Armed disarmed effect for oligosaccharide synthesis

Via gold catalyzed alkyne activation

THESIS

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By

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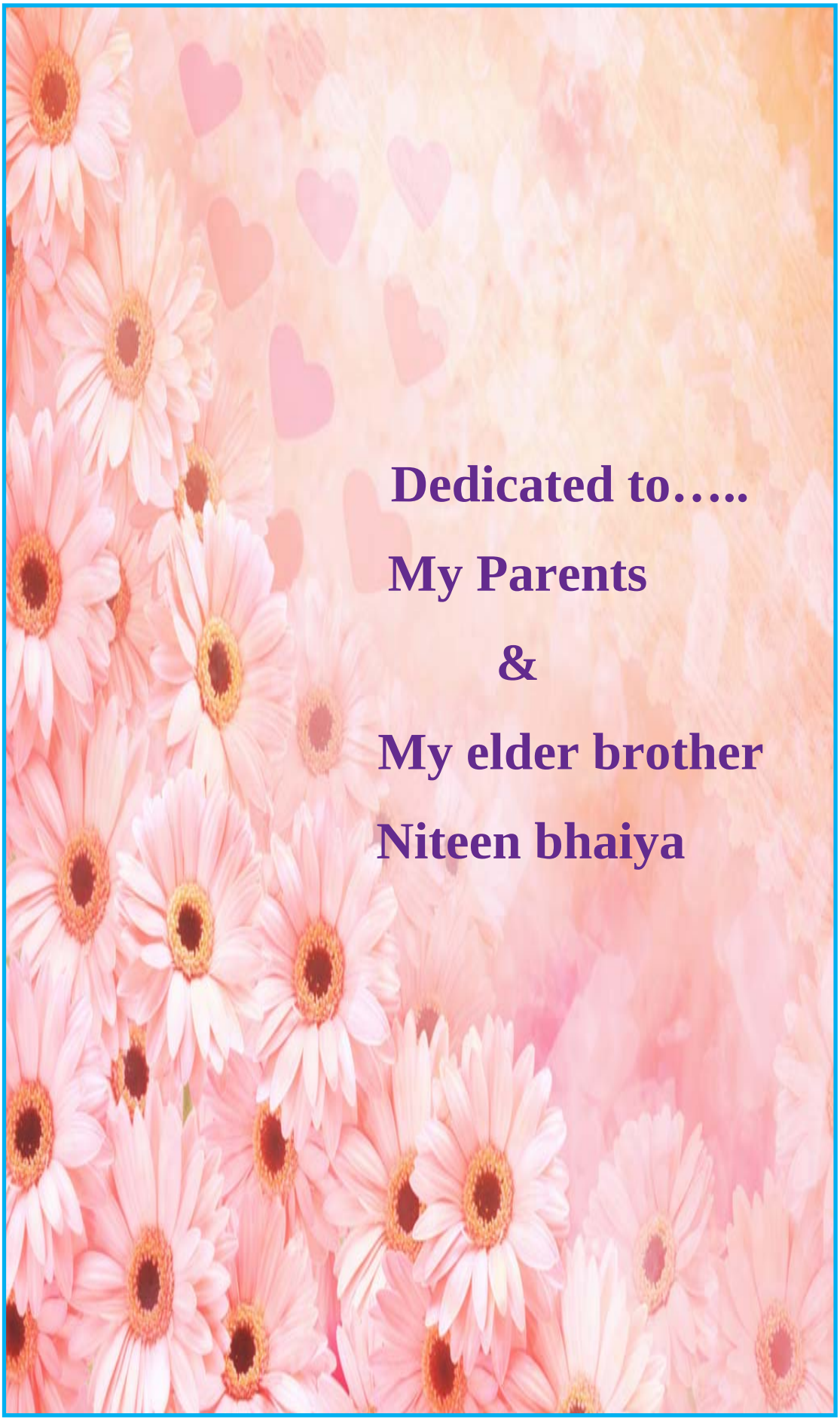
Dedicated to…..
My Parents
&
My elder brother
Niteen bhaiya

राष्ट्रीय रासायनिक प्रयोगशाला
(वैज्ञानिक तथा औद्योगिक अनुसंधान परिषद)
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CERTIFICATE

This is to certify that the research work presented in thesis entitled "***Armed disarmed effect for oligosaccharide synthesis via gold catalyzed alkyne activation"*** has been carried out under my supervision at National Chemical Laboratory, Pune and is a bonafide work of **Mr. Abhijeet K. Kayastha**. This work is original and has not been submitted for any other degree or diploma of this or any other University.

Pune- 411008
April 2013

(Dr. Srinivas Hotha)
Research Supervisor

Candidate's Declaration

I hereby declare that the research work incorporated in the thesis entitled ***"Armed disarmed effect for oligosaccharide synthesis via gold catalyzed alkyne activation"*** submitted for the degree of ***Doctor of Philosophy*** in ***Chemistry*** to the ***University of Pune***, has been carried out by me at National Chemical Laboratory, Pune- 411008, India, from February 2008 to April 2013 under the supervision of Dr. Srinivas Hotha. This work has not been submitted in part or full by me for a degree or diploma to this or any other University or Institution.

April 2013
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It gives me immense pleasure to express my deep sense of gratitude to my supervisor and mentor ***Dr. Srinivas Hotha*** *for his excellent guidance, continuous encouragement, and generous support in achieving this entire endeavor. Wholeheartedly, I am very much grateful to him for motivating me in the synthetic carbohydrate chemistry. Without his encouragement and constant guidance, I could not have finished my doctoral degree. I do sincerely acknowledge the freedom rendered by him in the laboratory for the independent thinking, planning and execution of research. Working with him was really a great pleasure and fetched me a lot of learning experience.*

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My stay here was made livelier by GJ hostel, a hostel unique in ways more than one. It provided the perfect atmosphere to spend leisure time and I thoroughly enjoyed all the sports & cultural activities that abounded in the hostel. It was a pleasure to share room with K. K. Suresh. I owe a big "thanks" to all my friends who made GJH such a wonderful place to stay in.

Friends make things go easy and life beautiful. Indeed I am blessed to have friends like Ankush, Ashif, Prasad, Mandeep, Satish and Vijay, where I don't have words to describe them as individuals and it should suffice to say that I am simply blessed to have them ever by my side; I've spent the best of times with them and all they have been great in putting up with a lot of my gibberish and form an indispensable part of my life. The care and emotional support of these people has been no less than that of my family and for all that they have done for me I don't want to thank them simply because I don't need to.

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I wish to express my gratitude towards "God-almighty", who gave me the strength and courage to fulfil my dreams and has showered upon me his choicest blessings. I believes on faith, which I feel, has always strengthen me in the deeps of difficulties and therefore it would be really appropriate to conclude this acknowledgement with the famous quotation of Mr. Paulo Coelho from his critically acclaimed Novel Alchemist "When you want something, all the universe conspires in helping you to achieve it."

.....Abhijeet

Contents

- ^{1}H NMR spectra were recorded on AV-200 MHz, AV-400 MHz, DRX-500 MHz, or JEOL ECX 400 MHz and Bruker Advance 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, DRX-125 or JEOL ECX 100 MHz and Bruker Advance 125 MHz spectrometer.
- Low resolution mass spectroscopy (LRMS) was performed on Waters Acquity UPLC-MS (H Class). High resolution mass spectroscopy (HRMS) was performed on ABI-MALDI-TOF mass spectrometer using TiO_2 as the solid matrix.
- 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 P-1020 or Rudolph polarimeter.
- GC Analyses were carried out on an Agilent 7890 instrument equipped with a hydrogen flame ionization detector and HP-5 capillary column (30m x 0.32mm x 0.25 µm, J & W Scientific). Nitrogen was used as the carrier gas at a flow rate of 1mL/min.
- 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.
- α-β ratio of anomeric position was determined by relative peak intensities of resonances from the most characteristic protons in the ^{1}H NMR spectrum of the partially purified product
- Scheme, Figure and Compound numbers in abstract and individual chapters are different.

Ac	Acetyl
Ac_2O	Acetic anhydride
AcOH	Acetic acid
AIBN	2,2-Azobisisobutyronitrile
Aq	Aqueous
$BF_3.Et_2O$	Boron trifluoride diethyl etherate
Bn	Benzyl
Bz	Benzoyl
BnCl	Benzyl chloride
BzCl	Benzoyl chloride
BnBr	Benzyl bromide
Cat	Catalytic
Conc	Concentrated
DBU	1,8-Diazabicycloundec-7-ene
DMAP	N,N-Dimethylaminopyridine
DMTST	Dimethyl sulphonium triflate
DMF	N,N-Dimethylformamide
DMSO	Dimethyl sulfoxide
DEPT	Distortionless Enhancement by Polarization Transfer
Ech-OH	1-Ethynylcyclohexanol
EtOAc	Ethyl Acetate
eq	Equivalents
g	Gram
h	Hour
Hz	Hertz
IDCP	Iodonium dicollidine perchlorate
J	Coupling constant
NIS	*N*-Iodosuccinimide
mL	Millilitre
mol	Mole
mmol	Millimole
Me	Methyl
MeOH	Methanol

4ÅMS	4Å Molecualar sieves
mg	Milligram
min	Minutes
NMR	Nuclear Magnetic Resonance
PMB	*para*- methoxy benzyl
PTSA, TsOH	*para*-Tolune sulphonic acid
rt	Room temperature
SBox	*S*-benzoxazolyl
TBAI	Tetra-*n*-butylammonium iodide
TESOTf	Triethylsilyl trifluoromethanesulfonate
tert-BuCl	*tert*-Butyl Chloride
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TfOH	Trifluoromethane sulphonic acid
TCA	Trichloroacetamidate
TLC	Thin Layer Chromatography
TMSOTf	Trimethylsilyl trifluoromethanesulfonate
Tr	Trityl

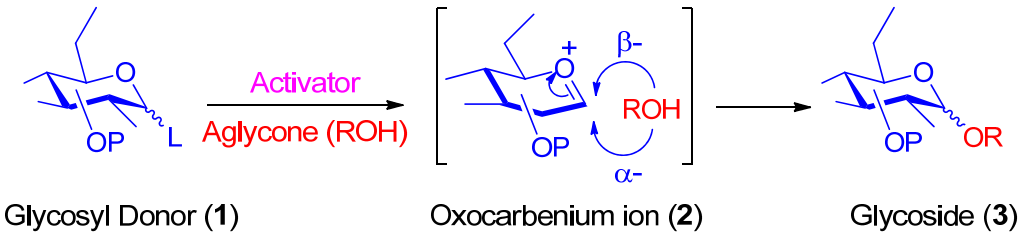
The thesis entitled, **"Armed Disarmed effect for oligosaccharide synthesis via gold catalyzed alkyne activation"** is divided into three chapters. Chapter one deals with the introduction to oligosaccharide synthesis and study of armed disarmed concept in propargyl glycosides. The second chapter describes development of a versatile gold catalyzed glycosidation reaction at room temperature. The third chapter shows the synthesis of glycoconjugates using room temperature gold catalyzed transglycosidation protocol.

Chapter 1: Armed disarmed effect in Propargyl glycosides.

Advances in glycobiology significantly highlighted the role of glycoconjugates and oligosaccharides in various biological processes such as information transfer between cells, immune response, metathesis, fertilization etc. The major hindrance to the understanding and eventual modulation of these biosynthetic pathways is the access to pure and well defined oligosaccharides and glycoconjugates. Isolation and purification of oligosaccharides and glyconjugates from a biological system is always a difficult task as they are present in microheterogenous forms; hence, chemical synthesis of such glycoconjugates is the most reliable technique.

The fundamental reaction for the synthesis of oligosaccharides is called as glycosidation, which involves a glycosyl donor (**1**), a glycosyl acceptor (R_1OH) and a promoter. The glycosyl donor contains a leaving group at the anomeric position which extrudes out under the influence of the promoter from the glycosyl donor to give an oxocarbenium ion intermediate (**2**) which will then be attacked by the aglycon to give glycoside (**3**).

Scheme: 1 General Glycosidation reaction



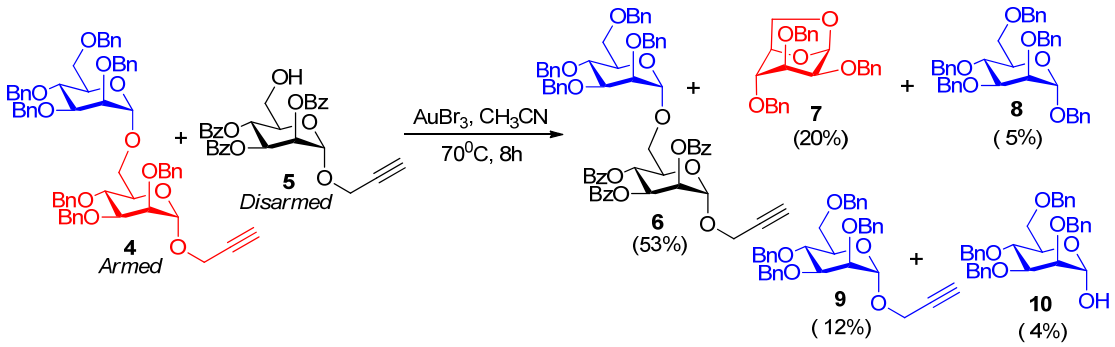
One of the ways to synthesize oligosaccharides is the chemoselective activation of glycosyl donor over another containing the same leaving group but in a different stereoelectronic environment, is called as *Armed-Disarmed effect* which was first coined by B. Fraser Reid in 1988 for *n*-pentenyl glycosides. The benzyl groups are electronically passive groups that encourage the development of positive charge in the pyranose ring, most commonly at *C-1*. Conversely the benzoates groups are electron withdrawing and so disfavor any build up of positive charge in the ring.

From our group, we have reported a novel transglycosidation methodology exploiting gold catalysis which activates the alkyne moiety of a propargyloxy group to make it a leaving group and then the resulting oxocarbenium ion was aptly trapped by an external nucleophile (aglycon or glycosyl acceptor) to give corresponding glycosides

or saccharides when the aglycon is a sugar moiety. While performing the reactions with our existing methodology, we understood that some appendages on the glycosyl moiety of the glycosyl donor would make the donor completely inactive or super active under the influence of gold catalysts. We took this concept to develop a method for the synthesis of higher saccharides using propargyl glycosides as glycosyl donors.

Initially Armed disaccharide **4** was allowed to react with disarmed aglycon **5** which should result into the formation of trisaccharide; which did not formed, instead after the conventional column purification we observed the cleavage of interglycosidic bond which then resulted in to the formation of two major products, disaccharide **6** and 1,6-anhydrosugar **7**. Formation of 1,6-anhydrosugar encouraged us to probe the prospect of propargyl glycosides as possible precursors for the synthesis of 1,6-anhydrosugars using catalytic $AuBr_3$ in a separate endeavor.

Scheme: 2

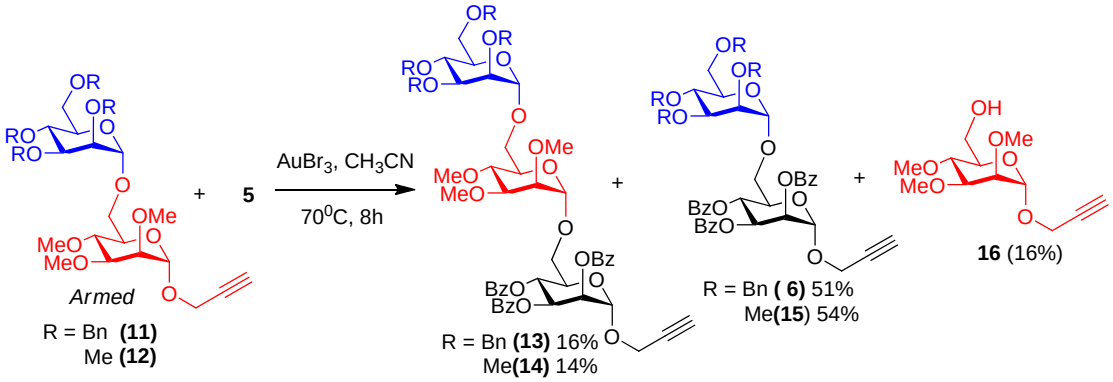


Further purification enabled us to isolate three more minor products from the reaction. Formation of compound **8** (5%) was attributed to the primary benzyl deprotection at high temperature where as compound **10** (4%) has formed due to the presence of moisture. Notably formation of compound **9** (12%) was quite surprising, as we have hypothesized previously, upon activation with gold salts the triple bond of propargyl group goes through some unidentified intermediates to get converted into cyclopropanone and therefore becomes traceless. However formation of compound **9** confirmed the liberation of propargyl alcohol during transglycosidation reaction**.**

Replacement of benzoyl groups of disaccharide **6** by methyl groups via a two step procedure gave armed disaccharide **11** with less directing methyl groups on the sugar at the reducing end. $AuBr_3$ catalyzed glycosidation gave us the trisaccharide **13**, disaccharide **6** and propargyl 2,3,4-tri-*O*-methyl mannoside **16** in 16, 51 and 16% respectively. Similar observations were noticed with the per *O*-methylated disaccharide **12** to give the trisaccharide **14**, disaccharide **15** and the monosaccharide **16**. These observations led us to understand that the propargyl glycosides are highly dependent on the electronic effect of the protecting groups. In contenuation this ongoing study, confirmed that during gold mediated transglycosidation reactions, both alkyne and interglycosidic oxygen are activating and cleaving-off interglycosidic bond, and so the reaction outcomes are highly dependent on the nature of interglycosidic linkage in association with sterics and

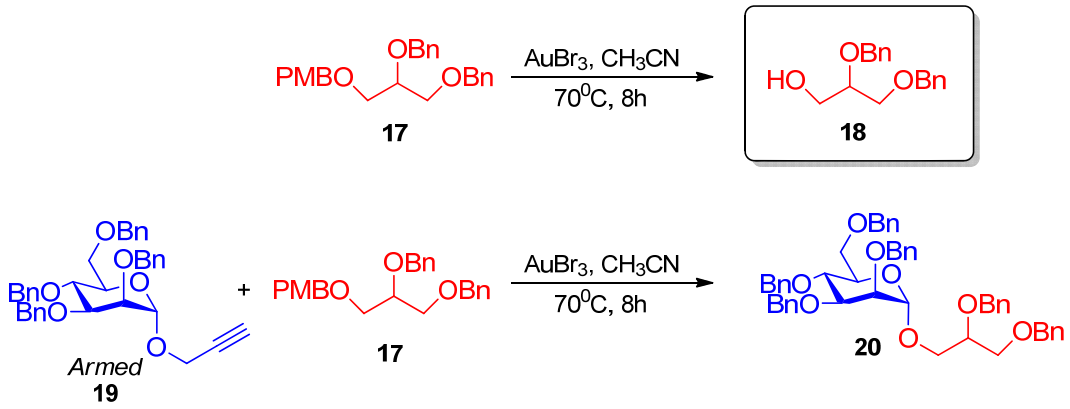
electronic factors.

Scheme: 3



Importantly the efficiency of primary benzyl deprotection in the presence of gold salts at high temperature is intriguing; for which we prepared compound **17** from acetonide protected glycerol and subjected to similar conditions ($AuBr_3$, 70 ^{0}C, and 8h), where we observed the quantitative deprotection of PMB group in presence of other benzyl groups, which can be rationalized as PMB group is more acid sensitive compare to OBn protecting group.

Scheme: 4



Similarly when we subjected the compound **18** with propargyl mannoside (**19)** we have observed the transglycosidation reaction following PMB deprotection and one pot glycosidation as shown in scheme 4.

In conclusion armed/disarmed effect of propargyl glycosides in presence of catalytic amount of $AuBr_3$ was studied. The cleavage of interglycosidic bond was observed which has resulted the formation of a disaccharide and 1,6-anhydrosugar as major products of the glycosidation reaction. The replacement of protecting group helped us to get anticipated trisaccharide in minor yield and eventually confirmed the importance of electronic effects of the protecting groups in oligosaccharide synthesis. High temperature of reaction was found responsible for other side reactions such as primary benzyl deprotection which then applied for PMB deprotection and one pot glycosidation. Significantly the extrusion of propargyl alcohol was observed and

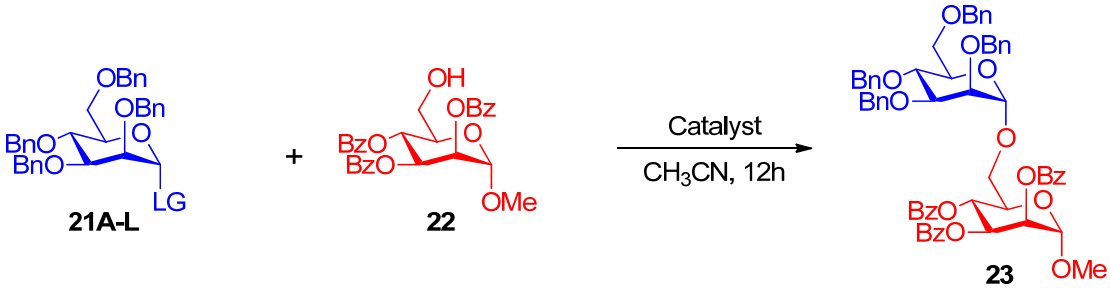
confirmed during transglycosidation process which inspired us to check for the role of gold salt and mechanism involved in transglycosidation reaction.

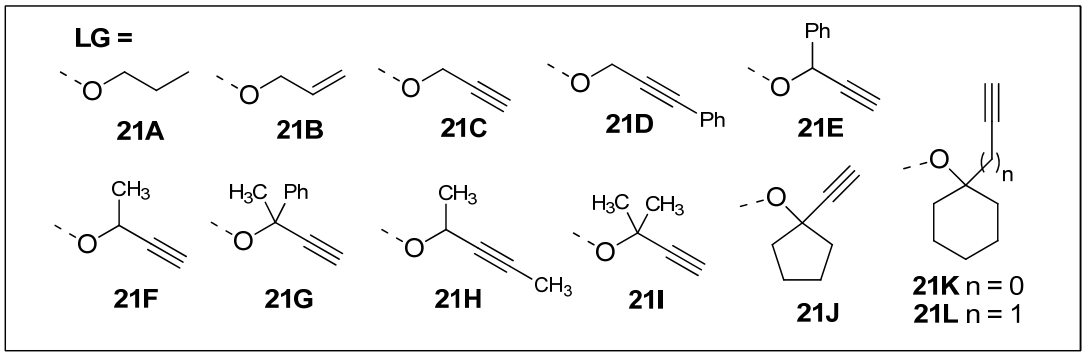
Chapter 2: Development of versatile gold catalyzed glycosidation reaction at room temperature.

Side reactions occurring in the high temperature activation protocol of propargyl glycosides in the presence of Au (III) salts, prompted us to investigate the reaction condition for carrying out the transglycosidation at room temperature, where it might be possible to rule out the cleavage of interglycosidic bond. Conceptually there are two ways to activate alkynes at room temperature for transglycosidation reaction (1) using catalytic silver salts with gold. (2) Substitution at propargyl group to make it more efficient leaving group. The substitution can be done either at *C-1*, *C-3* or both carbon atoms of propargyloxy group.

To begin with, synthesis of mannopyranosyl disaccharide (**23**) is considered as a model reaction (scheme 5) in view of previous observations that propargyl mannopyranosides give α-anomers only due to the bulky -OBn at the *C*-2 position as well as the anomeric effect. Aglycon **22** was selected among host of possible sugar alcohols in order to avoid competing side reactions.

Scheme: 5



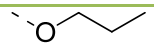
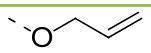
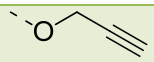
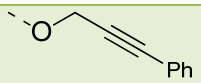
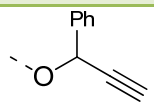
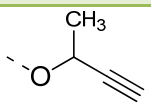
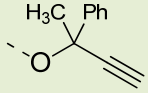
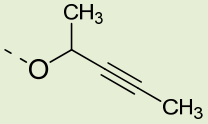
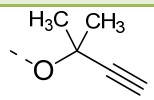
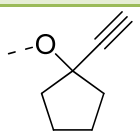
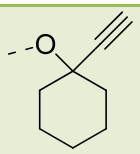
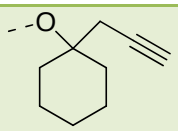


Alkyl substituted mannopyranosyl donors (**21A-21L**) were prepared. Aglycon **22** was allowed to react with potential mannosyl donors (**21A-21L**) in the presence of three widely available gold catalysts $AuBr_3$, $AuCl_3$ and $HAuCl_4$ at room temperature for 12h in CH_3CN.

Glycosyl donors **21A** and **21B** which possess no alkyne groups did not proceed satisfactorily and simple propargyl substitution (**21C**) was found to give about 18%

yield after 12h at room temperature in the presence of $AuCl_3$ (Table 1). Single aromatic substitution on the propargyl moiety (**21D** and **21E**) also failed to give good yields where methyl substitutions (**21F**, **21H**) showed good conversion with $AuCl_3$ but not with $AuBr_3$ and $HAuCl_4$. Between, *gem*-disubstituted donors **21G** and **21I**, dimethyl donor **21I** was found to be superior. However, placing the cyclic substitution (**21J**-**21L**) in place of *gem*-dimethyl was found to be highly beneficial. Nevertheless, best results in the screening process were observed with donors **21I**, **21K** and **21L**.

TABLE: 1 screening of leaving groups for gold-catalyzed transglycosidation at room temperature and corresponding yields

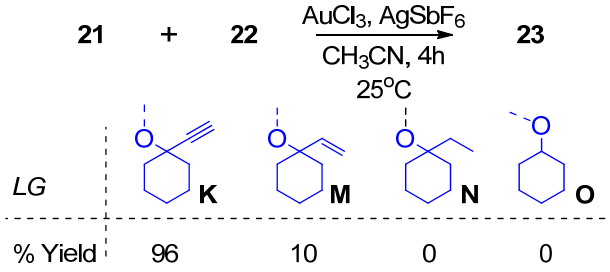
Donor	Leaving Group	% Yields			Donor	Leaving Group	% Yields		
		$AuCl_3$	$AuBr_3$	$HAuCl_4$			$AuCl_3$	$AuBr_3$	$HAuCl_4$
21A		0	8	0	**21B**		0	10	5
21C		15	18	17	**21D**		15	10	9
21E		0	26	8	**21F**		5	20	0
21G		0	0	15	**21H**		0	0	5
21I		8	30	10	**21J**		8	23	14
21K		16	32	15	**21L**		13	30	16

Significance of increased reactivity of *gem*-disubstituted donors can be attributed to the earlier reported Thorpe-Ingold like effect. Mannosyl donors **21F** and **21I** were not considered further because of the observed instability of the compound, ease in preparation and/or cost of the aglycon. Donor **21K** was found be better than **21L** purely because of the easy availability and low cost of **21K** though both **21K** and **21L** fared almost equally.

After considering all related facts 1-ethynylcyclohexanyl propargyl glycoside **21K** was chosen for optimization where it was observed that heating the donor **21K** and aglycon **22** to 45°C in the presence of $AuCl_3$ or $AuBr_3$ increased the yield of the reaction. Further increase to 70°C showed further improvement of yields to 80s. Inspired by several literature reports on the enhancement of performance in gold catalyzed reactions by the addition of Ag-salts, addition of Ag-based co-catalysts was then studied.[7] Among the combination of different gold and silver salts, $AuCl_3$-$AgSbF_6$ was found to be highly efficient (91% in 4h) at desired room temperature. The best result (96% in 4h) of disaccharide **23** was obtained when the transglycosidation reaction between **21K** and **22** was conducted in CH_3CN-CH_2Cl_2 (1:1) at room temperature for 4h in the presence of 5 mol% each of $AuCl_3$ and $AgSbF_6$.

The alkyne group in **21K** is essential for it to behave as a glycosyl donor since the partially reduced compound **21M** resulted in diminished yield whereas the fully saturated donor **21N** did not show any conversion at all and similar is the case with the simple cyclohexyl mannopyranosyl donor **21O** signifying the presence of alkyne in the glycosyl donor.

Scheme: 6 significance of Alkyne



The efficiency of 1-Ethynylcyclohexanyl glycosides were confirmed by GC study where THP protected 1-ethynylcyclohexanol was chosen as model glycosyl donor. The experimental results confirmed the quantitative formation of desired product and complete consumption of glycosyl donor. Similarly liberation of 1-ethynyl cyclohexanol was observed and confirmed through GC-study.

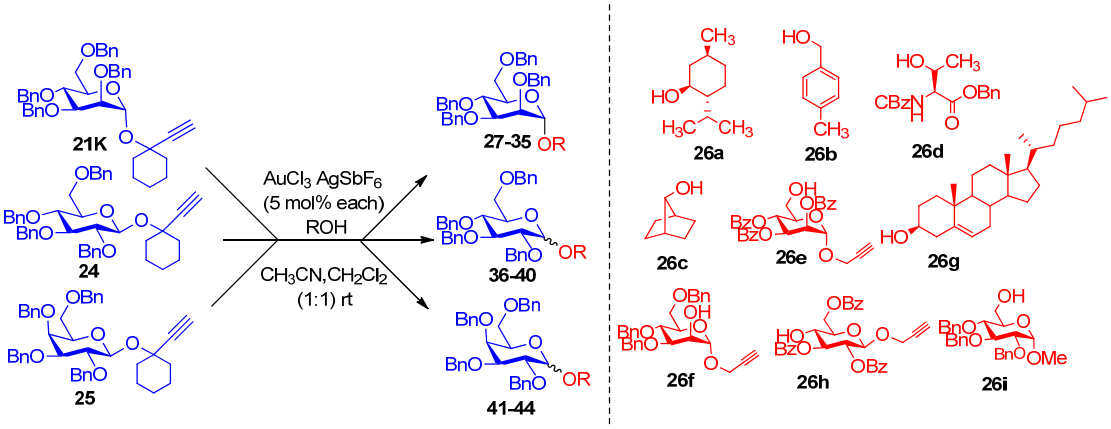
In conclusion we have discovered a method for transglycosidation at room temperature after screening a panel of substituted propargyl glycosyl donors. Where we have found that 1-ethynylcyclohexanyl (-Ech) glycosyl donor gives excellent transglycosidation. It was observed that during transglycosidation process 1-Ethynylcyclohexanol ejects out from reaction. Furthermore GC studies confirmed our observations and proved the quantitative formation of required product under similar conditions.

Chapter 3: Synthesis of glycoconjugates using room temperature gold catalyzed transglycosidation protocol.

After the screening with different substituted propargyl glycosyl donors 1-Ethynylcyclohexanyl (-Ech) propargyl glycosyl donor was proved to be superior to

other substituted propargyl glycosyl donors. It was observed that addition of catalytic amount of silver salt helps in transglycosidation and brings down the reaction temperature to 25 ^{0}C. The best condition for transglycosidation is the combination of $AuCl_3$ with $AgSbF_6$ (5 mol % each) in 1:1 mixture of CH_3CN and CH_2Cl_2.

Scheme: 7

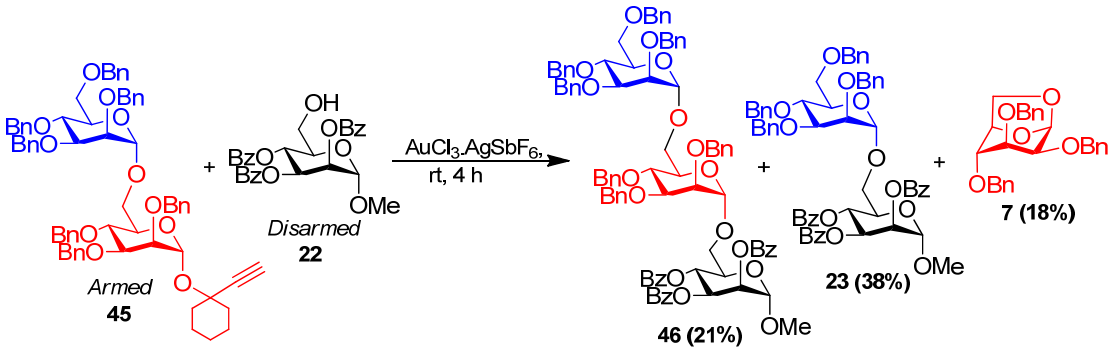


The generality of the newly identified glycosyl donor for transglycosidation was evaluated with set of aglycons (**26a-26i**). The reaction of mannopyranosyl donor **(21K)** with aromatic, acyclic and steroidal alcohol (**26a-26d**) formed the products in quantitative yields. Carbohydrate based primary alcohols (**26e** and **26i**) gave excellent yields where as carbohydrate based secondary alcohols (**26f** and **26h**) gave more than 70 % yield of required disaccharides. Furthermore, room-temperature transglycosidation using Ech-glycosides was successfully extended to glucosyl and galactosyl donors **24** and **25**. For example, aglycons which are alicyclic or carbohydrate derived primary alcohols resulted transglycosylated products in quantitative yields where as the secondary alcohols gave very high yields of transglycosylated products. Transglycosylated products resulting from glucosyl donor **24** and galactosyl donor **25** are found to be α-β mixture of anomers (**36-44**) with β-anomer being a major due to the participating nature of CH_3CN which is in complete agreement with earlier observations.

In order to check the efficiency of newly designed room temperature alkyne activation protocol for the synthesis of oligosaccharides using armed-disarmed effect, the armed disaccharide **45** was allowed to react with disarmed aglycon **22** in the presence of $AuCl_3/AgSbF_6/CH_3CN$-CH_2Cl_2(1:1)/rt under argon atmosphere for 6h. Purification by conventional silica gel column chromatography enabled us to characterize the anticipated trisaccharide **46** with 21% yield along with disaccharide **23** and anhydro sugar **7**. In the trisaccharide **46**, three anomeric protons were noticed at δ 4.88 (1H, d, J = 1.6Hz), 4.91 (1H, d, J = 1.6Hz), 5.61 (1H, dd, J = 1.6, 3.2Hz) ppm. The ^{13}C NMR spectrum revealed that there are three mannose residues with 1,2-*trans* configuration as their anomeric carbons were noticed at δ 98.1, 98.2 and 98.5 ppm and the molecular weight was found to be 1483.586 (M^{+}+23 for Na). Rests of the resonances in the

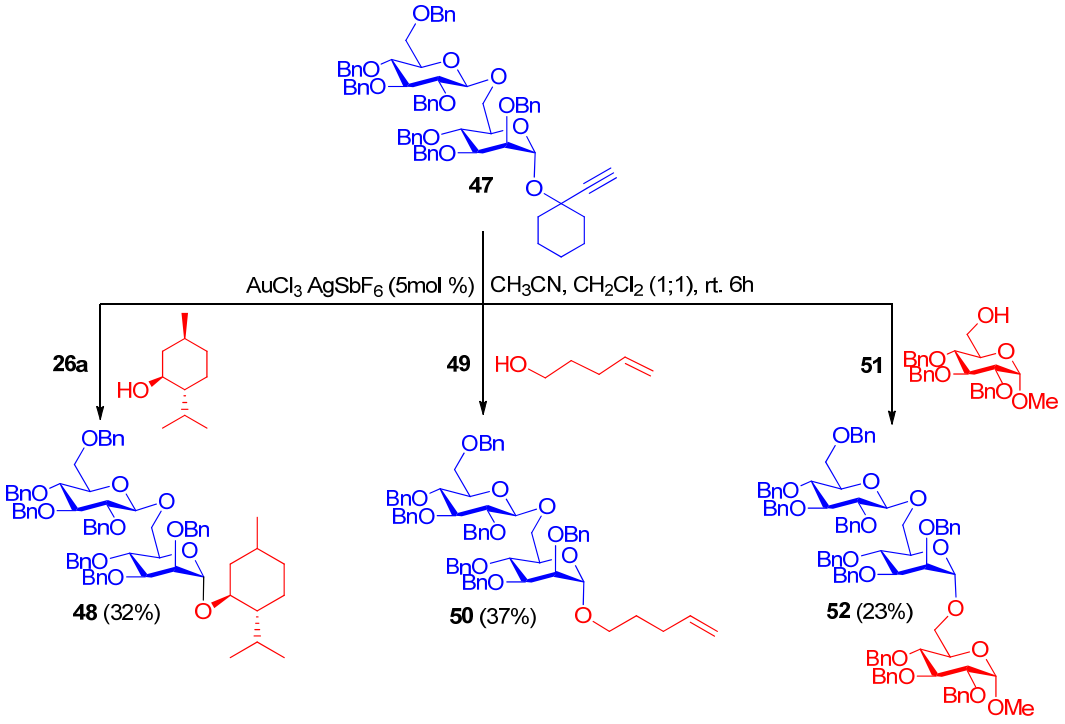
spectrum were completely in agreement with assigned structure of trisaccharide **46**. Formation of disaccharide **23** and anhydro sugar **7** can be rationalized on the basis of susceptibility of interglycosidic bond cleavage. Thus, it is proved that the Ech glycosides can be successfully utilized for oligosaccharide synthesis.

Scheme: 8



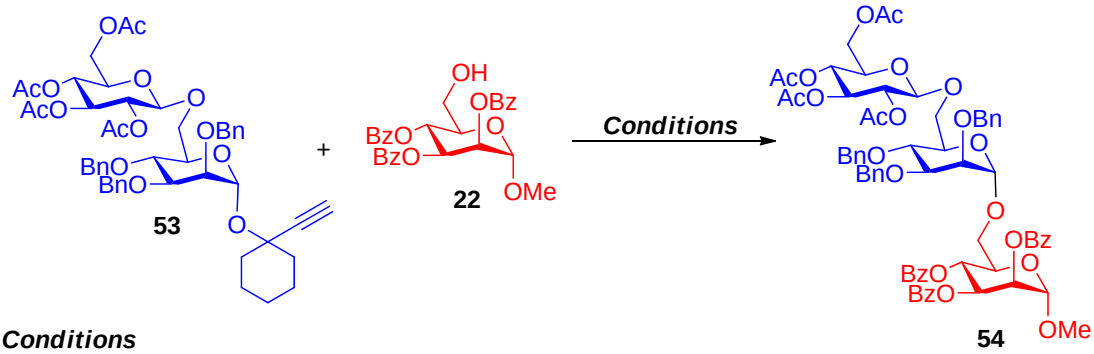
During our study of gold mediated transglycosidation reaction, it was observed that, intensity of unusual cleavage depends on nature of interglycosidic linkage. Generally the glycosyl donors with axial hydroxyl groups are considered more reactive then the glycosyl donors without any axial hydroxyl group. For example β-D-glucose is less reactive as compare to α-D-glucose and α-D-mannose. In order to check the effect of reactivity difference on interglycosidic bond cleavage, we prepared armed disaccharide **47**; and allowed to react with menthol (**26a)** in presence of 5 mol% $AuCl_3/AgSbF_6/CH_3CN$-CH_2Cl_2(1:1)/rt under argon atmosphere for 6h, to give the requisite disaccharide (**48**) in 32% yield. Similarly reaction between glucosyl donor **47** with 4-penten-1-ol (**49**) and methyl 2,3,4-tri-*O*-benzyl α-D-glucopyranoside (**51**) gave corresponding transglycosides in 37% and 23% respectively (Scheme 9).

Scheme: 9



Interestingly gold mediated transglycosidation reaction between disaccharide **53** and aglycon **22** gave corresponding trisaccharide **54** in good yield wherein cleavage of interglycosidic bond was not observed which further confirmed the importance of protecting groups in gold mediated glycosidation reactions.

Scheme: 10



Conditions

1) $AuCl_3$, $AgSbF_6$ (5 mol % each), CH_3CN, CH_2Cl_2 (1:1), rt, 4h, 53%

2) $AuCl_3$ (5mol %) CH_3CN, 70 ^{0}C, 6h, 78%

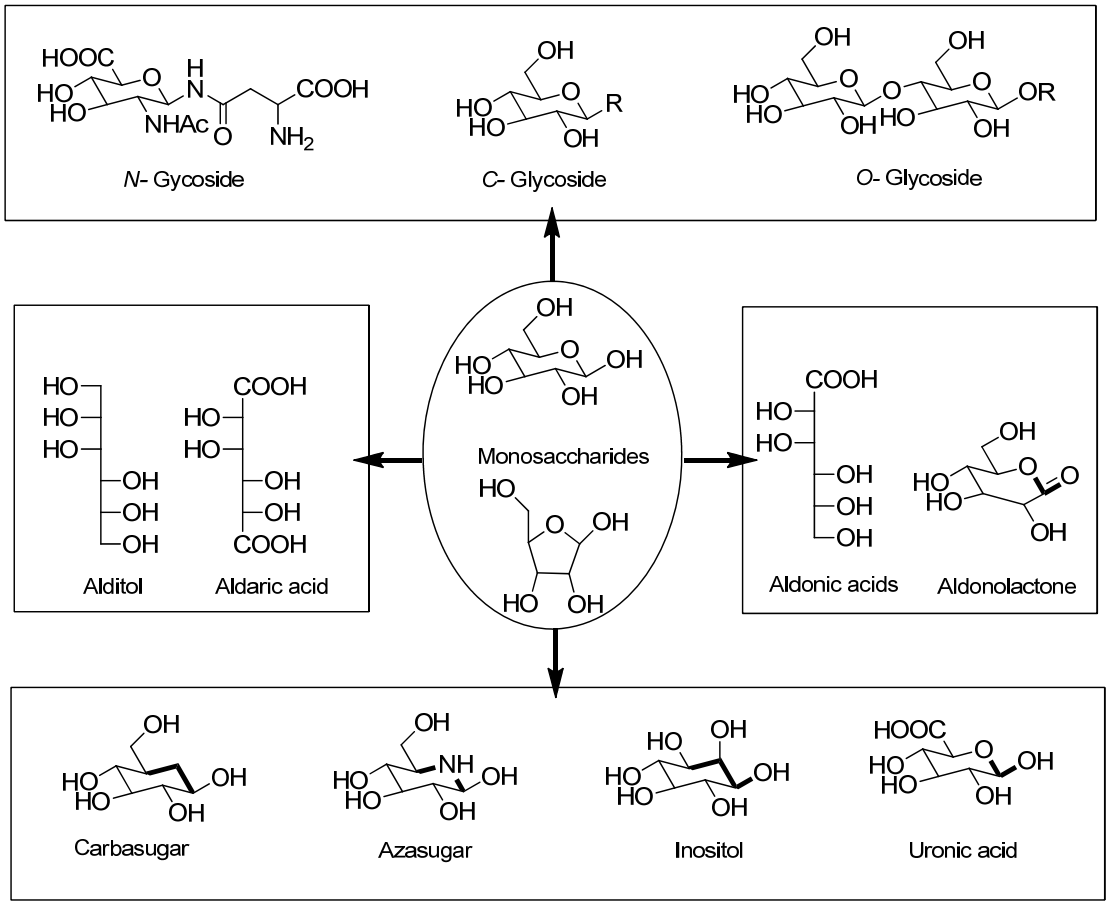
In conclusion, we have shown the utility of a gold-catalyzed transglycosidation that can be conducted at room temperature using 1-ethynylcyclohexanyl (Ech) glycosyl donors. The Ech glycosyl donors were found to be superior over the panel of aglycons including primary alcohols, alicyclic, steroidal alcohols which gave quantitative yields of transglycosylated products whereas carbohydrate-derived secondary alcohols and others result in high yields. Furthermore the gold mediated transglycosidation protocol has been successfully demonstrated for the synthesis of trisaccharide in moderate yields.

****

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

Carbohydrates are the most abundant natural products. They are primary biological substances, which are metabolized as monosaccharides and oligosaccharides. In general, the carbohydrates, with lower molecular weight (monosaccharides and disaccharides) are commonly referred as sugars.[1] the word saccharide comes from Greek word *sákkharon* meaning "sugar" while the scientific nomenclature of carbohydrate is complex; the names of the monosaccharides and disaccharides very often end in the suffix –ose. Carbohydrates are major nutrients, which play important role as energy stores and structural building blocks in plants and animals. Carbohydrates exist in a large elemental as well as stereochemical variety, as they are build up from monosaccharides of various kinds, forming diverse branched or linear oligomers as well as very different classes of polysaccharides.

Figure: 1 Carbohydrates



Carbohydrates possess a number of functionalities, at least one carbonyl and several hydroxyl functions per monosaccharide, and often carry further kind of functional groups. Carbohydrates are the compounds with several stereocenters and forms 5- and 6-membered heterocyclic rings, which constitute hemiacetals and acetals respectively. Moreover carbohydrates include substances derived from monosaccharides by reduction of carbonyl group or by oxidation of one or more terminal groups to form carboxylic acids. In addition to this the replacement of one or more hydroxyl groups by hydrogen,

an amino function, a thiol group or similar heteroatomic groups can considered as carbohydrates. Even the endocyclic oxygen atom may be replaced by a carbon or nitrogen which results into the formation of, the -carba and -aza sugars respectively, which are also carbohydrates.

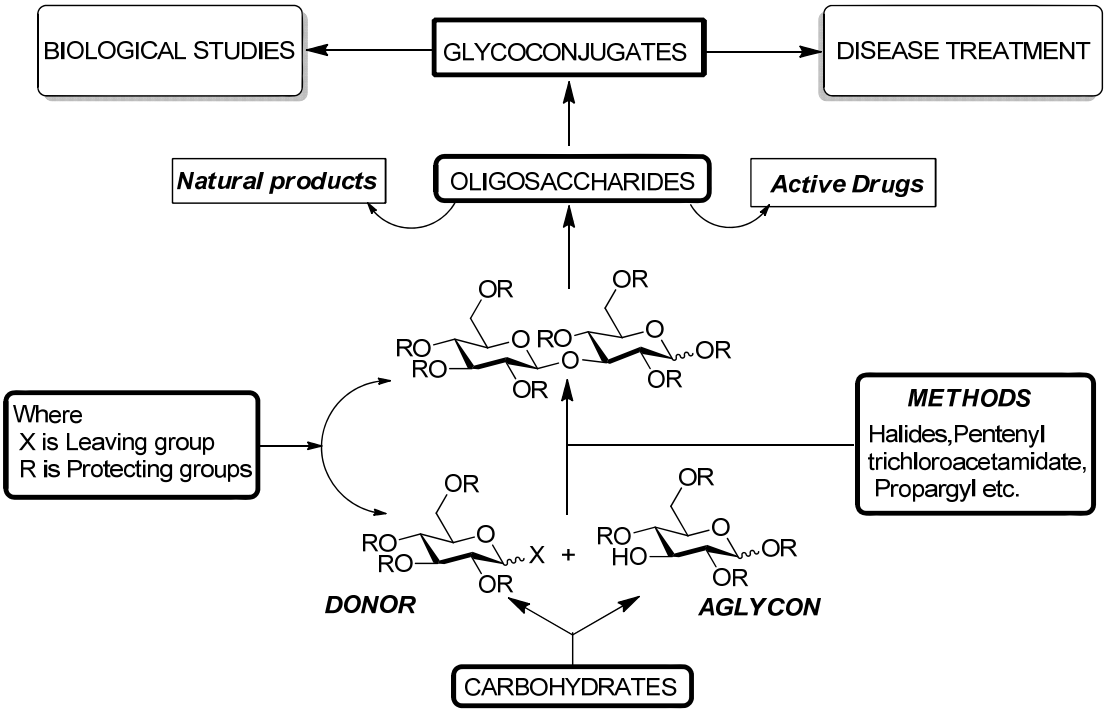
When the carbohydrates are covalently bound to non carbohydrate natural products of different kinds of proteins and lipids, are called glycoconjugates. The size of glycoconjugates varies from relatively small molecules to large biopolymers. Many of the smaller glycoconjugates possess antibiotic activity.[2] Many pharmaceuticals belong to this category, such as cardiac glycosides, anthracyclines, macrolides, ergot alkaloids, and calicheamycines. These molecules are glycosylated with oligosaccharides of varying complexity, which are important for biological storage and transport. On the other hand, even more complex carbohydrates are linked to proteins and lipids producing a large number of glycoconjugates which includes glycoproteins, proteoglycans, glycolipids and GPI-anchors. These glycoconjugates are found in dissolved form or in membrane bound form which belongs to the most important group of biomolecules in cell biology. These carbohydrate moieties comprise an enormous structural variety and these are used in communication process required in cell biology such as in cell adhesion processes.[3]

The glycoconjugates include, for example, glycolipid, whose lipid part serves as a means of anchorage in the double layer of the cell membrane. The oligosaccharide component protrudes out from the cell membrane[4] and is the determinant whose structure is decisive for the specificity of the immune reaction.[5] Glycoproteins found on the cell-surface membranes, in which the oligosaccharide residue is likewise exposed, play a role in intercellular recognition[6,7] acting as receptors for enzymes, hormones, proteins, and viruses. They are able to regulate the transportation of proteins between cells, and should thus be regarded as signal substances in cell metabolism.[8] Glycoproteins are also important in governing the water-molecule concentration at the membrane and the permeation of inorganic ions. In addition, they protect the peptide chain against proteolytic attack. Intensive studies are in progress for the purpose of a more detailed clarification of these many functions.

Two general strategies are used for oligosaccharide synthesis: enzymatic synthesis and chemical synthesis. In enzymatic synthesis, saccharide intermediates are elaborated with enzymes, typically glycosyltransferases, to generate oligosaccharides. Whereas in chemical synthesis, the appropriate building blocks are synthesized and assembled into oligosaccharides. In both approaches, the focus is on forming the critical connection that links saccharide building blocks to form the glycosidic bond. Chemical synthesis and enzyme-based routes are complementary. Enzymes can be used to effect glycosidation with absolute regio- and stereo-control. If the necessary enzyme is available, the desired bond can be formed, often with high efficiency, but from a biological perspective, glycans and glycoconjugates are intrinsically far more heterogeneous than proteins and nucleic acids; their biosynthesis is not template driven, and there are no selectivity and editing filters that ensure the biosynthesis of unique products. Thus, samples of glycans

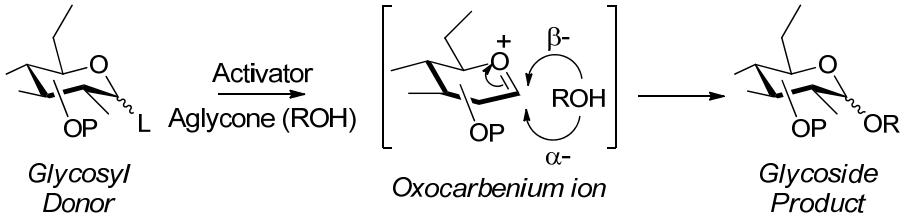
and glycoconjugates derived from nature are often complex mixtures of closely related materials that can be very difficult to analyze.

Figure: 2 The glycoconjugates synthesis and applications.



The major hindrance to the understanding and eventual modulation of these biosynthetic pathways is the access to pure well defined oligosaccharides and glycoconjugates, where chemical synthesis offers exceptional flexibility for the synthesis of Natural and non-natural saccharide building blocks. Although some enzymes will act on alternative substrates, chemical synthesis provides the means to generate any oligosaccharide, oligosaccharide analogs, or glycoconjugates. Hence the chemical synthesis is considered as the most reliable technique for oligosaccharide synthesis.[9] The chemical synthesis of glycosides usually involves the transformation of a sugar into a fully protected glycosyl donor with a leaving group at its anomeric centre and a suitably protected glycosyl acceptor, which generally contains only one free hydroxyl group. In other words, the "glycosyl donor", upon the activation of leaving group by suitable promoter forms oxocarbenium species which subsequently attacked by nucleophile (glycosyl acceptor or aglycon) leads into the formation of glycosidic bond, and the process is called as glycosidation. The schematic representation of general glycosidation reaction is given scheme 1.

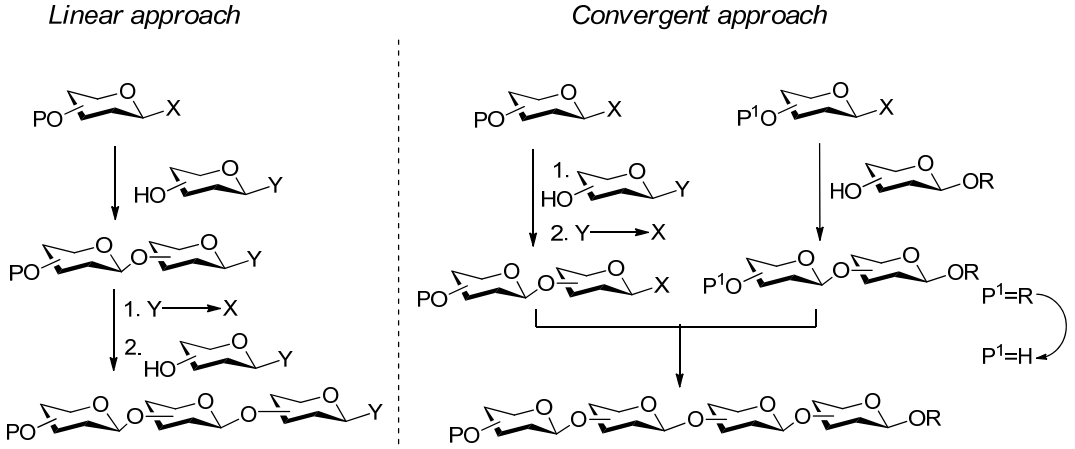
Scheme: 1 General Glycosidation reaction



The term '*glycoside*' when no other characteristics are specified refers to an *O*-glycoside. However, carbohydrate chemistry also deals with the synthesis of *N*-, *S*-, and *C*-glycosides. There are two major principal problems connected with the stereochemical outcome of glycosidation reaction. These are (i) the regiochemistry of the resultant glycosidic linkage, and (ii) the configuration of new glycosidic bond. The regiocontrol can be achieved by choosing a glycosyl acceptor with only hydroxyl group unprotected, which ought to be glycosylated. The stereochemical course of a glycosidation procedure determines whether an α- or β-glycoside will be the product of reaction. Generally when *C*-2 hydroxyl group is protected as ester, which results into 1,2-*trans* glycosides *stereospecifically*, via neighbouring group participation. Whereas glycosidation with a non-participating *C*-2 substituent results in the formation of both, 1,2-*trans* and 1,2-*cis* glycosides with more or less *stereoselectivity*. The protecting groups are the most fundamental parameters with respect to the yield and anomeric selectivity of glycosidation reactions.

Because of the complexities involved in oligosaccharide synthesis, none of the glycosidation methods is universal and reliable over the diverse range of reaction conditions.[10] So depending upon the requirement of desired oligosaccharide one can use either linear strategy in which a monosaccharide is converted into oligosaccharide through linear sequence of reactions else can use convergent strategy. (Figure 3) Yet the limitation for both the methods are, requirement of stoichiometric amount of metal salts, lesser yields and instability over the diverse range of conditions; limits the use of these strategies.

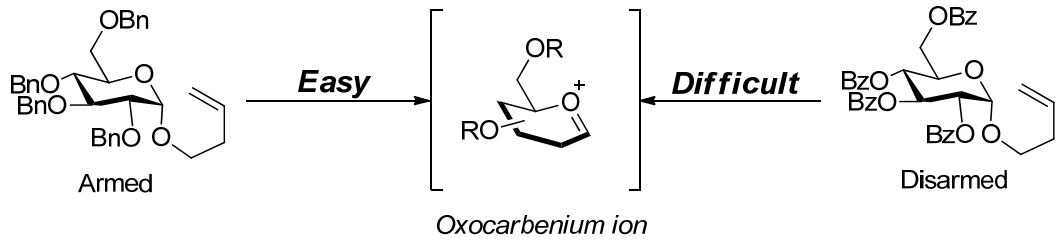
Figure: 3



The different reactivities of glycosyl donors can also be used for oligosaccharide synthesis. The reactivity of the anomeric centre depends on the configuration of the saccharide unit and to a larger degree on the substitution pattern. The nature of the *C*-2 protecting group is of particular importance for the reactivity of a given glycosyl donor. The fundamental work on this problem was published by *Paulsen*'s group in late 1970s.[11] It was observed that in general ester group at the *C*-2 position of glycosyl donor reduces the reactivity of anomeric centre. In 1980s this observation was extended

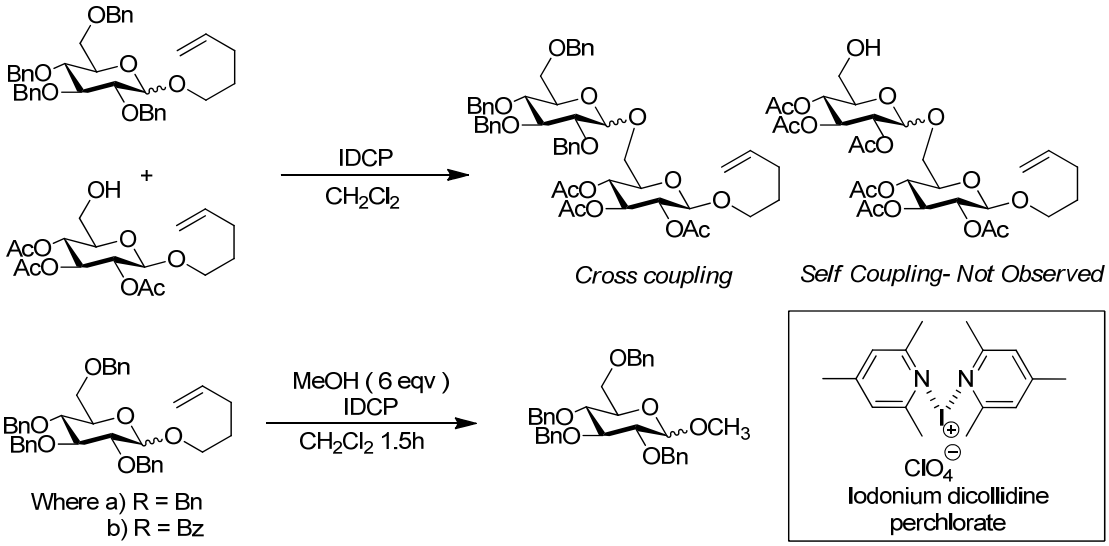
by *B. Fraser-Reid* et al. for *n*-pentenyl glycosides and coined the term 'Armed-disarmed' principal.[12]

Figure: 4 General Armed-disarmed principal



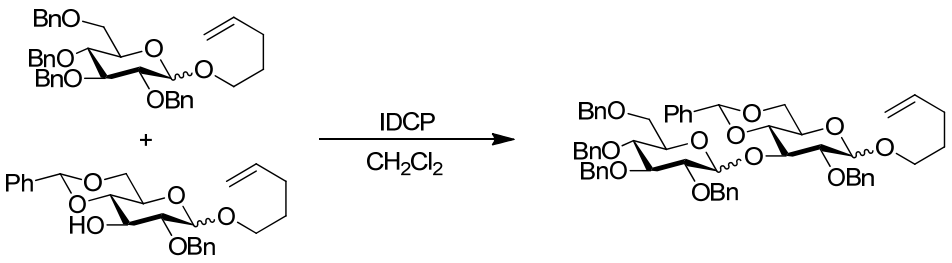
It was found that oxidative hydrolysis (NBS, H_2O) of *n*-pentenyl glycosides required minutes when the *C*-2 protecting group was an ether, but it took hours in case of ester. This notion opened the attractive possibility of condensing an armed pentenyl donor with a partially protected pentenyl acceptor to only obtain the cross coupled disaccharide, with none of the self coupled product.[12]

Scheme: 2 Armed disarmed effect in *n*-pentenyl glycosides



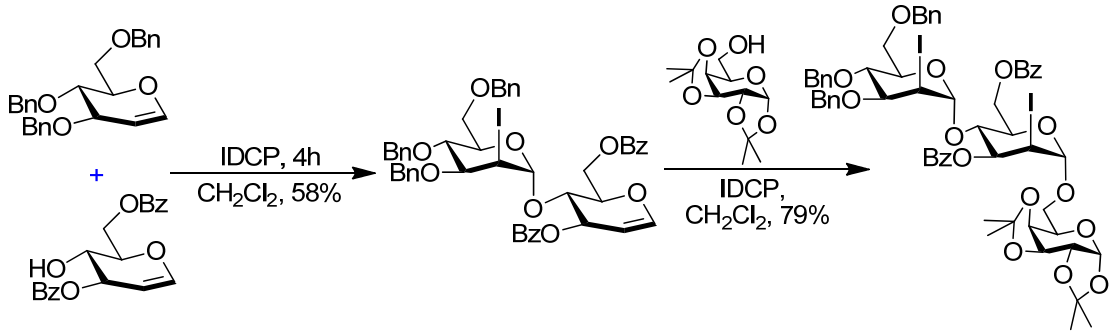
It has also been found that cyclic acetals reduce the reactivity of pentenyl glycosides[13] which is large enough to allow a chemoselective glycosidation of benzylated pentenyl glycosyl donor with cyclic acetal protected glycosyl acceptor to give a dimer as an anomeric mixture in a modest 52% yield (Scheme 3). Deactivation by cyclic acetals reflects presumably the torsial strain inflicted upon the developing cyclic oxocarbenium ion, the planarity of which is opposed by the cyclic protecting group.

Scheme: 3 Effect of cyclic acetal



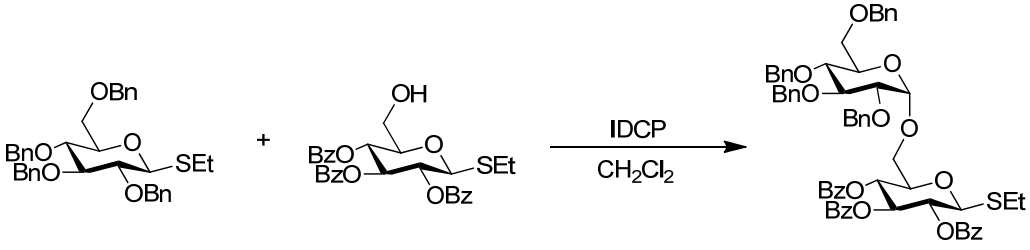
Thus, IDCP mediated chemoselective oxidative coupling of ether protected glycal with the partly acylated glycal gave stereoselectively disaccharide in a 58% yield. Which then again activated in presence of IDCP and glycosyl acceptor to give trisaccharide (79%)? Radical mediated dehalogenation of the trisaccharide afforded the 2-deoxy-glucoside containing trisaccharide (94%) as shown in scheme 4.

Scheme: 4



Chemoselective glycosidations have been developed for other types of glycosides. *Van Boom* et al. showed that similar to pentenyl glycosides, the reactivity of thioglycosides towards iodonium cations can be modulated by the choice of protecting groups[15] and it was found that a *C*-2 ether group activates and a *C*-2 ester deactivates the anomeric centre. Thus, iodonium cation mediated coupling of glycosyl donor with dispiroketal protected glycoside gave disaccharide mainly as the α-anomer with 84% yield (Scheme 5). In addition, it was established that a disarmed thioglycoside could be readily activated with the strong thiophilic promoter NIS/TfOH. It was also found that thioglycosides are more reactive than analogous pentenyl glycosides and give often better α-selectivity. In this case the chemoselective glycosydation approach was rationalised as follows: the electron density on the anomeric sulfur atom in a 2-*O*-acyl ethylthio glycoside is decreased, due to the inductive effect of the electron withdrawing ester functionality at *C*-2 and as a result, the nucleophilic complexation of the anomeric thio group with iodonium ions decreases and the thioglycoside can be regarded as disarmed with respect to an armed 2-*O*-alkyl thioglycoside.

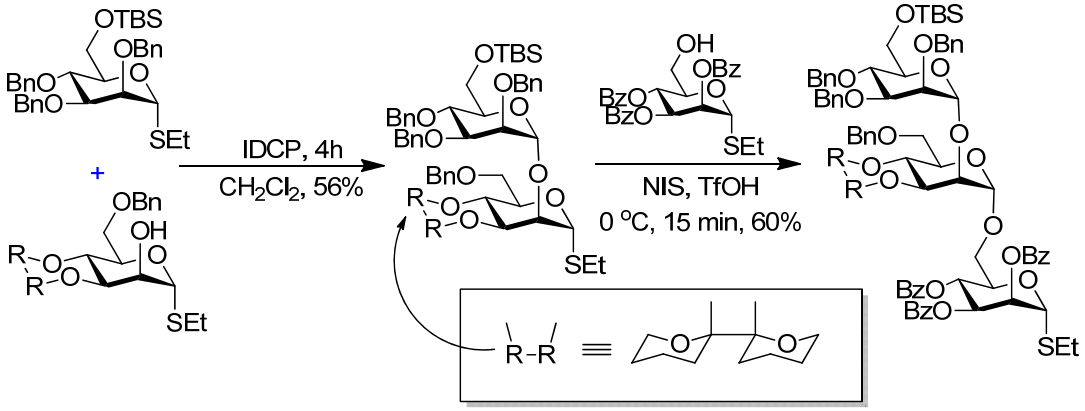
Scheme: 5 Armed disarmed effect in thioglycosides



Ley et al. proposed that the armed-disarmed glycosydation strategy could gain versatility by tuning the glycosyl donor leaving group ability. They described that a dispiroketal protecting group (R-R) has a marked effect on the reactivity of the anomeric centre[16] and it was found that a dispiroketal protected thioglycoside has a reactivity between an armed *C*-2 alkylated thioglycoside and a disarmed *C*-2 acyl

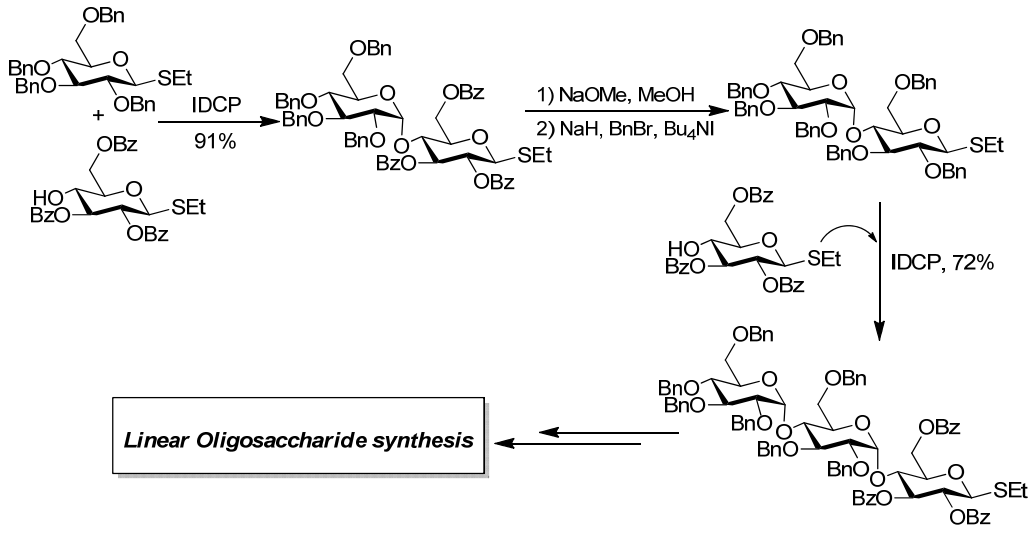
thioglycoside. Thus, iodonium dicollidine perchlorate mediated chemoselective glycosidation of glycosyl donor with dispiroketal protected acceptor gave disaccharide in an excellent yield. Further chemoselective glycosidation of the torsially deactivated donor with electronically deactivated acceptor in the presence of the more powerful activator NIS/TfOH gave a 63% yield of trisaccharide as one isomer. Similarly the three levels of anomeric reactivity were exploited in the preparation of a protected pentasaccharide unit common to the variant surface glycoprotein[17] of *Trypanosoma brucei.*

Scheme: 6



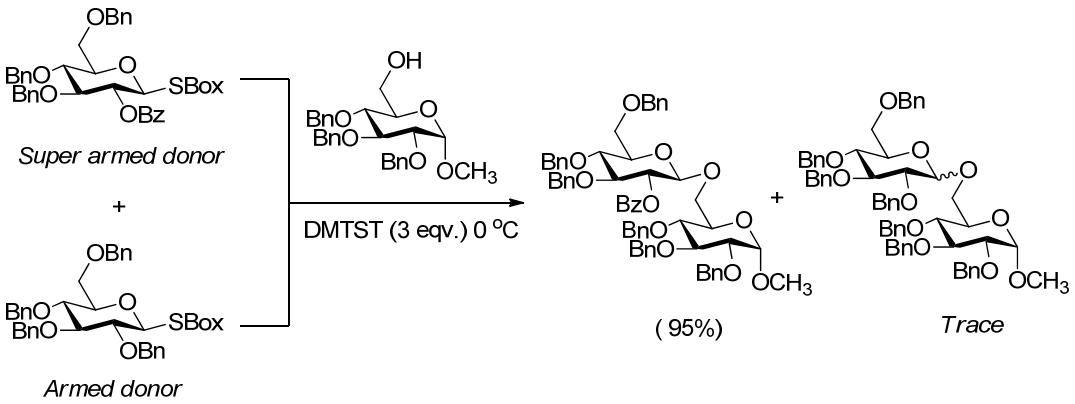
The dependence of reactivity on the substitution pattern also allows thioglycosides to be combined with oligosaccharides following the armed-disarmed concept, thus activation of an armed, benzyl protected , thioglycoside with iodonium ions, derived from iodonium dicollidine perchlorate (IDCP), allows the glycosidation of a partially protected disarm thioglycoside, giving only one disaccharide with the properties of the disarm glycosyl donor. This in turn can be converted to an armed glycoside by protecting group exchange and can subsequently be submitted to the next, analogous glycosidation step with a disarmed acceptor, yielding a disarmed trisaccharide. Consequently, this sequence has an iterative character which leads, in theory, to infinite growth of linear oligosaccharides.[18]

Scheme: 7 Thioglycosides for linear oligosaccharide synthesis



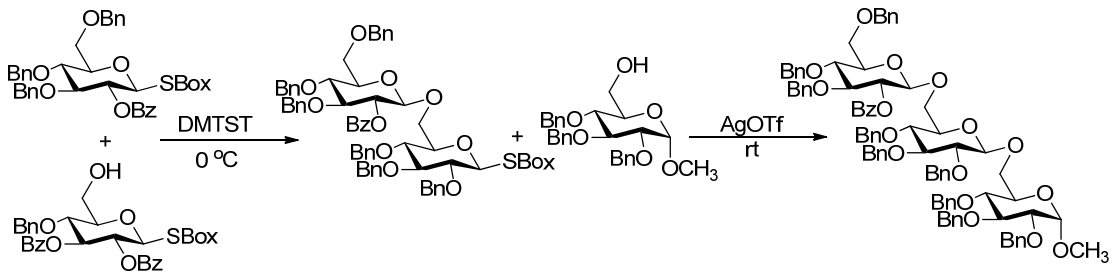
The concept has been extended to superarmed glycosyl donor by *Michel Bols* and his collaborators.[19] Where they have realized that hydroxyl functional groups of carbohydrates are less electron withdrawing toward the anomeric center when they are axial than equatorial, which means that glycosyl donor conformers with more axial oxy functions are more reactive, which *Bols* called superarmed. They showed that a superarmed donor can be coupled to an armed glycosyl donor/acceptor,[20] whereas, in a progressive research for chemoselective glycosidation, same concept was utilised by *Demchenko* et al. by strategic placement of common protecting groups to make a "super-armed" glycosyl donors.[21] Conceptualized from studies on the *O*-2/*O*-5 cooperative Effect,[22] it was determined that *S*-benzoxazolyl (SBox) glycosides possessing both a participating moiety at *C*-2 (benzoyl) and remote benzyl substituents that electronically arm the lone pair at *O*-5 are exceptionally reactive for superarming glycosyl donors. These easily accessible super armed glycosyl donors offer an entirely 1,2-*trans* stereoselective glycosidation. Consequently, the novelty of having both an armed and a 1,2-*trans* directing glycosyl donor can make this approach a very useful concept in many practical applications.

Scheme: 8 concept of superarming for competitive glycosidation



In extension of the armed-disarmed concept, utilizing the fact that the glycosyl donor reactivity can be graded by changing the substitution pattern of the donor molecule, a collection of glycosyl donors with gradual donor activity may be composed and used in one pot oligosaccharide synthesis as follows.[22]

Scheme: 9 Chemoselective sequential synthesis of trisaccharide in one pot

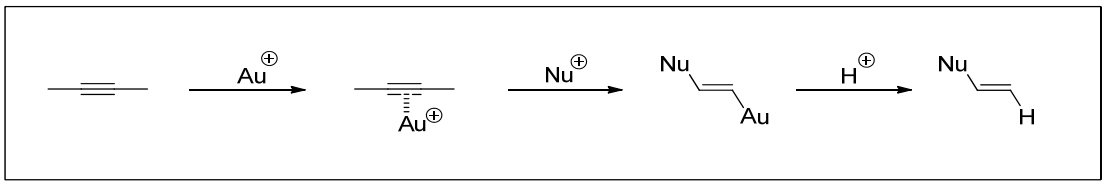


Recently armed disarmed approach with differential glycosyl donor activity has been elaborated in a computer assisted planning of oligosaccharide synthesis. This concept is

based on the preliminary assessment of the reactivity for a great number of protected or partially protected thioglycoside donors. During this program a database has been created for the reactivity of thioglycosides as glycosyl donor, based on structural effects of different monosaccharide cores and different protecting group on each glycosyl donor; which then correlated with chemical shift of the anomeric proton by ^{1}H NMR to generate a computer based program for oligosaccharide synthesis. Later the same program has been successfully demonstrated for rapid one pot assembly of various linear and branched oligosaccharide structures.[23]

The field of gold catalysis has gained significant attention during last two decades. From once being considered as inert metal, gold has now became the catalyst of choice for many organic transformations.[24] Co-ordination of Au(+1) or Au(+3) to the triple bond of alkynes renders them electrophilically activated and hence susceptible to nucleophilic attack by a plethora of nucleophiles. The alkynes are strong σ-donor and weak π-acceptor toward the gold species, hence specifically binds to gold which enhances the selectivity of gold catalysts over the other known transition metal catalysts (figure 5). Significantly, Gold-catalyzed reactions proceed without precautions to air, and hence oxygen, water, and alcohols are often well-tolerated, with gold catalysts in sharp contrast to most air- and moisture-sensitive Lewis acid or transition metal-catalyzed transformations. In addition, gold catalysts are not as oxophilic as most Lewis acids. Importantly, carbon-gold bonds are labile toward protodeauration, but not susceptible to β-hydride elimination, which frequently occurs in other transition metal-catalyzed reactions, thereby increasing the product selectivity.[25]

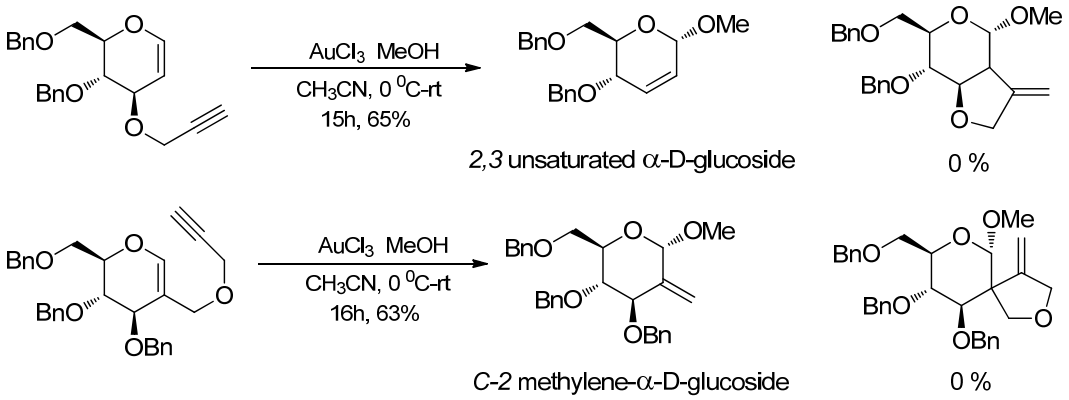
Figure: 5



Differential behavior of propargyloxy moiety was observed in our group while performing diversity oriented synthesis on carbohydrate templates to obtain novel molecular architecture.[26] To confirm this probe, 4,6-di-*O*-benzyl-3-*O*-propargyl glucal was treated with methanol and 3 mol% $AuCl_3$ in acetonitrile at room temperature. This reaction underwent a transformation to furnish 2,3 unsaturated-α-D-glucoside with 38% yield. Later to enhance the yield, reaction was carried out in presence of 5 mol% $AuCl_3$ under argon atmosphere at room temperature for 15 h, which improved yield to 67% (scheme 10). Notably during the whole process bicyclic product was not observed. Based on experimental output it was considered that reaction was initiated through co-ordination of gold salt with alkyne, but unable to trap the Au-alkyne complex via an alkoxycyclization, rather the propargyl moiety behaves like a leaving group thereby yielding a Ferrier-like reaction product.[27]

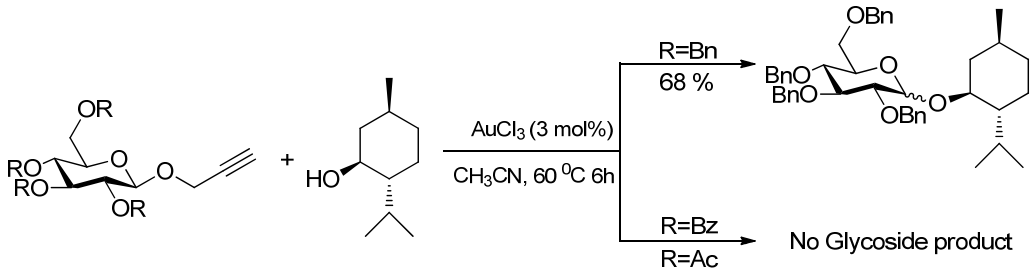
In continuation of aforementioned results, the utility of alkynophilic Au (+3) catalyst was studied for the synthesis of 2-deoxy-*C*-2-methylene glycosides using *C*-2-propargyloxy methyl glucal, which contain an enyne system very similar to 4,6-di-*O*-benzyl-3-*O*-propargyl glucal. Accordingly $AuCl_3$ mediated reaction was performed with 3,4,6-tri-*O*-benzyl-*C*-2-propargyloxy methyl glucal, as a novel substrate for Au-mediated Ferrier like reaction and methanol as glycosyl acceptor, in presence of acetonitrile at 0 ^{0}C to room temperature to get *C*-2 methylene-α-D-glucoside in 63% yield (scheme 10) and supported further, the differential behavior of the propargyloxy moiety in the presence of gold.[28]

Scheme: 10



The above observations showed that propargyloxy group becomes a leaving group under the influence of catalytic amount of Au(+3) salts. The efficiency of propargyloxy moiety as a leaving group for glycosidation reaction was evident when per-*O*-benzylated propargyl glucoside was treated with menthol in presence of 3 mol% $AuCl_3$ in acetonitrile at 70 ^{0}C, for 6h, to get an anticipated glucoside product as α,β mixture. Replacement of menthol by several aglycons resulted into corresponding glycosides with good yields, thereby a novel transglycosidation method using propargyloxy group as stable glycosyl donor in presence of catalytic amount of gold was discovered.[29] In further experiments, a solution of either per-*O*-acylated propargyl glucoside or per-*O*-benzoylated propargyl glucoside with menthol in presence of 3 mol% $AuCl_3$ in acetonitrile did not furnish transglycosidation at all. Even the increased reaction temperature or longer period for reaction failed to produce transglucoside. These observations suggested that propargyl glycosyl donors could become "*armed*" or "*disarmed*" depending on the type of substitution present at C-2 position.

