Identification of Novel Glycosyl Donor Chemistry and Syntheses of Oligosaccharides

A Thesis submitted

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Doctor of Philosophy

By

Mahesh Neralkar

ID: 20143298

Indian Institute of Science Education and Research, Pune

Thesis Supervisor

Prof. Srinivas Hotha, PhD
Department of Chemistry
Indian Institute of Science Education and Research, Pune

August 2019

DEDICATED TO....

Aai and Dada

भारतीय विज्ञान शिक्षा एवं अनुसंधान संस्थान पुणे
INDIAN INSTITUTE OF SCIENCE EDUCATION AND RESEARCH PUNE
डॉ. होमी भाभा मार्ग, पुणे 411008, महाराष्ट्र, भारत | Dr. Homi Bhabha Road, Pune 411008, Maharashtra, India
T +91 20 2590 8001 W www.iiserpune.ac.in
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Srinivas Hotha, PhD
Professor - Chemistry

CERTIFICATE

Certified that the work incorporated in the thesis entitled *"Identification of Novel Glycosyl Donor Chemistry and Syntheses of Oligosaccharides"* submitted by **Mr. Mahesh Renukadas Neralkar** 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, 2019
Place : Pune

Prof. Srinivas Hotha

DECLARATION

I declare that, this written submission represents my ideas in my own words and where ideas of others have been included; I have adequately cited and referenced the original sources. I also declare that I have adhered to all principles of academic honesty and integrity and have not misrepresented or fabricated or falsified any idea/data/fact/ source in my submission. I understand that violation of the above will be cause for disciplinary action by the Institute and can also evoke penal action from the sources which have thus not been properly cited or from whom proper permission has not been taken when needed.

RNeralkar

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Place : Pune

Mahesh Renukadas Neralkar

Institute ID: **20143298**

*First and foremost, I would like to express my sincere gratitude to my mentor and research supervisor **Prof. Srinivas Hotha.** Whatever I have achieved during my entire PhD expedition has been possible because of his limitless encouragement, outstanding guidance and kind supports. Without his encouragement and constant guidance, I could not have completed my doctoral degree. He is a constant source of inspiration for me. His guidance helped me in entire endeavour of my research. Working with him was really a great pleasure and fetched me lot of learning experience. I am really grateful to him for his effort and dedication to each project and freedom in the laboratory, priceless suggestion and guidance. I am really fortunate to have him as my PhD supervisor and it was a great pleasure to working with him.*

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MAHESH NERALKAR

- ^{1}H NMR spectra were recorded on AV 200, AV 400, DRX-500 MHz, JEOL ECX 400 or Bruker Avance 500 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 AV 50, AV 100, DRX-125 MHz, JEOL ECX 100 or Bruker Avance 125 MHz spectrometer.
- High resolution mass spectroscopy (HRMS) was performed on Waters Synapt G2 and Maldi-TOF.
- IR spectra were recorded on Perkin-Elmer 1310 and Perkin-Elmer 1600 FT-IR spectrometers with sodium chloride optics and are measured in cm^{-1}.
- Specific rotations were measured on a JASCO P-1020 or Rudolph polarimeter and measured in degree.
- All reactions were monitored by Thin-Layer Chromatography carried out on precoated Merck silica plates (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 dry freshly prepared solvents under anhydrous conditions and yields refer to chromatographically homogenous materials unless otherwise stated.
- All evaporators were carried out under reduced pressure on Büchi and Heildoph rotary evaporator below 45 °C unless otherwise specified.
- Silica gel (100-200) and (230-400) mesh were used for column chromatography.
- All gold and transition metal salts were purchased from multinational commercial vendors.
- Materials were obtained from commercial suppliers and were used without further purification.
- Scheme, Figure and Compound numbers in abstract and individual chapters are different.

Å – Angstrom
Ac – Acetate
AcBr – Acetyl bromide
AcCl – Acetyl chloride
AcOH – Acetic acid
Ac_2O – Acetic anhydride
AG – Arabinogalactan
Ara*f* – arabinofuranoside
Bn – Benzyl
BnBr – Benzyl bromide
Boc – *t*-butylcarbonyl
Bz – Benzoyl
BzCl – Benzoyl chloride
Calcd–Calculated
cat. – catalytic
$CDCl_3$ – Chloroform-D
$CHCl_3$ – Chloroform
d – days
DEPT –Distortionless Enhancement by Polarization Transfer
DIPEA – *N*,*N'*-Diisopropylethylamine
DMAP – *N*,*N'*-Dimethylaminopyridine
DMF – *N*,*N'*-Dimethyl formamide
D_2O – Deuterium oxide
δ –delta (in ppm)
eq. – equivalents
g – gram
Gal*f*–galactofuranoside
h – hour
HRMS – High-Resolution Mass Spectrometry
Hz – Hertz
Im. – Imidazole
IR – Infra Red
J – coupling constant
Kg – Kilogram
LAM – Lipoarabinomannan
Man*p*–mannopyranoside
mg – milligram
min. – minutes
MHz – Mega hertz
mL – milli Litre
mmol – milli molar
MS – Molecular sieves
Mtb – Mycobacterium tuberculosis
NGP – Neighbouring group participation
NIS –*N*-Iodosuccinimide
NMR –Nuclear Magnetic Resonance
NNGP – Non-neighbouring group participation
NPG – *n*-Pentenyl glycoside
PMB – *p*-Methoxy benzyl
Py – Pyridine
PTSA– *p*-Toluene sulfonic acid
ppm – parts per million
Rib*f* – ribofuranoside
rt – room temperature
sat – saturated
Tb – tuberculosis
TBAF – tetra-*n*-Butyl ammonium fluoride
TBAI – tetra-*n*-Butyl ammonium iodide
TBDPS – t-Butyldiphenylsilyl
TCA – trichloroacetimidate
TfOH – Trifluoromethane sulfonic acid
THF – Tetrahydrofuran
TLC – Thin Layer Chromatography
µg – micro gram
µmol– micromolar
µL – microliter

The thesis entitled *Identification of Novel Glycosyl Donor Chemistry and Syntheses of Oligosaccharides* is divided into four chapters. Chapter one reveals the discussion of carbohydrates and glycosylation; various types of glycosylations, factors determining the stereochemical outcome of glycosylation, a detailed study about the historical development of glycosyl donors and future scope for the field of glycosylation were discussed. Chapter two depicts the development of nucleofuge generating glycosylation by the remote activation of hydroxybenzotriazolyl glycosyl donors, activation, and their application for the synthesis of *O*-, *C*-, and *N*-glycosides. Chapter three illustrates utility of newly developed regenerative glycosylation by the synthesis of the linear and branched highmannan core of the HIV_1-gp120 complex. Chapter four describes efforts towards the synthesis of the most complex and branched oligosaccharide Arabinogalactan (AG) present on the surface of *Mycobacterium tuberculosis* cell wall.

Chapter 1: Historical Development of Glycosyl Donors

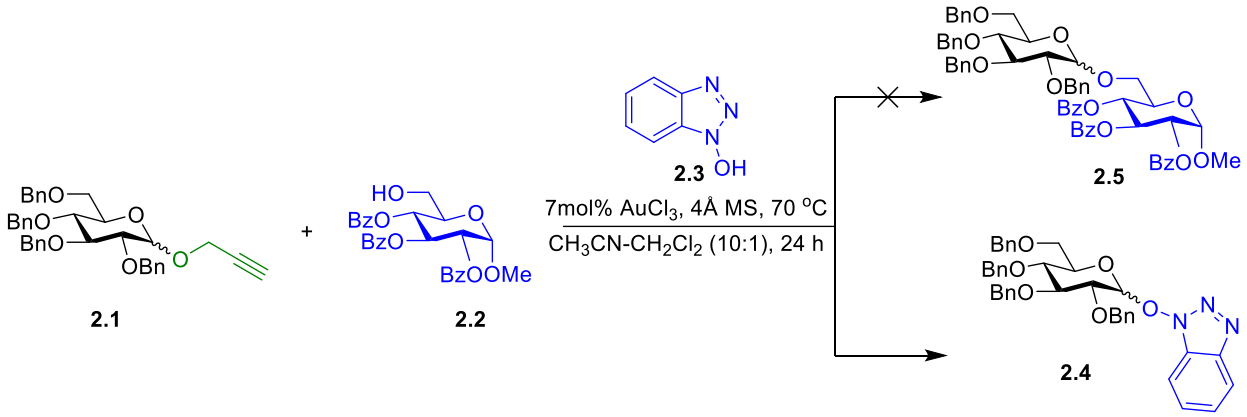
For a longtime, carbohydrates were simply viewed as powerhouses of energy to human body for driving biochemical processes. But with the development of analytical tools and biotechniques, saccharides are shown to play vital role in variety of biological processes such as cell-cell interactions, tissue engineering, drug delivery systems, viral and bacterial infection, hormone balance, metabolism, etc. Glycans are covalently linked to other biochemical substances such as proteins, lipids, nucleic acid, natural products, other sugar residues and distinct molecules having different biological activity. However, glycoconjugates occur in low concentrations and as micro-heterogeneous form which generally are difficult to isolate. Hence, chemical glycosylation methods for complex glycoconjugates with higher glycosylation yields are of great importance. In this context many synthetic methods have been developed in the literature and development of more techocommercially feasible novel glycosylation strategy is always exigent.

Chapter 2: Development of Nucleofuge Regenerative Hydroxybenzotriazolyl Glycosyl Donor Chemistry

Hotha and Kashyap identified propargyl glycosides **2.1** as stable glycosyl donors employing catalytic amount of $AuCl_3$ to afford anomeric mixture of glycosides. However, activation of propargyl glycosides occurred at 70 ºC, needed longer reaction time for activation, and also was suitable for glycosyl donors possessing ether functional group at *C*-2 position only. In addition

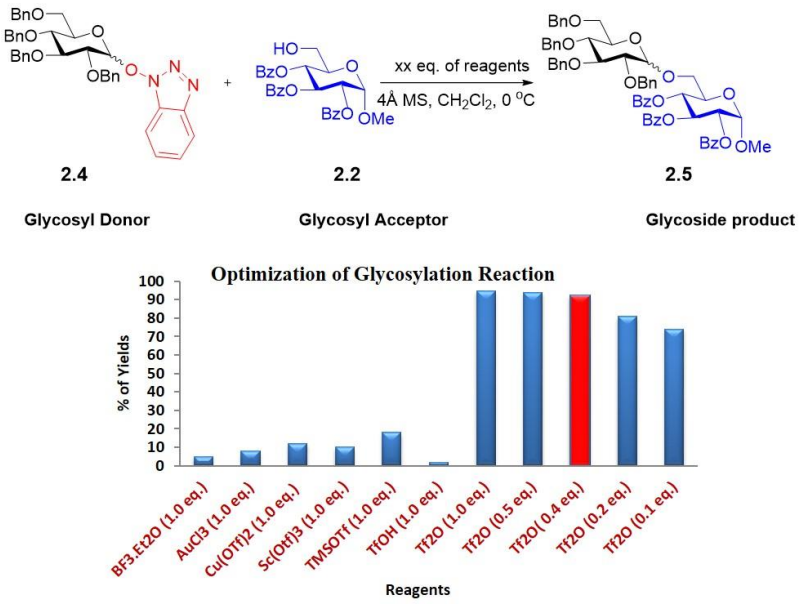
to this, cleavage of the inter-glycosidic bonds was noticed while synthesizing oligosaccharides in some cases. In this premise, bringing down the reaction temperature for the activation of propargyl glycosides with an eventual understanding that the glycosylation in the presence of disarmed substituents (i.e. C2-*O*-Bz) can also get facilitated due the increased turn over number (TON) of gold-catalyzed glycosidations is studied in this chapter.

Accordingly, inspiration was drawn upon from the peptide chemistry and hypothesized that addition hydroxybenzotriazole (HOBt) **2.3** in gold-catalyzed glycosylation will help to accelerate the overall reactivity of propargyl glycosides **2.2**. Propargyl glucosides **2.1** and glucosyl acceptor **2.2** were chosen as model substrates and treated with HOBt **2.3** and catalytic amount of $AuCl_3$ in the presence of 4Å MS powder at 70 ºC. To our dismay, HOBt glucoside **2.4** was observed as the sole product rather than expected disaccharide **2.5** (**Scheme 2.1**).



Scheme 2.1 Observation of HOBt Glucoside **4** Formation

Compound **2.4** was observed to be a solid with long shelf stability that warranted us to study its further utility for glycosylation. After screening various promoters, temperature and solvents, optimized glycosylation conditions were identified to be 0.4 equivalents of Tf_2O in CH_2Cl_2 at 0 ºC for 15 min that resulted in the much desired disaccharide in 95% yield (**Scheme 2.2**). The scope of glycosyl donor was further explored by the synthesis of a library of glycosides employed variety of glycosyl donors and acceptors under optimized reaction conditions.



Scheme 2.2 Optimization of Glycosylation Reaction

During the glycosylation, nuleofuge of the donor got regenerated as HOBt **2.1** at the end of the reaction. The regeneration of the nuleofuge was investigated by UPLC-MS studies (**Fig. 2.1**).

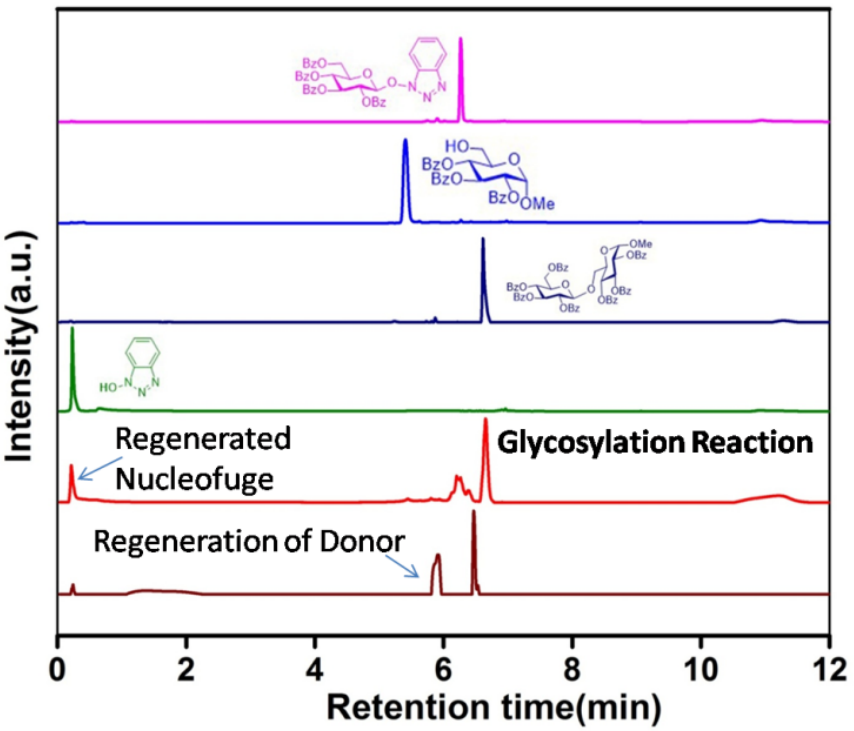
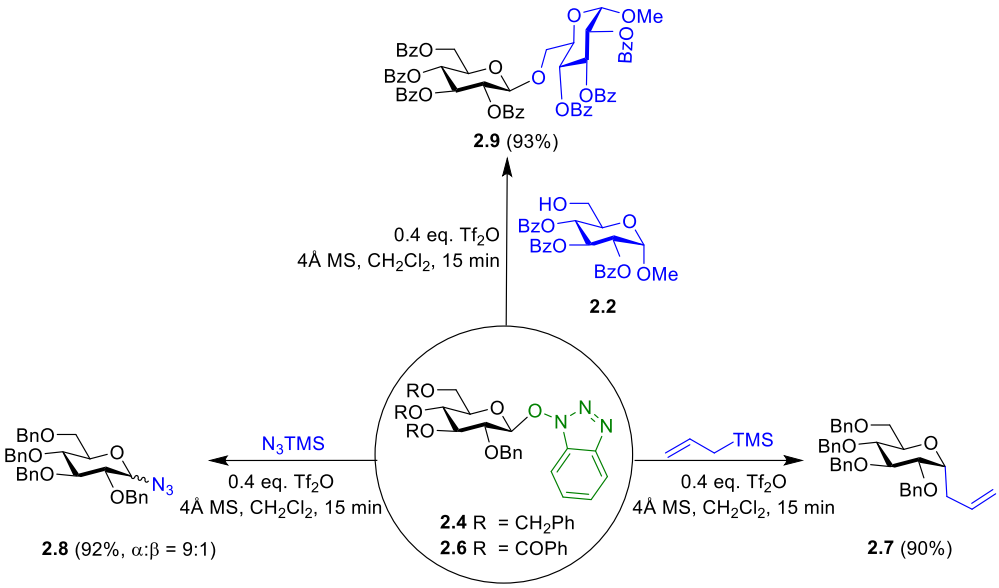


Fig. 2.1 UPLC traces of the chromatogram of the glycosidation reaction



Scheme 2.3 Extended Application of HOBt Glycosyl Donor

Furthermore, hydroxybenzotriazolyl glycosides (**2.4** and **2.6**) are explored for the synthesis of *C*-glucoside (**2.7**), azido (*N*-) glycosides (**2.8**) and Disaccharides **2.9** (**Scheme 2.3**).

Chapter 3: Utility of Hydroxybenzotriazolyl Glycosyl Donor to the Synthesis of Highmannan core of HIV$_{1\text{-gp120}}$ Complex

HIV expresses glycoproteins on their surfaces and the associated glycans are shown to play pivotal roles in the immune evasion. Trimeric gp120 of HIV$_1$ contains majority of 'high mannose' type glycans ($Man_{5\text{-}9}GlcNAc_2$ **3.1**) up to 62-79%, which is also known as 'high-mannose patch'. These glycan molecules play potential role in the life cycle of virus and have gained substantial attention as targets for the design of carbohydrate-based vaccine (**Fig 3.1**). The previous chapter illustrates the identification of HOBt glycosides as novel glycosyl donors; in this chapter, the utility of that glycosylation protocol was demonstrated by the successful synthesis of pentamannan (**3.2**) and trimannoside (**3.3**) structures present in the HIV$_{1\text{-gp120}}$ complex.

Synthesis of hydroxybenzotriazolyl donor is straight forward and can be prepared in one pot directly from commercially available parent sugar and is also cost effective. To probe utility of our HOBt-donor for oligosaccharide syntheses, synthesis of two glycan motifs from high mannose patch of HIV-gp120 were synthesized, first one is linear Man_3 by [1+1+1] strategy

(**Scheme 3.1**) and other is a highly branched pentamannan Man_5 oligosaccharide in [1+2+2] coupling strategy (**Scheme 3.2**).

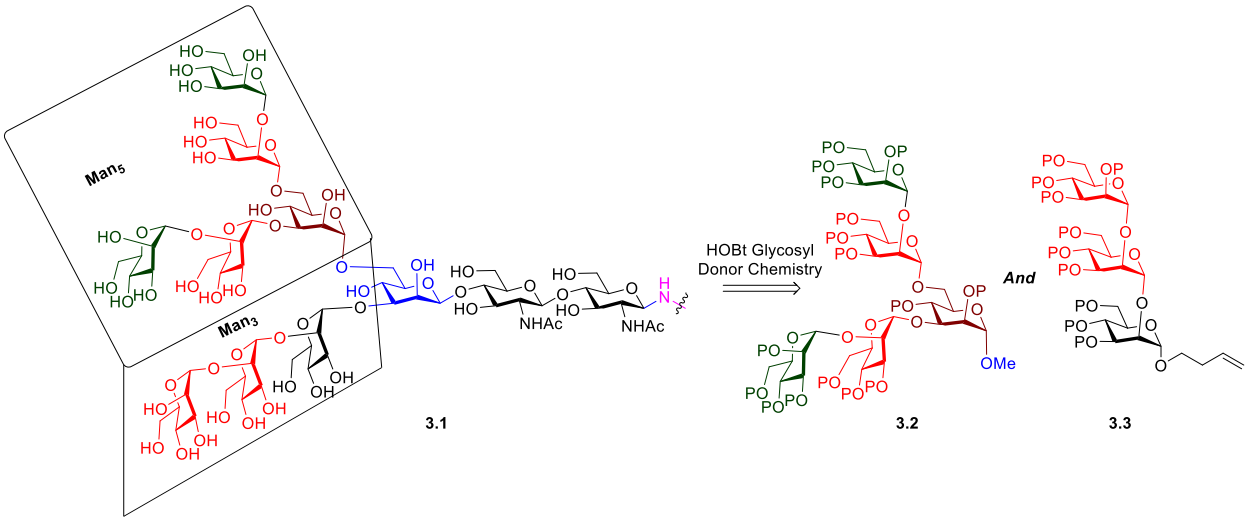
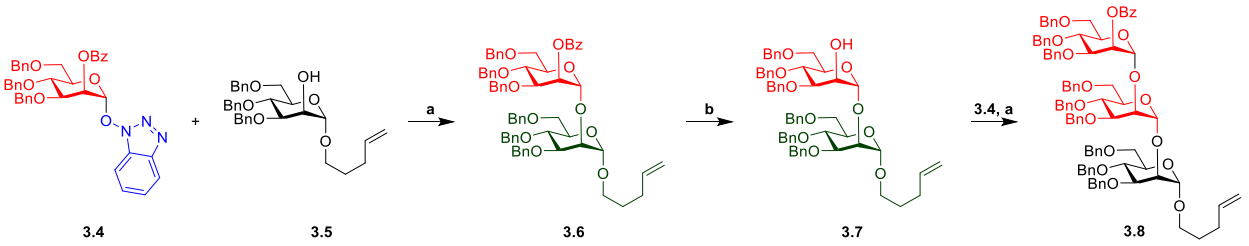
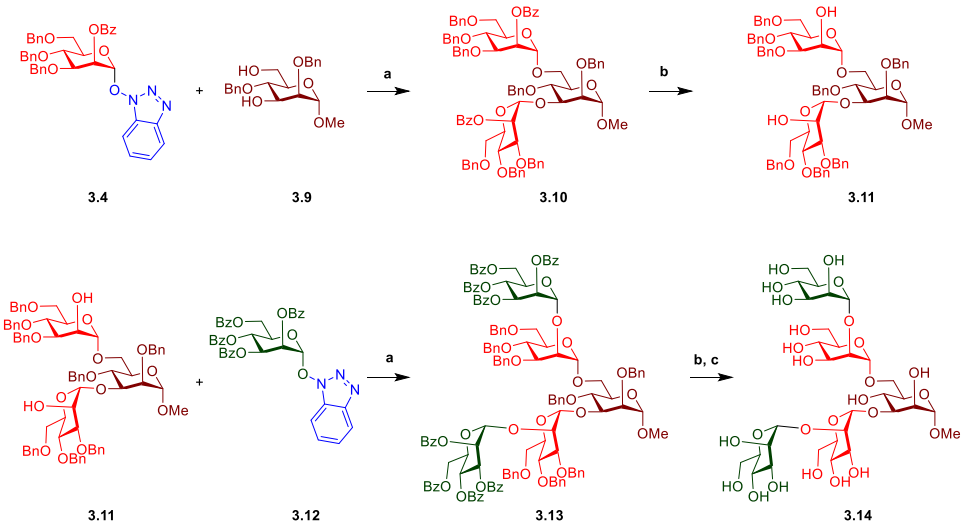


Fig 3.1 Structure of *N*-linked $Man_9GlcNAc_2$ present on the surface of HIVgp120



Scheme 3.1 Reagents a) 0.4 eq. Tf_2O, 4Å MS, CH_2Cl_2, 15 min, 92% for **3.6** 88% for **3.8**; b) NaOMe, MeOH and CH_2Cl_2, 25 ºC, 2 h, 95%.

Dimannoside **3.6** was synthesized by a coupling reaction between glycosyl donor **3.4** and glycosyl acceptor **3.5** under the standard 0.4 eq. of Tf_2O conditions. Disaccharide **3.6** was treated with NaOMe in CH_2Cl_2 and methanol to afford disaccharide acceptor **3.7** that was allowed to undergo glycosylation with another molar equivalent of glycosyl donor **3.4** under standard optimized conditions to afford the trimannoside **3.8** in excellent yield (**Scheme 3.1**). Encouraged by the successful synthesis of the linear trimannoside, a branched pentamannoside was chosen as the next target.

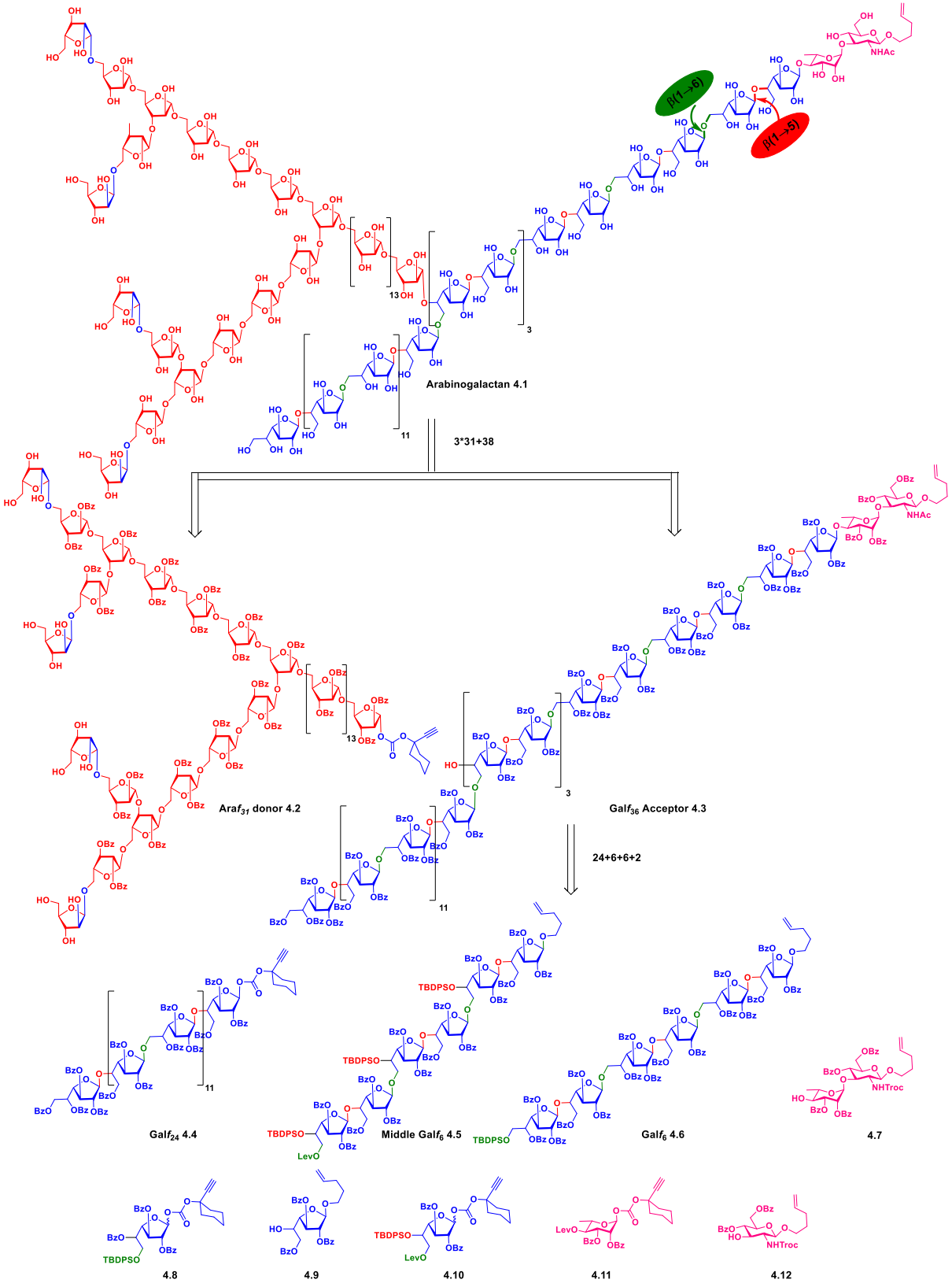


Scheme 3.2 Reagents a) 0.4 eq. Tf_2O, 4Å MS, CH_2Cl_2, 15 min, 81% for **3.10**, 77% for **3.13**; b) NaOMe, MeOH and CH_2Cl_2, 25 ºC, 2 h, 95% for **3.11**; c) H_2, Pd/C, EtOAc, 24 h, 84% (2 steps).

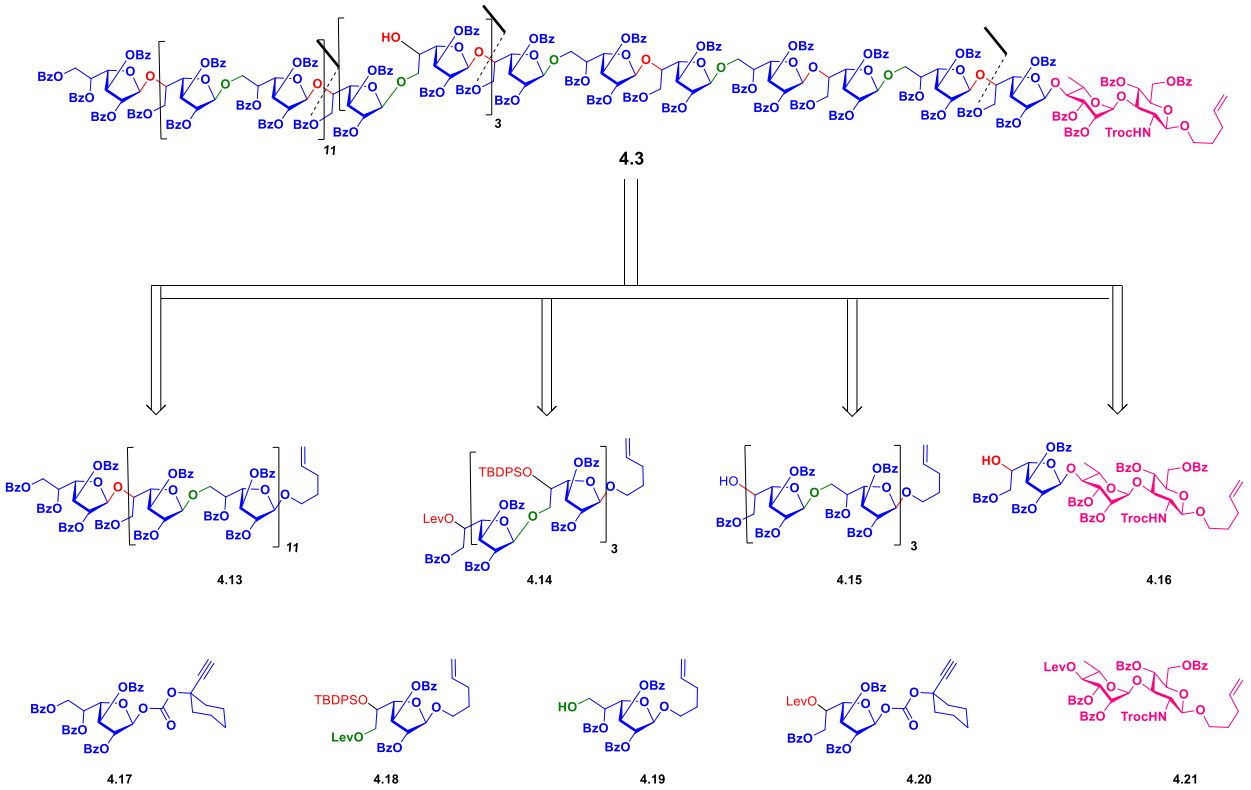
Using double glycosylation strategy, 2 equivalents of glycosyl donor **3.4** and 1 equivalent of glycosyl acceptor **3.9** under standard HOBt glycosylation conditions afforded the desired trisaccharide **3.10** in 82% yield. The trisaccharide **3.10** with two benzoyl groups reacted with NaOMe in 1:1 mixture of CH_2Cl_2 and MeOH as solvent afforded disaccharide diol **3.11** in good yield. In continuation, the trisaccharide diol **3.11** was allowed to undergo double glycosylation again with glycosyl donor **3.12** in the presence of 0.4 equivalents of Tf_2O as a promoter to afford desired target high pentamannan **3.13** in excellent yield. Astonishingly, formation of the product **3.13** only was observed without any partial glycosylated product such as tetrasaccharide. On global deprotection Man_5 **3.14** was isolated. The above two endeavours show the utility of newly developed hydroxybenzotriazolyl glycosyl donors.

Chapter 4: Studies Towards the Synthesis of Galactan Subunit of Arabinogalactan

Tuberculosis (TB) has existed for millennia and remains a major global health problem. *Mycobacterium tuberculosis* is the principal pathological bacterial species which is responsible for Tuberculosis disease in Humans. Cell wall of *Mycobacterium tuberculosis* contains Arabinogalactan (AG) **4.1** as major structural components. Access to various natural and their structural mimics are highly demanding due to their immense significance in overall and for the development of candidate vaccine or new drugs for disease treatment.



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



Scheme 4.2 New Retrosynthetic Analysis of Linear Chain Octatriacontanoside (38 mer) **4.3**

In this context, an attempt for full length synthesis of arabinogalactan (AG) **4.1** was made. Major challenges for the synthesis of Arabinogalactan **4.1** are: 1) The linear galactan chain consisting of 36 galactofuranose (Gal*f*) residues which are connected *via* alternating β(1→5) and β(1→6) linkages in linear fashion; 2) The linear galactan moiety connected to the disaccharide linker α-L-Rha*p*-(1→3)-α-D-GlcNAc; 3) The highly branched arabinan chains attached at the *C*-5 of β(1→6)Gal*f* residues selectively at 8th, 10th and 12th positions of the galactan chain. The synthetic endeavour started with the disconnection of giant arabinogalactan **4.1** into two sizeable fragments Araf_{31} donor (**4.2**) and the linear Galf_{38} acceptor (**4.3**). In this chapter, efforts towards the synthesis of linear Galf_{38} acceptor (**4.3**) are detailed (**Scheme 4.1**).

At first, required motifs middle hexasaccharide **Gal*f*$_6$** (**4.5**) with orthogonal protecting groups, common hexasaccharide Galf_6 (**4.6**) and disaccharide linker (**4.7**) was successfully synthesized. However, intramolecular migration of benzoyl group from O5→O6 position during the hydrolysis of C-6-O-silyl ether forced to revise the synthetic plan (**Scheme 4.2**)

Accordingly, problem of migration was circumvented by switching to the levulinoate at the reducing end of galactofuranose unit instead of silyl ether. The synthesis of the new hexasaccharide with alternating β(1→6) and β(1→5) linkages was accomplished with effective conquest over intramolecular migration of benzoyl group from O5→O6. The final glycosylation to synthesize the Galf_{36}+Rha*p*+GlcNHAc*p* is currently in progress and the resulting 38-mer will be coupled with the arabinan in due course of time.

******

Chapter 1

Historical Development of Glycosyl Donors

Chapter I

1.1 Discussion on Carbohydrates/Sugars

Sugars have been known to humankind since prehistoric times from Stone Age. In India, the use of honey is reported as far back as records go and the cultivation of sugarcane seem to have spread from north-eastern India to China and westward to Egypt and beyond by about *AD* 300.[1a]

Green plants utilize solar energy to convert atmospheric carbon dioxide into glucose and oxygen through complex sequence of reactions during the photosynthesis. Carbohydrates are considered to be exclusively of the use for energy until recently.[1b]

1.2 Etymological Roots

The origin of term 'sugar' came from the Sanskrit word '*Sharkara'*, which means sugar cane and its products. Synonym 'Carbohydrates' is due to the presence of Carbon (Latin *'carbo'*= coal) and water (Greek '*hydro*') in stoichiometric proportion with empirical formula $C_n(H_2O)_m$. Greek variant '*Sacchron*' and Latin form *'saccharum'* have led us to designate the class of compounds also as *'saccharides'*. The word 'Glycosides' goes back to the Greek term *'glykys'* means *'sweet'*.[2]

1.3 Historical Roots

In the 18th century, individual sugars were often named after their sources, for example, grape sugar for glucose and cane sugar for sucrose. In addition, a number of other monosaccharides were isolated by acid hydrolysis of respective polysaccharide sources and were given names ending with "–ose" such as mannose, galactose, xylose, arabinose, fucose and other disaccharides such as maltose and lactose.

In the middle of the 19th century, sugar refineries using sugarcane became commonplace in the developing world and sugar beet had been established as an economical source corp. Some major sugar manufacturing countries became interested in rationalizing international trade of sugars. Prices were to be determined by the application of the measured optical activities of sample by using polarimeter which was available to organic chemists. During the developmental phases of sugar industry, chemistry was in its infancy so understanding of comprehensive organic chemistry of sugars was difficult. However, the only available key physical technique – polarimetry- played a crucial role in the elucidation of the structure of sugars without which

progress in the development and understanding of their organic chemistry would not have been possible.[3]

Emil Fischer's contribution to the organic chemistry of carbohydrates such as studies of synthesis of simple carbohydrates and proof for the structures of monosaccharides became the classical part of the history of organic chemistry.[4]By the 1950s**,** massive improvement had been made with the development of the basic chemistry of sugars and the same principles had been applied to the study of oligosaccharides syntheses as well. The newly introduced chromatographic and NMR techniques made it possible to analyse detailed reaction progress of complex oligosaccharides along with detailed structural and stereochemical analysis.[5]

By the end of the 20th century**,** sugar chemistry had become much more diverse and several discoveries proved that carbohydrate play vita roles in the control of key biological process gave further impetus to the field of organic chemistry of sugars which is popularly called as carbohydrate chemistry or chemistry of saccharides. Dwek coined the term *Glycobiology* which became a bridge between the carbohydrate chemistry and biochemistry for understanding of the diverse cellular and molecular biology of *glycocalyx.*[6a]

1.4 Biological Significance of Carbohydrates

Before the birth of *Glycobiology*, carbohydrates were simply viewed as a powerhouse that only supplies energy to living beings to drive biomechanical processes. However advanced biological studies showed pivotal role played by carbohydrates in various biological processes such as cell-cell interactions, tissue engineering, bacterial infection, inflammation, immunological response, drug delivery systems, *etc*. Medicinal use of carbohydrates is also thoroughly studied. Commercially available Streptomycin is an antibiotic whereas Fondaparinux having trade name as Arixtra® and Heparin are anti-coagulant drugs.[6b-c]Many carbohydrate-based vaccines are currently under investigation for several diseases such as HIV, Cancer, and Tuberculosis etc.[6d] (**Fig. 1.1**)

However, saccharides are present in very low concentrations and as micro-heterogeneous forms which generate difficulty in isolation and characterization of pure and structurally well-defined glycoconjugates. Hence, chemical synthetic methods are most preferred for synthesis of pure and

structurally well-defined glycoconjugates for the exploration of their roles in various biological processes.

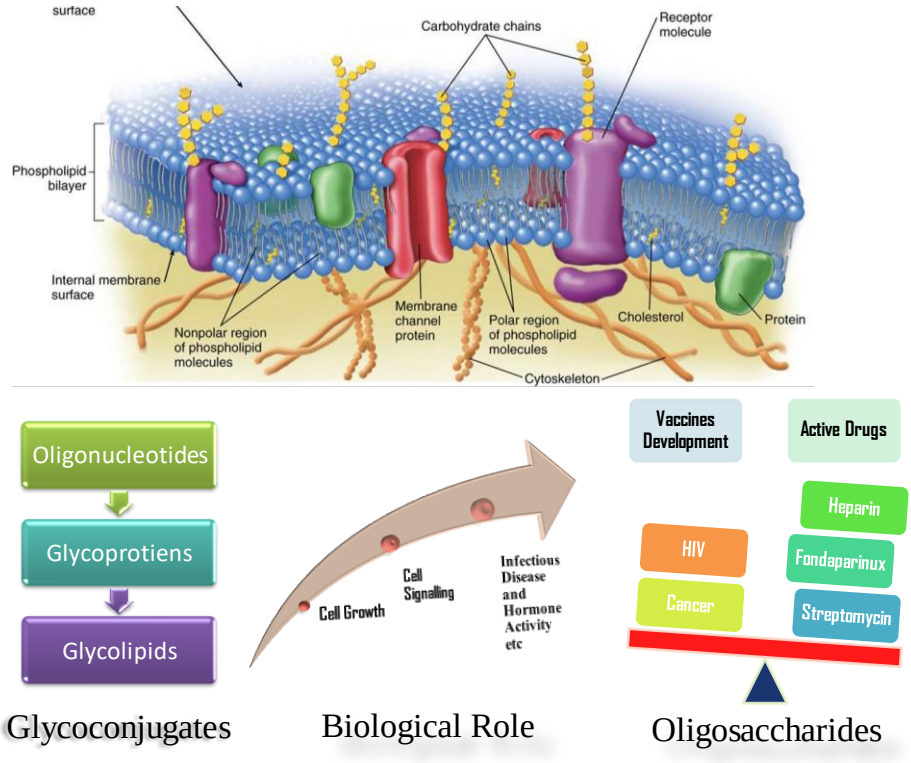


Fig 1.1 Biological Significance of Carbohydrates

1.5 Chemical Glycosylation[7]

Majority of glycans found in the Nature do not occur in free form but the monosaccharides are linked to each other or other type of compounds (aglycon) by glycosidic linkages. Depending upon glycosyl acceptor, the glycosyl linkages may be classified as *O*- linked Glycans, *N*- linked Glycans, and/or *S*- linked Glycans; among these, *O*- linked glycosides are the most abundant compounds in Nature. Chemical glycosylation reaction plays a central role in glycochemistry as it serves as a major tool for synthesizing homogenous materials for the study of their biological roles and applications.

Chemical glycosylation involves displacement of a leaving group from the anomeric centre of a sugar residue by a nucleophile to form glycosidic linkage. This reaction involves two reacting partners; one donates glycan moiety termed as glycosyl donor and the other one accepts the

donated glycan moiety which is termed as glycosyl acceptor. Glycosyl acceptor may or may not be a glycan. (**Fig. 1.2**)

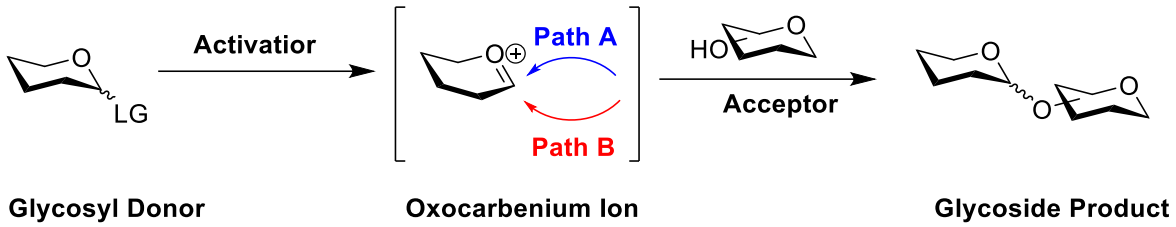


Fig 1.2 Chemical Glycosylation

1.6 Types of Glycosidic Linkages[7]

Further, in relation to the substituent at neighboring *C*-2 carbon, the glycosidic linkage can either be 1,2-*trans* or 1,2-*cis* at the anomeric or C-1 position (**Fig. 1.3**)

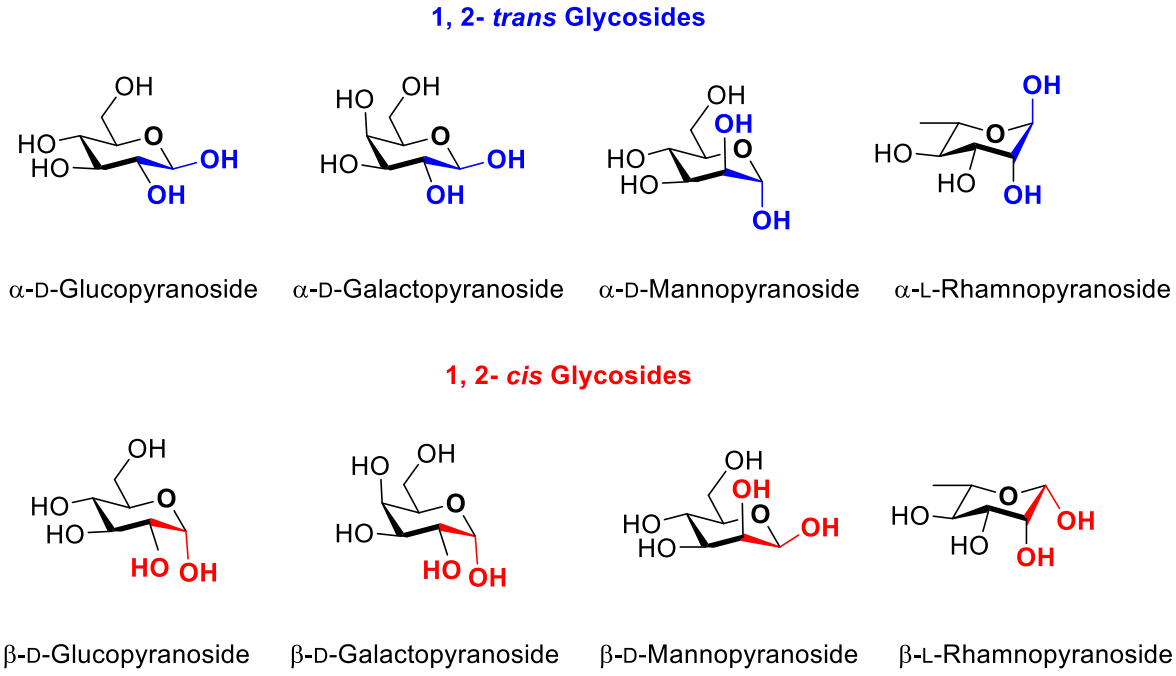


Fig 1.3 Different Types of Glycosidic Linkages

1.7 Nomenclature[8]

The IUPAC system of chemical nomenclature is based upon Cahn-Ingold-Prelog (R/S) assignments to stereogenic centers. Whereas in traditional name system, the *relative* configuration of the stereogenic centers of monosaccharides are embodied by prefixes such as

gluco-, galacto-, manno- and rhamno. The *absolute* configuration of monosaccharides is then designated using D/L- system of nomenclature. Configurational assignments of D or L enantiomers can be made on the basis of stereogenic center (R or S) farthest from the acetal or ketal moiety. (**Fig. 1.4 a**)

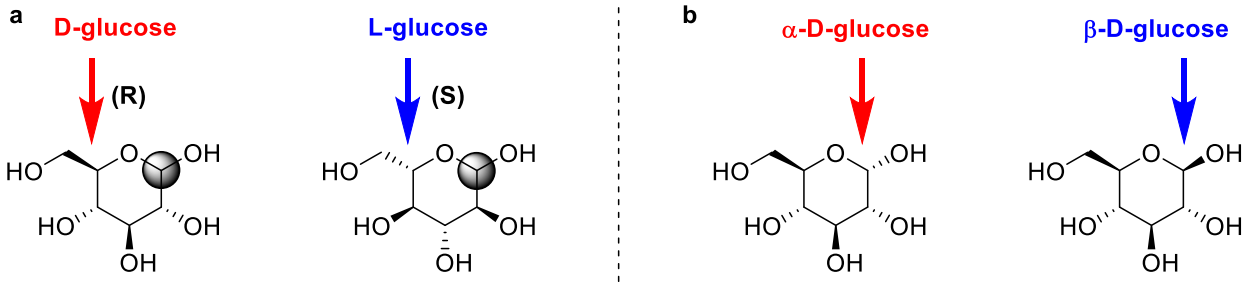


Fig. 1.4 a) Nomenclature of Carbohydrates; **b)** Anomeric Centre

1.8 Anomeric centre: The focal point for chemical reactivity[9]

In all naturally occurring glyconjugates, the acetal or ketal carbon is a stereogenic centre which is referred to as anomeric centre (**Fig. 1.4 b**). It can exist in two different configurations, referred as anomers. The two anomers are labelled as α– and β– anomers. Anomeric α–and β– configurations are designated on the basis of the relative orientation of the anomeric hydroxyl group and the substituent on the stereocenter farthest from anomeric centre.

1.9 Polar and Stereo-electronic Effects on the Anomeric Center[10]

In monosubtituted cyclohexane ring, substituents favour equatorial conformation. For example, in methoxy cyclohexane, alkoxy group shows modest preference for the equatorial position over the axial position by only about 0.6 kcal mol^{-1}due to unfavourable trans diaxial strain. In contrast to this, in methoxy perhydropyran, the axial anomer is more stable over equatorial anomer by 1.0 kcal mol^{-1}. This phenomenon is explained by two effects: 1) a lower dipole moment i.e. polar Effects and 2) more favourable donation of filled orbitals into unfilled orbitals i.e. stereoelectronic effect. It is found that in axial anomer the dipoles are almost in opposite direction which leads to a lower dipole moment. As far as stereoelectronic effect is concerned, axial anomers are better aligned for donation into the non-bonding orbital of the anomeric substituent. (**Fig 1.5**)

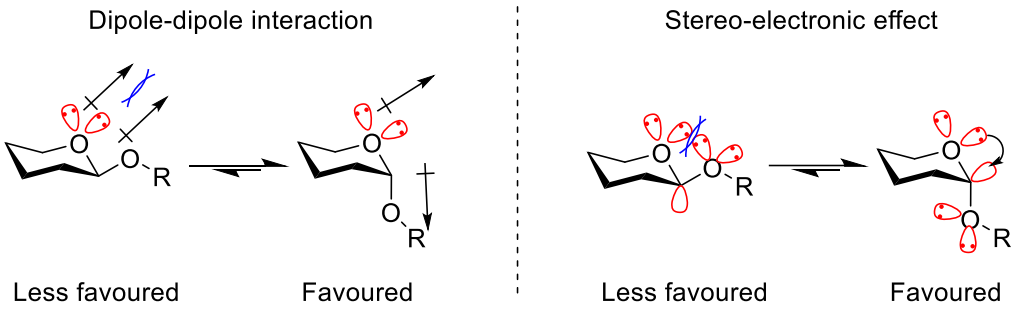


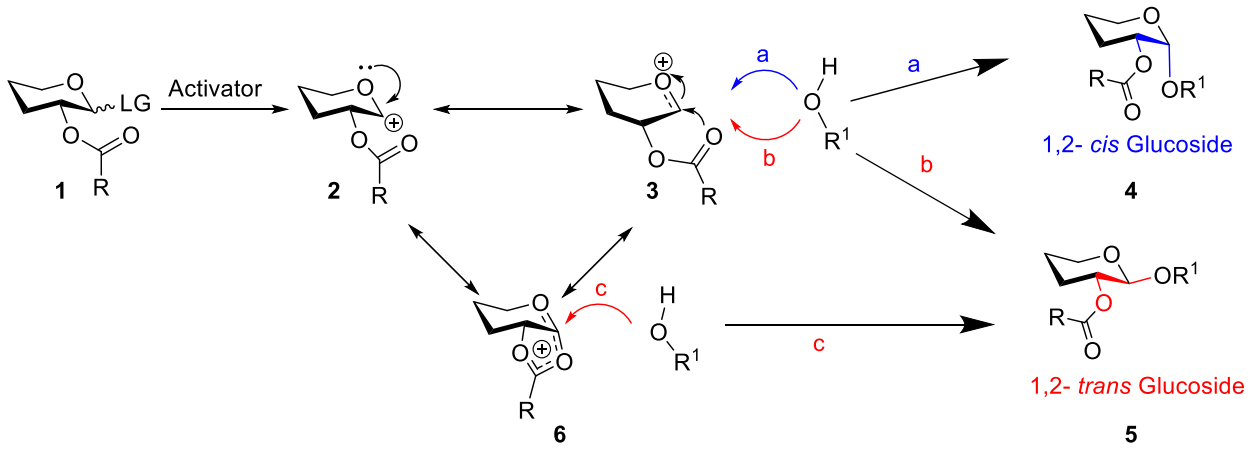
Fig 1.5 Polar and Stereo-electronic Effect Anomeric Center

1.10 Mechanism for the Glycosidic Bond Formation[1a]

Stereoselective formation of the glycosidic linkage at the chiral anomeric carbon atom is a crucial concern in the glycosylation reaction. The difficulties in accomplishing clean S_N2 reaction at the anomeric center occurs as a result of the ready participation of electron pair of the endocyclic oxygen in nucleophilic displacement of the leaving group with the nucleophile which leads to a considerable S_N1 component to these reactions.

Activator – assisted departure of the leaving group from the glycosyl donor **1** results in the formation of carbocation **2**, (**Scheme 1.1)** which is stabilized by the mesomeric release of electrons from the ring oxygen to give oxocarbenium ion **3**. The oxocarbenium ion**3** reacts with the hydroxyl component both from the *equatorial* (path a) or *axial* (path b) face affording the 1,2-*cis* **4** or 1,2-*trans* **5** glycosides respectively.

However, in the presence of a neighboring group active substituent (such as *O*- acyloxy, *O*-benzoyl and *O*-pivolyl for hydroxyl group, *N*-phthaloyl and *N*- trichloroethoxy carbonyl derivatives for amino groups) at adjacent carbon, the stereoselective synthesis of 1,2-*trans* can be achieved due to the neighboring group participation. This is because the reaction between acyloxonium ion**6** and hydroxyl group can take place from least hindered face of the ring (path c) which results into the formation of 1,2- *trans* glycoside **5** (β-glucoside in case of glucose and α-mannoside in case of mannose) exclusively. (**Scheme 1.1)**

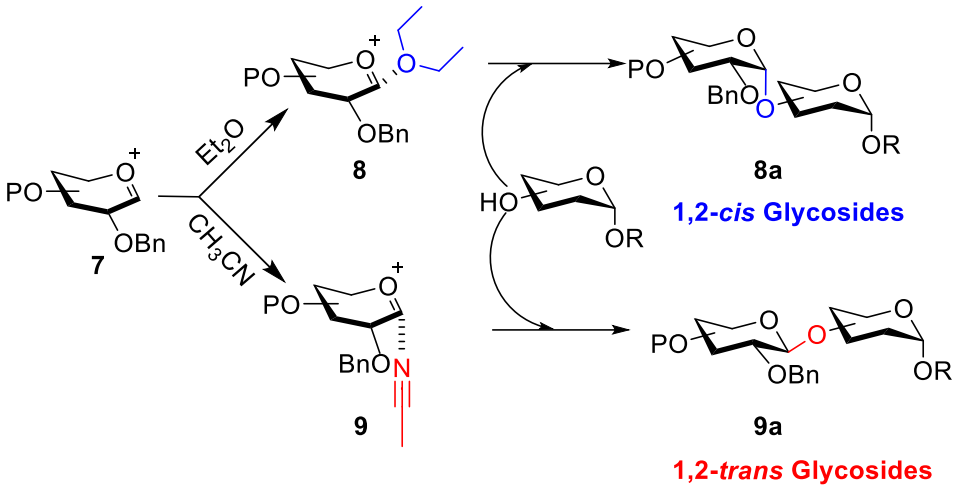


Scheme 1.1 General Reaction Mechanism for the Stereoselective Glycosidic Bond Formation

1.11Factors Affecting on Glycosylation Reaction

1.11.1 Solvent Effect[11a-b]

Stereoselectivity at the anomeric center is influenced by the reaction solvent. Generally, polar solvents increase the ratio of 1,2-*trans* glycosides via charge separation whereas non-polar solvents such as CH_2Cl_2, $ClCH_2Cl_2Cl$ or toluene favors the synthesis of 1,2-*cis* glycoside. In general, acetonitrile promotes formation of 1,2-*trans*-glycosides and diethyl ether promotes the formation of 1,2-*cis*-glycosides. Plausible explanation for this observation is during reaction in ether-type solvents participate from equatorial orientation **8** which allows the attack of upcoming nucleophile from axial orientation that leads to the formation of 1,2-cis glycosides **8a**. On the other hand, the nitrilium cation **9** forms *in situ* when the reaction is carried out in CH_3CN exclusively adopts an axial orientation allowing the attack of nucleophile from the equatorial orientation leading to the formation of 1,2-*trans* glycoside **9a** (**Scheme 1.2**).



Scheme 1.2 Solvents Effect on Glycosylation Reaction

1.11.2 Temperature and Pressure[11c-d]

If the glycosyl donor does not possess a participating neighboring group, lower temperatures promote kinetically controlled 1,2–*trans* glycoside formation during glycosylation reaction. However, higher temperature promotes 1,2-c*i*s glycoside formation. Influence of pressure on the fate of the glycosylation reaction is minimal; slight variation in the yields is noticed without significant improvement in the stereochemical outcome.

1.11.3 Activator (Catalyst) and Additives[11e-f]

Generally, mild activating conditions are advantageous for the 1,2-*cis* glycosylation. Different additives to the activator system often influence the stereo chemical product of the glycosylation.

1.12 Deciding Factors for Reactivity of Glycosyl Acceptor and Donor

1.12.1 Reactivity of the Glycosyl Acceptor [12a-d]

Structure and reactivity of nucleophile plays an active role in the glycosylation reaction. The least reactive nucleophiles give more stereoselectivity and more reactive nucleophile gives less stereoselectivity. Generally, spatial orientation of the hydroxyl group present in the sugar determines the reactivity of glycosyl acceptor. In general, *equatorial* hydroxyl group are more reactive than *axial* one. The general order of reactivity during glycosylation may be considered as 6-OH>> 3-OH>>2-OH>>4-OH for glucose.

1.12.2 Reactivity of Glycosyl Donor

1.12.2.1 Protecting Groups[13a-b]

Protecting groups of glycosyl donor are very important while controlling the region- and stereo-selectivity while executing the oligosaccharide syntheses. Carbohydrates possess large number hydroxyl groups which require regioselective protection. Reaction conditions for their introduction and removal, their stability and orthogonality while planning the synthesis of oligosaccharides shall be carefully planned.

Depending upon protecting group at the *C*-2 position of the glycosyl donor, Bert Fraser- Reid coined the term armed and disarmed glycosyl donor where disarmed donors are less reactive than armed donors because the positively charged oxocarbenium ion gets destabilized by presence of electron withdrawing groups such as –OBz or –OAc whereas electron donating group such –OBn at *C*-2 position stabilizes oxocarbenium ion intermediate (**Fig. 1.6**).

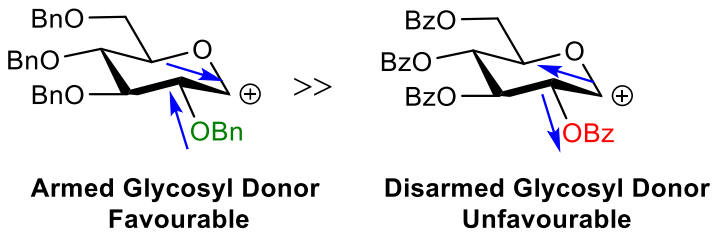


Fig 1.6 Armed and Disarmed Glycosyl Donor

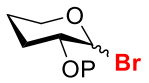
1.12.2.2 Leaving Group

A broad range of anomeric substituents are reported as leaving groups for the glycosylation reaction. Some of the most frequently used class of glycosyl donors are discussed in this section.

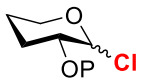
1.13 Historical Development of Glycosyl Donor

More than hundred years of research has been carried out to develop a practical synthesis protocol for glycosidic linkage. Emil Fischer and Arthur Michael are pioneers who perform chemical glycosylation first time in 1893, which is popularly known as 'Fischer Glycosylation'.[14a-c] Then, great efforts have been devoted for the development of different strategies and powerful tools for the glycosylation with different leaving groups at the anomeric position. These glycosylation approaches offer a concrete platform to access variety of complex oligosaccharides in pure and homogenous forms that are required for biological explorations.

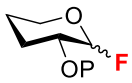
1.13.1 Glycosyl Halides



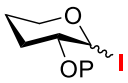
Glycosyl bromides (10)



Glycosyl Chlorides (11)



Glycosyl Fluorides (12)



Glycosyl Iodides (13)

Scheme 1.3 Glycosyl halide donors

1.13.1.1 Glycosyl Bromides and Chlorides:

Glycosylation with glycosyl bromides**10** and chlorides**11** in the presence of heavy metals salts is known as the Koenigs-Knorr reaction.[15a]The heavy metal salts frequently used as promoters include $Hg(OAc)_2$, Ag_2CO_3 and Ag_2O.[15b] Recently, Demchenko and co-workers reported that glycosyl chlorides can also be activated by using 20mol% of $FeCl_3$**.**[15c]Stability and reactivity of glycosyl bromides and chlorides is strongly influenced by the protecting groups on the sugar ring; electron-withdrawing groups decrease whereas electron-donating protecting groups increase their reactivity.

1.13.1.2 Glycosyl Fluorides:

Glycosyl fluorides **12**were introduced in 1981 by Mukaiyama.[15d]Compared with glycosyl bromides and chlorides, glycosyl fluorides have increased stability and have long shelf lives. Glycosyl fluorides can be activated under specific conditions using a combination of $SnCl_2$ and $AgClO_4$ giving rise to high yields and increased selectivity. They are commonly prepared by the reaction of a protected sugar with a free anomeric hydroxyl group with diethylaminosulfurtrifluoride (DAST).[15e]Fluoride ion serves as a weaker leaving group so enables it to give more controlled S_N2–type glycosylation.

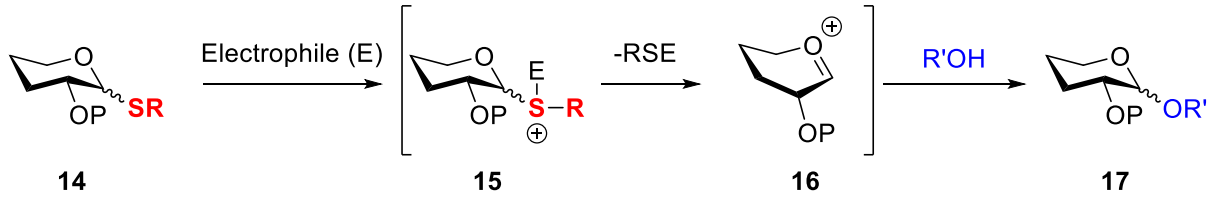
1.13.1.3 Glycosyl Iodides:

Glycosyl iodides**13** are too unstable and should be used directly. Formation of glycosidic linkage can be achieved by *in situ* generation of glycosyl iodide intermediate by activating glycosyl bromides with tetraalkylammonium iodides.[15f] However; Jacquelyn Gervay-Hague group has developed more practical procedure for the synthesis of glycosyl iodides.[15g]

1.13.2 Thioglycosides:

Thioglycosides are consistently used as glycosyl donors in the syntheses of several glycosidic linkages. Thioglycosides have proved their usefulness in the small-scale glycosylations for the construction of higher oligosaccharides. Thioglycosides show remarkable stability and tolerate very diverse carbohydrate protecting group chemical manipulations that are routinely utilized in carbohydrate chemistry.

Activation of thioglycosides**14** by electrophilic reagents or thiophilic reagents leads to the formation of sulphonium ion **15**, which then becomes a better leaving group. The loss of sulphonium ion generates common oxocarbenium ion intermediate**16** which will react with various *O*-nucleophiles to afford the *O*-glycoside **17**.[1a] (**Scheme. 1.4**)



Scheme 1.4 Thioglycosides Activation

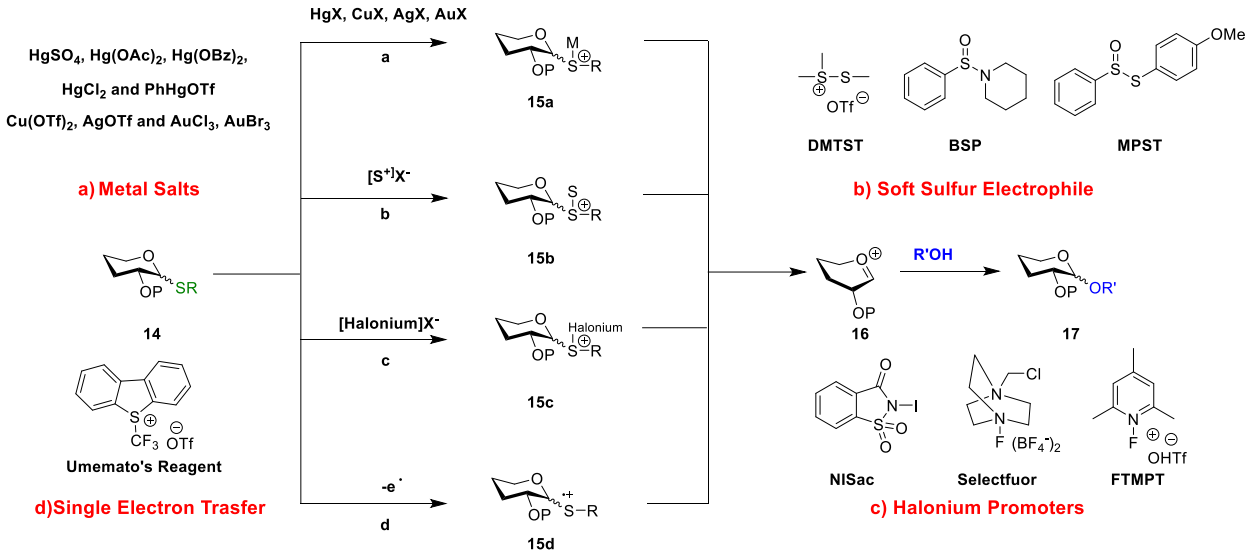
Depending upon potential for formation of sulphonium ion, thiophilic reagents are categorized into four types- a) metal salts, b) soft sulphur electrophiles, c) haloniumelectrophiles and d) single electron transfer (SET) reagents.[16a]

1.13.2.1Metal Salts

In the early 1979, thioglycosides were introduced as glycosyl donors by Ferrier and co-workers using mercury $HgSO_4$ as promoter.[16b]Other mercury salts such $Hg(OAc)_2$,[16b] $Hg(OBz)_2$,[16c] $HgCl_2$,[16d] and PhHgOTf[16e] were later tried. But, inherent toxicity associated with mercury salts encouraged researchers to develop more sustainable protocol. Thioglycosides can be activated by other Nobel metal salts such as Cu(II)[16f]to affords glycosides in good yields. However, stoichometric amount of metal salts are required for activation of thioglycosides. Sureshan *et al.*, in 2016, described the catalytic activation of thiglycosides using 3-5 mol % of Au(III) ($AuCl_3$ or $AuBr_3$) without any co-promoters.[16g]But soon after the report a correction appeared stating that in fact 0.8 eq. of Au(III) salt is needed. Reaction proceeds through formation of sulphonium ion **15a** by co-ordinating with metal as electrophile (**Scheme 1.5**).

1.13.2.2Activation by Soft Sulfur Electrophiles

Dimethyl(thiomethyl) sulfoniumtriflate (DMTST), first of its type, Fügedi and Garegg used as organosulfur promoter for the activation of thioglycosides.[17a] Idea behind the activation of is that the sulphur easily reacts with soft sulphur electrophile to form an intermediate **15b** (**Scheme 1.5**). In 2000, Crich and co-workers disclosed a combination of triflic acid and sufenylderivatives 1- benzenesulfinylpiperidine (BSP),[17b]*S*-(4-methoxyphenyl) benzenethiosufinate (MPBT)[17c]as activators for thioglycosides at ambient temperature.



Scheme 1.5 Formation of Different Intermediate Based upon Different Thiophilic Activator

1.13.2.3HaloniumPromoters:

As compared to metal salts and organosulfur promoters such as bromonium and iodonium species are more thiophilic and therefore are suitable for milder activation. In 1983, Nicolaou *et al.* reported that *N*-Bromosuccinimide(NBS) promotes glycosidation of armed thioglycosides.[18a]van Boom and Fraser-Reid independently made an important contribution to the field of glycosylation by the activation of thioglycosides by NIS/TfOH[18b] and NIS/AgOTf .[18c]

However, by-products formation due to the nucleophlicity of succinimide in NIS-promoted reaction is a major bottleneck in this protocol that can be overcome by the replacement of NIS

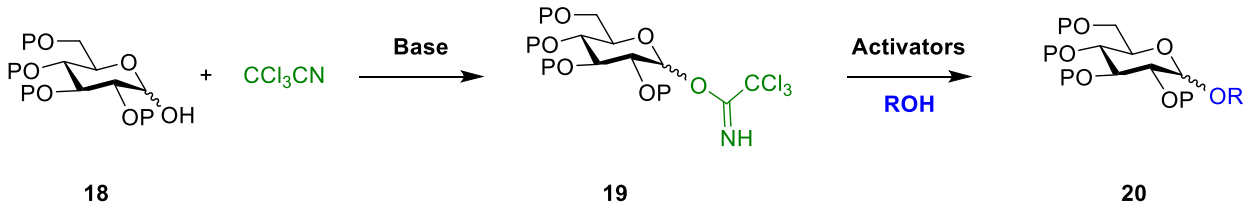
with another iodinating agent such *N*-iodosaccharin (NISac),[18d]Selectflour[18e]or 1-fluoropyridinium triflates (FTMPT).[18f]

1.13.2.4Activation by Single Electron Transfer (SET):

Sinäy *et al*. reported electro-oxidative glycosylation of thioglycosides through radical-cation intermediate that can collapse to thiyl radical and oxocarbenium ion species **3** via single electron transfer (SET) mechanism.[19a]Further, Bowers *et al*. disclosed a unique example of visible light mediated single electron oxidation on sulfur leading to *O*-glycosylation by using photoredox catalysis.[19b]Later on, Xin-Shan Ye published that thioglycosides can be activated upon UV irradiation by homolytic cleavage of C-S bond followed by in situ formation of reactive species **15d** affording glycosides.[19c]Thioglycosides can also be activated by using Umemoto's reagent under visible light irradiation to afford radical species which can be later oxidised to oxocarbenium ion in the presence of $Cu(OTf)_2$.[19d]

1.13.3 TrichloroacetamideGlycosyl Donors(TCA)

Historically, Schmidt's trichloroacetimide glycosyl donors **19** have been admired as one of the most versatile method for glycosylation. The rife popularity of trichloroacetimide been relied upon its straightforward base mediated access from free anomeric hydroxyl group. Schmidt and Michel in their first report, shown that the TCA donors were catalytically activated using both TsOH and BF_3•OEt_2(**Scheme 1.6**).[20a]



Scheme 1.6 Base Mediated Formation of TCA and its activation to form Glycoside

There have been numerous reports for the activation of TCA by using different promoters out of which some important activators reported in literature for TCA activation are delineated below.

1.13.3.1 Lewis acid and Bronsted Acid as promoters

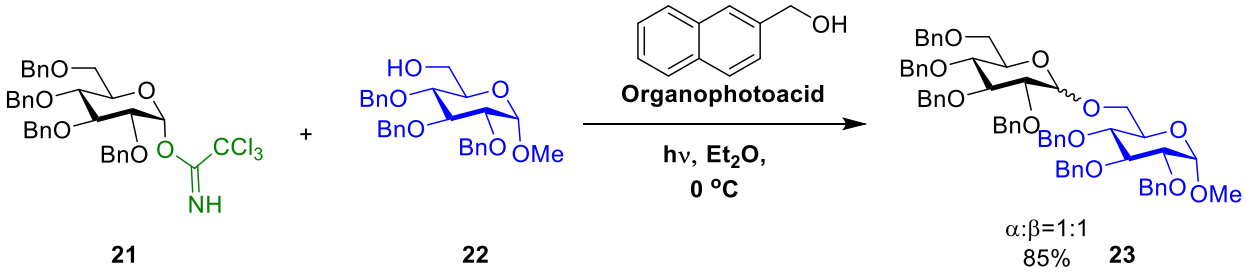
There have been various reports establishing activation of TCA donors by Lewis acids such as TMSOTf,[20b] $ZnBr_2$,[20c]$TMSNTf_2$/$NHTf_2$[20e]and I_2/Et_3H[20d] to synthesize anomeric mixture of glycosidic linkages.

1.13.3.2 TransitionMetal Salts as Promoters

Nguyen reported activation of glycosyl trichloroacetimidatesas donors using cationic Pd-$(CH_3CN)_4(BF_4)_2$ catalyst and demonstrated the formation of α-D-mannopyranoside without a participating group at *C*-2 position in a stereoselective fashion.[21a] Same group explored the utility of Ni(II) catalyst for activation of glycosyl trichloroacetamide using Ni(4-F-PhCN)$_4$(OTf)$_2$.[21b] Schmidt and co-workers published their results using $AuCl_3$ as the catalyst in TCA activation.[21c] Mukherjee and co-workers reported the use of $FeCl_3$ as an activator for the TCA donor.[21d]

1.13.3.3 Organophotoacid Catalysed Activation

Toshima group studied the activation of TCA glycosyl donor **21** under photoinduced excited state conditions by using organophotoacids to obtain glycosides **23**[21e](**Scheme 1.7**). In continuation of this, thiourea based photoacid as catalyst for TCA activation was also explored later on. They observed that high concentration of donor of donor and acceptor favours formation of β-glycoside and however dilute conditions prefer the formation of α-glycoside.[21f]



Scheme1.7 Organophotoacid as TCA Activator

1.13.4 C-C Triple bond Based Glycosyl Donors

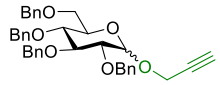
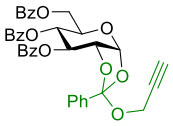
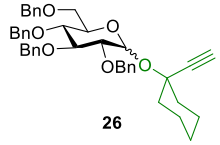
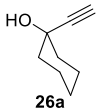
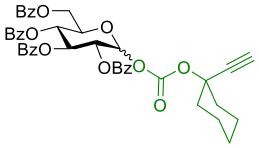
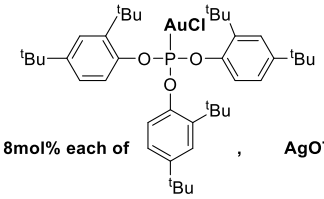
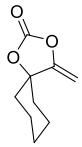
1.13.4.1 Au/Ag as Promoters

One of the most important events of last decade in glycosylation chemistry was the introduction of catalytic activation of alkyne by gold halides. Hotha and Kashyap reported for the first time a remarkable alkynophilicity by gold catalysts can be utilized for activation of propargyl glycosides **24** to synthesize glycosides.[22a]It was found that per-*O*-benzylated propargyl glycosyl donors only can be activated in presence of 3mol % of $AuCl_3$ in CH_3CN at 60 ˚C. The

hypothesized mechanism for the gold catalysed glycosidation of propargyl glycosides was attributed to the strong alkynophilicity of Au^{3+} leading to the formation of cyclopropanone**24a** as leaving group which was later noticed to be wrong. Yields obtained with various acceptors were good albeit in poor anomeric selectivity. In order to improve the anomeric selectivity Hotha group modified propargyl glycosides to propargyl 1,2-orthoesters**25**, which was able to synthesis disaccharide in presence of $AuBr_3$ at room temperature.[22b] Propargylorthoesters of more reactive furanosides were also found to be stable and were activated under similar reaction conditions.[22c]

It was found that activation propargyl orthoeter was much faster as compared to activation of propargyl glycosyl donors but has given rise to formation of a side product such as direct glycoside product. Improvisation in the reactivity and to minimise the formation of side products, Hotha Group systematically studied various alkynyl appendages at the anomeric carbon and found that *gem*-disubstituted donors were superior due to the well-known Thorpe–Ingold Effect. They have showed that 1-ethynylcyclohexanyl glycosides **26**as novel donors at room temperature by using silver salts such as AgOTf or $AgSbF_6$ in combination with $AuBr_3$ at room temperature.[22d]Gas chromatography led mechanistic investigation revealed that the 1-ethynylcyclohexanyl alcohol**26a**simply extrudes out as the leaving group. However, successfully brought down the reaction temperature from 60-25 $^{\circ}$C but still scope of reaction was limited only to per-*O*-benzylated donors and not suitable for disarmed sugars.

In continuation to this, Hotha group introduced ethynylcyclohexanyl glycosyl carbonates **27** as versatile glycosyl donors.[22e]Alkynyl glycosyl carbonates are shown to be stable glycosyl donors that can be activated catalytically by a combination of silver (AgOTf) and more alkynophilic gold (gold-phosphite) catalytic system at 25 $^{\circ}$C under 15 min to form glycosides in excellent yields. It is found that benzoyl carbonate donors are solids and are self-stable as well. They have shown cyclic carbonate with exomethylene **27a**formeddue the activation of the alkynyl aglycon without the release of CO_2 unlike many other previously reported glycosyl carbonates. Further, the method was found to be superior for the synthesis of a mannose-capped arabinan tridecasaccharide (**Scheme 1.8**).

Glycosyl Donor	Reagent(s)	Byproduct
 **24**	$AuBr_3$ (3mol%)	 **24a**
 **25**	$AuBr_3$ (5mol%)	Not specified
 **26**	5 mol% each of $AuCl_3$,$AgSbF_6$	 **26a**
 **27**	 8mol% each of , AgOTf	 **27b**

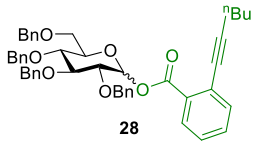
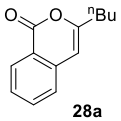
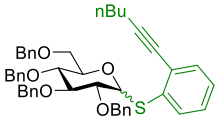
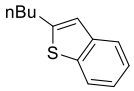
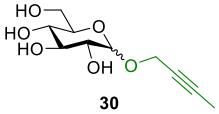
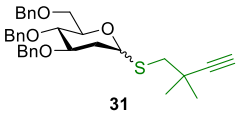
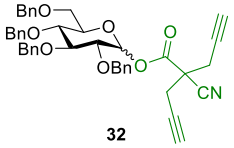
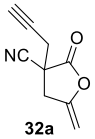
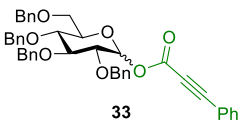
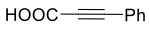
Scheme 1.8 Evolution of Alkyne-based Glycosyl Donors from Hotha Group

Early discoveries in Hotha group have led to a considerable interest among glycochemists′ inactivating other C1-alkynesby gold catalyst. In this direction, Yu grouphas developed *ortho*-alkynyl benzoate glycosides **28**, which were reacted with various aglycones upon activationby Au(I)-complex ($Ph_3PAuOTf$).[23a]Alkynyl-benzoate glycosyl donors are also explored in the synthesis of glycosides in continuous flow reactors.[23b] Yu group also shown that *ortho*-alkynylphenyl thioglycosides**29** can also under glycosidation under the catalysis of PPh_3AuOTf.[23c]

Apart from Hotha and Yu, several others also contributed toalkynyl family of glycosyl donors. For example, Finn group achieved glycosylation of unprotected sugars by using 2-butynyl glycosyl donors**30** in the presence of 5mol% of Au(III)-salt and excess of acceptors.[23d] Another major contribution by Zhu showed that*S*-but-3-ynylglycosides can form more reactive 2-*deoxy* sugars and later *gem*-dimethyl *S*-but-3-ynyl thioglycosides **31**as glycosyl donors under gold and silver catalytic system.[23e] Later glycosyl donor is more reactive as it has advantage of the

Thorpe-Ingold effect. Detailed NMR experiments showed that cyclised 4,4-dimethyl-2,3-dihydrothiophene**31a** was forced out as leaving group during the glycosylation reaction.

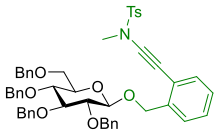
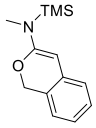
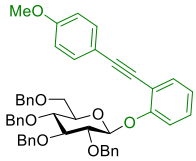
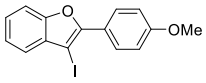
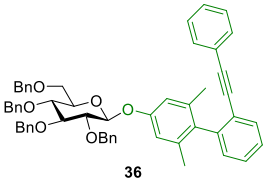
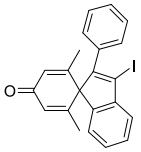
Recently, Balamurugan group found that the catalysis of gold and silver for the activation of dipropargyl–substituted cyanoacetyl glycosides **32**for glycosylation at room temperature.[23f] Amit Kumar group designed and developed phenylpropiolatates glycosides **33** as long shelf stable and effective glycosyl donors, which could be activated with catalytic $AuCl_3$ salt to produce desired glycosides in good to excellent yields. The noteworthy features of this glycosyl donors is the formation of hydrophilic phenylpropiolic acid**33a** as reusable leaving group (**Scheme 1.9**).[23g]

Glycosyl Donor	Research Group	Reagent(s)	Byproduct
 **28**	**Biao Yu**	**(Btz-Au-PPh_3)OTf (10mol%)**	 **28a**
 **29**	**Biao Yu**	**PPh_3AuOTf (10mol%)**	 **29a**
 **30**	**Finn**	**$AuCl_3$ (5mol%)**	Not Specified
 **31**	**Zhu**	**10mol% of $AuCl_3$, 30mol% of AgOTf**	 **31a**
 **32**	**Balamuragan**	**$AuCl_3$ (5mol%)**	 **32a**
 **33**	**Amit Kumar**	**$AuCl_3$ (10mol%)**	 **33a**

Scheme 1.9 Alkyne-based Glycosyl Donors

1.13.4.2 Non Au/Ag as Promoters

Further, electron rich alkyne moiety was also activated by other electrophiles apart from gold and silver metal salts. There have been reports where alkynoic acid residues are activated as leaving groups under mild and catalytic $Hg(OTf)_2$ conditions for the glycosylation reaction.[24a] Sen and co-workers showed that iodine can be used as promoters for the activation of glycosyl *ortho*-alkynylbenzoates**28** in glycosylation to form desired glycosidic linkages.[24b]

Glycosyl Donor	Research Group	Catalyst	Byproduct
 **34**	Biao Yu	TMSOTf (10mol%)	 **34a**
 **35**	Jian- Song Sun	1.5 eq. NIS, 0.5 eq.TMSOTf	 **35a**
 **36**	Biao Yu	1.5 eq. NIS, 0.5 eq.TMSOTf	 **35a**

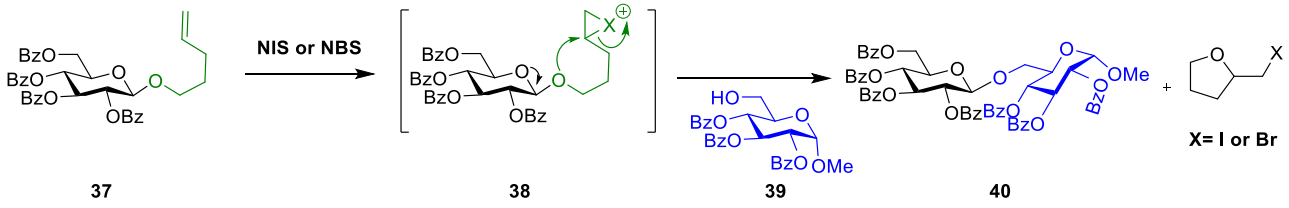
Scheme 1.10 Alkyne-based Donors

In an attempt to develop novel glycosyl donors Yu group introduced an electron rich substituent on the alkyne moiety to facilitate the glycosylation. *ortho*-(Methyl tosylaminoethynyl)benzyl glycosides **34**were explored as novel type of glycosyl donors which can be activated by a catalytic amount of TMSOTf. [24c] Jian-Song Sun established a novel alkyne-activation-based glycosylation protocol using *O*-(*p*-methoxyphenylethynyl)phenyl(MPEP) glycosides**35** using NIS and TfOH.[24d] Recently, Yu group reported another glycosylation protocol that uses 3,5-dimethyl-4-(2′-phenylethynylphenyl)phenyl(EPP) glycosides **35** as donors and NIS/TMSOTf as promoters;the proceeds through an unprecedented dearomative activation mechanism (**Scheme 1.10**) .[24e]

1.13.5 C-C Double Bond Based Glycosyl Donors

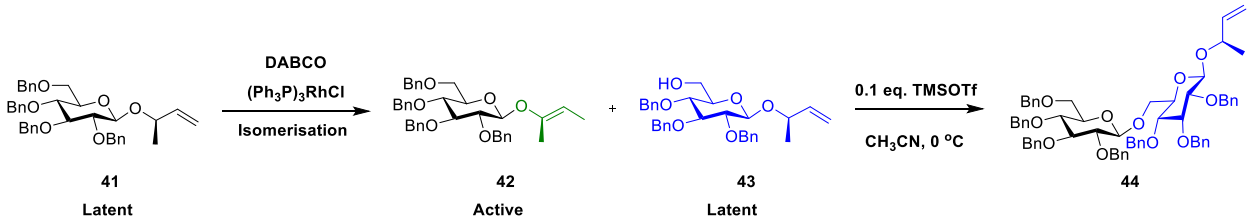
1.13.5.1 C-C Double Bond Remote from Sugar Ring

Fraser-Reid group discovered *n*-pentenyl glycosides**37** as glycosyl donors in 1980s. The *n*-pentenyl glycosyl donors get activated by an electrophilic addition of the iodinium/brominium ion to the double bond followed by the removal of a five membered tetrahydrofurfuryl iodide/ bromide **38** to form an oxocarbenium ion which can be later trapped by nucleophiles such as **39**(**Scheme 1.11**).Generally, used activators for *n*-pentenyl glycosyl donors are NBS, NIS, I_2, IDCP, NIS/TfOH or NIS/Yb(OTf)$_3$.[25a] Expensive nature of 4-penten-1-ol and removal of the tetrahydrofurfuryl alcohol from the reaction mixture are the major drawbacks.



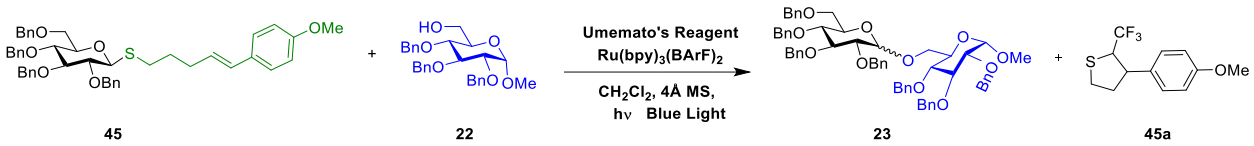
Scheme 1.11 n-pentenyl Glycosides

Boons and Isles introduced a novel latent-active glycosylation method which is based on the isomerization of substituted allyl glycosides**41** to afford vinyl glycosides**42** which can later be activated by using Lewis acid promoted glycosylation. In this approach, only 0.1 equivalent of TMSOTf was used to catalyze the glycosylation (**Scheme 1.12**).[25b]



Scheme 1.12 Allyl to Vinyl Isomerization-based Latent–active Glycosyl Donors

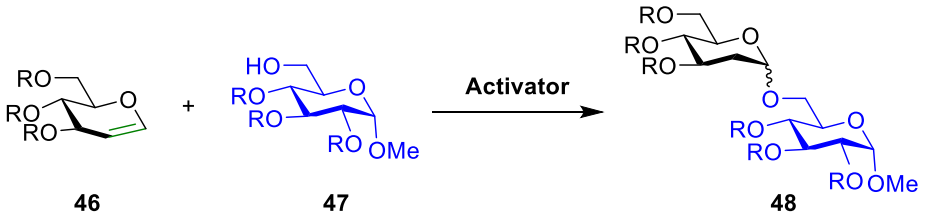
In yet another effort, Ragains and co-workers reported *O*-glycosylation using 4-*p*-methoxyphenyl-3-butenylthio-glucoside **45**as glycosyl donorin the presence of Umetoto′s reagent under visible-light irradiation (**Scheme. 1.13**).[25c]



Scheme 1.13 Visible-Light Mediated Activation of Alkenyl Glycosyl Donors

1.13.5.2C-C Double Bond Within Sugar Ring: Glycals as Glycosyl Donor

The acid-promoted addition of alcohols to glycals is straightforward approach for the synthesis of 2-*deoxy*glycosides where reactions favor the axial products. Bolitt and co-workers catalytically activated glycals with triphenylphosphinehydrobromide (HBr-PPh_3) to 2-*deoxy* products with high α-selectivity.[26a] However, the major problem associated with this reaction is allylic rearrangement of the oxocarbenium ion intermediate which leads to the formation of 2,3-unsaturated glycosides which is popularly known as the Ferrier reaction. To avoid, triphenylphosphine in combination with various other acids such as BF_3•OEt_2, TfOH, TMSOTf and $FeCl_3$ were tested and less side products were observed. But requirement of high acidic conditions prevents its utility in the synthesis of higher oligosaccharides.[26b]



Research Group	Activator
Bolitte	HBr-PPh_3 (5mol%)
Toste	[$ReOCl_3(SMe_2)(PPh_3PO)$] (1mol%)
Balmond	Organo-catalyst Thio Urea
Galan	$Pd(MeCN)_2Cl_2$ (25mol%)
Galan	[$(CF_3Ph)_3P$]AuCl (3mol%) and AgOTf (6mol%)

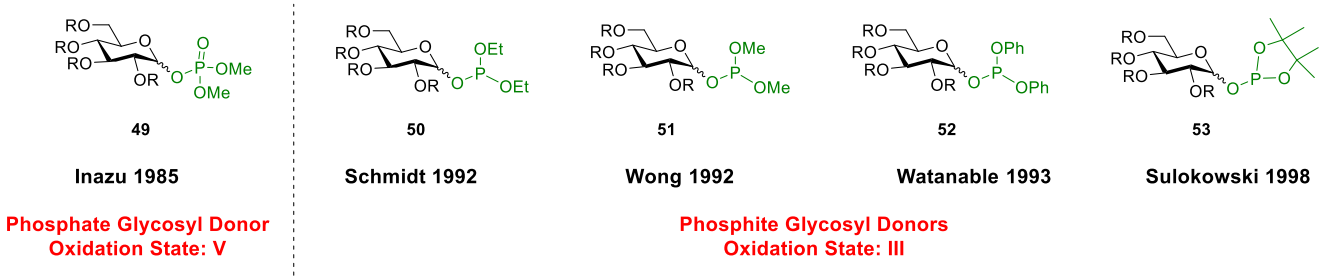
Scheme 1.14 Glycals as Glycosyl Donors with Different Activators

A major breakthrough in the activation of glucals came with Toste′s introduction of Rhenium(V) in combination with triphenylphosphine to form 2-*deoxy* glycosides with less percentage of side products.[26c]Balmond studied organo-catalysts such as thioureas for the activation of galactals to synthesize 2-*deoxy*glycoside.[26d]Galan and co-workers introduced the Pd(II) in combination with monodendate phosphine ligand for the activation of D-galactals.[26e] They were successful in achieving high α-selectivity as well as good to excellent yields albeit in longer periods. However, switching the catalyst from Pd to Au(I)([$(CF_3Ph)_3P$]AuCl in combination with AgOTf led to shorter reaction time as well as reactions could be carried out at room temperature (**Scheme 1.14**).[26f]

1.13.6 Glycosyl Phosphates and Phosphites

A wide range of phosphorus-based glycosyl donors have been reported in the literature. Depending on the oxidation state of phosphorus atom, these are sub-divided into two classes: one is phosphate glycosyl donors with an oxidation state of +5 and the others are the phosphite glycosyl donors with an oxidation state of +3.[27a]

To the best of our knowledge, Inazu and co-workers reported glycosyl phosphates **49** as glycosyl donors in 1980s by adding stoichiometric amount of TMSOTf.[27b]Schmidt and co-workers introduced the use of diethyl phosphate as leaving group in diethyl phosphate glycosyl donors **50**[27c] whereas Wong and co-workers developed dimethyl phosphate glycosyl donors**51.**[27d]Shortly after, dibenzyl phosphate glycosyl donors**52** were introduced by the Watanabe group.[27e] The Sulikowski and co-workers has shown modified cyclic pinacol phosphate glycosyl donor **53**in 1998.[27f](**Scheme 1.15**)



Scheme 1.15 Phosphate and Phosphite Glycosyl Donors

1.14 Summary and Future Directions

A universal glycosylation methodology has not yet found despite large number of glycosylation methods over the last one century. This is largely because of the highly complex nature of glycoconjugates and their intricate difficulties in the chemistry involved. From practical standpoint, search for technocommercially suitablenovel glycosyl donors and promoters along with mild and ideal reaction condition is expected to continue in future as well. In this regard, the development of novel methods, with different chemistry from the existing ones, can contribute to the progress in this field.

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Chapter 2

Development of Nucleofuge Regenerative Hydroxybenzotriazolyl Glycosyl Donor Chemistry

2.1 From where will be the New Innovation Come?

Stereoselective installation of glycosidic linkages is one of the greatest challenges of synthetic carbohydrate chemistry and organic chemistry *per se*. Comprehensive knowledge of detailed reaction mechanism of glycosylation is highly beneficial for synthesis of glycosidic bonds in more efficient ways and to achieve higher α/β stereoselectivity. In this concern, researchers have been making serious efforts to understand the reaction in a more systematic way. Existing efficient strategies and powerful tools with different leaving groups for synthesizing complex oligosaccharides and glycoconjugates of biological importance have been summarized in previous chapter along with major problems associated with the glycoside-bond formation. However, one should keep in mind that careful optimization of all parameters, such as the leaving group, promoters/catalyst, protecting groups and glycosidation conditions, play a crucial role in construction of any glycosidic linkage in high yield with high stereoselectivity. But the intricacy of glycosylation is accountable for countless drawbacks which are experienced by existing methods. Hence, the novel conceptual approaches for glycosylation are still welcomed to meet the intrinsic structural diversity of saccharides. However, further variation of the leaving groups need not lead to new innovation in glycosylation strategy.[1]So the big question is, from where will this new innovation come?[1]

2.2 Emerging Strategies in Glycosylation

2.2.1One-Pot Glycosylation

One-pot glycosylation has emerged as a highly powerful approach for the syntheses glycosidic linkages. One-pot glycosylation strategy claims to be the shortest possible route for synthesis of oligosaccharides as it relies on differences in relative reactivity of glycosylating agents. The concept of armed-disarmed sugar can potentially determine the chemoselective glycosylation. In pre-activation based glycosylation, the glycosyl donor is activated separately before the addition of the acceptor which contains a leaving group for the next glycosylation step. Orthogonal glycosylation is based on the selective activation of a leaving group. Generally two or three different glycosidic linkages can be prepared by this one-pot approach which shows the attractiveness of this approach **(Fig. 2.1)**.[2a-d]

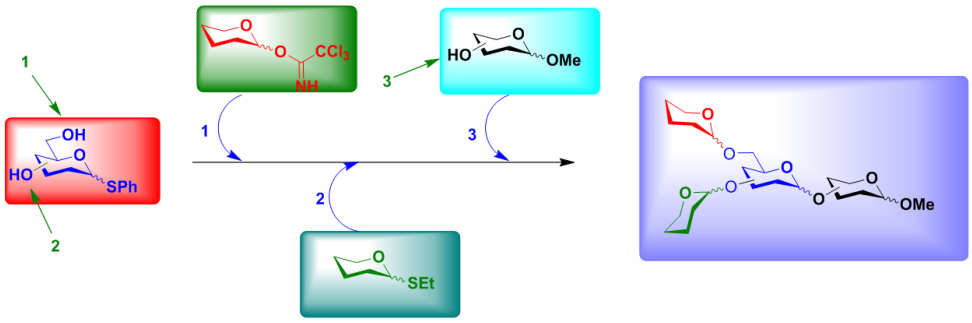


Fig. 2.1 One-Pot Glycosylation

2.2.2Solid-phase Oligosaccharide Synthesis (SPOS)

The development of efficient solid-phase organic reactions led the path for the solid phase synthesis of oligosaccharides and carbohydrate mimics due to the ease of production, isolation and purification. This modern strategy of oligosaccharide syntheses overcomes an assortment of drawbacks of solution phase synthesis and opens up many limitations due to the poor mass transfer.

Unlike solution-phase reaction, either the glycosyl acceptor is bound to a heterogeneous solid support linker or a resin that could be cleaved easily after completion of synthesis or the glycosyl donor is bound to the solid support (**Fig. 2.2**).This protocol is self-corrective as unused glycosyl donors or acceptor can be washed away after each coupling step and do not reemerge in the next cycle. Most common glycosyl donors have been investigated as glycosylating agents in the acceptor-bound strategy for SPOS, such as *O*-glycosyl trichloroacetimidates, glycosyl sulfoxides, thioglycosides, *n*-pentenyl glycosides and glycosyl phosphates.[3a-c]

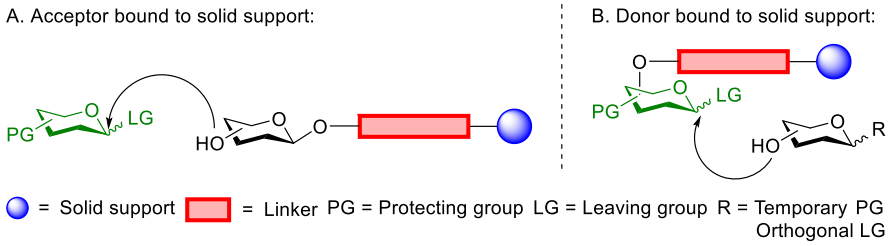


Fig. 2.2 Solid Phase Oligosaccharide Synthesis

Another important breakthrough in carbohydrate chemistry was the development of the automated oligosaccharide synthesizer by Seeberger and co-workers in 2001 using a solid-phase

peptide synthesizer employing *O*-glycosyl trichloroacetimidates and phosphates as glycosyl donors.[3d-e]

2.2.3Intramolecular Glycoside-Bond Formation

Inspired by enzymatic glycosidations which is closely related to an intramolecular glycosyl transfer from donor to the acceptor, a series of reports were published in an effort to overcome the challenges of synthesizing stereoselective 1,2-*cis* glycosides. In this unifying strategy, the temporary linker was used to tether glycosyl donor and the glycosyl acceptor, which results into the formation of the unidirectional attack of the aglycon producing 1,2-*cis* glycoside exclusively by allowing spatial orientation for delivery of glycosyl acceptor via a 5-membered transition state.[4a]

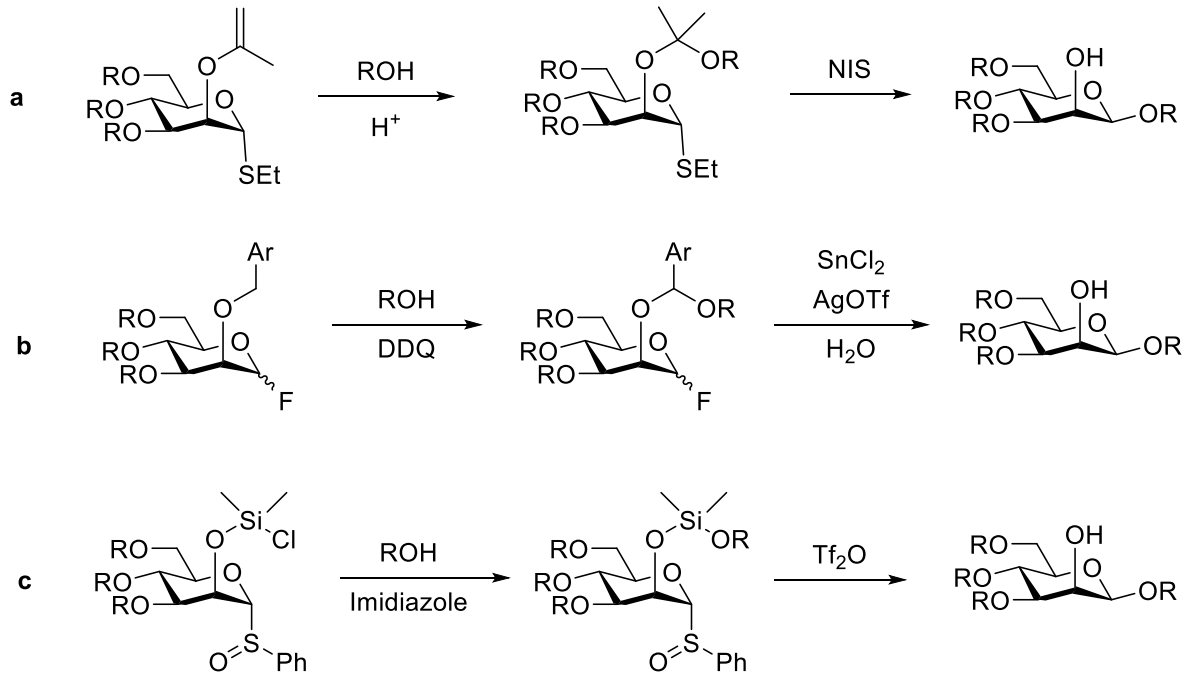


Fig. 2.3 Intramolecular Glycosidic Bond-Formation

Hindsgaul and coworkers introduced isopropylidine ether as a first temporary linkage for intramolecular aglycone delivery. Dimethyl ketal linker was formed in the presence of acid by reacting desired glycosyl acceptor with isopropylidine ether of donor and subsequentactivation of the thioethyl moiety with *N*-iodosuccinimide (NIS) resulted in the β-mannoside formation (**Equation a, Fig.2.3**).[4b]

Ito and Ogawa developed an alternative design for the intramolecular aglycone delivery using a C-2-*O*-*p*-methoxybenzyl protection which on treatment with DDQ and acceptor produced desired acetal linkage. Activation of glycosyl fluorides with AgOTf and $SnCl_2$ in the presence of water gave good yields of β-mannopyranoside exclusively (**Equation b, Fig. 2.3**).[4c] Stork and co-workers published dichlorodimethylsilane to link the C2-OH of the glycosyl donor andthe hydroxyl group on the acceptor resulting into the formation of dimethylsilyl-linker. The oxidized sulfur leaving group on subsequent treatment with Tf_2O provided β-mannoside as the only isolated anomer (**Equation c, Fig. 2.3**).[4d]

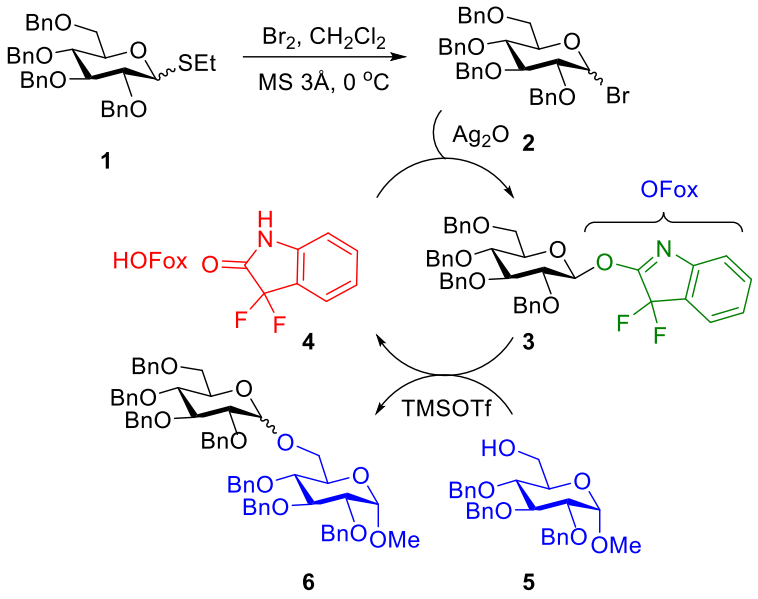
These systematic approaches have its own tribulations such as unwanted side products during reactions and difficulties in scale up of reactions. It seems that the field of carbohydrate chemistry is at a crossroad: either to scrutinize for a universal glycosylation policy or to focus on an alternative model for one particular type of coupling reaction. But during this continuous development in the field of catalytic glycosylation research, one should not ignore the environmental friendliness of reaction and also from industrial point of view cost efficiency needs to be considered. These factors appear to be the driving force for oligosaccharide synthesis and likely to be primary inspiration for years to come.[4e]

2.2.4 Regenerative Glycosylation

The regenerative approach seems to be promising in reducing side reactions which are commonly observed in conventional glycosylations. In 2014, Demchenko and co-workers first disclosed the concept of regenerative chemical glycosylation.[5a]They have identified that 3,3-difluro-3H-indol-2-yl (OFox)as a potential leaving group which is fundamentally similar to its cyclic analogue of departed leaving group 3,3-difluroxindole**4** (HOFox). First, precursor**2** will react with HOFox**4** to form highly reactive OFox imidatedonor**3** and which will then react with the acceptor**5** to form glycosides**6** along with regeneration of HOFox**4**. This regenerated HOFox **4**will then be available for the next catalytic cycle to regenerate the OFox imidate donor**3**. Resultantly, only a relatively small amount of the reactive donor is required i.e. HOFox catalysed regenerative glycosylation **(Scheme 2.1)**.[5a]

Further they have demonstrated its application by synthesizing an oligosaccharide by regenerative glycosylation.[5b]The importance of this inspection is that one should be able to

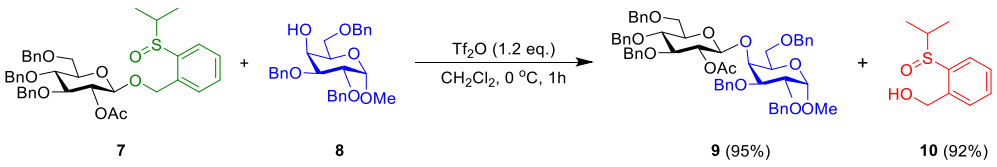
conduct both the *in situ* introduction and activation of the leaving group in the catalytic donor in a regenerative fashion which helps to minimize the side products.



Scheme 2.1 HOFox Catalyzed Regenerative Glycosylation

2.2.4.1 Regenerative and Recyclable Leaving Group

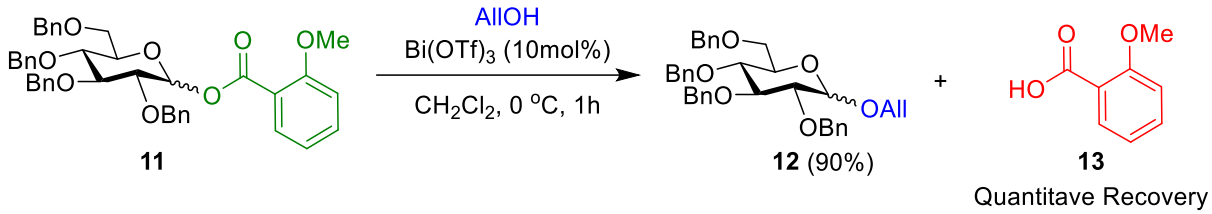
In 2015, Qian Wan and co-workers have identified 2-(2-proylsulfinyl) benzyl glycosides **7** as glycosyl donor. Initial transglycosylation was performed with glycosyl donor **7** and glycosyl acceptor **8** in presence of 1.2 eq. of triflic anhydride to afford the desired disaccharide **9** in 95% yield and observed that after coupling reaction, the leaving group is recycled as 2-(2-proylsulfinylbenzyl alcohol **10**in 92% yield which was used in the synthesis of the latent glycosyl donor **7**after a simple reduction **(Scheme 2.1)**.[6a]



Scheme 2.2 Regenerative and Recyclable Leaving Group

2.2.4.2 Quantitative Recovery of Leaving Group

Similar efforts were done by Jenson and coworkers, they have described a new type of glycosyl donor **11** having *O*-methoxybenzoate functionality which can be activated under catalytic Lewis acid condition to afford glycoside product **12** in high yield. The characteristic feature of this approach is after work up the leaving group can be easily removed and recovered as benzoic acid **13**in a quantitative yield **(Scheme 2.3)**.[6b]



Scheme 2.3 Quantitative Recovery of Leaving Group

It is found that regenerative glycosylation and recyclable leaving group approach faces difficulties such as two steps or work up is required for recovery of leaving group and *in situ* regeneration of glycosyl donor requires an additional step. Some of the explored donors have limited shelf stability and stoichometric amount of activators were reported. Formation of stereoselective glycosides still remains to be explored by this approach. Another obstacle is the nucleophilicity of the recycled leaving group which could potentially compete with the glycosyl acceptor during the glycosylation reaction. Regenerative glycosylation approach is currently at its nascent stage and has wide scope for future development.

2.3 Motivation from Peptide Chemistry for the New Glycosylation Approach

In this concern, one can take motivation from peptide chemistry. A plethora of peptides and proteins contain amide bond and the formation of amide bonds plays an important role in organic chemistry.[7a] Amide bond formation usually needs activation of a carboxylic acid moiety in the presence of coupling reagents/additives. Ideally, peptide bond formation should be fast and is carried out under mild conditions without affecting adjacent stereogenic center, without side reactions and with easily removable side products. But a key difficulty associated with the peptide bond formation is the racemization in α-amino acids. The racemization of amino acid usually occurs either β-proton abstraction (path a) or through azalactone formation (path b). Azalactone formation helps in removal of the most acidic proton from the chiral center which

results into resonance stabilization of the carbanion. The role of base is also important as it abstracts the most acidic proton (**Fig. 2.4**).[7b]

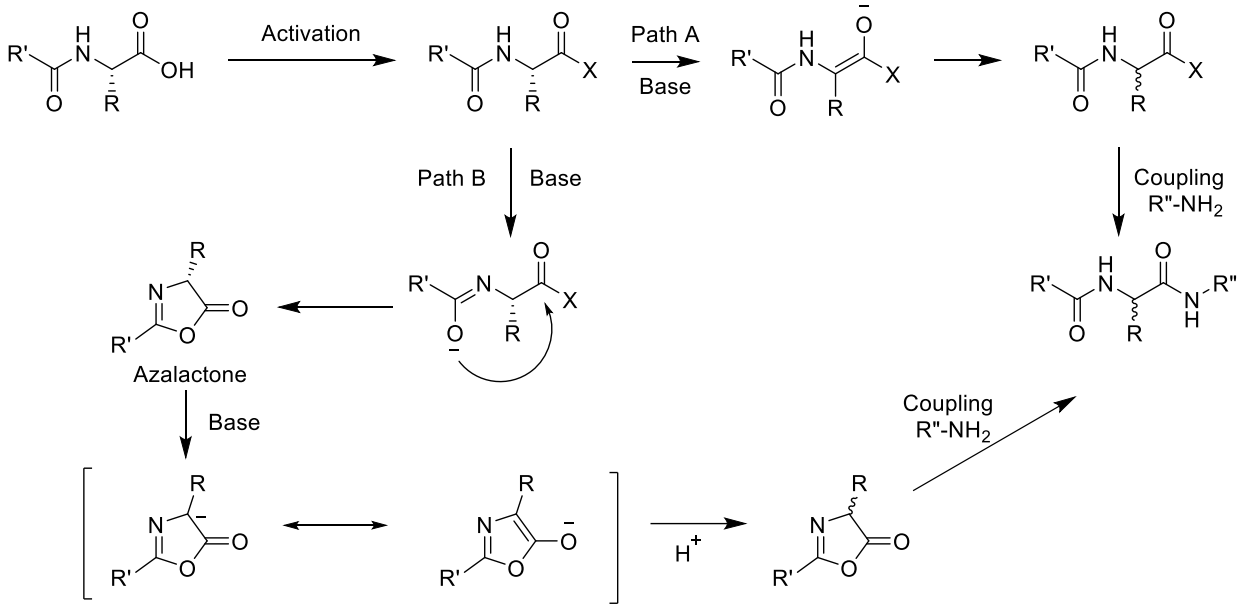


Fig 2.4 Mechanism of Base-catalyzed racemization during activation

A coupling additive not only enhances the reactivity of peptide coupling reagents but also reduces the extent of racemization. *N*-Hydroxysuccinimide (HOSu), *N*-hydroxy-5-norbornene-2,3-dicarboximide (HONB), 1-hydroxybenzotriazole (HOBt), 6-chloro-1-hydroxybenzotriazole (6-Cl-HOBt), 1-Hydroxy-7-azabenzotriazole (HOAt), 3-hydroxy-4-oxo-3,4-dihydro-1,2,3-benzotriazine (HODhbt) and its aza derivatives (HODhat) are some of the popular additives used in peptide chemistry (**Chart 2.1**).[7b]

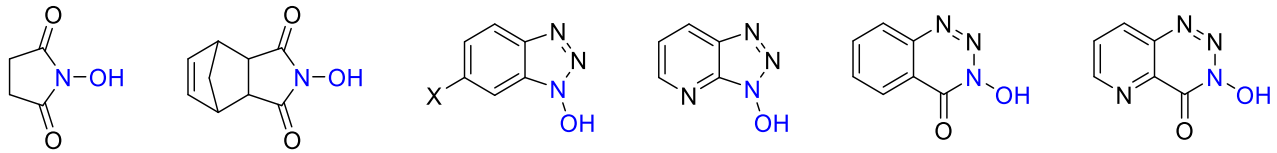
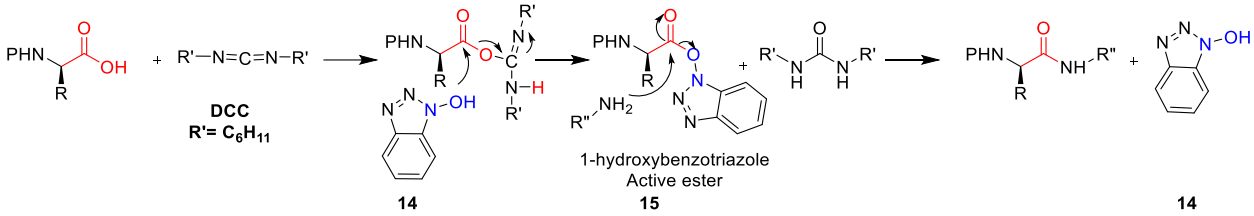


Chart 2.1 Common Coupling Additives

Among all coupling additives, 1-hydroxybenzotriazole (HOBt) **14** is frequently used in peptide coupling additive with dicyclohexylcarbodiimide (DCC).König and Geiger proposed that HOBt captures active species using hydroxylamine functionality to give corresponding active ester

15with the carboxylic acid that undergoes aminolysis with corresponding amine to form amide bond**(Scheme 2.4)**.[7c]



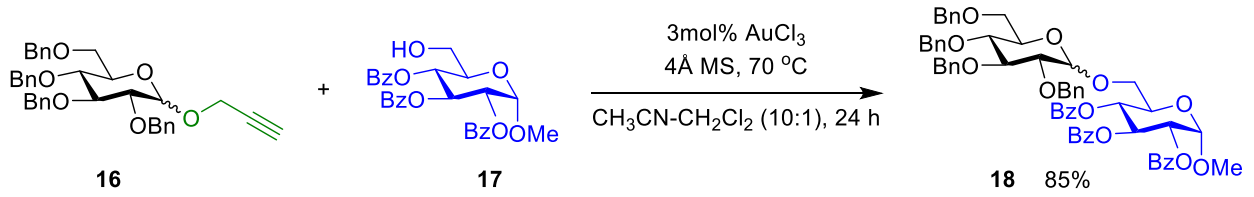
Scheme 2.4 Formation of 1-hydroxybenzotriazole Active Ester

One can clearly realize from the mechanism of amide bond formation that HOBt possesses distinguishing characteristics such as (i) better leaving group and (ii) comes out as recovered leaving group after completion of the reaction. It exhibits tautomeric isomerism between two heteroatoms. This encouraged us explore the utility of HOBt in glycosylation chemistry.

