STUDIES TOWARD OLIGOSACCHARIDE SYNTHESES USING PROPARGYL-1,2-ORTHOESTERS AND PROPARGYL GLYCOSIDES AS GLYCOSYL DONORS

Thesis Submitted to
The University of Pune for degree of

DOCTOR of PHILOSOPHY In CHEMISTRY

By

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PUNE – 411008 (INDIA)

JULY 2010

Dedicated

To

My Parents, Brothers, Grandfathers and

M.Sc. Professors Ganapathi and Varatharajan

CERTIFICATE

This is to certify that the research work presented in thesis entitled "***Studies Toward Oligosaccharide Syntheses Using Propargyl-1,2-Orthoesters And Propargyl Glycosides As Glycosyl Donors***" has been carried out under my supervision at National Chemical Laboratory, Pune and is a bonafide work of **Suresh Kumar G**. This work is original and has not been submitted for any other degree or diploma of this or any other University.

Pune- 411008 **(Dr. Srinivas Hotha)**

July 2010 **Research Supervisor**

DECLARATION

I hereby declare that the research work presented in this thesis was carried out by me at National Chemical Laboratory, Pune under the supervision of **Dr. Srinivas Hotha**, Scientist E-I, Division of Organic Chemistry, National Chemical Laboratory, Pune - 411 008. This work is original and has not been submitted in part or full, for any degree or diploma of this or any other university.

Division of Organic Chemistry
National Chemical Laboratory
Pune - 411008

(**Suresh Kumar G.**)

July 2010

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-Suresh Kumar

Contents

General Remarks

- ^{1}H NMR spectra were recorded on AV-200 MHz, AV-400 MHz, and DRX-500 MHz spectrometer using tetramethylsilane (TMS) as an internal standard. Chemical shifts have been expressed in ppm units downfield from TMS.
- ^{13}C NMR spectra were recorded on AV-50 MHz, AV-100 MHz, and DRX-125 MHz spectrometer.
- Mass spectra was recorded on Applied Biosystems API QSTAR Pulsar Mass Spectrometer (Electro spray ionization, direct infusion method, solvents used acetonitrile/methanol). EI Mass spectra were recorded on Finngan MAT-1020 spectrometer at 70 *eV* using a direct inlet system. Mass spectra were recorded on Waters LCMS-UPLC system.
- Elemental analysis was carried out on Thermo Finnigan Flash EA 1112 series analyzer.
- Infrared spectra were scanned on Shimadzu IR 470 and Perkin-Elmer 683 or 1310 spectrometers with sodium chloride optics and are measured in cm^{-1}.
- Optical rotations were measured with a JASCO DIP 370 digital polarimeter.
- All reactions are monitored by Thin Layer Chromatography (TLC) carried out on 0.25 mm E-Merck silica gel plates (60F-254) with UV light, I_2, and anisaldehyde in ethanol as developing agents.
- All reactions were carried out under nitrogen or argon atmosphere with dry, freshly distilled solvents under anhydrous conditions unless otherwise specified. Yields refer to chromatographically and spectroscopically homogeneous materials unless otherwise stated.
- All evaporations were carried out under reduced pressure on Büchi rotary evaporator below 45 °C unless otherwise specified.
- Silica gel (60–120), (100-200), and (230-400) mesh were used for column chromatography.
- Scheme, Figure and Compound numbers in abstract and individual chapters are different.

Abbreviations

Ac	Acetyl
Ac_2O	Acetic anhydride
AcOH	Acetic acid
AIBN	2,2-Azobisisobutyronitrile
aq	Aqueous
Bn	Benzyl
Bz	Benzoyl
BnCl	Benzyl chloride
BzCl	Benzoyl chloride
BnBr	Benzyl bromide
Cat	Catalytic
Conc	Concentrated
CuAAC	Copper catalyzed Alkyne Azide Cycloaddition
m-CPBA	*m*-Chloroperbenzoic acid
DBU	1,8-Diazabicycloundec-7-ene
DIPEA	N,N-Diisopropylethylamine
DMAP	N,N-Dimethylaminopyridine
DMDO	2,2-Dimethyldioxirane
DMF	N,N-Dimethylformamide
DMSO	Dimethyl sulfoxide
DMTrtCl	Dimethoxytrityl Chloride
DMTST	Dimethyl (methylthio) sulfonium triflate
DEPT	Distortionless Enhancement by Polarization Transfer
eq	Equivalents
g	Gram
gp120	Glycoprotein120
H	Hour
Hz	Hertz
J	Coupling constant
NIS	*N*-Iodosuccinimide

KLH	Keyhole Limpet Hemocyanin
L	*Leishmania*
mL	Millilitre
mol	Mole
mmol	Millimole
Me	Methyl
MeOH	Methanol
4ÅMS	4Å Molecualar sieves
MeOTf	Methyl triflate
mg	Milligram
min	Minutes
NMR	Nuclear Magnetic Resonance
Piv	Pivoloyl
PTSA, TsOH	*para*-Tolune sulphonic acid
rt	Room temperature
TBAI	Tetra-*n*-butylammonium iodide
TESOTf	Triethylsilyl trifluoromethanesulfonate
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TfOH	Trifluoromethane sulphonic acid
TLC	Thin Layer Chromatography
TMSOTf	Trimethylsilyl trifluoromethanesulfonate
Tr	Trityl
TBDPS	*tert*-Butyldiphenyl silyl
TBDMS	*tert*-Butyldimethyl silyl

Abstract

Abstract

The thesis entitled "*Studies Toward Oligosaccharide Syntheses Using Propargyl-1,2-Orthoesters And Propargyl Glycosides As Glycosyl Donors*" is organized into two chapters. The first chapter describes the development of propargyl 1,2-orthoesters as novel glycosyl donors in the presence of $AuBr_3$ for the stereoselective synthesis of glycosides, disaccharides, oligosaccharides and glycoconjugates. The second chapter explains the utilization of propargyl 1,2-orthoesters and propargyl glycosides for the synthesis of tetrasaccharide cap of the lipophosphoglycan expressed on the cell surface of the *Leishmania* parasite.

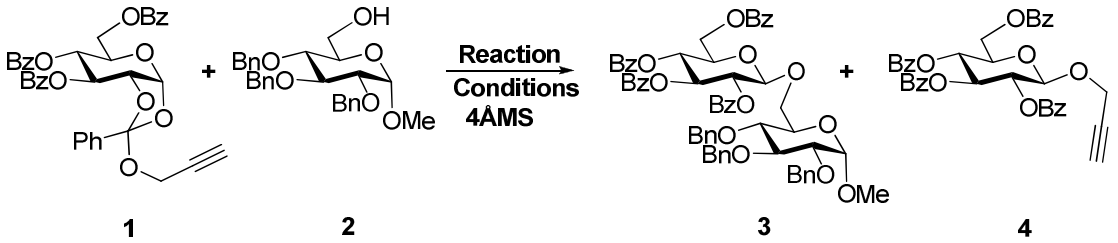
Chapter 1: Synthesis of glycosides, disaccharides, oligosaccharides and glycoconjugates from propargyl 1,2-orthoesters

Cell surface carbohydrates are present in the form of glycolipids and glycoproteins which mediates a variety of biological functions. For example, glycoproteins and glycolipids are reported to implicate information transfer between cells and have important roles in fertilization, embryogenesis, tumour cells etc. Further, oligosaccharides are capable of inducing a protective antibody response, which is a major contributor to the survival of the micro-organisms during infection. However, a major problem in the advanced study of saccharide-protein interactions is the lack of access to pure and structurally well-defined carbohydrates and glycoconjugates which are often found in low concentrations and as micro-heterogeneous forms thereby limiting their isolation and characterization. Hence, the chemical synthesis of oligosaccharides is the most preferred method.

In our laboratory, propargyl glycosides were identified as glycosyl donors in the presence of $AuCl_3$ in acetonitrile and the glycosylation yields often into an anomeric mixture of glycosides. Stereoselective method for the preparation of glycosides and saccharides is an important process as it reduces the laborious purification. In this premise, we thought of utilizing propargyl 1,2-orthoesters as glycosyl donors to effect stereoselective glycosidations in the presence of $AuCl_3$. Accordingly, 3,4,6-tri-*O*-benzoyl-α-D-glucopyranose-1,2-(prop-2-ynyl orthobenzoate) **1** was chosen as a model substrate and allowed to react with methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **2** in presence of various alkynophilic Lewis acids

(Scheme 1 & Table 1). The glycosyl donor **1** was resistant under conditions 5mol% $AuCl_3/CH_3CN/60^oC$; however, switching the solvent from acetonitrile to dichloromethane led to the formation of disaccharide **3** (30%) and prop-2-ynyl tetra-*O*-benzoyl-β-D-glucopyranoside **4** (50%) (Entries 1-2). Further, $AuBr_3$ and $HAuCl_4$ catalysed glycosylations gave 1,2-*trans* disaccharide **3** in 63% and 45% yields respectively whereas, attempted glycosylations with AuCl, Au_2O_3 and PPh_3AuCl were futile (Entries 3-7). The abovementioned experiments suggested that $AuBr_3$ in dichloromethane as an effective promoter for the activation of propargyloxy group present in the propargyl 1,2-orthoester to synthesize 1,2-*trans* disaccharide stereoselectively.

Scheme 1



1 **2** **3** **4**

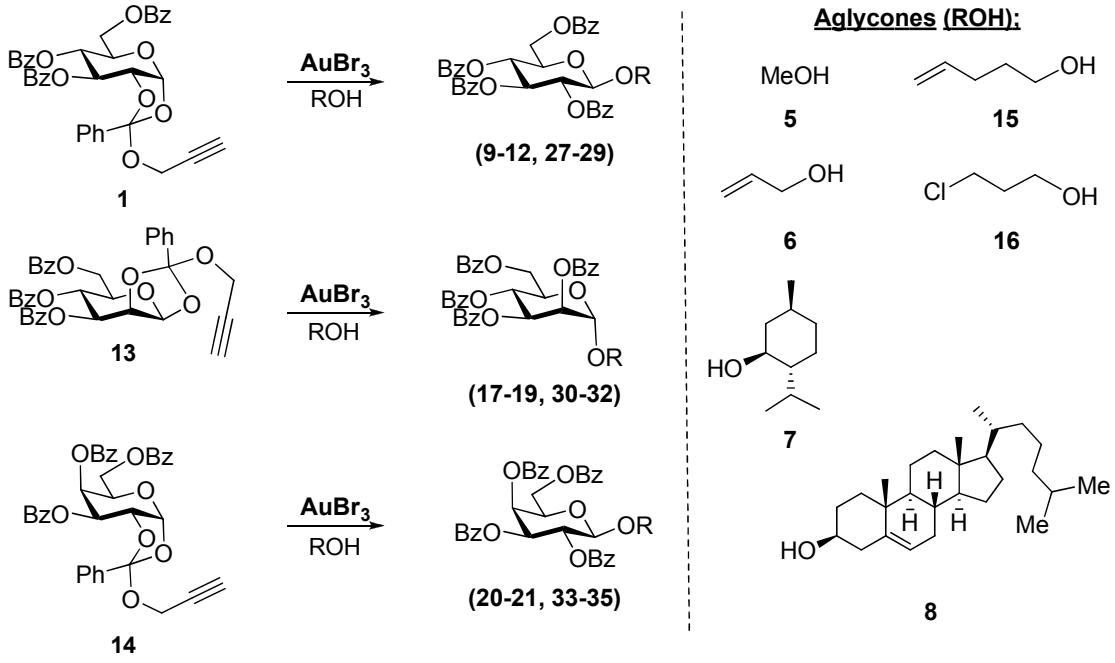
Table 1 *Optimization of catalyst*

Entries	Catalyst and Reaction Conditions	Time(h)	%**3**	%**4**
1	$AuCl_3$ (5 mol%)/ CH_3CN / 60 ^oC	36	0	0
2	$AuCl_3$ (10 mol%)/ CH_2Cl_2 / 25 ^oC	24	30	50
3	$AuBr_3$ (10 mol%)/ CH_2Cl_2 / 25 ^oC	5	63	20
4	$HAuCl_4$ (10 mol%)/ CH_2Cl_2 / 25 ^oC	1	45	28
5	Au_2O_3 (10 mol%)/ CH_2Cl_2 / 25 ^oC	72	0	0
6	AuCl (10 mol%)/ CH_2Cl_2 / 25 ^oC	36	0	0
7	PPh_3AuCl (10 mol%)/ CH_2Cl_2 / 25 ^oC	24	0	0

Identified protocol of $AuBr_3$ promoted glucosylation was tested with orthoester **1** and a panel of aglycones comprising methanol **5**, allyl alcohol **6**, menthol **7** and cholesterol **8** to give the corresponding glucosides (**9-12**) in a 1,2-*trans* stereoselective manner (Scheme 2). The current methodology has been extended to the other glycosyl donors namely propargyl 1,2-orthoesters of mannose **13** and galactose **14** with aglycones containing 4-penten-1-ol **15,** 3-chloro-1-propanol **16** and **8**. It is noteworthy

to mention that all glycosylations proceeded smoothly and afforded the respective mannosides (**17**-1**9**) and galactosides (**20**-**21**) in a 1,2-*trans* stereoselective fashion with good yields. The utility of propargyl 1,2-orthoesters of glucose **1**, mannose **13** and galactose **14** was further determined for the synthesis of disaccharides using sugar based aglycones comprising primary alcohols (**2, 22** and **23**), secondary alcohols (**24** and **25**) and a nucleoside based primary alcohol **26** (Scheme 2). Gratifyingly, all attempted glycosylations provided the respective 1,2-*trans* glucosylated disaccharides (**27-29)**, mannosylated disaccharides (**30-32**) and galactosylated disaccharides (**33-35**) from moderate to good yields.

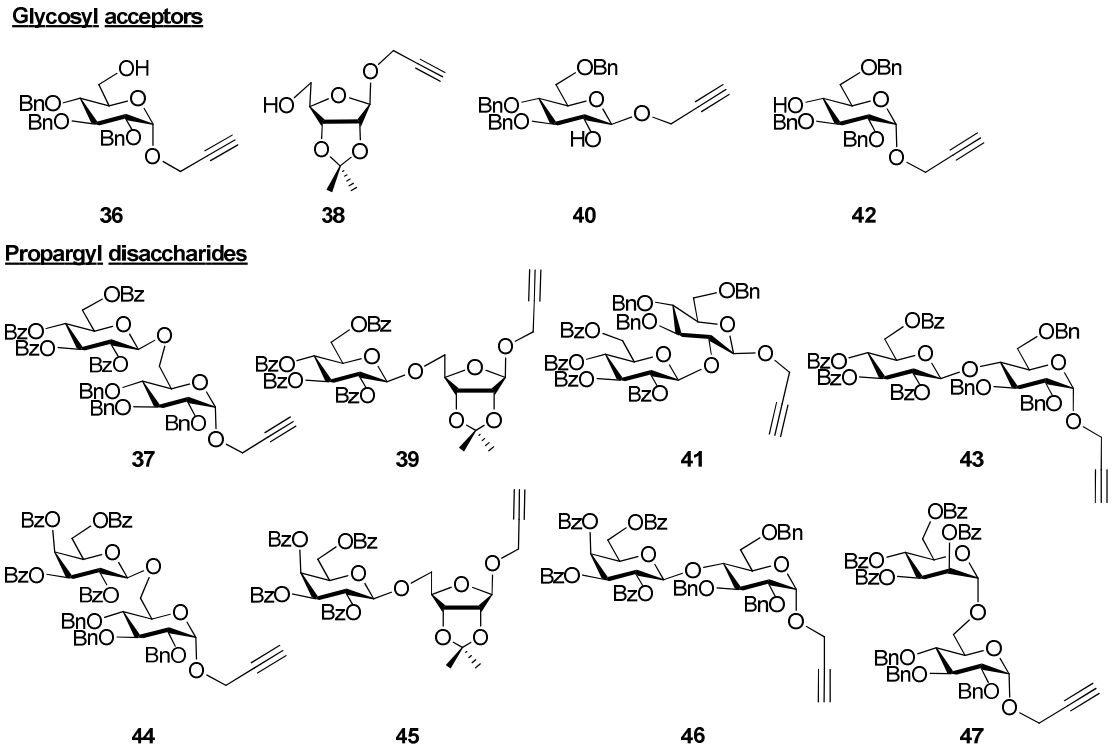
Scheme 2



Further, the glycosylation reaction carried out between a propargyl 1,2-orthoester **1** and propargyl glucoside **36** in the presence of 10mol% $AuBr_3/CH_2Cl_2$/4ÅMS powder at room temperature (Scheme 3) in order to get a 1,2-

trans disaccharide with propargyl group at the reducing end. Interestingly, $AuBr_3$ selectively activated propargyloxy group of the 1,2-orthoester **1** and made it to behave as a glycosyl donor in the presence of the propargyl glucoside **36** afforded a 1,2-*trans* disaccharide **37** as propargyl glycoside in good yield. This interesting observation was explored for the generality by treating with aglycones containing a ribofuranoside **38** and secondary alcohols (**40** and **42**) (Scheme 3). In all cases, the reaction proceeded smoothly and gave the corresponding 1,2-*trans* disaccharides (**39**, **41** and **43**) with propargyl group at the reducing end in good yields. The current protocol was extended to propargyl 1,2-orthoesters of galactose **14** and mannose **13**. Galactosyl 1,2-orthoester **14** reacted with glycosyl acceptor (**36**, **38** and **42**) afforded the respective 1,2-*trans* propargyl disaccharides **(44-46)** whereas mannosyl 1,2-orthoester **13** reacted with a glycosyl acceptor **36** resulting in 1,2-*trans* disaccharide **47** (Scheme 3) with propargyl group at the reducing end in good yields.

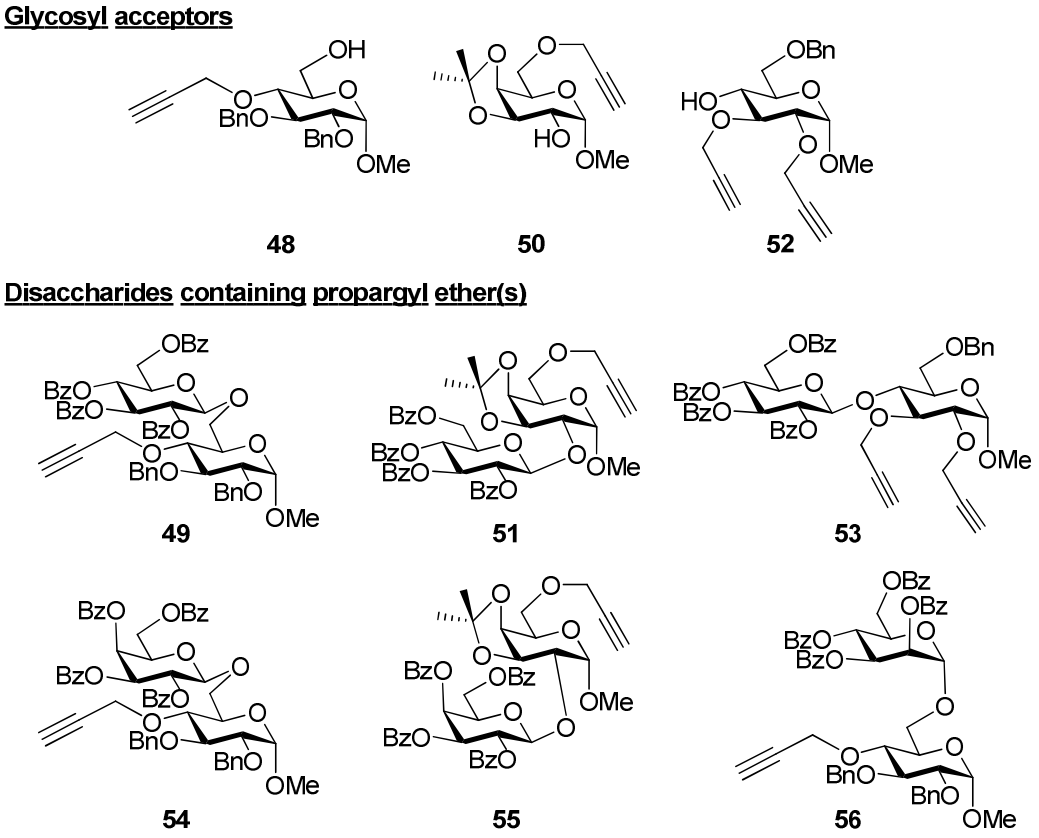
Scheme 3



The selectivity of $AuBr_3$ towards the propargyl 1,2-orthoester was also probed in the presence of propargyl ether(s) of monosaccharides (Scheme 4). Accordingly, glucosyl 1,2-orthoester **1** was treated with a glycosyl acceptor **48** under aforementioned conditions; observed the formation of 1,2-*trans* disaccharide **49** with

propargyl ether remains intact (Scheme 4). Similarly, the glycosylation reaction performed between a 1,2-orthoester **1** and the glycosyl acceptors **50** and **52** gave the corresponding 1,2-*trans* disaccharides with propargyl ether(s) (**51** and **53)** from moderate to good yields. The general applicability and scope of methodology was tested with propargyl 1,2-orthoester of galactose **14**, mannose **13** and the glycosyl acceptor containing a primary alcohol **48** and secondary alcohol **50**. Gratifyingly, all glycosyltions proceeded smoothly and gave the respective 1,2-*trans* disaccharides with intact propargyl ether moiety (**54-56**) in good yields.

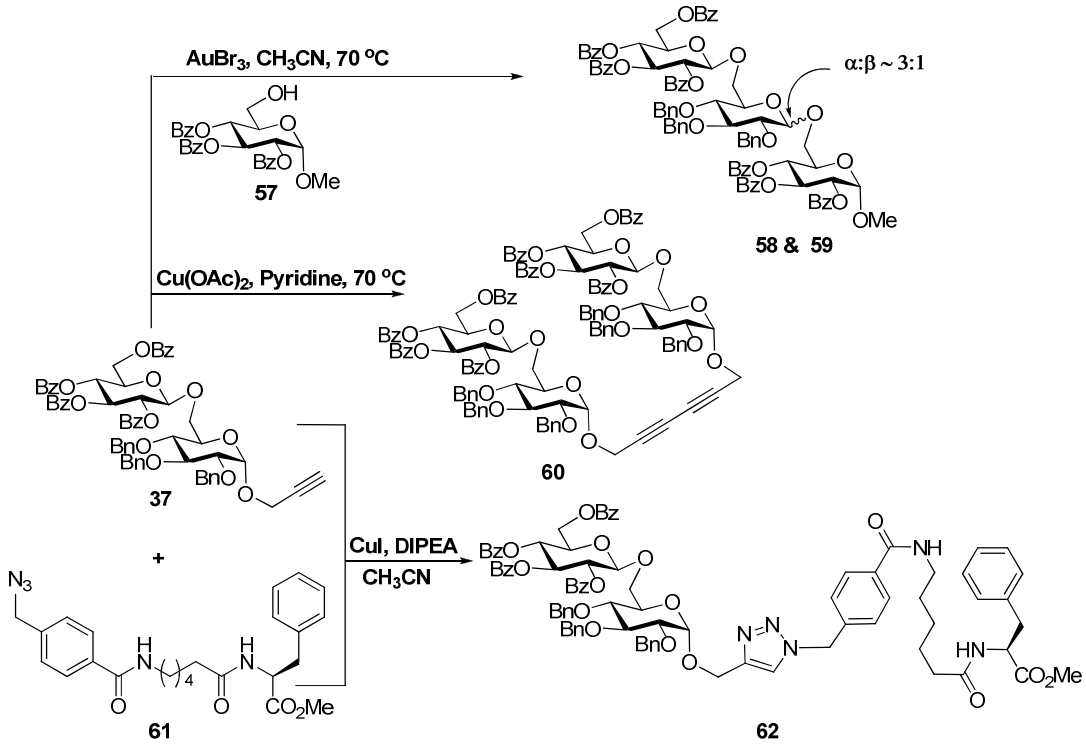
Scheme 4



Disaccharides synthesized *vide supra* as propargyl glycosides are thought to be excellent precursors for (a) the synthesis of higher oligomers by exploiting them as glycosyl donors, (b) the synthesis of symmetrical dimeric sugars under Eglinton's conditions and (c) the synthesis of amino acid glycoconjugates *via* CuAAC reaction. Accordingly, the glycosylation reaction was performed between a propargyl disaccharide **37** and methyl 2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside **57** in the presence of 15mol% $AuBr_3$ in acetonitrile at 70 ^oC to obtain the trisaccharide as a

mixture of anomers (**58** and **59**) (Scheme 5). In continuation, a homodimerized neoglycoside **60** was synthesized by the treatment of propargyl disaccharide **37** under Eglinton's conditions $Cu(OAc)_2$/pyridine/70 ^oC. Further, amino acid glycoconjugate **62** was prepared in excellent yield by treating the propargyl disaccharide **37** with azide **61** under CuI/DIPEA/CH_3CN conditions.

Scheme 5



In conclusion, we have developed a new *O*-glycosylation method that enables synthesis of 1,2-*trans* glycosides and disaccharides from propargyl 1,2-orthoesters stereoselectively. Identified procedure tolerates multiple functional groups such as ethers (propargyl ethers as well), esters, isopropylidene and benzylidene acetals which are routinely used in carbohydrate chemistry. It is noteworthy to mention that the propargyl 1,2-orthoester can be activated in the presence of propargyl glycosides and propargyl ether(s). Judicious blending of glycosylation and subsequent elaboration provided an entry to oligosaccharides, neoglycosides and aminoacid glycoconjugates.

Chapter 2: Synthesis of tetrasaccharide cap of the lipophosphoglycan expressed on the cell surface of the *Leishmania* parasite

Protozoan parasites of the genus *Leishmania* is the causative agent for the disease *Leishmaniasis* which annually affects more than 2.4 million people and kills over 59,000 people. The disease is still treated with old antimony-based drugs that are expensive and associated with significant side effects. *Leishmania* parasites initially lives as promastigotes in the digestive tract of the sand fly and are transmitted to the host mammal's bloodstream by the female *phlebotomine* sandfly while feeding blood. Promastigotes are enriched with lipophosphoglycan (LPG) on its entire surface and these lipophosphoglycans (LPGs) has been implicated in many roles. For instance, LPG (i) protects the parasites in the sand fly midgut; (ii) is implicated in binding and uptake by macrophages; (iii) protect the parasites from toxic macrophage products such as oxidants, hydrolytic enzymes. Therefore, the antigenic LPG is viewed as a new target for the idenfication of the chemotherapeutics and the vaccine development against *Leishmaniasis.*

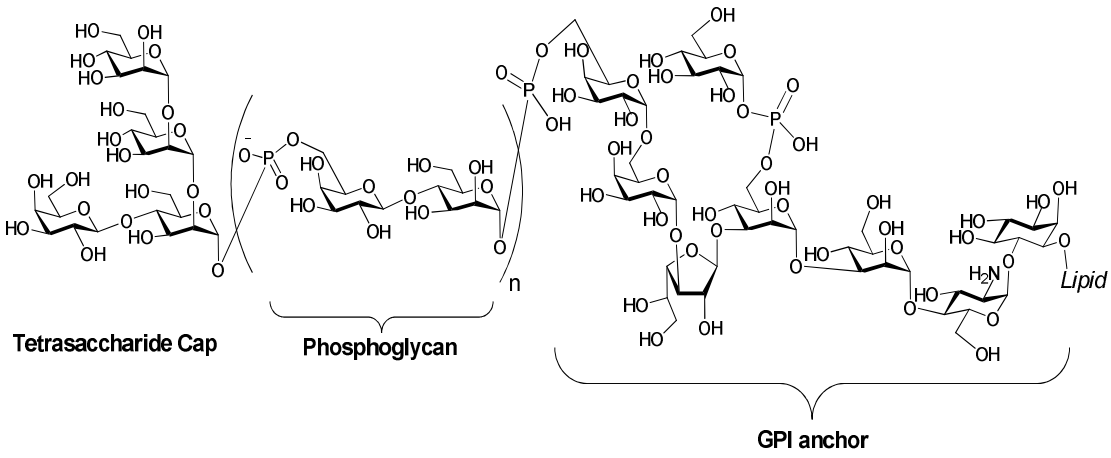


Figure 1

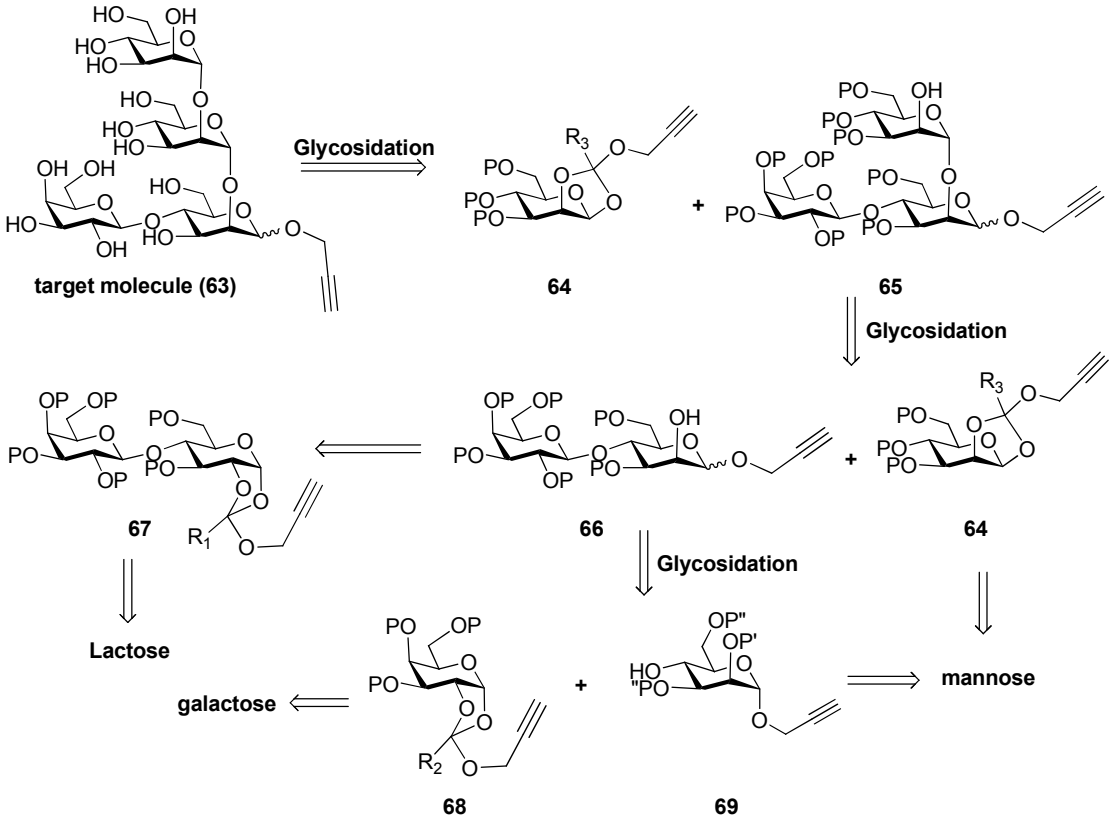
LPG is a glycoconjugate and contains four domains. They are 1) *lyso*-glycosyl phosphatidylinositol (GPI), (2) a conserved phosphosaccharide core with an internal galactofuranose residue (3) a variable repeating phosphorylated saccharide region and (d) neutral oligosaccharides. In this context, we got interested to synthesize the tetrasaccharide (Figure 1) cap of the *Leishmania LPG* as a propargyl glycoside using gold mediated activation of propargyl 1,2-orthoesters because $AuBr_3$ selectively

activates propargyloxy group of the propargyl 1,2-orthoesters in the presence of propargyl glycosides resulted in 1,2-*trans* propargyl disaccharides.

Accordingly, retrosynthetic analysis of the tetrasaccharide showed that the propargyl tetrasaccharide **63** can be obtained by the addition of a propargyl 1,2-orthoester of mannose **64** to the propargyl trisaccharide **65** using a catalytic amount of $AuBr_3$ in dichloromethane. The trisaccharide **65** can be accessed from the disaccharide **66** and propargyl 1,2-orthoester of mannose **64**. The propargyl disaccharide **66** in turn can be prepared from either lactose 1,2-orthoester **67** or from two monosaccharide building blocks **68** and **69** (Scheme 6).

Retrosynthetic analysis

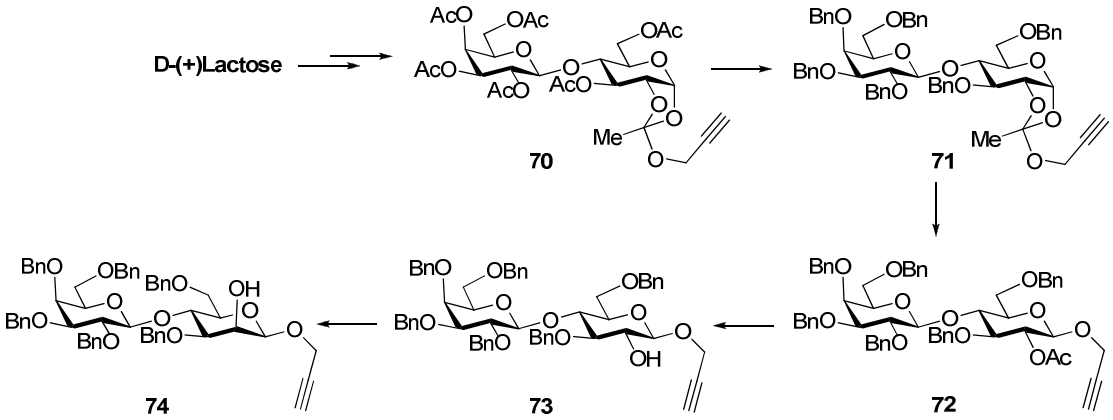
Scheme 6



The synthetic endeavour for the disaccharide acceptor **74** commenced from the starting material lactose (Scheme 7). One pot conversion of lactose into lactosyl bromide was accomplished under acetylation conditions Ac_2O/AcOH/Con.H_2SO_4 followed by the treatment with HBr in AcOH. Hepta-*O*-acetyl lactosyl bromide prepared *vide supra* was treated with propargyl alcohol, 2,6-lutidine and a catalytic

amount of TBAI in CH_2Cl_2 at 65 ^oC to give a per-*O*-acetylated propargyl 1,2-orthoester of lactose **70**. The *O*-acetyl groups of 1,2-orthoester were deprotected under Zemplén conditions NaOMe/MeOH and the resulting hydroxyl groups were benzylated using NaH/BnBr/TBAI to obtain a per-*O*-benzylated lactose 1,2-orthoester **71** which was subsequently converted into propargyl lactoside **72** using $Sc(OTf)_3$ and propargyl alcohol. The resulting 2-*O*-acetyl moiety was deprotected under Zemplén conditions. At last, the required disaccharide **74** was synthesized by oxidation of the disaccharide **73** under conditions DMSO/Ac_2O followed by reduction using $NaBH_4$ in CH_2Cl_2 and MeOH (Scheme 7). In parallel, propargyl 1,2-orthoester of mannose **75** was easily prepared from mannose *via* aforementioned procedures.

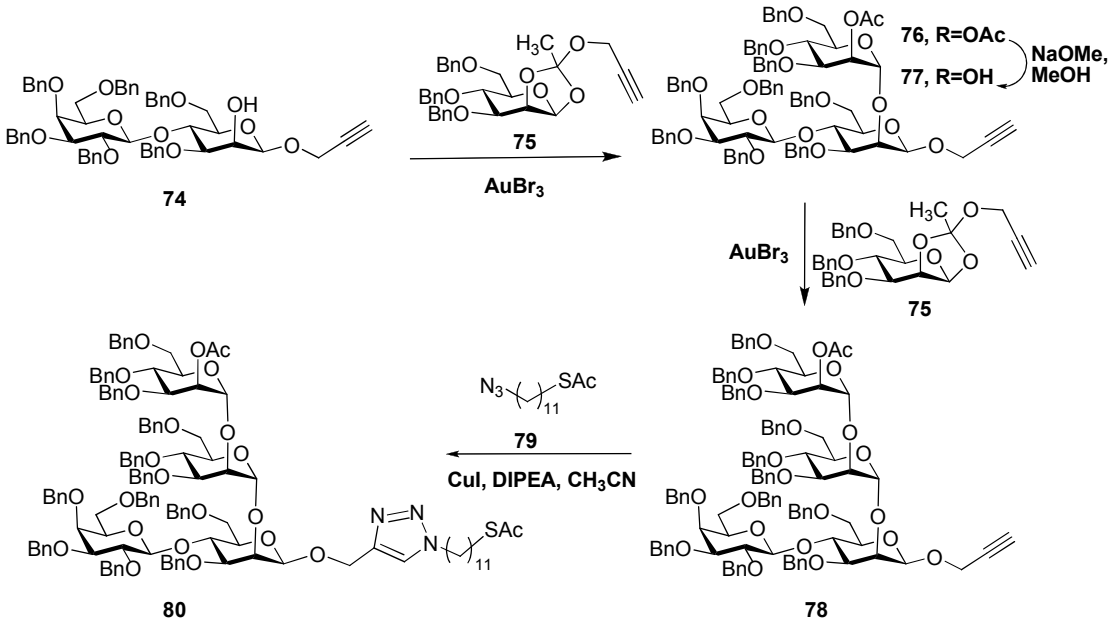
Scheme 7



Having the glycosyl donor **75** and acceptor **74** in hand, the glycosylation reaction carried out in the presence of 10mol% $AuBr_3/CH_2Cl_2$/rt/4ÅMS powder in order to get the trisaccharide **76** (Scheme 8) in good yield. But, the reaction proceeded very slowly and did not complete even after 24h. The reaction is completed when 20 mol% of catalyst is used and afforded the trisaccharide **76** in moderate yield. The resulting trisaccharide **76** was deacetylated under Zemplén conditions and subsequent coupling with mannosyl 1,2-orthoester **75** in the presence of 20mol% of $AuBr_3$ provided the propargyl tetrasaccharide **78**. The deprotection of *O*-benzyl ethers in the presence of propargyl group is extremely difficult process. However, the propargyl group can be clicked with azide under CuAAc reaction and the resulting product can be deprotected by either catalytic hydrogenation or by Birch reduction. Moreover, the impact of propargyl group in the synthesis of bioconjugates encouraged to functionalize the alkyne group of the propargyl tetrasaccharide with lipid containing

both azide and thiol functional groups. Accordingly, the tetrasaccharide **78** was treated with 11-azido-1-thioacetyl-undecane **79** under conditions CuI/DIPEA/CH_3CN to get a 1,2,3-triazole 'clicked' glycolipid **80** in excellent yield.

Scheme 8



In conclusion, the tetrasaccharyl cap portion of *Leishmania* LPG was assembled in an efficient manner using propargyl 1,2-orthoester protocol. The target oligosaccharide was prepared as a propargyl glycoside which allows further synthesis of bioconjugates *via* CuAAC reaction. Further, the propargyl group of tetrasaccharide can be converted into an alkene or carboxylic acid which is also useful for the synthesis of bioconjugates when proteins having amine and thiol functional groups are used.

Note: Compound numbers in abstract is different from those in the thesis.

Chapter I

Synthesis of Glycosides, Disaccharides, Oligosaccharides and Glycoconjugates from Propargyl 1,2-Orthoesters

Introduction

Carbohydrates are one of the diverse biomolecules produced by nature together with proteins and nucleic acids. In late 1880's, Emil Hermann Fischer exposed the structure of carbohydrates separated from natural sources based on the tetrahedral linkage of carbon atom suggested by Le Bel and Van't Hoff along with the other experiments. Further, elaboration of an aldose or a ketose into ascending order (Kiliani-Fischer synthesis) and descending order (Ruff degradation) had transformed the carbohydrates into an innovative field. Subsequently, cyclic structure was proposed for explaining the two optical rotations of (+)-glucose in aqueous solutions (Heidi and Heinz, 1891), W.N.Haworth (1926) suggestion towards the six membered cyclic structure with a hexagon plane and the conformational studies had been altered the entire face of carbohydrate chemistry.[1]

For decades, carbohydrates were simply viewed as the powerhouse that supplied energy to body to drive many biochemical processes. Meanwhile, many experiments and theories have been advanced to understand the nature and function of carbohydrates in various fields.[2] One of the inspired applications of carbohydrate chemistry is "glycobiology" which primarily deals with the studies on the preparation and biological role of carbohydrates from monosaccharides to complex oligosaccharides and their derivatives. It is now well understood that most of the cells from single-celled organism to human are completely covered with a carbohydrate layer termed as glycocalyx in which various oligosaccharide units are connected to proteins *via* *N*-atom of asparagine or *O*-atom of either serine or threonine (glycoproteins), and lipids (glycolipids) that are inserted to the cell membrane along with proteoglycans which may loosely bound on the cell surface. Glycocalyx are made up of few monosaccharide building blocks, primarily the hexoses (glucose, galactose, mannose, and fucose), *N*-acetyl aminosugars (*N*-acetyl glucosamine and *N*-acetyl galactosamine), and negatively charged glucuronic acid and sialic acid (Figure 1). Cell surface oligosaccharides act as ligands which can be recognized by a number of different molecules such as cells, lectins, selectins, enzymes, harmones, toxins etc. to distinguish each other and play vital roles in various biological processes for example; cell-cell communication, cell adhesion, cell growth, inflammation, fertilization, embryogenesis and hormone activities.[3]

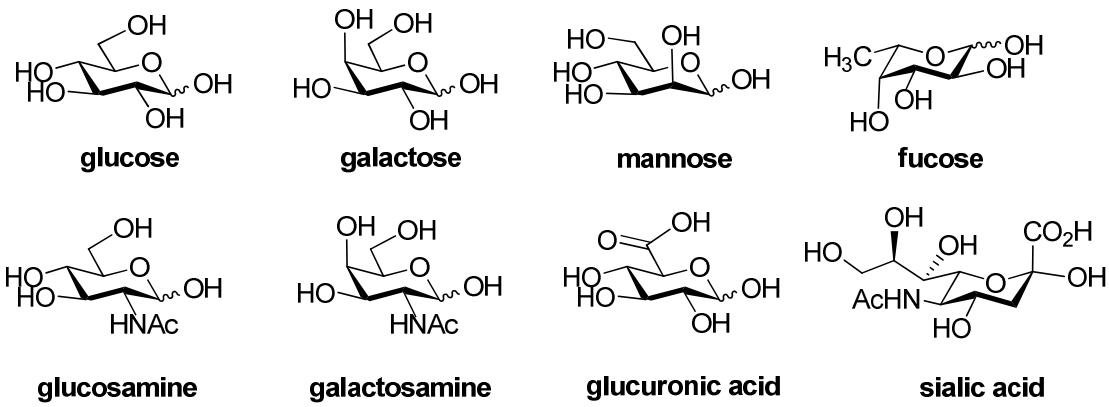


Figure 1

Further, oligosaccharides are determinant of human ABO blood system[4] which is antigenic, more immunogenic than other blood systems and plays crucial role in the transfusion medicine. The specificity of the human ABO blood system is determined based on oligosaccharide structure of glycoproteins and glycolipids present in the surface of red cell erythrocytes. As in the case of individuals with O type blood group possess a characteristic trisaccharide referred as H antigen (Figure 2). The antigen associated with the blood group A is a tetrasaccharide with an additional *N*-acetyl-D-galactosamine residue at the C-3 of galactose ring of H antigen. Moreover, the blood group B is also a tetrasaccharide with an additional D-galactose residue at the C-3 of galactose ring of H antigen as shown in figure 2.

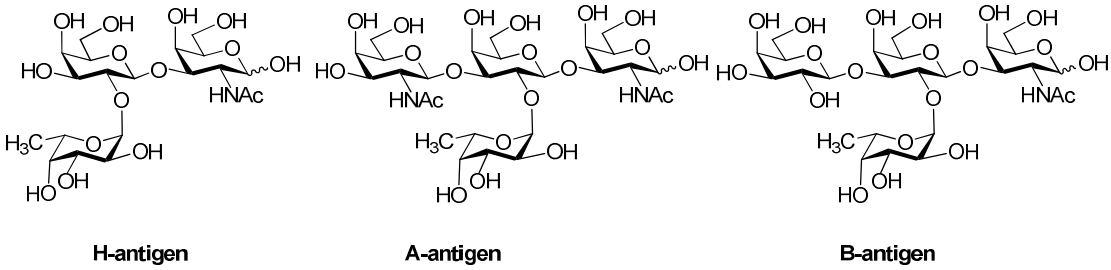
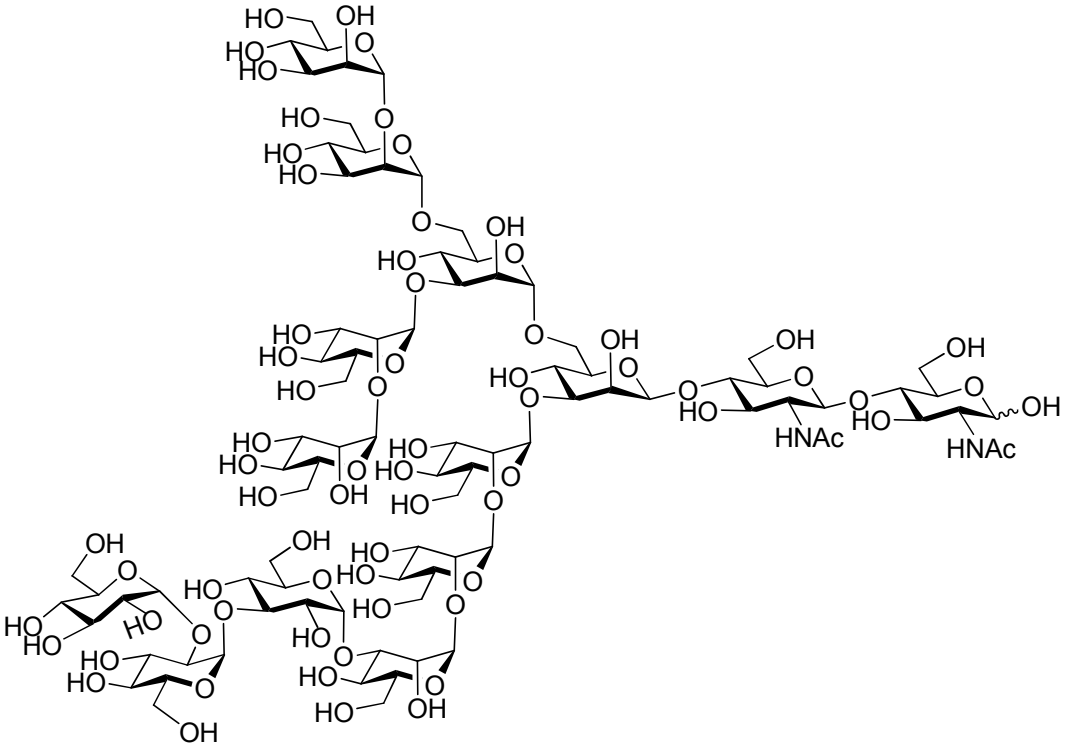


Figure 2

In addition, cell surface oligosaccharides present in the host cells can act as receptors for microbes such as bacteria, virus, influenza to adhesion and invasion of the cell.[3a,5] For example, the sialic acid present in host cell surface functions as a receptor to attach the surface of hemagglutinin which is present in influenza virus. Further, human immunodeficiency virus (HIV) has also an adhesion molecule called as gp120 to infect the cell. The biosynthesis of gp120 occurs from a precursor, Glc_3-

Man_9-$GlcNAc_2$ oligosaccharide (Figure 3). The viral infection is actually initiated by association of glycoprotein gp120 on the viral envelope with CD4 receptors which is expressed on the surface of T4 Lymphocyte cells. Sometimes, oligosaccharides expressed on the surface of microbes are major contributors to the survival of micro-organisms during infection. Further, the cell surface of bacteria, parasites and viruses exhibit oligosaccharides that are often distinct from those of their hosts. Often, specific types of glycoconjugates are highly expressed on the surface of tumours than on normal cells. Such cell-surface carbohydrate markers[6] are the basis for the discovery of new carbohydrate-based vaccines against various diseases.



Glc_3-Man_9-$GlcNAc_2$

Figure 3

However, the major obstacle to understand the function of carbohydrates in a better way and how they influence various biological events after attachment with either proteins or lipids is the lack of access to pure biologically important carbohydrate portions of glycolipids and glycoproteins from natural resources. Isolation and characterization of such oligosaccharides and glycoconjugates (glycolipids and glycoproteins) are difficult because they exist in very low

concentrations and micro-heterogeneous forms.[7] Hence, an alternative platform is always necessary for the synthesis of pure and structurally well-defined oligosaccharides to understand the biological activity in more detail. Chemical synthesis is one of the important routes to access oligosaccharides efficiently.

Oligosaccharides synthesis

An oligosaccharide is a polymer of monosaccharides which are interconnected by a bond called "glycosidic bond" usually through oxygen atom, sometimes nitrogen atom and rarely through sulphur and carbon atom. The glycosidic bond is formed by the displacement of a leaving group (X) attached to the anomeric carbon of the sugar moiety with nucleophiles such as alcohols, thiols, amines etc. The compound which donates the glycosyl moiety is called glycosyl donor and the compound that receives it, is known as glycosyl acceptor. The process involves the formation of glycosidic bond is called glycosylation and the reaction is generally performed in presence of an activator called promoter. The role of the promoter is to assist the departure of leaving group (Figure 4).

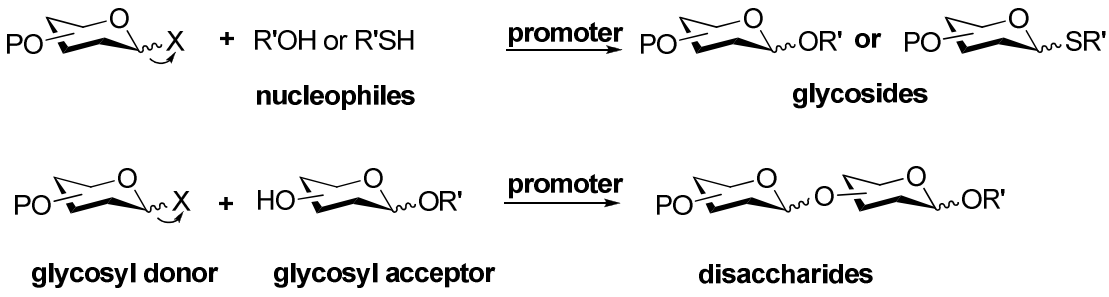


Figure 4

Because of the poly hydroxy functional groups present in saccharide units, it is very difficult to use glycosyl donor and glycosyl acceptor without the help of protecting group strategy for the oligosaccharides synthesis. Hence, the chemical synthesis of glycosides and saccharides frequently involves the coupling of a fully protected glycosyl donor bearing a leaving group at its anomeric centre with suitably protected glycosyl acceptors that contains a free hydroxyl group.[8] This strategy reduces the complexity of isolation and purification as compared to use of unprotected glycosyl donors and glycosyl acceptors in glycosylation. The alcohol used is non-carbohydrate unit then the resulting compound is called glycoside whereas, if

saccharide alcohols are used as glycosyl acceptors then the resulting glycosides are known as disaccharides, trisaccharides, tetrasaccharides etc.

The glycosylation proceeds through a general mechanistic pathway as represented in figure 5. In the case of a glycosyl donor having substituents such as ethers, azide etc. at C-2, the promoter activates a leaving group resulting in the formation of oxocarbenium ion which is then trapped by alcohol from both faces offers 1,2-*cis* and 1,2-*trans* isomers.

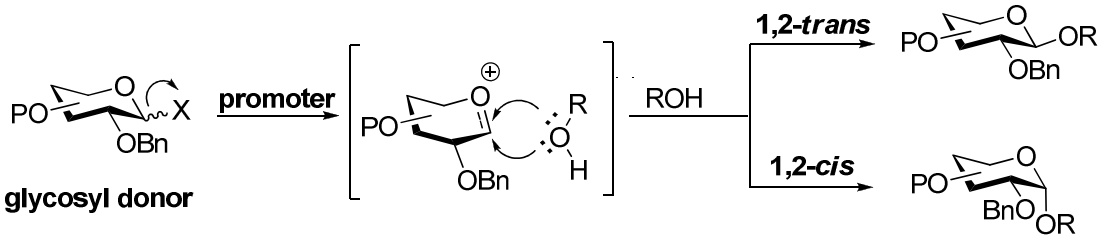


Figure 5

On the other hand, the glycosyl donor having substituents such as esters or amides at C-2 undergo glycosylation *via* initial formation of oxocarbenium ion which is then equilibrium to a stable dioxolenium ion formed by neighbouring group participation of 2-*O*-ester group that allows unidirectional attack of an alcohol from "*trans"* face (Figure 6). Sometimes, 1,2-*cis* isomer is formed in the case of glucosyl and galactosyl donor when competiting reaction takes place between an incoming nucleophile and ester group.

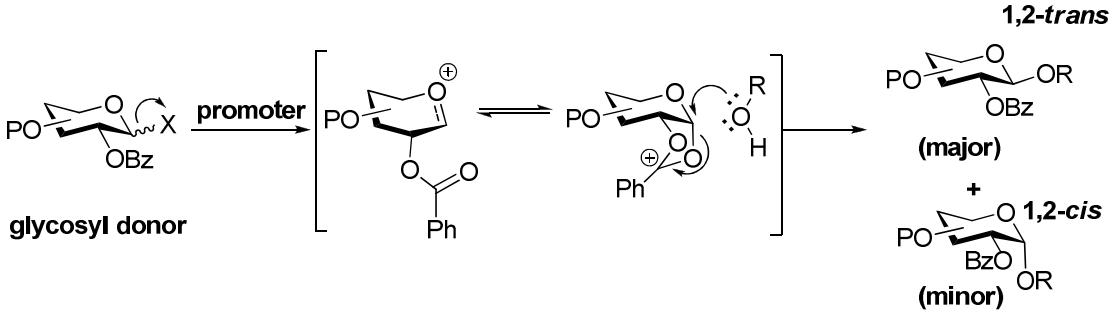


Figure 6

Glycosyl donors used for the synthesis of saccharides

Chemists have studied glycosylation for over a century and developed dozens of glycosylation protocols associated with hundreds of variants. There are several glycosylation methods involving different glycosyl donors[9] such as glycosyl

trichloroacetimidates,[10a] thioglycosides,[10b,c] glycosyl halides,[10d] 4-penten-1-yl glycosides,[10e] glycosyl sulfoxides,[10f] glycals,[10g] selenoglycosides,[10h] glycosyl phosphates,[10i] glycosyl phosphites,[10j] vinyl glycosides[10k] and 1,2-orthoesters[10l] (Figure 7). Recently, 1-Hydroxy sugars,[10m] 2-(hydroxycarbonyl) benzyl glycosides,[10n] glycosyl iodides[10o] and glycosyl thioimidates[10p,q] have also been reported as glycosyl donors for the synthesis of oligosaccharides. The name of the glycosylation method generally gives an idea about the functionality of the glycosyl donor except for the Fischer glycosylation that uses reducing sugars and the Koening-Knorr glycosylation that uses glycosyl bromides and chlorides as glycosyl donors.

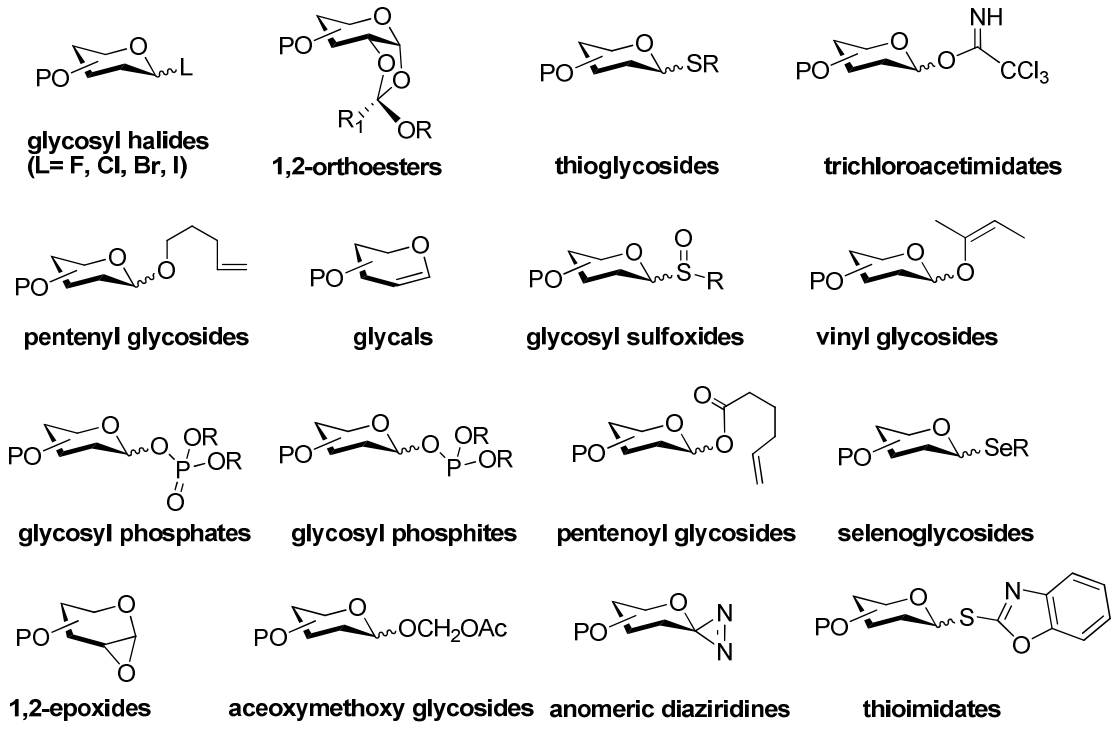


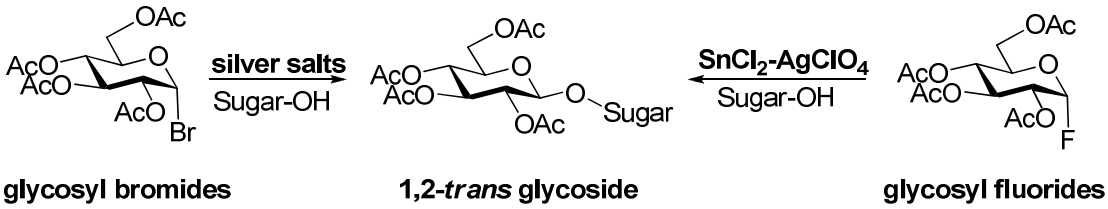
Figure 7

Glycosyl halides[10d,11]

The oldest and still most widely used method for the stereospecific synthesis of 1,2-*trans* glycosides is Köenings-Knorr reaction in which glycosyl bromides and chlorides are used as glycosyl donors in presence of insoluble promoters, Ag_2O and Ag_2CO_3 (Scheme 1). Soluble catalysts including $HgBr_2$ and $Hg(CN)_2$ (Helferich-Weiss, 1956),[11a] and AgOTf (Hanessian-Banoub, 1977)[11b] were exploited later as promoters. Short self-life of glycosyl bromides, excess use of silver salts usually four equivalents and the problem concerning the disposal of mercuric salts are major

drawbacks of this method. In 1981, Mukaiyama *et al*. introduced glycosyl fluorides as glycosyl donor in the presence of $SnCl_2$-$AgClO_4$.[11c] The introduction of fluorine as leaving group is good alternative to the Köenings-Knorr method in which C-F bond is stable.

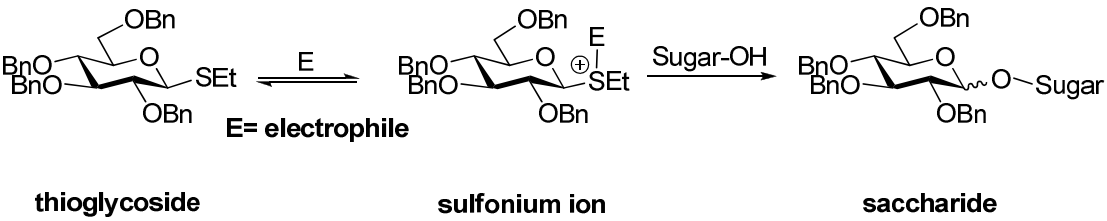
Scheme 1



Thioglycosides[10b,c,12]

Thioglycosides as glycosyl donors was first developed by Lönn *et al.* in 1980's. In this method, the promoter activates the sulphur of thioglycoside producing an intermediate sulfonium ion which in turn forms oxocarbenium ion and subsequently, trapped with the glycosyl acceptors offers glycosides and saccharides (Scheme 2). The promoters used for such reactions are MeOTf, DMTST, Iodinium dicollidine perchlorate, and NIS-TfOH.[12] The advantages of using thioglycosides are their stability under a wide range of reaction conditions. Additionally, thioglycosides act as temporary protecting groups at the anomeric position that helps to synthesize both glycosyl donors as well as glycosyl acceptors for the synthesis of oligosaccharides. But the unpleasant odour of thiols limits its use to make glycosyl donor.

Scheme 2

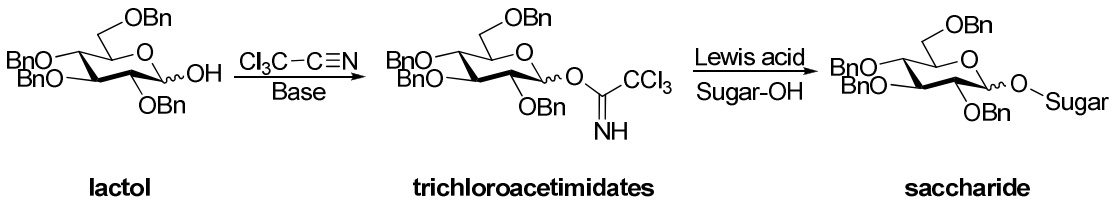


Trichloroacetimidates[10a,13]

Schmidt designed new glycosyl donors called trichloroacetimidates. In this approach, the anomeric trichloroacetimidates (formed by the treatment of hemiacetal

sugars using trichloroacetonitrile and base) are activated by Lewis acids such as $BF_3.OEt_2$, TMSOTf resulting in the formation of oxocarbenium ion which reacts with glycosyl acceptor to get glycosides and saccharides (Scheme 3). Trichloroacetimidates are useful to prepare both α-isomer and β-isomer at different conditions but, the intrinsic stability is too low.

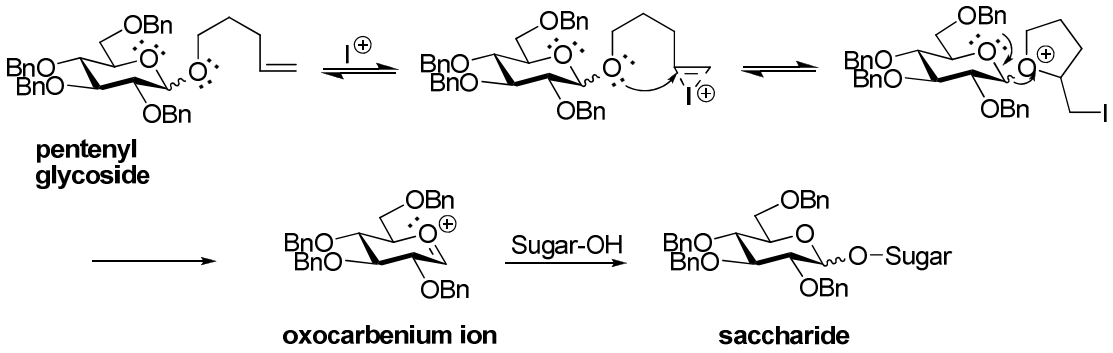
Scheme 3



4-Penten-1-yl glycosides[10e,14]

Fraser-Reid *et al*. introduced pentenyl glycosides as stable glycosyl donors in which the pentenyl group is activated by an electrophilic addition of iodinium ion to the double bond of glycosyl donor followed by an intramolecular displacement through an oxygen atom present at the anomeric centre and simultaneous removal of a cyclized product to form an oxocarbenium ion which is then trapped by glycosyl acceptor (Scheme 4). The promoters used for these reactions are NIS alone or NIS/Et_3SiOTf, NIS/TfOH and NIS/$Yb(OTf)_3$. Later, pentenyl 1,2-orthoester was also introduced by Fraser-Reid and successfully utilized along with pentenyl glycosides for the synthesis of oligosaccharides. But, the major limitation is the excess use of *N*-iodo succinimide along with harsh reagent, triflic acid.

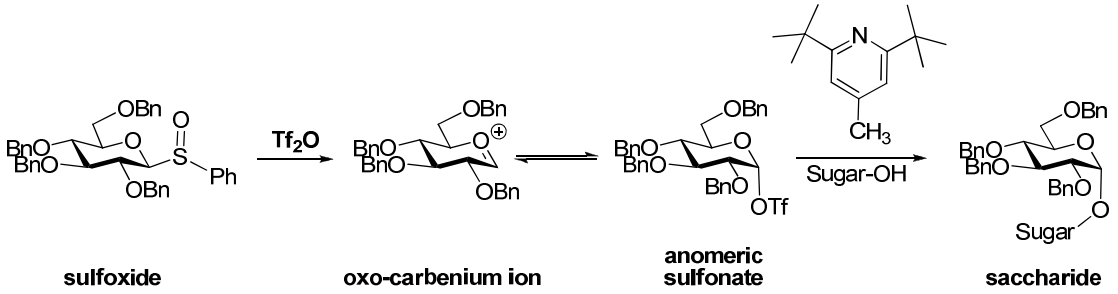
Scheme 4



Glycosyl sulfoxides[10f,15]

Kahne *et al*. introduced the sulfoxide method which is one of the most popular protocols especially for the synthesis of β-mannosides. Glycosyl sulfoxides can be prepared by oxidation of the corresponding thioglycosides, which is activated by triflic anhydride (Tf_2O) at -78 ^oC followed by the addition of 2,6-di-*tert*-butyl-4-methylpyridine and alcohols to get glycosides (Scheme 5). David Crich suggested that the formation of intermediate glycosyl sulfonates at low temperature enhances the 1,2-*cis* glycosylation.

Scheme 5



It is very difficult to predict which type of glycosyl donor will be most suitable to synthesize an oligosaccharide with controlled selectivity. However, there are some factors which influence the reactivity of glycosyl donor that should be taken into account and that can be further used in the optimization of an oligosaccharide synthesis. Beyond that, the success of glycosylation reaction depends on the reactivity of glycosyl acceptor and preferred selectivity of the product towards α- and β-isomers.

Reactivity of glycosyl donor

The reactivity of glycosyl donors mainly depends on the leaving ability of protecting group at the anomeric centre and the protecting groups attached to glycosyl donors. The leaving group attached to the anomeric carbon of glycosyl donor should be reactive in presence of promoter to facilitate the effective glycosylation. Apart from this, the substituent attached especially at C-2 in the glycosyl donor also influences the reactivity. Paulsen first observed, the glucosyl bromide having an ether group at C-2 is more reactive than the glucosyl donor having ester on C-2,[16] and it is very difficult to store per-*O*-benzylated glucopyranosyl bromide even at low temperature whereas per-*O*-benzoylated glucopyranosyl bromide can be stored at low

temperature for long time. Fraser-Reid noticed a similar type of observation while doing hydrolysis or methanolysis of *n*-pentenyl glycoside containing an ether and ester substituent attached on C-2 in the presence of NIS.[14b] The glycosyl donors are then classified into two main groups: armed donor which contains an ether substituent at C-2 whereas disarmed donor having an ester substituent. It was concluded that armed donors are more reactive than disarmed donors as an ester group can induce partial positive charge at the anomeric centre and slowly making the formation of oxocarbenium ion, and ether group accelerates the formation of oxocarbenium ion (Figure 8).

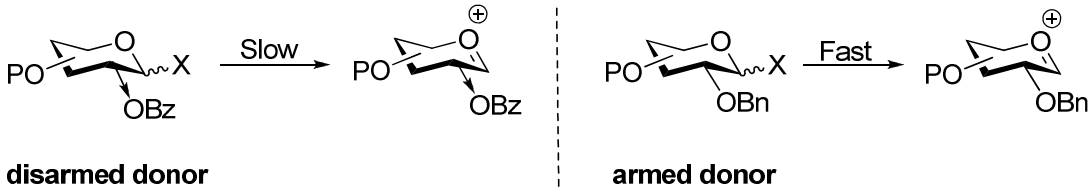


Figure 8

Based on the literature, a novel glycosyl donor must have the following characteristics to achieve glycosylation for the synthesis of oligosaccharides. 1) accessibility, 2) simple preparative procedure, 3) stability towards environmental conditions, 4) high stability toward protecting group manipulations, 5) anomeric protecting group should be reactive, 6) anomeric leaving group should be orthogonal with other protecting groups, 7) requires mild, catalytic activation conditions for the anomeric protecting group, 8) should provide stereoselective isomers at different conditions.

Reactivity of the glycosyl acceptor

There are several factors that influence the reactivity of glycosyl acceptors in the oligosaccharides synthesis. The first factor is the nucleophilicity of hydroxy groups in partially protected carbohydrates. In general, *primary* hydroxyl groups are more reactive than *secondary* hydroxyl groups in glycosylation. Second factor is the spatial orientation of the hydroxyl groups. For example, *equatorial* hydroxyl groups are more reactive than *axia*l hydroxyl groups due to more 1,3-diaxial interactions of the *axial* hydroxyl groups. The last factor is the nature of substituents present in the glycosyl acceptor which affect sometimes the nucleophilicity as well as reactivity of

glycosyl acceptors. For example, the electron-releasing groups such as benzyl ethers, isopropylidene groups increase the reactivity of acceptors whereas, the presence of electron-withdrawing groups and bulky substituents such as esters, TBDPS, TBDMS groups diminish the reactivity of glycosyl acceptors. When all hydroxyl groups attached to C-2, C-3, C-4 and C-6 in aldohexopyranoside have an *equatorial* orientation, the general order of reactivity in forming glycosidic linkages is: 6-OH >> 3-OH >>2-OH >>4-OH.

Anomeric effect[17]

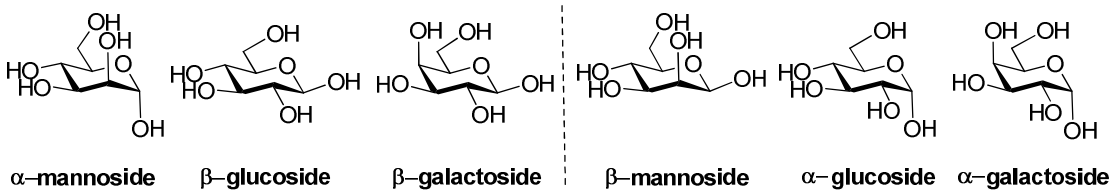


Figure 9

Two stereogenic isomers are generally possible at anomeric centre for any monosaccharide. They are termed as α- and β-isomers or 1,2-*cis* and 1,2-*trans* isomers (Figure 9). In general, the *equatorial* substituents of pyranose chair ring are most energetically favoured as compared to their *axial* counterparts because of steric reasons and 1,3-*diaxial* interactions. However, in D-pyranosides especially carbohydrate derivatives with electronegative group at anomeric centre, an *axial* position are often more stable than an *equatorial* position. The unusual preference of sterically unfavoured *axial* position over *equatorial* position at the anomeric centre has been termed as anomeric effect.[17] The anomeric effect is explained by Leimeux on the basis of intramolecular electrostatic interaction of two dipoles next to the anomeric centre. Anomeric configurations, where the two nearly perpendicular dipoles partially neutralize each other (an energetically more stable arrangement as in axial substituent) are favoured over the diastereomers where the anomeric configuration leads to intramolecular addition of the two parallel dipoles (an energetically unfavourable arrangement as in equatorial substituent) (Figure 10). The anomeric effect is different for each case and strongly influenced by the substituent situated at C-2 position. When the substituent at C-2 is an equatorial position as in the case of glucose and galactose, the anomeric effect is weakened whereas, the anomeric effect is enhanced in C-2 axial substituent of mannose.

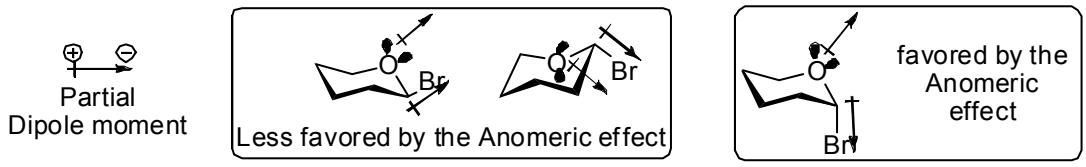


Figure 10

Anomeric selectivity

The formation of stereoselective anomers during glycosylation always proves the valuability of glycosyl donor, promoter and the success of glycosylation process. The achievement of anomeric selectivity still remains as a major problem especially in the case of glucosyl and galactosyl donors containing an ether substituent at C-2. The newly formed stereoisomeric mixture (α- and β-isomers) increases the complexity which is associated in the laborious purification. If these stereoisomers (anomers) are not separated after each glycosylation, the resulting complex mixtures cannot be used further to perform the desired biological studies. On the other hand, it is very difficult to prepare β-mannosides when mannosyl donor containing an ether substituent at C-2 due to the strong anomeric effect. Hence, the routine oligosaccharides synthesis will only be possible when robust stereoselective glycosylations become available. There are several approaches have been developed for a century to achieve stereoselective glycosylation. The following are the most reliable methods for the synthesis of stereoselective 1,2-*trans* glycosides:

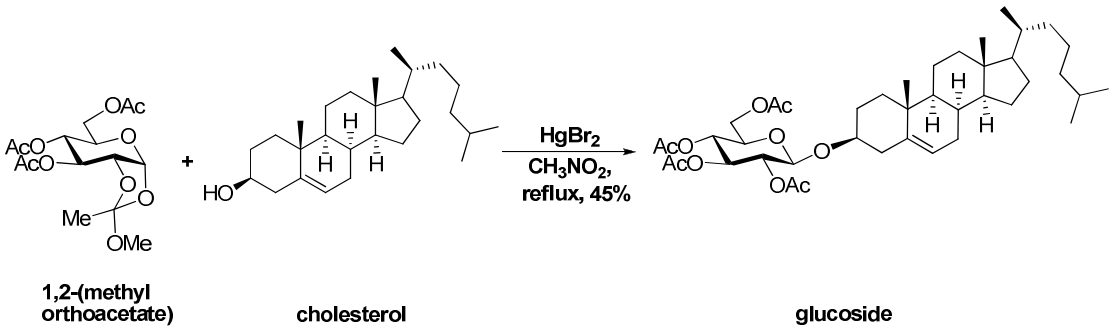
Neighbouring group participation of the 2-*O*-ester functionality

The substituent present at C-2 of glycosyl donor plays an important role in the stereoselective synthesis of 1,2-*trans* glycosides. When esters such as benzoate, acetate etc. are attached on C-2 of glycosyl donor, the promoter activates leaving group resulting in the formation of oxocarbenium ion which is in equilibrium with the stable dioxolenium ion formed by neighbouring group participation of carbonyl group of ester functionality that allows unidirectional attack of alcohols from *trans* side due to the steric influences exerted by this five membered ring offered 1,2-*trans* glycosides. Therefore, β-linked products is formed in the case of glucosyl-type donors whereas, mannosyl type-donors provides α-mannosides. This strategy is already shown in figure 6.

1,2-Orthoester strategy[10l,18]

1,2-Orthoester is a latent C-2 glycosyl donor, which is widely studied by Kochetkov *et al.* and employed for the stereoselective synthesis of 1,2-*trans* glycosides.[28a] The first paper with this work was published in 1964 using 3,4,6-tri-*O*-acetyl-α-D-glucopyranose-1,2-(methyl orthoacetate) and cholesterol in presence of $HgBr_2$ in nitromethane at reflux temperature (Scheme 6).[10l] Glucosyl and galactosyl donors offers β-glucosides and β-galactosides respectively, whereas, mannosyl 1,2-orthoester giving α-mannosides. Further, ethyl, isopropyl, *tert*-butyl and cyano 1,2-orthoesters as glycosyl donors have been studied by Kochetkov *et al*. for the effect of leaving ability of substituted alkyl group present in the 1,2-orthoester to the stereoselective synthesis of 1,2-*trans* glycosides.[18] Fraser-Reid *et al*. reported that pentenyl 1,2-orthoesters as glycosyl donors in the presence of NIS/$Yb(OTf)_3$ to get 1,2-*trans* glycosides and saccharides.[19] For 1,2-*trans* stereoselective glycosylation, benzoate and pivoloate protected 1,2-orthoesters are generally recommended as compared to acetate because the former reduces the formation of trans-orthoester.

Scheme 6



1,2-(methyl orthoacetate) cholesterol glucoside

Two routes are generally adopted for the mechanism to synthesize 1,2-*trans* glycosides using 1,2-orthoesters as glycosyl donors except for pentenyl 1,2-orthoester (Figure 11). They are

- **Direct glycosylation**

Promoter activates a leaving group attached to the quaternary carbon of 1,2-orthoester resulting in the formation of dioxolenium ion followed by unidirectional attack of an alcohol at the anomeric centre from *trans* face offers a 1,2-*trans* glycoside (Figure 11).

- **By two-stage glycosylation**

Initial trans-orthoesterification of 1,2-orthoester with an alcohol in the presence of promoter *via* the formation of dioxolenium ion, followed by isomerization leads to the formation of 1,2-*trans* glycoside (Figure 11).

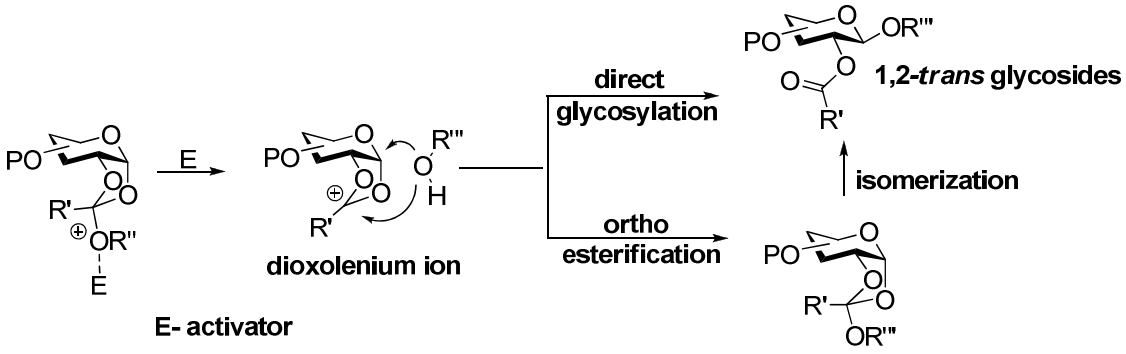


Figure 11

Synthesis of 1,2-*cis* glycosides

The introduction of 1,2-*cis* glycosidic linkage in glucosides, mannosides and galactosides requires glycosyl donors with non-assisting functionality like ethers at C-2. Use of these glycosyl donors always leads to the formation of mixture of compounds (α- and β-isomers). Consequently, the synthesis of 1,2-*cis* glycosides in a glycosylation is extremely difficult with respect to stereoselectivity and yield. However, the 1,2-*cis* stereoselectivity is sometimes enhanced with the use of diethyl ether solvent. Apart from this, there are several approaches have been addressed to solve this problem.

***In situ* anomerization or Halide catalysis**

Halide catalysis[20] is one of the popular methods for the synthesis of 1,2-*cis* glycosides. Lemieux's group first observed bromide anion of tetraalkyl ammonium bromide catalyzes the anomerization of α-pyranosyl bromides to β-pyranosyl bromides *in situ* which are highly reactive than α-pyranosyl bromides, and it is found that β-pyranosyl bromides utilized glycosylation gave α-glycosides in large proportions in a kinetically-controlled reaction. This method is known as *in situ* anomerization which gained a special inspiration in glycoworld (Figure 12). This protocol works effectively for galactose, fucose and glucose based glycosyl donors and not for mannose. Moreover, the yield of 1,2-*cis* glycoside is reduced with the use of less reactive glycosyl donor as well as glycosyl acceptor.

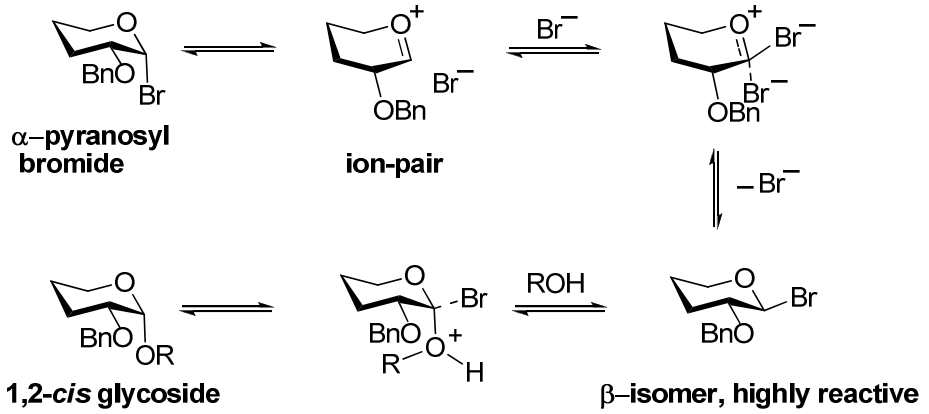


Figure 12

Intramolecular glycosidation

The reaction in which the glycosyl donor is linked to the glycosyl acceptor by means of a tether producing *O*-glycosidic bond *via* intramolecular delivery of aglycon is labelled as an intramolecular glycosidation. The tether may be either temporary which is eliminating during glycosylation or stable which is removed after glycosylation reaction (Figure 13).[21] This strategy has been widely utilized for the synthesis of 1,2-*cis* glycosides especially for β-mannosides and α-glucosides.

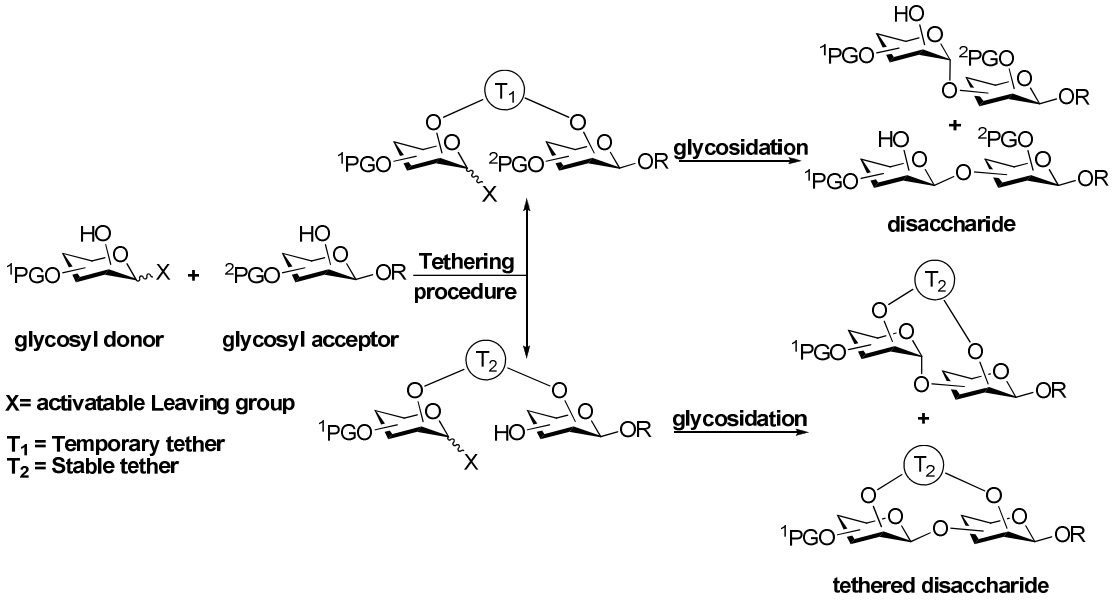
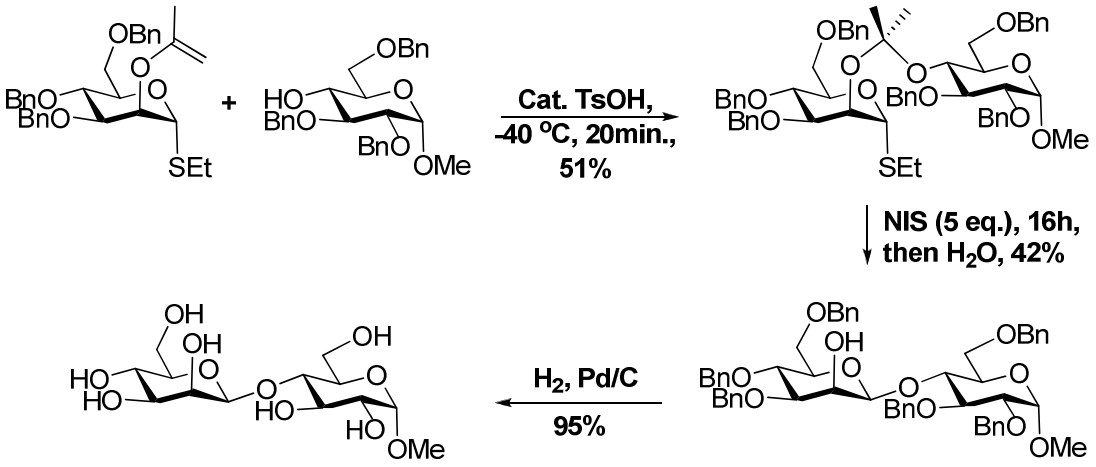


Figure 13

In 1991, Barresi and Hindsgaul[21a] reported the first example for an intramolecular glycosidation reaction in which vinyl ether of mannosyl donor linked to glucosyl acceptor was treated with NIS to afford β-mannoside *via* intramolecular delivery of aglycon (Scheme 7).

Scheme 7

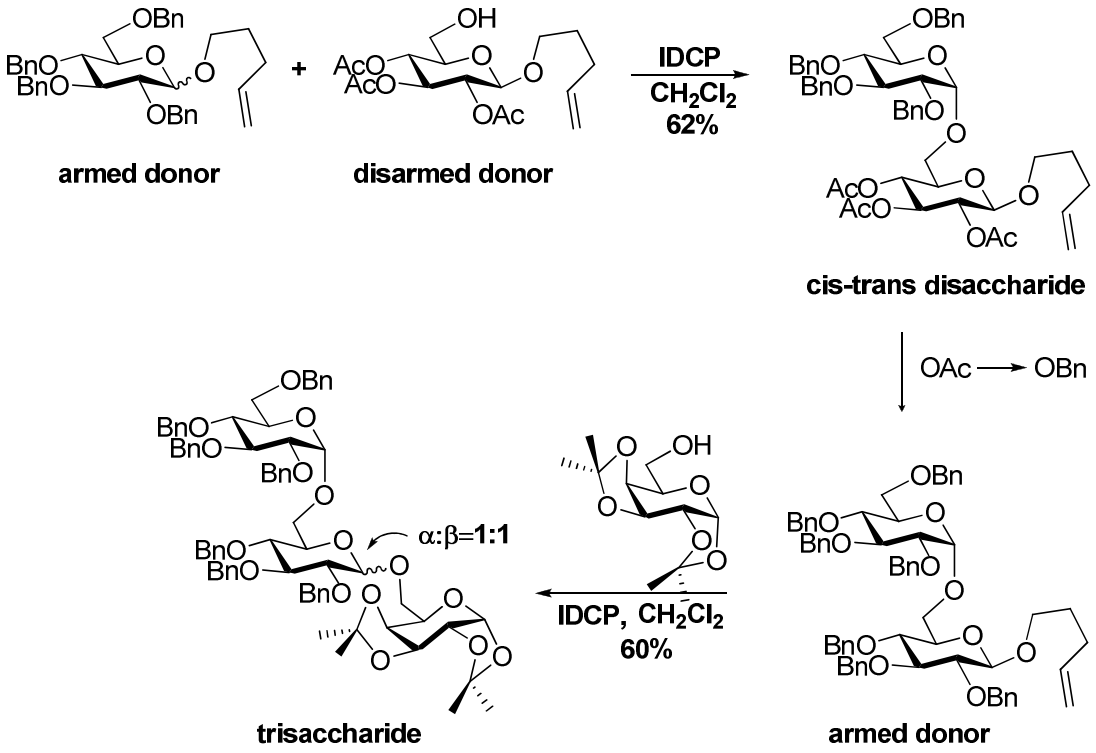


Synthesis of oligosaccharides[22]

Armed-Disarmed chemoselective glycosylation approach

When two glycosyl building blocks possess different reactivities at the anomeric centre due to the substituents present in C-2 are used, the more reactive building block enhances glycosylation in the presence of promoter as compared to a less reactive building block. The more reactive building block is known as an armed donor and the less reactive one is a disarmed donor.

Scheme 8



Fraser-Reid *et al*. demonstrated the utility of armed-disarmed effect[14a,b] for the synthesis of trisaccharide in which pentenyl glucoside containing benzyl ether substituents is activated chemoselectively with Iodinium dicollidine perchlorate (IDCP) in the presence of pentenyl glucoside containing acetate substituents. The resulting disaccharide is converted into an armed substrate in a two step process which in turn is activated with the acceptor derived from galactose in the presence of IDCP (Scheme 8). Similarly, various glycosyl donors such as thioglycosides, glycals etc. are utilized for the synthesis of oligosaccharides *via* an armed-disarmed strategy.[23]

Latent-Active approach[24]

In all differential donor activation approaches, an oligosaccharide is assembled from the non-reducing end to the reducing end. Roy *et al.* first coined the latent-active term for the different reactivity possessed by *p*-nitrophenyl thiosialoside and *N*-aminophenyl thiosialoside during glycosylation.[24a] Later, the latent-active strategy is applied for the synthesis of oligosaccharides *via* an aglycon moiety (Y) inert to glycosyl donor activation condition is installed at the anomeric centre of the acceptor. After glycosylation with glycosyl donor, the 'latent' group at the reducing end of newly formed saccharide is transformed to an activatable leaving group (X) which is now an 'active glycosyl donor' (Figure 14). The success of this approach crucially relies upon the ability to convert the latent aglycon into an activatable leaving group in high yield without affecting the protecting groups.

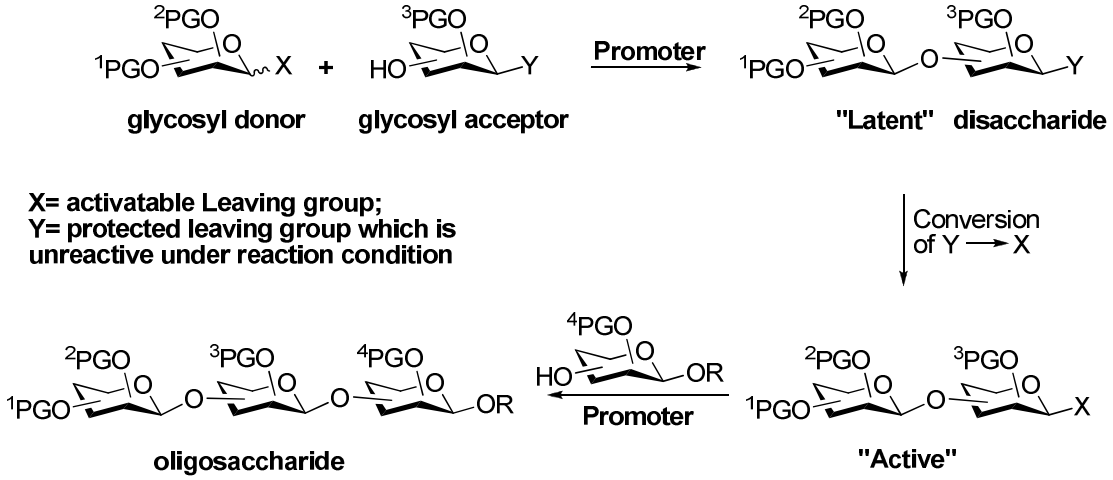
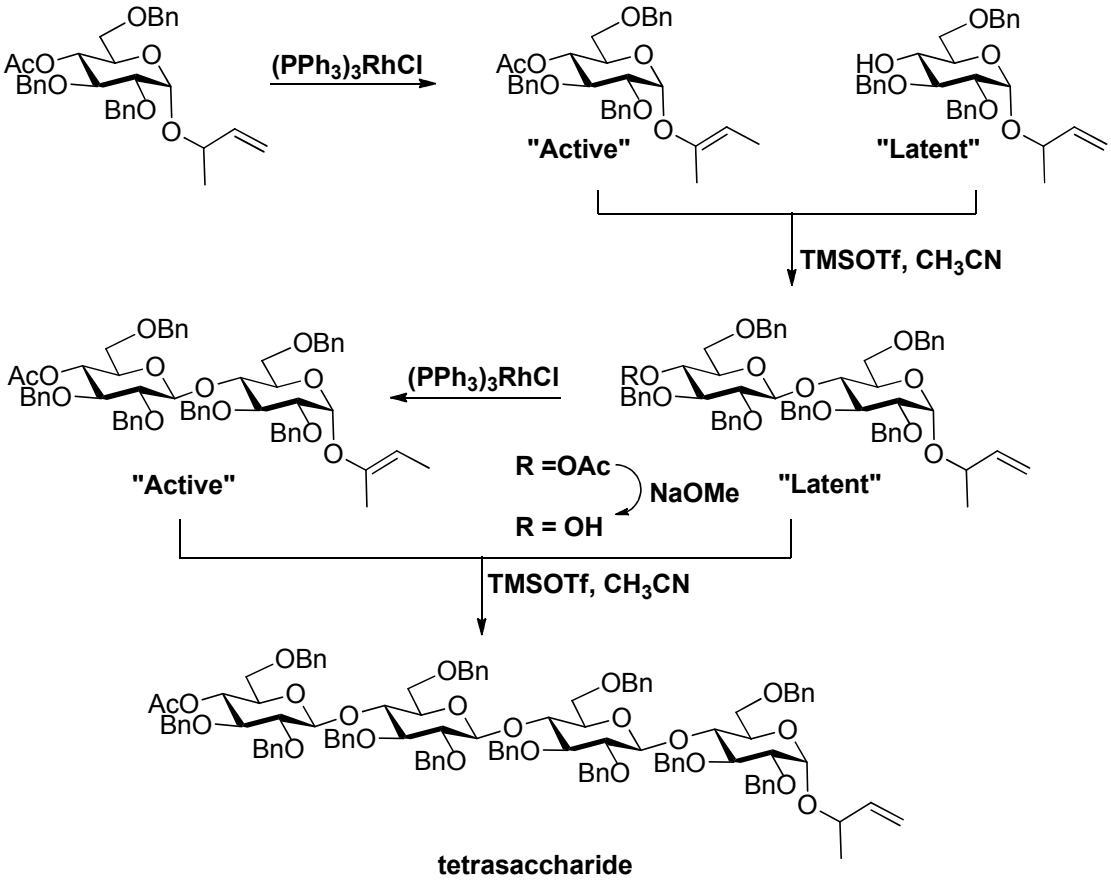


Figure 14

Geert-Jam Boons *et al*. utilized latent-active concept for the synthesis of tetrasaccharide[22,24b-d] in which 2-buten-2-yl glycoside formed from the isomerization

of 3-buten-2-yl glycoside using Wilkinson catalyst, is activated with 3-buten-2-yl glycoside in the presence of TMSOTf. The resulting 3-buten-2-yl saccharide is converted to an active glycosyl donor 2-buten-2-yl saccharide using Wilkinson catalyst which in turn is activated with 3-buten-2-yl glycoside in the presence of TMSOTf (Scheme 9).

Scheme 9



Orthogonal activation[25]

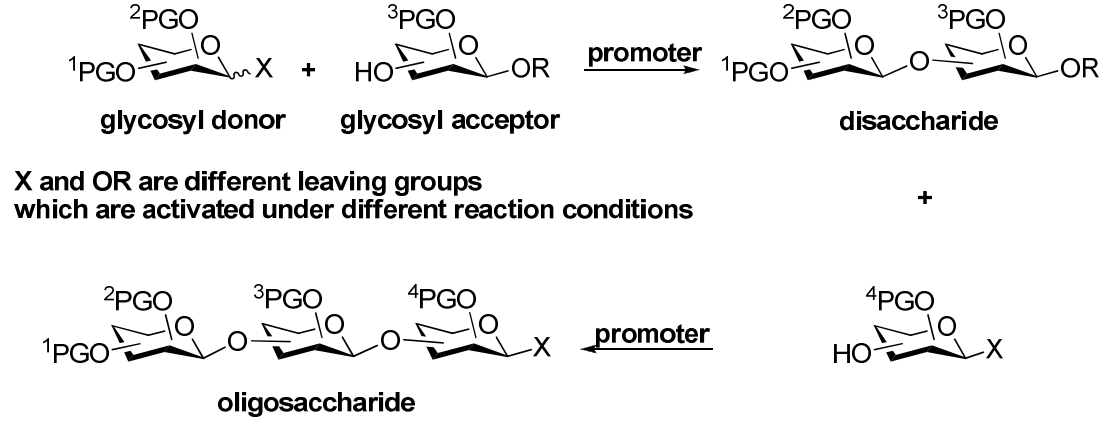
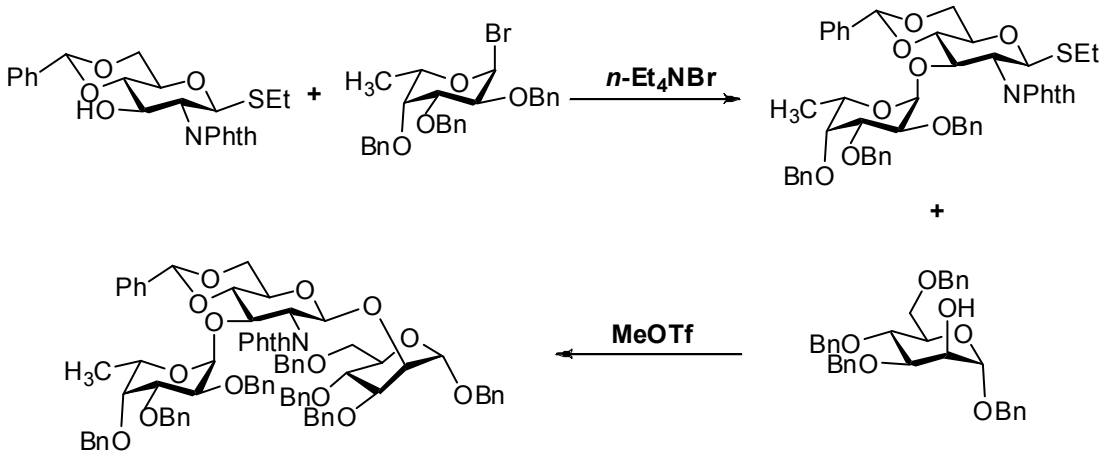


Figure 15

Baranay and Merrifield are the two scientists, introduced and exploited orthogonality in chemistry for the synthesis of peptides based on a system having set of completely independent classes of protecting group in which each class can be removed in presence of other classes.[25a,b] Later, Hans Lönn utilized the concept of orthogonality in carbohydrate chemistry (Figure 15) for the synthesis of trisaccharides and hexasaccharides in which thioglycoside is activated with methyl triflate and pyranosyl bromide is activated with *n*-tetraethylammonium bromide.[25c,d] For example, 2,3,5-tri-*O*-benzyl-α-L-fucopyranosyl bromide is treated with ethyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside in presence of *n*-tetraethylammonium bromide and the resulting disaccharide is converted to a required trisaccharide using methyl triflate activator (Scheme 10).

Scheme 10



Problems and Challenges in oligosaccharide syntheses

Till now, there are several methods have been reported based on the different glycosyl donors to synthesize glycosides and saccharides. However, problems associated in the glycosyl donors and promoters reduce its use in glycosylation reaction. For example, 1) the intrinsic stability of glycosyl halides and trichloroacetimidates are usually low. So, it is very difficult to store these compounds at low temperature for long time. 2) Toxic promoters such as MeOTf, Tf_2O, TMSOTf used glycosylation creates problem while handling as well as quenching, and further, these promoters are destroying the environment. Sometimes, the use of expensive heavy metal salts in large scale reactions is often dangerous. These difficulties can be

diminished by using a catalytic amount of mild promoter which should have low toxicity, an environmentally non-pollutant and easily accessible.

