glycosylation of per-*O*-benzoylated donors remained a mystery.

Thus, in 2016 Hotha and Mishra came up with yet another improved version of an alkyne donor chemistry by introducing a 1-ethynylcyclohexyl carbonate donor which was synthesized from the reaction of the protected hemiacetals and *p*-nitrophenyl ethynyl cyclohexyl carbonate in the presence of DBU base. This is indeed a remarkable discovery in the field of glycosyl donor chemistry. This donor is readily achievable, highly stable, and activated by a catalytic amount of commercially available Au(I)-Phosphite and AgOTf. All sorts of donors, e.g., armed donors (C2-Oalkyl), disarm donors (C2-O-acyl), acid-sensitive functional groups bearing donors (-Si, -THP,-MEM, -MOM etc), could be activated at room temperature within 15 min. Easy accessibility of donors, mild reaction conditions, ambient reaction temperature, short reaction time, and high stereoselectivity are the key highlights of this glycosylation method.[28] This glycosyl donor was exploited to synthesize oligosaccharides, e.g., tridecasaccharide

reminiscent, heneicosasaccharyl mannose capped arabinomannan, pentacosafuranoside of arabinogalactan, linear nonadecaarabinofuranoside, and branched heneicosafuranosyl arabinogalactan motif of *Mycobacterium tuberculosis* cell wall. Nevertheless, Fondaparinux pentasaccharide and *N*-glycosides were also synthesised utilizing the same donor chemistry.[29–32] Meanwhile, Yu's group also reported the gold-catalysed glycosylation method exploiting *ortho*-alkyne benzoate donor, which was activated by $PPh_3AuOTf$ catalyst[33].

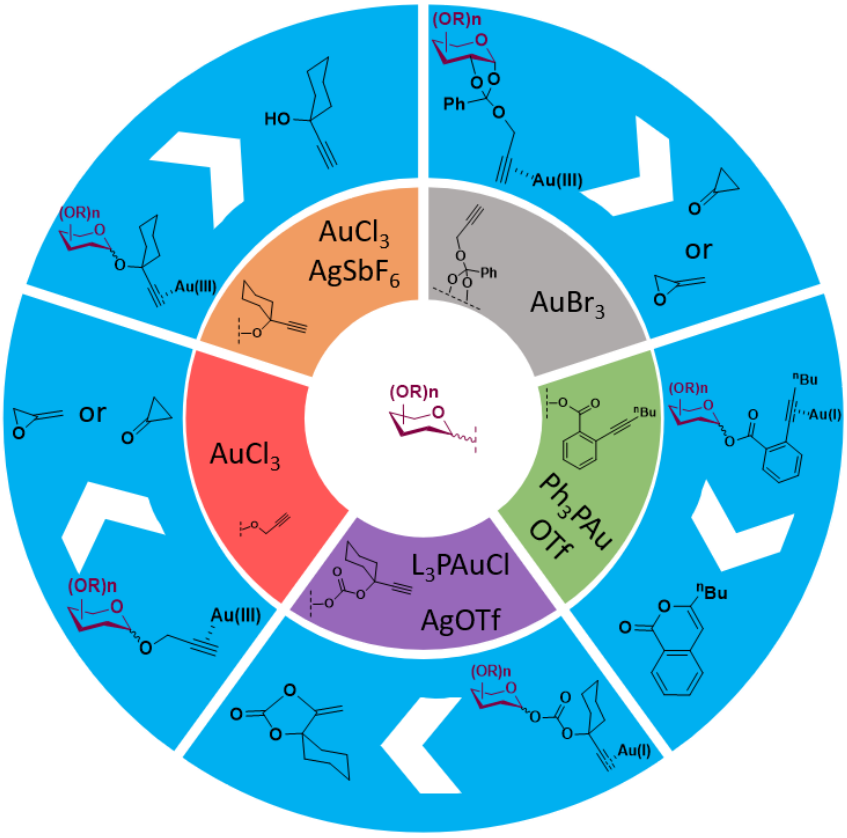



***Figure 1.8:*** *Different activators and donors with their mode of activation. Inner circle showing alkyne donors, middle circular sections showing different leaving groups and activators, outer circular sections showing mode of activation of glycosyl donors and their extruded products*

### 1.7 - Type of glycosides or glycosidic linkages

Glycosidic linkages can be classified based on atoms attached to the anomeric carbon and the orientation of the anomeric linkage.

#### 1.7.1 - Based on the atom attached to the anomeric carbon

Glycoconjugates are attached to an anomeric carbon atom of carbohydrates using different atoms. Nature has exploited mostly *O*-, *N*-, *S*-, and *C*- atoms for this purpose and these are commonly known as *O*-, *N*-, *S*-, and *C*-glycosides respectively.

*O-glycosides*: Glycosides attached to the sugar residue via oxygen atom are termed *O*-glycosides. All the disaccharides, oligosaccharides, and L-serine/L-threonine-*O*-glycosides fall in this category (**Figure 1.9**).

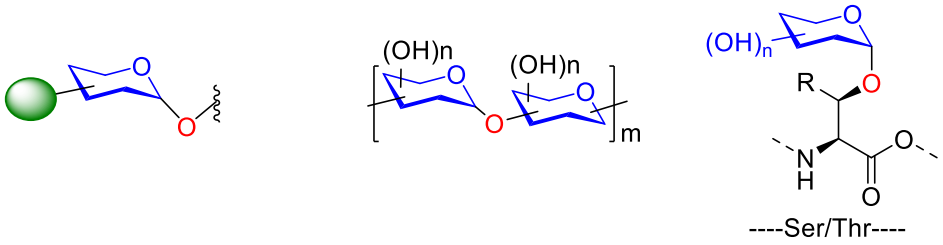



***Figure 1.9:*** *O-glycosides and some examples of O-glycosides*

*N-glycosides:* Glycosides attached to the sugar residues via nitrogen atom are *N*-glycosides.All the *N*-linked nucleosides and asparagine-linked glycoconjugates are a few examples (**Figure 1.10**).

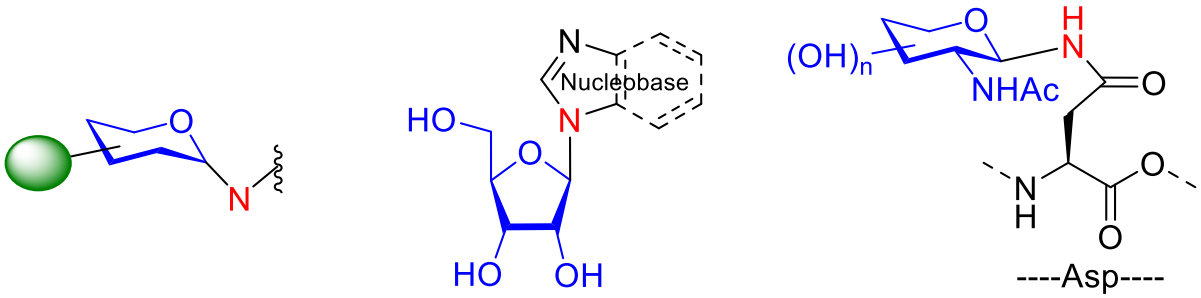



***Figure 1.10:*** *N-glycosides and some examples of N-glycosides*

*S-glycosides:*[34] Attachment of S-atom to the anomeric carbon of sugar moieties is rare. Raphanuside is an example of such kind of a *S*-glycoside (**Figure 1.11**).

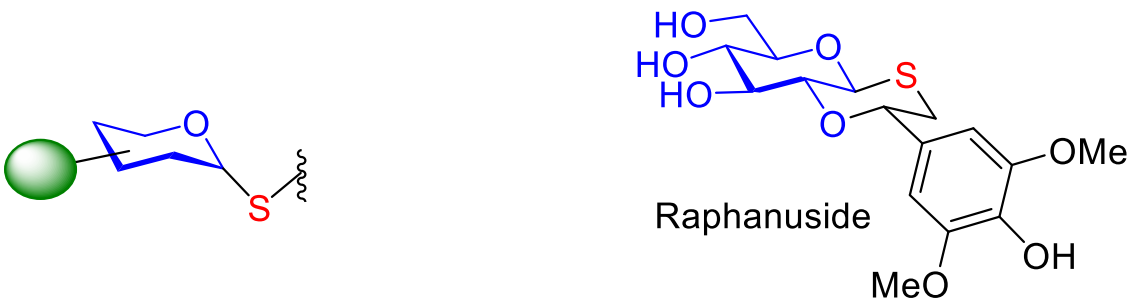



***Figure 1.11:*** *S-glycosides and one examples of S-glycoside*

*C-glycosides:*[35] When sugar and any aglycon are attached through C-C bond are known as *C-glycosides*, e.g., C-Mannosyl-Tryptophan (**Figure 1.12**).



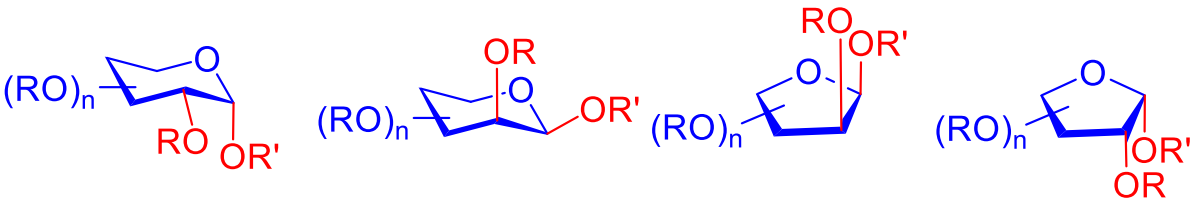

C-Manosyl-Tryptophan

***Figure 1.12:*** *C-glycosides and one examples of C-glycoside*

**1.7.2 – Based on orientation of the glycosidic linkage**

Based on the orientation of the linkage attached to the anomeric carbon atom of sugar residue, glycosidic linkages are classified into two types -

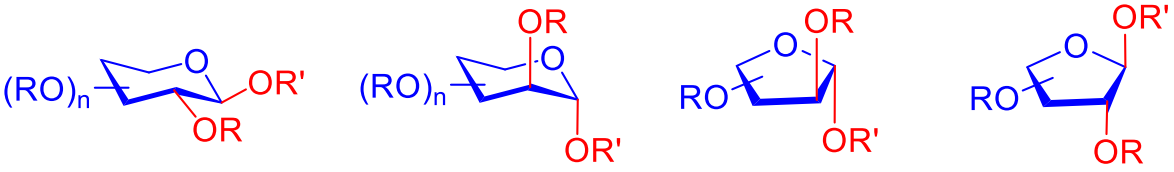
1,2-*Cis* linkages: Linkages attached to the C-1 & C-2 positions of the sugar residue are unidirectional (**Figure 1.13**).




1,2-*Cis* *α*-linkage | 1,2-*Cis* *β*-linkage | 1,2-*Cis* *β*-linkage | 1,2-*Cis* *α*-linkage

***Figure 1.13:*** 1,2-*Cis linkages in pyranose and furanose sugars*

1,2-*Trans* linkages: Linkages are in opposite direction at C-1 & C-2 positions of sugar residue (**Figure 1.14**).




1,2-*Trans* *β*-linkage | 1,2-*Trans* *α*-linkage | 1,2-Trans *α*-linkage | 1,2-*Trans* *β*-linkage

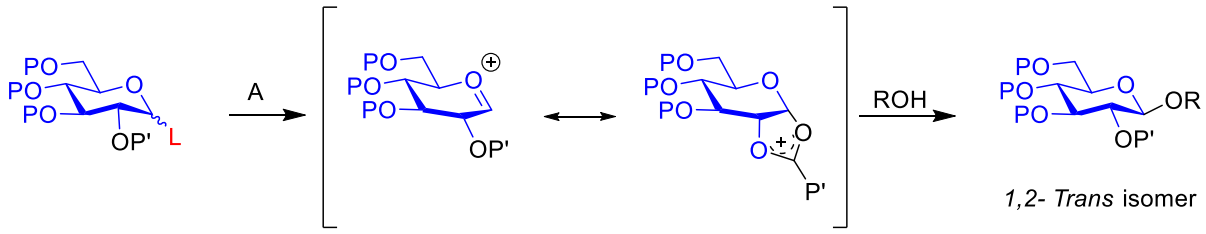
***Figure 1.14:*** 1,2-*Trans linkages in pyranose and furanose sugars*

**1.8 – Stereoselectivity in chemical glycosylation**

1, 2- *Cis* & 1, 2- *trans* are two possible products of glycosylation, commonly known *α* and *β*-stereoisomers. Stereoselective glycosylation is one of the major concerns during chemical glycosylation. Several methodologies have been developed by glycochemists' to control the stereoselectivity during chemical glycosylation.

### 1.8.1 - 1,2-*Trans* stereoselective approaches

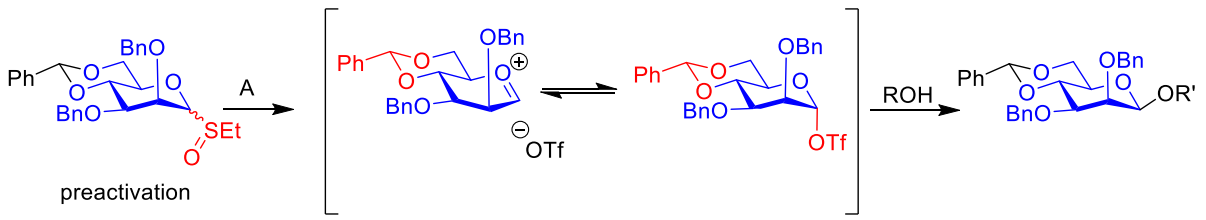
Synthesis of 1,2-*trans* stereoisomer can be achieved easily using the well-known concept of neighbouring group participation (NGP). In this approach, a participating group (mostly ester) present at the C-2 position to the anomeric carbon participates in stabilizing oxocarbenium resulted form after extrusion of leaving group, and block on the face, which favours the nucleophile attack from another face, leading to the 1,2-trans stereoisomer (**Scheme 1.5**).




***Scheme 1.5:*** *1,2-Trans stereoselective approach, P is protecting group, P' is participating group, L is leaving group, A is activator, ROH is nucleophile*

### 1.8.2 - *1,2-Cis* stereoselective approaches for pyranosides

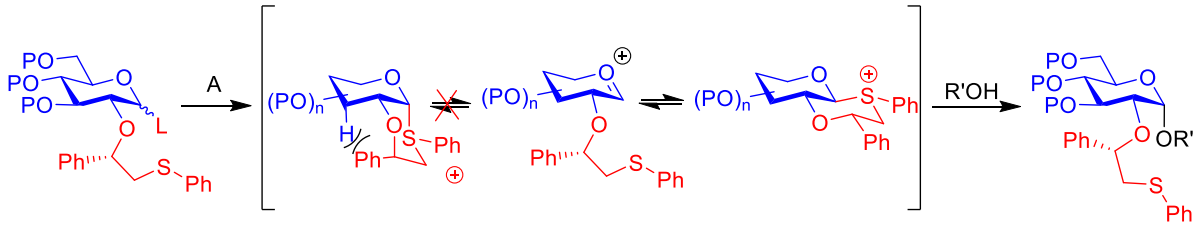
1,2-*Cis* stereoselectivity is one of the biggest hurdles in glycosides syntheses. No universal method is available for synthesizing exclusively 1,2-*cis* stereoisomers; different groups worldwide have developed different approaches for the same purpose. Some of the approaches are being discussed here. In 1997, Crich group introduced the concept of pre-activation of sulfoxide donor using a $Tf_2O$ activator at low temperature through triflate intermediate. The axial triflate ion is attacked by the acceptor from the equatorial position in an $S_N2$ manner, favouring the formation of 1,2-*cis* stereoisomer. However, this approach was limited to benzylidene-protected mannose glycosyl donors to give 1,2-cis mannosides (**Scheme 1.6**).[36]



***Scheme 1.6:*** *1,2-Cis stereoselective approach for mannose glycosides, A is activator, ROH is acceptor*

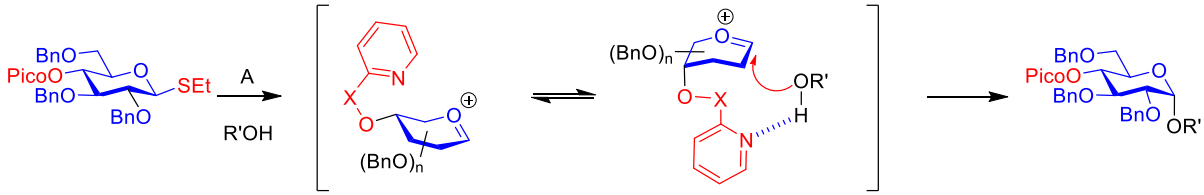
In 2005 Boon's group developed a methodology based on the participation from the C-2 position of glycosyl donor; (1*S*)-Phenyl-2-(phenyl sulfonyl) ether moiety was introduced at the C-2 position. After the generation of the oxocarbenium ion, the nucleophilic sulfanyl group participates from the C-2 position, leading to the formation of trans-decalin type of sulfonium ion intermediate, that remains in equilibrium with the oxocarbenium ion. However, the cis-decalin type intermediate formation was disfavoured by steric interactions.

The incoming nucleophile preferentially attacks from the axial side as the sulfonium ion intermediate coordinates from the equatorial side favouring the 1,2-cis stereoisomer. However, this method failed to facilitate exclusive stereoselectivity (**Scheme 1.7**).[37]




***Scheme 1.7:*** *1,2-Cis stereoselective approach, P is protecting group, L is leaving group, A is activator, R'OH is nucleophile*

A different type of approach was introduced by Demchenko group in 2012. Wherein, picolinyl or picoloyl was incorporated at different positions of the glycosyl donor as an "H-bond acceptor" for hydrogen bond-mediated aglycon delivery of nucleophiles, envisioning *syn*-glycosylation. 1,2-Cis stereoselective glycosylated product was observed from C-4 pico-functionality, which is possible through hydrogen bonding between the nitrogen atom of the picoloyl or picolinyl functionality and nucleophile moiety (**Scheme 1.8**).




***Scheme 1.8:*** *Hydrogen bond mediated aglycan delivery, A is activator, R'OH is nucleophile, X can be carbonyl or methylene*

Dilution significantly increases stereoselectivity, owing to decreased probability of a non-stereoselective attack of unbound nucleophiles. Moreover, adding DMSO to the reaction mixture also decreases the stereoselectivity (DMSO disturbs the H-bonding), suggesting the presence of H-bonding between the acceptor and pico-functionality. Nevertheless, TMS-protected acceptors were not stereoselective, which supports the role of hydrogen bonding in *syn* selectivity. Moreover, the benzylidene-protected donors did not enable *syn* selectivity; this suggests that flexibility in the sugar ring is also essential since the oxocarbenium ion generated in the reaction mixture remains in equilibrium between two flipped rings (all axial and all equilibrium) conformations - all axial conformation is crucial for the *syn* attack of the nucleophile. Stereoselective glycosylation was achieved in good to excellent facial selectivity using this method. However, complete stereoselectivity remains a challenge in this hydrogen bond assisted glycosylation reaction.[38]

### 1.8.3 - 1,2-Cis stereoselective approaches for furanosides

1,2-Cis selectivity in furanosides is much more challenging owing to the weak anomeric effect in furanosides and the inherent flexibility of furanose rings to adopt several twists and enveloped conformations. Pseudo-rotational itineraries explain these conformations. One way of achieving stereoselectivity can be by inhibiting the flexibility of furanose rings by locking or freezing the intermediate formed during the glycosylation reaction into a rigid conformation; using this approach several groups have developed different approaches.

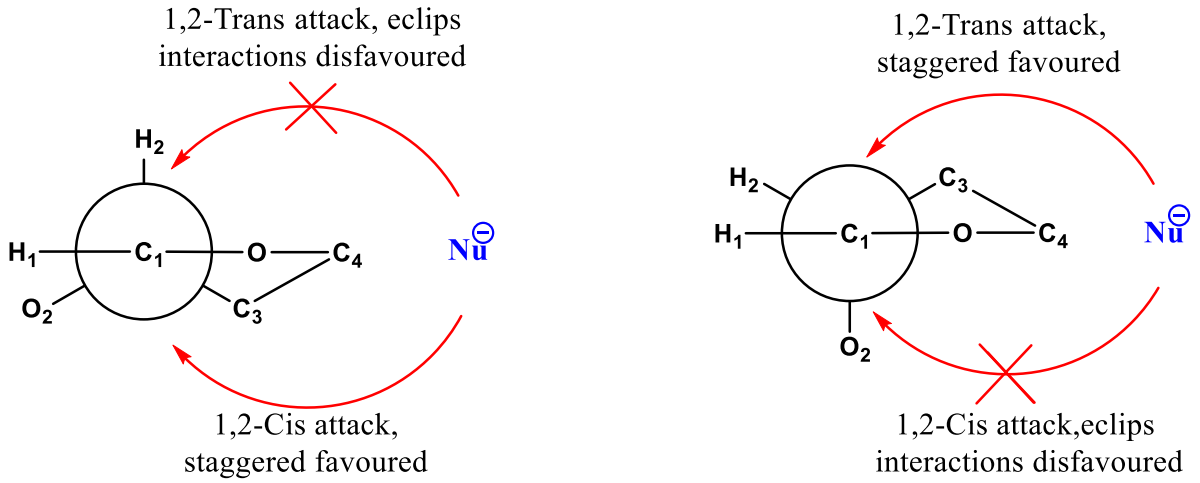
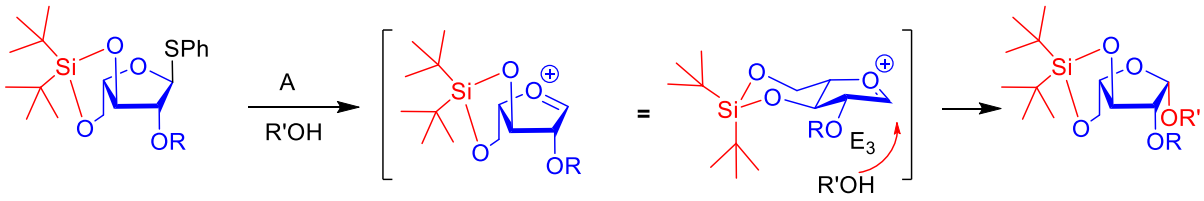



***Figure 1.15:*** *Nucleophilic approach in $E_3$ (left) and $^3E$ (right) conformers of oxocarbenium ion in their Newman projections showing disfavourable and favourable attack*

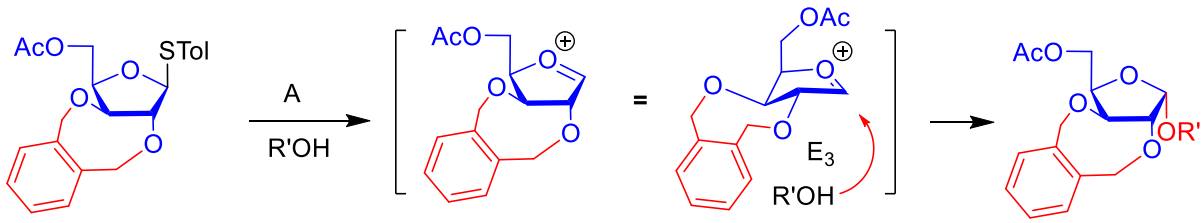
In this regard, Boons group in 2006, proposed one approach for stereoselective glycosylation of furanosides. They locked the C-3 and C-5 hydroxyl group by the di-*tert*-butyl silane protecting group, which was hypothesized to provide rigidity to the furanoside oxocarbenium ion intermediate formed during the glycosylation. Oxocarbenium ion has a double bond character between the ring oxygen and C-1 carbon atom, making C-4, ring oxygen, C-1, and C-2 become co-planar. C-3 carbon can either be below the plane ($E_3$-conformer) or above the plane ($^3E$-conformer) to minimize the oxocarbenium ion's potential energy and ring strain.

The Newman projection of $E_3$ and $^3E$ conformer suggests that the staggered attack favours the eclipsed attack because interactions in the eclipsed conformer disfavour the nucleophilic attack. However, it was suggested by DFT and other theoretical calculations that $^3E$ conformation is distorted and internal ring strain is responsible for less probability of product formation via this conformation. Hence, 1,2-*cis* stereoselective product formation occurs via *syn* attack of the nucleophile on the $E_3$ conformation (**Figure 1.15**).[39]




***Scheme 1.9:*** *Locked conformation directed 1,2- cis glycosylation, A is activator, R'OH is nucleophile*

Stereoselective glycosylation was accomplished by exploiting rigidity nourished by di-*tert*-butyl silane moiety in furanosides. However, complete selectivity in all the furanosides is impossible with this method. Thus, *cis*-stereoselective glycosylation remains an open field for researchers to work on (**Scheme 1.9**).

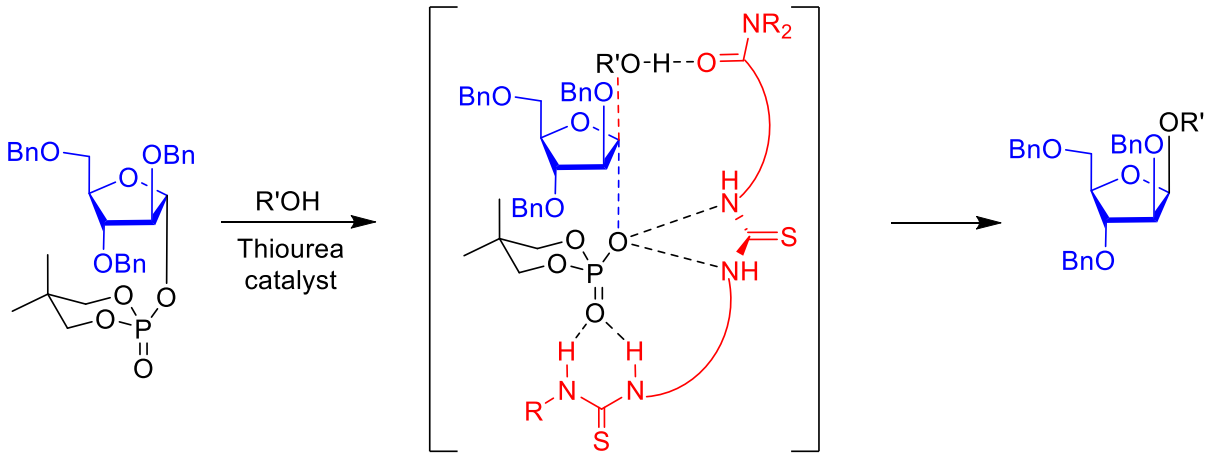



***Scheme 1.10:*** *Locked conformation directed 1,2- cis glycosylation, A is activator, R'OH is nucleophile*

A similar type of approach was introduced by Lowary group for the 1,2-*cis* selectivity by introducing 2,3-*O*-Xylylene protected glycosyl donor. The selectivity was obtained by locking

the oxocarbenium ion intermediate into the most stable and conformationally rigid $E_3$ conformation, wherein C-3 remains below the plane, and all other ring atoms should be in a plane owing to the partial double bond character between ring oxygen and C-1 carbon atoms. The disfavourable eclipse effect at the top of the plane forces nucleophiles to attack from the bottom of the plane (**Scheme 1.10**).[40]

However, complete stereocontrol remains the biggest challenge in obtaining *cis*-selectivity. All the strategies are highly specialized for specific cases and dependent on the specific protecting groups, which limits their substrate scope. Inspired by enzyme-catalyzed glycosylation, Jacobsen group introduced a bis-thio-urea-based catalyst for 1,2-*cis* glycosylation. Due to their highly reactive nature, they could not isolate aromatic phosphate donors, and aliphatic phosphate donors were less reactive toward the bis-thio-urea-based catalyst. In contrast, cyclic phosphate donor readily activated by hydrogen bonding between two oxygen atoms of the phosphate donor and two thiourea moieties, and activation of the acceptor occurred through general base interaction with one of the amides present in the bis-thiourea-based catalyst. The essentiality of two thiourea moieties in the catalyst was confirmed by a controlled experiment, wherein glycosylation was performed in the presence of mono-thiourea moiety, and selectivity decreased significantly.




***Scheme 1.11:*** *Thiourea catalysed 1,2- cis glycosylation, R'OH is nucleophile*

The activated acceptor attack from the backside of leaving the group in an $S_N2$ manner to furnish the highly stereospecific product (**Scheme 1.11**).[41]There are many other approaches for stereoselectivity other than those discussed here. Unfortunately, none of them claim to produce stereoselective products for all types of glycosyl donors. Hence, 1,2-*cis* selectivity remains as one of the biggest obstacles in the glycosylation and oligosaccharide syntheses.

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# *Chapter 2*

## *Chemical Synthesis of MTX-Capped Octasaccharide from Mtb Cell Envelope*

## 2.1 - Introduction

Tuberculosis is one of the major global health issues and causes ill health among millions of humans each year. After HIV, it was the second leading cause of death from an infectious disease worldwide until the Covid-19 pandemic. *Mycobacterium tuberculosis* is a causative agent of TB, which typically affects the lungs but can affect other parts of the body and is carried by air from one person to another.[1]

Around 8.6 million people developed TB, and 1.3 million deaths were reported (including 320000 deaths among HIV-positive people) in 2013. Without proper treatment of TB, the mortality rate is very high. The treatment success rate is around 85%. However, in the case of patients with multidrug-resistant TB (MDR-TB), the success rate is much low. In 1993, the world health organization (WHO) declared TB a global health emergency. Since then, significant progress has been made, and it has been observed that mortality rates are falling in most parts of the world (**Figure 2.2**).

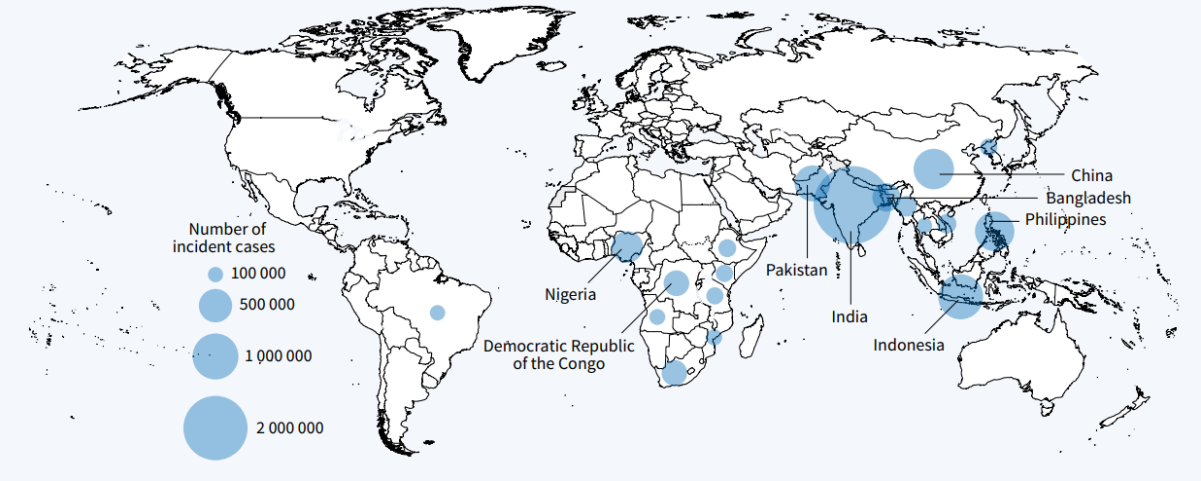



***Figure 2.1:*** *Estimated TB incidence in 2021, for counties with at least 100000 incident cases*[2]

In 2021, eight countries contributed to global TB incidence the most are: India (28%), Indonesia (9.2%), China (7.4%), Philippines (7.0%), Pakistan (5.8%), Nigeria (3.6%) and Bangladesh (3.6%), Democratic Republic of Congo (2.9%). Furthermore, it has been found that men were affected more than women, and children were affected the least. There are 150-400 cases of TB per 100000 population in most countries, contributing to a high number of cases. Drug-resistant (DR-TB) and multidrug-resistant (MDR-TB) is a significant concern, the number of cases of DR-TB and MDR-TB was constant during 2015-2020, and a significant increment was observed during 2020-2021 (**Figure 2.2**).[1]

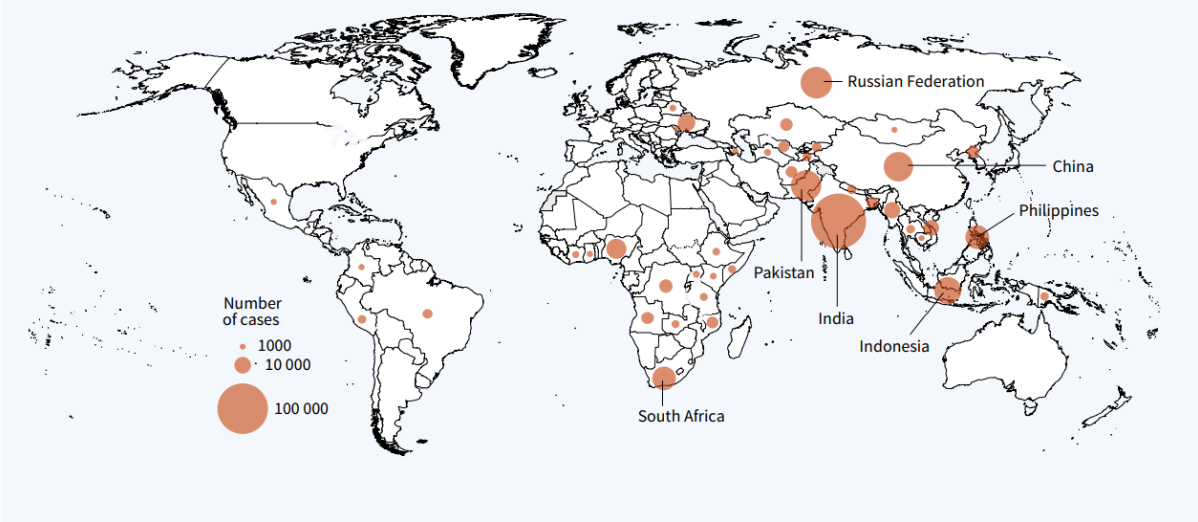



***Figure 2.2:*** *Estimated incidence of DR/MDR-TB in 2021, for countries with at least 1000 incident cases*[2]

Despite its relatively low sensitivity, sputum smear microscopy is the most widely used diagnostic test for TB. Culture in liquid media is another technique. However, culture-based diagnosis is only widely available in some parts of the world because it requires sophisticated laboratory and biosafety infrastructure, and test results take several weeks. Another breakthrough in TB diagnosis is rapid molecular tests used to diagnose TB and rifampicin-resistant TB at decentralized levels of health systems. However, TB remains unique among the major infectious diseases needing more accurate and rapid point-of-care tests, mainly due to insufficient progress in biomarker discovery despite ongoing research. There are several technologies endorsed by WHO for the diagnosis of tuberculosis, e.g., Xpert MTB/RIF, line probe assays are molecular technologies, Ziehl-Neelsen, and fluorescence microscopy is a microscopy-based technology. Commercial liquid culture systems and rapid speciation, and non-commercial culture and drug susceptibility testing methods are culture-based technologies.

Rifampicin, one of the most effective first-line drugs, was developed in the 1960s. Isoniazid, rifampicin, ethambutol, and pyrazinamide are a few other drugs developed later for treating TB. Vaccination is the most effective way of fighting against any epidemic; Bacille Calmette-Guérin (BCG) is the only vaccine currently used against TB. However, BCG applies to children. It has been observed that cellular immunity is a must for protection against TB. Hence, all the vaccines in the development of focusing on strong and durable cellular immune response.[2]

## 2.2 - Cell envelope of *Mycobacterium tuberculosis*

The cell envelope is a complex, dynamic, and multilayer structure responsible for the survival and protection of bacteria in a hostile environment. Based on the cell surface, bacteria are classified into gram-negative and gram-positive. Gram-negative bacteria contain inner as well as outer membranes. A thin peptidoglycan layer surrounds the inner membrane. The outer membrane contains polysaccharides from the outside and contains phospholipids inner side of the membrane. This outer membrane acts as a permeability barrier that controls the requirement of ions, nutrients, and toxins inside the cell in these bacteria.

In contrast, Gram-positive bacteria contain only an inner membrane surrounded by thick peptidoglycan (PG) layer from outside, which is further surrounded by different proteoglycans, oligosaccharides, capsular polysaccharides, carbohydrate-based, and phosphate-based polymers known as wall teichoic acids (WTA). WTAs are connected to the PG via the phosphodiester ligand at the reducing end and the main polymeric chain at the nonreducing end. Another class of anionic glycopolymers is lipoteichoic acids (LTA) comprised of the poly-glycerol phosphate chain anchored to glycolipid in cytoplasm membrane and, along with PG-bound WTA and extracellular proteins, play various role in their physiology and, interaction with the environment (**Figure 2.3**). [3]

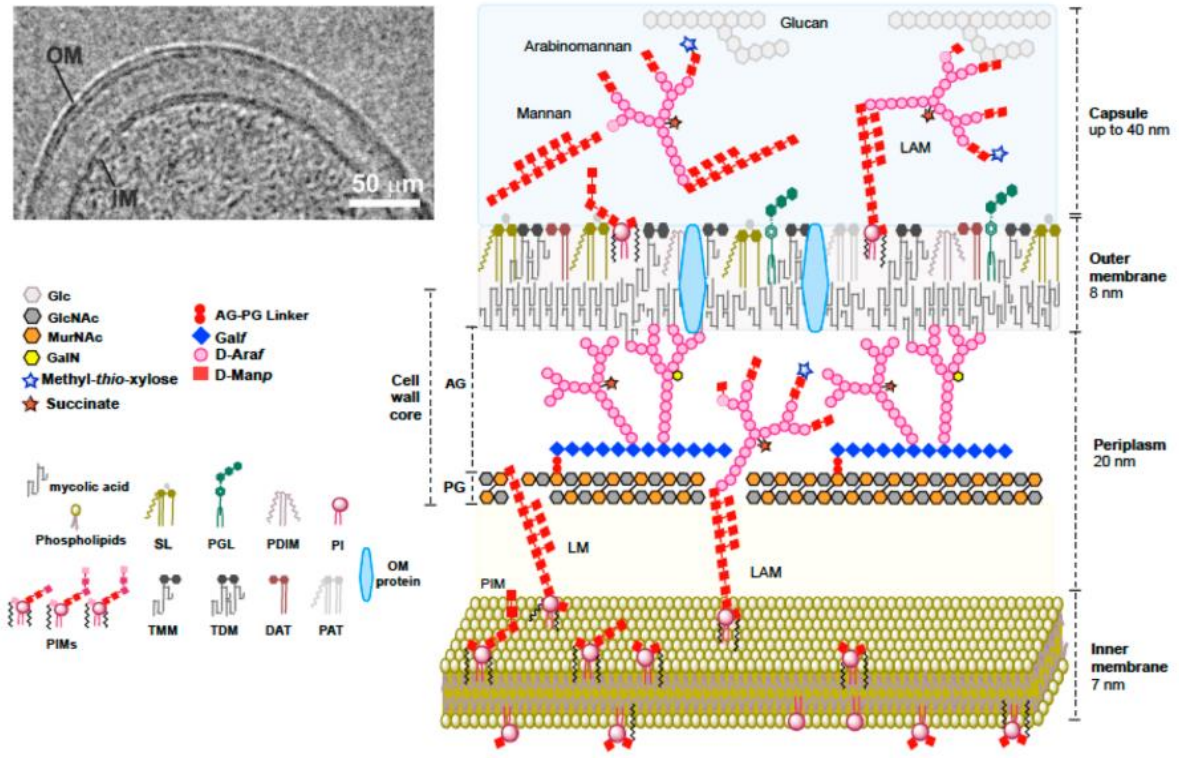



***Figure 2.3:*** *Cell envelope of mycobacterium tuberculosis*[4]

Structural components divide the cell envelope into three types: plasma membrane, wall, and capsule. The plasma membrane does not play any significant role in the pathological process. The wall contains a periplasmic region between peptidoglycans and membrane, and mycolate ester containing arabinogalactan proteoglycans (mAGP) are covalently attached to the PG. Non-reducing end of arabinogalactan is attached to the mycolates, which are esters of mycolic acids, one type of long-chain ($C_{60}$, $C_{90}$) fatty acids. The mAGP provides rigidity to the outside inner membrane, which is crucial for the structural integrity of the cell envelope. Loosely bonded peptides, lipids, and different polysaccharides are present in the capsular region, and these capsular components are involved in pathogenesis and host-pathogen interactions.[6] Cardiolipin (CL), phosphatidylethanolamine (PE), and phosphatidylinositol (PI) are the main phospholipids present in the mycobacterial inner membrane. Phosphatidylinositol mannosides (PIMs), lipomannan (LM), and lipoarabinomannan (LAM) are other phospholipids (**Figure 2.3**).[5–7]

### 2.3 - Symbolic diagrams of cell envelope glycans

Cell envelope is dominated by three major glycans: arabinogalactan (AG), lipomannan (LM), and lipoarabinomannan (LAM).

#### 2.3.1 - Arabinogalactan (AG)

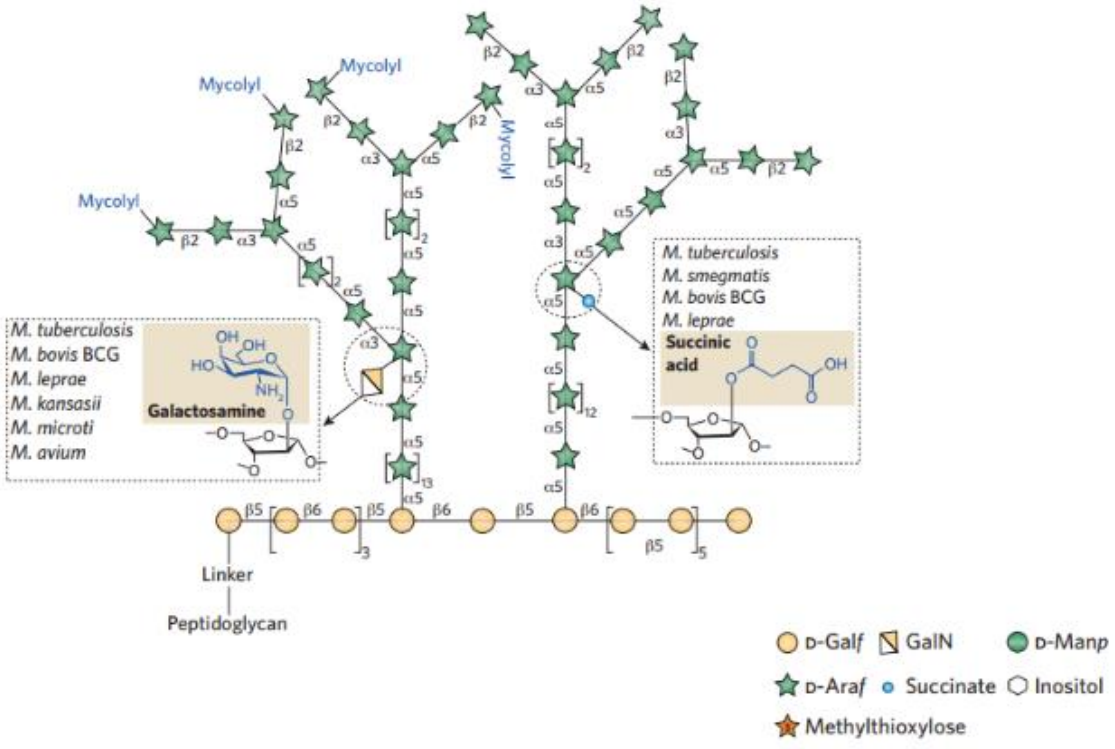



***Figure 2.4:*** *Symbolic representation of arabinogalactan in different mycobacteria*[8]

Arabinogalactan mainly contains three units: linker unit, D-galactan, and D-arabinan units. Arabinan and galactan contain arabinose and galactose residues in the furanose ring form, respectively. Galactan works as the backbone for the arabinogalactan; it contains around 30 galactofuranose (Gal*f*-) linked via *β*-(1→5) and *β*-(1→6) linkages alternatively and further linked to the L-rhamnose residue of the linker unit. Three arabinan units are attached as pendants to the galactan backbone through a *α*-(1→5) linkage at C-5 hydroxyl of *β*-(1→6)-linked Gal*f*- residue. Arabinan domain is a linear chain of *α*-(1→5)-arabinofuranose (Ara*f*-), occasionally substituted at the C-3 hydroxyl group of the arabinose residue via *α*-(1→3)-linkage forming 3,5-Ara*f*- branch points, and terminated by *β*-(1→2) Ara*f*- residues. The C-2 position of some of the 3,5-Ara*f*- branch point residue is modified with galactosamine (Gal*p*N) or succinyl substituents. Gal*p*N substituents have been found in *Mycobacterium tuberculosis* and other slow-growing pathogenic mycobacteria. However, succinyl residues have been found in both slow as well as fast-growing species (**Figure 2.4**).[9]

### 2.3.2 - Lipoarabinomannan (LAM)

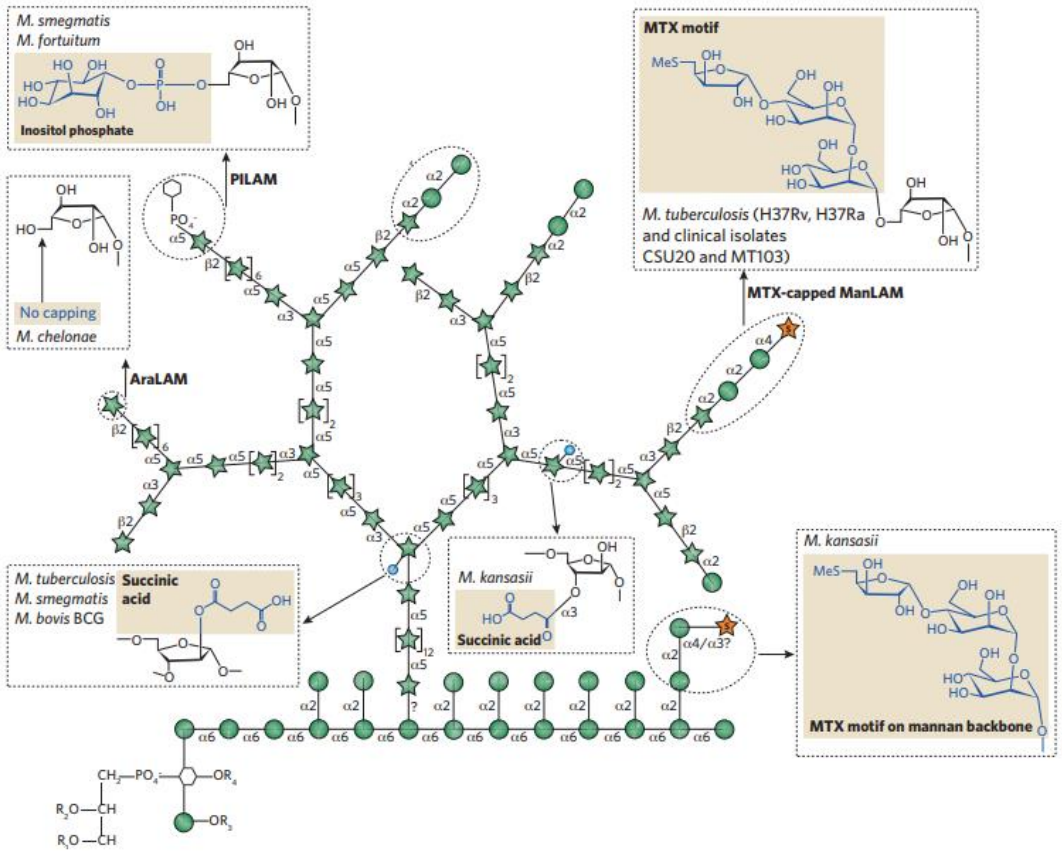



***Figure 2.5:*** *Symbolic representation of lipoarabinomannan in different mycobacteria*[10]

Lipoarabinomannan contains three major domains: MPI anchor, mannose polysaccharide backbone, and arabinan domain. MPI domain contains glycerol-3-phospho (1-D-*myo*-inositol) unit whose mannose residue is linked at *O*-2 and *O*-6 of *myo*-inositol. Mannose polysaccharide backbone is made up of $\alpha$-(1→6)-linked mannose residues and branched at the C-2 position by $\alpha$-(1→2)-linked one to three mannopyranosyl motifs. Arabinan domain is attached as a pendant to the mannose polysaccharide backbone at the C-6 hydroxyl group via $\alpha$-(1→6)-linkage. Arabinan domain is constructed by $\alpha$-(1→5)-linked arabinofuranose residues, occasionally branched at C-3 hydroxyl of arabinofuranose residue to form $\alpha$-(1→3)-linkages, and terminated by $\beta$-(1→2) Ara*f*- residues. LAM is further capped by one to three $\alpha$-(1→2)-linked mannose residues in *Mycobacterium tuberculosis* and other pathogenic mycobacteria, giving rise to the mannosylated LAM known as ManLAM.[12] Mannose caps of ManLAM are further substituted by $\alpha$-(1→4)-linked methyl-thio-D-xylofuranose residue (**Figure 2.5**).[11]

### 2.4 – Biological function of LAM, ManLAM, and MTX -capped ManLAM

Glycans on the cell surface play significant roles, including host-pathogen interaction and immune modulation. Owing to the structural complexity, ManLAM is recognized by several receptors. Mannose receptor (MR), DC-SIGN, and surfactant protein D recognize the mannose caps in ManLAM.[14,15] Dendritic cell immuno-activating receptor (DCAR), toll-like-receptor-2 (TLR-2), mannose-binding proteins (MBP), and CD1 recognize the PIM region of the

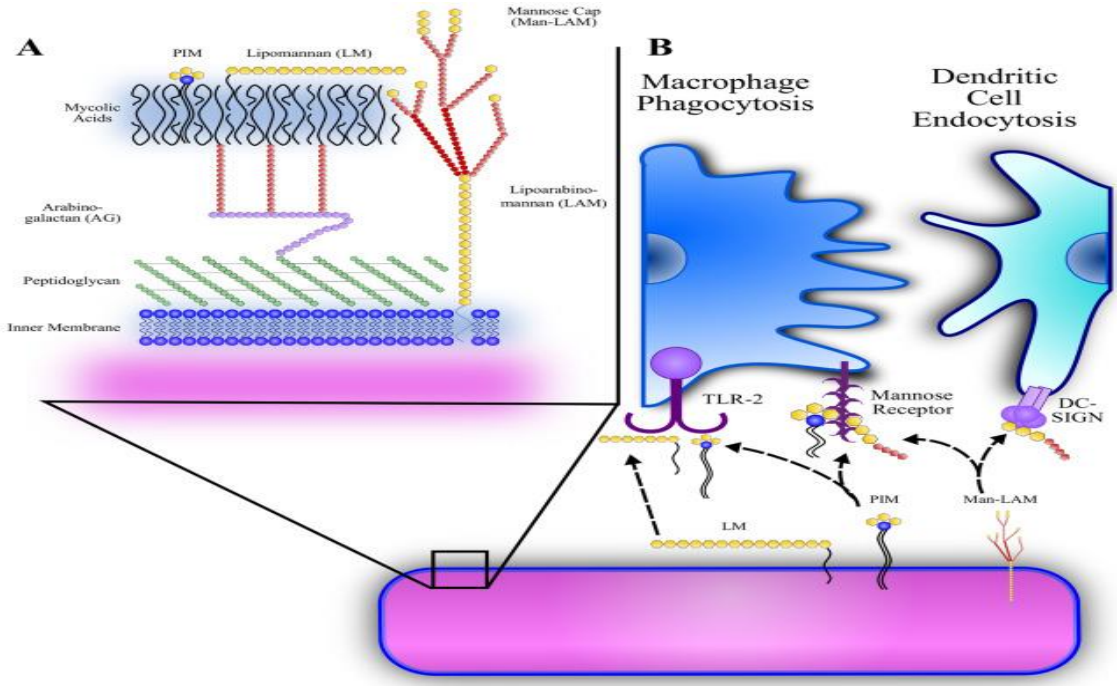



***Figure 2.6:*** *Recognition of cell surface Glycan of Mtb by different receptors (https://www.sciencedirect.com/topics/medicine-and-dentistry/lipomannan)*

ManLAM (**Figure 2.6**).[12–14] Pulmonary surfactant protein A (PS-A), Dectin-2, and CD44 are other molecules and receptors that bind to the ManLAM.[19–21] Macrophages and dendritic cells (DCs) are involved in phagocytosis and endocytosis of Mtb when mannose receptors and DC-SIGNs recognize ManLAM. T-cells recognize[22,23] LAM and other capping motifs with the help of the non-polymorphic MHC molecule CD1. These molecules are expressed on innate CD1-restricted T-cells and NKT-cells. Once the mycobacterial lipids are recognized, CD1-restricted T-cells activate and proliferate, starting secretion of Th1-type inflammatory cytokines (i.e., IFN-γ).[24] ManLAM are also involved in regulating T-cells response, and B-cell recognition of ManLAM generates more protective antibodies. Roles of ManLAM in reducing the immunosuppressive functions and limiting phagosome-lysosome fusion can be modulated by antibodies developed against it, and can also act as biomarkers for the Mtb infections.[15–17]

### 2.5 - Chemical synthesis of LAM and other capping motif of LAM

Owing to aforementioned significant role of LAM and the capping motif of LAM on the cell envelope of Mtb, the availability of these biomolecules is highly demanding. One way of availing these molecules is extraction from bacterial cells. However, purity is a major concern. The best alternative is chemical synthesis, which provides the desired molecule with desired stereoselectivity and regioselectivity. Many research groups across the world have chemically synthesized different fragments of LAM, and its capping motifs, some of the syntheses are mentioned below:

#### 2.5.1- Synthesis of 28-mer by Fraser-Reid *et al.*[18]

Fraser-Reid's group synthesized 28-mer, a fragment of ManLAM with an inositol motif at the reducing end, exploiting the [16+12] strategy to obtain the octacosasaccharide. In this journey, they mainly highlighted the importance of *n*-pentenyl ortho-ester donors, developed in their group and activated with ytterbium triflate and *N*-iodosuccinimide.

#### 2.5.2 - Synthesis of miniature LAM by Guo *et al*[19]

A highly convergent synthesis of miniature LAM mimetic was carried out by Guo's group, which contains all the three major domains of the LAM i.e., phosphatidyl inositol linked mannosyl domain, mannan, and arabinan domain, using thio-donor chemistry which was activated by *p*-toluenesulfenyl chloride (*p*-TolSCl) and silver triflate (AgOTf).

### 2.5.3 - Synthesis of arabino mannan fragments by Lowary *et al*[20]

Seven different arabinomannan fragments from the Mtb cell envelope were synthesized by Lowary group, exploiting an orthogonally protected mannose trisaccharide common motif. Reducing end of these oligosaccharides was attached to an amino-group containing linker for subsequent bioconjugation.

### 2.5.4 - Synthesis of 21-mer by Hotha *et al*[21]

A heinecosasaccharide from ManLAM was synthesized in 56 steps exploiting a convergent [5+(7+9)] approach with an overall 0.016% yield by Hotha group. Only alkyne carbonate donor chemistry was exploited for the glycosylation reaction employing gold-phosphite and silver triflate catalytic conditions. The synthesized 21-mer contained an arabinan domain with two 3,5 branch points and three *β*-arabinofuranose residues at the non-reducing end, each terminated by two mannopyranose capping motifs.

### 2.5.5 - Synthesis of tetrasaccharide motif of MTX-capped ManLAM by Mandal *et al*[22]

Mandal's group reported a sequential synthesis of thioxylose containing ManLAM tetrasaccharide, wherein tosylated xylofuranose precursor of the MTX was glycosylated with amino-linker containing arabinomannan disaccharide and late-stage modification of tosyl functional group of tosylated xylofuranose residue provided the desire amino-linker containing tetrasaccharide motif, which was further biotinylated for investigating their biological implications.

### 2.5.6 - Synthesis of hexasaccharide motif of MTX-capped ManLAM by Lowary *et al*[23]

Synthesis of hexasaccharide fragment of MTX-capped ManLAM was accomplished by Lowary's group exploiting a linear glycosylation approach. *α*-Linked xylofuranose and *β*-linked arabinofuranose were installed employing conformationally constrained 2,3-*O*-xylylene protected 5-*O*-mesylated xylofuranosyl-thio-donor and arabinofuranosyl-thio-donor respectively, under NIS and AgOTf catalyzed glycosylation conditions. Hexasaccharide was further treated with sodium thio-methoxide to get desired MTX-capped hexasaccharide motif. The synthesized motif were embedded with an amino-linker at the reducing end of the arabinofuranosyl residue and thio-methyl moiety at the non-reducing end of the xylofuranosyl residue, one mannosyl and three arabinofuranosyl residues in between them.

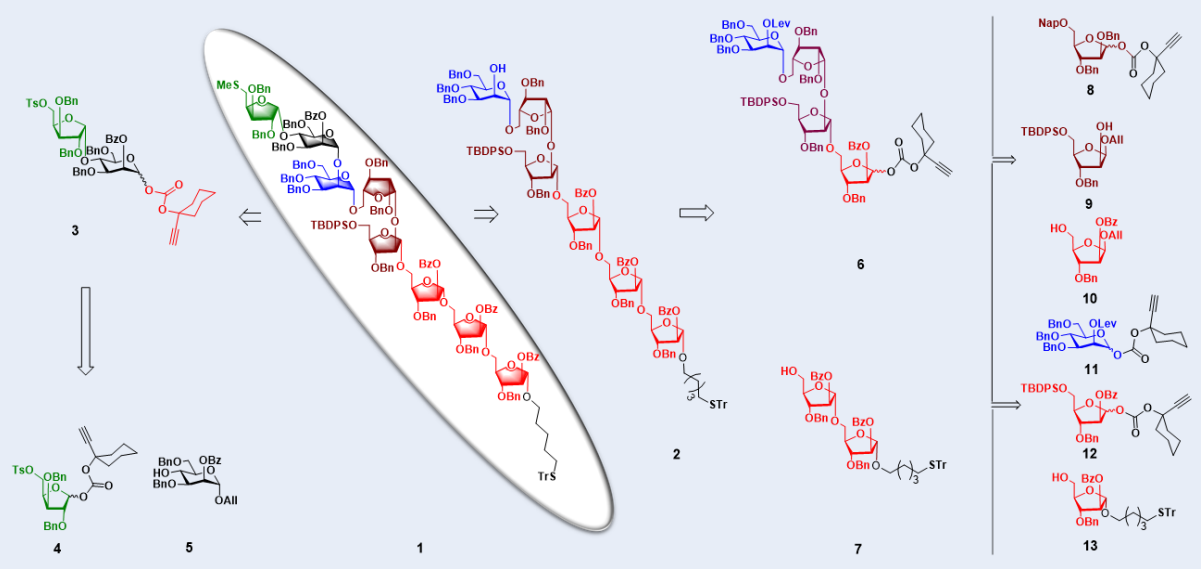
## 2.6 - Present work

*Mycobacterium tuberculosis* (Mtb) cell envelope consists of mainly arabinogalactan (AG), lipomannan (LM), and lipoarabinomannan (LAM). *M. tuberculosis* and other slow-growing pathogenic mycobacteria (M. bovis, M. leprae, M. avium, M. xenopi, M. marium, and M. kansasii*)* produce one to three $\alpha$-(1→4)-mannopyranosyl caps on LAM giving rise to the ManLAM, which can be further capped by $\alpha$-(1→4)-methyl-thio-xylose residue.[23,24] Only one MTX motif is present in the entire ManLAM molecule. The conservation and exposure of the MTX on the cell envelope of Mtb and other pathogenic mycobacteria suggest that it may play significant role in pathogenesis and host-pathogen interactions. In vitro studies found that the disaccharide mimetic of the MTX-capped ManLAM downregulates cytokine production by activated human macrophages in culture and showed antioxidant properties. So, these findings make this motif a more interesting synthetic target for glycochemists. There are very few reports on the chemical synthesis of the MTX-capped-ManLAM as detailed earlier. Here, we targeted an octasaccharide motif containing $\alpha$-(1→4)-methyl-thio-xylofuranose, two $\alpha$-(1→2)-mannopyranoses, one $\beta$-(1→2)-arabinofuranose, and four $\alpha$-(1→5)- arabinofuranose residues. An amino-terminated TEG (tetra ethylene glycol)-linker was also attached to the reducing end of the octasaccharide, which can be exploited for immunological and biomarker applications.

### 2.6.1 - Retrosynthetic analysis

The following are the major challenges in the synthesis of MTX capped LAM: presence of diverse sugar residues, different types of glycosidic linkages, two 1,2-*cis*-linkages, one rare sugar, i.e., MTX, which demand orthogonal protections at the monosaccharide level. Considering all the challenges associated, a careful retrosynthetic analysis was designed as depicted in **scheme 2.1**. The targeted compound **1** was envisioned to be synthesized in the split-react-couple manner exploiting [2+(4+2)] strategy. The molecule **1** contains both 1,2-*trans* and 1,2-*cis*, 1,2-trans linkages. 1,2-Trans arabinofuranosidation can be easily performed using neighbouring group participation (NGP) from the C-2 position by placing an ester moiety in the donor motif; however, installation of 1,2-*cis* linkages is challenging. We envisioned installation of 1,2-*cis* glycoside by invoking reactivity modulated selectivity concept during glycosylation. Accordingly, the protected octasaccharide **1** was picturized from hexasaccharide acceptor **2** and disaccharide donor **3**. Disaccharide donor **3** can be obtained from the corresponding allyl disaccharide motif, which can be synthesized after glycosylation of xylose

donor (**4**) and mannose acceptor (**5**) building blocks. Hexasaccharide acceptor (**2**) was envisioned can be obtained from tetrasaccharide



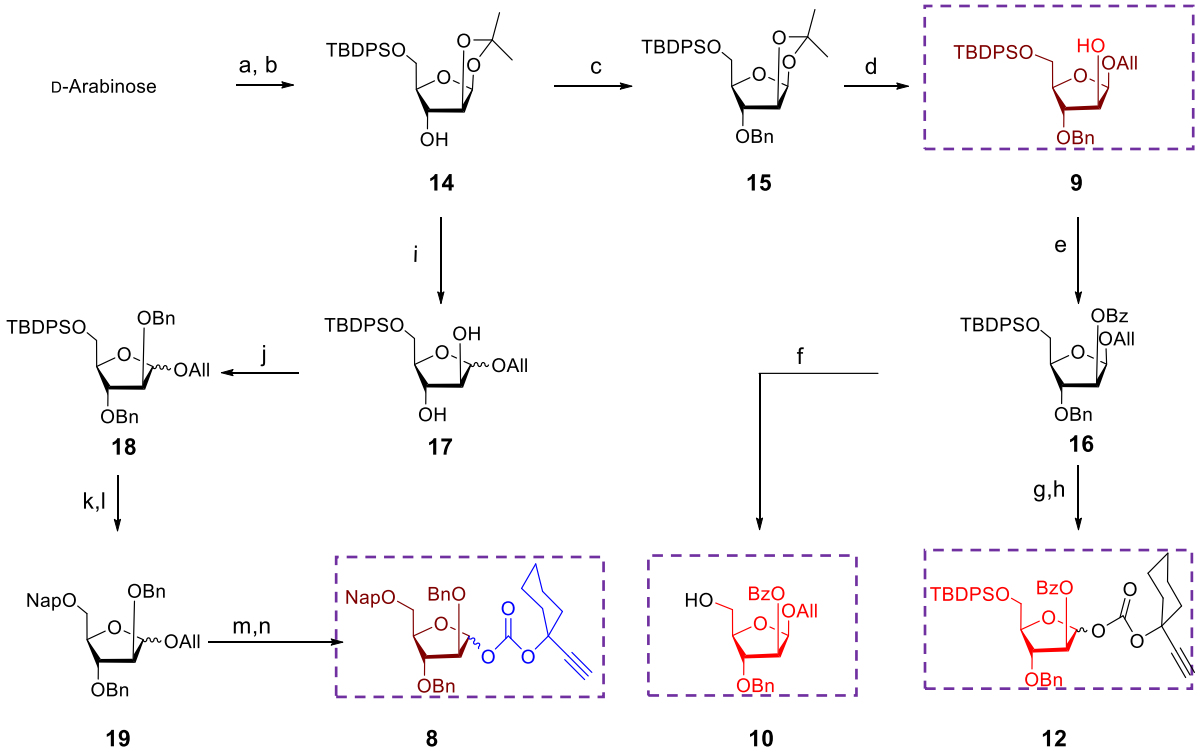
***Scheme 2.1:*** *Retrosynthesis of MTX-capped ManLAM octasaccharide motif*

donor **6** and disaccharide acceptor **7**. Linker containing disaccharide **7** was visualized from glycosyl donor **12** and acceptor **13**; and tetrasaccharide donor (**6**) can be obtained from the corresponding allyl tetrasaccharide motif, which can be imagined from a trisaccharide acceptor and mannose donor building block **11**. The trisaccharide motif can be obtained regioselectively from arabinose building blocks (**8**), (**9**), and (**10**) by functional group interconversions which in turn can be synthesized from commercially available D-arabinose. All the glycosylation reactions were visualized by using silver-assisted gold catalysis (**Scheme 2.1**).

### 2.6.2 – Synthesis of arabinofuranose building blocks

The stage for the forward synthesis of the octasaccharide started with the synthesis of arabinose building blocks in furanosyl form. To this end, we started with locking of D-arabinose into furanose form by TBDPS protection at the C-5 hydroxyl group and acetonide protection of C-1, C-2 hydroxyl groups, using TBDPSCl/imidazole and 2,2-dimethoxypropane/*p*-TSA respectively to get compound **14**. Compound **14** was split into two portions; one portion was treated with benzyl bromide/sodium hydride to furnish compound **15**, which was further exposed to the allyl alcohol under acidic conditions giving rise to the *α*/*β*-mixture of allyl glycosides that were separated by silica gel column chromatography lead to the secondary acceptor arabinose building block **9**. Keeping some of the quantity aside, compound **9** was treated with benzoyl chloride under the basic conditions to afford benzoate **16** which was

further divided into two portions; the first portion was treated with HF•py to furnish the primary acceptor building block **10**. The second portion was exposed to the $PdCl_2$ in a binary solvent (methanol, dichloromethane) system to convert into hemiacetal, which was further treated with easily accessible 1-ethynyl cyclohexyl(4-nitrophenyl) carbonate reagent[24] (**20**) and DMAP to furnish glycosyl donor building block (**12**), which was confirmed by NMR and HRMS experiments. Characteristic singlet for alkyne C-H proton was observed at δ 2.63 ppm and 9 protons of $^{tert}$butyl group in TBDPS at δ 0.97 ppm. In the $^{13}C$ NMR spectrum, resonances at δ 19.4 ppm corresponding to the quaternary carbon and at δ 26.9 ppm corresponding to the three-carbons in $^{tert}$butyl group indicated the presence of TBDPS protecting group.



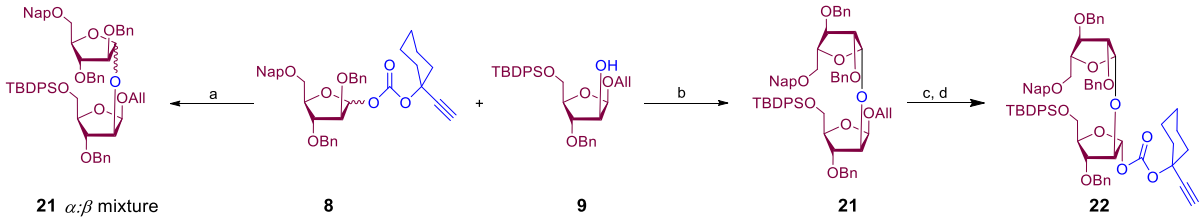

***Scheme 2.2:*** *Synthesis of arabinose building blocks*

Reagents: (a) TBDPSCl (1.0 eq.), Imidazole (2.0 eq.) DMF, 6 h; (b) 2,2-dimethoxypropane (2.0 eq.), *p*-TSA (0.2 eq.), acetone, 1 h, 70% over two steps; (c) benzyl bromide (1.2 eq.), NaH (1.2 eq.), TBAI, DMF, 0-25 °C, 1 h, 93%; (d) *p*-TSA (0.2 eq.), allyl alcohol (1.5 eq.), $CH_2Cl_2$, 60 °C, 2 h, 43%; (e) benzoyl chloride (1.2 eq.), DMAP (cat), pyridine, 0-25 °C, 3 h, 93%; (f) HF•py, pyridine, 0-25 °C, 2 h, 94%; (g) $PdCl_2$ (0.2 eq.), $CH_2Cl_2$:MeOH (1:2), 1.5 h; (h) carbonate reagent (**20**) (1.2 eq.), DMAP (1.2 eq.), $CH_2Cl_2$, 3 h, 81% over two steps; (i) *p*-TSA (0.2 eq.), AllylOH (2 eq.), $CH_2Cl_2$, 60 $^0$C, 1 h, 90%; (j) BnBr (2.4 eq.), NaH (2 eq.),TBAI, DMF, 0-25 °C, 1 h, 85%; (k) HF•p y, Pyridine, 0-25 °C, 1.5 h; (l) NapBr (1.3 eq.), NaH (1 eq.), DMF, 0-25 °C, 2 h, 91% over two steps; (m) $PdCl_2$ (0.15 eq.), $CH_2Cl_2$:MeOH (1:3), 2 h; (n) carbonate reagent (**20**) (1.3 eq.), DMAP (1.2 eq.), $CH_2Cl_2$, 3 h, 85% over two steps.

The second portion of compound **14** was treated with allyl alcohol under acidic conditions to accomplish a diol, which was converted onto di-*O*-benzylated compound **18** employing BnBr/NaH conditions. Compound **18** was exposed to the HF•py for the hydrolysis of the silyl ether; subsequently, treated with naphthylmethyl bromide/NaH delivered compound **19**. Furthermore, exposure to the $PdCl_2$ in a binary solvent (dichloromethane, methanol) system and easily accessible carbonate reagent (**20**) and DMAP conferred another glycosyl donor building block **8**. In the $^1$H NMR spectrum, one singlet at δ 2.65 ppm indicated the presence of alkyne C-H proton; in the $^{13}$C NMR spectrum, presence of quaternary carbon at δ 137.7 and 137.3 ppm are characteristic signals of the benzyl group, and at δ 135.6, 133.4, 133.1 ppm showed the presence of naphthylmethyl protecting group. Other signals at δ 151.5 ppm showed the presence of carbonyl carbon in the carbonyl donor, and δ 37.1, 36.8, and 25.1 ppm (2C) at δ 22.7 ppm indicated the presence of cyclohexyl group (**Scheme 2.2**).

### 2.6.3 – Synthesis of arabinan disaccharide donor

Synthesis of trisaccharide commenced with the synthesis of disaccharide **21**. The glycosylation reaction between glycosyl donor **8** and glycosyl acceptor **9** using Au/Ag catalyst[24] in 8 mol% each at room temperature afforded α: β mixture of compound **21** within 15 min. Intrigued by the reciprocal donor-acceptor selectivity (RDAS) concept and reactivity modulated selectivity (RMS) concept reported by Maidul et al.,[25] reactions were performed under the same catalytic conditions at a lower temperature (-78 ºC), to decrease the reactivity and increase the reaction time to 4 h. Decreased reactivity increased the selectivity of glycosylation reaction, and only *β*-isomer[21] of compound **21** was observed.




***Scheme 2.3:*** *Synthesis of disaccharide donor **22***

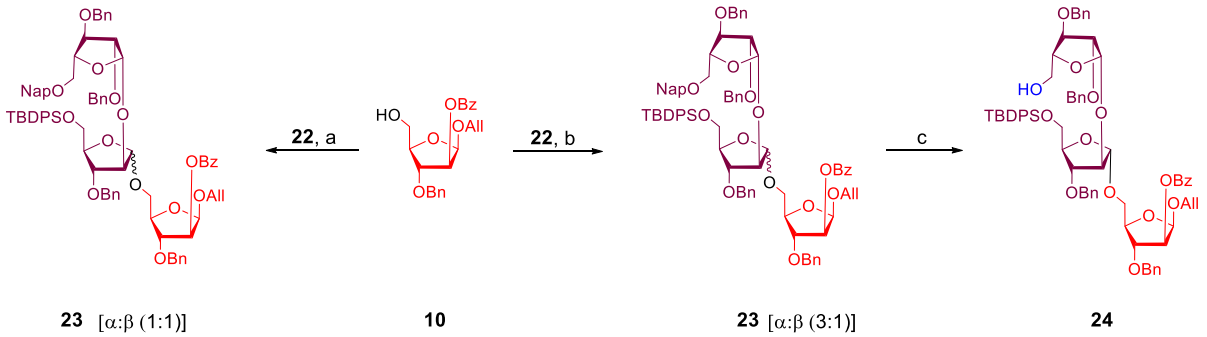
Reagents: (a) gold-phosphite (8 mol%), AgOTf (8 mol%), $CH_2Cl_2$, 4Å MS, 25 °C, 15 min., 96%; (b) gold-phosphite (8mol %), AgOTf (8 mol%), $CH_2Cl_2$, 4Å MS, -78 ºC, 4 h, 94%; (c) $PdCl_2$ (0.15 eq.), $CH_2Cl_2$: MeOH (1:3), 2 h; (d) carbonate reagent (**20**) (1.4 eq.), DMAP (1.2 eq.), $CH_2Cl_2$, 3 h, 78% over two steps.

Disaccharide **21** was thoroughly confirmed by NMR experiments; in the $^1$H NMR spectrum of disaccharide **21**, two anomeric protons appeared at δ 5.16 ppm (d, $J$ = 2.9 Hz, 1H) and 5.17

ppm (d, $J$ = 2.6 Hz, 1H) and in the $^{13}$C NMR spectrum, two signals at δ 98.7 and 99.0 ppm confirmed the 1,2-*cis* arabinofuranosidic linkages, which were further confirmed by HSQC-Coupled 2D NMR studies. Hydrolysis of the allyl glycosides by $PdCl_2$ in a binary solvent converted compound **21** into hemiacetals, which were further treated with carbonate reagent **20** and DMAP to furnish the disaccharide carbonate donor **22** (**Scheme 2.3**).

### 2.6.4 – Synthesis of arabinan trisaccharide acceptor

The successful synthesis of 1,2-*cis* linked disaccharide donor **22** prompted us to move towards the synthesis of trisaccharide acceptor. The primary acceptor **10** was glycosylated with disaccharide donor **22** under Au/Ag-catalysis conditions, leading to the trisaccharide in an equal ratio of *α* and *β*-trisaccharides; however, upon reducing the temperature of glycosylation to -78 ºC showed improvement in selectivity with compromised yield and longer reaction time. Improved selectivity can be rationalized by the steric hindrance of the TBDPS- protecting group present at the C-5 hydroxyl group of the disaccharide donor moiety **22**.



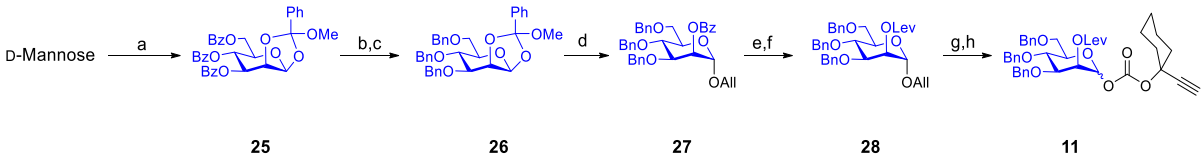

***Scheme 2.4:*** *Synthesis of arabinan trisaccharide acceptor **24***

Reagents: (a) gold-phosphite (8 mol %), AgOTf (8 mol %), $CH_2Cl_2$, 4Å MS, 25 °C, 15 min. 85%; (b) gold-phosphite (8 mol %), AgOTf (8 mol %), $CH_2Cl_2$, 4Å MS, -78 ºC, 3-4 h, 81%, (c) DDQ (3.5 eq.), $CH_2Cl_2$:MeOH (1:4), 4 h, 83%.

The *α*:*β*-ratio was confirmed from the $^1$H NMR spectrum and HSQC-coupled 2D NMR studies. Two $^1J_{CH}$ = 180 Hz and one $^1J_{CH}$ = 172 Hz in the anomeric region of the HSQC-coupled 2D NMR suggested that the major isomer contained two *cis* linkages and one *trans* linkage. Further, trisaccharide **23** was exposed to the DDQ to deprotect the naphthylmethyl protection, and desired isomer was isolated from a mixture of isomers to deliver the trisaccharide acceptor **24**. In the proton NMR spectrum of compound **23**, two 1,2-*cis* linkages appeared at δ 5.38 ppm (1H, $J$ = 4.5 Hz), 5.07 ppm (1H, $J$ = 4.4 Hz), and one *trans* linkage at δ 5.0 ppm (1H, s). In the $^{13}$C NMR spectrum, three anomeric carbons appear at δ 105.8, 100.0, and 99.7 ppm, confirming the presence of two *cis* and one *trans* linkage in the trisaccharide **24** (**Scheme 2.4**).

### 2.6.5 – Synthesis of mannose glycosyl donor

D-Mannose was converted into a benzylated ortho-ester **25** according to the reported procedure by Fraser-Reid's group.[25] Compound **25** was saponified under Zemplén conditions, and benzylation was performed without purification using BnBr/NaH to afford benzylated ortho-benzoate **26**, which was treated with allyl alcohol under the acidic conditions to give allyl mannopyranoside **27** (characteristic signals at δ 165.8 ppm and δ 117.9 ppm which is a characteristic signal of allylic functionality in $^{13}C$ NMR spectrum). Assembly of the oligosaccharide demands a protecting group orthogonal to benzoyl and also a participating group at the C-2 position of the mannose donor building block.



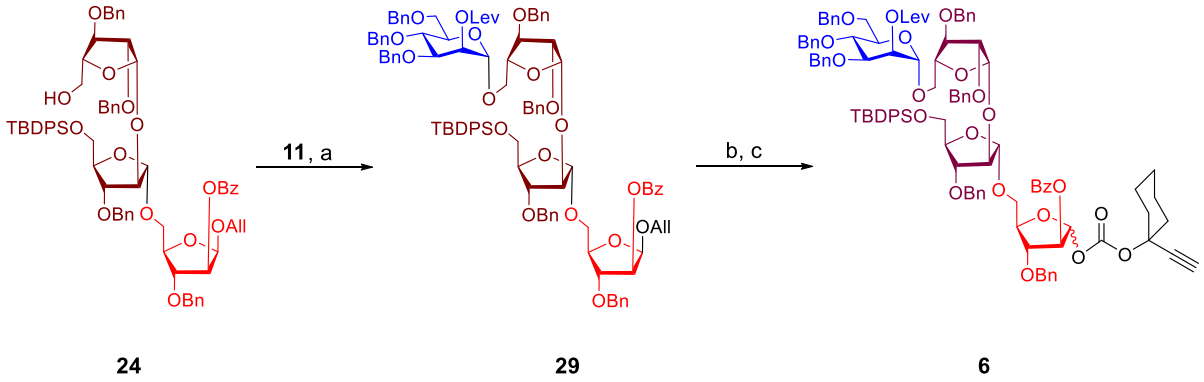

***Scheme 2.5:*** *Synthesis of mannose donor building block* ***11***

Reagents: (a) ref. 25; (b) NaOMe (0.6 eq.), $CH_2Cl_2$: MeOH (1:1), 1 h; (c) BnBr (7 eq.), NaH (9 eq.), THF, 0-25 ºC, 12 h; (d) AllOH (4 eq.) *p*-TSA (0.3 eq.), $CH_2Cl_2$, 4Å MS, 1 h, 80%; (e) NaOMe (0.4 eq.), $CH_2Cl_2$: MeOH (1:1), 1 h; (f) levulinic acid (1.5 eq.), DIC (1.5 eq), DMAP, $CH_2Cl_2$, 0 °C – 25 °C, 10 h, 93%; (g) $PdCl_2$ (0.2 eq.), DME:$CH_2Cl_2$: MeOH (3:1:1), 5 h; (h) carbonate reagent (**20**) (1.2 eq.), DMAP (1 eq.), $CH_2Cl_2$, 3 h, 70 %.

Hence, compound **27** was treated under Zemplén conditions (NaOMe/MeOH) to get the free alcohol at C-2 hydroxyl position which was reprotected as Lev-ester using levulinic acid, DIC, and DMAP. Presence of the lev-group in compound **28** was confirmed by $^1H$ NMR spectral studies; multiplets for 4H at δ 2.73 – 2.65 ppm, singlet for three protons at δ 2.12 ppm along with signals at δ 206.5 ppm, 172.2 ppm corresponding to the ketone and ester carbonyl and at δ 38.1, 29.9, 28.3 ppm methylene and methyl carbons of lev-ester protecting group in the $^{13}C$ NMR spectrum confirmed the structural homogeneity of compound **28**. HRMS spectrum further confirmed the molecular weight of the compound **28**. Thenceforward, allyl deprotection under $PdCl_2$ in ternary solvent system and further treatment with the carbonate reagent **20** and DMAP produced the desired carbonate donor **11**. Structural homogeneity of compound **11** was confirmed by the NMR experiments. In the $^{13}C$ NMR spectrum, signal at δ 150.3 ppm for the carbonyl carbon of carbonate, and in $^1H$ NMR, a singlet, a characteristic signal of alkyne proton was noticed at δ 2.61 ppm. As further confirmed by HRMS, the calculated value for $C_{41}H_{46}O_{10}[M+Na]^+$: 721.2989 and Found: 721.3005 (**Scheme 2.5**).

### 2.6.5 – Synthesis of tetrasaccharide donor

A tetrasaccharide donor is required to set the stage for the octasaccharide synthesis for exploiting the [2+(4+2)] glycosylation strategy. In this direction, trisaccharide acceptor compound **24** was glycosylated with mannose donor **11** using silver-assisted gold-catalysed glycosylation conditions to furnish tetrasaccharide **29** in 91% yield, confirmed by NMR and all the characteristic NMR peaks are shown in **Table 2.1**, compound **29** was further hydrolyzed under




**24** **29** **6**

***Scheme 2.6:*** *Synthesis of tetrasaccharide carbonate donor* ***6***

Reagents: (a) gold-phosphite (8 mol%), AgOTf (8 mol%), $CH_2Cl_2$, MS 4Å, 15 min., 91%; (b) $PdCl_2$ (0.2 eq.), MeOH: $CH_2Cl_2$ (2:1), 1 h; (c) carbonate reagent (**20**) (1.3 eq.), DMAP (1.2 eq.), $CH_2Cl_2$, 3 h, 70% over two steps.

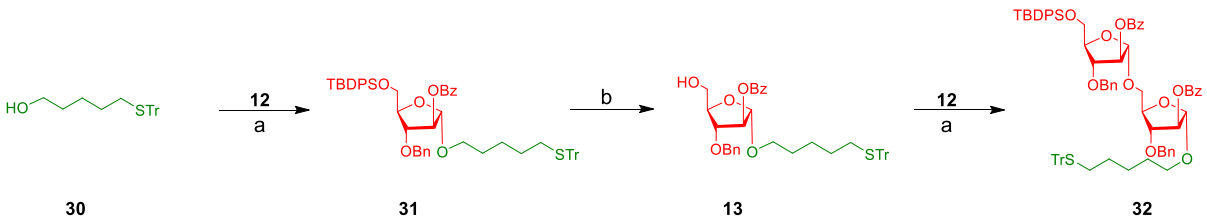
| Entry | $^1$H NMR (δ ppm) | $^{13}$C NMR (δ ppm) |
|---|---|---|
| H-1/C-1 | 5.36 (d, *J* = 4.5 Hz, 1H), 5.32 (s, 1H), 5.13 (s, 1H), 5.06 (d, *J* = 3.4 Hz, 1H) | 105.8, 100.4, 99.6, 97.9 |
| TBDPS | 1.03 (s, 9H), 7.13-7.67 (m, 10H) | 26.7 (3C), 19.5, 135.8 (4C), 133.5 (2C), 127.7-130.0 (6C) |
| Bz | 8.02 (d, *J* = 7.7 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.13-7.45 (2H) | 166.1 |
| Lev | 2.66 (m, 4H), 20.9 (s, 3H) | 206.4, 172.1, 38.1, 29.9, 28.3 |

***Table 2.1:*** *Only characteristics NMR peaks of compound* ***29***

$PdCl_2$ in methanol, dichloromethane binary solvent system to give hemiacetals which were transformed into the tetrasaccharide carbonate donor **6** using carbonate reagent **20** and DMAP. The carbonate donor was isolated in a 4:1 ratio (α:β) as confirmed by $^1$H NMR spectral studies (**Scheme 2.6**).

### 2.6.6 - Synthesis of linker containing disaccharide acceptor

Oligosaccharides are generally conjugated to an immunogenic protein to elicit their biological function. Often the immunogenic protein is attached to the non-reducing end of the glycan. Among different chemistries available for the bioconjugation, the Michael addition of thiolates to the maleimide is a very well deployed method for which the glycan shall contain a thiol at the terminal position. Therefore, we postulated to synthesize the disaccharide acceptor with a thio-trityl containing compound **32**. The synthesis started with the glycosylation of linker **30**[26] to arabinofuranosyl carbonate donor **12** in the presence of the gold and silver catalysts to obtain compound **31** with compromised yields in spite of adding stoichiometric Au/Ag salts and keeping the reaction for 24 h.




***Scheme 2.7:*** *Synthesis of linker containing disaccharide acceptor*

Reagents: (a) gold-phosphite (10-100 mol%), AgOTf (10-100 mol%), $CH_2Cl_2$, MS 4Å, 12 h; (b) HF-Py, Pyridine, 3 h.

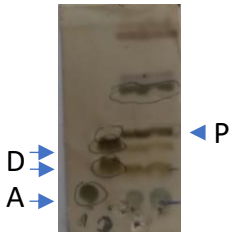
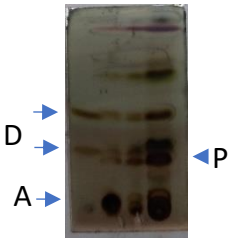
| TLC of first glycosylation | TLC of second glycosylation |
|---|---|
|  |  |



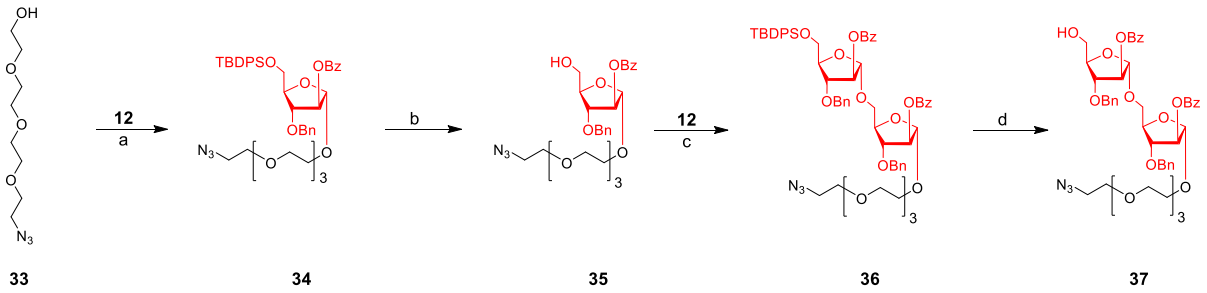
***Table 2.2:*** *TLCs of glycosylation reactions*

In spite of the compromised yield compound **31**, desilylation under HF•py conditions to get compound **13** was performed; the lone C5-OH was glycosylated again with another molar equivalent of donor **12** under the aforementioned gold-catalysed conditions to deliver the disaccharide compound **32**. The reaction was further slowed very similar to the first glycosylation. The very slow second glycosylation left some of the starting material unreacted even after using an excess amount of reagents. Further, it was observed by NMR experiments

that disaccharide **32** contains an inseparable mixture of compounds. It is well-known from previous reports that all the functionalities remain intact during glycosylation. However, poor yield, more catalyst loading, and less stability of the -STr moiety in the linker forced us to revise the linker chemistry for the disaccharide acceptor (**Scheme 2.7**).

### 2.6.7 – Revised linker containing disaccharide acceptor

After the unsuccessful attempt to install the thio-linker directly, we thought of introducing the thiol moiety at the end of the glycan synthesis. Initially, azide containing tether will be installed that can be converted into the amine later on and treated with the thiol containing NHS-ester so that the thiol can be introduced post-glycan synthesis. Accordingly, TEG-$N_3$[26] was treated with the glycosyl donor **12** under silver assisted gold-catalyzed glycosylation condition to afford the conjugate **34** in 96% yield. It was observed that an excess of gold and silver catalyst was required for the completion of the glycosylation reaction, which can be rationalized by the aggregation of tetra-ethylene-glycol around catalysts in solution. Also, the presence of the triethyleneglycol in the linker **33** would further increase the water solubility of the resulting glycan. Compound **34** was mapped by NMR spectral and mass analysis. In the $^1$H NMR spectrum, an anomeric proton resonated at δ 5.22 ppm, and two characteristic protons next to the azide moiety resonated at




**33** **34** **35** **36** **37**

***Scheme 2.8:*** *Synthesis of revised linker containing disaccharide acceptor **37***

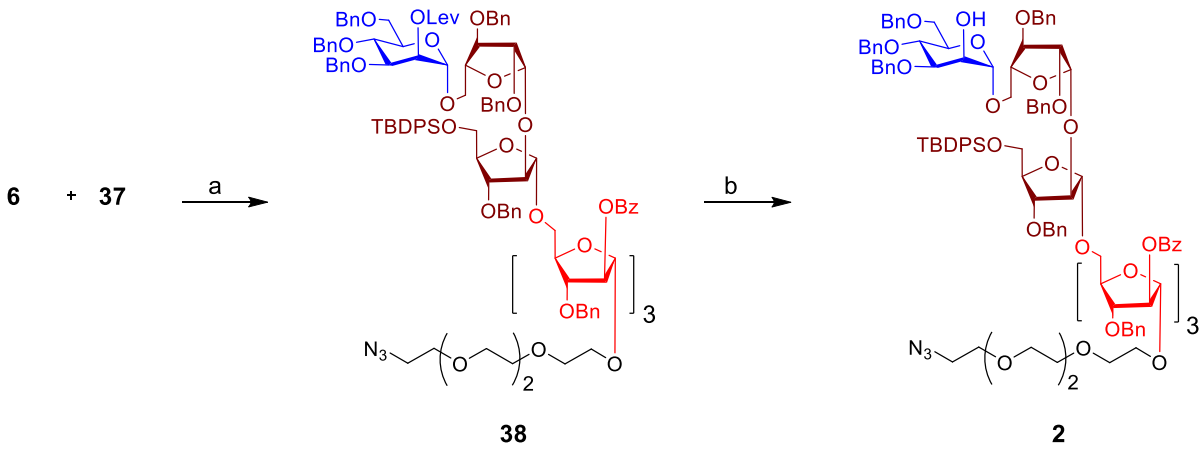
Reagents: (a) gold-phosphite (20 mol%), AgOTf (20 mol%), $CH_2Cl_2$, MS 4Å, 30 min., 96%; (b) HF•py, pyridine, 0-25ºC, 3 h, 94%; (c) Gold-phosphite (20 mol%), AgOTf (20 mol%), $CH_2Cl_2$, MS 4Å, 30 min., 95%; (b) HF•py, pyridine, 0-25 ºC, 3 h, 92%.

δ 3.33-3.36 ppm. In the $^{13}$C NMR spectrum of compound **34**, anomeric carbon at δ 106.42 ppm confirmed the presence of α-linkage and characteristic carbon next to the azide resonated at δ 50.77 ppm. Furthermore, a glycosylated linker containing compound **34** was exposed to the HF•py to convert compound **34** into compound **35** in 96% yield; subsequently, the lone hydroxyl group was glycosylated with the glycosyl donor **12** under the Au/Ag-catalyzed

glycosylation conditions to furnish the compound **36** in 95% yield, which was afterwards exposed to the HF•py condition to get the linker containing disaccharide acceptor **37** (**Scheme 2.8**). Compound **37** was confirmed by NMR studies; in the $^{1}$H NMR singlets from two anomeric protons resonated at δ 5.23 and 5.26 ppm, a triplet with $J$ = 5.1 Hz for two $CH_2$ protons next to the azido functionality appeared at δ 3.36 ppm. Distinguishable peaks of four ortho protons from two Bz protecting groups resonated at δ 7.98-8.05 ppm, and twenty aromatic protons suggested the presence of four aromatic rings in the compound. In the $^{13}$C NMR spectrum of compound **37**, two peaks at δ 165.6, and 165.4 ppm showed the presence of two carbonyl carbons inferring the presence of two Bz protecting groups, two quaternary carbons at δ 137.9 and 137.7 ppm belonging to the benzyl *ipso*-carbon, and at δ 106.3 ppm for two anomeric carbons of two sugar rings were noticed. Carbon next to the azido group resonated at δ 50.8 ppm. The calculated mass of the compound exactly matched with the observed mass in HRMS—calculated mass for $C_{46}H_{53}N_3O_{14}Si$ $[M+K]^+$: 894.3425 and Found: 894.3426.

**2.6.8 – Synthesis of hexasaccharide by [4+2] Strategy**

Synthesis of hexasaccharide acceptor commenced with the glycosylation between tetrasaccharide donor **6** and linker containing disaccharide acceptor **37** under Au/Ag-conditions to afford hexasaccharide **38** in 92% yield. The levulinoate moiety was hydrolysed by treating the hexasaccharide **38** with hydrazine acetate in the binary solvent system (THF and methanol) resulting in the formation of hexasaccharide acceptor **2**. Compound **38** was verified by NMR (**Table 2.2**) and mass spectroscopic data. Calculated mass for $C_{144}H_{157}N_3O_{34}Si$ $[M+Na]^+$: 2524.0349 Found: 2524.0344. All the NMR resonances were similar to that of compound **38** in compound **2** except for the missing levulinoate peaks confirming the deprotection of levulinic ester from the C-2 position of the mannose residue in compound **2** (**Scheme 2.9**).



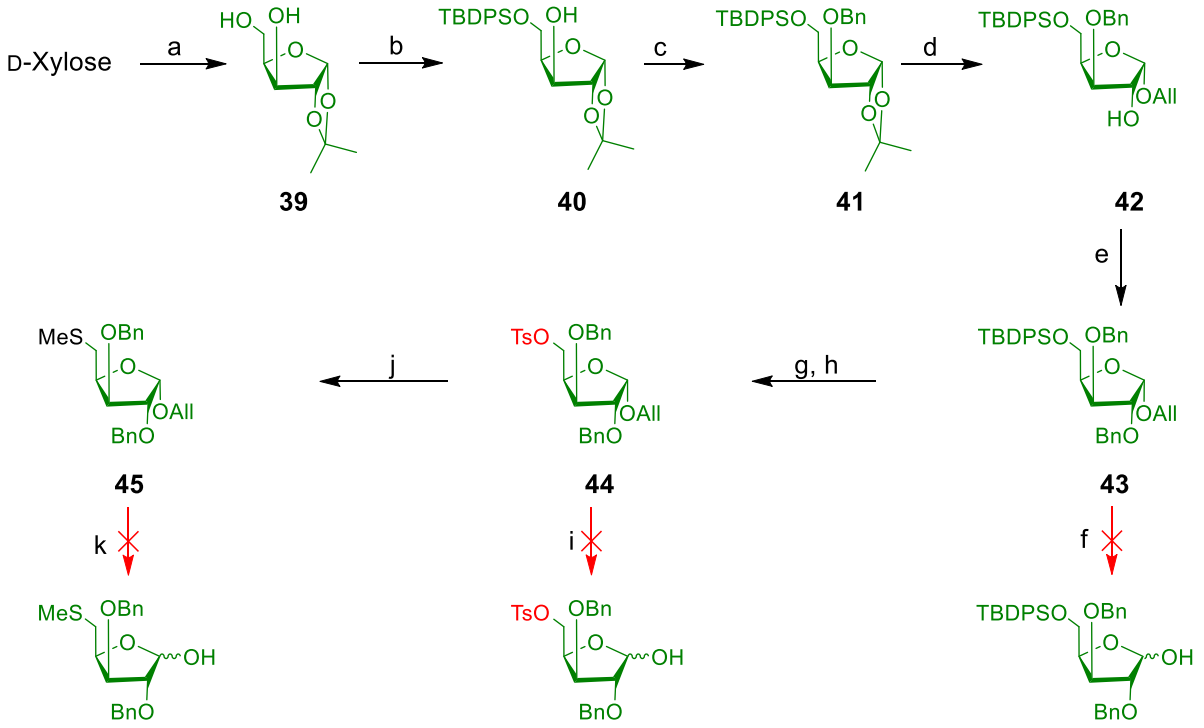

***Scheme 2.9:*** *Synthesis of revised linker containing disaccharide acceptor* ***2***

Reagents: (a) gold-phosphite (20 mol%), AgOTf (20 mol%), $CH_2Cl_2$, MS 4Å, 30 min., 92%; (b) $NH_2NH_2.CH_3COOH$, THF: MeOH (4:1), 1 h, 87%.

| Entry | $^1$H NMR (δ ppm) | $^{13}$C NMR (δ ppm) |
|---|---|---|
| H-1/ C-1 | 4.73 (d, *J* = 1.8 Hz, 1H), 4.98 (d, *J* = 1.5 Hz 1H), 5.04 (d, *J* = 4.3 Hz, 1H), 5.18 (s, 1H), 5.20 (s, 1H), 5.25 (s, 1H) | 106.2-106.1 (4C), 100.6, 97.8 |
| TBDPS | 1.01 (s, 9H), 7.13-7.67 (m, 10H) | 26.9(3C), 19.3, 135.6 (4C), 133.4 (2C), 127.6-129.8 (6C) |
| Bz | 7.95-8.04 (6H), 7.57 (1H), 7.13-7.45 (2H) | 165.5-165.3 (3C), |
| Lev | 2.66 (m, 4H), 20.9 (s, 3H) | 206.5, 172.0, 38.0, 29.8, 28.2 |

***Table 2.2:*** *Only characteristics NMR peaks of compound* ***38***

### 2.6.8 - Synthesis of xylose donor building block

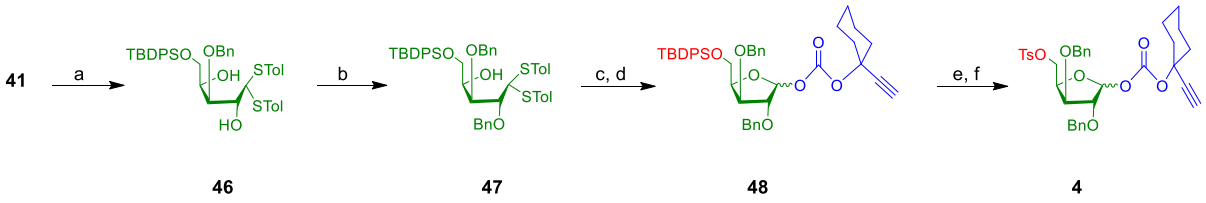



***Scheme 2.10:*** *Synthesis of xylose donor building block*

Reagents: (a) $H_2SO_4$, acetone, 30 min., 90%; (b) TBDPSCl (1 eq.), Imidazole (1.5 eq.), DMF, 6 h, 94%; (c) BnBr (1.2 eq.), NaH (1.1 eq.), DMF, 0 °C, 2 h, 85%; (d) *p*-TSA (0.2eq.), AllylOH (5 eq.), $CH_2Cl_2$, 60 ºC, 3 h, 75%; (e) BnBr (1.2 eq.), NaH (1.1 eq.), DMF, 0 ºC, 2 h, 89%;(g) HF•py, Pyridine, 0-25 °C, 3 h, 88%; (h) TsCl (1.2 eq.), Pyridine, 0-25 °C, 6 h, 96%; (f), (i), & (k) $PdCl_2$, $CH_2Cl_2$:MeOH; (j) NaSMe (3 eq), 18-crown-6, acetonitrile, 100 °C, 2 h, 75%.

Synthesis of the xylose building block commenced with the locking of the xylose into furanose conformation using concentrated sulfuric acid in acetone to get compound **39,** which was exposed to the TBDPSCl and imidazole in DMF solvent to convert it into silyl ether **40** and further BnBr and NaH to get benzyl ether protected compound **41**. Subsequently, benzyl ether **41** was treated with allyl alcohol under the acidic conditions to convert to allyl xyloside **42**, which was reacted with BnBr/NaH to install a non-participating group at the C-2 position of the xylofuranose; afterwards, an attempt was made to achieve hemiacetal by using $PdCl_2$ in $CH_2Cl_2$, MeOH. Unfortunately, a mixture of compounds was observed in TLC. It can be justified by the presence of acid sensitive TBDPS-ether protecting group that can cleave off by the HCl generated during the reaction from $PdCl_2$. To overcome this problem, we deprotected TBDPS protecting group using HF•py and protected with tosyl protecting group by using tosyl chloride in pyridine to afford compound **44** in 96% yield; subsequently, exposed to the allyl deprotection conditions; very little conversion into the product was observed. Thus, compound **44** was heated to 100 ºC in the presence of NaSMe in acetonitrile to furnish

compound **45**. Further transformation of compound **45** to the hemiacetal showed multiple indistinguishable compounds on the TLC (**Scheme 2.10**).




***Scheme 2.11:*** *New approach for the synthesis of xylose donor building block* ***4***

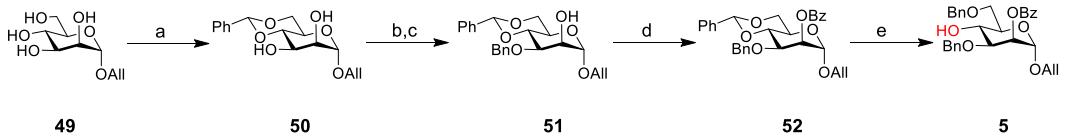
Reagents: (a) $BF_3$•$Et_2O$ (1eq.), TolSH (1.5 eq.), $CH_2Cl_2$, 0 ºC, 10 min., 65%; (b) BnBr (1.2 eq.), NaH (1.1 eq.), DMF, 0 ºC, 1 hr, 72%; (c) NBS (3 eq.), Acetone:water (9:1), 30 min.; (d) carbonate reagent (**20**) (1.2 eq.), DMAP (1.2 eq.), $CH_2Cl_2$, 3 h, 87% over two steps; (e) HF•py, Pyridine, 0 °C, 3 h; (f) TsCl (1.2 eq.), Pyridine, 0-25 °C, 6 h, 92% over two steps.

After unsuccessful attempts towards synthesizing desired hemiacetals, we came up with a new approach: compound **41** was treated with 4-methylbenzenethiol under Lewis acid condition to convert into *gem*-thiotol derivative **46**, characterized by NMR experiments. In the $^1$H NMR spectrum, two singlets at δ 2.33 ppm (3H) and 2.30 ppm (3H) and in the $^{13}$C NMR spectrum, two carbons resonating at δ 21.3 ppm showed the presence of two methyls from thiotol moiety. Compound **46** was further extrapolated into compound **47** by treating with BnBr and NaH, further treated with NBS in an acetone water solvent system to convert into hemiacetal, and subsequently, reacted with carbonate reagent **20** and DMAP to convert it into carbonate donor **48**. Exposure to HF•py converted it into a C-5 hydroxyl carbonate donor; furthermore, treatment with TsCl in pyridine converted into a tosylated carbonated donor **4**. Required carbonate donor building block **4** was thoroughly characterized by NMR and Mass spectroscopic techniques. Characteristic signals in the $^{13}$C NMR spectrum for carbonate carbonyl were identified at δ 151.3 ppm, and for cyclohexyl at δ 37.0, 36.6, 25.0, 22.6(2C) ppm. Additionally, compound **4** showed satisfactory molecular weight in the HRMS spectrum - calculated mass for $C_{35}H_{38}O_9S[M+Na]^+$: 657.2134 and Found: 657.2132.

### 2.6.9 - Synthesis of mannose acceptor building block

We initiated the synthesis of a mannose acceptor building block with the readily available allyl mannopyranoside compound **49** that was treated with benzaldehyde dimethyl acetal in catalytic amount of CSA to convert it into benzylidene protected diol compound **50** according to established protocols.[27–29] Stannylation mediated regioselective protection of C-3 hydroxyl group was performed on benzylidene **50**. Accordingly, compound **50** was treated with the

dibutyltin oxide to form stannylene-diol complex by refluxing in toluene for 8 h which was selectively opened by the fluoride ion from the equatorial side, allowing equatorial hydroxyl to attack the BnBr to protect the equatorial hydroxy group to afford monobenzyl ether **51**. Exposure to BzCl under basic conditions lead to compound **52**; subsequently, selective reductive opening using triethylsilane and trifluoroacetic acid afforded the compound **5** in dichloromethane solvent with 75% yield. NMR and HRMS spectroscopic analysis confirmed compound **5** (**Scheme 2.12**). Characteristic NMR peaks of the compound **5** were depicted in **Table 2.3.** Compound **5** was further confirmed in the HRMS spectrum as it showed matching mass - calculated mass for $C_{30}H_{32}O_7$ $[M+Na]^+$: 527.2046 Found: 527.2044.




***Scheme 2.12:*** *Synthesis of mannose acceptor building block* ***5***

Reagents: (a) $PhCH(OMe)_2$ (1eq.), CSA (0.2eq.), DMF, 25 °C, 24 h, 80%; (b) $Bu_2SnO$ (1 eq.), toluene, reflux, 8 h; (c) CsF (2 eq.), BnBr (1.5 eq.), DMF, 25 °C, 12 h, 79% over two steps; (d) BzCl ( 1.5 eq.), DMAP (0.5eq.), Py/$CH_2Cl_2$, 0-25 °C, 4 h, 98%; (e) $Et_3SiH$ ( 5eq.), $F_3CCOOH$ ( 5eq.), $CH_2Cl_2$, 0-25 °C, 1 h, 75%.

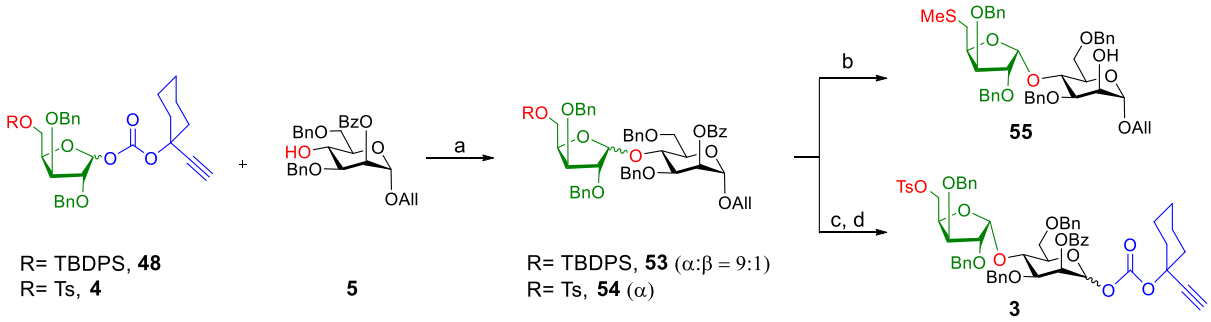
| Entry | $^1$H NMR (δ ppm) | $^{13}$C NMR (δ ppm) |
|---|---|---|
| H-1/C-1 | 5.03 (d, *J* = 1.8 Hz, 1H) | 97.17 |
| Allyl | 5.91 (m, 1H), 5.30 (dd, *J* = 17.2 Hz, 1.6 Hz, 1H), 5.22 (dd, *J* = 10.4 Hz, 1.5 Hz, 1H), 4.23 (dd, *J* = 12.9 Hz, 5.2 Hz, 1H), 4.04 (dd, *J* = 12.9 Hz, 6.2 Hz, 1H) | 133.0, 117.3, 68.3 |
| Bz | 8.05 (d, *J* = 6.9 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.20-7.40 (2H) | 129.9 (2C), 133.1, 127.9-128.9 (3C) |

***Table 2.3:*** *Characteristics NMR peaks of compound* ***5***

### 2.6.10 - Synthesis of Xyl*f*(1→4)-Man*p* disaccharide donor

With the two glycosyl donors **50** and **4** along with acceptor **5** in hand, we moved forward toward glycosylation in order to achieve the disaccharide donor **3**. Interestingly, we found that when C-5 TBDPS protected donor **50** was glycosylated with acceptor **5**, under gold and silver catalyzed conditions, glycosylated product **53** was observed in $\alpha$:$\beta$ = 9:1 with 91% yield. However, when C-5 tosyl containing glycosyl donor **4** glycosylated with acceptor **5**, only a

desired $\alpha$-isomer of disaccharide **54** was observed. Higher selectivity can be governed by the electron-withdrawing effect of the tosyl group, which reduces the reactivity and increase the selectivity. All the isomers were well characterized by 1D- and 2D- NMR spectral shows [**Table 2.4**].




***Scheme 2.13:*** *Synthesis of Xylo-Manno-disaccharide donor **3***

Reagents: (a) gold-phosphite (8 mol %), AgOTf (8 mol %), dry $CH_2Cl_2$, 4Å MS, 15 min., 94% for **53** ($\alpha$: $\beta$ = 9:1), 91% for **54** (only $\alpha$); (b) NaSMe (6 eq.), 18-crown-6, $CH_3CN$, 100 ºC, 3 h, 72% (c) $PdCl_2$ (0.2 eq.), $CH_2Cl_2$: MeOH (1:4), 2 h; (d) carbonate reagent (**20**) (1.3 eq.), DMAP (1.2 eq.), $CH_2Cl_2$, 3 h, 82% over two steps.

| Entry | $^1$H NMR (δ ppm) | $^{13}$C NMR (δ ppm) |
|---|---|---|
| Compound **53** ($\alpha$) | 5.49 (d, $J$ = 4.4 Hz, 1H), 5.05 (d, $J$ = 1.9 Hz, 1H) | 100.8, 96.8 |
| Compound **53** ($\beta$) | 5.42 (s, 1H), 4.97 (d, $J$ = 1.9 Hz, 1H) | 108.1, 96.9 |
| Compound **54** ($\alpha$) | 5.41 (d, $J$ = 4.5 Hz, 1H), 5.03 (d, $J$ = 2.2 Hz, 1H) | 100.9, 96.8 |

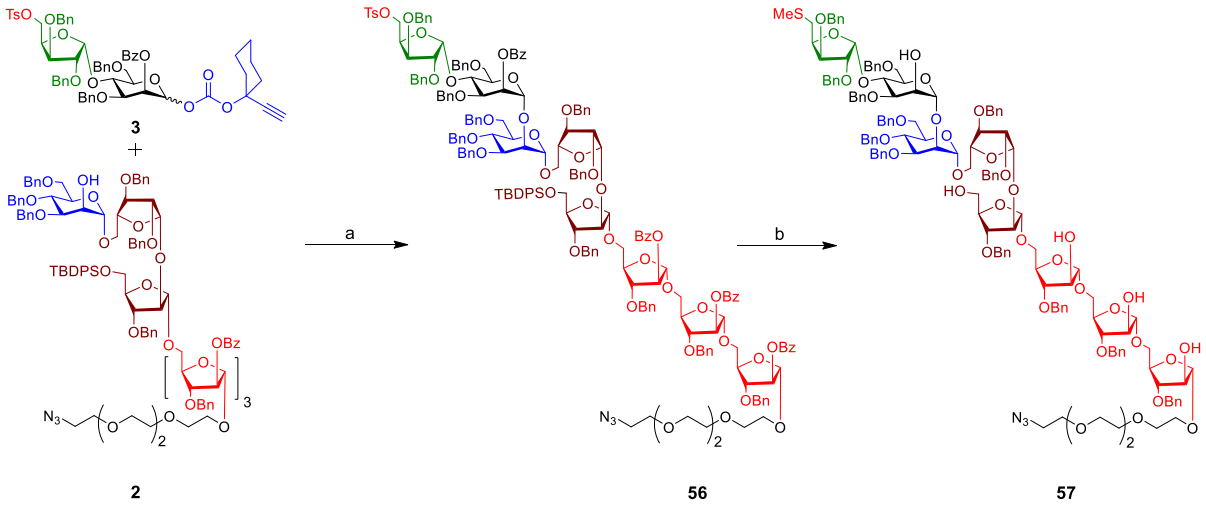
***Table 2.4:*** *Anomeric NMR peaks of compounds*

Furthermore, compound **54** was treated with $PdCl_2$ to free the allyl locking so that it gives hemiacetal; eventually, reaction with carbonate reagent **20** and DMAP addition converted it into carbonate donor **3** with 82% overall yield over two steps. Characterization of compound **3** was done by NMR and HRMS spectral analysis; in the $^1$H NMR spectrum, two anomeric protons of different rings resonate at δ 6.13 ppm (d, $J$ = 2.2, 1H) and 5.41 ppm (d, $J$ = 4.5, 1H) whereas in the $^{13}$C NMR spectrum, two anomeric carbons were noticed at δ 100.8 ppm and 94.1 ppm. Further, the characteristic singlet of alkyne proton appeared at δ 2.63 ppm (s, 1H) and signals at δ 37.1, 36.6, 25.0, and 22.7 ppm (2C) corresponding to the cyclohexyl, and signal at δ 150.4 ppm corresponding to the carbonyl carbon in the $^{13}$C NMR spectrum confirmed the carbonate donor **3**. Compound **54** was also converted into protected disaccharide mimetic of methyl-thio-xylofurnose compound **55** (**Scheme 2.13**). Compound **55** was confirmed by NMR spectroscopy; in the $^1$H NMR spectrum, protons of -$CH_2$ of xylose

moiety resonated at δ 2.69 ppm (dd, *J*=13.8, 4.4, 1H), 2.56 – 2.48 ppm (d, dd, *J*=13.0, 4.1, 1H), and one singlet of three protons appears at δ 2.05 ppm. In the $^{13}$C NMR, these characteristic peaks resonated at δ 34.8 and 16.7 ppm respectively.

**2.6.11 – Synthesis of partially deprotected octasaccharide**

Finally, octasaccharide **56** was assembled exploiting [2+6] glycosylation strategy. The disaccharide glycosyl donor **3** was glycosylated with hexasaccharide glycosyl acceptor **2** under gold and silver catalysed glycosylation condition to deliver octasaccharide **56** in 86% yield, Protected and unsubstituted octasaccharide **56** was fully characterized by NMR spectroscopic analysis. In the proton NMR, eight anomeric signals resonated at δ 5.30 ppm (d, *J* = 4.1 Hz, 1H), 5.25 ppm (s, 1H), 5.20 ppm (s, 1H), 5.17 ppm (2s, 2H), 5.05 ppm (d, *J* = 4.1 Hz, 1H), 5.03 (s, 1H), 4.98 (s, 1H), and they resonated in the $^{13}$C NMR spectrum at δ 106.4 ppm (4C), 100.7 ppm (2C), 99.4 ppm, 98.4 ppm. Two signals at δ 5.30 ppm and 5.05 ppm in proton NMR spectrum with coupling constant *J* = 4.1 Hz and corresponding signals at δ 100.7 ppm in the $^{13}$C NMR spectrum confirmed the presence of two 1,2-*cis* linkages in the octasaccharide. The signature peaks of two protons of the linker in $^{1}$H NMR spectrum were noticed at δ 3.35 ppm as a triplet confirming the presence of the linker in octasaccharide, and the singlet of three protons at δ 2.29 ppm confirmed the retention of the tosyl group. Eight ortho protons of four benzoyl protecting groups appear in between δ 7.95-8.05 ppm. Further, four carbonyl carbons ranging from d 165.6-165.4 ppm confirm the benzoate. Compound **55** was further confirmed by HRMS analysis, wherein the calculated mass for $C_{192}H_{203}N_3O_{44}SSi[M+Na]^+$: 3339.3194 and Found: 3339.3199. Finally, compound **56** was refluxed with sodium thio-methoxide in acetonitrile solvent to achieve substituted and partially deprotected compound **57** (**Scheme 2.14**), confirmed by NMR and mass spectral analysis. The compound **57**, can be subjected to global deprotection to accomplish conjugation ready glycoconjugate that can be utilized for different biological applications.



***Scheme 2.14:*** *Partially deprotected octasaccharide Synthesis* ***57***

Reagents: (a) gold-phosphite (20 mol %), AgOTf (20 mol %), dry $CH_2Cl_2$, 4Å MS, 30 min., 86% (b) NaSMe (20 eq.), 18-crown-6, $CH_3CN$, 100 ºC, 6 h, 67%.

**2.7 – Conclusion:** In summary, we have successfully synthesised a conjugation ready azido linker containing thio-methyl substituted octasaccharide by [2+(4+2)] glycosylation strategy. All the building blocks were synthesised using a convergent approach. 1,2-Cis selectivity was achieved by exploiting the reciprocal-donor-acceptor-reactivity concept at lower temperatures in arabinofuranosylation and using tosyl group as protecting group to reduce the reactivity of the donor in case of xylofuranosylation. All the glycosylations were done under silver-assisted gold catalysed glycosylation conditions, with good to excellent yield. Finally, late-stage substitution of the tosyl group by thio-methyl was successfully achieved. Global deprotection of the molecule is in progress, fully deprotected molecule can be employed as biomarker for tuberculosis, vaccine candidate, and other biological implications.

## 2.7 - Experimental section

**General procedure for TBDPS-protection of alcohols (14, 40)**

Alcohol (1.0 mmol) and imidazole (2.0 mmol) were dissolved in dry DMF (10 mL/g) and stirred for 10 minutes, and the solution was cooled to 0º C, TBDPS-Cl was added dropwise into the solution and stirred for a further 2 h, TLC monitored the reaction. After completion of the reaction, the mixture was diluted with ethyl acetate, and the combined organic layer was washed with ice-cold water and brine dried over $Na_2SO_4$. It evaporated in *vacuo* to obtain a crude residue, further purified on silica gel column chromatography (hexane: ethyl acetate) to afford the desired product.

**General procedure for TBDPS-ether deprotection (4, 10, 13, 19, 35, 37, 44)**

Silyl ether (1.0 mmol) was dissolved in pyridine (3 mL/g), HF.py (3 mmol) was added dropwise into it at 0 ºC, stirred for 2-3 h, after completion reaction mixture diluted with dichloromethane, washed with 1N HCl, cold water and after that $NaHCO_3$ and brine solution. The combined organic layer was dried over $Na_2SO_4$, evaporated in *vacuo* obtained residue was purified by column chromatography (hexane: ethyl acetate) to furnish the desired alcohols in good to excellent yields.

**General procedure for acetonide protection of 1,2-diols (Arabinofuranose) (14)**

In the stirring solution of 1,2-diol (58g, 149.28 mmol) in 900 mL dry acetone, 1,1-dimethoxy propane (36.58 mL, 298.56 mmol) and *p*-TSA (4.63g, 26.87 mmol) were added and stirred for 1 h. The reaction mixture was quenched by adding triethyl amine and dried in *vacuo*, purified by column chromatography to obtain 1,2 acetonide-protected arabinofuranose **14** (56g, 87.5 %).

**General procedure for acetonide protection of 1,2-diols (xylofuranose) (39)**

D-Xylose (25 g) was suspended in acetone (625 ml) containing conc$^n$ $H_2SO_4$ (25 mL), the mixture was stirred for 30 min. at room temperature. Then the solution of $Na_2CO_3$ (32.5 g) in water (325 mL) was added carefully in reaction mixture at 0º C, after addition the mixture was stirred for a further 3h, again solid $Na_2CO_3$ (25 g) was added in three portions over 30 min., reaction mixture was passed through a celite® pad and purified in dichloromethane and acetone (18:1) solvent system over silica gel column chromatography, white sticky compound was obtained with 90% yield.

**General procedure for Benzyl protection (15, 18, 26, 41, 43, 47)**

NaH (1.2 mmol per alcohol) was added into the stirring solution of alcohol (1.0 mmol) in DMF at 0º C & stirred for 10 minutes, benzyl bromide (1.2 mmol per alcohol) and catalytic tetra-n-butyl ammonium iodide was added into the reaction mixture and further stirred at room temperature for 2 h. After completion of the reaction mixture was poured into the cold water and extracted with ethyl acetate. The organic layer was washed with ice-cold water and brine solution and dried over $Na_2SO_4$. Evaporation of organic layer in *vacuo* and purification of residue on column chromatography leads to desire benzyl ether.

**General procedure for Naphthylmethyl protection (19)**

To the solution of alcohol (2.5 g, 6.75 mmol) in DMF (25 mL), NaH (210 mg, 8.77 mmol) was added and stirred for 5 to 10 minutes at 0 ºC, naphthyl methyl bromide (1.6 mL, 10.12 mmol) dropwise and a catalytic amount of tetra-n-butyl ammonium iodide was added and stirred for next 2 h. After completion of the reaction mixture was diluted with ethyl acetate, washed with cold water and brine solution, and dried over $Na_2SO_4$. The combined organic layer was

evaporated in *vacuo*, and the residue was purified by column chromatography (hexane: ethyl acetate) to obtain the desired compound (2.8 g, 6.36 mmol) with 94 % yield.

**General procedure for Naphthylmethyl ether deprotection (24)**

2,3-dichloro-5,6-dicyano-1,4-di benzoquinone (1.96g, 8.63 mmol) was added into the compound (3.2g, 2.47 mmol) solution in DCM: MeOH (1:3). After 4 h triethyl amine was added into the reaction mixture to stop the reaction, which was filtered off through celite® pad, the excess solvent was evaporated in *vacuo* and residue was purified by column chromatography (hexane: ethyl acetate) to obtain desired alcohol (2.4 g, 2.05 mmol) with 83% yield.

**General procedure for benzoate protection (16, 52)**

Alcohol (1.0 mmol) and DMAP (0.2 mmol) were dissolved in anhydrous pyridine/THF (10 mL/g), and benzoyl chloride (1.2 mmol) was added dropwise into it at 0 ºC and stirred for 3 h. The reaction mixture was diluted with dichloromethane, washed with 1N HCl, cold water, $NaHCO_3$ solution, and brine solution, and dried over $Na_2SO_4$. The combined organic layer was evaporated in *vacuo*, and the residue was suspended into the mixture of a saturated solution of $Na_2CO_3$: THF (1:1), stirred overnight, check TLC, and if benzoyl chloride is still in reaction mixture, add some solid $Na_2CO_3$, stirred for 4 h, dilute with ethyl acetate and wash with water and brine, dried over *vacuum*.

**Saponification of esters (26, 28)**

Benzoate protected compound (1.0 mmol) was dissolved in MeOH: DCM (3:1), sodium methoxide (0.2 mmol per benzoate) was added to it and stirred for 30 minutes. After completion of reaction, Amberlite IR 120 $H^+$ was added to neutralise the sodium methoxide, the reaction mixture was filtered off and concentrated in *vacuo*, and the residue was purified by column chromatography (hexane: ethyl acetate) to obtain the required alcohol. Yield of the reaction is very good.

**General procedure for allyl glycoside formation from 1,2-acetonide (9, 17, 42)**

Allyl alcohol (5.0 mmol) and *p*-TSA (0.2 mmol) were added into the solution of 1,2-acetonide-protected compound (1.0 mmol) in dry DCM (10 mL/g) and stirred for 2 h at 60 ºC. After completion of the reaction was neutralized by adding triethyl amine into the reaction mixture and evaporated in *vacuo*, the residue was purified by silica column chromatography (hexane: ethyl acetate) to obtain the desired allyl glycoside.

**General procedure for allyl glycoside formation from 1,2-orthoester (27)**

Allyl alcohol (15 g, 25.65 mmol) and *p*-TSA (1.33 g, 7.70 mmol) were added into the solution of 1,2-orthoester (7 mL, 103 mmol) and 4 Å molecular sieves in dry dichloromethane (15

mL/g) at room temperature and stirred for 2 h, the reaction mixture was passed through celite® bed on completion of the reaction and solvent was evaporated in *vacuo*, the residue was purified by column chromatography (hexane: ethyl acetate) to obtain allyl glycoside (12g, 20.52 mmol) with 80% yield.

**The general procedure of levulinate protection (28)**

Alcohol (1.4 g, 2.76 mmol), DMAP (168 mg, 1.38 mmol), and levulinic acid (481mg, 4.14 mmol) solution in dry $CH_2Cl_2$ (14 mL) was cooled to 0 ºC, and N, N-diisopropyl carbodiimide (573 mg, 4.14 mmol) was added dropwise under nitrogen atmosphere. The reaction mixture was gradually warmed to room temperature and stirred for 2 h. After completion of the reaction, dichloromethane was evaporated in *vacuo*, and the residue was purified by column chromatography (hexane: ethyl acetate) to obtain the required Lev ester compound (1.56 g, 2.56 mmol) in 93% yield as a white syrup.

**A general method for benzylidene protection (50)**

Benzaldehyde dimethyl acetal (20.45 mL, 136.23 mmol) and camphor sulfonic acid (4.22 g, 18.16 mmol) were added into the stirring solution of starting material (20g, 90.82 mmol) in dry DMF, and stirred for 6 h. After completion of the reaction, mixture was poured into the ice water, the compound was precipitated out and filtered off through Whatman filter paper, white solid was washed with water, dried, stirred with hexane (and minimum amount of dichloromethane) reprecipitated, and filtered off through Whatman filter paper, 2,3-time hexane washing gives pure white solid compound (22.5g, 72.97 mmol) in 80% yield.

**A general method for the reductive opening of benzylidene (5)**

Triethyl silane (3.65 mL, 22.88 mmol) was added into the solution of benzylidene protected compound (2.3 g, 4.58 mmol) in $CH_2Cl_2$ (23 mL), and stirred for 10 minutes at 0 ºC. Subsequently, trifluoro acetic acid (1.75 mL, 22.88 mmol) was added and stirred for 30 minutes. TLC monitored the reaction and, if not completed, stirred at room temperature even after 30 minutes. After completion of saturated reaction solution of $NaHCO_3$ was added into the reaction mixture to neutralize it, diluted with dichloromethane, and washed with cold water, brine, and died over $Na_2SO_4$, concentrated in *vacuo*, purified by column chromatography (hexane: ethyl acetate). Compound **5** (1.75 g, 3.47 mmol) was obtained in 75% yield.

**General procedure for selective benzyl protection (51)**

In the stirring solution of diol (9.30 g, 30.16 mmol) in toluene (93 mL), $Bu_2SnO$ (7.51 g, 30.16 mmol) was added and reflux for 6-8 h, toluene was evaporated in *vacuo*, and the compound was dried at a high vacuum. Subsequently, CsF (9.16g, 60.32 mmol) and BnBr (5.37 mL, 45.24 mmol) were added to the solution of the compound in DMF (186 mL), and the reaction mixture

was stirred for 10-12 h. The white precipitate was filtered off, and the mixture was diluted with ethyl acetate, washed with brine, dried over $Na_2SO_4$, evaporated in *vacuo*, and purified by column chromatography (hexane: ethyl acetate) to obtain the required benzyl ether compound **51** (9.5 g, 23.84 mmol) in 79% yield.

**Opening of 1,2-*O*-isopropylidene-D-xylofuranose by STol (46)**

$BF_3.Et_2O$ (4.28 mL, 34.70 mmol) was added to the stirring solution of 4-methylbenzenethiol (6.46g, 52.05 mmol) and 1,2-*O*-isopropylidene protected compound **41** (18g, 34.70 mmol) in dry dichloromethane (25 mL) and stirred for 15 min., $Na_2CO_3$ was added into the reaction mixture, washed with brine and water, dried over sodium sulphate, evaporated on rota, and purified by column chromatography (ethyl acetate: hexane) to furnish compound **46** (16g, 22.57mmol) in 65% yield.

**STol to Hemiacetal conversion (48)**

NBS (3.21g, 14.22 mmol) was added to the solution of compound **48** (3.20g**,** 4.74 mmol) in acetone/water (9:1, 25 mL) at 0 ºC, the reaction mixture was stirred for 30 min., after completion of the reaction, saturated solution of $Na_2CO_3$ was added into the reaction mixture to terminate the reaction. Acetone/water was evaporated on rota and mixture was diluted with dichloromethane and washed with brine and water, dried over sodium sulphate, concentrated, and purified by column chromatography to get desire hemiacetal (2.40g, 4.22 mmol) in 89% yield.

**General procedure for deprotection of allyl glycoside and installation of ethynyl cyclohexyl carbonate donor (3, 6, 8, 12, 11, 22)**

To the solution of allyl glycoside (1.0 mmol) in DCM: MeOH (3:1) (20 mL/g), $PdCl_2$ (0.2 mmol) was added into the reaction in portions under nitrogen atmosphere, vigorously stirred for 2- 3 h. after completion of the reaction, triethyl amine was added into it, and the solid residue was filtered off passing through celite® pad. The solvent was evaporated in *vacuo*, and the residue was purified by column chromatography (hexane: ethyl acetate) to obtain the desired hemiacetal.

Corresponding hemiacetals (1.0 mmol), DMAP (1.2 mmol), and ethynyl cyclohexyl(4-nitrophenyl) carbonate (1.3 mmol), were added in DCM (10mL/g) and stirred for 3h at room temperature. After completion of the reaction, DCM was evaporated, and the residue was purified by column chromatography (hexane: ethyl acetate) to afford ethynyl cyclohexyl glycosyl carbonate donor with a trace amount of 4-nitrophenol in order to remove 4-nitrophenol, the compound was diluted with DCM and washed with sat. aq. $NaHCO_3$ solution to obtain corresponding pure carbonate donors.

**General procedure for glycosylation (21, 23, 29, 31, 32, 53, 54)**

Under an atmosphere of nitrogen donor, (1.0 mmol) and acceptor (1.0 mmol) were dosed in dry $CH_2Cl_2$ (5mL/g). To seize moisture from the reaction mixture, activated 4Å molecular sieves powder was added and stirred for 10 minutes. 8 mol% of each AgOTf and chloro[tris(2,4-di-tert-butyl phenyl)phosphite]gold was added and further stirred for 15-30 minutes. If the reaction is at -78 ºC then stirred for 4-5 h, quenched by the addition of triethyl amine, the reaction mixture was filtered off through celite® pad, dichloromethane was evaporated, the residue was purified by column chromatography (hexane: ethyl acetate) to obtain the glycosylated desire products in excellent yields.

**General glycosylation procedure for azido-tetra-ethylene-glycol linker containing compounds (34, 36, 38, 56)**

Under an atmosphere of nitrogen donor, (1.0 mmol) and acceptor (1.0 mmol) were dosed in dry $CH_2Cl_2$ (5mL/g). To seize moisture from the reaction mixture, activated 4Å molecular sieves powder was added and stirred for 10 minutes. 20 mol% of each AgOTf and chloro[tris(2,4-di-tert-butyl phenyl)phosphite]gold was added and stirred for 1 h. after completion of reaction, mixture was filtered off through celite® pad, dichloromethane was evaporated, the residue was purified by column chromatography (hexane: ethyl acetate) to obtain the glycosylated products in good to moderate yields.

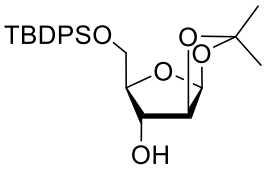
**General procedure for tosylation (4, 44)**

To the stirring solution of compound (1.0 mmol) at 0 ºC in pyridine was added tosyl chloride (1.5 mmol), further stirred for 6 h at room temperature. The reaction mixture was washed with 1N HCl, cold water, and $NaHCO_3$ solution after completion of reaction. Evaporated on rota and purified by column chromatography (hexane: ethyl acetate) to get desired tosylated compound.

**General method for substitution of tosyl by methyl-mercaptan (45, 55, 57)**

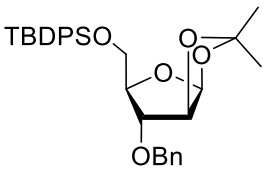
To the solution of compound (1.0 mmol) in acetonitrile, sodium methoxide (3.0 - 20.0 mmol), and 18-crown-6 were added. The reaction mixture was reflux for 2-10 h, diluted with acetonitrile and filtered through a celite® bed, concentrated on rota, and purified by column chromatography.

1,2-*O*-isopropylidine-5-*O*-$^{tert}$butyldiphenylsilyl-D-arabinofuranose (**14**):

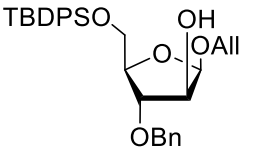



$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.67 (m, 4H), 7.44 – 7.36 (m, 6H), 5.88 (d, *J* = 4.5 Hz, 1H), 4.55 (d, *J* = 3.9 Hz, 1H), 4.43 (s, 1H), 4.10 – 4.04 (m, 1H), 3.83 (2d, *J* = 2.3 Hz, 2H), 2.08 (s, 1H), 1.33 (s, 3H), 1.29 (s, 3H), 1.07 (s, 9H); $^{13}$C NMR (101MHz, $CDCl_3$): δ 135.7(2C), 135.7 (2C), 133.3(2C), 129.9(2C), 127.9(4C), 112.7, 105.7, 87.5, 87.2, 76.4, 63.8, 27.0, 26.9, 26.2(3C), 19.3; HRMS (ESI-MS): m/z calcd for $C_{24}H_{32}O_5Si$ $[M+Na]^+$: 451.1917 Found: 451.1905.