2.4 Present Work

2.4.1 Gold-Catalyzed Glycosylation

Hotha and Kashyap identified propargyl glycosides**16** as glycosyl donors employing catalytic amount of $AuCl_3$ to afford anomeric mixture of glycosides **(Scheme 2.5)**.[8]

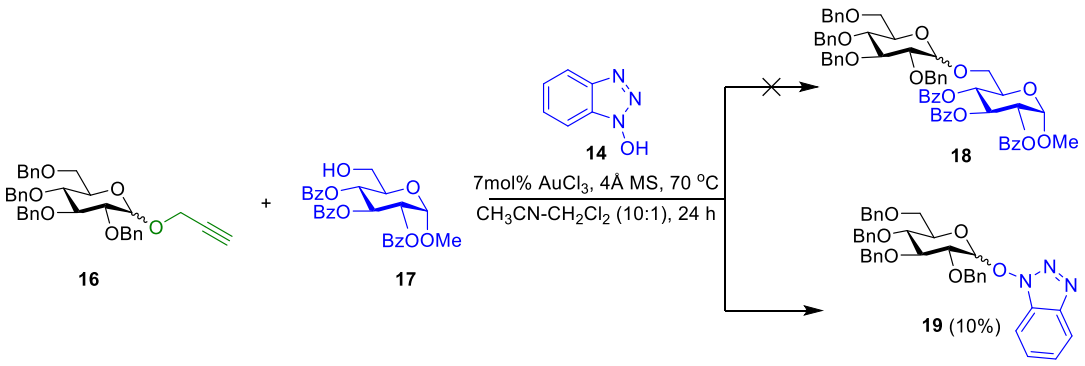


Scheme 2.5 Gold-catalyzed Glycosylation

The glycosylation requires elevated temperature (70 °C) and longer time (24 h) for activation and also they can be glycosylated only with armed sugar i.e. protection with C-2-*O*-benzyl ether. In addition, hydrolysis of the interglycosidic linkages was noticed while synthesizing oligosaccharides hypothesized to occur due to the elevated temperature. In this background, primary objectives of this project were to bring down the reaction temperature for the activation of propargyl glycosides with eventual understanding that glycosylations in the presence of disarmed substituents (i.e. C2-*O*-Bz) can also get facilitated at elevated temperatures,

stereoselective formation of glycosides and last but not least are to increase the turn over number (TON) of gold-catalyzed glycosidations.

To address these objectives, inspiration drew from peptide chemistry and hypothesized that addition hydroxybenzotriazole **14**(HOBt) in gold-catalyzed glycosylation will help to accelerate the reactivity of propargyl glycosides.[9]We started our experiments with the treatment of propargyl glucosides **16**as a model substrate with model glucosyl acceptor **17** and added HOBt **14**and catalytic amount of $AuCl_3$in the presence of 4Å MS powder at 70 °C. The reaction was monitored for 24 h to notice expected disaccharide**18**did not form; instead HOBt glucoside **19** was observed as side product that can be rationalized by the participation of the HOBt as the acceptor (**Scheme 2.6**).



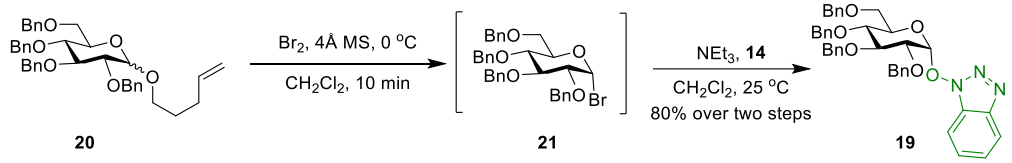
Scheme 2.6 Observation of HOBt Glucoside **19** Formation

HOBt glucoside **19** was isolated and separated by silica gel column chromatography and characterized thoroughly. In the ^{1}H NMR spectrum of glucoside **19**, a doublet of (*J*= 7.9 Hz) was observed at δ 5.40 ppm which is characteristic of anomeric proton and other six pyranoside ring protons were noticed between δ 3.10 – 5.30 ppm along with eight –CH_2 protons of four benzyl ethers. The aromatic protons (20H) of four benzyl ethers were identified as multiplets in the aromatic region at δ 7.10-7.35 ppm. The four characteristic aromatic resonances of HOBt were noticed atδ 7.55, 7.56, 7.76 and 8.05 ppm. In the^{13}C NMR spectrum of compound **19**, the *C*-1 carbon appeared at δ 109.4 ppm. Appearance of other five carbons of the pyranoside ring and four –CH_2 carbons of benzyl ether were observed between δ 68.4 – 84.5 ppm. Six carbons of HOBt were also noticed at δ 110.3, 119.9, 124.7, 128.6, 129.1 and 143.5 ppm out of which two peaks at δ 129.1 and 143.5 did not appear in DEPT giving confirmation about their quaternary

nature. Other 24 carbons belonging to four benzyl groups were also observed between δ 124.7 – 138.5 ppm

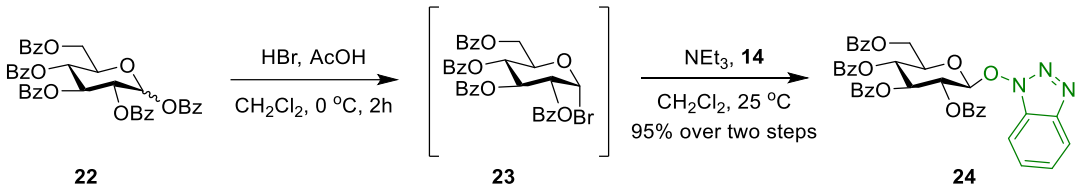
2.4.2 Preparation of HOBt Glucosides

The previous set-back made us to explore the utility of HOBt glucoside **19** as it was found to be solid with long shelf life. Remarkable stability of compound **19** and our interest in the development of stable glycosyl donors encouraged us to study its further utility for glycosylation. HOBt glucoside **19** can also be easily accessed in an alternative way from *n*-pentenyl glucoside **20**via glucosyl bromoside **21**in 80% over two steps (**Scheme 2.7**).



Scheme 2.7 Synthesis HOBt-glucosides via glucosyl bromoside

In fact, glucosyl bromide can also be conveniently prepared from per-*O*-benzoylated glucopyranose **22**by reaction with HBr to give glucosyl bromoside**23**(**Scheme 2.8**) which can be further subjected to aforementioned conditions to afford HOBt-glucoside **24** in very high yield; in addition, the reaction is suitable for scale-up as well.



Scheme 2.8 Synthesis of HOBt Glucosides in multiple gram scale

Formation of desired product **24**was confirmed by NMR and HRMS analysis, which is summarized in **Table 2.1**

Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
Anomeric	6.05 (t, *J* = 9.5 Hz, 1H),	106.4
Benzoates	7.21-8.06 (24H)	165.1, 165.2, 165.6, 165.8

Table 2.1 Characteristic^{1}H and ^{13}C NMR resonance identified in compound**24**

The above data clearly showed that the HOBt glucosides **19** and **24** could be successfully synthesized. From the NMR and MS data it is not very clear whether the HOBt is linked to the glucose through the oxygen atom or the nitrogen atom. Overlapping of resonances in the NMR spectra did not enable us to confirm the nature of the glycosidic linkage. However, to our luck, diffractable quality of single crystals of compound **24** could be obtained by careful but slow evaporation of a methanolic solution of compound **24**. The single crystal diffraction studies confirmed the structural integrity of the HOBt-glucoside **24**. From single crystal diffraction studies and the ORTEP diagram it is quite clear that HOBt is attached to anomeric centre through *O*-atom **(Fig. 2.5)**.

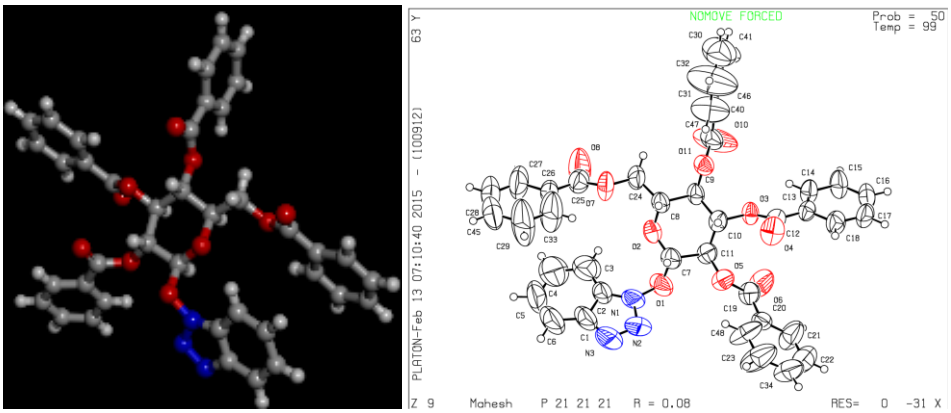
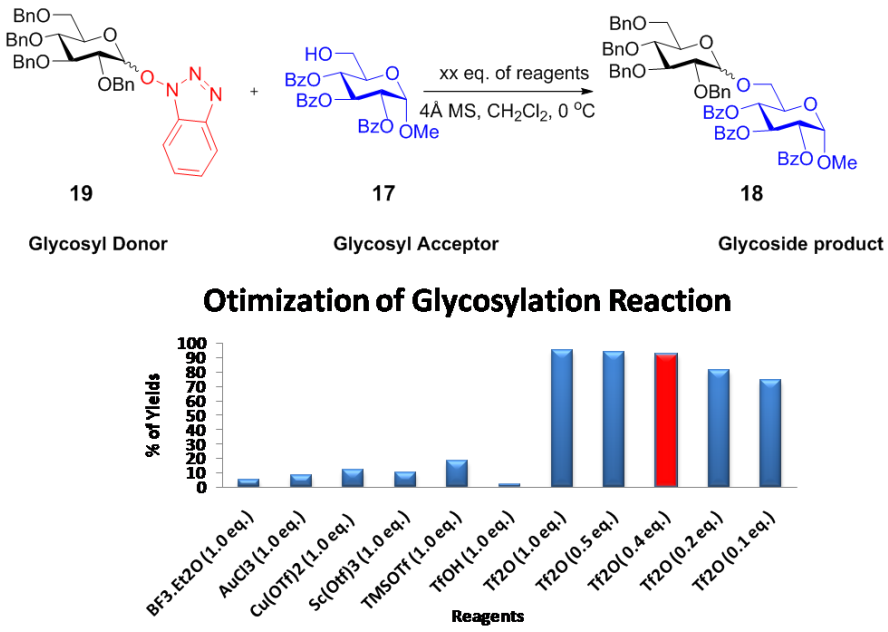


Fig 2.5 ORTEP diagram of Compound **24**

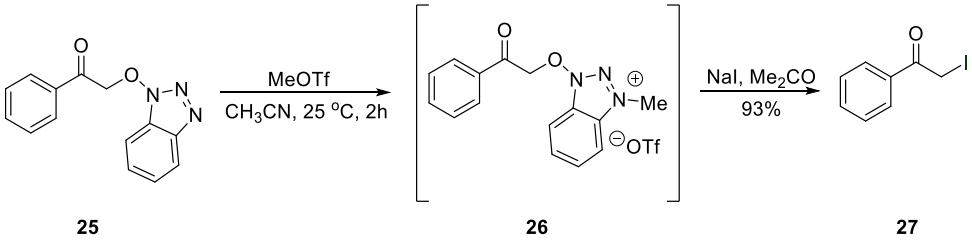
2.4.3 Optimization of Glycosylation Reaction Conditions

Once HOBt glucosyl donor **19** in hand, screening for glycosylation reaction was performed by treating HOBt glucoside **19** and glycosyl acceptor **17**as model compounds in the presence of a molar equivalent of various Lewis acids, Brønsted acids and metal salts as mentioned in **Scheme 2.9**. Chemical glycosylation did not occur with BF_3•Et_2O at 25 °C; however, Lewis acids which can produce Brønsted acids (HCl or TfOH) such as $AuCl_3$, $PdCl_2$, $Cu(OTf)_2$, $Sc(OTf)_3$ and TMSOTf offered the desired disaccharide **18** in 5-10% yield. Discouraging results were obtained even with 10 equivalents of TfOH.



Scheme 2.9 Optimization of Glycosylation Reaction

Diminished yields through the activation of exocyclic *C*1-oxygen sidetracked our efforts to the activation through the triazole moiety. During the period of optimization,Woerpel and coworkers reported independent investigation wherein they reported that the benzotriazole moiety present on ketone **25**can be alkylated by MeOTf through the distal N3-nitrogen into α-iodo ketone **27**through the proposed intermediate **26** (**Scheme 2.10**).[10]This study encouraged to look at the activation of the HOBt-glucoside through the distal nitrogen.



Scheme 2.10 Activation of Benzotriazole Moiety through N3-Nitrogen atom

Accordingly, we treated HOBt glucosides **19** with MeOTf; however, no desired disaaccharide was observed. Nevertheless, addition of molar equivalent of Tf_2O dramatically improved the performance of the reaction to afford required disaccharide **18** in 90% yields as α,β-mixture (3.5:1.0). Almost similar yield of disaccharide **18** was observed with 0.5 or 0.4 equivalent of

Tf_2O as well. The overall performance of the reaction has diminished on decreasing the amount of Tf_2O equivalents. Therefore, optimized glycosylation conditions were found to be 0.4 equivalents of Tf_2O in CH_2Cl_2 at 0 ^{O}C for 15 min. Disaccharide **18**was confirmed by the NMR, HRMS and other spectroscopic tools (**Table 2.3**).

Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
Anomeric	5.58(2H) and 6.19(2H)	96.8, 96.9, 97.3 and 104.1
-OMe	3.44 (6H)	56.6 and 56.7
Benzoates	7.16-8.07 (70H)	165.3, 165.5, 165.8, 165.9, 165.9 and 165.9

Table 2.3.Characteristic ^{1}H and ^{13}C NMR resonance of disaccharide **18**

2.5.4 Plausible Reaction Mechanism for the Activation of HOBt

A plausible mechanism can be advanced at this stage though a thorough mechanistic investigation is desirable. Mechanistically, one can hypothesize that electron push from the endocyclic oxygen of the donor due to the remote activation of distal N3-nitrogen of the triazole moiety can lead to the formation of the oxocarbenium ion **A** and a Zwitterionic species **B** along with TfO^{-}(**Fig. 2.6**). The TfO^{-} ion can regenerate Tf_2O and another intermediate **D**. Acceptor ROH can get transferred to RO^{-} extruding intermediate **E** which can exhibit desmotropism to get converted to HOBt **14.** Equilibration of intermediate **E** to HOBt makes the leaving group a non-competing nucloephile.Alkoxide RO^{-}shall attack on the oxocarbenium ion intermediate (R = -CH_2Ph) to affordα,β-mixture of glycosides or result in a 1,2-*trans* glycoside through trioxolenium ion **C** if the oxocarbenium ion **A** can be stabilized with groups such esters (-OBz) (**Fig. 2.6**).

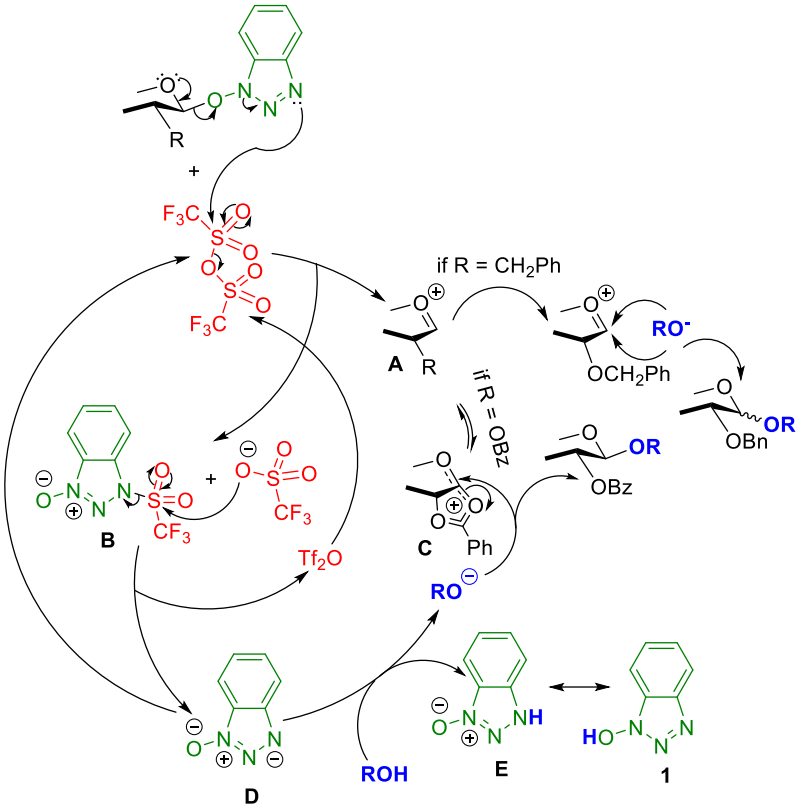


Fig 2.6 Plausible Reaction Mechanism for the HOBt activation

2.4.5 Substrate Scope

The stupendous yield of disaccharide **18** in case of hydoxybenzotriazolyl glucosides **19**enthused us to expand the scope of this glycosylation approach to other pyranosyl donors. Therefore, different HOBt glycosyl donors such asGlc*p*-(**24**), Man*p*-(**28**, **29**), Gal*p*-(**30**) and Rha*p*-(**31**) and GlcTroc- (**32**) have been synthesized by the aforementioned and optimized HOBt donor procedure. Synthesized library of glycosyl donors are subjected to the glycosidations with various acceptors such as **17**, **33-36**under optimized reaction condition (**Chart 2.2**).

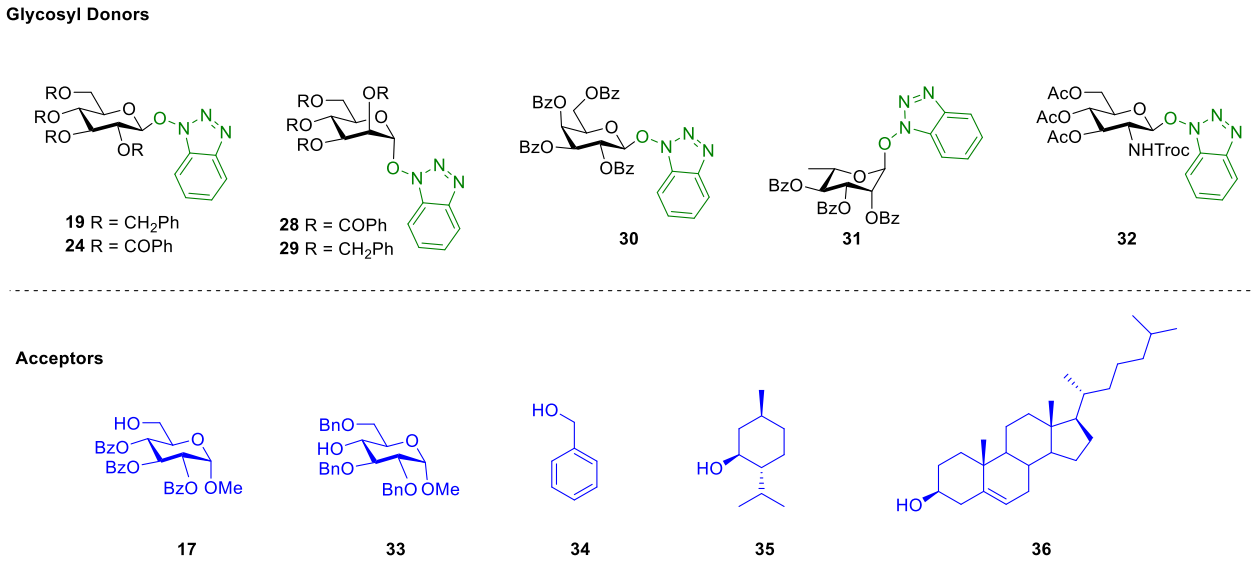
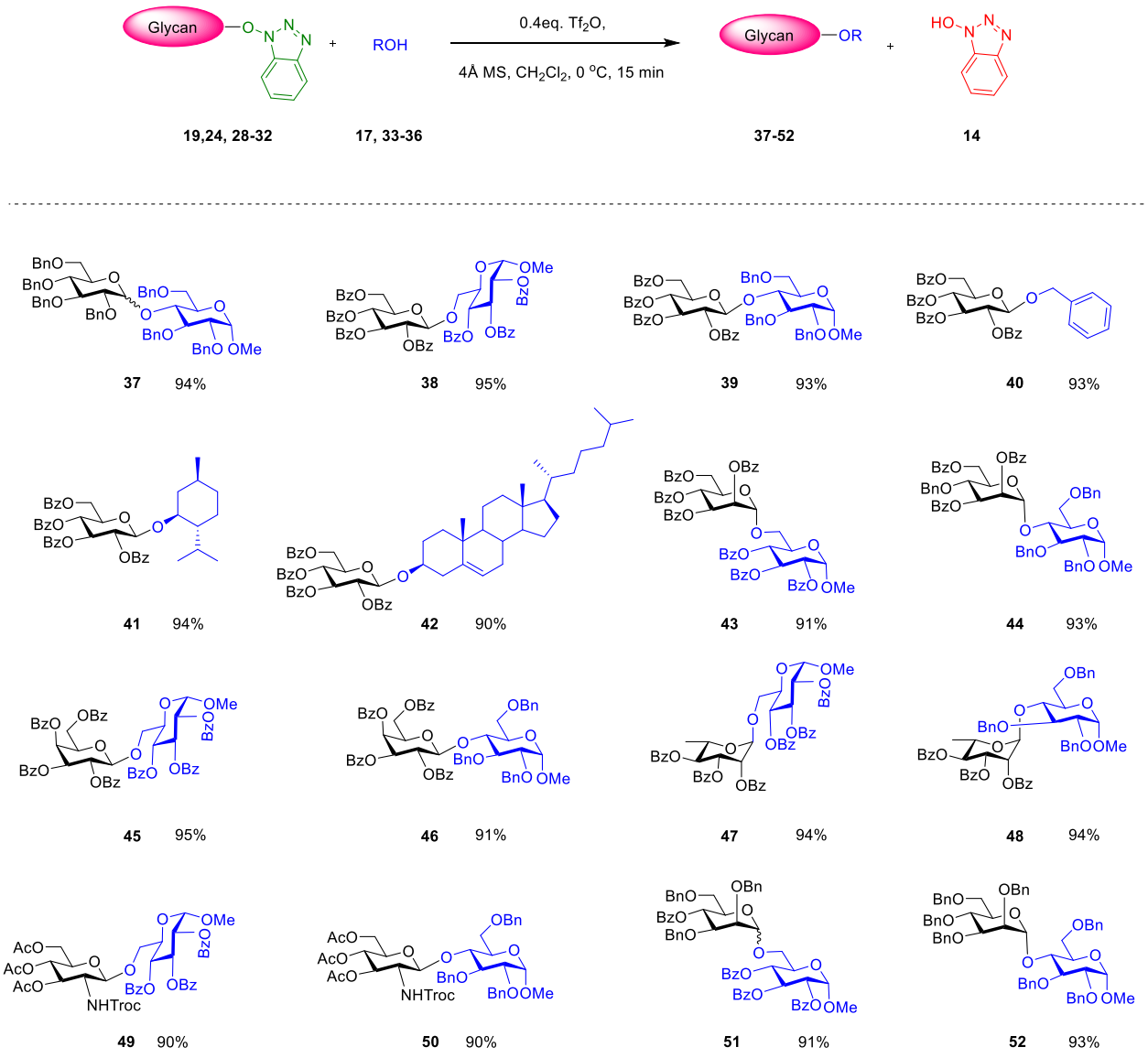


Chart 2.2 Panels of Glycosyl Donors and Acceptors

2.4.6 Synthesis of a Library of *O*-Glycosides

A library of *O*-glycosides was synthesized by using different HOBt-glycosyl donor. Diastereotopic mixture (α:β = 2.2:1.0) disaccharide **37** was isolated in high yield from donor **17**and secondary alcohol **33** as acceptor under optimized conditions. Disarmed donor of Glc*P***24** was treated separately with five different acceptors (**17**, **33-36**) under same reaction conditions to get respective glycosides (**38-42**) with exclusive 1,2-*trans* linkage in high yields. Similar set of reactions were performed using galactose, mannose, rhamnose and glucosamine HOBt glycosyl donors (**28-32**)with primary or secondary –OH glycosyl nucleophiles to afford corresponding disaccharide products (**43-52**) with more than 85% yields in all cases. All products were confirmed by ^{1}H, ^{13}C and DEPT NMR along with HRMS analysis (**Scheme 2.11**).



Scheme 2.11 Synthesis of Library of O-Glycosides Using HOBt Glycosyl Donor

2.4.8 Regeneration of Nucleofuge and Donor

During the glycosylation it was observed that the nuleofuge of the donor was getting regenerated as HOBt **14**.The regeneration of the nuleofuge was investigated by UPLC-MS studies (Fig. 2.7) wherein standards of HOBt glycosyl donor **24**, glycosyl acceptor **17**, disaccharide **38**and HOBt **14**samplesare individually injected into the RP-UPLC (Waters 1.7 µm silica column) to note down their standard retention times. Thereafter, the crude mixture of glycosylation reaction of **24+17** after passing it through a pad of celite was introduced into the UPLC column.

Gratifyingly, the retention time matched with that of the regenerated nucleofuge **14** along with the disaccharide **38**. Furthermore, the generated HOBt **14** was treated with glucosyl bromide **21**to regenerate the glycosyl donor **24**again (**Fig. 2.7**).

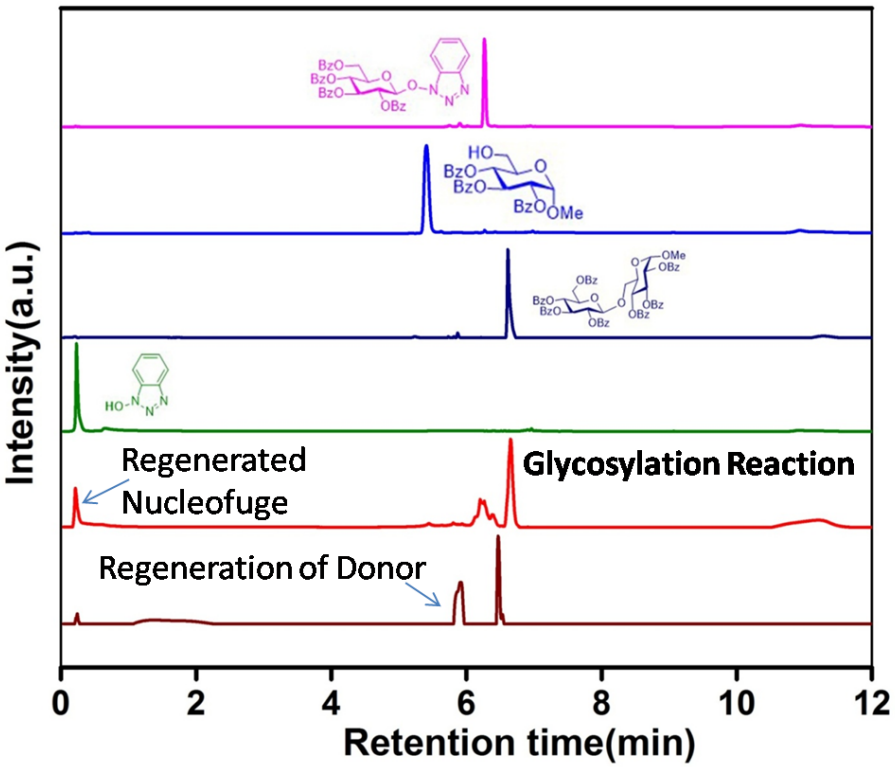
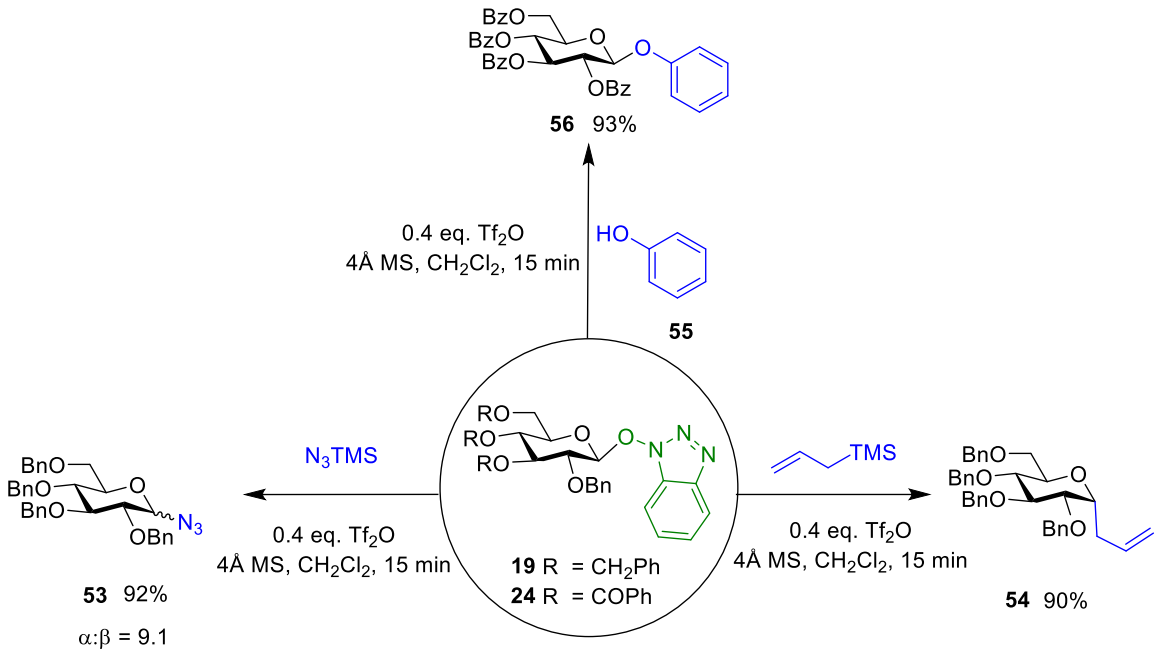


Fig. 2.7 UPLC traces of the chromatogram of the glycosidation between **24** and **17**

2.4.9 Synthesis of Other Glycosides Using HOBt Glycosyl Donors

After *O*-glycosides, *N*-glycosides are the most abundant in Nature. When anomeric carbon of sugar moiety is connected to an aglycon through *N*-atom then it is referred as *N*-glycosides. The azido glycosides are an important class of *N*-glycosides which are intermediates for the synthesis of various glycosyl amides. We have achieved successful synthesis of azido glycoside with HOBt glycosyl donor (**Scheme 2.12**). HOBt glycosyl donor **19** was treated with TMS-azide under standard optimized conditions to afford anomeric mixture of azido glycosides **53**(α:β=9:1) in 92% yields.



Scheme 2.12 Extended Application of HOBt Glycosyl Donor

In addition, the utility HOBt-glycosyl donors further explored to the preparation of *C*-glycosides which are considered as mimic of *O*-glycosides due to their inherent metabolic stability to oligosaccharides. Allyl-TMS was added to a well stirred mixture of HOBt glycosyl donor **19**in $CH_2Cl_2$and molecular sieves power under optimized condition to notice formation of α-allylic *C*-glucoside **54** as exclusive product in 15 min.

In addition, HOBt-glycosyl donors **19** and **24** were also investigated for the synthesis of phenolic and aminoxy glycosidic linkages. Phenol **55** was reacted with HOBt glucosyl donor **24** under optimized reaction conditions to get phenolic glucosides **56** in 92% yields within 15 min. **2.5**

2.5 Conclusions

In summary, hydroxybenzotriazolyl glycosides are identified as stable glycosyl donors that are suitable for the expedient synthesis of *O*-glycosides, azido (*N*-)glycosides and *C*- glycosides. Glycosidation with HOBt-glycosides occurs due to the remote activation the *N*3-nitrogen of benzotriazole by sub-stoichiometric amount of Tf_2O. Activation of the HOBt glycosyl donors can occur with both armed as well as disarmed glycosyl donors. Regenerative-donor glycosidation approach is promising as it reduces the chemical waste; therefore, enhances the overall atom and step economy during the glycosidation.

2.6 Experimental Section

A) General Experimental Procedure for the Synthesis of Hydroxylbenzotriazolyl Glycosyl Donors (24, 28, 30, 31, 32): From Glycosyl Bromide with Et_3N as base: Glycosyl bromide (1mmol in dry CH_2Cl_2 (5 mL) was stirred under nitrogen atmosphere for 5 min. Solid HOBt **14** (1.1 mmol) was added and followed by Et_3N(1mmol). The resulting reaction mixture was stirred for 2 h at 25 ^oC. At the end of the reaction as adjudged by TLC examination, the reaction mixture was concentrated in *vacuo.* The crude residue was purified by silica gel column chromatography to afford corresponding glycosyl donors **24, 28, 30, 31, 32**in 90-95% as white solid.

From Glycosyl Bromide with Phase Transfer Catayst: Solid HOBt **14**(1.1 mmol) was dissolved in 2.5ml of 1*N* solution of aqueous $NaHCO_3$. In another 25mL round bottom flask, the glycosyl bromide (1 mmol) was dissolved anhydrous CH_2Cl_2 (5 mL) was stirred under nitrogen for 5 min followed by addition of tetrabutylammonium hydrogensulphate (TBAHS) (1.5mmol) as a phase transfer catalyst. 1*N* Solution of $NaHCO_3$ containing HOBt **14**was added and resulting reaction mixture was stirred for 8 h. The reaction mixture was washed with 250 mL of water and organic phase was separated and was dried over Sodium sulphate and concentrated in *vacuo*. The resulting residue was purified by silica gel column chromatography to afford glycosyl donor in 84% yields.

B) General Procedure for conversion of pent-4-enyl glycosides to glycosyl bromosides: Pent-4-enyl glucoside (**19, 29**) (1mmol) in dry CH_2Cl_2 (10 mL) containing 4Å molecular sieves powder (0.5g) was cooled to -10 ^0C under nitrogen atmosphere. Molecular bromine (127 µL, 1.5mmol) in CH_2Cl_2 (1 mL) was added drop wise to the reaction mixture and stirred at -10 ^0C for additional 10 minutes. The reaction mixture was concentrated under reduced pressure to afford

2,3,4,6-tetra-O- benzyl glycopyranosyl bromide as solid along with 4Å molecular sieves powder which was immediately used in next step without any additional purification using before mentioned procedure to afford glycosyl donor **19** and **24** in 80-82% yield

C) General Procedure for Glycosylation: A solution of glycosyl donor (**19, 24, 28-32**) (1 mmol) and glycosyl acceptor **17, 33-36, 53** (1.1 mmol) in dry CH_2Cl_2 (2.5 ml) in the presence of 4Å molecular sieves (70 wt%) was stirred for 15 min at 0 ºC under N_2 atm. Tf_2O (0.4 mmol) dissolved in 0.5 mL of CH_2Cl_2 was added at 0 ºC and stirred for 30 min. The reaction was quenched by the addition of Et_3N (300 µL) and stirred for additional 15 min and filtered through a pad of celite, concentrated *invacuo* and the resulting residue was purified by silica gel column chromatography to afford glycosides **18, 37-52**, **56**in 80-94% yields.

1*H*-benzo[d][1,2,3]triazol-1-ol (14): $[\alpha]^{25}_D$ (H_2O, *c*1.0): 102.5º; IR(cm^{-1}, $CHCl_3$): 1454, 1362, 1271, 1209, 1153, 1090, 746, 700; ^{1}H NMR (399.78 MHz, CD_3OD): δ 7.20 (dddd, J= 9.4, 8.1, 6.9, 0.9Hz 2H), 7.45-7.41 (m,1H),7.56 (dd, J =8.3,10.1Hz, 1H); ^{13}C NMR (100.67 MHz, CD_3OD): δ 111.9, 118.9, 127.6, 128.6, 129.9, 143.0; HRMS (ESI-MS): m/z calcd for [$C_6H_4N_3ONa^+$]: 158.0339; Found: 158.0331.

Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α/β-D-glucopyranosyl)-α-D-glucopyranoside (18): $[\alpha]^{25}_D$ ($CHCl_3$, *c*1.0): 52.2º; IR(cm^{-1}, $CHCl_3$): 3031, 2929, 1730, 1600, 1494, 1453, 1317, 1209, 1098, 747, 706; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.44 (d, *J* = 22.8 Hz, 6H), 3.56 (ddd, *J* = 18.6, 10.3, 2.8 Hz, 4H), 3.61 – 3.94 (m, 10H), 4.01 (t, *J* = 9.3 Hz, 2H), 4.32 – 4.54 (m, 6H), 4.54 – 4.70 (m, 14H), 4.71 – 5.13 (m, 4H), 5.58 (s, 2H), 6.19 (s, 2H), 7.16 – 7.45 (m, 54H), 7.48 – 7.57 (m, 4H), 7.84 – 7.93 (m, 4H), 7.95 – 8.07 (m, 8H);^{13}C NMR (100.67 MHz, $CDCl_3$): δ 55.6, 55.7, 66.7, 68.3, 68.6, 68.7, 68.9, 69.1, 69.7, 70.0, 70.3, 70.6, 70.7, 72.2, 72.3, 73.2, 73.5, 73.5, 74.9, 75.0, 75.1, 75.6, 75.8, 77.4, 77.7, 80.0, 81.8, 82.4, 84.6, 96.8, 96.9, 97.3, 104.1, 127.6, 127.6, 127.6, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.8, 127.9, 128.0, 128.0, 128.0, 128.0, 128.0, 128.0, 128.0, 128.0, 128.1, 128.1, 128.1, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4,

128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 129.0, 129.1, 129.1, 129.2, 129.3, 129.3, 129.7, 129.7, 129.7, 129.8, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 133.1, 133.2, 133.4, 133.4, 133.4, 133.5, 138.0, 138.1, 138.2, 138.5, 138.5, 138.6, 138.7, 138.9, 165.3, 165.5, 165.8, 165.9, 165.9, 165.9; HRMS (ESI-MS): m/z calcd for [$C_{62}H_{60}O_{14}Na^+$]:1051.3881; Found: 1051.3877.

1*H*-benzo[*d*][1,2,3]triazol-1-yl-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (19): $[\alpha]^{25}_D$ ($CHCl_3$, *c*1.0): 30.5º; IR(cm^{-1}, $CHCl_3$): 3034, 2912, 1454, 1362, 1271, 1209, 1153, 1090, 746, 700; ^1H NMR (399.78 MHz, $CDCl_3$): δ 3.47 (d, *J* = 3.7 Hz, 1H), 3.57 – 3.65 (m, 1H), 3.71 (dd, *J* = 11.0, 4.1 Hz, 1H), 3.77 – 3.88 (m, 2H), 3.93 (t, *J* = 8.3 Hz, 1H), 4.38 – 4.58 (m, 2H), 4.64 (d, *J* = 10.9 Hz, 1H), 4.89 (dd, *J* = 11.0, 2.5 Hz, 2H), 4.94 (d, *J* = 10.8 Hz, 1H), 5.02 (d, *J* = 10.9 Hz, 1H), 5.26 (d, *J* = 10.7 Hz, 1H), 5.40 (d, *J* = 7.9 Hz, 1H), 7.19 – 7.48 (m, 20H), 7.54 (d, *J* = 6.6 Hz, 2H), 7.76 (d, *J* = 8.0 Hz, 1H), 8.05 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 68.4, 73.6, 75.1, 75.3, 75.4, 75.9, 76.9, 80.2, 84.4, 109.3, 110.3, 119.9, 124.7, 127.6, 127.6, 127.7, 127.8, 127.8, 127.9, 127.9, 127.9, 128.0, 128.0, 128.0, 128.0, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5,128.6, 128.6, 128.6, 129.1, 137.7, 137.9, 137.9, 138.3, 143.5; HRMS (ESI-MS): m/z calcd for [$C_{40}H_{39}N_3O_6Na^+$]: 680.2737; Found: 680.2737.

1*H*-benzo[*d*][1,2,3]triazol-1-yl 2,3,4,6-tetra-*O*-benzoyl β-D-glucopyranoside (24): $[\alpha]^{25}_D$ ($CHCl_3$, *c*1.0): 8.1º; IR(cm^{-1}, $CHCl_3$): 1730, 1603, 1450, 1366, 1266, 1030, 981, 755; ^1H NMR (399.78 MHz, $CDCl_3$): δ 4.15 (ddd, *J* = 9.2, 6.0, 2.8 Hz, 1H), 4.45 (dd, *J* = 12.3, 6.1 Hz, 1H), 4.57 (dd, *J* = 12.3, 2.8 Hz, 1H), 5.75 – 5.87 (m, 2H), 5.97 (dd, *J* = 9.6, 8.1 Hz, 1H), 6.05 (t, *J* = 9.5 Hz, 1H), 7.21 – 7.36 (m, 8H), 7.37 – 7.57 (m, 6H), 7.63 (d, *J* = 8.3 Hz, 1H), 7.73 (dd, *J* = 8.2, 1.2 Hz, 2H), 7.83 – 7.94 (m, 5H), 8.06 (dd, *J* = 8.2, 1.1 Hz, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$):δ 62.4, 68.9, 69.9, 72.4, 73.1, 106.4, 109.8, 119.7, 124.8, 128.3, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.6, 128.6, 128.9, 129.0, 129.1, 129.1, 129.6, 129.6, 129.8, 129.8, 129.9, 129.9, 130.1, 130.1, 133.2, 133.5, 133.7, 133.7, 143.3, 165.1, 165.2, 165.6, 165.8; HRMS (ESI-MS): m/z calcd for [$C_{40}H_{31}N_3O_{10}Na^+$]: 736.1907; Found: 736.1921.

1*H*-benzo[*d*][1,2,3]triazol-1-yl 2,3,4,6-tetra-*O*-benzoyl α-D-mannopyranoside (28): $[\alpha]^{25}_D$ ($CHCl_3$, *c*1.0): 37.7º; IR(cm^{-1}, $CHCl_3$): 1728, 1601, 1451, 1315, 1263, 1176, 1069, 1026, 937;^1H NMR (399.78 MHz, $CDCl_3$): δ 4.56 (dd, *J* = 12.6, 4.2 Hz, 1H), 4.78 (dd, *J* = 12.5, 2.3 Hz, 1H),

5.35 (ddd, *J* = 10.2, 3.9, 2.4 Hz, 1H), 6.01 (d, *J* = 1.7 Hz, 1H), 6.15 (dd, *J* = 10.1, 3.3 Hz, 1H), 6.23 (dd, *J* = 3.4, 1.8 Hz, 1H), 6.33 (t, *J* = 10.2 Hz, 1H), 7.27 – 7.33 (m, 2H), 7.35 – 7.42 (m, 7H), 7.43 – 7.48 (m, 1H), 7.49 – 7.63 (m, 4H), 7.65 – 7.70 (m, 1H), 7.90 (dd, *J* = 8.3, 1.1 Hz, 2H), 8.00 – 8.07 (m, 7H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 62.2, 65.9, 68.3, 69.5, 71.5,103.2, 108.2, 120.6, 125.0, 127.2, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 128.7, 128.7, 128.8, 128.8, 129.6, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 133.1, 133.5, 133.7, 134.0, 143.5, 165.3, 165.4, 165.5, 166.0; HRMS (ESI-MS): m/z calcd for [$C_{40}H_{31}N_3O_{10}Na^+$]: 736.1907; Found: 736.1908.

1*H*-benzo[*d*][1,2,3]triazol-1-yl 2,3,4,6-tetra-*O*-benzyl α-D-mannopyranoside (29): $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): -17.7º; IR(cm^{-1}, $CHCl_3$): 3063, 3031, 2869, 1496, 1453, 1362, 1092, 740, 697;^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.37 (ddd, *J* = 9.5, 5.1, 1.9 Hz, 1H), 3.56 – 3.66 (m, 2H), 3.73 (dd, *J* = 11.2, 5.1 Hz, 1H), 4.09 (t, *J* = 9.3 Hz, 1H), 4.34 (d, *J* = 11.9 Hz, 1H), 4.42 (d, *J* = 2.8 Hz, 1H), 4.47 (d, *J* = 11.9 Hz, 1H), 4.52 – 4.70 (m, 3H), 4.86 – 4.98 (m, 2H), 5.03 (d, *J* = 12.0 Hz, 1H), 5.41 (s, 1H), 7.14 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.18 – 7.40 (m, 18H), 7.43 – 7.58 (m, 2H), 7.67 – 7.83 (m, 1H), 7.94 (d, *J* = 8.3 Hz, 1H);^{13}C NMR (100.67 MHz, $CDCl_3$): δ 69.0, 72.0, 73.4, 73.5, 73.9, 74.6, 75.1, 76.3, 81.4, 107.0, 110.5, 119.6, 124.7, 127.4, 127.5, 127.5, 127.5, 127.7, 127.7, 127.8, 128.0, 128.0, 128.0, 128.0, 128.0, 128.0, 128.2, 128.2, 128.3, 128.3, 128.3, 128.4, 128.4, 128.5, 129.2, 137.7, 138.0, 138.1, 138.1, 143.4; HRMS (ESI-MS): m/z calcd for [$C_{40}H_{39}N_3O_6Na^+$]: 680.2737; Found:680.2738.

1*H*-benzo[*d*][1,2,3]triazol-1-yl 2,3,4,6-tetra-*O*-benzoyl β-D-galactopyranoside (30): $[\alpha]^{25}_D$ ($CHCl_3$, *c*1.0): 40.4º; IR(cm^{-1}, $CHCl_3$): 1727, 1451, 1226, 1093, 1025, 146, 708;^{1}H NMR (399.78 MHz, $CDCl_3$): δ 4.32 – 4.39 (m, 1H), 4.46 (dd, *J* = 11.6, 5.2 Hz, 1H), 4.58 (dd, *J* = 11.6, 7.5 Hz, 1H), 5.74 (dd, *J* = 10.3, 3.4 Hz, 1H), 5.82 (d, *J*= 8.4 Hz, 1H), 6.02 – 6.07 (m, 1H), 6.20 (dd, *J* = 10.3, 8.4 Hz, 1H), 7.21 – 7.31 (m, 5H), 7.33 – 7.55 (m, 8H), 7.61 – 7.73 (m, 4H), 7.81 (dd, *J* = 8.2, 1.2 Hz, 2H), 7.94 (d, *J* = 8.5 Hz, 1H), 8.04 – 8.16 (m, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 62.0, 67.7, 67.8, 71.6, 72.7, 107.1, 109.9, 119.9, 124.9, 128.4, 128.4, 128.5, 128.5, 128.6, 128.7, 128.8, 128.8, 128.8, 128.9, 129.0, 129.0, 129.1, 129.7, 129.7, 129.7, 129.9, 129.9, 130.1, 130.1, 130.1, 130.1, 133.3, 133.7, 133.8, 134.0, 143.5, 165.5, 165.5, 165.5, 165.9; HRMS (ESI-MS): m/z calcd for [$C_{40}H_{31}N_3O_{10}Na^+$]: 736.1907; Found: 736.1915.

1*H*-benzo[*d*][1,2,3]triazol-1-yl 2,3,4-tri-*O*-benzoyl β-D-rhamnopyranoside (31): $[\alpha]^{25}_D$ ($CHCl_3$, *c*1.0): 17.1º; IR(cm^{-1}, $CHCl_3$): 3067, 2983, 1729, 1353, 1261,1176 1069, 1027, 925,

907, 709;^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.49 (d, *J* = 6.2 Hz, 3H), 5.14 (dd, *J* = 9.9, 6.2 Hz, 1H), 5.88 – 5.99 (m, 2H), 6.12 (dd, *J* = 10.1, 3.6 Hz, 1H), 6.24 (dd, *J* = 3.6, 1.7 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.40 – 7.66 (m, 9H), 7.72 (d, *J* = 8.3 Hz, 1H), 7.93 (dd, *J* = 8.3, 1.2 Hz, 2H), 8.04 – 8.18 (m, 5H);^{13}C NMR (100.67 MHz, $CDCl_3$):δ17.4, 68.7, 69.5, 69.7, 70.9, 103.5, 108.3, 120.6, 124.9, 127.3, 128.4, 128.4, 128.6, 128.6, 128.6, 128.7, 128.8, 128.8, 128.8, 129.0, 129.8, 129.8, 129.9, 129.9, 130.0, 130.0, 133.4, 133.6, 133.9, 143.5, 165.5, 165.5, 165.7; HRMS (ESI-MS): m/z calcd for [$C_{33}H_{27}N_3O_8Na^+$]: 616.1696; Found: 616.1694.

1*H*-benzo[d][1,2,3]triazol-1-yl 2-*deoxy*-2-(((2,2,2-trichloroethoxy)carbonyl)amino)-3,4,6-tri-*O*-acetyl-β-D-glucopyranoside (32): $[\alpha]^{25}_D$ ($CHCl_3$, *c*1.0): 37.4^0; IR(cm^{-1}, $CHCl_3$): 3268, 3046, 1735, 1353, 1056, 928, 754;^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.88 (s, 3H), 2.03 (s, 3H), 2.08 (s, 3H), 3.81 (ddd, *J* = 10.0, 5.4, 2.3 Hz, 1H), 4.05 (dd, *J* = 12.3, 2.3 Hz, 1H), 4.12 – 4.21 (m, 1H), 4.26 (dd, *J* = 12.3, 5.4 Hz, 1H), 4.72 (d, *J* = 12.1 Hz, 1H), 4.86 (t, *J* = 18.6 Hz, 1H), 5.14 (t, *J* = 9.7 Hz, 1H), 5.48 – 5.57 (m, 1H), 5.68 (d, *J* = 8.8 Hz, 1H), 6.54 (d, *J* = 9.1 Hz, 1H), 7.35 – 7.44 (m, 1H), 7.51 (ddd, *J* = 10.6, 5.7, 2.2 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 1H);^{13}C NMR (100.67 MHz, $CDCl_3$):δ 20.6, 20.7, 20.7, 54.5, 61.7, 68.5, 71.5, 72.5, 74.7, 95.5, 106.3, 110.3, 119.9, 125.1, 128.6, 129.2, 143.4, 154.8, 169.6, 170.5, 170.7; HRMS (ESI-MS): m/z calcd for [$C_{21}H_{23}Cl_3N_4O_{10}Na^+$]:619.0377; Found: 619.0371.

Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl α,β-D-glucopyranosyl)-α-D-glucopyranoside [a:b(2.2:1)](37): $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 39.9^0; IR(cm^{-1}, $CHCl_3$): 3030, 2921, 2804, 1732, 1495, 1454, 1362, 1277, 1206, 1152, 1048, 911, 738; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.40 (d, *J* = 5.2 Hz, 6H), 3.44 (s, 6H), 3.56 – 3.72 (m, 6H), 3.76 (d, *J* = 10.5 Hz, 2H), 3.89 (td, *J* = 12.4, 10.6, 6.5 Hz, 4H), 3.96 (d, *J* = 9.6 Hz, 2H), 4.11 (t, *J* = 9.1, 9.1 Hz, 2H), 4.31 (d, *J* = 12.3 Hz, 2H), 4.38 – 4.50 (m, 4H), 4.50 – 4.61 (m, 8H), 4.64 (d, *J* = 11.1 Hz, 4H), 4.73 (d, *J* = 12.2 Hz, 2H), 4.78 – 5.03 (m, 10H), 5.01 – 5.78 (m, 4H), 7.11 – 7.49 (m, 70H);^{13}C NMR (100.67 MHz, $CDCl_3$): δ 55.2, 55.4, 67.9, 68.2, 69.1, 69.6, 70.1, 71.0, 72.3, 73.2, 73.3, 73.4, 73.5, 73.5, 73.7, 74.5, 74.9, 75.0, 75.0, 75.0, 75.2, 75.5, 75.6, 75.7, 76.7, 77.4, 77.7, 78.1, 78.9, 79.5, 80.3, 80.5, 82.1, 82.1, 82.9, 84.9, 96.7, 97.8, 98.5, 102.6, 126.8, 126.8, 126.8, 126.9, 126.9, 127.2, 127.2, 127.2, 127.3, 127.3, 127.3, 127.3, 127.3, 127.4, 127.4, 127.5, 127.6, 127.6, 127.7, 127.7, 127.7, 127.7, 127.8, 127.8, 127.8, 127.8, 127.8, 127.8, 127.9, 127.9, 127.9, 127.9, 127.9, 127.9, 127.9, 128.0, 128.1, 128.1, 128.1, 128.2, 128.3(12C), 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 137.9,

138.0, 138.1, 138.1, 138.2, 138.2, 138.4, 138.5, 138.6, 138.6, 138.7, 138.8, 139.0, 139.6; HRMS (ESI-MS): m/z calcd for [$C_{62}H_{66}O_{11}Na^+$]:1009.4503; found: 1009.4501.

Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl β-D-glucopyranosyl) α-D-glucopyranoside (38): $[\alpha]^{25}_D$ ($CHCl_3$, *c*1.0): 31.3º; IR(cm^{-1}, $CHCl_3$): 1735, 1452, 1360, 1315, 1093, 710;^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.10 (s, 3H), 3.79 (dd, *J* = 11.3, 7.6 Hz, 1H), 4.07 – 4.18 (m, 2H), 4.19 – 4.27 (m, 1H), 4.45 (dd, *J* = 12.2, 5.0 Hz, 1H), 4.61 (dd, *J* = 12.1, 3.1 Hz, 1H), 4.90 – 5.02 (m, 2H), 5.10 (dd, *J* = 10.2, 3.6 Hz, 1H), 5.32 (t, *J* = 9.9 Hz, 1H), 5.57 (dd, *J* = 9.7, 7.9 Hz, 1H), 5.66 (t, *J* = 9.7 Hz, 1H), 5.93 (t, *J* = 9.7 Hz, 1H), 6.08 (t, *J* = 9.8 Hz, 1H), 7.25 (td, *J* = 7.7, 4.2 Hz, 4H), 7.29 – 7.36 (m, 7H), 7.36 – 7.43 (m, 5H), 7.44 – 7.56 (m, 5H), 7.75 – 7.82 (m, 3H), 7.83 – 7.85 (m, 2H), 7.86 – 7.89 (m, 3H), 7.91 – 7.94 (m, 2H), 7.95 – 8.04 (m, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 55.1, 63.1, 68.8, 69.0, 69.7, 69.8, 70.4, 72.0, 72.1, 72.4, 72.9, 96.5, 101.9, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.8, 128.9, 128.9, 129.1, 129.3, 129.4, 129.6, 129.7, 129.7, 129.7, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 133.1, 133.2, 133.3, 133.3, 133.4, 133.5, 133.5, 165.3, 165.3, 165.5, 165.8, 165.8, 165.9, 166.2; HRMS (ESI-MS): m/z calcd for [$C_{62}H_{52}O_{18}Na^+$]:1107.3051; Found: 1107.3050.

Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-α-D-glucopyranoside (39): $[\alpha]^{25}_D$ ($CHCl_3$, *c*1.0):-25.2º; IR(cm^{-1}, $CHCl_3$):2925, 2856, 1725, 1600, 1451, 1370, 1259, 1173, 1029, 853, 736;^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.27 (s, 3H), 3.38 – 3.55 (m, 3H), 3.73 (ddt, *J* = 11.0, 7.8, 3.6 Hz, 2H), 3.89 (t, *J* = 9.2 Hz, 1H), 3.98 (t, *J* = 9.4 Hz, 1H), 4.27 (dd, *J* = 12.1, 5.0 Hz, 1H), 4.35 (d, *J* = 12.1 Hz, 1H), 4.41 (dd, *J* = 12.1, 3.4 Hz, 1H), 4.50 – 4.62 (m, 2H), 4.70 – 4.85 (m, 4H), 5.09 (d, *J* = 11.2 Hz, 1H), 5.48 (dd, *J* = 9.4, 8.2 Hz, 1H), 5.52 – 5.70 (m, 2H), 7.16 – 7.28 (m, 10H), 7.29 – 7.41 (m, 9H), 7.41 – 7.54 (m, 8H), 7.77 – 7.81 (m, 2H), 7.88 (d, *J* = 7.5 Hz, 4H), 7.95 – 7.98 (m, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 55.4, 63.2, 67.6, 69.5, 69.9, 71.9, 72.3, 73.2, 73.6, 73.7, 75.4, 77.3, 78.8, 80.0, 98.5, 100.5, 127.2, 127.5, 127.5, 127.8, 128.1, 128.1, 128.1, 128.1, 128.1, 128.1, 128.1, 128.3, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.9, 128.9, 128.9, 129.1, 129.7, 129.7, 129.7, 129.8, 129.8, 129.8, 129.8, 129.8, 133.0, 133.2, 133.4, 133.4, 137.9, 138.4, 139.3, 164.9, 165.1, 165.8, 166.1; HRMS (ESI-MS): m/z calcd for [$C_{62}H_{58}O_{15}Na^+$]:1065.3673; Found: 1065.3668.

Benzyl 2,3,4,6-tetra-*O*-benzoyl β-D-glucopyranoside (40):[$\alpha]^{25}_{D}$($CHCl_3$, *c*1.0): -27.1º; IR(cm^{-1}, $CHCl_3$): 2957, 2927, 1726, 1601, 1451, 1263, 1107, 1069, 709; ^{1}H NMR (399.78MHz, $CDCl_3$): δ 4.40 – 4.52 (m, 2H), 4.62 – 4.74 (m, 2H), 4.86 (d, *J* = 11.9 Hz, 1H), 5.18 (d, *J* = 1.7 Hz, 1H), 5.76 (dd, *J* = 3.3, 1.8 Hz, 1H), 5.96 (dd, *J* = 10.1, 3.4 Hz, 1H), 6.12 (t, *J* = 10.0 Hz, 1H), 7.21 – 7.30 (m, 2H), 7.32 – 7.46 (m, 12H), 7.46 – 7.53 (m, 1H), 7.53 – 7.65 (m, 2H), 7.83 (dd, *J* = 8.3, 1.1 Hz, 2H), 7.91 – 7.97 (m, 2H), 8.04 (dd, *J* = 8.3, 1.1 Hz, 2H), 8.11 (dd, *J* = 8.2, 1.3 Hz, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ63.0, 67.1, 69.2, 70.1, 70.3, 70.6, 97.1, 128.3, 128.3, 128.4, 128.4, 128.4, 128.6, 128.6, 128.6, 128.6, 128.7, 128.7, 128.8, 128.8, 129.1, 129.2, 129.4, 129.9, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.0, 133.2, 133.3, 133.6, 133.6, 136.5, 165.5, 165.6, 165.6, 166.3; HRMS (ESI-MS): m/z calcd for [$C_{41}H_{34}O_{10}Na^+$]:709.2050; Found: 709.2050.

(1*S*,2*R*,5*S*)-2-isopropyl-5-methylcyclohexyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranoside (**41**): $[\alpha]^{25}_{D}$($CHCl_3$, *c*1.0): -19.7º; IR(cm^{-1}, $CHCl_3$): 2953, 2951, 2866, 1729, 1601, 1452, 1373, 1265, 1175, 1101, 1020, 710; ^{1}H NMR (399.78MHz, $CDCl_3$): δ 0.60 – 0.92 (m, 14H), 1.56 (d, *J* = 12.3 Hz, 2H), 1.94 (d, *J* = 12.2 Hz, 1H), 2.12 – 2.33 (m, 1H), 3.48 (d, *J* = 4.0 Hz, 1H), 4.04 – 4.22 (m, 1H), 4.49 (dd, *J* = 12.0, 5.7 Hz, 1H), 4.57 – 4.74 (m, 1H), 4.93 (d, *J* = 8.0 Hz, 1H), 5.50 (dd, *J* = 9.8, 8.0 Hz, 1H), 5.65 (d, *J* = 9.7 Hz, 1H), 5.83 – 6.05 (m, 1H), 7.22 – 7.43 (m, 9H), 7.45 – 7.59 (m, 3H), 7.81 – 7.87 (m, 2H), 7.88 – 7.93 (m, 2H), 7.94 – 8.04 (m, 4H).^{13}C NMR (100.67 MHz, $CDCl_3$): δ 15.7, 20.9, 22.1, 23.1, 25.2, 31.5, 34.2, 40.9, 47.4, 63.6, 70.3, 72.1, 72.2, 73.3, 79.2, 99.1, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 129.0, 129.0, 129.0, 129.0, 129.0, 129.6, 129.6,129.7, 129.7, 129.8, 129.9, 129.9, 133.2, 133.2, 133.3, 133.5, 165.2, 165.4, 166.0, 166.2; HRMS (ESI-MS): m/z calcd for [$C_{44}H_{46}O_{10}Na^+$]:757.2989; Found: 757.2986.

Cholesteryl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranoside (**42**): $[\alpha]^{25}_{D}$($CHCl_3$, *c*1.0):-11.3º; IR(cm^{-1}, $CHCl_3$):2928, 2860, 1729, 1455, 1268, 1176, 1107, 711;^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.64 (s, 3H), 0.84 (d, *J* = 1.8 Hz, 3H), 0.86 (d, *J* = 1.7 Hz, 3H), 0.88 (s, 3H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.95 – 1.24 (m, 9H), 1.27 – 1.71 (m, 14H), 1.86 – 1.95 (m, 2H), 1.95 – 2.03 (m, 1H), 2.04 – 2.22 (m, 2H), 3.52 (dt, *J* = 10.6, 5.4 Hz, 1H), 4.14 (ddd, *J* = 9.5, 5.9, 3.4 Hz, 1H), 4.51 (dd, *J* = 12.0, 5.9 Hz, 1H), 4.59 (dd, *J* = 12.0, 3.3 Hz, 1H), 4.93 (d, *J* = 7.9 Hz, 1H), 5.21 (d, *J* = 5.1 Hz, 1H), 5.49 (dd, *J* = 9.8, 7.9 Hz, 1H), 5.62 (t, *J* = 9.7 Hz, 1H), 5.88 (t, *J* = 9.6 Hz, 1H), 7.20 – 7.42 (m, 9H), 7.43 – 7.57 (m, 3H), 7.77 – 7.85 (m, 2H), 7.89 (dd, *J* = 8.2, 1.2 Hz, 2H), 7.91 – 7.97 (m, 2H), 7.95 – 8.06 (m, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 12.0, 18.9, 19.4,

21.1, 22.7, 23.0, 23.9, 24.4, 28.2, 28.4, 29.7, 29.8, 31.9, 32.0, 35.9, 36.3, 36.8, 37.2, 39.0, 39.7, 39.9, 42.4, 50.2, 56.3, 56.9, 63.5, 70.2, 72.2, 72.2, 73.2, 80.6, 100.3, 122.1, 128.4, 128.4, 128.5, 128.5, 128.5, 128.6, 128.6, 128.9, 129.0, 129.6, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.0, 133.2, 133.3, 133.3, 133.6, 140.5, 165.2, 165.4, 166.0, 166.2; HRMS (ESI-MS): m/z calcd for $[C_{61}H_{72}O_{10}Na^+]$:987.5023; Found:987.5023.

Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl α-D-mannopyranosyl)-α-D-glucopyranoside (**43**): $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 8.7^0; IR(cm^{-1}, $CHCl_3$):3022, 1727, 1451, 1368, 1261, 1099, 973, 713; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.62 (s, 3H), 3.78 (dd, *J* = 10.7, 1.9 Hz, 1H), 4.10 (dd, *J* = 10.8, 6.2 Hz, 1H), 4.30 – 4.46 (m, 2H), 4.54 (ddd, *J* = 10.0, 4.8, 2.2 Hz, 1H), 4.63 (dd, *J* = 12.1, 2.2 Hz, 1H), 5.16 (d, *J* = 1.5 Hz, 1H), 5.26 (dd, *J* = 10.2, 3.7 Hz, 1H), 5.33 (d, *J* = 3.7 Hz, 1H), 5.58 (t, *J* = 9.9 Hz, 1H), 5.77 (dd, *J* = 3.2, 1.8 Hz, 1H), 5.99 (dd, *J* = 10.1, 3.3 Hz, 1H), 6.09 (t, *J* = 10.0 Hz, 1H), 6.21 (t, *J* = 9.8 Hz, 1H), 7.26 – 7.36 (m, 6H), 7.38 – 7.50 (m, 11H), 7.55 (t, *J* = 7.3 Hz, 2H), 7.58 – 7.65 (m, 2H), 7.85 – 7.89 (m, 2H), 7.92 – 7.96 (m, 2H), 7.97 – 8.05 (m, 6H), 8.06 – 8.15 (m, 4H);^{13}C NMR (100.67 MHz, $CDCl_3$): δ 55.8, 62.8, 66.6, 67.0, 68.4, 69.1, 69.5, 70.1, 70.5, 70.7, 72.2, 97.1, 97.6, 128.4, 128.4, 128.4,128.4, 128.4, 128.5, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.7, 128.7, 128.7, 128.9, 129.2, 129.3, 129.3, 129.4, 129.4, 129.9, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.0, 130.0, 130.1, 130.1, 130.1, 130.1, 133.2, 133.2, 133.3, 133.5, 133.6, 133.6, 133.7, 165.5, 165.5, 165.5, 165.7, 165.9, 165.9, 166.2; HRMS (ESI-MS):m/z calcd for $[C_{62}H_{52}O_{15}Na^+]$:1107.3051; Found: 1107.3049.

Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl α-D-mannopyranosyl)-α-D-glucopyranoside (**44**): $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 18.5^0; IR(cm^{-1}, $CHCl_3$):3030, 2921, 2864, 1732, 1495, 1363, 1282, 1100, 1050, 739, 698; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.40 (d, *J* = 5.2 Hz, 3H), 3.44 (s, 3H), 3.56 – 3.72 (m, 3H), 3.76 (d, *J* = 10.5 Hz, 1H), 3.89 (td, *J* = 12.4, 10.6, 6.5 Hz, 2H), 3.96 (d, *J* = 9.6 Hz,1H), 4.11 (t, *J* = 9.1, 9.1 Hz, 1H), 4.31 (d, *J* = 12.3 Hz, 1H), 4.38 – 4.50 (m, 2H), 4.50 – 4.61 (m, 4H), 4.64 (d, *J* = 11.1 Hz, 2H), 4.73 (d, *J* = 12.2 Hz, 1H), 4.78 – 5.03 (m, 5H), 5.01 – 5.78 (m, 2H), 7.11 – 7.49 (m, 35H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 55.3, 69.4, 69.8, 72.1, 72.3, 73.0, 73.2, 73.3, 74.9, 75.0, 75.0, 75.1, 76.3, 77.1, 77.8, 79.8, 80.0, 81.6, 97.7, 100.6, 126.8(2C), 127.2(2C), 127.5(2C), 127.6(2C), 127.7(4C), 127.8(2C), 128.7(3C), 128.1(2C), 128.2(2C), 128.3(8C), 128.4(2C), 128.4(2C), 128.5(2C), 137.9, 138.4, 138.4, 138.6, 138.6, 138.7, 138.9; HRMS (ESI-MS): m/z calcd for $[C_{62}H_{66}O_{11}Na^+]$:1009.4503; Found: 1009.4508.

Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl β-D-glucopyranosyl) α-D-galactopyranoside (**45**): $[\alpha]^{25}_{D}$($CHCl_3$, *c*1.0): 6.0^0; IR(cm^{-1}, $CHCl_3$): 3022, 1727, 1451, 1368, 1261, 1099, 973, 713; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.10 (s, 3H), 3.80 (dd, *J* = 11.3, 7.6 Hz, 1H), 4.18 (dd, *J* = 11.3, 1.6 Hz, 1H), 4.24 – 4.29 (m, 1H), 4.33 (s, 1H), 4.38 – 4.44 (m, 1H), 4.60 (dd, *J* = 11.2, 6.4 Hz, 1H), 4.90 – 4.98 (m, 2H), 5.06 (dd, *J* = 10.2, 3.6 Hz, 1H), 5.34 (t, *J* = 9.9 Hz, 1H), 5.64 (dd, *J* = 10.4, 3.5 Hz, 1H), 5.84 (dd, *J* = 10.4, 7.9 Hz, 1H), 6.00 (d, *J* = 3.3 Hz, 1H), 6.08 (t, *J* = 9.8 Hz, 1H), 7.20 – 7.30 (m, 4H), 7.32 – 7.60 (m, 17H), 7.75 – 7.82 (m, 4H), 7.91 (ddd, *J* = 18.1, 8.1, 1.0 Hz, 4H), 8.00 (ddd, *J* = 7.1, 3.4, 2.0 Hz, 4H), 8.04 – 8.08 (m, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 55.2, 62.0, 68.2, 68.8, 69.3, 69.7, 69.9, 70.5, 71.5, 71.7, 96.6, 102.4, 128.3, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 128.7, 128.7, 128.9, 128.9, 129.1, 129.2, 129.3, 129.3, 129.5, 129.5, 129.7, 129.7, 129.8, 129.9, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.1, 130.1, 130.1, 133.2, 133.4, 133.4, 133.4, 133.4, 133.6, 133.7, 165.5, 165.6, 165.6, 165.7, 165.8, 165.8, 166.1;HRMS (ESI-MS): m/z calcd for [$C_{62}H_{52}O_{18}Na^+$] :1107.3051; Found:1107.3051.

Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl β-D-galactopyranosyl)-α-D-glucopyranoside (**46**): $[\alpha]^{25}_{D}$($CHCl_3$, *c*1.0): -23.9^0; IR(cm^{-1}, $CHCl_3$): 3030, 2925, 1724, 1452, 1362, 1266, 1174, 1098, 708;^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.30 (d, *J* = 1.1 Hz, 3H), 3.44 (d, *J* = 10.7 Hz, 1H), 3.46 – 3.58 (m, 2H), 3.70 (d, *J* = 9.9 Hz, 1H), 3.86 – 3.97 (m, 2H), 3.99 – 4.08 (m, 1H), 4.19 (ddd, *J* = 11.2, 7.6, 1.3 Hz, 1H), 4.32 (d, *J* = 12.2 Hz, 1H), 4.34 – 4.45 (m, 1H), 4.58 (d, *J* = 3.6 Hz, 1H), 4.59 – 4.68 (m, 1H), 4.71 – 4.83 (m, 3H), 4.91 (d, *J* = 11.1 Hz, 1H), 5.18 (d, *J* = 11.1 Hz, 1H), 5.23 – 5.37 (m, 1H), 5.70 (ddd, *J* = 9.9, 8.0, 1.4 Hz, 1H), 5.85 (d, *J* = 3.3 Hz, 1H), 7.14 – 7.32 (m, 10H), 7.33 – 7.58 (m, 17H), 7.72 – 7.79 (m, 2H), 7.80 – 7.88 (m, 2H), 7.90 – 7.98 (m, 2H), 7.97 – 8.06 (m, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 55.5, 61.5, 67.7, 68.0, 69.6, 70.4, 71.1, 72.0, 73.7, 73.8, 75.4, 76.8, 78.8, 80.0, 98.7, 100.5, 127.3, 127.3, 127.3, 127.4, 127.9, 127.9, 128.2, 128.2, 128.2, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.7, 128.7, 128.9, 128.9, 128.9, 129.2, 129.3, 129.6, 129.8, 129.8, 129.8, 129.8, 129.9, 129.9, 130.0, 130.0, 133.3, 133.3, 133.4, 133.5, 137.9, 138.5, 139.5, 165.0, 165.6, 165.6, 166.0; HRMS (ESI-MS): m/z calcd for [$C_{62}H_{58}O_{15}Na^+$]:1065.3673; Found: 1065.3670.

Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3,4-tri-*O*-benzoyl β-D-rhamnopyranosyl)-α-D-glucopyranoside (47): $[\alpha]^{25}_{D}$($CHCl_3$, *c*1.0): 108.2^0; IR(cm^{-1}, $CHCl_3$): 3067, 2948, 1728, 1452, 1260, 1068, 703 ; ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.28 (s, 3H), 3.59 (s, 3H), 3.84 (dd, *J* = 11.8,

7.1 Hz, 1H), 3.94 (dd, *J* = 11.8, 2.1 Hz, 1H), 4.11 – 4.20 (m, 1H), 4.38 (dd, *J* = 9.1, 6.4 Hz, 1H), 5.16 (d, *J* = 1.5 Hz, 1H), 5.27 – 5.32 (m, 2H), 5.52 (t, *J* = 9.9 Hz, 1H), 5.64 (t, *J* = 9.9 Hz, 1H), 5.72 (dd, *J* = 3.4, 1.7 Hz, 1H), 5.79 (dd, *J* = 10.1, 3.4 Hz, 1H), 6.21 (t, *J* = 9.6 Hz, 1H), 7.22 – 7.32 (m, 4H), 7.39 (qd, *J* = 8.8, 7.5, 3.0 Hz, 8H), 7.46 – 7.54 (m, 5H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.79 – 7.82 (m, 2H), 7.86 – 7.90 (m, 2H), 7.94 – 8.02 (m, 6H), 8.07 – 8.11 (m, 2H);^{13}C NMR (100.67 MHz, $CDCl_3$): δ 18.0, 56.3, 67.3, 67.4, 70.0, 70.2, 70.3, 70.9, 71.1, 72.3, 72.6, 97.3, 98.7, 128.7, 128.7, 128.7, 128.7, 128.9, 128.9, 128.9, 128.9, 128.9, 128.9, 129.0, 129.0, 129.3, 129.6, 129.7, 129.7, 129.8, 129.9, 130.1, 130.1, 130.2, 130.2, 130.2, 130.2, 130.4, 130.4, 130.4, 130.4, 130.4, 130.4, 133.5, 133.5, 133.8, 133.8, 133.9, 133.9, 165.9, 165.9, 165.9, 166.2, 166.3, 166.3; HRMS (ESI-MS): m/z calcd for [$C_{55}H_{48}O_{10}Na^+$]:987.2840; Found: 987.2840.

Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4-tri-*O*-benzoyl β-D-rhamnopyranosyl)-α-D-glucopyranoside (**48**): $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): +41.3^0; IR(cm^{-1}, $CHCl_3$): 3067, 2948, 2961, 1728, 1600, 1450, 1260, 1006, 758; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.89 (d, *J* = 6.0 Hz, 3H), 3.41 (s, 3H), 3.62 – 3.69 (m, 1H), 3.74 (d, *J* = 11.0 Hz, 1H), 3.87 (dd, *J* = 20.5, 10.1 Hz, 2H), 3.94 – 4.07 (m, 2H), 4.38 (td, *J* = 7.7, 6.9, 3.0 Hz, 1H), 4.57 (q, *J* = 11.9 Hz, 2H), 4.62 – 4.67 (m, 2H), 4.74 – 4.80 (m, 1H), 4.86 (d, *J* = 11.1 Hz, 1H), 5.15 – 5.28 (m, 2H), 5.56 – 5.58 (m, 1H), 5.62 (t, *J* = 10.0, 1.8 Hz, 1H), 5.79 (dt, *J* = 10.2, 2.5 Hz, 1H), 7.09 – 7.22 (m, 6H), 7.24 – 7.35 (m, 9H), 7.36 – 7.50 (m, 7H), 7.50 – 7.63 (m, 2H), 7.79 – 7.96 (m, 4H), 8.02 – 8.14 (m, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 17.3, 55.4, 67.1, 68.4, 70.1, 70.2, 71.4, 71.8, 73.4, 73.5, 74.9, 75.6, 79.8, 80.4, 97.1, 98.1, 127.4 – 128.1(8C), 128.3 – 128.7(14C), 129.3 – 130.0(8C), 133.3, 133.4, 133.6, 137.8, 138.0, 138.8, 165.8, 165.9, 165.9; HRMS(ESI-MS): m/z calcd for [$C_{55}H_{54}O_{13}Na$]$^+$: 945.3462;Found: 945.3459.

Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2-*deoxy*-2-(((2,2,2-trichloroethoxy)carbonyl)amino)-3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl) α-D-glucopyranoside (**49**): $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): +41.3^0; IR(cm^{-1}, $CHCl_3$): 3293, 3021, 2932, 1729, 1604, 1453, 1267, 1103, 910, 709; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 2.00 (s, 3H), 2.01 (s, 3H), 2.02 (s, 3H), 3.44 (s, 3H), 3.56 – 3.70 (m, 3H), 3.81 (dt, *J* = 10.8, 8.5 Hz, 1H), 4.03 – 4.27 (m, 4H), 4.54 (d, *J* = 8.5 Hz, 1H), 4.62 – 4.83 (m, 2H), 5.06 (t, *J* = 9.6 Hz, 1H), 5.15 – 5.31 (m, 3H), 5.55 (t, *J* = 9.7 Hz, 1H), 5.72 (d, *J* = 8.8 Hz, 1H), 6.13 (t, *J* = 9.8 Hz, 1H), 7.25 (t, *J* = 7.7 Hz, 2H), 7.36 (dt, *J* = 10.2, 7.5 Hz, 4H), 7.50 (dt, *J* = 13.8, 7.4 Hz, 2H), 7.82 (d, *J* = 7.7 Hz, 2H), 7.91 – 7.99 (m, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 20.7, 20.8, 20.8, 55.8, 56.2, 62.0, 68.0, 68.5, 68.6, 69.3, 70.4, 71.9, 72.0, 72.6, 74.6,

95.7, 97.1, 101.5, 128.4, 128.4, 128.5, 128.5, 128.6, 128.6, 128.7, 129.1, 129.2, 129.7, 129.7, 130.0, 130.0, 130.0, 130.0, 133.2, 133.5, 133.8, 154.5, 165.7, 165.8, 165.9, 169.5, 170.7, 170.8; HRMS (ESI-MS): m/z calcd for $[C_{43}H_{44}Cl_3NO_{18}Na]^+$: 990.1522; Found: 990.1525.

Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2-*deoxy*-2-(((2,2,2-trichloroethoxy)carbonyl)amino)-3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl) α-D-glucopyranoside (**50**): $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): $+41.3^0$; IR(cm^{-1}, $CHCl_3$): 3293, 3021, 2932, 1729, 1604, 1453, 1267, 1103, 910, 709; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.90 (s, 3H), 1.97 (s, 3H), 1.99 (s, 3H), 3.32 (s, 3H), 3.45 – 3.61 (m, 3H), 3.66 (dd, *J* = 10.8, 2.6 Hz, 2H), 3.75 – 3.92 (m, 4H), 4.10 (dd, *J* = 12.3, 4.2 Hz, 1H), 4.18 (d, *J* = 8.3 Hz, 1H), 4.31 (d, *J* = 12.2 Hz, 1H), 4.54 (d, *J* = 3.3 Hz, 1H), 4.57 (s, 1H), 4.60 (s, 1H), 4.68 (s, 1H), 4.72 – 4.75 (m, 1H), 4.77 (d, *J* = 4.9 Hz, 1H), 4.83 (s, 1H), 4.86 (d, *J* = 6.3 Hz, 1H), 4.91 (d, *J* = 9.6 Hz, 1H), 4.97 (d, *J* = 11.5 Hz, 1H), 7.18 – 7.35 (m, 11H), 7.39 – 7.44 (m, 2H), 7.46 – 7.50 (m, 2H), 7.53 (d, *J* = 2.1 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 20.8, 20.8, 20.8, 55.4, 56.3, 61.9, 67.3, 68.7, 69.2, 71.3, 72.5, 73.6, 73.8, 74.5, 75.3, 77.2, 78.7, 80.3, 95.7, 98.5, 100.8, 127.2, 127.2, 127.9, 128.2, 128.2, 128.3, 128.3, 128.5, 128.5, 128.6, 129.2, 129.2, 129.3, 129.6, 129.6, 137.5, 138.3, 139.7, 154.0, 169.6, 170.5, 170.8; HRMS (ESI-MS): m/z calcd for $[C_{43}H_{50}Cl_3NO_{15}Na]^+$: 948.2144; Found: 948.2139.

Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl α,β-D-mannopyranosyl)-α-D-glucopyranoside (**51**): $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 52.2^0; IR(cm^{-1}, $CHCl_3$): 2944, 1733, 1453, 1366, 1276, 1214, 1102, 707; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.44 (d, *J* = 22.8 Hz, 6H), 3.56 (ddd, *J* = 18.6, 10.3, 2.8 Hz, 4H), 3.61 – 3.94 (m, 11H), 4.01 (t, *J* = 9.3 Hz, 2H), 4.32 – 4.54 (m, 6H), 4.54 – 4.70 (m, 11H), 4.71 – 5.13 (m, 4H), 5.21 – 5.34 (m, 2H), 5.58 (s, 2H), 6.19 (s, 2H), 7.16 – 7.45 (m, 54H), 7.48 – 7.57 (m, 4H), 7.84 – 7.93 (m, 4H), 7.95 – 8.07 (m, 8H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 55.6, 55.7, 66.7, 68.3, 68.6, 68.7, 68.9, 69.1, 69.7, 70.0, 70.3, 70.6, 70.7, 72.2, 72.3, 73.2, 73.5, 73.5, 74.9, 75.0, 75.1, 75.6, 75.8, 77.4, 77.6, 77.7, 80.0, 81.8, 82.4, 84.6, 96.8, 96.9, 97.3, 104.1, 127.6, 127.6, 127.6, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.7, 127.8, 127.9, 128.0, 128.0, 128.0, 128.0, 128.0, 128.0, 128.0, 128.0, 128.1, 128.1, 128.1, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 129.0, 129.1, 129.1, 129.2, 129.3, 129.7, 129.7, 129.7, 129.8, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 133.1, 133.2, 133.4, 133.4, 133.4, 133.5, 138.0, 138.1, 138.2, 138.5, 138.5,

138.6, 138.7, 138.9, 165.3, 165.5, 165.8, 165.9, 165.9, 165.9; HRMS (ESI-MS): m/z calcd for $[C_{62}H_{60}O_{14}Na^+]$:1051.3881; Found: 1051.3880.

Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl α-D-mannopyranosyl)-α-D-glucopyranoside (**52**): $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 18.5^0; IR(cm^{-1}, $CHCl_3$):3030, 2921, 2864, 1732, 1495, 1363, 1282, 1100, 1050, 739, 698; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.40 (d, *J* = 5.2 Hz, 3H), 3.44 (s, 3H), 3.56 – 3.72 (m, 3H), 3.76 (d, *J* = 10.5 Hz, 1H), 3.89 (td, *J* = 12.4, 10.6, 6.5 Hz, 2H), 3.96 (d, *J* = 9.6 Hz,1H), 4.11 (t, *J* = 9.1, 9.1 Hz, 1H), 4.31 (d, *J* = 12.3 Hz, 1H), 4.38 – 4.50 (m, 2H), 4.50 – 4.61 (m, 4H), 4.64 (d, *J* = 11.1 Hz, 2H), 4.73 (d, *J* = 12.2 Hz, 1H), 4.78 – 5.03 (m, 5H), 5.01 – 5.78 (m, 2H), 7.11 – 7.49 (m, 35H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 55.3, 69.4, 69.8, 72.1, 72.3, 73.0, 73.2, 73.3, 74.9, 75.0, 75.0, 75.1, 76.3, 77.1, 77.8, 79.8, 80.0, 81.6, 97.7, 100.6, 126.8(2C), 127.2(2C), 127.5(2C), 127.6(2C), 127.7(4C), 127.8(2C), 128.7(3C), 128.1(2C), 128.2(2C), 128.3(8C), 128.4(2C), 128.4(2C), 128.5(2C), 137.9, 138.4, 138.4, 138.6, 138.6, 138.7, 138.9; HRMS (ESI-MS): m/z calcd for $[C_{62}H_{66}O_{11}Na^+]$:1009.4503; Found: 1009.4508.

1-*deoxy*-1-azido 2,3,4,6-tetra-*O*-benzyl-α/β-D-glucopyranoside (**53**): $[\alpha]^{25}_D$ ($CHCl_3$, *c*1.0): 22.9^o; IR(cm^{-1}, $CHCl_3$): 3268, 3046, 2912, 2170, 1600, 1460, 1353, 1056, 928, 754;^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.65 (ddd, *J* = 9.8, 6.4, 4.2 Hz, 6H), 3.79 – 3.69 (m, 2H), 3.87 (t, *J* = 9.3 Hz, 2H), 4.48 (dd, *J* = 11.4, 3.8 Hz, 4H), 4.53 – 4.62(m, 2H), 4.65 (dd, *J* = 15.1, 7.5 Hz, 2H), 4.79 (dd, *J* = 15.1, 8.3 Hz, 4H), 4.85 (dd,*J* = 12.4, 7.4 Hz, 4H), 4.93 (t, *J* = 11.3 Hz, 2H), 5.23 (d, *J* = 4.1 Hz, 2H), 7.08 – 7.21 (m, 4H), 7.22 - 7.44 (m, 36H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 68.2, 68.5, 72.6, 73.6, 73.7, 73.9, 75.2, 75.3, 75.9, 76.0, 77.1, 77.2, 77.4, 79.5, 81.8, 81.8, 81.9, 85.0, 88.2, 90.3, 127.8, 127.9, 127.9, 127.9(3C), 128.1(4C), 128.1(5C), 128.2(2C), 128.3, 128.6(6C), 128.5(6C), 128.6(6C), 128.8(4C), 137.7, 137.8, 137.8, 137.9, 138.0, 138.1, 138.4, 138.6;HRMS (ESI-MS): m/z calcd for $[C_{34}H_{35}O_6N_3Na^+]$: 588.2424; Found: 588.2439.

1-*deoxy*-1-allyl 2,3,4,6-tetra-*O*-benzyl α-D-glucopyranoside (**54**): $[\alpha]^{25}_D$ ($CHCl_3$, *c* 1.0): 55.8^o; IR(cm^{-1}, $CHCl_3$): 3268, 3046, 2912, 1600, 1460, 1353, 1056, 928, 754;^{1}H NMR (399.78 MHz, $CDCl_3$): δ 2.37 - 2.7(m, 2H), 3.57 – 3.84 (m, 6H), 4.14 (dt, J=1.2, 5.1, 1H), 4.42 – 4.51 (m, 2H), 4.59 – 4.54 (m, 2H), 4.66 – 4.73 (m, 1H), 4.81 (dd, *J*=10.7, 1.6, 2H), 4.94 (d, *J*=10.9, 1H), 5.10 (dt, *J*=10.2, 5.2, 2H), 5.82 (ddt, *J*=17.2, 10.2, 6.8, 1H), 7.12 (dd, *J*=6.9, 2.5, 2H), 7.21 – 7.4 (m, 18H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 68.2, 71.2, 73.2, 73.6, 73.6, 75.2, 76.6, 78.2, 80.2, 80.2, 82.5, 117.0, 127.7, 127.8, 127.9, 127.9, 127.9(2C), 128.0(2C), 128.5(2C), 128.5(2C),

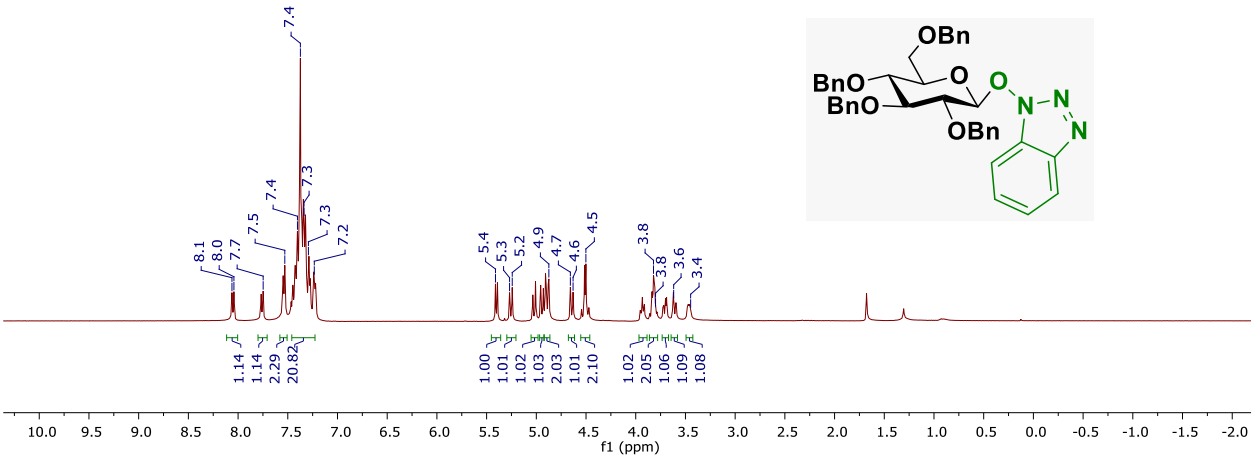
128.5(2C), 128.5(4C), 128.6(2C), 134.8, 138.1, 138.2, 138.3, 138.3; HRMS(ESI-MS): m/z calcd for [$C_{37}H_{40}O_5Na^+$]: 587.2773; Found: 587.2776.

Phenyl 2,3,4,6-tetra-*O*-benzoyl β-D-glucopyranoside (**56**): $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 29.7º; IR(cm-1, $CHCl_3$): 1725, 1597, 1492, 1451, 1260, 1071, 977, 844, 707; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 4.38 (ddd, *J* = 9.7, 6.7, 3.0 Hz, 1H), 4.57 (dd, *J* = 12.1, 6.7 Hz, 1H), 4.72 (dd, *J* = 12.1, 3.0 Hz, 1H), 5.44 (d, *J* = 7.8 Hz, 1H), 5.75 (t, *J* = 9.6 Hz, 1H), 5.86 (dd, *J*= 9.6, 7.8 Hz, 1H), 6.04 (t, *J* = 9.5 Hz, 1H), 7.00 – 7.11 (m, 3H), 7.16 – 7.24 (m, 2H), 7.33 (t, *J* = 7.8 Hz, 2H), 7.43 (dt, *J* = 23.4, 7.7 Hz, 7H), 7.50 – 7.63 (m, 3H), 7.88 – 7.92 (m, 2H), 7.98 (ddd, *J* = 9.9, 8.3, 1.1 Hz, 4H), 8.07 (dd, *J* = 8.2, 1.2 Hz, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 63.4, 69.8, 71.8, 72.7, 73.0, 99.8, 117.4, 117.4, 123.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.8, 128.9, 129.2, 129.6, 129.6, 129.7, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 133.3, 133.4, 133.5, 133.7, 157.1, 165.2, 165.4, 165.9, 166.2; HRMS (ESI-MS): m/z calcd for [$C_{40}H_{32}O_{10}Na^+$]:695.1893; Found: 695.1889.

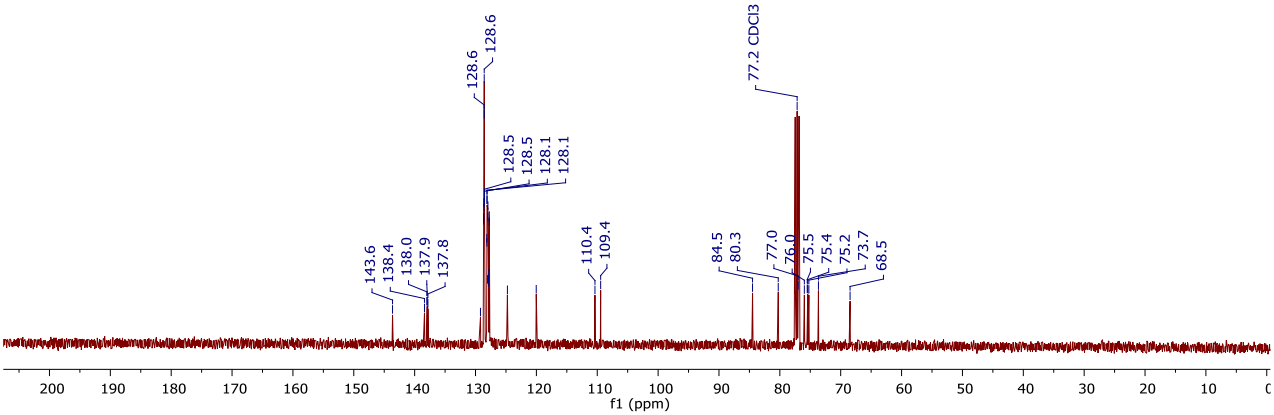
2.9 Representative Spectral Charts

Kindly see the supporting documents file in *J. Org. Chem.*, **2017**, *82*, 11494-11504 for spectral charts of compounds (**14**, **18**, **19**, **24**, **28**, **29**, **30**, **31**, **32**, **37**, **38**, **39**, **40**, **41**, **42**, **43**, **44**, **45**, **46**, **47**, **48**, **49**, **50**, **51**, **52**, **53**, **54** and **56**).

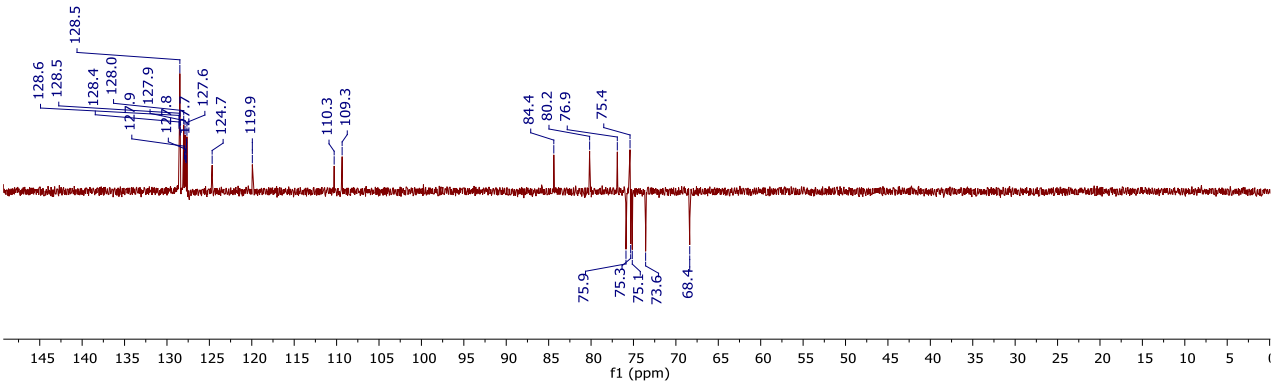
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **19**



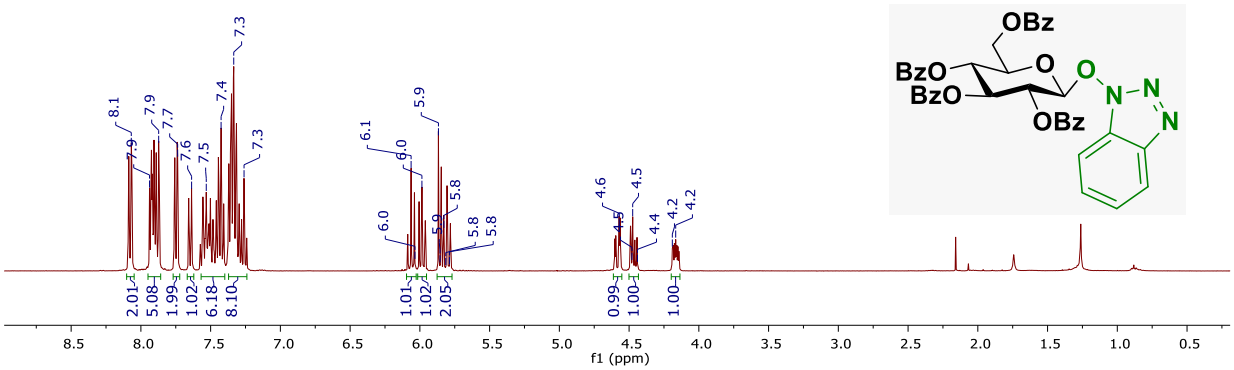
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **19**



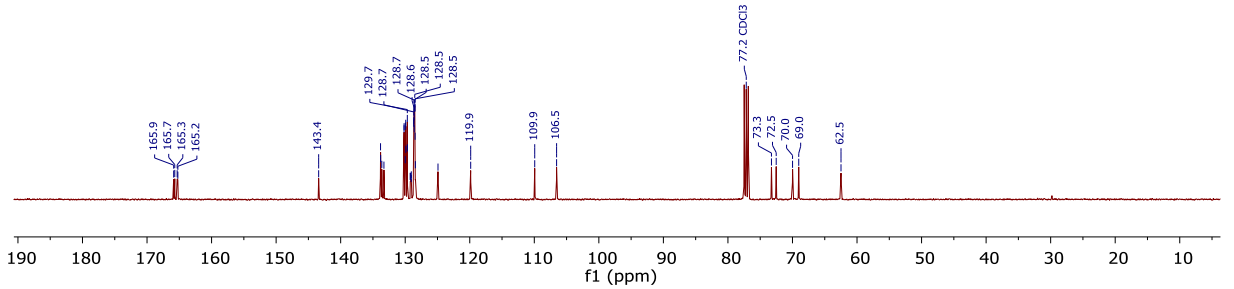
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **19**



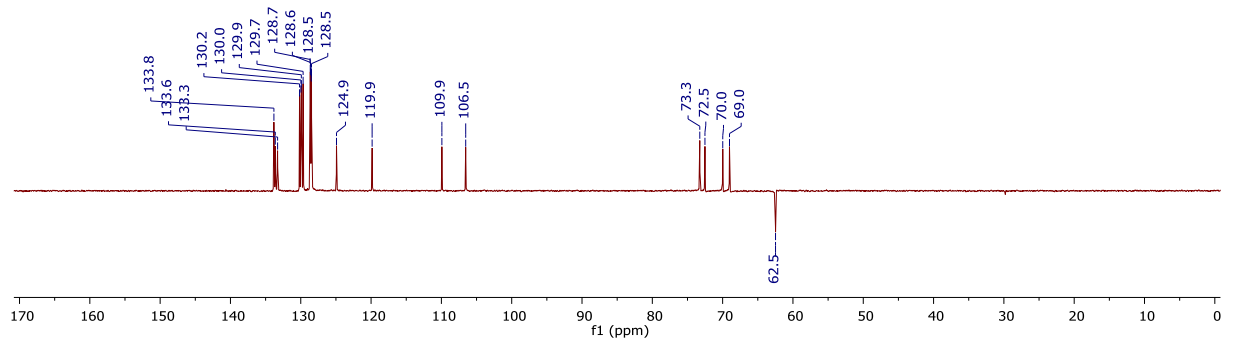
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **24**



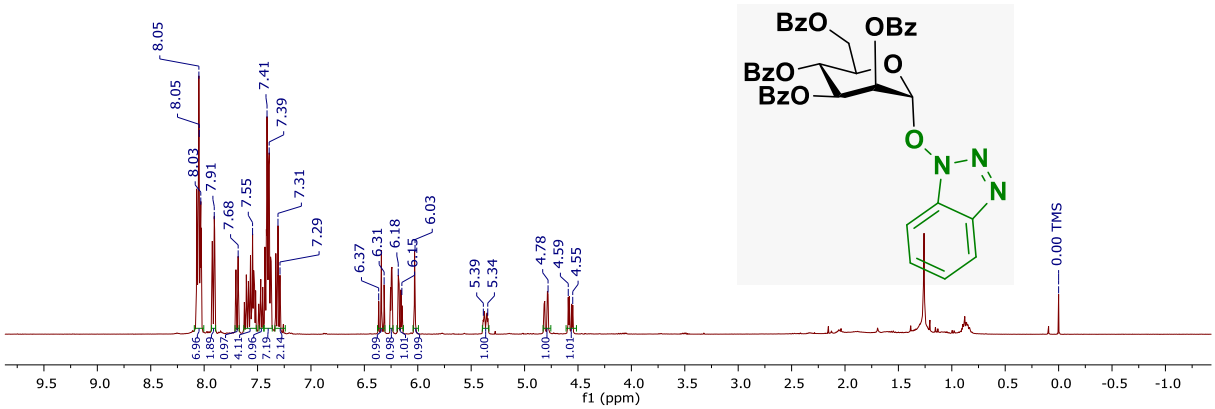
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **24**



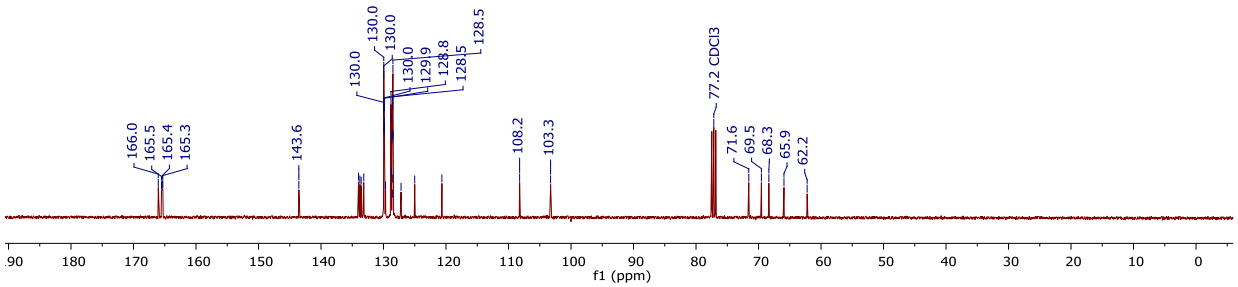
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **24**



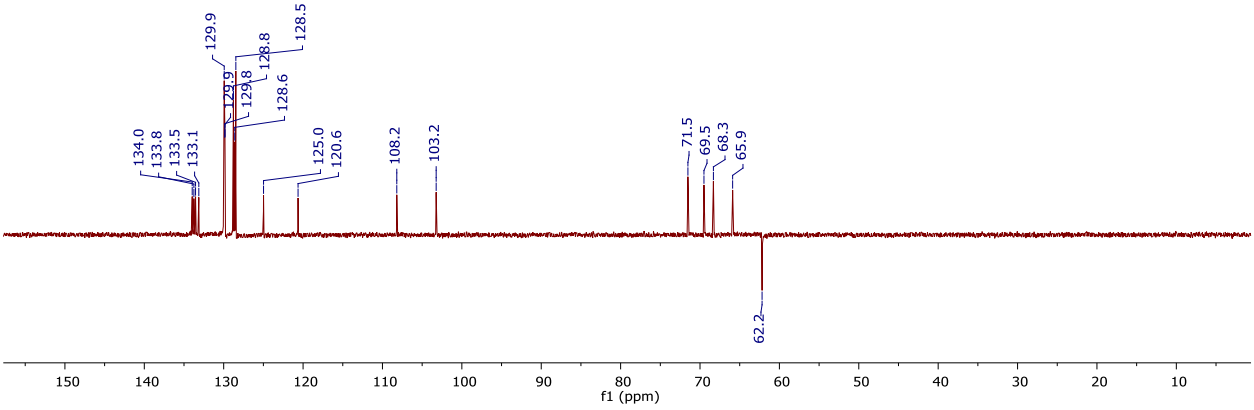
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **28**



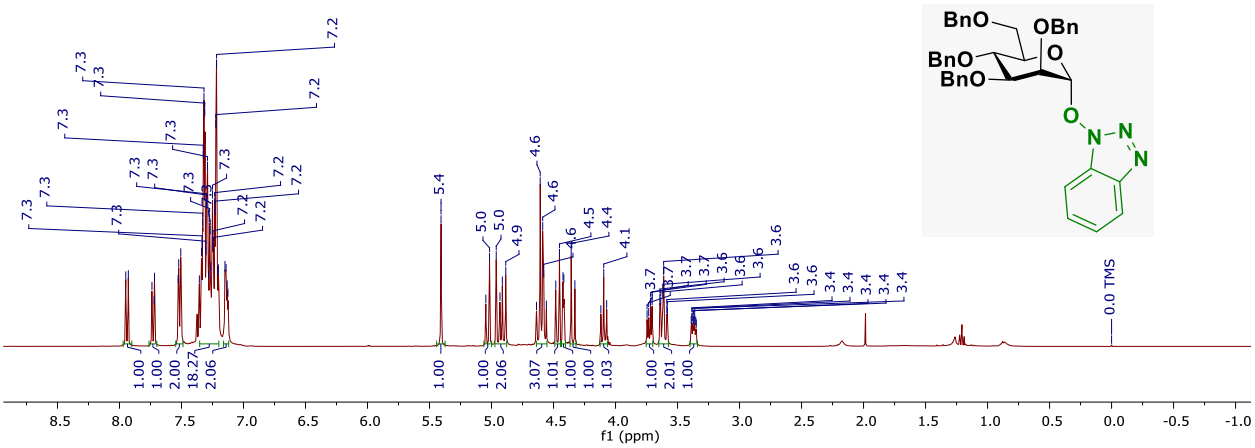
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **28**



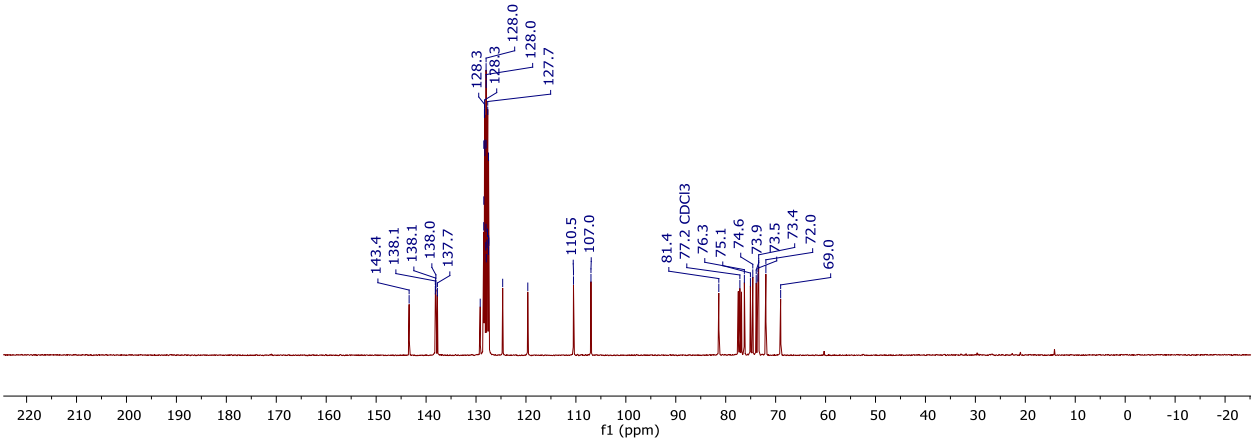
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **28**



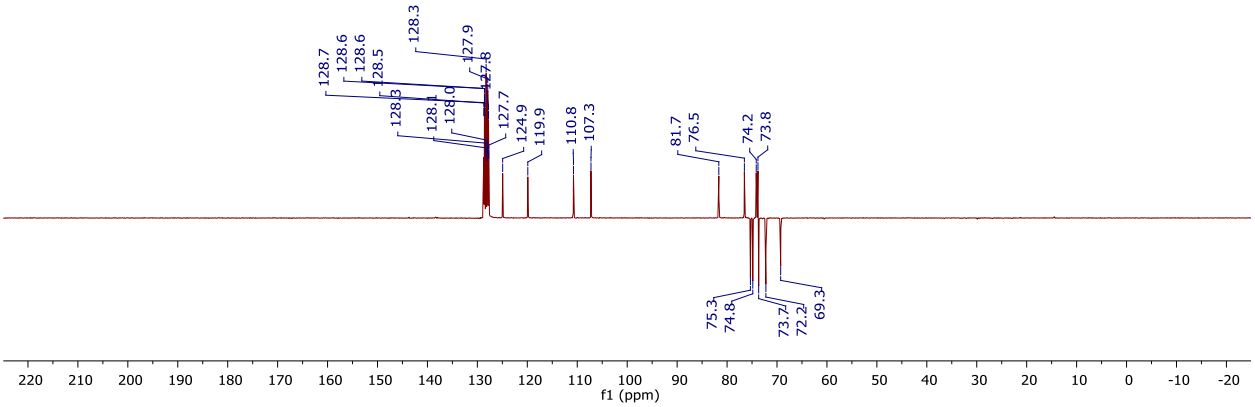
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **29**



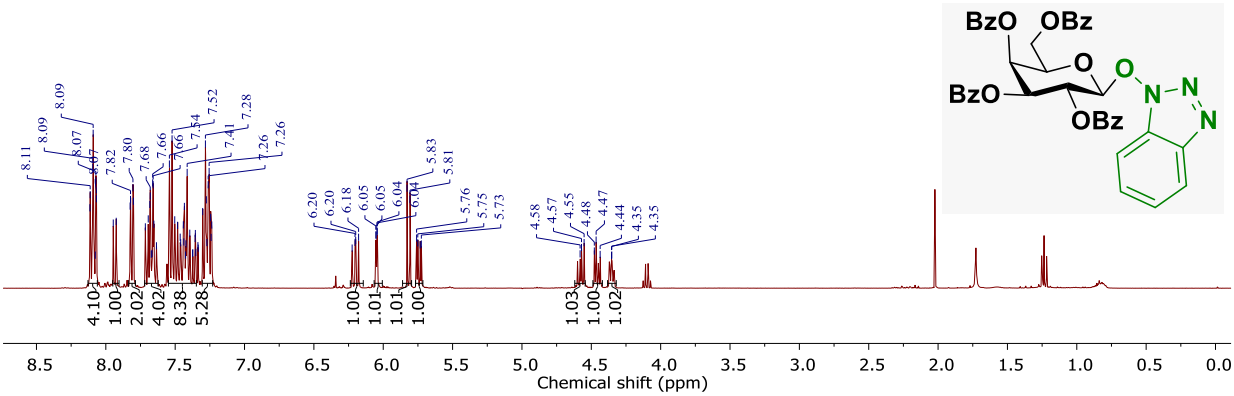
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **29**



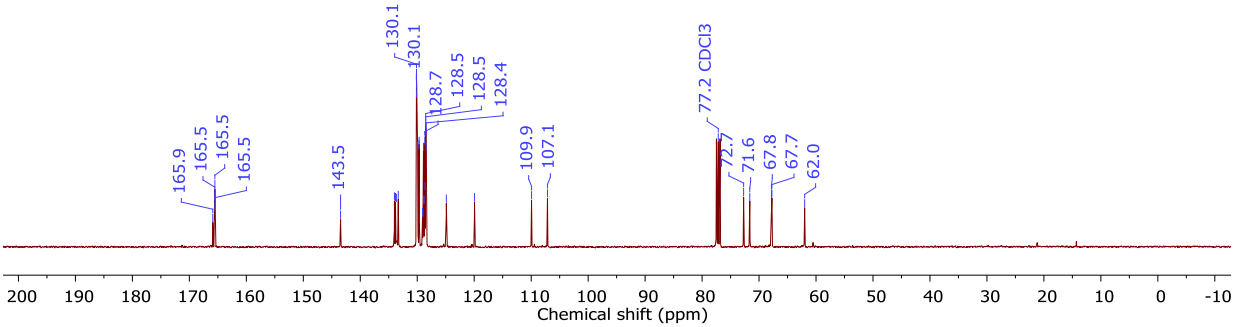
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **29**



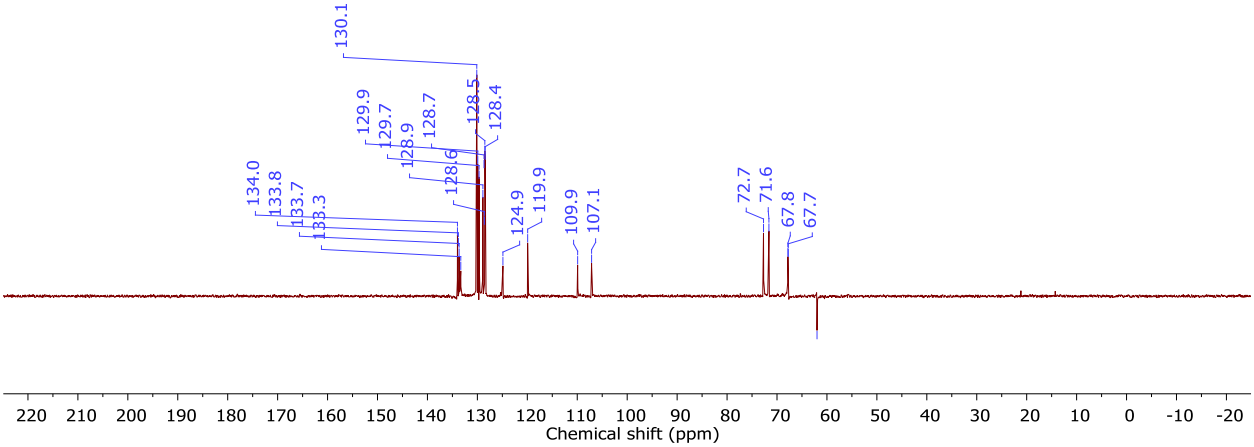
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **30**