Further, glycosyl donor activation often requires a combination of reagents, and the promoters are used in either stoichiometric or excess equivalents. Also, non-stoichiometry is observed in the ratio related to donor: acceptor equivalents owing to the instability of glycosyl donors under reaction conditions. Moreover, the anomeric selectivity is poor when benzyl ether is attached on C-2 of glucosyl and galactosyl donors. Sometimes, the reactivity of acceptor such as *axial*, *equatorial*, *primary*, *secondary* alcohols reduce the formation of stereoselective isomers due to the presence of substituents, steric and electronic effects. Even though, the formation of 1,2-*cis* or 1,2-*trans* linkages still remains an independent problem and difficult task which requires systematic research on both glycosyl donors as well as glycosyl acceptors.

Beyond that, there are several challenges exists while synthesizing oligosaccharides. For example, 1) minimum manipulation of protecting groups is always important as it reduces the number of steps involved in the formation of building blocks. 2) Selective activation of anomeric groups (If X, Y are orthogonal groups which have different reactivities, Y can be activated in the presence of X and *vice versa*) are difficult tasks for the synthesis of oligosaccharides as it reduces the manipulation of protecting groups involved in the oligosaccharide synthesis

All these facts clearly revealed that the chemical synthesis of oligosaccharides in a highly stereoselective manner is still a challenging and intriguing area. Owing to some basic disadvantages in the existing glycosylation methods and the synthetic challenges in oligosaccharides, most of the synthetic efforts have been explored on the discovery of novel glycosyl donors as well as promoters in order to get a high stereoselectivity.

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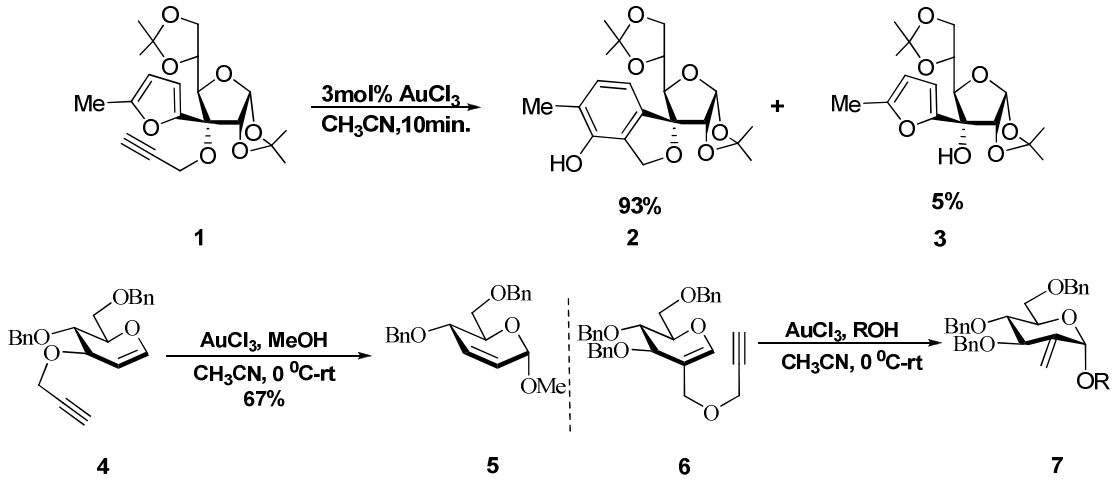
Present Work

Naturally and unnaturally produced oligosaccharides embedded with proteins and peptides in cells are well known to play key roles in various biologically important processes. The necessity to prepare such complex oligosaccharides is to better our understanding of how oligosaccharides influence the property of system to which they are attached. The synthesis of an oligosaccharide in definite composition generally needs the specific research to develop a new protocol based on the choice of protecting groups, possible participating groups, promoters/catalysts, reaction conditions, reactivity of donor leaving group and reactivity of glycosyl acceptor. As the formation of glycosidic linkage has been a major driving force for the oligosaccharide synthesis, most of the efforts have focused on the discovery of new glycosyl donors and promoters which have ability to produce high stereoselectivity in glycosylation. Thus, the area of oligosaccharides synthesis in a stereoselective manner is still a valuable and challenging task for chemists to design and develop the new *O*-glycosylation strategies for biological purpose.

In our laboratory, the propargyl ether attached to tertiary carbon cleaved 5% from the starting material 1,2:5,6-bis-*O*-(1-methylethylidene)-3-*C*-(5-methyl-2-furanyl)-3-*O*-prop-2-ynyl-allofuranose **1** when performed the intramolecular Diels-Alder reaction in the presence of 3mol% of $AuCl_3$ in acetonitrile (Scheme 11).[26] Similar observation was identified once again when a 3-*O*-prop-2-ynyl-4,6-di-*O*-benzyl-1,2-glucal **4** was treated with methanol in the presence of 3mol% of $AuCl_3$ in

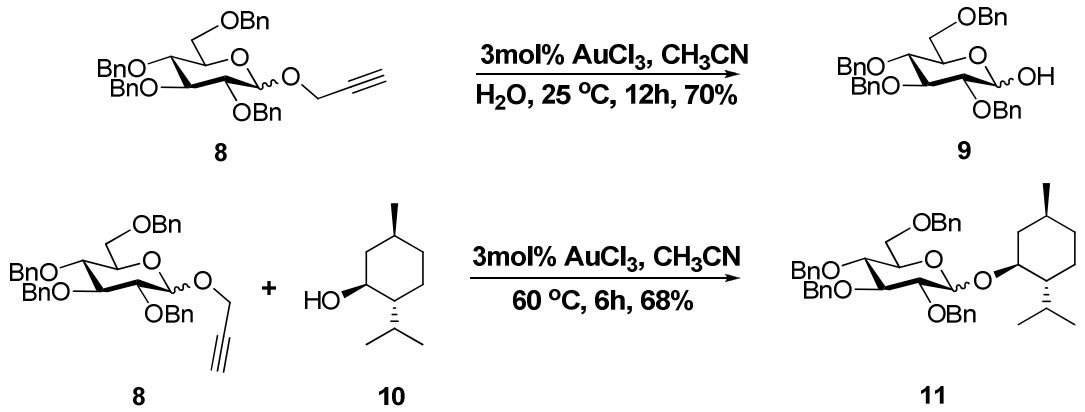
Scheme 11



CH_3CN and found an unexpected methyl 2,3-dideoxy glucoside **5** (Scheme 11).[27] In order to study the validity of $AuCl_3$ mediated propargyl ether deprotection, various alcohols were used to obtain glycosides and disaccharides. Initial coordination of carbon-carbon triple bond by $AuCl_3$ allowed the cleavage of propargyloxy moiety and simultaneous attack of alcohols from α-face at an anomeric centre to give the stereoselective α-glycosides. $AuCl_3$ mediated activation of propargyloxy moiety was utilized later for the synthesis of C-2 methylene glycosides **7** using per-*O*-benzylated C-2 propargyloxy methyl glycals **6** as glycosyl donors.[28]

Deprotection of propargyl ether in carbohydrates was already reported by different research groups using samarium iodide and water, dicobaltoctacarbonyl followed by TFA, low-valent titanium and metal catalyzed isomerization.[29] Unfortunately, none of the methods have ever been utilized for the synthesis of saccharides. Beyond that, a well known application of carbon-carbon triple bond, Click reaction[2c,30] to synthesize bioconjugates provides an enticing opportunity to utilize propargyl glycosides as possible glycosyl donors.

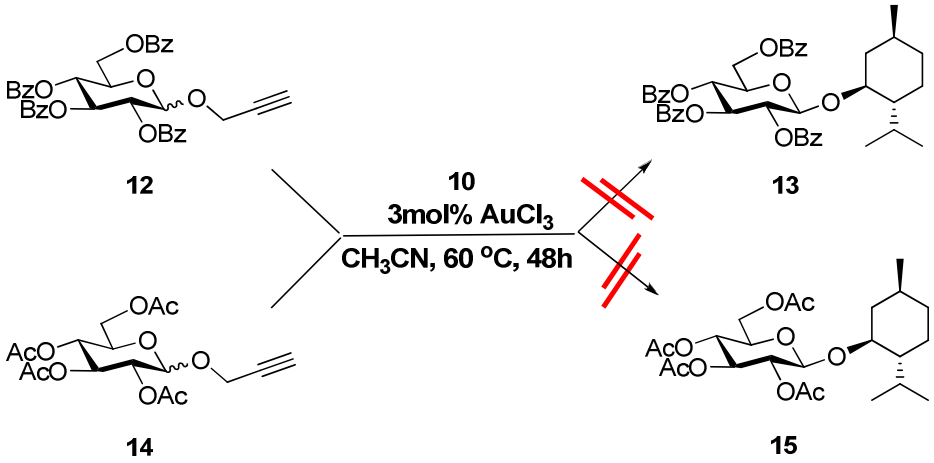
Scheme 12



For the first time, propargyl glycosides were activated in the presence of $AuCl_3$ for the synthesis of glycosides and disaccharides in our laboratory.[31] In this approach, initial treatment of prop-2-ynyl 2,3,4,6-tetra-*O*-benzyl-α,β-D-glucopyranosides **8** with water in presence of 3mol% $AuCl_3$ in acetonitrile for 12h at room temperature gave a mixture of per-*O*-benzylated lactols **9** (Scheme 12). Encouraging results suggested to swipe water with other nucleophilic alcohols to facilitate transglycosylation for the synthesis of glycosides and disaccharides. The glycosylation performed between

propargyl glucoside **8** and menthol **10** in the presence of 3mol% $AuCl_3/CH_3CN$/ 60 °C/6h afforded a mixture of menthyl glucosides in 68% yield. The same glycosylation failed when other alkyne activators namely $PtCl_2$, $Cu(OAc)_2$, $Co_2(CO)_8$ and $RuCl_3$ catalyst were used. Further, glycosylation failed to give 1,2-*trans* glycosides when the glycosylation was attempted between propargyl per-*O*-benzoylated **12** or per-*O*-acetylated **14** glucosides and an aglycone **10** in the presence of 3mol% $AuCl_3/CH_3CN$/60 °C (Scheme 13). Later, the glycosylation protocol has been applied to armed propargyl glucoside, mannoside and galactoside with various alcohols for the synthesis of glycosides and disaccharides. It was reported that propargyl glucoside and galactoside gave α,β mixture of glycosides whereas, mannosyl donor provided the α-isomer due to strong anomeric effect as well as bulky axially disposed benzyloxy group at C-2.

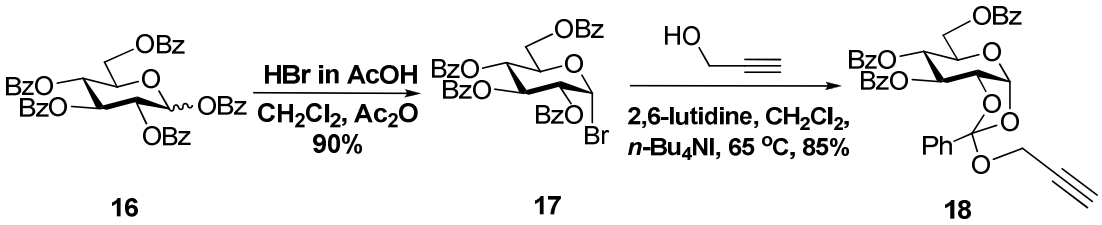
Scheme 13



The common advantages of propargyl glycosides are 1) stable towards the environmental conditions and protecting group manipulations, 2) glycosyl donor which required 3mol% of $AuCl_3$ for the activation of propargyloxy group, 3) easily accessible and 4) widely useful for the synthesis of bioconjugates *via* copper catalyzed cycloaddition reaction with azide derived from proteins and lipids. Unfortunately, a mixture of products formed during glycosylation when a propargyl glucoside and galactoside were used in the presence of $AuCl_3$ in acetonitrile at higher temperature. Glycosylation generally performed at higher temperature allowed the cleavage of protecting group(s) which is sensitive to acids either from an aglycone or from the glycosylated product led to the formation of complex mixtures, and the poor

selectivity was observed for the formation of 1,2-*trans* glycosylated product. In order to accomplish the gold catalyzed glycosylation in a 1,2-*trans* stereoselective manner, we envisioned to utilize gold mediated activation of propargyloxy group present in propargyl 1,2 *O*-orthoesters which might work as glycosyl donors and deliver glycosyl moiety to glycosyl acceptor to form a "*trans"* glycosidic bond. Sugar 1,2-orthoester is a masked glycosyl donor in which a leaving group attached to the quaternary carbon was activated by Lewis acids resulting in the formation of dioxolenium ion followed by unidirectional attack of an alcohol at the anomeric centre resulting in 1,2-*trans* glycoside stereoselectively.

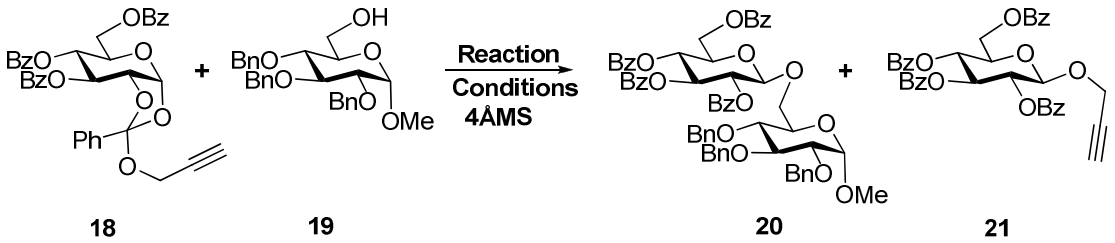
Scheme 14



16 **17** **18**

To commence our investigation, a 3,4,6-tri-*O*-benzoyl-α-D-glucopyranose-1,2-(prop-2-ynyl orthobenzoate) **18** was chosen as a model substrate and prepared from glucose in a two step manner.[32] The treatment of glucose penta-*O*-benzoate **16** with HBr in AcOH forms 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl bromide **17** that was subsequently reacted with propargyl alcohol, 2,6-lutidine and a catalytic amount of TBAI in dichloromethane at 65 ^{o}C for 2 days to give propargyl 1,2-orthoester **18** (Scheme 14). In the ^{1}H NMR spectrum of compound **18**, resonances at δ 2.40 ppm as a triplet and δ 3.99 ppm as a doublet attributed to methine proton and methylene protons of propargyl group along with a characteristic β-configured anomeric proton signal δ 6.11 ppm as a doublet (J = 5.31 Hz) were noticed. Rest of the signals in the spectrum were completely in agreement with the assigned structure **18**. In addition, ^{13}C NMR spectrum revealed the characteristic signals corresponding to α-anomeric carbon and the quaternary carbon at δ 97.7 and 121.1 ppm whilst rest of the other signals were in accordance to the assigned structure **18**. The structure was further supported by mass spectroscopic analysis (Mol. Wt. Calcd. 634.62, Found: 656.21 (M^{+} + 23 for Na)).

Scheme 15



18 **19** **20** **21**

Table 1

Entries	Catalysts & Reaction Conditions	Time (h)	%20	%21
1	$AuCl_3$ (5 mol%)/ CH_3CN / 60 ^oC	36	0	0
2	$AuCl_3$ (10 mol%)/ CH_2Cl_2 / 25 ^oC	24	30	50
3	$AuBr_3$ (10 mol%)/ CH_2Cl_2 / 25 ^oC	5	63	20
4	$HAuCl_4$ (10 mol%)/ CH_2Cl_2 / 25 ^oC	1	45	28
5	Au_2O_3 (10 mol%)/ CH_2Cl_2 / 25 ^oC	72	0	0
6	HCl/ Et_2O-CH_2Cl_2/ 60 ^oC	24	0	0
7	AuCl (10 mol%)/ CH_2Cl_2 / 25 ^oC	36	0	0
8	PPh_3AuCl (10 mol%)/ CH_2Cl_2 / 25 ^oC	24	0	0

The glycosylation reaction carried out between a propargyl 1,2-orthoester **18** and methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside **19** in the presence of 5mol% of $AuCl_3$ in acetonitrile at room temperature resulting in the formation of per-*O*-benzoylated lactol as sole product. We thought that the addition of 4Å molecular sieves powder (freshly activated) as dehydrating agent would assist in diminishing the

lactol formation. Accordingly, the glycosylation was conducted once again in the presence of 5mol% $AuCl_3/CH_3CN$/rt/4ÅMS powder under argon atmosphere. Unfortunately, we failed to observe disaccharide in spite of several attempts by changing temperature (from rt-60 ^oC) and for longer periods of time (36h) (Scheme 15, Table 1, entry 1). At that moment, we envisioned that the change of solvents might work to achieve glycosylation. For that, dichloromethane was initially replaced in place of acetonitrile. The glycosylation reaction performed between **18** and **19** in the presence of 5mol% $AuCl_3/CH_2Cl_2$/rt/4ÅMS powder under argon atmosphere resulting in the formation of two new compounds. However, the reaction did not complete even after 24h. The complete conversion of propargyl 1,2-orthoester **18** was accomplished under conditions 10mol% of $AuCl_3/CH_2Cl_2$/rt/24h/4ÅMS powder under argon atmosphere and the two compounds are identified as 1,2-*trans* disaccharide **20** in 30% yield along with prop-2-ynyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranoside **21** in 50% yield (entry 2). The two compounds were thoroughly confirmed by various spectroscopic techniques such as ^1H, ^{13}C, DEPT NMR and mass spectral analysis. In the ^1H NMR spectrum of compound **20**, disappearance of resonances due to propargylic methine proton, methylene protons and at the same time, signals corresponding to methoxy protons were observed at δ 3.20 ppm as a singlet. Further, aromatic protons corresponding to benzoates and benzyl ethers were noticed at δ 7.00-8.00 ppm as multiplets and the remaining peaks were completely in agreement with the assigned structure **20**. In addition, the ^{13}C NMR spectrum revealed the resonances corresponding to the 1,2-*trans* and 1,2-*cis* anomeric carbons at δ 101.3 and 97.9 ppm whilst the remaining resonances were in accordance to the assigned 1,2-*trans* disaccharide **20**. Further, DEPT NMR spectrum specified the five signals with negative intensity at δ 63.2, 68.3, 73.3, 74.7 and 75.5 ppm for the presence of five methylene groups ($-CH_2-$) in the assigned disaccharide **20**, and the mass spectrum showed a molecular ion base peak at 1065.65 (M^++ 23 for Na). Whereas, the ^1H NMR spectrum of compound **21** showed the resonances corresponding to methine proton and methylene protons of propargyl group at δ 2.41 ppm as a triplet and δ 4.42 ppm as double doublet along with aromatic protons of benzoate esters at δ 7.23-8.06 ppm as multiplets. Additionally, a characteristic peak of α-configured anomeric proton was evident at δ 5.16 ppm as a doublet with a coupling constant J = 7.86 Hz. Rest of the

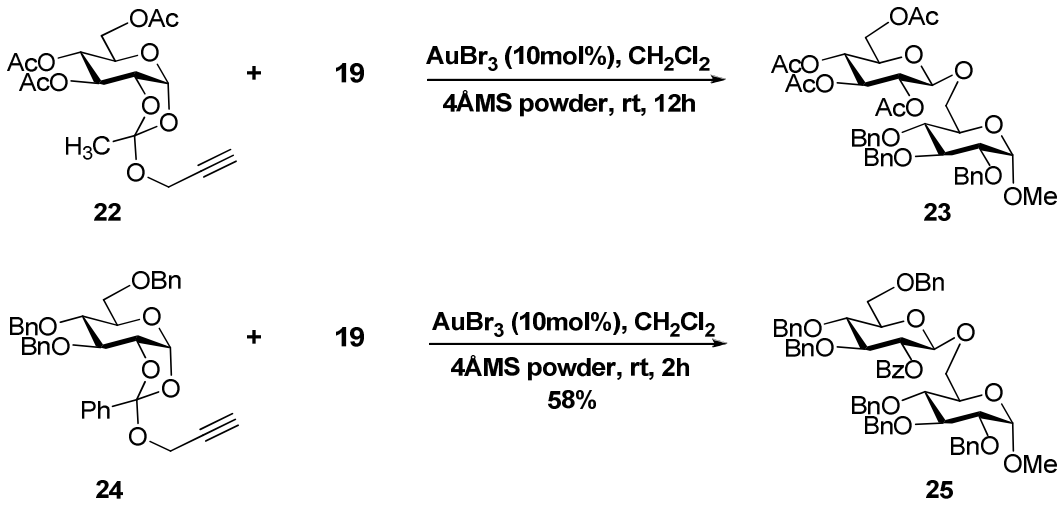
other signals in the spectrum were completely in agreement with the assigned structure **21**. Further, the ^{13}C NMR spectrum revealed resonance corresponding to the anomeric carbon at δ 98.4 ppm while rest of the resonances were in accordance to the assigned structure **21**.

The glycosylation results suggested that with 4Å molecular sieves powder, acetonitrile does not reduce the activation energy after complexation of $AuCl_3$ with propargyl group whereas, dichloromethane reduces the activation energy thereby $AuCl_3$ activating the propargyloxy group of propargyl 1,2-orthoester for the formation of stable glycosylated product. In addition, $AuCl_3$ solely is responsible for the excess formation of propargyl per-*O*-benzoylated glucoside due to its more Lewis acidic character. To improve the formation of 1,2-*trans* disaccharide and simultaneously suppress the formation of compound **21**, we decided to use a less Lewis acidic $AuBr_3$ as a catalyst. Accordingly, the glycosylation was conducted in presence of 10mol% $AuBr_3$ in dichloromethane and freshly activated 4Å molecular sieves powder at room temperature under argon atmosphere (entry 3). The glycosylation proceeded smoothly to afford satisfactorily 63% yield of 1,2-*trans* disaccharide **20** along with a propargyl per-*O*-benzoylated glucopyranoside **21** (20%).

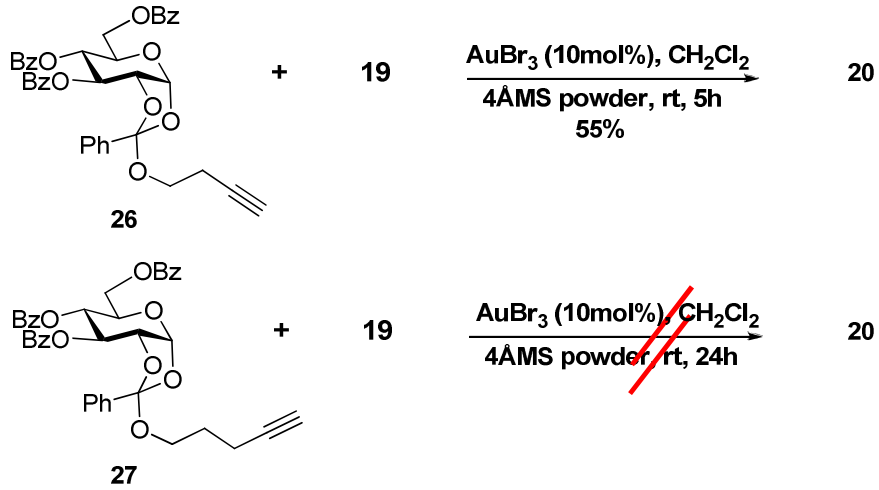
We understood that, the liberated acid also causes the formation of propargyl per-*O*-benzoylated glucopyranoside. To minimise such process, we decided to use organic bases after addition of $AuBr_3$. Accordingly, the glycosylation was performed in the presence of 10mol% of $AuBr_3$ with organic bases such as triethylamine, DBU DIPEA, N,N'-tetramethylurea etc. All attempts at the glycosylation were failed and the donor propargyl 1,2-orthoester resistant to these conditions which suggested that organic bases either quench the acid liberated from $AuBr_3$ thereby catalytic cycle was arrested or directly coordinate to $AuBr_3$ so the activity reduced towards the activation of propargyl 1,2-orthoester. Our efforts to promote the glycosylation in order to achieve high stereoselectivity, the glycosylation reaction was carried out with other gold (III) salts. The glycosylation performed in the presence of 10mol% of $HAuCl_4$ (entry 4) (which instantly liberates HCl *in situ*) in dichloromethane gave a 1,2-*trans* disaccharide **20** in 45% yield whereas glycosylation tried with Au_2O_3 (entry 5) failed to give a disaccharide, which clearly suggests Au (III) alone can't activate propargyl 1,2-orthoester. Further, the glycosylation was carried out with a saturated solution of HCl in diethyl ether and dichloromethane at 60 ^oC for 24h and the reaction was failed

to give 1,2-*trans* disaccharide that implies HCl alone is not enough to activate propargyl 1,2-orthoester for the synthesis of disaccharide (entry 6). Further, studies towards the 1,2-*trans* glycosylation with gold(I) salts namely AuCl and PPh_3AuCl were futile (entries 7 and 8). After optimization with several catalysts and different conditions, it was observed that 10mol% of $AuBr_3$ in dichloromethane as an effective promoter for the activation of propargyloxy group present in the propargyl 1,2-orthoester to synthesize 1,2-*trans* disaccharide stereoselectively, and the addition of freshly activated molecular sieves powder is always necessary to minimise the formation of per-*O*-benzoylated glucopyranose.

Scheme 16



Scheme 17



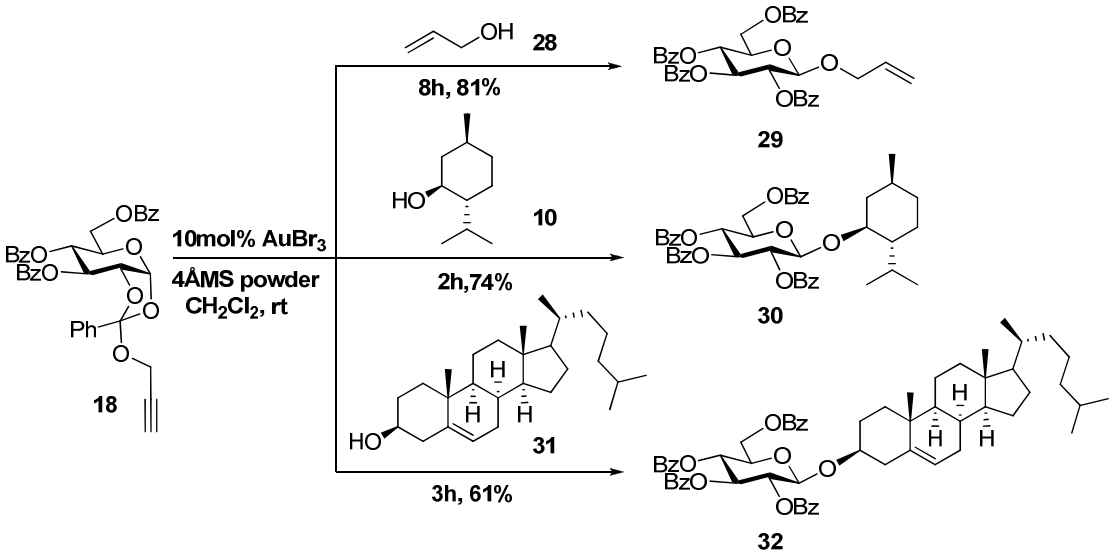
Having a optimized conditions in hand, the effect of $AuBr_3$ was studied for the stereoselective glycosylation between various alkynyl 1,2-orthoesters (**22**, **24**, **26** and

27) and the glycosyl acceptor **19**. In favour of that, we designed propargyl 1,2-orthoacetate **22**, propargyl per-*O*-benzylated 1,2-orthobenzoate **24**, homopropargyl 1,2-orthoester **26** and pentynyl 1,2-orthoester **27** *via* aforementioned procedures from the respective monosaccharides. A solution of 3,4,6-tri-*O*-acetyl-α-D-glucopyranose-1,2-(prop-2-ynyl orthoacetate) **22** in dichloromethane was treated with glycosyl acceptor **19** in the presence of 10mol% $AuBr_3$/rt/4ÅMS powder under argon atmosphere and observed incomplete conversion of starting materials giving a complex mixtures of products whereas the glycosylation of 3,4,6-tri-*O*-benzyl-α-D-glucopyranose-1,2-(prop-2-ynyl orthobenzoate) **24** with glycosyl acceptor **19** afforded a 1,2-*trans* disaccharide **25** in 58% yield (Scheme 16). In the ^{1}H NMR spectrum of compound **25**, methoxy group was identified at δ 3.19 ppm as a singlet, aromatic protons corresponding to six benzyl ethers and benzoate ester were noticed at δ 6.98-7.94 ppm as multiplets, and the remaining peaks were completely in agreement with the assigned structure **25**. In addition, the ^{13}C NMR spectrum showed the signals corresponding to 1,2-*cis* and 1,2-*trans* anomeric carbons at δ 97.9 and 101.1 ppm along with one carbonyl group resonance at δ 164.9 ppm. Rest of the spectrum was in accordance with the assigned structure **25**. The structure was further confirmed by mass spectrum which shows a molecular ion peak at 1024.06 (M^++23 for Na). Further, the glycosylation reaction conducted between a 3,4,6-tri-*O*-benzoyl-α-D-glucopyranose-1,2-(homopropargyl orthobenzoate) **26** and the glycosyl acceptor **19** in the presence of 10mol% $AuBr_3$/CH_2Cl_2/rt/4ÅMS powder under argon atmosphere gave 1,2-*trans* disaccharide **20** in 55% yield and the glycosylation of 3,4,6-tri-*O*-benzoyl-α-D-glucopyranose-1,2-(pentynyl orthobenzoate) **27** with **19** did not yield a disaccharide (Scheme 17). The aforementioned experiments confirmed that 1) propargyl 1,2-orthoesters are the best glycosyl donors, 2) 10mol% $AuBr_3$ is good for suppressing the rearranged isomerized product, 3) 4ÅMS powder is required, and 4) solvent should be CH_2Cl_2.

Further, propargyl 1,2-orthoester activation was investigated to demonstrate the applicability of 1,2-orthoester **18** for the synthesis of variety of 1,2-*trans* glucosides using a panel of aglycones. Accordingly, glucose 1,2-orthoester **18** was allowed to react with aglycones allyl alcohol **28**, menthol **10** and cholesterol **31** in the presence of 10mol% $AuBr_3$/CH_2Cl_2/rt/4ÅMS powder under argon atmosphere

(Scheme 18). It is pertinent to mention that all glycosylations proceeded smoothly and afforded the respective 1,2-*trans* glucosides (**29, 30** and **32**) in good yields. All glucosides were confirmed thoroughly by ^{1}H, ^{13}C, DEPT NMR and mass spectroscopic techniques. In the ^{1}H NMR spectrum of menthyl glucoside **30**, disappearance of peaks related to methine proton, methylene protons of propargyl group and at the same time, the new resonances attributed to menthol moiety were noticed in the aliphatic region. Additionally, a signal corresponding to the anomeric hydrogen of the β-glucoside was identified at δ 4.93 ppm as a doublet with coupling constant J = 7.93 Hz whilst the rest of other peaks were completely in agreement with the assigned structure **30**. Whereas, the ^{13}C NMR spectrum showed a signal corresponding to the anomeric carbon at δ 99.0 ppm and the remaining resonances were in accordance to the assigned structure **30**.

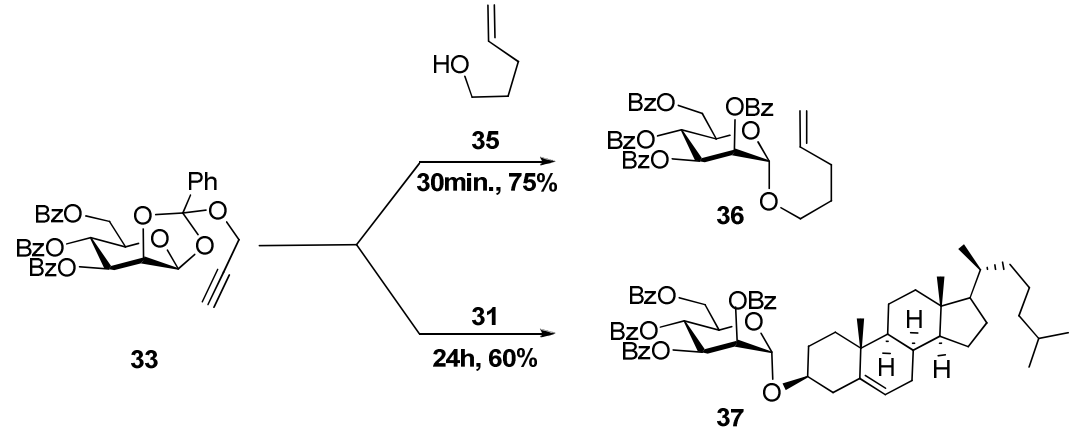
Scheme 18



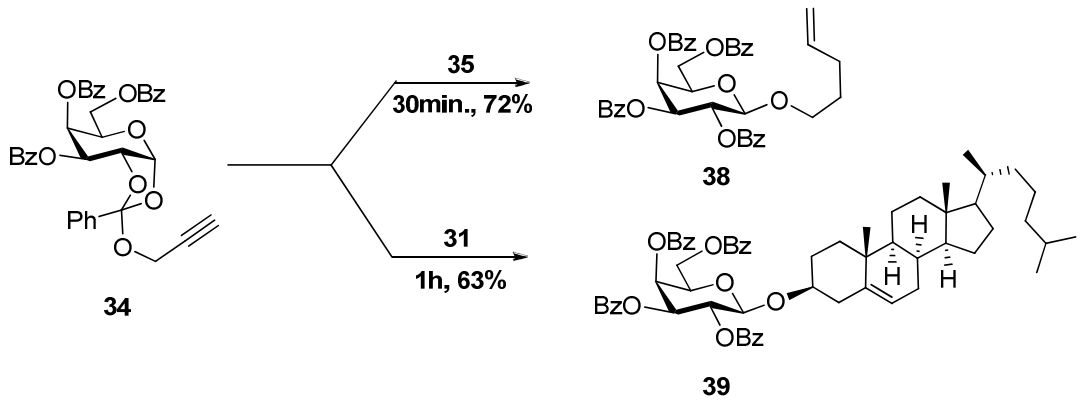
The 1,2-*trans* stereoselective glycosylation procedure has been extended to other glycosyl donors such as propargyl 1,2-orthoester of mannose **33** and galactose **34**. These orthoesters were prepared *via* the aforementioned procedures from the respective monosaccharides and characterized thoroughly by ^{1}H, ^{13}C and DEPT NMR spectroscopic analysis. In the ^{1}H NMR spectrum of propargyl 1,2-orthoester of mannose **33**, resonances corresponding to methine proton and methylene protons of propargyl group were noticed at δ 2.24 ppm as a triplet and δ 4.55 ppm as a double doublet along with α-faced anomeric proton signal at δ 5.83 ppm as a doublet with a

coupling constant J = 3.1 Hz. Rest of the spectrum was in accordance with the assigned structure **33**. In addition to this, ^{13}C NMR spectrum revealed resonances corresponding to the β-anomeric carbon and the quaternary carbon at δ 98.0 and 122.7 ppm respectively, while the rest of other signals were completely in agreement with the assigned structure **33**. Similarly, the ^{1}H NMR spectrum of galactosyl 1,2-orthoester **34** showed the signals corresponding to methine proton and methylene protons of propargyl group at δ 2.40 ppm as a triplet and at δ 4.06 ppm as a doublet. Further, the resonances corresponding to benzoate esters and the anomeric proton were identified at δ 7.20-8.05 ppm as multiplets and δ 6.26 ppm as a doublet with a coupling constant J = 5.2 Hz respectively. All other signals were completely in agreement with the assigned structure **34**. Furthermore, in the ^{13}C NMR spectrum, resonances attributed to the α-anomeric carbon and the quaternary carbon at δ 98.3 and 120.1 ppm were noticed whilst rest of the resonances were completely in accordance to the assigned structure **34**.

Scheme 19



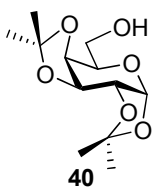
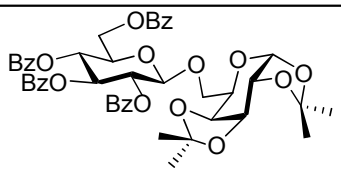
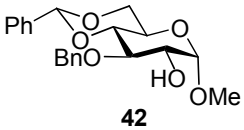
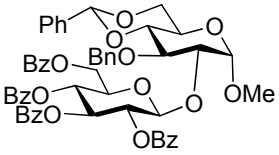
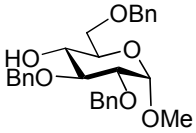
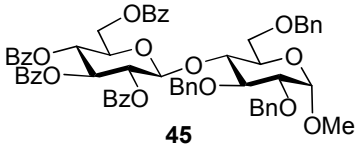
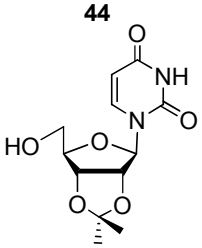
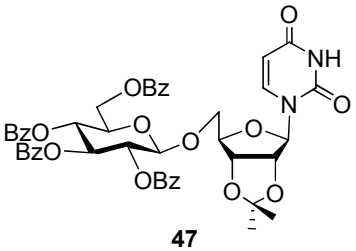
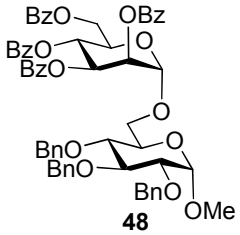
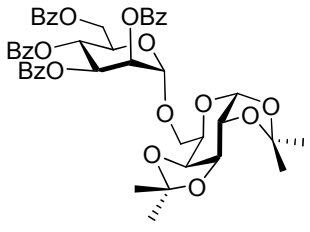
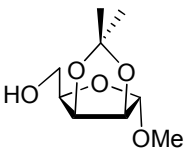
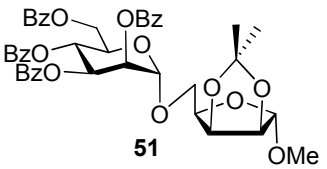
Reagents and Conditions: 10mol% $AuBr_3$, CH_2Cl_2, 4ÅMS powder, rt



The glycosylation reaction was carried out between a 3,4,6-tri-*O*-benzoyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthobenzoate) **33** and aglycones comprising 4-penten-1-ol **35** and cholesterol **31** in the presence of 10mol% $AuBr_3/CH_2Cl_2$/rt/4ÅMS powder under argon atmosphere to obtain the corresponding 1,2-*trans* mannosides (**36** and **37**) in good yields (Scheme 19). Similarly, the glycosylation of 3,4,6-tri-*O*-benzoyl-α-D-galactopyranose-1,2-(prop-2-ynyl orthobenzoate) **34** with aglycones such as 4-penten-1-ol **35** and cholesterol **31** in the presence of 10mol% $AuBr_3/CH_2Cl_2$/rt/4ÅMS powder under argon atmosphere afforded the corresponding 1,2-*trans* galactosides (**38** and **39**) in good yields. All glycosylated products were thoroughly characterized by the nuclear magnetic spectroscopic and mass spectral analysis. For example, the ^{1}H NMR spectrum of cholesteryl α-mannoside **37** showed disappearance of peaks corresponding to methine proton, methylene protons of propargyl group and simultaneously, the new signals corresponding to cholesterol moiety except alkenyl proton were evident in the aliphatic region. In addition, a signal corresponding to the anomeric proton of α-mannoside was noticed at δ 5.25 ppm as a doublet with a coupling constant J = 1.39 Hz along with the aromatic protons of benzoate esters signals at δ 7.20-8.11 ppm as multiplets. Rest of the spectrum was in accordance with the assigned structure **37**. Further, the ^{13}C NMR spectrum revealed resonance corresponding to the α-anomeric carbon at δ 95.9 ppm while other resonances were completely in agreement with the assigned structure **37**. In the case of the ^{1}H NMR spectrum of pentenyl galactoside **38**, disappearance of resonances corresponding to methine proton, methylene protons of propargyl group and at the same time, the new resonances attributed to pentenyl moiety were noticed at δ 1.59-1.75, 1.94-2.06 ppm as two multiplets, δ 3.59 ppm as a double triplet and δ 4.76-4.86 ppm as a multiplet. All other resonances were in alignment with the assigned structure **38**. Further, the structure **38** was confirmed by ^{13}C NMR spectrum wherein signal corresponding to the anomeric carbon of the β-galactoside was identified at δ 101.6 ppm along with the requisite resonances.

In addition, it has been envisioned that disaccharides also can be synthesized from the identified methodology by simply switching the aglycon to an alcohol derived from a monosaccharide unit. Accordingly, propargyl 1,2-orthoester of glucose **18** was treated with a 1,2:3,4-di-*O*-isopropylidene galactopyranose **40** in the presence

Table 2

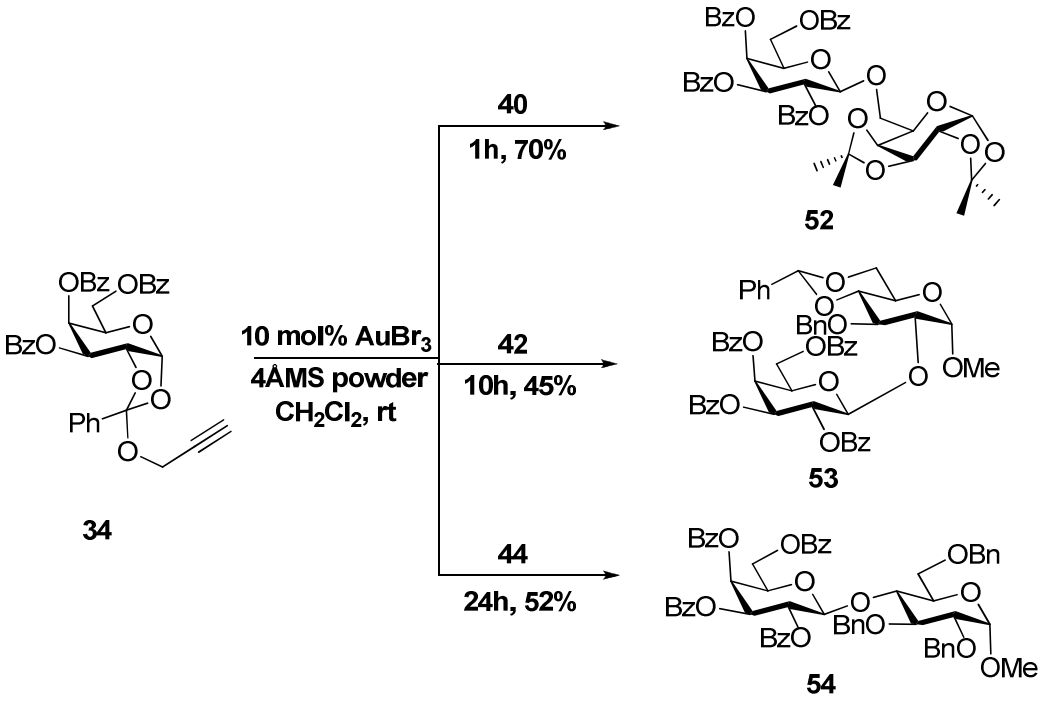
Propargyl 1,2-orthoesters	Glycosyl acceptors	1,2-*trans* disaccharides	Time & Yield
18	 **40**	 **41**	**30min., 80%**
18	 **42**	 **43**	**10h, 42%**
18	 **44**	 **45**	**8h, 45%**
18	 **46**	 **47**	**2h, 50%**
33	**19**	 **48**	**6h, 68%**
33	**40**	 **49**	**24h, 70%**
33	 **50**	 **51**	**2h, 77%**

*** Reagents and Conditions: 10mol% $AuBr_3$/ CH_2Cl_2 / rt / 4ÅMS powder**

of 10mol% $AuBr_3/CH_2Cl_2$/rt/4ÅMS powder under argon atmosphere for 30 min. to obtain 1,2-*trans* disaccharide **41** in 80% yield. Interestingly, the isopropylidene groups survived under $AuBr_3$ conditions. Similarly, glucosyl 1,2-orthoester **18** reacted smoothly with secondary alcohols (**42** and **44**) and a nucleoside based primary alcohol **46** in the presence of 10mol% $AuBr_3/CH_2Cl_2$/rt/4ÅMS powder under argon atmosphere provided the respective 1,2-*trans* disaccharides in moderate yields (**43**, **45** and **47**) (Table 2). The validity of current protocol was further determined with propargyl 1,2-orthoester of mannose **33**. The glycosylation reaction carried out between a mannose 1,2-orthoester **33** and glycosyl acceptor comprising primary alcohols (**19**, **40** and **50**) in the presence of 10mol% $AuBr_3/CH_2Cl_2$/rt/4ÅMS powder under argon atmosphere afforded the corresponding 1,2-*trans* disaccharides (**48**, **49** and **51**) in good yields (Table 2). All glycosylated disaccharides were thoroughly characterized by ^1H, ^{13}C and DEPT NMR spectral analysis. For example, in the ^1H NMR spectrum of compound **49**, resonances corresponding to the isopropylidene groups and two anomeric protons were identified at δ 1.36, 1.43, 1.63 ppm as three singlets, δ 5.16 (J = 1.65 Hz) and 5.57 ppm (J = 4.95 Hz) as two doublets. In addition to this, the signals corresponding to benzoate esters were noticed at δ 7.22-8.14 ppm as mutiplets while the remaining signals were completely in agreement with the assigned structure **49**. Further, the ^{13}C NMR spectrum revealed resonances corresponding to the anomeric carbons having two 1,2-*cis* linkages at δ 96.3 and 97.8 ppm whilst rest of the other signals were in accordance to the assigned structure **49**. Furthermore, DEPT NMR spectrum showed two signals with negative intensity at δ 62.9 and 67.6 ppm which confirming the presence of two methylene groups ($-CH_2-$) in the assigned disaccharide **49**. The structure was further confirmed by mass spectral analysis (Mol. Wt. calculated for $C_{46}H_{46}O_{15}$: 838.28, Found: 862.50 (M^++ 23 for Na)).

Further, the glycosylation of galactose 1,2-orthoester **34** was also attempted with primary alcohol **40** and secondary alcohols (**42** and **44**) in the presence of 10mol% $AuBr_3/CH_2Cl_2$/rt/4ÅMS powder under argon atmosphere. Performed glycosylations gave the respective 1,2-*trans* disaccharides (**52**, **53** and **54**) from moderate to good yields (Scheme 20). The newly galactosylated disaccharides were confirmed thoroughly by ^1H, ^{13}C, DEPT NMR and mass spectroscopic techniques.

Scheme 20

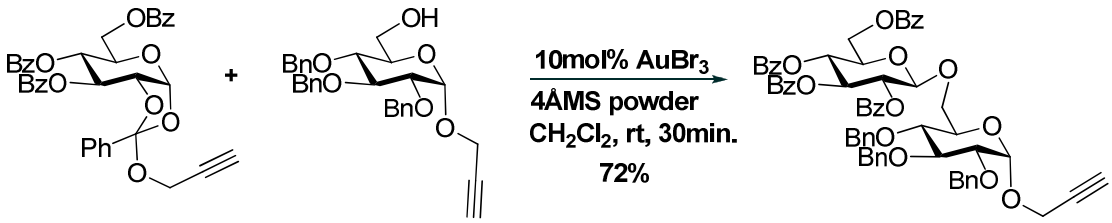


It is noteworthy to declare that propargyl 1,2-orthoesters behaved as glycosyl donors in all attempted glycosylations in the presence of $AuBr_3$ in dichloromethane and provided the respective 1,2-*trans* glycosides and disaccharides in a stereoselective fashion from moderate to good yields. Interestingly, the protecting groups such as isopropylidene and benzylidene acetals which are sensitive to acids were inert under reaction conditions.

Identified glycosylations *via* gold (III) salts mediated activation of propargyl group situated in the propargyl 1,2-orthoesters[32] as well as propargyl glycosides[31] provided us an additional interest to study the effect of $AuBr_3$ on the selective activation of propargyl 1,2-orthoesters and propargyl glycosides for the synthesis of oligosaccharides and glycoconjugates. As delineated above, propargyl glycosides can be activated by $AuCl_3$ in CH_3CN at 60 ^oC and propargyl 1,2-orthoesters were activated by $AuBr_3$ in CH_2Cl_2 at room temperature. The different reactivities exhibited by gold salts (solvent and temperature) gave motivation to conduct the glycosylation between propargyl 1,2-orthoesters and propargyl glycosides having hydroxyl functionality in $AuBr_3/CH_2Cl_2$/rt conditions. In order to elucidate our synthetic plan, prop-2-ynyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside **55** was chosen as a designer model substrate and synthesized by the literature reported procedure.[33] The glycosylation reaction was

carried out between glucosyl 1,2-orthoester **18** and propargyl glucoside **55** in the presence of 10mol% $AuBr_3/CH_2Cl_2$/rt/4ÅMS powder under argon atmosphere (Scheme 21). Gratifyingly, $AuBr_3$ selectively activated the propargyloxy group of propargyl 1,2-orthoester **18** and made it behave as a glycosyl donor in the presence of propargyl glucoside to afford 1,2-*trans* disaccharide stereoselectively with propargyl group at the reducing end in 72% yield. The 1,2-*trans* disaccharide was confirmed thoroughly by various spectroscopic techniques such as ^1H, ^{13}C, DEPT NMR and mass spectral analysis.

Scheme 21

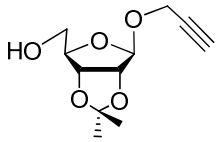
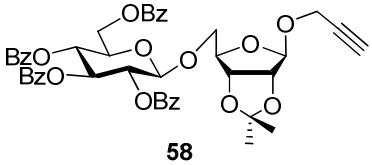
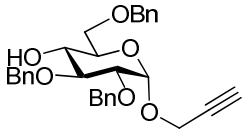
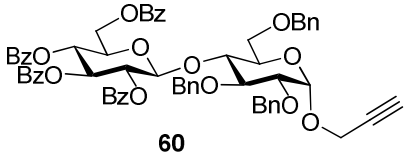
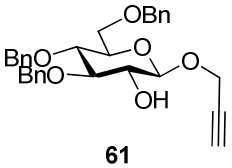
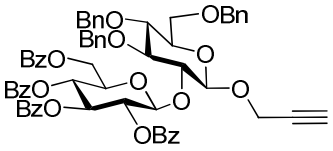
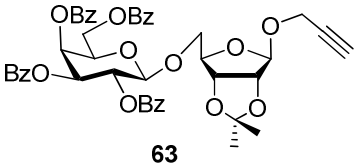
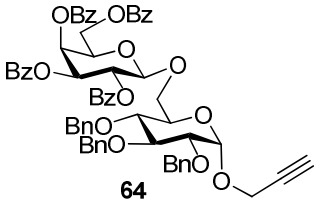
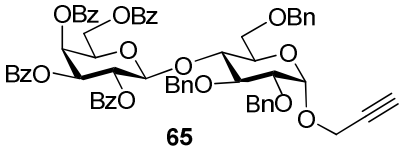
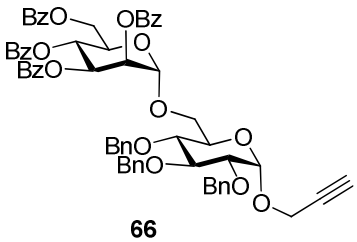


18 **55** **56**

In the ^1H NMR spectrum of compound **56**, resonances due to propargylic methine proton and methylene protons were disappeared and at the same time, a signal corresponding to methine proton of propargyl group from glycosyl acceptor **55** was evident at δ 2.38 ppm as a triplet. In addition, the signals attributed to aromatic protons of benzoate esters and benzyl ethers were observed at δ 7.01-8.01 ppm as multiplets and the remaining signals were completely in agreement with the assigned structure **56**. Further, the ^{13}C NMR spectrum showed the resonances corresponding to the two anomeric carbons having 1,2-*cis* and 1,2-*trans* linkages at δ 95.0 and 101.3 ppm while rest of the resonances were completely in agreement with the assigned structure **56**. The structure was further supported by DEPT NMR spectrum wherein the resonances at δ 54.3, 63.2, 68.1, 72.9, 74.7 and 75.5 ppm with negative intensity confirming the presence of six methylene groups ($-CH_2-$) in the assigned structure **56**.

Interesting selective activation of propargyl 1,2-orthoesters was explored for the generality by treating glucosyl 1,2-orthoester **18** with glycosyl acceptors ribofuranoside **57** and secondary alcohols (**59** and **61**) in the presence of 10mol% $AuBr_3/CH_2Cl_2$/rt/4ÅMS powder under argon atmosphere. It is worth mentioning that all attempted glycosylations proceeded smoothly and afforded the respective 1,2-*trans*

Table 3

Propargyl 1,2-orthoesters	Glycosyl acceptors	1,2-*trans* disaccharides	Time & Yield
18	 **57**	 **58**	15min., 63%
18	 **59**	 **60**	1h, 62%
18	 **61**	 **62**	2h, 68%
34	57	 **63**	15min., 60%
34	55	 **64**	5h, 65%
34	59	 **65**	10h, 55%
33	55	 **66**	2h, 72%

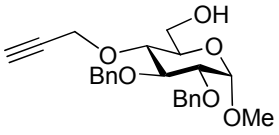
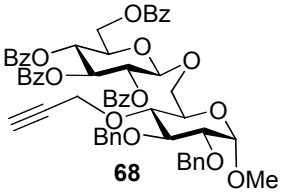
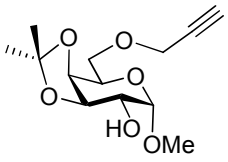
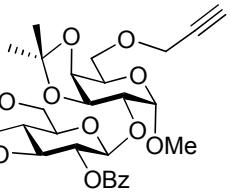
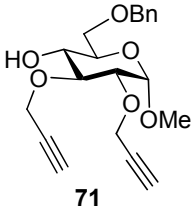
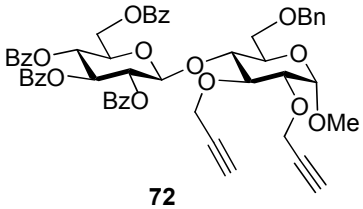
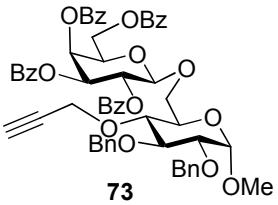
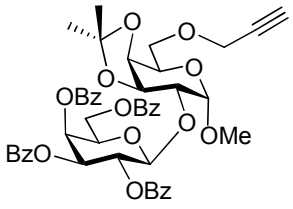
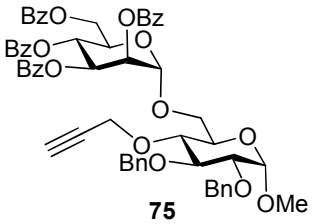
* Reagents and conditions: 10mol% $AuBr_3$/ CH_2Cl_2 / rt / 4ÅMS powder

disaccharides as propargyl glycosides (**58**, **60** and **62**) in good yields (Table 3). The glycosylation protocol has been extended to the propargyl 1,2-orthoesters of galactose **34** and mannose **33**. The glycosylation reaction was carried out between a galactosyl 1,2-orthoester **34** and glycosyl acceptors containing primary alcohols (**57** and **55**) and secondary alcohol **59** to obtain the corresponding 1,2-*trans* disaccharides as propargyl glycosides (**63**, **64** and **65**) in good yields whereas mannosyl 1,2-orthoester **33** reacted with sugar based primary alcohol **55** resulting in the formation of 1,2-*trans* disaccharide **66** (72%) in a stereoselective manner (Table 3). All glycosylated disaccharides were confirmed thoroughly by the spectroscopic techniques such as ^{1}H, ^{13}C, DEPT NMR and mass spectra. In the ^{1}H NMR spectrum of compound of **63**, the resonances corresponding to isopropylidene groups, methine proton and methylene protons of propargyl group were observed at δ 1.19, 1.38 as two singlets, δ 2.40 ppm as a triplet and δ 4.06 ppm as a double doublet respectively. In addition to this, resonances due to the anomeric carbons having 1,2-*trans* linkages and benzoate esters were noticed at δ 4.89 ppm as a doublet (J = 7.9 Hz), δ 5.18 ppm as a singlet and at δ 7.21-8.12 ppm as multiplets. Rest of the spectrum was in accordance with the assigned structure **63**. Further, the ^{13}C NMR spectrum revealed the signals attributed to the two β-anomeric carbons at δ 101.2 and 106.4 ppm. Further, a signal corresponding to the quaternary carbon of isopropylidene acetal was identified at δ 112.4 ppm whilst the remaining peaks were in accordance to the assigned structure **63**. Furthermore, DEPT NMR spectrum showed three signals with negative intensity at δ 53.9, 61.9 and 69.9 ppm for the presence of three methylene groups ($-CH_2-$) in the assigned structure **63**. The structure **63** was further supported by mass spectral analysis which showed a molecular ion peak at 829.26 (M^{+}+23 for Na).

The oligosaccharide synthesis often requires use of more than one protecting group and propargyl ethers are sometimes exploited in glycosylation as they are orthogonal to many of the other routinely used protecting groups. Further, propargyl ethers can be utilized for the synthesis of triazole clicked conjugates *via* CuAAC reaction. Thus, the effect of $AuBr_3$ towards the selectivity of the propargyl 1,2-orthoesters in the presence of propargyl ether(s) of monosaccharide was investigated. Accordingly, propargyl 1,2-orthoester of glucose **18** was treated with methyl 2,3-di-*O*-benzyl-4-*O*-prop-2-ynyl-α-D-glucopyranoside **67** in the presence of 10mol%

$AuBr_3/CH_2Cl_2$/rt/4ÅMS powder under argon atmosphere in order to get a 1,2-*trans* disaccharide without affecting the propargyl ether. As expected, the glycosylation

Table 4

Propargyl 1,2-orthoesters	Glycosyl acceptors	1,2-*trans* disaccharides	Time & Yield
18	 **67**	 **68**	**30min., 74%**
18	 **69**	 **70**	**1h, 71%**
18	 **71**	 **72**	**3h, 48%**
34	**67**	 **73**	**1h, 63%**
34	**69**	 **74**	**1h, 62%**
33	**67**	 **75**	**2h, 66%**

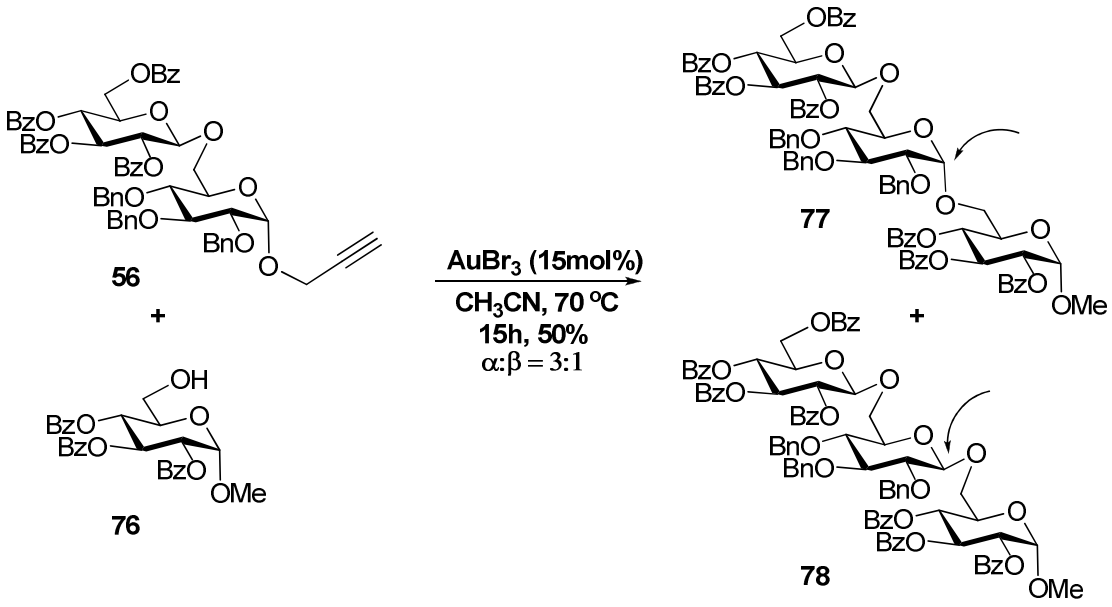
*** Reaction Condition: 10mol% $AuBr_3$/ CH_2Cl_2 / rt / 4ÅMS powder**

proceeded smoothly and afforded a 1,2-*trans* disaccharide **68** with propargyl ether in 74% yield (Table 4). The newly formed disaccharide was confirmed thoroughly by ^{1}H, ^{13}C, DEPT NMR and mass spectroscopic techniques. In the ^{1}H NMR spectrum of compound **68**, the resonances attributed to methine proton, methylene protons of propargyl group and methoxy protons were evident at δ 2.38 ppm as a triplet, δ 4.06 ppm as a double doublet and δ 3.17 ppm as a singlet respectively. In addition, aromatic protons corresponding to four benzoate esters and two benzyl ethers were noticed at δ 7.20-8.05 ppm as multiplets whilst rest of the peaks were completely in agreement with the assigned structure **68**. Further, in the ^{13}C NMR spectrum, the two characteristic signals for 1,2-*cis* and 1,2-*trans* anomeric carbons were noticed at δ 97.6 and 101.3 ppm whilst rest of the resonances were completely in agreement with the assigned structure **68**. Similarly, the glycosylation of glucose 1,2-orthoester **18** with methyl 3,4-*O*-isopropylidene-6-*O*-prop-2-ynyl-α-D-galactopyranoside **69** and methyl 2,3-di-*O*-prop-2-ynyl-6-*O*-benzyl-α-D-glucopyranoside **71** under aforementioned conditions offered the corresponding 1,2-*trans* disaccharides with propargyl ether(s) (**70** and **72**) in good yields (Table 4). The scope of the methodology was further determined towards the selective activation using propargyl 1,2-orthoester of galactose **34** and mannose **33**. The glycosylation carried out between a galactose 1,2-orthoester **34** and glycosyl acceptors comprising a primary alcohol **67** and secondary alcohol **69** afforded the respective 1,2-*trans* disaccharides with propargyl ether (**73** and **74**) in good yields. A mannosyl 1,2-orthoester **33** also reacted smoothly with primary alcohol **67** resulting in the formation of 1,2-*trans* disaccharide **75** in 66% yield (Table 4). The newly formed disaccharides were thoroughly characterized by ^{1}H, ^{13}C and DEPT NMR spectral and mass analysis.

Having a glycosylation protocol for the synthesis of propargyl disaccharides, our synthetic strategy turned towards the synthesis of higher saccharides by exploiting propargyl disaccharides as glycosyl donors in the presence of $AuBr_3/CH_3CN$ at higher temperature. Accordingly, the glycosylation reaction was carried out between a propargyl disaccharide **56** and methyl 2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside **76** in the presence of 5mol% of $AuBr_3$ in acetonitrile at 60 ^{o}C for 12h. The reaction did not proceed at 60 ^{o}C, and the temperature was raised to 70 ^{o}C; observed the 10% formation of trisaccharide after 12h. The glycosylation reaction performed in the

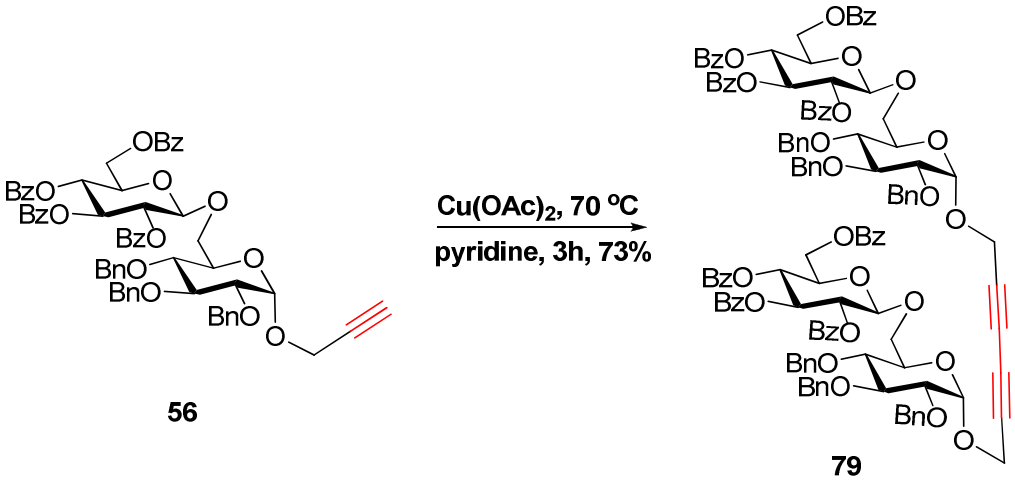
presence of 15mol% $AuBr_3/CH_3CN$/70 ^oC under argon atmosphere for 15h afforded an inseparable mixture (3:1~α:β) of trisaccharides **77** & **78** in 50% yield (Scheme 22). The trisaccharide was characterized thoroughly by the spectroscopic techniques such as ^1H, ^{13}C, DEPT NMR and mass spectral analysis.

Scheme 22



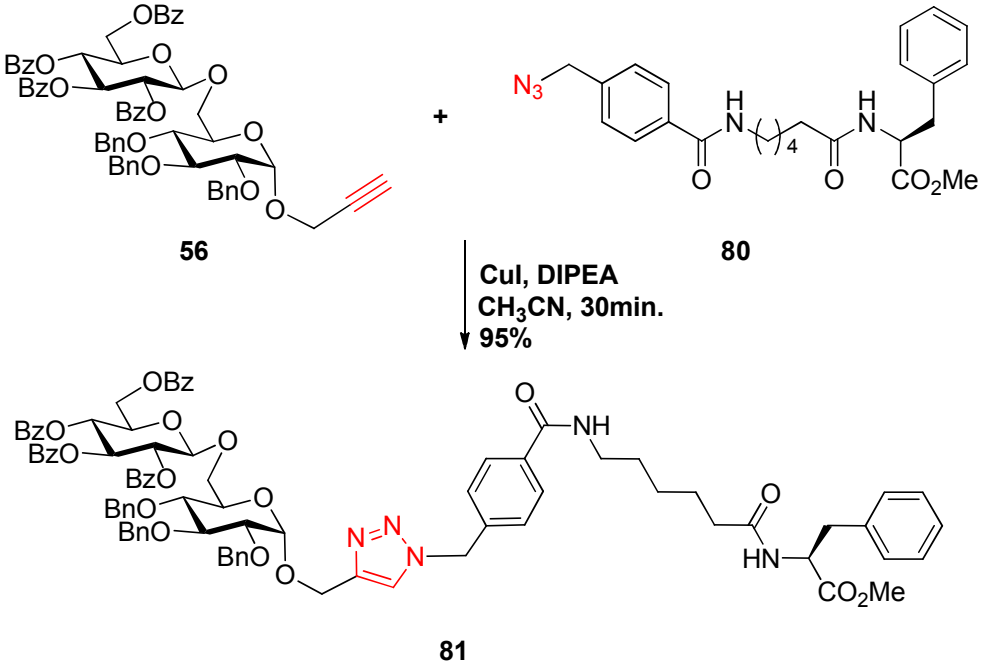
In the ^1H NMR spectrum of compound **77** & **78**, resonances attributed to methoxy group for α- and β-isomer were identified at δ 3.42 and 3.41 ppm as two single peaks along with the aromatic protons which showed the signals δ 6.98-8.01 ppm as multiplets. The remaining resonances were in accordance to the assigned structures **77** & **78**. Further, the ^{13}C NMR spectrum indicated the three signals corresponding to the three anomeric carbons present in the α-trisaccharide at δ 96.7, 97.0 and 101.2 ppm. Similarly, the resonances attributed to the three anomeric carbons for the β-isomer were noticed at δ 96.8, 101.3 and 103.6 ppm. Rest of the resonances in the spectrum were completely in agreement with the assigned structures **77** & **78**. ^{13}C NMR spectrum further revealed the ratio of the α- and β-isomers present in the trisaccharide (α:β ~ 3:1) from the relative intensity of signals attributed to the two methoxy carbons present at anomeric centre. The trisaccharide was further supported by the mass spectral analysis (Mol. Wt. calculated for $C_{89}H_{80}O_{23}$: 1516.51, Found: 1540.10 (M^++23 for Na)).

Scheme 23



56 **79**

Scheme 24



56 **80** **81**

Beyond the synthesis of oligosaccharides, we envisioned that propargyl disaccharides and disaccharides with propargyl ether(s) can be excellent precursors to molecular diversity with different connectivity. Dimerization of alkyne to produce sugar rods under Eglinton's conditions $Cu(OAc)_2$/pyridine/70 ^{o}C,[34] and Click reaction[30] in which alkyne reacts with azide in the presence of copper salts gives a regioselective 1,2,3-triazole were selected to utilize alkyne group of the propargyl moiety present in the disaccharides. Accordingly, the sugar rod, neoglycoside **79** was synthesized from a propargyl disaccharide **56** (73%) under Eglinton's conditions

(Scheme 23). A triazole clicked glycopeptide conjugate **81** was also synthesized (95%) by treatment of a propargyl disaccharide **56** with azide derived from peptide **80** under conditions CuI/DIPEA/CH_3CN/rt/30minutes (Scheme 24). All compounds were thoroughly characterized by ^{1}H, ^{13}C, DEPT NMR spectroscopic techniques and mass spectral analysis.

In a nutshell, we have identified a new *O*-glycosylation methodology in which solid $AuBr_3$ catalyzes the activation of propargyloxy moiety present in the propargyl 1,2-orthoesters and made it to behave as glycosyl donors in the presence of glycosyl acceptors to provide the 1,2-*trans* glycosides and disaccharides in a stereoselective manner. Identified methodology was further exploited for the preferential activation of propargyls 1,2-orthoesters in the presence of propargyl glycosides as well as propargyl ether(s). The disaccharide with propargyl group at the reducing end have been successfully extended to higher saccharides by exploiting them as glycosyl donor in the presence of $AuBr_3$ in acetonitrile whereas propargyl disaccharide was utilized for the synthesis of triazole 'clicked' glycopeptide. The temperature and solvent controlled selective activation of propargyl 1,2-orthoesters and subsequent elaboration provided the new route to make oligosaccharides, neoglycosides or pseudo oligosaccharides and aminoacid glycoconjugates. The new *O*-glycosylation protocol tolerates multiple functional groups such as ethers (propargyl ethers as well), esters, isopropylidene and benzylidene acetals which are routinely used in carbohydrate chemistry.

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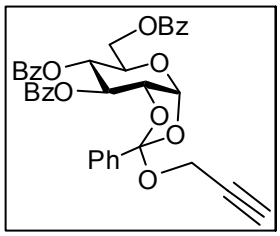
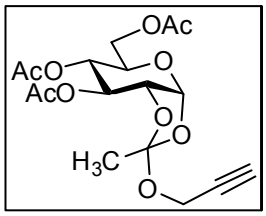
Experimental Section

Synthesis of 3,4,6-tri-*O*-benzoyl-α-D-glucopyranose-1,2-(prop-2-ynyl orthobenzoate) (18): To a solution of 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl bromide (20g, 30.3 mmol) in anhydrous CH_2Cl_2 (100mL) was added 2,6-lutidine (15mL), propargyl alcohol (9mL, 15.2 mmol) followed by a catalytic amount of tetra-*n*-butylammonium iodide (50mg) at room temperature under argon atmosphere. Then, the reaction mixture was refluxed at 65 °C for 48h, diluted with aqueous oxalic acid solution and extracted with CH_2Cl_2 (2x100mL). Combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate and concentrated *in vacuo.* The resulting brownish black residue was purified by silica gel column chromatography using petroleum ether-ethyl acetate as the mobile phase to afford 3,4,6-tri-*O*-benzoyl-α-D-glucopyranose-1,2-(prop-2-ynyl ortho-benzoate) **18** (16.3g, 85%) as a white solid. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = -3.55; IR (cm^{-1}): 1714, 1730, 1737, 3305; ^1H ($CDCl_3$, 200.13 MHz): δ 2.40 (1H, t, *J* 2.3 Hz), 3.99 (2H, d, *J* 2.3 Hz), 4.12-4.22 (1H, m), 4.40 (1H, dd, *J* 4.68, 12.00 Hz), 4.56 (1H, dd, *J* 3.04, 12.13 Hz), 4.85-4.92 (1H, m), 5.54 (1H, d, *J* 8.72 Hz), 5.79 (1H, dd, *J* 1.14, 2.78 Hz), 6.11 (1H, d, *J* 5.31 Hz), 7.21-7.65 (12H, m), 7.78-7.83 (2H, m), 7.92-7.98 (4H, m), 8.06-8.11 (2H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): 52.3, 63.9, 67.5, 68.4, 68.9, 72.0, 73.9, 79.1, 97.7, 121.1, 126.4-130.0, 132.9, 133.5, 133.6, 134.0, 164.1, 165.1, 165.9; Mol. Wt. calculated for $C_{37}H_{30}O_{10}$: 634.62, Found: 656.21 (M^++ 23 for Na).



3,4,6-Tri-*O*-acetyl-α-D-glucopyranose-1,2-(prop-2-ynyl orthoacetate) (22): Preparative protocol is same as described for compound **18** using 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide. $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +30.71; IR (cm^{-1}): 1227, 1745, 3279; ^1H NMR ($CDCl_3$, 200.13 MHz): δ 1.76 (3H, s), 2.10 (6H, s), 2.12 (3H, s), 2.45 (1H, t, *J* 2.44 Hz), 3.88-3.97 (1H, m), 4.18-4.21 (4H, m), 4.38 (1H, ddd, *J* 0.92, 2.90, 5.23 Hz), 4.90 (1H, ddd, *J* 0.87, 2.39, 9.51 Hz), 5.19 (1H, t, *J* 2.68 Hz), 5.75 (1H, d, *J* 5.28 Hz); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 20.4, 20.6, 20.6, 20.7, 51.6, 62.9, 66.8, 68.0, 69.7, 72.9, 73.9, 79.5, 96.9, 121.2, 168.9, 169.5, 170.6; Mol. Wt. calculated for $C_{17}H_{22}O_{10}$: 386.12, Found: 409.29 (M^++ 23 for Na).

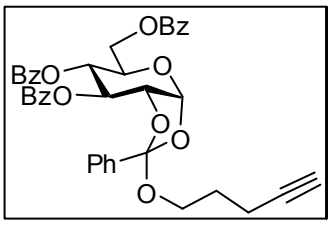


Synthesis of 3,4,6-tri-*O*-benzyl-α-D-glucopyranose-1,2-(prop-2-ynyl orthobenzoate) (24): To a solution of 3,4,6-tri-*O*-benzoyl-α-D-glucopyranose-1,2-(prop-2-ynyl orthobenzoate) **18** (10g, 15.75 mmol) in anhydrous THF (60mL) was added dropwise a solution of sodium methoxide in methanol. After completion of the reaction (as judged by TLC, ~ 2h), the reaction mixture was concentrated *in vacuo* and the resulting residue was purified by flash silica gel column chromatography using dichloromethane followed by combination of ethyl acetate and acetone as the mobile phase to afford the triol of glucose 1,2-orthoester (4.16g, 82%). To a solution of triol (4.16g, 12.93 mmol) in anhydrous DMF (30mL) was added NaH (1.39g, 58.18 mmol) at 0 ^{o}C and the resulting dark brown solution was stirred for 30min. at same temperature. To this was added benzyl bromide (6.2mL, 51.72 mmol) and the reaction mixture was stirred for additional 4h at 0 ^{o}C. After completion of the reaction, excess NaH was quenched by using methanol (10mL), diluted with water (100mL) and extracted with ethyl acetate (2×100mL). The pooled organic layers were dried over anhydrous Na_2SO_4, concentrated *in vacuo* and purified by silica gel column chromatography using petroleum ether and ethyl acetate as the mobile phase to obtain 3,4,6-tri-*O*-benzyl-α-D-glucopyranose-1,2-(prop-2-ynyl orthobenzoate) **24** (4.97g, 65 %) as a syrup. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.1) = +53.98; IR (cm^{-1}): 2343, 3305; ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ 2.36 (1H, t, *J* 2.40 Hz), 3.59 (2H, d, *J* 1.14 Hz), 3.73 (2H, d, *J* 1.14 Hz), 3.90-3.99 (3H, m), 4.29-4.75 (7H, m), 6.00 (1H, d, *J* 5.30 Hz), 7.10-7.17 (2H, m), 7.23-7.36 (16H, m), 7.60-7.69 (2H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 52.0, 69.0, 70.2, 71.9, 72.5, 73.1, 73.5, 75.1, 75.1, 77.5, 79.6, 98.3, 120.3, 126.3-129.6, 134.9, 137.6, 137.9, 138.1; Mol. Wt. calculated for $C_{37}H_{36}O_7$: 592.67, Found: 615.07 (M^++ 23 for Na).

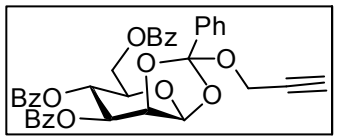
3,4,6-Tri-*O*-benzoyl-α-D-glucopyranose-1,2-(but-3-ynyl orthobenzoate) (26): The procedure for the preparation of compound **26** is same as delineated above for compound **18** using homopropargyl alcohol. $[\alpha]_D$ ($CHCl_3$, *c* 1.1) = -(0.5-0.9); IR (cm^{-1}): 1266, 1584, 1602, 1725, 2948, 2956, 3304; ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ 1.96 (1H, t, *J* 2.65 Hz), 2.40 (2H, td, *J* 2.61, 6.93 Hz), 3.33-3.54 (2H, m), 4.10-4.18 (1H, m), 4.38 (1H, dd, *J* 4.76, 12.02 Hz), 4.54 (1H, dd, *J* 2.98, 12.02 Hz), 4.86 (1H, ddd, *J* 1.22, 3.09, 5.17 Hz), 5.52 (1H, dt, *J* 1.28, 8.73 Hz), 5.77 (1H, dd,

J 1.2, 3.05 Hz), 6.08 (1H, d, *J* 5.22 Hz), 7.22-7.68 (12H, m), 7.77-7.82 (2H, m), 7.92-7.99 (4H, m), 8.06-8.11 (2H, m) ; ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 19.7, 62.3, 63.9, 67.4, 68.4, 69.0, 69.6, 71.9, 80.8, 97.5, 121.0, 126.3-129.9, 132.9, 133.5, 133.6, 134.8, 164.5, 165.1, 165.9; Mol. Wt. calculated for $C_{38}H_{32}O_{10}$: 648.19, Found: 671.24 (M^++ 23 for Na).

3,4,6-Tri-*O*-benzoyl-α-D-glucopyranose-1,2-(pent-4-ynyl orthobenzoate) (27): Preparative procedure is same as described for compound **18** using pent-4-ynol. $[\alpha]_D$ ($CHCl_3$, *c* 1.1) = -2.74; IR (cm^{-1}): 1266, 1585, 1602, 1727, 2887, 2960, 3307; ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ 1.72 (2H, quintet, *J* 6.52 Hz), 1.90 (1H, t, *J* 2.58 Hz) 2.23-2.27 (2H, m), 3.36-3.51 (2H, m), 4.13-4.17 (1H, m), 4.38 (1H, dd, *J* 4.94, 12.03 Hz), 4.54 (1H, dd, *J* 2.78, 12.07 Hz), 4.80-4.82 (1H, m), 5.51 (1H, d, *J* 1.28, 8.88 Hz), 5.78 (1H, dd, *J* 1.13, 2.87 Hz), 6.06 (1H, d, *J* 5.19 Hz), 7.24-7.28 (2H, m), 7.39-7.50 (8H, m), 7.56-7.63 (2H, m), 7.77-7.79 (2H, m), 7.93-7.97 (4H, m), 8.08-8.10 (2H, m) ; ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 15.1, 28.0, 62.2, 63.9, 67.4, 68.4, 68.9, 69.1, 72.0, 83.2, 97.5, 121.2, 126.2-129.9, 132.9, 133.5, 133.6, 135.2, 164.5, 165.1, 165.9; Mol. Wt. calculated for $C_{39}H_{34}O_{10}$: 662.21, Found: 685.38 (M^++ 23 for Na).

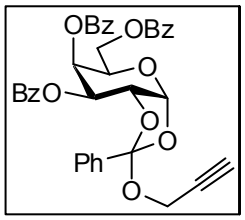


3,4,6-Tri-*O*-benzoyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthobenzoate) (33): The preparative procedure is same as described in the preparation of compound **18** using 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl bromide. $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = -96.59; IR (cm^{-1}): 1269, 1602, 1728, 1735, 3309; ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ 2.24 (1H, t, *J* 2.36 Hz), 4.05 (2H, dd, *J* 2.58, 3.24 Hz), 4.09-4.17 (1H, m), 4.36 (1H, dd, *J* 4.36, 12.08 Hz), 4.55 (1H, dd, *J* 3.32, 12.08 Hz), 5.16 (1H, t, *J* 3.39 Hz), 5.70 (1H, dd, *J* 3.86, 9.98 Hz), 5.83 (1H, d, *J* 3.1 Hz), 5.93 (1H, t, *J* 9.39 Hz), 7.25-7.57 (12H, m), 7.69-7.74 (2H, m), 7.88-8.06 (6H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 52.4, 63.1, 66.4, 70.7, 72.2, 73.8, 76.2, 79.2, 98.0, 122.7, 126.6-129.9, 132.9, 133.4, 133.5, 135.1, 165.1, 165.8, 165.9; Mol. Wt. calculated for $C_{37}H_{30}O_{10}$: 634.62, Found: 657.74 (M^++ 23 for Na).



3,4,6-Tri-*O*-benzoyl-α-D-galactopyranose-1,2-(prop-2-ynyl orthobenzoate) (34): Preparative protocol is same as delineated above for compound **18** using 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl bromide. $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +55.47; IR (cm^{-1}):

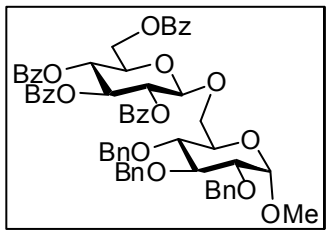
1269, 1602, 1728, 3309; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.40 (1H, t, *J* 2.3 Hz), 4.06 (2H, d, *J* 2.3 Hz), 4.40 (1H, dd, *J* 3.37, 9.10 Hz), 4.50-4.69 (2H, m), 4.84 (1H, t, *J* 5.3 Hz), 5.59 (1H, dd, *J* 4.20, 5.80 Hz), 5.83 (1H, dd, *J* 2.20, 4.00 Hz), 6.26 (1H, d, *J* 5.20 Hz), 7.18-7.60 (12H, m), 7.63-7.70 (2H, m), 7.83-8.05(6H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 52.0, 62.2, 66.3, 68.9, 69.9, 73.4, 73.8, 79.2, 98.3, 120.1, 126.0-130.0, 133.1, 133.3, 133.5, 135.1, 165.1, 165.1, 165.9; Mol. Wt. calculated for $C_{37}H_{30}O_{10}$: 634.63, Found: 657.52 (M^++23 for Na).



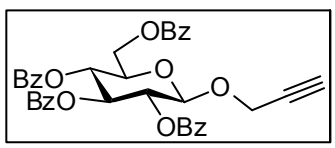
General procedure for $AuBr_3$ mediated glycosylation of propargyl 1,2-orthoester:

To a solution of glycosyl donor (0.1 mmol), glycosyl acceptor (0.11 mmol) and freshly activated 4Å molecular sieves powder (50mg) in anhydrous CH_2Cl_2 (5mL) was added $AuBr_3$ (10mol%) at room temperature under argon atmosphere. The reaction mixture was stirred at room temperature for the specified time. After completion of the reaction as checked by TLC, the reaction mixture was filtered and the filtrate was concentrated *in vacuo*. The resulting residue was purified by silica gel column chromatography using petroleum ether-ethyl acetate as the mobile phase.

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-α-D-glucopyranoside (20): $[\alpha]_D$ ($CHCl_3$, *c* 1.2) = +24.53; IR (cm^{-1}): 1267, 1602, 1730, 1735; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 3.20 (3H, s), 3.39 (1H, dd, *J* 1.47, 9.10 Hz), 3.42 (1H, dd, *J* 3.50, 9.61 Hz), 3.73 (1H, d, *J* 3.54 Hz), 3.73 (1H, ABq, *J* 4.22 Hz), 3.88 (1H, t, *J* 9.22 Hz), 4.05-4.17 (2H, m), 4.28 (1H, d, *J* 11.05 Hz), 4.47-4.92 (9H, m), 5.58 (1H, dd, *J* 7.69, 9.51 Hz), 5.67 (1H, t, *J* 9.51 Hz), 5.89 (1H, t, *J* 9.55 Hz), 7.18-7.56 (27H, m), 7.79-8.00 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 54.9, 63.3, 68.3, 69.5, 69.8, 71.8, 72.2, 72.9, 73.3, 74.7, 75.5, 77.4, 79.8, 81.9, 97.9, 101.3, 127.4-129.8, 133.1, 133.1, 133.2, 133.4, 138.1, 138.2, 138.8, 164.9, 165.2, 165.8, 166.1; Mol. Wt. calculated for $C_{62}H_{58}O_{15}$: 1042.38, Found: 1065.65 (M^++ 23 for Na).

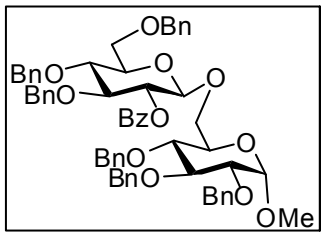


Prop-2-ynyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranoside (21): IR (cm^{-1}): 1267, 1583, 1600, 1714, 1730, 1737, 2121, 2873, 2931, 2958, 3303; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.41 (1H, t, *J* 2.38 Hz), 4.16-4.25 (1H, m), 4.42 (2H, dd, *J* 2.38, 5.03 Hz), 4.50 (1H, dd, *J* 5.08, 12.25 Hz), 4.66 (1H, dd, *J* 3.23, 12.25 Hz), 5.16 (1H, d, *J*



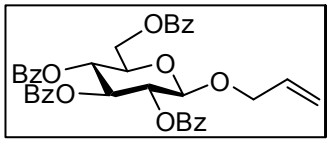
7.86 Hz), 5.55 (1H, dd, *J* 7.93, 9.63 Hz), 5.69 (1H, t, *J* 9.63 Hz), 5.69 (1H, t, *J* 9.57 Hz) 7.23-7.59 (12H, m), 7.81-8.06 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 56.0, 63.0, 69.7, 71.6, 72.4, 72.9, 75.6, 78.0, 98.4, 128.3-129.9, 133.1, 133.2, 133.2, 133.4, 165.1, 165.1, 165.8, 166.1; Mol. Wt. calculated for $C_{37}H_{30}O_{10}$: 634.18, Found: 657.22 (M^++ 23 for Na).

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl)-α-D-glucopyranoside (25):



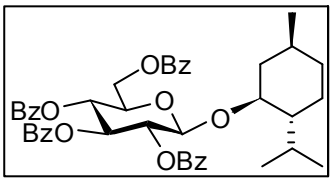
$[\alpha]_D$ ($CHCl_3$, *c* 1.2) = +25.56; IR (cm^{-1}): 1267, 1602, 1731, 2875, 2906, 2927; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 3.19 (3H, s), 3.37 (1H, t, *J* 9.43 Hz), 3.42 (1H, dd, *J* 3.40, 9.56 Hz), 3.52-3.91 (8H, m), 4.14 (1H, d, *J* 8.77 Hz), 4.26 (1H, d, *J* 10.96 Hz), 4.40-4.90 (13H, m), 5.35 (1H, t, *J* 8.50 Hz), 6.98-7.48 (33H, m), 7.90-7.94 (2H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 54.9, 67.9, 68.8, 69.4, 73.3, 73.4, 73.6, 74.6, 74.9, 75.1, 75.3, 75.4, 77.3, 77.9, 79.6, 81.8, 82.7, 97.9, 101.1, 127.3-129.7, 132.9, 137.6, 137.8, 138.0, 138.1, 138.2, 138.8, 164.9; Mol. Wt. calculated for $C_{62}H_{64}O_{12}$: 1001.16, Found: 1024.06 (M^++ 23 for Na).

Allyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranoside (29):



$[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +25.1; IR (cm^{-1}): 1267, 1583, 1602, 1731, 2879, 2958; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 4.11-4.22 (2H, m), 4.32-4.41(1H, m), 4.5 (1H, dd, *J* 5.25, 12.12 Hz), 4.65 (1H, dd, *J* 3.33, 12.12 Hz), 4.90 (1H, d, *J* 7.82 Hz), 5.09-5.27 (2H, m), 5.56 (1H, dd, *J* 7.82, 9.66 Hz), 5.68 (1H, t, *J* 9.63 Hz), 5.71-5.90 (1H, m), 5.91 (1H, t, *J* 9.58 Hz), 7.23-7.60 (12H, m), 7.81-8.05 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 63.2, 69.8, 70.1, 71.9, 72.2, 73.0, 99.8, 117.8, 128.2-129.7, 133.1, 133.2, 133.2, 133.3, 133.4, 165.1, 165.2, 165.8, 166.1; Mol. Wt. calculated for $C_{37}H_{32}O_{10}$: 636.64, Found: 659.81 (M^++ 23 for Na).

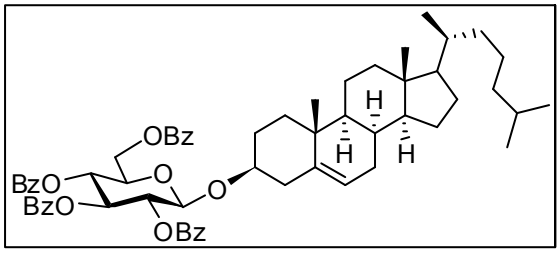
Menthyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranoside (30):



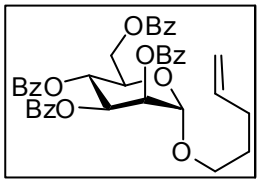
$[\alpha]_D$ ($CHCl_3$, *c* 1.0) = -30.9; IR (cm^{-1}): 1269, 1583, 1600, 1714, 1722, 1731, 1737, 2860, 2869, 2914, 2927, 2956; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 0.6-0.70 (2H, m), 0.71 (3H, d, *J* 7.03 Hz), 0.75 (3H, d, *J* 6.90 Hz), 0.82 (3H, d, *J* 7.07 Hz), 0.87-1.00 (1H, m), 1.11-1.26 (2H, m), 1.53-1.63 (2H, m), 1.96 (1H, d, *J* 12.01 Hz), 2.15-2.33 (1H, m), 3.48 (1H, dt, *J* 4.27, 10.55 Hz), 4.08-4.18 (1H, m), 4.47 (1H, dd, *J* 5.55, 12.02 Hz), 4.63 (1H, dd, *J* 3.49, 12.02 Hz), 4.93 (1H, d, *J* 7.93 Hz), 5.48 (1H, dd, *J*

7.92, 9.77 Hz), 5.63 (1H, t, *J* 9.68 Hz), 5.89 (1H, t, *J* 9.67 Hz), 7.24-7.58 (12H, m), 7.81-8.02 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 15.5, 20.8, 22.0, 23.0, 25.1, 31.3, 34.1, 40.7, 47.3, 63.4, 70.2, 72.0, 72.1, 73.2, 79.0, 99.0, 128.2-129.8, 133.0, 133.0, 133.1, 133.3, 165.0, 165.3, 165.8, 166.1; Mol. Wt. calculated for $C_{44}H_{46}O_{10}$: 734.83, Found: 757.75 (M^++ 23 for Na).

Cholesteryl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranoside (32): $[\alpha]_D$ ($CHCl_3$, *c* 1.1) = +8.90; IR (cm^{-1}): 1267, 1602, 1714, 1731, 1737, 2854, 2867, 2893, 2906, 2941; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 0.65 (3H, s), 0.85 (3H, s), 0.88 (6H, d, *J* 2.55 Hz), 0.92 (3H, d, *J* 7.46 Hz), 0.88-2.18 (28H, m), 3.48-3.61 (1H, m), 4.11-4.20 (1H, m), 4.51 (1H, dd, *J* 5.7, 12.10 Hz), 4.62 (1H, dd, *J* 3.30, 12.10 Hz), 4.95 (1H, d, *J* 7.94 Hz), 5.23 (1H, d, *J* 3.86 Hz), 5.50 (1H, dd, *J* 8.04, 9.38 Hz), 5.63 (1H, t, *J* 9.60 Hz), 5.91 (1H, t, *J* 9.57 Hz), 7.24-7.58 (12H, m), 7.82-8.03 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 11.8, 18.7, 19.2, 21.0, 22.5, 22.8, 23.8, 24.2, 28.0, 28.2, 29.5, 31.8, 31.9, 35.7, 36.2, 36.6, 37.1, 38.8, 39.5, 39.7, 42.3, 50.1, 56.1, 56.7, 63.4, 70.1, 72.1, 72.1, 73.0, 80.4, 100.1, 121.9, 128.2-129.8, 133.0, 133.1, 133.2, 133.4, 140.3, 165.1, 165.2, 165.8, 166.1; Mol. Wt. calculated for $C_{61}H_{72}O_{10}$: 965.22, Found: 988.12 (M^++ 23 for Na).

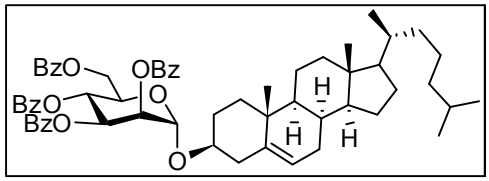


Pent-4-enyl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (36): $[\alpha]_D$ ($CHCl_3$, *c* 0.9) = -49.55; IR (cm^{-1}): 1265, 1602, 1730, 1735, 2883, 2933, 2950; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.82 (2H, quintet, *J* 6.88 Hz), 2.16-2.27 (2H, m), 3.59 (1H, dt, *J* 6.45, 9.59 Hz), 3.86 (dt, 1H, *J* 6.60, 9.64 Hz), 4.39-4.55 (2H, m), 4.66-4.74 (1H, m), 4.98-5.14 (2H, m), 5.09 (1H, d, *J* 1.6 Hz), 5.70 (1H, dd, *J* 1.78, 3.21 Hz), 5.75-5.92 (1H, m). 5.93 (1H, dd, *J* 3.13, 10.05 Hz), 6.11 (1H, t, *J* 9.95 Hz), 7.22-7.64 (12H, m), 7.82-8.13 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 28.5, 30.2, 62.9, 67.1, 67.9, 68.9, 70.1, 70.6, 97.7, 115.2, 128.3-129.9, 133.0, 133.1, 133.3, 133.4, 137.7, 165.4, 165.5, 165.5, 166.1; Mol. Wt. calculated for $C_{39}H_{36}O_{10}$: 664.7, Found: 687.76 (M^++ 23 for Na).

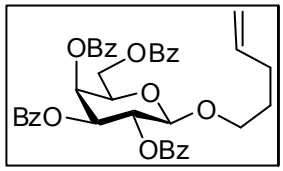


Cholesteryl 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranoside (37): $[\alpha]_D$ ($CHCl_3$, *c* 0.8) = +34.07; IR (cm^{-1}): 1267, 1602, 1728, 2854, 2867, 2908, 2948; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 0.69 (3H, s), 0.86 (6H, d, *J* 6.52 Hz), 0.93 (3H, d, *J* 6.33 Hz), 0.9-2.1

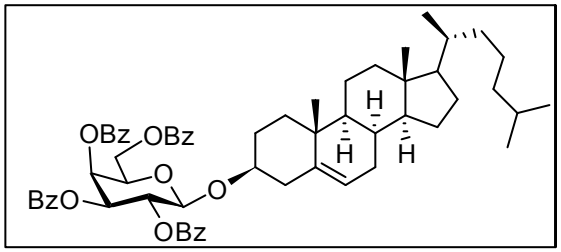
(26H, m), 1.04 (3H, s), 2.47 (2H, d, *J* 7.56 Hz), 3.55-3.71 (1H, m), 4.45-4.63 (2H, m), 4.68 (1H, d, *J* 9.65 Hz), 5.25 (1H, d, *J* 1.39 Hz), 5.27 (1H, d, *J* 4.04 Hz), 5.65 (1H, dd, *J* 1.77, 2.90 Hz), 5.94 (1H, dd, *J* 3.03, 10.13 Hz), 6.06 (1H, t, *J* 10.00 Hz), 7.23-7.63 (12H, m), 7.82-8.11 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 11.9, 18.7, 19.3, 21.0, 22.5, 22.8, 23.8, 24.3, 27.8, 28.0, 28.2, 31.8, 31.9, 35.8, 36.2, 36.7, 36.9, 39.5, 39.7, 40.0, 42.3, 50.1, 56.1, 56.8, 63.2, 67.2, 68.9, 70.1, 71.2, 78.6, 95.9, 122.2, 128.3-129.8, 132.9, 133.1, 133.4, 133.4, 140.2, 165.5, 165.5, 165.6, 166.2; Mol. Wt. calculated for $C_{61}H_{72}O_{10}$: 965.22, Found: 988.28 (M^++ 23 for Na).



Pent-4-enyl 2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranoside (38): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +86.03; IR (cm^{-1}): 1266, 1584, 1602, 1728, 2851, 2879, 2927; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.59-1.75 (2H, m), 1.94-2.06 (2H, m), 3.59 (1H, dt, *J* 6.69, 9.67 Hz), 3.99 (1H, dt, *J* 6.08, 9.71 Hz), 4.29-4.47 (2H, m), 4.70 (1H, dd, *J* 6.18, 10.77 Hz), 4.76-4.86 (3H, m), 5.55-5.75 (2H, m), 5.81 (1H, dd, *J* 7.88, 10.48 Hz), 6.00 (1H, d, *J* 3.18 Hz), 7.20-7.66 (12H, m), 7.77-7.81 (2H, m), 7.95-8.12 (6H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 28.5, 29.7, 61.9, 68.1, 69.6, 69.8, 71.2, 71.7, 101.6, 114.9, 128.2-130.0, 133.2, 133.3, 133.3, 133.5, 137.7, 165.2, 165.5, 165.6, 166.0; Mol. Wt. calculated for $C_{39}H_{36}O_{10}$: 664.7, Found: 687.55 (M^++ 23 for Na).

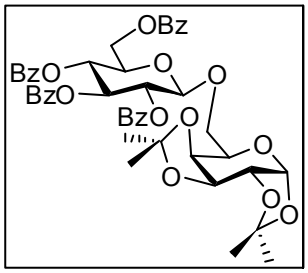


Cholesteryl 2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranoside (39): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +66.34; IR (cm^{-1}): 1265, 1584, 1602, 1729, 2862, 2901, 2937; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 0.66 (3H, s), 0.85 (3H, s), 0.90 (6H, d, *J* 5.82 Hz), 0.92 (3H, d, *J* 4.59 Hz), 0.98-2.04 (26H, m), 2.19 (2H, d, *J* 7.53 Hz), 3.49-3.64 (1H, m), 4.32 (1H, t, *J* 6.52 Hz), 4.42 (1H, dd, *J* 6.33, 10.87 Hz), 4.68 (1H, dd, *J* 6.65, 10.86 Hz), 4.92 (1H, d, *J* 7.92 Hz), 5.23 (1H, d, *J* 4.16 Hz), 5.59 (1H, dd, *J* 3.36, 10.41 Hz), 5.78 (1H, dd, *J* 7.92, 10.41 Hz), 5.99 (1H, d, *J* 3.15 Hz), 7.20-7.65 (12H, m), 7.77-7.81 (2H, m), 7.95-8.11 (6H, m) ; ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 11.8, 18.7, 19.3, 21.0, 22.5, 22.8, 23.7, 24.2, 27.9, 28.2, 29.6, 31.8, 31.9, 35.7, 36.1, 36.6, 37.1, 38.8, 39.5, 39.7, 42.3, 50.0, 56.1, 56.7, 62.0, 68.1, 69.9, 71.2, 71.9, 80.8, 100.7, 121.9, 128.2-130.0, 133.1, 133.2, 133.2, 133.5, 140.3,

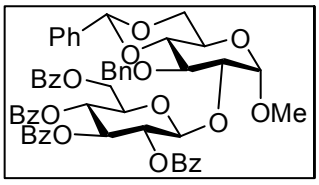


165.2, 165.5, 165.6, 165.9; Mol. Wt. calculated for $C_{61}H_{72}O_{10}$: 965.22, Found: 988.12 (M^++ 23 for Na).