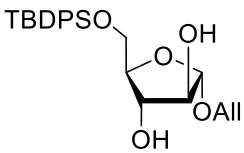
1,2-*O*-isopropylidine-3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-D-arabinofuranose (**15**): $^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.67 – 7.63 (m, 4H), 7.44 – 7.32 (m, 11H), 5.89 (d, *J* = 4.1 Hz, 1H), 4.66 (d, *J* = 4.0 Hz, 1H), 4.61 (2d, *J* = 1.6 Hz, 2H), 4.25 – 4.20 (m, 2H), 3.80 (m, 2H), 1.34 (s, 3H), 1.30 (s, 3H), 1.04 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 137.6, 135.7(2C), 135.7(2C), 133.4, 133.2, 129.9, 129.8, 128.6 (2C) 128.0, 127.9-127.8 (6C), 112.6, 105.9, 85.3, 85.2, 83.0, 71.8, 63.6, 27.1, 27.0, 26.3(3C), 19.3; HRMS (ESI-MS): m/z calcd for $C_{31}H_{38}O_5Si$ $[M+Na]^+$: 541.2386 Found: 541.2376.



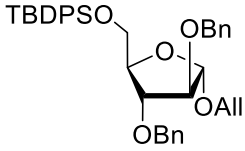

Allyl-3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*β*-D-arabinofuranose (**9**): $^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.71 – 7.65 (m, 4H), 7.37 (m, 7H), 7.31 – 7.28 (m, 4H), 5.80 (m, 1H), 5.18 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.12 (dq, *J* = 10.4, 1.3 Hz, 1H), 5.00 (d, *J* = 4.8 Hz, 1H), 4.76 (d, *J* = 11.8 Hz, 1H), 4.62 (d, *J* = 11.9 Hz, 1H), 4.27 (2d, *J* = 4.8, 1H), 4.18 (ddt, *J* = 12.8, 5.3, 1.5 Hz, 1H), 4.08 (q, *J* = 5.5 Hz, 1H), 4.01 – 3.94 (m, 2H), 3.75 (2d, *J* = 4.7 Hz, 2H), 1.06 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 138.2, 135.7(4C), 133.8, 133.4, 133.4, 129.8, 129.8, 128.4(2C), 127.8-127.7(7C), 117.7, 100.7, 84.7, 82.5, 78.2, 72.0, 68.7, 65.5, 26.9(2C), 19.4; HRMS (ESI-MS): m/z calcd for $C_{31}H_{38}O_5Si$ $[M+Na]^+$: 541.2386 Found: 541.2377.



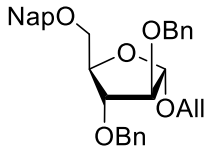

Allyl-5-*O*-$^{tert}$butyldiphenylsilyl-*α*-D-arabinofuranose (**17**): $^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.69 (m, 4H), 7.49 – 7.39 (m, 6H), 5.98 – 5.87 (m, 1H), 5.30 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.22 (dq, *J* = 10.4, 1.4 Hz, 1H), 5.15 (s, 1H), 4.25 (m, 1H), 4.19 (d, *J* = 11.4 Hz, 1H), 4.17 – 4.13 (m, 2H), 4.09 – 4.03 (m, 2H), 3.84 (dd, *J* = 11.4, 2.3 Hz, 1H), 3.76 (dd, *J* = 11.6, 1.7 Hz, 1H), 3.01 (d, *J* = 11.4 Hz, 1H), 1.07 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 135.8(2C), 135.7(2C), 133.8, 132.0, 131.9, 130.3, 130.2, 128.1(2C), 128.0(2C), 117.8, 107.6, 87.6, 78.6, 78.1, 68.2, 64.2, 26.8(3C), 19.1; HRMS (ESI-MS): m/z calcd for $C_{24}H_{32}O_5Si$ $[M+Na]^+$: 451.1917 Found: 451.1909.



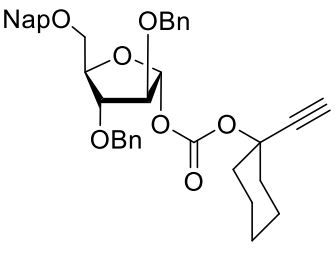
Allyl-2,3-*O*-dibenzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*α*-D-arabinofuranoside (**18**): $^1$H NMR (400 MHz, $CDCl_3$): δ 7.69 – 7.65 (m, 4H), 7.43 – 7.24 (m, 16H), 5.93 (m, 1H), 5.30 (dd, *J* = 17.2, 1.7 Hz, 1H), 5.19 (dd, *J* = 10.3, 1.6 Hz, 1H), 5.09 (d, *J* = 1.3 Hz, 1H), 4.57 – 4.47 (m, 4H), 4.25 – 4.20 (m, 1H), 4.17 (dd, *J* = 6.1, 4.5 Hz, 1H), 4.06 (dd, *J* = 3.1, 1.4 Hz, 1H), 4.03 (d, *J* = 6.3 Hz, 1H), 4.02 – 3.97 (m, 1H), 3.89 - 3.80 (2dd, *J* = 4.5, 1.1 Hz, 2H), 1.05 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 138.2, 137.9, 135.8(2C), 135.8(2C), 134.5, 133.6(2C), 129.8, 129.7, 128.5(2C), 128.5(2C), 127.9-127.8(10C), 117.4, 105.4, 88.5, 83.4, 82.5, 72.2, 72.0, 68.3, 64.0, 27.0(3C), 19.5; HRMS (ESI-MS): m/z calcd for $C_{38}H_{44}O_5Si$ $[M+Na]^+$: 631.2856 Found: 631.2850.



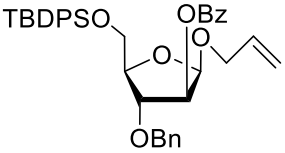

Allyl-2,3-*O*-dibenzyl-5-*O*-naphthylmethyl-*α*-D-arabinofuranoside (**19**): $^1$H NMR (400 MHz, $CDCl_3$): δ 7.84 – 7.74 (m, 4H), 7.48 – 7.42 (m, 3H), 7.33 – 7.28 (m, 5H), 7.24 – 7.18 (m, 5H), 5.92 (m, 1H), 5.30 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.19 (dq, *J* = 10.4, 1.4 Hz, 1H), 5.11 (d, *J* = 1.1 Hz, 1H), 4.77 – 4.68 (m, 2H), 4.58 – 4.53 (m, 2H), 4.47 (m, 2H), 4.28 – 4.21 (m, 2H), 4.06 (dd, *J* = 3.1, 1.3 Hz, 1H), 4.01 (ddt, *J* = 13.1, 6.2, 1.4 Hz, 1H), 3.94 (dd, *J* = 6.7, 3.1 Hz, 1H), 3.65 (qd, *J* = 10.8, 4.5 Hz, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 138.0, 137.7, 135.7, 134.4, 133.4, 133.1, 128.6(2C), 128.4(2C), 128.3, 128.0(3C), 128.0, 127.9(2C), 127.8(2C), 126.7, 126.2, 126.0(2C), 117.4, 105.5, 88.5, 83.7, 80.9, 73.6, 72.3, 72.1, 69.9, 68.2; HRMS (ESI-MS): m/z calcd for $C_{33}H_{34}O_5$[M+Na]$^+$: 533.2304 Found: 533.2311.




1-O-(((1-ethylnylcyclohexyl)oxy)carbonyl)-2,3-*O*-dibenzyl-5-*O*-naphthylmethyl-*α*-D-arabinofuranoside (**8**): $^1$H NMR (400 MHz, $CDCl_3$): δ 7.83 – 7.74 (m, 4H), 7.49 – 7.41 (m, 3H), 7.32 – 7.27 (m, 6H), 7.25 – 7.19 (m, 4H), 6.18 (s, 1H), 4.72 (s, 2H), 4.64 (d, *J* = 11.9 Hz, 1H), 4.52 – 4.48 (m, 3H), 4.42 (dt, *J* = 6.0, 4.9 Hz, 1H), 4.18 – 4.15 (m, 1H), 4.02 (dd, *J* = 5.9, 2.4 Hz, 1H), 3.67 (2d, *J* = 4.9 Hz, 2H), 2.65 (s, 1H), 2.26 – 2.14 (m, 2H), 1.93 – 1.84 (m, 2H), 1.65 (m, 4H), 1.32 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 151.5, 137.7, 137.3, 135.6, 133.4, 133.1, 128.6(2C), 128.5(2C), 128.3, 128.2(2C), 128.1, 128.1, 127.9, 127.9(2C), 127.8, 126.7, 126.2, 126.0, 125.9, 103.3, 87.1, 83.5, 83.5, 83.0, 78.2, 75.3, 73.7, 72.2, 72.2, 69.5, 37.1, 36.8, 25.1, 22.7(2C); HRMS (ESI-MS): m/z calcd for $C_{39}H_{40}O_7$[M+Na]$^+$: 643.2672 Found: 643.2674.

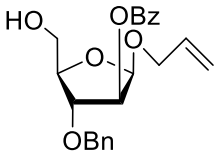



Allyl-2-*O*-bezoyl-3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*β*-D-arabinofuranoside (**16**): $^1$H NMR (400 MHz, $CDCl_3$): δ 8.07 – 8.03 (m, 2H), 7.72 (dd, *J* = 6.4, 1.8 Hz, 4H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.50 – 7.36 (m, 9H), 7.29 (s, 4H), 5.69 (m, 1H), 5.40 (d, *J* = 4.6 Hz, 1H), 5.25 (dd, *J* = 6.5, 4.6 Hz, 1H), 5.08

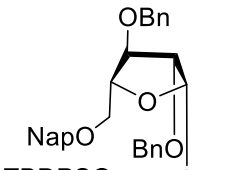


(dd, *J* = 17.4, 1.8 Hz, 1H), 5.01 (dd, *J* = 10.4, 1.7 Hz, 1H), 4.69 (s, 2H), 4.49 – 4.45 (m, 1H), 4.21 (q, *J* = 5.8 Hz, 1H), 4.12 – 4.06 (m, 1H), 3.94 – 3.87 (m, 1H), 3.84 (d, *J* = 6.2 Hz, 2H), 1.11 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.1, 137.9, 135.8(4C), 133.9, 133.5, 133.5, 133.3, 129.9(2C), 129.9, 129.9, 129.7, 128.5(2C), 128.5(2C), 127.9(4C), 127.8, 127.7(2C), 116.9, 99.7, 82.0, 81.7, 79.7, 72.4, 68.6, 65.9, 27.0(3C), 19.4; HRMS (ESI-MS): m/z calcd for $C_{38}H_{42}O_6Si[M+Na]^+$: 645.2648 Found: 645.2650.

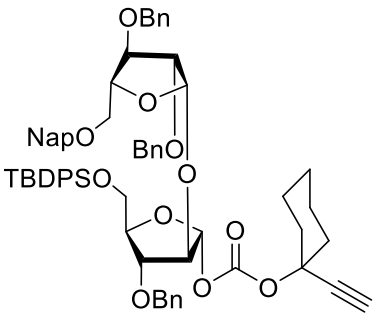
Allyl-2-*O*-bezoyl-3-*O*-benzyl-*β*-D-arabinofuranoside (**10**): $^1$H NMR (400 MHz, $CDCl_3$): δ 8.07 – 8.03 (m, 2H), 7.60 (m, 1H), 7.47 (m, 2H), 7.32 (m, 5H), 5.76 (m, 1H), 5.42 (d, *J* = 4.7 Hz, 1H), 5.25 – 5.22 (m, 1H), 5.22 – 5.16 (m, 1H), 5.10 (dd, *J* = 10.4, 1.4 Hz, 1H), 4.75 – 4.57 (m, 3H), 4.22 – 4.15 (m, 2H), 4.05 – 3.97 (m, 1H), 3.84 – 3.77 (m, 1H), 3.65 (m, 1H), 2.39 (dd, *J* = 8.5, 3.6 Hz, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.1, 137.7, 133.5, 133.5, 129.9(2C), 129.5, 128.6(4C), 128.1, 127.9(2C), 118.0, 100.1, 82.2, 79.8, 79.6, 72.7, 69.9, 63.5; HRMS (ESI-MS): m/z calcd for $C_{22}H_{24}O_6[M+Na]^+$: 407.1471 Found: 407.1407.




Allyl-2-*O*-(2,3-*O*-dibenzyl-5-*O*-naphthylmethyl-*β*-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*β*-D-arabinofuranoside (**21**): $^1$H NMR (400 MHz, $CDCl_3$): δ 7.84 – 7.74 (m, 3H), 7.69 (dd, *J* = 6.6, 1.5 Hz, 4H), 7.62 (s, 1H), 7.48 – 7.31 (m, 14H), 7.26 – 7.23 (m, 10H), 5.78 (m, 1H), 5.27 – 5.17 (m, 1H), 5.17 – 5.14 (m, 2H), 5.08 (dd, *J* = 10.3, 1.5 Hz, 1H), 4.83 (d, *J* = 11.5 Hz, 1H), 4.75 – 4.67 (m, 1H), 4.66 – 4.54 (m, 4H), 4.49 (d, *J* = 11.3 Hz, 2H), 4.44 (d, *J* = 12.2 Hz, 1H), 4.29 (dd, *J* = 6.9, 5.3 Hz, 1H), 4.23 – 4.07 (m, 5H), 3.97 – 3.90 (m, 1H), 3.76 (dd, *J* = 6.1, 4.1 Hz, 2H), 3.66 (d, *J* = 7.0 Hz, 1H), 3.61 (dd, *J* = 9.8, 4.9 Hz, 1H), 1.07 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 138.4, 138.3, 138.1, 135.8, 135.7 (4C), 134.0, 133.5 (2C), 133.4, 133.1, 129.8, 129.8, 128.5 (2C), 128.4 (2C), 128.4, 128.2 (3C), 128.0 (2C), 127.9 (7C), 127.8 (3C), 127.7, 127.6, 126.4, 126.1, 125.9, 125.8, 117.8, 99.0, 98.7, 84.0, 83.2, 82.9, 82.3, 81.0, 79.5, 73.3, 72.8, 72.4, 72.4, 71.8, 68.2, 66.0, 27.0 (3C), 19.4; HRMS (ESI-MS): m/z calcd for $C_{16}H_{66}O_9Si[M+Na]^+$: 993.4374 Found: 993.4386.

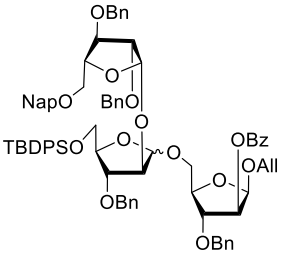



1-O-(((1-ethylnylcyclohexyl)oxy)carbonyl)-2-*O*-(2,3-*O*-dibenzyl-5-*O*-naphthylmethyl-*β*-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*α*-D-arabinofuranoside (**22**): $^1$H NMR (400 MHz, $CDCl_3$): δ 7.79 – 7.75 (m, 1H), 7.74 – 7.71 (m, 1H), 7.69 (d, *J*=4.4, 1H), 7.66 – 7.61 (m, 5H), 7.45 – 7.41 (m, 2H), 7.38 – 7.26 (m, 12H), 7.25 – 7.21 (m, 10H), 6.05 (s, 1H), 5.19 (d, *J*=3.8, 1H), 4.70 – 4.60 (m, 2H), 4.60 – 4.57 (m, 2H), 4.55 (d, *J*=4.9, 1H), 4.52 (d,

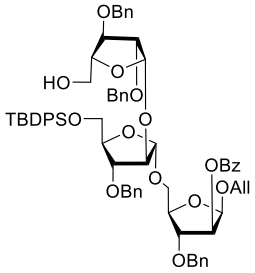


*J*=2.7, 2H), 4.51 – 4.44 (m, 2H), 4.36 (q, *J*=5.3, 1H), 4.15 (td, *J*=4.9, 1.7, 2H), 4.09 (dd, *J*=3.8, 1.3, 2H), 3.80 (dd, *J*=5.3, 1.5, 2H), 3.57 (dd, *J*=5.7, 3.6, 2H), 2.62 (s, 1H), 2.23 – 2.14 (m, 2H), 1.87 (q, *J*=11.6, 10.3, 2H), 1.63 (dd, *J*=14.2, 4.5, 4H), 1.35 – 1.27 (m, 2H), 1.02 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 151.6, 138.2, 138.0, 137.7, 135.8(2C), 135.7(2C), 135.5, 133.5, 133.4, 133.3, 133.1, 129.8, 129.8, 128.6(2C), 128.5(2C), 128.4(2C), 128.3, 128.1(2C), 128.0(2C), 127.9(4C), 127.8(4C), 127.7, 127.6(2C), 126.4, 126.2, 126.0, 125.7, 103.3, 100.3, 85.6, 84.7, 83.9(2C), 82.9, 82.9, 80.2, 78.1, 75.3, 73.3, 72.6, 72.5, 72.3, 72.2, 63.7, 37.0, 36.8, 27.0(3C), 25.1, 22.7(2C), 19.4; HRMS (ESI-MS): m/z calcd for $C_{67}H_{72}O_{11}Si[M+Na]^+$: 1103.4742 Found: 1103.4741.

Allyl-2-*O*-bezoyl-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-naphthylmethyl-*β*-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*α/β*-D-arabinofuranosyl)-*β*-D-arabinofuranoside [(*α*: *β*): 3:1] (**23**): $^1$H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 7.0 Hz, 2H), 7.81 – 7.54 (m, 10H), 7.46 – 7.40 (m, 5H), 7.38 – 7.26 (m, 15H), 7.19 (m, 10H), 5.71 (m, 1H), 5.37 (d, *J* = 4.5 Hz, 1H), 5.20 (dd, *J* = 6.6, 4.4 Hz, 1H), 5.15 – 5.07 (m, 2H), 5.01 (2d, *J* = 8.6 Hz, 2H), 4.69 – 4.54 (m, 7H), 4.51 (s, 1H), 4.44 (4d, *J* = 3.4 Hz, 4H), 4.25 – 4.04 (m, 8H), 3.96 – 3.85 (m, 2H), 3.82 – 3.76 (m, 2H), 3.60 – 3.54 (m, 2H), 1.04 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.1, 138.2, 138.2, 138.0, 137.8, 135.8(2C), 135.8(2C), 135.6, 134.0, 133.6, 133.5, 133.5, 133.4, 133.1, 130.0, 129.8, 129.7, 128.6-127.6(28C), 126.4, 126.2, 125.9, 125.7, 117.1, 106.0, 100.3, 99.6, 85.9, 84.1, 83.9, 83.2, 82.8, 82.3, 81.0, 80.2, 79.8, 79.7, 79.2, 73.3, 72.7, 72.5, 72.4, 72.3, 68.6, 64.1, 27.0(3C), 19.4; HRMS (ESI-MS): m/z calcd for $C_{80}H_{84}O_{14}Si[M+Na]^+$: 1319.5528 Found: 1319.5527.

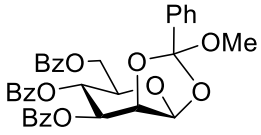



Allyl-2-*O*-bezoyl-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-*β*-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*α*-D-arabinofuranosyl)-*β*-D-arabinofuranoside (**24**): $^1$H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, *J* = 7.0 Hz, 2H), 7.67 (t, *J* = 7.1 Hz, 4H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.46 – 7.26 (m, 24H), 7.23 (m, 4H), 5.78 – 5.65 (m, 1H), 5.38 (d, *J* = 4.5 Hz, 1H), 5.21 (dd, *J* = 6.7, 4.5 Hz, 1H), 5.12 (dd, *J* = 17.2, 1.7 Hz, 1H), 5.07 (d, *J* = 4.4 Hz, 1H), 5.03 – 4.97 (m, 2H), 4.72 (d, *J* = 11.7 Hz, 1H), 4.65 – 4.60 (m, 4H), 4.57 (d, *J* = 7.6 Hz, 2H), 4.53 – 4.49 (m, 1H), 4.43 – 4.36 (m, 2H), 4.27 (t, *J* = 6.7 Hz, 1H), 4.25 – 4.19 (m, 1H), 4.19 – 4.12 (m, 3H), 4.07 (dd, *J* = 7.2, 4.4 Hz, 1H), 3.99 (m, 1H), 3.96 – 3.89 (m, 1H), 3.84 (m, 2H), 3.74 (dd, *J* = 11.3, 4.2 Hz, 1H), 3.63 (dd, *J* = 12.1, 3.1 Hz, 1H), 3.56 (m, 2H), 1.05 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.1, 138.2, 137.9(2C), 137.7, 135.8(2C), 135.8(2C), 133.9, 133.5, 133.4, 130.0(2C), 129.9, 129.8, 129.7, 128.7(2C), 128.6(2C),

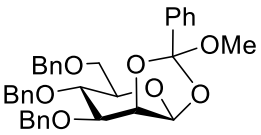


128.6(2C) 128.5(2C), 128.5(2C), 128.1(2C), 128.0-127.7(14C), 117.1, 105.8, 100.0, 99.7, 85.9, 84.2, 83.2, 82.2, 82.2, 82.1, 80.8, 79.7, 79.6, 72.8, 72.7, 72.4, 72.3, 69.3, 68.6, 64.0, 63.6, 27.0(3C), 19.4; HRMS (ESI-MS): m/z calcd for $C_{69}H_{76}O_{14}Si[M+Na]^+$:1179.4902 Found: 1179.4945.

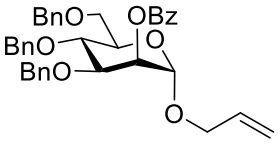
1,2-*O*-(methoxybenzylidene)-3,4,6-tri-*O*-benzoyl-*β*-D-mannopyranose (**25**): $^1$H NMR (400 MHz, $CDCl_3$): δ 8.02 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.93 – 7.87 (m, 4H), 7.74 – 7.67 (m, 2H), 7.58 – 7.42 (m, 3H), 7.41 – 7.26 (m, 9H), 5.90 (dd, *J* = 10.0, 9.2 Hz, 1H), 5.81 (d, *J* = 2.9 Hz, 1H), 5.67 (dd, *J* = 9.9, 4.0 Hz, 1H), 5.08 (dd, *J* = 4.1, 2.9 Hz, 1H), 4.53 (dd, *J* = 12.1, 3.3 Hz, 1H), 4.36 (dd, *J* = 12.1, 4.6 Hz, 1H), 4.10 (m, 1H), 3.23 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.08, 166.03, 165.20, 136.25, 133.53, 133.44, 133.01, 130.06 (2C), 129.81 (2C), 129.78 (2C), 129.74, 129.61, 129.33, 129.00, 128.94, 128.50, 128.46 (4C), 128.43 (2C), 128.33 (2C), 128.23 (2C), 126.51, 123.18, 97.94, 76.39, 72.07, 71.21, 66.49, 63.09, 51.50; HRMS (ESI-MS): m/z calcd for $C_{35}H_{30}O_{10}[M+Na]^+$: 633.1737 Found: 633.1741.



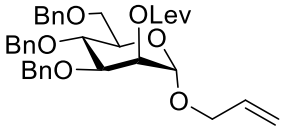

1,2-*O*-(methoxybenzylidene)-3,4,6-tri-*O*-benzyl-*β*-D-mannopyranose (**26**): $^1$H NMR (400 MHz, $CDCl_3$): δ 7.71 – 7.66 (m, 2H), 7.44 – 7.40 (m, 2H), 7.37 – 7.22 (m, 16H), 5.48 (d, *J* = 3.1 Hz, 1H), 4.88 (d, *J* = 10.9 Hz, 1H), 4.84 – 4.77 (m, 2H), 4.69 – 4.65 (m, 1H), 4.62 (d, *J* = 10.7 Hz, 1H), 4.45 – 4.35 (m, 2H), 3.93 (t, *J* = 9.1 Hz, 1H), 3.83 (dd, *J* = 9.3, 4.0 Hz, 1H), 3.66 (dd, *J* = 10.9, 4.7 Hz, 1H), 3.56 (dd, *J* = 10.9, 2.4 Hz, 1H), 3.48 (m, 1H), 3.26 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 138.5, 138.3, 138.0, 136.7, 129.1, 128.6(2C), 128.5(2C), 128.3(2C), 128.1(7C), 127.8, 127.6(2C), 127.5, 126.8(2C), 122.6, 97.9, 78.6, 76.4, 75.2, 75.1, 74.4, 73.3, 72.2, 69.2, 51.5; HRMS (ESI-MS): m/z calcd for $C_{35}H_{36}O_7[M+Na]^+$: 591.2359 Found: 591.2360.



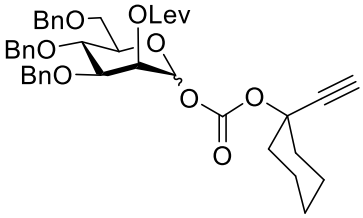

Allyl-2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-*α*-D-mannopyranoside (**27**): $^1$H NMR (400 MHz, $CDCl_3$): δ 8.07 (dd, *J* = 8.3 Hz, 1.4, 2H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.43 – 7.14 (m, 17H), 5.90 (dq, *J* = 16.8, 10.4, 6.2, 5.1 Hz, 1H), 5.64 (dd, *J* = 2.9, 2.0 Hz, 1H), 5.28 (dq, *J* = 17.2, 6.1, 1.6 Hz, 1H), 5.20 (dd, *J* = 10.4, 1.5 Hz, 1H), 5.02 (d, *J* = 1.9 Hz, 1H), 4.87 (d, *J* = 10.7 Hz, 1H), 4.77 (2d, *J* = 11.6 Hz, 2H), 4.55 (dd, *J* = 17.2, 11.2 Hz, 3H), 4.25 – 4.17 (m, 2H), 4.16 – 4.06 (m, 2H), 4.06 – 3.99 (m, 1H), 3.95 – 3.83 (m, 2H), 3.78 (d, *J* = 9.2 Hz, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.8, 138.5, 138.4, 138.0, 133.5, 133.16, 130.0, 129.9, 128.4 (2C), 128.4 (3C), 128.4(3C), 128.3(2C), 128.0(3C), 127.7, 127.647, 127.6(2C), 127.5, 117.9, 97.0, 78.3, 75.4, 74.4, 73.5, 71.7, 71.6, 69.1, 68.3; HRMS (ESI-MS): m/z calcd for $C_{37}H_{38}O_7[M+Na]^+$: 617.2515 Found: 617.2515.



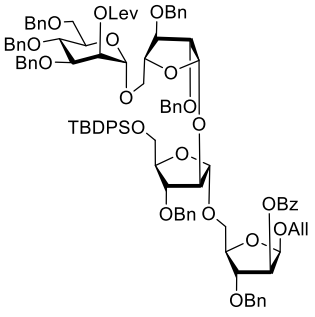
Allyl-2-*O*-(4-oxopentanoyl)-3,4,6-tri-*O*-benzyl-*α*-D-mannopyranoside (**28**): $^{1}$H NMR (400 MHz,$CDCl_3$): δ 7.37 – 7.25 (m, 13H), 7.17 – 7.13 (m, 2H), 5.86 (m, 1H), 5.39 – 5.36 (m, 1H), 5.28 – 5.15 (m, 2H), 4.88 – 4.82 (m, 2H), 4.68 (2dd, *J* = 11.8, 4.9 Hz, 2H), 4.49 (2dd, *J* = 14.2, 11.1 Hz, 2H), 4.49 (d, *J* = 14.2, 11.1 Hz, 1H), 4.15 (m, 1H), 4.02 – 3.93 (m, 2H), 3.89 – 3.77 (m, 3H), 3.72 – 3.67 (m, 1H), 2.73 – 2.65 (m, 4H), 2.12 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 206.5, 172.2, 138.4, 138.3, 138.1, 133.5, 128.4(5C), 128.1(2C), 128.1(2C), 127.9(2C), 127.7(2C), 127.7(2C), 117.8, 96.9, 78.2, 75.3, 74.4, 73.5, 71.7, 71.4, 68.9(2C), 68.2, 38.1, 29.9, 28.3; HRMS (ESI-MS): m/z calcd for $C_{35}H_{40}O_8$[M+Na]$^+$: 611.2621 Found: 611.2621.




1-O-(((1-ethylnylcyclohexyl)oxy)carbonyl)-2-*O*-(4-oxopentanoyl)-3,4,6-tri-*O*-benzyl-*α/β*-D-mannopyranoside [(α: β):1:3](**11**): $^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, *J* = 1.6 Hz, 2H), 7.31 (m, 5H), 7.30 – 7.26 (m, 6H), 7.17 (m, 2H), 5.98 (d, *J* = 2.0 Hz, 1H), 5.45 (dd, *J* = 3.3, 2.1 Hz, 1H), 4.86 (d, *J* = 10.7 Hz, 1H), 4.70 (d, *J* = 11.1 Hz, 1H), 4.65 (s, 1H), 4.55 – 4.51 (m, 2H), 4.50 (d, *J* = 5.6 Hz, 1H), 3.94 (2d, *J* = 7.5 Hz, 2H), 3.84 – 3.77 (m, 2H), 3.74 – 3.70 (m, 1H), 2.71 (m, 4H), 2.61 (s, 1H), 2.12 (s, 3H), 1.87 (d, *J* = 5.0, 2H), 1.68 – 1.48 (m, 6H), 1.37 – 1.27 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 206.3, 171.9, 150.3, 138.3, 138.3, 137.9, 128.5-127.7 (15C), 94.3, 82.6, 78.6, 77.7, 76.4, 75.4, 73.8, 73.7, 73.5, 72.0, 68.5, 67.7, 38.0, 36.9, 36.6, 29.9, 28.2, 25.0, 22.6 (2C); HRMS (ESI-MS): m/z calcd for $C_{41}H_{46}O_{10}$[M+Na]$^+$: 721.2989 Found: 721.3005.

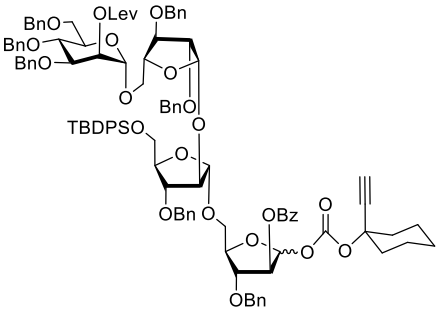



Allyl-2-*O*-bezoyl-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-*O*-dibenzyl-5-*O*-(2-*O*-(4-oxopentanoyl)-3,4,6-tri-*O*-benzyl-*α*-D-mannopyranosyl)-*β*-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*α*-D-arabinofuranosyl)-*β*-D-arabinofuranoside (**29**): $^{1}$H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, *J* = 7.0 Hz, 2H), 7.67 (t, *J* = 7.1 Hz, 4H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.47 – 7.27 (m, 24H), 7.23 (m, 4H), 5.78 – 5.65 (m, 1H), 5.38 (d, *J* = 4.5 Hz, 1H), 5.21 (dd, *J* = 6.7, 4.5 Hz, 1H), 5.12 (dd, *J* = 17.2, 1.7 Hz, 1H), 5.07 (d, *J* = 4.4 Hz, 1H), 5.03 – 4.98 (m, 2H), 4.72 (d, *J* = 11.7 Hz, 1H), 4.65 – 4.60 (m, 4H), 4.57 (d, *J* = 7.6 Hz, 2H), 4.53 – 4.49 (m, 1H), 4.42 – 4.37 (m, 2H), 4.27 (t, *J* = 6.7 Hz, 1H), 4.24 – 4.19 (m, 1H), 4.19 – 4.12 (m, 3H), 4.07 (dd, *J* = 7.2, 4.4 Hz, 1H), 3.99 (m, 1H), 3.96 – 3.89 (m, 1H), 3.84 (m, 2H), 3.74 (dd, *J* = 11.3, 4.2 Hz, 1H), 3.63 (dd, *J* = 12.1, 3.1 Hz, 1H), 3.56 (m, 2H), 1.05 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 206.4, 172.0, 166.1, 138.6, 138.4, 138.1(2C), 138.0, 138.0, 137.8, 135.8(2C), 135.8(2C), 133.9, 133.6, 133.5, 133.4, 130.0, 129.8, 129.7, 128.6-128.5(12C), 128.5-128.4(6C), 128.1(2C), 128.0(4C), 128.0(2C),

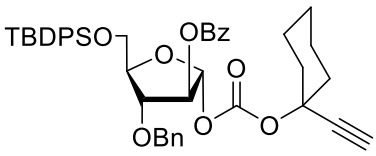


127.9-127.8(12C), 127.7(3C), 117.1, 105.8, 100.4, 99.6, 97.9, 85.9, 84.0, 83.9, 83.6, 82.7, 82.2, 79.8, 79.7, 79.4, 78.3, 75.3, 74.1, 73.5, 72.7, 72.5(2C), 72.3, 71.8, 71.7, 69.9, 69.1, 68.8, 68.7, 68.6, 63.9, 38.1, 29.9, 28.3, 27.0(3C), 19.4; HRMS (ESI-MS): m/z calcd for $C_{101}H_{110}O_{21}[M+Na]^+$: 1710.7240 Found: 1710.7362.

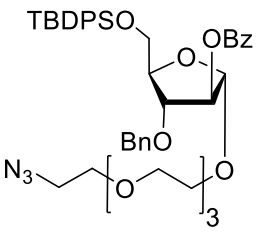
1-O-((1-ethylnylcyclohexyl)oxy)carbonyl-2-*O*-bezoyl-3-*O*-benzyl-5-*O*-(3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-2-*O*-(2,3-*O*-dibenzyl-5-*O*-(2-*O*-(4-oxopentanoyl)-3,4,6-tri-*O*-benzyl-*α*-D-mannopyranosyl)-*β*-D-arabinofuranosyl)- -D-arabinofuranosyl) -D-arabinofuranoside [(*α:β)*: 2.5:1] (**6**): $^1$H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 8.0 Hz, 2H), 7.64 (m, 5H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.35 – 7.26 (m, 25H), 7.22 (m, 10H), 7.18 – 7.17 (m, 4H), 7.13 (m, 3H), 6.23 (s, 1H), 5.54 (d, *J* = 1.9 Hz, 1H), 5.32 (s, 1H), 5.08 (d, *J* = 2.8 Hz, 1H), 4.96 (d, *J* = 1.6 Hz, 1H), 4.80 (m, 2H), 4.76 – 4.67 (m, 3H), 4.59 - 4.53 (m, 6H), 4.49 - 4.45 (m, 4H), 4.41 – 4.34 (m, 3H), 4.28 (m, 2H), 4.20 (dd, *J* = 5.6, 1.9 Hz, 1H), 4.03 – 4.00 (m, 4H), 3.87 (m, 3H), 3.73 (m, 4H), 3.54 (d, *J* = 10.1 Hz, 2H), 2.66 (m, 4H), 2.61 (s, 1H), 2.24 (m, 2H), 2.09 (s, 3H), 1.87 (m, 2H), 1.67 (m, 6H), 1.01 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 206.4, 172.0, 165.4, 151.4, 138.6, 138.4, 138.1, 138.0, 137.8, 137.8, 137.7, 135.8(4C), 133.7, 133.6, 133.5, 130.2, 130.0(2C), 129.8(2C), 129.2, 128.7-128.4(15C), 128.1-127.7(25C), 106.3, 102.9, 100.5, 98.0, 85.7, 83.9, 83.8, 83.4, 82.9, 82.8, 81.6, 79.4, 78.4(2C), 75.4, 75.3, 74.1, 73.5, 72.7, 72.6(2C), 72.4(2C), 72.3, 71.8, 71.7(2C), 70.0, 68.8, 68.7, 65.8, 38.1, 37.0, 36.8, 29.9, 28.3, 27.0(3C), 25.1, 22.7(2C), 19.4; HRMS (ESI-MS): m/z calcd for $C_{107}H_{116}O_{23}Si$ [M+Na]+: 1820.7607 Found: 1820.7603.



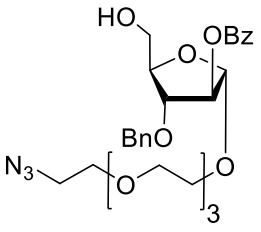

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-α-D-arabinofuranoside (**12**): IR ($cm^{-1}$, $CHCl_3$): 3289, 3069, 2931, 2858, 1758, 1728, 1264, 1237, 1107, 1070, 1009, 951, 911, 740, 702; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, *J* = 7.7 Hz, 2H), 7.73 – 7.50 (m, 4H), 7.33 (m, 14H), 6.26 (s, 1H), 5.59 (s, 1H), 4.83 (d, *J* = 12.0 Hz, 1H), 4.64 (d, *J* = 12.1 Hz, 1H), 4.46 (q, *J* = 4.7 Hz, 1H), 4.27 (d, *J* = 4.8 Hz, 1H), 3.82 (d, *J* = 5.4 Hz, 2H), 2.63 (s, 1H), 2.26 – 2.13 (m, 2H), 1.95 – 1.85 (m, 2H), 1.72 – 1.55 (m, 6H), 0.97 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.3, 151.4, 137.7, 135.7(4C), 133.6(2C), 133.2, 130.0(2C), 129.9, 129.8, 129.2, 128.6(2C), 128.5(2C), 128.0(2C), 127.9, 127.8(2C), 127.8(2C), 103.1, 85.9, 82.8, 82.7, 81.5, 78.3, 75.3, 72.4, 62.9, 37.0, 36.8, 26.9, 25.1, 22.7, 19.4; HRMS (ESI-MS): m/z calcd for $C_{44}H_{48}O_8Si$ [M+Na]$^+$: 755.3017; Found: 755.3026.



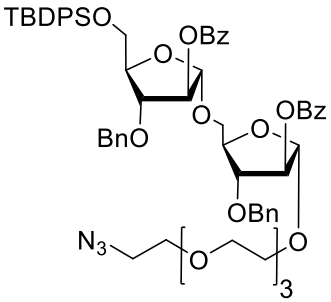
1-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethoxy)-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*α*-D-arabinofuranoside (**34**): IR (cm$^{-1}$, $CHCl_3$): 2929, 2861, 2101, 1722, 1453, 1265, 1106, 823; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 7.7 Hz, 2H), 7.63 (dd, *J* = 11.6, 6.9 Hz, 4H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.35 (m, 10H), 7.25-7.22 (m, 1H), 5.42 (m, 1H), 5.21 (s, 1H), 4.78 (d, *J* = 12.0 Hz, 1H), 4.56 (d, *J* = 11.7 Hz, 1H), 4.24 (d, *J* = 5.2 Hz, 1H), 4.13 (d, *J* = 5.6 Hz, 1H), 3.86 (d, *J* = 6.2 Hz, 1H), 3.82 (2d, *J* = 4.3 Hz, 2H), 3.72 – 3.65 (m, 6H), 3.62 (m, 8H), 3.34 (t, *J* = 5.1 Hz, 2H), 0.99 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.6, 137.8, 135.8(2C), 135.7(2C), 133.4(3C), 129.9(2C), 129.8, 129.8, 129.6, 128.5(2C), 128.5(2C), 128.0(2C), 127.8(3C), 127.8(2C), 106.4, 83.6, 83.2, 82.3, 72.4, 70.8, 70.8(2C), 70.7, 70.4, 70.1, 66.7, 63.2, 50.8, 26.9(3C), 19.4; HRMS (ESI-MS): m/z calcd for $C_{43}H_{53}N_3O_9Si$ $[M+K]^+$: 822. 3188 Found: 822.3486.




1-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethoxy)-2-*O*-benzoyl-3-*O*-benzyl-*α*-D-arabinofuranoside(**35**): $^1$H NMR (400 MHz, $CDCl_3$): δ 8.04 – 7.98 (d, *J* = 8.0 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.36 – 7.27 (m, 5H), 5.41 (d, *J* = 1.6 Hz, 1H), 5.22 (s, 1H), 4.82 (d, *J* = 11.9 Hz, 1H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.27 (dt, *J* = 6.2, 3.5 Hz, 1H), 4.04 (d, *J* = 5.8 Hz, 1H), 3.91 – 3.84 (m, 2H), 3.72 – 3.61 (m, 14H), 3.37 (t, *J* = 5.1 Hz, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.5, 137.7, 133.6, 129.9(2C), 129.5, 128.6(2C), 128.5(2C), 128.1(2C), 128.0, 106.5, 83.2, 83.1, 82.2, 72.6, 70.8, 70.8, 70.8, 70.7, 70.4, 70.1, 66.9, 62.2, 50.8; HRMS (ESI-MS): m/z calcd for $C_{43}H_{53}N_3O_9Si$ $[M+Na]^+$: 568.2271 Found: 568.2267.

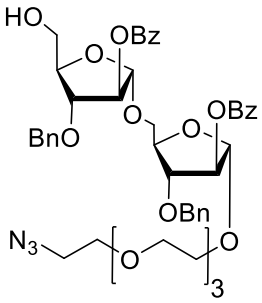



1-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethoxy)-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-benzoyl-3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*α*-D-arabinofuranosyl)-*α*-D-arabinofuranoside (**36**): IR (cm$^{-1}$, $CHCl_3$): 2930, 2864, 2104, 1721, 1453, 1263, 1104, 1026; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, *J* = 7.0 Hz, 2H), 7.95 (d, *J* = 7.0 Hz, 2H), 7.64 – 7.52 (m, 6H), 7.40 (m, 6H), 7.34 – 7.28 (m, 6H), 7.21 (m, 8H), 5.43 – 5.41 (m, 2H), 5.27 (s, 1H), 5.21 (s, 1H), 4.77 (d, *J* = 12.0 Hz, 1H), 4.64 – 4.57 (m, 2H), 4.46 (d, *J* = 12.1 Hz, 1H), 4.35 (d, *J* = 5.7 Hz, 1H), 4.17 – 4.08 (m, 3H), 3.94 – 3.86 (m, 2H), 3.78 – 3.74 (m, 2H), 3.72 – 3.61 (m, 14H), 3.36 (t, *J* = 5.1 Hz, 2H), 0.97 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.6, 165.4, 138.0, 137.9, 135.7 (2C), 135.7 (2C), 133.4 (2C), 133.4 (2C), 129.9 (4C), 129.8 (2C), 129.7 (2C), 128.6 (2C), 128.5 (2C), 128.4 (2C), 128.4 (2C), 128.0 (2C), 127.8 (2C), 127.8 (2C), 127.8 (3C), 127.7, 106.4,

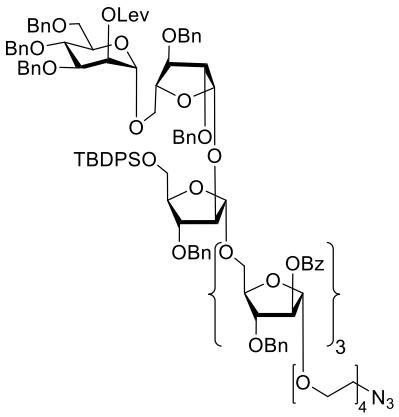


106.3, 83.9, 83.6, 83.1, 82.2, 82.1, 81.8, 72.5, 72.2, 70.9, 70.8, 70.8, 70.8, 70.4, 70.1, 66.9, 65.6, 63.2, 50.8, 26.9 (3C), 19.4; HRMS (ESI-MS): m/z calcd for $C_{62}H_{71}N_3O_{14}Si$ $[M+K]^+$: 1148.4342 Found: 1148.4606.

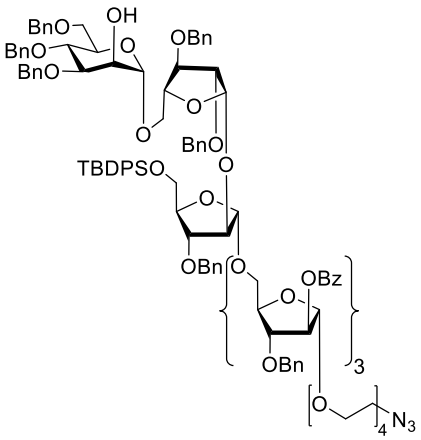
1-(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethoxy)-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-benzoyl-3-*O*-benzyl-*α*-D-arabinofuranosyl)-*α*-D-arabinofuranoside (**37**): IR ($cm^{-1}$, $CHCl_3$): 2915, 2108, 1722, 1454, 1269, 1112; $^1H$ NMR (400 MHz, $CDCl_3$): δ 8.05 – 7.98 (2d, *J* = 7.0 Hz, 4H), 7.57 (m, 2H), 7.47 – 7.40 (m, 4H), 7.36 – 7.31 (m, 2H), 7.31 – 7.26 (m, 2H), 7.26 – 7.18 (m, 6H), 5.43 (d, *J* = 1.4 Hz, 1H), 5.38 (d, *J* = 1.2 Hz, 1H), 5.26 (s, 1H), 5.22 (s, 1H), 4.81 (d, *J* = 12.0 Hz, 1H), 4.63 (dd, *J* = 12.1, 7.1 Hz, 2H), 4.46 (d, *J* = 12.1 Hz, 1H), 4.36 (dd, *J* = 9.6 Hz, 4.0, 1H), 4.14 (d, *J* = 5.7 Hz, 1H), 4.10 – 4.05 (m, 1H), 3.97 (d, *J* = 5.5 Hz, 1H), 3.94 – 3.87 (m, 2H), 3.81 – 3.73 (m, 2H), 3.72 – 3.65 (m, 6H), 3.64 – 3.52 (m, 9H), 3.36 (t, *J* = 5.1 Hz, 2H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 165.6, 165.4, 137.9, 137.7, 133.6, 133.5, 129.9 (2C), 129.8 (2C), 129.6, 129.5, 128.6 (4C), 128.5 (4C), 128.1 (2C), 127.9, 127.9 (2C), 127.8, 106.3, 106.3, 83.5, 83.5, 82.9, 82.1, 81.9, 81.7, 72.5, 72.3, 70.8, 70.8, 70.8, 70.7, 70.4, 70.1, 66.8, 65.9, 62.1, 50.8; HRMS (ESI-MS): m/z calcd for $C_{46}H_{53}N_3O_{14}Si$ $[M+K]^+$: 894.3425 Found: 894.3446.



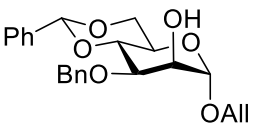

1-(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethoxy)-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-2-*O*-(2,3-di-*O*-benzyl-5-*O*-(2-*O*-(4-oxopentanoyl)-3,4,6-tri-*O*-benzyl-*α*-D-mannopyranosyl)-*β*-D-arabinofuranosyl)-*α*-D-arabinofuranosyl)-*α*-D-arabinofuranosyl)-*α*-D-arabinofuranosyl)-*α*-D-arabinofuranoside (**38**): IR ($cm^{-1}$, $CHCl_3$): 3014, 2110, 1722, 1453, 1267, 1216, 1111, 1027; $^1H$ NMR (400 MHz, $CDCl_3$): δ 8.05 – 7.94 (3d, J = 7.0 Hz, 6H), 7.66 – 7.60 (m, 4H), 7.56 – 7.46 (m, 3H), 7.44 – 7.26 (m, 22H), 7.23 – 7.09 (m, 35H), 5.42 (d, *J* = 1.6 Hz, 1H), 5.40 (d, *J* = 1.5 Hz, 1H), 5.33 – 5.31 (m, 2H), 5.25 (s, 1H), 5.19 (m, 2H), 5.04 (d, *J* = 4.3 Hz, 1H), 4.98 (d, *J* = 1.5 Hz, 1H), 4.82 – 4.72 (m, 3H), 4.62 – 4.46 (m, 10H), 4.43 (2d, *J* = 8.0 Hz, 2H), 4.40 – 4.30 (m, 4H), 4.25 (2d, *J* = 10.9 Hz, 2H), 4.18 – 4.11 (m, 2H), 4.09 – 4.03 (m, 3H), 4.00 (m, 4H), 3.96 – 3.77 (m, 8H), 3.76 – 3.56 (m, 23H), 3.56 – 3.49 (m, 2H), 3.35 (t, *J* = 5.1 Hz, 2H), 2.66 (m, 4H), 2.09 (s, 3H), 1.01 (s, 9H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 206.2, 171.9, 165.5, 165.3, 165.3, 138.5, 138.2, 137.9, 137.9, 137.8, 137.8, 137.7, 137.7, 137.6, 135.6 (2C), 135.6 (2C), 133.4, 133.4, 133.4, 133.3, 129.8-129.7 (6C),



129.5, 129.5, 129.4, 128.5-128.2 (30C), 127.9-127.5 (30C), 106.2, 106.2, 106.1, 106.1, 100.6, 97.8, 85.8, 83.9, 83.7, 83.4, 83.2, 83.2, 82.8, 82.1, 82.0, 82.0, 81.9, 81.8, 81.7, 79.3, 78.2, 75.2, 74.0, 73.4, 72.4, 72.4, 72.3, 72.3, 72.2, 72.2, 72.1, 71.7, 71.6, 70.7, 70.7, 70.7 (3C), 70.6, 70.2, 70.0, 68.6, 66.7, 65.6, 65.6, 65.5, 63.8, 50.7, 38.0, 29.8, 28.2, 26.9 (3C), 19.3; HRMS (ESI-MS): m/z calcd for $C_{144}H_{157}N_3O_{34}Si$ $[M+Na]^+$: 2524.0349 Found: 2524.0634.



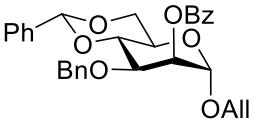

1-(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethoxy)-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-2-*O*-(2,3-di-*O*-benzyl-5-*O*-(3,4,6-tri-*O*-benzyl-*α*-D-mannopyranosyl)-*β*-D-arabinofuranosyl)-*α*-D-arabinofuranosyl)-*α*-D-arabinofuranosyl)-*α*-D-arabinofuranosyl)-*α*-D-arabinofuranoside (**2**): IR ($cm^{-1}$, $CHCl_3$): 3015, 2933, 2100, 1722, 1216, 1110; $^1H$ NMR (400 MHz, $CDCl_3$): δ 8.03 (d, *J* = 8.2 Hz, 2H), 8.00 (d, *J* = 8.2 Hz, 2H), 7.96 (d, *J* = 7.7 Hz, 2H), 7.63 (t, *J* = 7.7 Hz, 4H), 7.50 (m, 3H), 7.43 – 7.30 (m, 15H), 7.26 (m, 8H), 7.25 (m, 16H), 7.20 – 7.12 (m, 18H), 5.41 (m, 2H), 5.34 (s, 1H), 5.25 (s, 1H), 5.20 (m, 2H), 5.04 (d, *J* = 4.4 Hz, 1H), 4.99 (s, 1H), 4.85 – 4.75 (m, 3H), 4.63 – 4.42 (m, 13H), 4.41 – 4.27 (m, 5H), 4.15 (m, 2H), 4.11 – 3.99 (m, 7H), 3.98 – 3.79 (m, 8H), 3.78 – 3.71 (m, 5H), 3.67 (m, 7H), 3.62 (s, 9H), 3.57 – 3.50 (m, 2H), 3.35 (t, *J* = 5.1 Hz, 2H), 2.45 (s, 1H), 1.01 (s, 9H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 165.6, 165.4, 165.4, 138.5, 138.2, 138.0, 138.0, 137.9, 137.9, 137.9, 137.8, 137.7, 135.8 (2C), 135.7 (2C), 133.5, 133.5, 133.4, 133.4, 133.4, 129.9-129.8 (7C), 129.6, 129.6, 129.6, 128.6-128.3 (24C), 128.0-127.6 (32C), 106.3 (2C), 106.3, 106.2, 100.6, 99.4, 85.9, 83.9 (2C), 83.6, 83.5 (2C), 83.3 (2C), 82.9, 82.2 (2C), 82.0, 81.9, 81.8, 80.2, 79.3, 75.2, 74.1, 73.5, 72.5, 72.4, 72.3, 72.2, 72.2, 72.0, 71.5, 70.8 (2C), 70.8 (2C), 70.8 (2C), 70.7, 70.3, 70.1, 69.4, 68.8, 68.3, 66.8, 65.7, 63.9, 50.8, 27.0(3C), 19.4; HRMS (ESI-MS): m/z calcd for $C_{139}H_{151}N_3O_{32}Si$ $[M+Na]^+$: 2425.9948 Found: 2425.0483.



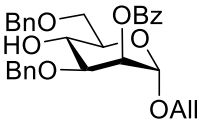

Allyl-3-*O*-benzyl-4,6-*O*-benzylidene-*α*-D-mannopyranoside (**51**): $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.53 – 7.47 (m, 2H), 7.41 – 7.28 (m, 8H), 5.89 (ddt, *J* = 16.2, 10.7, 5.7 Hz, 1H), 5.61 (s, 1H), 5.28 (d, *J* = 17.1 Hz, 1H), 5.21 (d, *J* = 10.5 Hz, 1H), 4.91 – 4.83 (m, 2H), 4.71 (d, *J* = 11.6 Hz, 1H), 4.27 (d, *J* = 5.8 Hz, 1H), 4.20 – 4.08 (m, 2H), 4.05 (d, *J* = 3.5 Hz, 1H), 4.02 – 3.92 (m, 2H), 3.86 (2d, *J* = 7.1 Hz, 2H), 2.81 (s, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 138.1, 137.6, 133.6, 129.0, 128.6 (2C), 128.3 (2C), 128.0, 127.9 (2C), 126.1 (2C), 118.0, 101.7, 99.3, 79.0, 75.8, 73.2, 70.1, 68.9,

68.3, 63.5; HRMS (ESI-MS): m/z calcd for $C_{46}H_{53}N_3O_{14}Si$ $[M+Na]^+$: 421.1627 Found: 421.1619.

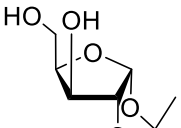
Allyl-2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-benzylidene-*α*-D-mannopyranoside (**52**): $^1$H NMR (400 MHz, $CDCl_3$): δ 8.11 (2d, *J* = 8.3, 1.4 Hz, 2H), 7.60 – 7.55 (m, 1H), 7.54 – 7.50 (m, 2H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.40 – 7.35 (m, 3H), 7.32 (dd, *J* = 7.8, 1.9 Hz, 2H), 7.27 – 7.21 (m, 3H), 5.90 (m, 1H), 5.69 (s, 1H), 5.63 (dd, *J* = 3.1, 1.7 Hz, 1H), 5.30 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.23 (dd, *J* = 10.4, 1.4 Hz, 1H), 4.98 (d, *J* = 1.6 Hz, 1H), 4.81 – 4.67 (m, 2H), 4.30 (dd, *J* = 9.4, 4.0 Hz, 1H), 4.23 – 4.11 (m, 3H), 4.02 (ddt, *J* = 12.9, 6.2, 1.4 Hz, 1H), 3.97 – 3.91 (m, 1H), 3.88 (m, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.9, 138.2, 137.6, 133.4, 133.3, 130.1 (2C), 129.9, 129.0, 128.5 (2C), 128.4 (2C), 128.3 (2C), 127.7 (2C), 127.6, 126.2 (2C), 118.2, 101.8, 98.0, 78.8, 74.2, 72.1, 70.4, 69.0, 68.5, 64.1; HRMS (ESI-MS): m/z calcd for $C_{46}H_{53}N_3O_{14}Si$ $[M+Na]^+$: 525.1889 Found: 525.1910.



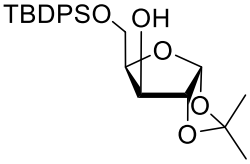

Allyl-2-*O*-benzoyl-3,6-di-*O*-benzyl-*α*-D-mannopyranoside (**5**): $^1$H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 6.9 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.39 – 7.31 (m, 6H), 7.28 (m, 4H), 7.25 – 7.16 (m, 2H), 5.92 (m, 1H), 5.61 (d, *J* = 1.3 Hz, 1H), 5.30 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.22 (dd, *J* = 10.4, 1.5 Hz, 1H), 5.03 (d, *J* = 1.8 Hz, 1H), 4.79 (d, *J* = 11.3 Hz, 1H), 4.69 (d, *J* = 12.0 Hz, 1H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.49 (d, *J* = 11.3 Hz, 1H), 4.23 (dd, *J* = 12.9, 5.2 Hz, 1H), 4.15 (t, *J* = 9.5 Hz, 1H), 4.04 (dd, *J* = 12.9, 6.2 Hz, 1H), 3.94 (dd, *J* = 9.4, 3.2 Hz, 1H), 3.91 – 3.79 (m, 3H), 2.65 (s, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.8, 138.4, 137.7, 133.5, 133.3, 130.0 (2C), 129.8, 128.5 (2C), 128.5 (2C), 128.4 (2C), 128.2 (2C), 128.0, 127.6, 127.5 (2C), 117.9, 97.2, 77.8, 73.7, 71.7, 71.5, 69.9, 68.5, 68.3, 67.3; HRMS (ESI-MS): m/z calcd for $C_{30}H_{32}O_7$ $[M+Na]^+$: 527.2046 Found: 527.2044.




1,2-*O*-isopropylidene-*α*-D-xylofuranose (**39**): $^1$H NMR (400 MHz, $CDCl_3$): δ 5.94 (d, *J* = 3.7 Hz, 1H), 4.49 (d, *J* = 3.7 Hz, 1H), 4.34 (s, 1H), 4.27 (d, *J* = 2.8 Hz, 1H), 4.14 (q, *J* = 3.5 Hz, 1H), 4.00 (qd, *J* = 12.3, 3.8 Hz, 2H), 3.52 (s, 1H), 1.45 (s, 3H), 1.29 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 111.9, 104.9, 85.6, 79.1, 76.6, 60.9, 26.8, 26.2; HRMS (ESI-MS): m/z calcd for $C_8H_{15}O_5$ $[M+H]^+$: 192.0953 Found: 192.0999.

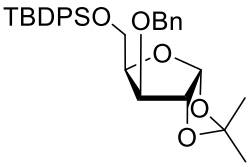



1,2-*O*-isopropylidene-5-*O*-$^{tert}$butyldiphenylsilyl-*α*-D-xylofuranose (**40**): $^1$H NMR (400 MHz, $CDCl_3$): δ 7.74 – 7.63 (m, 4H), 7.48 – 7.36 (m, 6H), 6.02 (d, *J* = 3.2 Hz, 1H), 4.56 (d, *J* = 3.5 Hz, 1H), 4.38 (s, 1H), 4.14 (s, 1H), 4.11 (dd, *J* = 7.5, 3.0 Hz, 2H), 4.11 (dd, *J* = 7.5, 3.0 Hz, 1H) 1.48 (s, 3H), 1.33 (s, 3H), 1.06 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 135.8 (2C), 135.6 (2C), 132.5,

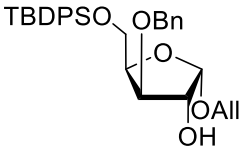


132.0, 130.2 (2C), 128.0 (2C), 128.0 (2C), 111.6, 105.1, 85.5, 78.5, 76.9, 62.9, 26.9, 26.8 (3C), 26.3, 19.2; HRMS (ESI-MS): m/z calcd for $C_{24}H_{32}O_5Si$ $[M+Na]^+$: 451.1917 Found: 451.1905.

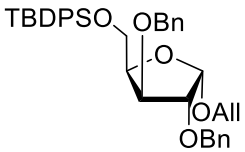
1,2-*O*-isopropylidene-3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*α*-D-xylofuranose (**41**): $^1$H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 7.2 Hz, 4H), 7.45 – 7.28 (m, 11H), 5.94 (d, *J* = 3.9 Hz, 1H), 4.72 (d, *J* = 11.7 Hz, 1H), 4.66 – 4.59 (m, 2H), 4.37 (m, 1H), 4.11 (d, *J* = 3.1 Hz, 1H), 4.03 (dd, *J* = 10.0, 7.8 Hz, 1H), 3.95 (dd, *J* = 10.0, 5.3 Hz, 1H), 1.53 (s, 3H), 1.35 (s, 3H), 1.10 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 137.8, 135.7 (2C), 135.7 (2C), 133.5, 133.3, 129.8, 129.8, 128.5 (2C), 127.9 (2C), 127.8 (3C), 127.6 (2C), 111.8, 105.2, 82.6, 81.6, 80.7, 77.4, 72.4, 60.8, 27.0, 26.7 (3C), 26.4, 19.3; HRMS (ESI-MS): m/z calcd for $C_{31}H_{38}O_5Si$ $[M+Na]^+$: 541.2386 Found: 541.2376.



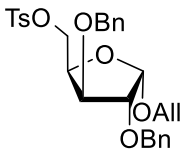

Allyl-3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*α*-D-xylofuranoside (**42**): $^1$H NMR (400 MHz, $CDCl_3$): δ 7.68 (s, 4H), 7.32 (m, 11H), 5.89 (m, 1H), 5.29 (d, *J*=1.9, 1H), 5.17 (d, *J*=10.5, 1H), 5.13 (d, *J* = 4.8 Hz, 1H), 4.74 (d, *J* = 11.9 Hz, 1H), 4.56 (d, *J* = 12.1 Hz, 1H), 4.38 – 4.26 (m, 3H), 4.08 (q, *J* = 4.8 Hz, 2H), 3.93 – 3.82 (m, 2H), 2.89 (s, 1H), 1.06 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 138.1, 135.7 (2C), 135.6 (2C), 133.9, 133.5, 133.4, 129.6 (2C), 128.3 (2C), 127.7 (2C), 127.6 (2C), 127.6 (3C), 117.7, 100.1, 83.4, 78.9, 76.6, 72.1, 69.1, 62.3, 26.8 (3C), 19.2; HRMS (ESI-MS): m/z calcd for $C_{31}H_{38}O_5Si$ $[M+Na]^+$: 541.2386 Found: 541.2377.




Allyl-2,3-di-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*α*-D-xylofuranoside (**43**): $^1$H NMR (400 MHz, $CDCl_3$): δ 7.75 – 7.66 (m, 5H), 7.46 – 7.27 (m, 15H), 5.96 (m, 1H), 5.33 (m, 1H), 5.24 – 5.19 (m, 1H), 5.02 (d, *J* = 4.4 Hz, 1H), 4.68 (dd, *J* = 11.8, 5.4 Hz, 2H), 4.58 (m, 2H), 4.37 – 4.23 (m, 3H), 4.17 (m, 1H), 4.05 (dd, *J* = 12.9, 6.4 Hz, 1H), 3.88 (dd, *J* = 11.1, 4.2 Hz, 1H), 3.80 (dd, *J* = 10.8, 4.6 Hz, 1H), 1.03 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 138.4, 138.0, 135.8 (2C), 135.8 (2C), 134.9, 133.7, 133.5, 129.8-127.6 (12C), 117.6, 98.8, 83.6, 81.6, 77.6, 72.8, 72.7, 68.7, 62.9, 26.9(3C), 19.3; HRMS (ESI-MS): m/z calcd for $C_{38}H_{44}O_5Si$ $[M+Na]^+$ : 631.2856 Found: 631.2850.

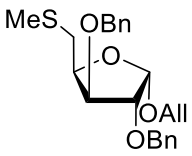



Allyl-2,3-di-*O*-benzyl-5-*O*-tosyl-*α*-D-xylofuranoside (**44**): $^1$H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.36 – 7.19 (m, 12H), 5.87 (m, 1H), 5.31 – 5.25 (d, *J* = 10 Hz, 1H), 5.19 (d, *J* = 10.1 Hz, 1H), 4.90 (d, *J* = 4.3 Hz, 1H), 4.62 – 4.56 (m, 2H), 4.49 (dd, *J* = 14.6, 11.8 Hz, 2H), 4.38 – 4.29 (m, 2H), 4.29 – 4.24 (m, 1H), 4.17 (dd, *J* = 12.5, 5.1 Hz, 1H), 4.07 (dd, *J* = 10.7, 6.3 Hz, 1H), 3.98 – 3.91 (m, 2H), 2.42 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 144.8, 137.8, 137.6, 134.0, 133.1, 129.8 (2C), 128.6 (2C), 128.5 (2C), 128.3 (2C), 128.1 (3C), 127.9, 127.8 (2C), 117.9, 98.6, 83.7, 81.2, 74.4, 72.7,

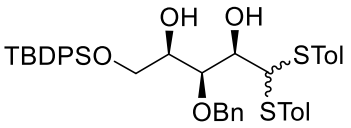


72.6, 69.3, 68.7, 21.8; HRMS (ESI-MS): m/z calcd for $C_{29}H_{32}O_7S$ $[M+Na]^+$ 547.1766 Found: 547.4881.

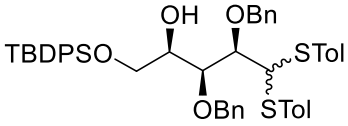
Allyl-2,3-di-*O*-benzyl-5-deoxy-5-methylmercapto-D-xylofuranoside (**45**): $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.27 (m, 10H), 6.01 – 5.87 (m, 1H), 5.35 – 5.28 (m, 1H), 5.23 – 5.17 (m, 1H), 5.02 (d, *J* = 3.7 Hz, 1H), 4.65 (dd, *J* = 11.8, 8.7 Hz, 2H), 4.54 (d, *J* = 11.7 Hz, 2H), 4.40 (q, *J* = 6.8 Hz, 1H), 4.26 (m, 2H), 4.07 – 3.99 (m, 2H), 2.82 (dd, *J* = 13.8, 5.4 Hz, 2H), 2.66 (dd, *J* = 13.8, 7.6 Hz, 1H), 2.13 (s, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 138.1, 137.8, 134.3, 128.5 (2C), 128.5 (2C), 128.2 (2C), 128.0, 127.8, 127.7 (2C), 117.7, 98.9, 84.0, 82.1, 77.0, 72.7, 72.5, 68.7, 34.2, 16.5; HRMS (ESI-MS): m/z calcd for $C_{23}H_{28}O_4S[M+Na]^+$ 423.1606 Found: 423.1610.



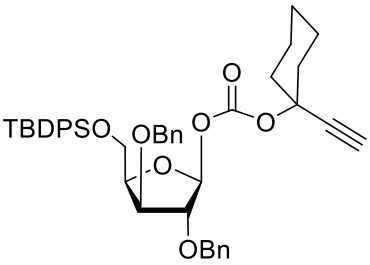

1-Dexoy-1,1-bis-(*p*-tolylthio)-3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-D-xylose (**46**): $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.65 (dt, *J* = 8.2, 1.5 Hz, 4H), 7.43 – 7.39 (m, 2H), 7.38 – 7.30 (m, 11H), 7.26 (d, *J* = 2.1 Hz, 2H), 7.07 (dd, *J* = 7.9, 5.1 Hz, 4H), 4.79 (d, *J* = 11.0 Hz, 1H), 4.72 (d, *J* = 11.0, 1H), 4.68 (s, 1H), 4.56 (d, *J* = 5.5 Hz, 1H), 4.33 (t, *J* = 3.7 Hz, 1H), 3.98 – 3.88 (m, 2H), 3.73 (d, *J* = 6.4 Hz, 2H), 3.15 (d, *J* = 5.3 Hz, 1H), 2.33 (s, 3H), 2.30 (s, 3H), 1.08 (s, 9H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 138.3, 138.3, 138.2, 135.7 (2C), 135.7 (2C), 133.3 (2C), 133.3 (2C), 132.9 (2C), 129.8 (3C), 128.7, 128.5 (2C), 128.2 (2C), 127.9 (2C), 127.1, 77.9, 75.0, 73.2, 73.1, 64.4, 63.8, 27.1 (3C), 21.3, 21.3, 19.4; HRMS (ESI-MS): m/z calcd for $C_{42}H_{48}O_4S_2Si[M+Na]^+$: 731.2661 Found: 731.2654.



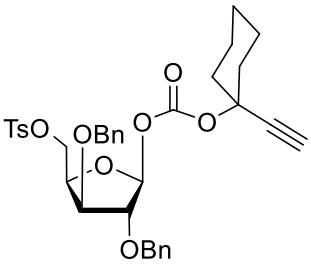

1-dexoy-1,1-bis-(*p*-tolylthio)-2,3-di-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-D-xylose (**47**): $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J* = 7.2, 4H), 7.44 – 7.25 (m, 18H), 7.12 – 7.01 (m, 6H), 4.94 (d, *J* = 11.1, 1H), 4.74 (dd, *J* = 11.0, 5.3 Hz, 2H), 4.68 (d, *J* = 2.2, 1H), 4.52 (d, *J* = 10.8 Hz, 1H), 4.23 (dd, *J* = 7.4, 1.9 Hz, 1H), 4.17 (dd, *J* = 7.4, 2.2 Hz, 1H), 3.89 (d, *J* = 7.2 Hz, 1H), 3.65 (dd, *J* = 7.0, 4.6 Hz, 2H), 2.33 (s, 3H), 2.28 (s, 3H), 2.25 (s, 1H), 1.05 (s, 9H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 138.6, 138.3, 137.8, 137.6, 135.7 (4C), 133.4, 133.3, 132.6 (2C), 132.3 (2C), 132.0, 131.1, 129.9 (6C), 128.4 (4C), 128.3 (2C), 128.0 (2C), 127.9 (4C), 127.9, 127.7, 81.9, 79.3, 75.6, 75.3, 71.5, 64.4, 61.9, 27.0 (3C), 21.3, 21.3, 19.3; HRMS (ESI-MS): m/z calcd for $C_{49}H_{54}O_4S_2Si[M+Na]^+$: 821.3130 Found: 821.3169.



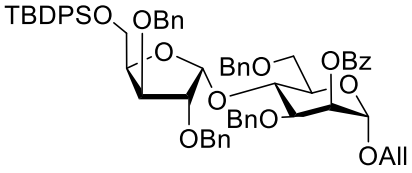
1-*O*-(((1-ethynylcylcohexyl)oxy)carbonyl)-2,3-di-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*β*-D-xylofuranoside (**48**): $^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.68 – 7.63 (m, 4H), 7.41 – 7.24 (m, 16H), 6.09 (d, *J* = 1.1 Hz, 1H), 4.67 (d, *J* = 11.9 Hz, 1H), 4.61 – 4.53 (m, 2H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.44 (q, *J* = 5.7 Hz, 1H), 4.27 (dd, *J* = 2.7 Hz, 1.2, 1H), 4.13 (dd, *J* = 5.5, 2.6 Hz, 1H), 4.00 (dd, *J* = 10.6, 6.3 Hz, 1H), 3.85 (dd, *J* = 10.6, 5.3 Hz, 1H), 2.60 (s, 1H), 2.20 – 2.08 (m, 2H), 1.90 – 1.80 (m, 2H), 1.60 (m, 6H), 1.03 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 151.7, 137.8, 137.3, 135.7 (2C), 135.6 (2C), 133.5, 133.3, 129.6, 129.6, 128.6 (2C), 128.4 (2C), 128.0, 127.9 (2C), 127.7 (6C), 127.7, 102.9, 85.1, 83.6, 83.0, 80.6, 75.0, 72.3, 72.2, 62.1, 37.0, 36.6, 26.8 (3C), 25.0, 22.5 (2C), 19.2; HRMS (ESI-MS): m/z calcd for $C_{44}H_{50}O_7Si[M+Na]^+$: 741.3224 Found: 741.3237.



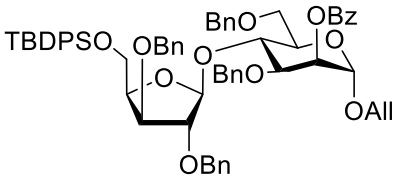

1-*O*-(((1-ethynylcylcohexyl)oxy)carbonyl)-2,3-di-*O*-benzyl-5-*O*-tosyl-*β*-D-xylofuranoside (**4**): $^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.0 Hz, 2H), 7.49 – 7.25 (m, 12H), 6.04 (s, 1H), 4.63 – 4.45 (m, 4H), 4.36 (m, 2H), 4.23 (m, 1H), 4.14 – 4.04 (m, 2H), 2.63 (s, 1H), 2.40 (s, 3H), 2.26 – 2.08 (m, 2H), 1.86 (m, 2H), 1.59 (m, 6H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 151.3, 144.8, 137.2, 136.9, 132.9, 129.9 (2C), 128.6 (2C), 128.5 (2C), 128.2, 128.0 (3C), 127.9 (2C), 127.8 (2C), 102.8, 84.6, 82.8, 80.7, 80.5, 78.1, 75.2, 72.3, 72.2, 68.3, 37.0, 36.6, 25.0, 22.6 (2C), 21.7; HRMS (ESI-MS): m/z calcd for $C_{35}H_{38}O_9S[M+Na]^+$: 657.2134 Found: 657.2122.



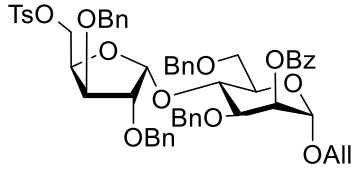

Allyl-2-*O*-benzoyl-3,6-di-*O*-benzyl-4-*O*-(2,3-di-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*α*-D-xylofuranosyl)-*α*-D-mannopyranoside (**53** *α*-isomer): $^{1}$H NMR (400 MHz, $CDCl_3$): δ 8.08 – 8.03 (d, *J* = 7.2 Hz, 2H), 7.65 – 7.52 (m, 5H), 7.39 – 7.23 (m, 15H), 7.20 (m, 10H), 7.10 – 7.06 (m, 2H), 5.95 (m, 1H), 5.67 (t, *J* = 2.3 Hz, 1H), 5.49 (d, *J* = 4.4 Hz, 1H), 5.32 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.24 (dq, *J* = 10.4, 1.3 Hz, 1H), 5.05 (d, *J* = 1.9 Hz, 1H), 4.90 (d, *J* = 11.2 Hz, 1H), 4.65 (d, *J* = 5.4 Hz, 1H), 4.64 – 4.58 (m, 2H), 4.52 – 4.39 (m, 3H), 4.31 – 4.16 (m, 5H), 4.06 (m, 3H), 3.97 (m, 1H), 3.84 (dd, *J* = 10.6, 2.1 Hz, 1H), 3.79 – 3.60 (m, 3H), 0.92 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.9, 138.7, 138.4, 138.0, 137.8, 135.8 (2C), 135.8 (2C), 133.6, 133.5, 133.3 (2C), 130.1 (2C), 129.9, 129.6, 129.6, 128.6 (2C), 128.4 (3C), 128.4 (2C), 128.4 (2C), 128.0 (2C), 127.8 (3C), 127.7 (2C), 127.7 (2C), 127.6 (2C), 127.5, 127.5, 127.3 (2C), 118.1, 100.7, 96.9, 82.1, 81.1, 78.6, 73.4, 73.0, 72.0, 71.7, 71.1, 71.0, 69.8, 68.4, 68.3, 63.0, 26.8 (3C), 19.2; HRMS (ESI-MS): m/z calcd for $C_{65}H_{70}O_{11}Si[M+Na]^+$: 1077.4585 Found: 1077.4592.



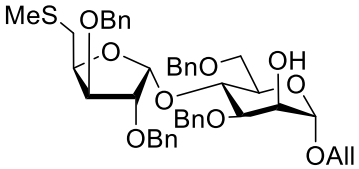
Allyl-2-*O*-benzoyl-3,6-di-*O*-benzyl-4-*O*-(2,3-di-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-*β*-D-xylofuranosyl)-*α*-D-mannopyranoside (**53** *β*-isomer): $^1$H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 7.8 Hz, 2H), 7.69 – 7.62 (m, 4H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.40 – 7.26 (m, 23H), 7.13 – 7.10 (m, 5H), 5.87 (m, 1H), 5.58 – 5.55 (m, 1H), 5.42 (s, 1H), 5.25 (dt, *J* = 17.2, 1.6 Hz, 1H), 5.16 (dt, *J* = 10.4, 1.5 Hz, 1H), 4.97 (d, *J* = 1.9 Hz, 1H), 4.67 (d, *J* = 10.9 Hz, 1H), 4.63 – 4.54 (m, 3H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.46 – 4.37 (m, 2H), 4.33 – 4.22 (m, 3H), 4.16 (dd, *J* = 10.4, 7.2 Hz, 2H), 4.12 – 4.04 (m, 2H), 4.02 – 3.96 (m, 2H), 3.87 (d, *J* = 9.2 Hz, 3H), 3.66 (d, *J* = 9.3 Hz, 1H), 1.03 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.9, 138.8, 138.2, 138.1, 137.8, 135.7 (4C), 133.7, 133.6, 133.5, 133.1, 130.0 (2C), 129.7, 129.7, 128.5 (4C), 128.4 (2C), 128.4 (2C), 128.2 (4C), 127.8 (3C), 127.8 (4C), 127.7 (3C), 127.5, 127.4, 127.3(2C), 117.8, 108.1, 96.9, 86.5, 81.9, 80.8, 73.5, 72.9, 72.3, 71.9, 71.8, 71.6, 69.4, 69.1, 68.3, 62.1, 27.0 (3C), 19.3; HRMS (ESI-MS): m/z calcd for $C_{65}H_{70}O_{11}Si[M+Na]^+$: 1077.4585 Found: 1077.4592.




Allyl-2-*O*-benzoyl-3,6-di-*O*-benzyl-4-*O*-(2,3-di-*O*-benzyl-5-*O*-tosyl-*α*-D-xylofuranosyl)-*α*-D-mannopyranoside (**54**): $^1$H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, *J*=7.7 Hz, 2H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.58 – 7.53 (m, 1H), 7.38 (q, *J* = 8.0, 7.1 Hz, 4H), 7.33 – 7.28 (m, 5H), 7.24 (m, 2H), 7.20 – 7.11 (m, 9H), 7.07 (m, 2H), 5.94 (m, 1H), 5.65 (d, *J* = 2.3 Hz, 1H), 5.41 (d, *J* = 4.5 Hz, 1H), 5.35 (d, *J* = 1.8 Hz, 1H), 5.24 (d, *J* = 10.8 Hz, 1H), 5.03 (d, *J* = 2.2 Hz, 1H), 4.86 (d, *J* = 10.9 Hz, 1H), 4.70 (d, *J* = 11.5 Hz, 1H), 4.61 – 4.46 (m, 3H), 4.39 – 4.31 (m, 2H), 4.29 – 4.23 (m, 1H), 4.20 – 4.09 (m, 5H), 4.08 – 4.04 (m, 1H), 4.03 – 3.98 (m, 2H), 3.86 (dd, *J* = 10.6, 6.1 Hz, 1H), 3.77 – 3.68 (m, 3H), 2.32 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.8, 144.7, 138.8, 137.9, 137.8, 137.4, 133.6, 133.4, 132.9, 130.1 (2C), 129.8 (2C), 129.7, 128.6 (2C), 128.5-127.5 (19C), 127.3 (2C), 118.2, 100.9, 96.8, 82.3, 80.7, 78.5, 74.5, 73.4, 72.7, 72.1, 70.9, 70.8, 69.4, 69.1, 68.5, 68.0, 21.7; HRMS (ESI-MS): m/z calcd for $C_{56}H_{58}O_{13}S[M+Na]$: 993.3496 Found: 993.3495.

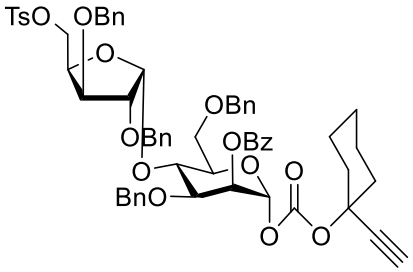



Allyl-3,6-di-*O*-benzyl-4-*O*-(2,3-di-*O*-benzyl-5-deoxy-5-methylmarcapto-*α*-D-xylofuranosyl)-*α*-D-mannopyranoside (**55**): $^1$H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.0 Hz, 2H), 7.34 – 7.20 (m, 16H), 7.17 – 7.13 (m, 2H), 5.92 (m, 1H), 5.51 (d, *J* = 4.3 Hz, 1H), 5.29 (dd, *J* = 17.2, 1.7 Hz, 1H), 5.21 (dd, *J* = 10.4, 1.5 Hz, 1H), 4.96 (d, *J* = 1.7 Hz, 1H), 4.71 (dd, *J* = 12.0, 2.2 Hz, 2H), 4.62 (d, *J*=11.9 Hz, 1H), 4.55 (d, *J* = 12.0 Hz, 2H), 4.46

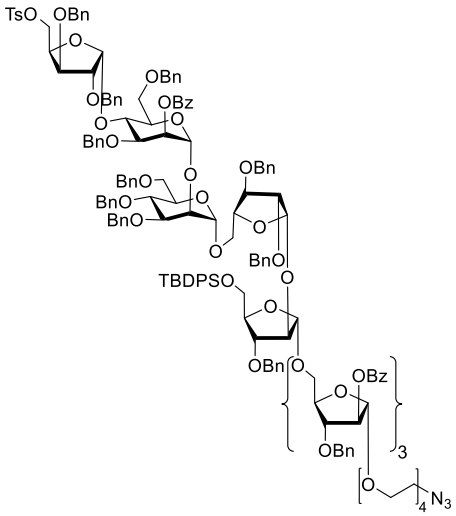


(dd, *J* = 11.7, 9.5 Hz, 2H), 4.31 (d, *J* = 11.9 Hz, 1H), 4.27 – 4.20 (m, 1H), 4.15 – 4.08 (m, 3H), 4.05 – 3.90 (m, 5H), 3.80 (dd, *J* = 10.7, 1.7 Hz, 1H), 3.70 (dd, *J* = 10.7, 6.3 Hz, 1H), 2.69 (dd, *J* = 13.8, 4.4 Hz, 1H), 2.56 – 2.48 (m, 1H), 2.05 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 138.6, 138.0, 137.8, 137.6, 133.8, 128.7 (2C), 128.4 (4C), 128.4 (2C), 127.9 (3C), 127.9, 127.8, 127.7 (2C), 127.6 (2C), 127.5, 127.2 (2C), 117.7, 100.8, 98.3, 82.7, 81.7, 80.6, 73.4, 72.6, 72.2, 71.5, 70.9, 70.6, 69.7, 68.1, 67.4, 34.8, 16.7; HRMS (ESI-MS): m/z calcd for $C_{43}H_{50}O_9S$[M+Na]: 765.3073 Found:765.3079.

1-*O*-(((1-ethynylcylcohexyl)oxy)carbonyl)-2-*O*-benzoyl-3,6-di-*O*-benzyl-4-*O*-(2,3-di-*O*-benzyl-5-*O*-tosyl-*α*-D-xylofuranosyl)-*α*-D-mannopyranoside (**3**): $^1$H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 8.0 Hz, 2H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.56 (t, *J* = 7.9 Hz, 1H), 7.41 – 7.32 (m, 5H), 7.31 – 7.25 (m, 7H), 7.21 – 7.06 (m, 12H), 6.13 (d, *J* = 2.2 Hz, 1H), 5.72 (t, *J* = 2.6 Hz, 1H), 5.41 (d, *J* = 4.5, 1H), 4.89 (d, *J* = 11.1, 1H), 4.66 (d, *J* = 11.9 Hz, 1H), 4.60 (d, *J* = 11.9 Hz, 1H), 4.55 (d, *J* = 11.9 Hz, 1H), 4.49 (d, *J* = 11.8 Hz, 1H), 4.40 – 4.35 (m, 2H), 4.30 – 4.22 (m, 2H), 4.20 (d, *J* = 2.6 Hz, 1H), 4.19 – 4.09 (m, 4H), 3.91 – 3.85 (m, 1H), 3.81 – 3.71 (m, 3H), 2.63 (s, 1H), 2.31 (s, 3H), 2.19 (m, 2H), 1.96 – 1.86 (m, 2H), 1.66 – 1.54 (m, 4H), 1.43 – 1.31 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.5, 150.4, 144.8, 138.7, 137.7, 137.6, 137.3, 133.6, 132.8, 130.1 (2C), 129.8 (2C), 129.3, 128.7 (2C), 128.5 (8C), 128.0 (5C), 127.9 (3C), 127.7 (3C), 127.5, 127.3 (2C), 100.8, 94.1, 82.5, 82.3, 80.6, 78.8, 78.1, 75.6, 74.6, 73.4, 73.2, 72.8, 72.1, 71.3, 71.1, 69.1, 69.0, 66.7, 37.1, 36.6, 25.0, 22.7 (2C), 21.7; HRMS (ESI-MS): m/z calcd for $C_{62}H_{64}O_{15}S$[M+Na]: 1103.3864 Found: 1103.3867.

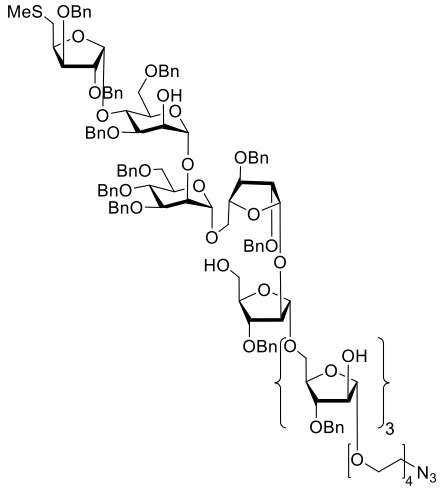



1-(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethoxy)-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(3-*O*-benzyl-5-*O*-$^{tert}$butyldiphenylsilyl-2-*O*-(2,3-di-*O*-benzyl-5-*O*-(3,4,6-tri-*O*-benzyl-2-*O*-(2-*O*-benzoyl-3,6-di-*O*-benzyl-4-*O*-(2,3-di-*O*-benzyl-5-*O*-tosyl-*α*-D-xylofuranosyl)-*α*-D-mannopyranosyl)-*α*-D-mannopyranosyl)-*β*-D-arabinofuranosyl)-*α*-D-arabinofuranosyl)-*α*-D-arabinofuranosyl)-*α*-D-arabinofuranoside (**56**): $^1$H NMR (600 MHz, $CDCl_3$): δ 8.02 (3d, *J* = 7.6 Hz, 6H), 7.96 (d, *J* = 7.6 Hz, 2H), 7.67 – 7.44 (m, 11H), 7.42 – 6.97 (m, 80H), 5.41 (m, 2H), 5.34 (s, 1H), 5.30 (d, *J* = 4.1 Hz, 1H), 5.25 - 5.19 (m, 4H),



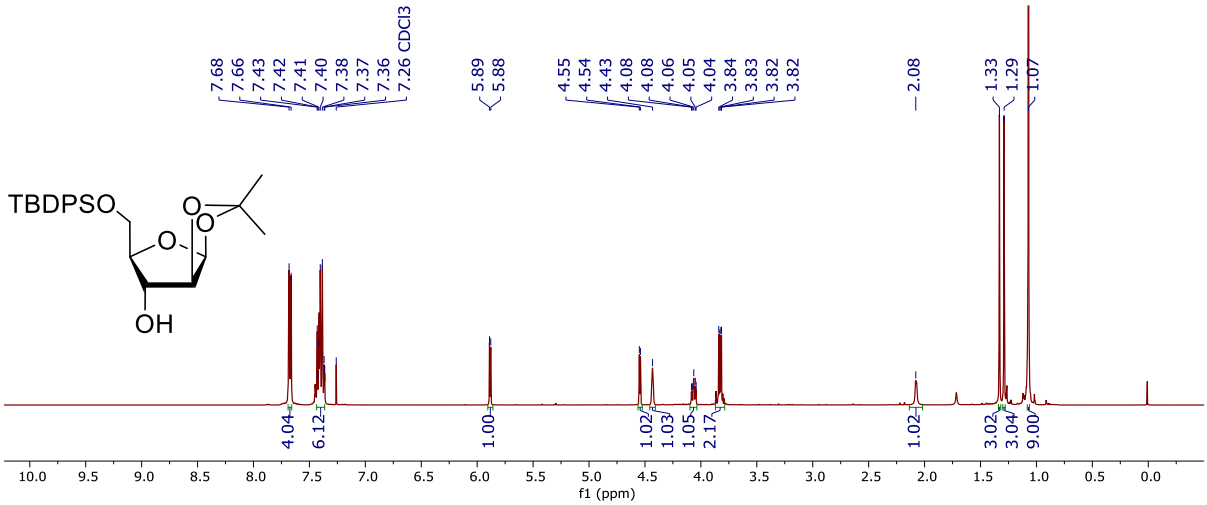
5.07 – 5.02 (m, 2H), 4.98 (s, 1H), 4.83 (t, *J* = 10.4 Hz, 1H), 4.77 (d, *J* = 12.0 Hz, 1H), 4.63 – 4.23 (m, 25H), 4.20 – 3.96 (m, 16H), 3.95 – 3.85 (m, 6H), 3.84 – 3.76 (m, 6H), 3.74 – 3.65 (m, 11H), 3.61 (d, *J* = 16.7 Hz, 13H), 3.37 – 3.32 (m, 2H), 2.29 (s, 3H), 1.00 (s, 9H); $^{13}$C NMR (151 MHz, $CDCl_3$): δ 165.6, 165.4, 165.4, 144.7, 138.7, 138.6, 138.2, 138.1, 138.0, 137.9, 137.9, 137.8, 137.7, 137.4, 135.8, 135.7, 133.5, 133.5, 133.4, 133.3, 133.1, 132.9, 130.1, 129.9, 129.9, 129.8, 129.7, 129.6, 129.6, 129.5, 128.6, 128.5, 128.4, 128.4, 128.0, 128.0, 127.8, 127.8, 127.7, 127.6, 127.4, 127.3, 106.4, 106.3, 106.3, 106.2, 100.9, 100.8, 99.5, 98.6, 86.2, 83.7 (3C), 83.5, 83.3, 82.9, 82.2, 82.2, 82.1, 82.0, 82.0, 81.9, 81.8, 80.7, 80.4, 80.1, 79.1, 78.3, 77.5, 75.2, 74.8, 74.5, 74.4, 73.4, 73.2, 72.7, 72.5, 72.5, 72.4, 72.3 (2C), 72.2, 72.0, 72.0, 71.9, 71.5, 70.8 (2C), 70.8 (2C), 70.8 (2C), 70.7, 70.4, 70.1, 69.6, 69.2, 69.1, 68.0, 66.8, 65.7, 65.7, 64.0, 50.8, 27.0 (3C), 21.7, 19.4; HRMS (ESI-MS): m/z calcd for $C_{192}H_{203}N_3O_{44}SSi[M+Na]^+$: 3339.3194 Found: 3339.4402.

1-(2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethoxy)-3-*O*-benzyl-5-*O*-(3-*O*-benzyl-5-*O*-(3-*O*-benzyl-5-*O*-(3-*O*-benzyl-2-*O*-(2,3-di-*O*-benzyl-5-*O*-(3,4,6-tri-*O*-benzyl-2-*O*-(3,6-di-*O*-benzyl-4-*O*-(2,3-di-*O*-benzyl-5-deoxy-5-methylmercapto-*α*-D-xylofuranosyl)-*α*-D-mannopyranosyl)-*α*-D-mannopyranosyl)-*β*-D-arabinofuranosyl)-*α*-D-arabinofuranosyl)-*α*-D-arabinofuranosyl)-*α*-D-arabinofuranoside (**57**): $^1$H NMR (600 MHz, $CDCl_3$): δ 7.39 – 7.14 (m, 65H), 5.48 – 3.45 (m, 87H), 3.38 (m, 2H), 2.57 - 2.35 (m, 4H), 2.01 – 1.72 (m, 7H); $^{13}$C NMR (151 MHz, $CDCl_3$): δ 138.5, 138.5, 138.5, 138.2, 138.1, 138.0, 137.8, 137.8, 137.6, 137.6, 137.5, 137.4, 137.3, 128.7-127.3 (65C), 108.6, 108.3, 105.4, 105.4, 101.1, 100.9, 100.8, 98.9, 85.3, 85.2, 85.0, 84.9, 84.0, 83.8, 83.7, 83.6, 83.2, 83.0, 83.0, 82.7, 82.5, 82.4, 81.5, 81.4, 80.3, 80.1, 80.1, 79.3, 78.7, 77.6, 75.2, 74.7, 74.2, 73.4, 73.3, 72.8, 72.7, 72.6, 72.5, 72.2, 71.8, 71.7, 71.5, 70.8 (2C), 70.8 (2C), 70.7 (2C), 70.7 (2C), 70.4, 70.1, 69.5, 69.2, 67.5, 66.9, 66.0, 65.6, 62.1, 57.5, 50.8, 32.0, 14.3; MALDI-TOF: m/z calcd for $C_{192}H_{203}N_3O_{44}SSi[M+Na]^+$: 2534.0869 Found: 2530.0270.

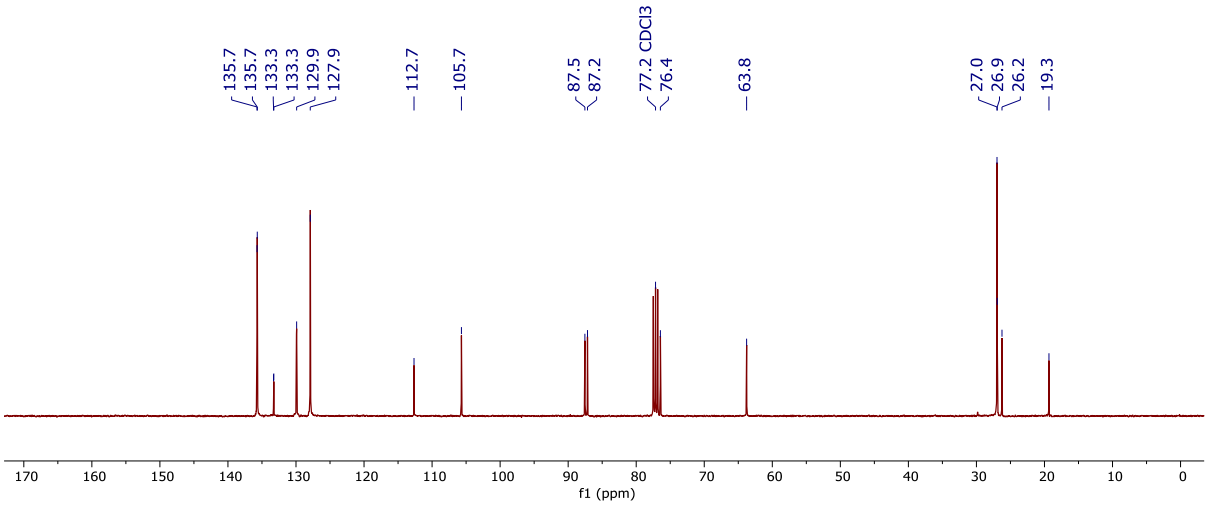


## 2.8 – Spectral charts

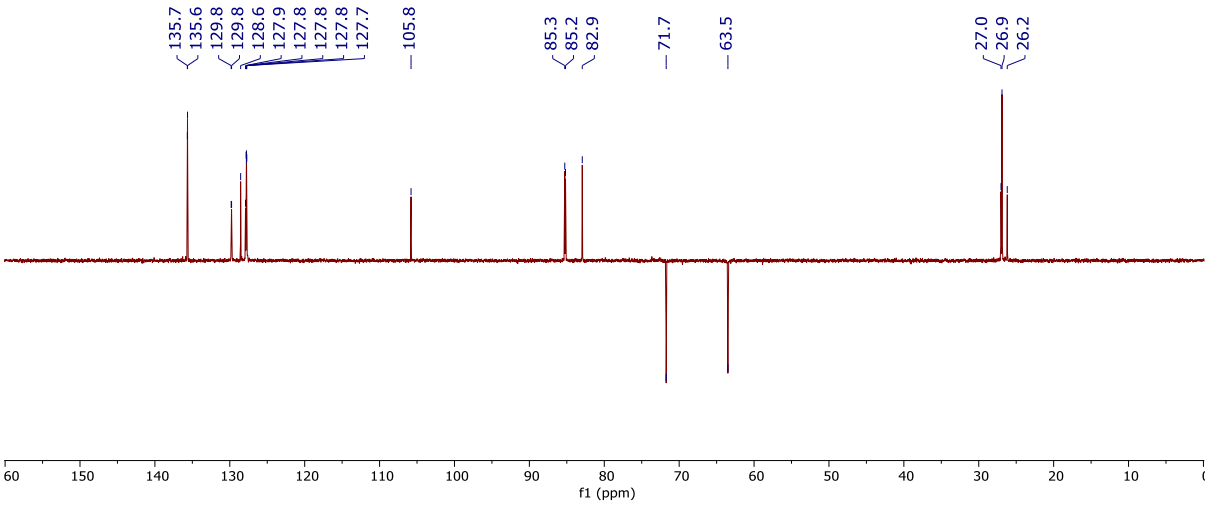
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **14**



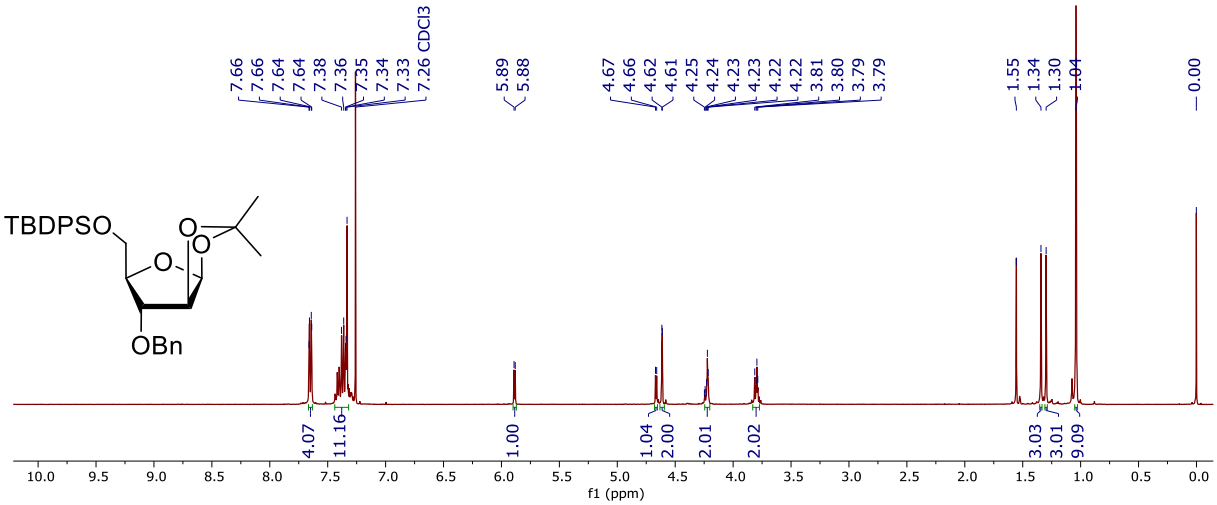

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **14**



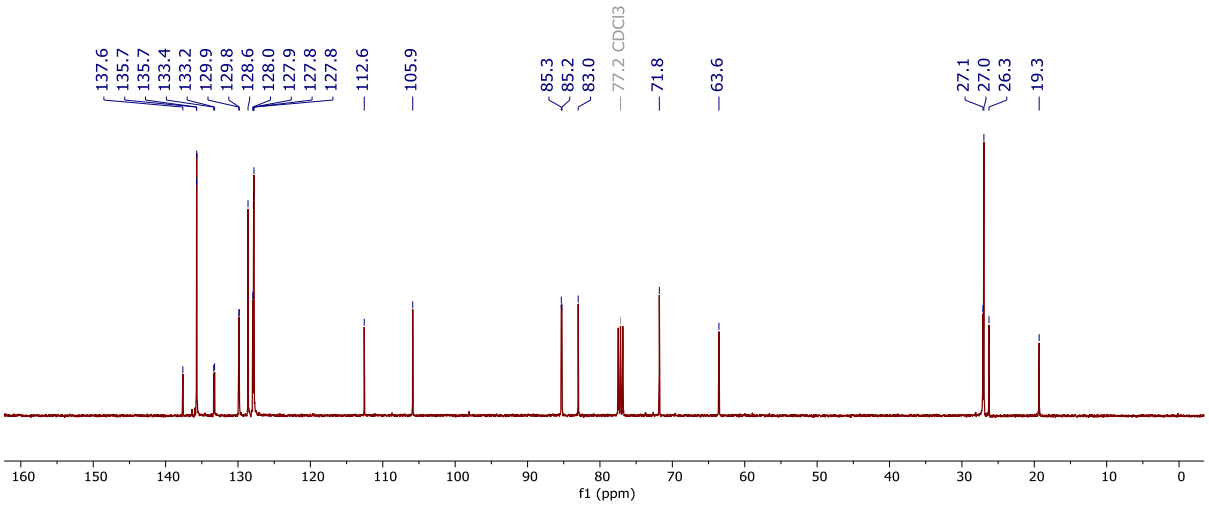

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **14**



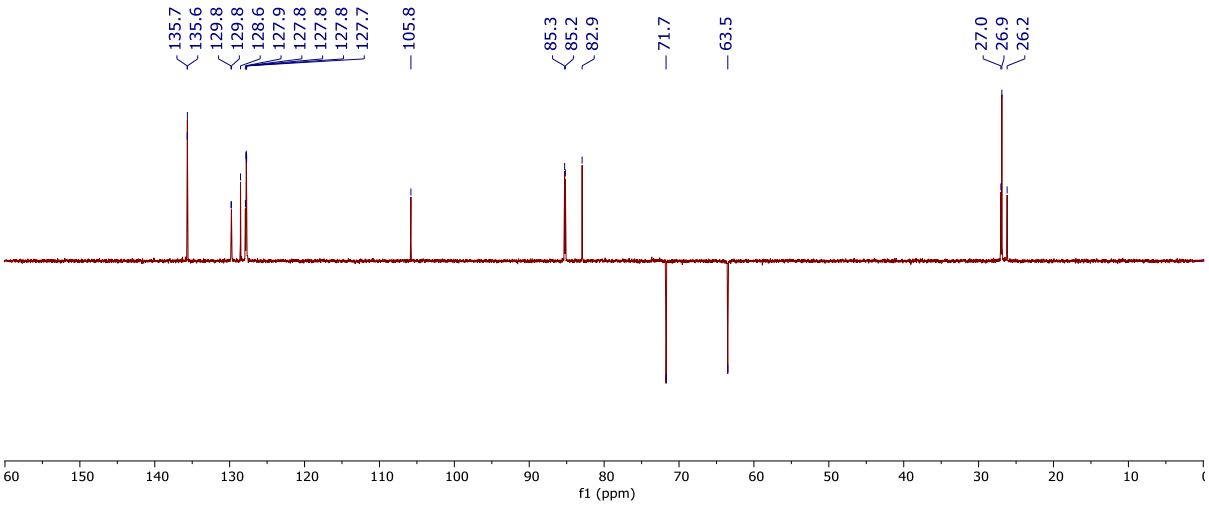
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **15**



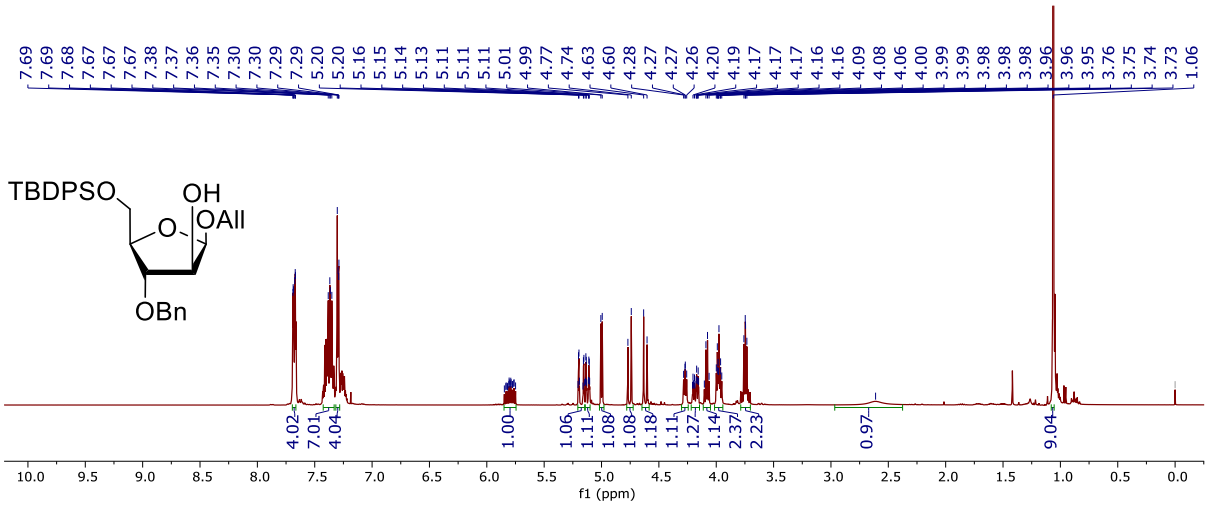

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **15**



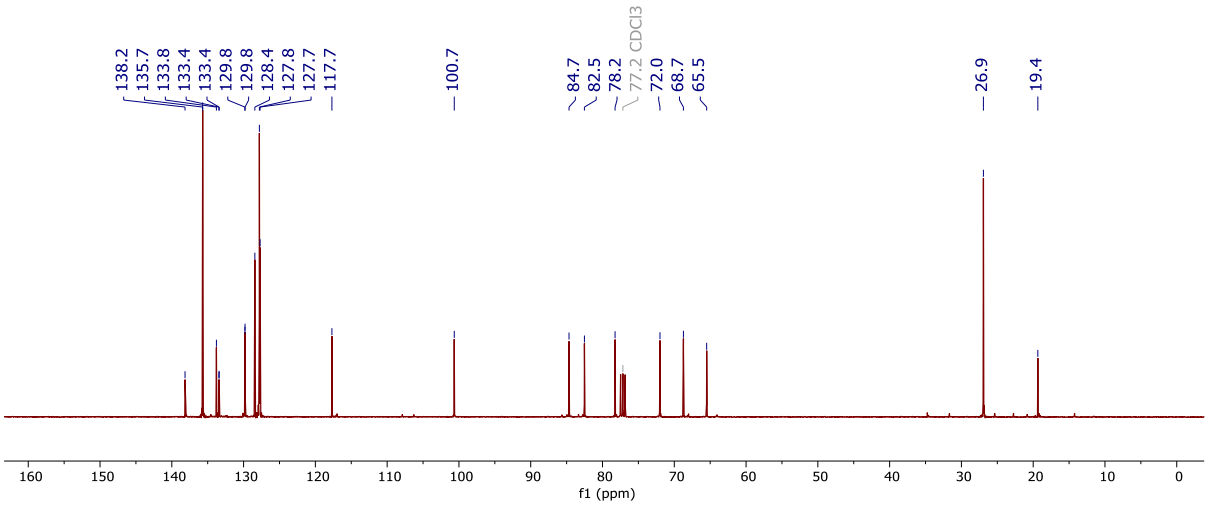

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **15**



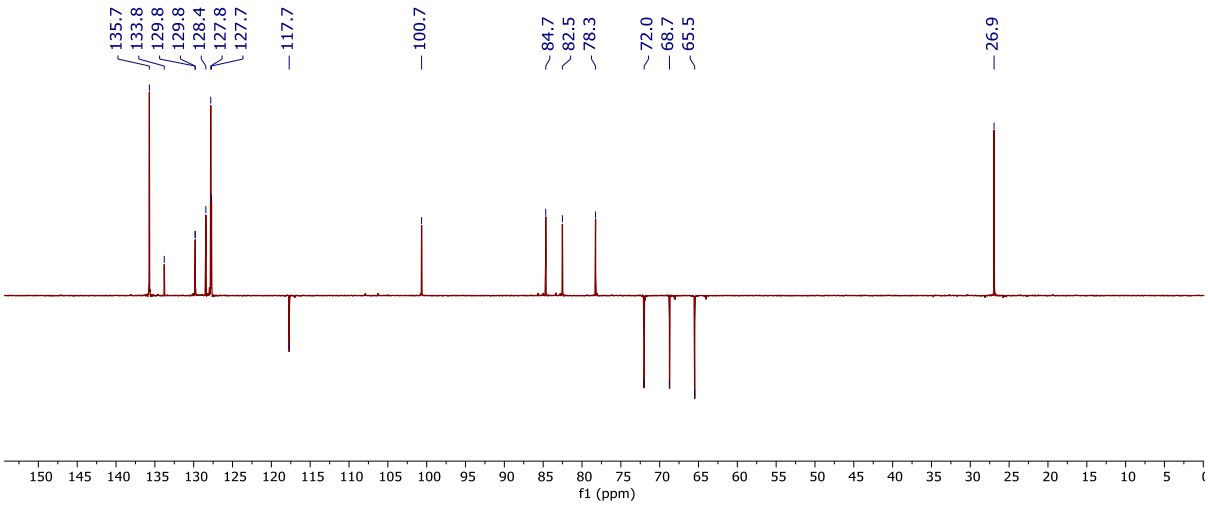
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **9**



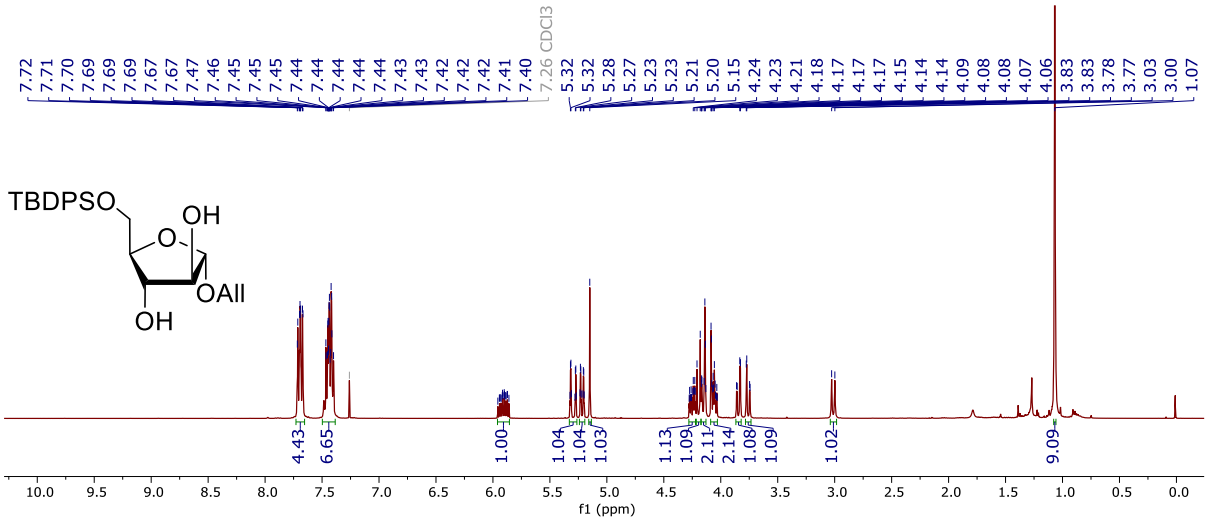

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **9**



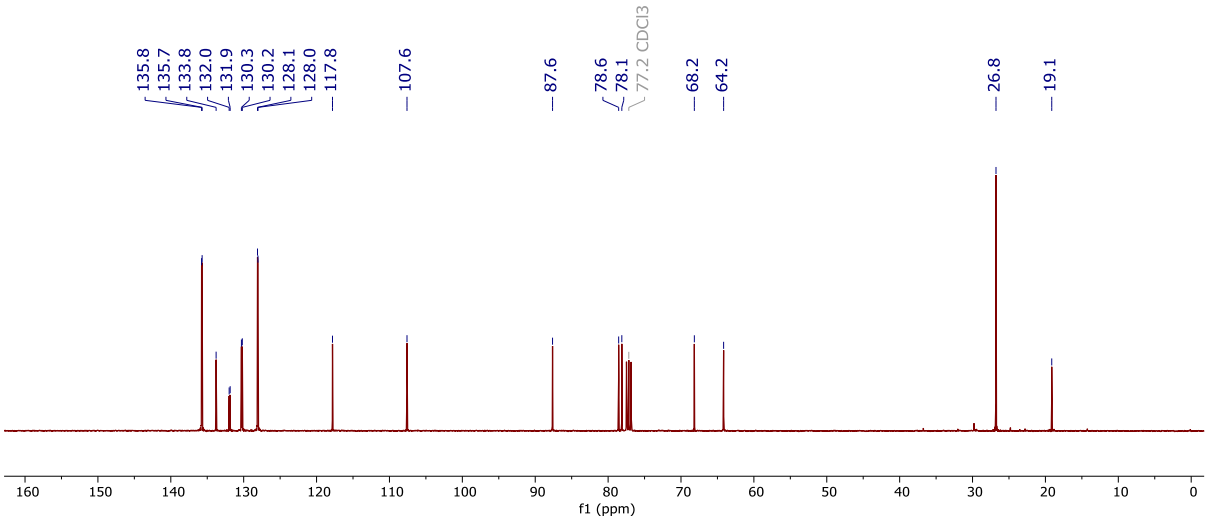

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **9**



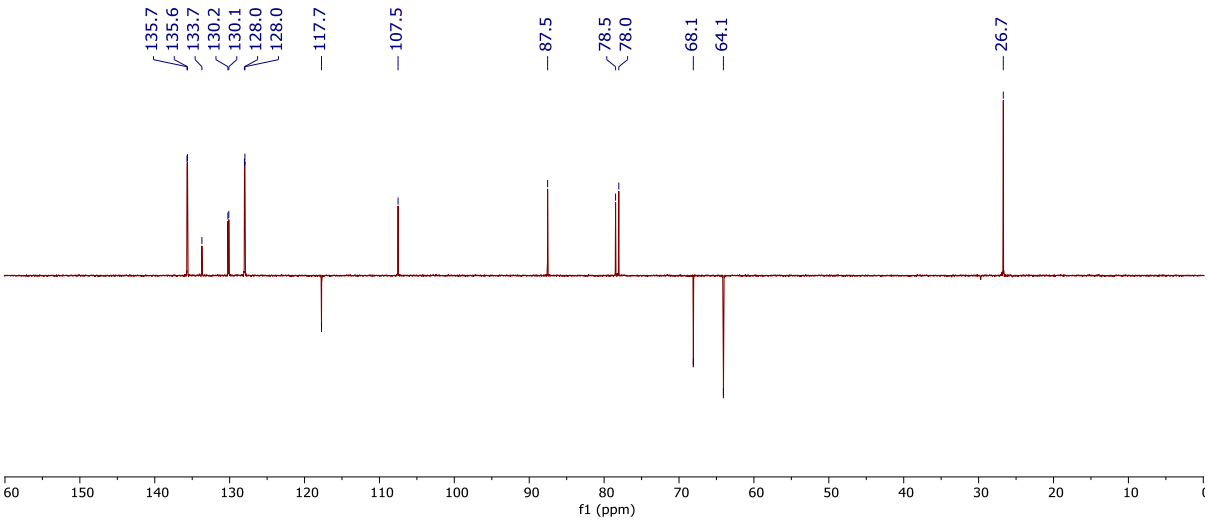
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **17**



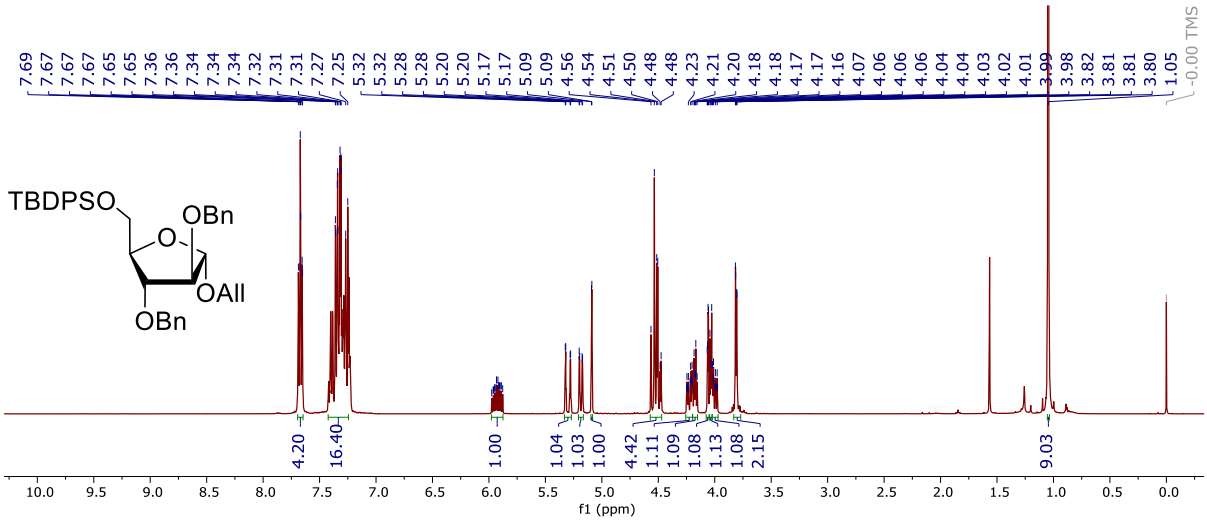

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **17**



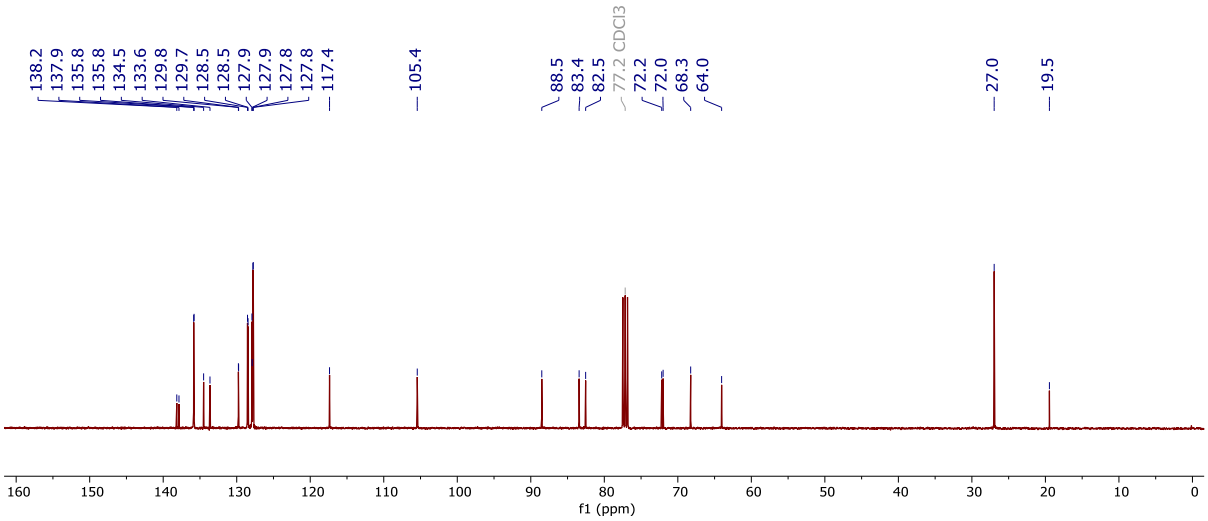

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **17**



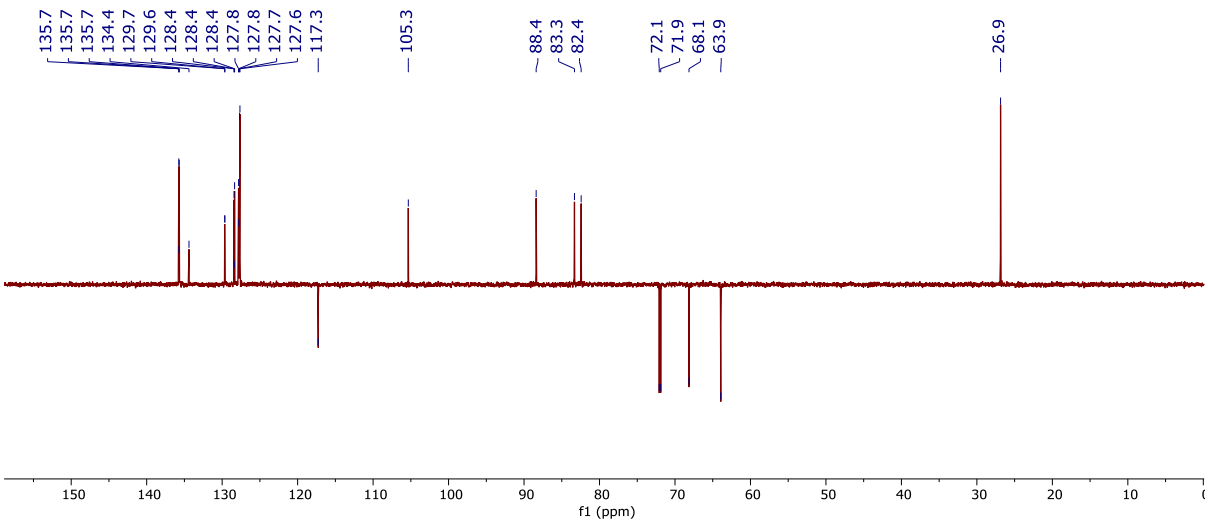
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **18**



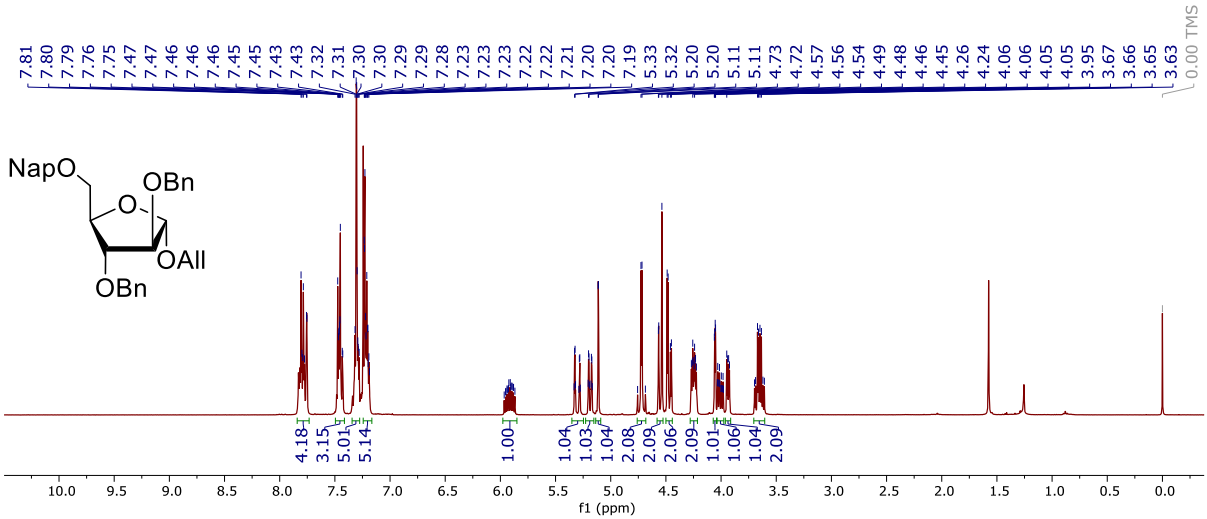

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **18**



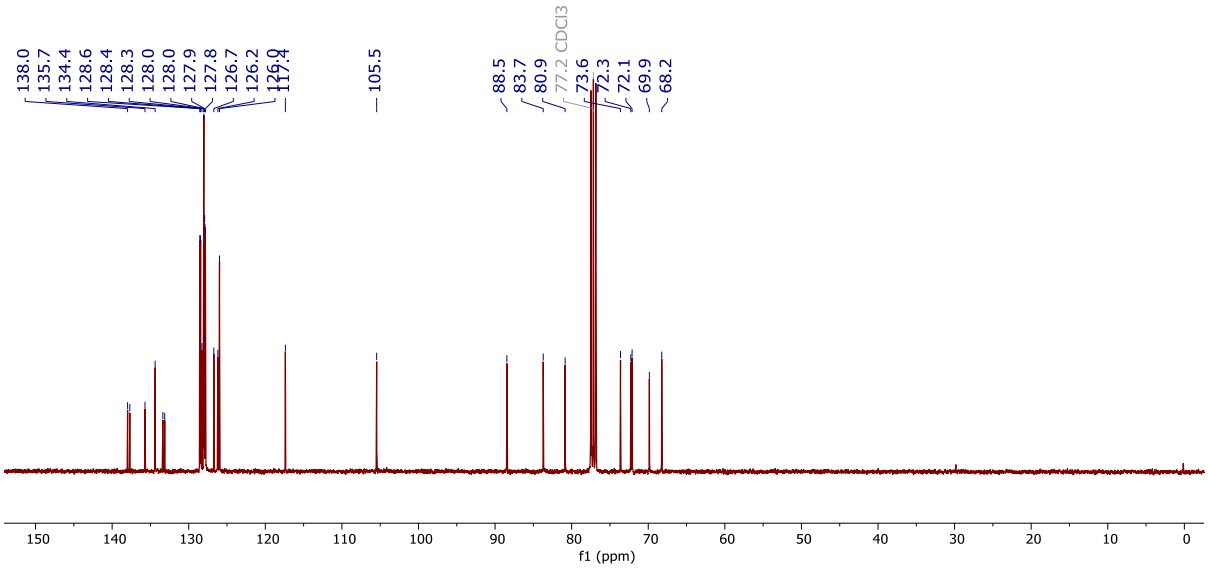

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **18**



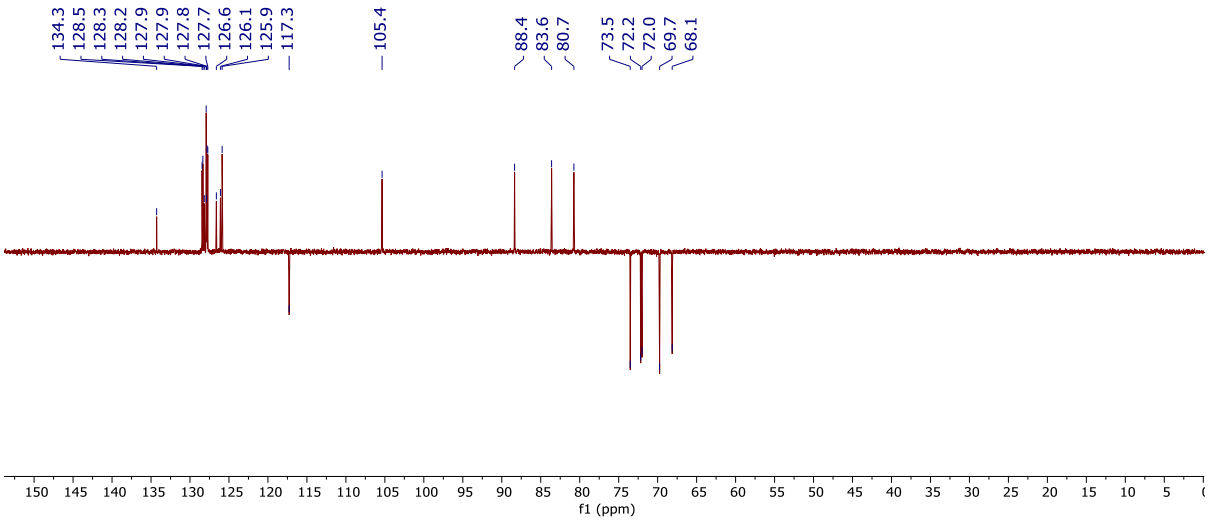
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **19**



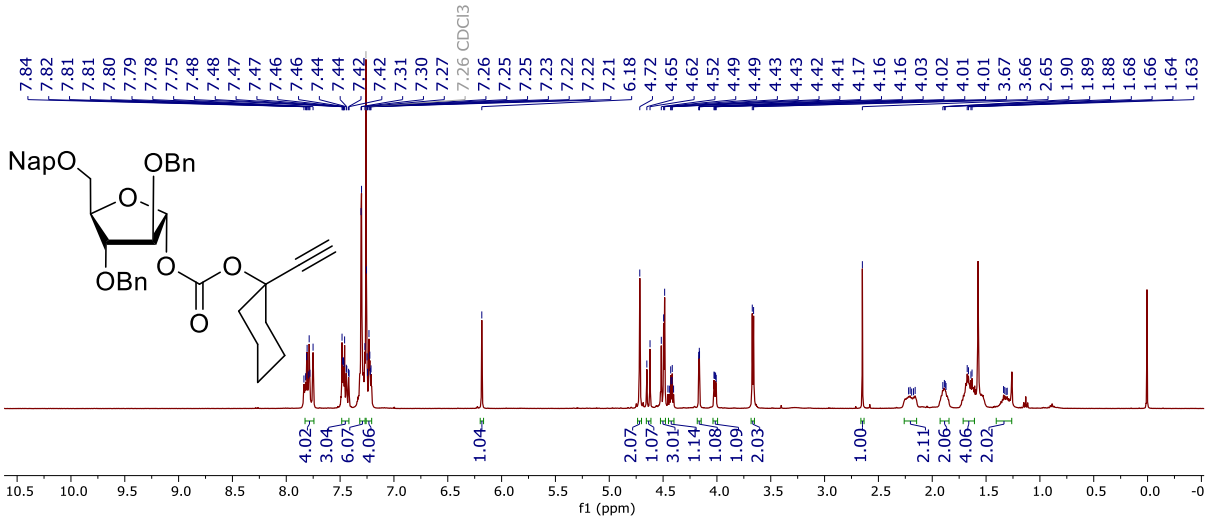

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **19**



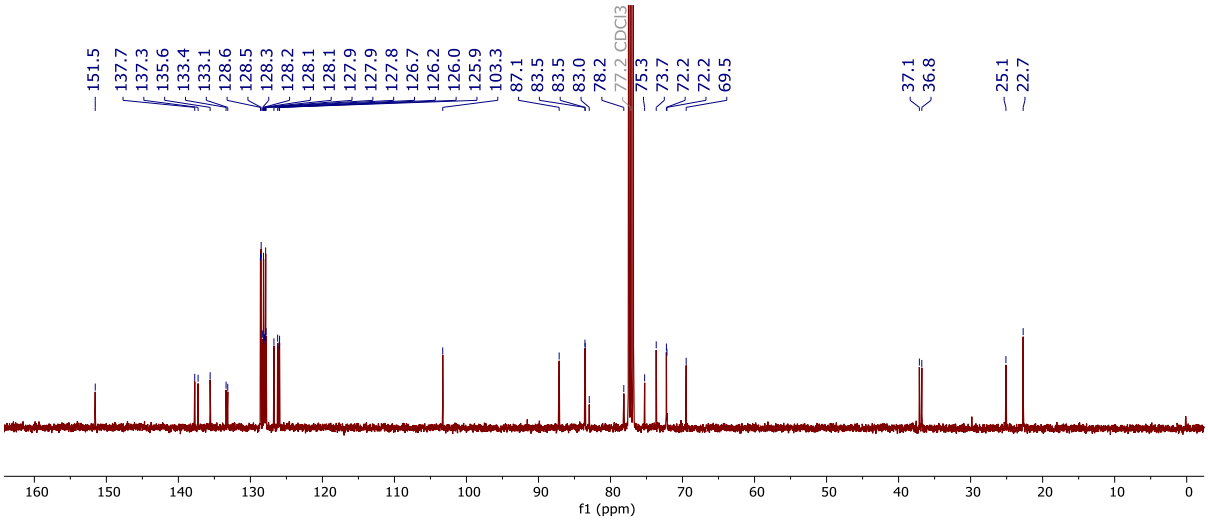

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **19**



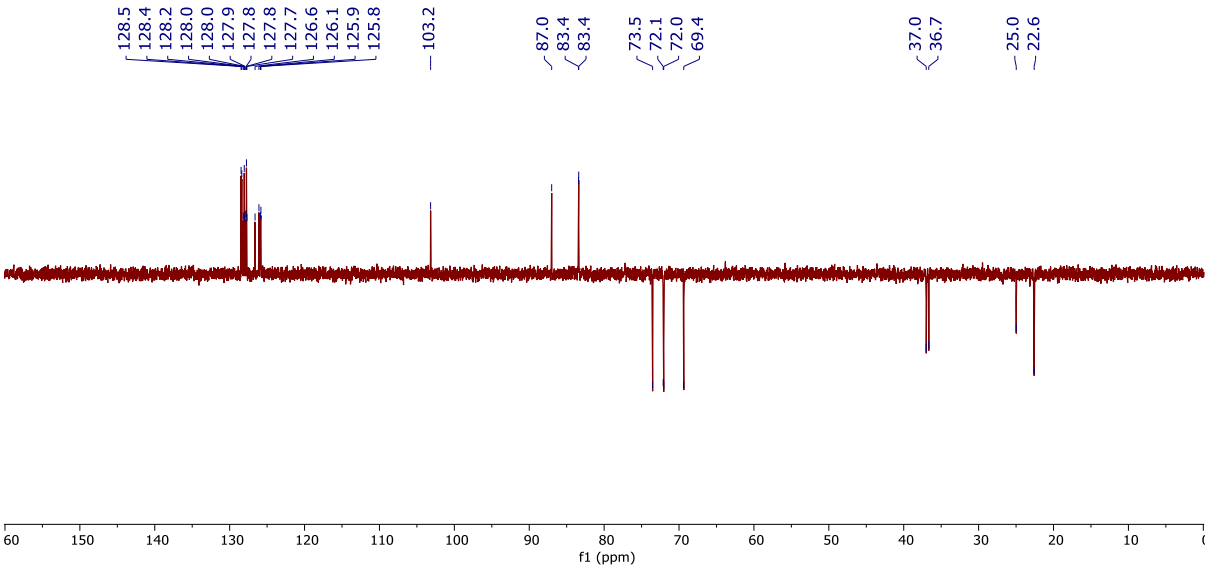
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **08**