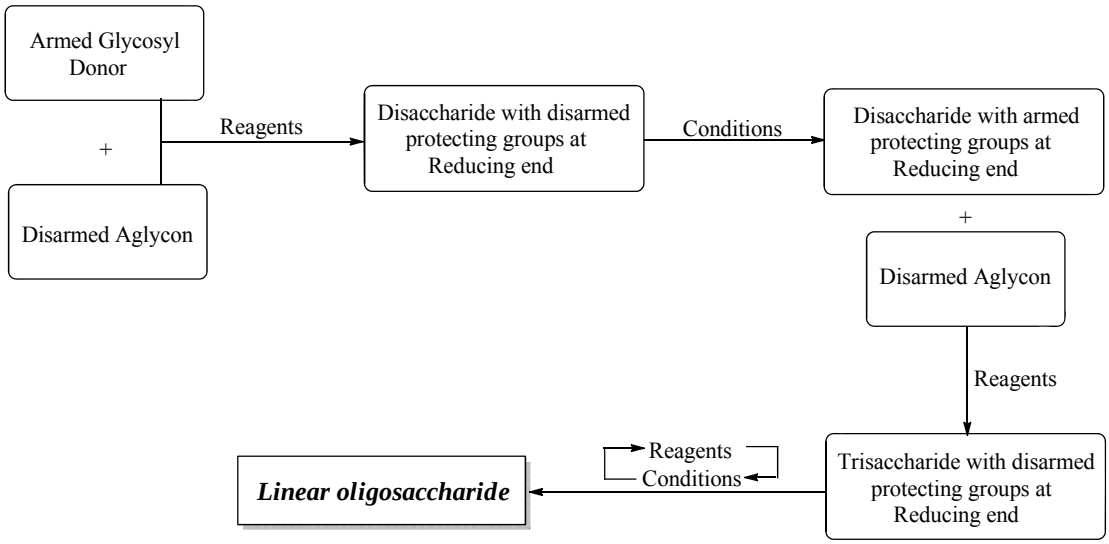
Scheme: 11



An armed-disarmed concept is an attractive strategy for synthesis of several linear as well as branched oligosaccharides. For example the partial synthesis of 28-mer oligosaccharide core of *Mycobacterial lipoarabinomannan* (LAM) can be achieved using this strategy in combination with other methods. A detail introduction for armed disarmed concept has been already covered earlier in this chapter, moreover propargyl glycosyl donors have shown similar effect under the influence of catalytic amount of gold (III), after the replacement of protecting groups, motivated us to utilize this concept for synthesizing some biologically significant oligosaccharides. A general

scheme for building oligosaccharides with an armed disarmed concept using propargyl glycosides would be as follows.

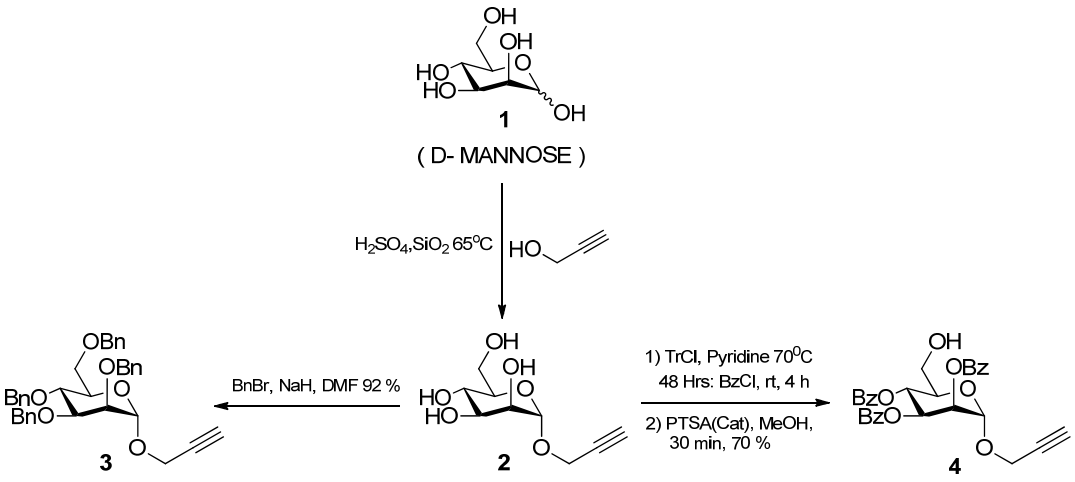
Scheme: 12 General armed-disarmed strategy for oligosaccharide synthesis.



In this context, initial set of experiments were planned with propargyl 2,3,4,6-tetra-*O*-benzyl α-D-mannopyranoside (**3**) as the armed glycosyl donor and the propargyl 2,3,4-tri-*O*-benzoyl α-D-mannopyranoside (**4**) as the disarmed aglycon, using D-mannose (**1**) as the starting material. In mannose the hydroxyl group on *C*-2, is important for guiding the glycoside synthesis, which positioned axially in contrast to the situation in glucose and galactose derivatives and can form only α–mannoside with or without neighboring group active substituent at *C*-2. The neighboring group participation with an ester group present at *C*-2 position prevents the attack of nucleophile from *β*–phase by forming an acetoxonium intermediate, where the opening of this acetoxonium ring by a nucliophile at *C*-1 is possible through *α*–phase only, and forms α-D-mannopyranoside. Even with the non participating groups at *C*-2, formation of α-mannoside is still a preferred reaction, as presence of axial hydroxyl group weakens the anomeric effect and allows to form stable α–mannoside.[30] Moreover the presence of axial substituent improves the reactivity of glycosyl donor, thus reaction with mannosyl donor has a practical advantage over glucose where it forms only α-isomer instead of α–β mixture, which removes difficulties from identification, characterization, and isolation of transglycosides.

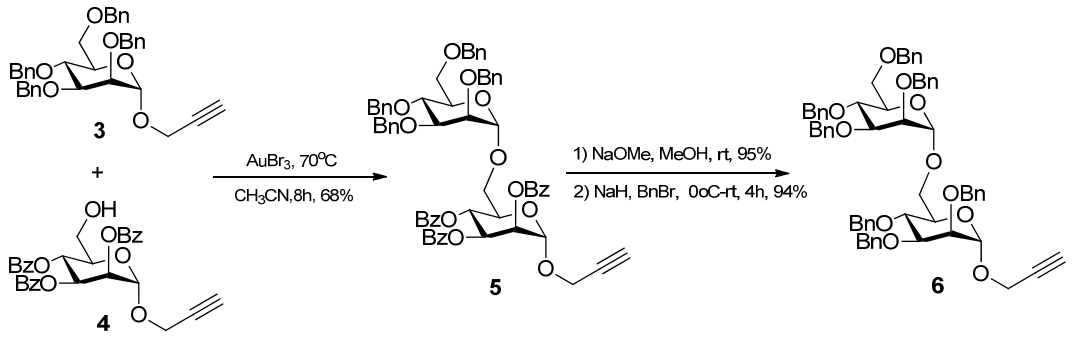
Initially anomeric hydroxyl group of mannose was protected using propargyl alcohol and H_2SO_4-silica gel catalyst[31] which on treatment with BnBr/NaH/TBAI in DMF, gave us armed glycosyl donor propargyl 2,3,4,6-tetra-*O*-benzyl α-D-mannopyranoside (**3**). Similarly propargyl mannoside (**2**) was used to get disarmed glycosyl acceptor by treatment of trityl chloride in pyridine for 48 hours followed by addition of benzoyl chloride to get 6-*O*-trityl-2,3,4-tri-*O*-benzoyl α-D-mannopyranoside, which upon subsequent trityl deprotection by adding catalytic amount of PTSA in methanol for 2h, gave us 6-hydroxyl-2,3,4-tri-*O*-benzoyl α-D-mannopyranoside (**4**).

Scheme: 13



Synthesis of required building blocks encouraged to investigate armed-disarmed strategy with propargyl glycosides under gold catalysis condition. Accordingly, the armed glycosyl donor **3** was allowed to react with aglycone **4** in the presence of $AuBr_3$ in CH_3CN at 70 ^oC for 8h and obtained the anticipated disaccharide **5** in 68% yield. It is important to mention that the replacement of gold salt from $AuCl_3$ to $AuBr_3$ for transglycosidation reaction is noteworthy as, $AuCl_3$ is highly hygroscopic in nature compare to $AuBr_3$ and starts decaying on elevated temperatures. Later the disarmed disaccharide was converted into an armed disaccharide **6** in two steps involving Zemplén debenzoylation (NaOMe/MeOH/rt) followed by benzylation using NaH and benzyl bromide in DMF in 94% yield (scheme 14).

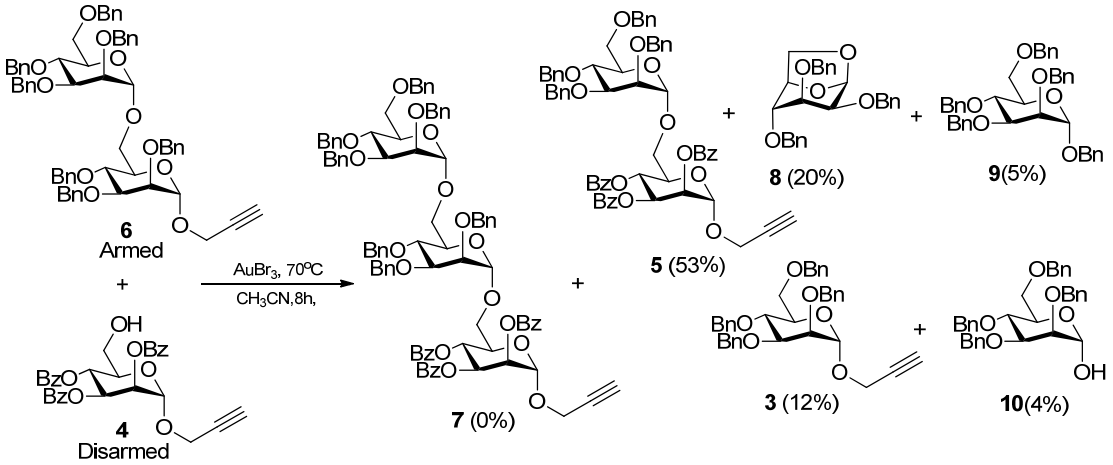
Scheme: 14



In continuation, the armed disaccharide **6** was allowed to react with disarmed aglycon **4** in anticipation of a trisaccharide **7**, surprisingly resulted in the isolation of two compounds. Purification by conventional silica gel column chromatography enabled us to characterize the major component not as the trisaccharide **7** but as disaccharide **5** (scheme 15). For instance, only two anomeric protons were noticed at δ 5.26 (1H, d, *J* 1.8Hz), 5.68(1H, dd, *J* 1.8, 2.9Hz) in the ^1H NMR spectrum instead of three if it were trisaccharide (**7**). The ^{13}C NMR spectrum revealed that there are two mannose residues with 1,2-*trans* configuration as their anomeric carbons were noticed at δ 96.2 and 98.2 ppm and the molecular weight was found to be 1076.622 [M^++23 for Na]. These

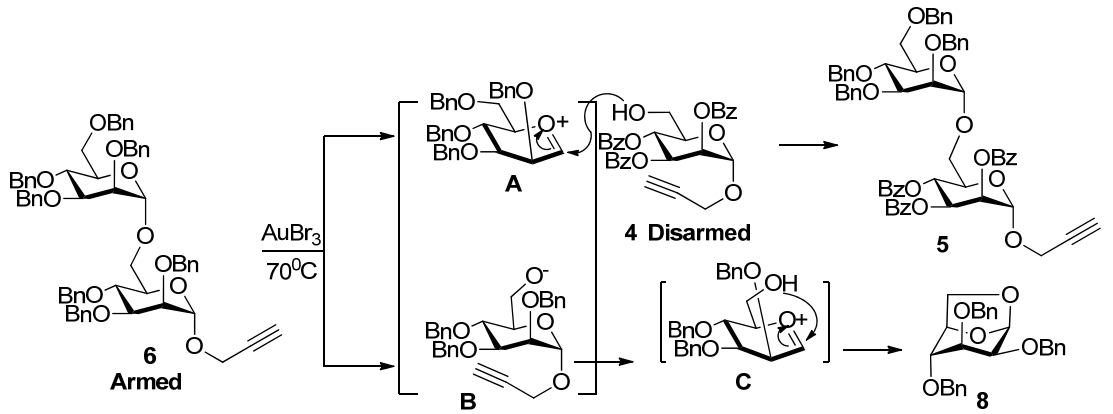
observations led us to assign the structure of the major component (53%) to be propargyl 2,3,4-tri-*O*-benzoyl-6-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-α-D-manno pyranoside **5**. The minor component was identified to be 1,6-anhydro derivative **8.** Further purification enabled us to isolate three more minor products from the reaction (scheme 15). Formation of compound **9** (5%) was attributed to the hydrolysis of benzyl ether at high temperature whereas compound **10** (4%) has formed may be due to the presence of moisture. Notably formation of compound **3** (12%) was quite surprising, as we have hypothesized previously, upon activation with gold salts the propargyloxy group goes through some unidentified intermediates to get converted into cyclopropanone and therefore becomes traceless.[29] However formation of compound **9** confirmed the extrusion of propargyl alcohol in the reaction.

Scheme: 15



The formation of disaccharide **5** and the 1,6-anhydro sugar formation can be rationalized by a double activation of the armed glycosyl donor **6** in the presence of $AuBr_3$ (Fig. 6). Initially, oxophilic $AuBr_3$ cleaves the interglycosidic bond leaving the intermediate oxocarbenium ion (**A**) with the extrusion of propargyl mannoside B. Intermediate (**A)** was then attacked by the disarmed aglycon **4** resulting in disaccharide **5** whereas the ejected product **B** led to the second oxocarbenium ion **C** which is trapped intramolecularly by the 6-OH group to give 1,6-anhydro derivative **8**.

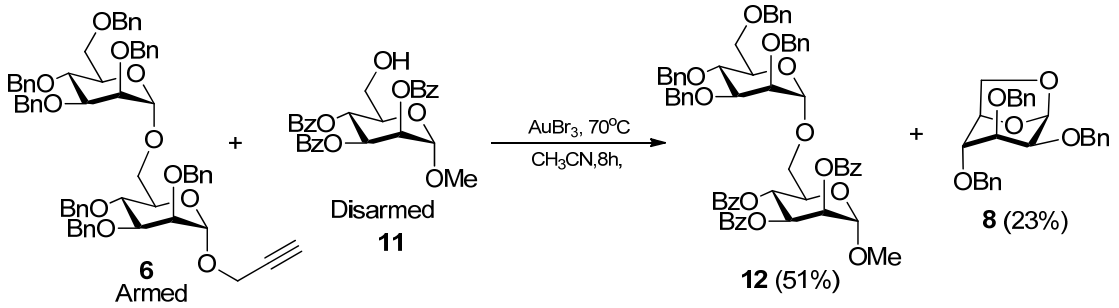
Figure: 6



The 2D HSQC (Heteronuclear Single-Quantum Correlation) experiment enables to obtain a correlation between directly-bonded hydrogen to the anomeric carbon. The HSQC spectrum correlates chemical shifts of anomeric carbon and hydrogen via the direct heteronuclear coupling $^{1}J_{C\text{-}H}$. These values of coupling constants are often useful in determination of glycosidic linkages.[32] In case of compound **5** we have observed two anomeric carbons at δ 96.2 and 98.2 ppm which when correlated with anomeric protons through HSQC experiment gave us two values as 175.5 Hz and 170.9 Hz, which again confirmed the presence of only two saccharide units in compound **5** with α–linkages.

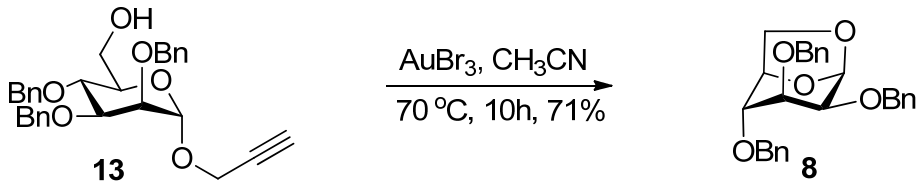
Similar results were obtained after replacing the aglycon **4** by methyl 2,3,4-tri-*O*-benzoyl α-D-mannopyranoside (**11**), which upon reaction with armed disaccharide **6** in the presence of $AuBr_3$ in CH_3CN at 70 ^{o}C for 8h, enabled us to isolate two major products from reaction mixture which were characterized as methyl 2,3,4-tri-*O*-benzoyl-6-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-α-D-manno pyranoside (**12**) and anhydro sugar (**8**) with slight variations in yields.

Scheme: 16



Observation of 1,6-anhydro sugars from the 6-OH propargyl glycosides needs a special mention as they are reported to be valuable synthons with significant biological activities. Most of the available methods for synthesizing the 1,6-anhydro compounds are rather forcing and require stoichiometric quantities of reagents which warrant further development of novel procedures by catalytic means. Aforementioned results enticed to probe the prospect of propargyl glycosides as possible precursors for the synthesis of 1,6-anhydro sugars using catalytic $AuBr_3$.[33] For example when propargyl 2,3,4-tri-*O*-benzyl α-D-mannopyranoside (**13**) was reacted with 5 mol% of $AuBr_3$ in CH_3CN at 70 ^{o}C, furnished with the 1,6-anhydro sugar (**8**) in 71 % yield.

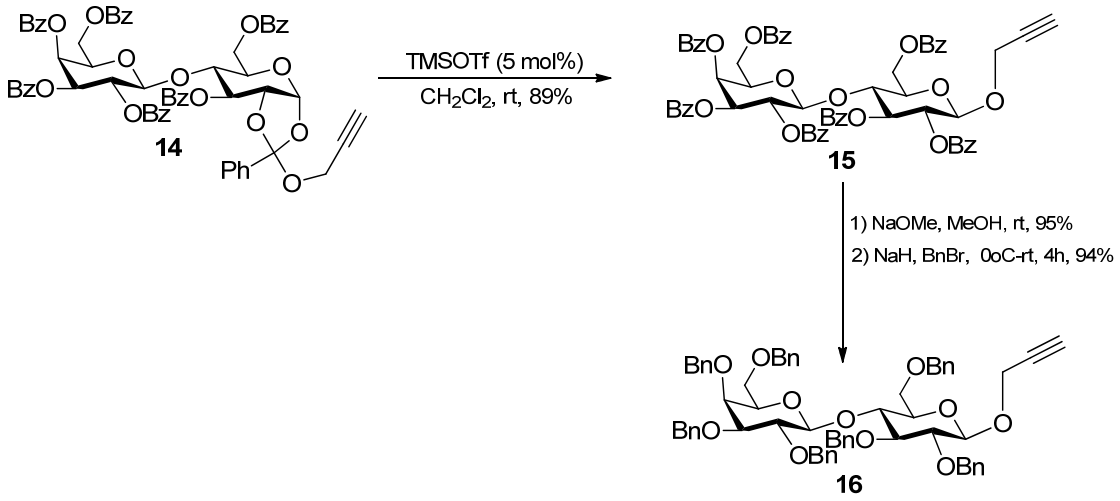
Scheme: 17



Stability of interglycosidic linkages between *C*-6 and *C*-4 vary significantly. Thus per-*O*-benzylated lactosyl donor might survive gold catalysis conditions for armed-disarmed

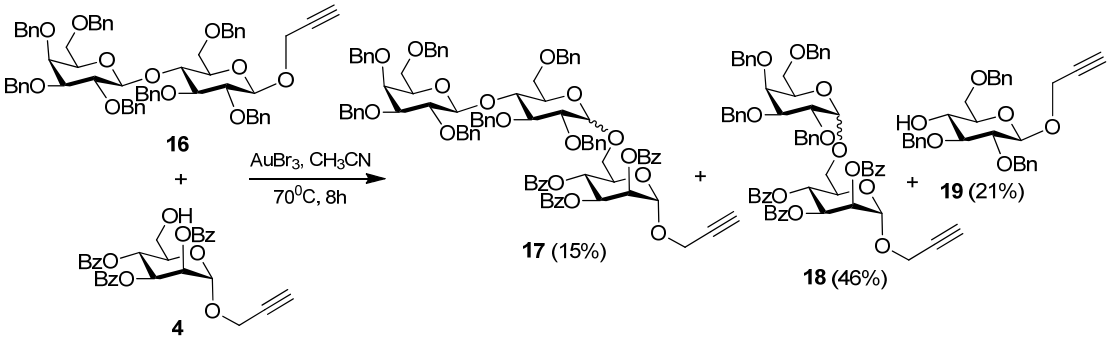
studies. Accordingly we have prepared per-*O*-benzylated lactosyl donor (**16**) starting from per-*O*-benzoylated propargyl lactose orthoester (**14**) in two steps as shown in scheme 18.

Scheme: 18



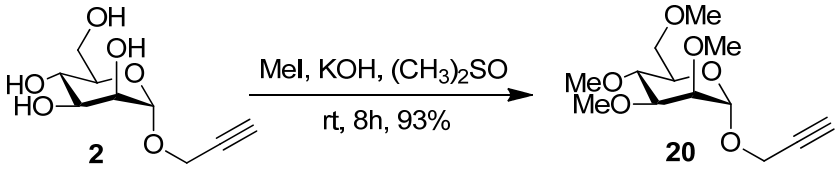
The newly prepared lactosyl donor (**16)** was allowed to react with disarmed aglycon (**4)**, with 5 mol% of $AuBr_3$ in CH_3CN at 70 ^oC for 8h, where for the first time; we were able to isolate α–β mixture of anticipated trisaccharide as minor product (**17**), along with two major products disaccharide (**18**) and monosaccharide (**19**) (scheme 19). Formation of compound **19** can be rationalized as unfavorable spatial arrangement which did not allows to further convert into anhydro sugar. Formation of trisaccharide (**17**) was confirmed by ^{13}C-NMR spectroscopy where three peaks were observed at δ 91.9 ppm, 96.1 ppm, and 97.3 ppm. Similarly the molecular weight of this compound was found to be 1507.5823, which was in perfect agreement with theoretical value 1507.5818 (M^+ 23 for Na).

Scheme: 19



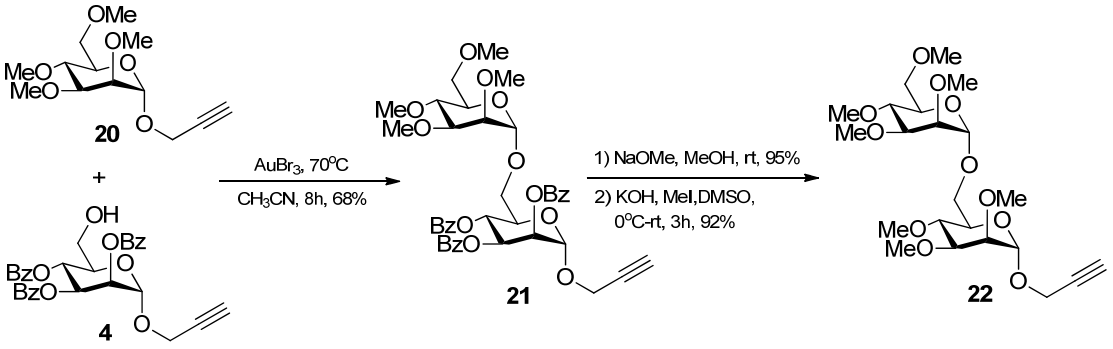
Formation of trisaccharide (**17**) encouraged us to understand, that the spatial arrangement of substituents, nature of interglycosidic linkages and stereochemistry along with electronic factors play an important role during transglycosidation reaction. To check our hypothesis, we took propargyl mannoside (**2**) and treated it with MeI in presence of potassium hydroxide and dimethyl sulphoxide to get propargyl 2,3,4,6-tetra-*O*-methyl α-D-mannopyranoside (**20**)

Scheme: 20



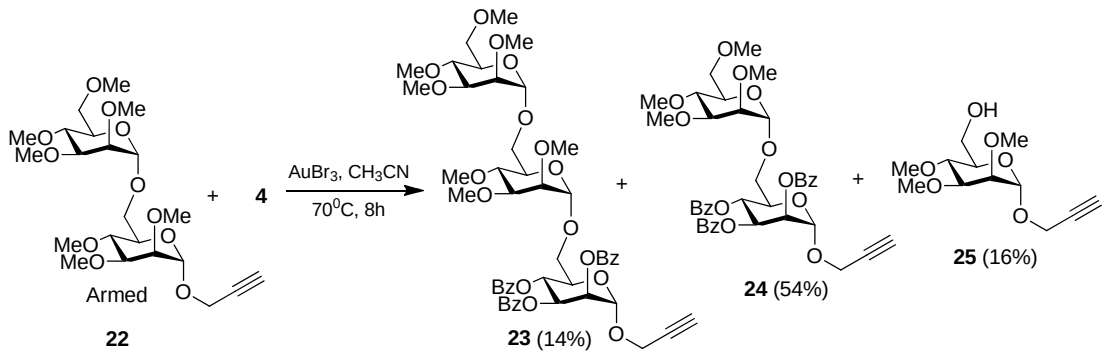
Further in order to make the per *O*-methylated disaccharide (**22**), gold catalyzed reaction of propargyl 2,3,4,6-tetra-*O*-methyl α-D-mannopyranoside (**20**) with aglycon (**4**), gave us the disaccharide (**21**) which on further debenzoylation followed by Wurtz's methylation reaction yielded per-*O*-methylated disaccharide (**22**) (scheme 21). Formation of requisite disaccharide was confirmed by ^{1}H and ^{13}C NMR Spectroscopy where all the resonances were in complete agreement with theoretical values. Further the molecular weight of compound **22** was found to be 501.2318 [M^{+}+23 for Na].

Scheme: 21



When this per-*O*-methyl disaccharide (**22**) was allowed to react with aglycon (**4**) in presence of 5 mol% of $AuBr_3$ in CH_3CN at 70 ^{o}C, gave us trisaccharide (**23**), disaccharide (**24**), and the ejected monosaccharide (**25**) in 14%, 54%, and 16%, respectively (scheme 22). Configuration of glycosidic linkages for trisaccharide **23** and were further confirmed with $^{1}J_{C\text{-}H}$ HSQC experiment. Where the three values 170.5 Hz, 169.7 Hz and 174.2 Hz authenticated all the linkages with α-configuration.

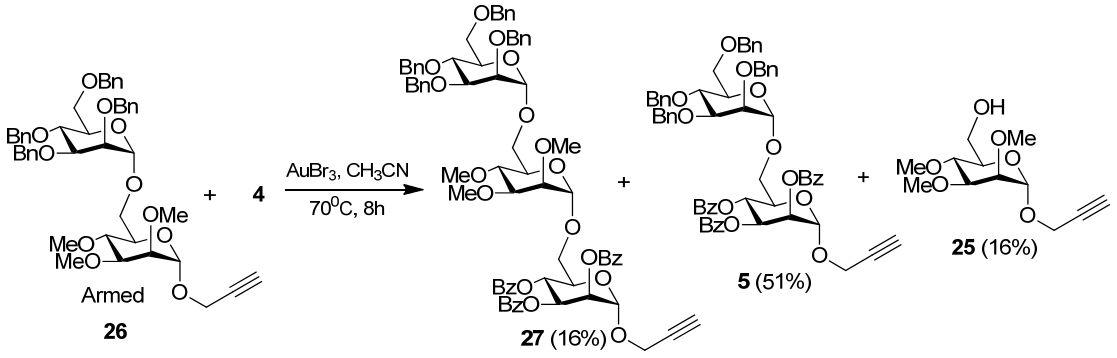
Scheme: 22



Similar observations were noticed when the benzoyl groups of disaccharide (**5**) were replaced by methyl groups via a two-step procedure gave us the armed disaccharide (**26**)

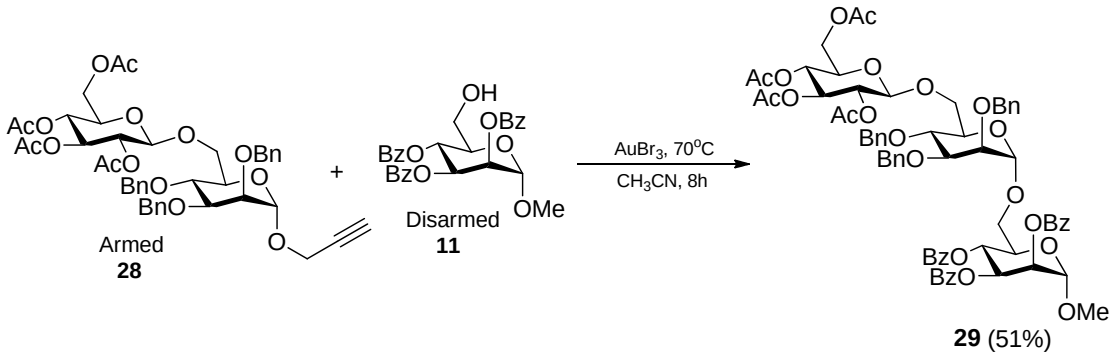
with less-directing methyl groups on the sugar at the reducing end (scheme 23). Armed disaccharide (**26**) was then reacted with aglycon (**4**), in presence of 5 mol% of $AuBr_3$ in CH_3CN at 70 ^oC for 8h, to give the anticipated trisaccharide (**27**) with 16% yield, in the midst of disaccharide (**5**), and propargyl 2,3,4-tri-*O*-methyl mannoside in (**25**) as major products of reaction with, 51%, and 16%, yields respectively. The above mentioned results led us to understand that the propargyl glycosides are highly dependent on the electronic effect of the protecting groups (scheme 23).

Scheme: 23



The ongoing study, confirmed that during gold mediated transglycosidation reactions, both alkyne and interglycosidic oxygen are activating and cleaving-off interglycosidic bond.[34] It was also observed that reaction outcomes are highly dependent on the nature of interglycosidic linkage in association with sterics and electronic factors. In addition to this, similar study from our group confirmed, the replacement of protecting group makes remarkable effect on cleavage of interglycosidic bond; as when saccharide unit is protected with ester groups, gold salt shows only alkynophilic behavior due to the less electron density on interglycosidic oxygen and forms desired product[35] as shown in scheme 24. However presence of armed participating group as substituent on saccharide unit enhances the electron density on interglycosidic oxygen which then allows gold salt to behave as oxophilic. The double activation was further considered as factor responsible for interglycosidic bond cleavage.

Scheme: 24

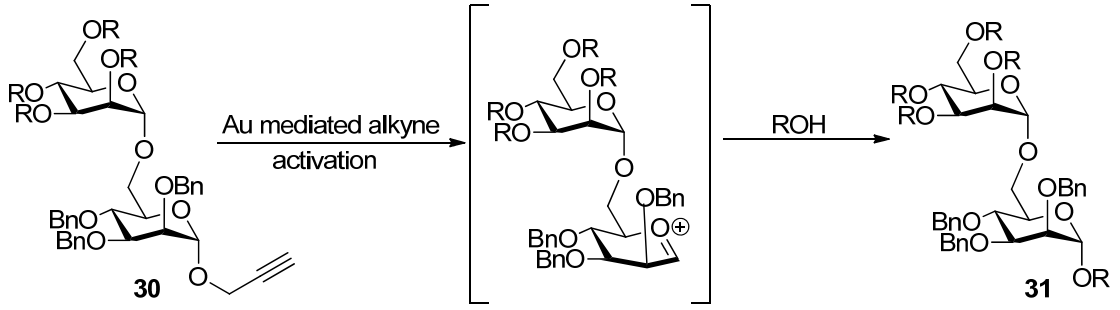


From the above observations, it was confirmed that the outcome of gold mediated glycosidation can be controlled by protecting group modification, where a desired modification can prevent the interglycosidic bond cleavage to get required product. But

such modifications have restrictions, which permits to use only ethereal protecting groups, as armed disarmed concept prohibit to use ester protecting groups in synthesizing glycosyl donor. In term of chemistry, etheral protecting groups are known for electron donation, which then stabilizes the formation of oxocarbenium intermediate, and hence termed as armed protecting groups, in contrast to ester protecting groups which are electron withdrawing and does not stabilize oxocarbenium intermediate and hence termed as disarmed protecting groups.

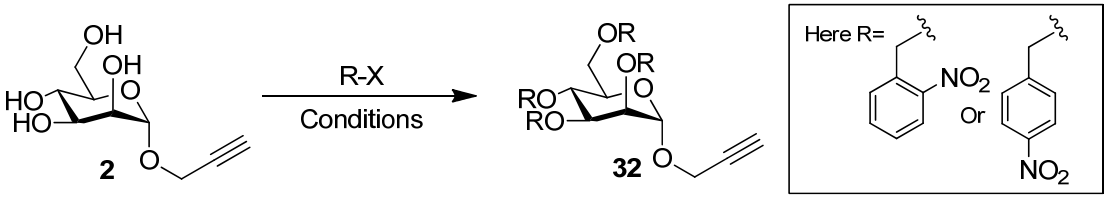
It might be possible to circumvent this problem by using substituted benzyl halides for protection of glycosyl donor. For example, compare to simple benzyl ethers, nitro substituted benzyl groups are more electron withdrawing, In this context, we thought to prepare nitro substituted per-*O*-benzylated glycosyl donor by assuming the fact, nitro substituted benzyl ethers might be helpful during the course of gold mediated transglycosidation by preventing the activation interglycosidic oxygen which could further rule out the possibility of interglycosidic bond cleavage. Such circumstances are highly beneficial for gold catalyzed glycosidation as in such cases only propargyloxy group will be activated to get desired transglycoside (scheme 25).

Scheme: 25



Accordingly propargyl α-D-mannopyranoside (**2**) and thought to prepare per-*O*-benzylated propargyl mannoside (**32**) using either *o*-nitro benzyl bromide or *p*-nitro benzyl bromide, as protecting group but unfortunately our all the attempts were failed to get the required product.

Scheme: 26

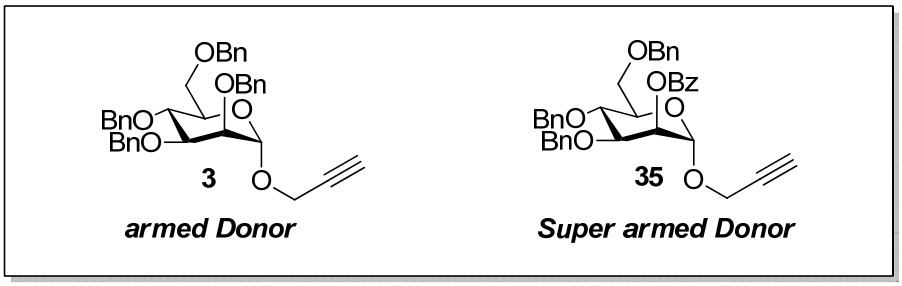


Here we have used either NaH or Ag_2O mediated *O*-alkylation method in different solvent mediums, but none of the reaction condition was successful in preparation of

required product. In all the cases, the progresses of reactions were slow, which eventually ended with multiple products without the full consumption of reactant.

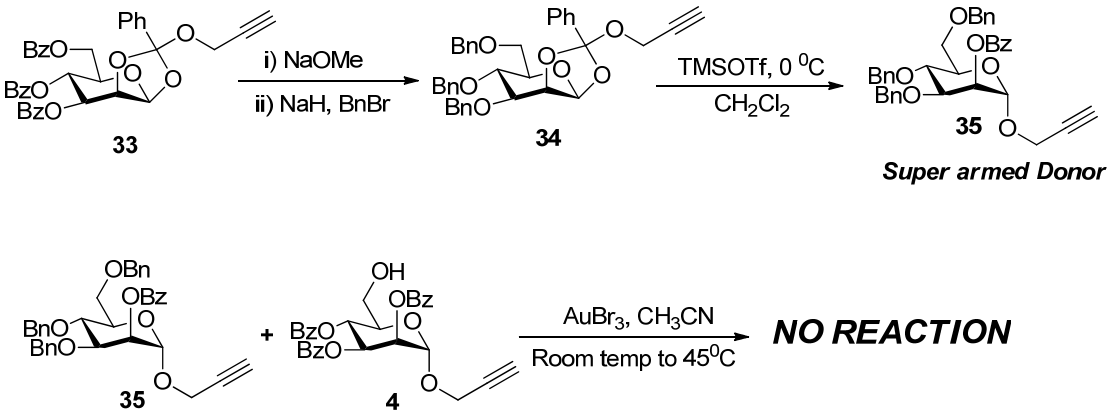
From the failures of above experimental results we then changed our strategy and thought to replace *C*-2 protecting group to enhance the reactivity of glycosyl donor by substituting ester protecting group on *C*-2 position of armed glycosyl donor. Inspired by several literature reports,[22] and conceptualized from studies on the *O*-2/*O*-5 cooperative effect, this strategic placement of common protecting groups are thought to improve the reactivity of glycosyl donor and make it "super-arming".

Figure: 7



Accordingly, we prepared 2-*O*-benzoyl-3,4,6-tetra-*O*-benzyl α-D-mannopyranoside (**35**) as super armed glycosyl donor starting from 3,4,6-tri-*O*-benzoyl mannose propargyl orthoester (**33**) by assuming the newly formed glycosyl donor can be activated at moderate temperature. Further 2-*O*-benzoyl-3,4,6-tetra-*O*-benzyl α-D-mannopyranoside (**35**) was treated with 6-hydroxyl-2,3,4-tri-*O*-benzoyl α-D-mannopyranoside (**4**) in presence of 5 mol% $AuBr_3$ at 0 ^{0}C for 6h, which did not shown any advance, afterward the enhancement of temperature up to 45 ^{0}C, also did not favor the reaction.

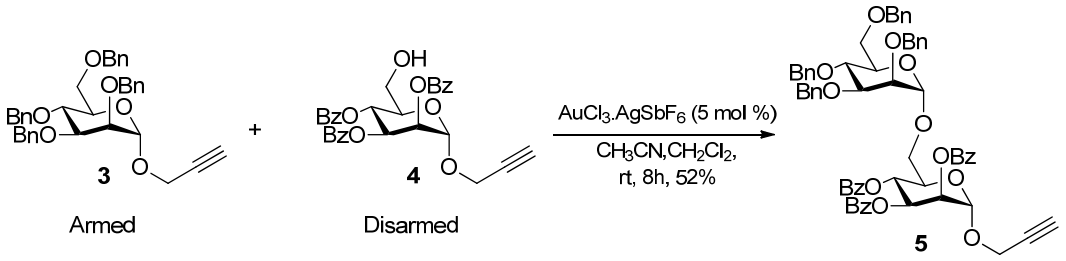
Scheme: 27



The primary suspect for unusual cleavage of interglycosidic bond was the high temperature of reaction; thus a low temperature version is highly desirable. Room temperature activation of propargyl group could be achieved through modification of the glycosyl donor through several ways; the modification with protecting groups can enhance the reactivity of glycosyl donors. Unfortunately our attempts for improving the reactivity of glycosyl donor by modifying protecting group strategy were failed

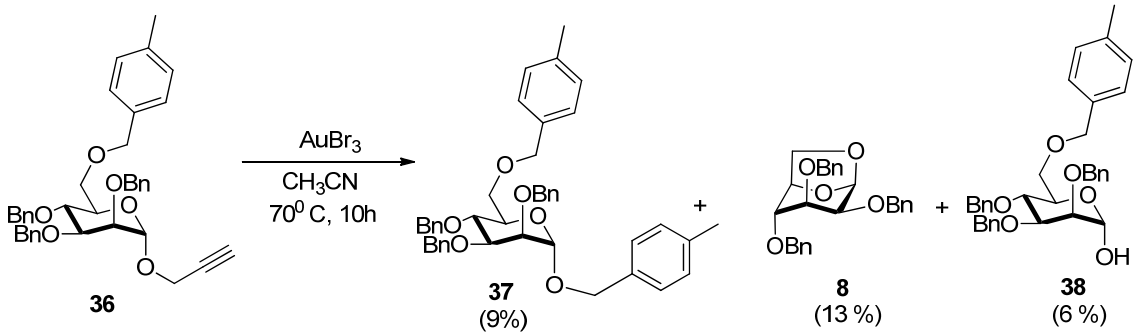
From the above observation, it was found that the modification of protecting group for improving the reactivity of glycosyl donor is difficult task. The other way of improving reactivity of propargyloxy glycosyl donor is the addition of co-catalyst in combination with gold.[36] Hence we employed combination of different silver salts as AgOTf, $AgBF_4$, $AgSbF_6$ with gold salts and found that combination of $AuCl_3$ and $AgSbF_6$ (5 mol% each) is sufficient to activate propargyl glycoside at room temperature (Scheme 28)). Although the yield of transglycosidation was only 52%, with the scope of improvement through other modifications.

Scheme: 28



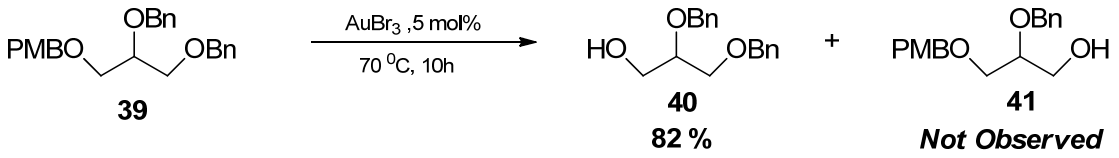
The former interpretations, of gold mediated transglycosidation reaction confirmed the elevated temperature of reaction is responsible for side reaction like primary benzyl deprotection, to authenticate our probe; we then prepared compound **36** and subjected to similar conditions ($AuBr_3$, 70 ^{0}C, and 8 hrs) where the formation of three compounds was observed. Formation of compound **8** is possible only after primary benzyl deprotection and compound **37** can be formed after the migration of benzyl group from 6-position to anomeric position. Compound **38** can form due to presence of traces of moisture. Formation of compound **8**, **37** and **38** was confirmed through LC-MS analysis where compound **8** has shown the mass 455.19 (M^+ +23 for Na), similarly Molecular weights for compound **37** and compound **38** were observed 681.34 (M^+ +23 for Na) and 577.24 (M^+ +23 for Na) respectively.

Scheme: 29



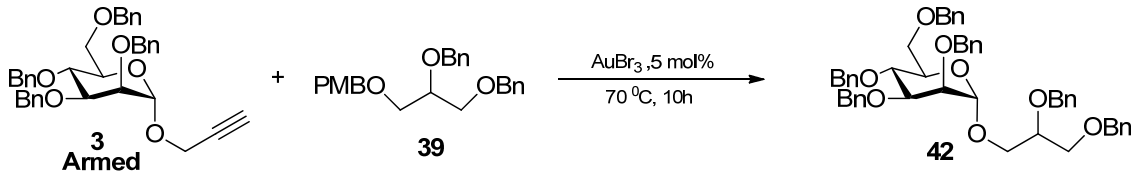
Later to check the efficiency of primary benzyl deprotection, compound **39** was prepared from acetonide protected glycerol and subjected to similar conditions ($AuBr_3$, 70 ^{0}C, and 8 hrs), where quantitave deprotection of PMB group was observed in presence of other benzyl groups, to get the compound **40** in 82% yield (Scheme 30), notably formation of compound **41** was not detected at all.

Scheme: 30



Similarly, the transglycosidation between compound **39** and armed mannosyl donor **3**, in presence of 5 mol% of $AuBr_3$ in CH_3CN at 70 ^oC for 8h, resulted in the formation of glycerol glycoside **42**. The formation of compound **42** is interesting as PMB ether got hydrolyzed and then participated in the transglycosidation reaction to afford compound **42** in one pot (Scheme 31).

Scheme: 31



In conclusion armed/disarmed effect of propargyl glycosides in presence of catalytic amount of $AuBr_3$ was studied. The cleavage of interglycosidic bond was observed. Moreover, the high temperature of reaction was found responsible for other side reactions like primary benzyl deprotection which then applied for PMB deprotection and one pot glycosidation.[37] significantly the extrusion of propargyl alcohol was observed and confirmed during transglycosidation process which inspired us to check the role of gold salt and mechanism involved in transglycosidation reaction. Importantly it was observed that addition of silver salt in gold mediated transglycosidation reaction can bring down the reaction temperature.

General experimental procedure for anomeric *O*-propargylation

In a simple reaction, D-mannose (1.80 gm, 1 equiv) was suspended in propargyl alcohol (2.9 mL, 5 equiv) and stirred at 65 ^{0}C. H_2SO_4–silica (0.5 gm) was added and stirring was continued until all the solids had dissolved (2.5 h). At this point, TLC (CH_2Cl_2–MeOH; 5:1) showed complete conversion of the starting D-mannose to a faster running component. After cooling to room temperature, the reaction mixture was transferred to a short silica gel column and the excess propargyl alcohol was eluted with CH_2Cl_2 (200 mL) followed by elution of the product glycoside with CH_2Cl_2–MeOH (15:1) to afford the desired propargyl mannoside in 75% yield.

General experimental procedure for *O*-benzylation

To a solution of propargyl mannoside (1 equiv) in anhydrous *N*,*N*-dimethylformamide (10 mL) at 0 ^{0}C was added sodium hydride (4.5 equiv) and stirred at room temperature for 30 min. The resulting dark brown solution was cooled to 0 ^{0}C and was added catalytic amount of *n*-$Bu_4N^+I^-$ (0.1 equiv) followed by dropwise addition of benzyl bromide (4.8 equiv) under nitrogen atmosphere, stirred at room temperature for 10 h. After completion of reaction (judged by TLC), excess of NaH was quenched by addition of 10 mL methanol. The reaction mixture was then diluted with 20 mL water and extracted with diethyl ether (3 x 25 mL), combined organic layers were dried over anhydrous sodium sulphate, concentrated *in vacuo* and the crude residue was purified by silica gel column chromatography to give corresponding per *O*-benzylated propargyl mannoside with 92% yield.

General experimental procedure for preparation of propargyl 2,3,4 tri-*O*-benzoyl α-D-mannopyranoside

To a solution of propargyl mannoside (1 equiv) in anhydrous pyridine (20 mL) at room temperature was added trityl chloride (1.2 equiv) and stirred at 70 ^{0}C for 48 h. Formation of desired product was confirmed by TLC. After protection of 6-hydroxyl group of propargyl mannoside, the reaction was allowed to cool at room temperature. Then to the same solution benzoyl chloride (3.6 equiv) was added in dropwise manner at 0 ^{0}C, after complete addition the reaction was stirred for 6h at room temperature. The completion of reaction was judged by TLC, the excess of pyridine was evaporated *in vacuo.* later, reaction mixture was diluted with 30 mL of water and extracted with ethyl acetate (3 x 25 mL), combined organic layers were dried over anhydrous sodium sulphate, concentrated *in vacuo* and the crude residue was purified by silica gel column chromatography to give desired product. In order to make 6-hydroxyl group free, the product was dissolved in 20 ml methanol followed by addition of PTSA (0.1 equiv), and kept on stirring for 2h, deprotection of trityl group was then confirmed by TLC, after which reaction mixture was evaporated *in vacuo* and purified through silica gel column chromatography to get anticipated propargyl 2,3,4 tri-*O*-benzoyl α-D-mannopyranoside in 70% yield.

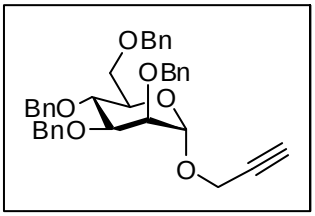
General experimental procedure for *O*-methylation

To a solution of propargyl mannoside (1 equiv) in anhydrous Dimethyl sulphoxide (10 mL) at 0 ^{0}C was added finely powdered Potassium hydroxide (5 equiv) and stirred at room temperature for 8 h, under nitrogen atmosphere. After completion of reaction (judged by TLC), the reaction mixture was then diluted with 20 mL water and extracted with diethyl ether (3 x 25 mL), the combined organic layers were dried over anhydrous sodium sulphate, concentrated *in vacuo* and the crude residue was purified by silica gel column chromatography to give corresponding per *O*-methylated propargyl mannoside in good yield.

General procedure for glycosylations using propargyl glycosides as glycosyl donor

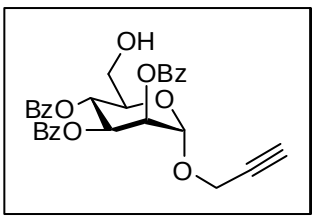
To a solution of glycosyl donor (1 equiv) and aglycone (1.2 equiv) in anhydrous acetonitrile (5 mL) was added a solution of 5 mol% of $AuBr_3$ in anhydrous acetonitrile (2 mL) under argon atmosphere at room temperature. The resulting mixture was heated to 70 ^{0}C and stirred till the completion of the reaction as judged by TLC analysis. The reaction mixture was concentrated *in vacuo* to obtain a crude residue which was purified by conventional silica gel column chromatography using ethyl acetate/petroleum ether as mobile phase.

Characterization data for compound **3**



$[\alpha]_D^{25}$ = +34.0 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.39 (t, 1H, *J* = 2.4Hz), 3.65-4.08 (m, 6H), 4.19 (d, 2H, *J* = 2.4Hz), 4.60 (ABq, 2H, *J* = 12.2Hz), 4.60 (s, 2H), 4.69 (ABq, 2H, *J* =10.6Hz) 4.74 (s, 2H,), 5.09 (d,1H, *J* = 1.7Hz), 7.08-7.41 (m, 20H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 54.1, 69.1, 72.0, 72.1, 72.6, 73.3, 74.3, 74.6, 74.7, 75.1, 78.1, 80.0, 96.4, 127.4-128.3, 138.1, 138.3, 138.4, 138.4 HRMS (MALDI-TOF): calcd. for $C_{37}H_{38}NaO_6$ [M^+ +Na]: 601.2566; Found: 601.2572.

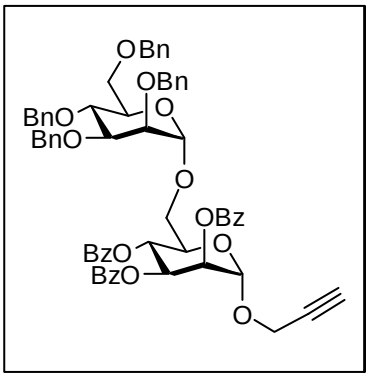
Characterization data for compound **4**



$[\alpha]_D^{25}$ = -88.3 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.66 (bs, 1H), 3.52 (d, 1H, *J* = 2.4Hz), 3.81 (m, 2H), 4.12 (dt, 1H, *J* = 3.0, 10.2Hz), 4.40 (d, 2H, , *J* = 2.4Hz), 5.32 (d, 1H, *J* = 1.8Hz), 5.71 (dd, 1H, *J* =1.8, 3.3Hz), 5.85 (t, 1H, *J* =10.2Hz), 6.00 (dd, 1H, *J* =3.3, 10.2Hz), 7.21-7.65 (m, 9H), 7.78-8.15 (m, 6H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.2, 61.2, 67.1, 69.5, 70.3, 71.4, 75.6, 78.1, 96.5, 128.2-129.9, 133.1, 133.5, 133.6, 165.3, 165.3, 166.3; HRMS (MALDI-TOF): calcd. for $C_{30}H_{26}NaO_9$ [M^+ +Na]: 553.1475; Found: 553.1468.

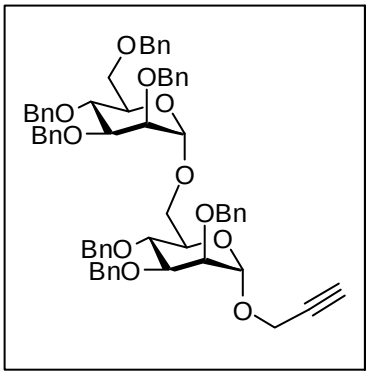
Characterization data for compound **5**

$[\alpha]_D^{25}$ = -23.3 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.50 (t, 1H, *J* = 2.4 Hz), 3.53–3.78 (m, 4H), 3.84 (dd, 1H, *J* = 3.3, 9.2 Hz), 3.88–4.05 (m, 2H), 4.22 (m,



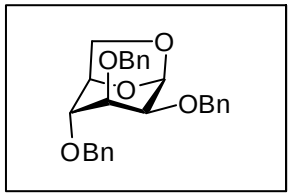
1H), 4.31 (d, 2H, *J* = 2.4 Hz), 4.37 (d, 2H, *J* = 4.5 Hz), 4.43 (s, 2H) 4.49 (ABq, 2H, *J* = 12.3 Hz), 4.63 (s, 2H), 4.86 (d, 1H, *J* = 10.9 Hz), 4.96 (d, 1H, *J* = 1.8 Hz), 5.26 (d, 1H, *J* = 1.8 Hz), 5.68 (dd, 1H, *J* = 1.8, 2.9 Hz), 5.89 (m, 2H),7.10–7.56 (m, 29H), 7.75–8.11 (m, 6H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.1, 66.6, 67.1, 69.0, 69.7, 69.8, 70.4, 71.8, 71.9, 72.5, 73.2, 74.7, 74.8, 74.9, 75.7, 78.1, 80.1, 96.2, 98.2, 127.3–128.9, 133.1, 133.3, 133.5, 138.3, 138.4, 138.5, 138.6,165.3, 165.4, 165.4; HRMS (MALDI-TOF): calcd. for $C_{64}H_{60}NaO_{14}$ [M^+ +Na]: 1075.388; found: 1075.3889.

Characterization data for compound **6**



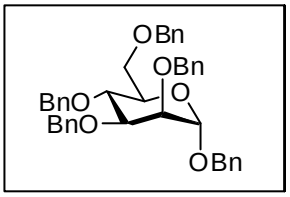
$[\alpha]_D^{25}$ = +31.4 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.37 (t, 1H, *J* = 2.4 Hz), 3.58–4.07 (m, 12H), 4.10 (dd, 2H, *J* = 0.7, 2.4 Hz), 4.42–4.71 (m, 8H), 4.61 (s, 2H), 4.68 (s, 2H), 4.87 (d, 2H, *J* = 10.8 Hz), 4.99 (d, 1H, *J* = 1.6 Hz), 5.11 (d, 1H, *J* = 1.6 Hz), 7.10–7.45 (m, 35H); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 54.1, 65.9, 69.1, 71.5, 71.8, 72.0, 72.1, 72.4, 72.9, 73.2, 74.4, 74.6, 74.7, 74.7, 74.9, 74.9, 75.0, 78.8, 79.3, 80.0, 96.5, 98.1, 127.3–128.4, 138.1, 138.4,138.4,138.4,138.4, 138.6, 138.7; HRMS (MALDI-TOF): calcd. for $C_{64}H_{66}NaO_{11}$ [M^+ +Na]: 1033.4503; found: 1033.4510.

Characterization data for compound **8**



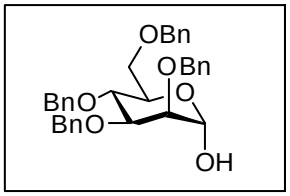
$[\alpha]_D^{25}$ = -16.6 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 3.47 (t, 1H, *J* = 1.8 Hz), 3.58 (dd, 1H, *J* = 1.8, 5.4 Hz), 3.73 (dd, 1H, *J* = 6.0, 7.1 Hz), 3.81 (qd, 1H, *J* = 1.6, 3.1, 5.0 Hz), 4.25 (dd, 1H, *J* = 0.9, 7.1 Hz), 4.43–4.57 (m, 5H), 4.52 (ABq, 2H, *J* = 12.4 Hz), 5.46 (s, 1H), 7.20–7.38 (m, 15H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 65.0, 71.3, 71.4, 73.4, 74.1, 74.4, 74.5, 76.5, 100.1, 127.7–128.5, 137.6, 137.9, 137.9; Mol. Wt. Calculated for $C_{27}H_{28}NaO_5$ [M^+ +Na]: 455.1825; found: 455.1830.

Characterization data for compound **9**



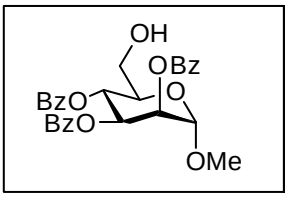
$[\alpha]_D^{25}$ = -38.5 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 3.45–3.51 (m, 2H), 3.79–3.96 (m, 4H), 4.67 (ABq, 2H, *J* = 3.0 Hz), 4.69 (ABq, 2H, *J* = 5.2 Hz), 4.56-4.70 (m, 4H), 4.92 (m, 2H), 5.05 (m, 1H), 7.17-7.47 (m, 25H); ^{13}C NMR (50.32 MHz, $CDCl_3$): 69.6, 70.7, 71.4, 73.4, 73.8, 73.8, 74.8, 75.0, 75.9, 82.3, 100.2, 127.2-128.3, 137.4, 138.0, 138.3, 138.4, 138.7; HRMS (MALDI-TOF): calcd. for $C_{41}H_{42}NaO_6$ [M^+ +Na]: 653.2879; found: 653.2875.

Characterization data for compound **10**



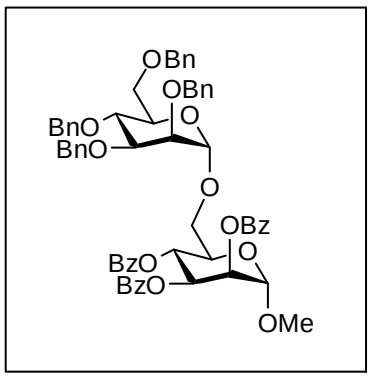
$[\alpha]_D^{25}$ = +9.5 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 3.42–4.08 (m, 7H), 4.53 (m, 1H), 4.60 (s, 2H), 4.72 (d, 2H, *J* = 1.9 Hz), 4.72 (ABq, 2H, *J* = 11.3 Hz), 4.85 (t, 1H, *J* = 5.5 Hz), 5.24 (d, 1H, *J* = 1.2 Hz); ^{13}C NMR (50.32 MHz, $CDCl_3$): 69.6, 71.5, 72.1, 72.6, 73.2, 74.8, 75.0, 75.2, 79.7, 92.7, 127.6-128.5, 138.0, 138.1, 138.3, 138.5; HRMS (MALDI-TOF): calcd. for $C_{34}H_{36}NaO_6$ [M^+ +Na]: 563.2410; found: 563.2416.

Characterization data for compound **11**



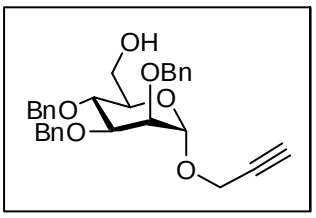
$[\alpha]_D^{25}$ = -113.6 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 3.4 (bs, 1H), 3.52 (s, 3H,), 3.81 (m, 2H), 4.12 (dt, 1H, *J* = 3.0, 9.4Hz), 5.01 (d, 1H, , *J* = 1.7Hz), 5.68 (dd, 1H, *J* = 1.7, 3.3Hz), , 5.84 (t, 1H, *J* =10.2Hz), 5.96 (dd, 1H, *J* =3.3, 10.2Hz), 7.21-7.65 (m, 9H), 7.78-8.13 (m, 6H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.4, 61.4, 67.2, 69.6, 70.5, 70.8, 98.7, 128.2-130.1, 133.1, 133.5, 133.6, 165.4, 165.5, 166.4; HRMS (MALDI-TOF): calcd. for $C_{28}H_{26}NaO_9$ [M^+ +Na]: 529.1475; Found: 529.1752.

Characterization data for compound **12**



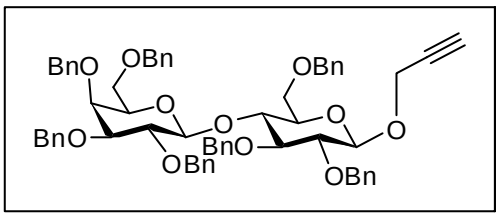
$[\alpha]_D^{25}$ = -43.8 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 3.43 (s, 3H), 3.54–3.75 (m, 5H), 3.81-4.01 (m 3H), 4.18 (m, 1H), 4.37 (d, 2H, *J* = 2.5 Hz), 4.49 (t, 2H, *J* = 10.3 Hz), 4.49 (ABq, 2H, *J* = 12.3 Hz), 4.68 (s, 2H), 4.95 (dd, 2H, *J* = 1.7, 5.6 Hz), 5.62 (dd, 1H, *J* = 1.8, 2.9 Hz), 5.89 (m, 2H),7.13–7.53 (m, 29H), 7.78–8.10 (m, 6H); ^{13}C NMR (125.76 MHz, $CDCl_3$): δ 55.4,66.7, 67.8, 68.9, 69.0, 69.9, 70.6, 71.7, 71.8, 72.4, 73.2, 74.6, 74.7, 75.0, 80.1, 98.1, 98.4, 127.3–129.8, 133.1, 133.3, 133.5, 138.3, 138.4, 138.5, 138.6,165.3, 165.4, 165.4; HRMS (MALDI-TOF): calcd. for $C_{62}H_{60}NaO_{14}$ [M^+ +Na]: 1051.388; found: 1051.3889.

Characterization data for compound **13**



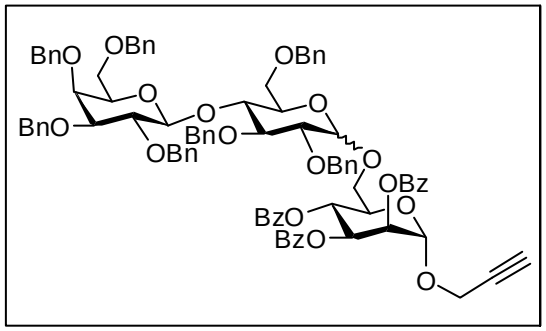
$[\alpha]_D^{25}$ = +56.1 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.21 (bs, 1H), 2.40 (t, 1H, *J* =2.4 Hz), 3.62-3.68 (m, 1H), 3.76-4.05 (m, 5H), 4.16 (d, 2H, *J* = 2.4Hz), 4.62 (s, 2H), 4.74 (ABq, 2H, *J* =12.7 Hz), 4.87 (ABq, 2H, *J* =10.9 Hz), 5.20 (d, 1H, *J* = 1.8 Hz), 7.23-7.37 (m, 15H); ^{13}C NMR (50.32 MHz, $CDCl_3$): 54.3, 62.2, 72.3, 72.7, 73.1, 74.6, 74.6, 75.0, 75.3, 78.8, 80.0, 96.8, 127.6-128.5, 138.1, 138.4, 138.5; HRMS (MALDI-TOF): calcd. for $C_{30}H_{32}NaO_6$ [M^+ +Na]: 511.2097; found: 511.2089.

Characterization data for compound **16**



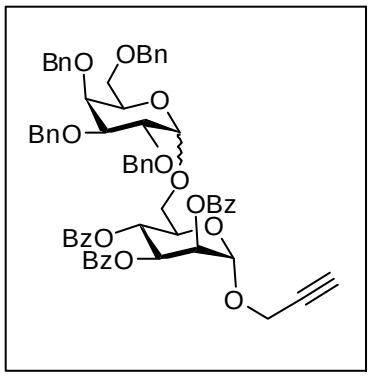
$[\alpha]_D^{25}$ = +5.3 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.44 (t, 1H, *J* = 2.4 Hz), 3.25–4.05 (m, 12H), 4.28 (ABq, 2H, *J* = 11.8 Hz), 4.40 (m, 3H), 4.48–4.65 (m, 3H), 4.62–4.83 (m, 7H), 4.97 (ABq, 2H, *J* = 9.1 Hz), 4.98 (ABq, 1H, *J* = 12.8 Hz), 7.10–7.42 (m, 35H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.8, 68.0, 68.1, 72.5, 72.9, 73.0, 73.3, 73.5, 74.7, 74.8, 74.9, 75.1, 75.2, 75.4, 77.2, 79.0, 79.9, 81.4, 82.4, 82.8, 101.3, 102.7, 127.0-128.4, 138.0, 138.2, 138.5, 138.6, 138.7, 139.0, 139.1; HRMS (MALDI-TOF): calcd. for $C_{64}H_{66}NaO_{11}$ [M^+ +Na]: 1033.4503; found: 1033.4509.

Characterization data for compound **17**



$[\alpha]_D^{25}$ = +5.3 ($CHCl_3$, *c* 1.0); Overall α/β = 9:1; Data for the major isomer: ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 2.52 (t, 1H, *J* = 2.4 Hz), 3.43–3.78 (m, 10H), 3.83–3.98 (m, 4H), 4.02 (dd, 1H, *J* = 3.7, 9.8 Hz), 4.16 (t, 1H, *J* = 6.7 Hz), 4.29–5.00 (m, 17H), 5.29 (m, 1H), 5.74 (dd, 1H, *J* = 1.8, 3.1 Hz), 5.88 (m, 1H), 5.96 (t, 1H, *J* = 10.2 Hz), 7.10–7.55 (m, 44H), 7.78–8.14 (m, 6H); ^{13}C NMR (125.76 MHz, $CDCl_3$): δ 54.9, 66.7, 67.1, 68.9, 69.2, 69.6, 70.1, 70.2, 70.2, 70.3, 70.8, 72.8, 72.9, 73.3, 73.5, 73.6, 74.6, 74.7, 75.2, 75.8, 76.6, 78.2, 78.7, 79.7, 81.3, 91.9, 96.1, 97.3, 127.4–130.1, 133.1, 133.4, 133.5, 137.9, 138.0, 138.2, 138.3, 138.5, 138.6, 138.9, 165.4, 165.4, 165.6; HRMS (MALDI-TOF): calcd. for $C_{91}H_{88}NaO_{19}$ [M^+ +Na]: 1507.5818; found: 1507.5823.

Characterization data for compound **18**

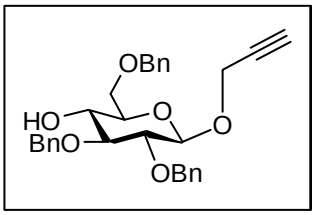


$[\alpha]_D^{25}$ = -19.2 ($CHCl_3$, *c* 1.0); Overall α/β = 3:1; Data for the major isomer: ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.31–2.48 (m, 1H), 3.36–5.12 (m, 21H), 5.26 (m, 1H), 5.72 (m, 1H), 5.81–5.98 (m,1H), 7.09–7.63 (m, 29H), 7.76–8.12 (m, 6H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 54.7, 66.9, 67.1, 68.6, 69.1, 70.1, 70.1, 70.2, 72.9, 73.0, 73.1, 74.7, 75.0, 75.8, 77.2, 78.1, 78.7, 95.8, 97.9, 127.3–130.0, 133.1, 133.4, 133.4, 138.0, 138.6, 138.7, 138.9, 165.4, 165.4, 165.8; HRMS (MALDI-TOF): calcd. for $C_{64}H_{60}Na\ O_{14}$ [M^+ +Na]: 1075.3881; found: 1075.3889.

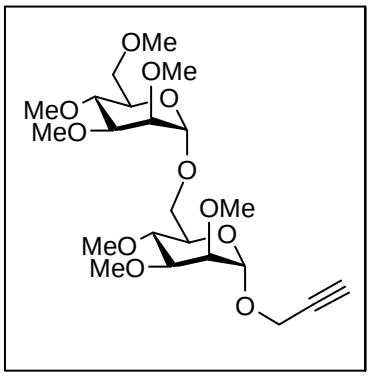
Characterization data for compound **19**

$[\alpha]_D^{25}$ = -11.0 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.47 (t, 1H, J = 2.4 Hz), 2.51 (bs, 1H), 3.38–3.82 (m, 6H), 4.43 (t, 2H, J = 2.4 Hz), 4.58 (d, 2H, J = 1.8 Hz),

4.63–4.76 (m, 3H), 4.90-5.03 (m, 2H), 7.23–7.44 (m, 15H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 56.0, 70.0, 71.2, 73.7, 74.1, 74.7, 75.0, 75.3, 78.9, 81.4, 83.9, 101.5, 127.5–128.6, 137.9, 138.3, 138.6; HRMS (MALDI-TOF): calcd. for $C_{30}H_{32}NaO_6$, [M^+ +Na]: 511.2097; found: 511.2090.

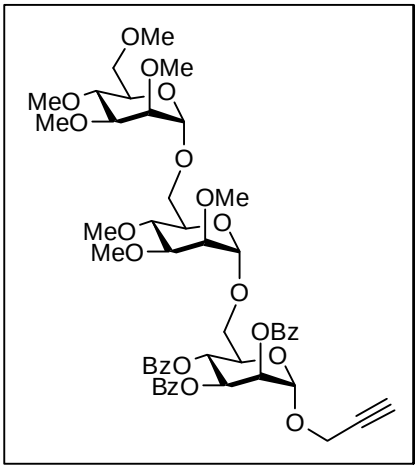


Characterization data for compound **22**



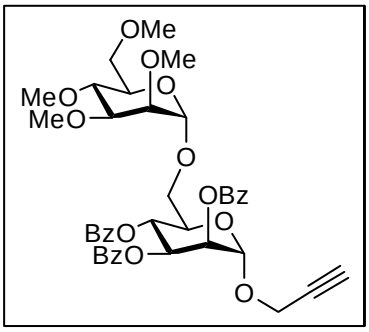
$[\alpha]_D^{25}$ = 106.9 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.46 (t, 1H, *J* = 2.4 Hz), 3.4, 3.5, 3.5, 3.5, 3.5, 3.5, 3.5 (7s, 21H), 3.42 (m, 1H), 3.50–3.72 (m, 10H), 3.92 (dd, 1H, *J* = 3.7, 11.5 Hz), 4.22 (t, 2H, *J* = 2.4 Hz), 5.07 (d, 1H, *J* = 1.5 Hz), 5.09 (d, 1H, *J* = 1.8 Hz); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 54.2, 57.6, 57.6, 58.7, 58.8, 59.1, 60.6, 60.8, 65.8, 71.2, 71.6, 71.9, 74.8, 75.7, 76.3, 76.8, 76.8, 78.6, 81.1, 81.1, 95.3, 97.0; HRMS (MALDI-TOF): calcd. for $C_{22}H_{38}NaO_{11}$ [M^+ +Na]: 501.2312; found: 501.2318.

Characterization data for compound **23**



$[\alpha]_D^{25}$ = -7.1($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.57 (t, 1H, J = 2.3 Hz), 3.34, 3.37, 3.38, 3.38, 3.44, 3.49, 3.52 (7s, 21H), 3.38–3.59 (m, 8H), 3.69 (m, 3H), 3.78 (dd, 1H, J = 3.3, 4.8 Hz), 3.9 (dd, 1H, J = 3.5, 11.1 Hz), 4.14–4.36 (m, 2H), 4.40 (d, 2H, J = 2.3 Hz), 4.92 (d, 1H, J = 1.3 Hz), 4.94 (d, 1H, J = 1.3 Hz), 5.29 (d, 1H, J = 1.5 Hz), 5.69 (dd, 1H, J = 1.8, 3.2 Hz), 5.88 (dd, 1H, J = 3.2, 10.1 Hz), 6.02 (t, 1H, J = 9.9 Hz), 7.20–7.71 (m, 9H), 7.75–8.18 (m, 6H); 13C NMR (100.61 MHz, CDCl3): d 55.3, 57.4, 57.6, 58.6, 58.6, 59.1, 60.6, 60.8, 65.6, 66.1, 67.3, 69.9, 69.9, 70.5, 71.1, 71.5, 71.6, 75.6, 75.7, 76.3, 76.6, 77.2, 78.1, 81.2, 81.2, 96.5, 96.9, 96.9, 128.2–130.0, 133.2, 133.5, 133.6, 165.3, 165.4, 165.4; HRMS (MALDI-TOF): calcd. for $C_{49}H_{60}NaO_{19}$ [M^+ +Na]: 975.3626; found: 975.3631.

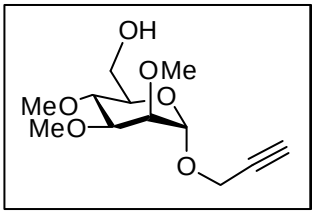
Characterization data for compound **24**



$[\alpha]_D^{25}$ = -144.3 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.56 (t, 1H, *J* = 2.4 Hz), 3.21, 3.36, 3.36, 3.50 (4s, 12H), 3.18–3.59 (m, 6H), 3.71 (dd, 1H, *J* = 3.7, 11.1 Hz), 3.96 (dd, 1H, *J* = 3.8, 11.1 Hz), 4.29 (td, 1H, *J* = 3.6, 7.3, 9.8 Hz), 4.40 (d, 2H, *J* = 2.4 Hz), 4.94 (s, 1H), 5.31 (d, 1H, *J* = 1.5 Hz), 5.69 (dd, 1H, *J* = 1.8, 3.1 Hz), 5.87 (dd, 1H, *J* = 3.3, 10.1 Hz), 6.02 (t, 1H, *J* = 9.9 Hz), 7.21–7.68 (m, 9H), 7.79–8.14 (m, 6H); ^{13}C NMR (50.32

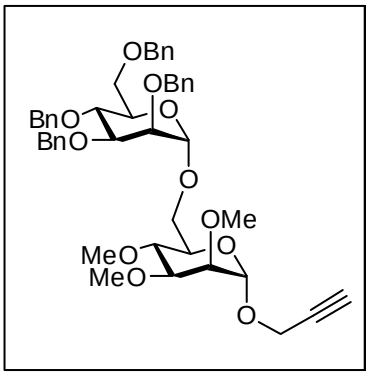
MHz, $CDCl_3$): d 55.3, 57.5, 58.8, 58.9, 60.6, 66.1, 67.2, 69.8, 69.9, 70.4, 71.2, 71.3, 75.6, 76.2, 76.7, 78.1, 80.9, 96.4, 97.0, 128.2–129.9, 133.1, 133.3, 133.6, 165.3, 165.4, 165.4; HRMS (MALDI-TOF): calcd. for $C_{40}H_{44}NaO_{14}$ [M^+ +Na]: 771.2629; found: 771.2620.