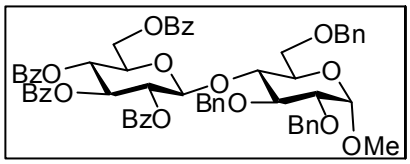
1,2:3,4-Di-*O*-isopropylidene-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-α-D-galactopyranose (41): $[\alpha]_D$ ($CHCl_3$, *c* 0.9) = -9.96; IR (cm^{-1}): 1267, 1602, 1714, 1730, 1735, 2914, 2939, 2989; ^1H NMR (200.13 MHz, $CDCl_3$): δ 1.20 (6H, s), 1.24 (3H, s), 1.37 (3H, s), 3.80-4.18 (5H, m), 4.22 (1H, dd, *J* 2.34, 4.96 Hz), 4.43 (1H, dd, *J* 2.45, 7.78 Hz), 4.48 (1H, dd, *J* 5.13, 11.91 Hz), 4.65 (1H, dd, *J* 3.25, 12.09 Hz), 5.05 (1H, d, *J* 7.82 Hz), 5.42 (1H, d, *J* 5.01 Hz), 5.53(1H, dd, *J* 7.84, 9.50 Hz), 5.68 (1H, t, *J* 9.55 Hz), 5.91 (1H, t, *J* 9.55 Hz), 7.23-7.58 (12H, m), 7.80-8.05 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 24.2, 24.8, 25.6, 25.8, 63.2, 67.5, 68.3, 69.8, 70.4, 70.5, 70.9, 71.8, 72.2, 73.0, 96.1, 101.2, 108.5, 109.2, 128.1-130.0, 133.0, 133.0, 133.1, 133.4, 165.1, 165.2, 165.8, 166.1; Mol. Wt. calculated for $C_{46}H_{46}O_{15}$: 838.28, Found: 861.13 (M^++ 23 for Na).



Methyl 2-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (43): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +16.45; IR (cm^{-1}): 1215, 1714, 1730, 1737; ^1H NMR (200.13 MHz, $CDCl_3$): δ 3.38 (3H, s), 3.68-3.82 (3H, m), 3.93 (1H, t, *J* 9.19 Hz), 4.10-4.19 (1H, m), 4.26 (1H, dd, *J* 4.07, 9.50 Hz), 4.36-4.78 (5H, m), 4.96 (1H, d, *J* 3.53 Hz), 5.19 (1H, d, *J* 7.84 Hz), 5.49 (1H, s), 5.67 (1H, dd, *J* 3.32, 9.65 Hz), 5.72 (1H, dd, *J* 5.09, 9.63 Hz), 5.92 (1H, t, *J* 9.55 Hz), 6.96-7.62 (22H, m), 7.78-8.05 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.4, 62.1, 62.7, 69.1, 69.6, 72.0, 72.3, 73.1, 74.7, 77.2, 80.7, 82.1, 100.3, 101.3, 102.3, 125.9-129.8, 133.1, 133.2, 133.2, 133.5, 137.2, 138.4, 165.0, 165.2, 165.8, 166.0; Mol. Wt. calculated for $C_{55}H_{50}O_{15}$: 950.31, Found: 973.58 (M^++ 23 for Na).

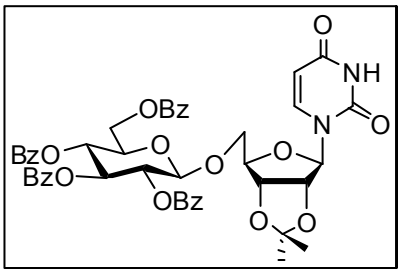


Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-α-D-glucopyranoside (45): $[\alpha]_D$ ($CHCl_3$, *c* 1.1) = -1.20; IR (cm^{-1}): 1263, 1600, 1733, 2869, 2910, 2937; ^1H NMR (200.13 MHz, $CDCl_3$): δ 3.27 (3H, s), 3.39-3.52 (3H, m), 3.67-3.76 (2H, m), 3.92 (1H, ABq, *J* 8.86 Hz), 3.92 (1H, d, *J* 0.78 Hz), 4.21-4.44 (3H, m), 4.54-4.82 (6H, m), 5.07 (1H, d, *J* 11.25 Hz), 5.42-5.67 (3H, m), 7.17-7.56 (27H, m), 7.76-7.98 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.3, 63.1, 67.5, 69.4, 69.8, 71.8, 72.2, 73.1, 73.5, 73.6, 75.3, 77.2, 78.7, 79.9, 98.4, 100.1, 127.1-

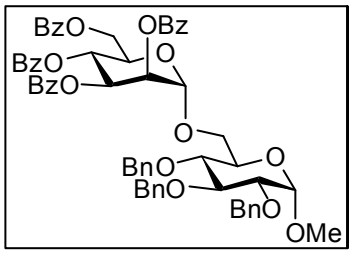


129.7, 132.9, 133.1, 133.3, 133.3, 137.8, 138.3, 139.2, 164.8, 165.1, 165.9, 165.7; Mol. Wt. calculated for $C_{62}H_{58}O_{15}$: 1042.38, Found: 1065.65 (M^++ 23 for Na).

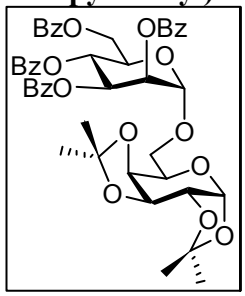
2,3-*O*-Isopropylidene-5-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl) uridine (47): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = -5.60; IR (cm^{-1}): 1267, 1602, 1693, 1730, 2933, 2947; ^1H NMR (200.13 MHz, $CDCl_3$): δ 0.91, 1.47 (6H, 2s), 3.65 (1H, dd, *J* 3.35, 11.60 Hz), 4.13-4.22 (1H, m), 4.28-4.56 (5H, m), 4.67 (1H, dd, *J* 3.19, 12.18 Hz), 4.85 (1H, d, *J* 7.91 Hz), 5.48 (1H, dd, *J* 7.98, 9.81 Hz), 5.69 (1H, t, *J* 9.68 Hz), 5.81 (1H, dd, *J* 2.24, 8.14 Hz), 5.90 (1H, d, *J* 3.16 Hz), 5.96 (1H, t, *J* 9.75 Hz), 7.26-7.60 (13H, m), 7.83-8.05 (8H, m), 8.56 (1H, s); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 24.6, 26.9, 62.8, 69.5, 69.6, 71.7, 72.2, 72.5, 80.3, 84.2, 84.5, 91.9, 101.5, 102.4, 114.2, 128.3-129.8, 133.3, 133.4, 133.5, 133.7, 140.7, 150.2, 163.0, 165.0, 165.1, 165.8, 166.1; Mol. Wt. calculated for $C_{46}H_{42}N_2O_{15}$: 862.83, Found: 885.90 (M^++ 23 for Na).



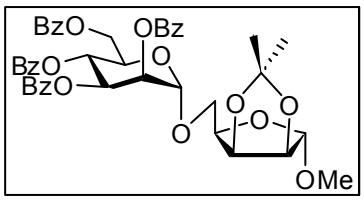
Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-glucopyranoside (48): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +3.39; IR (cm^{-1}): 1267, 1602, 1714, 1730, 1737, 2840, 2929; ^1H NMR (200.13 MHz, $CDCl_3$): δ 3.45 (3H, s), 3.53-3.61 (2H, m), 3.78-3.96 (3H, m), 4.04 (1H, t, *J* 9.22 Hz), 4.30-4.44 (2H, m), 4.60-4.86 (6H, m), 4.99 (1H, d, *J* 1.57 Hz), 5.04 (1H, d, *J* 1.12 Hz), 5.15 (1H, d, *J* 1.62 Hz), 5.73 (1H, dd, *J* 1.79, 3.20 Hz), 5.87 (1H, dd, *J* 3.28, 10.07 Hz), 6.07 (1H, t, *J* 9.89 Hz), 7.22-7.63 (27H, m), 7.80-8.11 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.2, 62.7, 66.6, 66.9, 68.9, 69.8, 69.9, 70.3, 73.4, 74.9, 75.6, 77.7, 80.2, 82.0, 97.7, 97.9, 127.5-129.9, 132.9, 133.1, 133.3, 133.3, 138.1, 138.2, 138.7, 165.2, 165.3, 165.4, 166.0; Mol. Wt. calculated for $C_{62}H_{58}O_{15}$: 1042.38, Found: 1065.65 (M^++ 23 for Na).



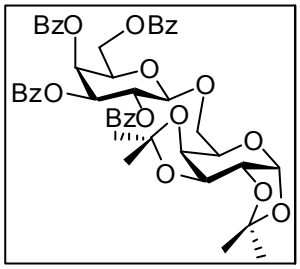
1,2:3,4-Di-*O*-isopropylidene-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-galactopyranose (49): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = -60.50; IR (cm^{-1}): 1265, 1585, 1602, 1728, 1731, 2935, 2991; ^1H NMR (200.13 MHz, $CDCl_3$): δ 1.36 (6H, s), 1.43 (3H, s), 1.63 (3H, s), 3.84-4.01 (2H, m), 4.11 (1H, td, *J* 1.61, 6.06 Hz), 4.32-4.37 (2H, m), 4.49 (1H, dd, *J* 3.79, 11.74 Hz), 4.55-4.73 (3H, m), 5.16 (1H, d, *J* 1.65 Hz), 5.57 (1H, d, *J* 4.95 Hz), 5.74 (1H, dd, *J* 1.84, 3.21 Hz), 5.90 (1H, dd, *J*



3.28, 10.11 Hz), 6.14 (1H, t, *J* 9.88 Hz), 7.22-7.64 (12H, m), 7.81-8.14 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 24.4, 24.9, 25.9, 26.1, 62.9, 66.7, 66.8, 67.6, 68.8, 70.2, 70.3, 70.6, 70.6, 70.9, 96.3, 97.8, 108.7, 109.4, 128.2-129.9, 132.9, 133.1, 133.2, 133.3, 165.3, 165.4, 165.5, 166.1; Mol. Wt. calculated for $C_{46}H_{46}O_{15}$: 838.28, Found: 862.50 (M^++ 23 for Na).



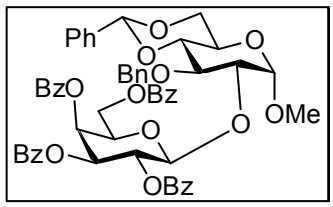
Methyl 2,3-*O*-isopropylidene-5-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-lyxofuranoside (51): $[\alpha]_D$ ($CHCl_3$, *c* 0.9) = -21.38; IR (cm^{-1}): 1267, 1602, 1730, 1735, 2937, 2993; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.32, 1.42 (6H, 2s), 3.40 (3H, s), 3.86 (1H, dd, *J* 5.07, 10.55 Hz), 4.08 (1H, dd, *J* 6.49, 10.55 Hz), 4.24-4.31 (1H, m), 4.48 (1H, dd, *J* 4.16, 11.66 Hz), 4.50-4.63 (2H, m), 4.72 (1H, dd, *J* 2.10, 11.79 Hz), 4.79 (1H, dd, *J* 3.64, 5.86 Hz), 4.93 (1H, s), 5.16 (1H, d, *J* 1.65 Hz), 5.75 (1H, dd, *J* 1.76, 3.19 Hz), 5.94 (1H, dd, *J* 3.28, 10.11 Hz), 6.13 (1H, t, *J* 9.89 Hz), 7.22-7.64 (12H, m), 7.81-8.15 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 24.8, 26.0, 54.7, 62.9, 66.4, 66.9, 68.9, 70.1, 70.4, 78.3, 79.6, 84.9, 97.7, 107.3, 112.7, 128.9-129.9, 132.9, 133.1, 133.4, 133.4, 165.3, 165.4, 165.5, 166.2; Mol. Wt. calculated for $C_{43}H_{42}O_{14}$: 782.79, Found: 806.22 (M^++ 23 for Na).



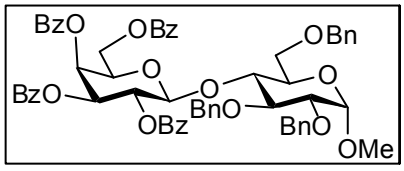
1,2:3,4-Di-*O*-isopropylidene-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-α-D-galactopyranose (52): $[\alpha]_D$ ($CHCl_3$, *c* 0.9) = +40.29; IR (cm^{-1}): 1267, 1585, 1602, 1731, 2935, 2989; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.20 (3H, s), 1.22 (3H, s), 1.24 (3H, s), 1.39 (3H, s), 3.86-4.14 (4H, m), 4.21 (1H, dd, *J* 2.40, 5.01 Hz), 4.31-4.47 (3H, m), 4.67 (1H, dd, *J* 6.07, 10.64 Hz), 5.02 (1H, d, *J* 7.93 Hz), 5.42 (1H, d, *J* 5.03 Hz), 5.62 (1H, dd, *J* 3.30, 10.48 Hz), 5.81 (1H, dd, *J* 7.93, 10.48 Hz), 5.99 (1H, d, *J* 3.17 Hz), 7.19-7.65 (12H, m), 7.95-8.11 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 24.1, 24.8, 25.6, 25.8, 61.9, 67.4, 68.1, 68.3, 69.6, 70.2, 70.4, 70.9, 71.2, 71.7, 96.1, 101.6, 108.4, 109.2, 128.1-129.9, 133.0, 133.2, 133.2, 133.5, 165.2, 165.4, 165.5, 165.9 ; Mol. Wt. calculated for $C_{46}H_{46}O_{15}$: 838.28, Found: 861.33 (M^++ 23 for Na).

Methyl 2-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (53): $[\alpha]_D$ ($CHCl_3$, *c* 0.9) = +71.84; IR (cm^{-1}): 1267, 1602, 1728, 2867, 2933; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 3.45 (3H, s), 3.51-3.86 (4H, m), 3.98 (1H, t, *J* 9.20 Hz), 4.24-4.69 (6H, m), 5.02 (1H, d, *J* 3.35 Hz), 5.18

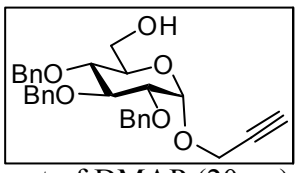
(1H, d, *J* 7.94 Hz), 5.50 (1H, s), 5.59 (1H, dd, *J* 3.35, 10.32 Hz), 5.93-6.02 (2H, m), 6.98-7.67 (22H, m), 7.75-8.13 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.6, 62.1, 62.2, 68.2, 69.1, 69.7, 71.5, 71.9, 74.6, 77.1, 81.2, 81.9, 100.25, 101.3, 102.7, 126.0-130.0, 133.1, 133.2, 133.3, 133.6, 137.2, 138.3, 165.1, 165.5, 165.6, 165.9; Mol. Wt. calculated for $C_{55}H_{50}O_{15}$: 950.31, Found: 973.50 (M^++ 23 for Na).



Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-α-D-glucopyranoside (54): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +7.49; IR (cm^{-1}): 1267, 1602, 1728, 2869, 2929; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 3.30 (3H, s), 3.40-3.55 (3H, m), 3.70 (1H, dd, *J* 2.44, 10.59 Hz), 3.87-4.07 (3H, m), 4.18 (1H, dd, *J* 7.49, 11.02 Hz), 4.32 (1H, d, *J* 12.26 Hz), 4.40 (1H, dd, *J* 6.24, 11.17 Hz), 4.56-4.93 (6H, m), 5.17 (1H, d, *J* 11.26 Hz), 5.30 (1H, dd, *J* 3.44, 10.32 Hz), 5.69 (1H, dd, *J* 7.96, 10.31 Hz), 5.85 (1H, d, *J* 3.25 Hz), 7.16-7.62 (27H, m), 7.74-8.04 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.4, 61.4, 67.5, 67.8, 69.4, 70.2, 70.9, 71.8, 73.5, 73.6, 75.2, 76.7, 78.5, 79.8, 98.5, 100.3, 127.2-129.8, 133.2, 133.2, 133.3, 133.4, 137.7, 138.3, 139.3, 164.8, 165.4, 165.4, 165.8; Mol. Wt. calculated for $C_{62}H_{58}O_{15}$: 1042.38, Found: 1065.55 (M^++ 23 for Na).

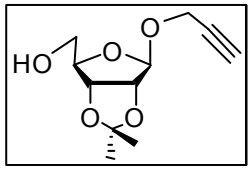


Synthesis of prop-2-ynyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (55): To a solution of propargyl-α,β-glucopyranosides (5g, 22 mmol) in pyridine (50mL) was added trityl chloride (7g, 25 mmol) followed by a catalytic amount of DMAP (20mg). The resulting reaction mixture was stirred for 48h at room temperature, concentrated *in vacuo*, redissolved in ethyl acetate and washed with water (3x50mL). Organic layer was concentrated *in vacuo* to get a thick syrup which was purified by silica gel column chromatography using petroleum ether-ethyl acetate as the mobile phase to obtain prop-2-ynyl 6-*O*-trityl-α,β-glucopyranosides (6.3g, 60%). To a solution of tritylated product prepared *vide supra* (4g, 8.7 mmol) in anhydrous DMF (30mL) was added 60% suspension of NaH in paraffin (1.62g, 40.5 mmol) at 0 ^oC under argon atmosphere. The resulting solution was stirred for 30min. at room temperature. Benzyl bromide (3.4mL, 28.7 mmol) followed by a catalytic amount of tetra-*n*-butyl ammonium iodide were added at 0 ^oC and the resulting reaction mixture was stirred at



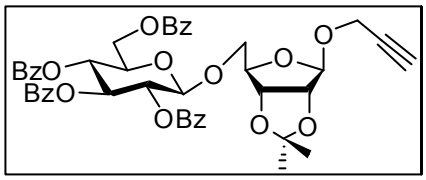
room temperature under argon atmosphere for 10h. After completion of the reaction as judged by TLC, excess NaH was quenched with methanol followed by cold water and extracted with diethyl ether (2x50mL). Combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The resulting crude was purified by flash silica gel column chromatography (230-400 mesh) using petroleum ether-ethylacetate as mobile phase to give prop-2-ynyl 6-*O*-trityl-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (4.4g, 70%) as thick syrup. To a solution of prop-2-ynyl 6-*O*-trityl-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside in CH_2Cl_2 and MeOH was added a catalytic amount of PTSA. The reaction mixture was stirred for 5h at room temperature, quenched with triethylamine and the solvent was removed *in vacuo*. The resulting yellowish crude oil was purified by silica gel column chromatography to afford prop-2-ynyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (2.65g, 90%). Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +49.4; IR (cm^{-1}): 3298, 3461; ^1H NMR (200.13 MHz, $CDCl_3$): δ 2.45 (1H, t, *J* 2.4 Hz), 3.56 (2H, dd, *J* 3.6, 9.6 Hz), 3.65-3.80 (3H, m), 4.02 (1H, t, *J* 8.8 Hz), 4.26 (2H, d, *J* 2.4 Hz), 4.60-5.06 (7H, m), 7.24-7.45 (15H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 54.4, 61.7, 71.3, 73.0, 74.9, 75.1, 75.8, 77.1, 78.8, 79.4, 81.7, 95.1, 127.5-128.5, 137.9, 138.0, 138.7; Mol. Wt. calculated for $C_{30}H_{32}O_6$: 488.57, Found: 511.02 (M^++23 for Na).

Prop-2-ynyl 2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-α-D-glucopyranoside (56): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +30.5; IR (cm^{-1}): 1215, 1585, 1602, 1733, 2869, 2921, 2941, 3305; ^1H NMR (200.13 MHz, $CDCl_3$): δ 2.38 (1H, t, *J* 2.3 Hz), 3.21-3.52 (2H, m), 3.89 (1H, t, *J* 9.2 Hz), 3.72-3.92 (2H, m), 4.10-4.32 (5H, m), 4.45-5.02 (9H, m), 5.58 (1H, dd, *J* 8.0, 9.6 Hz), 5.67 (1H, t, *J* 9.6 Hz), 5.90 (1H, t, *J* 9.5 Hz), 7.00-7.57 (27H, m), 7.78-8.02 (8H, m); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 54.3, 63.2, 68.1, 69.8, 70.1, 71.8, 72.2, 72.9, 72.9, 74.6, 74.7, 75.5, 77.2, 79.0, 79.3, 81.7, 95.0, 101.3, 127.4-129.7, 133.1, 133.1, 133.2, 133.4, 138.0, 138.2, 138.8, 165.0, 165.1, 165.2, 165.8; Mol. Wt. calculated for $C_{64}H_{58}O_{15}$: 1067.13, Found: 1090.52 (M^++23 for Na).

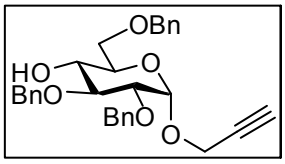


Synthesis of prop-2-ynyl 2,3-*O*-isopropylidene-β-D-ribofuranoside (57): To a solution of D-ribose (2g, 13.3 mmol) in propargyl alcohol (15mL) was added a few drops of H_2SO_4 at room temperature under argon atmosphere. The reaction mixture

was stirred for 15h at room temperature, neutralized with triethylamine. The unreacted propargyl alcohol was removed *in vacuo* and the resulting yellow syrup was directly taken for the next step without purification. To a solution of prop-2-ynyl β-D-ribofuranoside in acetone (10mL) was added 2,2'-dimethoxy propane (3mL) followed by a catalytic amount of PTSA at room temperature under nitrogen atmosphere. The resulting reaction mixture was stirred for 2h at room temperature, neutralized with triethylamine and concentrated *in vacuo* followed by flash silica gel column purification using petroleum ether-ethyl acetate solvent to obtain prop-2-ynyl 2,3-*O*-isopropylidene-β-D-ribofuranoside (1.3g, 43% over two steps). Characterization data : $[\alpha]_D$ ($CHCl_3$, *c* 0.8) = -97.3; IR (cm^{-1}): 3321, 3422; ^1H NMR (200.13 MHz, $CDCl_3$): δ 1.33, 1.49 (6H, 2s), 2.52 (1H, t, *J* 2.4 Hz), 2.97 (1H, dd, *J* 4.6, 8.4 Hz), 3.60-3.75 (2H, m), 4.30 (2H, d, *J* 2.4 Hz), 4.42 (1H, t, *J* 3.8 Hz), 4.72 (2H, ABq, *J* 5.9 Hz), 5.27 (1H, s); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 24.6, 26.2, 55.0, 63.7, 75.3, 78.3, 81.3, 85.7, 88.4, 107.5, 112.2; Mol. Wt. calculated for $C_{11}H_{16}O_5$: 228.24, Found: 251.12 (M^++23 for Na).



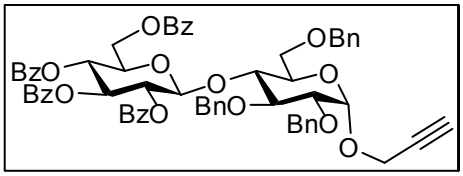
Prop-2-ynyl 2,3-*O*-isopropylidene-5-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-β-D-ribo-furanoside (58): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = -18.8; IR (cm^{-1}): 1267, 1585, 1602, 1731, 2869, 2887, 2943, 2954, 3305; ^1H NMR (200.13 MHz, $CDCl_3$): δ 1.17, 1.38 (6H, 2s), 2.40 (1H, t, *J* 2.4 Hz), 3.65 (1H, dd, *J* 6.6, 10.3 Hz), 3.87 (1H, dd, *J* 7.6, 10.1 Hz), 4.04 (1H, q, *J* 2.4 Hz), 4.10-4.22 (2H, m), 4.31 (1H, t, *J* 7.1 Hz), 4.40-4.72 (4H, m), 4.91 (1H, d, *J* 7.9 Hz), 5.17 (1H, s), 5.56 (1H, dd, *J* 7.8, 9.6 Hz), 5.68 (1H, t, *J* 9.8 Hz), 5.91 (1H, t, *J* 9.6 Hz), 7.21-7.62 (12H, m), 7.76-8.10 (8H, m) ; ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 24.6, 26.2, 53.9, 63.0, 69.6, 69.7, 71.6, 72.3, 72.8, 74.7, 78.7, 81.5, 84.9, 85.0, 100.7, 106.4, 112.3, 128.2-129.8, 133.1, 133.2, 133.2, 133.4, 165.0, 165.1, 165.8, 166.1; Mol. Wt. calculated for $C_{45}H_{42}O_{14}$: 806.80, Found: 829.26 (M^++23 for Na).



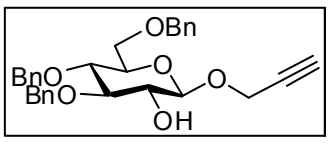
Synthesis of prop-2-ynyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (59): Prop-2-ynyl 4,6-*O*-benzylidene-α-D-glucopyranoside was benzylated under conditions NaH/DMF/BnBr/*n*-Bu_4NI/(0-25)^oC/95% as delineated above. The resulting product (2g, 4.11 mmol) was dissolved in anhydrous THF (10mL). To that was added sodium cyanoborohydride (2.2g, 34.9 mmol) followed by a saturated solution of HCl gas in

diethyl ether at 0 ^{o}C dropwise till the disappearance of frothing. The reaction mixture was quenched with water and extracted with ethyl acetate. Combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The resulting crude was purified by silica gel column chromatography using petroleum ether-ethyl acetate as eluent to give prop-2-ynyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside **8** (1.65g, 82%). Characterization data : $[\alpha]_D$ ($CHCl_3$, *c* 0.8) = +58.0; IR (cm^{-1}): 1215, 3305, 3496; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.44 (1H, t, *J* 2.4 Hz), 3.53-3.51 (6H, m), 4.28 (2H, d, *J* 2.4 Hz), 4.55 (2H, d, *J* 3.7 Hz), 4.71 (2H, s), 4.86 (2H, ABq, *J* 3.9 Hz), 5.10 (1H, d, *J* 3.95 Hz), 7.21-7.43 (15H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 54.3, 61.2, 70.4, 70.5, 72.6, 73.5, 74.8, 75.4, 78.8, 78.9, 81.2, 95.0, 127.4-128.6, 137.8, 137.9, 138.7; Mol. Wt. calculated for $C_{30}H_{32}O_6$: 488.57, Found: 511.14 (M^++23 for Na).

Prop-2-ynyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-α-D-glucopyranoside (60): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +17.8; IR (cm^{-1}): 1215, 1585, 1602, 1733, 2869, 2921, 2941, 3305; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.27 (1H, t, *J* 2.2 Hz), 3.41 (1H, dd, *J* 1.5, 10.8 Hz), 3.50 (1H, dd, *J* 3.7, 9.3 Hz), 3.56 (1H, d, *J* 9.8 Hz), 3.62-3.78 (2H, m), 3.93 (1H, d, *J* 2.5 Hz), 3.94 (1H, ABq, *J* 8.8 Hz), 4.15 (2H, d, *J* 2.2 Hz), 4.21-4.46 (3H, m), 4.55-5.10 (7H, m), 5.40-5.68 (3H, m), 7.12-7.58 (27H, m), 7.75-8.05 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 54.7, 63.1, 67.3, 69.8, 70.1, 71.8, 72.2, 73.0, 73.2, 73.6, 74.7, 75.3, 77.1, 78.3, 78.8, 79.7, 95.6, 100.3, 127.1-129.7, 132.9, 133.1, 133.2, 133.3, 137.8, 138.2, 139.2, 164.7, 165.0, 165.7, 166.0; Mol. Wt. calculated for $C_{64}H_{58}O_{15}$: 1067.13, Found: 1090.52 (M^++23 for Na).

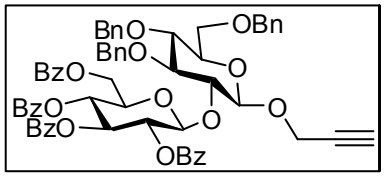


Synthesis of prop-2-ynyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranoside (61): To a solution of tri-*O*-benzyl glucal (1g, 2.41 mmol) in chloroform (5mL) was added a solution of *m*-CPBA (1g, 6.02 mmol) in chloroform (10mL) at 0 ^{o}C under argon atmosphere. The reaction mixture was stirred at room temperature for 15h, diluted with water and extracted with chloroform. Combined organic layers were washed water, aq $NaHCO_3$ solution, water, dried over anhydrous sodium sulfate and concentrated *in vacuo.* The resulting crude was purified by silica gel column chromatography to give 1-*m*-chlorobenzoyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranose (0.6g, 43%). 1-*m*-Chloro

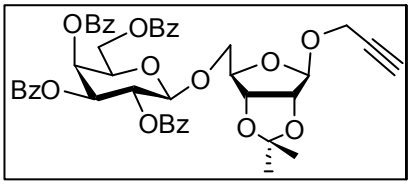


benzoyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranose (0.84g, 1.43 mmol) prepared *vide supra* was acetylated at C-2 position under conditions Ac_2O (1.5 eq.)/Et_3N (2 eq.)/DMAP/CH_2Cl_2/88%. The resulting acetylated product (2g, 3.16 mmol) was dissolved in anhydrous CH_2Cl_2 (15mL) along with propargyl alcohol (0.95mL, 15.8 mmol). $BF_3.Et_2O$ (1.2mL, 9.50 mmol) was added dropwise at 0 ^oC under argon atmosphere. The reaction mixture was stirred for 2h at room temperature, quenched with $NaHCO_3$ solution and extracted with CH_2Cl_2 (2x25mL). Combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate and concentrated *in vacuo* to obtain black residue which was purified by silica gel column chromatography using petroleum ether-ethyl acetate as eluent to afford a mixture of prop-2-ynyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α,β-glucopyranosides (1.25g, 74%). To a solution of the mixture of prop-2-ynyl 2-*O*-aceyl-3,4,6-tri-*O*-benzyl-α,β-glucopyranosides (1.25g, 2.35 mmol) in anhydrous methanol (15mL) was added a catalytic amount of sodium metal at room temperature under argon atmosphere. The reaction mixture was stirred for 30min. at room temperature and the excess methanol was removed *in vacuo*. The resulting crude residue was purified by flash silica gel (230-400 mesh) column chromatography using petroleum ether-ethyl acetate as the mobile phase to give prop-2-ynyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranoside (0.62g, 52%). Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = -25.2; IR (cm^{-1}): 3303, 3446; ^1H NMR (200.13 MHz, $CDCl_3$): δ 2.39 (1H, t, *J* 2.3 Hz), 2.48 (1H, bs), 3.39-3.67 (6H, m), 4.33 (2H, t, *J* 2.8 Hz), 4.41 (1H, d, *J* 6.1 Hz), 4.49 (2H, ABq, *J* 12.3 Hz), 4.60 (2H, ABq, *J* 10.6 Hz), 4.82 (2H, ABq, *J* 11.2 Hz), 7.04-7.33 (15H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.9, 68.6, 73.4, 74.3, 74.9, 75.1, 75.2, 75.3, 77.3, 78.3, 84.4, 100.4, 127.6-128.4, 137.9, 138.0, 138.5; Mol. Wt. calculated for $C_{30}H_{32}O_6$: 488.57, Found: 511.23 (M^++23 for Na).

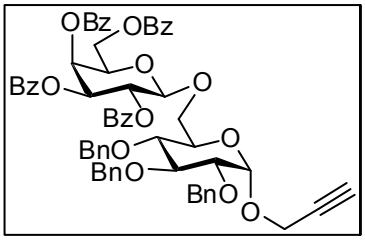
Prop-2-ynyl 2-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside (62): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +25.6; IR (cm^{-1}): 1267, 1585, 1602, 1731, 2869, 2927, 3305; ^1H NMR (200.13 MHz, $CDCl_3$): δ 2.47 (1H, t, *J* 2.4 Hz), 3.30-3.68 (5H, m), 3.80 (1H, t, *J* 8.2 Hz), 4.14-4.85 (12H, m), 5.35 (1H, d, *J* 7.8 Hz) 5.59 (1H, dd, *J* 7.8, 9.2 Hz), 5.72-5.92 (2H, m), 6.93-7.58 (27H, m), 7.72-8.10 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 56.2, 63.0, 68.5, 69.4, 72.0, 72.5, 73.4, 73.4, 74.6, 74.8, 75.2, 75.3, 77.3, 78.9, 81.4, 84.1, 100.2, 100.3, 127.1-129.9, 133.0,



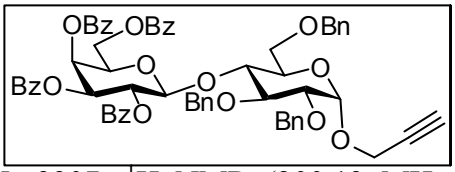
133.0, 133.1, 133.3, 137.8, 137.9, 138.3, 165.1, 165.1, 165.8, 166.2; Mol. Wt. calculated for $C_{64}H_{58}O_{15}$: 1067.13, Found: 1090.08 (M^++23 for Na).



Prop-2-ynyl 2,3-*O*-isopropylidene-5-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-β-D-ribo-furanoside (63): $[\alpha]_D$ ($CHCl_3$, *c* 1.2) = +49.2; IR (cm^{-1}): 1269, 1585, 1602, 1716, 1731, 1737, 2869, 2939, 3303; ^1H NMR (200.13 MHz, $CDCl_3$): δ 1.19, 1.38 (6H, 2s), 2.40 (1H, t, *J* 2.3 Hz), 3.68 (1H, dd, *J* 6.8, 10.3 Hz), 3.84-4.00 (1H, m), 4.06 (2H, dd, *J* 2.4, 5.6 Hz), 4.23-4.48 (3H, m), 4.51-4.75 (3H, m), 4.89 (1H, d, *J* 7.9 Hz), 5.18 (1H, s), 5.60 (1H, dd, *J* 3.2, 10.3 Hz), 5.81 (1H, dd, *J* 7.9, 10.5 Hz), 6.00 (1H, d, *J* 3.1 Hz), 7.20-7.65 (12H, m), 7.75-8.13 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 24.7, 26.3, 53.9, 61.9, 68.0, 69.4, 69.9, 71.4, 71.7, 74.7, 78.7, 81.6, 84.9, 85.0, 101.2, 106.4, 112.4, 128.2-130.1, 133.2, 133.3, 133.3, 133.6, 165.1, 165.5, 165.6, 166.0; Mol. Wt. calculated for $C_{45}H_{42}O_{14}$: 806.80, Found: 829.26 (M^++23 for Na).

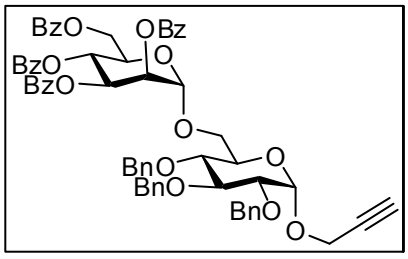


Prop-2-ynyl 2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-α-D-glucopyranoside (64): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +89.8; IR (cm^{-1}): 1267, 1585, 1602, 1730, 2869, 2927, 3305; ^1H NMR (200.13 MHz, $CDCl_3$): δ 2.30 (1H, t, *J* 2.1 Hz), 3.35 (1H, d, *J* 10.3 Hz), 3.45 (1H, dd, *J* 3.6, 9.9 Hz), 3.67-3.98 (3H, m), 4.09-5.03 (14H, m), 5.61 (1H, dd, *J* 3.32, 10.4 Hz), 5.84 (1H, dd, *J* 8.1, 10.4 Hz), 5.97 (1H, d, *J* 2.5 Hz), 7.05-7.68 (27H, m), 7.72-8.18 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 54.3, 61.9, 68.0, 68.3, 69.7, 70.2, 71.3, 71.5, 72.9, 74.7, 74.7, 75.5, 77.2, 78.9, 79.3, 81.7, 94.9, 101.9, 127.4-130.0, 133.1, 133.3, 133.3, 133.6, 137.9, 138.1, 138.7, 165.1, 165.5, 165.6, 166.0; Mol. Wt. calculated for $C_{64}H_{58}O_{15}$: 1067.13, Found: 1090.52 (M^++23 for Na).



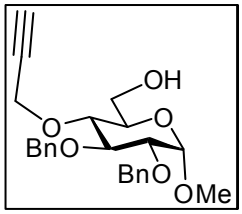
Prop-2-ynyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-α-D-glucopyranoside (65): $[\alpha]_D$ ($CHCl_3$, *c* 0.8) = +40.0; IR (cm^{-1}): 1215, 1602, 1730, 2869, 2925, 3307; ^1H NMR (200.13 MHz, $CDCl_3$): δ 2.30 (1H, t, *J* 2.3 Hz), 3.51 (2H, ABq, *J* 10.6 Hz), 3.55 (1H, dd, *J* 3.9, 9.5 Hz), 3.69 (1H, dd, *J* 2.7, 10.4 Hz), 3.85-4.10 (3H, m), 4.17 (2H, d, *J* 2.3 Hz), 4.23-4.48 (3H, m), 4.61-4.84 (4H, m), 4.98 (2H, ABq, *J* 11.2 Hz), 5.01 (1H, d, *J* 3.6 Hz), 5.30 (1H, dd, *J* 3.4, 10.4 Hz), 5.69 (1H, dd, *J* 8.0, 10.4 Hz), 5.85 (1H, d, *J* 3.0 Hz), 7.12-

7.61 (27H, m), 7.70-8.08 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 54.7, 61.3, 67.3, 67.7, 70.1, 70.2, 70.9, 71.8, 73.2, 73.6, 74.7, 75.3, 76.5, 78.2, 78.8, 79.6, 95.7, 100.4, 127.1-129.8, 133.1, 133.2, 133.3, 133.4, 137.7, 138.1, 139.3, 164.8, 165.3, 165.3, 165.8; Mol. Wt. calculated for $C_{64}H_{58}O_{15}$: 1067.13, Found: 1090.02 (M^++23 for Na).



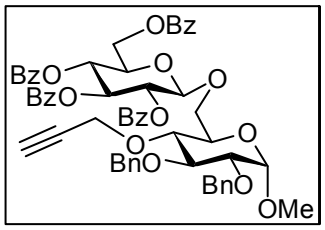
Prop-2-ynyl 2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-gluco-pyranoside (66): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +18.8; IR (cm^{-1}): 1215, 1602, 1728, 2875, 2893, 2927, 3307; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.47 (1H, t, *J* 2.3 Hz), 3.48-3.69 (2H, m), 3.75-4.12 (4H, m), 4.15-4.87 (10H, m), 4.48-5.16 (3H, m), 5.69-5.76 (1H, m), 5.87 (1H, dd, *J* 3.2, 10.1 Hz), 6.09 (1H, t, *J* 10.1 Hz), 7.10-7.65 (27H, m), 7.78-8.15 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 54.6, 62.7, 66.7, 66.8, 68.9, 70.0, 70.2, 70.6, 73.0, 75.0, 75.0, 75.7, 77.6, 78.9, 79.7, 81.9, 95.0, 97.7, 127.4-130.0, 133.0, 133.1, 133.4, 133.4, 138.0, 138.1, 138.7, 165.2, 165.4, 165.4, 166.1; Mol. Wt. calculated for $C_{64}H_{58}O_{15}$: 1067.13, Found: 1090.52 (M^++23 for Na).

Synthesis of methyl 2,3-di-*O*-benzyl-4-*O*-prop-2-ynyl-α-D-glucopyranoside (67): Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside (2.0g, 53.5 mmol) was tritylated at C-6 position selectively under conditions ($(C_6H_5)_3CCl$/DMAP/pyridine/50 ^oC/85%. The resulting trityl ether (2.0g, 32.4 mmol) was propargylated under NaH/DMF/propargyl bromide/*n*-Bu_4NI/0 ^oC and the resulting crude was purified by flash silica gel (230-400 mesh) column chromatography using petroleum ether-ethyl acetate as the mobile phase to give methyl 2,3-di-*O*-benzyl-4-*O*-prop-2-ynyl-6-*O*-trityl-α-D-gluco-pyranoside (2.0g, 95%) that was redissolved in CH_2Cl_2 (10mL) and methanol. To that was added a catalytic amount of PTSA at room temperature. The reaction mixture was stirred for 5h at room temperature, quenched with triethylamine and the solvent was concentrated *in vacuo* to obtain a yellow syrupy residue which was purified by silica gel column chromatography using petroleum ether-ethyl acetate as mobile phase to obtain methyl 2,3-di-*O*-benzyl-4-*O*-prop-2-ynyl-α-D-glucopyranoside **67** (1.1g, 90%). Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 0.9) = +64.4; IR (cm^{-1}): 3305, 3496; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.00 (1H, bs), 2.46 (1H, t, *J* 2.4 Hz), 3.36 (3H, s), 3.40-3.52 (2H, m), 3.59 (1H, td, *J* 3.3, 10.0 Hz), 3.81 (2H, dd, *J* 3.2, 6.1 Hz), 3.95 (1H, t, *J* 9.1 Hz), 4.38 (2H, d, *J* 2.4 Hz), 4.56 (1H, d, *J* 12.3 Hz), 4.71 (2H, ABq, *J* 12.3 Hz), 4.87

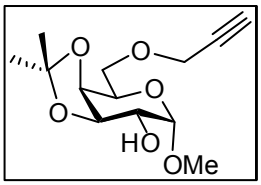


(2H, ABq, *J* 10.7 Hz), 7.21-7.39 (10H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.2, 59.8, 61.6, 70.3, 73.3, 74.4, 75.7, 76.6, 79.8, 80.1, 81.7, 98.0, 127.6-128.5, 137.9, 138.4; Mol. Wt. calculated for $C_{24}H_{28}O_6$: 412.47, Found: 435.64 (M^++23 for Na).

Methyl 2,3-di-*O*-benzyl-4-*O*-prop-2-ynyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-gluco-pyranosyl)-α-D-glucopyranoside (68): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +62.2; IR (cm^{-1}): 1266, 1584, 1602, 1733, 2933, 3306; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.38 (1H, t, *J* 2.4 Hz), 3.17 (3H, s), 3.24 (1H, t, *J* 9.4 Hz), 3.37 (1H, dd, *J* 9.6 Hz), 3.62-3.89 (3H, m), 4.06 (2H, dd, *J* 2.4, 7.7 Hz), 4.13-4.28 (2H, m), 4.42-5.0 (8H, m), 5.64 (1H, t, *J* 9.9 Hz), 5.65 (1H, dd, *J* 9.7, 19.4 Hz), 5.91 (1H, t, *J* 9.6 Hz), 7.20-7.57 (22H, m), 7.78-8.05 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 54.9, 59.7, 63.2, 68.5, 69.2, 69.7, 71.7, 72.1, 72.8, 73.2, 74.5, 75.4, 76.9, 79.6, 79.8, 81.6, 97.6, 101.3, 127.5-129.8, 133.1, 133.2, 133.2, 133.4, 137.9, 138.5, 164.9, 165.1, 165.8, 166.1; Mol. Wt. calculated for $C_{58}H_{54}O_{15}$: 991.04, Found: 1014.65 (M^++23 for Na).

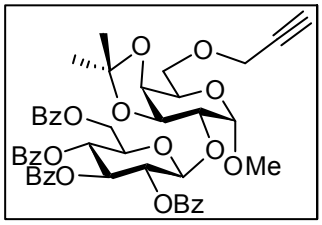


Synthesis of methyl 3,4-*O*-isopropylidene-6-*O*-prop-2-ynyl-α-D-galactopyranoside (69): 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (3g, 0.1154 mol) was propargylated using NaH/DMF/propargyl bromide/*n*-Bu_4NI/0 ^oC followed by conventional silica gel column purification to obtain 1,2:3,4-di-*O*-isopropylidene-6-*O*-prop-2-ynyl-α-D-galactopyranose (2.9g, 85%) that was redissolved in anhydrous methanol. A catalytic amount of PTSA was added at room temperature and the reaction mixture was stirred for 10h at 80 ^oC under argon atmosphere. After completion of the reaction as judged by TLC, the reaction mixture was neutralized with triethylamine and the excess methanol was concentrated *in vacuo*. The resulting crude residue was directly taken for the next step without purification. To a solution of mixture of methyl 6-*O*-prop-2-ynyl-α,β-glucopyranosides in acetone (15mL) was added 2,2'-dimethoxypropane (5mL) followed by a catalytic amount of PTSA at room temperature under nitrogen atmosphere. The reaction mixture was stirred for 5h at room temperature, neutralized with triethylamine and concentrated *in vacuo*. The resulting crude was purified by flash silica gel (230-400 mesh) column chromatography using petroleum ether-ethyl acetate as the mobile phase to obtain methyl 3,4-*O*-isopropylidene-6-*O*-prop-2-ynyl-α-D-galactopyranoside (0.8g, 30% over 2 steps). Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +94.4; IR (cm^{-1}): 3307, 3421; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.35, 1.51 (6H,

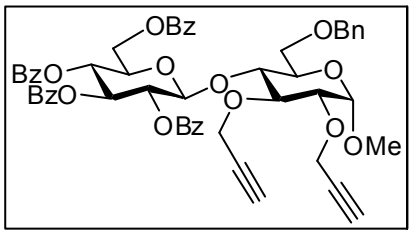


2s), 2.47 (1H, t, *J* 2.4 Hz), 2.55 (1H, bs), 3.46 (3H, s), 3.58-3.89 (3H, m), 4.12-4.29 (5H, m), 4.78 (1H, d, *J* 3.8 Hz); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 25.9, 27.7, 55.5, 58.6, 67.1, 69.3, 69.5, 73.2, 74.7, 76.1, 79.4, 98.4, 109.6; Mol. Wt. calculated for $C_{13}H_{20}O_6$: 272.29, Found: 295.67 (M^++23 for Na).

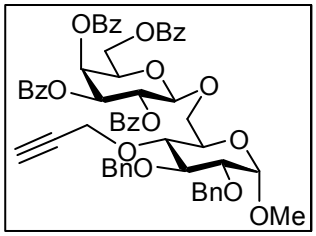
Methyl 2-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-3,4-*O*-isopropylidene-6-*O*-prop-2-ynyl-α-D-galactopyranoside (70): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +65.2; IR (cm^{-1}): 1266, 1585, 1602, 1732, 1733, 2936, 3306; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.20, 1.36 (6H, 2s), 2.45 (1H, t, *J* 2.4 Hz), 3.32 (3H, s), 3.65-3.86 (3H, m), 4.04-4.20 (4H, m), 4.21 (2H, dd, *J* 2.4, 4.5 Hz), 4.46 (1H, dd, *J* 5.2, 12.2 Hz), 4.67 (1H, dd, *J* 3.1, 12.2 Hz), 4.86 (1H, d, *J* 3.4 Hz), 5.19 (1H, d, *J* 7.7 Hz), 5.56 (1H, dd, *J* 7.9, 9.7 Hz), 5.67 (1H, t, *J* 9.7 Hz), 5.92 (1H, t, *J* 9.7 Hz), 7.20-7.59 (12H, m), 7.81-8.05 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 26.3, 28.2, 55.6, 58.6, 63.0, 66.4, 69.2, 69.5, 71.8, 72.3, 72.8, 73.8, 74.7, 75.0, 79.0, 79.5, 98.9, 101.9, 109.0, 128.0-129.9, 132.9, 133.1, 133.2, 133.4, 165.0, 165.1, 165.8, 166.0; Mol. Wt. calculated for $C_{47}H_{46}O_{15}$: 850.85, Found: 873.60 (M^++23 for Na).



Methyl 2,3-di-*O*-prop-2-ynyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-6-*O*-benzyl-α-D-glucopyranoside (72): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +65.67; IR (cm^{-1}): 1265, 1585, 1602, 1732, 2868, 2938, 3307; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.33 (1H, t, *J* 2.33 Hz), 2.41 (1H, t, *J* 2.26 Hz), 3.31 (3H, s), 3.38-3.64 (4H, m), 3.83 (2H, ABq, *J* 8.71 Hz), 3.81-3.97 (1H, m), 4.28-4.82 (10H, m), 5.45 (1H, dd, *J* 7.98, 9.62 Hz), 5.58-5.75 (2H, m), 7.22-7.58 (17H, m), 7.76-7.93 (6H, m), 8.03-8.07 (2H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.2, 59.3, 60.3, 62.9, 67.4, 69.2, 69.5, 71.8, 72.1, 72.9, 73.4, 73.8, 74.6, 77.8, 77.9, 79.7, 80.2, 80.3, 98.4, 100.7, 128.1-129.7, 132.9, 133.1, 133.4, 133.4, 137.9, 164.8, 165.0, 165.7, 166.1; Mol. Wt. calculated for $C_{54}H_{50}O_{15}$: 938.96, Found: 961.80 (M^++ 23 for Na).

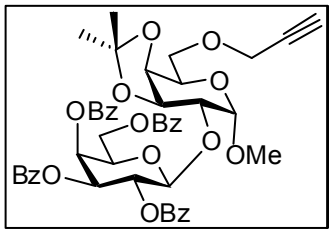


Methyl 2,3-di-*O*-benzyl-4-*O*-prop-2-ynyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galacto pyranosyl)-α-D-glucopyranoside (73): $[\alpha]_D$ ($CHCl_3$, *c* 0.9) = +86.2; IR (cm^{-1}): 1267, 1583, 1602, 1730, 2932, 3306; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.39 (1H, t, *J* 2.3 Hz), 3.17 (3H, s), 3.24 (1H, t, *J* 9.3 Hz), 3.34 (1H, dd, *J* 3.6, 9.6 Hz), 3.65-3.90 (3H, m), 4.13 (2H, dd, *J* 2.5, 3.6 Hz), 4.22-4.74 (9H, m), 4.91 (2H, t, *J* 9.6

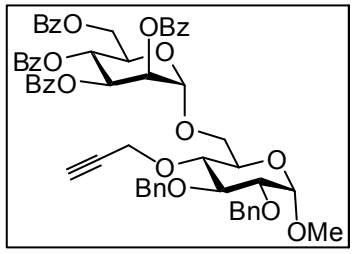


Hz), 5.61 (1H, dd, *J* 3.4, 10.4 Hz), 5.85 (1H, dd, *J* 3.2 Hz), 7.10-7.65 (22H, m), 7.70-8.11 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 54.9, 59.7, 61.9, 68.1, 68.9, 69.3, 69.7, 71.3, 71.6, 73.2, 74.6, 75.4, 76.9, 79.7, 79.9, 81.7, 97.6, 102.0, 127.5-130.0, 133.1, 133.2, 133.2, 133.5, 138.0, 138.5, 165.1, 165.5, 165.5, 166.0; Mol. Wt. calculated for $C_{58}H_{54}O_{15}$: 991.04, Found: 1013.87 (M^++23 for Na).

Methyl 2-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-3,4-*O*-isopropylidene-6-*O*-prop-2-ynyl-α-D-galactopyranoside (74): $[\alpha]_D$ ($CHCl_3$, *c* 0.9) = +128.9; IR (cm^{-1}): 1267, 1585, 1602, 1730, 2935, 3307; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.20, 1.36 (6H, 2s), 2.45 (1H, t, *J* 2.4 Hz), 3.36 (3H, s), 3.74-3.80 (2H, m), 3.84 (1H, dd, *J* 3.4 Hz), 4.06-4.18 (3H, m), 4.22 (2H, dd, *J* 2.6, 5.1 Hz), 4.25-4.37 (1H, m), 4.45 (1H, dd, *J* 6.2, 11.1 Hz), 4.63 (1H, dd, *J* 6.7, 11.2 Hz), 4.90 (1H, d, *J* 3.2 Hz), 5.15 (1H, d, *J* 7.8 Hz), 5.61 (1H, dd, *J* 3.3, 10.4 Hz), 5.82 (1H, dd, *J* 7.8, 10.3 Hz), 5.99 (1H, d, *J* 3.0 Hz), 7.20-7.68 (12H, m), 7.70-8.14 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 26.3, 28.2, 55.7, 58.7, 62.2, 66.4, 68.1, 69.2, 69.6, 71.5, 71.8, 73.8, 74.7, 75.0, 79.3, 79.5, 98.9, 102.4, 109.1, 128.0-130.1, 132.9, 133.2, 133.3, 133.5, 165.2, 165.6, 165.6, 166.0; Mol. Wt. calculated for $C_{47}H_{46}O_{15}$: 850.85, Found: 873.31 (M^++23 for Na).

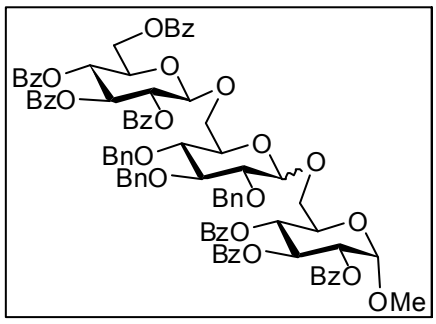


Methyl 2,3-di-*O*-benzyl-4-*O*-prop-2-ynyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-manno pyranosyl)-α-D-glucopyranoside (75): $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +6.6; IR (cm^{-1}): 1266, 1585, 1602, 1729, 2932, 3306; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.56 (1H, t, *J* 2.3 Hz), 3.46 (3H, s), 3.53 (2H, dd, *J* 3.9, 9.7 Hz), 3.71-4.08 (4H, m), 4.40-5.05 (10H, m), 5.21 (1H, d, *J* 1.5 Hz), 5.73 (1H, dd, *J* 1.8, 3.3 Hz), 5.93 (1H, dd, *J* 3.3, 10.0 Hz), 6.09 (1H, t, *J* 10.0 Hz), 7.20-7.65 (22H, m), 7.80-8.14 (8H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.2, 59.8, 62.8, 66.6, 67.0, 68.8, 69.5, 69.9, 70.3, 73.3, 75.1, 76.3, 75.5, 79.8, 80.1, 82.0, 97.6, 97.7, 127.5-129.9, 133.0, 133.1, 133.3, 133.4, 138.0, 138.5, 165.3, 165.4, 165.4, 166.1; Mol. Wt. calculated for $C_{58}H_{54}O_{15}$: 991.04, Found: 1014.65 (M^++23 for Na).

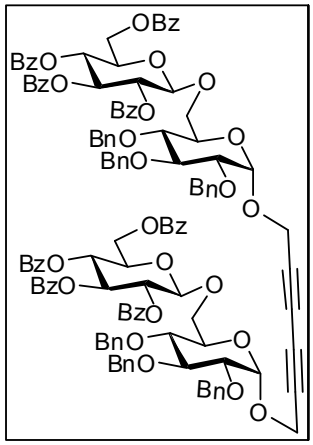


Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-α,β-D-glucopyranosyl)-α-D-glucopyranoside (77 & 78): To a solution of propargyl disaccharide **56** (0.1g, 0.0937 mmol) and methyl 3,4,6-tri-*O*-benzoyl-α-D-glucopyranoside **76** (57mg, 0.1124 mmol) in acetonitrile (3mL) was

added 15mol% of solid $AuBr_3$ (6mg) at room temperature under argon atmosphere. The reaction mixture was stirred for 15h at 70 ^oC under argon atmosphere, concentrated *in vacuo* and the resulting crude was purified by flash silica gel chromatography using petroleum ether-ethyl acetate as the mobile phase to obtain an inseparable (3:1~α:β) mixture of trisaccharides as a colourless solid (72mg, 50%). Characterization data of **77 & 78**: $[\alpha]_D$ ($CHCl_3$, *c* 1.1) = +42.33; IR (cm^{-1}): 1266, 1584, 1602, 1731, 2879, 2836; ^1H NMR (500.13 MHz, $CDCl_3$): δ 3.20-3.53 (3H, m), 3.42 (3H, s), 3.62-3.83 (3H, m), 3.88 (1H, t, *J* 9.21 Hz), 4.00-4.25 (4H, m), 4.29-4.68 (6H, m), 4.70 (1H, d, *J* 6.69 Hz), 4.72 (1H, d, *J* 2.23 Hz), 4.80-5.03 (2H, m), 5.17-5.40 (2H, m), 5.50-5.58 (1H, m), 5.62-5.71 (1H, m), 5.83-6.07 (1H, m), 6.08-6.25 (1H, m), 6.95-7.60 (36H, m), 7.78-8.05 (14H, m); ^{13}C NMR (125.76 MHz, $CDCl_3$): δ 55.5, 63.2, 66.3, 67.9, 68.6, 69.3, 69.4, 69.7, 70.6, 71.7, 72.1, 72.2, 72.8, 73.0, 74.3, 75.2, 77.0, 79.8, 81.4, 96.7, 97.0, 101.2, 127.0-130.0, 133.0, 133.1, 133.2, 133.2, 133.3, 133.3, 133.4 138.3, 138.5, 138.9, 164.8, 165.1, 165.1, 165.8, 165.8, 165.8, 166.1; Mol. Wt. calculated for $C_{89}H_{80}O_{23}$: 1516.51, Found: 1540.10 (M^++23 for Na).

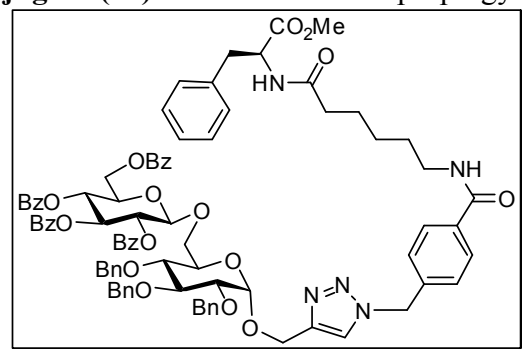


2,4-Hexynyl bis(2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-α-D-glucopyranoside (79): To a solution of propargyl disaccharide **56** (0.1g, 0.094 mmol) in pyridine (7mL) was added solid copper(II)acetate (0.17g, 0.94 mmol) at room temperature. The reaction mixture was stirred at 70 ^oC for 3h, quenched with dilute HCl and extracted with dichloromethane (2x20mL). Combined organic layers were washed with water, brine solution, dried over anhydrous Na_2SO_4 and filtered off. The filtrate was concentrated *in vacuo* and the resulting crude was purified by silica gel column chromatography using petroleum ether-ethyl acetate as eluent to give homodimerized product **79** as a viscous liquid (73%). Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +39.41; IR (cm^{-1}): 1269, 1602, 1714, 1731, 1737, 2856, 2927; ^1H NMR (400.13 MHz, $CDCl_3$): δ 3.37 (1H, t, *J* 9.41 Hz), 3.44 (1H, dd, *J* 3.71, 9.71 Hz), 3.70-3.75 (2H, m), 3.87 (1H, t, *J* 9.25 Hz), 4.04-4.10 (1H, m), 4.13 (1H, d, *J* 9.36 Hz), 4.19 (2H, s), 4.29 (1H, d, *J* 11.01



Hz), 4.48-4.68 (6H, m), 4.79 (1H, d, *J* 7.93 Hz), 4.88 (1H, d, *J* 8.26 Hz), 4.89 (1H, d, *J* 3.27 Hz), 5.57 (1H, dd, *J* 7.83, 9.65 Hz), 5.66 (1H, t, *J* 9.72 Hz), 5.88 (1H, t, *J* 9.63 Hz), 7.04-7.06 (2H, m), 7.20-7.52 (25H, m), 7.80-7.82 (2H, m), 7.87-7.91 (4H, m), 7.97-7.99 (2H, m); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 54.6, 63.2, 68.1, 69.8, 70.2, 70.6, 71.8, 72.2, 72.8, 73.1, 74.6, 74.7, 75.5, 77.2, 79.2, 81.6, 95.2, 101.3, 127.5-129.8, 133.1, 133.2, 133.2, 133.4, 137.8, 138.1, 138.7, 164.9, 165.1, 165.8, 166.1; Mol. Wt. calculated for $C_{128}H_{114}O_{30}$: 2132.26, Found: 2156.37 (M^++23 for Na).

Triazole 'clicked' disaccharide peptide conjugate (81): To a solution of propargyl disaccharide **56** (50mg, 0.0468 mmol) and azide **80** (21mg, 0.0465 mmol) in CH_3CN (3mL) was added CuI (10mg, 0.054 mmol) followed by DIPEA (16μL, 0.094 mmol). The reaction mixture was stirred at room temperature for 30min., quenched with a saturated solution of ammonium chloride and extracted with ethyl acetate (2x10mL). Combined organic layers were washed with water, dried over sodium sulfate and concentrated *in vacuo*. The resulting crude was purified by silica gel chromatography using ethyl acetate as the eluent to give the triazole 'clicked' glycopeptide as a colourless solid (68mg, 95%). Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.1) = +39.06; IR (cm^{-1}): 1650, 1714, 1731, 1737, 2860, 2929, 3426; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.26-1.35 (4H, m), 1.47-1.67 (4H, m), 2.17 (2H, t, *J* 7.24 Hz), 3.09 (2H, t, *J* 6.27 Hz), 3.35-3.46 (4H, m), 3.69 (3H, s), 3.71-3.87 (3H, m), 4.07-4.16 (2H, m), 4.25 (1H, d, *J* 11.05 Hz), 4.38-4.66 (6H, m), 4.79-4.92 (4H, m), 5.45 (2H, s), 5.57 (1H, dd, *J* 7.98, 9.64 Hz), 5.67 (1H, t, *J* 9.65 Hz), 5.89 (1H, t, *J* 9.48 Hz), 6.00 (1H, d, *J* 7.81 Hz), 6.48 (1H, t, *J* 5.41 Hz), 6.99-7.55 (36H, m), 7.71-8.00 (9H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 24.6, 26.1, 28.9, 35.9, 37.8, 39.6, 52.3, 52.9, 53.5, 60.6, 63.2, 68.2, 69.7, 69.8, 71.8, 72.2, 72.8, 72.9, 74.7, 75.3, 77.2, 79.6, 81.6, 96.2, 101.2, 123.1, 127.1-129.8, 133.1, 133.1, 133.2, 133.4, 135.8, 137.0, 138.0, 138.0, 138.7, 164.9, 165.2, 165.7, 166.1, 166.7, 172.1, 172.5; Mol. Wt. calculated for $C_{88}H_{87}N_5O_{19}$: 1518.65, Found: 1544.19 (M^++23 for Na).



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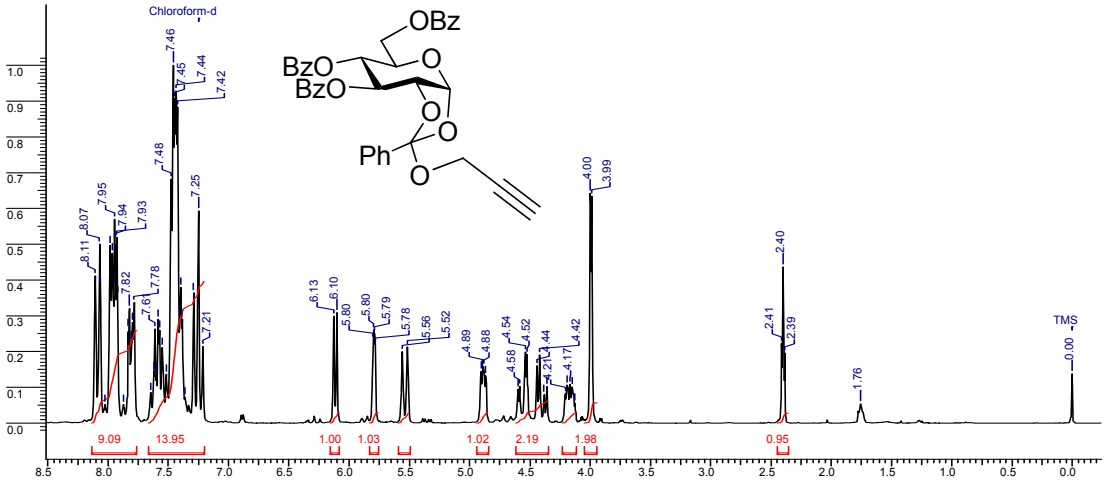
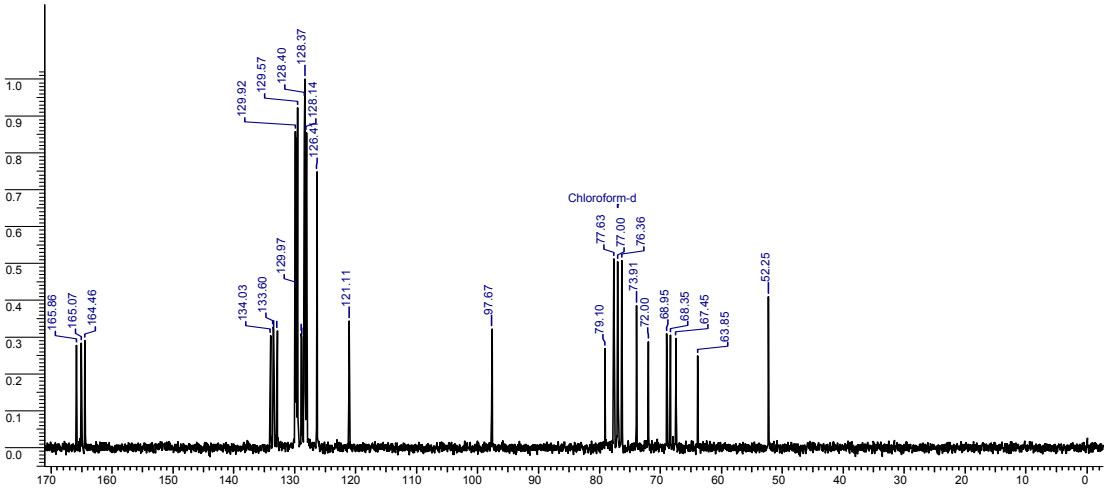
Spectral Charts

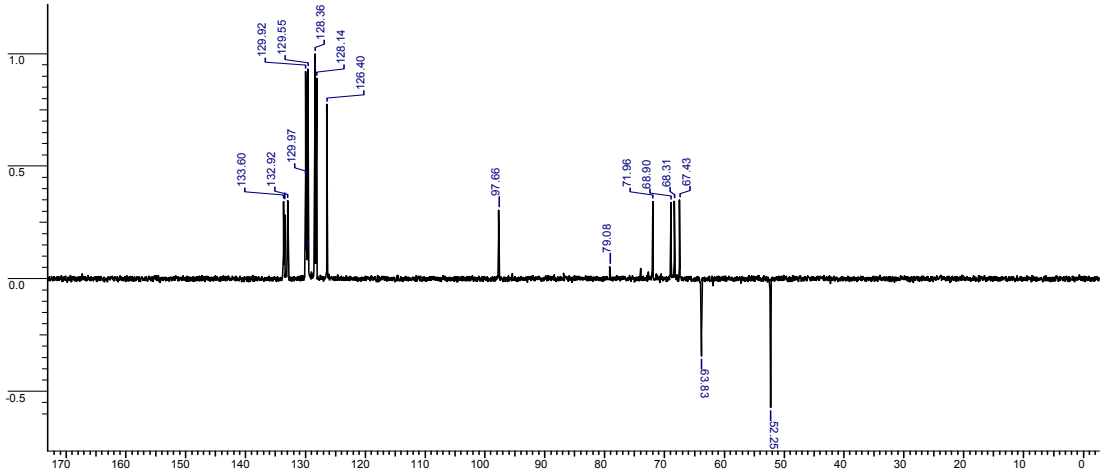
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **18**



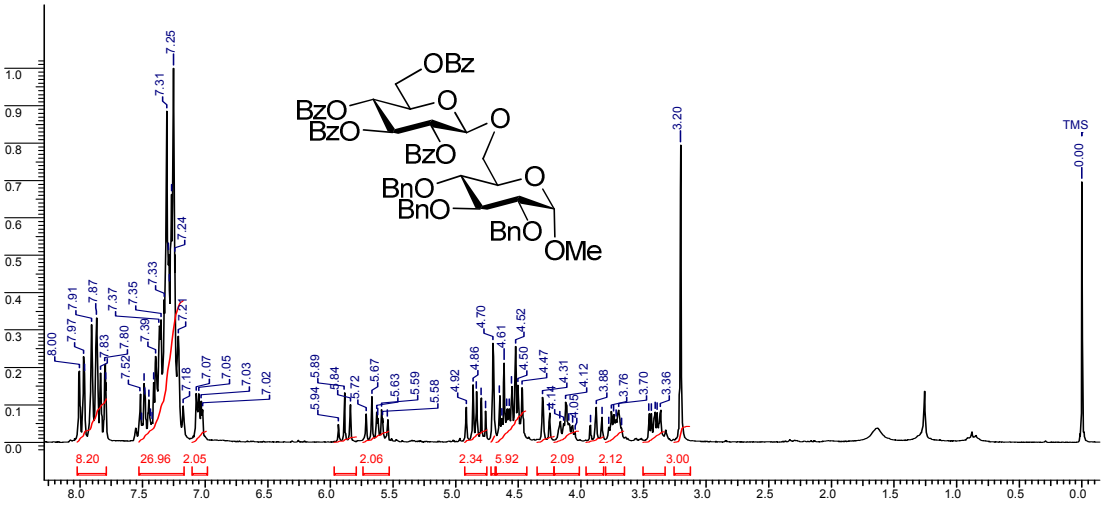
^{13}CNMR ($CDCl_3$, 50.32 MHz) of Compound **18**



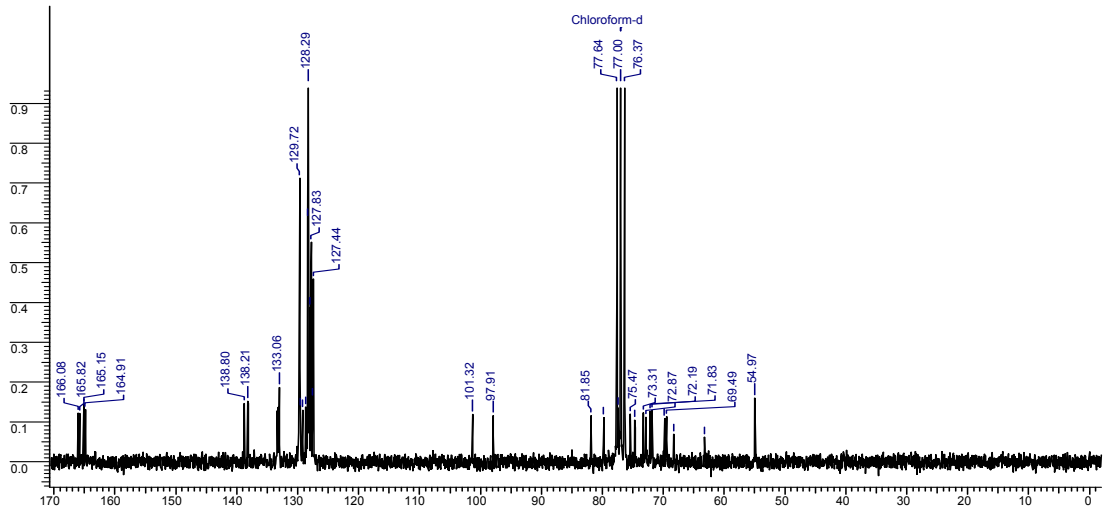
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **18**



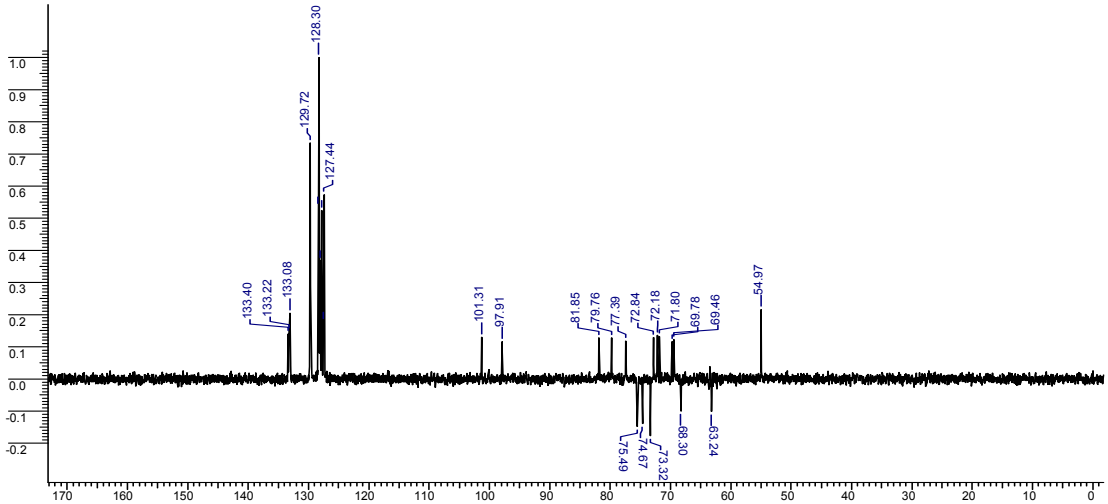
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **20**



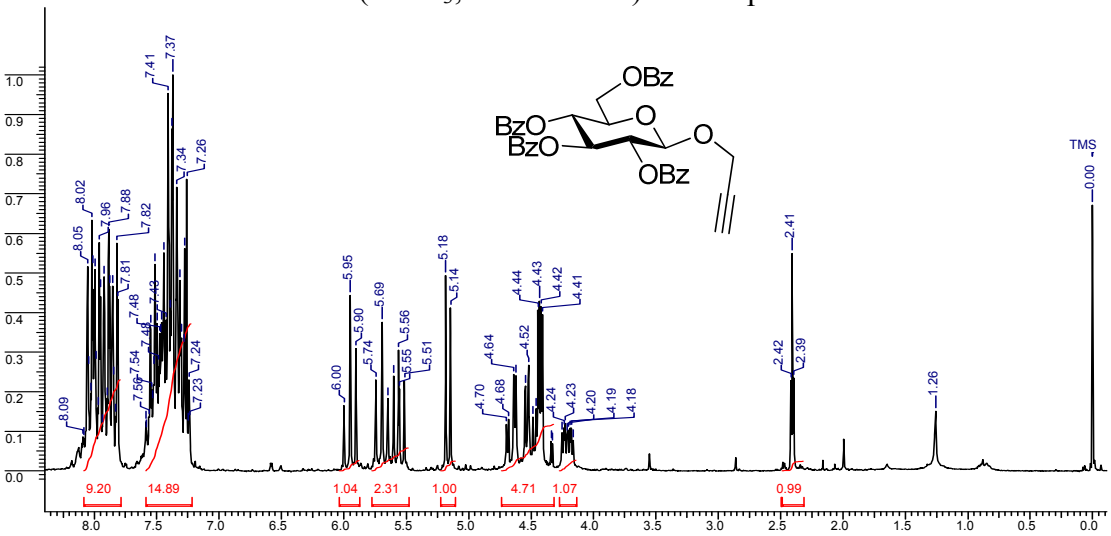
^{13}CNMR ($CDCl_3$, 50.32 MHz) of Compound **20**



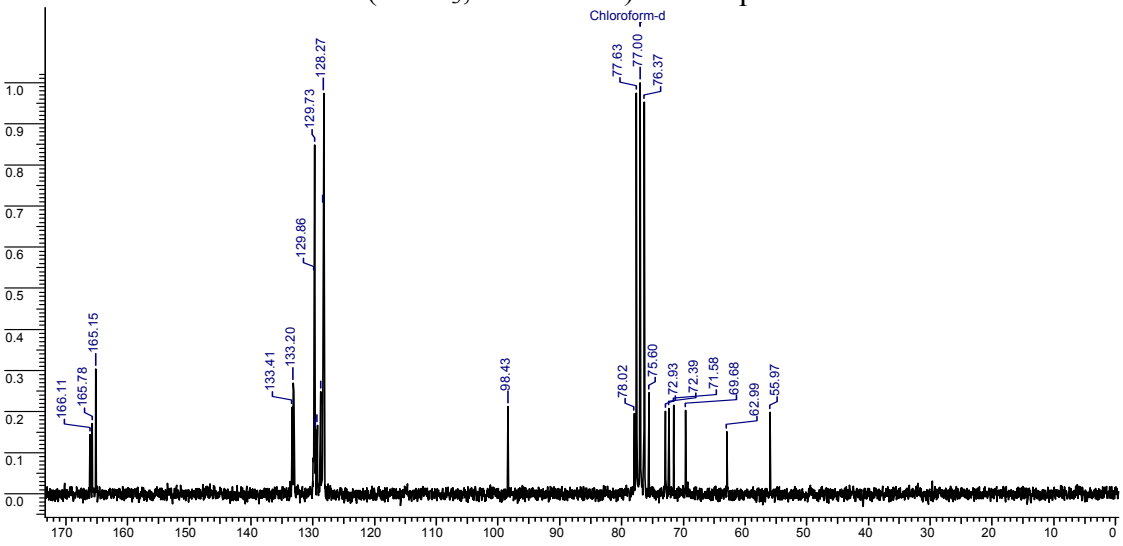
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **20**



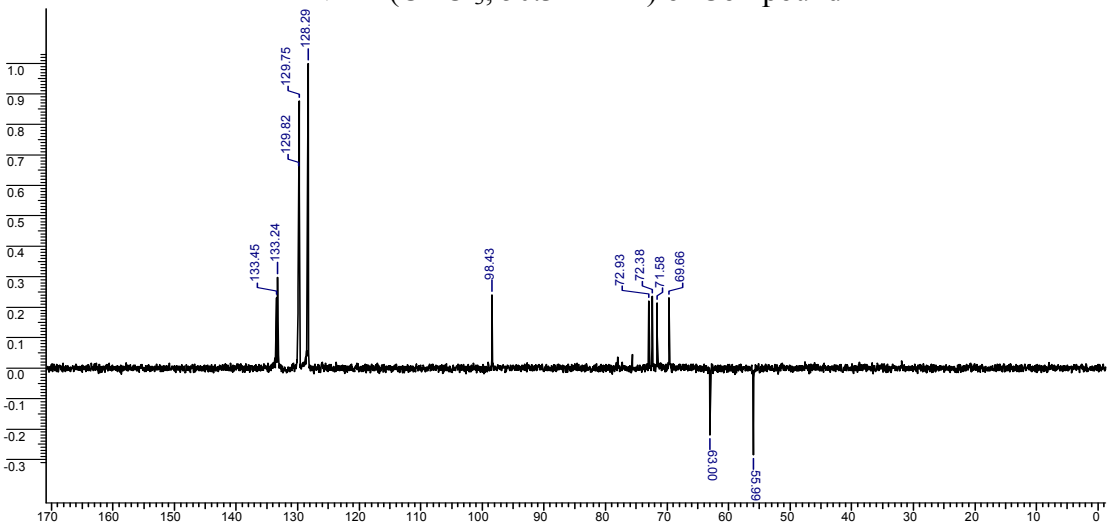
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **21**



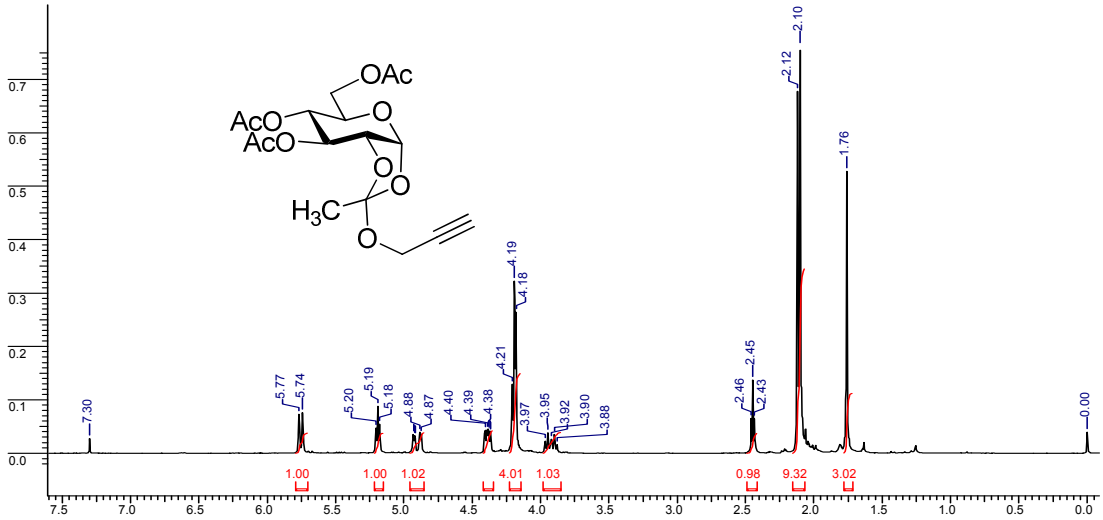
^{13}CNMR ($CDCl_3$, 50.32 MHz) of Compound **21**



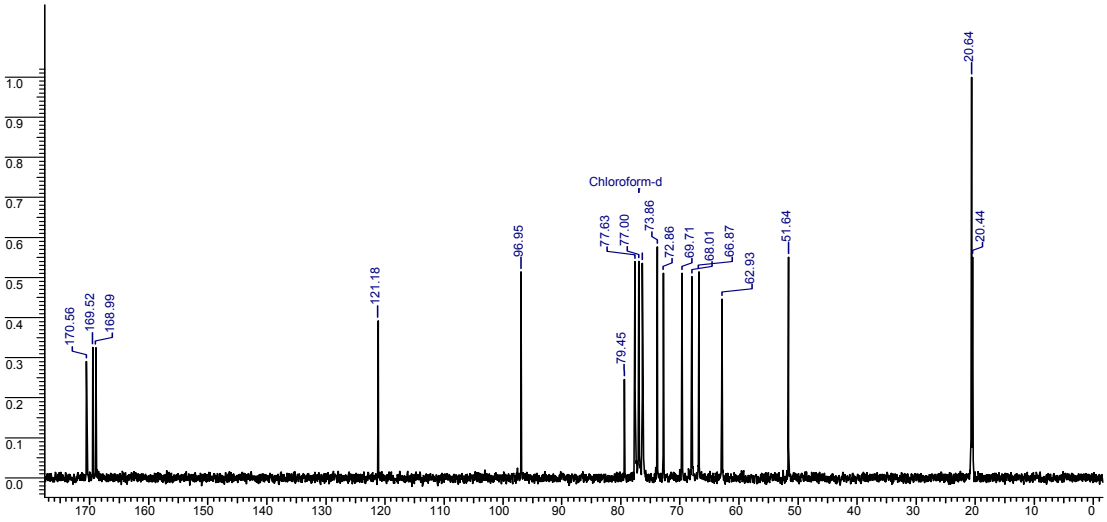
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **21**



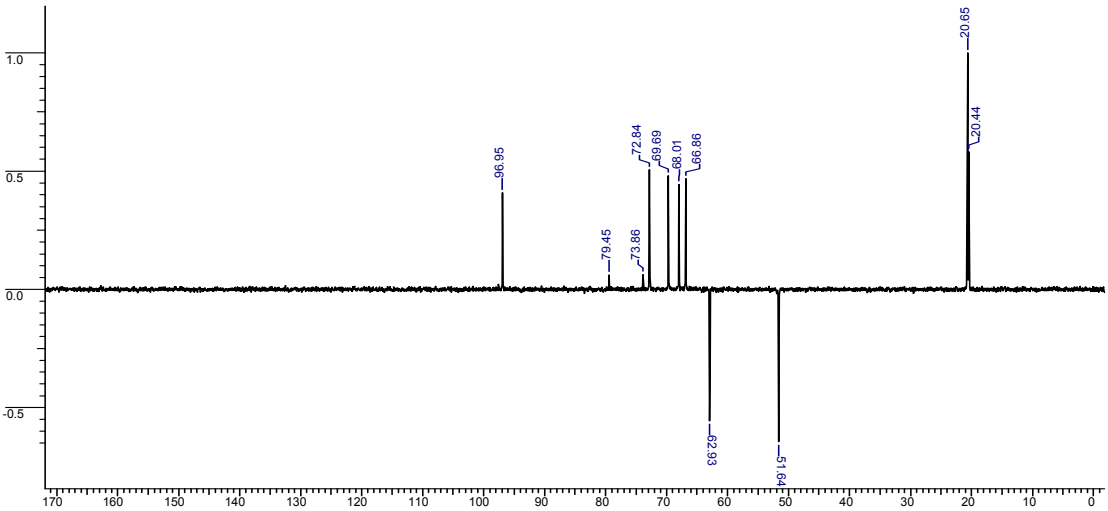
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **22**



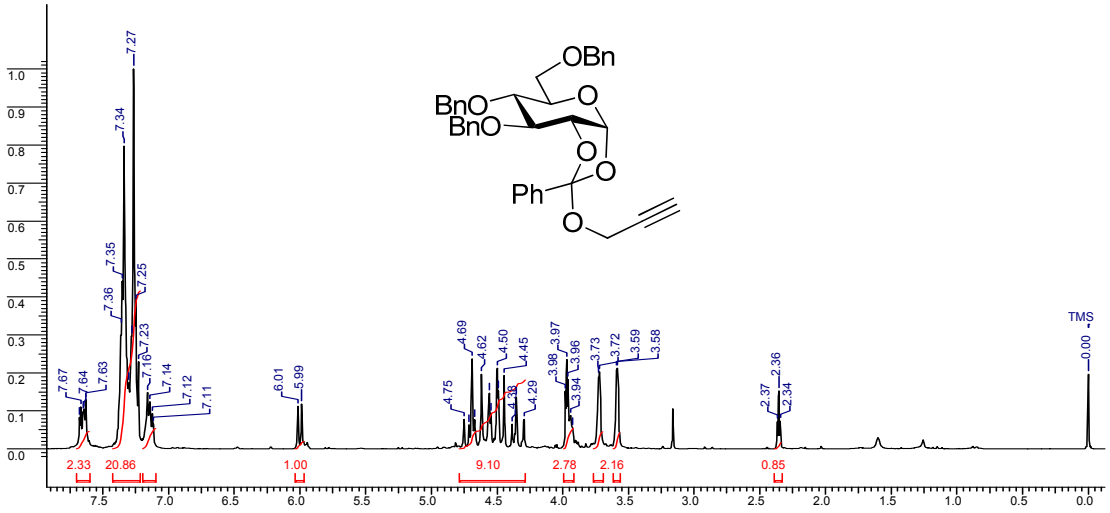
^{13}CNMR ($CDCl_3$, 50.32 MHz) of Compound **22**



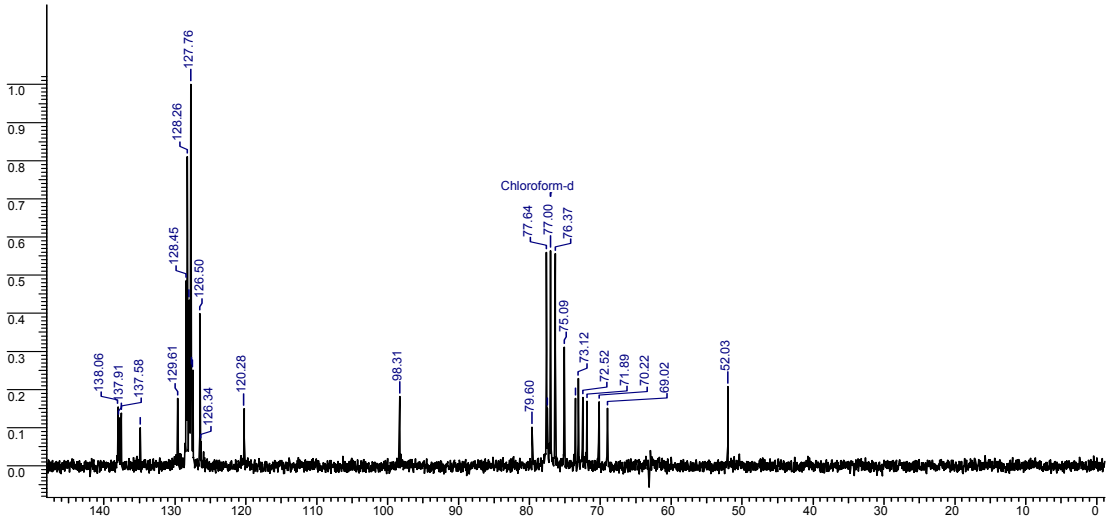
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **22**



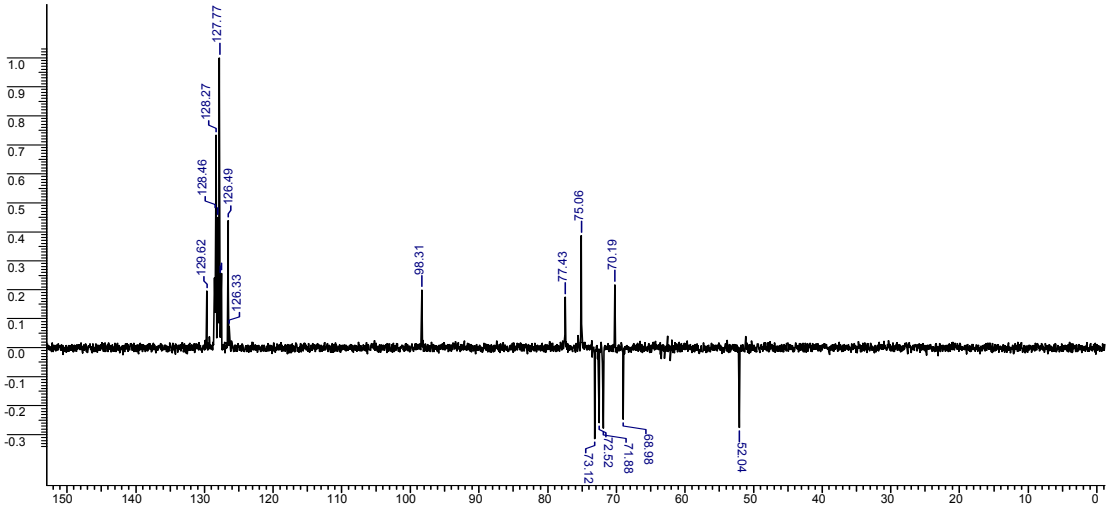
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **24**



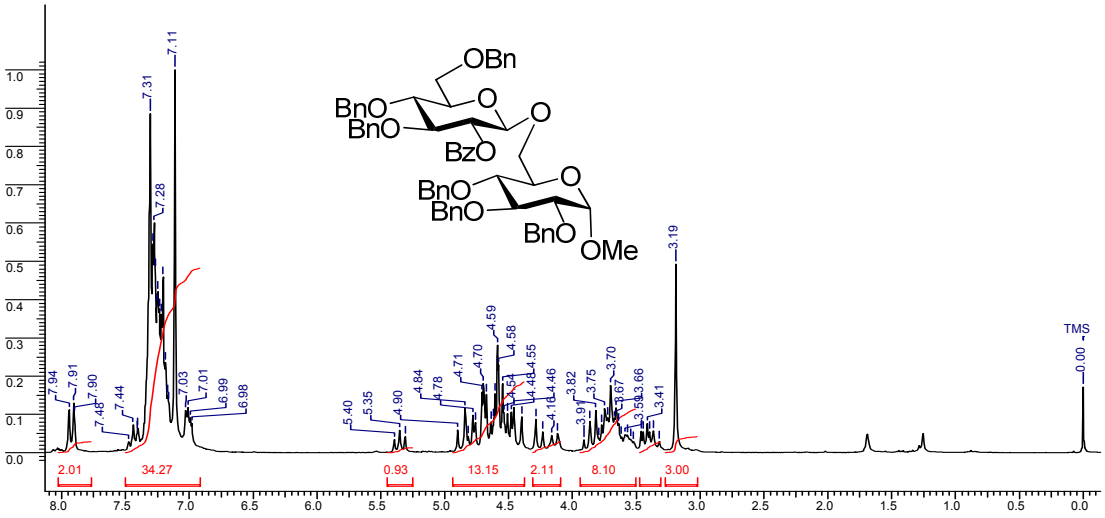
^{13}CNMR ($CDCl_3$, 50.32 MHz) of Compound **24**



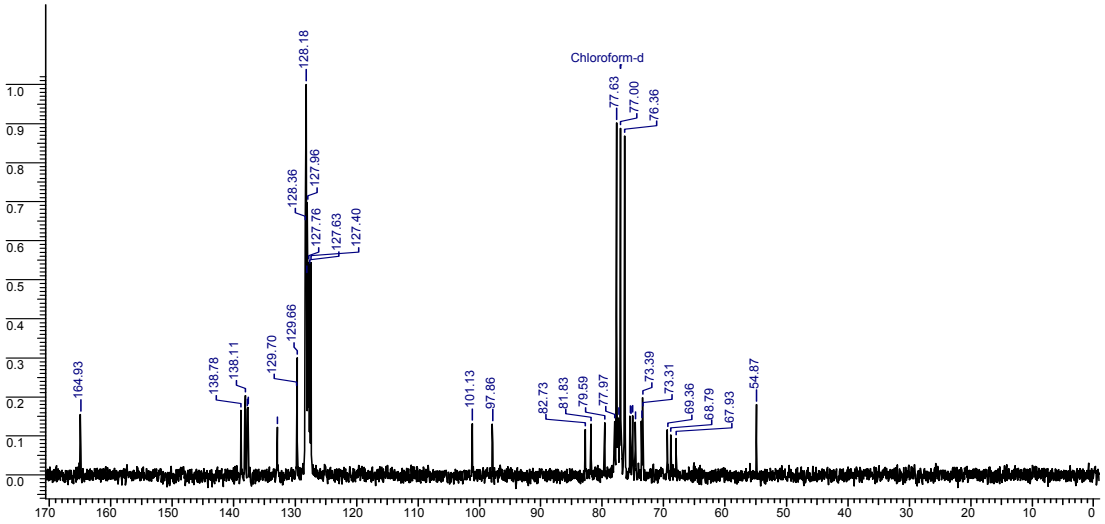
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **24**



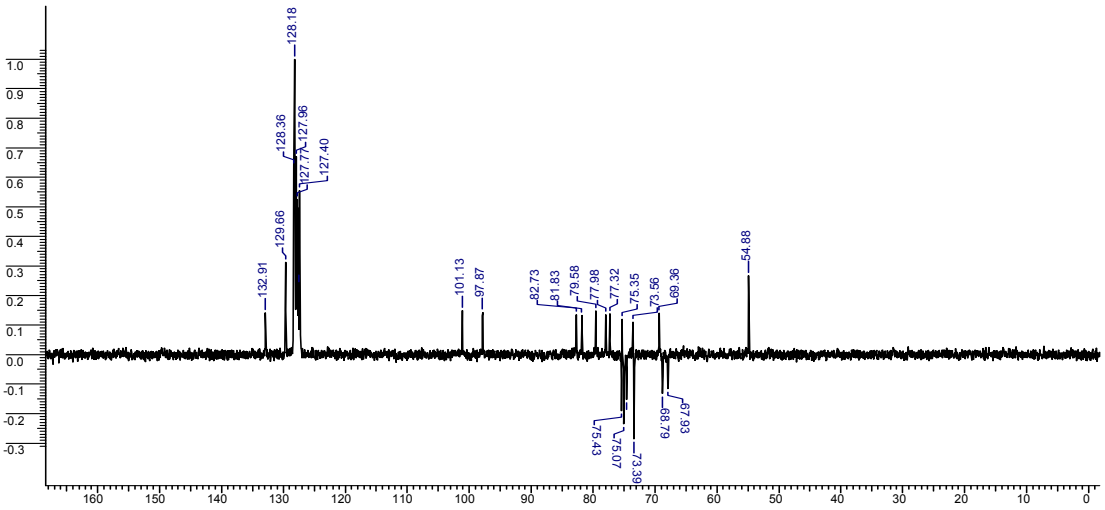
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **25**



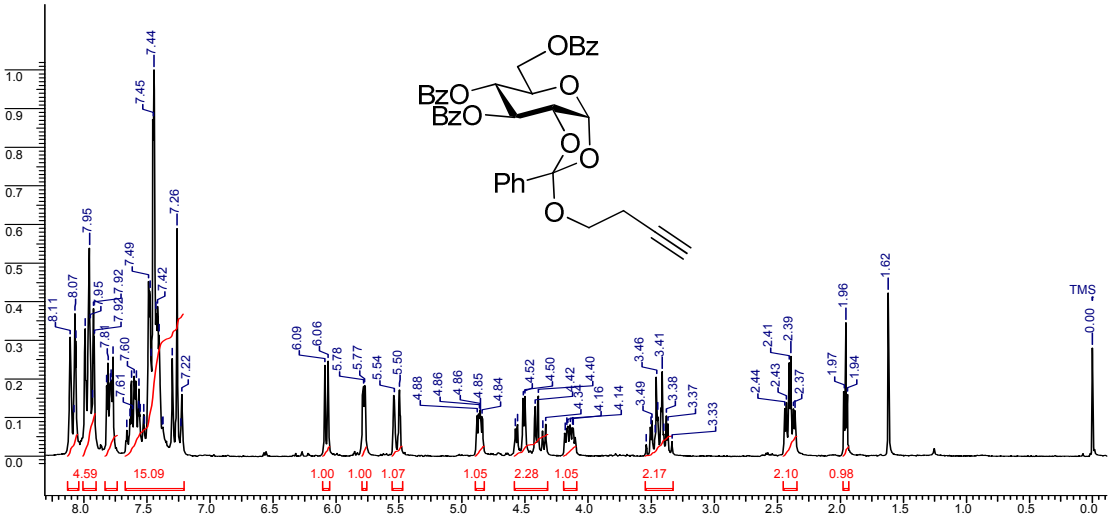
^{13}CNMR ($CDCl_3$, 50.32 MHz) of Compound **25**



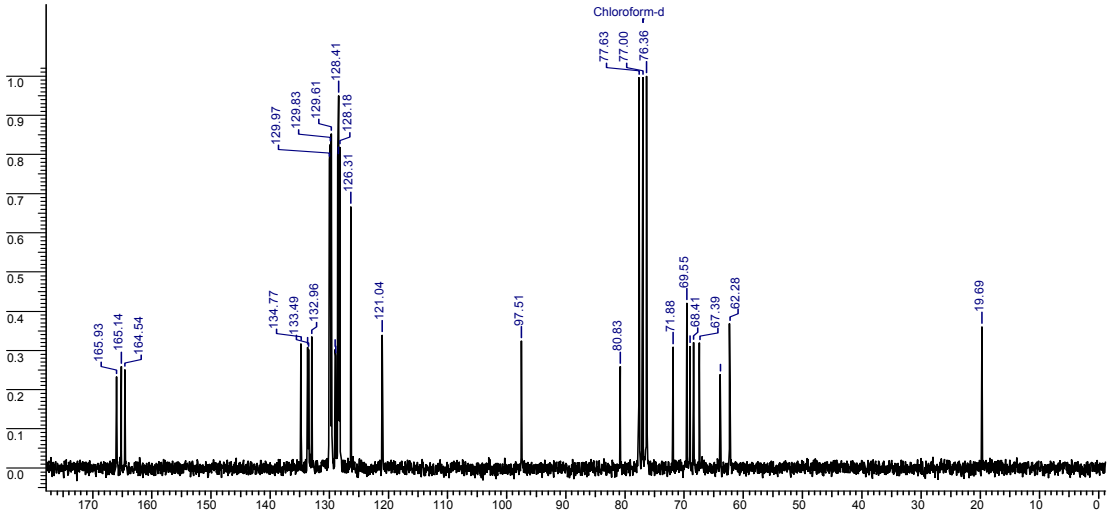
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **25**



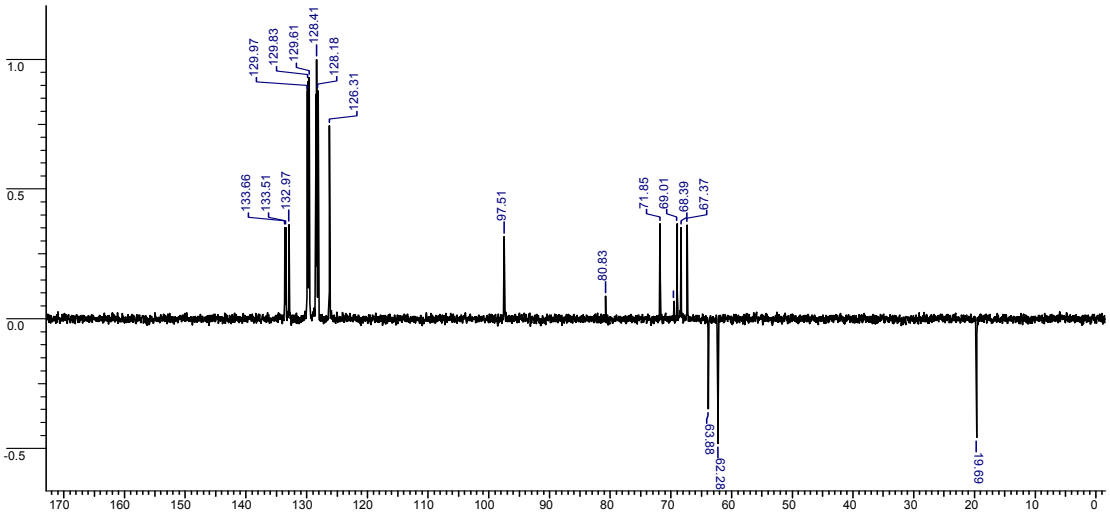
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **26**