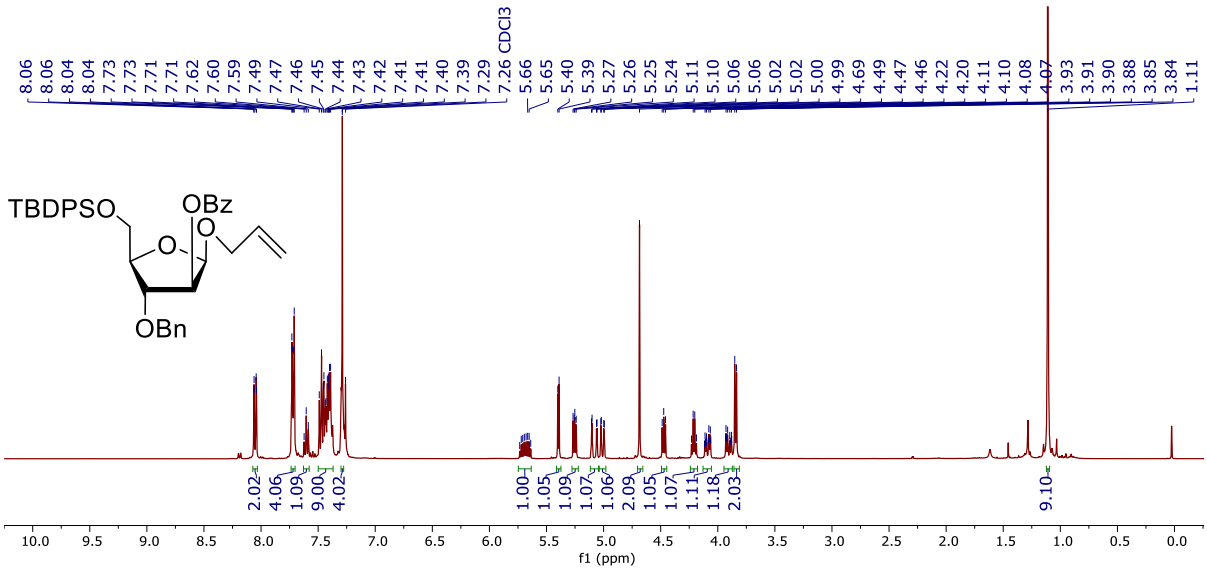

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **08**



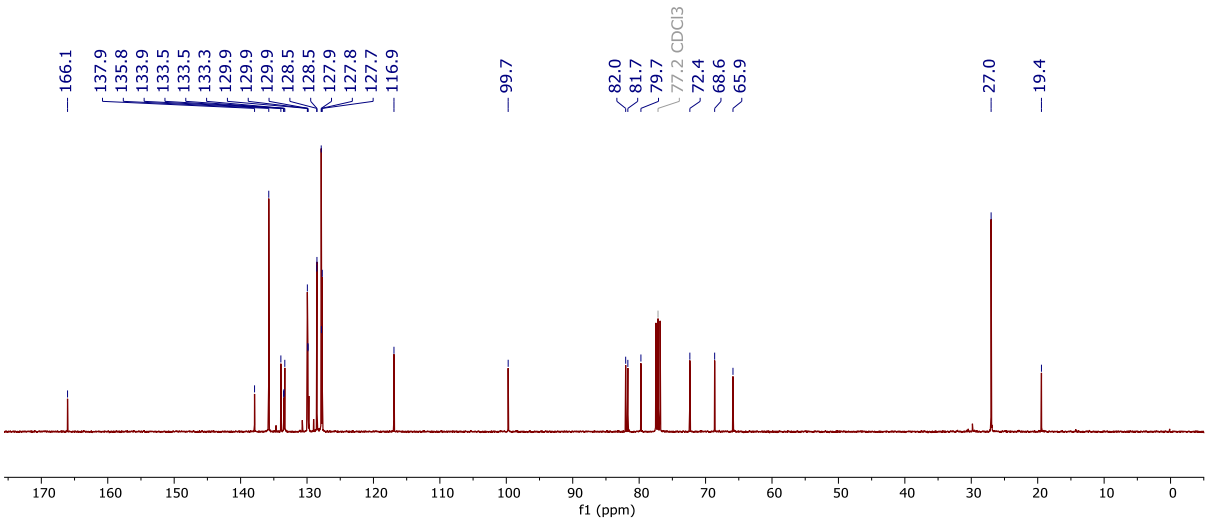

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **08**



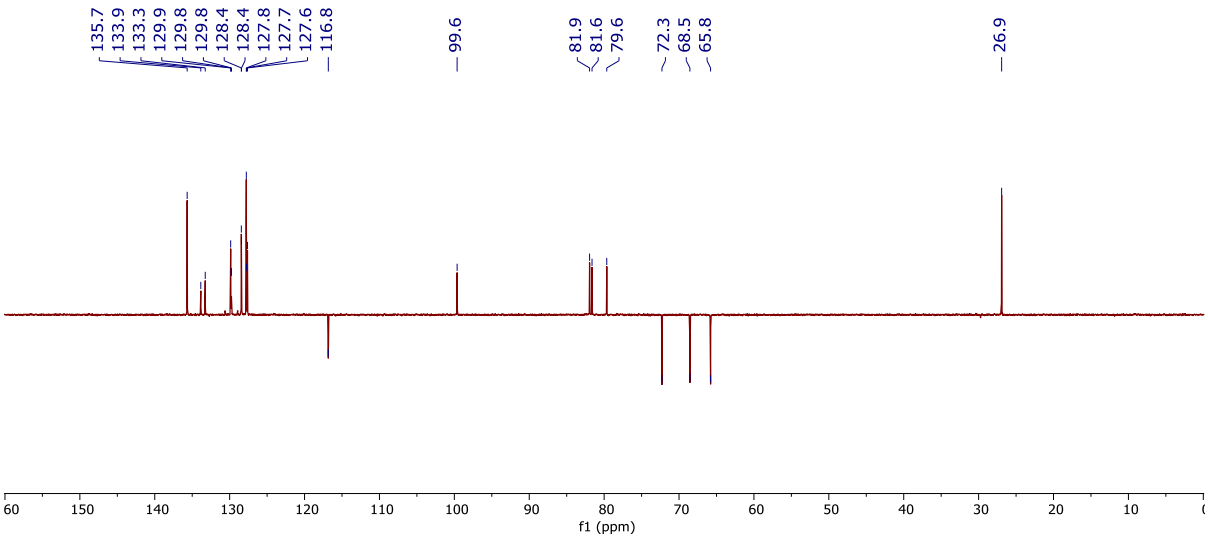
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **16**



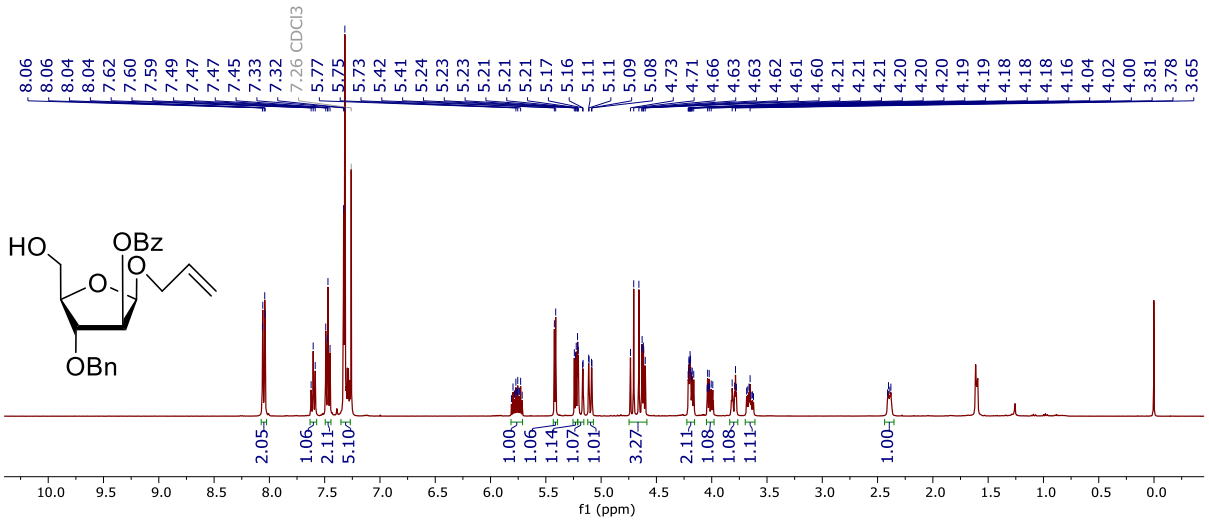

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **16**



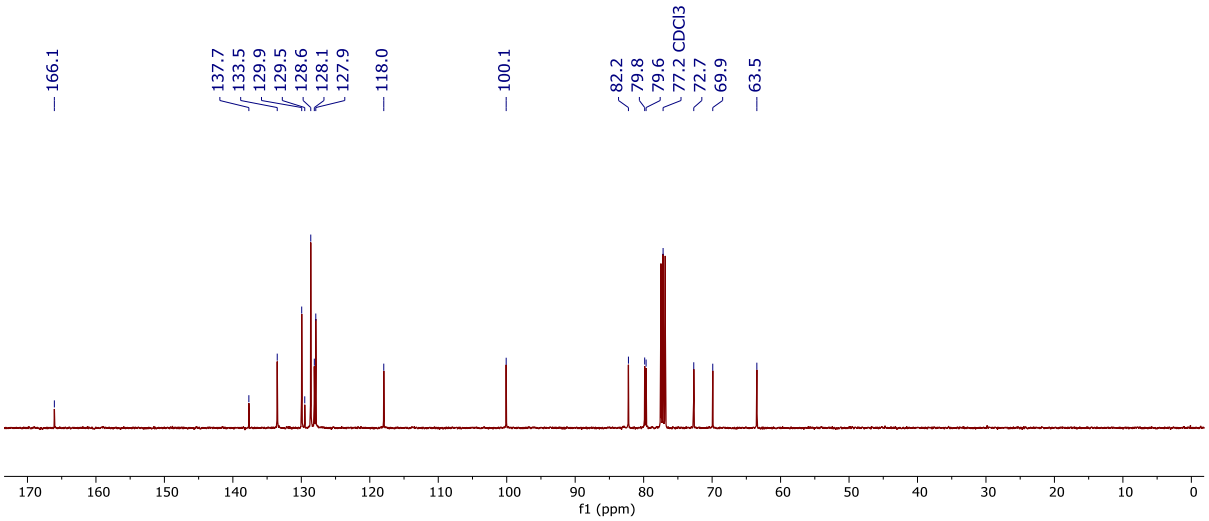

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **16**



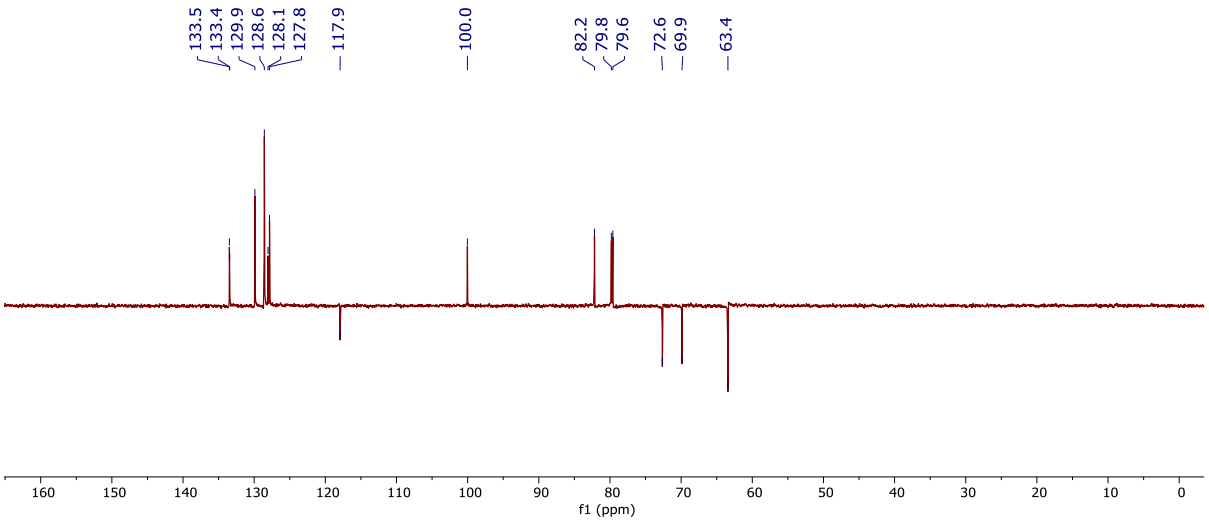
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **10**



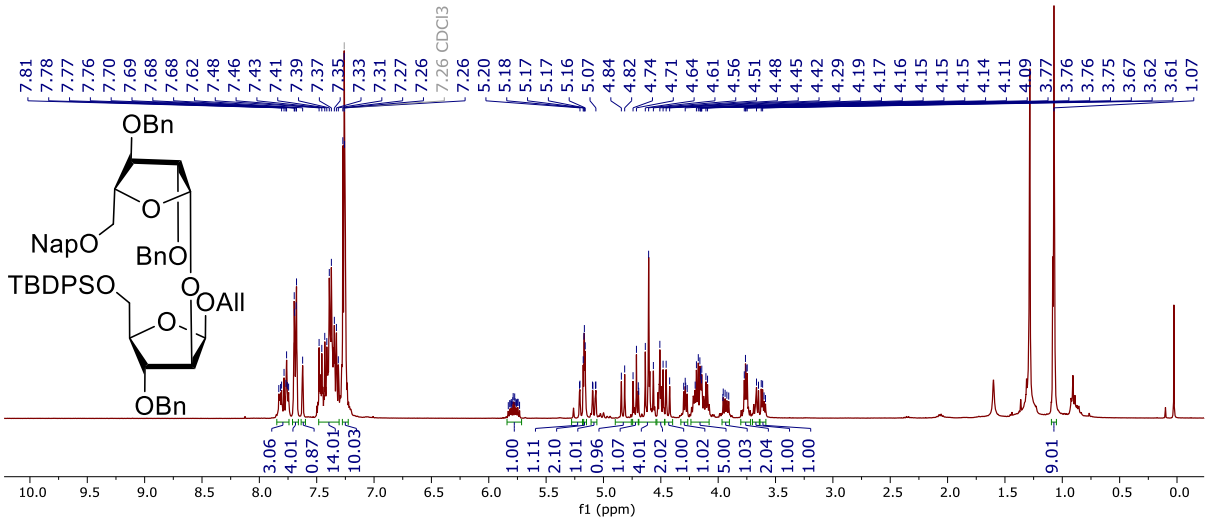

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **10**



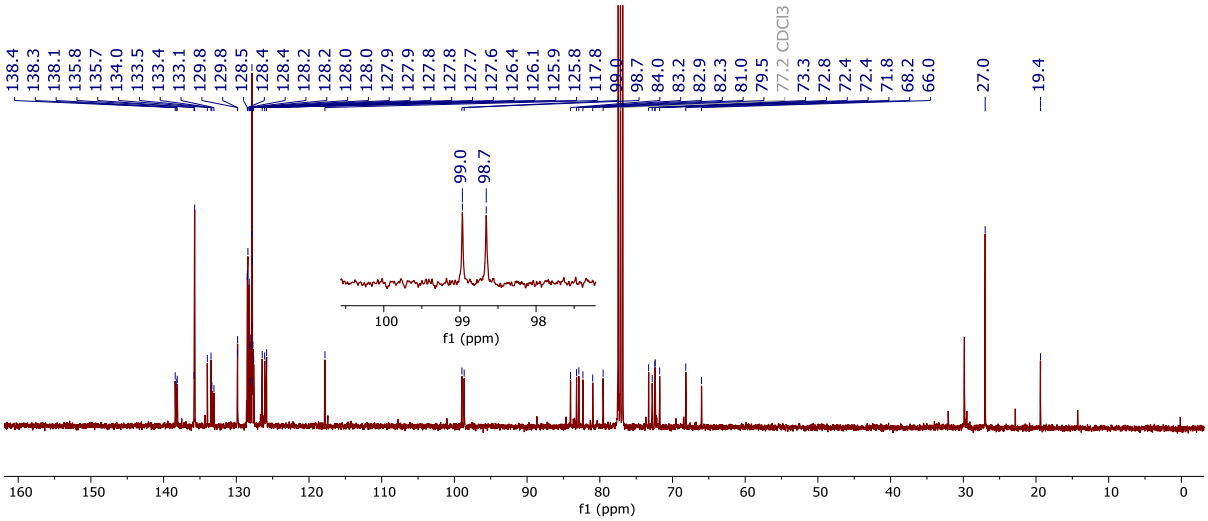

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **10**



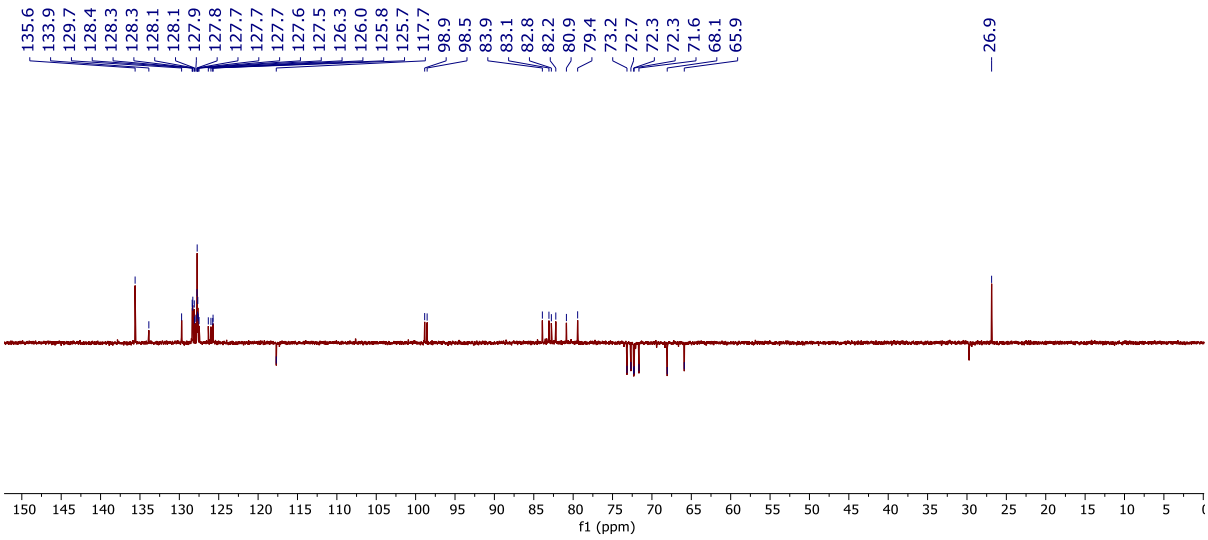
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **21**



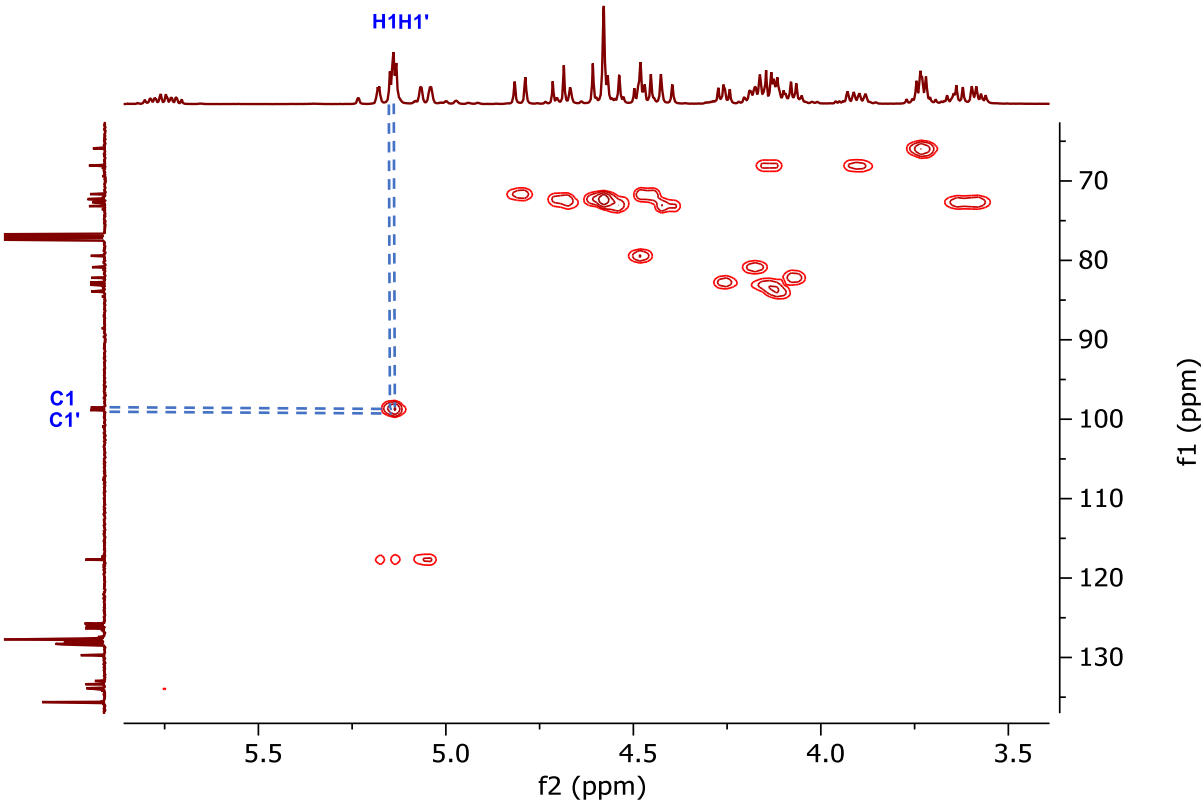

$^{13}$C Spectrum (101 MHz, $CDCl_3$) of compound **21**



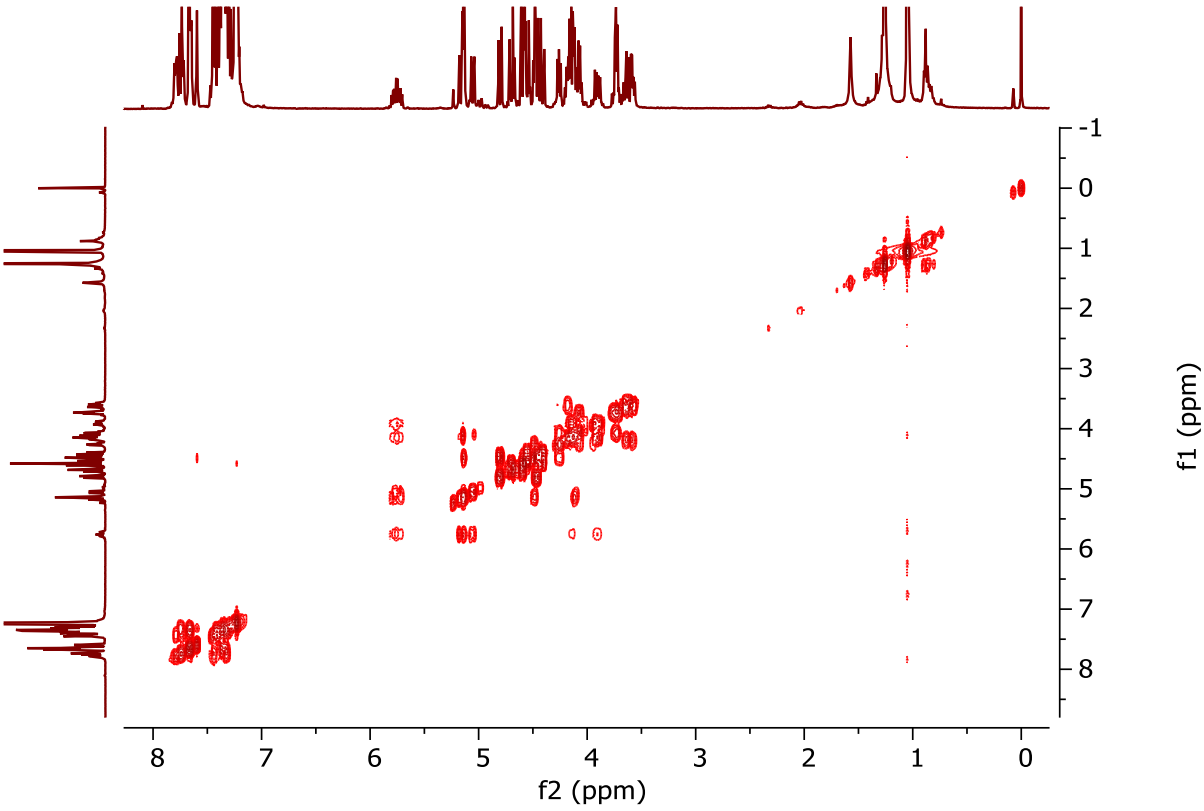

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **21**



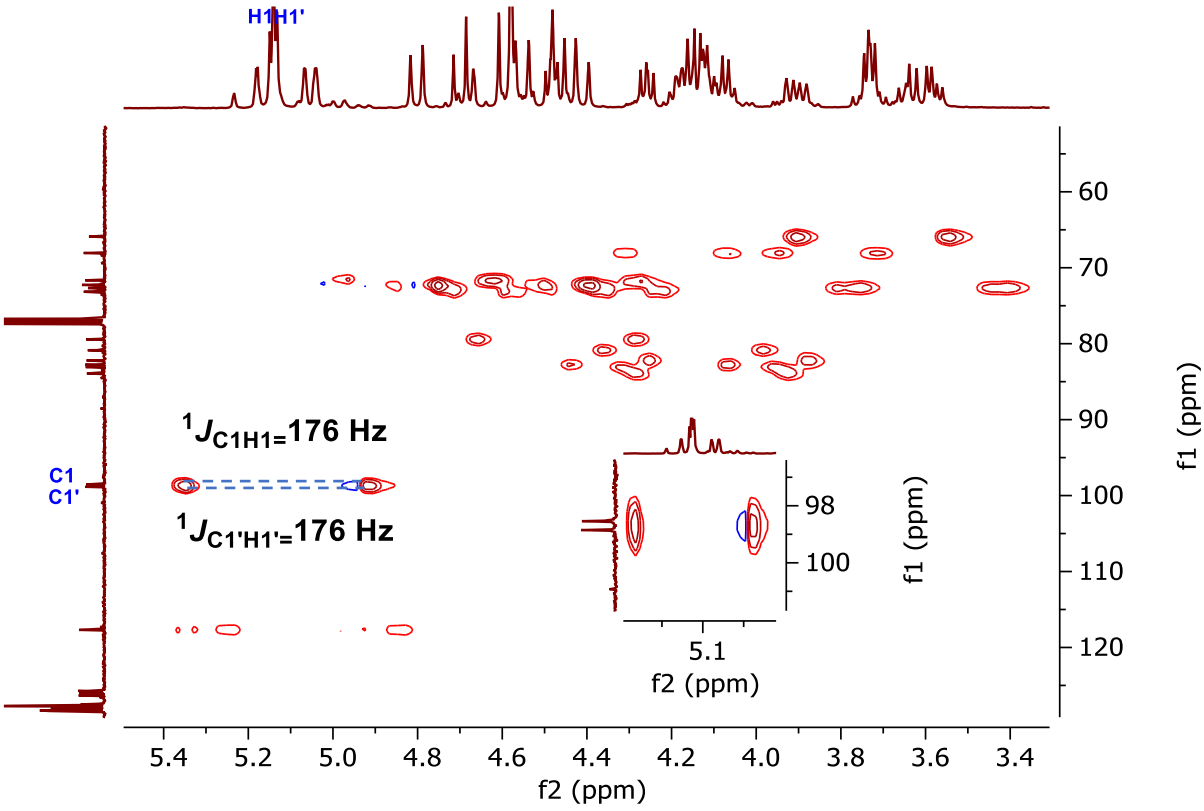
$^{1}H$, $^{13}C$-HSQC NMR Spectrum (400, 101 MHz, $CDCl_3$) of compound **21**



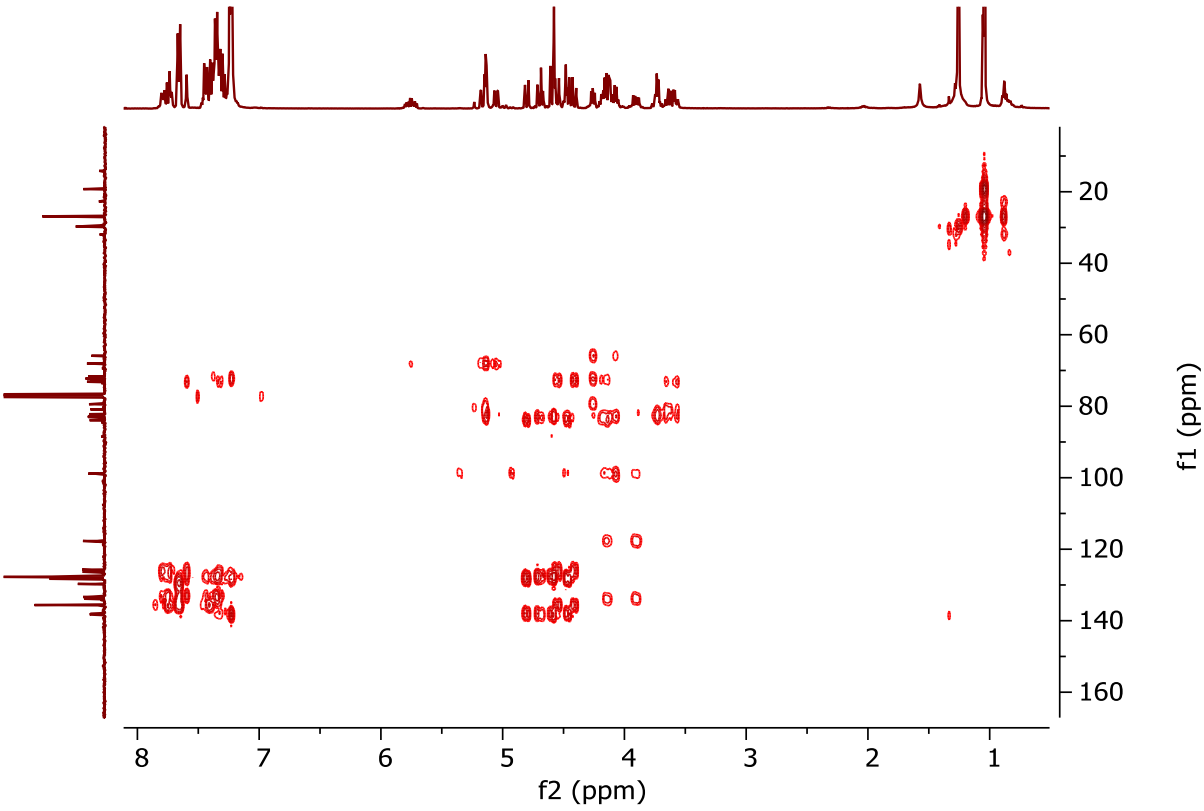

$^{1}H$, $^{1}H$ COSY NMR Spectrum (400, 101 MHz, $CDCl_3$) of compound **21**



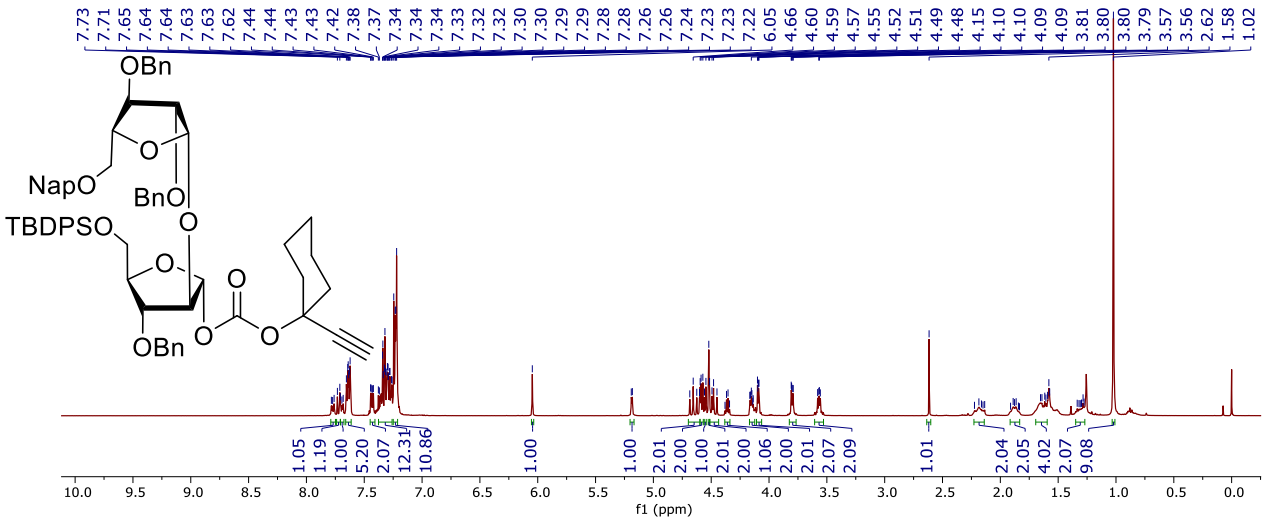
$^{1}$H, $^{13}$C HSQC-Coupled NMR Spectrum (400, 101 MHz, $CDCl_3$) of Compound **21**



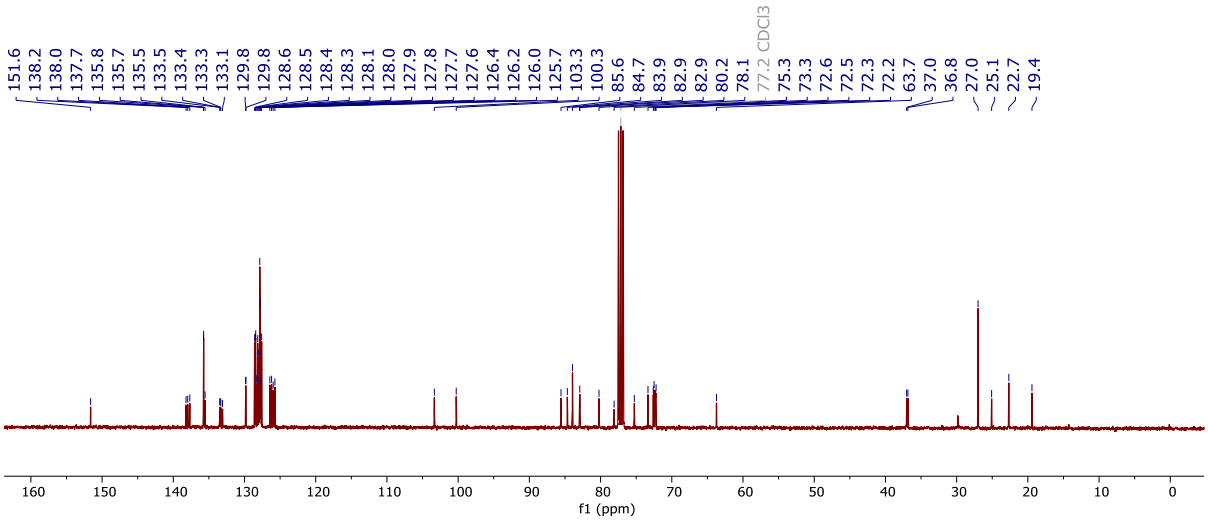

$^{1}$H, $^{13}$C HMBC NMR Spectrum (400, 101 MHz, $CDCl_3$) of compound **21**



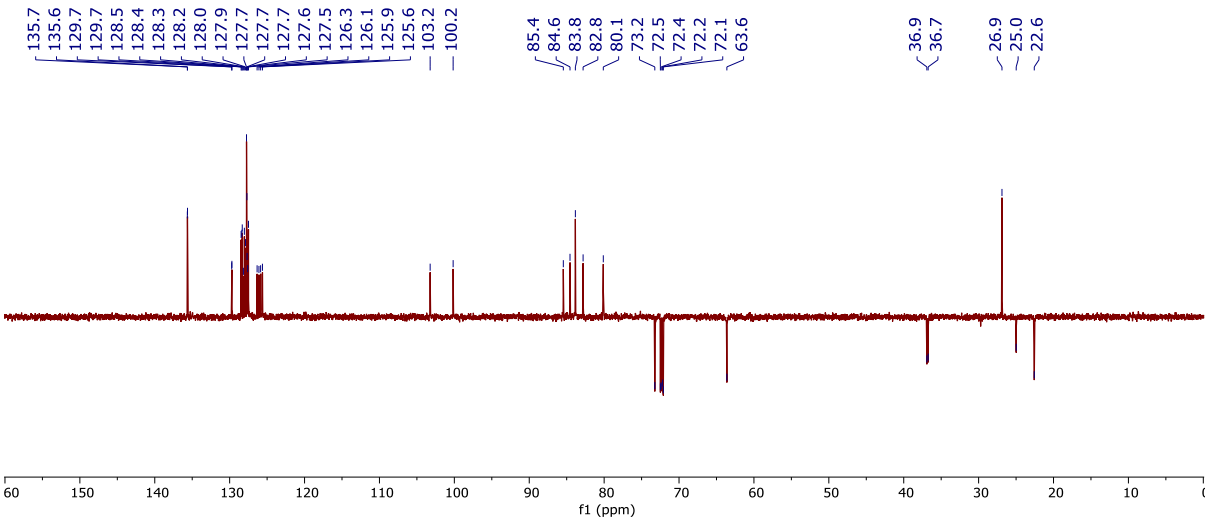
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **22**



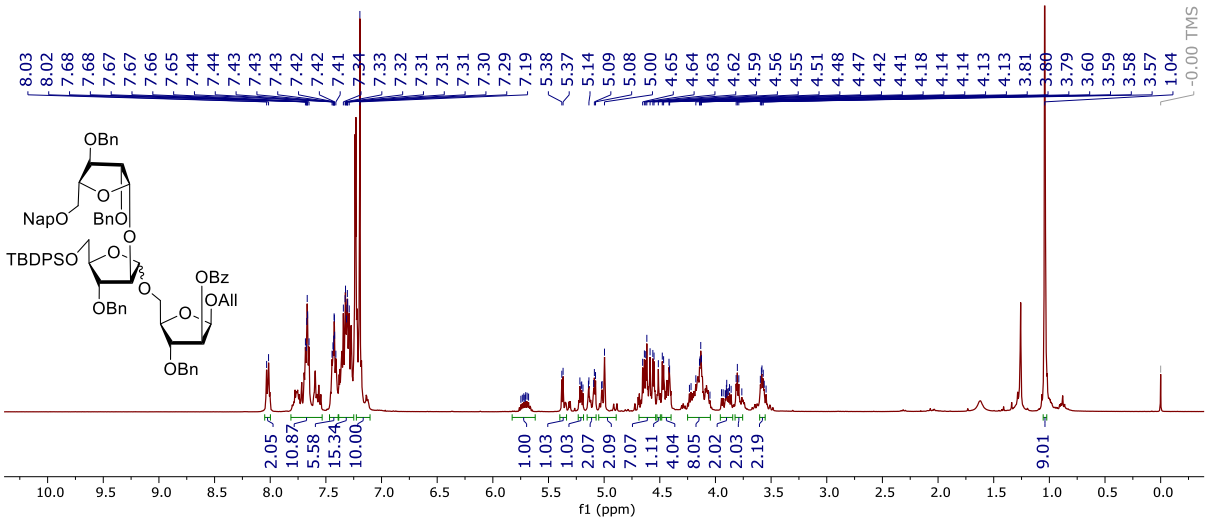

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **22**



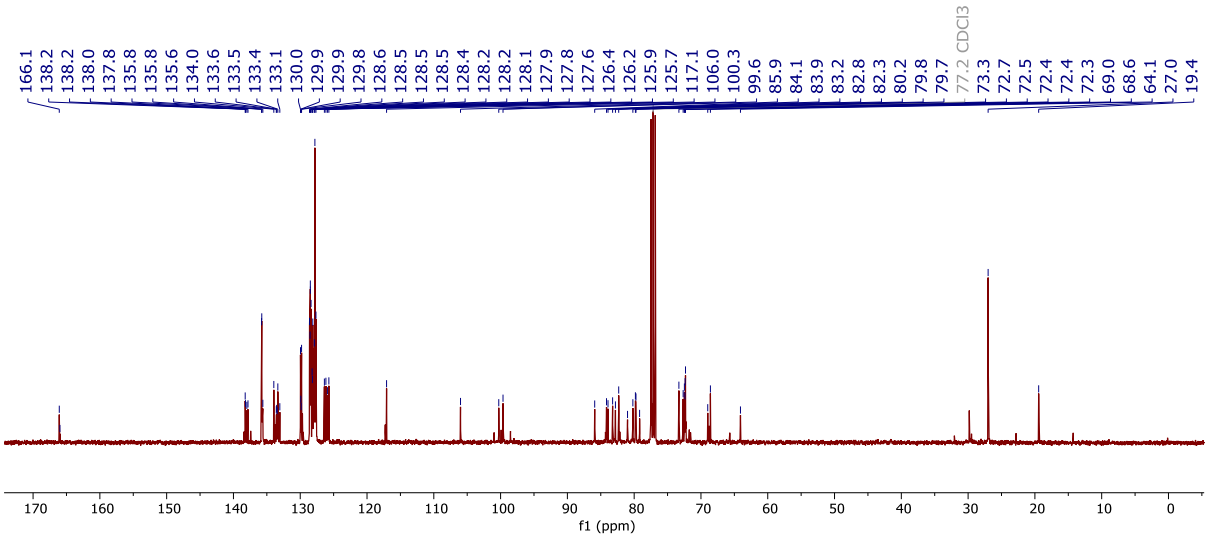

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **22**



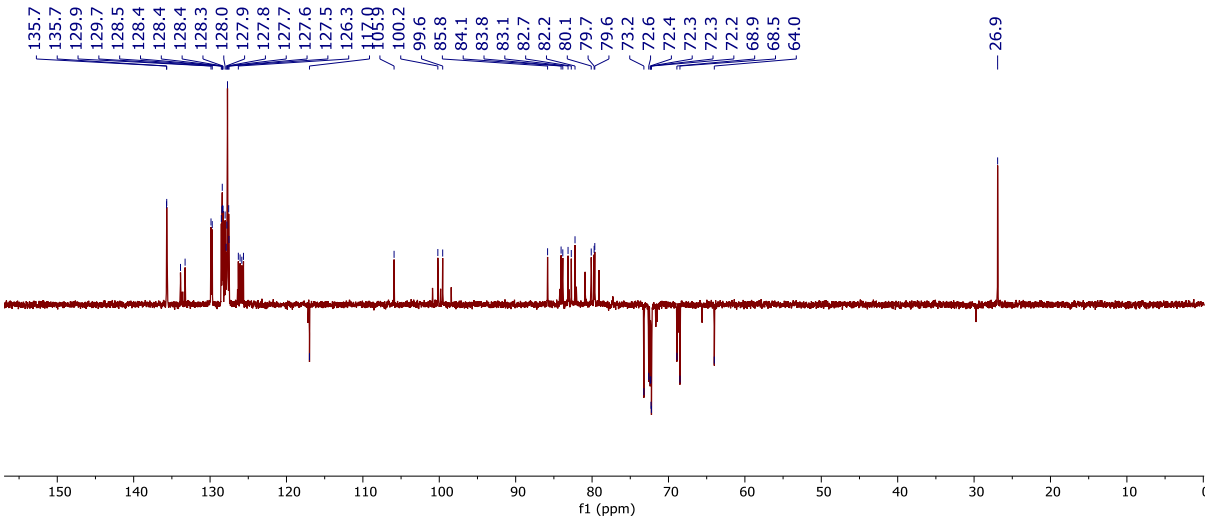
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **23**



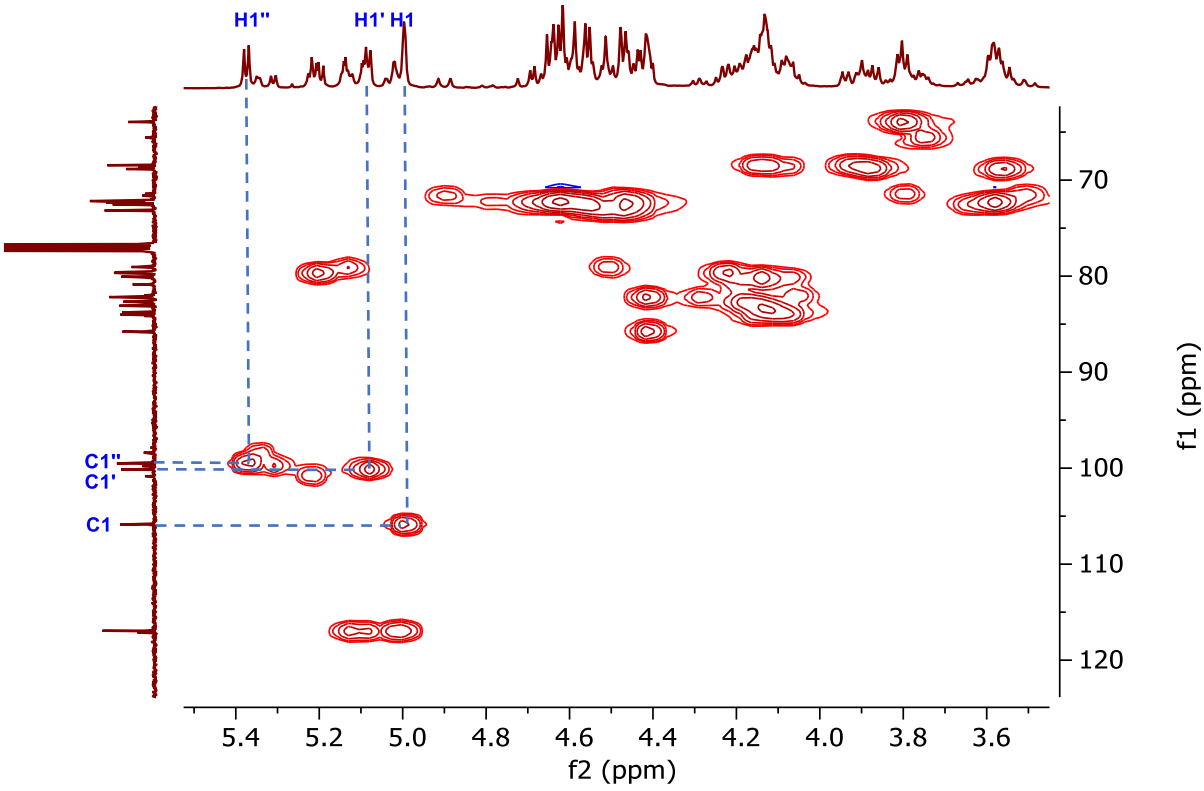

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **23**



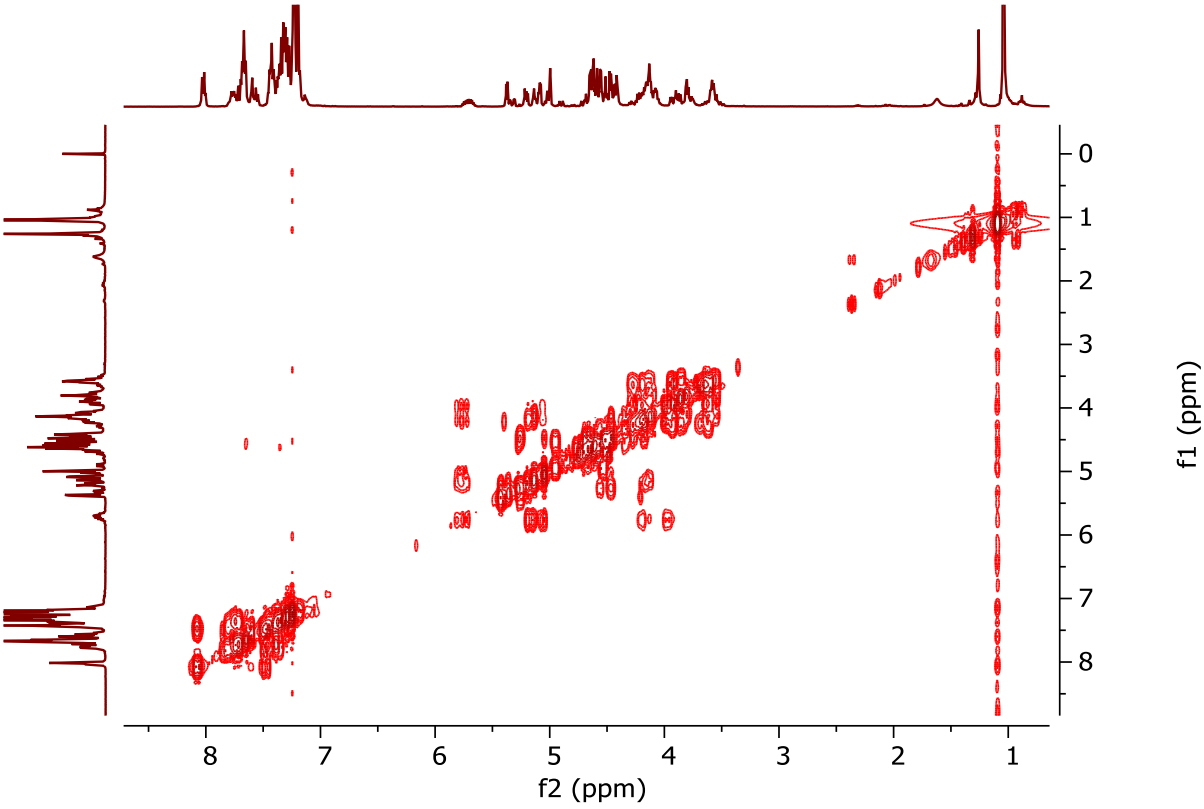

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **23**



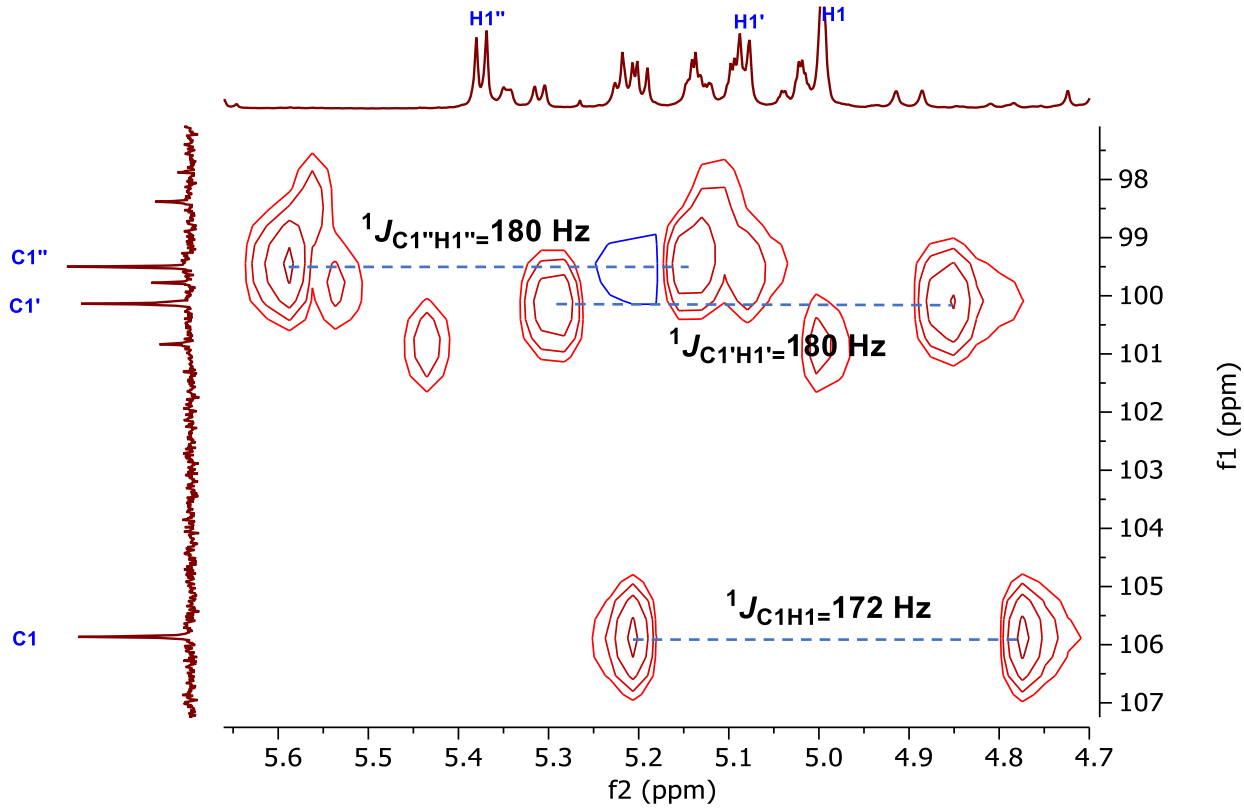
$^{1}H$, $^{13}C$ HSQC NMR Spectrum (400, 101 MHz, $CDCl_3$) of compound **23**



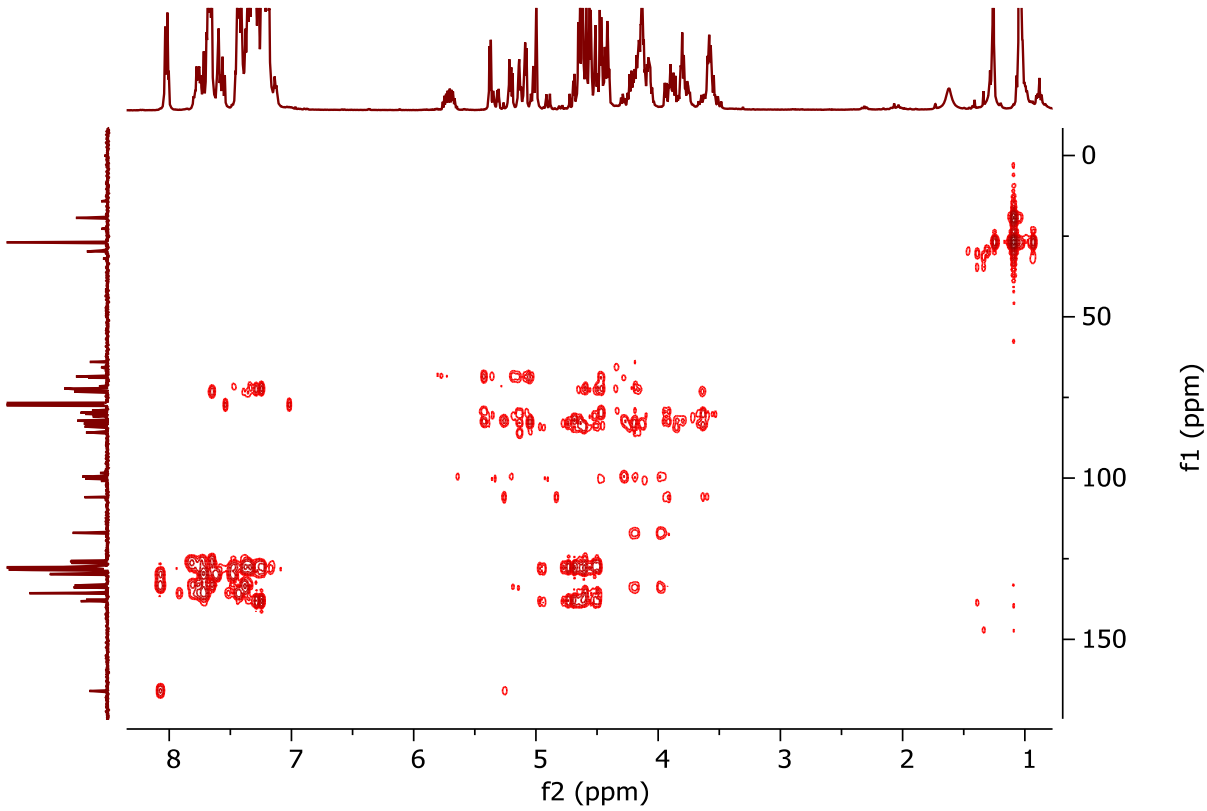

$^{1}H$, $^{1}H$ COSY NMR Spectrum (400, 101 MHz, $CDCl_3$) of compound **23**



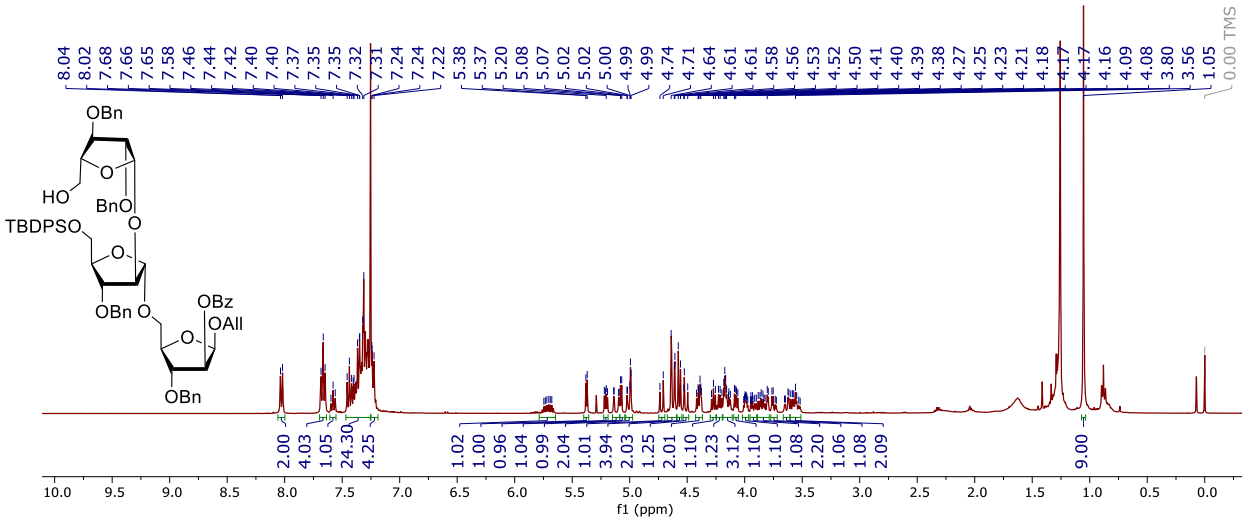
$^{1}H$, $^{13}C$ HSQC-Coupled NMR Spectrum (400, 101 MHz, $CDCl_3$) of Compound **23**



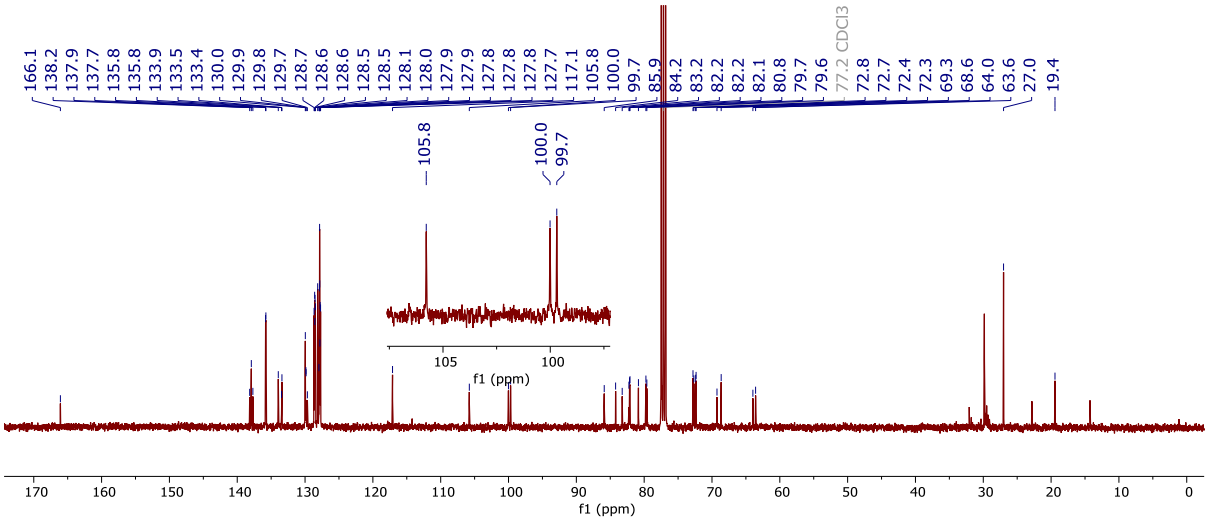

$^{1}H$, $^{13}C$ HMBC NMR Spectrum (400, 101 MHz, $CDCl_3$) of compound **23**



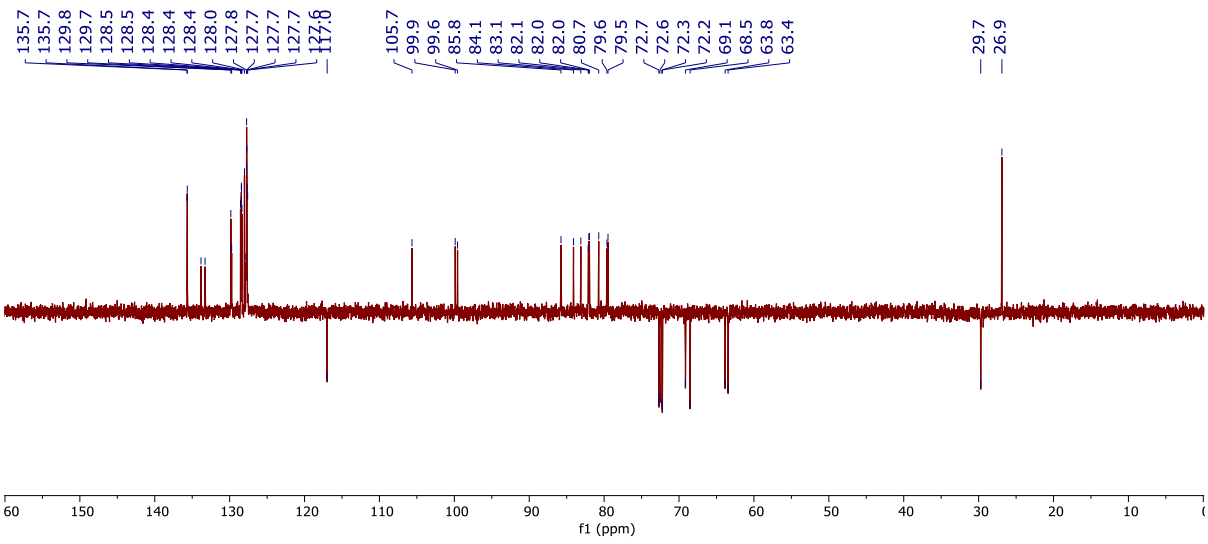
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **24**



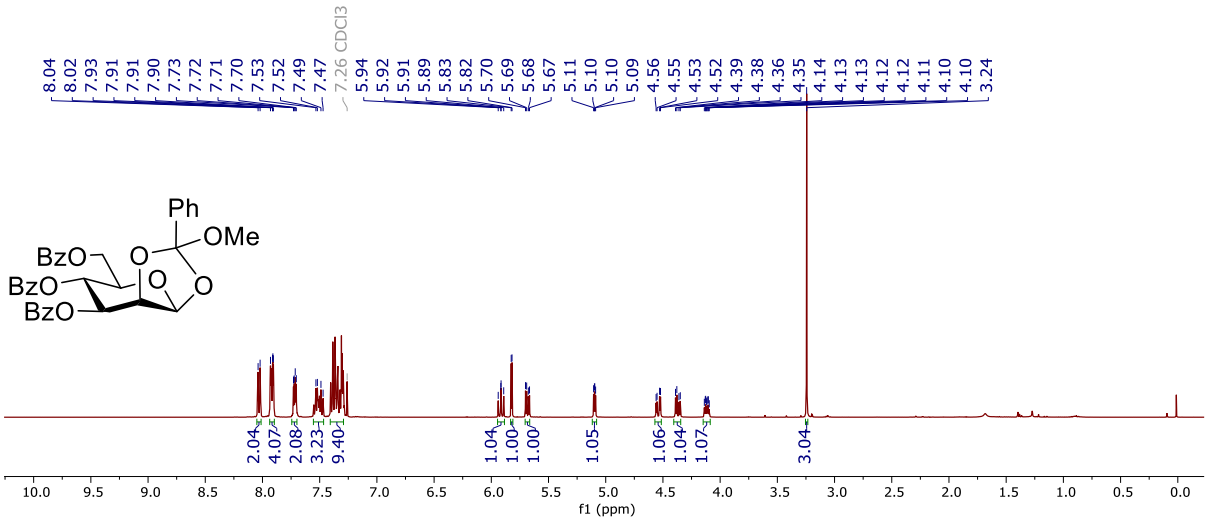

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **24**



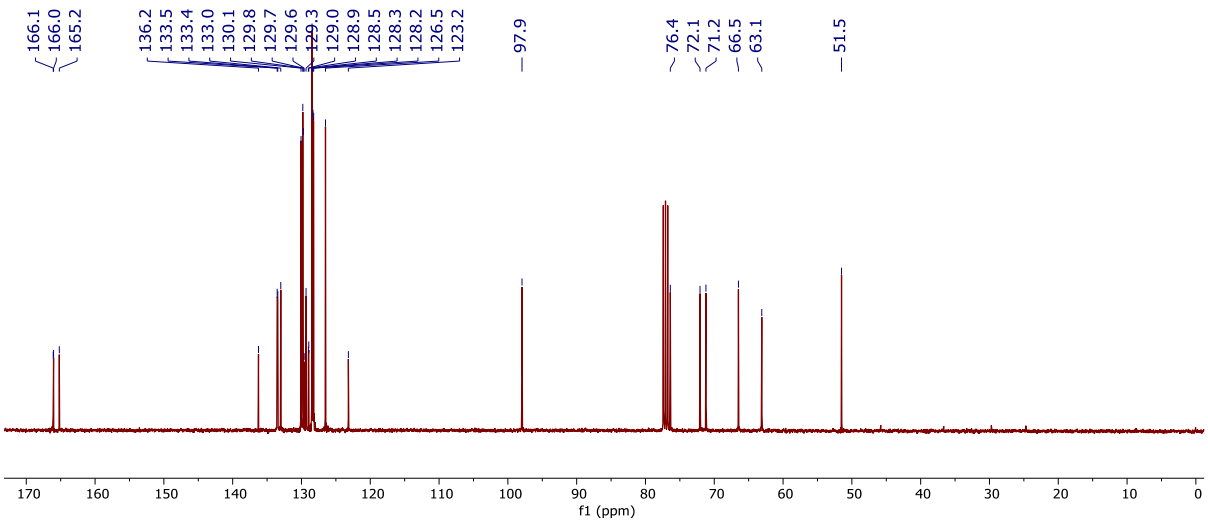

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **24**



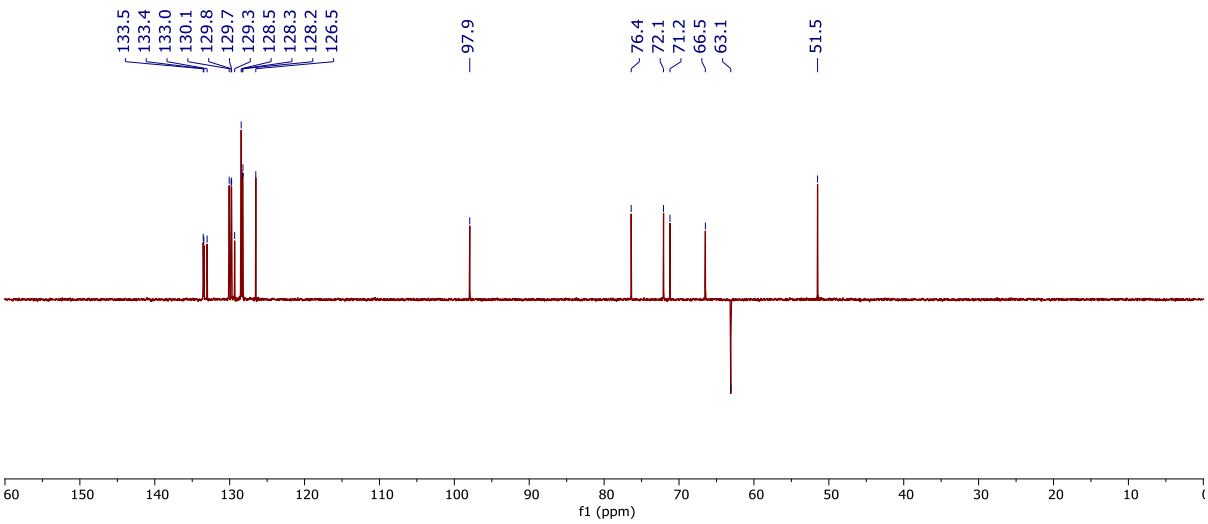
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **25**



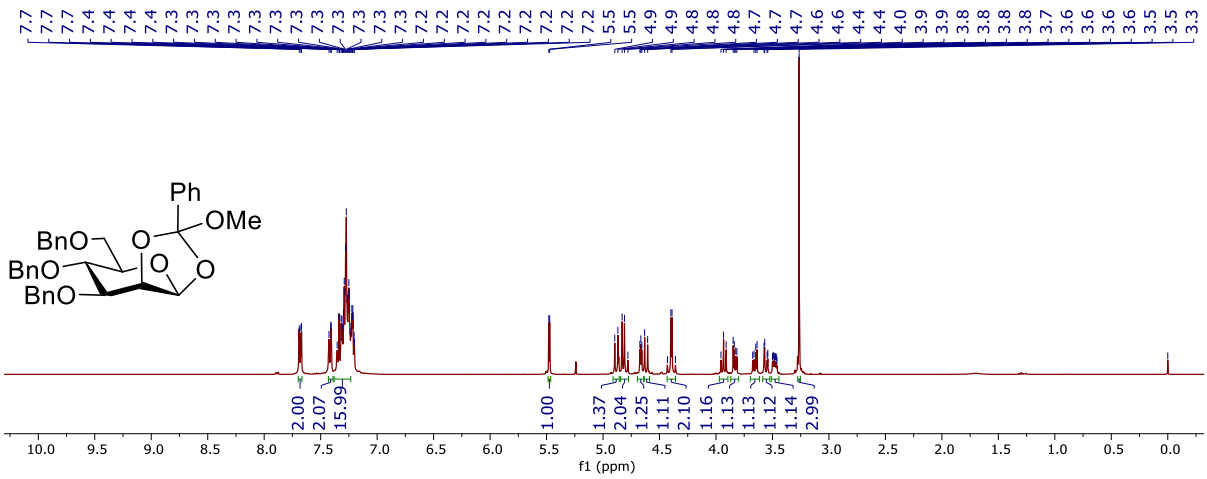

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **25**



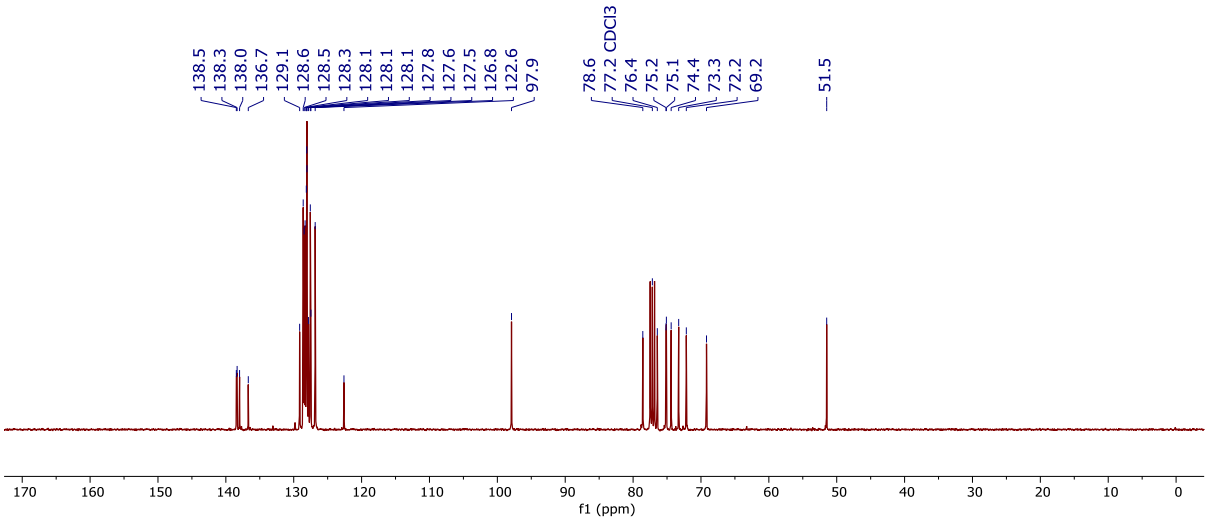

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **25**



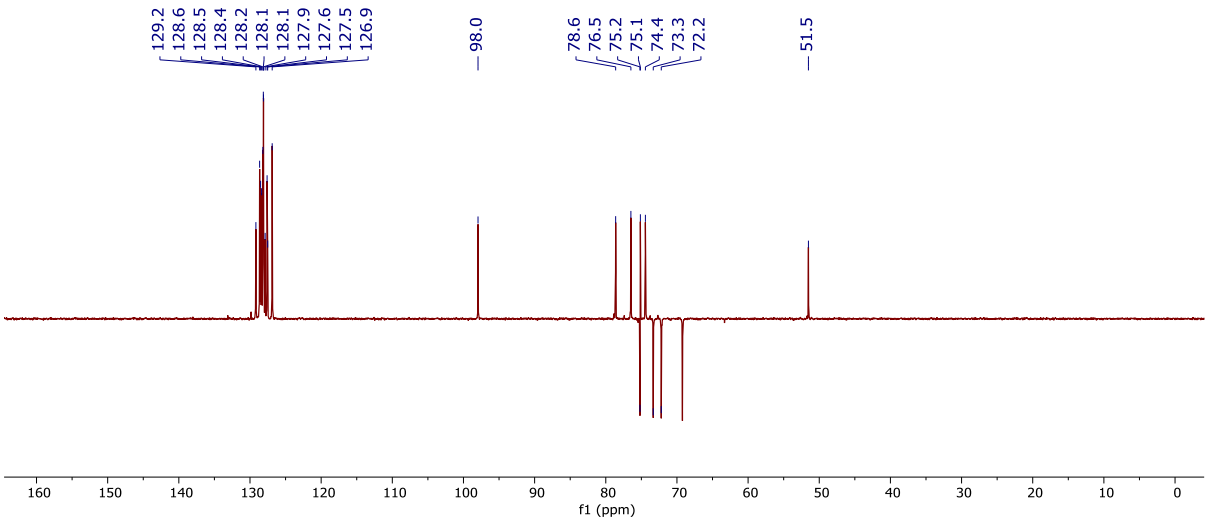
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **26**



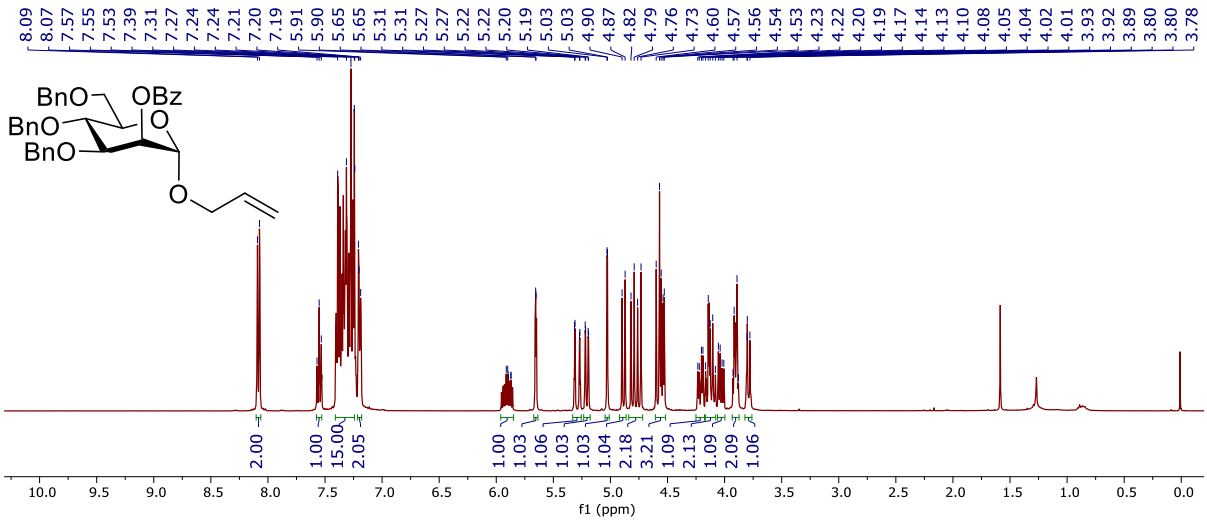

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **26**



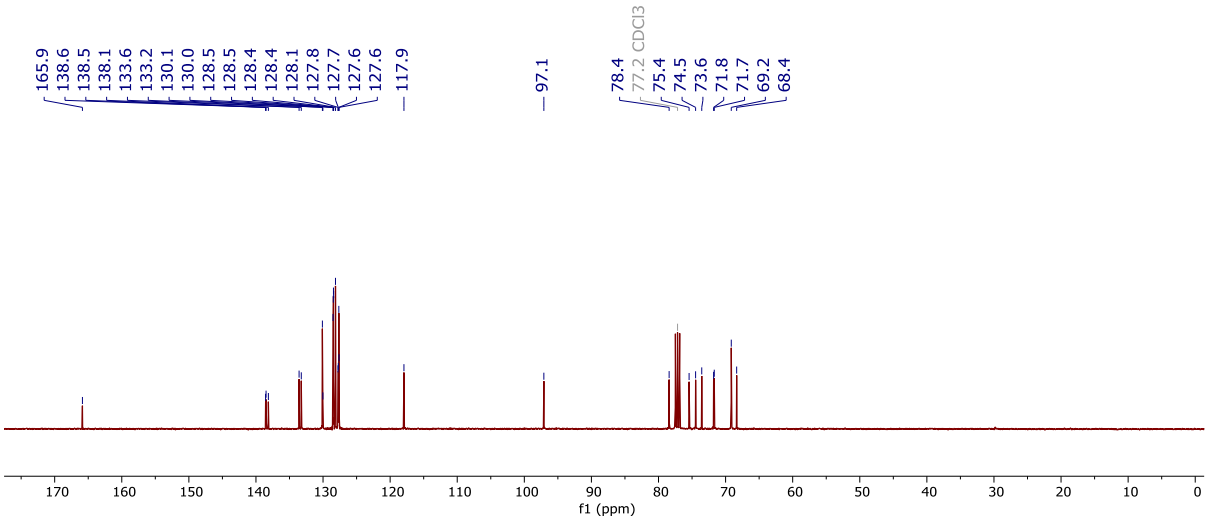

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **26**



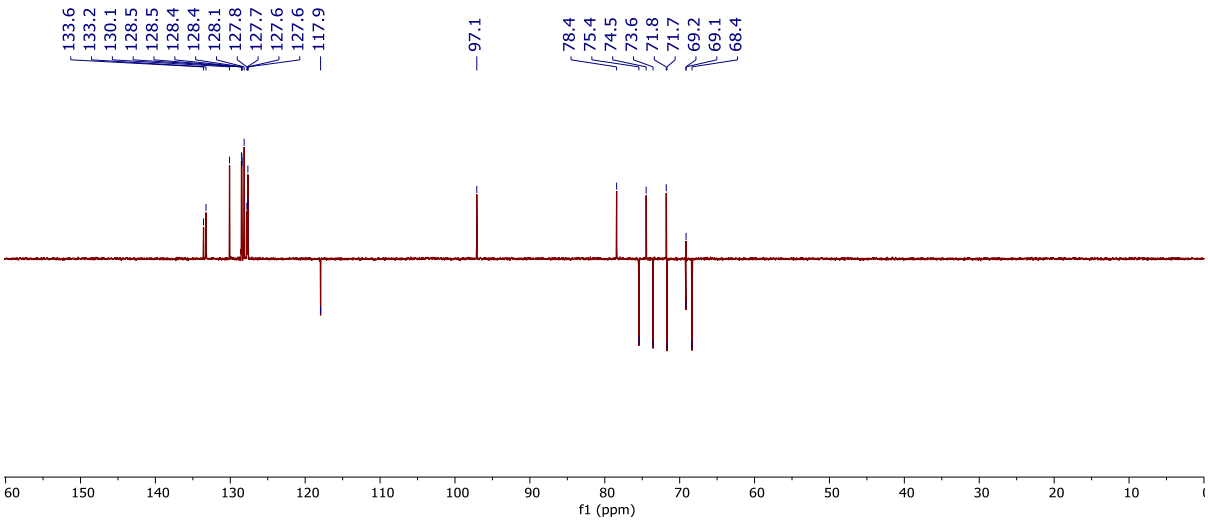
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **27**



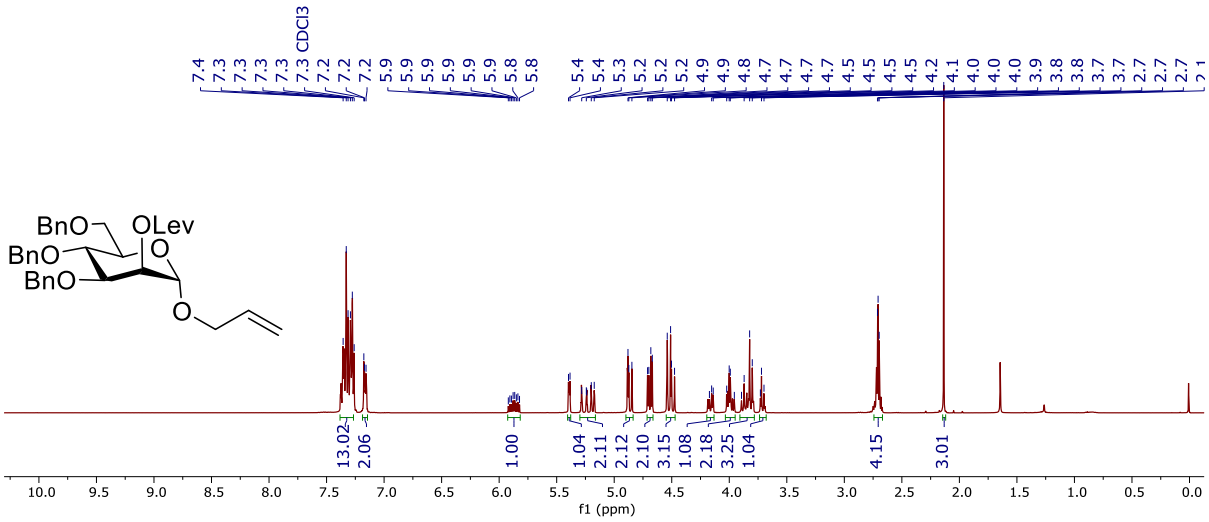

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **27**



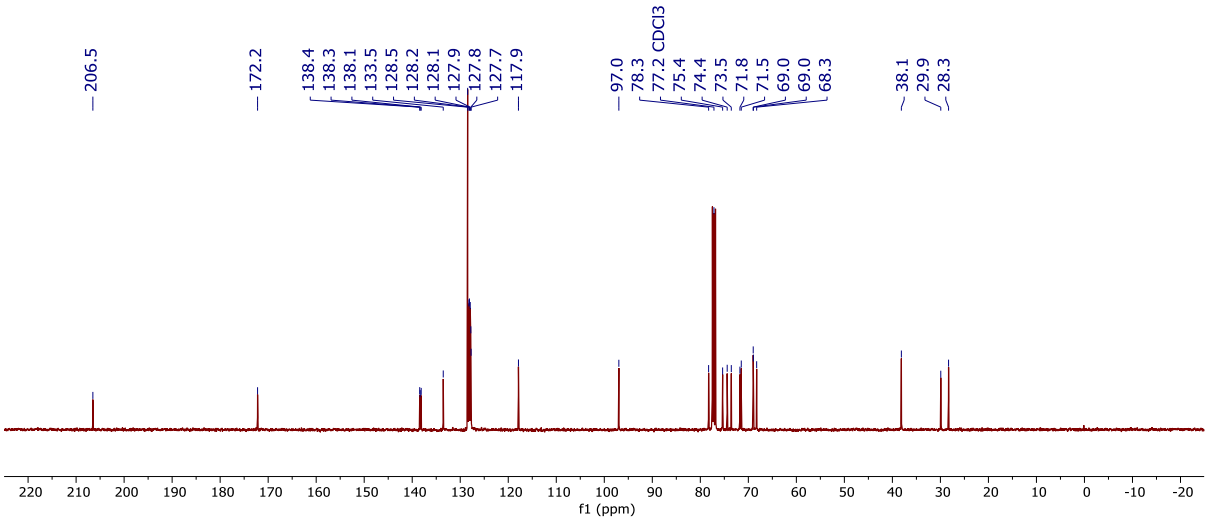

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **27**



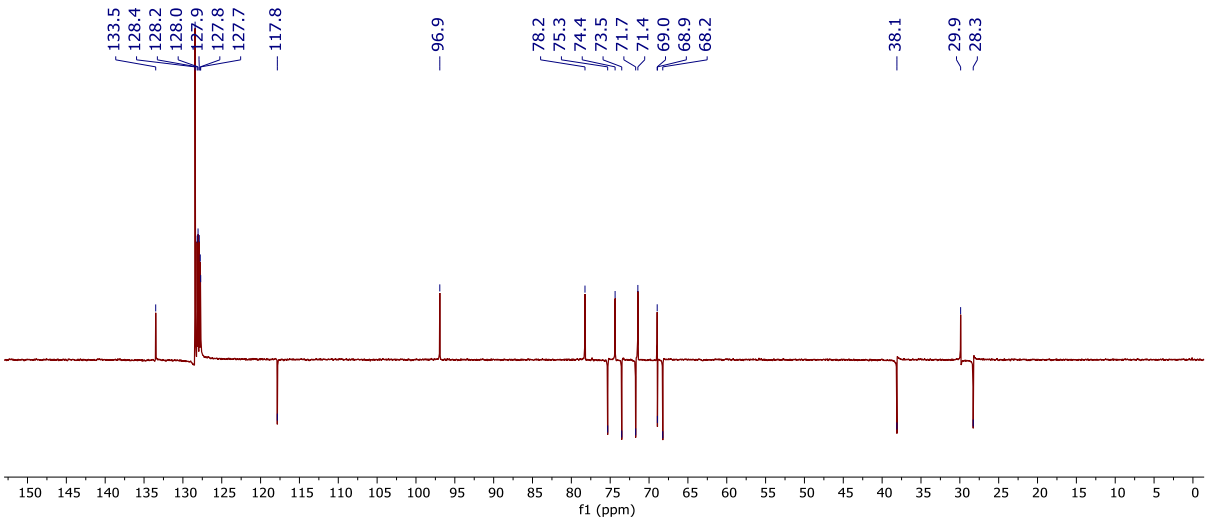
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **28**



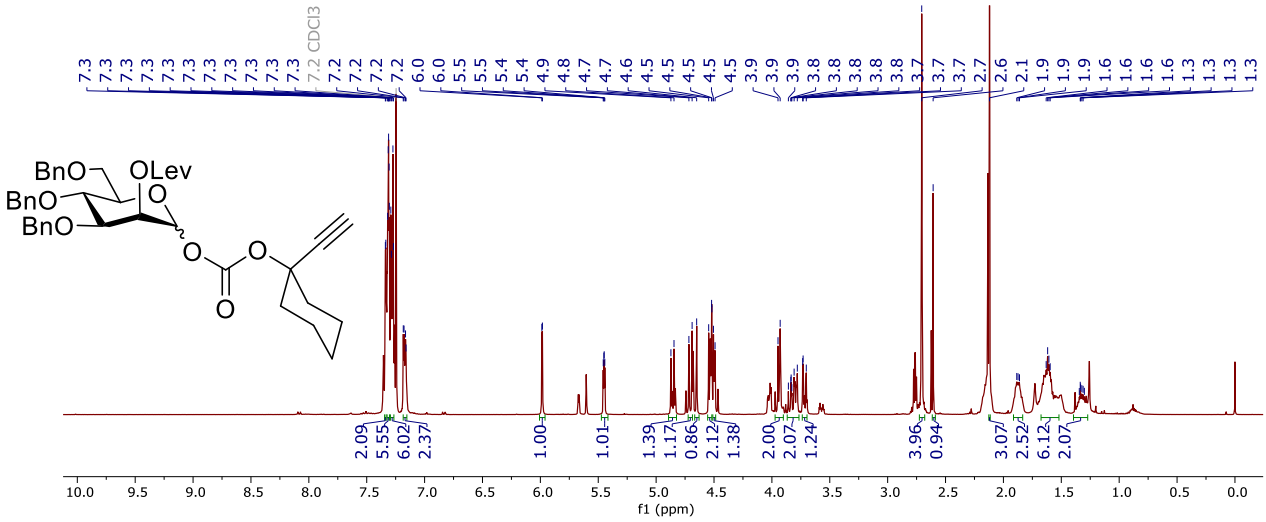

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **28**



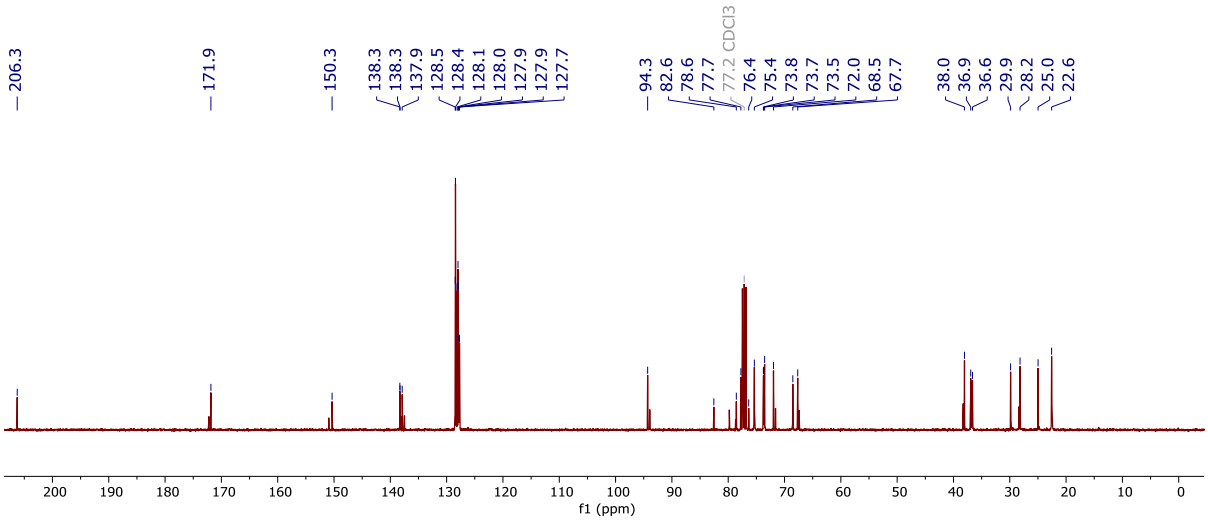

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **28**



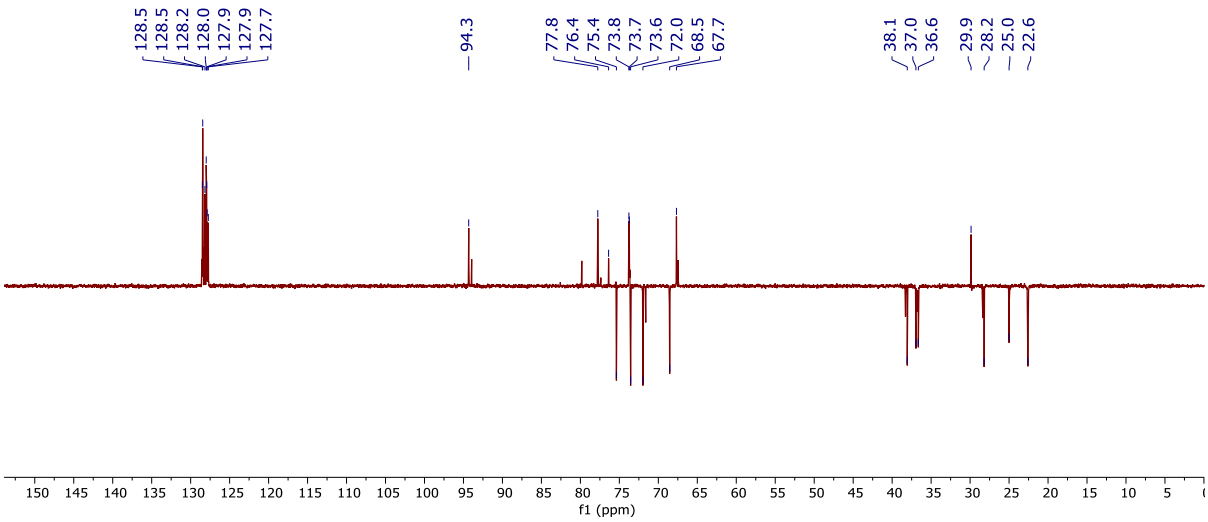
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **11**



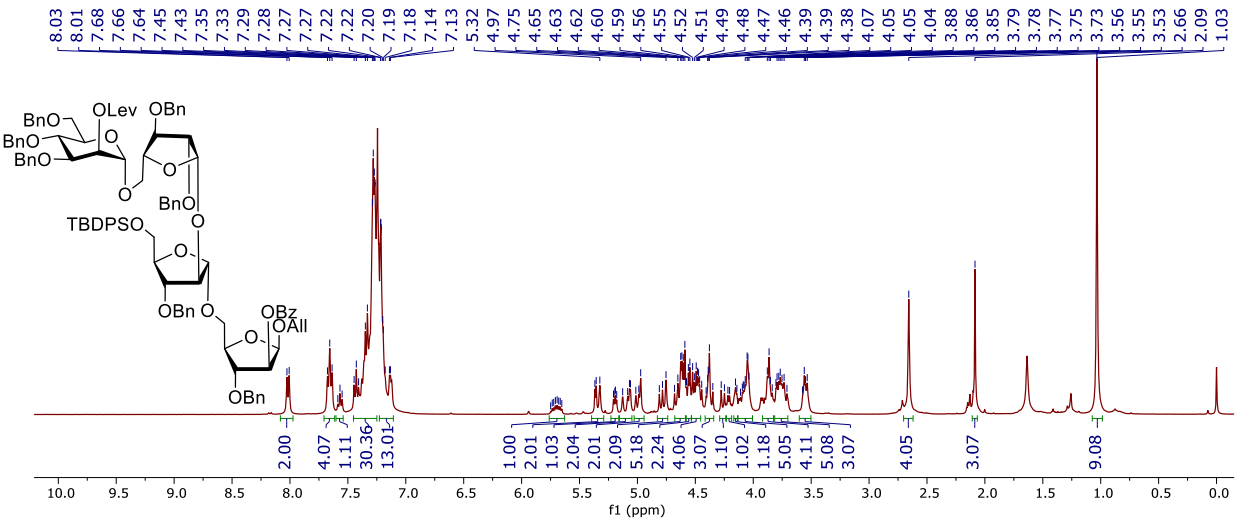

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **11**



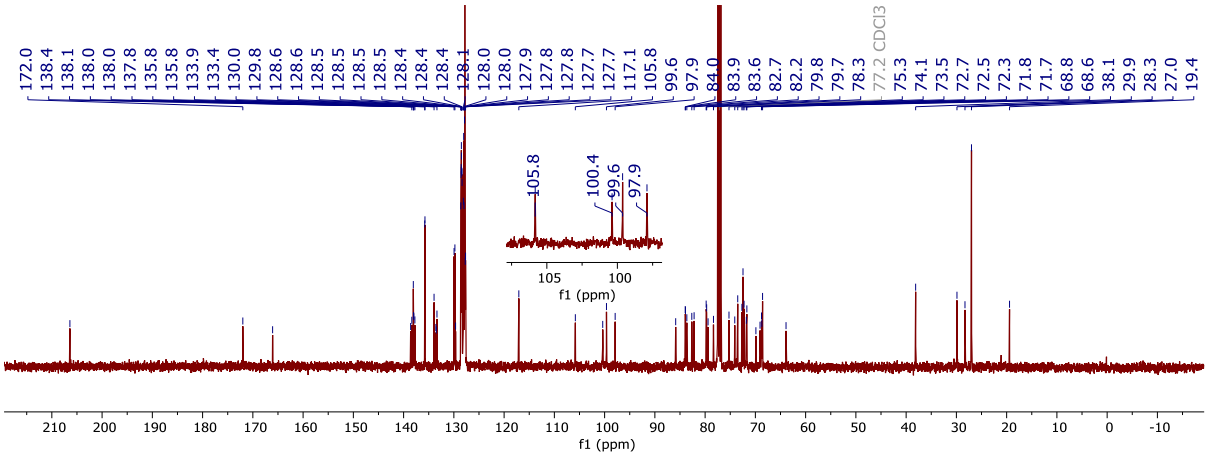

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **11**



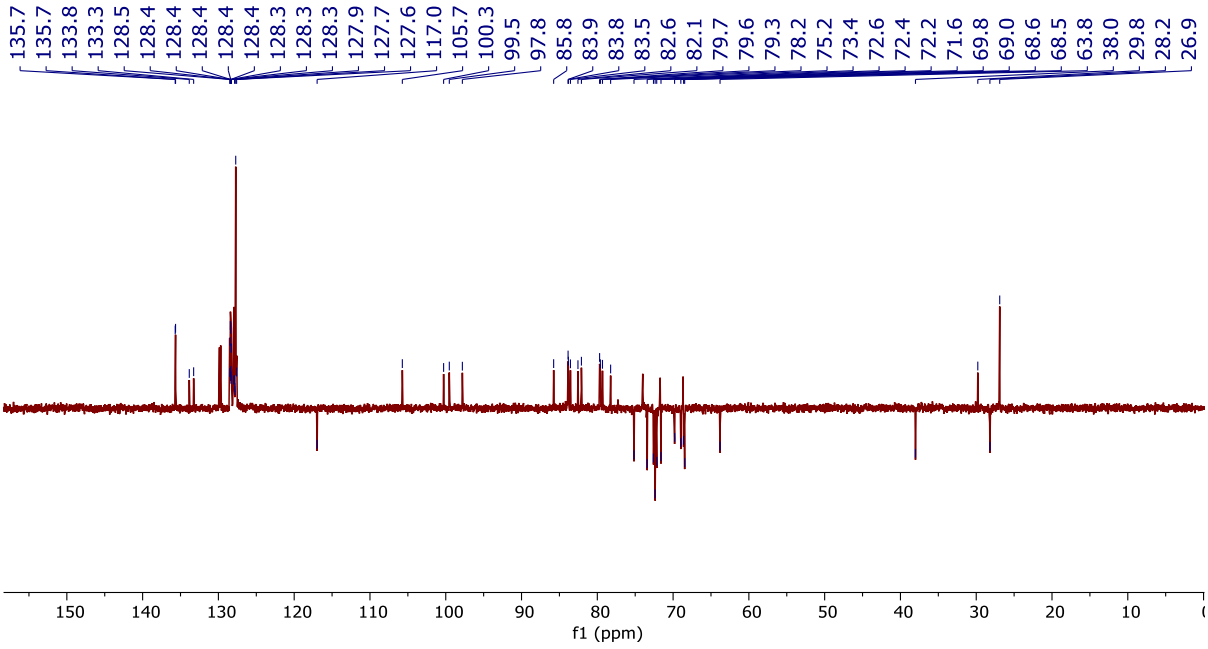
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **29**



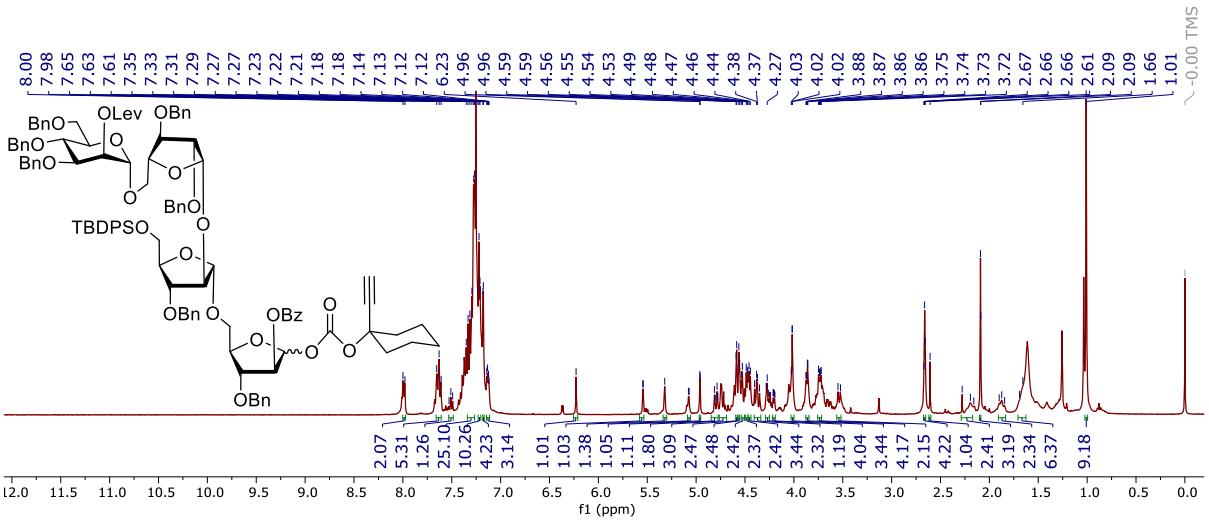

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **29**



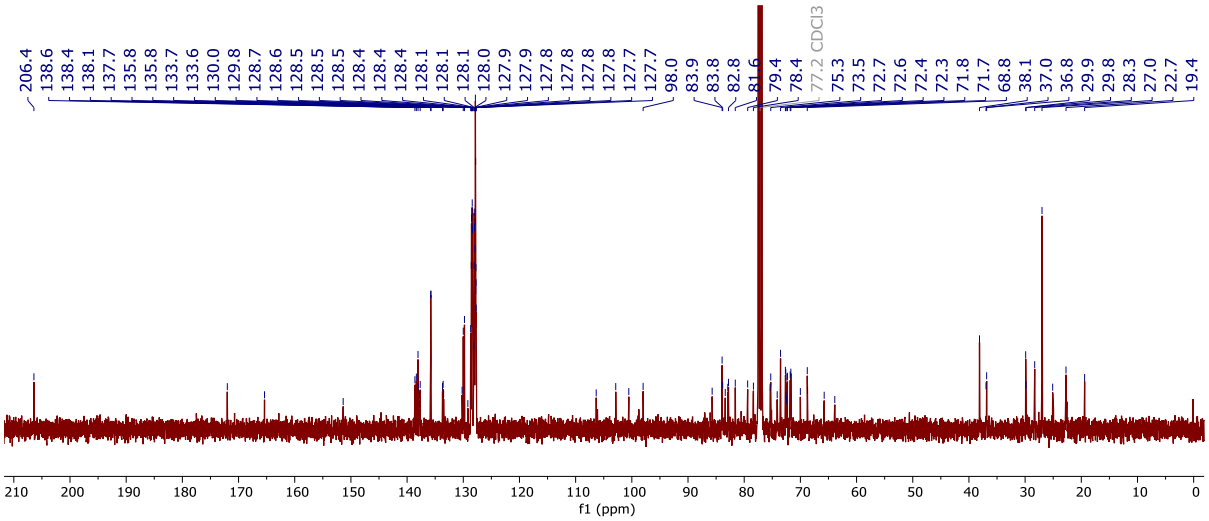

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **29**



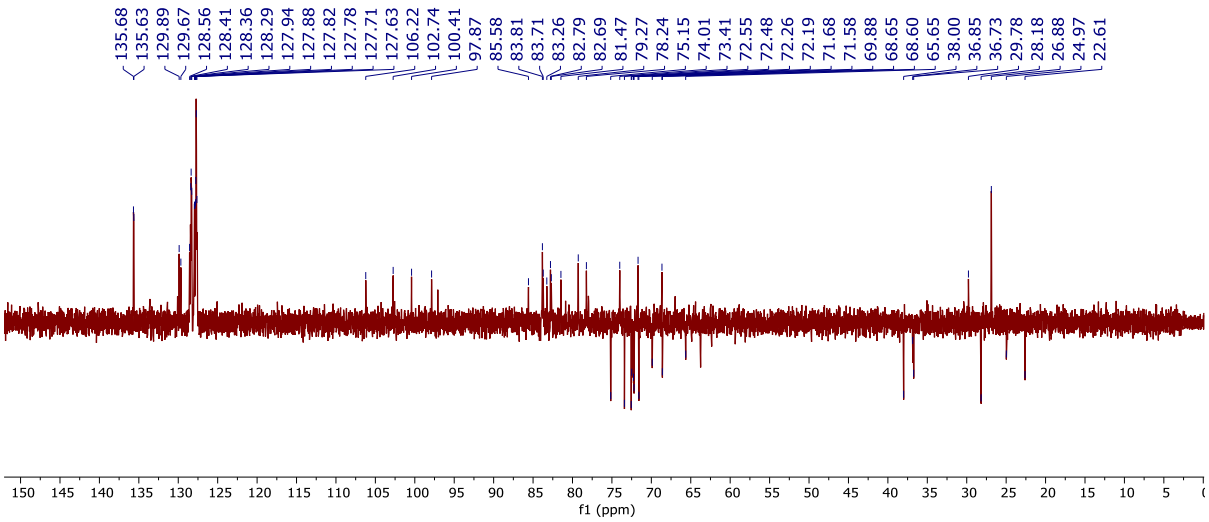
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **06**



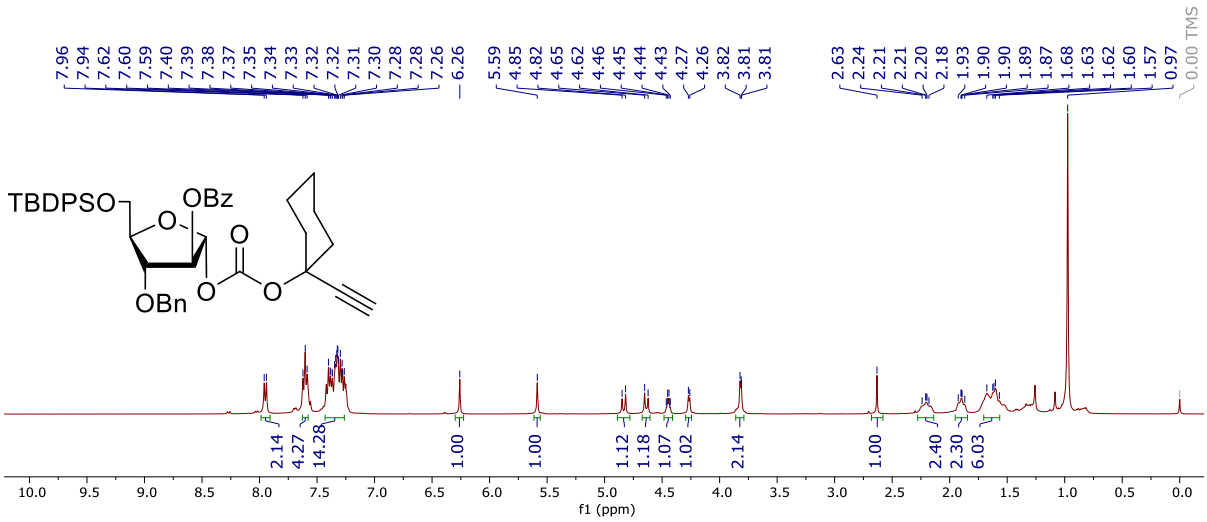

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **06**



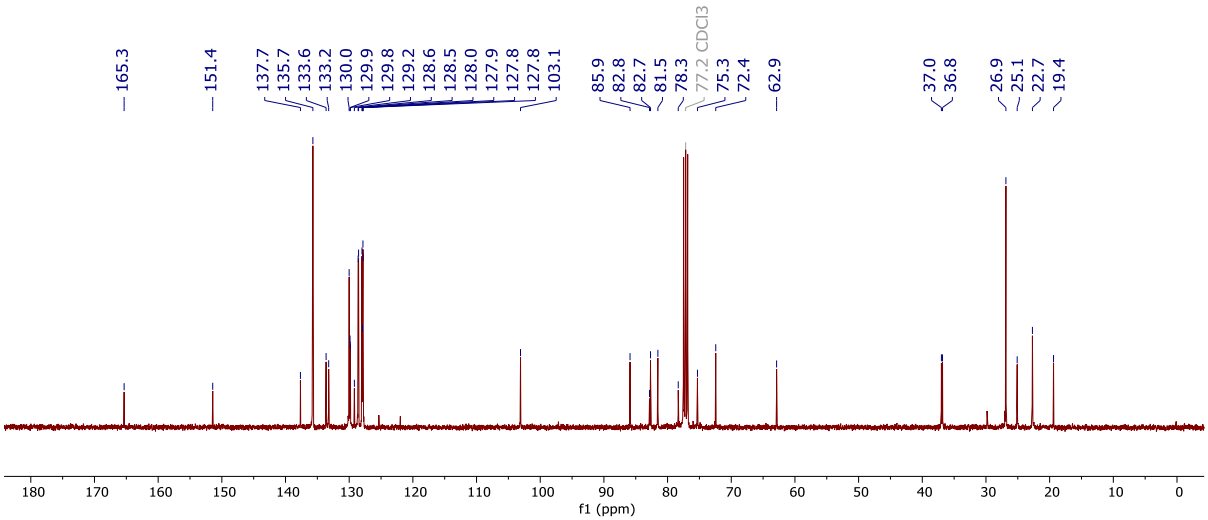

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **06**



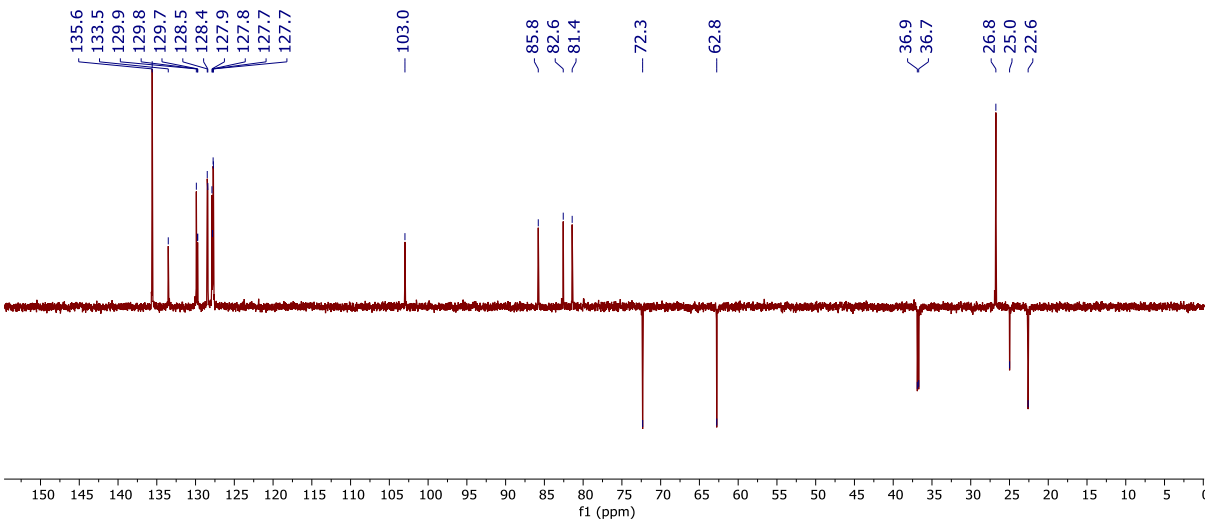
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **12**



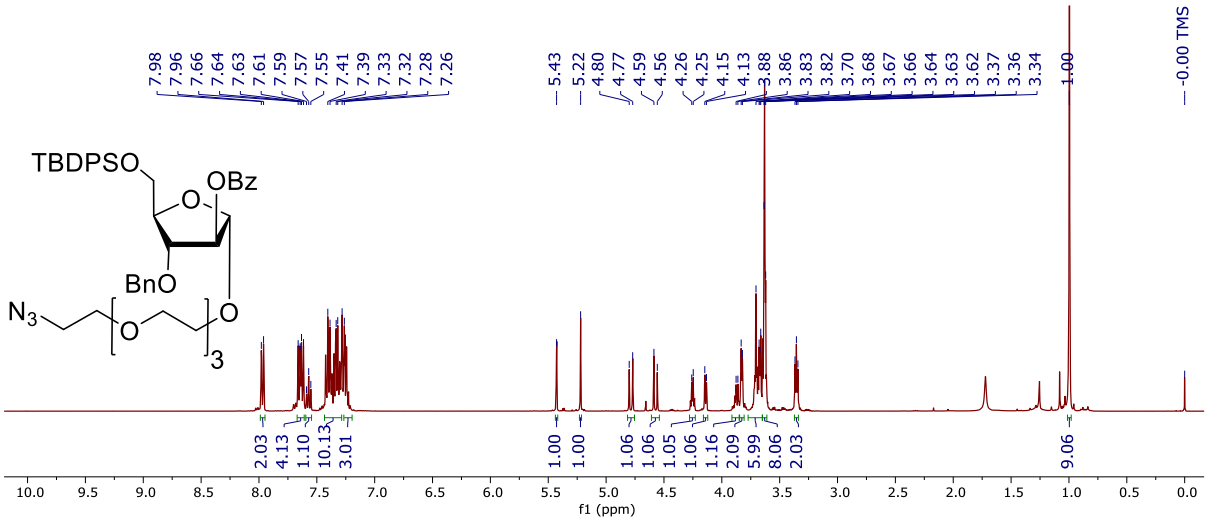

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **12**



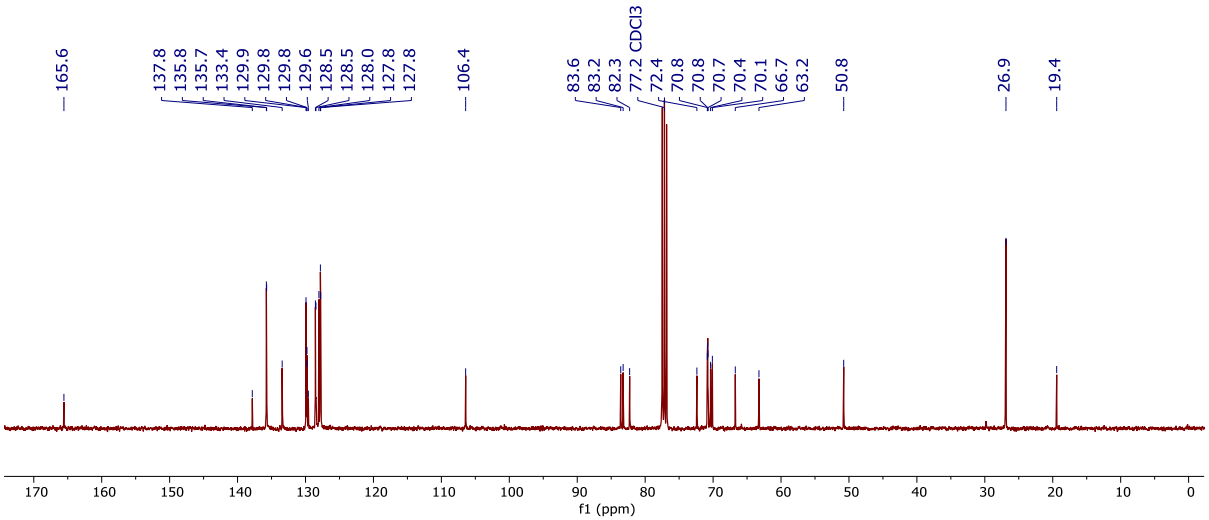

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **12**



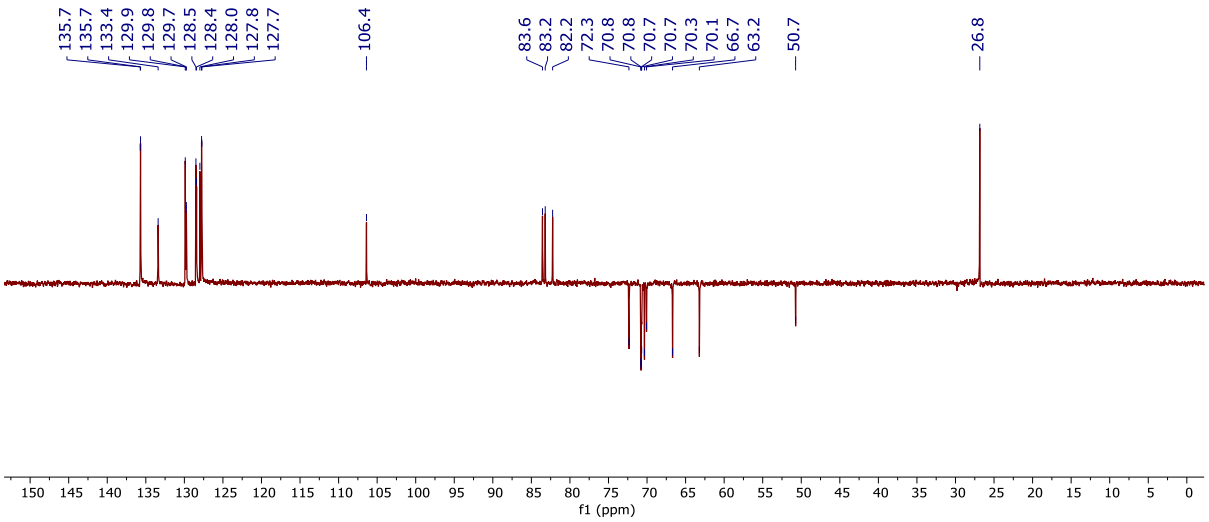
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **34**



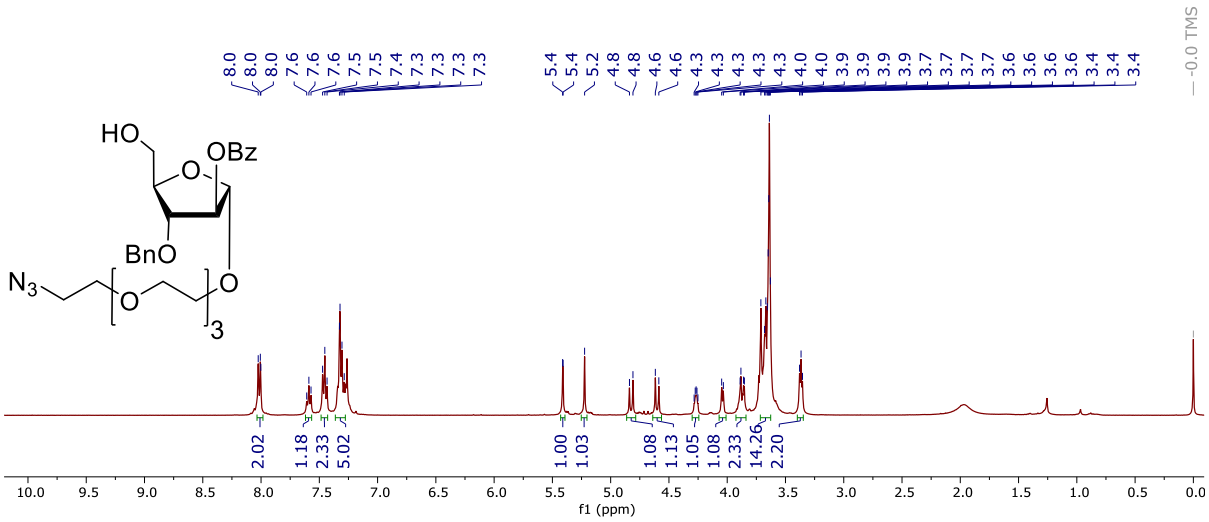

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **34**



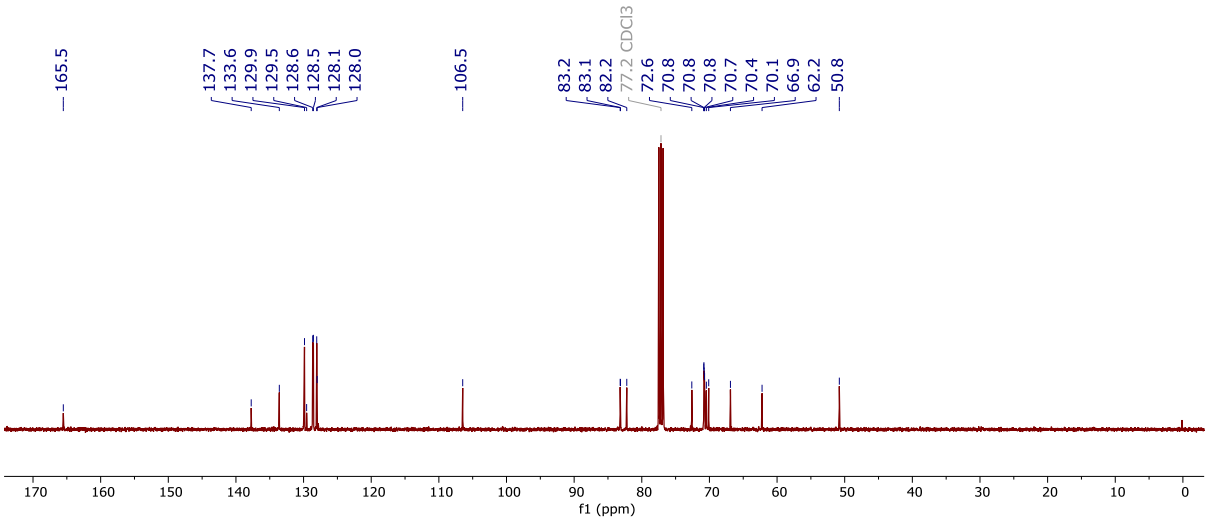

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **34**



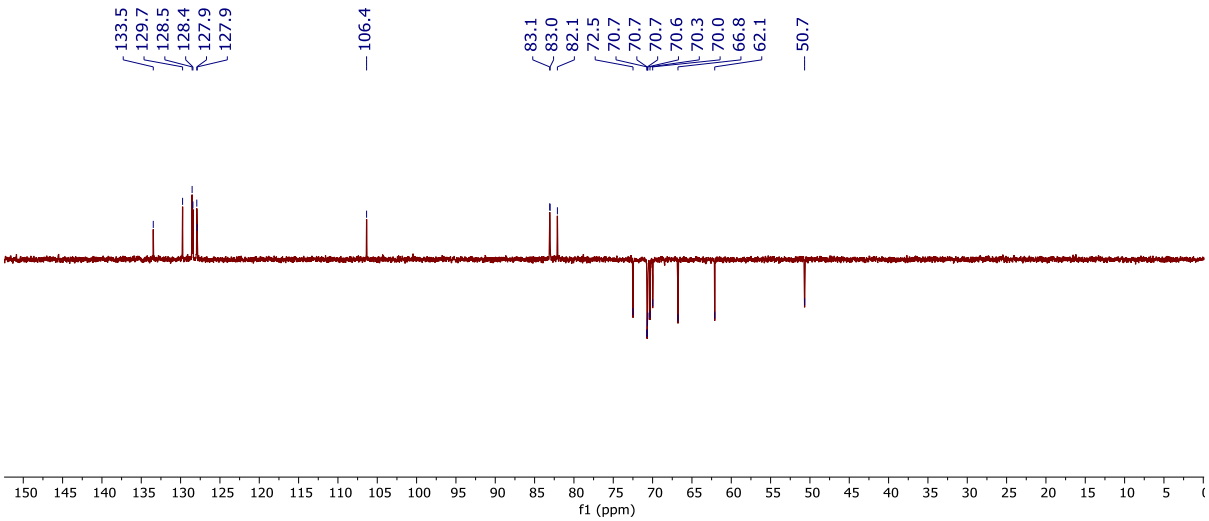
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **35**



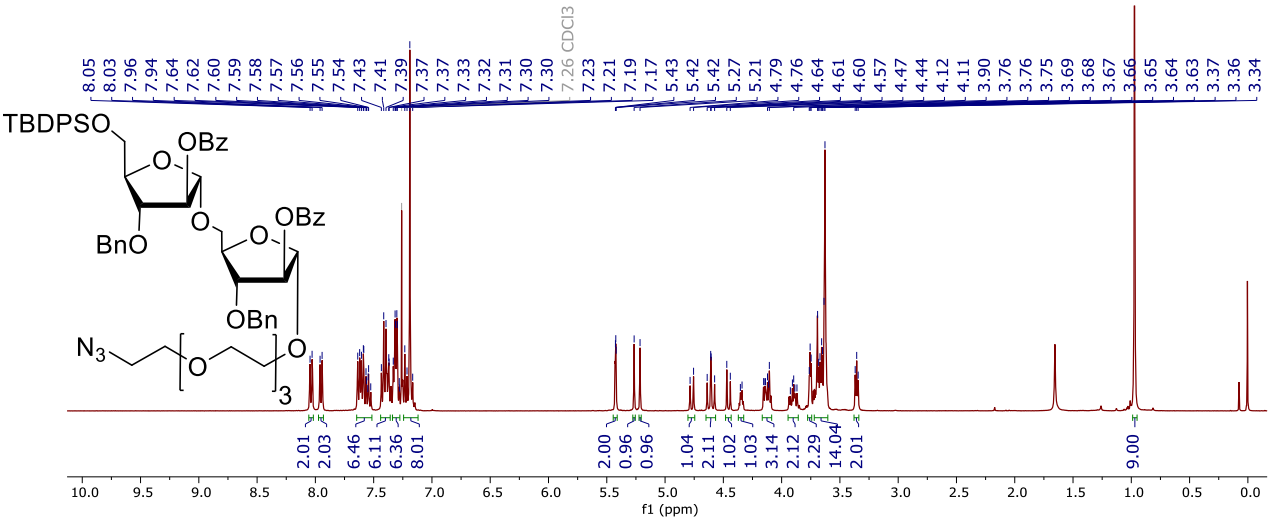

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **35**



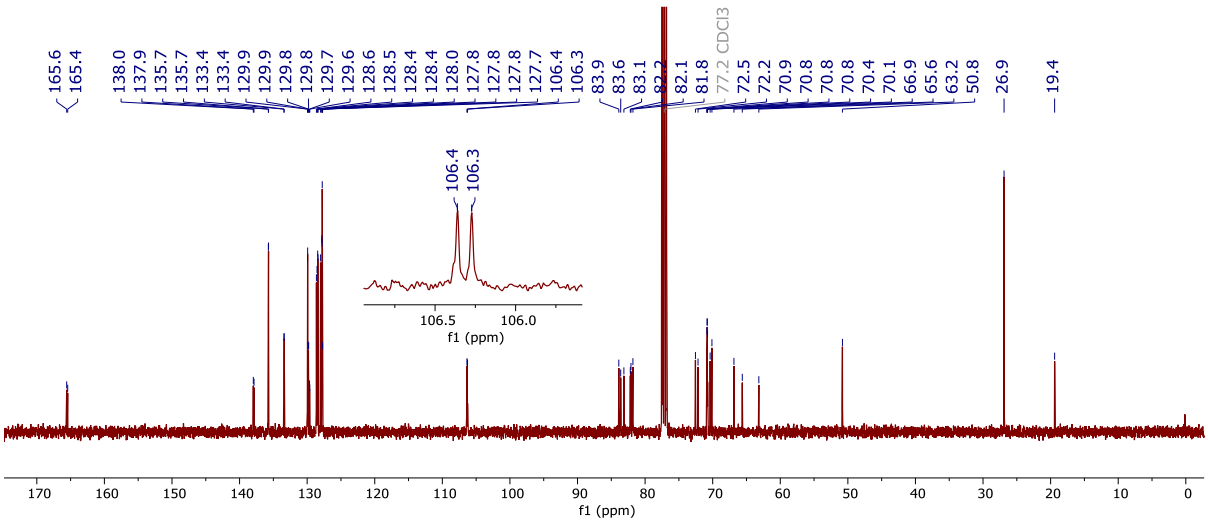

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **35**



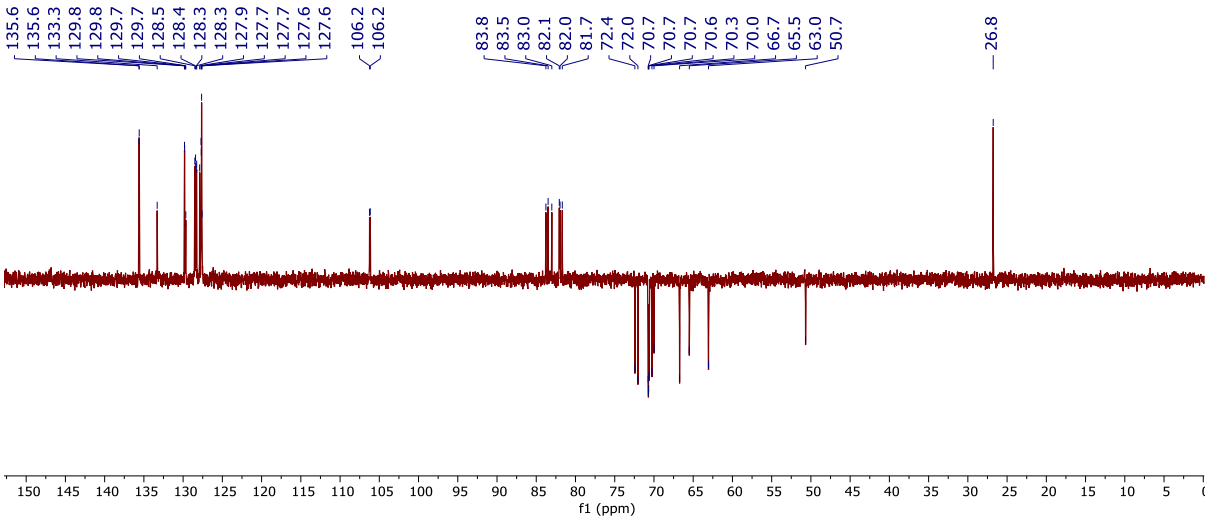
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **36**



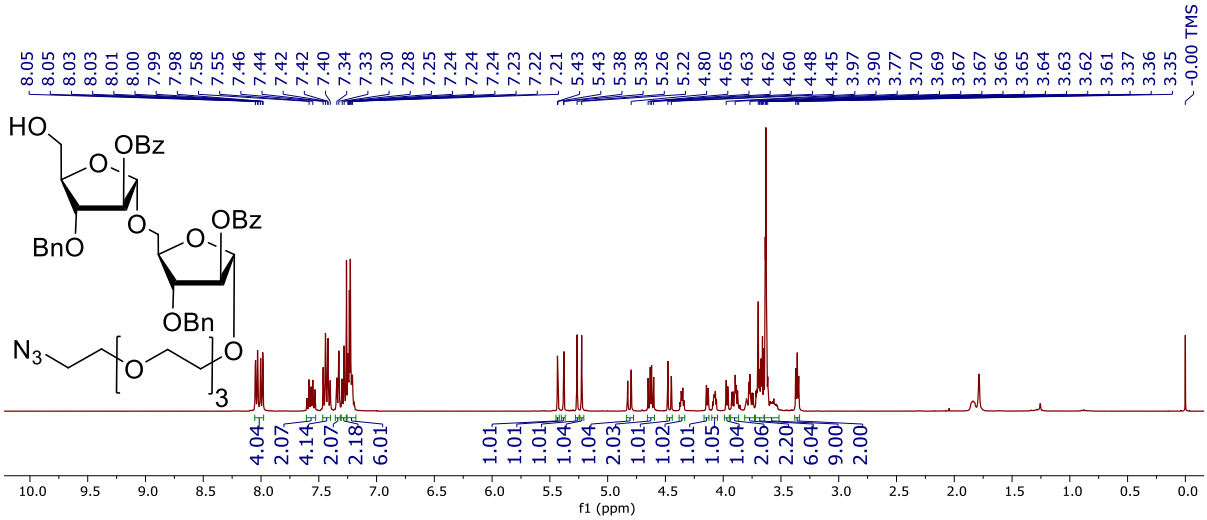

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **36**



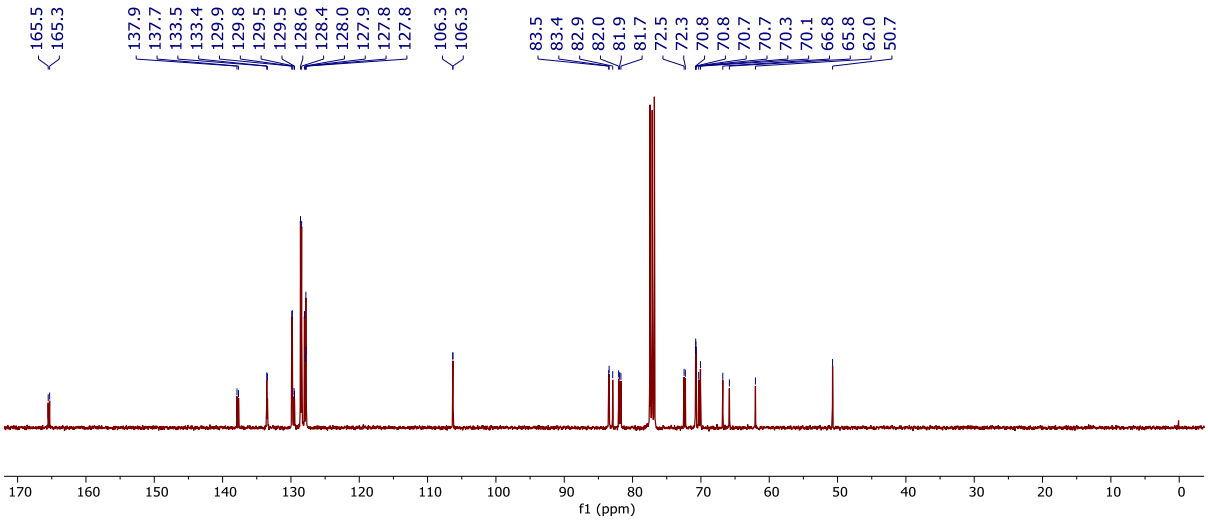

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **36**



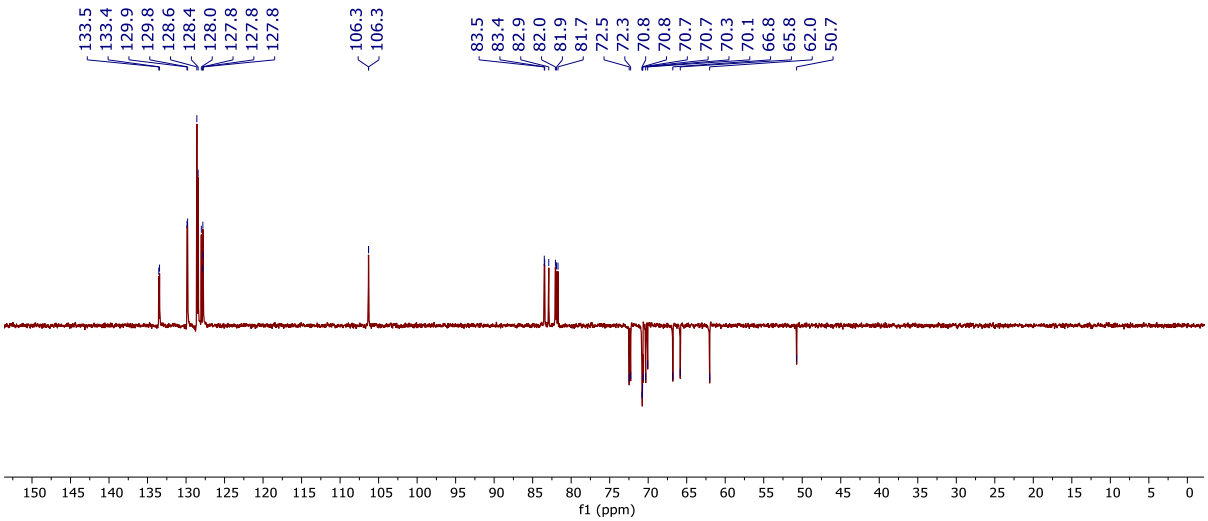
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **37**