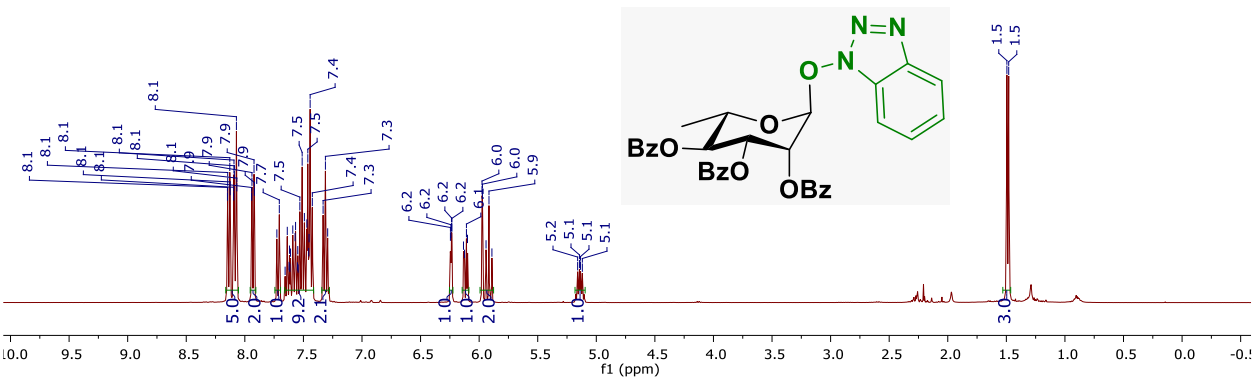
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **30**



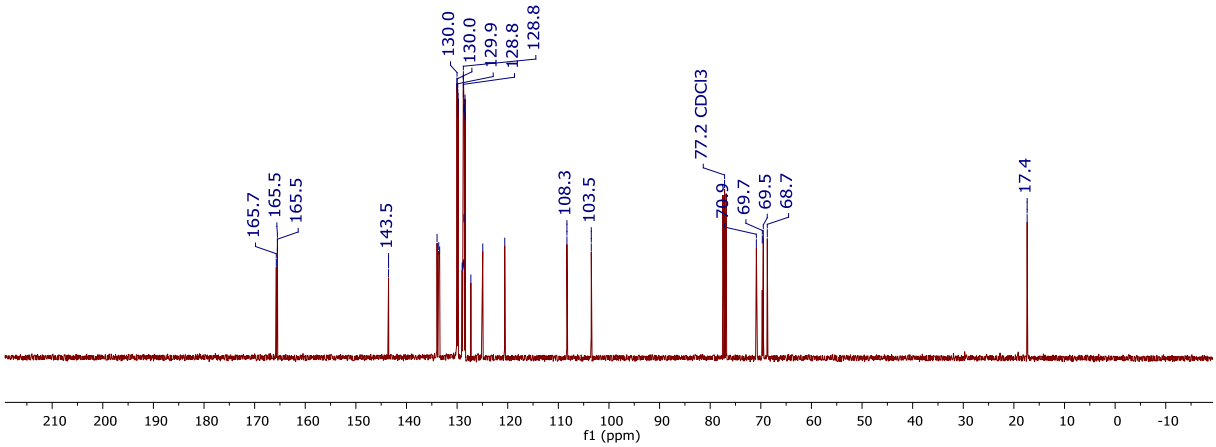
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **30**



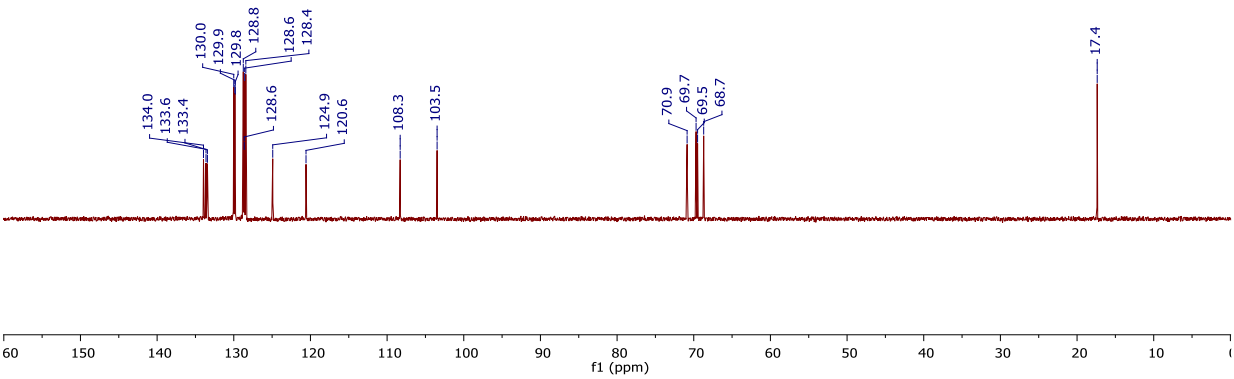
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **31**



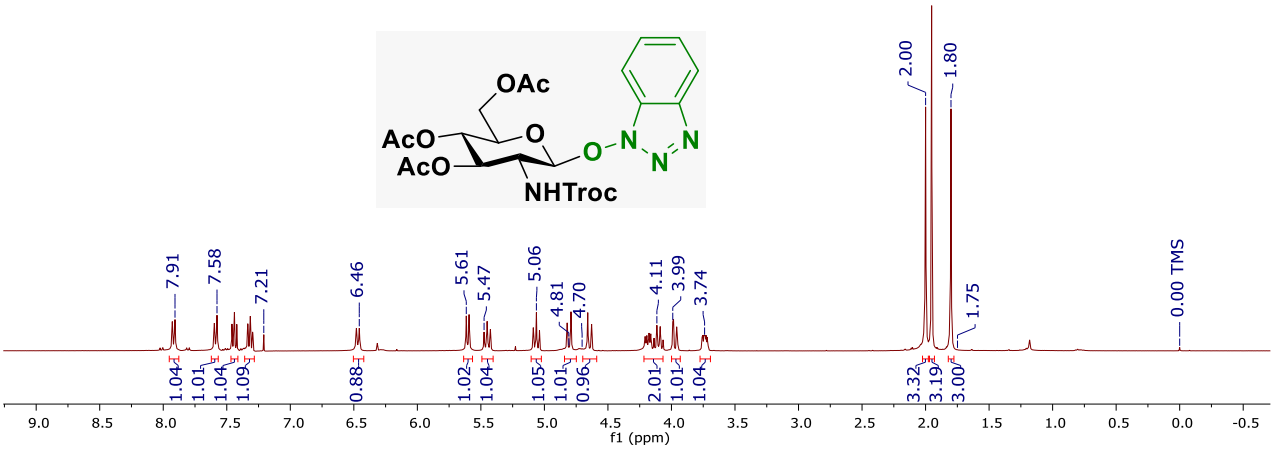
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **31**



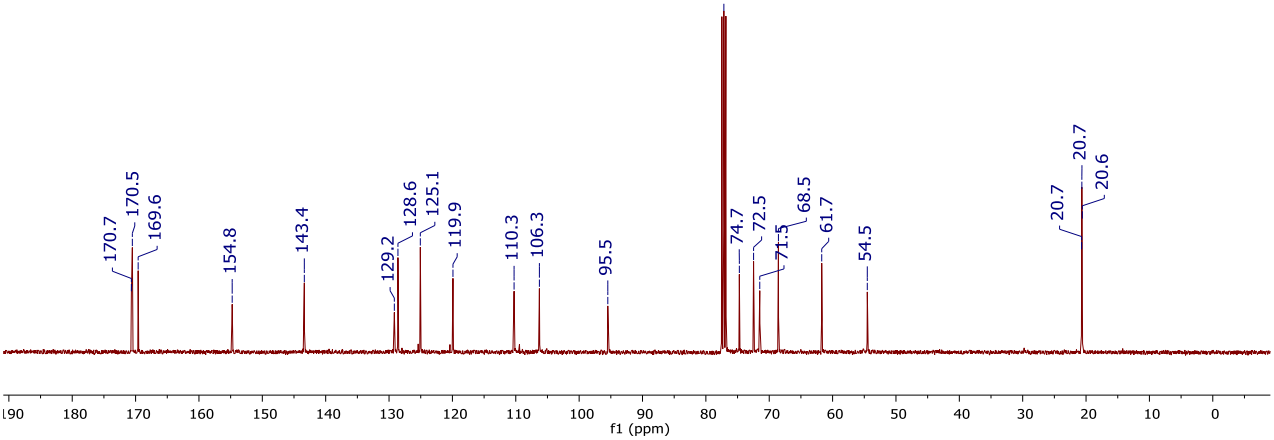
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **31**



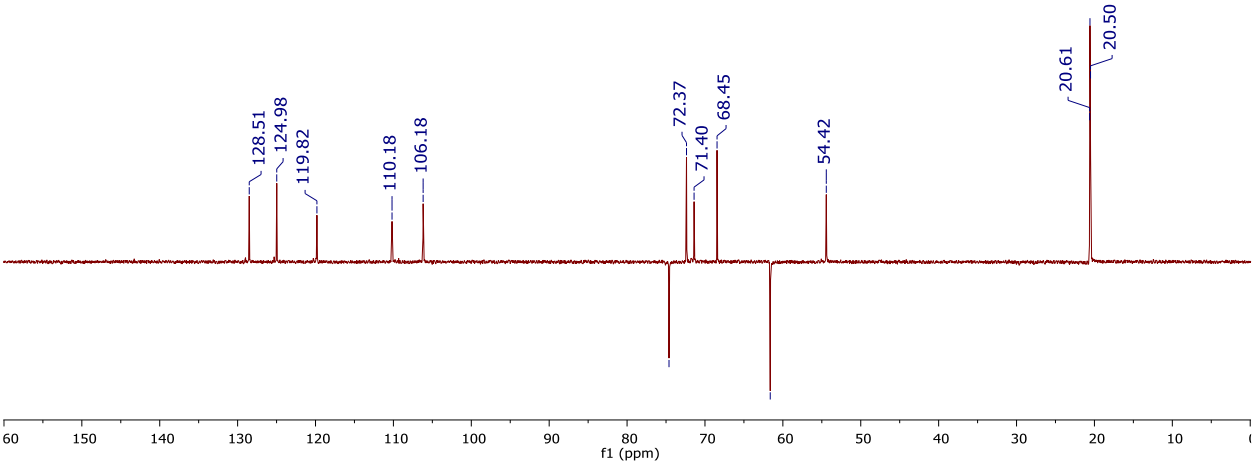
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **31**



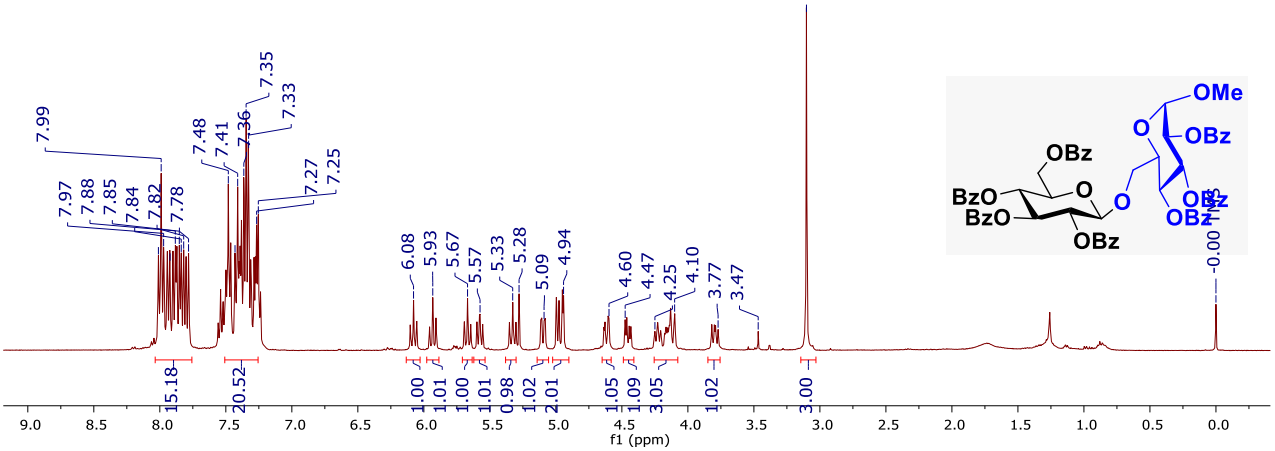
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **31**



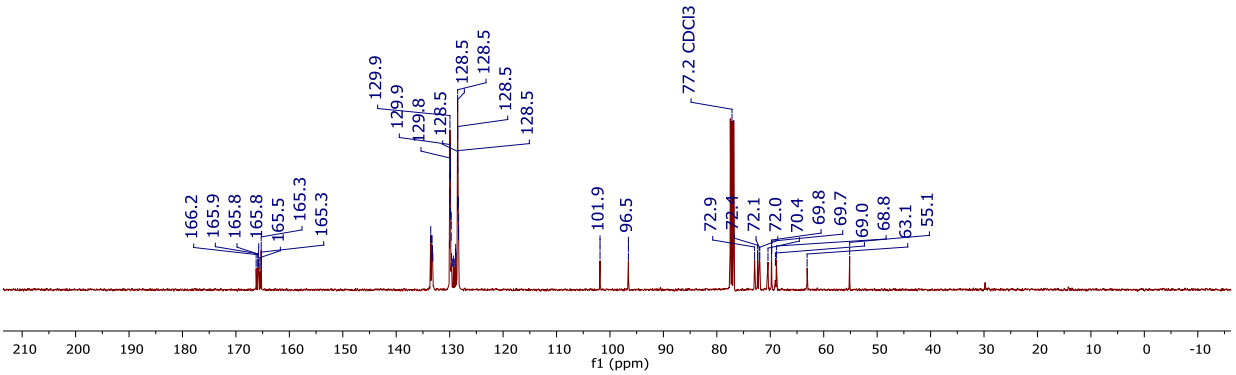
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **31**



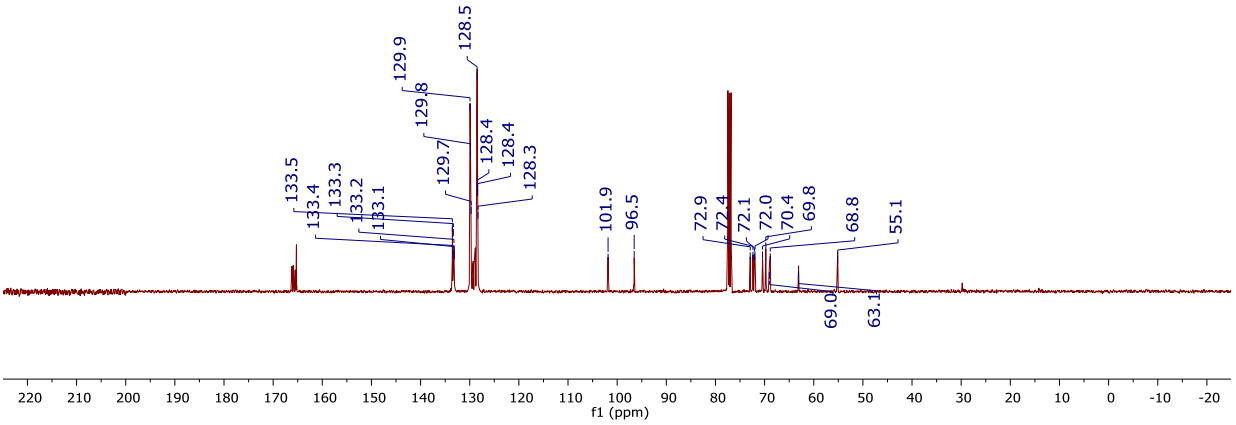
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **38**



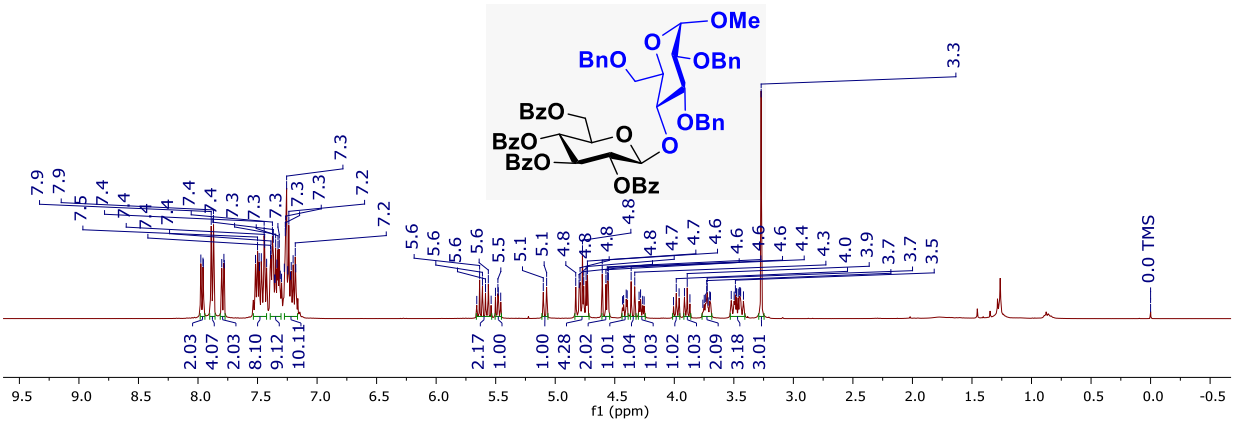
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **38**



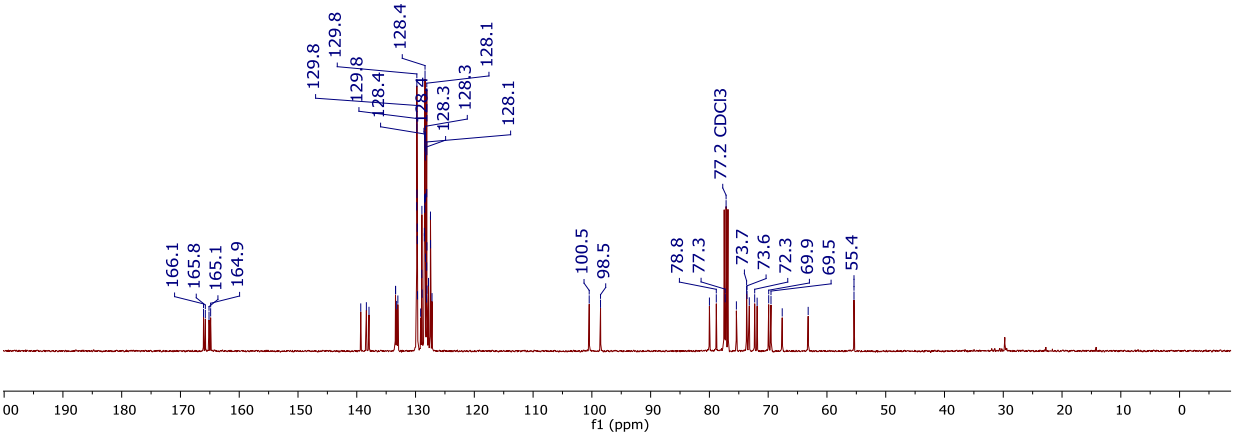
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **38**



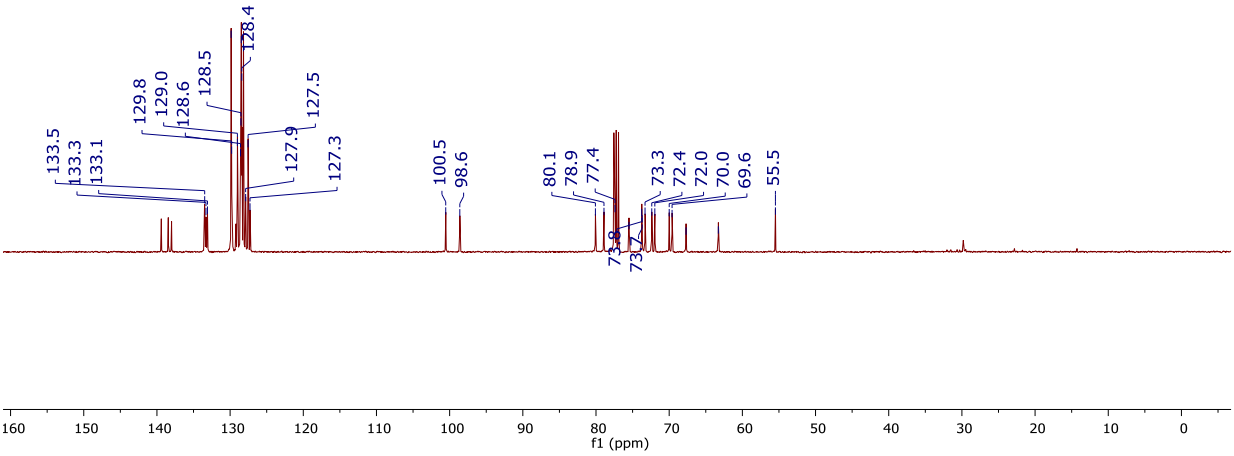
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **39**



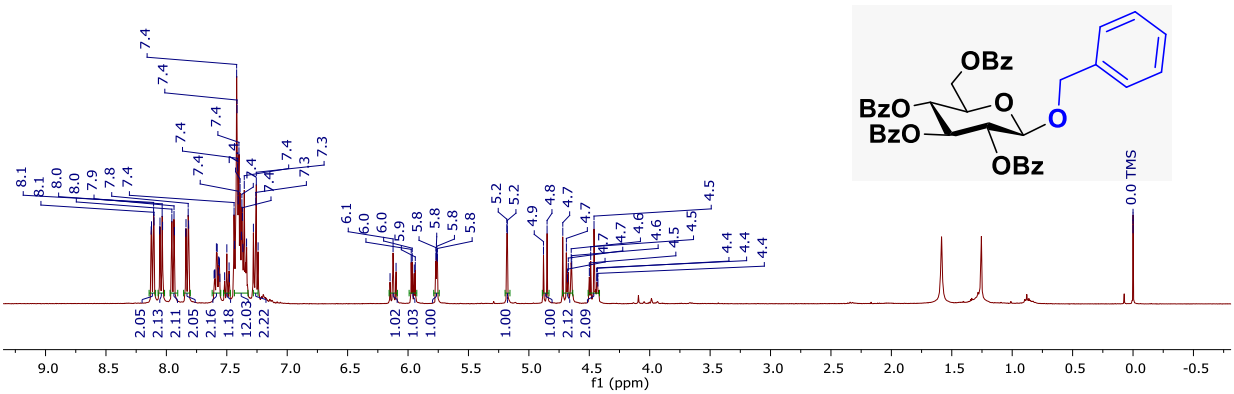
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **39**



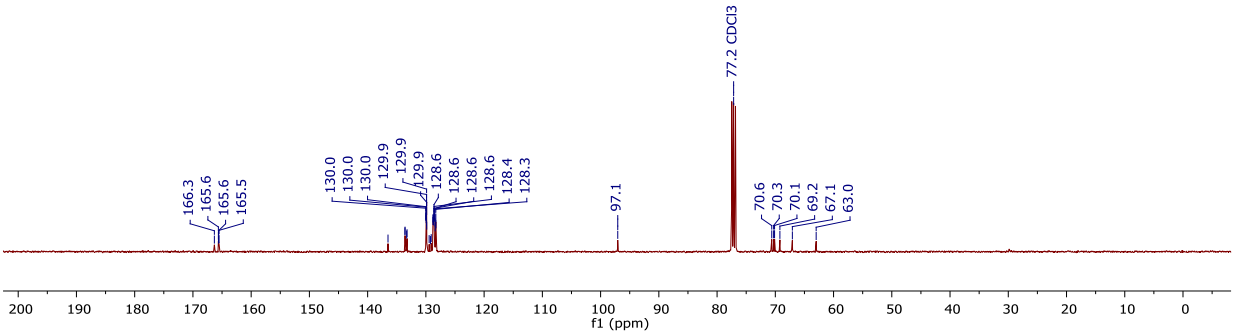
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **39**



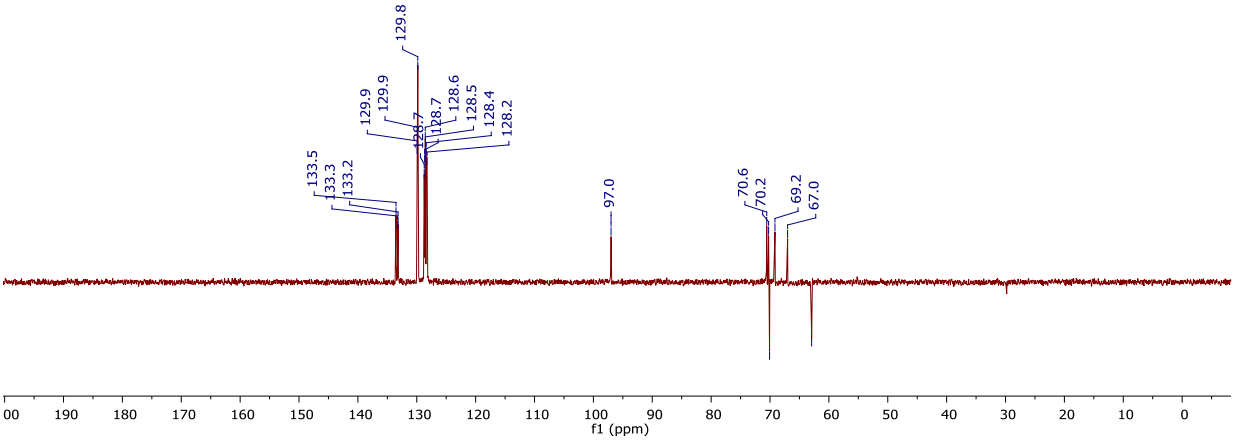
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **40**



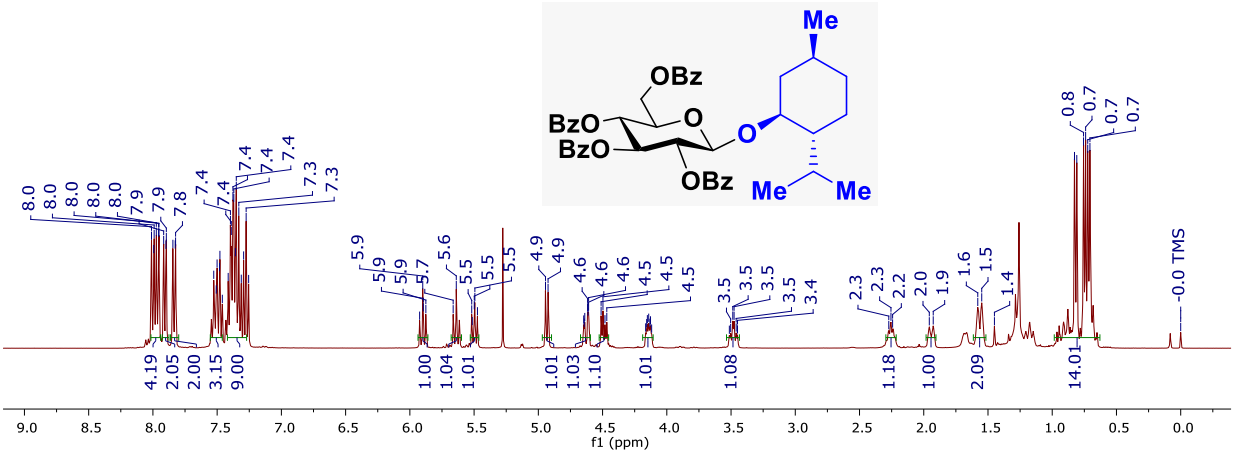
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **40**



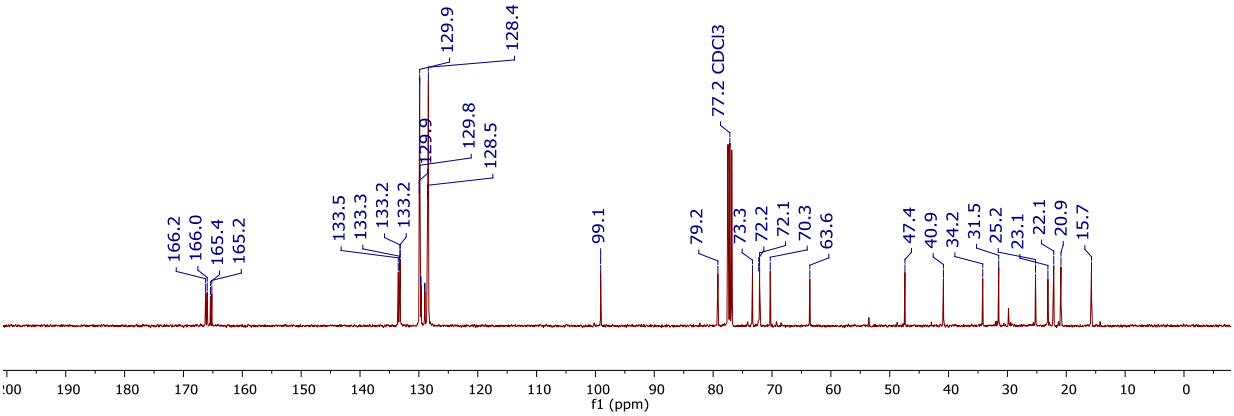
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **40**



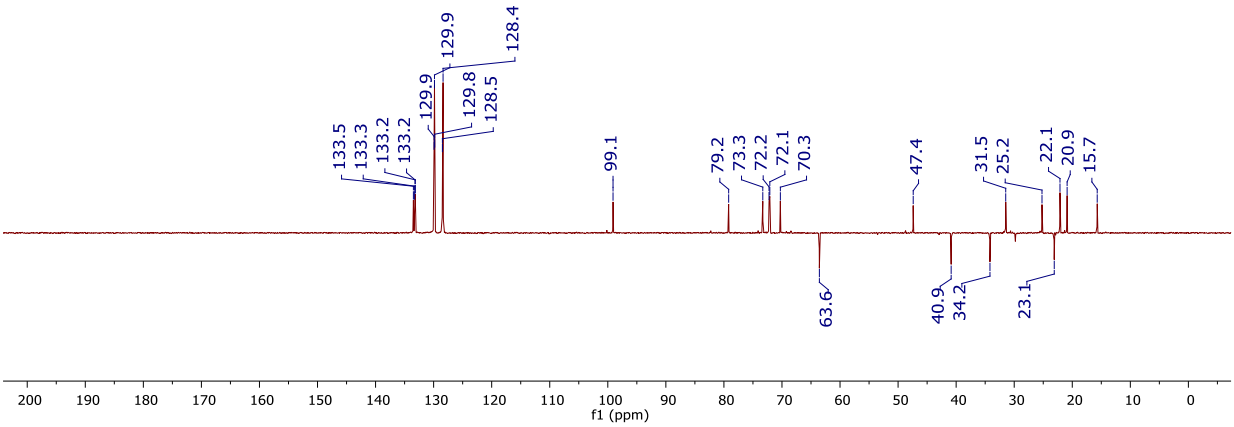
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **41**



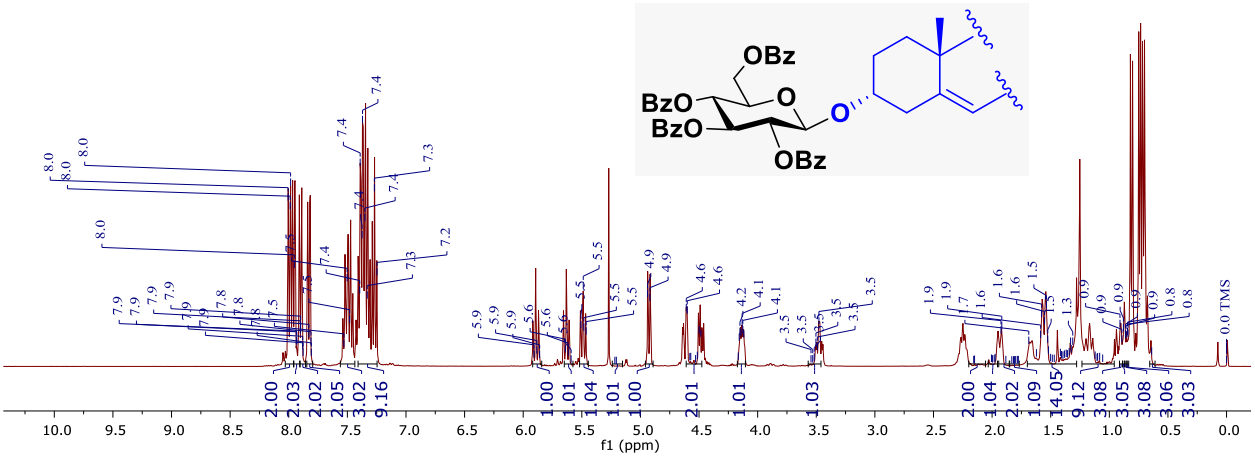
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **41**



DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **41**



^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **42**



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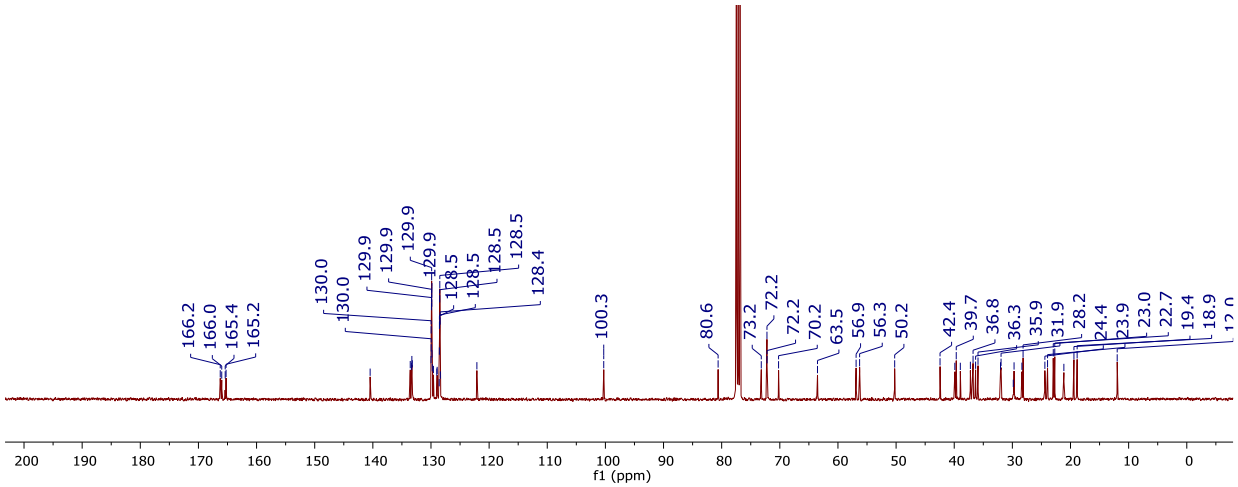

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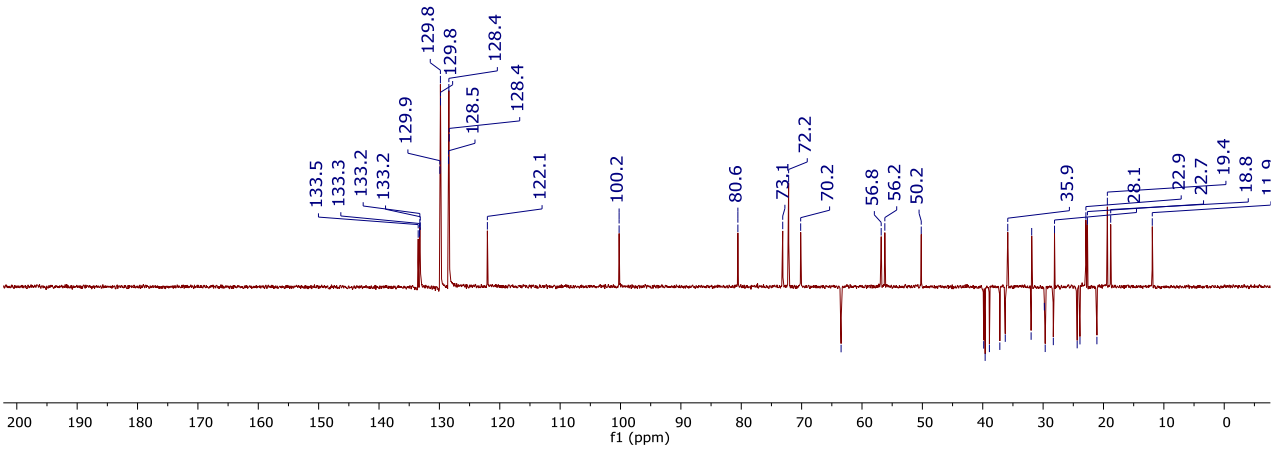

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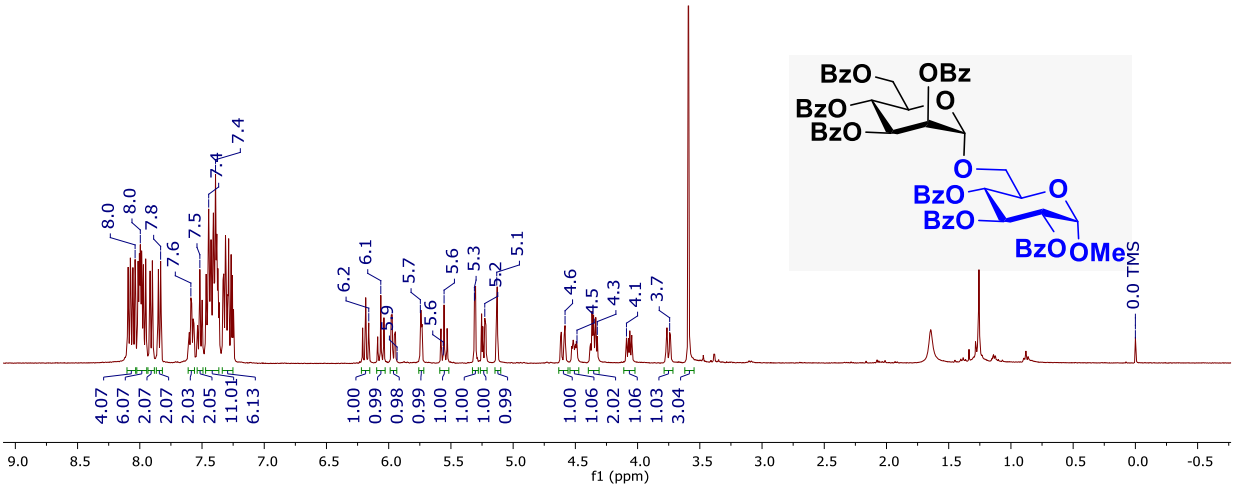

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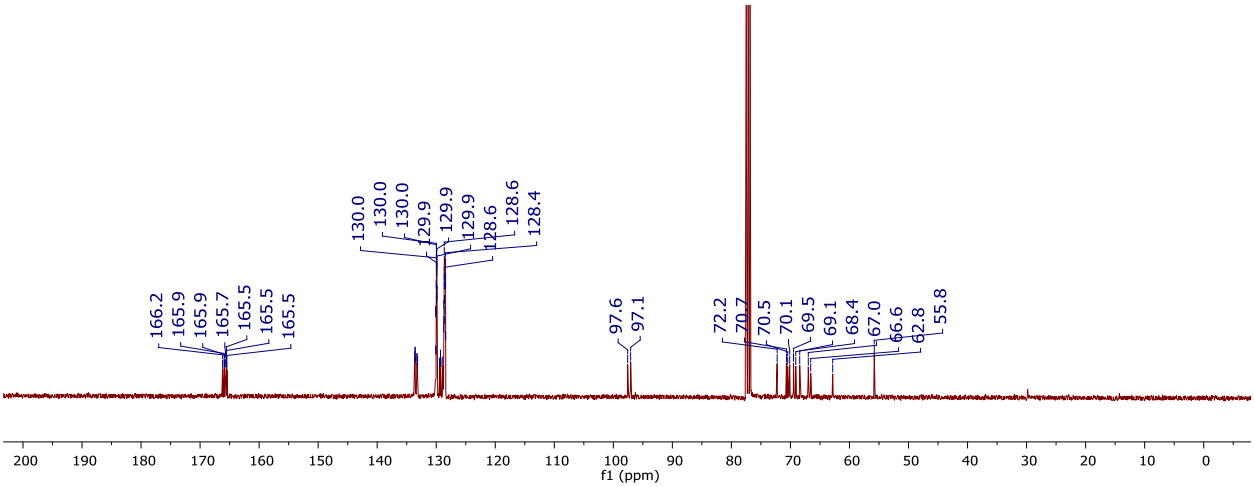

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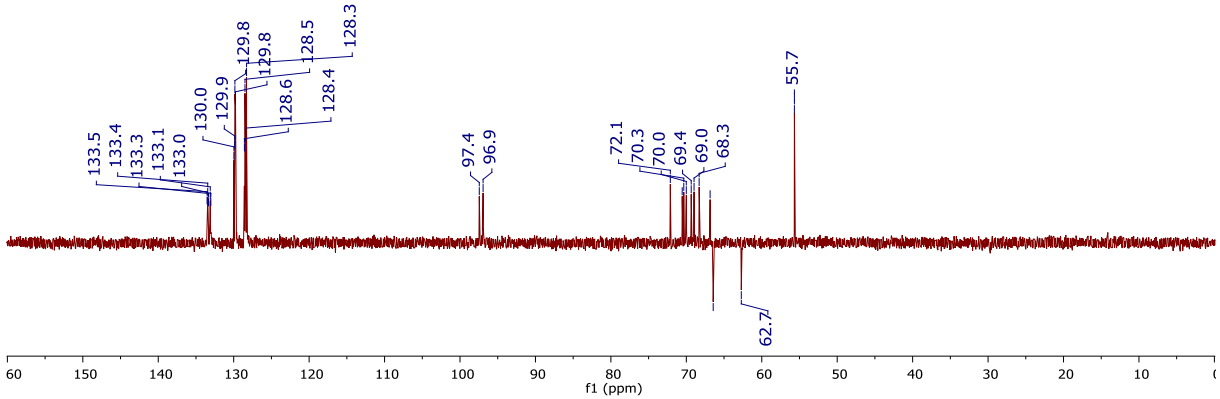

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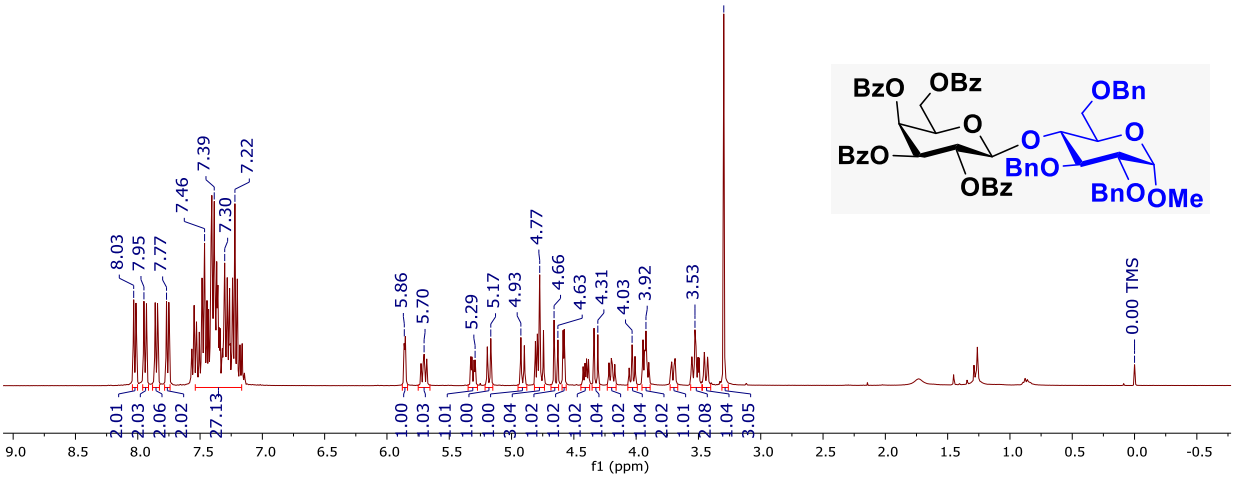

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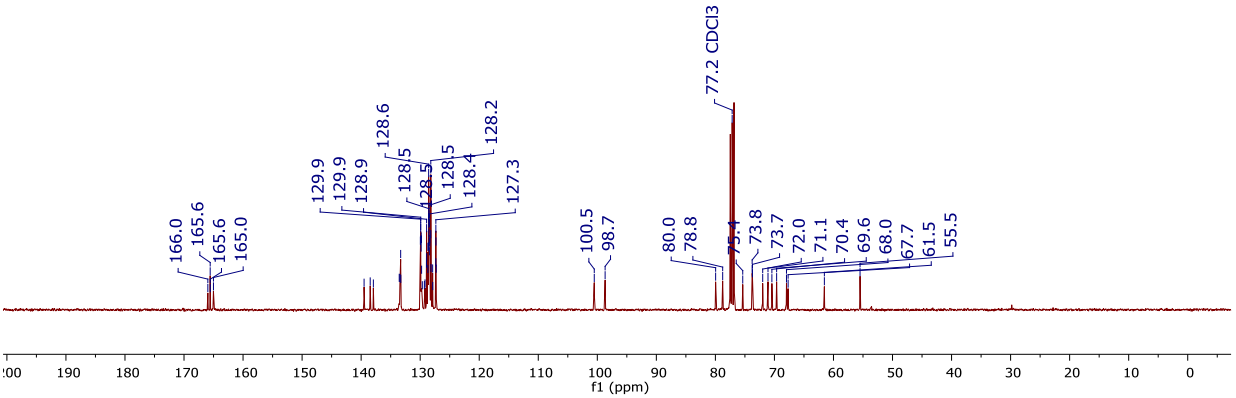

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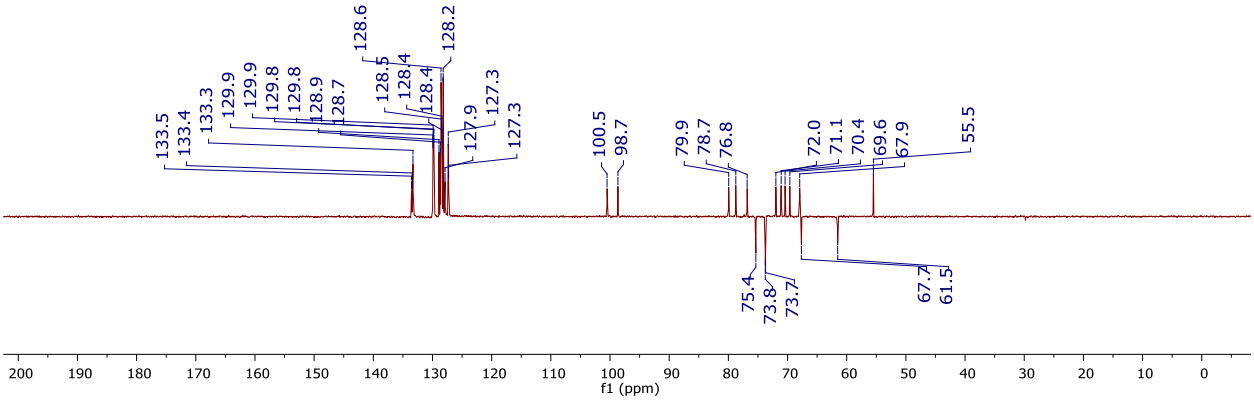

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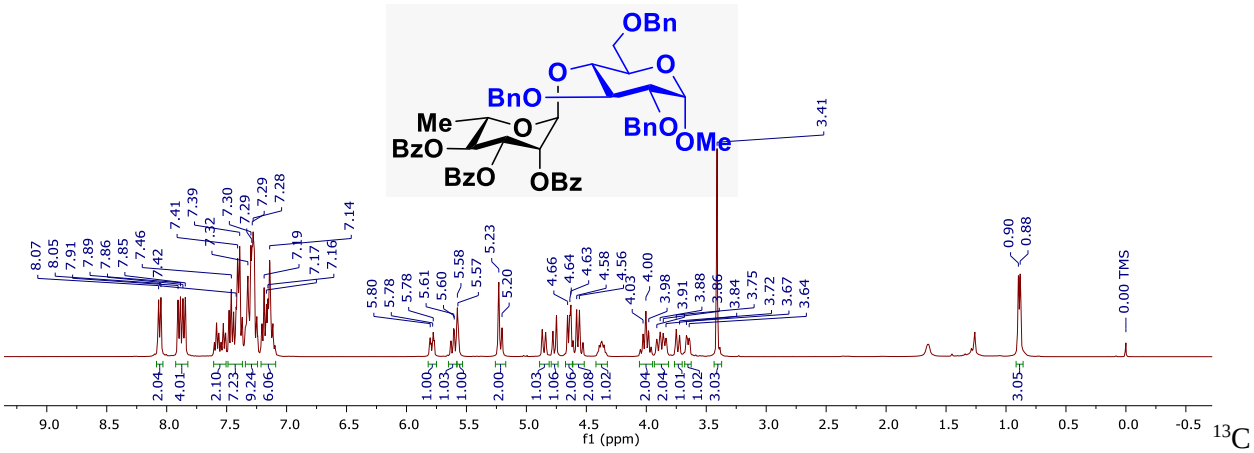

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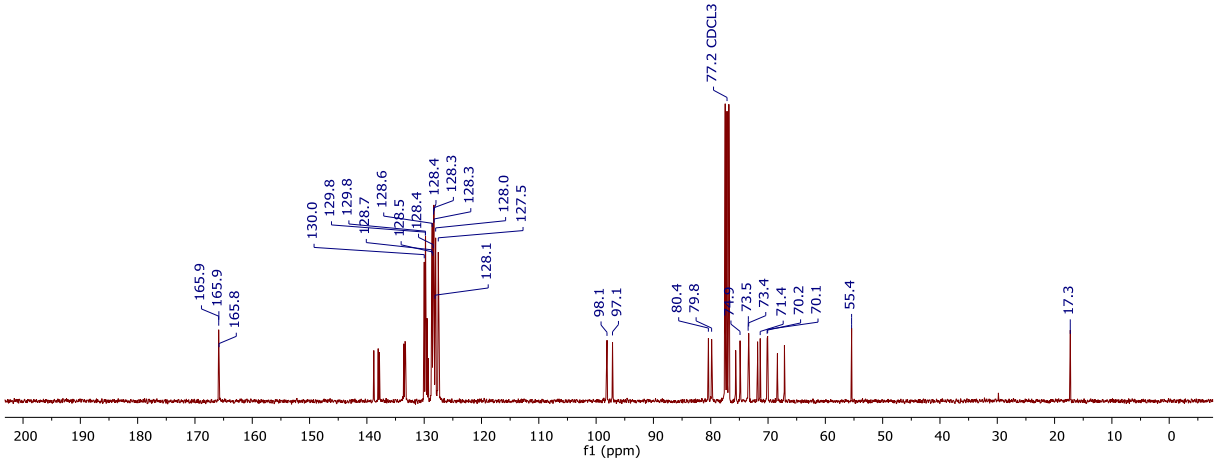

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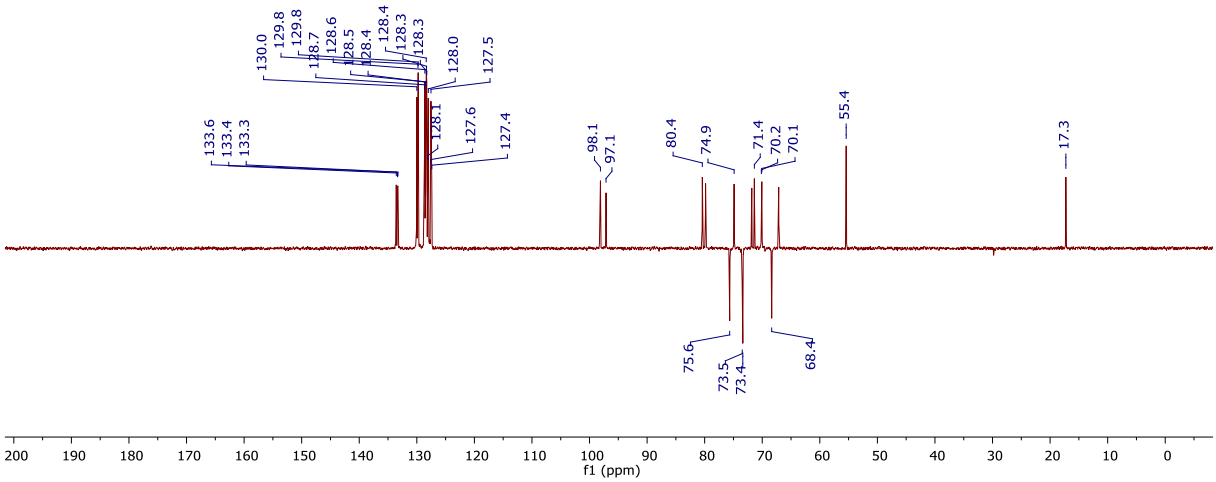

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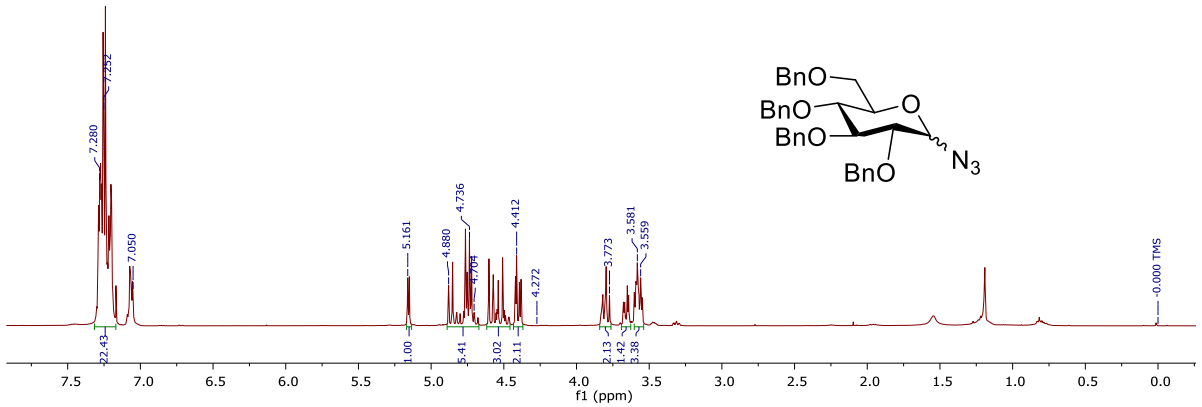

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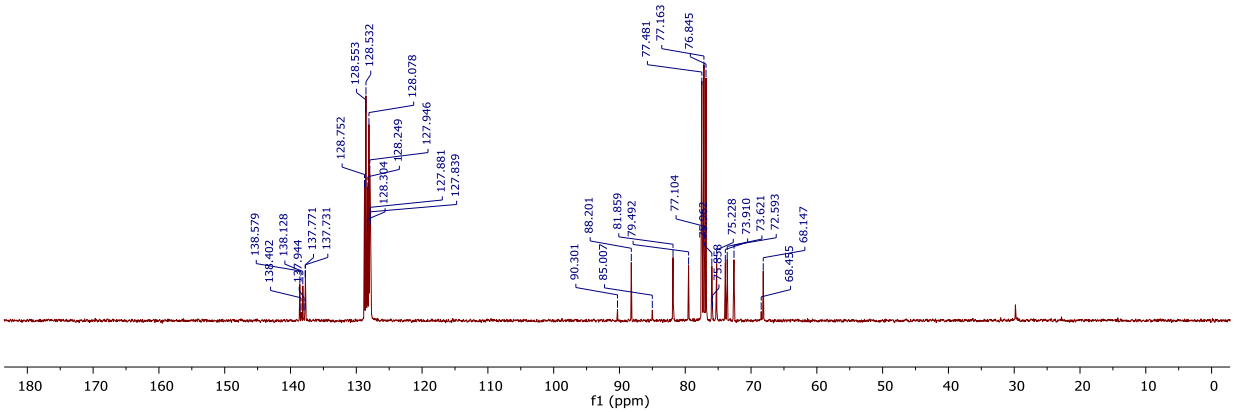

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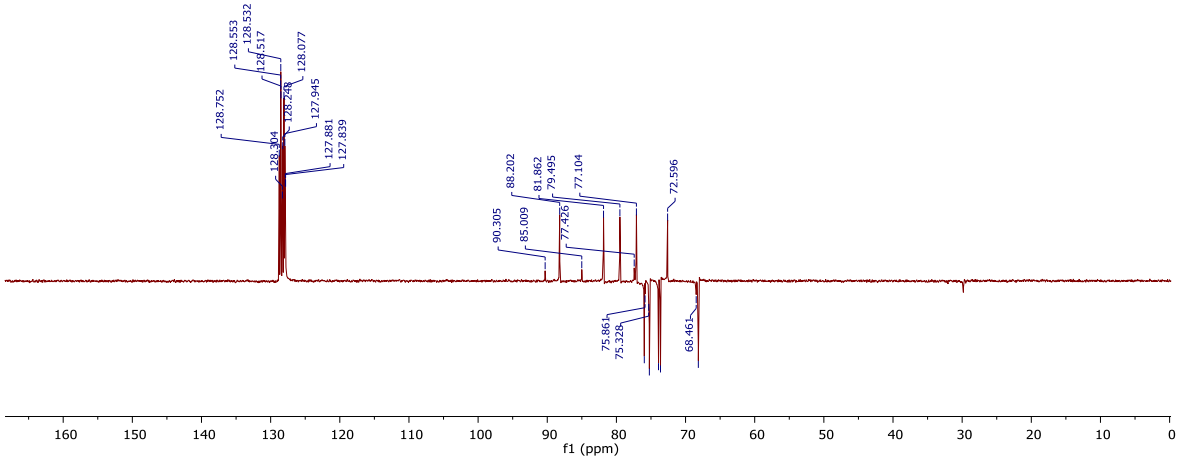

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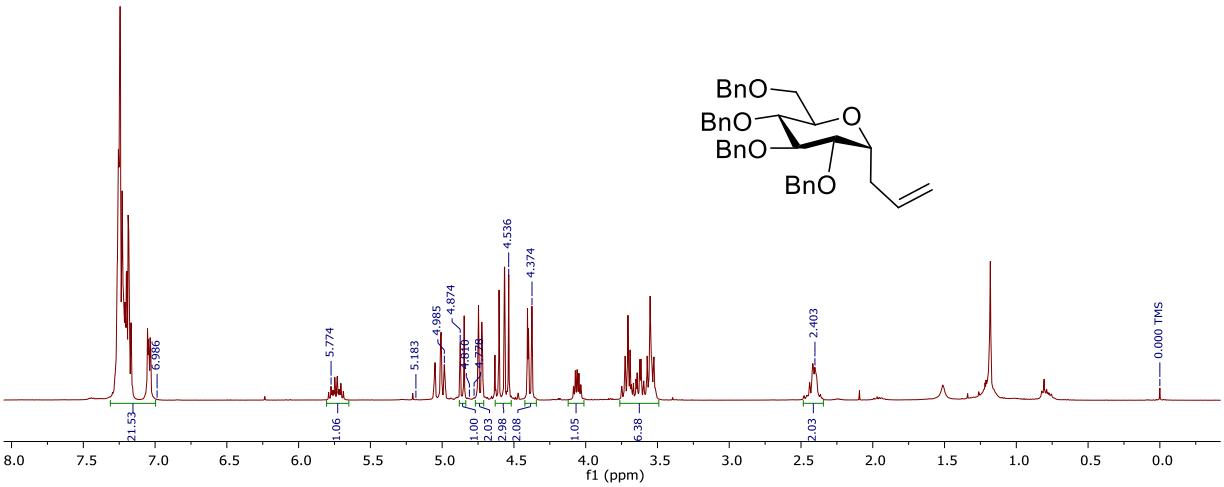

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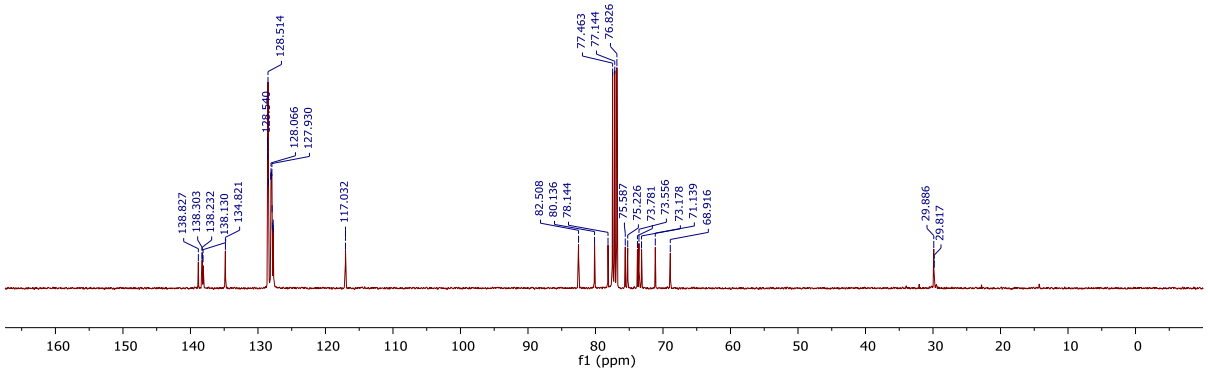

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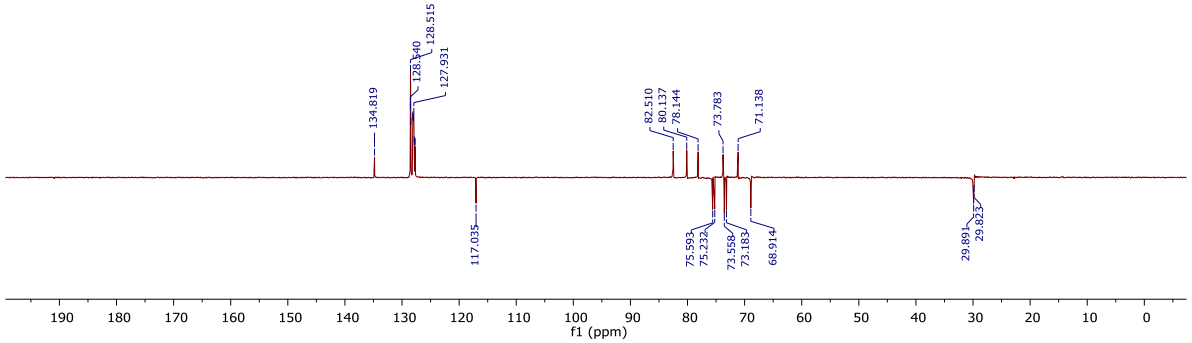

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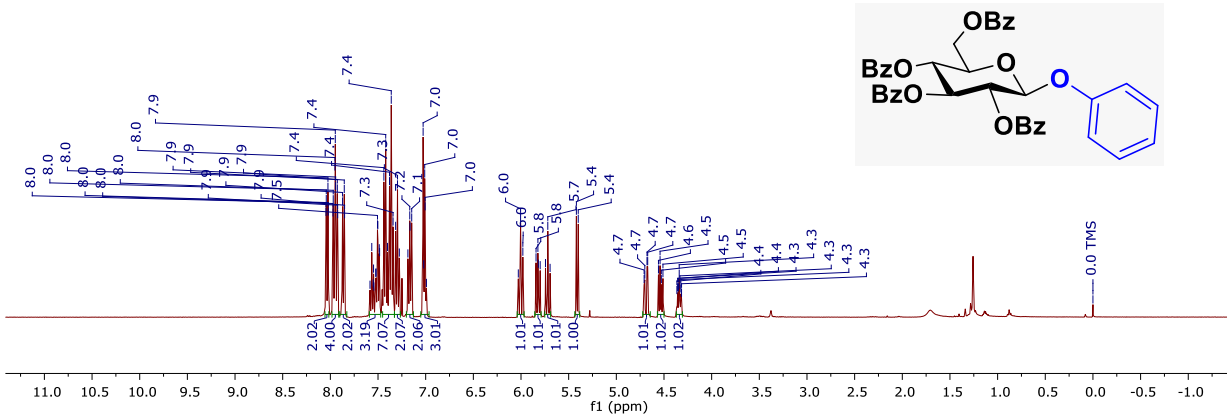

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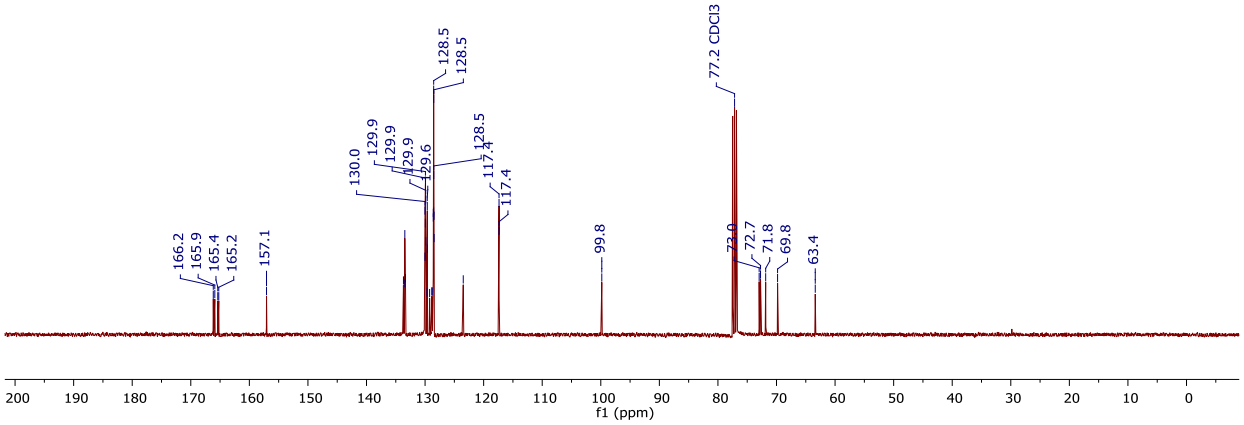
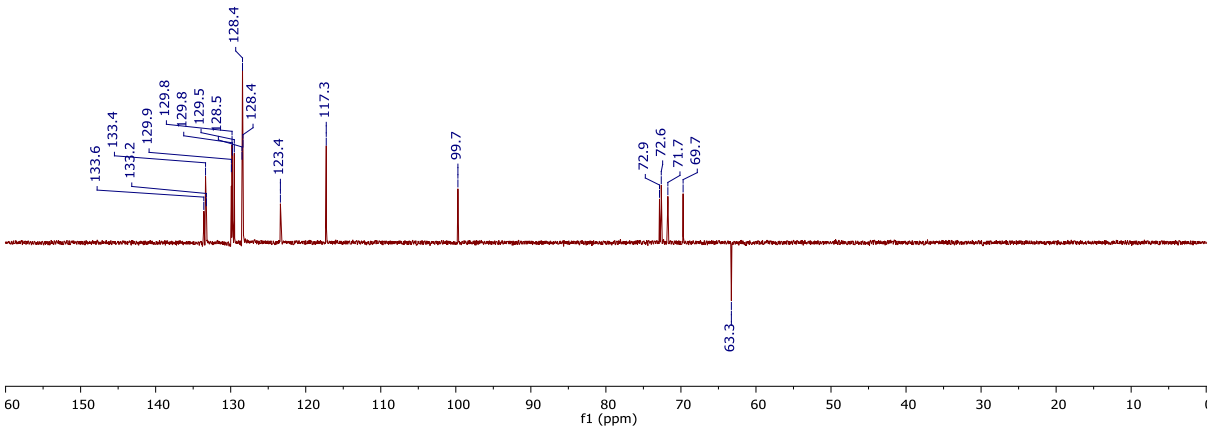


DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **56**



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Chapter 3

Utility of Hydroxybenzotriazolyl Glycosyl Donor in Oligosaccharide synthesis

3.1 Introduction

Structural diversity and dense distribution of carbohydrate moieties on cell surfaces of invasive bacteria, parasites and viruses needs special attention as potential drug and vaccine targets (**Fig. 3.1**).[1]Many microbes attach to cell surface glycans to gain entry into host cells and initiate infection. Vaccines provide protection by inducing immunity to disease-causing pathogens.[2]As they are among the most abundant molecules found on surfaces of sinister pathogens and malignant cells, they possesses the ability to produce protective immune responses against human infectious diseases.[3]Currently,*Haemophilus infuenzae serotype b* (Hib) vaccine is the only example of an approved and commercially available fully synthetic carbohydrate conjugate vaccine where as several promising vaccine candidates against various kinds of infectious diseases are in different phases of clinical trials.[4]

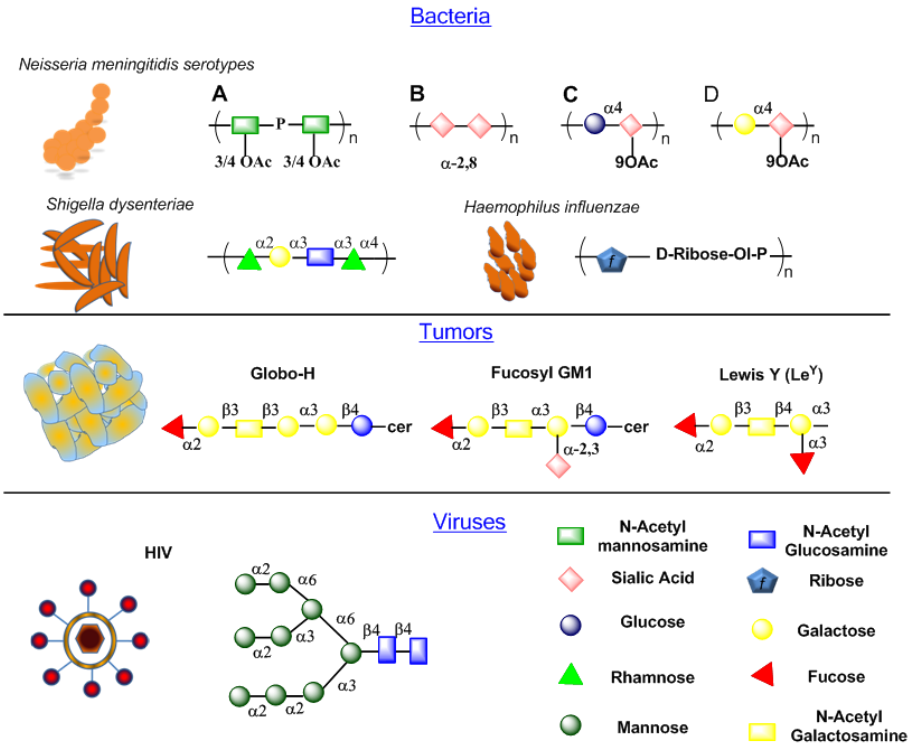


Figure 3.1. Different types of microbes and their associated glycan antigens

3.2 Carbohydrate-Based-Vaccines

Carbohydrate-based-vaccines are of two types – the first ones are 'polysaccharide vaccines', which contain only carbohydrates as immunogens and the second ones are 'conjugate vaccines',

in which immunogensare glycan antigens covalently bound to immunogenic proteins (**Fig 3.1**).Polysaccharide vaccines made of glycansmolecules alone show poor immune response to antibodies because carbohydrates are T-cell-independent antigens.[5]However,polysaccharides have ability to activate B-cells leading to production of low affinity antibodies. But such T-cell-independent responses are short-lasting and less robust and cannot provide adequate protection for high-risk groups such as infants and children under two years.[6]

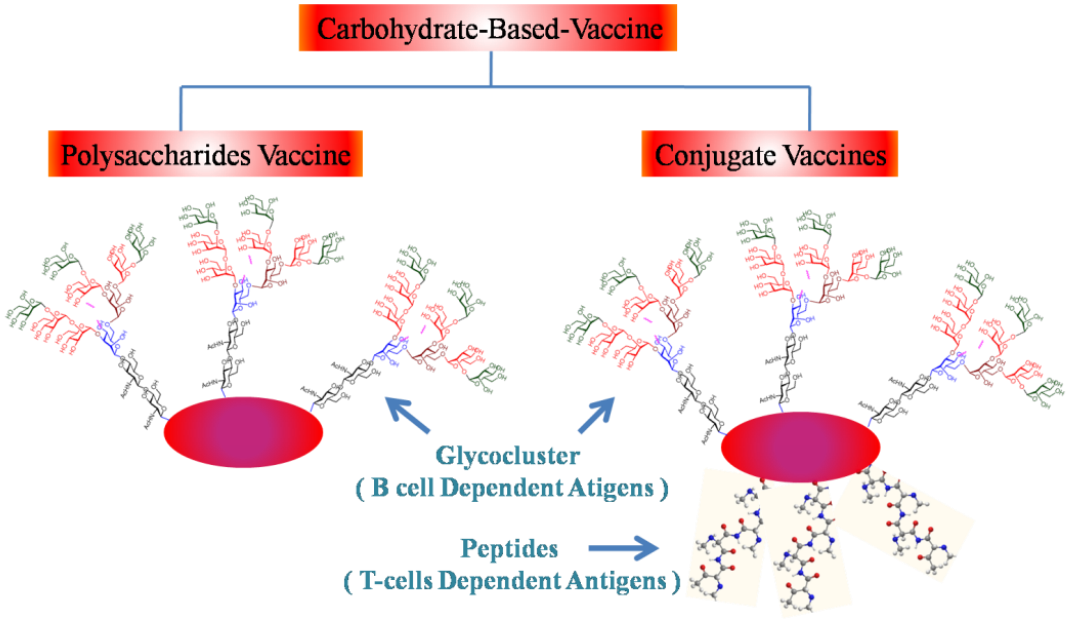


Fig. 3.1 Carbohydrate- Based-Vaccine Design

In order to achieve a high-affinity towards antibodies, the B cells need to interact with T cells. On the other hand, zwitterionic polysaccharides, proteins and peptides have ability to generate T cell-dependent responses and can generate high affinity which results into long-lived antibody-mediated protection.[7]It is well know that, conjugation of carbohydrate moieties to a suitable protein scaffold induces activation of CD4+ T-cells antibody response which provide protection with the long-lasting immunogenicity of carbohydrates and also confer protection even in the high-risk groups.[8]This concept of 'conjugate vaccine' triggered the field significantly.[9]

The carbohydrate-based-vaccine development became a giant stride for researchers as there is a steady and continuous emergence of antibiotic resistance; so synthetic-carbohydrate-based-vaccine strategy offers a resilient solution to sticky problem in the upcoming years.

3.3.1 Development of Carbohydrate-Based-Vaccine for Global Pandemic: Human Immunodeficiency Virus (HIV)

Human Immunodeficiency Virus (HIV) is a retrovirus and the causative agent of acquired immunodeficiency syndrome that is popularly known as AIDS.[10] It remains as a major threat to human health in many countries. In spite of the major progress in antiretroviral drugs which improved survival of HIV patients, the high cost of these drugs and increased resistance forced to search long-term solution to curb the infection rate globally such as preventive vaccine.[11]

3.3.2 Structure of HIV Envelope

HIV expresses glycoproteins on their surfaces and the associated glycans are shown to play pivotal roles in the immune evasion.[1]The functional envelope spike of HIV contains gp160 glycoprotein which is C_3-symmetric and undergoes proteolytic cleavage to produce of two glycoproteins gp120 and gp 41 (**Fig. 3.2a**). These two glycoproteins remain non-covalently associated through transmembrane.[12]Gp120 plays a crucial role in the first step of viral infection as it serves as a high-affinity ligand for the T-cell receptor. After binding to CD4+, gp41 is responsible for fusion of virus-host cell membrane that helps in release of virus into the host cell.[13]

Gp120 is densely glycosylated protein with about 50% of its molecular weight comprising high mannooligosacchrides. These glycan molecules have potential dual role in the virus life cycle - first, the high mannose glycan have affinity towards the DC-SIGN receptor of dendritic cells, which enable the virus to accumulate on the surface of these cells and facilitate its presentation to CD4+ cells for infection.[14] Second, this dense array of *N*-glycans on surface sterically provide protection to the underlying polypeptide surface from interaction with potentially neutralizing antibodies and this dense canopy is referred as '*glycan shield'*.[13]Trimeric gp120 contains majority of 'high mannose' type glycans ($Man_{5\text{-}9}GlcNAc_2$) in around 62-79%, which is also known as 'high-mannose patch' and remaining are 'complex' or 'hybrid-type' glycans.[13] (**Fig. 3.2b**)

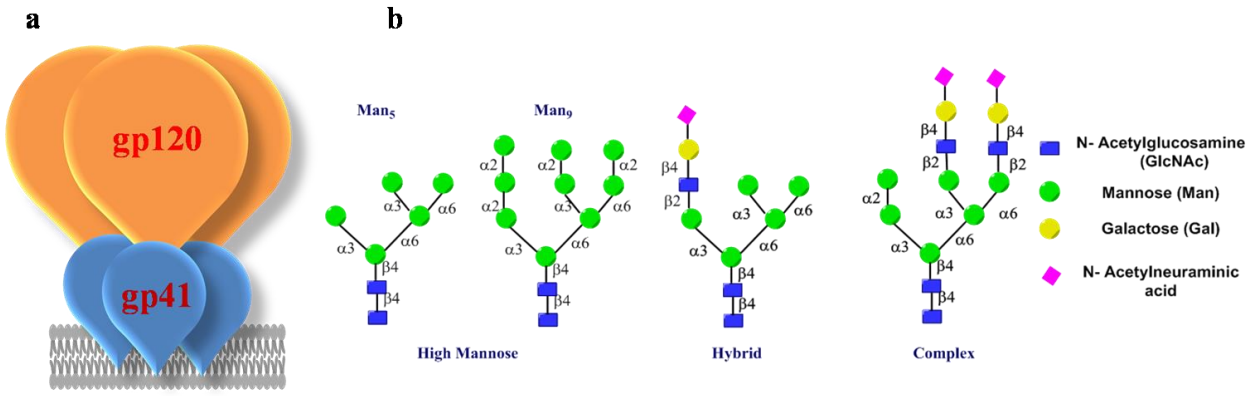


Fig. 3.2a) Gp120-gp41 Trimeric Envelope of HIV. **b)** Types of mammalian *N*-glycans present on the surface of gp120.

3.3.3 Antibody Targeting Carbohydrate-Based-Vaccine Design

Over the last two decades, vast amount of data has been collected about broadly neutralizing antibodies (bnAbs) against HIV, like 2G12, which is isolated from the serum of HIV infected individuals.[15,16]These antibodies neutralize a wide range of HIV strains and provide protection in animal models from infection by binding specifically to associated cluster of high-oligomannose glycans on the envelope glycoprotein. As a result, the high-mannose patch has gained substantial attention as a target for vaccine design. This observation provides clue for vaccine design by producing adequate mimicry of glycan shield which will produce specificity for antibodies.[1]

3.4 Challenges in Designing of Carbohydrate-Based-Vaccine

So far, the active carbohydrates used in commercial vaccine production are extracted from bacteria *via* techniques such as large-scale pathogens culture, digestion, hydrolysis and finally chromatography to remove low-molecular weight and less immunogenic portion to derive the well purified and characterized prevailing dogma as a protective B-cell epitopes which should be comprised of 10-20 units of monosaccharides.[3]However, several small epitopes composed of 3-5 sugar residues are adequate enough to induce antibody against whole organism and to provide protection.[17]

The vaccines prepared from extracted glycan antigens have been verified to be safe and relatively effective after many long-running trials, albeit vaccine production cost remains high

due to necessary facilities for safety precautions. Moreover, despite advanced technologies of culturing bacteria, they bear the risk of leaking pathogens causing disaster and risk of being contaminated which always remains a threat and reduce the titer of effective antibodies induction.[3]Furthermore, in general, carbohydrates survive as a family of closely related species that vary in their degree of polymerization, so even the purified carbohydrate antigens by chromatography suffers heterogeneity which create difficulties in the process of quality control.[2]So these heterogeneous glycan antigens isolated from natural sources reduces the efficacy of carbohydrate vaccines. Additionally, as far as designing of conjugate vaccines concern, the partial purified carbohydrate antigens necessitate to be modified in order to covalently link to the immunogenic proteins. Such modification could occur at the reducing end, non-reducing end or both terminals of the glycan moiety.[18]

3.5 Chemical Synthesis: A Solution for Sticky Challenges in Carbohydrate-Based-Vaccine

The problem related to accessing homogenous, well-purified and well-characterized specific carbohydrate antigens can be solved by using chemical synthesis instead of purifying from pathogens. Chemical synthesis provides pertinent solution for the availability of relevant carbohydrates with required modification, length and amount. Also, the production of homogenous oligosaccharides by chemical synthesis is moretechnoeconomical.[3]

3.6.1 Present Work

For the chemical synthesis of carbohydrate, the major setback is to build glycosidic linkages with proper stereo-and regiochemical orientation. A survey of existing glycosyl donor was discussed in chapter I whereas Chapter II described how existing strategies in glycosylation helped the development of regenerative hydroxybenzotriazolyl glycosyl donor. Synthesis of hydroxybenzotriazolyl donor is straight forward and can be prepared in one pot directly from commercially available parent sugar and is also cost effective. It has been experimentally shown that hydroxybenzotriazolyl glycosyl donors are useful in synthesis of *O*-, *C*- and *N*- glycosidic linkages with excellent yields. Here, the regenerative glycosylation strategy has been explored for the synthesis higher oligosaccharides.

To probe utility of our HOBt-donor for oligosaccharide syntheses, synthesis of two glycan motifs from high mannose patch of HIV-gp120 are chosen as targets. First target is trisaccharide

Man_3:(α-Man*p*-(1→2)-α-Man*p*-(1→2)-α-Man*p*) corresponding to the *C*-3branch of $Man_9GluNAc_2$**1** and second is the high pentamannan Man_5:(α-Man*p*-(α-Man*p*-(1→3)-α-Man*p*-(1→2))-(α-Man*p*-(1→6)-α-Man*p*-(1→2)) corresponding to the *C*-6 branch of $Man_9GluNAc_2$ **1**present on surface of the HIV-gp120 **(Fig. 3.4)**.

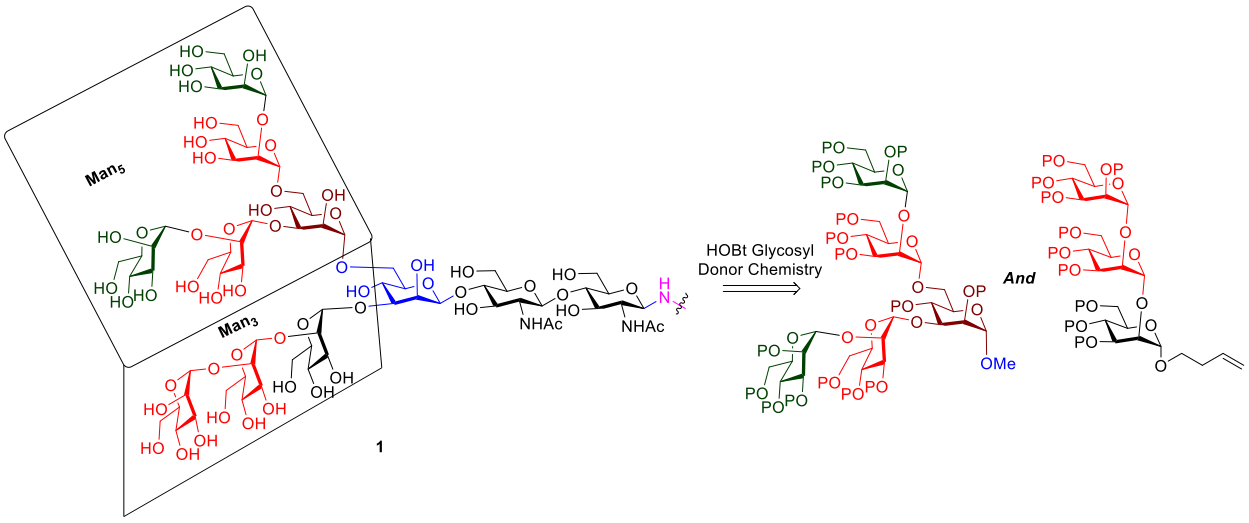
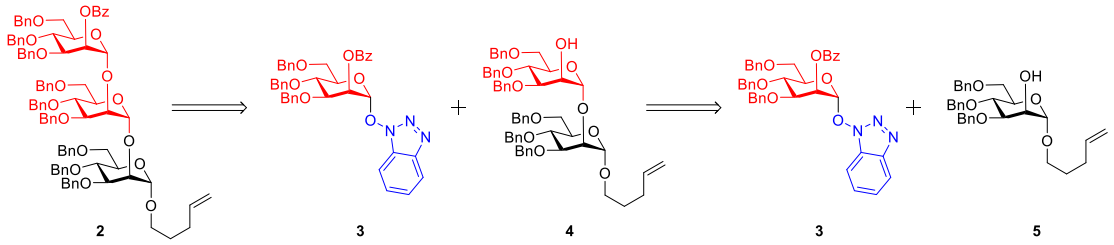


Fig 3.4 Complete Structure *N*-linked oligomannose **1** ($Man_9GlcNAc_2$)present on surface of high mannose patch of HIVgp120

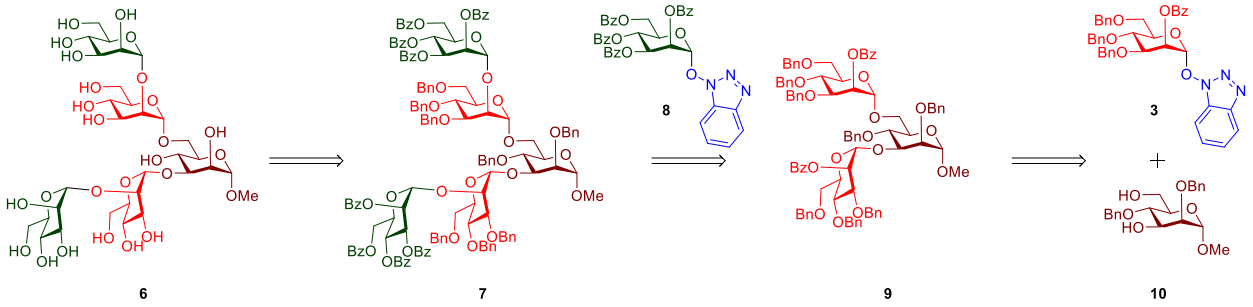
3.6.2 Retrosynthesis of Man_3 and Man_5 high oligomannose

From the perspective of installation of stereoselective 1,2-*trans*linkages in Man_3**2,** retrosynthetic analysiswas envisioned for Man_3**2** by using convergent block synthesis strategy (**Scheme 3.1**). 1,2-*trans*Linkages can be achieved by exploiting neighboring group participation from the *C*2-benzoyl protecting group of benzotriazolyl glycosyl donors **3.** Orthogonal protecting group strategy was applied for the synthesis for *C*2-OH free acceptor **5.**



Scheme 3.1 Retrosynthetic analysis of Man_3 **2**

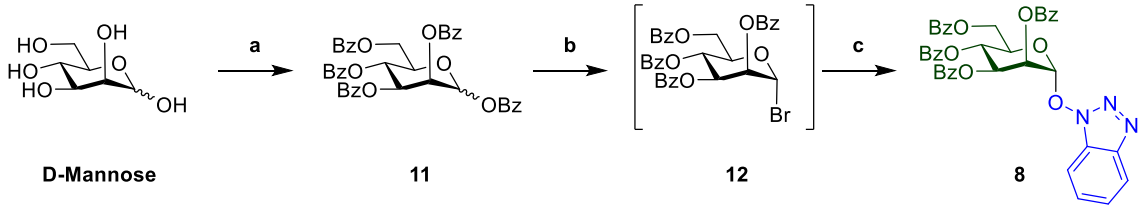
The retrosynthetic analysis of fully deprotected high pentamannan oligosaccharide Man_5 6 begins with 3,6-OH free mannose diol **10** serving as an acceptor for the selectively protected *C*-2glycosyl donor **3** to form trisaccharide **9** which could be further extended to synthesize protected high pentamannan Man_5**7. (Scheme3.2)**



Scheme 3.2 Retrosynthetic analysis of high petamannan oligosaccharide Man_5**6**

3.6.3 Synthesis of Building Block 8

Our synthesis endeavor begun with the preparation of per-*O*-benzoylated benzotriazolyl mannosyl donor **8** that was synthesized in two steps from commercially available D-mannose. All free hydroxyl groups of D-mannose were protected as benzoates by using benzoyl choride and anhydrous pyridine in 5 hours at 0 ºC to give per-*O*-benzoylated mannose **11.**Compound **11** was treated with 40% HBr in glacial acetic acid to afford known intermediate mannosyl bromide **12**,which was directly treated with commercially available hydroxyl benzotriazole (HOBt) and NEt_3in dry CH_2Cl_2 at room temperature to afford glycosyl donor **8**in 1 hour (87% over three steps) (**Scheme 3.3**).Gratifyingly, column chromatography was performed only once over three steps to get access to glycosyl donor **8.**



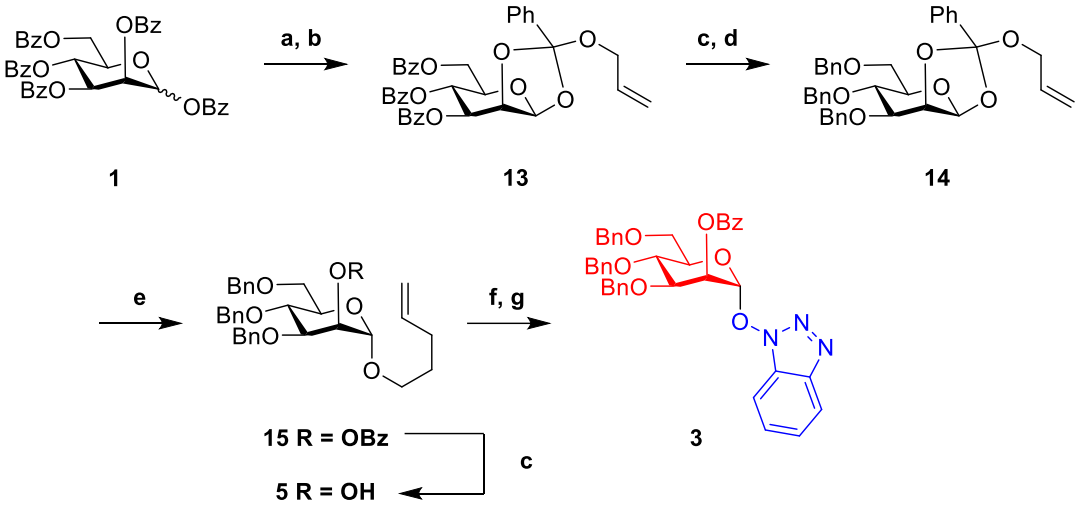
Scheme 3.3 Reagentsa) BzCl, pyridine, DMAP, 0-25 ºC, 5h; b) HBr in acetic acid, CH_2Cl_2, 0 ºC, 2h; c) HOBt, NEt_3, CH_2Cl_2, 1h, 87% over three steps.

Formation of compound **8** was confirmed by NMR and HRMS analysis. In the^{1}H NMR spectrum of compound **8**,anomeric protons of 1,2-*trans* mannose linkage appeared as doublets at δ6.23 ppm with a coupling constant *J*=3.4 Hz and 24 aromatic protons are identified between δ 7.27-8.07 ppm that include extra 4 protons of HOBt moiety as well apart from those of benzoates. In the^{13}C NMR spectrum of compound **8**, anomeric carbon was noticed at δ103.2 and six characteristic carbons of HOBt were characterized at δ108.2, 120.7, 125.0, 127.2, 129.7 and 143.6 out of which two tertiary carbons disappeared in DEPT NMR spectra confirming the formation of compound **8.**

3.6.4 Synthesis of Building Block 3 and 5

Other required building blocks for the convergent synthesis of Man_3 and Man_5 were compounds**3** and compound **5** which could be accessed from the same precursor **15.** In order to synthesize compound **15,** per-*O*-benzoylated mannoside **1**was treated with 40% HBr in glacial acetic acid at 0 ºC to form mannopyranosyl bromoside which was further reacted with allyl alcohol, 2,6-lutidine and TBAI in dry CH_2Cl_2 at 60 °C for 8 hours to afford allyl mannose orthoester **13**in 78% yield over two reactions. Compound **13**was subjected to modified Zemplén conditions (NaOMe in MeOH and CH_2Cl_2) in order to deprotect three benzoyl groups to afford highly unstable allyl mannose intermediate which was without purification treated with benzyl bromide and NaH in dry DMF at 0 °C to afford per-*O*-benzyl protected allyl orthoester **14** in 76 % yield over two steps. Compound **14**was allowed to undergo orthoester opening with 4-penten-1-ol under acidic conditions to afford compound **15**with C2-*O*-Bz group and pentenyl group at the anomeric position.

In continuation, compound **15**was split into two fractions. One fraction was treated with Br_2 in dry CH_2Cl_2 to form mannopyranosyl bromide, which was subsequently treated with HOBt and NEt_3 to afford compound **3**. The second fraction of compound **15** was treated with NaOMe to deprotect *C*2-benzoyl group to afford compound **5** with C2- free hydroxyl group (**Scheme 3.4**).



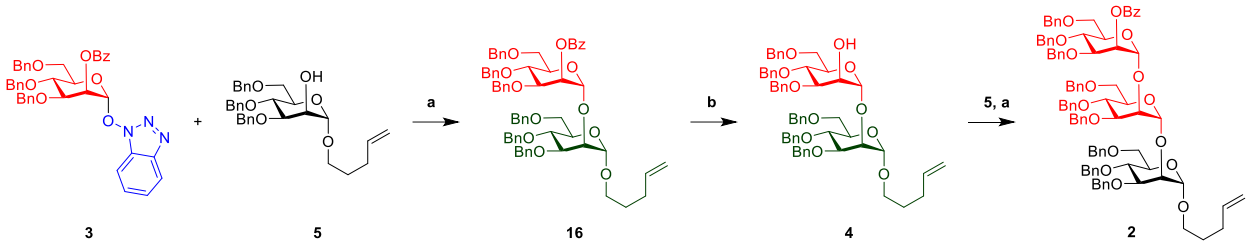
Scheme3.4 Reagents a) HBr in Acetic acid, CH_2Cl_2, 0 ºC, 2h, 85%; b) allyl alcohol, 2,6-lutidine, TBAI, CH_2Cl_2, 4Å MS, 60 ºC, 8h, 78%; c) NaOMe, MeOH and CH_2Cl_2, 25 ºC, 2h, 82%; d) BnBr, NaH, TBAI, DMF, 0 ºC, 6h, 76%; e) TMSOTf, pent-4-en-1-ol, 4Å MS, CH_2Cl_2, 1h, 92%; f) Br_2, 4Å MS, CH_2Cl_2, 15 min, g) HOBt, NEt_3, CH_2Cl_2, 2h, 76% over two steps.

The formation of compound **3**and compound **5** was confirmed by NMR and mass spectral analysis. In ^1H and ^{13}C NMR spectrum of compound **3**, anomeric protons resonated at δ 5.90, anomeric carbon at δ104.9 ppm and benzoyl ester carbon at δ165.6 respectively. In the ^1H NMR of compound **5**, characteristic vinylic protons and secondary hydroxyl group signals resonated at δ6.12 and δ3.24 ppm respectively. Similiarly, in ^{13}C NMR spectrum, carbon value of δ114.7 and δ143.1 ppm confirmed the formation compound **5.**

3.6.5 Synthesis of Trisaccharide Man_3 2

In order to check utility of newly developed glycosyl donor for the synthesis of mannose trisaccharide **2,** glycosyl donor **3**and glycosyl acceptor **5**were coupled first under the standard optimized reaction conditions such as 0.4 eq. of Tf_2O as activator to afford disaccharide **4**in an excellent yield of 92%. Disaccharide **4**was treated with NaOMe in CH_2Cl_2 and methanol to afford disaccharide acceptor**16** in 95% yields. In continuation, disaccharide acceptor**16** was allowed to undergo glycosylation with glycosyl donor **5**under standard optimization reaction conditions to afford the trimannoside**2**in more than 88% yields (**Scheme 3.5**). These preliminary results showed that hydroxybenzotrizolyl glycosyl donor is useful for oligosaccharide synthesis

in 1+1+1 fashion. This result further encouraged us to synthesize new target oligosaccharide with more number of monosaccharide units.

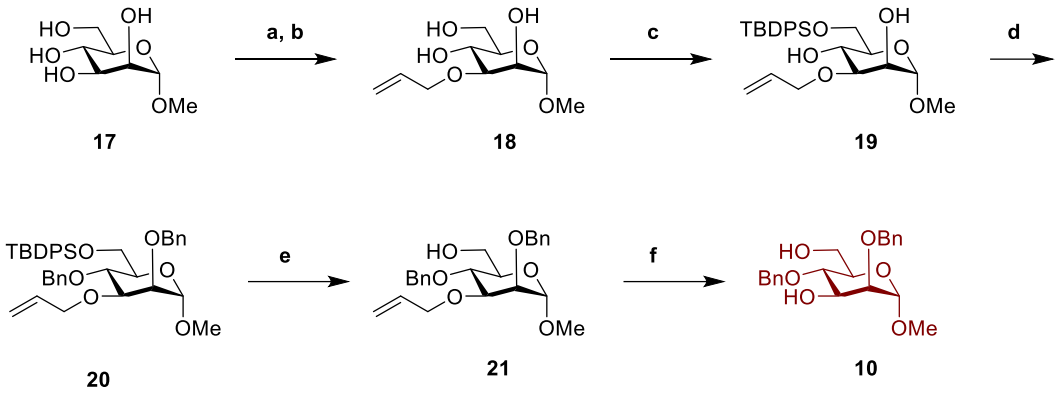


Scheme 3.5 Reagents a) 0.4 eq. Tf_2O, 4Å MS, CH_2Cl_2, 15 min, 92% for **4**, 88% for **2**; b) NaOMe, MeOH and CH_2Cl_2, 25 ^{0}C, 2h, 95%.

3.6.6 Synthesis of 3,6-OH Free Mannose Diol 10

The synthesis of high pentamannan oligosaccharide **7**in 1+2+2 fashionrequired3,6-OH free mannose diol **10** as acceptor. Synthesis of compound **10**commenced from commercially available α-methyl mannopyranoside **17**. Compound **17**was first refluxed with dibutyl tin oxide in MeOH for 2 hours to form *insitu*stannylidene complex which underwent reductive opening with allyl bromide and TBAI in toluene to afford compound **18** with allyl group at C3-position in 64% yield. Now, selective protection of TBDPS group at primary of compound **18**was carried with TBDPSCl and imidazole in dry DMF as solvent in 9 hours to afford compound **19**in 82% yield.

Subsequently, compound **19**was reacted with benzyl bromide and NaH in dry DMF at 0 ºC to protect both hydroxyl groups as benzyl ethers to afford mannoside **20.** Further, silyl group in compound **20**was removed with the help of HF•pyridine in 1:1 binary solvent mixture containing THF and pyridine to afford compound **21** in 90% yield. Finally, the allyl glycoside was converted into hemiacetal **21** with the help 0.15 equivalents of of $PdCl_2$ in 1:1 mixture of methanol and $CH_2Cl_2$to afford desired compound **10**in 78% yield.



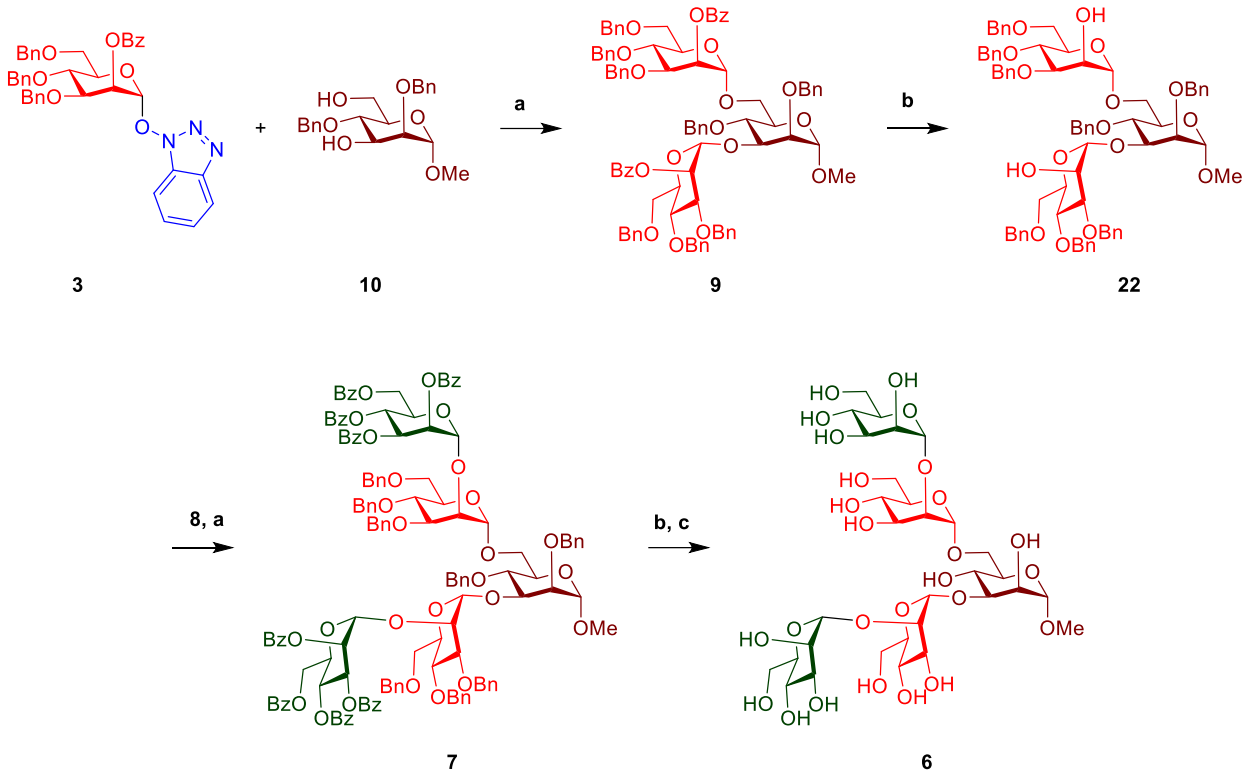
Scheme 3.6 Reagents a) Bu_2SnO, MeOH, 80 ºC, 2h; b) AllylBr, TBAI, DMF, 25 ºC, 3h, 64% over two steps; c) TBDPSCl, Imidazol, DMF, 0 ºC, 9h, 82%; d) BnBr, NaH, DMF, 0 ºC, 6h, 88%; e) HF•py, pyridine, 0 ºC, 4h, 90%; f) $PdCl_2$, MeOH and CH_2Cl_2,5h, 78%.

Formation of compound **10** was confirmed by NMR and mass spectral analysis. In the^{1}H NMR spectrum of compound **10**, a singlet for three protons of methyl group resonated at δ3.30 ppm whereas those of anomeric protons resonated at δ5.9 and signals for vinylic –CH at δ5.94, along with carbon signal for methyl at δ54.8 and anomeric at δ99.4 ppm in the ^{13}C NMR spectrum confirmed the formation of compound **10.**

3.6.7 Synthesis of High Pentamannan Man_5 6

With these encouraged results and all required building blocks in hands, we stepped forward to assemble high pentamannan **6**by using (1+2+2) coupling strategy. Double glycosylation using 2 eq. of glycosyl donor **3**and 1 eq. of glycosyl acceptor **10**under standard reaction conditions for glycosylation afforded the desired trisaccharide **9**in 82% yield. The trisaccharide **9**with two benzoyl groups reacted with NaOMe in 1:1 mixture of CH_2Cl_2 and MeOH as solvent afforded disaccharide diol **22**in good yield.

In continuation, the disaccharide diol **22**was allowed to undergo double glycosylation with glycosyl donor **8** in the presence of 0.4 equivalents of Tf_2O as promoter to afford desired target high pentamannan oligosaccharide **7** in excellent yield. Astonishingly, formation of product **8**only was observedwithout any partial glycosylated product such as tetrasaccharide.Thus we accomplished the synthesis of Man_5**7** by using newly developed hydroxybenzotriazolyl glycosyl donors(**Scheme 3.7**).



Scheme 3.7 Reagents a) 0.4 eq. Tf_2O, 4Å MS, CH_2Cl_2, 15 min, 81% for **9**, 77% for **7**; b) NaOMe, MeOH and CH_2Cl_2, 25 ^{0}C, 2h, 95% for **22**; c) H_2, Pd/C, EtOAc, 24h, 84% over two steps.

Formation of compound **8**was confirmed by NMR and mass analysis. The characteristic signals for compound **7**are summarized in **Table 3.2**

Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
OMe	3.24 (s, 3H)	54.9
Anomeric	6.16 (d, Hz, 3H), 5.99 – 5.95 (m, 1H), 5.93 (d, *J* = 3.1 Hz, 1H), 5.91 (d, *J* = 2.9 Hz, 1H) and 5.85 (d, 1H).	98.3, 99.5, 99.5, 99.8, 101.1
Benzoates	7.1-8.1 (m, 40)	165.2, 165.2, 165.4, 165.5, 165.5, 165.6, 166.2, 166.3

Table 3.1 Characteristic ^{1}H and ^{13}C NMR resonancesfor high pentamannan Man_5**7**

Saponification of compound **7**under modified Zemplén conditions followed by hydrogenolysis using Pd/C in H_2atmosphere (balloon pressure) afforded targeted pentasaccharide **6.**

Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
OMe	3.37 (s, 3H)	54.9
Anomeric	4.69 (s, 1H), 4.98 (t, *J* = 14.7 Hz, 2H), 5.11 (s, 1H), 5.30 (s, 1H)	97.9, 100.8, 101.0, 102.3,102.3

Table 3.1 Characteristic ^{1}H and ^{13}C NMR resonances of high pentamannan Man_5**6**

3.7 Conclusion

In conclusion, we have shown that the utility of newly developed hydroxybenzotriazolyl glycosyl donor chemistry through successful synthesis of linear trisaccharide of mannose and branched pentasaccharide of high mannan present on surface of HIV-gp120. Due to its simple operational protocol and excellent glycosylation yields, hydroxybenzotriazolyl glycosyl donors are useful for the rapid synthesis of oligosaccharide which are useful for in vaccine design.

3.8 General Experimental Procedure

Unless otherwise noted, materials were obtained from Sigma-Aldrich and were used without further purification. Unless otherwise reported all reactions were performed under Nitrogen atmosphere. Removal of solvent *in vacuo* refers to distillation using a rotary evaporator attached to an efficient vacuum pump. Products obtained as solids or syrups were dried under high vacuum. Analytical thin-layer chromatography was performed on pre-coated silica plates (F_{254}, 0.25 mm thickness); compounds were visualized by UV light or by staining with anisaldehyde spray. Optical rotations were measured on a digital polarimeter. IR spectra were recorded on a FT-IR spectrometer. NMR spectra were recorded either on a 400 or a 500 MHz with $CDCl_3$ or CD_3OD as the solvent and TMS as the internal standard. High resolution mass spectroscopy (HRMS) was performed using an ESI-TOF mass analyzer.

A) General Experimental Procedure for the Synthesis of Hydroxylbenzotriazolyl Glycosyl Donors (3, 8): Glycosyl bromide (1 eq.) in dry CH_2Cl_2 (5 mL) was stirred under nitrogen atmosphere for 5 min. Solid HOBt (113 mg, 834 mmol, 1.1 eq.) was added and followed by Et_3N (53 µL, 379 mmol, 0.5 eq.). The resulting reaction mixture was stirred for 2 h at 25 ^{o}C. At the end of the reaction as adjudged by TLC examination,

the reaction mixture was concentrated in *vacuo.* The crude residue was purified by silica gel column chromatography to afford corresponding glycosyl donor as white solid.

B) General Procedure for conversion of pent-4-enyl glycosides to glycosyl bromosides (for 3): Pent-4-enyl glucoside (1 mmol) in dry CH_2Cl_2 (10 mL) containing 4Å molecular sieves powder was cooled to -10 ^{0}C under nitrogen atmosphere. Molecular bromine (2 mmol) in CH_2Cl_2 (1 mL) was added drop wise to the reaction mixture and stirred at -10 ^{0}C for additional 10 minutes. The reaction mixture was concentrated under reduced pressure to afford glycosyl bromide along with 4Å molecular sieves powder which was immediately used in next step without any additional purification using aforementioned procedure.

C) General Procedure for Glycosylation for (2, 4, 7, 9): A solution of glycosyl donor (1 mmol) and glycosyl acceptor (1.1 mmol) in dry CH_2Cl_2 (2.5 ml) in the presence of 4Å molecular sieves (70 wt%) was stirred for 15 min at 0 ^{o}C under N_2 atm. Tf_2O (4o mol%) dissolved in 0.5 mL of CH_2Cl_2 was added at 0 ^{o}C and stirred for 30 min. The reaction was quenched by the addition of Et_3N (300 µL) and stirred for additional 15 min and filtered through a pad of celite, concentrated *invacuo* and the resulting residue was purified by silica gel column chromatography to glycoside product.

D) General procedure for 3-OH substitution of mannose (for 18): To a solution of compound a-methyl pyranoside (1 mmol) in 250 mL of MeOH, Bu_2SnO (1 mmol) was added and refluxed for 2 h at 90 ^{O}C. After two hours, methanol was completely evaporated under diminished pressure. The crude residue was redissolved in toluene and allyl bromide (2 mmol) and TBAI (1 mmol) were added. The reaction mixture heated at 70 ^{o}C for 24 h. Solvent was evaporated under diminished pressure and the resulting residue was separated by silica gel column chromatography using CH_2Cl_2 and methanol as mobile phase to afford desired product.

E) General Procedure for TBDPSCl protection (for 21): To stirred solution of starting material(1mmol) dissolved in dry DMF as a solvent and cooled to 0 ^{o}C, imidazole (2 mmol) was added and stirred for 30 min at 0 ^{o}C followed by addition of TBDPSCl (0.9 eq) at 0 ^{o}C and reaction mixture was stirred at 25 ^{o}C for 12 h. The reaction mixture was diluted with ethyl acetate (50 mL) and washed with brine solution and ethyl acetate (3x50 ml). The organic layer was separated and dried over anhydrous Na_2SO_4. The organic

solvent was evaporated under vacuum and the crude residue was purified by silica gel column chromatography to afford desired product.

F) General procedure for benzyl protection (for 14, 21): Starting compound (1 eq) dissolved in 35 mL of dry DMF was cooled to 0 ^{o}C and sodium hydride (1.5 eq. for each free hydroxyl group) was added and stirred for 30 min at 0 ^{o}C. Benzyl bromide (1.2 eq. for each hydroxyl group) was added and stirred for 6 h at 25 ^{o}C. The reaction mixture was diluted with water and washed ethyl acetate (3x40 mL) and combined organic layers were washed with brine solution. The organic layer was separated, dried (Na_2SO_4) and concentrated *invacuo* to obtain a residue that was purified by the silica gel column chromatography using ethyl acetate and n-hexane as mobile phase to afford desired product.

G) General procedure for TBDPS-deprotection (for 21): To a solution of silyl ether in solvent THF:Py (1:1) was added HF·Py (3ml) at 0 ^{0}C, allowed to warm to 25 ^{0}C and stirred for 3 h. The reaction mixture was concentrated *in vacuo* to obtain a residue which was purified by silica gel column chromatography (ethyl acetate and n-hexane) to afford desired compound.

H) General procedure for allyl group deprotection (for 10): Starting material (1 mmol) was dissolved in dry methanol:CH_2Cl_2(1:1) (50 ml for each 1g of compound) and $PdCl_2$ (15 mol %) dissolved in 5 mL methanol was added dropwise. The reaction mixture was stirred for additional 3 h at 25 ^{o}C and quenched with Et_3N and filtered through celite. The filtrate was concentrated *invacuo* and the resulting residue was purified by silica gel column chromatography to afford compound expected product.

I) General procedure for benzoyl group protection (for 5, 14, 16, 22): To a solution starting compound with Bz-protecting group (1 mmol) methanol-CH_2Cl_2 (1:1) (8 mL) and catalytic amount of freshly prepared NaOMe was added and stirred for 1 h. The NaOMe was quenched with Amberlite IR-120 and filtered, the filtrate was concentrated *invacuo*.The crude residue was purified by silica gel column chromatography to afford desired compound.

J) General procedure for benzyl deprotection by hydrogenation (for 7): The starting compoundwas dissolved in a 1:1 mixture of methanol and ethyl acetate (5mL), 10% Pd/C (15 mg) was added and stirred vigorously for 48 h under H_2 atmosphere (balloon). The

reaction mixture was filtered through a pad of celite, the filtrate was concentrated *invacuo*. The residue was purified by BIO-RAD Bio-Gel P-4 Gel using distilled water as mobile phase. The desired compound was obtained by lyophilization.

K) General procedure for opening of orthoester by using TMSOtf (for 15): To a solution of allyl-1,2-orthoester (1.0 mmol) in anhydrous CH_2Cl_2 (4 mL), pent-1-ene-ol (6 mmol) and freshly activated 4Å MS powder (0.200 g) were added under argon atmosphere and stirred for 15 min at 25 °C. TMSOT (5 mol%) was added drop wise by dissolving in CH_2Cl_2 and the reaction mixture was allowed to stir for 3-4 h and was passed through a bed of Celite®. The filtrate was concentrated *in vacuo* and purified by silica gel column chromatography using ethyl acetate and hexane as mobile phase to obtain corresponding glycoside with C-2 benzoate or acetate in 75-90% yield.