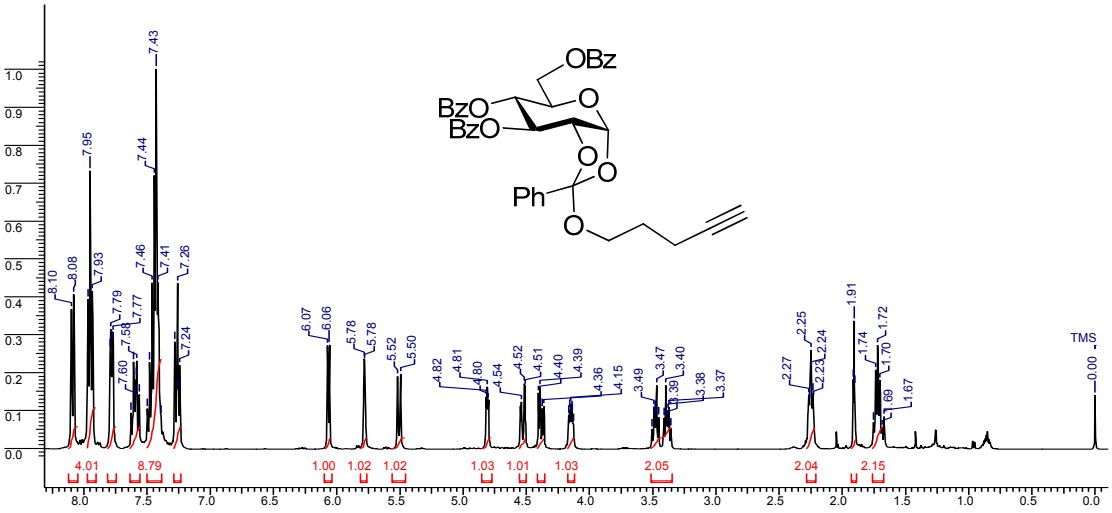
^{13}CNMR ($CDCl_3$, 50.32 MHz) of Compound **26**



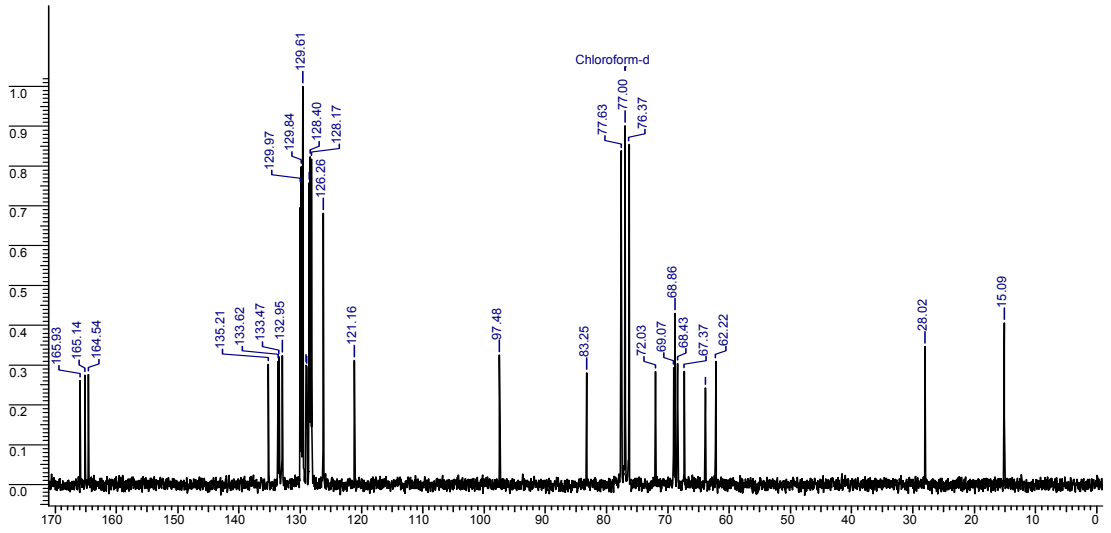
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **26**



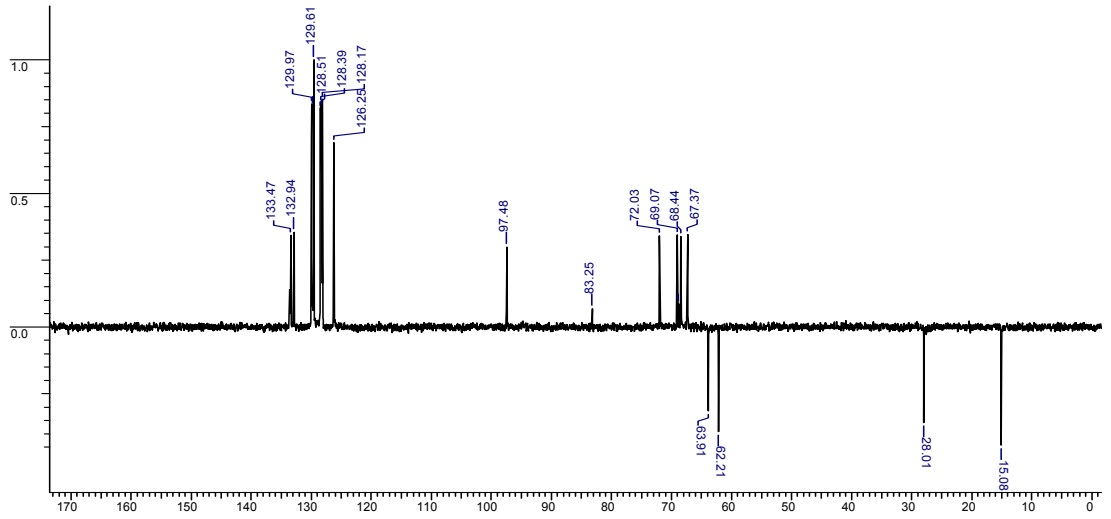
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **27**



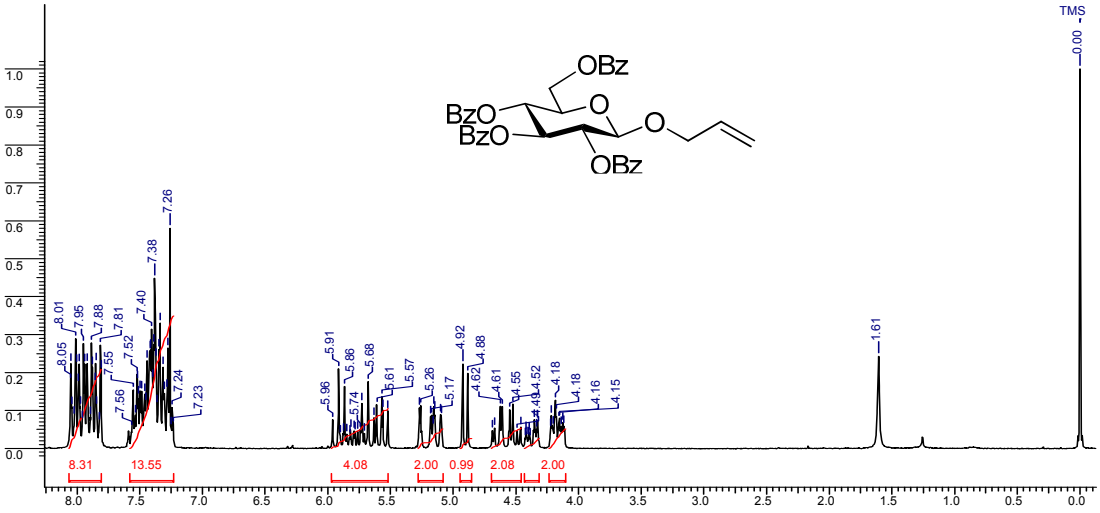
^{13}CNMR ($CDCl_3$, 50.32 MHz) of Compound **27**



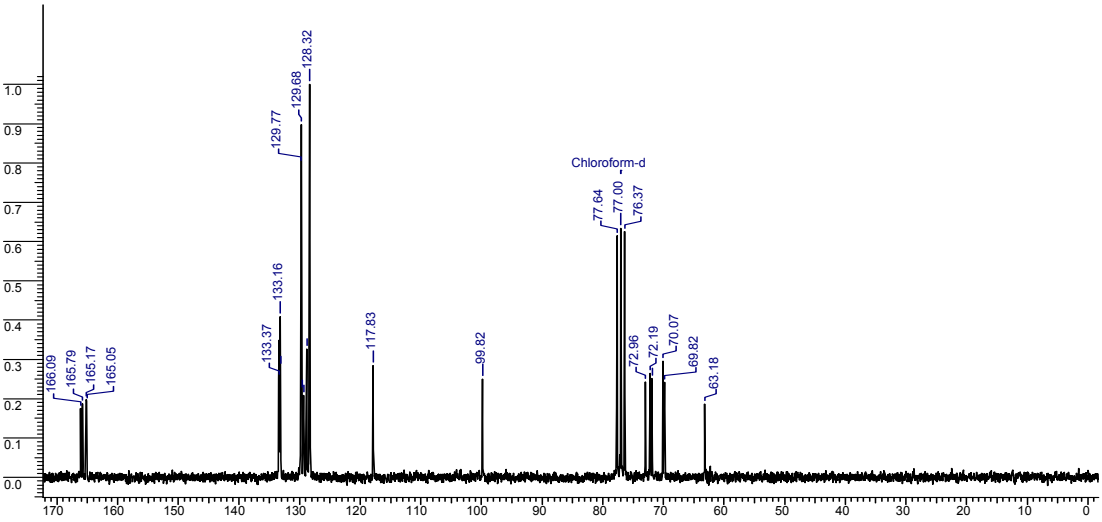
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **27**



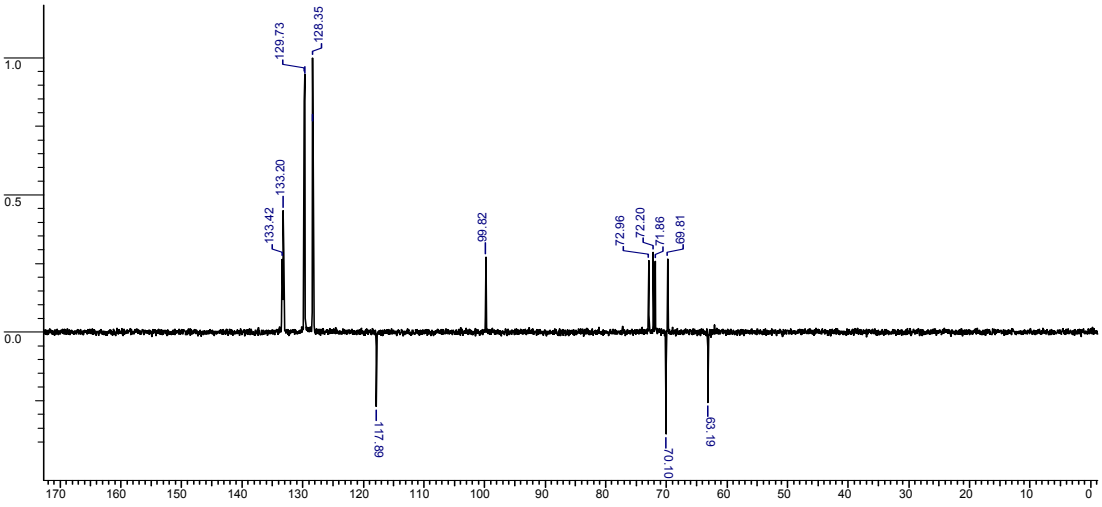
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **29**



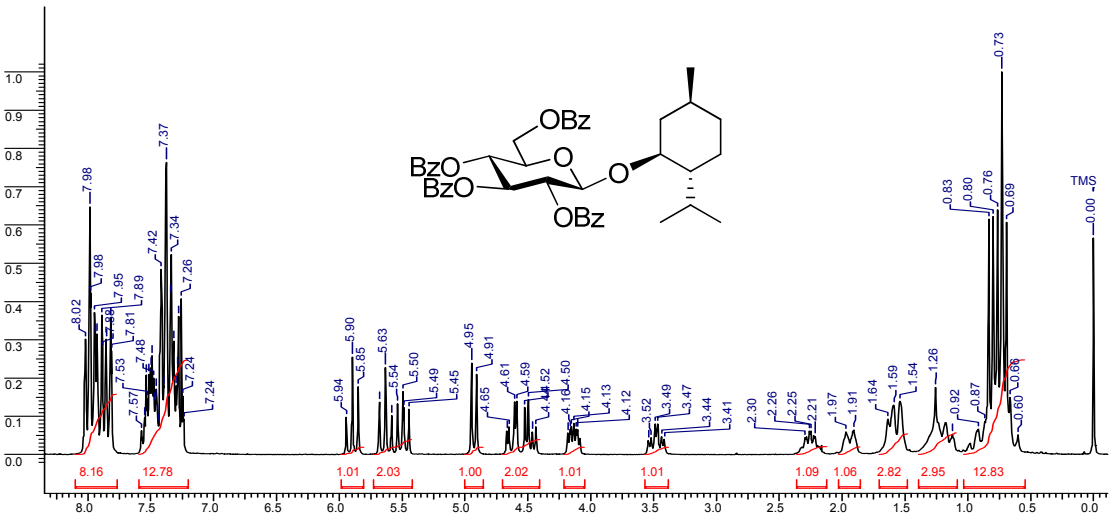
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **29**



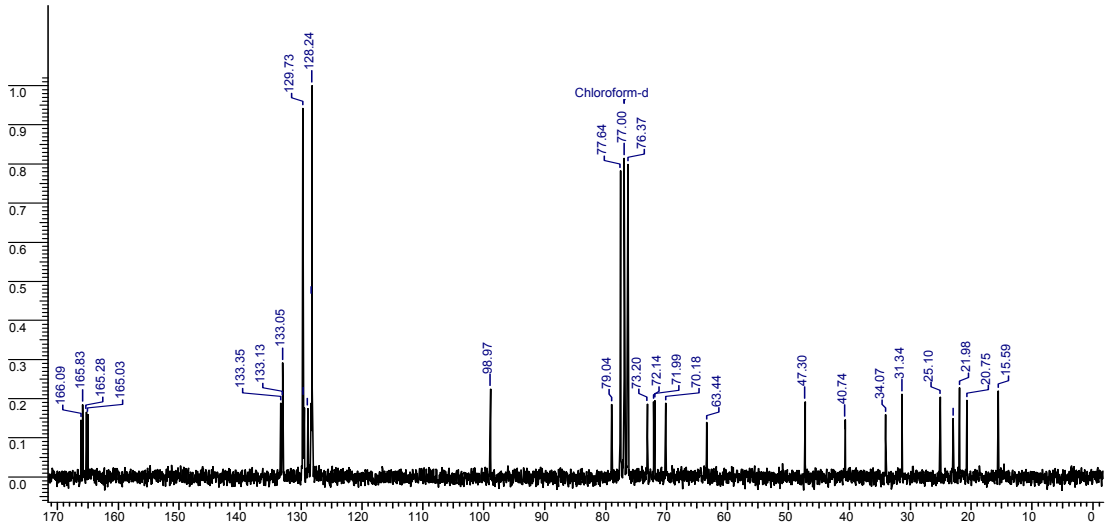
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **29**



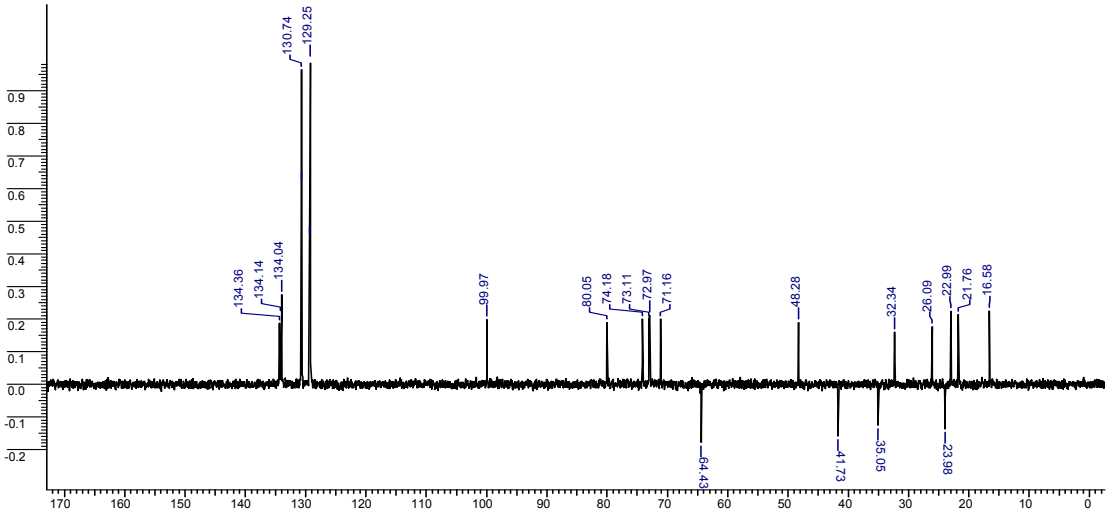
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **30**



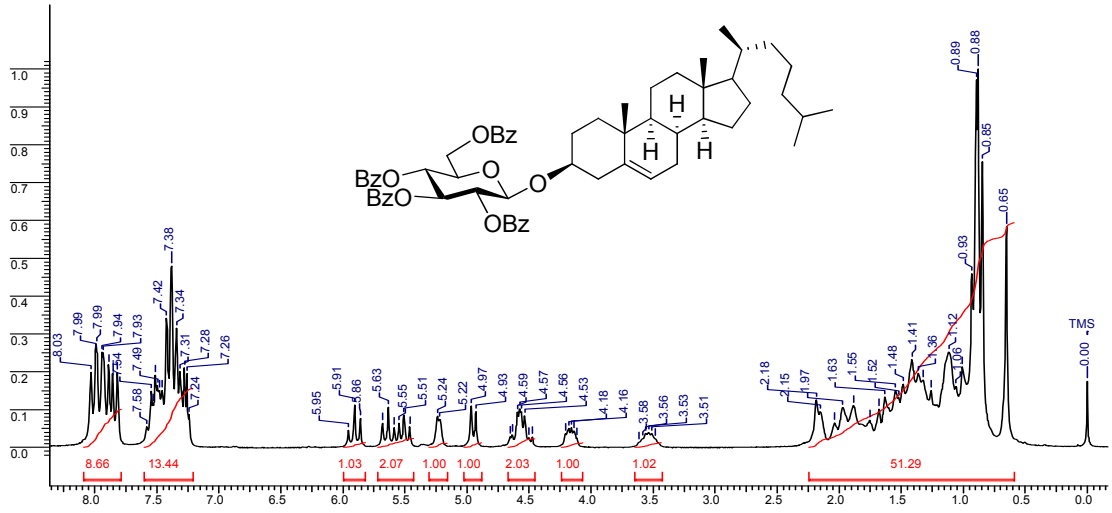
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **30**



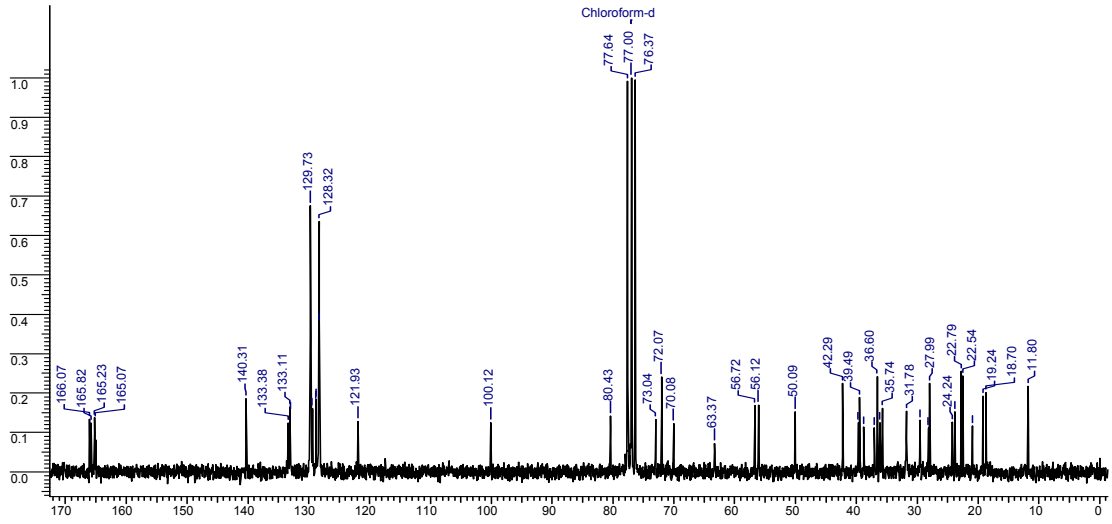
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **30**



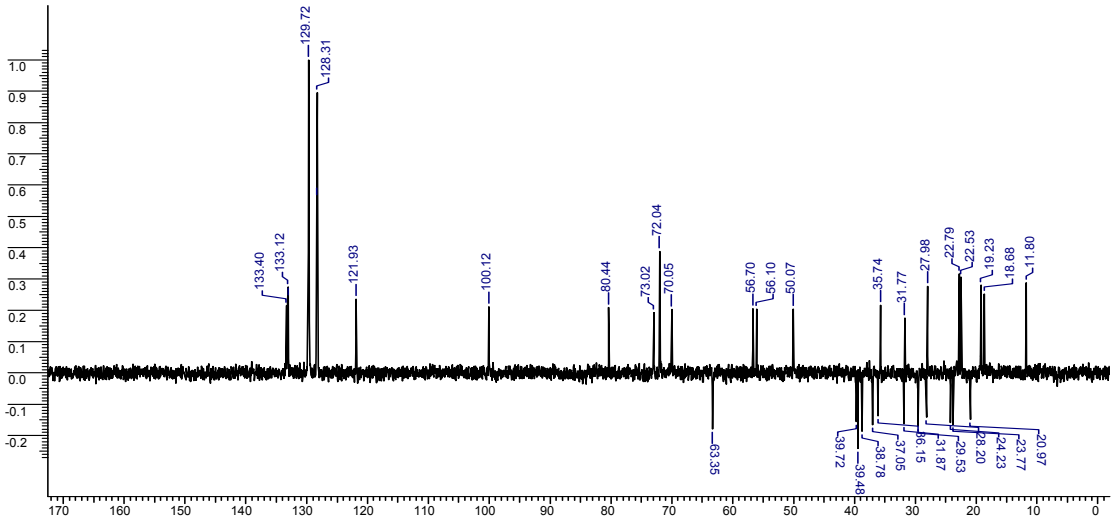
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **32**



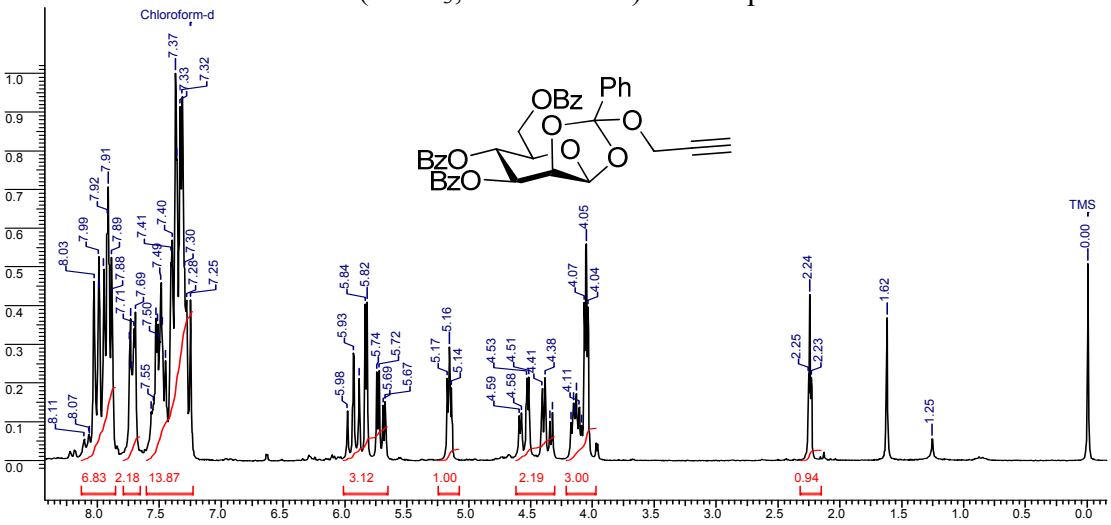
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **32**



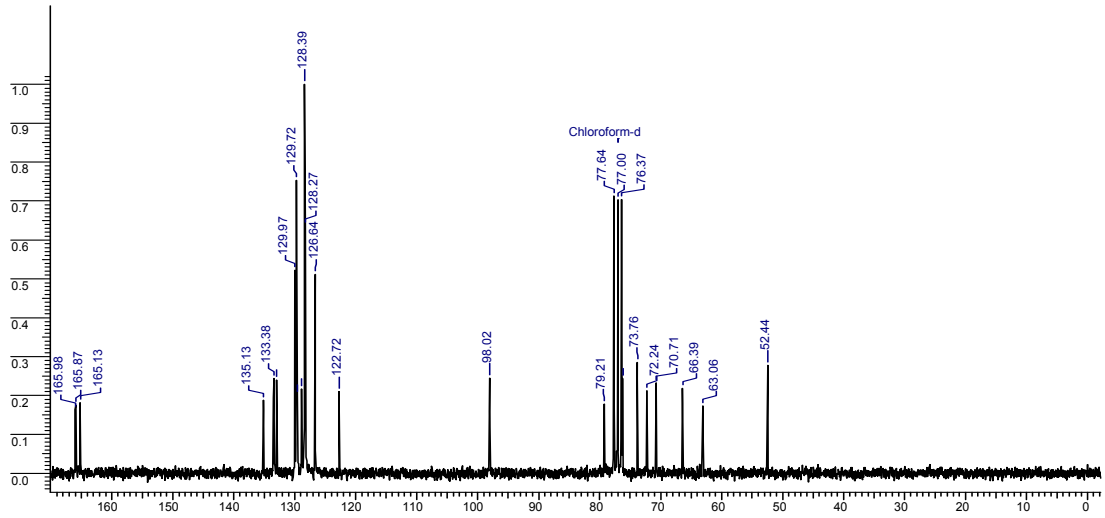
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **32**



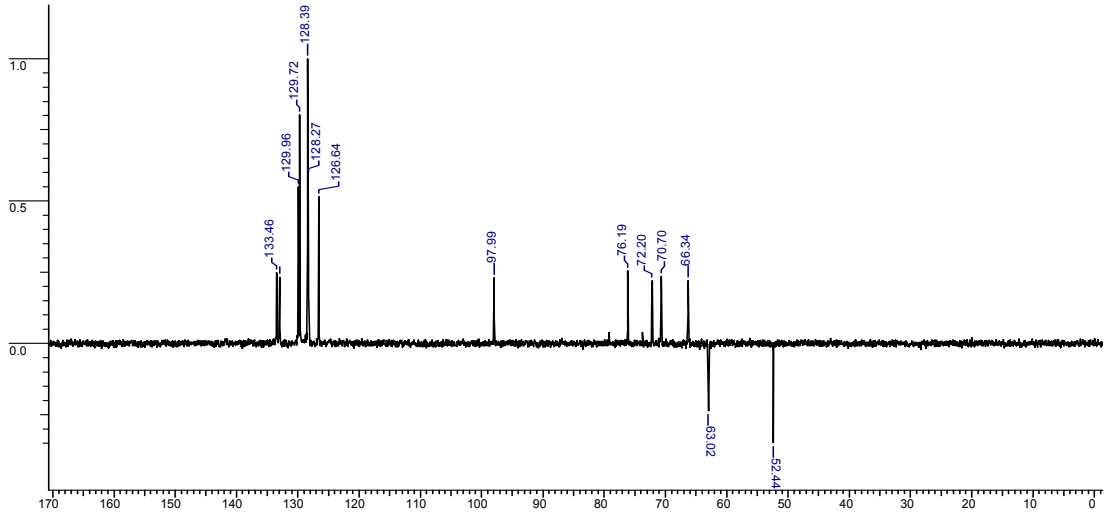
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **33**



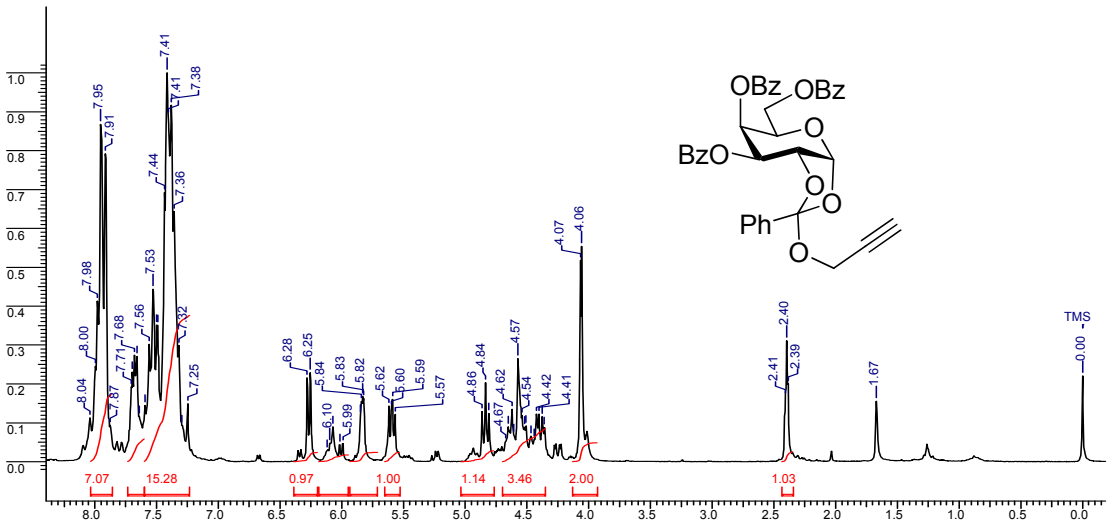
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **33**



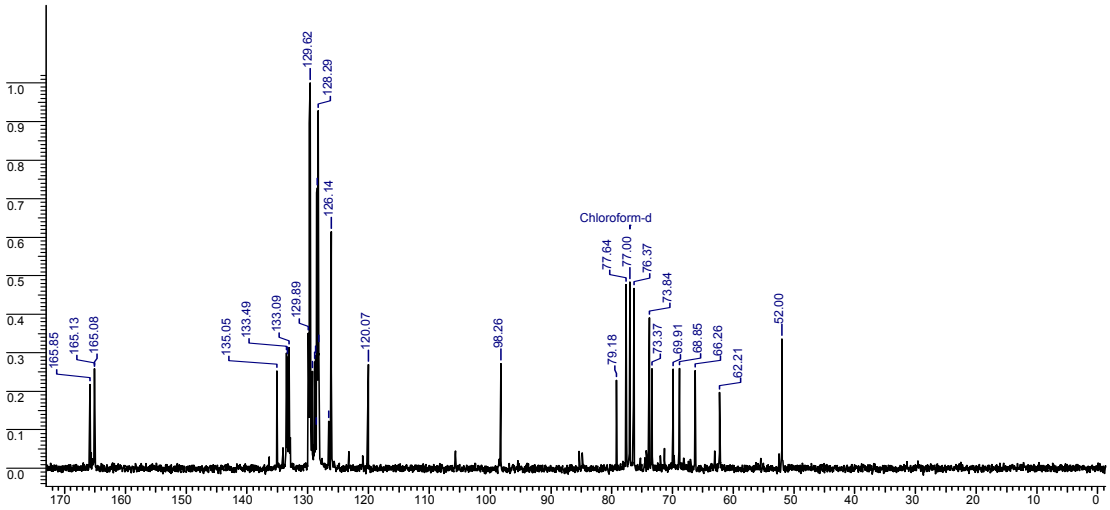
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **33**



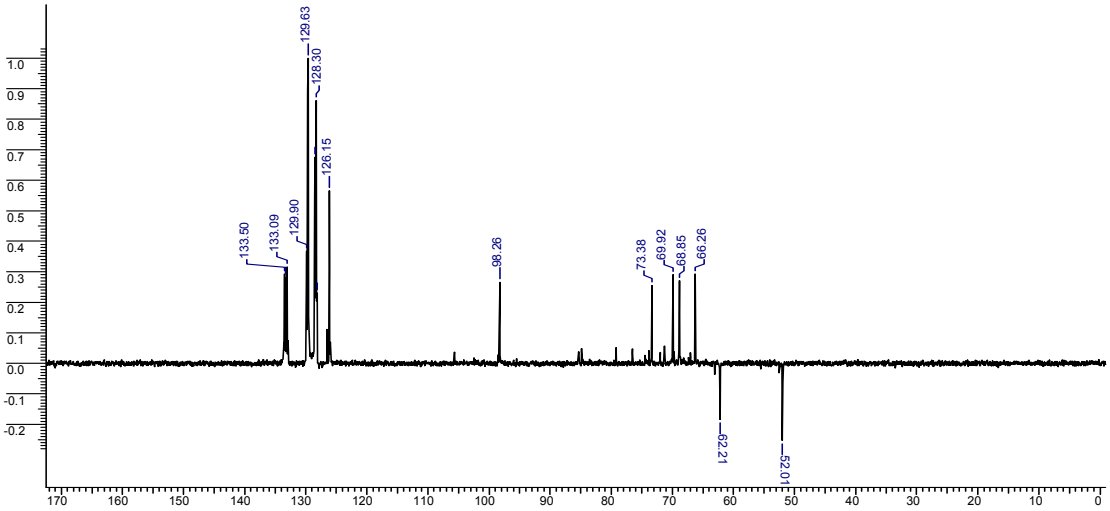
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **34**



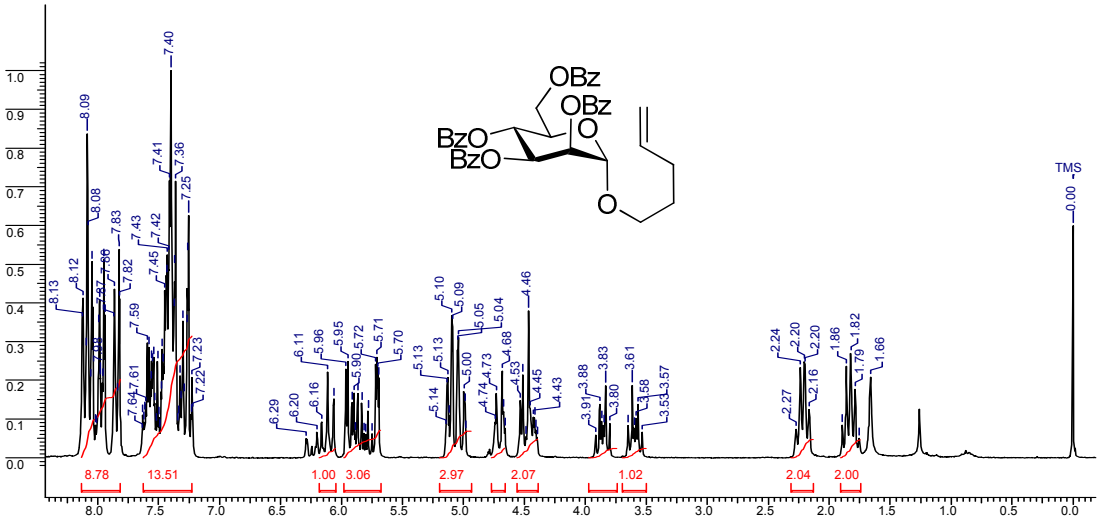
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **34**



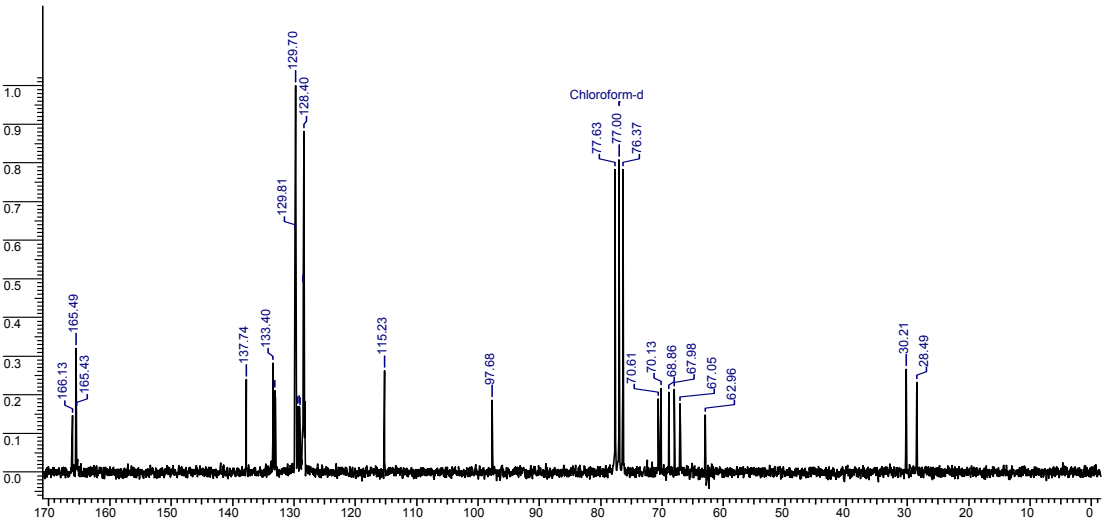
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **34**



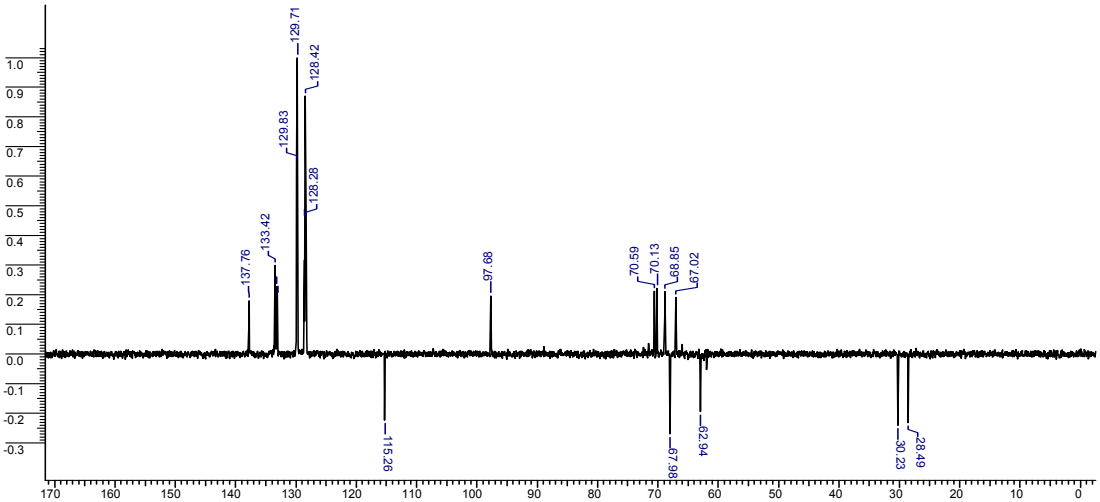
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **36**



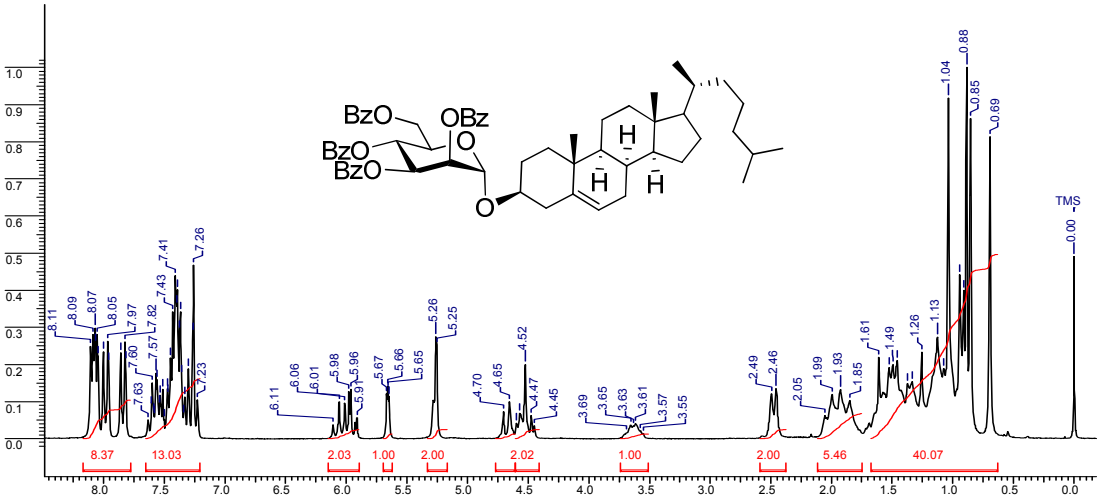
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **36**



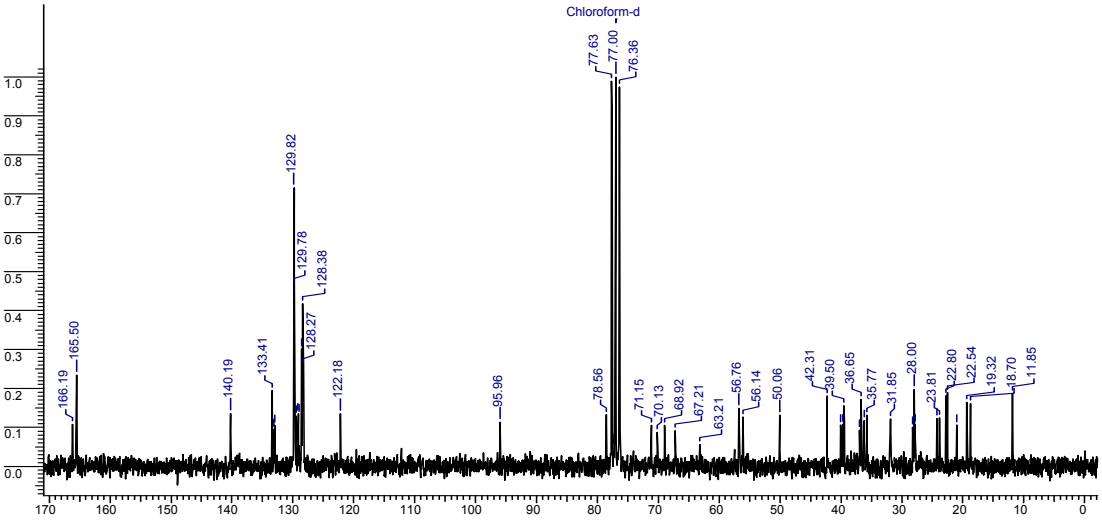
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **36**



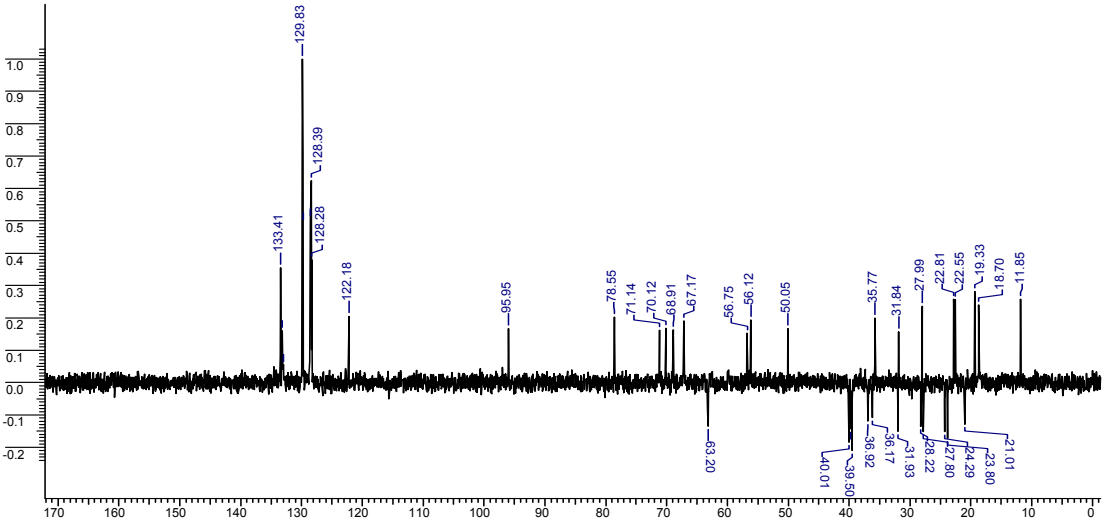
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **37**



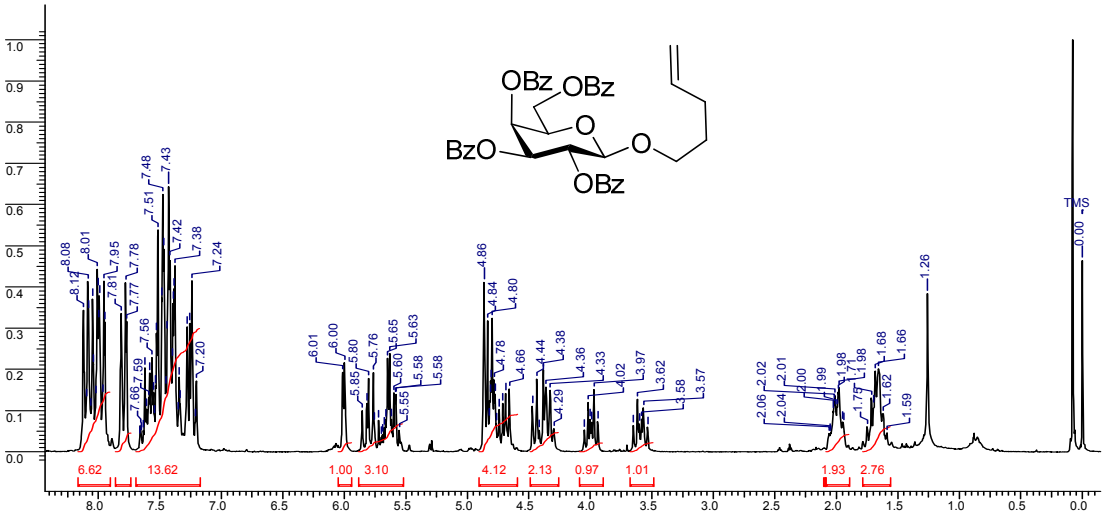
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **37**



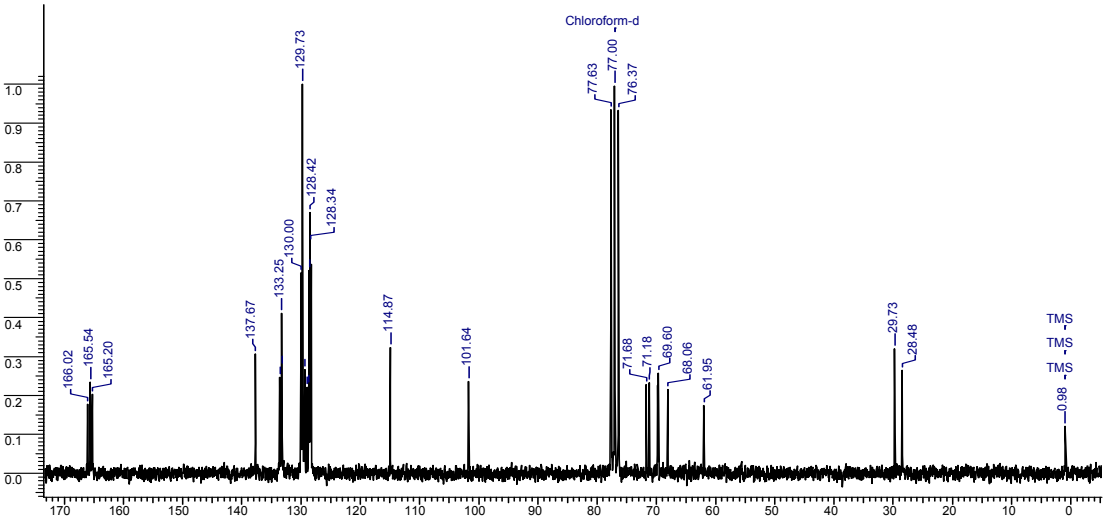
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **37**



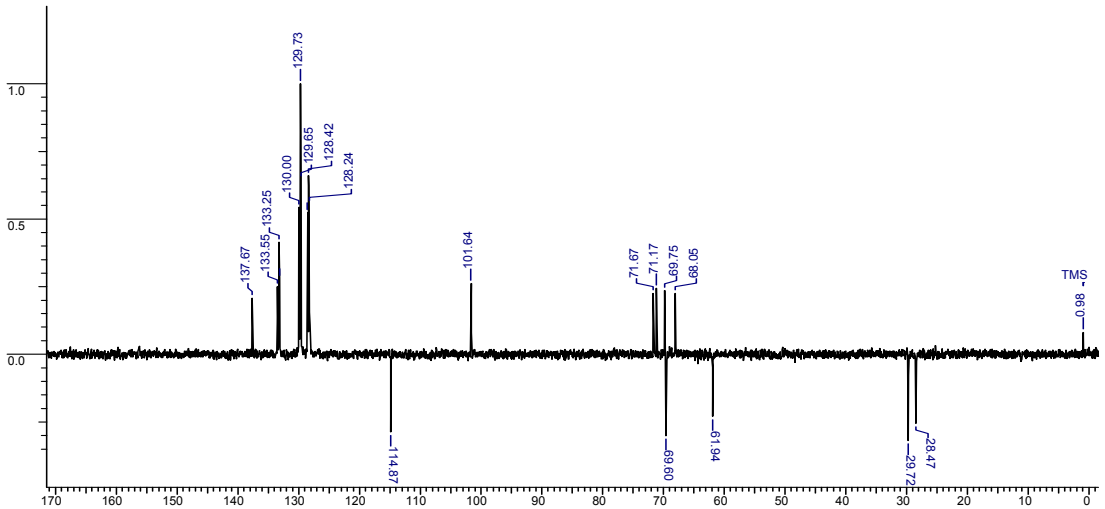
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **38**



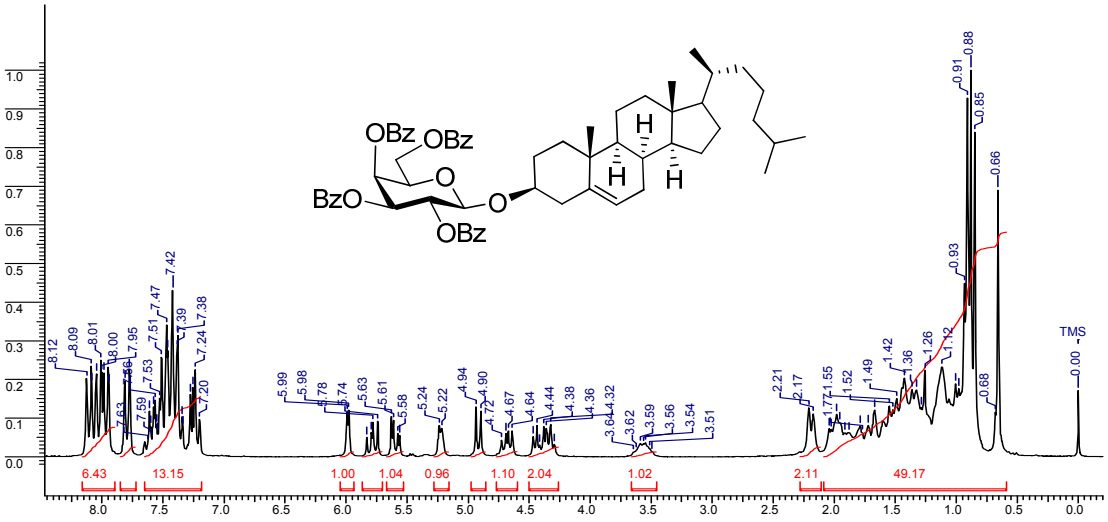
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **38**



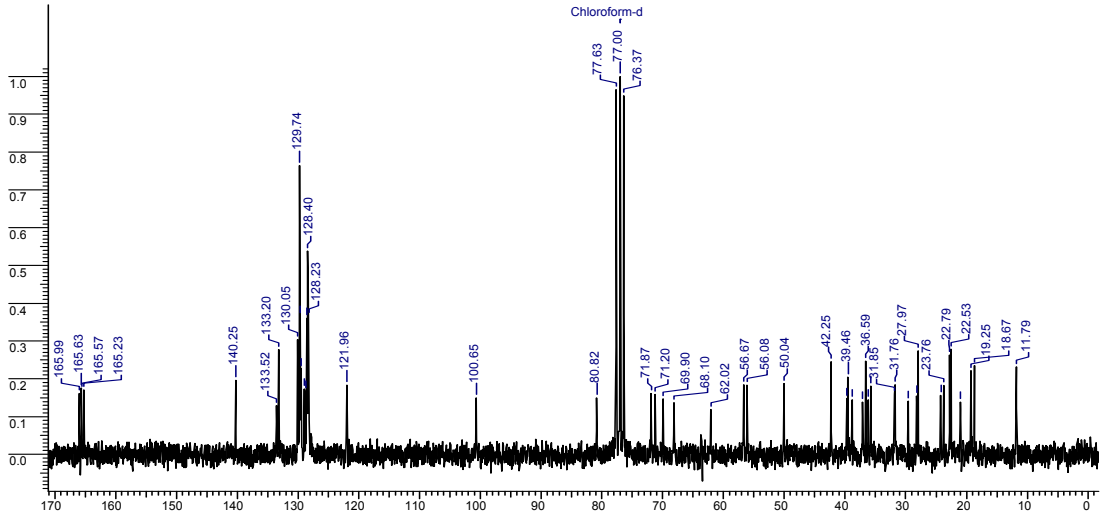
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **38**



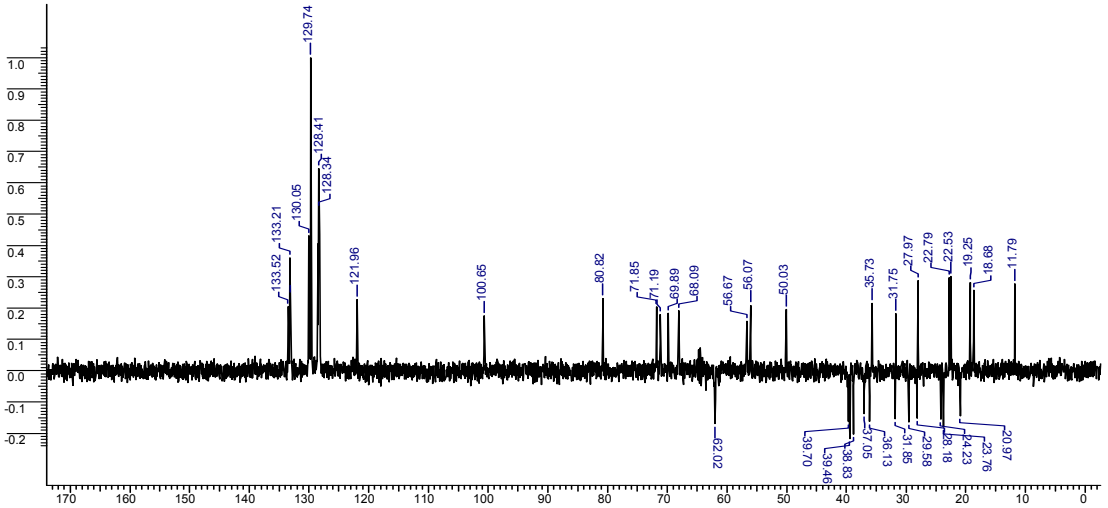
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **39**



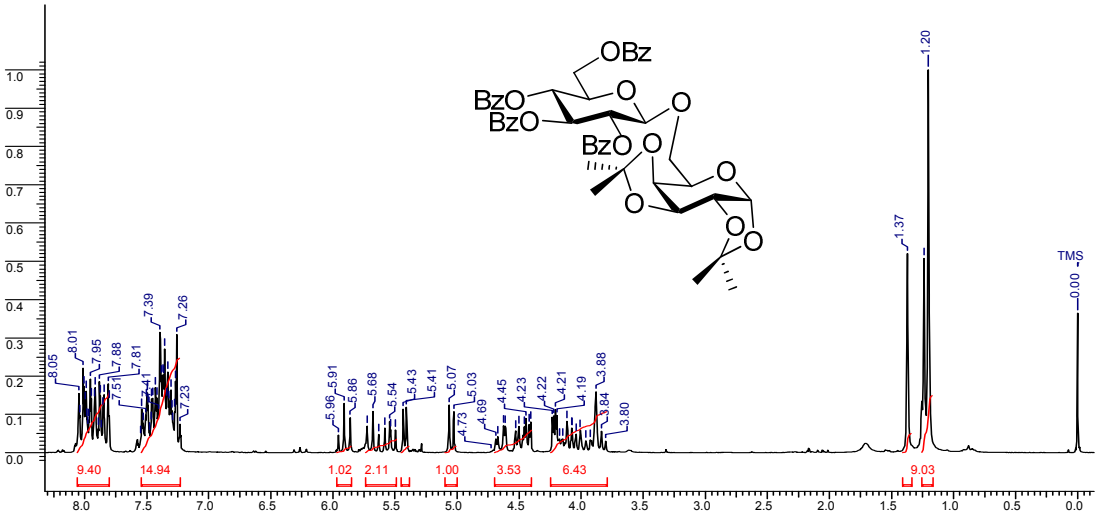
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **39**



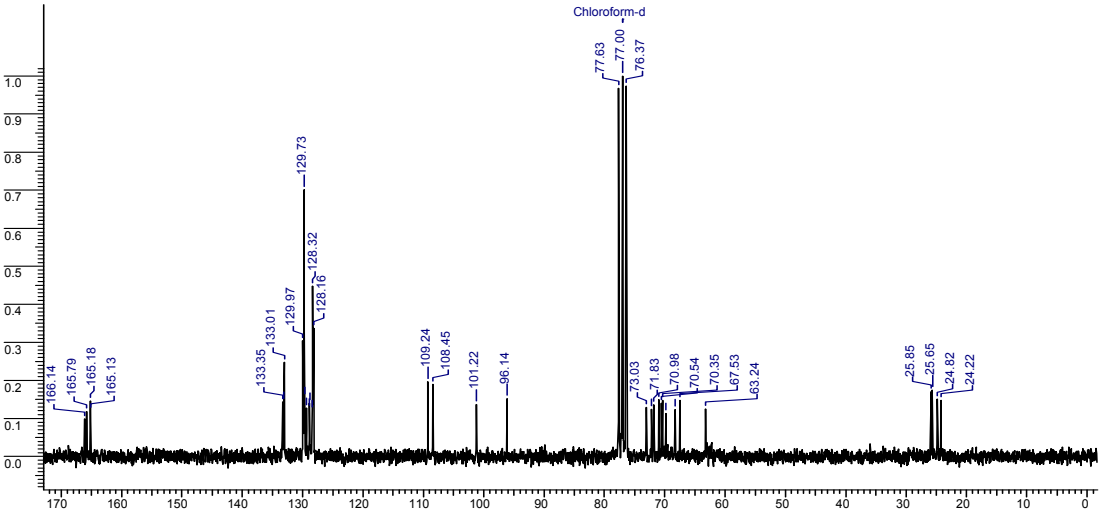
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **39**



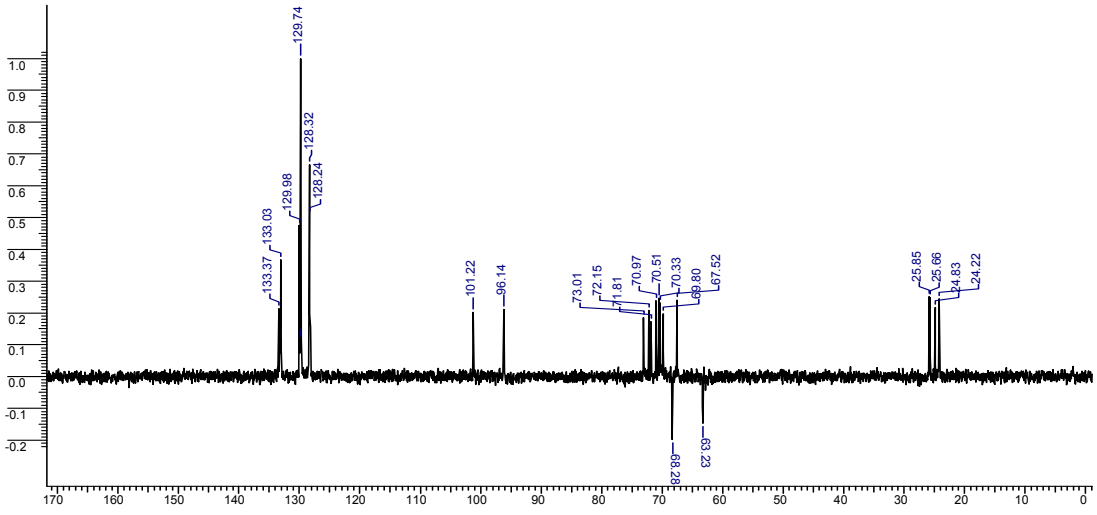
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **41**



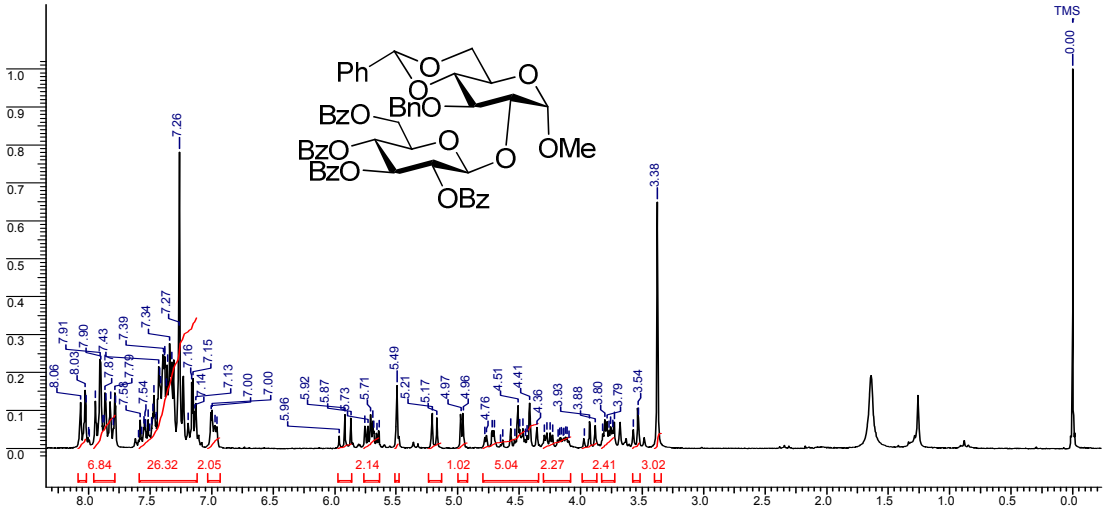
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **41**



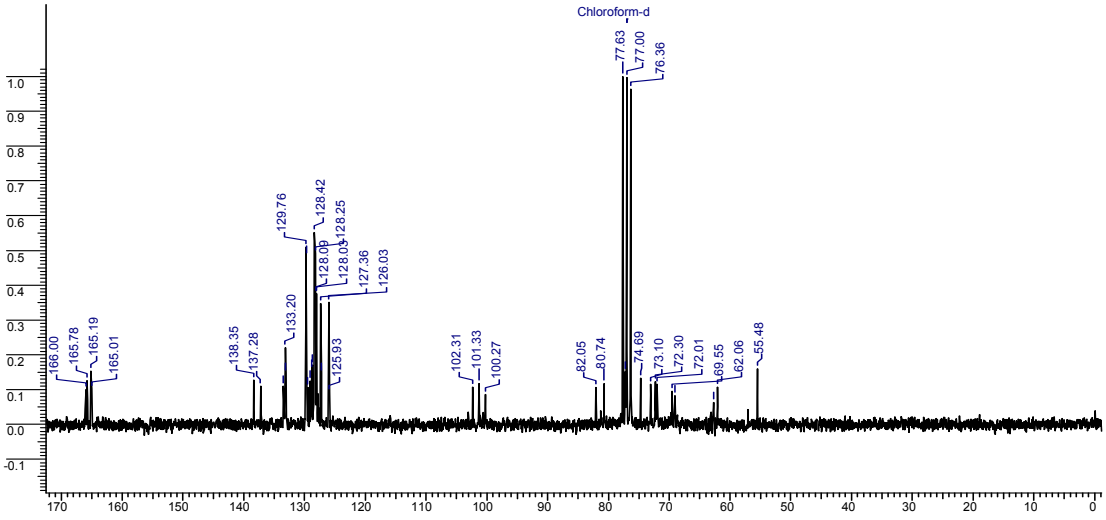
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **41**



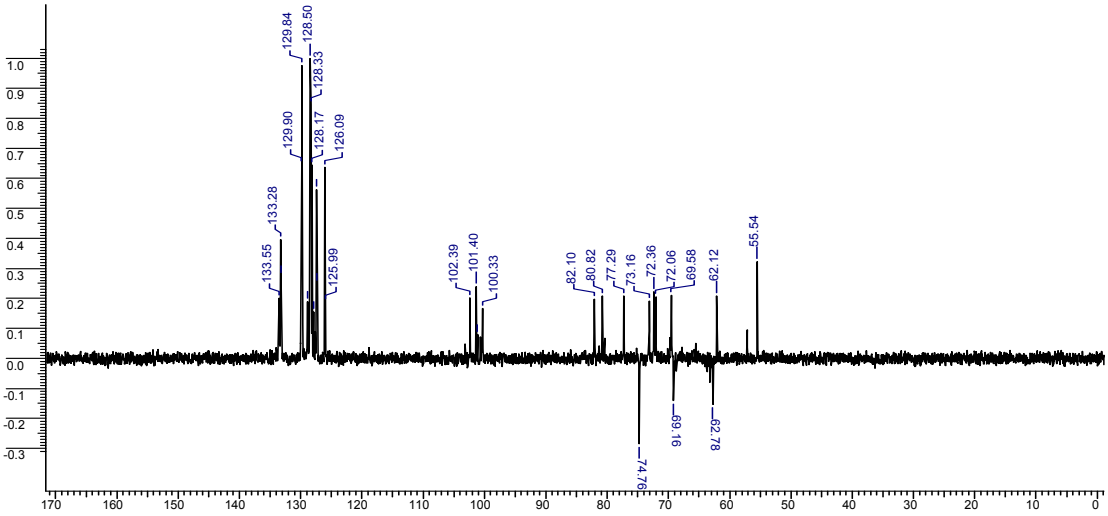
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **43**



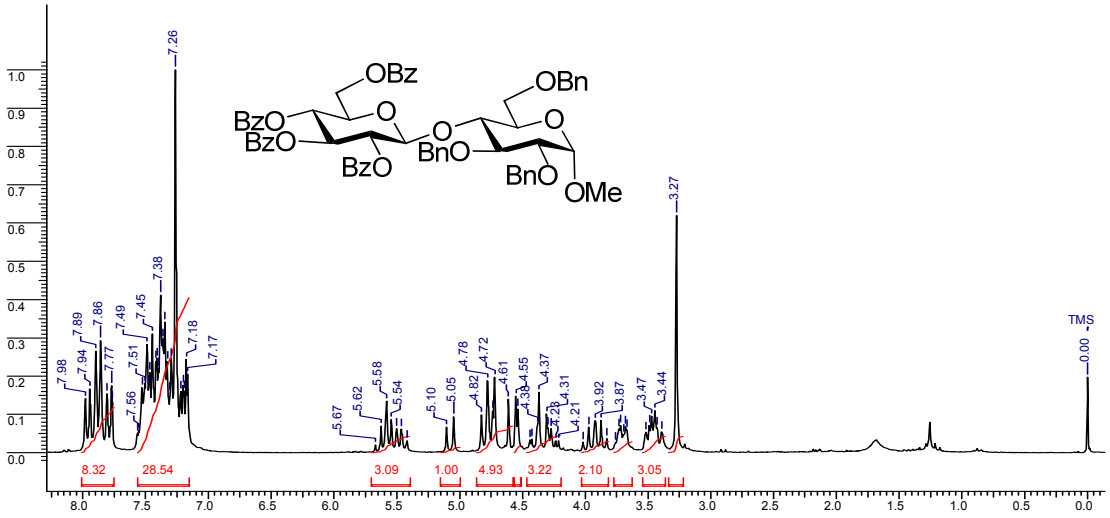
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **43**



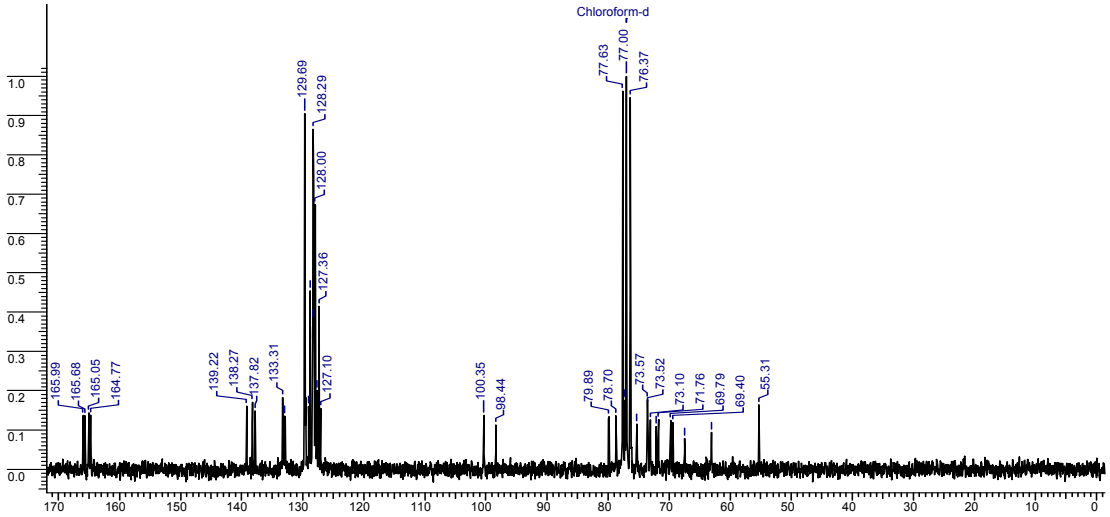
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **43**



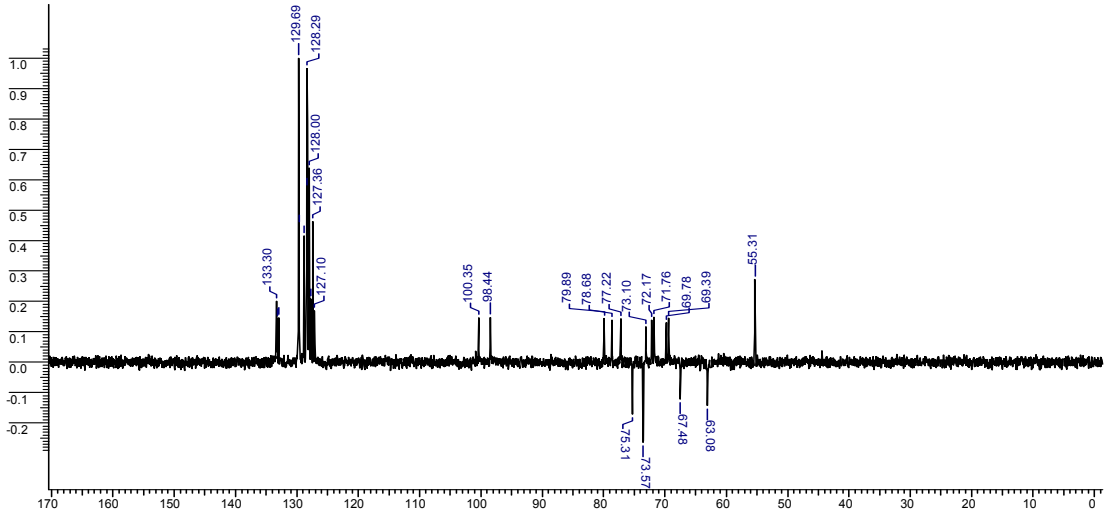
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **45**



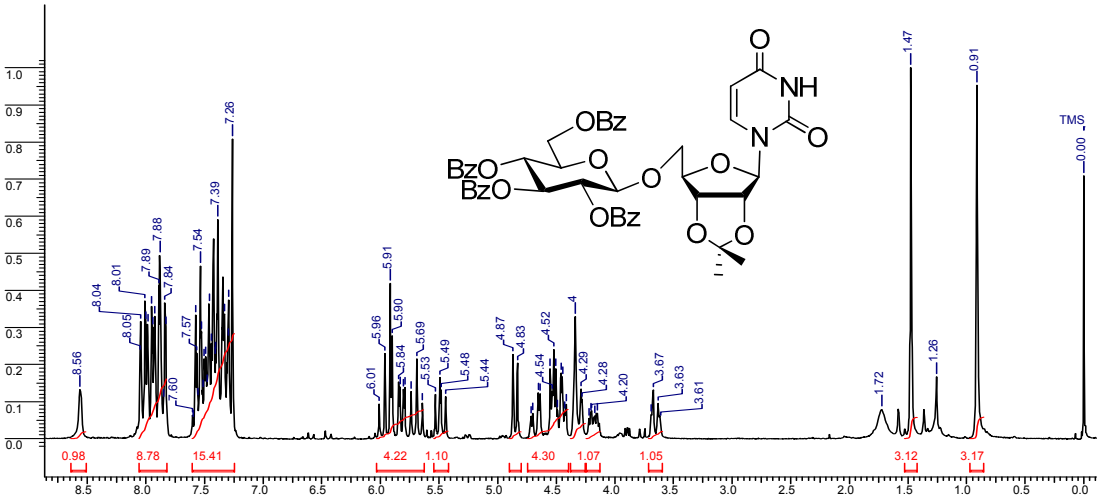
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **45**



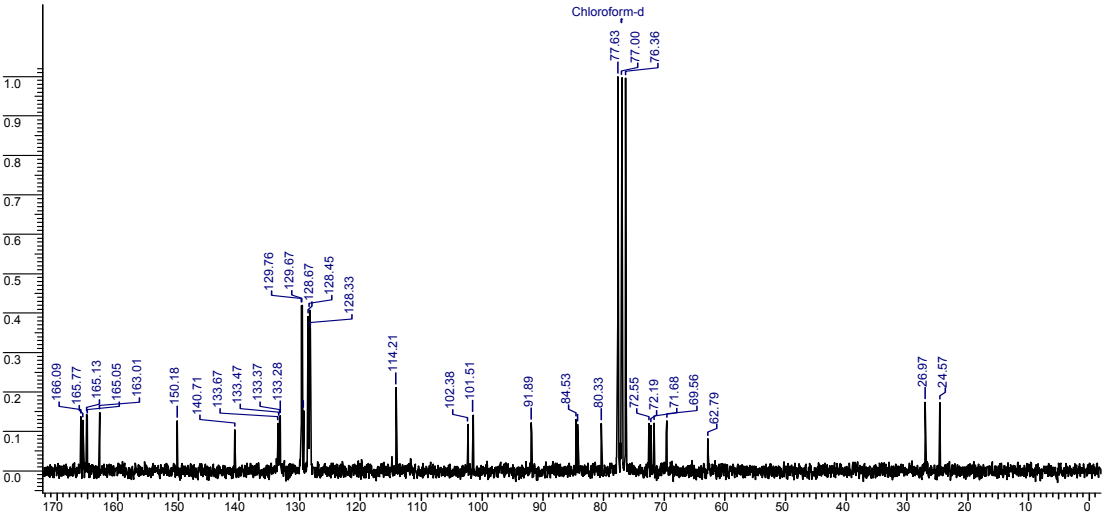
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **45**



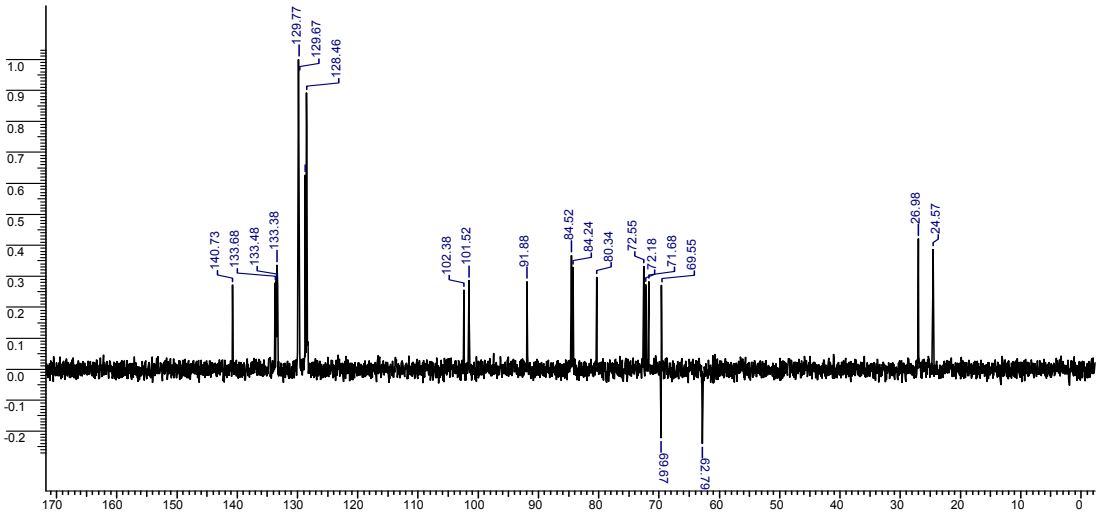
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **47**



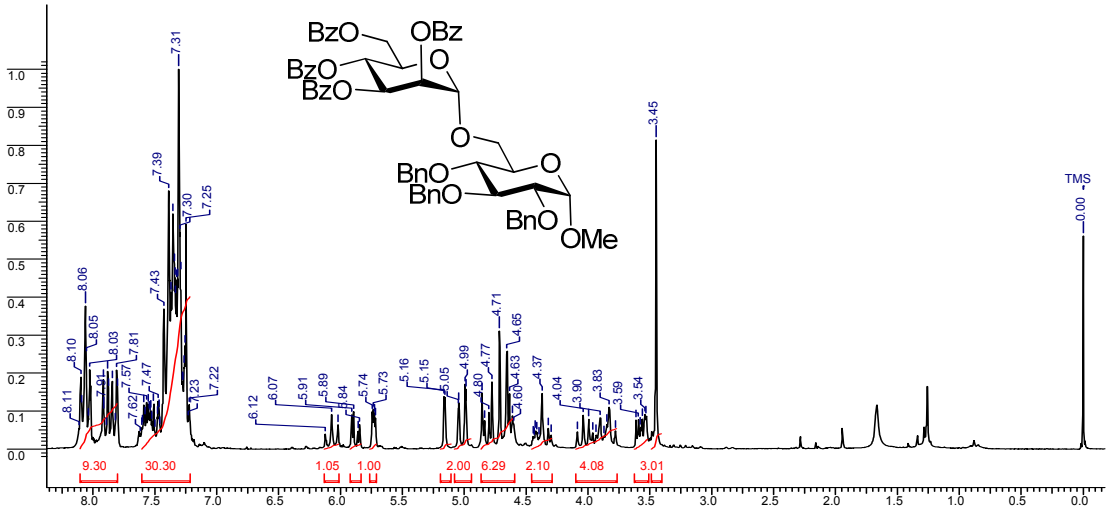
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **47**



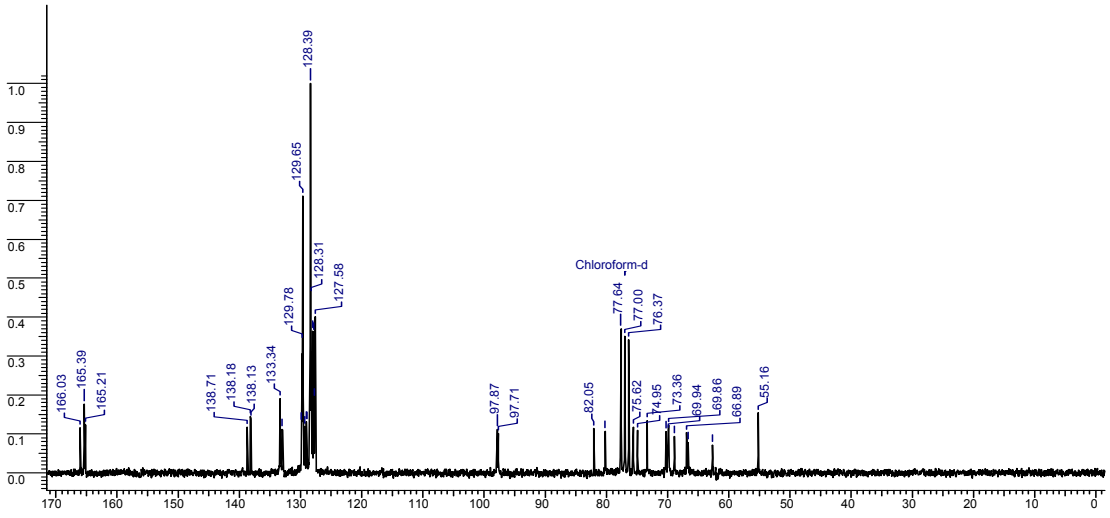
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **47**



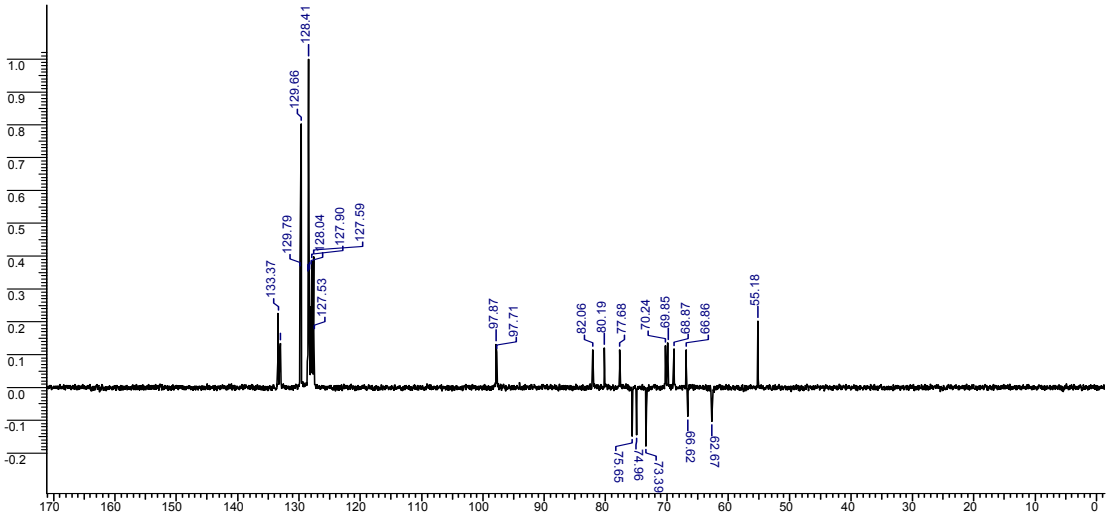
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **48**



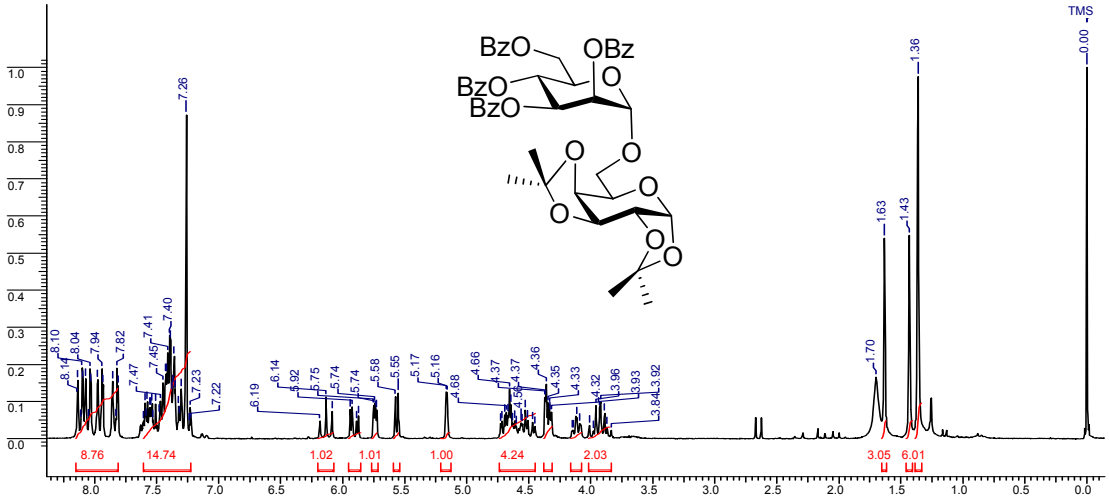
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **48**



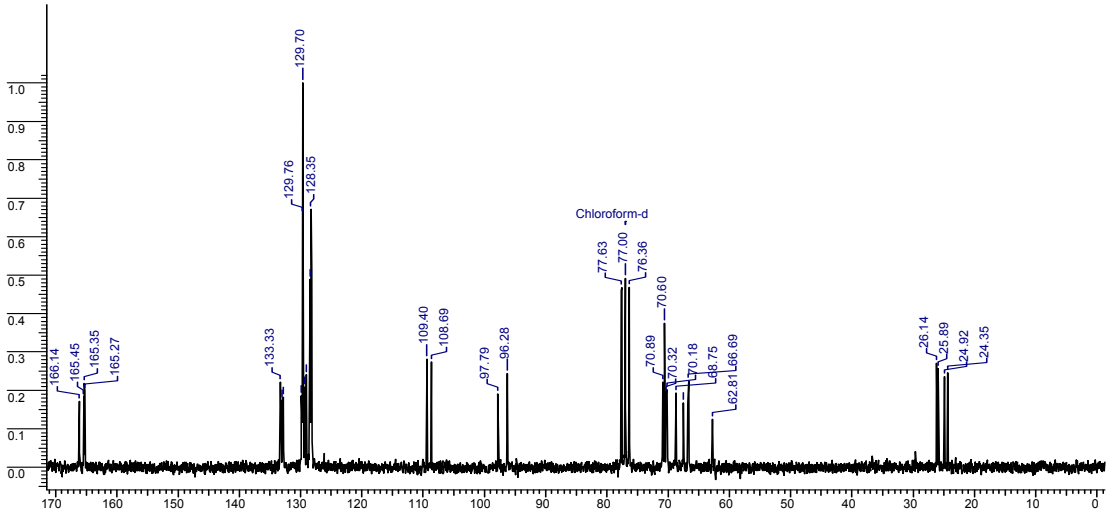
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **48**



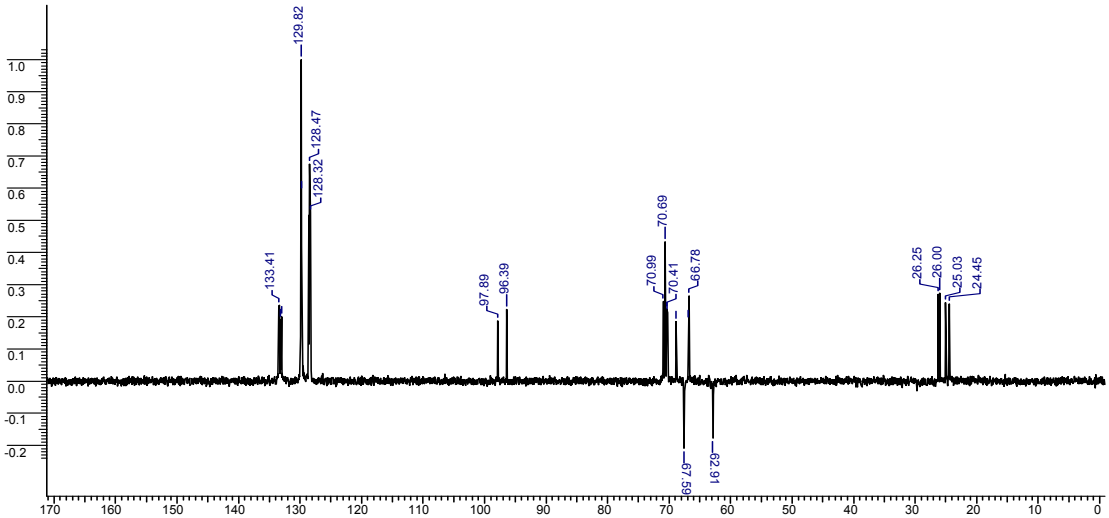
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **49**



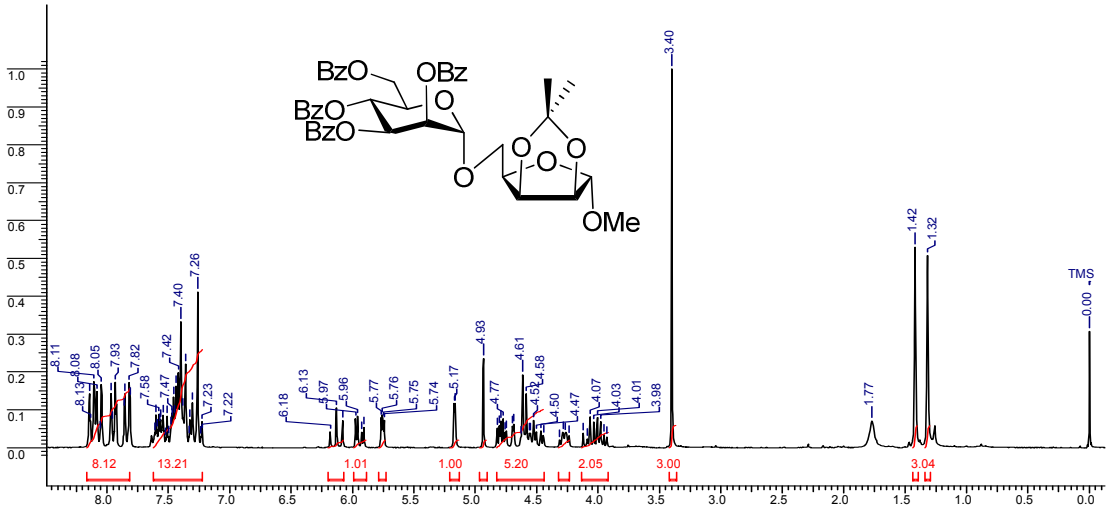
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **49**



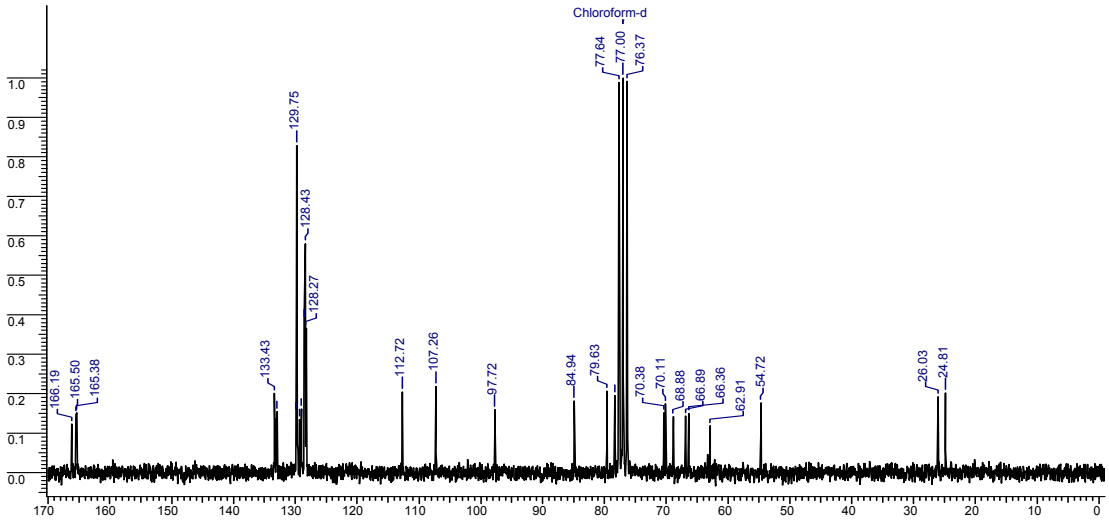
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **49**



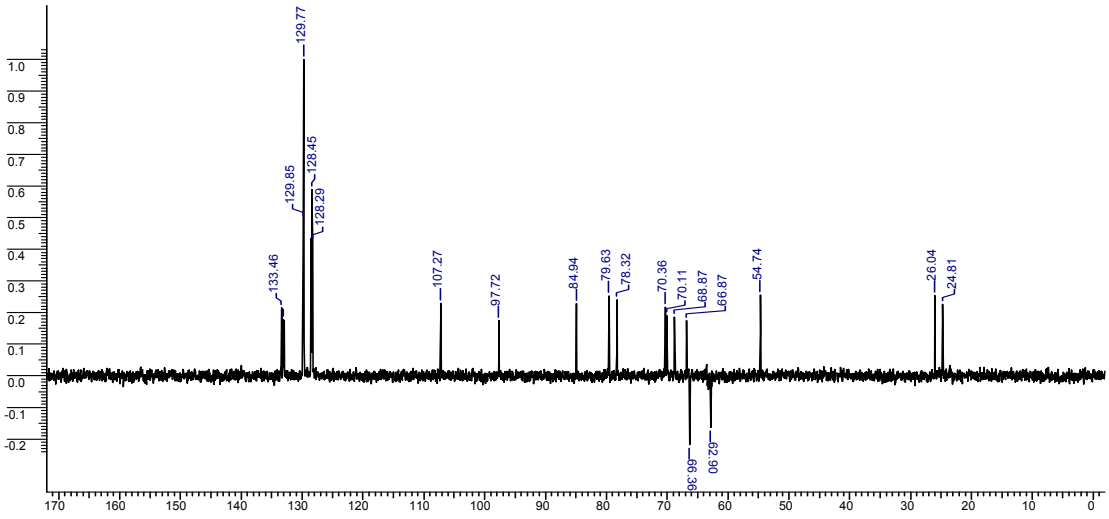
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **51**



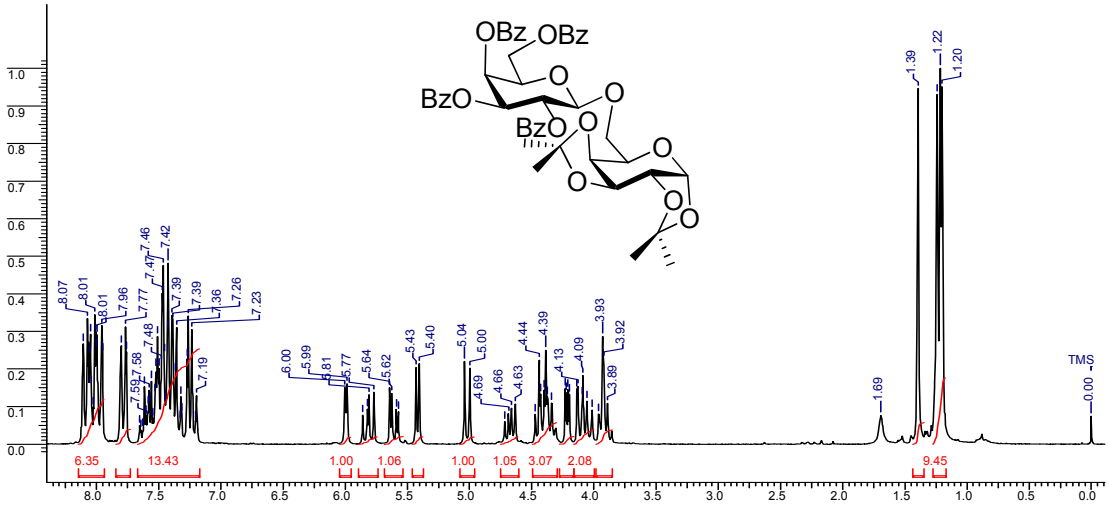
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **51**



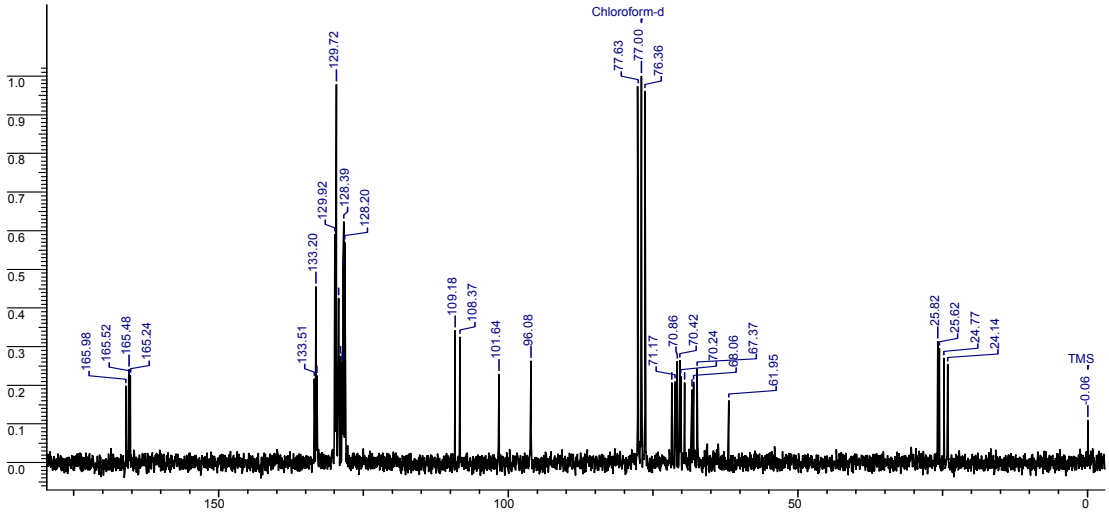
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **51**



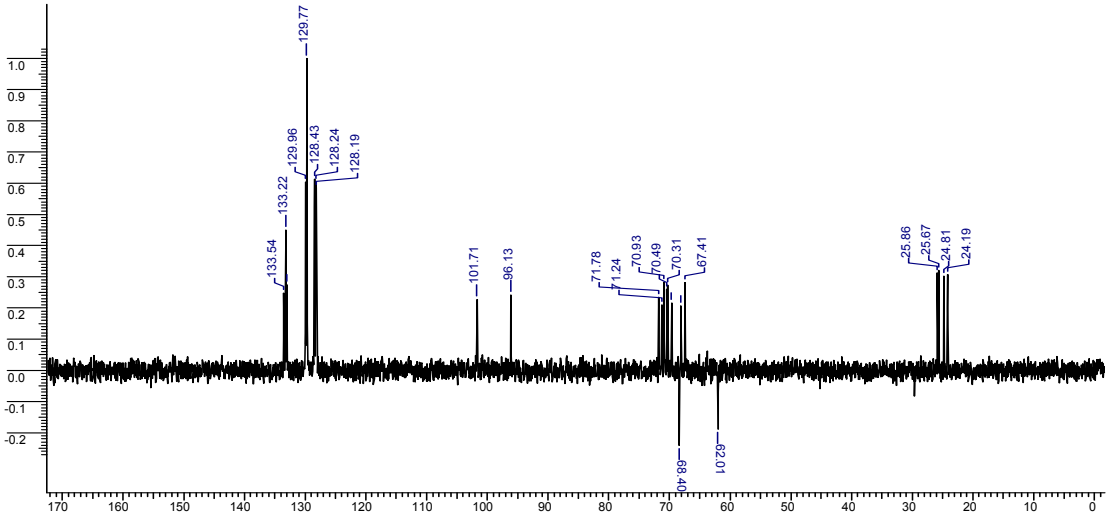
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **52**