Characterization data for compound **25**



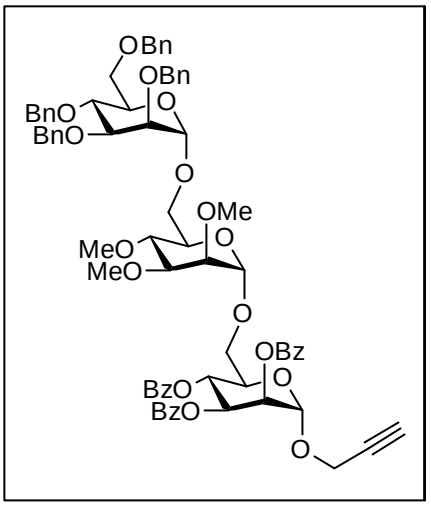
$[\alpha]_D^{25}$ = +75.5 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.18 (bs, 1H), 2.47 (t, 1H, J = 2.4 Hz), 3.50, 3.51, 3.55 (3s, 9H), 3.52 (m, 3H), 3.62 (m, 1H), 3.71–3.90 (m, 2H), 4.23 (d, 2H, J = 2.4 Hz), 5.09 (d, 1H, J = 1.7 Hz); 13C NMR (50.32 MHz, CDCl3): d 54.3, 57.7, 59.1, 60.8, 62.1,72.4, 74.9, 76.3, 76.9, 78.6, 80.9, 95.6; HRMS (MALDI-TOF): calcd. for $C_{12}H_{20}NaO_6$ [M^+ +Na]: 283.1158; found: 283.1164.

Characterization data for compound **26**



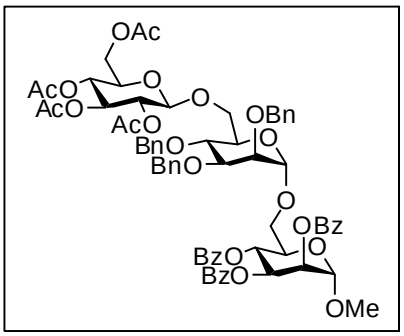
$[\alpha]_D^{25}$ = +56.6 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.42 (t, 1H, *J* = 2.4 Hz), 3.44, 3.46, 3.48 (3s, 9H), 3.46 (m, 2H), 3.55 (td, 1H, *J* = 2.4, 11.5 Hz), 3.63–4.02 (m, 9H), 4.14 (t, 2H, *J* = 2.4 Hz), 4.60 (ABq, 2H, *J* = 12.0 Hz), 4.61 (s, 2H), 4.70 (ABq, 2H, *J* = 10.9 Hz), 4.73 (s, 2H), 5.02 (d, 1H, *J* = 1.5 Hz), 5.09 (d, 1H, *J* = 1.3 Hz), 7.04–7.45 (m, 20H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 54.1, 57.9, 58.9, 60.8, 65.8, 69.2, 71.7, 71.8, 71.8, 72.3, 73.2, 74.7, 74.8, 74.9, 74.9, 75.9, 76.8, 78.7, 79.7, 81.1, 95.2, 98.0, 127.3-128.3, 138.3, 138.4, 138.5, 138.6; HRMS (MALDI-TOF): calcd. for $C_{46}H_{54}NaO_{11}$ [M^+ +Na]: 805.3564; found: 805.3560.

Characterization data for compound **27**



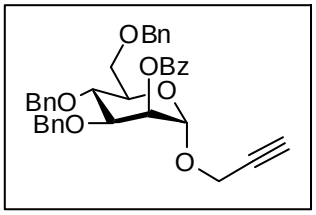
$[\alpha]_D^{25}$ = -11.1 ($CHCl_3$, *c* 1.0); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.50 (t, 1H, *J* = 2.4 Hz), 3.30, 3.36, 3.46 (3s, 9H), 3.45 (m, 4H), 3.58–4.09 (m, 10H), 4.24 (m, 1H), 4.35 (d, 2H, *J* = 2.4 Hz), 4.43–4.71 (m, 7H), 4.86 (dd, 2H, *J* = 4.8, 6.2 Hz), 4.99 (d, 1H, *J* = 1.7 Hz), 5.26 (d, 1H, *J* = 1.7 Hz), 5.67 (dd, 1H, *J* = 1.7, 3.2 Hz), 5.86 (dd, 1H, *J* = 3.2, 10.2 Hz), 6.03 (t, 1H, *J* = 10.2 Hz), 7.09–7.66 (m, 29H), 7.75–8.17 (m, 6H); ^{13}C NMR (125.76 MHz, $CDCl_3$): δ 55.4, 57.4, 58.7, 60.7, 65.6, 66.1, 67.3, 69.3, 69.9, 69.9, 70.5, 71.6, 71.7, 71.8, 72.3, 73.3, 74.8, 75.0, 75.0, 75.6, 75.8, 76.7, 78.2, 79.9, 81.2, 96.6 ($^1J_{C-H}$ = 170.5 Hz), 97.1 ($^1J_{C-H}$ = 169.7), 98.1 ($^1J_{C-H}$ = 174.2), 127.3–130.2, 133.1, 133.4, 133.6, 138.5, 138.5, 138.7, 138.7, 165.3, 165.4, 165.4; HRMS (MALDI-TOF): calcd. for $C_{73}H_{76}NaO_{19}$ [M^+ +Na]: 1279.4878; found: 1279.4870.

Characterization data for compound **29**



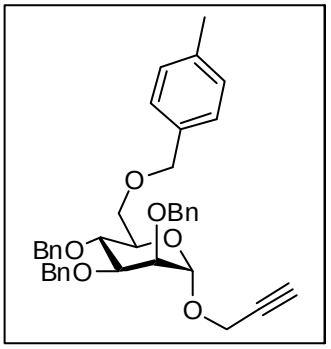
$[\alpha]_D^{25}$ = -33.6; ($CHCl_3$, *c* 1.00); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.95 (s, 3H), 1.99 (s, 3H), 2.01 (s, 3H), 2.02 (s, 3H), 3.50-4.21 (m, 13H), 4.33-4.37 (m, 3H), 4.52 (d, 1H, *J* = 11.4 Hz), 4.58 (s, 2H), 4.90-4.96 (m, 3H), 5.01 (t, 1H, *J* = 9.8 Hz), 5.03 (t, 1H, *J* = 10.1Hz), 5.13 (t, 1H, *J* = 9.4 Hz), 5.63 (dd, 1H, *J* = 1.8, 3.2 Hz), 5.84 (dd, 1H, *J* = 3.2, 9.8 Hz), 7.23-7.54 (m, 24H), 7.81-8.11 (m, 6H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 20.5, 20.5, 20.6, 20.6, 55.4, 61.8, 66.6, 67.8, 68.3, 68.7, 69.1, 69.9, 70.5, 71.0, 71.1, 71.5, 71.5, 72.5, 72.8, 74.4, 74.6, 74.8, 80.1, 98.0, 98.4, 100.9, 127.4-129.8, 133.0, 133.3, 133.4, 138.2, 138.3, 138.5, 165.3, 165.4, 165.5, 169.0, 169.4, 170.3, 170.6 ;HRMS (MALDI-TOF): calcd. for $C_{69}H_{72}NaO_{23}$ [M^++Na]: 1291.4362; found: 1291.4377.

Characterization data for compound **35**



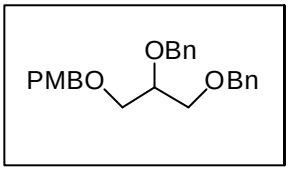
$[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.0) = +7.1; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 2.43 (t, 1H, *J* = 2.4 Hz), 3.77-3.90 (m, 3H), 4.10 (m, 2H), 4.26 (d, 2H, *J* = 2.5 Hz), 4.49-4.60 (m, 3H), 4.72-4.88 (m, 3H), 5.17 (d, 1H, *J* = 1.8 Hz), 5.67 (s, 1H), 7.17-7.56 (m, 18H), 8.07 (m, 2H);^{13}C NMR (100.53 MHz, $CDCl_3$): 54.4, 68.6, 68.8, 71.5, 72.0, 73.4, 74.0, 75.0, 75.2, 78.0, 96.4, 127.4-129.9, 133.1, 137.9, 138.2, 138.3, 165.5; HRMS (MALDI-TOF): calcd. for $C_{37}H_{36}NaO_7$ [M^+ +Na]: 615.2359; found: 615.2364.

Characterization data for compound **36**



$[\alpha]_D^{25}$ = +34.7 ($CHCl_3$, *c* 1.0); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 2.31 (s, 3H), 2.38 (t, 1H, *J* = 2.4 Hz), 3.68-3.77 (m, 3H), 3.83 (dd, 1H, *J* = 1.9, 1.2 Hz), 3.88 (dd, 1H, *J* = 3.2, 9.2 Hz), 3.99 (t, 1H, *J* = 9.5 Hz), 4.10 (d, 2H, *J* = 2.2 Hz), 4.58 (ABq, 2H, *J* = 11.9 Hz), 4.59 (s, 2H), 4.65 (ABq, 2H, *J* = 11.0 Hz), 4.73 (q, 2H, *J* = 2.8, 15.2 Hz), 5.08 (d, 1H, *J* = 1.8 Hz), 7.09-7.39 (m, 19H); ^{13}C NMR (100.53 MHz, $CDCl_3$): 21.2, 54.0, 68.7, 72.0, 72.2, 72.6, 73.2, 74.3, 74.6, 74.7, 75.0, 78.8, 79.9, 96.4, 127.4-128.9, 135.1, 137.1, 138.1, 138.3, 138.4; Mol. Wt. Calculated for $C_{38}H_{40}NaO_6$ [M^+ +Na]: 615.2723; found: 615.2731.

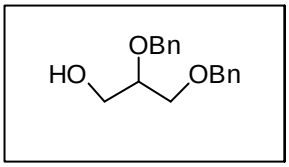
Characterization data for compound **39**



$[\alpha]_D^{25}$ = N/R (racemic); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.56–3.65 (m, 4H), 3.80 (s, 4H), 4.46 (s, 2H), 4.53 (s, 2H), 4.69 (s, 2H), 6.86 (d, 2H *J* = 8.2 Hz), 7.22-7.34 (m, 12H); ^{13}C NMR (100.53 MHz, $CDCl_3$): 55.2, 69.9, 70.3, 72.1, 73.0, 73.3,

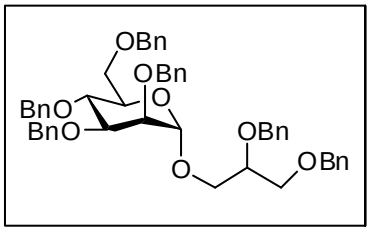
77.2, 113.7, 127.4-130.3, 138.2, 138.6, 159.1; HRMS (MALDI-TOF): calcd. for $C_{25}H_{28}NaO_4$ [M^+ +Na]: 415.1885; found: 415.1889.

Characterization data for compound **40**



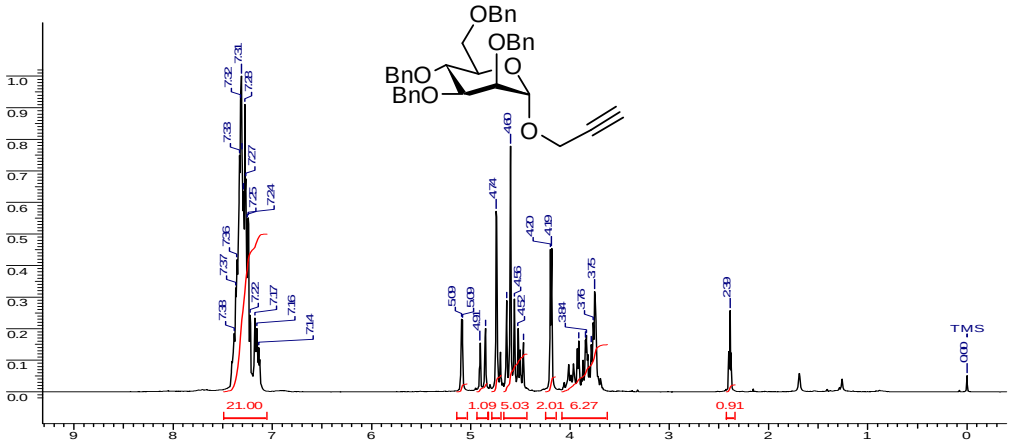
$[\alpha]_D^{25}$ = N/R (racemic); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.15 (bs, 1H), 3.59-3.73 (m, 5H), 4.54 (s, 2H), 4.65 (dd, 2H, *J* = 10.1, 12.0 Hz), 7.24-7.36 (m, 10H); ^{13}C NMR (50.32 MHz, $CDCl_3$): 62.8, 70.1, 72.1, 73.5, 78.0, 127.6-128.4, 137.9, 138.2; HRMS (MALDI-TOF): calcd. for $C_{17}H_{20}NaO_3$ [M^+ Na]: 295.1310; found: 295.1318.

Characterization data for compound **42**

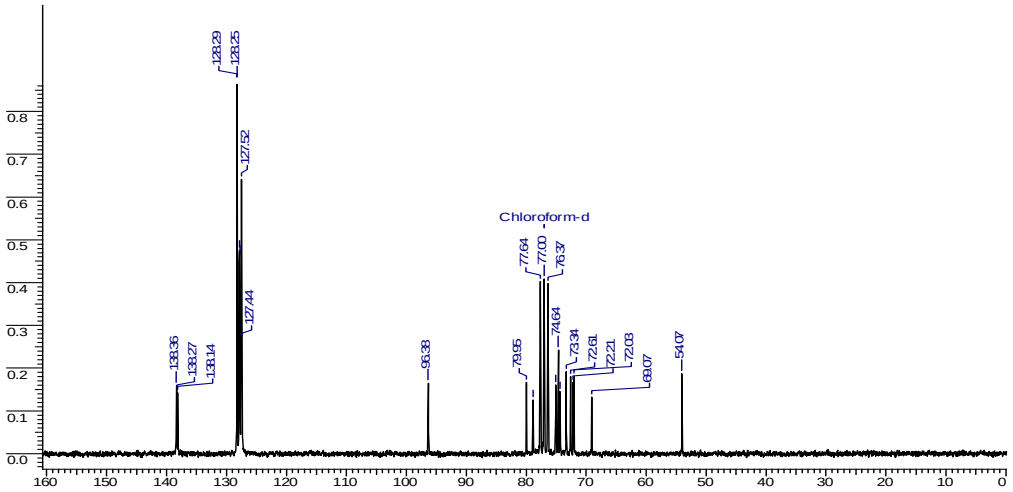


$[\alpha]_D^{25}$ = N/R (racemic); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.50-3.57 (m, 3H), 3.65-3.87 (m, 7H), 4.00 (m, 1H), 4.46-4.52 (m, 4H), 4.59-4.70 (m,7H), 4.86-4.90 (m, 2H), 7.15-7.36 (m, 30H); ^{13}C NMR (100.53 MHz, $CDCl_3$): 67.2, 69.0, 69.8, 71.7, 72.1, 72.2, 72.4, 73.2, 73.3, 74.6, 74.8, 75.0, 76.7, 79.9, 98.0, 127.4-128.3, 138.1, 138.3, 138.3, 138.3, 138.5, 138.6; HRMS (MALDI-TOF): calcd. for $C_{51}H_{54}NaO_8$ [M^+ +Na]: 817.3716; found: 817.3723.

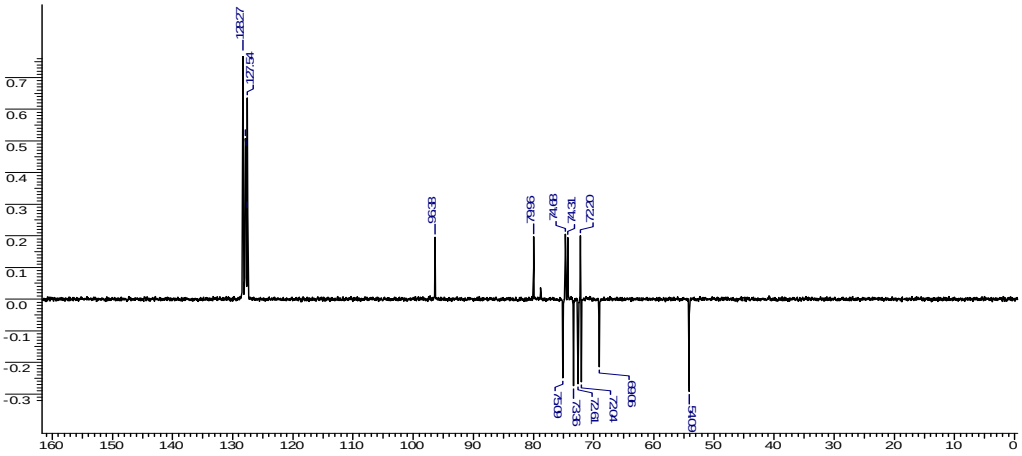
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **3**



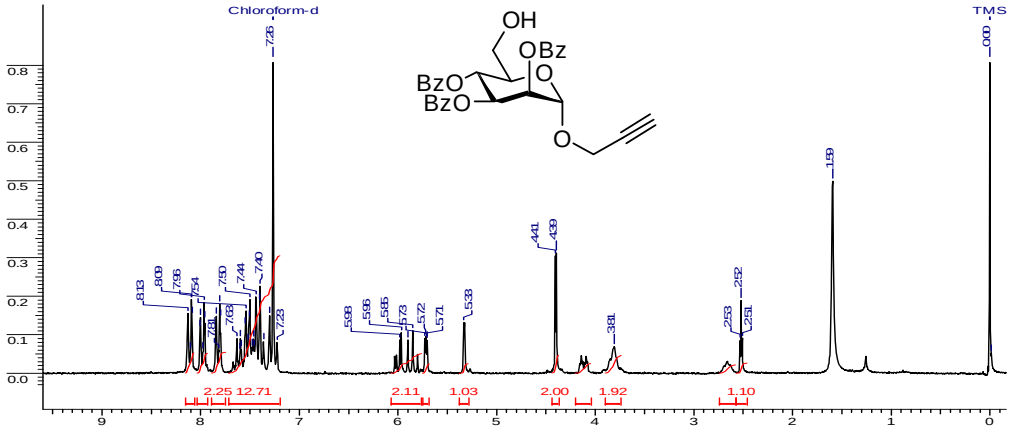
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **3**



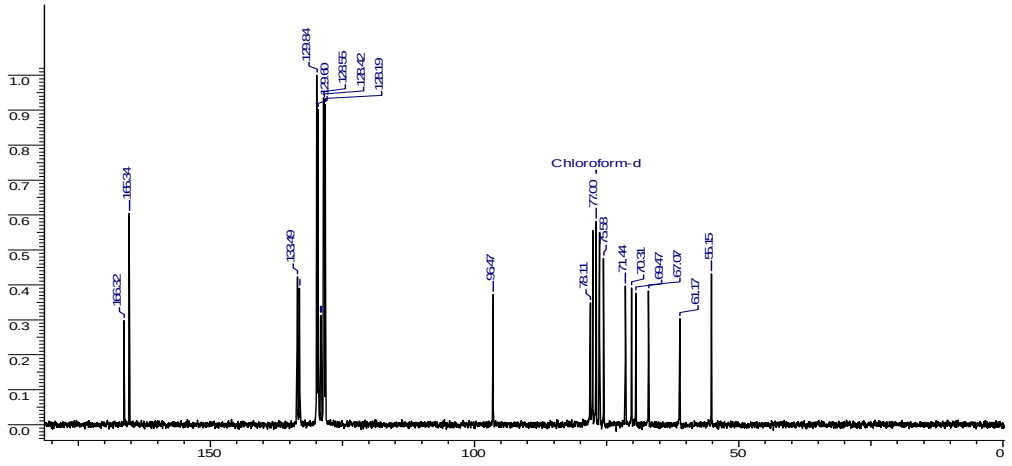
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **3**



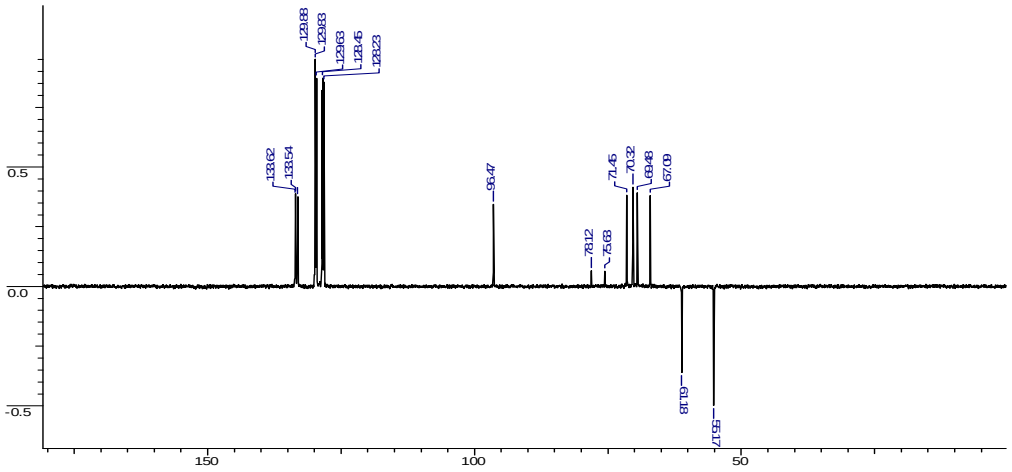
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **4**



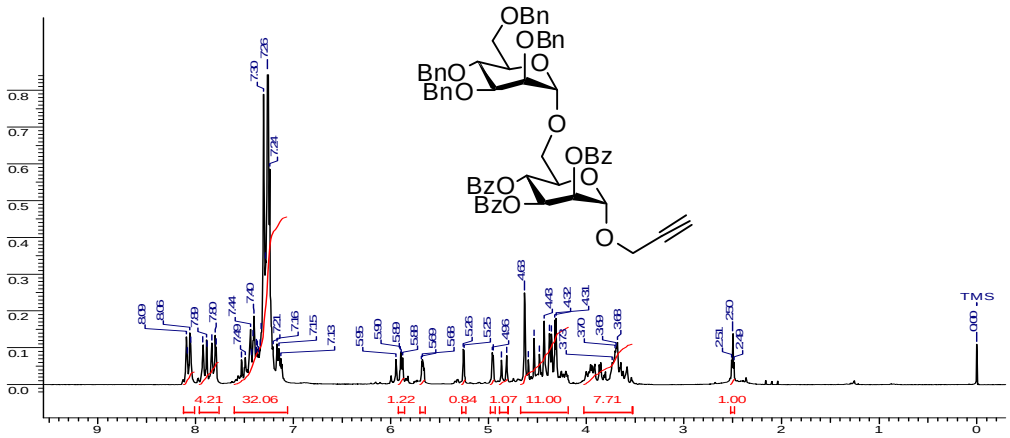
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **4**



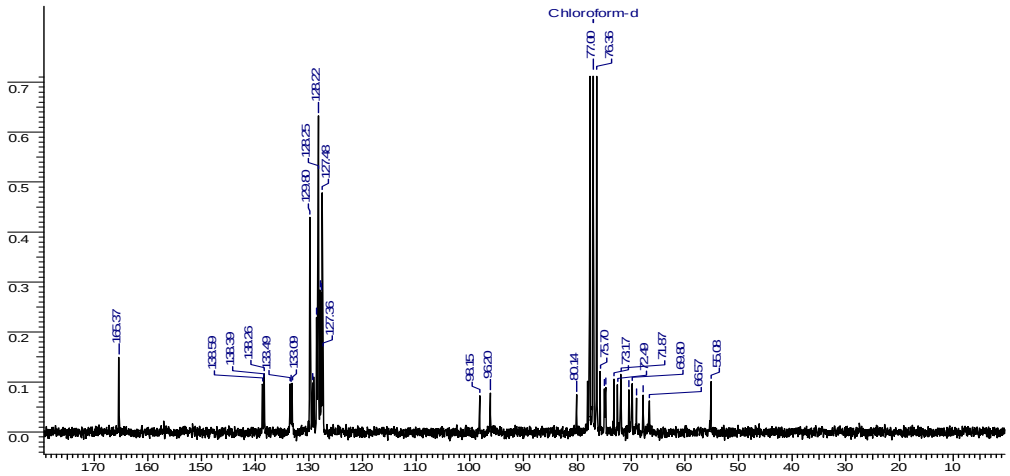
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **4**



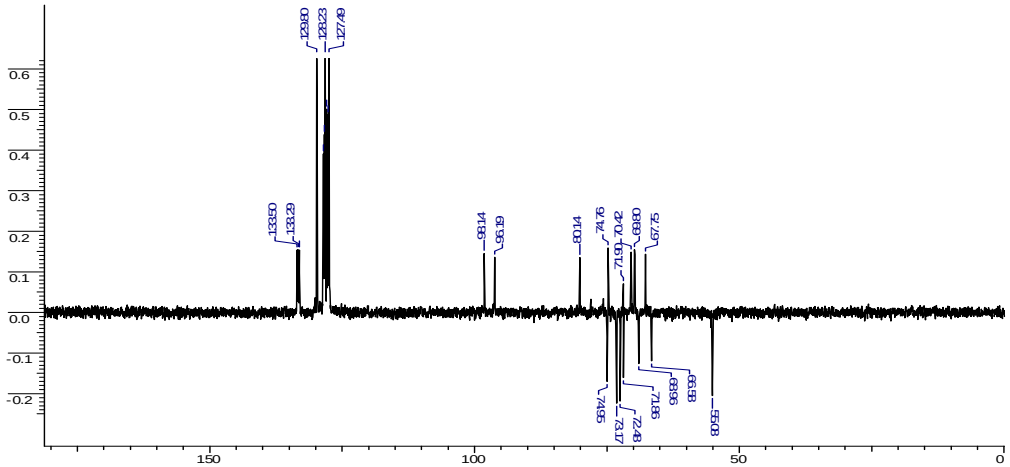
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **5**



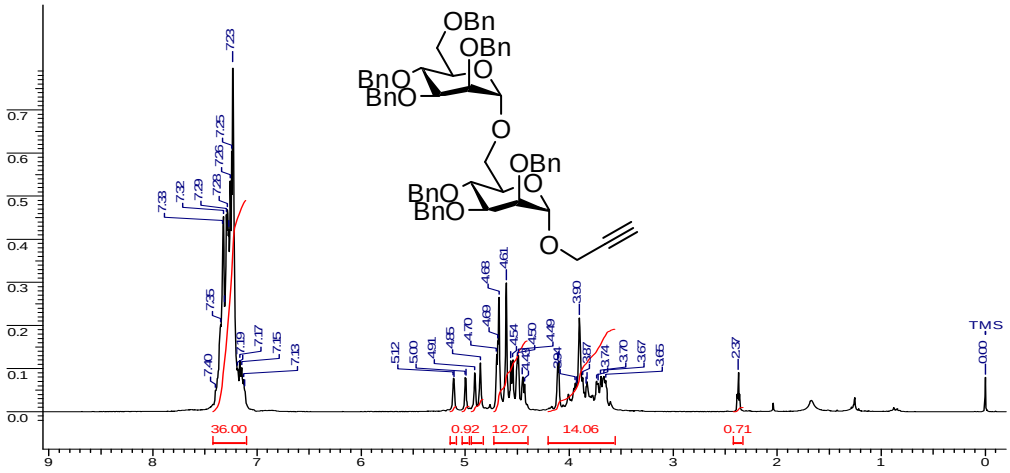
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **5**



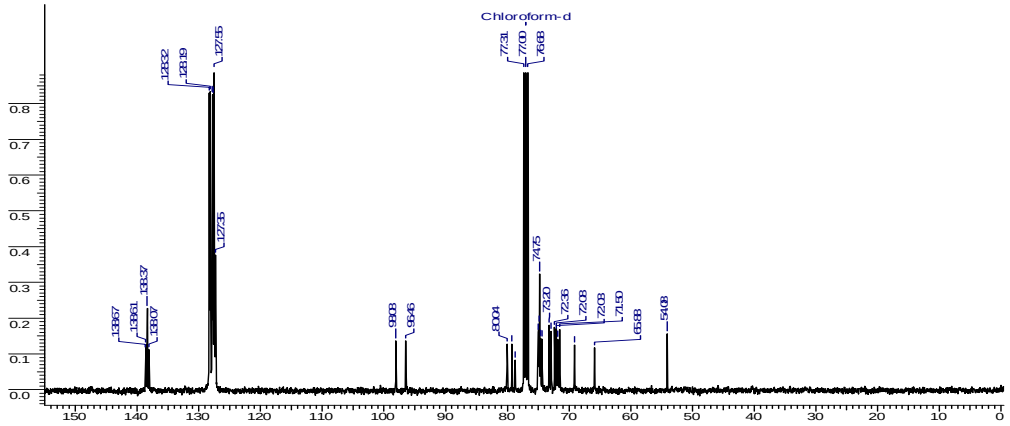
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **5**



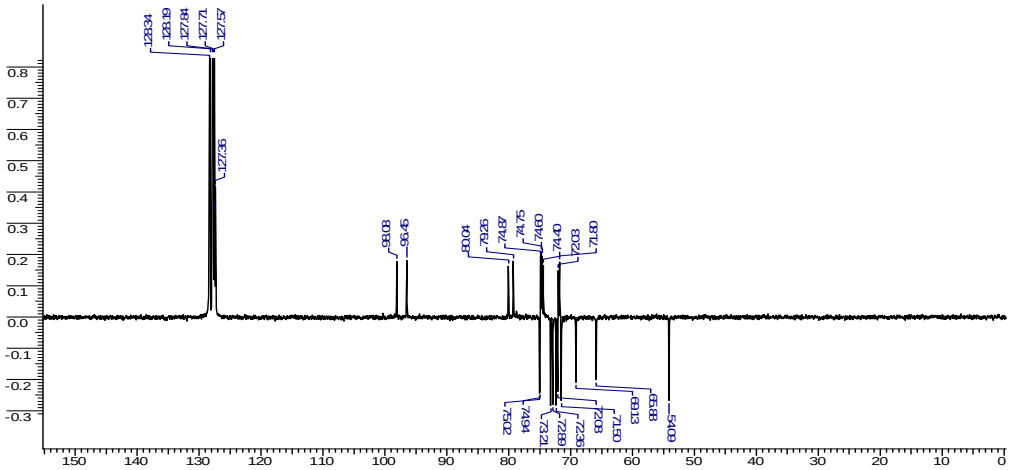
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **6**



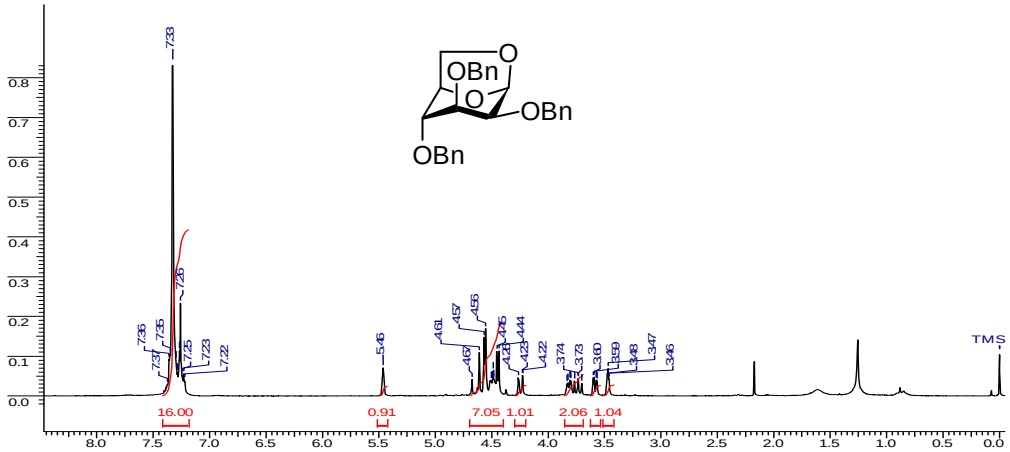
^{13}C NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **6**



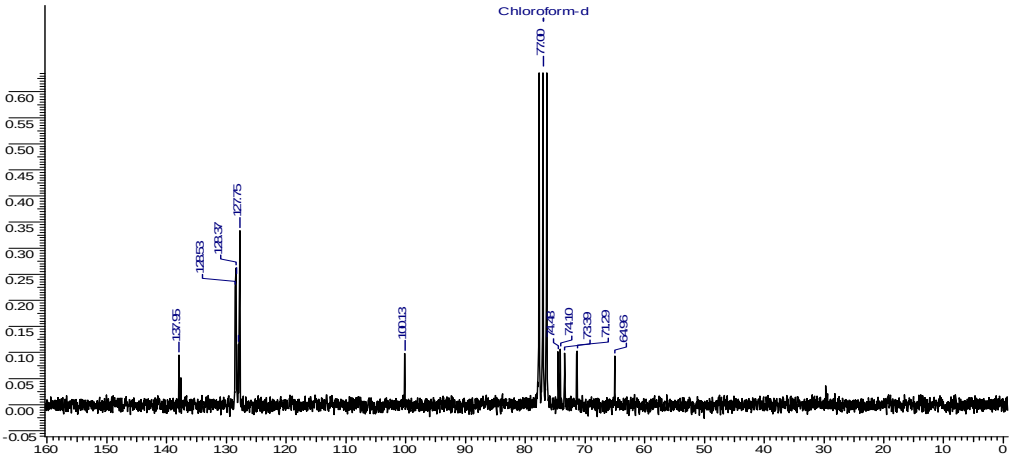
DEPT NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **6**



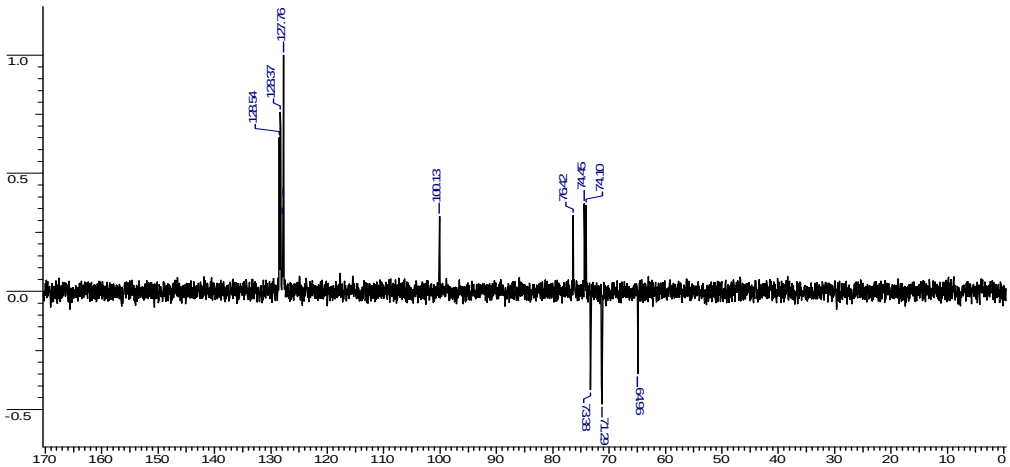
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **8**



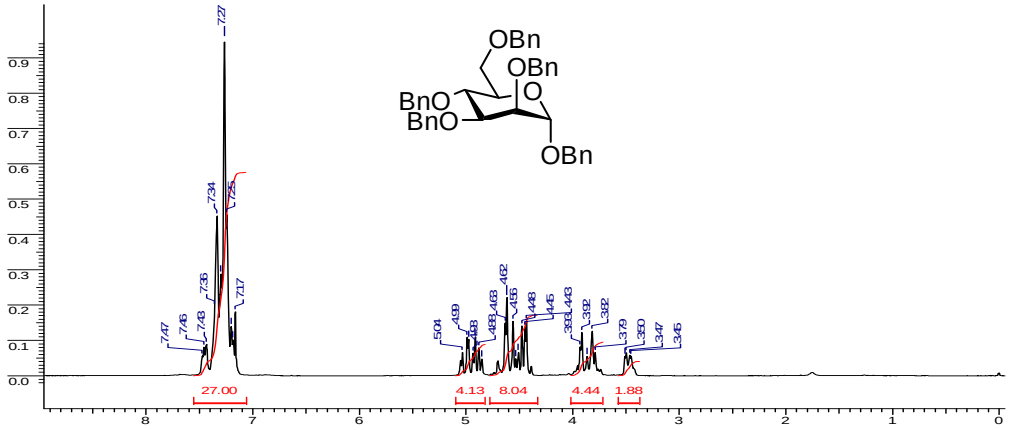
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **8**



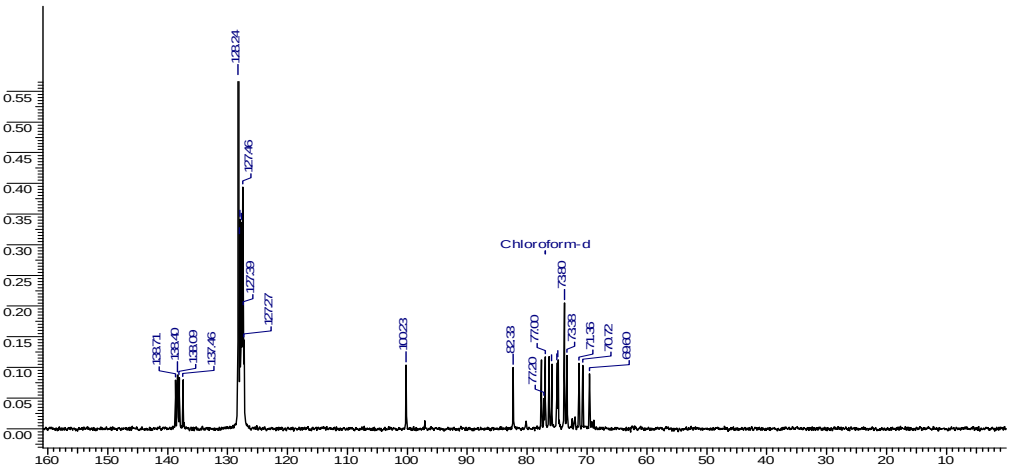
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **8**



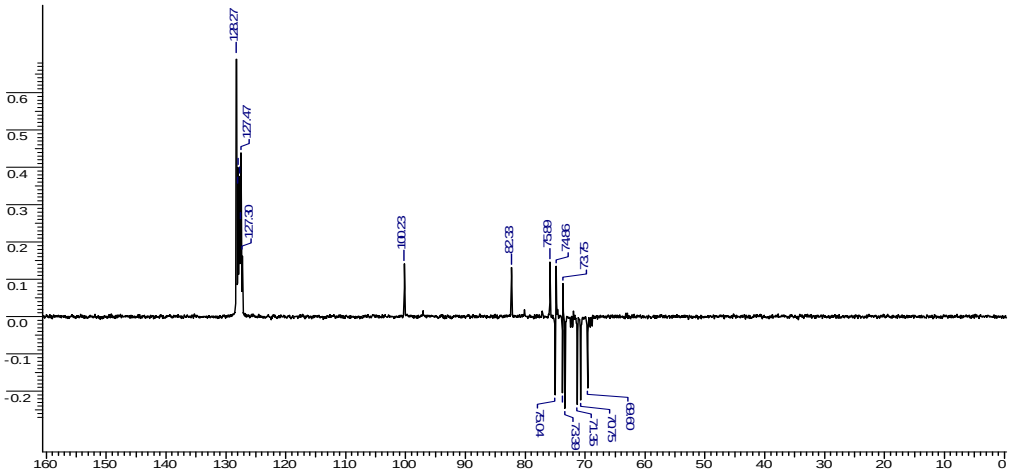
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **9**



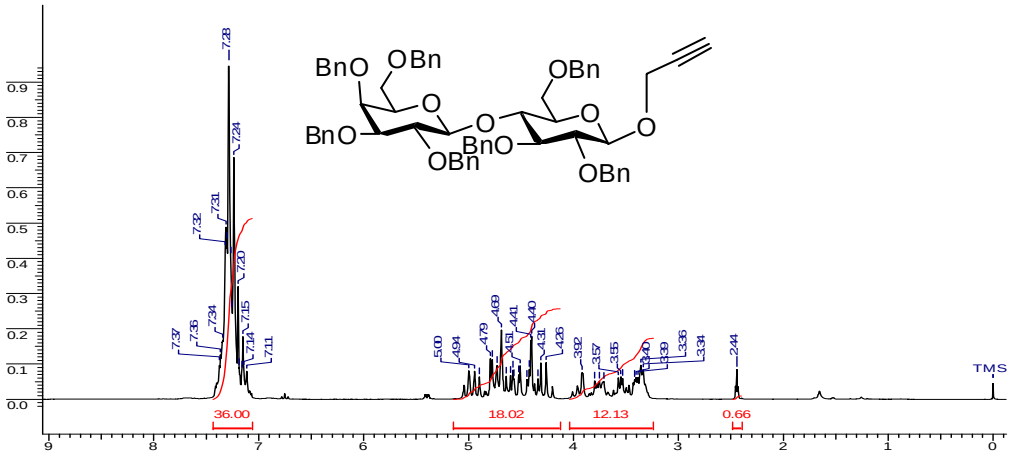
^{13}C NMR Spectrum (50. 32MHz, $CDCl_3$) of Compound **9**



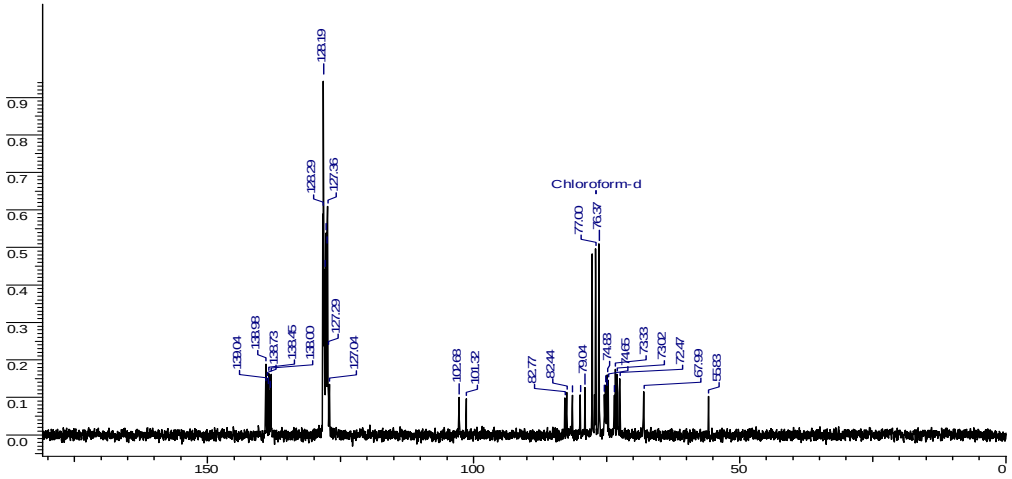
DEPT NMR Spectrum (50. 32MHz, $CDCl_3$) of Compound **9**



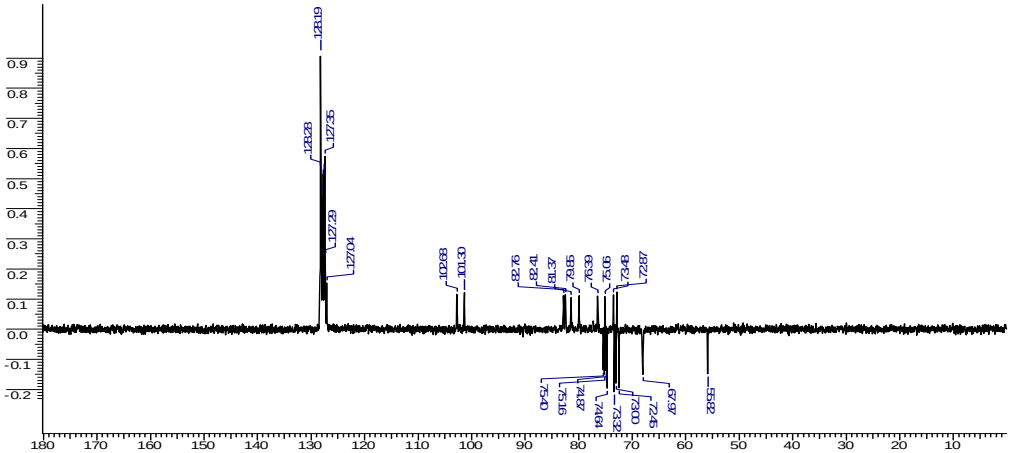
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **16**



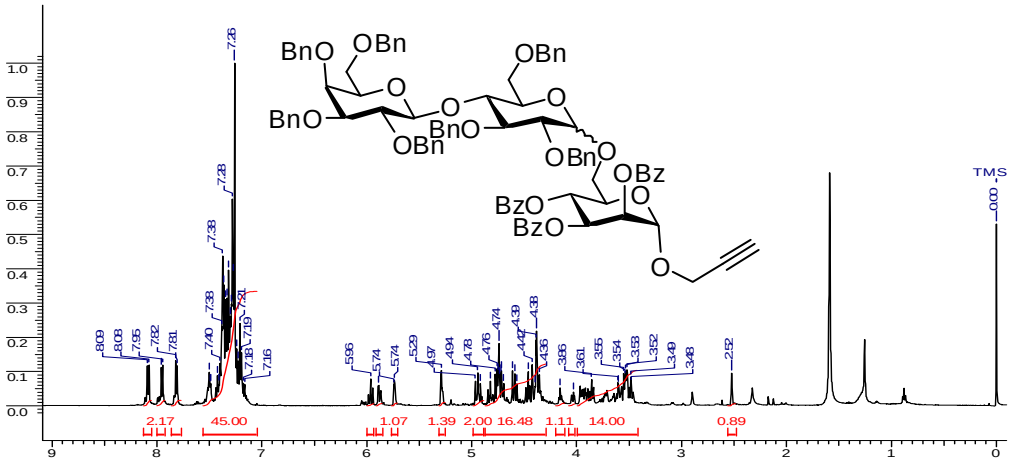
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **16**



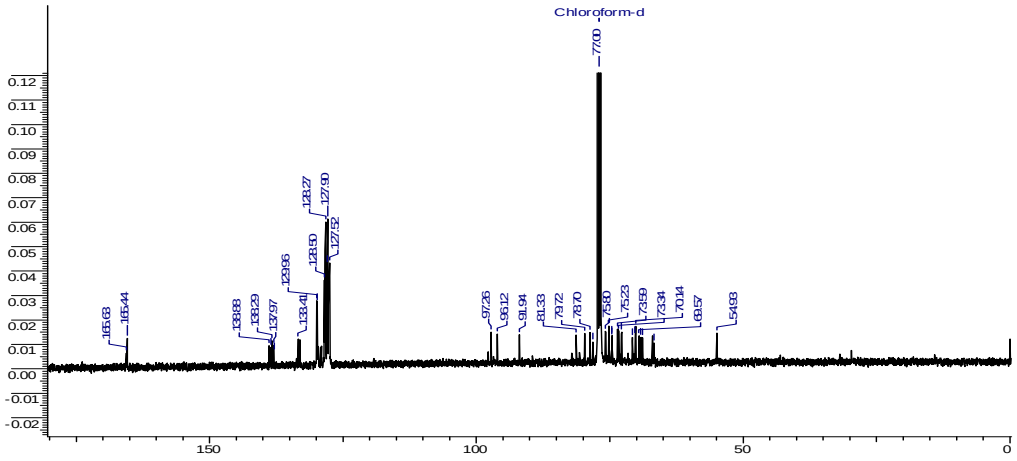
EPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **16**



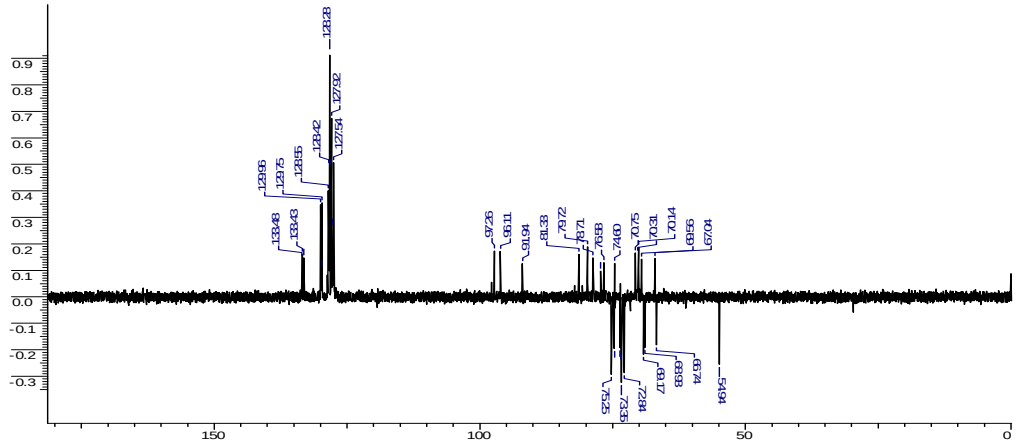
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **17**



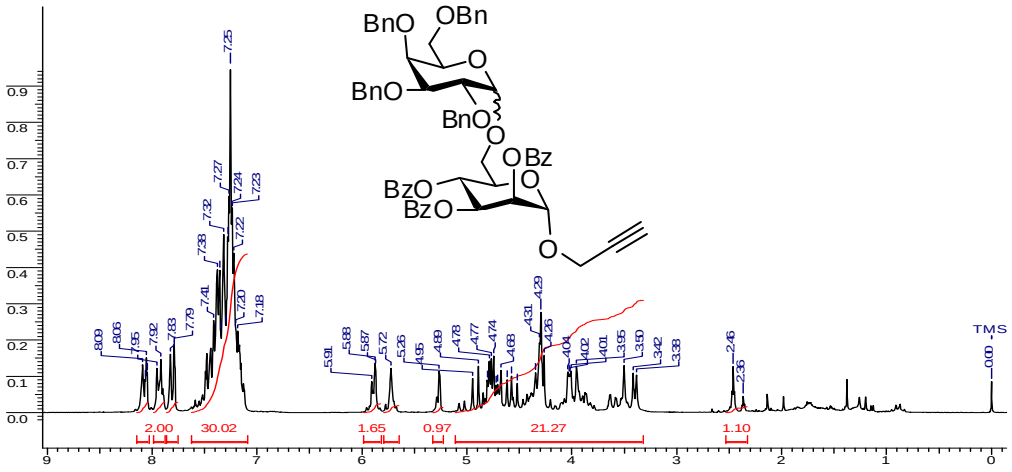
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **17**



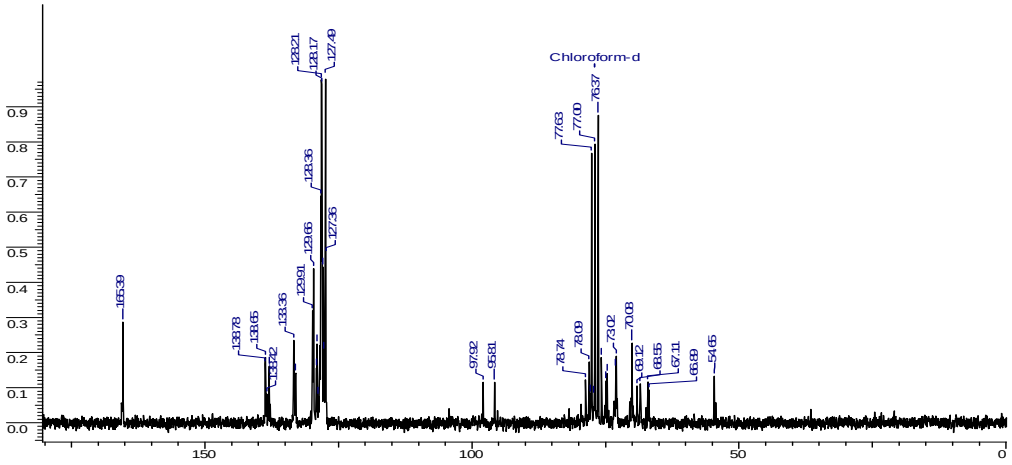
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **17**



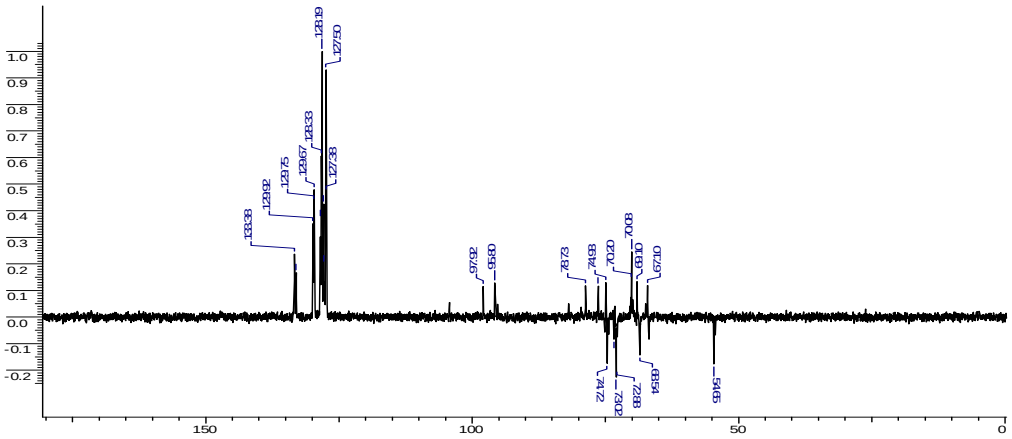
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **18**



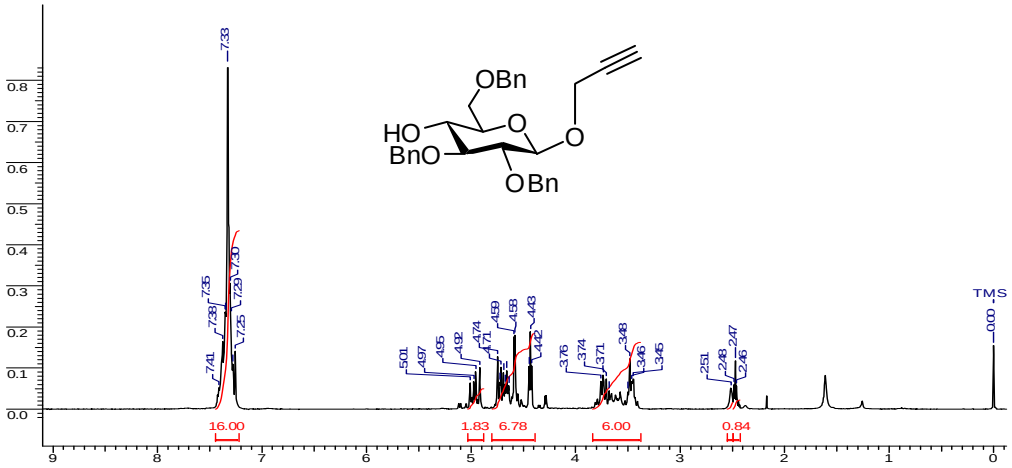
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **18**



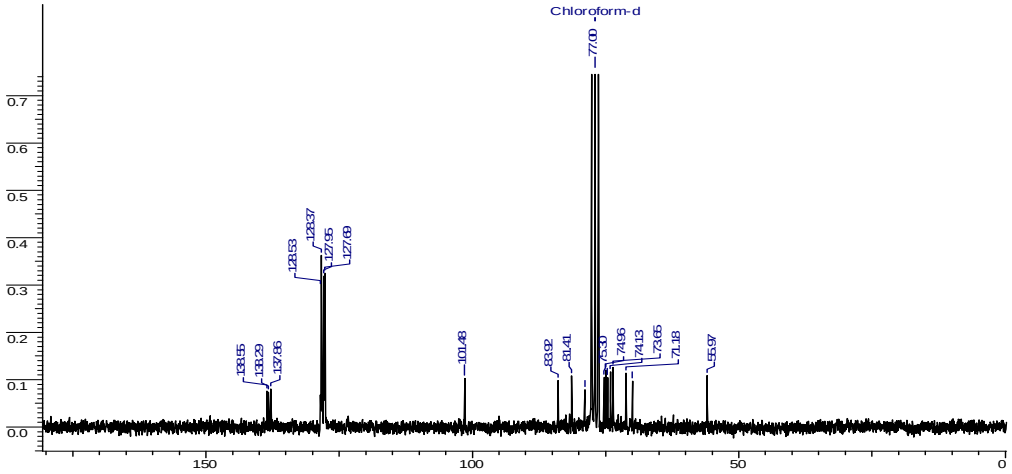
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **18**



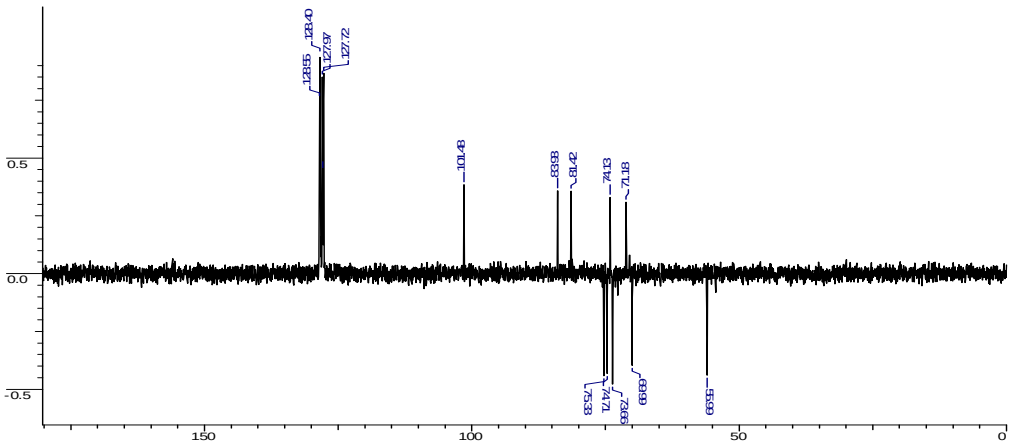
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **19**



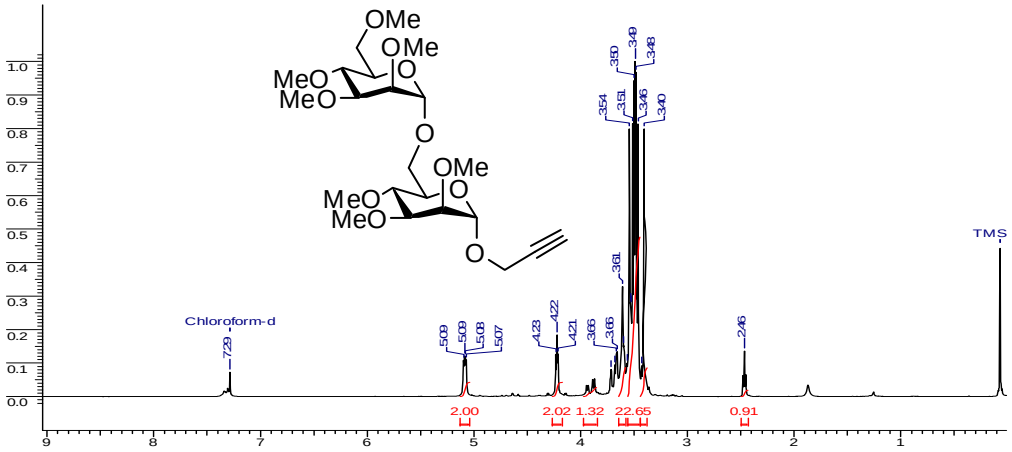
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **19**



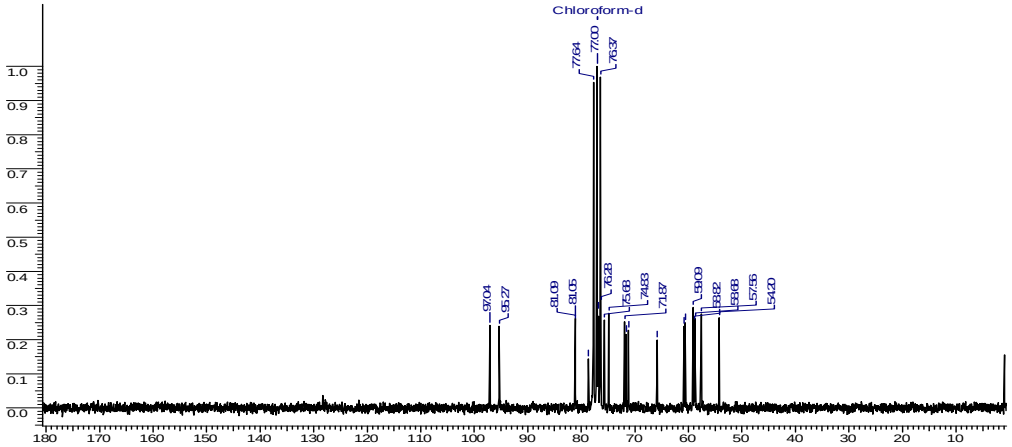
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **19**



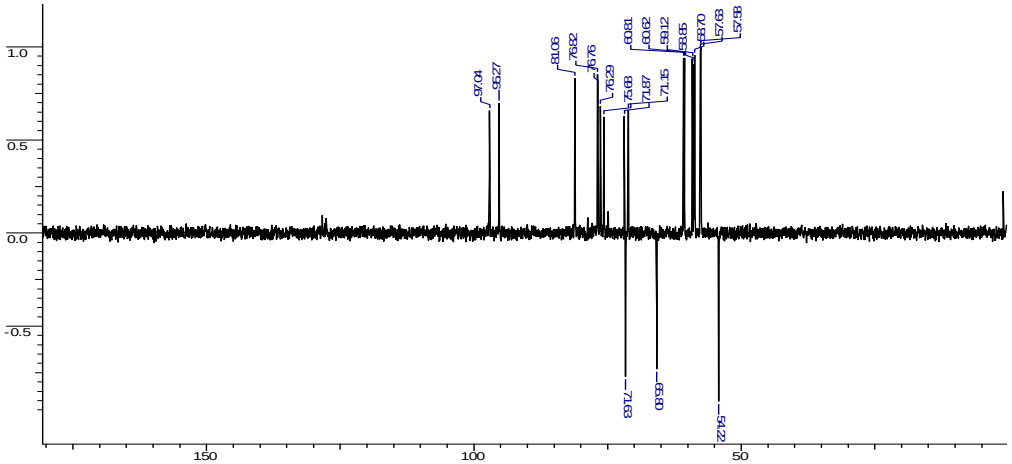
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **22**



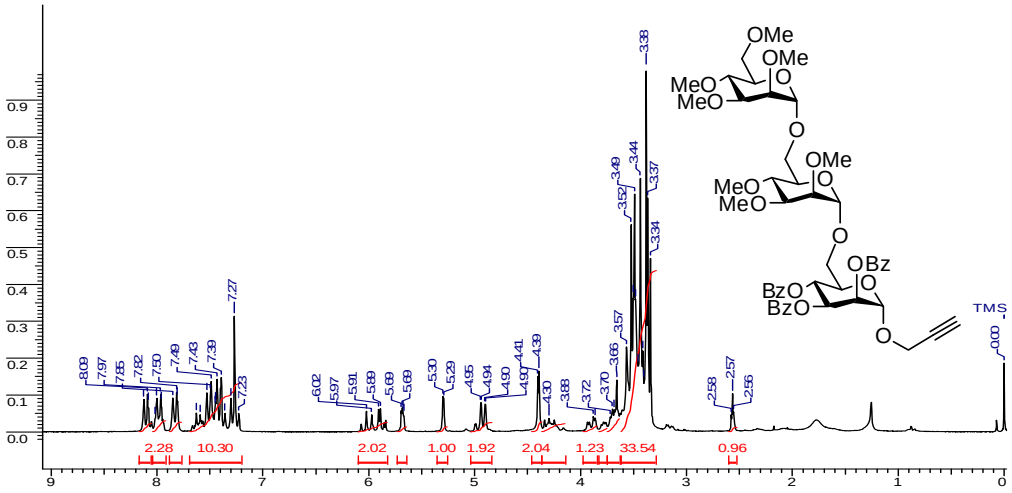
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **22**



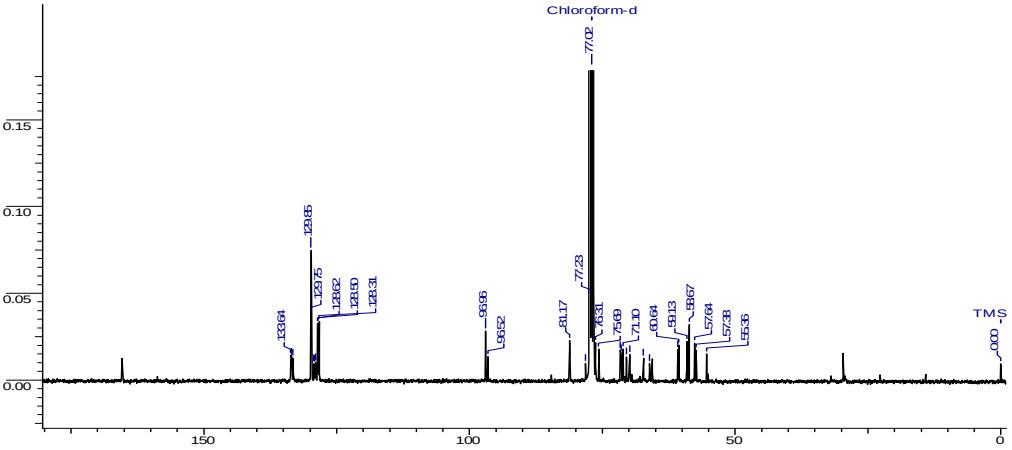
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **22**



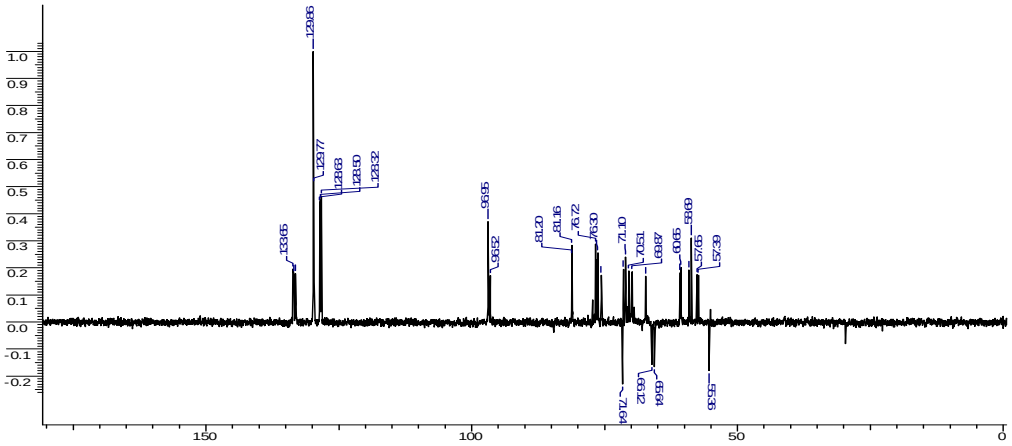
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **23**



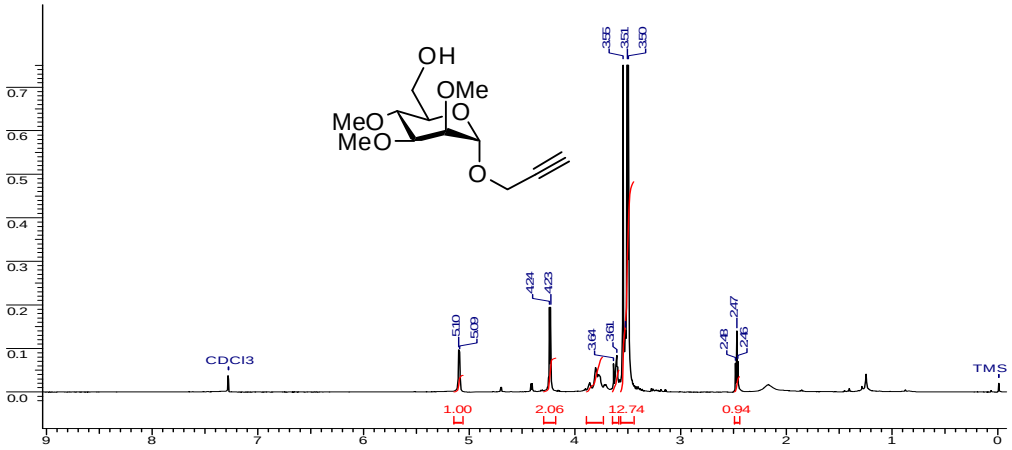
^{13}C NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **23**



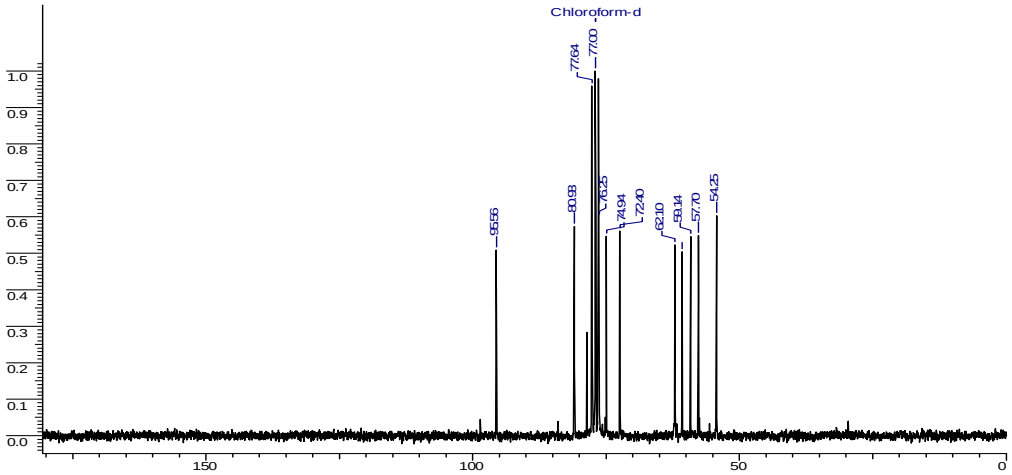
DEPT NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **23**



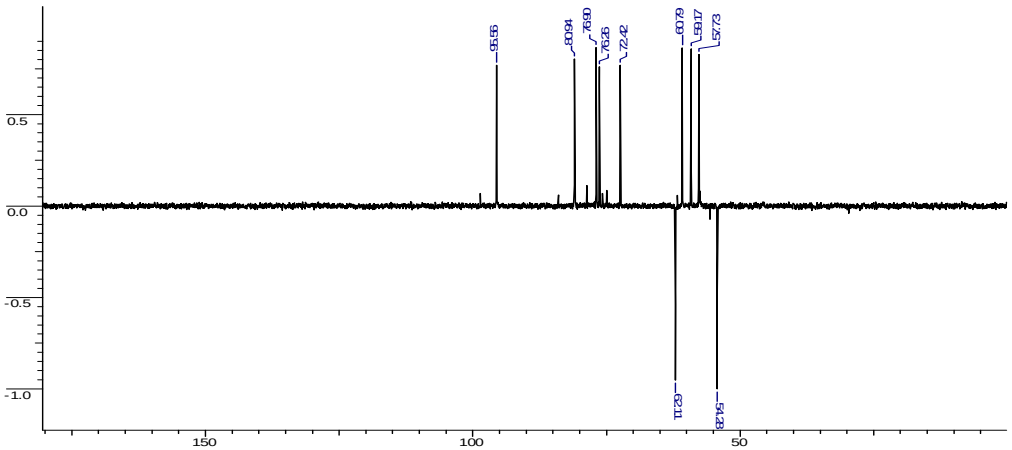
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **25**



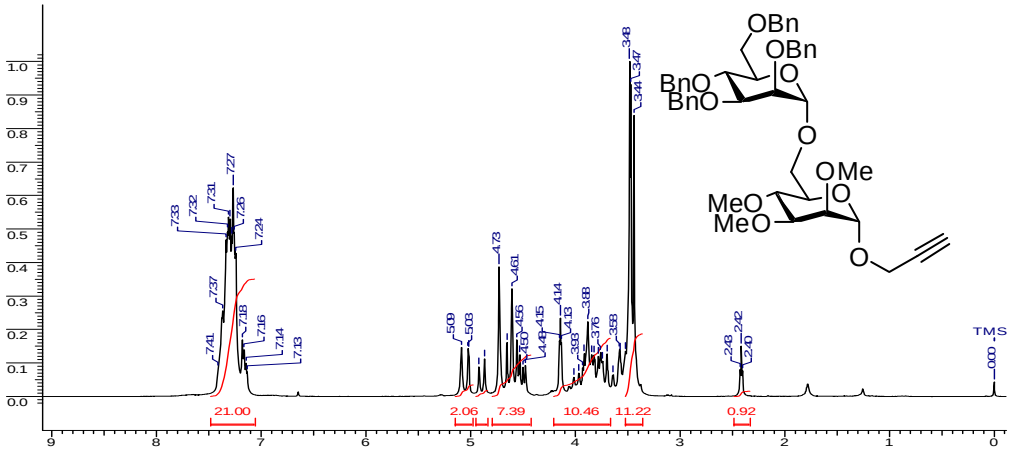
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **25**



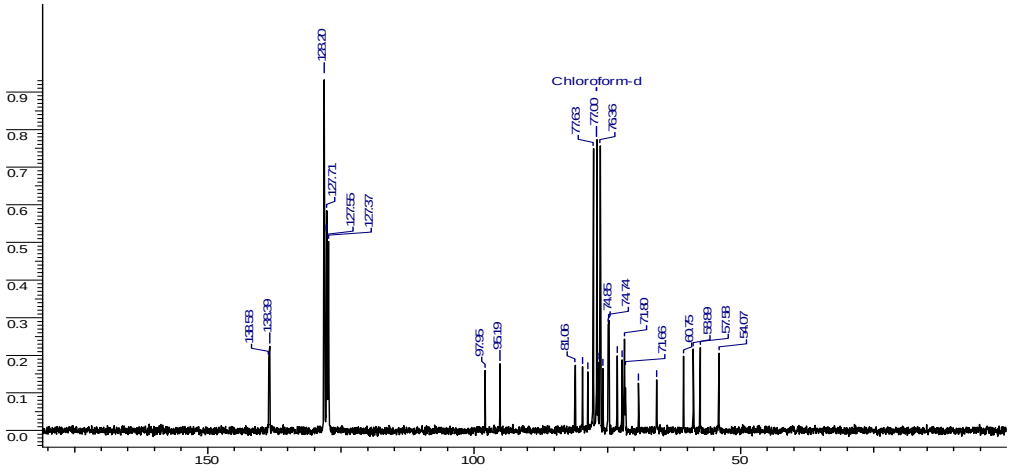
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **25**