L) General procedure for orthoester formation (for 13): Per-*O*-benzoylatedmannose (1.0 mmol) were dissolved in anhydrous CH_2Cl_2 and cooled to 0 °C. 40% HBr in glacial acetic (1 mmol) was added to the reaction mixture and stirred at 0 °C for 2 h. After complete conversion of the starting material, the reaction mixture was diluted with CH_2Cl_2 and poured over ice-water mixture and was extracted with CH_2Cl_2 (3x50 mL). The organic layer was washed with ice-cold saturated $NaHCO_3$ (1x25 mL), brine solution (1x25 mL), dried over Na_2SO_4 and concentrated *in vacuo* to afford corresponding furanosyl bromide as a white foam which was immediately carried forward without any further purification. To a solution of the crude furanosyl bromide prepared *vide supra* in anhydrous CH_2Cl_2, allyl alcohol (2.0 mmol), 2,6-lutidine (2.2 mmol) and tetra *n*-butyl ammonium iodide (0.5 mmol) were added and the reaction mixture was allowed to stir at 25 °C. After 15 h, the reaction mixture was diluted with CH_2Cl_2 and water, extracted with saturated aqueous oxalic acid solution (3x25 mL), saturated $NaHCO_3$ (1x25 mL), brine solution (1x25 mL), dried over Na_2SO_4 and concentrated *in vacuo* to obtain a crude product that was purified by silica gel column chromatography using EtOAc and Hexane as mobile phase to obtain the corresponding orthoester.

M) General procedure for benzoate ester protection of alcohols (for 11) : To a solution of alcohol (1 mmol) in anhydrous pyridine (10 mL), benzoyl chloride/acetic anhydride (1.2 mmol per alcohol) was added dropwise at 0 ^{0}C under nitrogen atmosphere. The reaction mixture was gradually warmed up to 25 ^{0}C and stirred for 6-12 h. Progress of

the reaction and consumption of starting alcohol was checked by TLC. After completion of the reaction, the reaction mixture was quenched by adding ice cooled water and extracted with CH_2Cl_2 (50 mL) and the CH_2Cl_2 layer was washed with 1*N*HCl (2x50 mL), water, sat. aq. $NaHCO_3$ solution and finally with brine solution. Combined organic layers were dried over anhydrous Na_2SO_4, concentrated *in vacuo* and the resulting crude residue was purified by silica gel column chromatography (*n*-hexane/EtOAc) to obtain the desired compound.

3.9 Supporting Information

1*H*-benzo[*d*][1,2,3]triazol-1-yl 2,3,4,6-tetra-*O*-benzoyl α-D-mannopyranoside (**8**): mp(^{0}C): 124.0; $[\alpha]^{25}_D$ ($CHCl_3$, *c*1.0): 37.7º; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 4.56 (dd, *J* = 12.6, 4.2 Hz, 1H), 4.78 (dd, *J* = 12.5, 2.3 Hz, 1H), 5.35 (ddd, *J* = 10.2, 3.9, 2.4 Hz, 1H), 6.01 (d, *J* = 1.7 Hz, 1H), 6.15 (dd, *J* = 10.1, 3.3 Hz, 1H), 6.23 (dd, *J* = 3.4, 1.8 Hz, 1H), 6.33 (t, *J* = 10.2 Hz, 1H), 7.27 – 7.33 (m, 2H), 7.35 – 7.42 (m, 7H), 7.43 – 7.48 (m, 1H), 7.49 – 7.63 (m, 4H), 7.65 – 7.70 (m, 1H), 7.90 (dd, *J* = 8.3, 1.1 Hz, 2H), 8.00 – 8.07 (m, 7H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 62.2, 65.9, 68.3, 69.5, 71.5,103.2, 108.2, 120.6, 125.0, 127.2, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 128.7, 128.7, 128.8, 128.8, 129.6, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 133.1, 133.5, 133.7, 134.0, 143.5, 165.3, 165.4, 165.5, 166.0; HRMS (ESI-MS): m/z calcd for [$C_{40}H_{31}N_3O_{10}Na^+$]: 736.1907; Found: 736.1908.

3,4,6-tri-O-benzoyl-α-D-mannopyranoside-(allyloxy)-1,2-orthobenzoate (13): mp(^{0}C): 104.0; $[\alpha]^{25}_D$ ($CHCl_3$, *c*1.0): 45.9º; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.98 (dt, *J* = 5.6, 1.4 Hz, 2H), 4.10 – 4.23 (m, 1H), 4.43 (dd, *J* = 12.1, 4.4 Hz, 1H), 4.61 (dd, *J* = 12.1, 3.1 Hz, 1H), 5.02 – 5.12 (m, 1H), 5.14 – 5.18 (m, 1H), 5.20 – 5.26 (m, 1H), 5.77 (dd, *J* = 10.0, 4.0 Hz, 1H), 5.81 – 5.91 (m, 2H), 6.01 (t, *J* = 9.6 Hz, 1H), 7.26 – 7.41 (m, 9H), 7.42 – 7.58 (m, 3H), 7.74 – 7.86 (m, 2H), 7.90 – 8.00 (m, 4H), 8.04 (dd, *J* = 8.3, 1.1 Hz, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 63.1, 65.5, 66.6, 71.3, 72.1, 76.5, 98.1, 117.0, 123.1, 126.7, 126.8, 128.4, 128.4, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 129.0, 129.1, 129.5, 129.8, 129.8, 129.9, 129.9, 129.9, 130.1, 130.2, 133.2, 133.6, 133.7, 133.9, 136.6, 165.3, 166.1, 166.2; HRMS (ESI-MS): m/z calcd for [$C_{37}H_{32}O_{10}Na^+$]: 659.1893; Found: 659.1890.

Pent-4-enyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-β-D-mannopyranoside (15): mp(^{0}C): 98.8; $[\alpha]^{25}_D$ ($CHCl_3$, *c*1.0): 68.5º; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.67 – 1.84 (m, 2H), 2.11 – 2.30 (m,

2H), 3.52 (dt, *J* = 9.7, 6.5 Hz, 1H), 3.68 – 3.87 (m, 2H), 3.94 (td, *J* = 9.4, 8.2, 4.0 Hz, 2H), 4.10 – 4.26 (m, 2H), 4.54 – 4.68 (m, 3H), 4.79 (d, *J* = 12.0 Hz, 1H), 4.86 (d, *J* = 11.3 Hz, 1H), 4.93 (d, *J* = 10.8 Hz, 1H), 4.98 – 5.12 (m, 3H), 5.67 (t, *J* = 2.3 Hz, 1H), 5.86 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 7.21 – 7.48 (m, 17H), 7.56 – 7.65 (m, 1H), 8.13 (dd, *J* = 8.3, 1.2 Hz, 2H).; ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.7, 30.4, 67.4, 69.2, 69.2, 71.7, 71.7, 73.5, 74.5, 75.4, 78.4, 97.9, 115.1, 127.6, 127.6, 127.6, 127.7, 127.8, 128.1, 128.1, 128.1, 128.2, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 130.1, 130.1, 130.1, 130.1, 133.2, 138.0, 138.1, 138.5, 138.6, 165.9; HRMS (ESI-MS): m/z calcd for [$C_{39}H_{42}O_7Na^+$]: 645.2828; Found: 645.2890.

Pent-4-enyl 3,4,6-tri-*O*-benzyl-β-D-mannopyranoside (5): mp(^{0}C): 102.0; [α]$^{25}_D$ ($CHCl_3$, *c*1.0): 44.9^o; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.73 (p, *J* = 6.8 Hz, 2H), 2.08 – 2.22 (m, 2H), 2.78 (s, 1H), 3.49 (dt, *J* = 9.7, 6.5 Hz, 1H), 3.73 – 3.80 (m, 2H), 3.78 – 3.90 (m, 2H), 3.89 – 4.01 (m, 2H), 4.06 – 4.14 (m, 1H), 4.49 – 4.65 (m, 2H), 4.67 – 4.83 (m, 3H), 4.90 (d, *J* = 10.8 Hz, 1H), 4.96 (d, *J* = 1.6 Hz, 1H), 4.99 – 5.18 (m, 2H), 5.86 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 7.22 – 7.28 (m, 2H), 7.31 – 7.52 (m, 13H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.7, 30.3, 67.1, 68.5, 69.0, 71.1, 72.0, 73.5, 74.4, 75.2, 77.2, 80.3, 99.3, 115.0, 127.6, 127.7, 127.9, 127.9, 127.9, 127.9, 127.9, 128.0, 128.0, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 138.0, 138.0, 138.3, 138.4; HRMS (ESI-MS): m/z calcd for [$C_{23}H_{38}O_6Na^+$]: 541.2566; Found: 541.2568.

1*H*-benzo[*d*][1,2,3]triazol-1-yl 2-*O*-benzoyl-3,4,6-tetra-*O*-benzyl-α-D-mannopyranoside (**3**): mp(^{0}C): 91.0; [α]$^{25}_D$($CHCl_3$, *c*1.0): 17.1^0; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.79 (dd, *J* = 11.1, 1.7 Hz, 1H), 3.96 (dd, *J* = 11.1, 3.6 Hz, 1H), 4.21 – 4.36 (m, 2H), 4.45 (d, *J* = 11.8 Hz, 1H), 4.63 (dd, *J* = 11.4, 7.0 Hz, 3H), 4.71 (d, *J* = 11.5 Hz, 1H), 4.90 (dd, *J* = 21.1, 11.2 Hz, 2H), 5.82 – 5.91 (m, 1H), 6.01 – 6.14 (m, 1H), 7.21 – 7.46 (m, 19H), 7.59 (ddd, *J* = 10.1, 8.7, 4.7 Hz, 2H), 8.01 (d, *J* = 8.3 Hz, 1H), 8.05 – 8.10 (m, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 67.5, 68.6, 72.3, 73.6, 73.7, 74.5, 75.4, 77.5, 104.9, 108.6, 120.5, 124.9, 127.6, 127.7, 127.7, 127.7, 127.9, 128.0, 128.1, 128.1, 128.2, 128.2, 128.5, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.7, 128.7, 129.3, 130.2, 130.2, 133.7, 137.7, 138.2, 138.3, 143.6, 165.6; HRMS (ESI-MS): m/z calcd for [$C_{40}H_{37}N_3O_7Na^+$]: 694.2529; Found: 694.2529.

Pent-4-enyl 3,4,6-tri-*O*-benzyl-2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-a-D-mannopyranosyl)-α-D-mannopyranoside (16): mp(^{0}C): 89.1; [α]$^{25}_D$ ($CHCl_3$, *c*1.0): 54.9^o; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.50 – 1.79 (m, 2H), 2.04 (q, *J* = 6.6 Hz, 2H), 3.30 (dt, *J* = 9.7, 6.5 Hz, 1H), 3.55 – 3.67 (m, 1H), 3.75 (ddd, *J* = 14.6, 6.8, 4.1 Hz, 4H), 3.80 – 3.89 (m, 2H), 3.92 (dd, *J* = 9.2, 2.9

Hz, 1H), 3.95 – 4.06 (m, 3H), 4.11 (dd, *J* = 9.2, 3.1 Hz, 1H), 4.45 (d, *J* = 11.1 Hz, 1H), 4.50 (d, *J* = 2.2 Hz, 1H), 4.51 – 4.55 (m, 2H), 4.57 (d, *J* = 4.0 Hz, 1H), 4.65 (s, 1H), 4.68 (t, *J* = 2.8 Hz, 3H), 4.76 (d, *J* = 11.1 Hz, 1H), 4.84 (d, *J* = 4.3 Hz, 1H), 4.87 (d, *J* = 4.2 Hz, 1H), 4.89 (d, *J* = 1.8 Hz, 1H), 4.94 – 4.98 (m, 2H), 5.19 (d, *J* = 1.9 Hz, 1H), 7.02 – 7.46 (m, 33H), 8.07 (dd, *J* = 8.3, 1.2 Hz, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.8, 30.4, 67.1, 69.2, 69.4, 69.5, 71.8, 72.0, 72.1, 72.3, 73.4, 73.5, 74.5, 74.8, 75.3, 75.3, 75.4, 77.2, 78.3, 79.9, 98.8, 99.7, 115.0, 127.5, 127.6, 127.6, 127.6, 127.7, 127.7, 127.7, 127.8, 128.0, 128.0, 128.2, 128.2, 128.2, 128.2, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 130.1, 130.2, 133.2, 138.2, 138.2, 138.2, 138.4, 138.5, 138.5, 138.6, 138.7, 165.6.; HRMS (ESI-MS): m/z calcd for [$C_{66}H_{70}O_{12}Na^+$]: 1077.4765; Found: 1077.4769.

Pent-4-enyl 3,4,6-tri-*O*-benzyl-2-*O*-(3,4,6-tri-*O*-benzyl-2-*O*-*(*2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranoside (2): mp(^{0}C): 92.8; $[\alpha]^{25}_D$ ($CHCl_3$, *c*1.0): 59.0^o; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.49 – 1.79 (m, 2H), 1.89 – 2.22 (m, 2H), 3.29 (dd, *J* = 8.1, 4.7 Hz, 1H), 3.64 (dd, *J* = 8.1, 5.0 Hz, 2H), 3.70 – 3.86 (m, 7H), 3.87 – 4.06 (m, 6H), 4.14 (d, *J* = 8.2 Hz, 3H), 4.41 (d, *J* = 11.8 Hz, 1H), 4.50 – 4.62 (m, 9H), 4.67 (dd, *J* = 17.3, 5.1 Hz, 4H), 4.76 – 5.06 (m, 7H), 5.15 (s, 1H), 5.27 (s, 1H), 5.75 – 5.85 (m, 1H), 6.97 – 7.55 (m, 47H), 7.60 (t, *J* = 7.4 Hz, 1H), 8.13 (d, *J* = 6.8 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.7, 30.3, 67.0, 69.1, 69.1, 69.4, 69.6, 71.6, 71.8, 72.1, 72.2, 72.2, 72.3, 73.3, 73.3, 73.3, 74.4, 74.8, 75.0, 75.0, 75.2, 75.2, 75.3, 75.6, 77.3, 78.1, 79.3, 79.6, 98.8, 99.5, 100.7, 114.8, 127.4, 127.4, 127.4, 127.4, 127.5, 127.5, 127.5, 127.5, 127.5, 127.5, 127.5, 127.6, 127.6, 127.6, 127.6, 127.6, 127.6, 127.6, 127.7, 127.7, 128.0, 128.0, 128.0, 128.0, 128.1, 128.1, 128.1, 128.1, 128.1, 128.2, 128.2, 128.2, 128.2, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 130.0, 130.1, 133.1, 138.1, 138.3, 138.5, 138.5, 138.6, 165.5.; HRMS (ESI-MS): m/z calcd for [$C_{93}H_{98}O_{17}Na^+$]: 1510.6735; Found: 1510.6758.

Methyl 3-*O*-allyl-α-D-mannopyranoside(18): mp(^{0}C): 71.0; $[\alpha]_{25}{}^D$ (MeOH, *c* 1.0): 76.4^0; ^{1}H NMR (399.78MHz, CD_3OD): δ 3.40 (s, 3H), 3.47 – 3.57 (m, 2H), 3.67 – 3.78 (m, 2H), 3.85 (dd, *J* = 11.8, 2.4 Hz, 1H), 3.97 (dd, *J* = 3.3, 1.8 Hz, 1H), 4.09 – 4.31 (m, 2H), 4.68 (d, *J* = 1.9 Hz, 1H), 4.85 (s, 3H), 5.18 (dq, *J* = 10.4, 1.4 Hz, 1H), 5.34 (dd, *J* = 17.3, 1.7 Hz, 1H), 5.90 – 6.20 (m, 1H);^{13}C NMR (100.67 MHz, CD_3OD): δ 55.2, 62.8, 67.4, 68.8, 71.7, 74.4, 80.0, 102.5, 117.3, 136.5; HRMS (ESI-MS): m/z calcd for [$C_{10}H_{18}O_6Na]^+$:257.1001; Found: 257.1001.

Methyl 3-*O*-allyl-6-*O*-(*tert*-butyldiphenylsilyl)-α-D-mannopyranoside(19): mp(^{0}C): 81.0; $[\alpha]_{25}^{D}$($CHCl_3$, *c* 1.0): 31.7^0; ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.07 (s, 9H), 2.58 – 2.68 (m, 1H), 2.99 (s, 1H), 3.33 (s, 3H), 3.61 (dd, *J* = 9.1, 3.4 Hz, 1H), 3.68 (dt, *J* = 9.8, 5.0 Hz, 1H), 3.84 – 4.02 (m, 4H), 4.16 (dd, *J* = 10.0, 6.4 Hz, 2H), 4.74 (s, 1H), 5.12 – 5.25 (m, 1H), 5.26 – 5.38 (m, 1H), 5.88 – 6.03 (m, 1H), 7.40 (t, *J* = 8.2 Hz, 6H), 7.67 – 7.76 (m, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$):δ 19.3, 26.9, 26.9, 26.9, 54.8, 65.1, 67.7, 68.5, 70.9, 71.3, 79.1, 100.4, 117.9, 127.8(8C), 129.8, 133.0, 133.1, 134.5, 135.7; HRMS (ESI-MS): m/z calcd for $[C_{26}H_{36}O_6SiNa]^+$: 495.6428; Found: 495.6427.

Methyl 2,4-Di-*O*-benzyl-3-*O*-allyl-6-*O*-(*tert*-butyldiphenylsilyl)-α-D-mannoside(20): mp(^{0}C): 81.0; $[\alpha]_{25}^{D}$ ($CHCl_3$, *c* 1.0): 12.4^0; ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.06 (s, 9H), 3.30 (s, 3H), 3.65 (d, *J* = 14.2 Hz, 1H), 3.73 – 3.85 (m, 2H), 3.88 – 4.03 (m, 3H), 4.11 (d, *J* = 6.8 Hz, 2H), 4.55 (d, *J* = 10.8 Hz, 1H), 4.66 – 4.78 (m, 2H), 4.82 (d, *J* = 12.4 Hz, 1H), 4.90 (d, *J* = 10.8 Hz, 1H), 5.16 (d, *J* = 11.8 Hz, 1H), 5.31 (d, *J* = 19.0 Hz, 1H), 5.94 (d, *J* = 27.7 Hz, 1H), 7.11 – 7.29 (m, 4H), 7.31 – 7.44 (m, 10H), 7.73 (dd, *J* = 15.1, 7.3 Hz, 6H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 19.7, 27.0, 27.2, 27.2, 54.9, 63.8, 71.6, 73.1, 73.4, 75.2, 75.5, 75.6, 80.4, 99.2, 117.1, 127.9(2C), 128.0(2C), 128.0, 128.1(2C), 128.1, 128.4(4C), 128.7, 129.9(2C), 130.1, 133.9, 134.3, 135.2, 135.5, 135.6, 136.1, 136.3, 139.0, 139.0; HRMS (ESI-MS): m/z calcd for $[C_{40}H_{48}O_6SiNa]^+$: 675.8928; Found: 675.8928.

Methyl 2,4-Di-*O*-benzyl-3-*O*-allyl-α-D-mannopyranoside (21): mp(^{0}C): 84.0; $[\alpha]_{25}^{D}$ ($CHCl_3$, *c* 1.0): 40.6^0; ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.25(s,1H), 3.29 (s, 3H), 3.60 (dd, *J* = 8.7, 5.6 Hz, 1H), 3.72 – 3.86 (m, 4H), 3.93 (d, *J* = 9.3 Hz, 1H), 4.10 (d, *J* = 5.4 Hz, 2H), 4.60 – 4.74 (m, 3H), 4.80 (d, *J* = 12.4 Hz, 1H), 4.93 (d, *J* = 10.9 Hz, 1H), 5.18 (dq, *J* = 10.5, 1.4 Hz, 1H), 5.27 – 5.38 (m, 1H), 5.84 – 6.01 (m, 1H), 7.24 – 7.42 (m, 10H); ^{13}C NMR (100.67 MHz, $CDCl_3$):δ 54.8,

62.5, 71.2, 72.1, 73.1, 74.7, 74.9, 75.3, 80.0, 99.5, 116.8, 127.8 (2C), 128.0(2C), 128.2(2C), 128.5(2C), 128.5(2C), 135.0, 138.4, 138.6; HRMS (ESI-MS): m/z calcd for $[C_{24}H_{30}O_6Na]^+$: 437.4878; Found: 437.4876.

Methyl 2,4-di-*O*-benzyl-α-D-mannopyranoside (10): mp(^{0}C): 86.0; $[\alpha]_{25}^{D}$ ($CHCl_3$, *c* 1.0): 30.4^0; ^{1}H NMR (399.78MHz, $CDCl_3$): δ 2.56 (d, *J* = 8.6 Hz, 2H), 3.27 (s, 3H), 3.41 – 3.90 (m, 5H), 3.97 (s, 1H), 4.48 – 4.76 (m, 4H), 4.87 (d, *J* = 11.2 Hz, 1H), 7.31 (d, *J* = 6.9 Hz, 10H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 54.8, 62.1, 71.4, 71.7, 73.1, 74.8, 76.3, 78.4, 98.3, 127.7, 127.8(2C), 127.9(2C), 128.0, 128.4(2C), 128.5(2C), 137.7, 138.4.; HRMS (ESI-MS): m/z calcd for $[C_{21}H_{26}O_6Na]^+$: 397.1627; Found: 397.1620.

Methyl 2,4-di-*O*-benzyl-3,6-di-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**9**): mp(^{0}C): 87.0; $[\alpha]^{25}{}_D$($CHCl_3$, *c*1.0): 5.5^0; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.21 (s, 3H), 3.65 – 3.68 (m, 2H), 3.70 (d, *J* = 3.2 Hz, 1H), 3.75 (s, 1H), 3.83 (d, *J* = 4.6 Hz, 2H), 3.88 – 3.93 (m, 1H), 4.02 (d, *J* = 7.1 Hz, 2H), 4.09 (d, *J* = 8.5 Hz, 2H), 4.17 (dd, *J* = 9.4, 2.9 Hz, 2H), 4.46 (s, 1H), 4.49 (t, *J* = 3.2 Hz, 3H), 4.51 (s, 1H), 4.52 (s, 2H), 4.56 (s, 1H), 4.64 – 4.69 (m, 5H), 4.71 (d, *J* = 4.2 Hz, 1H), 4.73 (d, *J* = 1.9 Hz, 1H), 4.75 – 4.82 (m, 2H), 4.85 – 4.92 (m, 3H), 5.09 (d, *J* = 1.8 Hz, 1H), 5.33 (d, *J* = 1.6 Hz, 1H), 5.73 (t, *J* = 2.1 Hz, 1H), 5.74 – 5.77 (m, 1H), 7.17 (m, 8H), 7.20 (m, 7H), 7.26 (m, 15H), 7.30 (m, 2H), 7.32 – 7.37 (m, 10H), 7.54 (m, 3H), 8.05 (m, 5H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 54.9, 66.6, 68.8, 68.8, 69.1, 69.2, 69.5, 71.1, 71.2, 71.7, 71.7, 71.8, 72.5, 72.5, 73.5, 73.5, 73.6, 73.6, 74.3, 74.5, 75.2, 75.2, 75.3, 75.3, 78.3, 78.7, 98.3, 98.3, 99.8, 127.5, 127.6, 127.6, 127.6, 127.6, 127.7, 127.7, 127.7, 127.7, 127.8, 127.8, 127.8, 127.8, 127.8, 127.9, 127.9, 127.9, 128.0, 128.0, 128.0, 128.1, 128.1, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 130.0, 130.1, 130.1, 130.1, 130.1, 130.1, 130.1, 130.1, 133.2, 133.2, 138.0,

138.0, 138.0, 138.3, 138.6, 138.6, 138.7, 138.8, 165.6, 165.7; HRMS (ESI-MS): m/z calcd for $[C_{89}H_{90}O_{18}Na^+]$:1469.6025; Found: 1469.6024.

Methyl 2,4-di-*O*-benzyl-3,6-di-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (22): mp(^{0}C): 114.0; $[\alpha]^{25}_D$($CHCl_3$, *c*1.0):45.3^0; ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.83 (s, 1H), 2.44 (s, 1H), 3.17 – 3.28 (m, 3H), 3.54 – 4.04 (m, 16H), 4.08 – 4.18 (m, 2H), 4.43 – 4.72 (m, 15H), 4.84 (t, *J* = 10.7 Hz, 2H), 5.09 (s, 1H), 5.23 (s, 1H), 7.14 – 7.36 (m, 40H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 54.9, 66.2, 68.2, 68.8, 68.9, 69.5, 71.2, 71.5, 71.6, 72.0, 72.1, 72.4, 73.5, 73.6, 74.3, 74.5, 75.0, 75.0, 75.1, 75.2, 77.8, 79.1, 79.6, 80.2, 98.2, 99.8, 101.6, 127.6, 127.6, 127.6, 127.6, 127.7, 127.7, 127.7, 127.7, 127.7, 127.8, 127.8, 127.8, 127.8, 127.9, 127.9, 127.9, 127.9, 127.9, 128.0, 128.0, 128.0, 128.0, 128.0, 128.0, 128.1, 128.1, 128.1, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 128.6, 138.0, 138.0, 138.2, 138.3, 138.4, 138.4, 138.5, 138.6; HRMS (ESI-MS):m/z calcd for $[C_{75}H_{82}O_{18}Na^+]$:1261.5501; Found: 1261.5504.

Methyl 2,4-di-*O*-benzyl-3,6-di-*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 (7): mp(^{0}C): 89.0; $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): -1.5^0; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.24 (s, 3H), 3.56 – 3.73 (m, 5H), 3.73 – 3.87 (m, 3H), 3.91 (t, *J* = 9.6 Hz, 3H), 4.00 (t, *J* = 10.1 Hz, 5H), 4.13 (s, 2H), 4.28 (dd, *J* = 12.4, 2.8 Hz, 1H), 4.37 – 4.45 (m, 3H), 4.51 (s, 2H), 4.55 (d, *J* = 4.9 Hz, 5H), 4.58 (d, *J* = 4.8 Hz, 2H), 4.61 (d, *J* = 5.5 Hz, 3H), 4.65 (d, *J* = 2.8 Hz, 2H), 4.66 – 4.75 (m, 2H), 4.79 (s, 1H), 4.92 (t, *J* = 10.6 Hz, 2H), 5.03 (s, 1H), 5.12 (s, 1H), 5.20 (s, 1H), 5.33 (s, 1H), 5.83 – 6.00 (m, 4H), 6.15 (dt, *J* = 25.4, 10.1 Hz, 2H), 6.89 – 7.04 (m, 5H), 7.10 (q, *J* = 7.5 Hz, 5H), 7.15 – 7.22 (m, 10H), 7.27 (ddd, *J* = 12.7, 6.3, 2.0 Hz, 25H), 7.34 – 7.48 (m, 15H), 7.52 – 7.63 (m, 4H), 7.81 – 7.90 (m, 8H), 8.04 (d, *J* = 8.0 Hz, 4H), 8.12 (d, *J* = 7.9 Hz, 4H); ^{13}C NMR

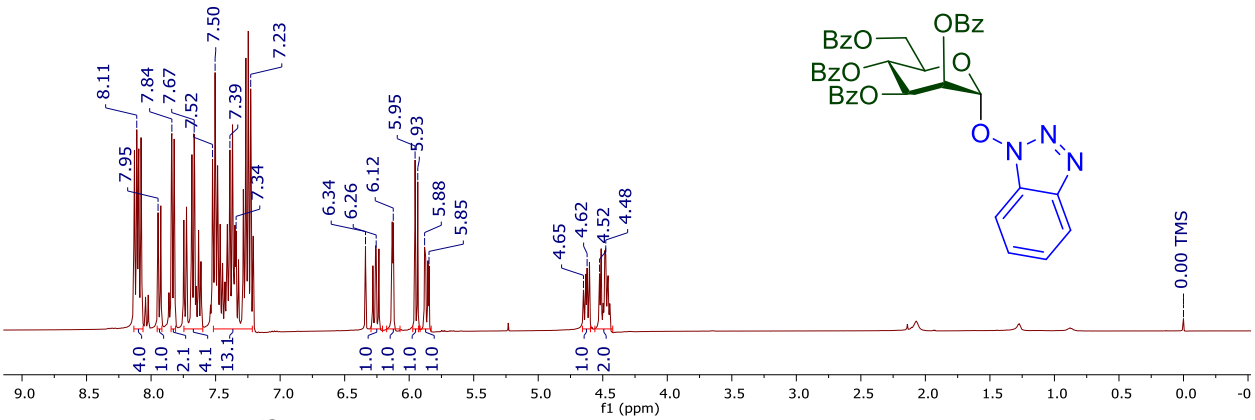
(100.67 MHz, $CDCl_3$): δ 54.9, 62.7, 62.7, 66.4, 66.7, 66.9, 69.2, 69.3, 69.4, 69.6, 70.3, 70.3, 70.5, 70.6, 71.7, 71.8, 71.9, 72.2, 72.6, 72.7, 73.2, 73.4, 74.7, 74.8, 74.9, 74.9, 75.1, 75.4, 77.1, 77.4, 77.9, 78.7, 79.4, 79.7, 98.3, 99.5, 99.5, 99.8, 101.1, 127.1, 127.1, 127.1, 127.4, 127.4, 127.5, 127.5, 127.5, 127.5, 127.6, 127.6, 127.6, 127.7, 127.7, 127.7, 127.7, 127.7, 127.9, 127.9, 127.9, 128.0, 128.0, 128.0, 128.0, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 128.7, 128.7, 128.7, 128.7, 129.2, 129.2, 129.4, 129.5, 129.7, 129.7, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.1, 130.2, 133.0, 133.1, 133.1, 133.1, 133.4, 133.4, 133.4, 133.5, 138.2, 138.3, 138.3, 138.3, 138.5, 138.5, 138.7, 138.8, 165.2, 165.2, 165.4, 165.5, 165.5, 165.6, 166.2, 166.3; HRMS (ESI-MS): m/z calcd for $[C_{143}H_{134}O_{34}Na^+]$:2418.8688; Found: 2418.8686.

Methyl 3,6-di-*O*-(2-*O*-α-D-mannopyranosyl)-α-D-mannopyranosyl-α-D-mannopyranoside (6): mp(^{0}C): 70.0; $[\alpha]^{25}_D$(H_2O, *c*1.0): 21.5^0; ^{1}H NMR (399.78 MHz, D_2O): δ 3.37 (s, 3H), 3.56 – 4.14 (m, 30H), 4.69 (s, 1H), 4.97 (d, *J* = 14.7 Hz, 1H), 4.99 (d, *J* = 14.7 Hz, 1H),5.11 (s, 1H), 5.30 (s, 1H) [16 protons exchanged due to D_2O];^{13}C NMR (100.67 MHz, D_2O): δ 54.9, 60.9, 60.9, 61.1, 65.3, 65.6, 66.7, 66.8, 66.8, 66.9, 69.9, 69.5, 69.9, 70.1, 70.2, 70.3, 70.3, 70.8, 72.7, 73.2, 73.2, 73.2, 73.3, 78.4, 78.6, 78.8, 97.9, 100.8, 101.0, 102.3, 102.3; HRMS (ESI-MS): m/z calcd for $[C_{31}H_{54}O_{26}Na^+]$:865.2801; Found: 865.2789.

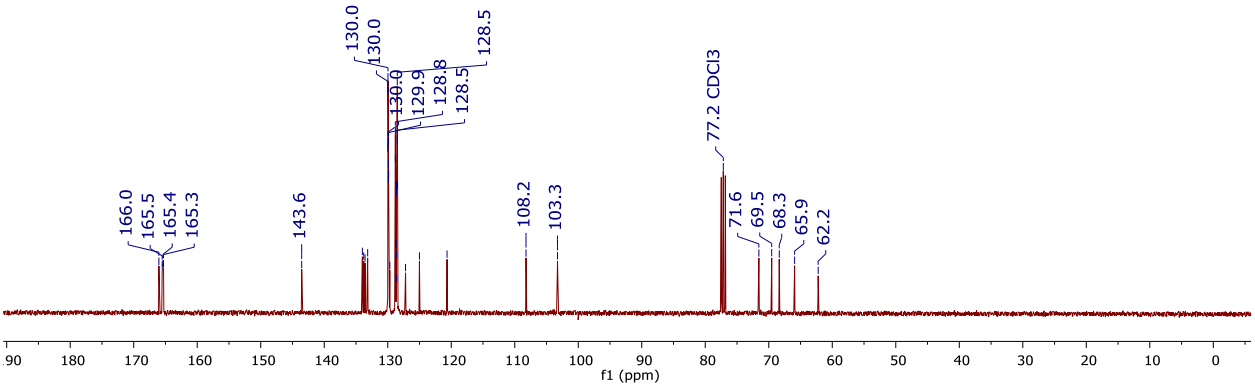
3.10 Representative Spectral Charts

Kindly see the supporting documents file in *J. Org. Chem.*, **2017**, *82*, 11494-11504 for spectral charts of compounds (**3, 6, 7, 8, 9, 10, 18, 19, 20, 21, and 22**)

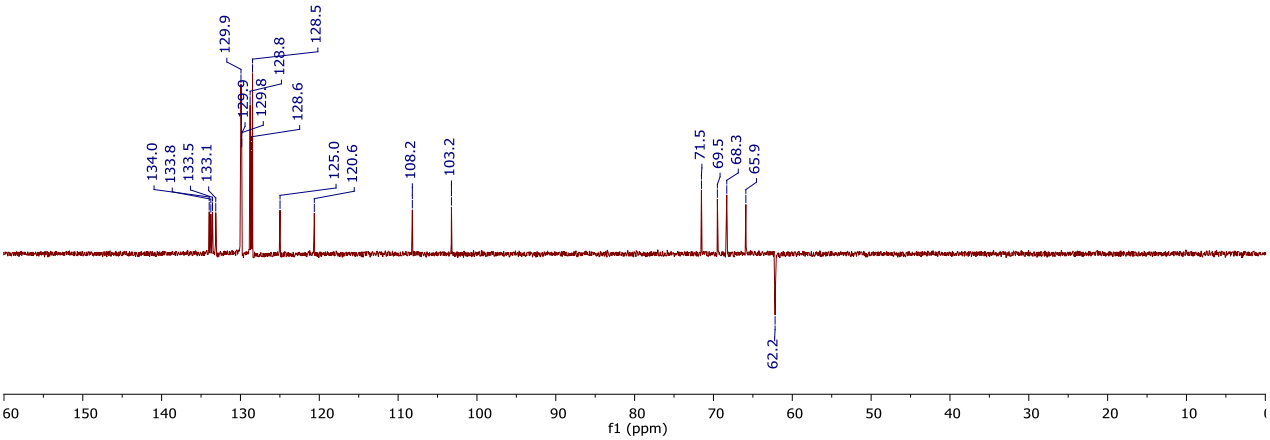
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **8**



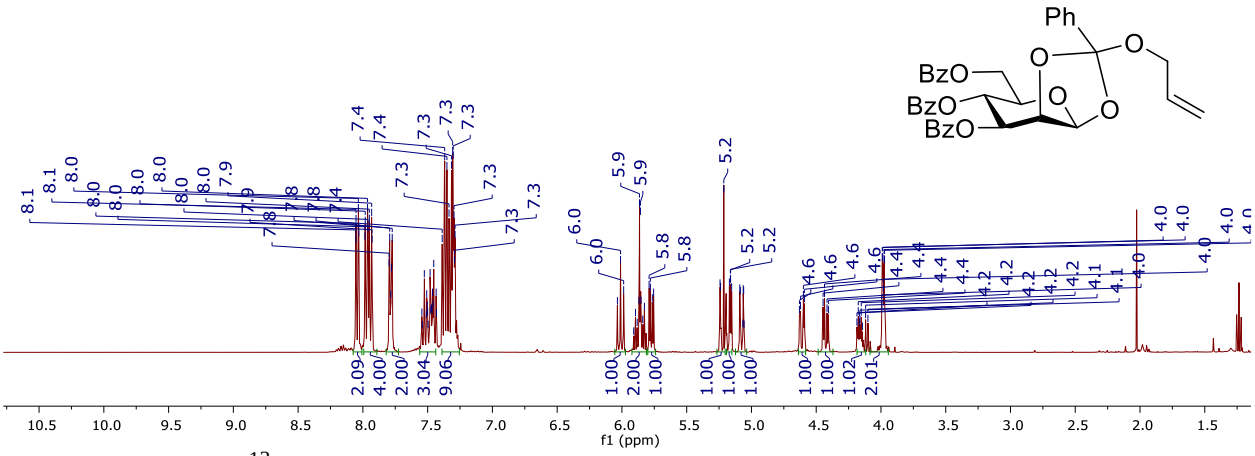
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound **8**



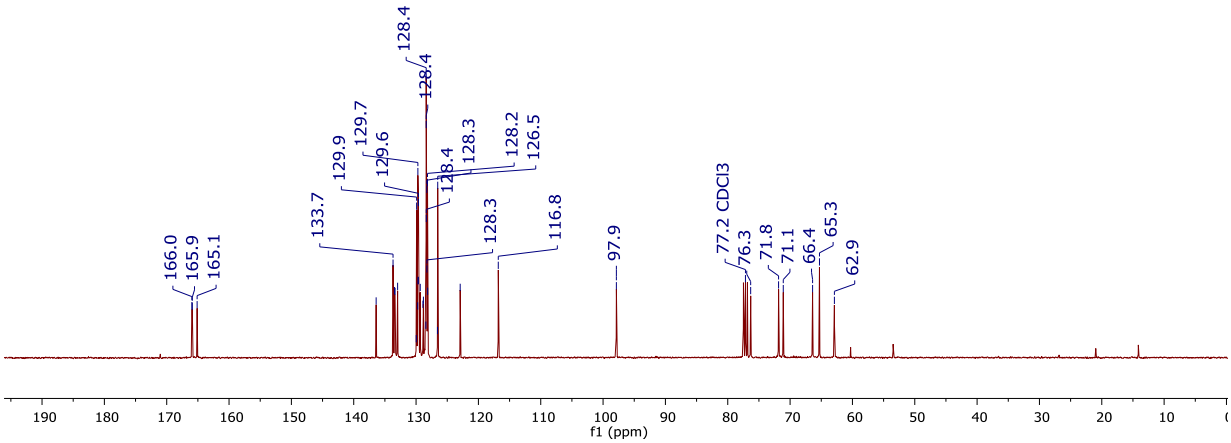
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **8**



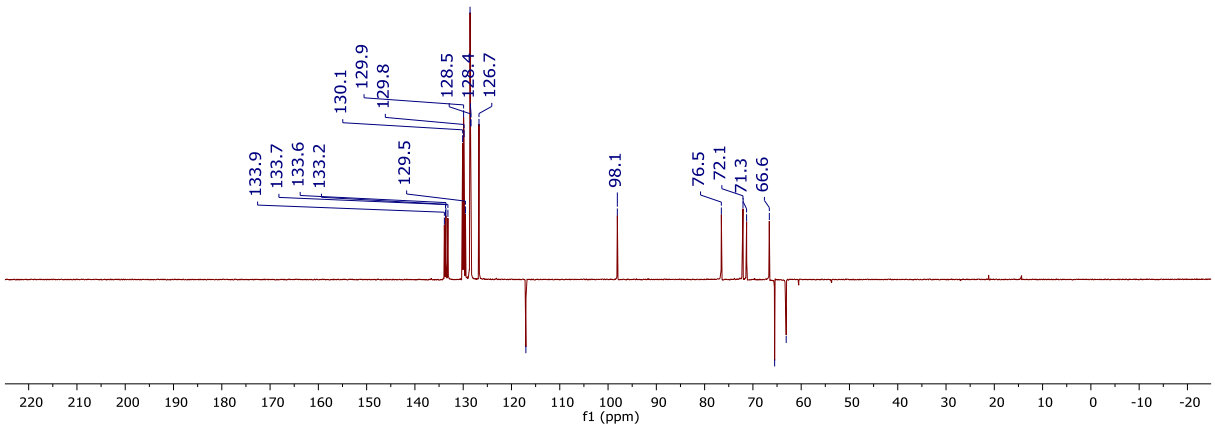
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **13**



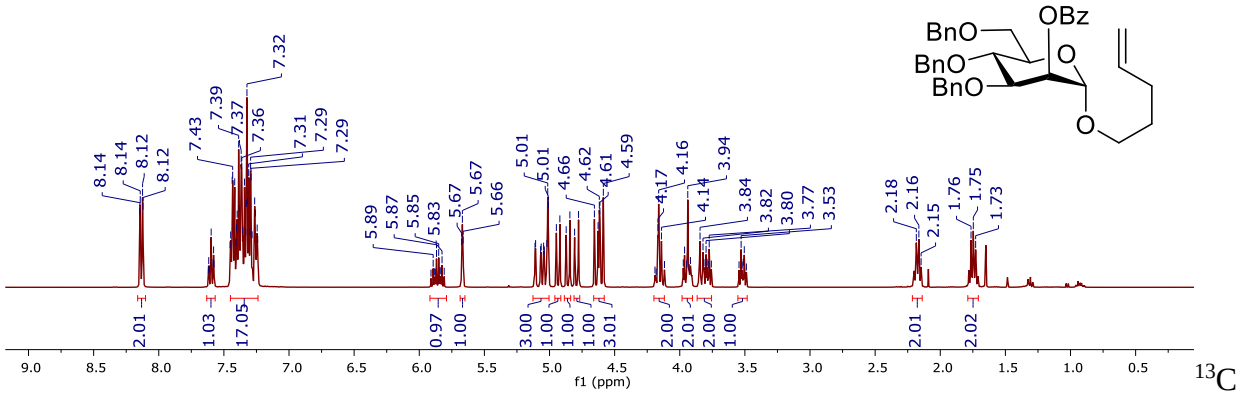
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound **13**



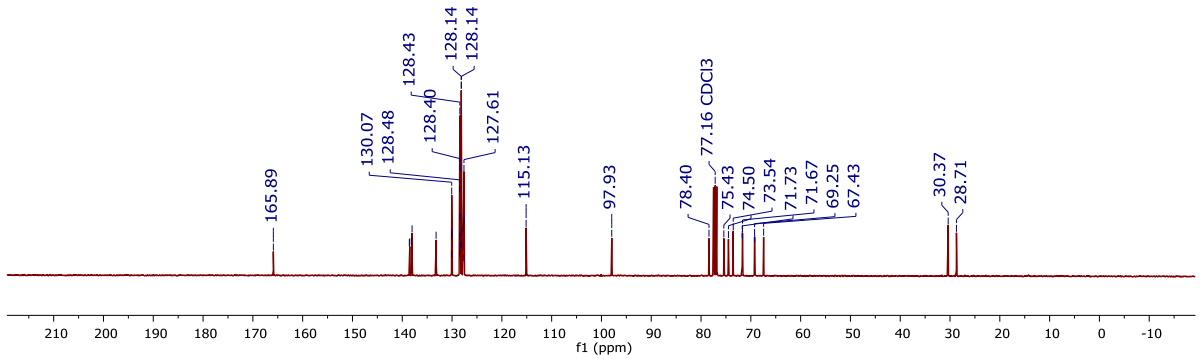
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **13**



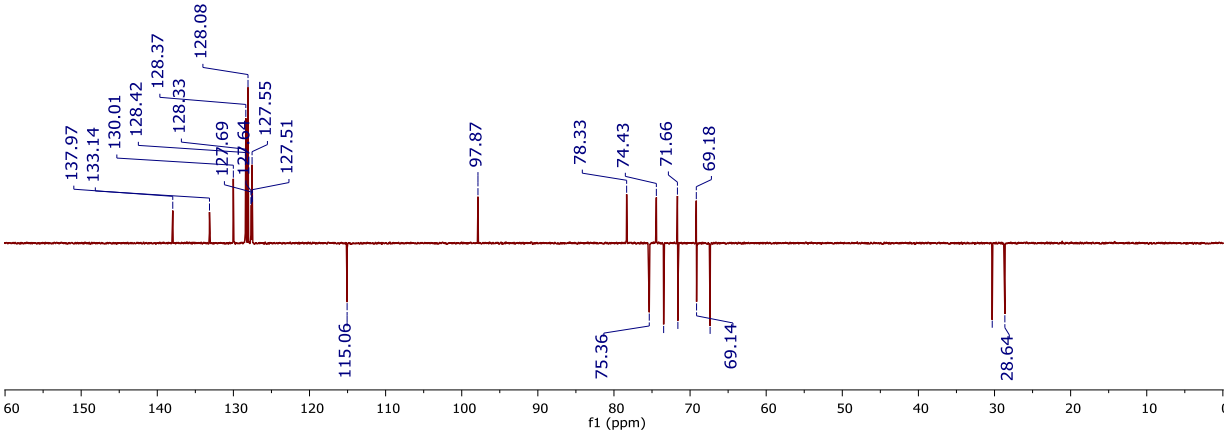
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **15**



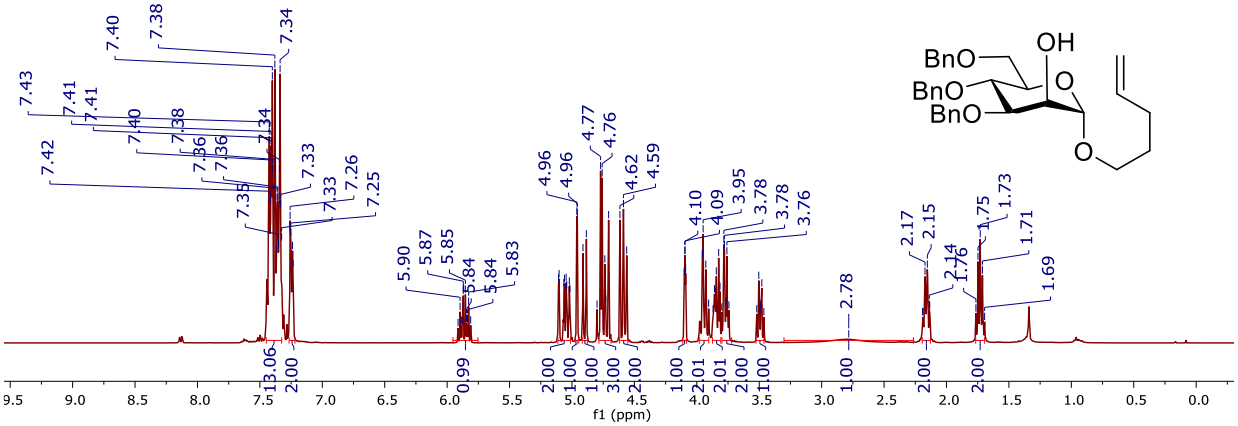
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound **15**



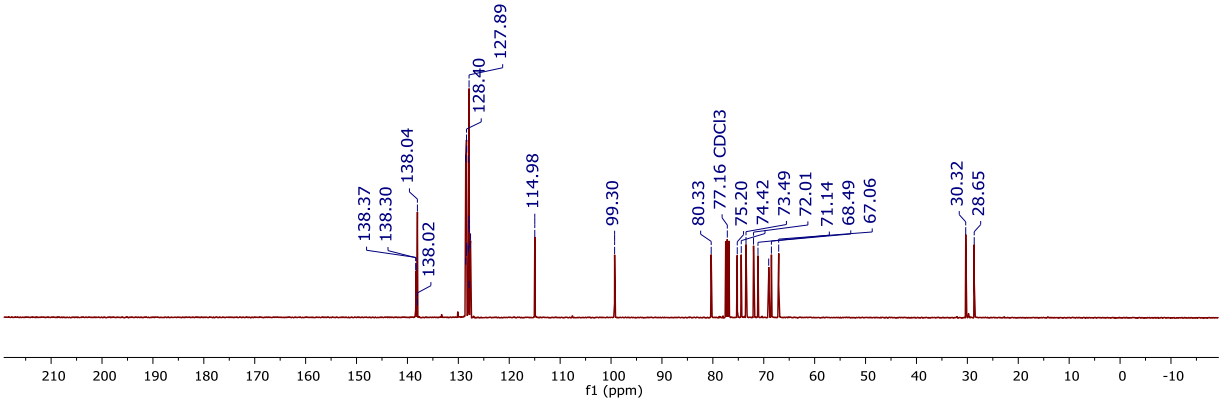
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **15**



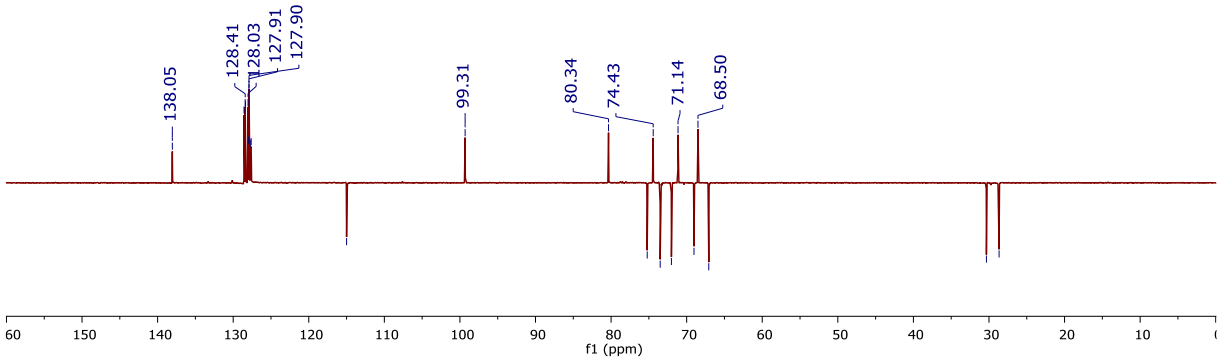
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **5**



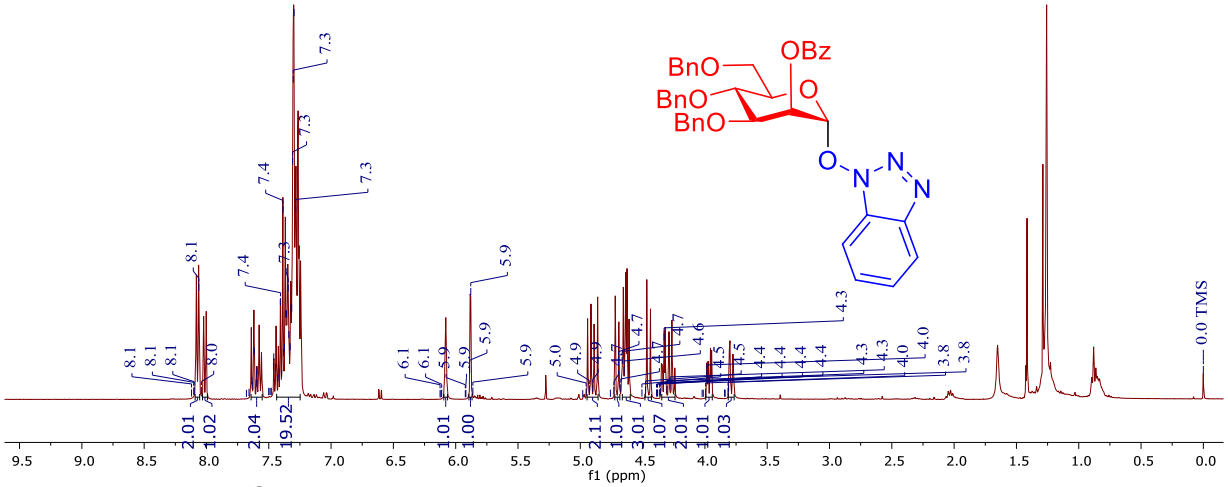
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound **5**



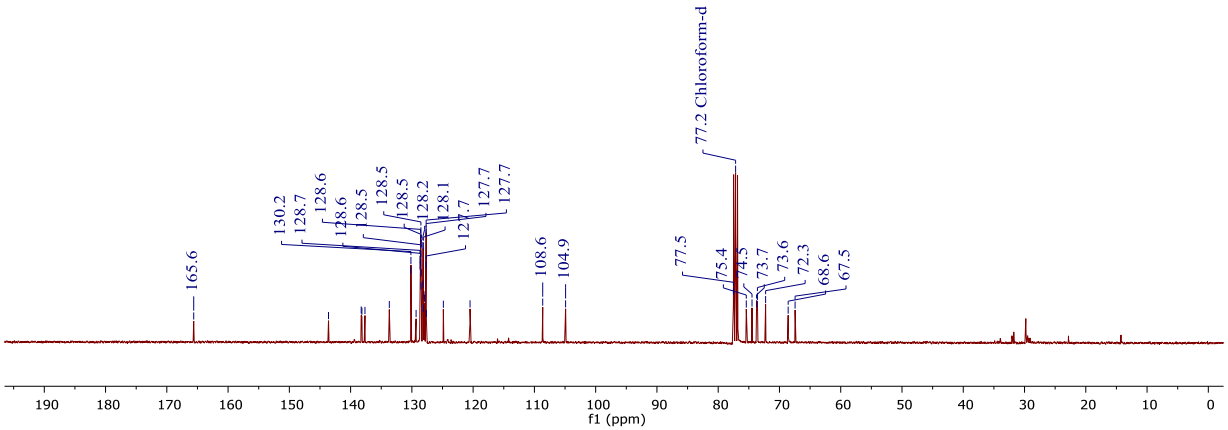
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **5**



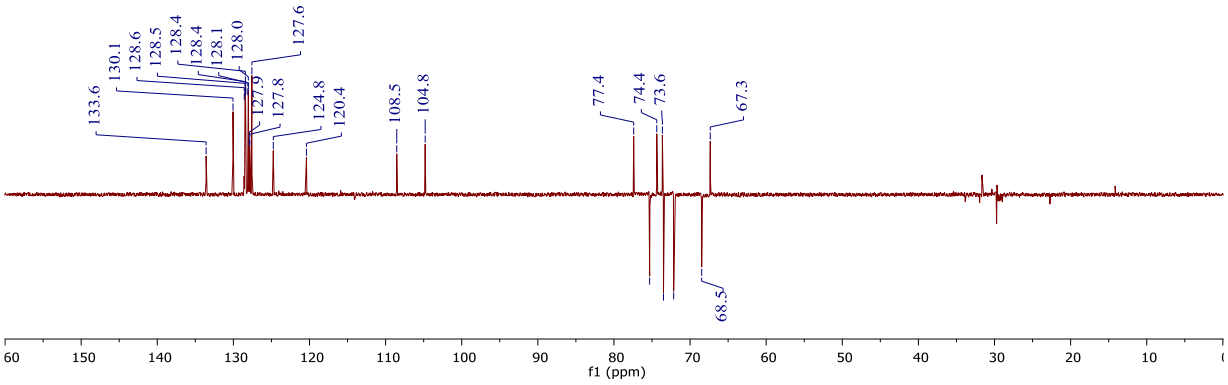
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **3**



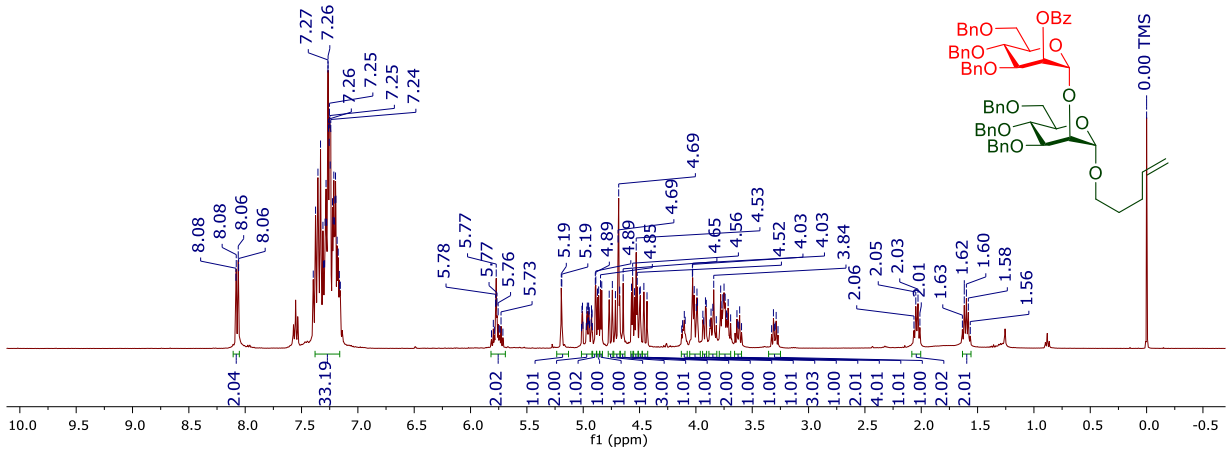
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound **3**



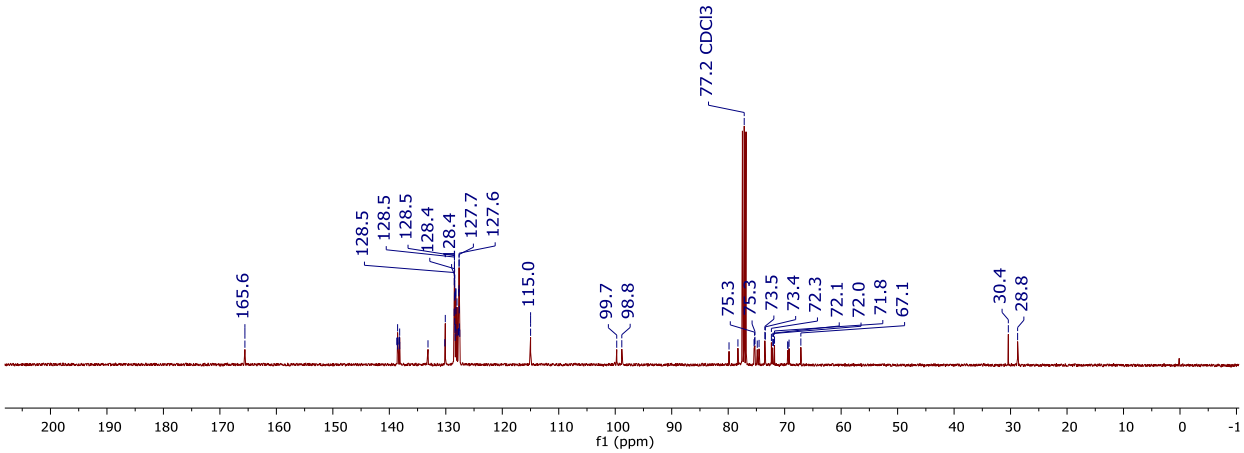
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **3**



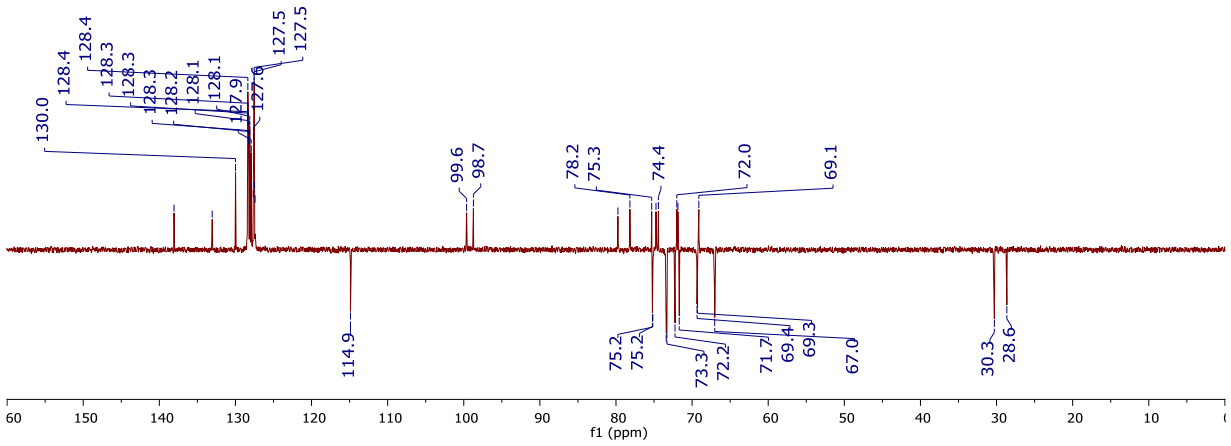
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **16**



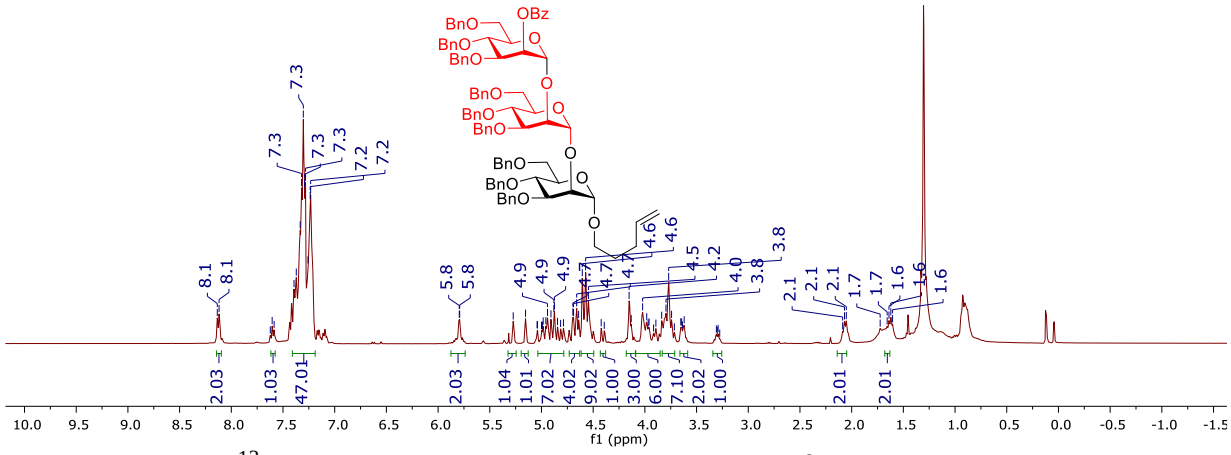
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound **16**



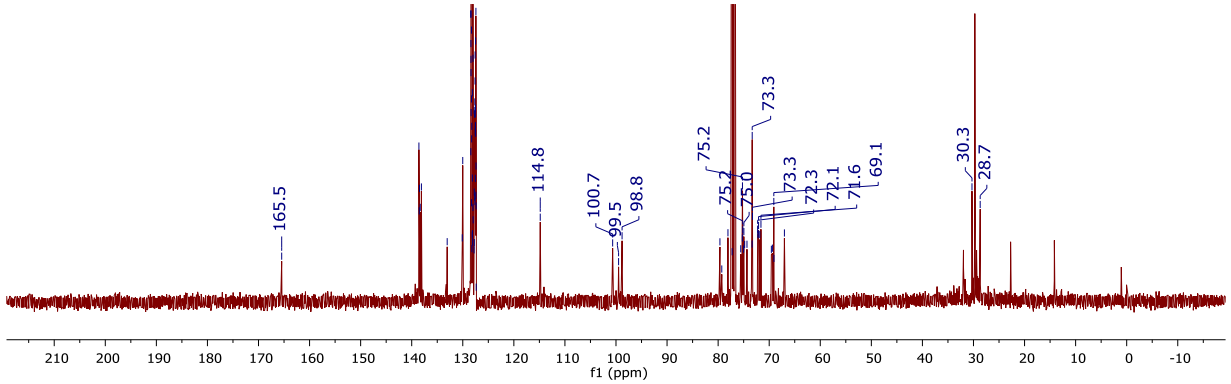
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **16**



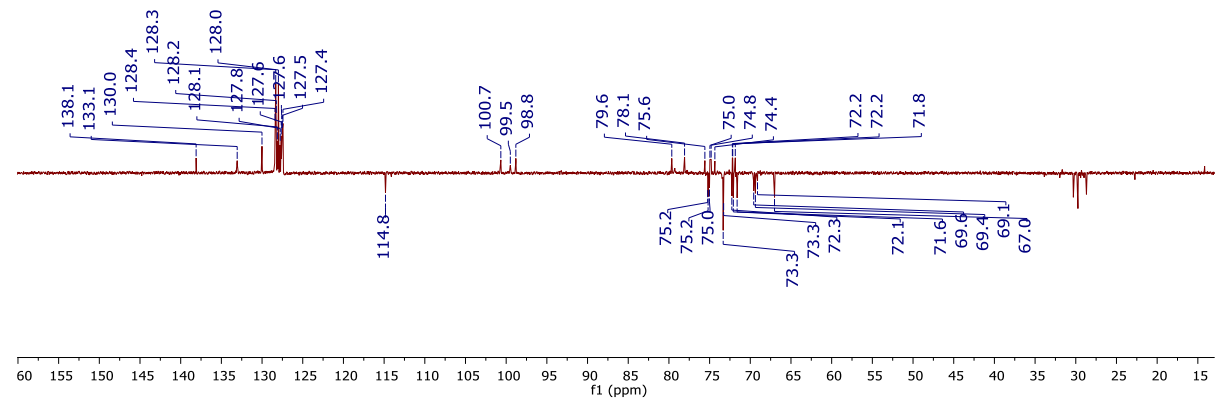
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **2**



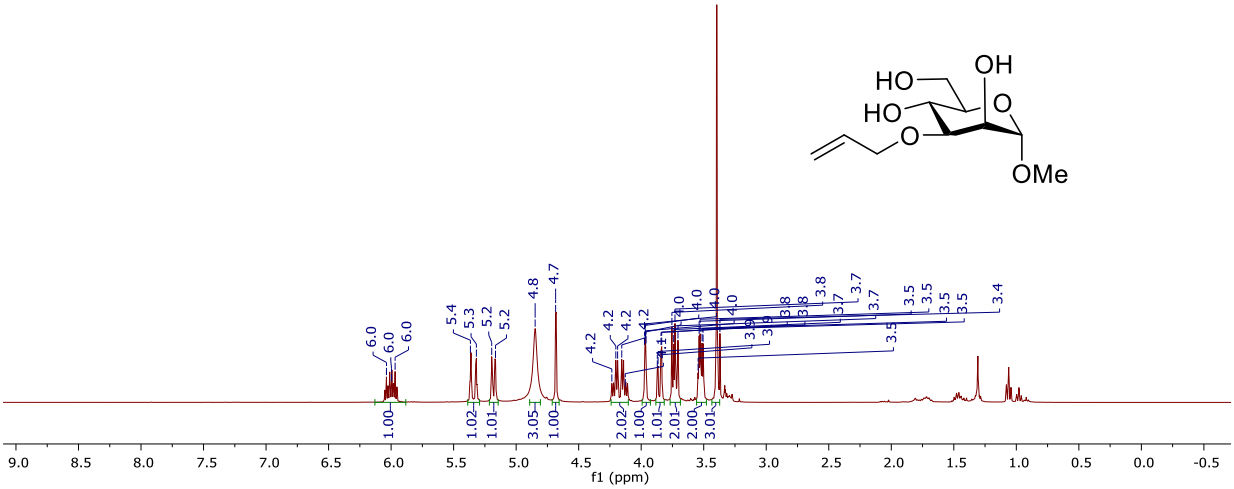
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound **16**



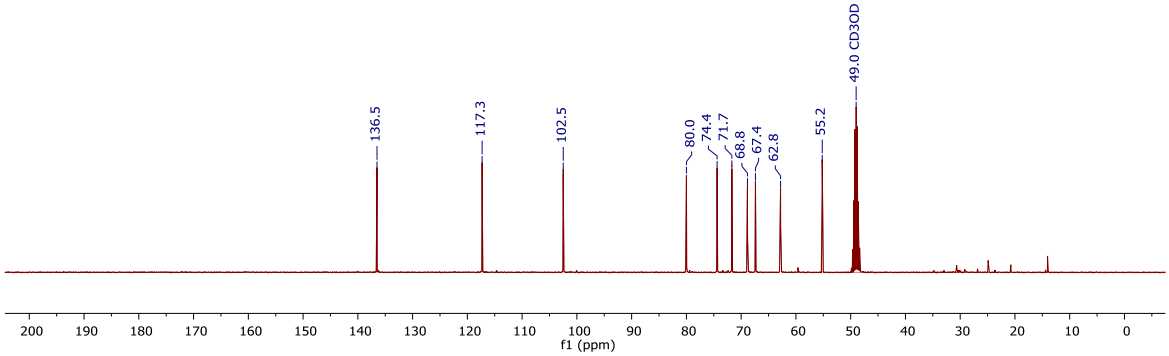
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **2**



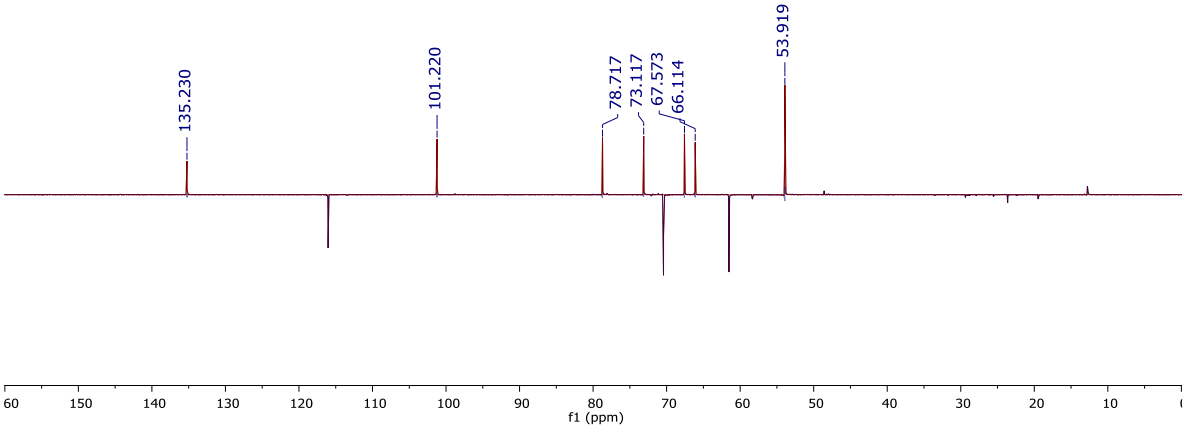
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **18**



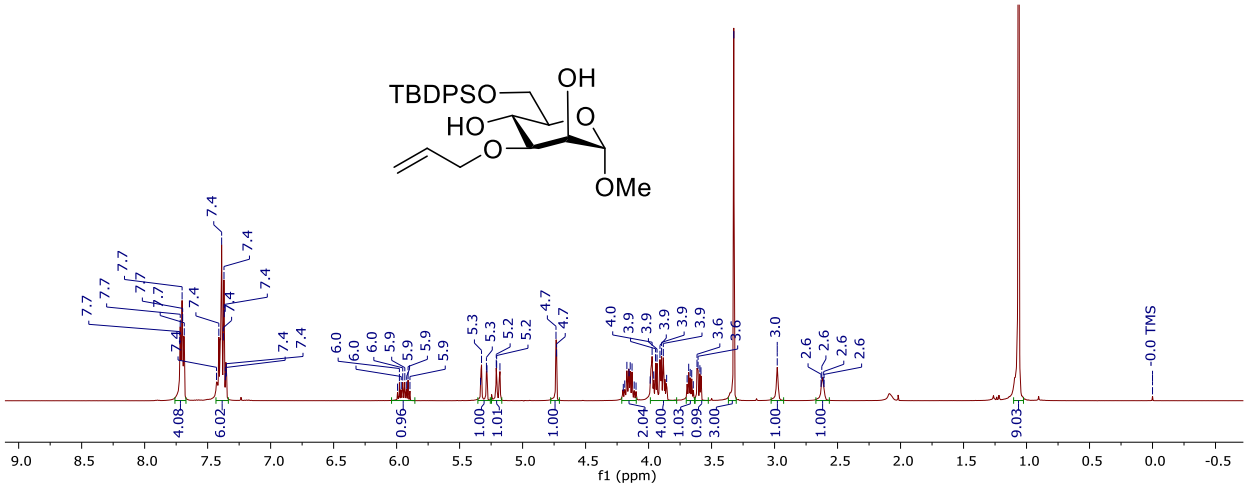
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound **18**



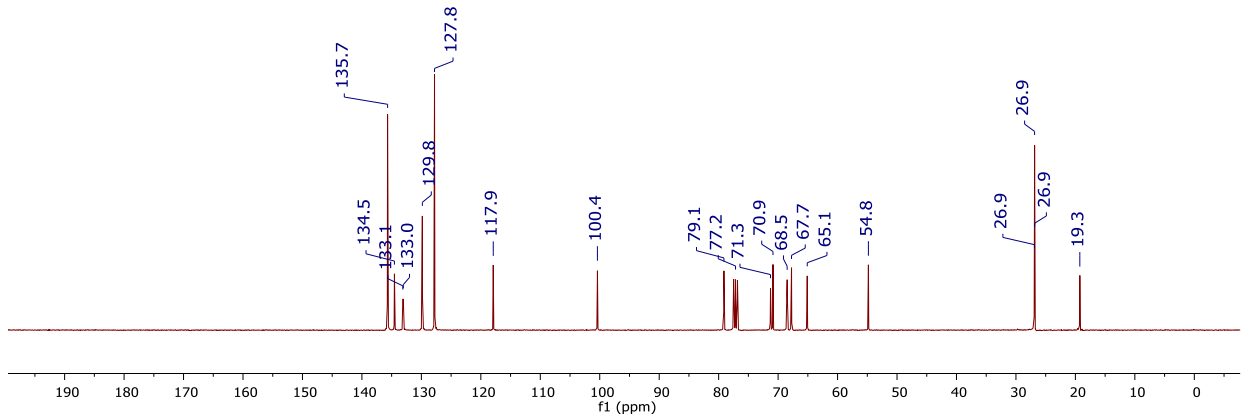
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **18**



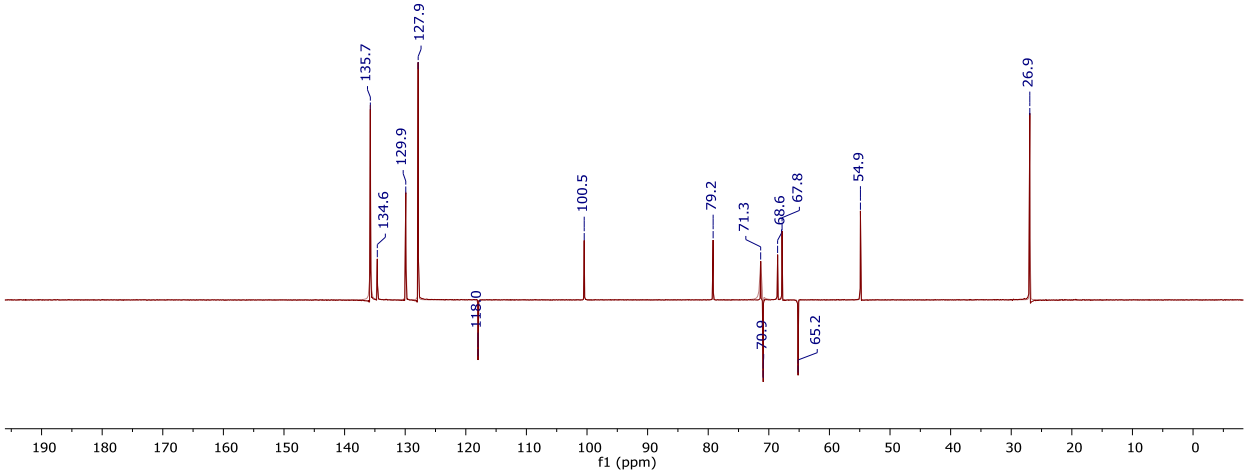
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **19**



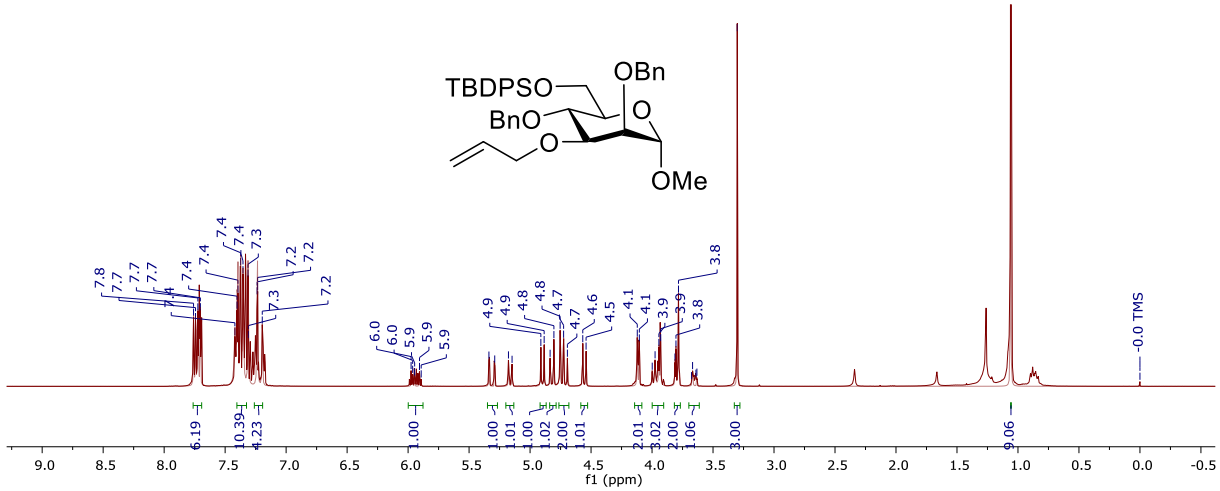
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound **19**



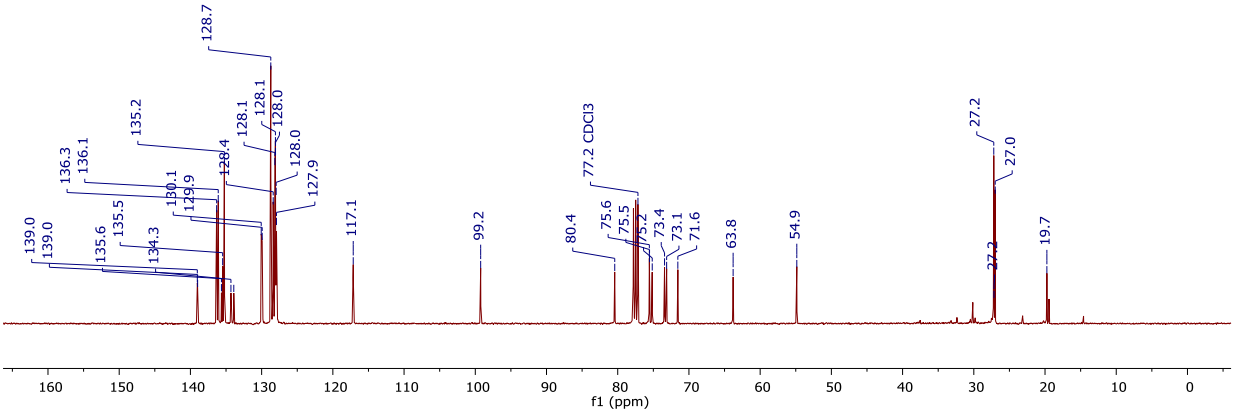
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **19**



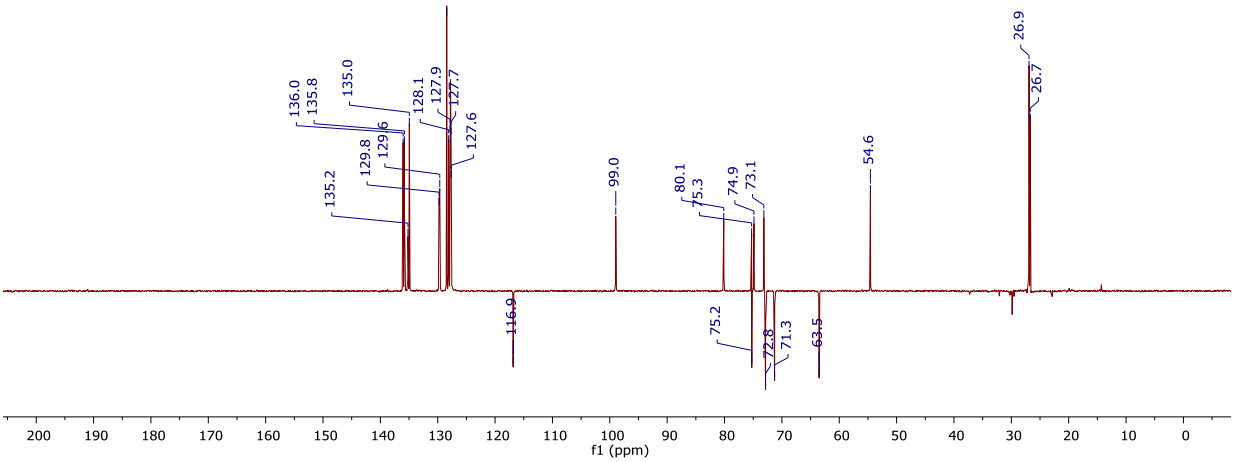
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **20**



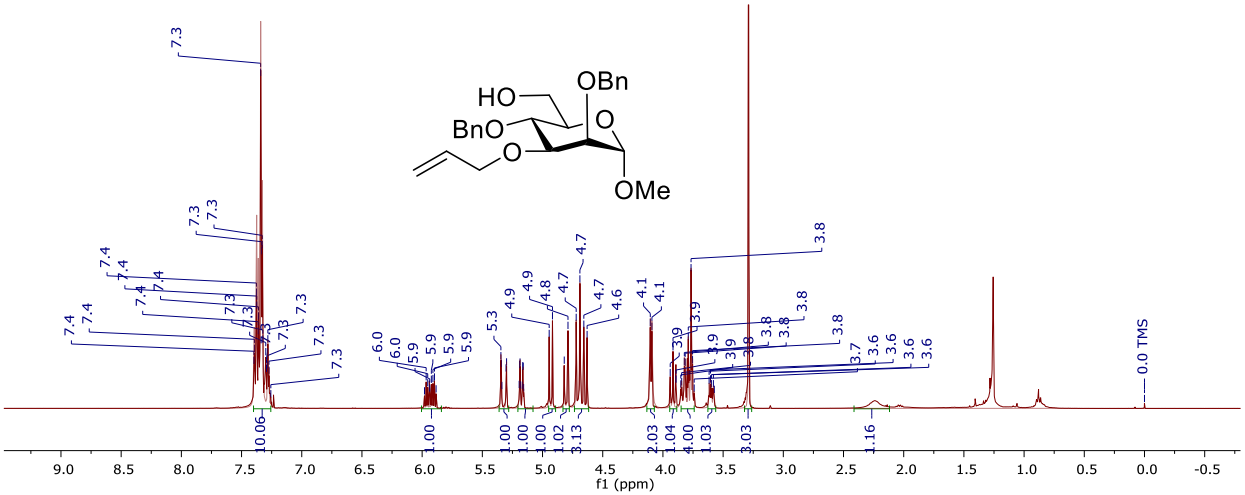
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound **20**



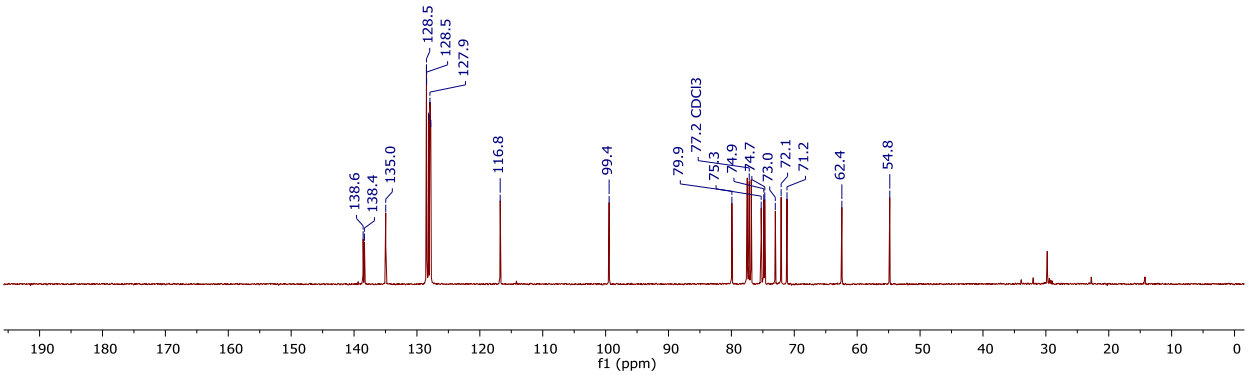
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **20**



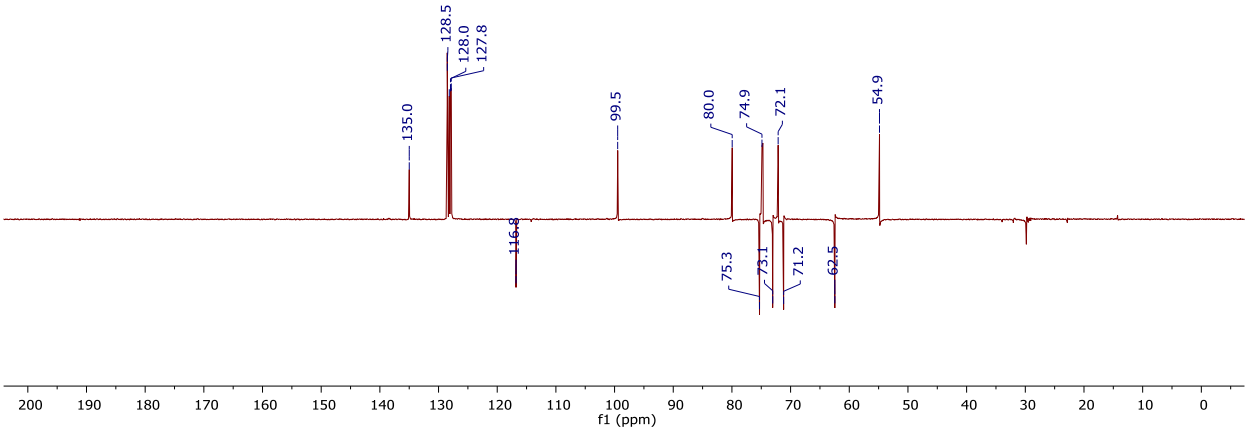
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **21**



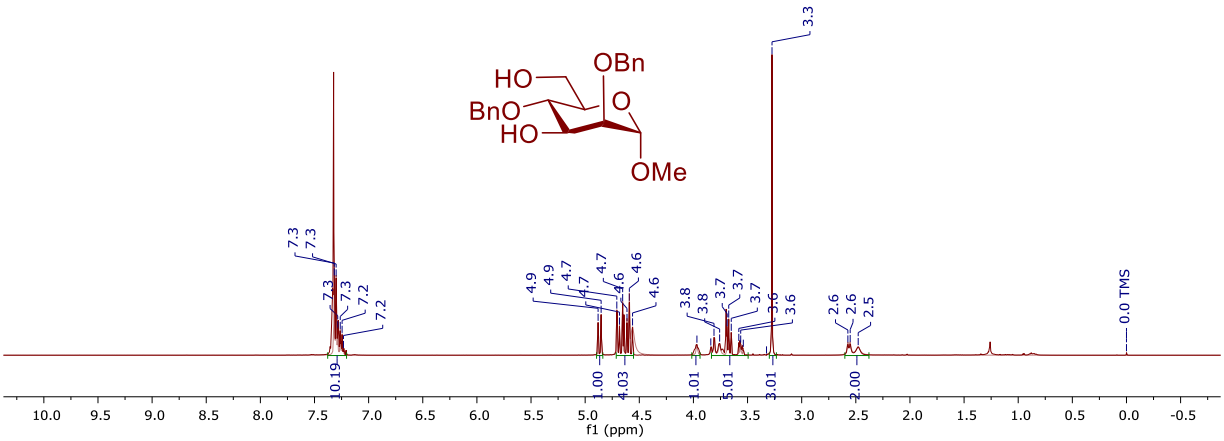
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound **21**



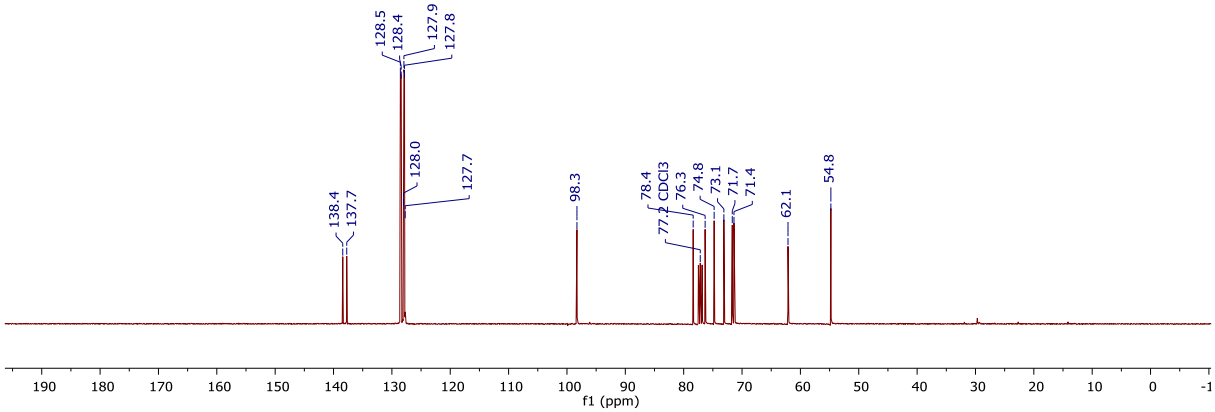
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **20**



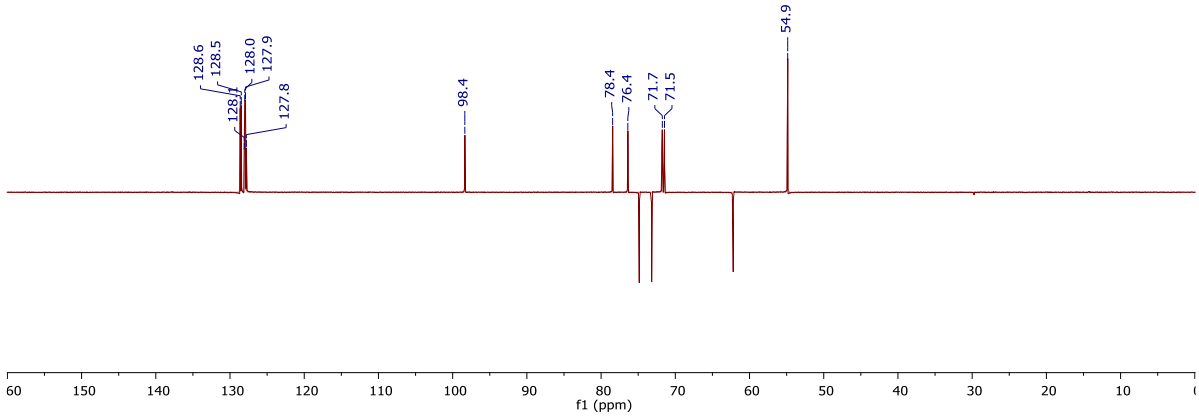
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **10**



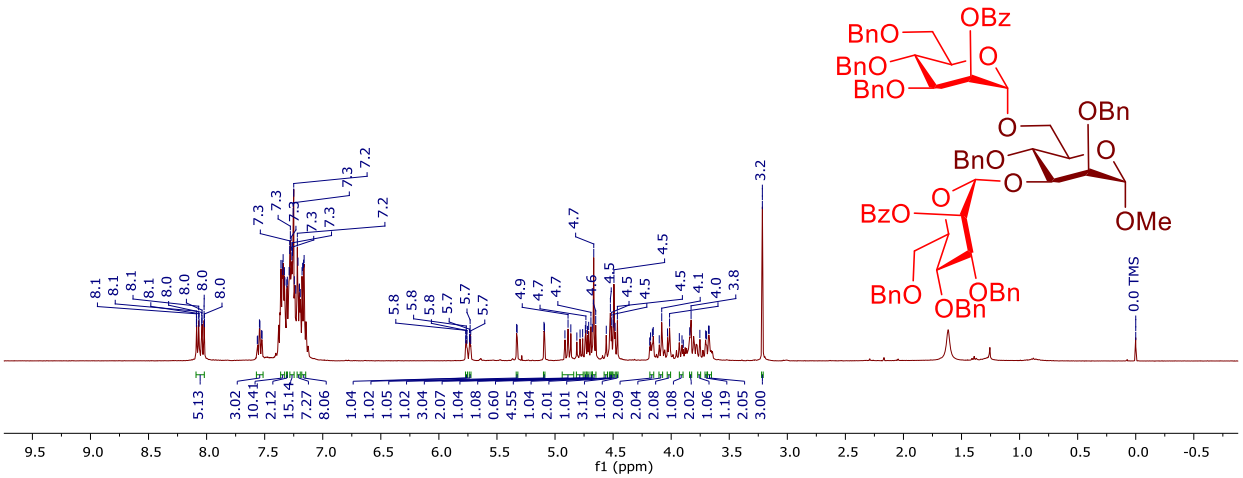
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound **10**



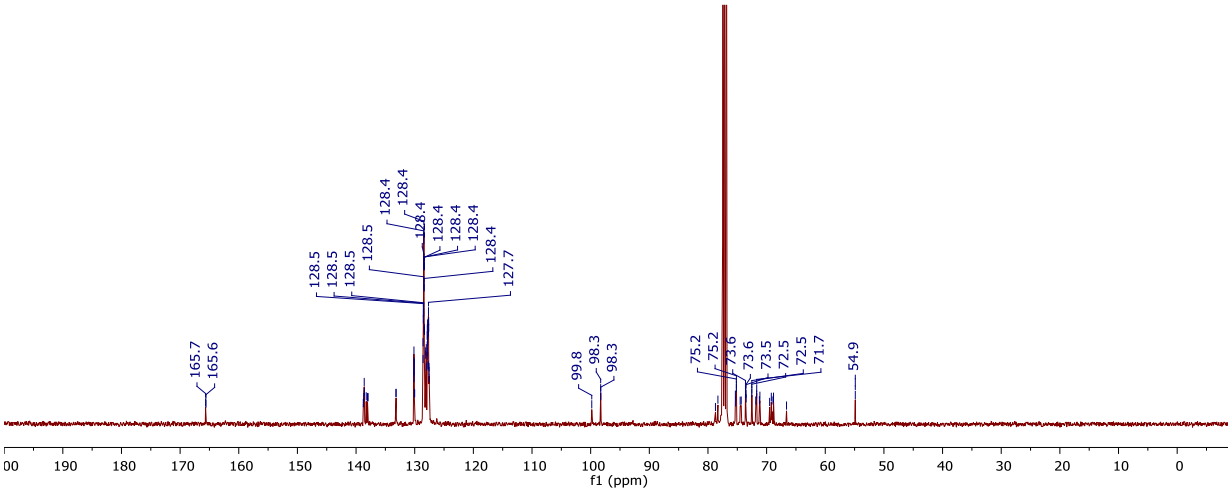
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **10**



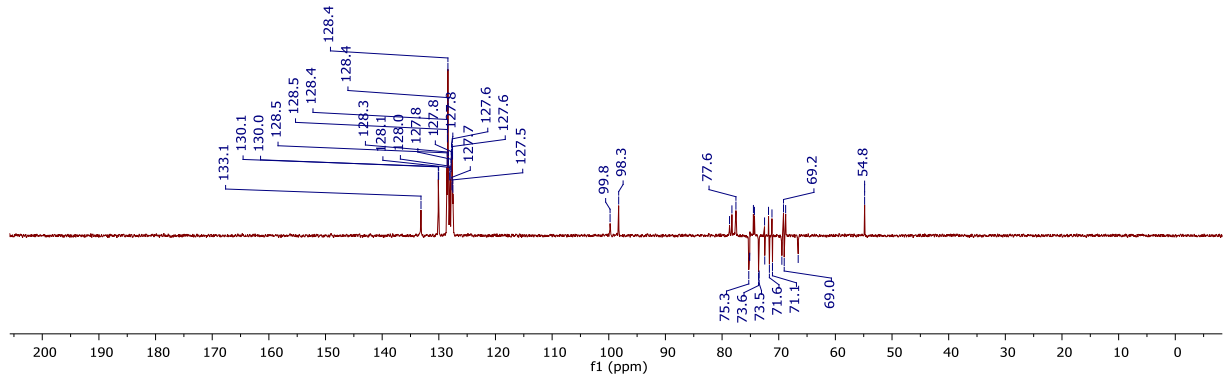
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **9**



^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound **9**



DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **9**



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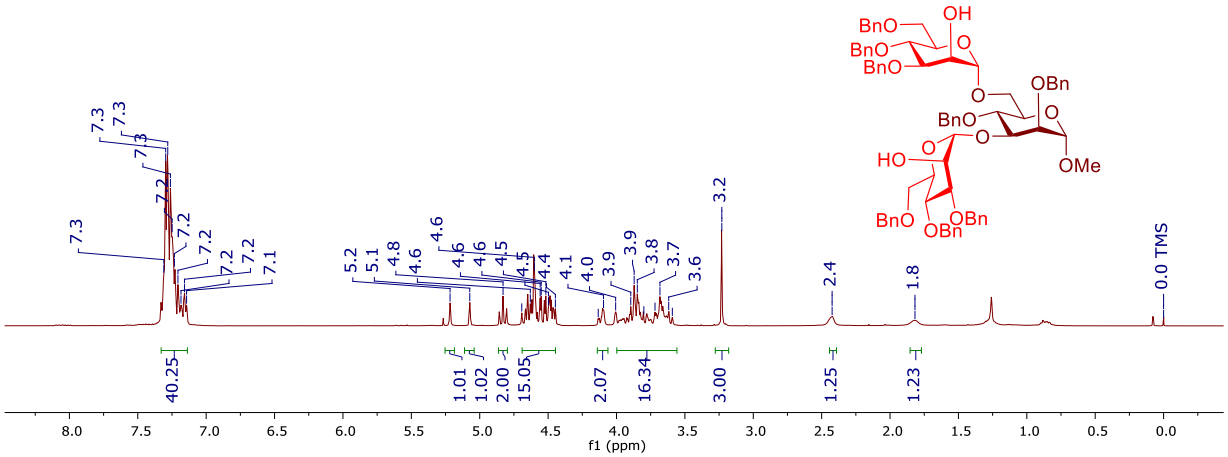
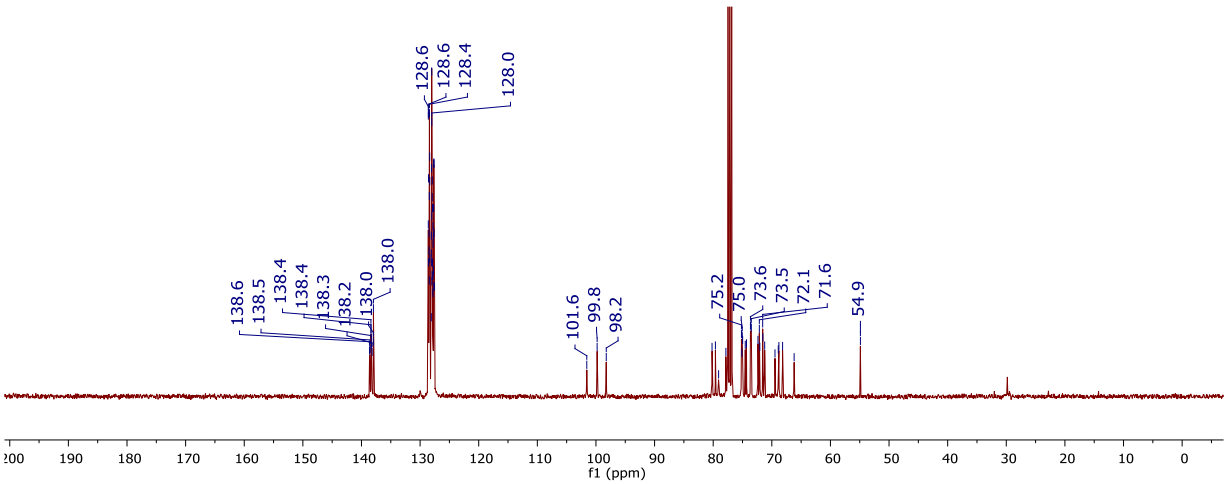
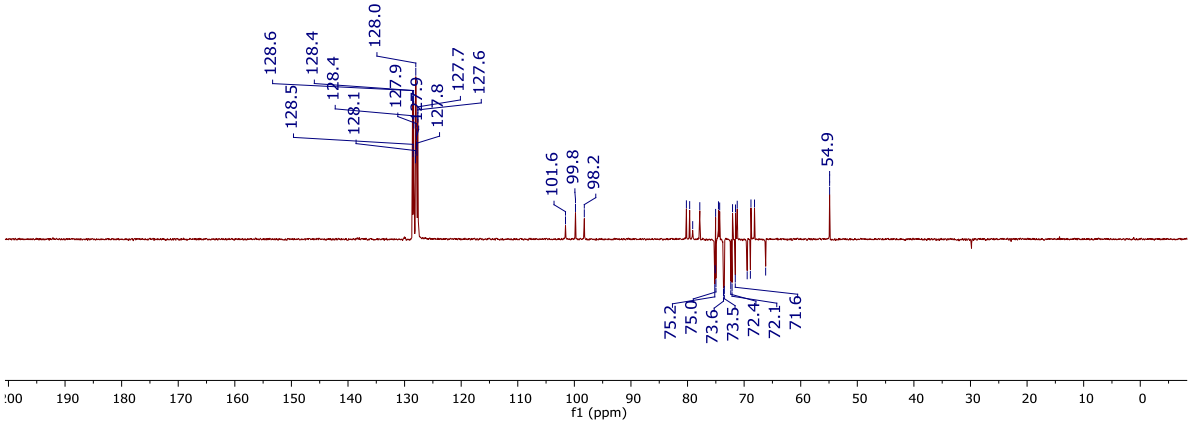


^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound **22**



DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **22**



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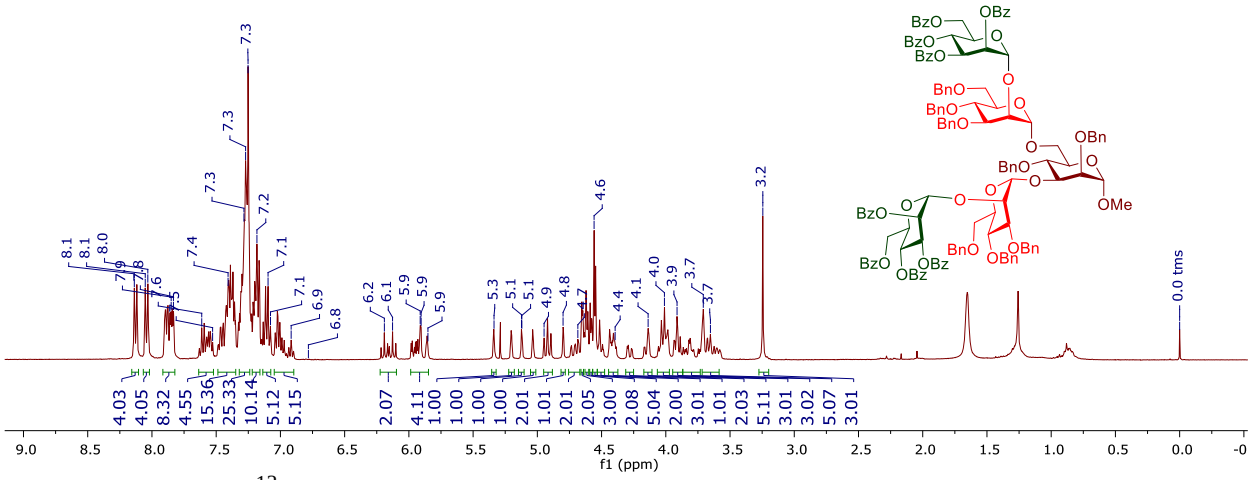

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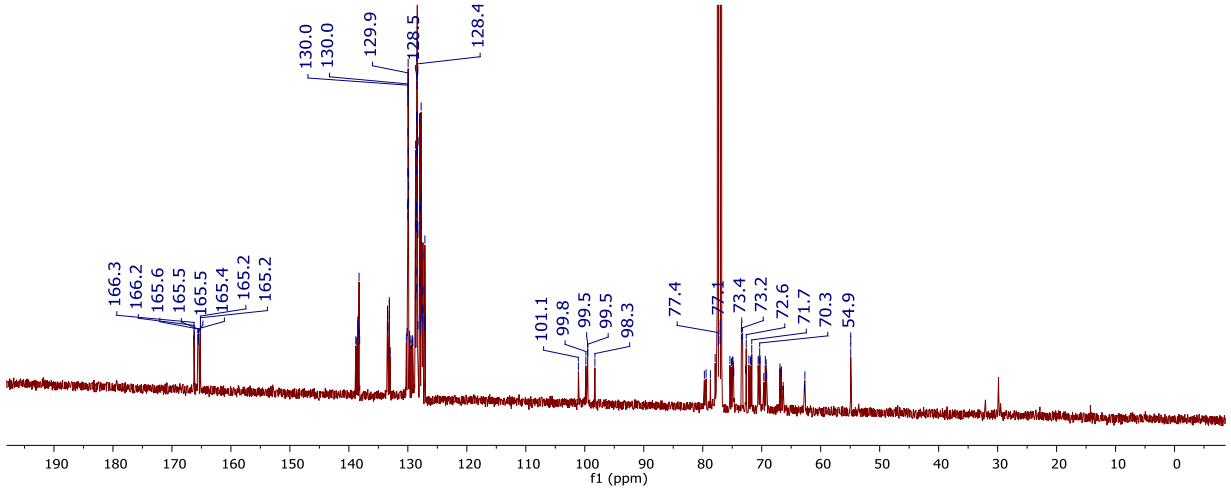
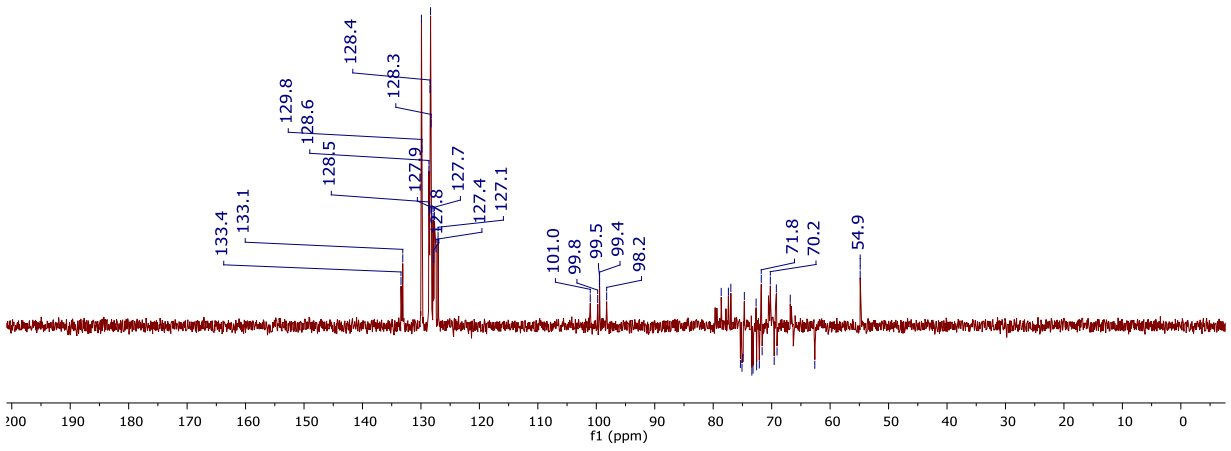


DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **7**



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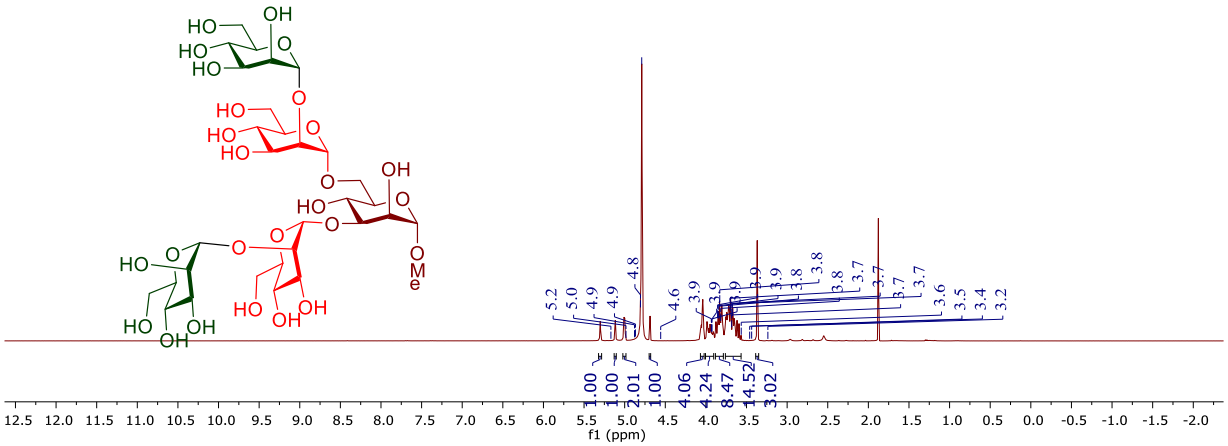
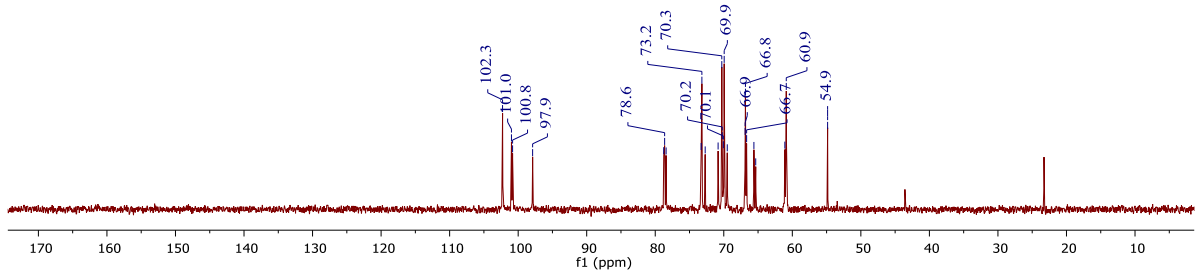
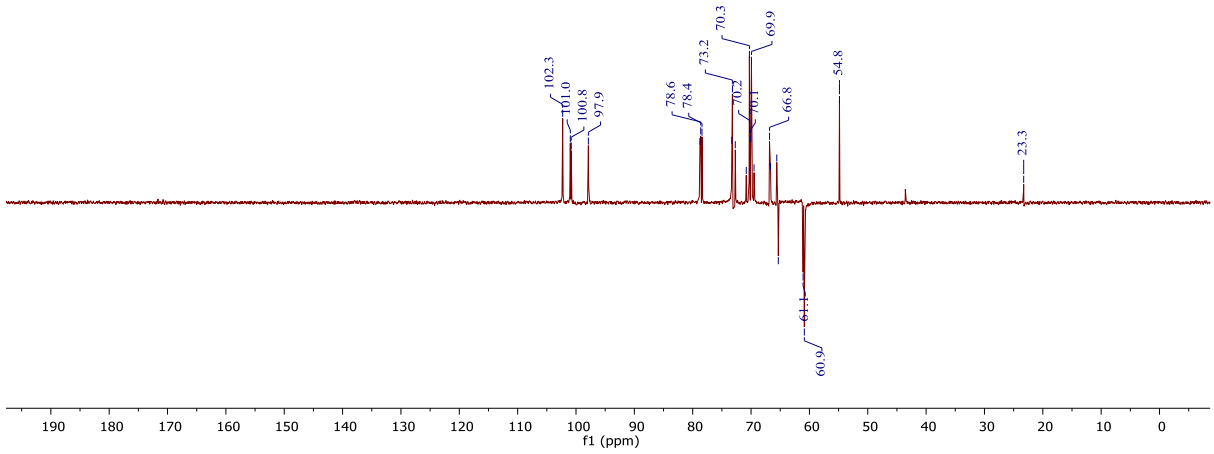


^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound **6**



DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **6**



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Chapter 4

Studies Towards the Synthesis of Galactan Subunit of Arabinogalactan

4.1 Introduction:

Tuberculosis (TB) has existed for millennia and remains a major global health problem. It is one of the top 10 leading causes of death form a single infectious agent after the human immunodeficiency virus (HIV). As per Global Tuberculosis Report 2018 by WHO, TB caused an estimated 1.3 million deaths among HIV-negative people and there were an additional 300 000 deaths from TB among HIV-positive people in 2017. TB affects all counties and all age groups. Globally, there were an estimated 10.0 million incident cases of TB which is equivalent to 133 cases per 10 000 humans in 2017. The 30 high burden countries accounted for 87% of all estimated incident cases worldwide and India tops the list of seven nations which had 64% of all new TB cases (**Fig. 4.1**).[1]World Health Organization (WHO) declared TB a global public health emergency in 1993.