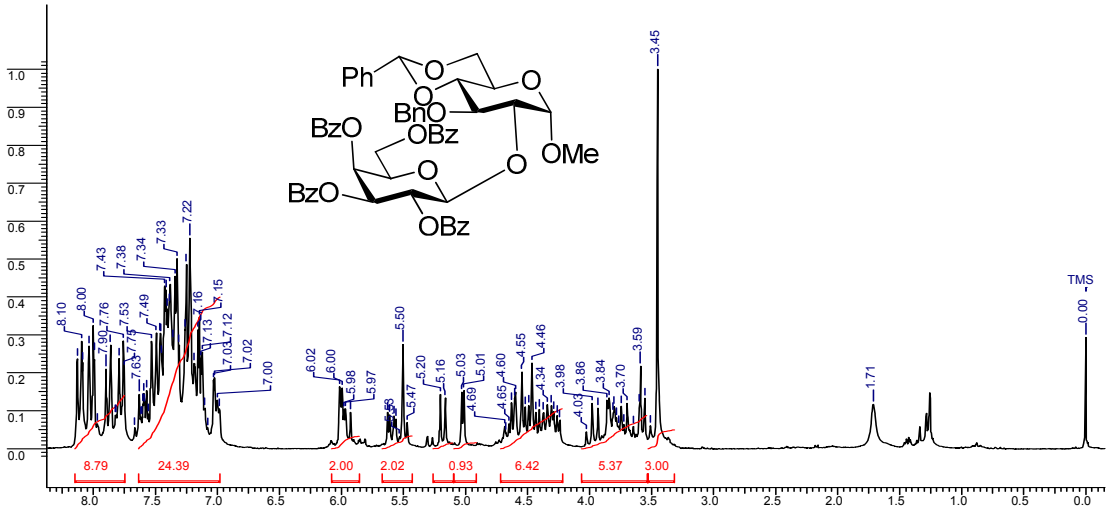
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **52**



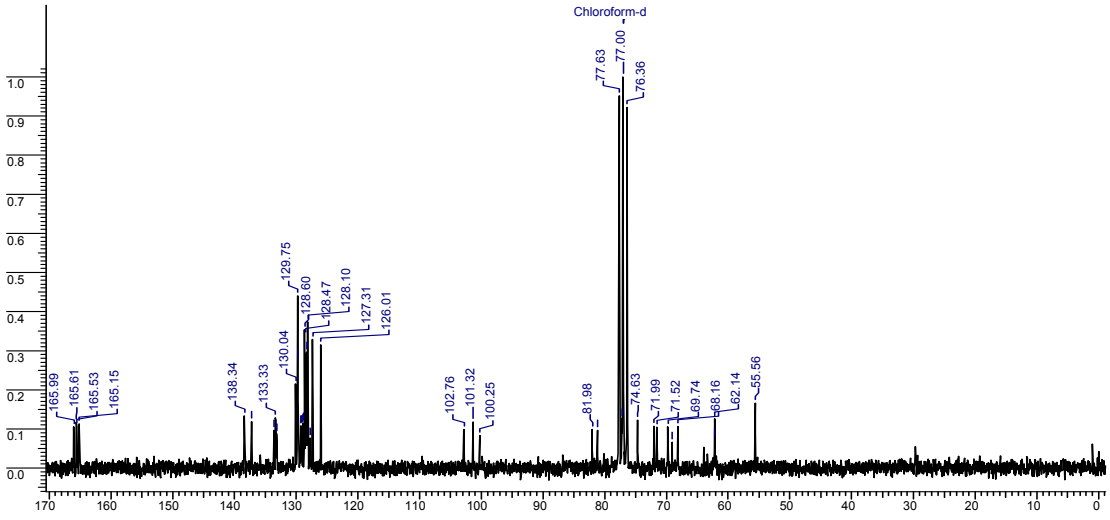
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **52**



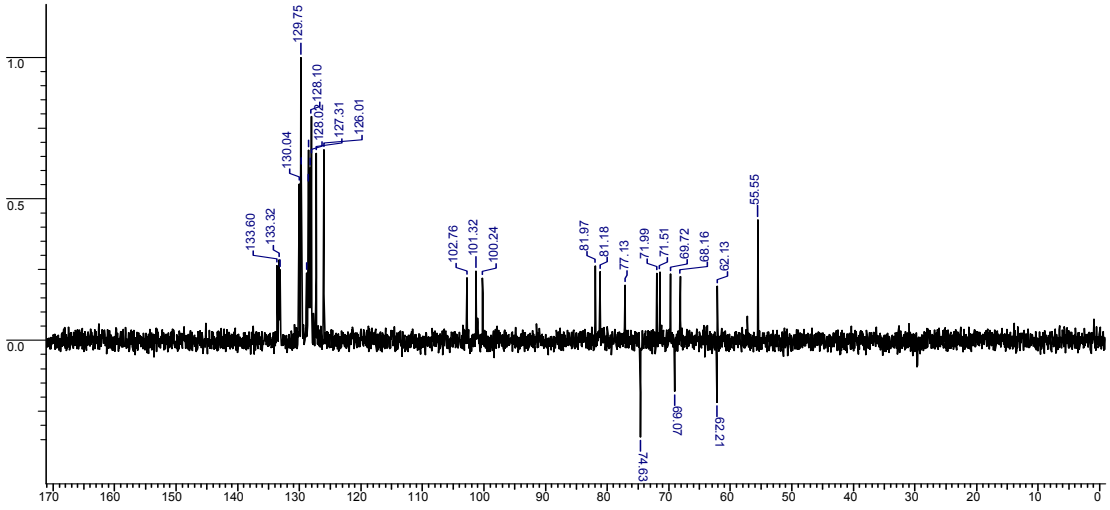
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **53**



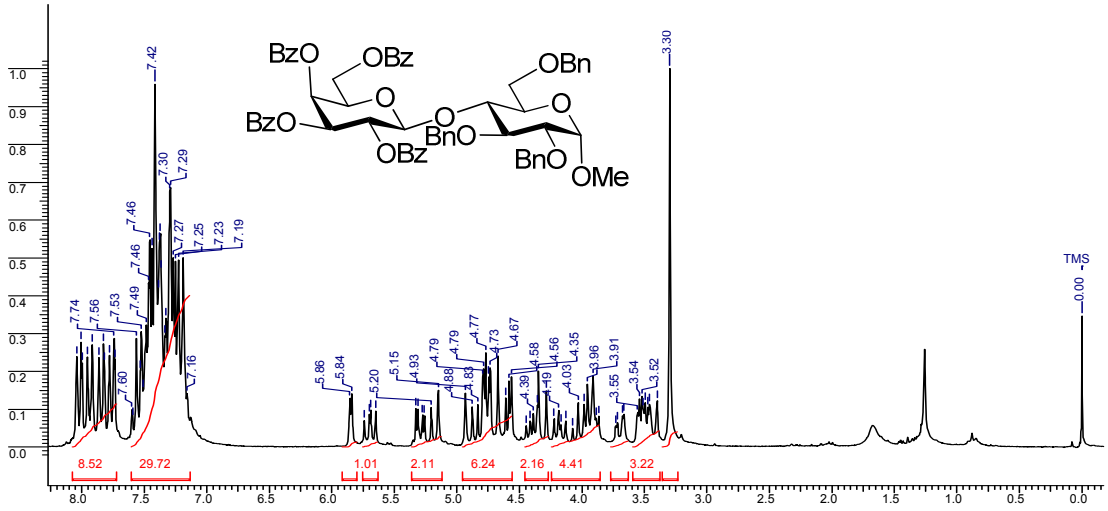
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **53**



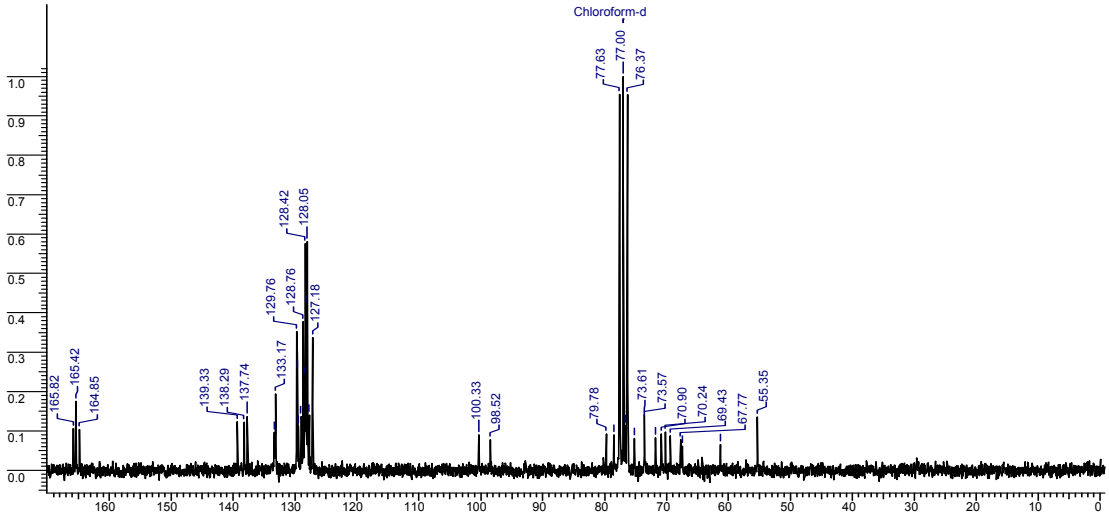
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **53**



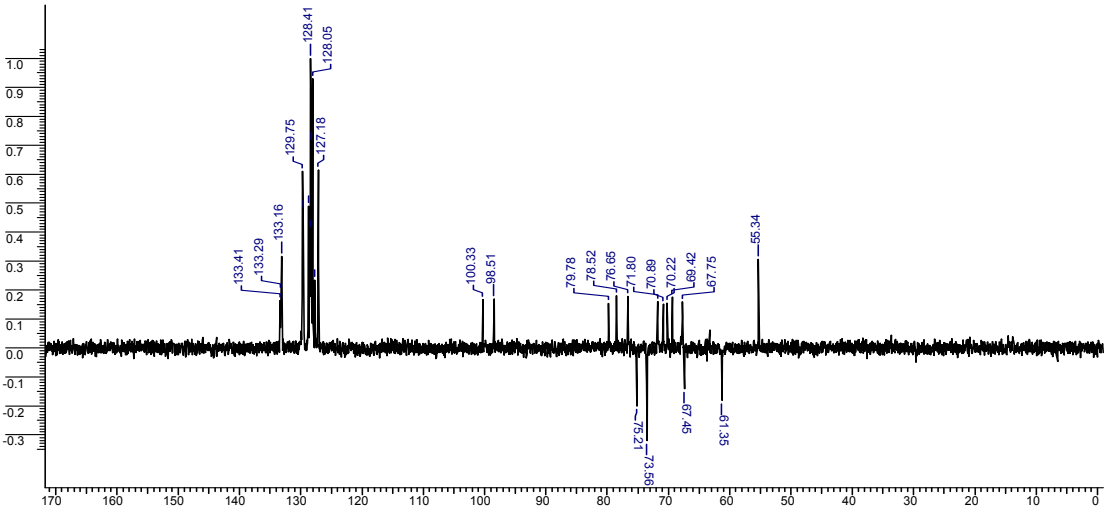
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **54**



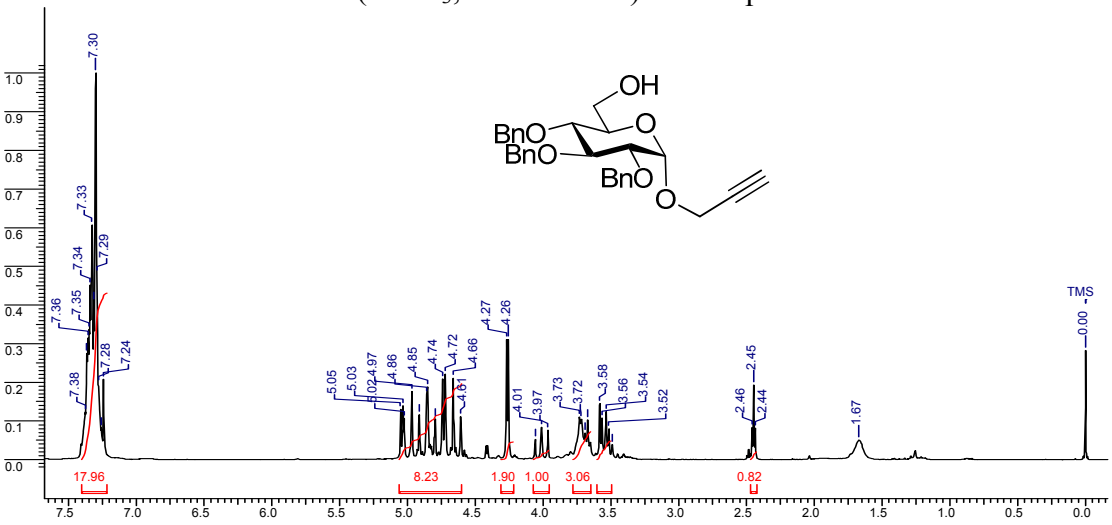
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **54**



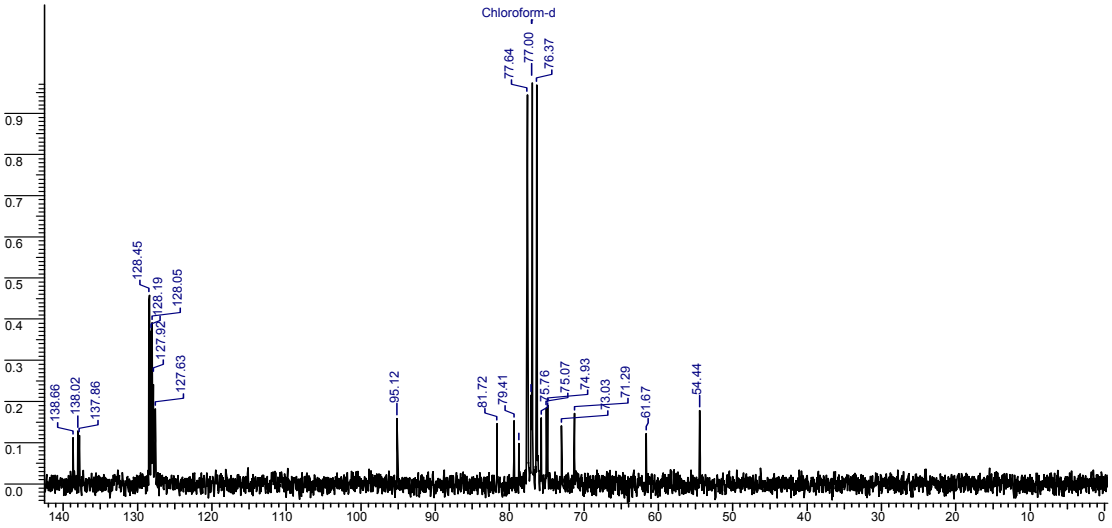
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **54**



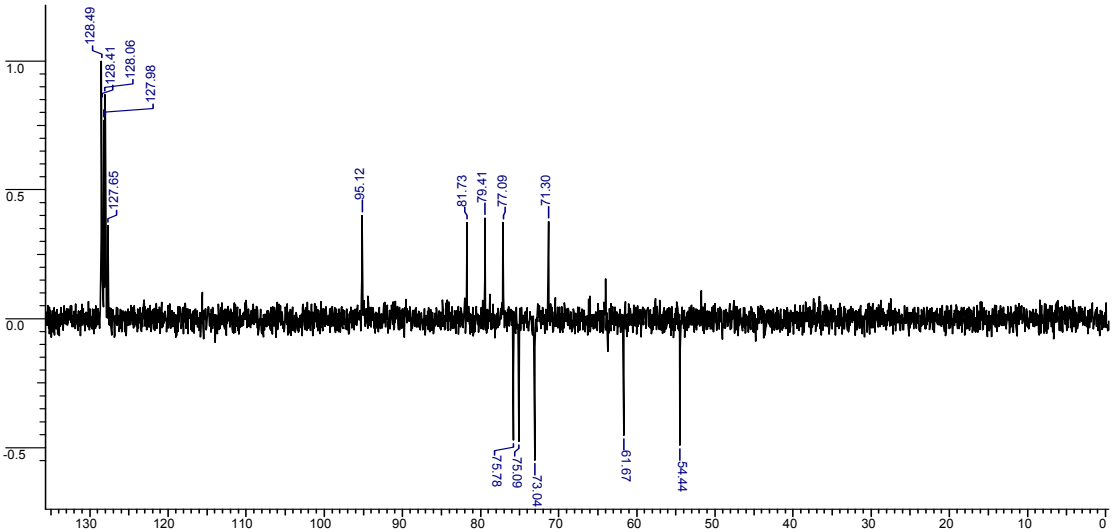
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **55**



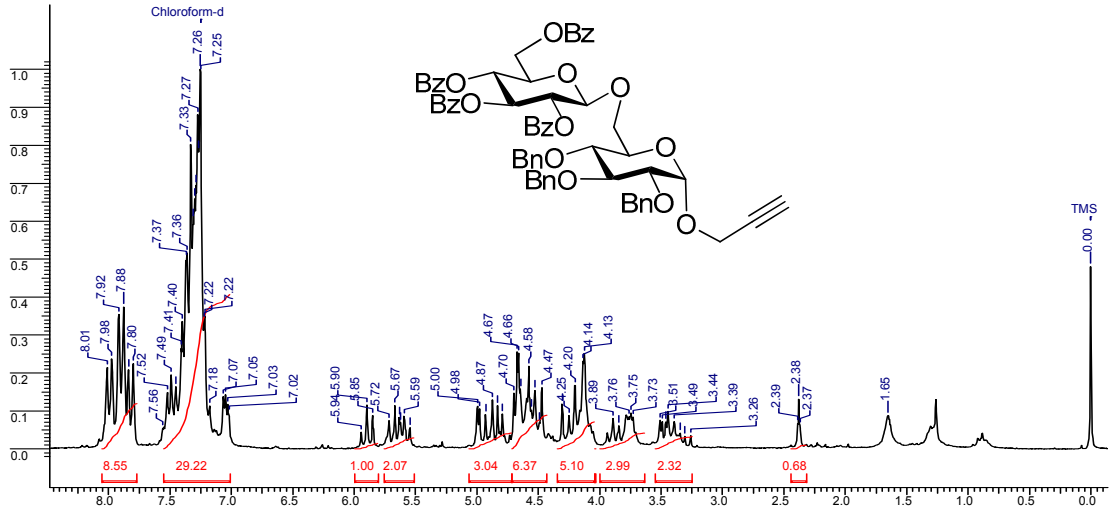
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **55**



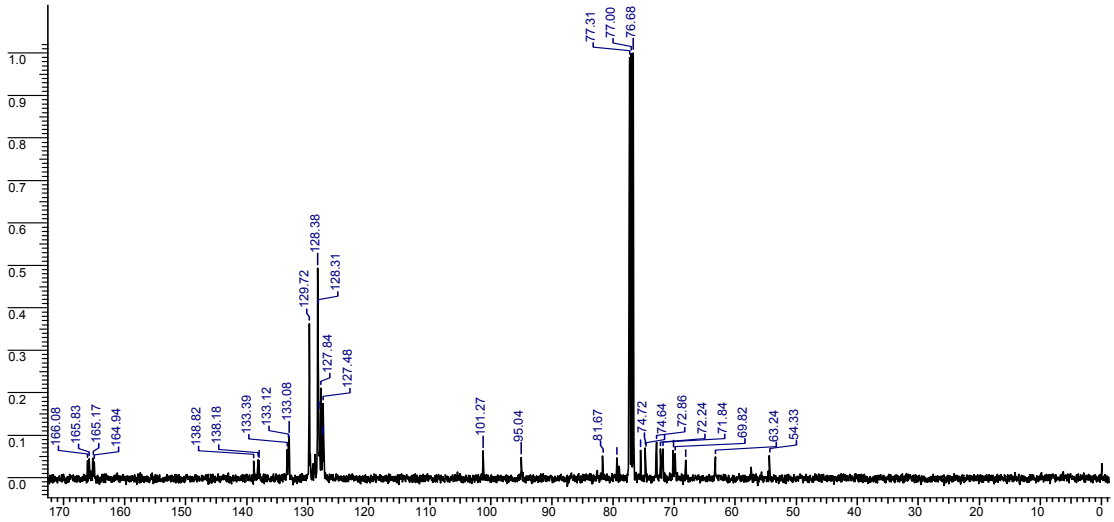
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **55**



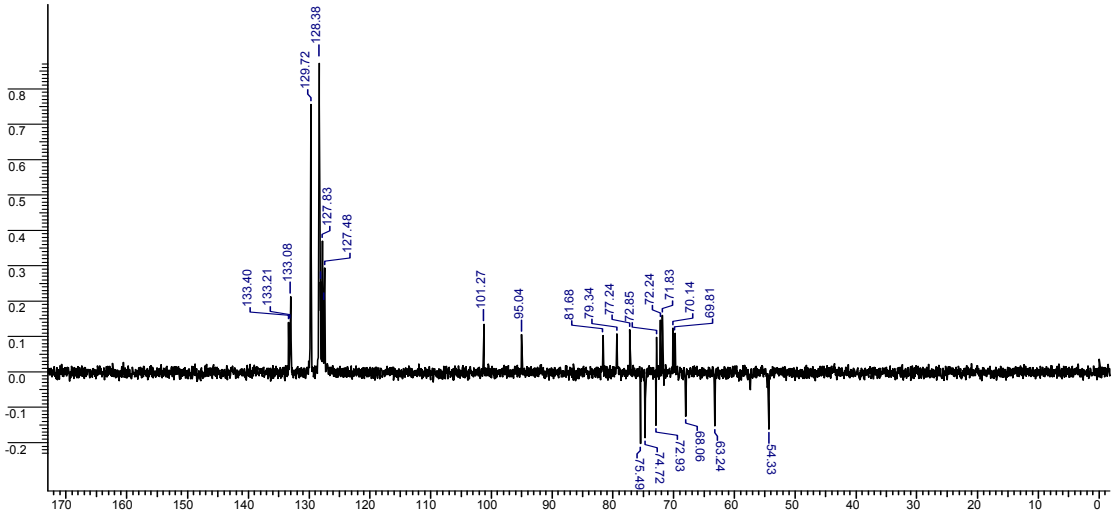
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **56**



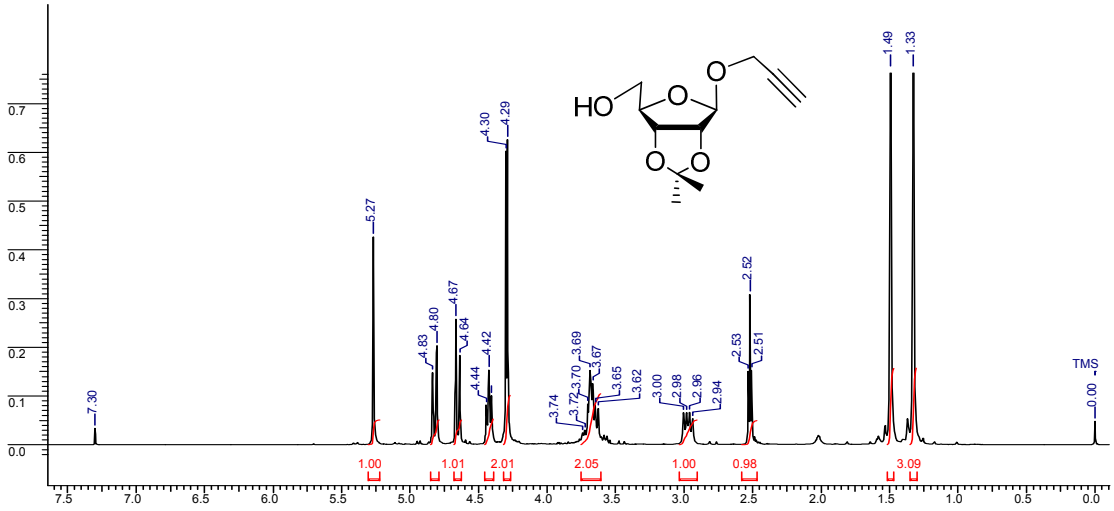
^{13}C NMR ($CDCl_3$, 100.61 MHz) of Compound **56**



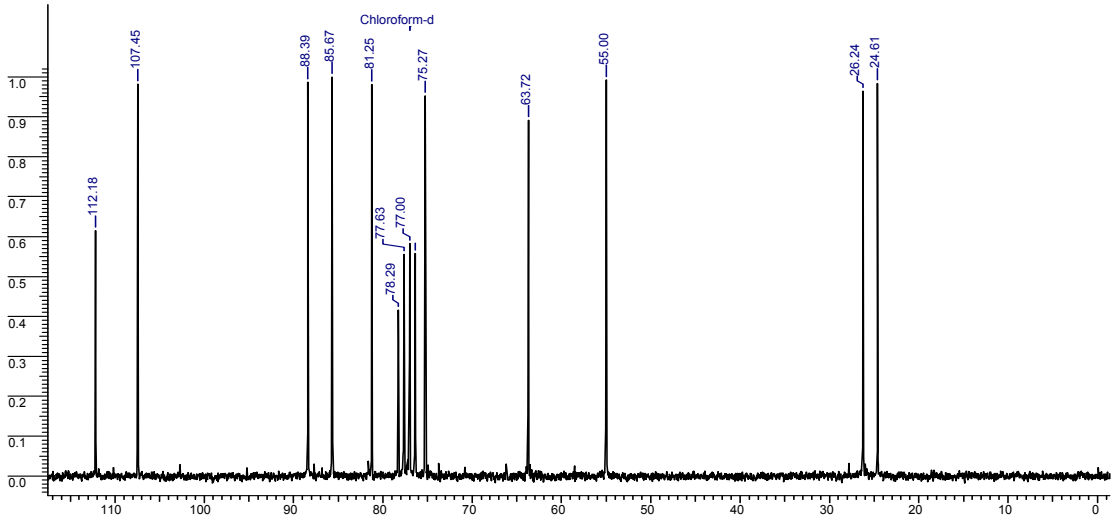
DEPT NMR ($CDCl_3$, 100.61 MHz) of Compound **56**



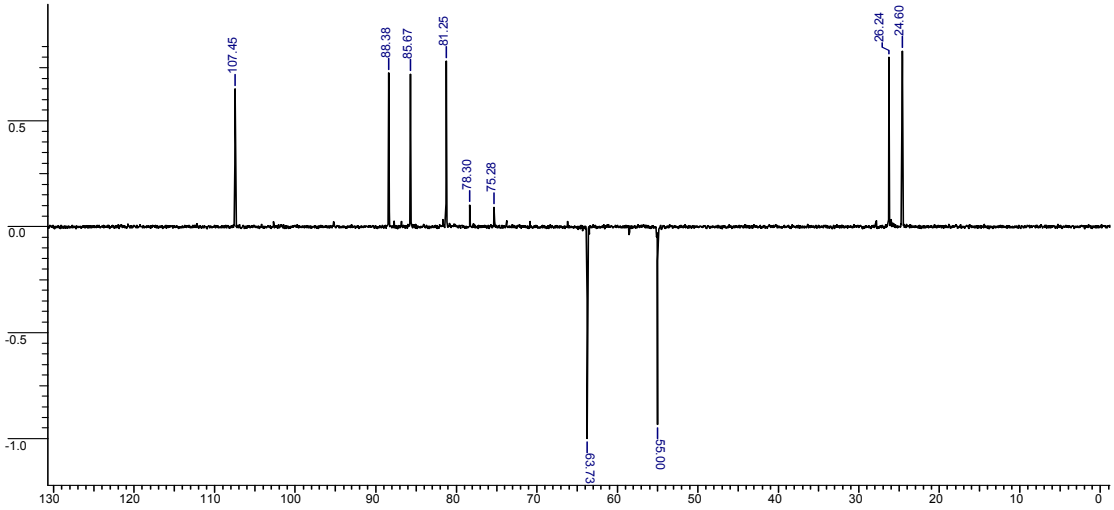
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **57**



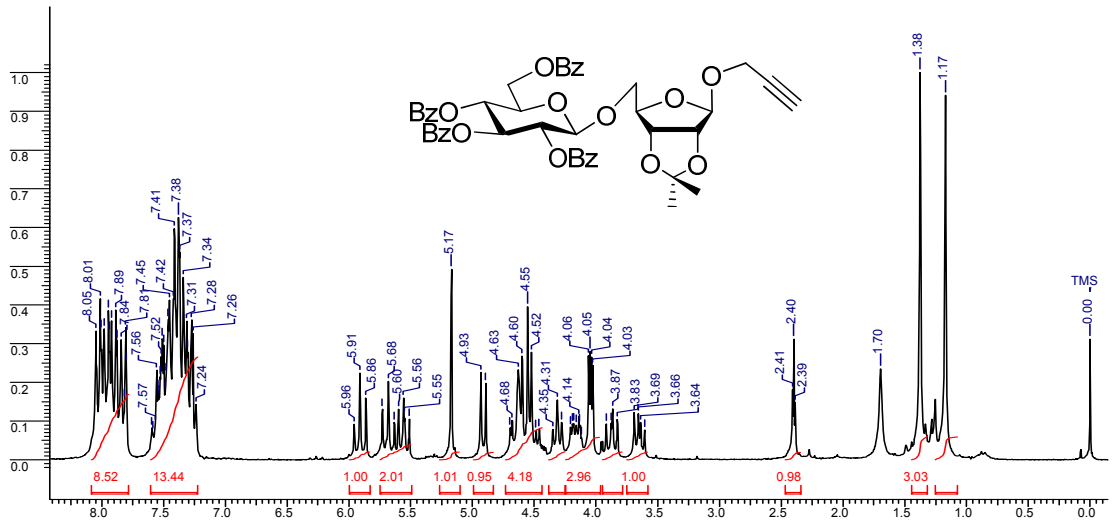
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **57**



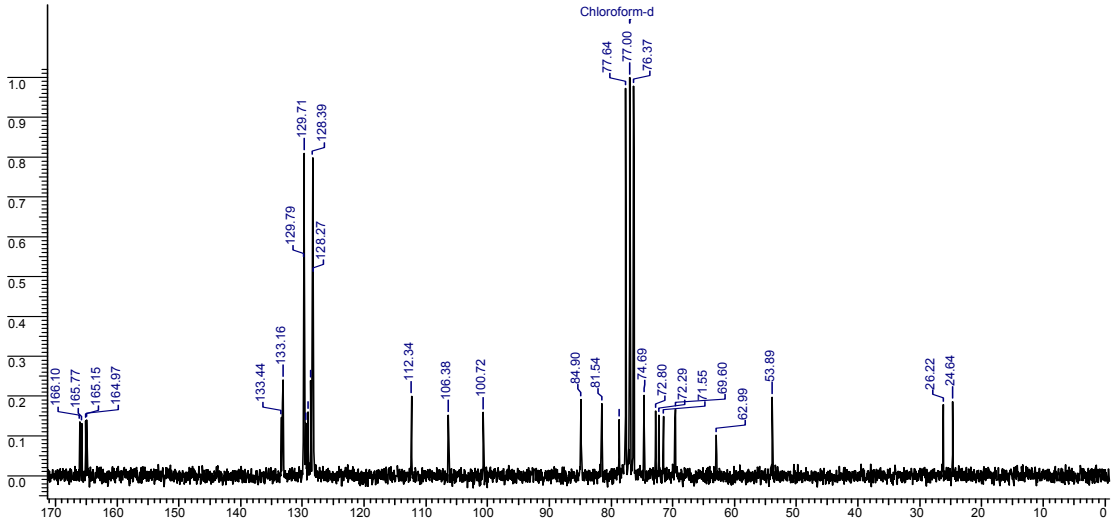
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **57**



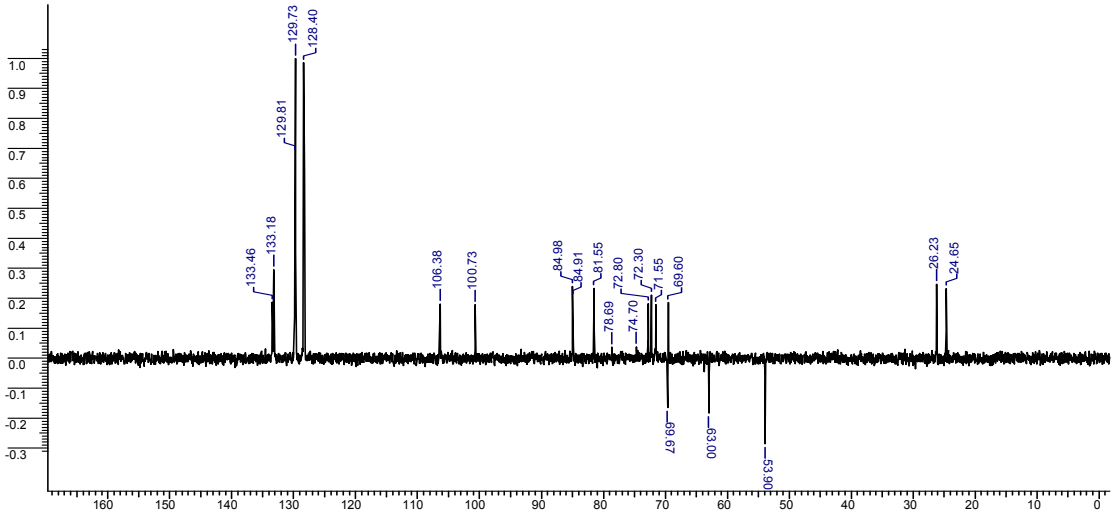
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **58**



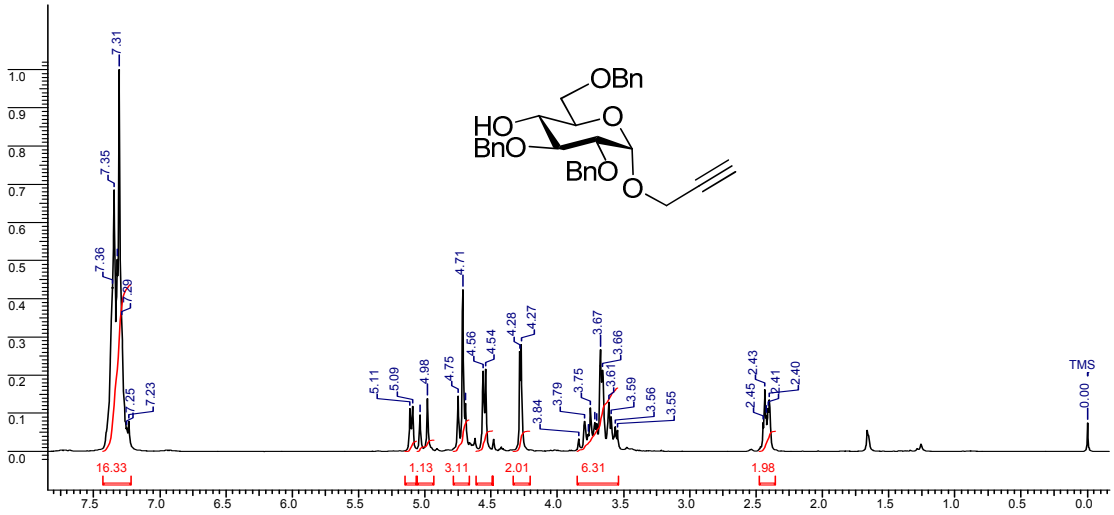
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **58**



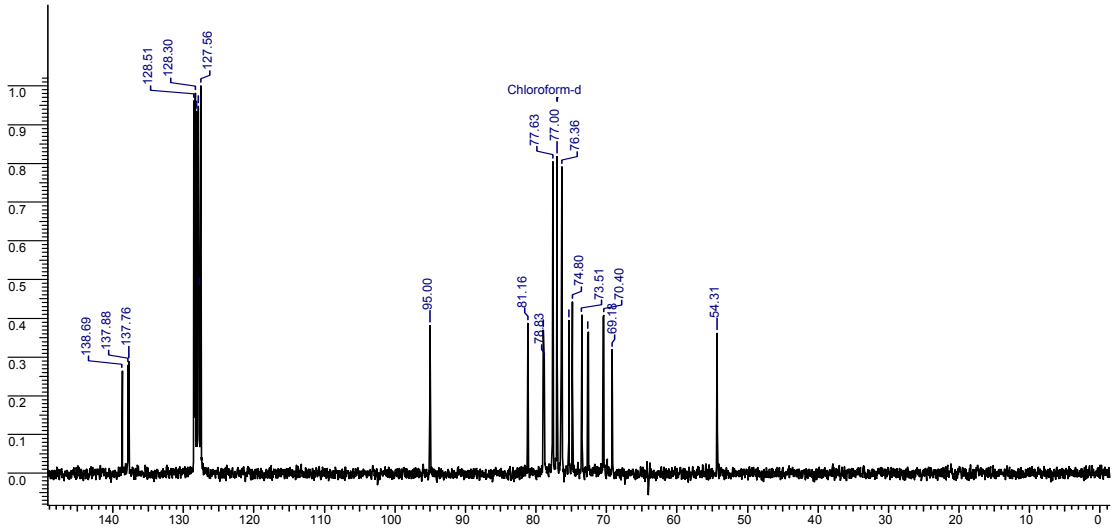
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **58**



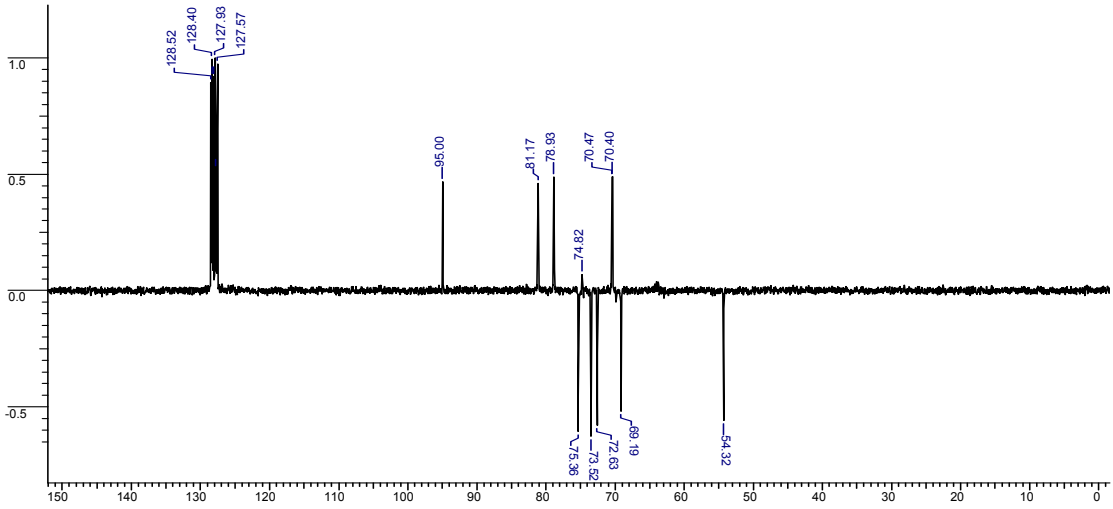
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **59**



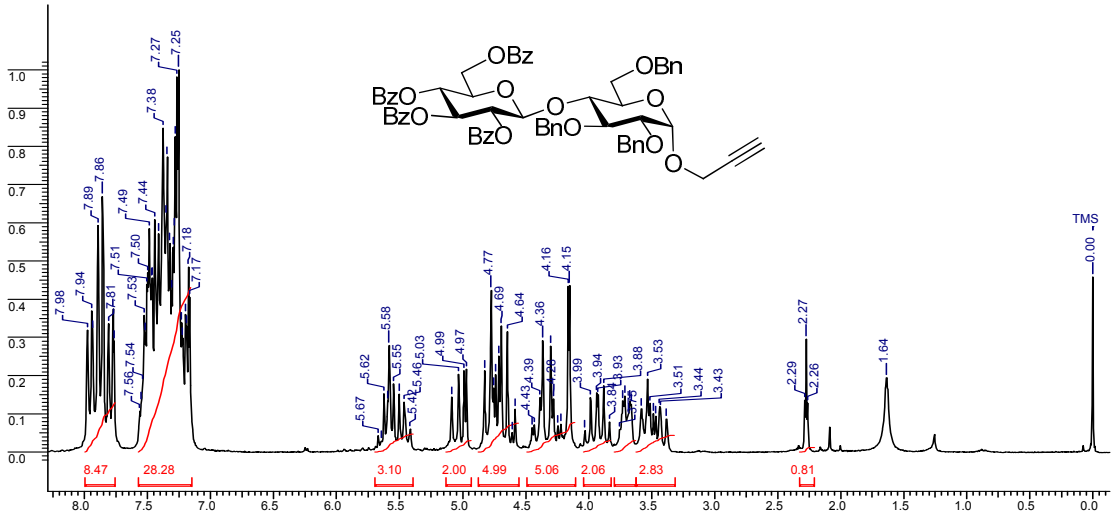
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **59**



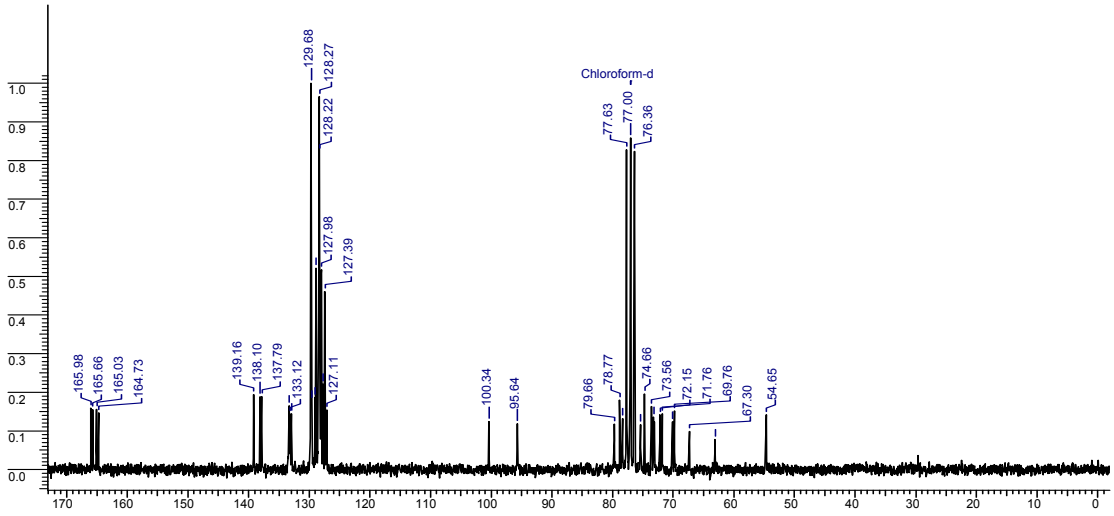
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **59**



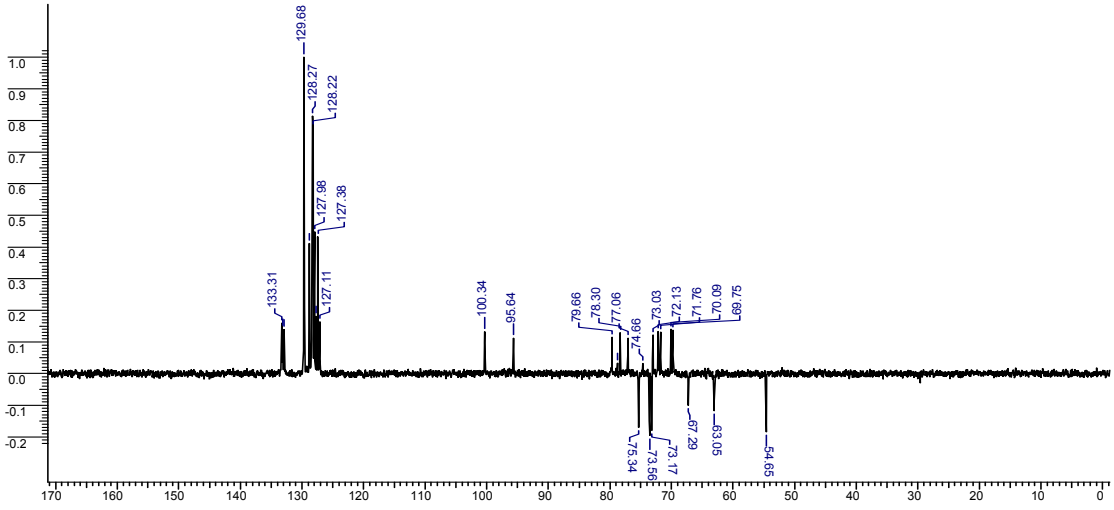
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **60**



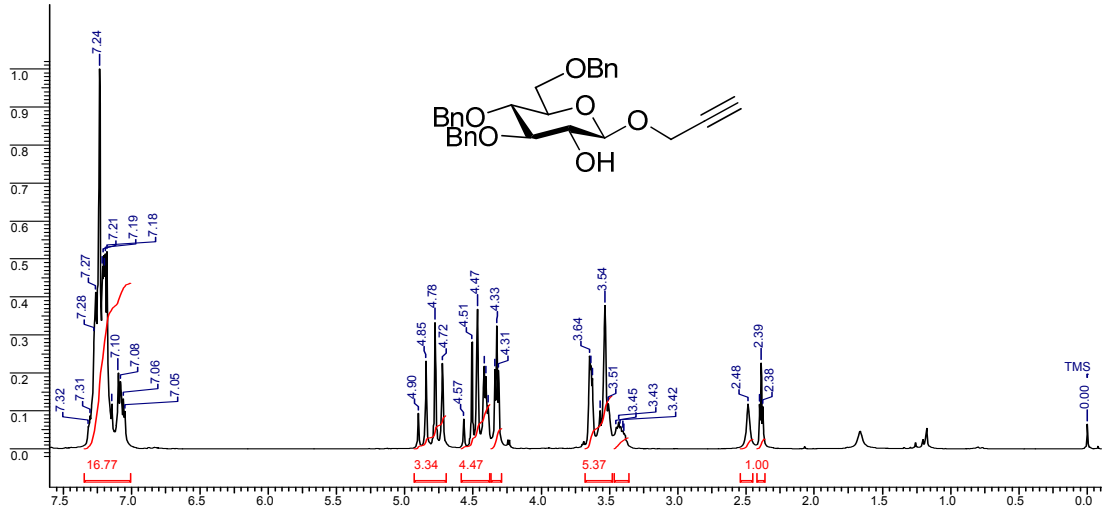
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **60**



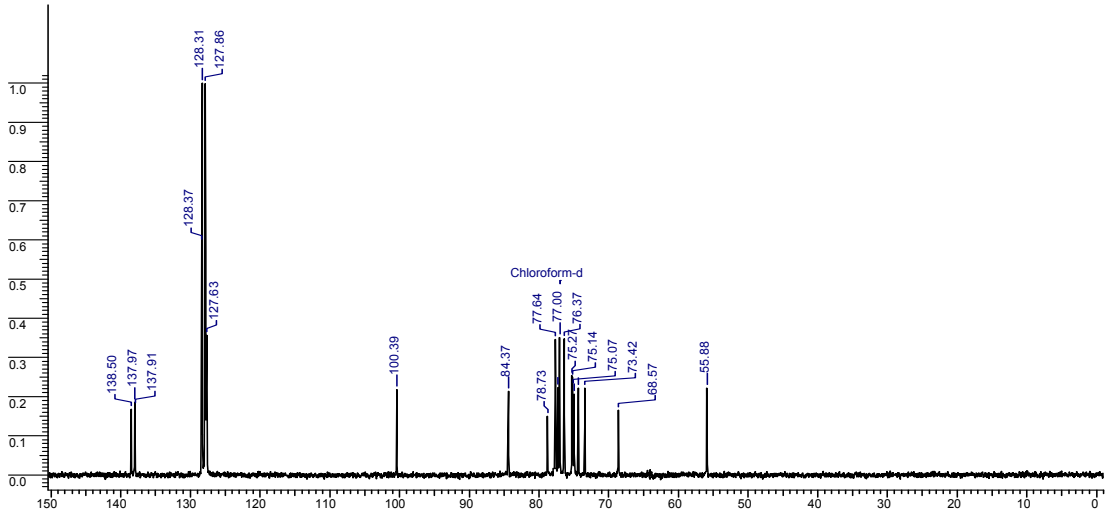
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **60**



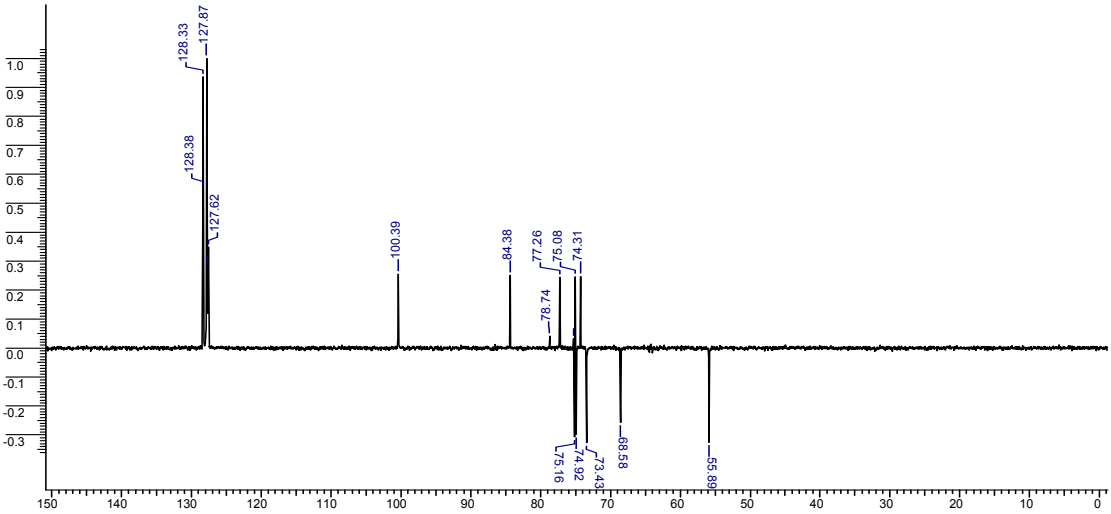
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **61**



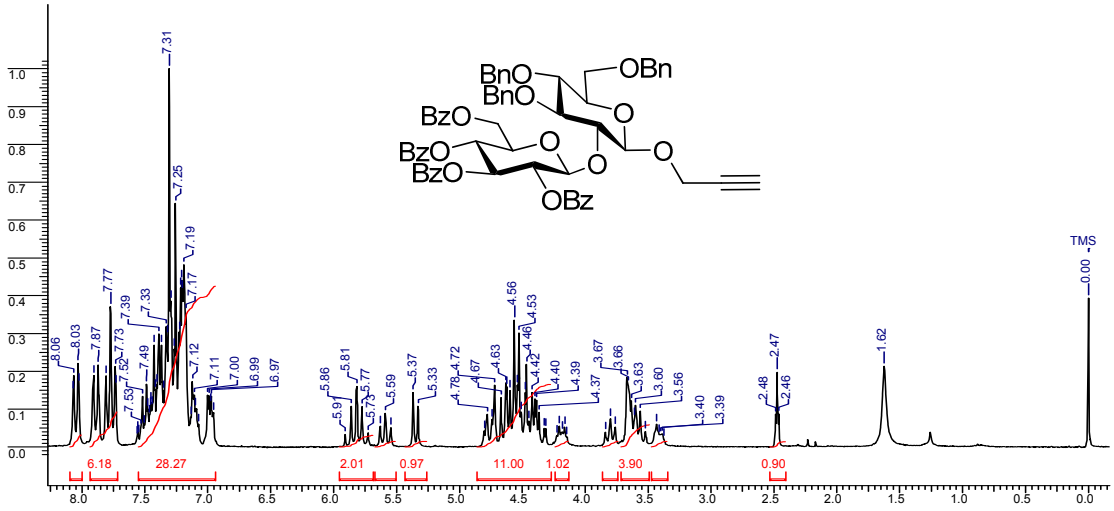
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **61**



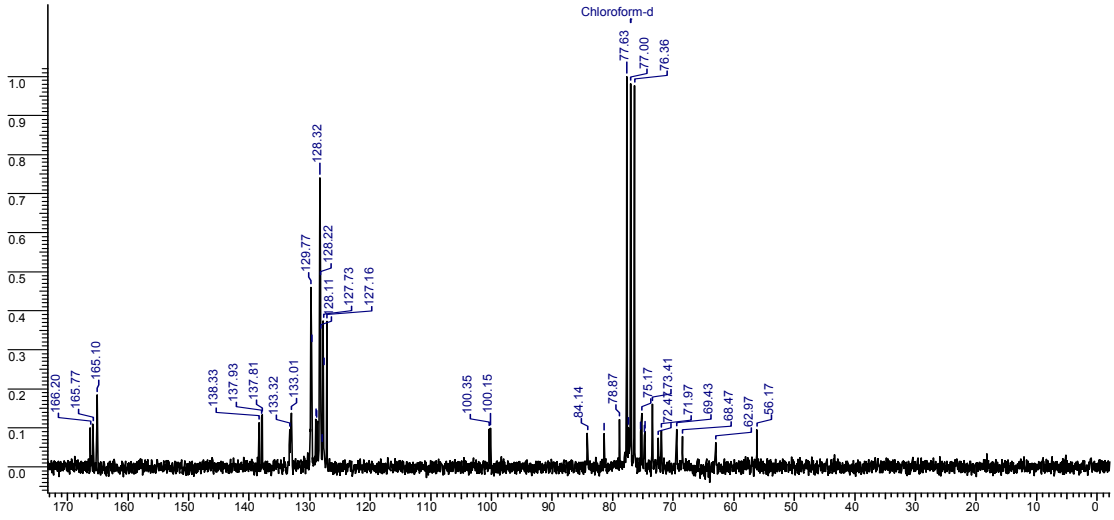
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **61**



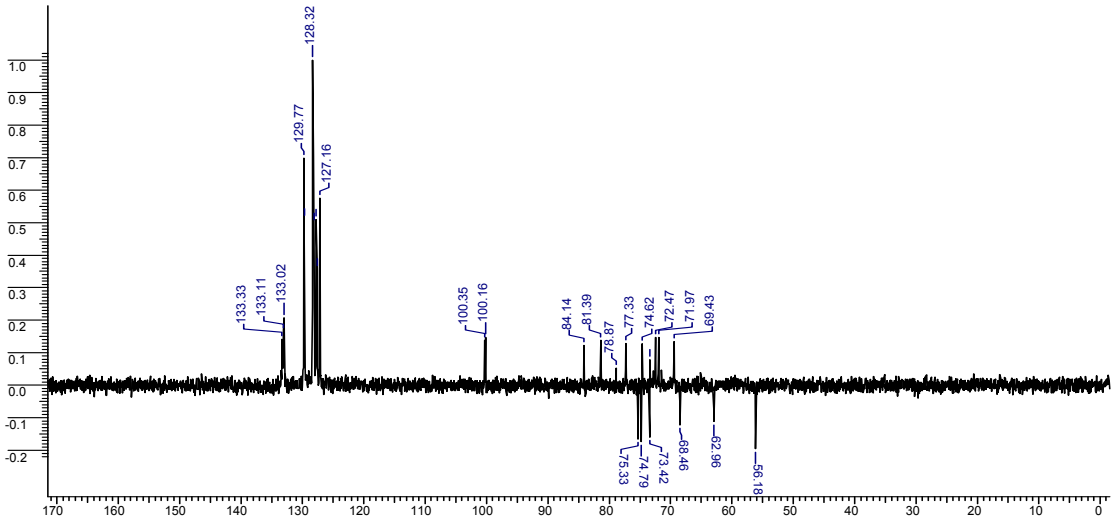
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **62**



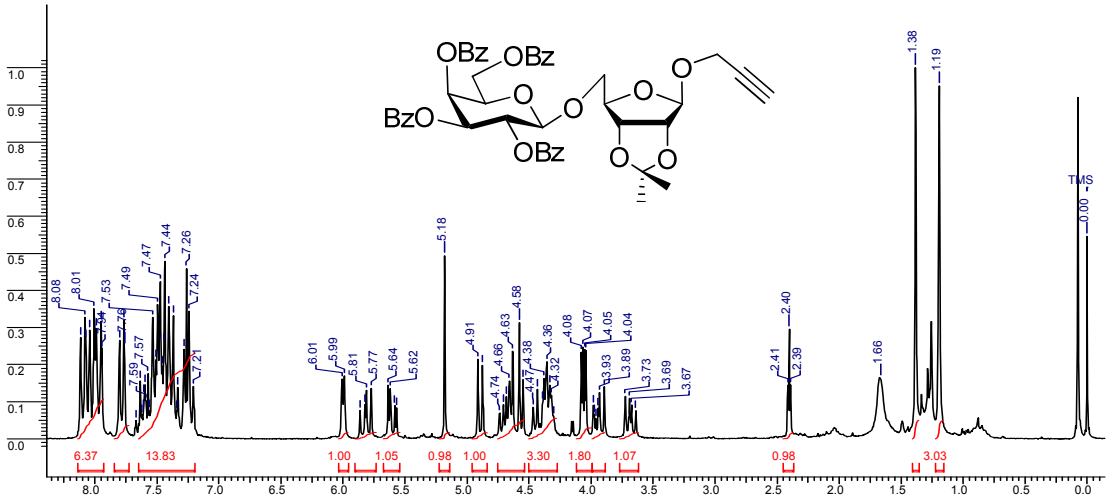
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **62**



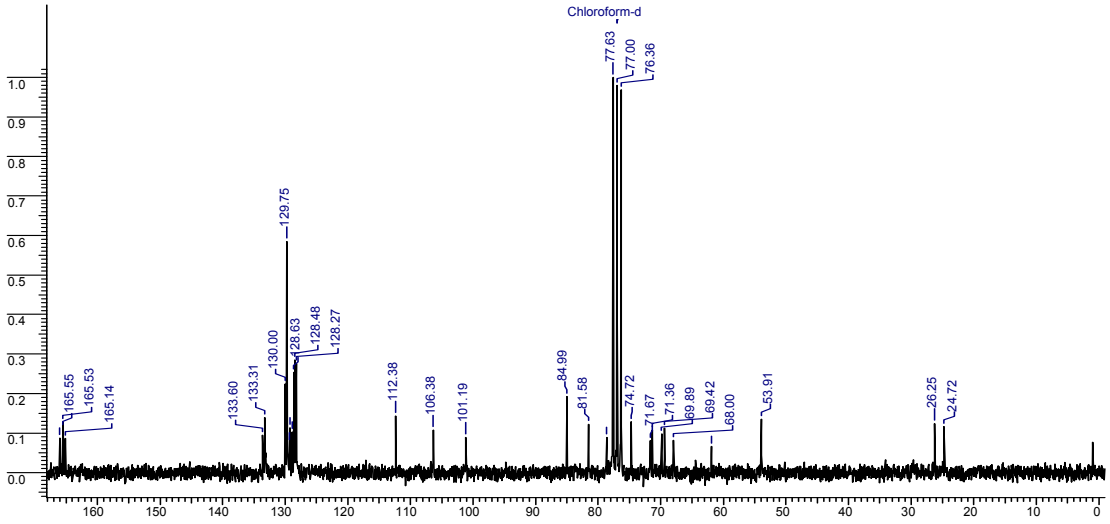
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **62**



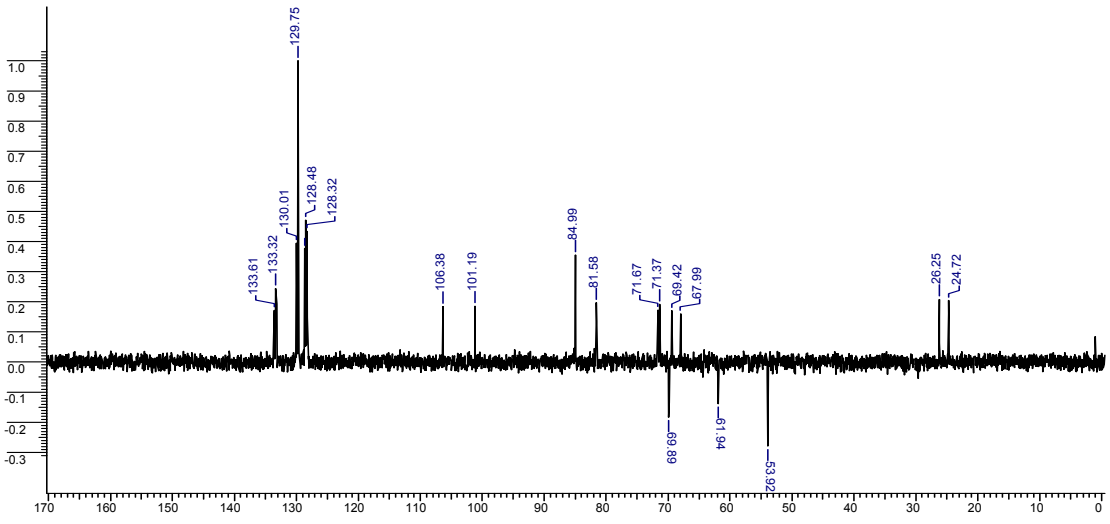
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **63**



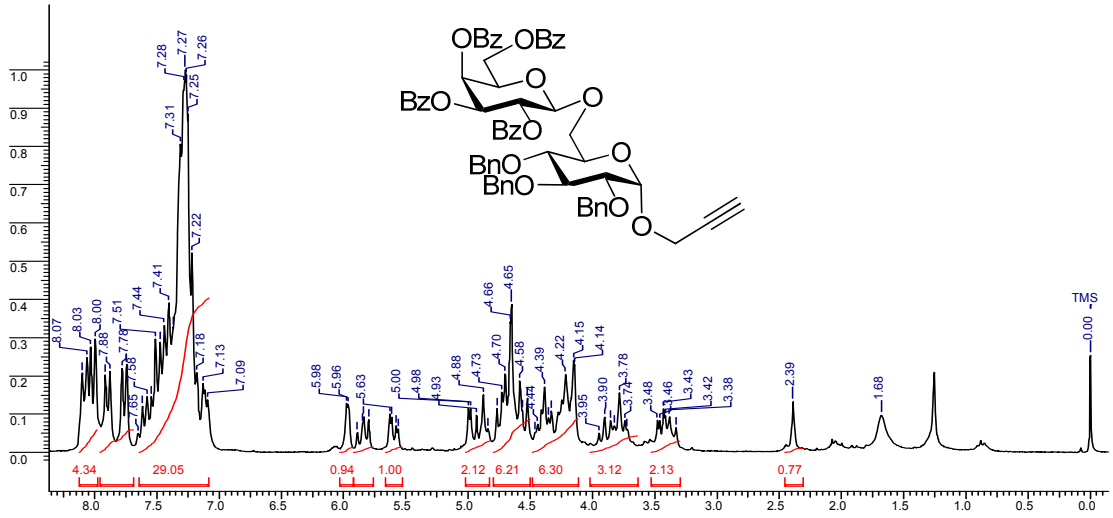
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **63**



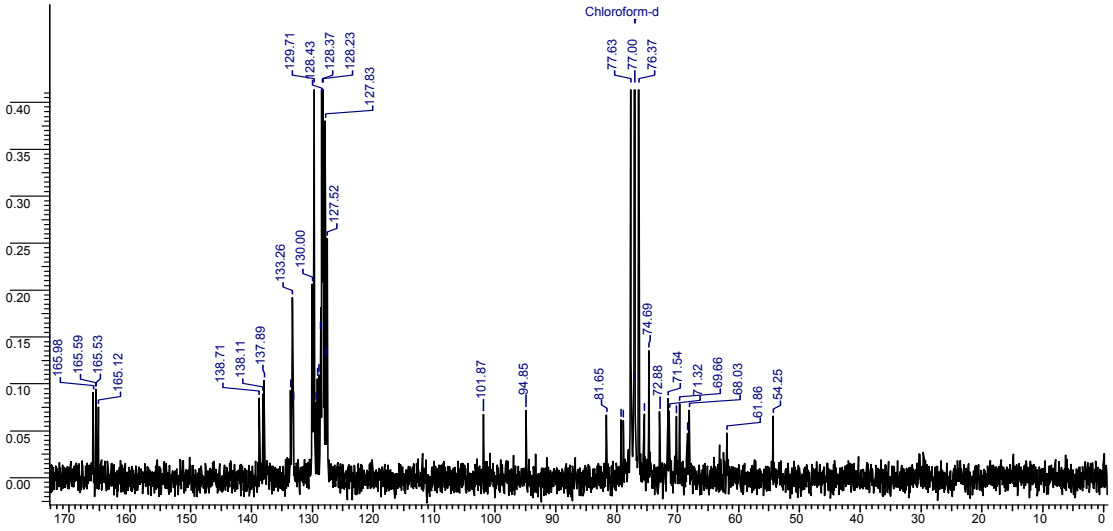
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **63**



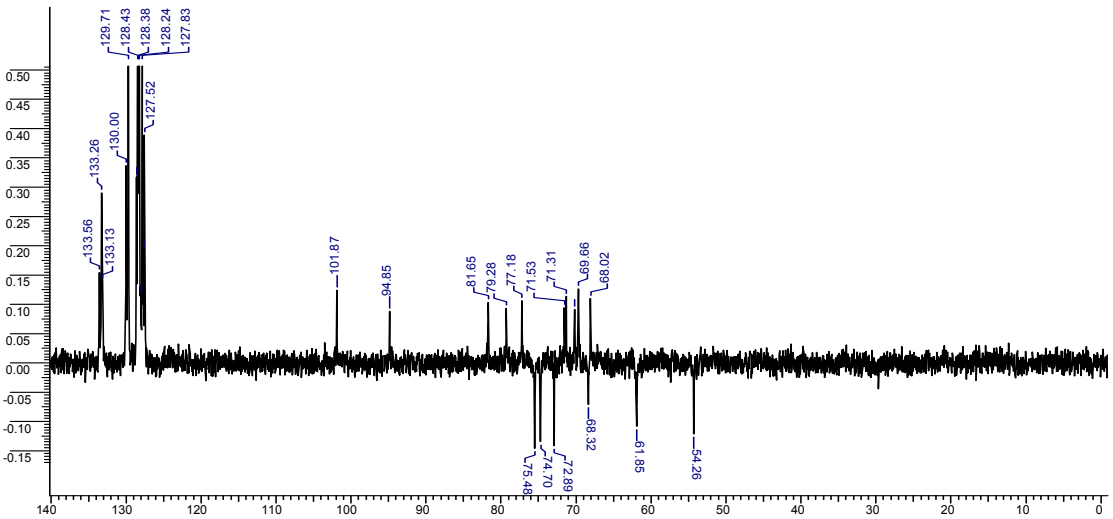
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **64**



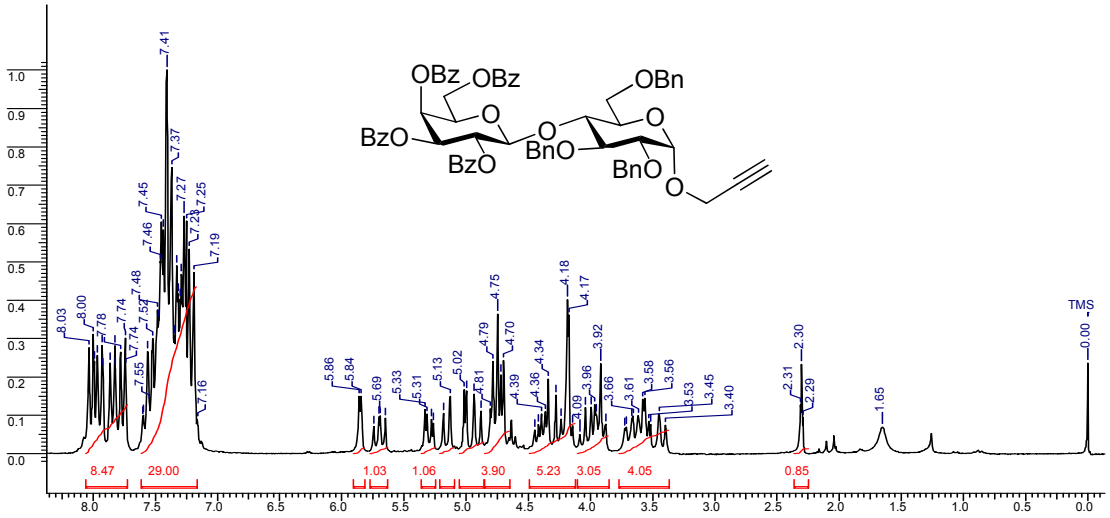
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **64**



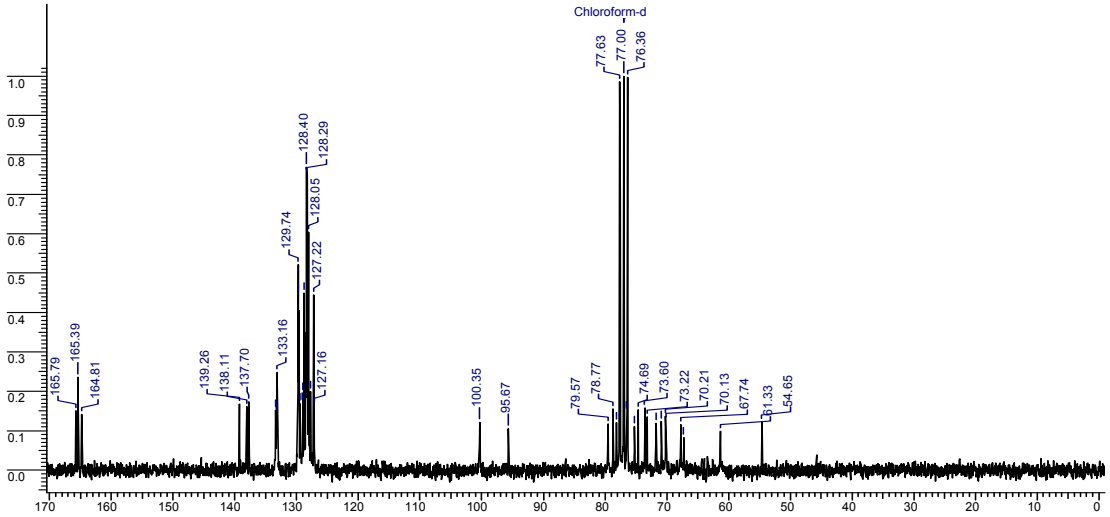
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **64**



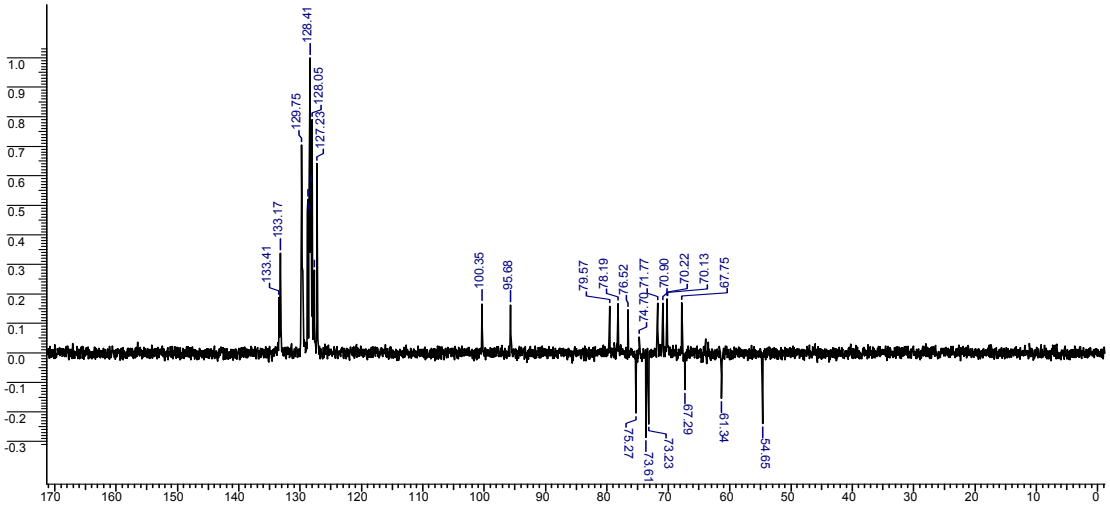
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **65**



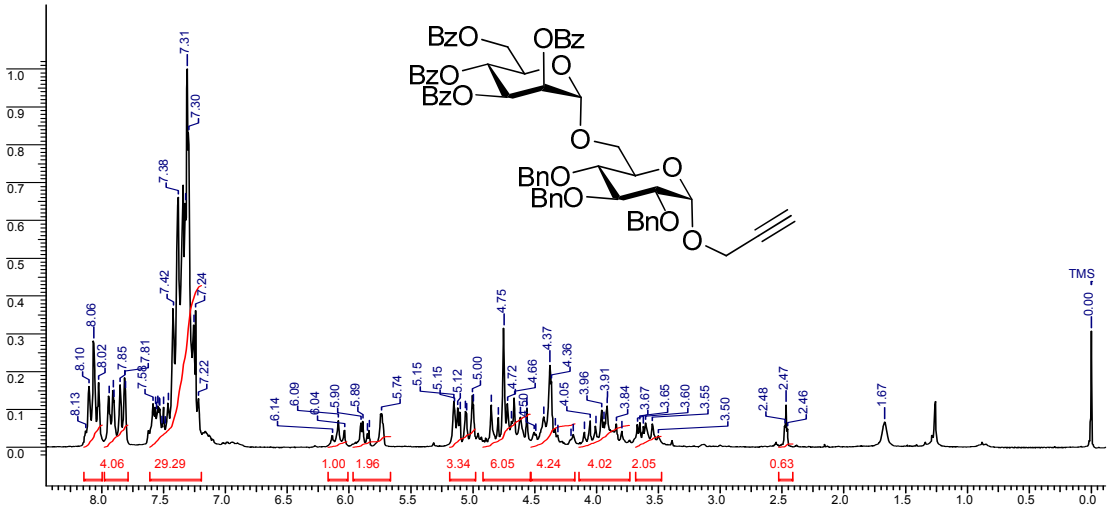
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **65**



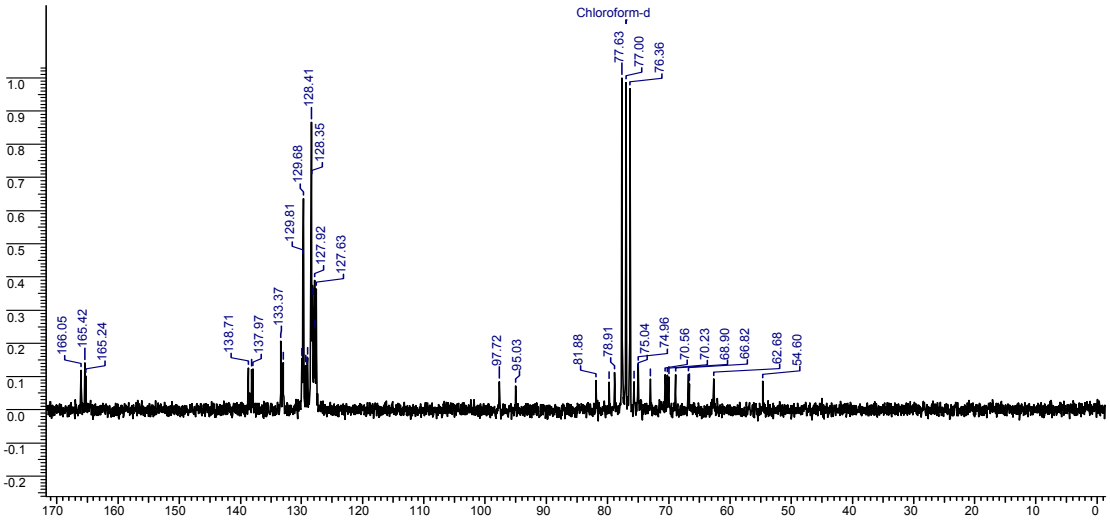
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **65**



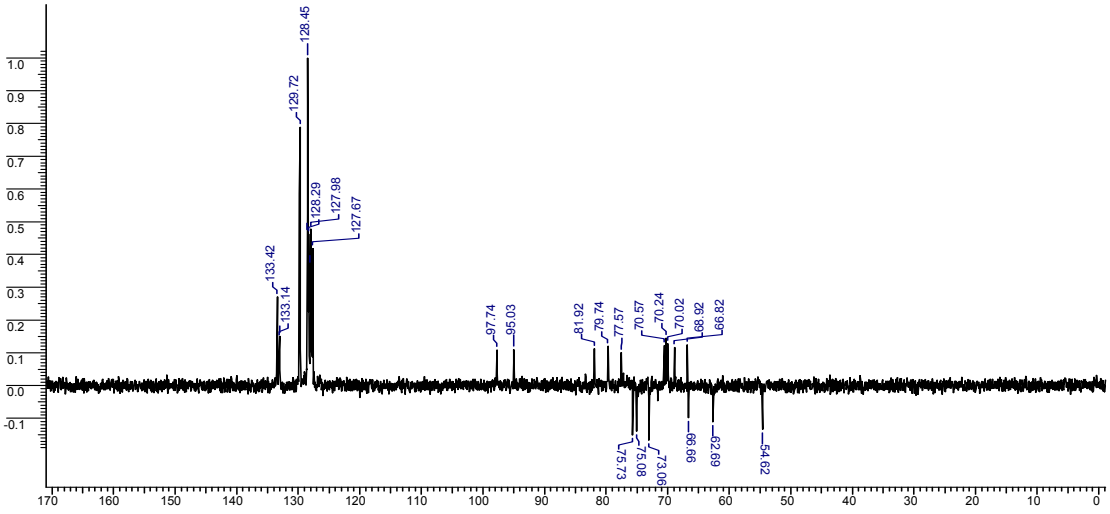
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **66**



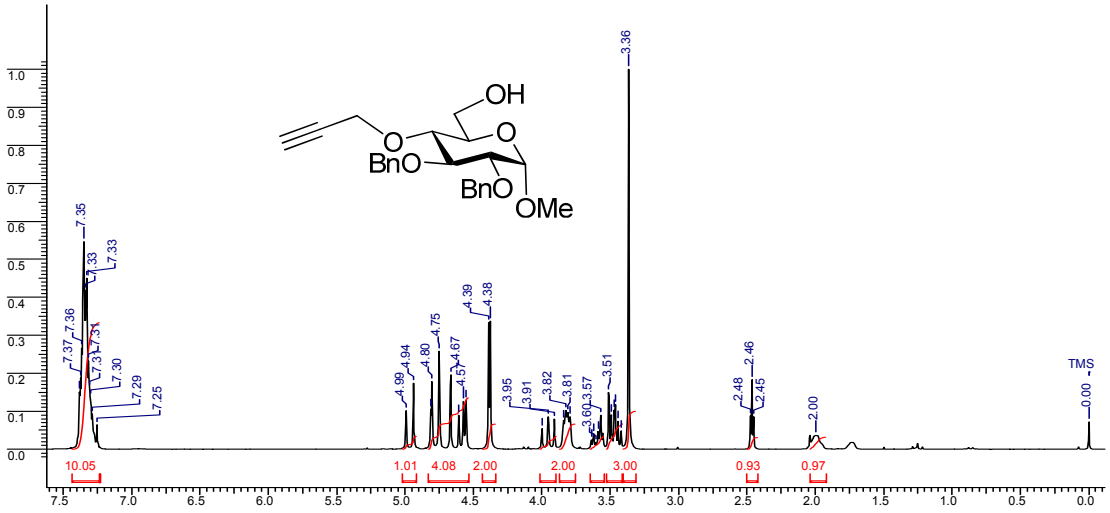
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **66**



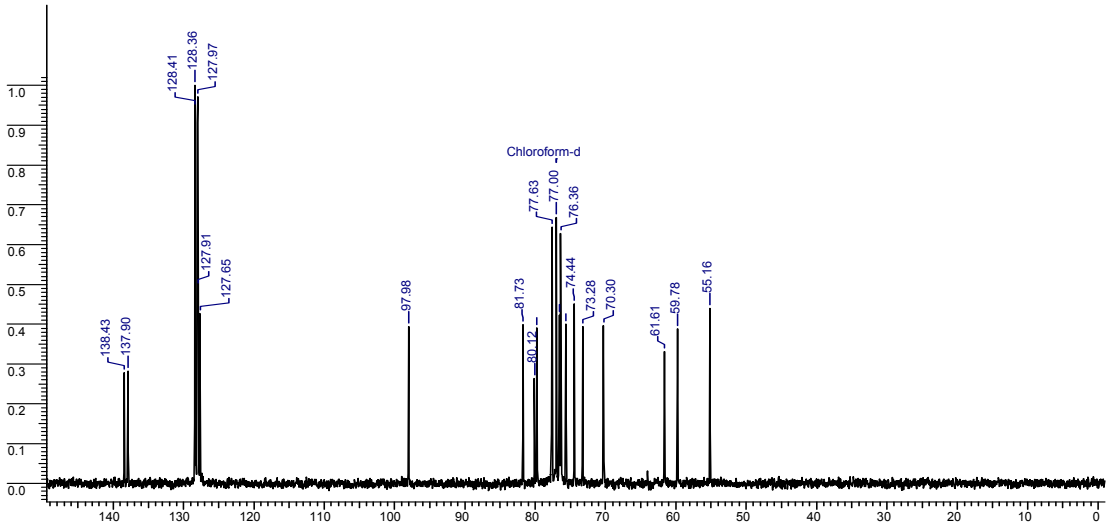
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **66**



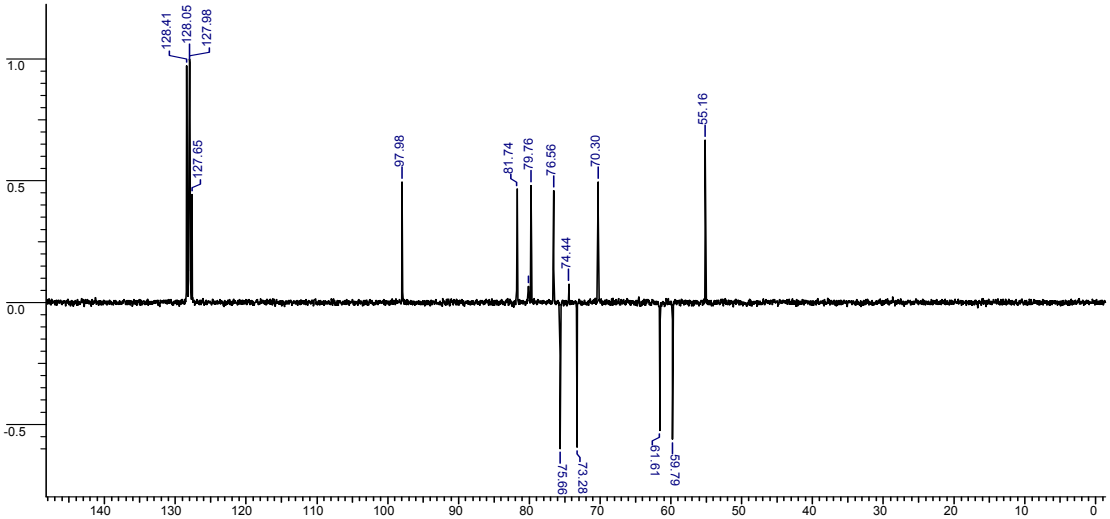
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **67**



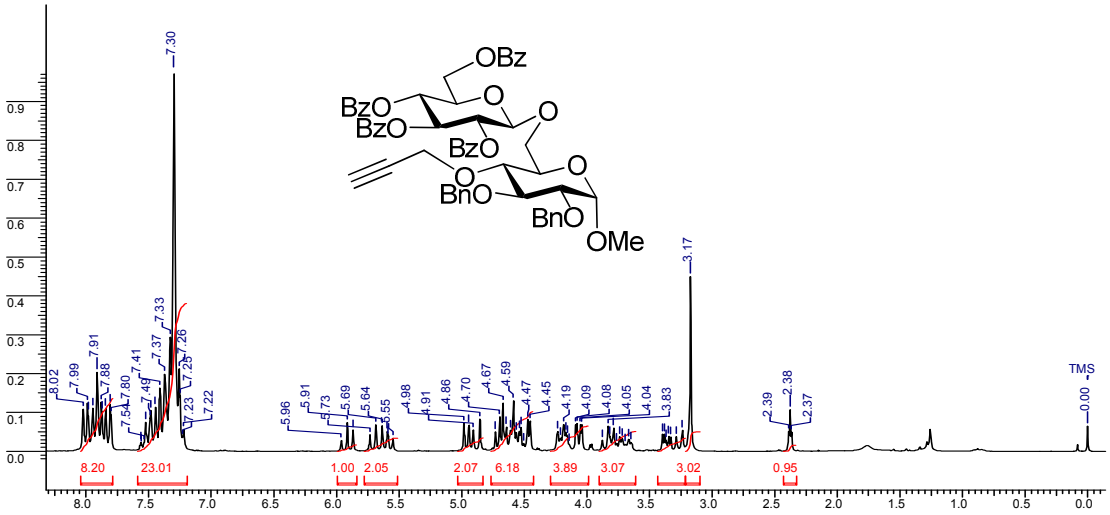
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **67**



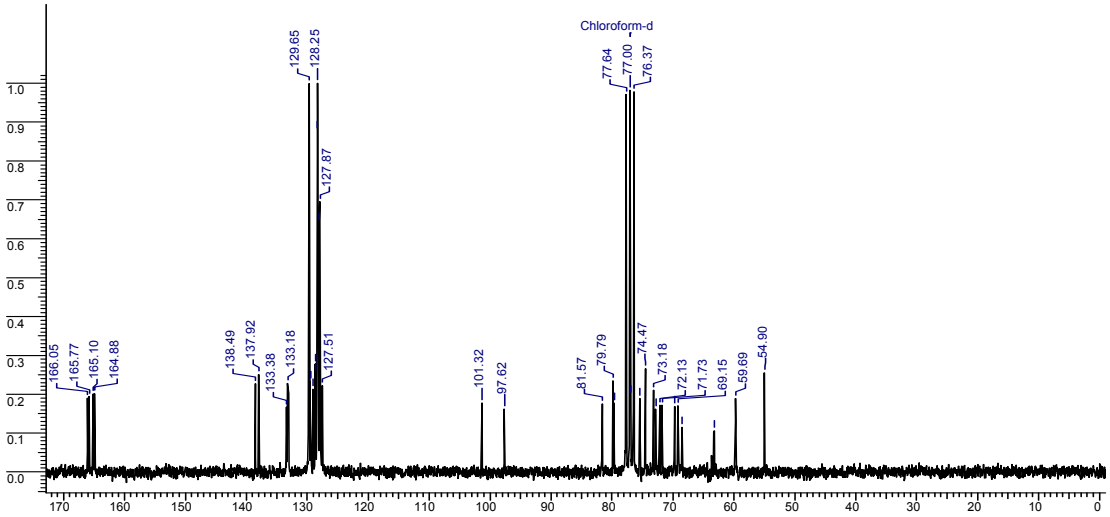
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **67**



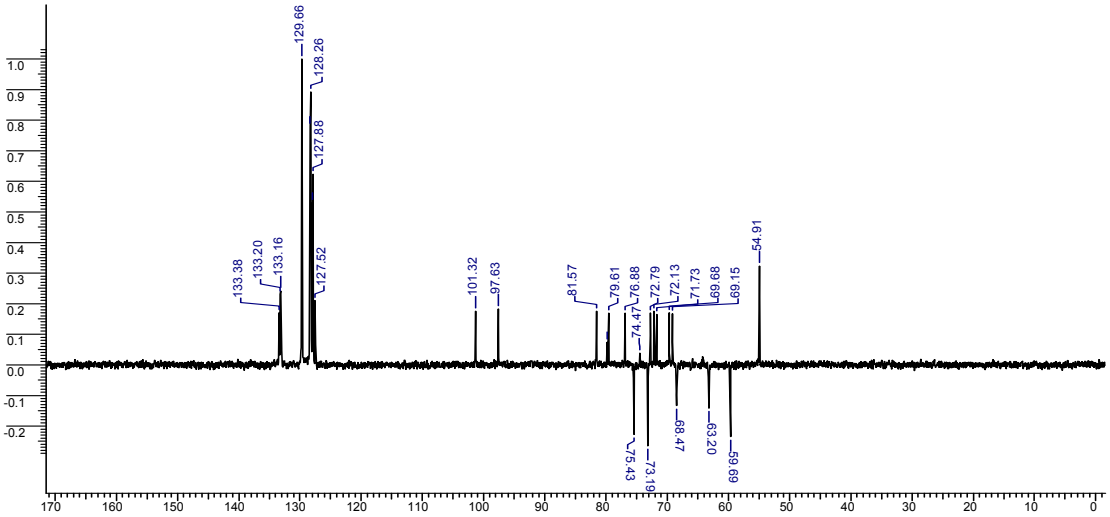
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **68**



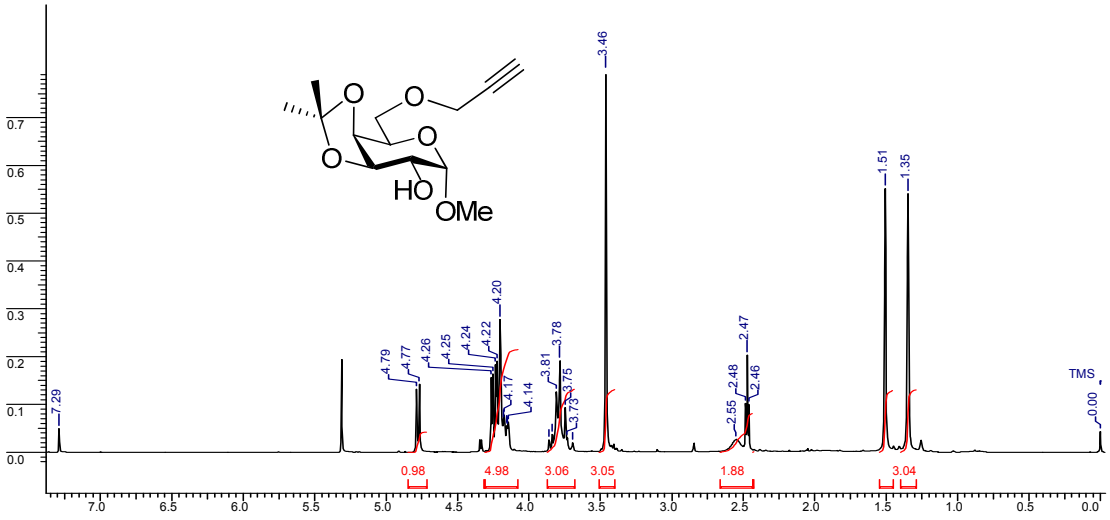
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **68**



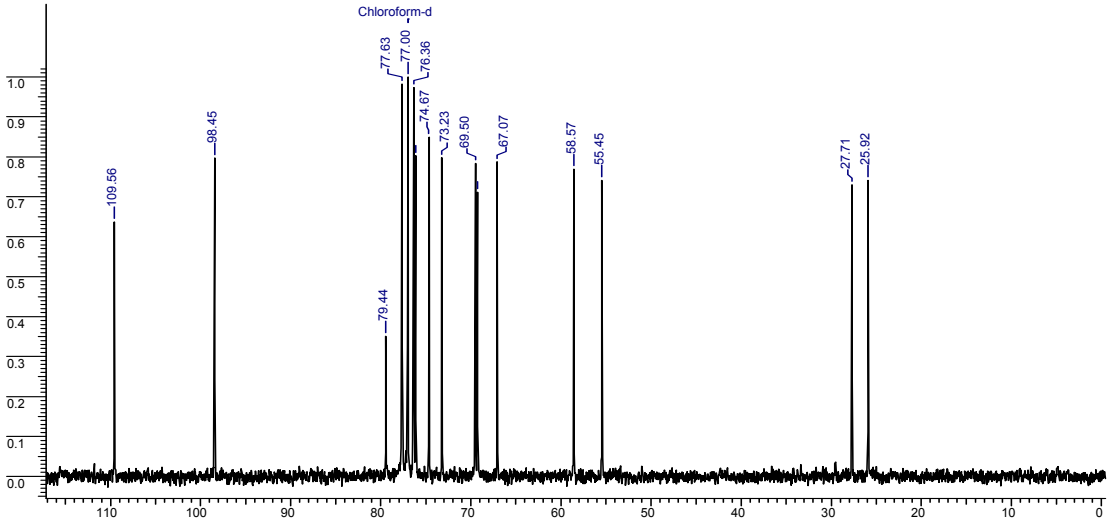
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **68**



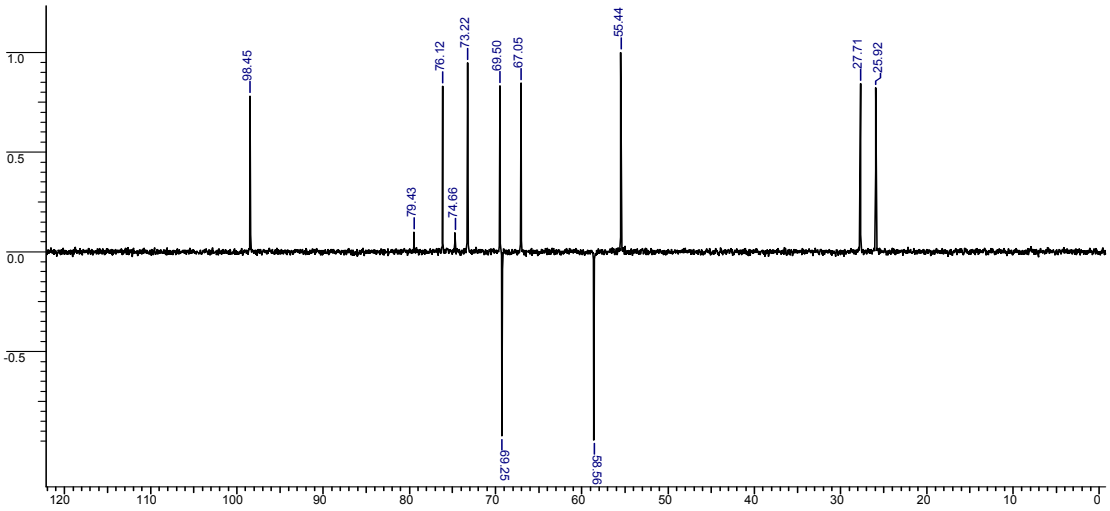
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **69**



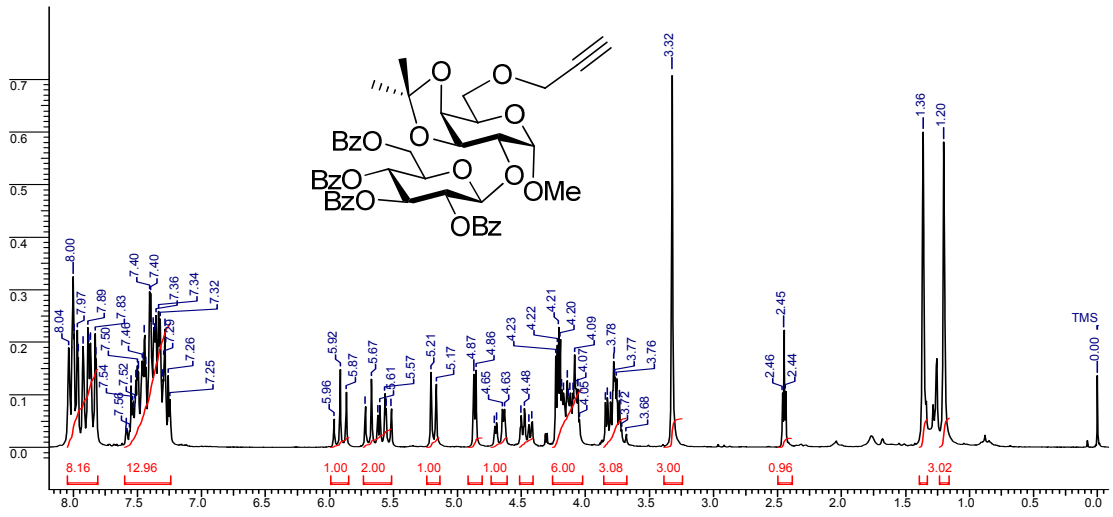
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **69**



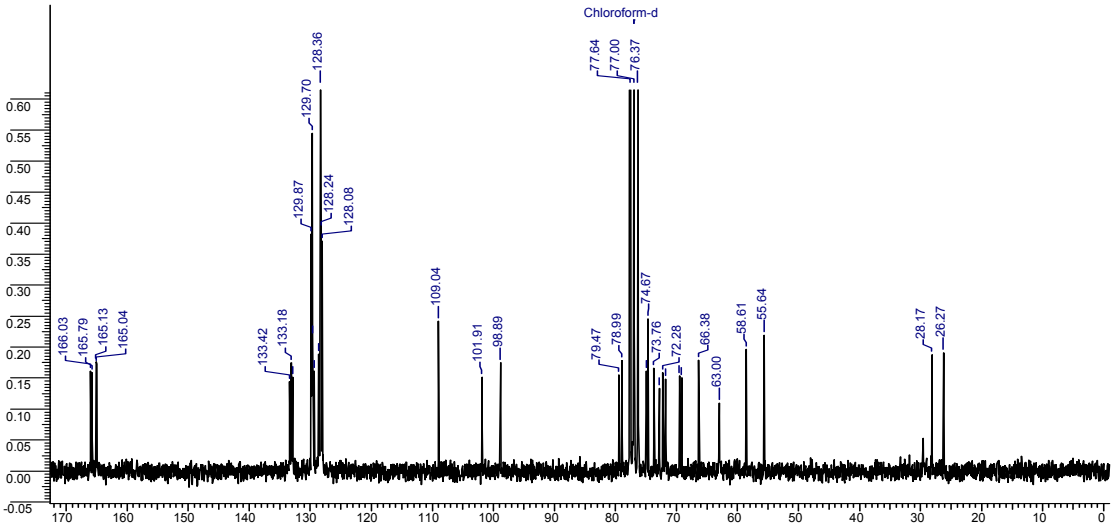
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **69**



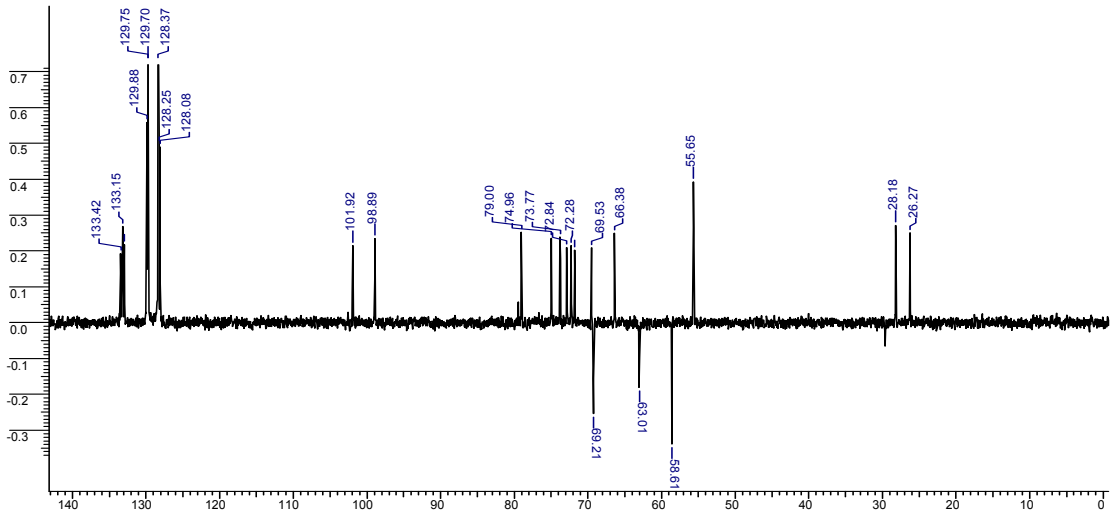
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **70**



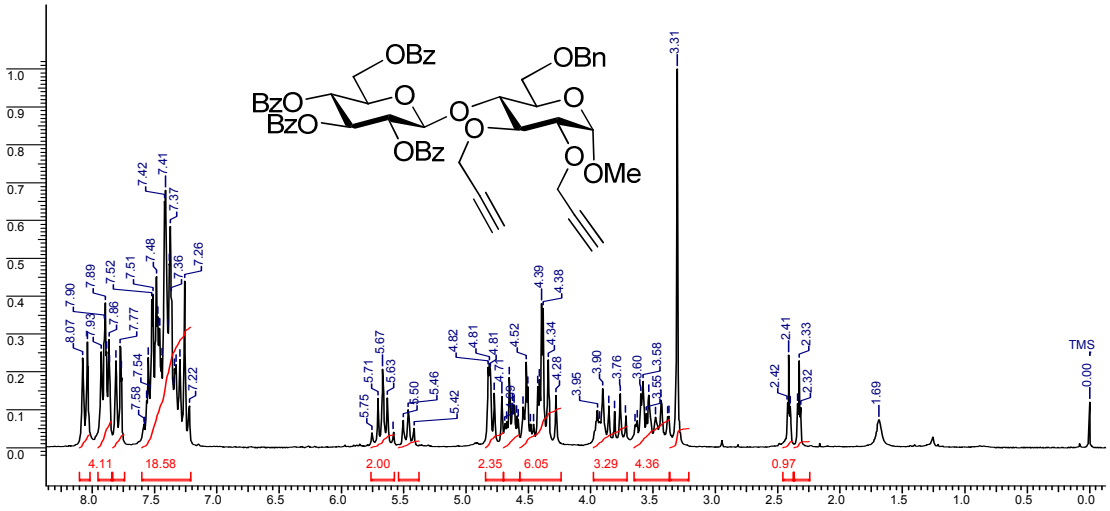
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **70**