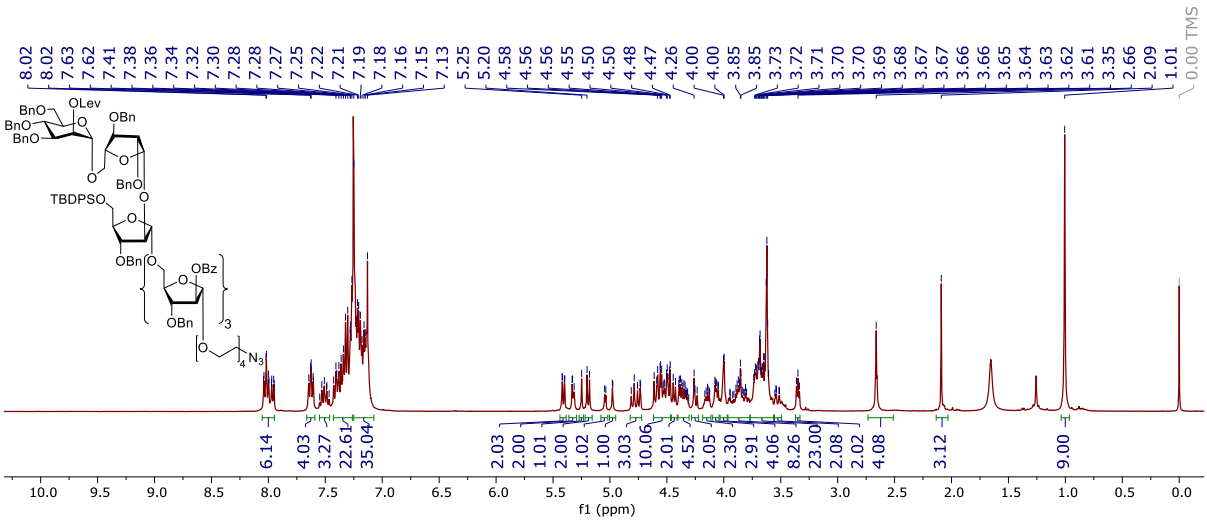

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **37**



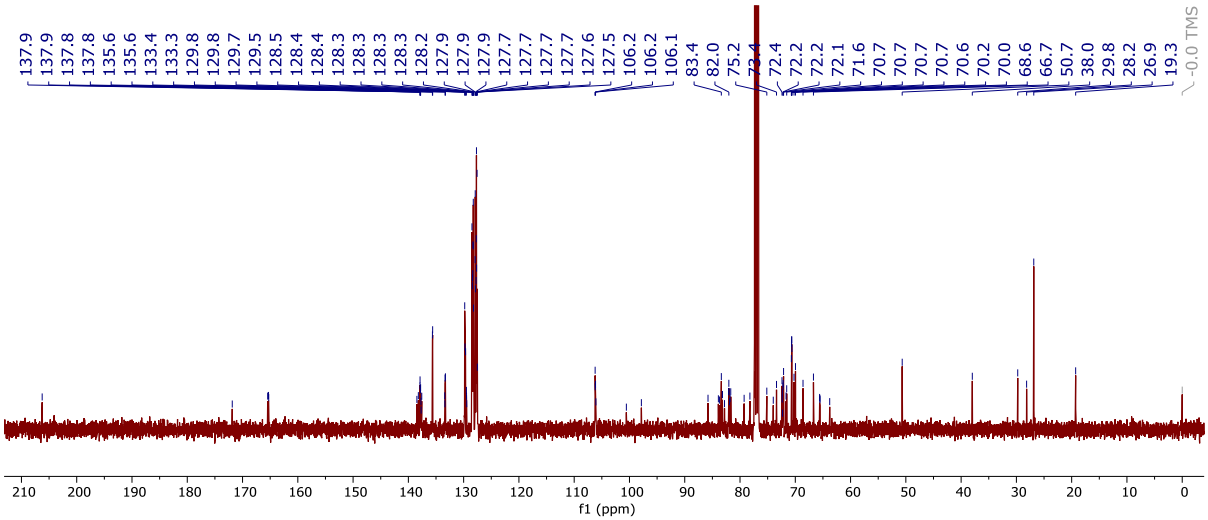

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **37**



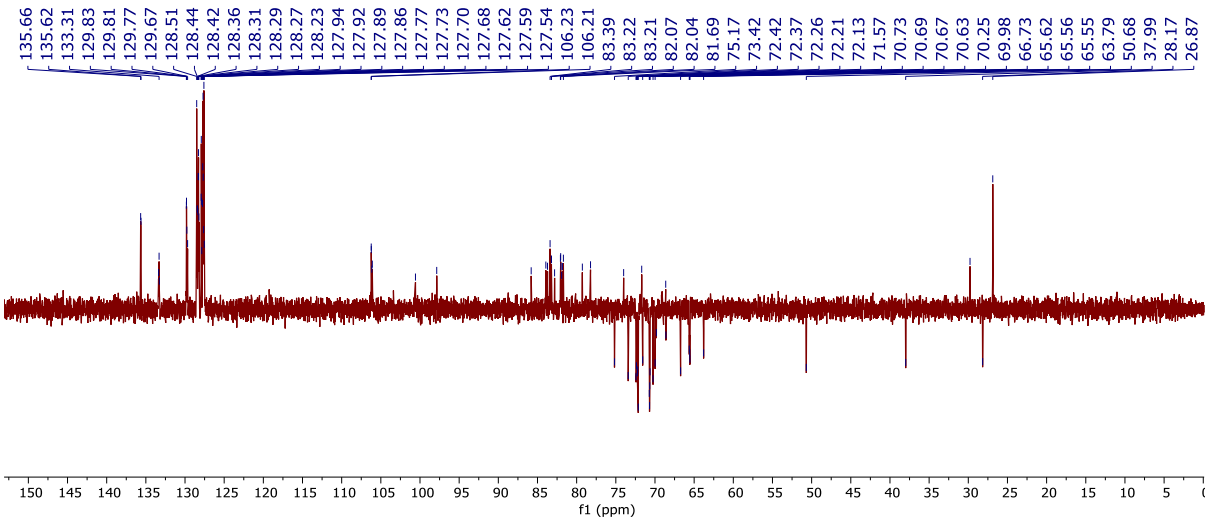
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **38**



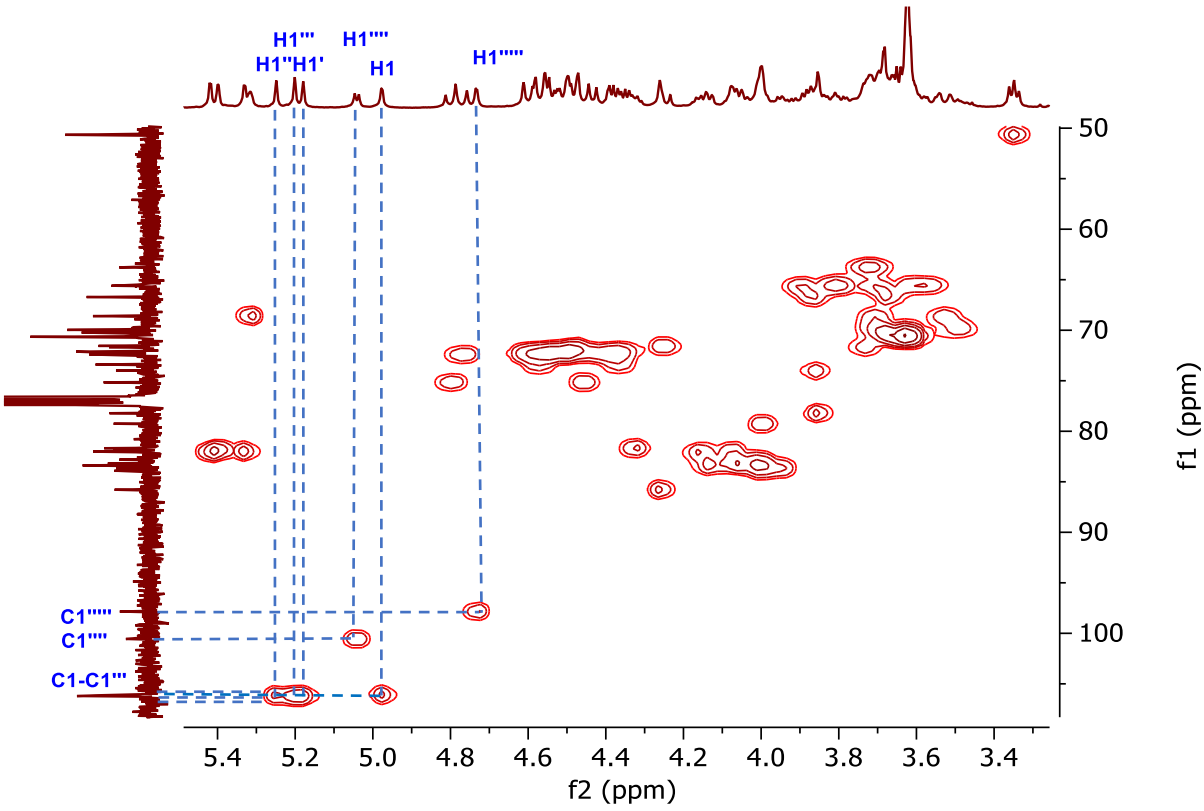

$^{13}$C NMR Spectrum of compound **38**



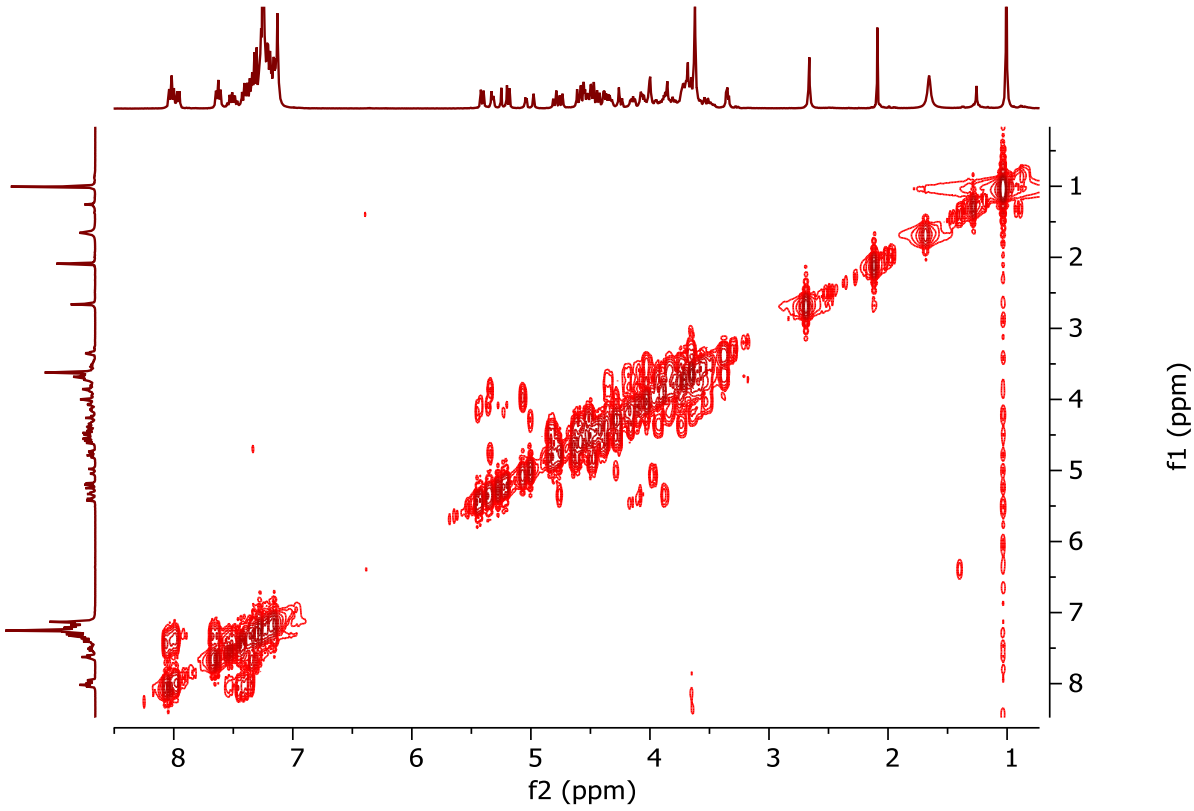

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **38**



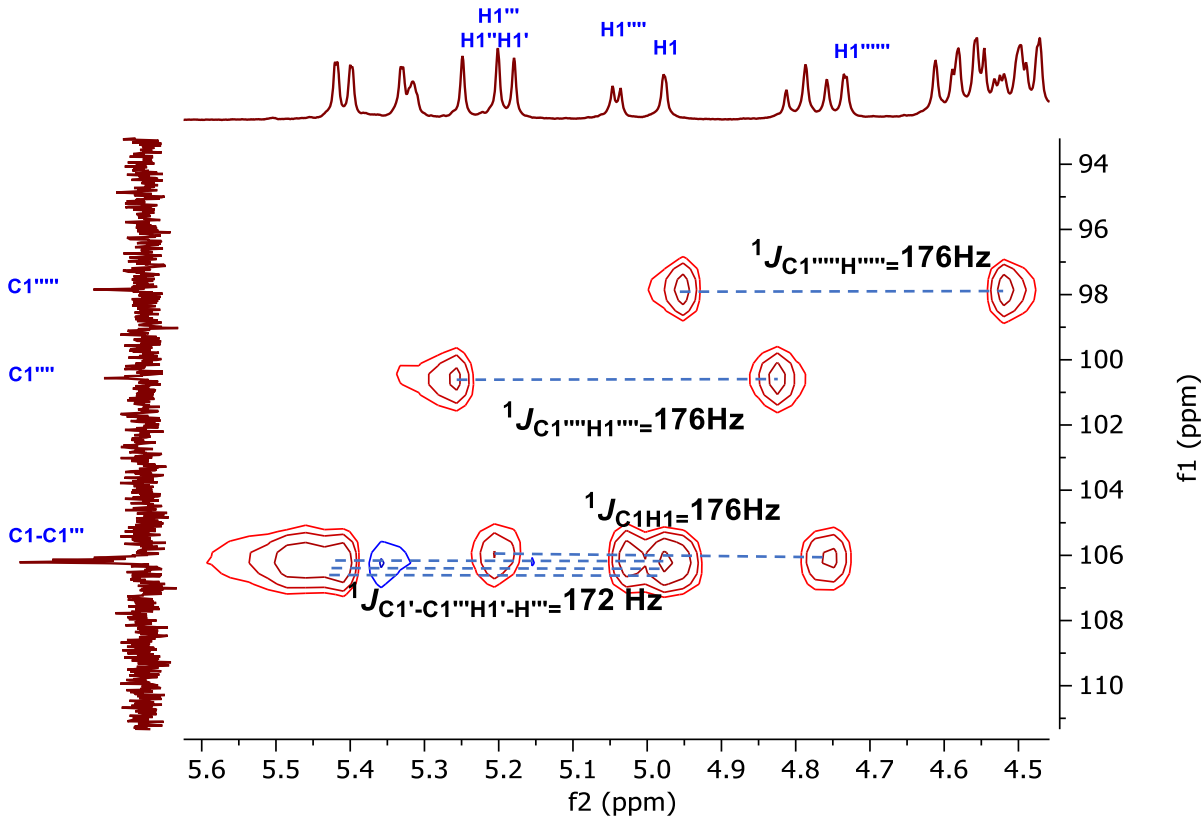
$^{1}H$, $^{13}C$-HSQC NMR Spectrum (400, 101 MHz, $CDCl_3$) of Compound **38**



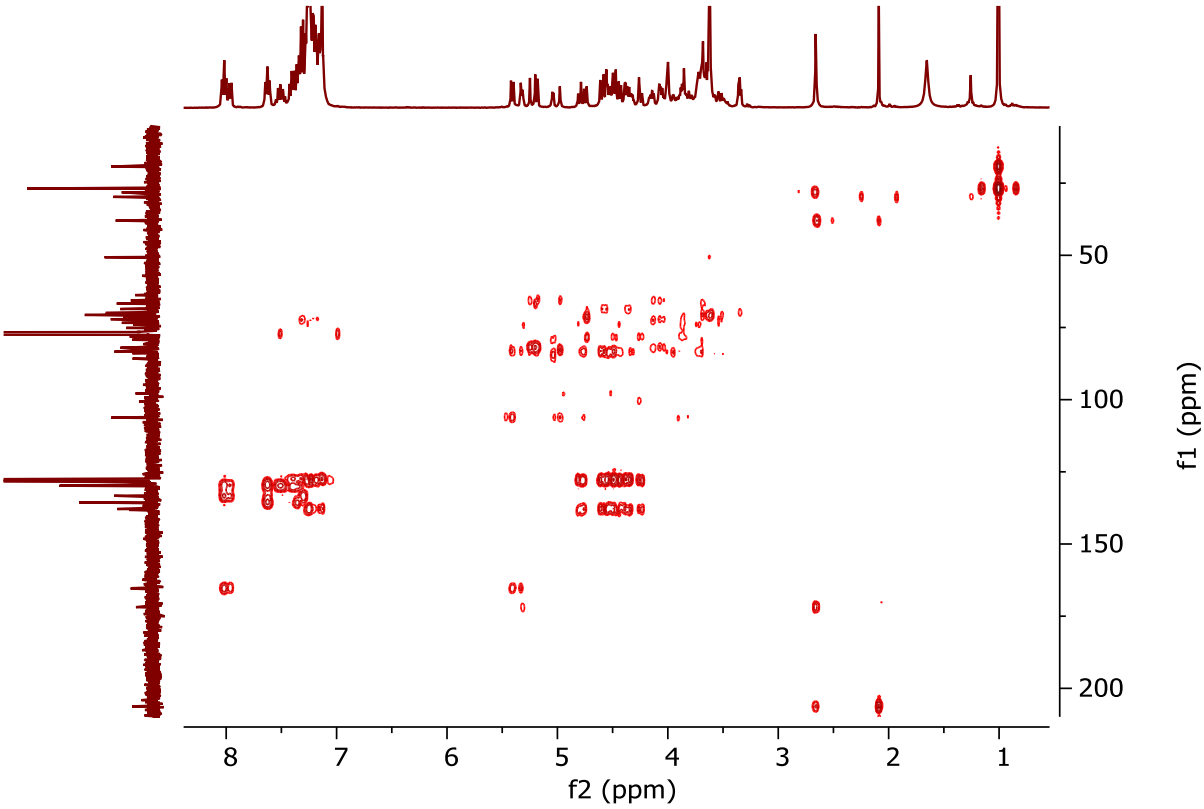

$^{1}H$, $^{13}C$-COSY NMR Spectrum (400, 101 MHz, $CDCl_3$) of Compound **38**



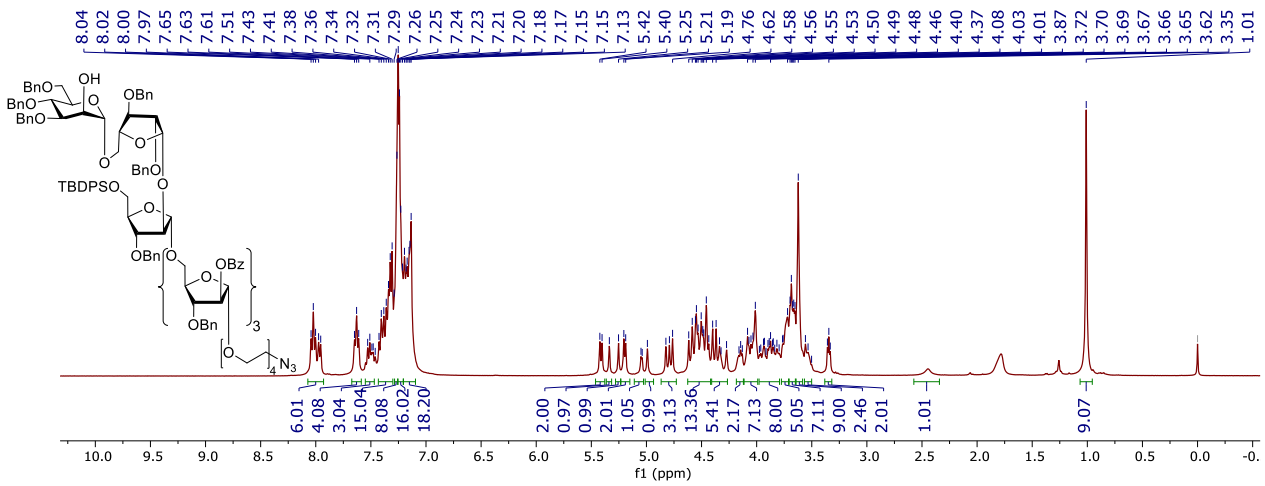
$^{1}H$, $^{13}C$-HSQC-Coupled NMR Spectrum (400, 101 MHz, $CDCl_3$) of Compound **38**



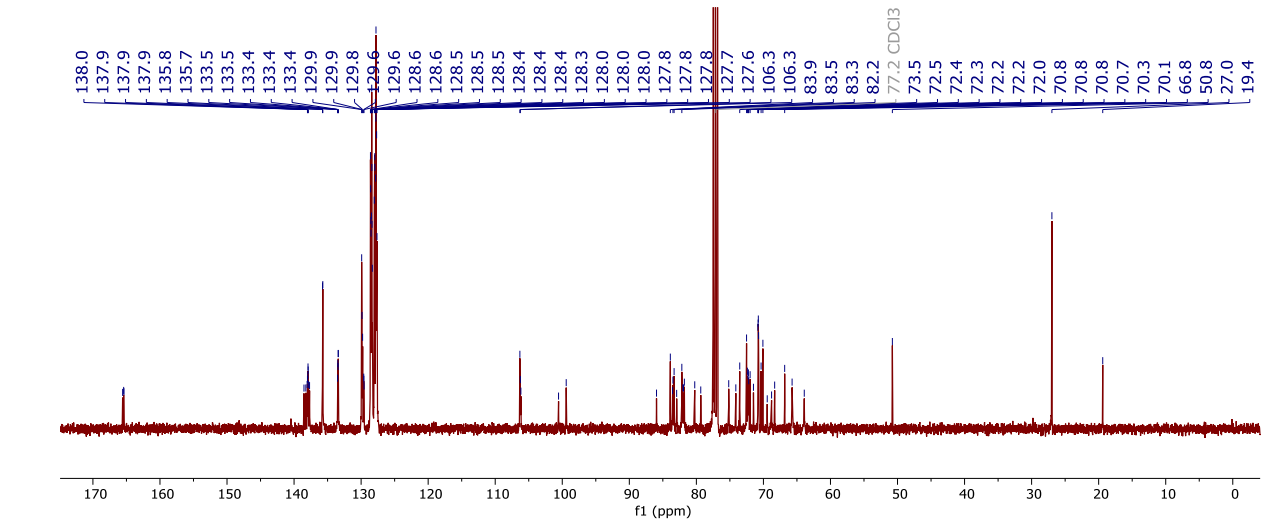

$^{1}H$, $^{13}C$-HMBC NMR Spectrum (400, 101 MHz, $CDCl_3$) of Compound **38**



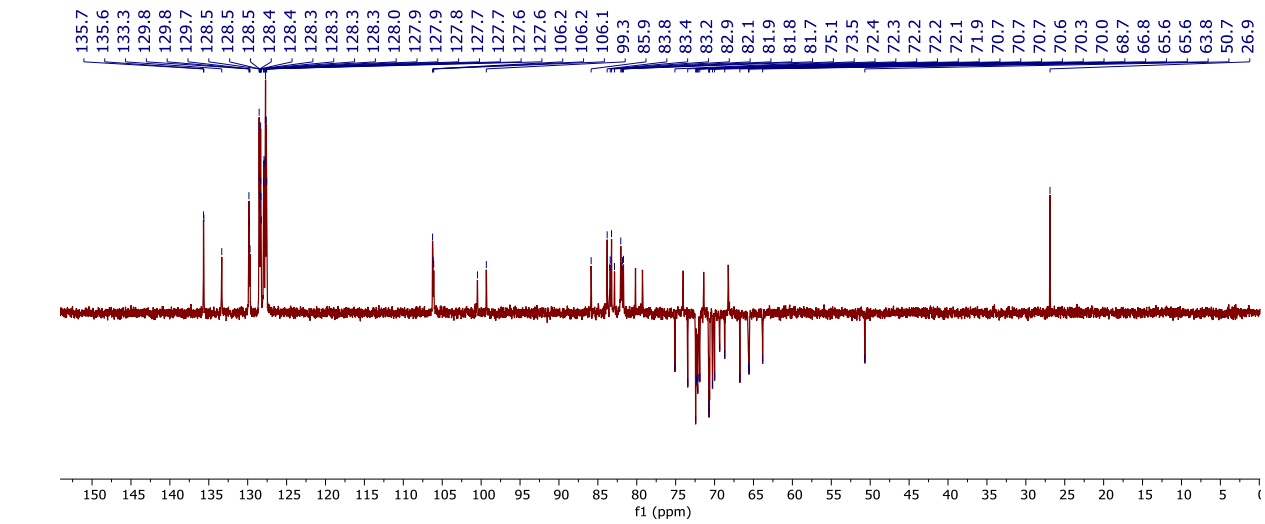
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **02**



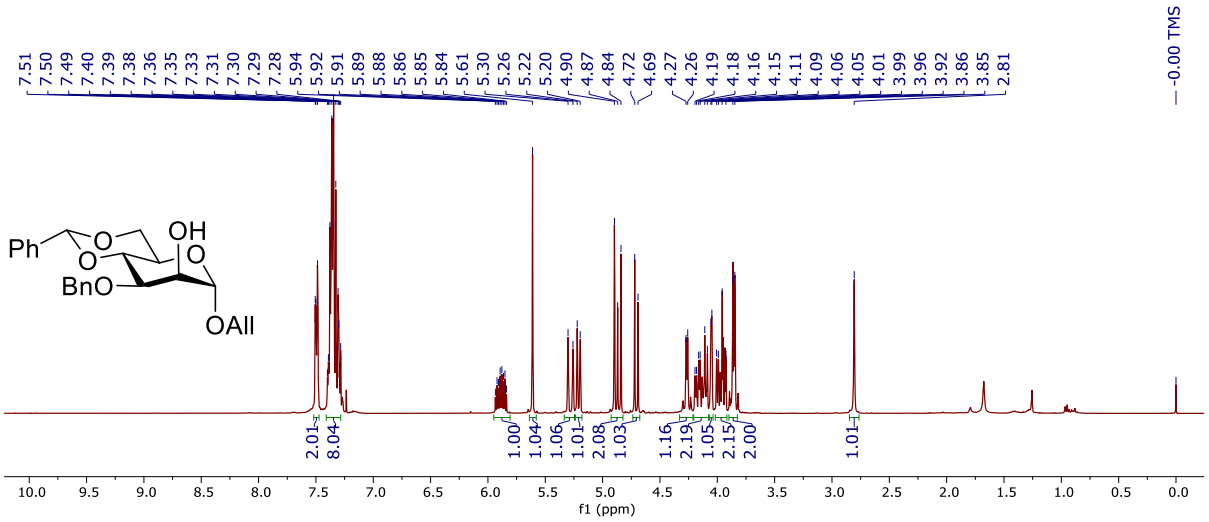

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **02**



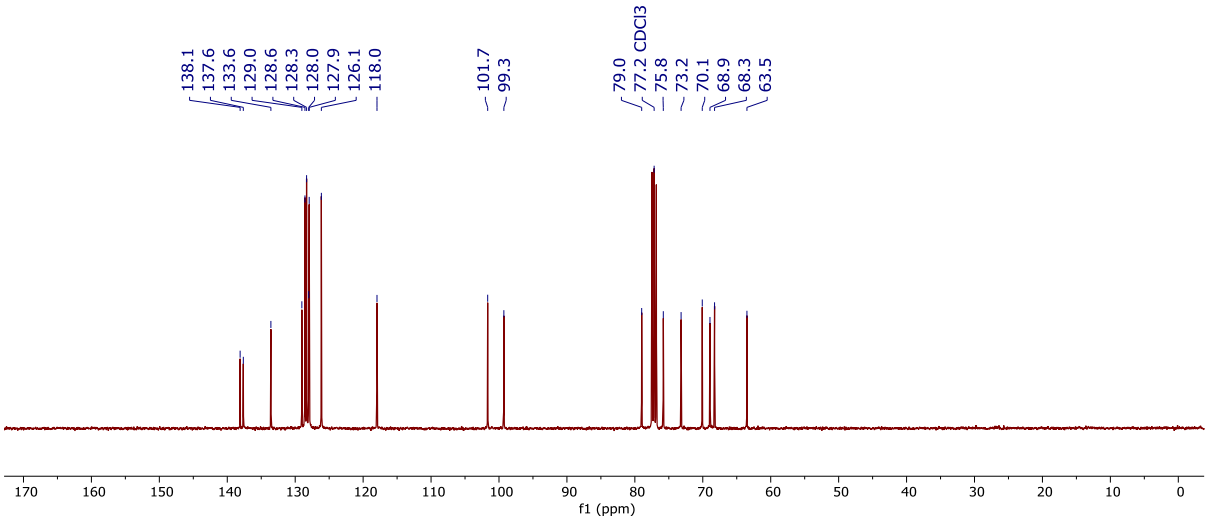

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **02**



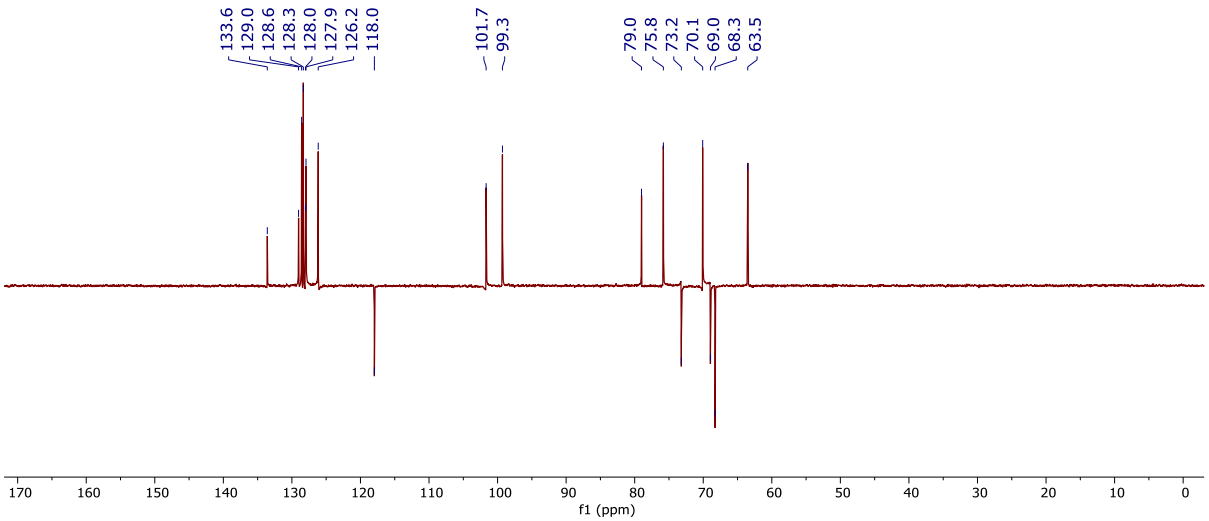
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **51**



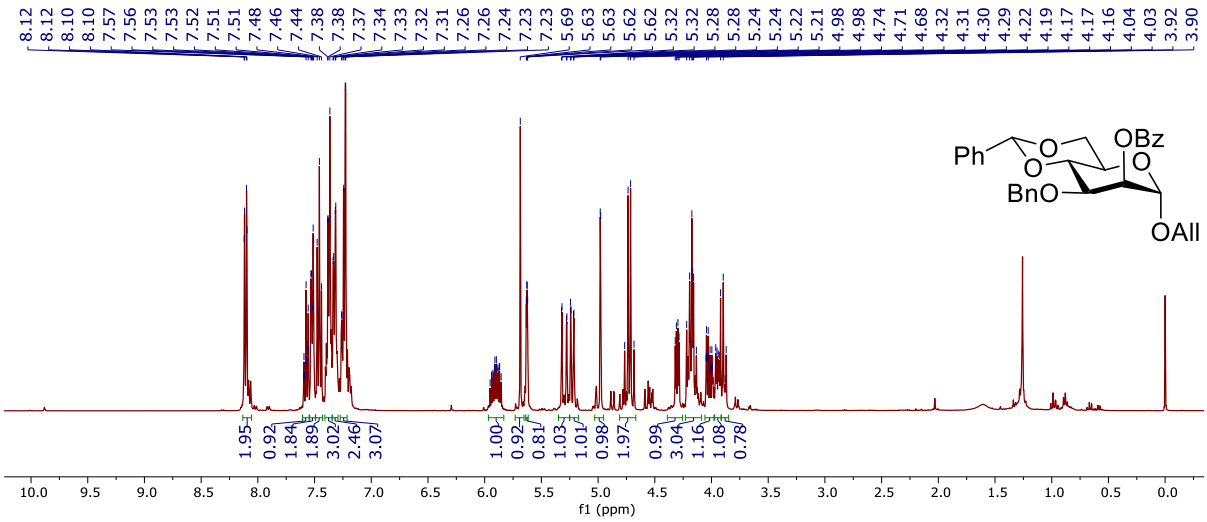

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **51**



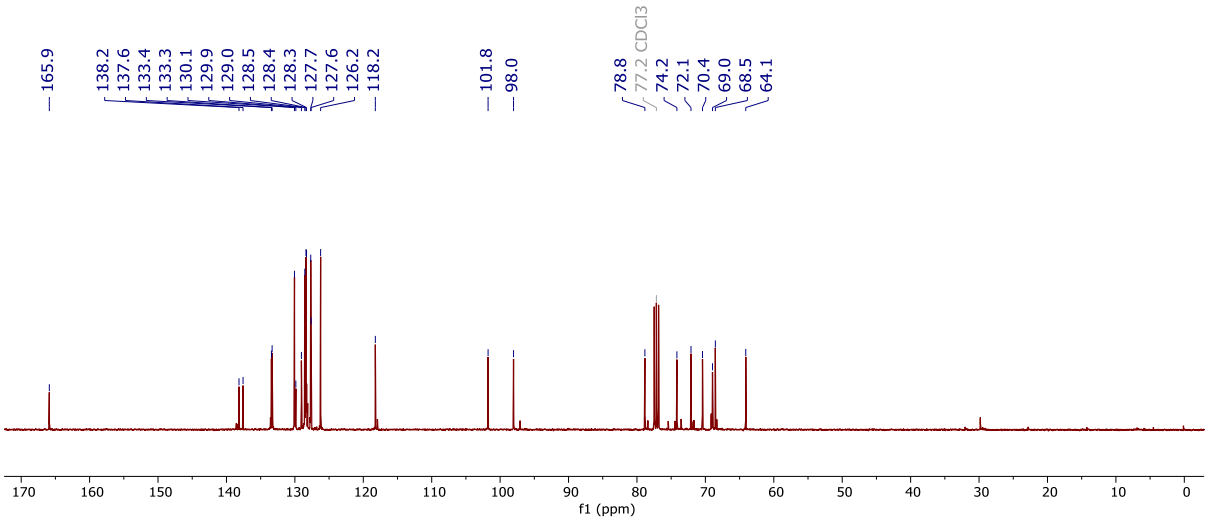

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **51**



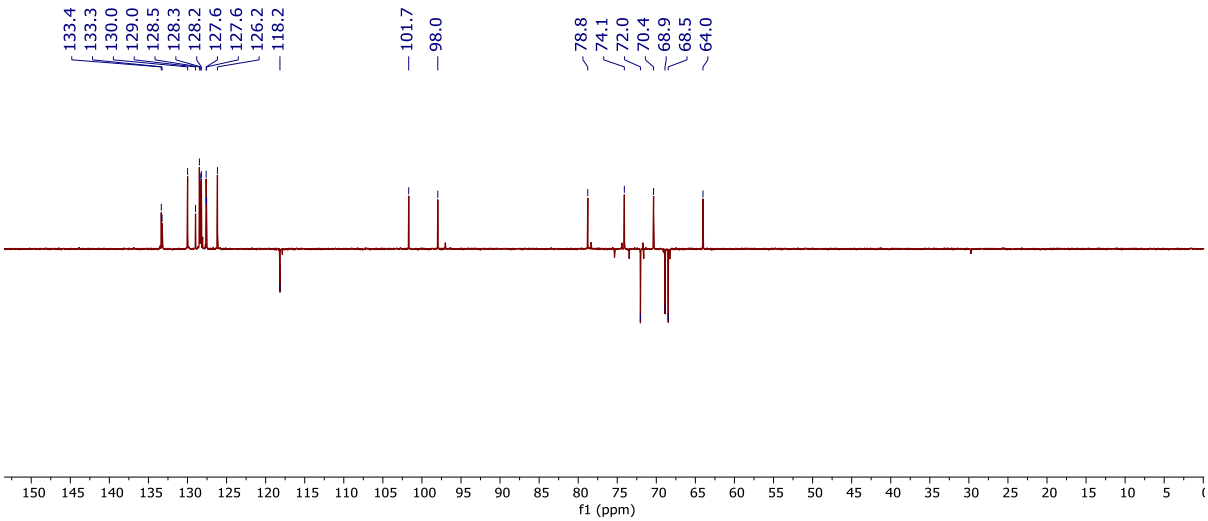
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **52**



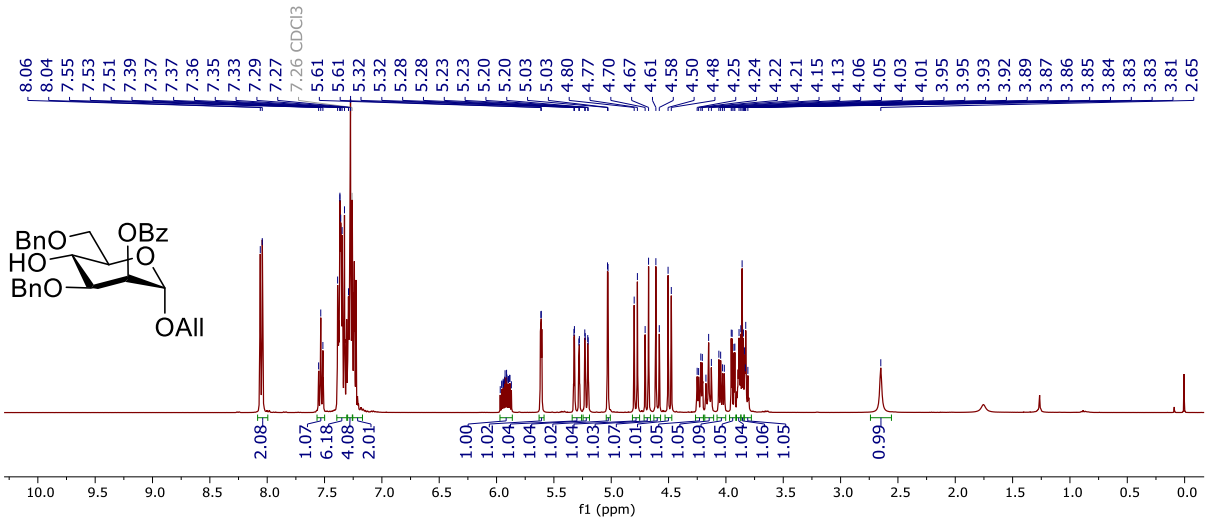

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **52**



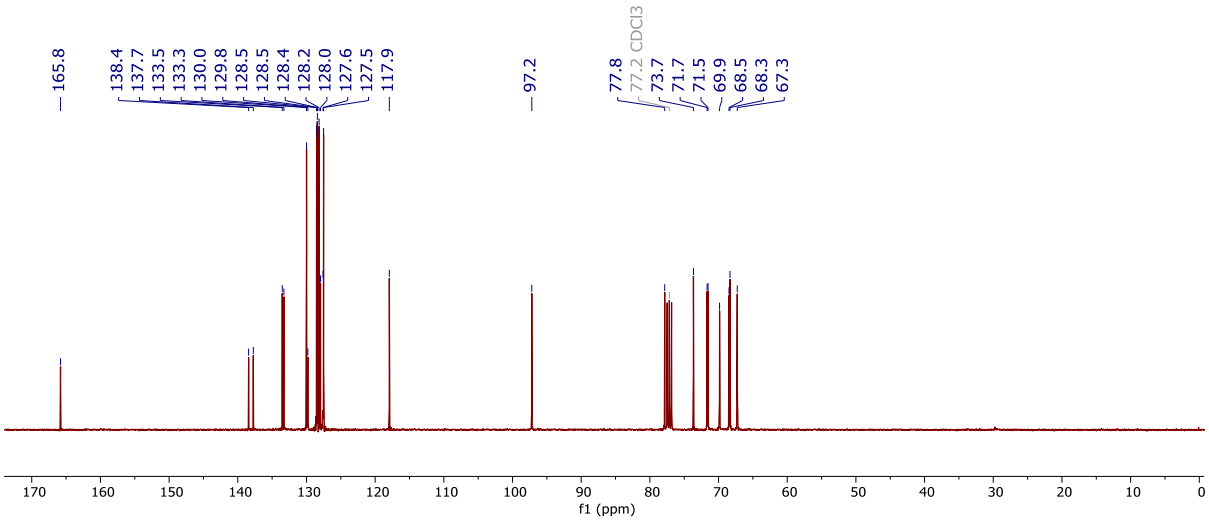

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **52**



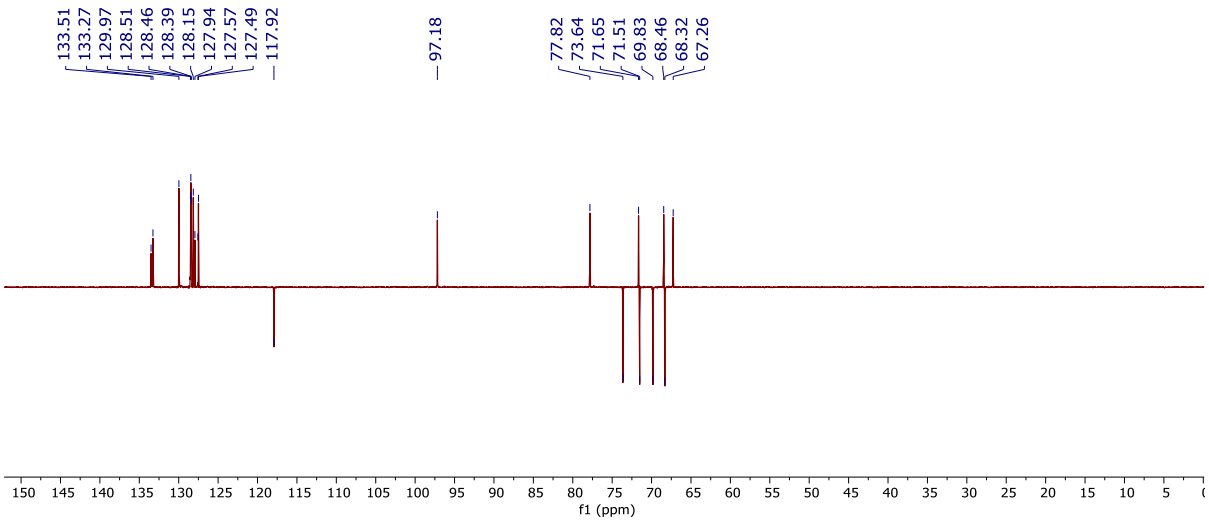
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **05**



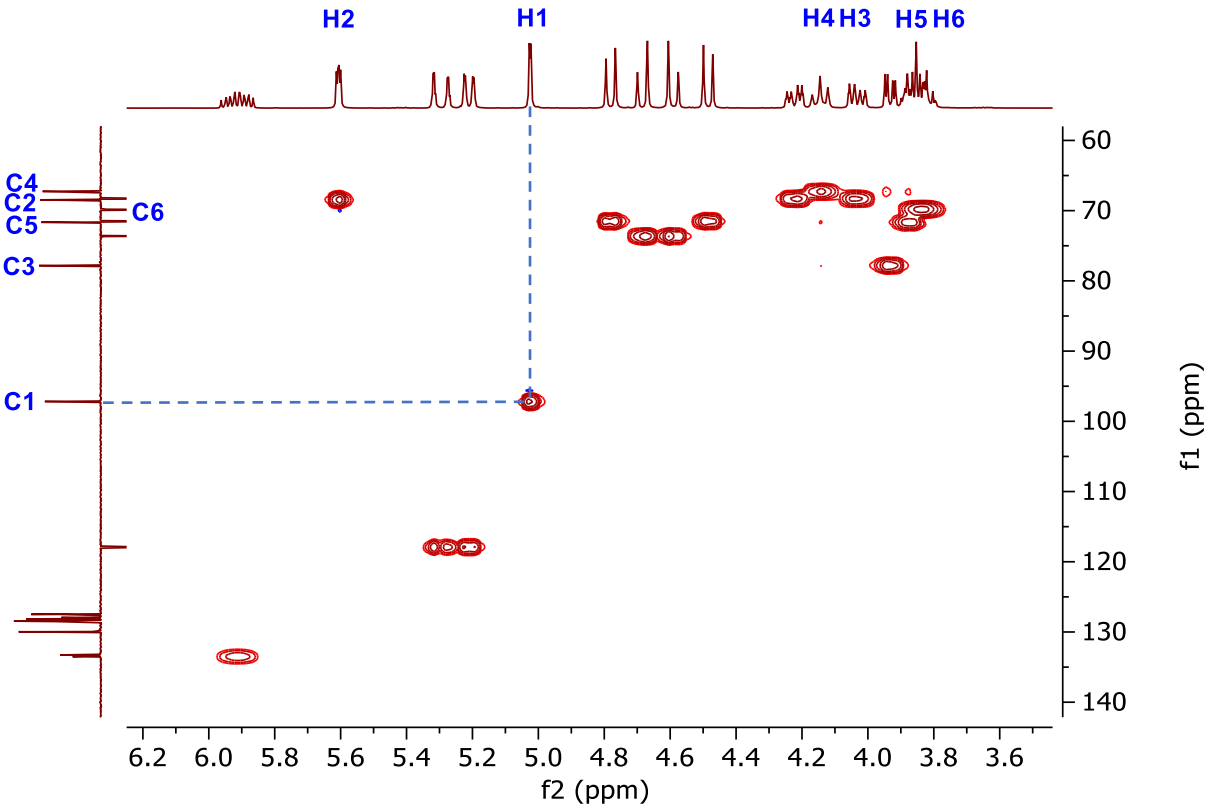

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **05**



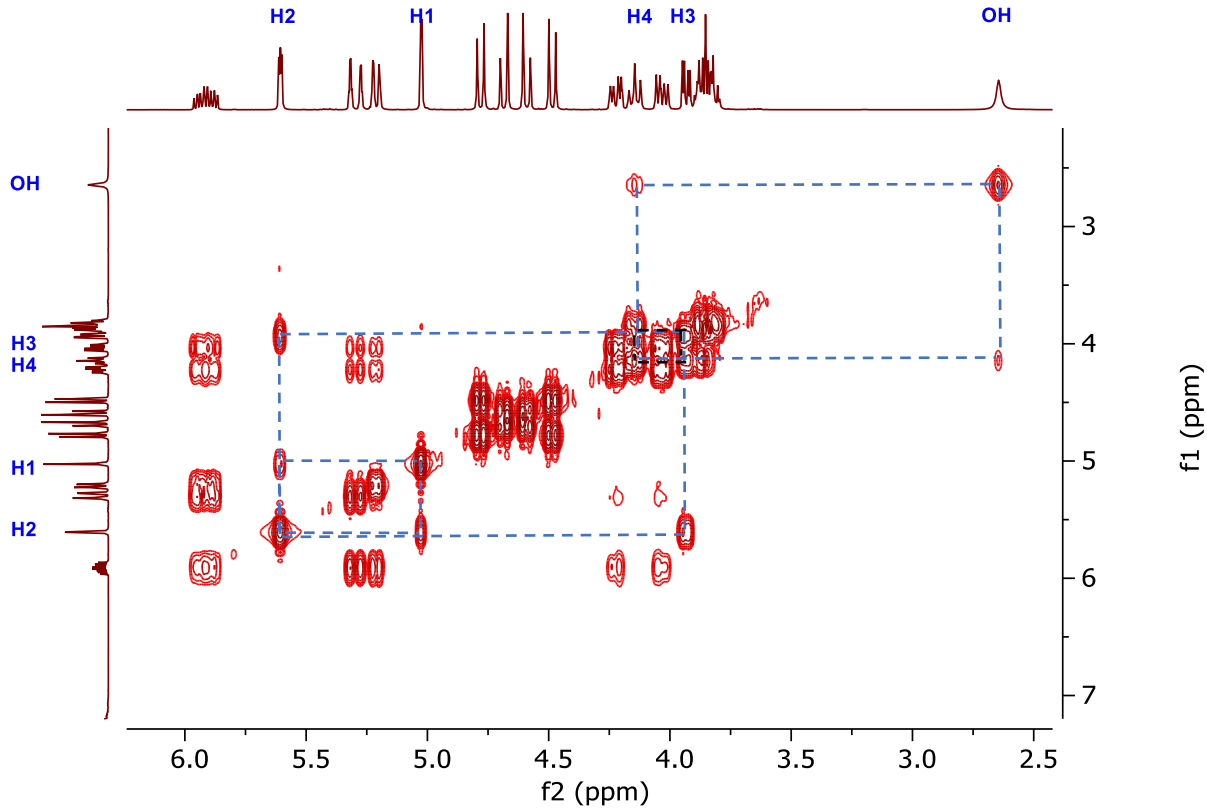

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **05**



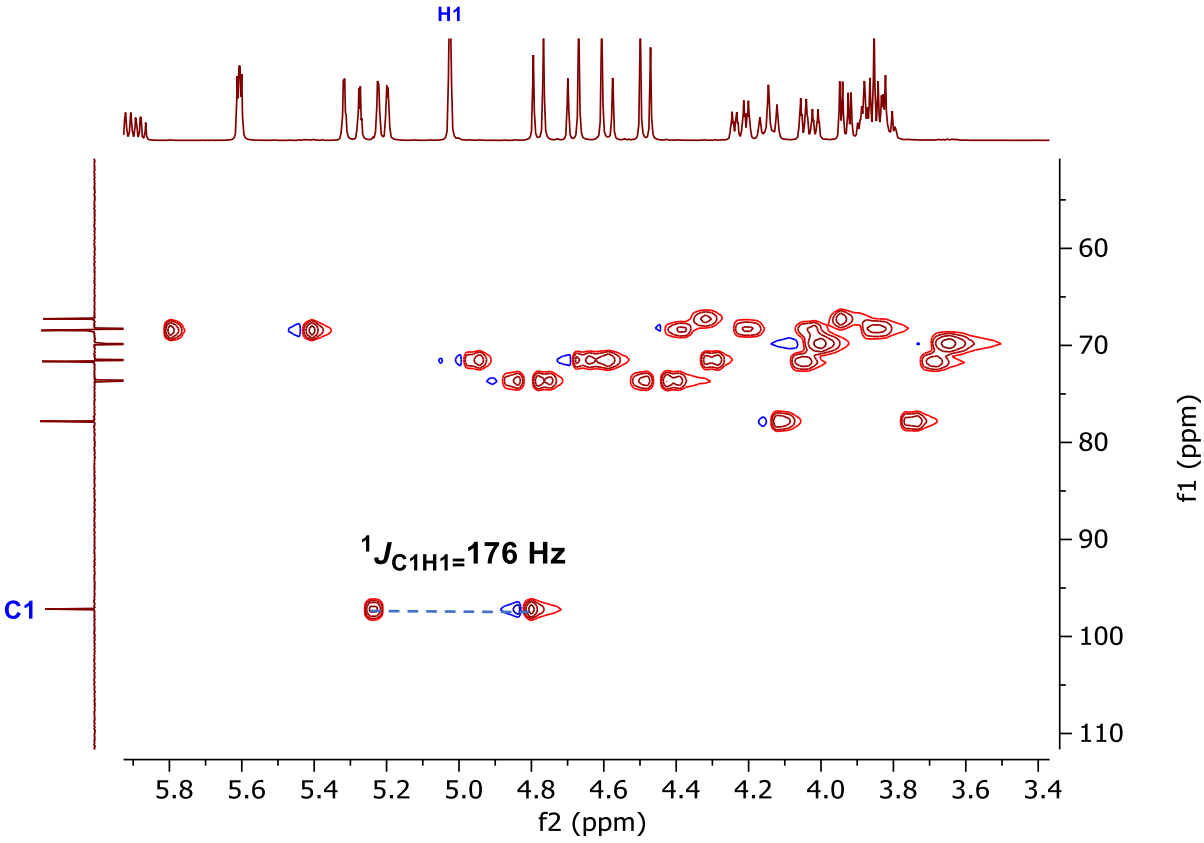
$^{1}H$, $^{13}C$-HSQC NMR Spectrum (400, 101 MHz, $CDCl_3$) of Compound **05**



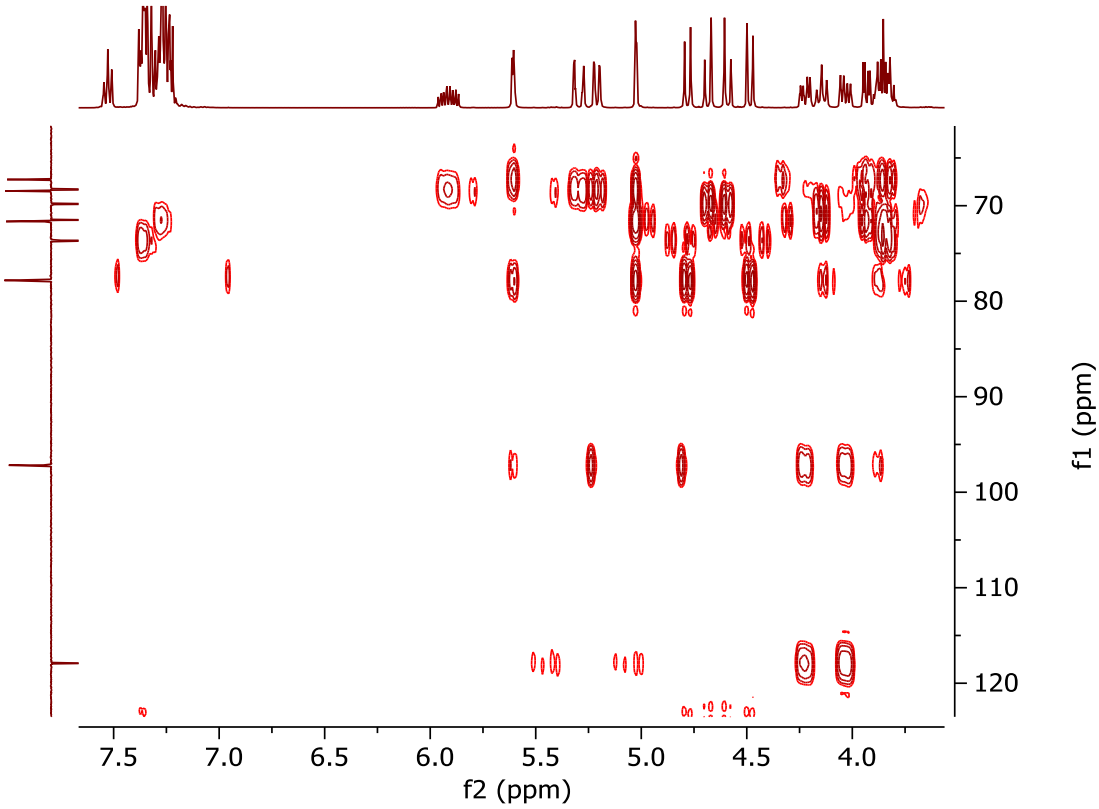

$^{1}H$, $^{13}C$-COSY NMR Spectrum (400, 101 MHz, $CDCl_3$) of Compound **05**



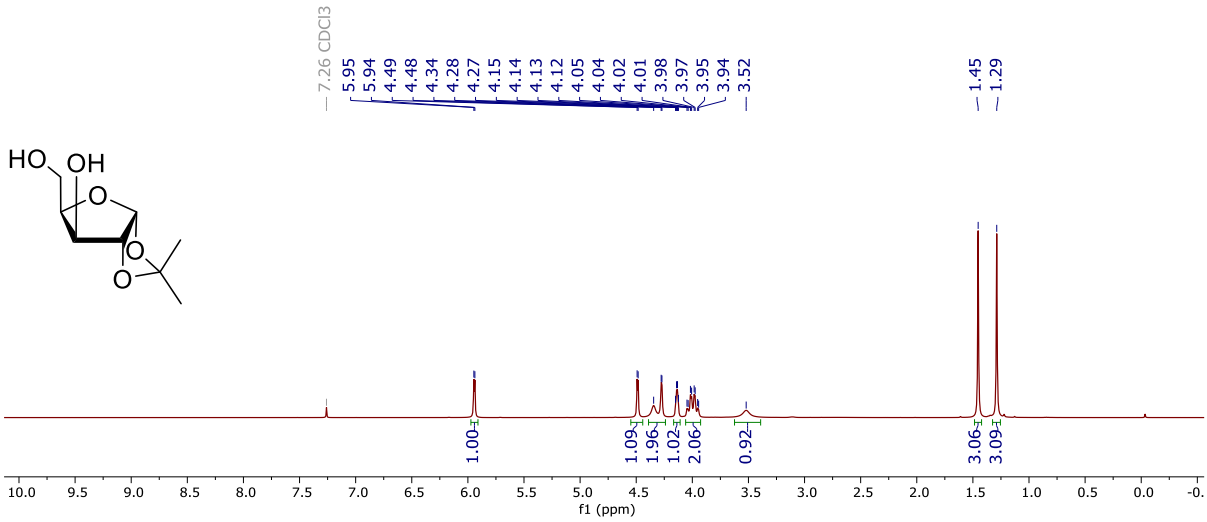
$^{1}$H, $^{13}$C-HSQC-Coupled NMR Spectrum (400, 101 MHz, $CDCl_3$) of Compound **05**



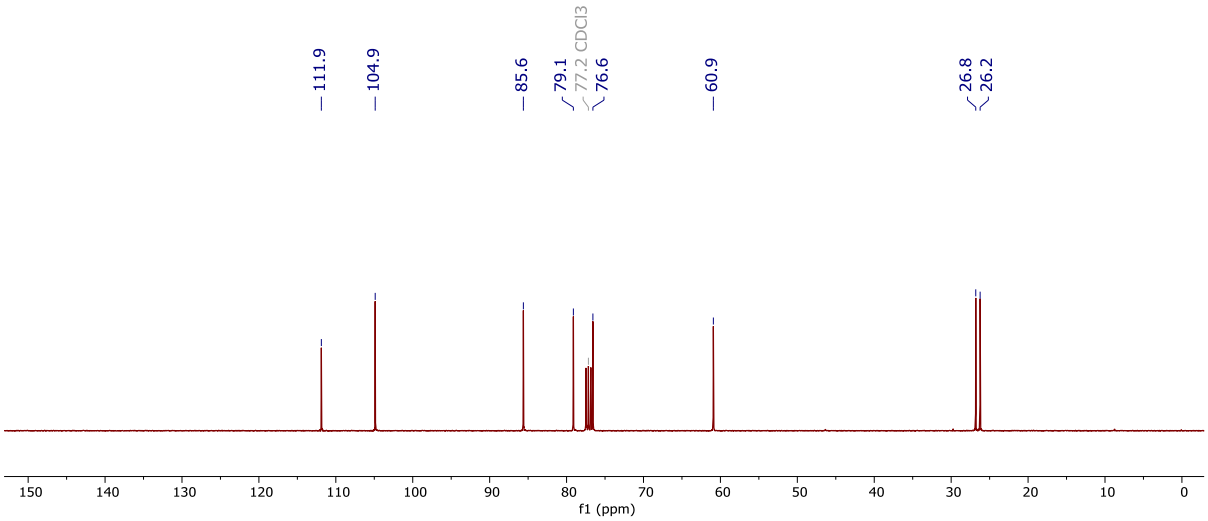

1H, $^{13}$C-HMBC NMR Spectrum (400, 101 MHz, $CDCl_3$) of Compound **05**



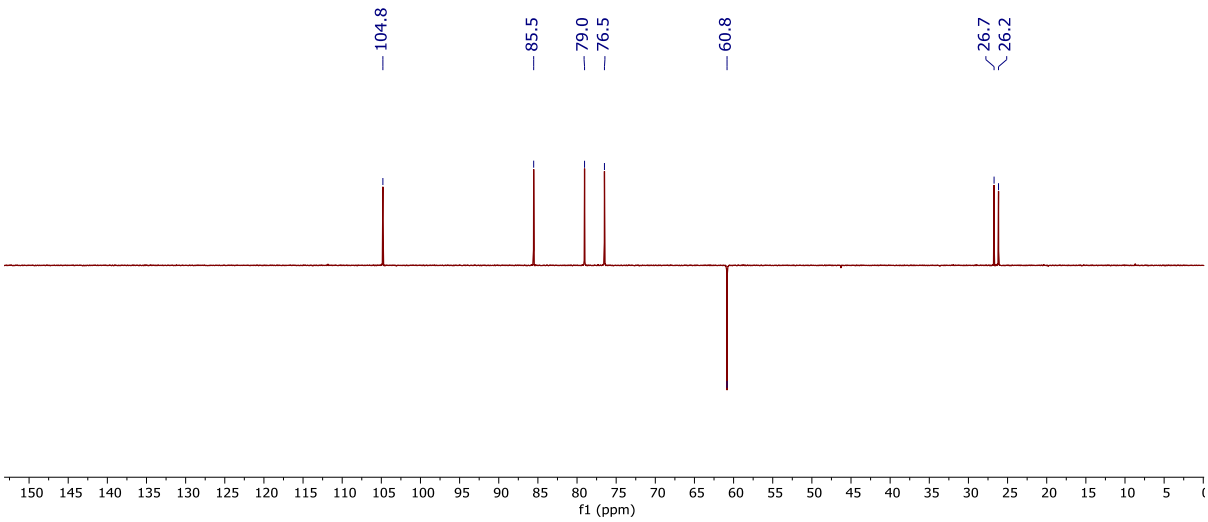
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **39**



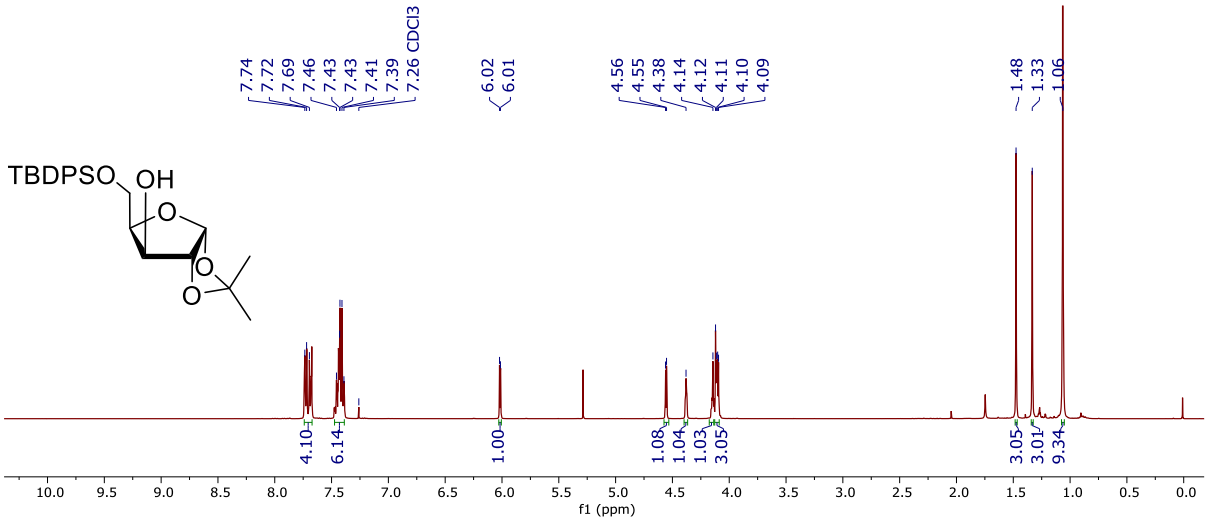

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **39**



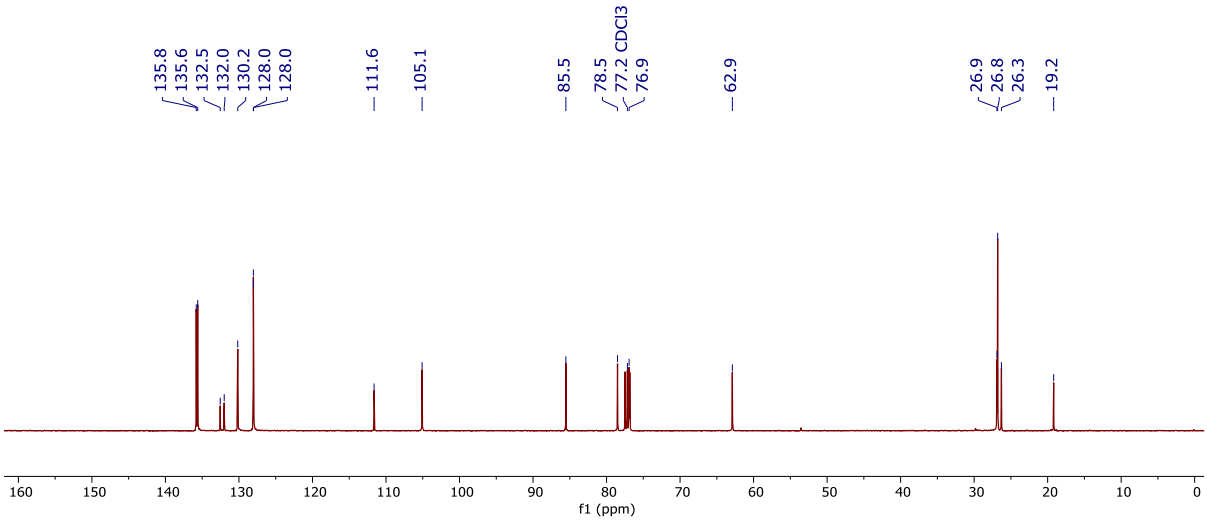

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **39**



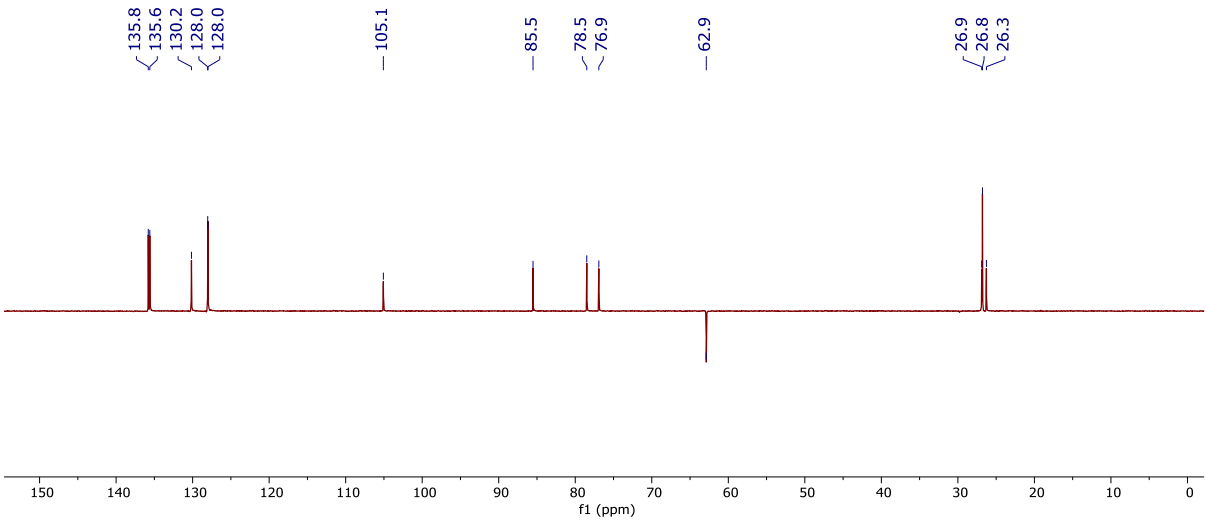
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **40**



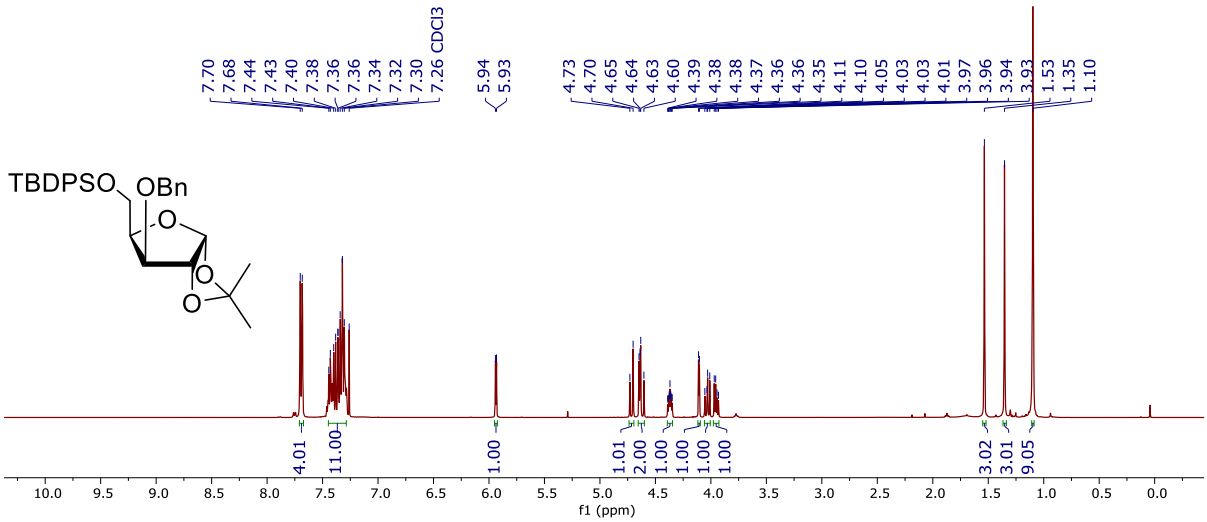

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **40**



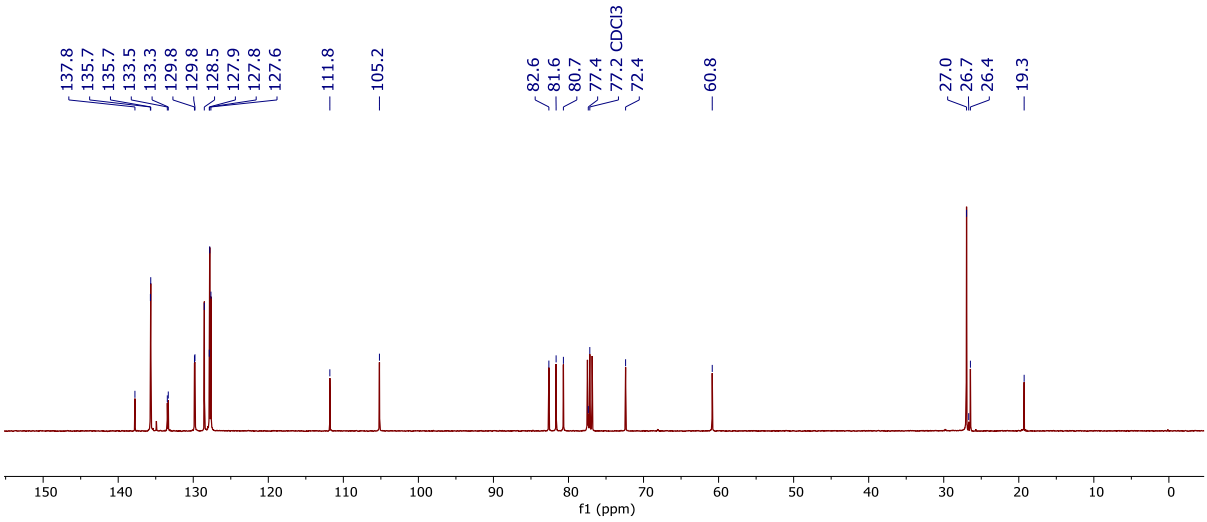

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **40**



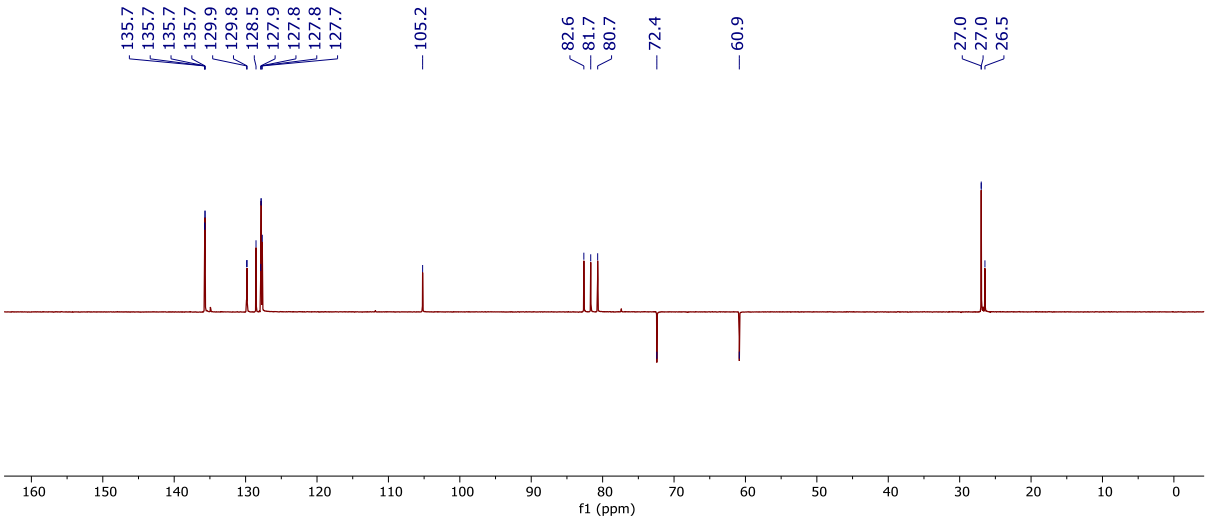
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **41**



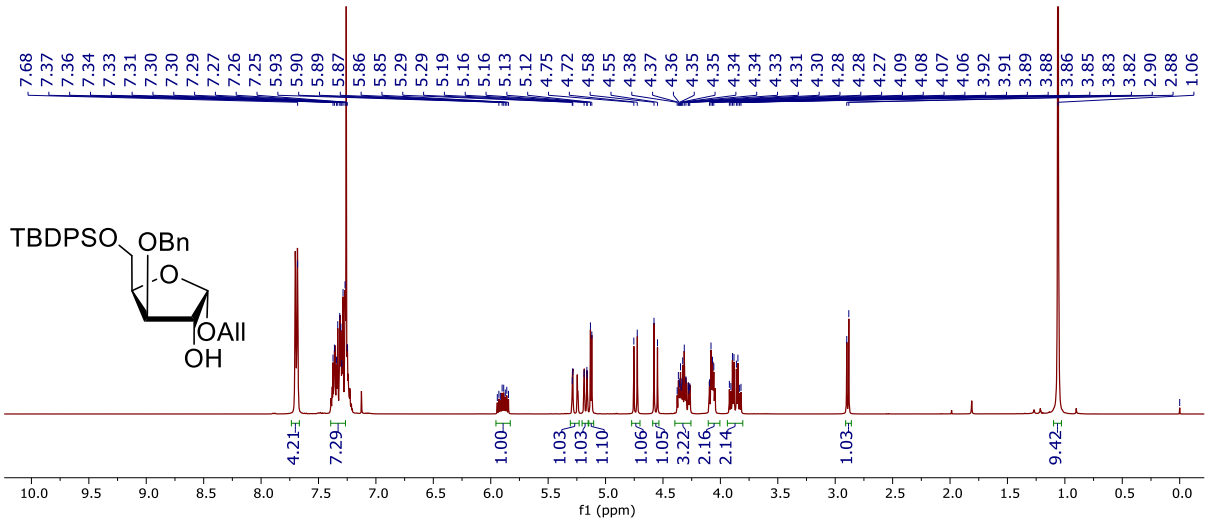

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **41**



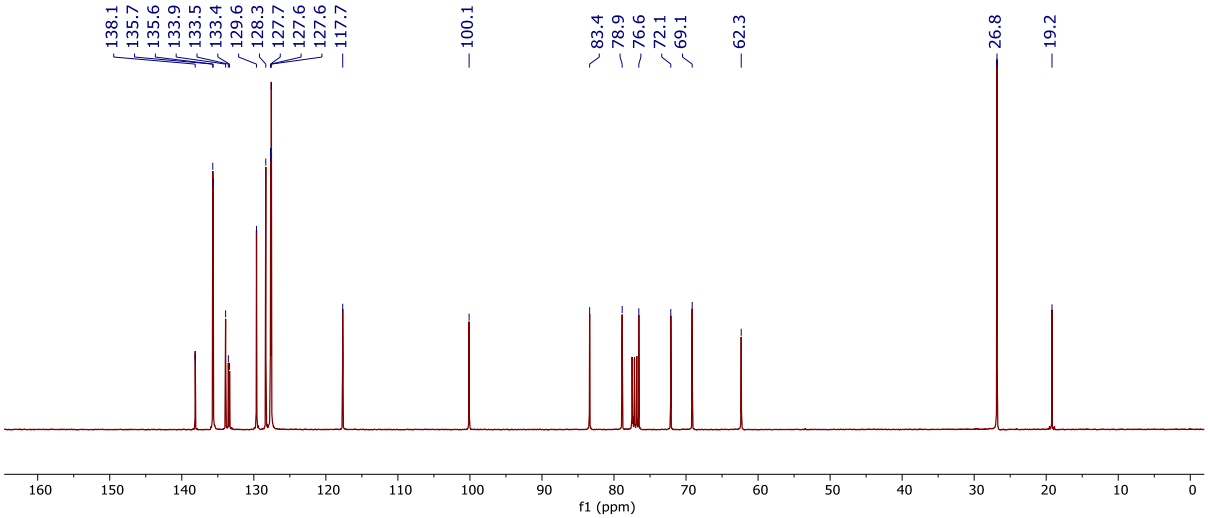

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **41**



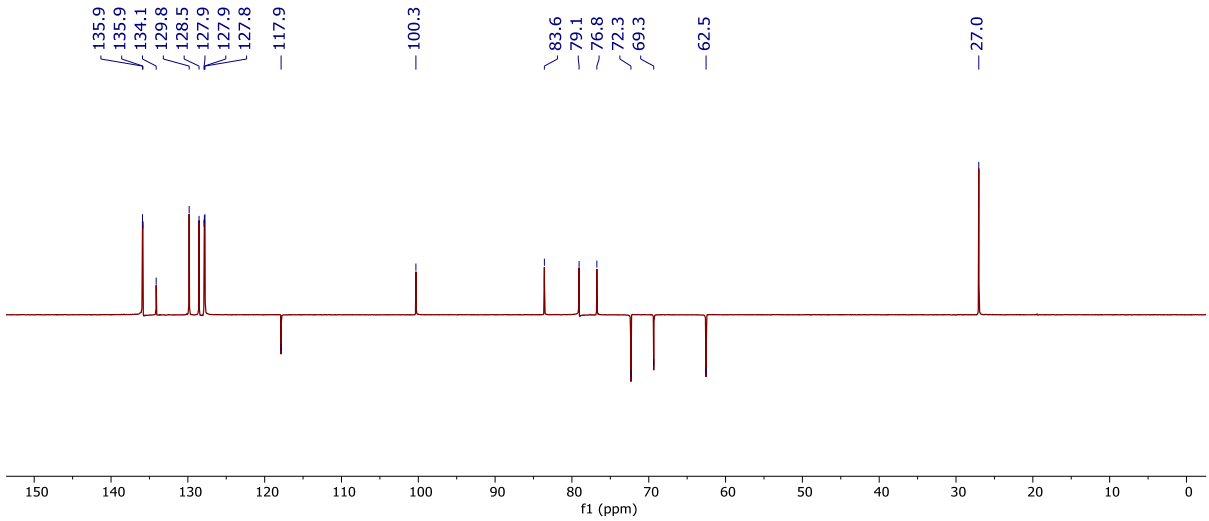
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **42**



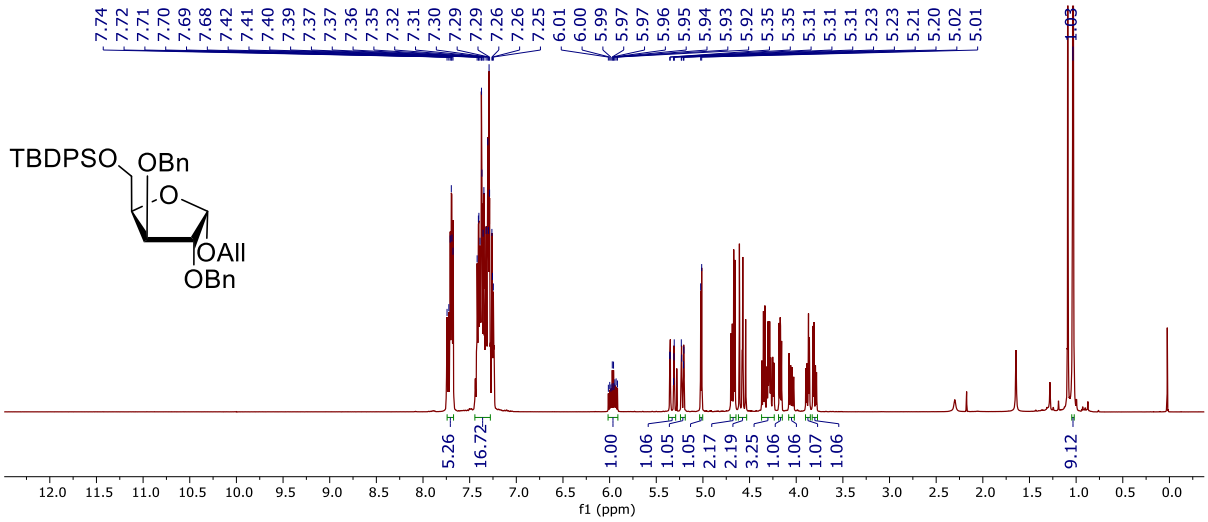

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **42**



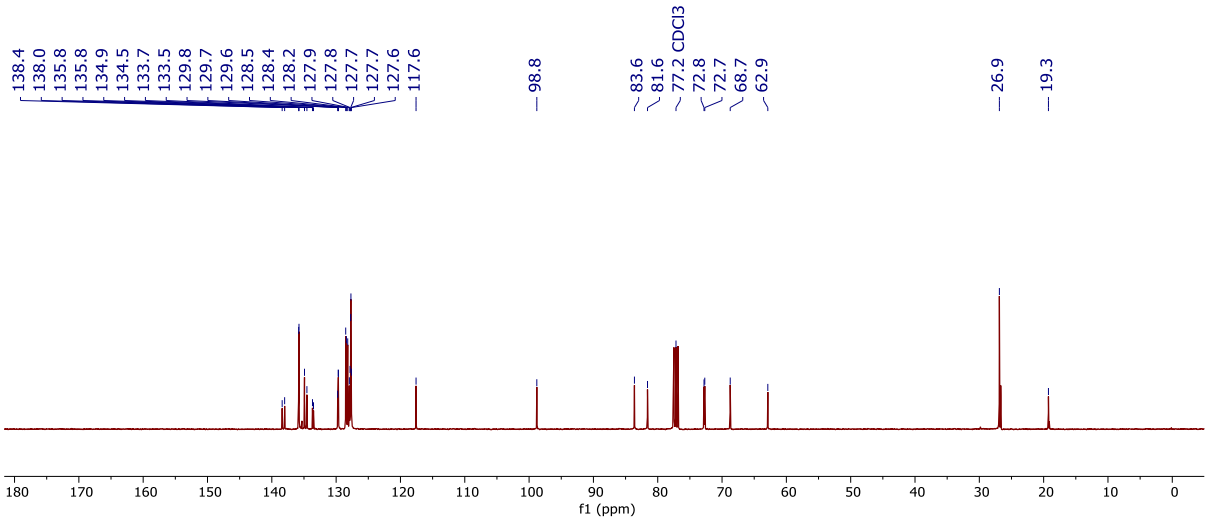

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **42**



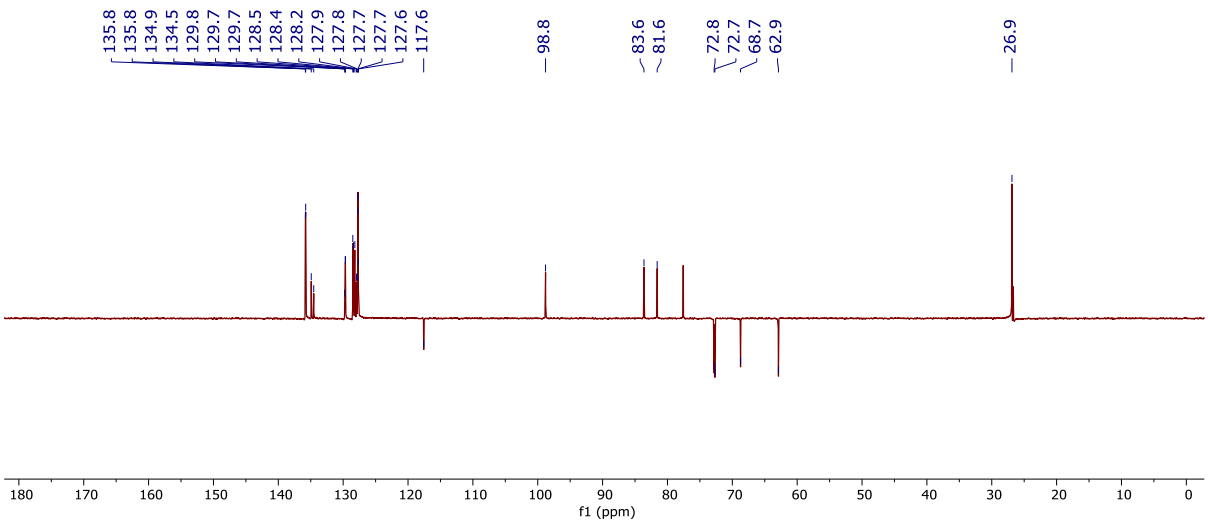
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **43**



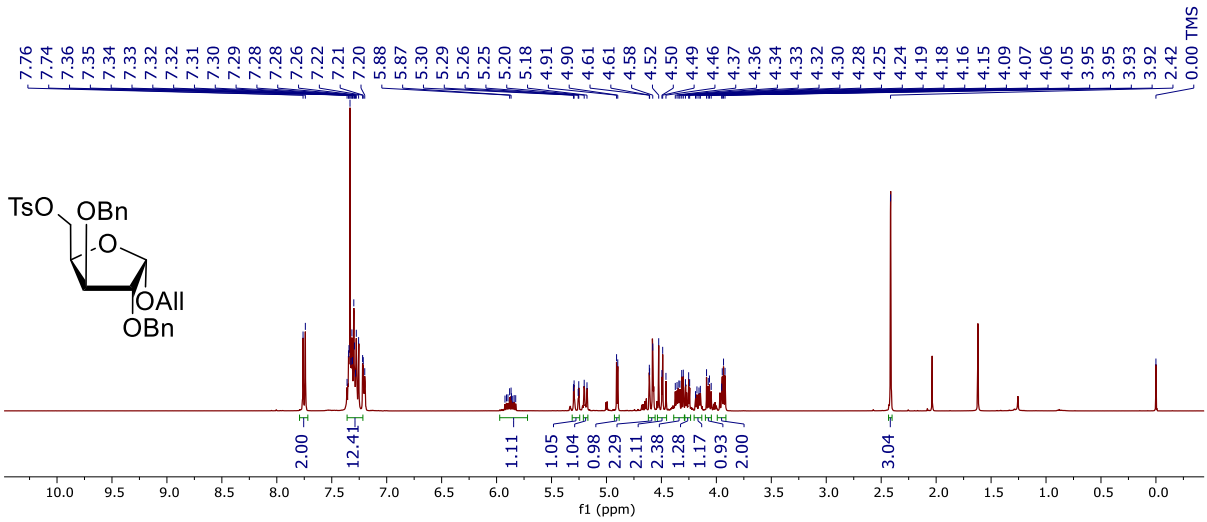

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **43**



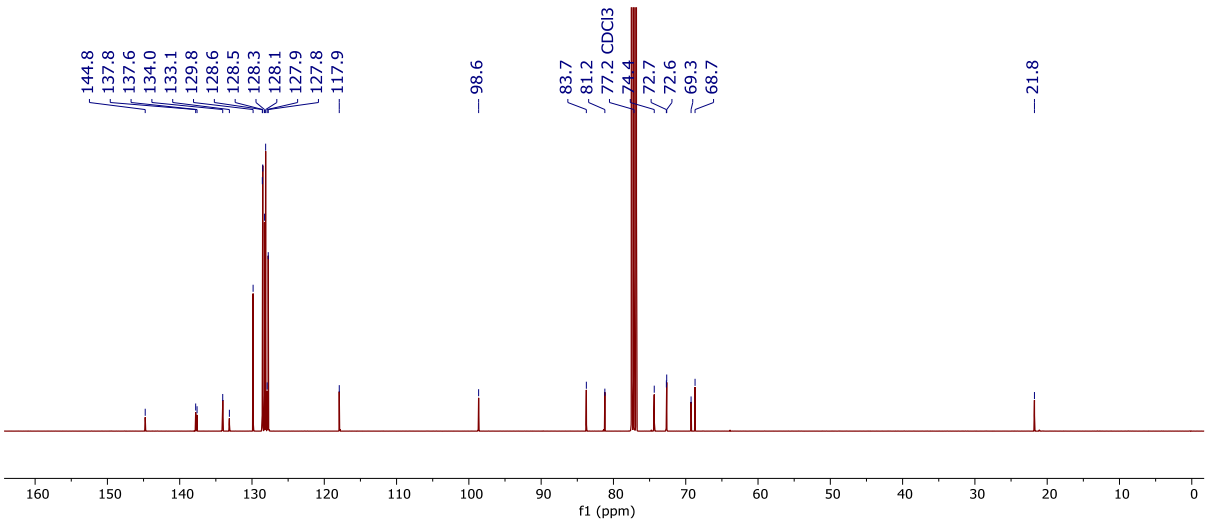

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **43**



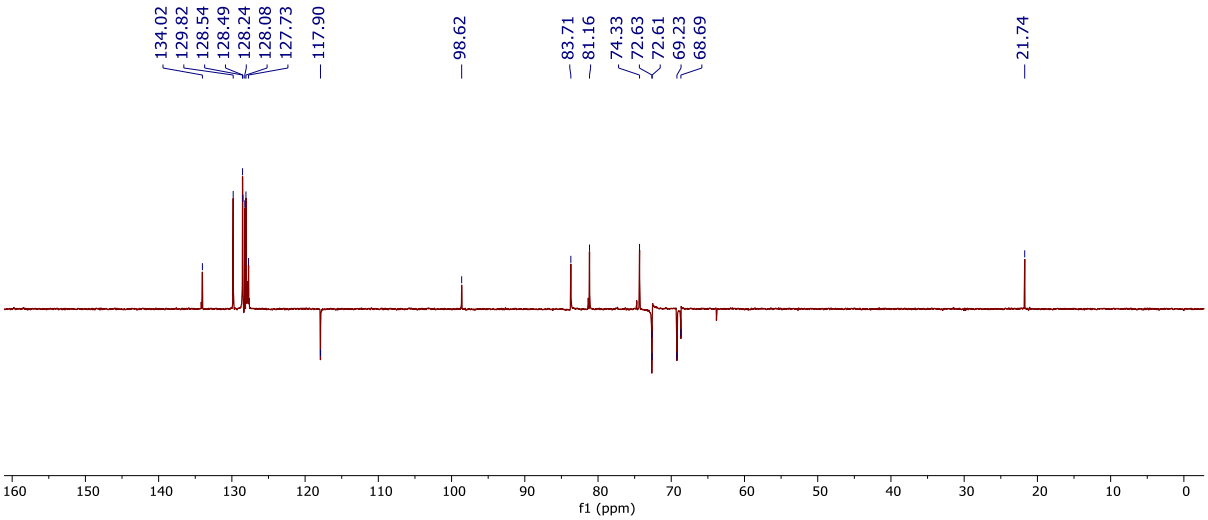
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **44**



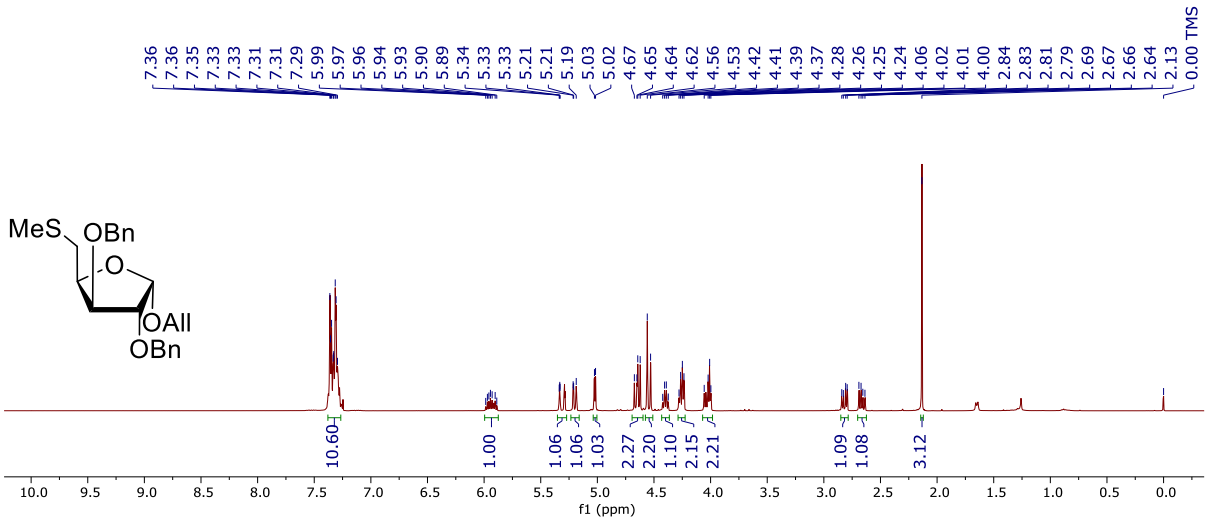

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **44**



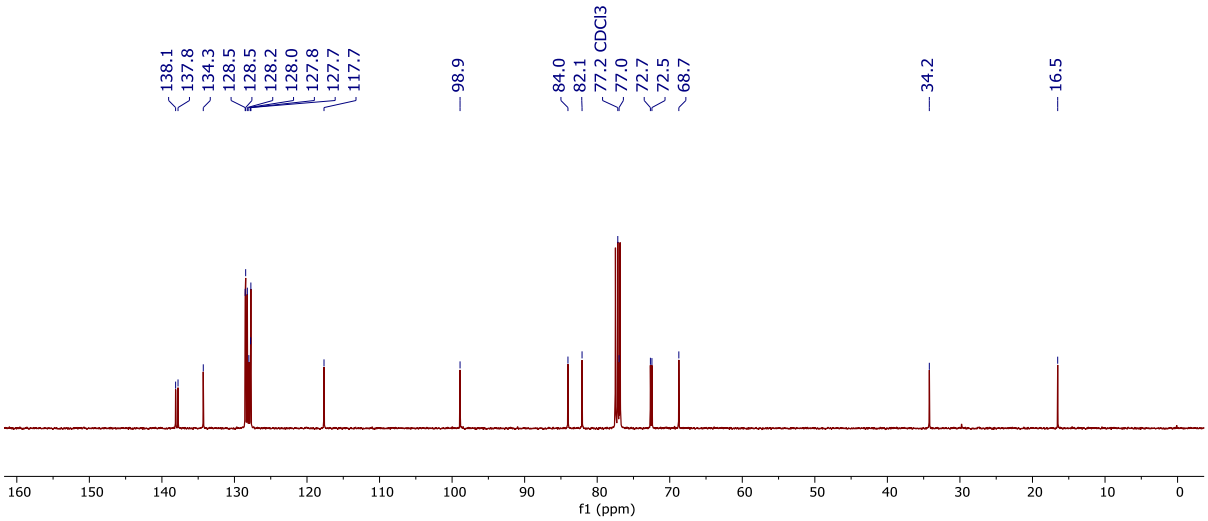

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **44**



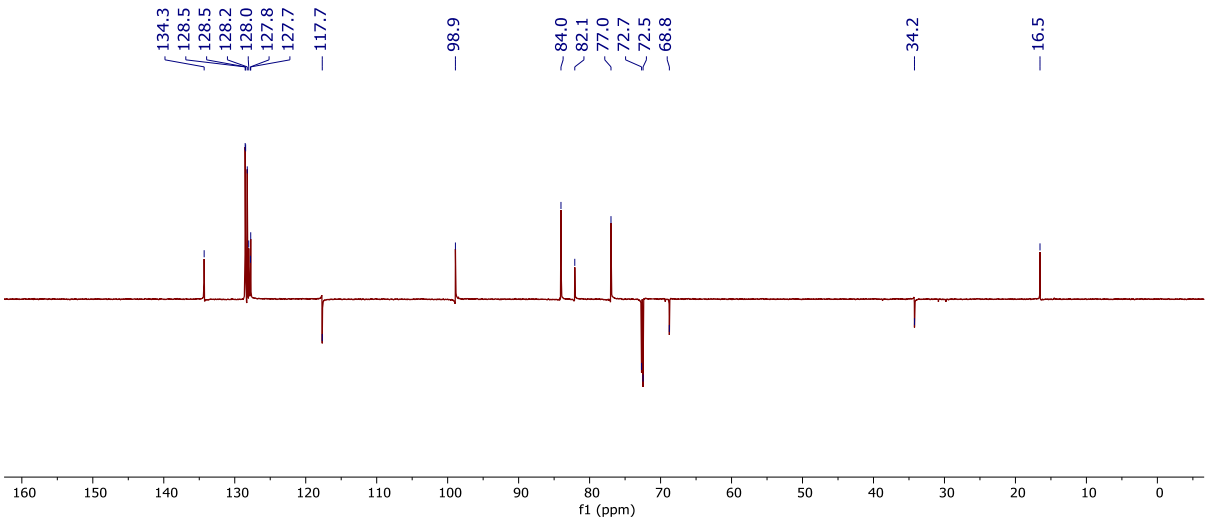
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **45**



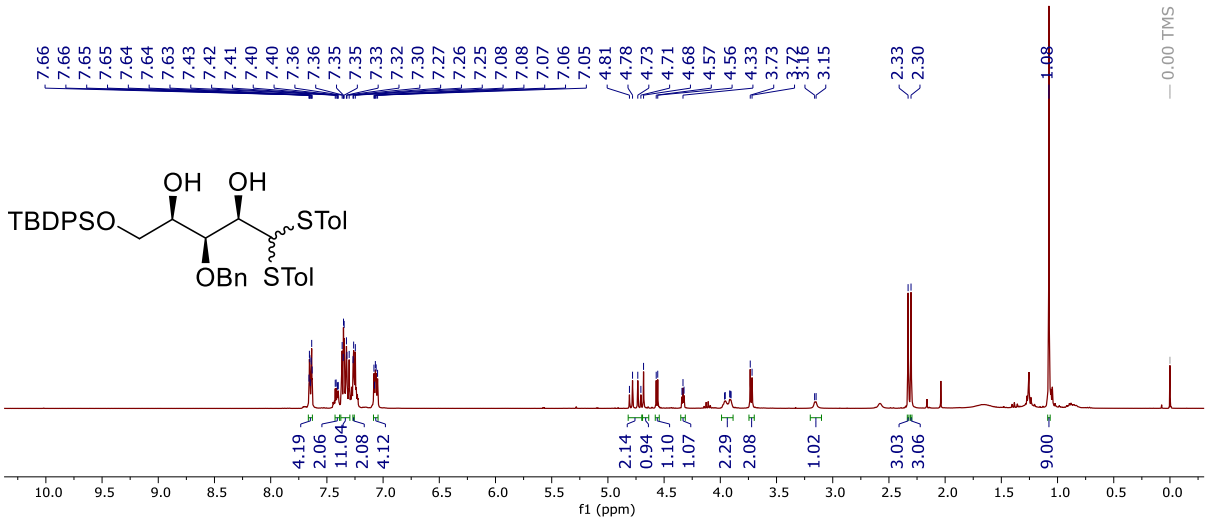

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **45**



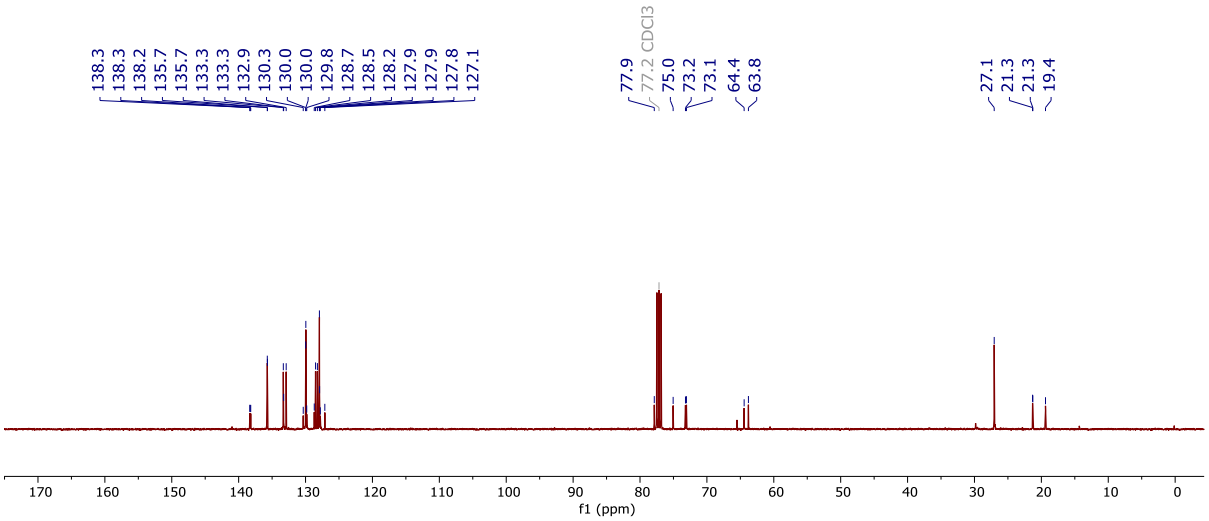

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **45**



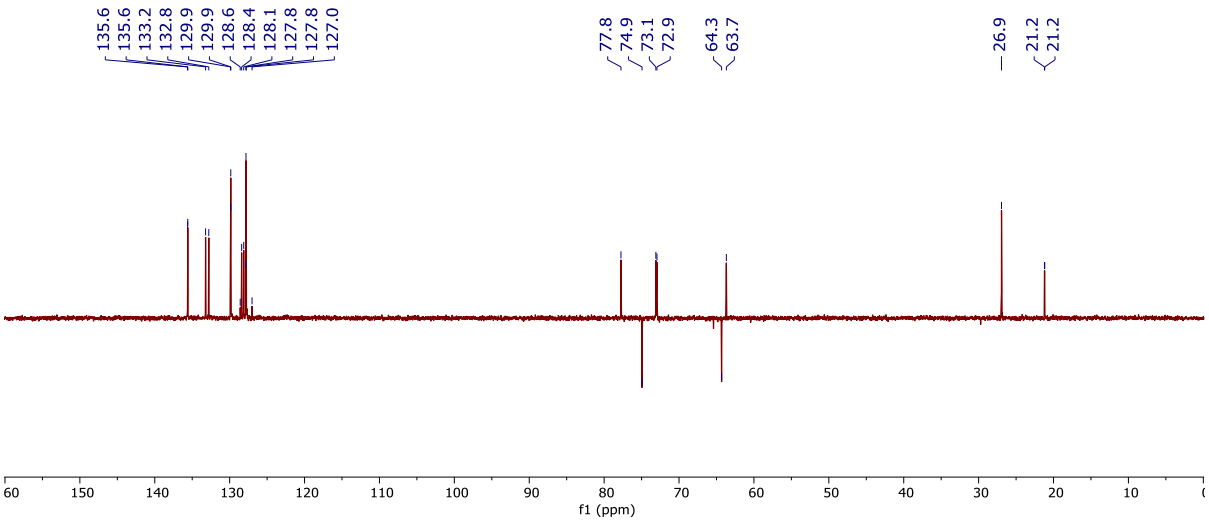
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **46**



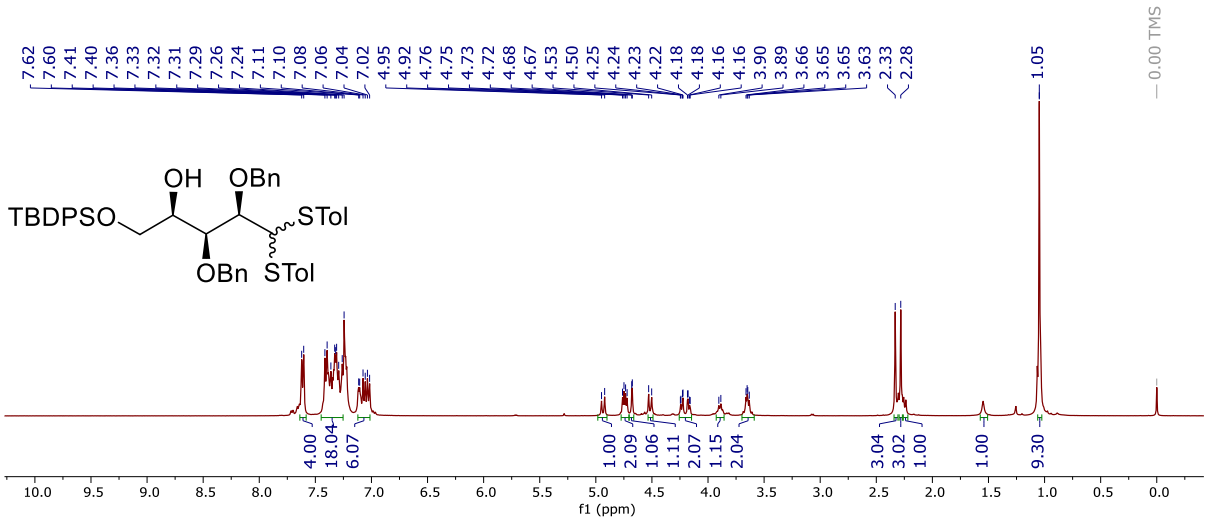

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **46**



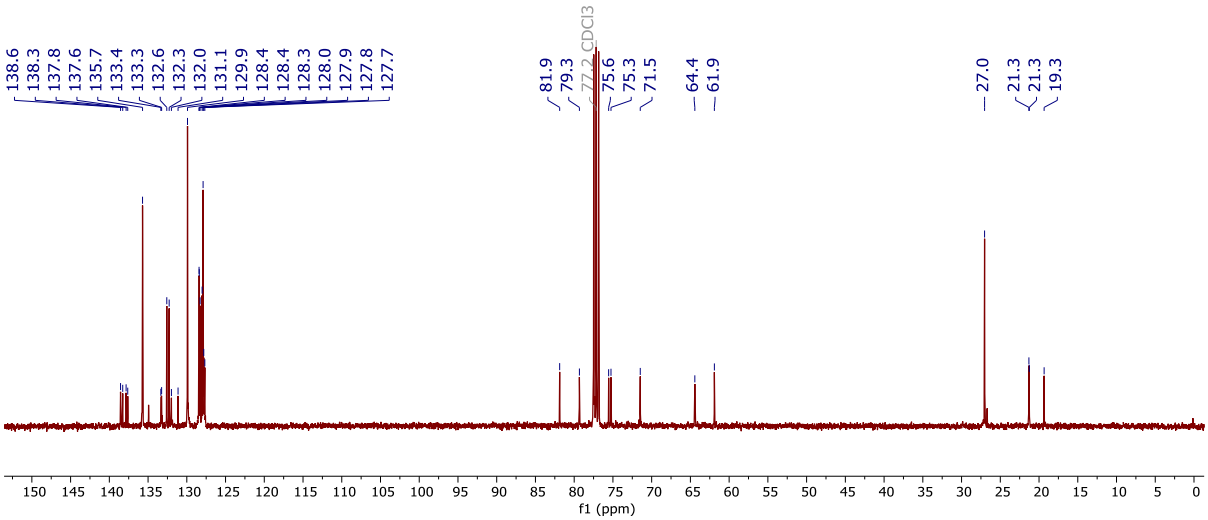

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **46**



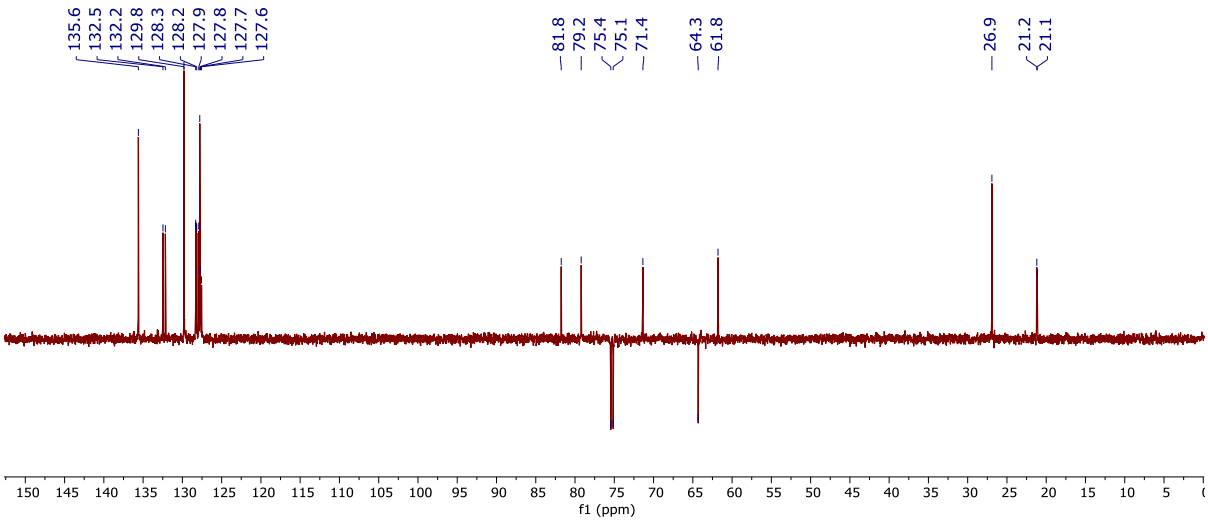
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **47**



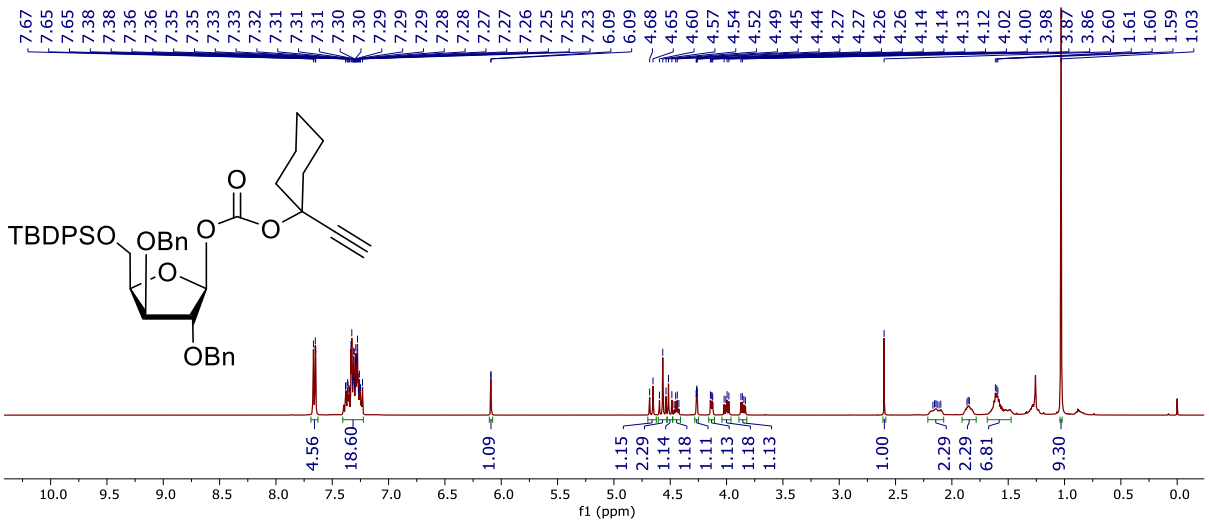

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **47**



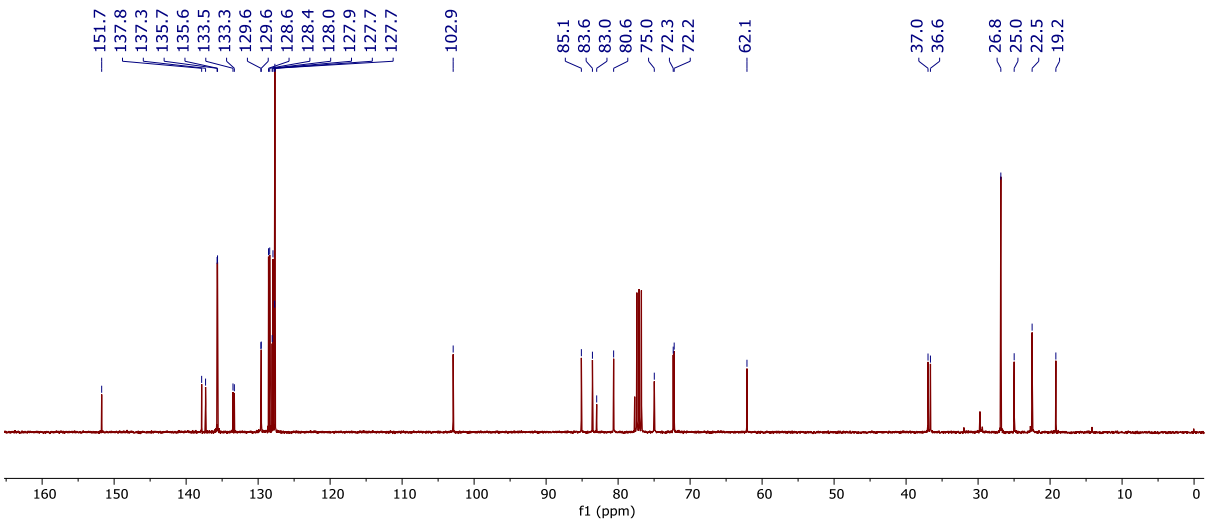

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **47**



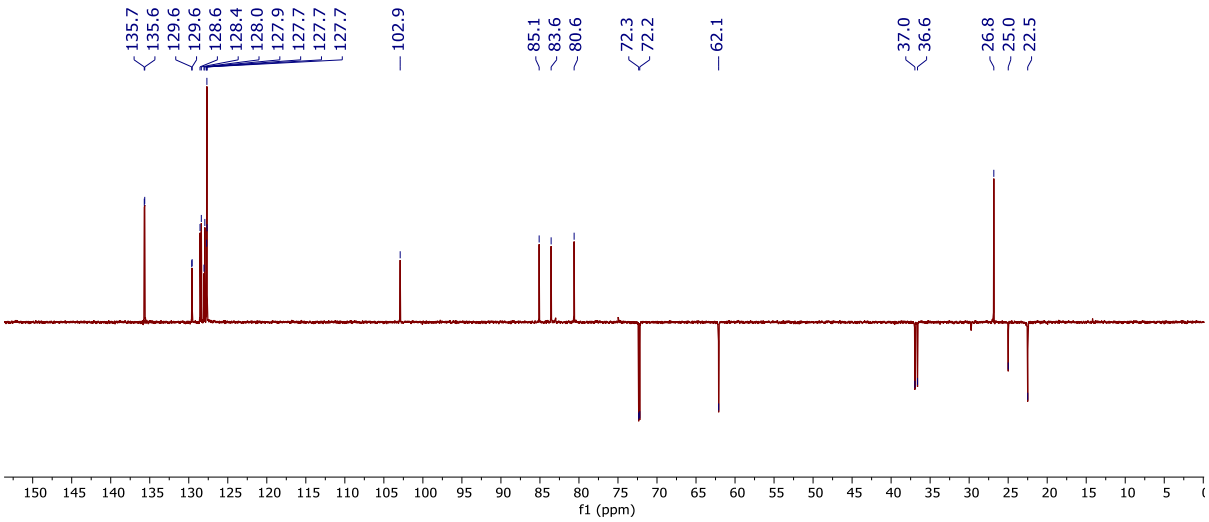
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **48**



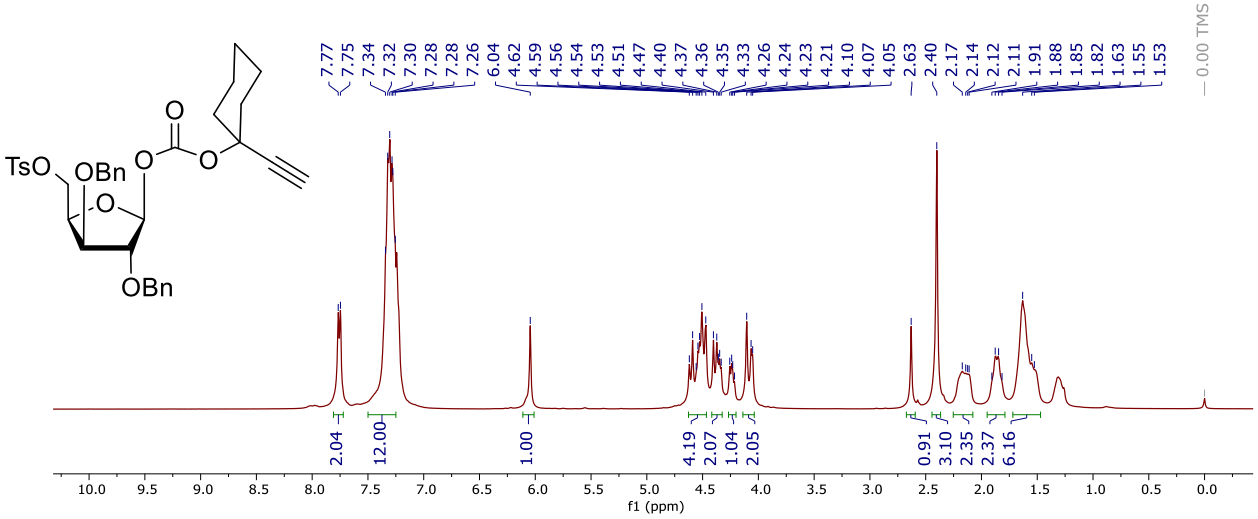

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **48**



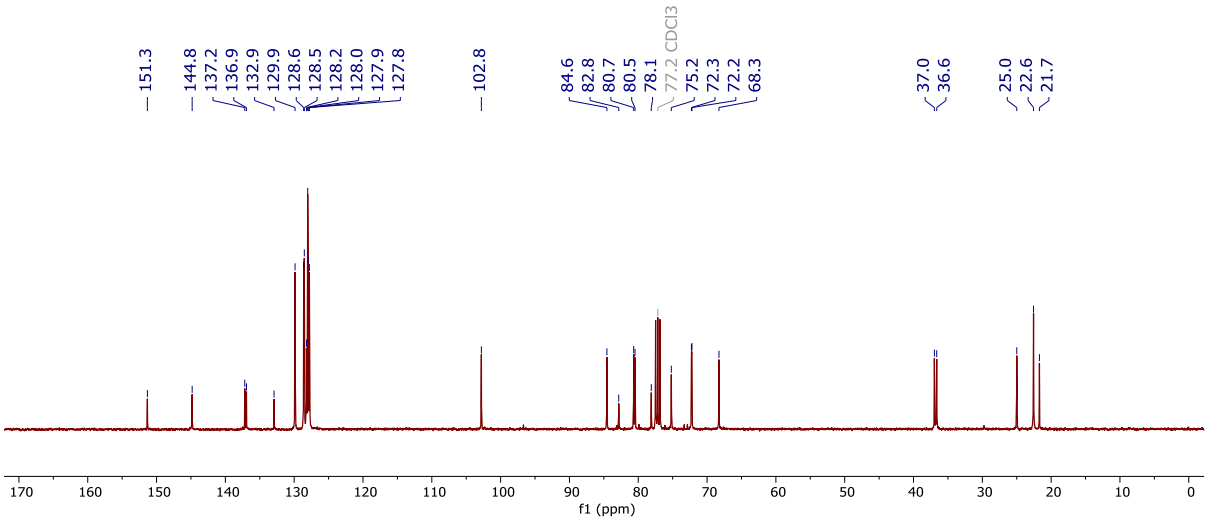

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **48**



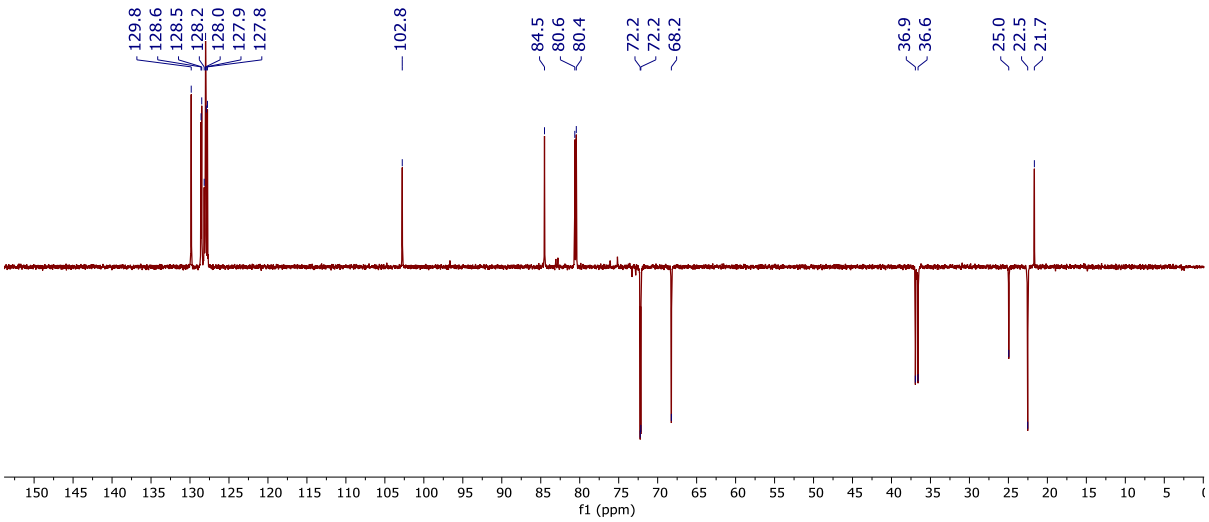
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **04**



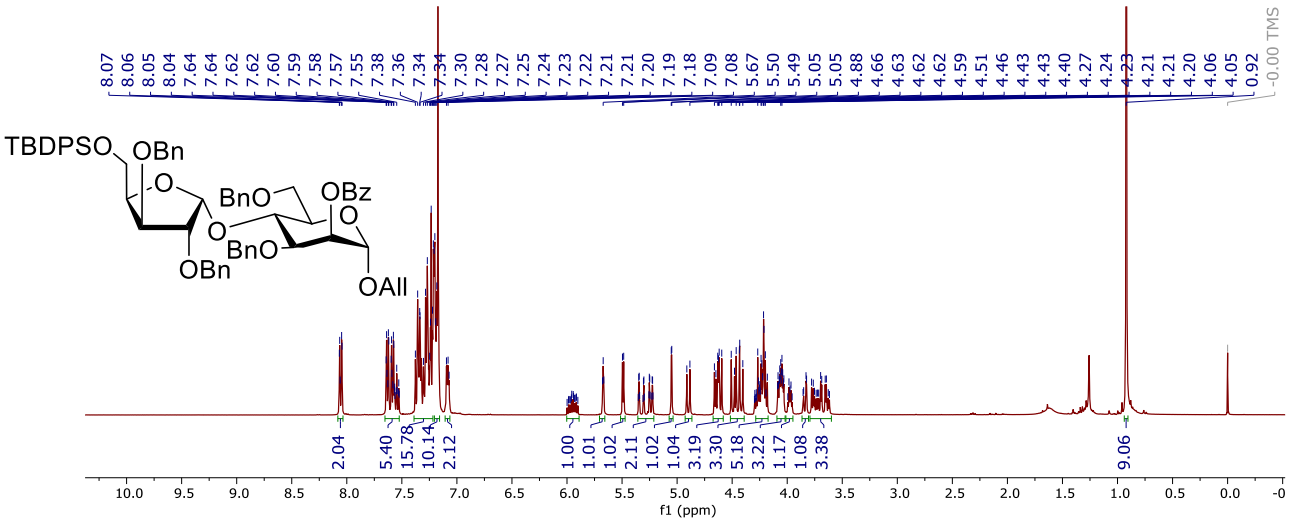

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **04**



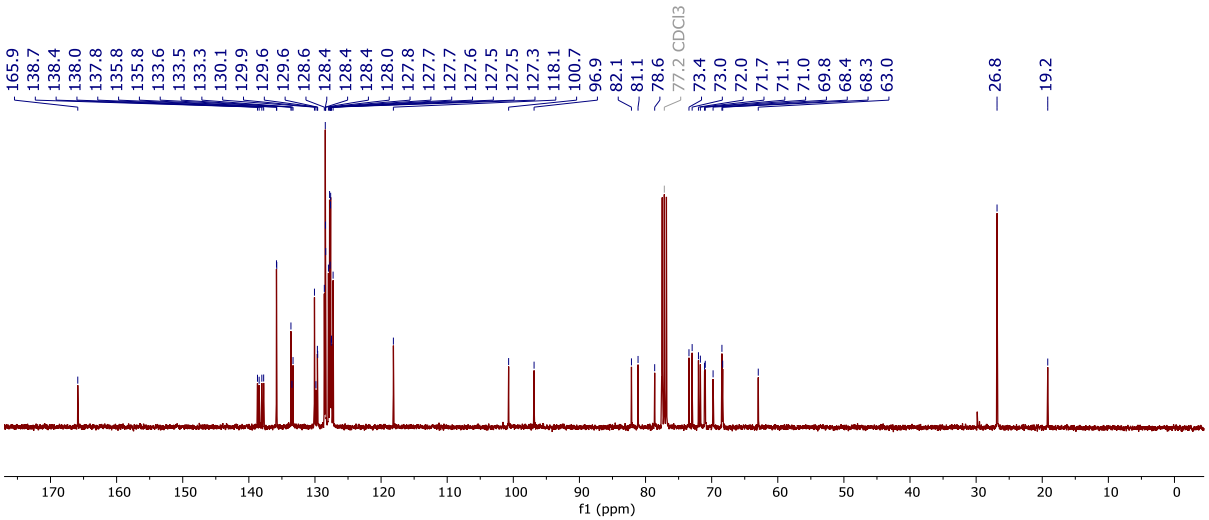

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **04**



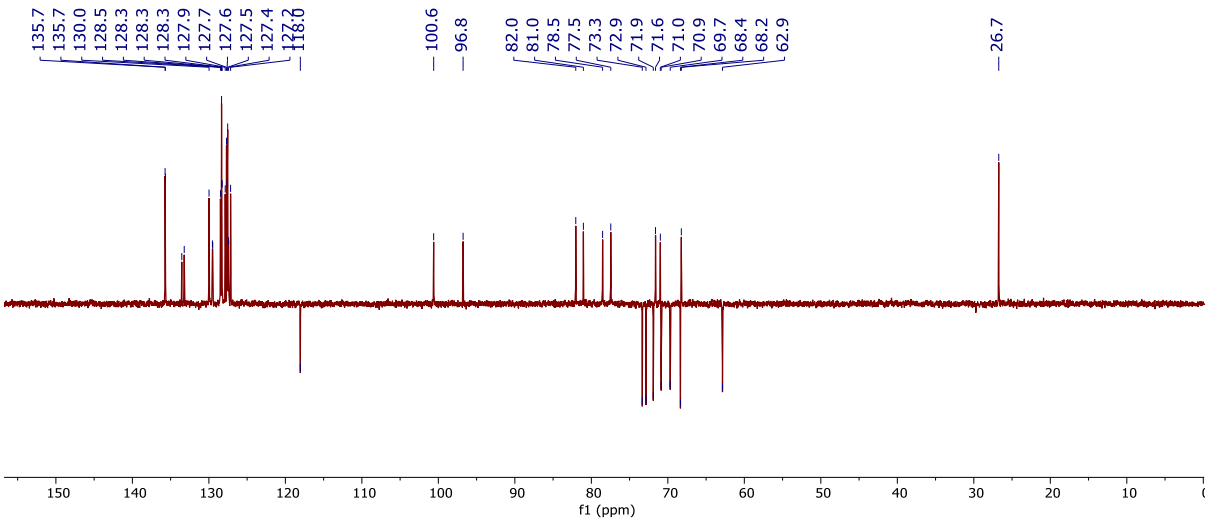
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **53**