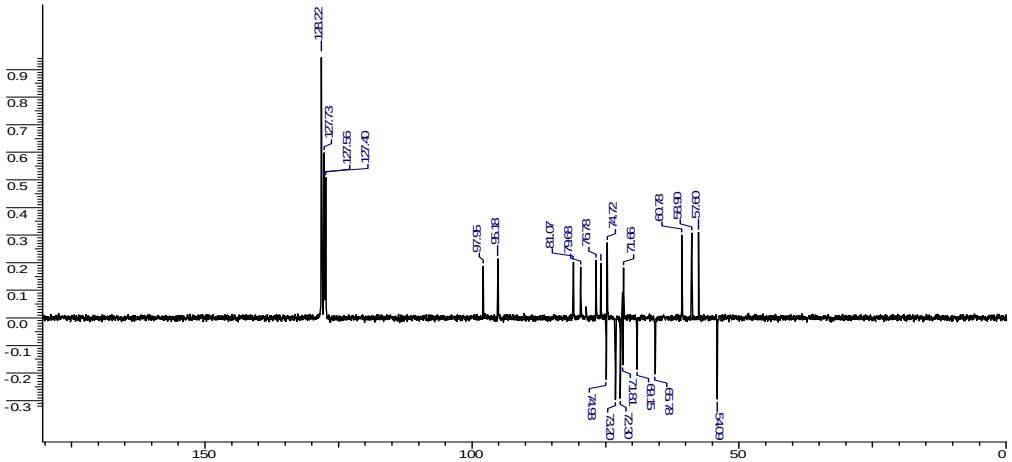
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **26**



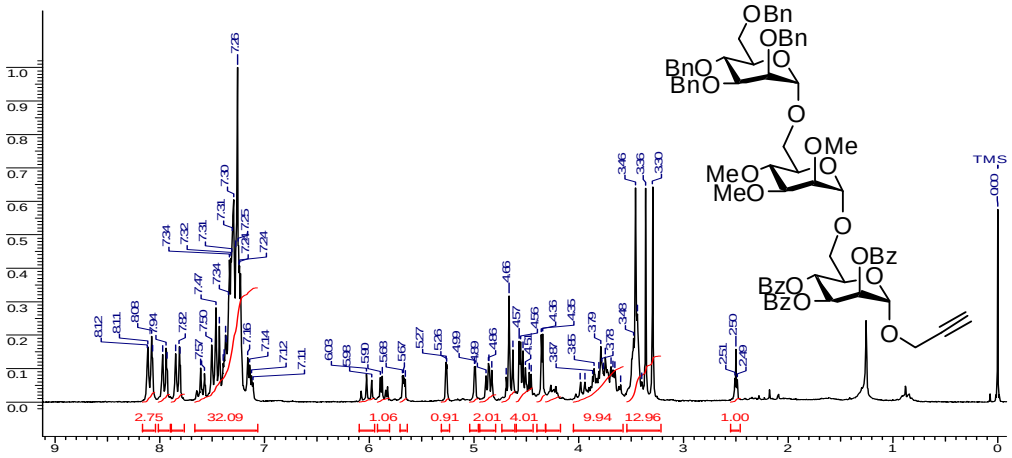
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **26**



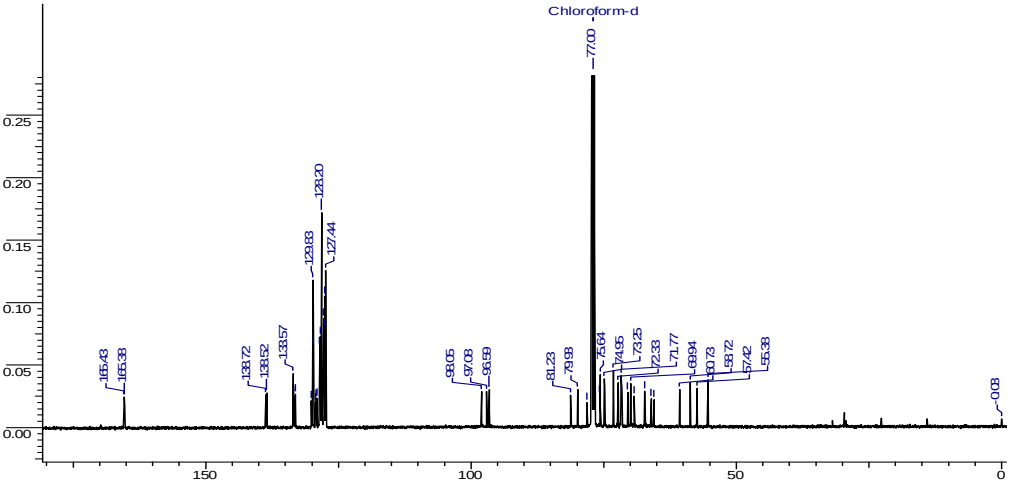
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **26**



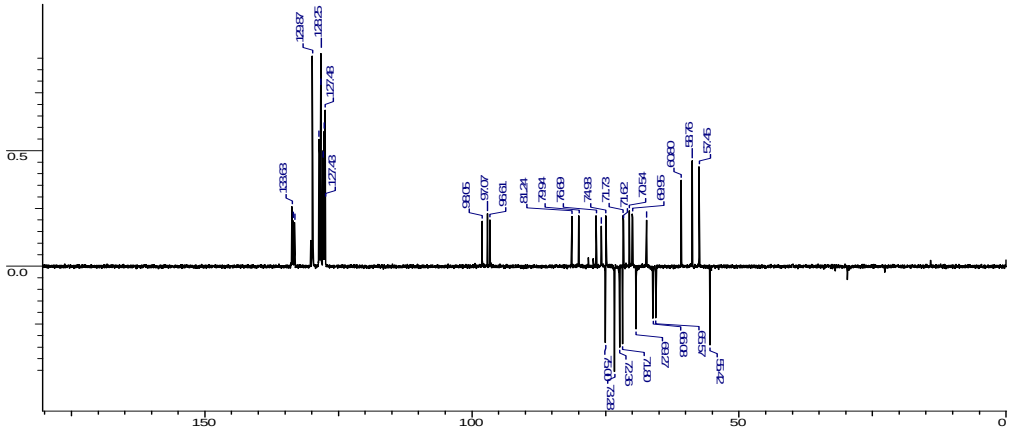
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **27**



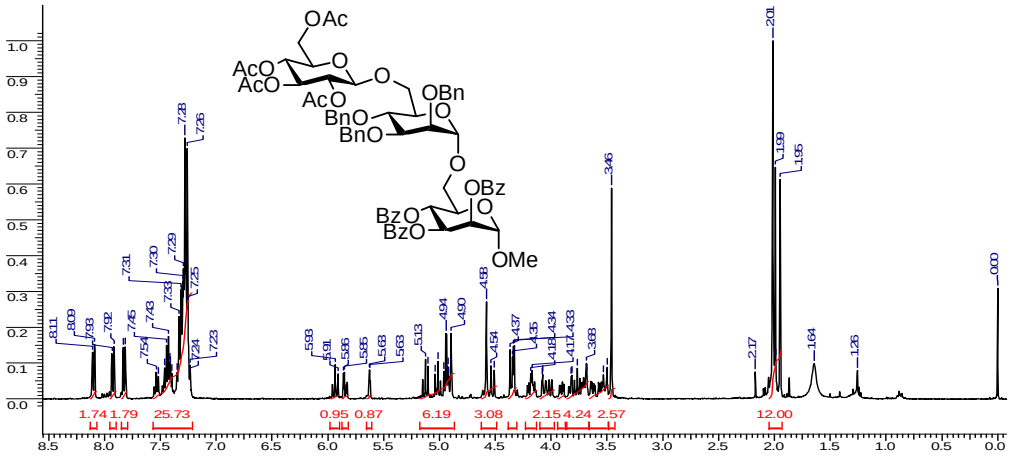
^{13}C NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **27**



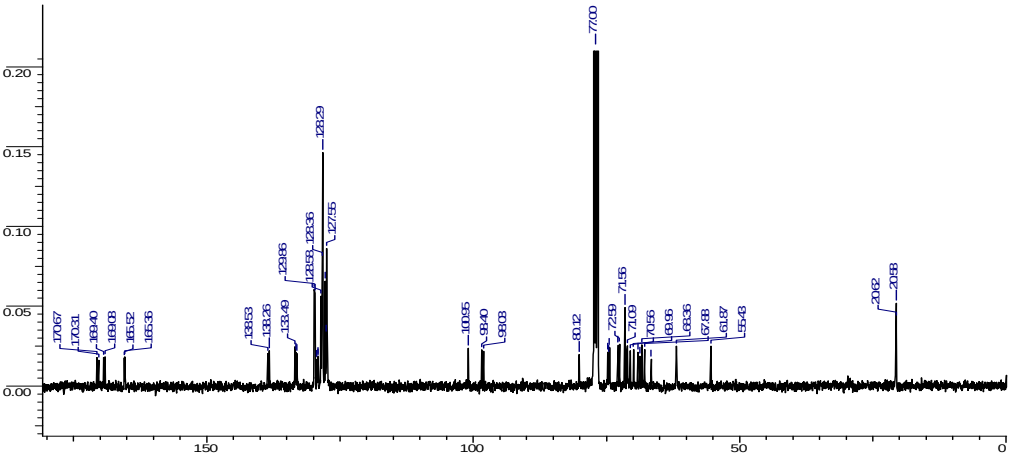
DEPT NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **27**



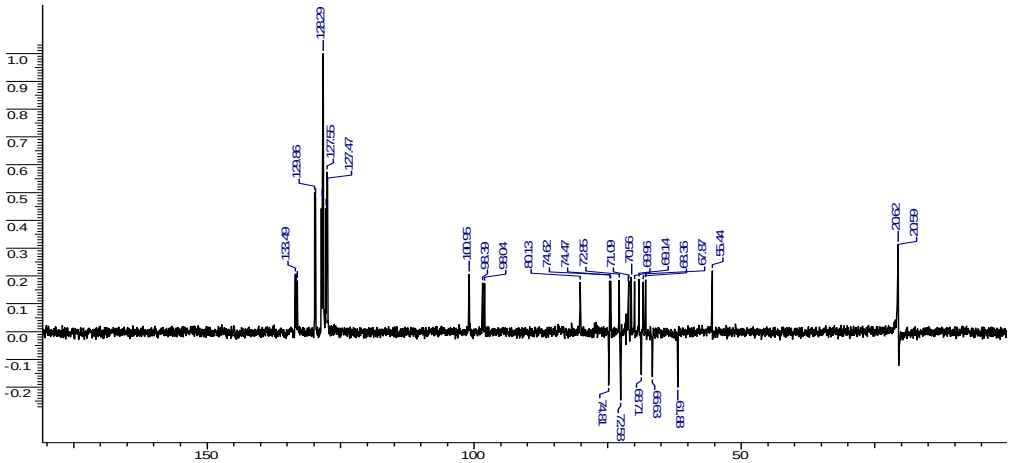
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **29**



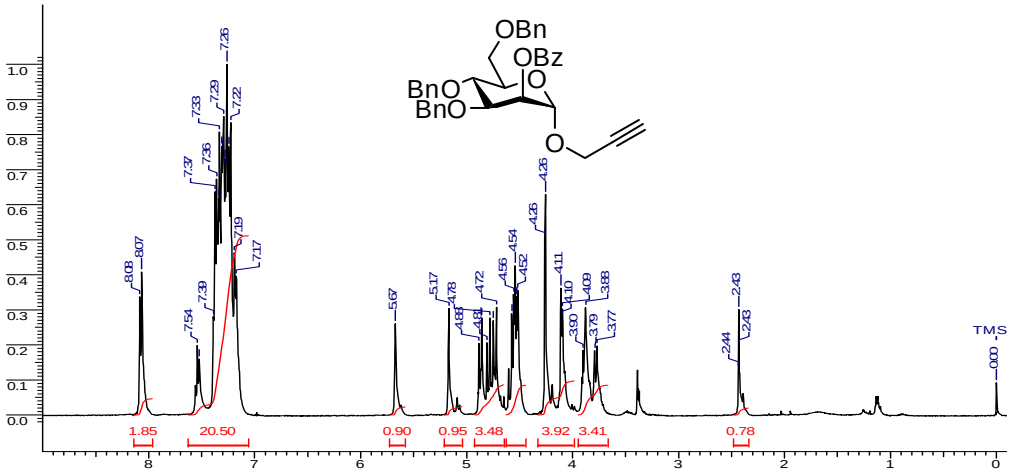
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **29**



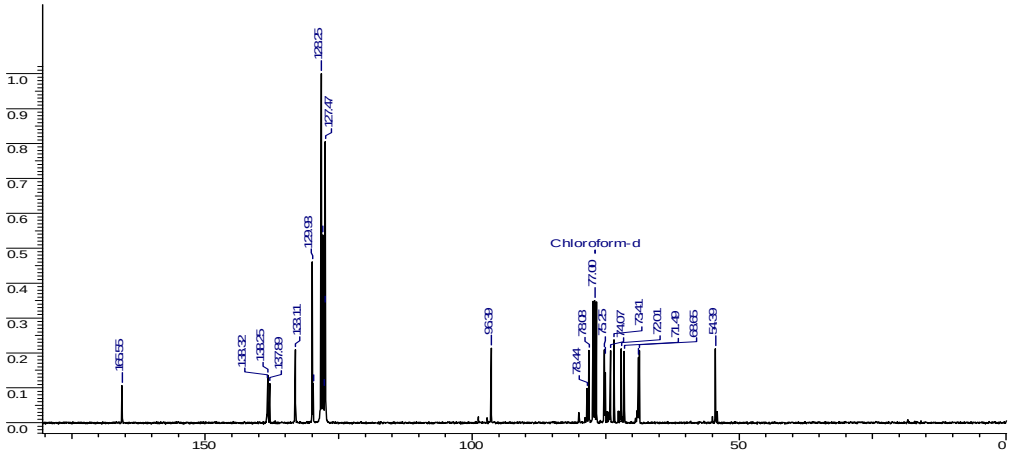
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **29**



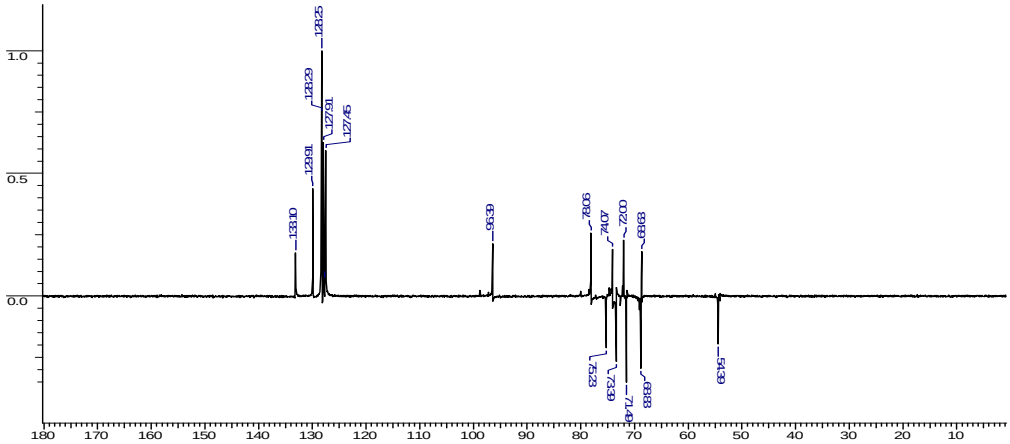
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **35**



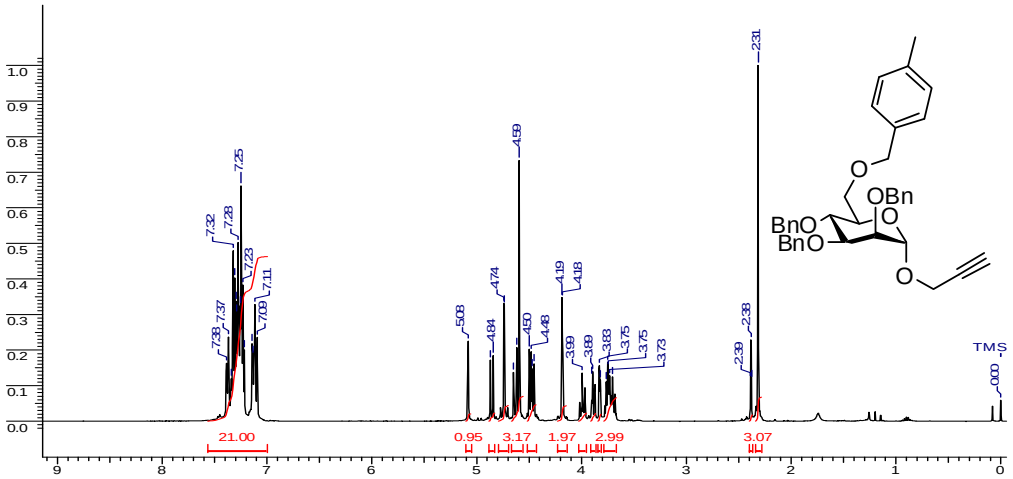
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **35**



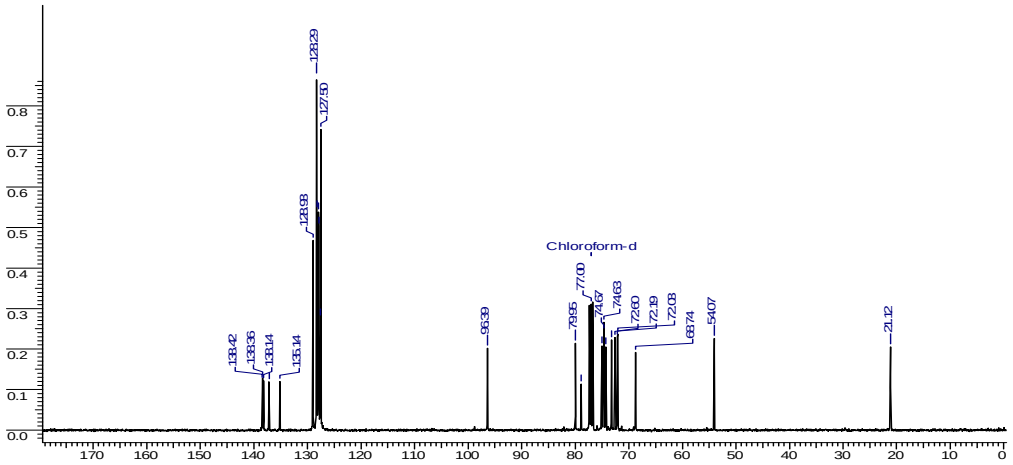
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **35**



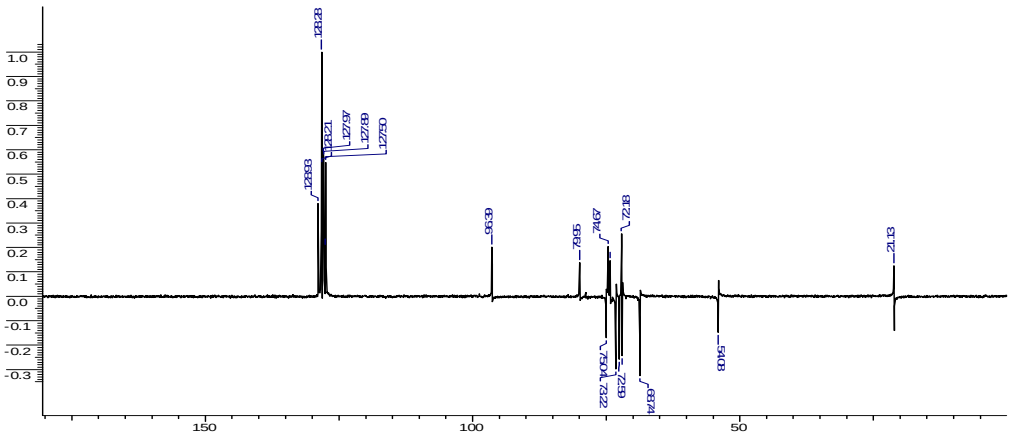
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **36**



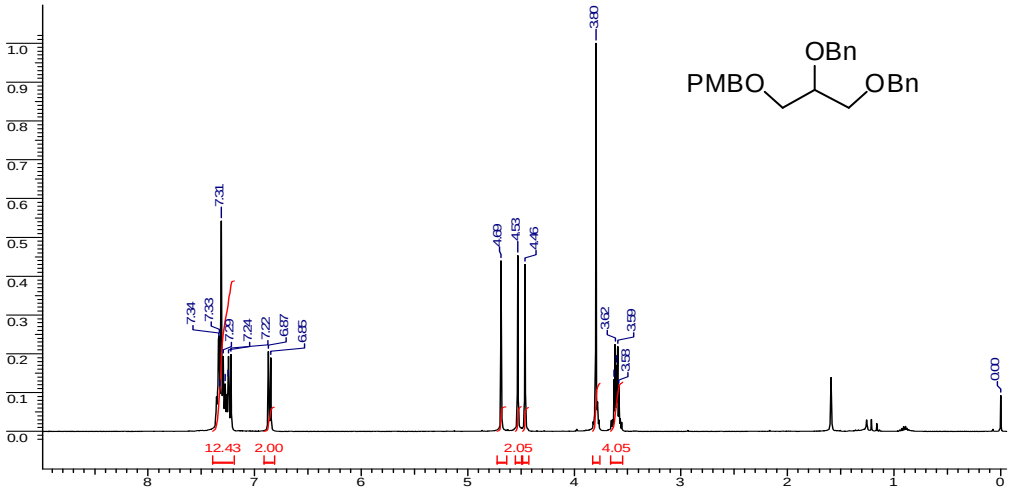
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **36**



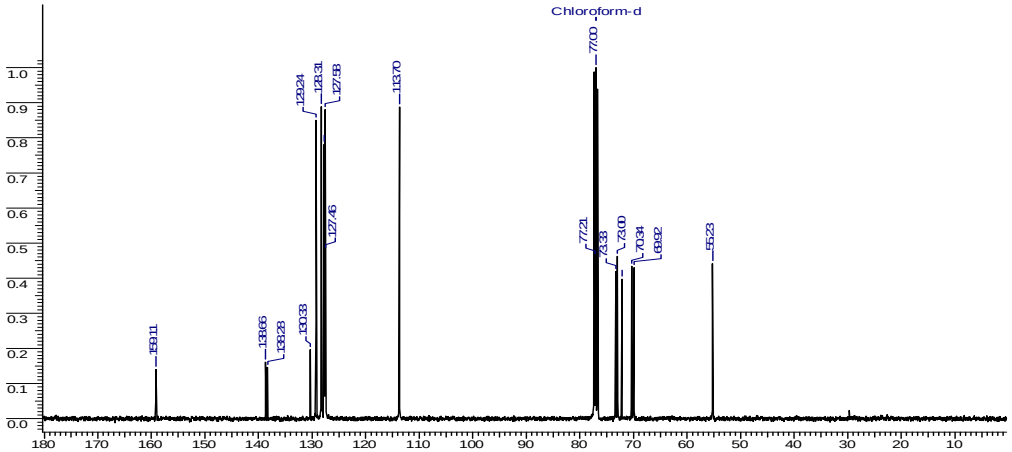
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **36**



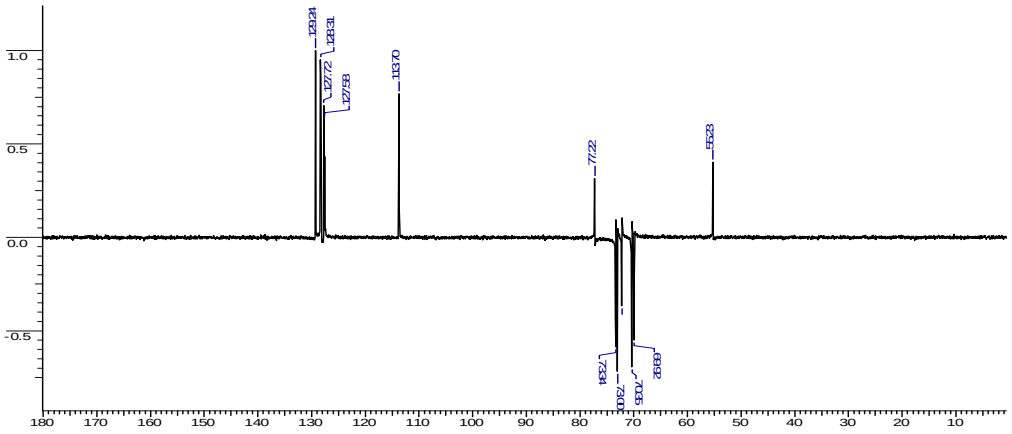
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **39**



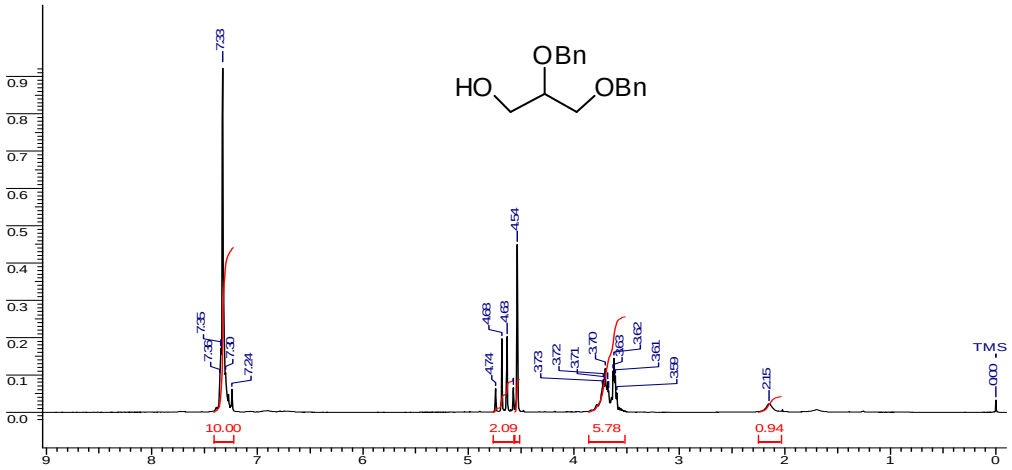
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **39**



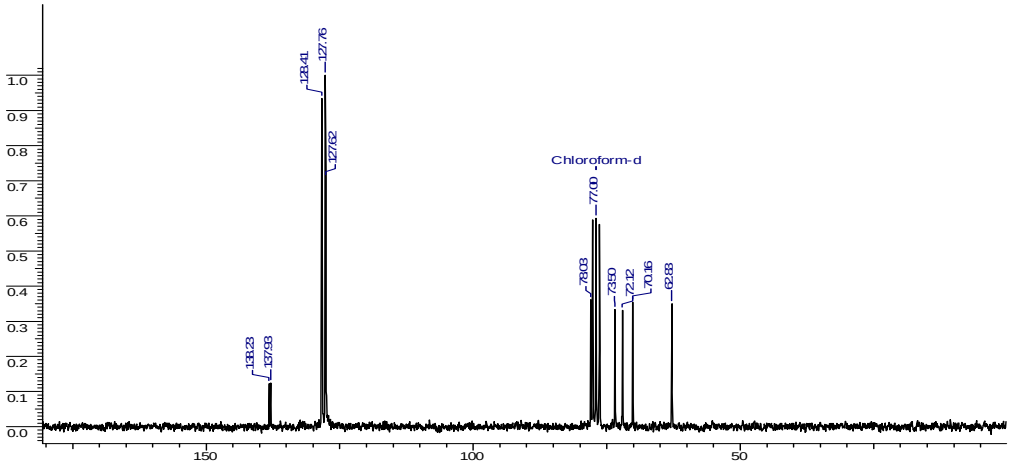
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **39**



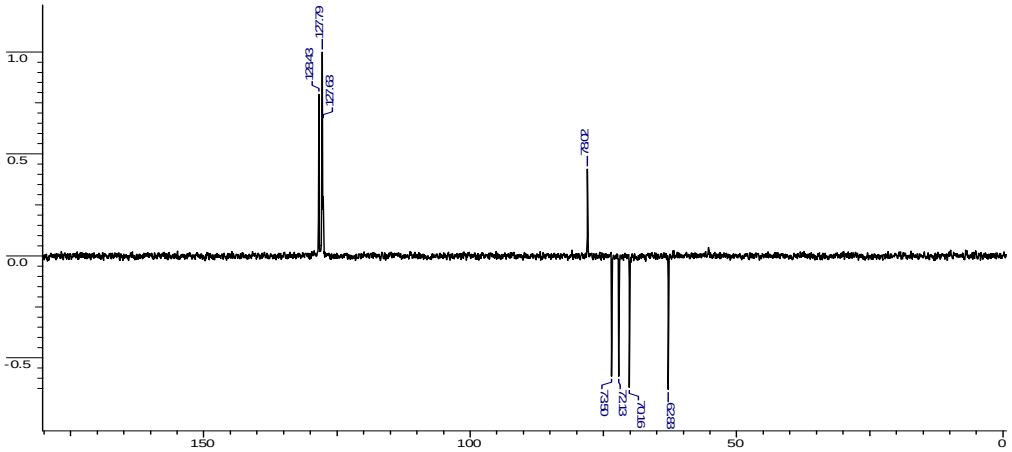
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **40**



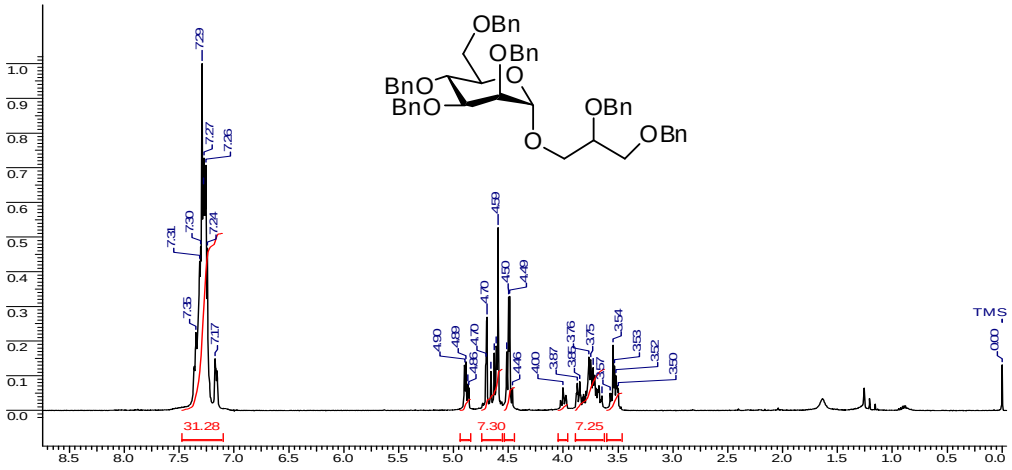
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **40**



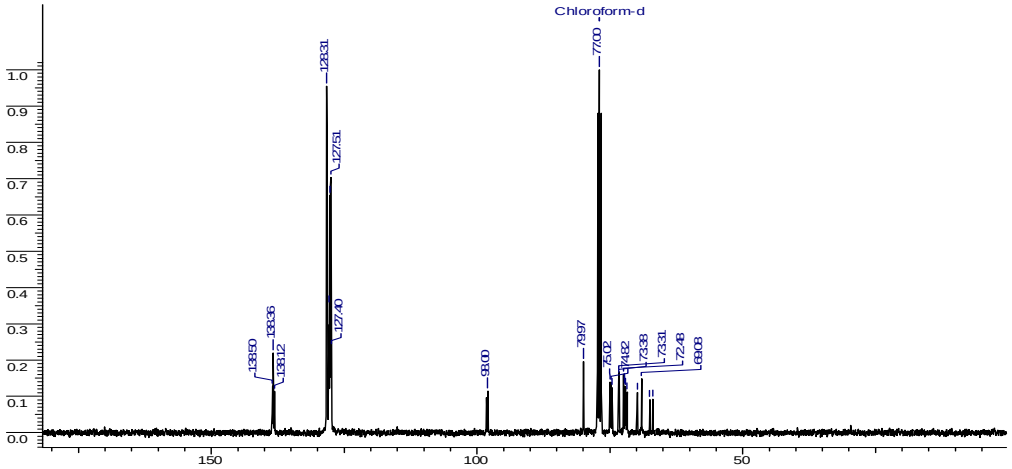
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **40**



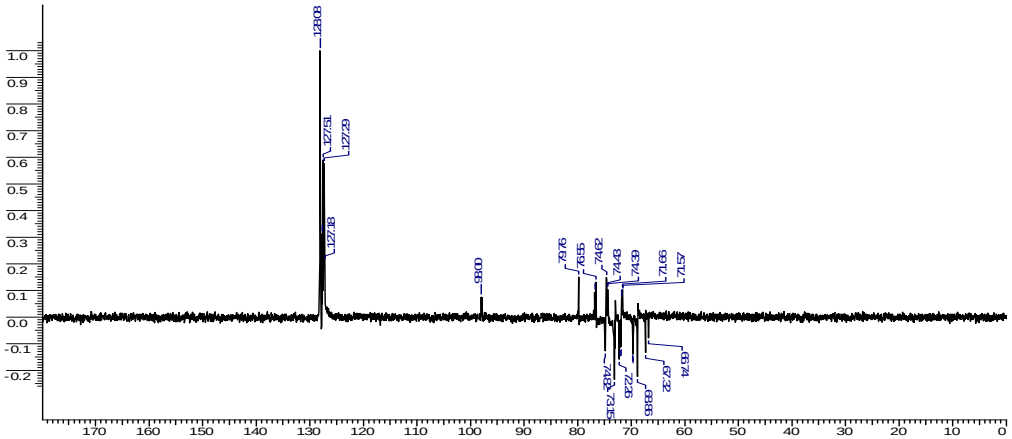
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **42**



^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **42**



DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **42**



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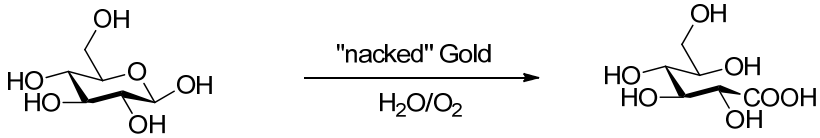
Gold is always been precious, a highly positive normal potential is responsible for occurrence of gold in elemental form, for example, as nuggets. Since ancient times, the desire to possess gold has been the driving force for many activities in human civilization and continuing its reputation in this modern era as valuable investment. Apart from the praiseworthy importance of gold in various fields, it has been heavily neglected for the early development of science and chemistry; especially in organic transformations, probably because of two reasons (i) the low reactivity of gold and (ii) the high value associated with gold, which leads to the assumption that such a catalyst would be unaffordable, which may not be true because the price of a catalyst is often dominated by the ligand rather than by the metal.[1]

Over the period of last two decades gold has gained a significant attention and rapidly became a hot topic in organic transformations by catalyzing different reactions and proved equally effective for homogeneous and heterogeneous reaction medium. Out of the different oxidation states possible for gold, in the presence of organic substrates, Au (0), Au (I), and Au (III) are possible. In aqueous solution, in the absence of stabilizing ligand, Au (I) spontaneously disproportionate to Au (III) and Au (0). In 1973 when *Bond* et al.[2] reported the hydrogenation of olefins over supported gold catalysts, which proved the fabulous activity of gold for driving reaction over the other known catalysts. More than a decade later, Haruta and Hutchings simultaneously [3] and independently reported gold to be an extraordinally good catalyst and subsequently demonstrated it experimentally. *Haruta* et al. investigated the low-temperature oxidation of CO[4] and Hutchings the hydrochlorination of ethyne to vinyl chloride.[5] Here both reactions have been done in heterogeneous medium. For the first time these studies showed gold to be the best catalyst for these reactions. *Haruta* et al. demonstrated that high selectivity in the heterogeneous oxidation of propene to propene oxide, one of the top targets in industrial chemistry, could be achieved with gold on titania.[6] The positional-selective oxidation of different alcohols and even carbohydrates with molecular oxygen, as developed by *Rossi* et al, represents another milestone in the story of gold catalysis.[7]

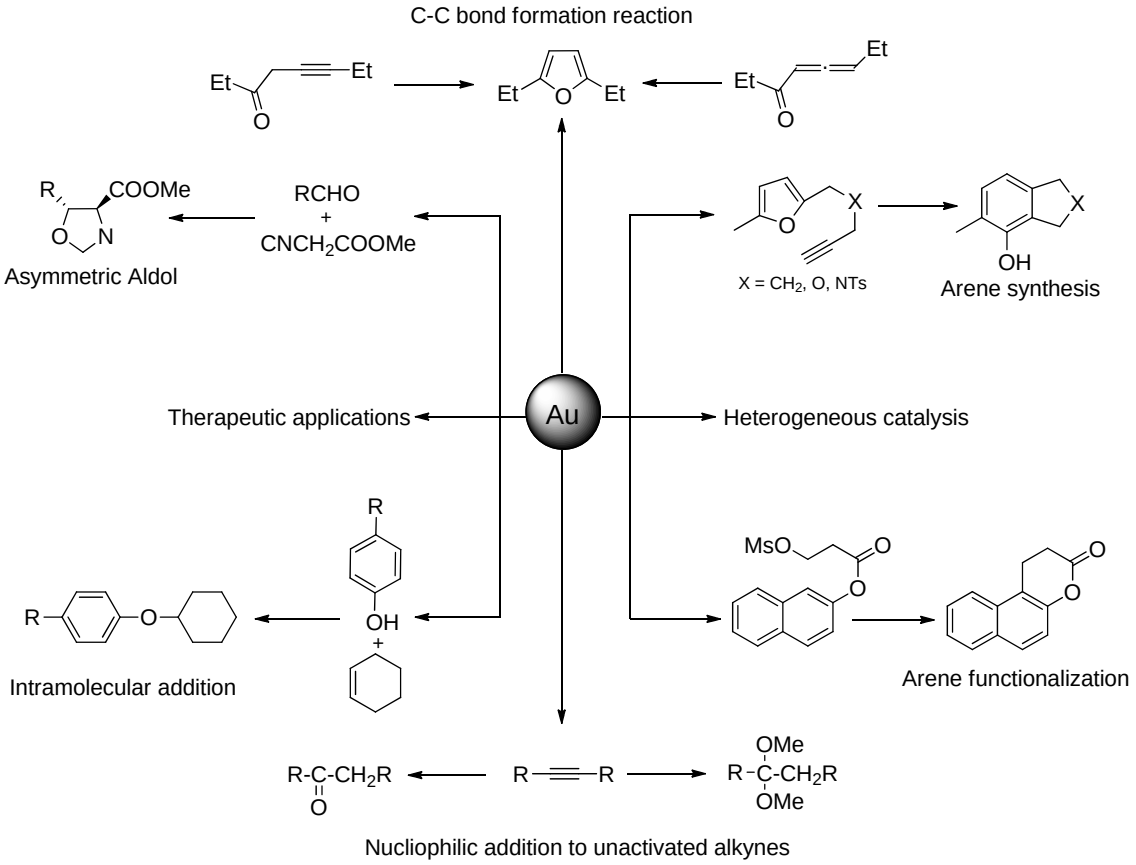
Scheme: 1



At about the same time a unique milestone in homogeneous asymmetric catalysis was established, when Ito et al. reported the first example of a catalytic asymmetric aldol reaction. They applied a Au (I) catalyst and an enantiomerically pure ferrocene diphosphane ligand for the addition of a carbon nucleophile to a carbonyl group.[8] The next important step in homogeneous catalysis was the addition of nucleophiles to alkynes, This approach was first investigated for alcohols, water, and amines by Fukuda and Utimoto.[9] A next crucial step for homogeneous catalysis followed in 2000 when *Hashmi* et al. extended the nucleophilic additions from alkynes to olefins for both the intramolecular additions of alcohols and the intermolecular addition of arenes.[10]

Subsequent studies by Yang and He investigated intermolecular reactions of alkenes with O nucleophiles[11] and provided evidence that the reactions with electron-rich arenes proceeded by an initial activation of an aryl C-H bond.[12] The other development initiated in 2000 by *Hashmi* et al. was the gold-catalyzed isomerization of ω-alkynylfurans,[13] which possess an enyne substructure, to phenols. Echavarren and co-workers[14] later finally demonstrated the involvement in this reaction of gold carbene species, one of the newest facets of gold catalysis.

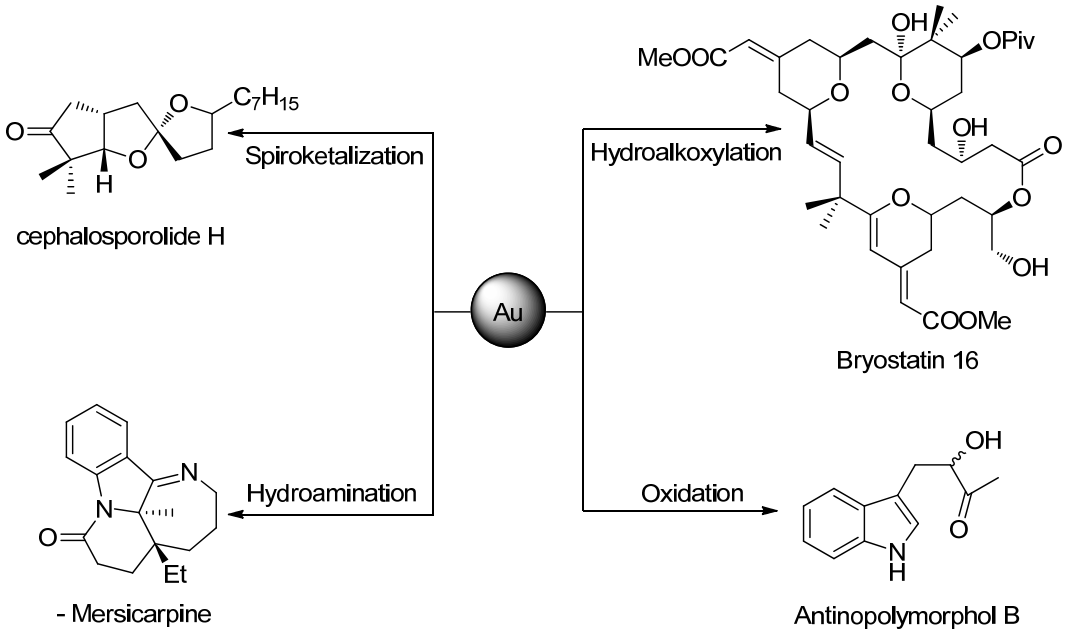
Figure: 1



Development in gold catalysis influenced the other fields as well, inspired from various gold catalyzed transformations, several total synthesis were reported based on gold catalyzed reactions as a key step. For example in the synthesis of Antinopolymorphol B, gold mediated transformation has been used for oxidation of alkene to corresponding ketone,[15] similarly in the synthesis of Bryostatin 16, hydroalkoxylation of alkyne has been done in the presence of gold catalyst, where this transformation, represents an impressive example of the high chemoselectivity. Moreover the gold-catalysed step is late in the synthesis, a plethora of functional groups must be tolerated and it is remarkable that only the alkyne is addressed even if several unsaturated moieties are present.[16] In continuation, gold mediated spiroketalization is used for the total synthesis of Ushikulide A,[17] Okadic acid,[18] Cephalosporolide H,[19] and Spirasterellolide F.[20] similarly Hydroamination of alkyne with gold catalysis has been addressed in the synthesis of (-) Mersicarpine[21] and Nitidine.[22] In an account for gold catalysis, several

other reports are available, in which gold mediated transformations were the key steps for synthesizing corresponding target molecules.

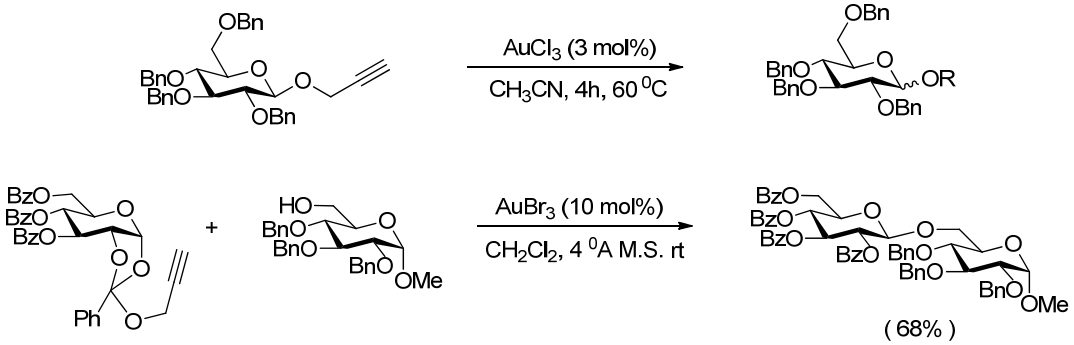
Figure: 2



The gold has worth's its importance in the field of medical science. The frequent use of gold in medicine confirmed the utility of metallic gold with high biocompatibility without any toxic effect.[23]

Apart from the reports by *Rossi* et al, gold mediated transformations in carbohydrates were completely unknown, until the first report from *Hotha* et al in 2006; who showed the utility of catalytic amount of gold (III) salts for transglycosidation.[24] This was achieved by keeping propargyloxy group at anomeric position, and later selectively activated to generate oxocarbenium, to make available for further glycosidation. The salient feature of this reaction is requirement of catalytic amount of gold salt, good reaction yields and mild reaction condition. Whereas the high temperature of reaction can be considered as a major drawback of this method.

Scheme: 2

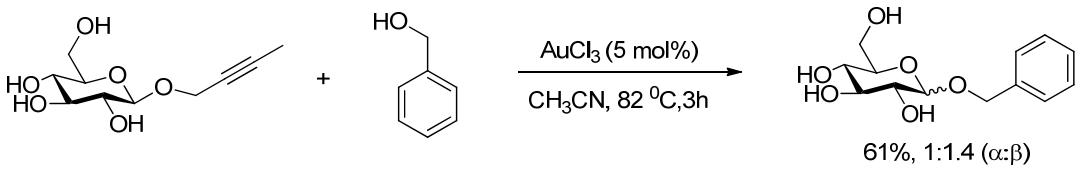


In order to get a stereoselective 1,2 *trans* glycosides, the same group came up with the concept of propargyl orthoesters, which subsequently used for stereoselective 1,2 *trans*

glycosidation with a wide range of aglycones in presence of 10 mol% of $AuBr_3$ in Dichloromethane and 4 ^{0}A molecular sieves powder at room temperature.[25]

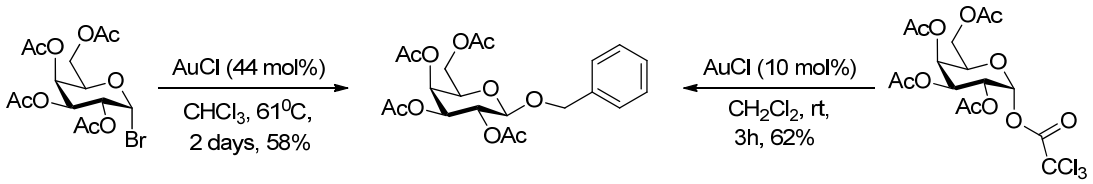
About the same time three more approaches were reported for gold catalyzed glycosidations. *Finn* et al showed the utility of Au(III) salt for unprotected propargyl glycosyl donors.[26] Where they have reported that donors containing the 2-butynyl group were more reactive, giving good yields of glycoside products. Secondary alcohols were also used but with diminished efficiency. The major drawback of this methodology was the high temperature of reaction and high molar concentration of aglycon (about 5 to 10 folds when compared to glycosyl donor).

Scheme: 3



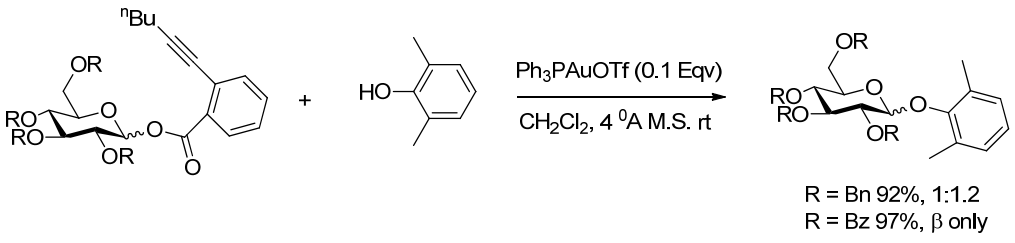
In a separate endeavor, Kunz and co-workers have reported gold (I) chloride catalyzed glycosylation reactions using the common glycosyl donors, glycosyl halides and glycosyl trichloroacetamidates. The Au(I) activation of glycosyl halide, requires high amount of catalytic gold salts, elevated reaction temperature and gives poor yields, this insufficient activation of glycosyl halides was rationalized on the basis of catalyst inhibition by halide anions. On the other hand the glycosyl trichloroacetamidates were activated at room temperature in presence of 5 mol% AuCl, furnished a transglycosides in 71% yield.[27]

Scheme: 4



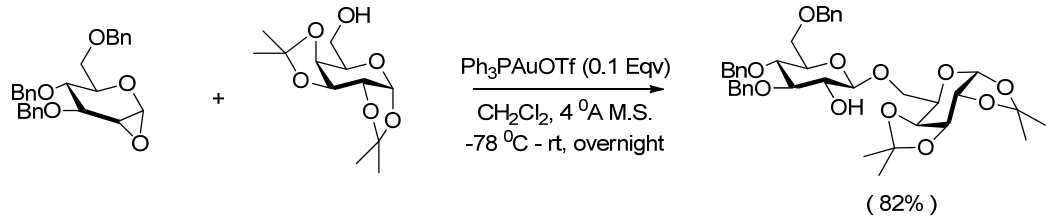
A significant development in the field of gold catalyzed glycosidation was reported by the group of Biao Yu, where catalytic amount of $Ph_3PAuOTf$ is used for the activation of glycosyl *ortho*-alkynylbenzoates.[28] This new method has significant merits as the glycosidic coupling yields are generally excellent, the donors are readily available and stable, the promotion is catalytic and mild reaction condition. The major disadvantage of this method is the sensitivity of leaving group towards basic reaction media, which restricts the manipulation of protecting groups and hence not suitable for the strategies like an armed-disarmed concept.

Scheme: 5



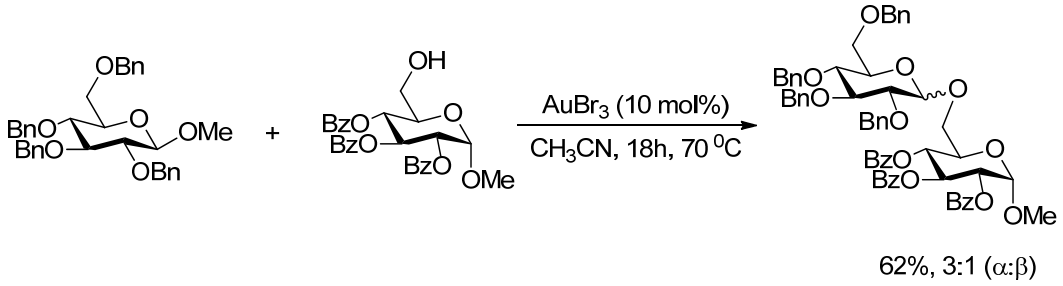
The glycosidation reaction of 1,2-anhydrosugars and its application in the construction of complex carbohydrates have been well elaborated by Danishefsky and co-workers.[29] where, multi equivalents of $ZnCl_2$ is mostly employed as a promoter in coupling with ordinary alcohol acceptors. However lower reaction yields or sometime failure to get desired product with Zn mediated methodology is common. To avoid this *Yu* et al reported the utility of $Ph_3PAuOTf$ as an effective catalyst for the glycosidation with 1,2-anhydrosugars.[30]

Scheme: 6



In 2009, *Hotha* et al reported methyl glycosides also activated in presence of gold (III) salts and thereby exploited methyl glycosides as stable glycosyl donors.[31] A diverse range of aglycons are shown to react with methyl glycosides, resulting in the formation of corresponding glycosides and disaccharides in good yields. Here, anomeric methyl group was activated in presence of $AuBr_3$, Proposed the oxophilic behavior of gold at elevated temperature. During the program in synthesis of oligosaccharide using armed-disarmed concept, we then observed the cleavage of interglycosidic bond, which further confirmed the oxophilic behavior of gold at elevated temperature.[32]

Scheme: 7



With a remarkable development in gold catalyzed glycosidation, over a period of last two decades, still a lot can be expected to come out in future. The increased understanding of the important roles that oligosaccharides and glycoconjugates play in biological processes has led to a demand for significant amounts of these materials for biological, medicinal, and pharmacological studies. Therefore, tremendous effort has been made to develop new procedures for the synthesis of glycosides. In this premise, further developments in gold catalyzed glycosidation can make a significant contribution. Depending on previous clarification, these reactions have the characteristics like gentle reaction conditions, atom economic, high yielding, and compatible with panel of different glycosyl acceptors. These inbuilt qualities of gold catalyzed glycosidation assure a systematic approach in this field has a potential to

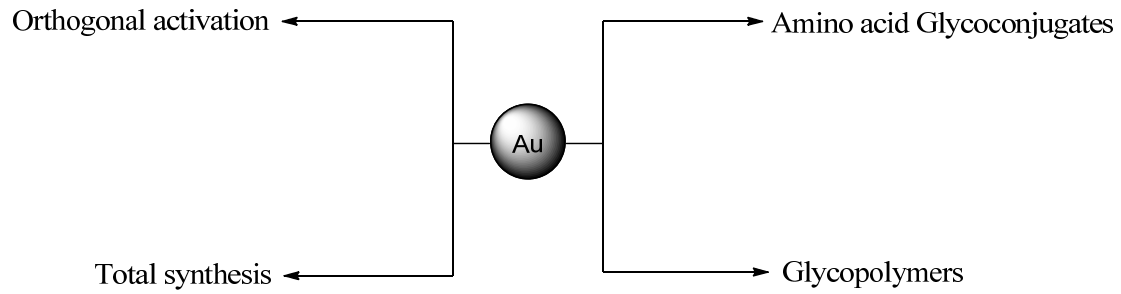
generate a multipurpose method which can fulfill the majority criteria's of ideal glycosidation.

Addition of a silver salt as co-catalyst is the one way of improving the performance of gold catalyzed transformations. In gold catalysis, a silver salt with a non-coordinating counter ion is often added to abstract a halogen from the gold species, leaving the homogenous gold catalytic system and extremely insoluble silver halides. Phosphorus NMR studies also revealed that the gold complexes in solution were influenced by silver, which promotes catalytic activity of gold and, suggesting a cooperative catalytic system between gold and silver salts.[33] Based on this hypothesis a wide range of gold catalyzed reactions are reported in the literature with the "silver effect" on the reactivity of the catalytic systems. Even our earlier studies, recommend to use silver as co-catalyst for improving the performance of gold catalyzed glycosidation reactions.

Glycoconjugates are the class of biomolecules which play important role in various intracellular and extracellular events. Chemical synthesis of such glycoconjugates, worth's due to their limited access; as these glycoconjugates are present in microheterogenious form. Chemical synthesis of glycans depends upon two important building blocks which are called glycosyl donor and glycosyl acceptor (or aglycon). A glycosyl donor is defined as any substance which upon activation forms the oxocarbenium ion by departing the leaving group attached to anomeric carbon and makes itself available for further attack of nucleophile or acceptor through an interglycosidic bond and form glycoside product. Thus development of efficient glycosylation methods which are reliable and with diverse substrate scope would be a right step for the synthesis of oligosaccharides. An ideal glycosylation should have one or more of the following characteristics: (i) easy to prepare/access; (ii) stable to diverse chemical reactions; (iii) regio- and stereoselective; (iv) use catalytic reagents; (v) generate minimum amount of waste; and (vi) avoid use of toxic metals in order to make glycosylation as an efficient reaction.[34]

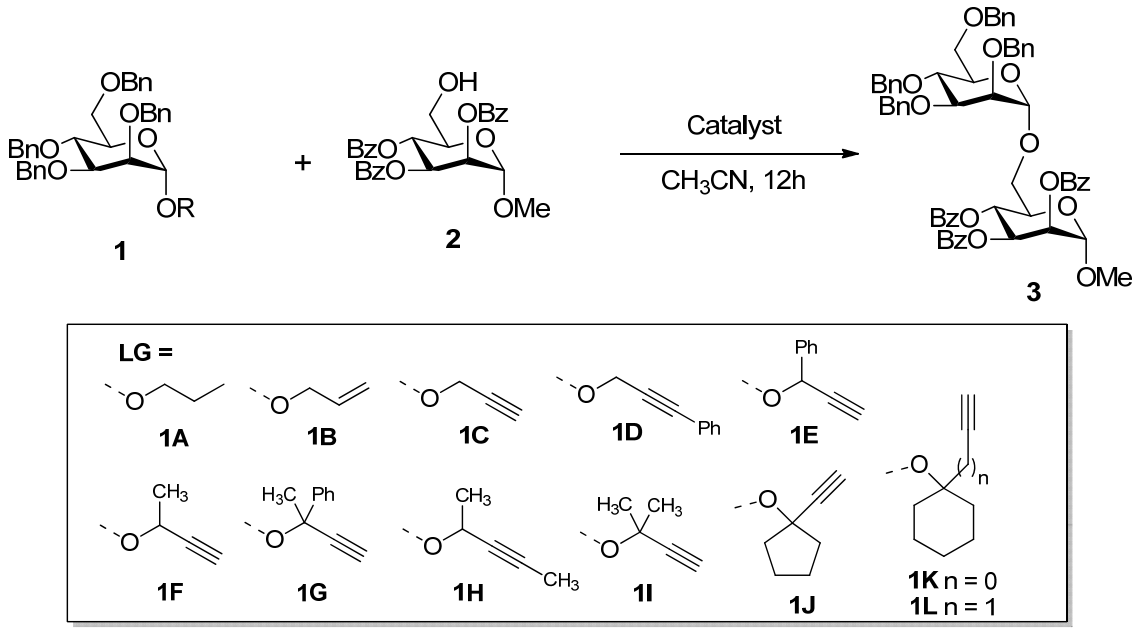
From our laboratory, stable propargyl glycosides were discovered to act as glycosyl donors when activated in the presence of catalytic amount of gold (III) halides. Salient features of this gold-catalyzed transglycosidation using propargyl glycosides are: (i) glycosyl donors can be prepared from aldoses under modified Fischer glycosidation conditions; (ii) propargyl group is stable to many of the diverse chemical manipulations; (iii) the activation by catalytic quantity of noble gold halide; and (iv) no byproduct formation.

Figure: 3



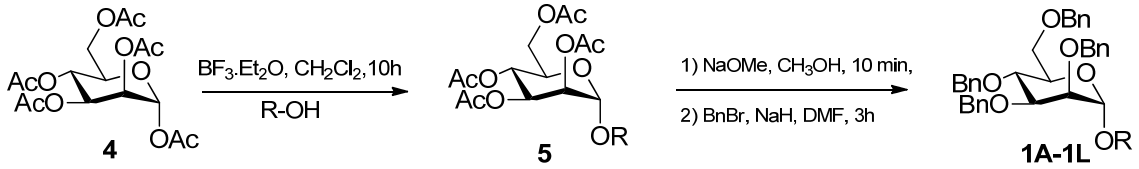
During the period of last six years, the utility of gold catalyzed glycosidation proved significant in the areas like synthesis of amino acid glycoconjugates,[35] oligosaccharide synthesis by orthogonal activation,[36] and total synthesis of tetrasaccharide cap of the lipophosphoglycan expressed on the cell surface of the surface of *Leishmania* parasite.[37] Gold-catalyzed glycosidation strategy was also found to be superior for the synthesis of glycopolymers with acrylate, acrylamide and polypeptide backbones.[38] However, a major impediment for improving the scope of gold-catalyzed transglycosidation was found to be the high reaction temperature and oxophilicity of gold salts. Thus, systematic investigation of various alkyne bearing appendages was carried out to find a leaving group that would facilitate transglycosidation at ambient temperatures.

Scheme: 8



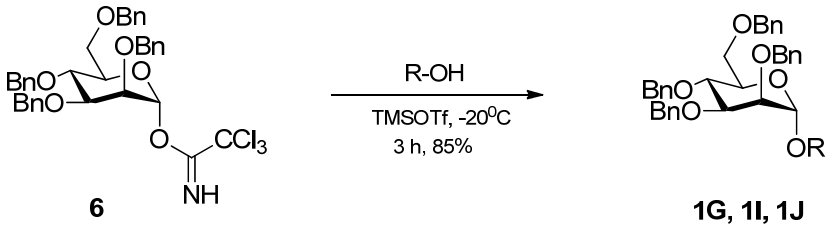
To begin with, synthesis of mannopyranosyl disaccharide (**3**) is considered as a model reaction (scheme 8) in view of previous observations that propargyl mannopyranosides give α-anomers only due to the bulky -OBn at the *C*-2 position as well as the anomeric effect.[24] Aglycon **2** was selected among host of possible sugar alcohols in order to avoid competing side reactions. Alkyl substituted mannopyranosyl donors (**1A**-**1L**) were prepared in parallel in three simple steps; first, per-*O*-acetyl mannospyranose was reacted with alcohols **A**-**L** using $BF_3.Et_2O$ and then deacetylated under Zemplén conditions and per-*O*-benzylated using NaH, BnBr in DMF.

Scheme: 9



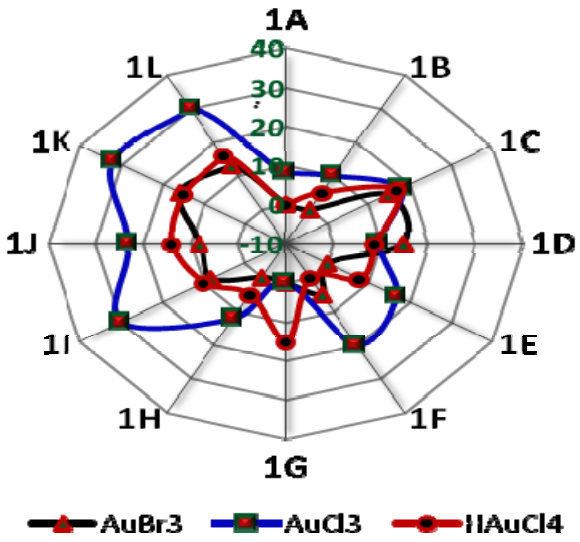
The synthesis of mannopyranosyl donor **1G**, **1I** and **1J** is carried out by using trichloacetamidate method.[3] As per-*O*-acetyl mannopyranoside on reaction with corresponding alcohols in presence of $BF_3.Et_2O$, were insufficient to get required products in good yields.

Scheme: 10



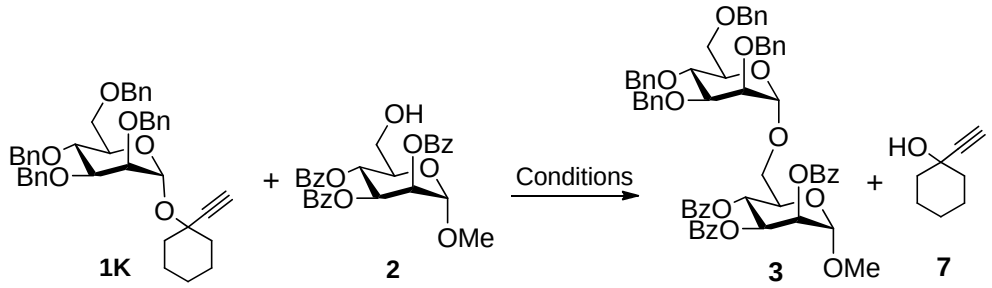
In order to check the efficiency of potential mannosyl donors (**1A**-**1L**), were allowed to react with Aglycon **2** in the presence of three widely available gold catalysts $AuBr_3$, $AuCl_3$ and $HAuCl_4$ at room temperature for 12h in CH_3CN (Figure **4**). Glycosyl donors **1A** and **1B** which do not possess alkyne groups did not proceed satisfactorily and simple propargyl substitution (**1C**) was found to give about 18% yield after 12h at room temperature in the presence of $AuCl_3$ (Figure 4). Single aromatic substitution on the propargyl moiety (**1D** and **1E**) also failed to give good yields where methyl substitutions (**1F**, **1H**) showed good conversion with $AuCl_3$ but not with $AuBr_3$ and $HAuCl_4$. Between, *gem*-disubstituted donors **1G** and **1I**, dimethyl donor **1I** was found to be superior. However, placing the cyclic substitution (**1J**-**1L**) in place of *gem*-dimethyl was found to be highly beneficial. Nevertheless, best results in the screening process were observed with donors **1I**, **1K** and **1L**. Significance of increased reactivity of *gem*-disubstituted donors can be attributed to the earlier reported Thorpe-Ingold like effect.[40]

Figure: 4



Mannosyl donors **1F** and **1I** were not considered further because of the observed instability of the compound, ease in preparation and/or cost of the aglycon. Donor **1K** was found be better than **1L** purely because of the easy availability and low cost of **1K** though both **1K** and **1L** fared almost equally. The $AuBr_3$ catalyzed reaction of mannopyranosyl donor **1K** with aglycon **2** at room temperature gave 14% yield of required disaccharide, but in presence of 5 mol% $AuCl_3$; the yield of anticipated product was improved to 36% similarly reaction of mannopyranosyl donor **1K** with aglycon **2** in presence of 5 mol% $HAuCl_4$ gave only 14% yield. While doing this reaction in presence of different gold salts, we have successfully isolated 1-ethynyl cyclohexanol (**4**) which was quite similar with our earlier observations, where liberation of propargyl alcohol was observed when propargyl glycosyl donors were activated in presence of gold. Identification of good leaving group for the gold-catalyzed transglycosidation reaction prompted us to optimize for the right catalytic conditions (Table 1).

Table: 1



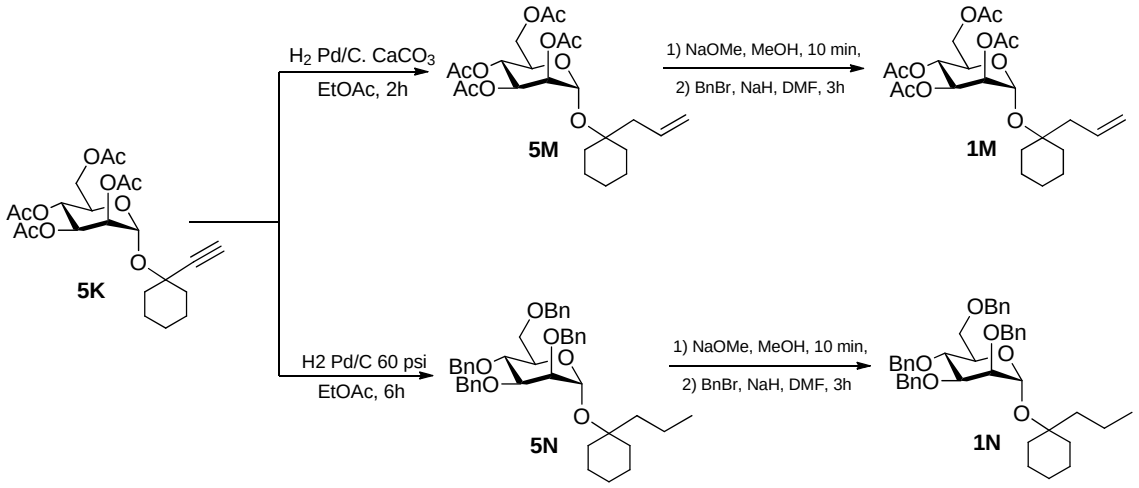
Entry	Catalyst	Solvent	Time (h)	Temp (^oC)	% Yield
1	$AuCl_3$	CH_3CN	8	45	71
2	$AuBr_3$	CH_3CN	8	45	74
3	**$AuCl_3$**	**CH_3CN**	**8**	**70**	**86**
4	$AuBr_3$	CH_3CN	8	70	82
5	$AuCl_3$+AgOTf	CH_3CN	3	25	83
6	**$AuCl_3$+$AgSbF_6$**	**CH_3CN**	**4**	**25**	**91**
7	$AuBr_3$+$AgSbF_6$	CH_3CN	12	25	90
8	**$AuCl_3$+$AgSbF_6$**	**CH_3CN+CH_2Cl_2**	**4**	**25**	**96**

Heating the donor **1K** and aglycon **2** to 45^{o}C in the presence of $AuCl_3$ or $AuBr_3$ increased the yield of the reaction substantially (Table 1, entry 1,2); further increase to 70 ^{o}C showed further improvement to 80s (Table 1 entry 3,4). Inspired by several literature reports on the enhancement of performance in gold catalyzed reactions by the addition of Ag-salts, addition of Ag-based co-catalysts was then studied.[33] Accordingly, optimization of glycosidation with 5mol% each of $AuCl_3$ and AgOTf showed that the reaction can be carried out at room temperature without compromising yields (entry 5). Nevertheless, transglycosidation between **1K** and **2** in the presence of AuX_3-$AgSbF_6$ was found to be highly efficient (91% in 4h) at desired room temperature (entry **6**,**7**). The best result (96% in 4h) of disaccharide **3** was obtained when the transglycosidation reaction between **1K** and **2** was conducted in acetonitrile-dichloromethane (1:1) at room temperature for 4h in the presence of 1:1 quantity of 5mol% of $AuCl_3$ and $AgSbF_6$ (entry 8) and thus all further studies were conducted with these optimized reaction conditions only.

Furthermore, in a control experiment, reaction **1K** + **2** failed to proceed in the presence of Et_2O.HCl Besides, addition of a drop of Et_3N to the reaction mixture quenched the progress of the reaction suggesting the presence of Brønsted acid. Reaction with Au_2O_3 which has Au(III) but not a Lewis acid showed no reaction suggesting a role for both Lewis and Brønsted acidity for the transglycosidation process. The liberation of 1-Ethynyl cyclohexanol, encouraged us to check the role of alkyne for gold mediated transglycosidation reaction. Accordingly we prepared mannopyranosyl donor **1M** by

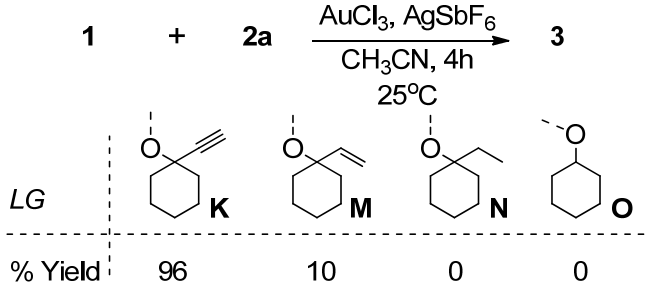
partial reduction of alkyne to alkene. Similarly mannopyranosyl donor **1N** was prepared through hydrogenation of alkyne to get simple alkane. Similarly mannopyranosyl donor **1O** was prepared to check the significance of substitution on cyclohexanol (scheme 11).

Scheme: 11



In the presence of aforementioned condition the treatment of aglycon **2** with mannopyranosyl donors **1K**, **1M**, **1N**, and **1O** confirmed the significance of alkyne group; as the partially reduced compound **1M** resulted in diminished yield whereas the fully saturated donor **1N** did not show any conversion at all and similar is the case with the simple cyclohexyl mannopyranosyl donor **1O** signifying, the presence of alkyne in the glycosyl donor.

Scheme: 12

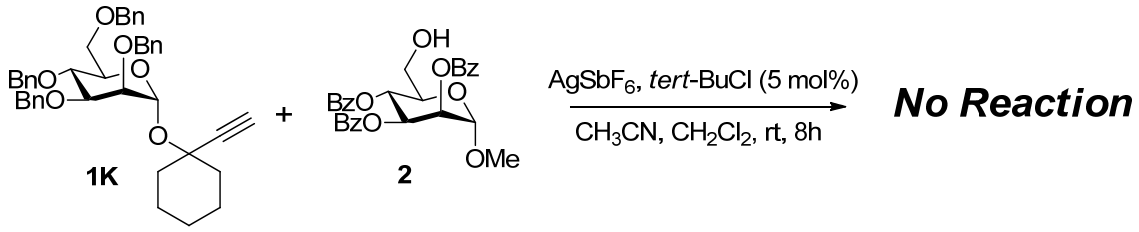


It is essential to mention here; on room temperature only silver salts are incapable to activate propargyl glycosides, whereas propargyl glycosides can be activated in presence of gold with poor yields. But addition of catalytic amount of silver salt in presence of gold dynamically improves the performance of transglycosidation reaction and forms anticipated product in quantitative yields, where both Lewis acidity and Brønsted acidity plays an important role.

In order to check the role of hidden Brønsted acidity,[41] later we have carried out a reaction in presence of $AgSbF_6$ and *t*-BuCl, with mannopyranosyl donor **1K** and aglycon **2**, in presence of acetonitrile and dichloromethane (1:1 mixture) at room temperature for 8h, but found insufficient for transglycosidation reaction, which then

ruled out the possibility of hidden Brønsted acid catalysis, and further confirmed the importance of gold for activating propargyl glycosides.

Scheme: 13



To understand the mechanism, THP protected 1-ethynylcyclohexanol **11**(Ech-OH) was chosen as model glycosyl donor for GC studies since glycosyl donor **1K** and THP-Ech ether (**8**) are both acetals and hence, the later should be sufficient to act as a glycosyl donor for the transglycosidation with 4-methylbenzyl alcohol (**9**). Initially, individual components such as THP-Ech ether (**8**), aglycon (**9**), required transglycosylated product (**10**), leaving group (**7**) and 4-methylbenzyl bromide (**11**) were injected into the gas chromatograph and obtained well separated retention times and followed by which the reaction mixture was injected. Independently, 4-methylbenzyl alcohol was found to give bromide **11** in the presence of $AuBr_3$.

Scheme 14:

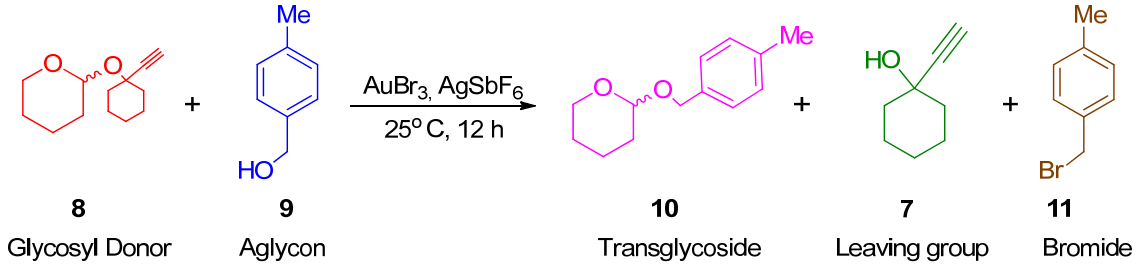
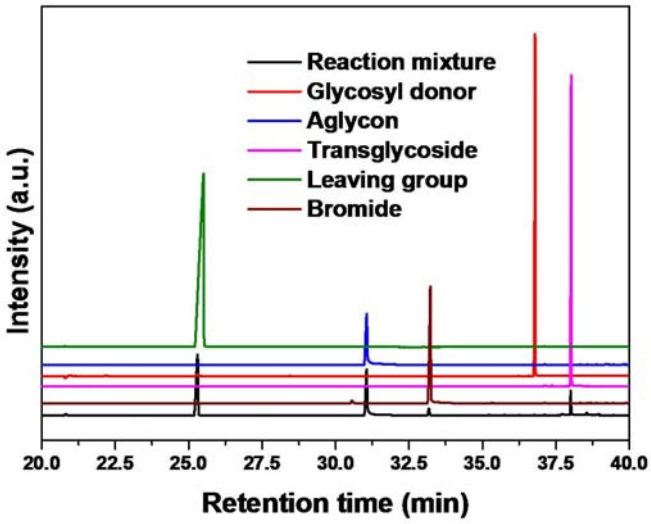


Figure: 5

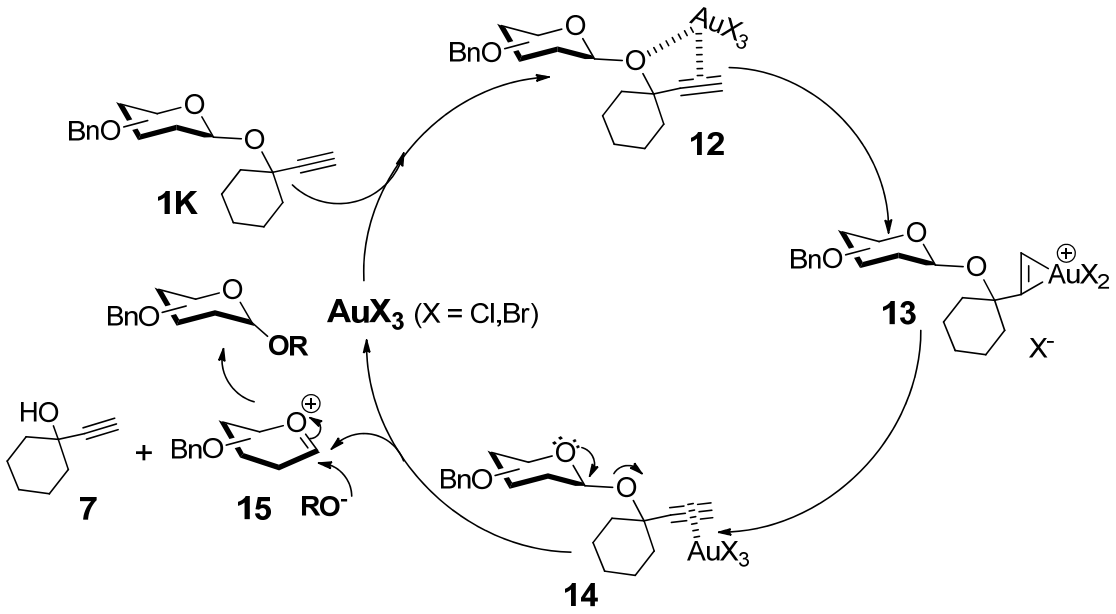


The donor **8** at retention time (Rt) 36.5min got disappeared completely in 4h and newly formed transglycosylated product **10** (Rt 38.0min) coincided with that of the standard and to our surprise, we observed simple 1-ethynylcyclohexanol **7** at retention time (Rt)

of 25.3min and 4-methylbenzyl bromide **11** at Rt 33.2 min (figure **5**). Formation of intermediate **10** is surprising since it contradicts earlier studies which postulated that propargyloxy group gets converted to cyclopropanone through a series of unidentified intermediates.[24]

Depending upon the observations made during the development of versatile gold catalyzed glycosidation, the plausible mechanism for the same can be envisaged as shown in Figure **6**.