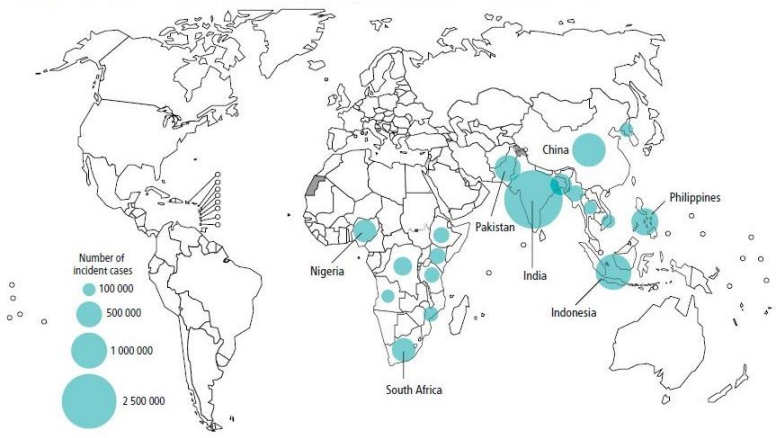


Figure 4.1. Estimated TB incidence in 2017, for countries with at least 10000 incident cases (*source: Global Tuberculosis Report 2018 by WHO*)

4.2 Basic Facts about Tuberculosis (TB):

Studies of human skeletons show that Tuberculosis (TB) has affected humans for thousands of years but the cause remained unknown until 24 March 1882 when Dr. Robert Koch discovered that the TB is an infectious disease caused by bacillus *Mycobacterium tuberculosis* that event is now commemorated as World TB day every year.[2] TB typically affects the lungs and disease is spread in air when people who are sick with pulmonary TB expel bacteria, for example, by coughing. People infected with HIV have high probability of developing TB disease. The risk of TB is also higher among people affected such under nutrition, diabetes, smoking and alcohol

consumption. It is found that about 90% of cases occur among adults with male: female ratio among adults is approximately 2:1.

4.3 Diagnostic Tests for TB disease:

1) Sputum Smear Microscopy:

The most common and old method for diagnosing TB is sputum smear microscopy, in which bacteria are examined under a microscope in sputum samples.

2) Rapid Molecular Tests:

In 2013, WHO recommended Xpert®MTB/RIF assay as only rapid test for diagnosis of TB. It can provide results rapidly within 2 hours. The test has much better accuracy than previous test.

3) Culture-based methods:

It requires more developed laboratory capacity and can take up to 12 weeks to provide results.[3]

4.4 Treatment for Tuberculosis:

For drug- susceptible TB patients, the currently recommended treatment by WHO is a 6-month course of four first-line drugs i.e. isoniazid, rifampicin, ethambutol and pyrazimadie.[4a]

The drug-susceptible TB cases, the success rate of treatment is around 85%. While treatment for rifampicin- resistant TB (RR-TB) and multidrug resistant TB (MDR-TB) is more expensive and more toxic drugs.[4b] According Global Report on TB 2018 by WHO, currently there are 20 TB drugs which are under clinical trials.

The only licensed vaccine is Bacilli-Chalmette-Guerin (BCG) vaccine, which was developed in 1918 and still widely used. However, it has shown its little effectiveness in infant to prevent severe forms of TB.[4c]

However, currently there is no vaccine to combat or prevent with TB disease in adults, either before or after exposure of TB infection. There are 12 TB vaccines in different phase trials. Development globally effective novel anti-tuberculosis drugs or vaccine to combat TB disease is dire need. In this concern, World Health Organization (WHO) launched 'The END TB' strategy with 'A World Free of TB' as a motive with strong coalition with Government Body, Civil society organizations and communities of respective countries.

4.5 *MycobacteriumTuberculosis*:

Mycobacteriumtuberculosis is the principal pathological bacterial species which is responsible for Tuberculosis disease in Humans. It is a macrophage intracellular pathogen having complex cellular envelope which establishes its infection preferentially to the pulmonary system and along with this it may also affect central nervous system, bones and skin. *Mtb* is a rod-shaped weak Gram-positive bacterium having width from 0.3 to 0.6 µm and height from 1 to 4µm. There are currently 60 known species among the Mycobacterium genera, out of which *M. tuberculosis*, *M. bovis* and *M. africanum* are the most common pathogenic species that cause TB in humans.[5]

4.6 Detailed Structural Analysis of Cell Wall of *MycobacteriumTuberculosis*:

Hallmark of mycobacteria is their complex cell wall. Understanding of cell wall biosynthesis has been a major research objective over the last few decades. More recent developments in analytical techniques such as NMR and Mass Spectral Analysis combined with M. tuberculosis genome enabled pioneering microbiologist Patrick Brennan to unravel the chemical structure of the mycobacterium cellular envelope along with lipids and its basic genetics.[6a-6b]

The cell wall of *Mycobacteriumtuberculosis* is composed of three major structural segments: a) the long-chain mycolic acids, b) a highly branched arabinogalactan (AG) glycan and Lipoarabinomannan (LAM) and c) a cross linked network of peptidoglycan. The core cell wall assembly is termed as the mycolyl arabinogalactan-peptidoglycan (mAGP) complex (**Fig. 4.2**).[7a] In addition, mAGP envelope of *M. tuberculosis* composed of an outer member segment that contains lipids, such as inert waxes and glycolipids, intercalates and mycolates layer and outermost capsule consisting of glycans and proteins.[7b]

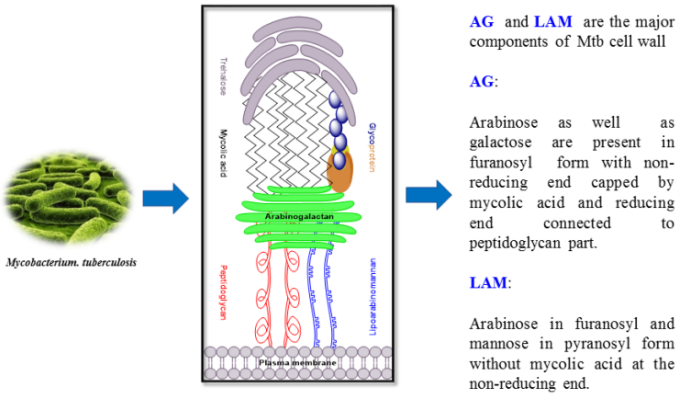


Figure 4.2. Representative Structure of Cell Wall of *Mycobacteriumtuberculosis*

a) Mycolic Acids:

Nearly 60% of mycobacterial cell wall is composed lipids that consist of long-chain fatty acids with 60-90 carbons which are termed as mycolic acids. It helps the cell wall in modulating the fluidity and permeability.[8a]They are covalently attached to polysaccharides. They are present in three different types: α-mycolic acids which exists only in *cis*-cyclopropane configuration whereas methoxy mycolic acids and keto mycolic acids consist of cyclopropane rings in either a *cis*- or *trans*- configuration with an adjacent methyl group (**Fig. 4.3**).[8b-d]

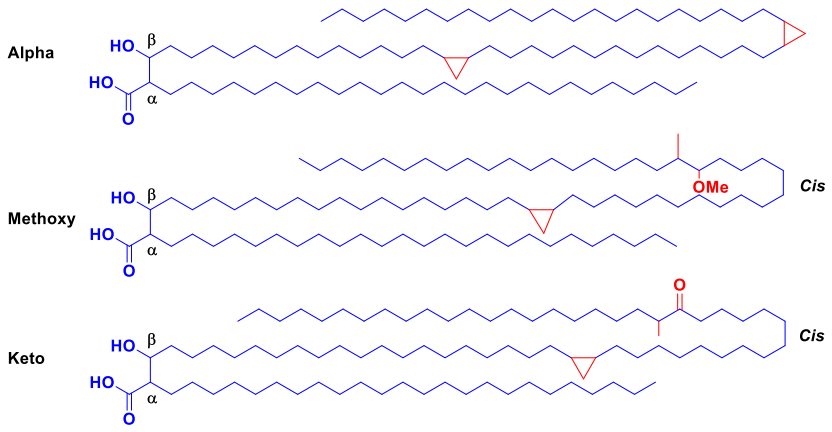


Figure 4.3. Mycolic Acids in *Mycobacteriumtuberculosis*

b) Peptidoglycan:

Almost all bacteria contain peptidoglycan (PG) which provides shape, rigidity and osmotic stability to both gram negative and gram positive bacilli.[9a]PGs have same basic structure which is composed of a glycan backbone and cross-linked peptide side chains.[9b] Mycobacterial PG consists of alternating units of *N*-acetylglucosamine (GlcNAc) and oxidized muramic acid (Mur). [9c-d]Another unique feature of mycobacterial PG is that the 6 position of muramyl unit of PG backbone provides a site for AG attachment *via*α-L-Rha*p*-(1→3)-α-D-GlcNAc-(1-P) bridge.[9e]

c) Arabinogalactan:

Arabinogalactan of Mtbis a highly branched polysaccharide molecule comprising mainly furanosyl (*f*) form of galactose (Gal) and arabinose (Ara) sugar residues.[10a] The galactan component was isolated and was found to consist of nearly 36 Gal*f* residues of alternating linearly (1→5)-/(1→6) linked β-D-Gal*f* residues. The highly branched three arabinan chains, each containing roughly 31 Ara*f* residues, are connected to galactan chain at positions 8th, 10th and 12th.[10b]The terminal β-Ara*f* units at non-reducing terminal of arabinan structure are linked to

the mycolic acids and also possesses 1,2-*cis* linkages i.e. [β-D-Ara*f*-(1→2)-α-D-Ara*f*]$_2$(**Fig 4.4**).[10c]

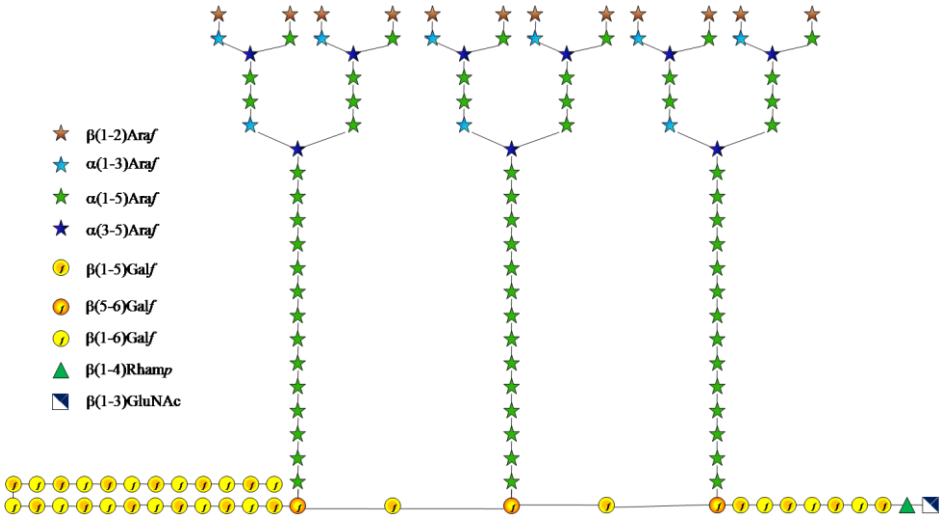


Figure 4.4. Structure of Mycobacterial Arabinogalactan

In addition to the Arabinogalactan (AG), M. tuberculosis also consists of another important class of immunologically active polysaccharide i.e. lipoarabinomannan (LAM) and an inactive lipomannan (LM) which are abundant in inner and outer membranes of Mycobacterial species.[11a] LAM and LM both have structural similarities in mannan backbone which is linked to *C*6-O position inositol of phosphatidyl-*myo*-inositol mannosides (PIMs).[11b] LAM and LM both possesses a mannan chain approximately 21-34 linearly linked α-(1→6)-Man*p* sugar residues further branched with 5-10 units of single α-(1→2)-Man*p* linkages at *C*2- position.[11c] The non-reducing end of mannan is covalently attached to a domain of 55-70 Ara*f*units which have structural resemblance with AG.[11d]

4.7 Importance of Homogenous Glycansin Anti-TB Drug Development:

In recent years, multi-drug resistance (MDR) cases of TB are increasing at an alarming rate along with extensively drug resistance (XDR) TB cases. The structural complexity of Mtb cell wall is considered to be the main reason behind this as glycans present of Mtb cell wall surface play a vital role as permeability barrier to extracellular compounds such as drugs or vaccines and also known to modulate the host immune system.[12a] This pressing need of antitubercular drugs resulted in many new lead compounds which are now at various stages of the drug discovery and preclinical development pipeline.

It has now become very clear that glycan part of Mtb cell wall is an essential immune-modulating motif that exerts wide range of effects on the host human system and contributes in pathogenicity of the mycobacterial infection. It has been observed that this polysaccharide promotes the survival of the mycobacteria in host macrophages as well.[12b] The future prospectus shall dwell on the development of new drugs regimes for anti-TB chemotherapy by mimicking the large naturally occurring oligosaccharide motif either by biosynthetic pathway or chemical synthetic pathway. To do so, pure and homogenous form of glycans is essential for understanding the biosynthetic machinery for eventual development of more effective vaccine to combat TB infection. But isolation of pure carbohydrates from natural sources is a tedious task or very intimidating in most cases. Therefore, the chemical synthesis is ultimate approach to obtain well-defined carbohydrates.

4.8 Chemical Synthesesof Mtb Cell Wall Fragments:

The major pentaarabinofuranosyl motif from Mtb Cell wall was synthesized byMereyala, Hotha and Gurjar using *n*-pentenyl arabinofuranoside and thiopyridyl arabinofuranosides as glycosyl donors for the first time in 1998.[13] Synthesis of various AG and LM fragments was achieved by Seeberger group by using their own developed automated solid phase syntheser.[14a] Utilizing glycosyl phosphate donor, they were able to prepare a dodecasaccharide arabinomannan (AM) fragment by coupling of six α-D-Ara*f* and α-D-Man*p* residues *via* 6+6 coupling strategy.[14b]In 2006, a 28-mer heterooligosaccharide of that period was accomplished by Fraser-Reid group using only two *n*-pentenyl orthoester progenitors. They used 12+16 coupling strategy to couple arabinomannan-trichloroacetimidate donor and mannosylated inositol acceptor to get 28-mer.[15]

Todd Lowary group reported the total synthesis of dodecaarbinan domain of mycobacterial arabinogalactan in 2007.[16] The key feature of their report was the highly convergent [(2x5) +7+5] coupling strategy by using trichloroacetimidate and thiotolyl glycosyl donors. In 2011, Ito group utilized the intramolecular aglycon delivery (IAD) to synthesize stereoselective 1,2-*cis*-arabinose linkages while accomplishing the 22-mer arabinan by [(2x7)+8) coupling strategy.[17]

Hotha group introduced Au-catalyzed glycosylation to activate the propargyl 1,2-orthoester glycosyl donor and demonstrated the utility of their method by synthesizing branched hexaarbinofuranoside which is a common motif in both AG and LAM fragments of Mtb cell wall.[18a]Subsequently, they extended to a full length 21-mer arabinogalactan residue in highly

convergent [(2x4)+7+6] manner by single glycosylation strategy;the key feature being the introduction of galactofuran (Gal*f*) disaccharide moiety to arabinan residue for the first time.[18b]

Later, Hotha group developed alkynyl carbonate glycosyl donor which can be activated under Au/Ag catalysis[18c]and successfully utilized their method for the total synthesis of linear nonadecaarabinofuanoside motif[18d] as well as the highly branched tridecasaccharide reminiscent of mycobacterial cell wall envelope.[18c] Along with this, Hotha group also successfully synthesizeda heneicosasaccharyl mannose capped arabinomannan[18e] and pentacosafuranoside subunit[18f] of mycobacterial arabinogalactan by using one strategic Au/Ag-catalyzed glycosylation protocol.

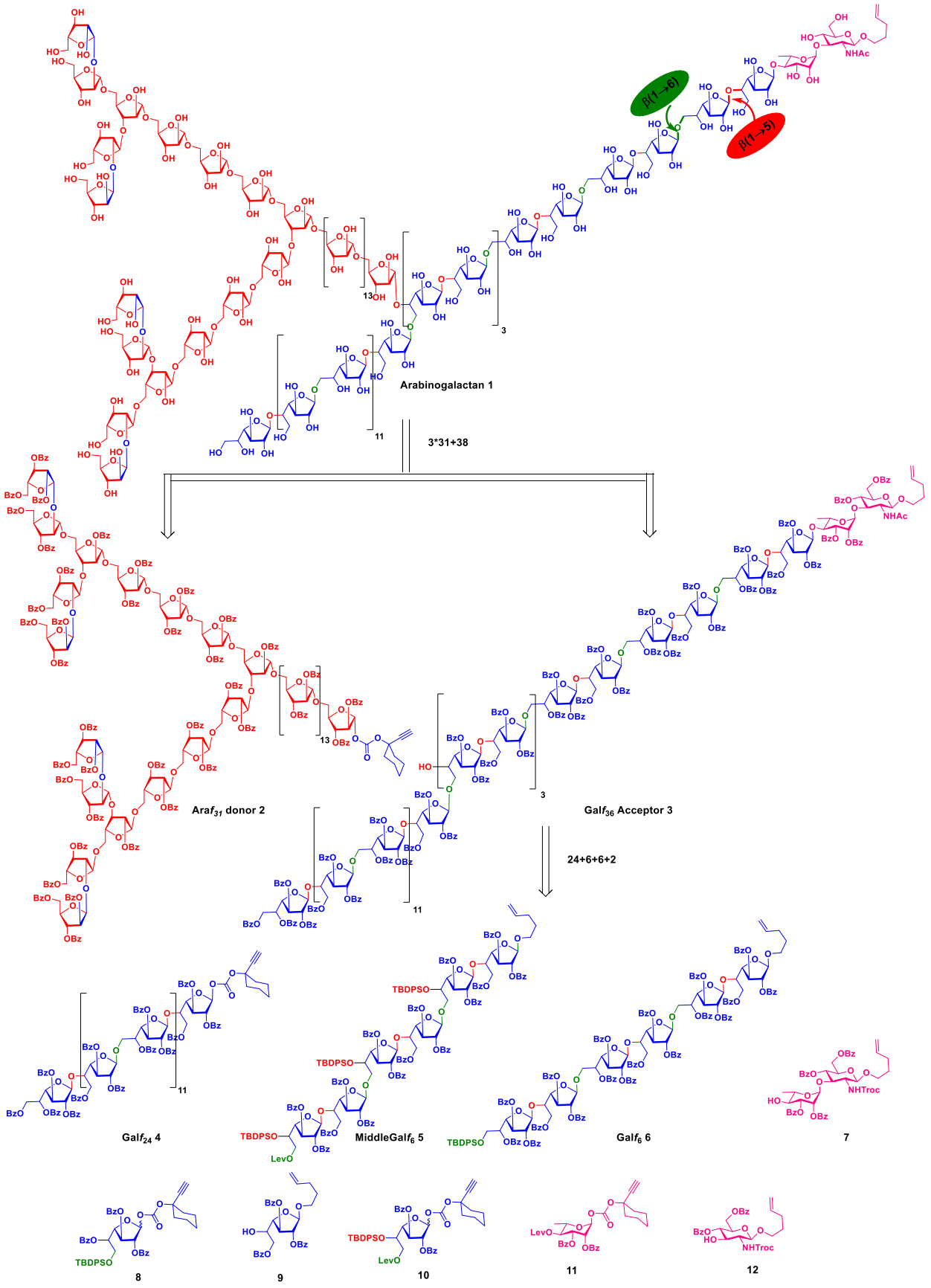
In 2017, Xin-Shan Ye group created the World record by synthesizing the longest well-defined carbohydrate chain of mycobacterial arabinogalatan containing 92-units of monosaccharides by utilizing the pre-activation based one-pot glycosidation protocol.[19]

4.9 Present Work:

Most of the cells use common sugars to construct their own complex and hetero- cell wall but they manage to differentiate from each other *via* endless possibilities of sequences and linkages.[20a]Thanks to some microorganism which differentiate themselves from other organism by incorporating sugars in their furanosyl form rather in their pyranosyl forms.[20b] Glycoconjugates containing D-Gal*f* and D-Ara*f*are found in pathogenic microorganism like mycobacteria cell wall but absent in the mammalian cell wall.[20c] So synthesis of oligosaccharides containing furanosyl forms in itself is a challenging task. In addition to this, major challenges for the synthesis of Arabinogalactan **1** are: 1) The linear galactan chain consisting of 36 galactofuranose (Gal*f)* residues which are connected *via* alternating β(1→5) and β(1→6) linkages in linear fashion; 2) The linear galactan moiety connected to the disaccharide linker α-L-Rha*p*-(1→3)-α-D-GlcNAc; 3) The highly branched arabinan chains attached at the*C*-5 of β(1→6) Gal*f* residues selectively at 8th, 10th and 12th positions of the galactan chain.

Our synthetic endeavour started with the disconnection of giant target oligosaccharide arabinogalactan **1** into two sizeable fragments Araf_{31}**2** donor and the linear Galf_{38}**3** acceptor. The branched Arf_{31}**2** donors was targeted by my colleague Dr. Sandip Pasari and this chapter deals with synthesis of linear Galf_{38}**3**acceptor (**Scheme 4.1**).

4.9.1 Retrosynthetic Disconnection of Arabinogalactan 1:


β(1→6)
β(1→5)
Arabinogalactan 1
3*31+38
Araf31 donor 2
Galf36 Acceptor 3
24+6+6+2
Galf24 4
MiddleGalf6 5
Galf6 6
7
8
9
10
11
12

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

In an effort to synthesize the Galf_{38}**3** acceptor, we have developed a highly convergent Split-React-Couple strategy wherein we opted 24+6+6+2 coupling strategy (Scheme 4.1). We disconnected Galf_{24}**3** in such a way that both glycosyl donorand glycosyl acceptor can be synthesized from an identical precursor **6**. Strategically *n*-pentenyl group was kept at the reducing end as it can be suitably converted to hemiacetal that can be extended to corresponding carbonate glycosyl donor at a later stage in the presence of Au/Ag catalytic system.[18c]The choice of TBDPS group as a temporary protection was argued by its stability under many reaction conditions as well as it can be selectively protect at primary hydroxyl group over the other competing secondary hydroxyl groups. To install three arabinan chains at three branching points, Galf_6**5**was envisioned separately with orthogonal protecting groups such as TBDPS and Lev group. In all other precursors, *C*2- OH was protected as a benzoate ester to ensure 1,2-*trans*selective glycosylation and one step saponification (**Scheme 4.1**).

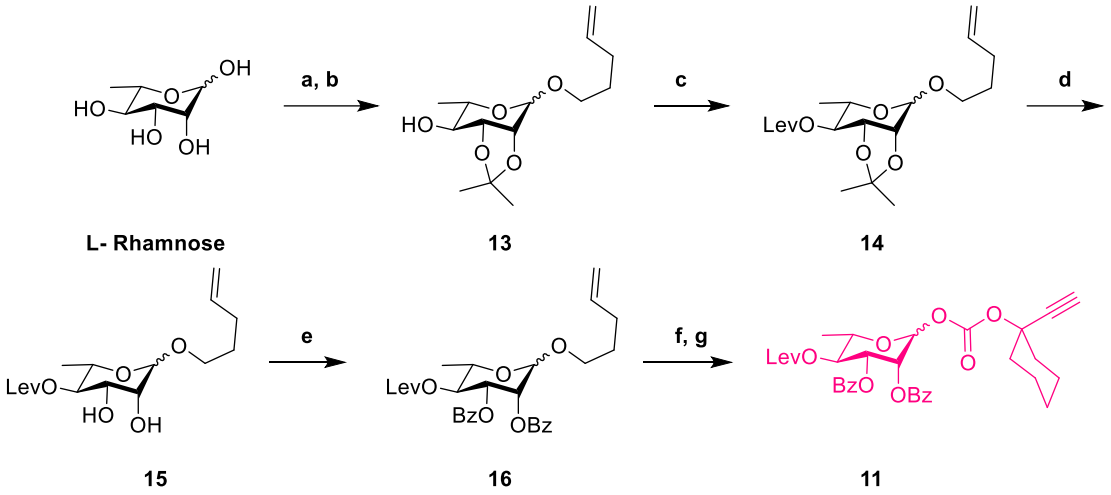
4.9.2 Synthesis of Building Block 11:

Reaction of commercially available L-Rhamnose with 4-penten-1-ol in the presence of AcCl at 0 ºC for 5 h, followed by acetonide protection using 2,2-dimethoxy propane and catalytic amount of PTSA in dry acetone at 25 ºC for 5 hours produced the acetonide protected *n*-pentenylrhamnoside **13** in 80% over two steps. Free hydroxyl group of compound **13** was protected as a levulinate by coupling with levulinic acid in presence of DIC and DMAP in CH_2Cl_2 at room temperature to afford compound **14** in 94% (**Scheme 4.2**).

Subsequent deprotection of acetonide group in acidic medium gave free diol **15** in 74% yield which on benzoate protection with benzoyl chloride resulted into dibenzoate**16**in 92% yield. Pentenyl group of compound **16** was hydrolyzedemploying NIS and TfOH at -20 ºC to form a hemiacetal which was directly reacted with available 1-ethynylcyclohexyl (4-nitrophenyl) carbonate **17** in presence of DMAP to afford desired rhamnopyranosyl carbonate donor **11** in 80% yield over two steps (**Scheme 4.2)**.

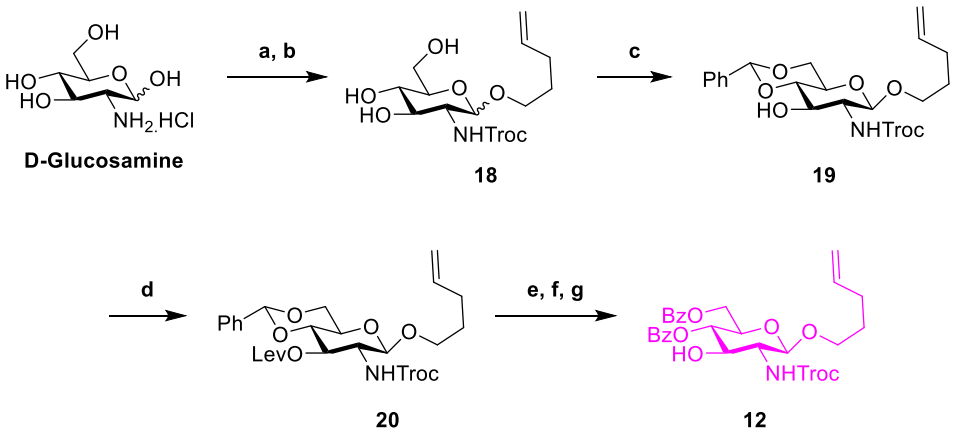
4.9.3 Synthesis of Building Block 12:

Free amine group of D-Glucosamine was protected with TrocCl in presence of $NaHCO_3$ and was further treated with *n*-pentenyl alcohol and acetyl chloride at 0 ºC to protect anomeric hydroxyl group to form pentenyl glycoside**18** in 78% yield over two steps. Compound **18** was directly



Scheme 4.2. Synthesis of Building Block 11. Reagents: a) 4-pent-1-ol, AcCl, 0-25 ºC, 5 h; b) 2,2-dimethoxypropane, CSA, dry acetone, 25 ºC, 5 h, over two steps 80%; c) Lev-acid, DIC, DMAP, CH_2Cl_2, 0-25 ºC, 1 h, 94%; d) PTSA, CH_3OH:CH_2Cl_2 (1:1), 25 ºC, 6 h, 74%; e) BzCl, pyridine, DMAP, 0-25 ºC, 5 h, 92%; f) 1.5 eq. NIS, 0.2 eq. TfOH, CH_3CN:CH_2Cl_2:H_2O (3:5:0.5), -20 to 0 ºC, 2 h; g) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate (**17**),CH_2Cl_2, DMAP, 25 ºC, 8 h, over two steps 80%.

taken for benzylidine protection using benzaldehyde di-methylacetal and catalytic amount of PTSA in DMF at 60 ºC for 4 hours in 82% yield and thus resultingcompound **19**was treated with levulinic acid, DIC and DMAP that ended in lev protection of the free hydroxyl group **20**.

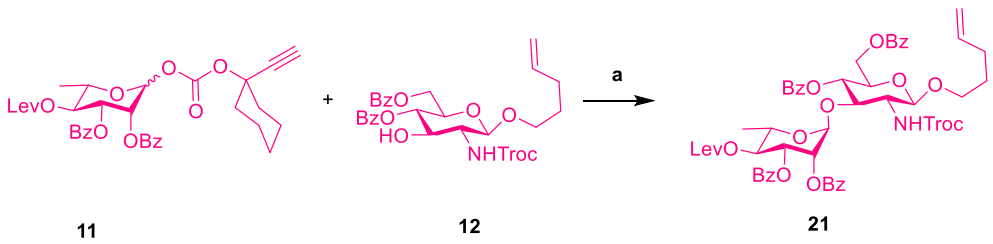


Scheme 4.3. Synthesis of Building Block 12. Reagents: a) TrocCl, $NaHCO_3$, H_2O, 5 h, 0 ºC; b) 4-pentene-1-ol, AcCl, 0-25 ºC, 5 h, over two steps 78%; c) $PhCH(OMe)_2$, PTSA, DMF, 25 ºC, 4 h, 82%; d) Lev-Acid, DIC, DMAP, CH_2Cl_2, 0-25 ºC, 1 h, 88%; e) PTSA, CH_3OH: CH_2Cl_2 (1:1), 25 ºC, 6 h; f) BzCl, pyridine, DMAP, 0-25 ºC, 5 h; g) NH_2NH_2, AcOH: Pyridine (12:17 eq.), CH_2Cl_2, 2 min, over three steps 48%.

Benzylidine group of compound **20** was deprotected under acidic conditions and subsequently treated with benzoyl chloride in pyridine to form dibenzoyl protection;which was treated with hydrazine hydrate in buffer solution of acetic acid and pyridine for 10 min to unblock lev moiety which resulted in the formation of building block **12**in 48% yield (**Scheme 4.3**).

4.9.4 Synthesis of Disaccharide 21:

Disaccharide **21**was assembled by [Au]/[Ag]-catalyzed glycosylation betweenthe glycosyl donor **11** and glycosyl acceptor **12** in 81% yield (**Scheme 4.4**).

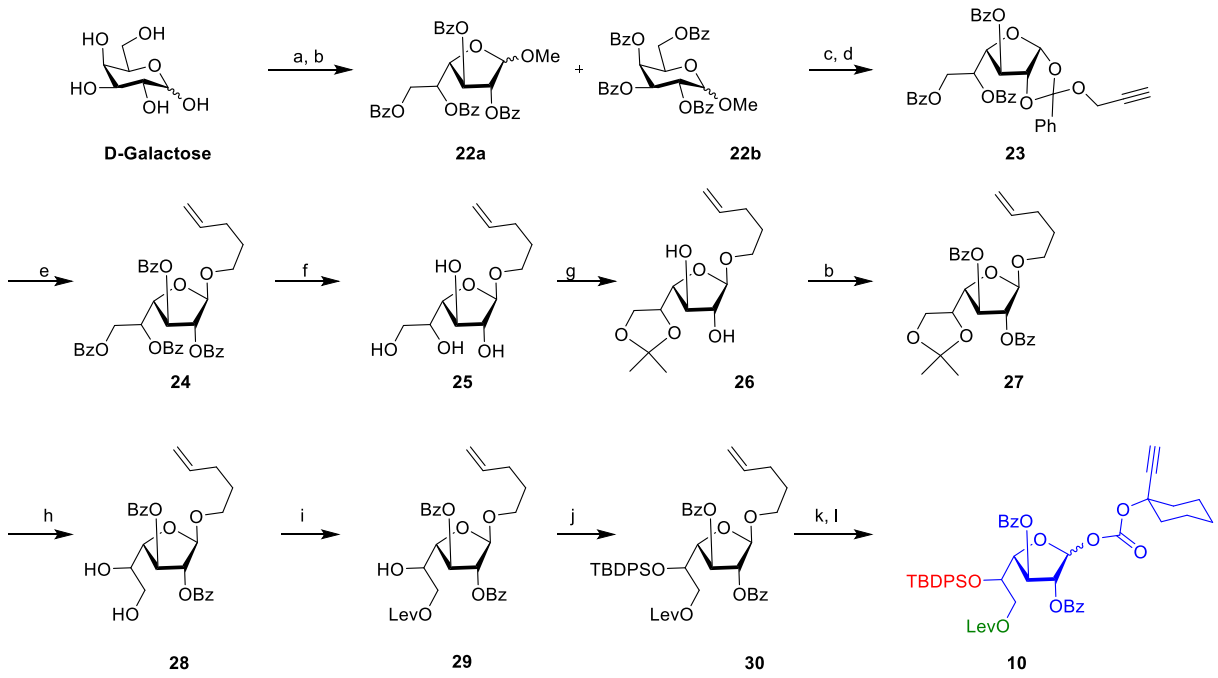


Scheme 4.4. Synthesis of Disaccharide 7. Reagents: a) 8mol% chloro[2,4-di-*tert*-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ºC, 20 min, 81%

4.9.5 Synthesis of Building Block 10:

Commercially available D-galactose was refluxed with $FeCl_3$ in dry methanol for 2 days to lock galactose into galactofuranosyl form by a literature reported method, followed by benzoylation using benzoyl chloride in pyridine to form mixture of methyl per-*O*-benzoylated galactofuranoside **22a** and galactopyranoside **22b** in 40% and 60% yield respectively in overall two steps which could be easily separated on silica gel column chromatography.[21] Propargyl galactofuranoside 1,2-*O*-orthobenzoate **23** was obtained by reaction of AcBr/MeOH at 0 ºC for 2 hours to form *insitu* generation of HBr resulting in furanosyl bromide which was treated with propargyl alcohol and 2,6-lutidine. Gold-catalyzed glycosylation was carried out between

orthoester **23** and 4-penten-1-ol in CH_2Cl_2 to afford **24** in 95% yield. Benzoyl groups in compound **24** were deprotected under Zemplén condition (NaOMe/MeOH) to form tetraol**25**in 92% yield. Major fraction **25**in anhydrous acetone was treated with 1,2-dimethoxy propane and catalytic amount of PTSA to afford diol **26**which was again protected as benzoatesemploying benzoyl chloride in pyridine to form compound **27** in 95% yield.[22]In continuation, compound **27**was treated with PTSA in CH_2Cl_2 and methanol for the hydrolysis of the isopropylidene to obtain desired compound **28** in 76% yield.



Scheme 4.5. Synthesis of Building Block 10. Reagents: a) $FeCl_3$, CH_3OH, 80 ºC, 2 d, for **22a** 40% and for **22b** 60%; b) BzCl, pyridine, DMAP, 0-25 ºC, 5 h, over two steps for **22a** 40% and for **22b** 60%, for **27** 95%; c) AcBr, CH_3OH, 0 ºC, 4h; d) Propargyl alcohol, 2,6- lutidine, TBAI, CH_2Cl_2, 25 ºC, 8 h, over two steps 45%; e) 10mol% $AuCl_3$, 5mol% AgOTf, 4-pentene-1-OH, CH_2Cl_2, 4Å MS powder, 25 ºC, 20 min, 95%; f) NaOMe, CH_2Cl_2: CH_3OH (1:1), 25 ºC, 2 h, 92%; g) 2,2-dimethoxypropane, CSA, Dry Acetone, 25 ºC, 5 h, 80%; h) PTSA, CH_3OH:CH_2Cl_2 (1:1), 25 ºC, 6 h, 76%; i) Lev-anhydride, 1,4- dioxane, DMAP, 0 ºC, 4 h, 60%; j) TBDPS-Cl, Im., DMF, 60 ºC, 10 h, 82%; k) 1.5 eq. NIS, 0.2 eq. TfOH, CH_3CN:CH_2Cl_2:H_2O (3:5:0.5), -20 - 0 ºC, 2 h; l) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate **(17),** CH_2Cl_2, DMAP, 25 ºC, 8 h, over two steps 84%.

Further, compound **28** was selectively protected as*C*6-*O*-levulinic ester using *in situ* prepared levulinic anhydride and the reaction was monitored by TLC for 4 hours at 0 ºC to get compound **29** in 60% yield which upon treatment with TBDPS-Cl in DMF for 10 hours at 60 ºC protected the lone C5-OHassilyl ether in 82% yield. Pentenyl moiety of compound **29** was released by the reaction with NIS and TfOH at -20 ºC to form hemiacetal which was directly reacted with available 1-ethynylcyclohexyl (4-nitrophenyl) carbonate **17** in presence of DMAP to afford desired carbonate glycosyl donor **10** in 84% yield over two steps (**Scheme 4.5**). Formation of desired building block **10** was confirmed by NMR and MALDI-ToF (**Table 4.1**).

Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
Anomeric	5.19 (d, *J* = 82.9 Hz, 1H) and 6.22 (s, 1H)	102.2 and 105.5
Benzoates	7.23 - 8.11 (m, 20H)	19.5 (2C) and 26.9 (6C)
Levulinoate	2.10 (d, *J* = 4.5 Hz, 6H),	172.3, 172.4, 206.4, 206.4.
OTBDPS	δ 0.99 (d, *J* = 4.1 Hz, 18H) and 7.23 - 8.11 (m, 20H)	19.5, 26.9, 26.9 and 26.9

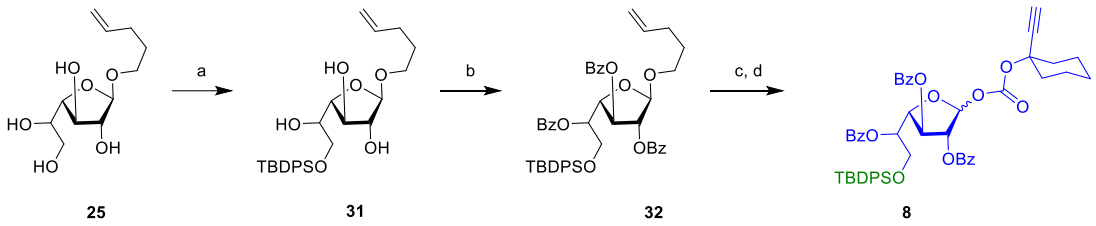
Table 4.1. Characteristic ^{1}H and ^{13}C NMR resonancesofcompound **10**

4.9.6 Synthesis of Building Block 8:

Portion of compound **25**prepared *vide supra* was selectively protected as TBDPS-ether at C6-OH position under TBDPS-Cl/Imidazole/DMF to obtain compound **31** in 82% yieldafter 10 hours. Remaining three hydroxyl groups of compound **31** was protected with benzoyl group by reaction with benzoyl chloride in pyridine in 91% yield and further, compound **31** was transformed to carbonate glycosyl donor **8**, in 88% yields by aforementioned two successive reactions*viz* hydrolysis of the pentenyl group to obtain hemiacetal followed by the conversation of hemiacetal to carbonate by the treatment of reagent **17** in the presence of DMAP in CH_2Cl_2in 6 hours **(Scheme 4.6)**. Desired carbonate glycosyl donor **8** was confirmed by spectroscopic techniques such NMR and MALDI-ToF analysis (**Table 4.2**).

Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
Anomeric	6.29 – 6.79 (d, 2H)	96.6 and 102.3
Benzoates	7.16 –8.22 (m, 20H)	165.2, 165.5, 165.6, 165.6, 165.7 and 165.8
OTBDPS	7.16 –8.22 (m, 20H)	19.2, 19.3,22.6, 22.6 and 22.6

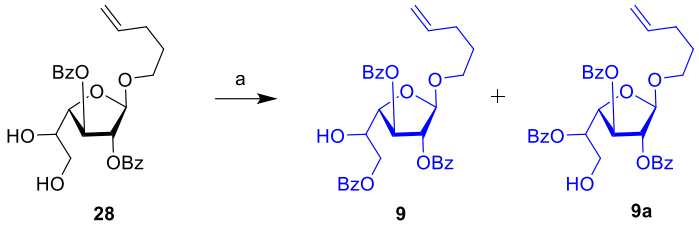
Table 4.2. Characteristic ^{1}H and ^{13}C NMR resonancesfor building block **8**



Scheme 4.6: Synthesis of Building Block 8. Reagents: a) TBDPS-Cl, Im., DMF, 0 ºC, 10 h, 82%; b) BzCl, pyridine, DMAP, 0-25 ºC, 5 h, 91%, c) 1.5 eq. NIS, 0.2 eq. TfOH, CH_3CN:CH_2Cl_2:H_2O (3:5:0.5), -20 - 0 ºC, 2 h; d) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate **17,** CH_2Cl_2, DMAP, 25 ºC, 6 h, over two steps 88%.

4.9.7 Synthesis of Building Block 9:

Product **9** with a free -OH group at 5-OH is useful as a convenient precursor for the synthesis of 5-*O*-linked galactofuranoside chain. Compound **28**was selectively protected as benzoate by reacting with benzoic anhydride in presence of NEt_3in CH_2Cl_2 to get compound **9**as a major product along with formation of the compound **9a** in as minor product which could be easily separated by silica gel column chromatography.

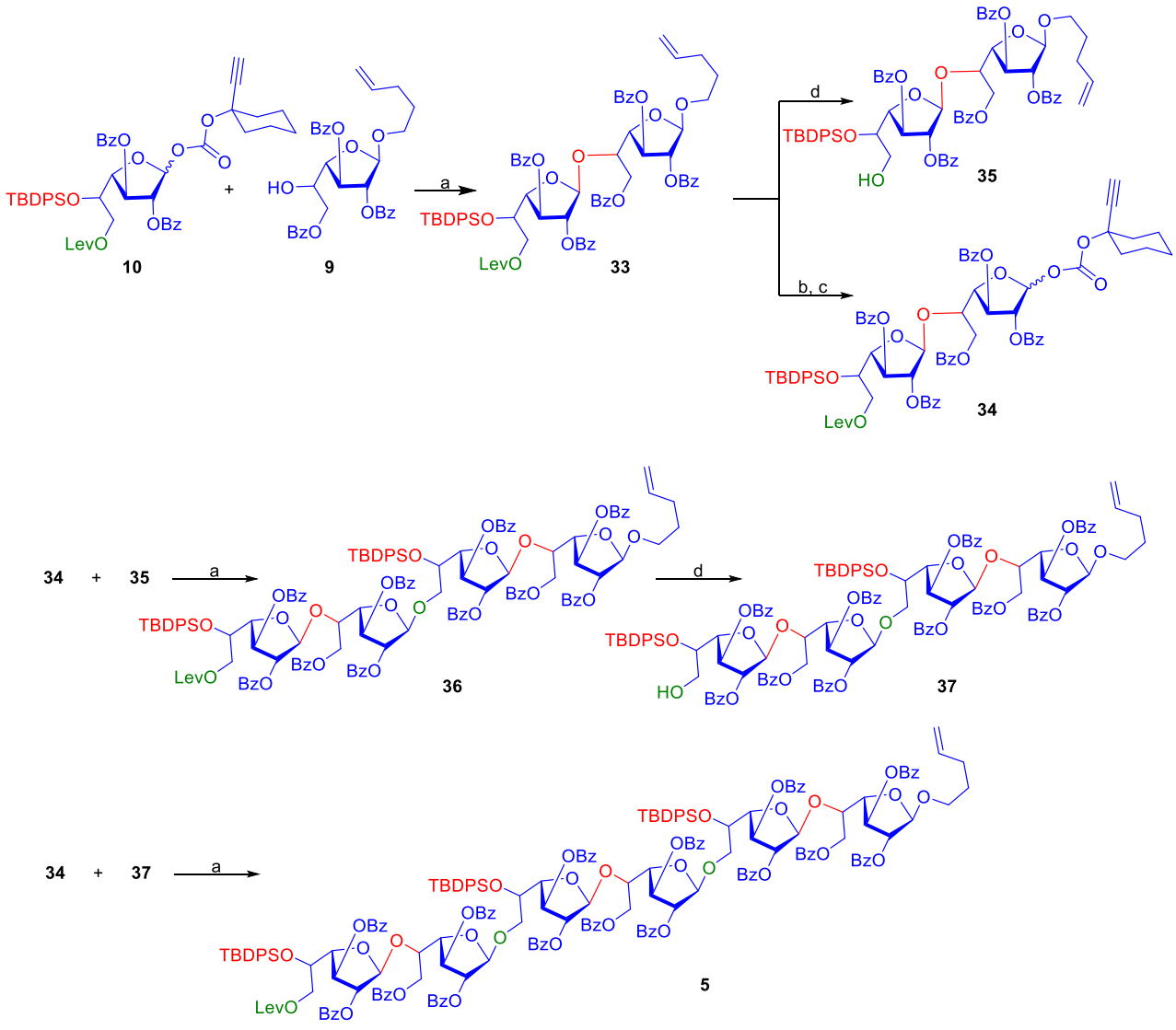


Scheme 4.7. Synthesis of Building Block 9. Reagents: a) 1.1 eq., Benzoic Anhydride, 1 eq., NH_3, CH_2Cl_2, 0 ºC, 5 h, 70% for **9** and 10% for **9a**.

4.9.8 Synthesis of Middle Gal*f*$_6$ Hexasaccharide Motif 5:

Having synthesized glycosyl donor **10** and glycosyl acceptor **9**, glycosylation was carried out under[Au]/[Ag] catalytic conditions to furnish disaccharide **33** in 75% yield. Subsequently, disaccharide**33** was divided into two portions - one portion was converted to disaccharide carbonate glycosyl donor **34** and the other portion was transformed into disaccharide glycosyl acceptor **35** by deprotection of Lev group using hydrazine.

With these disaccharide donor **34** and acceptor **35** in our hand we started assembly of middle hexasaccharide motif **5**. In this regard, tetrasaccharide **36** was conveniently accomplished by 2+2 coupling of compounds**34** and **35**under gold-catalyzed glycosylation conditions. Lev deprotection was carried out on compound **36** to afford compound **37** by using hydrazine and resulting alcohol was used as tetrasaccharide acceptor for 2+4 coupling. [Au]/[Ag]-catalyzed glycosylation was performed between tetrasaccharide acceptor **37** and disaccharide donor **34** to afford middle hexasaccharide Gal*f*$_6$**5** in 65% yield (**Scheme 4.8**). Successful synthesis of desired middle hexasaccharide motif **5** was confirmed by NMR and MALDI-ToF techniques (**Table 4.3**).



Scheme 4.8. Synthesis of Middle Gal*f*$_6$ Hexasaccharide Motif 5. Reagents: a) 8mol% chloro[2,4-di-*tert*-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ºC, 20 min, 81% for **33**, 75% for **36**, 65% for **5**; b) 1.5 eq. NIS, 0.2 eq. TfOH, CH_3CN:CH_2Cl_2:H_2O (3:5:0.5), -20 - 0 ºC, 2 h; c) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate **(17),** CH_2Cl_2, DMAP, 25 ºC, 8 h, over two steps 78%; d) NH_2NH_2, AcOH: Pyridine (12:17 eq.), CH_2Cl_2, 2 min, 80% for **35**, 78% for **37**.

Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
-OTBDPS	0.8 (s, 9H), 0.9 (s, 9H), 0.9 (s, 9H) and 7.0 – 8.1 (m, 30H)	19.4, 19.5, 19.5, 26.8, 26.8, 26.8, 26.9, 26.9, 26.9, 27.0, 27.0 and 27.0
Anomeric	5.4 (s, 1H), 5.5 (s, 2H) and 5.6 (s, 3H)	105.1, 105.6, 105.6, 106.1, 106.1 and 106.1
Benzoates	7.0 – 8.1 (m, 75H)	164.7, 164.9, 165.0, 165.2, 165.2, 165.2, 165.4, 165.4, 165.6, 165.7, 165.7, 165.8, 166.0, 166.0 and 166.2
Levulinoate	1.7 (dd, *J* = 14.9, 6.8 Hz, 2H), 1.7 – 1.8 (m, 2H) and 2.0 (s, 3H)	29.8, 30.4, 37.7, 172.2 and 206.4

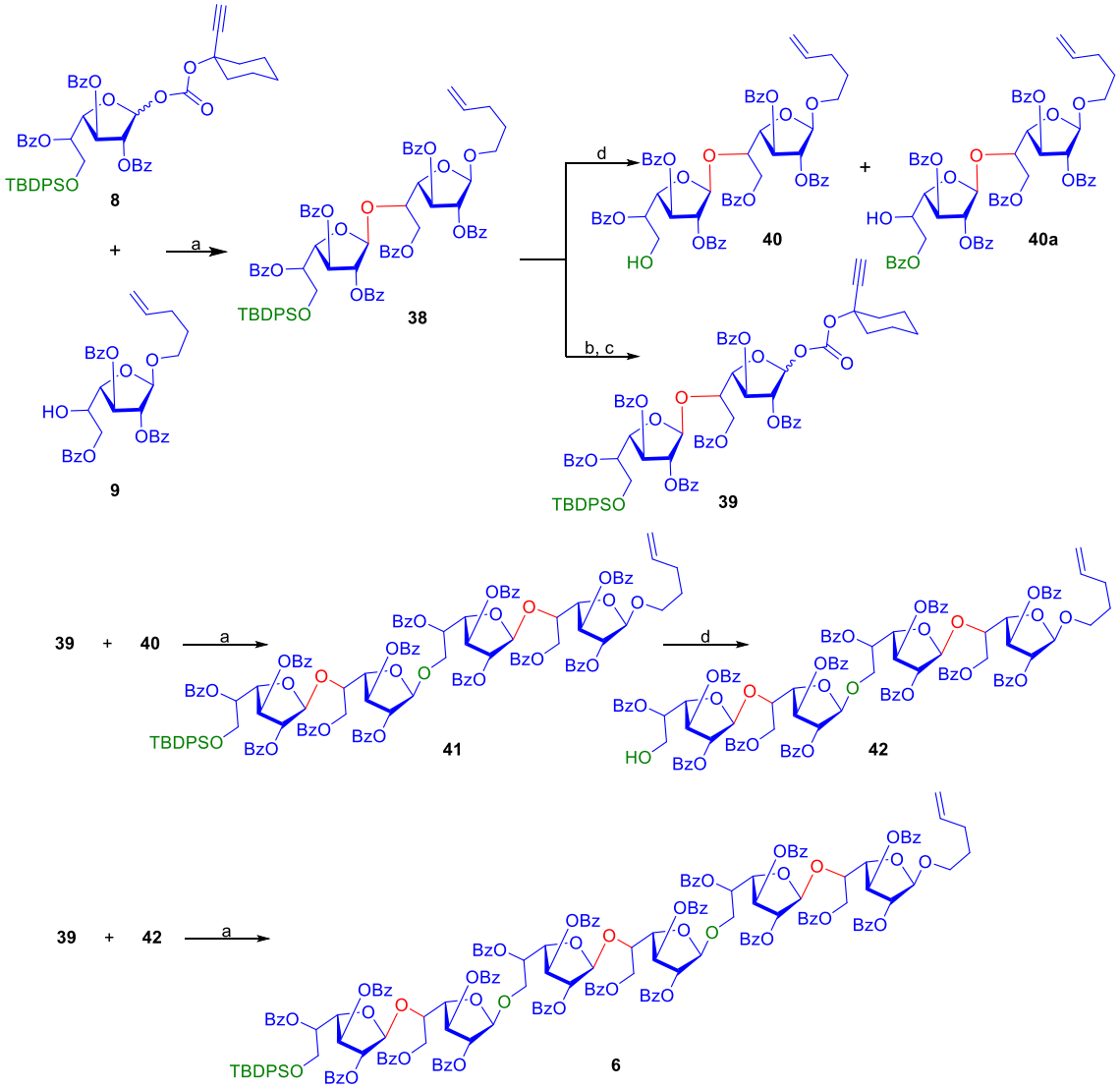
Table 4.3. Characteristic ^{1}H and ^{13}C NMR Signals for hexasaccharide motif **5**

4.9.9 Synthesis of Common Gal*f*$_6$ Hexasaccharide Motif 6:

Synthesis of disaccharide **38**commenced withthe between glycosyl donor **8** and glycosyl acceptor **9**under aforementioned Au/Ag catalysis conditions. Further, disaccharide **38**was converted into glycosyl donor **39** and glycosyl acceptor **40** by adopting the same route as delineated above. The smooth sail all the while until now has all of a sudden got shattered as the simple deprotection of TBDPS protecting group from compound **38** using HF•pyridine to obtain compound **40**. Along with the desired compound **40**, we noticed another compound whose spectral and other characteristics are very similar to compound **40**; later, the new compound was identified to be an isomer of compound **40** and assigned the structure as compound **40a**. Luckily, the two regioisomers could be easily separated on simple silica gel column chromatography. The formation of isomer **40a**can be attributed to the intramolecular migration of benzoyl group from O5→O6 position.

Similar benzoyl migration was observed while removal of trityl- group or Fmoc- protecting group as well as silyl groups under acidic conditions.[23a, b] Further, the rate of intramolecular ester

group migration is solvent polarity dependent and it is slower in polar solvents[24]and thus, silyl deprotections were carried out at different ratios of pyridine and THF at lower temperature to minimize the formation of compound **40a** up to 10% by using 1:5 ratio of pyridine and THF at -10 ºC by HF•pyridine. Similar migrations are noticed by others hypothesized through five membered orthoester type of transition state.[25]



Scheme 4.9. Synthesis of Common Gal*f*$_6$ Hexasaccharide Motif 6. Reagents: a) 8mol% chloro[2,4-di-*tert*-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ºC, 20 min, 84% for **38**, 76% for **41**, 65% for **6**; b) 1.5 eq. NIS, 0.2 eq. TfOH, CH_3CN:CH_2Cl_2:H_2O (3:5:0.5), -20 - 0 ºC, 2 h; c) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate **(17),** CH_2Cl_2, DMAP,

25 ºC, 8 h, over two steps 78%; d) HF•py, THF:Pyridine(5:1), -10 ºC, 2 h, 72% for **40**, 70% for **42**.

Having obtained sufficient quantity of the aglycon **40**, synthesis of tetrasaccharide **41** by Au/Ag-mediated glycosylation was performed between compounds **40** and **39**. Thus obtained tetrasaccharide**41**was treated with HF•py under aforementioned reaction conditions to unblock TBDPS protecting group to obtain tetrasaccharide **42**. Gratifyingly, the other isomer of tetrasaccharide was minimized to <5% at this level. This prompted us to attend the glycosylation between acceptor**42** and donor**39** under Au/Ag catalyzedconditions to afforddesired hexasaccharide Gal*f*$_6$**6** in 69% yield (**Scheme 4.9**).Common Gal*f*$_6$ Hexasaccharide Motif **6**was confirmed by NMR and MALDI-ToF experiments (**Table 4.4**).

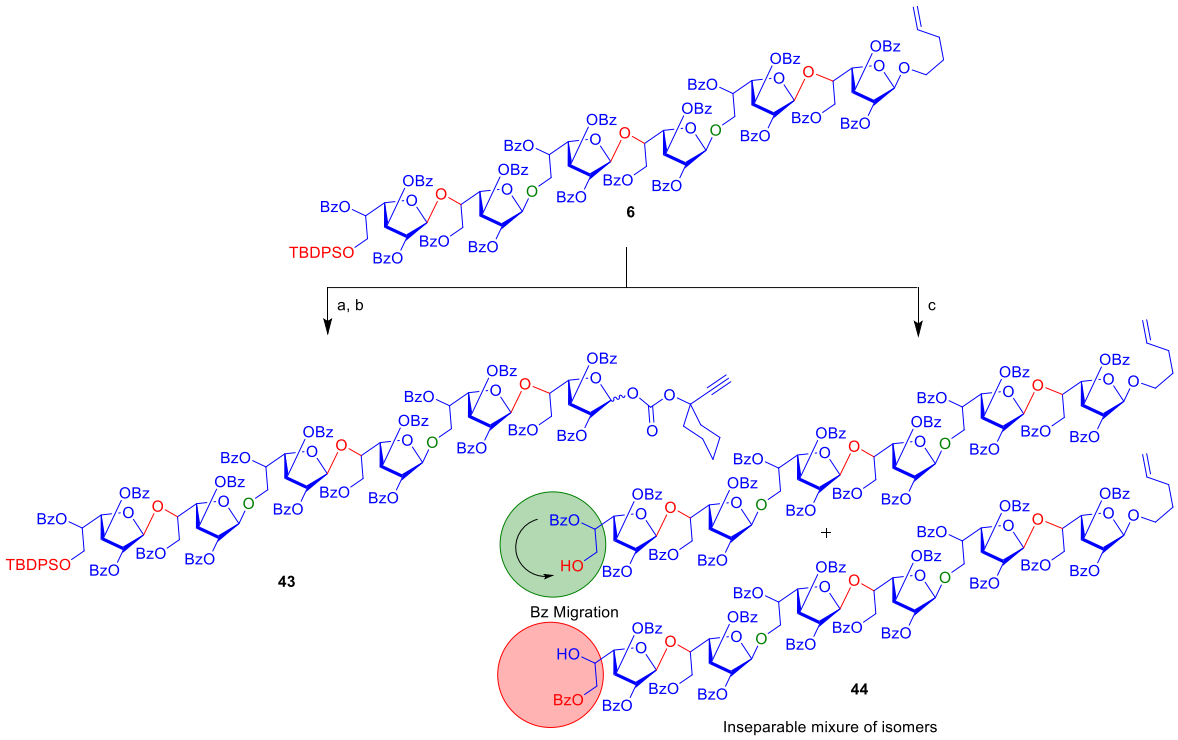
Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
Anomeric	5.67-5.87 (s, 6H)	105.4, 105.4, 105.5, 105.9, 106.7, 106.7
OTBDPS	6.90 – 8.20 (m, 10H)	19.0, 26.5, 26.6, 26.6
Benzoates	6.90 – 8.20 (m, 90H)	165.0, 165.0, 165.1, 165.2, 165.2, 165.2, 165.3, 165.3, 165.4, 165.5, 165.5, 165.5, 165.7, 165.7, 165.8, 165.8, 165.9, 165.9, 166.0, 166.0, 166.2, 166.2

Table 4.4. Characteristic ^{1}H and ^{13}C NMR Signals for Common Gal*f*$_6$ Hexasaccharide Motif **6**

4.9.10 Synthesis of Linear Gal*f*$_{24}$ Motif 4:

With 3.1g hexasaccharide **6** in hand, we continued our split-react-couple strategy for the synthesis of Gal*f*$_{24}$ motif **4**. The hexasaccharide **6** was split into two portions and the first fraction was converted to hexasaccharide carbonate donor **43** in 81% yields (**Scheme 4.10**). At this point, the hexasaccharide acceptor **44**was subjected to the hydrolysis of TBDPS moiety with HF•pyridine in pyridine and THF (1:5) solvent under -10 ºC; to our dismay,equal amount of the ***inseparable***mixture of desired compound **44** and its corresponding isomer **44a**were obtained. Several attempts to separate them have resulted in frustrating results and we could not successfully separate even on Flash chromatographic and Semi-preparative columns.

Moving forward with this mixture of compound **44**was obviously not a very good option due to the loss of material at each and every stage of the synthesis. Hence, revision in the synthetic plan was highly desirable.

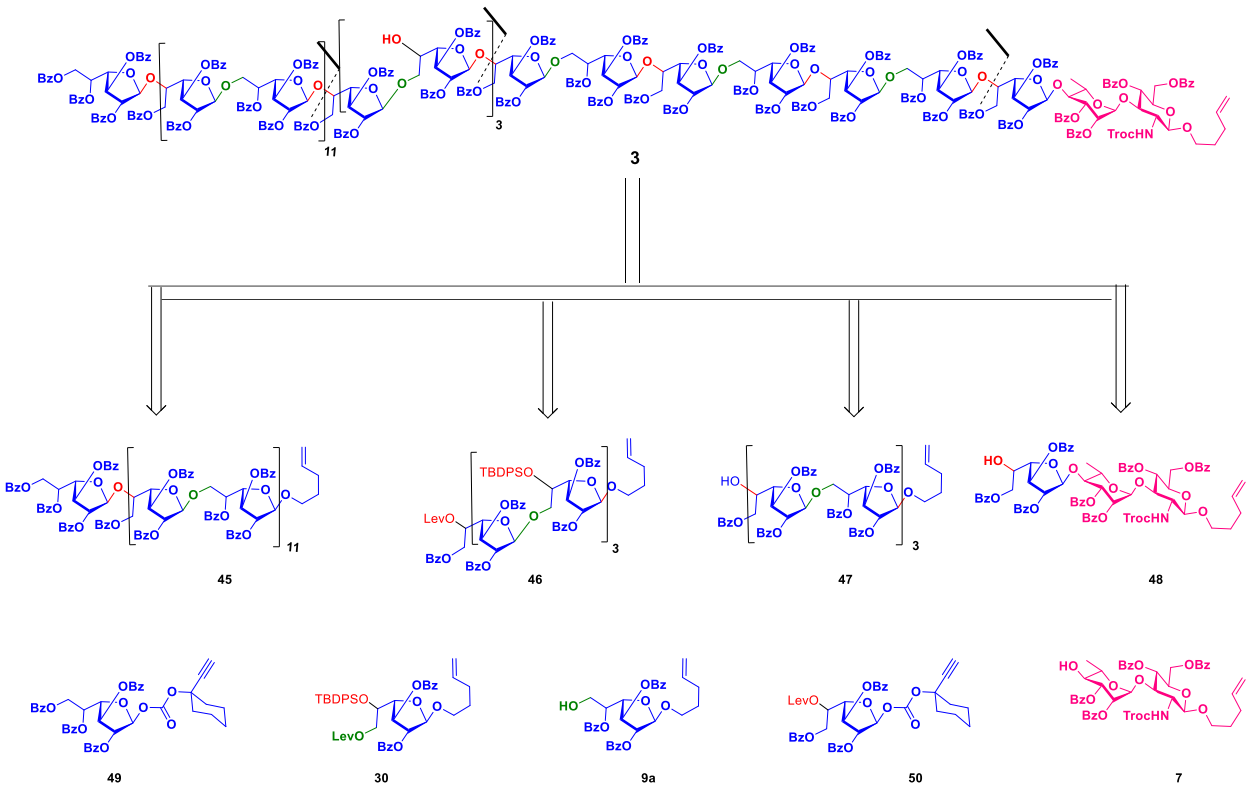


Scheme 4.10. Synthesis of Common Gal*f*$_6$ Hexasaccharide Motif 6. Reagents: a)1.5 eq. NIS, 0.2 eq. TfOH, CH_3CN:CH_2Cl_2:H_2O (3:5:0.5), -20 - 0 ºC, 2 h; b) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate **(17),** CH_2Cl_2, DMAP, 25 ºC, 8 h, over two steps 81% for **43**; c) HF•py, THF:Pyridine(5:1), -10ºC, 2 h, 82% for **44**, d) 8mol% chloro[2,4-di-*tert*-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ºC, 20 min.

4.9.11 New Retrosynthetic Analysis of Linear Chain Octatriacontanoside

Facile migration of unpredictable migration of benzoate even at oligosaccharide levelunder acidic conditions prevented us from using TBDPS and trityl moieties as protecting groups while revising the synthesisof Gal*f*$_{38}$**3**with alternating β(1→5) and β(1→6) linkages in linear fashion. Based on previous experience, it is concluded that *O*5→*O*6 migration of benzoate group cannot be stopped completely; however,the reverse *O*6→*O*5migration does not occur. Hence, shifting of one single Gal*f* residue would be ideal. Accordingly, a 3+6+23 coupling strategy was conceived so that there will be minimal perturbation to the original plan of synthesis (**Scheme 4.11**). We disconnectedGal*f*$_{38}$**3** in such way that both glycosyl donor and glycosyl acceptor can be

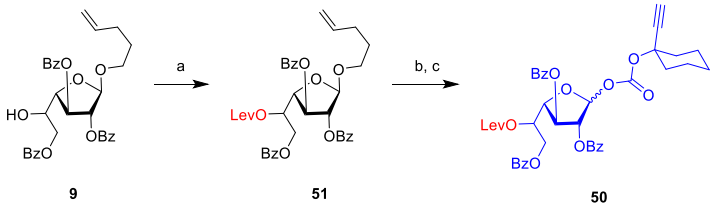
synthesized from the same precursor**48** and the 1,2-*trans* selective glycosylationsoccur due to the neighboring group participation at *C*2-OBz. We kept the*n*-pentenyl group at the reducing end as it can be conveniently converted into carbonate glycosyl donor as delineated above. Among all other protecting groups,levulinoate protection at non-reducing end of galactofuranoside ring was selected because levulinoates undergo saponification undernear neutral/buffer conditions. This new strategy required some additional building blocks and some from the previous pool ofbuilding blocks.



Scheme 4.11.New Retrosynthetic Analysis of Linear Chain Octatriacontanoside (38 mer)

4.9.12 Synthesis of Building Block 50:

Monosaccharide**9** (ref.**Scheme 4.5** and **4.9**) was protected as levulinoatethrough a coupling reaction of compound **9** with levulinic acid, DIC in CH_2Cl_2at 0 ºC to afford compound **51**. *n*-Pentenyl moiety from anomeric position of compound **51**was deprotected by employing NIS and TfOH at -20 ºC to form hemiacetal which was directly reacted with 1-ethynylcyclohexyl (4-nitrophenyl) carbonate **17** in the presence of DMAP to afford desired carbonate glycosyl donor **50** in 87% yield over two successive steps (**Scheme 4.12**).



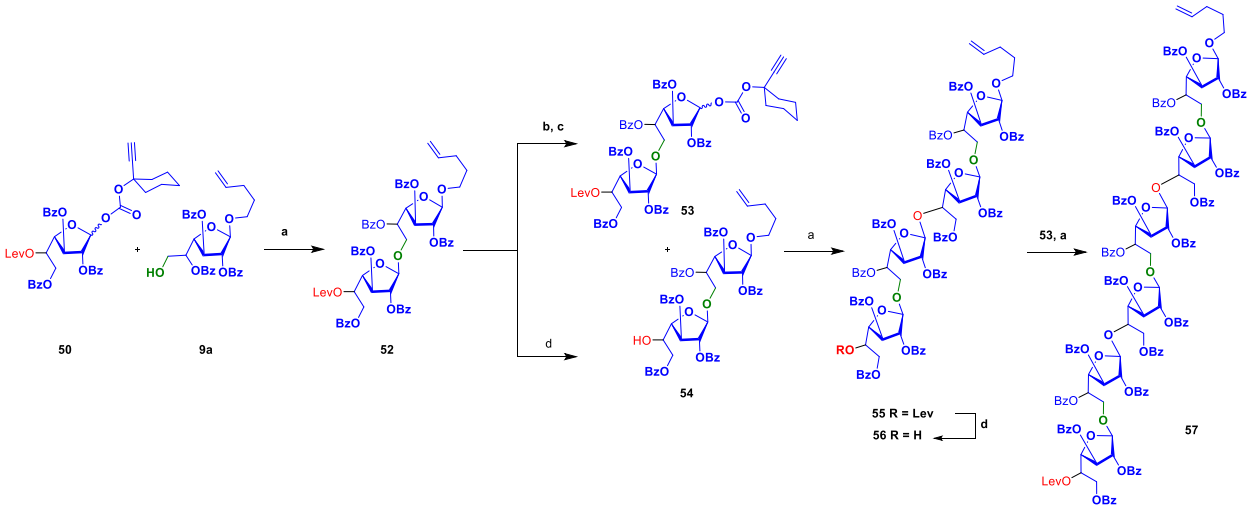
Scheme 4.12.Synthesis of building Block 51 Reagents:a) Levulinic acid, DIC, DMAP, 0 ºC, 1 h, 93%; c) 1.5 eq. NIS, 0.2 eq. TfOH, CH_3CN:CH_2Cl_2:H_2O (3:5:0.5), -20 - 0 ºC, 2 h; d) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate (**17**),CH_2Cl_2, DMAP, 25 ºC, 8 h, over two steps 87%.

4.9.13 Synthesis of Gal*f*$_6$ 57:

Glycosyl donor **50**and glycosyl acceptor **9a**were subjected to [Au]/[Ag]-catalyzed glycosylation to furnish disaccharide **52**that was divided into two portions - one portion was converted to the disaccharide carbonate glycosyl donor **53**and the other was transformed into disaccharide glycosyl acceptor **54** bydeprotectingthe Lev group using hydrazine. To our luck, no migration of benzoate from O6-O5 position was noticed. Subsequently, tetrasaccharide **55**was conveniently synthesized by 2+2 coupling of compounds**53** and **54** in under standard glycosylation conditionsin 68% yield; Lev group was deprotected using hydrazine hydrate to afford tetrasaccharide-acceptor **56**. Finally, acceptor **56**was treated with disaccharide glycosyl donor **53** under catalytic [Au]/[Ag] conditions to afford desired hexasaccharide **57** in 64% yield (**Scheme 4.13**). Structural homogeneity of hexasaccharide **57**was unequivocally confirmed by spectroscopic analysis (**Table 4.5**).

Entry	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)
Anomeric	5.70 – 5.86 (m, 6H)	105.7, 105.8, 105.9, 106.1, 106.7, 106.8
Levulinoate	1.68 (t, *J* = 6.8 Hz, 2H), 1.98 (s, 3H), 2.33 – 2.67 (t, 2H)	28.0, 28.6, 37.9,172.0, 205.9
Benzoates	6.94 – 7.60 (m, 50H), 7.73 – 8.11 (m, 40H)	165.0, 165.1, 165.2, 165.2, 165.3, 165.5, 165.5, 165.5, 165.5, 165.5, 165.7, 165.7, 165.7, 165.9, 165.9, 166.0, 166.0, 166.1

Table 4.5. Characteristic ^{1}H and ^{13}C NMR Signals for Gal*f*$_6$ Hexasaccharide Motif **57**



Scheme 4.13. Synthesis of Common Gal*f*$_6$ Hexasaccharide Motif 58. Reagents: a) 8mol% chloro[2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ºC, 20 min, 82% for **52**, 70% for **55**, 64% for **57**; b) 1.5 eq. NIS, 0.2 eq. TfOH, CH_3CN:CH_2Cl_2:H_2O (3:5:0.5), -20 - 0 ºC, 2 h; c) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate **(17),** CH_2Cl_2, DMAP, 25 ºC, 8 h, over two steps 78%; d) NH_2NH_2, AcOH: Pyridine (12:17 eq.), CH_2Cl_2, 10 min, 80% for **54**, 78% for **56**.

4.9.14 Conclusion:

In conclusion, synthesisof the most complex and larger oligosaccharide of arabinogalactan molecule by using carbonate glycosyl donor strategy was identified. Chemistry for the synthesis of all required building blocks including disaccharide linker comprising of L-Rha*p* and D-GlcNHAc*p* was developed. Advanced milestones such as middle hexasaccharide with orthogonal protecting groups, linear hexasaccharide of galactofuranose with alternating β(1→5) and β(1→6) and linkages was also synthesized in sufficient quantities. Intramolecular *O*5→*O*6 migration of benzoate group during the hydrolysis of primary TBDPS group posed as a significant bottleneck. Revised retrosynthesis by the change of protecting groups eventually was successful. The synthesis of new hexasaccharide with alternating β(1→6) and β(1→5) linkages was accomplished. The final glycosylation to synthesize the Gal*f*$_{36}$+Rha*p*+GlcNHAc*p* is currently in progress and the resulting 38-mer will be coupled with the arabinan in due course of time.

4.10 Experimental Procedures:

a) General Procedure for synthesis of pentenyl glycosides (for 13 and 21): AcCl (0.3 mmol) was added drop wise to a rapidly stirring pent-4-en-ol as solvent at 0 ^{0}C under nitrogen atmosphere. After 30 min, sugar (1.0 mmol) was added and stirred at 25 ^{0}C for 1h. The reaction mixture was further heated 80 ^{0}C and refluxed for 6h. After completion of reaction, the reaction mixture was cooled to 0 ^{0}C and quenched with Et_3N and concentrated in *vacuo* to obtain a light brown residue which was purified by column chromatography (CH_2Cl_2/MeOH) to obtain the desired pentenyl glycoside.

b) General Procedure for acetonide protection (for13 and 26): To a solution of deprotected sugar in anhydrous acetone, 2,2-dimethoxy propane (1.2 mmol) and PTSA (0.2 mmol) was added. The reaction mixture was allowed to stir at room temperature for 6 hours. After complete consumption of starting material, the reaction was quenched with Et_3N and concentrated in *vacuo* to obtain a light yellow residue which was purified by column chromatography (n-hexane/ EtOAc) to obtain the desired acetonide product as white solid.

c) General procedure for Levulinoate ester protection of alcohols (for 14, 20, 29 and 51): To a solution of alcohol (1.0 mmol) in anhydrous CH_2Cl_2 (4 ml), DMAP (1.0 mmol), levulinic acid (1.5 mmol) and *N*,*N*′-Diisopropylcarbodiimide (1.5 mmol) were added sequentially at 0 ^{0}C under inert atmosphere. The reaction mixture was gradually warmed up to 25 ^{0}C and stirred for 4 h. After complete consumption of the starting alcohol, the reaction mixture was concentrated in *vacuo* and purified on silica gel column chromatography (*n*-hexane/ EtOAC) to afford corresponding levulinoate ester.

d) General procedure for deprotection of Isopropylidene group (for 15 and 28): To a solution of isopropylidene compound (1 mmol) in CH_2Cl_2 and Methanol (10 mL), 0.2 eq. of PTSA was added at 25 ^{0}C and the reaction mixture was allowed to stir at 55 ^{0}C for 3 h. Progress of the reaction and complete consumption of the starting material was checked by TLC.At the end of reaction, the reaction mixture was quenched NEt_3 (2 mL) at 0 ^{0}C evaporated *in vacuo* to obtain a crude residue which was purified on silica gel column chromatography (*n*-hexane/EtOAc) to afford the desired product.

e) General procedure for benzoate/acetate ester protection of alcohols (for 16, 21, 22a, 22b, and 24): To a solution of alcohol (1 mmol) in anhydrous pyridine (10 mL), benzoyl chloride/acetic anhydride (1.2 mmol per alcohol) was added dropwise at 0 ^{0}C under nitrogen atmosphere. The reaction mixture was gradually warmed up to 25 ^{0}C and stirred for 6-12 h. Progress of the reaction and consumption of starting alcohol was checked by TLC. After completion of the reaction, the reaction mixture was quenched by adding ice cooled water and extracted with CH_2Cl_2 (50 mL) and the CH_2Cl_2 layer was washed with 1*N*HCl (2x50 mL), water, saturated aqueous $NaHCO_3$ solution and finally with brine solution. Combined organic layers were dried over anhydrous Na_2SO_4, concentrated *in vacuo* and the resulting crude residue was purified by silica gel column chromatography (*n*-hexane/EtOAc) to obtain the desired compound.

f) General procedure for deprotection of Pent-4-ene-1-ol Glycosides (for 11, 10, 8, 34, 39, 43, 51 and 53): The pent-4-enyl glycoside (1.0 mmol) was dissolved in a mixture of solvents $CH_2Cl_2/CH_3CN/H_2O$ (5.0:3.0:0.5) and the reaction mixture was cooled to -10 °C. After 15 min, NIS (2.2 mmol) and TfOH (0.2 mmol) were added to the reaction mixture simultaneously and the reaction was allowed to stir at 0 °C for another 1 h. After completion, the reaction mixture was quenched with $NaHCO_3$ solution and diluted with CH_2Cl_2. The organic layer was successively washed with water (25 mL), brine solution (25 mL), dried over Na_2SO_4 and concentrated in *vacuo* to obtain crude that was purified by silica gel column chromatography using ethyl acetate and hexane to furnish corresponding *C*-1 alcohol.

g) General procedure for synthesis of ethynylcyclohexyl glycosyl carbonate donors (for 11, 10, 8, 34, 39, 43, 51 and 53): DMAP (1 mmol) was added to a stirring solution of hemiacetal (1mmol) in anhydrous CH_2Cl_2 (10 mL) at 25 ^{0}C. After 20 min, reagent **22** (1.2 mmol) was added portion-wise (3x) after every 30 min and stirred at 25 ^{0}C for 2-3 h. After completion of reaction as indicated by TLC, the reaction mixture was concentrated *in vacuo* and the oily residue was partially purified by silica gel column chromatography (*n*-hexane/EtOAc). Eluents containing alkynyl glycosyl carbonate along with trace quantities of 4-nitrophenol were concentrated under diminished pressure. Further, the crude residue was redissolvedin CH_2Cl_2 (30 mL) and washed with sat. aq. $NaHCO_3$ (3x10 mL) and brine solution to remove 4-nitrophenol. The organic layer

was dried over Na_2SO_4 and concentrated *in vacuo* toobtain the alkynyl glycosyl carbonate donor in excellent yields.

h)General Procedure for Troc- protection of amine (for 18): To ice cooled solution of glucosamine hydrochloride salt in water, 2.0 N solution of $NaHCO_3$ was added and allowed to stir solution for an hour. After an hour 1.0 eq. of TrocCl was added dropwise to same solution and allowed to stir for another 2 hours. Solid precipitate was filtered, dried and used for further reaction without purification.

i)General procedure for benzylidine protection (for 19): To a rapidly stirring solution of sugar (1.0 mmol) in anhydrous DMF, benzaldehyde 1,1-dimethylacetal (1.5 mmol) and PTSA (0.2 mmol) were added and the reaction mixture was stirred at 25 °C for overnight (12 h). After complete consumption of the di-ol, the reaction mixture was quenched with Et_3N and extracted with ethyl acetate (3x20 mL). The combined organic layer was washed with water (2x50 mL), brine solution (1x50 mL), dried over Na_2SO_4 and evaporated *in vacuo* to obtain a crude residue which was purified on silica gel column chromatography (*n*-hexane/EtOAc) to afford the desired product.

j)General procedure for deprotection of benzylidinegroup (for 21): To a solution of benzylidine compound (1 mmol) in MeOH and CH_2Cl_2, PTSA (0.2 mmol) was added and the reaction mixture was stirred at 25 °C for 30 minute. After completion of the reaction (as indicated by TLC), the reaction mixture was quenched with Et_3N and concentrated *in vacuo*to obtain a light yellow residue which was purified by column chromatography (*n*-hexane/EtOAc) to afford the desired product.

k)General procedure for deprotection of levulinoate ester protection (for 7, 35, 37, 54 and 56): To a solution of levulinoate (1.0 mmol) in CH_2Cl_2 (5 mL), a buffer solution of py/AcOH (27:22 mmol) and 70% hydrazine hydrate (6 mmol) were added and the reaction mixture was stirred at 25 °C for 3-4 h. After completion, the reaction was quenched by the addition of acetone (2 mL) and the reaction mixture was extracted with ethyl acetate. The organic layer was washed with 1*N* HCl (25 mL), brine (50 mL), dried over Na_2SO_4 and concentrated *in vacuo* and the crude residue was purified by silica gel column chromatography to achieve the desired product in 85-95% yield.

l)General Procedure for Glycosylation (for 7a, 33, 36, 5, 38, 41, 6, 53, 55 and 57): To a stirred solution of alkynyl carbonate donor (1 mmol) and acceptor (1 mmol) in anhydrous

CH_2Cl_2 containing 4Å MS powder Au-phosphite complex (0.08 mmol) and AgOTf salt (0.15 mmol) were added and stirred at 25 ^{0}C. Upon completion of reaction, the reaction mixture was quenched with Et_3N and concentrated *in vacuo* to obtain a residue that was purified by silica gel column chromatography (*n*-hexane/EtOAc) to afford the desired glycoside.

m)Procedure for synthesis of galactofuranoside (for 22a): To a suspension of D-galactose (1 mmol) in anhydrous methanol (100 mL) containing ferric chloride (8 mmol) was heated to 60 ^{0}C for 24 h and then refluxed for 3 h under argon atmosphere. After cooling to 25 °C, Celite (1.0 g) and saturated aqueous solution of $NaHCO_3$ (10 mL) were added. The reaction mixture was stirred for additional 1 h at 25 °C. The precipitate was filtered off through a pad of Celite, washed with methanol and the filtrate was concentrated in *vacuo*. The resulting solid was extracted with boiling ethyl acetate-ethanol (2:1, v/v, 4 x 80 mL) and the combined organic extracts were concentrated under diminished pressure to obtain a residue that was redissolved in THF, filtered and evaporated to dryness to obtain methyl galactofuranoside (2.90 g, 83%). The crude product was pure enough to proceed to the next step without any further purification.

n)General procedure for orthoester formation (for 23): Per-*O*-acyl methyl galacto-furanosides (1.0 mmol) were dissolved in anhydrous CH_2Cl_2 and cooled to 0 °C. Acetyl bromide (6.5 mmol) was added to the reaction mixture followed by the drop-wise addition of MeOH (4.5 mmol) and stirred at 0 °C for 2 h. After complete conversion of the starting material, the reaction mixture was diluted with CH_2Cl_2 and poured over ice-water mixture and was extracted with CH_2Cl_2 (3x50 mL). The organic layer was washed with ice-cold saturated $NaHCO_3$ (1x25 mL), brine solution (1x25 mL), dried over Na_2SO_4 and concentrated *in vacuo* to afford corresponding furanosyl bromide as a white foam which was immediately carried forward without any further purification. To a solution of the crude furanosyl bromide prepared *vide supra* in anhydrous CH_2Cl_2, propargyl alcohol (2.0 mmol), 2,6-lutidine (2.2 mmol) and tetra *n*-butyl ammonium iodide (0.5 mmol) were added and the reaction mixture was allowed to stir at 25 °C. After 15 h, the reaction mixture was diluted with CH_2Cl_2 and water, extracted with saturated aqueous oxalic acid solution (3x25 mL), saturated $NaHCO_3$ (1x25 mL), brine solution (1x25 mL), dried over Na_2SO_4 and concentrated *in vacuo* to obtain a crude product that was purified by silica gel column chromatography using EtOAc and Hexane as mobile phase to obtain the corresponding orthoester.

o) General procedure for opening of orthoester by using $AuBr_3$(for 24): To a solution of propargyl-1,2-orthoester (1.0 mmol) in anhydrous CH_2Cl_2 (4 mL), allyl or pent-1-ene-ol (6 mmol) and freshly activated 4Å MS powder (0.200 g) were added under argon atmosphere and stirred for 15 min at 25 °C. $AuBr_3$ (10mol%) was added and the reaction mixture was allowed to stir for 3-4 h and was passed through a bed of Celite®. The filtrate was concentrated *in vacuo* and purified by silica gel column chromatography using ethyl acetate and hexane as mobile phase to obtain corresponding glycoside with C-2 benzoate or acetate in 75-90% yield.

p)General procedure for TBDPS-protection of alcohols (for 31): Toarapidly stirring solution of alcohol (1.0 mmol) and imidazole (1.3 mmol) in anhydrous DMF (10 mL) was added TBDPSCl (1.2 mmol) dropwise and stirred for 4 h at 25 °C. At the end of reaction, the reaction mixture was extracted with ethyl acetate (3x20 mL). The combined organic layer was washed with water (2x50 mL), brine solution (1x50 mL), dried over Na_2SO_4 and evaporated *in vacuo*to obtain a crude residue which was purified on silica gel column chromatography (*n*-hexane/EtOAc) to afford the desired product.

q)General procedure for deprotection of the TBDPS-ethers(for 40, 42 and 44): To a solution of silyl ether compound (1mmol) in 5:1 mixture of THF-Py (5:1) (10 mL), HF·py (3 mmol) was added drop wise at -10^oC under nitorgen atmosphere and stirred at 25 ^oC. After 4 h,the reaction mixture was quenched with 2N HCl at 0 ^oC, diluted with EtOAc (30mL) and washed with ice cold water (2x20 mL), sat. aq. $NaHCO_3$ (20 mL) and brine solution (20 mL) sequentially. The EtOAc layer was dried over anhydrous Na_2SO_4 andconcentrated *in vacuo*.The crude residue was purified by silica gel column chromatography (*n*-hexane/EtOAc) to furnish corresponding alcohol in very high yield.

r)General procedure for selective benzoate ester protection of alcohol (for 9): To a solution of alcohol (1 mmol) and anhydrous Et_3N (5 mmol) in anhydrous CH_2Cl_2 (10 mL), Benzoic anhydride (1.2 mmol) was added portion wise over a period of 3 h at 0 ^0C under nitrogen atmosphere. The reaction mixture was continued to stir for another 6 h at 0 ^0C. Progress of the reaction and consumption of starting alcohol was checked by TLC. After completion of the reaction, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with 1*N* HCl (20 mL), water, saturated aq. $NaHCO_3$ solution and finally with brine solution. Combined organic layers were dried over anhydrous Na_2SO_4, concentrated *in vacuo* and the resulting crude residue

was purified by silica gel column chromatography (*n*-hexane/EtOAc) to obtain the desired compound.

4.11Supporting Information

Pent-4-enyl 2,3-*O*-isopropylidine-α-L-rhamnopyranoside (13):syrup; $[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 1.0): -19.5; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.28 (d, *J* = 6.3 Hz, 3H), 1.35 (s, 3H), 1.52 (s, 3H), 1.69 (p, *J* = 7.8, 7.3 Hz, 2H), 2.07 – 2.22 (m, 2H), 3.29 – 3.39 (m, 1H), 3.43 (dt, *J* = 9.7, 6.4 Hz, 1H), 3.56 – 3.77 (m, 3H), 4.02 – 4.23 (m, 2H), 4.95 (s, 1H), 4.96 – 5.09 (m, 2H), 5.80 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H);^{13}C NMR (100.67 MHz, $CDCl_3$): δ 17.4, 26.1, 28.0, 28.5, 30.2, 65.6, 66.8, 74.4, 75.9, 78.6, 96.9, 109.3, 115.0, 137.8.; HRMS (ESI-MS): m/z calcd for $[C_{14}H_{24}O_5Na]^+$: 295.1521; Found: 295.1520.

Pent-4-enyl 2,3-*O*-isopropylidine-4-*O*(4-oxopentanoyl)-α-L-rhamnopyranoside (14): syrup; $[\alpha]^{25}_{D}$($CHCl_3$, *c*1.0): -11.1^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.18 (d, *J* = 6.3 Hz, 3H), 1.34 (s, 3H), 1.55 (s, 3H), 1.69 (p, *J* = 7.0 Hz, 2H), 2.14 (q, *J* = 7.1 Hz, 2H), 2.19 (s, 3H), 2.51 – 2.61 (m, 1H), 2.61 – 2.68 (m, 1H), 2.70 (q, *J* = 5.0, 4.3 Hz, 1H), 2.81 – 2.94 (m, 1H), 3.44 (dt, *J* = 9.8, 6.4 Hz, 1H), 3.61 – 3.82 (m, 2H), 4.09 – 4.21 (m, 2H), 4.85 (dd, *J* = 10.1, 7.6 Hz, 1H), 4.91 – 5.10 (m, 3H), 5.82 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 17.0, 26.5, 27.8, 28.1, 28.7, 29.9, 30.4, 38.0, 64.0, 67.1, 75.0, 75.9, 76.2, 97.0, 109.8, 115.1, 138.0, 172.2, 206.5; HRMS (ESI-MS): m/z calcd for $[C_{19}H_{30}O_7Na^+]$: 393.1889; Found: 393.1882.

Pent-4-enyl 4-*O*-(4-oxopentanoyl)-α-L-rhamnopyranoside (15): syrup; $[\alpha]^{25}_{D}$($CHCl_3$, *c*1.0): -9.3^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.2 (d, *J* = 6.3 Hz, 3H), 1.6 – 1.8 (m, 2H), 2.1 (d, *J* = 7.4 Hz, 2H), 2.6 (td, *J* = 6.1, 3.2 Hz, 3H), 2.60 (td, *J* = 6.1, 3.2 Hz, 2H), 2.8 (dt, *J* = 7.0, 3.7 Hz, 2H), 3.4 (d, *J* = 9.7 Hz, 1H), 3.5 (s, 1H), 3.6 (s, 1H), 3.6 – 3.8 (m, 2H), 3.9 (d, *J* = 22.1 Hz, 2H), 4.8 (s, 1H), 4.9 (t, *J* = 9.7 Hz, 1H), 4.9 – 5.1 (m, 2H), 5.7 – 5.9 (m, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 17.3, 28.1, 28.6, 29.8, 30.2, 38.1, 65.7, 67.0, 69.9, 71.0, 75.1, 99.5, 114.9, 138.0, 173.2, 207.5; HRMS (ESI-MS): m/z calcd for $[C_{16}H_{26}O_7Na^+]$: 353.1576; Found: 353.1582.

Pent-4-enyl 2,3-di-*O*-benzoyl-4-*O*-(4-oxopentanoyl)-α-L-rhamnopyranoside (16): mp (^{0}C): 97.5; $[\alpha]^{25}_{D}$($CHCl_3$, *c*1.0): -10.7^0;^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.33 (d, *J* = 6.3 Hz, 3H), 1.77

(pd, *J* = 6.8, 1.9 Hz, 2H), 2.07 (s, 3H), 2.20 (q, *J* = 6.7 Hz, 2H), 2.34 – 2.57 (m, 2H), 2.56 – 2.74 (m, 2H), 3.52 (dt, *J* = 9.6, 6.4 Hz, 1H), 3.77 (dt, *J* = 9.6, 6.6 Hz, 1H), 4.05 (dq, *J* = 9.9, 6.2 Hz, 1H), 4.94 (d, *J* = 1.6 Hz, 1H), 4.99 – 5.13 (m, 2H), 5.40 (t, *J* = 9.9 Hz, 1H), 5.59 (dd, *J* = 3.4, 1.7 Hz, 1H), 5.67 (dd, *J* = 10.1, 3.5 Hz, 1H), 5.85 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.48 (dt, *J* = 15.2, 7.5 Hz, 3H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.80 – 7.94 (m, 2H), 8.06 (dd, *J* = 8.3, 1.3 Hz, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 17.6, 28.1, 28.7, 29.7, 30.4, 38.0, 66.5, 67.7, 70.2, 71.0, 71.7, 97.6, 115.3, 128.5, 128.5, 128.7, 128.7, 129.5, 129.6, 129.9, 129.9, 130.0, 130.0, 133.3, 133.5, 138.0, 165.6, 165.7, 172.2, 206.2; HRMS (ESI-MS): m/z calcd for [$C_{30}H_{34}O_9Na^+$]: 561.2101; Found: 561.2119.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3-di-*O*-benzoyl-4-*O*-(4-oxopentanoyl)-α-L-rhamnopyranoside [α:β=0.3:1] (11):foam;mp (^{0}C): 66.5;[α]$^{25}_D$($CHCl_3$, *c*1.0): -39.6^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.35 (d, *J* = 6.2 Hz, 6H), 1.56 – 1.83 (m, 10H), 1.84 – 2.00 (m, 4H), 2.07 (d, *J* = 2.1 Hz, 6H), 2.15 – 2.28 (m, 4H), 2.31 – 2.47 (m, 2H), 2.51 – 2.63 (m, 4H), 2.66 – 2.74 (m, 4H), 3.41 (qd, *J* = 10.6, 5.4 Hz, 1H), 3.55 (ddd, *J* = 15.6, 8.9, 6.2 Hz, 1H), 3.73 – 3.85 (m, 1H), 4.13 (ddd, *J* = 62.8, 9.8, 6.2 Hz, 2H), 4.63 – 4.80 (m, 1H), 4.96 (d, *J* = 1.4 Hz, 2H), 5.38 – 5.50 (m, 1H), 5.60 (dd, *J* = 3.4, 1.7 Hz, 1H), 5.65 – 5.68 (m, 1H), 5.69 – 5.76 (m, 1H), 7.35 (t, *J* = 7.8 Hz, 4H), 7.43 – 7.55 (m, 6H), 7.56 – 7.64 (m, 2H), 7.89 (dt, *J* = 8.5, 2.0 Hz, 4H), 7.98 – 8.13 (m, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 14.1, 17.6, 22.4, 22.6, 25.0, 25.2, 25.2, 28.0, 28.0, 29.7, 30.8, 30.8, 36.7, 36.8, 37.0, 37.0, 37.9, 37.9, 66.6, 67.5, 67.6, 68.9, 70.1, 70.8, 71.6, 75.1, 75.6, 76.0, 76.0, 78.0, 78.9, 82.9, 93.7, 97.5, 128.4, 128.4, 128.4, 128.5, 128.6, 128.6, 128.6, 128.7, 129.1, 129.2, 129.4, 129.5, 129.8, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 130.0, 133.3, 133.4, 133.5, 133.7, 150.4, 152.3, 165.2, 165.5, 165.5, 165.6, 172.0, 172.1, 206.0, 206.1.; HRMS (ESI-MS): m/z calcd for [$C_{34}H_{36}O_{11}Na^+$]: 543.2155; Found: 544.7136.

Pent-4-enyl 2-deoxy-2-(((2,2,2-trichloroethoxy)carbonyl)amino)-β-D-glucopyranoside [α:β=1:3] (18):mp (^{0}C): 144.2; [α]$^{25}_D$($CHCl_3$, *c*1.0): 27.1^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.71 (p, *J* = 6.8 Hz, 2H), 2.14 (dd, *J* = 4.4, 2.2 Hz, 2H), 3.08 (s, 1H), 3.40 (dt, *J* = 9.7, 6.5 Hz, 1H), 3.52 (t, *J* = 9.1 Hz, 1H), 3.66 – 3.75 (m, 2H), 3.75 – 3.95 (m, 3H), 4.23 (dd, *J* = 9.9, 4.5 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.76 – 4.89 (m, 2H), 4.95 – 5.12 (m, 2H), 5.35 (d, *J* = 9.1 Hz, 1H), 5.52 (s, 1H), 5.80 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 7.32 – 7.41 (m, 3H), 7.45 – 7.55 (m, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.5, 30.4, 55.9, 62.6, 67.8, 68.9, 70.0, 74.9, 81.9, 95.5,

97.9, 102.0, 115.4, 126.4, 126.4, 128.4, 128.4, 129.4, 137.1, 137.9, 155.0; HRMS (ESI-MS): m/z calcd for [$C_{14}H_{22}Cl_3NO_7Na^+$]: 444.0360; Found: 444.1549.

Pent-4-enyl 2-deoxy-2-(((2,2,2-trichloroethoxy)carbonyl)amino)-4,6-*O*-benzylidine-β-D-glucopyranoside (19): mp (^{0}C): 87.5; $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 37.8^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.54 – 1.86 (m, 4H), 2.02 – 2.35 (m, 4H), 2.89 (d, *J* = 0.6 Hz, 2H), 2.96 – 3.12 (m, 2H), 3.24 – 3.55 (m, 10H), 3.61 (dq, *J* = 7.8, 2.7 Hz, 1H), 3.64 – 3.69 (m, 3H), 3.73 – 3.85 (m, 4H), 3.86 – 3.97 (m, 2H), 4.41 (d, *J* = 8.2 Hz, 1H), 4.72 (dd, *J* = 12.2, 1.9 Hz, 2H), 4.82 (d, *J* = 2.3 Hz, 2H), 4.93 – 4.99 (m, 2H), 4.98 – 5.12 (m, 3H), 5.84 (dddd, *J* = 17.1, 10.4, 6.7, 3.9 Hz, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 30.0, 30.2, 31.4, 31.6, 57.7, 59.4, 62.9, 63.0, 68.5, 70.2, 72.3, 72.4, 73.0, 73.9, 75.8, 75.8, 76.0, 78.0, 97.3, 98.9, 103.1, 103.1, 115.5, 115.6, 139.6, 139.6, 157.0, 157.2; HRMS (ESI-MS): m/z calcd for [$C_{21}H_{26}Cl_3NO_7Na^+$]: 532.0673; Found: 532.0770.

Pent-4-enyl 2-deoxy-2-(((2,2,2-trichloroethoxy)carbonyl)amino)-3-*O*-(4-oxopentanoyl)-4,6-*O*-benzylidine-β-D-glucopyranoside (20): mp (^{0}C): 110.5; $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 39.1^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.74 (p, *J* = 6.9 Hz, 2H), 2.13 (s, 3H), 2.14 – 2.25 (m, 2H), 2.50 – 2.80 (m, 4H), 3.43 (dt, *J* = 9.7, 6.5 Hz, 1H), 3.64 – 3.83 (m, 3H), 3.90 (td, *J* = 9.9, 4.7 Hz, 1H), 4.05 (td, *J* = 10.2, 3.7 Hz, 1H), 4.28 (dd, *J* = 10.2, 4.7 Hz, 1H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.79 – 4.91 (m, 2H), 4.97 – 5.11 (m, 2H), 5.35 (dt, *J* = 10.0, 5.0 Hz, 2H), 5.52 (s, 1H), 5.80 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 7.30 – 7.42 (m, 3H), 7.46 (dd, *J* = 6.6, 3.0 Hz, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.1, 28.5, 29.9, 30.5, 38.0, 54.7, 63.0, 68.0, 68.9, 70.5, 74.8, 79.2, 95.6, 98.2, 101.6, 115.5, 126.3, 126.3, 128.3, 128.3, 129.2, 137.0, 137.9, 154.5, 172.8, 206.1; HRMS (ESI-MS): m/z calcd for [$C_{26}H_{32}Cl_3NO_9Na^+$]: 630.1040; Found: 630.1033

Pent-4-enyl 2-deoxy-2-(((2,2,2-trichloroethoxy)carbonyl)amino)-4,6-di-*O*-benzoyl-β-D-glucopyranoside (12):mp(^{0}C): 82.5; $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 26.0^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.78 (q, *J* = 6.9 Hz, 2H), 2.16 (dt, *J* = 13.4, 7.0 Hz, 2H), 3.49 (dt, *J* = 9.7, 6.5 Hz, 1H), 4.04 (ddd, *J* = 9.9, 4.2, 2.2 Hz, 2H), 4.20 (td, *J* = 10.4, 3.7 Hz, 1H), 4.49 (s, 1H), 4.57 (dd, *J* = 12.2, 2.2 Hz, 1H), 4.71 (s, 1H), 4.74 – 4.82 (m, 1H), 4.92 (d, *J* = 3.7 Hz, 1H), 4.94 – 5.13 (m, 2H), 5.31 – 5.47 (m, 2H), 5.81 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 7.44 (dt, *J* = 20.8, 7.7 Hz, 4H), 7.52 – 7.68 (m, 2H), 7.90 – 8.18 (m, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.6, 30.6, 53.9, 63.5, 68.0, 69.5, 70.7, 74.5, 75.0, 95.3, 97.6, 115.5, 128.5, 128.6, 128.6, 128.6, 129.2, 129.7, 129.9,

130.0, 130.2, 130.2, 133.5, 133.7, 137.9, 154.4, 167.1, 167.8; HRMS (ESI-MS): m/z calcd for [$C_{28}H_{30}Cl_3NO_9Na^+$]: 652.0884; Found: 652.4462

Pent-4-enyl2-deoxy-2-(((2,2,2-trichloroethoxy)carbonyl)amino)-4,6-di-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-4-*O*-(4-oxopentanoyl)-α-L-rhamnopyranosyl)-β-D-glucopyranoside (21): mp(^{0}C): 98.5; $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 16.0^0; ^{1}H NMR (400.31MHz, $CDCl_3$): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 0.77 (d, *J* = 6.2 Hz, 3H), 1.76 – 1.92 (m, 2H), 2.06 (s, 3H), 2.14 – 2.28 (m, 2H), 2.29 – 2.49 (m, 2H), 2.58 (dq, *J* = 19.8, 6.0, 5.4 Hz, 2H), 3.51 (dt, *J* = 9.7, 6.7 Hz, 1H), 3.77 – 3.96 (m, 2H), 4.21 (ddd, *J* = 14.3, 8.2, 3.4 Hz, 3H), 4.43 (d, *J* = 12.0 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.91 (d, *J* = 3.6 Hz, 1H), 4.94 – 5.02 (m, 1H), 5.03 – 5.15 (m, 2H), 5.19 (d, *J* = 1.5 Hz, 1H), 5.28 (d, *J* = 10.0 Hz, 1H), 5.41 (d, *J* = 10.3 Hz, 2H), 5.49 – 5.60 (m, 1H), 5.59 – 5.66 (m, 1H), 5.71 (dd, *J* = 10.9, 9.1 Hz, 1H), 5.80 – 5.94 (m, 1H), 7.32 – 7.61 (m, 14H), 7.85 – 7.99 (m, 4H), 7.98 – 8.15 (m, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 16.9, 27.9, 28.4, 29.6, 30.4, 37.7, 54.6, 62.6, 67.5, 68.1, 69.4, 69.5, 71.0, 71.1, 72.4, 74.3, 77.3, 95.1, 97.3, 98.8, 115.4, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.6, 129.1, 129.2, 129.4, 129.7, 129.8, 129.8, 129.8, 129.9, 129.9, 130.1, 130.1, 133.1, 133.3, 133.4, 133.5, 137.8, 154.3, 165.5, 165.5, 166.0, 166.5, 171.9, 205.9; HRMS (ESI-MS): m/z calcd for [$C_{52}H_{54}Cl_3NO_{17}Na^+$]: 1104.2355; Found: 1104.2356.

3, 5, 6- Tri-*O*-benzyoyl-α-D-galactofuranosidepropyn-3-yl-1,2-orthobenzoate (23):mp(^{0}C): 88.5; $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 18.9^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 2.39 (t, *J* = 2.5 Hz, 1H), 4.01 (dd, *J* = 5.5, 2.5 Hz, 2H), 4.49 (dd, *J* = 12.4, 5.0 Hz, 1H), 4.55 – 4.98 (m, 2H), 5.23 (d, *J* = 4.3 Hz, 1H), 5.48 – 5.54 (m, 1H), 5.63 (d, *J* = 2.8 Hz, 1H), 6.34 (d, *J* = 4.3 Hz, 1H), 7.10 – 7.56 (m, 11H), 7.64 – 7.81 (m, 2H), 7.76 – 8.22 (m, 7H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 52.1, 63.2, 71.5, 73.9, 76.7, 79.4, 85.0, 85.5, 105.9, 123.5, 126.7, 128.3, 128.4, 128.4, 128.4, 128.5, 128.5, 128.6, 128.6, 128.8, 129.6, 129.7, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 129.9, 130.1, 133.1, 133.1, 133.8, 134.3, 165.3, 165.3, 165.8; HRMS (ESI-MS): m/z calcd for [$C_{39}H_{36}O_{10}Na^+$]: 657.1731; Found: 657.1736.

Pent-4-enyl 2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranoside (24):mp(^{0}C): 77.5; $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 38.6^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.53 – 1.88 (m, 2H), 2.02 – 2.36 (m, 2H), 3.45 – 3.65 (m, 1H), 3.79 (dt, *J* = 9.5, 6.7 Hz, 1H), 4.68 (dd, *J* = 5.1, 3.6 Hz, 1H), 4.73 – 4.84 (m, 2H), 4.92 – 5.07 (m, 2H), 5.32 (s, 1H), 5.49 (d, *J* = 0.8 Hz, 1H), 5.66 (d, *J* = 5.1 Hz, 1H), 5.81 (dd, *J* = 17.0, 10.3 Hz, 1H), 6.10 (dt, *J* = 7.2, 4.4 Hz, 1H), 7.23 – 7.44 (m, 8H), 7.46 – 7.62 (m, 4H), 7.91

(dd, *J* = 8.1, 1.0 Hz, 2H), 7.95 – 8.02 (m, 2H), 8.03 – 8.12 (m, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.7, 30.3, 63.5, 66.9, 70.4, 77.6, 81.3, 82.1, 105.7, 115.1, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 129.0, 129.1, 129.5, 129.6, 129.7 (2C), 129.9 (2C), 130.0 (2C), 130.0 (2C), 133.1, 133.3, 133.4, 133.5, 138.0, 165.5, 165.7, 165.8, 166.1; HRMS (ESI-MS): m/z calcd for [$C_{39}H_{36}O_{10}Na^+$]: 687.2206; Found: 687.2211.

Pent-4-enyl β-D-galactofuranoside (25):syrup; $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 42.6^0; ^{1}H NMR (400.31 MHz, Methanol-D_4) δ 1.4 – 1.9 (m, 2H), 1.7 – 2.4 (m, 2H), 3.4 (dt, *J* = 9.7, 6.5 Hz, 1H), 3.5 – 3.6 (m, 2H), 3.6 – 3.7 (m, 2H), 3.8 – 3.9 (m, 2H), 4.0 (dd, *J* = 6.7, 4.0 Hz, 1H), 4.8 (d, *J* = 1.9 Hz, 1H), 4.9 – 5.0 (m, 2H), 5.8 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H); ^{13}C NMR (100.67 MHz, METHANOL-D_4) δ 28.7, 30.1, 63.2, 66.9, 71.0, 77.3, 82.1, 82.7, 108.1, 113.9, 138.1; HRMS (ESI-MS): m/z calcd for [$C_{11}H_{20}O_6Na^+$]: 271.1158; Found: 271.1197

Pent-4-enyl 5,6-*O*-isopropylidene-β-D-galactofuranoside (26): syrup; $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 22.6^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.39 (s, 3H), 1.42 (s, 3H), 1.68 (p, *J* = 7.1 Hz, 2H), 2.04 – 2.15 (m, 2H), 3.07 (d, *J* = 11.6 Hz, 1H), 3.47 (dt, *J* = 9.8, 6.4 Hz, 1H), 3.76 (dt, *J* = 9.7, 6.7 Hz, 1H), 3.90 – 4.16 (m, 6H), 4.35 (td, *J* = 7.8, 1.7 Hz, 1H), 4.91 – 5.12 (m, 3H), 5.79 (ddt, *J* = 16.9, 10.1, 6.6 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ δ 25.7, 25.7, 28.7, 30.4, 65.8, 67.3, 75.8, 78.2, 78.7, 85.7, 108.6, 110.3, 115.3, 137.9; HRMS (ESI-MS): m/z calcd for [$C_{14}H_{24}O_6Na^+$]: 311.1471; Found: 311.1478

Pent-4-enyl 2,3-di-*O*-benzoyl-5,6-*O*-isopropylidene-β-D-galactofuranoside (27): mp(^{0}C): 111.5;$[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 18.1^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.42 (s, 3H), 1.47 (s, 3H), 1.68 – 1.84 (m, 2H), 2.12 – 2.27 (m, 2H), 3.56 (dt, *J* = 9.6, 6.2 Hz, 1H), 3.84 (dt, *J* = 9.5, 6.6 Hz, 1H), 4.02 (dd, *J* = 8.6, 6.3 Hz, 1H), 4.17 (dd, *J* = 8.6, 6.8 Hz, 1H), 4.33 (dd, *J* = 5.4, 4.6 Hz, 1H), 4.54 (q, *J* = 6.3 Hz, 1H), 4.92 – 5.09 (m, 2H), 5.29 (s, 1H), 5.46 (d, *J* = 1.0 Hz, 1H), 5.49 (d, *J* = 4.5 Hz, 1H), 5.83 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 4H), 7.54 – 7.61 (m, 2H), 7.98 – 8.16 (m, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 25.3, 26.4, 28.8, 30.3, 65.7, 66.8, 75.7, 77.6, 81.7, 83.3, 105.7, 110.0, 115.0, 128.4, 128.5, 128.5, 128.5, 129.2, 129.2, 129.9, 129.9, 129.9, 130.1, 133.5, 133.5, 138.0, 165.3, 165.6; HRMS (ESI-MS): m/z calcd for [$C_{28}H_{32}O_8Na^+$]: 519.1995; Found: 519.1993

Pent-4-enyl 2,3-di-*O*-benzoyl-β-D-galactofuranoside (28):mp(^{0}C): 87.6;$[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 24.9^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.72 (dq, *J* = 13.0, 6.6 Hz, 2H), 1.99 – 2.32 (m, 2H), 2.92 (s, 1H), 3.25 (s, 1H), 3.52 (dt, *J* = 9.5, 6.1 Hz, 1H), 3.68 – 3.91 (m, 3H), 4.14 (s, 1H), 4.31

(dd, *J* = 4.5, 3.4 Hz, 1H), 4.90 – 5.10 (m, 2H), 5.24 (s, 1H), 5.49 (d, *J* = 1.2 Hz, 1H), 5.60 (d, *J* = 4.4 Hz, 1H), 5.80 (ddt, *J* = 16.9, 10.1, 6.6 Hz, 1H), 7.35 – 7.49 (m, 4H), 7.50 – 7.63 (m, 2H), 8.05 (d, *J* = 8.2 Hz, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.7, 30.3, 64.3, 66.9, 71.0, 78.0, 81.5, 83.9, 105.8, 115.0, 128.5, 128.6, 128.6, 128.6, 129.1, 129.1, 129.9, 129.9, 129.9, 130.0, 133.6, 133.6, 138.0, 165.5, 166.1; HRMS (ESI-MS): m/z calcd for [$C_{25}H_{28}O_8Na^+$]: 489.1682; Found: 489.1683

Pent-4-enyl 2,3-di-*O*-benzoyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranoside (29): mp(^{0}C): 94.5;[α]$^{25}_D$($CHCl_3$, *c*1.0): 38.7;^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.79 (m, 2H), 2.15 (s, 3H), 2.20 (m, 2H), 2.59 (t, *J* = 6.4 Hz, 2H), 2.74 (t, *J* = 6.6 Hz, 2H), 2.84 – 2.91 (m, 1H), 3.54 (dt, *J* = 9.5, 6.1 Hz, 1H), 3.77 (dt, *J* = 9.4, 6.6 Hz, 1H), 4.20 – 4.39 (m, 4H), 4.92 – 5.06 (m, 2H), 5.25 (s, 1H), 5.50 (s, 1H), 5.61 (d, *J* = 4.5 Hz, 1H), 5.74 – 5.89 (m, 1H), 7.45 (q, *J* = 7.4 Hz, 4H), 7.59 (q, *J* = 7.3 Hz, 2H), 8.07 (t, *J* = 6.6 Hz, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 27.9, 28.7, 29.8, 30.3, 38.0, 65.8, 66.8, 68.8, 77.9, 81.5, 82.9, 105.7, 115.0, 128.5, 128.5, 128.6, 128.6, 129.1, 129.2, 129.9, 129.9, 129.9, 129.9, 133.6, 133.6, 138.1, 165.4, 166.0, 172.7, 206.7; HRMS (ESI-MS): m/z calcd for [$C_{30}H_{34}O_{10}Na^+$]: 577.2050; Found: 577.2040

Pent-4-enyl 2,3-di-*O*-benzoyl-5-*O*-tert-butyldiphenylsilyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranoside (30): mp(^{0}C): 72.4;[α]$^{25}_D$($CHCl_3$, *c*1.0): 11.1^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.00 (s, 9H), 1.62 – 1.78 (m, 2H), 1.97 – 2.07 (m, 1H), 2.09 (s, 3H), 2.12 – 2.21 (m, 2H), 2.25 (s, 1H), 2.48 (d, *J* = 18.7 Hz, 2H), 3.40 – 3.49 (m, 1H), 3.59 – 3.71 (m, 1H), 4.28 (d, *J* = 4.4 Hz, 3H), 4.35 (t, *J* = 4.7 Hz, 1H), 4.94 – 5.08 (m, 2H), 5.10 (s, 1H), 5.33 – 5.39 (m, 1H), 5.75 – 5.89 (m, 2H), 7.23 – 7.38 (m, 6H), 7.45 (m, 4H), 7.58 (m, 2H), 7.65 – 7.75 (m, 4H), 7.96 – 8.12 (m, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 19.5, 26.7, 26.9, 27.0, 27.6, 28.8, 29.9, 30.4, 37.8, 66.0, 66.7, 70.5, 76.4, 82.0, 82.5, 105.5, 115.0, 127.6, 127.6, 127.8, 127.8, 128.4, 128.5, 128.6, 128.6, 129.2, 129.5, 129.7, 129.7, 129.9, 130.0, 130.1, 130.2, 132.7, 133.4, 133.5, 133.9, 134.9, 135.9, 136.1, 136.1, 138.2, 165.5, 165.5, 172.4, 206.5; HRMS (ESI-MS): m/z calcd for [$C_{46}H_{52}O_{10}SiNa^+$]: 815.3227; Found: 815.3230

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3-di-*O*-benzoyl-5-*O*-tert-butyldiphenylsilyl-6-*O*-(4-oxopentanoyl)-α/β-D-galactofuranoside[α:β (1:0.2)] (10):foam; mp(^{0}C): 66.9;**[**α]$^{25}_D$($CHCl_3$, *c*1.0): 32.4^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 0.99 (d, *J* = 4.1 Hz, 18H), 1.66 (dt, *J* = 10.2, 5.2 Hz, 10H), 1.85 – 2.06 (m, 8H), 2.10 (d, *J* = 4.5 Hz, 6H), 2.23 (td, *J* = 12.4, 11.4, 6.3 Hz, 6H), 2.34 – 2.56 (m, 4H), 3.26 – 3.45 (m, 2H), 4.17 – 4.34 (m, 6H), 4.46 – 4.71 (m,

2H), 5.19 (d, *J* = 82.9 Hz, 1H), 5.32 – 5.64 (m, 2H), 5.73 – 5.89 (m, 2H), 6.22 (s, 1H), 7.23 – 7.40 (m, 12H), 7.45 (td, *J* = 7.7, 5.5 Hz, 8H), 7.55 – 7.63 (m, 4H), 7.63 – 7.72 (m, 8H), 7.93 – 8.11 (m, 8H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 19.5, 19.5, 22.7, 22.8, 25.1, 25.2, 26.9 (6C), 27.6, 27.6, 29.8, 29.8, 29.9, 29.9, 36.7, 36.8, 36.9, 37.1, 37.8, 37.9, 65.7, 65.9, 70.3, 70.5, 75.1, 75.5, 75.8, 75.9, 78.4, 78.5, 81.2, 81.2, 82.6, 82.7, 84.9, 84.9, 102.2, 105.5, 127.6, 127.6, 127.6, 127.6, 127.8, 127.8, 127.8, 127.8, 128.5, 128.5, 128.5, 128.5, 128.6, 128.7, 128.7, 128.7, 128.8, 128.8, 129.2, 129.3, 129.7, 129.7, 130.0, 130.0, 130.1, 130.2, 130.2, 130.2, 130.2, 130.2, 130.2, 130.3, 132.4, 132.4, 133.5, 133.6, 133.6, 133.8, 133.9, 133.9, 135.8, 135.9, 135.9, 135.9, 136.1, 136.2, 136.2, 136.2, 151.0, 151.0, 165.2, 165.2, 165.3, 165.5, 172.3, 172.4, 206.4, 206.4; HRMS (ESI-MS): m/z calcd for [$C_{50}H_{54}O_{12}SiNa^+$]: 897.3282; Found: 897.3288

Pent-4-enyl 6-*O*-tert-butyldiphenylsilyl-β-D-galactofuranoside (31): syrup;$[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 19.1^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.07 (s, 9H), 1.48 – 1.81 (m, 2H), 1.87 – 2.23 (m, 2H), 2.84 (d, *J* = 0.6 Hz, 1H), 2.91 (s, 1H), 3.14 (d, *J* = 11.2 Hz, 1H), 3.41 (dt, *J* = 9.7, 6.4 Hz, 1H), 3.63 – 3.86 (m, 3H), 3.97 (d, *J* = 6.2 Hz, 2H), 4.06 (d, *J* = 11.0 Hz, 1H), 4.11 (t, *J* = 1.7 Hz, 1H), 4.87 – 5.05 (m, 3H), 5.76 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 7.27 – 7.51 (m, 6H), 7.67 (dt, *J* = 6.6, 1.5 Hz, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 19.3, 26.9 (3C), 28.7, 30.3, 64.7, 67.0, 71.6, 78.5, 78.9, 86.2, 108.3, 115.2, 127.9 (4C), 129.9, 130.0, 133.0, 133.1, 135.6 (4C), 137.9; HRMS (ESI-MS): m/z calcd for [$C_{27}H_{38}O_6SiNa^+$]: 509.2335; Found: 509.2340.