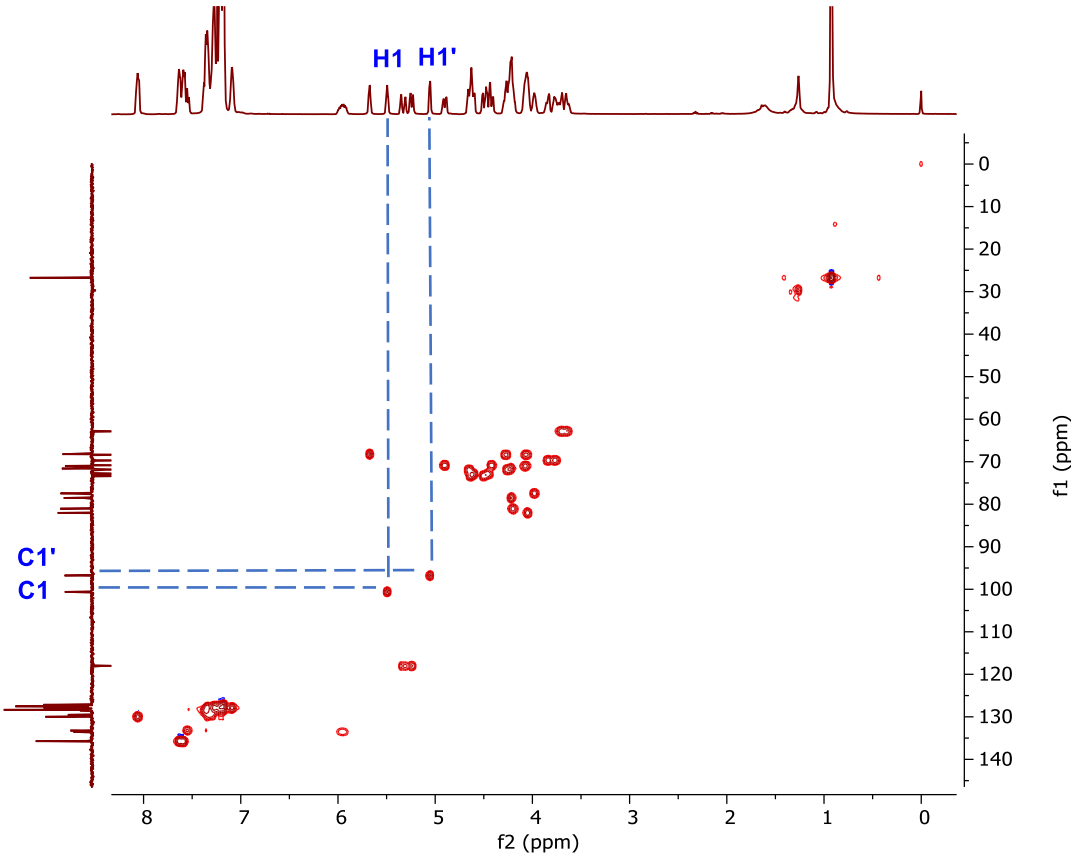

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **53**



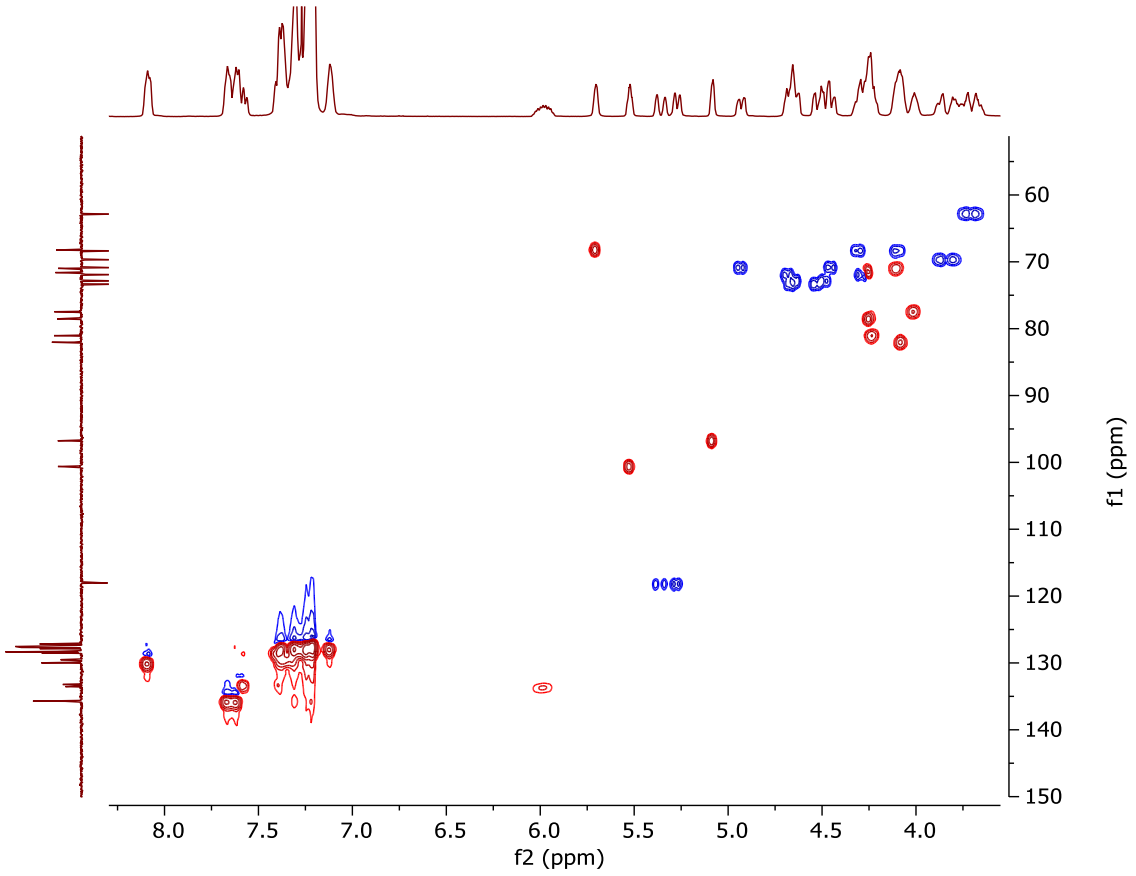

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **53**



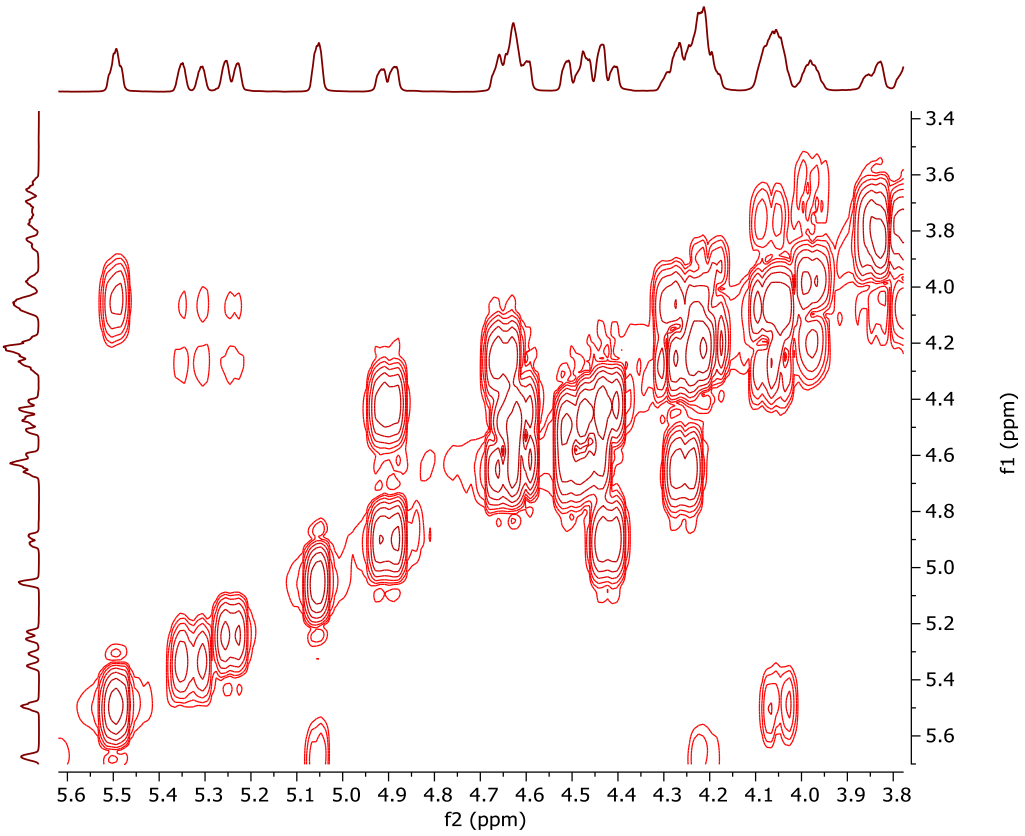
$^{1}H$, $^{13}C$ HSQC NMR Spectrum (400, 101 MHz, $CDCl_3$) of compound **53**



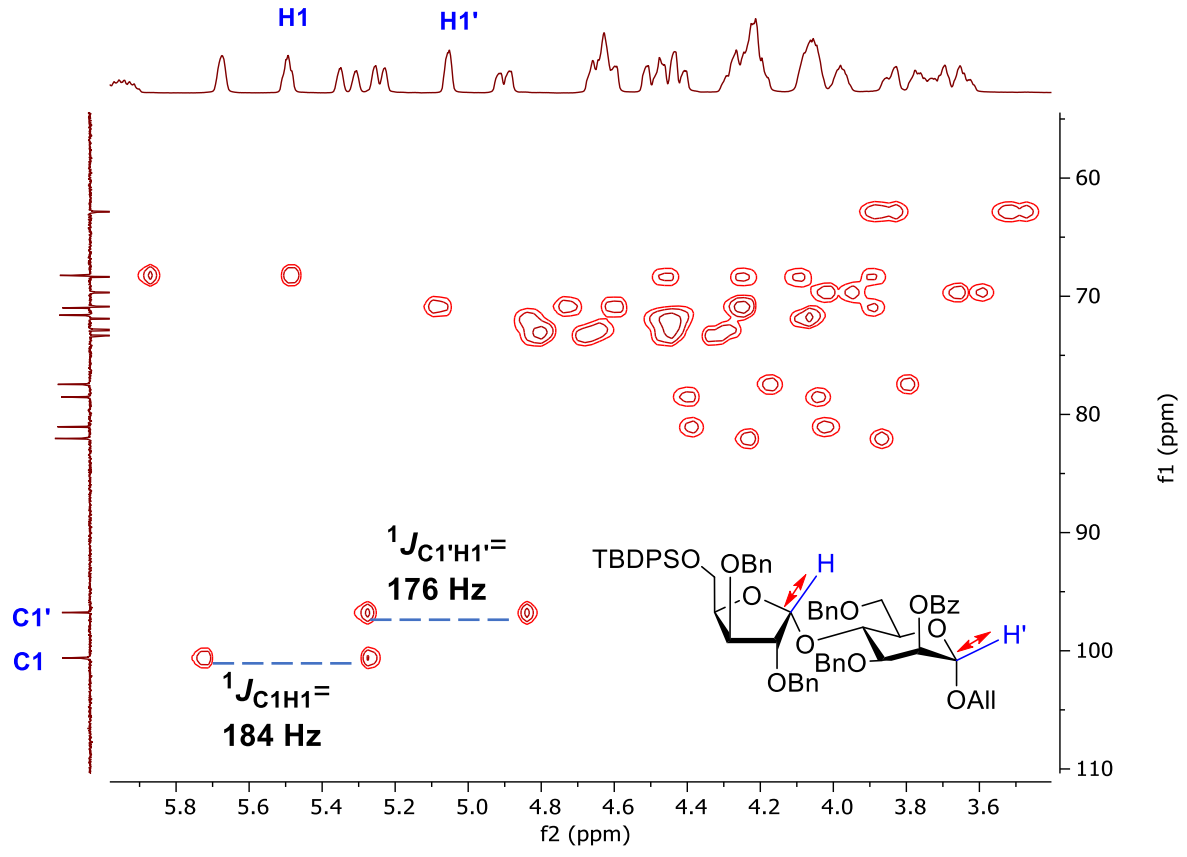

$^{1}H$, $^{13}C$ HSQC-EDITED NMR Spectrum (400, 101 MHz, $CDCl_3$) of compound **53**



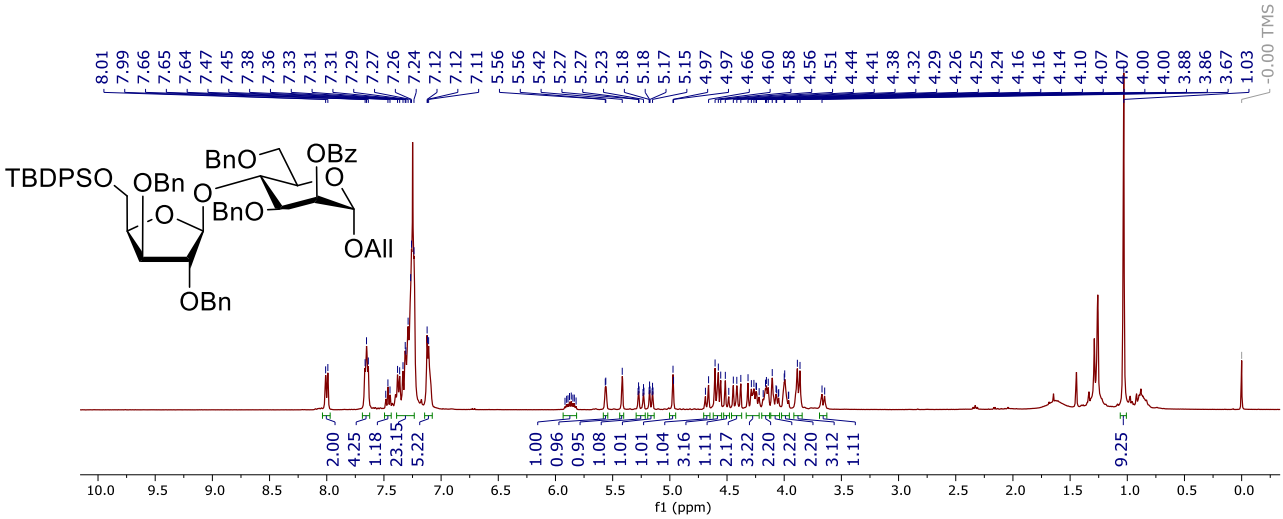
$^{1}$H, $^{1}$H COSY NMR Spectrum (400 MHz, $CDCl_3$) of compound **53** (*α*-isomer)



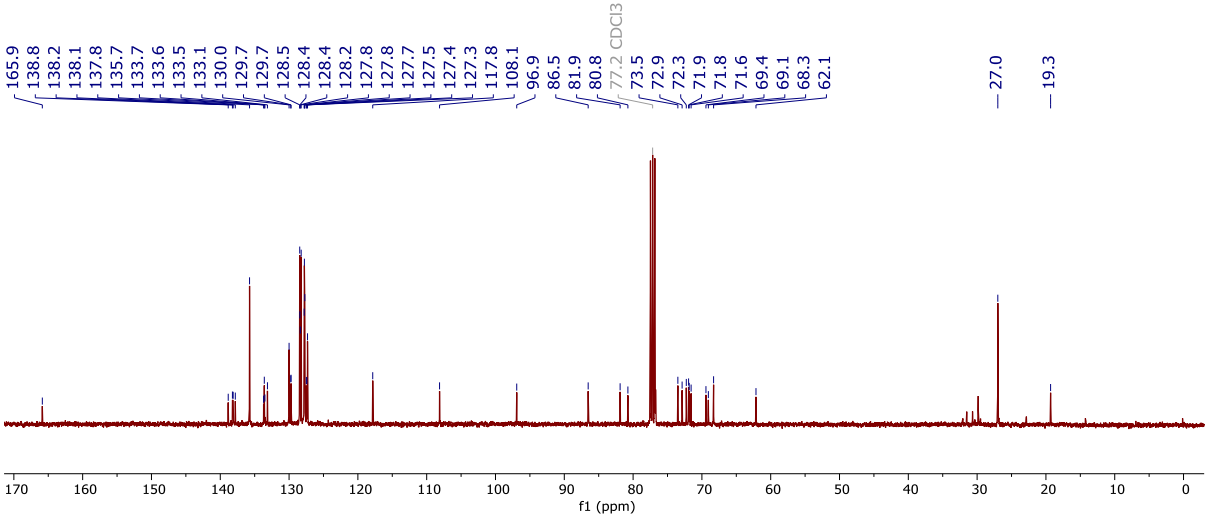

$^{1}$H, $^{13}$C HSQC-Coupled NMR Spectrum (400, 101 MHz, $CDCl_3$) of compound **53** (*α*-isomer)



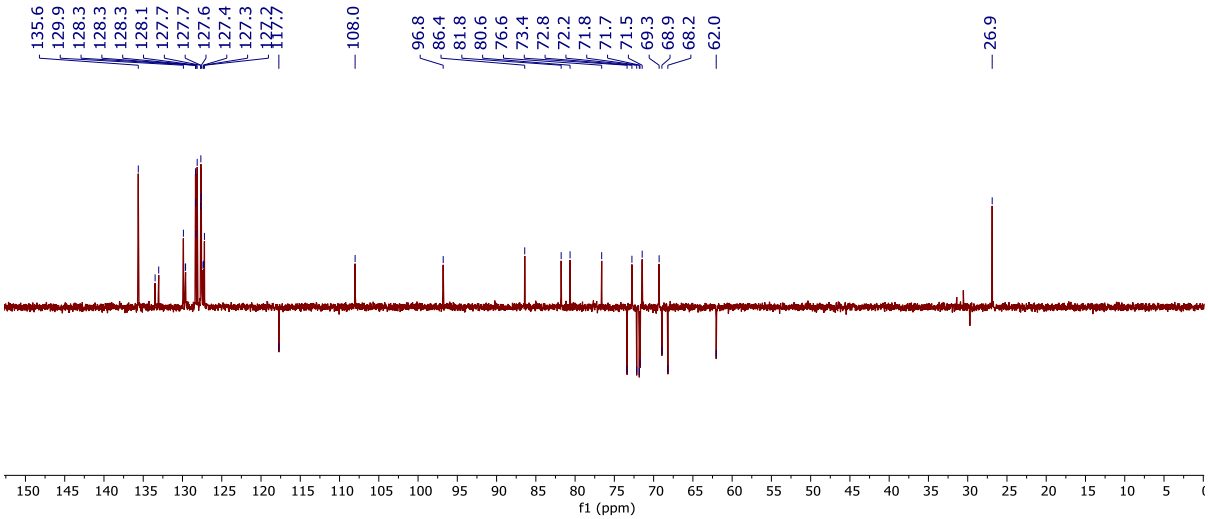
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **53** (*β*-isomer)



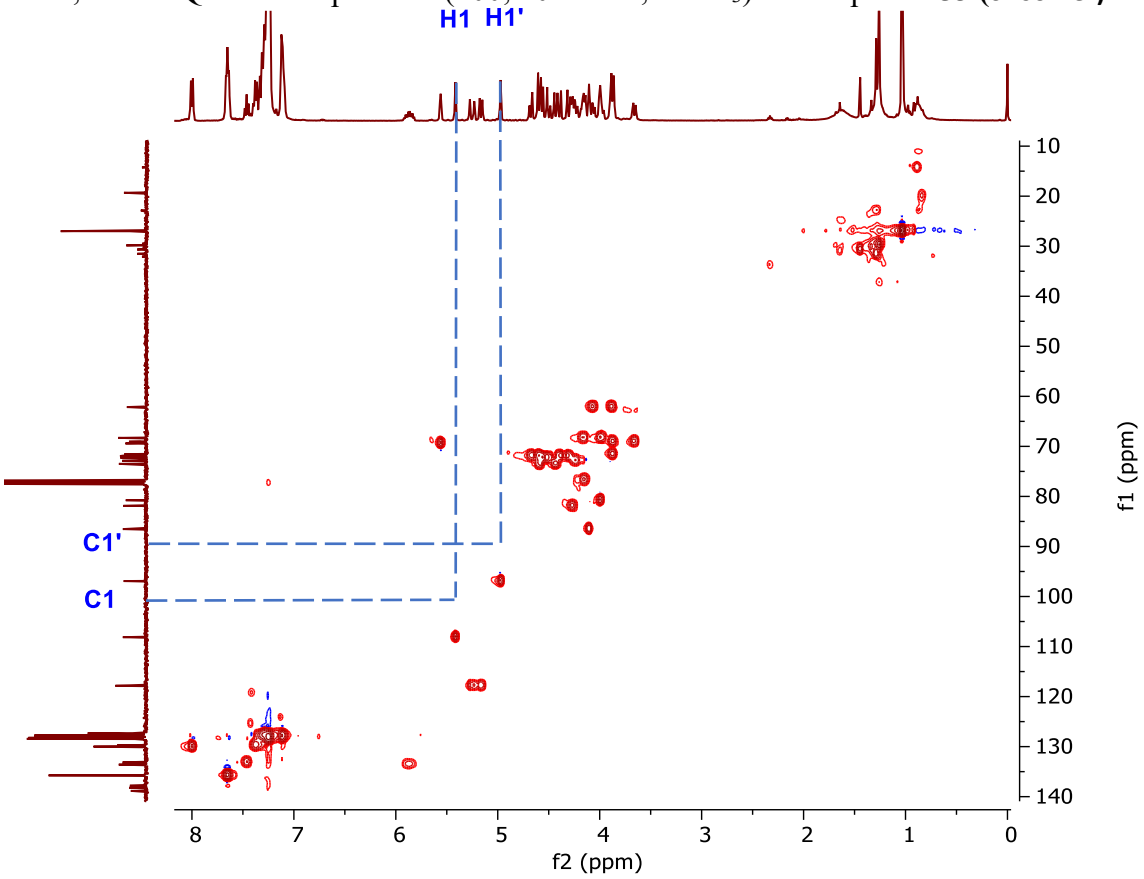

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **53** (*β*-isomer)



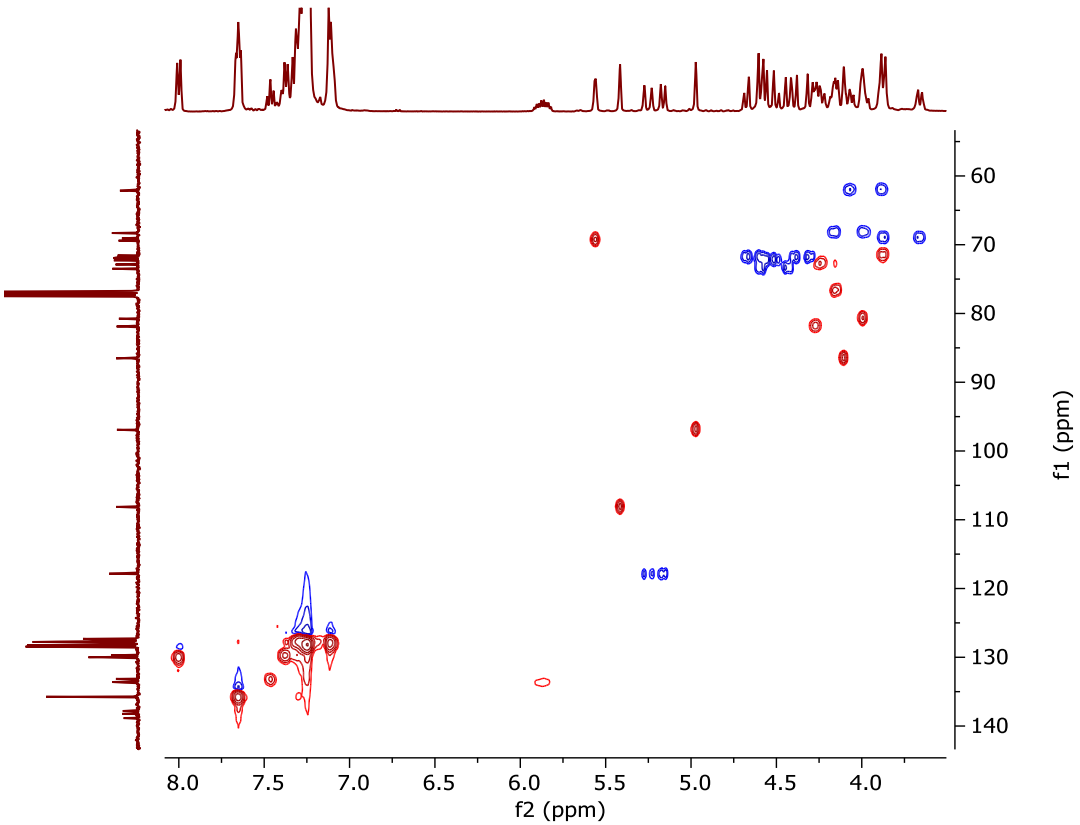

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **53** (*β*-isomer)



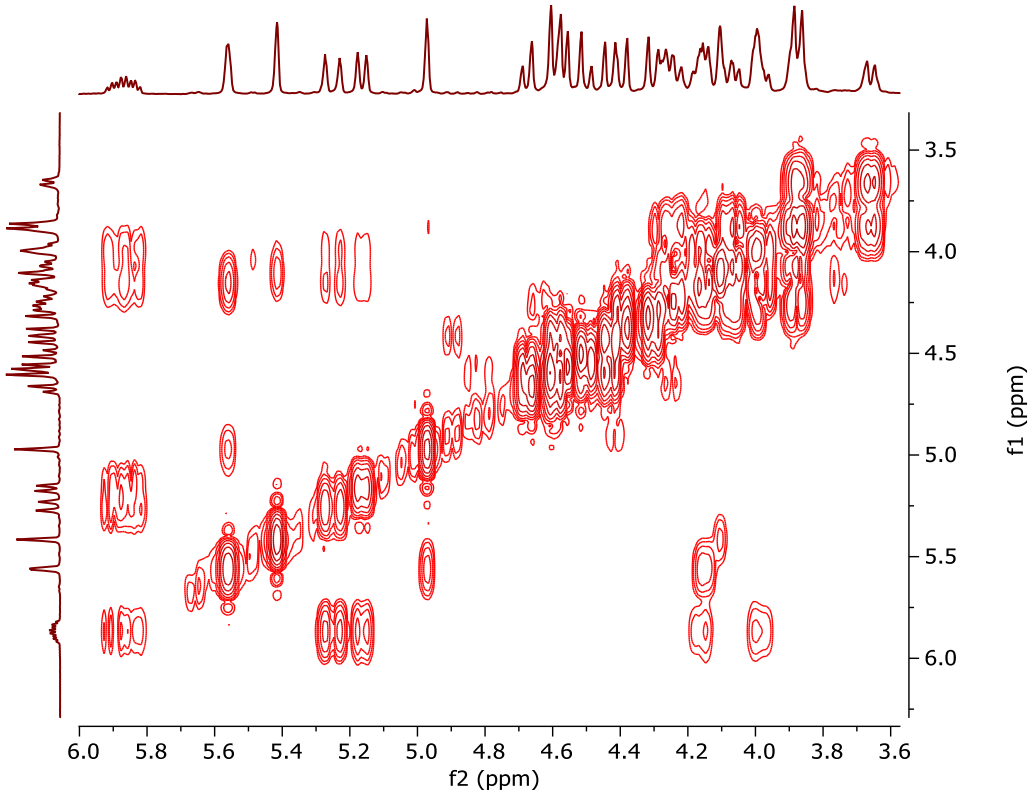
$^{1}H$, $^{13}C$ HSQC NMR Spectrum (400, 101 MHz, $CDCl_3$) of compound **53** (*β*-isomer)



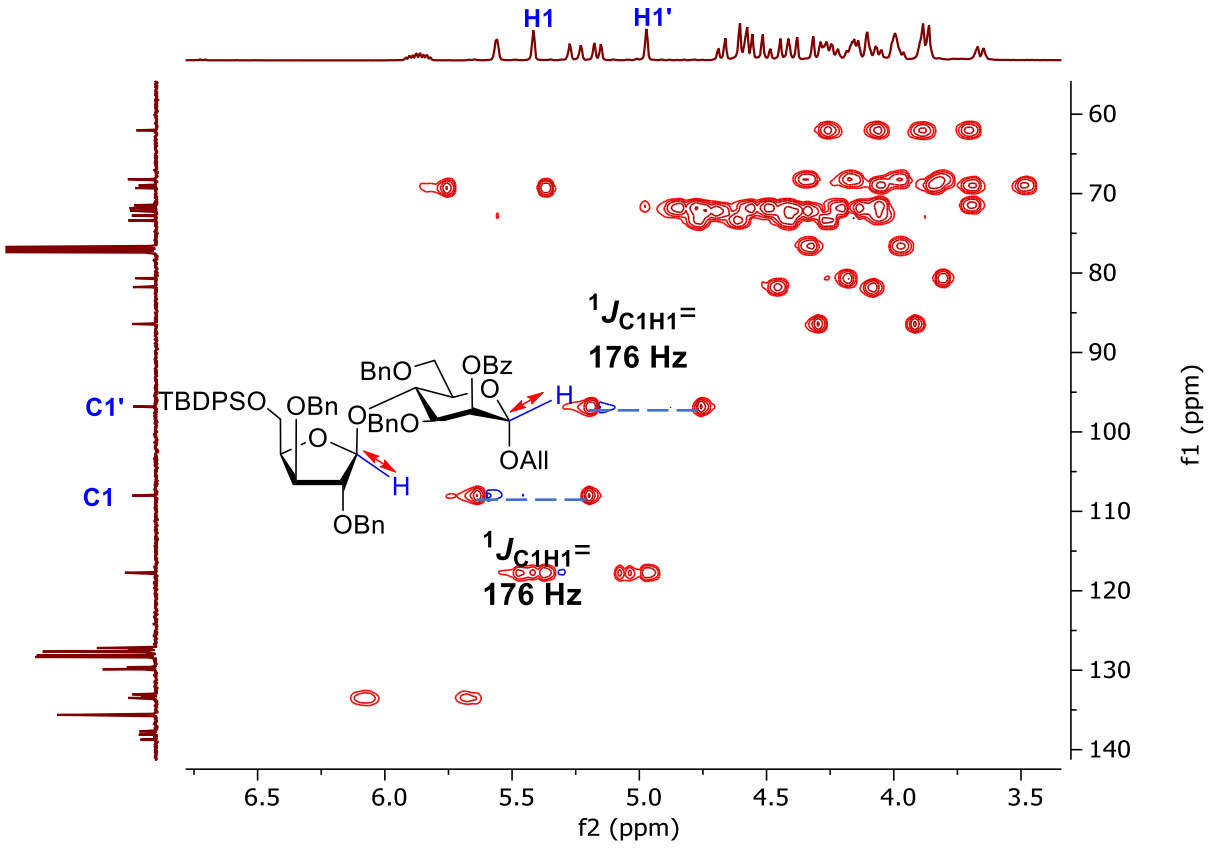

$^{1}H$, $^{13}C$ HSQC-EDITED NMR Spectrum (400, 101 MHz, $CDCl_3$) of compound **53** (*β*-isomer)



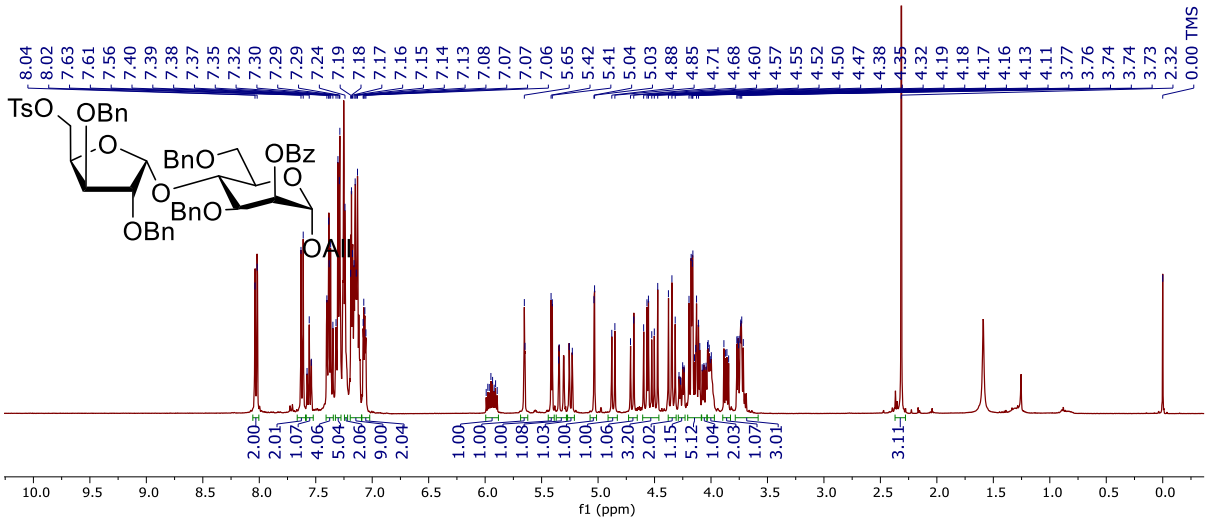
$^{1}H$, $^{1}H$ COSY NMR Spectrum (400 MHz, $CDCl_3$) of compound **53** (*β*-isomer)



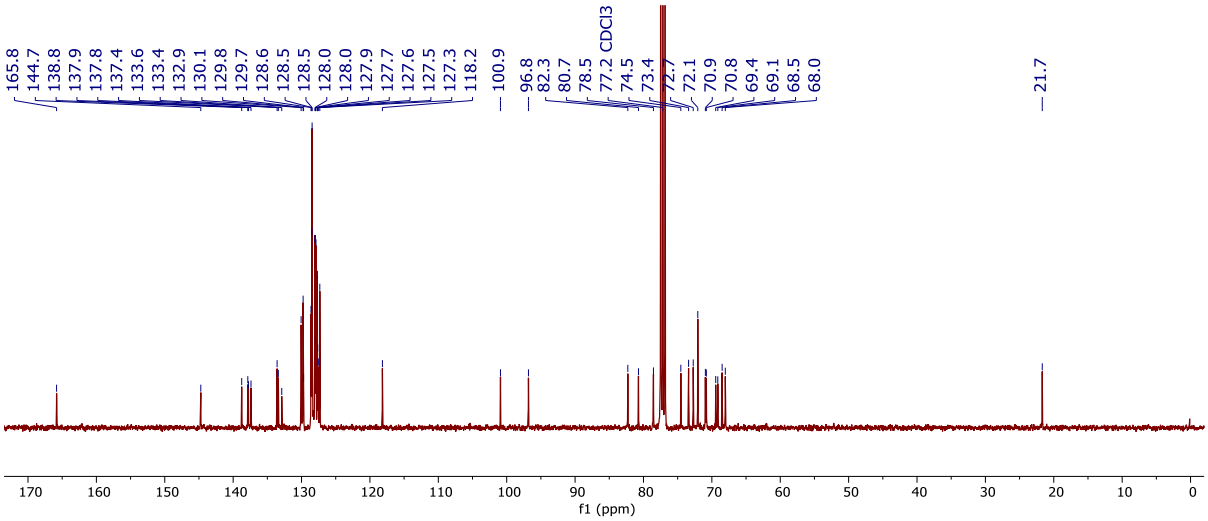

$^{1}H$, $^{13}C$ HSQC-Coupled NMR Spectrum (400, 101 MHz, $CDCl_3$) of compound **53** (*β*-isomer)



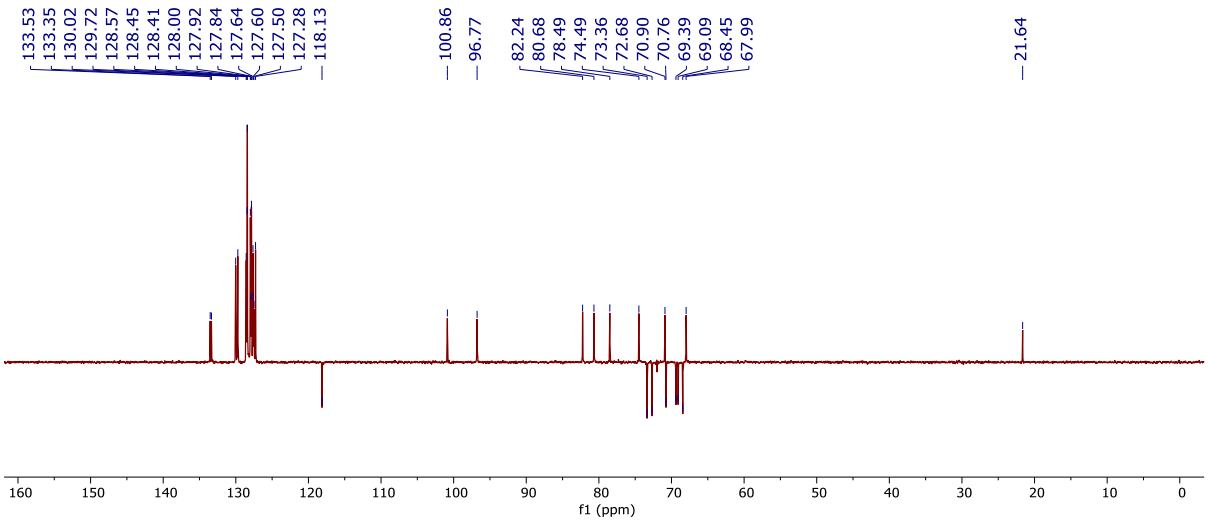
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **54**



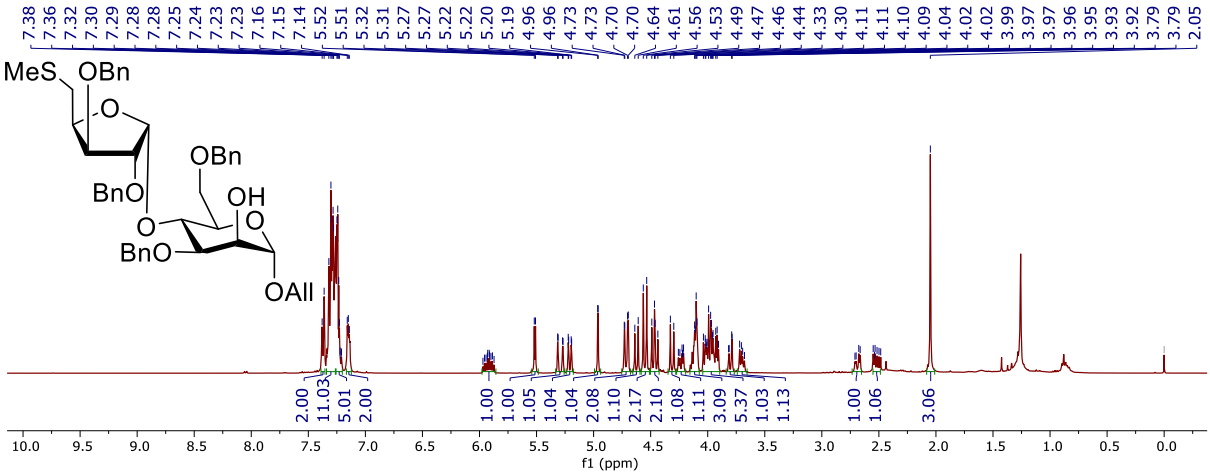

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **54**



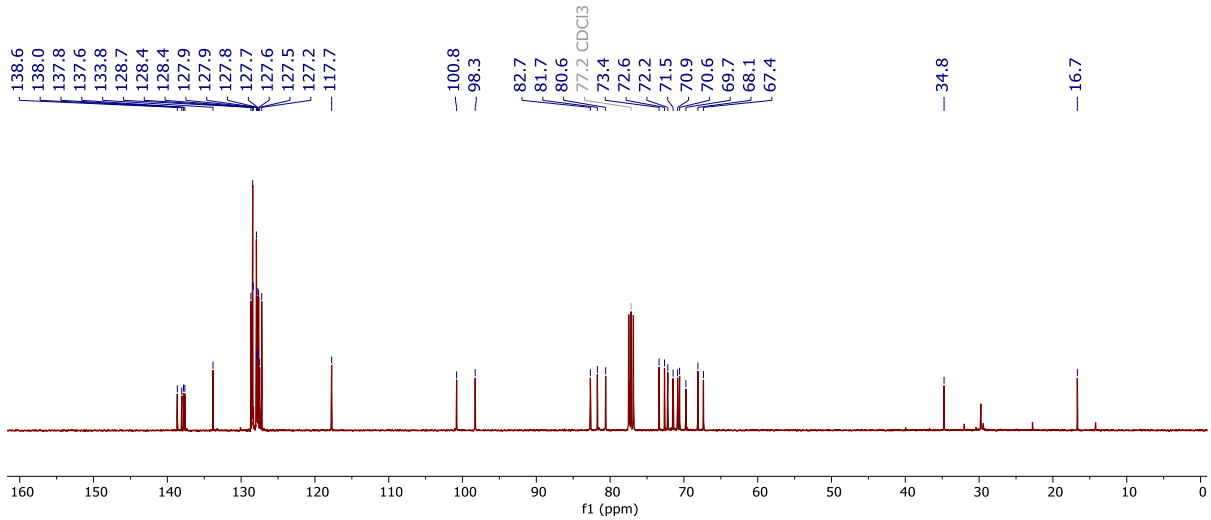

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **54**



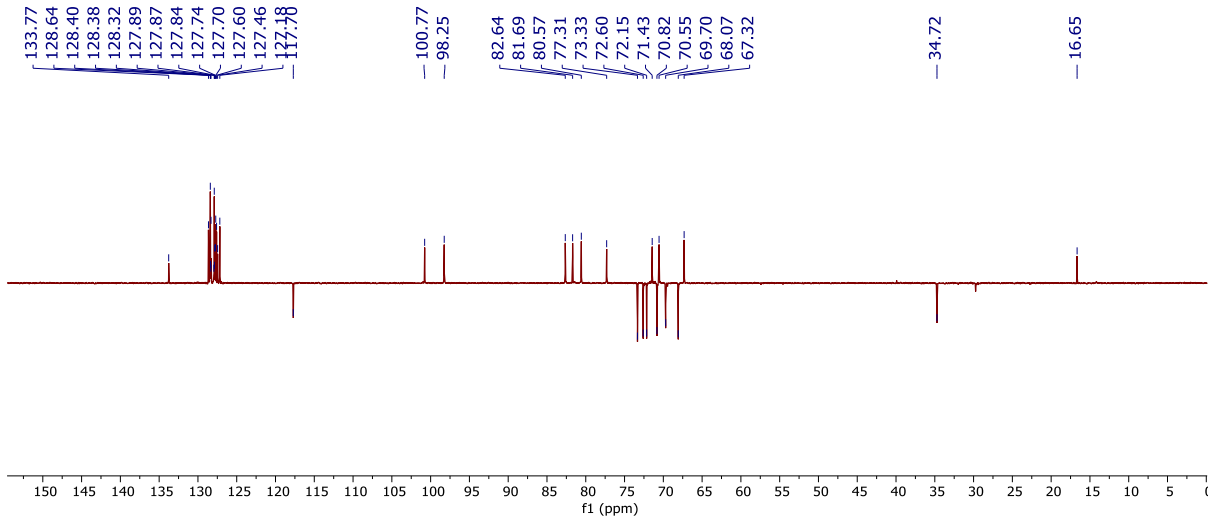
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **55**



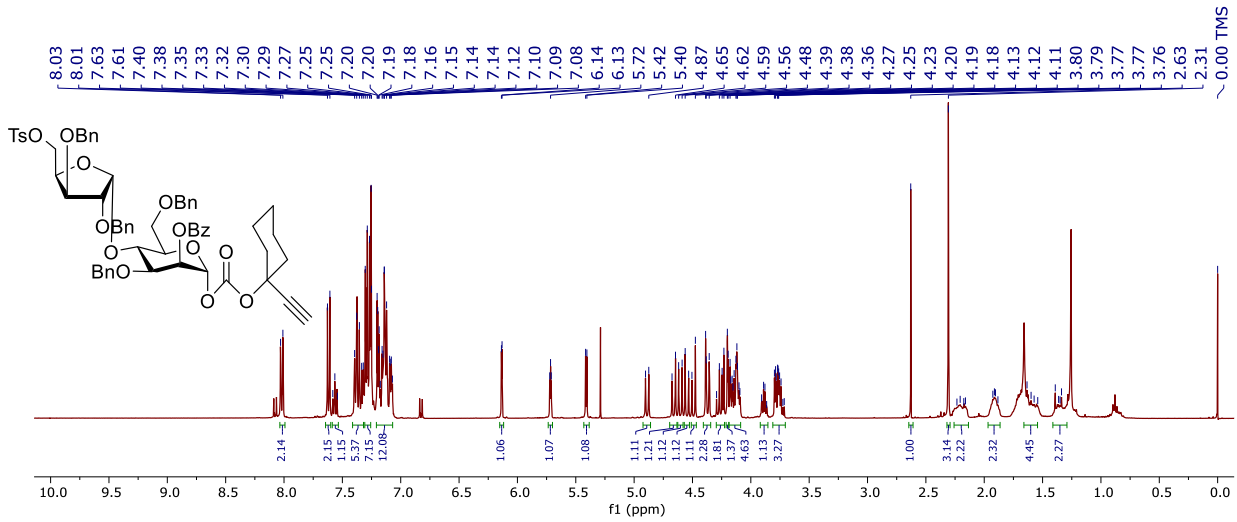

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **55**



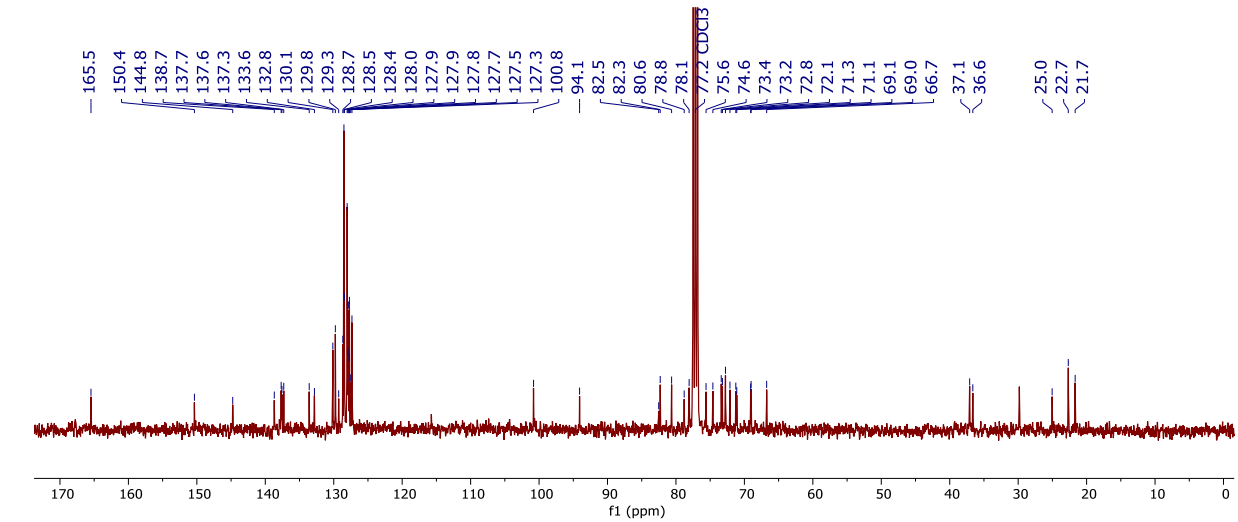

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **55**



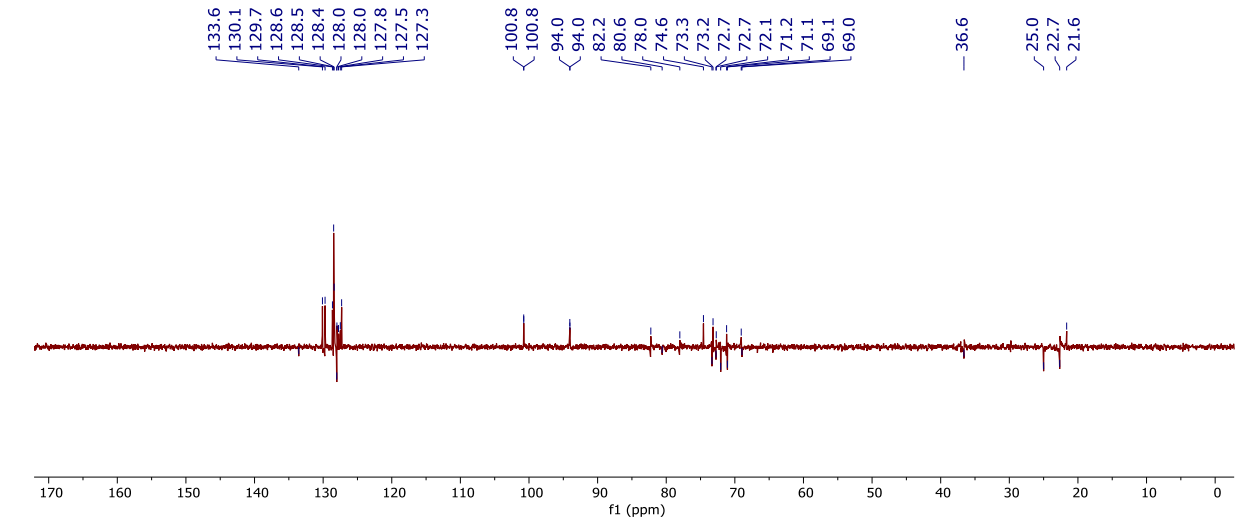
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of compound **03**



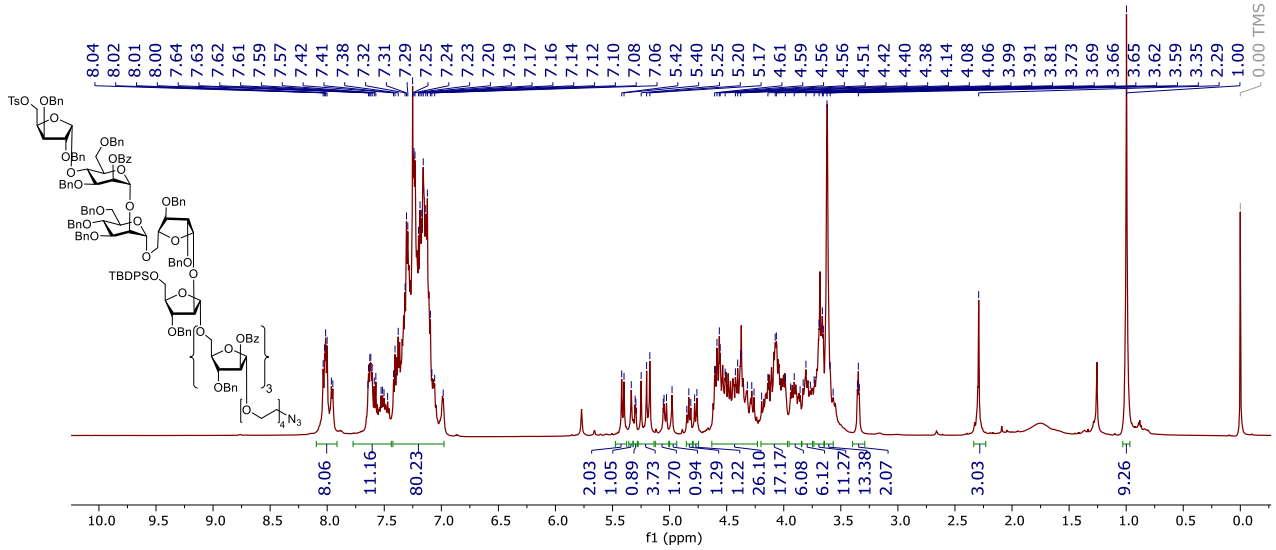

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of compound **03**



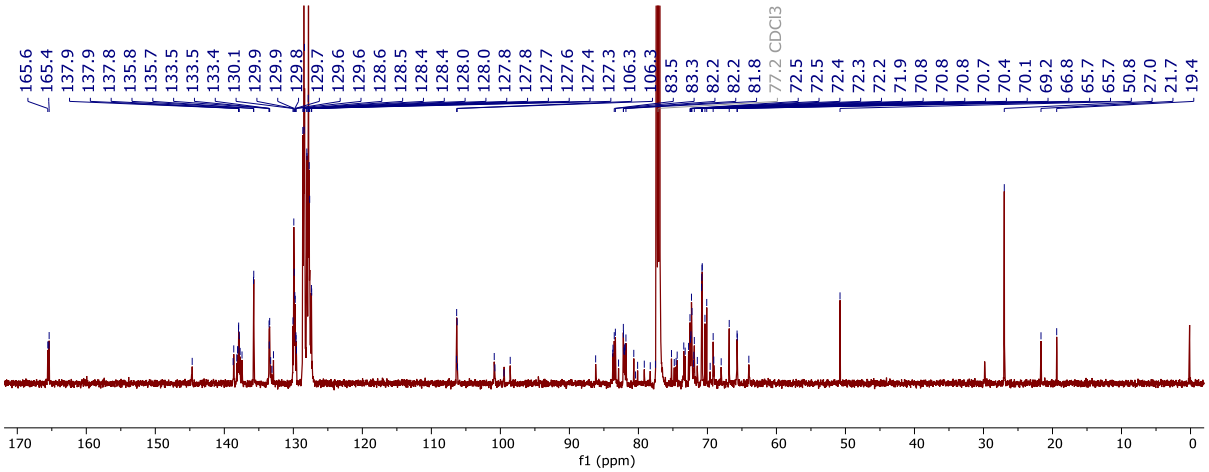

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of compound **03**



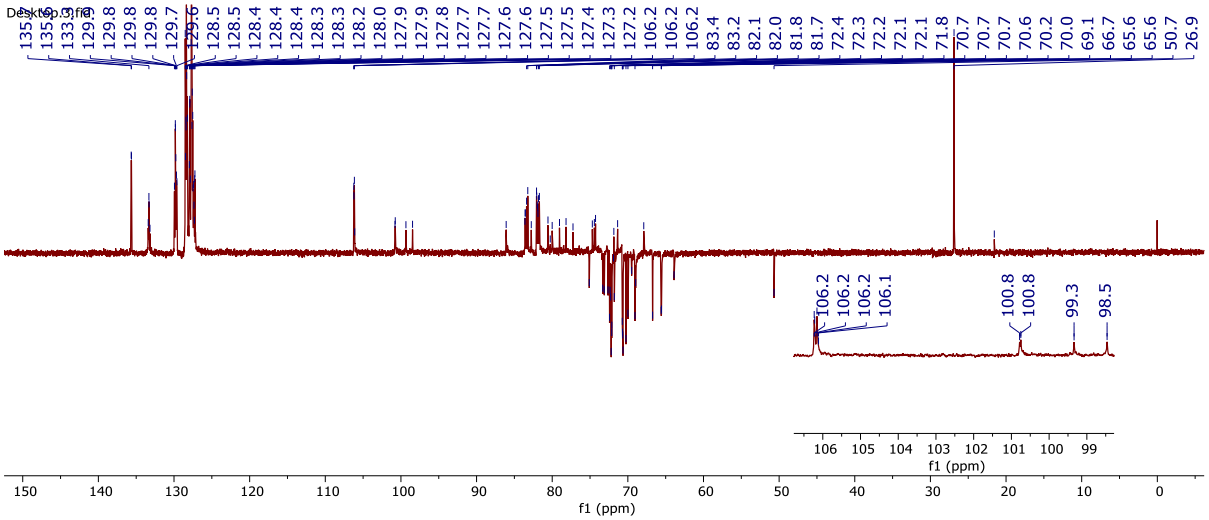
$^{1}$H NMR Spectrum (600 MHz, $CDCl_3$) of compound **56**



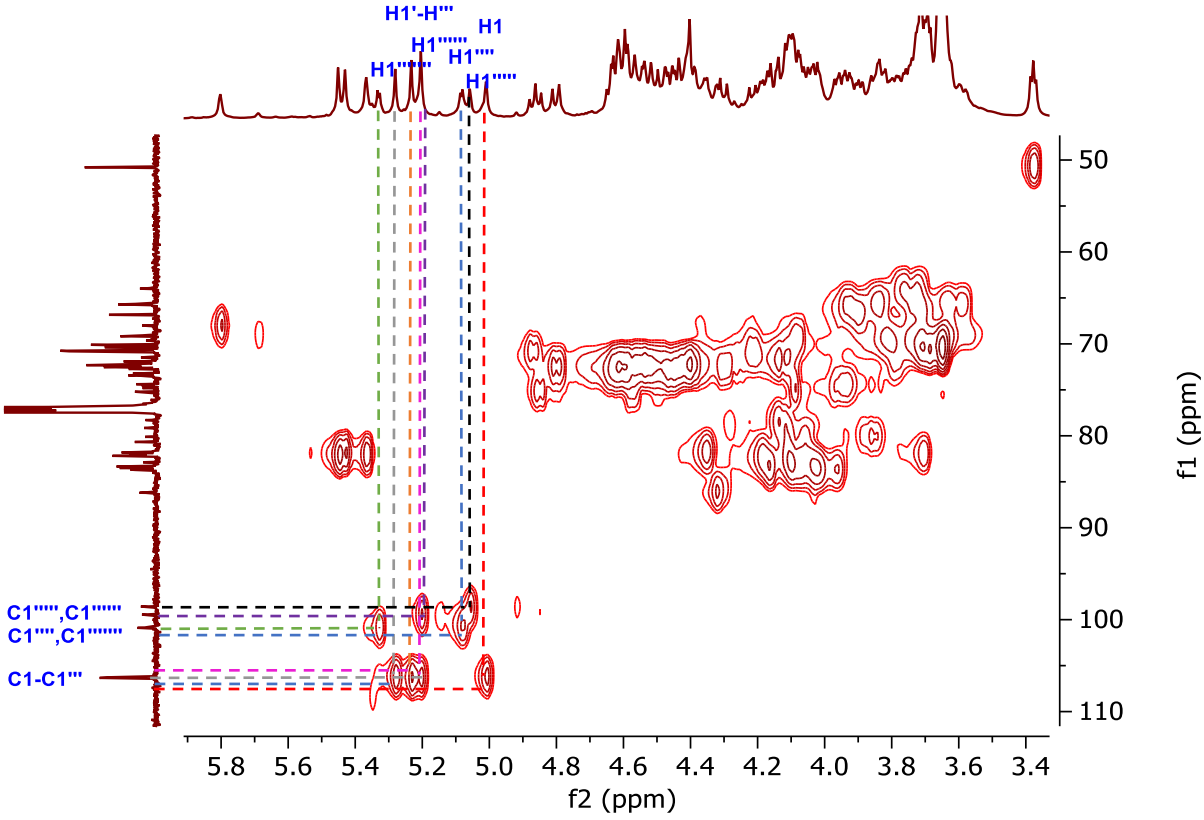

$^{13}$C NMR Spectrum (151 MHz, $CDCl_3$) of compound **56**



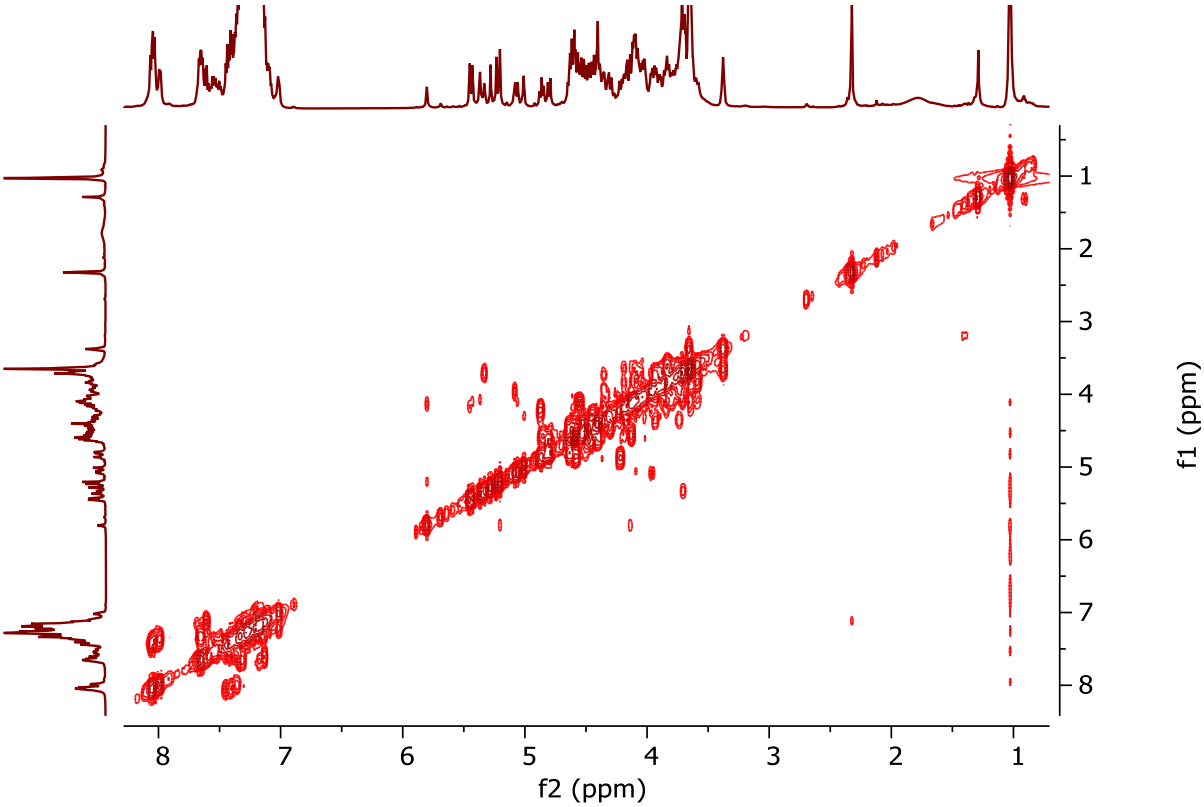

$^{13}$C DEPT-135 NMR Spectrum (151 MHz, $CDCl_3$) of compound **56**



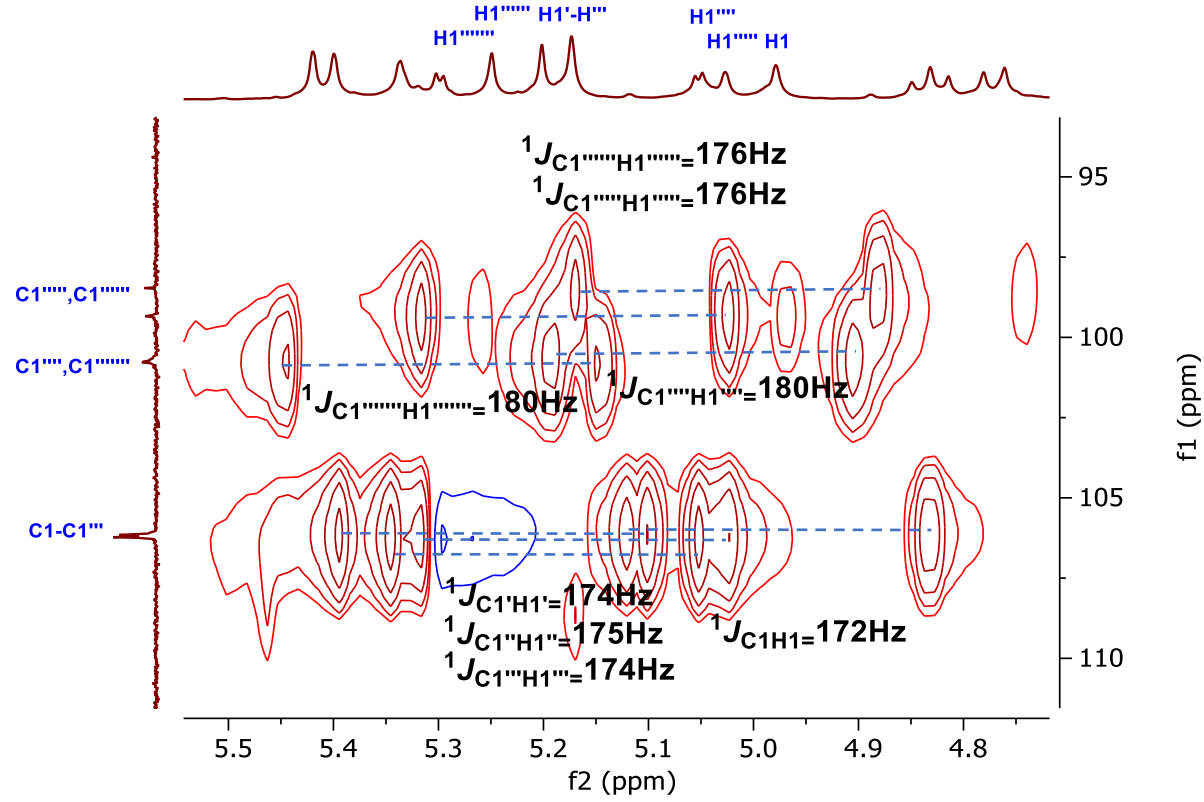
$^{1}H$, $^{13}C$ HSQC NMR Spectrum (600, 151 MHz, $CDCl_3$) of compound **56**



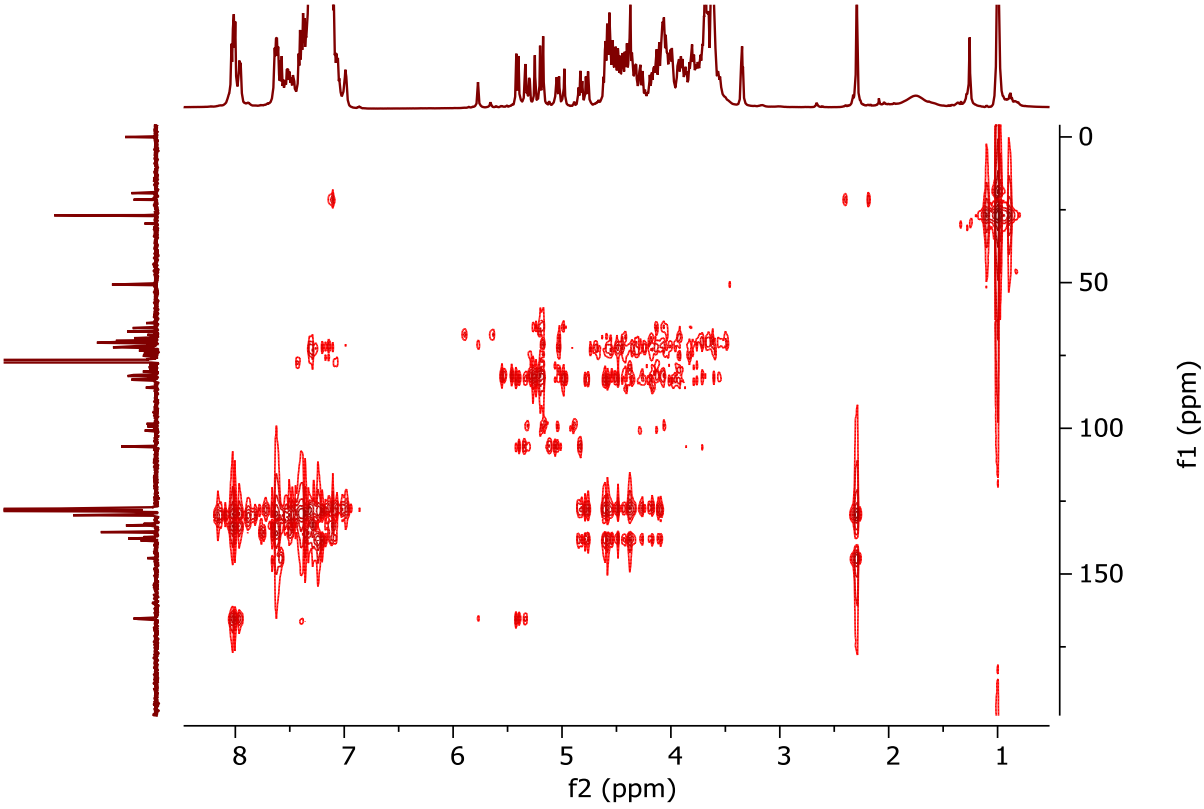

$^{1}H$, $^{1}H$ COSY NMR Spectrum (600, 151 MHz, $CDCl_3$) of compound **56**



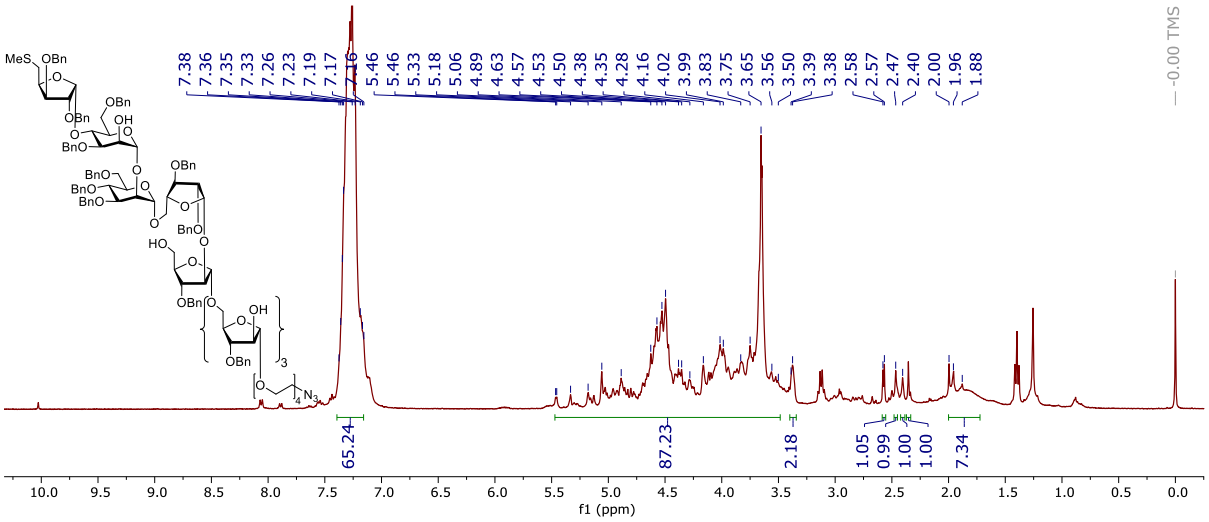
$^{1}H$, $^{13}C$ HSQC-Coupled NMR Spectrum (600, 151 MHz, $CDCl_3$) of compound **56**



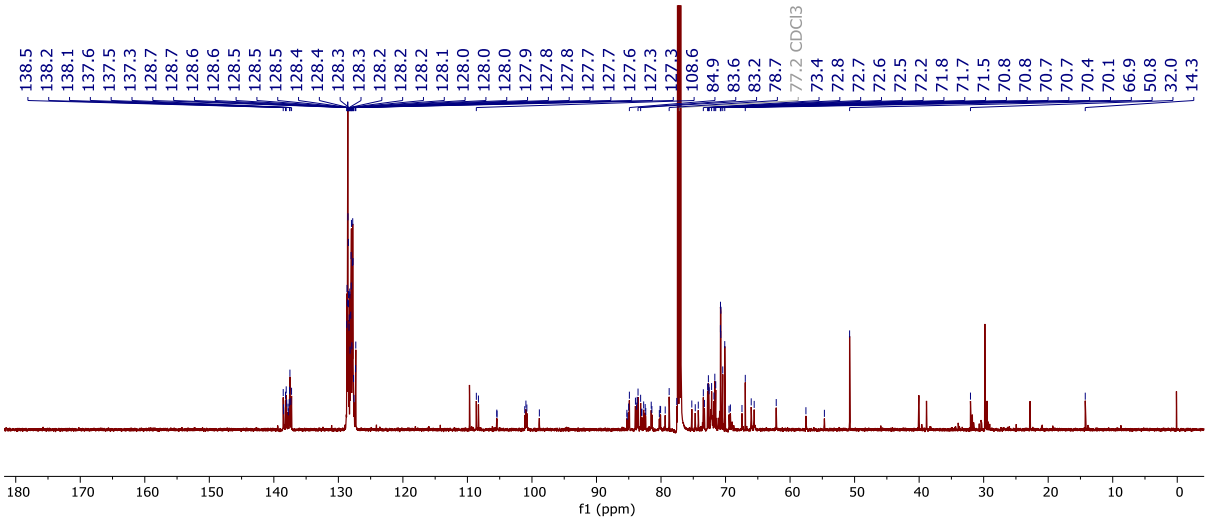

$^{1}H$, $^{13}C$ HMBC NMR Spectrum (600, 151 MHz, $CDCl_3$) of compound **56**



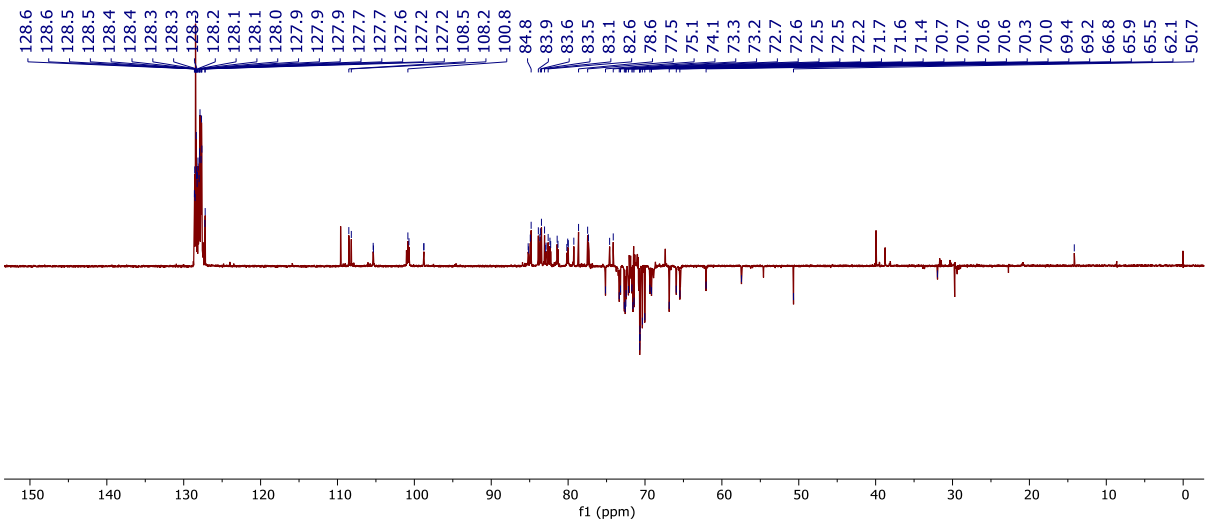
$^{1}$H NMR Spectrum (600 MHz, $CDCl_3$) of compound **57**




$^{13}$C NMR Spectrum (151 MHz, $CDCl_3$) of compound **57**




$^{13}$C DEPT-135 NMR Spectrum (151 MHz, $CDCl_3$) of compound **57**



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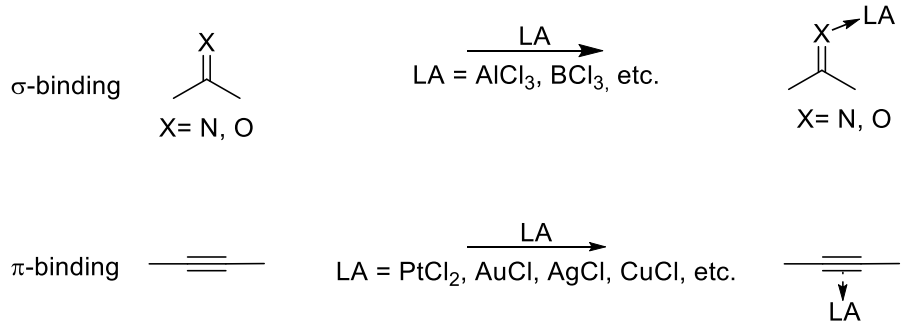
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# *Chapter 3*

## *Metal-free Activation of Alkynyl Glycosyl Carbonate Donors*

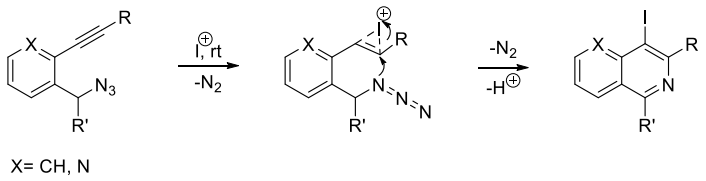
### 3.1 - Introduction

The coordination of Lewis acid with different functional groups, such as imine, carbonyl, alkene, and alkyne, is an important method for activating these functional groups that facilitate many organic transformations. Recently, gold and platinum complexes with alkyne have been of keen interest to several organic chemists.[1] Molecular transformations, such as cyclization, cyclo-isomerization, cycloaddition, etc., are well explored. Thus, it has been known that main-group Lewis-acids such as $BX_3$ make much stronger complexes with heteroatoms (*N* and *O*) of these functional groups than with carbon-carbon multiple bonds (*σ*-electrophilic Lewis-acids). However, coinage metal salts ($CuL_n$, $AgL_n$, $AuL_n$) and Pt salts strongly coordinate with carbon-carbon multiple bonds (*π*-electrophilic Lewis-acids). Computational studies indicate that main group halides show *σ*-electrophilicity, whereas coinage metal and Pt halides exhibit significant *π*-electrophilicity (**Scheme 3.1**).[2]




***Scheme 3.1:*** *σ-binding and π-binding of Lewis acid to heteroatoms and C-C multiple bonds.*

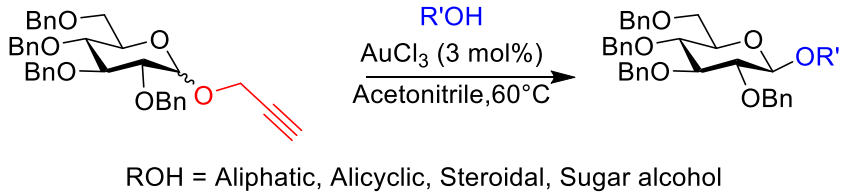
Besides a plethora of transition metal catalysts, the stoichiometric use of simple electrophilic agents such as electrophilic iodonium source became popular in the cyclization and other organic transformations.[3] It is well known that iodonium or protonium ions are intermediates when iodine or Brϕnsted acid is added to the alkyne-containing compounds. Taking advantage of this concept, Yamamoto group reported iodonium ion-catalyzed cyclization and its utility in the synthesis of complex organic compounds. In one of the examples, 2-alkynyl-1-methylene azide aromatic compound gave highly substituted cyclization products, 1,3-disubstituted 4-iodoisoquinolines; the reaction proceeded through the formation of iodonium ion intermediate followed by nucleophilic cyclization of the azide and subsequent elimination of the nitrogen gas (**Scheme 3.2**).[4]




***Scheme 3.2:*** *Iodonium catalysed cyclization reaction by Yamamoto*

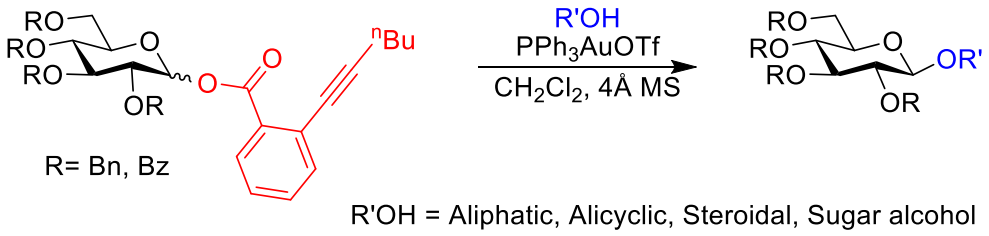
**3.2 - π-binding of Lewis acid with alkynes in the activation of glycosyl donors**

Apart from cyclization, cyclo-isomerization, and cycloaddition of organic compounds, these Lewis-acids are also well explored by glycochemists for glycosylation reactions using alkyne as an activation center at the anomeric position. In this direction, the first gold catalyzed glycosylation was started by Hotha group in 2006, wherein, $AuCl_3$-activated per-*O*-benzylated propargyl glucosides to afford several glycosides using this protocol (**Scheme 3.3**).



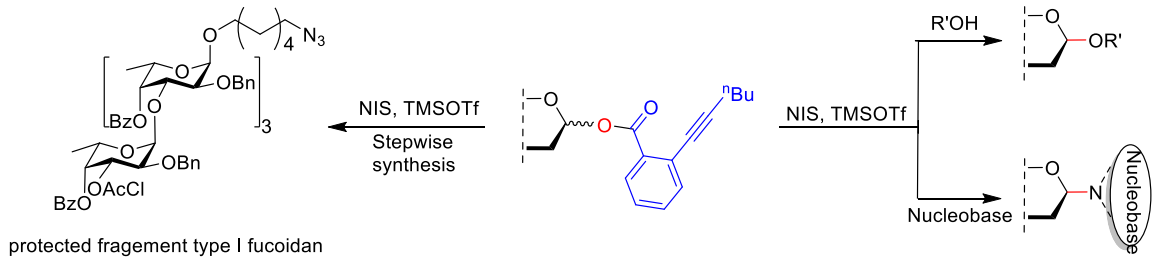

***Scheme 3.3:*** *The First gold catalysed glycosylation protocol*

However, this method was restricted for armed donors (those which armed to react by having C2-*O*-ether) and did not react with per-*O*-benzoate donors (disarmed donors) towards the gold catalytic system.[5]



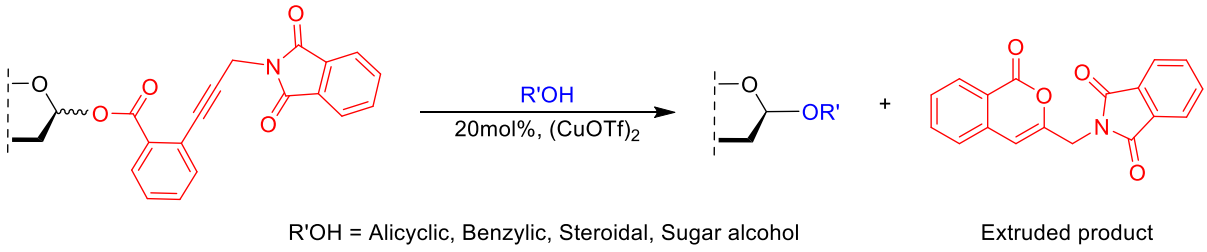

***Scheme 3.4:*** *Alkynyl esters as glycosyl donors*

Subsequently, Yu group reported the gold-catalysed ($PPh_3AuOTf$) glycosylation method exploiting *ortho*-alkyne benzoate donor wherein the coordination of gold with alkyne initiates the reaction[6] (**Scheme 3.4**). Later, Yang group activated the *ortho*-alkyne benzoate (ABz) donor using *N*-iodosuccinimide (NIS) and trimethylsilyl-trifluoromethanesulfonate (TMSOTf) and utilized it for the synthesis of *O*-glycosides and *N*-glycosides. Furthermore, to evaluate the synthetic ability of this glycosylation protocol, they also synthesized tetrasaccharide fragment of the type I fucoidan, which is known for its important biological activities, such as anticancer, antiangiogenic, immunomodulation, and antiviral properties. (**Scheme 3.5**).[7]




***Scheme 3.5:*** *NIS/TMSOTf activation of o-alkynyl benzoate donor*

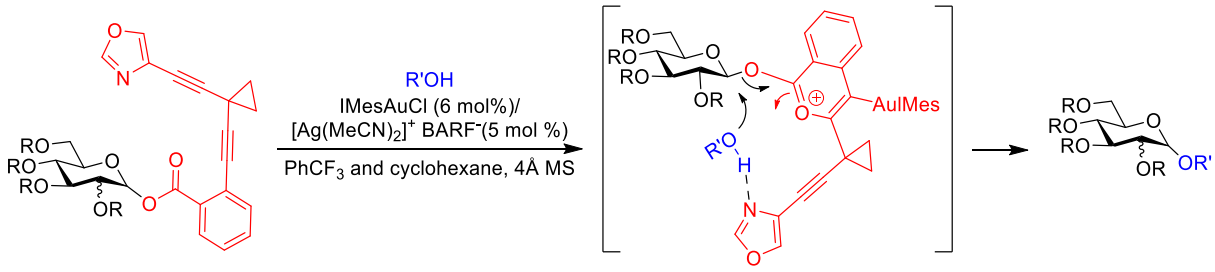
To make Yu's ortho-alkyne benzoate (ABz) donor more economical, it was slightly modified at the alkyne terminal by introducing *N*-phthalimidoylpropynyl to develop *ortho*-N-phthalimidoylpropynyl benzoates (NPPBs) as donor, which is a modified version of original donor (ABz donor) reported by Yu. The inexpensive copper catalyst was employed in the glycosylation to catalyze the modified donor. Primary investigation on mechanistic path suggested that Cu(II) is involved in the coordination with alkyne and amide functionality which play an essential role in the activation of donor, later carbonyl carbon of the ester coordinated with the alkyne bond to form a cyclic compound which forms the extruded product, and intermediate oxocarbenium ion is attacked by incoming nucleophilic acceptor to produce the desired glycoside (**Scheme 3.6**).[8]




***Scheme 3.6:*** *Cu(II) activation of ortho-N-phthalimidoylpropynyl benzoates donor*

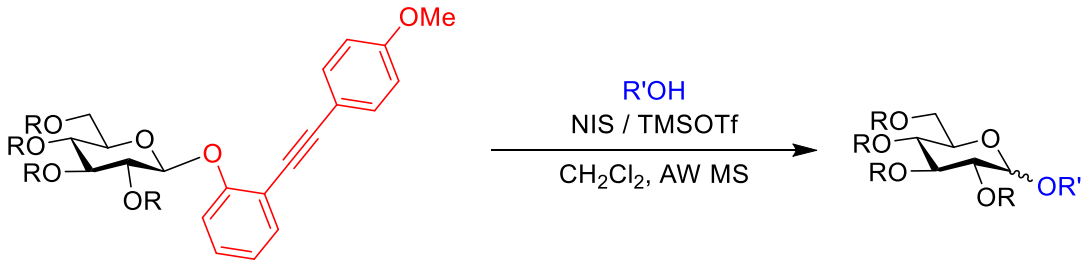
Taking inspiration from several reports on innovative and hydrogen-bond-assisted stereoselective glycosylation,[9-12] Liu co-workers engineered Yu's donor by the introducing oxazole-based traceless directing group on the alkyne terminal of the leaving group for the stereoselectivity glycosylation, which was catalysed by gold(I) catalyst. The alkyne terminal of Yu's donor terminated by the alkyne cyclopropyl group featuring mild basic oxazole ring which shows hydrogen bonding with acceptor moiety, and direct the acceptor attack from opposite to the leaving group, hence realising the desired $S_N2$ glycosylation under gold {chloro[1,3-bis(2,4,6-trimethylphenyl) imidazol-2-ylidene] gold(I)} and silver {tetrakis(3,5-bis(trifluoromethyl)phenyl) silver(I)borate} catalysed conditions. After formation of

isochromenylium intermediate, the hydrogen bonded acceptor attacks from opposite side of leaving group affording the inverted product (**Scheme 3.7**).[13]



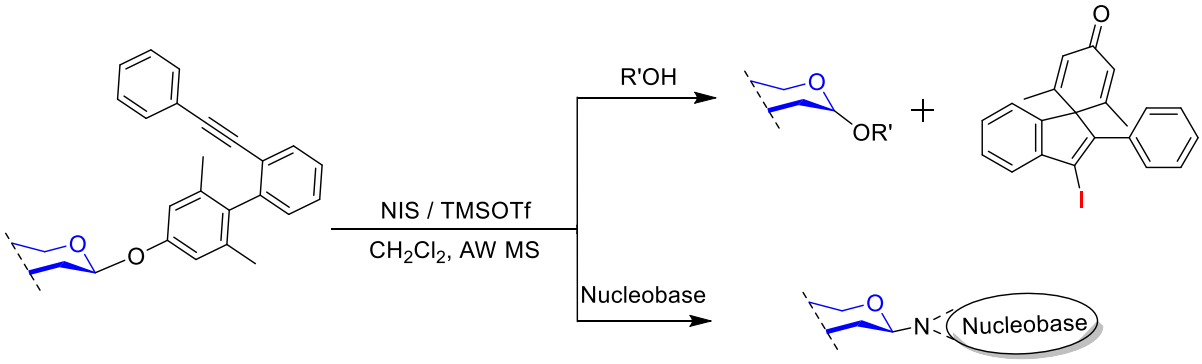

***Scheme 3.7:*** *Oxazole-based traceless directing group mediated gold catalysed glycosylation*

Sun et al., introduced an alkyne-based glycosyl donor, i.e., *O*-(*p*-methoxyphenyl ethynyl) phenyl, catalysed by *N*-iodosuccinimide (NIS) and trimethylsilyl-trifluoromethanesulfonate (TMSOTf). This donor was shelf-stable and could be prepared efficiently via Sonogashira reaction from the corresponding *o*-iodophenyl glycosides. The outstanding stability of both *o*-iodophenyl (IP) as well as *O*-(*p*-methoxyphenyl ethynyl) phenyl (MPEP) glycosides make them applicable for the latent-active oligosaccharide and glycoconjugate synthesis strategy with IP glycosides as the latent form and MPEP glycosides as the active form. Moreover, MPEPs were also utilized in the selective one-pot glycosylation strategy as exemplified by the syntheses of oligosaccharides via successive glycosylation with glycosyl TCAI (Schmidt's donor), ABz (Yu's donor), and EPMP as donor (**Scheme 3.8**).[14]



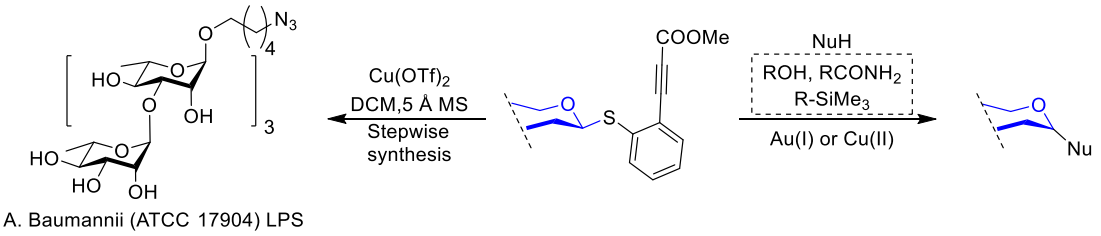

***Scheme 3.8:*** *NIS/TMSOTf activation of o-* (*p*-methoxyphenyl ethynyl) phenyl donor

A highly effective and versatile glycosylation method was developed by Yu *et al.* which uses 3,5-dimethyl-4-(2'-phenylethynylphenyl) phenyl (EPP) glycosides as donors by activating with the NIS/TMSOTf promoters proceeding via an unprecedented dearomatized activation mechanism. EPP donor was utilized for *O*-glycosides, *N*-glycosides, and oligosaccharides synthesis (**Scheme 3.9**).[15]



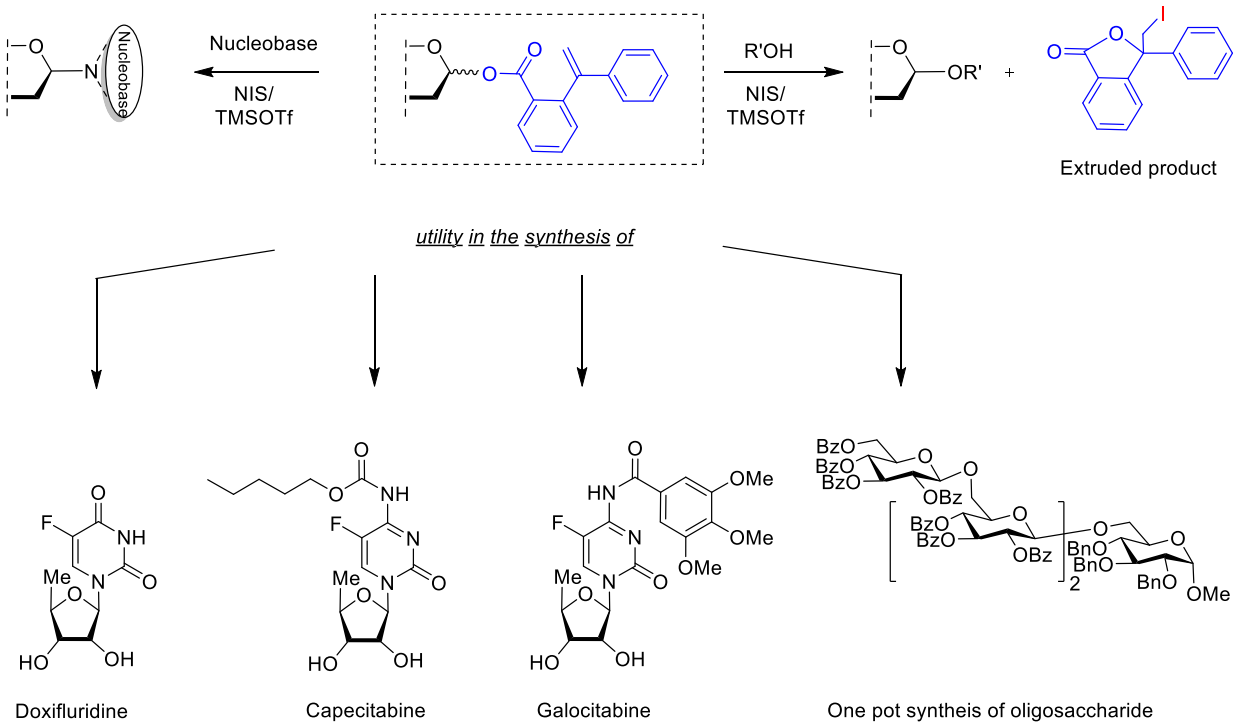

***Scheme 3.9:*** *NIS/TMSOTf activation of 3,5-dimethyl-4-(2'-phenylethynylphenyl) phenyl donor*

Sun et al., came up with *ortho*-methoxycarbonylethynylphenyl-thio-glycoside donor, which was catalysed by either Au (I) complexes or economic $Cu(OTf)_2$. This glycosylation protocol was exploited for the synthesis of *O*-glycosides, amide glycosides. Moreover, one pot synthesis and orthogonality with Yu's donor was also investigated and a practical synthesis of surface polysaccharide subunits of A. baumannii was accomplished via a latent-activation strategy (**Scheme 3.10**).[16]




***Scheme 3.10:*** *Cu(II) or Au(I) activation of ortho-Methoxycarbonylethynylphenyl Thioglycosides*

Xiao group highlighted the *ortho*-(1-phenylvinly) benzoates as versatile donors activated by cheap and readily available promoter (NIS/TMSOTf), utilized for the synthesis of *O*- and *N*-glycosides, further its application in the synthesis of nucleoside-based antibiotics Capecitabine, Doxifluridine, and Galocitabine was demonstrated. Furthermore, biologically active oligosaccharides were synthesised in one pot exploiting orthogonality of *p*-tolysl (Tol), ortho-alkylbenzoates (ABz), ortho-(1-phenylvinyl) benzoate, pentenyl (Pen), trichloroacetimidate (TCAI) (**Scheme 3.11**).[17]

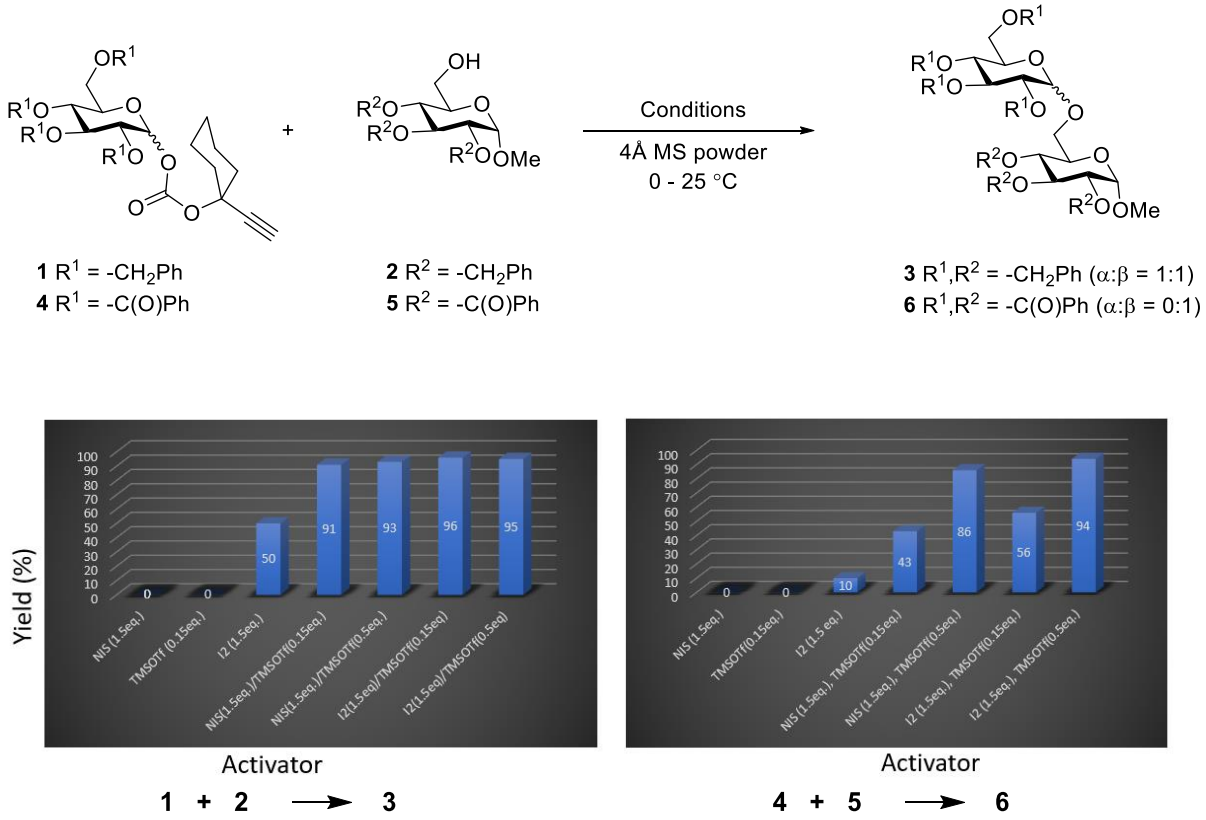



***Scheme 3.11:*** *NIS/TMSOTf activation of ortho-(1-phenylvinly) benzoates*

### 3.2 - Present work

The inception of golden era of glycosylation was a breakthrough by Hotha and co-workers in 2006, as aforementioned in **Scheme 3.3**. To overcome the limitation of the first gold catalysed glycosyl donor (propargyl donor), a stable, versatile, and easily accessible carbonate donor (ethynyl cyclohexyl carbonate) was discovered exactly after ten years in 2016, which was catalysed by gold {chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold} and silver {silver triflate} salts, performed better in terms of yield of glycosylation reaction.[18] Carbonate donor was exploited for synthesizing several oligosaccharides[19-21] and *N*-glycosides, including amide glycosides.[22] To make the reported donor metal activation free and reduce the glycosylation reaction's cost, we envisioned a metal-free and cost-effective activator for the activation of ethynyl cyclohexyl carbonate donor. So, in this regard, we commenced with the ethynyl carbonate donor as a model substrate for our exploration. The alkynophilicity of iodonium reagents drew our attention to the metal-free activation of ethynyl cyclohexyl carbonate donor.

#### 3.2.1 – Optimisation of glycosylation reaction



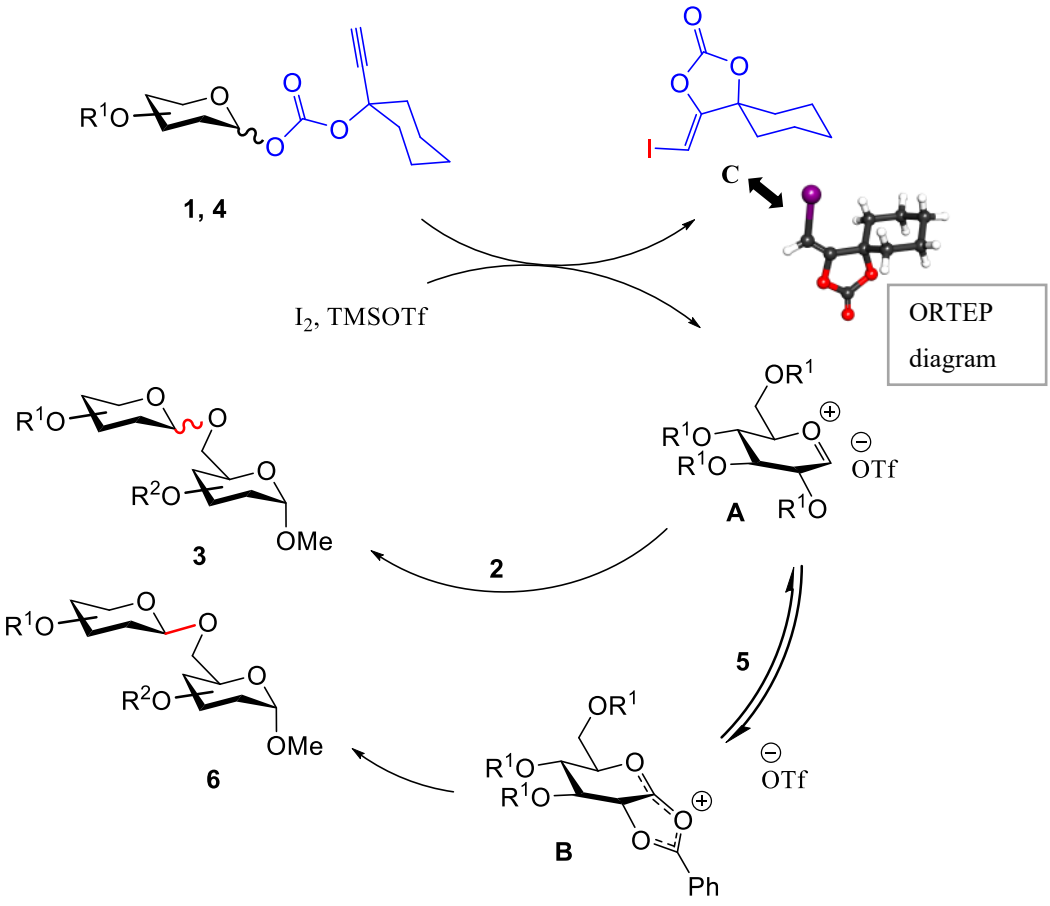

***Scheme 3.12:*** *Screening of reaction conditions for the model glycosylation reaction*

The first glycosylation reaction between carbonate donor **1** and acceptor **2** demonstrated under *N*-iodosuccinimide (NIS) catalyst was failed to produce the desired disaccharide **3**. Similarly, only trimethylsilyl-trifluoromethanesulfonate (TMSOTf) as a catalyst also failed to produce any glycosylated product. However, a combination of NIS (1.5 eq.) and TMSOTf (0.15 eq.) afforded excellent yield (91%) when glycosyl donor **1** was glycosylated with glycosyl acceptor **2**. Moreover, the glycosylation reaction between glycosyl donor **4** and glycosyl acceptor **5** produced glycosylated product **6** in only 43% yield, which can be explained by the disarmed nature of the benzoylated donor.[23] Addition of 0.5 eq. of TMSOTf with 1.5 eq. of NIS significantly improved the reaction yield to 86% with disarmed donor and acceptor. The hygroscopic nature of NIS prompted us to search for an alternate catalyst for better reaction yield. Thus, the same glycosylation reactions were performed under molecular iodine to notice the formation of disaccharides **3** and **6** in 50% and 10% respective yield, and further addition of TMSOTf (0.15 - 0.50 eq.) with molecular iodine drastically improved the reaction yield to 96% (**1**+**2**→**3**) and (**4**+**5**→**6**) 94% (**Scheme 3.12**). Compound **3** was isolated in an equimolar mixture of two isomers *α* and *β*, were characterized by NMR spectroscopy. In the $^{13}C$ NMR spectrum, four peaks at δ 103.9, 98.1, 98.1, 97.3 ppm belong to the anomeric carbons indicating the presence of two isomers, remaining ring carbons, and benzyl (-$CH_2$-) carbons resonated in

between δ 84.9 - 66.1 ppm. Fourteen quaternary carbons of benzyl rings in disaccharides appeared at δ 138.9, 138.9, 138.9, 138.6, 138.6, 138.5, 138.5, 138.5, 138.4, 138.3, 138.3, 138.2, 138.2, and 138.1 ppm, other seventy aromatic carbons resonate from δ 128.5 to 127.6 ppm. Two methyl carbons of methoxy group (-$OCH_3$) were noticed at δ 55.3 & 55.2 ppm. Disaccharide was further confirmed by HRMS spectroscopy, in HRMS (ESI-MS): *m/z* calculated for $C_{62}H_{66}O_{11}[M+Na]^+$: 1009.4503; Found: 1009.4509. Similarly, compound **6** was confirmed by the NMR and mass spectral analysis. In the $^1H$ NMR spectrum, two anomeric protons were recognized at δ 4.98 ppm (d, $J$ = 7.9 Hz, 1H) and δ 4.94 ppm (d, $J$ = 3.7 Hz, 1H), indicating the *β*- and *α*- linkages respectively, rest of the ring (sugar ring) protons resonated between δ 6.07 - 3.79 ppm. Thirty-five aromatic benzoyl ring protons appear between δ 8.15 - 7.26 ppm, and three methoxy protons were noticed at δ 3.10 ppm as a singlet. Further characterised by mass analysis: in HRMS (ESI-MS): *m/z* calculated for $C_{62}H_{52}O_{18}$ $[M+Na]^+$: 1084.3154; Found: 1084.3148 confirmed the disaccharide **6**.

**3.2.2 – Mechanistic investigation of glycosylation**

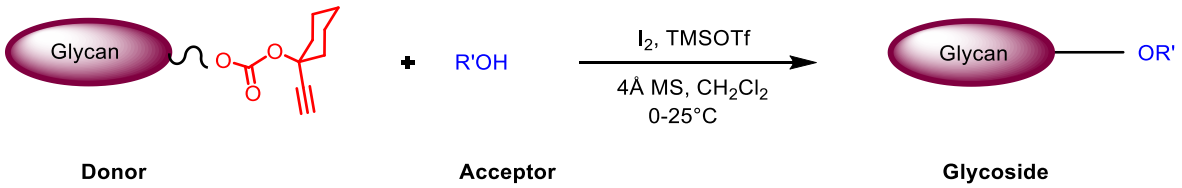
Mechanistically, co-ordination of molecular iodine to the alkyne would activate the ethynyl cyclohexyl carbonate, producing iodonium species that would be attacked by carbonyl oxygen atom resulting in the extrusion of cyclized iodine-containing extruded product, which was characterised by Single Crystal X-ray Diffraction (SCXRD)[24] and intermediate **A** would then be available for the attack of the acceptor **2** in a non-stereoselective fashion to afford an anomeric mixture of disaccharide **3**. Intermediate **A** (oxocarbenium ion) remains in equilibrium with

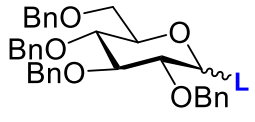
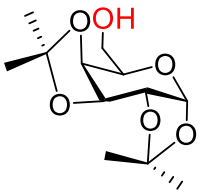
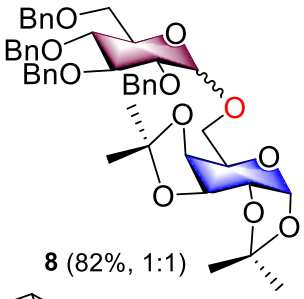
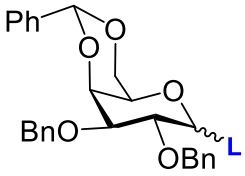
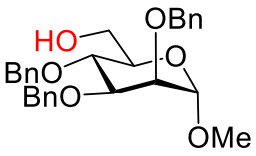
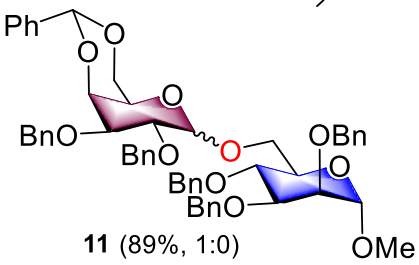
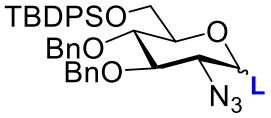
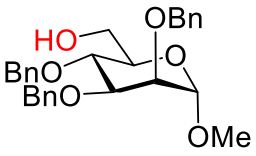
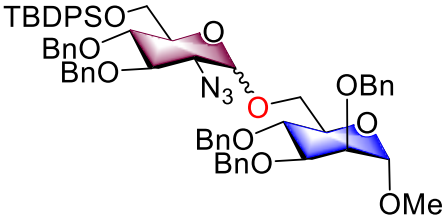
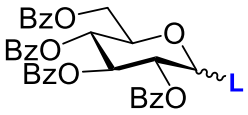
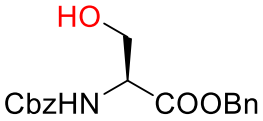
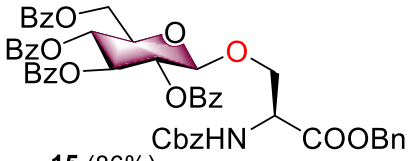


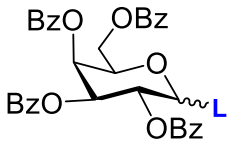

***Scheme 3.13:*** *plausible mechanism for the activation of ethynyl cyclohexyl carbonate glycoside by $I_2$/TMSOTf*

intermediate **B** (trioxolenium ion), if any ester participating group is present at C-2 position, that would be amenable for the attack by the acceptor **5** in a 1,2-*trans* selective fashion to produce disaccharide **6**. The stereoselectivity of the reaction is independent of anomeric ratio of the starting material (donor's stereochemistry). The protodeauration step in Au-catalysed glycosylation reaction was absent in this mechanism, hence, this metal-free activation requires stoichiometric quantities of molecular iodine (**Scheme 3.13**).

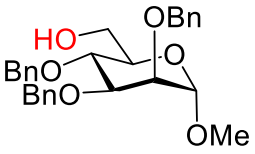
### 3.2.3 – Substrate scope for *O*-glycoside



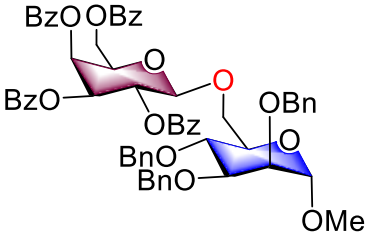
| Donor | Acceptor | Glycoside (yield, $\alpha$:$\beta$ ratio) |
|---|---|---|
|  **1** |  **7** |  **8** (82%, 1:1) |
|  **9** |  **10** |  **11** (89%, 1:0) |
|  **12** |  **10** |  **13** (91%, 3:1) |
|  **4** |  **14** |  **15** (86%) |



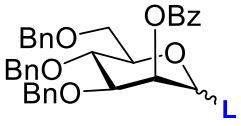

**16**



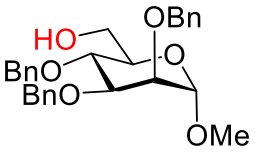

**10**



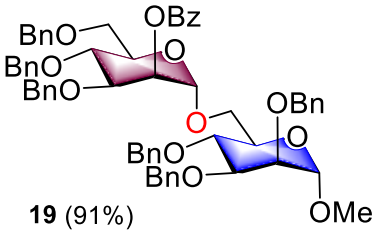

**17** (90%)



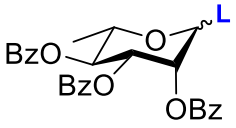

**18**



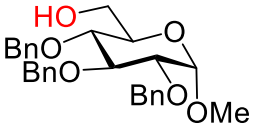

**10**



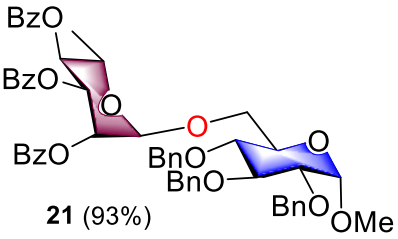

**19** (91%)



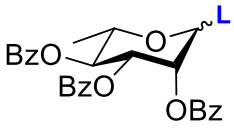

**20**



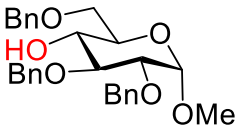

**2**



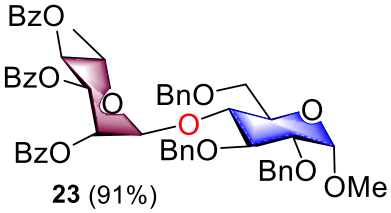

**21** (93%)



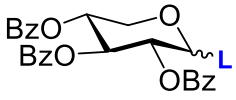

**20**



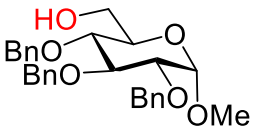

**22**



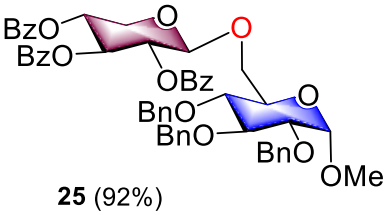

**23** (91%)



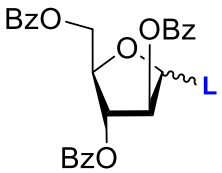

**24**



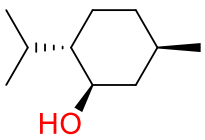

**2**



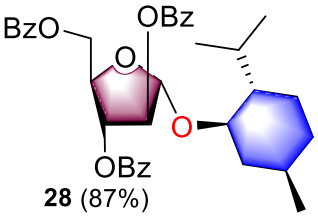

**25** (92%)



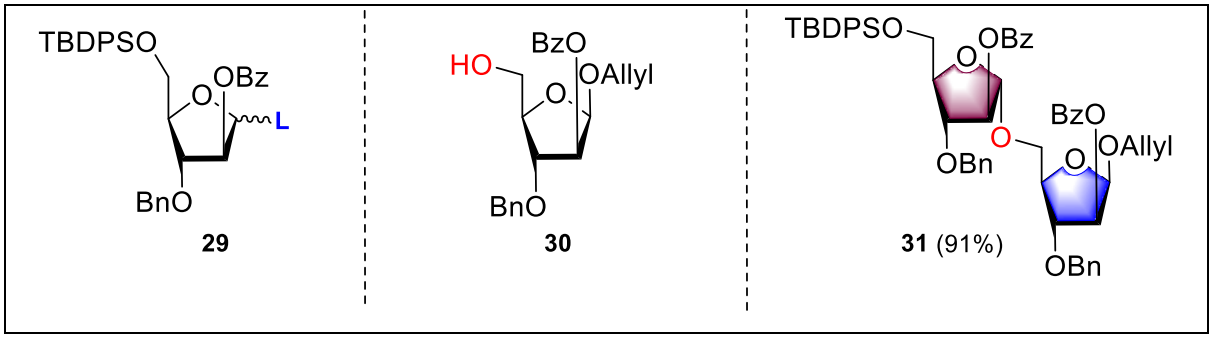

**26**




**27**




**28** (87%)




***Scheme 3.14:*** *Substrate scope for the O-glycosylation*

After optimization of the reaction conditions for the iodine-catalyzed glycosylation reaction, we moved forward towards the substrate scope for the generalization of the method. For example, the utility of this metal-free activation of glycosyl donors was evaluated with the plethora of donors (**1**, **4**, **9**, **12**, **16**, **18**, **20**, **24**, **26**, **29**) comprising all sorts of donors, pyranosyl (**1**, **4**, **9**, **12**, **16**, **18**, **20**, **24**), furanosyl (**26**, **29**) derived from pentoses as well as hexoses. The reaction was well-suited with different reacting partners and glycosyl donors were successfully glycosylated with different acceptors (**2**, **7**, **10**, **14**, **22**, **27**, **30**), to produce a broad range of *O*-glycosides (**8**, **11**, **13**, **15**, **17**, **19**, **21**, **23**, **25**, **28**, **31**). Interestingly, different functional groups: benzylidene, silyl-ether, iso-propylidene, Cbz, and allyl, tolerated well during the glycosylation reaction. All the donors having C2-benzyl protection afforded a mixture of 1,2-*cis* and 1,2-*trans* glycoside (**8**, **11**, **13**), whereas those embedded with C2-benzoate produced 1,2-*trans* glycoside (**15**, **17**, **19**, **21**, **23**, **25**, **28**, **31**) in a stereoselective fashion (**Scheme 3.14**). All the synthesized glycosides were confirmed by NMR, mass, and IR spectroscopic analysis. Thus, proton NMR confirmed that disaccharide **8** contains two isomers $\alpha$ & $\beta$ in a 1:1 ratio. Further, the appearance of forty aromatic protons was noticed between δ 7.44 – 7.13 ppm, forty-four protons from the pyranosyl ring and benzylic (-$CH_2$-) resonates between δ 5.57 – 3.41 ppm, and twenty-four methyl protons of iso-propylidene groups were noticed between δ 1.53 – 1.28 ppm. Moreover, in $^{13}C$ NMR spectrum, eight quaternary carbons of the benzyl protecting groups show its presence between δ 139.0 - 138.1 ppm, rest of the forty aromatic carbons were noticed between δ 128.7-127.6 ppm, quaternary carbons of iso-propylidene in between δ 109.5, 109.3, 108.7, and 108.7 ppm, however, characteristic anomeric carbons resonate at δ 104.5, 97.2, 96.5, 96.4 ppm as per our expectation, rest of the carbons from pyranosyl ring and benzylic (-$CH_2$-) positions resonates between δ 84.7 - 65.8 ppm, and methyl protons were observed at δ 26.3, 26.2, 26.2, 26.1, 25.1, 25.0, 24.8, and 24.6 ppm and finally, disaccharide **8** was confirmed by HRMS analysis. In HRMS (ESI-MS): m/z calculated for

$C_{46}H_{54}O_{11}[M+Na]^+$: 805.3564; Found: 805.3566. Similarly, compound **11** was confirmed by NMR, HRMS, and IR spectroscopy; in the proton NMR spectrum, thirty aromatic protons were identified between δ 7.54 – 7.23 ppm, one proton of benzylidene appeared at δ 5.44 ppm as a singlet along with other pyranosyl ring protons and benzylic (-$CH_2$-) protons were noticed from δ 5.10 ppm to 3.79 ppm, and three protons of methyl group at the reducing end of the disaccharide **11** come into sight at δ 3.19 ppm as a singlet for three protons. Furthermore, in the $^{13}C$ NMR spectrum, quaternary carbons of the benzyl and benzylidene protecting groups were seen at δ 138.9, 138.9, 138.8, 138.6, 138.3, and 138.0 ppm, thirty carbons from aromatic rings were noticed between δ 129.0-126.5 ppm, characteristic peak of benzylidene protecting group was noticed at δ 101.2 ppm, two anomeric carbons from disaccharide **11** were observed at δ 99.0 & 98.1 ppm, other pyranosyl rings and benzylic (-$CH_2$-) carbons were seen in between δ 80.4 - 62.7 ppm, and one carbon from methyl at the anomeric position of the disaccharide δ 54.7 ppm. Mass spectral analysis by HRMS further confirmed the disaccharide **11** - HRMS (ESI-MS): m/z calculated for $C_{55}H_{58}O_{11}$ $[M+Na]^+$: 917.3877; Found: 917.3876. Further compound **13** was also fully characterized by IR, NMR, and mass spectroscopy. In the IR spectroscopy, the signature peak at 2109 $cm^{-1}$ indicated that the azide functionality remained intact during the reaction in disaccharide **13**. Protected serine amino acid **14** was successfully glycosylated with per-*O*-benzoate glucopyranosyl carbonate donor **4** to yield glycosylated product **15**, characterized by IR, NMR, and mass spectroscopy. In the proton NMR spectrum, eight ortho protons from four benzoate protecting groups appear between δ 8.01- 7.81 ppm, other twenty-two aromatic protons resonate between δ 7.55 - 7.26 ppm, anomeric proton of the compound **15** was noticed at δ 4.78 ppm as a doublet with coupling constant $J$ = 7.9 Hz (between H-2 and anomeric proton). In the $^{13}C$ NMR spectrum, four characteristic peaks at δ 166.2, 165.9, 165.2, 165.2 ppm represent the carbonyl carbon of the benzoate protection in the ring, carbonyl carbon of ester functionality in amino-acid was observed at δ 169.4 ppm, however, carbonyl carbon of the Cbz protecting group resonate at δ 156.0 ppm, all the aromatic carbons resonate in between δ 136.3 - 128.2 ppm, characteristic anomeric carbon seen at δ 101.4 ppm, carbon between N- and C-terminal resonate at δ 54.4 ppm. Similarly, all the other glycosides were also thoroughly characterized by IR, NMR, and Mass spectroscopy.

### 3.2.4 – Introduction of nucleosides

After successful synthesis of a library of compounds utilising the newly developed methodology, we were highly motivated to explore it for the synthesis of *N*-glycosides. In this regard, we targeted the synthesis of nucleosides. Nucleosides are composed of a nucleobase (such as adenine, guanine, cytosine, thymine, or uracil) and a sugar residue (ribose or deoxyribose), which have various applications in different fields. Some of the notable applications are mentioned herein.

Antiviral Drugs: Several synthesised nucleoside analogs are in use as antiviral drugs. These analogs can interfere with viral replication by incorporating into the viral DNA or RNA during synthesis, leading to termination of the viral chain. Acyclovir and ganciclovir are some examples of antiviral drugs used for the treatment of herpes and cytomegalovirus infections, respectively.[25]

**Cancer Therapy:** Nucleoside analogs play a crucial role in chemotherapy for treating cancer. Drugs like cytarabine, gemcitabine, and fluorouracil (5-FU) are commonly used in the treatment of various types of cancers. They inhibit DNA synthesis and induce cell death in rapidly dividing cancer cells.[26]

**Research Tools:** Nucleosides are widely used in biochemical and molecular biology research. They serve as building blocks for the synthesis of nucleotides, which are essential components of DNA and RNA. Nucleosides labelled with radioactive isotopes or fluorescent dyes are often employed to study DNA replication, transcription, translation, and other cellular processes.[27]

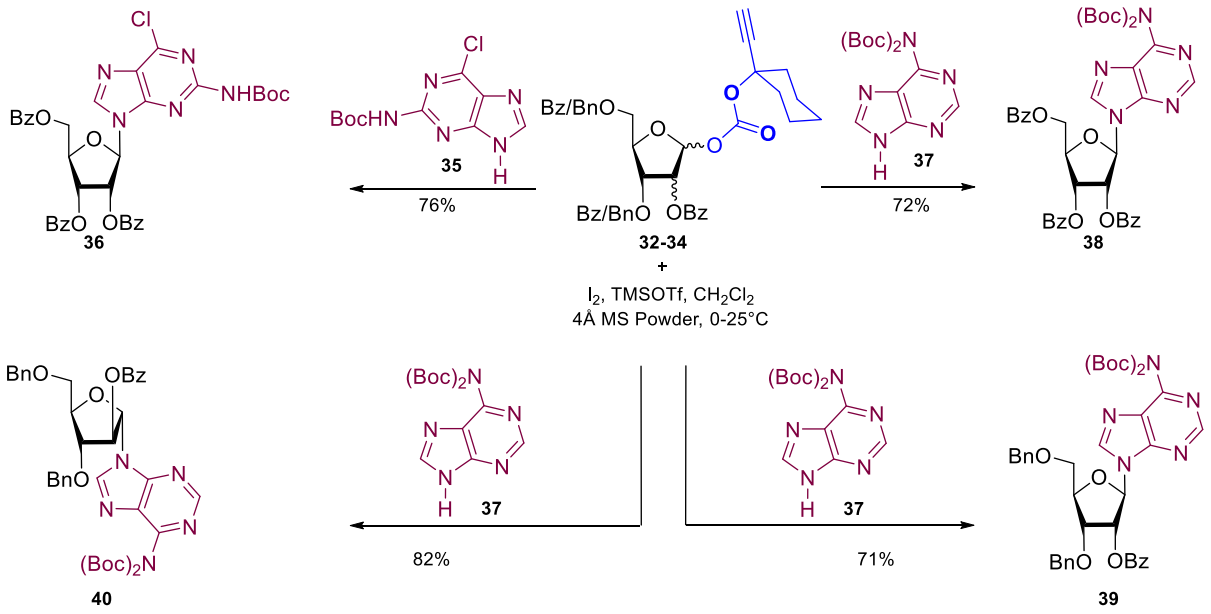
**Diagnostic Techniques:** Nucleosides are employed in diagnostic techniques like polymerase chain reaction (PCR) and DNA sequencing. In PCR, nucleoside triphosphates (dNTPs) are used as substrates for DNA synthesis, enabling amplification of specific DNA sequences. In DNA sequencing, dideoxy nucleotides (modified nucleosides lacking a 3'-OH group) are utilized to terminate DNA synthesis at specific positions, enabling the determination of the DNA sequence.[28]

**Nucleic Acid Therapeutics:** Modified nucleosides are used in the development of nucleic acid-based therapeutics. For instance, nucleoside analogs can be incorporated into therapeutic oligonucleotides (such as antisense oligonucleotides and siRNA) to enhance their stability, specificity, and delivery to target cells.[29]

### 3.2.5 – Utility of current glycosylation protocol in chemical synthesis of nucleosides

To demonstrate the utility of the metal-free activation, we have investigated the synthesis of purine and pyrimidine nucleosides. Accordingly, easily accessible benzoylated ribofuranosyl (Rib*f*) carbonate donor **32** was treated with the Bis-Boc-protected adenine derivative **37** to

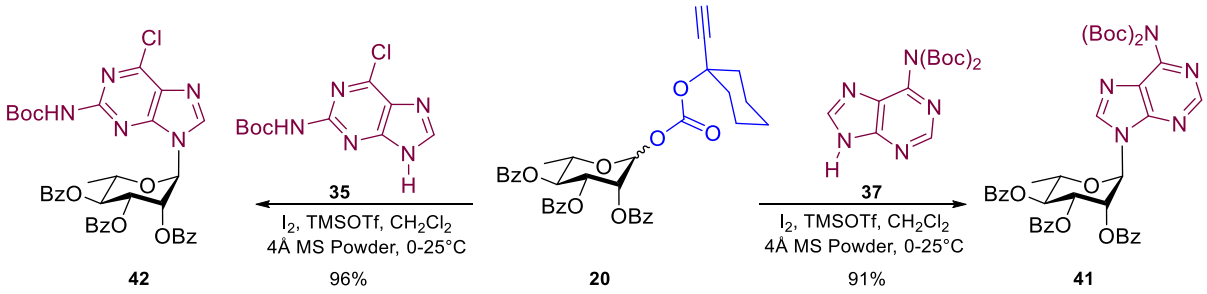
afford the adenosine **38** in 72% yield. The presence of bis-Boc moiety serves the dual role of increasing the solubility of the nucleobase in dichloromethane and N7/N9-regioselectivity in favour of N9-regioselectivity.[30] The metal-free activation of alkynyl glycosyl carbonate donor **32** produced the chloropurine derivative **36** in 76% yield. Furthermore, nucleosides containing 2'-modifications are important for *si*RNA-based therapeutics and probes. In a separate set of experiments, easily synthesized super-armed donor ribofuranosyl carbonate **33** produced the adenosine derivative **39** in 71% yield, and glycosylation of super-armed arabinose **34** with adenosine yielded unnatural nucleoside **40** in 82% yield (**Scheme 3.15**).




***Scheme 3.15:*** *Synthesis of purine N-glycosides*

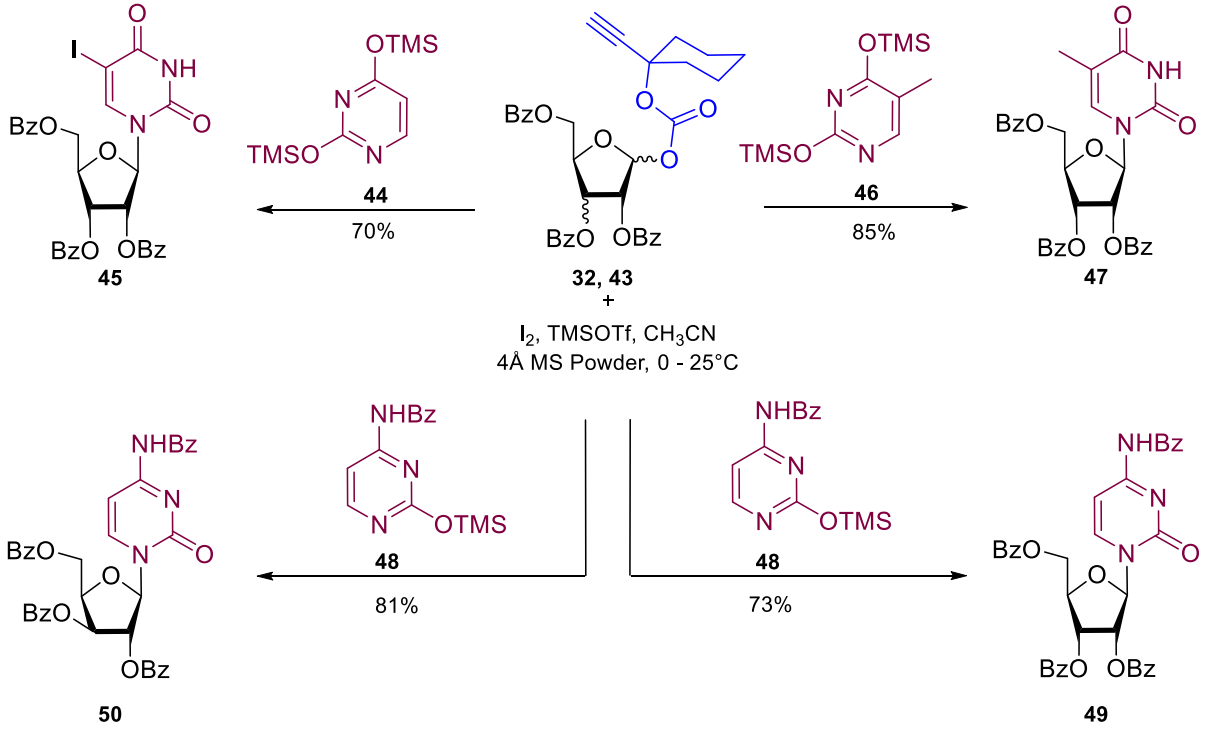
All the N-glycosides (nucleosides) were characterized by NMR and Mass spectroscopy. In the proton NMR spectrum of compound **38**, two aromatic protons of aromatic ring (of nucleobase) were noticed as two singlets at δ 8.76 and 8.24 ppm. Three benzoyl rings (six ortho-proton) protons resonate at δ 8.12 - 7.90 ppm as doublet of two protons, other benzoyl ring protons appears between δ 7.61 - 7.34 ppm. All the furanosyl ring protons were assigned between δ 6.53 - 4.70 ppm, however, eighteen protons from $^{tert}$butyl group were noticed at 1.43 ppm. In the $^{13}$C NMR spectrum of compound **38**, three carbonyl carbons from benzoyl protecting group resonated at δ 166.2, 165.3, and 165.0 ppm. Four quaternary carbons (two from carbonyl carbons of Boc-protecting group and two carbons from nucleobase rings) were noticed at δ 152.9, 152.5, 150.7, and 150.3 ppm, non-quaternary carbons (=CH-) from nucleobase ring were

observed at δ 152.5 and 143.3 ppm, other aromatic carbons resonate between δ 134.0 - 128.5 ppm. Anomeric carbon was marked at δ 87.1 ppm, two quaternary carbons from Boc-protecting group resonated at δ 84.0 ppm, furanosyl ring carbons were observed between δ 81.0 - 63.7 ppm, and six methyl carbons from two Boc- protecting group at δ 27.9 ppm. In HRMS (ESI-MS): m/z calculated for $C_{41}H_{41}N_5O_{11}$ $[M+H]^+$: 780.2881; found: 780.2889. Similarly other nucleosides were characterized.




***Scheme 3.16:*** *Synthesis of non-natural purine N-glycosides*

This glycosylation protocol was also tested for the synthesis of the non-natural *N*-glycosides synthesis. In this direction, L-rhamnopyranosyl donor **20** was glycosylated with di-Boc-protected adenine **37** to afford glycosylated *N*-glycoside **41** in 91% yield, Further, same donor was glycosylated with 2-amino-6-chloropurine derivative **35**, afforded the non-natural nucleoside **42** in 96 % yield. Notably, yield obtained for non-natural nucleoside was higher than the yield of natural nucleosides (**Scheme 3.16**).




***Scheme 3.17:*** *Synthesis of pyrimidine N-glycosides*

Other than purine nucleosides, we also synthesized pyrimidine nucleosides. It is well known that pyrimidines are less soluble in the organic solvent. To make pyrimidines soluble, *N*, *O*-Bis-(Trimethylsilyl) trifluoroacetamide (BSTFA) was added into pyrimidines before glycosylation, which silylate these bases and make them soluble in acetonitrile solvent. After the silylation of nucleobase, a donor and activator were added to the reaction mixture for further reaction.

When benzoylated donor **32** was added into the silylated uracil **44**, surprisingly, 5-iodouridine derivative **45** was obtained in 70% yield as a glycosylated product that can be utilized for the further exploration to many important chemical probes through the Sonogahira coupling.[31] However, glycosylation between the donor **32** and silylated thymine derivative resulted in the benzoylated thymidine **47** in 85% yield. Similarly, donor **32** produces the cytidine derivative **49** in 73% yield after glycosylation with silylated cytosine **48**. Non-natural nucleoside was also synthesized by glycosylation of donor **43** (xylofuranosyl donor) and silylated cytosine **48** in 81% yield. Compound **45** was first characterized by NMR analysis; in proton NMR, one of the ring protons was missing from the uracil ring, and $^{13}C$ NMR confirmed that one extra quaternary carbon was noticed δ 70 ppm, which is possible only if iodine is attached to the uracil ring. The mass analysis confirmed the presence of iodine; HRMS (ESI-MS): m/z calculated for $C_{30}H_{23}IN_2O_9$ $[M+H]^+$: 683.0527; found: 683.0533.

Compound **47** was also fully characterized. In $^1H$ NMR of compound **47**, an anomeric proton was noticed at δ 6.43 ppm as a doublet of a proton with a coupling constant of $J$ = 6.3 Hz. Three methyl protons of thymine ring resonate at δ 1.59 ppm, which shows four bound coupling with ring proton and appears as a doublet with coupling constant $J$ = 1.3 Hz. In $^{13}C$ NMR, anomeric carbon appears at δ 87.0 ppm, quaternary carbon next to the methyl in the thymine ring was seen at δ 112.3 ppm, and methyl carbon was noticed at δ 12.2 ppm. Thymidine derivative was also confirmed by HRMS (ESI-MS) spectroscopy; m/z calculated for $C_{31}H_{26}N_2O_9$ $[M+H]^+$: 571.1717; found: 571.1733.

Moreover, in $^1H$ NMR, of cytidine derivative **49**, anomeric proton resonates at δ 6.46 ppm as a doublet with vicinal coupling constant $J$ = 4.6 Hz and NH proton was noticed at δ 8.81ppm. In $^{13}C$ NMR, anomeric carbon was observed at 89.6 ppm, compound **49** was further confirmed by mass analysis, in HRMS (ESI-MS): m/z calculated for $C_{37}H_{29}N_3O_9$ $[M+H]^+$: 660.1982; found: 660.1987. Similarly, compound **50** was well characterized.