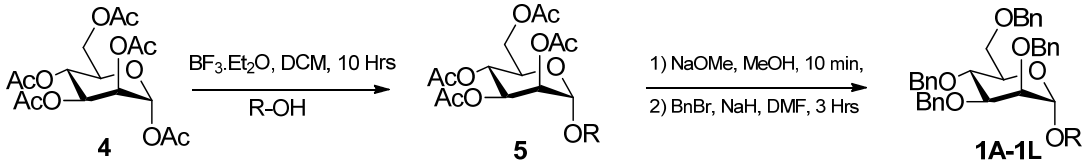
Figure: 6



Initially alkynophilic AuX_3 co-ordinates with exocyclic oxygen and the alkyne (**12**) which can collapse to give cyclopropenyl gold bromide intermediate **13** releasing halide ion (Figure 6). Subsequently, exocyclic oxygen can get protonated to give intermediate **14** that could further get converted to the oxocarbenium ion **15** which is available for the attack of RO^- to result in the transglycosylated product. Prototropic demetallation would result in the regeneration of AuX_3 for further catalytic action and 1-ethynylcyclohexanol (Ech-OH) **7**. Important to mention that the leaving group can be removed easily under high vacuum from the reaction mixture thereby making leaving group traceless after the reaction.

In conclusion, gold catalyzed method for transglycosidation at room temperature has been discovered, after screening a panel of substituted propargyl glycosyl donors. Where we have found that 1-ethynylcyclohexanyl (-Ech) glycosyl donor gives excellent transglycosidation. It was observed that during transglycosidation process 1-ethynylcyclohexanol ejects out from reaction. Furthermore GC studies confirmed our observations and proved the quantitative formation of required transglycosides under similar conditions.

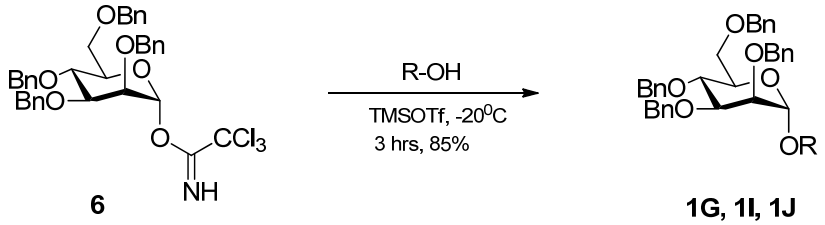
General experimental procedure for preparation of substituted propargyl mannosides using $BF_3.Et_2O$



To a solution of penta-*O*-acteyl-D-mannose (1 equiv) in dichloromethane (25 mL) was added an alcohol (2 equiv). The reaction was cooled to 0 ^{0}C and $BF_3.Et_2O$ (1.5 equiv) was added slowly. The mixture was allowed to warm to room temperature with stirring, while monitoring the reaction progress by TLC. Upon completion (10 h) the reaction was diluted with dichloromethane and neutralized with aq. K_2CO_3. The organic layer was washed with water, separated and dried (Na_2SO_4). The solvent was removed and the crude product was purified by flash column chromatography to give compound **5** as a hygroscopic white solid with 75-80 % yield.

To a solution of **5** (1 equiv) in methanol (15 mL) was added 2N NaOMe (1.0 mL). The reaction was stirred at room temperature, monitoring by TLC. Upon completion (1 h) the mixture was neutralized with Amberlite IR 120 (H+) resin. The resin was filtered and solvent was evaporated to give a white solid compound in 92 % yield. The same compound (1 equiv) was then dissolved in DMF (5 mL) and allowed to cool at 0 ^{0}C followed by addition of NaH (4.5 equiv) and catalytic amount of *n*-$Bu_4N^+I^-$ (0.1 equiv). Then reaction was stirred at room temperature for 1h followed by dropwise addition of benzyl bromide (4.8 equiv) under nitrogen atmosphere, and finally kept on stirring at room temperature for another 5h. The progress of reaction was monitored by TLC and when completed it was neutralized with ice cold water. The reaction mixture was extracted with diethyl ether (3 X 25 mL), washed with water. The organic layer was separated, dried (Na_2SO_4) and evaporated to give the required per-*O*-benzyl akynelated mannoside (mannosyl donor's **1A-1L**) as pale yellow syrup.

General experimental procedure for preparation of substituted propargyl mannosides using Trichloracatamidate method.



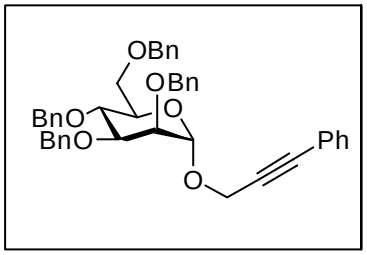
Mannosyl trichloroacetamidate **6** (1 equiv) and glycosyl acceptor (1.5 Equiv) was dissolved in dry Diethyl ether (25 mL). The mixture is cooled to -20 ^{0}C under nitrogen atmosphere and is then treated dropwise with TMSOTf in Et_2O (0.05 equiv) and kept on stirring for 3h. The progress of reaction was monitored by TLC analysis, after completion of reaction, solid $NaHCO_3$ was added. The mixture was filtered and

concentrated. The residue is purified by column chromatography to yield the required per-*O*-benzyl akynelated mannoside (mannosyl donor's **1G, 1I,** and **1J**) as pale yellow syrup.

General experimental procedure for GC analysis

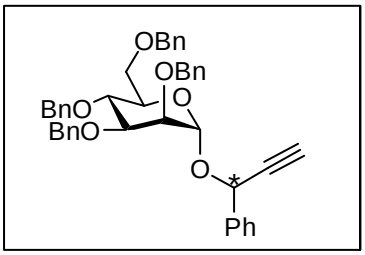
GC Analyses were carried out on an Agilent 7890 instrument equipped with a hydrogen flame ionization detector and HP-5 capillary column (30m x 0.32mm x 0.25 μm, J & W Scientific). Nitrogen was used as the carrier gas at a flow rate of 1mL/min. Initially the column temperature was maintained at 30°C for 15 min followed by a temperature gradient from 30°C to 120°C at 5°C/min and then finally temperature gradient was raised from 120°C to 220°C at 20°C/min. Total time for one GC was 45min.

Characterization data for compound **1D**



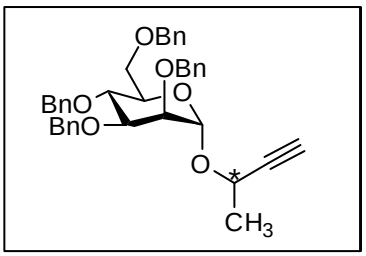
$[\alpha]_D^{25}$ = +27.9 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 3.73-3.85 (m, 3H), 3.87 (dt, 1H, *J* = 0.7, 1.9, 2.8 Hz), 3.93 (dd, 1H, *J* = 2.8, 8.9 Hz), 3.99 (dd, 1H, *J* = 9.0, 17.5 Hz), 4.42 (s, 2H), 4.60 (ABq, 2H, *J* = 12.2 Hz), 4.61 (s, 2H), 4.70 (ABq, 2H, *J* = 10.8 Hz), 4.75 (s, 2H), 5.19 (s, 1H), 7.10-7.48 (m, 25H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 54.8, 69.1, 72.0, 72.2, 72.6, 73.4, 74.3, 74.8, 75.1, 80.0, 84.2, 86.3, 96.3, 122.4, 127.5-128.5, 138.1, 138.2, 138.4, 138.4; HRMS (MALDI-TOF): calcd. for $C_{43}H_{42}NaO_6$[M^++Na]: 677.2879; found: 677.2856.

Characterization data for compound **1E**



$[\alpha]_D^{25}$ = +5.9 ($CHCl_3$, *c* 1.00); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 2.54-2.65 (m, 2H), 3.51-4.15 (m, 12H), 4.29-5.05 (m, 18H), 5.32-5.75 (m, 2H), 7.10-7.62 (m, 50H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 67.3, 67.9, 68.3, 68.9, 69.1, 69.4, 71.4, 72.1, 72.2, 72.4, 72.5, 72.5, 73.3, 73.4, 73.9, 74.2, 76.6, 74.8, 75.0, 75.1, 80.1, 80.6, 81.9, 82.4, 95.5, 95.7, 127.3-128.9, 137.3, 137.4, 137.8, 137.9, 138.2, 138.2, 138.4, 138.4, 138.5, 138.6; HRMS (MALDI-TOF): calcd. for $C_{43}H_{42}NaO_6$ [M^++Na]: 677.2879; found: 677.2869.

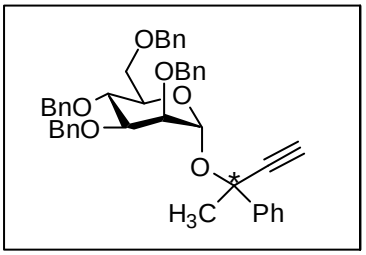
Characterization data for compound **1F**



$[\alpha]_D^{25}$ = +34.1 ($CHCl_3$, *c* 1.00); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 1.39 (d, 3H, *J* = 6.7 Hz), 2.36 (t, 1H, *J* = 2.0 Hz), 3.66-3.82 (m, 3H), 3.83 (d, 1H, *J* = 2.0 Hz), 3.90 (dd, 1H, *J* = 2.8, 9.3 Hz), 4.01 (t, 1H, *J* = 9.5 Hz), 4.47 (dd, 1H, *J* = 4.9, 6.8 Hz), 4.59 (ABq, 2H, *J* = 12.2 Hz), 4.60 (s, 2H), 4.71 (ABq, 2H, *J* = 12.0 Hz), 4.75 (s, 2H), 5.28 (s, 1H), 7.10-7.45 (m, 20H); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 21.8, 61.1, 69.2,

71.9, 72.3, 72.5, 73.1, 73.4, 74.5, 74.8, 75.8, 80.0, 82.8, 95.2, 127.3-128.3, 138.2, 138.3, 138.4, 138.5 ; HRMS (MALDI-TOF): calcd. for $C_{38}H_{40}NaO_6$ [M^++Na]: 615.2723; found: 615.2723.

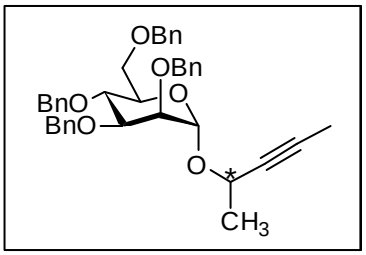
Characterization data for compound **1G**



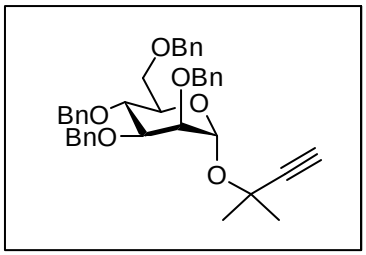
$[\alpha]_D^{25}$ = +25.0 ($CHCl_3$, *c* 1.00); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 1.77(s, 3H), 2.62 (s, 1H), 3.64 (t, 1H, *J* = 2.2 Hz), 3.76 (d, 1H, *J* = 10.8 Hz), 3.86 (dd, 1H, *J* = 3.8, 10.8 Hz), 3.98 (dd, 1H, *J* = 2.7, 8.6 Hz), 4.03-4.13 (m, 2H), 4.57 (ABq, 2H, *J* = 12.3 Hz), 4.58 (d, 1H, *J* = 9.3 Hz), 4.59 (ABq, 2H, *J* = 12.4 Hz), 4.62 (ABq, 2H, *J* = 12.0 Hz), 4.93 (d, 1H, *J* = 10.8 Hz), 5.44 (s, 1H), 7.14-7.55 (m, 25H); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 32.1, 69.2, 71.9, 71.9, 79.2, 72.4, 73.3, 74.7, 75.0, 75.3, 75.6, 76.0, 77.2, 79.7, 83.8, 94.4, 125.5, 127.3-128.4, 138.2, 138.4, 138.5, 138.5, 142.8; HRMS (MALDI-TOF): calcd. for $C_{44}H_{44}NaO_6$ [M^++Na]: 691.3036; found: 691.3035.

Characterization data for compound **1H**

$[\alpha]_D^{25}$ = +37.6 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.29-1.30 (m, 3H), 1.75-1.84 (m, 3H), 3.73-4.00 (m, 6H), 4.36-5.30 (m, 10H), 7.10-7.45 (m, 20H); ^{13}C NMR (125.76 MHz, $CDCl_3$): δ 3.5, 22.2, 61.5, 69.3, 70.0, 72.2, 72.5, 73.4, 74.6, 75.0, 75.2, 78.2, 80.2, 81.3, 95.0, 127.4-128.4, 138.3, 138.4, 138.5, 138.6; HRMS (MALDI-TOF): calcd. for $C_{39}H_{42}NaO_6$ [M^++Na]: 629.2879; found: 629.2894.



Characterization data for compound **1I**

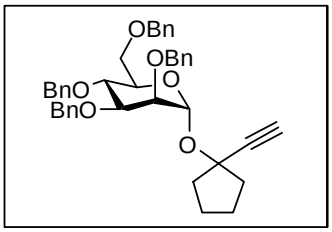


$[\alpha]_D^{25}$ = +37.7 ($CHCl_3$, *c* 1.00); ^{1}H NMR(200.13 MHz, $CDCl_3$): δ 1.41, 1.53 (2s, 6H), 2.37 (s, 1H), 3.65-4.10 (m, 6H), 4.59 (s, 2H), 4.60 (ABq, 2H, *J* = 12.1 Hz), 4.68 (ABq, 2H, *J* = 10.6 Hz), 4.76 (s, 2H), 5.52 (d, 1H, *J* = 2.0 Hz), 7.10-7.45 (m, 20H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 29.1, 30.2, 69.2, 71.7, 71.9, 72.0, 72.2, 72.5, 73.3, 75.0, 75.0, 75.1, 80.0, 84.4, 94.3, 127.3-128.3, 138.4, 138.4, 138.5, 138.5; HRMS (MALDI-TOF): calcd. for $C_{39}H_{42}NaO_6$ [M^++Na]: 629.2879; found: 629.2892.

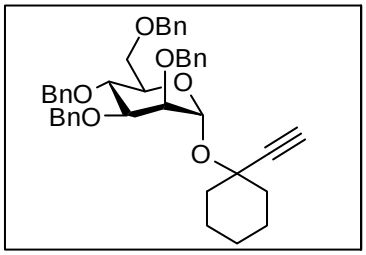
Characterization data for compound **1J**

$[\alpha]_D^{25}$ = +21.5 ($CHCl_3$, *c* 1.00); ^{1}H NMR(200.13 MHz, $CDCl_3$): δ 1.60-1.98 (m, 8H), 2.38 (s, 1H), 3.65-4.10 (m, 6H), 4.59 (s, 2H), 4.60 (ABq, 2H, *J* = 12.2 Hz), 4.70 (ABq, 2H, *J* = 10.5 Hz), 4.76 (s, 2H), 5.47 (d, 1H, *J* = 2.0 Hz), 7.15-7.40 (m, 20H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 22.8, 23.1, 39.3, 40.9, 69.3, 71.9, 72.2, 72.5, 72.9, 73.3, 74.5,

75.0, 75.2, 80.0, 81.5, 84.8, 94.9, 127.3-128.3, 138.4, 138.5, 138.5, 138.5; HRMS (MALDI-TOF): calcd. for $C_{41}H_{44}NaO_6$ [M^++Na]: 655.3036; found: 655.3045.

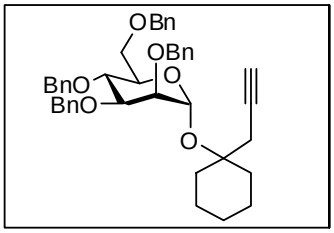


Characterization data for compound **1K**



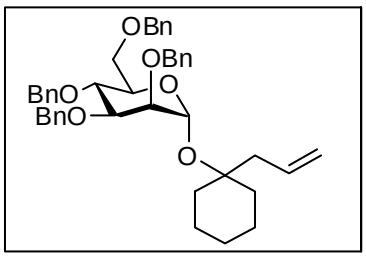
$[\alpha]_D^{25}$ = +28.2 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.10-2.15 (m, 10H), 2.40 (s, 1H), 3.65-4.12 (m, 6H), 4.59 (s, 2H), 4.60 (ABq, 2H, *J* = 12.6 Hz), 4.71 (ABq, 2H, *J* = 10.6 Hz), 4.76 (s, 2H), 5.56 (d, 1H, *J* = 1.8 Hz), 7.13-7.42 (m, 20H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 22.7, 22.7, 25.0, 37.6, 38.2, 69.3, 71.9, 72.1, 72.3, 73.3, 74.1, 75.0, 75.2, 75.2, 75.5, 80.0, 84.6, 94.0, 127.3-128.3, 138.4, 138.5, 138.5, 138.5; HRMS (MALDI-TOF): calcd. for $C_{42}H_{46}NaO_6$ [M^++Na]: 669.3192; found: 669.3173.

Characterization data for compound **1L**



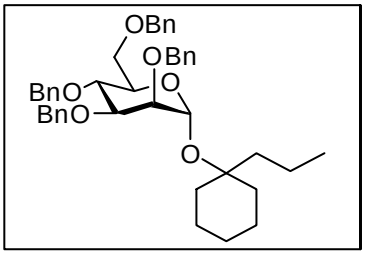
$[\alpha]_D^{25}$ = +54.5 ($CHCl_3$, *c* 1.00); ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.05-1.75 (m, 10H), 1.90 (t, 1H, *J* = 2.8 Hz), 2.36 (d, 2H, *J* = 2.6 Hz), 3.62 (t, 1H, *J* = 2.5 Hz), 3.70 (dd, 1H, *J* = 1.6, 10.7 Hz), 3.81 (dd, 1H, *J* = 4.1, 10.7 Hz), 3.95 (dd, 1H, *J* = 2.9, 9.1 Hz), 3.99 (ddd, 1H, *J* = 1.5, 4.0, 6.1 Hz), 4.04 (d, 1H, *J* = 9.8 Hz), 4.71 (ABq, 2H, *J* = 10.8 Hz), 4.67-4.72 (m, 2H), 4.60 (ABq, 2H, *J* = 11.9 Hz), 4.72 (ABq, 2H, *J* = 11.5 Hz), 5.05 (d, 1H, *J* = 1.5 Hz), 7.18-7.45 (m, 20H); ^{13}C NMR (125.76 MHz, $CDCl_3$): δ 21.7, 21.8, 25.3, 29.6, 33.1, 34.9, 69.3, 70.5, 72.1, 72.4, 72.5, 73.3, 75.0, 75.2, 76.0, 76.9, 79.8, 81.0, 92.1, 127.3-128.3, 138.4, 138.5, 138.6, 138.6; HRMS (MALDI-TOF): calcd. for $C_{43}H_{48}NaO_6$ [M^++Na]: 683.3349; found: 683.3361.

Characterization data for compound **1M**



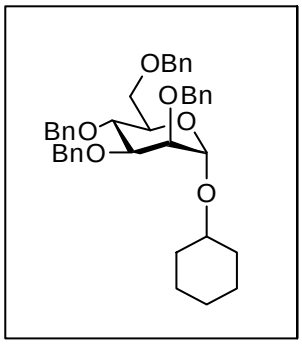
$[\alpha]_D^{25}$ = -11.9 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.07-1.90 (m, 10H), 3.50 (t, 1H, *J* = 2.0 Hz), 3.68 (dd, 1H, *J* = 0.8, 10.3 Hz), 3.82 (dd, 1H, *J* = 3.7, 10.3 Hz), 3.92 (m, 3H), 4.59 (ABq, 2H, *J* = 12.1 Hz), 4.63 (ABq, 2H, *J* = 11.8 Hz), 4.68 (s, 2H), 4.71 (ABq, 2H, *J* = 10.6 Hz), 4.97 (d, 1H, *J* = 1.8 Hz), 5.03 (dd, 1H, *J* = 1.2, 7.2 Hz), 5.01 (s, 1H), 5.65 (m, 1H), 7.15-7.37 (m, 20H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 21.9, 21.9, 25.5, 33.9, 35.4, 69.3, 72.0, 72.1, 72.2, 73.3, 75.1, 75.2, 75.6, 77.9, 79.8, 92.6, 115.1, 127.3-128.3, 138.3, 138.5, 138.5, 138.5, 142.7; HRMS (MALDI-TOF): calcd. for $C_{42}H_{48}NaO_6$ [M^++Na]: 671.3349; found: 671.3360.

Characterization data for compound **1N**



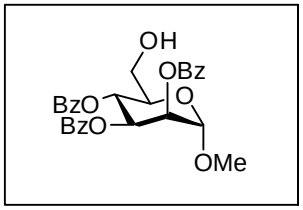
$[\alpha]_D^{25}$ = +48.2 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 0.68 (t, 3H, *J* = 7.9 Hz), 1.08-1.65 (m, 12H), 3.53 (t, 1H, *J* = 2.2 Hz), 3.68 (dd, 1H, *J* = 1.2, 9.5 Hz), 3.83 (dd, 1H, *J* = 3.3, 10.4 Hz), 3.98 (m, 3H), 4.60 (ABq, 2H, *J* = 12.0 Hz), 4.68 (ABq, 2H, *J* = 11.8 Hz), 4.68 (ABq, 2H, *J* = 10.3 Hz), 4.72 (ABq, 2H, *J* = 12.1 Hz), 4.98 (d, 1H, *J* = 1.9 Hz), 7.20-7.39 (m, 20H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 7.5, 21.9, 22.1, 25.7, 30.3, 33.6, 34.4, 69.3, 71.8, 72.4, 72.4, 73.3, 75.1, 75.2, 75.9, 78.4, 79.8, 91.4, 127.3-128.3, 138.4, 138.5, 138.6, 138.6; HRMS (MALDI-TOF): calcd. for $C_{42}H_{50}NaO_6$ [M^++Na]: 673.3505; found: 673.3507.

Characterization data for compound **1O**



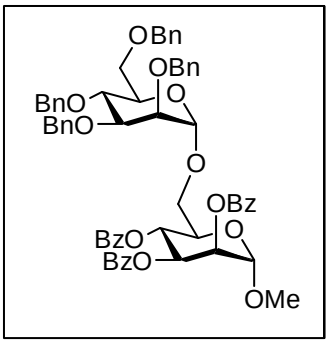
$[\alpha]_D^{25}$ = +36.2 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.08-1.95 (m, 10H), 3.45-4.08 (m, 7H), 4.61 (ABq, 2H, *J* = 12.1 Hz), 4.63 (s, 2H), 4.69 (ABq, 2H, *J* = 10.6 Hz), 4.74 (ABq, 2H, *J* = 12.4 Hz), 5.00 (d, 1H, *J* = 1.8 Hz), 7.15-7.38 (m, 20H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 23.7, 24.0, 25.6, 31.2, 33.2, 69.3, 71.6, 72.1, 72.5, 73.2, 74.6, 75.1, 75.1, 75.2, 80.2, 95.6, 127.3-128.3, 138.4, 138.4, 138.4, 138.6; HRMS (MALDI-TOF): calcd. for $C_{40}H_{46}NaO_6$ [M^++Na]: 645.3192; found: 645.3164.

Characterization data for compound **2**



$[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.0) = -113.6; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 3.4 (bs, 1H), 3.52 (s, 3H,), 3.81 (m, 2H), 4.12 (dt, 1H, *J* = 3.0, 9.4Hz), 5.01 (d, 1H, , *J* = 1.7Hz), 5.68 (dd, 1H, *J* = 1.7, 3.3Hz), , 5.84 (t, 1H, *J* =10.2Hz), 5.96 (dd, 1H, *J* =3.3, 10.2Hz), 7.21-7.65 (m, 9H), 7.78-8.13 (m, 6H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.4, 61.4, 67.2, 69.6, 70.5, 70.8, 98.7, 128.2-130.1, 133.1, 133.5, 133.6, 165.4, 165.5, 166.4; HRMS (MALDI-TOF): calcd. for $C_{28}H_{26}NaO_9$ [M^++Na]: 529.1475 Found: 529.1452.

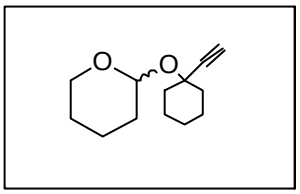
Characterization data for compound **3**



$[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.0) = -43.8; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 3.43 (s, 3H), 3.54–3.75 (m, 5H), 3.81-4.01(m 3H), 4.18 (m, 1H), 4.37 (d, 2H, *J* = 2.5 Hz), 4.49 (t, 2H, *J* = 10.3 Hz), 4.49 (ABq, 2H, *J* = 12.3 Hz), 4.68 (s, 2H), 4.95 (dd, 2H, *J* = 1.7, 5.6 Hz), 5.62 (dd, 1H, *J* = 1.8, 2.9 Hz), 5.89 (m, 2H),7.13–7.53 (m, 29H), 7.78–8.10 (m, 6H); ^{13}C NMR (125.76 MHz, $CDCl_3$): δ 55.4,66.7, 67.8, 68.9, 69.0, 69.9, 70.6, 71.7, 71.8, 72.4, 73.2, 74.6, 74.7, 75.0, 80.1, 98.1,

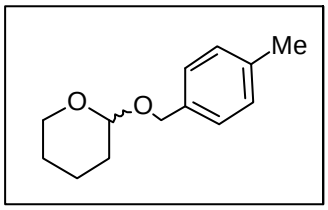
98.4, 127.3–129.8, 133.1, 133.3, 133.5, 138.3, 138.4, 138.5, 138.6,165.3, 165.4, 165.4; HRMS (MALDI-TOF): calcd. for $C_{28}H_{26}NaO_9$ [M^++Na]: $C_{62}H_{60}NaO_{14}$, 1051.3881; found, 1051.3889.

Characterization data for compound **8**



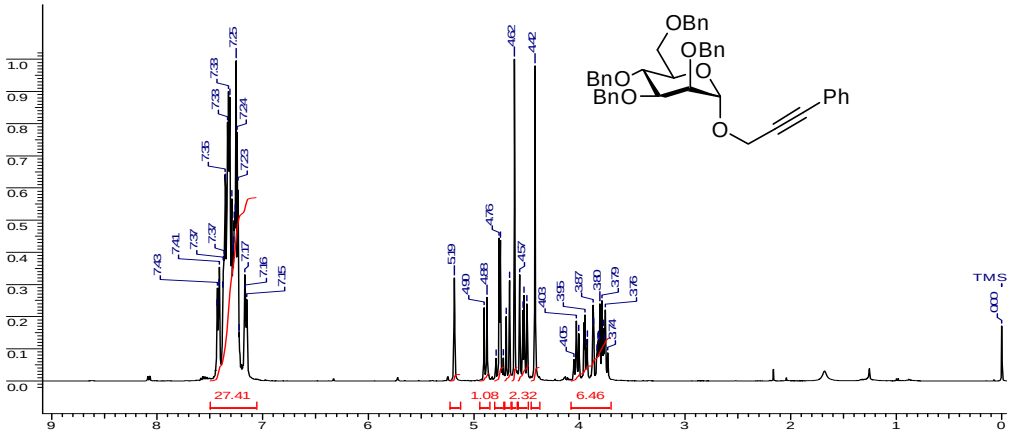
$[\alpha]_D^{25}$ = +5.3 ($CHCl_3$, *c* 1.00); ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.26(m, 1H), 1.45-2.08 (m, 15H), 2.48 (s, 1H), 3.51 (quintet, 1H, *J* = 5.2 Hz), 3.96 (t, 1H, *J* = 10.5 Hz), 5.13 (t, 1H, *J* = 4.1 Hz); ^{13}C NMR(125.76 MHz, $CDCl_3$): δ 20.5, 23.0, 23.0, 25.3, 25.4, 32.1, 38.4, 38.7, 63.5, 73.8, 74.8, 85.4, 95.7; HRMS (MALDI-TOF): calcd. for $C_{13}H_{20}NaO_2$ [M^++Na]: 231.1361; found: 231.1364.

Characterization data for compound **10**

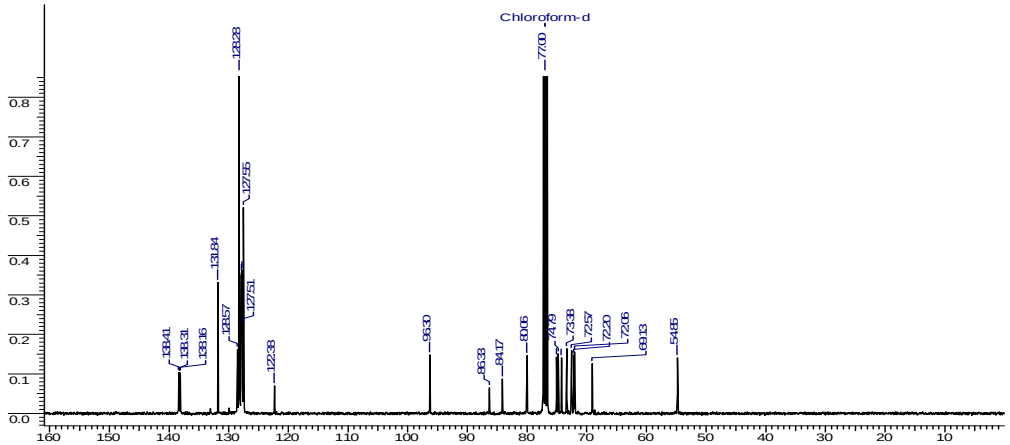


$[\alpha]_D^{25}$ = +5.6 ($CHCl_3$, *c* 1.00); ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.48-1.93 (m, 6H), 2.34 (s, 3H), 3.54 (m, 1H), 3.92 (ddd, 1H, *J* = 3.0, 8.6, 11.5 Hz), 4.60 (ABq, 2H, *J* = 11.9 Hz), 4.69 (t, 1H, *J* = 3.3 Hz) 7.15 (d, 2H, *J* = 7.9 Hz), 7.26 (d, 2H, *J* = 7.91 Hz); ^{13}C NMR (125.76 MHz, $CDCl_3$): δ 19.3, 21.1, 25.5, 30.5, 62.0, 68.6, 97.5, 127.9, 127.9, 129.0, 129.0, 135.2, 137.1; HRMS (MALDI-TOF): calcd. for $C_{13}H_{18}NaO_2$ [M^++Na]: 229.1204; found: 229.1225.

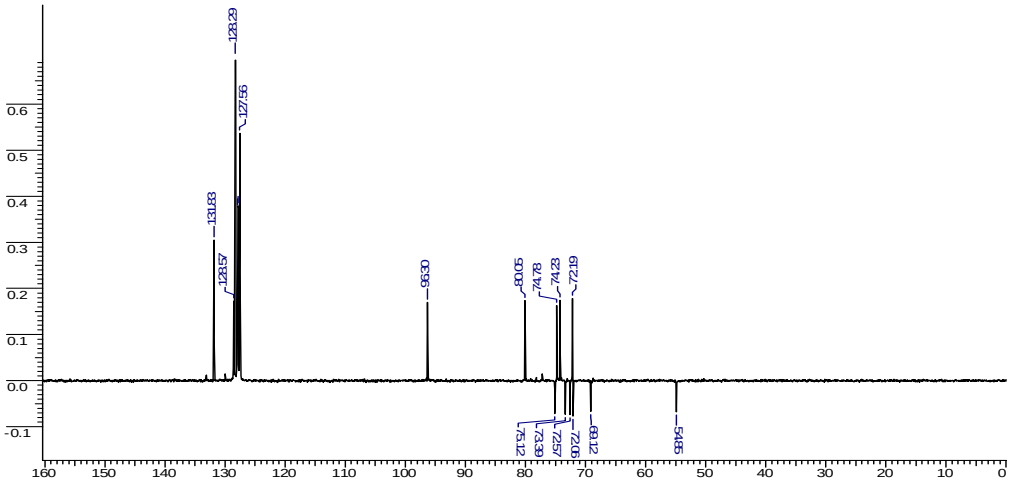
^{1}H NMR Spectrum (400.13 MHz, $CDCl_3$) of Compound **1D**



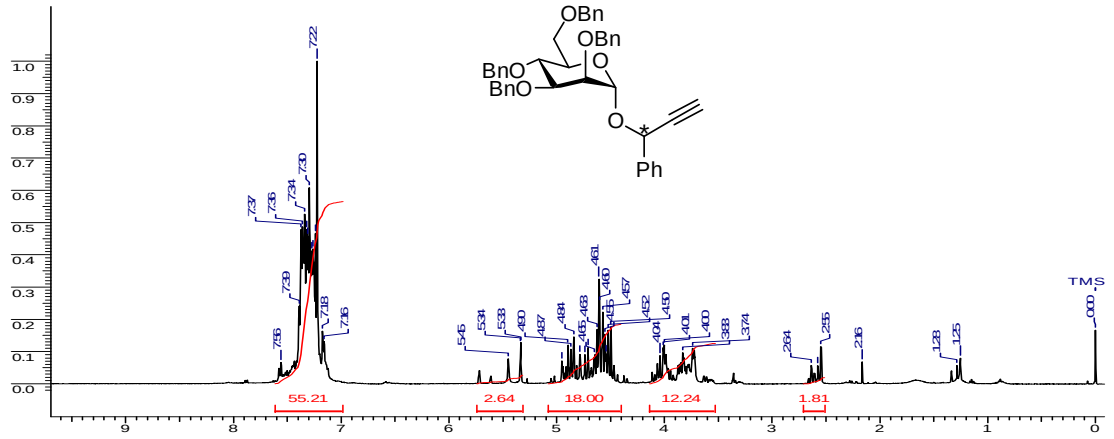
^{13}C NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **1D**



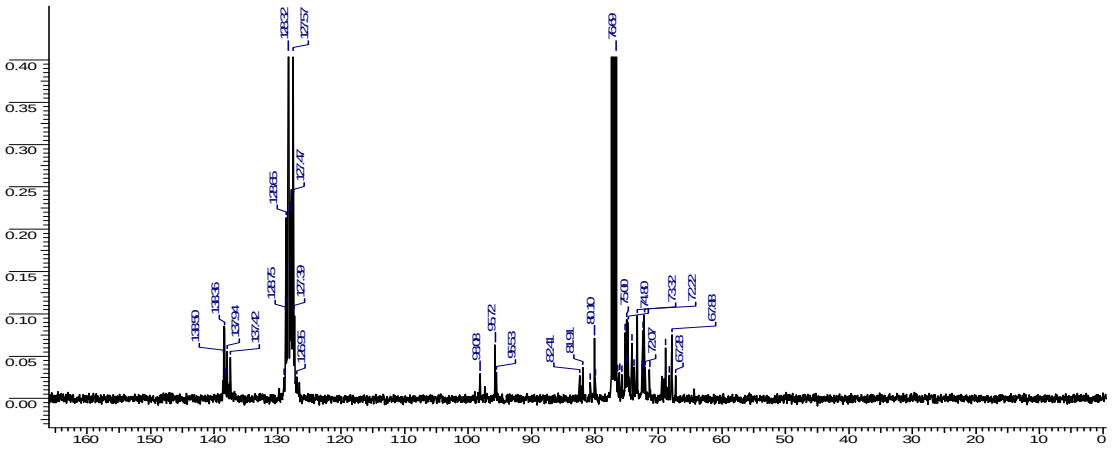
DEPT NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **1D**



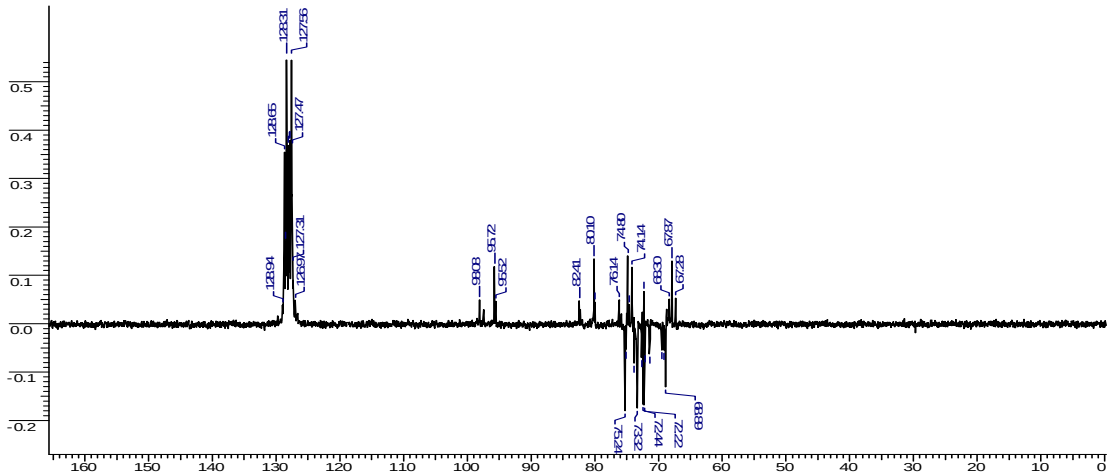
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **1E**



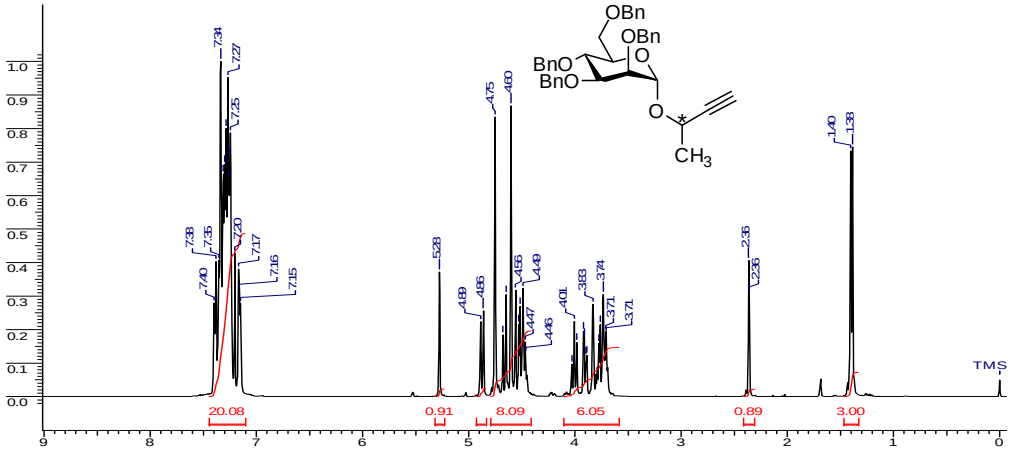
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **1E**



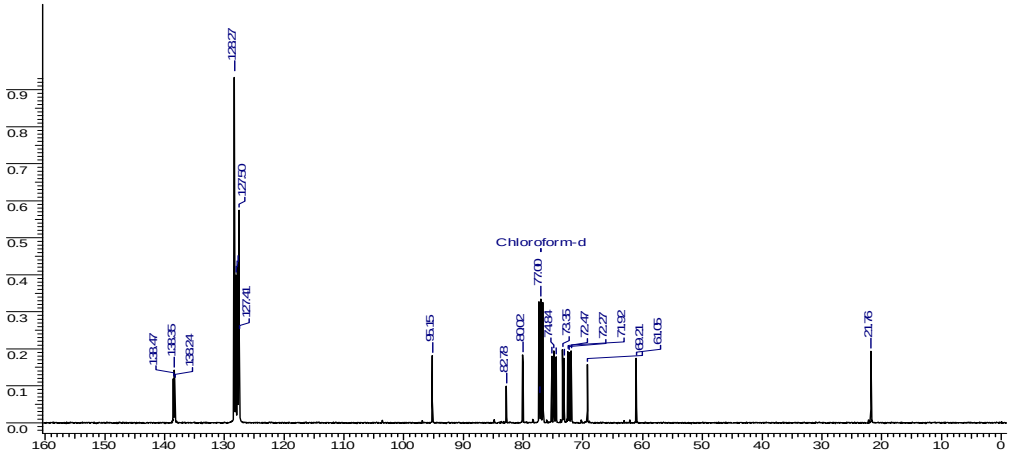
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **1E**



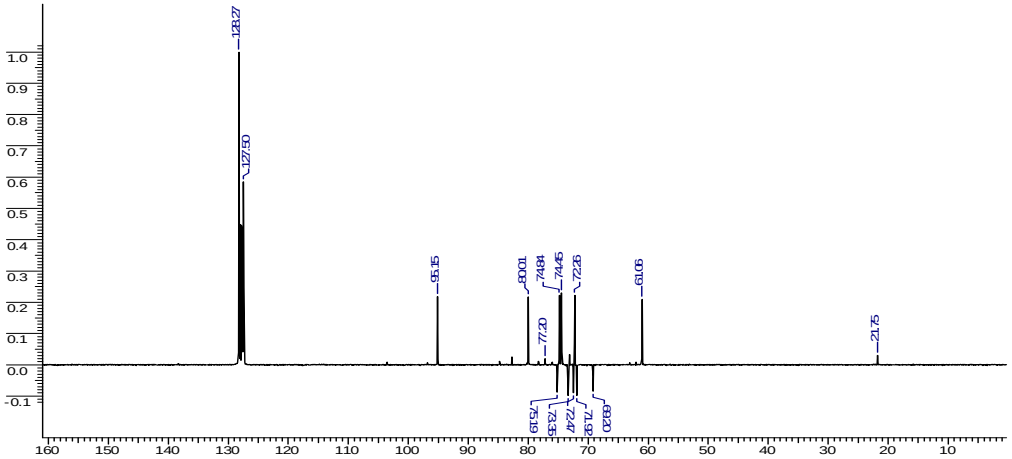
^{1}H NMR Spectrum (400.13 MHz, $CDCl_3$) of Compound **1F**



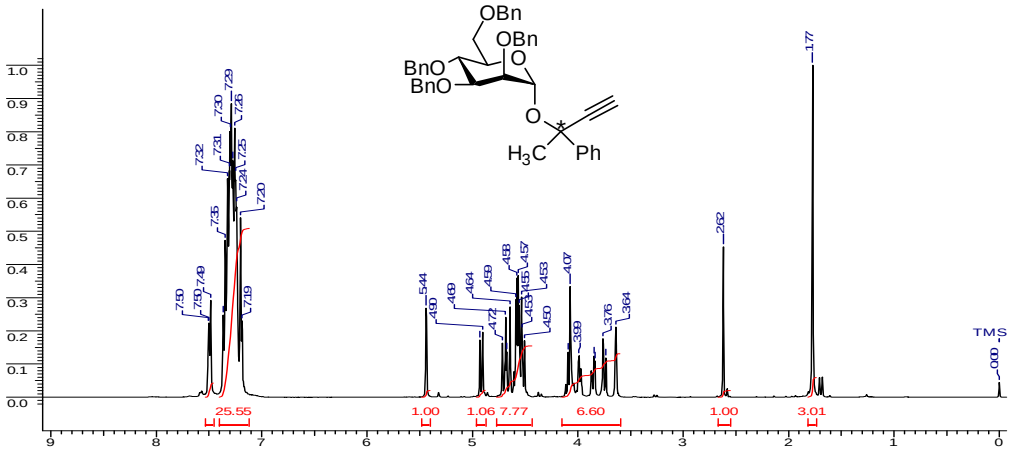
^{13}C NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **1F**



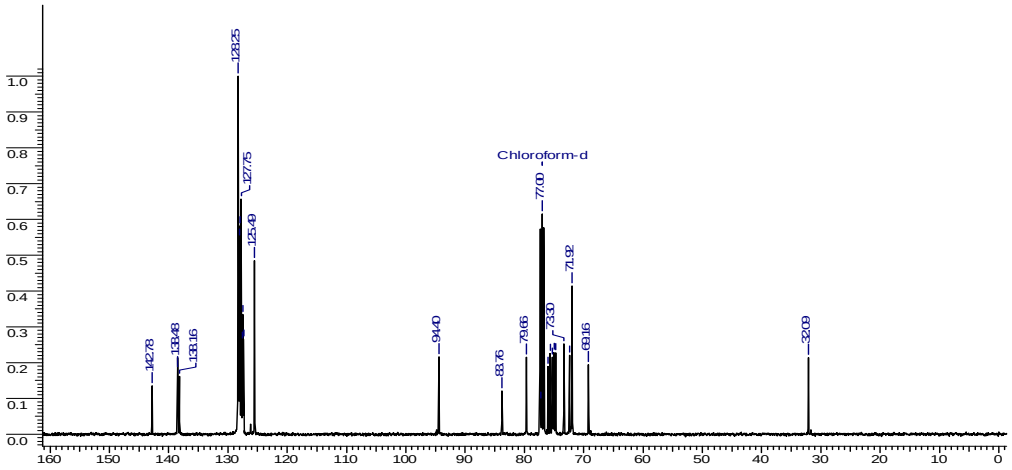
DEPT NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **1F**



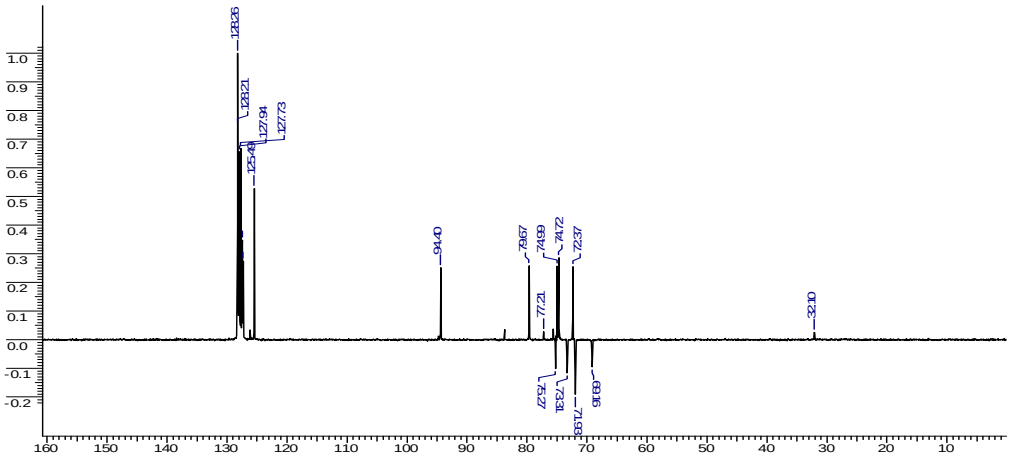
^{1}H NMR Spectrum (400.13 MHz, $CDCl_3$) of Compound **1G**



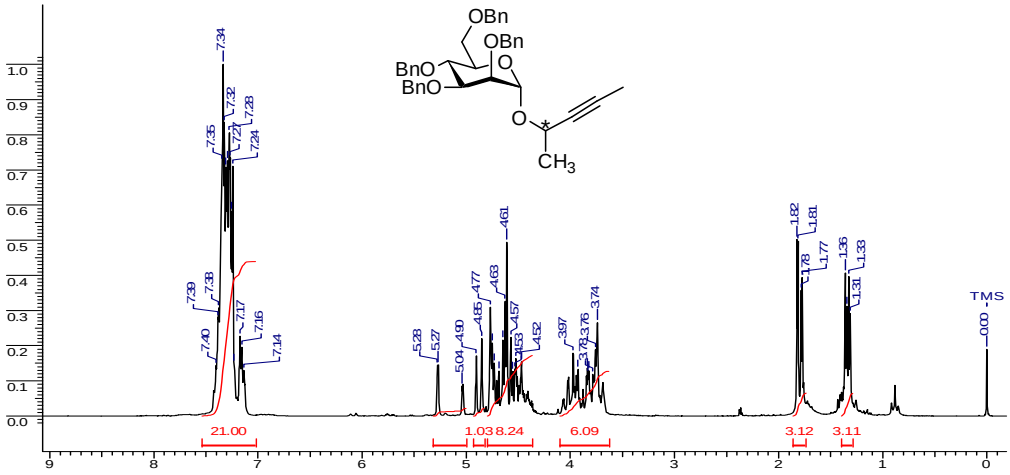
^{13}C NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **1G**



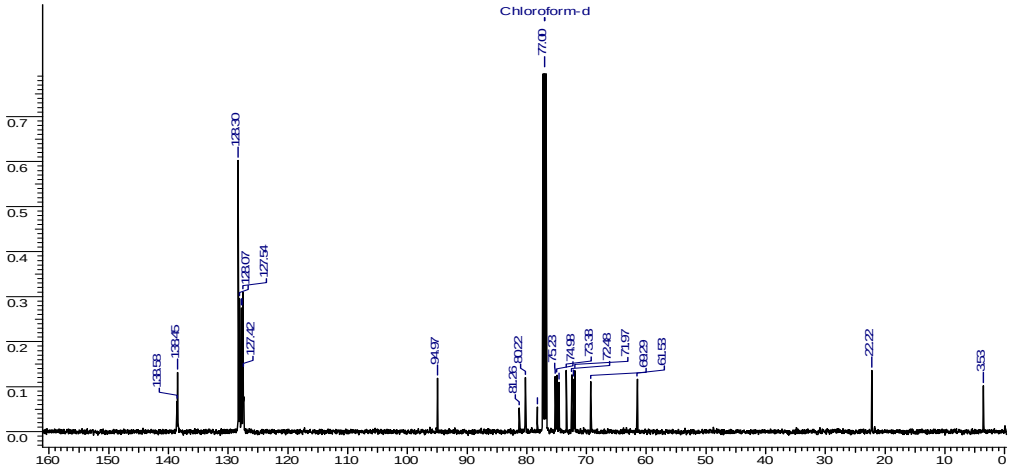
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **1G**



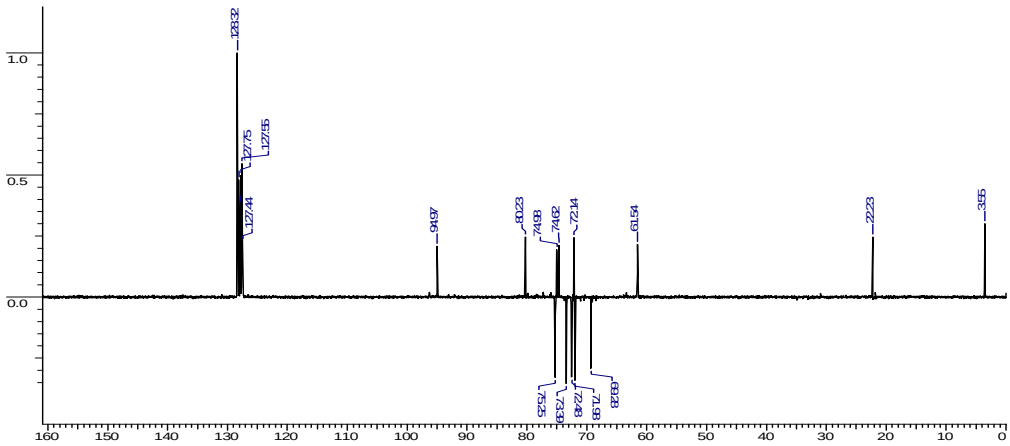
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **1H**



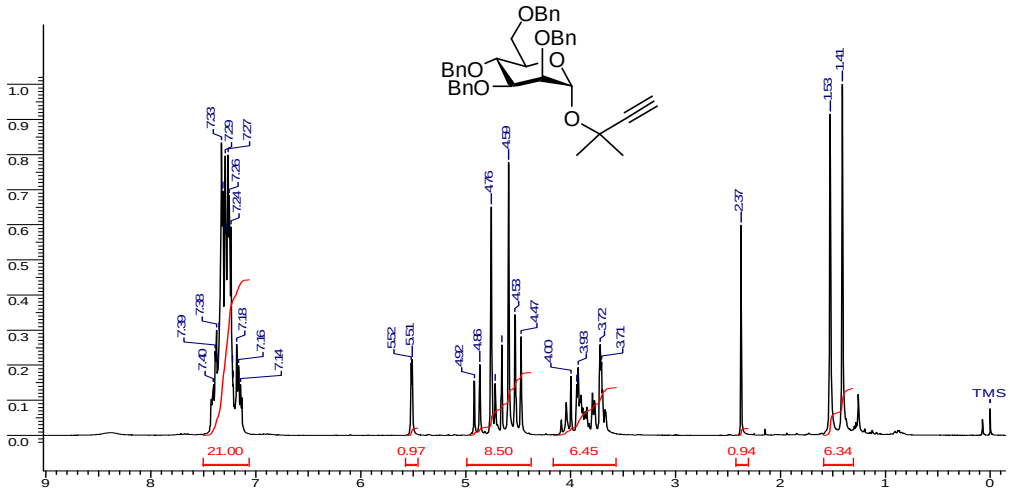
^{13}C NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **1H**



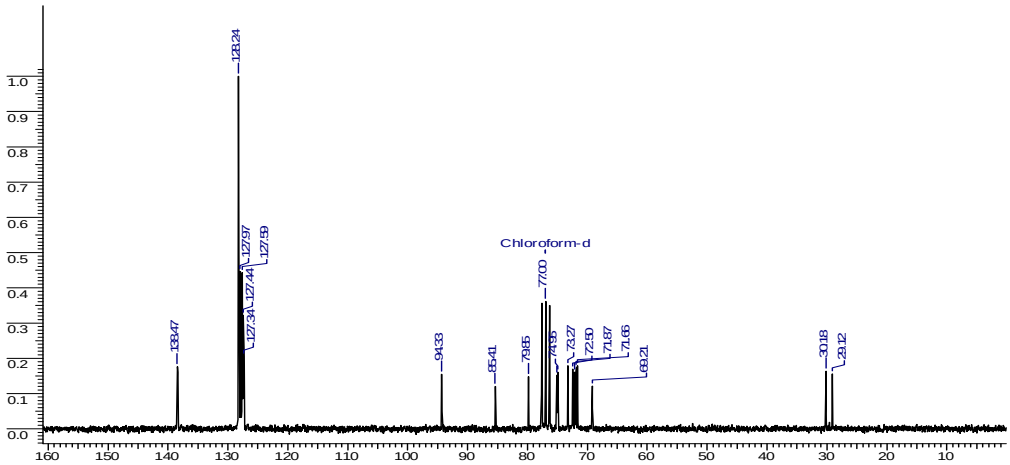
DEPT NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **1H**



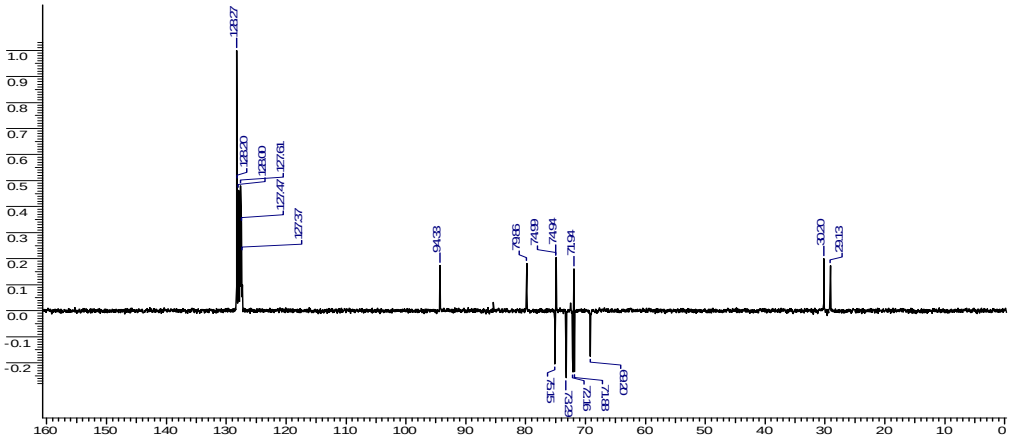
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **1I**



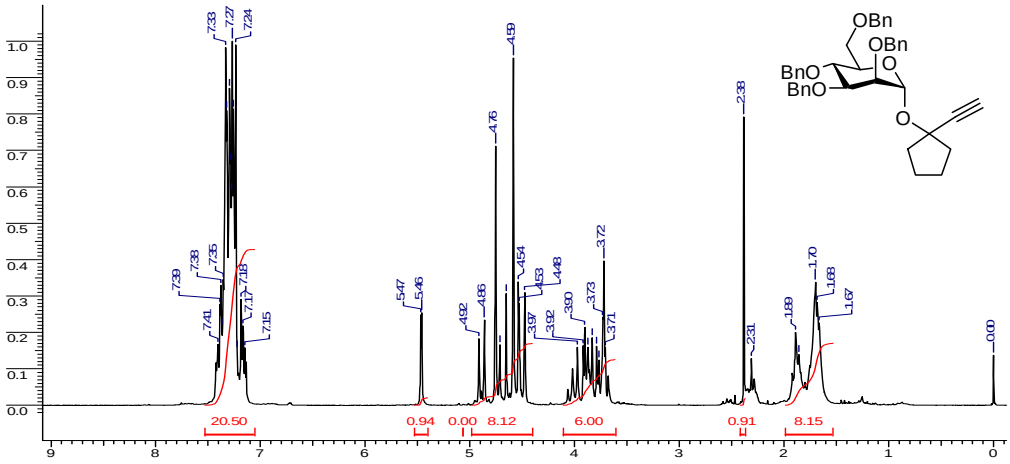
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **1I**



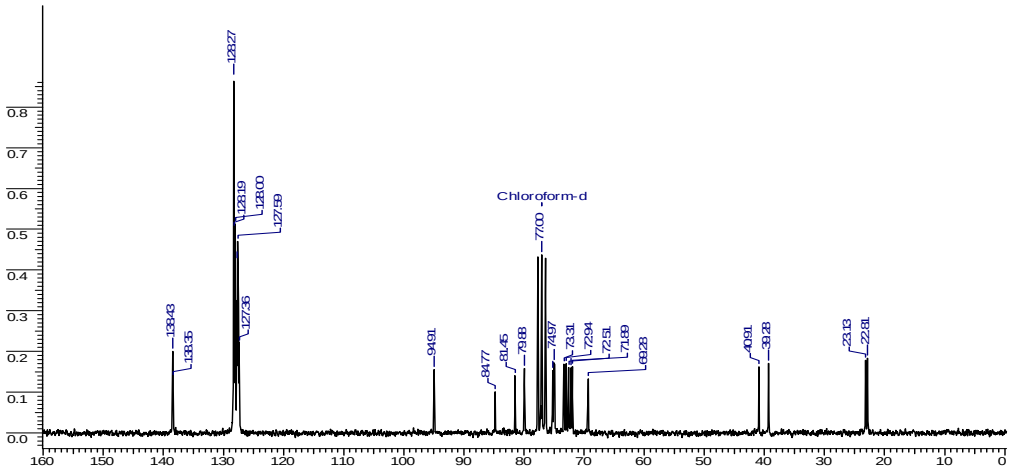
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **1I**



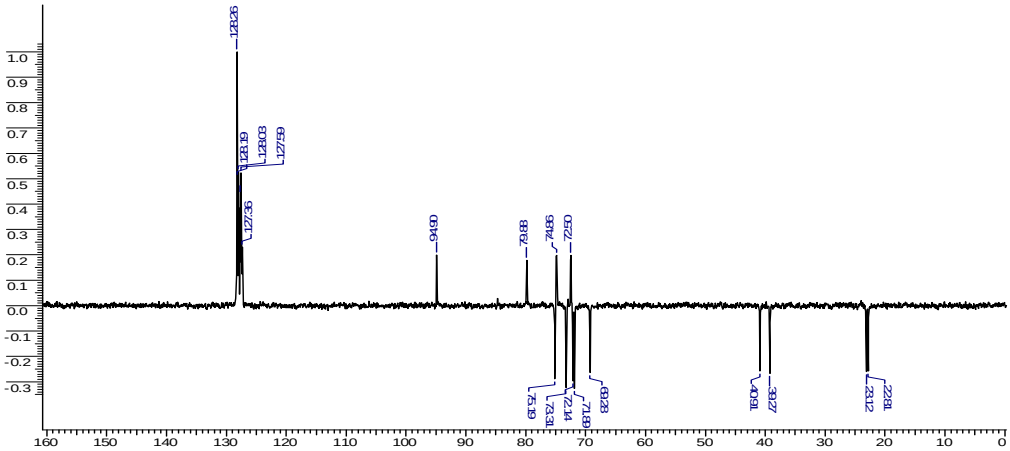
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **1J**



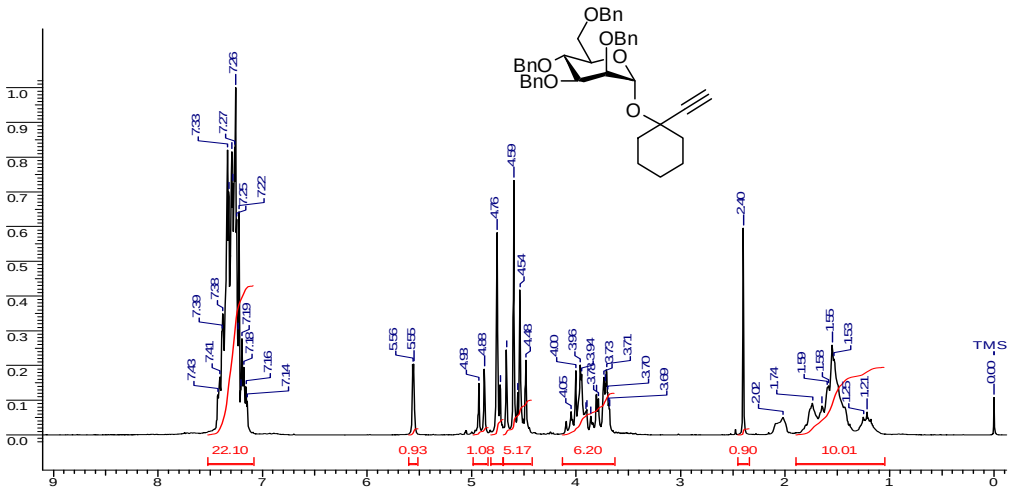
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **1J**



DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **1J**



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



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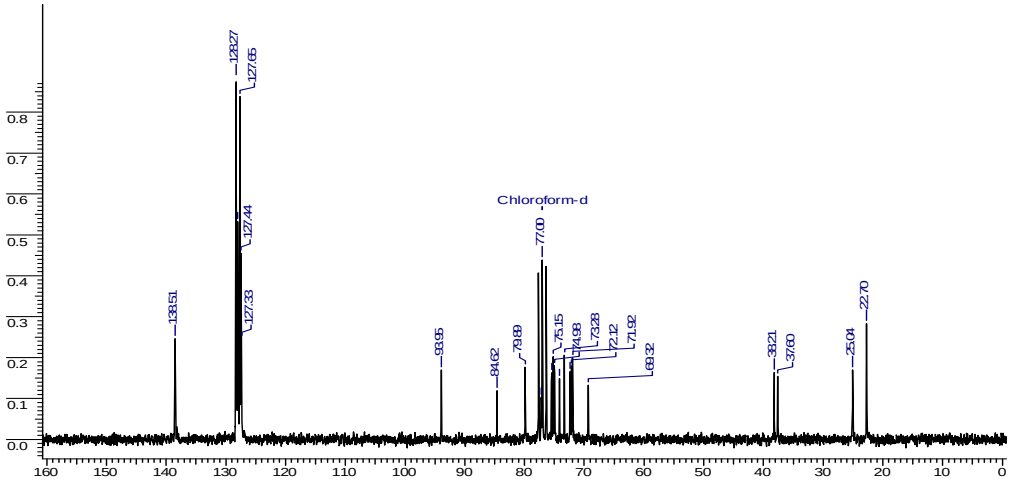
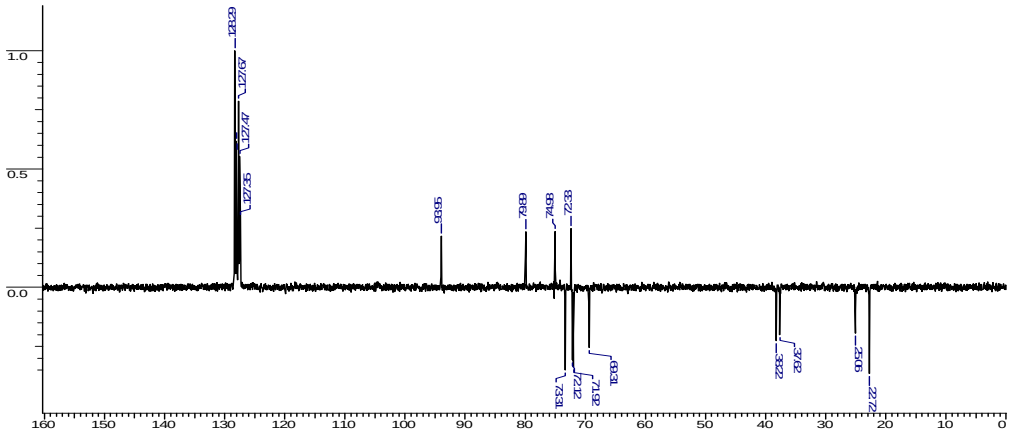
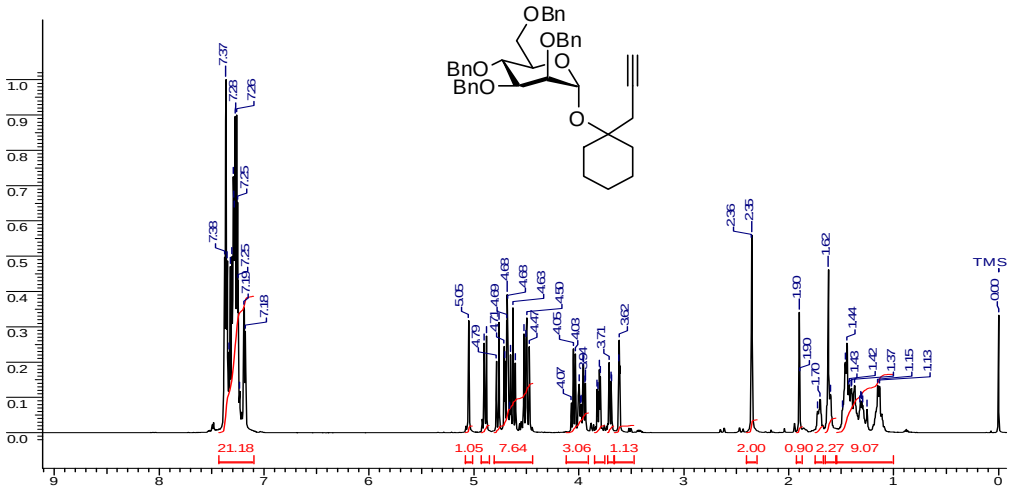


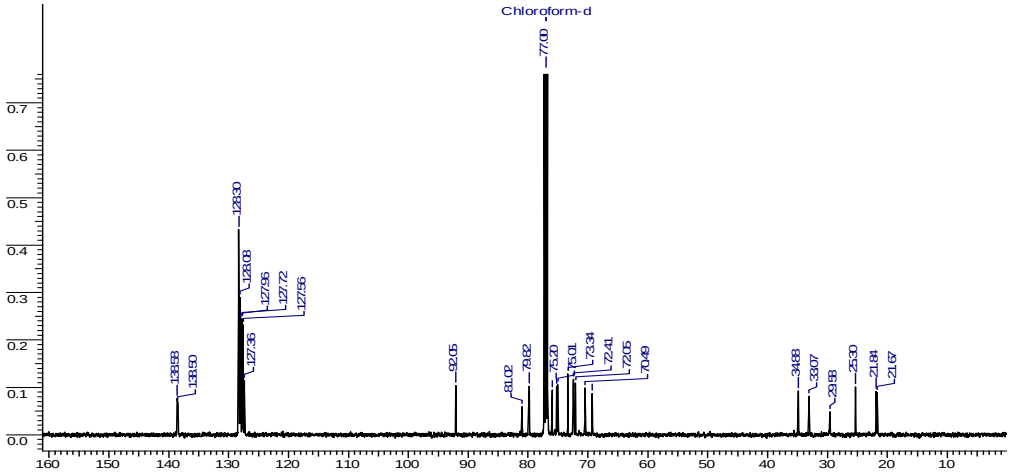
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **1K**



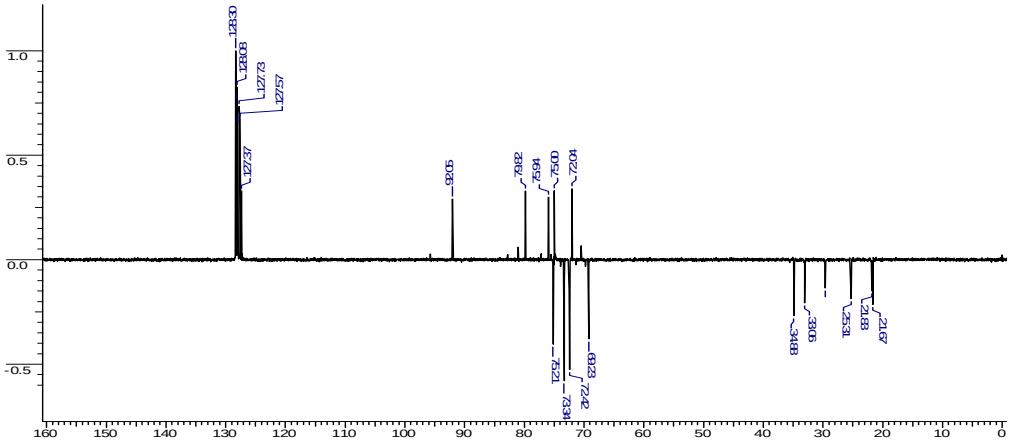
^{1}H NMR Spectrum (500.13 MHz, $CDCl_3$) of Compound **1L**



^{13}C NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **1L**



DEPT NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **1L**



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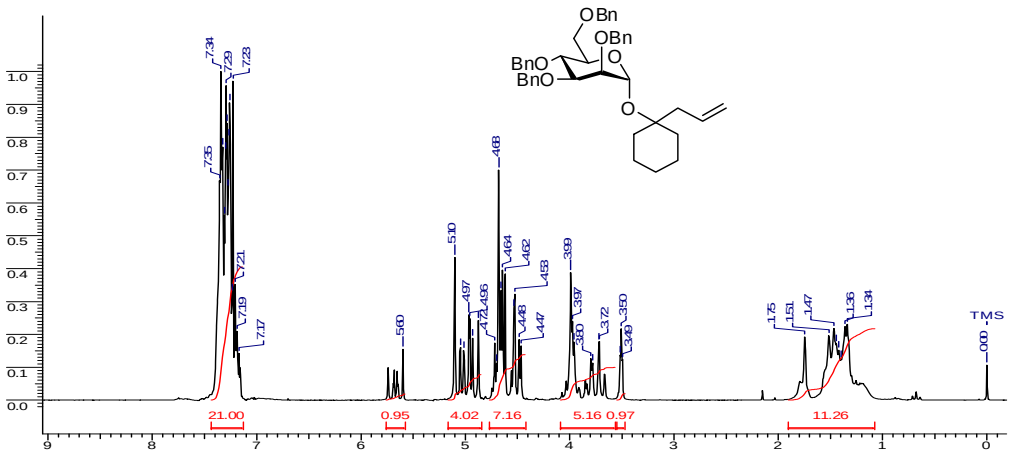
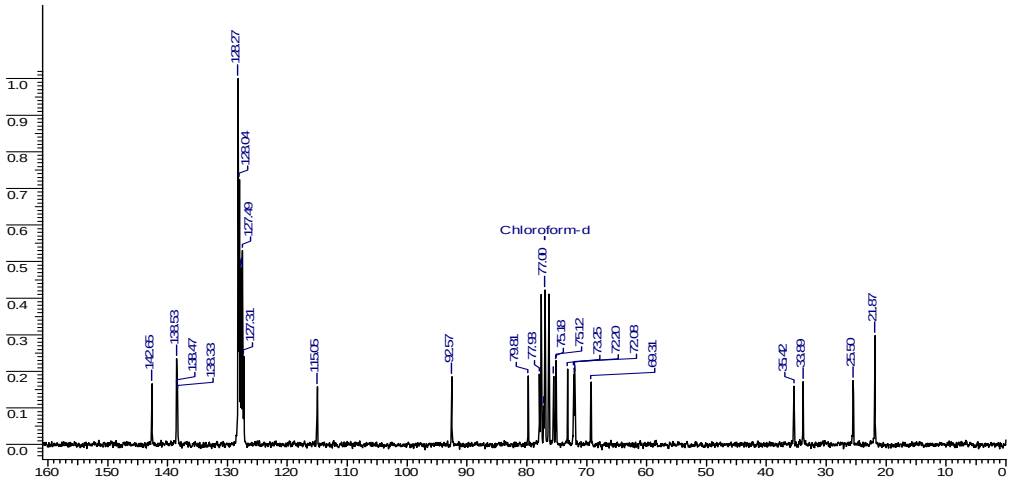
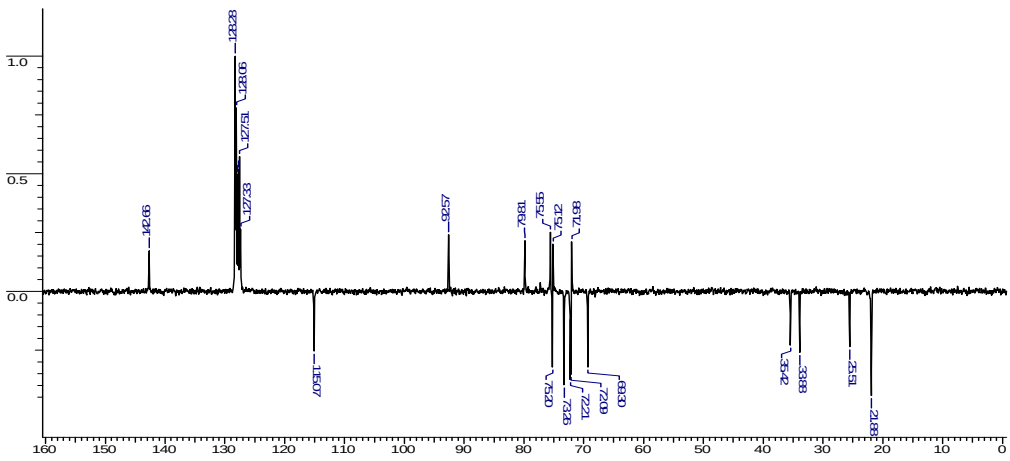