Pent-4-enyl 2,3,5-tri-*O*-benzoyl-6-*O*-tert-butyldiphenylsilyl-β-D-galactofuranoside (32):mp(^{0}C): 71.5;$[\alpha]^{25}_D$($CHCl_3$, *c*1.0): +16.4^0;^{1}H NMR (400.31MHz, $CDCl_3$): δ 0.98 (s, 9H), 1.65 – 1.80 (m, 2H), 2.10 – 2.23 (m, 2H), 3.54 (dt, *J* = 9.5, 6.3 Hz, 1H), 3.79 (dt, *J* = 9.5, 6.7 Hz, 1H), 3.96 – 4.12 (m, 2H), 4.76 – 4.82 (m, 1H), 4.87 – 5.05 (m, 2H), 5.26 (s, 1H), 5.43 (s, 1H), 5.56 (d, *J* = 4.9 Hz, 1H), 5.69 – 5.88 (m, 2H), 7.18 – 7.31 (m, 6H), 7.40 – 7.47 (m, 2H), 7.47 – 7.57 (m, 3H), 7.56 – 7.68 (m, 6H), 7.83 – 7.90 (m, 2H), 7.97 – 8.15 (m, 6H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 19.3, 26.8 (3C), 28.9, 30.4, 62.5, 66.9, 73.2, 77.8, 80.8, 82.4, 105.6, 115.0, 127.8, 127.8, 127.8, 127.8, 128.4, 128.5, 128.5, 128.6, 128.6, 128.6, 129.2, 129.4, 129.4, 129.8, 129.9, 130.0, 130.1, 130.1, 130.3, 133.0, 133.1, 133.2, 133.4, 133.5, 133.9, 133.9, 135.6, 135.6, 135.7, 135.7, 138.2, 165.7, 165.8, 165.9; HRMS (ESI-MS): m/z calcd for [$C_{48}H_{50}O_9SiNa^+$]: 821.3122; Found: 821.319

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,5-tri-*O*-benzoyl-6-*O*-tert-butyldiphenylsilyl-β-D-galactofuranoside [α:β=0.2:1] (8): mp(^{0}C): 71.4;$[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 17.1^0;^{1}H NMR

(400.31MHz, $CDCl_3$): δ 0.98 (d, *J* = 2.2 Hz, 18H), 1.44 – 1.73 (m, 10H), 1.90 (q, *J* = 9.4 Hz, 4H), 2.19 (s, 4H), 2.59 (s, 2H), 3.94 – 4.13 (m, 4H), 4.82 – 5.04 (m, 2H), 5.01 – 5.57 (m, 2H), 5.61 – 6.30 (m, 6H), 6.29 – 6.79 (m, 2H), 7.16 – 7.69 (m, 38H), 7.94 (ddd, *J* = 54.8, 8.1, 1.0 Hz, 4H), 8.04 – 8.22 (m, 8H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 19.2, 19.3, 22.5, 22.6, 22.6, 22.6, 25.0, 25.0, 26.7, 26.7, 26.7, 26.8, 26.8, 26.8, 36.6, 36.7, 36.8, 36.9, 61.6, 62.2, 72.6, 73.3, 74.0, 75.1, 75.5, 76.5, 77.3, 78.3, 78.5, 79.7, 81.5, 82.5, 82.6, 83.2, 96.6, 102.3, 127.7, 127.8, 127.8, 127.8, 127.9, 127.9, 128.3, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.7, 128.9, 129.0, 129.1, 129.1, 129.8, 129.8, 129.8, 130.0, 130.0, 130.0, 130.1, 130.1, 130.1, 130.2, 130.2, 130.2, 130.3, 132.9, 132.9, 132.9, 133.0, 133.0, 133.1, 133.2, 133.2, 133.2, 133.5, 133.6, 133.6, 133.6, 133.6, 133.7, 135.5, 135.5, 135.6, 135.6, 135.7, 135.7, 135.7, 135.7, 135.7, 151.0, 151.1, 165.2, 165.5, 165.6, 165.6, 165.7, 165.8; HRMS (ESI-MS): m/z calcd for $[C_{52}H_{52}O_{11}SiNa^+]$: 903.3177; Found: 903.3180

Pent-4-enyl 2,3,6-tri-*O*-benzoyl-β-D-galactofuranoside (9): mp(^{0}C): 85.0; $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 47.6^0; ^1H NMR (400.31MHz, $CDCl_3$): δ 1.55 – 1.90 (m, 2H), 2.14 (qd, *J* = 7.4, 6.9, 3.9 Hz, 2H), 2.79 (s, 1H), 3.51 (dt, *J* = 9.6, 6.2 Hz, 1H), 3.75 (dt, *J* = 9.5, 6.6 Hz, 1H), 4.38 (dd, *J* = 4.8, 2.2 Hz, 1H), 4.49 (dd, *J* = 8.2, 4.6 Hz, 2H), 4.55 – 4.65 (m, 1H), 4.87 – 5.05 (m, 2H), 5.26 (s, 1H), 5.52 (d, *J* = 1.3 Hz, 1H), 5.65 (d, *J* = 4.8 Hz, 1H), 5.79 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 7.35 – 7.50 (m, 6H), 7.49 – 7.65 (m, 3H), 7.91 – 8.15 (m, 6H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.8, 30.3, 66.2, 67.0, 69.2, 78.2, 81.6, 83.2, 105.8, 115.1, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 129.1, 129.2, 129.8, 129.8, 129.9, 130.0, 130.0, 130.0, 130.0, 133.2, 133.7, 133.7, 138.1, 165.5, 166.2, 166.6; HRMS (ESI-MS): m/z calcd for $[C_{32}H_{32}O_9Na^+]$: 583.1944; Found: 583.5387

Pent-4-enyl 2,3,6-tri-*O*-benzoyl-β-D-galactofuranoside (9a): mp(^{0}C): 85.7; $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 47.6^0; ^1H NMR (400.31MHz, $CDCl_3$): δ 1.64 – 1.90 (m, 2H), 2.01 – 2.28 (m, 2H), 2.68 – 3.04 (m, 1H), 3.51 (dt, *J* = 9.5, 6.2 Hz, 1H), 3.75 (dt, *J* = 9.5, 6.6 Hz, 1H), 4.33 – 4.56 (m, 3H), 4.57 – 4.71 (m, 1H), 4.82 – 5.05 (m, 2H), 5.27 (s, 1H), 5.52 (d, *J* = 1.2 Hz, 1H), 5.61 – 5.73 (m, 1H), 5.78 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 7.28 – 7.47 (m, 6H), 7.48 – 7.63 (m, 3H), 7.99 – 8.09 (m, 6H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ δ 28.7, 30.3, 66.2, 66.9, 69.0, 78.2, 81.5, 83.1, 105.8, 115.0, 128.3, 128.4, 128.5, 128.5, 128.6, 128.6, 129.1, 129.1, 129.7, 129.7, 129.8, 129.9, 129.9, 129.9, 130.0, 133.1, 133.6, 133.6, 138.0, 165.4, 166.1, 166.5; HRMS (ESI-MS): m/z calcd for $[C_{32}H_{32}O_9Na^+]$: 583.1944; Found: 583.5751

Pent-4-enyl2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldiphenylsilyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (33): mp(^{0}C): 94.1;$[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 11.2^0;^{1}H NMR (400.31MHz, $CDCl_3$): δ 0.96 (s, 9H), 1.63 – 1.87 (m, 3H), 2.04 (s, 3H), 2.10 – 2.22 (m, 3H), 2.34 (dd, *J* = 26.0, 6.8 Hz, 2H), 3.51 (dt, *J* = 9.6, 6.2 Hz, 1H), 3.77 (dt, *J* = 9.5, 6.6 Hz, 1H), 4.26 (tt, *J* = 12.3, 6.6 Hz, 3H), 4.48 – 4.60 (m, 1H), 4.61 – 4.82 (m, 4H), 4.90 – 5.04 (m, 2H), 5.20 (s, 1H), 5.52 (s, 1H), 5.68 (d, *J* = 7.4 Hz, 2H), 5.74 – 5.88 (m, 3H), 7.18 – 7.38 (m, 12H), 7.39 – 7.49 (m, 7H), 7.57 (td, *J* = 7.3, 5.4 Hz, 2H), 7.63 – 7.69 (m, 2H), 7.72 – 7.76 (m, 2H), 7.82 (d, *J* = 7.4 Hz, 2H), 8.02 (dt, *J* = 22.0, 8.0 Hz, 8H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 19.5, 26.9(3C), 27.4, 28.8, 29.8, 30.3, 37.7, 64.5, 66.1, 66.8, 70.5, 72.3, 76.8, 77.2, 81.5, 82.2, 82.8, 83.1, 105.0, 105.6, 115.0, 127.5, 127.5, 127.7, 127.7, 128.2, 128.2, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 129.0, 129.1, 129.2, 129.3, 129.5, 129.7, 129.7, 129.8, 129.8, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.1, 130.2, 132.3, 133.1, 133.2, 133.4, 133.4, 133.5, 134.1, 135.7, 135.7, 136.1, 136.1, 138.1, 165.2, 165.4 (2C), 165.7, 166.2, 172.2, 206.3; HRMS (ESI-MS): m/z calcd for [$C_{73}H_{74}O_{18}SiNa^+$]: 1289.4552; Found: 1289.5128

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldiphenylsilyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranoside [α:β=0.1:1](34):mp(^{0}C): 82.5;$[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 29.1^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 0.95 (s, 18H), 1.36 – 1.62 (m, 4H), 1.67 (dd, *J* = 9.3, 4.7 Hz, 7H), 1.80 – 1.95 (m, 7H), 2.04 (s, 6H), 2.17 (dt, *J* = 10.2, 4.3 Hz, 6H), 2.26 – 2.51 (m, 4H), 2.62 (s, 2H), 3.15 – 3.81 (m, 1H), 4.21 (td, *J* = 10.2, 9.1, 4.2 Hz, 6H), 4.42 – 4.61 (m, 2H), 4.61 – 4.68 (m, 4H), 4.75 (d, *J* = 8.5 Hz, 3H), 4.91 – 5.28 (m, 1H), 5.46 – 5.70 (m, 4H), 5.72 – 5.82 (m, 3H), 5.87 (dd, *J* = 21.0, 4.1 Hz, 2H), 6.31 (s, 2H), 7.10 – 8.20 (m, 70H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 19.5, 22.7, 25.0, 26.9, 26.9, 26.9, 27.4, 29.8, 29.8, 36.8, 36.8, 37.8, 64.4, 66.0, 70.5, 72.6, 75.5, 76.6, 76.7, 78.6, 80.7, 82.1, 82.6, 83.3, 85.1, 102.3, 105.2, 127.5, 127.5, 127.7, 127.7, 128.2, 128.3, 128.3, 128.4, 128.4, 128.5, 128.5, 128.5, 128.6, 128.6, 128.6, 128.7, 129.1, 129.2, 129.5, 129.7, 129.8, 129.8, 129.9, 129.9, 130.0, 130.1, 130.1, 130.2, 130.2, 130.2, 130.2, 132.4, 133.1, 133.3, 133.5, 133.7, 133.7, 134.1, 135.8, 135.8, 136.1, 136.1, 150.8, 165.1, 165.2, 165.4, 165.6, 166.2, 172.2, 206.4; HRMS (ESI-MS): m/z calcd for [$C_{77}H_{76}O_{20}SiNa^+$]: 1371.4597; Found: 1371.4622

Pent-4-enyl2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldiphenylsilyl-β-D-galactofuranosyl)-β-D-galactofuranoside (35): mp(^{0}C): 77.5;$[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 6.7^0; ^{1}H

NMR (400.31MHz, $CDCl_3$): δ 1.04 (s, 9H), 1.73 (dd, *J* = 12.8, 6.5 Hz, 2H), 2.16 (p, *J* = 6.7 Hz, 2H), 2.87 (s, 1H), 3.45 – 3.67 (m, 2H), 3.67 – 3.89 (m, 2H), 4.04 (dd, *J* = 7.2, 3.3 Hz, 1H), 4.45 – 4.63 (m, 1H), 4.60 – 4.88 (m, 4H), 4.85 – 5.09 (m, 2H), 5.24 (s, 1H), 5.52 (s, 1H), 5.67 – 5.70 (m, 1H), 5.73 (s, 1H), 5.73 – 5.93 (m, 3H), 6.99 – 7.36 (m, 12H), 7.40 (d, *J* = 7.8 Hz, 7H), 7.57 (d, *J* = 7.6 Hz, 2H), 7.63 – 7.85 (m, 6H), 7.92 – 8.10 (m, 8H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 19.6, 27.1 (3C), 28.8, 30.4, 63.2, 64.9, 66.9, 72.3, 73.0, 76.6, 77.7, 81.7, 82.1, 82.7, 82.8, 105.4, 105.6, 115.1, 127.7, 127.7, 127.8, 127.8, 128.2, 128.2, 128.4, 128.4, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 129.0, 129.0, 129.1, 129.4, 129.7, 129.7, 129.7, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 130.0, 130.1, 130.1, 130.1, 130.1, 132.6, 133.1, 133.4, 133.5, 133.8, 134.0, 135.8, 135.8, 136.0, 136.0, 138.1, 165.4, 165.5, 165.7, 166.2, 166.5; HRMS (ESI-MS): m/z calcd for $[C_{68}H_{68}O_{16}SiNa^+]$: 1191.4174; Found: 1191.4265

Pent-4-enyl2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldiphenylsilyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldiphenylsilyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (36): mp(^0C): 79.5;$[\alpha]^{25}_D$($CHCl_3$, *c*1.0): -5.0^0; ^1H NMR (400.31MHz, $CDCl_3$): δ 0.87 (s, 9H), 0.92 (s, 9H), 1.71 (dd, *J* = 14.6, 6.8 Hz, 2H), 1.77 (dd, *J* = 11.8, 5.0 Hz, 2H), 2.01 (s, 3H), 2.13 (dd, *J* = 13.6, 6.7 Hz, 2H), 2.30 (dt, *J* = 21.3, 6.8 Hz, 2H), 3.50 (dt, *J* = 9.4, 4.3 Hz, 2H), 3.65 – 3.87 (m, 1H), 3.95 (dd, *J* = 10.5, 4.2 Hz, 1H), 4.06 – 4.34 (m, 5H), 4.33 – 4.55 (m, 3H), 4.59 (s, 3H), 4.67 (d, *J* = 7.1 Hz, 4H), 4.70 (d, *J* = 5.5 Hz, 1H), 4.94 (dd, *J* = 21.9, 13.6 Hz, 2H), 5.18 (d, *J* = 5.6 Hz, 1H), 5.50 (d, *J* = 10.3 Hz, 2H), 5.54 – 5.69 (m, 4H), 5.72 – 5.81 (m, 2H), 5.83 (d, *J* = 4.5 Hz, 2H), 7.26 (dddt, *J* = 58.6, 29.4, 16.2, 7.9 Hz, 40H), 7.53 – 8.20 (m, 30H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 19.5, 19.5, 26.8, 26.9, 26.9, 26.9, 27.0, 27.0, 27.4, 28.8, 29.8, 30.4, 37.7, 64.3, 65.4, 66.0, 66.9, 69.3, 70.4, 72.1, 72.3, 73.4, 76.4, 76.7, 77.4, 77.8, 81.2, 81.9, 82.0, 82.1, 82.5, 82.9, 83.1, 85.4, 105.1, 105.6, 105.7, 106.1, 115.0, 127.5, 127.5, 127.5, 127.5, 127.5, 127.5, 127.7, 127.7, 128.2, 128.2, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.6, 129.1, 129.1, 129.2, 129.2, 129.3, 129.4, 129.4, 129.5, 129.6, 129.7, 129.7, 129.7, 129.8, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.0, 130.0, 130.1, 130.2, 130.2, 130.2, 132.3, 132.9, 133.0, 133.1, 133.1, 133.1, 133.3, 133.3, 133.4, 133.4, 133.4, 133.5, 134.2, 134.2, 135.7, 135.7, 135.8, 135.8, 135.8, 135.8, 136.1, 136.1, 136.1, 136.1, 136.2, 136.2, 136.2, 136.3, 138.2,

164.8, 165.2, 165.2, 165.4, 165.4, 165.6, 165.7, 165.8, 166.0, 166.2, 172.2, 206.4; MALDI-TOF (ESI-MS): m/z calcd for [$C_{136}H_{132}O_{33}Si_2Na^+$]: 2372.8121; Found: 2372.5277

Pent-4-enyl2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldiphenylsilyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldiphenylsilyl-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (37): mp(^{0}C): 72.4;[α]$^{25}_D$($CHCl_3$, *c*1.0): 2.7^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 0.9 (s, 9H), 1.0 (s, 9H), 1.6 – 1.8 (m, 2H), 2.0 – 2.2 (m, 2H), 2.9 (d, *J* = 33.4 Hz, 1H), 3.3 – 3.6 (m, 3H), 3.6 – 3.8 (m, 2H), 3.9 (ddt, *J* = 10.8, 7.5, 4.4 Hz, 2H), 4.2 (q, *J* = 5.3 Hz, 1H), 4.4 (dd, *J* = 4.8, 2.4 Hz, 1H), 4.4 – 4.6 (m, 5H), 4.7 (d, *J* = 3.5 Hz, 5H), 4.7 – 5.0 (m, 2H), 5.1 (s, 1H), 5.2 (s, 1H), 5.5 (s, 1H), 5.5 (s, 1H), 5.6 (d, *J* = 7.1 Hz, 3H), 5.7 (s, 1H), 5.7 – 5.8 (m, 2H), 5.8 (d, *J* = 4.8 Hz, 2H), 7.0 – 7.5 (m, 40H), 7.5 – 7.6 (m, 2H), 7.6 – 7.7 (m, 8H), 7.7 – 7.8 (m, 2H), 7.8 – 7.8 (m, 4H), 7.9 – 8.0 (m, 10H), 8.0 – 8.1 (m, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 14.5, 14.5, 27.2, 27.3, 27.3, 27.4, 27.4, 27.4, 29.2, 30.7, 63.3, 64.7, 66.1, 67.2, 67.9, 69.7, 72.5, 72.6, 73.2, 73.8, 76.8, 77.0, 77.7, 78.6, 81.6, 81.8, 82.4, 82.9, 82.9, 83.5, 85.5, 105.9, 106.0, 106.0, 106.5, 115.3, 127.8, 127.8, 127.9, 127.9, 128.0, 128.0, 128.1, 128.1, 128.5, 128.5, 128.5, 128.7, 128.7, 128.7, 128.8, 128.8, 128.8, 128.9, 128.9, 128.9, 128.9, 129.2, 129.4, 129.5, 129.5, 129.5, 129.6, 129.6, 129.7, 129.7, 129.8, 129.8, 129.9, 129.9, 130.0, 130.0, 130.0, 130.1, 130.1, 130.1, 130.1, 130.2, 130.2, 130.2, 130.2, 130.2, 130.2, 130.3, 130.3, 130.3, 130.3, 130.3, 130.4, 130.4, 130.4, 130.4, 132.9, 133.3, 133.4, 133.4, 133.4, 133.4, 133.6, 133.6, 133.6, 133.7, 133.8, 133.9, 134.4, 134.5, 136.1, 136.1, 136.1, 136.1, 136.1, 136.1, 136.3, 136.3, 136.3, 136.3, 136.3, 136.4, 136.5, 136.5, 138.5, 165.4, 165.5, 165.7, 165.7, 165.8, 165.9, 166.0, 166.3, 166.6, 167.0; MALDI-TOF (ESI-MS): m/z calcd for [$C_{131}H_{126}O_{31}Si_2Na^+$]: 2274.7753; Found: 2274.7786

Pent-4-enyl2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldiphenylsilyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldiphenylsilyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-tert-butyldiphenylsilyl-6-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (5):mp(^{0}C): 78.4;[α]$^{25}_D$($CHCl_3$, *c*1.0): -5.9^0; ^{1}H NMR (400.31MHz, $CDCl_3$): 0.8 (s, 9H), 0.9 (s, 9H), 0.9 (s, 9H), 1.7 (dd, *J* = 14.9, 6.8 Hz, 2H), 1.7 – 1.8 (m, 2H), 2.0 (s, 3H), 2.1 – 2.2 (m, 2H), 2.3 – 2.4 (m, 2H), 3.3 (dd, *J* = 10.1, 5.6 Hz, 1H), 3.5 (ddd, *J* = 25.2, 9.8, 6.2 Hz, 2H), 3.7 (dt, *J* = 10.3, 6.3 Hz, 2H), 4.0 (dd, *J* = 10.1, 3.9 Hz, 1H), 4.1 – 4.2 (m, 4H), 4.2 – 4.3 (m, 2H), 4.3 – 4.4 (m, 5H), 4.5 (s, 3H), 4.6 – 4.7 (m, 5H), 4.7

(d, *J* = 6.2 Hz, 4H), 4.9 – 5.1 (m, 2H), 5.1 (d, *J* = 5.1 Hz, 1H), 5.2 (s, 1H), 5.4 (s, 1H), 5.5 (s, 1H), 5.5 (s, 2H), 5.6 (s, 3H), 5.6 (s, 2H), 5.7 – 5.8 (m, 3H), 5.8 – 5.9 (m, 2H), 7.0 – 7.5 (m, 65H), 7.6 – 8.1 (m, 40H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 19.4, 19.5, 19.5, 26.8, 26.8, 26.8, 26.9, 26.9, 26.9, 27.0, 27.0, 27.0, 27.4, 28.8, 29.8, 30.4, 37.7, 64.3, 65.2, 65.5, 66.0, 66.9, 67.6, 69.3, 69.4, 70.4, 72.1, 72.2, 72.3, 73.3, 76.1, 76.5, 76.7, 77.9, 78.1, 81.1, 81.6, 81.7, 81.9, 81.9, 82.0, 82.1, 82.5, 82.9, 83.1, 85.2, 85.5, 105.1, 105.6, 105.6, 106.1, 106.1, 106.1, 115.0, 127.4, 127.4, 127.4, 127.5, 127.5, 127.5, 127.5, 127.5, 127.6, 127.7, 127.7, 127.7, 127.7, 128.1, 128.1, 128.1, 128.2, 128.2, 128.2, 128.2, 128.2, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 128.6, 128.7, 129.1, 129.1, 129.2, 129.2, 129.2, 129.2, 129.3, 129.3, 129.3, 129.4, 129.4, 129.5, 129.5, 129.7, 129.7, 129.7, 129.7, 129.7, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.1, 130.1, 130.2, 132.3, 132.9, 132.9, 133.0, 133.0, 133.0, 133.1, 133.1, 133.1, 133.1, 133.2, 133.3, 133.3, 133.4, 133.4, 133.4, 133.4, 133.4, 133.5, 134.2, 134.2, 135.7, 135.7, 135.7, 135.7, 135.7, 135.7, 135.7, 135.8, 135.8, 135.8, 135.8, 136.1, 136.1, 136.1, 136.1, 136.1, 136.1, 136.1, 136.2, 136.2, 136.2, 138.2, 164.7, 164.9, 165.0, 165.2, 165.2, 165.2, 165.4, 165.4, 165.6, 165.7, 165.7, 165.8, 166.0, 166.0, 166.2, 172.2, 206.4; MALDI-TOF (ESI-MS): m/z calcd for [$C_{199}H_{190}O_{48}Si_3Na^+$]: 3456.1699; Found: 3456.4353

Pent-4-enyl2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-tert-butyldiphenylsilyl-β-D-galactofuranosyl)-β-D-galactofuranoside (38): mp(^{0}C): 84.0;[α]$^{25}_D$($CHCl_3$, *c*1.0): 21.8^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 0.78 – 1.05 (m, 9H), 1.72 (tt, *J* = 12.8, 6.6 Hz, 2H), 2.16 (td, *J* = 13.4, 12.4, 5.4 Hz, 2H), 3.49 (dd, *J* = 8.6, 4.9 Hz, 1H), 3.72 (dd, *J* = 9.0, 5.3 Hz, 1H), 4.09 (d, *J* = 6.8 Hz, 1H), 4.48 – 4.60 (m, 1H), 4.61 – 4.80 (m, 2H), 4.73 – 4.84 (m, 1H), 4.91 – 5.12 (m, 3H), 5.17 (s, 1H), 5.47 – 5.59 (m, 1H), 5.63 (s, 1H), 5.68 (s, 1H), 5.76 – 5.86 (m, 3H), 5.88 – 5.98 (m, 1H), 7.26 (dd, *J* = 12.9, 4.9 Hz, 10H), 7.34 (dd, *J* = 17.3, 9.2 Hz, 9H), 7.50 (dt, *J* = 24.3, 7.6 Hz, 6H), 7.63 (d, *J* = 6.8 Hz, 4H), 7.84 (d, *J* = 7.8 Hz, 2H), 7.89 (d, *J* = 7.6 Hz, 2H), 7.95 (d, *J* = 7.9 Hz, 2H), 8.00 (d, *J* = 7.3 Hz, 4H), 8.10 (d, *J* = 7.7 Hz, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 19.0, 26.6, 26.6, 26.6, 28.7, 30.3, 63.2, 64.6, 66.8, 66.8, 73.1, 73.6, 77.2, 78.0, 81.7, 81.8, 82.1, 82.6, 115.0, 127.6, 127.6, 127.7, 127.7, 128.2, 128.2, 128.2, 128.3, 128.3, 128.3, 128.3, 128.3, 128.4, 128.4, 128.5, 128.5, 128.9, 129.0, 129.0, 129.1, 129.6, 129.6, 129.6, 129.7, 129.7, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.1, 132.9, 133.0, 133.0, 133.1, 133.2,

133.2, 133.3, 133.4, 135.5, 135.5, 135.5, 135.6, 138.0, 165.2, 165.4, 165.5, 165.5, 165.8, 166.1; MALDI-TOF (ESI-MS): m/z calcd for [$C_{75}H_{72}O_{17}SiNa^+$]: 1295.4436; Found: 1295.4459

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-tert-butyldiphenylsilyl-β-D-galactofuranosyl)-β-D-galactofuranoside [α:β=0.4:1] (39): mp(^{0}C): 77.5;[α]$^{25}_D$($CHCl_3$, *c*1.0): 44.8^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 0.90 (s, 18H), 1.21 – 1.36 (m, 3H), 1.62 (ddt, *J* = 39.5, 25.3, 10.9 Hz, 12H), 1.79 – 1.96 (m, 4H), 2.18 (s, 4H), 2.61 (s, 1H), 3.14 – 4.23 (m, 5H), 4.39 – 4.81 (m, 8H), 4.81 – 5.17 (m, 2H), 5.37 – 5.61 (m, 4H), 5.60 – 5.79 (m, 4H), 5.84 (d, *J* = 2.9 Hz, 3H), 6.22 (s, 1H), 7.09 – 7.64 (m, 50H), 7.73 – 8.21 (m, 30H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 19.1, 19.1, 22.4, 22.6, 22.6, 22.7, 25.0, 25.1, 26.6, 26.6, 26.7, 26.7, 26.7, 26.7, 36.7, 36.8, 36.9, 37.1, 63.3, 63.4, 64.6, 64.7, 73.0, 73.2, 73.6, 73.8, 75.2, 75.2, 75.6, 76.0, 76.1, 76.6, 77.3, 77.8, 77.9, 78.1, 81.9, 82.0, 82.1, 82.2, 82.5, 82.8, 83.0, 85.1, 102.3, 105.3, 105.5, 105.6, 127.7, 127.7, 127.7, 127.7, 128.2, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 128.6, 128.7, 128.7, 128.7, 128.7, 128.9, 129.0, 129.0, 129.0, 129.0, 129.1, 129.1, 129.2, 129.6, 129.6, 129.6, 129.7, 129.7, 129.7, 129.7, 129.7, 129.8, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.1, 130.1, 130.1, 130.1, 130.1, 130.1, 130.1, 130.2, 130.2, 130.2, 130.3, 132.9, 132.9, 133.0, 133.0, 133.1, 133.1, 133.1, 133.3, 133.3, 133.5, 133.6, 133.6, 135.6, 135.6, 135.6, 135.6, 135.7, 150.8, 152.3, 165.0, 165.3, 165.3, 165.3, 165.5, 165.5, 165.6, 165.6, 165.9, 165.9, 166.1, 166.2; HRMS (ESI-MS): m/z calcd for [$C_{79}H_{74}O_{19}SiNa^+$]: 1377.4491; Found: 1377.4628

Pent-4-enyl2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranoside (40): mp(^{0}C): 87.5;[α]$^{25}_D$($CHCl_3$, *c*1.0): 30.1^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.64 – 1.81 (m, 2H), 2.16 (dd, *J* = 14.4, 6.8 Hz, 2H), 3.21 (s, 1H), 3.53 (dt, *J* = 9.6, 6.1 Hz, 1H), 3.76 (dt, *J* = 9.3, 6.6 Hz, 1H), 3.90 – 4.14 (m, 2H), 4.56 (dd, *J* = 5.1, 3.0 Hz, 1H), 4.66 – 4.83 (m, 3H), 4.90 – 5.10 (m, 3H), 5.26 (s, 1H), 5.52 (s, 1H), 5.55 – 5.63 (m, 2H), 5.71 (s, 1H), 5.76 – 5.83 (m, 2H), 5.82 – 5.89 (m, 1H), 7.19 – 7.61 (m, 18H), 7.80 – 7.90 (m, 4H), 7.92 – 8.11 (m, 8H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.7, 30.3, 61.4, 64.8, 66.9, 73.0, 73.5, 77.2, 77.5, 77.7, 81.7, 81.9, 82.2, 82.4, 105.6, 105.6, 115.1, 128.2, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.6, 128.6, 128.6, 128.6, 128.6, 128.8, 128.9, 129.6, 129.7, 129.8, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 133.1, 133.2, 133.4, 133.4, 133.5,

133.8, 138.0, 165.3, 165.6, 165.7, 166.1, 166.2, 166.5; MALDI-TOF (ESI-MS): m/z calcd for [$C_{59}H_{54}O_{17}Na^+$]: 1057.3259; Found: 1257.8037

Pent-4-enyl2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,6-tri-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranoside (40a): mp(^{0}C): 88.4;[α]$^{25}_D$(CHCl$_3$, *c*1.0): 34.5^0; ^{1}H NMR (400.31MHz, CDCl$_3$): δ 1.69 (dt, *J* = 14.3, 6.7 Hz, 2H), 2.12 (dt, *J* = 14.2, 7.1 Hz, 2H), 2.91 (s, 1H), 3.47 (dt, *J* = 9.6, 6.2 Hz, 1H), 3.71 (dt, *J* = 9.2, 6.6 Hz, 1H), 4.34 – 4.47 (m, 1H), 4.46 – 4.60 (m, 3H), 4.62 – 4.87 (m, 4H), 4.88 – 5.07 (m, 2H), 5.19 (s, 1H), 5.46 (s, 1H), 5.67 (d, *J* = 4.7 Hz, 1H), 5.76 (d, *J* = 13.6 Hz, 4H), 7.05 – 7.76 (m, 20H), 7.83 (d, *J* = 7.4 Hz, 2H), 7.99 (m, 8H); ^{13}C NMR (100.67 MHz, CDCl$_3$): δ 28.7, 30.3, 53.6 64.7, 66.3, 66.8, 69.5, 73.2, 77.1, 78.1, 81.7, 81.9, 82.2, 83.6, 105.6, 105.6, 115.0, 128.3, 128.3, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.7, 128.7, 128.8, 129.0, 129.0, 129.7, 129.7, 129.7, 129.7, 129.8, 129.9, 129.9, 130.0, 130.0, 133.1, 133.2, 133.4, 133.6, 133.6, 133.6, 138.1, 165.2, 165.6, 165.8, 166.0, 166.2, 166.5; MALDI-TOF (ESI-MS): m/z calcd for [$C_{59}H_{54}O_{17}Na^+$]: 1057.3259; Found: 1257.8035

Pent-4-enyl2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-tert-butyldiphenylsilyl-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (41): mp(^{0}C): 91.7;[α]$^{25}_D$(CHCl$_3$, *c*1.0): -5.8^0; ^{1}H NMR (400.31MHz, CDCl$_3$): δ 0.9 (s, 9H), 1.6 – 1.9 (m, 2H), 2.2 (hept, *J* = 7.3, 6.8 Hz, 2H), 3.5 (dt, *J* = 9.4, 6.1 Hz, 1H), 3.8 (dt, *J* = 9.2, 6.6 Hz, 1H), 4.1 (d, *J* = 5.1 Hz, 3H), 4.1 (dd, *J* = 11.2, 3.8 Hz, 1H), 4.6 – 4.6 (m, 2H), 4.7 (s, 3H), 4.7 – 4.9 (m, 3H), 4.9 – 5.0 (m, 4H), 5.2 – 5.3 (m, 2H), 5.4 (s, 1H), 5.5 (s, 1H), 5.6 – 5.6 (m, 1H), 5.7 (dd, *J* = 13.9, 5.6 Hz, 3H), 5.8 – 5.9 (m, 6H), 5.9 – 6.0 (m, 1H), 7.1 – 7.6 (m, 50H), 7.8 – 7.9 (m, 10H), 7.9 – 8.1 (m, 10H); ^{13}C NMR (100.67 MHz, CDCl$_3$): δ 19.0, 26.6, 26.6, 26.6, 28.7, 30.3, 63.2, 64.7, 65.3, 66.8, 66.8, 67.4, 71.8, 72.8, 73.2, 73.7, 77.4, 77.8, 78.0, 81.7, 81.7, 81.8, 82.0, 82.0, 82.4, 82.5, 83.2, 105.5, 105.5, 105.6, 106.7, 115.0, 127.6, 127.6, 128.1, 128.1, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.2, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.6, 128.6, 128.6, 128.9, 128.9, 128.9, 128.9, 128.9, 129.0, 129.0, 129.0, 129.0, 129.0, 129.0, 129.1, 129.6, 129.6, 129.6, 129.6, 129.7, 129.7, 129.7, 129.7, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.0, 130.0, 130.1, 130.1, 130.1, 132.8, 132.9, 133.0, 133.1, 133.1, 133.1, 133.2, 133.2, 133.2, 133.3, 133.4, 133.5, 135.5, 135.5, 138.1, 165.1, 165.2, 165.3, 165.4, 165.5, 165.5,

165.5, 165.7, 165.8, 165.9, 165.9, 166.2; MALDI-TOF (ESI-MS): m/z calcd for [$C_{129}H_{116}O_{33}SiNa^+$]: 2244.7099; Found: 2244.5864

Pent-4-enyl2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (42): mp(^{0}C): 84.6;[α]$^{25}_D$($CHCl_3$, *c*1.0): 2.0^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.7 (dt, *J* = 8.5, 5.9 Hz, 2H), 2.0 – 2.2 (m, 2H), 2.9 (d, *J* = 8.0 Hz, 1H), 3.5 (dt, *J* = 9.6, 6.1 Hz, 1H), 3.6 – 3.8 (m, 1H), 4.0 (dd, *J* = 11.4, 7.6 Hz, 1H), 4.1 (dd, *J* = 11.5, 4.1 Hz, 1H), 4.3 (dd, *J* = 7.6, 4.0 Hz, 1H), 4.5 (d, *J* = 5.4 Hz, 2H), 4.5 (dd, *J* = 5.1, 3.2 Hz, 1H), 4.6 – 4.6 (m, 2H), 4.6 – 4.8 (m, 6H), 4.9 – 5.0 (m, 3H), 5.2 (d, *J* = 6.7 Hz, 2H), 5.4 (d, *J* = 1.6 Hz, 1H), 5.5 (d, *J* = 1.4 Hz, 1H), 5.6 – 5.7 (m, 3H), 5.7 – 5.9 (m, 6H), 6.0 (dt, *J* = 7.7, 3.9 Hz, 1H), 7.0 – 7.6 (m, 40H), 7.7 – 7.9 (m, 10H), 7.9 – 8.1 (m, 10H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.8, 30.3, 64.7, 65.3, 66.2, 66.9, 67.7, 69.6, 71.9, 73.2, 73.4, 76.9, 77.2, 77.9, 77.9, 81.7, 81.9, 81.9, 82.0, 82.5, 82.5, 82.5, 83.6, 105.6, 105.6, 105.9, 106.7, 115.0, 128.2, 128.2, 128.3, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 128.6, 128.8, 128.9, 128.9, 129.0, 129.0, 129.1, 129.1, 129.2, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.7, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.0, 130.0, 133.0, 133.0, 133.0, 133.1, 133.2, 133.3, 133.3, 133.4, 133.4, 133.5, 133.5, 133.5, 138.1, 165.2, 165.2, 165.3, 165.5, 165.6, 165.7, 165.9, 165.9, 166.0, 166.0, 166.2, 166.5; MALDI-TOF (ESI-MS): m/z calcd for [$C_{113}H_{98}O_{33}Na^+$]: 2006.6922; Found: 2006.4052

Pent-4-enyl2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-tert-butyldiphenylsilyl-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (6): mp(^{0}C): 77.5;[α]$^{25}_D$($CHCl_3$, *c*1.0): 9.0^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 0.85 (s, 9H), 1.28 (dq, *J* = 27.1, 7.0 Hz, 2H), 1.63 – 1.76 (m, 2H), 3.40 – 3.54 (m, 1H), 3.71 (q, *J* = 6.8 Hz, 1H), 3.84 – 3.91 (m, 1H), 3.98 (s, 2H), 4.03 (d, *J* = 9.0 Hz, 1H), 4.09 (d, *J* = 8.3 Hz, 1H), 4.51 (s, 2H), 4.55 (d, *J* = 4.7 Hz, 1H), 4.62 (d, *J* = 21.0 Hz, 6H), 4.69 (d, *J* = 7.9 Hz, 3H), 4.77 (dd, *J* = 20.2, 5.7 Hz, 2H), 4.85 (s, 1H), 4.91 (d, *J* = 9.1 Hz, 2H), 4.97 (d, *J* = 17.1 Hz, 1H), 5.03 – 5.22 (m, 3H), 5.35 (d, *J* = 14.8 Hz, 2H), 5.48 (s, 1H), 5.51 – 5.61 (m, 3H), 5.63 (d, *J* = 16.3 Hz, 3H), 5.67 – 5.76 (m, 4H), 5.77 –

5.84 (m, 5H), 5.91 – 5.97 (m, 1H), 6.98 – 7.56 (m, 65H), 7.69 – 8.11 (m, 35H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 19.1, 26.6, 26.6, 26.7, 28.8, 30.4, 63.3, 64.8, 65.4, 65.5, 66.9, 67.6, 67.6, 71.9, 72.1, 72.9, 73.2, 73.2, 73.7, 76.8, 76.9, 76.9, 77.5, 77.8, 77.9, 78.0, 81.7, 81.7, 81.8, 81.9, 81.9, 82.1, 82.4, 82.5, 82.7, 82.7, 83.2, 105.5, 105.5, 105.6, 106.0, 106.8, 106.8, 115.0, 127.7- 128.4 (40C), 128.4-130.0 (20C), 130.0-130.2 (40C), 132.9, 132.9-135.6(20C), 138.1, 165.1, 165.1, 165.2, 165.2, 165.3, 165.3, 165.3, 165.5, 165.5, 165.6, 165.6, 165.7, 165.9, 166.0, 166.0, 166.0, 166.2, 166.2; MALDI-TOF (ESI-MS): m/z calcd for [$C_{183}H_{160}O_{49}Si\ Na^+$]: 3193.9762; Found: 3193.1108.

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)- 2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-tert-butyldiphenylsilyl-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside [α:β=1:1] (43): mp(^{0}C): 79.5;$[\alpha]^{25}_D$($CHCl_3$, *c*1.0): -20.6; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 0.87 (d, *J* = 7.7 Hz, 18H), 1.50 – 1.76 (m, 12H), 1.89 (d, *J* = 12.7 Hz, 4H), 2.18 (d, *J* = 7.5 Hz, 4H), 2.66 (s, 2H), 4.03 (tdd, *J* = 41.2, 11.7, 5.6 Hz, 10H), 4.63 (s, 14H), 4.69 (d, *J* = 8.3 Hz, 10H), 4.85 (ddt, *J* = 29.8, 13.5, 6.5 Hz, 10H), 5.14 (s, 1H), 5.21 (d, *J* = 2.4 Hz, 2H), 5.32 – 5.44 (m, 3H), 5.53 – 5.62 (m, 5H), 5.67 (d, *J* = 16.4 Hz, 9H), 5.71 – 5.84 (m, 14H), 5.92 (d, *J* = 4.4 Hz, 4H), 6.37 (s, 2H), 7.02 – 7.54 (m, 130H), 7.72 – 8.10 (m, 70H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 19.0, 19.0, 22.4, 22.4, 22.4, 22.4, 22.5, 22.5, 26.5, 26.5, 26.5, 26.6, 26.6, 26.6, 34.1, 34.1, 34.1, 34.1, 63.2, 63.2, 63.3, 64.6, 64.7, 64.7, 64.7, 65.3, 65.3, 65.3, 65.5, 65.6, 65.6, 67.3, 67.3, 67.3, 67.5, 67.6, 71.8, 71.9, 71.9, 72.0, 72.6, 72.6, 72.6, 72.7, 72.8, 73.1, 73.2, 73.3, 73.4, 73.6, 73.7, 75.5, 76.6, 76.9, 77.3, 77.7, 77.7, 77.9, 77.9, 78.0, 78.5, 78.5, 81.0, 81.6, 81.7, 81.7, 81.7, 81.8, 81.8, 81.8, 81.9, 81.9, 82.0, 82.4, 82.6, 82.6, 82.7, 82.7, 82.7, 83.4, 83.4, 83.5, 84.4, 84.5, 102.2, 105.1, 105.3, 105.4, 105.4, 105.4, 105.5, 105.7, 105.8, 105.8, 105.8, 105.9, 127.5-128.6 (40C), 128.6-129.2 (40C), 129.6-130.1 (80C), 132.8-135.5 (40C), 150.2, 150.8, 165.0, 165.1, 165.1, 165.1, 165.1, 165.1, 165.1, 165.2, 165.2, 165.4, 165.4, 165.4, 165.4, 165.4, 165.4, 165.5, 165.5, 165.5, 165.5, 165.6, 165.6, 165.6, 165.8, 165.8, 165.8, 165.8, 165.8, 165.9, 165.9, 165.9, 166.0, 166.0, 166.1, 166.1, 166.1, 166.1; MALDI-TOF (ESI-MS): m/z calcd for [$C_{187}H_{162}O_{51}Na^+$]: 3275.9817; Found: 3275.9855

Pent-4-enyl2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside and Pent-4-enyl2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,6-tri-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (inseparable mixture of 44): mp(^{0}C): 91.9;$[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 4.1^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.53 – 1.80 (m, 4H), 2.06 – 2.20 (m, 4H), 3.20 – 3.60 (m, 5H), 3.66 – 4.23 (m, 14H), 4.53 (s, 4H), 4.58 – 4.66 (m, 10H), 4.64 – 4.74 (m, 10H), 4.78 (d, *J* = 14.5 Hz, 4H), 4.84 – 5.04 (m, 9H), 5.19 (d, *J* = 7.0 Hz, 4H), 5.31 – 5.41 (m, 3H), 5.51 (dd, *J* = 14.6, 6.7 Hz, 7H), 5.59 – 5.63 (m, 2H), 5.62 – 5.68 (m, 6H), 5.69 (s, 1H), 5.70 – 5.76 (m, 4H), 5.77 (s, 6H), 5.82 (d, *J* = 5.2 Hz, 5H), 5.95 (s, 2H), 7.03 – 7.57 (m, 108H), 7.57 – 8.22 (m, 72H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.8, 28.8, 30.4, 30.4, 60.5, 61.1, 61.2, 61.3, 64.8, 65.3, 65.4, 65.5, 65.8, 66.9, 67.5, 67.6, 67.8, 71.9, 71.9, 72.0, 72.2, 72.2, 72.8, 72.9, 72.9, 73.0, 73.1, 73.2, 73.2, 73.3, 73.3, 73.3, 73.7, 73.7, 74.0, 77.0, 77.4, 77.6, 77.7, 77.9, 77.9, 77.9, 81.4, 81.4, 81.4, 81.6, 81.6, 81.8, 81.8, 81.9, 82.0, 82.1, 82.1, 82.4, 82.4, 82.4, 82.5, 82.5, 82.6, 82.8, 82.9, 82.9, 83.3, 83.3, 83.5, 105.3, 105.6, 105.6, 105.7, 106.0, 106.2, 106.2, 106.7, 106.7, 106.8, 106.8, 106.8, 115.0, 115.0, 128.2- 128.6 (72C), 128.6-128.9 (36C), 129.6-130.2 (72C), 132.8-133.6 (36C), 138.1, 138.1, 165.2, 165.3, 165.3, 165.3, 165.4, 165.4, 165.6, 165.6, 165.6, 165.6, 165.6, 165.7, 165.7, 165.7, 165.8, 165.8, 165.8, 165.9, 165.9, 165.9, 166.0, 166.0, 166.0, 166.0, 166.1, 166.1, 166.1, 166.1, 166.2, 166.3, 166.3, 166.5, 166.5, 166.5, 166.5, 166.6.; HRMS (ESI-MS): m/z calcd for [$C_{167}H_{142}O_{49}Na^+$]: 2954.8551; Found: 2954.1754

Pent-4-enyl 2,3,6-tri-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-β-D-galactofuranoside (51):mp(^{0}C): 89.6;$[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 26.9^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.72 – 1.84 (m, 2H), 2.08 (s, 3H), 2.14 – 2.26 (m, 2H), 2.50 – 2.58 (m, 2H), 2.61 – 2.75 (m, 2H), 3.57 (dt, *J* = 9.6, 6.2 Hz, 1H), 3.80 (dt, *J* = 9.6, 6.6 Hz, 1H), 4.45 – 4.62 (m, 3H), 4.89 – 5.11 (m, 2H), 5.30 (s, 1H), 5.46 (d, *J* = 1.1 Hz, 1H), 5.56 (d, *J* = 5.1 Hz, 1H), 5.76 – 5.96 (m, 2H), 7.25 – 7.37 (m, 4H), 7.39 – 7.46 (m, 2H), 7.48 – 7.61 (m, 3H), 7.91 (dd, *J* = 8.4, 1.3 Hz, 2H), 8.07 (ddd, *J* = 8.4, 5.5, 1.3 Hz, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 27.8, 28.7, 29.7, 30.3, 37.8, 63.1, 66.9, 70.2, 76.8, 77.1, 77.5, 77.5, 81.2, 82.1, 105.6, 115.0, 128.4, 128.4, 128.4, 128.5, 128.5, 129.0, 129.1, 129.5, 129.8,

129.8, 129.9, 129.9, 130.0, 130.0, 133.3, 133.4, 133.5, 138.0, 165.4, 165.6, 165.7, 172.3, 206.2; HRMS (ESI-MS): m/z calcd for [$C_{37}H_{38}O_{11}Na^+$]: 681.2312; Found: 681.2316

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)-2,3,6-tri-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-α/β-D-galactofuranoside [α:β (1:1)] (50): foam; mp(^{0}C): 66.9; **[**α]$^{25}_D$($CHCl_3$, *c*1.0): 32.4^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.42 – 1.60 (m, 3H), 1.61 – 1.75 (m, 6H), 1.90 (ddd, *J* = 22.7, 9.7, 3.9 Hz, 7H), 2.08 (d, *J* = 6.0 Hz, 6H), 2.10 – 2.26 (m, 4H), 2.42 – 2.83 (m, 10H), 3.14 – 3.84 (m, 2H), 4.44 – 4.80 (m, 7H), 5.28 (d, *J* = 5.3 Hz, 3H), 5.60 – 5.82 (m, 3H), 6.39 (s, 1H), 7.15 – 7.77 (m, 18H), 7.89 – 8.16 (m, 12H); ^{13}C NMR (100.67 MHz, $CDCl_3$): 22.5, 22.5, 22.6, 22.6, 24.9, 25.0, 28.0, 28.0, 29.6, 29.7, 36.6, 36.7, 36.8, 37.0, 37.9, 38.0, 53.5, 63.2, 63.3, 66.9, 66.9, 69.8, 70.0, 75.1, 75.5, 75.9, 76.6, 77.9, 78.6, 80.9, 81.1, 81.8, 82.4, 83.4, 102.1, 105.6, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.7, 128.7, 128.7, 128.9, 128.9, 128.9, 129.0, 129.0, 129.1, 129.5, 129.5, 129.6, 129.7, 129.7, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.0, 130.0, 130.1, 130.1, 130.1, 130.2, 133.0, 133.1, 133.2, 133.2, 133.5, 133.6, 133.6, 133.7, 133.8, 133.8, 165.0, 165.4, 165.4, 166.0, 166.0, 166.0, 171.9, 172.0, 205.9, 205.9; HRMS (ESI-MS): m/z calcd for [$C_{41}H_{40}O_{13}Na^+$]: 763.2367; Found: 763.2442

Pent-4-enyl2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (52): mp(^{0}C): 80.0;[α]$^{25}_D$($CHCl_3$, *c*1.0): 11.4^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.18 – 1.43 (m, 3H), 1.56 – 1.82 (m, 2H), 2.04 (s, 3H), 2.14 (q, *J* = 7.9, 7.3 Hz, 1H), 2.40 – 2.68 (m, 2H), 3.45 – 3.63 (m, 1H), 3.76 (dt, *J* = 9.6, 6.5 Hz, 1H), 4.03 (dd, *J* = 10.6, 6.7 Hz, 1H), 4.17 (dd, *J* = 10.7, 5.4 Hz, 2H), 4.57 (dd, *J* = 12.0, 7.4 Hz, 1H), 4.66 (dt, *J* = 13.9, 4.3 Hz, 3H), 4.84 – 5.05 (m, 2H), 5.26 (s, 1H), 5.35 (s, 1H), 5.42 (d, *J* = 8.8 Hz, 2H), 5.47 (d, *J* = 5.0 Hz, 1H), 5.59 (d, *J* = 5.0 Hz, 1H), 5.69 – 5.83 (m, 2H), 5.90 (q, *J* = 5.7 Hz, 1H), 7.19 – 7.56 (m, 21H), 7.80 – 8.12 (m, 10H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 14.2, 22.5, 28.1, 28.7, 29.8, 30.3, 38.0, 63.6, 66.4, 67.2, 70.1, 71.4, 77.2, 77.3, 77.6, 81.6, 81.7, 81.8, 82.3, 105.9, 106.3, 115.1, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 129.0, 129.1, 129.2, 129.2, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.0, 130.0, 130.1, 130.1, 130.1, 133.2, 133.2, 133.4, 133.5, 133.5, 133.6, 138.1, 165.2, 165.6, 165.7, 165.8, 165.9, 166.2, 172.1, 206.0; HRMS (ESI-MS): m/z calcd for [$C_{37}H_{38}O_{11}Na^+$]: 1155.3626; Found: 1155.4951

1-*O*-(((1-ethynylcyclohexyl)oxy)carbonyl)- 2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranoside [α:β=0.3:1] (53): mp(^{0}C): 76.6;$[\alpha]^{25}_D$($CHCl_3$, *c*1.0): -9.3^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.42 – 1.73 (m, 9H), 1.78 – 1.96 (m, 9H), 2.07 (s, 2H), 2.10 – 2.26 (m, 6H), 2.34 – 2.95 (m, 10H), 3.09 – 3.87 (m, 2H), 3.93 – 4.32 (m, 4H), 4.54 – 4.81 (m, 7H), 4.93 (t, *J* = 4.1 Hz, 1H), 5.26 – 5.38 (m, 2H), 5.37 – 5.55 (m, 5H), 5.58 – 5.75 (m, 3H), 5.77 – 6.10 (m, 3H), 6.43 (s, 1H), 7.18 – 7.67 (m, 36H), 7.86 – 8.16 (m, 24H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 22.3, 22.5, 24.9, 24.9, 28.0, 28.0, 29.6, 29.6, 29.6, 29.7, 36.5, 36.6, 36.9, 37.0, 37.9, 37.9, 63.5, 63.8, 65.0, 70.0, 70.1, 70.8, 70.9, 71.4, 73.9, 75.0, 75.2, 75.7, 75.9, 76.0, 77.2, 77.5, 77.8, 78.5, 80.0, 81.4, 81.5, 81.6, 81.9, 82.5, 82.9, 84.0, 102.4, 105.1, 105.6, 105.8, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.7, 128.8, 128.8, 128.9, 129.0, 129.0, 129.1, 129.1, 129.1, 129.4, 129.5, 129.6, 129.6, 129.6, 129.7, 129.7, 129.8, 129.8, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.0, 130.1, 130.1, 130.1, 130.1, 130.3, 133.0, 133.0, 133.1, 133.1, 133.2, 133.3, 133.4, 133.5, 133.5, 133.5, 133.6, 133.6, 151.0, 152.2, 165.1, 165.1, 165.2, 165.5, 165.6, 165.6, 165.7, 165.7, 165.8, 166.0, 166.0, 166.1, 172.0, 172.1, 205.9, 205.9; HRMS (ESI-MS): m/z calcd for [$C_{68}H_{62}O_{21}Na^+$]: 1237.3681; Found: 1237.5927

Pent-4-enyl2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranoside (54): mp(^{0}C): 93.5;$[\alpha]^{25}_D$($CHCl_3$, *c*1.0): 7.4^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.61 – 1.86 (m, 2H), 2.08 – 2.40 (m, 2H), 2.81 (d, *J* = 8.0 Hz, 1H), 3.56 (dt, *J* = 9.6, 6.3 Hz, 1H), 3.78 (dt, *J* = 9.6, 6.6 Hz, 1H), 4.06 (dd, *J* = 10.8, 6.7 Hz, 1H), 4.19 (dd, *J* = 10.8, 5.3 Hz, 2H), 4.44 – 4.53 (m, 1H), 4.55 (dd, *J* = 4.8, 2.4 Hz, 1H), 4.59 – 4.65 (m, 1H), 4.69 (dd, *J* = 4.9, 3.9 Hz, 1H), 4.92 – 5.08 (m, 2H), 5.29 (s, 1H), 5.39 (s, 1H), 5.47 (dd, *J* = 6.7, 1.2 Hz, 2H), 5.58 – 5.72 (m, 2H), 5.73 – 5.88 (m, 1H), 5.91 – 6.00 (m, 1H), 7.29 (q, *J* = 7.6 Hz, 4H), 7.35 – 7.46 (m, 8H), 7.47 – 7.61 (m, 6H), 7.95 (ddd, *J* = 18.5, 8.3, 1.2 Hz, 4H), 8.01 – 8.12 (m, 8H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.6, 30.2, 66.3, 66.4, 67.0, 69.2, 71.4, 77.5, 78.0, 81.4, 81.5, 82.1, 83.6, 105.8, 106.4, 115.0, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.9, 128.9, 129.0, 129.1, 129.7, 129.7, 129.7, 129.8, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 130.0, 130.0, 133.0, 133.1, 133.3, 133.4, 133.5, 133.5, 138.0, 165.1, 165.5, 165.7, 165.8, 166.1, 166.5; MALDI-TOF (ESI-MS): m/z calcd for [$C_{59}H_{54}O_{17}Na^+$]: 1057.3259; Found: 1257.8035

Pent-4-enyl2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (55): mp(^{0}C): 97.5;$[\alpha]^{25}_D$($CHCl_3$, *c*1.0): -2.9^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.67 (p, *J* = 7.1 Hz, 2H), 1.76 (d, *J* = 6.7 Hz, 2H), 1.99 (s, 3H), 2.12 (q, *J* = 7.2 Hz, 2H), 2.44 – 2.64 (m, 2H), 3.51 (dt, *J* = 9.5, 6.3 Hz, 1H), 3.74 (dt, *J* = 9.4, 6.5 Hz, 1H), 3.98 (ddd, *J* = 29.7, 10.9, 7.5 Hz, 2H), 4.13 (ddd, *J* = 21.7, 10.8, 4.4 Hz, 2H), 4.52 (dd, *J* = 12.1, 7.4 Hz, 1H), 4.55 – 4.63 (m, 3H), 4.65 – 4.74 (m, 4H), 4.85 (t, *J* = 3.8 Hz, 1H), 4.89 – 5.02 (m, 2H), 5.19 (s, 1H), 5.25 (s, 1H), 5.27 – 5.35 (m, 2H), 5.42 (t, *J* = 7.8 Hz, 3H), 5.60 (dd, *J* = 13.9, 8.5 Hz, 3H), 5.69 – 5.83 (m, 4H), 5.91 (dq, *J* = 9.4, 5.8, 5.0 Hz, 2H), 7.13 – 7.53 (m, 35H), 7.72 – 8.06 (m, 25H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.1, 28.7, 29.7, 30.3, 37.9, 63.6, 65.3, 66.1, 67.1, 67.5, 70.2, 71.3, 71.9, 73.2, 77.4, 77.6, 77.8, 81.5, 81.6, 81.7, 81.9, 81.9, 82.2, 82.6, 82.8, 105.8, 106.1, 106.7, 128.2, 128.2, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 128.9, 128.9, 128.9, 129.0, 129.0, 129.0, 129.1, 129.1, 129.1, 129.1, 129.2, 129.3, 129.7, 129.7, 129.7, 129.7, 129.8, 129.8, 129.8, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.0, 130.0, 130.1, 130.1, 130.1, 133.0, 133.0, 133.0, 133.1, 133.1, 133.2, 133.3, 133.4, 133.4, 133.4, 133.4, 133.5, 138.1, 165.1, 165.3, 165.3, 165.6, 165.6, 165.6, 165.8, 165.8, 165.9, 166.0, 166.1, 166.2, 206.1; MALDI-TOF (ESI-MS): m/z calcd for [$C_{118}H_{104}O_{35}Na^+$]: 2104.6289; Found: 2104.6289

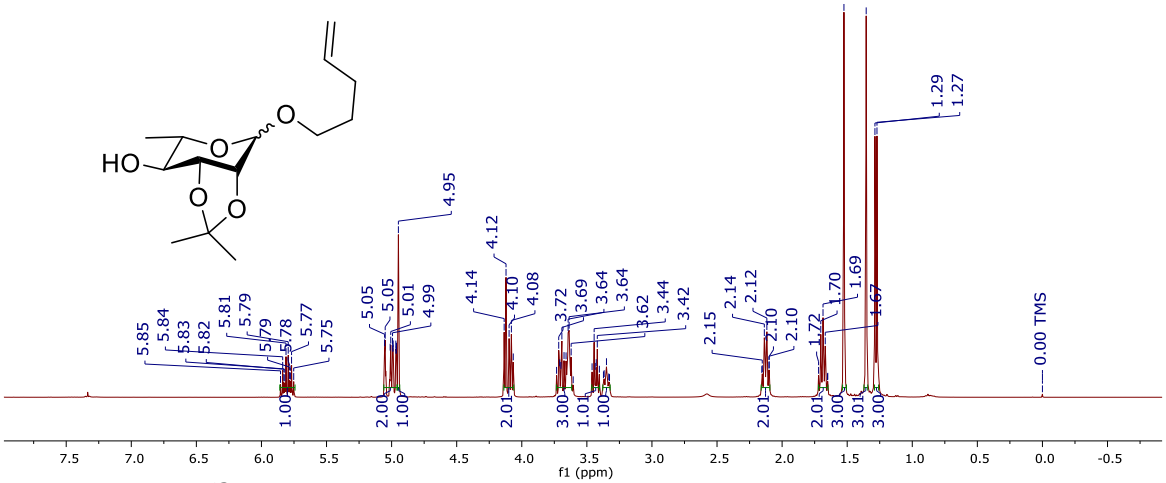
Pent-4-enyl2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (56): mp(^{0}C): 92.5; $[\alpha]^{25}_D$($CHCl_3$, *c*1.0): -8.9^0; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.68 (q, *J* = 6.9 Hz, 2H), 2.06 – 2.25 (m, 2H), 2.76 (d, *J* = 8.2 Hz, 1H), 3.51 (dt, *J* = 9.7, 6.3 Hz, 1H), 3.74 (dt, *J* = 9.7, 6.5 Hz, 1H), 4.06 (dddd, *J* = 48.9, 24.4, 11.0, 6.7 Hz, 5H), 4.32 – 4.55 (m, 4H), 4.61 (dd, *J* = 5.1, 2.4 Hz, 1H), 4.68 (ddd, *J* = 12.0, 6.2, 2.8 Hz, 3H), 4.81 – 4.89 (m, 1H), 4.89 – 5.04 (m, 2H), 5.18 (s, 1H), 5.25 (s, 1H), 5.30 – 5.40 (m, 2H), 5.44 (dd, *J* = 9.4, 1.3 Hz, 2H), 5.53 (d, *J* = 4.7 Hz, 1H), 5.55 – 5.66 (m, 3H), 5.71 – 5.82 (m, 2H), 5.92 (dd, *J* = 8.0, 3.8 Hz, 2H), 7.13 – 7.55 (m, 35H), 7.73 – 8.10 (m, 25H).; ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.6, 30.2, 65.1, 66.1, 66.2, 67.0, 67.8, 69.4, 71.3, 71.8, 73.3, 77.3, 77.6, 77.7, 77.9, 81.4, 81.4, 81.8, 81.9, 82.2, 82.4, 82.8, 83.7, 105.7, 105.7, 106.1, 106.8, 115.0, 128.1, 128.2, 128.3, 128.3,

128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.5, 128.8, 128.8, 128.9, 128.9, 128.9, 128.9, 128.9, 128.9, 129.0, 129.0, 129.2, 132.9, 132.9, 133.0, 133.0, 133.1, 133.2, 133.3, 133.3, 133.4, 133.4, 133.4, 133.5, 138.0, 165.0, 165.2, 165.2, 165.5, 165.5, 165.7, 165.7, 165.8, 165.9, 166.1, 166.1, 166.5; MALDI-TOF (ESI-MS): m/z calcd for [$C_{113}H_{98}O_{33}Na^{+}$]: 2006.5922; Found: 2006.6791

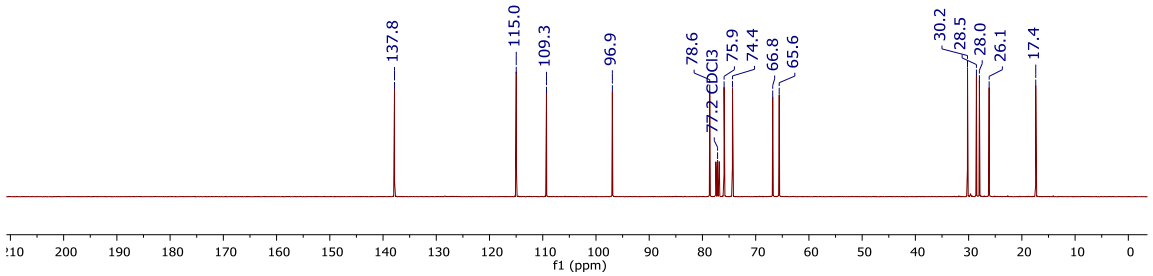
Pent-4-enyl2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(2,3,5-tri-*O*-benzoyl-6-*O*-(2,3,6-tri-*O*-benzoyl-5-*O*-(4-oxopenanoyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranosyl)-β-D-galactofuranoside (57): mp(^{0}C): 71.5; $[\alpha]^{25}_{D}$($CHCl_3$, *c*1.0): -4.0^{0}; ^{1}H NMR (400.31MHz, $CDCl_3$): δ 1.68 (p, *J* = 6.8 Hz, 2H), 1.98 (s, 3H), 2.13 (d, *J* = 6.4 Hz, 2H), 2.33 – 2.67 (m, 4H), 3.53 (q, *J* = 6.7 Hz, 1H), 3.67 – 3.79 (m, 1H), 3.88 – 4.27 (m, 5H), 4.49 – 4.87 (m, 12H), 4.85 – 5.09 (m, 3H), 5.23 (s, 6H), 5.42 (dd, *J* = 37.4, 14.9 Hz, 6H), 5.64 (d, *J* = 20.7 Hz, 4H), 5.70 – 5.86 (m, 6H), 5.93 (s, 2H), 6.94 – 7.60 (m, 50H), 7.73 – 8.11 (m, 40H); ^{13}C NMR (100.67 MHz, $CDCl_3$): δ 28.0, 28.6, 29.6, 30.2, 37.9, 63.5, 63.6, 65.2, 65.5, 66.0, 66.9, 67.0, 67.7, 67.9, 70.2, 71.3, 71.9, 72.0, 72.1, 73.2, 77.1, 77.8, 77.8, 81.4, 81.6, 81.7, 81.8, 81.9, 81.9, 81.9, 82.0, 82.2, 82.3, 82.5, 82.6, 82.7, 82.8, 105.7, 105.8, 105.9, 106.1, 106.7, 106.8, 115.0, 128.1-128.4(36C), 128.7-129.1 (18C), 129.6-129.9(36C), 132.9-133.8(18C), 138.0, 165.0, 165.1, 165.2, 165.2, 165.3, 165.5, 165.5, 165.5, 165.5, 165.5, 165.7, 165.7, 165.7, 165.9, 165.9, 166.0, 166.0, 166.1, 172.0, 205.9.; MALDI-TOF (ESI-MS): m/z calcd for [$C_{172}H_{148}O_{51}Na^{+}$]: 3052.8919; Found: 3054.1738.

4.12 Spectral Charts

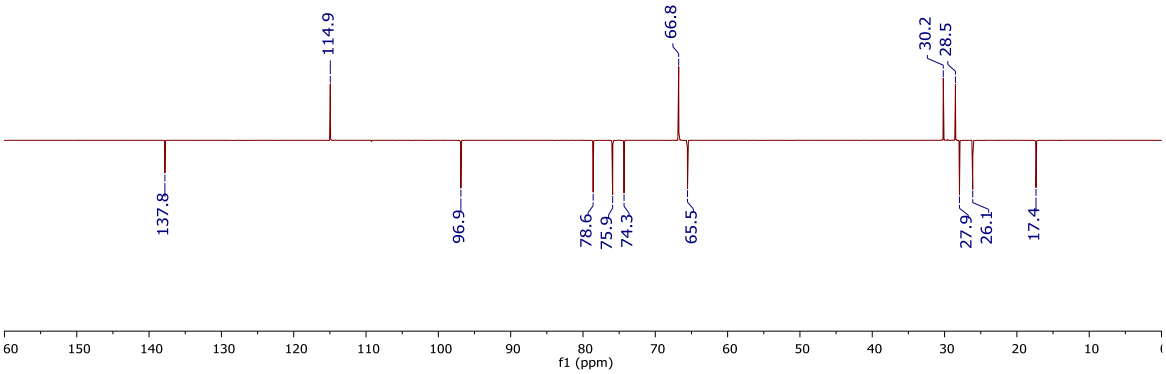
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **13**



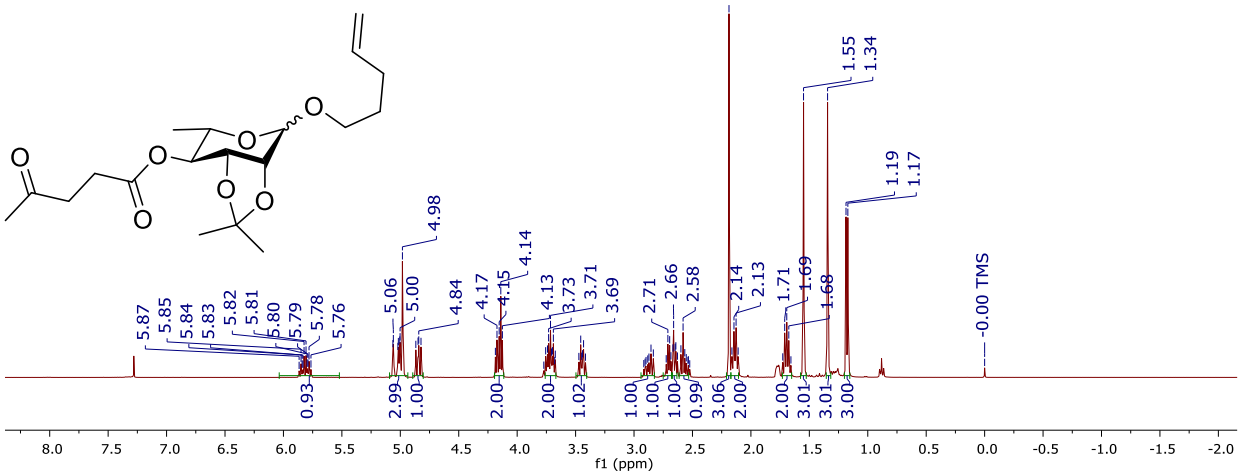
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**13**



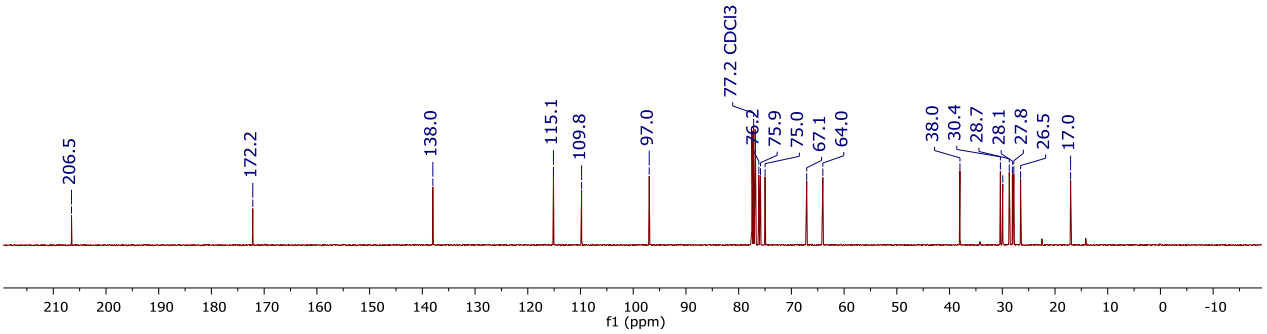
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**13**



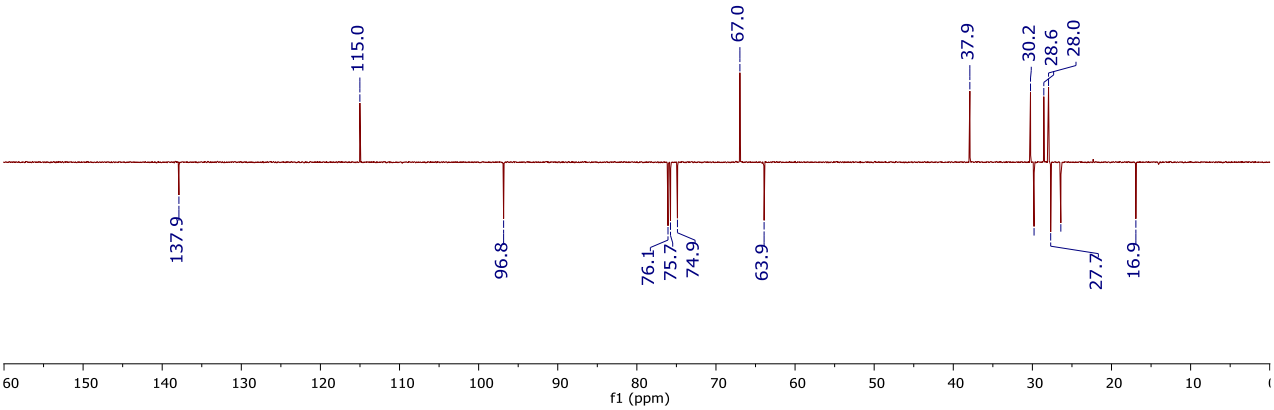
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **14**



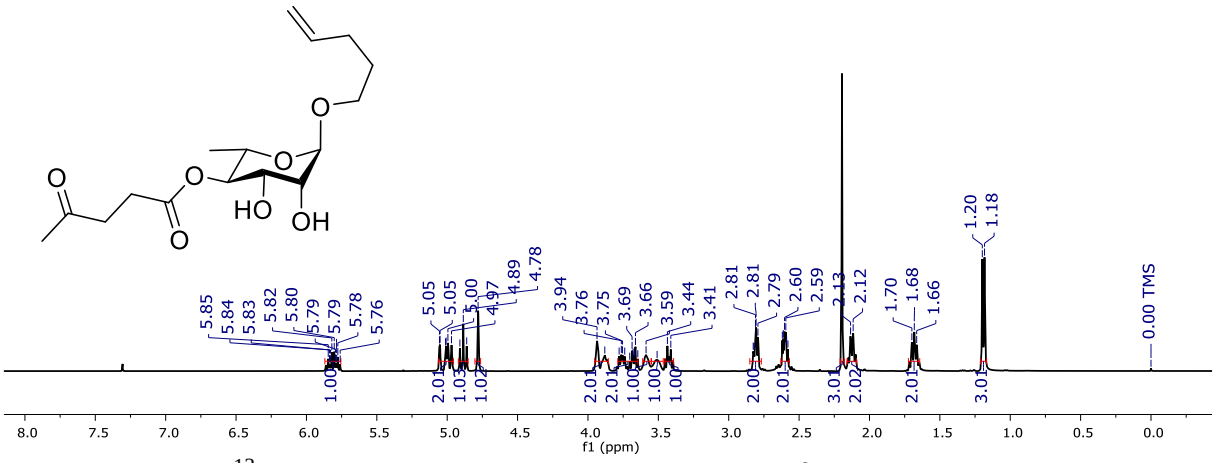
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**14**



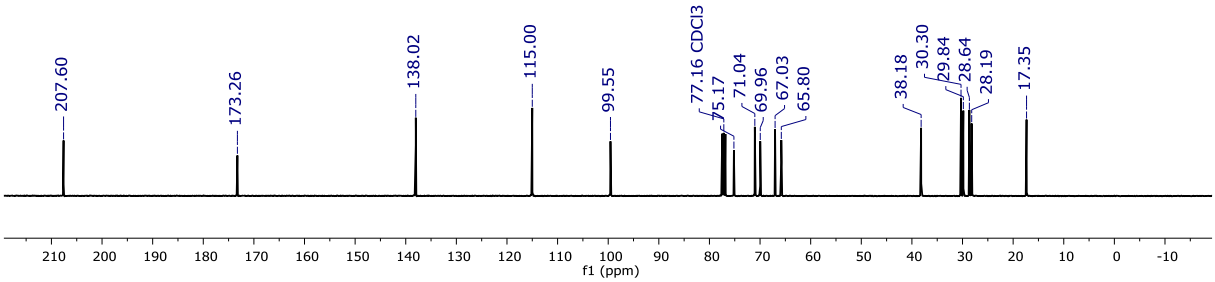
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**14**



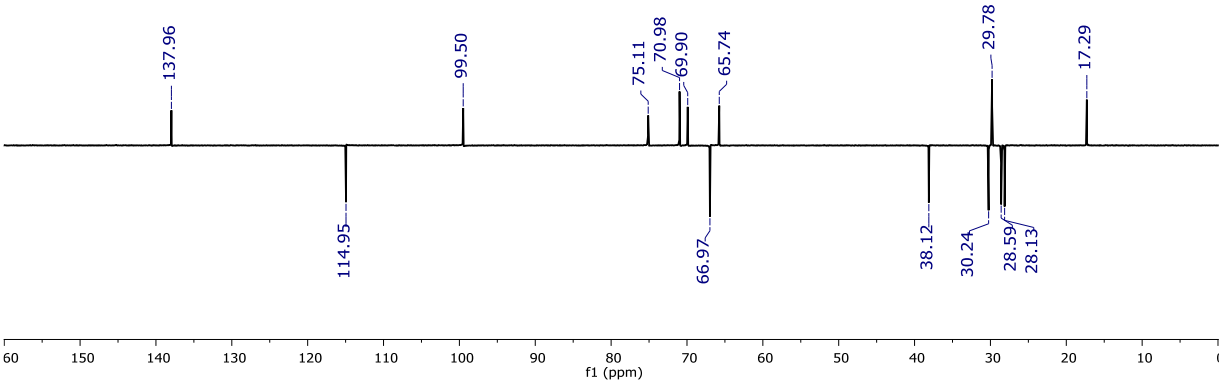
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **15**



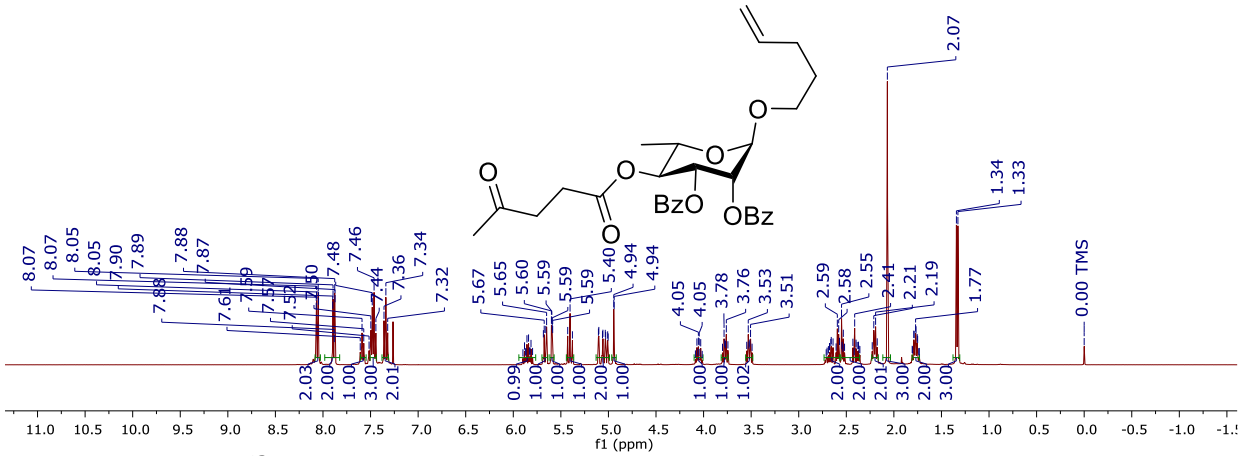
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**15**



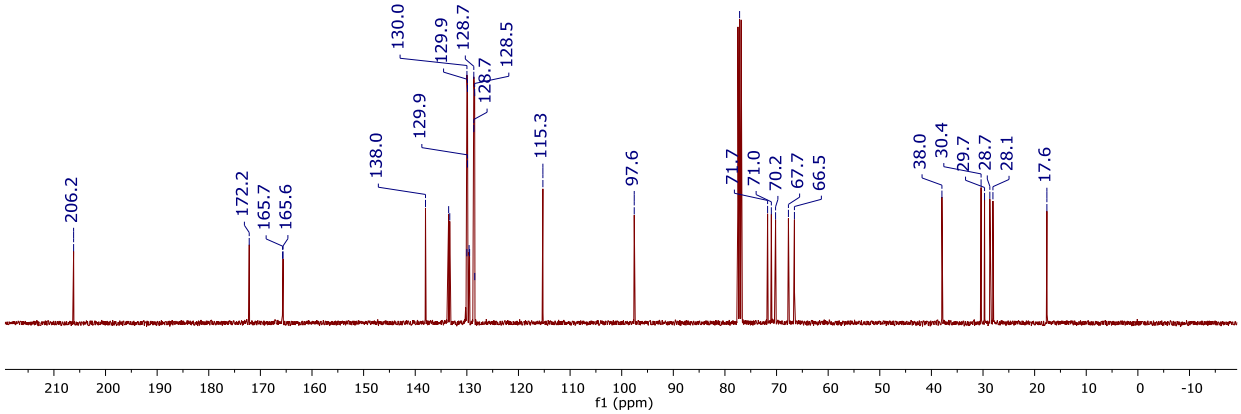
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**15**



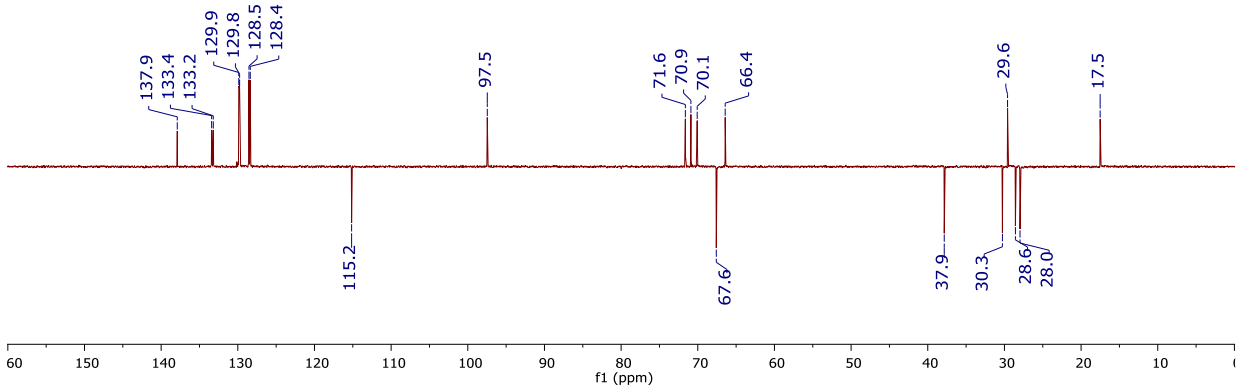
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **16**



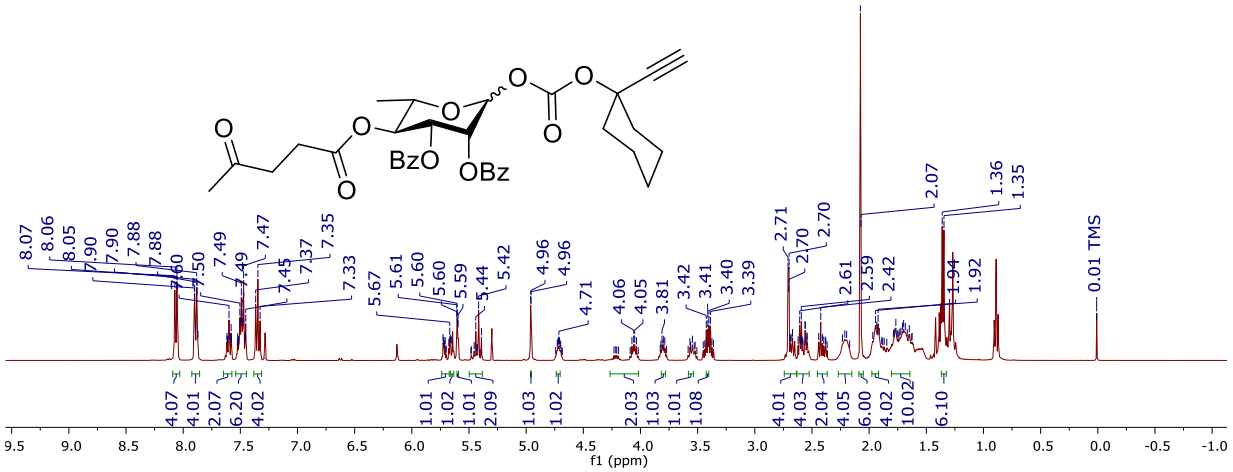
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**16**



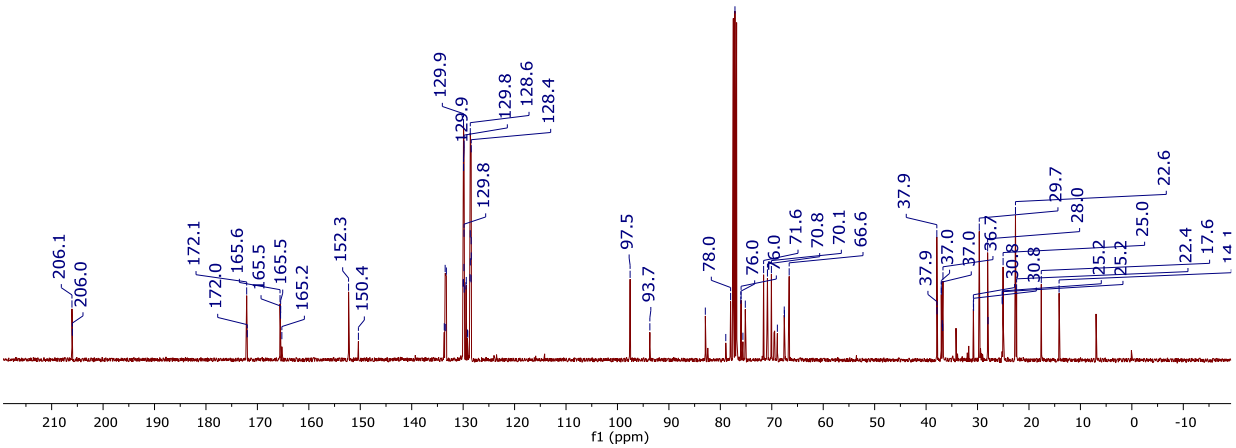
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**16**



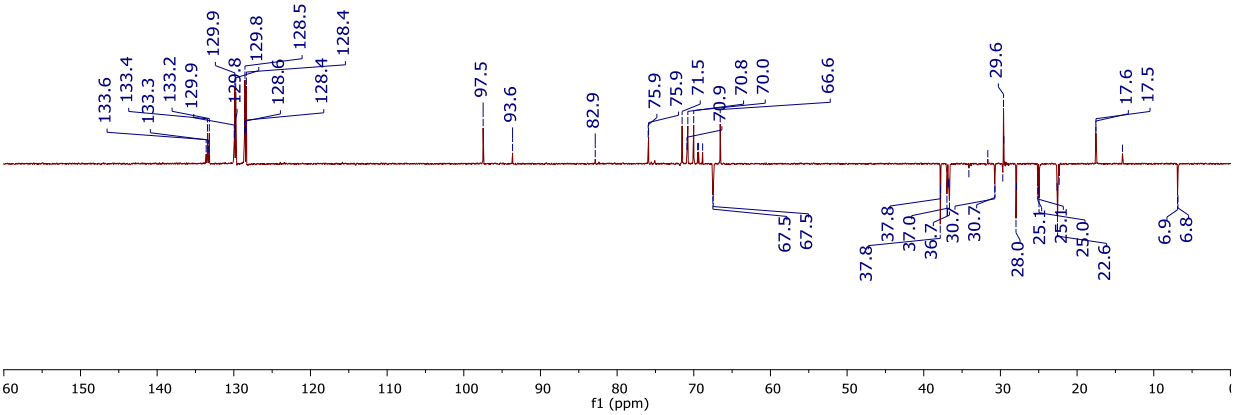
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **11**



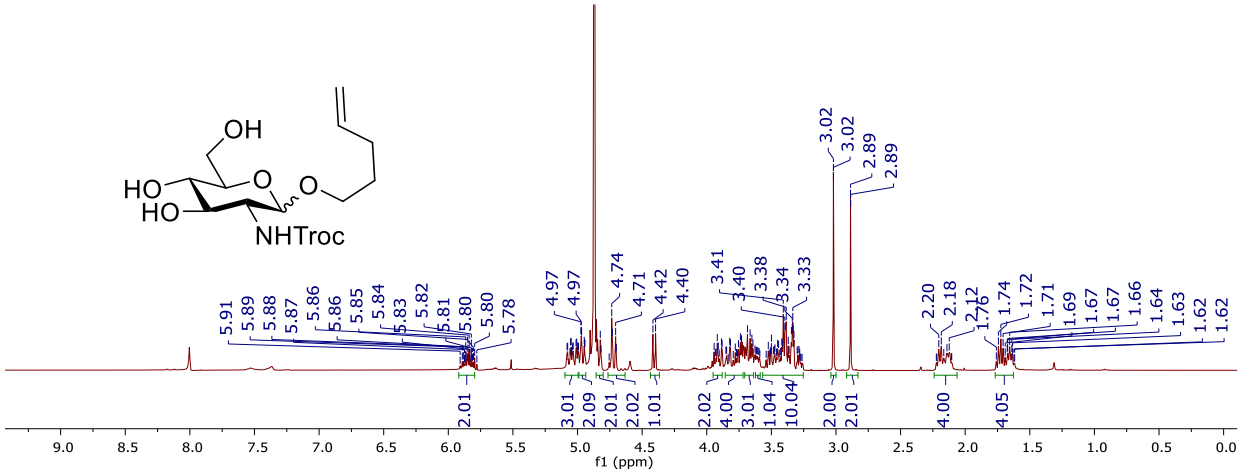
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**11**



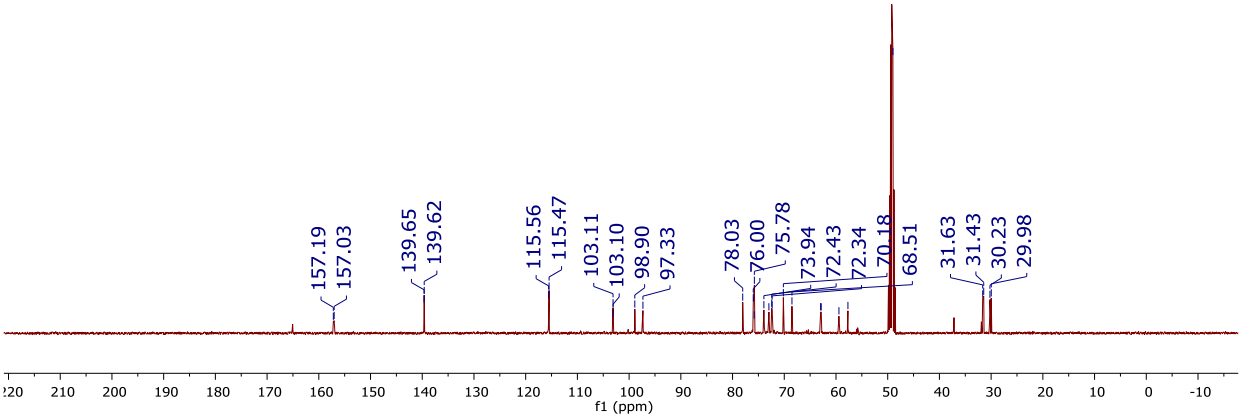
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**19**



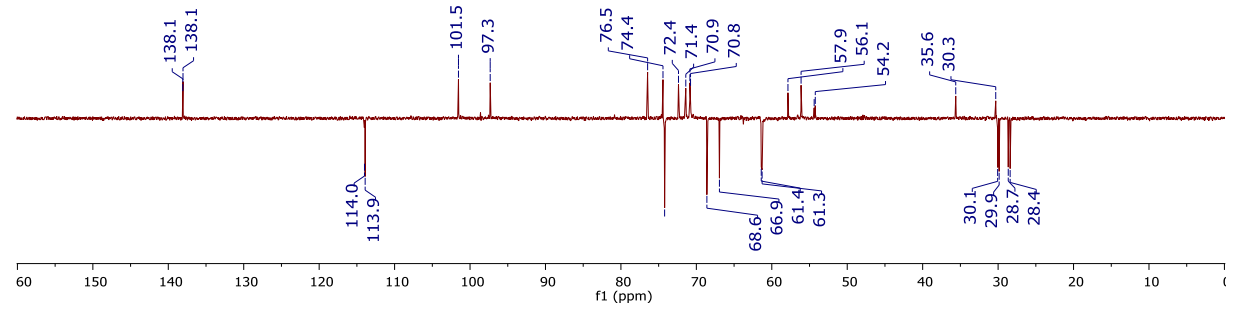
^{1}H NMR Spectrum (400.31 MHz, $MeOD_4$) of compound **18**



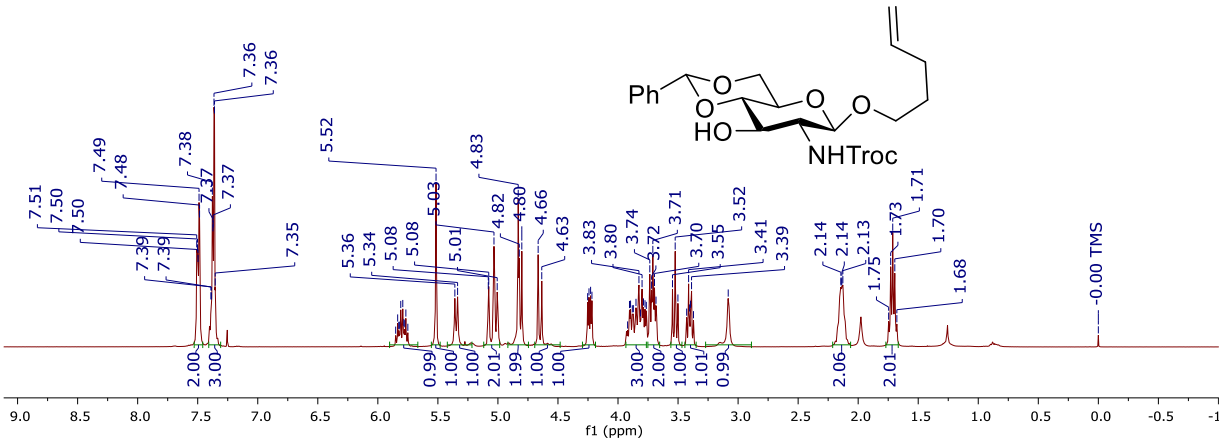
^{13}C NMR Spectrum (100.67MHz, $MeOD_4$) of compound**18**



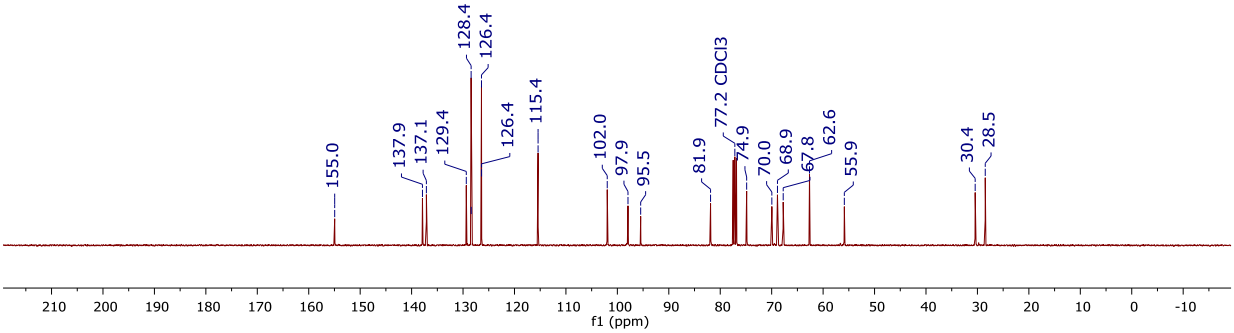
DEPT NMR Spectrum (100.67MHz, $MeOD_4$) of compound**18**



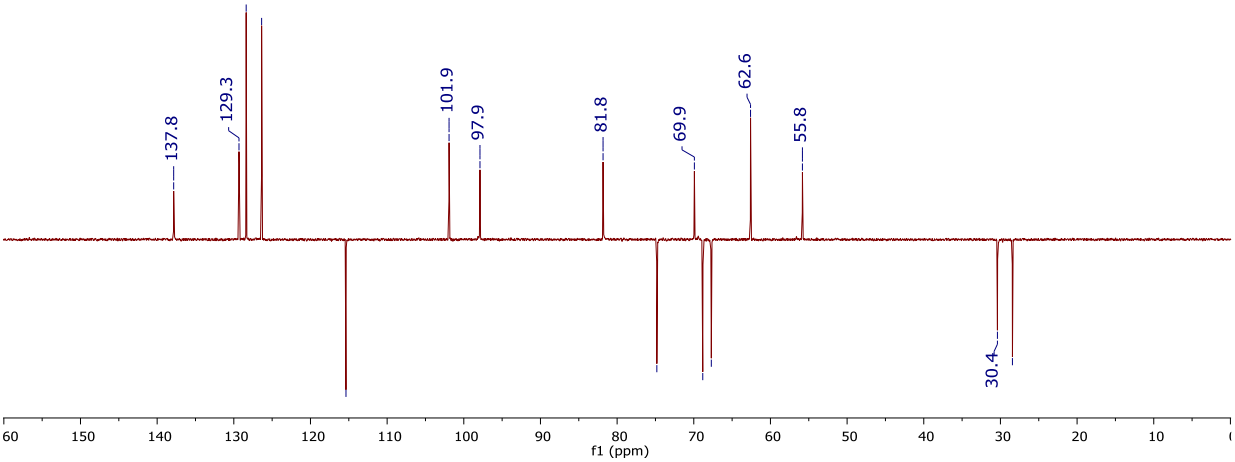
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **19**



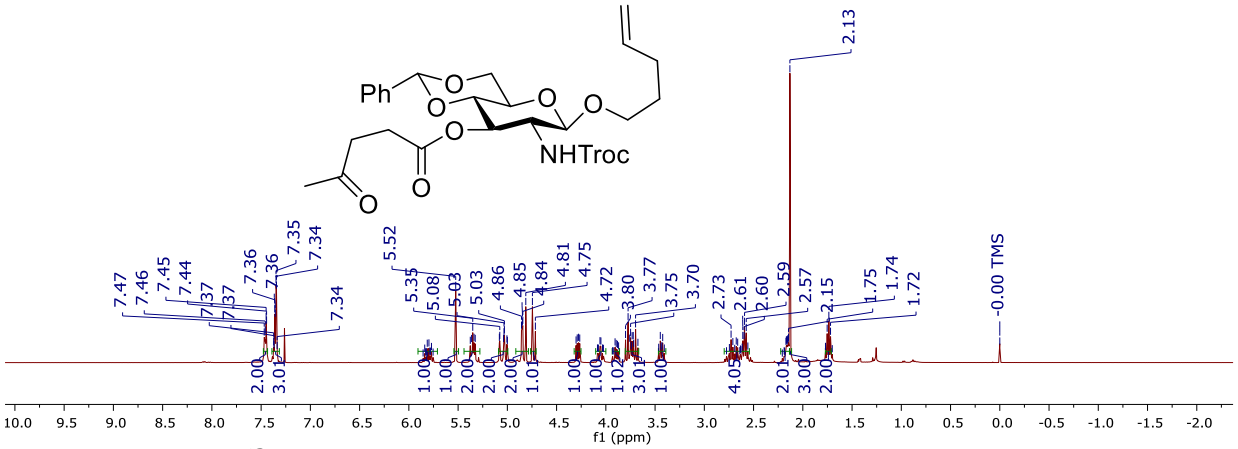
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**19**



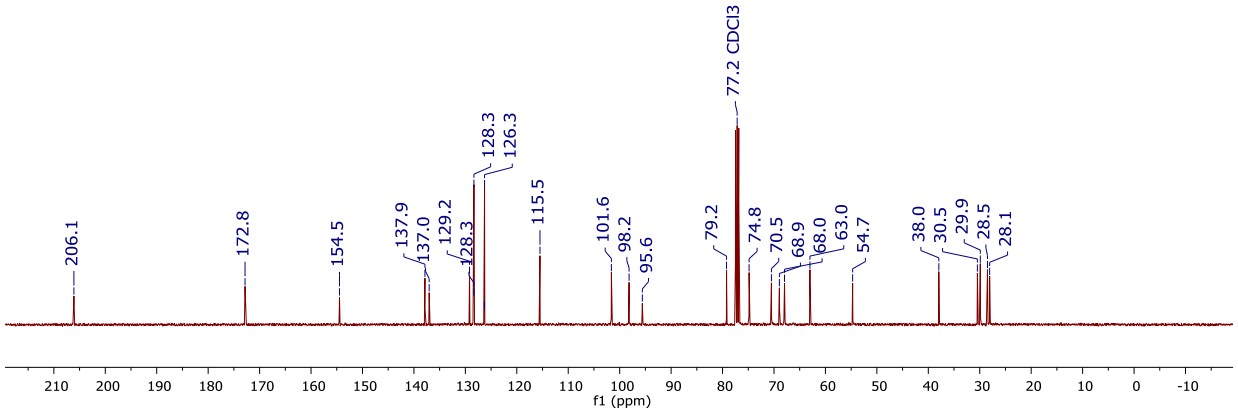
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**19**



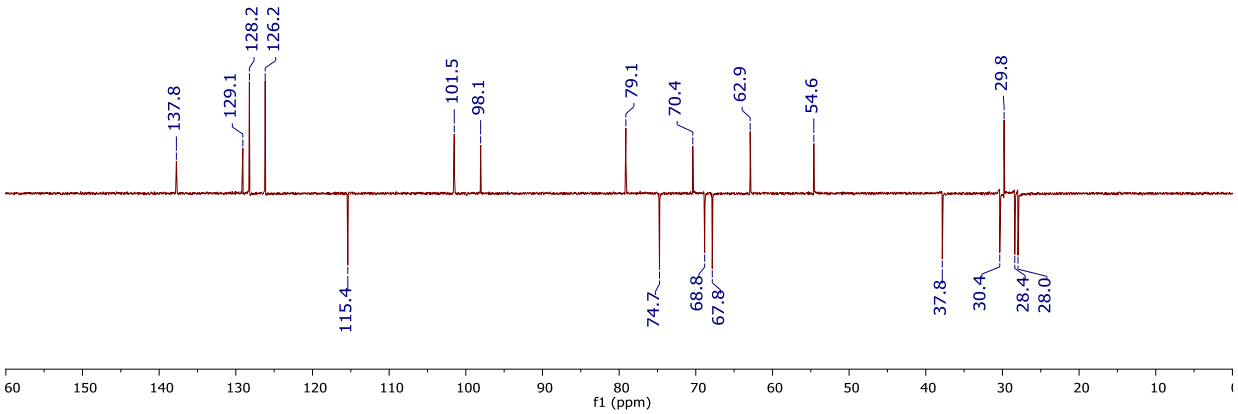
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **20**



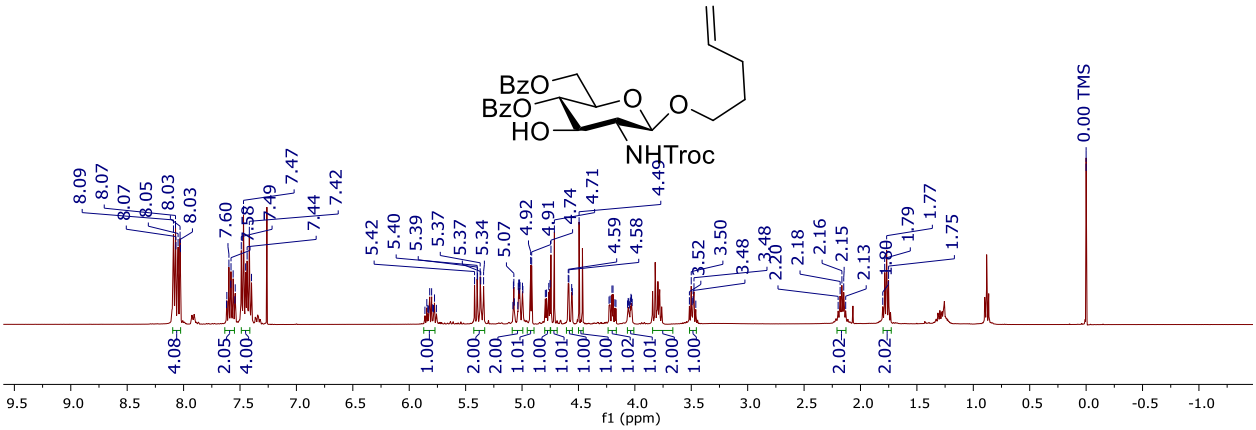
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**20**



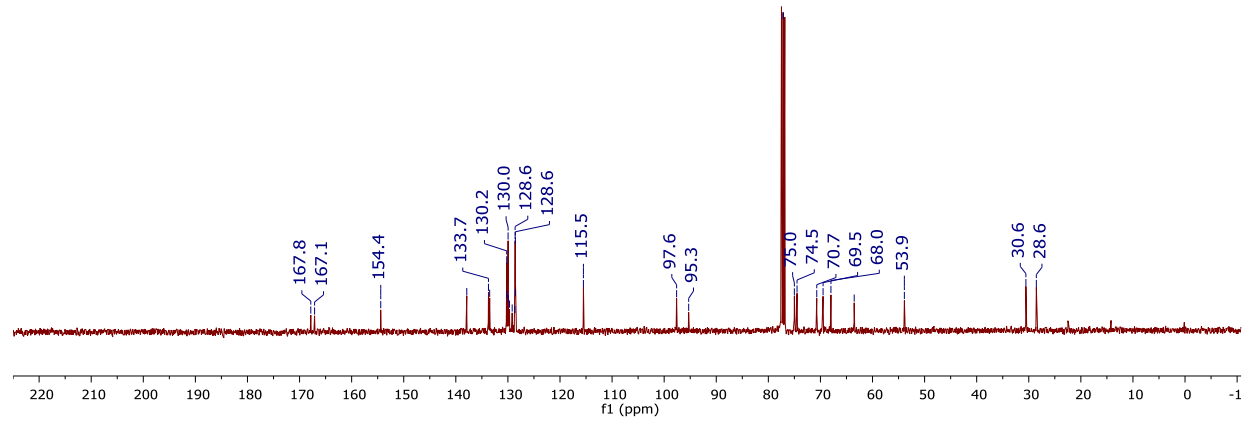
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**20**



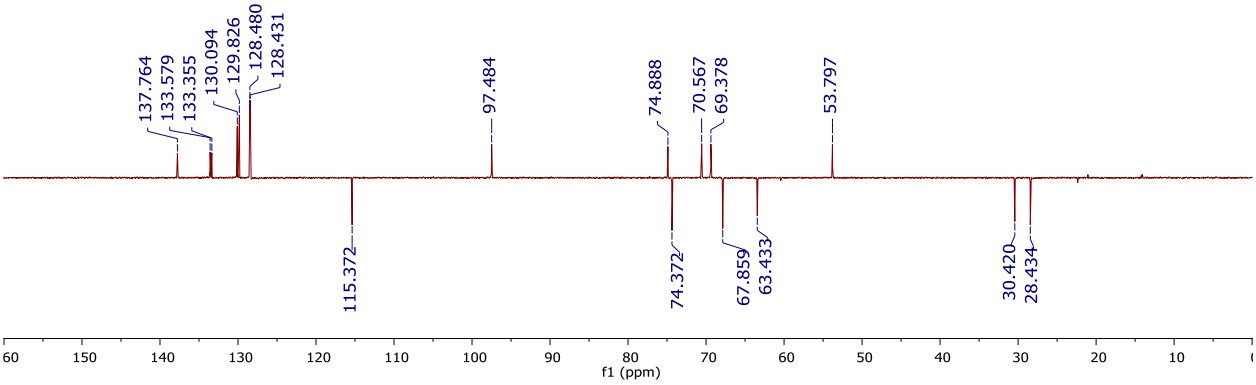
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **12**



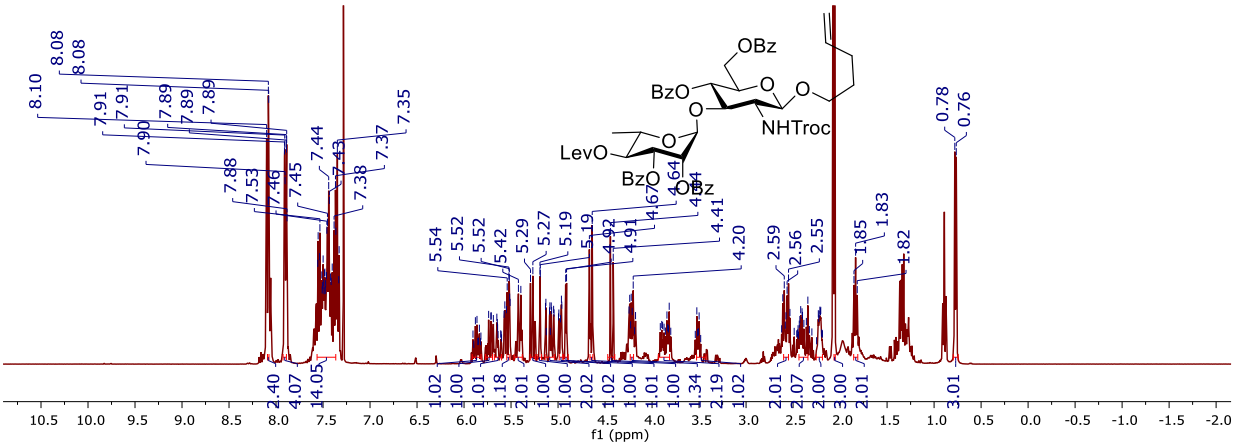
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**12**



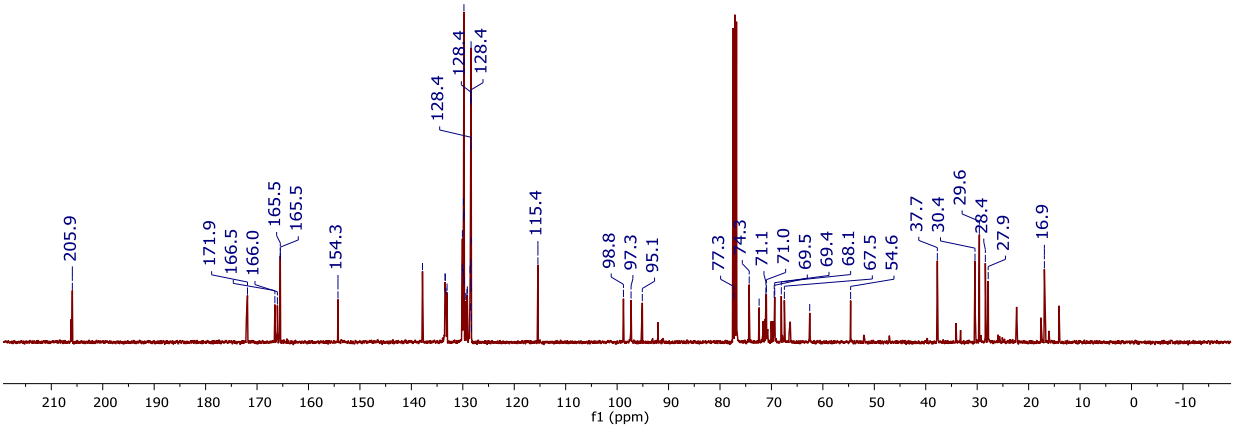
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**12**



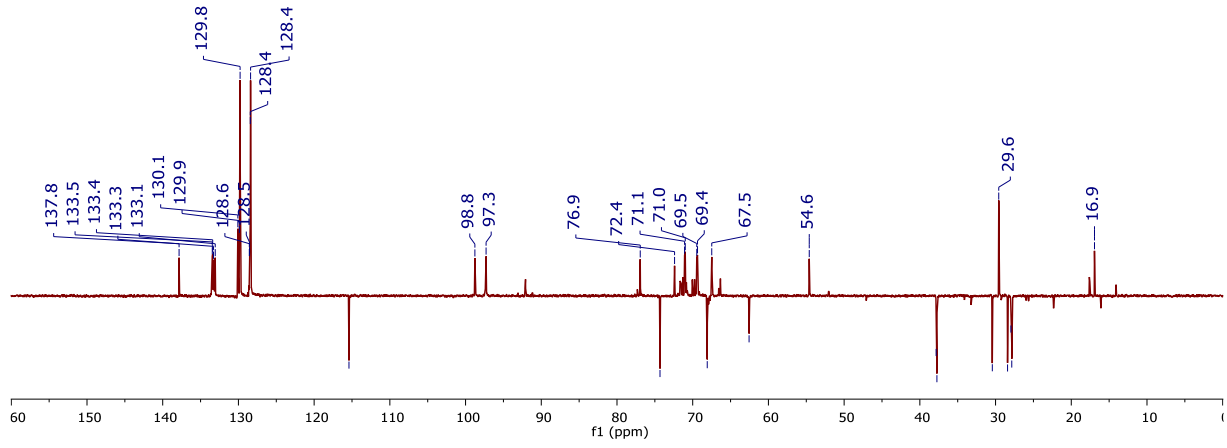
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **21**