### 3.2.6 – Synthesis of pentasacchride repeating unit of *Klebsiella Pneumoniae (O-3-Antigen)*

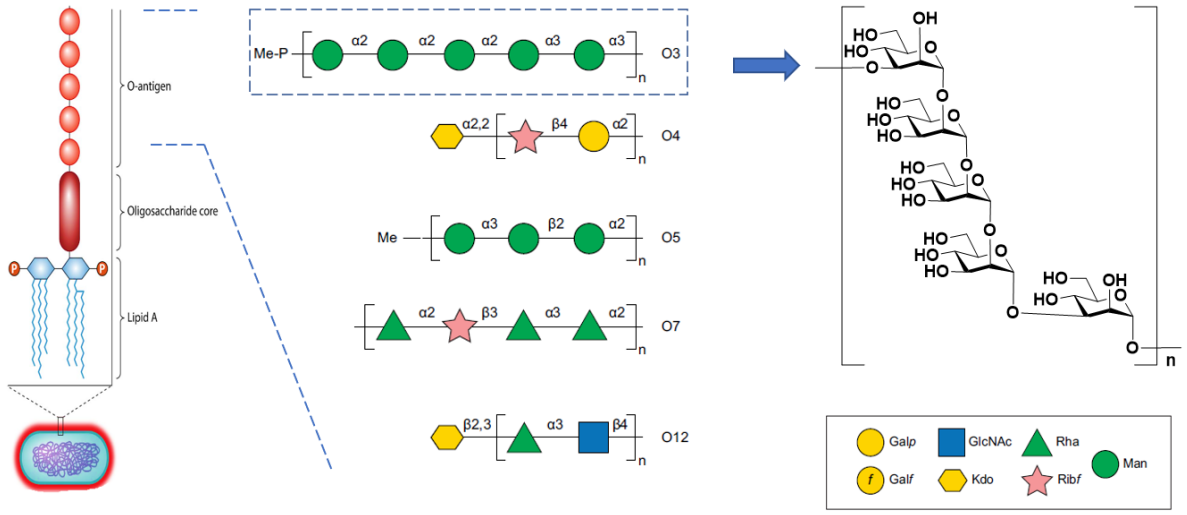
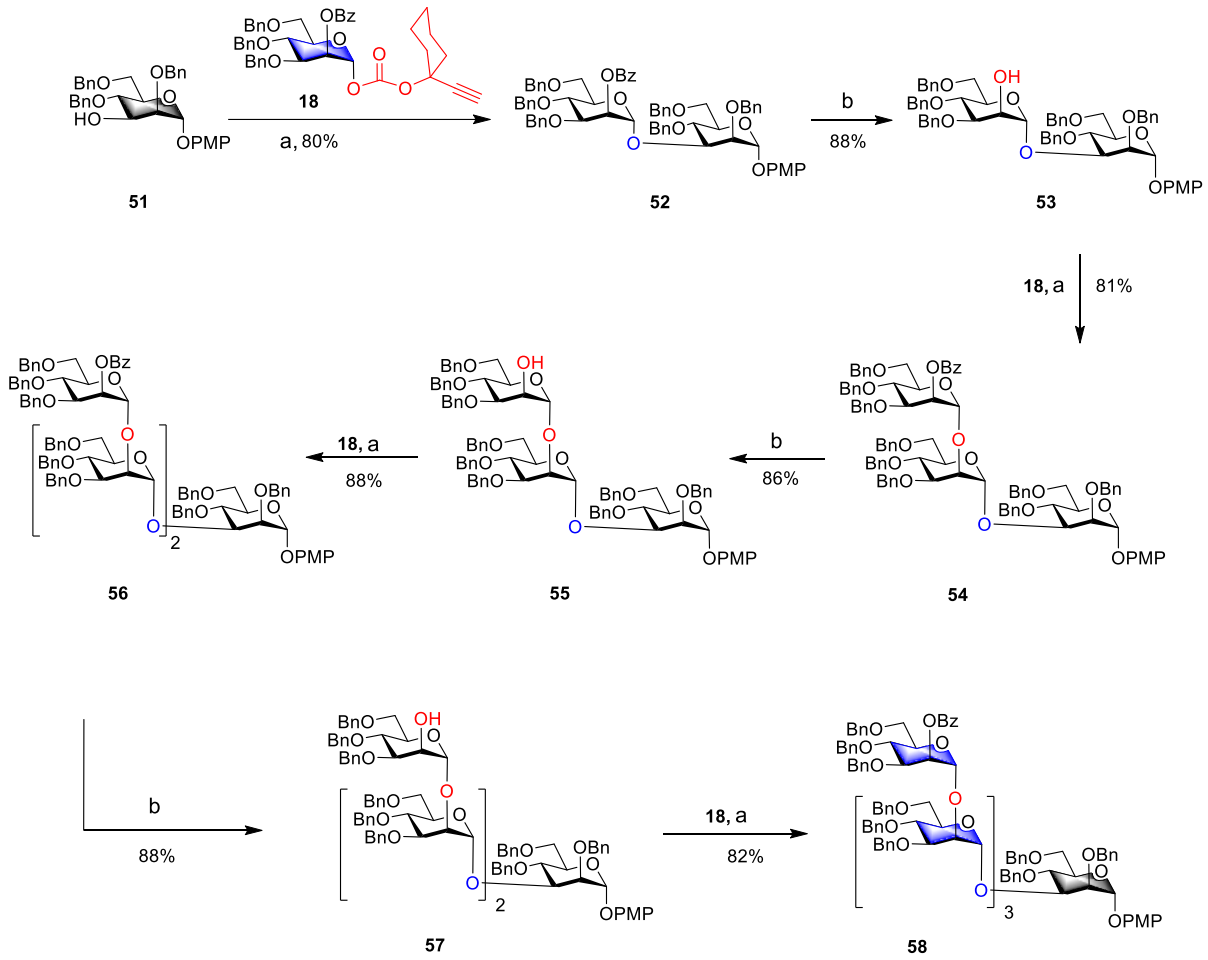



***Figure 3.1:*** *Pentasaccharide repeating unit of Klebsiella Pneumoniae (O-3-Antigen)*

Experience and successful synthesis of the glycosides, disaccharides and nucleosides has encouraged us to apply metal free activation of alkynyl glycosyl carbonate donor to the synthesis of a pentasaccharide motif reminiscent of *Klebsiella Pneumoniae* (O-3 antigen). *Klebsiella pneumoniae* is responsible for the wide range of infections, including pneumonias, urinary tract infections, bacteremias, and liver abscesses. *K. pneumoniae* strains have become increasingly resistant to antibiotics, so infection cause by these strains is challenging to treat.[32] So, vaccine development is an alternative initiative to combat this challenge, here we targeted the synthesis of the pentasaccharide repeating unit of O-3-antigen of *K. pneumoniae,* which can be a vaccine candidate for the treatment of the disease caused by *Klebsiella Pneumoniae*. To this end, we started the synthesis of targeted pentasaccharide **58** with glycosylation of donor **18** with easily accessible acceptor **51**[33] to achieve disaccharide **52** with 80% glycosylated yield, subsequently, saponification under zemplén condition, and converted into disaccharide acceptor **53** in 88% yield, which was again glycosylated with glycosyl donor **18** to access trisaccharide **54** in 81% yield. Further, saponified under zemplén condition furnished trisaccharide acceptor **55** in 86% yield. Furthermore, one more cycle of glycosylation with donor **18** → saponification → glycosylation with donor **18** afforded the desired pentasaccharide **58** in a very facile manner with an overall yield of 37% from monosaccharides donor and acceptor (**Scheme 3.18**).




(a) $I_2$ (1.5eq.), TMSTOf (0.5eq.), $CH_2Cl_2$, 4Å MS (b) NaOMe (0.2eq.), MeOH: $CH_2Cl_2$ (3:1)

***Scheme 3.18:*** *Synthesis of Pentasaccharide repeating unit of O-3-Antigen*

Pentasaccharide **58** was fully characterised by NMR and mass analysis. In $^1$H NMR; five anomeric protons resonate between δ 5.77 - 5.11 ppm, characteristic ortho protons of two benzoate group were noticed at δ 8.07 ppm, two set of two protons form PMP protection at anomeric position were observed at δ 6.91 ppm and 6.73 ppm. In $^{13}$C NMR; presence of benzoate was confirmed by a peak at δ 165.5 ppm which belongs to the carbonyl carbon of benzoate group. Two quaternary carbons of PMP were noticed at δ 155.0 and 150.6 ppm. Fifteen benzyl quaternary carbons were seen between δ 138.8 - 138.2 ppm. Five anomeric carbons at δ 101.4, 101.2, 100.8, 99.6, and 96.5 ppm confirmed the pentasaccharide. Further, pentsaccharide **58** was confirmed by mass analysis, in HRMS (ESI-MS); m/z calculated for $C_{149}H_{152}O_{28}$ $[M+Na]^+$:2413.0401; found: 2413.3660.

**3.3- Conclusion:** In summary, stable easily accessible and versatile alkynyl glycosyl donors were activated under metal-free conditions using stoichiometric quantity of readily available molecular iodine and TMSOTf. The extrusion product resulting from the carbonate moiety was

characterised by the SCXRD. Apart from the use of stoichiometric quantities, glycosylations happen in a smooth manner producing glycosides, disaccharides, and nucleoside in a very simple fashion. The reaction conditions are tolerated well by the most of the protecting groups (benzyl, benzoyl, TBDPS, benzylidene acetal, iso-propylidene). The glycosylation produced anomeric mixture when C2-position of the donor was occupied by the benzyl ethers or azide; whereas, 1,2-trans glycosides were obtained stereoselective when the C2-position was equipped with the participating benzoates owing to the anchimeric assistant. Finally, the utilised of synthesis of a pentasaccharide motif reminiscent of *Klebsiella Pneumoniae* (O-3 antigen). These results demonstrate that the alkynyl glycosyl carbonates can be activated by combination of readily available $I_2$ and TMSOTf.

### 3.2.7 – Experimental section

**General Procedure A:** Synthesis of 1-ethynylcyclohexyl carbonate donors (**1**, **4**, **9, 12, 16, 18, 20, 24, 26, 29**): To a solution of dichloromethane (6 mL/g) hemiacetals (for preparation procedure – see **Table S1**) (1.0 mmol), 1-ethynylcyclohexyl (4-nitrophenyl) carbonate (**S1**) (1.2 mmol) and DMAP (1.2 mmol) were added and stirred for 4 h at 25 °C. After complete conversion of the hemiacetals as adjudged by the TLC analysis, the reaction mixture was diluted by adding $CH_2Cl_2$ and washed with aqueous saturated $NaHCO_3$ to remove the 4-nitrophenol. Combined organic layers were dried over anhydrous sodium sulphate, filtered and the filtrate was concentrated *in vacuo* to obtain an oily residue that was purified by silica gel column chromatography (Petroleum ether /EtOAc) to obtain pure ethynyl cyclohexyl carbonate donors (**1**, **4**, **9, 12, 16, 18, 20, 24, 26, 29**) in more than 90% yield.

| Compound | Reference |
|---|---|
| **S1** | B. Mishra, M. Neralkar, S. Hotha, *Angewandte Chemie International Edition* **2016**, *128*, 7917 –7922 |
| **Hemiacetal of 16** | A. E. Vigo, A. C. Stortz, C. Marino, *Beilstein J. Org. Chem.* **2019,** *15,* 2982–2989 |
| **18**, **29** | M. Islam, G. P. Shinde, S. Hotha, *Chem. Sci.* **2017**, *8*, 2033–2038. |
| **12** | G. Walke, N. Kasdekar, Y. Sutar, S. Hotha, *Commun. Chem*. **2021**, *4*, 15. |
| **Hemiacetal of 26** | N. Kasdekar, G. Walke, K. Deshpande, S. Hotha, *J. Org. Chem.,* **2022**, *87*, 5472−5484. |
| **24** | B. Mishra, S. Manmode, G. Walke, S. Chakraborty, M. Neralkar, S. Hotha, *Org. Biomol. Chem.* **2021**, *19*, 1315-1328. |
| **Hemiacetal of 32** | D. Lengeler, K. Weisz, *Tetrahedron Letters* **2001**, *42*, 1479–1481 |
| **Hemiacetal 33** | Chakraborty, S., Mishra, B., Das, P. K., Pasari, S., & Hotha, S. *Angewandte Chemie International Edition* **2023**, *62*(6), e202214167. |

***Table S1.*** *Literature reference for the synthesis of hemiacetals*

**General Procedure B:** General procedure for *O*-glycosides synthesis (**3**, **6**, **8, 11, 13, 15, 17, 19, 21, 23, 25, 28, 31, 52, 54, 56, 58**): To a solution of glycosyl donor (1.0 mmol) and glycosyl acceptor (1.0 mmol) in anhydrous $CH_2Cl_2$ (3 mL/g of donor), activated 4Å MS powder was added and stirred for 15 min, molecular iodine (1.5 mmol) and TMSOTf (0.1 mmol for armed

donors, 0.5 mmol for disarmed donor) were added and stirred for 30 min. Triethylamine was added to quench the reaction, filtered through a bed of Celite®, the filtrate was concentrated *in vacuo*, and purified by silica gel column chromatography (Petroleum ether/EtOAc).

**General Procedure C:** General procedure for purine nucleosides syntheses (**36**, **38**, **39**, **40**): Glycosyl donor (1.0 mmol) and protected purine base (1.0 mmol) were dissolved in anhydrous $CH_2Cl_2$ (6 mL/g of donor) containing freshly activated 4Å MS powder. After stirring for 15 min, molecular iodine (1.5 mmol) and TMSOTf (0.5 mmol) were introduced into the reaction mixture, continued stirring for 3 h. Triethylamine was added to arrest the reaction, filtered through a bed of Celite®, the filtrate was concentrated *in vacuo* and the resulting residue was purified by silica gel column chromatography (Petroleum ether /EtOAc).

**General Procedure D:** General procedure for pyrimidine nucleosides syntheses (**45**, **47**, **49, 50**): To a suspension of pyrimidine base (1.5 mmol) in acetonitrile (10 mL/g of donor), BSTFA (4.0 mmol) was added and stirred vigorously at 25 °C for 30 min or until a clear solution was noticed. In a separate round bottom flask, glycosyl donor (1.0 mmol) and activated 4Å MS powder in acetonitrile solvent was stirred for 15 mins under nitrogen atmosphere and the above prepared silylated nucleobase was cannulated into this flask. The reaction vessel was cooled to 0 °C, $I_2$ (1.5 mmol) and TMSOTf (0.5 mmol) was added, reaction temperature was warmed to the room temperature (25 °C) and stirred for another 3 h. Triethylamine was added to arrest the reaction, passed through a pad of Celite®, the filtrate was concentrated *in vacuo*, and purified by silica gel column chromatography (Petroleum ether/EtOAc).

**Synthesis of acceptor:** All the acceptors were synthesised according to the know literature.

| Acceptor | Reference |
|---|---|
| **2**,**5** | V. Dimkos, S. M. Taylor, *Chem. Rev*. **2018**, *118*, 11457−11517. |
| **22** | A. Gucchait, M. Kundu, T. Manna. P. Shit, A. K. Mishra, A. K., *Eur. J. Org. Chem*. **2020**, 3398–3409. |
| **10** | A. Kayastha, S. Hotha, *Chem. Commun.* **2012**, *48*, 7161-7163. |
| **7** | P. J. Meloncelli, T. M. Williams, P. E. Hartmann, R. V. Stick, *Carbohydrate Res.* **2007**, *342,* 1793–1804. |
| **30** | M. Islam, G. P. Shinde, S. Hotha, *Chem. Sci.* **2017**, *8*, 2033–2038. |
| **14** | M. Emmadi, S. S. Kulkarni, *Org. Biomol. Chem.* **2013**, *11*, 3098–3102. |
| **27** | Purchased from Sigma Aldrich |
| **35**, **37** | Q. Zhang, J. Sun, Y. Zhu, F. Zhang, B. Yu, *Angew. Chem. Int. Ed.* **2011**, *50*, 4933-4936 |

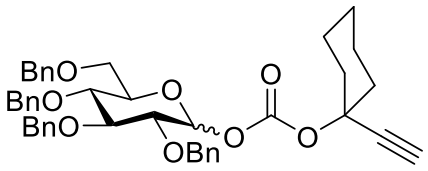
***Table S2.*** *Literature references for the synthesis of acceptors*

**General procedure for saponification under Zemplén conditions (53, 55, 57):** Benzoyl protected compound (1 mmol) was dissolved in 10 mL of 1:3 $CH_2Cl_2$: MeOH mixture, sodium

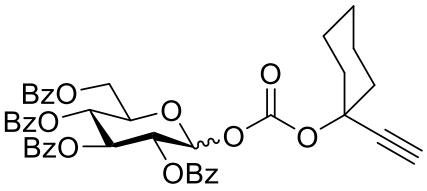
methoxide (0.2 mmol) was added into it and stirred for 30 min. After completion of the reaction, reaction mixture was passed through an acidic resin (Amberlite® IR 120 ($H^+$)) for neutralization, concentrated under vacuum, and purified by silica gel column chromatography (Petroleum ether/EtOAc) to get desired saponified compounds **53**, **55**, **57**.

### 3.2.8 - Compound characterisation data

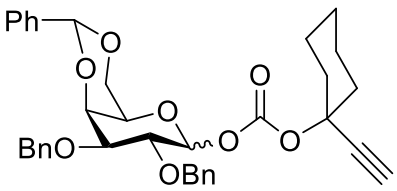
1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,4,6-tetra-*O*-benzyl α/β-D-glucopyranoside [α:β : 1:2] (**1**): Syrup; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 1.0): +29.7°; IR ($cm^{-1}$, $CHCl_3$): 3288, 3030, 2862, 1761, 1496, 1452, 1359, 1267, 1238, 1146, 1074, 1012, 902, 735, 697; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.26 (m, 36H), 7.16 (m, 4H), 6.23 (d, *J* = 3.5 Hz, 1H), 5.52 (d, *J* = 8.1 Hz, 1H), 4.94 (m, 2H), 4.88 – 4.82 (m, 4H), 4.81 (s, 1H), 4.77 (d, *J* = 2.7 Hz, 1H), 4.74 (d, *J* = 3.2 Hz, 1H), 4.70 – 4.59 (m, 3H), 4.58 – 4.53 (m, 2H), 4.53 – 4.46 (m, 2H), 4.02-3.93 (m, 1H), 3.79-3.69 (m, 8H), 3.66-3.57 (m, 3H), 2.62 (s, 1H), 2.60 (s, 1H), 2.26 – 2.10 (m, 4H), 1.92 (m, 4H), 1.74 – 1.62 (m, 6H), 1.53 (m, 2H), 1.33 (m, 4H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 151.5, 151.6, 138.8, 138.5, 138.3, 138.2, 138.1, 138.1, 138.0, 137.8, 128.6, 128.5-128.5(17C), 128.3-128.2(4C), 128.1-127.8(19C), 97.6, 93.7, 84.7, 83.0, 82.7, 81.6, 81.1, 79.1, 78.4, 78.0, 75.9(3C), 75.3, 75.3, 75.2, 75.2, 75.1(2C), 73.6, 73.6, 73.3, 73.0, 68.2, 68.2, 36.9(2C), 36.8, 36.7, 25.1(2C), 22.6(4C); HRMS (ESI-MS): m/z: calcd for $C_{43}H_{46}O_8$ $[M+Na]^+$: 713.3090; Found: 713.3090.



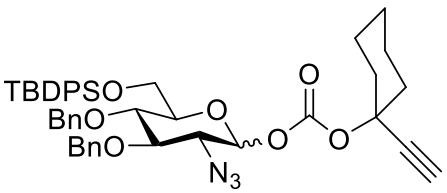

1-*O*-(((1-ethynylcylcohexyl)oxy)carbonyl)-2,3,4,6-tetra-*O*-benzoyl α/β-D-glucopyranoside [α:β : 1:1](**4**): mp (ºC): 62.5; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 1.0): +41.6°; IR ($cm^{-1}$, $CHCl_3$): 3020, 2941, 2866, 1731, 1451, 1265, 1214, 1092, 1026, 901, 744, 708, 667; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.05 (m, 4H), 8.00 – 7.81 (m, 12H), 7.59 – 7.47 (m, 7H), 7.46 – 7.40 (m, 5H), 7.40 – 7.37 (m, 3H), 7.37 – 7.33 (m, 5H), 7.33 – 7.27 (m, 4H), 6.51 (d, *J* = 3.7 Hz, 1H), 6.23 (t, *J* = 10.0 Hz, 1H), 6.02 (d, *J* = 8.0 Hz, 1H), 5.94 (t, *J* = 9.5 Hz, 1H), 5.81 – 5.73 (m, 2H), 5.72 – 5.64 (m, 1H), 5.56 (dd, *J* = 10.3, 3.7 Hz, 1H), 4.70 – 4.58 (m, 3H), 4.48 (m, 2H), 4.30 (m, 1H), 2.47 (s, 1H), 2.38 (s, 1H), 2.23 – 1.96 (m, 4H), 1.90 –1.72 (m, 4H), 1.58-1.40 (m, 10H), 1.58 – 1.40 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.1, 166.1, 165.8, 165.7, 165.4, 165.1, 165.1, 164.9, 150.9, 150.6, 133.5(2C), 133.4(2C), 133.3, 133.3, 133.2, 133.1, 130.1-128.7(16C), 128.6-128.5(8C), 128.5-128.4(16C), 95.1, 92.6, 82.2, 82.2, 79.0, 78.9, 75.3, 75.2, 73.2, 72.8, 70.8, 70.5, 70.4, 70.2, 69.0, 68.7, 62.7, 62.4, 36.7, 36.6, 36.5(2C), 24.9, 24.8, 22.6(2C), 22.4, 22.3; HRMS (ESI-MS): m/z calcd for $C_{43}H_{38}O_{12}$ $[M+Na]^+$: 769.2261; Found: 769.2268.



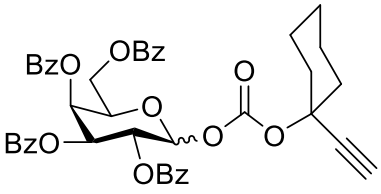
1-*O*-(((1-ethynylcyclohexyl) oxy) carbonyl)-2,3-di-*O*-benzyl-4,6-*O*-benzylidene α/β-D-galactopyranoside [α:β : 1:4] (**9**): mp (ºC): 150; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 0.3): +57.8°; IR ($cm^{-1}$, $CHCl_3$): 3305, 3017, 2943, 2867, 1758, 1452, 1364, 1269, 1241, 1214, 1093, 1012, 919, 743; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.61 – 7.52 (m, 4H), 7.42 – 7.29 (m, 26H), 6.39 (d, *J* = 3.5 Hz, 1H), 5.54 (d, *J* = 8.2 Hz, 1H), 5.51 (s, 2H), 4.90 – 4.83 (m, 3H), 4.83 – 4.74 (m, 5H), 4.37 – 4.19 (m, 2H), 4.17 – 4.12 (m, 2H), 4.07 – 3.99 (m, 3H), 3.90 (m, 1H), 3.66 (dd, *J* = 9.6, 3.5 Hz, 2H), 3.47 (q, *J* = 1.5 Hz, 2H), 2.64 (s, 1H), 2.62 (s, 1H), 2.19 (m, 4H), 1.93 (m, 4H), 1.74 – 1.67 (m, 4H), 1.63 – 1.27 (m, 8H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 151.6, 151.4, 138.7, 138.5, 138.2, 138.2, 137.8, 137.7, 129.1, 129.0, 128.5-127.7(24C), 126.6-126.4(4C), 101.4, 101.1, 97.5, 95.0, 82.9, 82.7, 79.4, 78.3, 78.1, 77.3, 75.6, 75.5, 75.2, 75.2, 74.7, 74.3, 73.6, 73.5, 72.2, 72.1, 69.1, 68.9, 67.3, 65.0, 37.1, 36.9, 36.8, 36.5, 25.0(2C), 22.6(2C), 22.5(2C); HRMS (ESI-MS): m/z calcd for $C_{36}H_{38}NaO_8$ $[M+Na]^+$: 621.2464; Found: 621.2459.




1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2-*deoxy*-2-azido-3,4-di-*O*-benzyl-6-*O*-*tert*butyldi-phenylsilyl α/β-D-glucopyranoside [α:β : 1:2] (**12**): Syrup; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 1.0): +5.3°; IR ($cm^{-1}$, $CHCl_3$): 3302, 2932, 2858, 2110, 1763, 1453, 1427, 1359, 1267, 1236, 1073, 1010, 901, 751, 696; $^1$H NMR (400 MHz, $CDCl_3$) δ = 7.79 – 7.63 (m, 8H), 7.48 – 7.30 (m, 28H), 7.23 (m, 4H), 6.16 (d, *J* = 3.5 Hz, 1H), 5.37 (d, *J* = 7.6 Hz, 1H), 4.93 (m, 6H), 4.77 (m, 2H), 4.11 – 3.84 (m, 8H), 3.68 – 3.56 (m, 3H), 3.45 (dt, *J* = 9.7, 2.5 Hz, 1H), 2.67 (s, 1H), 2.64 (s, 1H), 2.22 (m, 5H), 2.07 – 1.84 (m, 5H), 1.80 – 1.61 (m, 10H), 1.08 (2s, 18H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 151.0, 150.9, 138.0, 137.9, 137.7, 137.6, 136.0, 135.9, 135.7, 135.6, 133.5, 133.4, 132.9, 132.8, 129.7(2C), 129.7, 129.6, 128.6-127.6(32C), 95.9, 94.2, 83.3, 82.6, 82.5, 80.6, 78.7, 78.3, 77.5 (3C), 76.5, 76.0, 75.9, 75.4, 75.2, 75.2, 74.3, 65.0, 63.1, 62.1, 62.0, 36.9(2C), 36.7, 36.6, 26.9(3C), 26.8(3C), 25.0(2C), 22.5(2C), 22.5(2C), 19.4, 19.3; HRMS (ESI-MS): m/z calcd for $C_{45}H_{51}O_7Si$ $[M+Na]^+$: 796.3394; Found: 796.3387.

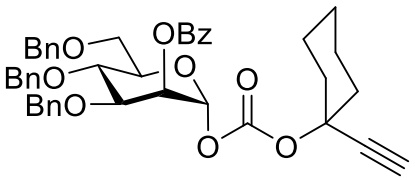



1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,4,6-tetra-*O*-benzoyl α/β-D-galactopyranoside [α:β:1:2.5](**16**): Syrup; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 0.3): +22.5°; IR ($cm^{-1}$, $CHCl_3$): 3022, 2932, 1766, 1727, 1601, 1451, 1265, 1216, 1094, 1070, 1025, 899, 754, 730, 669; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 7.5 Hz, 4H), 8.01 (d, *J* = 8.0 Hz, 4H), 7.96 (d, *J* = 7.8 Hz, 4H), 7.80 (d, *J* = 7.7 Hz, 4H), 7.67 – 7.31

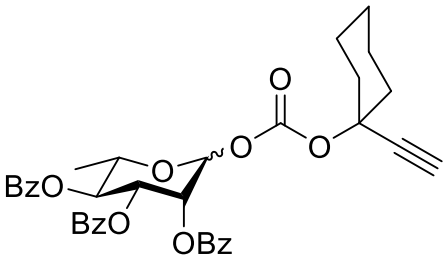


(m, 24H), 6.60 (d, *J* = 3.6 Hz, 1H), 6.17 – 5.99 (m, 3H), 5.98 – 5.82 (m, 2H), 5.76 – 5.58 (m, 2H), 4.85 (m, 1H), 4.68 (m, 1H), 4.63 – 4.35 (m, 4H), 2.46 (s, 1H), 2.39 (s, 1H), 2.21 – 1.95 (m, 4H), 1.91 – 1.70 (m, 4H), 1.69 – 1.40 (m, 12H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.0, 166.0, 165.6, 165.6, 165.5, 165.5, 165.4, 165.0, 150.9, 150.8, 133.7, 133.6, 133.4, 133.4, 133.4, 133.3, 133.3, 133.2, 130.0-129.7 (16C), 129.5-128.8(8C), 128.7-128.6(4C), 128.5-128.3(12C), 95.5, 93.3, 82.3, 82.2, 79.0, 78.7, 75.2, 75.2, 72.4, 71.8, 69.6, 68.8, 68.6, 68.2, 67.8, 67.6, 62.0, 61.8, 36.6(2C), 36.5(2C), 24.9, 24.8, 22.5, 22.5, 22.4, 22.3; HRMS (ESI-MS): m/z calcd for $C_{43}H_{38}O_{12}$ $[M+Na]^+$: 769.2261; Found: 769.2267.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2-*O*-benzoyl-3,4,6-tri-*O*-benzyl α-D-mannopyranoside (**18**): mp (ºC): 95.8; [α] $^{25}$D ($CHCl_3$, *c* 1.0): +73.6°; IR ($cm^{-1}$, $CHCl_3$): 3028, 2935, 1758, 1722, 1452, 1362, 1266, 1239, 1176, 1091, 1012, 908, 851, 746, 697, 665; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.13 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.61 – 7.54 (m, 1H), 7.43 – 7.27 (m, 15H), 7.21 (dd, *J* = 7.3, 2.2 Hz, 2H), 5.95 (dd, *J* = 3.0, 1.1 Hz, 1H), 5.74 (d, *J* = 1.0 Hz, 1H), 4.87 (dd, *J* = 11.0, 6.0 Hz, 2H), 4.80 (d, *J* = 12.0 Hz, 1H), 4.58 (dd, *J* = 11.5, 4.3 Hz, 3H), 4.12 (t, *J* = 9.5 Hz, 1H), 3.97 – 3.83 (m, 3H), 3.68 (ddd, *J*=9.7, 3.7, 1.9 Hz, 1H), 2.64 (s, 1H), 2.24 – 2.08 (m, 2H), 1.93 – 1.78 (m, 2H), 1.72 – 1.47 (m, 6H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.8, 151.1, 138.5, 138.2, 137.5, 133.2, 130.3, 130.0, 128.5(9C), 128.3(2C), 128.1(2C), 128.0, 127.9, 127.7(2C), 127.6, 94.2, 82.6, 80.1, 78.8, 76.5, 75.5, 75.4, 73.7, 73.6, 71.6, 68.7, 67.8, 36.9, 36.7, 25.0, 22.6(2C); HRMS (ESI-MS): m/z calcd for $C_{43}H_{44}O_9$ $[M+Na]^+$: 727.2883; Found: 727.2889.

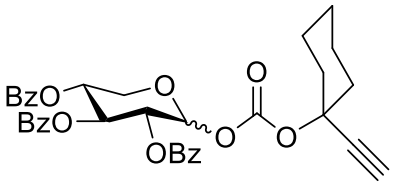



1-*O*-(((1-ethynylcyclohexyl) oxy) carbonyl)-2,3,4-tri-*O*-benzoyl α/β-L-rhamnopyranoside [α:β : 1:2] (**20**): Syrup; [α]$^{25}$D ($CHCl_3$, *c* 0.3): +73.9°; IR ($cm^{-1}$, $CHCl_3$): 3020, 1728, 1264, 1242, 1241, 1093, 1028, 915, 743, 667; $^1$H NMR (400 MHz, $CDCl_3$) δ: 8.14 – 8.05 (m, 4H), 7.96 (dd, *J*=7.8, 6.1, 4H), 7.81 (dd, *J*=6.1, 2.8, 4H), 7.68 – 7.58 (m, 2H), 7.56 – 7.46 (m, 7H), 7.46 – 7.36 (m, 7H), 7.30 – 7.27 (m, 2H), 6.18 (d, *J*=2.0, 1H), 6.02 (s, 1H), 5.89 (m, 1H), 5.78 (m, 1H), 5.71 (m, 1H), 5.67 – 5.58 (m, 1H), 4.35 (m, 1H), 4.00 (m, 1H), 2.70 (s, 1H), 2.65 (s, 1), 2.21 (m, 4H), 2.02 – 1.80 (m, 4H), 1.78 – 1.67 (m, 4H), 1.58 (m, 2H), 1.50 – 1.39 (m, 6H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.7, 165.6, 165.5, 165.5, 165.5, 165.3, 150.8, 150.4, 133.7, 133.5, 133.4(2C), 133.3, 133.2, 130.1-29.0(9C), 129.4-128.8(6C), 128.7-128.3(9C), 93.8, 93.4, 82.4, 82.4, 79.0, 78.9, 75.6, 75.4, 71.8, 71.4, 71.2, 71.1, 69.5, 69.5, 69.1, 69.0, 36.9, 36.8, 36.7, 36.5,

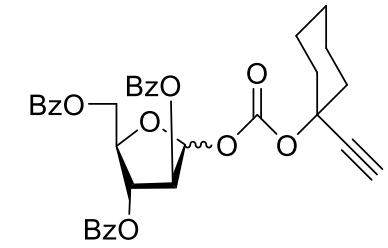


25.0, 24.9, 22.7, 22.5, 17.8, 17.7; HRMS (ESI-MS): m/z calcd for $C_{36}H_{35}O_{10}$ $[M+H]^+$: 649.2050; Found: 649.2061.

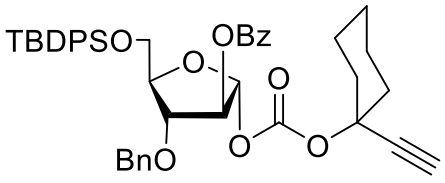
1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,4-tri-*O*-benzoyl α/β-D-xylopyranoside [α:β:1:1.1] (**24**): mp (ºC): 58.7; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 1.0): +8.4°; IR ($cm^{-1}$, $CHCl_3$): 3277, 2939, 2862, 1727, 1600, 1451, 1263, 1096, 908, 709; $^1H$ NMR (400 MHz, $CDCl_3$): δ 8.09 (d, *J* = 7.7 Hz, 2H), 8.04 – 7.90 (m, 10H), 7.59 – 7.50 (m, 4H), 7.48 – 7.29 (m, 14H), 6.42 (d, *J* = 3.7 Hz, 1H) 6.20 (t, *J* = 9.9 Hz, 1H), 6.08 (d, *J* = 3.9 Hz, 1H), 5.75 (t, *J* = 5.4 Hz, 1H), 5.56 – 5.38 (m, 3H), 5.28 (d, *J* = 4.4 Hz, 1H), 4.53 (dd, *J* = 12.8, 3.4 Hz, 1H), 4.26 (dd, *J* = 11.2, 5.8 Hz, 1H), 4.09 – 3.92 (m, 2H), 2.60 (s, 1H), 2.43 (s, 1H), 2.24 – 2.01 (m, 4H), 1.98 – 1.76 (m, 4H), 1.55 – 1.15 (m, 12H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 165.9, 165.6(2C), 165.5, 165.1, 165.0, 151.0, 150.9, 133.7(3C), 133.6, 133.5, 133.5, 130.2-129.9(12C), 129.3, 129.2(2C), 129.0(2C), 128.9, 128.6-128.5(12C), 94.4, 92.9, 82.5, 82.5, 78.8, 78.6, 75.4, 75.3, 70.4, 69.8, 69.6, 68.1, 68.1, 67.8, 61.5, 61.3, 36.8(2C), 36.8, 36.7, 25.0(2C), 22.6(2C), 22.6, 22.5; HRMS (ESI-MS): m/z calcd for $C_{35}H_{32}O_{10}$ $[M+Na]^+$: 635.1893; Found: 635.1895.




1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,5-tri-*O*-benzoyl α/β-D-arabinofuranoside [α:β : 2.5:1] (**26**): Syrup; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 0.15): -13.3°; IR ($cm^{-1}$, $CHCl_3$): 2939, 1758, 1720, 1451, 1262, 1094, 938, 752, 705; $^1H$ NMR (400 MHz, $CDCl_3$): δ 8.13 – 8.08 (m, 5H), 8.02 (m, 7H), 7.63 – 7.55 (m, 4H), 7.54 – 7.35 (m, 12H), 7.29 (d, *J* = 7.9 Hz, 2H), 6.53 (d, *J* = 4.6 Hz, 1H), 6.39 (s, 1H), 5.94 (m, 1H), 5.73 (d, *J* = 1.4 Hz, 1H), 5.66 – 5.54 (m, 2H), 4.78 (m, 3H), 4.73 – 4.49 (m, 3H), 2.66 (s, 1H), 2.38 (s, 1H), 2.30 – 1.89 (m, 8H), 1.75 – 1.44 (m, 10H), 1.39-1.34 (m, 2H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 166.3, 166.3, 165.9, 165.7, 165.6, 165.2, 151.0, 151.0, 133.9, 133.8, 133.8, 133.7, 133.2, 133.2, 130.3-129.7 (15C), 129.1-128.4 (15C), 102.4, 96.9, 83.4, 82.6, 82.5, 81.3, 80.2, 80.1, 78.6, 78.4, 76.2, 75.5, 75.2, 75.1, 65.1, 63.6, 37.0, 36.8, 36.7, 36.6, 25.1, 25.0, 22.7 (2C), 22.5 (2C); HRMS (ESI-MS): m/z calcd for $C_{35}H_{32}NaO_{10}$ $[M+Na]^+$: 635.1893; Found: 635.1891.

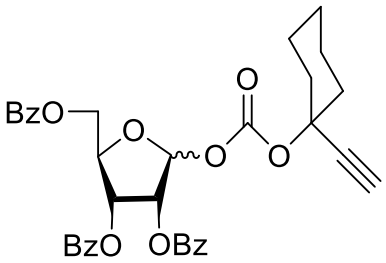



1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-*tert*-butyldiphenylsilyl α-D-arabinofuranoside (**29**): Syrup; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 0.15): +18.5°; IR ($cm^{-1}$, $CHCl_3$): 3289, 3069, 2931, 2858, 1758, 1728, 1264, 1237, 1107, 1070, 1009, 951, 911, 740, 702; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 7.7 Hz,

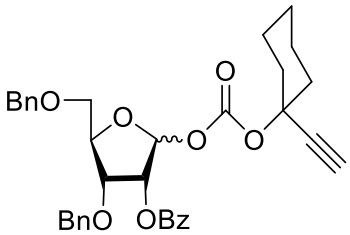


2H), 7.73 – 7.50 (m, 4H), 7.33 (m, 14H), 6.26 (s, 1H), 5.59 (s, 1H), 4.83 (d, *J* = 12.0 Hz, 1H), 4.64 (d, *J* = 12.1 Hz, 1H), 4.45 (q, *J* = 4.7 Hz, 1H), 4.27 (d, *J* = 4.8 Hz, 1H), 3.82 (d, *J* = 5.4 Hz, 2H), 2.63 (s, 1H), 2.26 – 2.13 (m, 2H), 1.95 – 1.85 (m, 2H), 1.72 – 1.55 (m, 6H), 0.97 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.3, 151.4, 137.7, 135.7(4C), 133.6(2C), 133.2, 130.0(2C), 129.9, 129.8, 129.2, 128.6(2C), 128.5(2C), 128.0(2C), 127.9, 127.8(2C), 127.8(2C), 103.1, 85.9, 82.8, 82.7, 81.5, 78.3, 75.3, 72.4, 62.9, 37.0, 36.8, 26.9(3C), 25.1, 22.7(2C), 19.4; HRMS (ESI-MS): m/z calcd for $C_{44}H_{48}O_8Si$ $[M+Na]^+$: 755.3016; Found: 755.3021.

1-*O*-(((ethynylcyclohexyl)oxy)carbonyl)-2,3,5-tri-*O*-benzoyl α/β-D-ribofuranoside [α:β:6:1] (**32**): $[\alpha]^{25}_D$ ($CHCl_3$, *c* 0.3): +18.4°; IR ($cm^{-1}$, $CHCl_3$): 3277, 2939, 2863, 1723, 1601, 1451, 1315, 1262, 1235, 1176, 1106, 1024, 1010, 938, 919, 753, 706, 668; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.13 – 8.06 (m, 4H), 8.05 – 7.97 (m, 4H), 7.90 – 7.84 (m, 4H), 7.61 – 7.56 (m, 3H), 7.55 – 7.48 (m, 4H), 7.42 (m, 4H), 7.32 (m, 4H), 6.58 (m, 3H), 6.34 (s, 1H), 5.95 (dd, *J* = 7.1, 4.8 Hz, 1H), 5.86 (d, *J* = 4.8 Hz, 2H), 5.81 (dd, *J* = 6.6, 2.6 Hz, 2H), 4.80 (dt, *J* = 7.4, 4.1 Hz, 2H), 4.77 – 4.70 (m, 2H), 4.64 – 4.50 (m, 2H), 2.63 (s, 1H), 2.47 (s, 1H), 2.22 – 2.06 (m, 4H), 1.60 (m, 14H), 1.26 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.3, 166.2, 165.9, 165.8, 165.4, 165.1, 151.2, 150.9, 133.8, 133.7, 133.7, 133.6, 133.5, 133.3, 130.2-129.5(15C), 129.0-128.4(15C), 101.3, 97.5, 82.8, 82.5, 82.4, 80.2, 78.8, 78.8, 75.5, 75.2, 75.1, 73.5, 71.5, 71.3, 64.0, 63.9, 37.0, 36.9, 36.7, 36.5, 25.0, 24.9, 22.7(2C), 22.5(2C); HRMS (ESI-MS): m/z calcd for $C_{35}H_{32}NaO_{10}$ $[M+Na]^+$: 635.1893; Found: 635.1891.

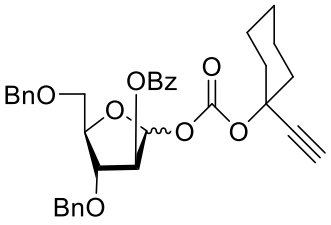



1-*O*-(((ethynylcylcohexyl)oxy)carbonyl)-2-*O*-benzoyl-3,5-*O*-dibenzyl *α/β*-D-ribofuranoside [ *α:β* : 5:1] (**33**): Syrup; $[\alpha]^{25}_D$ ($CHCl_3$, c 0.3): +19.2; IR (cm-1, $CHCl_3$): 2978, 1789, 1727, 1600, 1579, 1452, 1369, 1269, 1214, 1107, 851, 753, 616; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.08 (dt, J=8.5, 1.7, 4H), 7.60 – 7.52 (m, 2H), 7.43 (td, J=7.8, 6.2, 4H), 7.35 – 7.21 (m, 20H), 6.45 (d, J=4.5, 1H), 6.22 (s, 1H), 5.63 (d, J=4.1, 1H), 5.40 (dd, J=6.6, 4.6, 1H), 4.65 (d, J=11.5, 2H), 4.62 – 4.51 (m, 4H), 4.50 – 4.41 (m, 4H), 4.40 – 4.23 (m, 2H), 3.76 – 3.39 (m, 4H), 2.61 (s, 1H), 2.48 (s, 1H), 2.29 – 2.07 (m, 4H), 1.93 – 1.75 (m, 4H), 1.70 – 1.42 (m, 12H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.6, 165.4, 151.6, 150.9, 138.3, 137.8, 137.8, 137.3, 133.5, 133.3, 130.2-127.6(30C), 101.5, 98.0, 84.2, 82.8, 82.6, 82.1, 78.4, 77.8, 76.8, 75.4, 75.3, 75.0, 74.0, 73.6, 73.5, 73.2, 73.1, 72.1, 69.6, 69.1, 37.0,

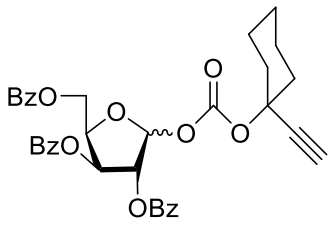


36.8, 36.6, 36.5, 25.0, 25.0, 22.6, 22.6, 22.6, 22.5; HRMS (ESI-MS): m/z calcd for $C_{35}H_{36}NaO_8$ [M+Na]+: 607.2308; Found: 607.2307.

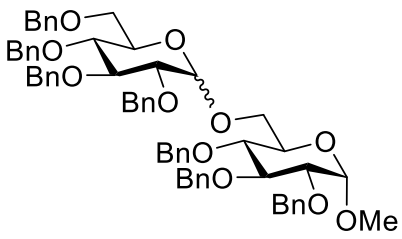
1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2-*O*-benzoyl-3,5-di-*O*-benzyl α/β-D-arabinofuranoside [α:β:3:1] (**34**): $^1$H NMR (400 MHz, $CDCl_3$): δ = 8.03 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.96 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.61 – 7.55 (m, 2H), 7.47 – 7.38 (m, 4H), 7.37 – 7.23 (m, 20H), 6.39 (d, *J* = 4.5 Hz, 1H), 6.28 (s, 1H), 5.55 (d, *J* = 1.5 Hz, 1H), 5.52 (dd, *J* = 7.2, 4.5 Hz, 1H), 4.83 (d, *J* = 12.1 Hz, 2H), 4.66 – 4.63 (m, 2H), 4.62 – 4.55 (m, 2H), 4.50 (m, 5H), 4.13 (d, *J* = 5.0 Hz, 1H), 3.73 – 3.58 (m, 4H), 2.63 (s, 1H), 2.33 (s, 1H), 2.28 – 2.14 (m, 3H), 2.10 – 1.83 (m, 4H), 1.77 – 1.41 (m, 13H); 13C NMR (101 MHz, $CDCl_3$): δ 165.5, 165.3, 151.4, 151.0, 138.1, 137.9, 137.6, 137.6, 133.6, 133.5, 130.2, 129.9, 129.3, 129.2, 128.6 - 128.4(12C), 128.0 - 127.8(12C), 102.9, 97.3, 84.5, 82.9, 82.8, 82.6, 81.5, 81.2, 80.2, 78.4, 78.1, 78.0, 75.4, 75.0, 73.6, 73.5, 72.5, 72.4, 71.0, 69.0, 37.0, 36.8, 36.8, 36.6, 25.1, 25.0, 22.7(2C), 22.5(2C); HRMS (ESI-MS): m/z: calcd for $C_{35}H_{36}NaO_8$ [M+Na]+: 607.2308; Found: 607.2311.




1-O-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,5-tri-O-benzoyl *α/β*-D-xylofuranoside [α:β : 1:1] (**43**): $^1$H NMR (400 MHz, $CDCl_3$): δ 8.12 – 8.04 (m, 6H), 8.03 – 7.95 (m, 6H), 7.63 – 7.51 (m, 5H), 7.42 (m, 13H), 6.57 (d, *J* = 4.4 Hz, 1H), 6.32 (s, 1H), 6.12 (t, *J* = 6.8 Hz, 1H), 5.92 (d, *J* = 4.9 Hz, 1H), 5.88 – 5.83 (m, 1H), 5.70 (s, 1H), 5.03 (p, *J* = 5.0, 4.3 Hz, 3H), 4.67 (td, *J* = 11.5, 6.1 Hz, 2H), 4.56 (qd, *J* = 12.5, 4.8 Hz, 2H), 2.62 (s, 1H), 2.44 (s, 1H), 2.23 – 1.65 (m, 12H), 1.59 – 1.30 (m, 8H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.1, 166.0, 165.7, 165.4, 165.0, 164.8, 151.0, 150.8, 133.9, 133.7, 133.7, 133.6, 133.3, 133.2, 130.1 - 129.5 (15C), 129.5- 128.3 (15C), 101.7, 96.0, 82.6, 82.4, 80.5, 80.0, 78.4, 78.2, 76.0, 75.9, 75.2, 75.1, 74.3, 74.2, 62.9, 62.2, 36.9, 36.7, 36.6, 36.5, 24.9, 24.9, 22.4 (4C); HRMS (ESI-MS): m/z calcd for $C_{35}H_{32}NaO_{10}$ $[M+Na]^+$: 635.1893; Found: 635.1898.



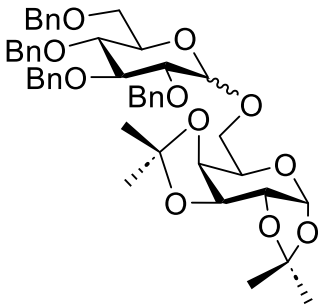

Methyl-2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl α/β-D-glucopyranosyl) α-D-glucopyranoside [α:β : 1:1] (**3**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 10/1) giving 138mg as syrup (yield 96 %) from 100 mg (0.145 mmol) donor **1**; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 1.0): +24.6°; IR ($cm^{-1}$, $CHCl_3$): 2916, 1456, 1218, 750, 670; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.24 (m, 63H), 7.20 – 7.15 (m, 7H), 4.97 (m, 4H), 4.92 (d, *J* = 3.7 Hz,



1H), 4.90 (d, *J* = 4.1 Hz, 1H), 4.84 – 4.78 (m, 5H), 4.77 (d, *J* = 2.7 Hz, 2H), 4.74 – 4.69 (m, 3H), 4.66 (m, 3H), 4.63 (s, 1H), 4.61 (d, *J* = 3.8 Hz, 1H), 4.58 (d, *J* = 3.9 Hz, 2H), 4.55 (m, 3H), 4.53 – 4.51 (m, 1H), 4.51 – 4.39 (m, 3H), 4.35 (d, *J* = 7.8 Hz, 1H), 4.18 (dd, *J* = 10.9, 2.1 Hz, 1H), 4.02 – 3.93 (m, 3H), 3.80 (m, 4H), 3.66 (m, 8H), 3.53 (m, 6H), 3.44 (m, 2H), 3.35 (s, 3H), 3.33 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 138.9, 138.9, 138.9, 138.6, 138.6, 138.5, 138.5, 138.5, 138.4, 138.3, 138.3, 138.2, 138.2, 138.1, 128.5-128.3(30C), 128.2-127.9(20C), 127.8-127.6(20C), 103.9, 98.1, 98.1, 97.3, 84.9, 82.2, 82.2, 82.1, 81.8, 80.2, 80.1, 79.9, 78.1, 78.0, 77.8, 77.7, 75.8, 75.8(2C), 75.6, 75.1, 75.1, 75.1, 75.0(3C), 73.5, 73.5, 73.5, 73.4, 72.5, 70.4, 70.3, 69.9, 69.1, 68.6, 68.6, 66.1, 55.3, 55.2; HRMS (ESI-MS): m/z calcd for $C_{62}H_{66}O_{11}[M+Na]^+$: 1009.4503; Found: 1009.4509.

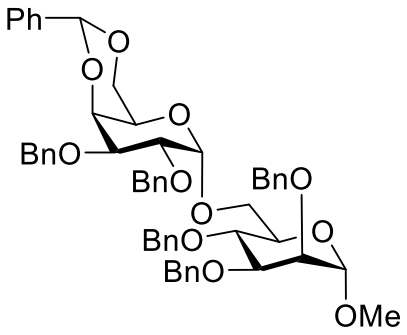
Methyl-2,3,4-tri-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl β-D-glucopyranosyl) α-D-glucopyranoside (**6**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 4/1) giving 131mg as syrup (yield 94 %) from 100 mg (0.126 mmol) donor **4**; [α] $^{25}_D$ ($CHCl_3$, c 0.3): +34.0°; IR ($cm^{-1}$, $CHCl_3$): 3007, 2950, 1721, 1601, 1584, 1451, 1333, 1249, 1179, 1089, 1066, 1025, 703; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.15 – 7.72 (m, 14H), 7.66 – 7.26 (m, 21H), 6.07 (t, *J*=9.8, 1H), 5.93 (t, *J*=9.7, 1H), 5.66 (t, *J*=9.7, 1H), 5.57 (t, *J*=8.8, 1H), 5.32 (t, *J*=9.9, 1H), 5.09 (dd, *J*=10.3, 3.7, 1H), 4.98 (d, *J* = 7.9 Hz, 1H), δ 4.94 (d, *J* = 3.7 Hz, 1H), 4.61 (dd, *J*=12.3, 3.2, 1H), 4.45 (dd, *J*=12.2, 5.1, 1H), 4.23 (t, *J*=8.9, 1H), 4.18 – 4.05 (m, 2H), 3.79 (dd, *J*=11.4, 7.6, 1H), 3.10 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.2, 165.9, 165.8, 165.8, 165.6, 165.3(2C), 133.6(2C), 133.4, 133.4(2C), 133.2, 133.2, 130.0-129.7(14C), 129.5, 129.3,129.2, 128.9, 128.9, 128.9, 128.6, 128.5-128.3(14C), 101.9, 96.6, 72.9, 72.4, 72.1, 72.0, 70.4, 69.8, 69.7, 69.1, 68.9, 63.1, 55.2; HRMS (ESI-MS): m/z calcd for $C_{62}H_{52}O_{18}$ $[M+Na]^+$: 1084.3154; Found: 1084.3148.

1,2:3,4-di-*O*-isopropylidene-6-*O*-(2,3,4,6-tetra-*O*-benzyl α/β D-glucopyranosyl) α-D-galactopyranoside [α: β ： 1:1] (**8**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 4/1) giving 93 mg as syrup (yield 82 %) from 100 mg (0.119 mmol) donor **1**; [α]$^{25}_D$ ($CHCl_3$, *c* 0.3): -7.2°; IR ($cm^{-1}$, $CHCl_3$): 2984, 2863, 1453, 1379, 1254, 1204, 1066; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.39 (m, 2H), 7.38 – 7.23 (m, 34H), 7.13 (m, 4H), 5.57 (d, *J* = 5.0 Hz, 1H), 5.52 (d, *J* = 5.0 Hz, 1H), 5.05 (d, *J* = 11.2 Hz, 1H), 5.00–4.93 (m, 3H), 4.84 – 4.70 (m, 7H), 4.65 – 4.56 (m, 4H), 4.55 – 4.43 (m, 5H), 4.35 (dd, *J* = 7.9,



1.9 Hz, 1H), 4.31 (dt, *J* = 4.8, 2.3 Hz, 2H), 4.24 (dd, *J* = 7.9, 1.9 Hz, 1H), 4.16 (dd, *J* = 10.6, 3.7 Hz, 1H), 4.09 (m, 1H), 4.06 – 3.95 (m, 2H), 3.85 – 3.55 (m, 12H), 3.49 – 3.41 (m, 2H), 1.53 (s, 3H), 1.50 (s, 3H), 1.45 (s, 3H), 1.46 (s, 3H), 1.35 – 1.28 (2s, 12H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 139.0, 138.8, 138.8, 138.5, 138.4, 138.3, 138.2, 138.1, 128.7-127.6(40C), 109.5, 109.3, 108.7, 108.7, 104.5, 97.2, 96.5, 96.4, 84.7, 82.1, 81.7, 79.9, 77.8, 77.7, 75.8, 75.7, 75.1(2C), 74.9, 74.5, 73.6, 73.6, 72.5, 71.5, 70.9, 70.9, 70.8(2C), 70.6, 70.3, 69.8, 68.9, 68.5, 67.5, 66.3, 65.8, 26.3, 26.2, 26.2, 26.1, 25.1, 25.0, 24.8, 24.6; HRMS (ESI-MS): m/z calcd for $C_{46}H_{54}O_{11}[M+Na]^+$: 805.3564; Found: 805.3566.

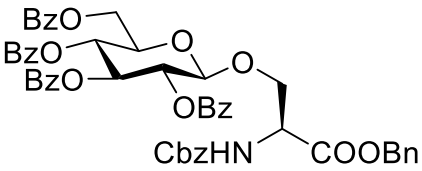
Methyl-2,3,4-tri-*O*-benzyl-6-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene α-D-galactopyranosyl) α-D-mannopyranoside (**11**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 7/1) giving 200 mg as syrup (yield 89 %) from 150 mg (0.250 mmol) donor **9**; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 0.3): +33.4°; IR ($cm^{-1}$, $CHCl_3$): 3032, 2911, 1495, 1453, 1363, 1096, 1048, 1025, 914, 696; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.54 – 7.49 (m, 2H), 7.40 – 7.23 (m, 28H), 5.44 (s, 1H), 5.10 (d, *J* = 3.4 Hz, 1H), 4.89 (d, *J* = 11.3 Hz, 1H), 4.80 – 4.72 (m, 3H), 4.67 (m, 4H), 4.60 (s, 2H), 4.54 (d, *J* = 11.4 Hz, 1H), 4.15 (d, *J* = 12.5 Hz, 1H), 4.07 (m, 2H), 3.98 (dd, *J* = 10.0, 3.4 Hz, 1H), 3.93 – 3.82 (m, 4H), 3.79 (m, 4H), 3.19 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 138.9, 138.9, 138.8, 138.6, 138.3, 138.0, 129.0-126.5(30C), 101.2, 99.0, 98.1, 80.4, 75.9, 75.2, 75.1, 75.1, 75.0, 74.9, 73.2, 72.9, 72.2, 72.0, 71.5, 69.6, 66.9, 62.7, 54.7; HRMS (ESI-MS): m/z calcd for $C_{55}H_{58}O_{11}$ $[M+Na]^+$: 917.3877; Found: 917.3876.



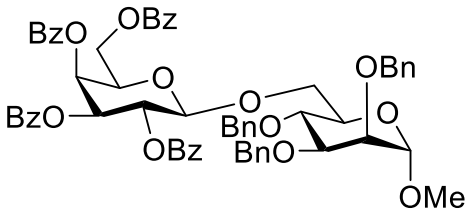
Methyl-2,3,4-tri-*O*-benzyl-6-*O*-(2-*deoxy*-2-azido-3,4-di-*O*-benzyl-6-*O*-$^{tert}$butyldiphenylsilyl α/β-D-glucopyranosyl) α-D-mannopyranoside [$\alpha:\beta$ : 3:1] (**13**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 10/1) giving 137 mg as syrup (yield 91 %) from 110 mg (0.142 mmol) donor **12**; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 0.3): +21.2°; IR ($cm^{-1}$, $CHCl_3$): 3008, 2930, 2858, 2109, 1454, 1359, 1269, 1110, 1055, 914, 695; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.76 – 7.64 (m, 8H), 7.41 – 7.23 (m, 58H), 7.17 (m, 4H), 5.05 (d, *J* = 3.5 Hz, 1H), 5.02 – 4.77 (m, 9H), 4.76 – 4.57 (m, 14H), 4.32 (d, *J* = 7.9 Hz, 1H), 4.25 – 3.99 (m, 2H), 3.98 – 3.71 (m, 19H), 3.57 – 3.37 (m, 2H), 3.36 – 3.25 (m, 6H), 1.05 (s, 9H), 1.03 (s, 9H);$^{13}$C NMR (101 MHz,

$CDCl_3$): δ 138.7, 138.6, 138.5, 138.5, 138.4, 138.4, 138.3, 138.1, 138.0, 138.0, 135.9, 135.7, 135.6, 135.6, 133.7, 133.6, 133.2, 133.0, 129.7, 129.7, 129.7, 129.6, 128.6 -128.2(31C), 128.0-127.6(31C), 102.4, 99.3, 98.8, 97.8, 83.4, 80.5, 80.4, 80.0, 78.4, 77.6, 75.9, 75.8, 75.5, 75.2, 75.0, 75.0, 75.0(4C), 74.9, 74.7, 74.5, 72.8, 72.7, 72.2, 72.1, 71.9, 71.7, 71.3, 68.7, 66.7, 66.6, 63.8, 62.5, 54.8, 54.7, 26.9 (3C), 26.8 (3C), 19.4, 19.3; HRMS (ESI-MS): m/z calcd for $C_{64}H_{71}N_3O_{10}Si$ $[M+Na]^+$: 1092.4806; Found: 1092.4811.

Benzyl-*N*-benzyloxycarbonyl-L-serine-2,3,4,6-tetra-*O*-benzoyl β-D-glucopyranoside (**15**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 7/1) giving 105 mg as syrup (yield 86 %) from 100 mg (0.134 mmol) donor **4**; $[\alpha]$ $^{25}_D$ ($CHCl_3$, *c* 0.3): +10.0°; IR ($cm^{-1}$, $CHCl_3$): 3032, 2967, 1722, 1601, 1506, 1452, 1260, 1176, 1090, 1066, 1026, 704; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 7.7 Hz, 2H), 7.92 (d, *J* = 7.8, 2H), 7.91 (d, *J* = 13.9, 2H), 7.82 (d, *J* = 7.7 Hz, 2H), 7.56 – 7.26 (m, 22H), 5.86 (t, *J* = 9.7 Hz, 1H), 5.64 (t, *J* = 9.7 Hz, 1H), 5.57 (d, *J* = 8.2 Hz, 1H), 5.45 (t, *J* = 8.8 Hz, 1H), 5.19 – 5.08 (m, 2H), 5.02 (d, *J* = 12.4 Hz, 1H), 4.94 (d, *J* = 12.3 Hz, 1H), 4.78 (d, *J* = 7.9 Hz, 1H), 4.60 (dd, *J* = 12.2, 3.2 Hz, 1H), 4.51 (dd, *J* = 7.9, 3.7 Hz, 1H), 4.40 (dd, *J* = 11.2, 4.0 Hz, 2H), 4.02 (dt, *J* = 9.1, 4.1 Hz, 1H), 3.91 (dd, *J* = 10.3, 3.5 Hz, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 169.4, 166.2, 165.9, 165.2, 165.2, 156.0, 136.3, 135.3, 133.6, 133.4(2C), 133.3, 129.9-129.8(8C), 129.6, 129.1, 128.8(2C), 128.7-128.2(18C), 101.4, 72.7, 72.4, 71.9, 69.6, 69.5, 67.6, 67.0, 63.0, 54.4; HRMS (ESI-MS): m/z calcd for $C_{52}H_{45}NO_{14}$ $[M+H]^+$: 908.2918; Found: 908.2913.

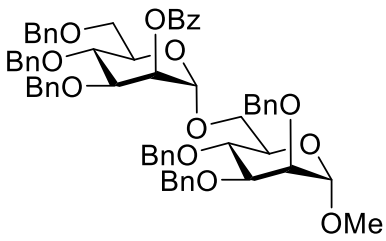



Methyl-2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl β-D-galactopyranosyl) α-D-mannopyranoside (**17**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 8/1) giving 129 mg as syrup (yield 90 %) from 100 mg (0.134 mmol) donor **16**; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 0.3): +24.6°; IR ($cm^{-1}$, $CHCl_3$): 2922, 2853, 1725, 1601, 1494, 1451, 1263, 1093, 1065, 1025, 697; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.15 – 8.06 (m, 2H), 8.04 – 8.00 (m, 2H), 7.92 – 7.88 (m, 2H), 7.80 – 7.75 (m, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.56 – 7.36 (m, 8H), 7.35 – 7.27 (m, 14H), 7.23 (m, 4H), 5.99 (d, *J* = 3.5 Hz, 1H), 5.85 (dd, *J* = 10.5, 7.9 Hz, 1H), 5.61 (dd, *J* = 10.4, 3.5 Hz, 1H), 4.92 (d, *J* = 7.9 Hz, 1H), 4.77 (d, *J* = 11.1 Hz, 1H), 4.72 – 4.64 (m, 3H), 4.51 (m, 3H), 4.48 – 4.38 (m, 2H), 4.34 – 4.25 (m, 2H), 3.78 (m, 3H), 3.69 (m, 2H), 2.99 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.1, 165.6, 165.6, 165.2, 138.4, 138.4, 138.3, 133.6, 133.3, 133.3, 133.0, 130.1, 129.8(4C), 129.6, 129.4, 129.1, 128.8, 128.6, 128.5(2C), 128.4(3C),

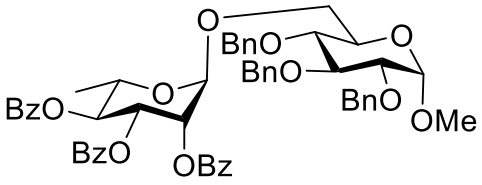


128.4(3C), 128.3(3C), 128.3(2C), 128.3(2C), 127.9(2C), 127.7(2C), 127.7, 127.6(2C), 127.5(3C), 102.2, 98.7, 80.3, 75.1, 74.9, 74.3, 72.7, 72.0, 71.8, 71.3, 71.2, 69.9, 69.9, 68.2, 61.9, 54.3; HRMS (ESI-MS): m/z calcd for $C_{62}H_{58}O_{15}$ $[M+Na]^+$: 1065.3673; Found: 1065.3673.

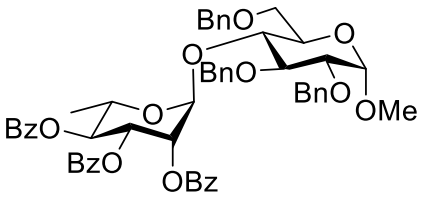
Methyl-2,3,4-tri-*O*-benzyl-6-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl α-D-mannopyranosyl) α-D-mannopyranoside (**19**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 9/1) giving 130 mg as syrup (yield 89 %) from 100 mg (0.142 mmol) donor **18**; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 0.3): +14.1°; IR ($cm^{-1}$, $CHCl_3$): 3032, 2926, 1722, 1495, 1452, 1361, 1266, 1097, 1058, 1026, 973, 909, 696; $^1H$ NMR (400 MHz, $CDCl_3$): δ 8.16 – 8.08 (m, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.45 – 7.26 (m, 29H), 7.21 (d, *J* = 7.6, 2H), 7.20 (d, *J* = 5.5 Hz, 1H), 5.78 (d, *J* = 2.2 Hz, 1H), 5.13 (d, *J* = 2.1 Hz, 1H), 4.96 (d, *J* = 11.2 Hz, 1H), 4.92 (d, *J* = 10.9 Hz, 1H), 4.79 – 4.72 (m, 5H), 4.64 (s, 2H), 4.57 – 4.49 (m, 4H), 4.14 (m, 2H), 4.00 – 3.93 (m, 3H), 3.90 (m, 1H), 3.84 (m, 2H), 3.79 – 3.69 (m, 3H), 3.30 (s, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 165.6, 138.7, 138.6, 138.6, 138.6, 138.4, 138.0, 133.1, 130.1-127.5(35C), 98.9, 98.2, 80.4, 77.6, 75.2, 75.1, 74.7, 74.7, 74.3, 73.5, 72.8, 72.1, 71.7, 71.1, 71.1, 69.1, 68.9, 66.8, 54.8; HRMS (ESI-MS): m/z calcd for $C_{62}H_{64}O_{12}$ $[M+Na]^+$: 1023.4295; Found: 1023.4249.



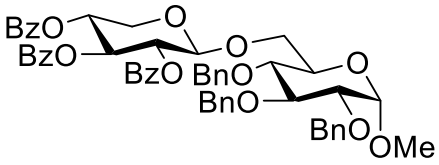

Methyl-2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4-tri-*O*-benzoyl α-D-rhamnopyranosyl) α-D-glucopyranoside (**21**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 8/1) giving 137 mg as syrup (yield 93 %) from 100 mg (0.160 mmol) donor **20**; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 0.3): +45.3°; IR ($cm^{-1}$, $CHCl_3$): 3065, 2930, 1726, 1601, 1584, 1452, 1315, 1260, 1092, 1067, 1026, 706; $^1H$ NMR (400 MHz, $CDCl_3$): δ 8.09 (d, *J* = 8.1, 1.4 Hz, 2H), 7.97 (dd, *J* = 8.2, 1.5 Hz, 2H), 7.81 (dd, *J* = 8.2, 1.5 Hz, 2H), 7.63 – 7.57 (m, 1H), 7.54 – 7.45 (m, 3H), 7.43 – 7.21 (m, 20H), 5.81 (dd, *J* = 10.1, 3.4 Hz, 1H), 5.68 – 5.62 (m, 2H), 5.03 (d, *J* = 10.9 Hz, 1H), 4.99 – 4.93 (m, 2H), 4.89 – 4.80 (m, 2H), 4.71 (d, *J* = 12.1 Hz, 1H), 4.68 – 4.61 (m, 2H), 4.18 (dq, *J* = 12.3, 6.2 Hz, 1H), 4.06 (t, *J* = 9.2 Hz, 1H), 3.96 (dd, *J* = 10.9, 1.7 Hz, 1H), 3.90 – 3.85 (m, 1H), 3.63 (td, *J* = 10.4, 9.4, 4.6 Hz, 2H), 3.52 (t, *J* = 9.5 Hz, 1H), 3.47 (s, 3H), 1.32 (d, *J* = 6.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 165.9, 165.6, 165.6, 138.8, 138.3, 138.3, 133.5, 133.4, 133.2, 130.0 - 129.8(6C), 129.6, 129.4, 129.4, 128.7-127.7(21C), 98.1, 98.0, 82.3, 80.3, 77.9, 75.9, 75.2, 73.6, 71.9, 70.8, 70.2, 70.0, 67.2, 66.8, 55.4, 17.7; HRMS (ESI-MS): m/z calcd for $C_{55}H_{54}O_{13}$ $[M+Na]^+$: 945.3462; Found: 961.3169.



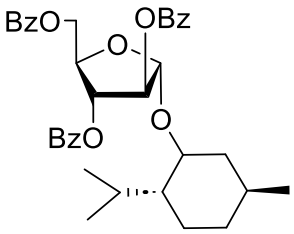
Methyl-2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4-tri-*O*-benzoyl α-D-rhamnopyranosyl) α-D-glucopyranoside (**23**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 8/1) giving 201 mg as syrup (yield 91 %) from 150 mg (0.240 mmol) donor **20**; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 0.3): +23.0°; IR ($cm^{-1}$, $CHCl_3$): 3032, 2929, 1723, 1601, 1584, 1451, 1260, 1093, 1026, 911, 706; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.09 – 8.03 (m, 2H), 7.92 – 7.88 (m, 2H), 7.87 – 7.83 (m, 2H), 7.62 – 7.36 (m, 10H), 7.35 – 7.27 (m, 8H), 7.21 – 7.09 (m, 6H), 5.78 (dd, *J* = 10.2, 3.4 Hz, 1H), 5.64 – 5.54 (m, 2H), 5.26 – 5.16 (m, 2H), 4.85 (d, *J* = 11.1 Hz, 1H), 4.76 (d, *J* = 12.1 Hz, 1H), 4.67 – 4.60 (m, 2H), 4.60 – 4.51 (m, 2H), 4.41 – 4.30 (m, 1H), 4.00 (d, *J* = 9.1 Hz, 2H), 3.93 – 3.81 (m, 2H), 3.73 (dd, *J* = 11.1, 1.9 Hz, 1H), 3.65 (dd, *J* = 9.0, 3.5 Hz, 1H), 3.41 (s, 3H), 0.89 (d, *J* = 6.1 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.9(2C), 165.8, 138.8, 138.1, 137.9, 133.6, 133.4, 133.3, 130.0-129.8(6C), 129.6(2C), 129.4, 128.7-127.4(21C), 98.1, 97.2, 80.5, 79.9, 75.7, 75.0, 73.5, 73.4, 71.9, 71.4, 70.2, 70.1, 68.4, 67.2, 55.4, 17.3; HRMS (ESI-MS): m/z calcd for $C_{55}H_{54}O_{13}$ $[M+Na]^+$: 945.3462; Found: 945.3465.




Methyl-2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4-tri-*O*-benzoyl β-D-xylopyranosyl) α-D-glucopyranoside (**25**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 7/1) giving 137 mg as syrup (yield 92 %) from 100 mg (0.163 mmol) donor **24**; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 0.3): +1.0°; IR ($cm^{-1}$, $CHCl_3$): 3006, 2929, 2855, 1724, 1622, 1452, 1257, 1068, 1026, 706; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, *J* = 7.3 Hz, 2H), 7.95 (d, *J* = 7.5 Hz, 2H), 7.92 (d, *J* = 7.7 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.47 – 7.28 (m, 18H), 7.25 – 7.21 (m, 3H), 7.09 (dd, *J* = 7.5, 2.1 Hz, 2H), 5.76 (t, *J* = 7.6 Hz, 1H), 5.43 (dd, *J* = 7.6, 5.7 Hz, 1H), 5.31 (td, *J* = 7.4, 4.3 Hz, 1H), 4.93 (d, *J* = 10.8 Hz, 1H), 4.82 – 4.72 (m, 3H), 4.66 – 4.60 (m, 2H), 4.58 (d, *J* = 3.5 Hz, 1H), 4.43 (dd, *J* = 12.0, 4.5 Hz, 1H), 4.39 (d, *J* = 11.0 Hz, 1H), 4.08 (d, *J* = 9.2 Hz, 1H), 3.93 (t, *J* = 9.3 Hz, 1H), 3.74 (d, *J* = 9.5 Hz, 2H), 3.64 (dd, *J* = 12.1, 7.5 Hz, 1H), 3.53 – 3.42 (m, 2H), 3.27 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.5, 165.5, 165.0, 138.8, 138.2 (2C), 133.4-129.8(7C), 129.2(2C), 129.1, 128.5-127.5(23C), 100.4, 98.1, 82.0, 79.9, 77.4, 75.6, 74.9, 73.4, 70.6, 70.4, 69.6, 69.2, 67.8, 61.4, 55.1; HRMS (ESI-MS): m/z calcd for $C_{54}H_{52}O_{13}$ $[M+Na]^+$: 931.3306; Found: 931.3305.

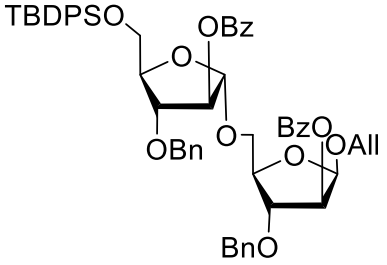


1*R*,2*S*,5*R*-(-)-Menthyl-2',3',5'-tri-*O*-benzoyl α-D-arabinofuranoside (**28**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 10/1) giving 85 mg as syrup (yield 89 %) from 100 mg (0.163 mmol) donor **26**; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c*0.3): +16.8°; IR ($cm^{-1}$, $CHCl_3$): 2953, 2923, 2854, 1720, 1602, 1451, 1315, 1262, 1177, 1095, 1025, 705; $^1H$ NMR (400 MHz, $CDCl_3$): δ 8.06 (m, 6H), 7.63 – 7.55 (m, 2H), 7.55 – 7.50 (m, 1H), 7.47 (2d, *J* = 7.8 Hz, 2H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.32 (t, *J* = 7.8 Hz, 2H), 5.58 (d, *J* = 4.4 Hz, 1H), 5.50 (s, 1H), 5.37 (s, 1H), 4.87 – 4.79 (m, 1H), 4.73 – 4.65 (m, 2H), 3.49 (td, *J* = 10.6, 4.3 Hz, 1H), 2.30 (m, 1H), 2.25 – 2.17 (m, 1H), 1.70 – 1.60 (m, 2H), 1.49 – 1.28 (m, 2H), 1.16 – 1.06 (m, 1H), 1.00 (m, 1H), 0.92 (m, 7H), 0.81 (d, *J* = 6.9 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 166.3, 165.9, 165.6, 133.6, 133.5, 133.1, 130.0-128.4(12C), 106.8, 82.5, 80.8, 79.9, 78.0, 64.1, 48.6, 42.9, 34.4, 31.7, 25.7, 23.4, 22.3, 21.2, 16.4; HRMS (ESI-MS): m/z calcd for $C_{36}H_{40}O_8$ $[M+Na]^+$: 623.2621; Found: 623.2614.

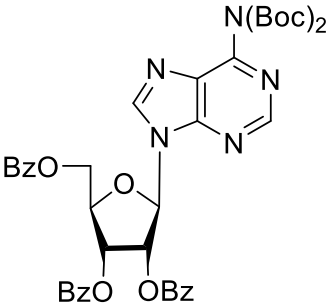



Allyl-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-benzoyl-3-*O*-benzyl-5-*O*-*tert*butyldiphenylsilyl α-D-arabinofuranosyl) α-D- arabinofuranoside (**31**):

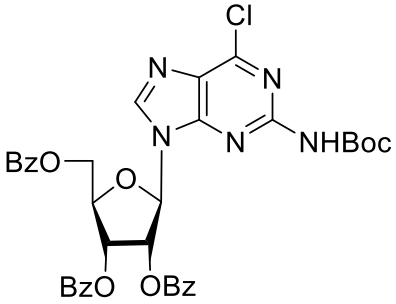
The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 15/1) giving 100 mg as syrup (yield 91 %) from 89 mg (0.136 mmol) donor **29**; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 0.3): -7.0°; IR ($cm^{-1}$, $CHCl_3$): 2929, 2856, 1722, 1452, 1267, 1109, 1026, 699; $^1H$ NMR (400 MHz, $CDCl_3$): δ 8.03 (d, *J* = 7.8 Hz, 2H), 7.98 (d, *J* = 7.8 Hz, 2H), 7.69 – 7.55 (m, 6H), 7.47 – 7.27 (m, 16H), 7.25 – 7.18 (m, 4H), 5.71 (dd, *J* = 10.8, 5.5 Hz, 1H), 5.46 (s, 1H), 5.38 (d, *J* = 4.5 Hz, 1H), 5.27 – 5.19 (m, 2H), 5.11 (d, *J* = 12.3 Hz, 1H), 5.00 (d, *J* = 10.5 Hz, 1H), 4.78 (d, *J* = 11.9 Hz, 1H), 4.74 – 4.65 (m, 2H), 4.58 (d, *J* = 12.0 Hz, 1H), 4.49 (t, *J* = 6.0 Hz, 1H), 4.28 (m, 2H), 4.22 (d, *J* = 5.7 Hz, 1H), 4.15 (dd, *J* = 13.3, 5.1 Hz, 1H), 3.92 (m, 2H), 3.84 (t, *J* = 3.5 Hz, 2H), 3.66 (dd, *J* = 10.3, 6.9 Hz, 1H), 1.01 (s, 9H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 166.1, 165.6, 138.0, 137.8, 135.8, 135.7, 133.9, 133.5, 133.4, 133.4, 133.4, 130.0-129.8(6C), 129.7, 129.6, 128.6-28.5(8C), 128.5-127.8(12C), 117.0, 106.5, 99.7, 83.7, 83.2, 82.4, 82.3, 79.8(2C), 72.5, 72.4, 68.9, 68.6, 63.2, 26.9(3C), 19.4; HRMS (ESI-MS): m/z calcd for $C_{57}H_{60}O_{11}Si$ $[M+Na]^+$: 971.3803; Found: 971.3802.



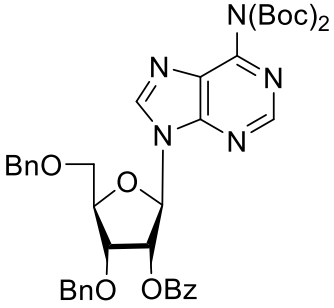
*N, N'*-Di-$^{tert}$Butyloxycarbonyl-9-(2',3',5'-tri-*O*-benzoyl β-D-ribofuranosyl) adenine (**38**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 6/1) giving 458 mg as syrup (yield 72 %) from 500 mg (0.816 mmol) donor **32**; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 0.3): -35.7°; IR ($cm^{-1}$, $CHCl_3$): 2982, 1788, 1723, 1601, 1452, 1369, 1249, 1093, 1025, 707; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.76 (s, 1H), 8.24 (s, 1H), 8.11 (d, *J* = 7.9 Hz, 2H), 8.02 (d, *J* = 7.8 Hz, 2H), 7.91 (d, *J* = 7.8 Hz, 2H), 7.55-7.58 (m, 3H), 7.45-7.38 (m, 6H), 6.50 (d, *J* = 5.4 Hz, 1H), 6.39 (t, *J* = 5.6 Hz, 1H), 6.26 (t, *J* = 5.3 Hz, 1H), 4.88 (m, 2H), 4.73 (dd, *J* = 12.2, 4.2 Hz, 1H), 1.43 (2s, 18H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.2, 165.3, 165.0, 152.9, 152.5(2C), 150.7, 150.3, 143.3, 133.9, 133.8, 133.5, 129.8(4C), 129.8(2C), 129.5, 129.3, 128.7, 128.7(2C), 128.6(2C), 128.5(2C), 128.3, 87.0, 83.9(2C), 80.9, 73.9, 71.4, 63.6, 27.8(6C); HRMS (ESI-MS): m/z calcd for $C_{41}H_{41}N_5O_{11}$ $[M+H]^+$: 780.2881; found: 780.2889.




2-*N*-($^{tert}$Butyloxycarbonyl)-amino-9-(2',3',5'-tri-*O*-benzoyl β-D-ribofuranosyl) 6-chloropurine (**36**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 5/1) giving 325 mg as syrup (yield 76 %) from 300 mg (0.490 mmol) donor **32**; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 0.3): -26.3°; IR ($cm^{-1}$, $CHCl_3$): 2980, 1723, 1523, 1509, 1450, 1399, 1261, 1126, 924, 702; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.08 (s, 1H), 8.01-7.99 (m, 4H), 7.93 (d, *J* = 7.0 Hz, 2H), 7.65 – 7.51 (m, 4H), 7.43 – 7.33 (m, 6H), 6.60 (t, *J* = 5.9 Hz, 1H), 6.37 – 6.24 (m, 2H), 4.96 (dd, *J* = 11.8, 3.9 Hz, 1H), 4.92 – 4.86 (m, 1H), 4.78 (dd, *J* = 11.8, 5.4 Hz, 1H), 1.47 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.3, 165.4, 165.3, 152.7, 152.1, 151.9, 149.8, 143.1, 133.9, 133.7, 133.4, 130.0(2C), 129.9(2C), 129.7(2C), 129.5, 129.0, 128.7(2C), 128.6(2C), 128.6(2C), 128.6, 128.5, 88.3, 81.7, 80.9, 74.9, 71.9, 64.0, 28.2(3C); HRMS (ESI-MS): m/z calcd for $C_{36}H_{32}N_5O_9Cl$ $[M+H]^+$:714.1967; found: 714.1970.

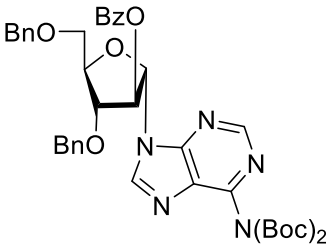



*N, N'*-Di-$^{tert}$Butyloxycarbonyl-9-(2'-*O*-benzoyl-3',5'-di-*O*-benzyl β-D-ribofuranosyl) adenine (**39**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 8/1) giving 274 mg as syrup (yield 71 %) from 300 mg (0.364 mmol) donor **33**; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 0.3): + 0.9°; IR ($cm^{-1}$, $CHCl_3$): 2923, 1722, 1601, 1452, 1272, 1119, 1069, 1029, 700, $^1$H NMR (600 MHz, $CDCl_3$): δ 8.84 (s, 1H), 8.50 (s, 1H), 8.12 – 7.94 (m, 2H), 7.72 – 7.52 (m, 1H), 7.45

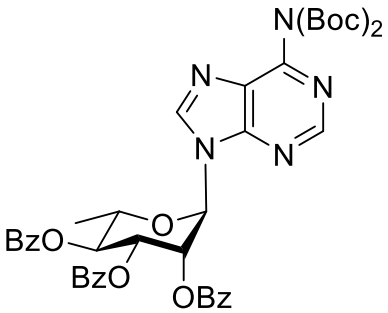


(t, *J* = 7.8 Hz, 2H), 7.40 – 7.29 (m, 5H), 7.28 – 7.18 (m, 5H), 6.53 (d, *J* = 3.7 Hz, 1H), 5.95 (t, *J* = 4.9, 3.7 Hz, 1H), 4.66 – 4.64 (m, 2H), 4.61 – 4.59 (d, *J* = 12 Hz, 1H), 4.54-4.52 (d, *J* = 12.0 Hz, 1H), 4.49-4.47 (d, *J* = 11.9 Hz, 1H), 4.44-4.42(m, 1H) 3.85 (dd, *J* = 10.8, 2.6 Hz, 1H), 3.61 (dd, *J* = 10.8, 3.2 Hz, 1H), 1.45 (2s, 18H); $^{13}$C NMR (151 MHz, $CDCl_3$): δ 165.6, 152.9, 152.4(2C), 150.6, 150.5, 143.5, 137.4, 137.2, 133.8, 130.1(2C), 129.4, 129.1, 128.8(2C), 128.7(2C), 128.6(2C), 128.2(3C), 128.2, 128.0(2C), 87.2, 84.0(2C), 82.5, 76.3, 75.4, 73.7, 73.4, 68.6, 27.9(6C); HRMS (ESI-MS): m/z calcd for $C_{41}H_{45}N_5O_9$ $[M+H]^+$:752.3296 ; found: 752.3331.

*N, N'*-Di-$^{tert}$Butyloxycarbonyl-9-(2'-*O*-benzoyl-3',5'-di-*O*-benzyl β-D-arabinofuranosyl) adenine (**40**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 8/1) giving 274 mg as syrup (yield 71 %) from 300 mg (0.364 mmol) donor **34**;1H NMR (400 MHz, Chloroform-d) δ = 8.86 (s, 1H), 8.50 (s, 1H), 7.99 – 7.91 (m, 2H), 7.66 – 7.58 (m, 1H), 7.48 – 7.40 (m, 2H), 7.34 – 7.22 (m, 10H), 6.56 (d, J=1.6, 1H), 6.02 (t, J=1.8, 1H), 4.79 – 4.66 (m, 3H), 4.56 (s, 2H), 4.36 (dd, J=3.7, 1.8, 1H), 3.67 (qd, J=10.4, 5.3, 2H), 1.44 (s, 18H); 13C NMR (101 MHz, CDCl3) δ 165.27, 153.08, 152.39(2C), 150.54, 150.44, 143.58, 137.61, 136.78, 133.94, 129.98(2C), 129.00, 128.75(2C), 128.73, 128.71(2C), 128.55(2C), 128.29, 128.06(2C), 127.97, 127.82(2C), 88.40, 85.38, 83.86(2C), 82.76, 80.93, 73.68, 72.69, 69.23, 27.90(6C). HRMS (ESI-MS): m/z calcd for $C_{41}H_{45}N_5O_9$ $[M+H]^+$:752.3296 ; found: 752.3331.

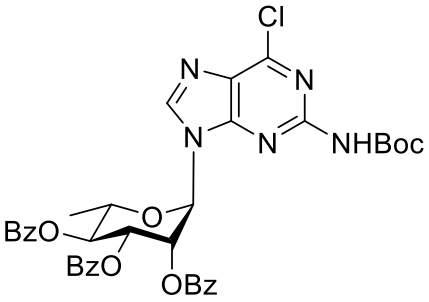



N, N-Di-$^{tert}$Butyloxycarbonyl-9-(2',3',4'-tri-*O*-benzoyl β-D-rhamnopyranosyl) adenine (**41**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 7/1) giving 288 mg as syrup (yield 91 %) from 250 mg (0.399 mmol) donor **20**; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 0.3): -3.5°; IR ($cm^{-1}$, $CHCl_3$): 2982, 1790, 1727, 1600, 1578, 1452, 1247, 1103, 1026, 850, 748, 706; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.94 (s, 1H), 8.44 (s, 1H), 8.16 – 8.05 (m, 2H), 7.99 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.95 – 7.79 (m, 2H), 7.62 – 7.50 (m, 3H), 7.44 (m, 4H), 7.36 (t, *J* = 7.8 Hz, 2H), 6.61 (dd, *J* = 5.8, 3.5 Hz, 1H), 6.50 (d, *J* = 5.7 Hz, 1H), 6.15 (dd, *J* = 6.3, 3.5 Hz, 1H), 5.62 (t, *J* = 6.1 Hz, 1H), 4.47 – 4.37 (m, 1H), 1.61 (d, *J* = 6.7 Hz, 3H), 1.40 (2s, 18H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.4, 165.2, 165.1, 153.3, 152.7(2C), 150.8, 150.4, 143.2, 133.9, 133.8, 133.7, 129.9(2C), 129.8, 129.0,

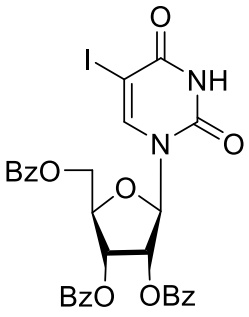


128.9(7C), 128.7(3C), 128.6, 128.4, 83.9(2C), 79.0, 72.2, 71.9, 69.8, 68.7, 27.8(6C), 17.0; HRMS (ESI-MS): m/z calcd for $C_{42}H_{43}N_5O_{11}$ $[M+H]^+$: 794.3037; found: 794.3038.

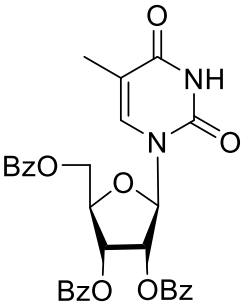
2-*N*-($^{tert}$Butyloxycarbonyl)-amino-9-(2',3',4'-tri-*O*-benzoyl α-L-rhamnopyranosyl) 6-chloropurine (**42**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 6/1) giving 279 mg as syrup (yield 96 %) from 250 mg (0.399 mmol) donor **20**; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 0.3): +32.4; IR ($cm^{-1}$, $CHCl_3$): 2982, 1724, 1604, 1573, 1450, 1260, 1091, 1026, 918, 748, 706; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.22 (s, 1H), 8.11 (s, 1H), 8.02 (dd, *J* = 6.7, 1.7 Hz, 3H), 7.96 (dt, *J* = 7.1, 1.4 Hz, 2H), 7.63 – 7.47 (m, 3H), 7.48 – 7.32 (m, 6H), 6.70 (t, *J* = 3.7 Hz, 1H), 6.38 (dd, *J* = 8.0, 3.6 Hz, 1H), 6.28 (d, *J* = 3.8 Hz, 1H), 5.70 (t, *J* = 7.9 Hz, 1H), 4.31 – 4.18 (m, 1H), 1.83 (s, 1H), 1.52 (s, 9H), 1.49 (d, *J* = 6.4 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.6, 165.4, 165.3, 152.9, 152.5, 152.2, 150.0, 143.2, 133.9, 133.7, 133.6, 130.0, 130.0, 129.9, 129.0, 129.0, 128.7(3C), 128.7, 128.6(3C), 128.6(3C), 127.8, 81.4, 81.4, 71.6, 71.3, 70.4, 69.1, 28.2 (3C), 17.3; HRMS (ESI-MS): m/z calcd for $C_{37}H_{34}ClN_5O_9$ $[M+H]^+$: 728.2123; found: 728.2128.



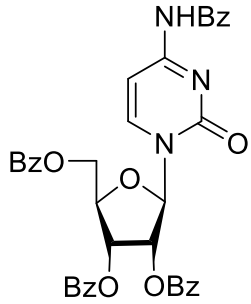

5-Iodo-1-(2',3',5'-tri-*O*-benzoyl α-D-ribofuranosyl) uracil (**45**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 4/1) giving 156 mg as syrup (yield 70 %) from 200 mg (0.229 mmol) donor **32**; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 0.3): -125.7°; IR ($cm^{-1}$, $CHCl_3$): 3034, 1718, 1689, 1603, 1450, 1315, 1259, 1118, 1091, 704; $^1$H NMR (400 MHz, $CDCl_3$): δ 9.21 (s, 1H), 8.12 (d, *J* = 7.8 Hz, 2H), 7.95 (2d, *J* = 7.9 , 4H), 7.85 (s, 1H), 7.54 (m, 5H), 7.37 (m, 4H), 6.35 (d, *J* = 6.1 Hz, 1H), 5.95 – 5.85 (m, 1H), 5.76 (t, *J* = 6.2 Hz, 1H), 4.81 (m, 1H), 4.71 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.1, 165.4, 165.3, 159.6, 149.8, 144.0, 133.9, 133.8, 133.7, 129.9, 129.8, 129.8, 129.1, 128.9(3C), 128.6(3C), 128.5(4C), 128.2, 87.7, 81.0, 73.8, 71.4, 69.8, 63.9; HRMS (ESI-MS): m/z calcd for $C_{30}H_{23}IN_2O_9$ $[M+H]^+$: 683.0527; found: 683.0533.



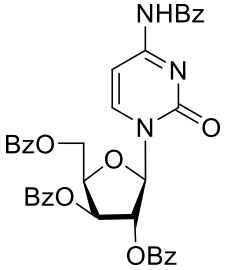
1-(2',3',5'-Tri-*O*-benzoyl α-D-ribofuranosyl) thymine (**47**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 4/1) giving 65 mg as syrup (yield 85 %) from 100 mg (0.163 mmol) donor **32**; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 0.3): -32.3°; IR ($cm^{-1}$, $CHCl_3$): 3064, 1717, 1688, 1601, 1451, 1260, 1096, 1024, 706; $^1$H NMR (400 MHz, $CDCl_3$): δ 9.02 (s,1H), 8.17 – 8.12 (m, 2H), 7.96 (m, 4H), 7.65 – 7.47 (m, 5H), 7.38 (m, 4H), 7.16 (d, *J* = 1.5 Hz, 1H), 6.43 (d, *J* = 6.3 Hz, 1H), 5.92 (dd, *J* = 6.0, 3.7 Hz, 1H), 5.76 (t, *J* = 6.2 Hz, 1H), 4.88 (dd, *J* = 12.1, 2.6 Hz, 1H), 4.70 (q, *J* = 3.3 Hz, 1H), 4.65 (dd, *J* = 12.1, 3.5 Hz, 1H), 1.59 (d, *J* = 1.3 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.1, 165.5, 165.4, 163.6, 150.5, 134.9, 133.8, 133.8, 133.8, 130.0, 129.9, 129.7, 129.3, 128.9, 128.6(6C), 128.4(4C), 112.3, 87.0, 80.6, 73.4, 71.5, 64.0, 12.2; HRMS (ESI-MS): m/z calcd for $C_{31}H_{26}N_2O_9$ $[M+H]^+$: 571.1717; found: 571.1733.




*N*-Benzoyl-1-(2',3',5'-tri-*O*-benzoyl α-D-ribofuranosyl) cytosine (**49**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 4/1) giving 79 mg as syrup (yield 73 %) from 100 mg (0.163 mmol) donor **32**; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 0.3): +0.6; IR ($cm^{-1}$, $CHCl_3$): 3067, 2925, 2852, 1726, 1626, 1554, 1482, 1315, 1264, 1070, 1026, 708; $^1$H NMR (600 MHz, $CDCl_3$): δ 8.81 (s, 1H), 8.11 (d, *J* = 7.7 Hz, 2H), 7.95 (m, 5H), 7.89 (d, *J* = 7.6 Hz, 2H), 7.66 – 7.58 (m, 2H), 7.55 (m, 2H), 7.50 (m, 5H), 7.37 (2d, *J* = 7.6 Hz, 4H), 6.46 (d, *J* = 4.6 Hz, 1H), 5.92 (t, *J* = 5.6 Hz, 1H), 5.86 (t, *J* = 5.2 Hz, 1H), 4.86 (dd, *J* = 12.3, 2.9 Hz, 1H), 4.79 (dt, *J* = 6.1, 3.4 Hz, 1H), 4.73 (dd, *J* = 12.3, 4.0 Hz, 1H); $^{13}$C NMR (151 MHz, $CDCl_3$): δ 166.2, 165.4, 165.3, 162.7, 154.9, 144.5, 133.8, 133.8, 133.8, 133.4,133.0, 130.1(2C), 129.9(2C), 129.7(2C), 129.3, 129.1(2C), 128.9(2C), 128.7, 128.7, 128.6(5C), 127.7(2C), 97.3, 89.6, 80.7, 74.8, 71.0, 63.7; HRMS (ESI-MS): m/z calcd for $C_{37}H_{29}N_3O_9$ $[M+H]^+$: 660.1982; found: 660.1987.

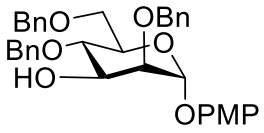



*N*-Benzoyl-1-(2',3',5'-tri-*O*-benzoyl α-D-xylofuranosyl) cytosine (**50**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 4/1) giving 88 mg as syrup (yield 81 %) from 100 mg (0.163 mmol) donor **43**; $^1$H NMR (400 MHz, $CDCl_3$): δ 8.36 (s, 1H), 8.11 (d, *J* = 7.8 Hz, 2H), 7.92 (m, 6H), 7.67 – 7.38 (m, 14H), 6.35 (s, 1H), 5.86 (d, *J* = 3.5 Hz, 1H), 5.77 (s, 1H), 4.98 (s, 1H), 4.85 (dd, *J* = 12.2, 6.4 Hz, 1H), 4.75 (dd, *J* = 12.3, 4.1 Hz, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$): δ 166.2, 164.7, 164.5, 162.8, 154.7, 144.3, 134.1, 133.9, 133.5, 133.3, 133.1, 130.1(2C), 129.9(2C), 129.7(2C), 129.2, 129.0(2C), 128.8,

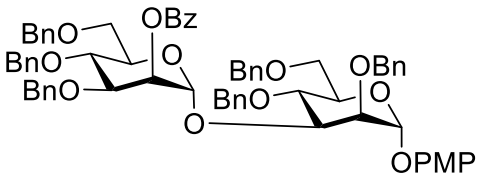


128.7(2C), 128.6(2C), 128.5(3C), 128.2, 127.8(2C), 96.7, 90.7, 80.9, 80.4, 74.8, 61.6; HRMS (ESI-MS): m/z calcd for $C_{37}H_{29}N_3O_9$ $[M+H]^+$: 660.1982; found: 660.1980.

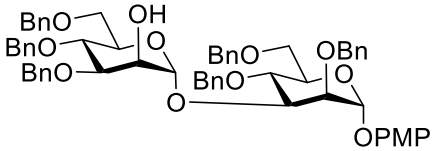
*p*-Methoxyphenyl-2,4,6-tri-*O*-benzyl α-D-mannopyranoside (**51**): The title compound was synthesised according to the reported methods form D-mannose, as a syrup; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 0.3): +23.5°; IR ($cm^{-1}$, $CHCl_3$): 2923, 2856, 1505, 1224, 1094, 1027, 827, 733, 690; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.22 (m, 15H), 6.99 (d, *J* = 9.1 Hz, 2H), 6.78 (d, *J* = 9.1 Hz, 2H), 5.53 (d, *J* = 1.8 Hz, 1H), 4.87 (d, *J* = 11.0 Hz, 1H), 4.81 (d, *J* = 11.8 Hz, 1H), 4.64 (dd, *J* = 11.8, 8.3 Hz, 2H), 4.55 (d, *J* = 11.0 Hz, 1H), 4.46 (d, *J* = 11.9 Hz, 1H), 4.18 (td, *J* = 8.5, 3.5 Hz, 1H), 3.96 – 3.77 (m, 4H), 3.75 (s, 3H), 3.69 (dd, *J* = 11.0, 1.9 Hz, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 155.1, 150.4, 138.5, 138.4, 137.7, 128.7(2C), 128.5(2C), 128.4(2C), 128.2, 128.1(2C), 128.1(2C), 127.9(2C), 127.8, 127.6, 117.9(2C), 114.7(2C), 96.2, 78.3, 76.5, 75.0, 73.4, 73.1, 71.8, 71.6, 69.1, 55.8; HRMS (ESI-MS): m/z calcd for $C_{34}H_{36}O_7$ $[M+Na]^+$: 579.2379; found: 579.2371.




*p*-Methoxyphenyl-2,4,6-tri-*O*-benzyl-3-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl α-D-mannopyranosyl) α-D-mannopyranoside (**52**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 10/1) giving 1.43 g as syrup (yield 80 %) from 1.2 g (1.7 mmol) acceptor **51**; $[\alpha]^{25}_D$ ($CHCl_3$, *c* 0.3): +16.4°; IR ($cm^{-1}$, $CHCl_3$): 2927, 2866, 1723, 1505, 1453, 1267, 1094, 1027, 828, 734, 696; $^1H$ NMR (400 MHz, $CDCl_3$): δ 8.05 (d, *J* =7.8 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.53-7.16 (m, 32H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.76 (d, *J* = 8.5 Hz, 2H), 5.77 (d, *J* = 3.1 Hz, 1H), 5.45 (s, 1H), 5.40 (s, 1H), 4.90 (d, *J* = 11.1 Hz, 1H), 4.78 (dd, *J*=16.6, 11.1 Hz, 2H), 4.72 – 4.61 (m, 4H), 4.56 – 4.43 (m, 5H), 4.38 (dd, *J* = 9.3, 3.0 Hz, 1H), 4.14 (dd, *J* = 11.8, 7.5 Hz, 2H), 4.04 (m, 3H), 3.87 (dd, *J* = 9.9, 4.0 Hz, 1H), 3.79 (d, *J* = 5.8 Hz, 3H), 3.74 (s, 3H), 3.65 (d, *J* = 11.0 Hz, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 165.6, 155.0, 150.4, 138.7, 138.5, 138.4, 138.1, 138.0, 138.0, 133.2, 130.1(2C), 130.0, 128.6-128.4(15C), 128.2, 128.2, 127.9-127.6(15C), 117.9(2C), 114.7(2C), 100.0, 96.6, 78.6, 78.2, 75.3, 75.2, 75.0, 74.5, 73.6, 73.4, 72.5(4C), 71.7, 69.5, 69.2, 69.0, 55.8; HRMS (ESI-MS): m/z calcd for $C_{68}H_{68}O_{13}$ $[M+Na]^+$: 1115.4558; found: 1115.4556.

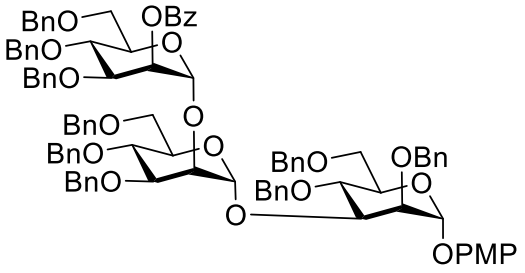



*p*-Methoxyphenyl-2,4,6-tri-*O*-benzyl-3-*O*-(3,4,6-tri-*O*-benzyl α-D-mannopyranosyl) α-D-mannopyranoside (**53**): The titled compound was obtained after saponification under Zemplén conditions, followed by column purification (petroleum ether/ethyl acetate = 7/1)

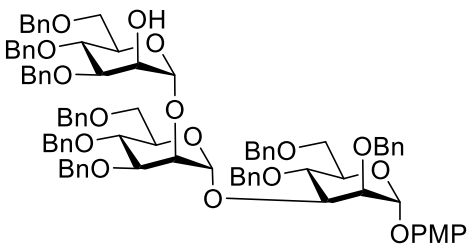


giving 1.21 g as syrup (yield 88 %) from 1.43 g (1.31 mmol) compound **52**; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 0.3): +24.9°; IR ($cm^{-1}$, $CHCl_3$): 2918, 2862, 1723, 1505, 1453, 1267, 1026, 733, 696; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.15 (m, 30H), 6.93 (d, *J* = 8.6 Hz, 2H), 6.76 (d, *J* = 8.7 Hz, 2H), 5.43 (s, 1H), 5.29 (s, 1H), 4.85 (d, *J* = 11.1 Hz, 1H), 4.70 – 4.61 (m, 6H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.50 (m, 3H), 4.45 (d, *J* = 11.9 Hz, 1H), 4.33 (dd, *J* = 9.3, 3.1 Hz, 1H), 4.15 – 4.04 (m, 2H), 3.98 (m, 2H), 3.93 – 3.85 (m, 2H), 3.84 – 3.77 (m, 2H), 3.74 (s, 3H), 3.71 – 3.62 (m, 3H), 2.40 (s, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 155.0, 150.4, 138.7, 138.4, 138.3, 138.2(2C), 138.0, 128.6-128.4(12C), 128.0-127.6(18C), 118.0(2C), 114.6(2C), 101.5, 96.7, 80.1, 78.5, 77.6, 75.1(2C), 75.0, 74.5, 73.6, 73.4, 72.4(2C), 72.2, 72.0, 69.4, 69.0, 68.8, 55.7; HRMS (ESI-MS): m/z calcd for $C_{61}H_{64}O_{12}$ $[M+Na]^+$: 1011.4295; found: 1011.4294**.**

*p*-Methoxyphenyl-2,4,6-tri-*O*-benzyl-3-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl α-D-mannopyranosyl)3,4,6-tri-*O*-benzyl α-D-mannopyranosyl) α-D-mannopyranoside (**54**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 8/1) giving 1.13 g as syrup (yield 81 %) from 898 mg (0.908 mmol) acceptor **53**; $[\alpha]^{25}_{D}$ ($CH_3Cl$, *c* 0.3): +30.6; IR ($cm^{-1}$, $CHCl_3$): 3031, 2930, 2865, 1723, 1505, 1453, 1362, 1267, 1027, 828, 747, 695; $^1H$ NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 7.6 Hz, 2H), 7.54 (t, *J* = 7.6 Hz, 2H), 7.41 – 7.07 (m, 46H), 6.94 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.6 Hz, 2H), 5.75 (s, 1H), 5.41 (s, 1H), 5.27 (m, 2H), 5.11 (s, 1H), 4.86 (m, 2H), 4.74 (t, *J* = 11.3 Hz, 2H), 4.67 – 4.61 (m, 4H), 4.55 (m, 6H), 4.46 (d, *J* = 12.7 Hz, 2H), 4.38 (t, *J* = 10.0 Hz, 2H), 4.30 (d, *J* = 9.2 Hz, 1H), 4.12 (m, 3H), 4.07 – 3.93 (m, 5H), 3.89 – 3.77 (m, 3H), 3.74 (s, 3H), 3.64 (m, 3H), 3.52 (d, *J* = 10.9 Hz, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 165.5, 155.0, 150.6, 138.7-138.2(9C), 133.1, 130.2(2C), 130.1, 128.5-128.3(22C), 128.0-127.5(25C), 118.0(2C), 114.6(2C), 101.3, 99.5, 96.5, 79.6, 78.1, 77.8, 75.6(2C), 75.3, 74.9, 74.8(2C), 74.3(2C), 73.6, 73.3(2C), 72.7, 72.5, 72.4, 72.4, 72.2(2C), 71.7, 69.9, 69.1, 68.9, 55.7; HRMS (ESI-MS): m/z calcd for $C_{95}H_{96}O_{18}$ $[M+Na]^+$: 1547.6494; found: 1548.6496.



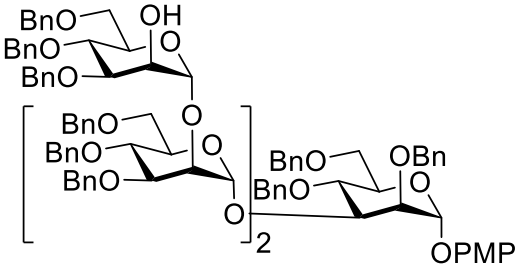

*p*-Methoxyphenyl-2,4,6-tri-*O*-benzyl-3-*O*-(2-*O*-(3,4,6-tri-*O*-benzyl α-D-mannopyranosyl)3,4,6-tri-*O*-benzyl α-D-mannopyranosyl) α-D-mannopyranoside (**55**): The titled compound was obtained after saponification under Zemplén conditions, followed by column



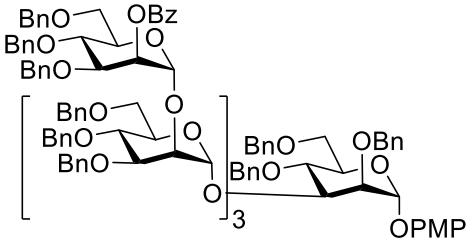
purification (petroleum ether/ethyl acetate = 6/1) giving 800 mg as syrup (yield 86 %) from 1.00 g (0.675 mmol) compound **54**; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 0.3): +21.8°; IR ($cm^{-1}$, $CHCl_3$): 3012, 1506, 1454, 1215, 1042, 744, 697; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.19 (m, 40H), 7.17 – 7.11 (m, 5H), 6.93 (d, *J* = 8.9 Hz, 2H), 6.74 (d, *J* = 8.9 Hz, 2H), 5.41 (d, *J* = 2.0 Hz, 1H), 5.29 (s, 1H), 5.12 (s, 1H), 4.85 (d, *J* = 11.1 Hz, 1H), 4.79 (d, *J* = 11.0 Hz, 1H), 4.72 (d, *J* = 11.5 Hz, 1H), 4.67 – 4.51 (m, 11H), 4.49 – 4.33 (m, 5H), 4.28 (dd, *J* = 9.4, 3.0 Hz, 1H), 4.12 (q, *J* = 2.6 Hz, 2H), 4.06 – 3.95 (m, 4H), 3.93 – 3.82 (m, 4H), 3.78 (d, *J* = 9.6 Hz, 1H), 3.74 (s, 3H), 3.72 – 3.58 (m, 5H), 3.49 (d, *J* = 10.6 Hz, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 155.0, 150.6, 138.8, 138.6, 138.5, 138.5, 138.5, 138.4, 138.3, 138.2, 138.2, 128.6-128.3(18C), 128.0-127.5(27C), 118.1(2C), 114.6(2C), 101.4, 101.0, 96.5, 80.0, 79.6, 77.8, 77.4, 75.2, 75.1, 75.0, 75.0, 74.8, 74.7, 74.3, 73.6, 73.3, 73.3, 72.8, 72.4, 72.4, 72.2, 72.2, 71.8, 69.9, 69.2, 68.7, 68.7, 55.7; HRMS (ESI-MS): m/z calcd for $C_{88}H_{92}O_{17}$ $[M+Na]^+$:1443.6232; found: 1443.6227.

*p*-Methoxyphenyl-2,4,6-tri-*O*-benzyl-3-*O*-(2-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl α-D-mannopyranosyl) α-D-mannopyranoside (**56**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 7/1) giving 1.02 g as syrup (yield 88 %) from 840 mg (0.591 mmol) acceptor **55**; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 0.3): +20.9°; IR ($cm^{-1}$, $CHCl_3$): 2919, 2864, 1505, 1453, 1362, 1224, 1027, 828, 732, 695; $^1H$ NMR (400 MHz, $CDCl_3$): δ 8.07 (d, *J* = 7.8 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.38 – 7.23 (m, 34H), 7.22 – 7.17 (m, 18H), 7.11 (m, 7H), 6.98 (t, *J* = 7.3 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.74 (d, *J* = 8.7 Hz, 2H), 5.76 (s, 1H), 5.39 (s, 1H), 5.30 (s, 1H), 5.23 (s, 1H), 5.14 (s, 1H), 4.84 (dd, *J* = 11.0, 6.1, 2H), 4.83(m, 1H), 4.73 (dd, *J* = 11.3, 8.2 Hz, 2H), 4.67 – 4.47 (m, 14H), 4.46 – 4.32 (m, 5H), 4.28 (d, *J* = 11.8 Hz, 2H), 4.12 (m, 6H), 4.06 (s, 1H), 4.04 – 3.87 (m, 7H), 3.84 (dd, *J* = 10.2, 4.4 Hz, 1H), 3.74 (s, 3H), 3.68 (m, 5H), 3.59 (d, *J* = 10.8 Hz, 1H), 3.50 (d, *J* = 10.8 Hz, 2H); $^{13}C$ NMR (101 MHz, $CDCl_3$): δ 165.5, 155.0, 150.6, 138.8(2C), 138.7, 138.7, 138.6, 138.5(3C), 138.5, 138.3, 138.2(2C), 133.1-128.1(36C), 128.0-127.4(31C), 118.1(2C), 114.6(2C), 101.4, 100.7, 99.5, 96.5, 79.6, 79.4, 78.3, 77.8, 77.4, 75.5, 75.4, 75.4(2C), 75.2, 75.1, 74.9, 74.7, 74.4, 73.6, 73.4, 73.3, 73.2, 72.8, 72.6, 72.4, 72.3, 72.3, 72.2, 72.2, 71.7, 69.9, 69.2, 69.2, 69.1, 69.0, 69.0, 55.7; HRMS (ESI-MS): m/z calcd for $C_{122}H_{124}O_{23}$ $[M+Na]^+$:1980.8465; found: 1980.9170.

*p*-Methoxyphenyl-2,4,6-tri-*O*-benzyl-3-*O*-(2-*O*-(2-*O*-(3,4,6-tri-*O*-benzyl α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl α-D-mannopyranosyl) α-D-mannopyranoside (**57**): The titled compound was obtained after saponification under Zemplén conditions, followed by column purification (petroleum ether/ethyl acetate = 4/1) giving 814 mg as syrup (yield 86 %) from 1.00 g (0.522 mmol) compound **56**; $[\alpha]^{25}_{D}$($CHCl_3$, *c* 0.15): +52.0°; IR ($cm^{-1}$, $CHCl_3$): 3010, 2925, 2865, 1505, 1454, 1362, 1221, 1051, 745, 695; $^1$H NMR (600 MHz, $CDCl_3$): δ 7.39 – 7.05 (m, 60H), 6.91 (d, *J* = 8.9 Hz, 2H), 6.73 (d, *J* = 9.0 Hz, 2H), 5.39 (d, *J* = 2.0 Hz, 1H), 5.30 (s, 1H), 5.22 (d, *J* = 2.0 Hz, 1H), 5.16 (s, 1H), 4.84 (d, *J* = 11.0 Hz, 1H), 4.80 (d, *J* = 10.8 Hz, 2H), 4.72 (d, *J* = 11.3 Hz, 1H), 4.67 – 4.61 (m, 2H), 4.59 – 4.48 (m, 12H), 4.44 (m, 3H), 4.39 (d, *J* = 11.3 Hz, 1H), 4.33 (d, *J* = 12.4 Hz, 1H), 4.28 (dd, *J* = 9.4, 3.1 Hz, 1H), 4.24 (d, *J* = 12.2 Hz, 1H), 4.14 – 4.09 (m, 3H), 4.05 (t, *J* = 2.4 Hz, 1H), 4.00 (dd, *J* = 10.2, 6.4 Hz, 2H), 3.96 (dd, *J* = 9.3, 2.8 Hz, 1H), 3.92 – 3.84 (m, 7H), 3.74 (s, 3H), 3.71 – 3.63 (m, 5H), 3.60 – 3.55 (m, 2H), 3.49 (d, *J* = 10.8 Hz, 1H), 3.44 (d, *J* = 10.5 Hz, 1H), 2.40 (s, 1H); $^{13}$C NMR (151 MHz, $CDCl_3$): δ 155.0, 150.6, 138.8, 138.8, 138.8, 138.7, 138.5(4C), 138.4, 138.3, 138.2(2C), 128.6-128.3(25C), 128.1-127.9(11C), 127.8-127.4(25C), 118.1(2C), 114.6(2C), 101.4, 101.0, 100.9, 96.5, 80.2, 79.6, 79.5, 77.7, 75.4, 75.2, 75.1(3C), 74.9, 74.8, 74.8, 74.3, 73.6, 73.5, 73.3, 73.2, 72.7, 72.6, 72.5, 72.4, 72.2, 72.2(3C), 71.7, 69.9, 69.2, 69.1, 68.8, 68.6, 55.8; HRMS (ESI-MS): m/z calcd for $C_{115}H_{120}O_{22}$ $[M+Na]^+$:1876.8202; found: 1876.8209.




*p*-Methoxyphenyl-2,4,6-tri-*O*-benzyl-3-*O*-(2-*O*-(2-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl α-D-mannopyranosyl) α-D-mannopyranoside (**58**): The titled compound was obtained after column purification (petroleum ether/ethyl acetate = 5/1) giving 0.114 mg as syrup (yield 88 %) from 100 mg (0.054 mmol) acceptor **57**; $[\alpha]^{25}_{D}$($CHCl_3$, *c* 0.3): +12.2°; IR ($cm^{-1}$, $CHCl_3$): 3031, 2918, 2863, 1724, 1505, 1453, 1268, 1051, 733, 694; $^1$H NMR (600 MHz, $CDCl_3$): δ 8.07 (d, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.7 Hz, 2H), 7.32 – 7.06 (m, 73H), 7.00 (t, *J* = 7.5 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 6.73 (d, *J* = 8.8 Hz, 2H), 5.77 (s, 1H), 5.39 (s, 1H), 5.32 (s, 1H), 5.26 (s, 1H), 5.22 (s, 1H), 5.11 (s, 1H), 4.86 (dd, *J* = 10.9, 3.0 Hz, 2H), 4.83 – 4.78 (m, 2H), 4.74

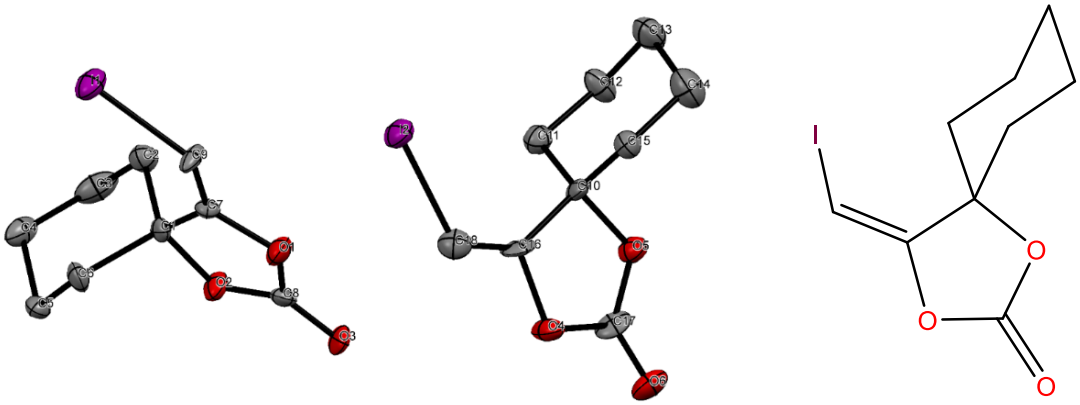


(dd, *J* = 11.2, 8.2 Hz, 2H), 4.66 – 4.60 (m, 2H), 4.60 – 4.58 (m, 1H), 4.56 (d, *J* = 4.1 Hz, 2H), 4.55 (s, 3H), 4.53 – 4.49 (m, 7H), 4.42 (m, 7H), 4.33 (d, *J* = 12.4 Hz, 1H), 4.29 (dd, *J* = 9.3, 3.1 Hz, 1H), 4.25 (t, *J* = 11.9 Hz, 2H), 4.15 – 4.05 (m, 6H), 4.02 – 3.81 (m, 11H), 3.74 (s, 3H), 3.71 – 3.67 (m, 4H), 3.65 (d, *J* = 5.8 Hz, 1H), 3.63 – 3.57 (m, 2H), 3.54 – 3.47 (m, 3H); $^{13}$C NMR (151 MHz, $CDCl_3$): δ 165.5, 155.0, 150.6, 138.8(5C), 138.6, 138.5(4C), 138.4, 138.3, 138.3, 138.2(2C), 133.1, 130.2, 130.1(2C), 128.5-128.1(38C), 128.0, 127.9-127.4(38C), 118.1(2C), 114.6(2C), 101.4, 101.2, 100.8, 99.6, 96.5, 79.7, 79.5, 79.4, 78.4(2C), 77.7, 75.8, 75.5(2C), 75.4, 75.3, 75.1(2C), 75.0, 74.8, 74.8(2C), 74.5, 73.6, 73.4(3C), 73.3, 73.2, 72.7, 72.6, 72.5, 72.4, 72.4, 72.3, 72.3, 72.2, 72.1, 71.7, 69.9, 69.3, 69.2, 69.2, 69.1, 69.0, 55.8; HRMS (ESI-MS): m/z calcd for $C_{149}H_{152}O_{28}$ $[M+Na]^+$:2413.0401; found: 2413.3660.

### 3.2.9 - Crystallographic Information of extruded product C

Crystals of compound **C** were grown by slow evaporation from a solution of chloroform at 25 °C. A single crystal (0.15×0.007×0.18 mm) was mounted on a loop with a small amount of paraffin oil. The X-ray data were collected at 150 K on a Bruker APEX(II) DUO CCD diffractometer using Mo $K_\alpha$ radiation ($\lambda$ = 0.71073 Å), $\omega$-scans ($2\theta$ = 56.906), for a total of 21317 independent reflections. Space group P $2_1$, a = 6.994 (1), b = 15.419 (2), c = 9.467 (12), $\alpha$ = 90, $\beta$ = 97.595 (4), $\gamma$ = 90, V = 1012.0 (2) Å$^3$, Monoclinic, Z = 4 for chemical formula $C_9H_{11}I\ O_3$, with two molecules in the asymmetric unit; $\rho$ calcd = 1.93 gcm$^{-3}$, $\mu$ = 3.137 mm$^{-1}$, F (000) = 568. The structure was obtained by direct methods using SHELXS-97. The final R value was 0.0307 (wR2 = 0.1011) 5051 observed reflections ($F_0 \geq 4\sigma$ ($|F_0|$)) and 237 variables, S = 0.785.

ORTEP Diagram of Compound **C**

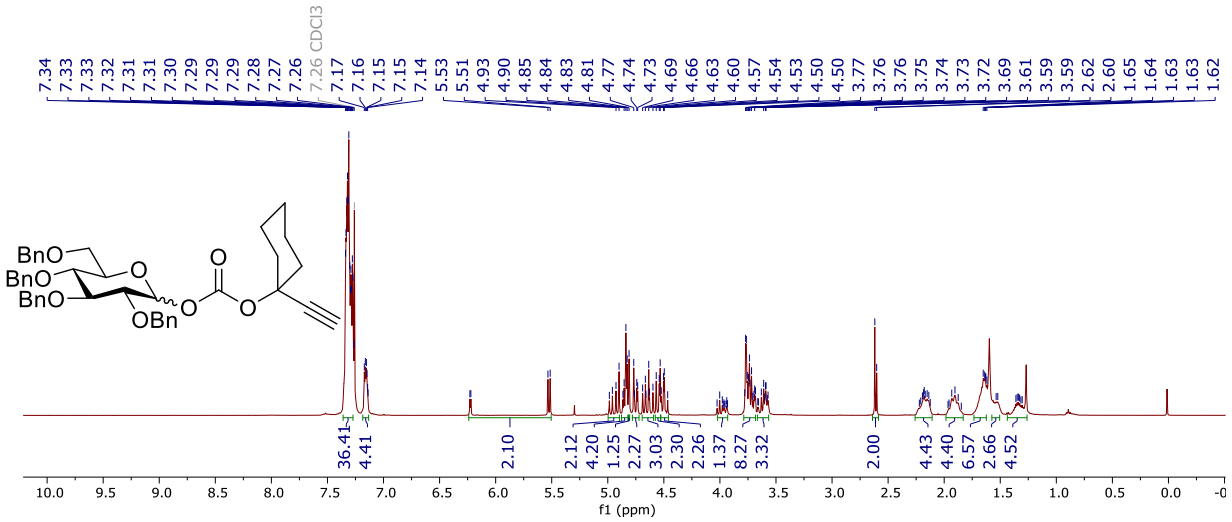


CCDC No. 2246866 **C**

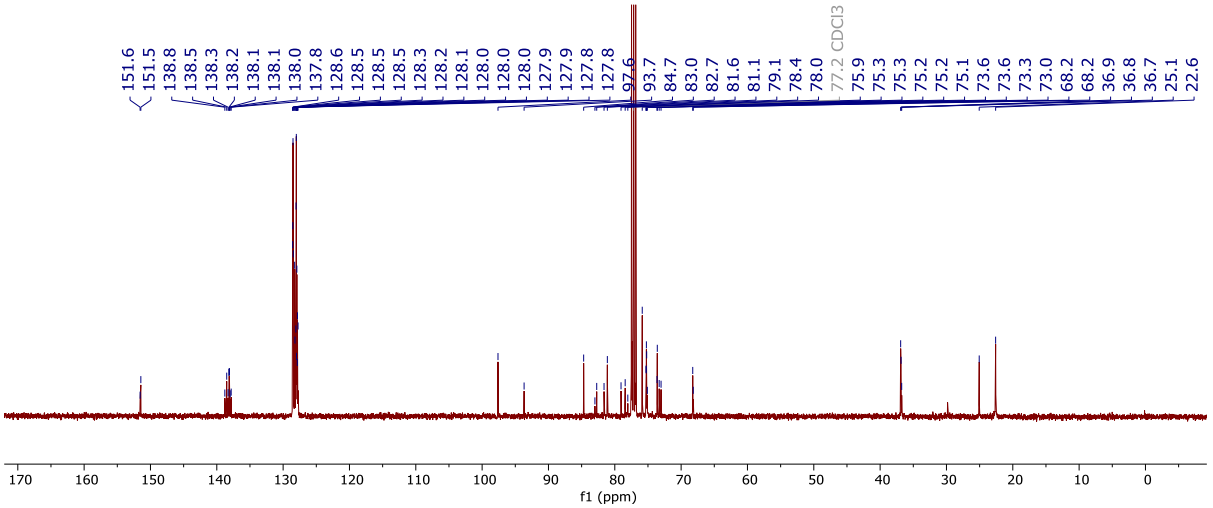
**Figure 3.2**: ORTEP diagram of compound **C**. H-atoms are omitted for clarity. Ellipsoids are drawn at 50% probability.