^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **1M**



DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **1M**



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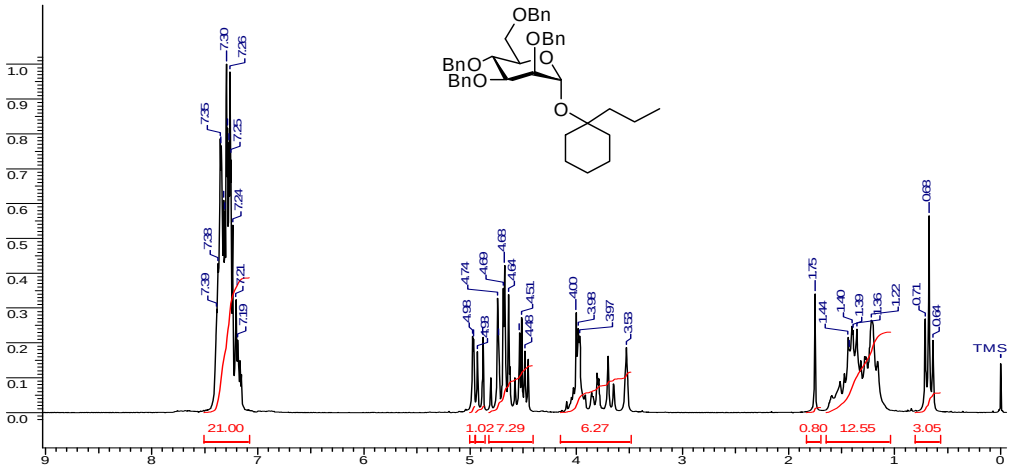
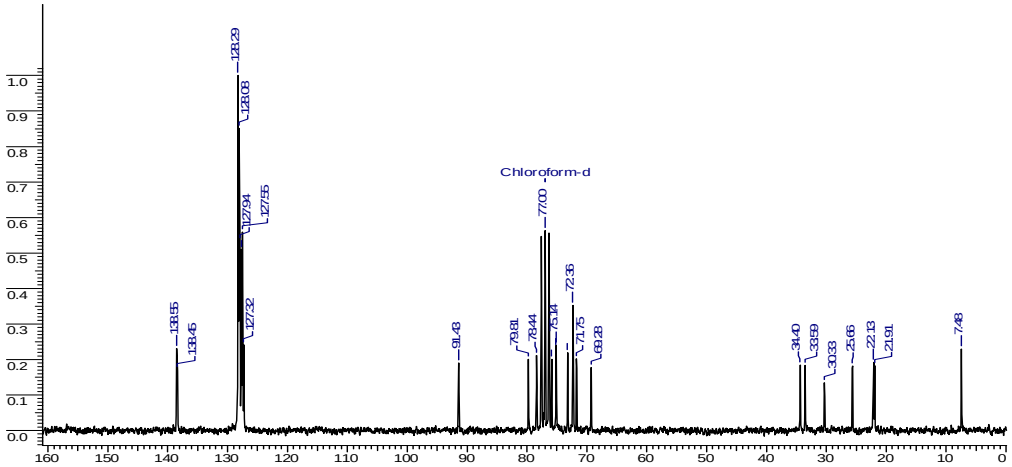


^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **1N**



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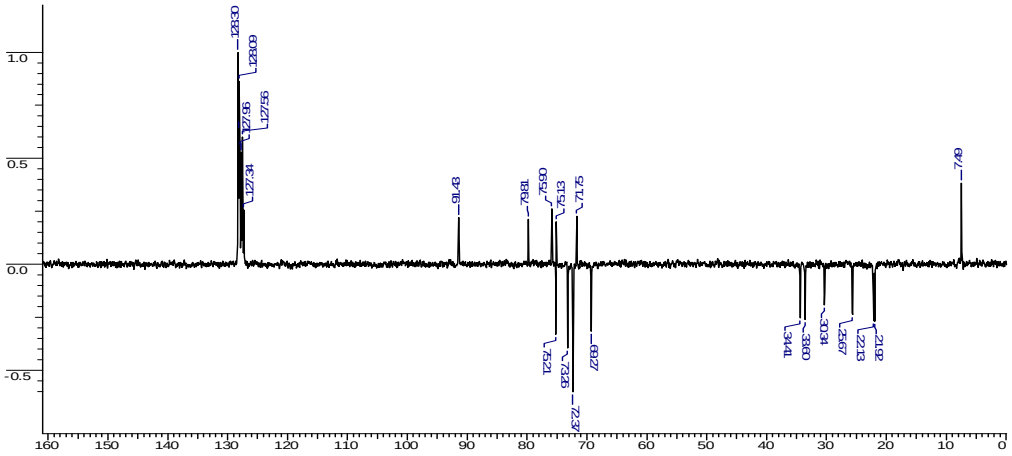
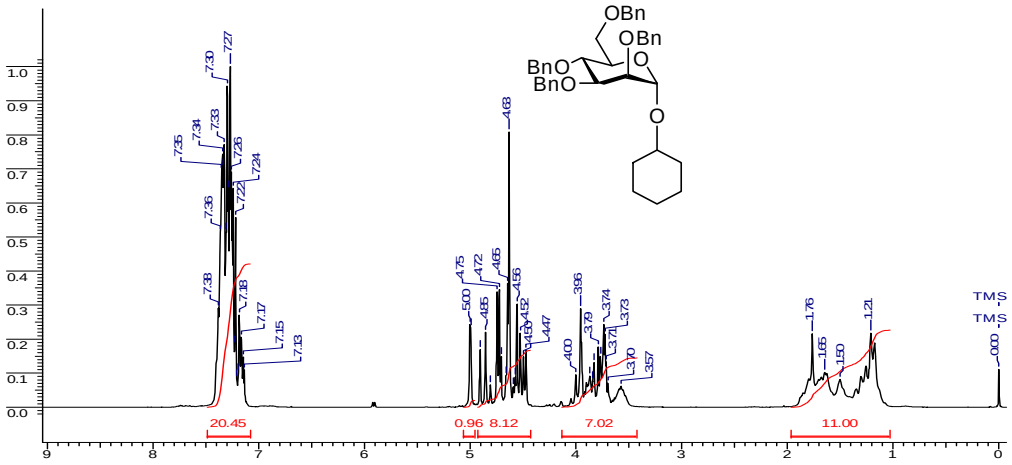


^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **1O**



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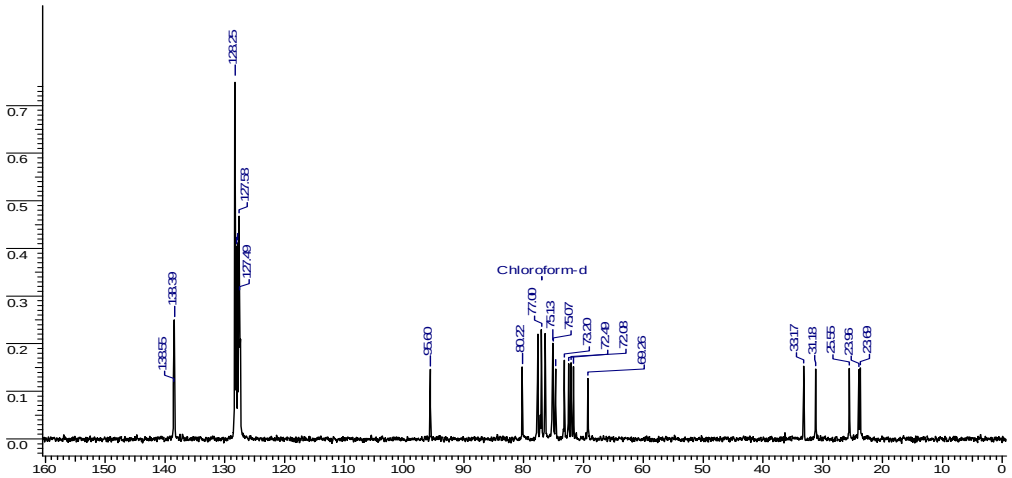
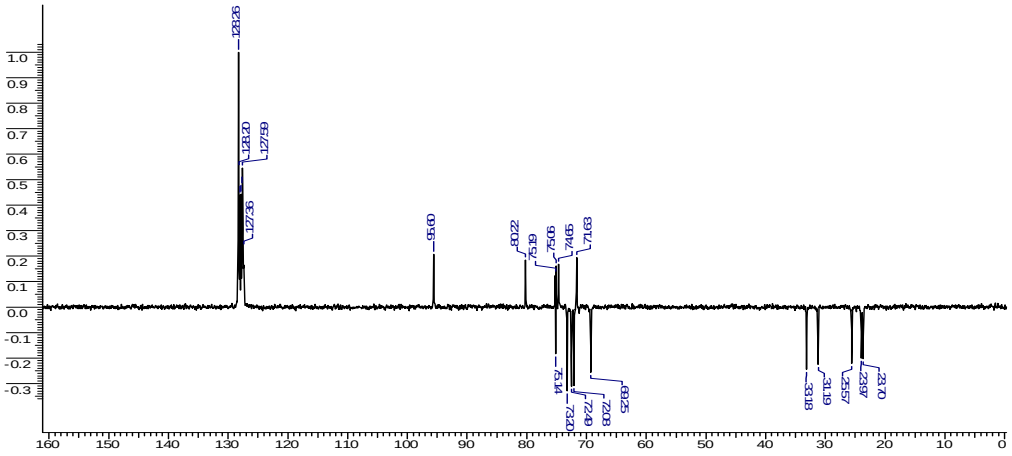
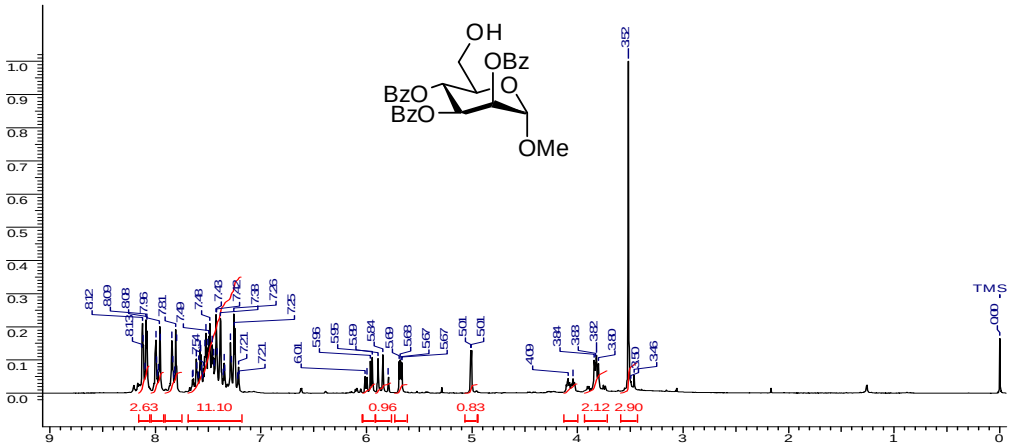


DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **1O**



^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **2**



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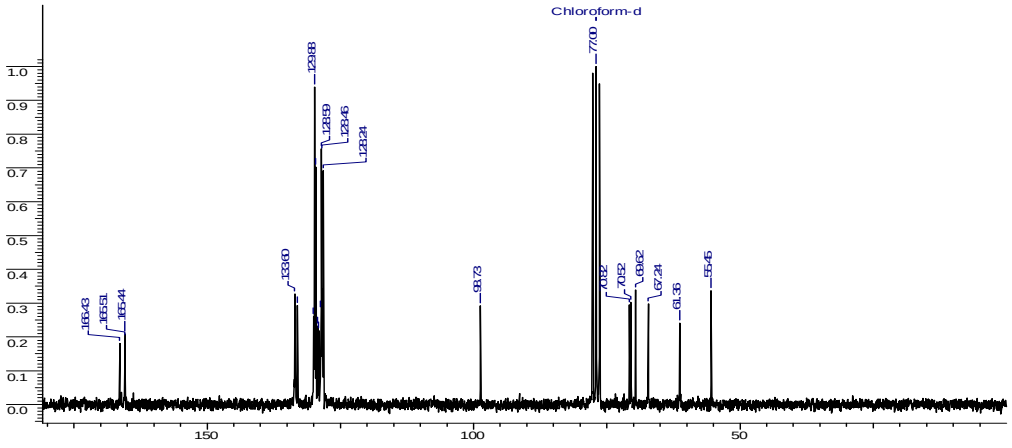
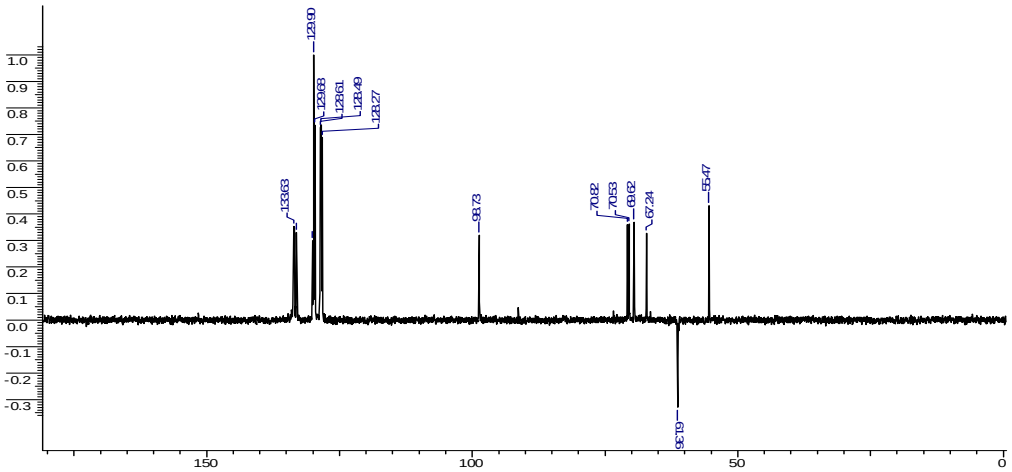
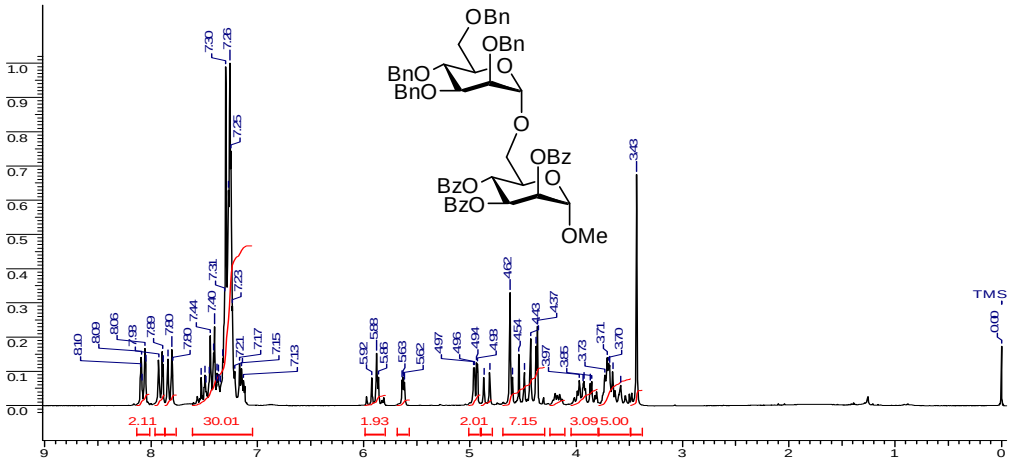


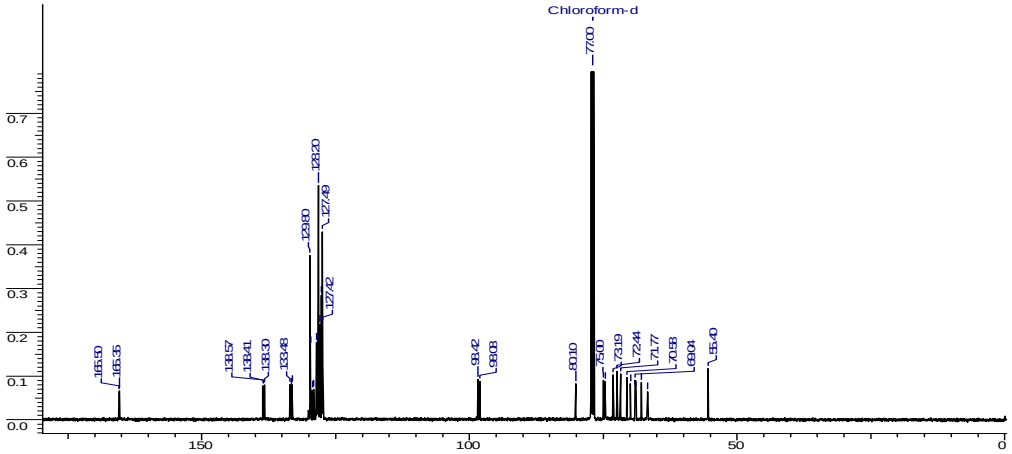
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **2**



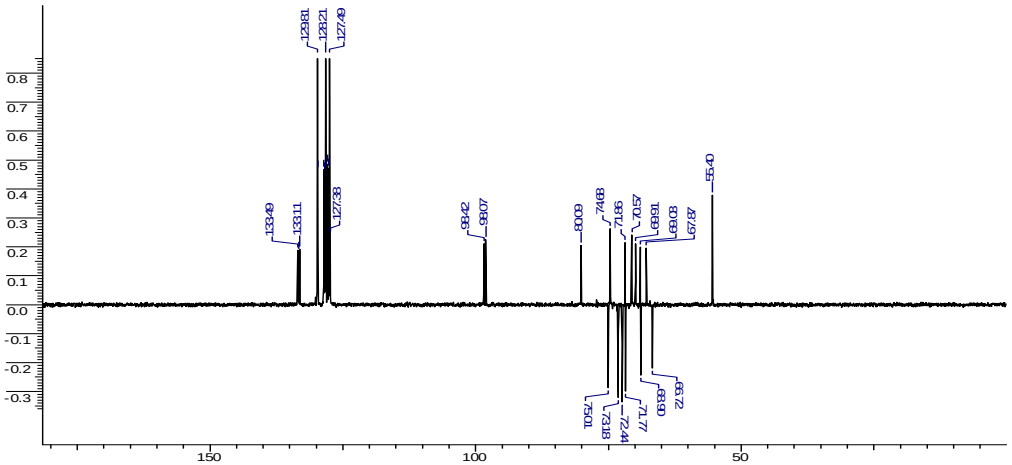
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **3**



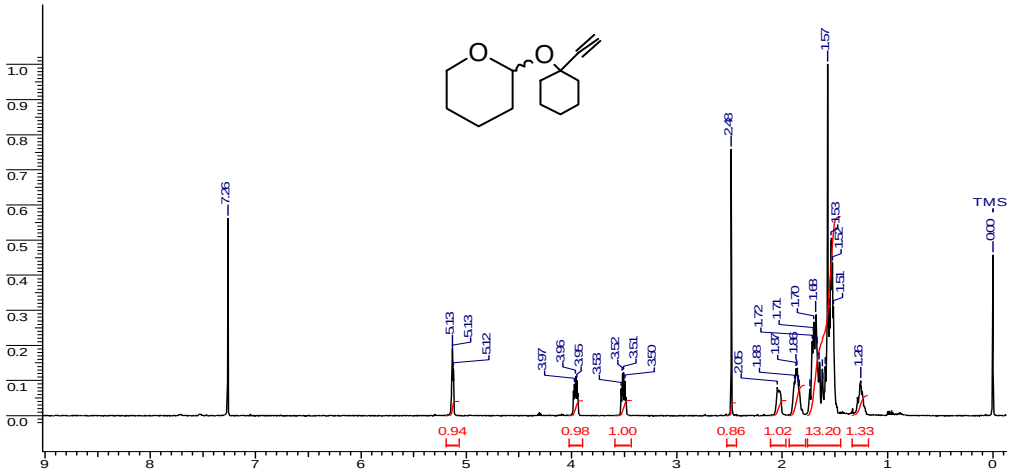
^{13}C NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **3**



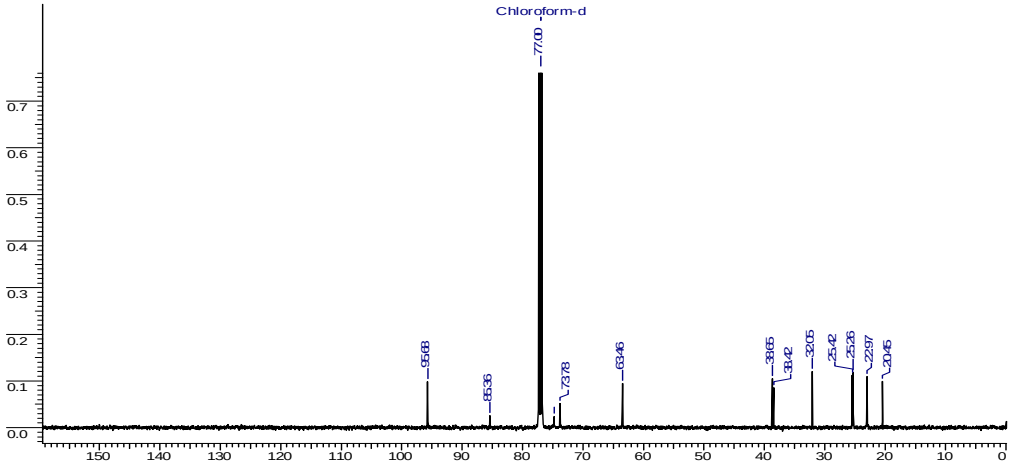
DEPT NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **3**



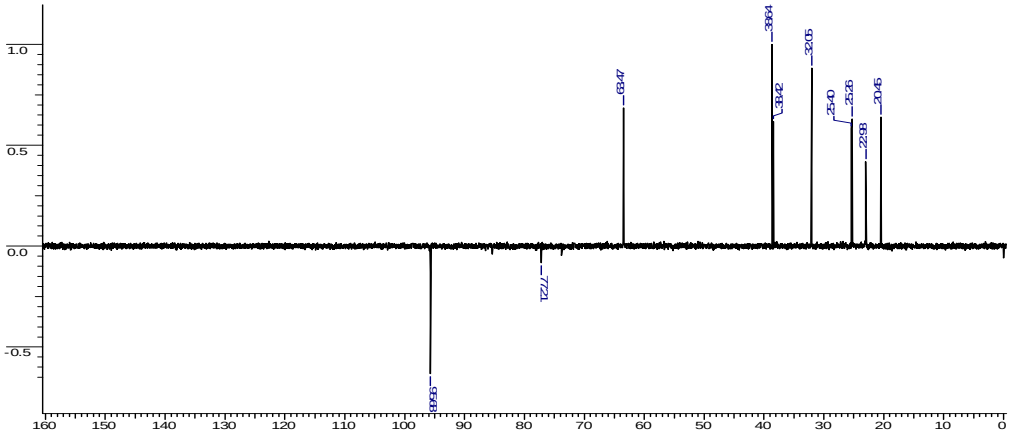
^{1}H NMR Spectrum (500.13 MHz, $CDCl_3$) of Compound **8**



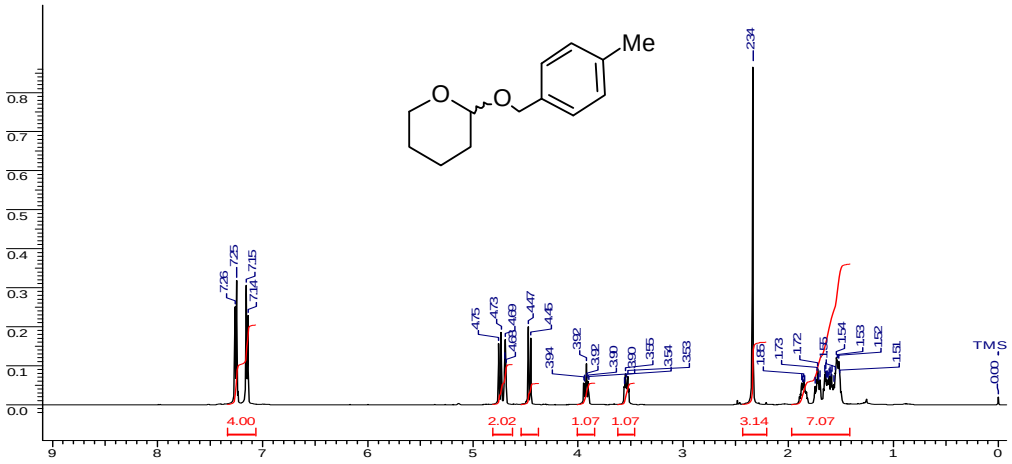
^{13}C NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **8**



DEPT NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **8**



^{1}H NMR Spectrum (500.13 MHz, $CDCl_3$) of Compound **10**



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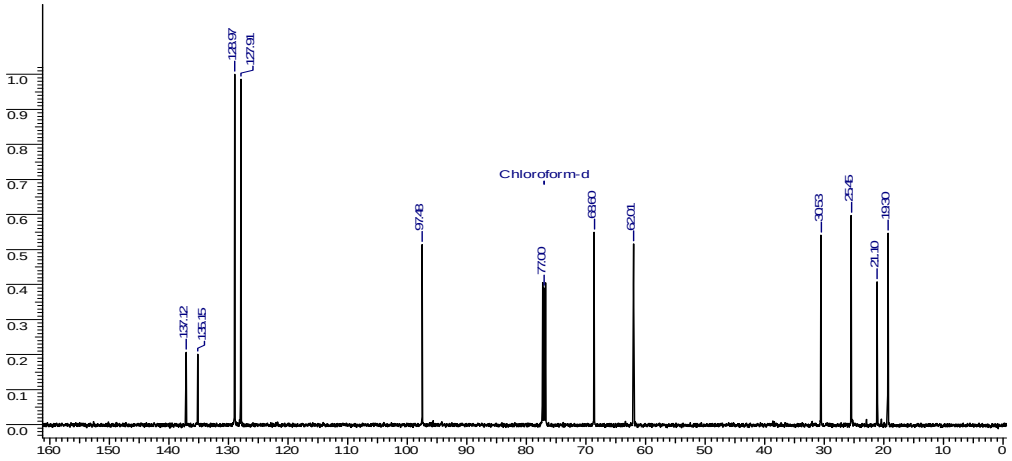
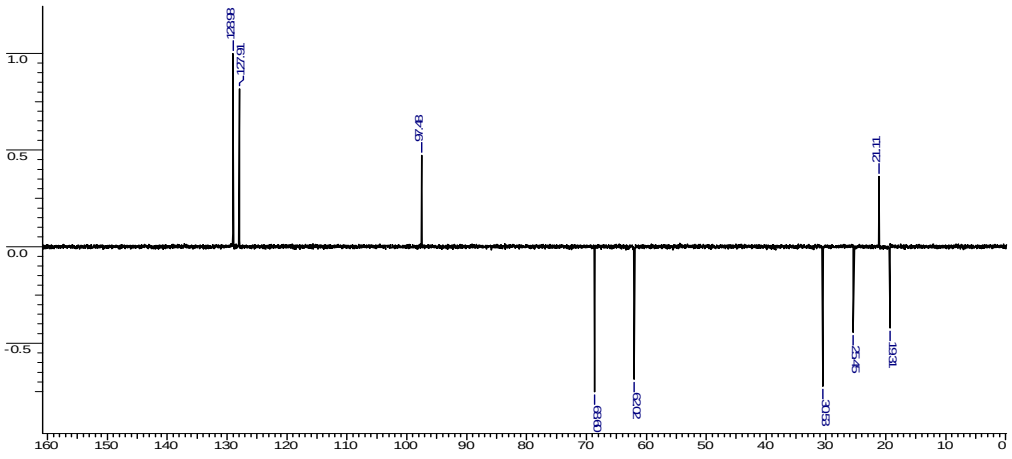


DEPT NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **10**



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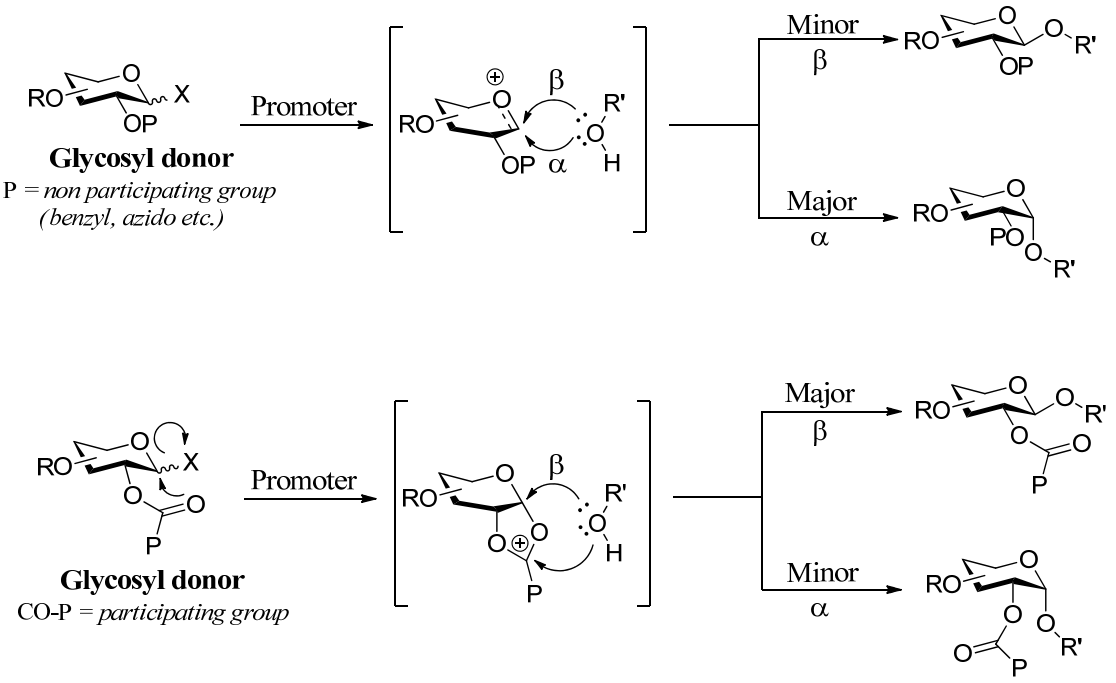
Complex carbohydrates covalently linked to proteins and lipids were long considered to be biological compounds that lack any biological specificity serving merely as structural components, it has become evident within the last three decades that complex carbohydrates in particular those covalently linked to proteins and lipids form highly diverse and complex class of biomolecules that are almost ubiquitous in any living organism and mediate a large number of biological functions.[1] In general Glycoconjugates are biopolymers formed when an oligosaccharide is attached to a protein or lipid moiety. These glycoconjugates are present in the membrane of cells responsible for large number of diverse and important biological functions like inflammation, immune response, metastasis, and fertilization. Specific carbohydrates cover different kind of functions, for example they act as markers of certain types of tumors, and some of the glycoconjugates can perform as signal molecules of symbiotic processes in legume plants where as in some cases these operate as binding sites for bacterial and viral pathogens.[2]

Glycobiology is a division of organic chemistry which deals with the study, preparation and biological role of sugars from monosaccharides to complex oligosaccharides and their analogues. The important role of carbohydrates in biology and biomedicine provides opportunities for development of new methods for the chemical and enzymatic synthesis of this class of molecules. The biological role of sugars depends on many factors, compared with other biopolymers such as nucleic acids, proteins and peptides, in which their biological activity depends on their sequence of nucleotides or amino acids; in the case of oligosaccharides the situation is more complex. For oligosaccharides, besides the sequence of the monomeric structures, other aspects such as the functional groups and their stereochemistry, the conformation of sugar ramification, the stereoselective formation of glycosidic linkages, etc. must be considered. All these facts have made the area of oligosaccharide synthesis an ideal and challenging area for the development and testing new synthetic methodologies.[3]

The formation of glycosidic bond is an important step for oligosaccharide synthesis which forms through displacement of leaving group attached to the anomeric carbon of a sugar moiety by an alcohol ROH, or by the OH group of partially protected sugar moiety. The reaction is generally performed in the presence of an activator called promoter. The role of promoter is to assist in the departure of the leaving group. Promoters are often used in catalytic amounts, although in some instances they are used stoichiometrically. The general mechanistic pathways for glycosidic bond formation can be represented as below. The timing of events heavily depends on the structure of the glycosyl donors, acceptors and promoters. There are some exceptions to this general mechanism, such as *in situ* anomerization,[4] intramolecular aglycon delivery[5] and use of additives such as acetonitrile,[6] which appears to react at anomeric centre itself.

Figure: 1

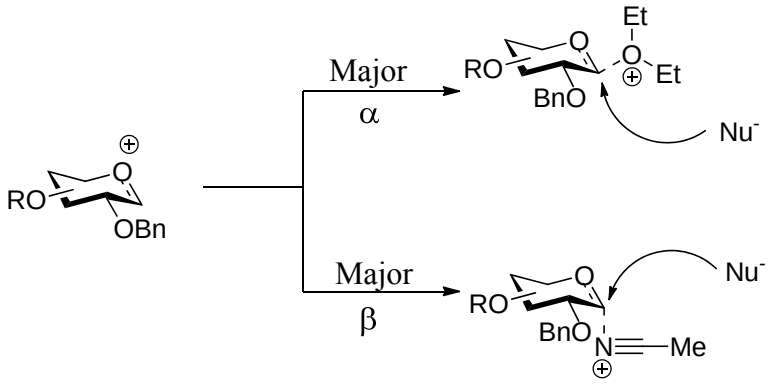


A success of glycosidation depends on several factors. In chapter 1, it has been demonstrated that the reactivity of glycosyl donor can be tuned by interchanging protecting groups. Whereas the reactivity of glycosyl acceptor depends on the nucleophilicity of the hydroxyl groups in partially protected carbohydrates that in turn depends on their nature (1^0 more reactive than 2^0), their spatial orientation (equatorial more reactive than axial), conformation of sugar ring and presence of protecting groups on glycosyl acceptors. The nature of promoter, generally a Lewis acid, also has been an effect on glycosidation. In addition the nature of Lewis acid classifies the reaction as homogenous or heterogeneous.

The solvent also has significant influence on the overall rate of the process and on the stereochemistry, especially in the case of non-participating glycosyl donors. Anhydrous solvents are required to avoid competition from water. Solvents of low polarity, such as dichloromethane or diethyl ether are frequently used. Sometimes polar aprotic solvents such as acetonitrile or nitromethane are used. On the other hand, some solvents may also form complexes with the intermediate sugar oxocarbenium ion, affecting the orientation of the incoming nucleophile. For instance, diethyl ether enhances the formation of α–glycosides[7] while acetonitrile favors the accumulation of β-anomer. This can be explained by the formation of an exocyclic complex with the solvent that hinders the β– and α– faces respectively. The influence of acetonitrile on the stereochemical outcome of glycosidation is called as '*nitrile effect*' and can be explained by the formation of an axial α-acetonitrilium ion.[6] Many different types of glycosyl donors feature the ability to form highly reactive nitrilium intermediates with acetonitrile. However it has been shown that the acetonitrile effect does not apply for

the synthesis of β-mannosides. The methodology is most commonly applied for the preparation of β-glucosides and β-galactosides and in general the best β selectivities are obtained with reactive alcohols at low temperatures such as -20 ^{0}C.

Figure: 2



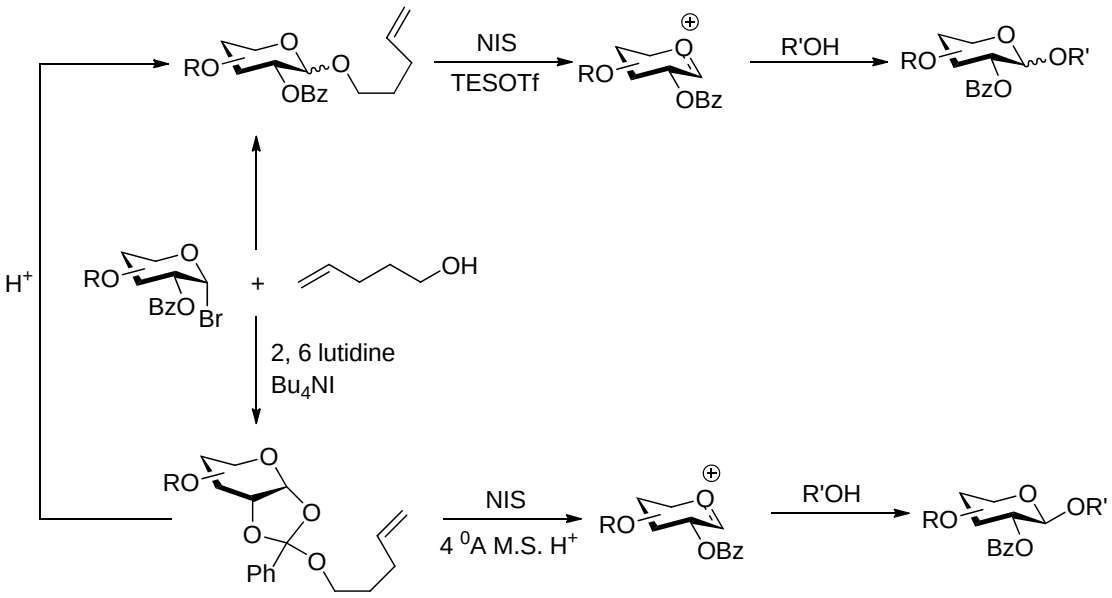
From a chemical point of view, the synthesis of oligosaccharides still presents an important challenge to synthetic chemists in spite of major advances in the area. During the period of last five decades several synthetic methods were developed for glycoside bond formation. Although some methods for glycoside synthesis are more popular than others, but still there is no universal protocol that can be applied to any combinations of donors and acceptors without consideration of their substitution patterns, configurations, or position of the hydroxyl groups. In terms of utility and wide applications, *n*-pentenyl activation developed by Bert Fraser-Reid and trichloroacetimidate activation, developed by Robert R. Schmidt are well-liked methods over other glycosidation methods.

The *n*-pentenyl glycosidation method was introduced by Fraser-Reid in 1988.[8] The activation of leaving group is based on an electrophilic addition to the double bond of aglycon, followed by an intramolecular displacement of the ring oxygen and eventual expulsion of the pentenyl chain to form oxocarbenium species. Trapping with a glycosyl acceptor, then leads to desired glycoside. The promoter of the choice is any source of halonium ion. NBS or NIS alone or activated by Lewis acid. NIS/Et_3SiOTf is commonly used. The use of NBS or NIS alone, affects the progress of reaction and often takes hours or days for completion of reaction. This method is further extended for stereoselective glycosidation using *n*-pentenyl 1,2-orthoester (NPOEs) for the synthesis of 1,2-*trans* glycosides. The usual choice of catalyst for activation of NPOEs is NIS along with lanthanide triflates.[9]

The *n*-pentenyl glycosides are stable under most condition which enables them for wide range of applications in carbohydrate chemistry. The *n*-pentenyl glycosides are also useful in the convergent synthesis of larger oligosaccharide units.[10] The potential of this glycosyl donor is further increased by the observation that acetyl and ether protected *n*-pentenyl glycosides displays different reactivities. This finding is known

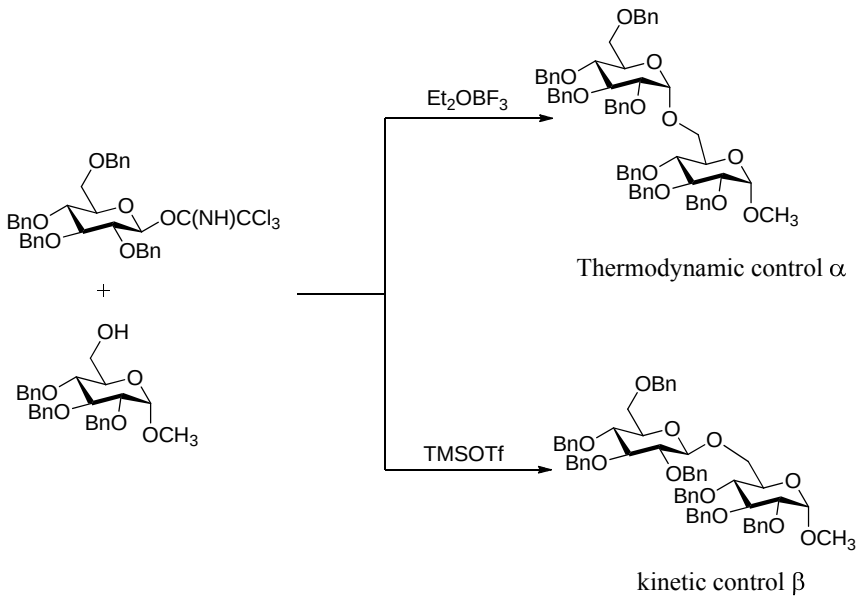
as the armed- disarmed glycosidation strategy which has been discussed earlier in chapter 1.

Figure: 3



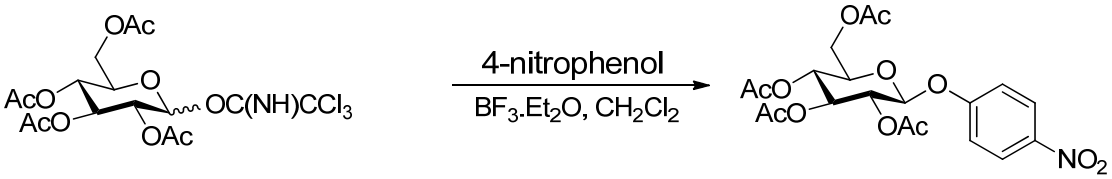
The Trichloroacetimidate method was developed into a widely applicable method by R. R. Schmidt after treating hemiacetals sugars with trichloroacetonitrile in the presence of base which gives rise to the replacement of anomeric oxygen in to a good leaving group.[11] These newly formed trichloroacetimidates are highly sensitive towards acidic or basic condition. Importantly the real strength of TCA method lies in the synthesis of glycosidic linkages; for example strong Lewis acids like TMSOTf gives rise to thermodynamically controlled α glycosides whereas weak Lewis acids like ZnBr, AgOTf and $BF_3.Et_2O$ forms kinetically controlled β glycoside.[12]

Scheme: 1



In general glycosidation with glycosyl trichloroacetimidates gives good yield in small scale as well as in large scale. Notably the trichloroacatimidate can be activated even when the glycosyl donor with disarmed protecting groups such as acetates and benzoates. But ether protected trichloroacetimidates are more reactive than their ester protected counterparts, as ether groups stabilize the oxocarbenium ion, which occurs as intermediate of the glycosidation reaction.

Scheme: 2

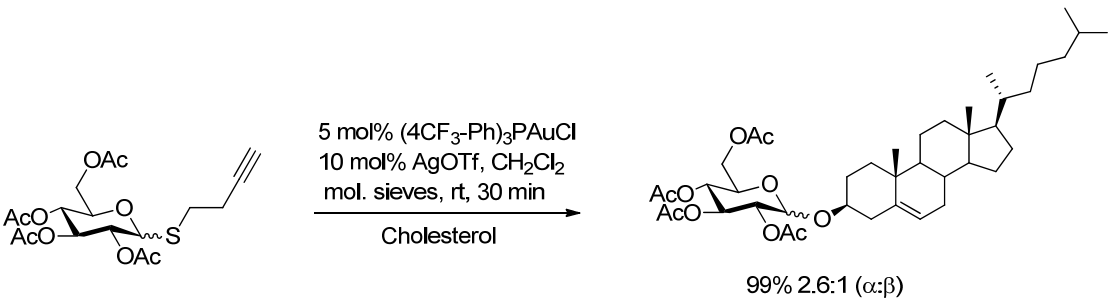


1,2 *trans* selective

Despite of having numerous literature reports showing utility of trichloroacetimidates, the major disadvantage is stability of these glycosyl donors which does not allow them to store it for longer period of time.

Apart from these two methods several other methods were developed for the synthesis of oligosaccharides and glycoconjugates, few of them are thioglycosides,[13] sulphoxides,[14] selenoglycosides,[15] and glycals.[16] During the period of last seven years gold catalyzed glycosidation has added a new flavor to the field of glycochemistry where Hotha *et al* has demonstrated the utility of catalytic gold (III) salts for anomeric activation using simple propargyloxy group.[17] The utility of catalytic gold (III) has a potential for solving some of the problems in the field of Glycobiology. After the disclosure of gold catalyzed glycosidation, the same concept has been utilized by several other groups which have been discussed in the last chapter. Recently, in a systematic development we have disclosed a gold catalyzed glycosidation protocol at ambient temperature[18] which has broadened the scope this methodology to a larger extent. In 2012 Yu *et al* had shown the utility of *ortho*-alkynylphenyl thioglycosides, which could undergo glycosidation in presence of gold (I) complex.[19]

Scheme: 3

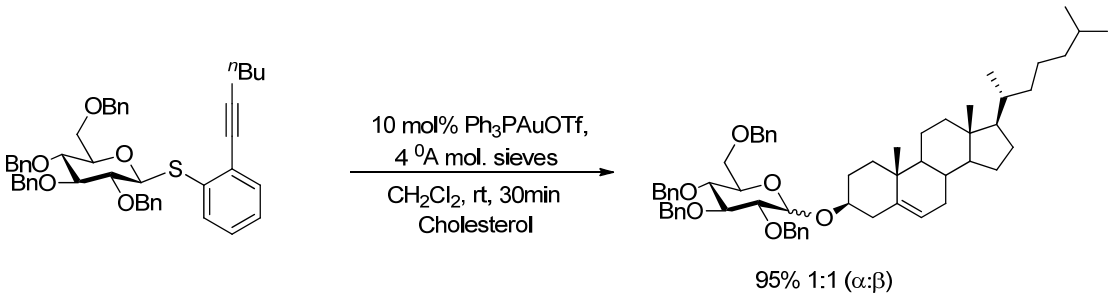


99% 2.6:1 (α:β)

The latest development in this field is made by Jianglong Zhu and co workers, who demonstrated a mild and atom-economic gold (I)-catalyzed glycosylation for stereoselective synthesis of 2-deoxy α- glycosides using bench-stable 2-deoxy S-But-3-ynyl thioglycoside donors. Under optimal conditions, 2-deoxy and 2,6-dideoxy

thioglycoside donors were able to react with a variety of primary, secondary, and tertiary alcohol acceptors to afford α-selective glycosides in good to excellent yields.[20]

Scheme: 4



95% 1:1 (α:β)

In our laboratory, we have developed a glycosidation methodology where alkyne leaving group can be activated at ambient temperature. The versatility has been proved by treating 1-ethynylcyclohexanyl glycosyl donors with a range of glycosyl acceptors including aromatic, cyclic and steroidal alcohols in quantitative yields. Moreover carbohydrate-based primary and secondary alcohols shown excellent conversions. In addition the Ech glycosyl donors have been successfully utilized for the synthesis of oligosaccharides in moderate yields but need further improvement. Thus systematic improvisation to the newly developed glycosidation methodology has a promising potential to serve as glycosyl donor with numerous application in field of carbohydrate chemistry.

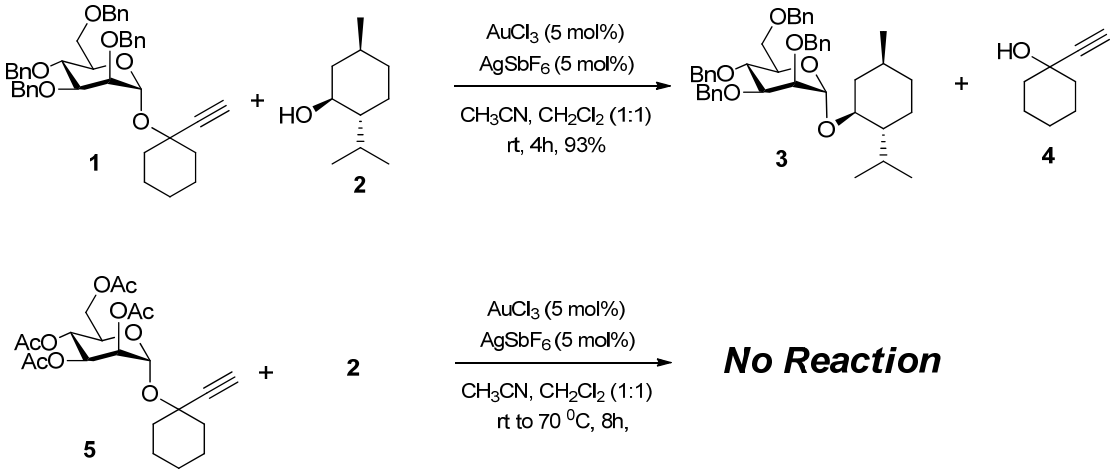
The majority of human proteins are co- or post-translationally modified by mono- or oligosaccharides. These glycoconjugates contribute physiochemical properties, influencing protein conformation or increasing stability against proteolytic activity. With their unique structural diversity and complexity, carbohydrates attached on proteins or lipids are involved in numerous cell-surface binding events, such as cell growth and differentiation, cell proliferation, cell adhesion, binding of pathogens, fertilization and immune responses. Furthermore, glycans assist in intracellular protein folding and transport. Pathogenic processes, such as chronic inflammation, viral and bacterial infections, tumour growth and metastasis, and autoimmune disorders, all involve glycan cell–cell communication.[1,2] The availability of structurally defined glycopeptides and glycoproteins, which contain information about the glycan structure and glycosidation sites, is valuable for functional biological studies. Glycopeptides have, for instance, been applied to evaluate the role of conformational and proteolytic stability. In other studies, synthetic glycopeptides have been employed in vaccines to induce specific immune responses or for the inhibition of protein binding events. This awareness of the biological importance of carbohydrates has led to glycoscience becoming an intriguing and fascinating field of interdisciplinary research. However, the structural diversity found in the carbohydrate regime is unparalleled. Which makes the biological study of carbohydrate recognition and understanding the processes involved rather complicated. In addition, the multivalent nature of most carbohydrate ligands constitutes a special challenge in glycoscience.

Since the isolation of those complex glycoconjugates, which are active in cellular communication is problematic. Moreover these glycoconjugates exist in microheterogenious form; hence, cannot be isolated in acceptable amount and purity, where chemical synthesis provides an opportunity for obtaining structurally well defined and chemically pure glycoconjugates for biological studies. To date no general method or strategy exists for complex oligosaccharides and glycoconjugate synthesis. Moreover, what Professor Hans Paulsen, one of the greatest exponents of glycoside synthesis, observed in 1982 still holds true today: [21] "*Although we have now learned to synthesize oligosaccharides, it should be emphasized that each oligosaccharide synthesis remains an independent problem, whose resolution requires considerable systematic research and a good deal of know-how. There are no universal reaction conditions for oligosaccharide syntheses.*"

It is therefore not surprising that the majority of contributions in the field of glycoscience, deals with development of new methodologies for oligosaccharide synthesis. In this continuation, gold catalyzed glycosidation has already made a significant impact to this field. Although any imperative method with the characteristics like mildness, atom economic and high yielding is highly valuable for further advancement of this field. Recently, we have demonstrated a versatile transglycosidation protocol by keeping 1-ethynylcyclohexanyl (-Ech) at anomeric position.[15] This newly developed method is suitable for activation of leaving group at

ambient temperatures; formation of transglycosides in quantitative yield is the important feature of this method. Whereas newly developed glycosyl donors executed the characteristic activation depending on armed-disarmed effect is another critical aspect of this protocol. For example when armed mannosyl donor 1-ethynyl cyclohexanyl 2,3,4,6-tetra-*O*-benzyl α-D-mannopyranoside (**1)** was treated with menthol (**2**) in presence of 5 mol% each of $AuCl_3$ and $AgSbF_6$, in presence of 1:1 mixture of acetonitrile and dichloromethane, at room temperature, furnished 93% of required product (**3**) in 4h. Contradictorily disarmed mannosyl donor 1-ethynyl cyclohexanyl 2,3,4,6-tetra-*O*-acetyl α-D-mannopyranoside (**5**) upon treatment with menthol (**2**) under similar set of conditions was incapable to form required tranglycoside. Increase in the temperature also failed to give the required transglycoside, which further proved the existence of armed-disarmed effect in Ech-glycosides.

Scheme: 5

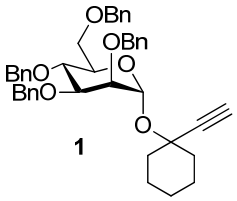
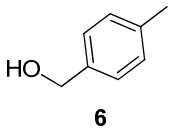
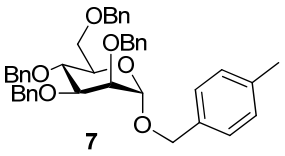
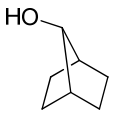
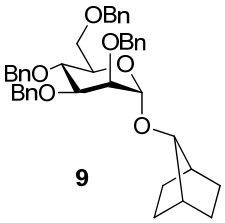
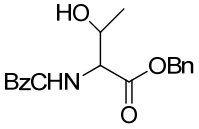
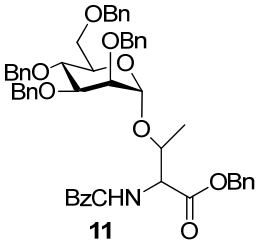
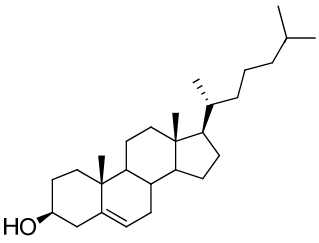
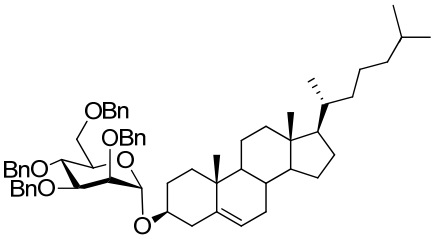


The generality of the newly identified gold-catalyzed transglycosidation at room temperature was evaluated with a panel of aglycons. Accordingly armed mannosyl donor, 1-ethynyl cyclohexanyl 2,3,4,6-tetra-*O*-benzyl α-D-mannopyranoside (**1**) was allowed to react with 4-methyl benzyl alcohol (**6**), cholesterol (**12**), exo-norbornyl (**8**) and CBz-protected threonine (**10**) in the presence of 5 mol% each of $AuCl_3$ and $AgSbF_6$ in 1:1 solution of acetonitrile and dichloromethane at room temperature for 4h, under argon atmosphere. It is imperative to mention that all glycosidations proceeded smoothly and afforded the respective transglycosides in quantitative yields. All the resultant mannosides were confirmed through ^{1}H, ^{13}C, DEPT and mass spectroscopic techniques.

The utility of newly identified gold catalyzed transglycosidation condition was extended for the synthesis of disaccharides. Interestingly monosaccharide based primary alcohols resulted in quantitative yields to give disaccharides, whereas carbohydrate-based secondary alcohol gave greater than 70% yields. For example a reaction of mannosyl donor (**1**) with propargyl 2,3,4-tri-*O*-benzoyl α-D-mannopyranoside (**14**) in the presence of $AuCl_3$ and $AgSbF_6$ (5 mol% each) in 1:1

solution of acetonitrile and dichloromethane at room temperature for 4h, under argon atmosphere gave required disaccharide (**15**) with 91% yield (Table 1).

Table: 1

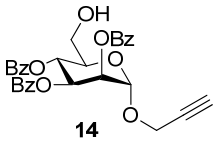
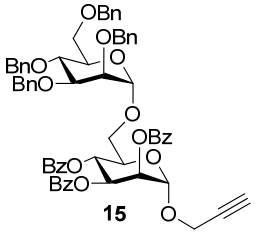
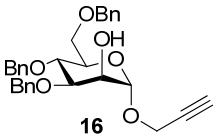
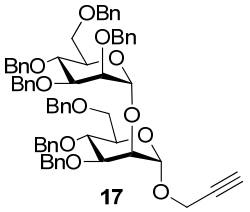
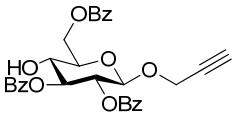
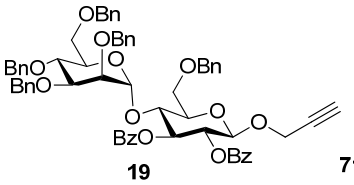
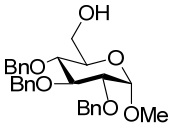
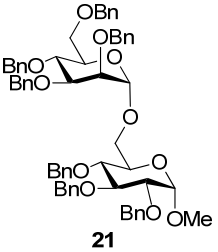
Mannosyl donor	Aglycon	Corresponding Mannoside	Yield
 **1**	 **6**	 **7**	**95**
1	 **8**	 **9**	**68**
1	 **10**	 **11**	**74**
1	 **12**	 **13**	**90**

^{1}H NMR spectrum, of compound **15** showed two doublets at δ 4.96 (J =1.8 Hz) and δ 5.26 (J =1.8 Hz) which are the characteristic signals for anomeric protons. Similarly in ^{13}C NMR two signals were observed at δ 96.2 ppm and δ 98.2 ppm further confirmed the formation of requisite disaccharide. Similarly when mannosyl donor (**1**) was treated with methyl 2,3,4-tri-*O*-benzyl α-D-Gluopyranoside (**20**) under similar set of conditions, gave anticipated disaccharide in 96% yield.

This newly designed gold catalyzed transglycosidation protocol was further utilized for building *1,2*- and *1,4*- linkages of disaccharides, for example a reaction of mannosyl donor (**1**) with propargyl 3,4,6-tri-*O*-benzyl α-D-Mannopyranoside (**16**) under 5 mol% $AuCl_3/AgSbF_6/CH_3CN$-CH_2Cl_2(1:1)/rt/8h gave requisite disaccharide

(17) with 78% yield. Similarly reaction of mannosyl donor (**1**) with aglycone (**18**) gave required disaccharide (**19**) in 71% yield.

Table: 2

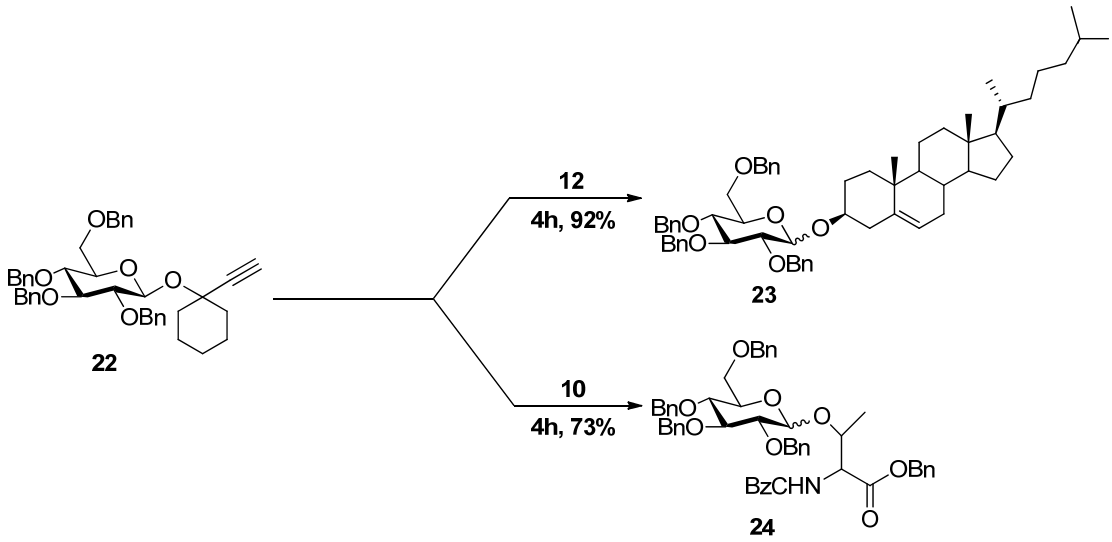
Mannosyl donor	Aglycon	Corresponding Mannoside	Yield
1	 **14**	 **15**	**91**
1	 **16**	 **17**	**78**
1	 **18**	 **19**	**71**
1	 **20**	 **21**	**96**

In an attempt to extend the applicability of room temperature transglycosidation protocol, the glucosyl donor and galactosyl donor were prepared by trichloroacetamidate method from respective monosaccharides and characterized through ^{1}H, ^{13}C, DEPT NMR spectroscopic analysis. In the ^{1}H NMR spectrum of 1-ethynyl cyclohexanyl 2,3,4,6-tetra-*O*-benzyl β-D-glucopyranoside (**22**) corresponding signal for methine proton and cyclohexane ring protons were observed at δ 2.55ppm as a singlet and δ 1.15-2.15 ppm as a multiplet. In addition the characteristic anomeric proton was observed at d 4.55 ppm as a doublet with coupling constant J = 10.3 Hz, the all other signals were completely agreement the assigned structure of glucosyl donor (**22**). In addition, ^{13}C spectrum showed resonance at δ 99.3 ppm confirmed the β configuration of compound **22**.

Similarly the ^{1}H NMR spectrum of galactosyl donor (**28**) showed the signal corresponding to methine proton and cyclohexane ring protons at δ 2.51 ppm as singlet for 1 proton and δ 1.05-2.10 ppm as multiplet for 10 protons. Further the resonance attributed to anomeric proton was observed at δ 4.97 ppm as a doublet with J = 7.8 Hz. All other signals were completely in agreement with the assigned structure of galactosyl donor (**28**). Moreover in ^{13}C NMR spectrum, resonance occurred at δ 99.6 ppm confirmed the exclusive β-configuration of compound **28**.

Later, the glycosidation reaction was carried out between glucosyl donor (**22**) aglycons comprising cholesterol (**12**) and CBz-protected threonine (**10**) in presence of 5 mol% $AuCl_3/AgSbF_6/CH_3CN$-CH_2Cl_2(1:1)/rt/ under argon atmosphere to obtain α,β–mixture of corresponding glycoside with excellent yields. The β-anomer was observed as a major isomer in comparison to the α-anomer due to the participating nature of CH_3CN, which is in complete agreement with earlier observations.[17]

Scheme: 6

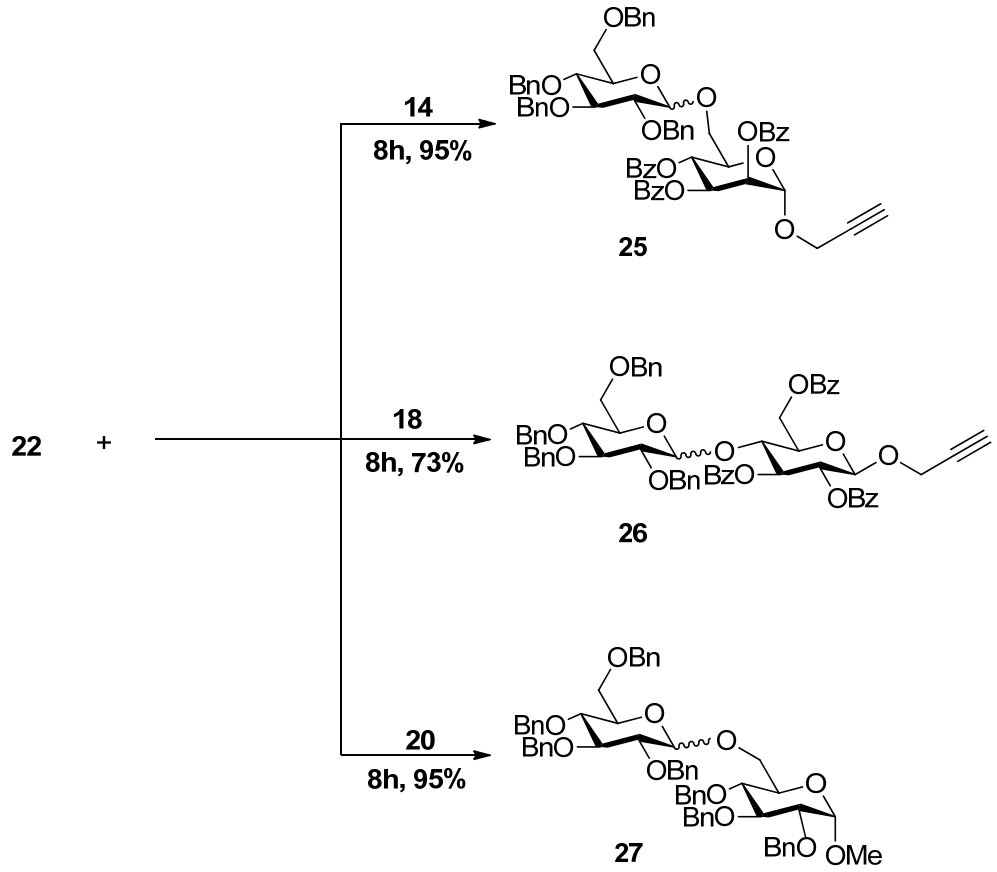


In addition, synthesis of disaccharides has been visualized through glycosidation of glucosyl donor (**22**) with an alcohol derived from monosaccharide unit. Accordingly glucosyl donor (**22**) was treated with propargyl 2,3,4-tri-*O*-benzoyl α-D-mannopyranoside (**14**) in presence of 5 mol% $AuCl_3/AgSbF_6/CH_3CN$-CH_2Cl_2(1:1)/rt under argon atmosphere for 8h, to obtain α–β mixture of estimated disaccharide (**25**) with 95% yield. Similarly the reactions of glucosyl donor (**22**) with carbohydrate-based alcohols **18** and **20** gave α,β–mixture of corresponding disaccharides **26** and **27** in good yields.

All the glycosylated disaccharides were thoroughly characterized by ^{1}H, ^{13}C, DEPT and mass spectroscopic analysis. For example ^{1}H NMR spectrum of disaccharide (**25**) showed two signals corresponding to methine proton of propargyl group at δ 2.39 ppm and 2.46 ppm as two individual triplets with coupling constant J = 2.44 Hz. In addition the resonance occurred at δ 7.75-8.15 ppm as multiplet for 12 protons confirmed the presence of benzoates in disaccharide. Further, the ^{13}C NMR spectrum

showed the two signals corresponding to the two anomeric carbons present in a disaccharide at δ 95.9 ppm and δ 97.4 ppm. Similarly resonances attributed to the two anomeric carbons for β–isomer were noticed at δ 95.4 ppm and δ 104.1 ppm. Rests of the resonances in the spectrum were completely in agreement with assigned structure of disaccharide **25**. The α,β– ratio was determined by comparing peak heights of corresponding signals of anomeric carbons of α– and β– isomers. Moreover the mass peak at 1075.3871 (M^++Na) confirmed the formation of disaccharide **25**, where the theoretical molecular weight for compound **25** is 1075.3881 (M^+ Na).

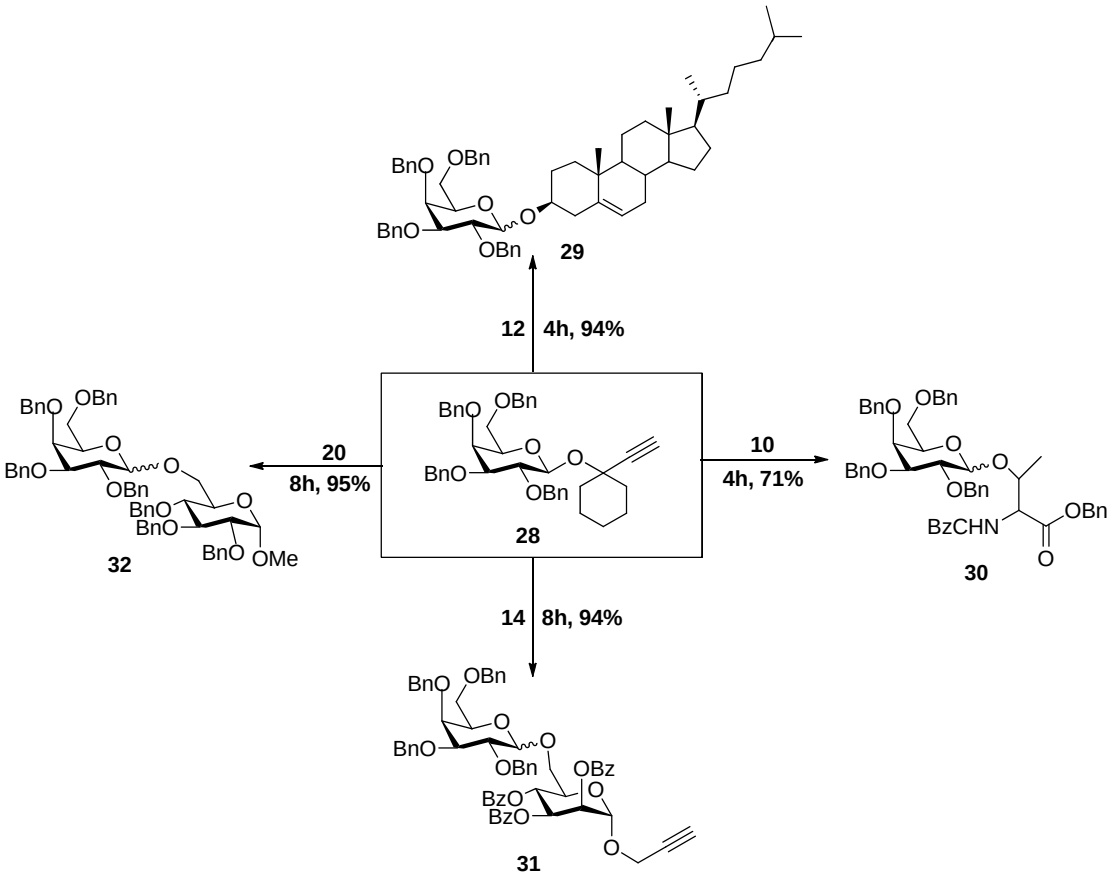
Scheme: 7



Further the glycosidation of galactosyl donor (**28**) with cholesterol (**12**) and CBz-protected threonine (**10**) in presence of 5 mol% $AuCl_3/AgSbF_6/CH_3CN$-CH_2Cl_2(1:1)/rt under argon atmosphere gave corresponding transgalactosides **29** and **30** as a inseparable mixture of α,β–isomers in excellent yields. Similarly the same reaction condition was used to get disaccharides. The galactosyl donor (**28**) was allowed to react with carbohydrate-based alcohols **14** and **20**, to get α,β– mixture of requisite disaccharides **31** and **32**. The newly galactosylated disaccharides were confirmed thoroughly by ^1H, ^{13}C, DEPT and mass spectroscopic analysis. For example formation of disaccharide **32** was confirmed with two doublets at δ 4.52 (d, 1H, J = 3.5 Hz) and δ 4.55 (d, 1H, J = 5.1 Hz), in the ^1H NMR spectrum. Whereas, ^{13}C NMR spectrum confirmed the β–galactosides as major isomer of reaction with anomeric signals at

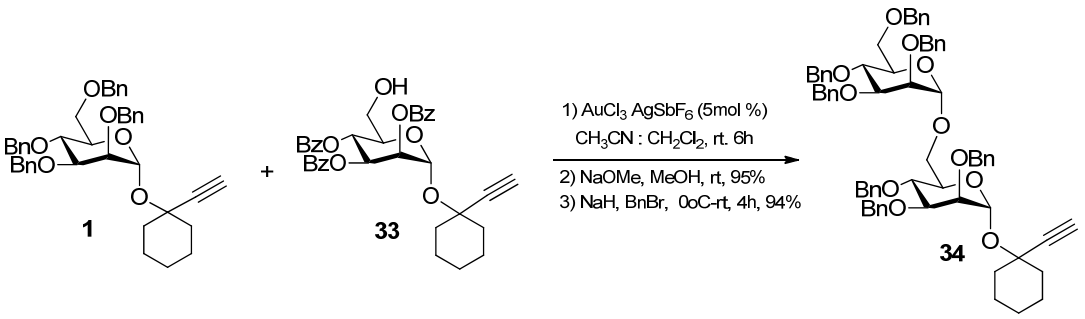
δ 97.8 ppm and δ 97.9 ppm. Rests of the resonances in the spectrum were completely in agreement with assigned structure of disaccharide **32**. Finally the assigned compound **32** was confirmed by mass spectroscopy which was observed at 1009.4508 [M^+ + Na], shown the complete agreement with theoretical molecular weight of compound **32** [$C_{62}H_{66}O_{11}$+Na] i.e. 1009.4503.

Scheme: 8



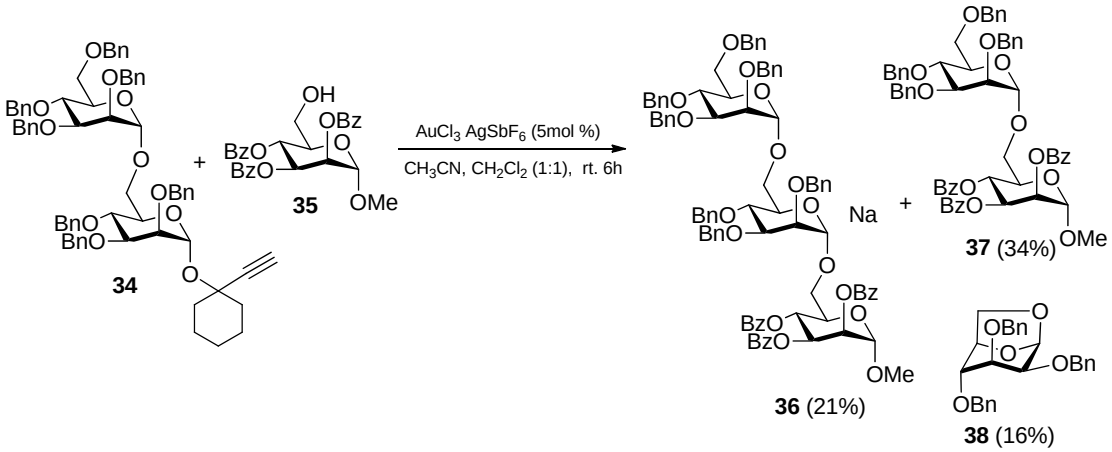
In order to check the efficiency of newly designed room temperature alkyne activation protocol for the synthesis of oligosaccharides using armed-disarmed effect, the armed glycosyl donor (**1**) was allowed to react with aglycone **33** in presence of 5 mol% $AuCl_3/AgSbF_6/CH_3CN$-CH_2Cl_2(1:1)/rt under argon atmosphere gave corresponding disaccharide in 91% yield, which subsequently converted into an armed disaccharide **34** in two steps involving Zemplén debenzoylation (NaOMe/MeOH/rt) followed by benzylation using NaH and benzyl bromide in DMF.

Scheme: 9



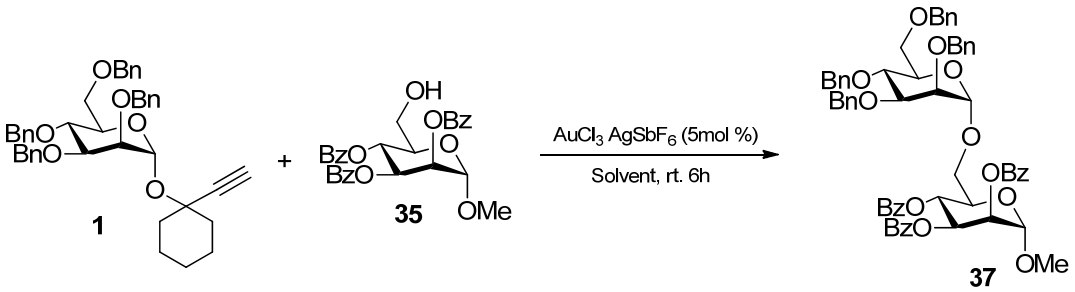
Later, the armed disaccharide **34** was allowed to react with disarmed aglycon **35** in the presence of $AuCl_3/AgSbF_6/CH_3CN$-CH_2Cl_2(1:1)/rt under argon atmosphere for 6h. Purification by conventional silica gel column chromatography enabled us to characterize the anticipated trisaccharide **36** with 21% yield along with disaccharide **37** and anhydro sugar **38**. In the trisaccharide **36**, three anomeric protons were noticed at δ 4.88 (1H, d, *J* = 1.6Hz), 4.91 (1H, d, *J* = 1.6Hz), 5.61 (1H, dd, *J* = 1.6, 3.2Hz) ppm. The ^{13}C NMR spectrum revealed that there are three mannose residues with 1,2-*trans* configuration as their anomeric carbons were noticed at δ 98.1, 98.2 and 98.5 ppm and the molecular weight was found to be 1483.586 (M^++23 for Na). Rest of the resonances in the spectrum were completely in agreement with assigned structure of trisaccharide **36**. Formation of disaccharide **37** and anhydro sugar **38** can be rationalized on the basis of susceptibility of interglycosidic bond cleavage. Thus, it is proved that the Ech glycosides can be successfully utilized for oligosaccharide synthesis.