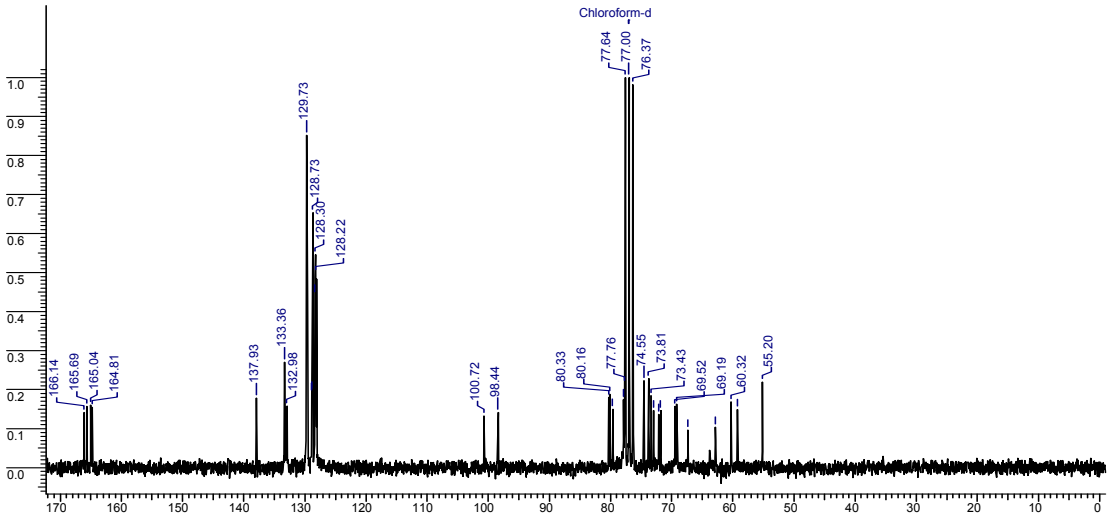
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **70**



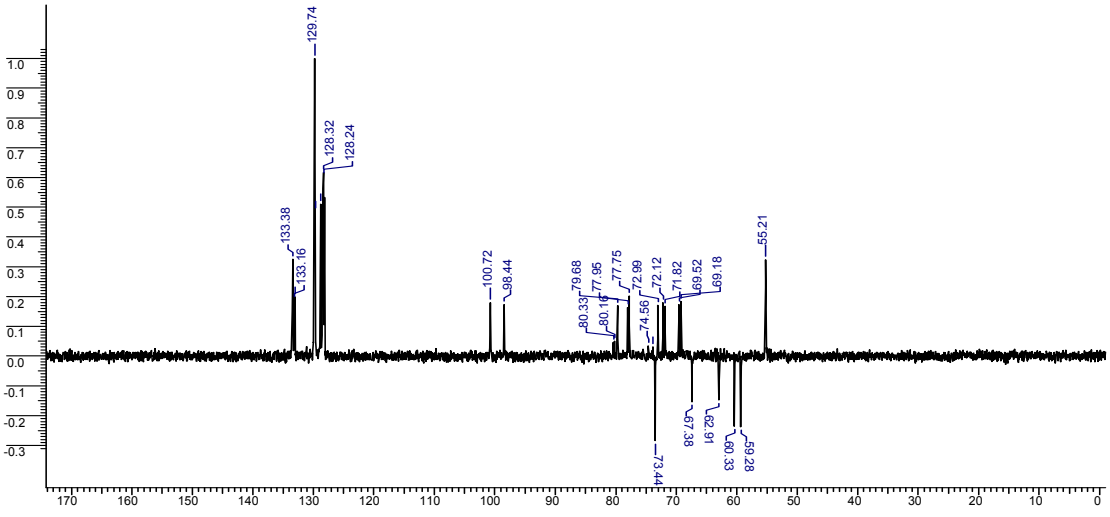
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **72**



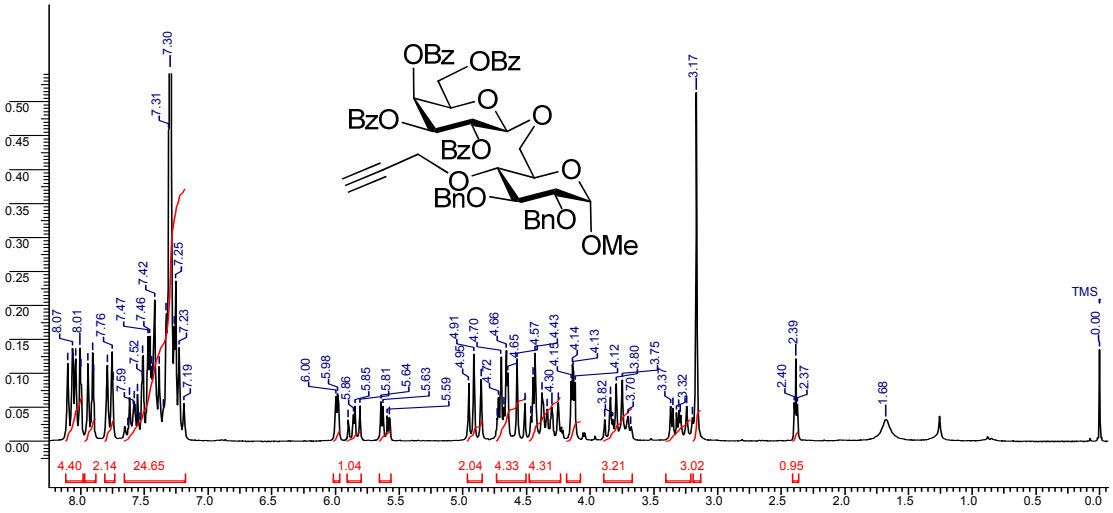
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **72**



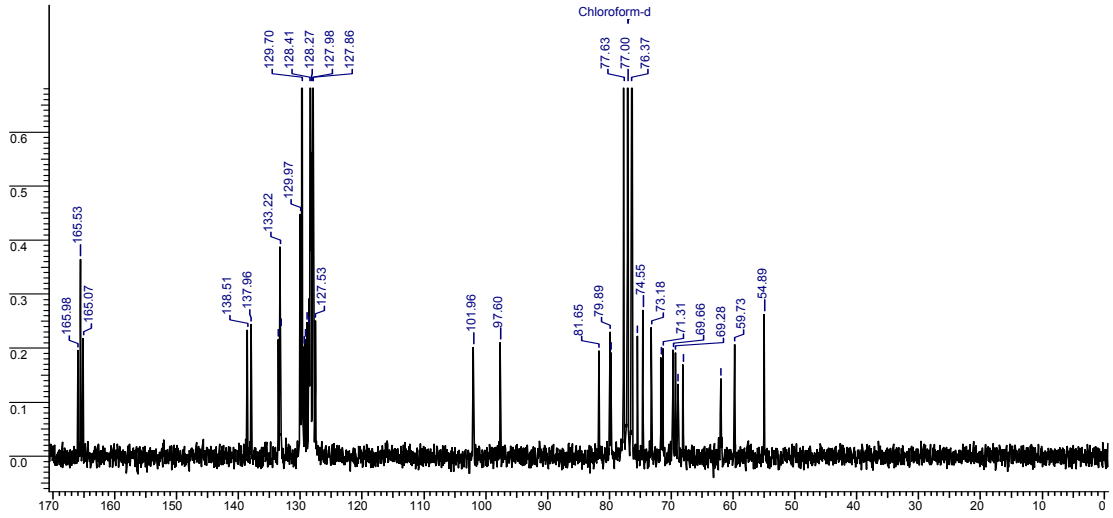
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **72**



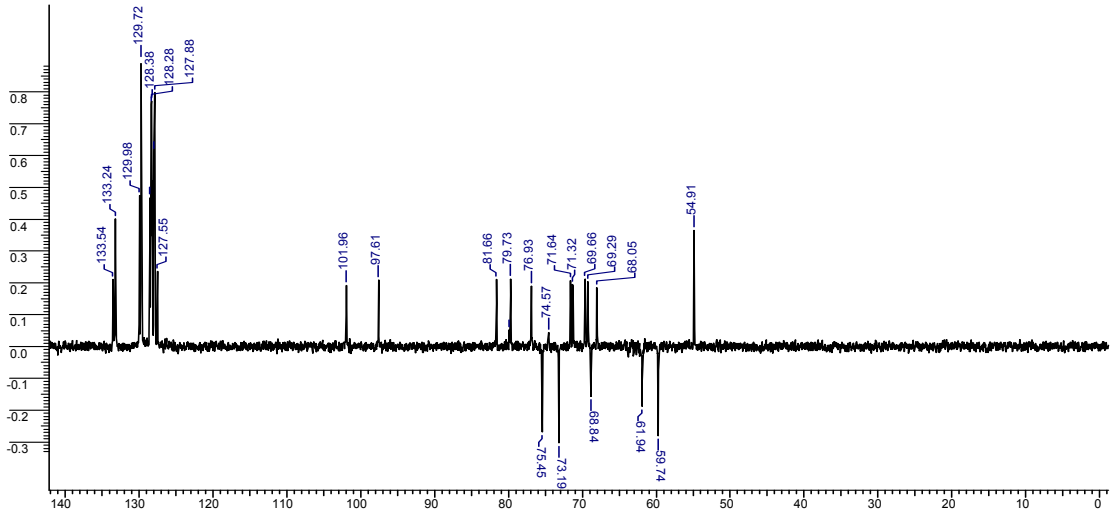
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **73**



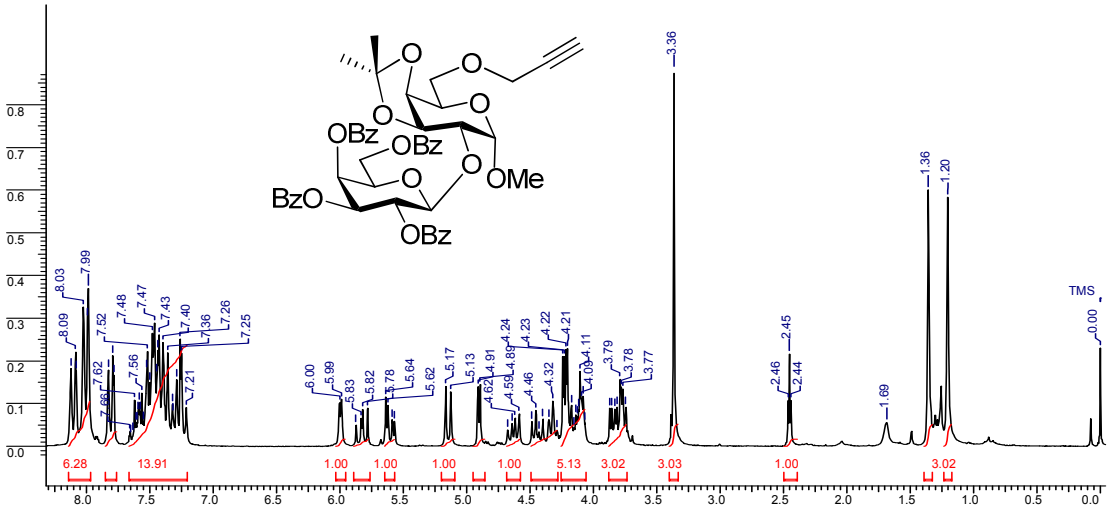
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **73**



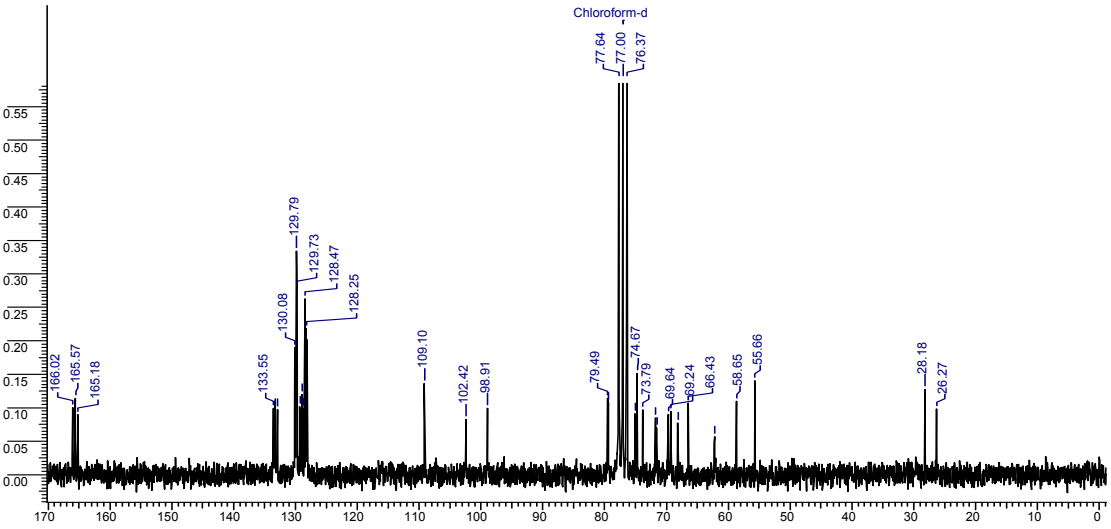
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **73**



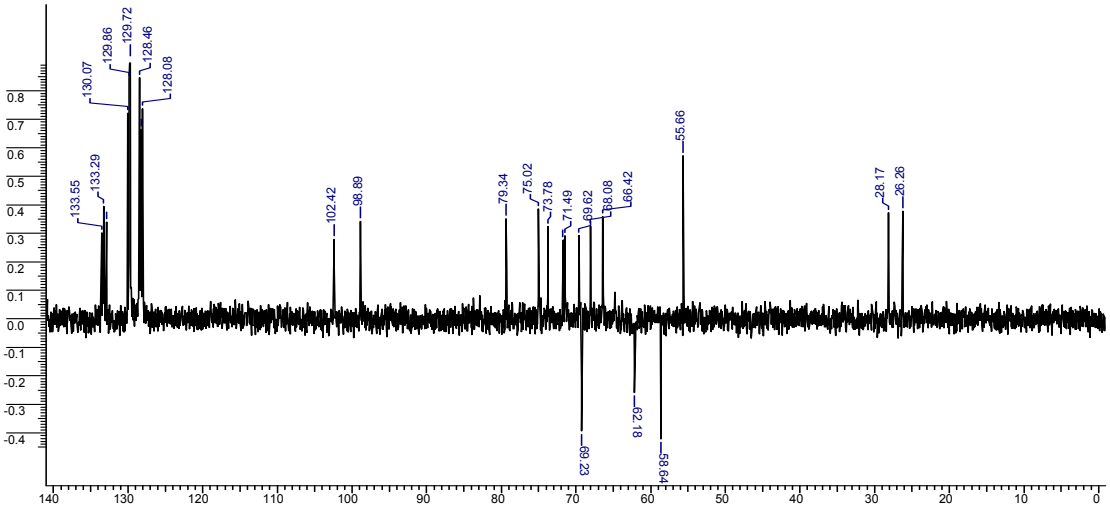
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **74**



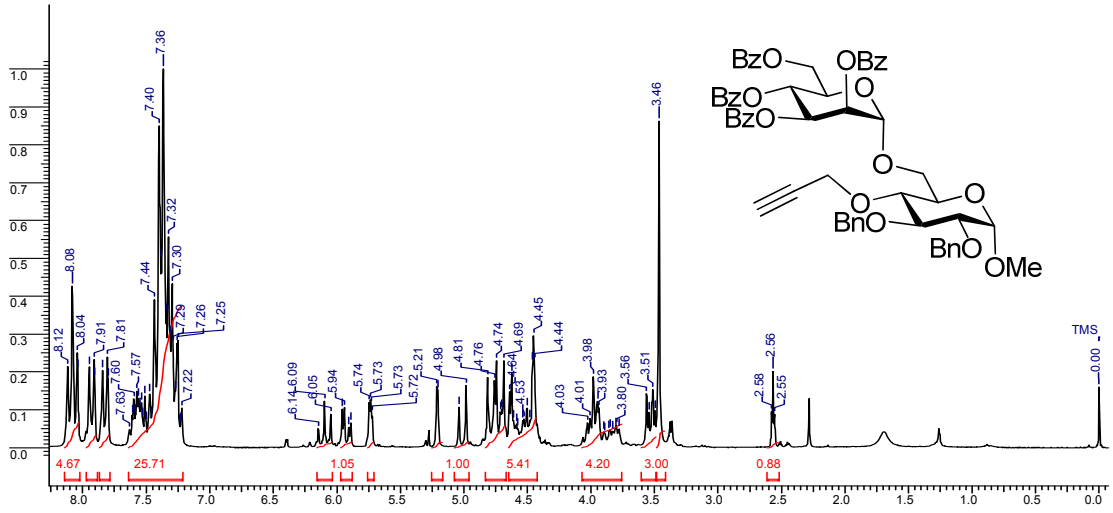
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **74**



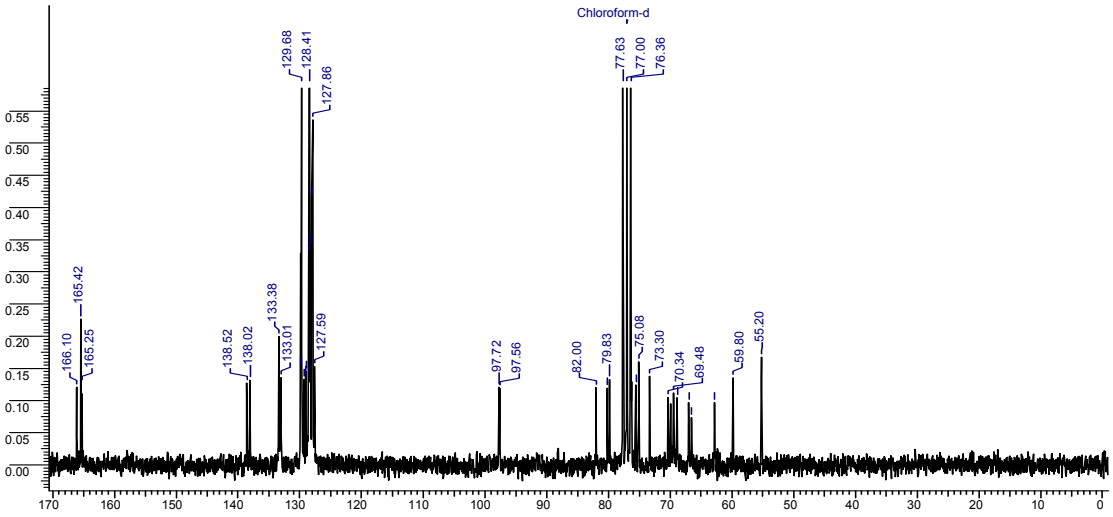
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **74**



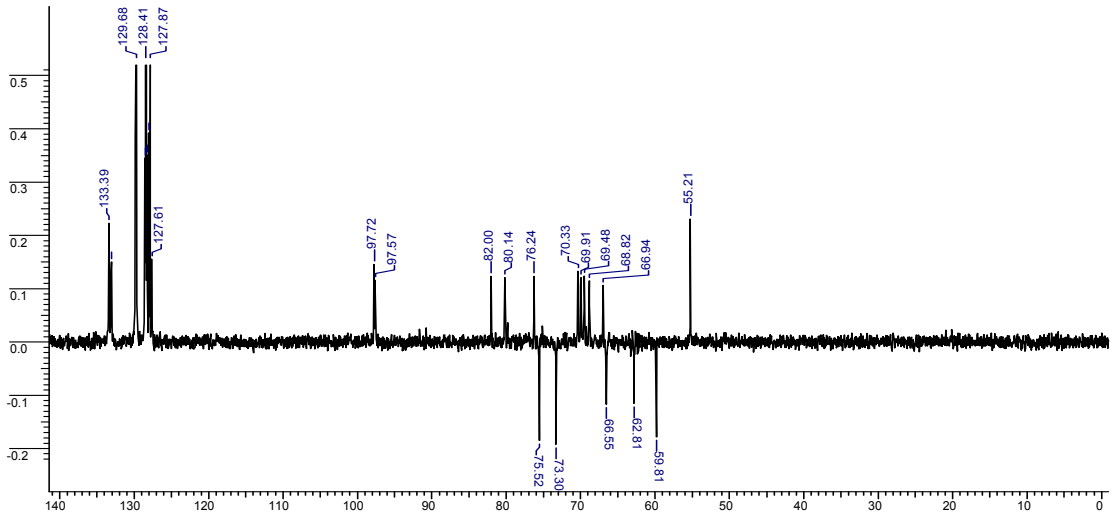
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **75**



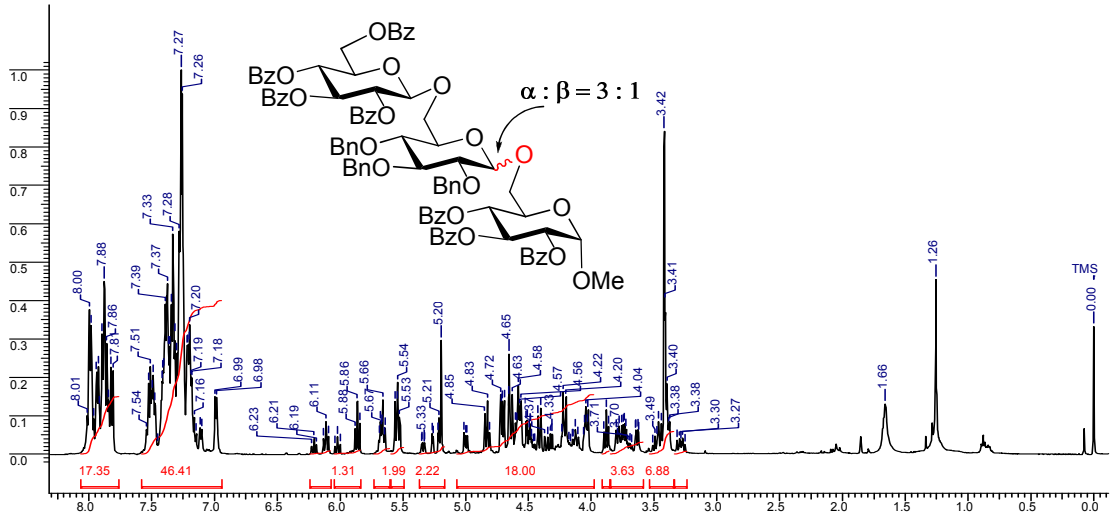
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **75**



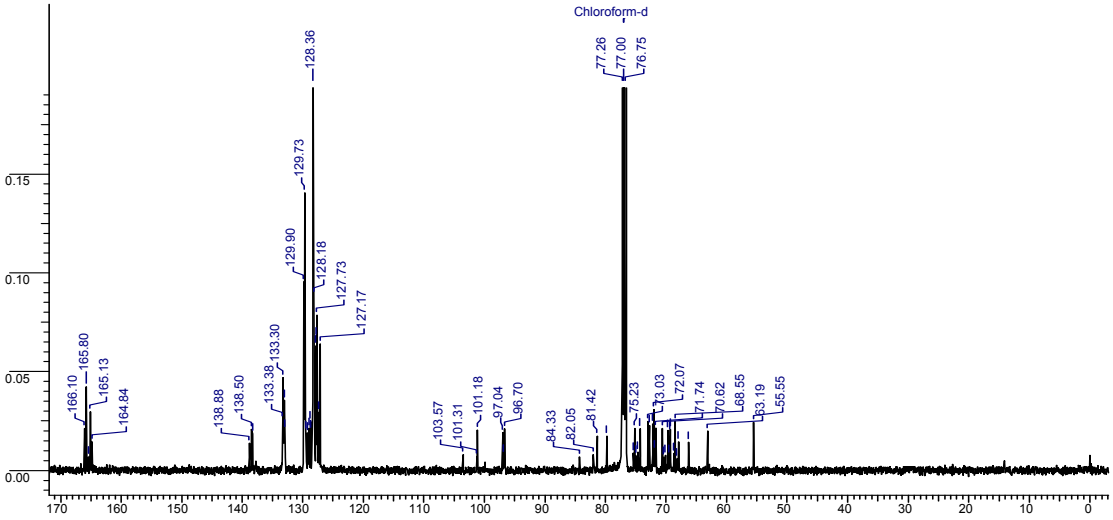
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **75**



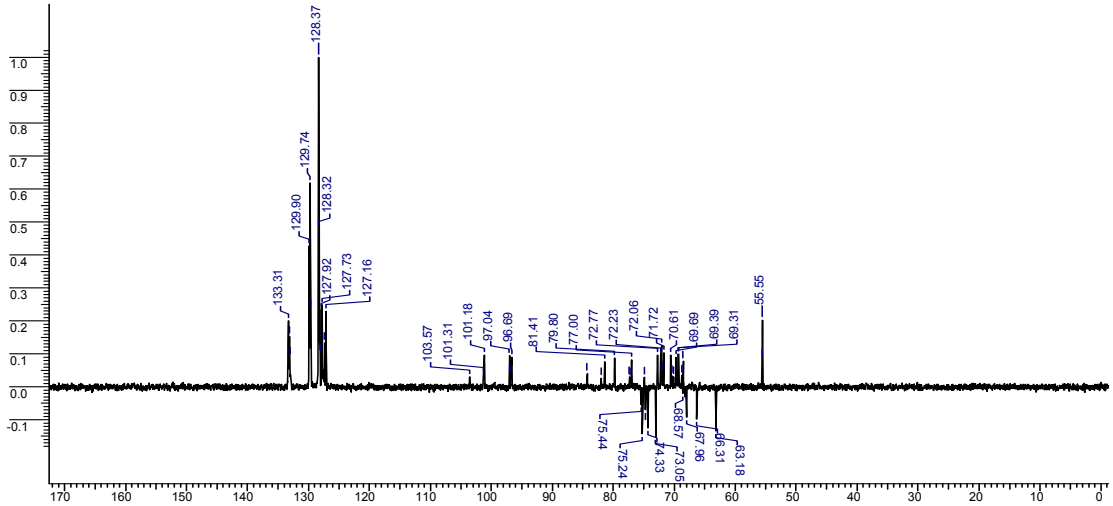
^{1}H NMR ($CDCl_3$, 500.13 MHz) of Compound **77 & 78**



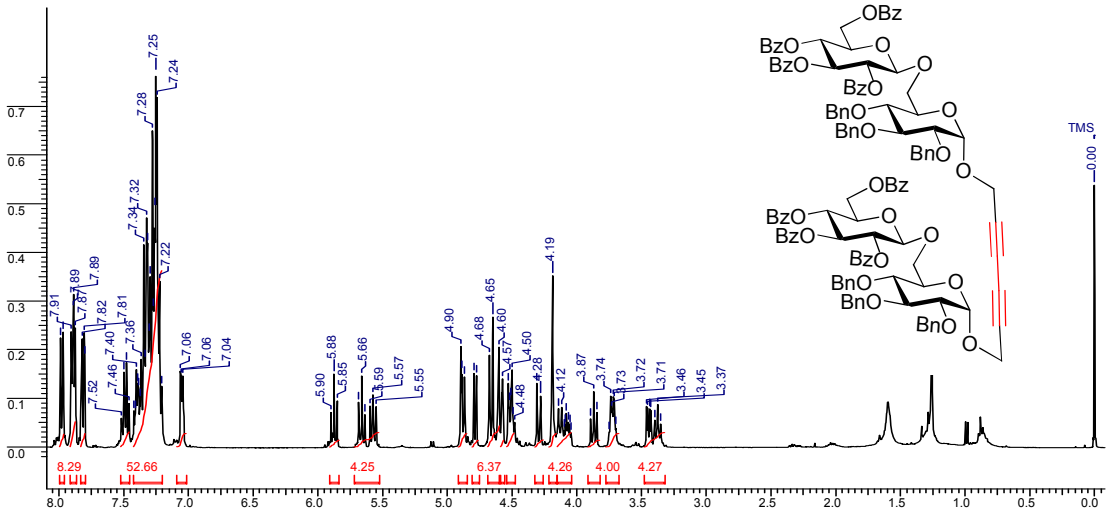
^{13}C NMR ($CDCl_3$, 125.76 MHz) of Compound **77 & 78**



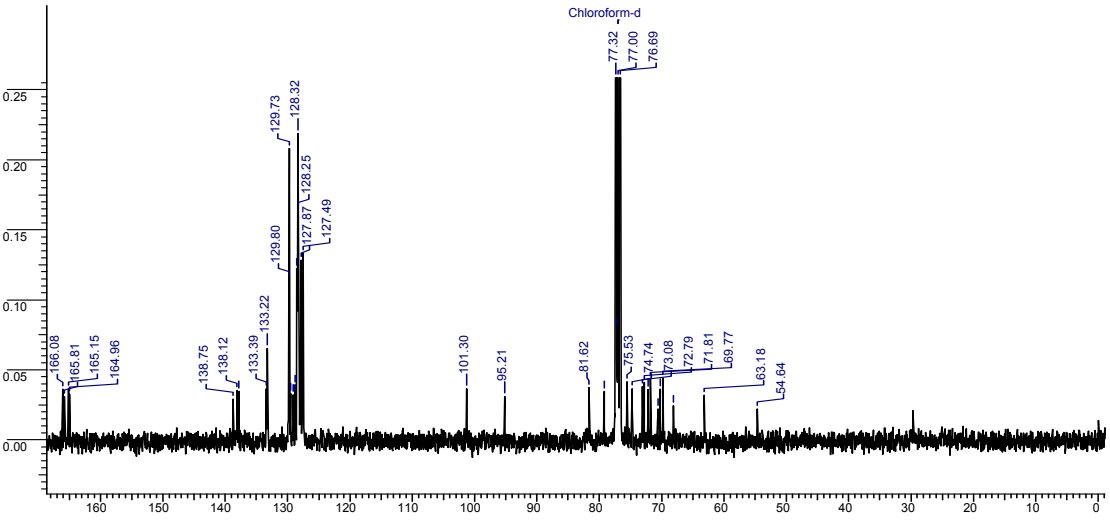
DEPT NMR ($CDCl_3$, 125.76 MHz) of Compound **77 & 78**



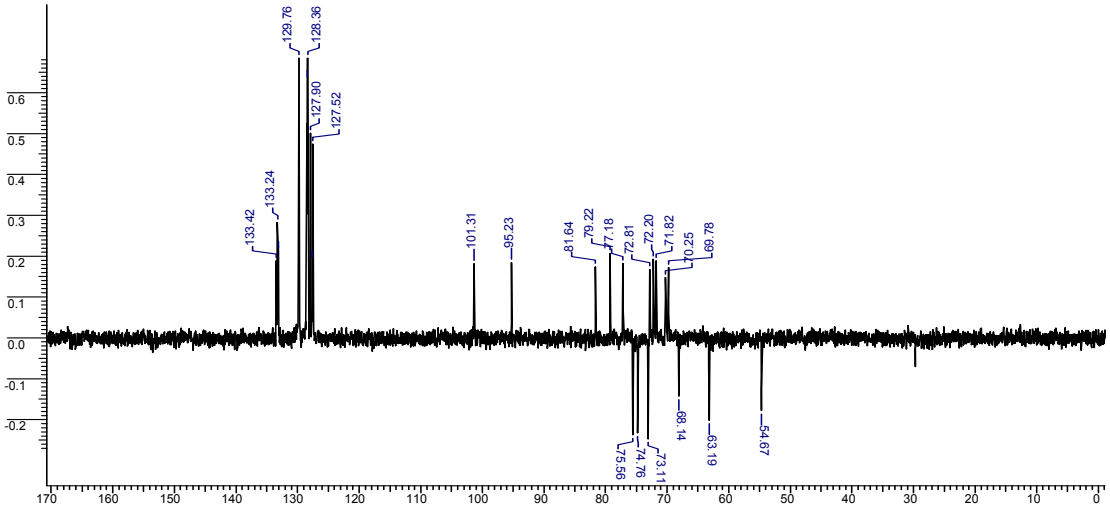
^{1}H NMR ($CDCl_3$, 400.13 MHz) of Compound **79**



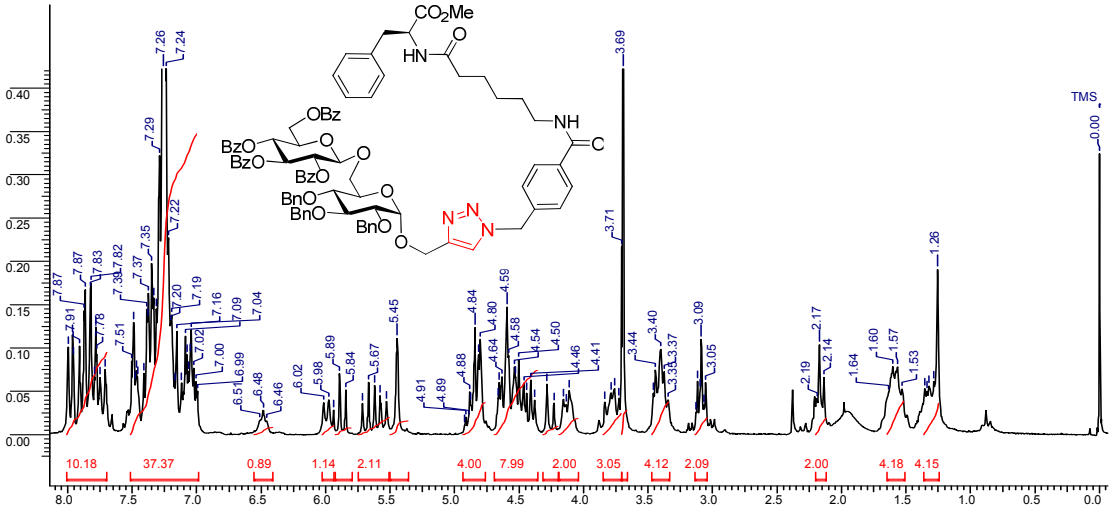
^{13}C NMR ($CDCl_3$, 100.61MHz) of Compound **79**



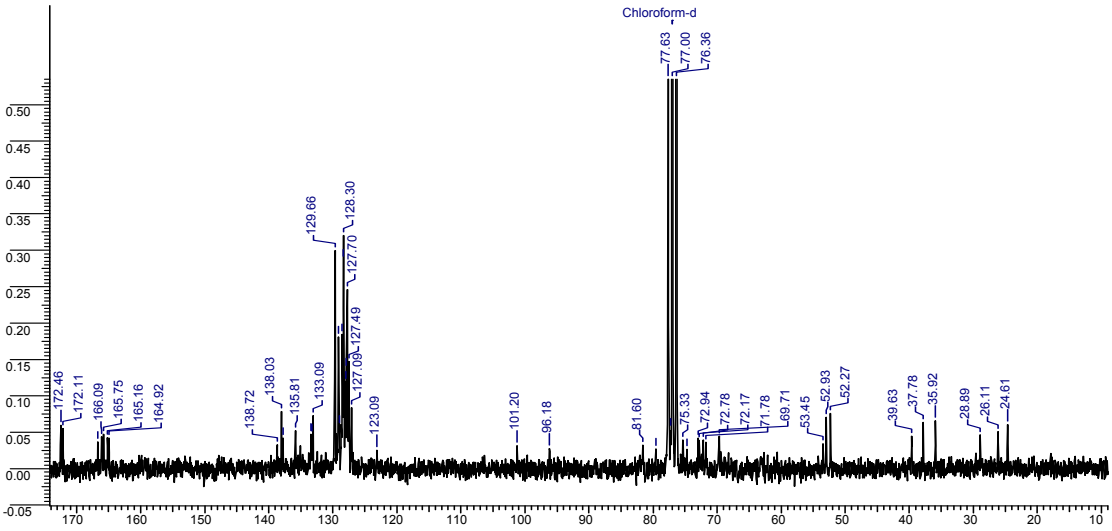
DEPT NMR ($CDCl_3$, 100.61MHz) of Compound **79**



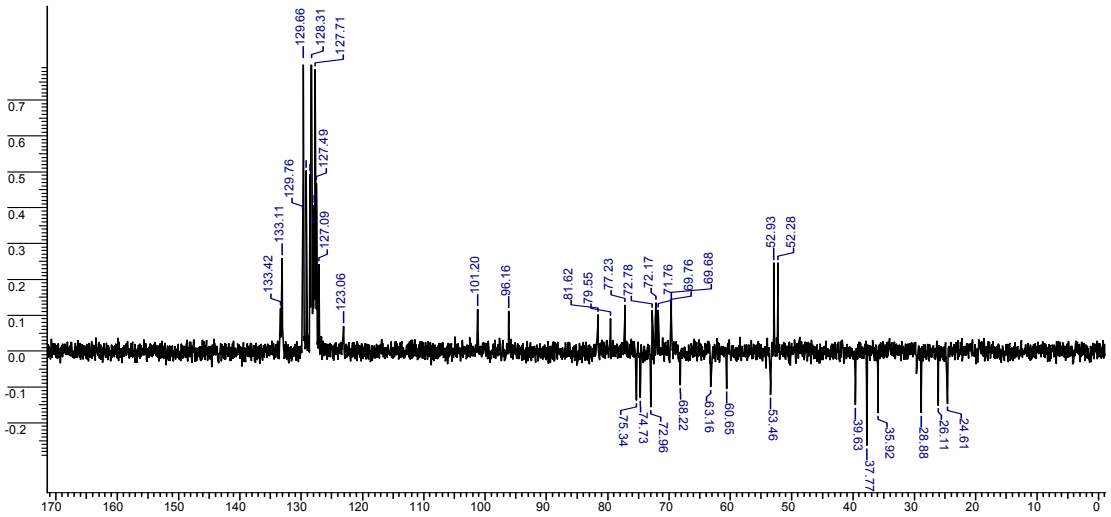
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **81**



^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **81**



DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **81**



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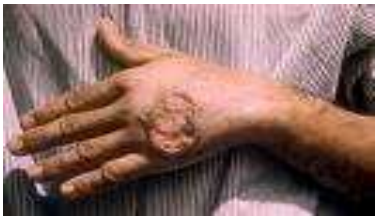
Chapter II

Synthesis of Tetrasaccharide Cap of The Lipophosphoglycan Expressed on The Cell Surface of Leishmania Parasite

Introduction

The wide spread disease *Leishmaniasis* is caused by protozoan parasites of the genus *Leishmania* and is currently found in nearly 88 countries where *Leishmaniasis* annually affects more than 2.4 million people and kills over 59,000 people.[1] In 1901, Scottish pathologist William Boog Leishman identified certain organisms in smears taken from the spleen of a patient who had died from *"dum-dum fever"*. Initially, these organisms were considered to be trypanosomes, but in 1903 Donovan described them as being new. The link between these organisms and kala azar was eventually discovered by Major Ross, who named them *Leishmania donovani*. The *Leishmania* genus had been discovered and the disease is recalled as *Leishmaniasis.* Before that, the disease is known with different names such as White leprosy, Black fever, Orient Boils, Valley sickness, Andean sickness etc. Later, *Leishmaniasis* divided into three forms namely *cutaneous Leishmaniasis, mucocutaneous Leishmaniasis* and *visceral Leishmaniasis.*[2]

Cutaneous Leishmaniasis



It is caused by various *Leishmania* species such as *L. braziliensis, L. major, L. tropica* and *L. mexicana*. *Cutaneous Leishmaniasis* normally produces skin ulcers on the exposed parts of the body such as the face, arms and legs. The disease can produce a large number of lesions sometimes up to 200 causing serious disability and invariably leaving the patient permanently scarred. Cutaneous infections are most common in Afghanistan, Brazil, Iran, Peru, Saudi Arabia and Syria.

Mucocutaneous Leishmaniasis

In *mucocutaneous Leishmaniasis*, lesions can lead to partial or total destruction of the mucous membranes of the nose, mouth and throat cavities and surrounding tissues. These disabling and degrading forms of *Leishmaniasis* result in victims being humiliated and cast out from society. Mucocutaneous infections are most common in Bolivia, Brazil and Peru.

Visceral Leishmaniasis

It is well characterized by irregular bouts of fever, substantial weight loss, swelling of the spleen and liver, and sometimes anaemia. *Leishmania* species such as

L. donovani, *L. infantum* are the causative agents for *visceral Leishmaniasis*. The parasite mainly attacks the internal organs such as liver, spleen (hence 'visceral') and bone marrow and if left untreated will almost result in death of the host. It is the second-largest parasitic killer in the world after malaria and the death due to *visceral Leishmaniasis* is non-countable as compared to the other two forms. *Visceral Leishmaniasis* are found in tropical and subtropical areas of all continents except Australia and the visceral infections are most common in Bangladesh, Brazil, India, Nepal, Sudan and some parts of china such as Sichuan Province, Gansu Province.

Treatment for *Leishmaniasis*[3]

Pentavalent antimonials, meglumine antimoniate (Glucantime), sodium stibogluconate (Pentostam) and pentamidine are initially used as drugs for various *Leishmaniasis*. Unfortunately, pentavalent antimonials based drugs are resistant to several patients in many parts of the world, also have significant side effects and moreover, they are expensive. Later, pentamidine is used when antimonials based drugs are ineffective. In parallel, another drug Miltefosine (Impavido) is identified for *Leishmaniasis*. Interestingly, it is observed that Miltefosine is effective against *L. braziliensis*, *L. mexicana* and towards the patients who are residing in the area of Africa. It is the first oral drug identified for *visceral* and *cutaneous Leishmaniasis.* Another drug paromomycin is reintroduced for the treatment of *visceral Leishmaniasis* and had originally been identified in 1960's. But, it is abandoned because it would not be profitable as the disease mostly affects poor people. Despite of many efforts in chemotherapy, no effective vaccine for any form of *Leishmaniaisis* has emerged yet.

Life Cycle of the *Leishmania* parasites[4]

The life cycle of *Leishmania* parasites is complex, which is implicated in the sand fly as well as the host macrophages as shown in figure 1. The *Leishmania* parasites are transmitted to the host mammal's blood stream by female sand flies of the genus *Phlebotomus* or *Lutzomyia* while feeding blood. Generally, *Leishmania* parasitic cells have two morphological forms: (i) promastigote and (ii) amastigote. The parasite initially lives as an extracellular, flagellate promastigote form in the digestive tract of sand fly and these promastigotes are enriched with lipophosphoglycans (LPGs) on its entire surface including flagellum.[4a]

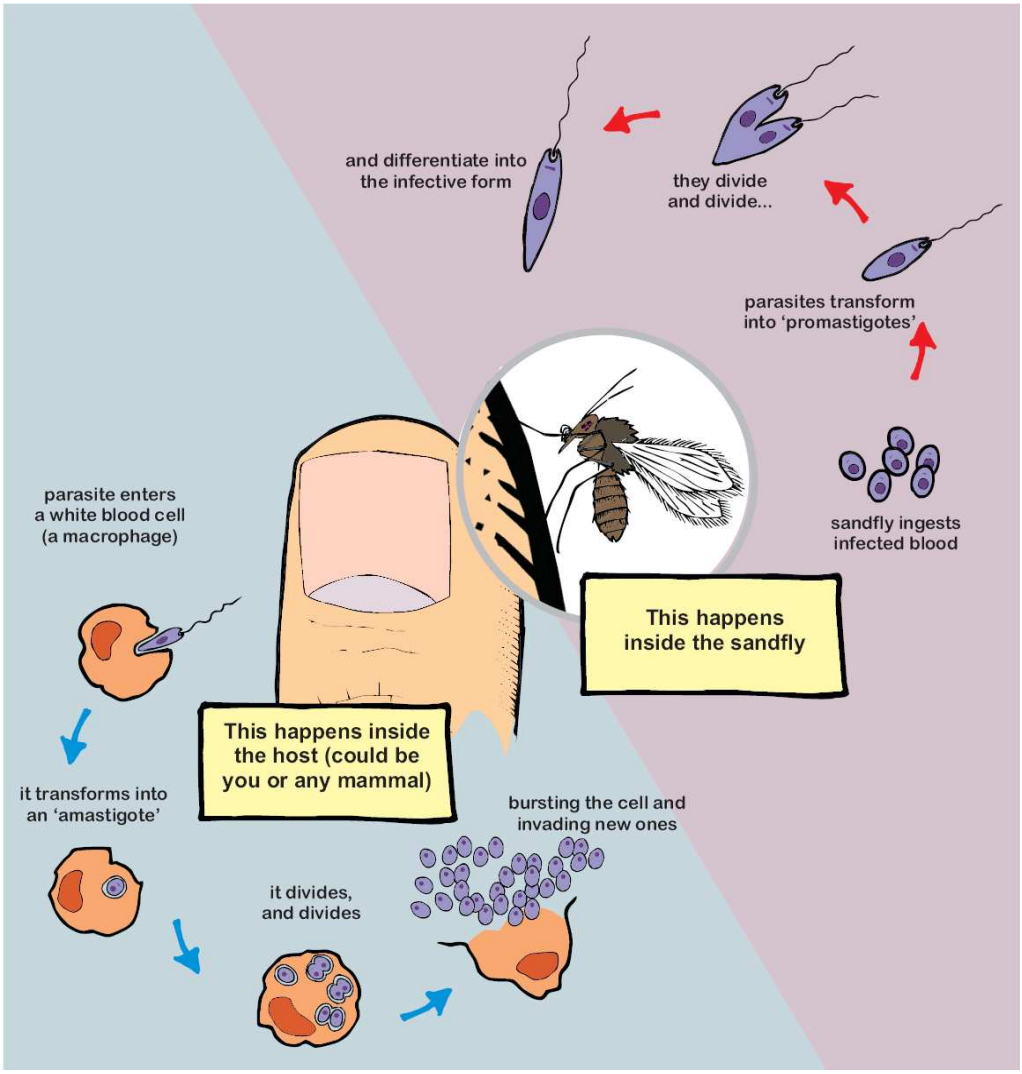


Figure 1

While biting, infective promastigotes of the *Leishmania* resist lysis by complement, a process mediated by lipophosphoglycan (LPG) and at the same time, the macrophages ingested the parasites. Macrophages are white blood cells that ingest foreign materials and key players in the immune response to foreign invaders such as infectious microorganisms. Later, the parasites are taken up into the phagolysosome. During this period, some of the LPG is deposited on the surface of the macrophage and internal vesicles to play a significant role in modulating the host signal transduction. Soon after entry, the parasites opposing the host defences such as oxidants and hydrolytic enzymes, inhibit macrophage activation required to kill the foreign materials and subsequently, transformed from flagellate promastigote to non-

flagellate amastigote. The newly formed amastigote is survived under hydrolytic conditions and further replicates within an acidified phagolysosome.[4b] Upon maximum multiplication of amastigote, the infected macrophages lyse and release amostigotes to the surrounding environment where they can infect other macrophages. All promastigotes synthesize LPG. In contrast, amastigotes do not synthesize LPG but they contain several glycoconjugates related to LPG such as proteophosphoglycan, acid phosphatise and glycophosphatidylinositol lipids. The resultant macrophages infected with amastigotes ingested by a second sand fly which initially resides within the blood meal. The released amastigotes from the macrophages differentiate into the procyclic promastigote in the peritrophic membrane of the sand fly midgut and subsequently, they acquire a coat of procyclic form of LPG and begun to multiply. After the blood meal is digested, the parasites cease dividing and transformed into the metacyclic promastigotes which is then moved to midgut wall of the sand fly.[4c] These virulent forms detach from the gut wall and migrate to mouthparts of the sand fly for the next infectious bite. The life cycle is completed when a sandfly bites an infected host and the parasite is present in the bloodmeal.

Lipophosphoglycan[5-12]

The promastigote form of *Leishmania* parasites is covered with a thick glycocalyx composed primarily of a single macromolecule termed lipophosphoglycan (LPG).[5] LPG has been implicated in many biologically important roles. For example, LPG (i) protects the parasites in the sand fly midgut; (ii) attaches the parasites to the sand fly midgut epithelium; (iii) protects the parasites against complement attack; (iv) is implicated in binding and uptake by macrophages; (v) modulating the macrophage signal transduction; (vi) protects the parasites from toxic macrophage products such as oxidants, hydrolytic enzymes; (vii) allowing the parasites to establish successful infections. Therefore, the cell-surface lipophosphoglycans (LPGs) of the *Leishmania* pramastigotes play a key role in the protection, survival and the infectivity of the *Leishmania* parasites throughout their life cycle. Each parasite cell contains several million molecules of LPG which is heterogeneous, lipid containing polysaccharide and contains four domains[6] namely a neutral oligosaccharides cap at the terminal non-reducing end, a variable phosphoglycan repeating units, [6Gal*p*-(β1 ⟶4)-Man*p*-α1-phosphate]$_n$ (M_r 5000-40000), a conserved phosphosaccharide core with an internal

galactofuranose residue, and a 1-*O*-alkyl.*lyso*glycosylphosphatidylinositol (GPI) anchor as shown in figure 2.

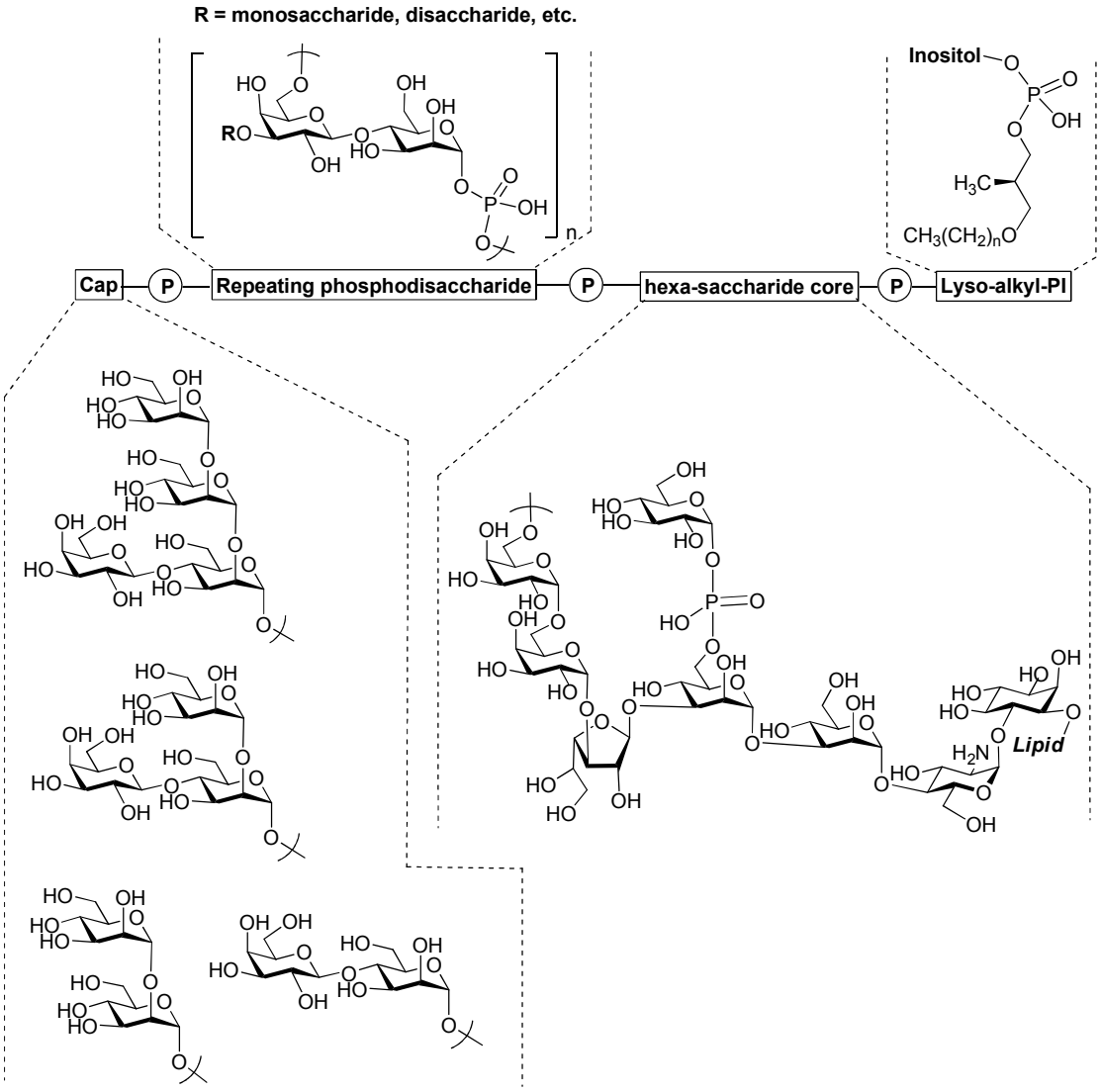


Figure 2

Structural features of lipophosphoglycans (LPGs)

Lipid Anchor of LPG

- The polysaccharide portion of LPG is attached by the unusual phospholipid derivative 1-*O*-alkyl-2-*lyso*-phosphatidyl-*myo*-inositol. LPGs of the *Leishmania* species *L. donovani*, *L. major and L. mexicana* contains an aliphatic hydrocarbon chain either C_{24} or C_{26} saturated and unbranched (Figure 2).[6c-d,7]

- Tentative structure activity relationship suggested that the lipid moiety helps to anchor the oligosaccharide (or protein) to the plasma membrane.[8]

Phosphosaccharide core of LPG

- Attached to the inositol of the lipid anchor of LPG is the phosphosaccharide core region. In *L. donovani*, *L. major,* and *L. mexicana*, the glycan core composed of an unacetylated glucosamine, two mannoses, a galactose-6-phosphate, a galactopyranose and a galactofuranose (Figure 2).[6b,e,9]
- The presence of internal galactofuranose is extremely unusual in eukaryotic glycoconjugates. As with all reported GPI anchored proteins reported so for[10], LPG possesses Man*p*-(α1⟶4)-GlcN*p*-(αl⟶6)-*myo*-inositol-l-PO_4 *motif*. The LPG of *L. donovani* and *L. mexicana* possess a glucosyl-α1-phosphate attached in phosphodiester linkage to the C-6 hydroxyl of the proximal mannose residue.[6d,e] A substantial percentage of the *L. major* LPG also contains the identical glucosyl-αl-phosphate substitution, while the remainder does not.[6b]
- Another interesting sequence in the core region is the Gal(αl⟶3)Gal unit, which is reportedly the epitope for circulating antibodies in patients with *Leishmaniasis*.[11]

Repeating units of LPG

- The repeating phosphoglycan contain multiple units of a backbone structure of [6Gal*p*-(β1⟶4)-Man*p*-α1-phosphate]$_n$ as shown in figure 2.[6a-b,11] One of the noteworthy features of the backbone is the 4-*O*-substituted mannose residue, which is not present in any other known eukaryotic glycoconjugate.
- The LPG of *L. donovani*[6a,12] contains no other substitutions in the backbone sequence whereas in the *L. mexicana* LPG, approximately 25% of galactose residues are substituted at the C-3 hydroxyl with βGlc residues.[6e] As in the case of *L. major* LPG, the repeating units are more complex; however, approximately 87% of the galactose residues in the back bone structure are further substituted with small monosaccharides such as galactose, glucose and arabinose (in furanose form) from one to four residues.[6b]
- The structure activity relationship[8] revealed that phosphoglycan repeats to form a helical structure and is presumed to form a macromolecular diffusion barrier thereby it prevents the binding of host's antibodies to the LPG epitopes.

Neutral oligosaccharides cap of LPG

- LPG is terminated at the non-reducing end with several small neutral oligosaccharides containing galactose and mannose residues. *Leishmania* species contains the tetrasaccharide Gal*p*-(β1⟶4)-Man*p*-(α1⟶2)-Man*p*-(α1⟶2)-Man*p*(α1), the trisaccharide Gal*p*-(β1⟶4)-Man*p*-(α1⟶2)-Man*p*-(α1⟶2) and the disaccharides Gal*p*-(β1⟶4)-Man*p*(α1) and Man*p*-(α1⟶2)-Man*p*(α1) as shown in figure 2.[6b,e]
- Also, the tetrasaccharide contains Gal*p*-(β1⟶4)-Man*p* linkages like phosphoglycans which is unusual and is not present in any other known eukaryotic glycoconjugate.
- Tentative structure activity relationship[8] revealed that the oligosaccharide cap is thought to attach the parasite to the digestive tract of the sand fly and may also contain an epitope responsible for recognition by the mammalian host macrophages.

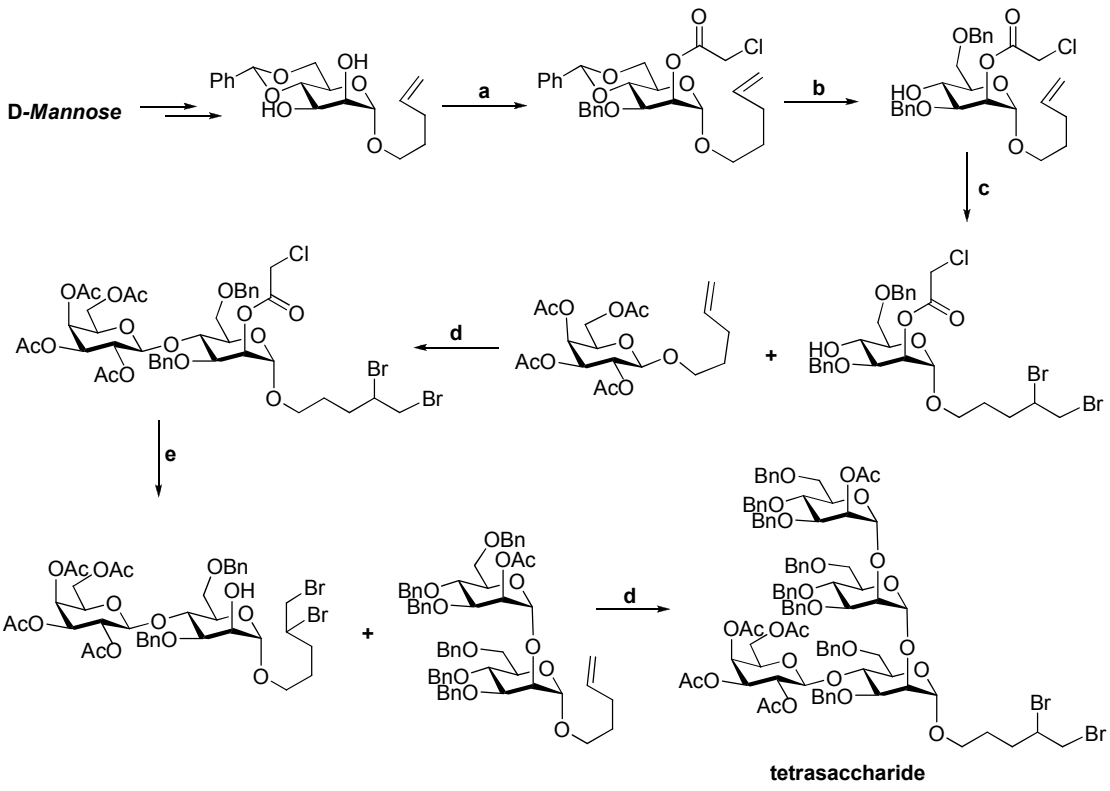
Because of the most abundant nature of LPG in the promastigotes of the *Leishmania* parasites and its role in the parasite's life cycle, LPG is viewed as a new target for identification of the chemotherapeutics. Also, the presence of unique oligosaccharide structures on the surface of various *Leishmania* species has been attracted synthetic carbohydrate chemists to create possible vaccines against *Leishmaniasis*. In particular, a unique tetrasaccharide and a variable phosphoglycans, which shows the unusual galactose-(β1⟶4)-mannosidic linkage that is xenobiotic to the human cells and is too attractive from a synthetic point. Though the synthetic work towards LPG is tough task for chemists, several groups have been interested to synthesize various structural fragments of the LPG[13] for further studies either to find out the significant roles in the human macrophages with more detail or to develop the vaccine against *Leishmaniasis*. Some approaches related to the synthesis of tetrasaccharide cap[13a-e], phosphoglycans[13f-m] and heptasaccharyl *myo*-inositol[13n] are described below.

Synthesis of tetrasaccharide cap

In 1996, Fraser-Reid *et al*. reported first synthesis for the tetrasaccharide cap of LPG by using *n*-pentenyl glycosides as glycosyl donor *via* convergent as well as linear approach (Scheme 1).[13a] In a convergent approach, initial attempt of glycosylation between *n*-pentenyl galactoside and the mannosyl acceptor in the presence of

NIS/TESOTf/CH_2Cl_2 offered the 1,2-*trans* disaccharide in 87%. Subsequently, the chloroacetyl group is removed using thiourea in refluxing ethanol to give the disaccharide acceptor. Final coupling of the dimannan donor (prepared from *n*-pentenyl glycoside) with the acceptor resulted in the formation of the tetrasaccharide in good yield.

Scheme 1

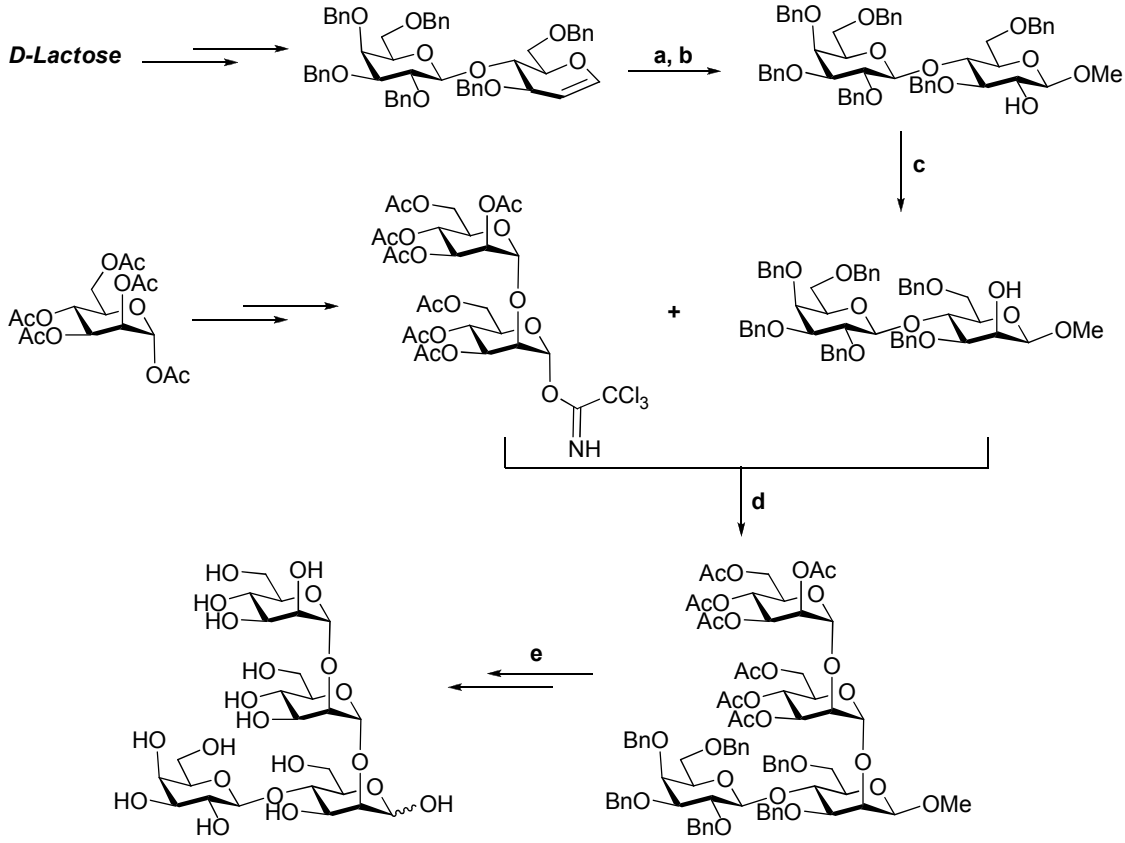


Reagents and conditions:
a) (i) Bu_2SnO, MeOH, reflux, 1h; (ii) Bnbr, DMF, 80-110 °C, 2h, 59% for two steps; (iii) $(ClCH_2CO)_2O$, Pyridine, CH_2Cl_2, 0-10 °C, 30min., 84%; b) Et_3SiH, CF_3CO_2H, CH_2Cl_2, 0-20 °C, 2h, 84%; c) Et_4NBr, Br_2, CH_2Cl_2, 0 °C, 86%; d) NIS, TESOTf, CH_2Cl_2, 87% for disaccahride and 69% for tetrasaccharide; e) Thiourea, $NaHCO_3$, EtOH/EtOAc, reflux, 2h, 86%

Four years later, Vishwakarma's group[13b] used linear strategy for the synthesis of the tetrasaccharide wherein hexa-*O*-benzyl lactal is treated with DMDO in acetone to undergo stereoselective α-epoxidation and subsequent ring opening of the epoxide with excess of anhydrous methanol at room temperature provided the corresponding β-lactoside in quantitative yield (Scheme 2). Further, an *equatorial* alcohol is inverted to an *axial* alcohol by oxidation followed by reduction. The upper half of the mannobiose donor is prepared as a trichloroacetimidate from mannose penta-*O*-acetate, which is allowed to react with the lower half Gal-Man acceptor in the presence

of TMSOTf/CH_2Cl_2/-30 ^oC to obtain the tetrasaccharide (67%). Global deprotection is achieved by debenzylation, deacetylation, acetylation, acetolysis and deacetylation to afford the fully deprotected tetrasaccharide in 41% yield.

Scheme 2

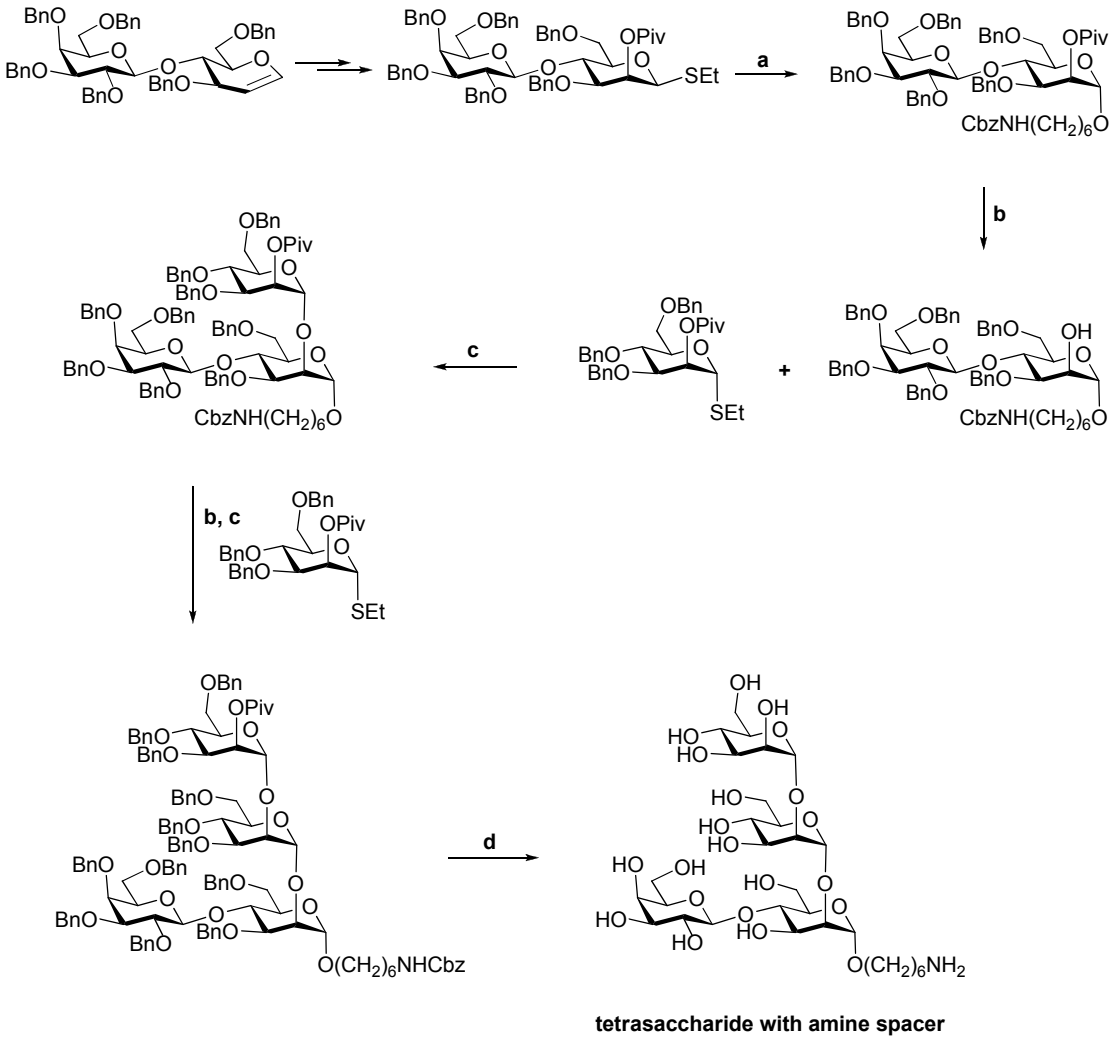


Reagents and conditions:
a) DMDO, CH_2Cl_2, 0 ^oC, 2h, 90%; b) MeOH, rt, 4h, 96%; c) (i) $(COCl)_2$, DMSO, -78 ^oC; (ii) $NaBH_4$, rt, 4h, 64% for two steps; d) TMSOTf, CH_2Cl_2, 45min., -30 ^oC, 67%; e) (i) $Pd(OH)_2$, H_2, 4h; (ii) NaOMe, MeOH, quant; (iii) Ac_2O/AcOH/H_2SO_4, rt; (iv) Na_2CO_3, MeOH, rt, 41% for two steps

Seeberger *et al*. reported the synthesis of tetrasaccharide in 2001,[13c] but an amine spacer is installed at the reducing end for the subsequent studies to develop a vaccine (Scheme 3). In this approach, epoxidation of hexa-*O*-benzyl lactal using DMDO followed by ring opening of the epoxide with ethanethiol in the presence of trace amounts of acid resulting in thioethyl lactose. Further, the stereochemistry of the hydroxyl group at the C-2 position is inverted by a two step oxidation-reduction process to give thioethyl galactose-β-(1 ⟶ 4)-mannoside. After pivoloyalation, thioethyl glycoside undergoes glycosylation with *N*-Cbz protected aminohexanol in

the presence of MeOTf to give α-glycoside. The resultant C-2-pivoloyl protected disaccharide is deprotected using sodium hydroxide to afford the disaccharide acceptor which is coupled with ethyl 2-pivaloyl-thio-α-D-mannopyranoside in the presence of MeOTf to obtain a trisaccharide in 66% yield. Further, elongation is carried out by repetition of the deprotection/coupling steps to get the fully protected cap tetrasaccharide equipped with an aminohexyl spacer on the reducing terminus. Global deprotection of the tetrasaccharide is achieved *via* a two step protocol involving saponification followed by palladium catalyzed hydrogenation.

Scheme 3

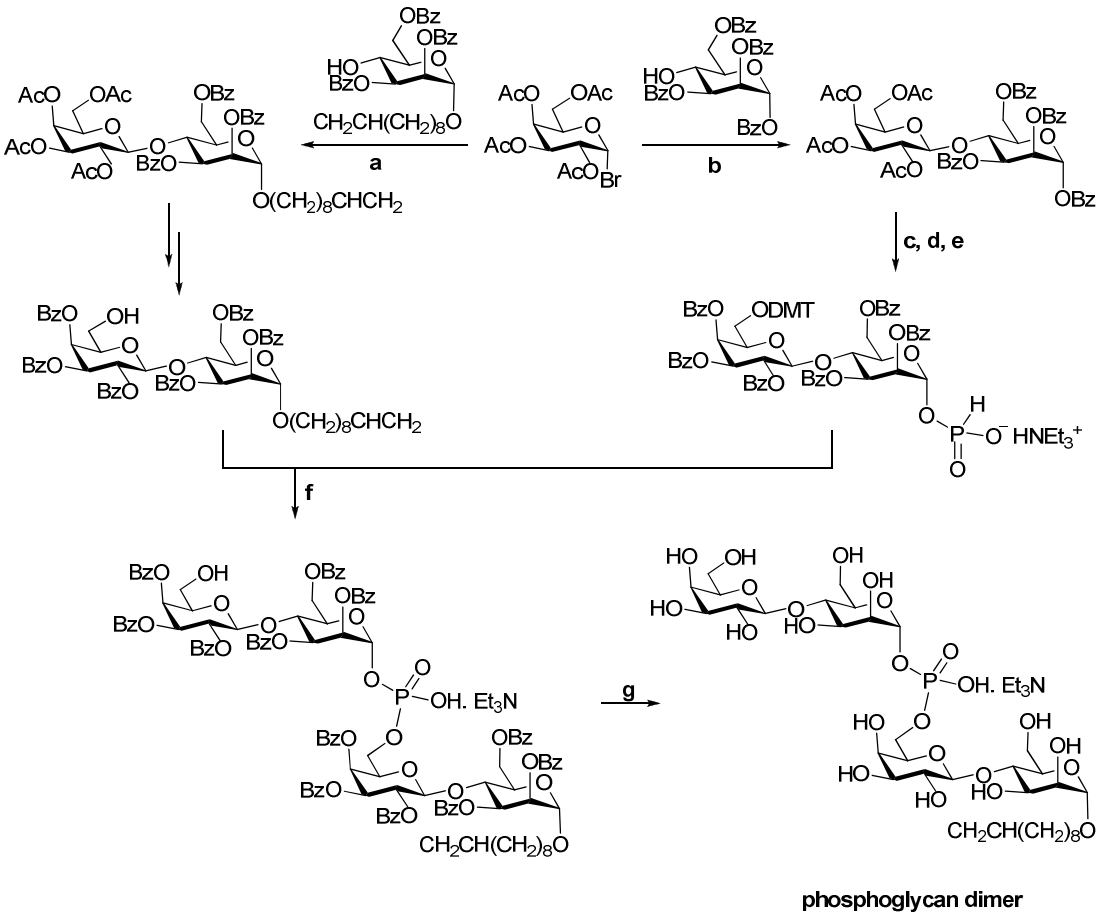


Reagents and conditions:
a) MeOTf, $HO(CH_2)_6NHCbz$, 54%; b) NaOH, MeOH/THF, 76%; c) MeOTf; d) H_2, Pd/C, CH_3OH, 53%

Synthesis of phosphoglycan

Nikolaev's group reported first synthesis for the *dimer, trimer* and *tetramer* of phosphoglycans (Scheme 4).[13f] In this approach, glycosylation reaction is carried out between 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide and 1,2,3,6-tetra-*O*-benzoyl-α-D-mannopyranose in the presence of silver triflate and 2,6-lutidine to get 1,2-*trans* disaccharide which is then treated with $Mg(OMe)_2$ in methanol to deprotect acetates selectively in the presence of benzoates. The resultant disaccharide is allowed to undergo dimethoxytritylation and benzoylation using dimethoxytrityl chloride in pyridine and benzoyl chloride. Further, 1-*O*-deacylation is achieved with diethylamine in acetonitrile and the resulting lactol undergo phosphitylation using

Scheme 4

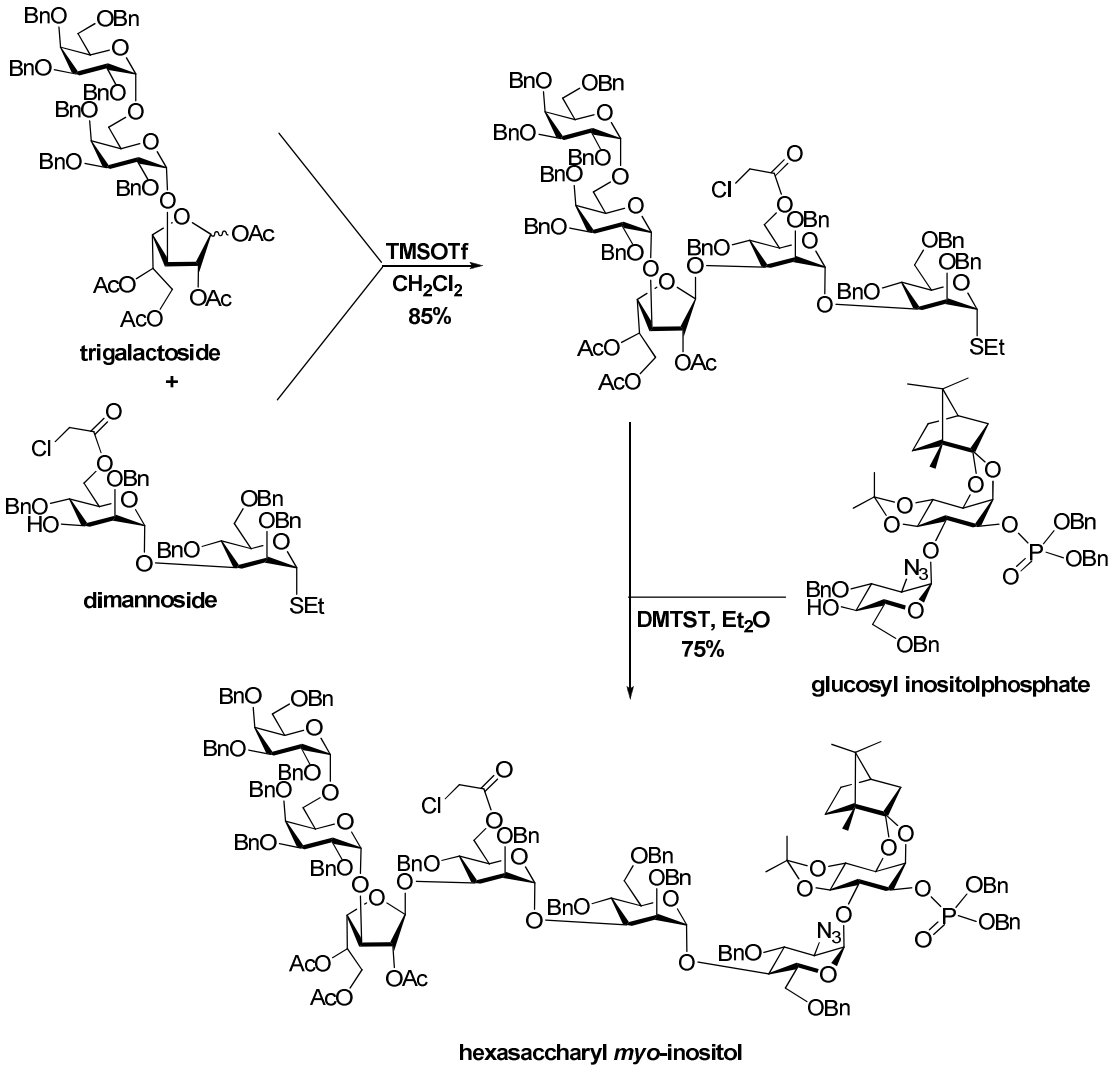


Reagents and conditions:
a) AgOTf, CH_2Cl_2, 67%; b) AgOTf, CH_2Cl_2, 71%; c) (i) $Mg(OMe)_2$, MeOH (ii) DMTrtCl, pyridine; (iii) BzCl, 66% (over three steps); d) Me_2NH, CH_3CN, 77%; e) PCl_3, imidazole, CH_3CN, Et_3N, Et_3NHHCO_3 (TEAB), H_2O, 92%; f) (i) 1-adamantanecarbonyl chloride, I_2, pyridine-water; (ii) TFA, CH_2Cl_2, 0 °C, 81% (over two steps); g) MeONa, MeOH, 90%.

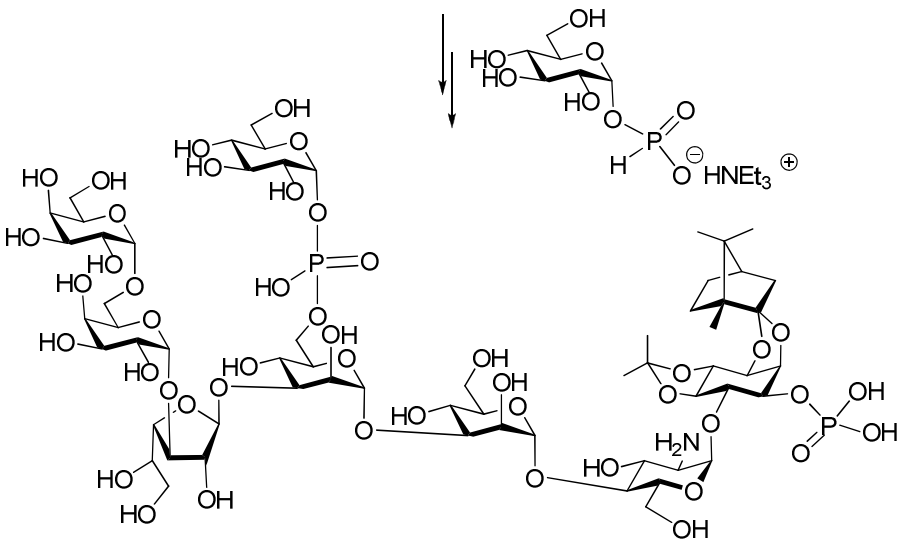
tri-imidazolylphosphine followed by mild hydrolysis to give the H-phosphonate derivative which is a common intermediate for the synthesis of phosphoglycan polymers. Condensation of phosphonate and hydroxyl acceptor in the presence of 1-adamantanecarbonyl chloride in pyridine followed by *in situ* oxidation with iodine in pyridine-water and mild detritylation (1% TFA/CH_2Cl_2, 0°C) resulting in the partially benzoylated tetrasaccharide phosphoric diester. The deprotection of benzoate protecting group is achieved with sodium methoxide in methanol in order to get a phosphoglycan dimer. Moreover, elongation is carried out by repetition of the condensation/deprotection steps to obtain the protected *trimer* and *tetramer* of phosphoglycan.

Synthesis of Heptasaccharyl *myo*-Inositol[13n]

Scheme 5



hexasaccharyl *myo*-inositol



heptasaccharyl *myo*-inositol

Konradsson's group synthesized heptasaccharyl *myo*-inositol related to GPI of LPG using four building blocks namely trigalactoside, dimannoside, glucosyl inositol phosphate and glucosyl-R-1-H-phosphonate *via* convergent block synthetic strategy (Scheme 5). In this approach, the trigalactoside is linked to the dimannoside followed by glycosylation with the glucosyl inositolphosphate to obtain the fully protected hexasaccharyl *myo*-inositol. Subsequent oxidative coupling of the glucosyl-H-phosphonate resulting in the formation of protected heptasaccharyl *myo*-inositol which is deprotected in order to get heptasaccharyl *myo*-inositol.

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Present Work

Leishmaniasis is an ancient disease and is still a major problem for the human-beings, which is caused by the bite of the female *phlebotomine* sandfly through protozoan parasites of the genus *Leishmania*. A major component present in large quantities on the cell surface of the *Leishmania* parasite is lipophosphoglycan (LPG) which plays many roles in adhesion, survival and infection of the parasites. For example, it is implicated in the binding of the parasite in epithelial cells of the sandfly midgut and receptor mediated phagocytosis by macrophage *via* direct interaction with carbohydrate binding sites; it protects the parasites against complement and oxidants. Therefore, the lipophosphoglycan is an antigenic and important virulence factor essential for the survival and infectivity of the parasites. LPG is a glycoconjugate, which is synthesized by promastigotes of all *Leishmania* parasites and is composed of glycosyl phosphatidylinositol (GPI), a repeating phosphorylated saccharide region ([6Gal*p*-(β1→4)-Man*p*-(α1)-phosphate]$_n$) and different oligosaccharides cap.

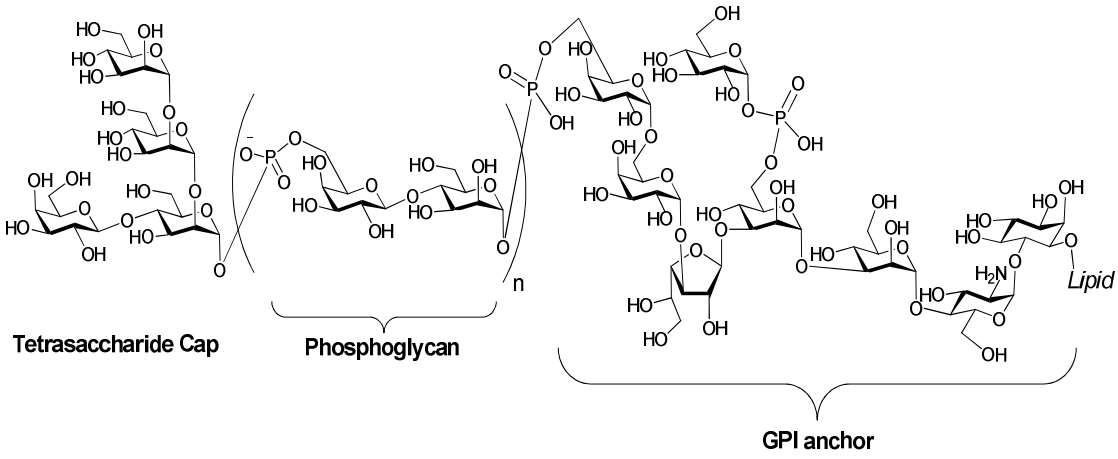


Figure 3

Interesting biological functions of lipophosphoglycans in the parasites as well as the human macrophages encouraged us to synthesize various portions of the LPG which is useful either to understand the role of LPG in the human macrophage in more detail or to develop the synthetic vaccine[14] against *Leishmaniasis*. In this context, we got interested in synthesizing the tetrasaccharide fragment of LPG expressed on the surface of the *Leishmania donovani*[13a-e] (Figure 3) because the neutral oligosaccharide

- contains a signal for termination of phosphoglycan assembly.

- is responsible for the binding of the parasite to the digestive tract of the sand fly and the human macrophages.
- contains an epitope for recognition by macrophages.

Further, it has been thought that the synthesis of tetrasaccharide with propargyl group at the reducing end would be an ideal target instead of synthesizing the tetrasaccharide alone owing to the useful application of alkyne group to synthesize various bioconjugates (**b**, **e** and **f**) (Figure 4).[15] For instance, the propargyl group in the tetrasaccharide can be subjected to 1,3-dipolar cycloaddition reaction under copper catalyst with either azide derived carrier proteins or lipids. In addition, the propargyl group could be converted into either an acid or alkene which is also useful for connecting the proteins having amine and thiol functional groups.

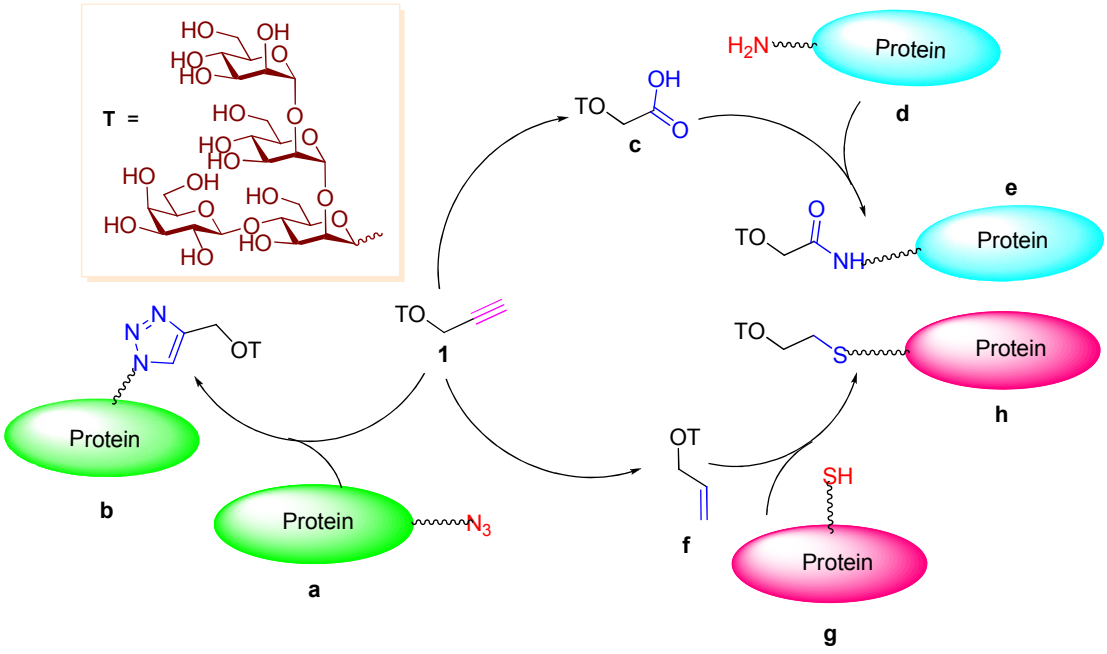


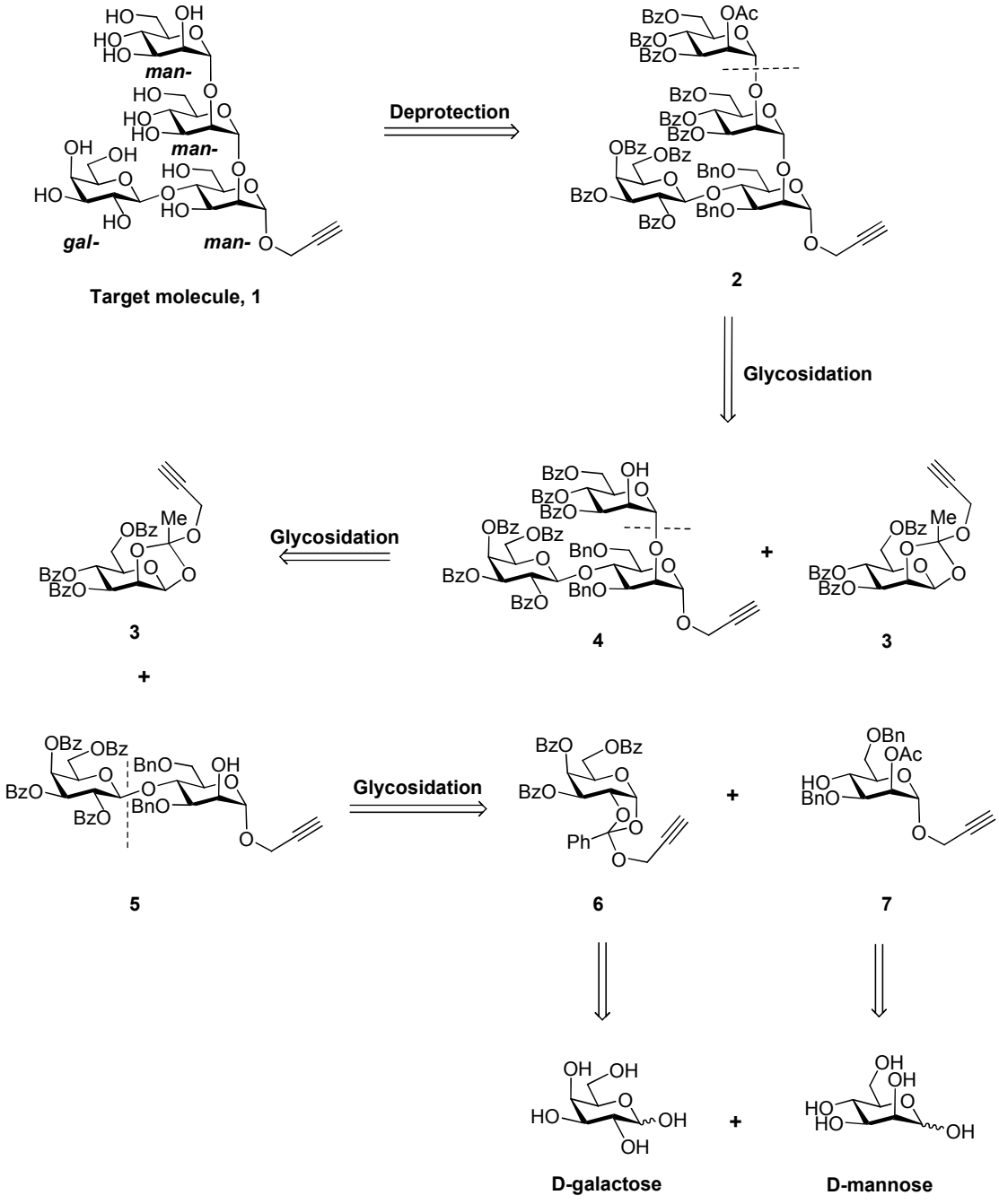
Figure 4

we envisioned that $AuBr_3$ mediated glycosidations *via* propargyl 1,2-orthoesters activation as delineated in chapter I should facilitate the stereoselective synthesis of tetrasaccharide cap with propargyl group at the reducing end because $AuBr_3$ selectively activates propargyloxy moiety situated in the propargyl 1,2-orthoesters in the presence of propargyl glycosides.

A close examination of the target molecule revealed that the tetrasaccharide is composed of two monosaccharides namely galactose and mannose (Scheme 6).

Retrosynthetic analysis 1

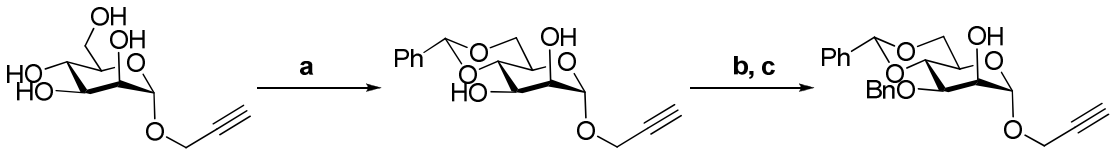
Scheme 6



Mannose derivative is linked to galactose at the C-4 position in β-configuration and at the same time, mannose is linked to another mannose at the C-2 position in α-configuration. The target molecule **1** can be obtained from the deprotection of protected propargyl tetrasaccharide **2** (Scheme 6). The propargyl tetrasaccharide **2** in turn can be synthesized by the addition of a propargyl 1,2-orthoester of mannose **3** to a

propargyl trisaccharide **4** using a catalytic amount of $AuBr_3$ in dichloromethane. The trisaccharide **4** can be easily made from $AuBr_3$ mediated glycosidation of the disaccharide **5** and a propargyl 1,2-orthoester of mannose **3**. The propargyl disaccharide **5** can be accessed from the two monosaccharide building blocks, propargyl 1,2-orthoester of galactose **6** and mannose derivative **7** *via* glycosylation under $AuBr_3$ catalyst. Finally, the monosaccharide building blocks can be prepared from the starting materials, D-(+)-galactose and D-(+)-mannose.

Scheme 7



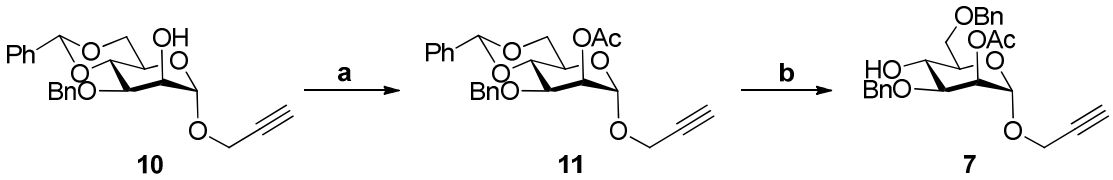
8 **9** **10**

Reagents and Conditions: a) $C_6H_5CH(OMe)_2$, PTSA, DMF, 50 ^oC, 5h, 65%; b) Bu_2SnO, MeOH, 90 ^oC, 4h; c) BnBr, DMF, 120 ^oC, 8h, 93% (over two steps)

Our synthetic endeavour started for the building block **7** from D-mannose which was converted into propargyl mannopyranoside **8** from the literature reported procedure.[16] Prop-2-ynyl α-D-mannopyranoside **8** was treated with benzylidene dimethyl acetal in anhydrous DMF in the presence of PTSA catalyst at 50 ^oC under reduced pressure for 5h to give prop-2-ynyl 4,6-*O*-benzylidene-α-D-mannopyranoside **9** in 65% yield (Scheme 7).[17] The resulting diol **9** was allowed to undergo selective benzylation at C-3 position in a two step process. For that, diol was first protected as stannylene acetal by treatment with dibutyltin oxide in anhydrous methanol at 90 ^oC for 4h under argon atmosphere which was subsequently reacted with benzyl bromide in anhydrous DMF at 120 ^oC for 8h under argon atmosphere to afford prop-2-ynyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside **10** in 93% yield.[12a,18] The structure was characterized thoroughly by the spectroscopic techniques such as ^1H, ^{13}C and DEPT NMR. In the ^1H NMR spectrum of compound **10**, resonances attributed to methine proton and methylene protons of propargyl group were observed at δ 2.46 ppm as a triplet and δ 4.23 ppm as a doublet. In addition to this, resonances due to the anomeric proton and benzylidene methine proton were evident at δ 5.06 ppm as a doublet (J = 1.26 Hz) and δ 5.61 ppm as a singlet respectively. Further, resonances

corresponding to aromatic protons were located around δ 7.25-7.52 ppm as a multiplet. Rest of the spectrum was in complete agreement with the assigned structure **10**. Whereas, in the ^{13}C NMR spectrum, resonances attributed to the anomeric carbon and benzylidene carbon were noticed at δ 98.6 and 101.6 ppm whilst rest of the resonances were completely in agreement with the assigned structure **10**.

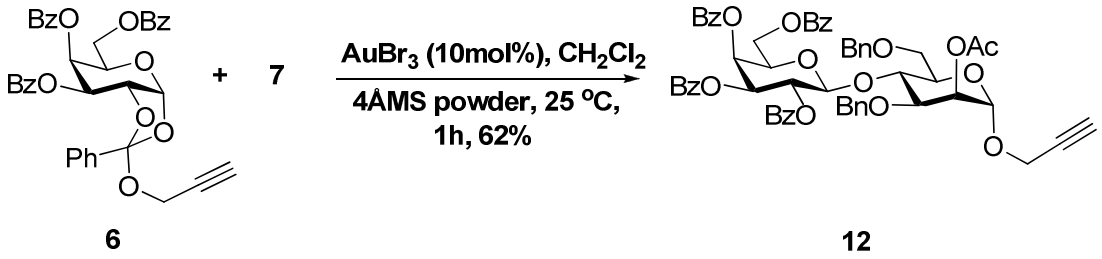
Scheme 8



Reagents and Conditions: a) Ac_2O, Et_3N, DMAP, CH_2Cl_2, 0-25 ^oC, 2h, 100% ; b) $NaCNBH_3$, THF, HCl-Et_2O, 0 ^oC, 30min., 70%.

The lone C-2 hydroxyl group was thought to be protected as acetate due to the prospect of deprotection of acetate (-OAc) at a later stage in the presence of benzoates using acids such as PTSA, $HBF_4 \cdot Et_2O$ in MeOH, HCl/MeOH.[19-21] Thus, prop-2-ynyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside **10** was acetylated under conditions Ac_2O/DMAP/Et_3N/CH_2Cl_2/2h and subsequently, the compound **11** was treated with $NaCNBH_3$ in anhydrous THF followed by a dropwise addition of saturated solution of HCl gas in anhydrous diethyl ether at 0 ^oC for 30min. to afford prop-2-ynyl 2-*O*-acetyl-3,6-di-*O*-benzyl-α-D-mannopyranoside[22] **7** in 70% yield (Scheme 8). The newly formed product **7** was thoroughly characterized by the NMR and mass spectral analysis. In the ^1H NMR spectrum of compound **7**, resonances corresponding to the propargylic methine proton and methylene protons were identified at δ 2.45 ppm as a triplet and δ 4.24 ppm as a doublet respectively. Additionally, the resonances corresponding to acetyl group and the anomeric proton were observed at δ 2.12 as a singlet and δ 5.04 ppm as a doublet (J = 1.58 Hz) whilst all other resonances were completely in agreement with the assigned structure **7**. Further, ^{13}C NMR spectrum showed resonance attributed to the anomeric carbon having α-linkage at δ 96.5 ppm whilst rest of the resonances were in accordance to the assigned structure **7**. The structure **7** was further supported by mass spectral analysis (Mol. Wt. calculated for $C_{25}H_{28}O_7$: 440.485, Found: 463.480 (M^++ 23 for Na)).