### 3.2.10 - NMR Spectral Charts

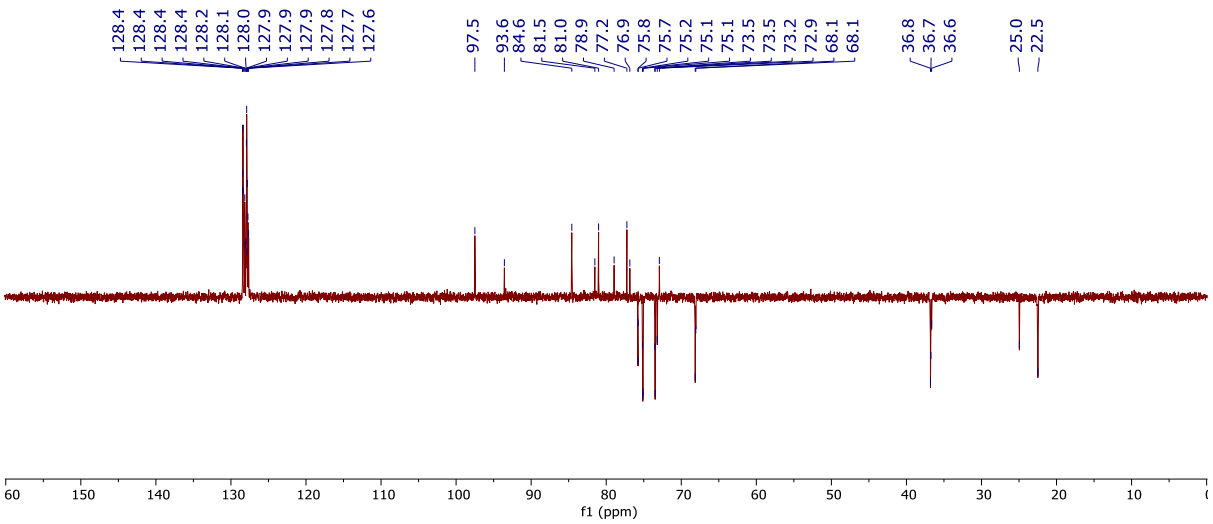
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **1**



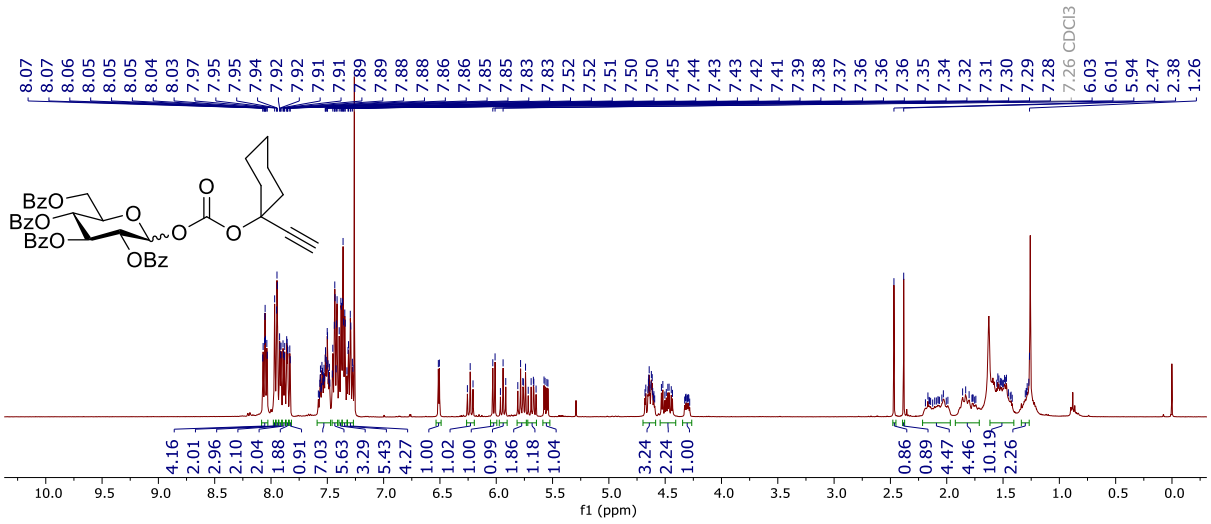

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **1**



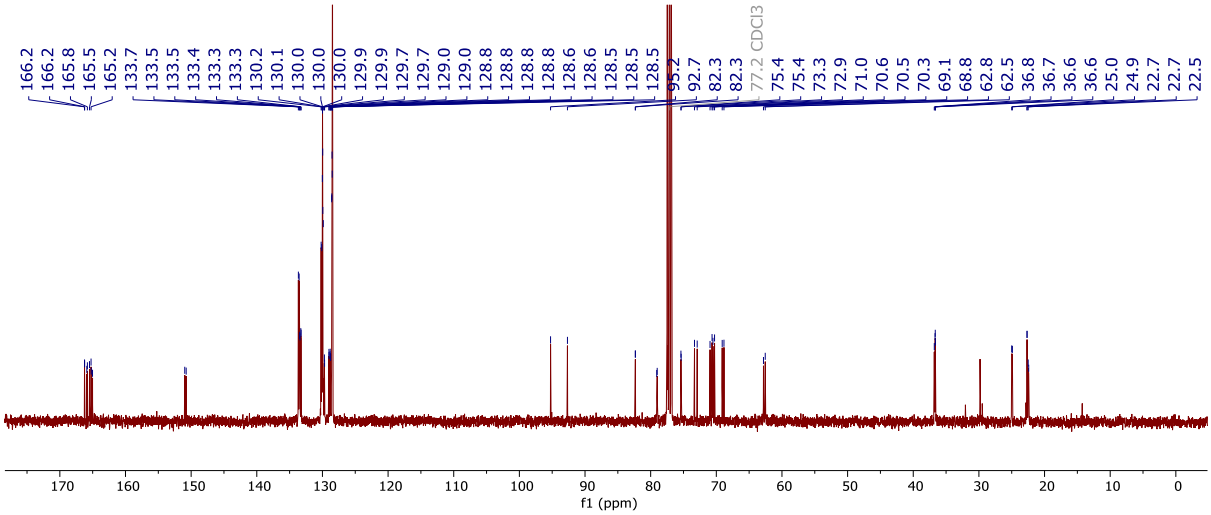

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **1**



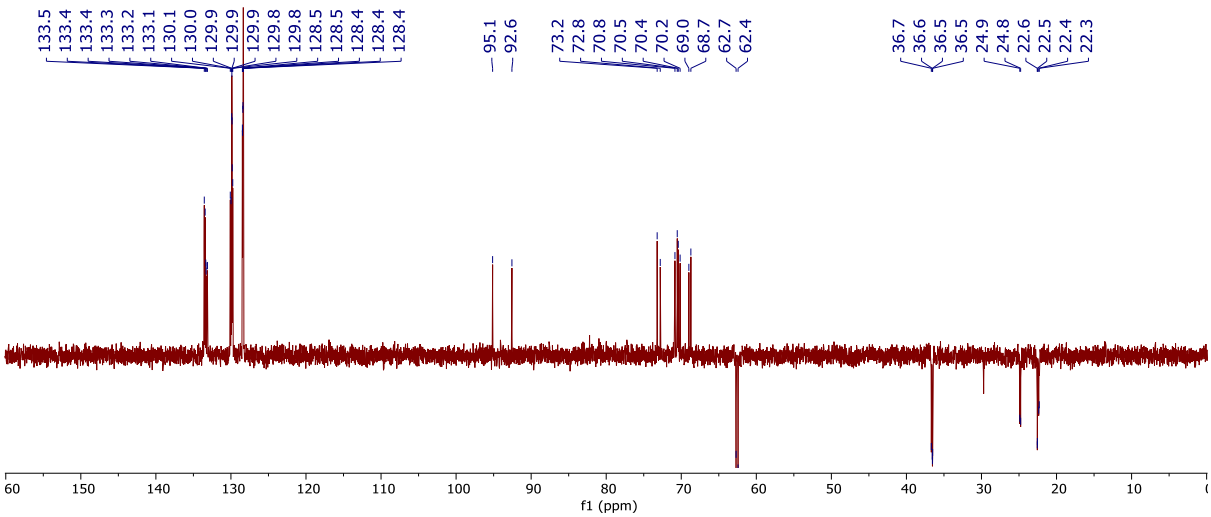
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **4**



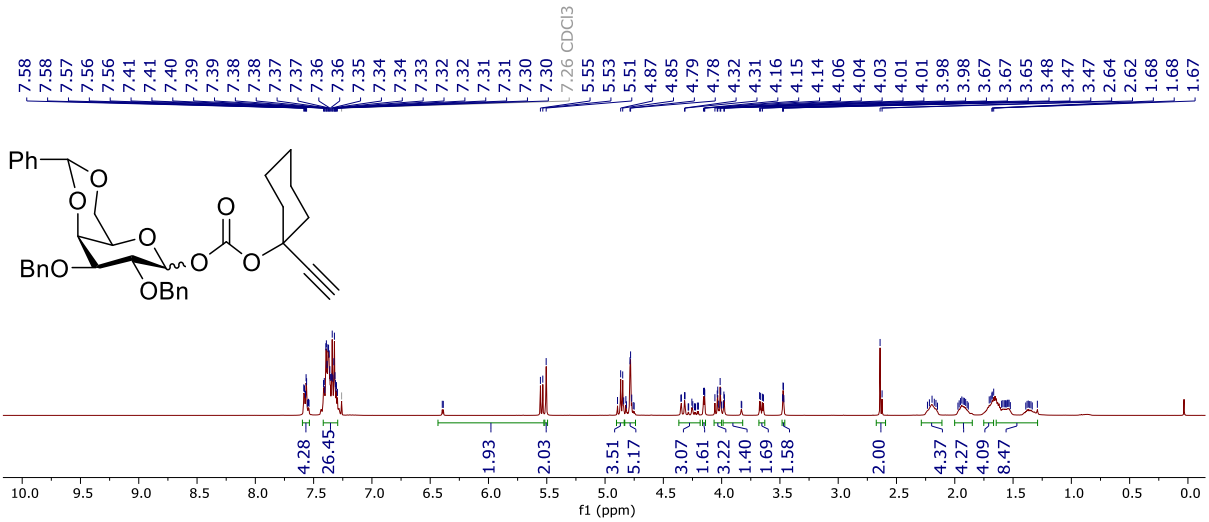

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **4**



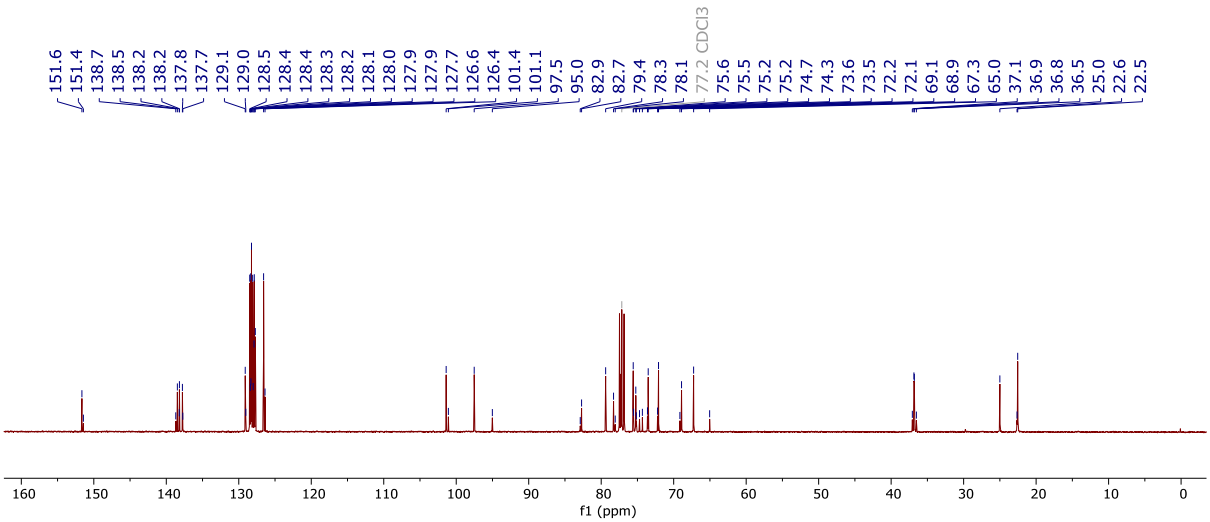

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **4**



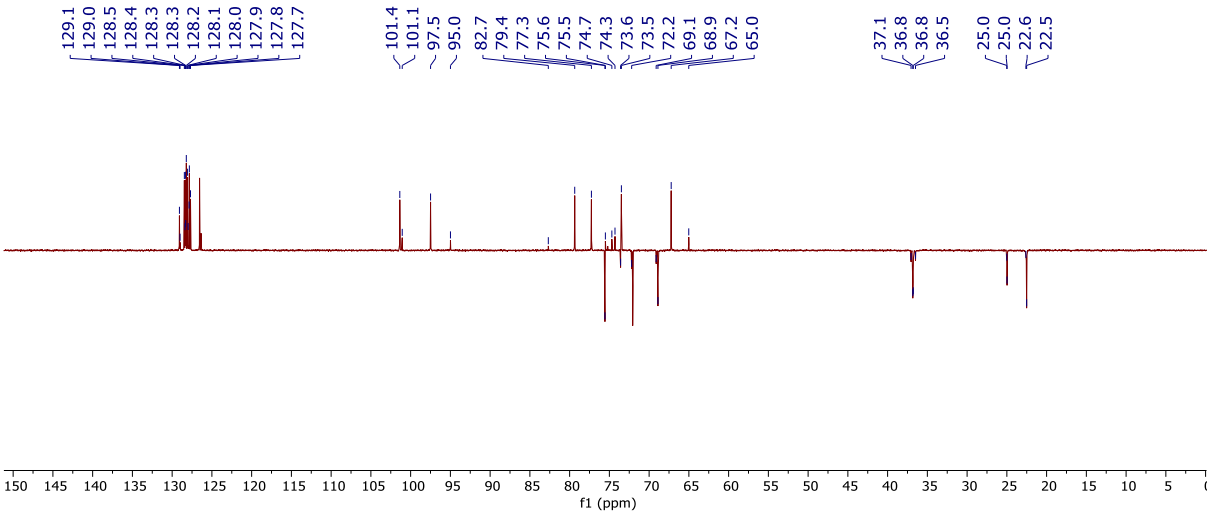
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **9**



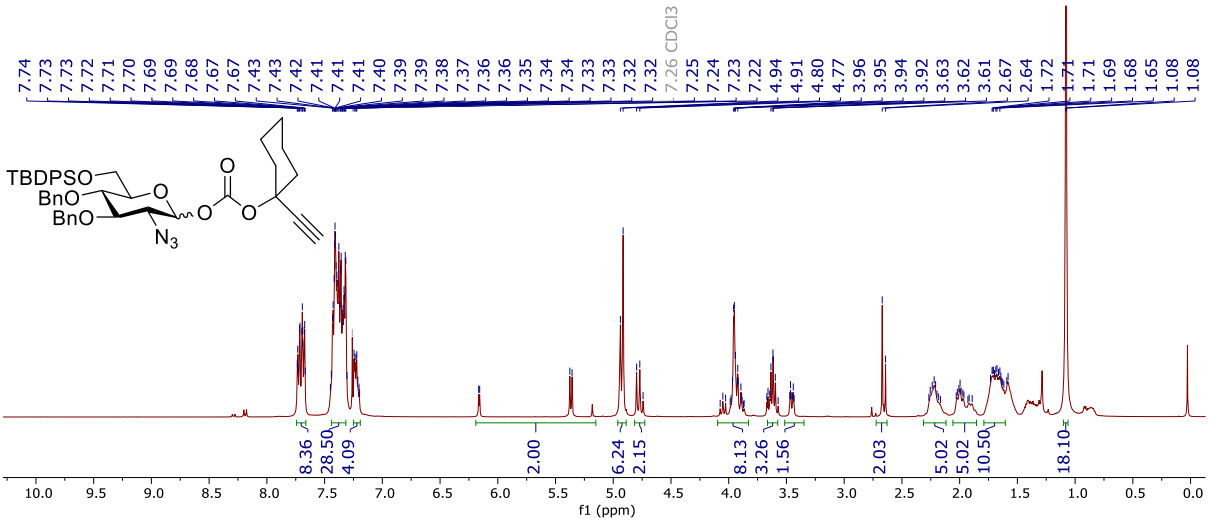

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **9**



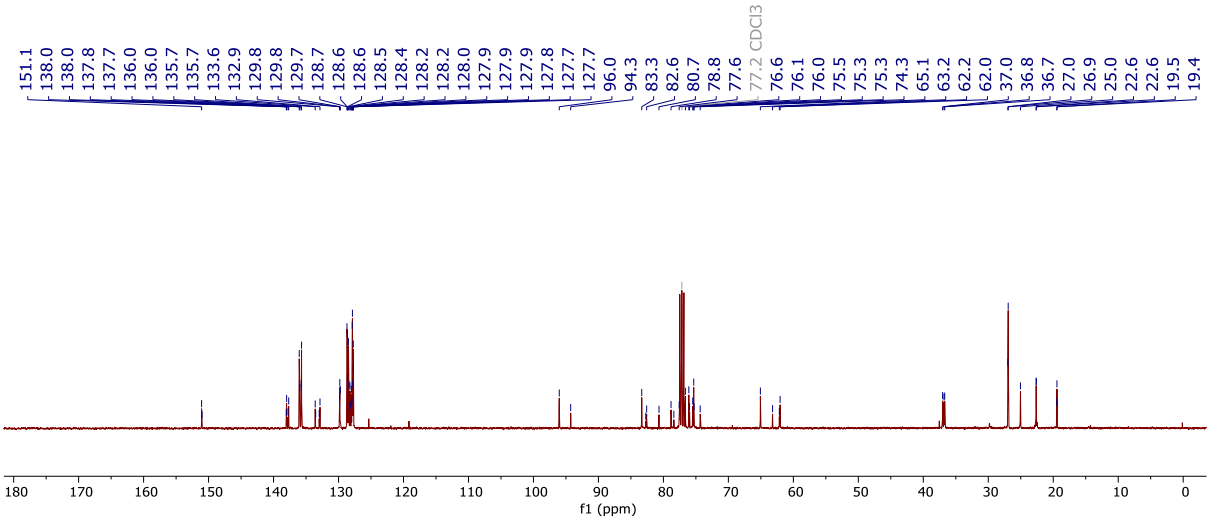

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **9**



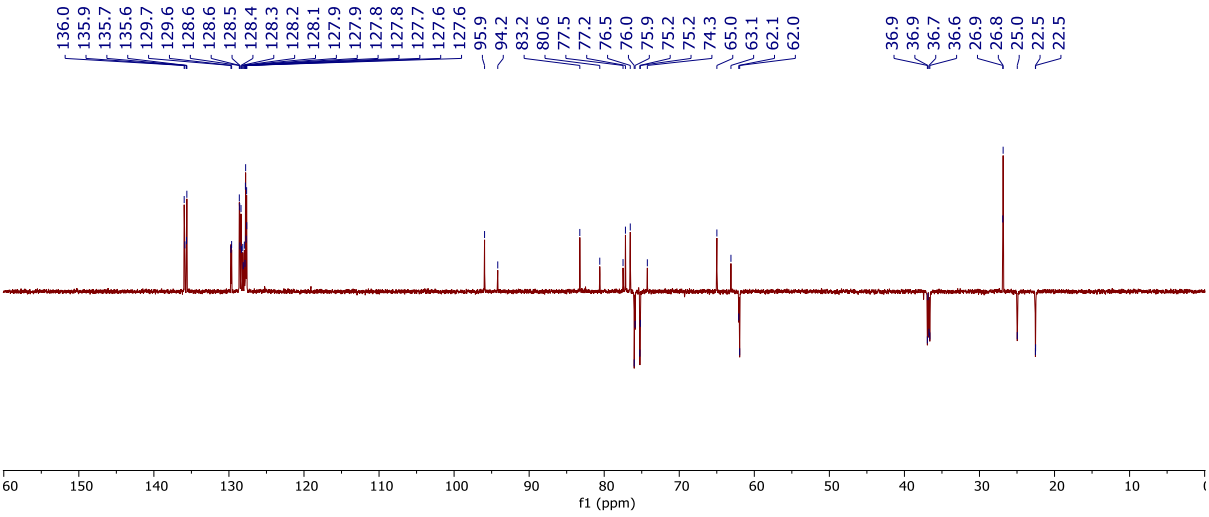
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **12**



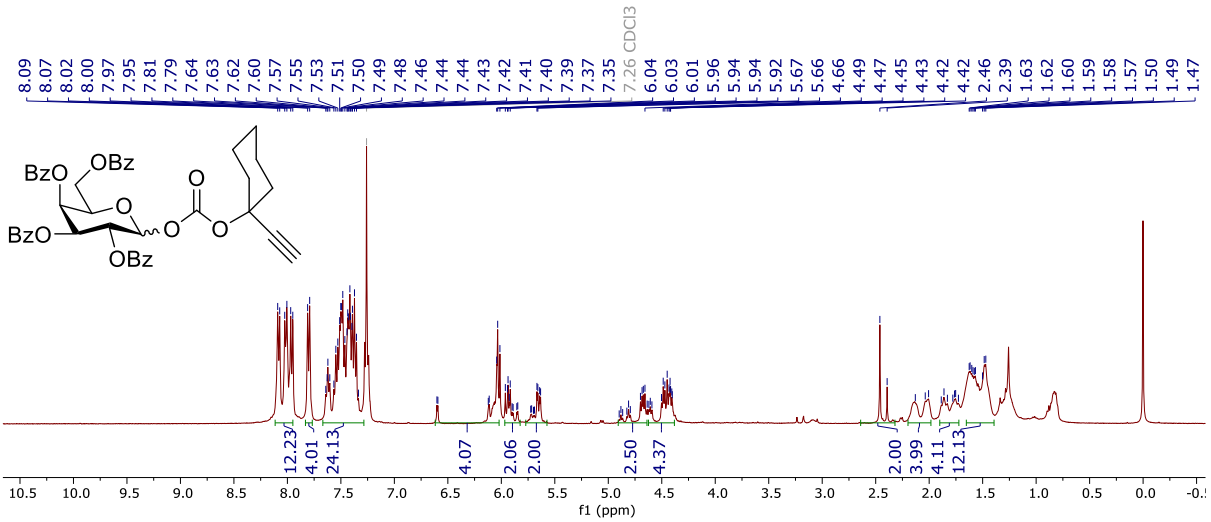

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **12**



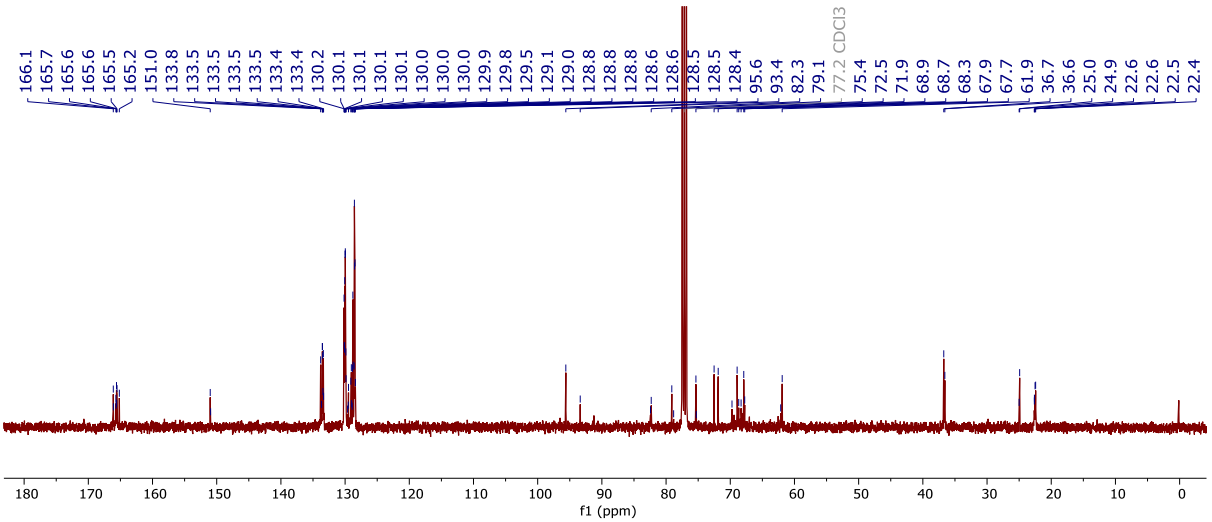

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **12**



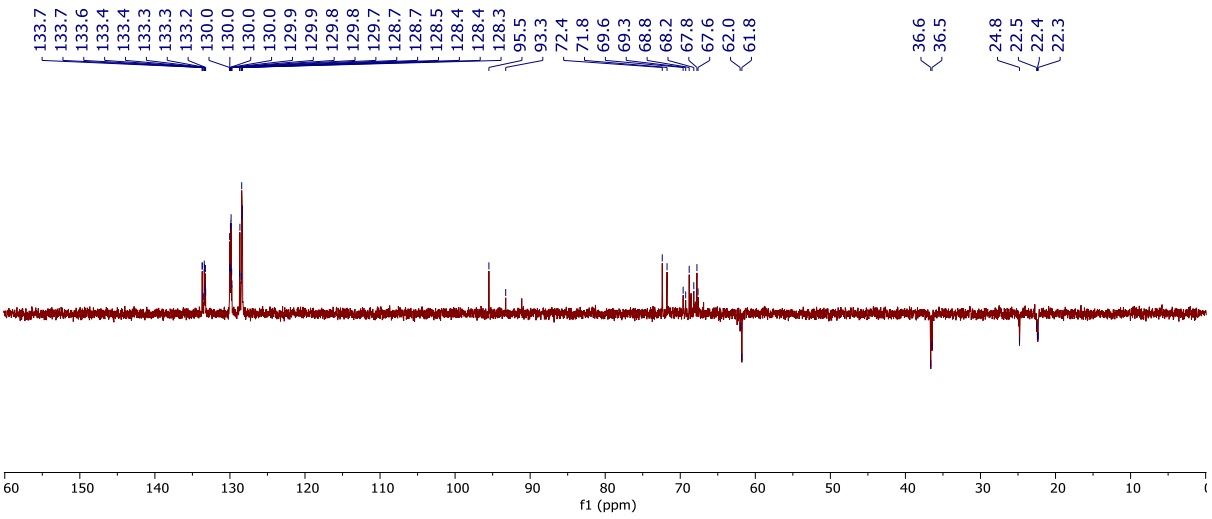
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **16**



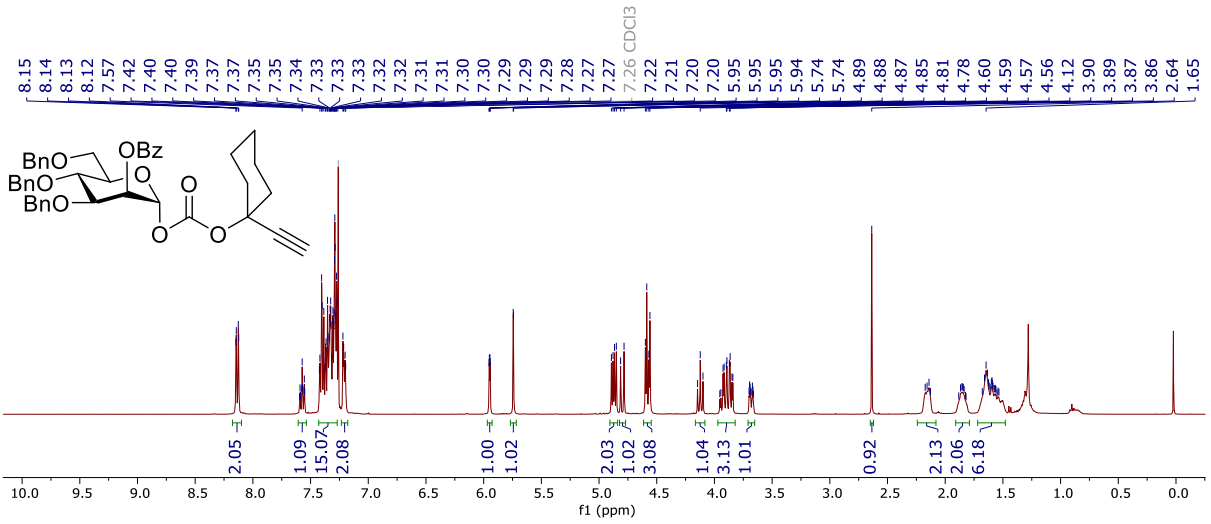

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **16**



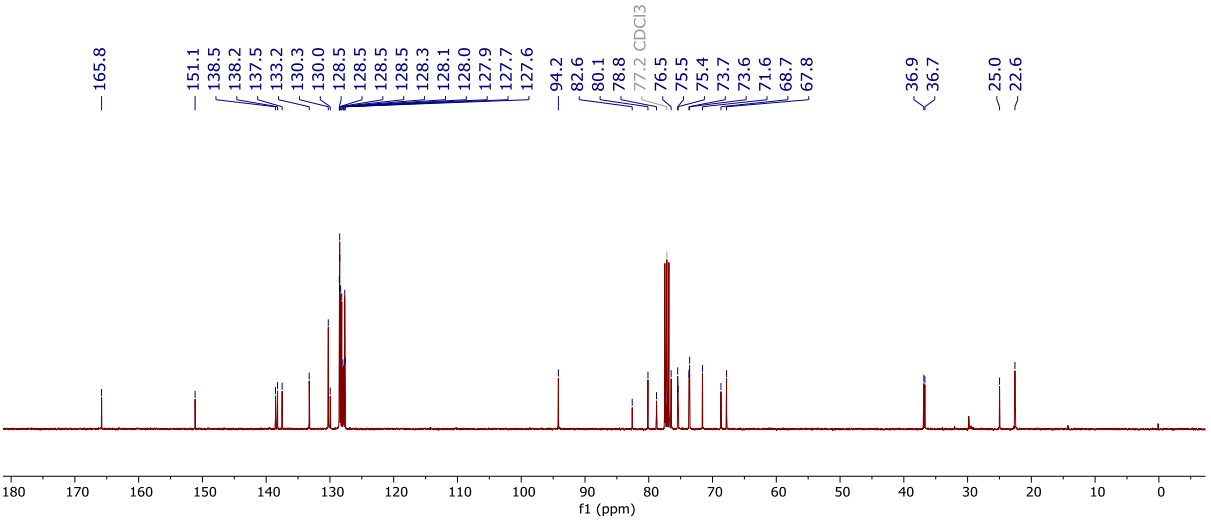

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **16**



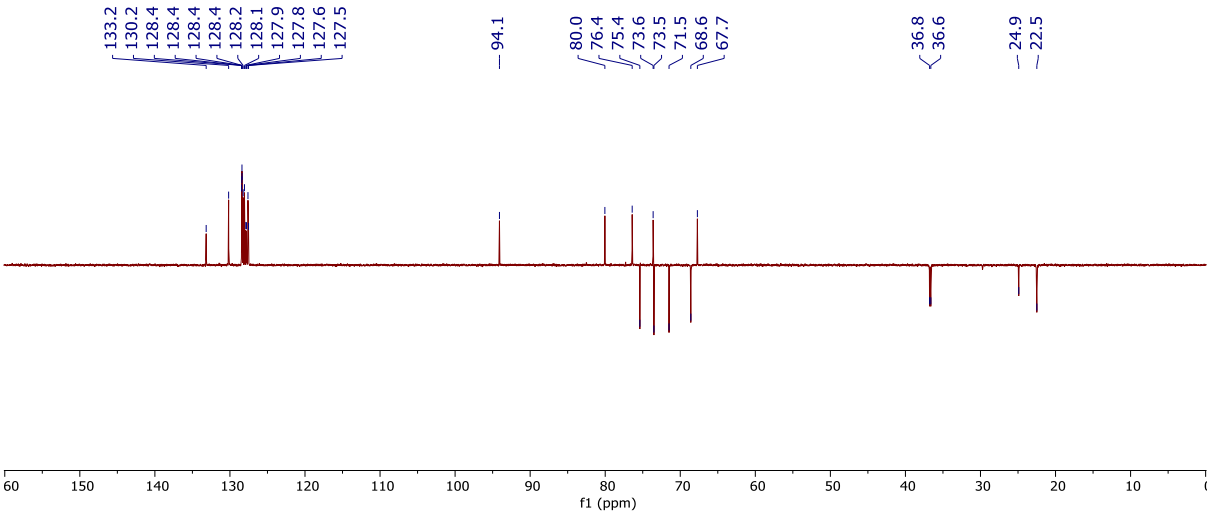
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **18**



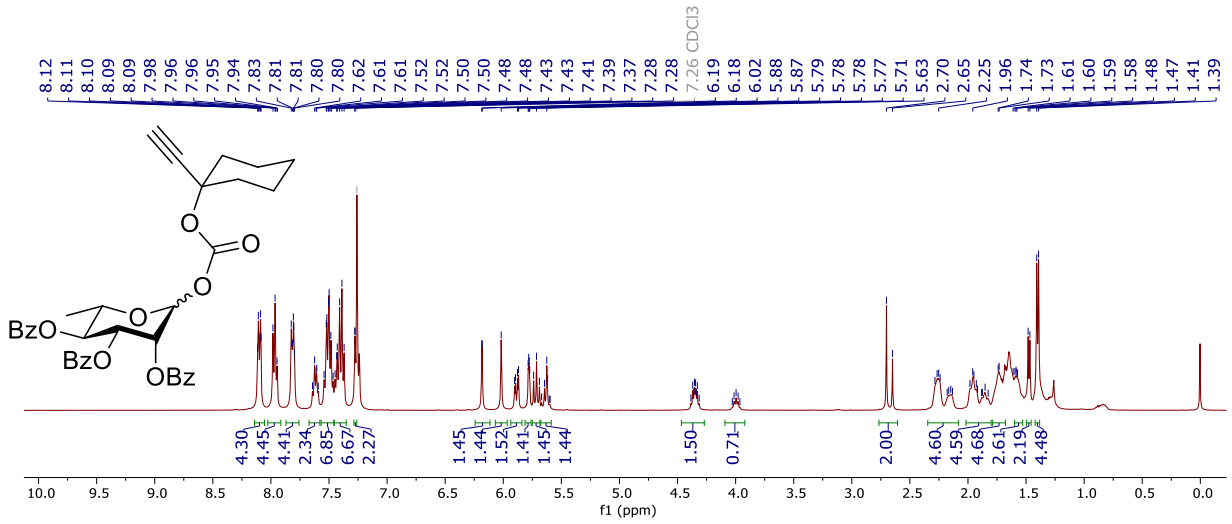

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **18**



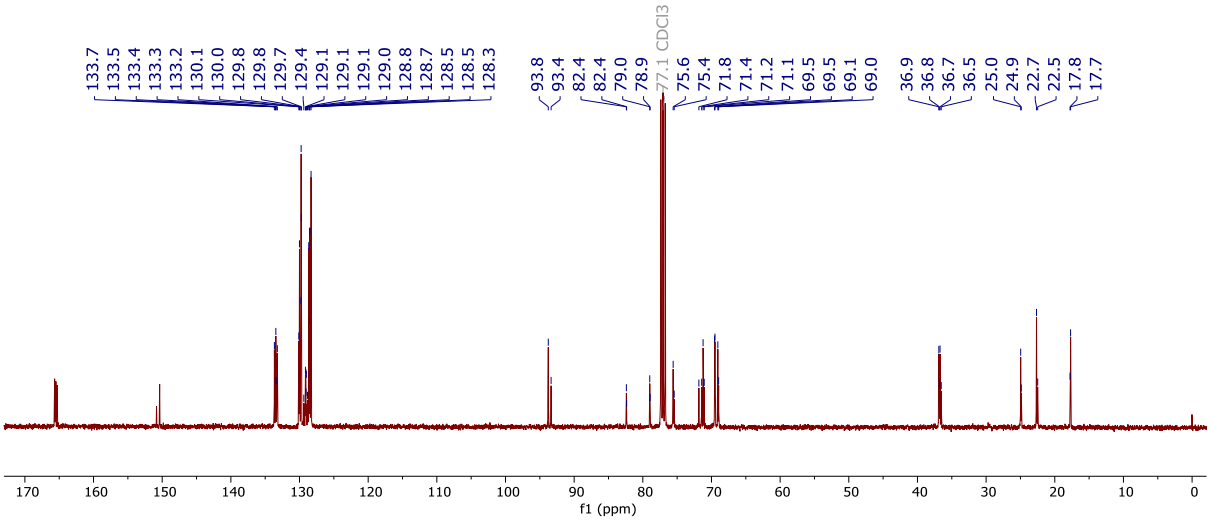

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **18**



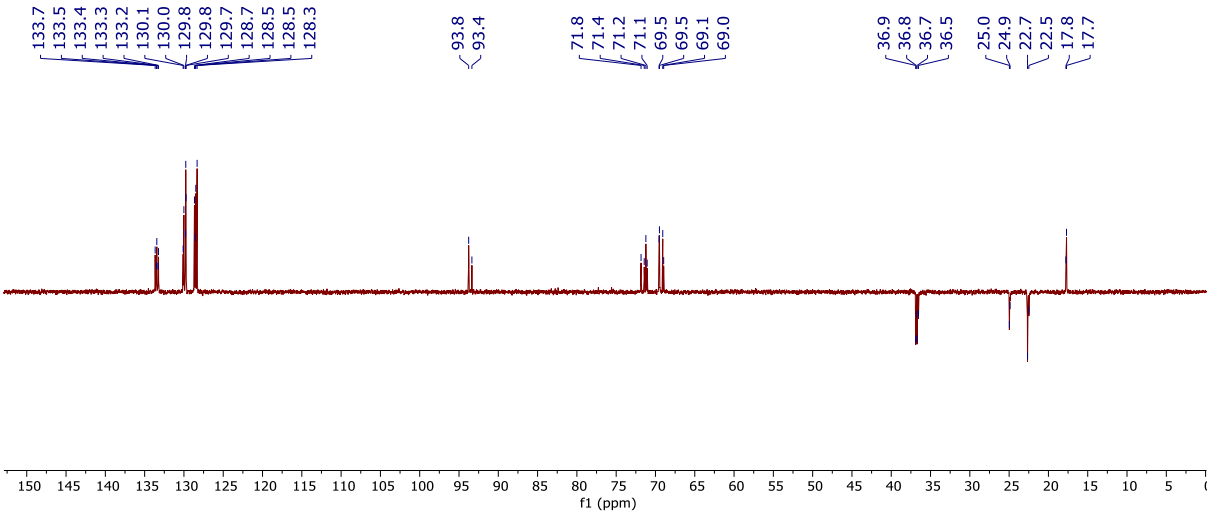
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **20**



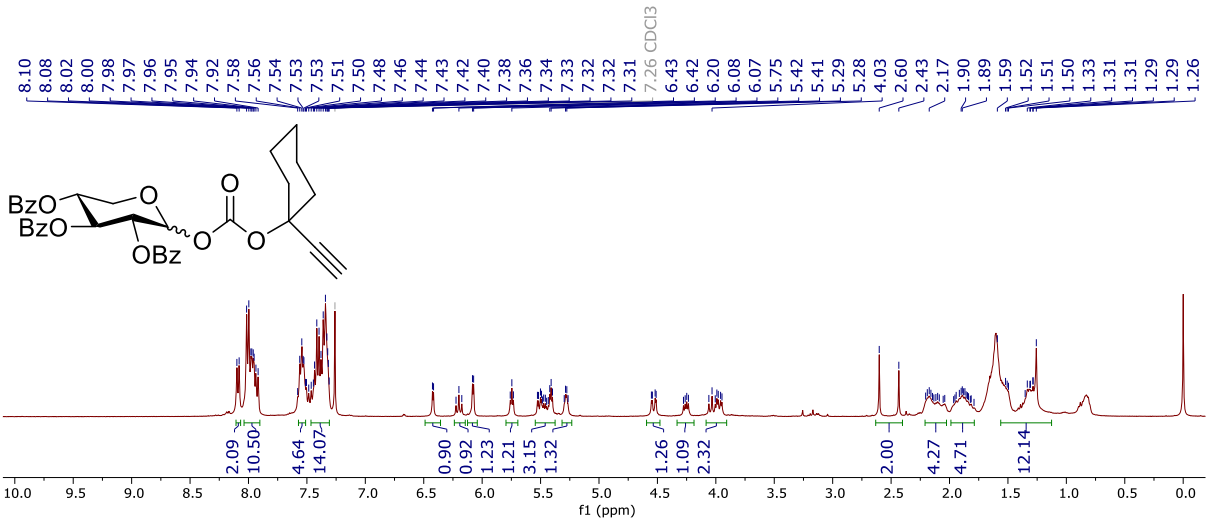

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **20**



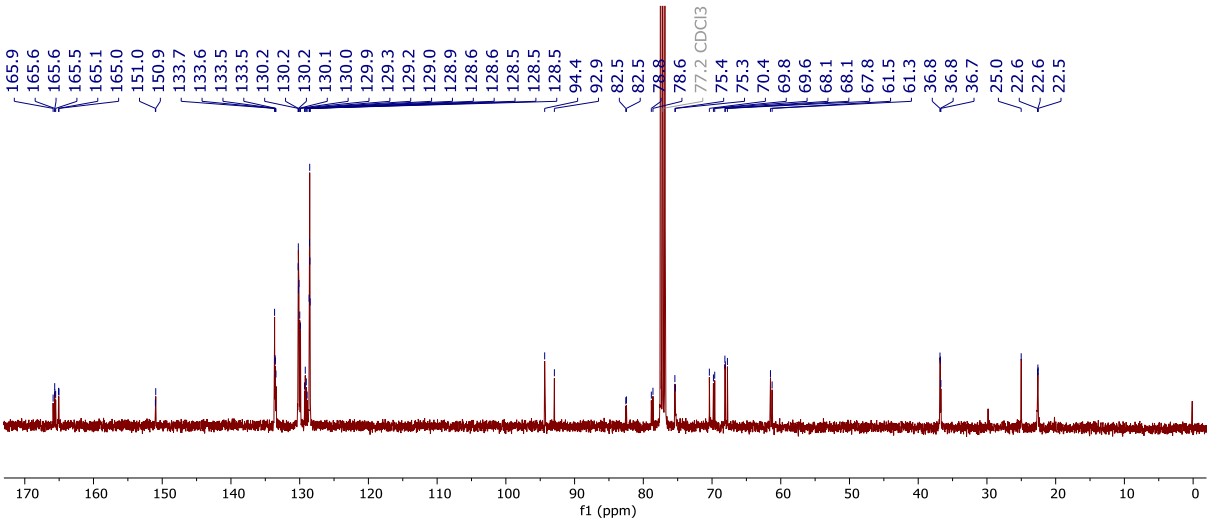

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **20**



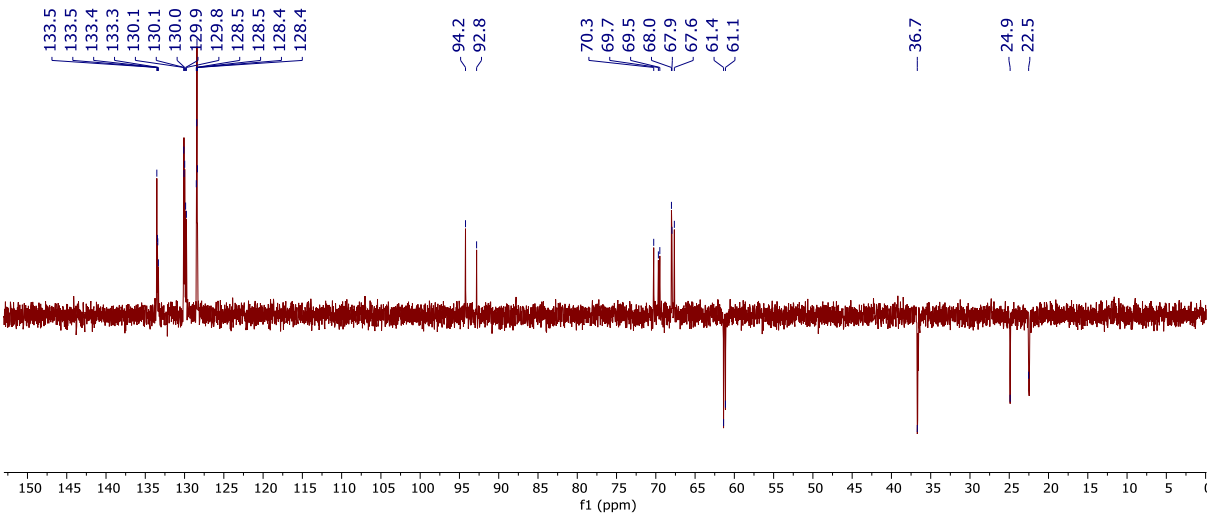
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **24**



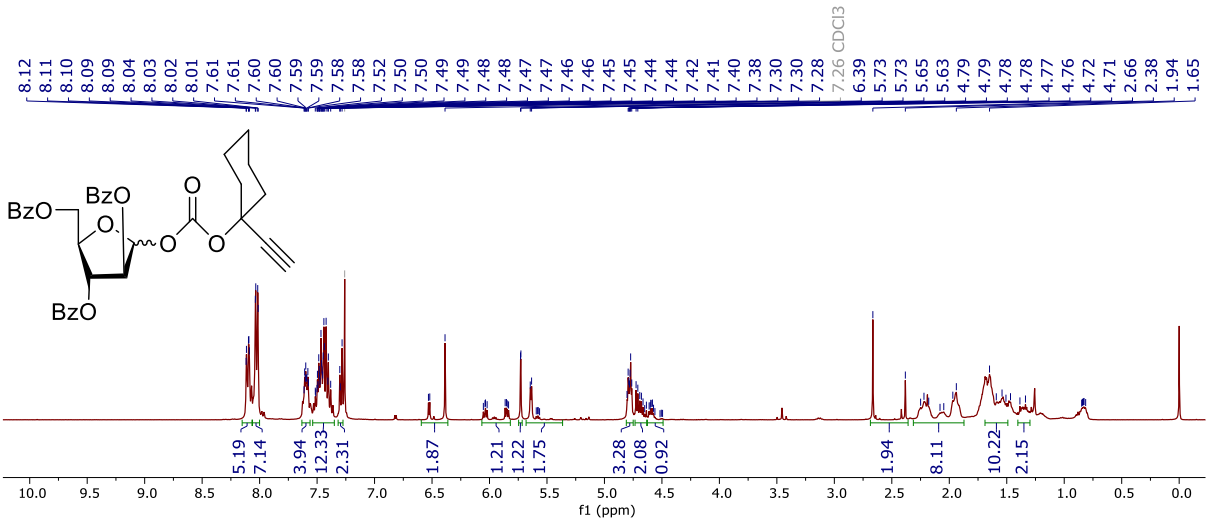

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **24**



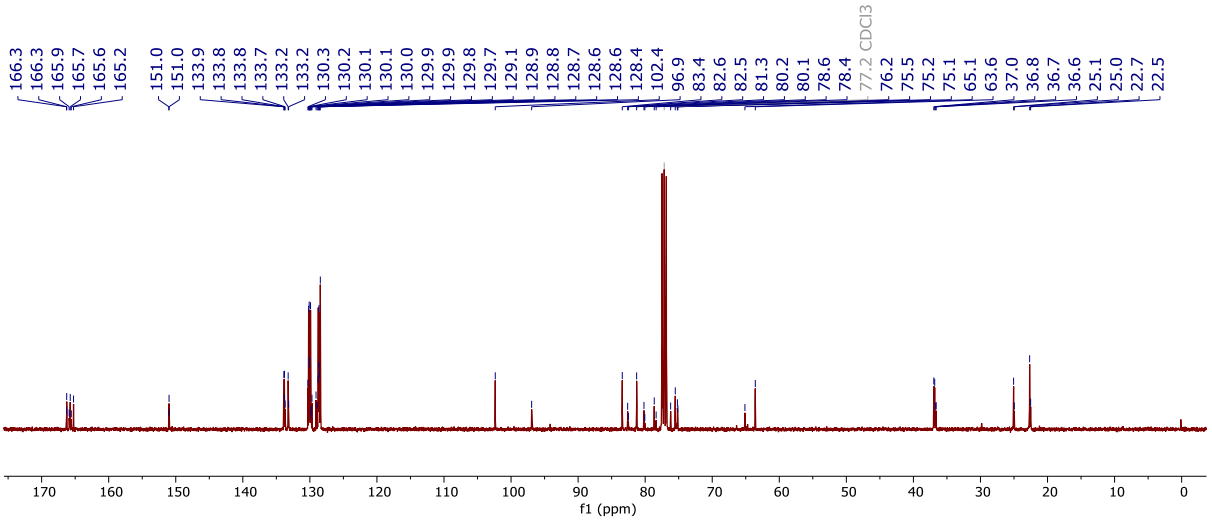

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **24**



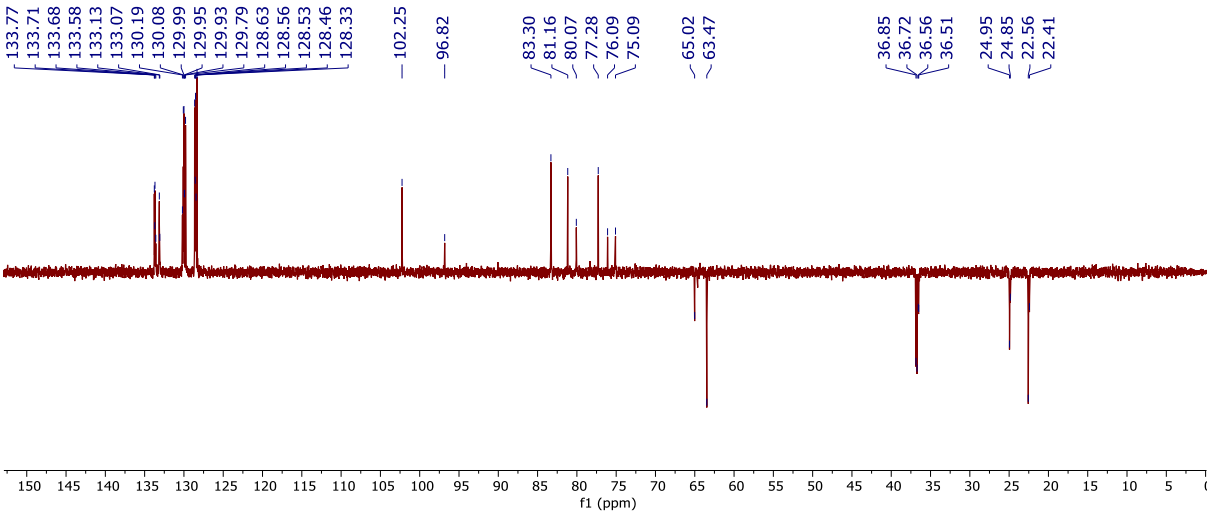
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **26**



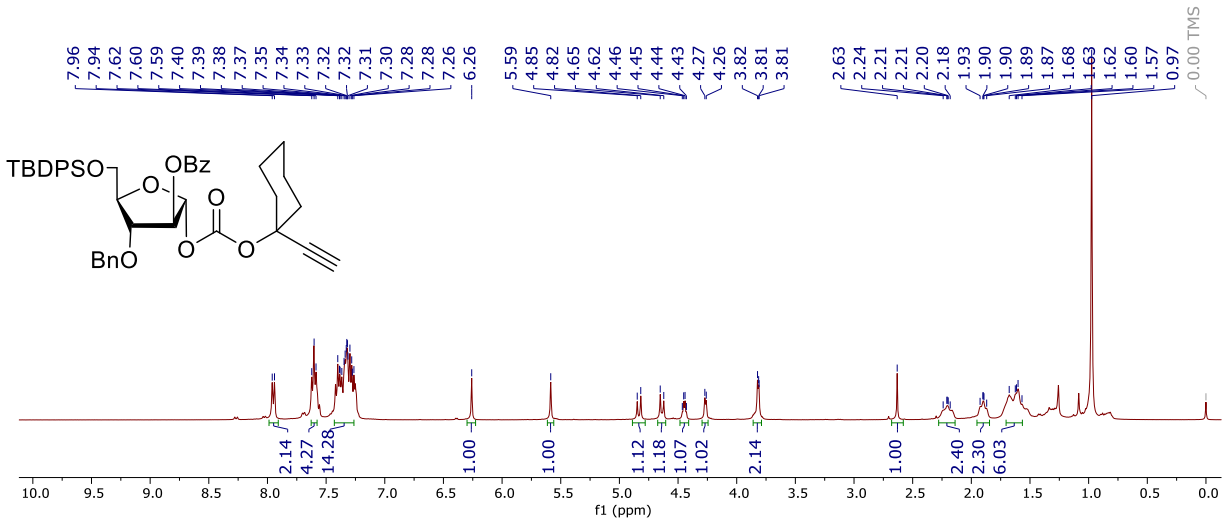

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **26**



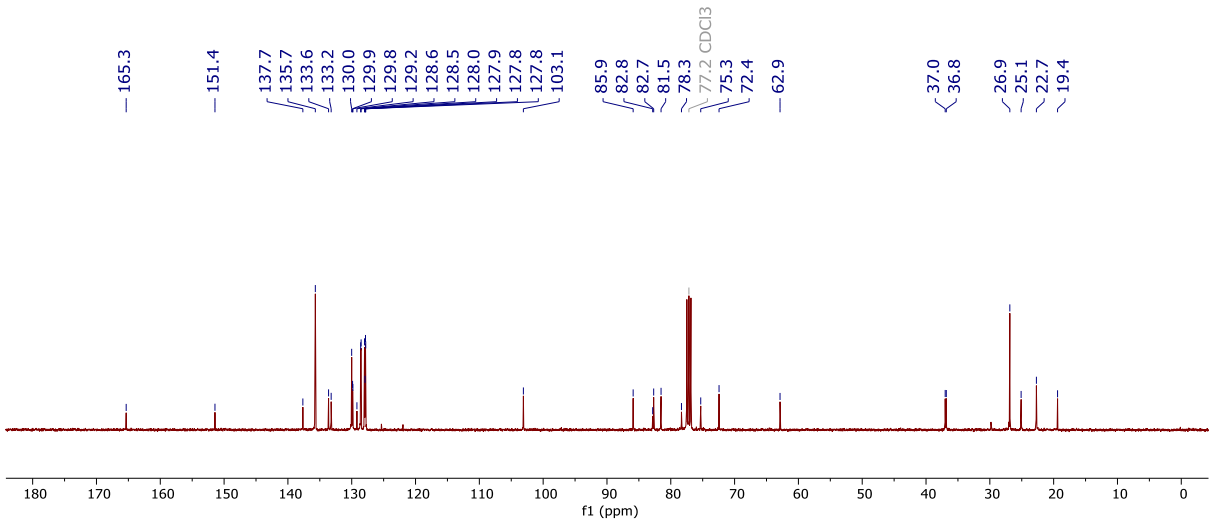

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **26**



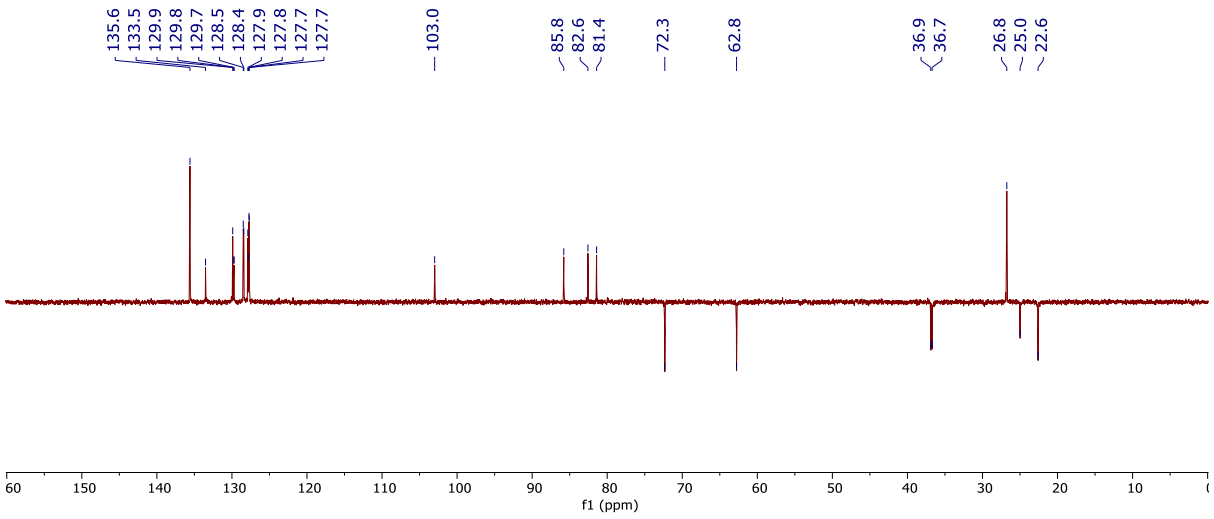
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **29**



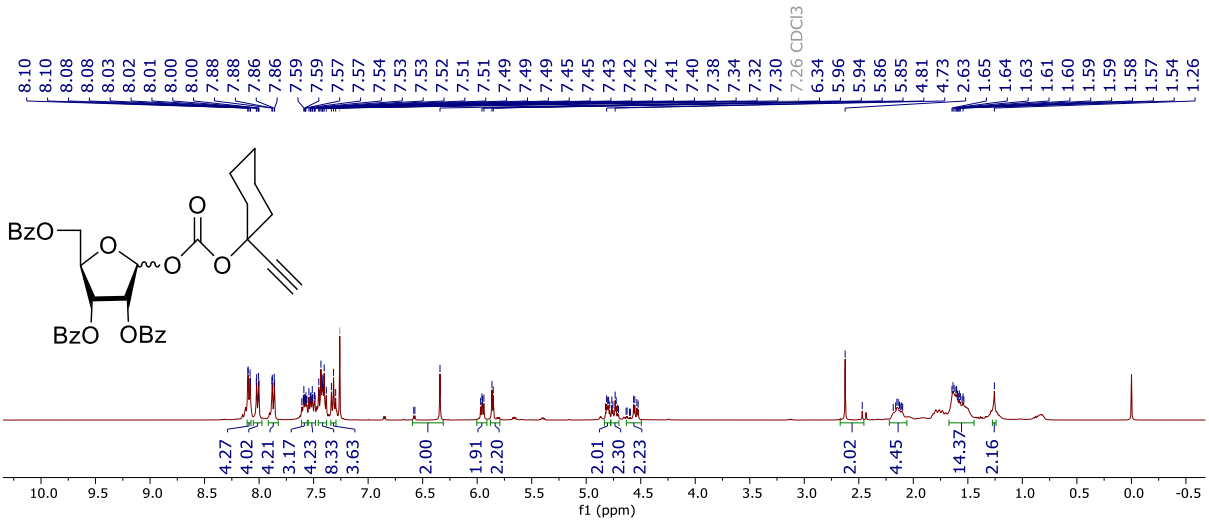

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **29**



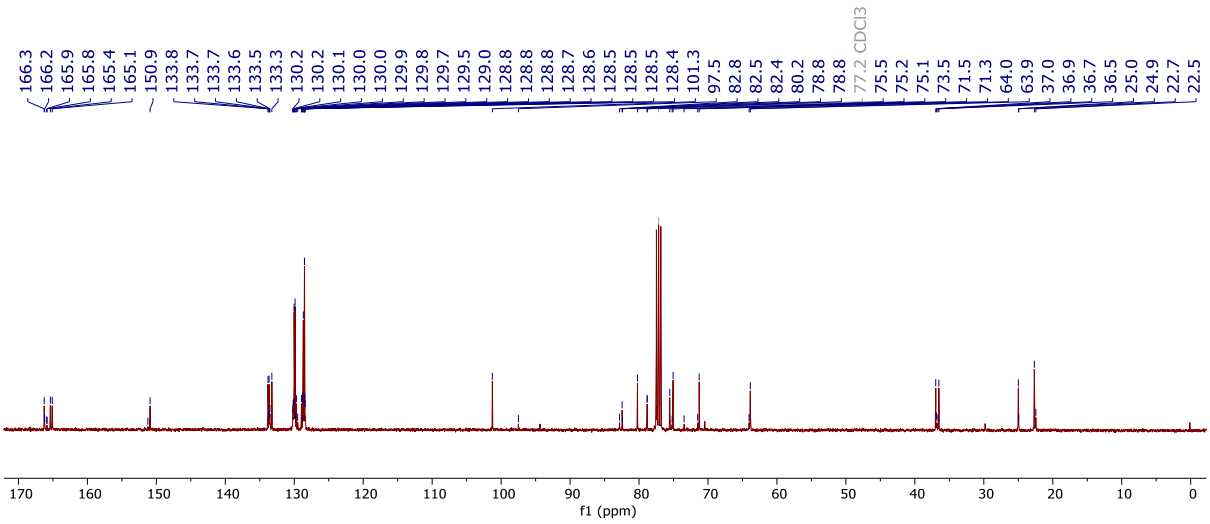

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **29**



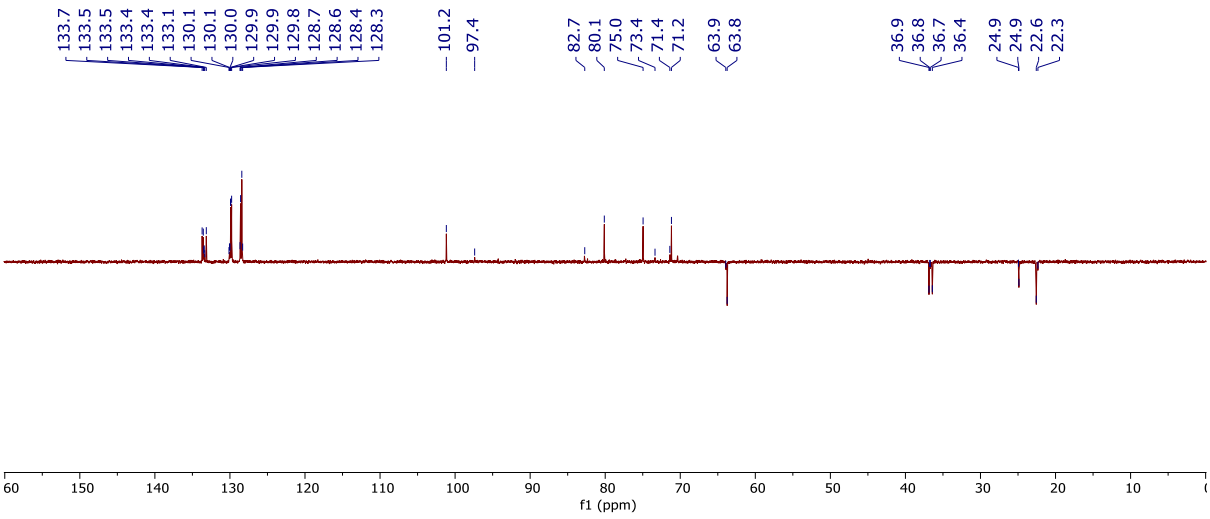
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **32**



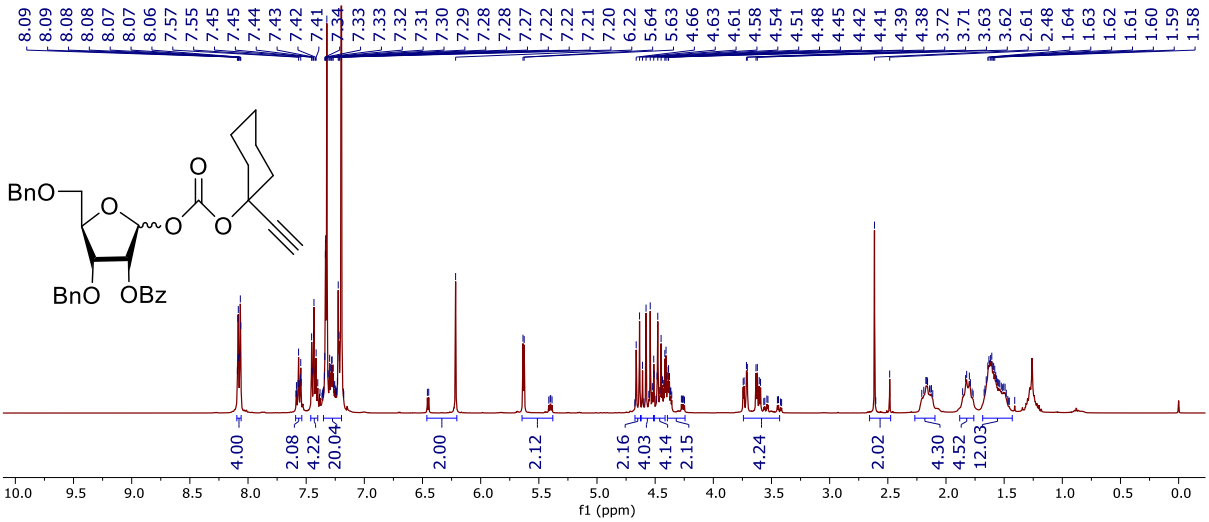

$^{13}$C NMR Spectrum (400 MHz, $CDCl_3$ of Compound **32**



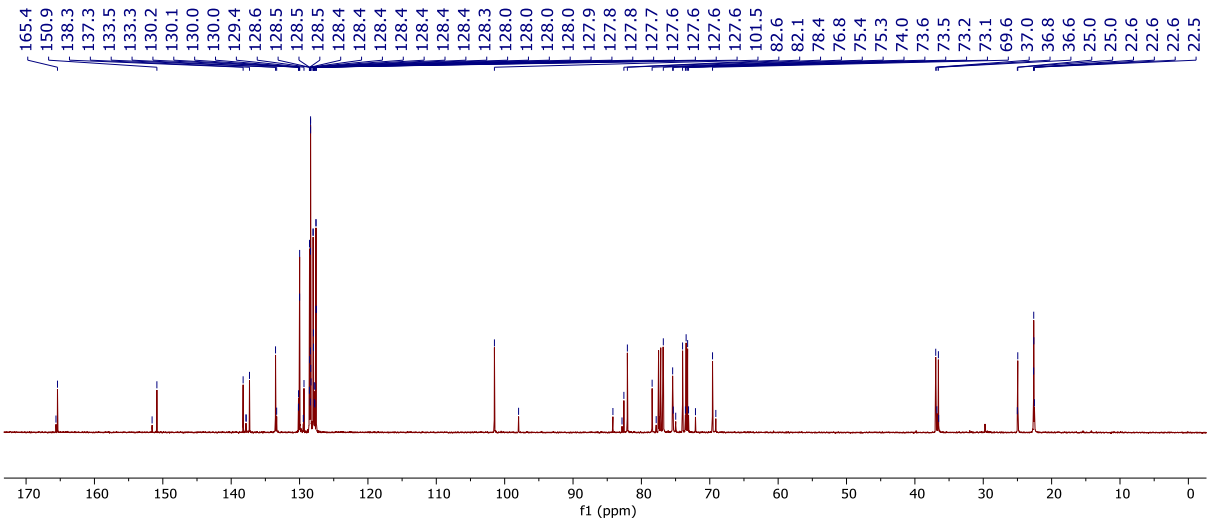

$^{13}$C DEPT-135 NMR Spectrum (400 MHz, $CDCl_3$ of Compound **32**



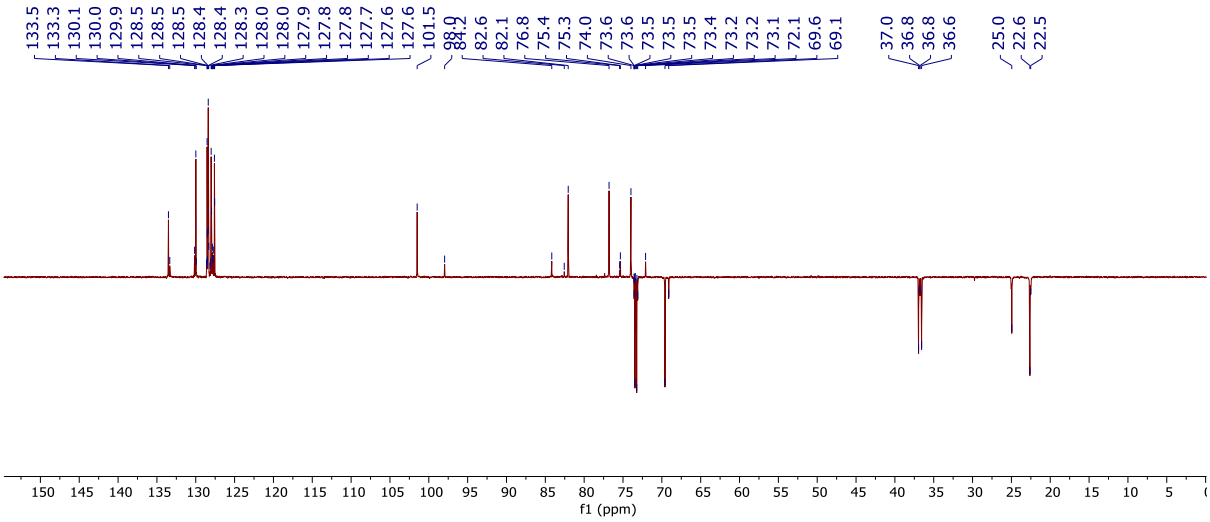
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **33**



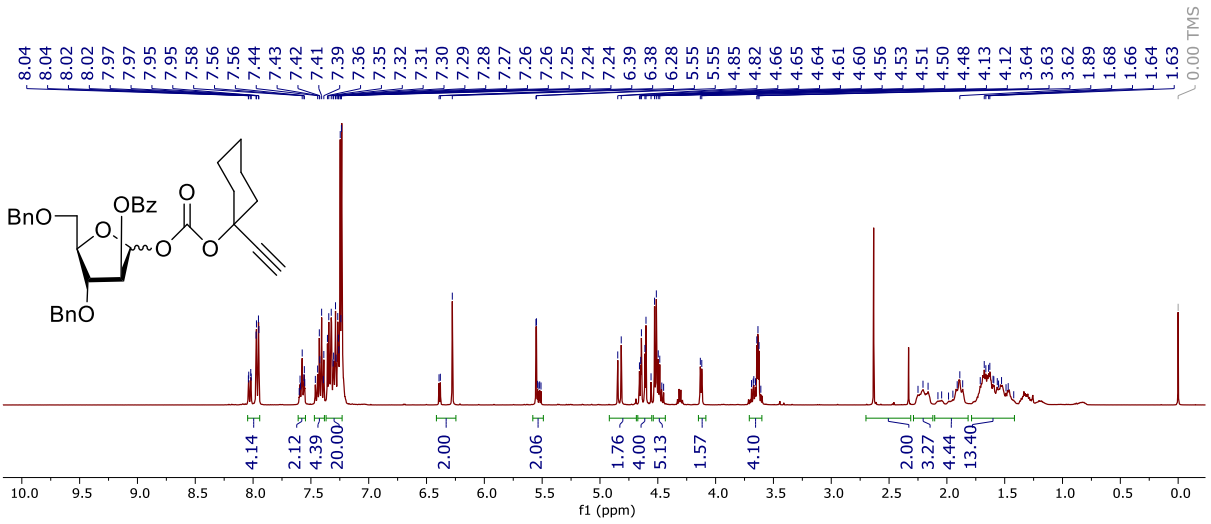

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **33**



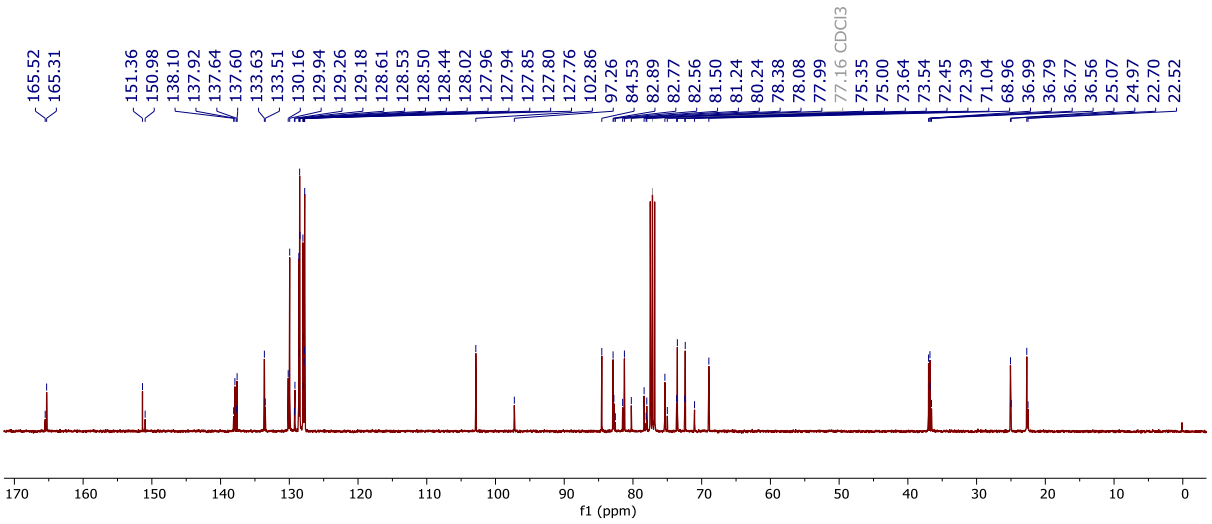

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **33**



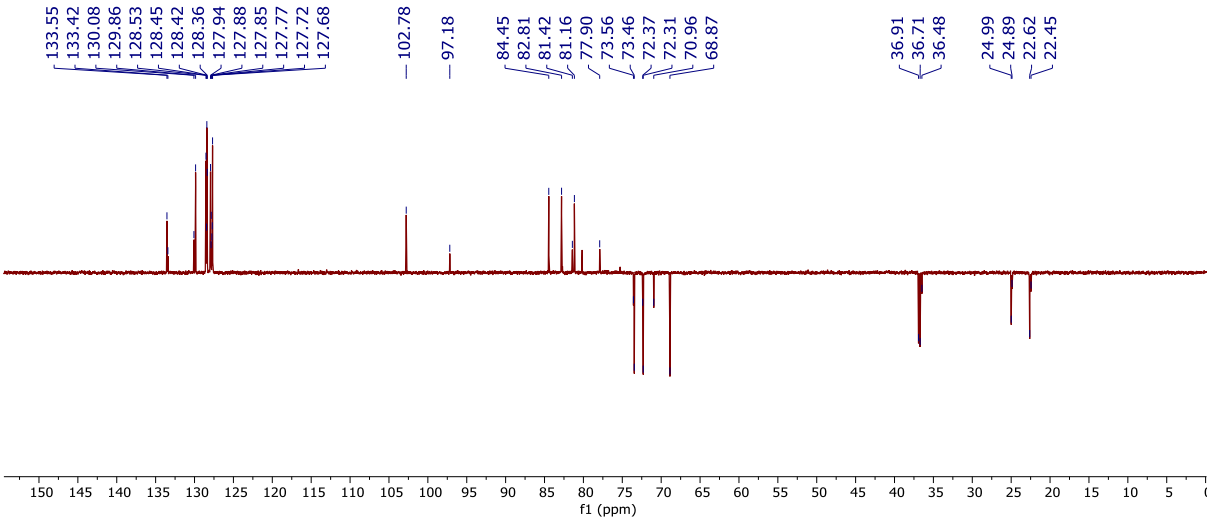
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **34**



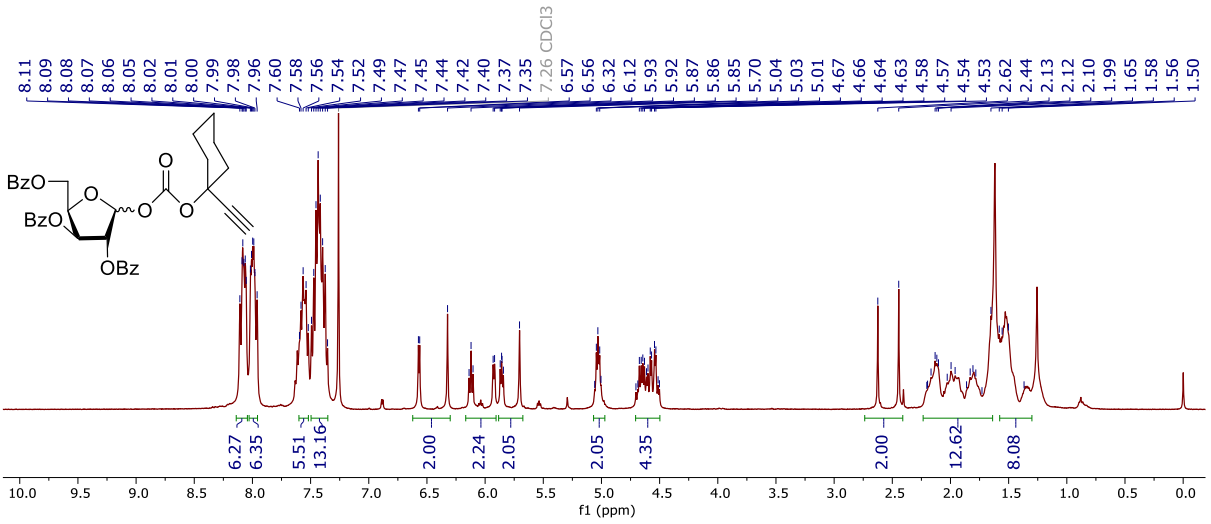

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **34**



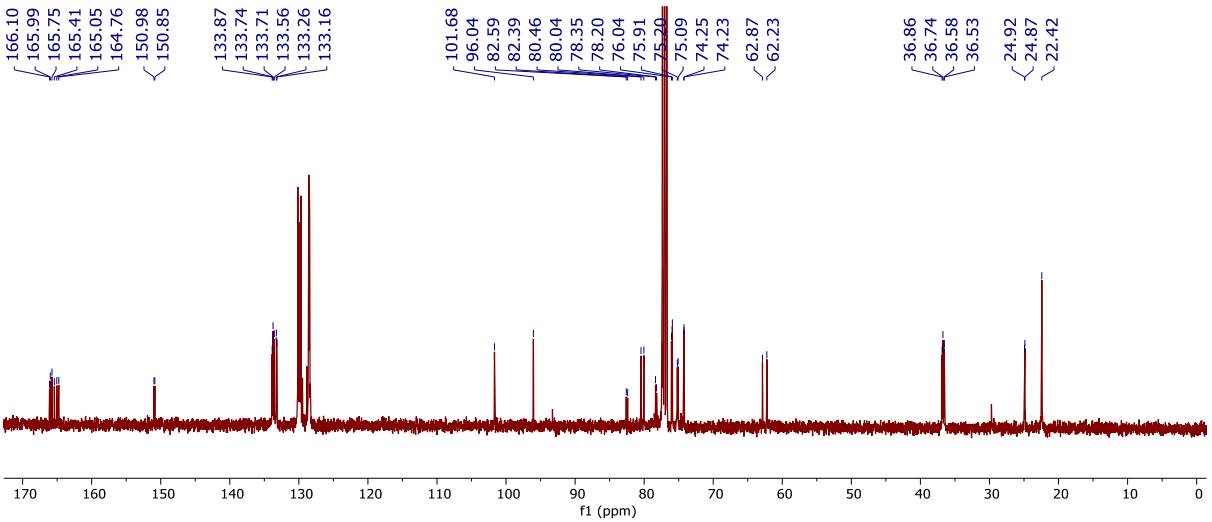

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **34**



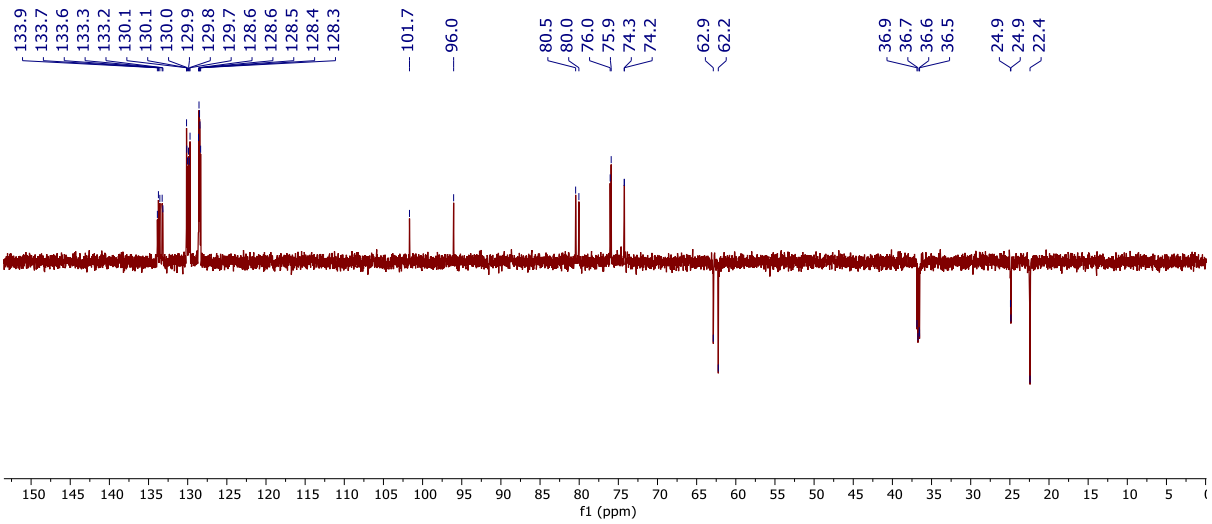
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **43**



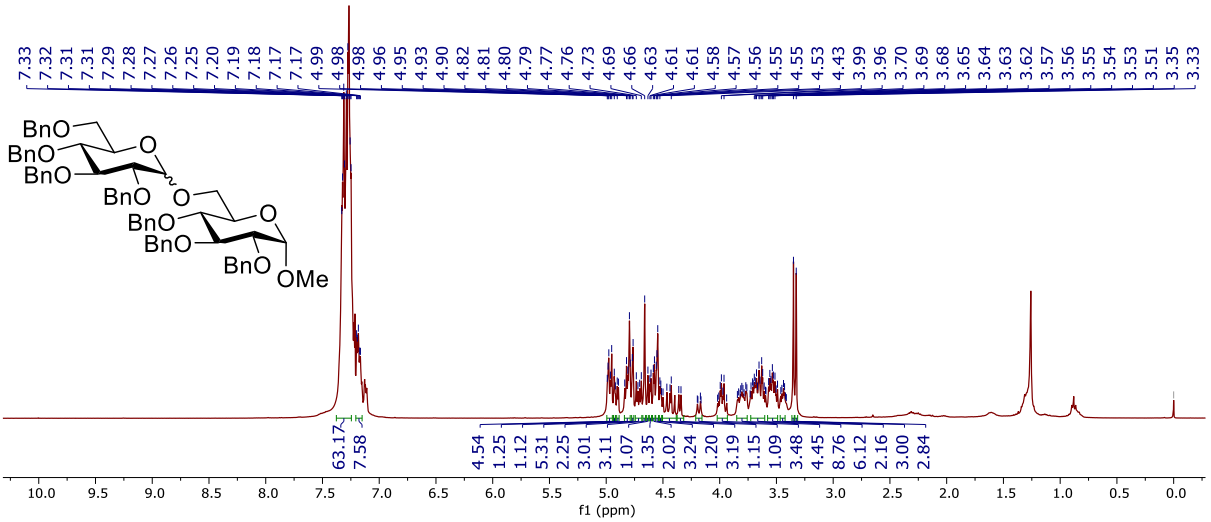

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **43**



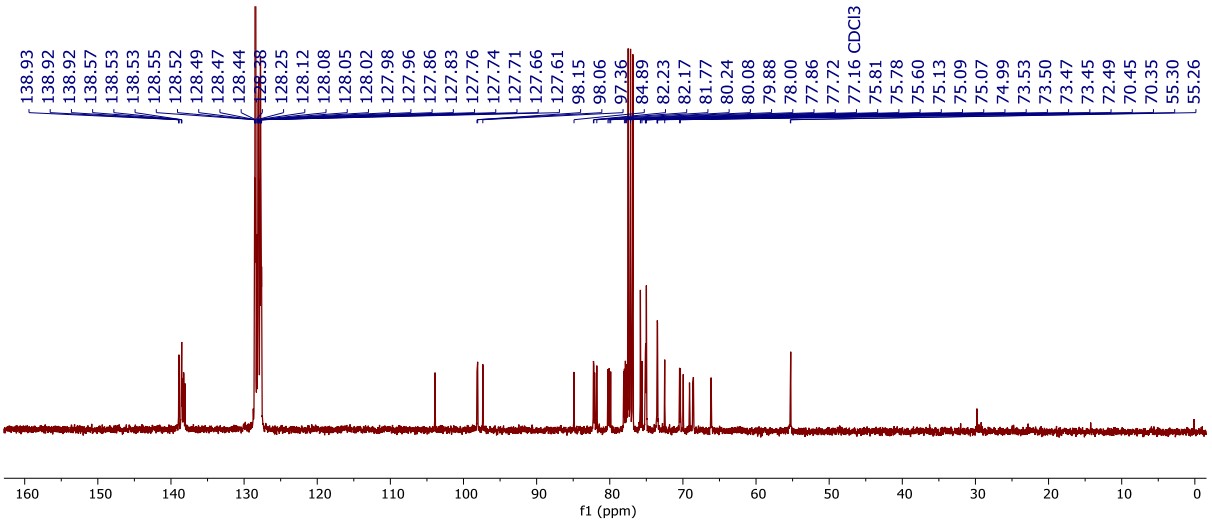

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **43**



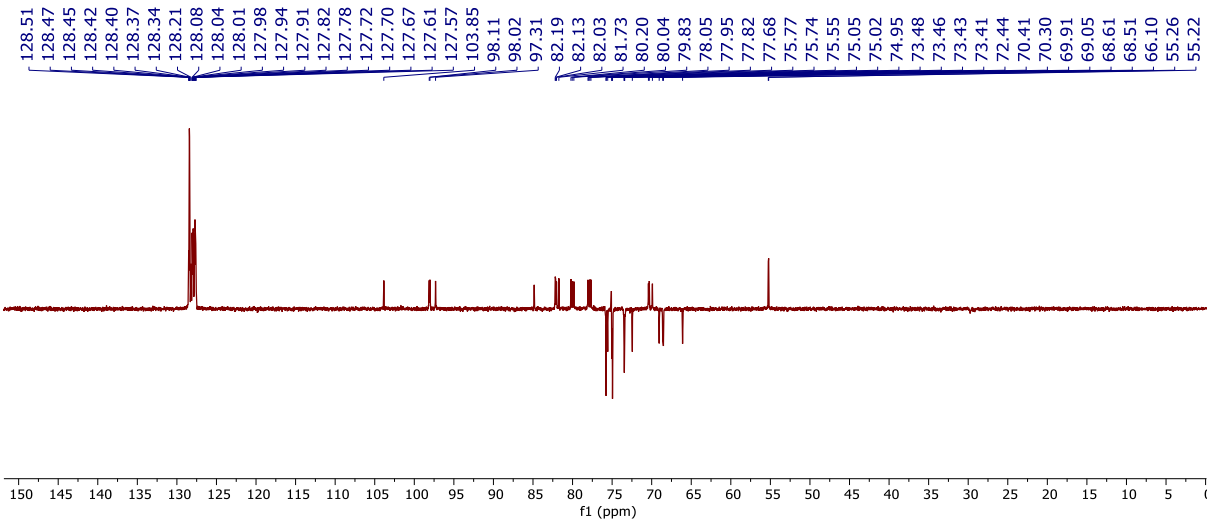
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **3**



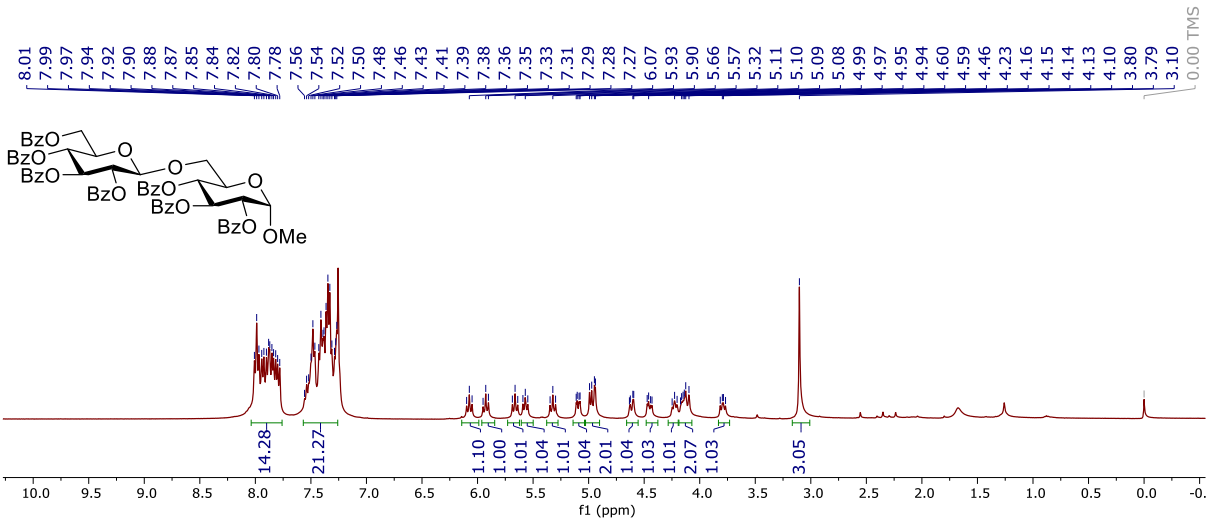

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **3**



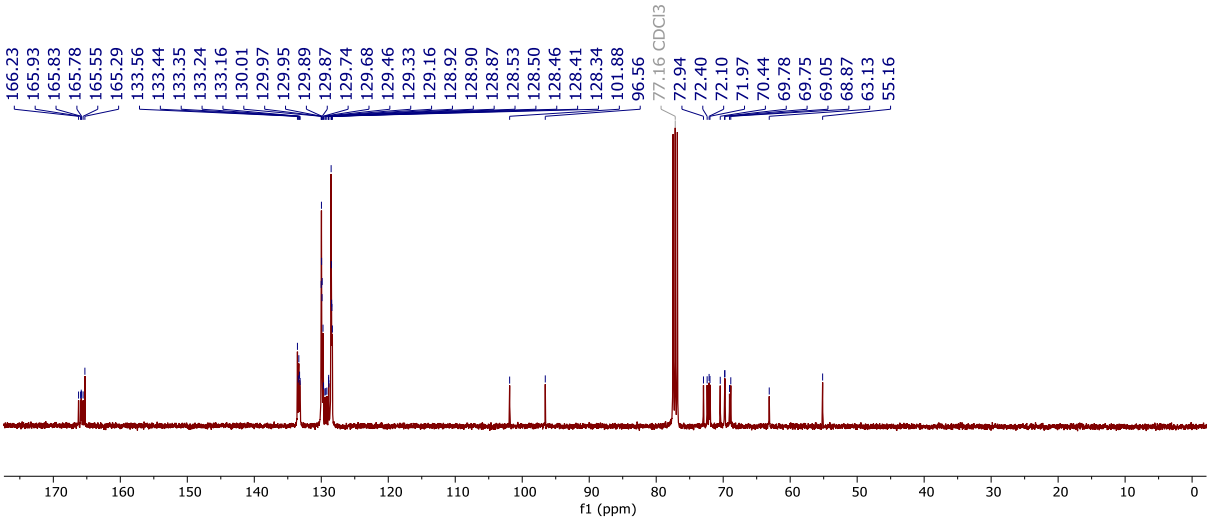

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **3**



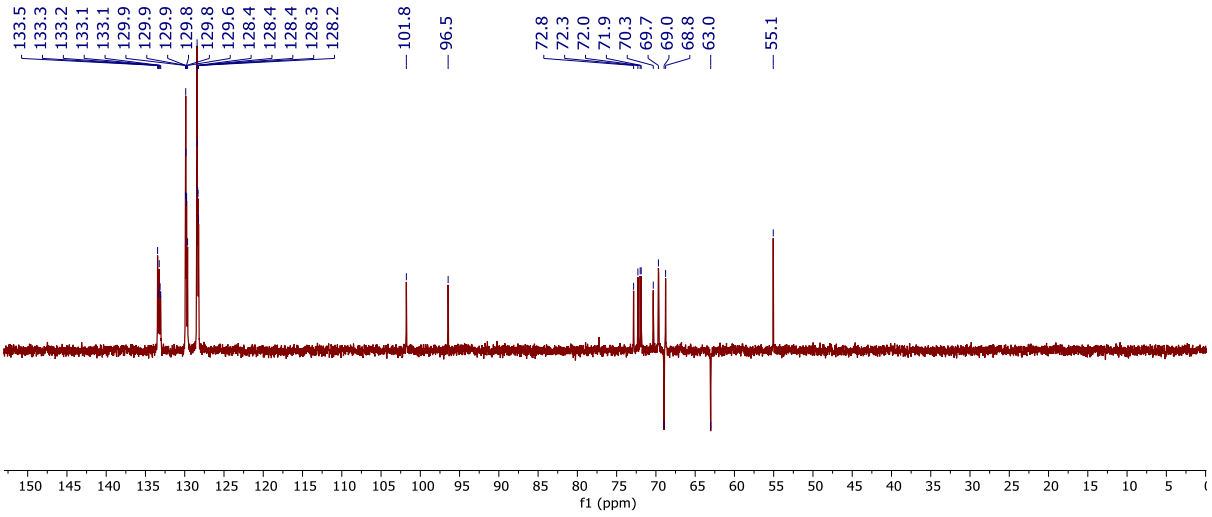
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **6**



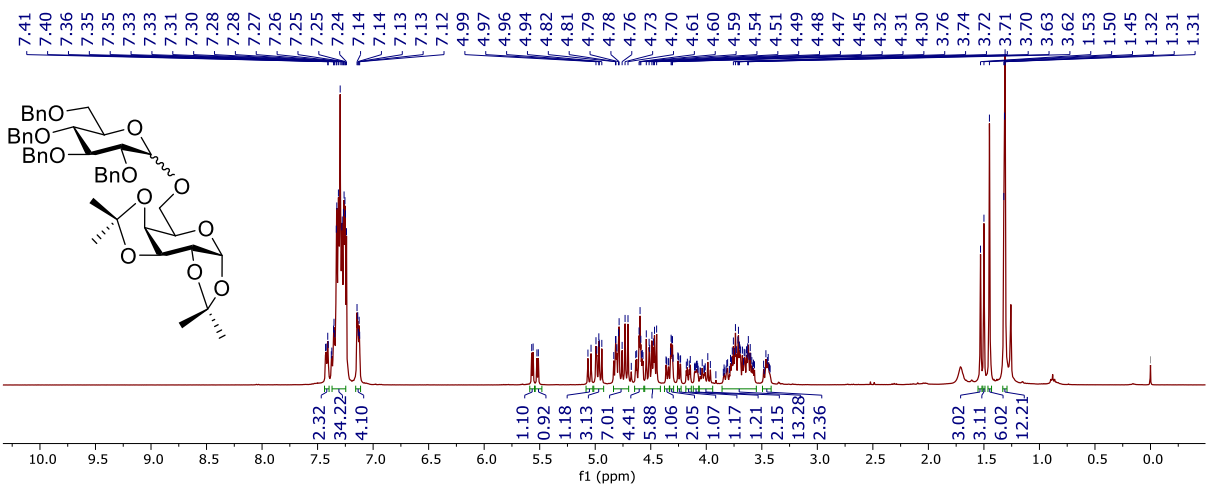

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **6**



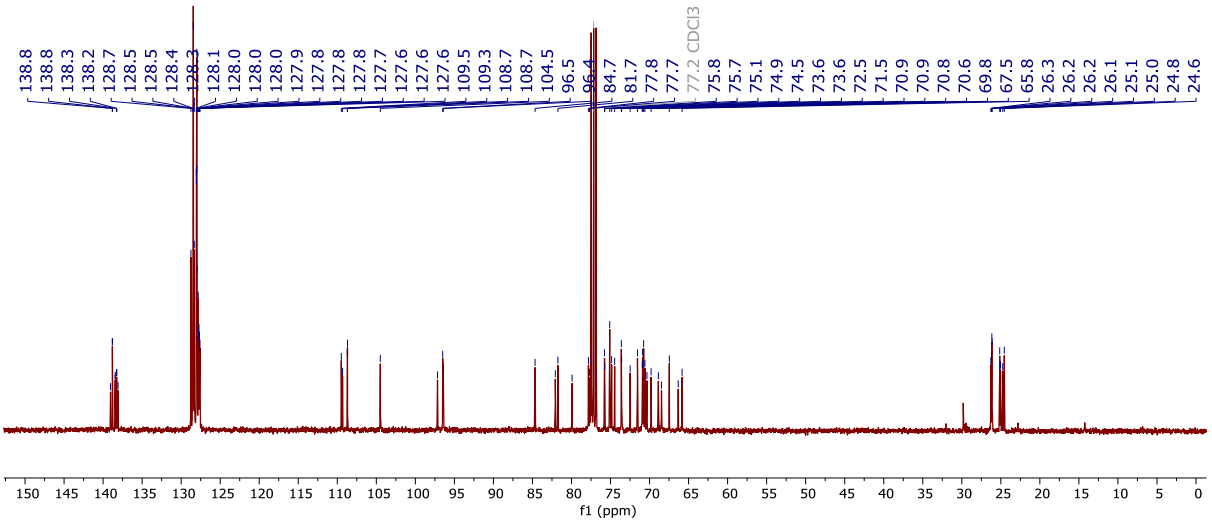

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **6**



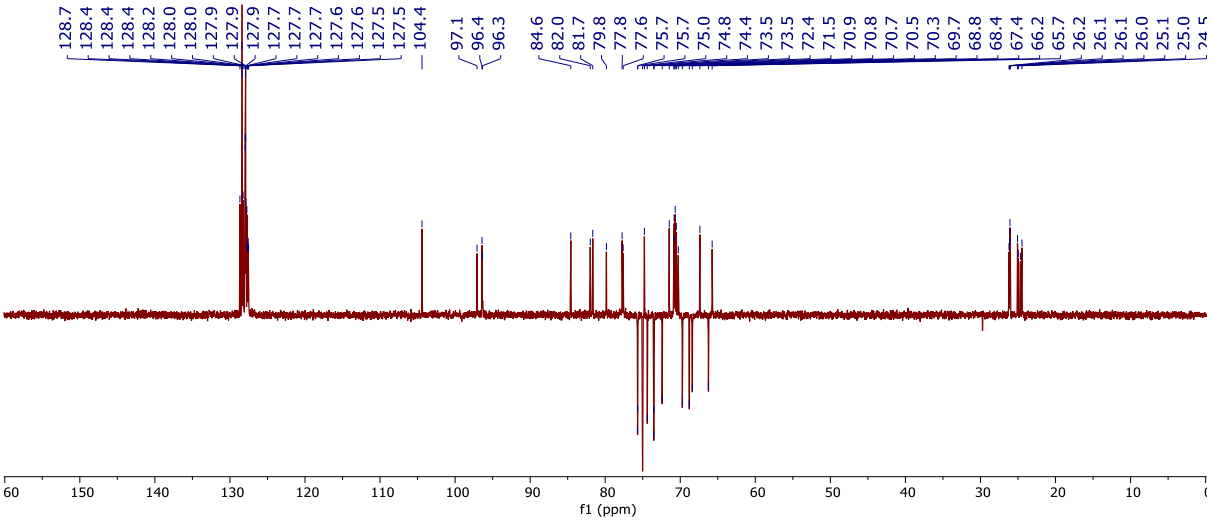
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **8**



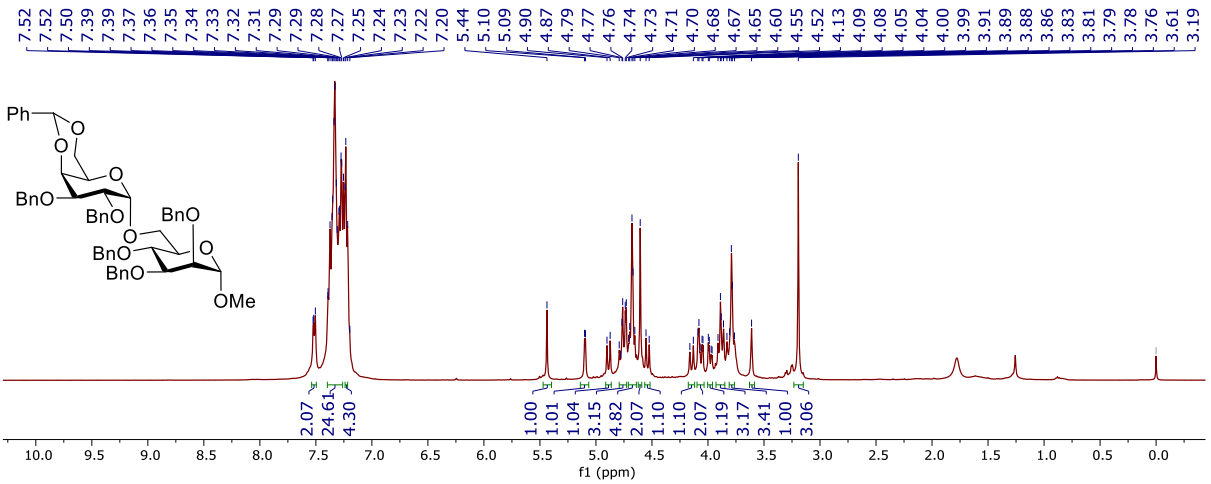

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **8**



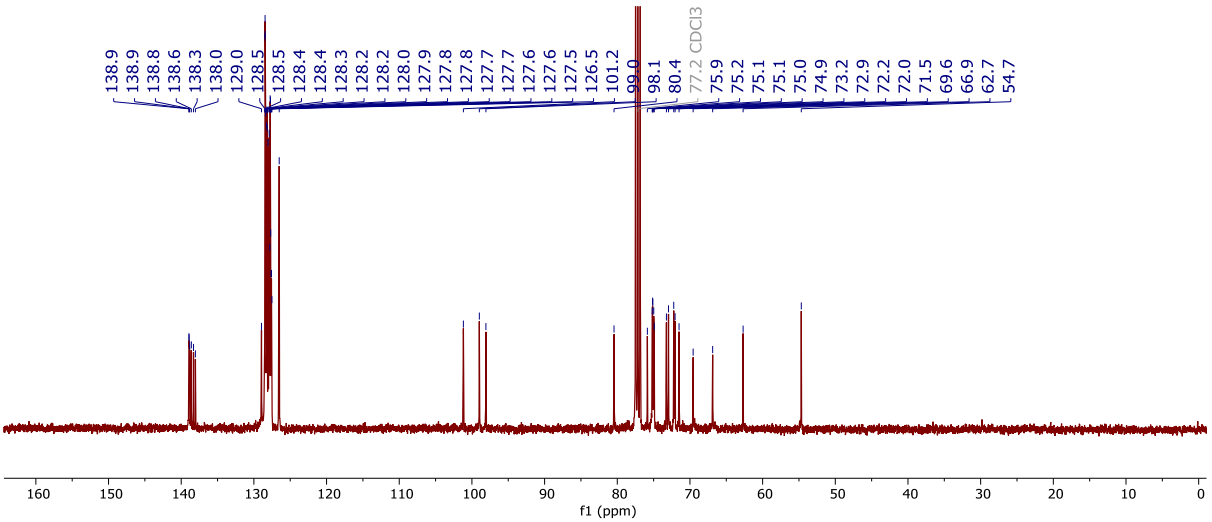

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **8**



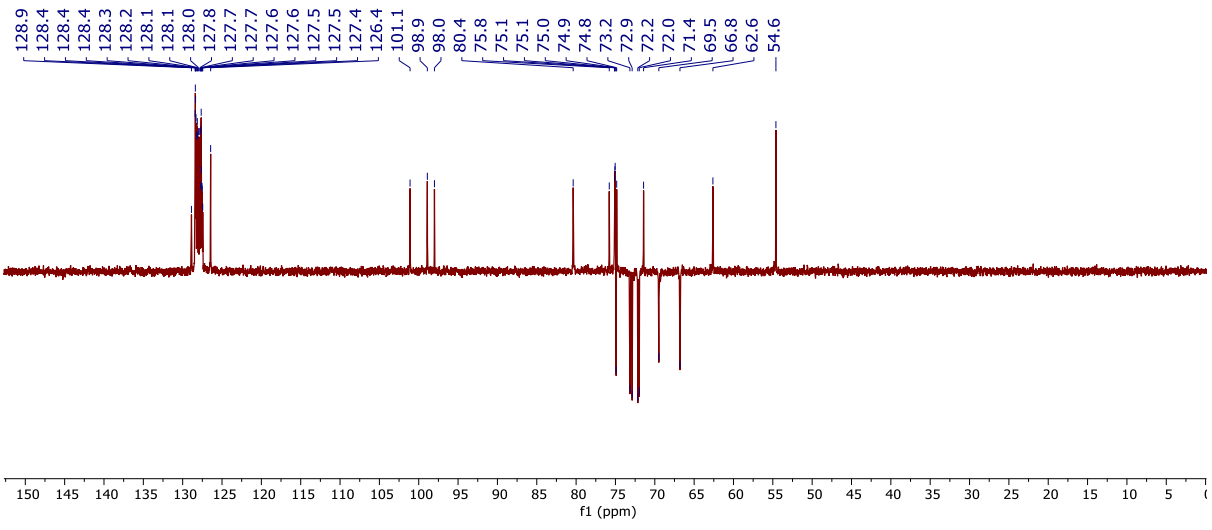
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **11**



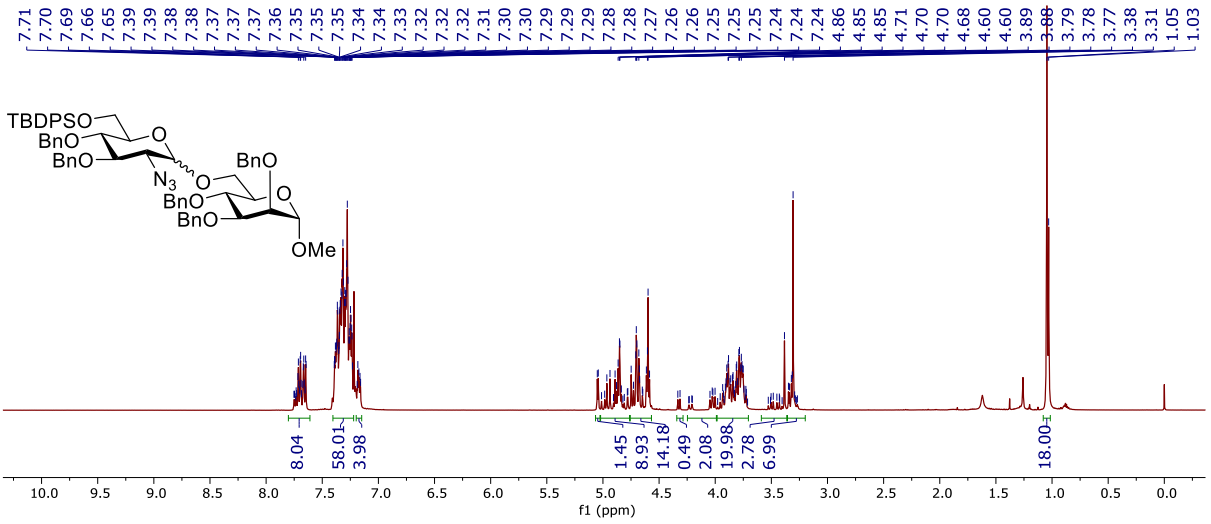

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **11**



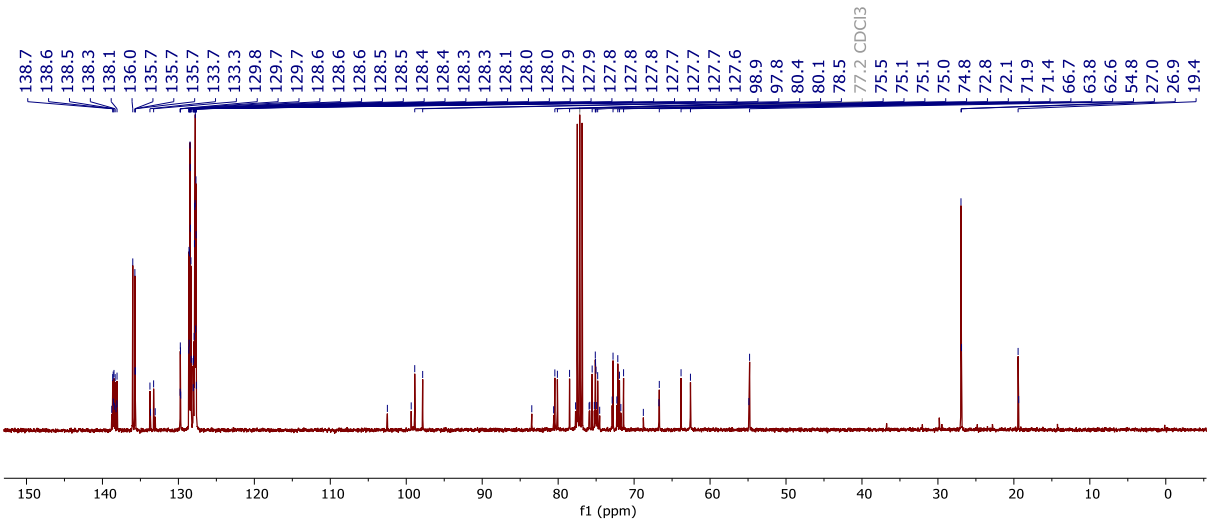

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **11**



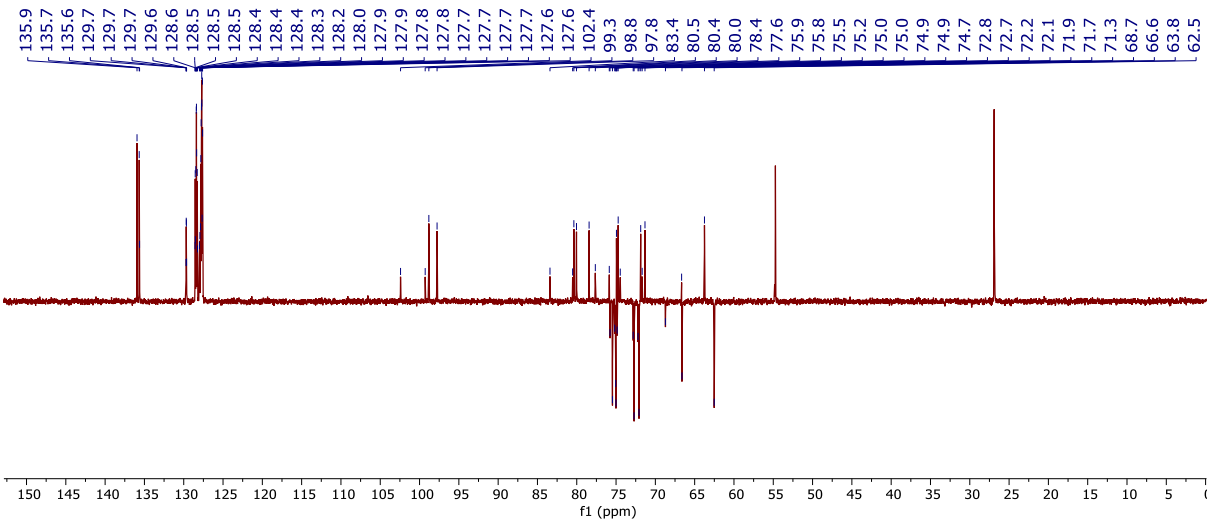
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **13**



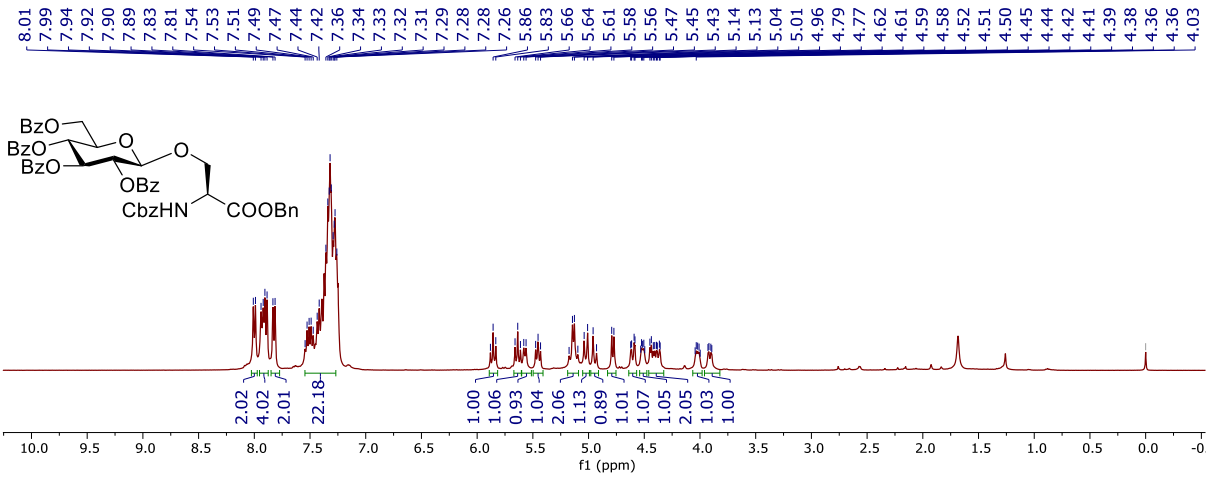

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **13**



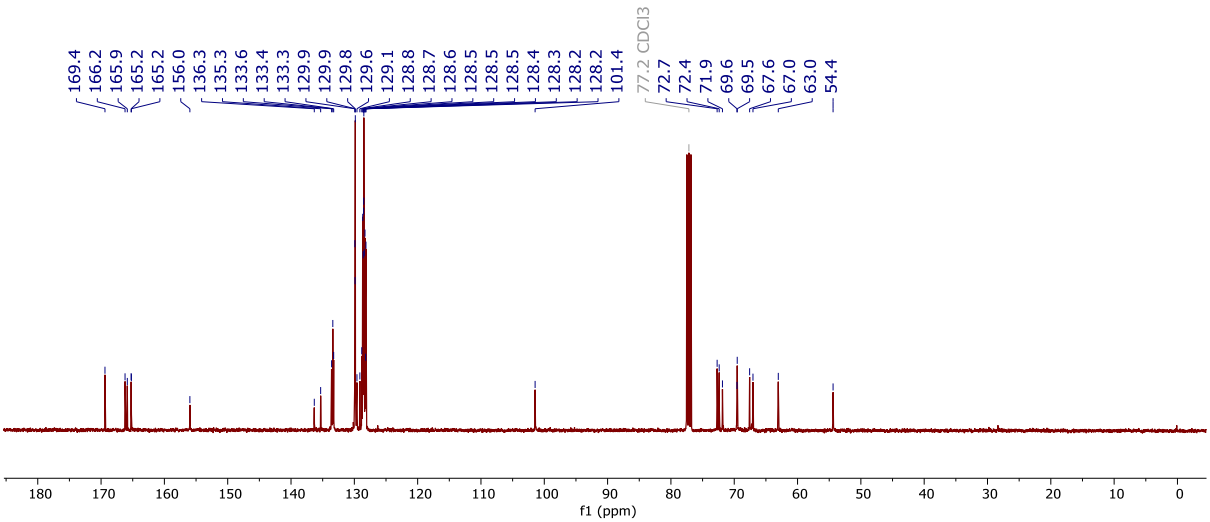

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **13**



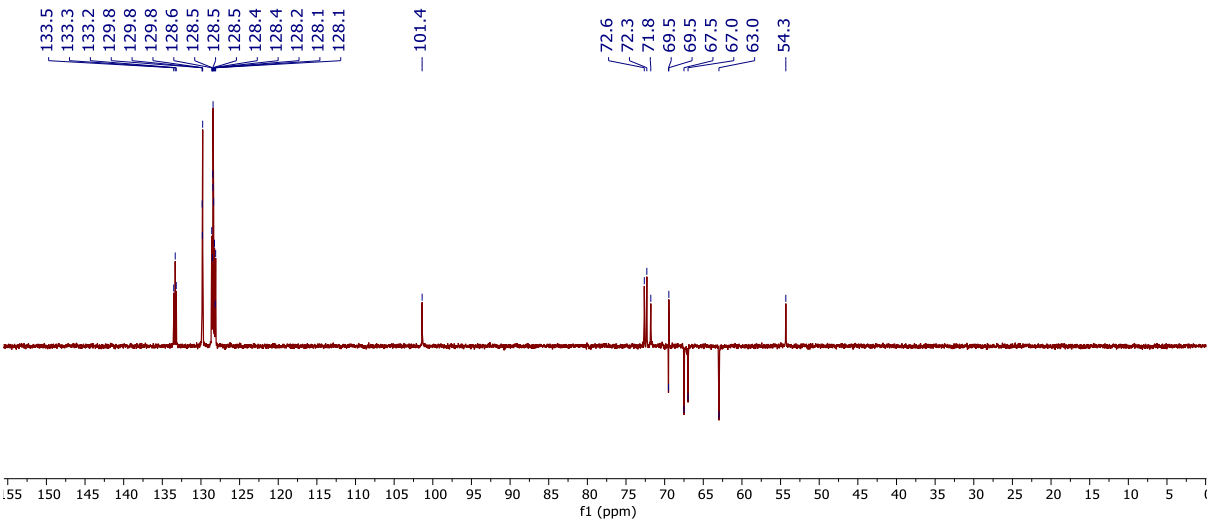
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **15**



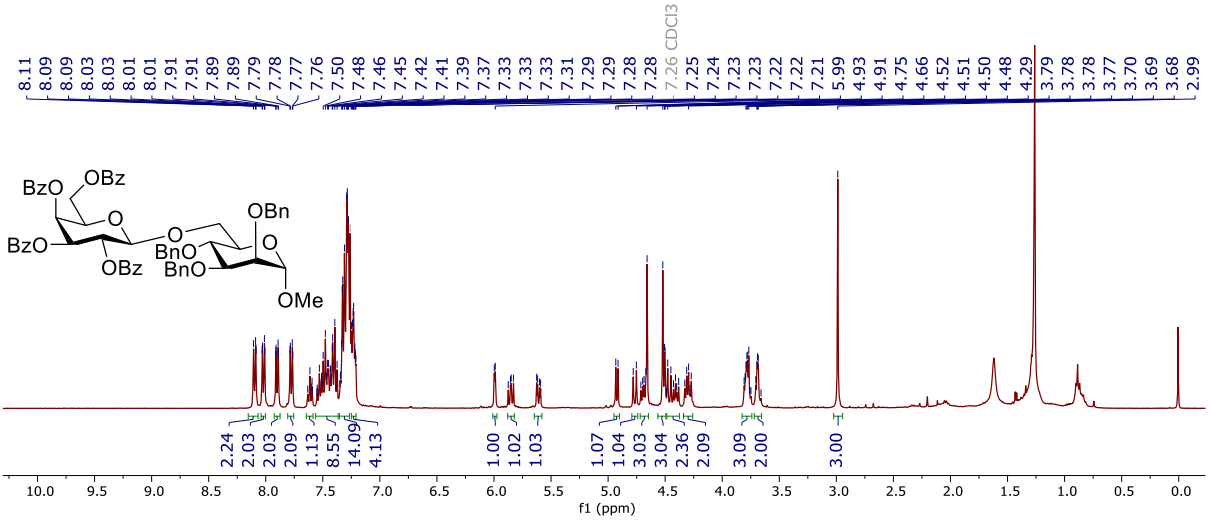

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **15**



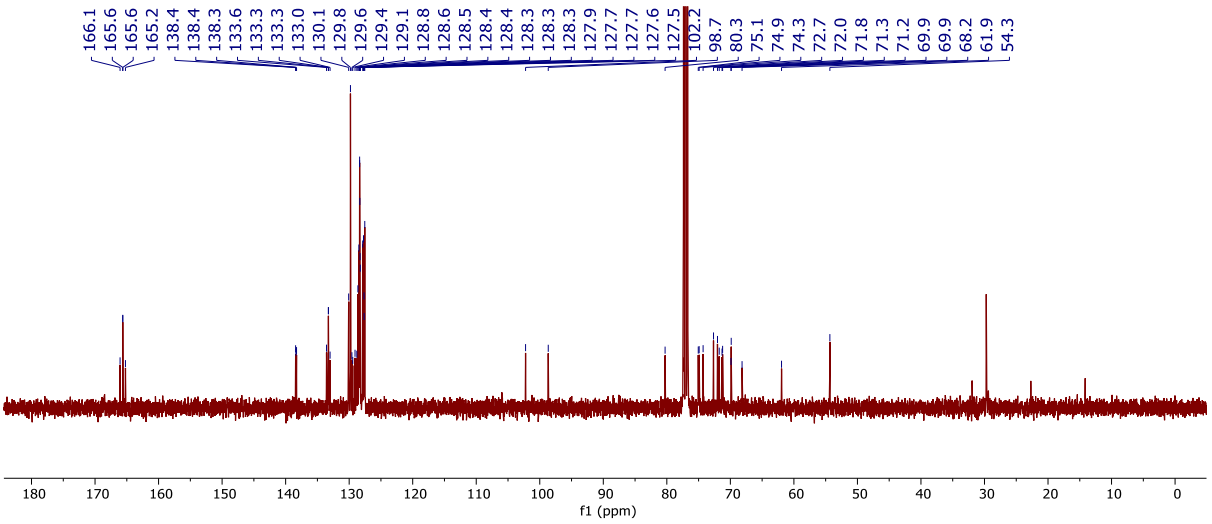

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **15**



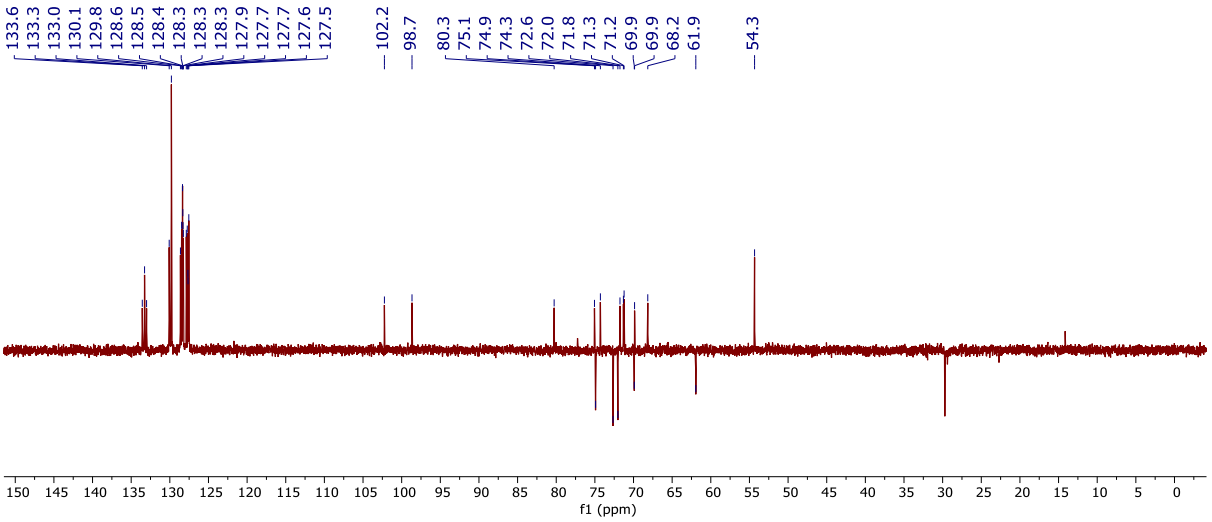
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **17**



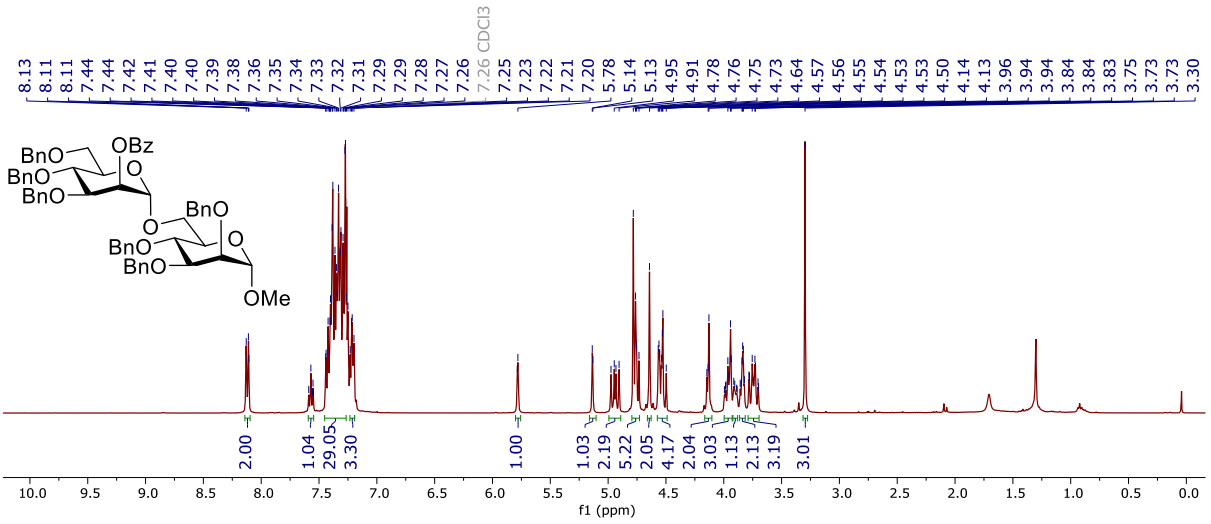

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **17**



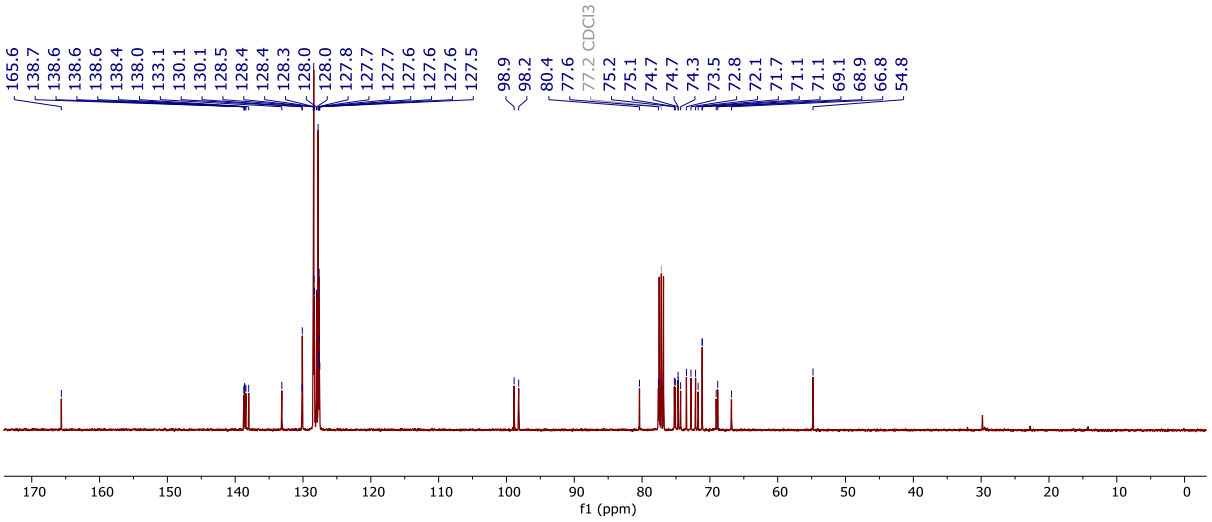

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **17**



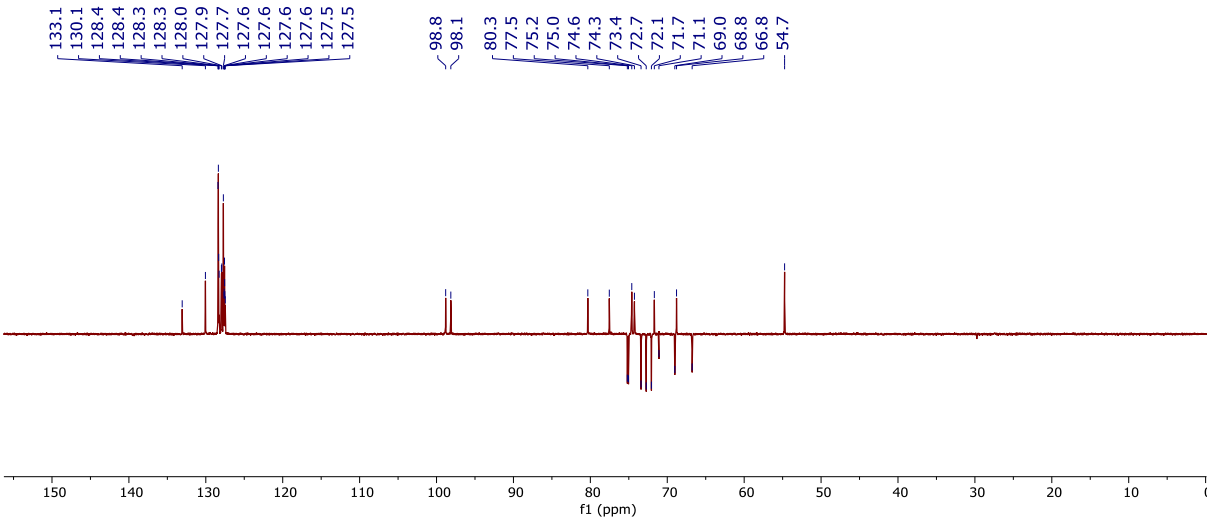
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **19**



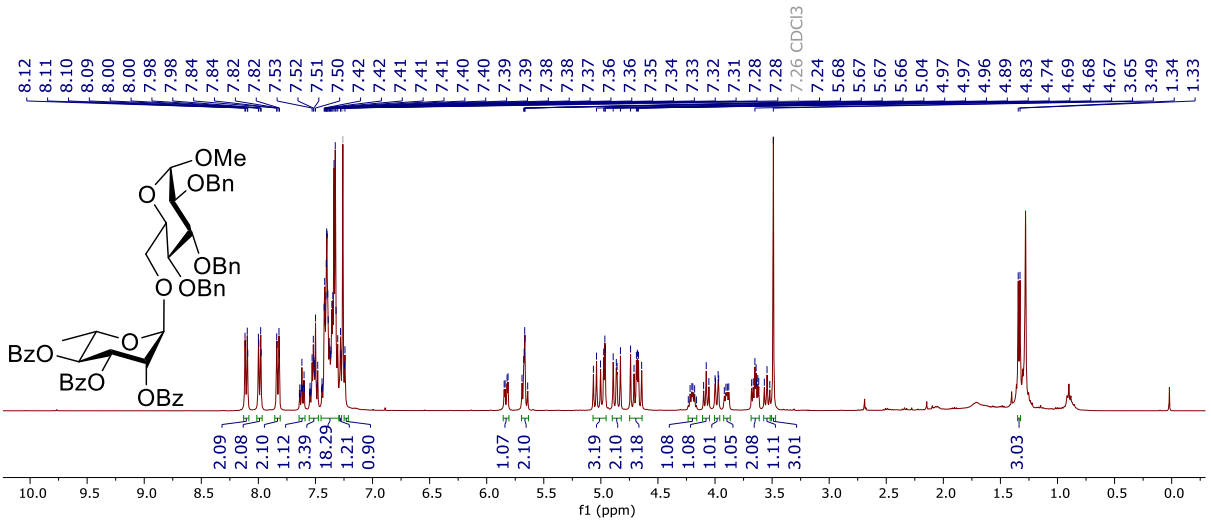

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **19**



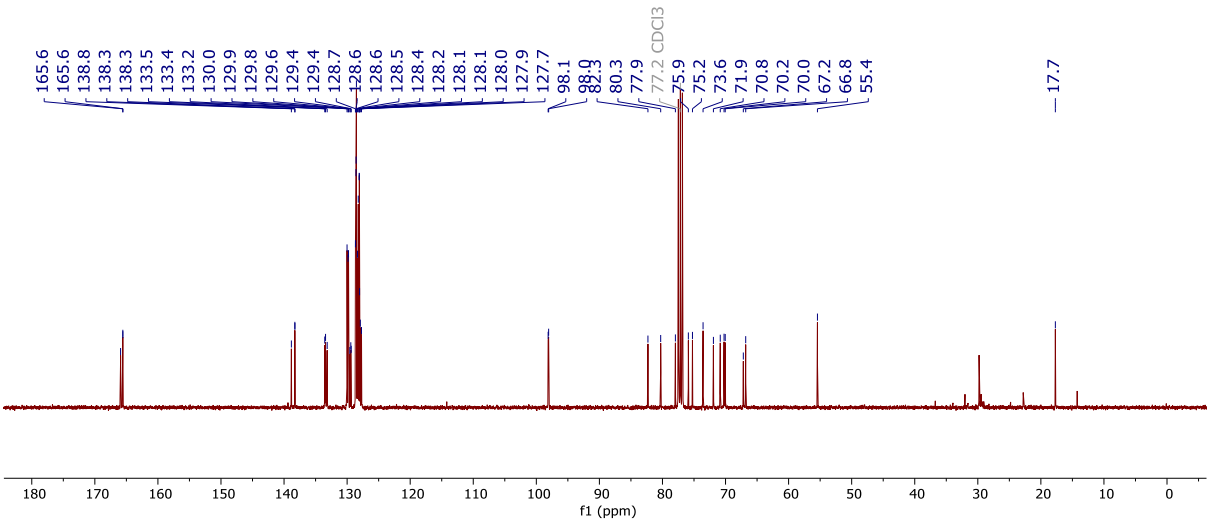

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **19**



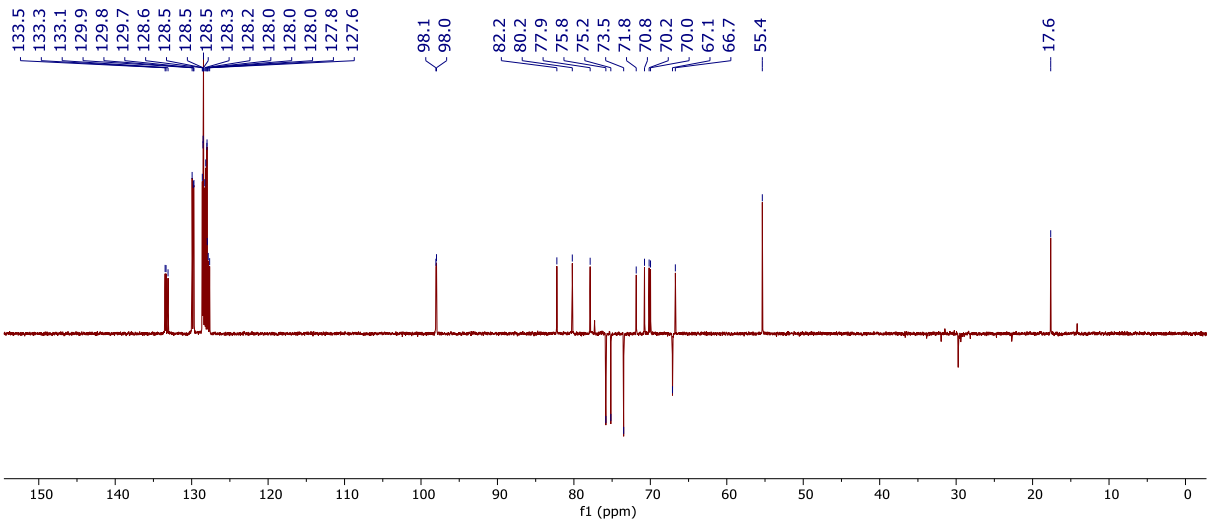
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **21**



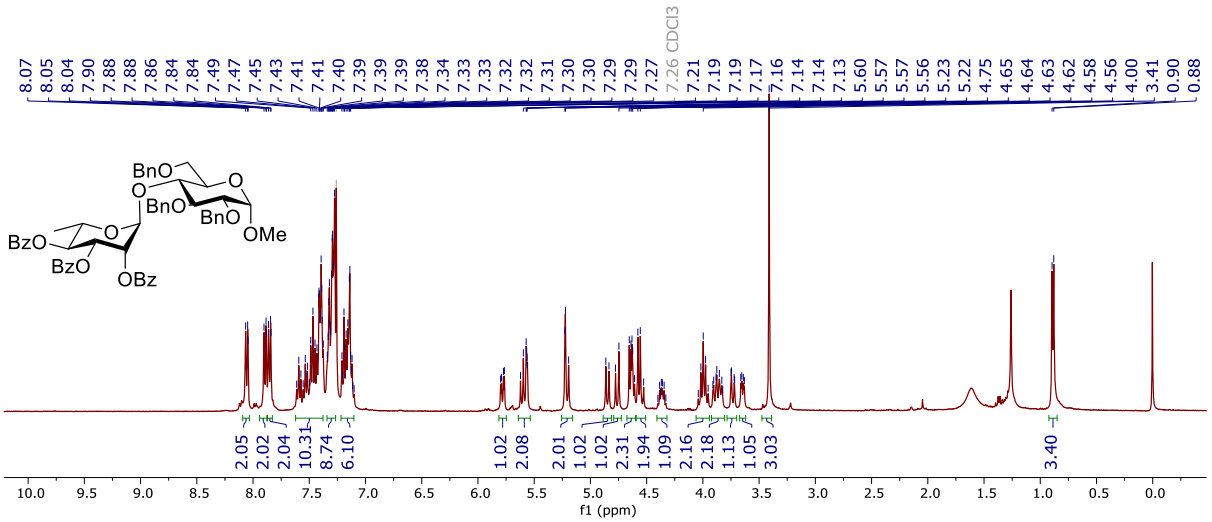

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **21**



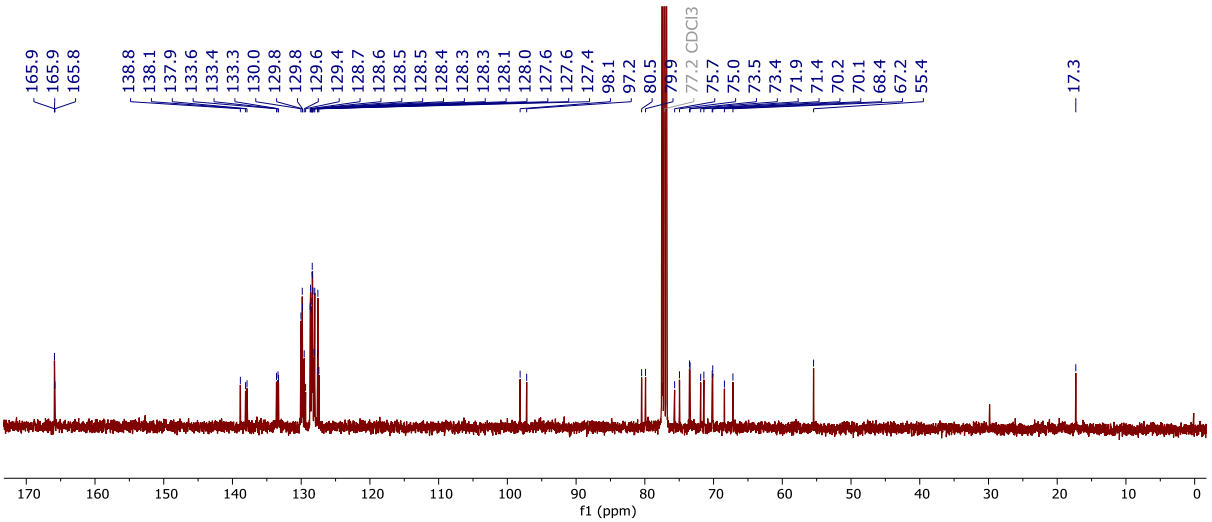

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **21**



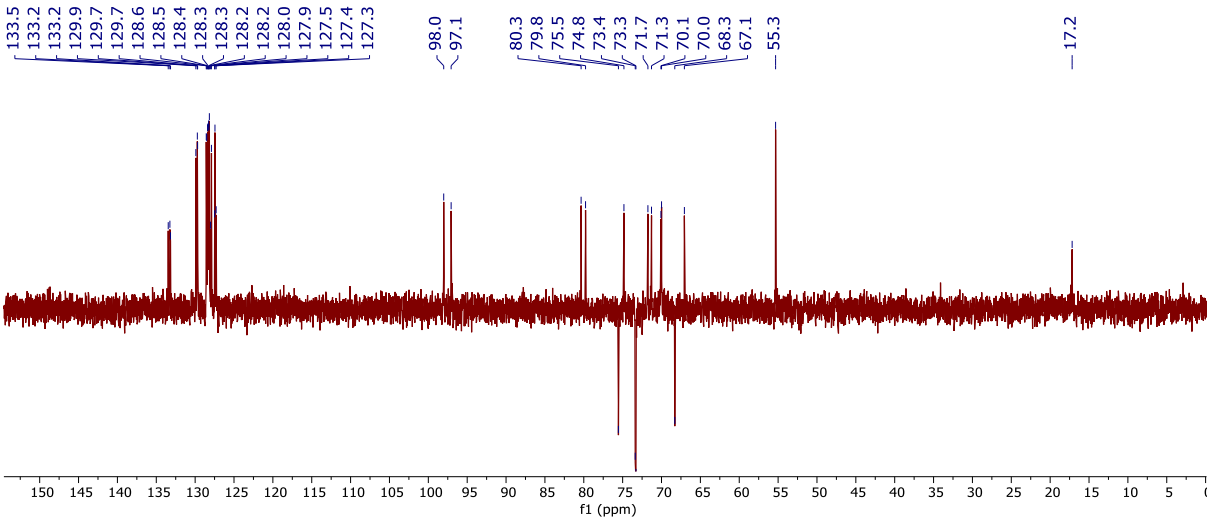
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **23**