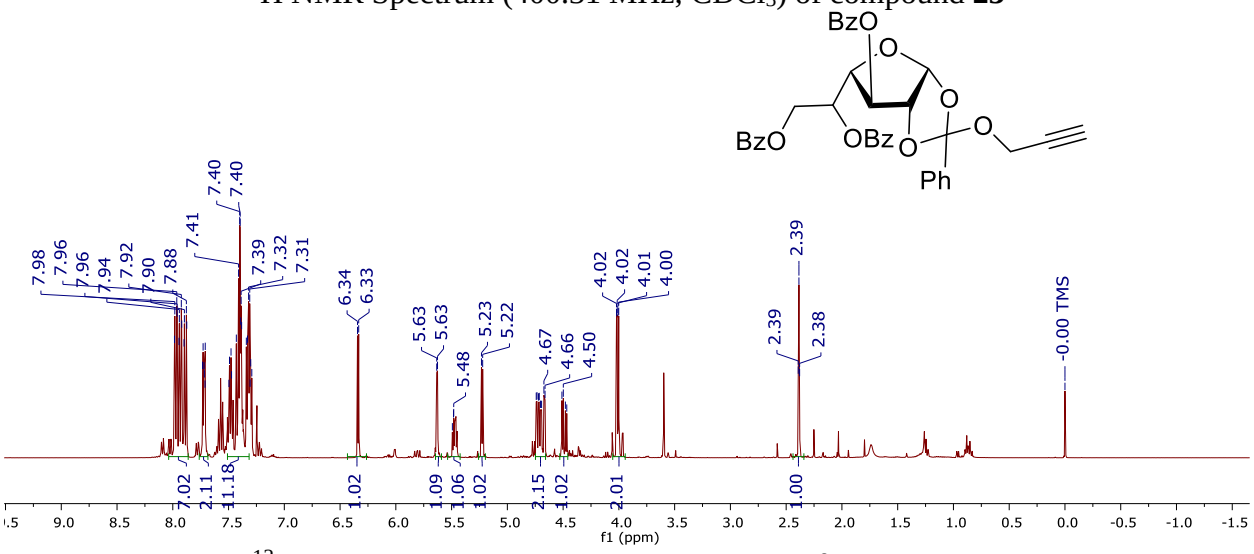
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**21**



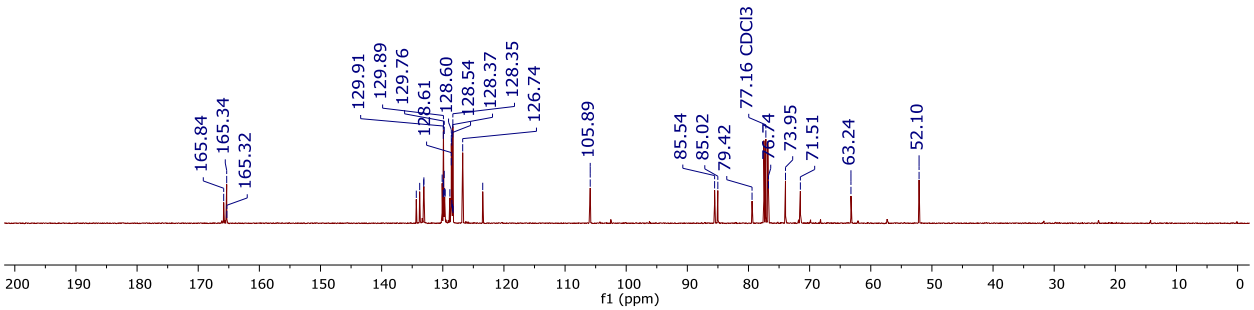
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**21**



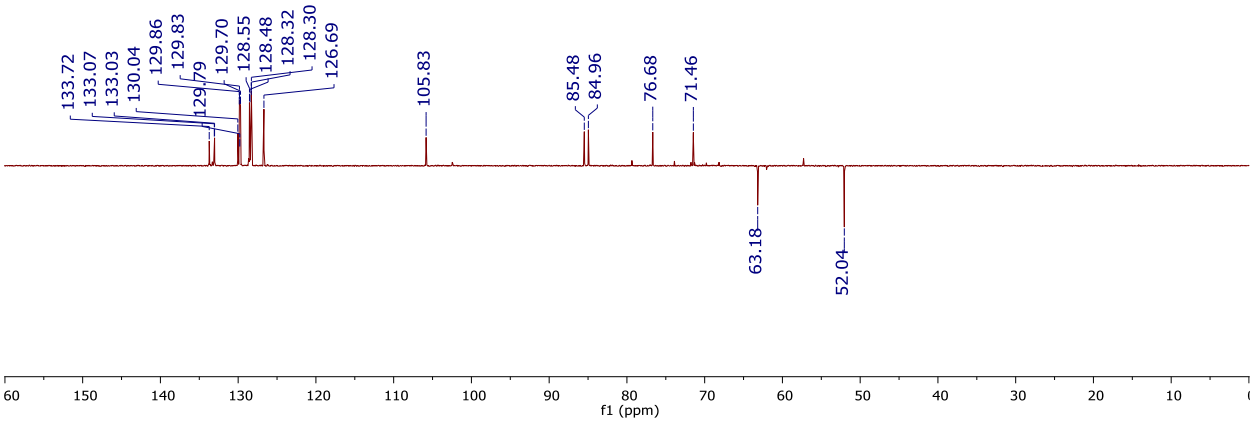
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **23**



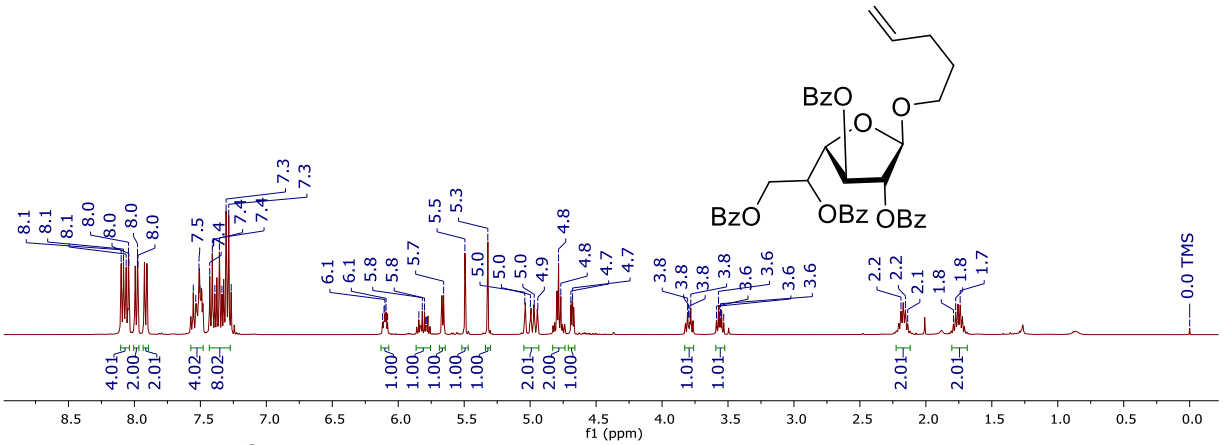
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**23**



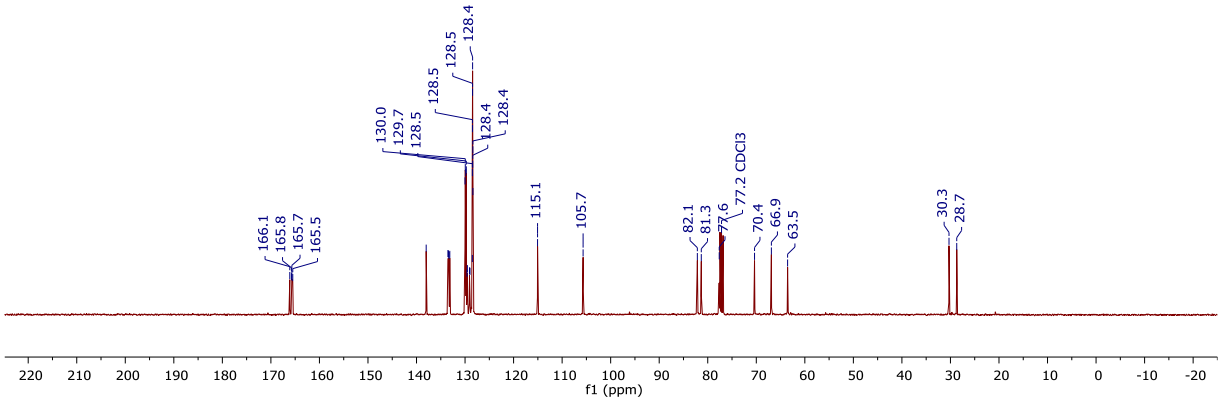
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**23**



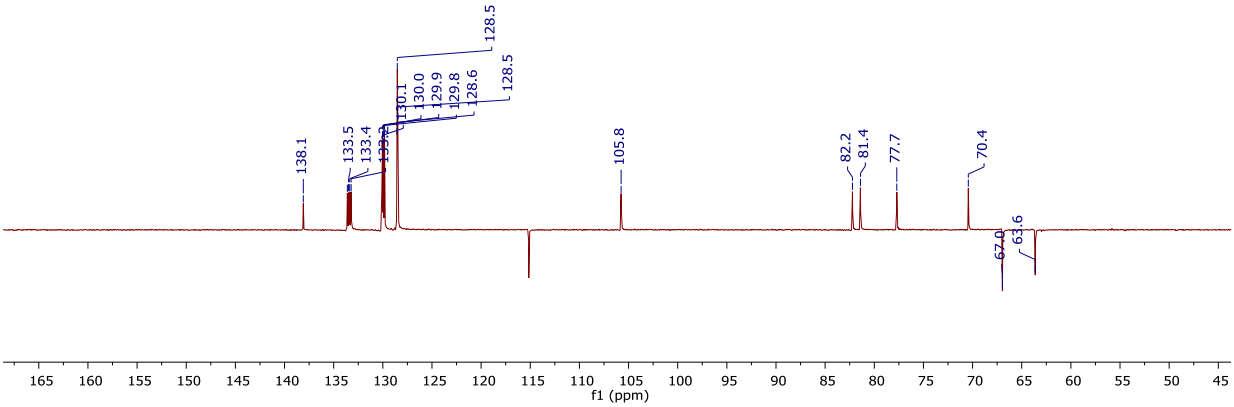
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **24**



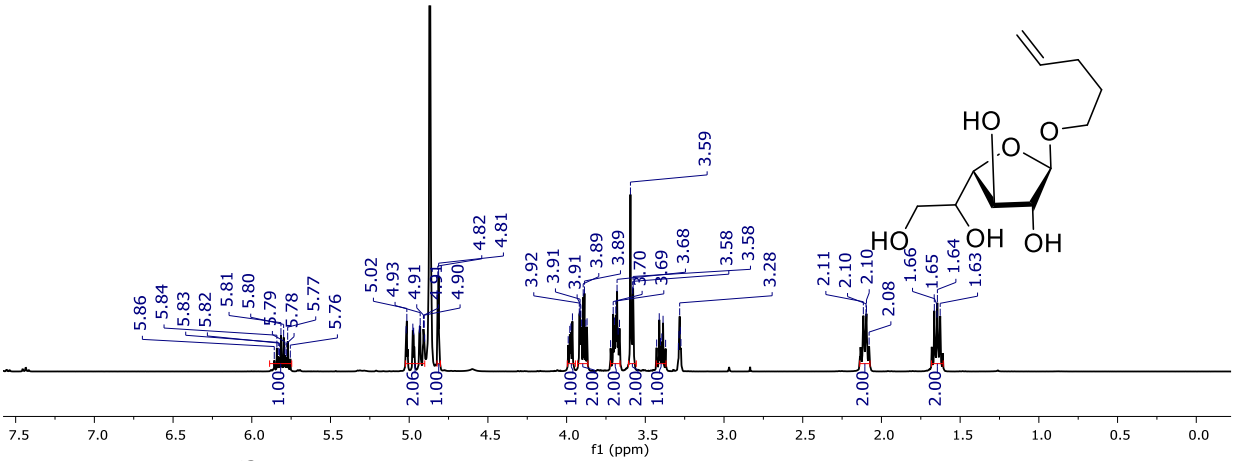
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**24**



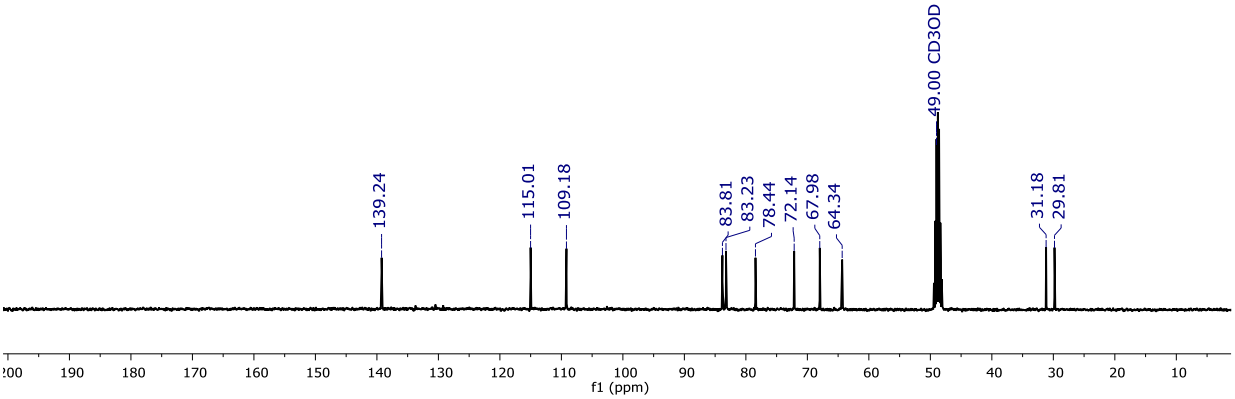
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**24**



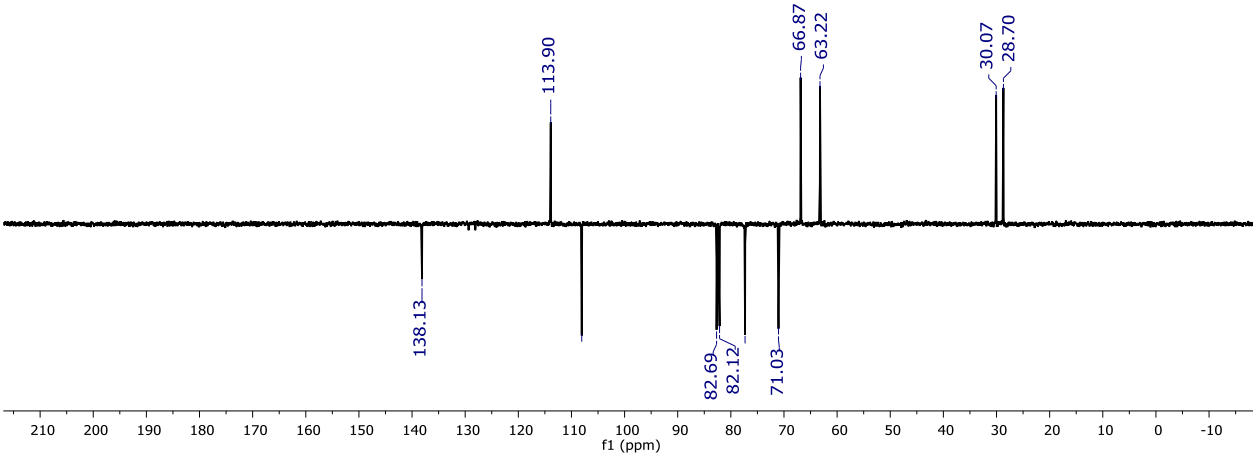
^{1}H NMR Spectrum (400.31 MHz, $MeOD_4$) of compound **25**



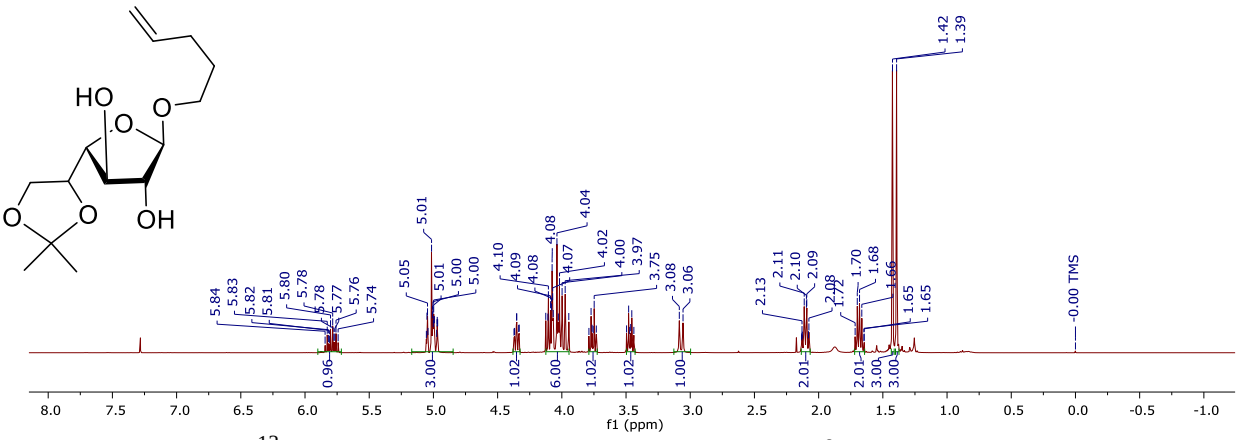
^{13}C NMR Spectrum (100.67MHz, $MeOD_4$) of compound**25**



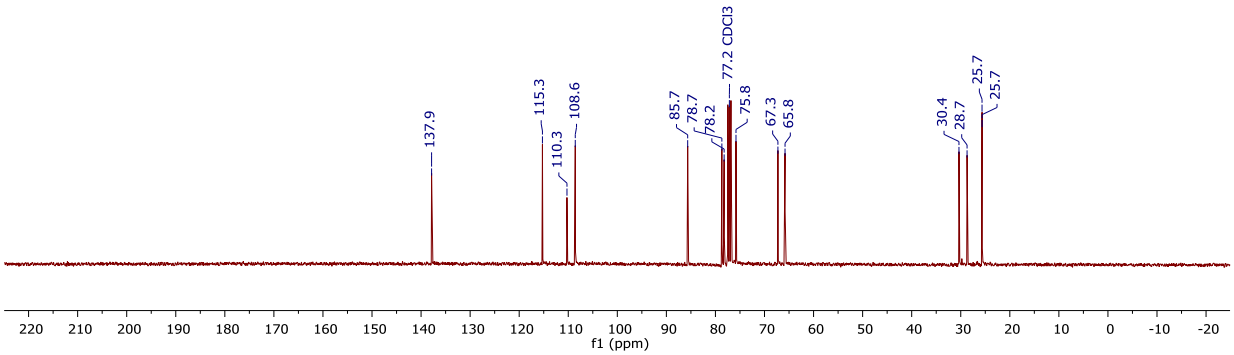
DEPT NMR Spectrum (100.67MHz, $MeOD_4$) of compound**25**



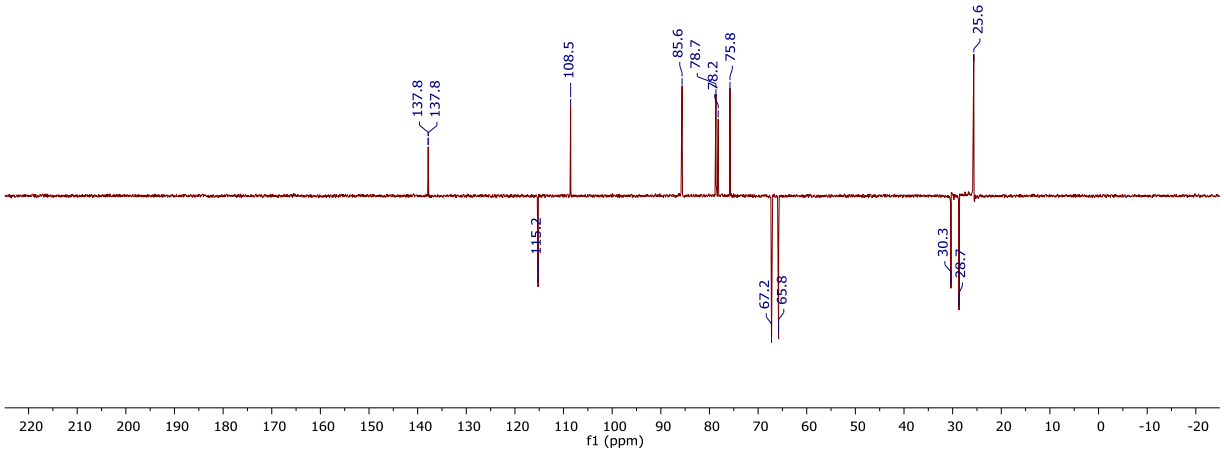
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **26**



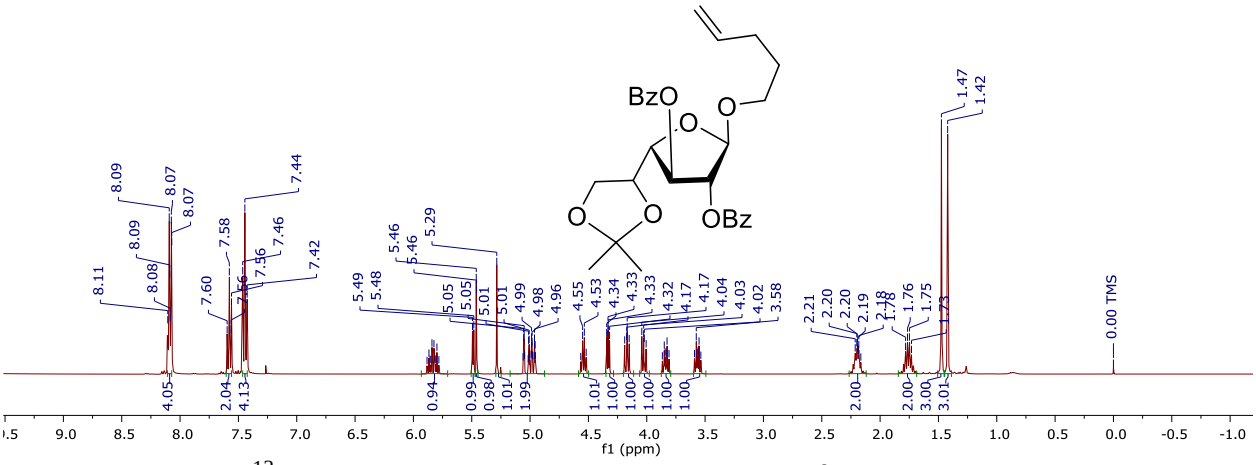
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**26**



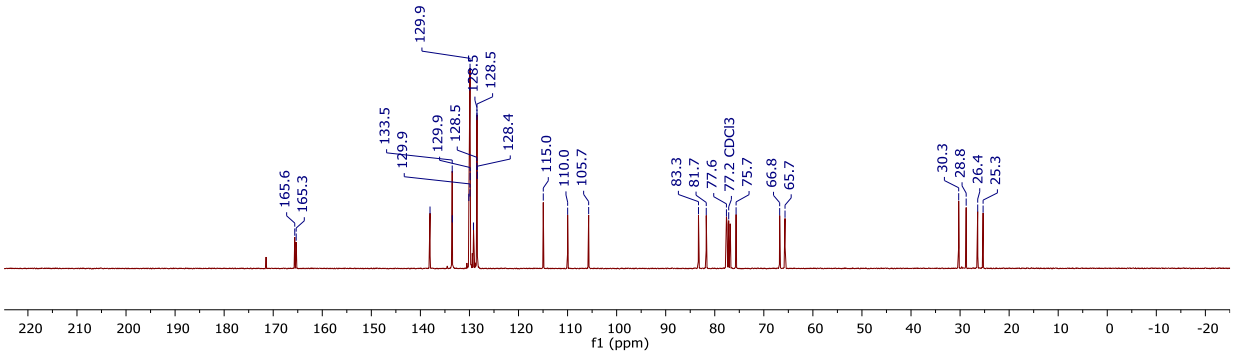
DEPT NMR Spectrum (100.67MHz, $MeOD_4$) of compound**26**



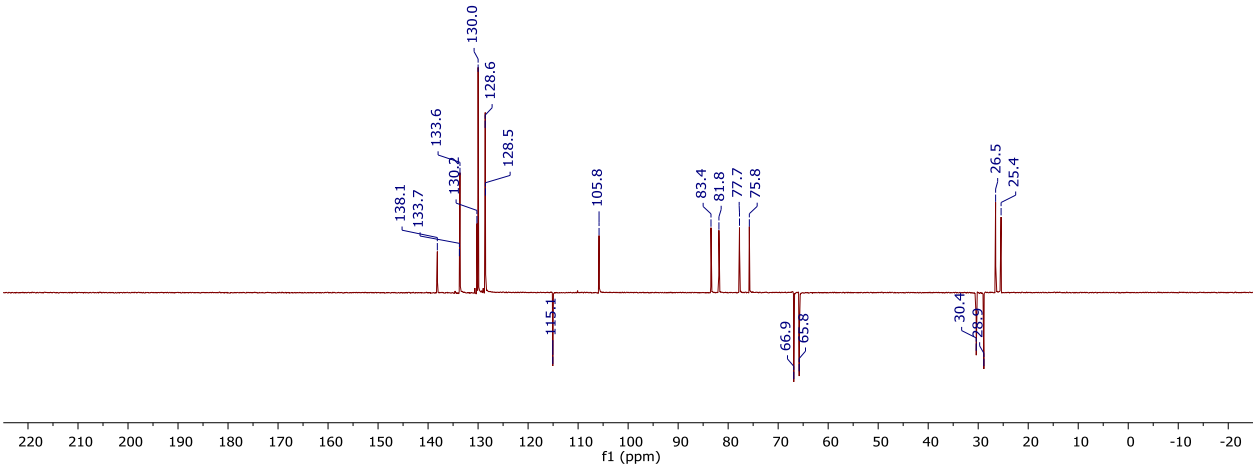
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **27**



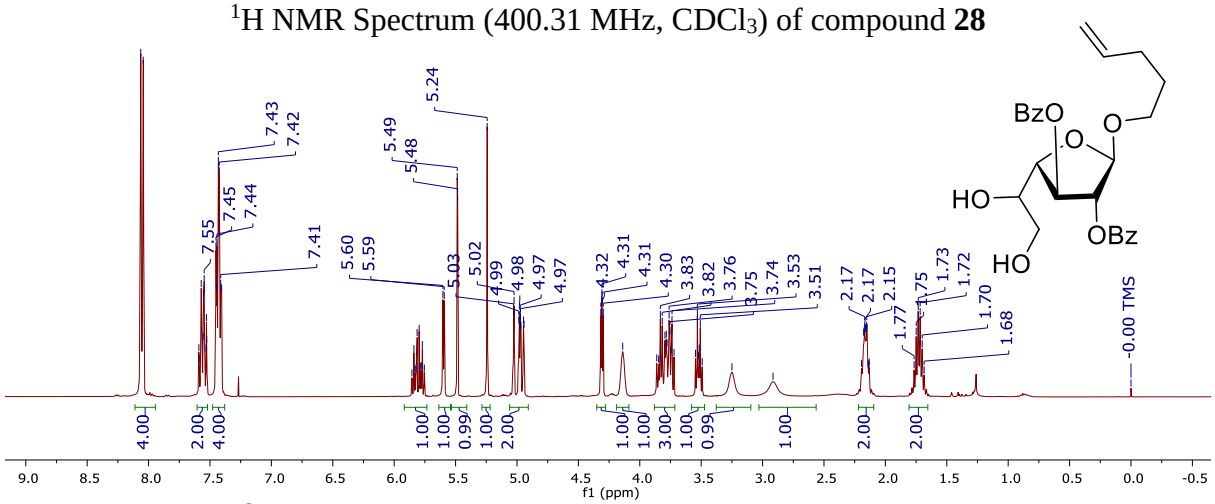
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**27**



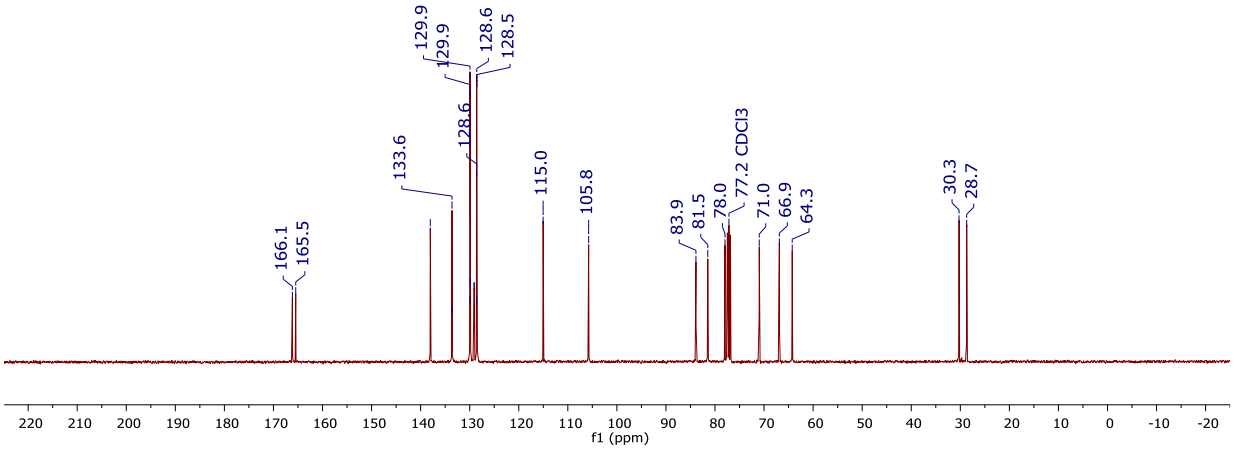
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**27**



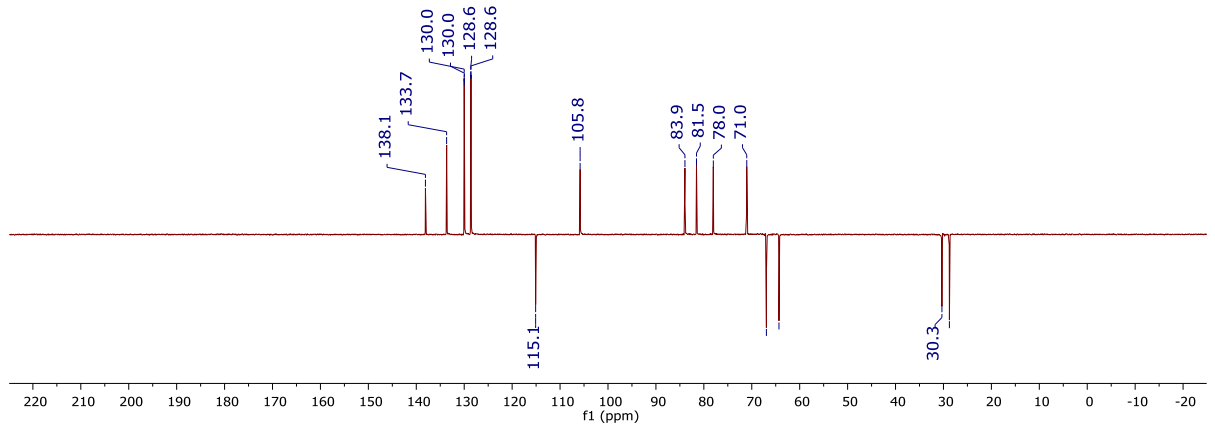
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **28**



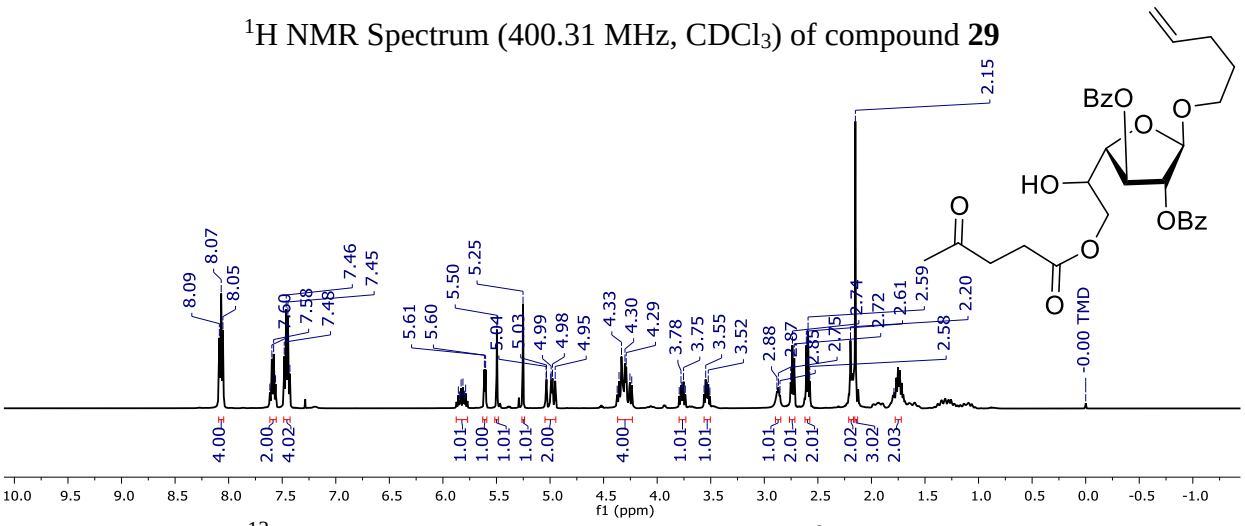
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**28**



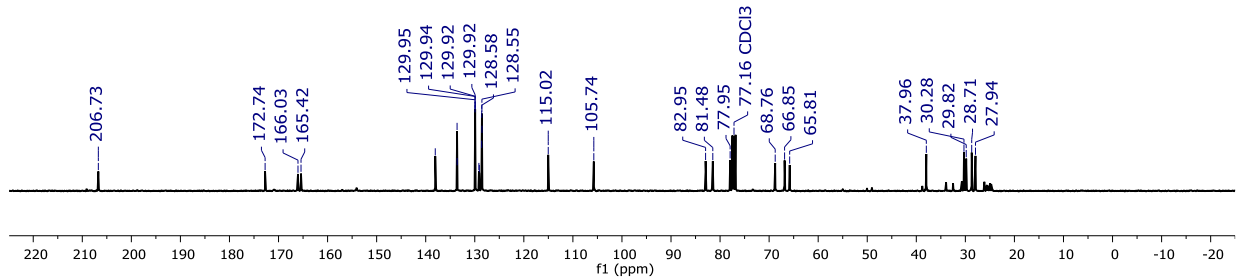
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**28**



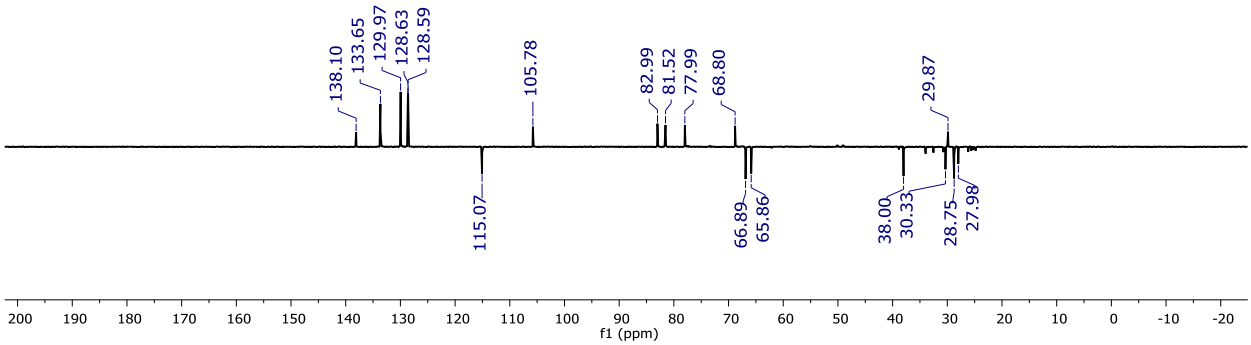
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **29**



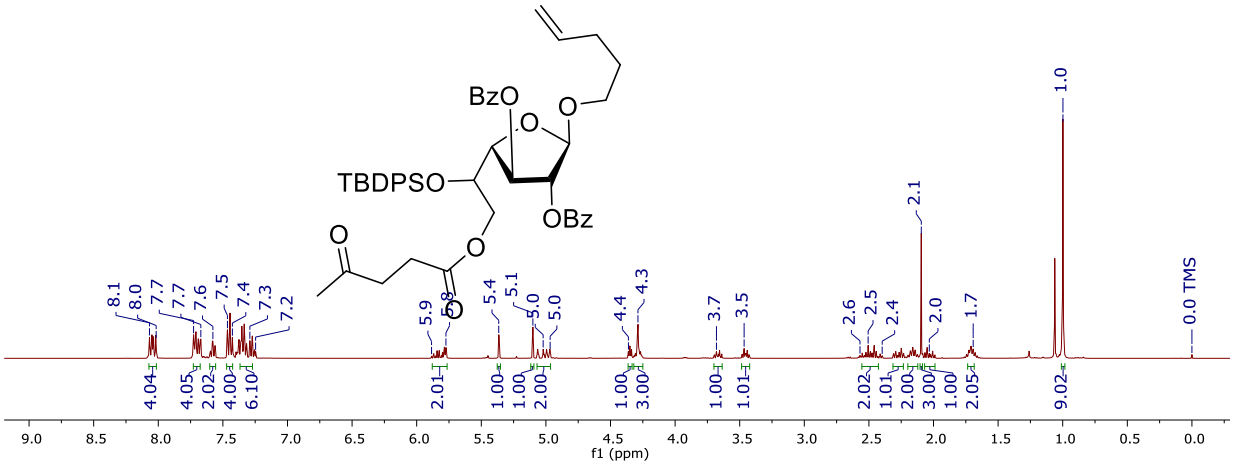
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**29**



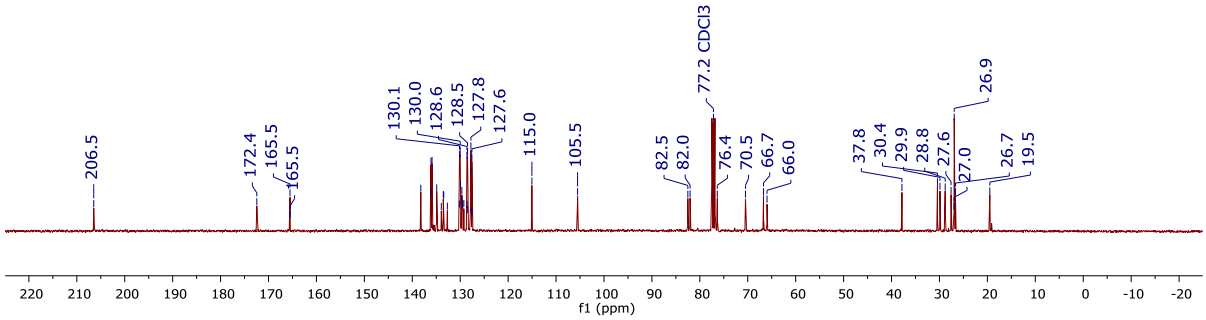
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**29**



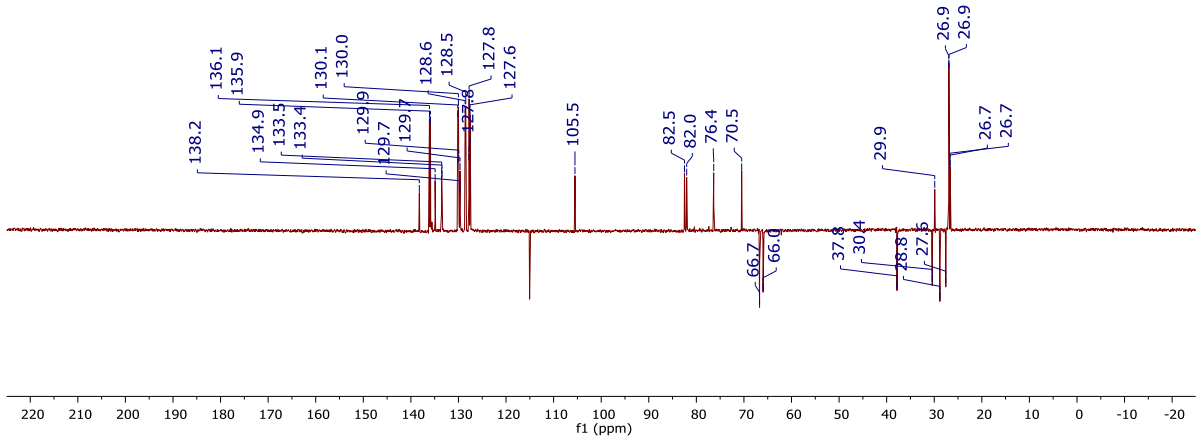
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **30**



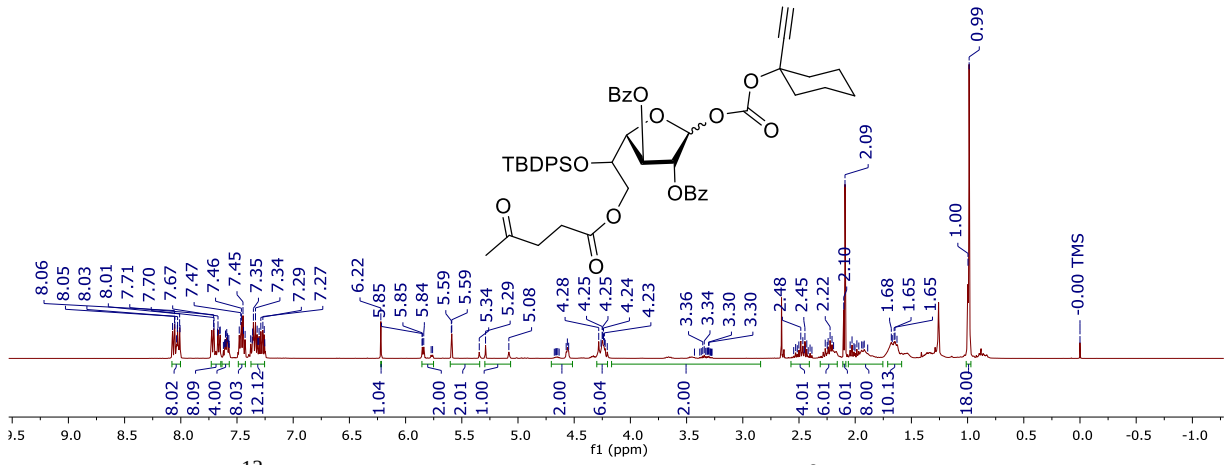
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**30**



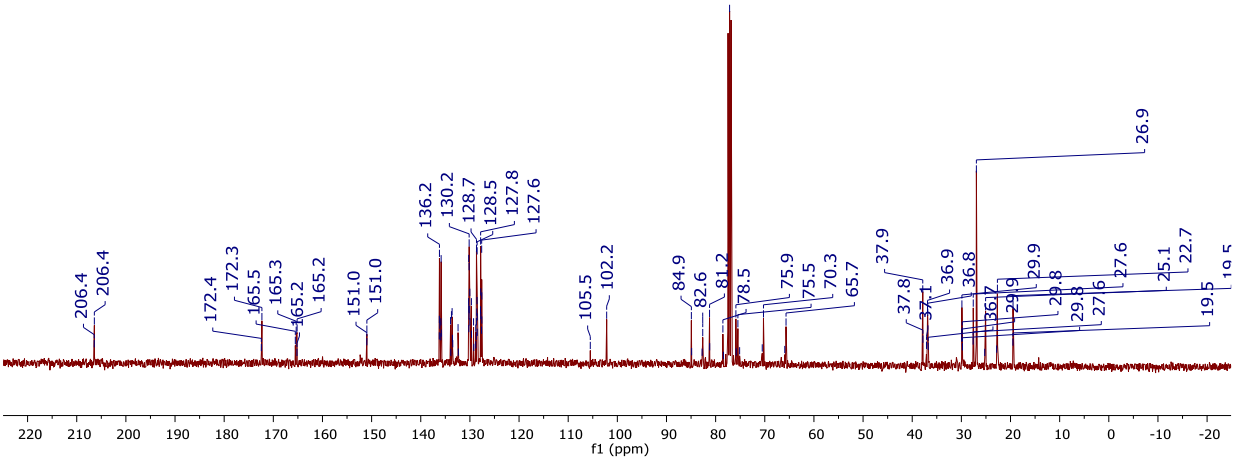
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**30**



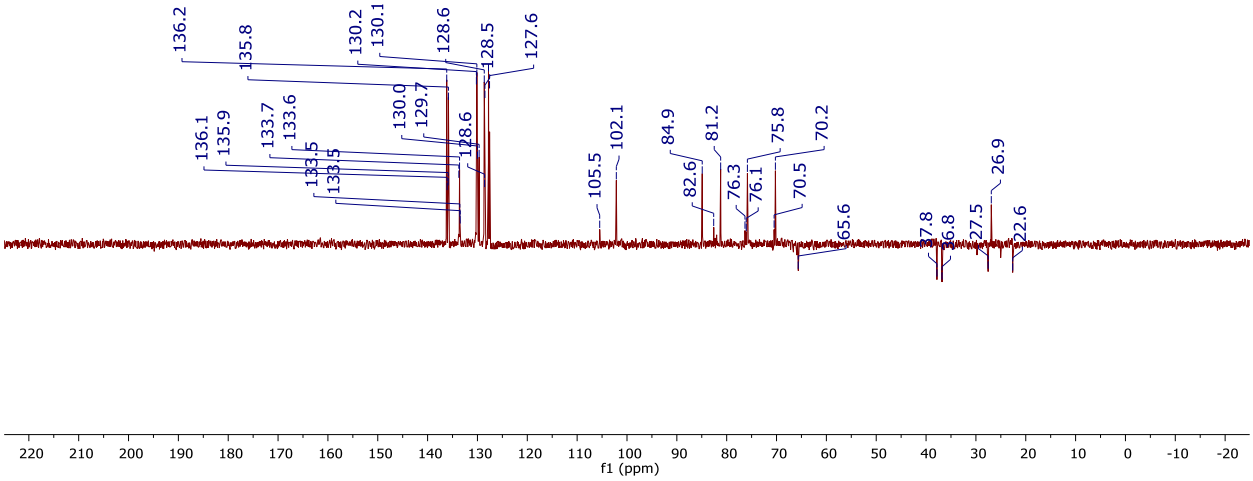
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **10**



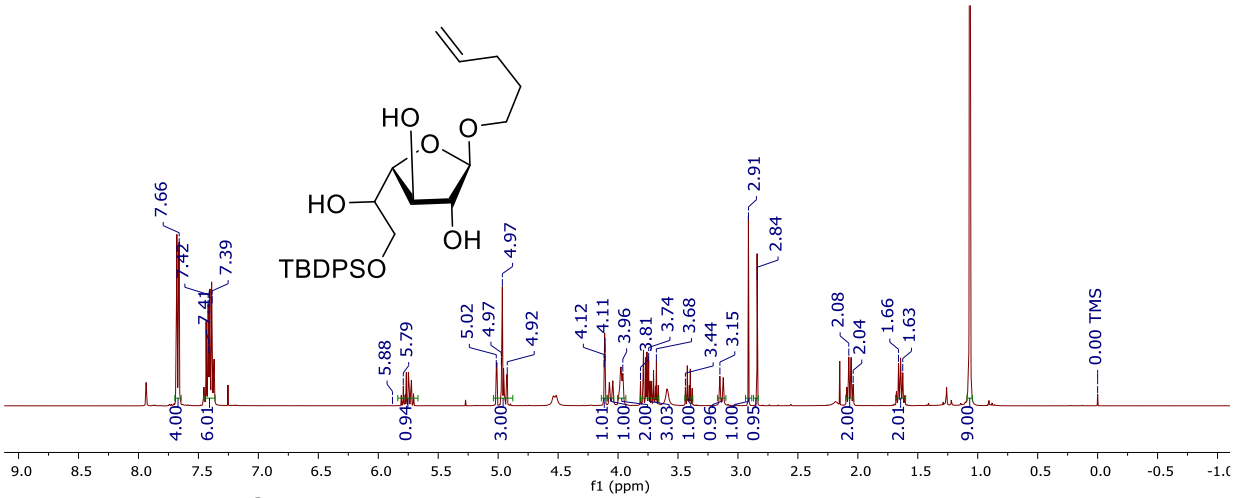
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**10**



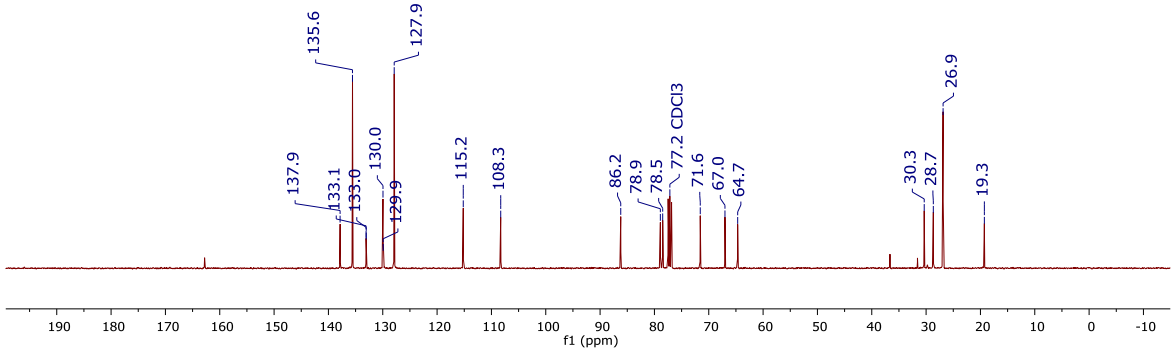
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**10**



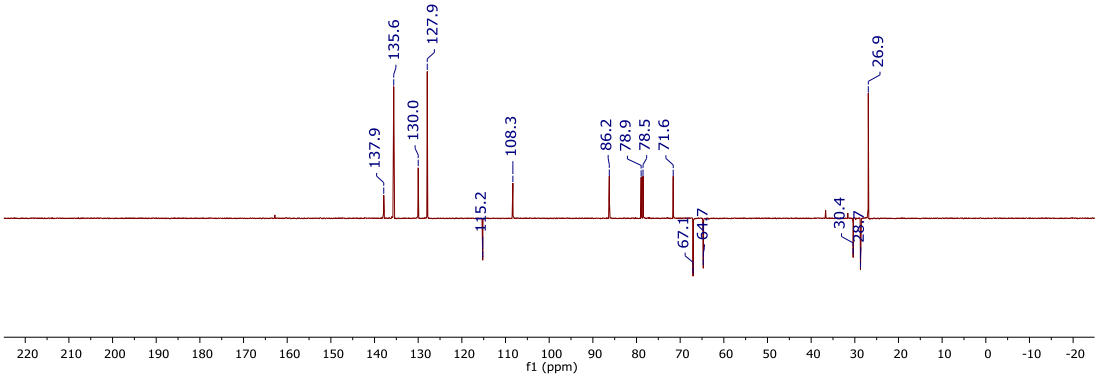
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **31**



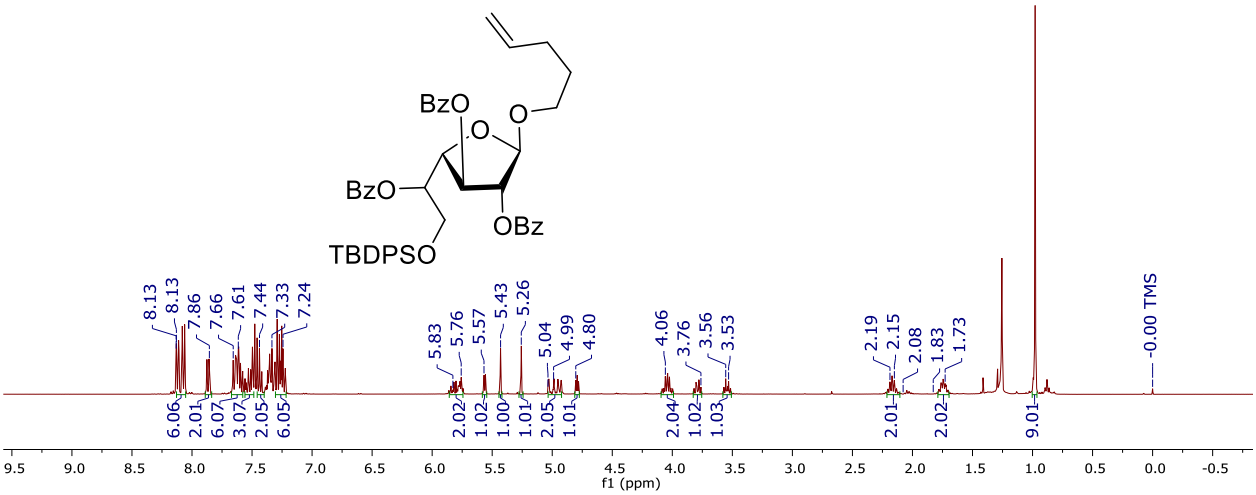
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**31**



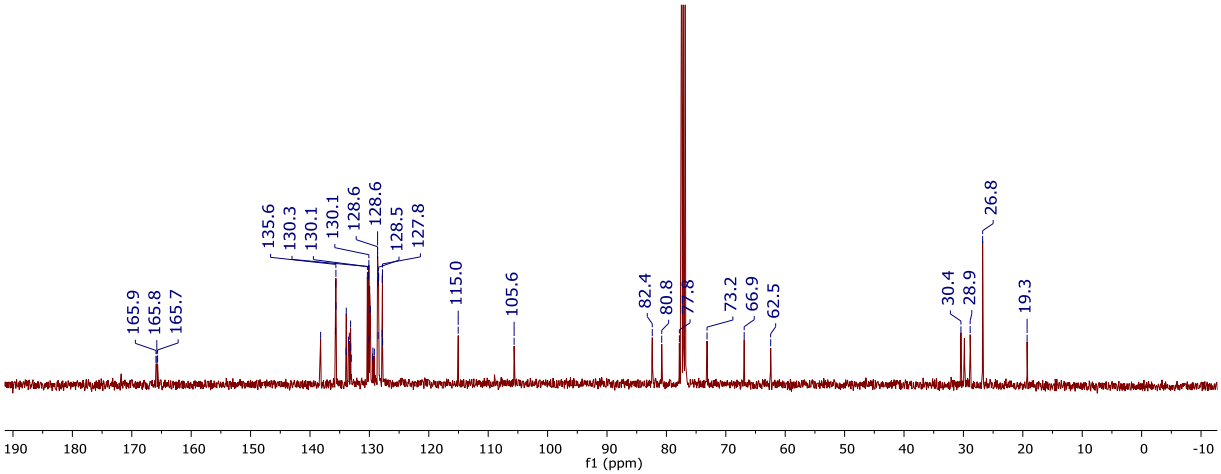
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**31**



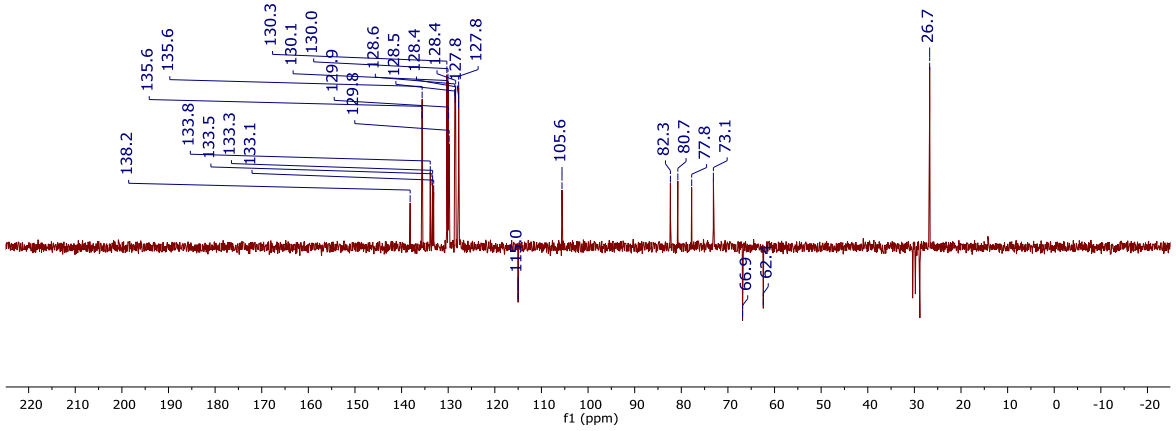
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **32**



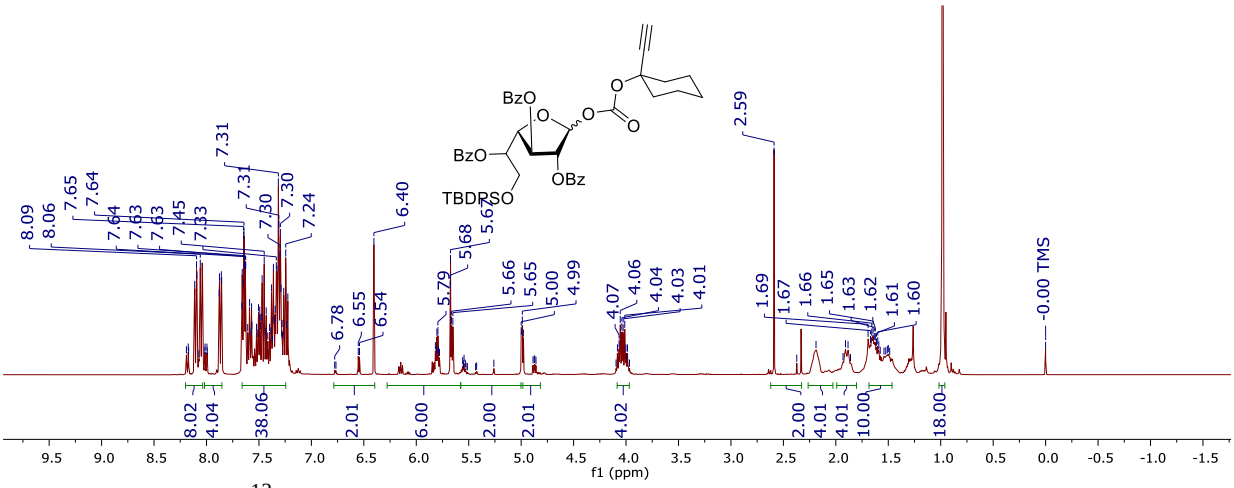
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**32**



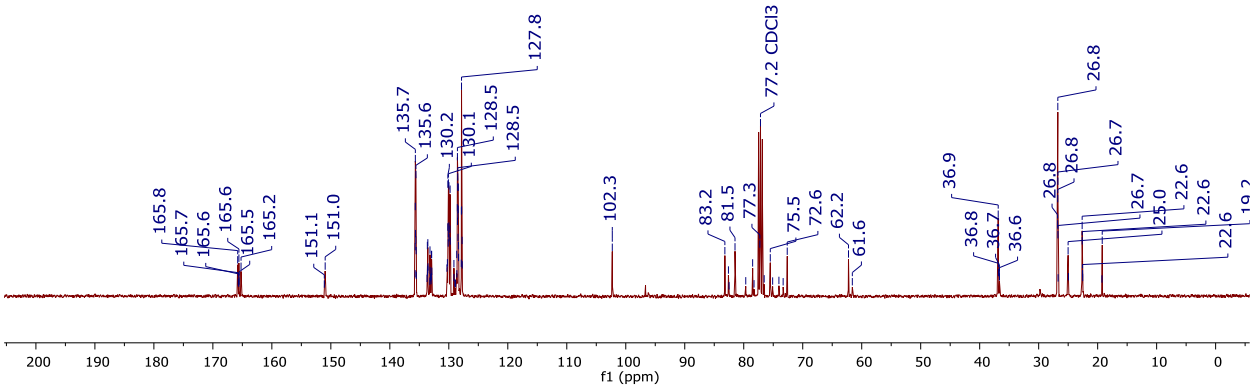
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**32**



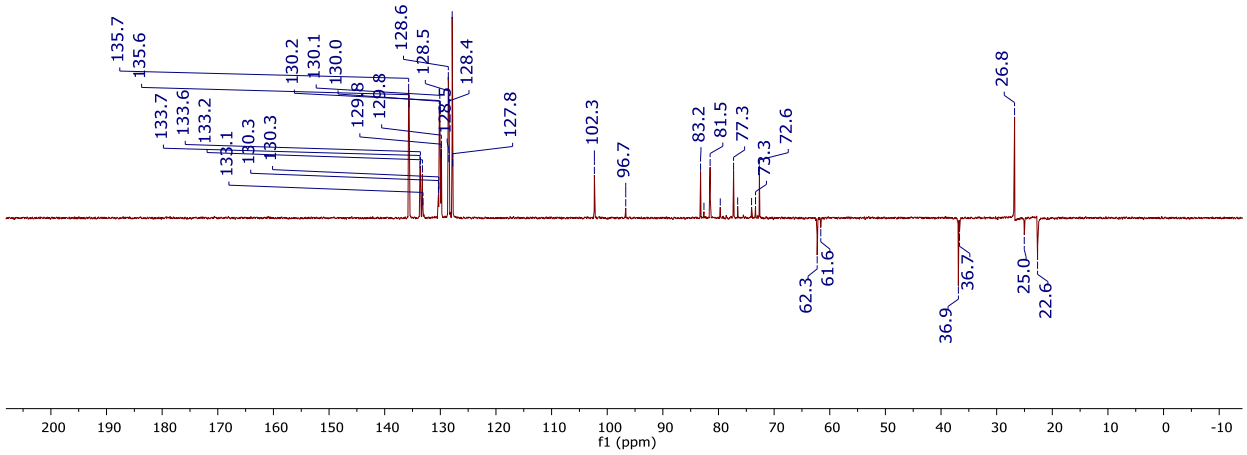
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **8**



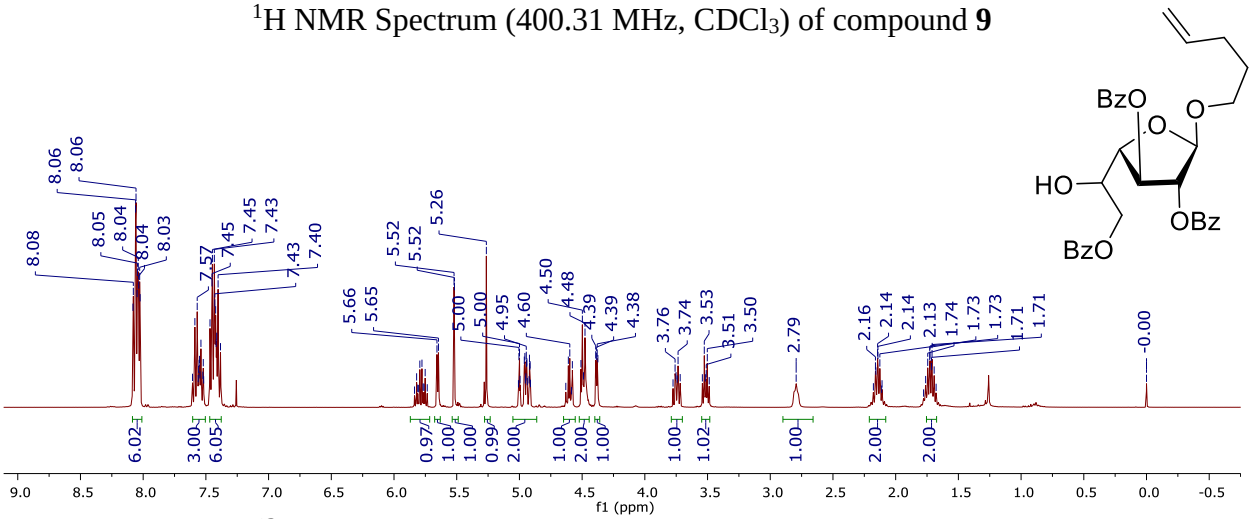
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**8**



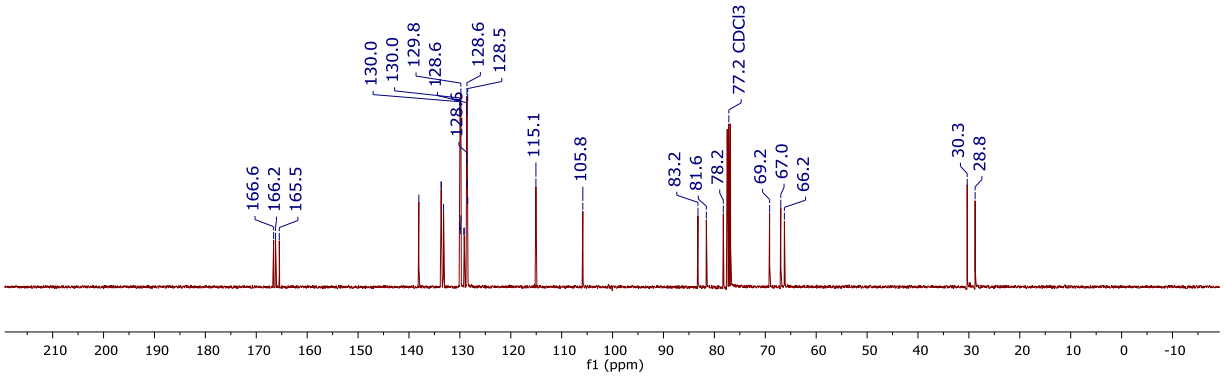
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**8**



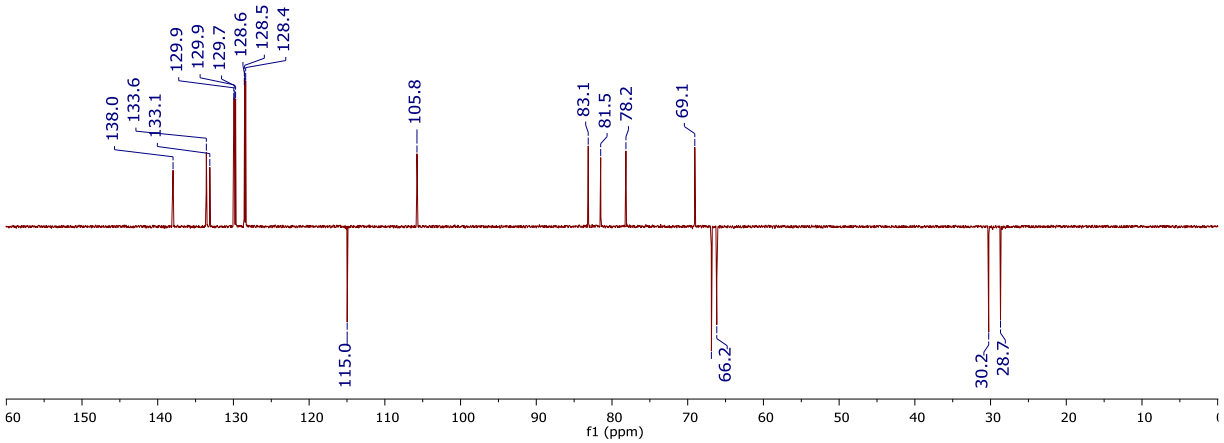
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **9**



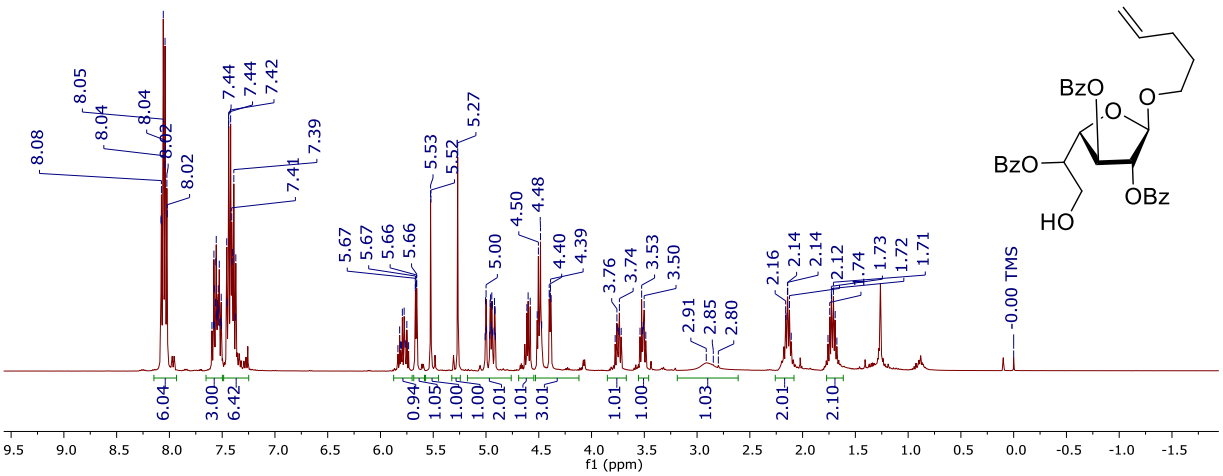
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**9**



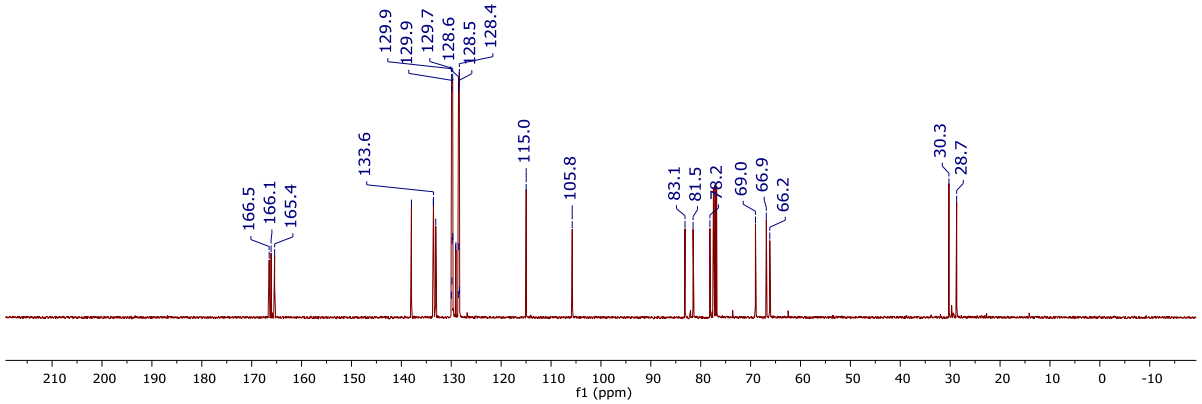
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**9**



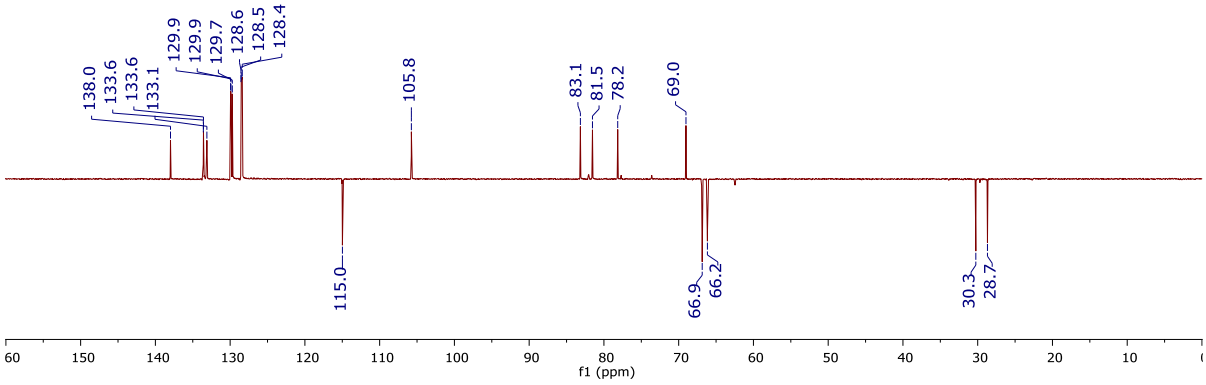
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **9a**



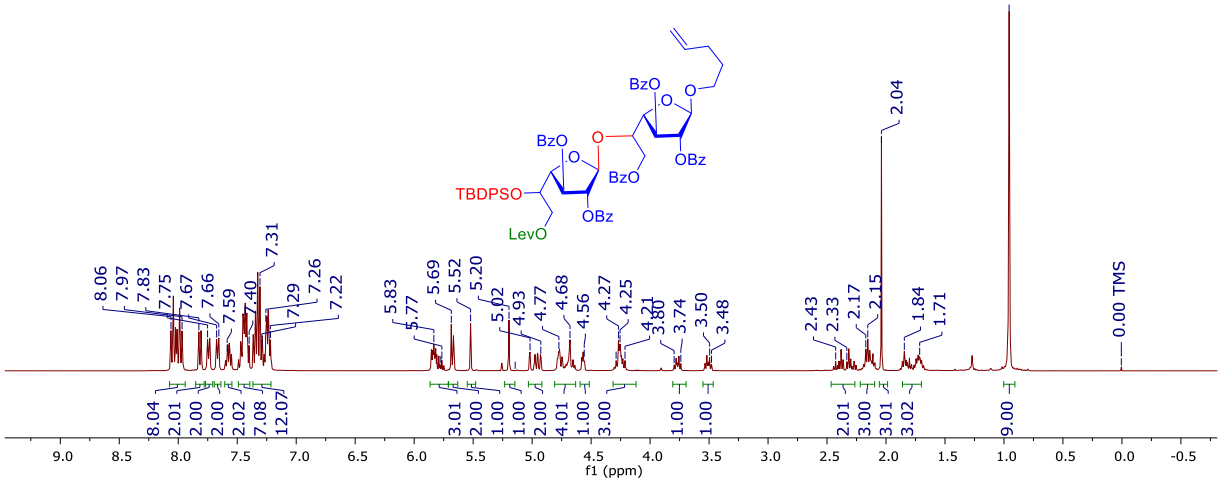
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**9**



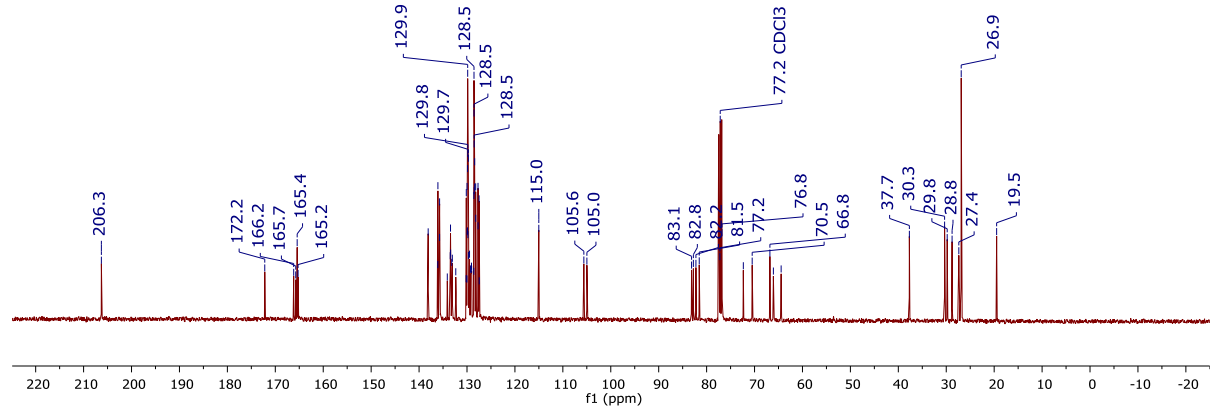
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**9**



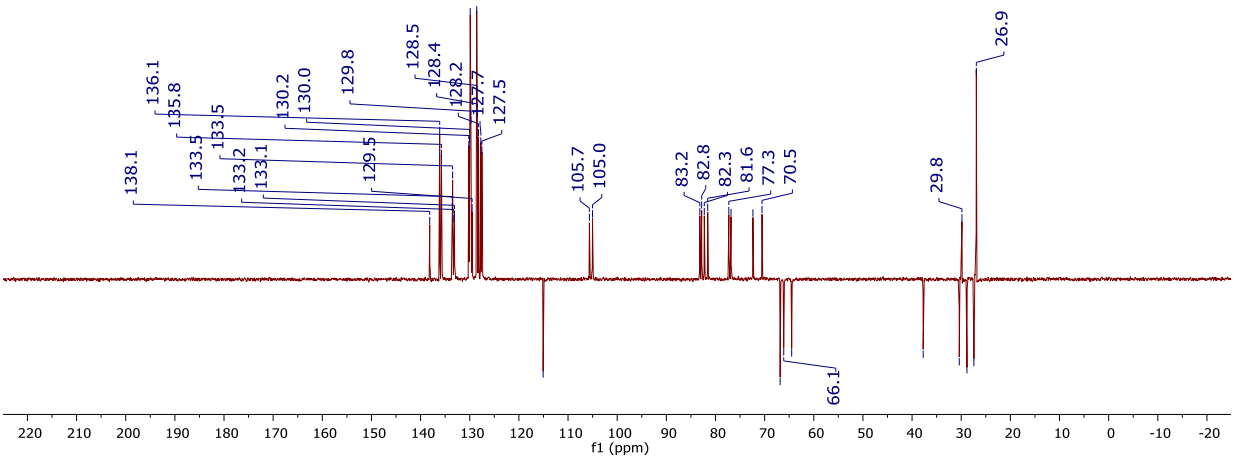
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**33**



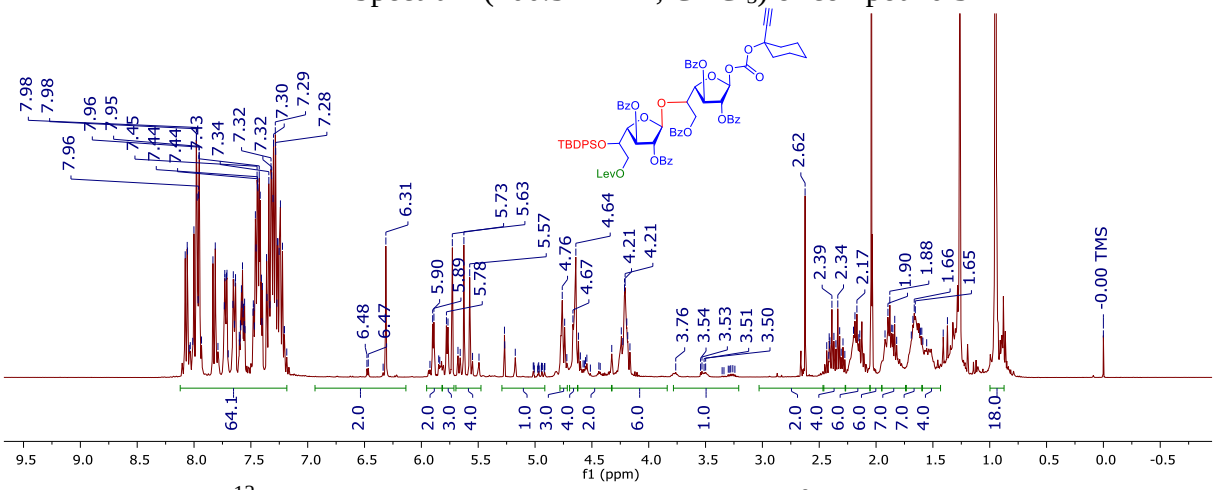
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**33**



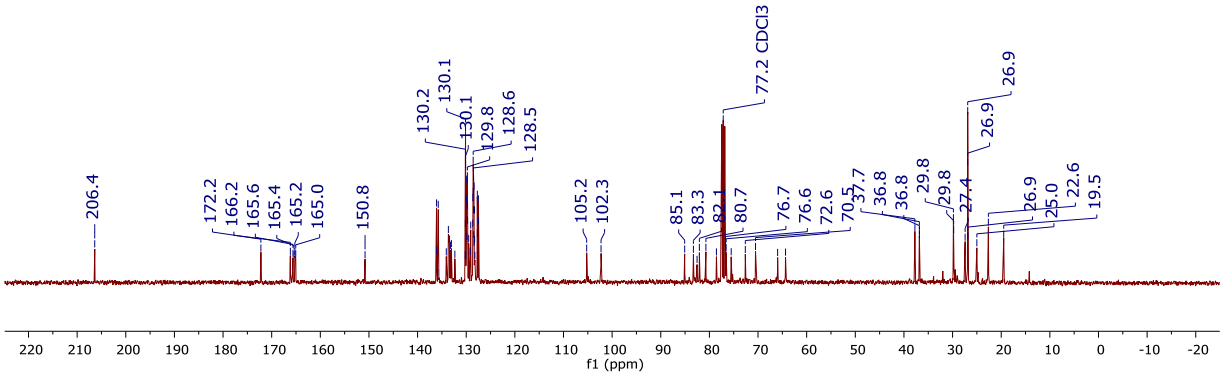
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**33**



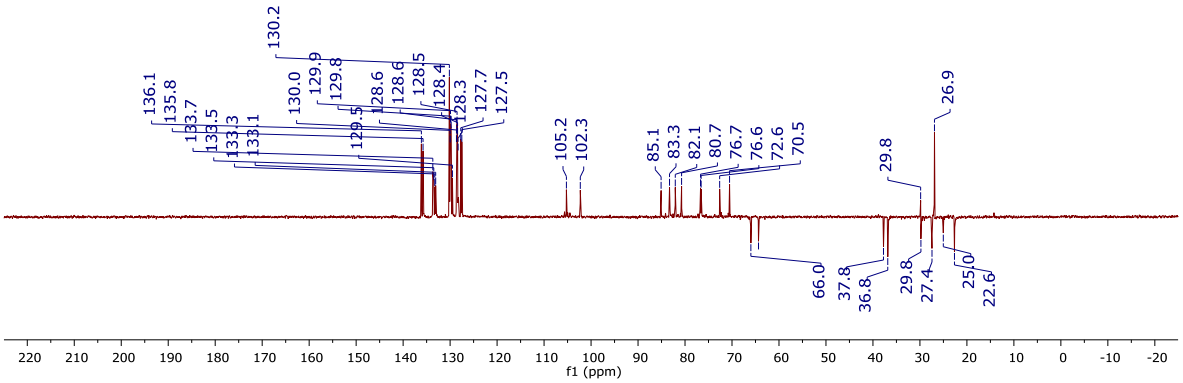
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **34**



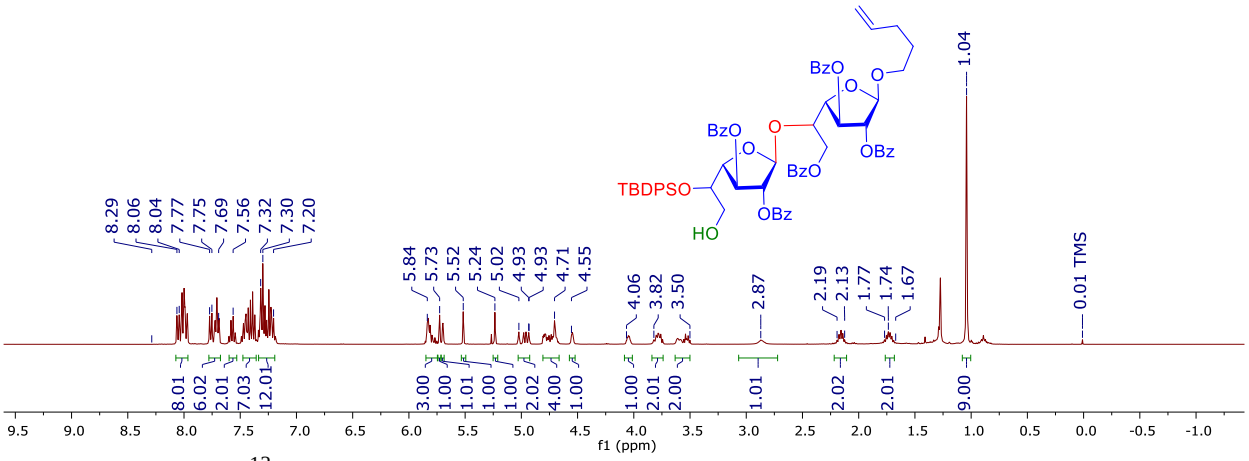
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**34**



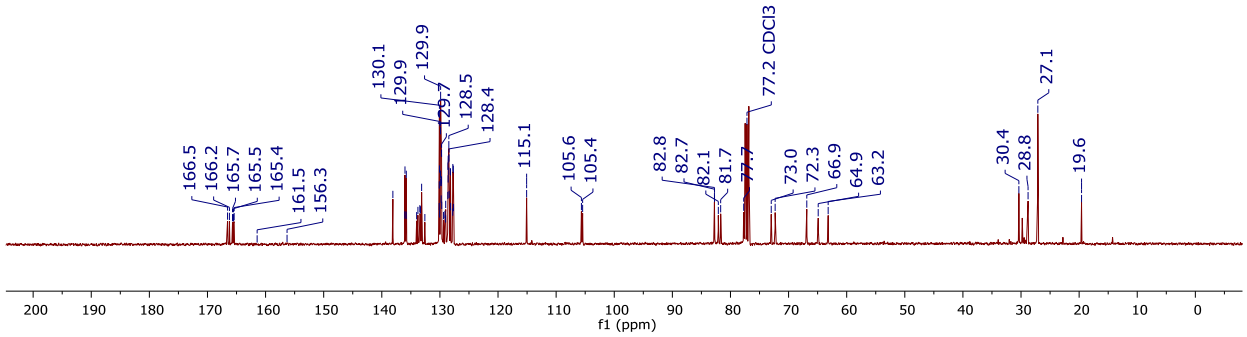
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**34**



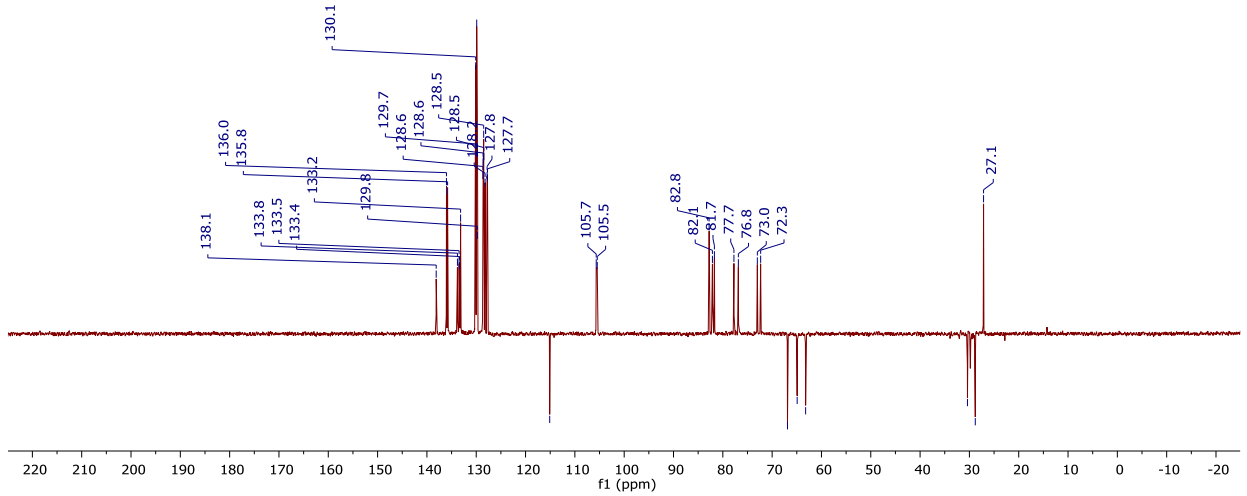
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**35**



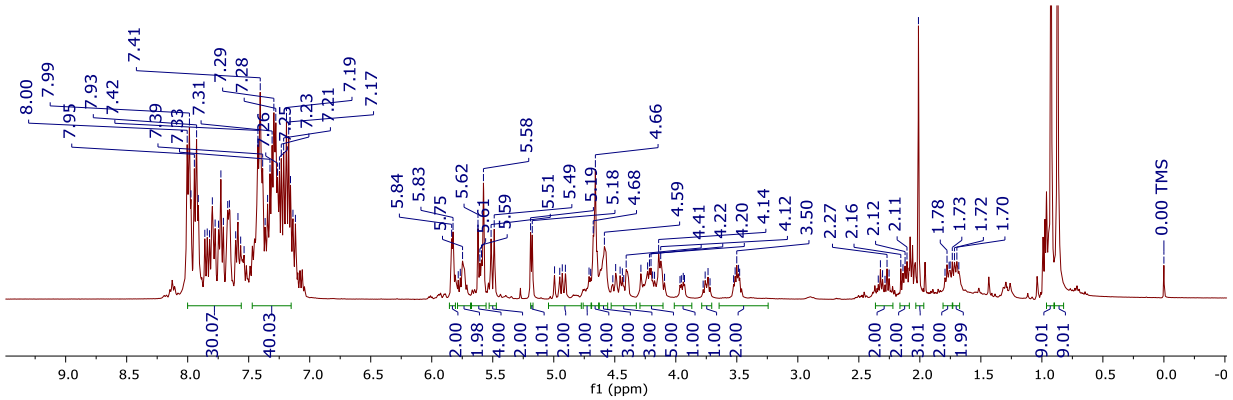
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**35**



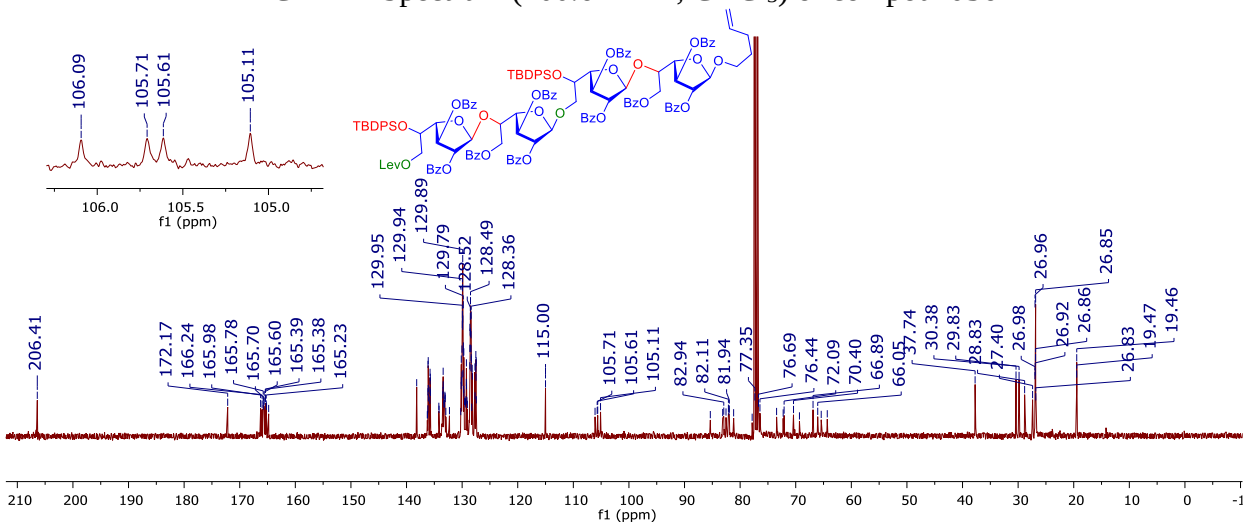
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**35**



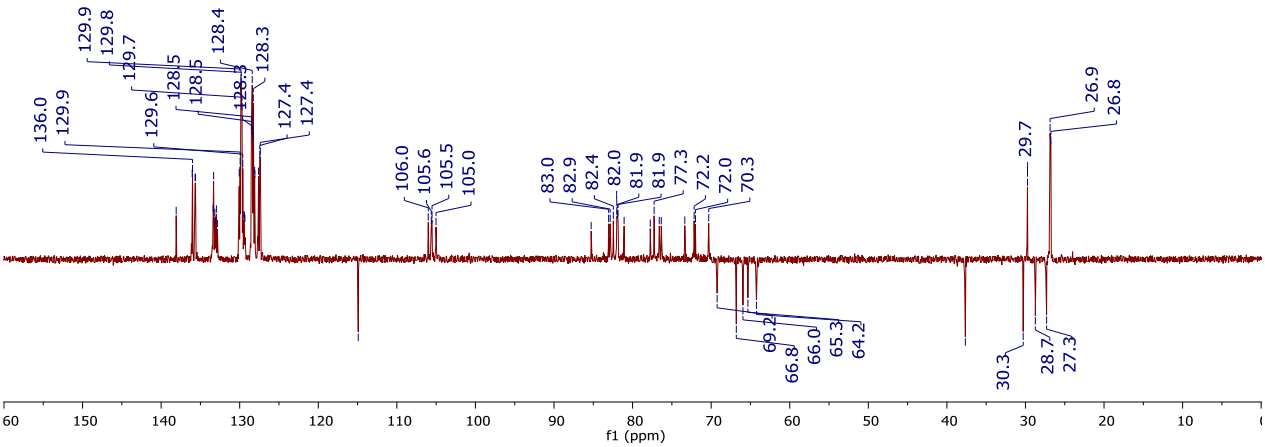
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**36**



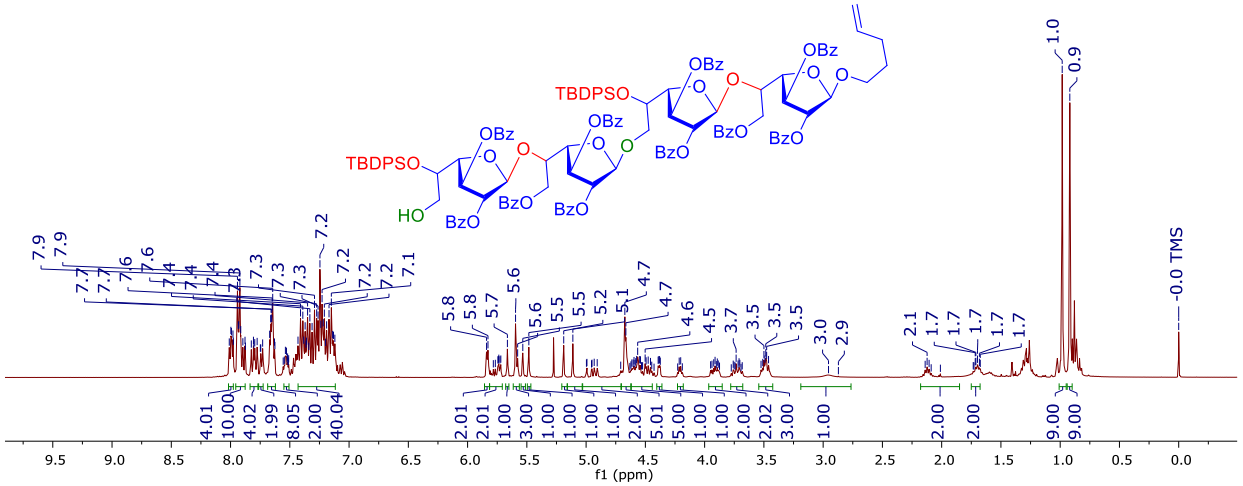
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**36**



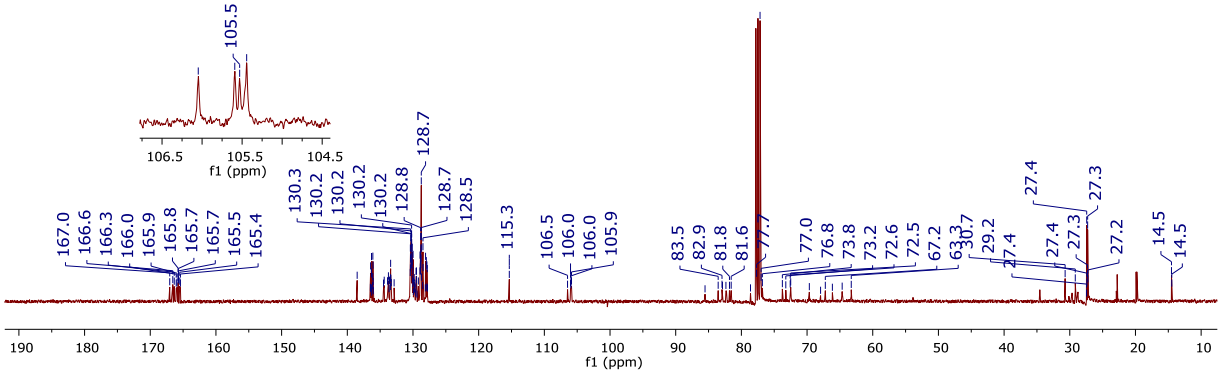
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**36**



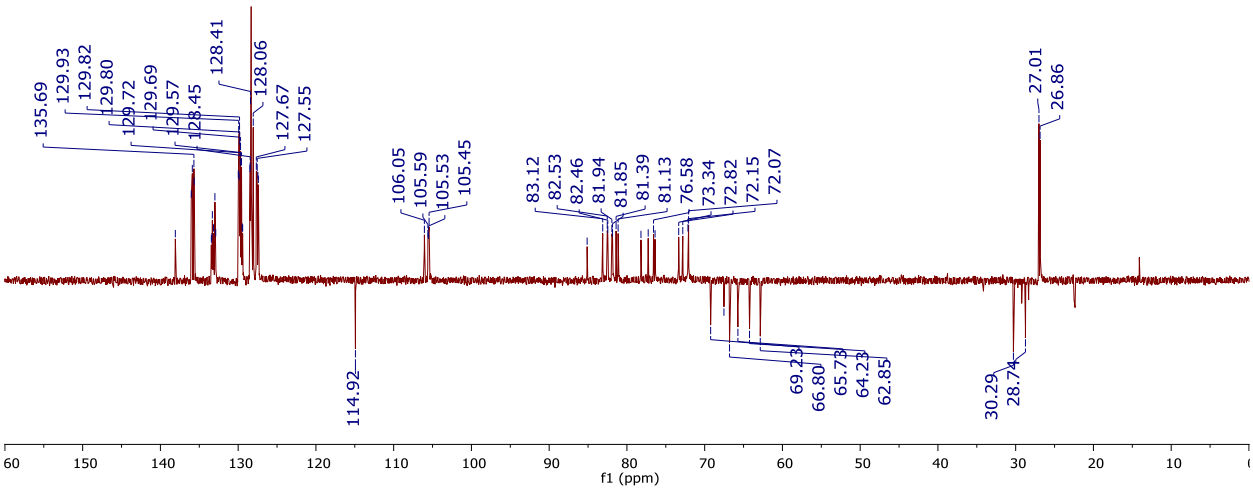
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**37**



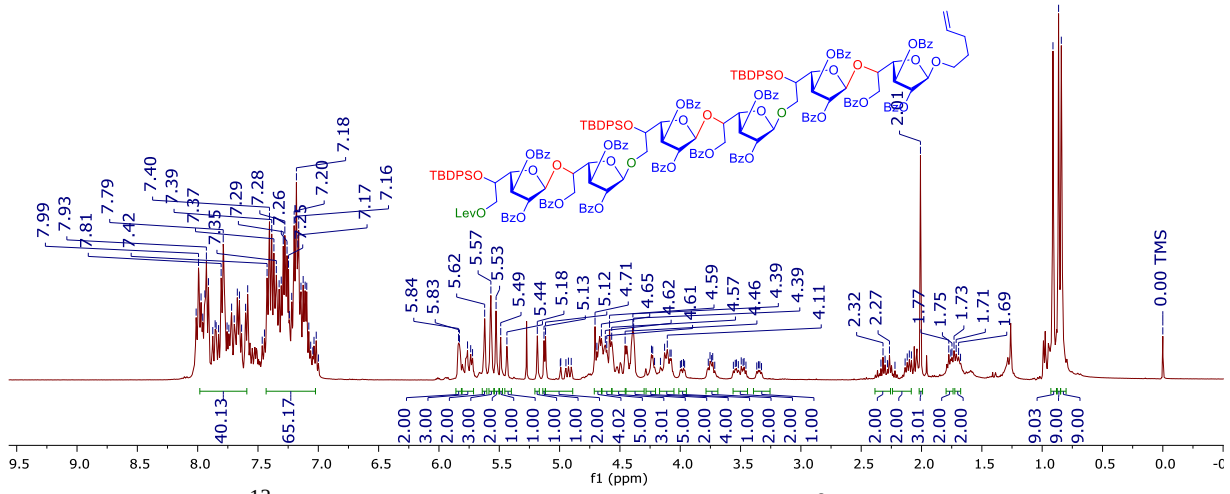
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**37**



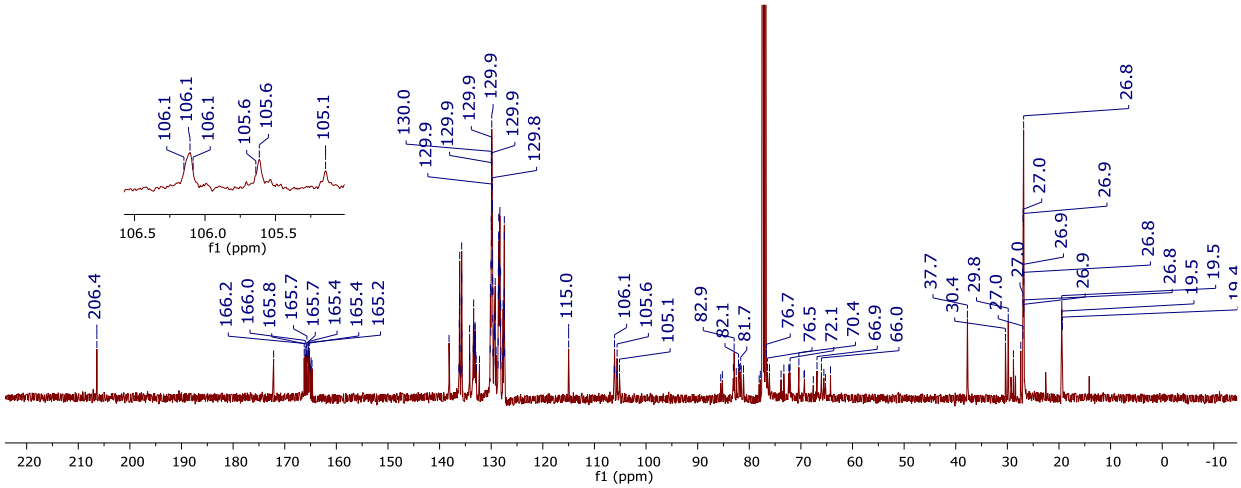
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**37**



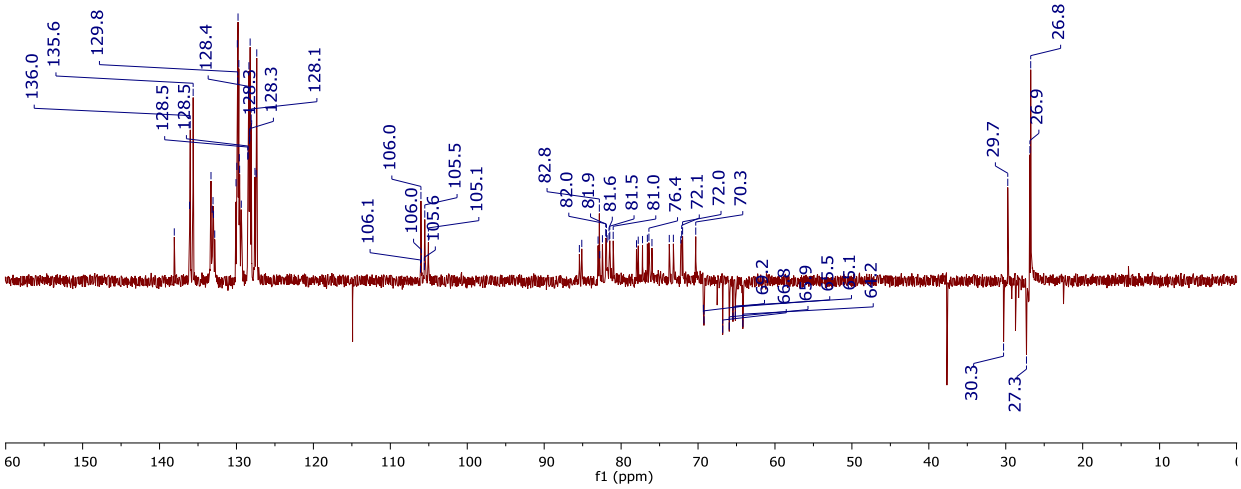
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**5**



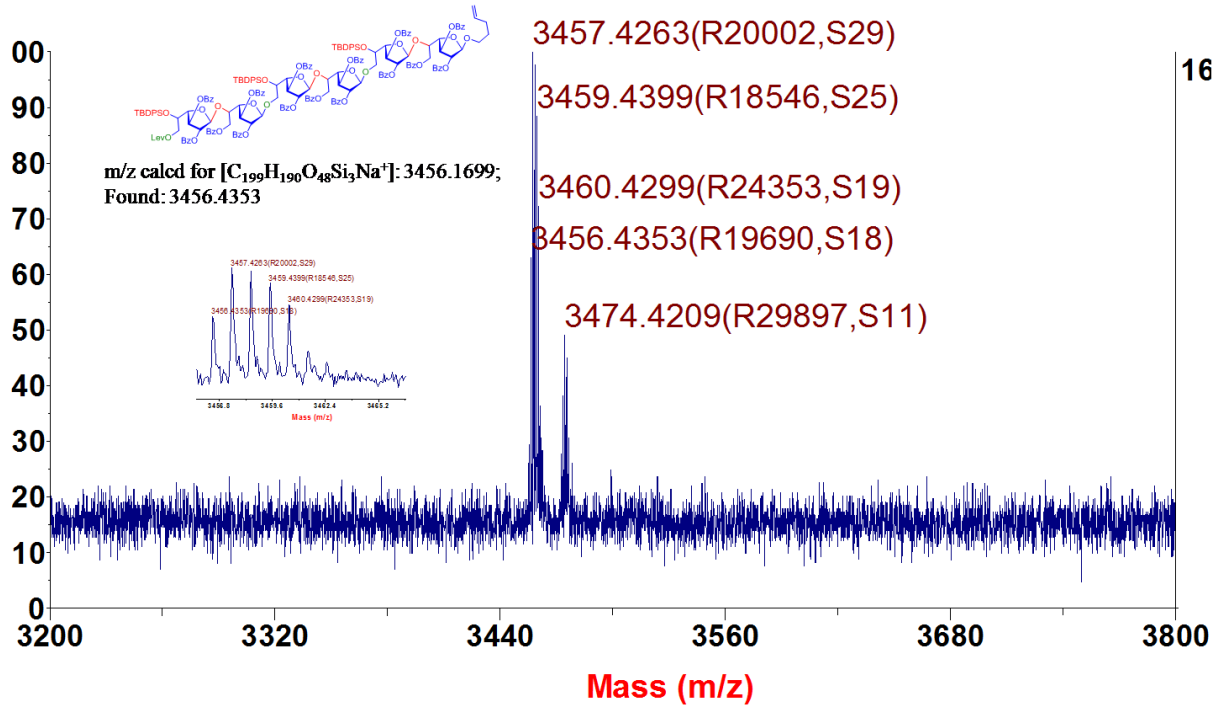
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**5**



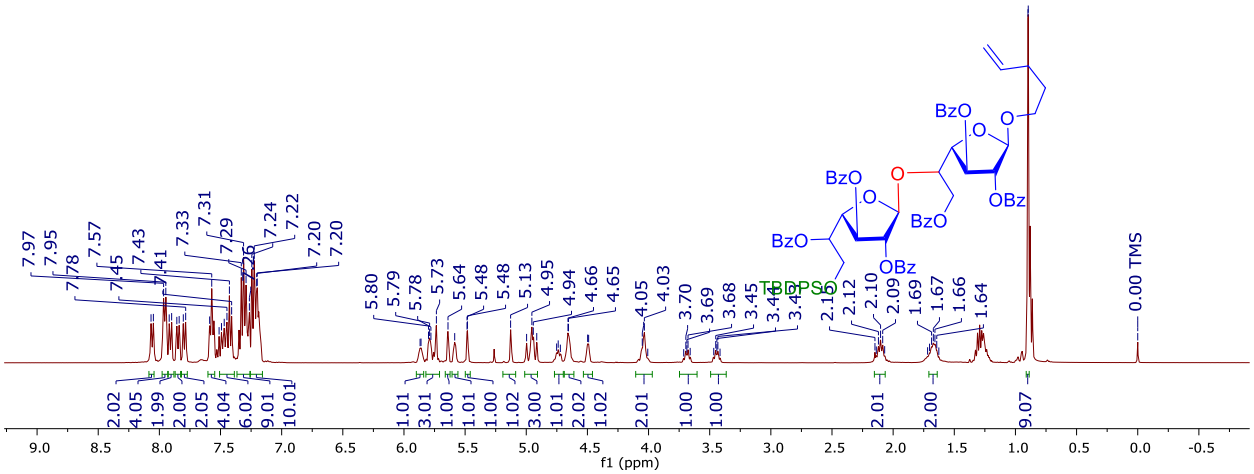
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**5**



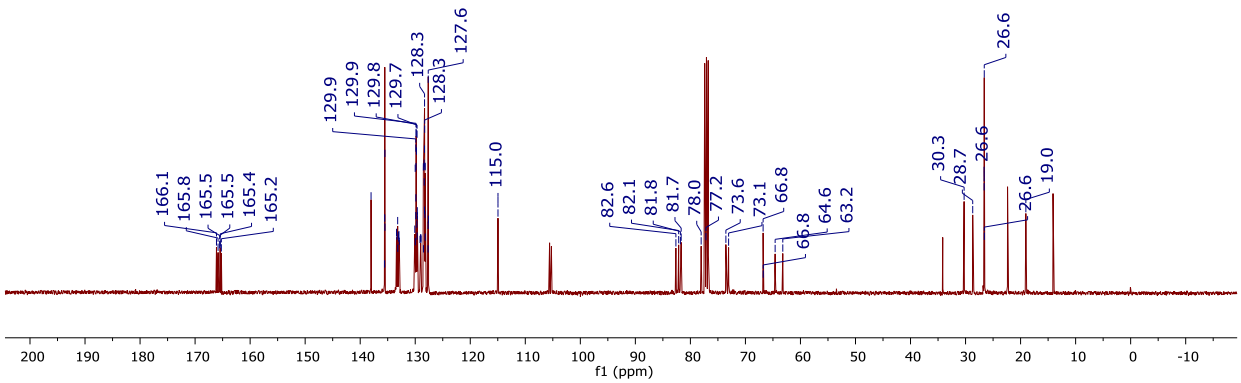
MALDI-TOF Spectrum of compound **5**



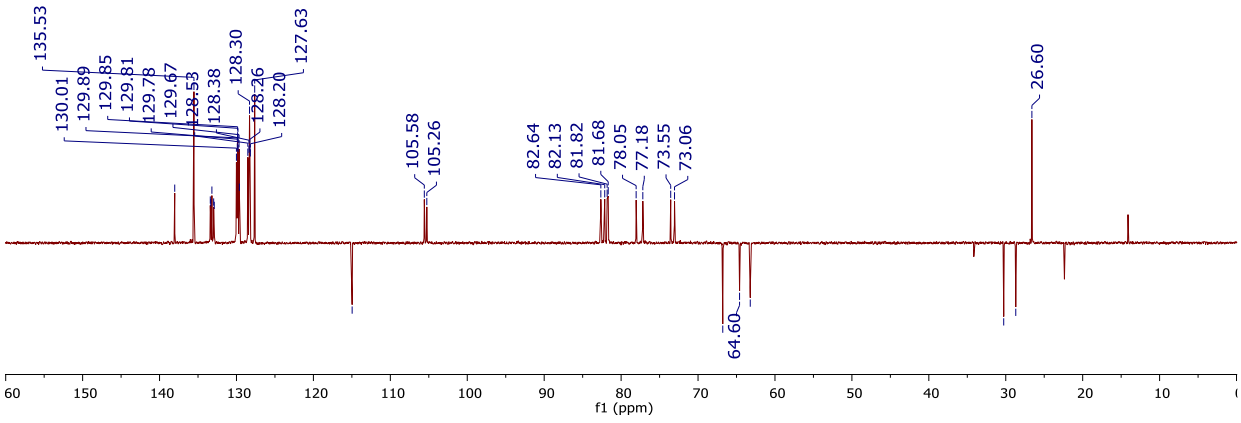
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**38**



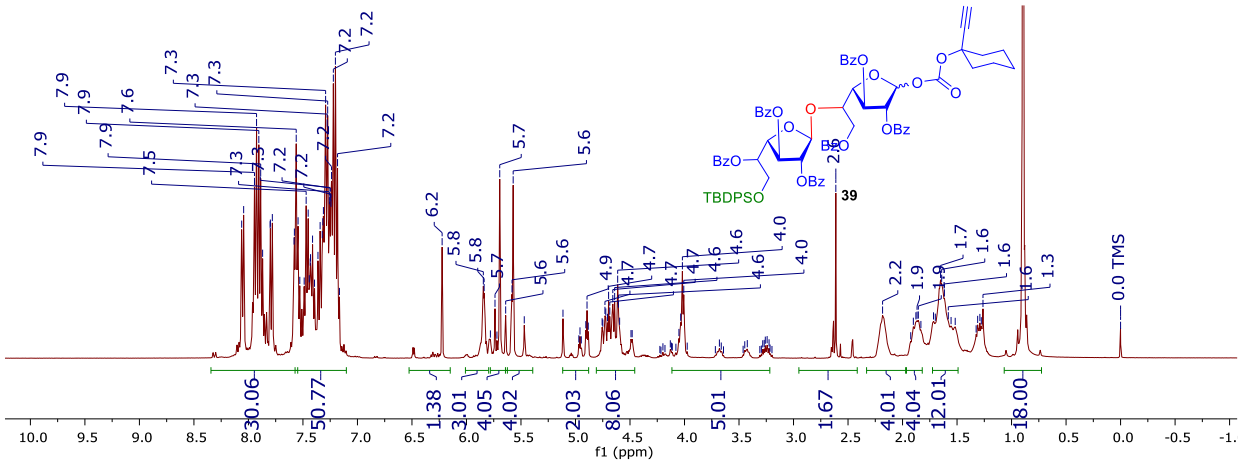
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**38**