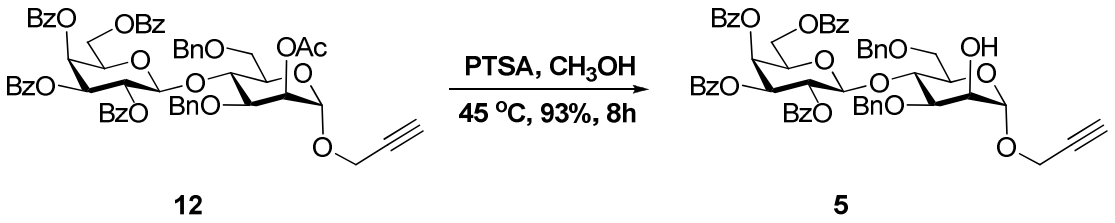
Scheme 9



6 **12**

Having the mannose building block **7** in hand, our synthesis has been extended with the utilization of gold mediated glycosidations using propargyl 1,2-orthoesters as glycosyl donors.[22-23] Accordingly, the glycosylation reaction carried out between an equimolar amount of galactose 1,2-orthoester **6** (preparative procedure is described in Chapter I) and mannosyl acceptor **7** in the presence of 10mol% of $AuBr_3$ in dichloromethane and freshly activated 4Å molecular sieves powder at room temperature under argon atmosphere. Attempted glycosylation offerd the desired 1,2-*trans* disaccharide **12** in 35% yield (Scheme 9). Further, to improve the yield of the disaccharide **12**, the glycosylation reaction performed with 2 mmol of galactose 1,2-orthoester **6** under same conditions. Gratifyingly, the glycosylation proceeded smoothly and gave 1,2-*trans* disaccharide **12** in 62% yield. The obtained 1,2-*trans* disaccharide was thoroughly characterized by the nuclear magnetic resonance spectroscopic techniques and mass spectral analysis. In the ^1H NMR spectrum of compound **12**, resonances corresponding to methine proton and methylene protons of propargyl moiety at δ 2.33 ppm as a triplet and δ 4.13 ppm as a doublet along with a resonance corresponding to acetyl group at δ 2.08 ppm as a singlet were noticed. Additionally, resonances attributed to the two anomeric protons were identified as two doublets at δ 4.91 ppm (J = 8.03 Hz) and δ 4.99 ppm (J = 1.66 Hz) whilst all other signals were completely in agreement with the assigned structure **12**. Further, ^{13}C NMR spectrum showed the resonances attributed to the two anomeric carbons having α-linkage and β-linkage at δ 96.3 and 100.7 ppm respectively, while rest of the resonances were in accordance with the assigned structure **12**. The structure was further supported by the mass spectral analysis (Mol. Wt. calculated for $C_{59}H_{54}O_{16}$: 1018.34, Found: 1041.75 (M^++ 23 for Na)).

Scheme 10

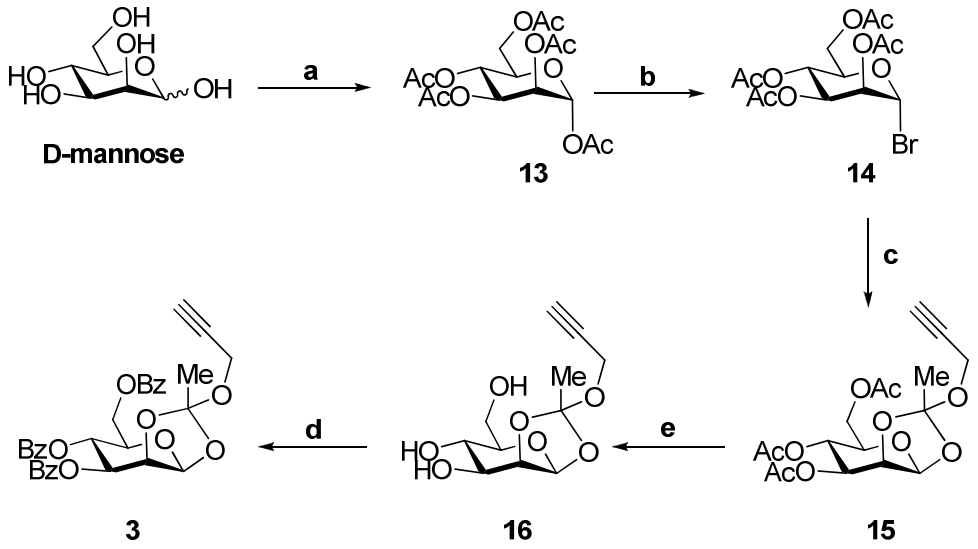


12 **5**

Further, propargyl disaccharide **12** was treated with PTSA in anhydrous methanol at 45 ^{o}C under argon atmosphere for 8h for the selective deprotection of acetate in the presence of benzoates.[19] As expected, PTSA selectively deprotected acetate group in the presence of benzoates and at the same time, offered the required alcohol **5** in 93% yield (Scheme 10). It is interesting to note that the interglycosidic bond is stable under these conditions may be because of the electron withdrawing substituent (-OBz) present at C-2 position of the disaccharide **12**. The deacetylated product **5** was characterized thoroughly by ^{1}H, ^{13}C, DEPT NMR and mass spectroscopic techniques. In the ^{1}H NMR spectrum of compound **5**, disappearance of resonances corresponding to acetyl group and at the same time, C-2 hydrogen shift of the disaccharide acceptor compared to starting material along with the hydroxyl group resonance at δ 2.59 ppm as a broad singlet were noticed whilst all other peaks were completely in agreement with the assigned structure **5**. Further, ^{13}C NMR spectrum showed the disappearance of resonances due to methyl group and carbonyl group whilst rest of the signals were in accordance with the assigned structure **5**.

In continuation of the synthesis towards the target molecule, we required a glycosyl donor 3,4,6-tri-*O*-benzoyl-β-D-mannopyranose-1,2-(prop-2-ynyl ortho-acetate) **3** which was prepared from mannose by following five step sequence (Scheme 11). One pot conversion of D-mannose into 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide **14** was achieved using acetylation conditions Ac_2O/AcOH/ Conc.H_2SO_4/30min. followed by the addition of 33% hydrobromic acid in glacial acetic acid at room temperature.[24] Subsequently, mannopyranosyl bromide **14** was treated with 2,6-lutidine, propargyl alcohol and a catalytic amount of tetra-*n*-butylammonium iodide at 70 ^{o}C under argon atmosphere for 24h to obtain 3,4,6-tri-*O*-acetyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthoacetate) **15** in 63% yield.[23] The 1,2-orthoester **15** was confirmed thoroughly by ^{1}H, ^{13}C and DEPT NMR spectral analysis.

Scheme 11

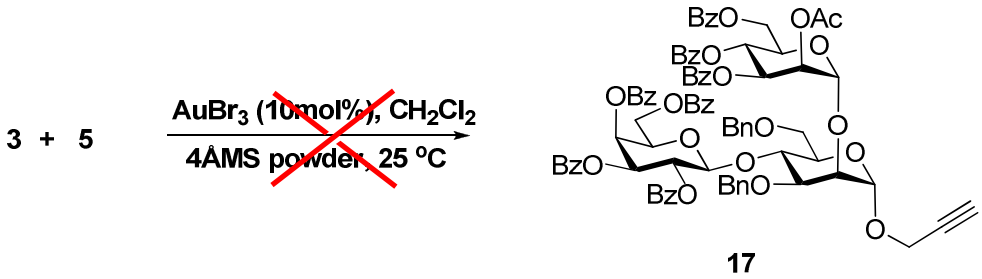


Reagents and Conditions : a) Ac_2O, AcOH, Conc. H_2SO_4, 30min.; b) HBr-AcOH, 5h, 90%; c) 2,6-lutidine, *n*-Bu_4NI, propargyl alcohol, CH_2Cl_2, 70 ^oC, 63%; d) NaOMe, MeOH, 2h, 97%; e) Et_3N, DMAP, CH_2Cl_2, BzCl, 0-25 ^oC, 15h, 40%

In the ^1H NMR spectrum of compound **15**, resonances corresponding to methine proton and methylene protons of propargyl moiety at δ 2.39 as a triplet and 4.19 ppm as a doublet along with a resonance due to the methyl group attached to the quaternary carbon of orthoester at δ 1.79 ppm as a singlet were identified. In addition to this, resonances corresponding to the three acetyl groups and anomeric proton were observed at δ 2.06, 2.08, 2.12 ppm as three singlets and δ 5.51 ppm (J = 2.63 Hz) as a doublet respectively. Rest of the spectrum was in accordance with the assigned structure **15**. Further, ^{13}C NMR spectrum revealed the resonances corresponding to the anomeric carbon and quaternary carbon at δ 97.4 and 124.1 ppm respectively, while rest of the signals in the spectrum were in accordance to the assigned structure **15**. Deprotection of acetyl groups in 1,2-orthoester **15** was achieved *via* Zemplén conditions NaOMe/MeOH and the resulting triol of 1,2-orthoester **16** was treated with triethylamine, N,N-dimethylaminopyridine and benzoyl chloride in dichloromethane at 0-25 ^oC for 15h to give 3,4,6-tri-*O*-benzoyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthoacetate) **3** (40%) as a colourless solid. The newly formed 1,2-orthoester **3** was thoroughly confirmed by ^1H, ^{13}C, DEPT NMR spectroscopic techniques and mass spectral analysis. In the ^1H NMR spectrum of compound **3**, resonances corresponding to the propargylic methine proton and methylene protons were located at δ 2.28 ppm

as a triplet and δ 4.18 ppm as a doublet. Apart from that, resonances attributed to methyl group and the anomeric proton were observed at δ 1.81 ppm as a singlet and δ 5.69 ppm (J = 2.65 Hz) as a doublet whilst rest of the peaks were completely in agreement with the assignment structure **3**. Further, in the ^{13}C NMR spectrum, resonances corresponding to the methyl group, anomeric carbon and the quaternary carbon were identified at δ 24.5, 97.7 and 124.2 ppm respectively. All others resonances in the spectrum were in accordance to the assigned structure **3**.

Scheme 12



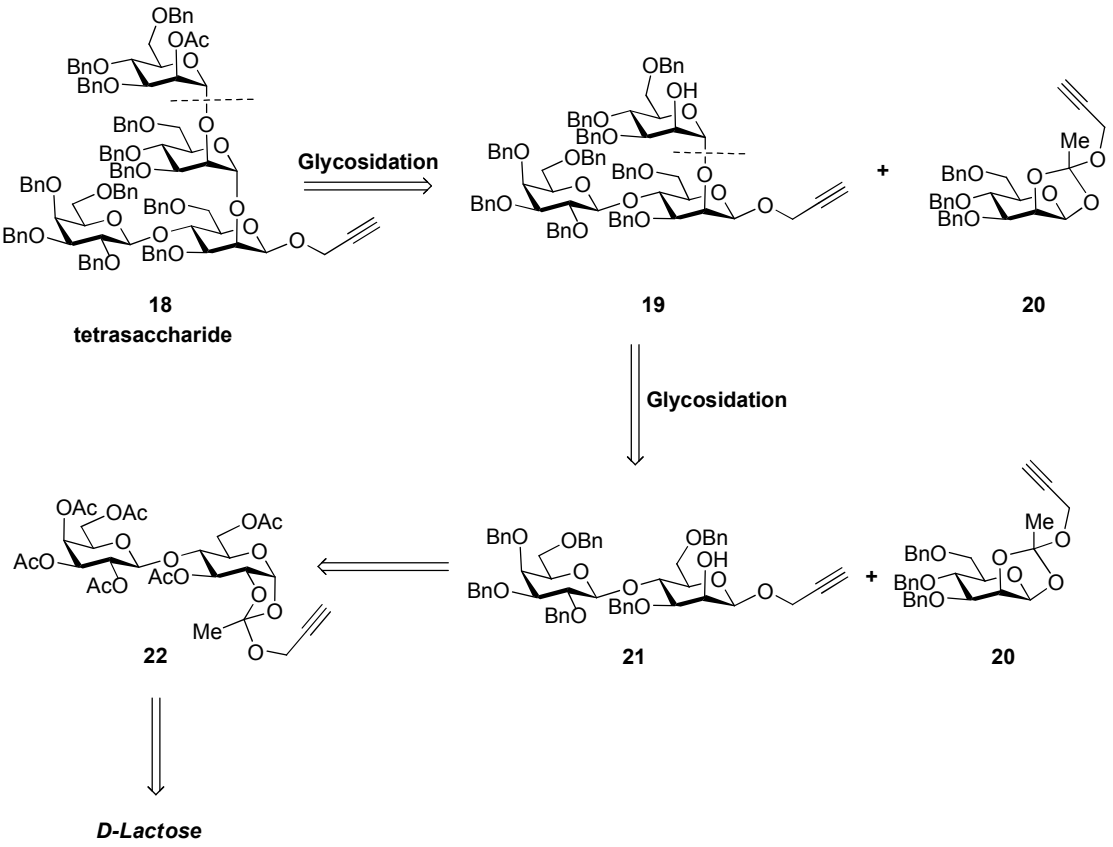
17

Having both glycosyl donor **3** and glycosyl acceptor **5** in hand, the glycosylation reaction was performed between a propargyl 1,2-orthoester of mannose **3** and disaccharide acceptor **5** under 10mol% $AuBr_3$/4ÅMS/rt/CH_2Cl_2 conditions for 24h to get a trisaccharide **17** exclusively (Scheme 12). But, the reaction failed to give the trisaccharide **17**. Increasing the temperature to 60 ^oC or switching the solvent from CH_2Cl_2 to $ClCH_2CH_2Cl$ did not give any encouraging results. It has been assumed that the reactivity of 1,2-orthoester and disaccharide acceptor are not sufficient for the synthesis of the trisaccharide **17**. Thus, we thought of increasing the reactivity of glycosyl donor as well as glycosyl acceptor to get the desired trisaccharide under similar conditions. Benzyl ether substituents are generally more reactive than benzoate ester substituents.[25] Therefore, we decided to check the effect of per-*O*-benzylated mannose propargyl 1,2-orthoester with a fully benzylated disaccharide acceptor (which was prepared from lactose instead of mannose and galactose) under same condition. Thus, a new retrosynthetic analysis revealed that the propargyl tetrasaccharide **18** can be synthesized by the addition of a propargyl 1,2-orthoester of mannose **20** to a propargyl trisaccharide **19** using a catalytic amount of $AuBr_3$ in dichloromethane. The trisaccharide **19** can be easily made from $AuBr_3$ mediated glycosidation of the disaccharide **21** and a propargyl 1,2-orthoester of mannose **20**.

The disaccharide **21** in turn can be prepared conveniently from propargyl 1,2-orthoester of lactose **22** (Scheme 13).

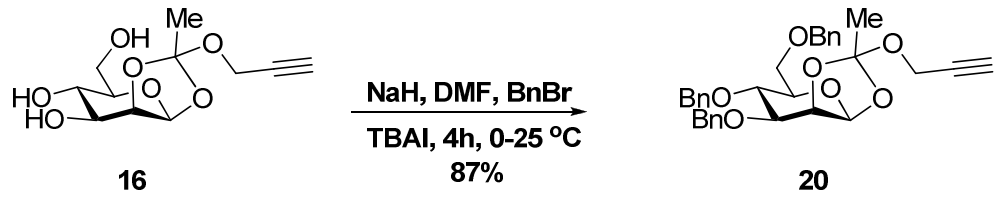
Retrosynthetic analysis 2

Scheme 13



Accordingly, a new glycosyl donor 3,4,6-tri-*O*-benzyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthoacetate) **20** was prepared by treating the triol of mannose 1,2-orthoester **16** under conditions NaH/DMF/BnBr/TBAI/0-25 ^{o}C/4h (Scheme 14). The product, per-*O*-benzylated mannose 1,2-orthoester **20** was characterized thoroughly by various spectroscopic techniques such as ^{1}H, ^{13}C, DEPT NMR and mass spectral analysis. In the ^{1}H NMR spectrum of compound **20**, resonances corresponding to

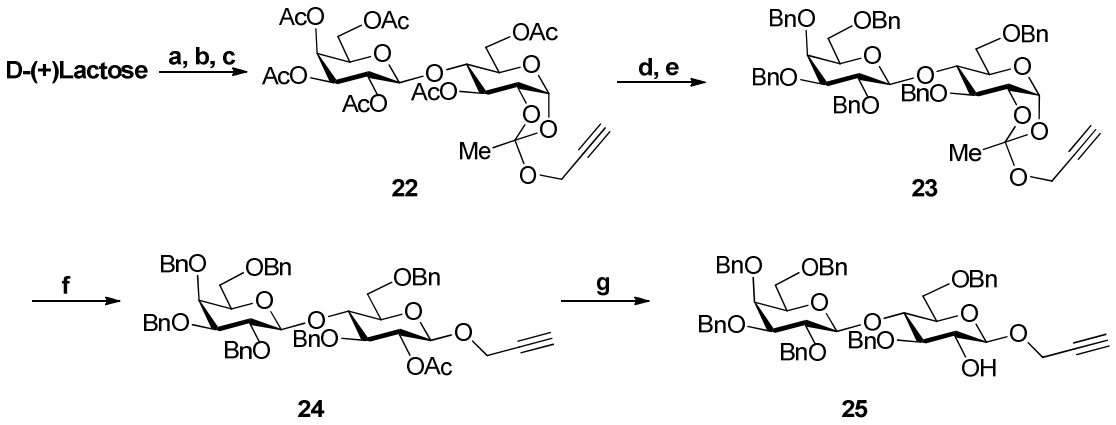
Scheme 14



methine proton and methylene protons of propargyl group were noticed at δ 2.41 ppm as a triplet and δ 4.18 ppm as a doublet. In addition, resonances corresponding to the aromatic protons of benzyl groups and anomeric proton were observed at δ 7.19-7.45 ppm as a multiplet and δ 5.37 ppm (J = 2.61 Hz) as a doublet whilst all other resonances were in accordance to the assigned structure **20**. Further, in the ^{13}C NMR spectrum, resonances attributed to the anomeric carbon and quaternary carbon were located at δ 97.6 and 123.7 ppm respectively. Rest of the signals in the spectrum were completely in agreement with the assigned structure **20**.

In parallel, per-*O*-benzylated propargyl 1,2-orthoester of lactose **23** was prepared *via* aforementioned protocols starting from lactose (Scheme 15). The structure was confirmed thoroughly by ^{1}H, ^{13}C, DEPT NMR and mass spectroscopic techniques. In the ^{1}H NMR spectrum of compound **23**, the characteristic resonances due to methine proton and methylene protons of propargyl group at δ 2.36 ppm as a triplet and δ 4.14 ppm as a doublet along with a resonance corresponding to methyl group at δ 1.67 ppm as a singlet were identified. Further, resonances attributed to the anomeric proton of 1,2-orthoester and aromatic protons were located at δ 5.73 ppm (J = 5.24 Hz) as a doublet and δ 7.15-7.40 ppm as a multiplet. Rest of the resonances in the spectrum were completely in agreement with the assigned structure **23**. Whereas, ^{13}C NMR spectrum showed the resonances corresponding to the two anomeric carbons

Scheme 15



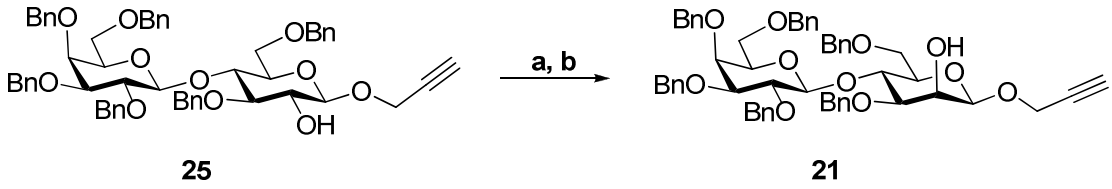
Reagents and conditions: a) Ac_2O, AcOH, Conc. H_2SO_4, 30min.; b) HBr-AcOH, 5h, 90%; c) 2,6-lutidine, *n*-Bu_4NI, propargyl alcohol, CH_2Cl_2, 65 °C, 55%; d) NaOMe, MeOH, 2h, 95%; e) NaH, DMF, BnBr, TBAI, 4h, 0-25 °C, 85%; f) $Sc(OTf)_3$, CH_2Cl_2, propargyl alcohol, 25 °C, 30min., 63%; g) NaOMe, MeOH, 25 °C, 2h, 90%

and quaternary carbon of the 1,2-orthoester at δ 97.5, 105.3 and 120.9 ppm respectively, while rest of the resonances were in accordance with the assigned structure **23**. The structure was further supported by DEPT NMR spectrum wherein the signals with negative intensity at δ 51.5, 68.5, 68.9, 71.7, 72.8, 73.1, 73.3, 74.6 and 74.9 ppm revealed the presence of nine methylene (-CH_2-) groups in the assigned disaccharide 1,2-orthoester **23**. Thereafter, ring opening of 1,2-orthoester **23** to propargyl lactoside **24** was achieved in the presence of 10mol% of scandium triflate and propargyl alcohol in dichloromethane at room temperature under argon atmosphere (Scheme 15). Further, propargyl lactoside **24** was deacetylated under Zemplén conditions NaOMe/MeOH to obtain β-propargyl per-*O*-benzylated lactopyranoside **25** (90%). The structure was confirmed thoroughly by using ^{1}H, ^{13}C, DEPT NMR spectroscopic techniques and mass spectral analysis. In the ^{1}H NMR spectrum of compound **25**, resonances attributed to the propargylic methine proton and methylene protons were identified at δ 2.46 ppm as a triplet and δ 4.39 ppm as a doublet along with resonances corresponding to the aromatic hydrogens of benzyl ethers at δ 7.10-7.40 ppm as a multiplet whilst all other signals were completely in agreement with the assigned structure **25**. Whereas, in the ^{13}C NMR spectrum, the characteristic resonances due to the two anomeric carbons having 1,2-*trans* linkages were evident at δ 100.1 and 102.6 ppm whilst the rest of peaks were in accordance with the assigned structure **25**. The structure was further supported by DEPT NMR spectrum which indicated the resonances with negative intensity at δ 55.6, 67.9, 68.0, 72.4, 73.0, 73.3, 74.5, 74.7 and 75.1 ppm due to nine methylene (-CH_2-) groups present in the assigned structure **25**. At this stage, inversion of the hydroxyl group was required in order to convert *gluco*-configuration to *manno*-configuration. This could be achieved using a two step procedure which involves oxidation and reduction.[13c,26]

Accordingly, propargyl lactopyranoside containing an *equatorial* alcohol **25** was oxidized under conditions DMSO/Ac_2O/25 ^{o}C/24h to give the *ulose* which was reduced with $NaBH_4$ in 1:1 mixture of dichloromethane and methanol for 4h at room temperature under argon atmosphere to obtain the desired disaccharide **21** having axial hydroxyl functional group (Scheme 16). The oxidation and reduction reactions are selective for the inversion of alcohol from the *equatorial* position to *axial* position, when the anomeric protecting group was situated at the β-position only.[13c,26] The

disaccharide *axial* alcohol **21** was confirmed thoroughly by the NMR and mass spectral analysis. In the ^{1}H NMR spectrum of compound **21**, appearance of resonances corresponding to methine proton of propargyl group and aromatic protons were noticed at δ 2.43 ppm as a triplet and δ 7.11-7.40 ppm as a multiplet whilst rest of the resonances were completely in agreement with the structure **21**. Further, ^{13}C NMR spectrum revealed the characteristic resonances for the presence of two anomeric carbons having β-linkages at δ 96.9 and 103.1 ppm. Rest of the resonances in the spectrum were in accordance with the assigned structure **21**. The structure was further supported by DEPT NMR spectrum wherein nine signals with negative intensity at δ 55.4, 68.3, 68.6, 72.4, 72.5, 73.1, 73.4, 74.5 and 75.1 ppm confirming the nine methylene (-CH_2-) groups present in the assigned structure **21**. To understand the configuration of the newly formed disaccharide **21** in a better way, ^{1}H and ^{13}C NMR data of the starting material and the product are shown in table 1.

Scheme 16



25 **21**

Reagents and Conditions
a) DMSO, Ac_2O, 24h, 25 °C ; b) $NaBH_4$, CH_2Cl_2 : CH_3OH (1:1), 4h, 82% (over two steps)

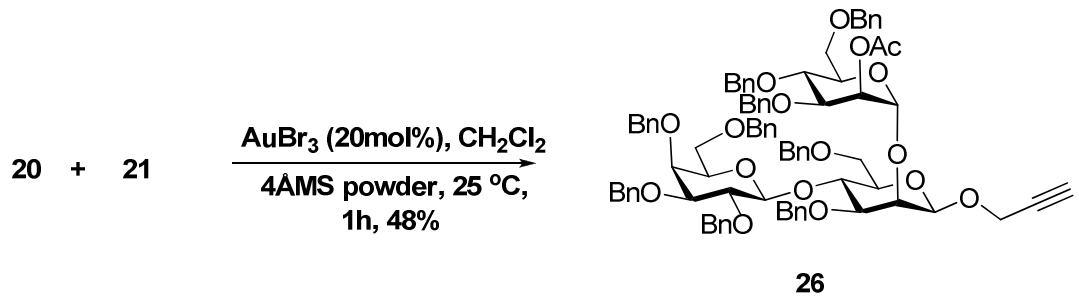
Table 1: Comparison of β-*gluco*-configuration and β-*manno*-configuration

Disaccharide **25** having *gluco*-configuration (starting material)	Disaccharide **21** having *manno*-configuration (product)
^{1}H NMR ($CDCl_3$, 200.13 MHz): δ **2.45** (1H, bs), **2.46** (1H, t, *J* 2.35 Hz), 3.30-3.60 (7H, m), 3.65-4.05 (5H, m), 4.23-4.57 (9H, m), 4.65-4.74 (3H, m), 4.79 (2H, d, *J* 3.44 Hz), 4**.96** (1H, d, *J* 11.51 Hz), **5.08** (1H, d, *J* 11.08 Hz), **7.10-7.40** (30H, m).	^{1}H NMR ($CDCl_3$, 200.13 MHz): δ, **2.43** (1H, t, *J* 2.33 Hz), **2.50** (1H, bs) 3.37-3.60 (6H, m), 3.72 (1H, d, *J* 7.83 Hz), 3.79 (2H, d, *J* 3.31 Hz), 3.91 (1H, d, *J* 2.56 Hz), 4.11 (2H, d, *J* 7.74 Hz), 4.25-4.85 (15H, m), **4.96** (1H, d, *J* 11.52 Hz), **7.11-7.40** (30H, m).

^{13}C NMR ($CDCl_3$, 50.32 MHz): δ **55.6**, **67.9**, **68.0**, **72.4**, 72.9, **73.0**, 73.1, **73.3**, 73.4, **74.5**, **74.7**, **75.1**, 75.1, 75.4, 75.9, 78.7, 79.8, 82.3, 82.5, **100.1**, **102.6**, 127.2, 127.2, 127.3, 127.4, 127.4, 127.6, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.1, 128.2, 128.3, 128.3, **137.9**, **138.1**, **138.4**, **138.7**, **138.8**, **138.9**.	^{13}C NMR ($CDCl_3$, 50.32 MHz): δ **55.4**, **68.3**, 68.5, **68.6**, **72.4**, **72.5**, 72.9, **73.1**, **73.4**, 73.4, 74.1, **74.5**, 75.0, **75.1**, 75.3, 78.7, 79.1, 79.8, 82.4, **96.9**, **103.1**, 127.4, 127.4, 127.5, 127.6, 127.7, 127.8, 127.8, 128.1, 128.2, 128.2, 128.3, 128.4, **137.9**, **138.3**, **138.4**, **138.4**, **138.6**, **138.9**.

After successful preparation of the fully benzylated mannose 1,2-orthoester donor **20** and disaccharide acceptor **21**, our synthetic endeavour begun a journey to achieve the synthesis of the tetrasaccharide with propargyl group at the reducing end using gold mediated activation of propargyl 1,2-orthoesters. Accordingly, the glycosylation reaction carried out between a mannosyl donor **20** and disaccharide acceptor **21** in the presence of 10mol% $AuBr_3/CH_2Cl_2$/25 ^oC/4ÅMS powder under argon atmosphere in order to get a trisaccharide **26** (Scheme 17). The glycosylation reaction proceeded very slowly and did not complete even after 24h. At this stage, the trisaccharide **26** was isolated in low yield (15%) along with the starting materials, **20** (50%) and **21** (75%**)**. To further increase the yield of trisaccharide **26**, we decided to conduct the same glycosylation with 20mol% of $AuBr_3$ catalyst. Surprisingly, the glycosylation performed in the presence of 20mol% $AuBr_3/CH_2Cl_2$/rt/4ÅMS powder under argon atmosphere offered the desired trisaccharide as a propargyl glycoside **26** in moderate yield (48%). Further, to improve the yield of trisaccharide, the glycosylation carried out with more equivalents of glycosyl donor **20** was futile.

Scheme 17

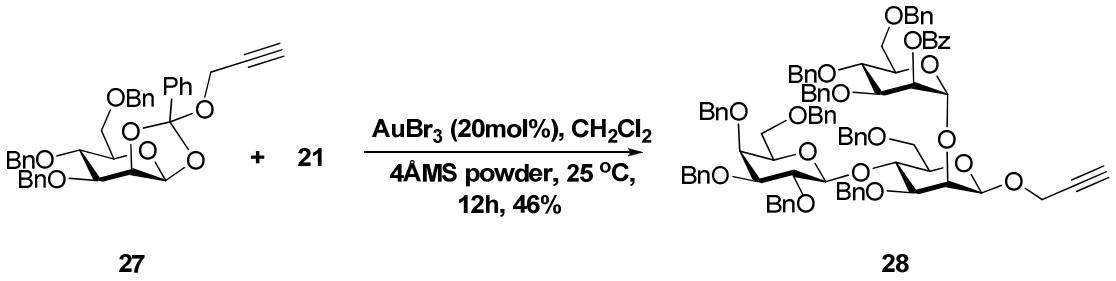


26

The trisaccharide **26** was thoroughly characterized by ^{1}H, ^{13}C and DEPT NMR spectroscopic techniques and mass spectral analysis. In the ^{1}H NMR spectrum of compound **26**, resonances attributed to acetyl group and the propargylic methine proton at δ 2.03 ppm as a singlet and δ 2.35 ppm as a triplet along with one of the three anomeric protons resonance at δ 5.16 ppm (J = 1.14 Hz) as a doublet were noticed. Other two anomeric protons were merged in the spectrum. Further, resonances corresponding to the aromatic protons of nine benzyl groups were observed at δ 7.10-7.35 ppm as a multiplet. Rest of the spectrum was completely in agreement with the assigned structure **26**. Whereas, in the ^{13}C NMR spectrum, resonances attributed to the three anomeric carbons were evident at δ 97.0, 98.9 and 103.1 ppm along with the resonances due to acetyl group at δ 21.2 and 169.8 ppm. Rest of the peaks in the spectrum were in accordance with the assigned structure **26**. Furthermore, DEPT NMR spectrum indicated thirteen signals with negative intensity at δ 55.4, 67.9, 68.7, 68.9, 71.9, 72.1, 72.4, 73.1, 73.2, 73.3, 74.4, 74.8 and 75.1 ppm for the presence of thirteen methylene groups (-CH_2-) in the assigned trisaccharide **26**. The structure was further supported by mass spectral analysis (Mol. Wt. calculated for $C_{86}H_{90}O_{17}$: 1395.62; Found: 1419.24 (M^++ 23 for Na)).

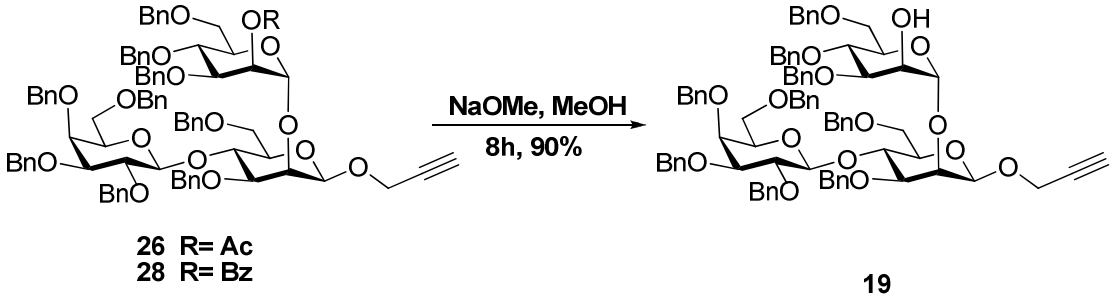
Further, we studied the effect of glycosylation between disaccharide acceptor **21** and 3,4,6-tri-*O*-benzyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthobenzote) **27** in order to get a trisaccharide. The glycosylation reaction performed in the presence of 20mol% $AuBr_3$/CH_2Cl_2/rt/4ÅMS powder under argon atmosphere (Scheme 18), which resulted in the formation of the trisaccharide with propargyl group at the reducing end **28** in 46% yield. The trisaccharide structure **28** was thoroughly confirmed by using ^{1}H, ^{13}C, DEPT NMR and mass spectroscopic techniques. In the ^{1}H NMR spectrum of compound **28**, resonances corresponding to the propargylic methine proton and one of the three anomeric protons were identified at δ 2.36 ppm as a triplet and δ 5.32 ppm as a singlet respectively. Further, resonances attributed to the aromatic protons of nine benzyl groups and benzoate were noticed at δ 6.98-8.07 ppm as multiplets along with resonance corresponding to the hydrogen present at the C-2 of mannose ring containing benzoate ester at δ 5.85 ppm. Rest of the spectrum was in accordance with the assigned structure **28**. The structure was further supported by ^{13}C NMR spectrum in which the resonances corresponding to the three anomeric carbons having two β-

Scheme 18



linkages and one α-linkage were noticed at δ 97.0, 98.8 and 103.1 ppm along with a resonance attributed to one carbonyl group at δ 165.1 ppm. Rest of the signals in the spectrum were in accordance to the assigned trisaccharide **28**. The structure was further confirmed with mass spectral analysis which showed the molecular ion peak at 1481.42 (M^++23 for Na).

Scheme 19

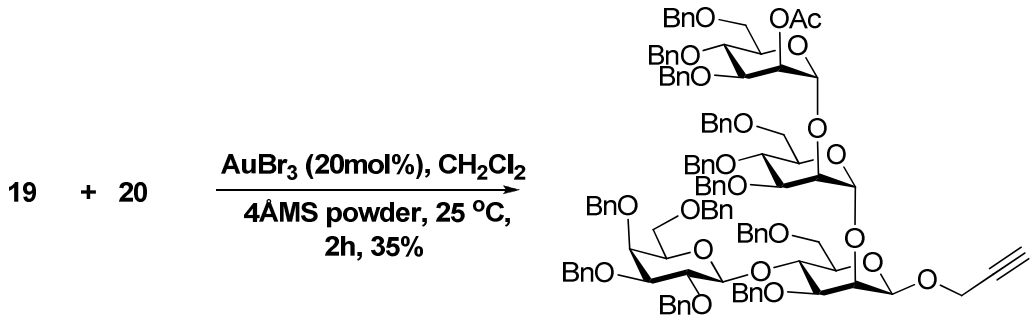


After successful preparation of the trisaccharide, deprotection of ester in the trisaccharide (**26** & **28**) was accomplished using Zemplén conditions NaOMe/MeOH to obtain the precursor **19** for the synthesis of propargyl tetrasaccharide (Scheme 19). The structure **19** was confirmed thoroughly by various spectroscopic techniques such as ^{1}H, ^{13}C, DEPT NMR and mass spectral analysis. In the ^{1}H NMR spectrum of compound **19**, disappearance of resonances corresponding to acetyl group was observed. At the same time, resonances corresponding to the propargylic methine proton and methylene protons were identified at δ 2.34 ppm as a triplet and δ 4.43 ppm as a doublet along with resonances attributed to hydroxyl functional group at δ 2.25 ppm as a broad singlet. Additionally, resonances corresponding to the aromatic protons of benzyl ethers and one of the three anomeric protons were observed at δ 7.10-7.38 ppm as a multiplet and δ 5.27 (J = 1.22 Hz) as a doublet. The remaining

signals were completely in agreement with the assigned structure **19**. Further, ^{13}C NMR spectrum **19** revealed the resonances corresponding to the three anomeric carbons having one α-linkage and two β-linkages at δ 97.2, 100.1 and 102.9 ppm respectively. Rest of the resonances in the spectrum were in accordance with the assigned structure **19**. Furthermore, DEPT NMR spectrum showed resonances with negative intensity at δ 55.3, 68.6, 68.7, 68.8, 71.8, 72.6, 72.8, 73.1, 73.3, 73.4, 74.5, 74.8 and 75.2 ppm which confirming the presence of thirteen methylene ($-CH_2-$) groups in the assigned structure **19**. The structure was further supported by mass spectral analysis wherein the molecular ion showed a peak at 1376.39 (M^++ 23 for Na).

Having 3,4,6-tri-*O*-benzyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthoacetate) **20** and the trisaccharide acceptor **19** in hand, the glycosylation reaction was carried out under conditions 20mol% $AuBr_3/CH_2Cl_2$/rt/4ÅMS powder for 2h in order to synthesize the tetrasaccharide with propargyl group at the reducing end **18**. As expected, the glycosylation proceeded well and gave the required propargyl tetrasaccharide in 35% yield (Scheme 20). The propargyl tetrasaccharide **18** was

Scheme 20



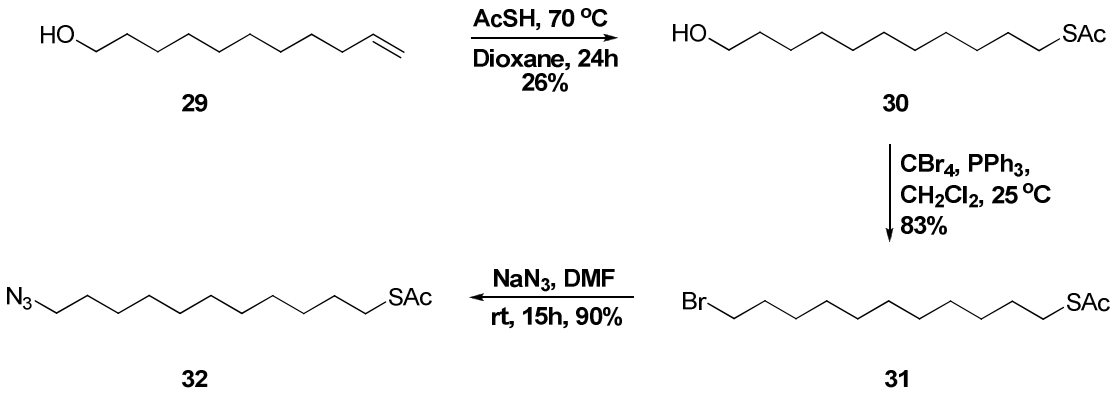
18

thoroughly characterized by the spectroscopic experiments such as ^1H, ^{13}C and DEPT NMR, and mass spectral analysis. In the ^1H NMR spectrum of tetrasaccharide **18**, resonances corresponding to acetyl group and the propargylic methine proton were noticed at δ 2.06 ppm as a singlet and δ 2.34 ppm as a triplet respectively. Further, resonances attributed to one of the four anomeric carbons and the aromatic protons of twelve benzyl ethers were observed at δ 5.19 ppm as a singlet and δ 7.07-7.38 ppm as a multiplet. Rest of the resonances in the spectrum were completely in agreement with

the assigned structure **18**. Further, in the ^{13}C NMR spectrum, resonances due to the four anomeric carbons were evident at δ 97.1, 99.3, 100.0 and 102.6 ppm along with the resonances corresponding to acetyl group at δ 21.1 and 170.0 ppm respectively. Rest of the signals in the spectrum were in accordance with the assigned structure **18**. Furthermore, DEPT NMR spectrum revealed the resonances with negative intensity at δ 55.2, 68.1, 68.8, 69.0, 69.2, 71.8, 71.9, 72.4, 72.6, 73.1, 73.1, 73.2, 73.3, 74.6, 74.8, 74.9 and 75.2 ppm for the seventeen methylene (-CH_2-) groups present in the assigned tetrasaccharide **18**. The structure **18** was also supported by mass spectral analysis (Molecular weight calculated for $C_{113}H_{118}O_{22}$: 1827.81; Found: 1849.78 (M^++23 for Na)).

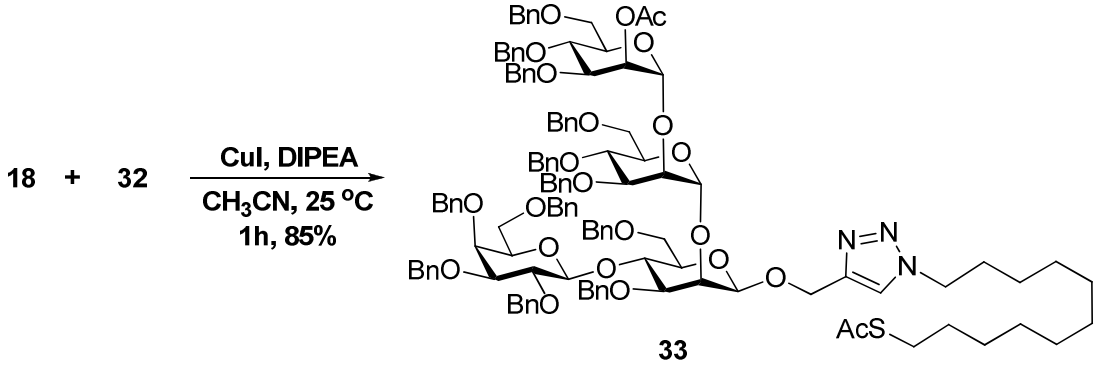
At last, the tetrasaccharide **18** was synthesized efficiently as a propargyl glycoside with benzyl ether protecting groups. Selective deprotection of benzyl ethers in the presence of propargyl moiety is extremely difficult to accomplish the target molecule **1**. However, we thought that the propargyl group can be clicked with azide under CuAAc reaction and the resulting product can be deprotected by either catalytic hydrogenation or by Birch reduction. Moreover, the impact of propargyl group in the synthesis of bioconjugates as delineated above motivated us to functionalize the propargyl group of the tetrasaccharide with lipid containing both azide and thiol functional groups under CuAAC reaction. Later, the thiol functionality can be useful to develop the synthetic antigens using various carrier proteins such as KLH, virosomes.[13c,e] For that reason, we selected 11-azido-1-thioacetyl-undecane as a model substrate and synthesized from easily available material 10-undecen-1-ol **29** which was converted into thioacetyl hydroxy compound **30** *via* the treatment with excess thioacetic acid in anhydrous dioxane in the presence of free radical initiator AIBN

Scheme 21



at 70 ^{o}C under argon atmosphere.[27a] Subsequently, the hydroxy compound **31** was treated with carbon tetrabromide and triphenylphosphine in dichloromethane at room temperature to give thioacetyl-undecyl bromide **32** which was allowed to react with sodium azide in anhydrous DMF at room temperature under argon atmosphere to obtain 11-azido-1-thioacetyl-undecane **32** in 90% yield (Scheme 21).[27b] The structure was confirmed by ^{1}H NMR spectrum in which resonances attributed to undecyl groups at δ 1.20-1.43 ppm as a multiplet, δ 1.56 ppm as a quintet, δ 2.86 ppm as a triplet and δ 3.26 ppm as a triplet along with a resonance due to thioacetyl group at δ 2.32 ppm were noticed.

Scheme 22



Having both linker and propargyl tetrasaccharide in hand, the propargyl tetrasaccharide **18** was treated with 11-azido-1-thioacetyl-undecane **32** under conditions CuI/DIPEA/rt/1h to obtain the triazole 'clicked' glycolipid **33** with thioacetyl functionality at the terminal position in 85% yield (Scheme 22). The glycolipid **33** was characterized thoroughly using the spectroscopic techniques such as ^{1}H, ^{13}C, DEPT NMR and mass spectral analysis. In the ^{1}H NMR spectrum of glycolipid **33**, disappearance of resonance related to the propargylic methine proton and at the same time, appearance of a characteristic resonance due to the aromatic proton of triazole ring at δ 7.45 ppm as a singlet were observed. In addition, resonances attributed to acetyl group and thioacetyl group were identified at δ 2.05 and 2.31 ppm as two singlets along with the resonances corresponding to the aromatic protons of benzyl ethers at δ 7.02-7.32 ppm as a multiplet. Rest of the resonances in the spectrum were completely in agreement with the assigned structure **33**. Whereas, in the ^{13}C NMR spectrum, the resonances attributed to the four anomeric carbons were

identified at δ 98.8, 99.3, 99.6 and 102.7 ppm. Additionally, resonances corresponding to acetyl group and thioacetyl group were noticed at δ 21.1, 170.0 and 26.4, 196.1 ppm respectively. Rest of the resonances were in accordance with the assigned structure **33**. The structure was further supported by the mass spectral analysis which indicated a molecular ion peak at 2123.61 (M^++23 for Na).

In conclusion, we synthesized a tetrasaccharyl cap portion of lipophosphoglycan (LPG) present in the *Leishmania* parasite in an efficient manner using $AuBr_3$ mediated activation of propargyl 1,2-orthoesters. The target tetrasaccharide was synthesized as a per-*O*-benzylated propargyl glycoside. The propargyl group in the tetrasaccharide can be useful for the synthesis of saccharide-protein conjugation, saccharide-lipid conjugation and saccharides conjugation under CuAAC reaction. For instance, we utilized the propargyl tetrasaccharide with 11-azido-1-thioacetyl-undecane for the synthesis of triazole 'clicked' glycolipid with thioacetate group at the terminal end that could be useful to construct various synthetic antigens by treating with carrier proteins such as KLH, virosomes etc. In addition, the propargyl tetrasaccharide is a valuable intermediate to synthesize various derivatives such as carboxylic acid, alkene that are useful for connecting the proteins having amines and thiol functional groups.

****

Experimental Section

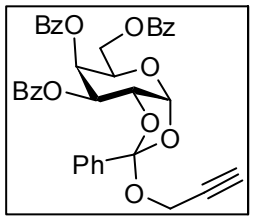
Synthesis of prop-2-ynyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (10): To a solution of prop-2-ynyl α-D-mannopyranoside (2g, 9.16 mmol) and benzylidene dimethyl acetal (1.8mL, 11.92 mmol) in anhydrous DMF (15mL) was added a catalytic amount of PTSA (100mg) at room temperature. A round bottom flask containing the reaction mixture was attached to the *rotavapor* and methanol formed from the reaction mixture was removed at 50 ^{o}C under reduced pressure for 5h. The reaction mixture was neutralized with aq $NaHCO_3$ solution and extracted with diethyl ether (2x50mL). Combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The resulting crude was purified by silica gel column chromatography using petroleum ether-ethyl acetate as the mobile phase to give prop-2-ynyl 4,6-*O*-benzylidene-α-D-mannopyranoside (1.83g, 65%) as a white solid. Subsequently, a solution of prop-2-ynyl 4,6-*O*-benzylidene-α-D-mannopyranoside (1.7g, 5.55 mmol) in anhydrous methanol (25mL) was treated with dibutyltin oxide (1.38g, 5.55 mmol) to form the stannylene acetal and the reaction mixture was stirred for 4h at 90 ^{o}C. The completion of reaction was observed by formation of clear solution in the reaction mixture. The solvent was concentrated *in vacuo* to obtain a stannylene acetal of propargyl mannoside that was redissolved in anhydrous DMF (15mL). Benzyl bromide (2.0mL, 16.65 mmol) was added at room temperature and the reaction mixture was stirred at 120 ^{o}C for 8h under argon atmosphere, quenched with water and extracted with diethyl ether (2x50mL). Combined organic layers were washed with water, dried over anhydrous sodium sulfate and filtered off. The filtrate was concentrated *in vacuo* to obtain the yellowish crude residue which was purified by silica gel column chromatography using petroleum ether-ethyl acetate as the eluent to afford prop-2-ynyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside **10** (2.05g, 93%) as a viscous liquid. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.00) = +124.44; IR (cm^{-1}): 2120, 2868, 2920, 3285, 3481; ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ 2.46 (1H, t, *J* 2.38 Hz), 2.79 (1H, s), 3.83-3.95 (2H, m), 3.85 (1H, d, *J* 7.38 Hz), 4.06-4.20 (2H, m), 4.23 (2H, d, *J* 2.39 Hz), 4.27 (1H, d, *J* 5.99 Hz), 4.77 (2H, ABq, *J* 11.85 Hz), 5.06 (1H, d, *J* 1.26 Hz), 5.61 (1H, s), 7.25-7.52 (10H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 54.4, 63.7, 68.6, 69.7,

73.0, 75.0, 75.4, 78.5, 78.6, 98.6, 101.6, 126.0-128.9, 137.4, 137.9; Mol. Wt. calculated for $C_{23}H_{24}O_6$: 396.43, Found: 419.45 (M^++ 23 for Na).

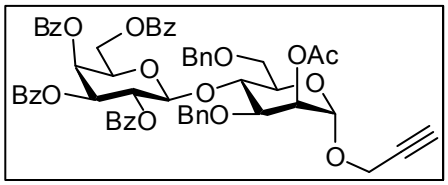
Synthesis of prop-2-ynyl 2-*O*-acetyl-3,6-di-*O*-benzyl-α-D-mannopyranoside (7): To a solution of prop-2-ynyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (1.9g, 4.79 mmol), triethylamine (1.3mL, 9.58 mmol) and a catalytic amount of DMAP (50mg) in anhydrous dichloromethane (15mL) was added acetic anhydride (0.93mL, 9.58 mmol) at 0 ^oC under argon atmosphere. The reaction mixture was stirred at room temperature for 2h, diluted with water and extracted with dichloromethane (2x30mL). Combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate and filtered off. The filtrate was evaporated under reduced pressure to give prop-2-ynyl 2-*O*-acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (2.1g, 100%) as a pale yellow liquid which was taken for the next step without purification. To a solution of acetylated compound prepared *vide supra* (2.1g, 4.79 mmol) in anhydrous THF (20mL) was added sodium cyanoborohydride (2.56g, 40.91 mmol) at 0 ^oC under argon atmosphere. Then, a saturated solution of HCl gas in diethyl ether (25mL) was added carefully and dropwise at 0 ^oC till the disappearance of frothing. The reaction mixture was quenched slowly with water and extracted with diethyl ether (2x30mL). Combined organic layers were washed with water (2x50mL), dried over anhydrous sodium sulfate and concentrated *in vacuo*. The resulting yellowish liquid was purified by flash silica gel column chromatography using petroleum ether-ethyl acetate as eluent to obtain prop-2-ynyl 2-*O*-acetyl-3,6-di-*O*-benzyl-α-D-mannopyranoside **7** (1.48g, 70%) as a thick syrup. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.00) = +36.28; IR (cm^{-1}): 1585, 1604, 1745, 2120, 2868, 2921, 3284, 3472 ; ^1H NMR ($CDCl_3$, 200.13 MHz): δ 2.12 (3H, s), 2.45 (1H, t, *J* 2.42 Hz), 2.48 (1H, bs), 3.73-3.83 (4H, m), 3.93 (1H, d, *J* 9.24 Hz), 4.24 (2H, d, *J* 2.36 Hz), 4.44 (1H, d, *J* 11.13 Hz), 4.61 (2H, ABq, *J* 12.12 Hz), 4.72 (1H, d, *J* 11.22 Hz), 5.04 (1H, d *J* 1.58 Hz), 5.40 (1H, dd, *J* 1.72, 3.23 Hz), 7.22-7.40 (10H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 20.9, 54.4, 67.0, 67.7, 69.5, 71.6, 71.7, 73.5, 75.1, 77.4, 78.4, 96.5, 127-128.5, 137.5, 138.1, 170.2; Mol. Wt. calculated for $C_{25}H_{28}O_7$: 440.485, Found: 463.480 (M^++ 23 for Na).

Synthesis of 3,4,6-tri-*O*-benzoyl-α-D-galactopyranose-1,2-(prop-2-ynyl orthobenzoate) (6): A solution of 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl bromide (20g, 30.3 mmol) in anhydrous CH_2Cl_2 (75mL) was treated with 2,6-lutidine

(15mL), propargyl alcohol (9mL, 15.2 mmol) followed by tetra *n*-butylammonium iodide (50mg) at room temperature under argon atmosphere. The reaction mixture was refluxed at 65 °C for 48h, diluted with aqueous oxalic acid solution and extracted with CH_2Cl_2 (2x100mL). Combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate and concentrated *in vacuo.* The resulting brownish black residue was purified by silica gel column chromatography using petroleum ether-ethyl acetate as the mobile phase to give 3,4,6-tri-*O*-benzoyl-α-D-galactopyranose-1,2-(prop-2-ynyl orthobenzoate) **6** (16.3g, 85%) as a amorphous white solid. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.0) = +55.47; IR (cm^{-1}): 1269, 1602, 1728, 3309; ^1H NMR (200.13 MHz, $CDCl_3$): δ 2.40 (1H, t, *J* 2.3 Hz), 4.06 (2H, d, *J* 2.3 Hz), 4.40 (1H, dd, *J* 3.37, 9.10 Hz), 4.50-4.69 (2H, m), 4.84 (1H, t, *J* 5.3 Hz), 5.59 (1H, dd, *J* 4.20, 5.80 Hz), 5.83 (1H, dd, *J* 2.20, 4.00 Hz), 6.26 (1H, d, *J* 5.20 Hz), 7.18-7.60 (12H, m), 7.63-7.70 (2H, m), 7.83-8.05(6H, m); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 52.0, 62.2, 66.3, 68.9, 69.9, 73.4, 73.8, 79.2, 98.3, 120.1, 126.0-130.0, 133.1, 133.3, 133.5, 135.1, 165.1, 165.1, 165.9; Mol. Wt. calculated for $C_{37}H_{30}O_{10}$: 634.63, Found: 657.52 (M^++23 for Na).

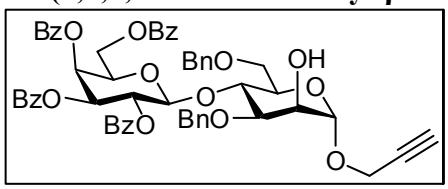


Synthesis of prop-2-ynyl 2-*O*-acetyl-3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-α-D-mannopyranoside (12): Propargyl 1,2-orthoester of galactose **6** (1.44g, 2.27 mmol), mannosyl acceptor **7** (0.5g, 1.14 mmol) were mixed in anhydrous dicholoromethane (15mL). Freshly activated 4Å molecular sieves powder (0.7g) followed by 10mol% of solid $AuBr_3$ (49mg) was added at room temperature under argon atmosphere. The reaction mixture was stirred for 1h, filtered through a celite pad and the filtrate was concentrated *in vacuo*. The resulting crude was purified by silica gel column chromatography using petroleum ether-ethyl acetate as eluent to afford 1,2-*trans* disaccharide **12** (0.72g, 62%) as a colourless solid. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.00) = +107.12; IR (cm^{-1}): 1267, 1584, 1602, 1731, 2126, 2873, 2925, 3298; ^1H NMR ($CDCl_3$, 200.13 MHz): δ 2.08 (3H, s), 2.33 (1H, t, *J* 2.37 Hz), 3.49 (1H, d, *J* 9.31 Hz), 3.60-3.75 (2H, m), 3.90-4.02 (2H, m), 4.13 (2H, d, *J* 2.33 Hz), 4.16-4.33 (3H, m), 4.49 (1H, dd, *J* 5.86, 11.15 Hz), 4.67 (1H, d, *J* 12.07 Hz), 4.77 (2H, s), 4.91 (1H, d, *J* 8.03 Hz), 4.99 (1H, d, *J* 1.66 Hz), 5.35 (1H, dd, *J* 1.11, 3.45 Hz), 5.38 (1H, dd, *J* 3.40, 10.48 Hz), 5.73 (1H, dd, *J*



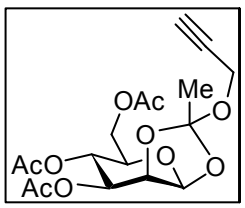
8.02, 10.45 Hz), 5.89 (1H, d, *J* 3.29 Hz), 7.15-7.62 (22H, m), 7.77-8.05 (8H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 20.9, 54.5, 61.5, 67.8, 67.9, 68.9, 70.3, 70.9, 71.2, 71.7, 71.8, 73.4, 74.3, 75.1, 75.4, 78.3, 96.3, 100.7, 126.9-129.8, 133.2, 133.2, 133.3, 133.4, 138.1, 138.4, 164.9, 165.4, 165.4, 165.8, 170.2; Mol. Wt. calculated for $C_{59}H_{54}O_{16}$: 1018.34, Found: 1041.75 (M^++ 23 for Na).

Synthesis of prop-2-ynyl 3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-α-D-mannopyranoside (5):

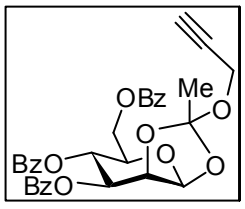


To a solution of disaccharide **12** (1.1g, 1.08 mmol) in anhydrous methanol (20mL) was added an equimolar amount of PTSA (0.19g, 1.08 mmol) at room temperature. The resulting solution was stirred for 8h at 45 ^{o}C. After completion of the reaction, the reaction mixture was quenched with triethylamine and the solvent was concentrated *in vacuo* to obtain the crude residue which was purified by silica gel column chromatography using petroleum ether and ethyl acetate as the mobile phase to give prop-2-ynyl 3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-α-D-mannopyranoside **5** (0.98g, 93%) as a white solid. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.00) = +116.46; IR (cm^{-1}): 1267, 1585, 1602, 1731, 2862, 2924, 3296, 3445; ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ 2.32 (1H, t, *J* 2.34 Hz), 2.59 (1H, bs), 3.45-3.63 (2H, m), 3.69 (1H, dd, *J* 3.20, 10.57 Hz), 3.81 (1H, dd, *J* 3.36, 9.18 Hz), 3.95-4.05 (2H, m), 4.13 (2H, d, *J* 2.35 Hz), 4.23-4.40 (3H, m), 4.50 (1H, dd, *J* 6.68, 11.13 Hz), 4.73 (2H, d, *J* 12.02 Hz), 4.88 (1H, d, *J* 8.03 Hz), 5.02 (1H, d, *J* 11.65 Hz), 5.05 (1H, s), 5.37 (1H, dd, *J* 3.42, 10.44 Hz), 5.72 (1H, dd, *J* 8.09, 10.39 Hz), 5.88 (1H, d, *J* 3.11 Hz), 7.10-7.60 (22H, m), 7.74-8.05 (8H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 54.4, 61.7, 67.7, 67.9, 69.1, 70.2, 70.9, 71.0, 71.8, 72.8, 73.5, 73.9, 74.9, 77.2, 78.7, 97.8, 100.6, 127.2-129.8, 133.2, 133.2, 133.3, 133.4, 138.1, 138.4, 164.9, 165.4, 165.5, 165.9; Mol. Wt. calculated for $C_{57}H_{52}O_{15}$: 977.01, Found: 1000.73 (M^++ 23 for Na).

Synthesis of 3,4,6-tri-*O*-acetyl-β-D-mannopyranose-1,2-(prop-2-ynyl ortho acetate) (15): To a suspension of D-mannose (5g, 27.75 mmol) in glacial acetic acid (20mL) was added acetic anhydride (18mL, 180.39 mmol) followed by Conc. H_2SO_4 (4 drops) and the reaction mixture was stirred at room temperature for 30min. Then, 33% HBr in glacial acetic acid (60mL) was added at 0 ^{o}C and the resulting solution was stirred for additional 5h at room temperature. After completion of the reaction as

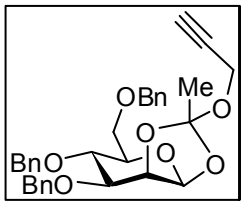


judged by TLC, the reaction mixture was poured into ice and extracted with dichloromethane (2x100mL). Combined organic layeres were washed with water (3x100mL), saturated $NaHCO_3$ solution, water, dried over anhydrous sodium sulfate and concentrated *in vacuo* to give 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide (10.24g, 90%) that was redissolved in anhydrous dichloromethane (50mL). To that, 2,6-lutidine (10mL), propargyl alcohol (7.3mL, 124.02 mmol) followed by a catalytic amount of tetra-*n*-butylammonium iodide (0.2g) were added at room temperature under argon atmosphere. The reaction mixture was stirred for 24h at 70 ^{o}C under argon atmosphere, quenched with a saturated solution of oxalic acid and extracted with dichloromethane (2x100mL). Combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate and concentrated *in vacuo* to obtain the brownish black residue which was purified by silica gel column chromatography using petroleum ether-ethyl acetate as the mobile phase to give 3,4,6-tri-*O*-acetyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthoacetate) **15** (6.07g, 63%). Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.00) = +3.59; IR (cm^{-1}): 1050, 1230.1748, 2120, 2947, 3279; ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ 1.79 (3H, s), 2.06 (3H, s), 2.08 (3H, s), 2.12 (3H, s), 2.39 (1H, t, *J* 2.46 Hz), 3.69 (1H, ddd, *J* 2.84, 4.84, 9.21 Hz), 4.15-4.29 (1H, m), 4.16 (1H, d, *J* 2.87 Hz), 4.19 (2H, d, *J* 2.47 Hz), 4.66 (1H, dd, *J* 2.66, 3.83 Hz), 5.16 (1H, dd, *J* 3.89, 9.90 Hz), 5.27 (1H, d, *J* 9.45 Hz), 5.51 (1H, d, *J* 2.63 Hz); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 20.6, 20.7, 20.7, 24.4, 50.8, 62.3, 65.3, 70.2, 71.4, 73.6, 76.3, 79.4, 97.4, 124.1, 169.4, 170.3, 170.8; Mol. Wt. calculated for $C_{17}H_{22}O_{10}$: 386.35, Found: 409.37 (M^++ 23 for Na).



Synthesis of 3,4,6-tri-*O*-benzoyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthoacetate) (3): To a solution of 3,4,6-tri-*O*-acetyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthoacetate) **15** (2g, 5.18 mmol) in anhydrous methanol (25mL) was added a piece of sodium metal at room temperature under argon atmosphere and the reaction mixture was stirred for 2h at same temperature. After completion of the reaction as judged by TLC, the reaction mixture was concentrated under reduced pressure to give the triol of mannose 1,2-orthoester (1.3g, 97%) which was taken for the next step without further purification. The triol was dissolved in anhydrous dichloromethane (15mL) along with DMAP (50mg) and triethylamine (10mL, 74.93 mmol). Benzoyl chloride (2mL, 17.48 mmol) was added dropwise at 0 ^{o}C under argon atmosphere. The reaction

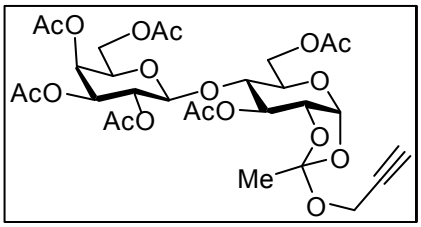
mixture was stirred for 15h at room temperature, quenched with water and extracted with dichloromethane (2x25mL). Combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate and concentrated *in vacuo* followed by flash silica gel (230-400 mesh) column purification to obtain 3,4,6-tri-*O*-benzoyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthoacetate) **3** (1.14g, 40%) as a white solid. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.1) = -34.68; IR (cm^{-1}): 1215, 1585, 1602, 1725, 2879, 2934, 3307; ^1H NMR ($CDCl_3$, 200.13 MHz): δ 1.81 (3H, s), 2.28 (1H, t, *J* 2.43 Hz), 4.05-4.16 (1H, m), 4.18 (2H, d, *J* 2.42 Hz), 4.46 (1H, dd, *J* 4.66, 12.09 Hz), 4.65 (1H, dd, *J* 3.20, 12.09 Hz), 4.91 (1H, dd, *J* 2.76, 3.76 Hz), 5.60 (1H, dd, *J* 3.90, 10.03 Hz), 5.69 (1H, d, *J* 2.65 Hz) 5.93 (1H, t, *J* 9.73 Hz), 7.26-7.58 (9H, m), 7.86-8.05 (6H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 24.5, 50.8, 63.1, 66.2, 71.1, 71.7, 73.6, 76.5, 79.4, 97.7, 124.2, 128.3-130.0, 133.1, 133.4, 133.6, 165.2, 165.9, 166.1; Mol. Wt. calculated for $C_{32}H_{28}O_{10}$: 572.55, Found: 595.43 (M^++ 23 for Na).



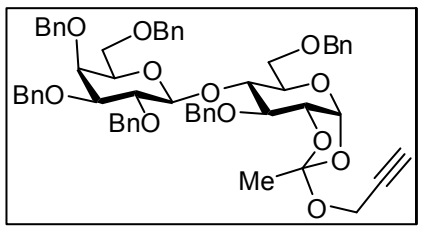
Synthesis of 3,4,6-tri-*O*-benzyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthoacetate) (20): To a solution of 3,4,6-tri-*O*-acetyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthoacetate) **15** (5g**,** 12.94 mmol) in anhydrous methanol (75mL) was added sodium metal (~50mg) at room temperature under argon atmosphere and the reaction mixture was stirred for 2h at the same temperature. After completion of the reaction, the reaction mixture was concentrated under reduced pressure to give the triol of mannose 1,2-orthoester (3.37g). The triol (3.37g, 12.94 mmol) was dissolved in anhydrous DMF (30mL). To that was added NaH (1.81g, 45.29 mmol) at 0 ^oC and the reaction mixture was stirred for 1h at room temperature. Benzyl bromide (5.4mL, 45.29 mmol) followed by a catalytic amount of TBAI (0.2g) were added at 0 ^oC under argon atmosphere and the stirring was continued for additional 4h at room temperature. After completion of the reaction as judged by TLC, excess NaH was quenched by slow addition of methanol followed by cold water and subsequently extracted with diethyl ether (2x70mL). Combined organic layers were washed water, brine and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the resulting crude was purified by conventional silica gel column chromatography using petroleum ether and ethyl acetate as the mobile phase to give 3,4,6-tri-*O*-benzyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthoacetate) **20** (5.97g, 87%) as a white amorphous solid. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.00)

= +28.54; IR (cm^{-1}): 1588, 1605, 2126, 2869, 2923, 3284; ^1H NMR ($CDCl_3$, 200.13 MHz): δ 1.77 (3H, s), 2.41 (1H, t, *J* 2.42 Hz), 3.43 (1H, ddd, *J* 2.61, 4.10, 9.25 Hz), 3.71 (1H, d, *J* 2.72 Hz), 3.73 (2H, dd, *J* 4.00, 6.80 Hz), 3.91 (1H, t, *J* 9.23 Hz), 4.18 (2H, d, *J* 2.39 Hz), 4.44 (1H, dd, *J* 2.66, 3.91 Hz), 4.57 (2H, d, *J* 3.26 Hz), 4.59 (1H,d, *J* 11.47 Hz), 4.79 (2H, s), 4.88 (1H, d, *J* 10.74 Hz), 5.37 (1H, d, *J* 2.61 Hz), 7.19-7.45 (15H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 24.6, 50.6, 68.9, 72.3, 73.3, 73.4, 74.0, 74.2, 75.2, 76.9, 78.8, 79.8, 97.6, 123.7, 127.5-128.5, 137.7, 138.1, 138.1; Mol. Wt. calculated for $C_{32}H_{34}O_7$: 530.60, Found: 553.47 (M^++ 23 for Na).

Synthesis of 3,6-di-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-glucopyranose-1,2-(prop-2-ynyl orthoacetate) (22): Preparative procedure is same as delineated above for compound **15**. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.1) = +74.89; IR (cm^{-1}): 1218, 1749, 2879, 2972, 3302; ^1H NMR ($CDCl_3$, 200.13 MHz): δ 1.76 (3H, s), 1.98 (3H, s), 2.04 (3H, s), 2.06 (3H, s), 2.12 (6H, s), 2.18 (3H, s), 2.43 (1H, t, *J* 2.41 Hz), 3.65 (1H, d, *J* 9.61 Hz), 3.76-3.88 (1H, m), 3.94 (1H, t, *J* 6.64 Hz), 4.05-4.17 (3H, m), 4.19 (2H, d, *J* 2.38 Hz), 4.25 (1H, dd, *J* 2.24, 12.05 Hz), 4.37 (1H, dd, *J* 2.54, 4.86 Hz), 4.61 (1H, d, *J* 7.81 Hz), 5.00 (1H, dd, *J* 3.40, 10.41 Hz), 5.19 (1H, dd, *J* 7.89, 10.29 Hz), 5.38 (1H, d, *J* 3.07 Hz), 5.55 (1H, d, *J* 2.73 Hz), 5.70 (1H, d, *J* 5.15 Hz); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 20.1, 20.4, 20.5, 20.5, 20.6, 20.7, 20.8, 51.7, 60.8, 63.2, 66.7, 66.9, 68.7, 69.6, 70.7, 70.8, 72.4, 73.8, 77.4, 79.5, 96.9, 102.3, 121.4, 168.9, 169.3, 169.9, 170.2, 170.3, 170.6; Mol. Wt. calculated for $C_{29}H_{38}O_{18}$: 674.60, Found: 697.52 (M^++ 23 for Na).



Synthesis of 3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-α-D-glucopyranose-1,2-(prop-2-ynyl orthoacetate) (23): Preparative protocol is same as described above for compound **20**. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 0.9) = +71.44; IR (cm^{-1}): 1099, 1605, 1585, 2867, 2921, 3289; ^1H NMR ($CDCl_3$, 200.13 MHz): δ 1.67 (3H, s), 2.36 (1H, t, *J* 2.39 Hz), 3.35-3.57 (4H, m), 3.60-3.65 (2H, m), 3.76 (2H, dd, *J* 7.82, 9.33 Hz), 3.87 (1H, d, *J* 2.91 Hz), 3.98 (1H, d, *J* 9.18 Hz), 4.13-4.19 (1H, m), 4.14 (2H, d, *J* 2.40 Hz), 4.23-4.45 (6H, m), 4.50-4.78 (7H, m), 4.93 (1H, d, *J* 11.52 Hz), 5.73 (1H, d, *J* 5.24 Hz), 7.15-7.40 (30H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 20.5, 51.5, 68.5,

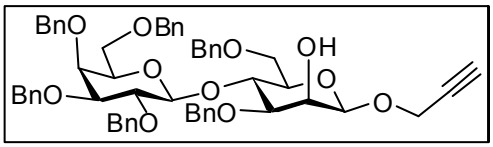


68.9, 69.8, 71.7, 72.8, 73.1, 73.2, 73.3, 73.5, 73.5, 73.6, 74.6, 74.9, 75.5, 76.7, 79.1, 79.9, 81.9, 97.5, 105.3, 120.9, 127.4-128.3, 137.6, 138.0, 138.1, 138.3, 138.5, 138.5; Mol. Wt. calculated for $C_{59}H_{62}O_{12}$: 963.11, Found: 985.81 (M^++ 23 for Na).

Synthesis of prop-2-ynyl 3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galacto pyranosyl)-β-D-glucopyranoside (25): To a solution of propargyl 1,2-orthoester of lactose **23** (3.3g, 3.43 mmol), propargyl alcohol (0.2mL, 3.42 mmol) and freshly activated 4Å molecular sieves powder (0.5g) in dichloromethane (20mL) was added 10mol% of scandium triflate (84mg) at room temperature under argon atmosphere. The reaction mixture was stirred for 30min., filtered through a celite pad and the filtrate was concentrated *in vacuo.* The resulting crude was purified by silica gel column chromatography using petroleum ether-ethyl acetate as eluent to give prop-2-ynyl 2-*O*-acetyl-3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-β-D-glucopyranoside (2.08g, 63%) as a colourless liquid. Prop-2-ynyl lactoside (2.08g, 2.16 mmol) prepared *vide supra* was dissolved in anhydrous methanol (25mL). Sodium metal (~50mg) was added at room temperature under argon atmosphere and the reaction mixture was stirred till completion of the reaction. The solvent was concentrated *in vacuo* and the resulting crude was purified by silica gel column chromatography using petroleum ether-ethylacetate as the mobile phase to afford prop-2-ynyl 3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galacto-pyranosyl)-β-D-glucopyranoside **25** (1.79g, 90%) as a colourless oil. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.00) = -30.15; IR (cm^{-1}): 1091, 1585, 1605, 2120, 2869, 2912, 3289, 3444.13; ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ 2.45 (1H, bs), 2.46 (1H, t, *J* 2.35 Hz), 3.30-3.60 (7H, m), 3.65-4.05 (5H, m), 4.23-4.57 (9H, m), 4.65-4.74 (3H, m), 4.79 (2H, d, *J* 3.44 Hz), 4.96 (1H, d, *J* 11.51 Hz), 5.08 (1H, d, *J* 11.08 Hz), 7.10-7.40 (30H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 55.6, 67.9, 68.0, 72.4, 72.9, 73.0, 73.1, 73.3, 73.4, 74.5, 74.7, 75.1, 75.1, 75.4, 75.9, 78.7, 79.8, 82.3, 82.5, 100.1, 102.6, 127.2-128.3, 137.9, 138.1, 138.4, 138.7, 138.8, 138.9; Mol. Wt. calculated for $C_{57}H_{60}O_{11}$: 921.07, Found: 943.74 (M^++ 23 for Na).

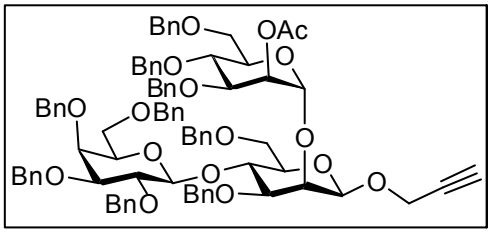
Synthesis of prop-2-ynyl 3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galacto pyranosyl)-β-D-mannopyranoside (21): Propargyl lactoside **25** (1.7g, 1.84 mmol) was dissolved in 30mL of mixture of DMSO and Ac_2O (2:1). The resulting solution was stirred for 24h at room temperature under argon atmosphere, concentrated directly

under reduced pressure and the resulting crude was directly taken for the next step without further purification. The disaccharide ketone



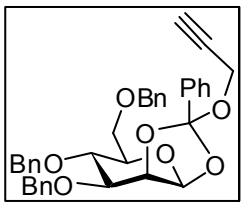
(1.69g, 1.83 mmol) was dissolved in 100mL of CH_2Cl_2:MeOH (1:1). To that, sodium borohydride (0.25g, 6.43 mmol) was added at 0 ^oC under argon atmosphere. The reaction mixture was stirred for 4h at room temperature, quenched with water and extracted with dichloromethane (2x50mL). Combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate and concentrated *in vacuo* to obtain a yellowish crude oil which was purified by flash silica gel (230-400 mesh) column chromatography using petroleum ether-ethyl acetate as eluent to afford prop-2-ynyl 3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-β-D-mannopyranoside **21** (1.39g, 82% over two steps) as a white solid. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.00) = -30.91; IR (cm^{-1}): 1099, 1585, 1605, 2868, 2920, 3285, 3510; ^1H NMR ($CDCl_3$, 200.13 MHz): δ, 2.43 (1H, t, *J* 2.33 Hz), 2.50 (1H, bs) 3.37-3.60 (6H, m), 3.72 (1H, d, *J* 7.83 Hz), 3.79 (2H, d, *J* 3.31 Hz), 3.91 (1H, d, *J* 2.56 Hz), 4.11 (2H, d, *J* 7.74 Hz), 4.25-4.85 (15H, m), 4.96 (1H, d, *J* 11.52 Hz), 7.11-7.40 (30H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 55.4, 68.3, 68.5, 68.6, 72.4, 72.5, 72.9, 73.1, 73.4, 73.4, 74.1, 74.5, 75.0, 75.1, 75.3, 78.7, 79.1, 79.8, 82.4, 96.9, 103.1, 127.4-128.4, 137.9, 138.3, 138.4, 138.4, 138.6, 138.9; Mol. Wt. calculated for $C_{57}H_{60}O_{11}$: 921.07,Found: 943.81 (M^++ 23 for Na).

Synthesis of prop-2-ynyl 2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-manno pyranosyl)-3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-β-D-mannopyranoside (26): To a solution of mannose 1,2-orthoester **20** (0.1g, 0.188 mmol) and disaccharide acceptor **21** (0.173g, 0.188 mmol) in anhydrous dichloromethane (5mL)



was added freshly activated powdered 4Å molecular sieves (50mg) followed by solid $AuBr_3$ (16mg, 0.038 mmol) at room temperature under argon atmosphere. The reaction mixture was stirred for 1h at room temperature. After completion of the reaction as judged by TLC, the reaction mixture was filtered through a celite pad and the filtrate was concentrated *in vacuo*. The resulting crude was purified by flash silica gel column chromatography using petroleum ether-ethyl acetate as eluent to obtain the trisaccharide **26** (125mg, 48%) as a thick syrup. Characterization data: $[\alpha]_D$ ($CHCl_3$,

c 0.9) = -15.57; IR (cm^{-1}): 1100, 1588, 1605, 1746, 2867, 2928, 3297; ^{1}H NMR ($CDCl_3$, 500.13 MHz): δ 2.03 (3H, s), 2.35(1H, t, *J* 2.33 Hz), 3.38 (2H, ddd, *J* 4.90, 8.49, 19.73 Hz), 3.44 (1H, dd, *J* 2.82, 9.78 Hz), 3.46-3.51 (1H, m), 3.51 (1H, t, *J* 8.49 Hz), 3.57 (1H, dd, *J* 2.83, 8.78 Hz), 3.66 (1H, dd, *J* 1.67, 10.76 Hz), 3.70 (1H, dd, *J* 7.77, 9.57 Hz), 3.77 (1H, dd, *J* 5.44, 10.99 Hz), 3.79-3.90 (4H, m), 4.02 (1H, dd, *J* 3.33, 9.58 Hz), 4.14 (1H, t, *J* 8.94 Hz), 4.20 (1H, d, *J* 2.65 Hz), 4.21 (1H, d, *J* 11.74 Hz), 4.29-4.35 (5H, m), 4.38 (1H, d, *J* 12.02 Hz), 4.41 (1H, d, *J* 5.59 Hz), 4.44 (1H, d, *J* 7.10 Hz), 4.50 (1H, t, *J* 11.54 Hz), 4.52 (1H, d, *J* 6.81 Hz), 4.54 (1H, d, *J* 2.35 Hz), 4.59-4.68 (5H, m), 4.71 (2H, d, *J* 11.57 Hz), 4.79 (2H, dd, *J* 4.15, 10.97 Hz), 4.86 (1H, d, *J* 11.56 Hz), 4.93 (1H, d, *J* 12.13 Hz), 5.16 (1H, d, *J* 1.14 Hz), 5.61 (1H, dd, *J* 1.71, 3.28 Hz), 7.10-7.35 (45H, m); ^{13}C NMR ($CDCl_3$, 125.76 MHz): δ 21.1, 55.4, 67.9, 68.5, 68.7, 68.9, 70.9, 71.9, 72.1, 72.4, 72.6, 73.0, 73.0, 73.1, 73.2, 73.3, 74.3, 74.4, 74.8, 74.8, 74.9, 75.1, 75.7, 78.6, 78.9, 79.8, 80.0, 82.6, 97.0, 98.9, 103.1, 126.5-128.3, 138.0, 138.3, 138.4, 138.4, 138.5, 138,7, 138.7, 138.8, 138.9, 169.8 ; Mol. Wt. calculated for $C_{86}H_{90}O_{17}$: 1395.62, Found: 1419.24 (M^{+}+ 23 for Na).



Synthesis of 3,4,6-tri-*O*-benzyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthobenzoate) (27): To a solution of 3,4,6-tri-*O*-benzoyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthobenzoate) (2.5g, 3.94 mmol) in anhydrous THF (20mL) was added a solution of sodium methoxide in methanol at room temperature under argon atmosphere. The resulting solution was stirred for 1h at room temperature, concentrated *in vacuo* to obtain a yellowish crude oil which was purified by flash silica gel (230-400 mesh) column chromatography using dichloromethane followed by a mixture of ethyl acetate and acetone solvent to get the triol of mannose 1,2-orthobenzoate (1.17g, 92%) as a viscous liquid. The triol prepared *vide supra* was dissolved in anhydrous DMSO (10mL). Powdered KOH (1.83g, 32.59 mmol) followed by benzyl chloride (2.5mL, 21.72 mmol) were added at room temperature under argon atmosphere. The reaction mixture was stirred for 4h, quenched with water and extracted with diethyl ether (2x50mL). Combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate and concentrated *in vacuo* to obtain a dark yellow oil which was purified by silica gel column chromatography using petroleum ether-ethyl acetate as the mobile phase to give 3,4,6-tri-*O*-benzyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthobenzoate) **27** (1.89g, 88%) as

a colourless viscous liquid. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.2) = -36.43; IR (cm^{-1}): 1100, 1588, 1605, 2869, 2925, 3287; ^1H ($CDCl_3$, 200.13 MHz): δ 2.40 (1H, t, *J* 2.42 Hz), 3.46-3.60 (2H, m), 3.67 (1H, dd, *J* 4.91, 10.74 Hz), 3.90 (1H, d, *J* 3.83 Hz), 3.91 (1H, ABq, *J* 9.17 Hz), 4.09 (2H, d, *J* 2.44 Hz), 4.42 (2H, s), 4.62 (1H, d, *J* 10.81 Hz), 4.75-4.94 (4H, m), 5.53 (1H, d, *J* 3.04 Hz), 7.20-7.45 (18H, m), 7.65-7.75 (2H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 52.3, 69.1, 71.9, 73.2, 73.7, 74.2, 75.0, 75.2, 76.0, 78.1, 79.7, 98.0, 122.2, 126.8-129.4, 135.6, 137.7, 138.2, 138.3; Mol. Wt. calculated for $C_{37}H_{30}O_{10}$: 592.67, Found: 615.60 (M^++ 23 for Na).

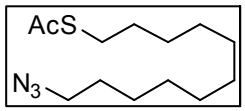
Synthesis of prop-2-ynyl 2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-manno pyranosyl)-3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-β-D-mannopyranoside (28): To a solution of propargyl 1,2-orthoester of mannose **27** (100mg, 0.169 mmol) and disaccharide acceptor **21** (0.156g, 0.169 mmol) in anhydrous dichloromethane (7mL) was added freshly activated 4Å molecular sieves powder (100mg) followed by solid $AuBr_3$ (15mg, 0.034 mmol) at room temperature under argon atmosphere and the reaction mixture was stirred for 12h at same temperature. The reaction mixture was filtered through a celite pad and the filtrate was concentrated *in vacuo* to obtain a gummy residue which was purified by flash silica gel column chromatography (230-400 mesh) using petroleum ether-ethyl acetate as eluent to afford the propargyl trisaccharide **28** (0.113g, 46%) as a colourless viscous liquid. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.00) = -53.83; IR (cm^{-1}): 1070, 1269, 1585, 1602, 1724, 2867, 2923, 3301; ^1H NMR ($CDCl_3$, 500.13 MHz): δ 2.36 (1H, t, *J* 2.46 Hz), 3.40 (1H, dd, *J* 3.44, 8.56 Hz), 3.43-3.55 (4H, m), 3.58 (1H, m), 3.69-3.95 (6H, m), 4.07 (1H, td, *J* 3.50, 9.59 Hz), 4.14-4.22 (3H, m), 4.24 (1H, dd, *J* 3.59, 11.68 Hz), 4.31-4.37 (3H, m), 4.38 (2H, t, *J* 3.98 Hz), 4.41 (1H, d, *J* 3.24 Hz), 4.46-4.82 (14H, m), 4.85 (1H, dd, *J* 3.39, 11.56 Hz), 4.94 (1H, dd, *J* 3.40, 12.17 Hz), 5.32 (1H, s), 5.82-5.85 (1H, m), 6.98-7.54 (48H, m), 8.00-8.07 (2H, m); ^{13}C NMR ($CDCl_3$, 125.76 MHz): δ 55.4, 67.9, 68.9, 69.0, 69.1, 71.4, 71.6, 72.4, 72.5, 72.6, 73.1, 73.2, 73.2, 73.3, 73.7, 74.4, 74.5, 74.8, 74.9, 75.0, 75.2, 75.8, 78.6, 78.9, 79.7, 79.9, 82.5, 97.0, 98.8, 103.1, 126.7-129.9, 132.7, 138.1, 138.3, 138.4, 138.5, 138.6, 138.7, 138.7, 138.8, 138.9, 165.1; Mol. Wt. calculated for $C_{91}H_{92}O_{17}$: 1457.69, Found: 1481.42 (M^++ 23 for Na).

Synthesis of prop-2-ynyl 2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-β-D-mannopyranoside (19): Preparative procedure is same as described in the preparation of compound **25**, which provided the trisaccharide acceptor **19** as colourless viscous liquid. Characterization data: $[\alpha]_D$ (CH_3OH, *c* 1.00) = +1.72; IR (cm^{-1}): 1099, 1585, 1603, 2867, 2917, 3296, 3447; ^1H NMR ($CDCl_3$, 500.13 MHz): δ 2.25 (1H, bs), 2.34 (1H, t, *J* 2.37 Hz), 3.37-3.44 (3H, m), 3.44 (1H, dd, *J* 2.90, 9.92 Hz), 3.50-3.57 (2H, m), 3.67 (1H, dd, *J* 1.80, 10.78 Hz), 3.71-3.79 (2H, m), 3.78 (1H, dd, *J* 3.85, 10.74 Hz), 3.84 (1H, dd, *J* 4.95, 11.37 Hz), 3.86-3. 91 (3H, m), 4.05 (1H, s), 4.15 (1H, t, *J* 8.91 Hz), 4.21 (1H, d, *J* 2.76 Hz), 4.25 (1H, d, *J* 11.80 Hz), 4.30 (2H, t, *J* 2.74 Hz), 4.38 (2H, d, *J* 11.92 Hz), 4.43 (2H, d, *J* 2.54 Hz), 4.46 (1H, d, *J* 5.18 Hz), 4.48 (1H, d, *J* 6.67 Hz), 4.51 (1H, d, *J* 7.62 Hz), 4.54 (1H, d, *J* 11.54 Hz), 4.59 (1H, d, *J* 12.05 Hz), 4.61-4.72 (5H, m), 4.70 (1H, d, *J* 3.90 Hz), 4.76 (1H, d, *J* 10.60 Hz), 4.76 (2H, ABq, *J* 11.03 Hz), 4.85 (1H, d, *J* 12.05 Hz), 4.93 (1H, d, *J* 11.37 Hz), 5.27 (1H, d, *J* 1.22 Hz), 7.10-7.38 (45H, m); ^{13}C NMR ($CDCl_3$, 125.76 MHz): δ 55.3, 68.5, 68.6, 68.7, 68.8, 70.7, 71.8, 72.6, 72.8, 73.1, 73.2, 73.3, 73.3, 73.4, 73.6, 74.3, 74.4, 74.5, 74.8, 74.9, 75.2, 75.9, 78.9, 79.9, 79.9, 80.1, 82.5, 97.2, 100.1, 102.9, 127.2-128.5, 138.0, 138.2, 138.4, 138.5, 138.5, 138.7, 138.7, 138.7, 138.8; Mol. Wt. calculated for $C_{84}H_{88}O_{16}$: 1353.58, Found: 1376.39 (M^++ 23 for Na).

Synthesis of prop-2-ynyl 2-*O*-(2-*O*-(2-*O*-acetyl-3,4,6-tri-O-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-β-D-mannopyranoside (18): To a solution of mannose 1,2-orthoester **20** (78mg, 0.148 mmol), trisaccharide acceptor **19** (0.2g, 0.148 mmol) and freshly activated 4Å molecular sieves powder (100mg) in anhydrous dichloromethane (5mL) was added solid $AuBr_3$ (13mg, 0.03 mmol) at room temperature under argon atmosphere. The reaction mixture was stirred at room temperature for 2h. After completion of the reaction as judged by TLC, the reaction mixture was filtered through a celite pad and the filtrate was concentrated *in vacuo*.

The resulting crude was purified by flash silica gel column chromatography using petroleum ether-ethyl acetate as eluent to obtain the propargyl tetrasaccharide **18** (94mg, 35%) as colourless viscous liquid. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 0.9) = -15.20; IR (cm^{-1}): 1096, 1585, 1605, 1742, 2866, 2917, 3285; ^1H NMR ($CDCl_3$, 400.13 MHz): δ 2.06 (3H, s), 2.34 (1H, t, *J* 2.27 Hz), 3.32-3.45 (5H, m), 3.48 (1H, d, *J* 10.40 Hz), 3.53-3.63 (2H, m), 3.68 (1H, dd, *J* 1.29, 11.34 Hz), 3.73 (2H, dd, *J* 7.65, 9.63 Hz), 3.76-3.83 (3H, m), 3.85 (1H, d, *J* 9.54 Hz), 3.87-3.92 (2H, m), 3.94 (1H, d, *J* 2.50 Hz), 3.98 (1H, dd, *J* 3.18, 9.03 Hz), 4.01 (1H, d, *J* 2.07 Hz), 4.04 (1H, t, *J* 2.14 Hz), 4.08 (1H, t, *J* 8.71 Hz), 4.21 (2H, ABq, *J* 11.56 Hz), 4.25 (1H, d, *J* 1.23 Hz), 4.26 (1H, d, *J* 11.10 Hz), 4.30 (2H, t, *J* 2.90 Hz), 4.36 (1H, d, *J* 10.75 Hz), 4.40 (2H, dd, *J* 2.28, 11.81 Hz), 4.41 (1H, d, *J* 10.88 Hz), 4.45-4.72 (14H, m), 4.74 (2H, d, *J* 5.23 Hz), 4.80 (2H, dd, *J* 2.81, 10.85 Hz), 4.91 (1H, d, *J* 1.46 Hz), 4.93 (1H, d, *J* 11.55 Hz), 5.19 (1H, s), 5.50 (1H, dd, *J* 0.99, 1.78 Hz), 7.07-7.38 (60H, m); ^{13}C NMR ($CDCl_3$, 100.61 MHz): δ 21.1, 55.2, 68.1, 68.8, 68.8, 69.0, 69.2, 71.6, 71.7, 71.8, 71.9, 72.4, 72.6, 72.6, 73.1, 73.1, 73.2, 73.3, 74.1, 74.3, 73.3, 74.5, 74.6, 74.7, 74.8, 74.9, 74.9, 75.2, 75.5, 75.7, 78.2, 79.1, 79.5, 79.5, 79.9, 82.5, 97.1, 99.3, 100.0, 102.6, 127.0-128.4, 137.9, 138.1, 138.4, 138.4, 138.5, 138.6, 138.7, 138.7, 138.7, 138.8, 138.9, 139.0, 170.0; Mol. Wt. calculated for $C_{113}H_{118}O_{22}$: 1827.81, Found: 1849.78 (M^++ 23 for Na).

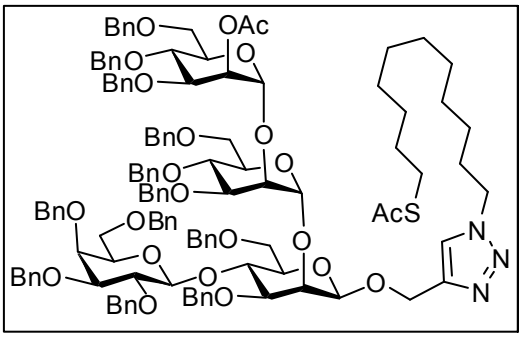
Synthesis of 11-azido-1-thioacetyl-undecane (32): A solution of



10-undecen-1-ol (1g, 5.87 mmol) in anhydrous dioxane (5mL) was purged with argon balloon. To that was added excess of thioacetic acid (6.1mL, 117.4 mmol) followed by AIBN (50mg) at room temperature. The reaction mixture was purged once again with argon balloon, stirred for 24h at 75 ^oC under argon atmosphere, concentrated *in vacuo* and the resulting crude was purified by silica gel column chromatography using petroleum ether-ethylacetate as eluent to afford 11-thioacetyl-undecan-1-ol (0.37g, 26%) as a dark liquid that was redissolved in anhydrous dichloromethane (15mL). To that was added carbon tetrabromide (1.0g, 3.00 mmol) follwed by a solution of triphenylphosphine (0.79g, 3.00 mmol) in dichloromethane (5mL) at 0 ^oC under argon atmosphere. The reaction mixture was stirred for 1h at room temperature, quenched with water and extracted with dichloromethane (2x20mL). Combined organic layers were washed with water, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The resulting crude residue

was purified by silica gel column chromatography using petroleum ether-ethyl acetate as the mobile phase to obtain 11-thioacetyl-undecyl bromide (0.38g, 83%) as dark oil. To a solution of 11-thioacetyl-undecyl bromide (0.36g, 1.16 mmol) in anhydrous DMF (5mL) was added carefully NaN_3 (0.38g, 5.82 mmol) at room temperature under argon atmosphere. The reaction mixture was stirred for 20h at same temperature, quenched with water and extracted with diethyl ether (2x20mL). Combined organic layers were washed with water, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The resulting crude was purified by silica gel column chromatography using petroleum ether and ethyl acetate as the mobile phase to give 11-azido-1-thioacetyl-undecane **32** (0.28g, 90%) as a brown coloured liquid. Characterization data: IR (cm^{-1}): 1693, 2096, 2855, 2928; ^1H NMR ($CDCl_3$, 200.13 MHz): δ 1.20-1.43 (14H, m), 1.56 (4H, quintet, *J* 7.10 Hz), 2.32 (3H, s), 2.86 (2H, t, *J* 7.37 Hz), 3.26 (2H, t, *J* 6.89 Hz); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 26.6, 28.7, 28.8, 29.0, 29.1, 29.1, 29.3, 29.3, 29.3, 29.4, 30.6, 51.4, 196.0; Mol. Wt. calculated for $C_{13}H_{25}N_3OS$: 271.42, Found: 294.28 (M^++ 23 for Na).

Synthesis of triazole 'clicked' glycolipid (33): To a solution of propargyl tetrasaccharide **18** (0.3g, 0.16 mmol), 11-azido-1-thioacetyl-undecane **32** (45mg, 0.16 mmol) and DIPEA (57μL, 0.33 mmol) in CH_3CN (5mL) was added CuI (33mg, 0.17 mmol) at room temperature. The reaction mixture was stirred for 1h at room temperature, quenched with a saturated solution of ammonium chloride and extracted with ethyl acetate (2x20mL). Combined organic layers were washed with water, dried over anhydrous Na_2SO_4 and the solvent was concentrated *in vacuo*. The resulting crude was purified by silica gel column chromatography using petroleum ether and ethyl acetate as the mobile phase to afford a 1,2,3-triazole 'clicked' glycolipid **33** (0.29g, 85%) as a colourless viscous oil. Characterization data: $[\alpha]_D$ ($CHCl_3$, *c* 1.10) = -(2-6); IR (cm^{-1}): 1098, 1688, 1740, 2856, 2926; ^1H NMR ($CDCl_3$, 400.13 MHz): δ 1.05-1.35 (14H, m), 1.51-1.63 (4H, m), 2.05 (3H, s), 2.31 (3H, s), 2.85 (2H, t, *J* 7.34 Hz), 3.33-3.43 (4H, m), 3.45 (3H, d, *J* 10.74 Hz), 3.54 (2H, dd, *J* 3.26, 11.12 Hz), 3.60 (1H, t, *J* 7.80 Hz), 3.70-3.80 (1H, m), 3.74 (1H, ABq, *J* 7.66 Hz), 3.81-3.92 (7H, m), 3.94 (1H, t, *J* 3.02 Hz), 3.99 (1H, dd, *J* 2.53, 9.53 Hz), 4.03 (1H, d, *J* 2.09 Hz), 4.05



(1H, t, *J* 1.88 Hz), 4.10 (1H, t, *J* 8.84 Hz), 4.22 (2H, d, *J* 11.86 Hz), 4.23 (2H, ABq, *J* 11.63 Hz), 4.30-4.57 (12H, m), 4.60-4.82 (11H, m), 4.91 (2H, dd, *J* 1.89, 3.72 Hz), 4.94 (1H, d, *J* 5.25 Hz), 5.23 (1H, s), 5.49 (1H, dd, *J* 0.93, 1.88 Hz), 7.02-7.32 (60H, m), 7.45 (1H, s); ^{13}C NMR ($CDCl_3$, 100.61 MHz): δ 21.1, 26.4, 28.8, 29.0, 29.1, 29.1, 29.4, 29.4, 29.4, 29.5, 30.2, 30.6, 49.9, 62.5, 68.2, 68.8, 68.9, 69.0, 69.1, 71.5, 71.7, 71.8, 71.8, 72.5, 72.5, 72.6, 73.1, 73.1, 73.2, 73.3, 73.3, 73.8, 74.2, 74.4, 74.6, 74.8, 74.9, 75.1, 75.2, 75.2, 75.6, 78.2, 79.8, 79.9, 80.0, 82.6, 98.8, 99.3, 99.6, 102.7, 122.9, 127.0-128.3, 137.9, 138.1, 138.4, 138.4, 138.5, 138.5, 138.6, 138.7, 138.7, 138.8, 138.8, 138.9, 144.4, 170.0, 196.1; Mol. Wt. calculated for $C_{126}H_{143}N_3O_{23}S$: 2099.55, Found: 2123.61 (M^++ 23 for Na).