Scheme: 10



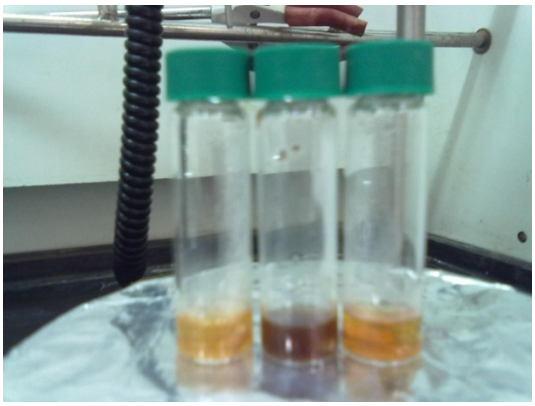
However the current protocol is insufficient to prevent the cleavage of interglycosidic bond. Here the systematic restrain in reaction temperature has successfully demonstrated the synthesis of trisaccharide in moderate yield and further proved the influence of reaction temperature on the outcome of reaction along with other important factors like choice of solvent, reaction conditions and reaction time. Moreover in case of non participating glycosyl donors, the resultant glycosidic linkage depends on choice of solvent. Non participating solvents like dichloromethane and diethyl ether gives α-glycosides whereas a polar and participating solvent like acetonitrile gives β-glycosides. Generally a glycosidation reaction follows S_N1 pathway, where the polarity of solvent plays an important role, because polar solvents stabilizes the oxonium cation intermediate and improves the rate of reaction. Nitromethane is polar aprotic solvent, which is also frequently used for glycosidation reactions.[22] Nitromethane is slightly more polar than acetonitrile, the dielectric constant of nitromethane is 39.4 compare to acetonitrile with dielectric constant 37.5.

Scheme: 11



In an attempt to further improve in reaction condition, we thought out to compare the utility of acetonitrile against nitromethane. Accordingly, we made three sets of reactions, by reacting glycosyl donor **1** with aglycon **35** in presence of 5 mol% $AuCl_3$ for 4h in argon atmosphere at room temperature, with different solvent combinations. When acetonitrile was used as solvent, 35% product formation was observed without any color change to reaction mixture. In contrast when nitromethane was used, the initial pale yellow color of reaction was changed to dark brown, the glycosyl donor was completely consumed and gave complex TLC mixture through formation of multiple spots without formation of desired product. Similarly when the same reaction is performed using mixture of acetonitrile and nitromethane (1:1), gave 25% of desired product with slight color change to reaction mixture. Changing the temperature from rt to 0 ^{0}C, also failed to improve the yield of reaction, thereby confirming the importance of acetonitrile in gold mediated transglycosidation reaction.

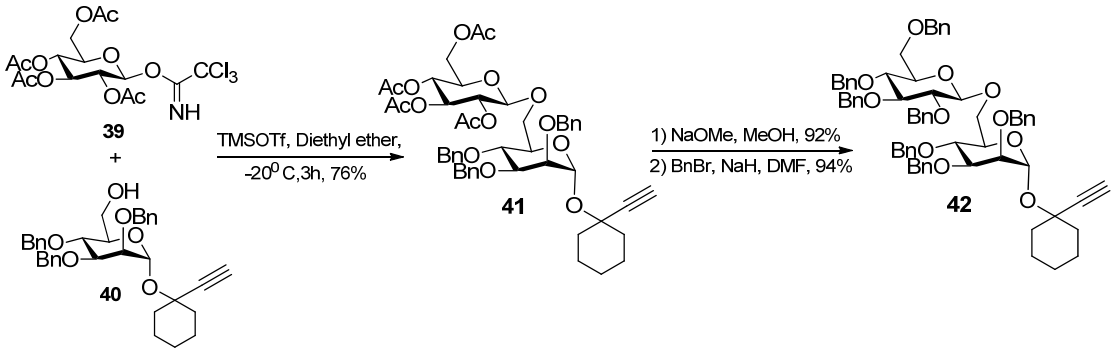
Figure: 4



During our study of gold mediated transglycosidation reaction, it was observed that, intensity of unusual cleavage depends on nature of interglycosidic linkage. Generally the glycosyl donors with axial hydroxyl groups are considered more reactive then the glycosyl donors without any axial hydroxyl group. For example β-D-glucose is less reactive as compare to α-D-glucose and α-D-mannose. In order to check the effect of reactivity difference on interglycosidic bond cleavage, we prepared armed disaccharide **42** by treating 2,3,4,6-tet-*O*-acetyl α-D-mannose trichloroacetimidate (**40**) with 1-ethynyl cyclohexanyl 2,3,4-tri-*O*-benzoyl α-D-mannopyranoside (**40**) in presence of diethyl ether and catalytic amount of TMSOTf at -20 ^{0}C followed by

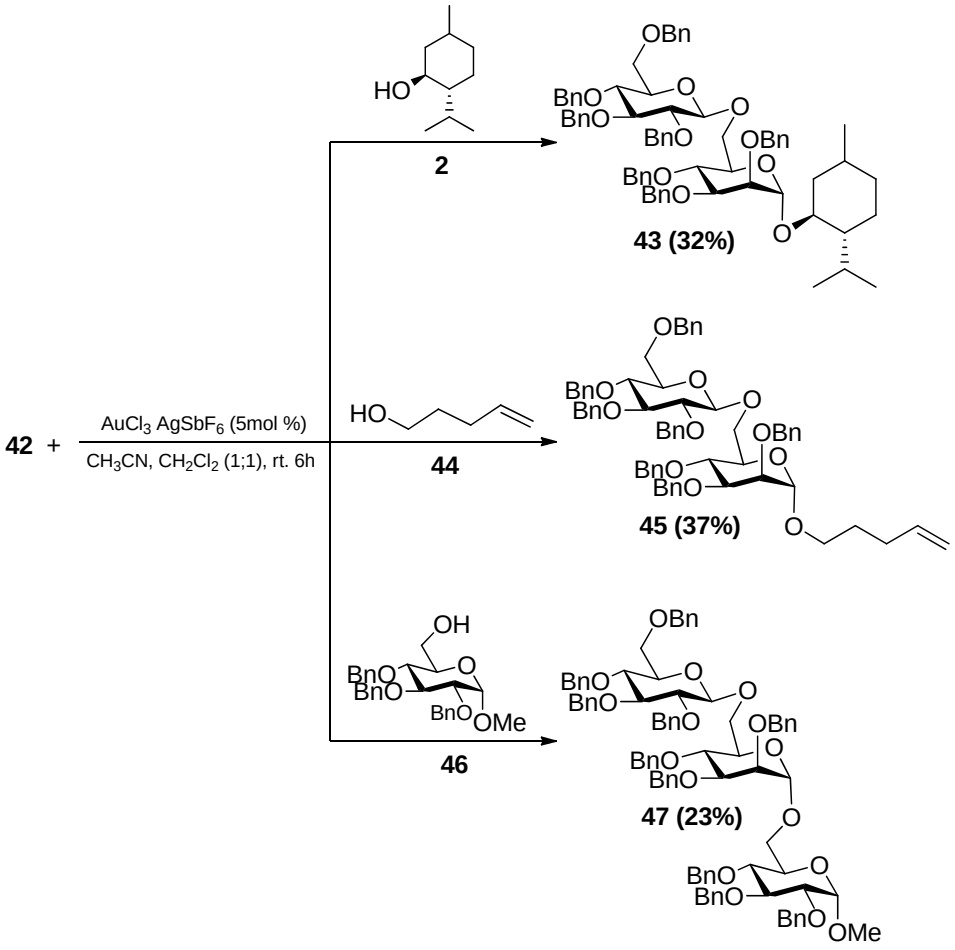
deacetylation (NaOMe/MeOH/rt) and benzylation using NaH and benzyl bromide in DMF.

Scheme: 12



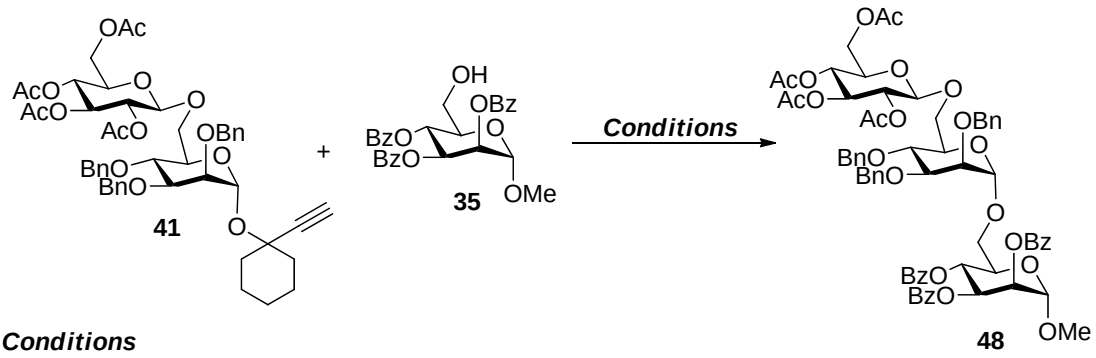
In an attempt to check the efficiency of newly prepared glycosyl donor, the armed disaccharide **42** was allowed to react with menthol (**2)** in presence of 5 mol% $AuCl_3/AgSbF_6/CH_3CN$-CH_2Cl_2(1:1)/rt under argon atmosphere for 6h, to give the requisite disaccharide (**43**) in 32% yield. Similarly reaction between glucosyl donor **42** with 4-penten-1-ol (**44**) and methyl 2,3,4-tri-*O*-benzyl α-D-glucopyranoside (**46**) gave corresponding transglycosides in 37% and 23% respectively.

Scheme: 13



Interestingly gold mediated transglycosidation reaction between disaccharide **41** and aglycon **35** gave corresponding trisaccharide **48** in good yield wherein cleavage of interglycosidic bond was not observed which further confirmed the importance of protecting groups in gold mediated glycosidation reactions.

Scheme: 14



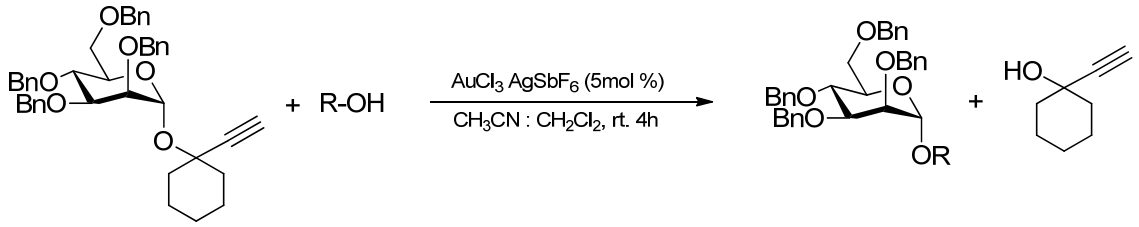
Conditions

1) $AuCl_3$, $AgSbF_6$ (5 mol % each), CH_3CN, CH_2Cl_2 (1:1), rt, 4h, 53%

2) $AuCl_3$ (5mol %) CH_3CN, 70 ^{0}C, 6h, 78%

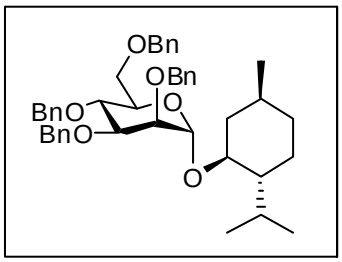
In conclusion, we have shown the utility of a gold-catalyzed transglycosidation that can be conducted at room temperature using 1-ethynylcyclohexanyl (Ech) glycosyl donors. The Ech glycosyl donors were found to be superior over the panel of aglycons including primary alcohols, alicyclic, steroidal alcohols which gave quantitative yields of transglycosylated products whereas carbohydrate-derived secondary alcohols and others result in high yields. Furthermore the gold mediated transglycosidation protocol has been successfully demonstrated for the synthesis of trisaccharide in moderate yields but needs further refinement to prevent complete interglycosidic bond cleavage.

General transglycosidation procedure for room temperature activation of 1-ethynylcyclohexanol glycosides:



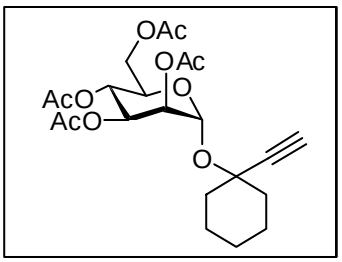
To a 3mL 1:1 CH_3CN-CH_2Cl_2 solution of glycosyl donor (1 equiv) and aglycon (1.1 equiv) was added a solution of $AuCl_3$ (5 mol%) and $AgSbF_6$ (5 mol%) in 3mL of 1:1 CH_3CN-CH_2Cl_2 and stirred at 25^o C for 4 h, under argon atmosphere. After completion of reaction (judged by TLC)., dark brown reaction mixture was concentrated *in vacuo* and the crude residue was purified through silica gel column chromatography using 1:5 ethyl acetate-petroleum ether to give corresponding transglycosides.

Characterization data for compound **3**



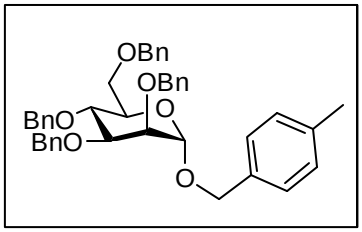
$[\alpha]_D^{25}$ = +5.2 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 0.64 (d, 3H, *J* = 6.7 Hz), 0.80 (d, 3H, *J* = 1.3 Hz), 0.84 (d, 3H, *J* = 2.0 Hz), 0.87-1.85 (m, 9H), 2.15 (m, 1H), 3.23 (dt, 1H, *J* = 4.3, 10.5 Hz), 3.67 (q, 1H, *J* = 2.0, 4.1 Hz), 3.76 (dd, 1H, *J* = 1.6, 4.7 Hz), 3.84-3.98 (m, 3H), 4.63 (ABq, 2H, *J* = 12.1 Hz), 4.63 (d, 1H, *J* = 1.4 Hz), 4.67 (ABq, 2H, *J* = 11.5 Hz), 4.68 (ABq, 2H, *J* = 12.1 Hz), 4.70 (ABq, 2H, *J* = 10.7 Hz), 7.10-7.38 (m, 20H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 16.2, 21.0, 22.2, 23.2, 25.7, 31.6, 34.2, 42.8, 48.6, 69.4, 71.7, 72.2, 72.4, 73.3, 74.3, 75.2, 75.2, 80.0, 81.0, 99.8, 127.3-128.4, 138.2, 138.4, 138.5, 138.5; HRMS (MALDI-TOF): calcd. for $C_{44}H_{54}NaO_6$ [M^++Na]: 701.3818; found: 701.3821.

Characterization data for compound **5**



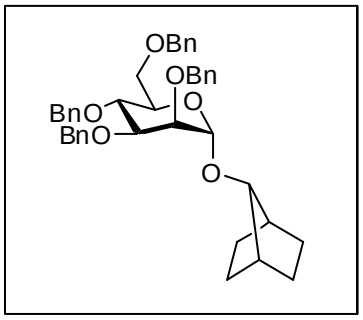
$[\alpha]_D^{25}$ = +65.6 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.20-1.92 (m, 10H), 2.00 (s, 3H), 2.05 (s, 3H), 2.09 (s, 3H), 2.18 (s, 3H), 2.57 (s, 1H), 4.08 (dd, 1H, *J* = 2.0, 11.6 Hz), 4.15-4.34 (m, 1H), 4.25 (t, 1H, *J* = 5.1 Hz), 5.18 (dd, 1H, *J* = 2.0, 3.1 Hz), 5.24-5.43 (m, 2H), 5.48 (d, 1H, *J* = 1.8 Hz); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 20.7, 20.7, 20.7, 20.9, 22.8, 22.8, 24.9, 37.8, 38.0, 62.5, 66.3, 68.8, 69.1, 70.6, 75.5, 77.2, 83.3, 93.7, 169.7, 169.9, 170.1, 170.6; HRMS (MALDI-TOF): calcd. for $C_{22}H_{30}NaO_{10}$ [M^++Na]: 477.1737; found:477.1753.

Characterization data for compound **7**



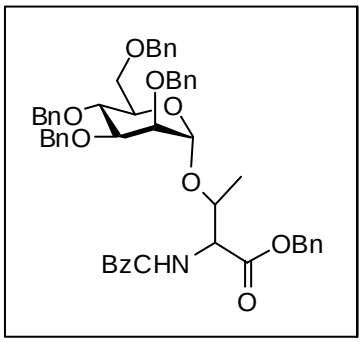
$[\alpha]_D^{25}$ = +15.4 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.34 (s, 3H), 3.68-4.08 (m, 6H), 4.48 (ABq, 2H, *J* = 11.8 Hz), 4.60 (s, 2H), 4.68 (ABq, 2H, *J* = 10.6 Hz), 4.69 (ABq, 2H, *J* = 10.7 Hz), 4.70 (s, 2H), 4.96 (d, 1H, *J* = 1.8 Hz), 7.10-7.40 (m, 24H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 21.2, 68.8, 69.2, 72.0, 72.1, 72.5, 73.3, 74.6, 74.9, 75.1, 80.2, 97.0, 127.3-128.3, 129.0, 129.0, 134.2, 137.4, 138.2, 138.3, 138.4, 138.5; HRMS (MALDI-TOF): calcd. for $C_{42}H_{44}NaO_6$ [M^++Na]: 667.3036; found: 667.3032.

Characterization data for compound **9** *(isomers at the norbornol 2^o-alcohol)*



$[\alpha]_D^{25}$ = +34.8 ($CHCl_3$, *c* 1.00); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 0.88-1.58 (m, 18H), 1.63 (s, 2H), 2.25 (m, 2H), 3.55-4.05 (m, 12H), 4.45-4.98 (m, 18H), 7.12-7.40 (m, 40H); ^{13}C NMR(100.61 MHz, $CDCl_3$): δ 24.2, 24.5, 28.4, 28.4, 34.6, 35.0, 35.1, 35.1, 39.5, 39.6, 39.6, 41.9, 69.3, 69.4, 71.7, 71.8, 72.1, 72.1, 72.4, 72.5, 73.2, 73.2, 75.1, 75.2, 75.2, 75.2, 75.3, 75.4, 78.5, 80.2, 80.3, 81.1, 96.0, 96.8, 127.3-128.4, 138.4, 138.4, 138.4, 138.4, 138.5, 138.5, 138.6, 138.6; HRMS (MALDI-TOF): calcd. for $C_{41}H_{46}NaO_6$ [M^++Na]: 657.3192; found: 657.3178.

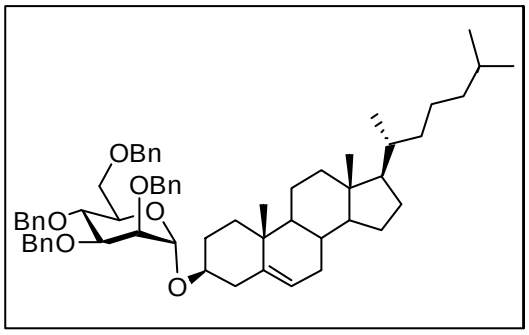
Characterization data for compound **11**



$[\alpha]_D^{25}$ = +16.5 ($CHCl_3$, *c* 1.00); ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.28 (d, 3H, *J* = 6.3 Hz), 3.50 (t, 1H, *J* = 2.4 Hz), 3.58-3.85 (m, 4H), 3.93 (t, 1H, *J* = 9.2 Hz), 4.34 (ddd, 1H, *J* = 2.1, 6.7, 8.7 Hz), 4.38 (dd, 1H, *J* = 1.8, 10.1 Hz), 4.46 (d, 1H, *J* = 10.6 Hz), 4.54 (s, 2H), 4.54 (ABq, 2H, *J* = 12.5 Hz), 4.57 (ABq, 2H, *J* = 12.5 Hz), 4.83 (dd, 2H, *J* = 5.0, 6.3 Hz), 5.02 (ABq, 2H, *J* = 12.2 Hz), 5.12 (ABq, 2H, *J* = 12.3 Hz), 5.29 (d, 1H, *J* = 9.8 Hz), 7.13-7.41 (m, 30H); ^{13}C NMR (125.76 MHz, $CDCl_3$): δ 18.5, 58.8, 67.2, 67.3, 69.1, 72.0, 72.3, 72.4, 73.3, 74.7, 74.7, 75.1, 76.4, 79.3, 99.6, 127.6-128.7, 135.0, 136.0, 138.2, 138.2, 138.3, 138.3, 156.6, 170.4; HRMS (MALDI-TOF): calcd. for $C_{53}H_{55}NNaO_{10}$ [M^++Na]: 888.3724; found: 888.3728.

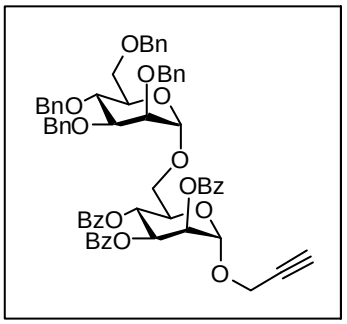
Characterization data for compound **13**

$[\alpha]_D^{25}$ = +19.1 ($CHCl_3$, *c* 1.00); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 0.61 (s, 3H), 0.86 (d, 3H, *J* = 1.6 Hz), 0.87 (d, 3H, *J* = 1.6 Hz), 0.89-2.10 (m, 31H), 2.16 (s, 1H), 2.24 (t, 1H, *J* = 12.3 Hz), 2.33 (dd, 1H, *J* = 4.7, 12.3 Hz), 3.48 (m, 1H), 3.37 (dd, 1H, *J* = 1.8, 14.7 Hz), 3.75 (s, 1H), 3.81 (dd, 1H, *J* = 4.7, 10.7 Hz), 3.87 (m, 1H), 3.94 (dd, 1H, *J* =



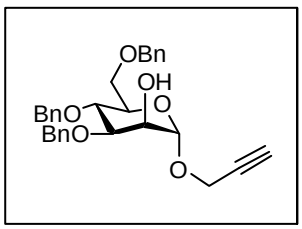
2.7, 9.3 Hz), 3.99 (dd, 1H, *J* = 9.1, 18.8 Hz), 4.60 (ABq, 2H, *J* = 12.0 Hz), 4.63 (s, 2H), 4.70 (ABq, 2H, *J* = 10.8 Hz),4.74 (ABq, 2H, *J* = 12.6 Hz), 5.03 (d, 1H, *J* = 1.5 Hz), 5.27 (d, 1H, *J* = 5.0 Hz), 7.10-7.40 (m, 20H); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 11.8, 18.7, 19.3, 21.0, 22.5, 22.8, 23.8, 24.3, 27.5, 28.0, 28.2, 31.8, 31.9, 35.8, 36.2, 36.6, 37.0, 39.5, 39.7, 39.8, 42.2, 50.0, 56.1, 56.7, 69.3, 71.7, 72.1, 72.5, 73.3, 75.1, 75.1, 76.5, 77.2, 80.3, 95.7, 121.8, 127.3-128.3, 138.4, 138.4, 138.5, 138.6, 140.6; HRMS (MALDI-TOF): calcd. for $C_{61}H_{80}NaO_6$ [M^++Na]: 931.5853; found: 931.5849.

Characterization data for compound **15**



$[\alpha]_D^{25}$ = -23.3($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.50 (t, 1H, *J* = 2.4 Hz), 3.53-3.78 (m, 4H), 3.84 (dd, 1H, *J* = 3.3, 9.2 Hz), 3.88-4.05 (m, 2H), 4.22 (m, 1H), 4.31 (d, 2H, *J* = 2.4 Hz), 4.37 (d, 2H, *J* = 4.5 Hz), 4.43 (s, 2H), 4.49 (ABq, 2H, *J* = 12.3 Hz), 4.63 (s, 2H), 4.86 (d, 1H, *J* = 10.9 Hz), 4.96 (d, 1H, *J* = 1.8 Hz), 5.26 (d, 1H, *J* = 1.8 Hz), 5.68 (dd, 1H, *J* = 1.8, 2.9 Hz), 5.89 (m, 2H), 7.10-7.56 (m, 29H), 7.75-8.11 (m, 6H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.1, 66.6, 67.1, 69.0, 69.7, 69.8, 70.4, 71.8, 71.9, 72.5, 73.2, 74.7, 74.8, 74.9, 75.7, 78.1, 80.1, 96.2, 98.2, 127.3-128.9, 133.1, 133.3, 133.5, 138.3, 138.4, 138.5, 138.6, 165.3, 165.4, 165.4; HRMS (MALDI-TOF): calcd. for $C_{64}H_{60}NaO_{14}$ [M^++Na]: 1075.3881; found: 1075.3889.

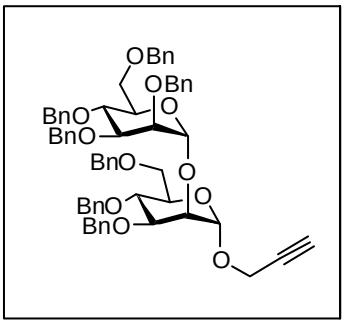
Characterization data for compound **16**



$[\alpha]_D^{25}$ = -51.70 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.44 (t, 1H, *J* = 2.3 Hz), 2.46 (bs, 1H), 3.45 (m, 1H), 3.60 (dd, 1H, *J* = 3.0, 9.1 Hz), 3.75 (m, 2H), 3.90 (t, 1H, *J* = 9.3 Hz), 4.12 (d, 1H, *J* = 2.6 Hz), 4.42 (d, 2H, *J* = 2.4 Hz), 4.50-4.66 (m, 3H), 4.67 (ABq, 2H, *J* = 11.8 Hz), 4.68 (ABq, 2H, *J* = 10.4 Hz), 7.17-7.35 (m, 15H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.3, 67.9, 68.8, 71.2, 73.3, 73.9, 74.9, 75.1, 75.1, 78.5, 81.3, 96.9, 127.4-128.3, 137.6, 138.0, 138.0 ; HRMS (MALDI-TOF): calcd. for $C_{30}H_{32}NaO_6$ [M^++Na]:511.2097; found: 511.2062.

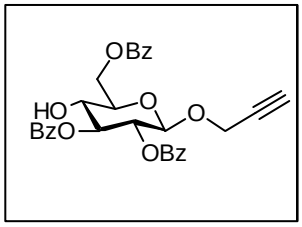
Characterization data for compound **17**

$[\alpha]_D^{25}$ = -22.6 ($CHCl_3$, *c* 1.00); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 2.35 (t, 1H, *J* = 2.4 Hz), 3.42 (ddd, 1H, *J* = 1.7, 4.7, 6.5 Hz), 3.58 (dd, 1H, *J* = 2.3, 9.2 Hz), 3.73 (m, 4H), 3.80-3.88 (m, 2H), 3.94 (ddd, 1H, *J* = 1.5, 3.1, 4.7 Hz), 4.04 (dd, 1H, *J* = 1.4, 10.3 Hz), 4.26 (dd, 2H, *J* = 1.8, 18.4 Hz), 4.32 (m, 2H), 4.35-4.63 (m, 9H), 4.66 (ABq, 2H, *J* = 12.0 Hz), 4.68 (ABq, 2H, *J* = 11.0 Hz), 4.84 (d, 1H, *J* = 1.9 Hz), 4.87 (d, 1H, *J* = 1.7



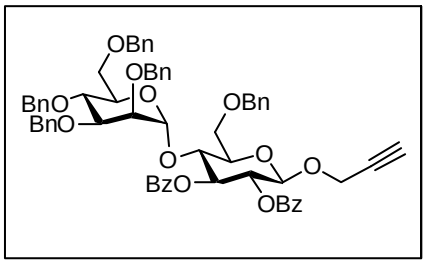
Hz), 5.28 (m, 1H), 7.13-7.41 (m, 35H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 55.4, 69.2, 69.3, 71.4, 71.8, 72.1, 72.6, 72.7, 73.2, 73.5, 74.7, 74.9, 74.9, 75.0, 75.1, 75.7, 77.2, 78.9, 79.8, 82.7, 97.1, 98.4, 127.2-128.6, 137.7, 138.2, 138.3, 138.5, 138.7, 138.8, 138.8; HRMS (MALDI-TOF) calcd. for $C_{64}H_{66}NaO_{11}$[M^++Na]: 1033.4503; found: 1033.4517.

Characterization data for compound **18**



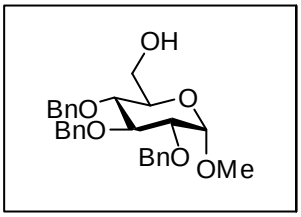
$[\alpha]_D^{25}$ = +41.77 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.39 (t, 1H, *J* = 2.3 Hz), 3.86 (bs, 1H), 3.91 (m, 2H), 4.40 (ddd, 2H, *J* = 2.3, 16.3, 21.0), 4.73 (m, 2H), 5.05 (d, 1H, *J* = 7.5 Hz), 5.40-5.60 (m, 2H), 7.26-7.63 (m, 9H), 7.94-8.11 (m, 6H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.8, 63.3, 69.3, 71.2, 74.5, 75.4, 76.2, 78.1, 98.3, 128.2-129.8, 133.1, 133.2, 133.4, 165.3, 166.8, 167.0; HRMS (MALDI-TOF): calcd. for $C_{30}H_{26}NaO_9$ [M^++Na]:553.1475; found: 553.1484

Characterization data for compound **19**



$[\alpha]_D^{25}$ = +16.4 ($CHCl_3$, *c* 1.00); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 2.36 (t, 1H, *J* = 2.4 Hz), 3.55 (dd, 1H, *J* = 1.6, 7.7 Hz), 3.57 (d, 1H, *J* = 1.8 Hz), 3.70 (dd, 1H, *J* = 3.7, 10.4 Hz), 3.79 (m, 1H), 3.87 (d, 1H, *J* = 11.6 Hz), 3.89 (ddd, 1H, *J* = 2.0, 4.5, 7.1 Hz), 4.97 (t, 1H, *J* = 9.3 Hz), 4.12 (d, 1H, *J* = 10.8 Hz), 4.19 (t, 1H, *J* = 9.1 Hz), 4.39 (ABq, 2H, *J* = 12.1 Hz), 4.36 (ABq, 2H, *J* = 12.5 Hz), 4.36 (ABq, 2H, *J* = 11.1 Hz), 4.39-4.56 (m, 3H), 4.74 (d, 1H, *J* = 10.8 Hz), 4.81 (dd, 1H, *J* = 2.1, 12.1 Hz), 5.03 (d, 1H, *J* = 7.7 Hz), 5.14 (d, 1H, *J* = 2.1 Hz), 5.40 (dd, 1H, *J* = 8.0, 9.8 Hz), 5.78 (t, 1H, *J* = 9.6 Hz), 6.90-7.60 (m, 29H), 7.90-8.15 (m, 6H); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 55.9, 63.3, 68.7, 71.6, 71.8, 72.6, 73.2, 73.3, 73.4, 74.3, 74.9, 75.3, 75.5, 76.1, 76.3, 78.1, 79.4, 98.1, 100.7, 127.0-129.9, 133.1, 133.2, 133.7, 138.1, 138.3, 138.3, 138.5, 165.3, 165.6, 166.1; HRMS (MALDI-TOF) calcd. for $C_{64}H_{60}NaO_{14}$ [M^++Na]: 1075.3881; found: 1075.3891.

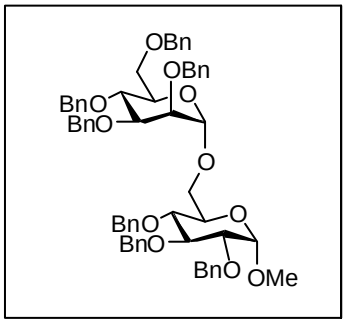
Characterization data for compound **20**



$[\alpha]_D^{25}$ = +22.98 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 3.21 (bs, 1H), 3.35 (s, 3H), 3.46-3.74 (m, 5H), 4.01 (t, 1H, *J* = 9.1 Hz), 4.56 (d, 1H, *J* = 3.7 Hz), 4.61-4.86 (m, 5H), 4.96 (t, 1H, *J* = 10.9 Hz), 7.22-7.37 (m, 15H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 55.2, 61.8, 70.7, 73.4, 75.0, 75.7, 77.4, 80.0, 82.0, 98.2, 127.6-128.5, 138.1, 138.2, 138.8 ; HRMS (MALDI-TOF): calcd. for

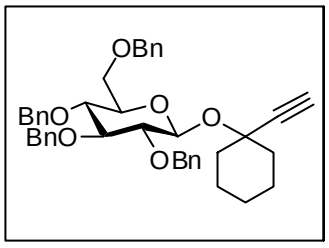
$C_{28}H_{32}NaO_6$ [M^++Na]:487.2097; found: 487.2070.

Characterization data for compound **21**



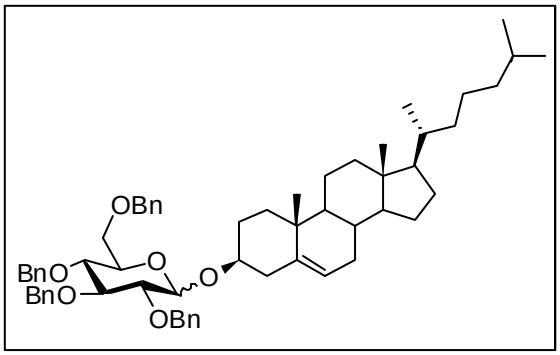
$[\alpha]_D^{25}$ = +41.8 ($CHCl_3$, *c* 1.00); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 3.3 (s, 3H), 3.39 (t, 1H, *J* = 9.3 Hz), 3.45 (dd, 1H, *J* = 3.5, 9.3 Hz), 3.60 (dt, 2H, *J* = 1.3, 8.8 Hz), 3.69 (m, 3H), 3.78 (t, 1H, *J* = 2.3 Hz), 3.83 (dd, 1H, *J* = 3.8, 10.5 Hz), 3.86 (dd, 1H, *J* = 3.0, 7.0 Hz), 3.98 (q, 2H, *J* = 9.2 Hz), 4.48 (d, 1H, *J* = 1.5 Hz), 4.50 (d, 1H, *J* = 1.7 Hz), 4.61 (ABq, 2H, *J* = 11.7 Hz), 4.61(s, 2H), 4.66 (m, 2H), 4.67 (ABq, 2H, *J* = 11.1 Hz), 4.70 (ABq, 2H, *J* = 12.6 Hz), 4.73 (ABq, 2H, *J* = 12.1 Hz), 4.84 (ABq, 2H, *J* = 10.6 Hz), 7.11-7.42 (m, 35H); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 55.0, 65.7, 69.0, 69.7, 71.8, 71.9, 72.4, 73.2, 73.2, 74.6, 74.8, 74.9, 75.0, 75.7, 77.6, 79.5, 79.9, 82.1, 97.8, 98.2, 127.3-128.5, 138.1, 138.1, 138.3, 138.3, 138.4, 138.6, 138.6; HRMS (MALDI-TOF) calcd. for $C_{62}H_{66}NaO_{11}$ [M^++Na]: 1009.4503; found: 1009.4508.

Characterization data for compound **22**



$[\alpha]_D^{25}$ = +16.0 ($CHCl_3$, *c* 1.00); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.15-2.15 (m, 10H), 2.55 (s, 1H), 3.52 (m, 2H), 3.57 (t, 1H, *J* = 9.1 Hz), 3.64 (dd, 1H, *J* = 5.0, 10.7 Hz), 3.69 (m, 2H), 4.55 (d, 1H, *J* = 10.3 Hz), 4.56 (ABq, 2H, *J* = 12.3 Hz), 4.75 (ABq, 2H, *J* = 11.0 Hz), 4.85 (ABq, 2H, *J* = 10.7 Hz), 5.02 (s, 1H), 5.04 (d, 1H, *J* = 2.8 Hz), 7.13-7.43 (m, 20H); ^{13}C NMR(100.53 MHz, $CDCl_3$): δ 22.9, 23.0, 25.1, 38.6, 38.8, 69.1, 73.2, 74.4, 74.7, 74.8, 75.3, 75.6, 76.8, 77.8, 82.1, 84.4, 84.9, 99.3, 127.3-128.4, 138.1, 138.2, 138.4, 138.6; HRMS (MALDI-TOF): calcd. for $C_{42}H_{46}NaO_6$ [M^++Na]: 669.3192; found: 669.3207.

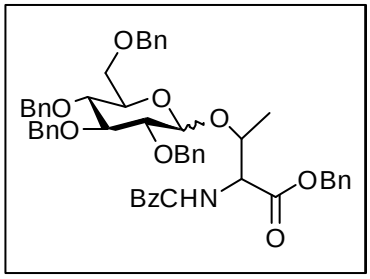
Characterization data for compound **23** *(1:8.9* α*: β)*



$[\alpha]_D^{25}$ = -1.6($CHCl_3$, *c* 1.00); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 0.68 (s, 3H), 0.86 (d, 3H, *J* = 1.8 Hz), 0.88 (d, 3H, *J* = 1.8 Hz), 0.89-2.48 (m, 34H), 3.44 (m, 2H), 3.54 (t, 1H, *J* = 9.3 Hz), 3.63 (m, 3H), 3.73 (dd, 1H, *J* = 1.7, 10.7 Hz), 4.50 (d, 1H, *J* = 7.7 Hz), 4.57 (ABq, 2H, *J* = 12.3 Hz), 4.68 (ABq, 2H, *J* = 10.9 Hz), 4.82 (ABq, 2H, *J* = 10.9 Hz), 4.88 (ABq, 2H, *J* = 10.8 Hz), 5.35 (d, 1H, *J* = 4.7 Hz), 7.10-7.38 (m, 20H); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 11.8, 18.7, 19.4, 21.1, 21.6, 22.8, 23.8, 24.3, 28.0, 28.2, 30.0, 31.9, 31.9, 35.8, 36.2, 36.7, 37.3, 39.1, 39.5, 39.8, 42.3, 50.2, 56.1, 56.7, 69.1, 73.4, 74.8, 74.9, 75.0, 75.7, 78.0, 79.7, 82.3, 84.8, 102.2, 121.9, 127.4-128.4, 138.1, 138.3, 138.5, 138.6,

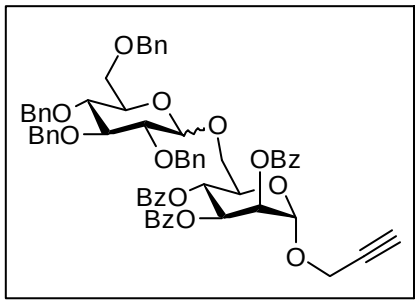
140.6; HRMS (MALDI-TOF) calcd. for $C_{61}H_{80}NaO_6[M^+ + Na]$: 931.5853; found: 931.5850.

Characterization data for compound **24** *(1:1.3 α: β)*



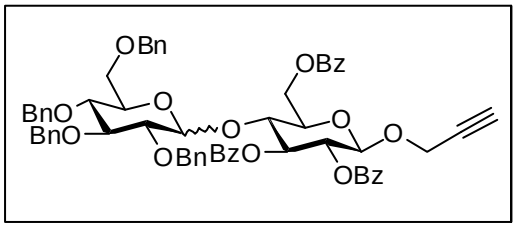
$[\alpha]_D^{25}$ = +22.6 ($CHCl_3$, *c* 1.00); ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.27, 1.30 (2d, 6H, *J* = 7.0 Hz), 3.25 (td, 1H, *J* = 2.4, 5.6 Hz), 3.33 (t, 1H, *J* = 8.2 Hz), 3.45 (dd, 1H, *J* = 3.6, 9.7 Hz), 3.50-3.65 (m, 6H), 3.71 (dd, 1H, *J* = 3.2, 10.5 Hz), 3.79 (td, 1H, *J* = 2.9, 5.0 Hz), 3.88 (t, 1H, *J* = 9.3 Hz), 4.30-5.20 (m, 30H) 5.80, 5.91 (2d, 2H, *J* = 8.4 Hz), 7.10-7.51 (m, 60H); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 17.7, 19.1, 58.9, 59.1, 67.1, 67.1, 67.1, 67.2, 68.3, 68.8, 70.9, 73.1, 73.4, 73.5, 74.7, 74.7, 74.9, 75.0, 75.2, 75.5, 75.5, 75.6, 77.2, 77.2, 77.6, 79.6, 81.6, 81.8, 98.0, 101.4, 127.5-128.5, 135.2, 135.4, 136.3, 136.3, 137.8, 137.9, 138.1, 138.1, 138.1, 138.2, 138.6, 138.6, 156.8, 156.8, 170.2, 170.5; HRMS (MALDI-TOF): calcd. for $C_{53}H_{55}NNaO_{10}$ $[M^+ + Na]$: 888.3724; found: 888.3721.

Characterization data for compound **25** *(1:3.1 α : β)*



$[\alpha]_D^{25}$ = -14.3 ($CHCl_3$, *c* 1.00); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 2.39, 2.46 (2t, 2H, *J* = 2.4 Hz), 3.35-4.30 (m, 16H), 4.16-4.98 (m, 22H), 5.00 (d, 1H, *J* = 10.3 Hz), 5.09 (d, 1H, *J* = 10.7 Hz), 5.27 (d, 1H, *J* = 1.7 Hz), 5.31 (d, 1H, *J* = 1.7 Hz), 5.67-5.93 (m, 6H), 7.10-7.61 (m, 58H), 7.75-8.15 (m, 12H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 54.5, 54.9, 67.2, 67.3, 67.4, 68.2, 68.7, 69.1, 69.9, 70.0, 70.2, 70.2, 70.3, 70.4, 70.5, 73.1, 73.3, 73.4, 73.5, 74.8, 74.8, 74.9, 75.0, 75.6, 75.7, 75.7, 75.8, 77.5, 77.6, 77.9, 78.0, 81.7, 81.8, 82.4, 95.4, 95.9, 97.4, 104.1, 127.3-130.5, 131.1, 131.1, 133.2, 133.2, 133.4, 133.4, 138.0, 138.0, 138.1, 138.1, 138.3, 138.4, 138.5, 138.8, 165.2, 165.2, 165.3, 165.4, 165.4, 165.6; HRMS (MALDI-TOF): calcd. for $C_{64}H_{60}NaO_{14}$ $[M^+ + Na]$: 1075.3881; found: 1075.3871.

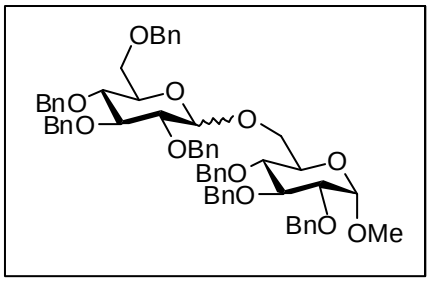
Characterization data for compound **26** *(1:3.2 α: β)*



$[\alpha]_D^{25}$ = +23.6 ($CHCl_3$, *c* 1.00); ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 2.37, 2.48 (2t, 2H, *J* = 2.4 Hz), 2.98-3.98 (m, 16H), 4.10-4.90 (m, 24H), 5.03 (m, 2H), 5.49 (m, 2H), 5.87 (m, 2H), 5.75 (m, 2H), 7.00-7.65 (m, 58H), 7.95-8.15 (m, 12H); ^{13}C NMR (125.76 MHz, $CDCl_3$): δ 55.2, 55.8, 62.5, 63.2, 66.9, 68.2, 68.3, 68.8, 71.2, 71.6, 71.7, 71.8, 72.8, 73.0, 73.2, 73.4, 73.7, 74.1, 74.3, 74.7, 74.8, 74.9, 75.0, 75.1, 75.4, 75.5, 75.5, 75.6, 78.1, 78.2, 78.7, 78.9, 81.4, 81.7, 98.1, 99.8, 102.2, 104.8, 127.3-130.2, 132.8, 133.0,

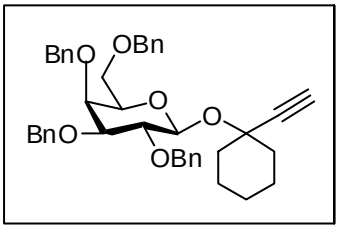
133.1, 133.2, 133.5, 133.7, 137.9, 138.1, 138.2, 138.3, 138.4, 138.5, 138.6, 138.6, 165.4, 165.5, 165.8, 165.9, 165.9, 166.0; HRMS (MALDI-TOF): calcd. for $C_{64}H_{60}NaO_{14}$ [M^++Na]: 1075.3881; found: 1075.3888.

Characterization data for compound **27** *(1:2.8 α: β)*



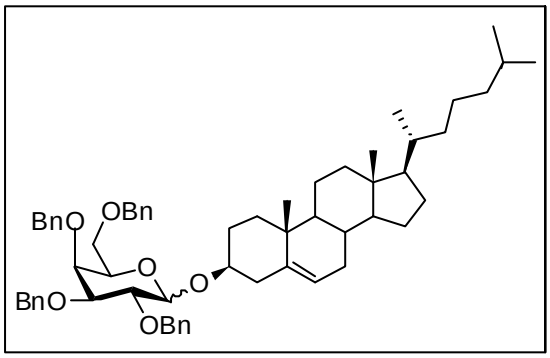
$[\alpha]_D^{25}$ = +31.0 ($CHCl_3$, *c* 1.00); ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 3.32, 3.35 (2s, 6H), 3.39-4.25 (m, 24H), 4.32-5.00 (m, 32H), 7.10-7.39 (m, 70H); ^{13}C NMR(100.61 MHz, $CDCl_3$): δ 55.1, 55.2, 68.4, 68.5, 69.0, 69.8, 70.2, 70.3, 72.3, 72.3, 73.3, 74.3, 74.9, 74.9, 74.9, 75.0, 75.0, 75.5, 75.6, 75.7, 75.7, 77.6, 77.7, 77.8, 77.9, 79.7, 79.9, 80.1, 81.6, 81.9, 82.0, 82.1, 84.7, 97.2, 97.9, 98.0, 103.8, 127.3-128.5, 137.9, 138.0, 138.0, 138.1, 138.1, 138.2, 138.3, 138.3, 138.4, 138.4, 138.4, 138.5, 138.8, 138.8; HRMS (MALDI-TOF): calcd. for $C_{62}H_{66}NaO_{11}$ [M^++Na]: 1009.4503; found: 1009.4512.

Characterization data for compound **28**



$[\alpha]_D^{25}$ = +6.6 ($CHCl_3$, *c* 1.00); ^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.05-2.10 (m, 10H), 2.51 (s, 1H), 3.55 (m, 4H), 3.84 (dd, 1H, *J* = 7.8, 9.7 Hz), 3.87 (d, 1H, *J* = 2.9 Hz), 4.40 (ABq, 2H, *J* = 11.4 Hz), 4.70 (ABq, 2H, *J* = 11.6 Hz), 4.80 (ABq, 2H, *J* = 11.9 Hz), 4.86 (ABq, 2H, *J* = 10.8 Hz), 4.97 (d, 1H, *J* = 7.8 Hz), 7.20-7.45 (m, 20H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 23.0, 23.1, 25.1, 38.6, 38.7, 69.2, 73.2, 73.3, 73.4, 73.4, 74.4, 75.1, 75.1, 76.7, 79.5, 82.6, 84.7, 99.6, 127.3-128.5, 138.0, 138.6, 138.7, 138.8; HRMS (MALDI-TOF): calcd. for $C_{42}H_{46}NaO_6$ [M^++Na]: 669.3192; found: 669.3181.

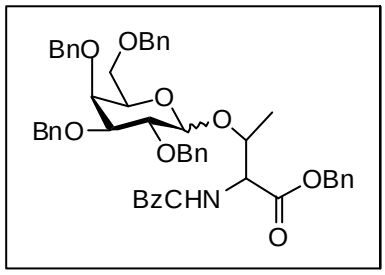
Characterization data for compound **29** *(1:2.7 α: β)*



$[\alpha]_D^{25}$ = +13.5($CHCl_3$, *c* 1.00); ^{1}H NMR (500.20 MHz, $CDCl_3$): δ 0.60-2.51 (m, 86H), 3.54 (m, 7H), 3.93-4.08 (m, 7H), 4.36-5.02 (m, 18H), 5.26 (d, 1H, *J* = 4.8 Hz), 5.32 (d, 1H, *J* = 4.8 Hz), 7.10-7.38 (m, 40H); ^{13}C NMR (125.78 MHz, $CDCl_3$): δ 11.8, 11.8, 18.7, 18.8, 19.4, 19.4, 21.0, 21.0, 22.6, 22.5, 22.8, 22.8, 23.8, 23.8, 24.3, 24.4, 27.6, 27.6, 28.0, 28.1, 28.2, 28.2, 29.7, 29.8, 31.9, 31.9, 35.6, 35.6, 36.2, 36.3, 36.8, 36.8, 37.1, 37.3, 39.0, 39.1, 39.5, 39.5, 39.8, 39.9, 42.3, 42.4, 50.1, 50.2, 56.1, 56.2, 56.7, 56.8, 67.5, 69.0, 69.1, 73.1, 73.2, 73.4, 74.4, 74.4, 74.7, 74.9, 75.2, 75.2, 75.3, 75.4, 76.5, 76.5, 79.2, 79.2, 79.4, 79.7, 95.4, 102.4, 121.6, 121.7, 127.3-128.6, 137.3, 138.0, 138.0, 138.6, 138.7,

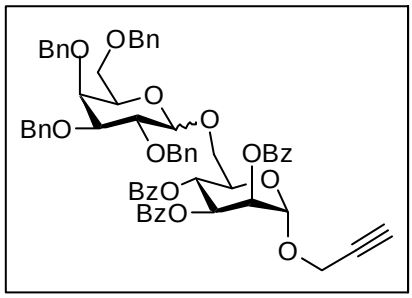
138.7, 138.8, 138.9, 140.8, 140.9; HRMS(MALDI-TOF) calcd for $C_{61}H_{80}NaO_6$ [M^++Na]: 931.5853; found: 931.5862.

Characterization data for compound **30** *(1:8.1 α: β)*



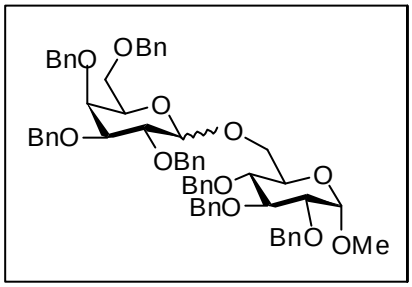
$[\alpha]_D^{25}$ = +34.0 ($CHCl_3$, *c* 1.00); ^{1}H NMR(500.13 MHz, $CDCl_3$): δ 1.13 (d, 3H, *J* = 6.3 Hz), 3.53 (m, 2H), 3.88 (dd, 1H, *J* = 2.3, 10.3 Hz), 3.97 (m, 3H), 4.35 (dd, 1H, *J* = 2.3, 8.6 Hz), 4.40 (m, 1H), 4.44-4.57 (m, 2H), 4.56 (d, 1H, *J* = 11.5 Hz), 4.61 (ABq, 2H, *J* = 11.7 Hz), 4.68 (s, 2H), 4.90 (d, 1H, *J* = 3.6 Hz), 4.94 (d, 1H *J* = 11.4 Hz), 5.06 (s, 2H), 5.15 (s, 2H), 6.05 (d, 1H, *J* = 8.6 Hz), 7.20-7.51 (m, 30H); ^{13}C NMR (125.76 MHz, $CDCl_3$): δ 19.1, 59.1, 67.0, 67.2, 68.8, 69.9, 72.8, 73.5, 73.5, 74.7, 74.8, 74.8, 76.0, 78.8, 98.3, 127.4-128.6, 133.3, 136.3, 137.9, 138.3, 138.6, 138.6, 156.9, 170.6; HRMS (MALDI-TOF): calcd. for $C_{53}H_{55}NNaO_{10}$ [M^++Na]: 888.3724; found: 888.3834.

Characterization data for compound **31** *(1:8.2 α: β)*



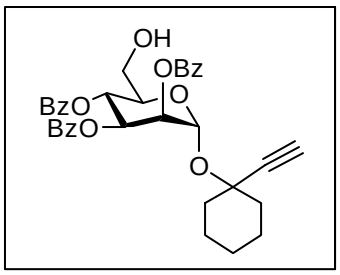
$[\alpha]_D^{25}$ = -23.0 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.46 (t, 1H, *J* = 2.4 Hz), 3.40 (d, 1H, *J* = 6.5 Hz), 3.58 (dt, 1H, *J* = 2.1, 11.2 Hz), 3.85-4.13 (m, 5H), 4.20-5.10 (m, 13H), 5.25 (d, 1H, *J* = 1.4 Hz), 5.72 (t, 1H, *J* = 2.4 Hz), 5.87 (d, 1H, *J* = 1.4 Hz), 5.89 (dd, 1H, *J* = 10.1, 12.1Hz), 7.10-7.56 (m, 29H), 7.72-8.15 (m, 6H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 54.7, 66.9, 67.2, 68.6, 69.1, 70.1, 70.1, 70.2, 72.9, 73.1, 73.2, 74.7, 75.0, 75.8, 76.4, 78.1, 78.7, 95.8, 98.0, 127.3-130.0, 133.1, 134.0, 134.0, 138.0, 138.6, 138.7, 138.8, 165.4, 165.5, 165.5 ; HRMS (MALDI-TOF): calcd. for $C_{64}H_{60}NaO_{14}$ [M^++Na]: 1075.3881; found: 1075.3868.

Characterization data for compound **32** *(1:7.9 α:β)*



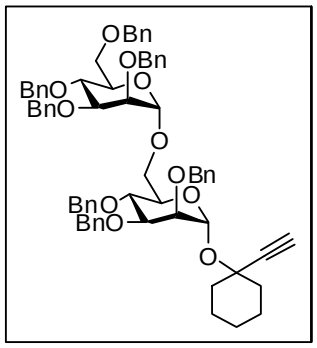
$[\alpha]_D^{25}$ = +40.8 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 3.29 (s, 3H), 3.29 (m, 1H), 3.41 (dd, 1H, *J* = 3.4, 9.5 Hz), 3.50 (m, 2H), 3.58 (t, 1H, *J* = 9.2 Hz), 3.68-3.82(m, 2H), 3.91(dd, 1H, *J* = 3.3, 12.8 Hz), 3.92(s, 1H), 3.96 (m, 2H), 4.03 (dd, 1H, *J* = 3.3, 9.2 Hz), 4.39 (ABq, 2H, *J* = 12.2 Hz), 4.52 (d, 1H, *J* = 3.5 Hz), 4.55 (d, 1H, *J* = 5.1 Hz), 4.5-4.98 (m, 11H), 5.00(d, 1H, *J* = 3.7 Hz), 7.10-7.48(m, 35H); ^{13}C NMR(125.76 MHz, $CDCl_3$): δ 55.0, 66.4, 68.9, 69.3, 70.3, 72.5, 72.8, 73.3, 73.3, 74.7, 75.0, 75.1, 75.7, 76.5, 78.0, 78.2, 80.1, 82.0, 97.8, 97.9, 127.3-128.4, 138.0, 138.2, 138.4, 138.7, 138.7, 138.8, 138.8 ; HRMS (MALDI-TOF): calcd. for $C_{62}H_{66}NaO_{11}$ [M^++Na]: 1009.4503; found: 1009.4508

Characterization data for compound **33**



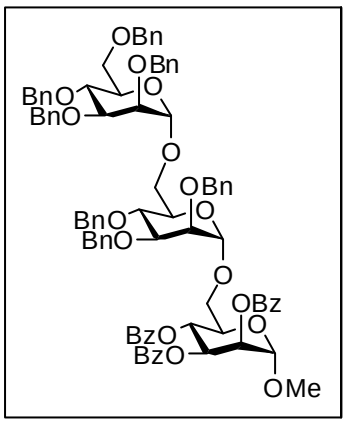
$[\alpha]_D^{25}$ = +3.3 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.27–2.07 (m, 10H), 2.60 (s, 1H), 2.60 (bs, 1H), 3.78 (m, 2H), 4.28 (dt, 1H, *J* = 3.7, 9.8 Hz), 5.61 (dd, 1H, *J* = 2.0, 3.1 Hz), 5.73 (d, 1H, *J* = 1.8 Hz), 5.85 (t, 1H, *J* = 10.1 Hz), 6.00 (dd, 1H, *J* = 3.3, 10.1 Hz), 7.22-7.65 (m, 9H), 7.81-8.14 (m, 6H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 22.8, 22.8, 25.0, 37.7, 38.2, 61.4, 67.4, 69.7, 71.3, 71.6, 75.4, 76.2, 83.7, 93.7, 128.2-129.8, 133.1, 133.4, 133.5, 165.5, 165.5, 166.4; HRMS (MALDI-TOF): calcd. for $C_{35}H_{34}NaO_9$ [M^++Na]: 621.2101; found: 621.2114.

Characterization data for compound **34**



$[\alpha]_D^{25}$ = +26.5 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz): δ 1.26-1.73 (m, 10H), 2.41 (s, 1H), 3.61-4.01 (m, 12H), 4.43-4.69 (m, 12H), 4.87 (dd, 2H, *J* = 3.1, 10.8 Hz), 5.11 (d, 1H, *J* = 1.3 Hz), 5.46 (d, 1H, J = 1.8 Hz), 7.11-7.41 (m, 35H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 22.6, 22.6, 25.0, 37.6, 38.1, 66.3, 69.0, 71.4, 71.6, 71.9, 72.1, 72.3, 72.3 73.1, 74.2, 74.5, 74.6, 74.8, 74.9, 75.0, 75.3, 75.3, 79.4, 79.9, 84.4, 93.9, 98.1, 127.2-128.4, 138.2, 138.3, 138.3, 138.4, 138.4, 138.4, 138.6; HRMS (MALDI-TOF): calcd. for $C_{69}H_{74}NaO_{11}$ [M^++Na]: 1101.5129; found: 1101.5134.

Characterization data for compound **36**

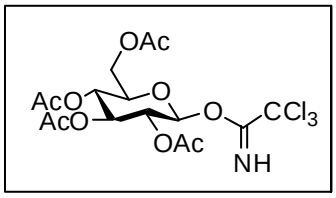


$[\alpha]_D^{25}$ = -10.6 ($CHCl_3$, *c* 1.00); ^{1}H NMR (500.13 MHz, $CDCl_3$):δ 3.42 (s, 3H), 3.51-3.69 (m, 8H), 3.80 (dd, 1H, *J* = 3.9, 11.6 Hz), 3.84-3.88 (m, 4H), 3.95 (dt, 2H, *J* = 9.4, 25.7 Hz), 4.14 (dt, 1H, *J* = 4.2, 9.6 Hz), 4.35-4.4.62 (m, 8H), 4.41 (ABq, 2H, *J* = 11.0 Hz), 4.61 (s, 2H), 4.84 (ABq, 2H, *J* = 11.0 Hz), 4.88 (d, 1H, *J* = 1.5 Hz), 4.90 (d, 1H, *J* = 1.5 Hz), 5.03 (t, 1H, *J* = 10.0 Hz), 5.06 (d, 1H, *J* = 1.3 Hz), 5.84 (dd, 1H, *J* = 3.3, 10.2 Hz), 7.11-7.51 (m, 44H), 7.81-8.08 (m, 6H); ^{13}C NMR (125.76 MHz, $CDCl_3$): δ 55.4, 65.6, 66.6, 69.0, 69.1, 69.8, 70.6, 71.3, 71.7, 71.7, 71.7, 71.7, 72.2, 72.7, 73.2, 74.2, 74.6, 74.8, 74.9, 74.9, 75.0, 79.2, 80.2, 98.1, 98.2, 98.4, 127.2-129.8, 133.1, 133.3, 133.5, 138.3, 138.3, 138.4, 138.4, 138.6, 138.6, 138.7, 165.3, 165.4, 165.5; HRMS (MALDI-TOF): calcd. for $C_{89}H_{88}NaO_{19}$ [M^++Na]: 1483.5818; found: 1483.5837.

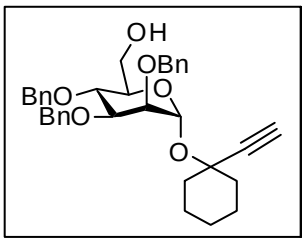
Characterization data for compound **39**

$[\alpha]_D^{25}$ = N/R; ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 2.03-2.08 (4s, 12H), 4.13 (dd, 1H, *J* = 2.2, 12.2 Hz), 4.22 (ddd, 1H, *J* = 1.8, 3.9, 10.1 Hz), 4.28 (dd, 1H, *J* = 4.1, 12.4 Hz),

5.12-5.21 (m, 2H), 5.57 (t, 1H, *J* = 9.8 Hz), 6.56 (d, 1H, *J* = 3.8 Hz), 8.71 (s, 1H); ^{13}C NMR (100.53 MHz, $CDCl_3$): 20.3, 20.5, 20.6. 20.6, 61.3, 67.7, 69.6, 69.7, 69.9, 90.6, 92.8, 160.7, 169.4, 169.8, 169.9, 170.5; HRMS (MALDI-TOF): calcd. for $C_{16}H_{20}Cl_3NNaO_{10}$ [M^++Na]: 514.0050; found: 514.0063.

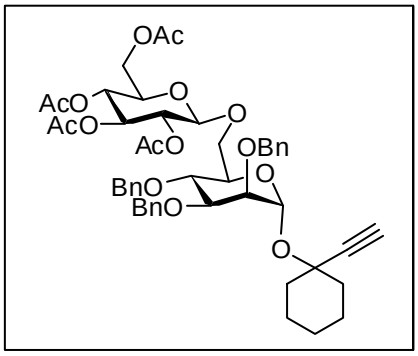


Characterization data for compound **40**



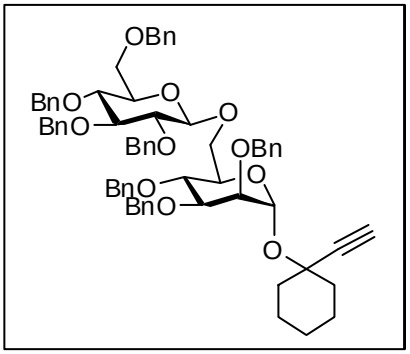
$[\alpha]_D^{25}$ = +28.0 ($CHCl_3$, *c* 1.00); ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.54 (m, 10H), 2.08 (bs, 1H), 2.41 (s, 1H), 3.69-3.95 (m, 6H), 4.63 (s, 2H), 4.70 (ABq, 2H, *J* = 5.8 Hz), 4.95 (m, 2H), 5.45 (d, 1H, *J* = 1.8 Hz), 7.24-7.39 (m, 15H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 22.6, 22.6, 24.9, 37.7, 37.9, 62.4, 72.0, 72.5, 72.5, 74.2, 75.1, 75.2, 75.2, 75.4, 79.7, 84.5, 94.1, 127.5-128.3, 138.2, 138.3, 138.4; HRMS (MALDI-TOF): calcd. for $C_{35}H_{40}NaO_6$ [M^++Na]: 579.2723; found: 579.2738.

Characterization data for compound **41**



$[\alpha]_D^{25}$ = +11.5 ($CHCl_3$, *c* 1.00); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.25-1.72 (m, 10H), 1.99-2.03 (4s, 12H), 2.42 (s, 1H), 3.58 (dq, 1H, *J* = 2.5, 9.6 Hz), 3.71 (m, 2H), 3.80 (m, 1H), 3.92 (dd, 2H, *J* = 2.7, 9.1 Hz), 4.12 (m, 2H), 4.22 (dd, 1H, *J* = 4.6, 12.6 Hz), 4.53 (ABq, 2H, *J* = 7.8 Hz), 4.57 (s, 2H), 4.71 (ABq, 2H, *J* = 12.8 Hz), 4.95-5.16 (m, 4H), 5.48 (d, 1H, *J* = 1.6 Hz), 7.26-7.38 (m, 15H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 20.5, 20.5, 20.6, 20.6, 22.6, 22.7, 25.0, 37.5, 38.2, 61.9, 68.3, 69.0, 71.1, 71.6, 71.7, 72.0, 72.2, 73.0, 74.3, 74.7, 74.9, 75.0, 75.7, 79.7, 84.4, 93.8, 100.7, 125.5-128.4, 138.2, 138.3, 138.4, 169.1, 169.3, 170.3, 170.7; HRMS (MALDI-TOF): calcd. for $C_{49}H_{58}NaO_{15}$ [M^++Na]: 909.3673; found: 909.3678.

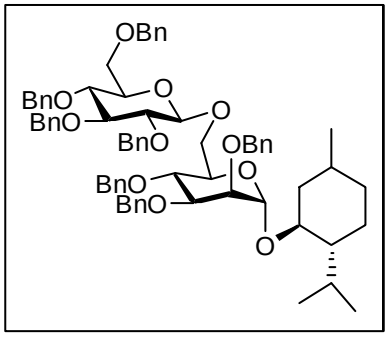
Characterization data for compound **42**



$[\alpha]_D^{25}$ = +20.3 ($CHCl_3$, *c* 1.00); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.42-1.75 (m, 10H), 2.34 (s, 1H), 3.43 (ddd, 1H, *J* = 1.8, 4.3, 9.0 Hz), 3.49-3.76 (m, 7H), 3.97 (m, 2H), 4.08 (t, 1H, *J* = 9.6 Hz), 4.23 (dd, 1H, *J* = 1.4, 3.5, Hz), 4.48-4.83 (m, 8H), 4.54 (ABq, 2H, *J* = 7.8 Hz), 4.58 (s, 2H), 4.80 (d, 1H, *J* = 2.9 Hz), 5.02 (ABq, 2H, *J* = 11.1 Hz), 5.57 (d, 1H, *J* = 1.7 Hz), 7.16-7.40 (m, 35H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 22.7, 22.7, 24.9, 37.5, 38.2, 68.8, 69.0, 71.7, 71.9,

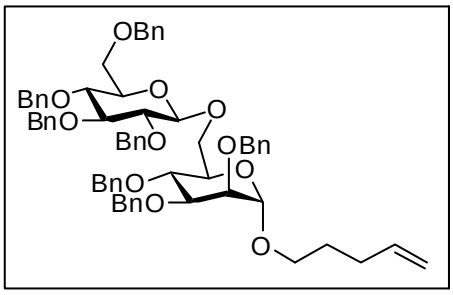
72.2, 73.3, 74.1, 74.8, 74.8, 74.9, 74.9, 75.0, 75.2, 75.5, 75.6, 77.9, 79.8, 82.1, 84.5, 84.7, 94.0, 104.0, 127.3-129.5, 138.1. 138.2, 138.4, 138.5, 138.6, 138.6, 138.7; HRMS (MALDI-TOF): calcd. for $C_{69}H_{74}NaO_{11}$ [M^++Na]: 1101.5129; found: 1101.5138.

Characterization data for compound **43**



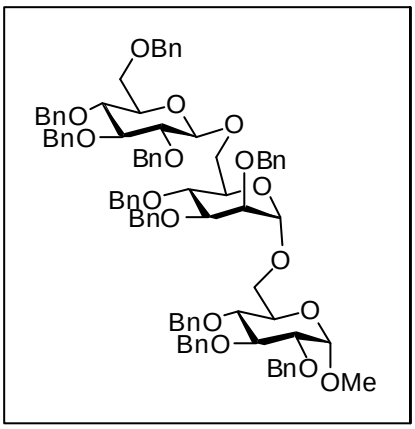
$[\alpha]_D^{25}$ = +19.3 ($CHCl_3$, *c* 1.00); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.58 (d, 2H *J* = 6.7 Hz), 0.73 (m, 2H), 0.81 (t, 6H, *J* = 7.4Hz), 0.93 (t, 1H, *J* = 12.0 Hz), 1.06 (t, 1H, *J* = 10.7 Hz), 1.23 (t, 1H, *J* = 7.0 Hz), 1.51 (m, 2H), 1.59 (s, 2H), 1.73 (m, 1H), 2.08 (d, 1H, *J* = 12.4 Hz), 3.16 (dt, 1H, *J* = 4.4, 14.8, Hz), 3.42-4.04 (m, 11H), 4.27-5.11 (m, 11H), 4.64 (ABq, 2H, *J* = 11.1 Hz), 4.87 (d, 1H, *J* = 1.4 Hz), 5.02 (ABq, 2H, *J* = 10.8 Hz), 7.15-7.42 (m, 35H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 16.1, 21.0, 22.2, 23.0, 25.5, 31.5, 34.1, 42.8, 48.7, 69.0, 69.2, 71.1, 72.0, 72.4, 73.4, 74.1, 74.9, 74.9, 75.0, 75.0, 75.1, 75.7, 77.8, 80.1, 80.6, 82.2, 84.6, 99.8, 104.2, 127.4-128.5, 138.1, 138.1, 138.2, 138.5, 138.6, 138.6, 138.6; HRMS (MALDI-TOF): calcd. for $C_{71}H_{82}NaO_{11}$ [M^++Na]: 1133.5755; found: 1133.5763.

Characterization data for compound **45**



$[\alpha]_D^{25}$ = +18.4 ($CHCl_3$, *c* 1.00); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.54 (t, 2H, *J* = 7.2 Hz), 1.59 (s, 2H), 1.99 (m, 2H), 3.26-3.98 (m, 12H), 4.25-5.06 (m, 18H), 5.73 (m, 1H), 7.15-7.37 (m, 35H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 28.4, 30.2, 66.8, 68.9, 69.0, 71.3, 72.0, 72.6, 73.4, 74.7, 74.7, 74.9, 74.9, 74.9, 75.0, 75.7, 77.8, 80.2, 82.0, 84.6, 97.7, 104.0, 114.8, 126.9-128.5, 137.9, 138.1, 138.2, 138.3, 138.5, 138.5, 138.6 ; HRMS (MALDI-TOF): calcd. for $C_{66}H_{72}NaO_{11}$ [M^++Na]: 1063.4972; found: 1063.4994.

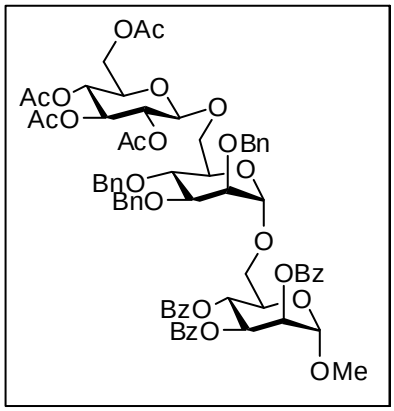
Characterization data for compound **47**



$[\alpha]_D^{25}$ = +23.1 ($CHCl_3$, *c* 1.00); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.17 (s, 3H), 3.25-3.94 (m, 17H), 4.11 (dd, 1H, *J* = 1.8, 9.1 Hz), 4.24-4.96 (m, 23H), 7.04-7.32 (m, 50H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 55.0, 65.6, 68.7, 69.0, 69.8, 71.3, 71.8, 72.5, 73.2, 73.4, 73.4, 74.5, 74.6, 74.7, 74.8, 74.9, 74.9, 74.9, 74.9, 77.5, 77.8,79.5, 79.9, 82.0, 82.0, 84.6, 97.6, 98.1, 104.0, 127.3-128.4, 138.1, 138.1, 138.1, 138.2, 138.3, 138.3, 138.5, 138.6, 138.6, 138.7; HRMS (MALDI-TOF): calcd. for

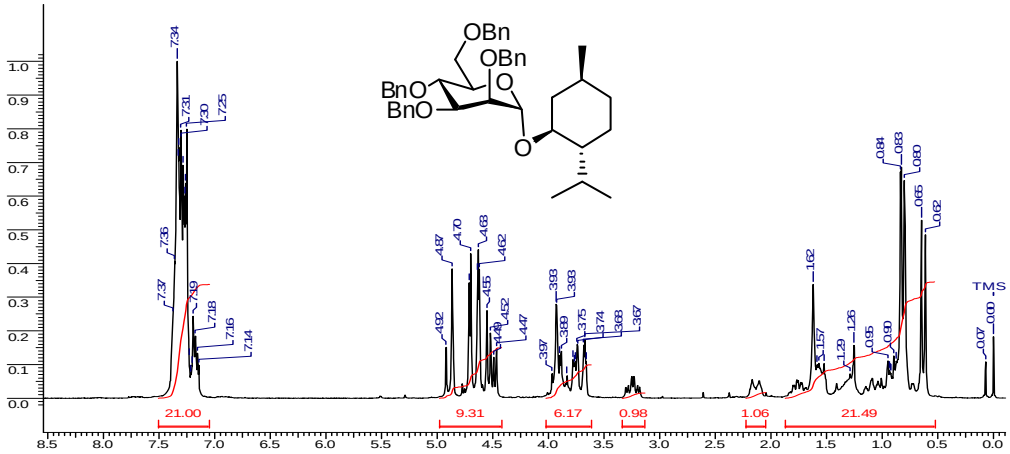
$C_{89}H_{94}NaO_{16}$ [M^++Na]: 1441.6440; found: 1441.6457.

Characterization data for compound **48**

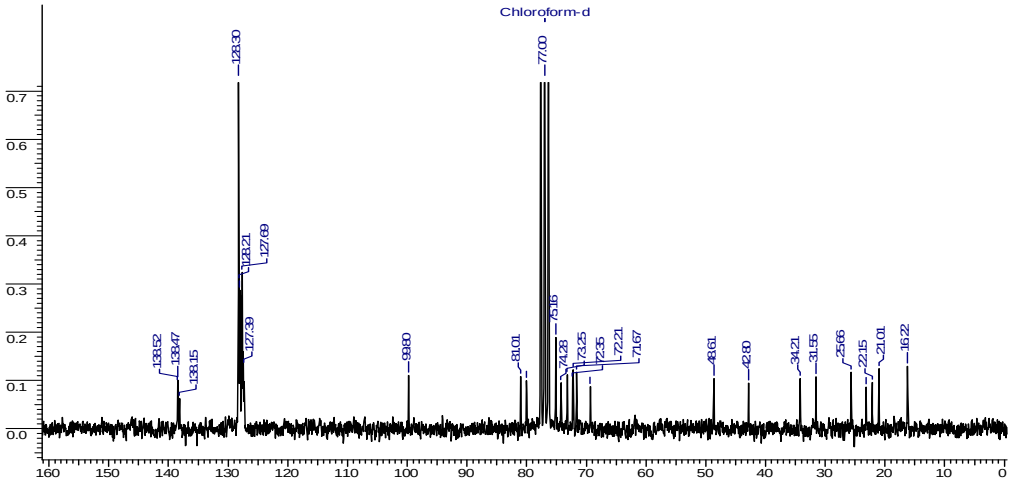


$[\alpha]_D^{25}$ = -63.8 ($CHCl_3$, *c* 1.00); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.95 (s, 3H), 1.99 (s, 3H), 2.01 (s, 3H), 2.02 (s, 3H), 3.50-4.21 (m, 13H), 4.33-4.37 (m, 3H), 4.52 (d, 1H, *J* = 11.4 Hz), 4.58 (s, 2H), 4.90-4.96 (m, 3H), 5.01 (t, 1H, *J* = 9.8 Hz), 5.03 (t, 1H, *J* = 10.1Hz), 5.13 (t, 1H, *J* = 9.4 Hz), 5.63 (dd, 1H, *J* = 1.8, 3.2 Hz), 5.84 (dd, 1H, *J* = 3.2, 9.8 Hz), 7.23-7.54 (m, 24H), 7.81-8.11 (m, 6H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 20.5, 20.5, 20.6, 20.6, 55.4, 61.8, 66.6, 67.8, 68.3, 68.7, 69.1, 69.9, 70.5, 71.0, 71.1, 71.5, 71.5, 72.5, 72.8, 74.4, 74.6, 74.8, 80.1, 98.0, 98.4, 100.9, 127.4-129.8, 133.0, 133.3, 133.4, 138.2, 138.3, 138.5, 165.3, 165.4, 165.5, 169.0, 169.4, 170.3, 170.6 ; HRMS (MALDI-TOF): calcd. for $C_{69}H_{72}NaO_{23}$ [M^++Na]: 1291.4362; found: 1291.4377.