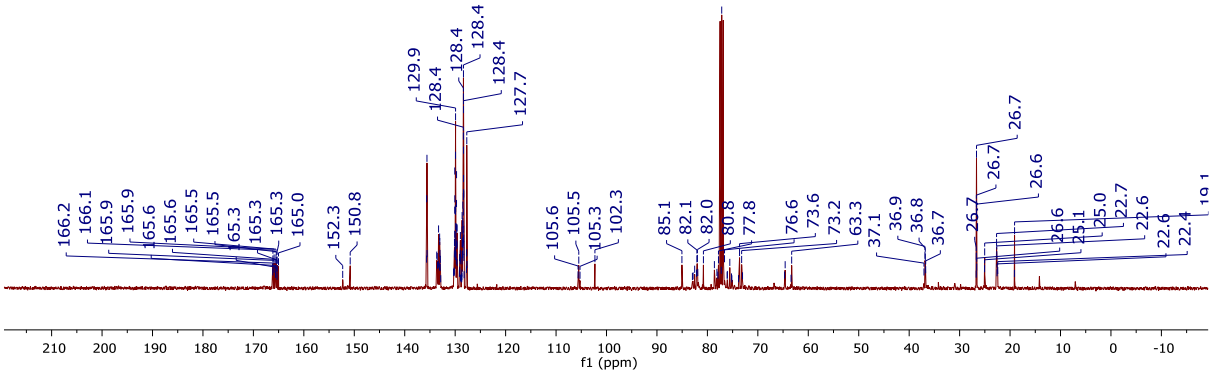
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**38**



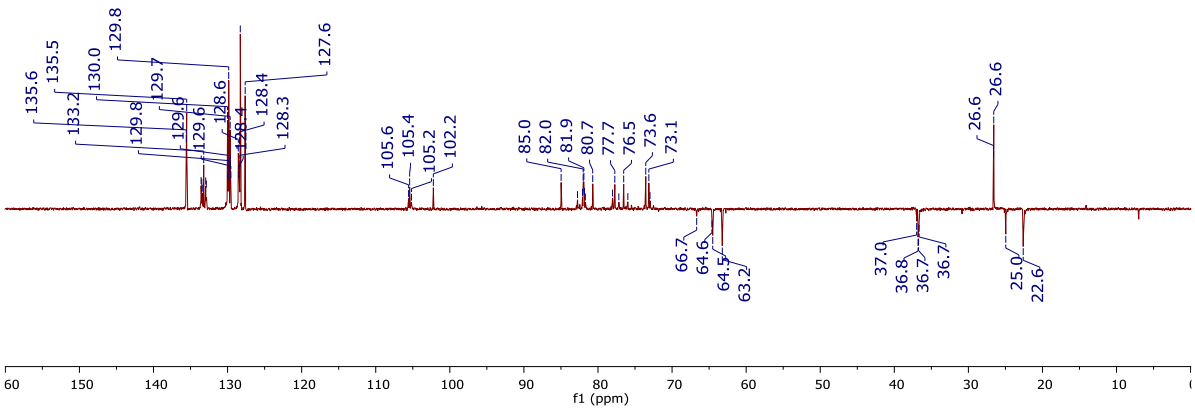
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**39**



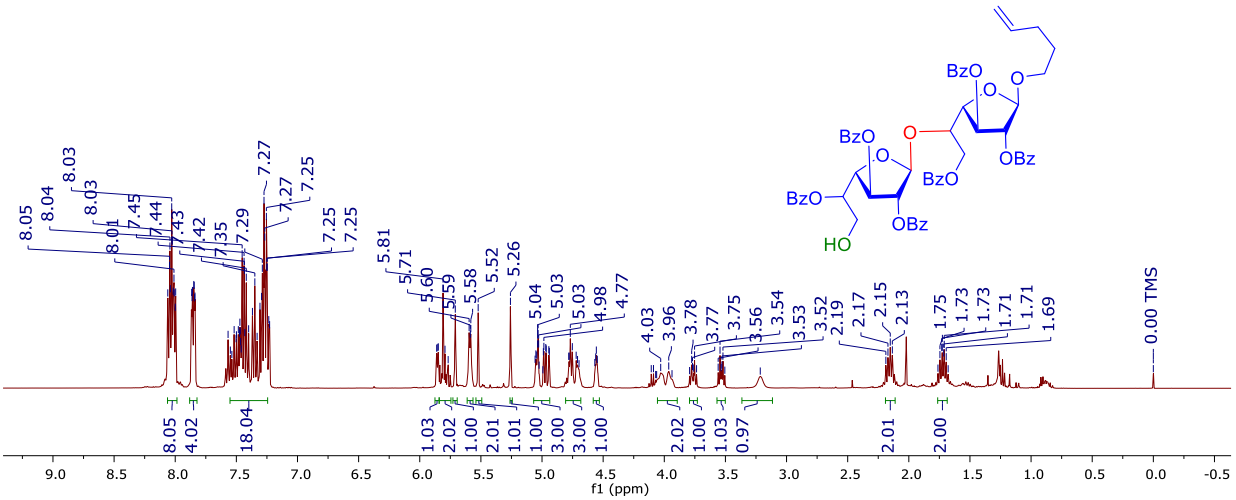
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**39**



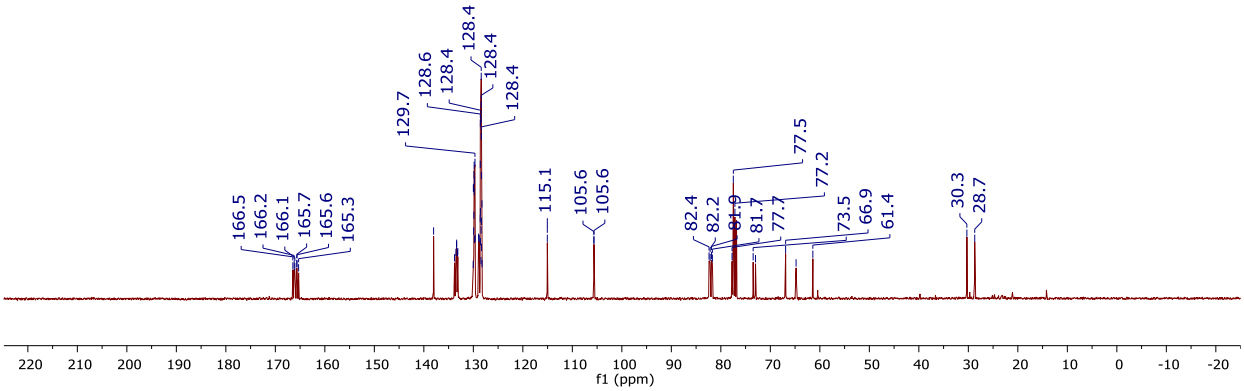
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**39**



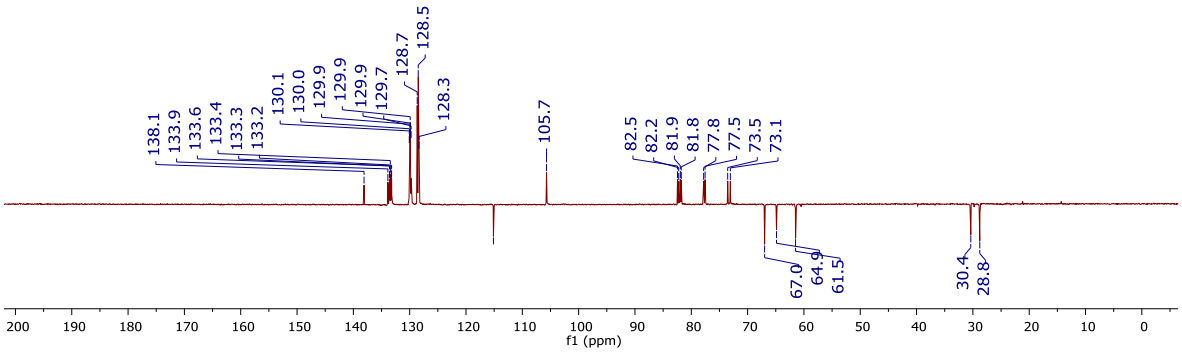
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound **40**



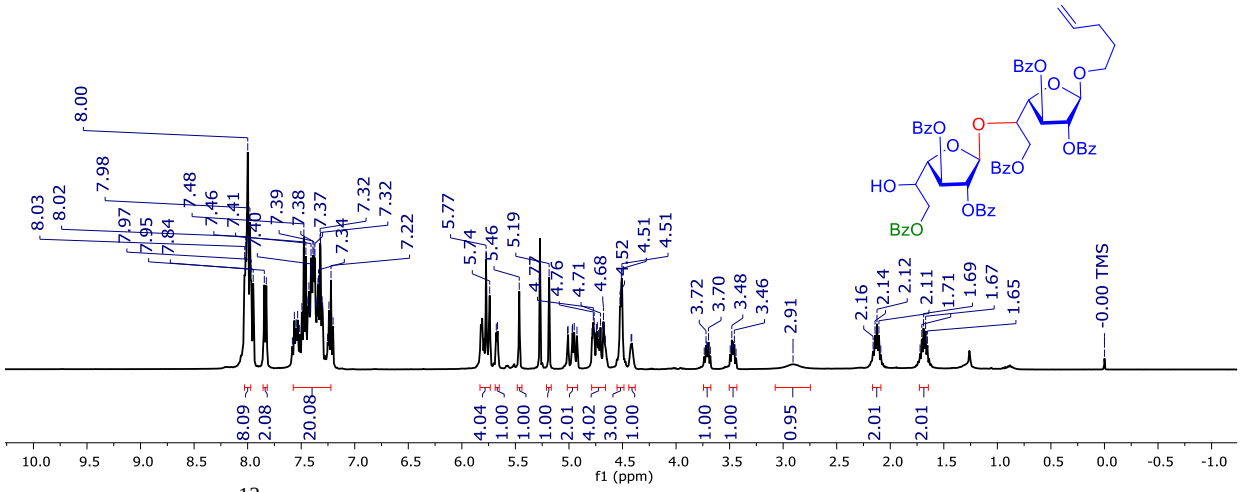
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**40**



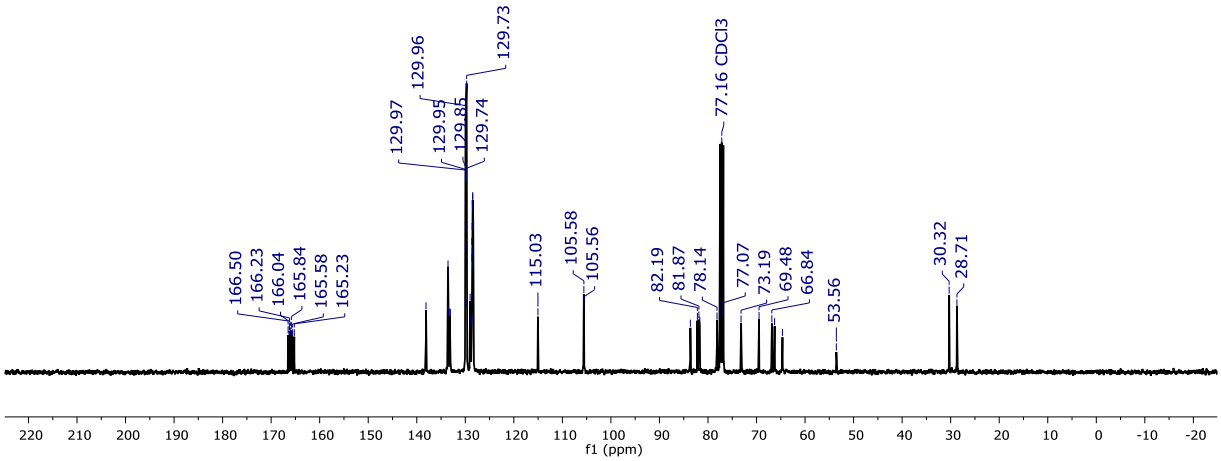
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**40**



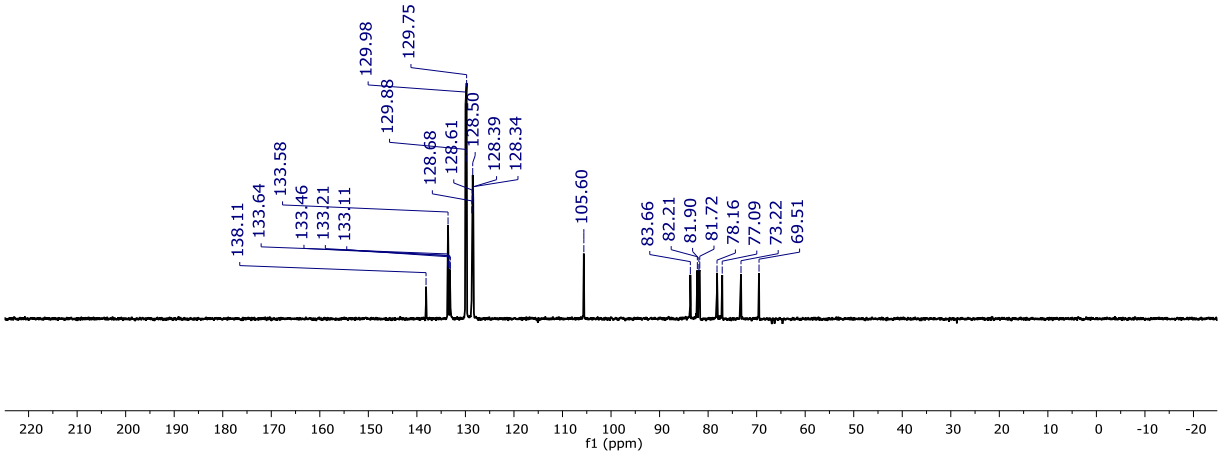
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**40a**



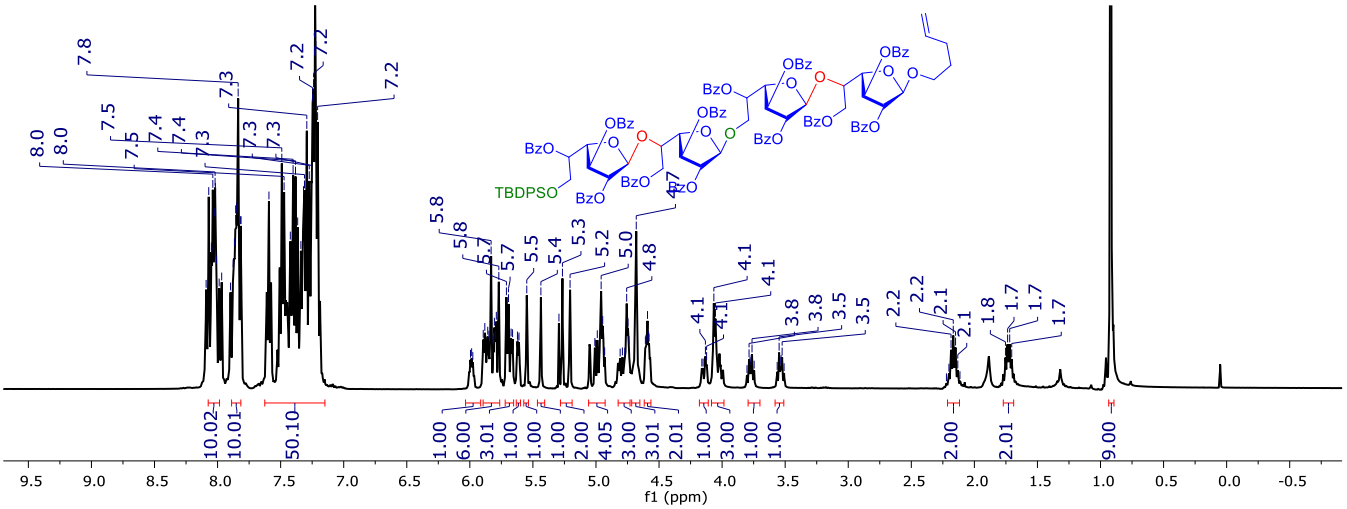
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**40a**



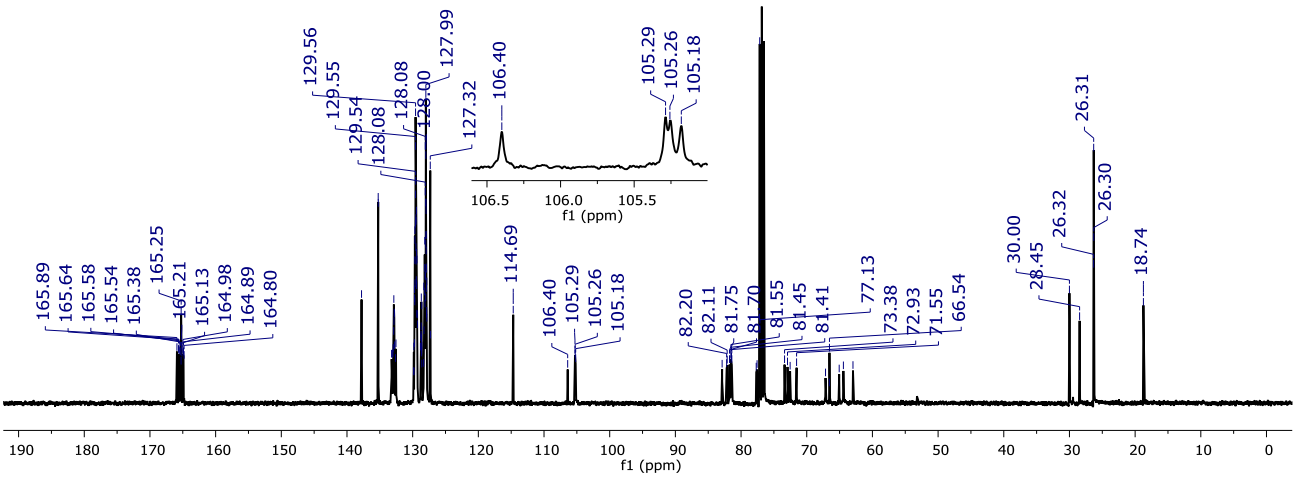
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound **40a**



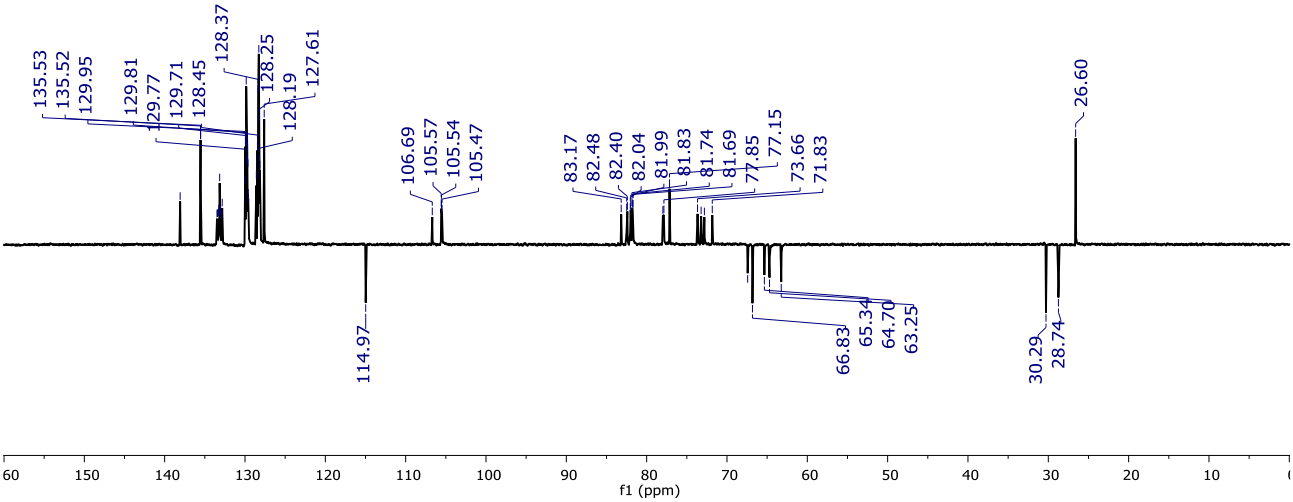
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**41**



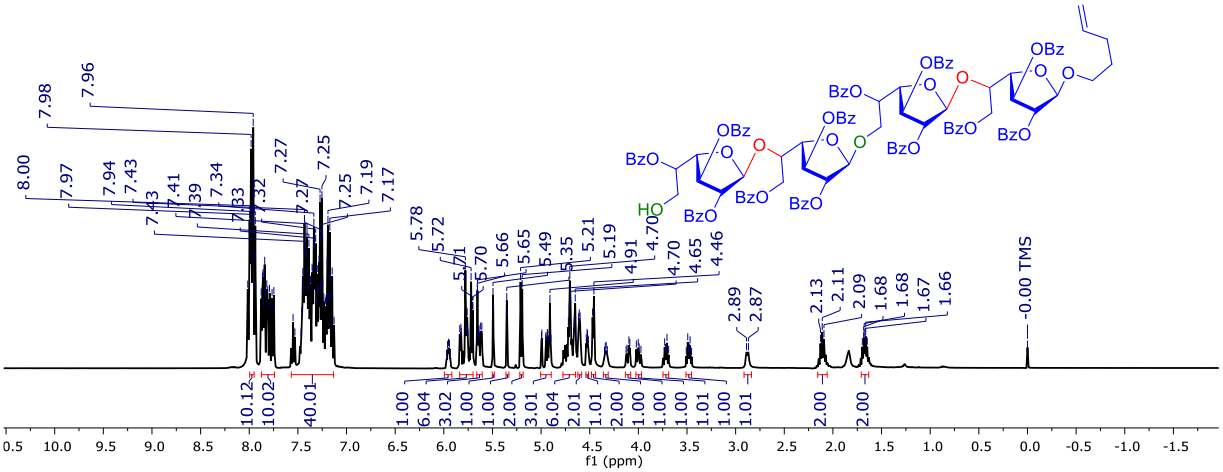
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**41**



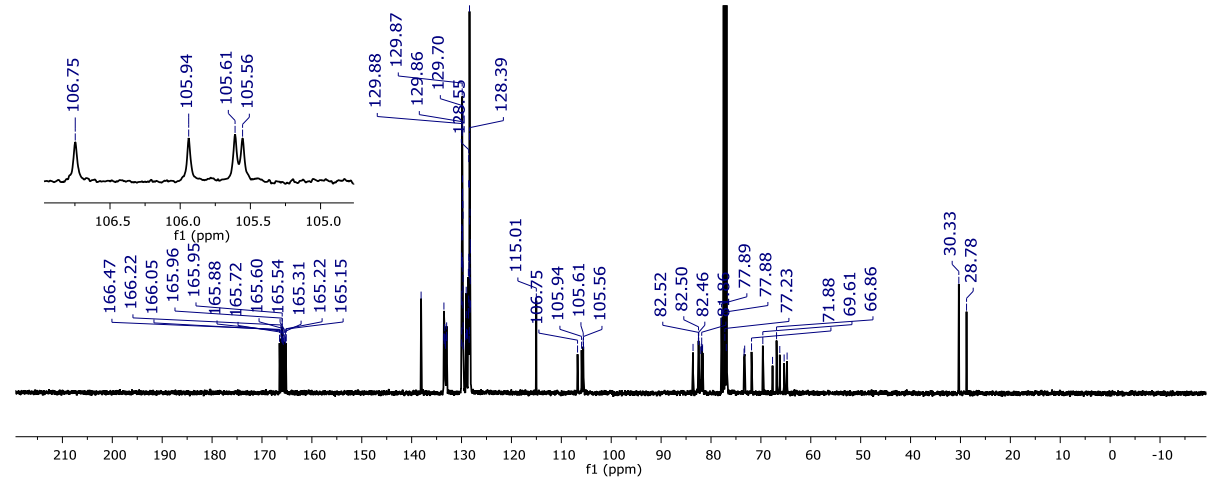
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**41**



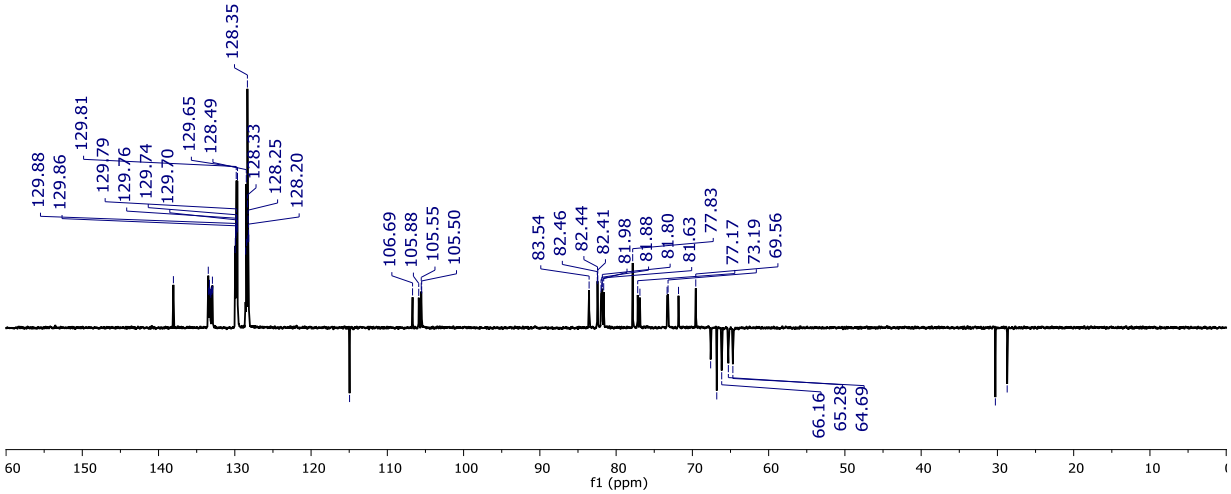
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**42**



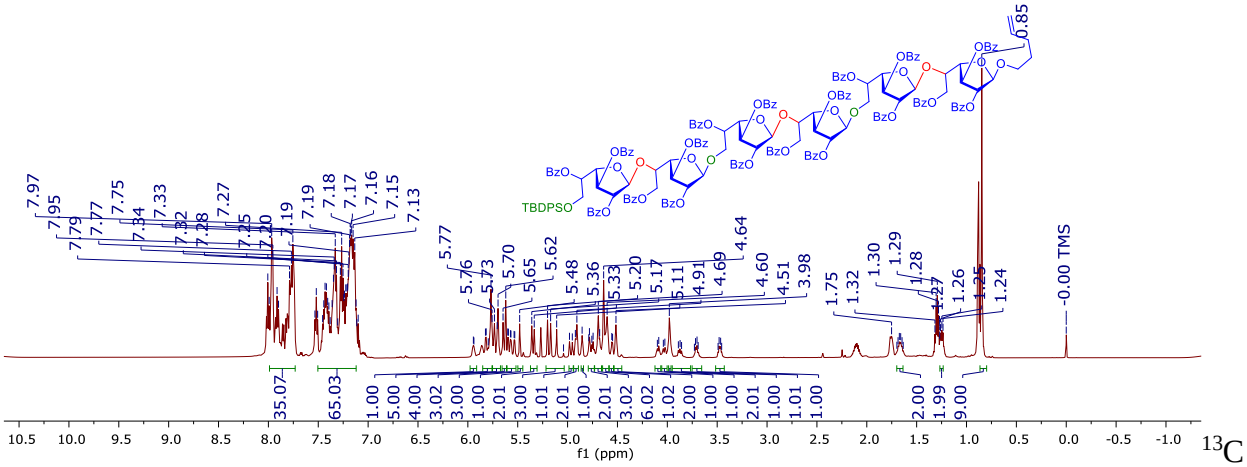
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**42**



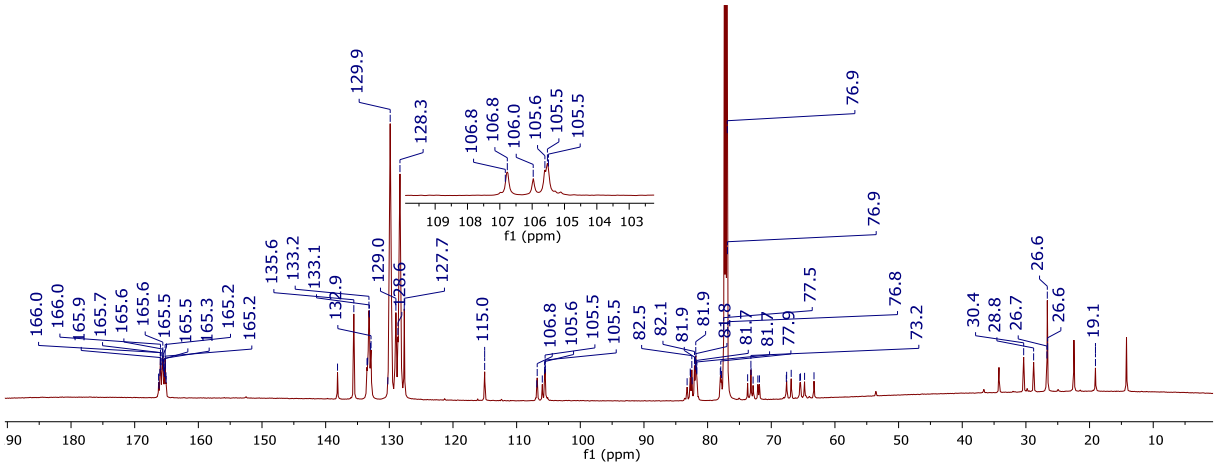
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**42**



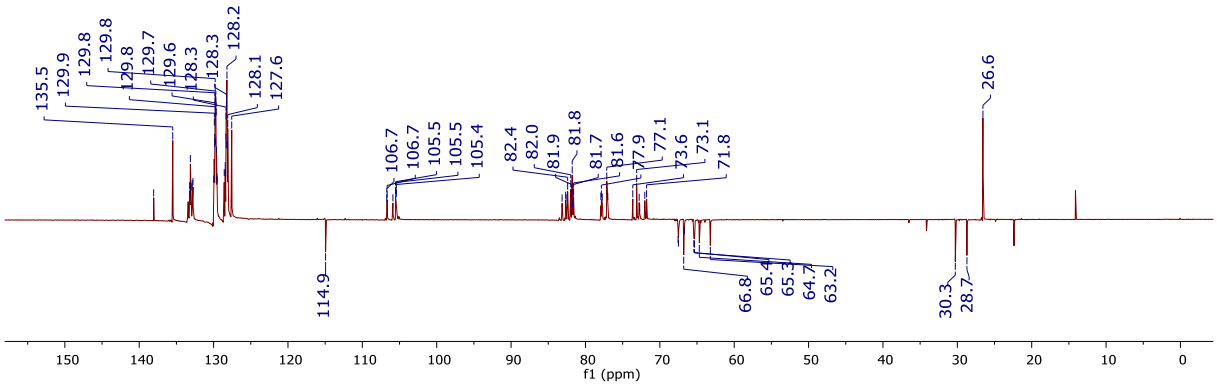
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**6**



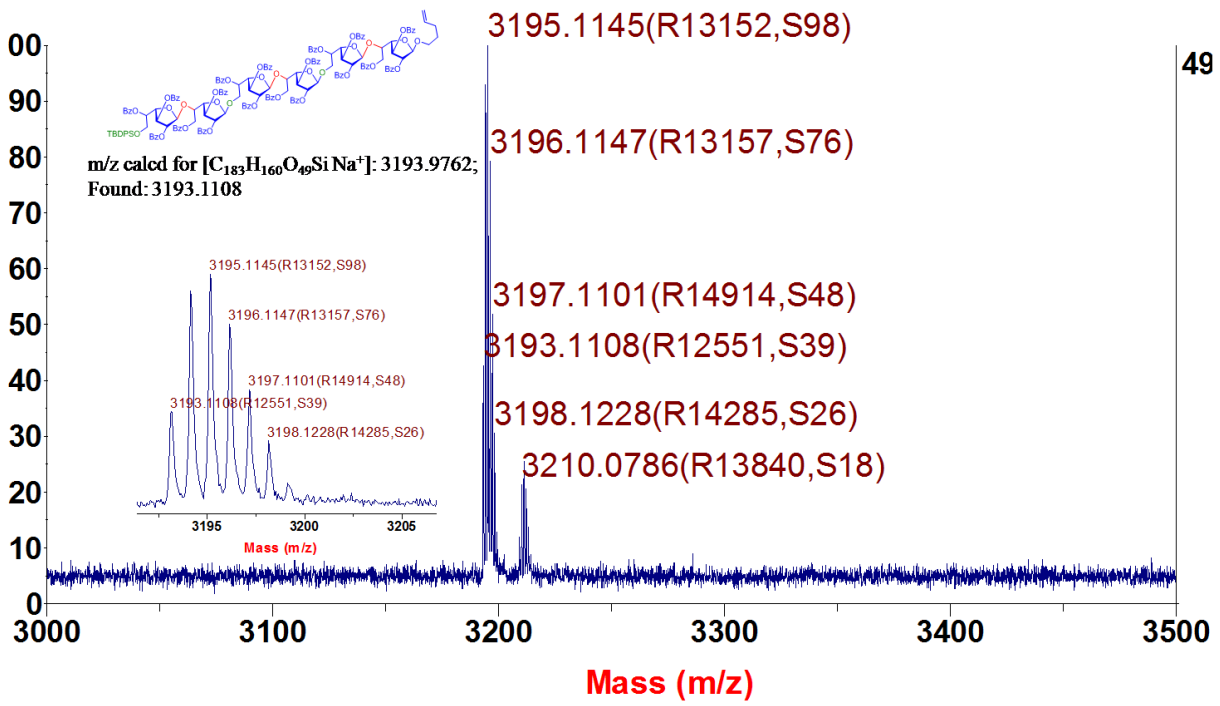
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**6**



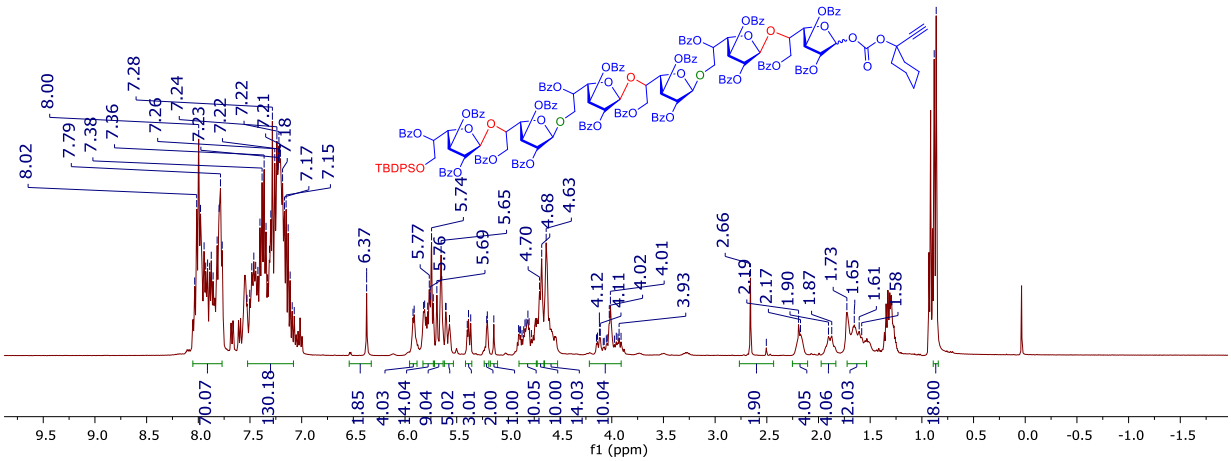
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**6**



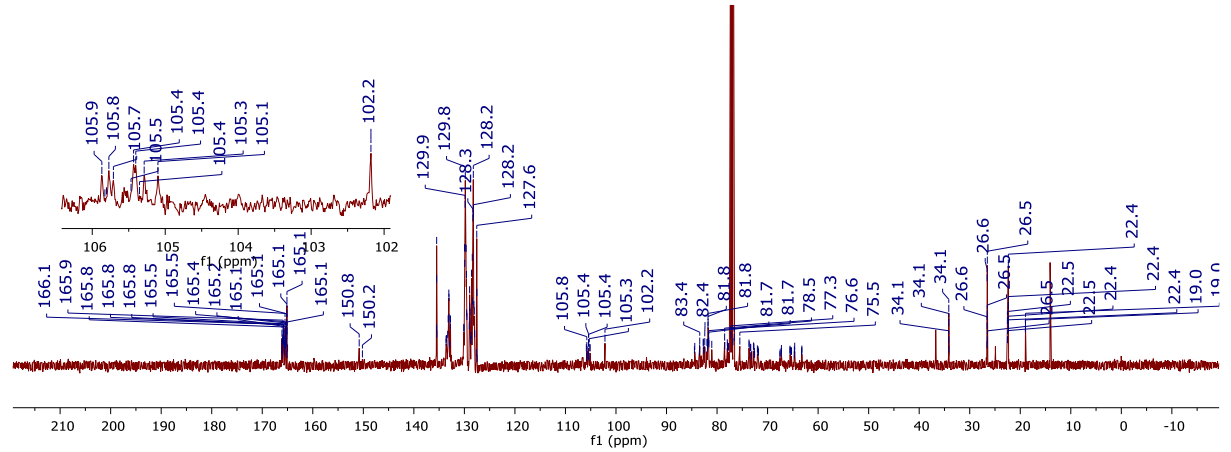
MALDI-TOF spectrum of compound **6**



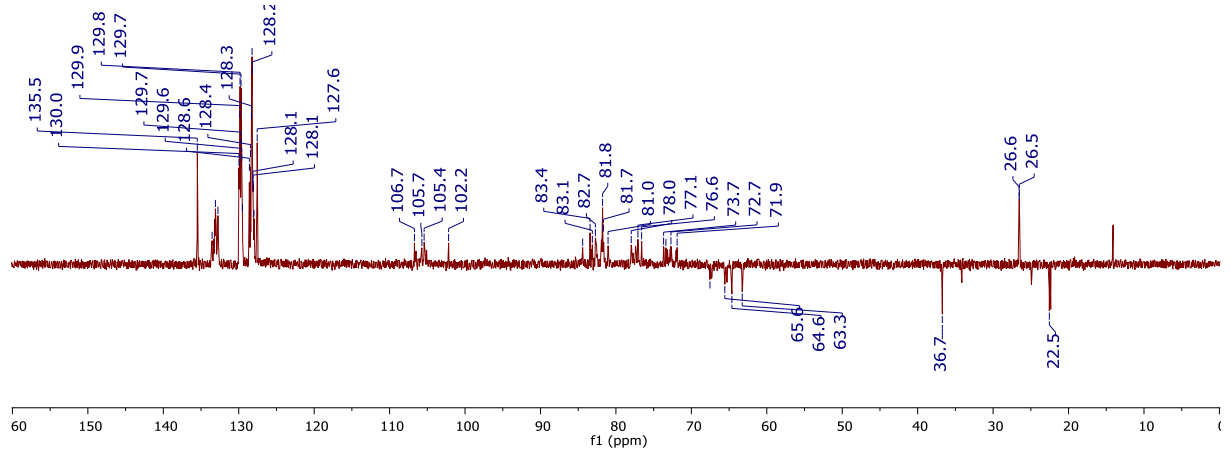
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**43**



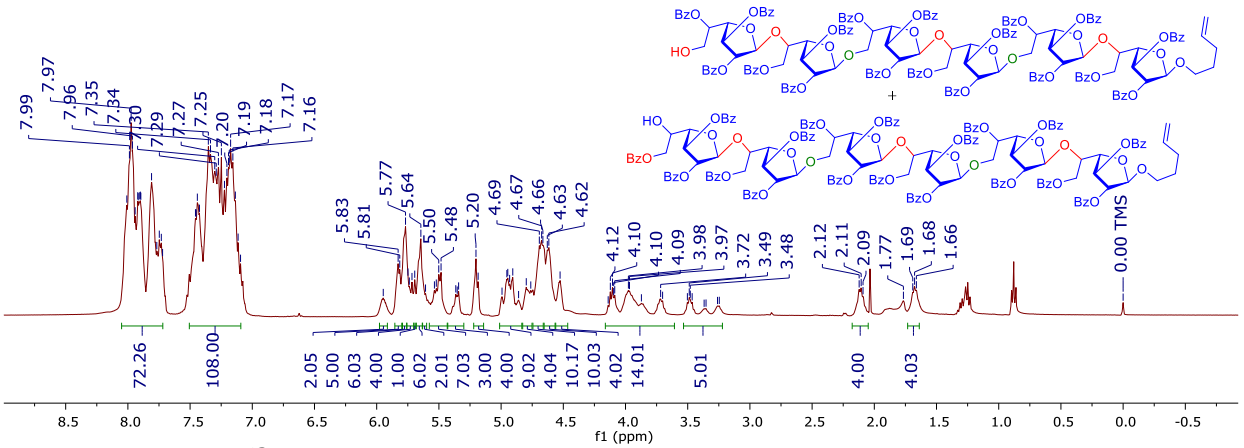
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**43**



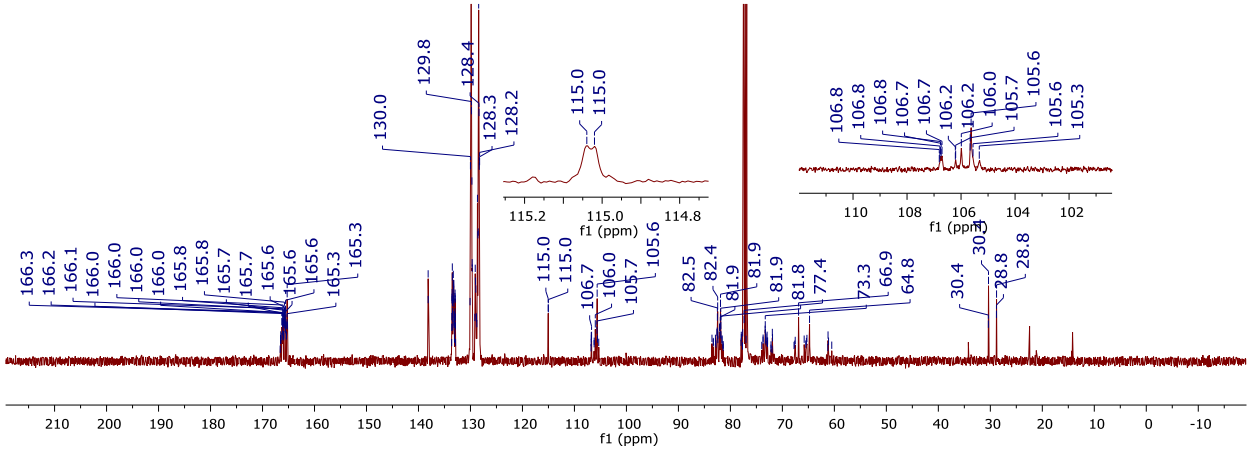
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**44**



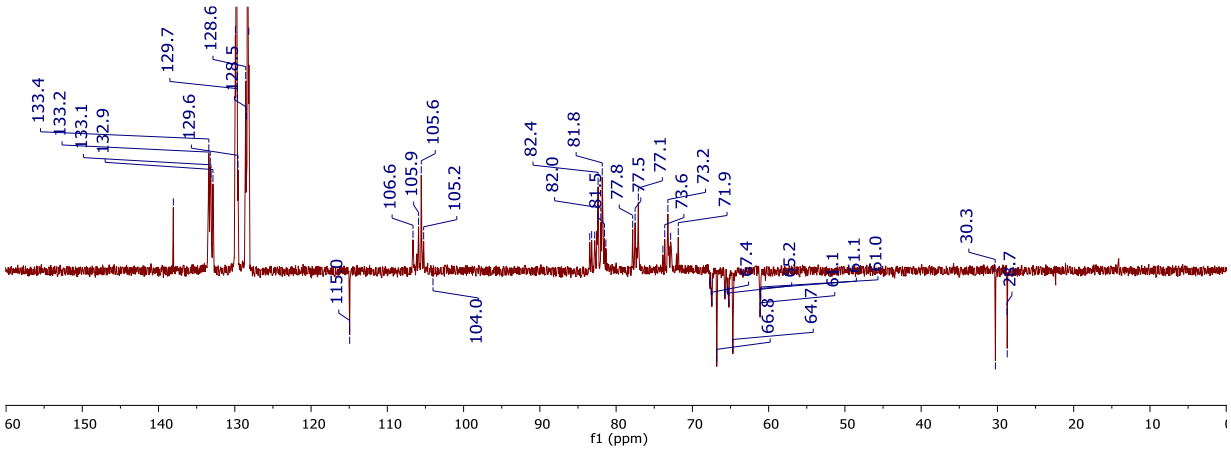
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**44**



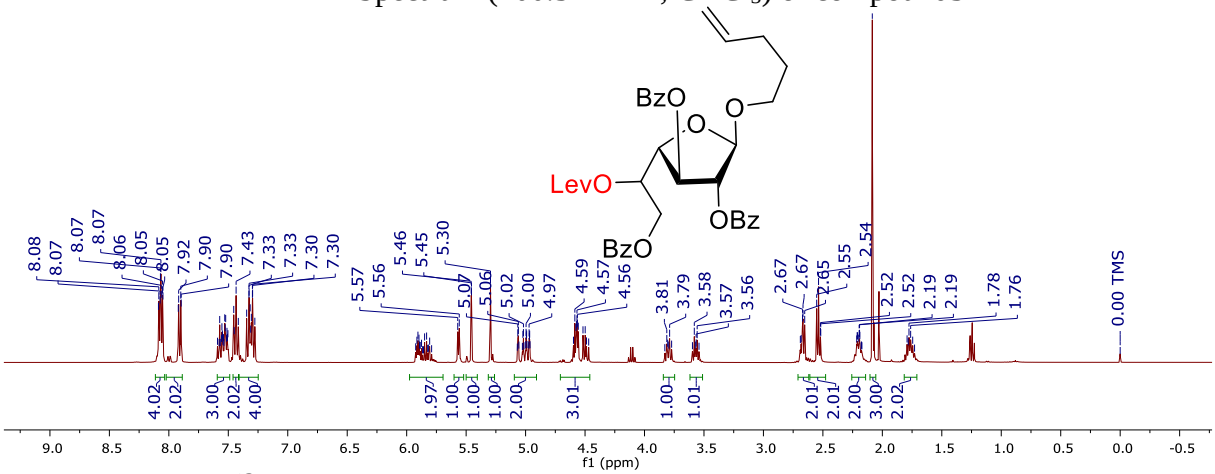
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**44**



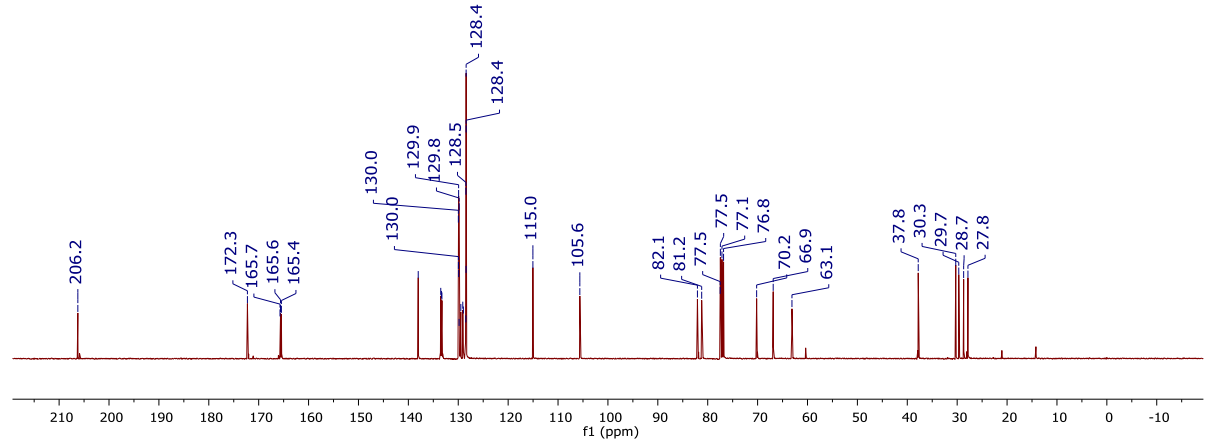
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**44**



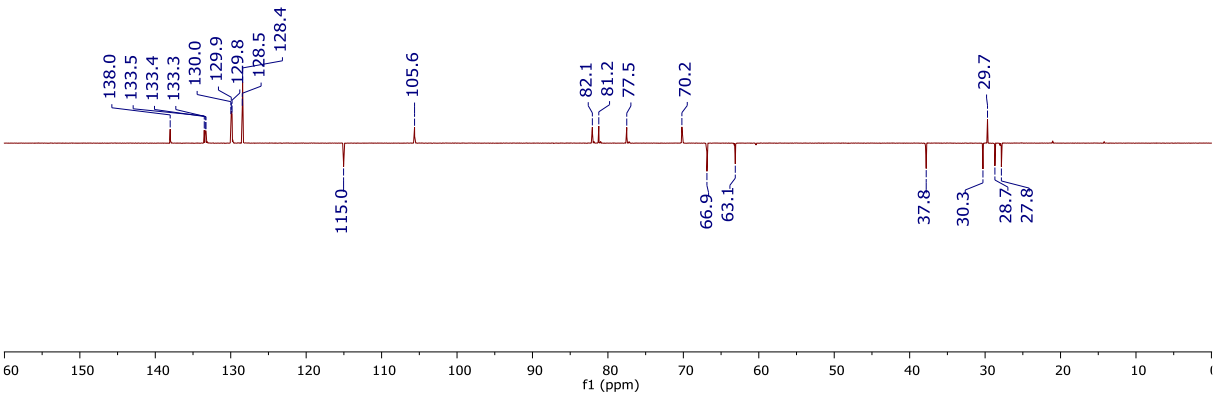
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**51**



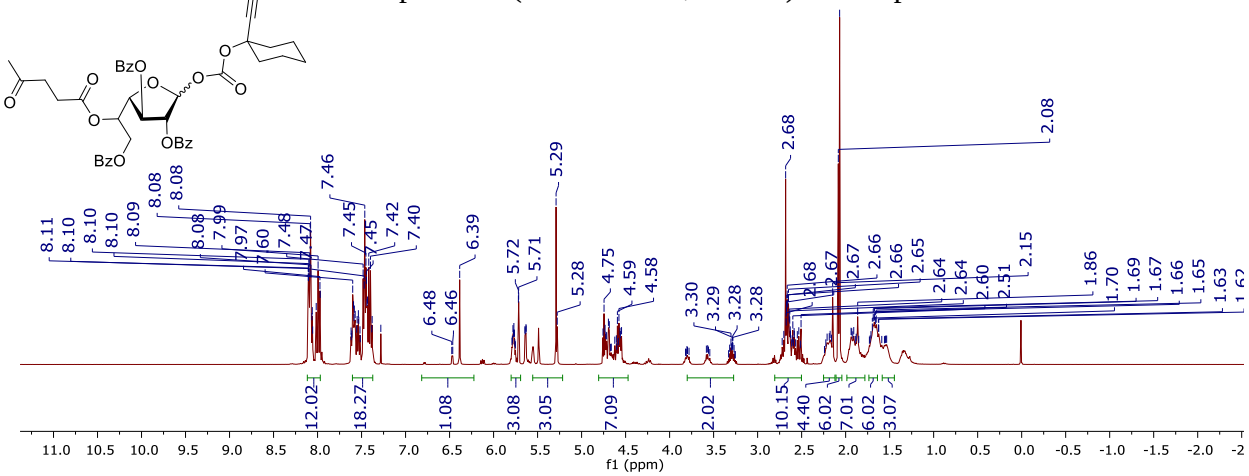
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**51**



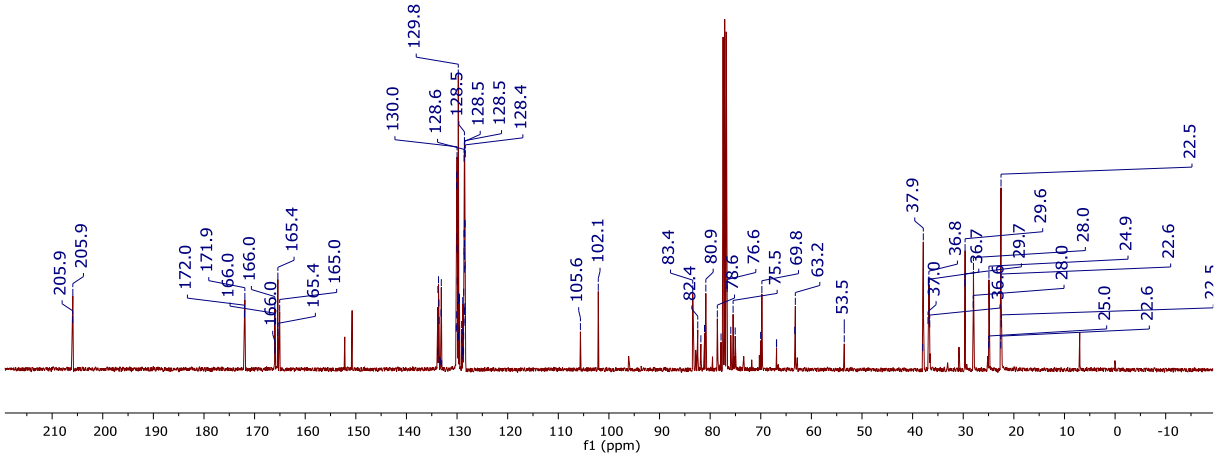
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**51**



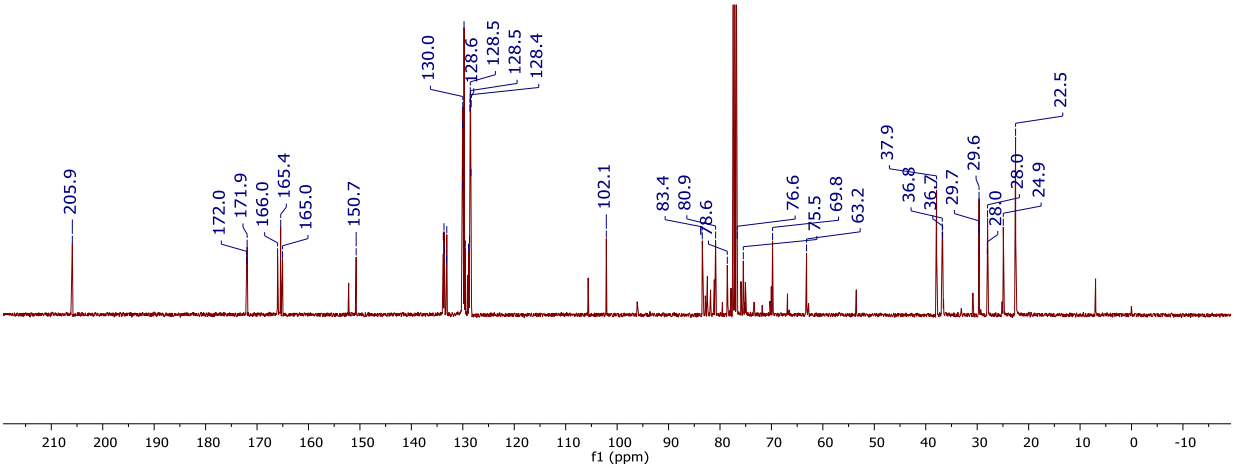
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**50**



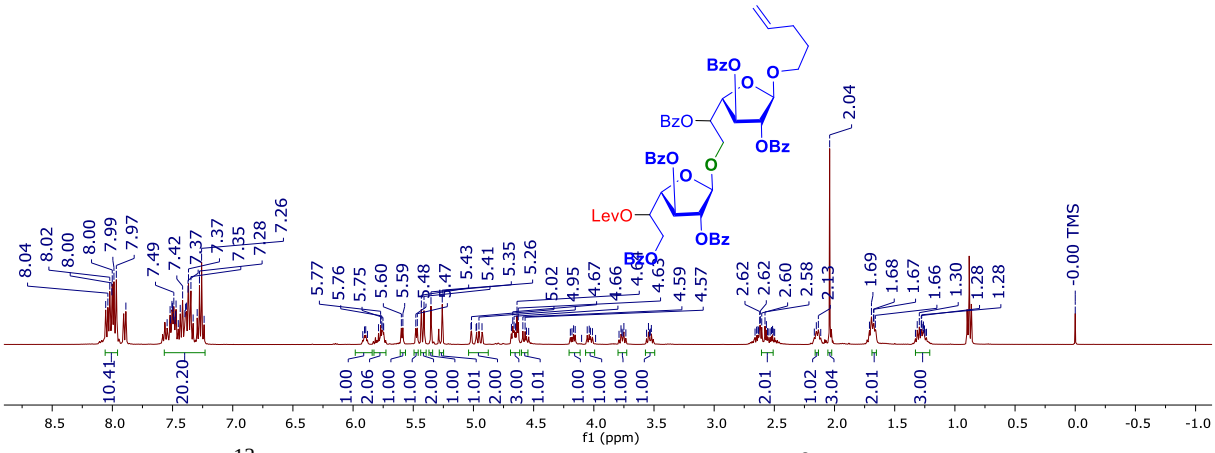
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**50**



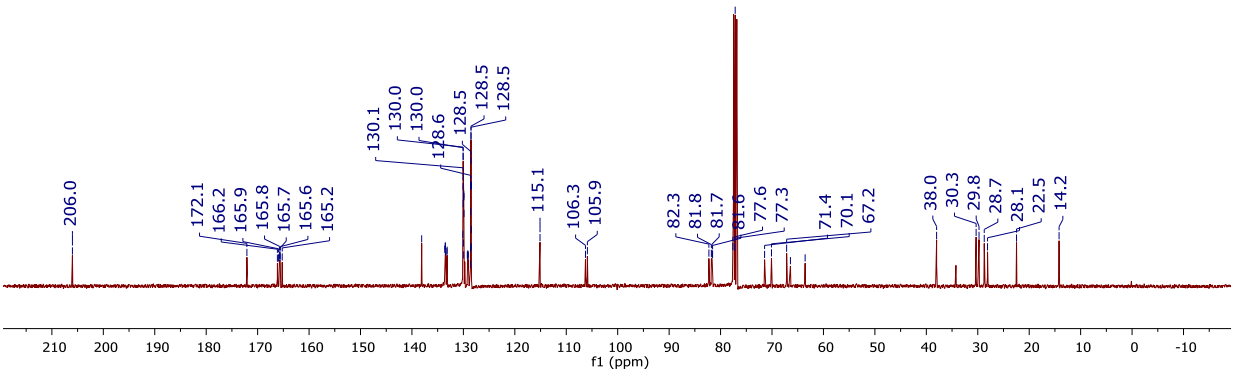
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**50**



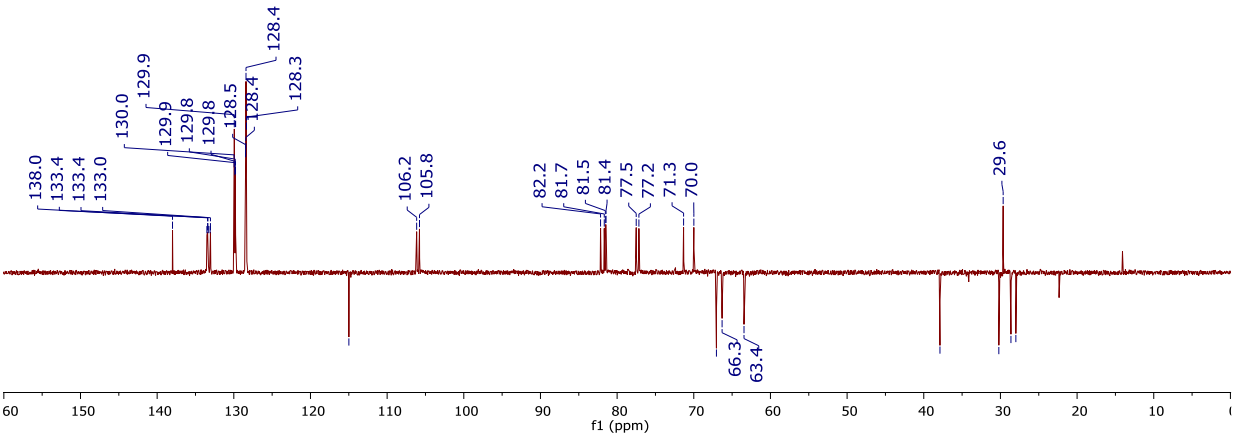
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**52**



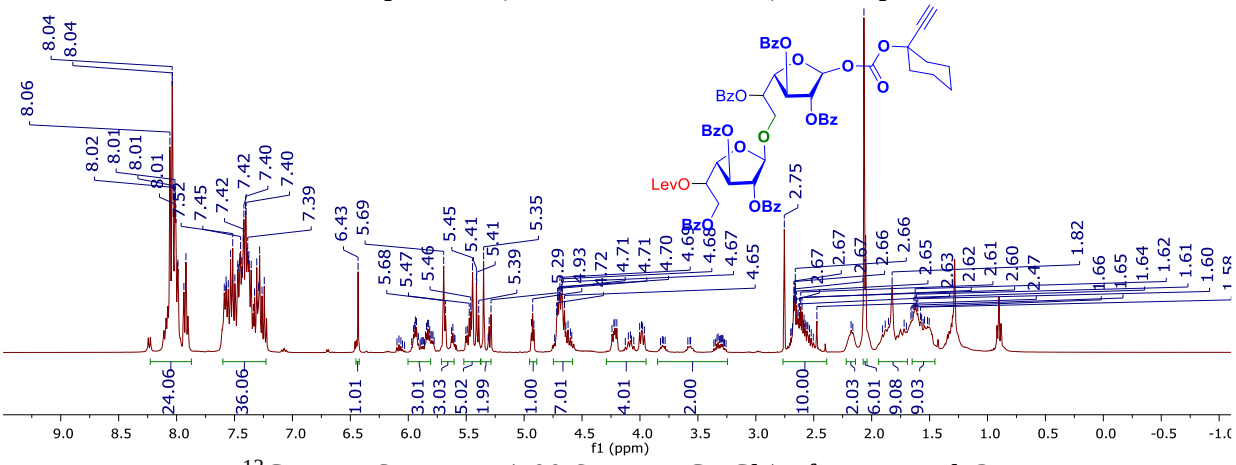
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**52**



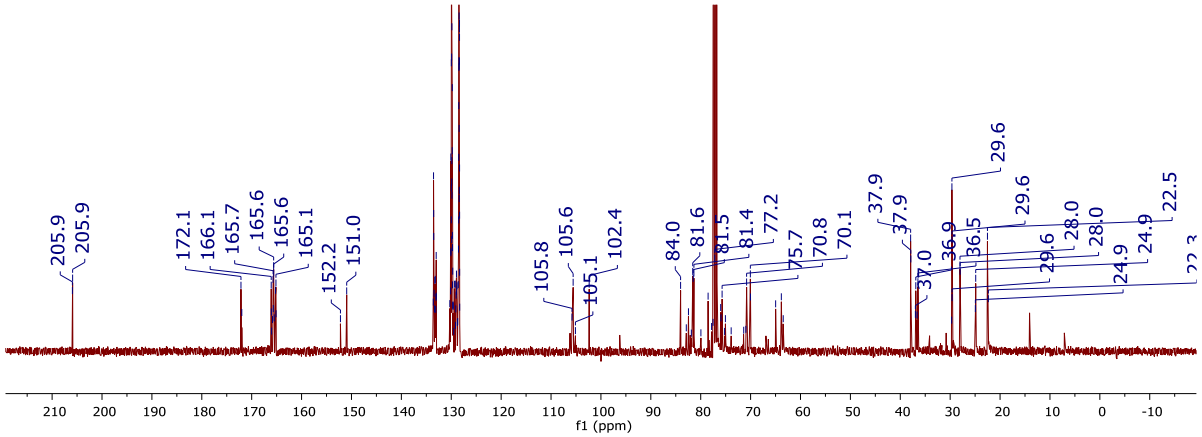
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**52**



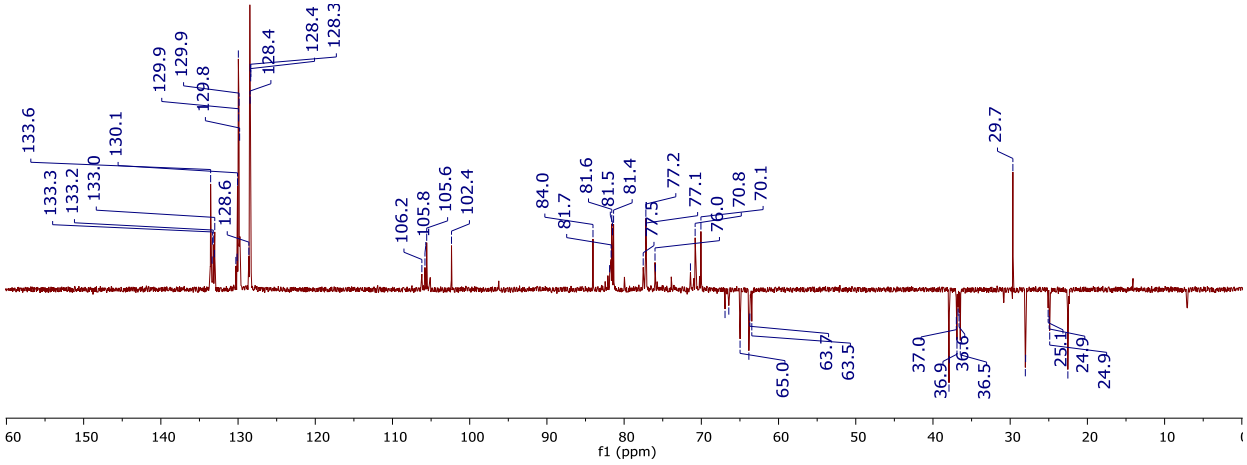
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**53**



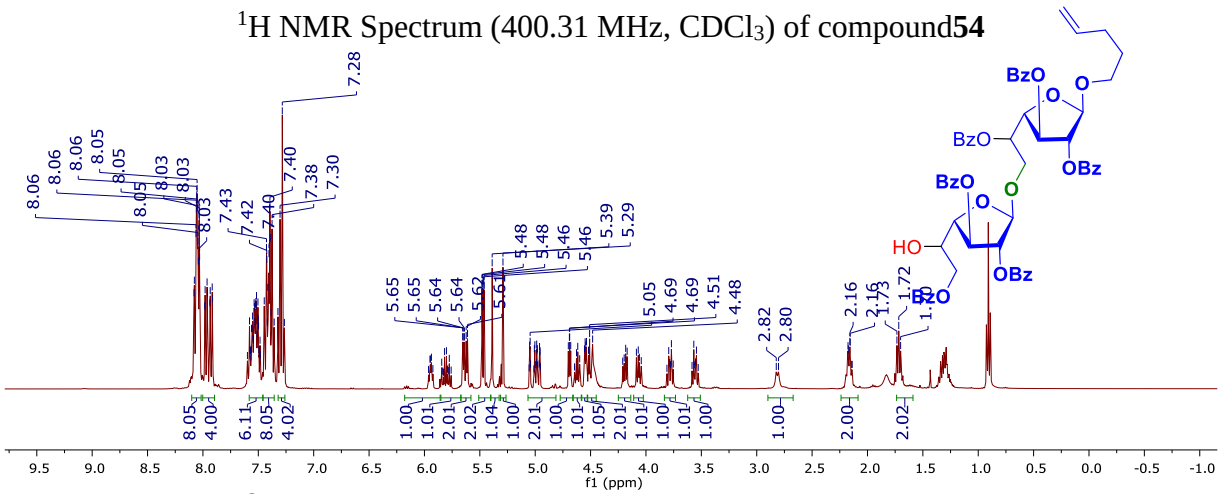
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**53**



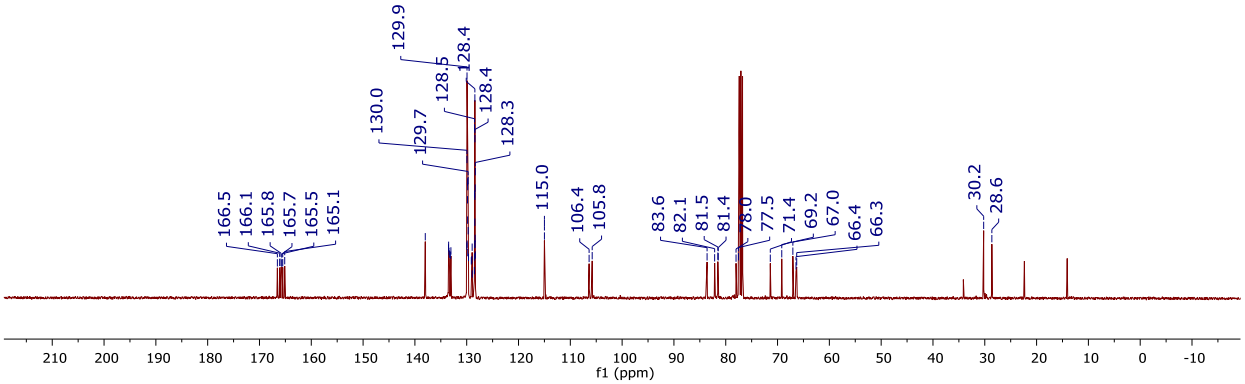
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**53**



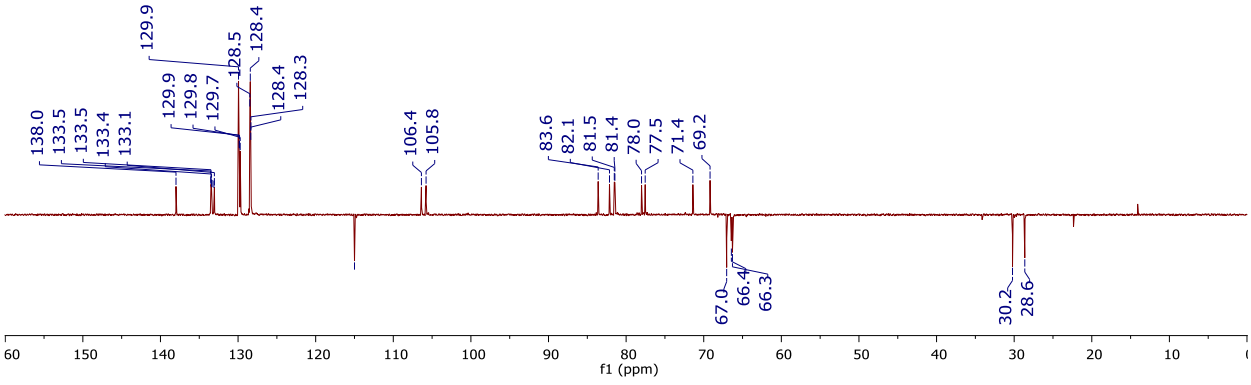
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**54**



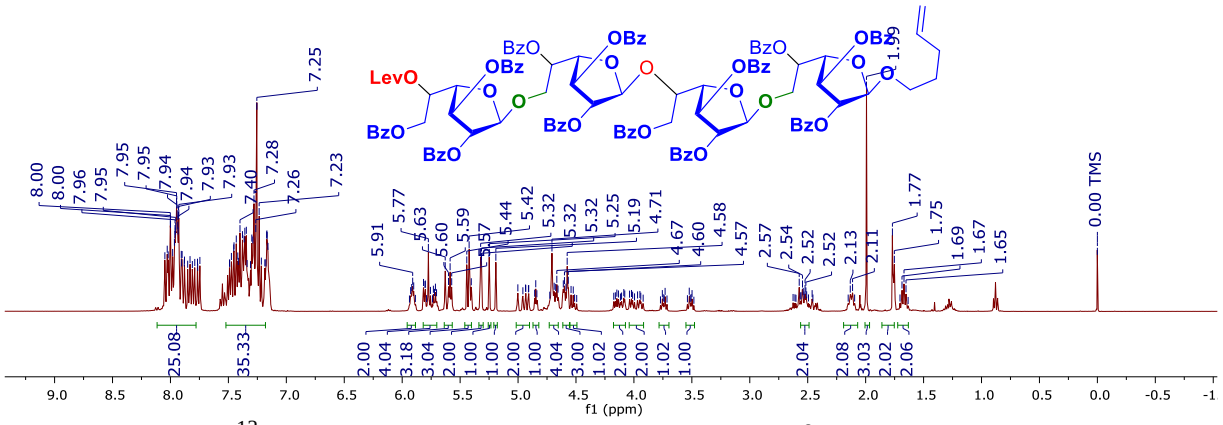
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**54**



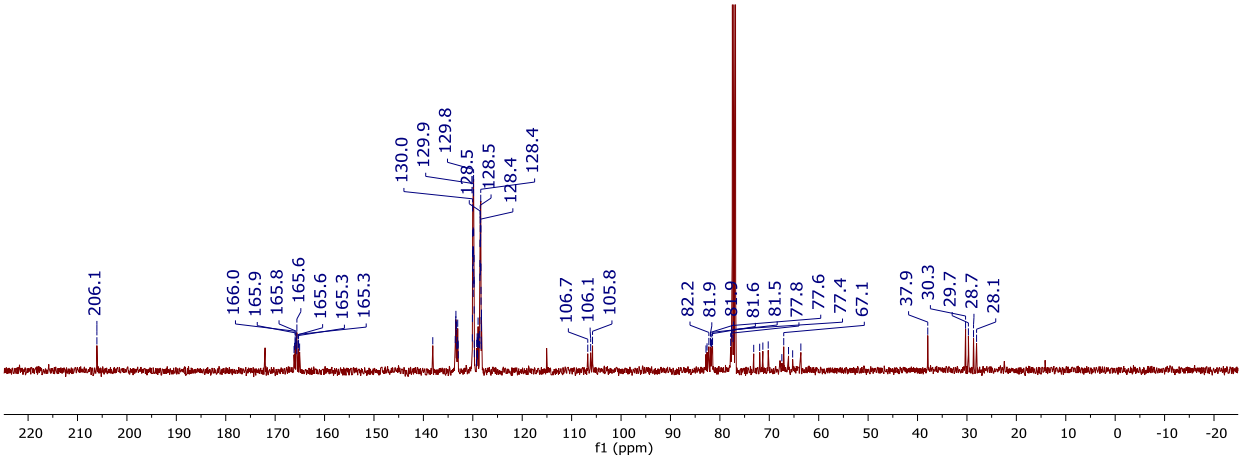
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**54**



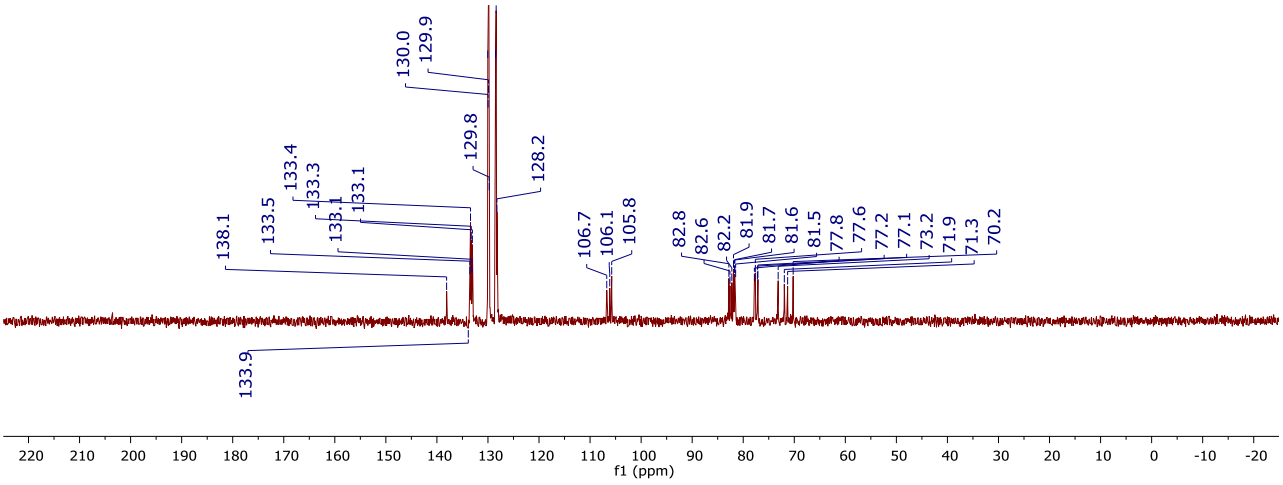
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**55**



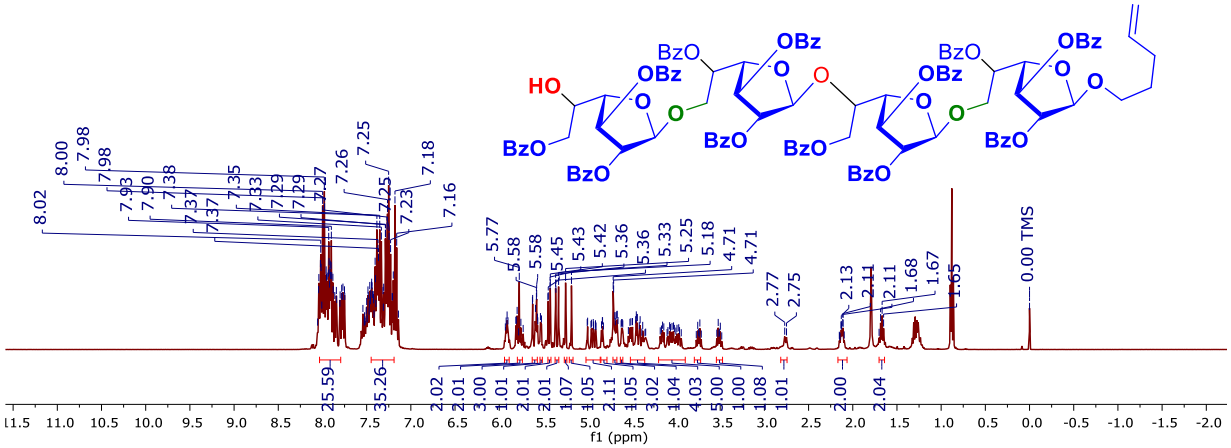
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**55**



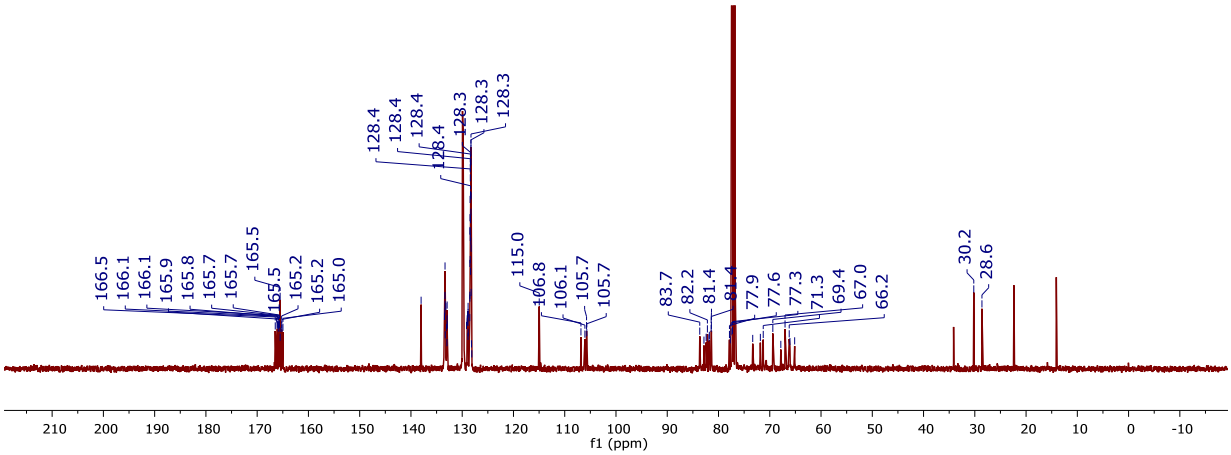
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**55**



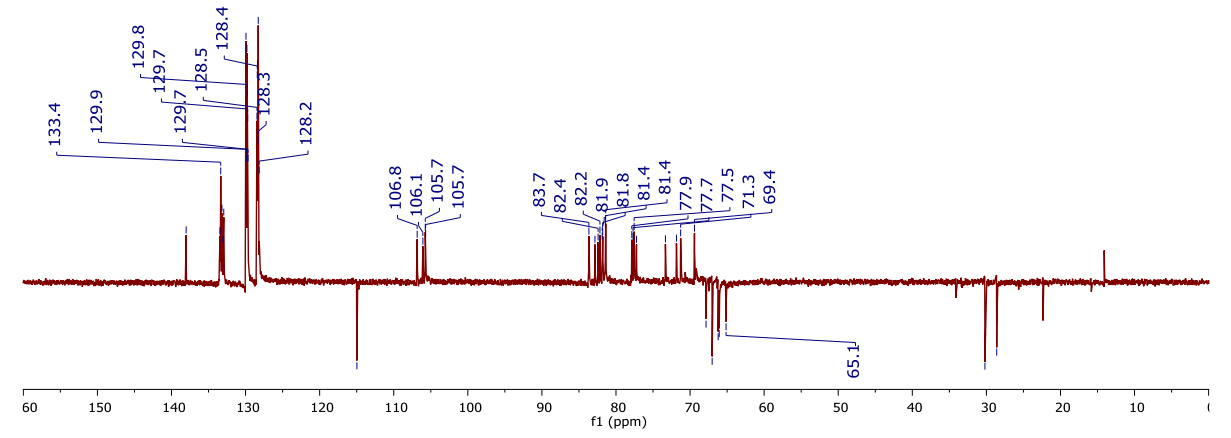
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**56**



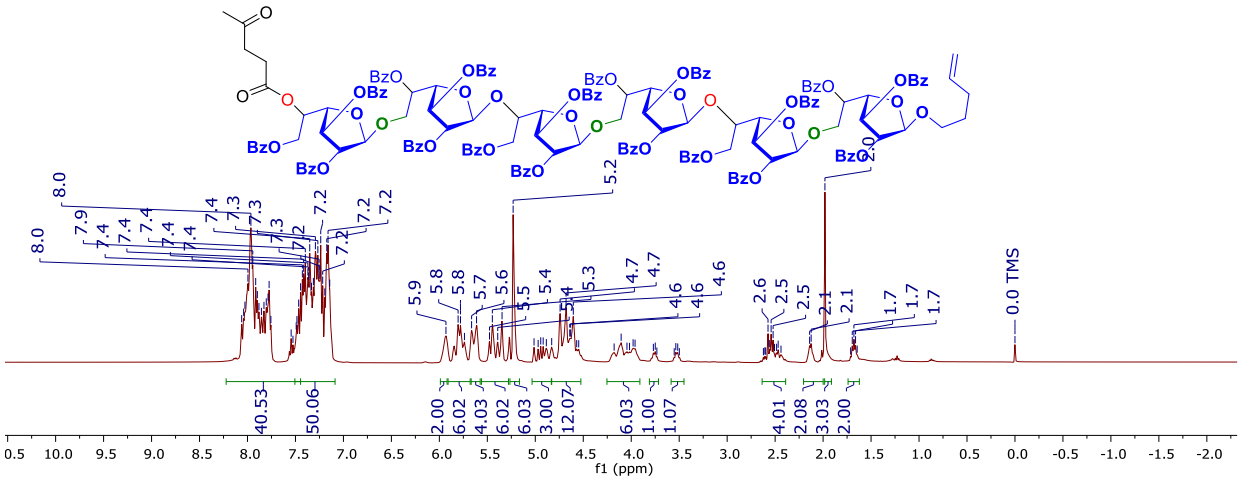
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**56**



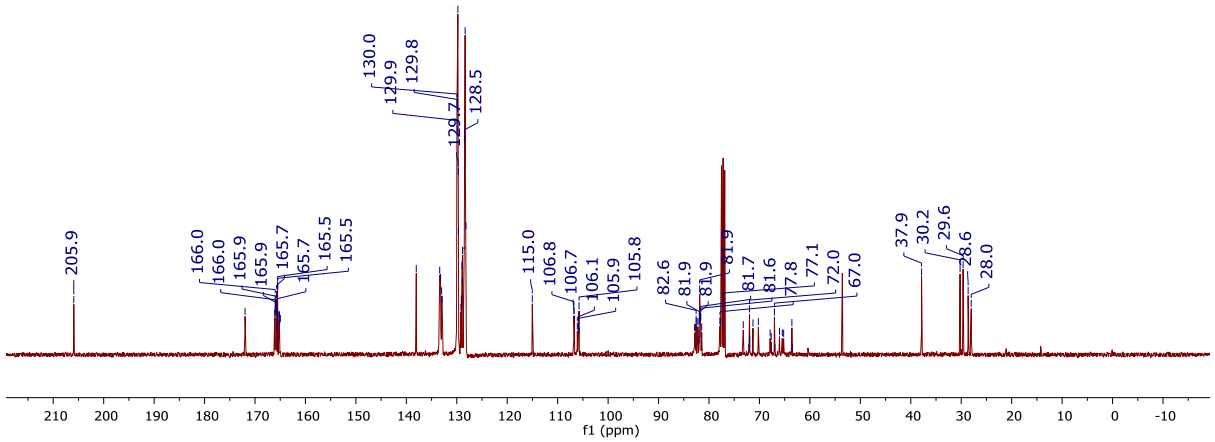
DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**56**



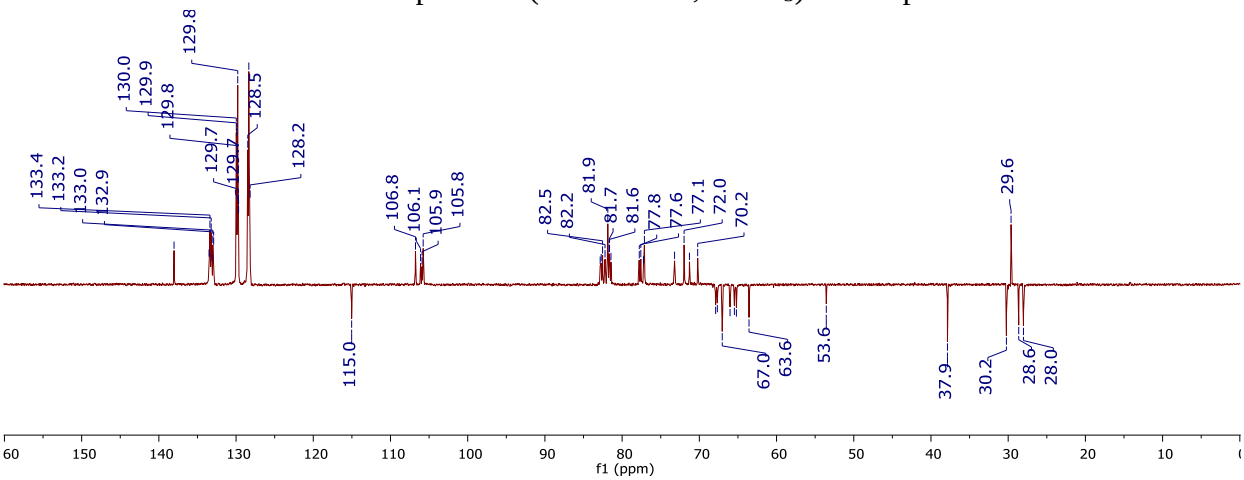
^{1}H NMR Spectrum (400.31 MHz, $CDCl_3$) of compound**57**



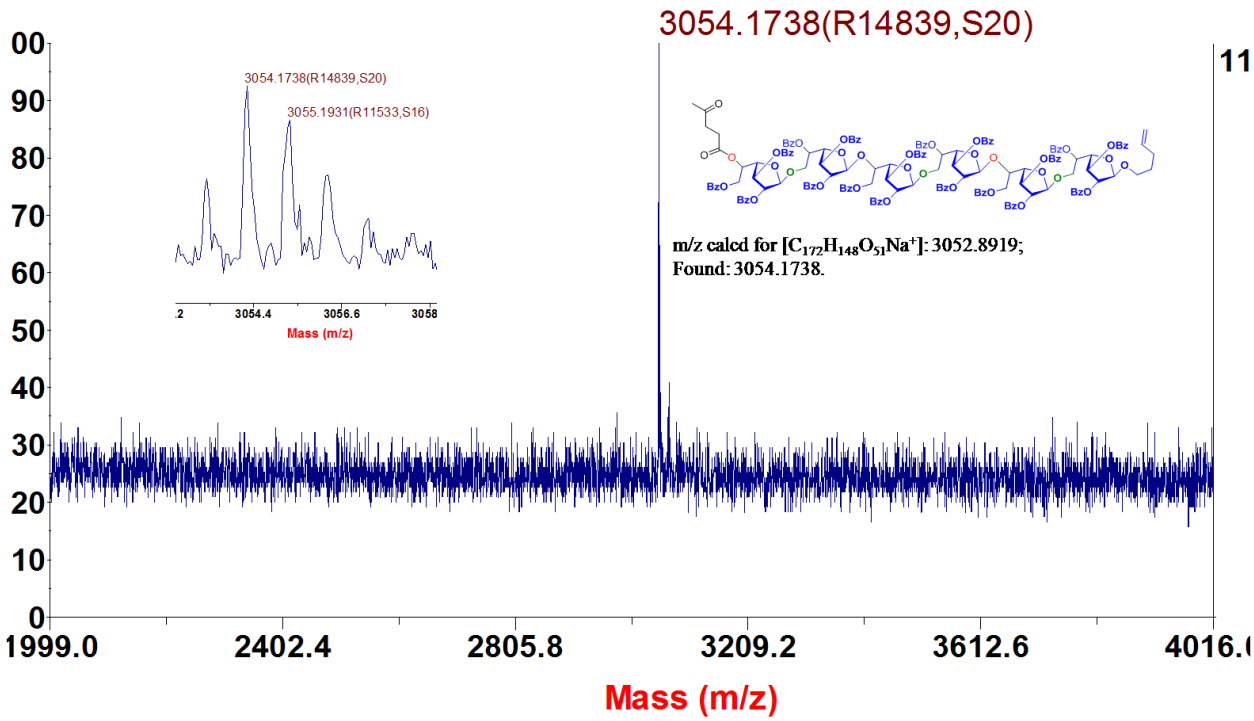
^{13}C NMR Spectrum (100.67MHz, $CDCl_3$) of compound**57**



DEPT NMR Spectrum (100.67MHz, $CDCl_3$) of compound**57**



MALDI-TOF Spectrum of compound **57**



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List of Publications

- Nucleofuge Generating Glycosidations by the Remote Activation of Hydroxybenzotriazolyl Glycosides, **Mahesh Neralkar**, Bijoyananda Mishra, and Srinivas Hotha*, *J. Org. Chem***, 2017**, *82*, 11491-11504
- Stable Alkynyl Glycosyl Carbonates: Catalytic Anomeric Activation and Synthesis of Tridecasaccharide Reminiscent of Mycobacterium tuberculosis Cell Wall Lipoarabinomannan, Bijoyananda Mishra, **Mahesh Neralkar**, and Srinivas Hotha*, *Angew*. *Chem. Int. Ed*., **2016**, *55*, 7786-7791
- [Au]/[Ag]-Catalysed expedient synthesis of branched heneicosafuranosyl arabinogalactan motif of Mycobacterium tuberculosis cell wall, Shivaji A. Thadke, Bijoyananda Mishra, Maidul Islam, Sandip Pasari, Sujit Manmode, Venkateswara Rao Boddu, **Mahesh Neralkar**, Ganesh P. Shinde, Gulab Walke and Srinivas Hotha*, *Nature Communication,* **2017**, 14019
- Facile synthesis of aminooxy glycosides by gold(III)-catalyzed glycosidation, Shivaji Thadke, **Mahesh Neralkar** and Srinivas Hotha*, *Carbohydrate Research***, 2016**, *430*, 16–23
- Stable Benzylic (1-Ethynylcyclohexanyl) Carbonates Protect Hydroxyl Moieties by the Synergistic Action of [Au]/[Ag] Catalytic System Saptashwa Chakraborty, Bijoyananda Mishra, **Mahesh Neralkar** and Srinivas Hotha*, *J. Org. Chem.*, **2019**, *84*, 6604-6611.
- First total synthesis of full length 131-mer of Arbinogalacatan Present on Mycobacterium Tuberculosis cell wall Sandip Pasari, **Mahesh Neralkar** and Srinivas Hotha (Work is under progress)
- Total Synthesis of Glycan Epitope Present on HIV-1 Envelope Trimer GP-41 by using by using regenerative Hydroxybenzotriazolyl Glycosyl Donor, **Mahesh Neralkar**, Bijoyananda Mishra and Srinivas Hotha*(Manuscript under preparation)
- Total synthesis of Highly Branched N-linked Core Hexasaccharide from Chloroviruses, Bijoyanda Mishra, Sujit Manmode, Gulab Walke, **Mahesh Neralkar**, Saptashwa Chakraborty and Srinivas Hotha (Manuscript under preparation)

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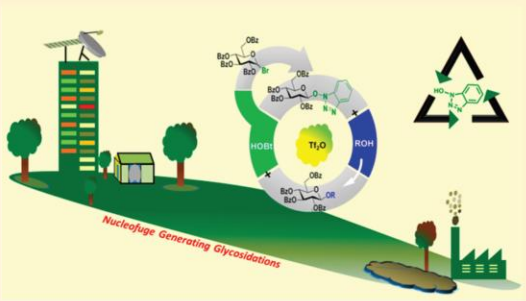
Nucleofuge Generating Glycosidations by the Remote Activation of Hydroxybenzotriazolyl Glycosides

Mahesh Neralkar, Bijoyananda Mishra, and Srinivas Hotha*

Department of Chemistry, Indian Institute of Science Education and Research, Pune, 411 008 MH, India

Supporting Information

ABSTRACT: Hydroxybenzotriazole is routinely used in peptide chemistry for reducing racemization due to the increased reactivity. In this article, very stable hydroxybenzotriazolyl glucosides were identified to undergo glycosidation. The reaction was hypothesized to go through the remote activation by the Tf_2O at the N3-site of HOBt followed by the extrusion of the oxocarbenium ion that was attacked by the glycosyl acceptor. Further, equilibration of the zwitterionic benzotriazolyl species makes the leaving group noncompetitive and generates the nucleofuge that has been reconverted to the glycosyl donor. The reaction is mild, high yielding, fast and suitable for donors containing both C2-ethers and C2-esters as well. The regenerative-donor glycosidation strategy is promising as it enables us to regenerate the glycosyl donor for further utilization. The utility of the methodology for the oligosaccharide synthesis was demonstrated by the successful synthesis of the branched pentamannan core of the HIV1−gp120 complex.



INTRODUCTION

Burgeoning growth in all the allied fields of glycosciences led to the identification of myriad roles played by glycoconjugates and oligosaccharides in many physiological and pathological processes.[1,2] A major impediment holding the exponential growth of the glycosciences is the lack of pure, well characterized and homogeneous oligosaccharides or glycoconjugates.[3] Isolating oligosaccharides from natural sources is a challenging task since they exist in tiny quantities as microheterogeneous forms.[3] Often, totally chemical[4] or chemoenzymatic[5] syntheses are the most popular strategies for obtaining sufficient quantity of oligosaccharides using a bottoms-up approach, wherein saccharide residues are sequentially condensed by a glycosidation reaction.[3] The glycosidation reaction involves two partners termed as glycosyl donor and glycosyl acceptor.[4] The glycosyl donor often contains a nucleofuge at the anomeric carbon which generates an oxocarbenium ion intermediate that will be attacked by the glycosyl acceptor upon the activation by a promoter. Several decades of research culminated into the development of numerous glycosyl donors' viz. glycosyl halides,[6−8] esters,[9] phosphates,[10] imidates,[11] carbonates,[12] thioglycosides,[13] selenyl glycosides,[14] glycals,[15] hemiacetals,[16,17] alkenyl,[18] and alkynyl[19] glycosides.[4]

Propargyl glycosides are observed to undergo glycosidation in the presence of catalytic amount of gold(III) halides in CH_2Cl_2 at 70 °C.[19] They undergo glycosidation when *C*-2 position is protected as a benzyl ether only.[19] Enhanced reactivity by the addition of hydroxybenzotriazole (HOBt) (**1**) is well documented in the peptide chemistry through the formation of activated ester **2** (Figure 1).[20] In this premise,

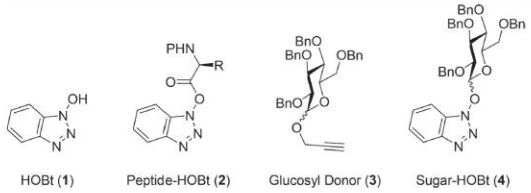


Figure 1. Structures of hydroxybenzotriazole (HOBt) and peptide-HOBt and sugar-HOBt.

addition of HOBt in the gold-catalyzed glycosidation was hypothesized to further increase the overall turnover number (TON) of the gold-catalyzed glycosidation (Scheme 1).

RESULTS AND DISCUSSION

Accordingly, donor **3** was treated with Sug−OH (**5**) and HOBt (**1**, 1.0 equiv) and catalytic amount of $AuCl_3$ in the presence of 4 Å MS powder at 70 °C for 24 h. To our surprise, the required disaccharide **6** was not noticed; instead HOBt glucoside **4** (6%) was observed as the sole product that can be rationalized by the participation of the HOBt as the glycosyl acceptor. HOBt-

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Glycosidation

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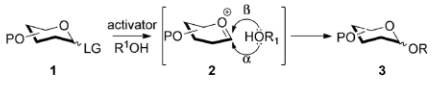
Stable Alkynyl Glycosyl Carbonates: Catalytic Anomeric Activation and Synthesis of a Tridecasaccharide Reminiscent of *Mycobacterium tuberculosis* Cell Wall Lipoarabinomannan

*Bijoyananda Mishra, Mahesh Neralkar, and Srinivas Hotha**

Abstract: *Oligosaccharide synthesis is still a challenging task despite the advent of modern glycosidation techniques. Herein, alkynyl glycosyl carbonates are shown to be stable glycosyl donors that can be activated catalytically by gold and silver salts at 25 °C in just 15 min to produce glycosides in excellent yields. Benzoyl glycosyl carbonate donors are solid compounds with a long shelf life. This operationally simple protocol was found to be highly efficient for the synthesis of nucleosides, amino acids, and phenolic and azido glycoconjugates. Repeated use of the carbonate glycosidation method enabled the highly convergent synthesis of tridecaarabinomannan in a rapid manner.*

The chemical synthesis of oligosaccharides has emerged as a viable approach offering advantages including homogeneity, scalability, and the ability to synthesize unnatural glycoconjugates, which can have great ramifications in modern medicine and materials science.[1] Two saccharides are chemically coupled by a glycosidation reaction that involves a glycosyl donor **1**, a fully protected saccharide with a leaving group at the anomeric position, and a glycosyl acceptor (R^1OH), usually containing a single hydroxy group.[2] Promoters activate the leaving group to give a highly reactive oxocarbenium ion intermediate **2** that will be susceptible to the attack of the acceptor, thus resulting in a glycoside **3** (Scheme 1).[2]

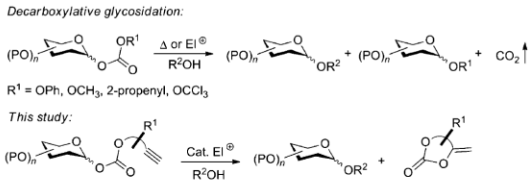


Scheme 1. General glycosidation reaction. LG = leaving group, P = protecting group.

Glycosidation methods that are reliable and scalable and involve stable glycosyl donors are still scarce even after several decades since the first glycoside synthesis. Well-studied glycosyl donors[3] include glycosyl halides,[3a–d] glycosyl esters,[3e] glycosyl trichloroacetamidates,[3f] glycals,[3g] selenoglycosides,[3h] thioglycosides,[3i–k] *n*-pentenyl glycosides,[3l] alkynyl glycosides,[3m] alkyl 1,2-*O*-orthoesters,[3n–p] glycosyl phosphates,[3q] and hemiacetals.[3r] The identification of alkyl glycosyl and thioglycosyl donors has been a transformative advance in the glycosciences, as the alkyl and thio groups serve as stable appendages at the anomeric position, and the compounds can be triggered to become glycosyl donors with an appropriate promoter.

Our own research efforts identified propargyl glycosides as glycosyl donors in the presence of a catalytic amount of $AuCl_3$.[3m] Subsequently, Yu and co-workers reported *o*-alkynyl esters[3s] and Zhu and co-workers reported *S*-but-3-ynyl glycosides[3t] as glycosyl donors with gold catalysts. Gold-catalyzed transglycosidation[3m] has proven to be a robust reaction for the synthesis of glycosides, but has limitations including I) the suitability of only an ether functional group at the C2 position,[3m] II) the lack of stereocontrol through anchimeric assistance,[4a] and III) the hydrolysis of the interglycosidic bond in some instances.[4b,c] Propargyl 1,2-orthoesters were utilized to enable 1,2-*trans* diastereoselectivity.[3p] In the search for a versatile and stable glycosyl donor that can be activated in a catalytic fashion, our attention was drawn to the most popular trichloroacetamidates. However, some glycosyl trichloroacetamidates have a short life time. The hemiacetal precursor to imidates is readily accessible and highly stable; hence, we hypothesized that the conversion of the hemiacetal into a stable, versatile, and reactive glycosyl donor could be highly rewarding.

Methods for the decarboxylative glycosidation of carbonate donors is known; however, they have not been widely utilized owing to forcing reaction conditions and poor yields.[5] Yu and co-workers reported gold-catalysis conditions that can activate *o*-alkynyl esters but not 2-butynyl carbonates even at an elevated temperature (Scheme 2).[6a] The failure to activate 2-butynyl carbonates can be attributed to the possible higher degree of freedom of the leaving group, thereby diminishing the chances of gold–alkyne coordination. In our



Scheme 2. Hypothesis for the use of alkynyl carbonate glycosyl donors.

[*] B. Mishra, M. Neralkar, Prof. S. Hotha
Department of Chemistry
Indian Institute of Science Education and Research
Dr. Homi Bhabha Road, Pune (India)
E-mail: s.hotha@iiserpune.ac.in

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Facile synthesis of aminooxy glycosides by gold(III)-catalyzed glycosidation

Shivaji A. Thadke, Mahesh Neralkar, Srinivas Hotha *

Department of Chemistry, Indian Institute of Science Education & Research, Pune 411 008, India

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ABSTRACT

The *O*-glycosidation of hydroxysuccinimides and hydroxyphthalimides with a variety of aldose derived propargyl 1,2-orthoesters under the gold(III)-catalyzed glycosidation conditions is reported. A wide range of hydroxysuccinimidyl and hydroxyphthalimidyl glycosides were synthesized from corresponding glycosyl orthoesters including glucosyl, mannosyl, galactosyl, ribofuranosyl, arabinofuranosyl, lyxofuranosyl and xylofuranosyl using gold catalysis repertoire. The protocol is identified to be compatible for the synthesis of aminooxy glycosides of higher oligosaccharides as well.

1. Introduction

The occurrence of aminooxy glycosides in calicheamicin[1] and observed increase in the biological significance of drosocin[2] renewed interest in the development of protocols for their synthesis (Fig. 1a and b). In addition, the relative ease in preparation and stability of oximes resulted in the widespread use of aminooxy moiety as a unique linker for the ligation of various biomolecules (Fig. 1c).[3,4]

Aminooxy glycosides are traditionally synthesized from corresponding glycosyl bromides, which have varied shelf life and it is better to convert them into more stable forms as soon as possible.[5–15] Aminooxy glycoside synthesis using *N*-pentenoyl hydroxamate as the acceptor followed by the deprotection of the *n*-pentenyl moiety is the latest addition to the methods for aminooxy glycoside synthesis.[6] In this premise, hitherto unexplored glycosyl 1,2-*O*-orthoesters, which can be conveniently and quickly synthesized from glycosyl bromides, for aminooxy glycosides are hypothesized to be advantageous as they are stable, easily accessible and reactive under mild conditions.

Over the last several years, propargyl 1,2-orthoesters were found to be promising glycosyl donors in the presence of a catalytic amount of Au(III) halides with various glycosyl acceptors.[16–22] Gold(III)-catalyzed glycosidation affords full 1,2-*trans* diastereoselectivity and is found to be suitable for the synthesis of carbohydrate epitopes of infectious bacteria,[18,19] glycopolymers,[20] glycopolypeptides,[21,22] and glycomimetics.[16–22] Knowledge about the significance of aminoxy glycosides and our continued interest in the gold(III)-catalyzed glycosidation attracted the attention to apply the gold(III)-catalyzed glycosidation repertoire for their synthesis. The exploration started with a model reaction between propargyl 1,2-orthoester 1a[16] and the *N*-hydroxysuccinimide 2a under standard gold(III)-catalyzed glycosidation conditions.[16]

2. Results and discussion

Glycosyl donor **1a**[16] and commercially available acceptor **2a** were dissolved in CH_2Cl_2 and treated with 7 mol% of $AuBr_3$ and 4Å MS powder for 48h to observe formation of the required hydroxysuccinimidyl glucoside **3a** (10%) along with the propargyl glucoside **4a**[16] in 70% yield (Table 1).[23] The diminished yield of glucoside **3a** was ascribed to the poor solubility of **2a** in CH_2Cl_2. *N*-Hydroxysuccinimide dissolves well in CH_3CN and hence, the glycosidation was conducted in CH_3CN to observe formation of compound **3a** in 20%. Earlier studies showed that CH_2Cl_2 as the preferred solvent for the activation of propargyl 1,2-orthoesters under gold(III) catalysis conditions.[16] Following many experiments, a mixture of CH_2Cl_2 and CH_3CN in 4:1 ratio was observed to be the most suitable for affording hydroxysuccinimidyl glucoside **3a** in very good yield (72%). Discouraging results were obtained with other solvent mixtures such as CH_2Cl_2-DMF and CH_2Cl_2-THF. In addition, $HAuCl_4$ was also found to be suitable for the glycosidation; however, hygroscopicity of $HAuCl_4$ prevented us to consider its further use (Table 1).

Aminooxy glycosides can also be synthesized using hydroxyphthalimide as yet another glycosyl acceptor. Accordingly, glucosyl orthoester **1a** was treated with commercially available

* Corresponding author. Department of Chemistry, Indian Institute of Science Education & Research, Pune 411 008, India. Tel.: +91 20 2590 8015; fax: +91 20 2589 9790
E-mail address: s.hotha@iiserpune.ac.in (S. Hotha).

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[Au]/[Ag]-catalysed expedient synthesis of branched heneicosafuranosyl arabinogalactan motif of *Mycobacterium tuberculosis* cell wall

Shivaji A. Thadke[1,*], Bijoyananda Mishra[1,*], Maidul Islam[1], Sandip Pasari[1], Sujit Manmode[1], Boddu Venkateswara Rao[1], Mahesh Neralkar[1], Ganesh P. Shinde[1], Gulab Walke[1] & Srinivas Hotha[1]

Emergence of multidrug-resistant and extreme-drug-resistant strains of *Mycobacterium tuberculosis* (MTb) can cause serious socioeconomic burdens. Arabinogalactan present on the cellular envelope of MTb is unique and is required for its survival; access to arabinogalactan is essential for understanding the biosynthetic machinery that assembles it. Isolation from Nature is a herculean task and, as a result, chemical synthesis is the most sought after technique. Here we report a convergent synthesis of branched heneicosafuranosyl arabinogalactan (HAG) of MTb. Key furanosylations are performed using [Au]/[Ag] catalysts. The synthesis of HAG is achieved by the repetitive use of three reactions namely 1,2-*trans* furanoside synthesis by propargyl 1,2-orthoester donors, unmasking of silyl ether, and conversion of *n*-pentenyl furanosides into 1,2-orthoesters. Synthesis of HAG is achieved in 47 steps (with an overall yield of 0.09%) of which 21 are installation of furanosidic linkages in a stereoselective manner.

[1] Department of Chemistry, Indian Institute of Science Education and Research, Dr Homi Bhabha Road, Pune, Maharashtra 411 008, India. * These authors contributed equally to this work. Correspondence and requests for materials should be addressed to S.H. (email: s.hotha@iiserpune.ac.in).

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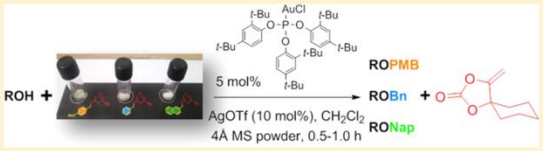
Stable Benzylic (1-Ethynylcyclohexanyl)carbonates Protect Hydroxyl Moieties by the Synergistic Action of [Au]/[Ag] Catalytic System

Saptashwa Chakraborty, Bijoyananda Mishra, Mahesh Neralkar, and Srinivas Hotha*

Department of Chemistry, Indian Institute of Science Education and Research, Pune 411 008, India

Supporting Information

ABSTRACT: Chemical syntheses of oligosaccharides and glycosides call utilization of many protecting groups that can be installed or deprotected without affecting other functional groups present. Benzyl ethers are routinely used in the synthesis of glycans as they can be subjected to hydrogenolysis under neutral conditions. However, installation of benzyl ethers is often carried out under strong basic conditions using benzyl halides. Many a times, strongly basic conditions will be detrimental for some of the other sensitive functionalities (e.g., esters). Later introduced reagents such as benzyl trichloroacetimidate and BnOTf are not shelf-stable, and hence, a new method is highly desirable. Taking a cue from the [Au]/[Ag]-catalyzed glycosidations, we have identified a method that enables protection of hydroxyl groups as benzyl, *p*-methoxybenzyl, or naphthylenemethyl ethers using easily accessible and stable carbonate reagent. A number of saccharide-derived alcohols were subjected to the benzylation successfully using a catalytic amount of gold phosphite and silver triflate. Furthermore, the protocol is suitable for even protecting menthol, cholesterol, serine, disaccharide OH, and furanosyl-derived alcohol easily. The often-utilized olefins and benzoates, as well as benzylidene-, silyl-, Troc-, and Fmoc-protecting groups do not get affected during the newly identified protocol. Regioselective protection and one-pot installation of benzyl and *p*-methoxybenzyl ethers are demonstrated.



INTRODUCTION

Chemical glycosidation is a condensation reaction involving a glycosyl donor and an acceptor, which will be repeatedly utilized while synthesizing oligosaccharides. Chemical synthesis of oligosaccharides is still a challenging task as regioselectivity among multiple reactive alcohols is highly demanding.[1] Often, the glycosyl donor and the acceptor are protected to reduce undesirable competition among similarly reactive alcohols.[2] Often, glycosyl donors are prepared in a fully protected form with a leaving group at the C-1 position, whereas the acceptor (ROH) is synthesized in such a way that a lone hydroxyl group is left for undergoing glycosylation. A facile syntheses of large and branched oligosaccharides generally exploits protection and deprotection strategies on demand.[3,4]

Several decades of research culminated into the development of chemistry for the protection and/or deprotection of alcohols.[5] Benzylation of alcohols to afford benzyl ethers is one of the most celebrated reactions that many oligosaccharide syntheses utilize. Frequently, benzylations are conducted under NaH/dimethylformamide/benzyl halide conditions, which are strongly alkaline, and hence, base-labile protecting groups also get affected.[6] Later introduced BnOTf[7] permits benzylation under neutral conditions, whereas benzyl trichloroacetimidates[8a−d] enable syntheses of benzyl ethers under acid catalysis using a catalytic amount of TfOH. A gold-catalyzed microwave-assisted synthesis of unsymmetrical ethers using alcohols as alkylating agents has been recently reported by Liu et al.[8e] However, moisture sensitivity and instability of BnOTf and benzyl trichloroacetamidates are the major limitations of these two methods.[8] Therefore, installation of benzylic ethers under mild catalytic conditions that provide excellent yields will be highly rewarding.

RESULTS AND DISCUSSION

Recently, glycosyl (1-ethynylcyclohexyl)carbonates (e.g., **1**) have been identified as glycosyl donors under the synergistic catalytic action of Au phosphite (**2**) and AgOTf to afford glycosides **3** with the extrusion of the spirocyclic carbonate **4**.[9] The reaction was postulated to undergo activation of alkyne by the [Au]/[Ag] catalytic system resulting in the formation of a carbocation at the C-1 position extruding the Au-alkylidene **B**.[9] Thus, the formed carbocation is highly stabilized due to the formation of the oxocarbenium-ion intermediate **A1**, which will be in equilibrium with the trioxolenium-ion intermediate **A2** (Scheme 1). Attack of the aglycon ROH led to glycosides, and the protodeauration resulted in the formation of the spirocyclic carbonate **4**. Push of electrons from the exocyclic oxygen is envisaged as one of the possible factors for the stabilization of the carbocation at the anomeric position. In this scenario, we hypothesized that the benzylic carbonates shall also undergo a similar reaction to afford benzylic cation **A3**, releasing the intermediate **B**, and thus formed benzylic cation shall be available for the attack of nucleophiles. To verify our hypothesis, benzylic carbonates **5** and **6** were,

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