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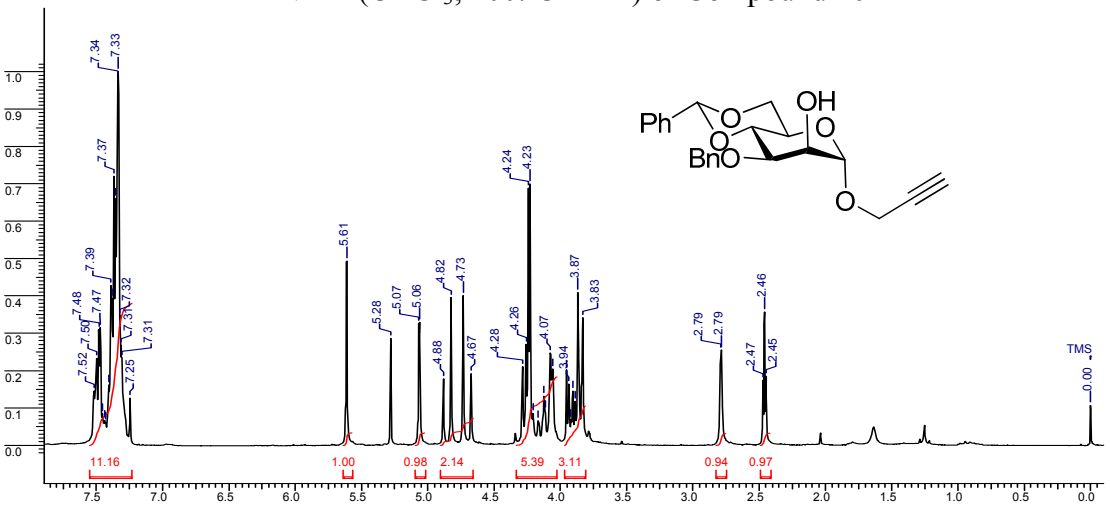
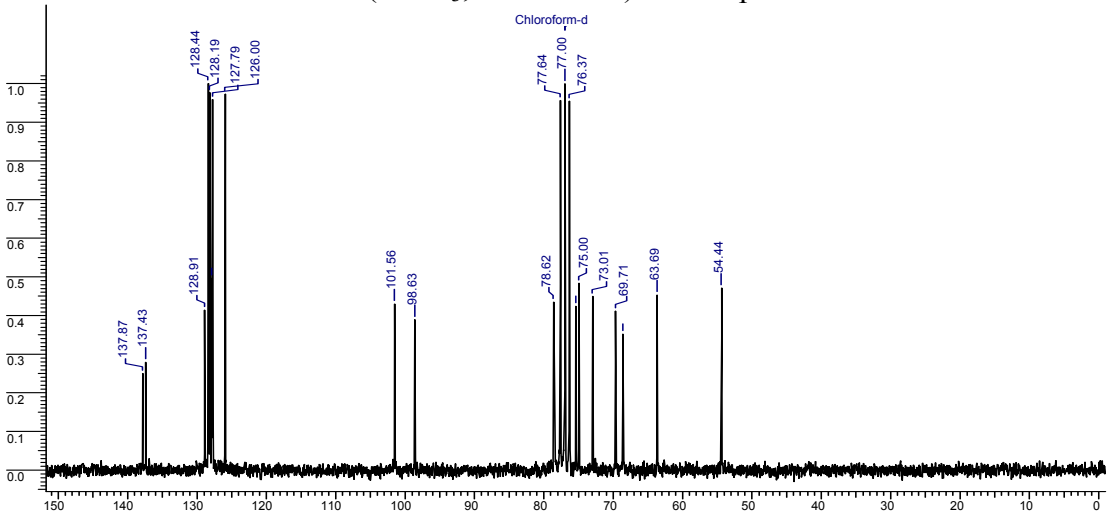
Spectral Charts

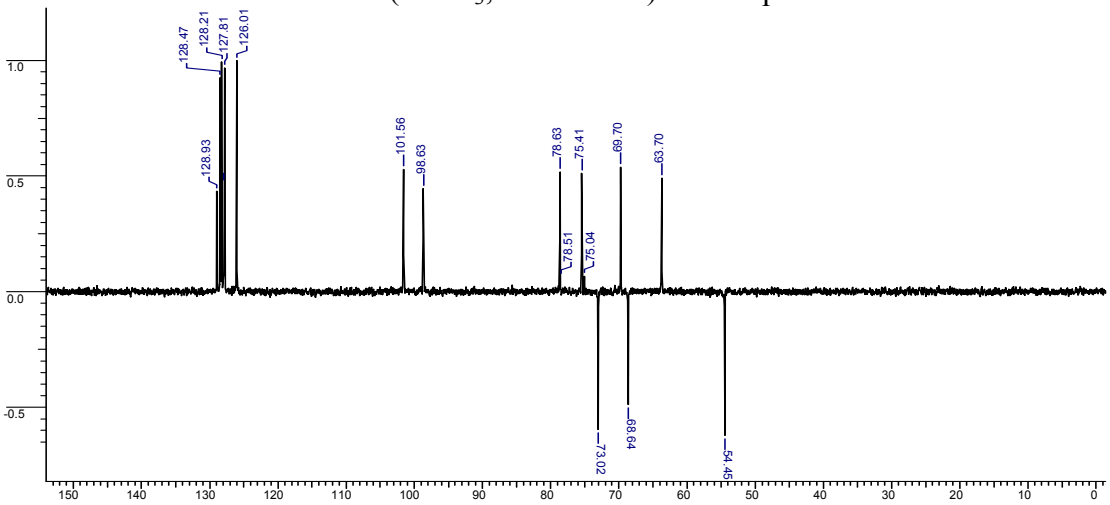
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **10**



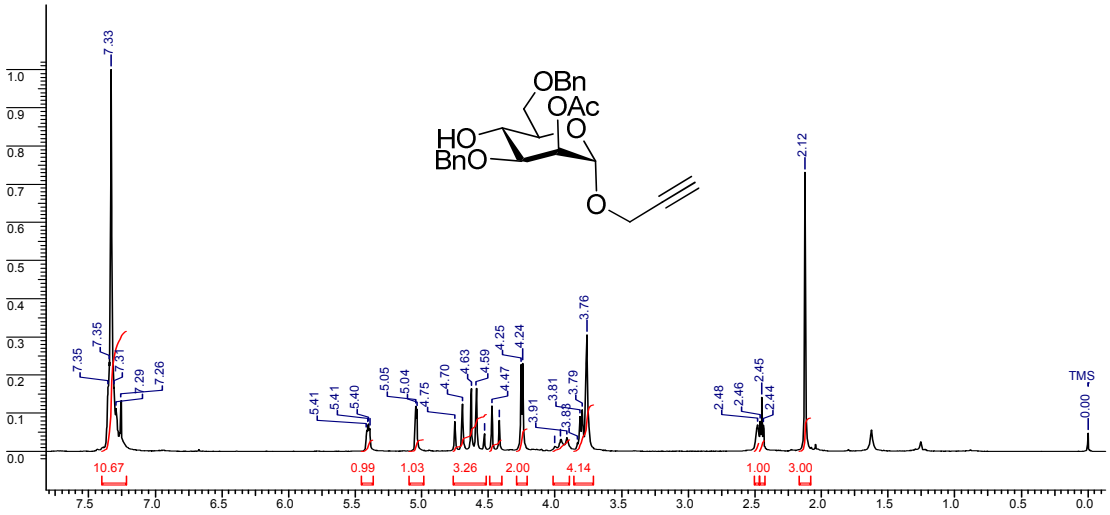
^{13}CNMR ($CDCl_3$, 50.32 MHz) of Compound **10**



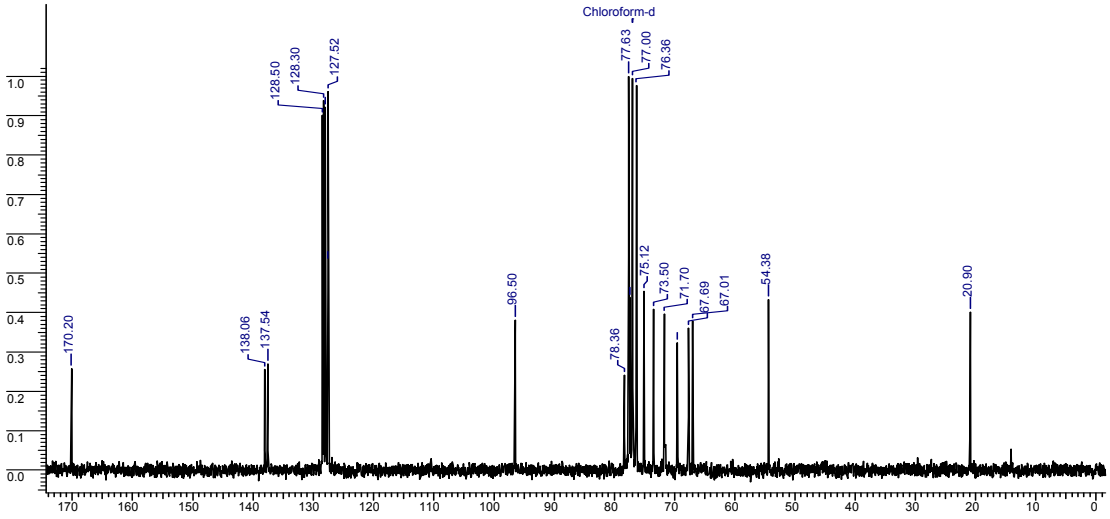
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **10**



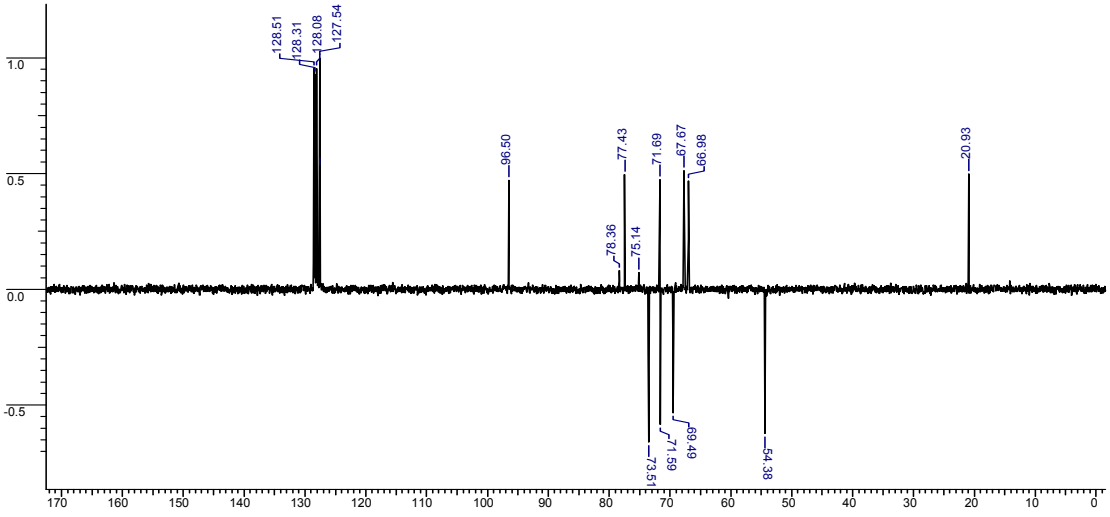
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **7**



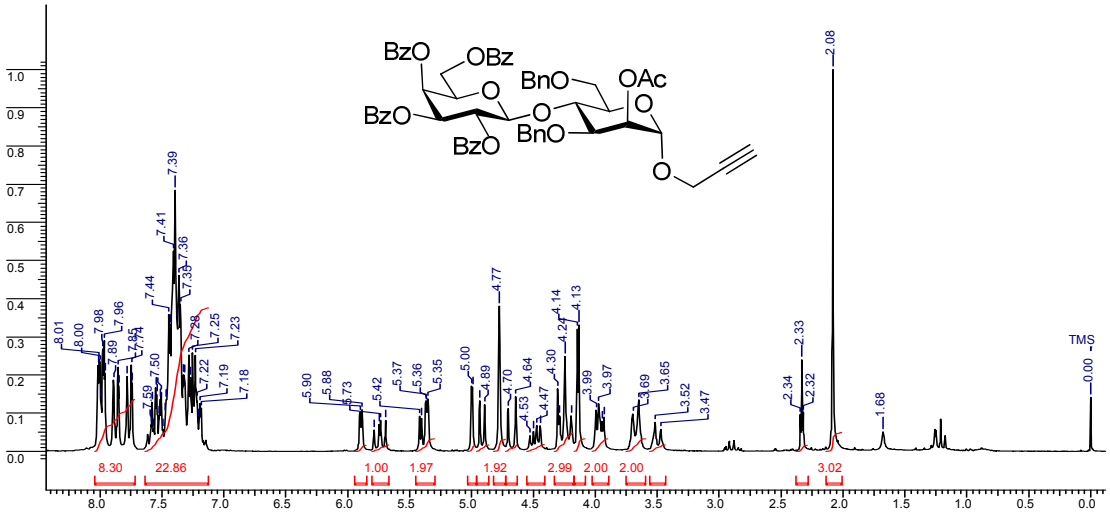
^{13}CNMR ($CDCl_3$, 50.32 MHz) of Compound **7**



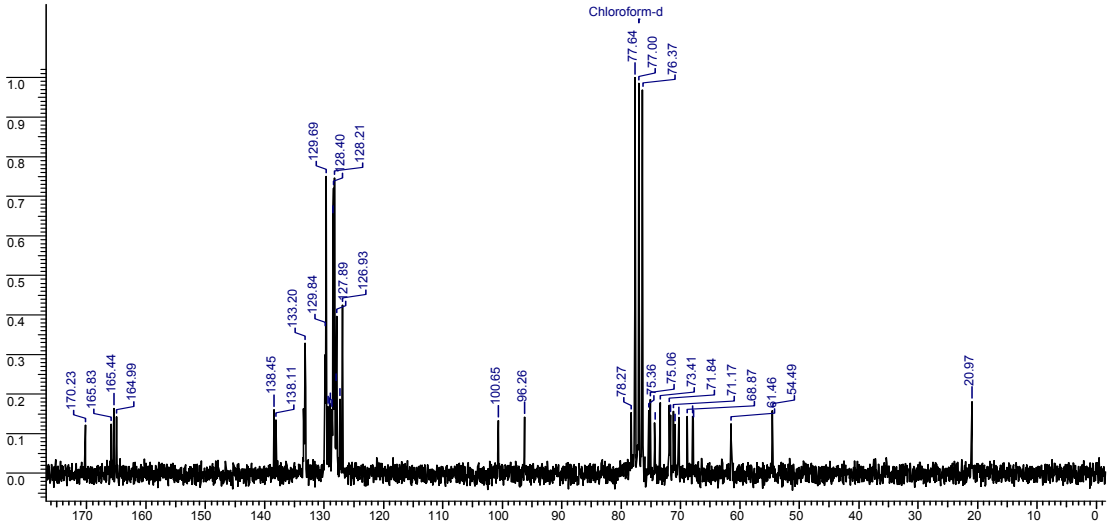
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **7**



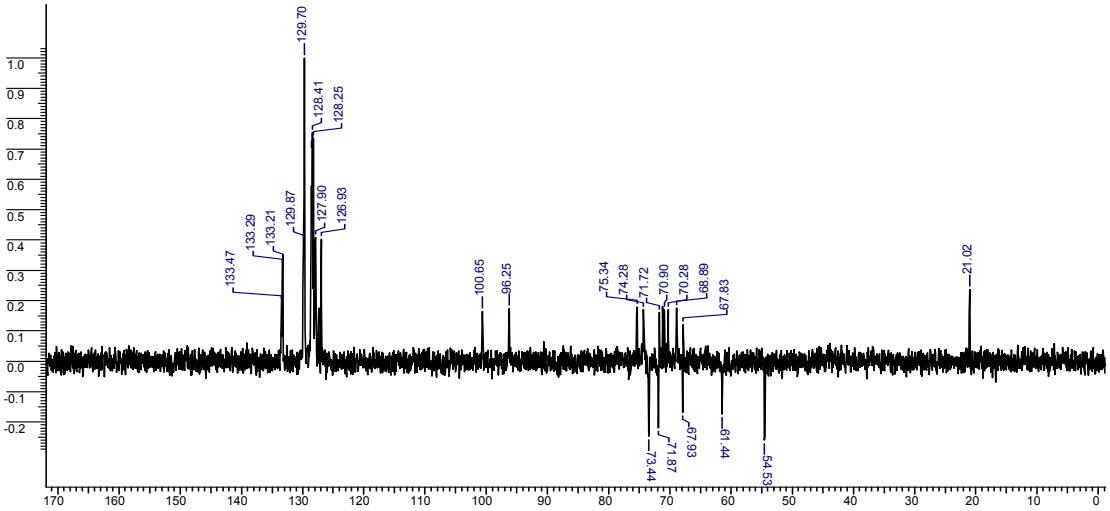
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **12**



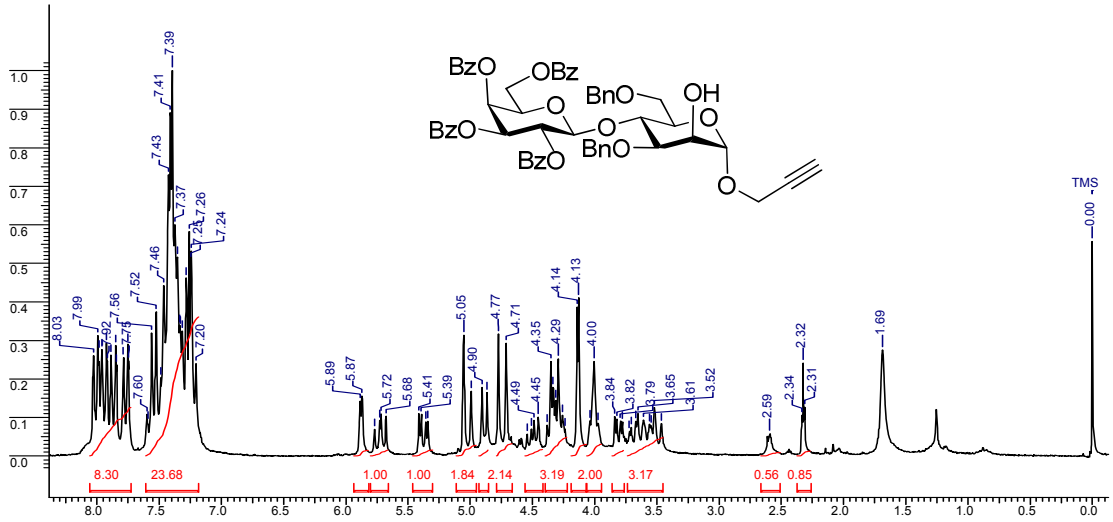
^{13}CNMR ($CDCl_3$, 50.32 MHz) of Compound **12**



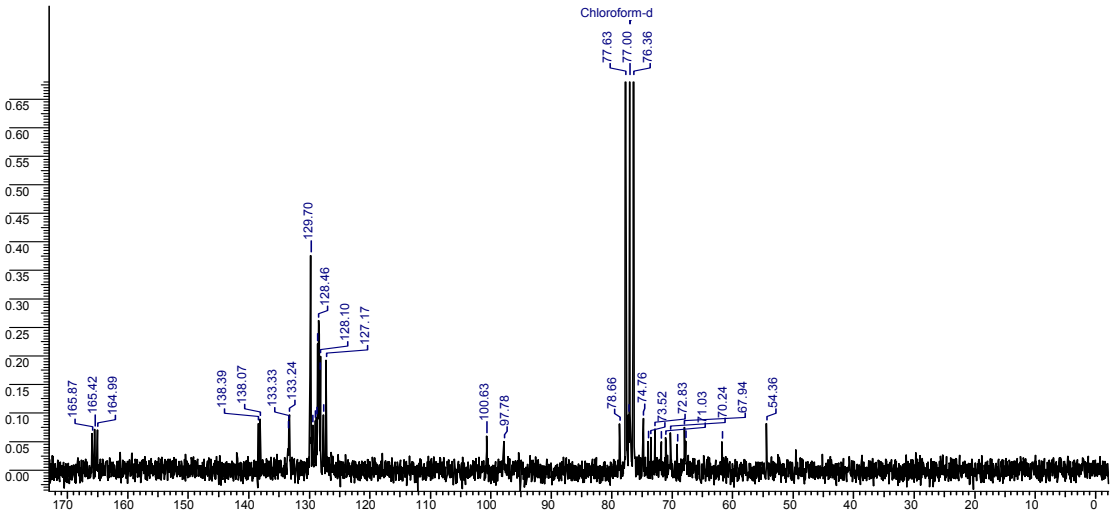
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **12**



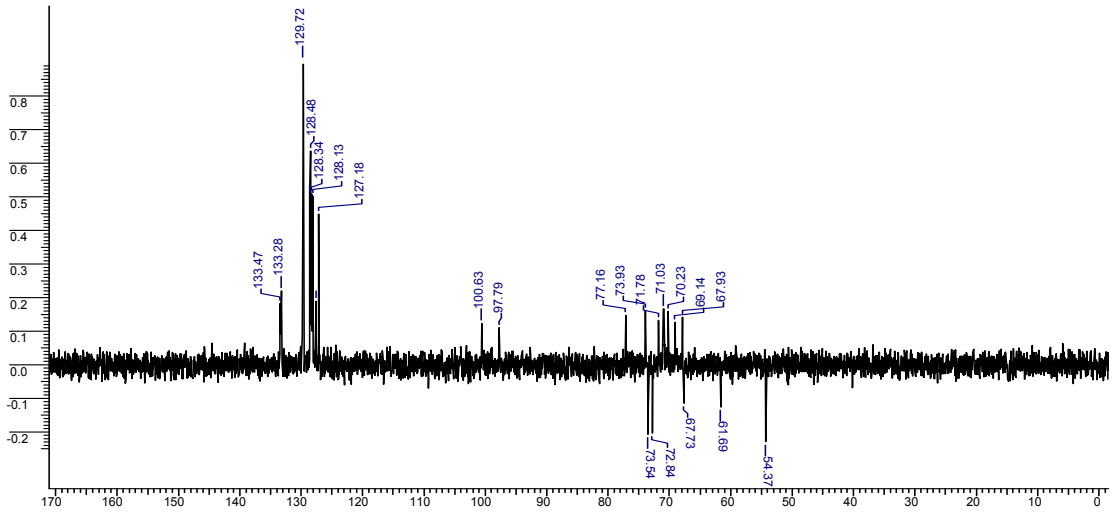
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **5**



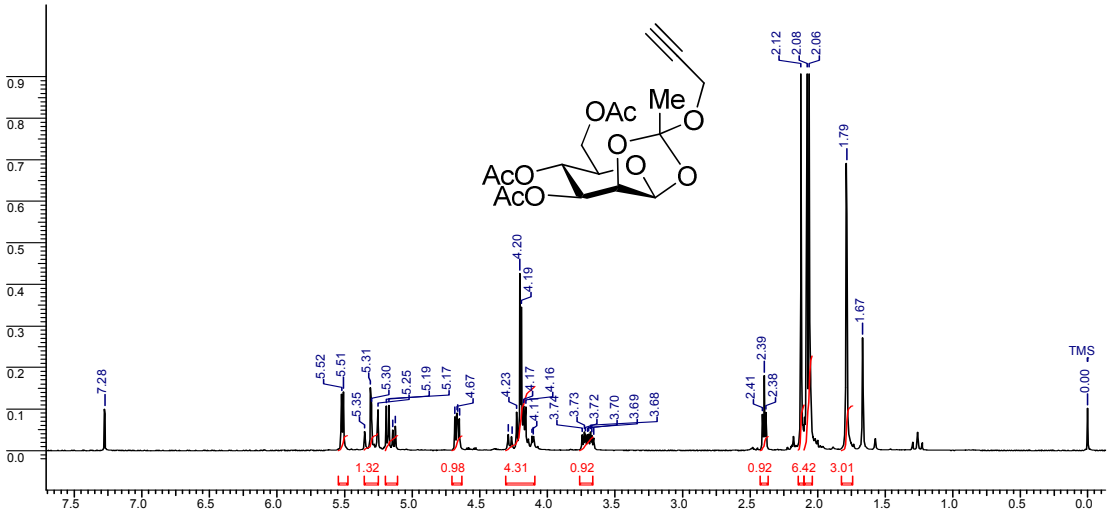
^{13}CNMR ($CDCl_3$, 50.32 MHz) of Compound **5**



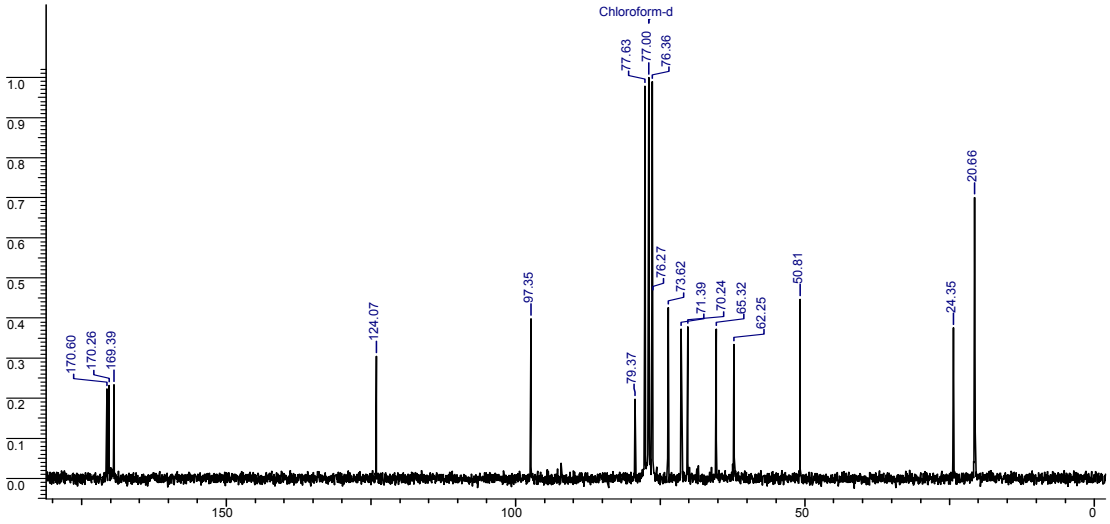
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **5**



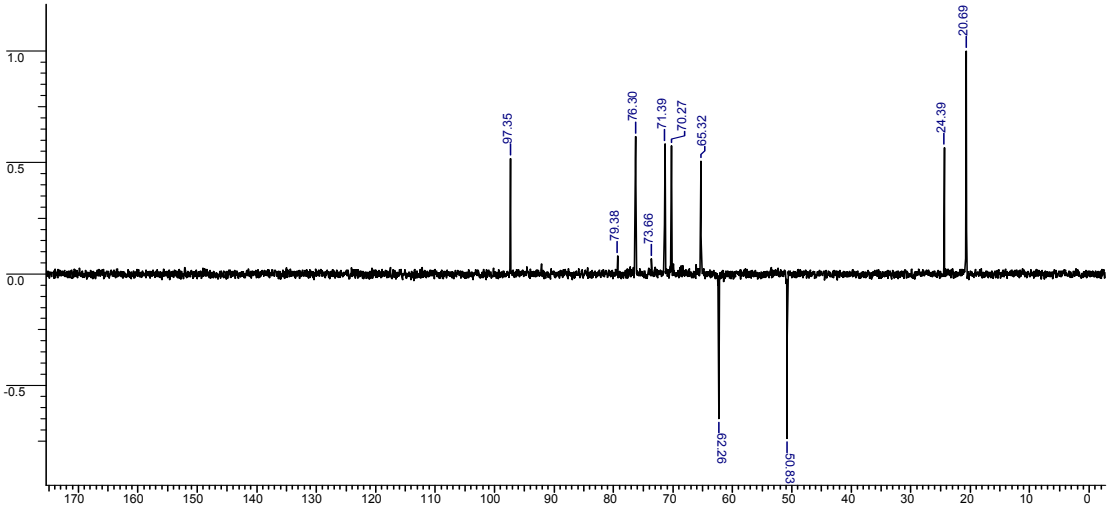
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **15**



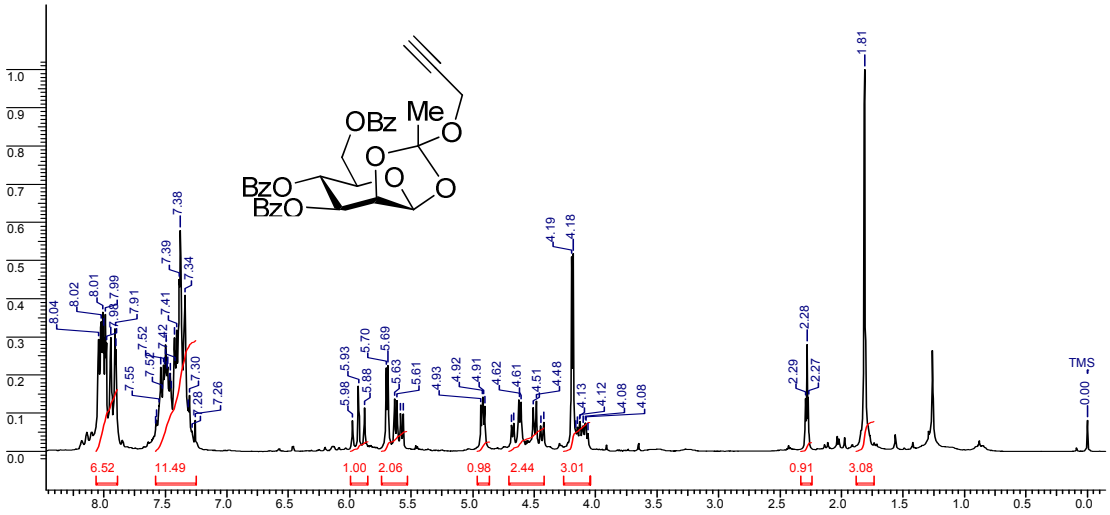
^{13}CNMR ($CDCl_3$, 50.32 MHz) of Compound **15**



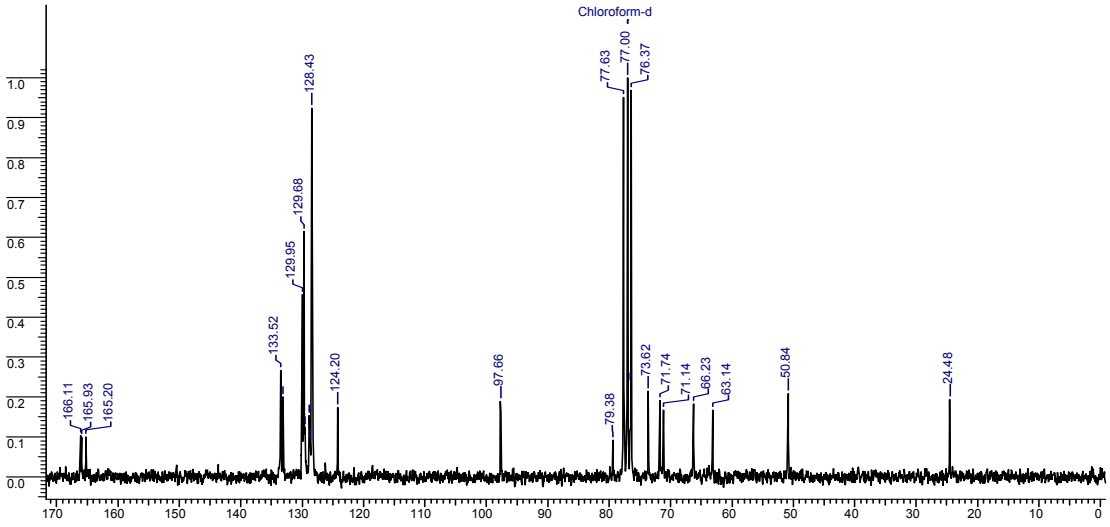
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **15**



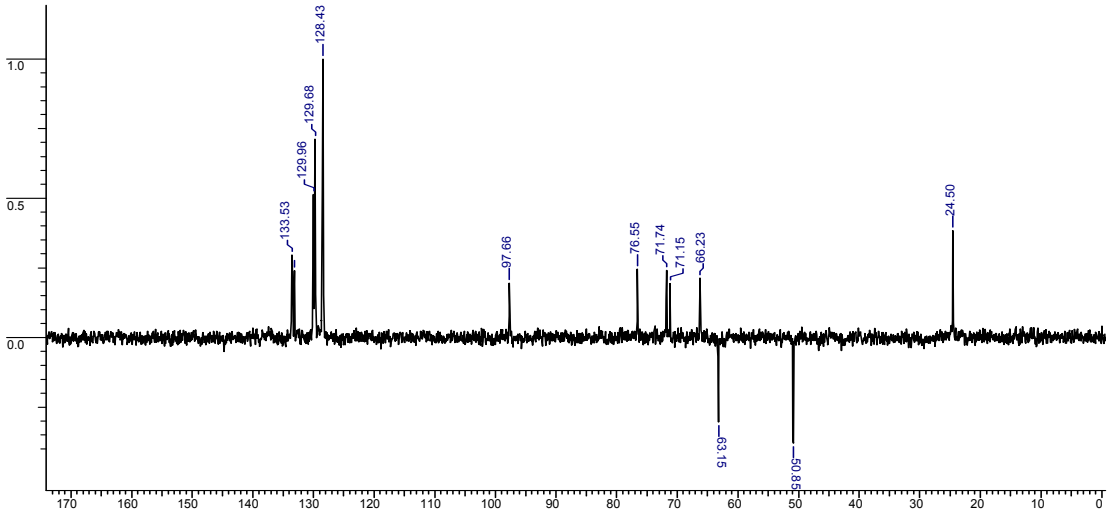
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **3**



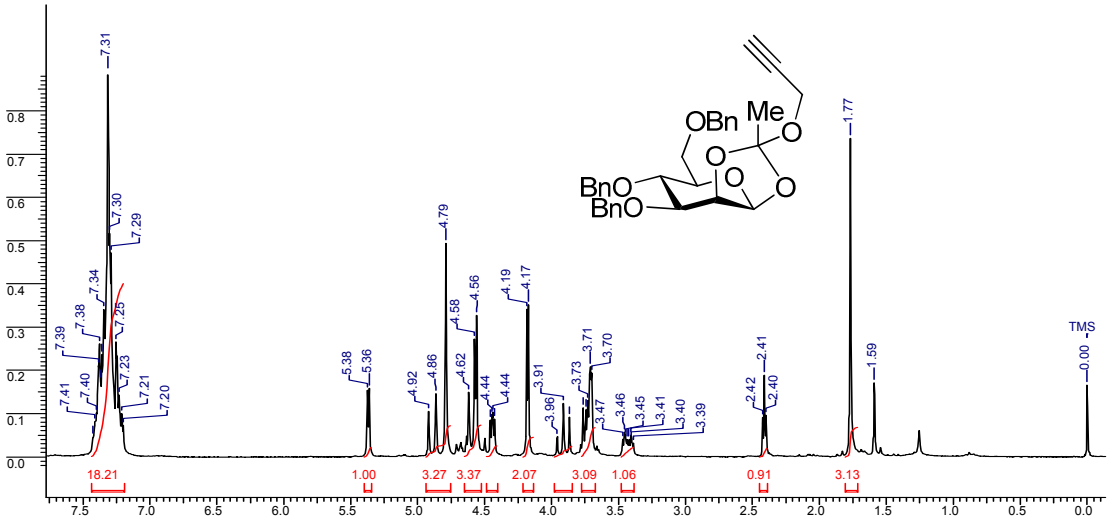
^{13}CNMR ($CDCl_3$, 50.32 MHz) of Compound **3**



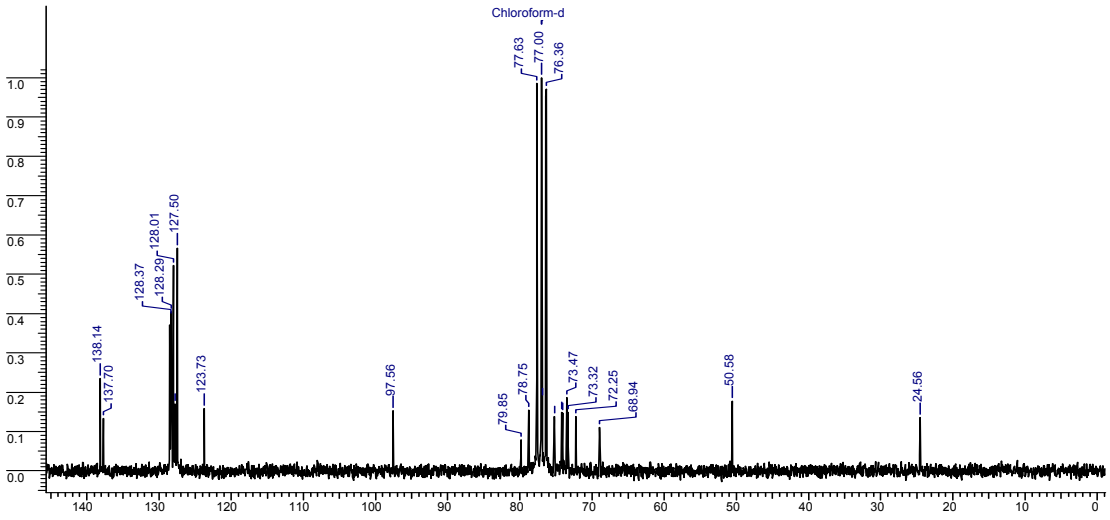
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **3**



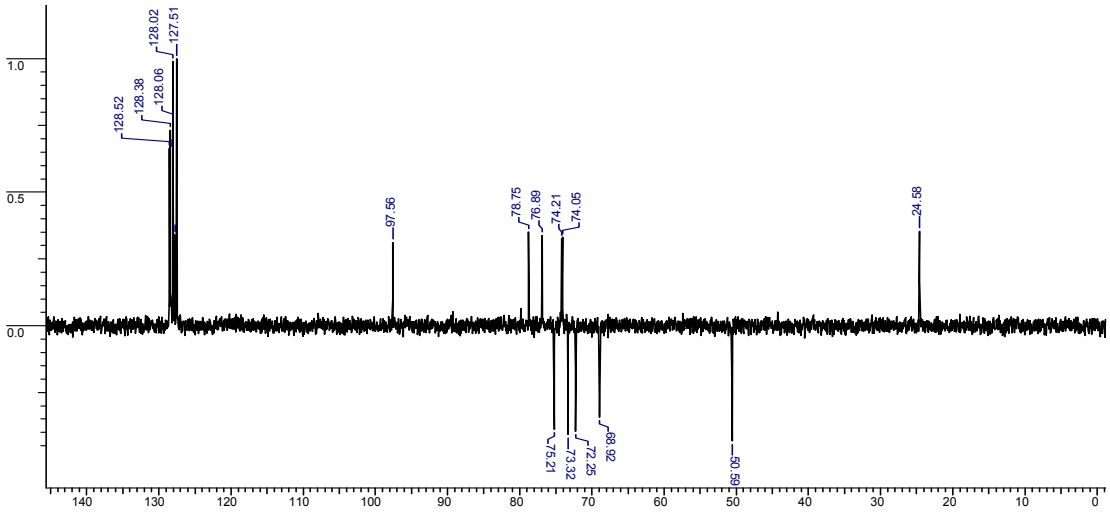
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **20**



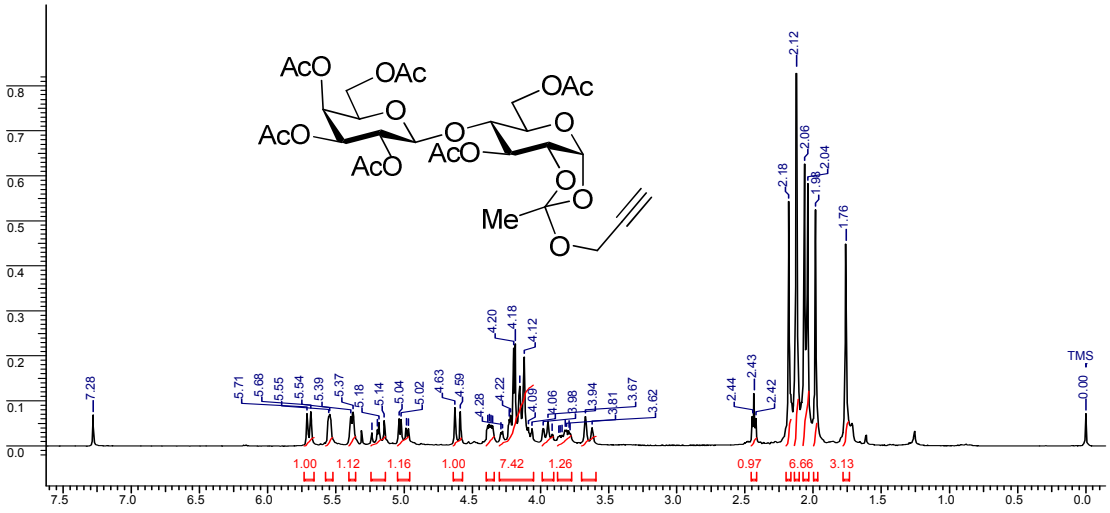
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **20**



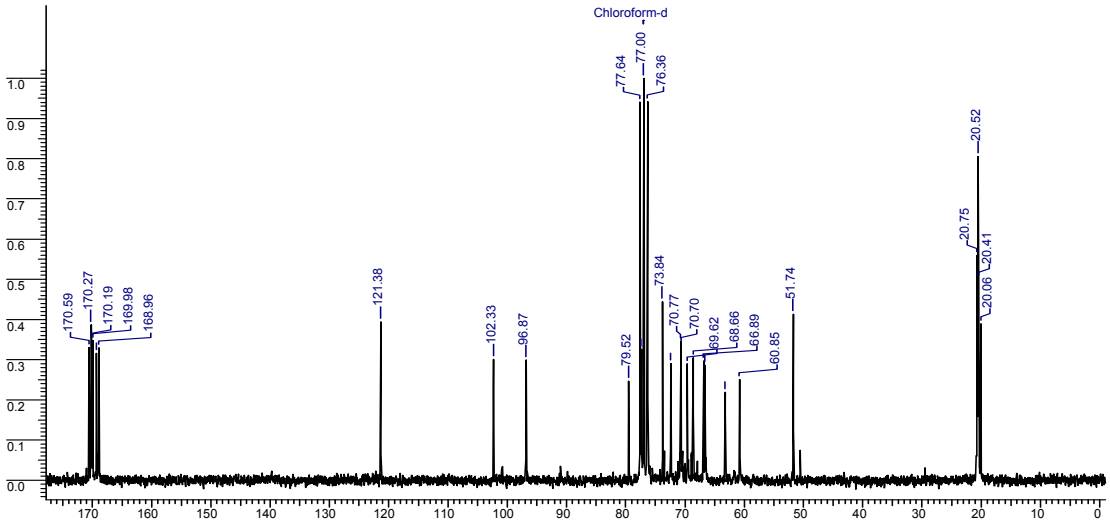
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **20**



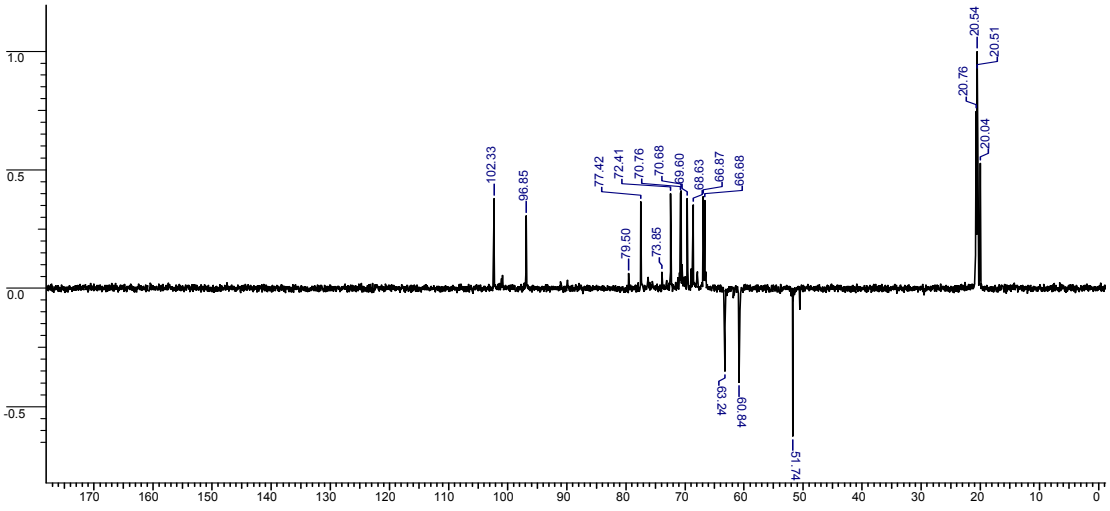
^{1}H NMR ($CDCl_3$, 400.13 MHz) of Compound **22**



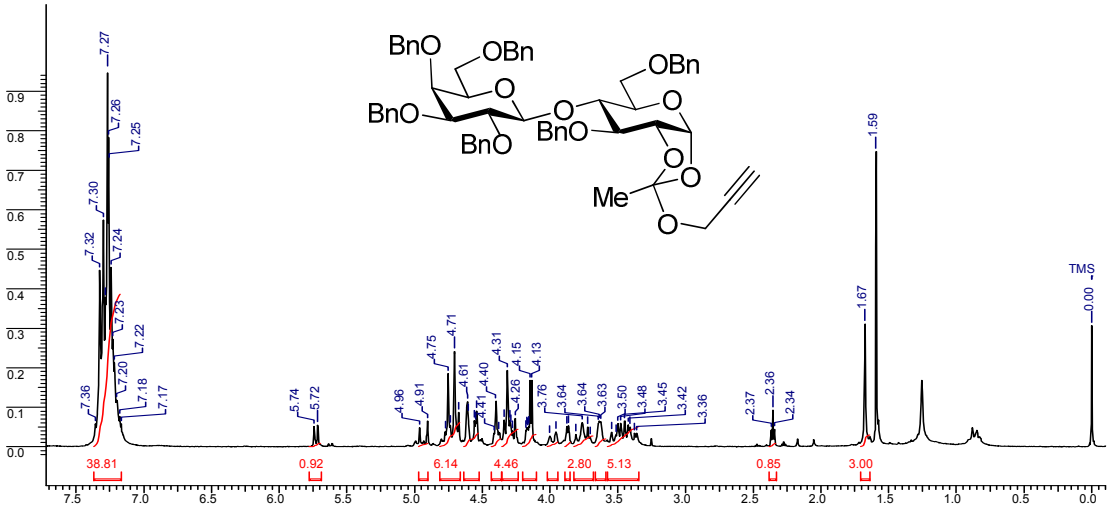
^{13}CNMR ($CDCl_3$, 50.32 MHz) of Compound **22**



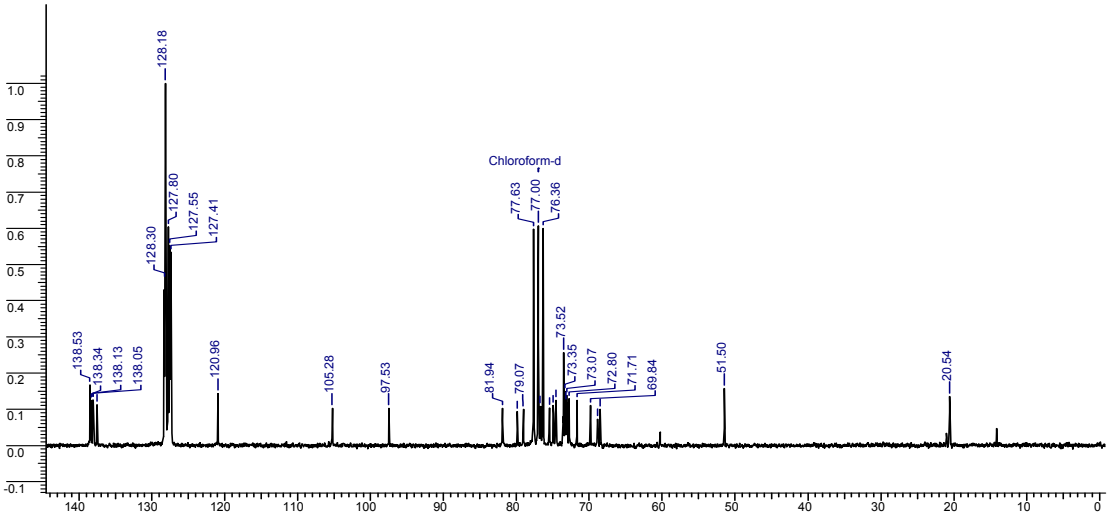
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **22**



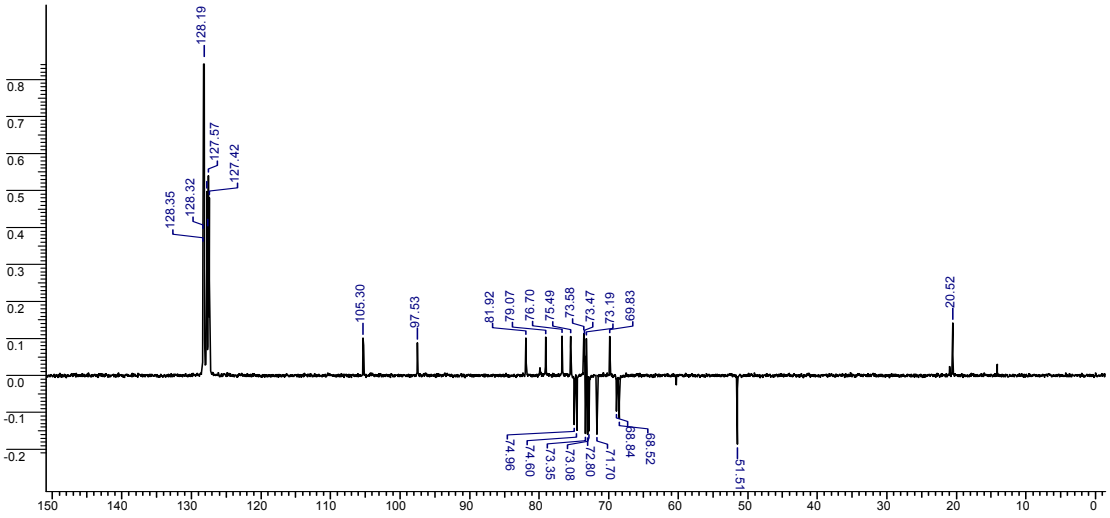
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **23**



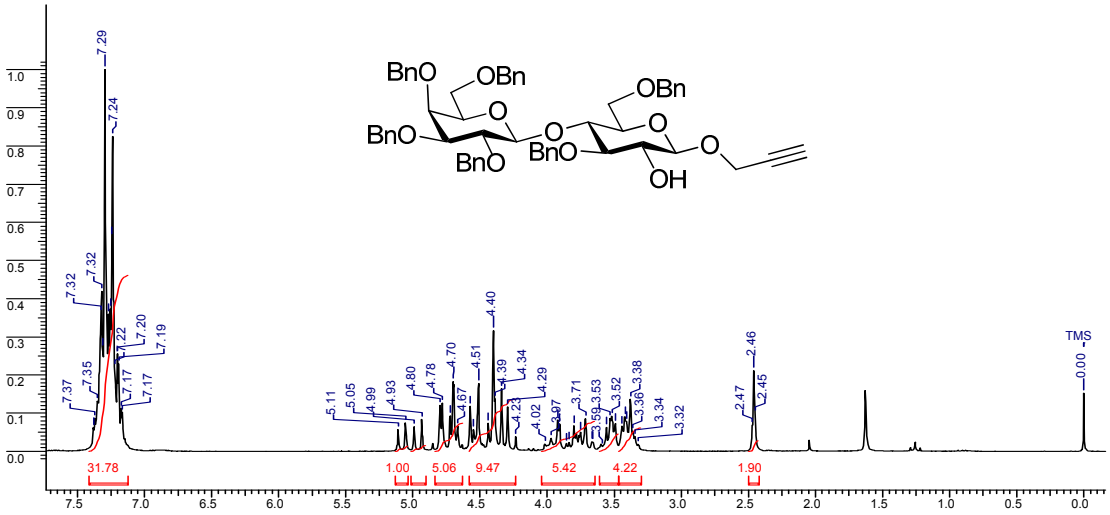
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **23**



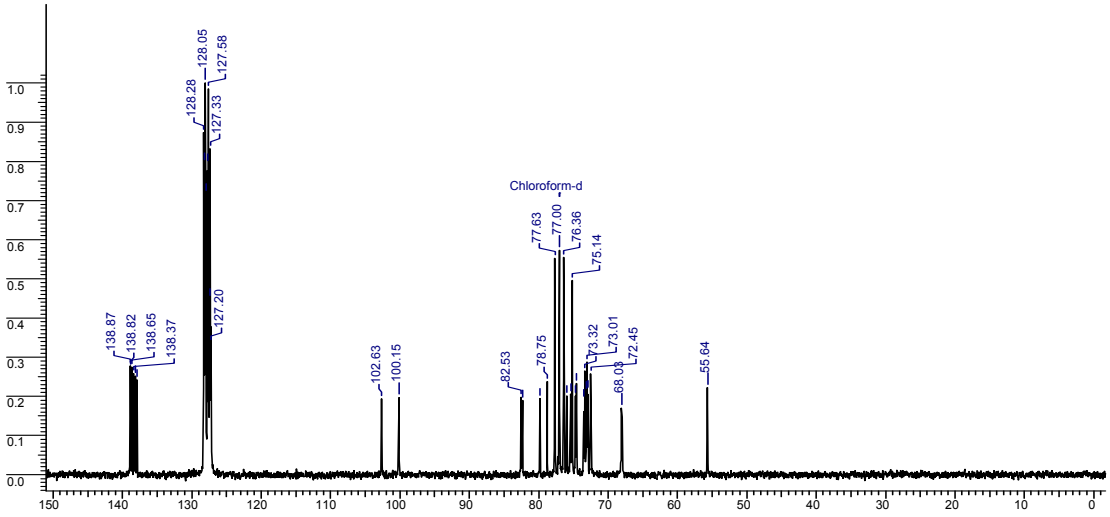
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **23**



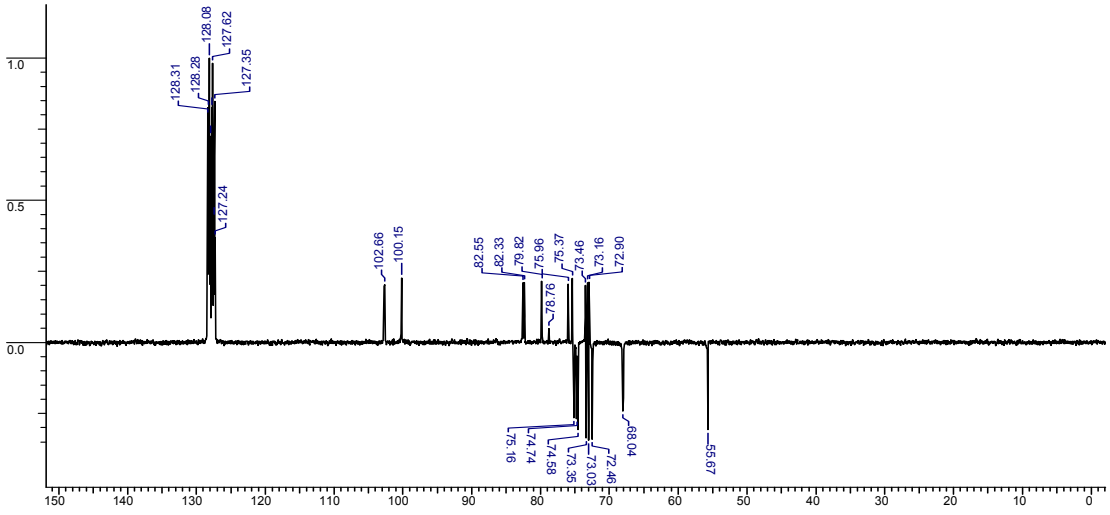
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **25**



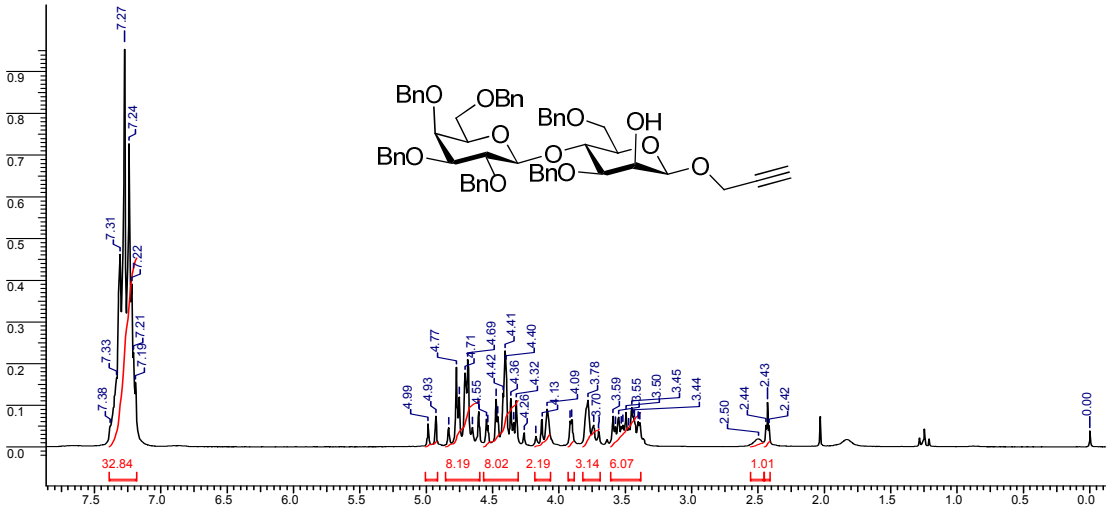
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **25**



DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **25**



^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **21**



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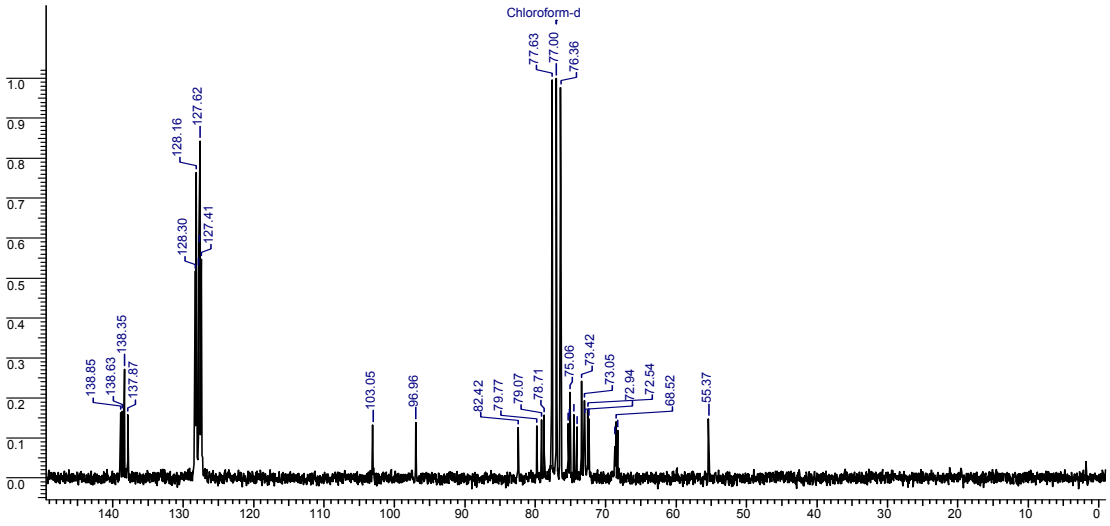
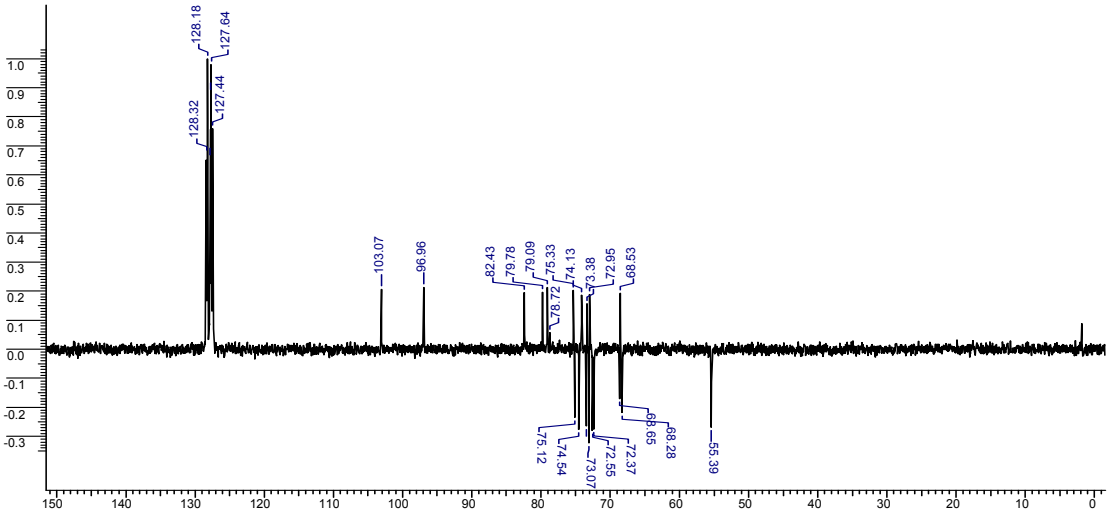
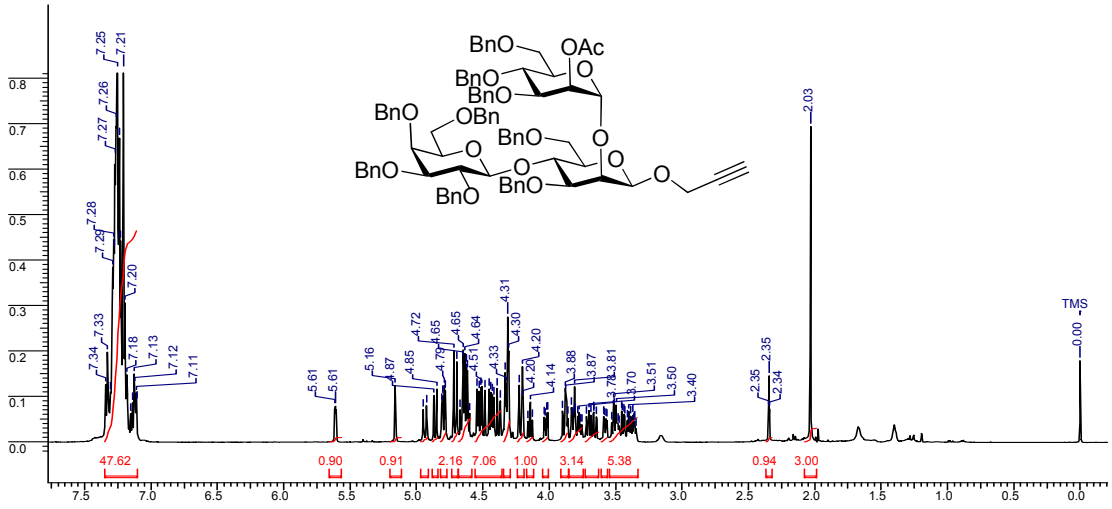


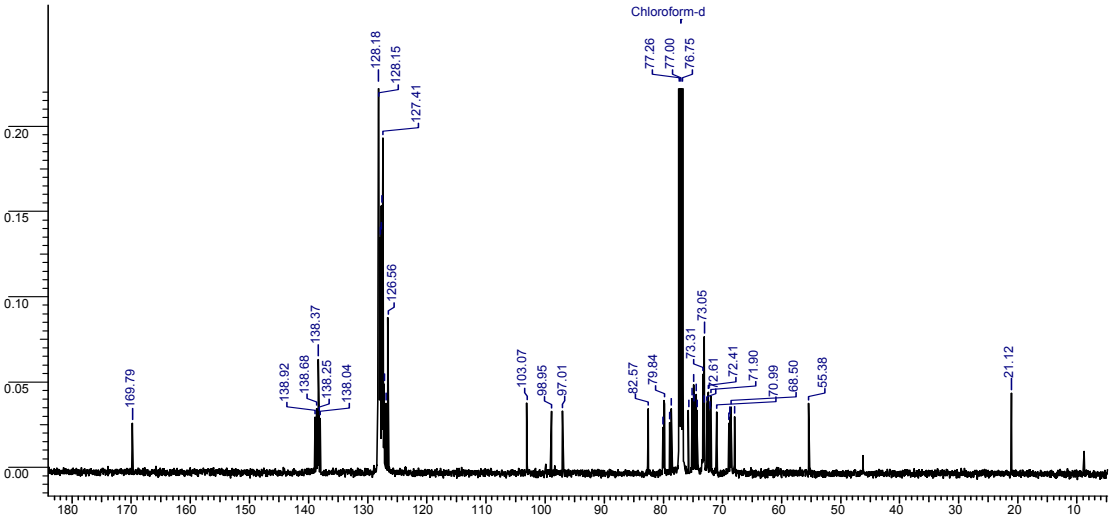
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **21**



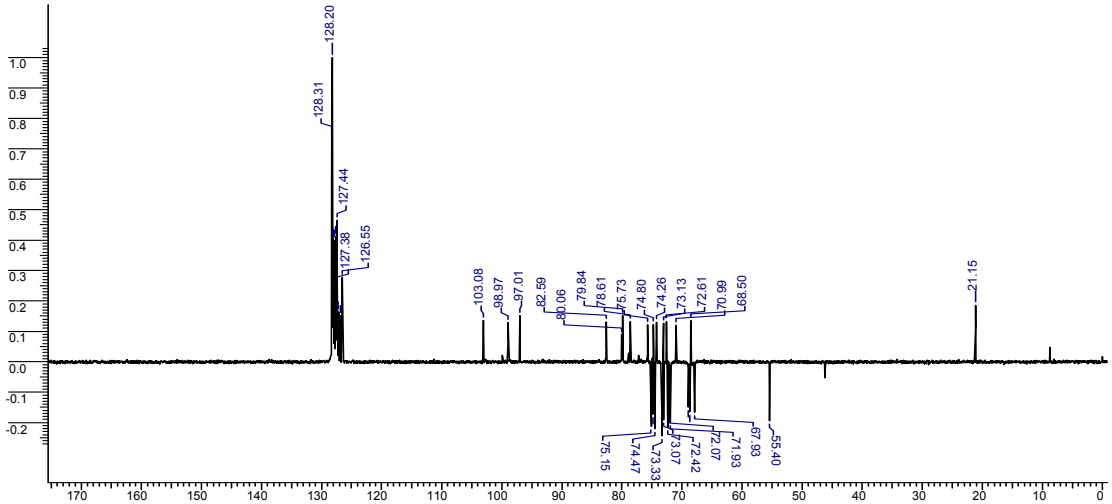
^{1}H NMR ($CDCl_3$, 500.13 MHz) of Compound **26**



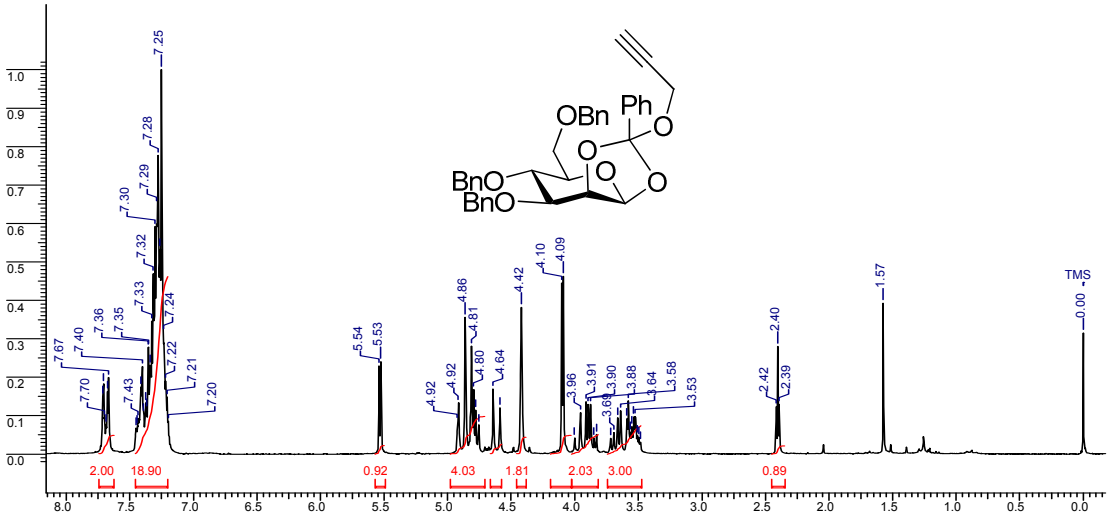
^{13}C NMR ($CDCl_3$, 125.76 MHz) of Compound **26**



DEPT NMR ($CDCl_3$, 125.76 MHz) of Compound **26**



^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **27**



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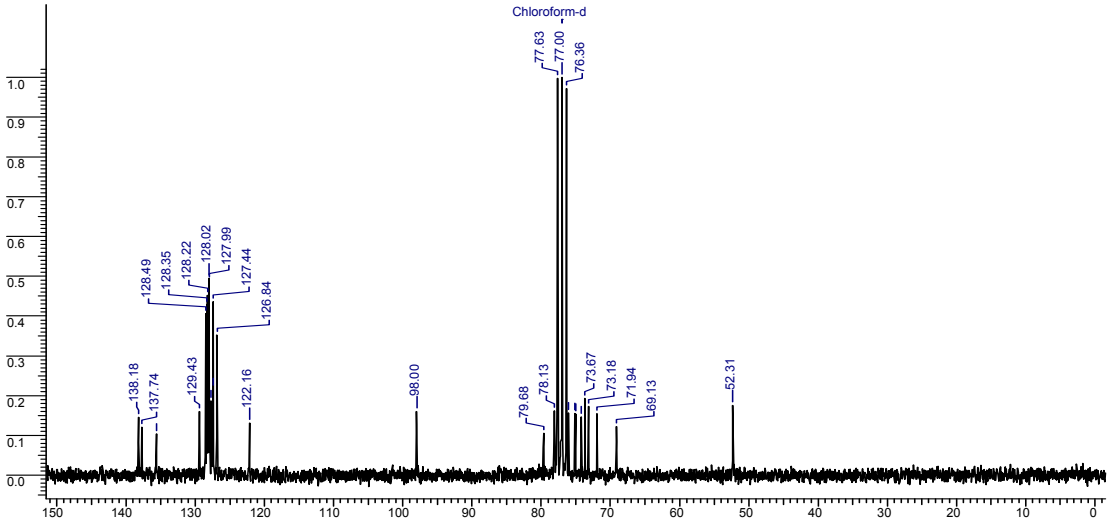
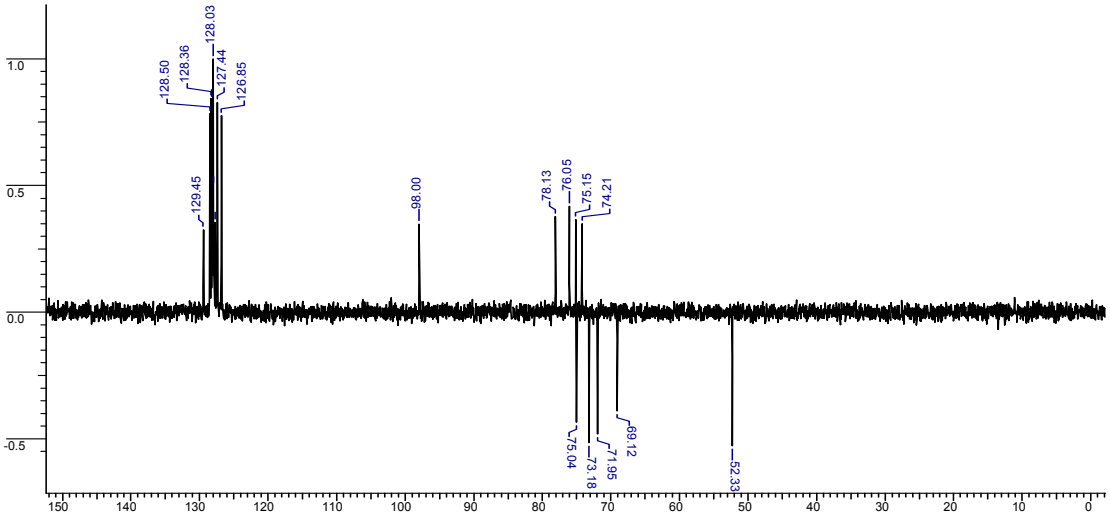
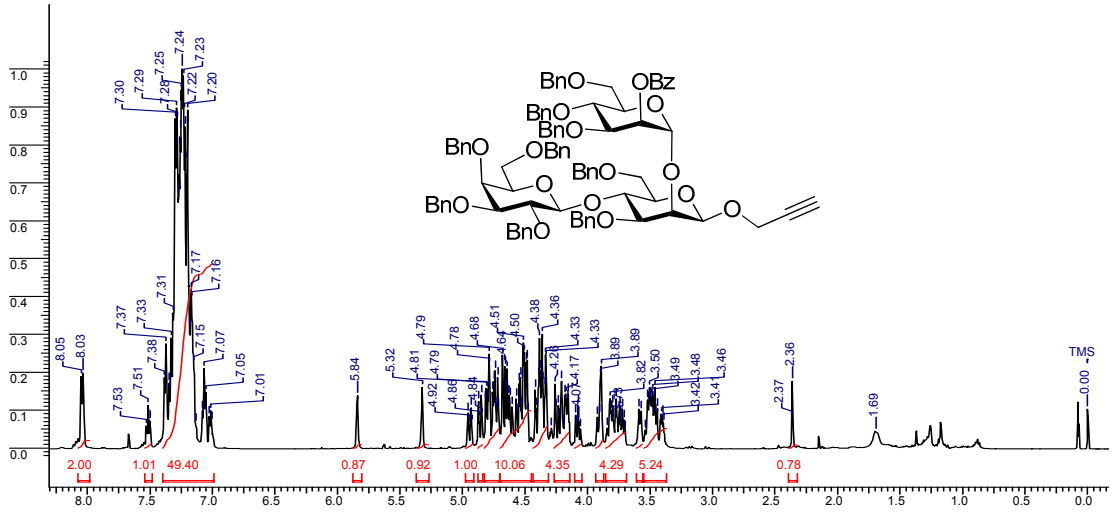


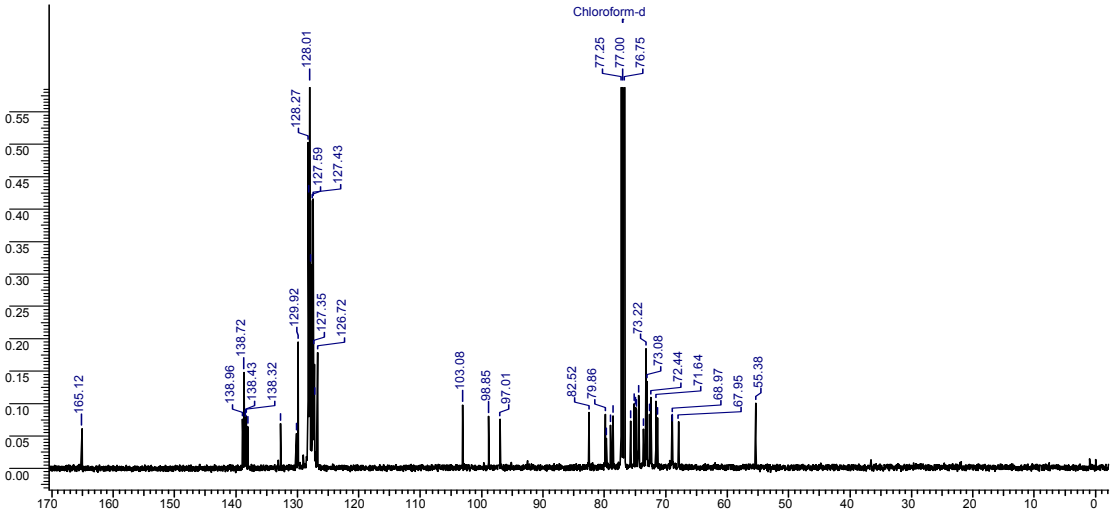
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **27**



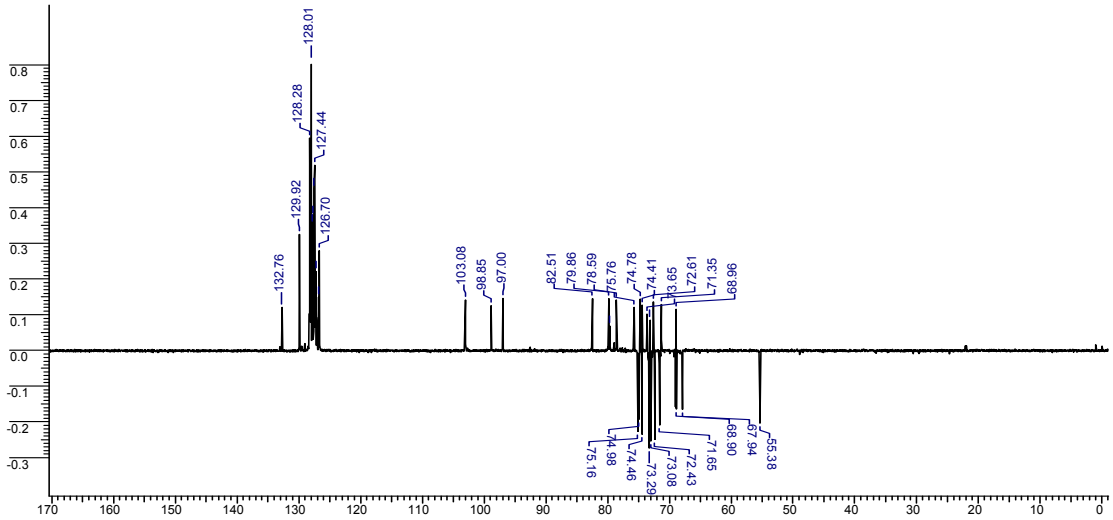
^{1}H NMR ($CDCl_3$, 500.13 MHz) of Compound **28**



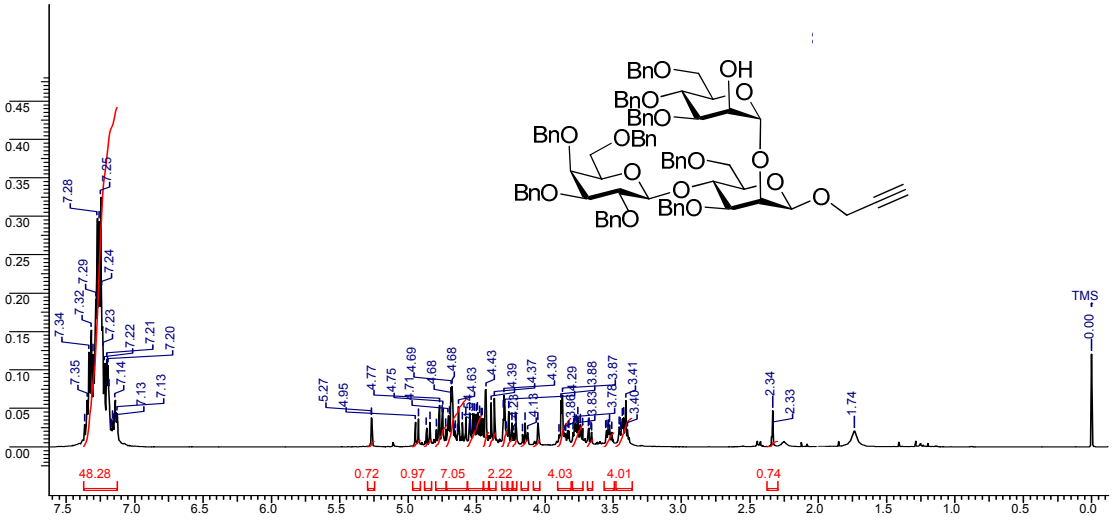
^{13}C NMR ($CDCl_3$, 125.76 MHz) of Compound **28**



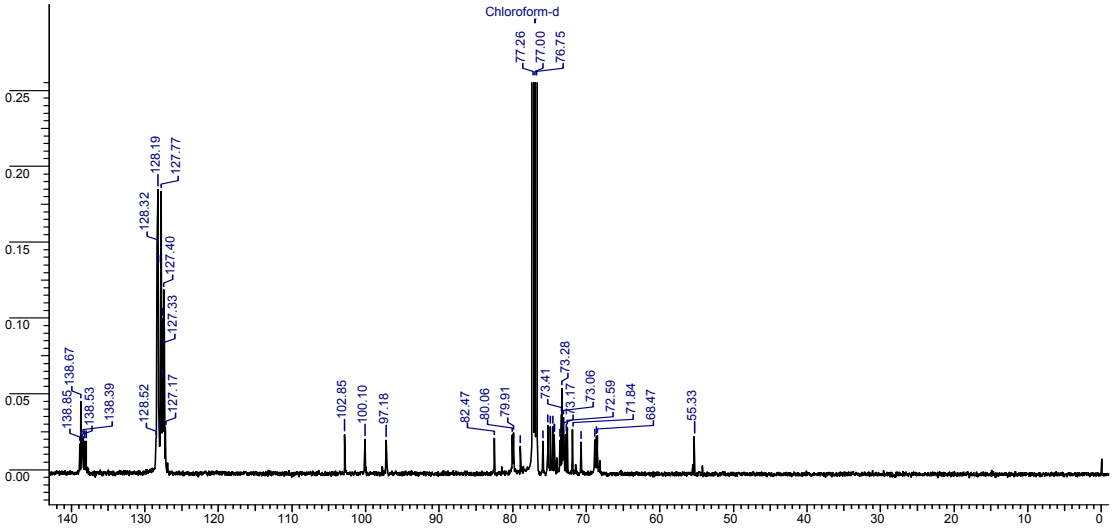
DEPT NMR ($CDCl_3$, 125.76 MHz) of Compound **28**



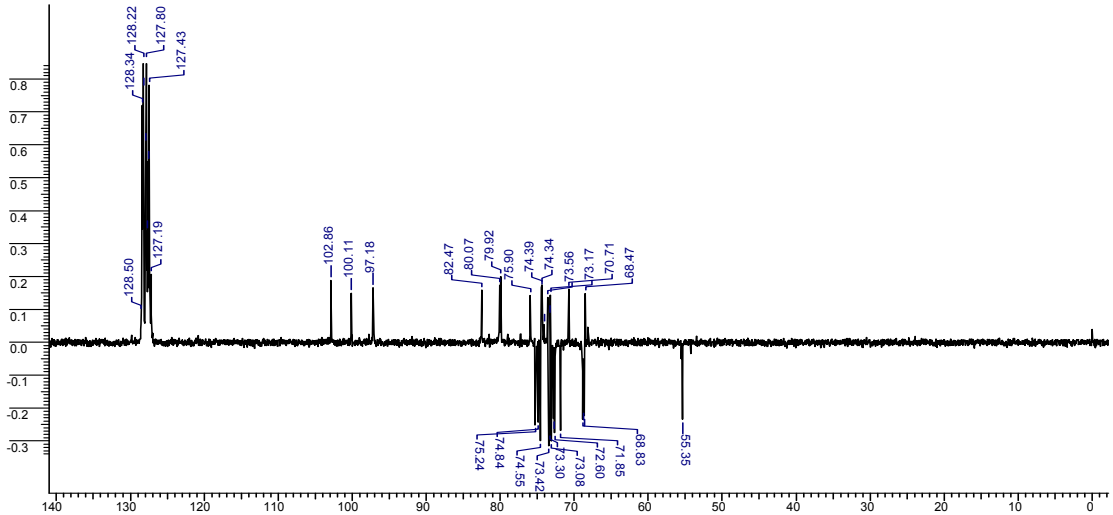
^{1}H NMR ($CDCl_3$, 500.13 MHz) of Compound **19**



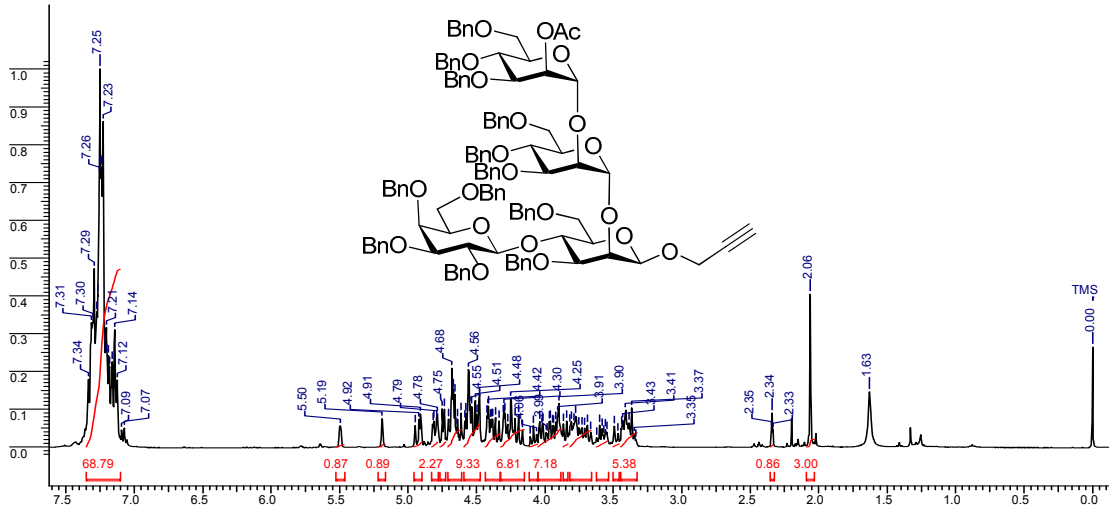
^{13}C NMR ($CDCl_3$, 125.76 MHz) of Compound **19**



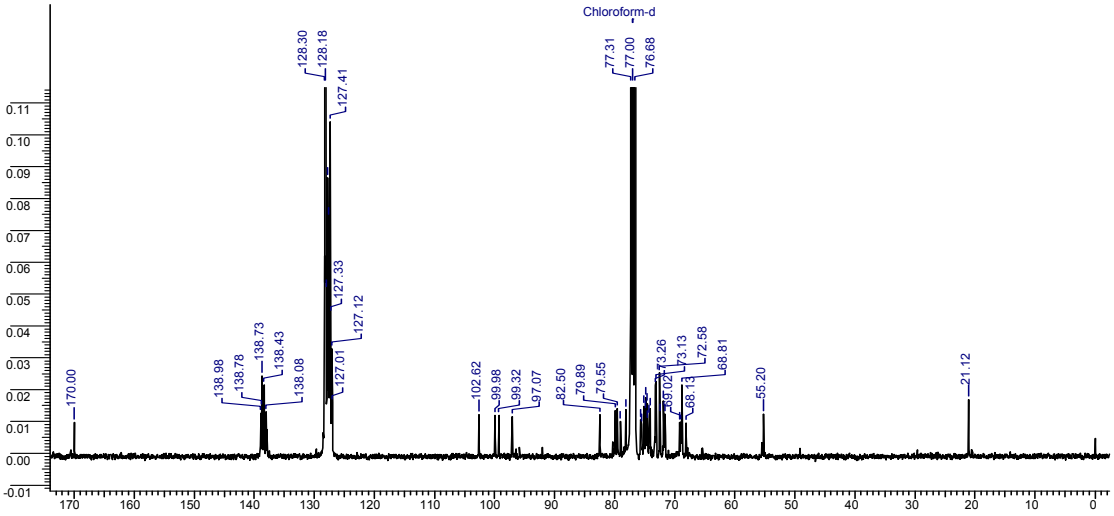
DEPT NMR ($CDCl_3$, 125.76 MHz) of Compound **19**



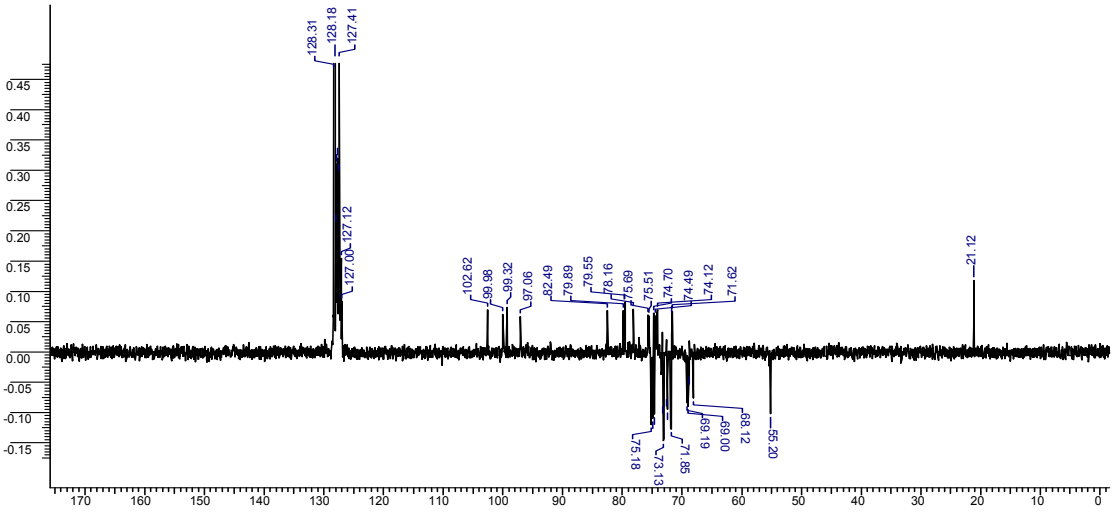
^{1}H NMR ($CDCl_3$, 400.13 MHz) of Compound **18**



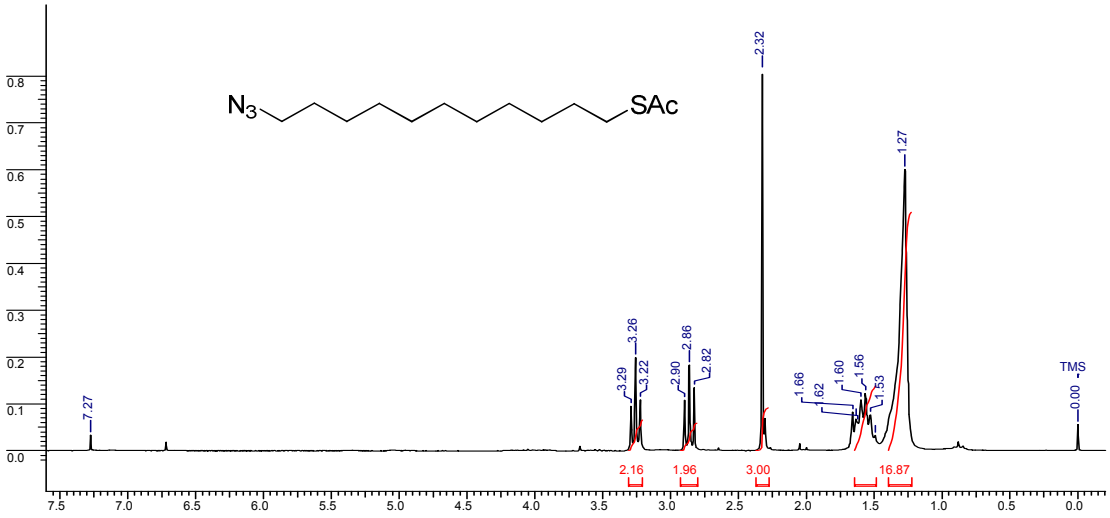
^{13}C NMR ($CDCl_3$, 100.61 MHz) of Compound **18**



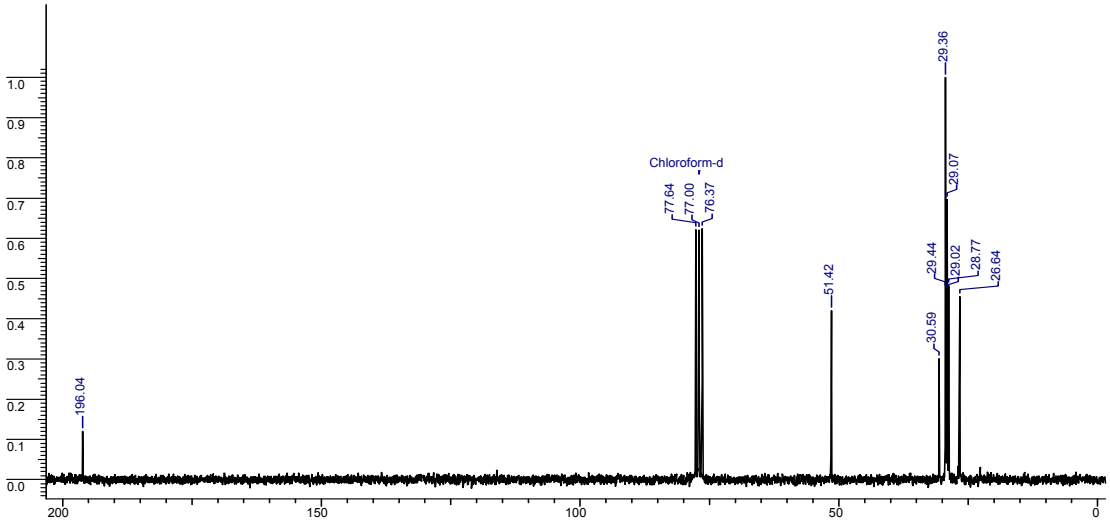
DEPT NMR ($CDCl_3$, 100.61 MHz) of Compound **18**



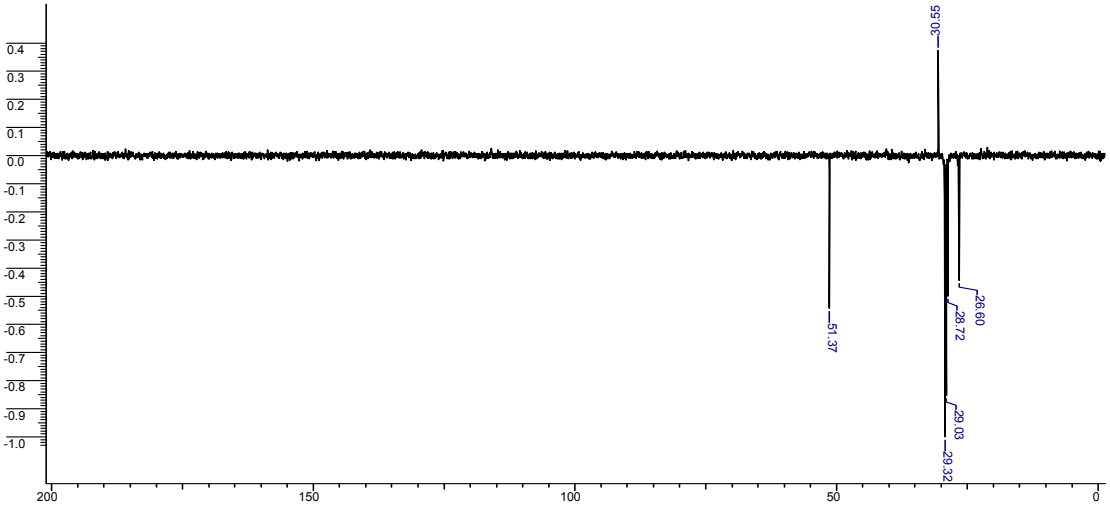
^{1}H NMR ($CDCl_3$, 200.13 MHz) of Compound **32**



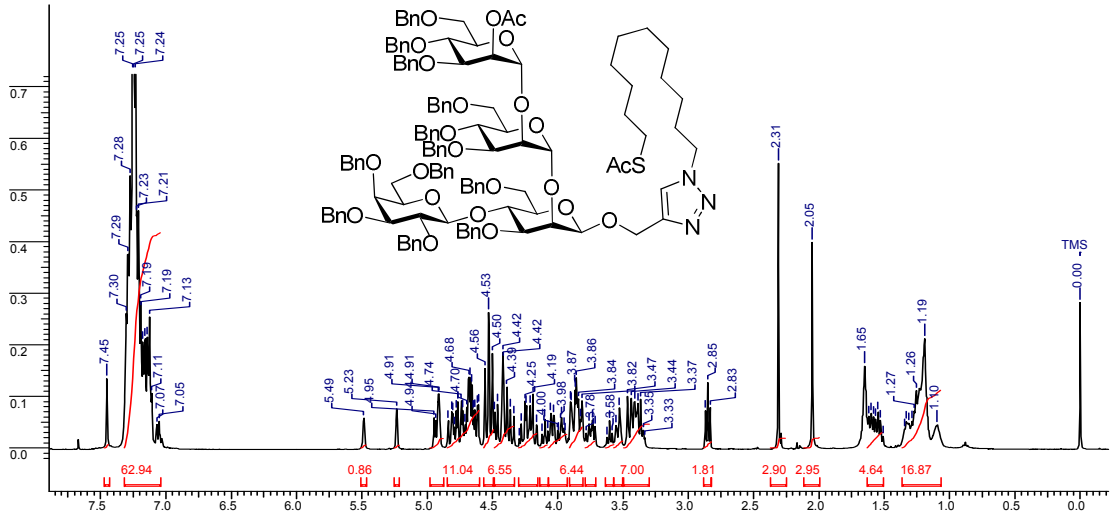
^{13}C NMR ($CDCl_3$, 50.32 MHz) of Compound **32**



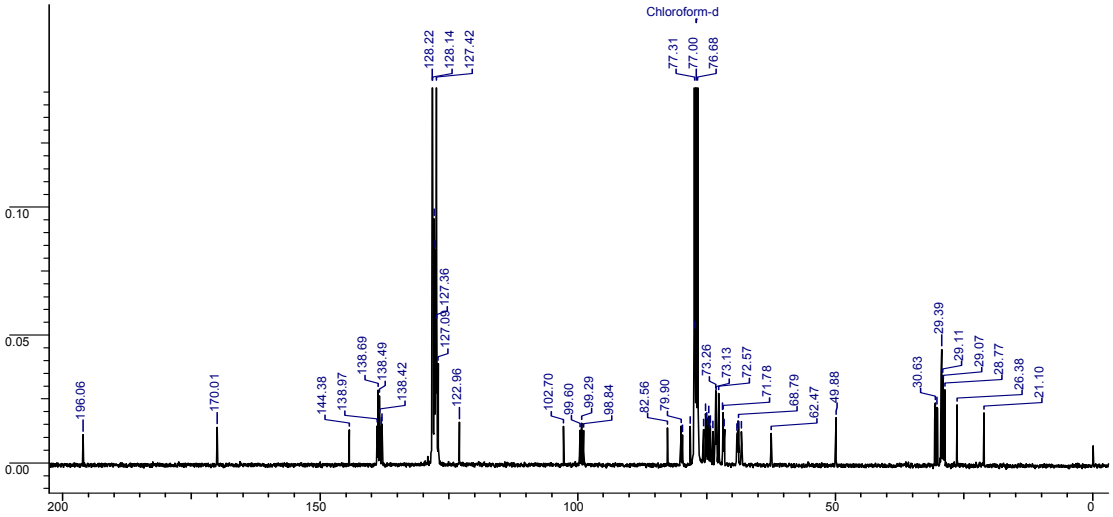
DEPT NMR ($CDCl_3$, 50.32 MHz) of Compound **32**



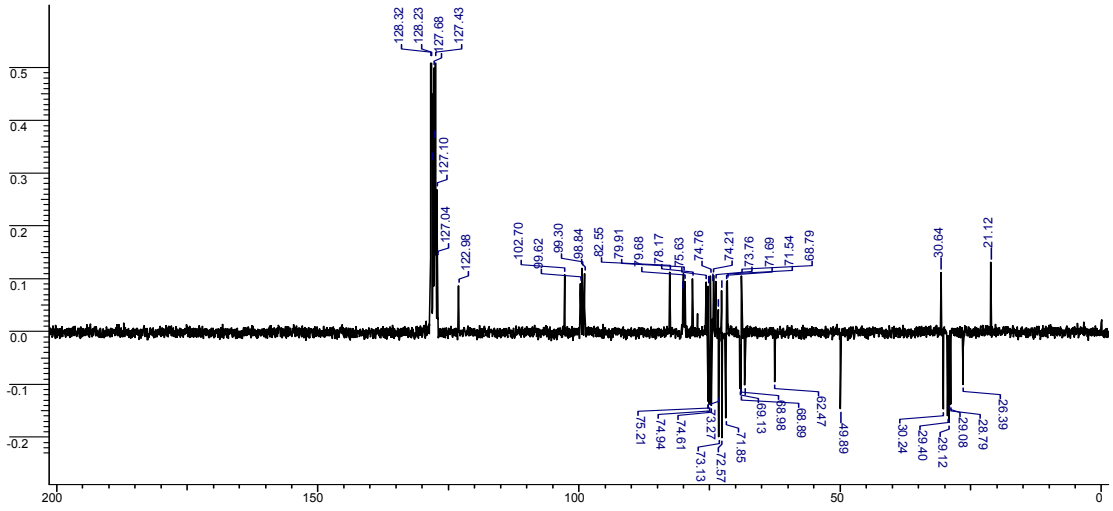
^{1}H NMR ($CDCl_3$, 400.13 MHz) of Compound **33**



^{13}C NMR ($CDCl_3$, 100.61 MHz) of Compound **33**



DEPT NMR ($CDCl_3$, 100.61 MHz) of Compound **33**



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List of Publications

- Gold mediated Glycosidations: Selective Activation of Propargyl 1,2-orthoesters in the presence of Aglycones containing a Propargyl moiety, **Sureshkumar, G** and Hotha, S. *Chem. Comm.* 2008, 4284-4286.

- Propargyl 1,2-orthoesters as glycosyl donors: Stereoselective synthesis of glycosides and disaccharides, **Sureshkumar, G** and Hotha, S. *Tetrahedron Lett.* **2007,** *48*(*37*), 6564-6568.

- Gold Catalyzed Glycosidations: Synthesis and Utility of Glycomonomers, Shivaji A. Thadke, Ashif Y. Shaikh, Debasis Pati, Mritunjoy Kar, **Gopalsamy Sureshkumar**, Sayam Sen Gupta, and Srinivas Hotha (*Communicated*).

- Spectroscopic and DNA binding properties of 9-ω-aminoalkyl ether derivatives of berberine, Md. Maidul Islam, Anirban Basu, Maidul Hossain, **Gopalsamy Sureshkumar**, Srinivas Hotha, Gopinatha Suresh Kumar (*Communicated*).

- Synthesis of tetrasaccharide *motif* of the lipophosphoglycan expressed on the cell surface of the *Leishmania Donovani*, **Gopalsamy Sureshkumar** and Srinivas Hotha (*manuscript under preparation*).