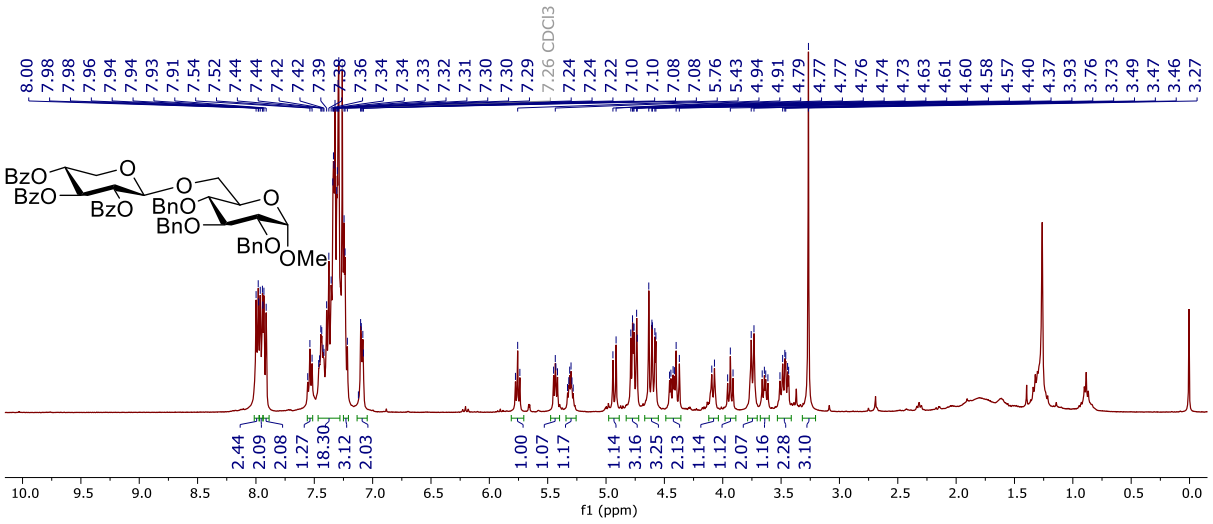

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **23**



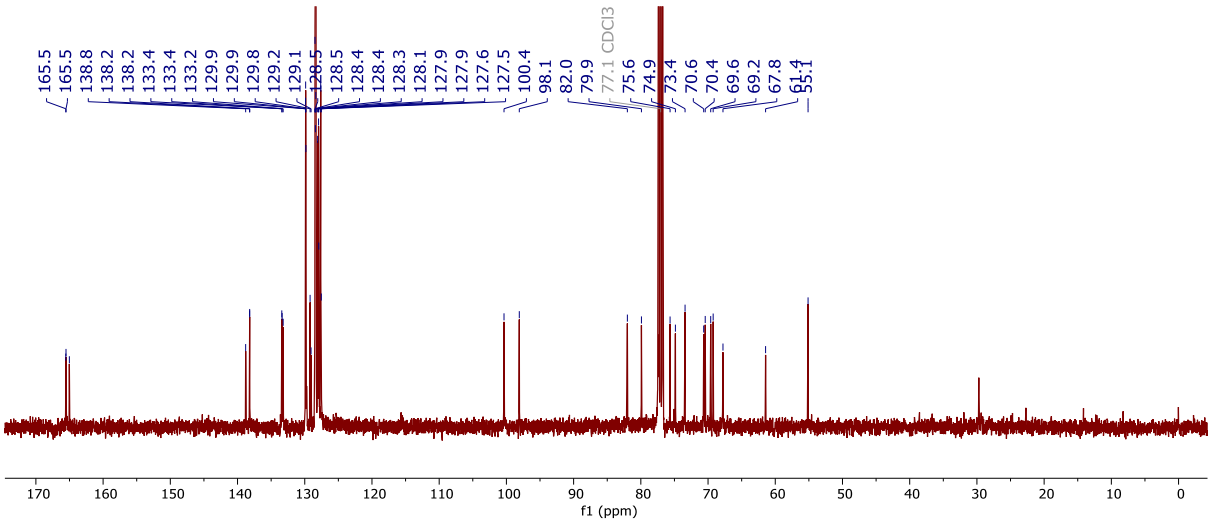

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **23**



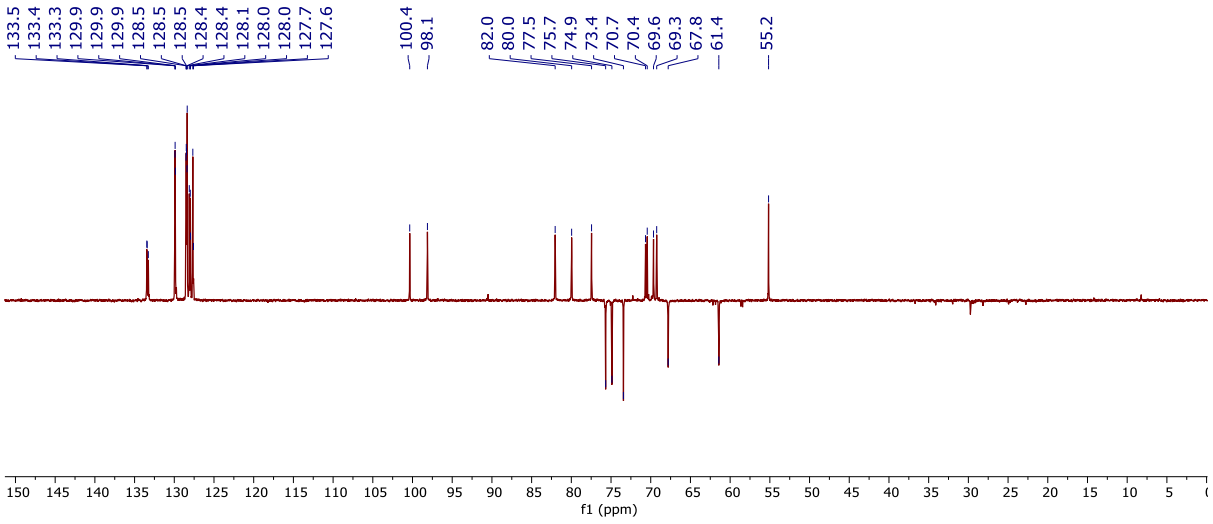
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **25**



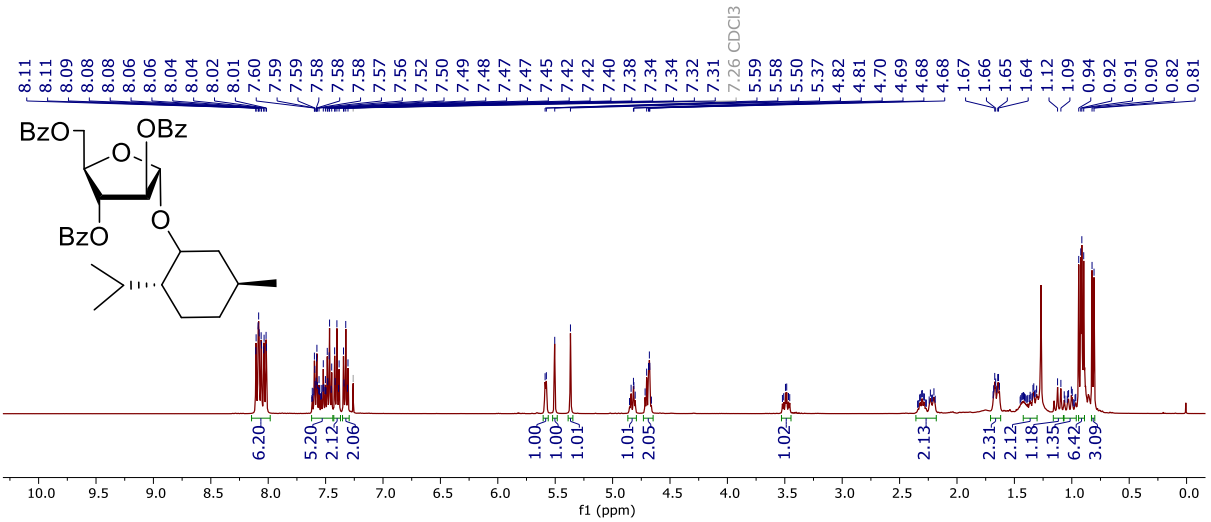

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **25**



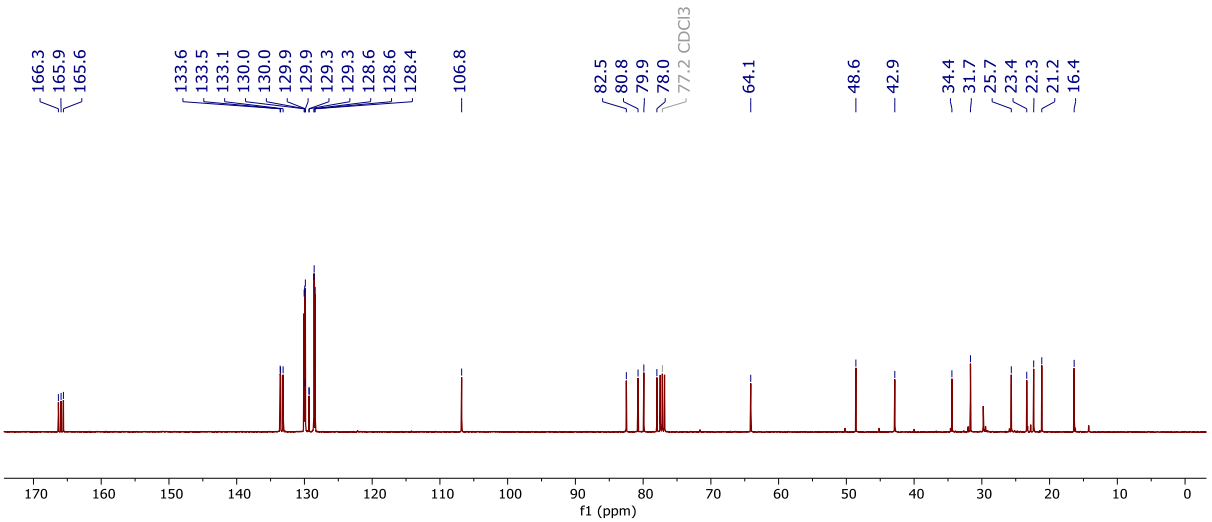

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **25**



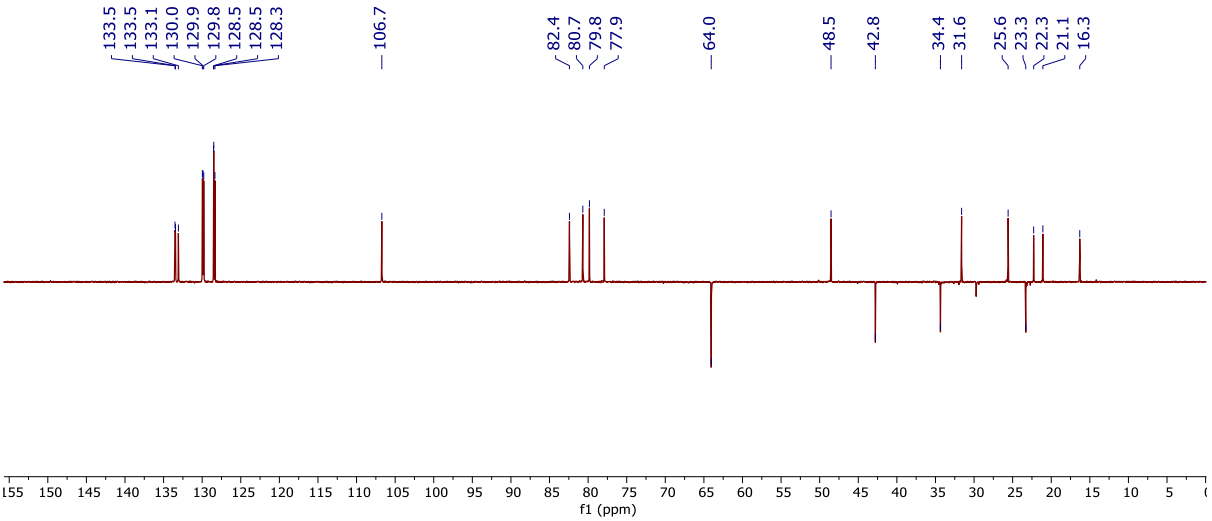
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **28**



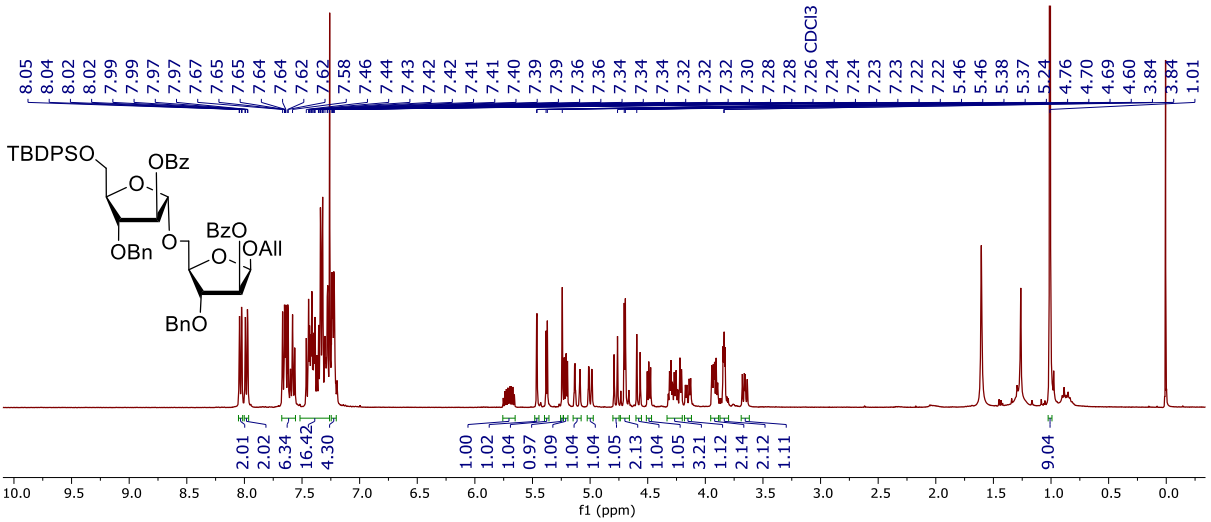

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **28**



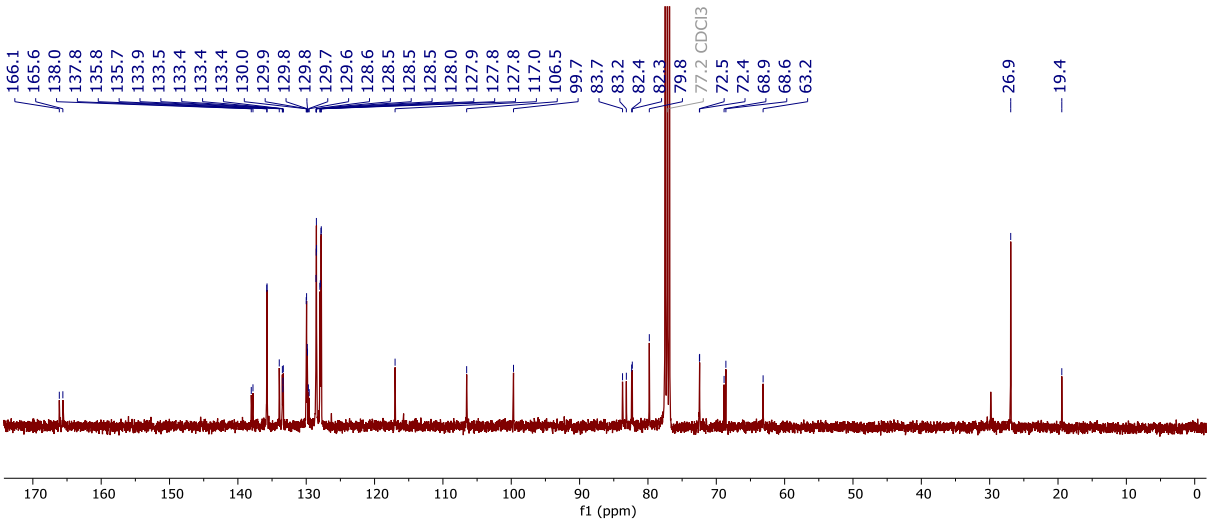

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **28**



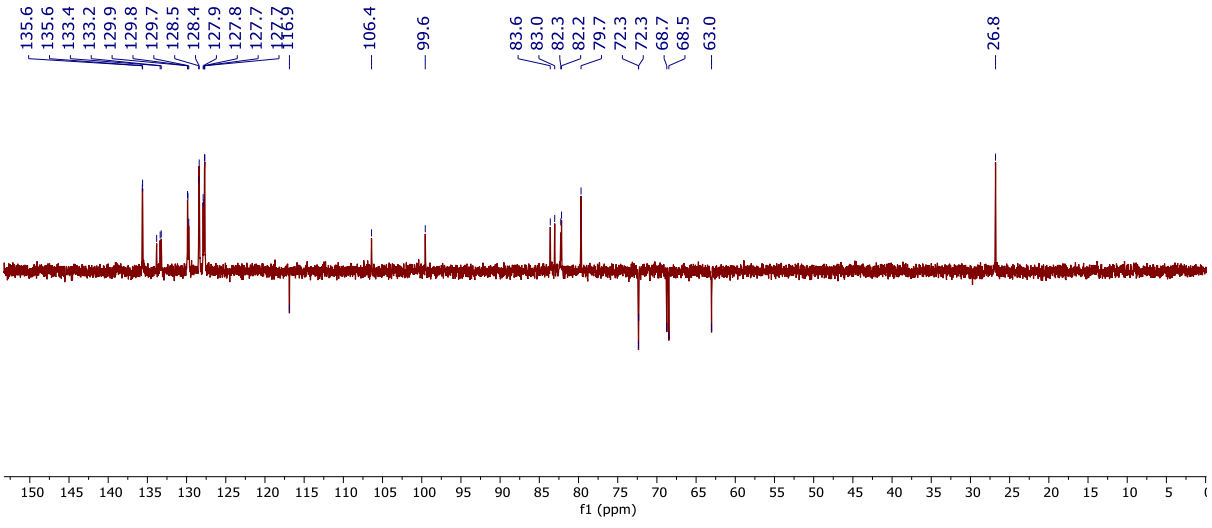
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **31**



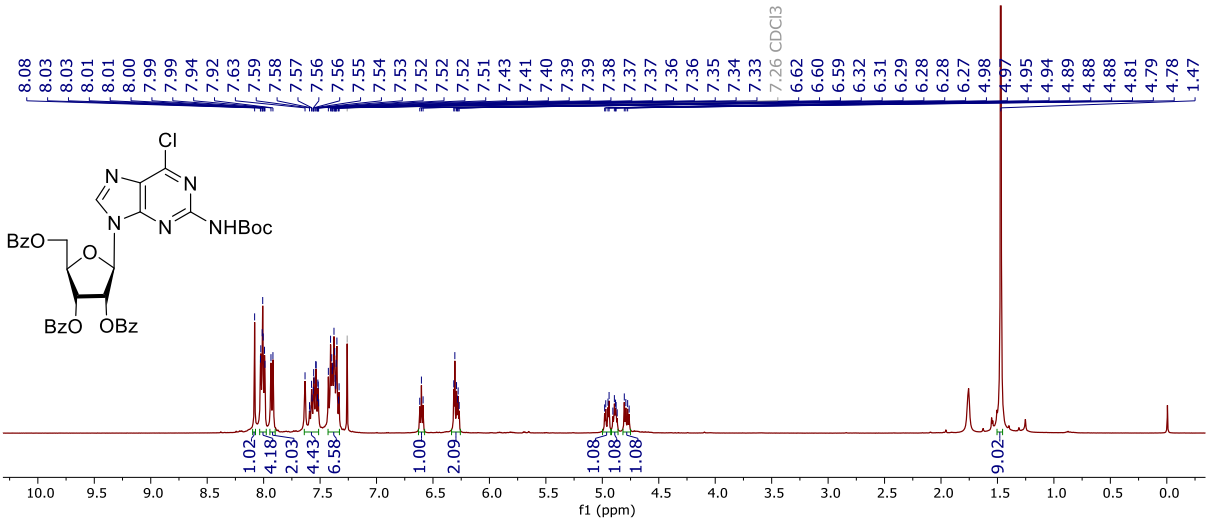

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **31**



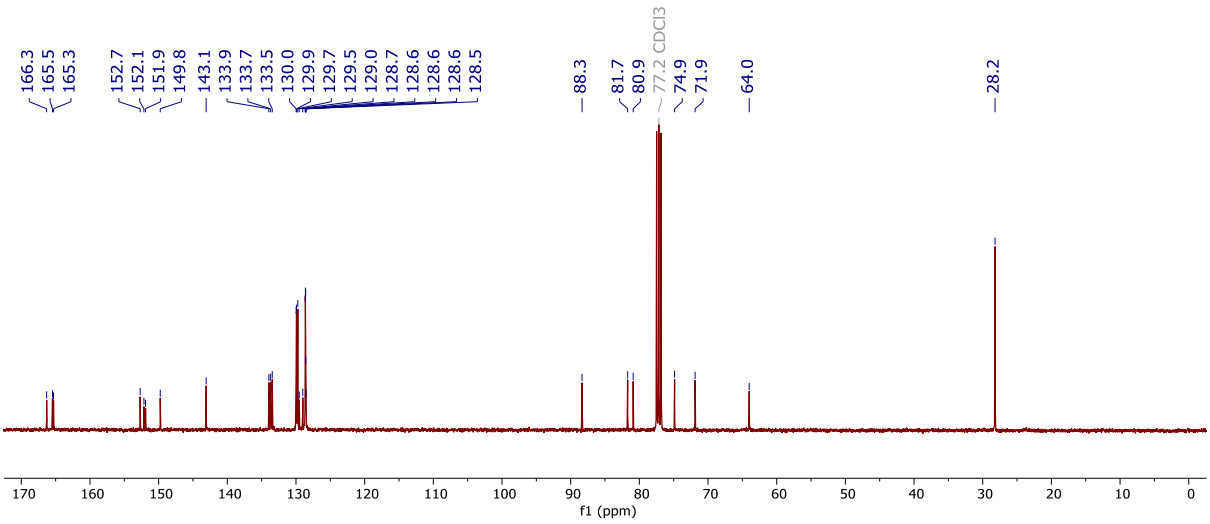

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **31**



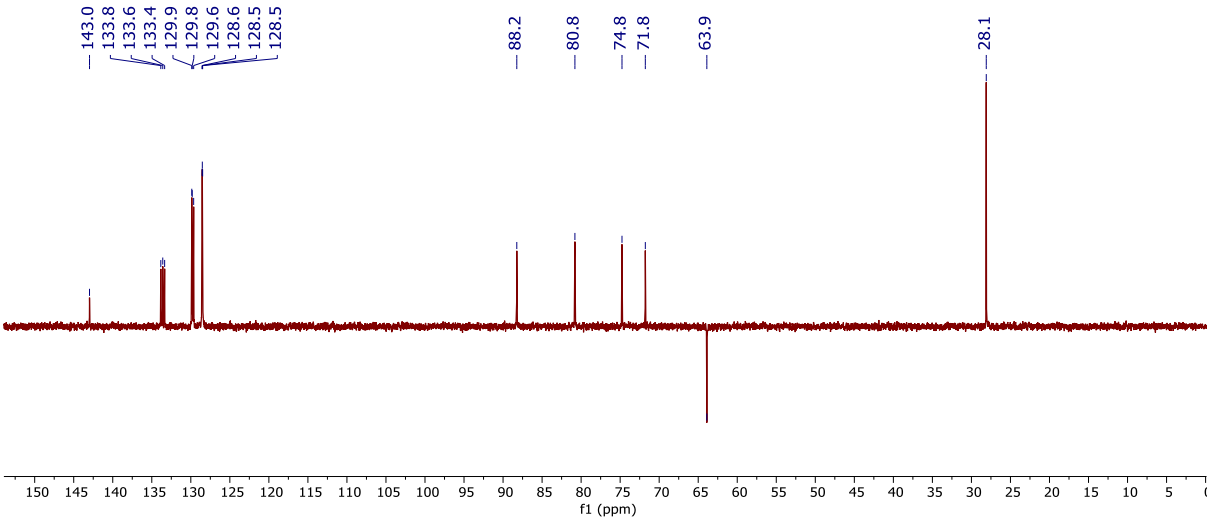
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **36**



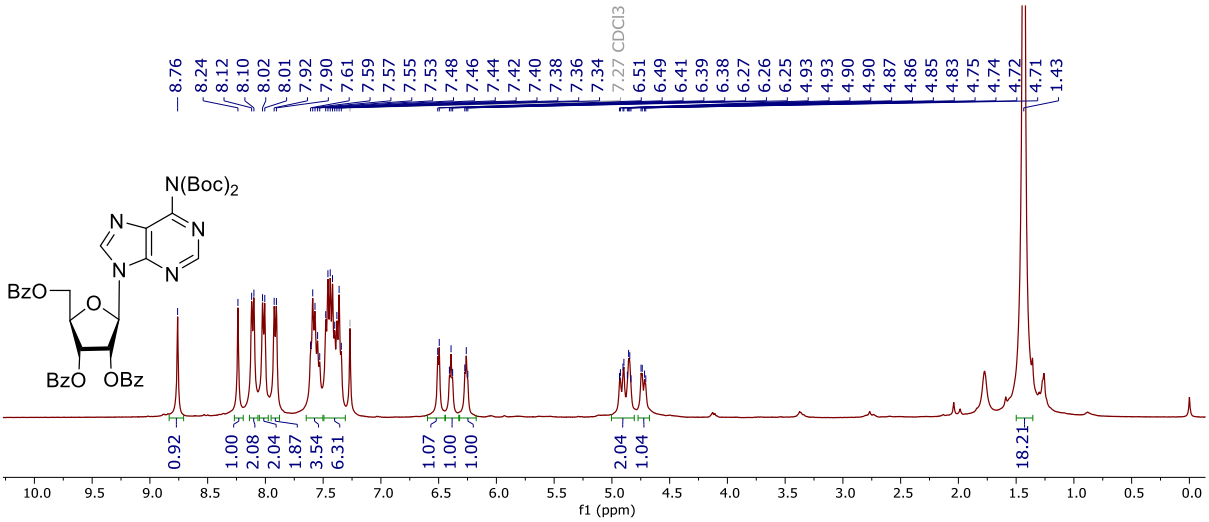

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **36**



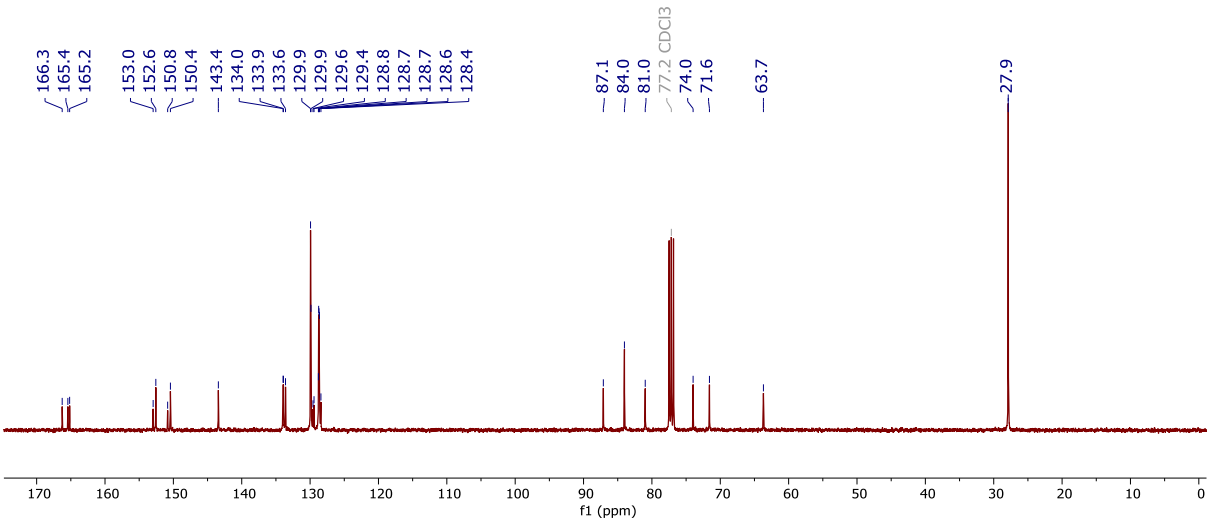

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **36**



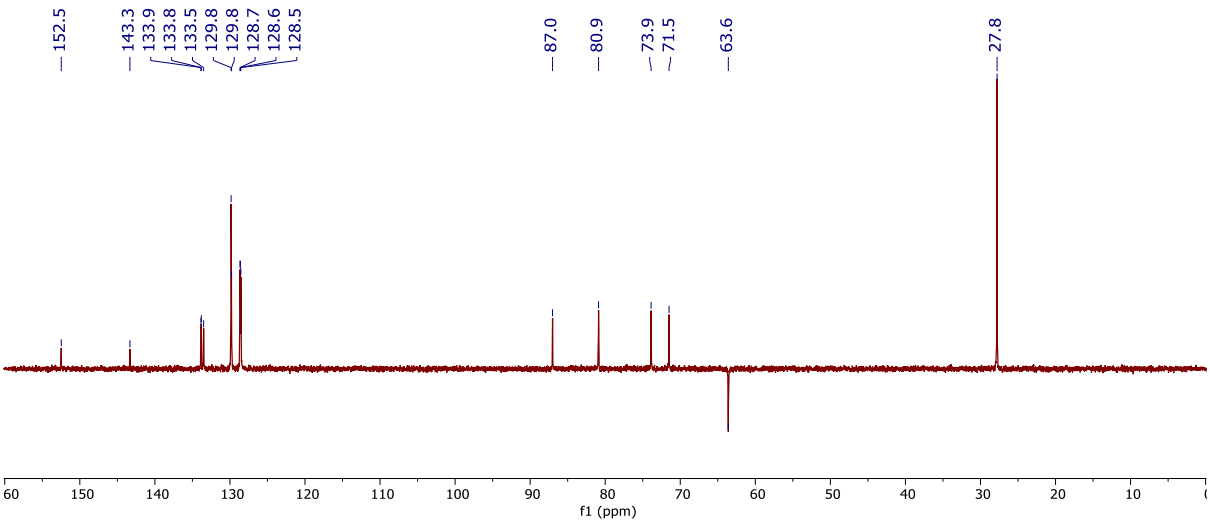
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **38**



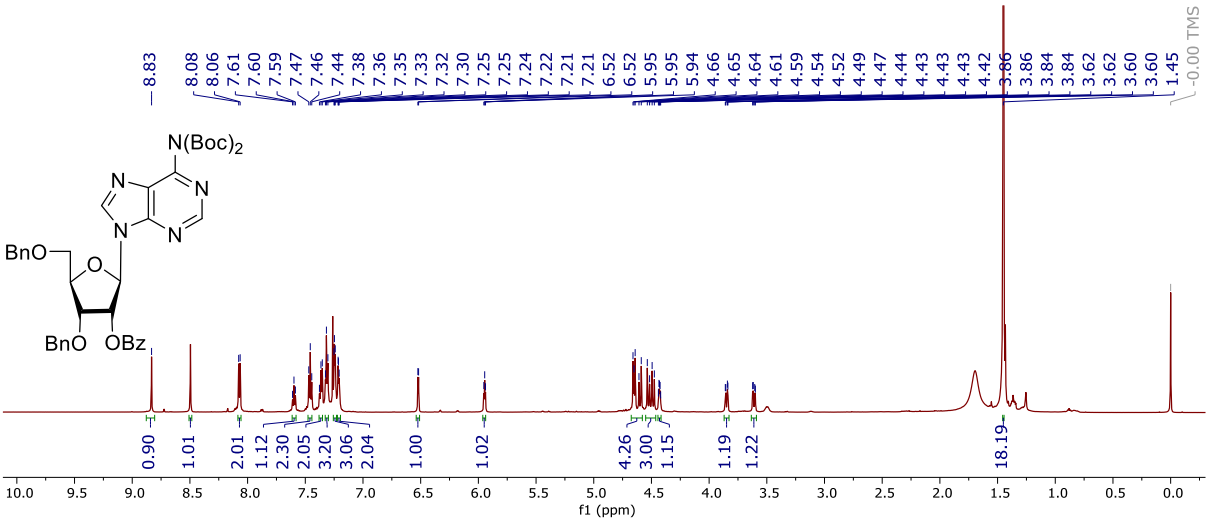

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **38**



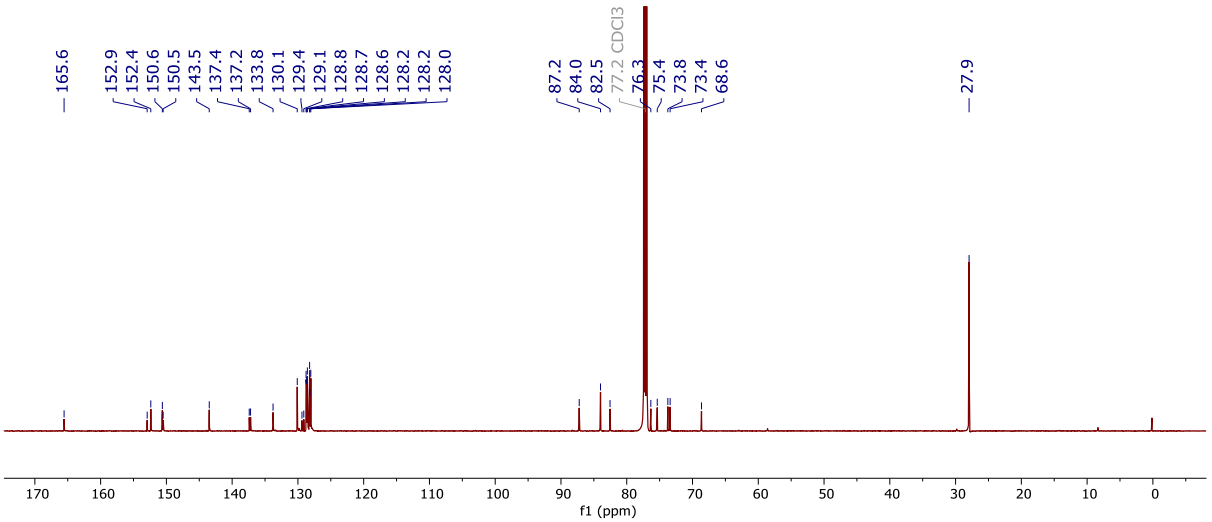

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **38**



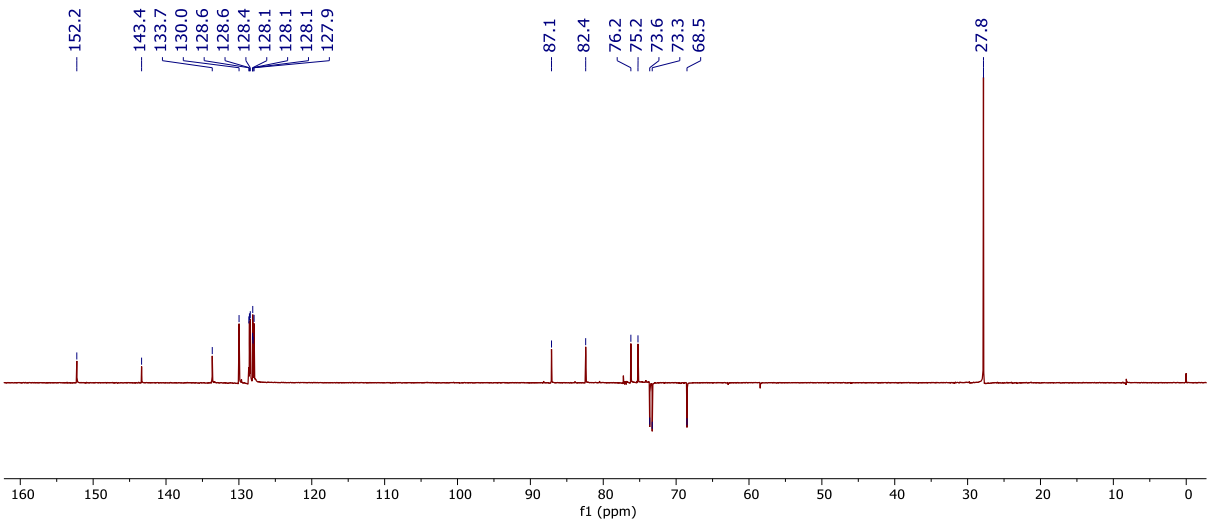
$^{1}$H NMR Spectrum (600 MHz, $CDCl_3$) of Compound **39**



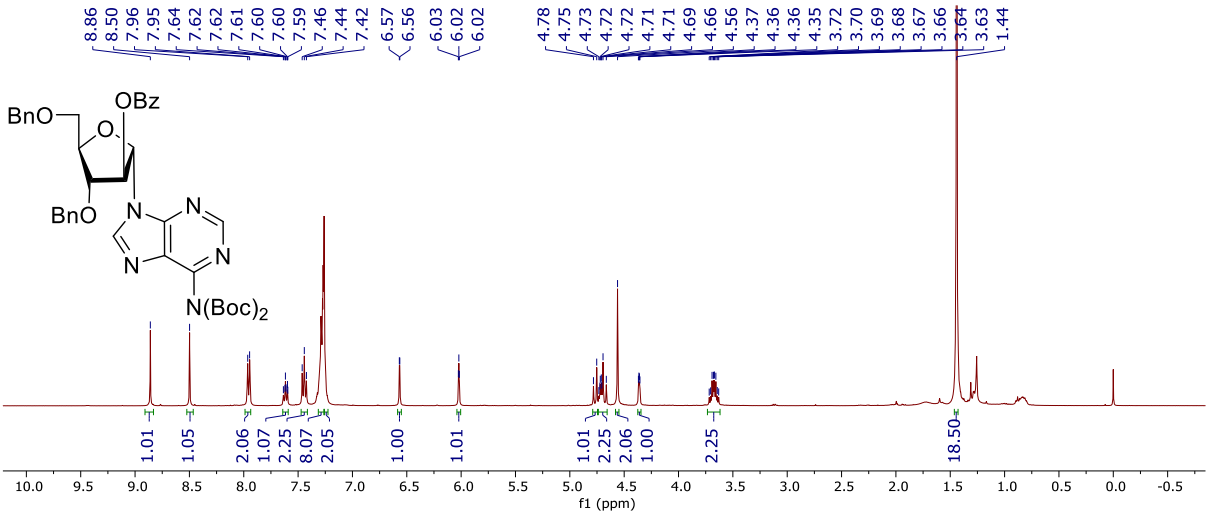

$^{13}$C NMR Spectrum (151 MHz, $CDCl_3$) of Compound **39**



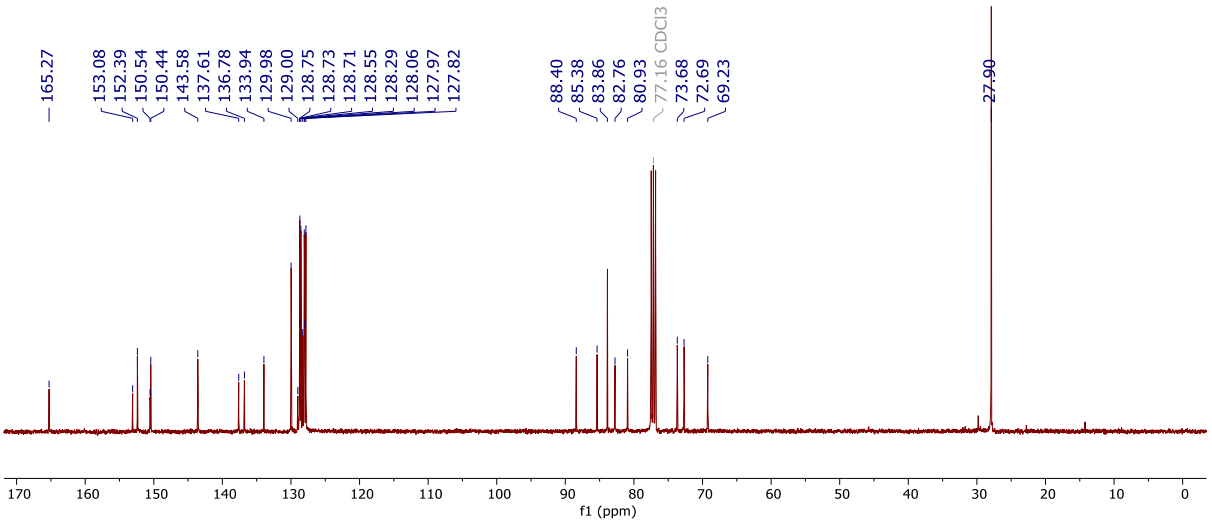

$^{13}$C DEPT-135 NMR Spectrum (151 MHz, $CDCl_3$) of Compound **39**



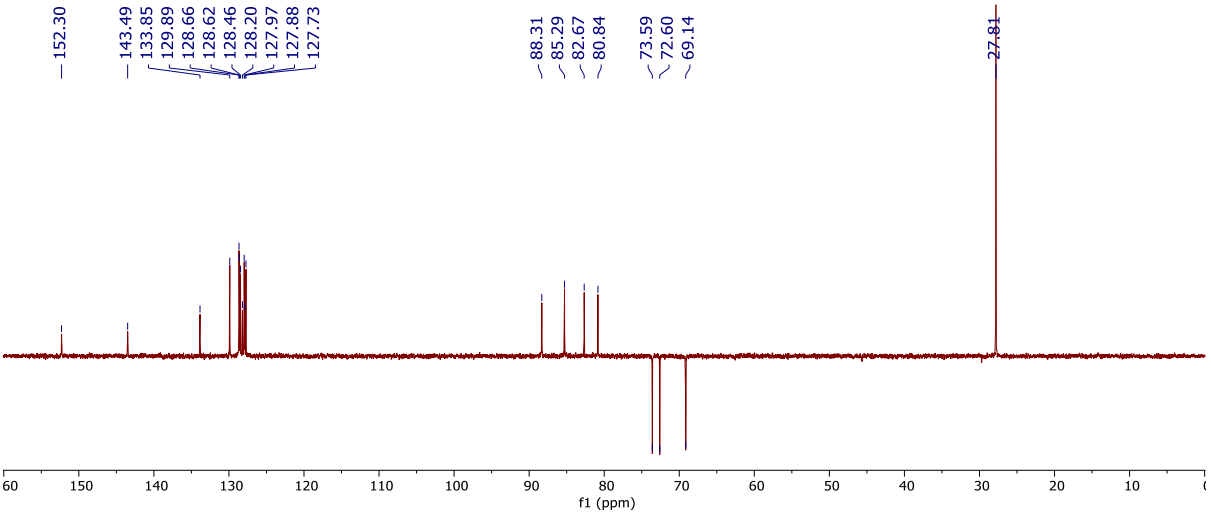
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **40**



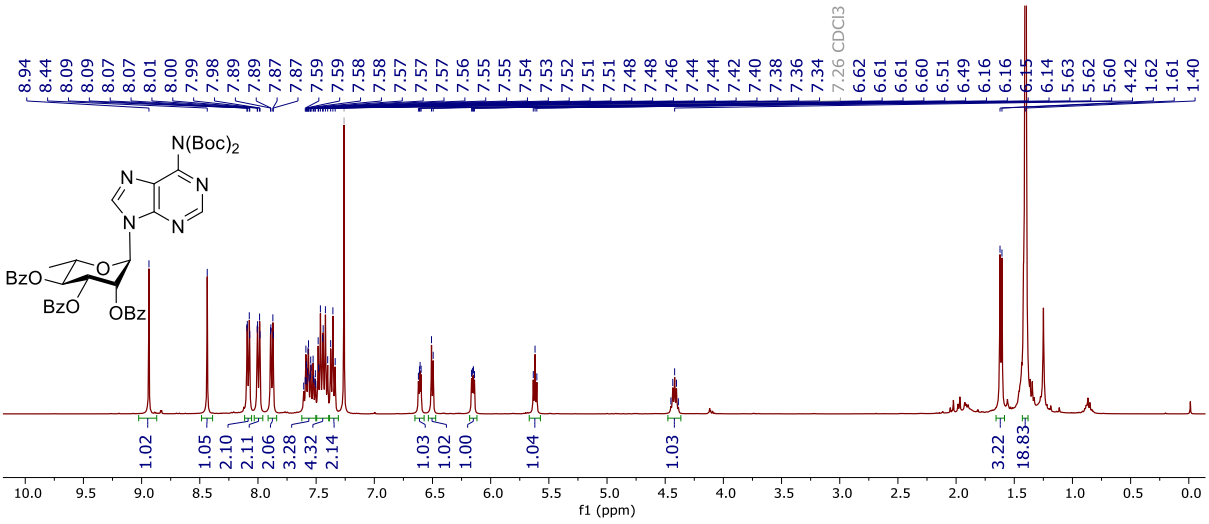

$^{13}$C NMR Spectrum (400 MHz, $CDCl_3$) of Compound **40**



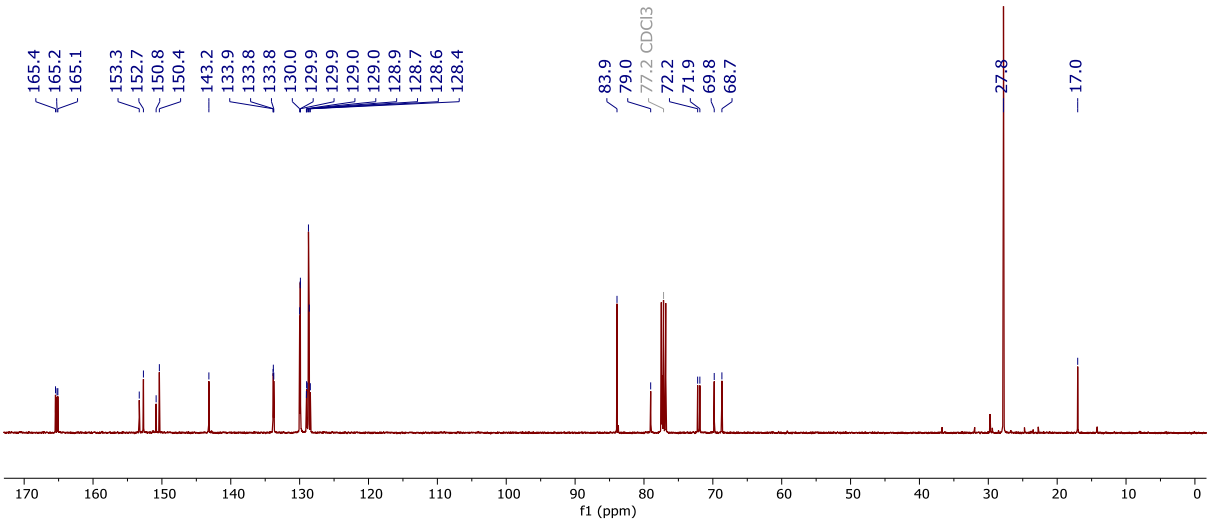

$^{13}$C DEPT-135 NMR Spectrum (400 MHz, $CDCl_3$) of Compound **40**



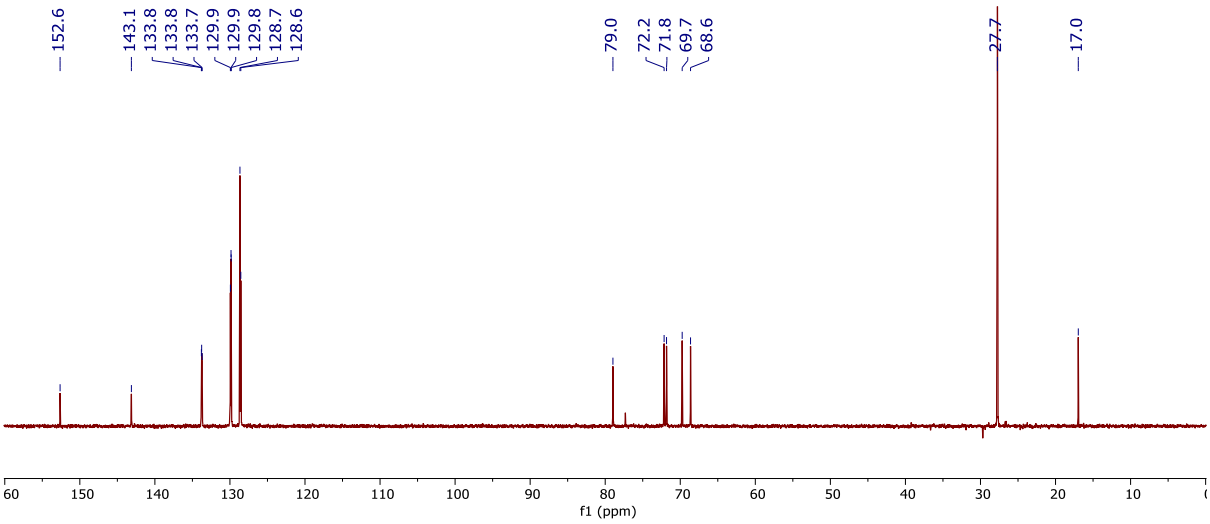
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **41**



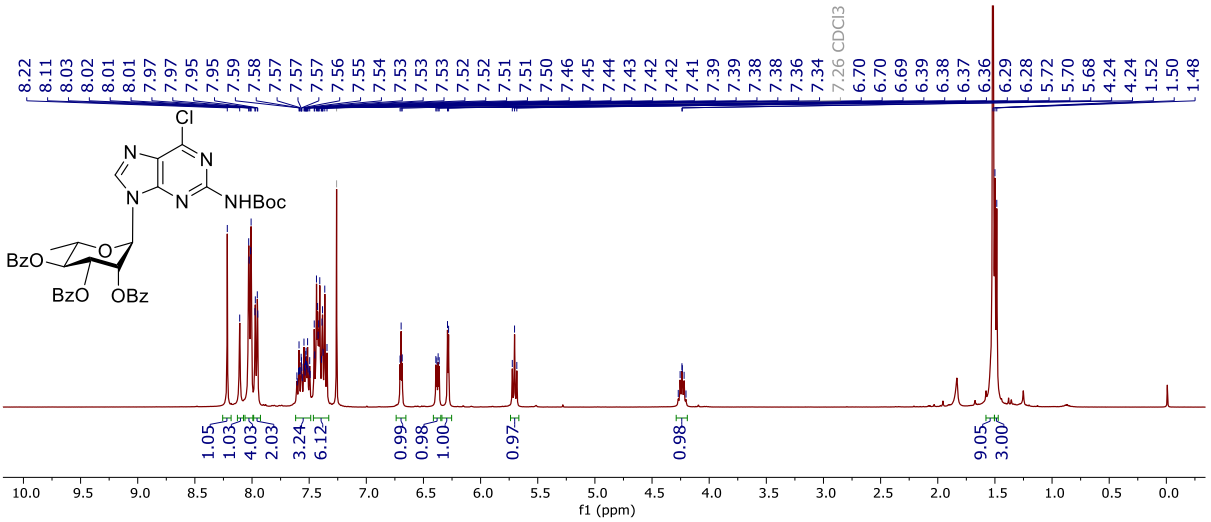

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **41**



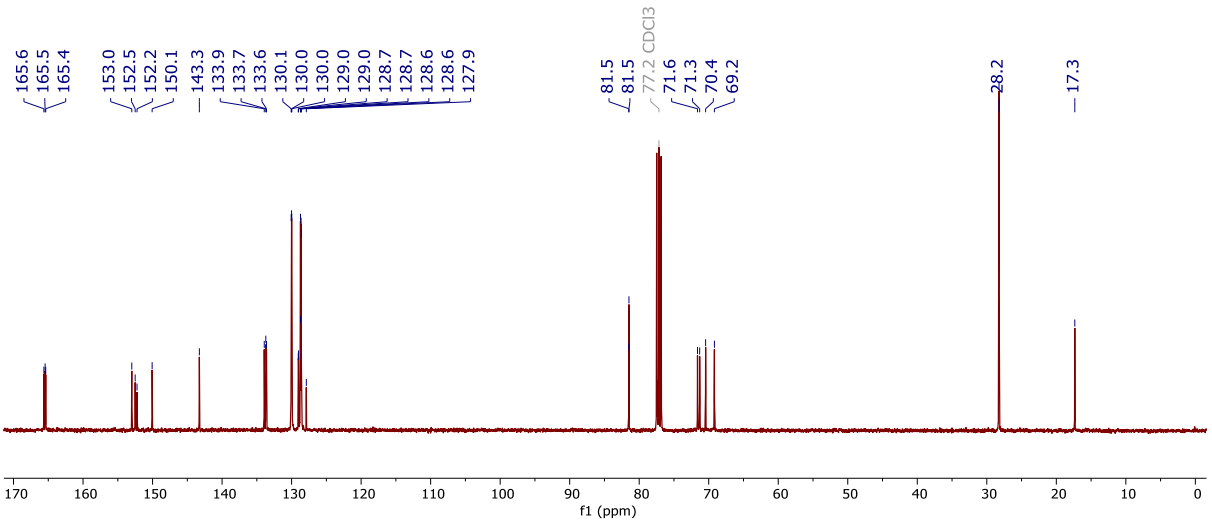

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **41**



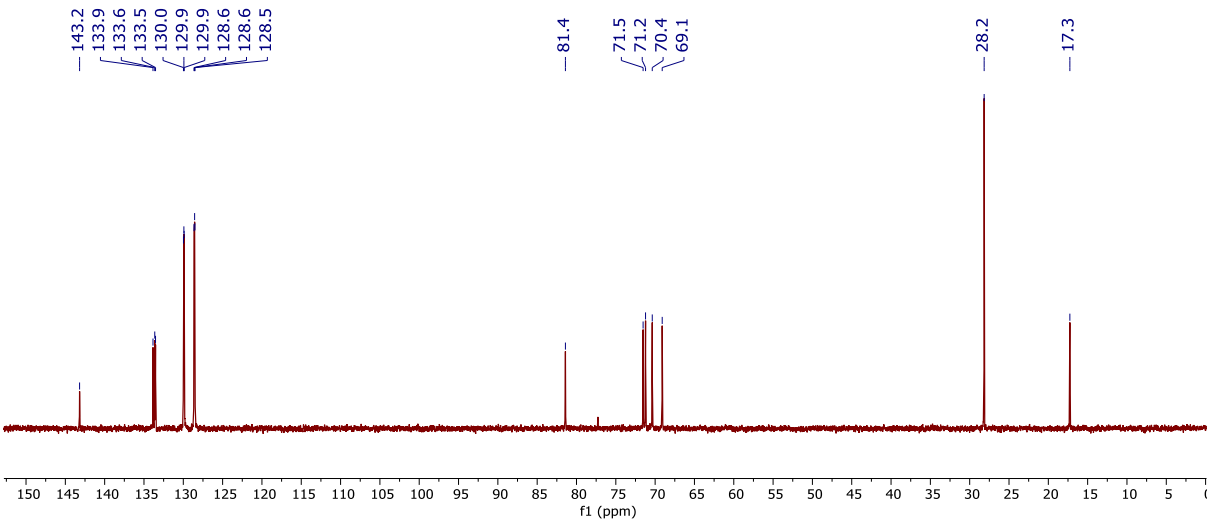
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **42**



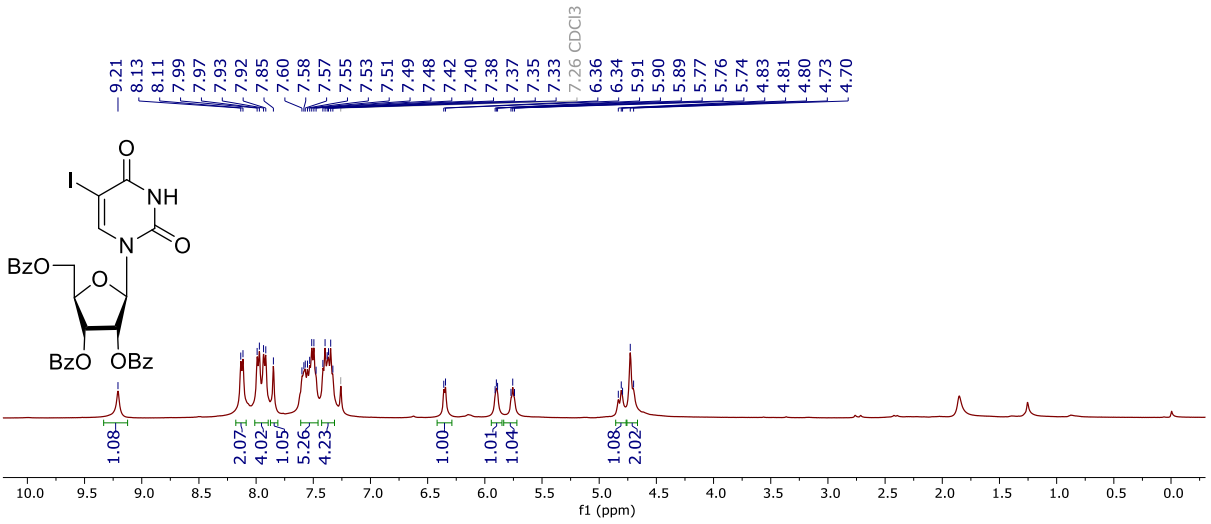

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **42**



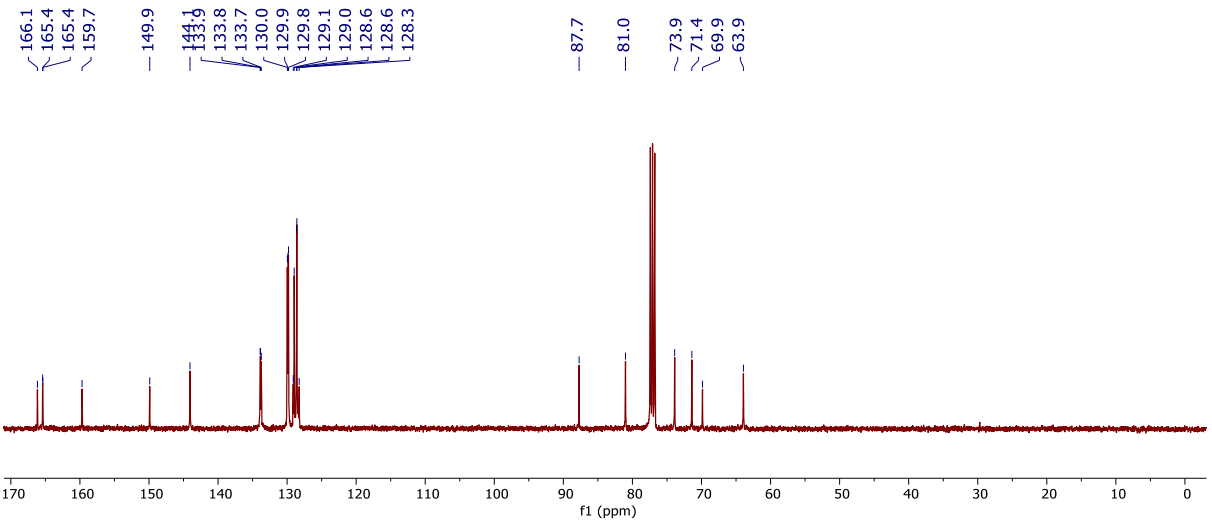

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **42**



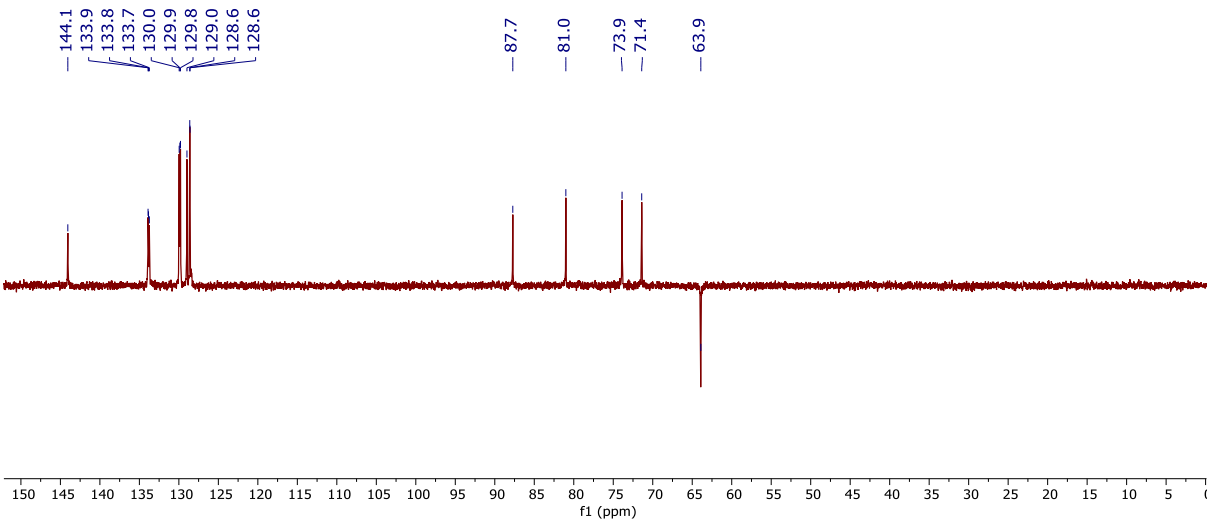
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **45**



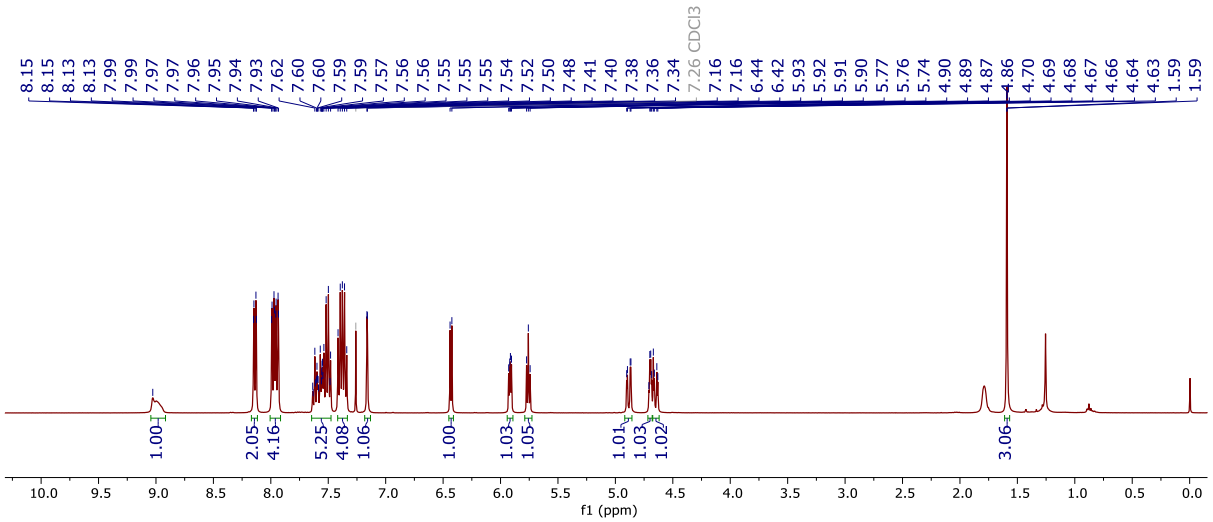

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **45**



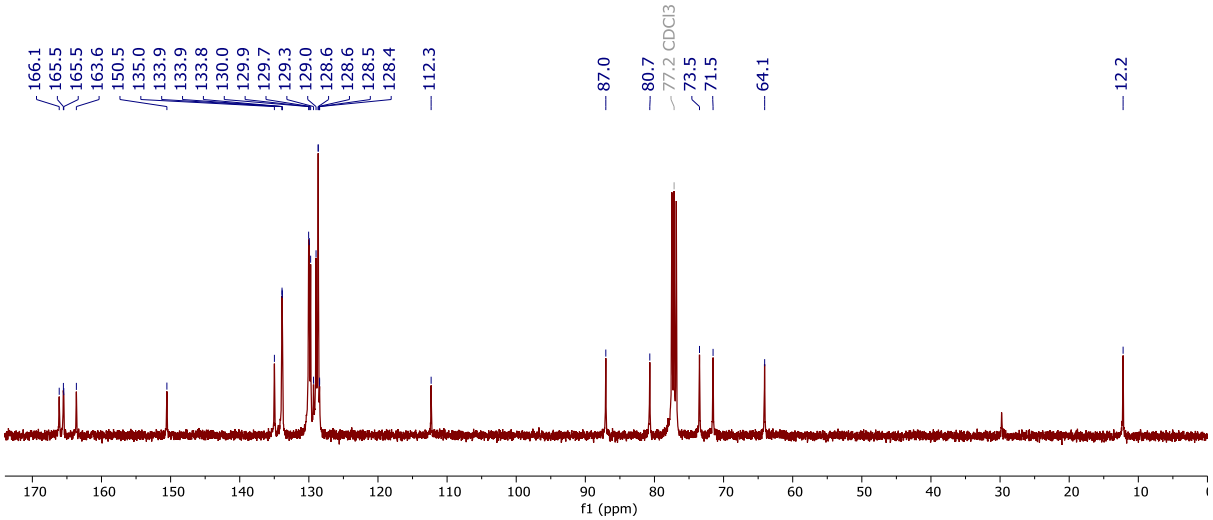

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **45**



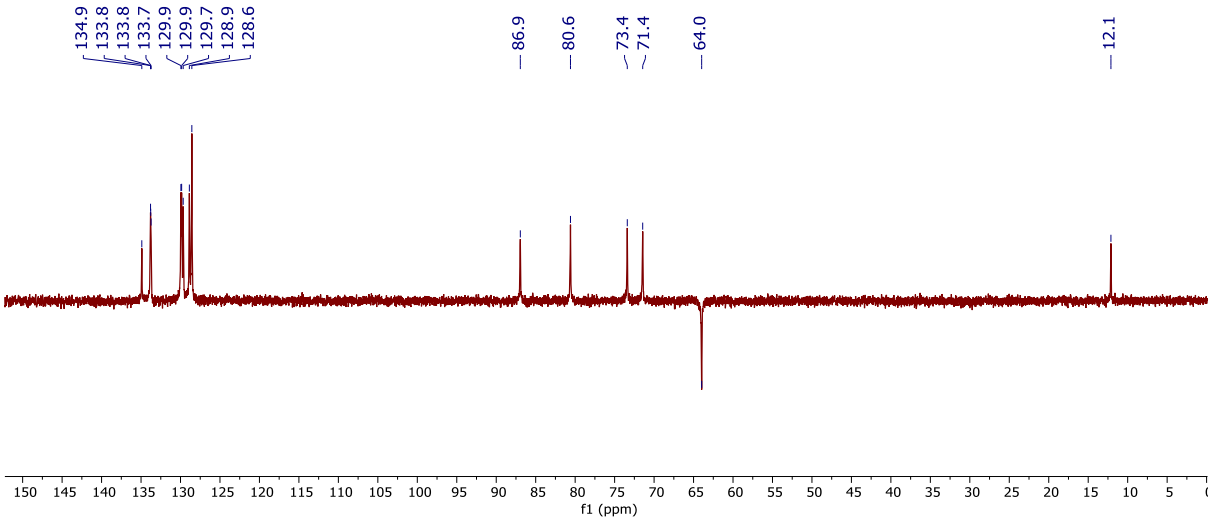
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **47**



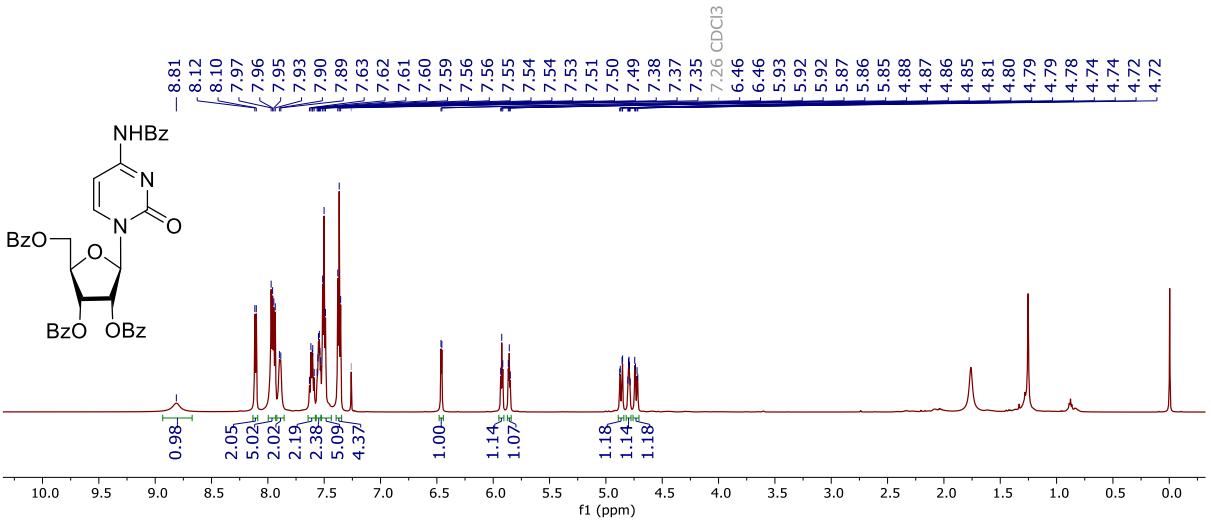

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **47**



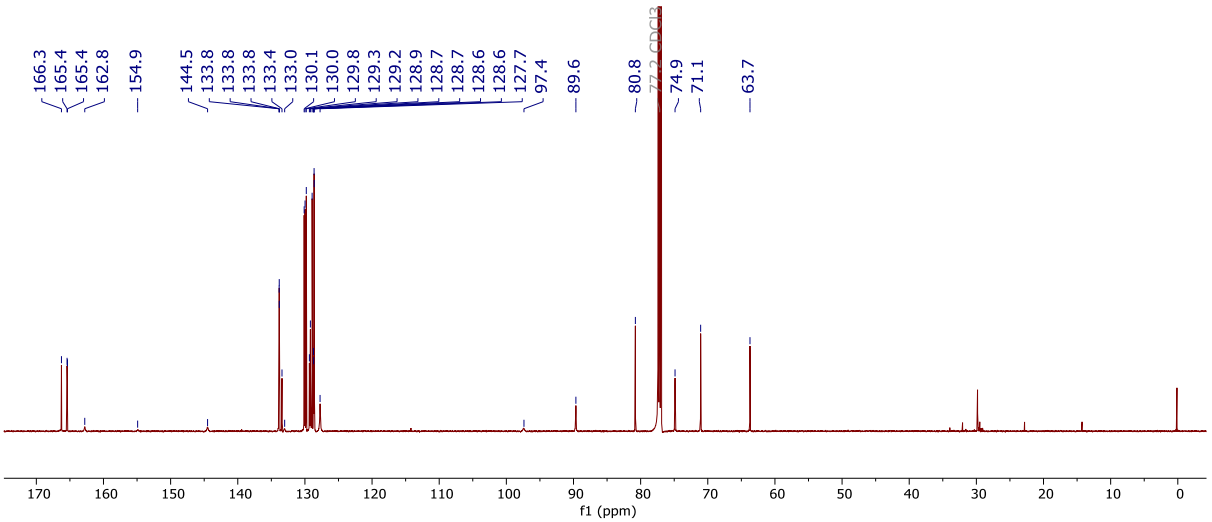

$^{13}$C DEPT-135 NMR Spectrum (101 MHz, $CDCl_3$) of Compound **47**



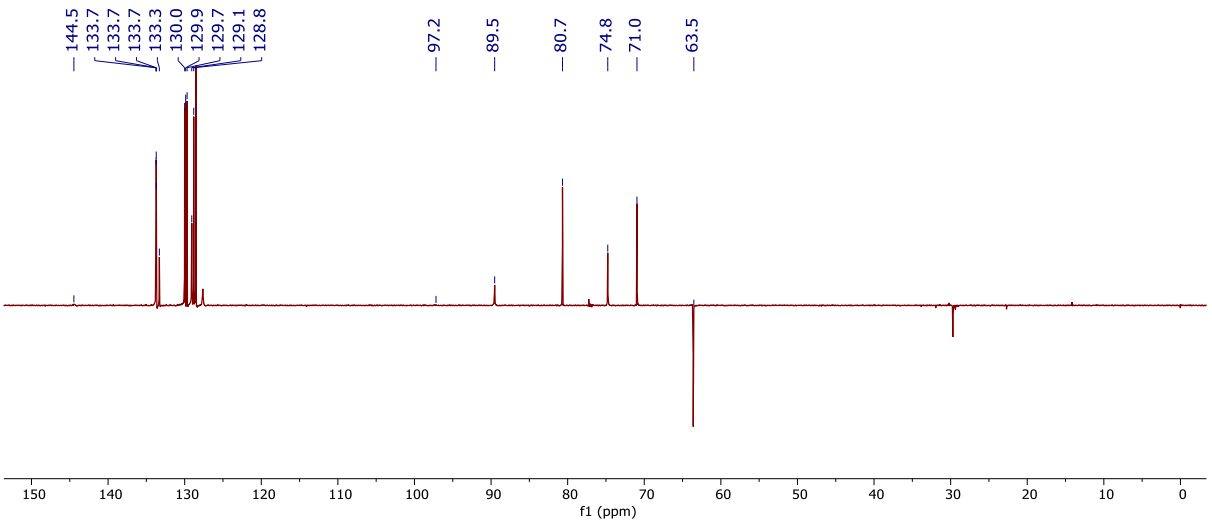
$^{1}$H NMR Spectrum (600 MHz, $CDCl_3$) of Compound **49**



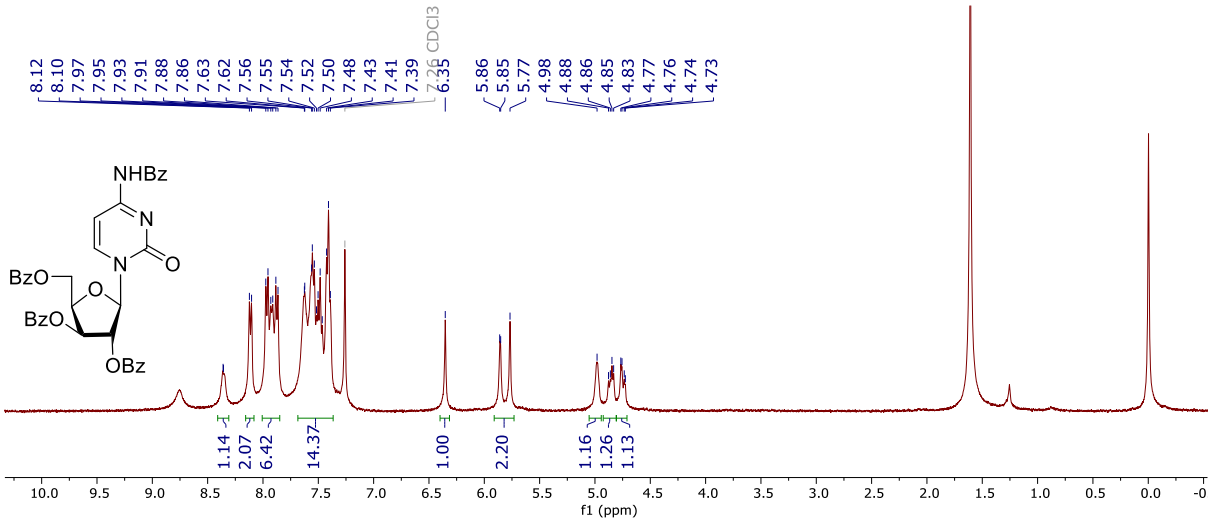

$^{13}$C NMR Spectrum (151 MHz, $CDCl_3$) of Compound **49**



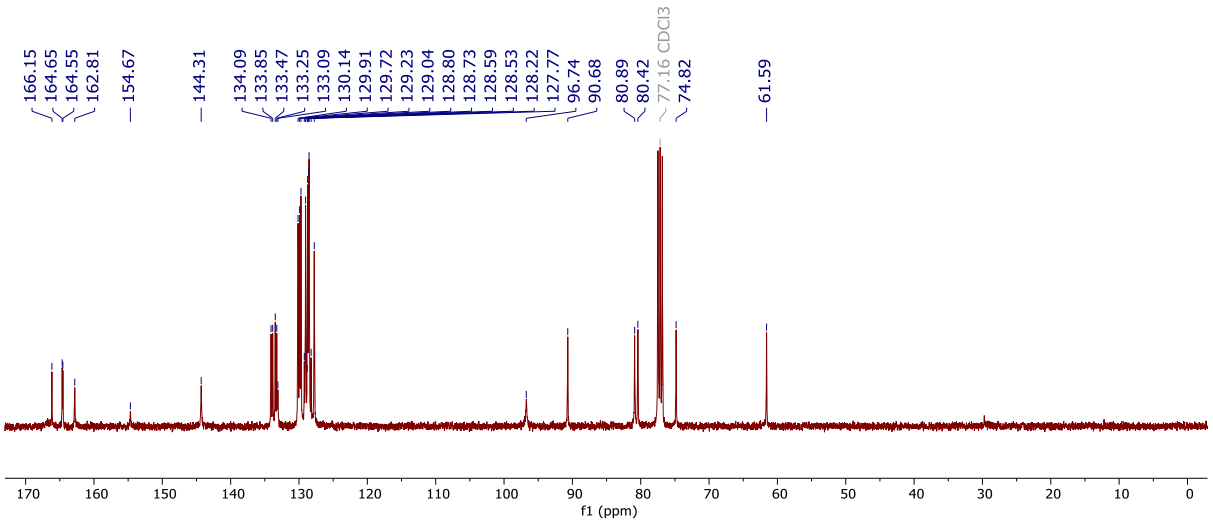

$^{13}$C DEPT-135 NMR Spectrum (151 MHz, $CDCl_3$) of Compound **49**



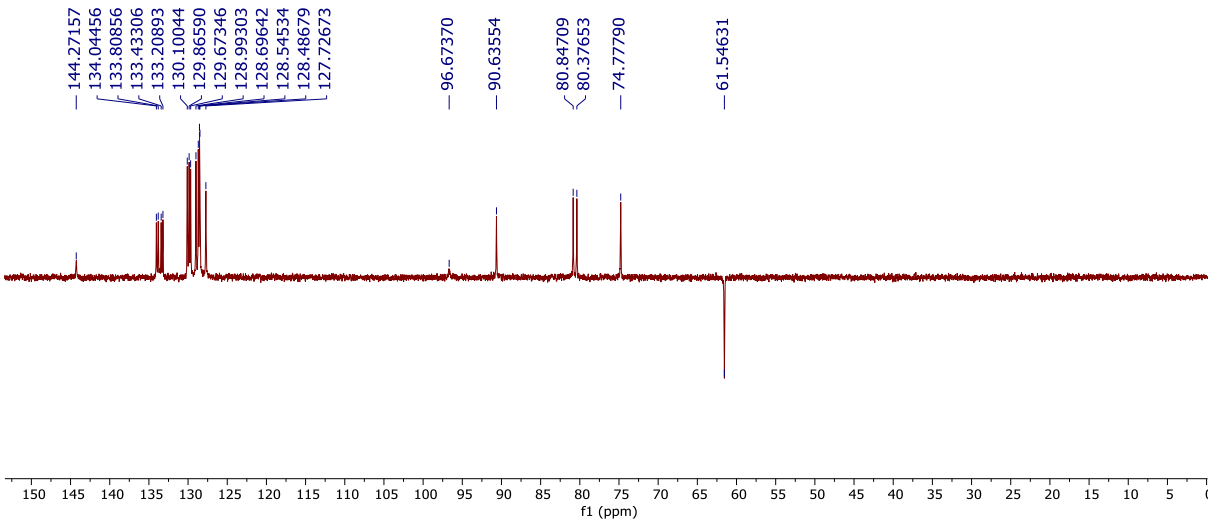
$^{1}$H NMR Spectrum (600 MHz, $CDCl_3$) of Compound **50**



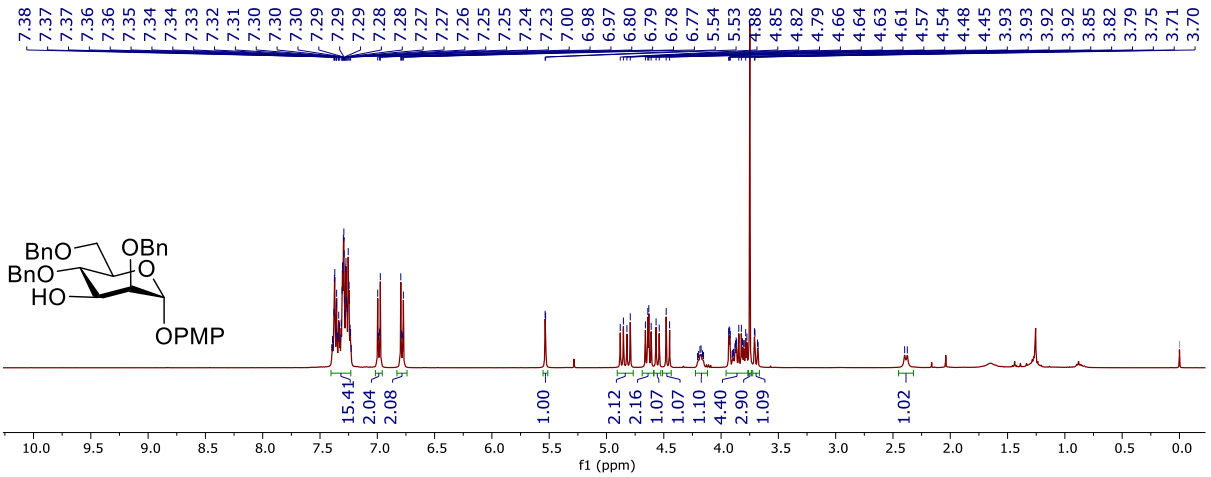

$^{13}$C NMR Spectrum (151 MHz, $CDCl_3$) of Compound **50**



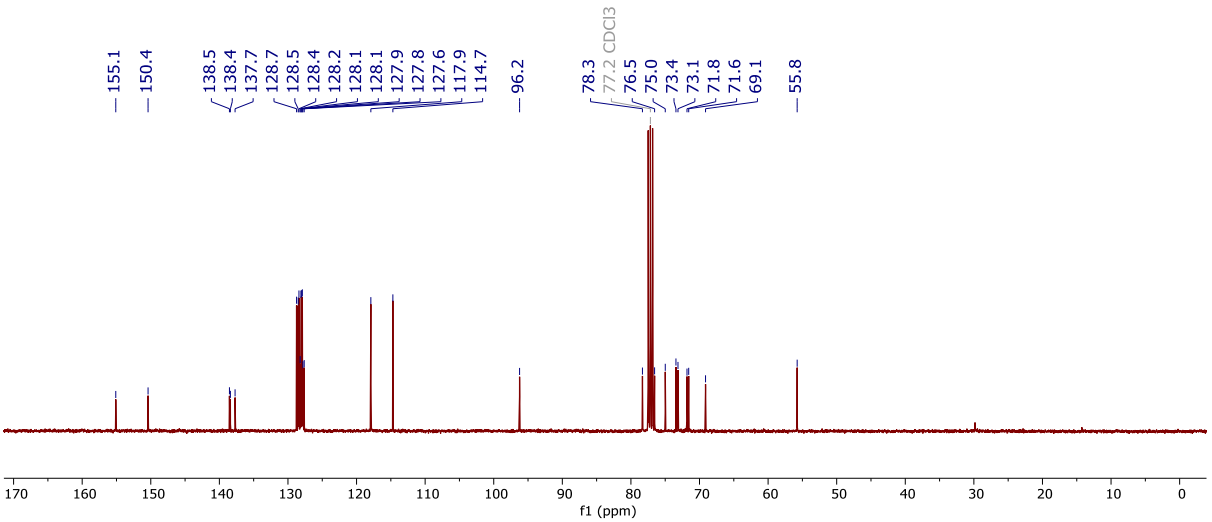

$^{13}$C DEPT-135 NMR Spectrum (151 MHz, $CDCl_3$) of Compound **50**



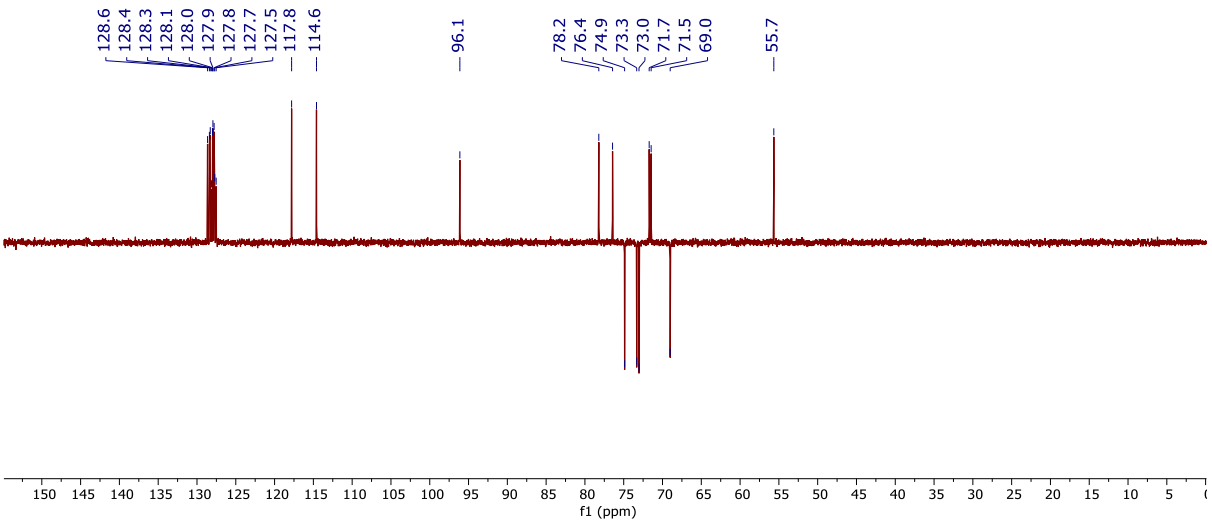
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **51**



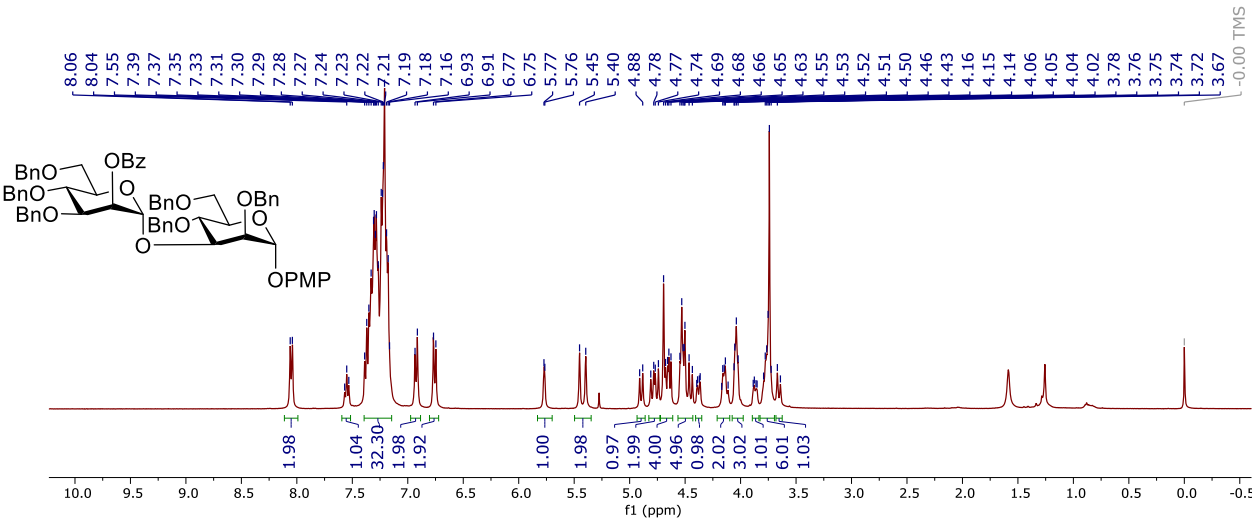

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **51**



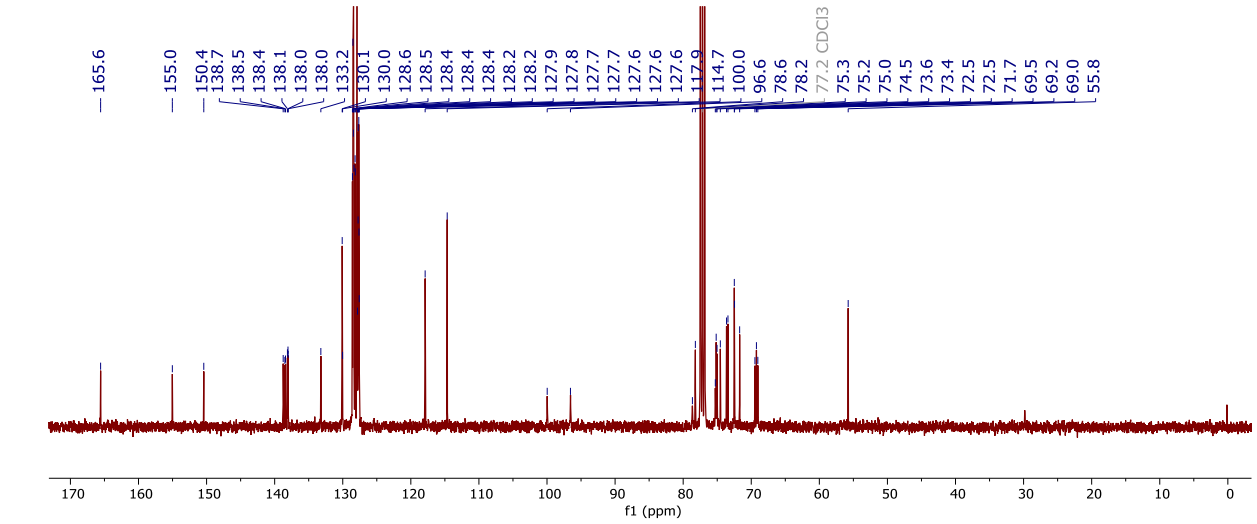

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **51**



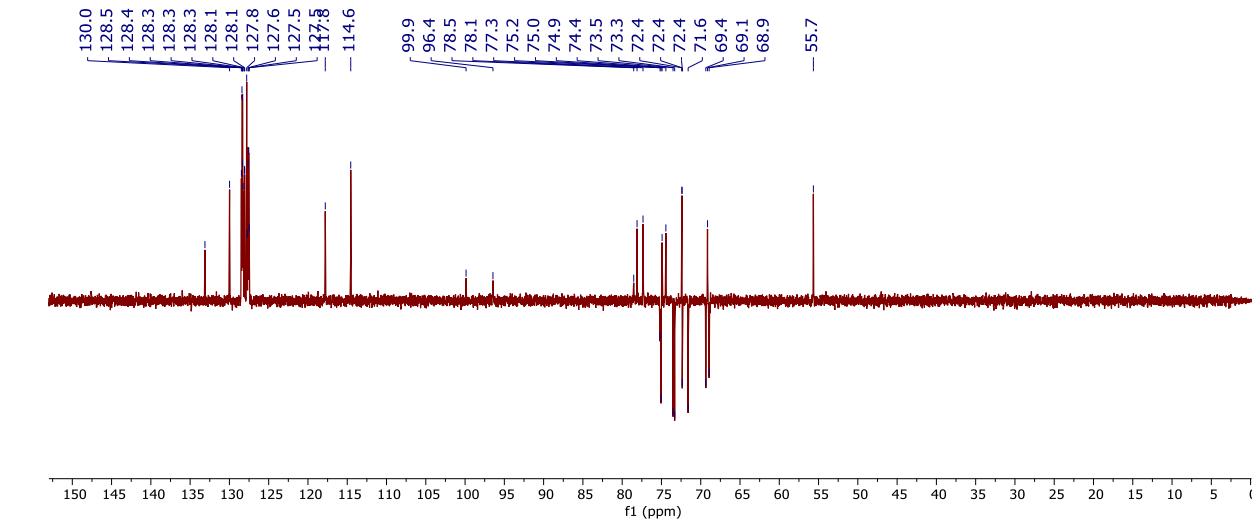
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **52**



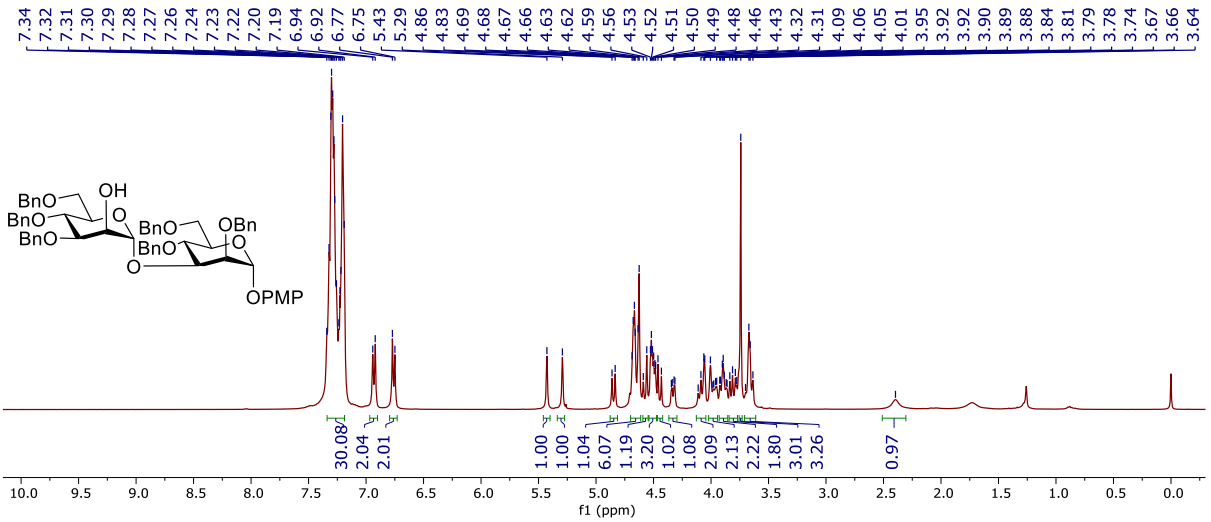

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **52**



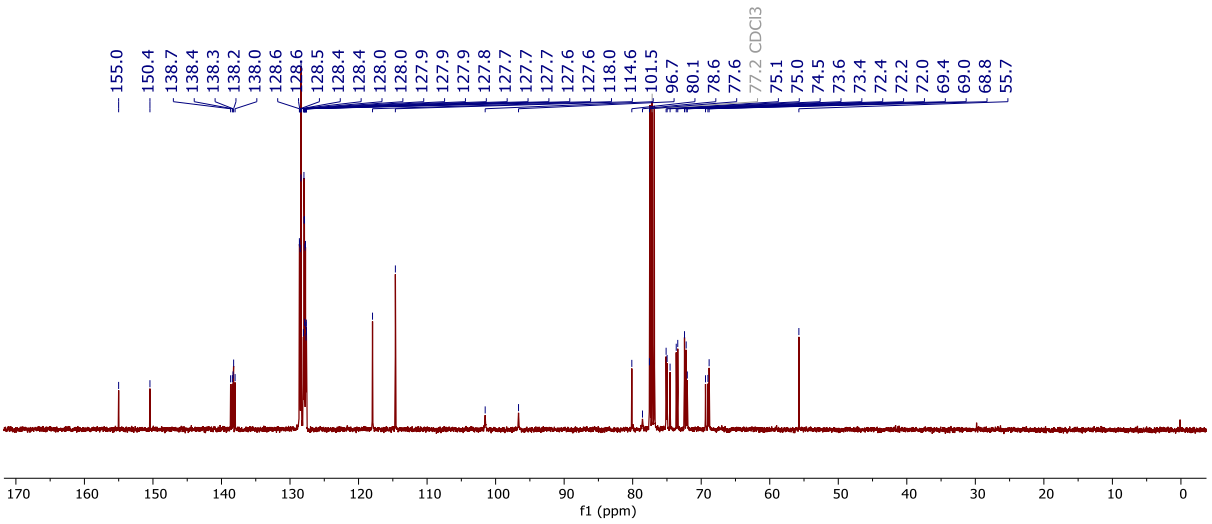

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **52**



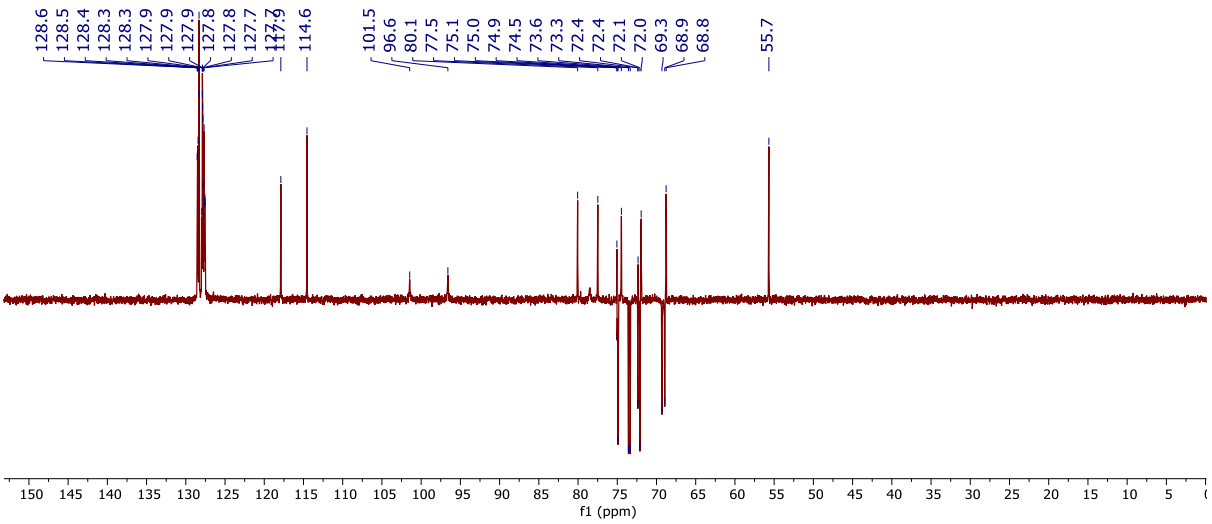
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **53**



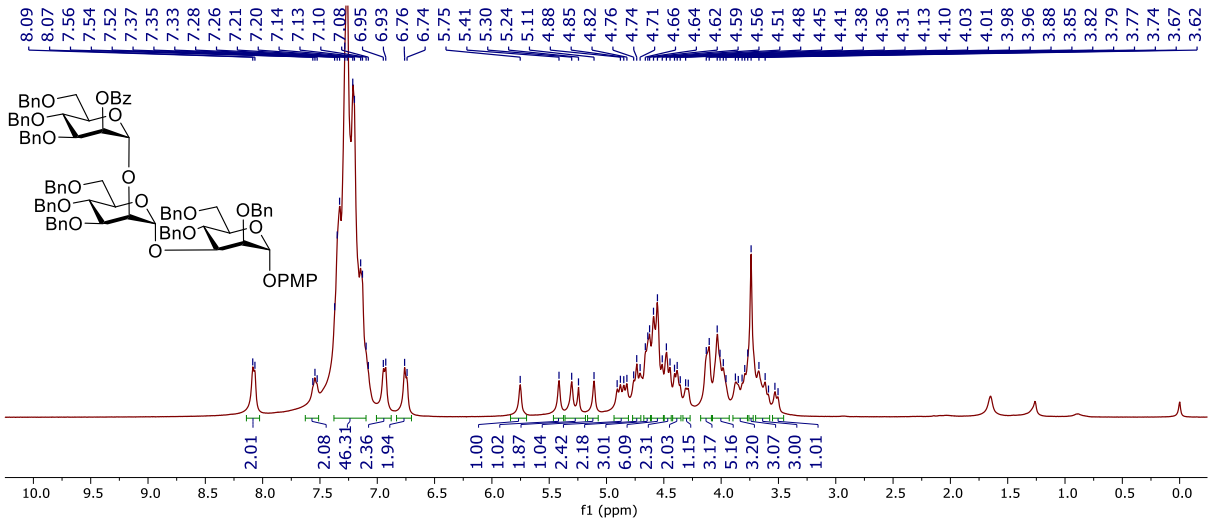

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **53**



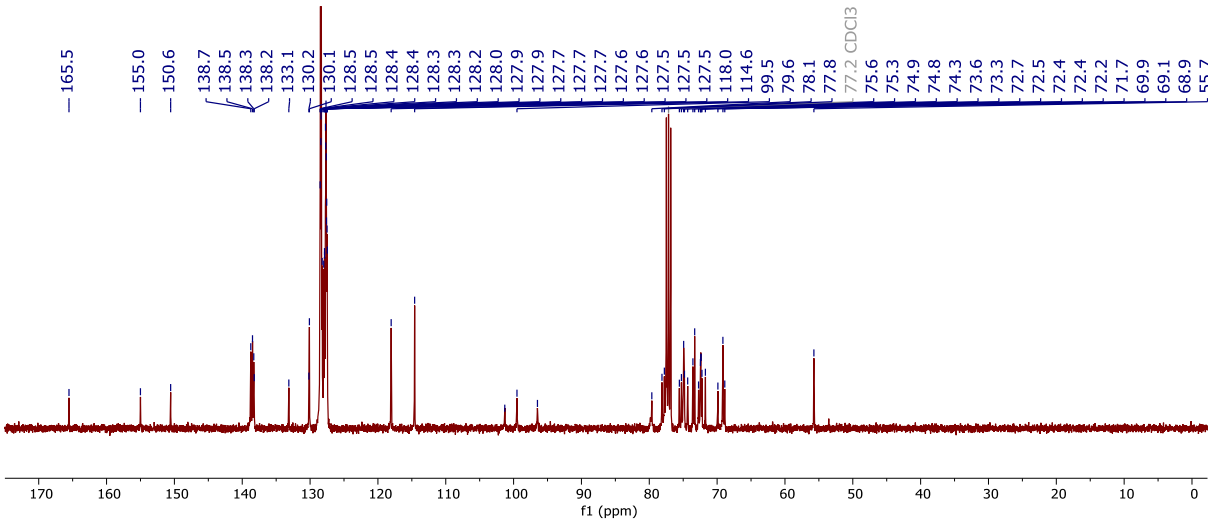

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **53**



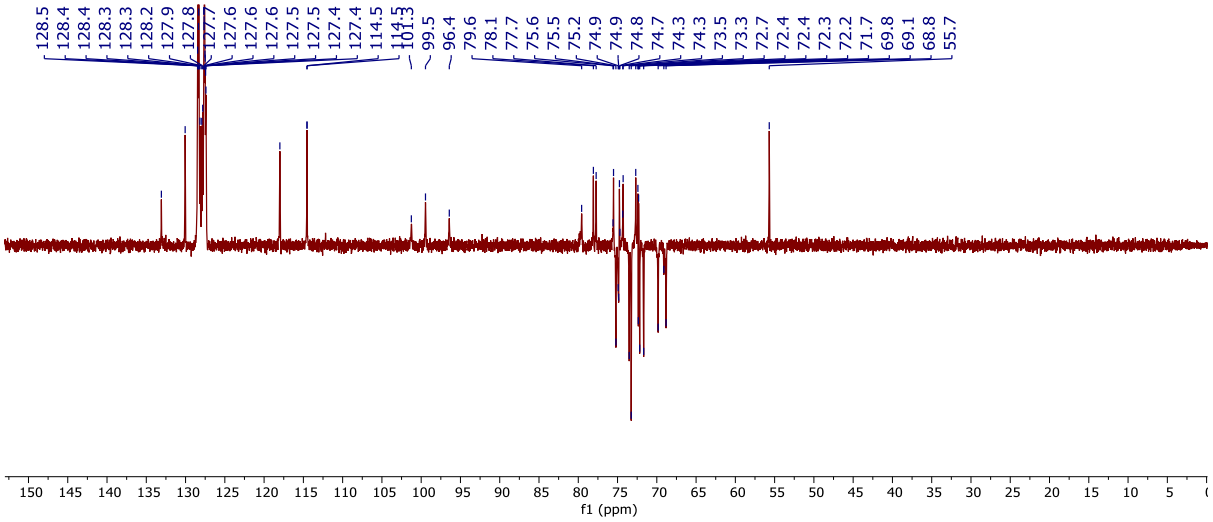
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **54**



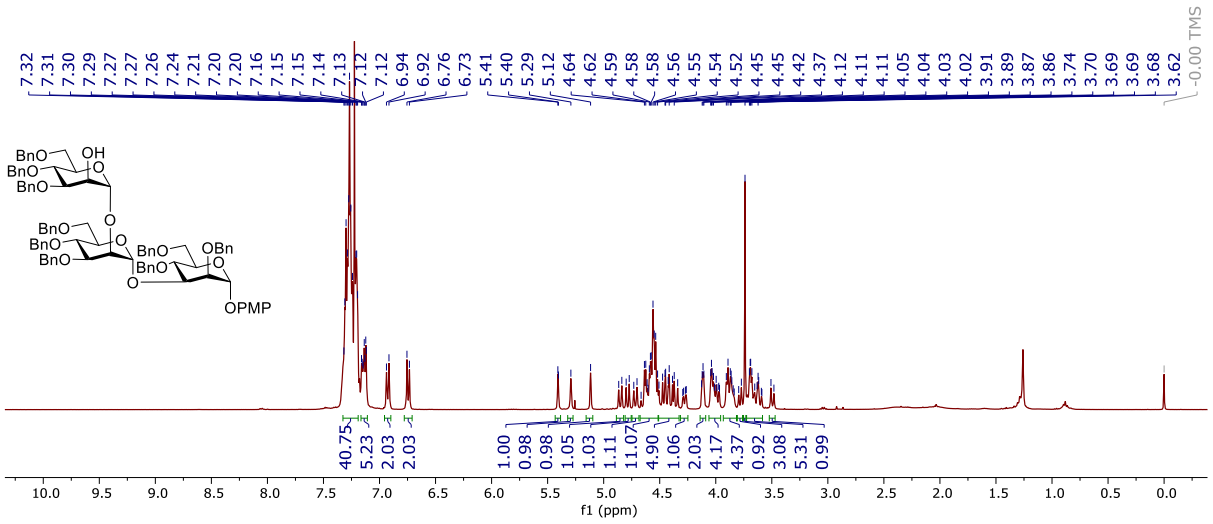

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **54**



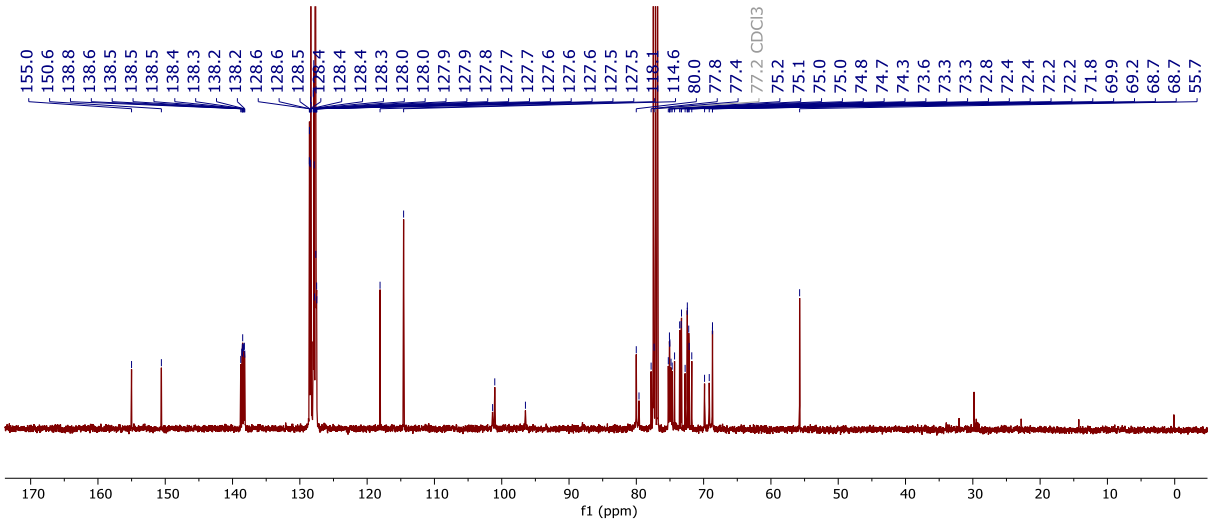

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **54**



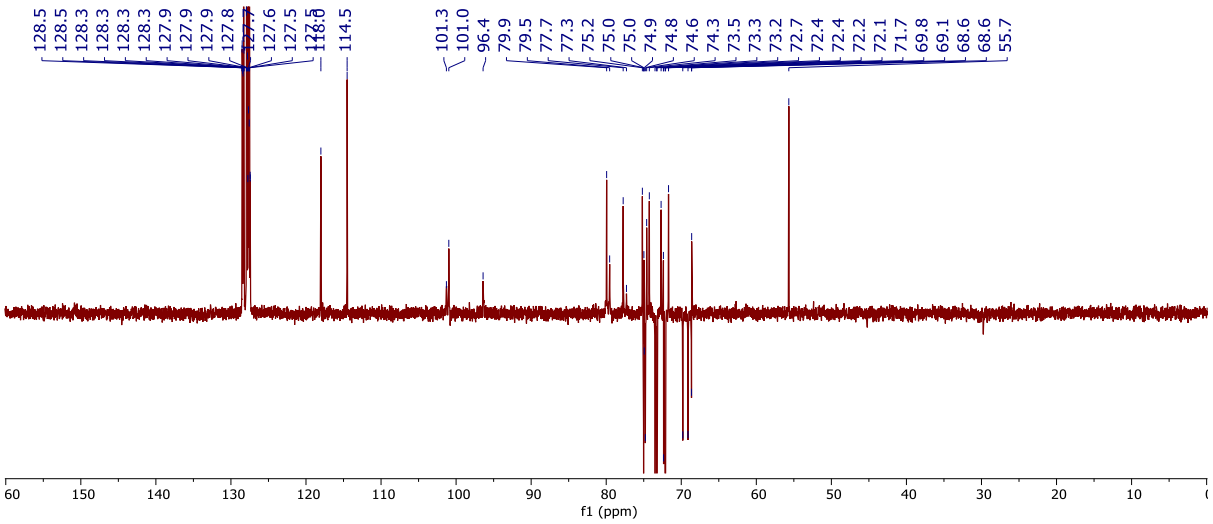
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **55**



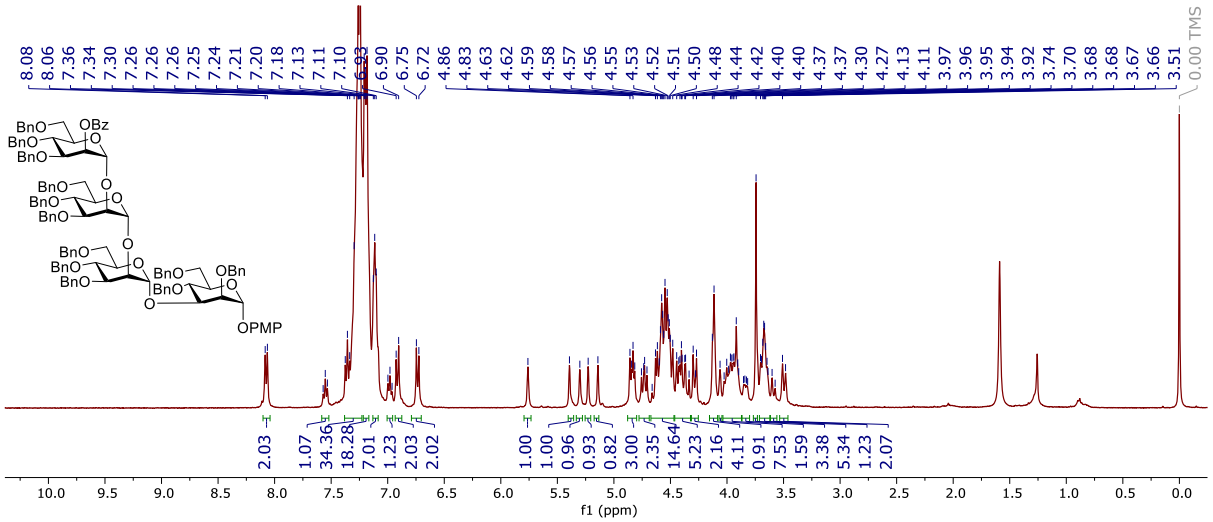

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **55**



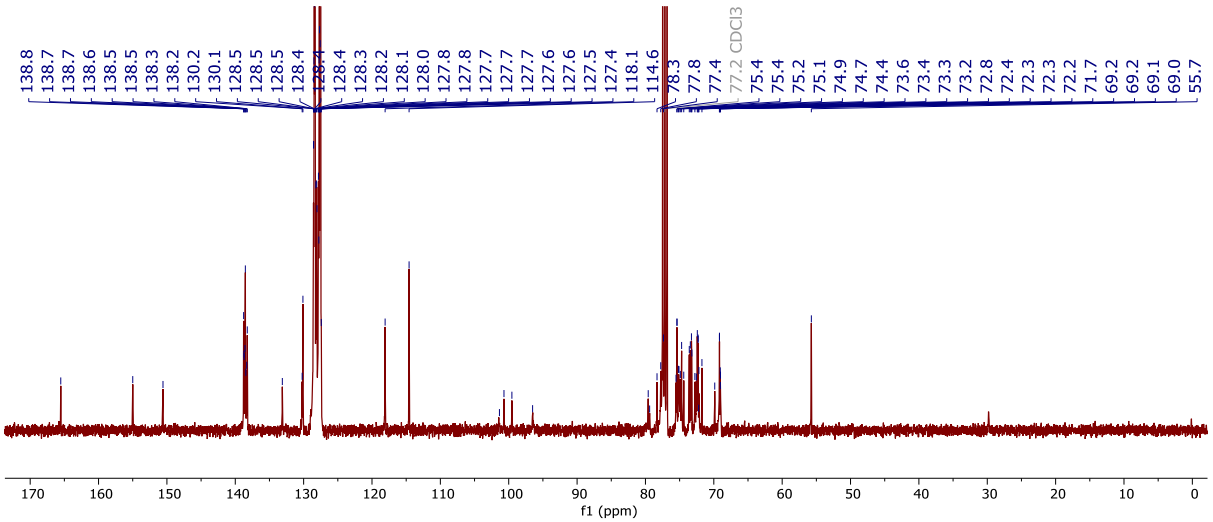

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **55**



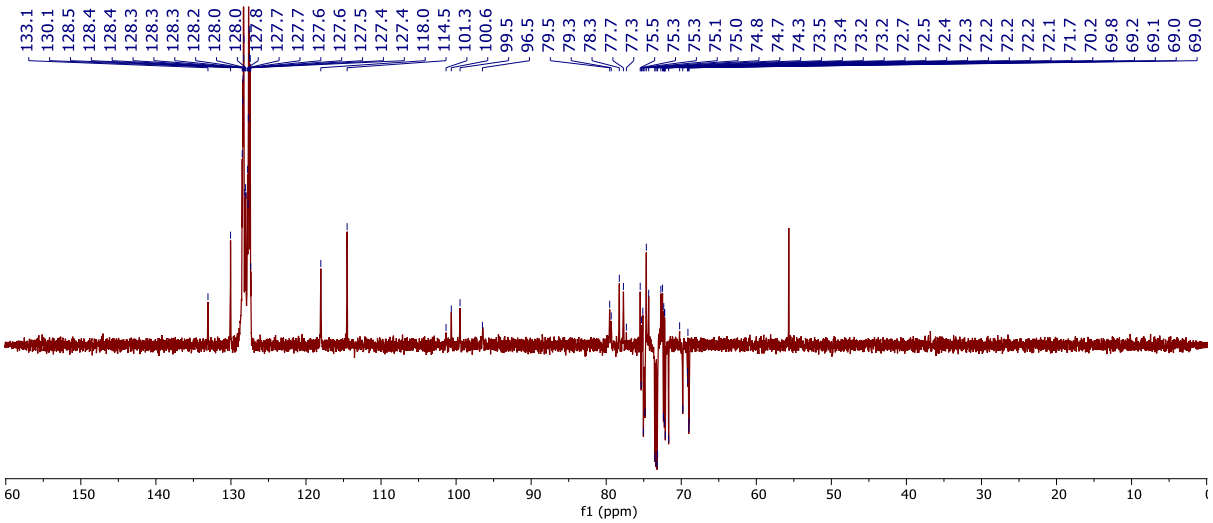
$^{1}$H NMR Spectrum (400 MHz, $CDCl_3$) of Compound **56**



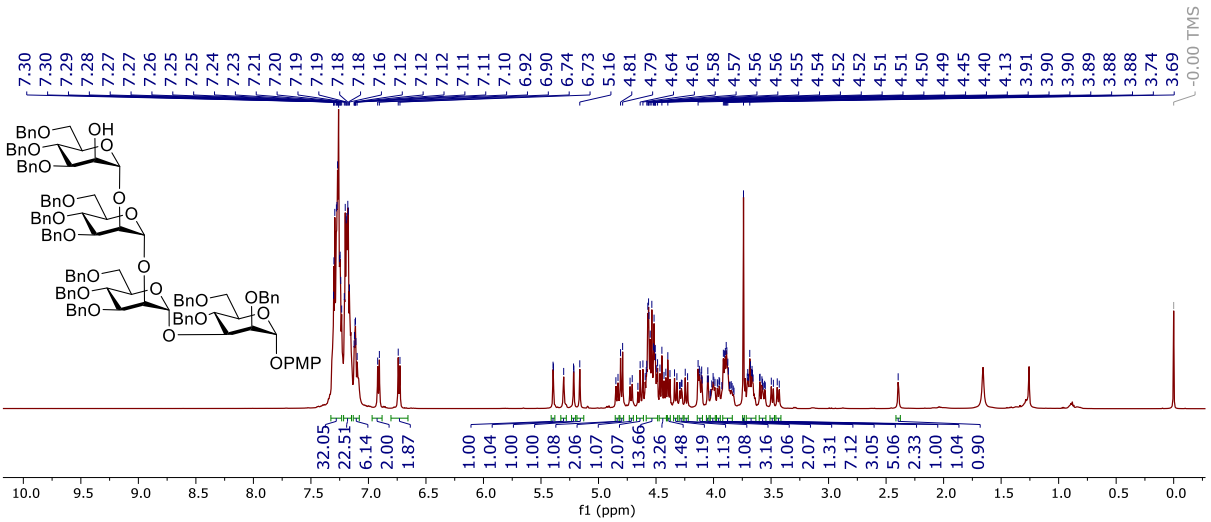

$^{13}$C NMR Spectrum (101 MHz, $CDCl_3$) of Compound **56**



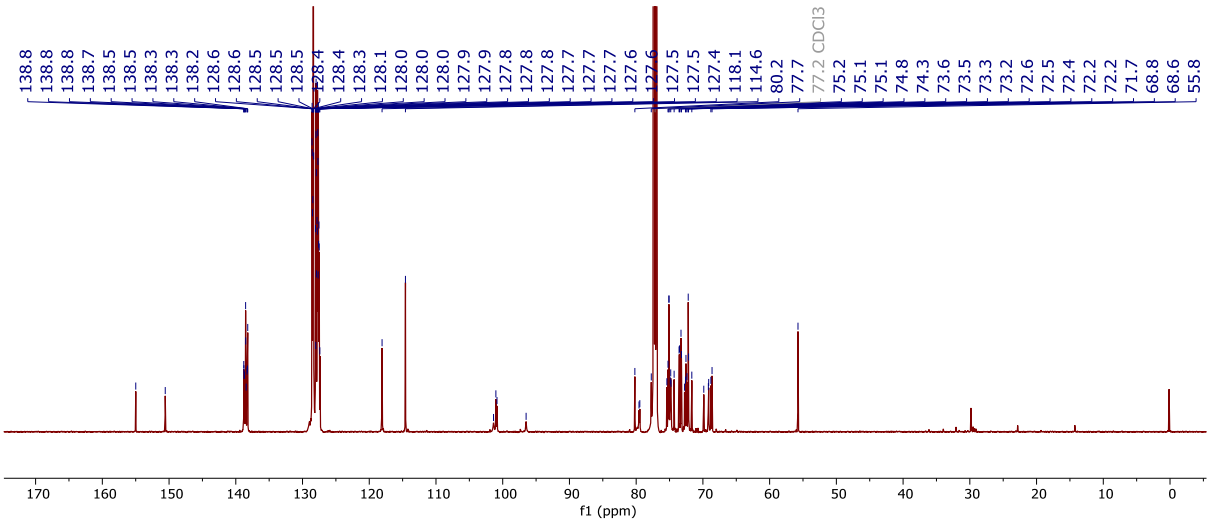

$^{13}$C DEPT-135 Spectrum (101 MHz, $CDCl_3$) of Compound **56**



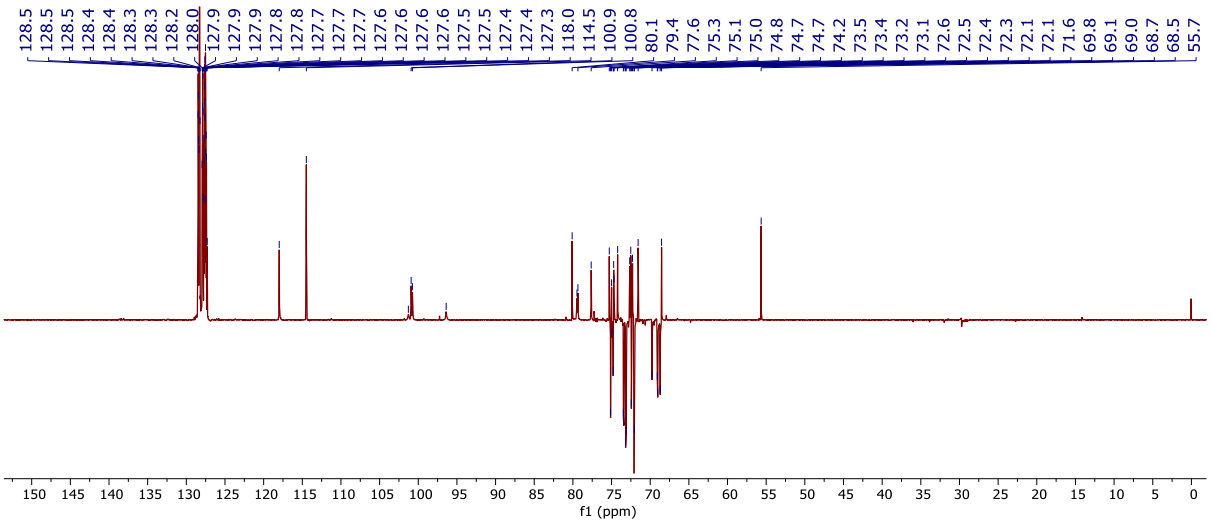
$^{1}$H NMR Spectrum (600 MHz, $CDCl_3$) of Compound **57**



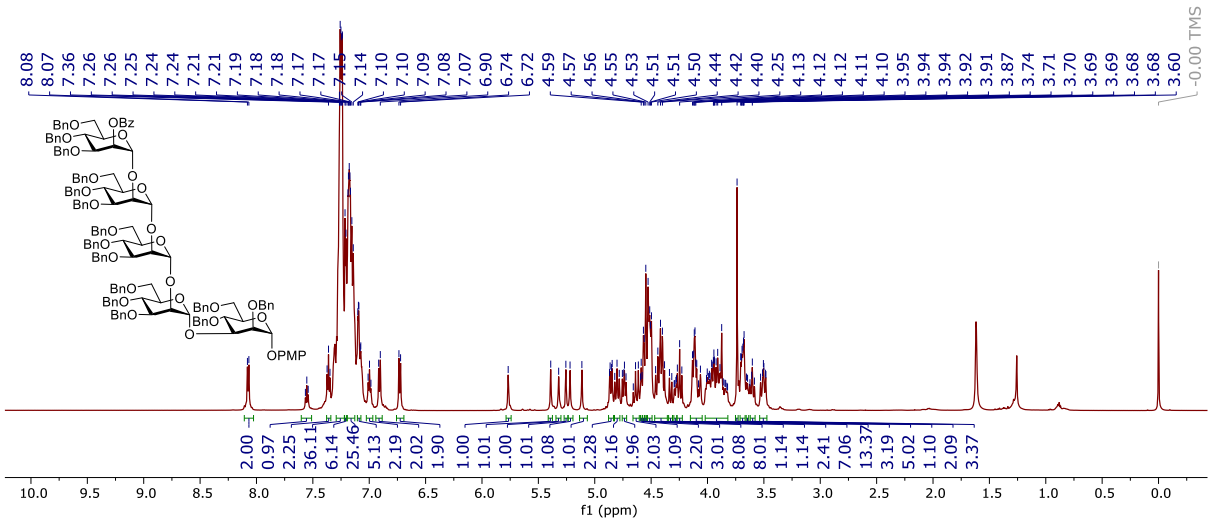

$^{13}$C NMR Spectrum (151 MHz, $CDCl_3$) of Compound **57**



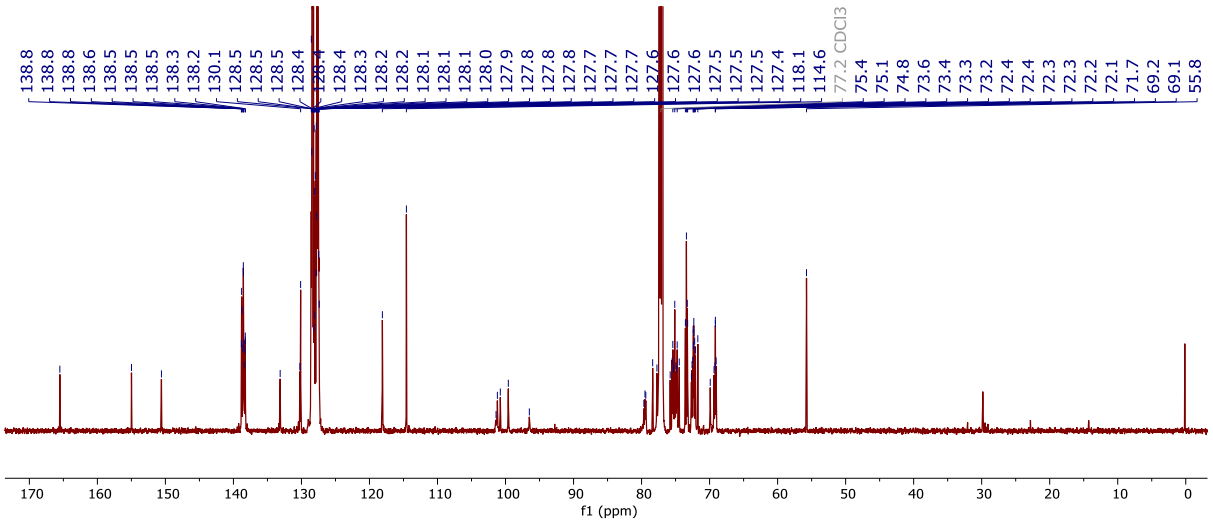

$^{13}$C DEPT-135 Spectrum (151 MHz, $CDCl_3$) of Compound **57**



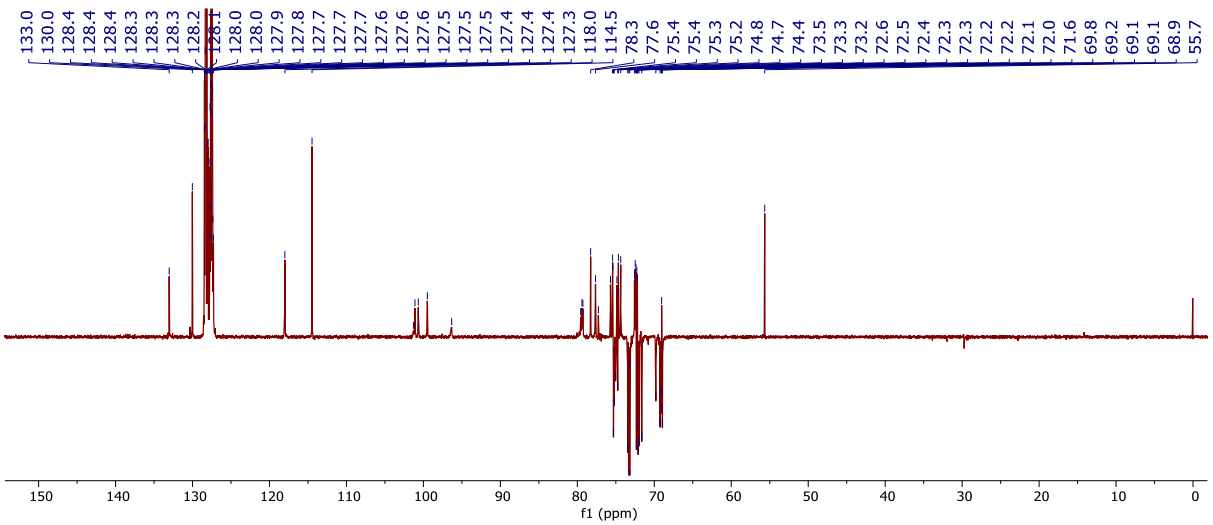
$^{1}$H NMR Spectrum (600 MHz, $CDCl_3$) of Compound **58**




$^{13}$C NMR Spectrum (151 MHz, $CDCl_3$) of Compound **58**




$^{13}$C DEPT-135 Spectrum (151 MHz, $CDCl_3$) of Compound **58**



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1. **Kameshwar Prasad**, Ananay Sharma, Soumyaranjan Pati, Marc Taillefer, Florian Jaroschik, Srinivas Hotha * Metal-free activation of alkynyl glycosyl carbonate donors (Advance synthesis & catalysis. doi.org/10.1002/adsc.202300251)

2. **Kameshwar Prasad**, Srinivas Hotha* Synthesis of MTX-capped Octasaccharide of LAM in *Mtb* (Manuscript under preparation)

3. Niteshlal Kashdekar, Gulab Walke, **Kameshwar Prasad**, Srinivas Hotha* Gold catalysed glycosylation of alkyne acetate donors (Manuscript under preparation)

4. Soumyaranjan Pati, **Kameshwar Prasasd**, Srinivas Hotha, Marc Taillefer, Florian Jaroschik, * Lewis acid activation of pyridyl ethynyl cyclohexyl carbonate donors (work is under progress)

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# Metal Free Activation of Alkynyl Glycosyl Carbonate Donors

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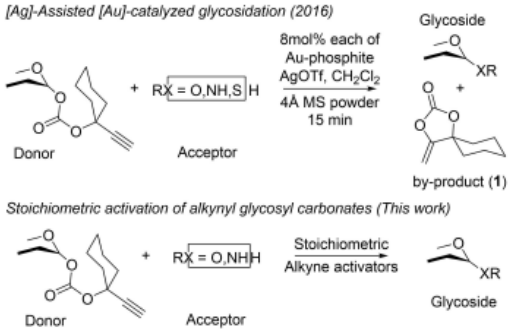
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**Abstract:** Accessing homogenous glycoconjugates is of significance for assessing their biophysical activities and sometimes as vaccine candidate. Synthesis of glycoconjugates involves two species of which, glycosyl donor plays pivotal role in controlling the outcome of the glycosylation. Recently discovered alkynyl glycosyl carbonate donors possess self-stability, high reactivity, and fast reaction time (15–30 min) when activated with [Au]/[Ag]-catalysts. Herein, we report metal free conditions for the activation of the same alkynyl glycosyl carbonate donors using $I_2$/TMSOTf in stoichiometric quantities. Extrusion product was characterized to be the vinylidene iodide by single crystal X-ray analysis. The reaction conditions were illustrated to be suitable for synthesis of various glycosides, purine/pyrimidine nucleosides and a pentasaccharide repeating unit of *Klebsiella pneumoniae* (O-3-antigen).

**Keywords:** Glycosides; Glycosylation; Glycoconjugates; Nucleosides; Oligosaccharides

Most of the living organisms require glycoconjugates and/or carbohydrates for energy storage, cell-cell communication, embryogenesis, protein folding, fertilization, structural support.[1] Many pioneering studies culminated in the development of excellent strategies for the synthesis of glycosides, nucleosides and assembly of complex oligosaccharides.[2] Glycosylation is one of the key reactions that enables rapid synthesis of glycoconjugates. In spite of developing excellent glycosylation methods, the synthesis of all glycosides is still a major challenge.[3] Discovery of novel glycosylation methods can be augmented by the identification of new reactivity patterns and reaction conditions for already existing glycosylation protocols.[4]

Glycosylation by silver-assisted gold-catalyzed activation of alkynyl glycosyl carbonates has emerged as one of the versatile alternatives for the rapid, stereoselective and catalytic synthesis of *O*-glycosides,[5a] nucleosides,[5a] *N*-glycosides[5b] and oligosaccharides (Scheme 1).[5] Whereas alkynyl glycosyl carbonate donors can be synthesized easily, [Au]/[Ag]-catalysts are not routinely available in all organic chemistry laboratories though the glycosylation is quite efficient, high yielding and catalytic. In addition, access to gold and silver salts has become difficult during pandemic; therefore, an alternate mode of activation of carbonates was investigated. Herein, we present activation of alkynyl glycosyl carbonates donors by other routinely available alkynophilic reagents drawing inspiration from the exceptional affinity of iodonium reagents towards unsaturated compounds.[6]




**Scheme 1.** General representation of the synthesis of glycosides by the activation of alkynyl glycosyl donors. Au-phosphite: chloro [tris(2,4-di-tert-butylphenyl)phosphite] gold. MS: molecular sieves.



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