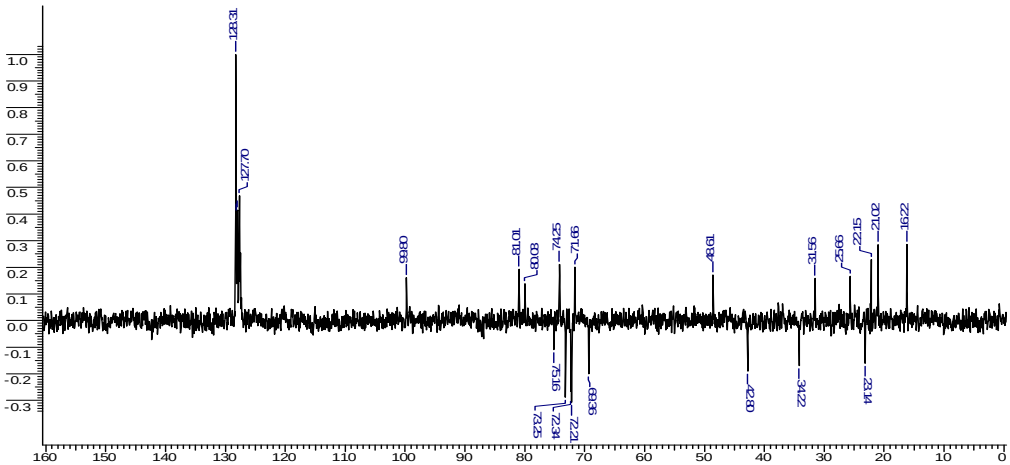
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **3**



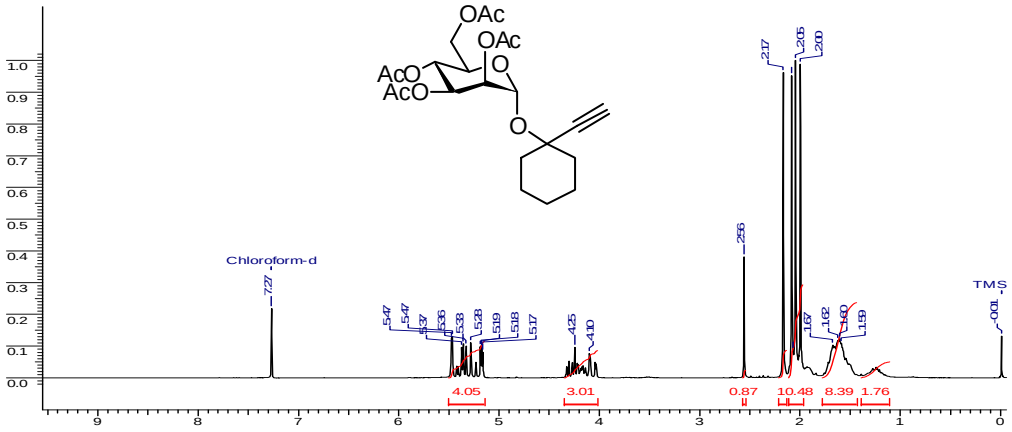
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **3**



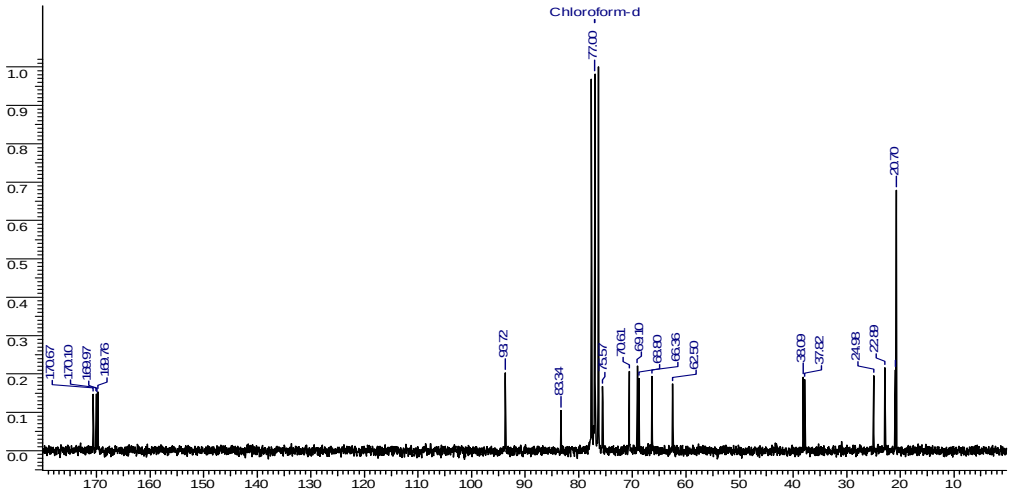
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **3**



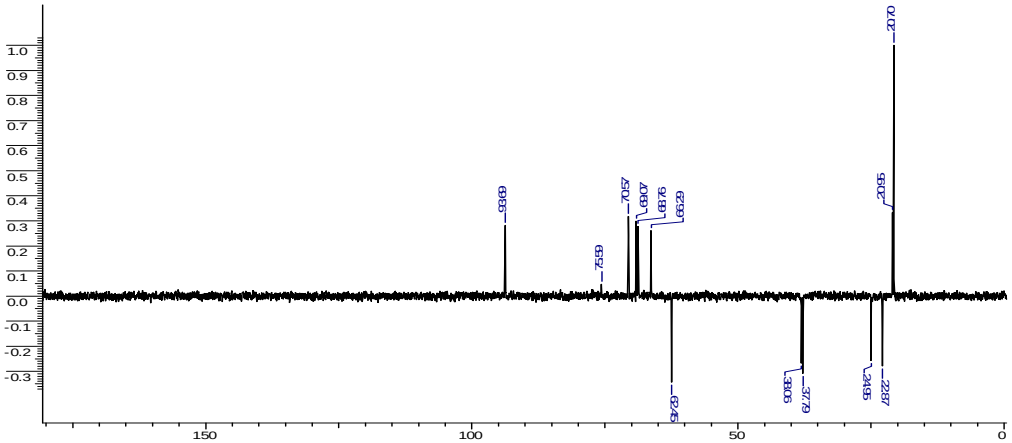
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **5**



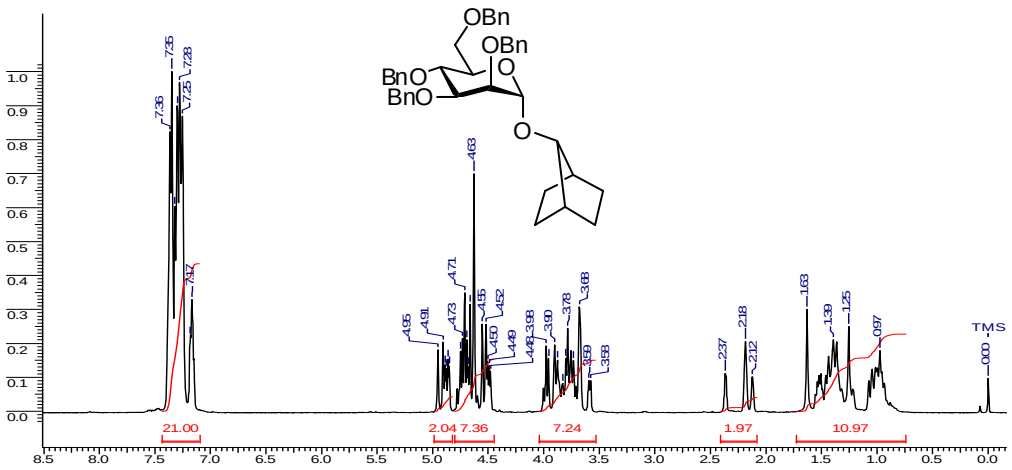
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **5**



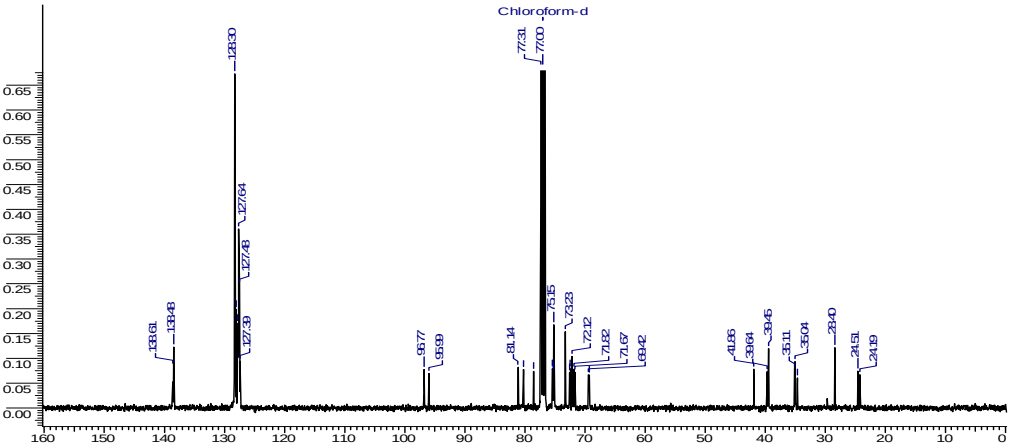
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **5**



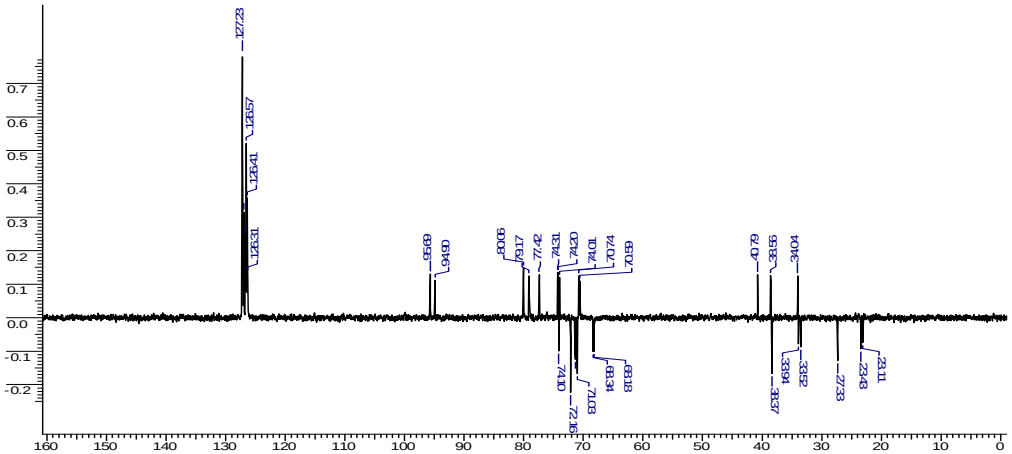
^{1}H NMR Spectrum (400.13 MHz, $CDCl_3$) of Compound **9**



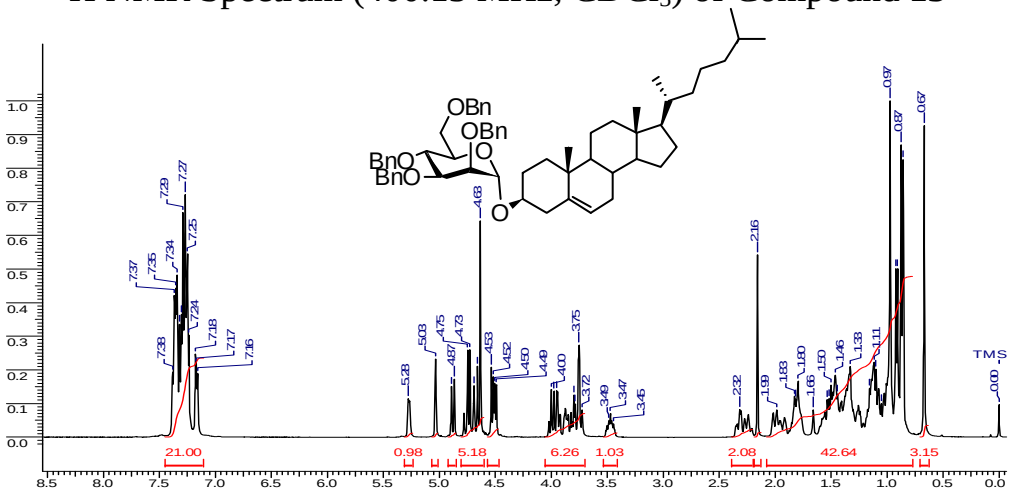
^{13}C NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **9**



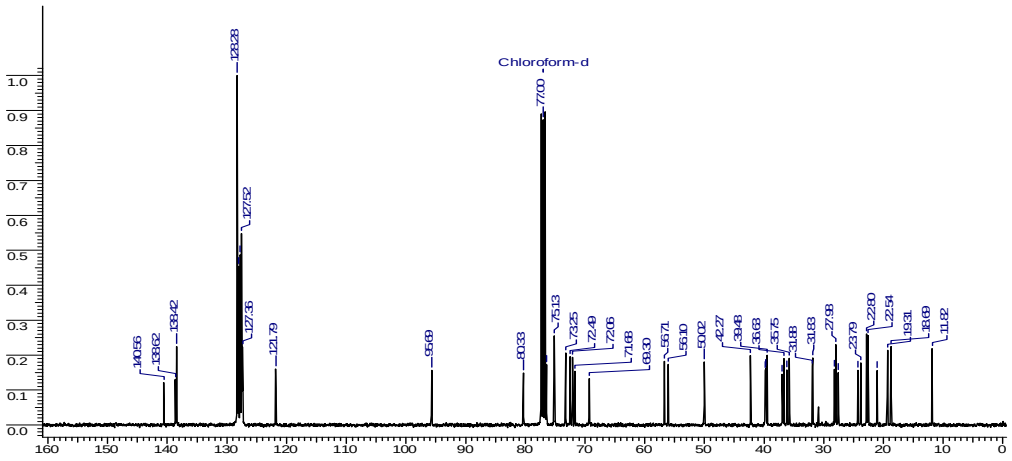
DEPT NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **9**



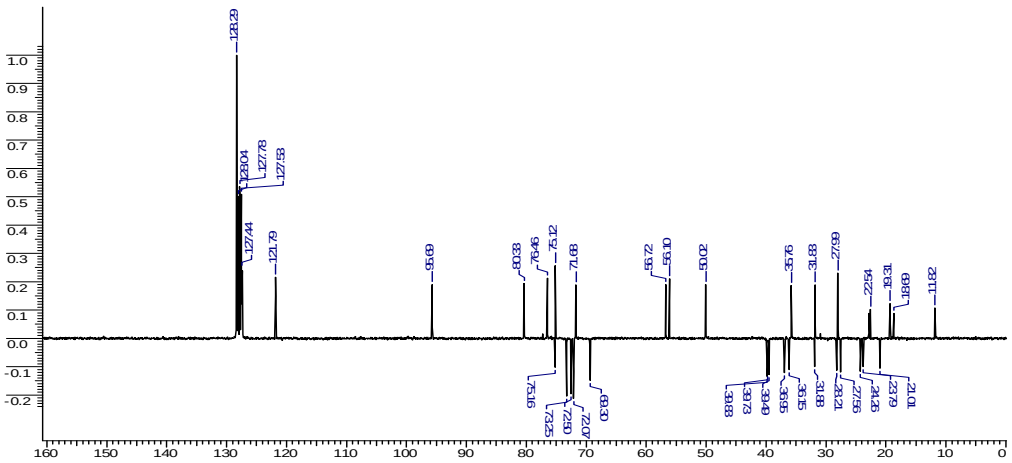
^{1}H NMR Spectrum (400.13 MHz, $CDCl_3$) of Compound **13**



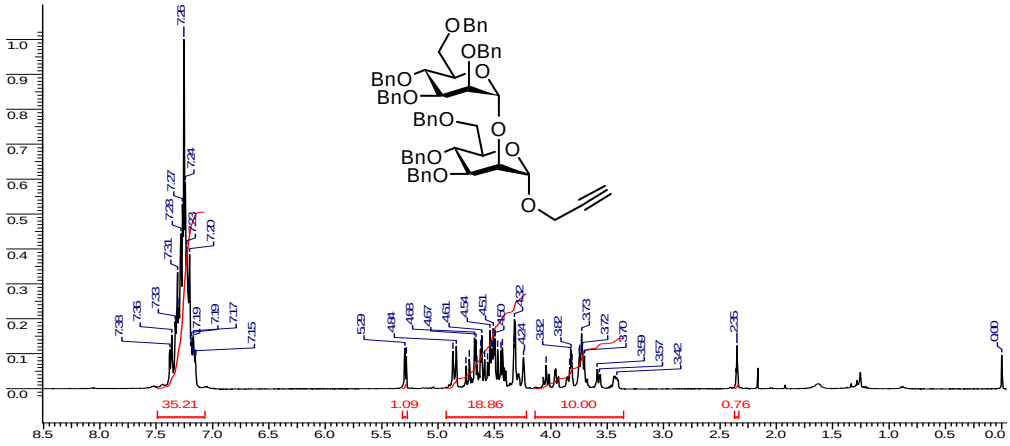
^{13}C NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **13**



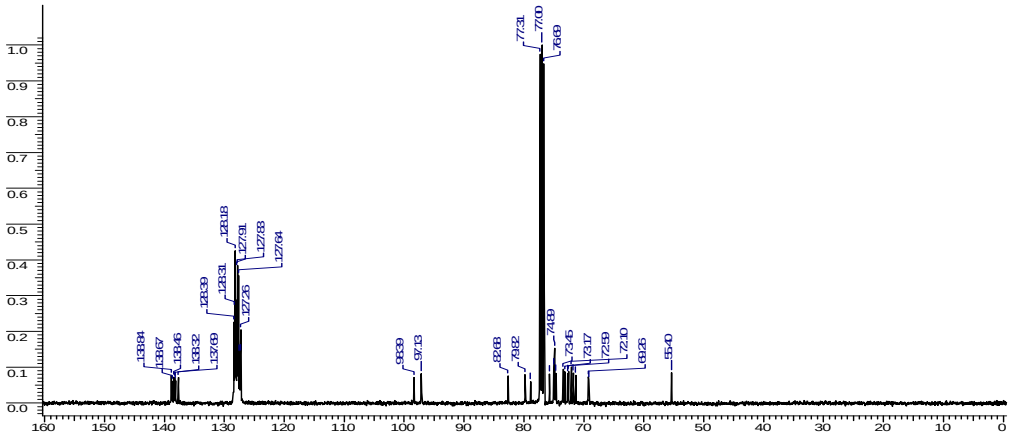
DEPT NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **13**



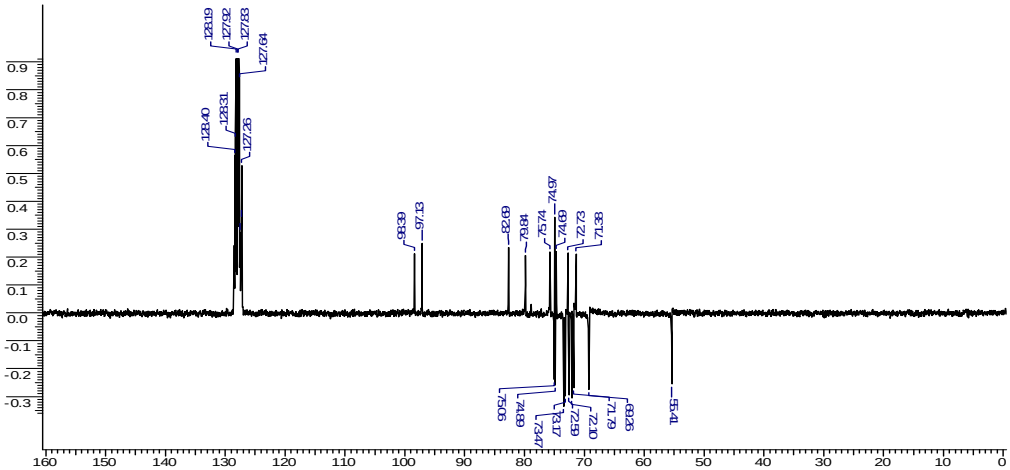
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **17**



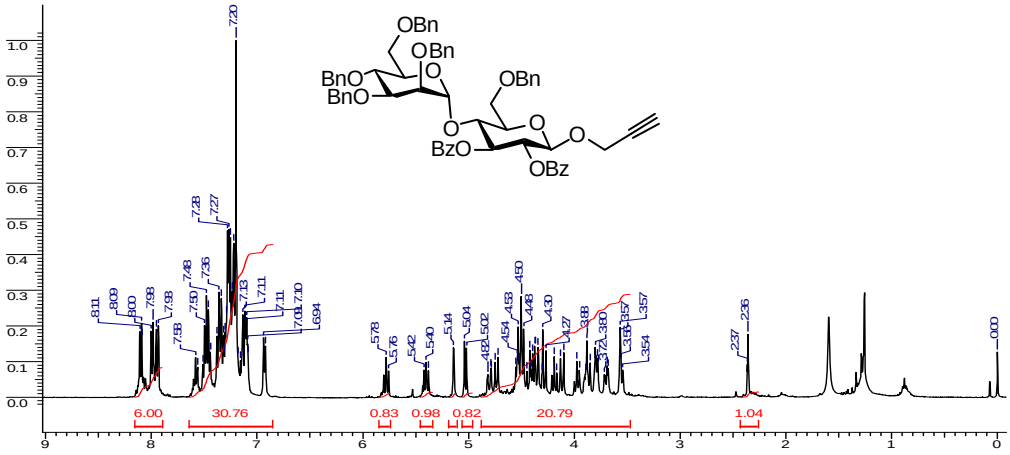
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **17**



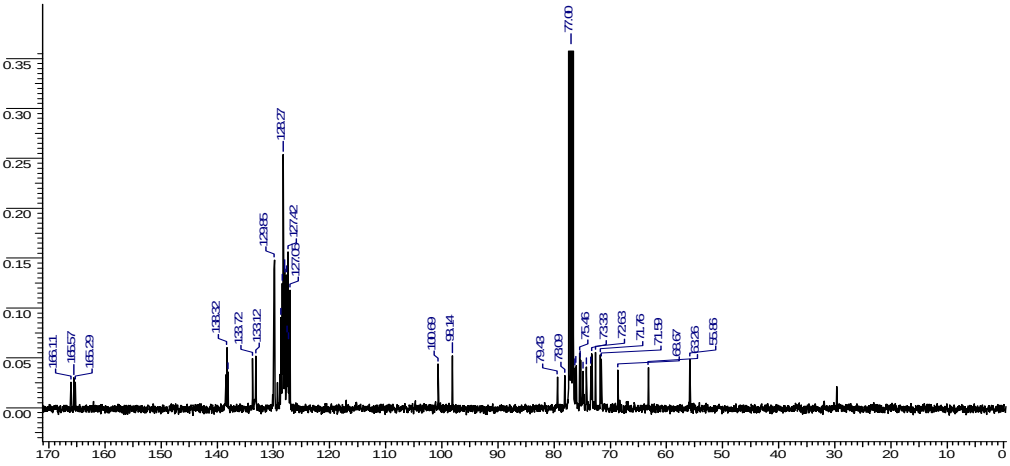
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **17**



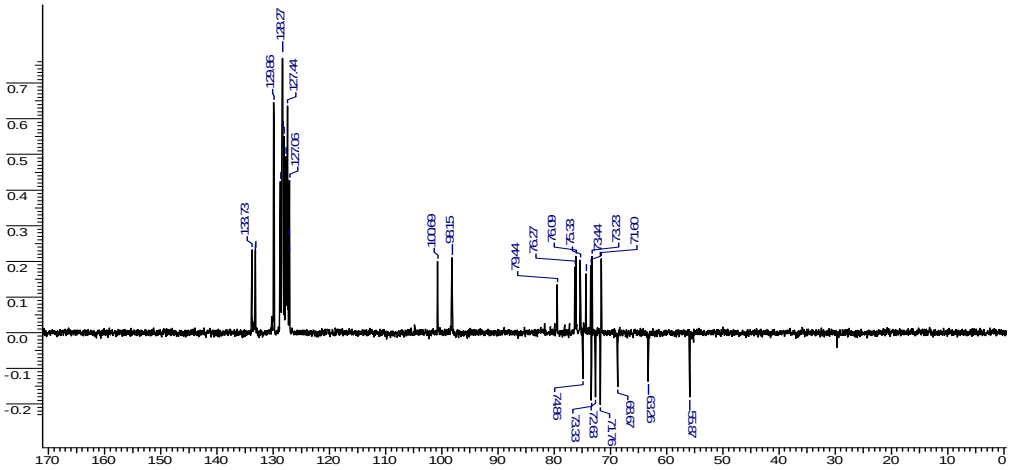
^{1}H NMR Spectrum (400.13 MHz, $CDCl_3$) of Compound **19**



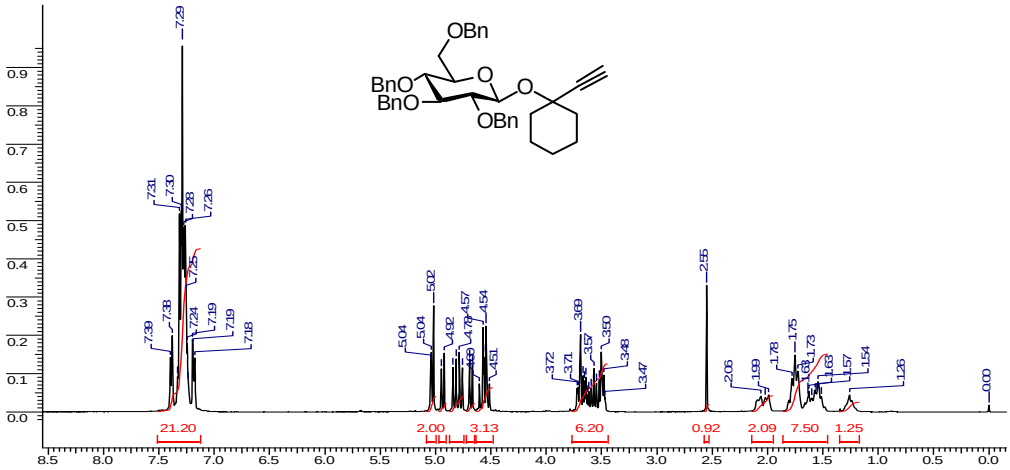
^{13}C NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **19**



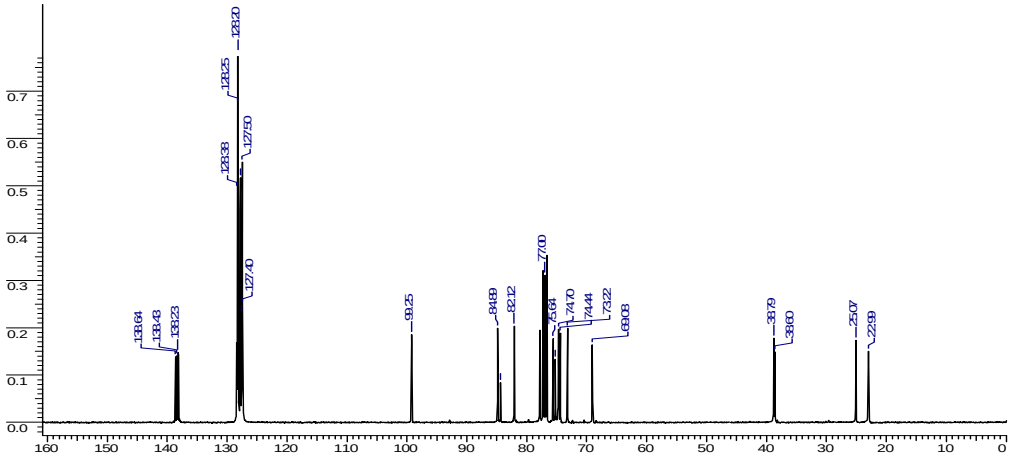
DEPT NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **19**



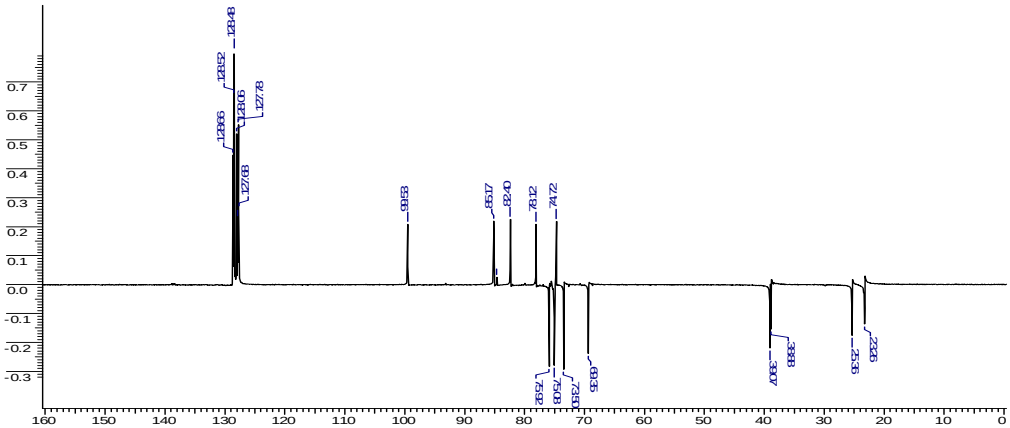
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **22**



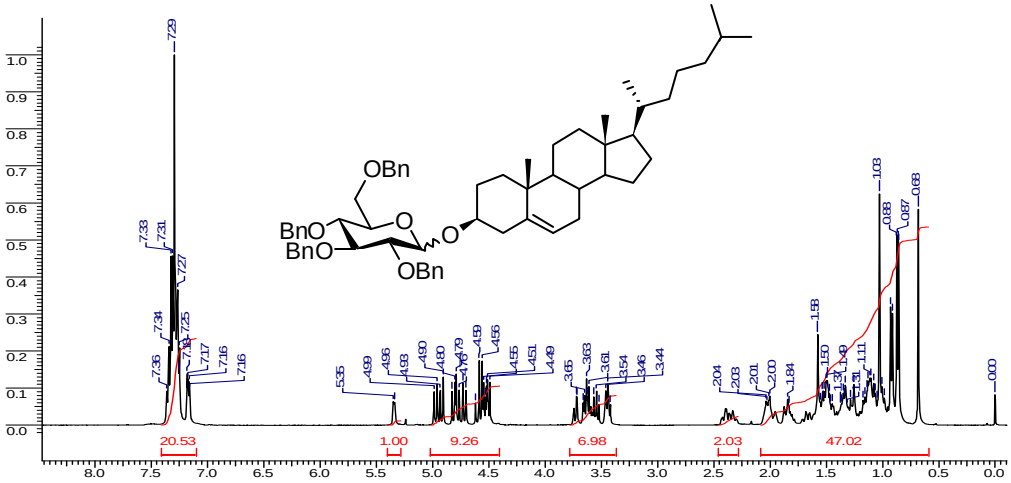
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **22**



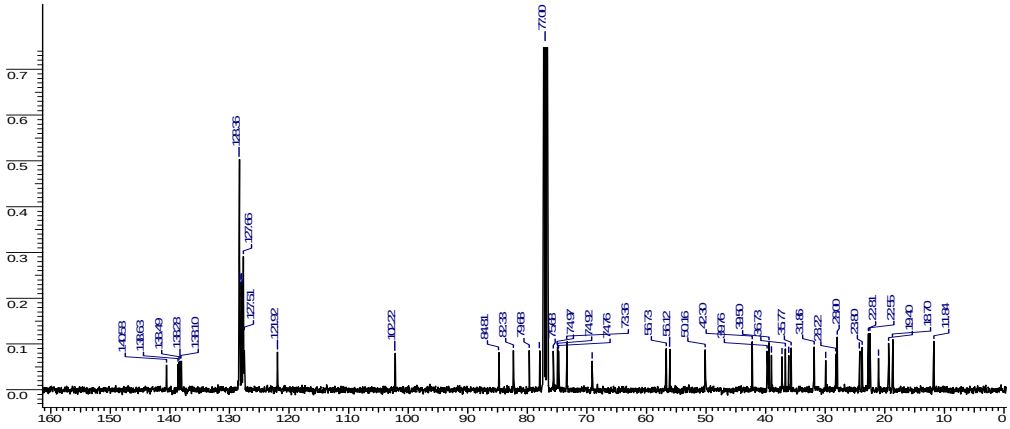
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **22**



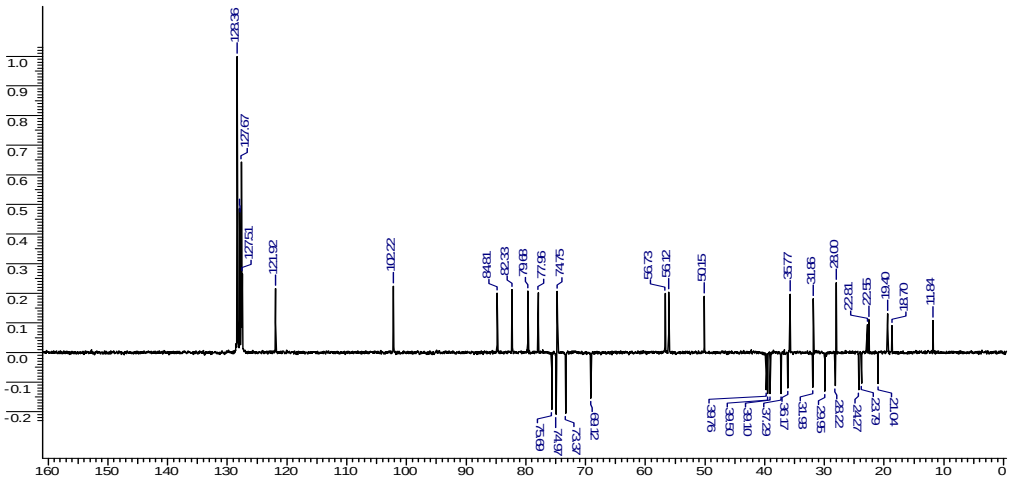
^{1}H NMR Spectrum (400.13 MHz, $CDCl_3$) of Compound **23**



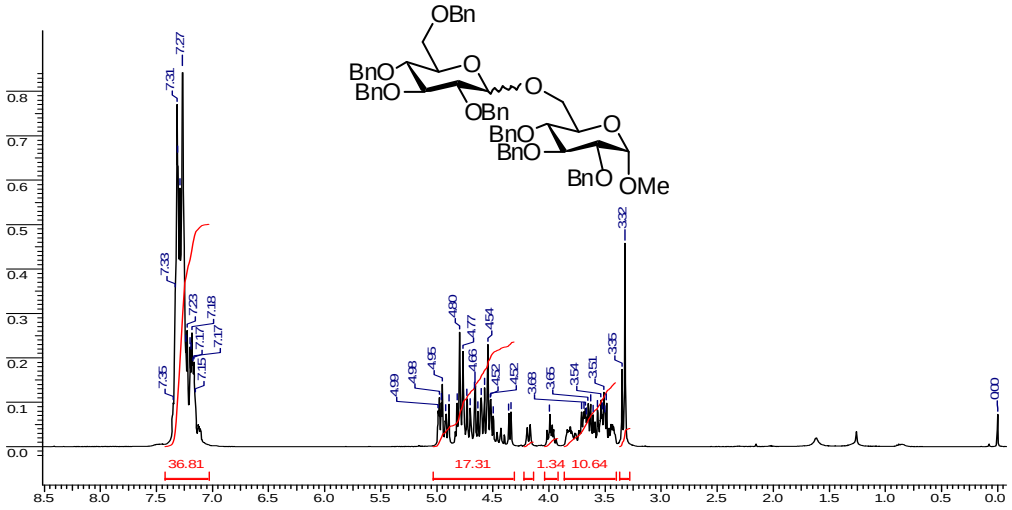
^{13}C NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **23**



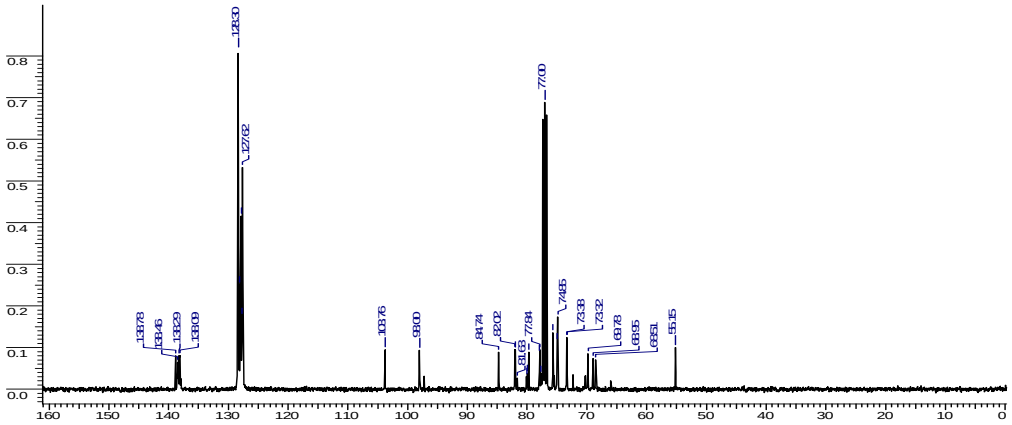
DEPT NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **23**



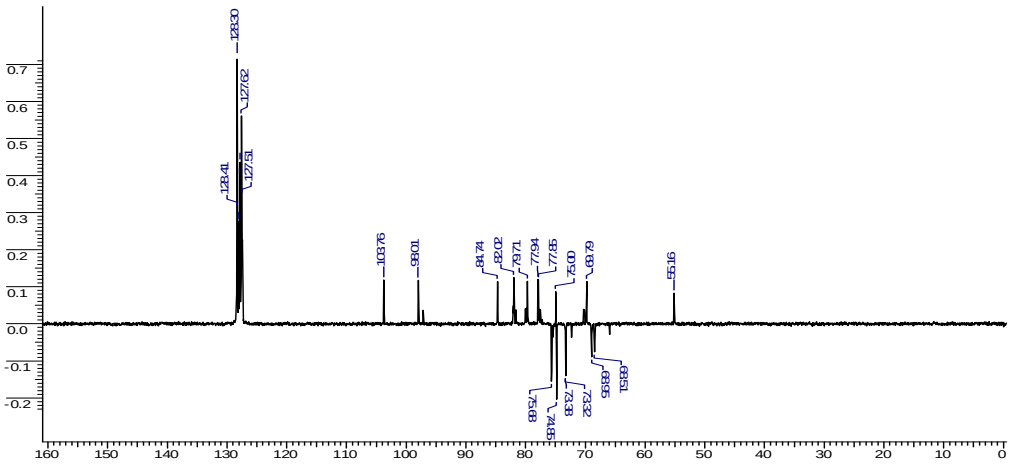
^{1}H NMR Spectrum (400.13 MHz, $CDCl_3$) of Compound **27**



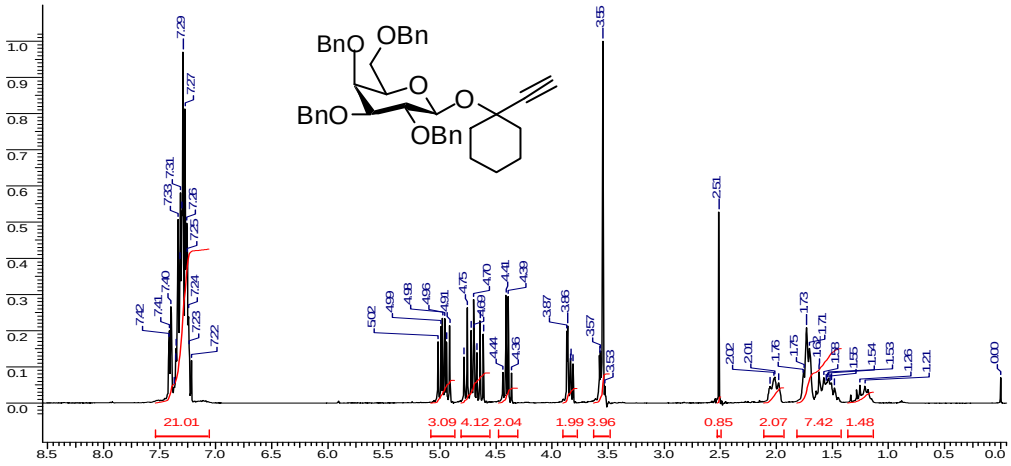
^{13}C NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **27**



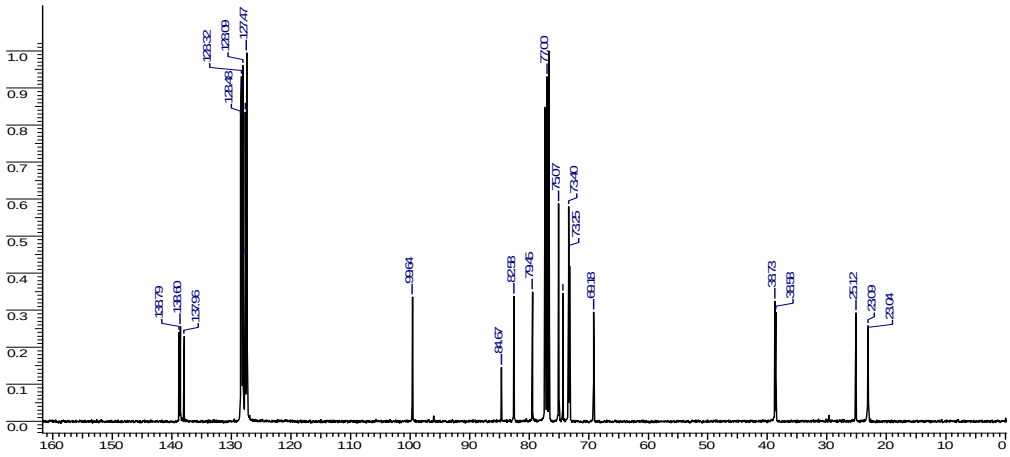
DEPT NMR Spectrum (100.61 MHz, $CDCl_3$) of Compound **27**



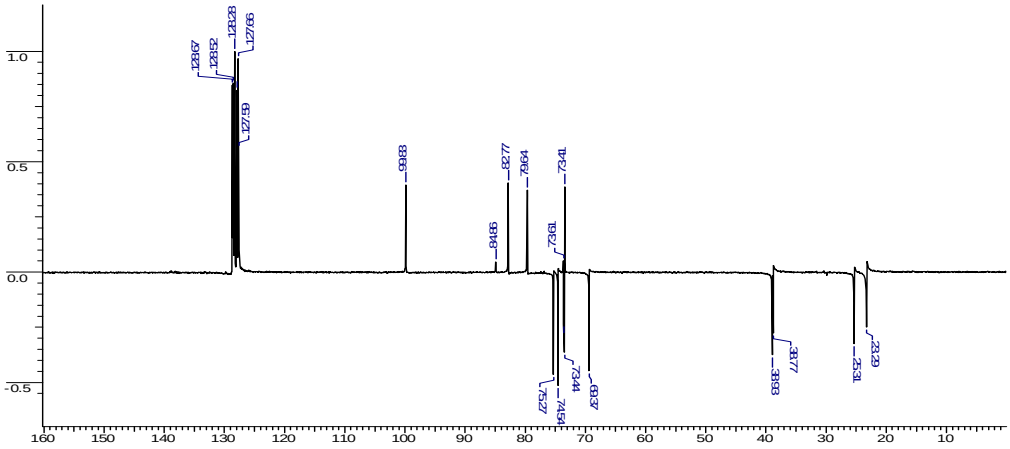
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **28**



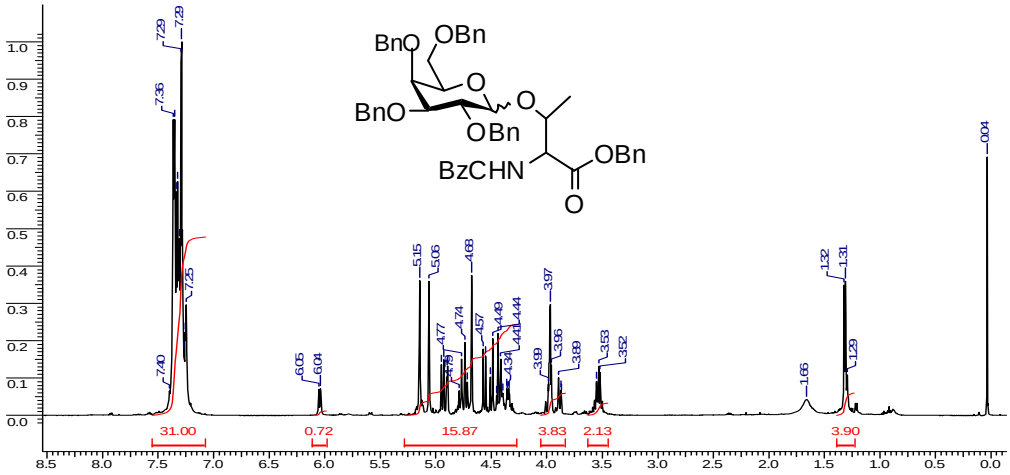
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **28**



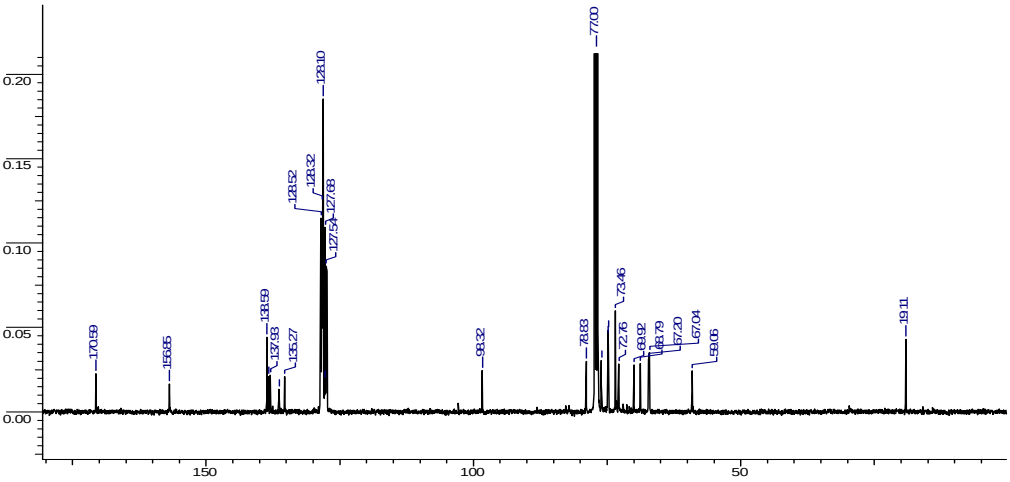
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **28**



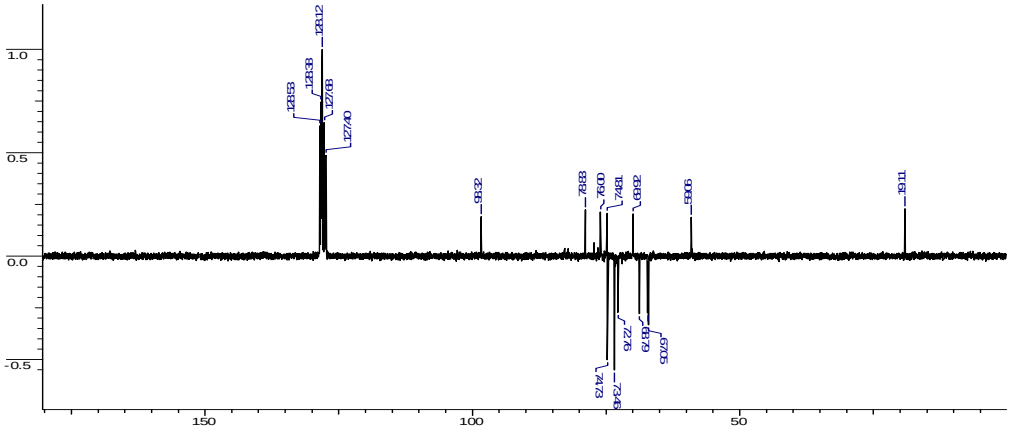
^{1}H NMR Spectrum (500.13 MHz, $CDCl_3$) of Compound **30**



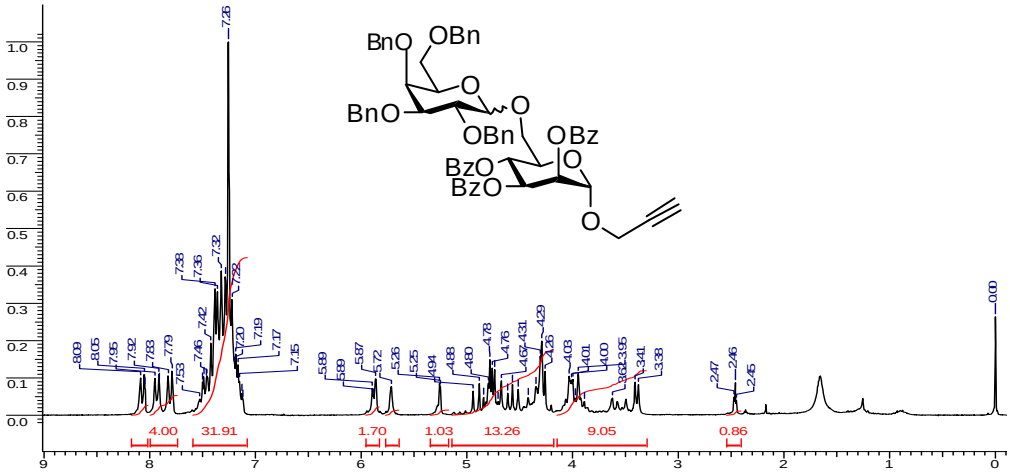
^{13}C NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **30**



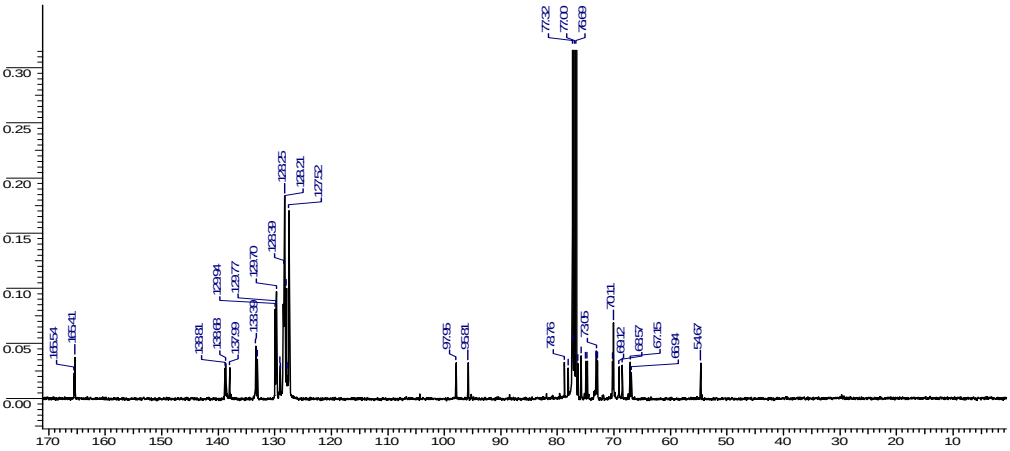
DEPT NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **30**



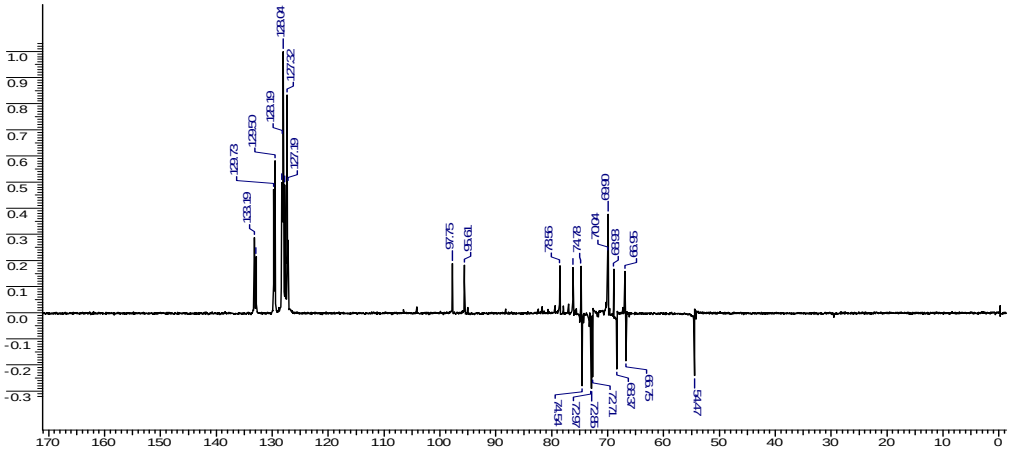
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **31**



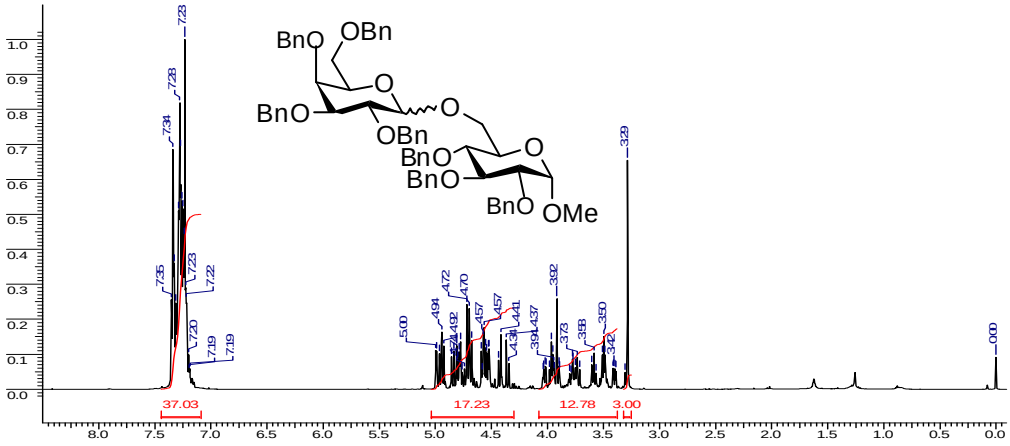
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **31**



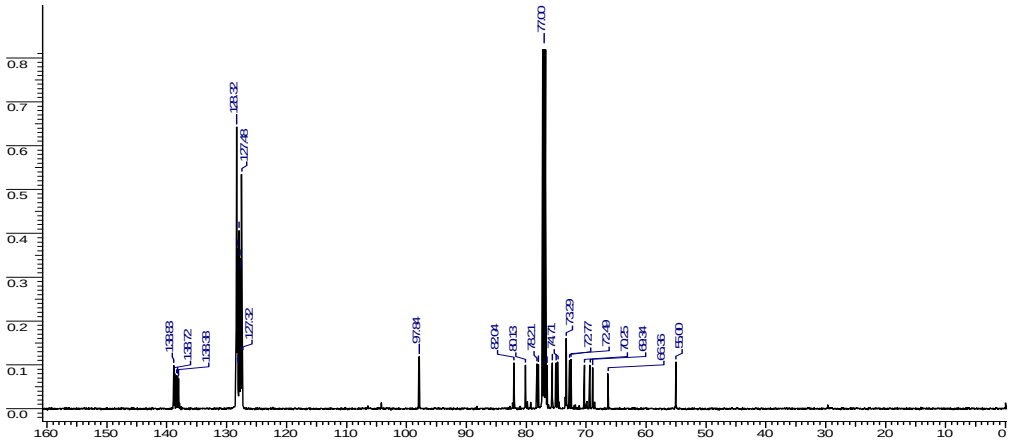
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **31**



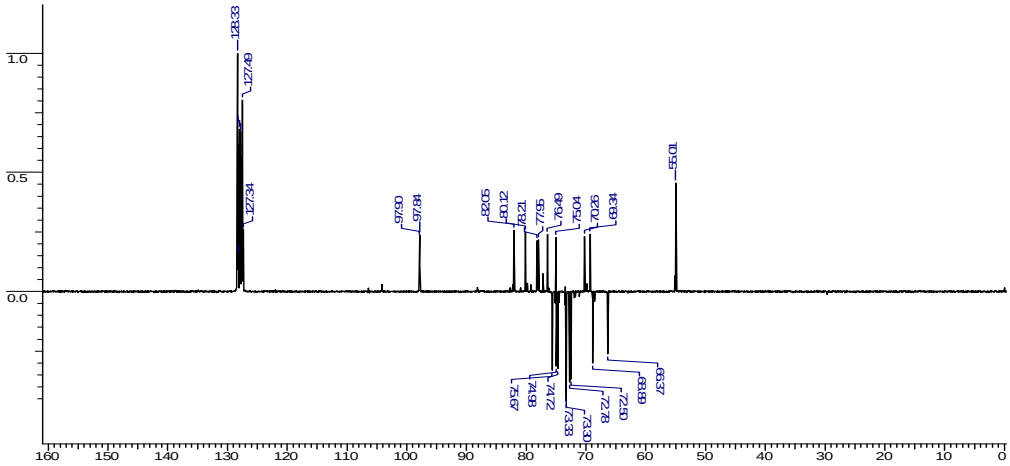
^{1}H NMR Spectrum (500.13 MHz, $CDCl_3$) of Compound **32**



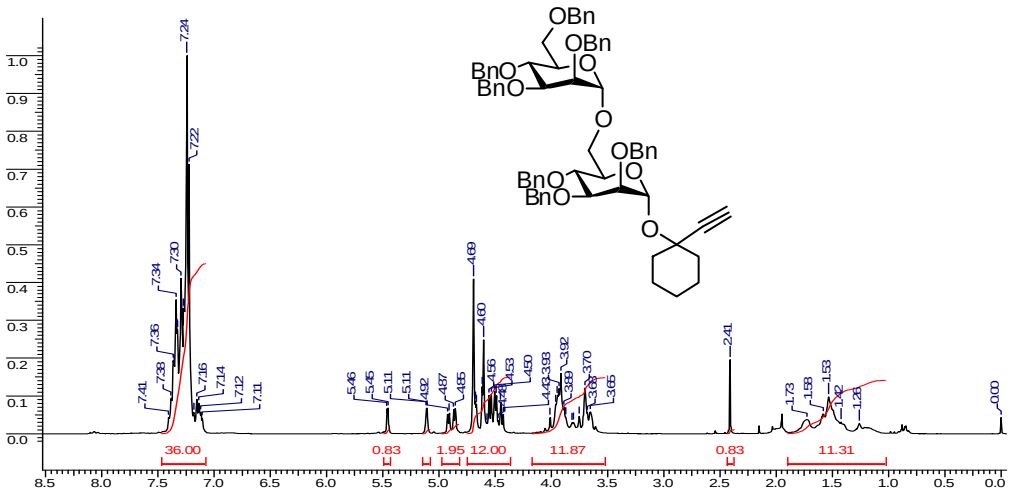
^{13}C NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **32**



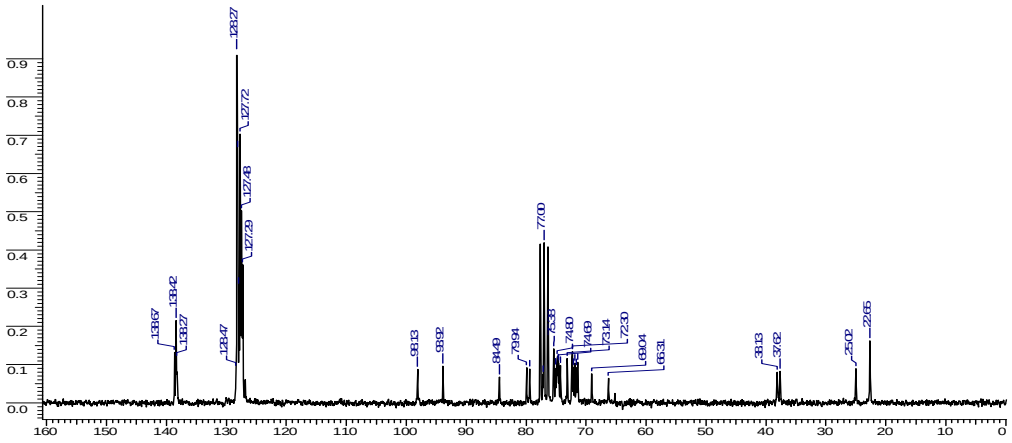
DEPT NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **32**



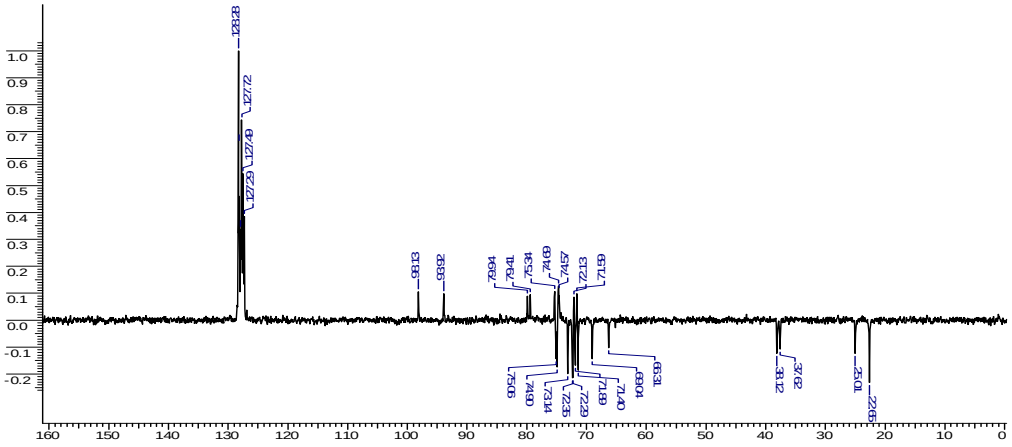
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **34**



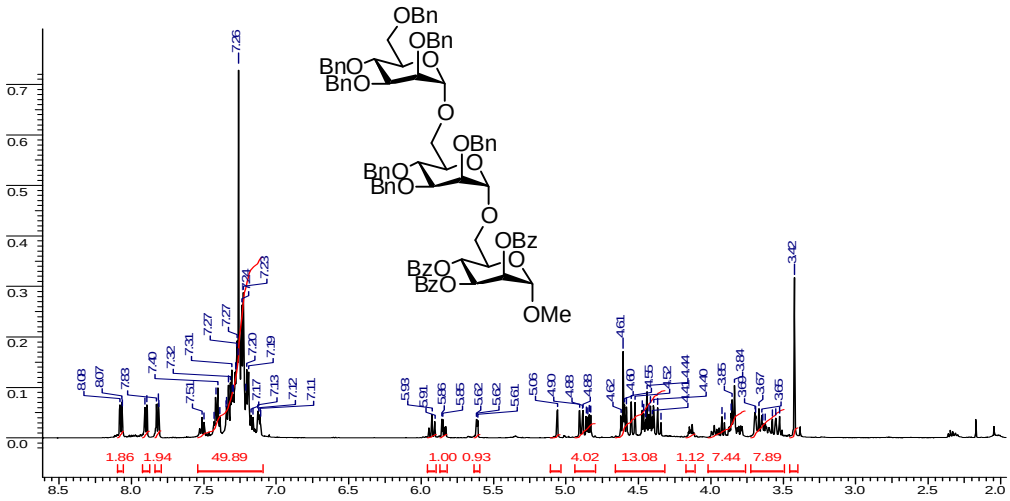
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **34**



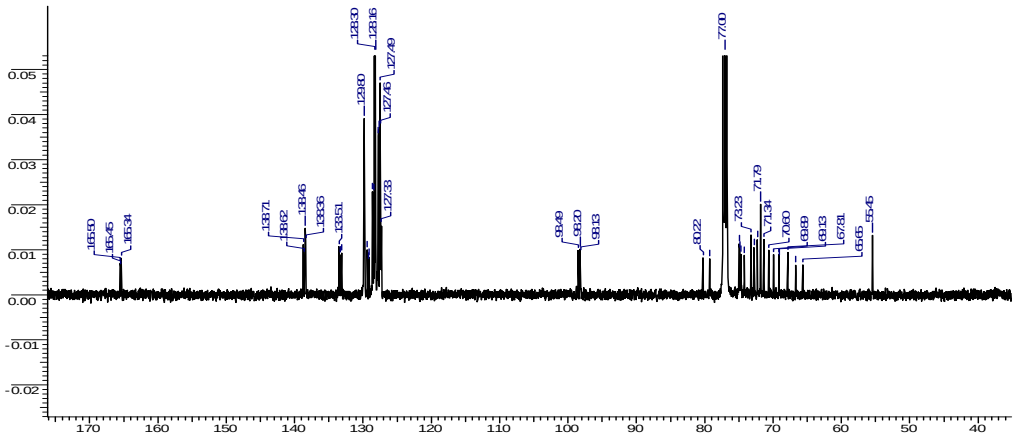
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **34**



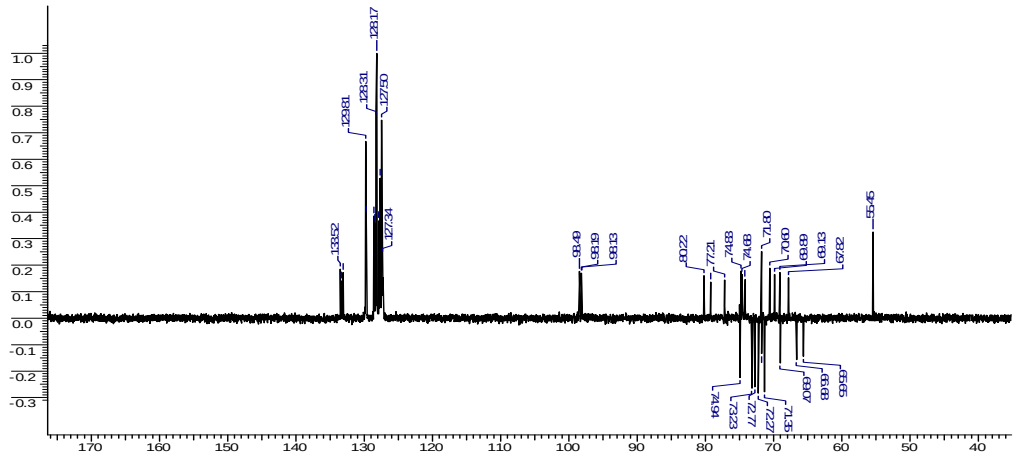
^{1}H NMR Spectrum (500.13 MHz, $CDCl_3$) of Compound **36**



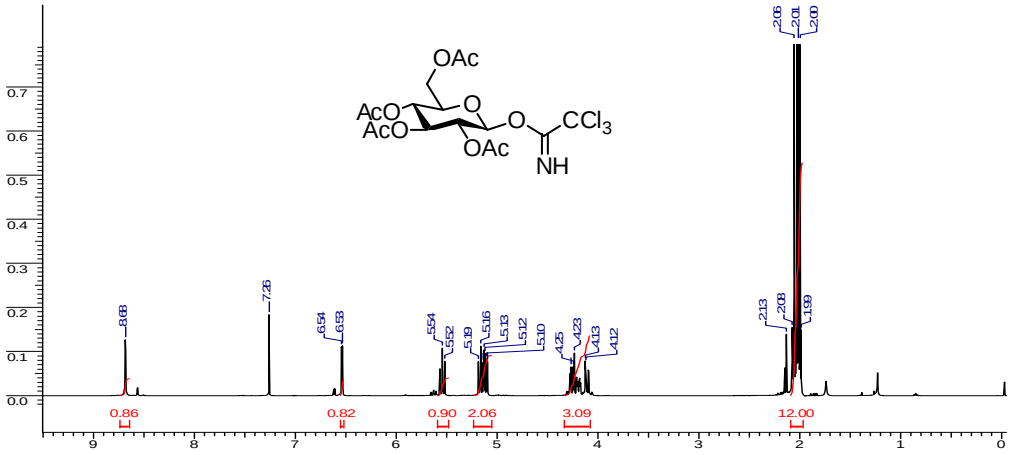
^{13}C NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **36**



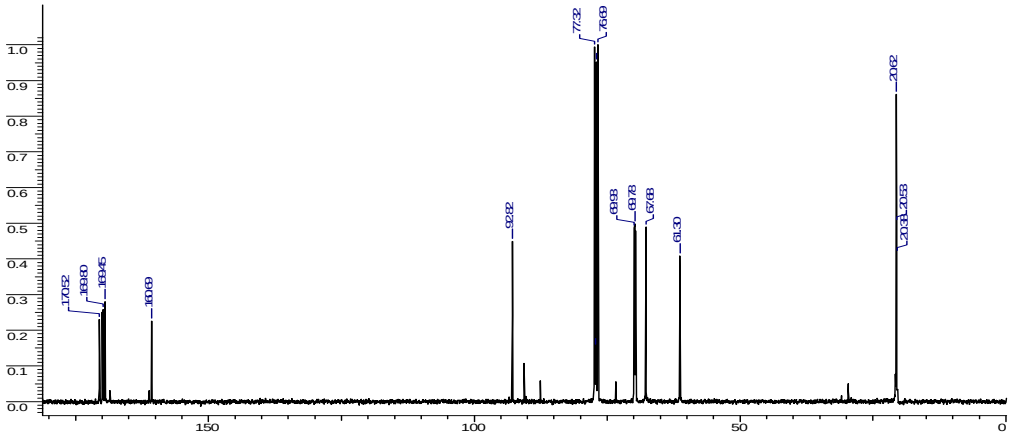
DEPT NMR Spectrum (125.76 MHz, $CDCl_3$) of Compound **36**



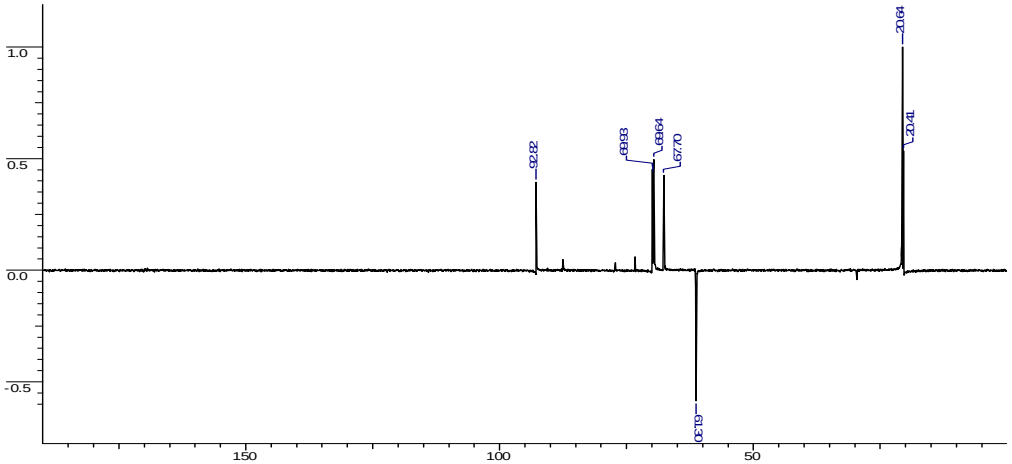
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **39**



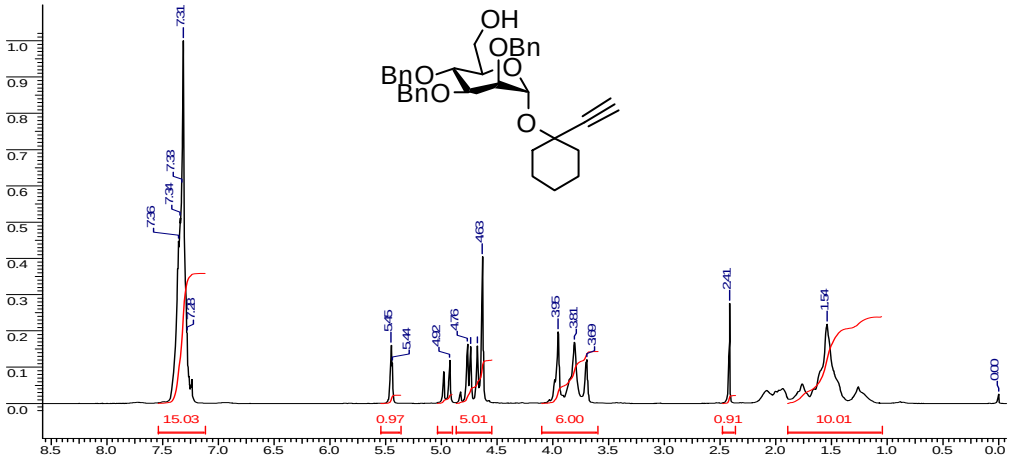
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **39**



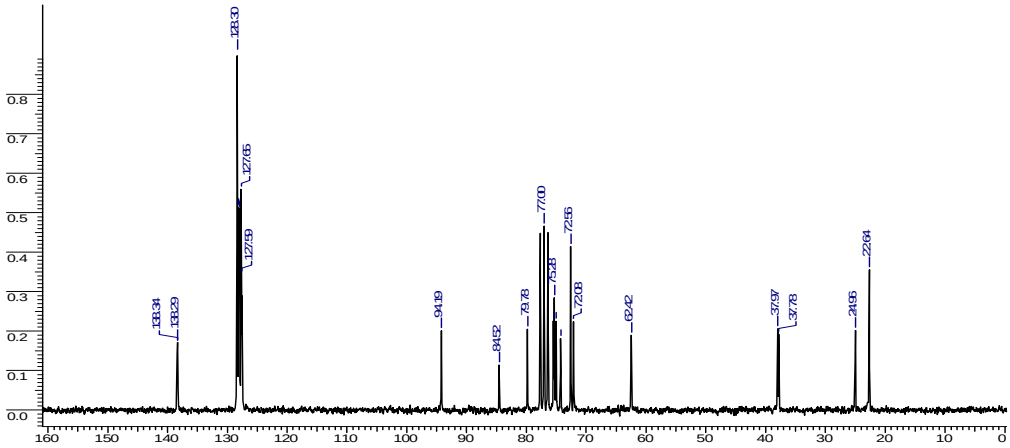
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **39**



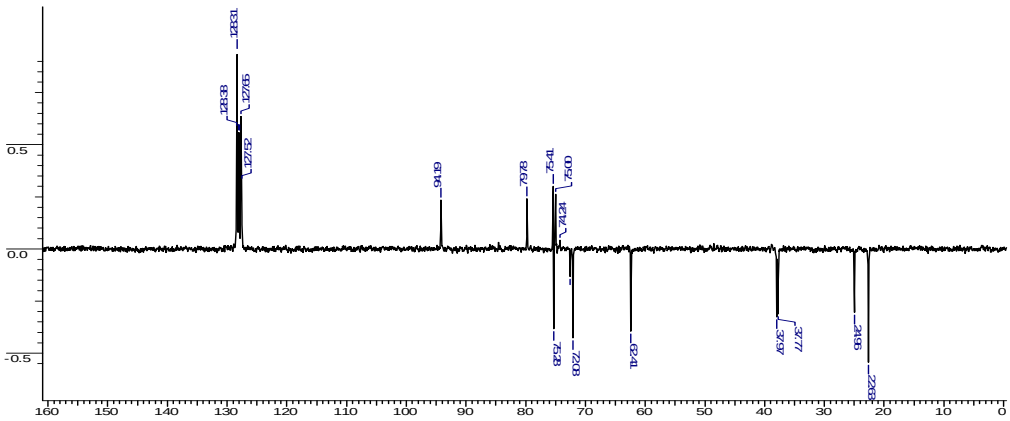
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of Compound **40**



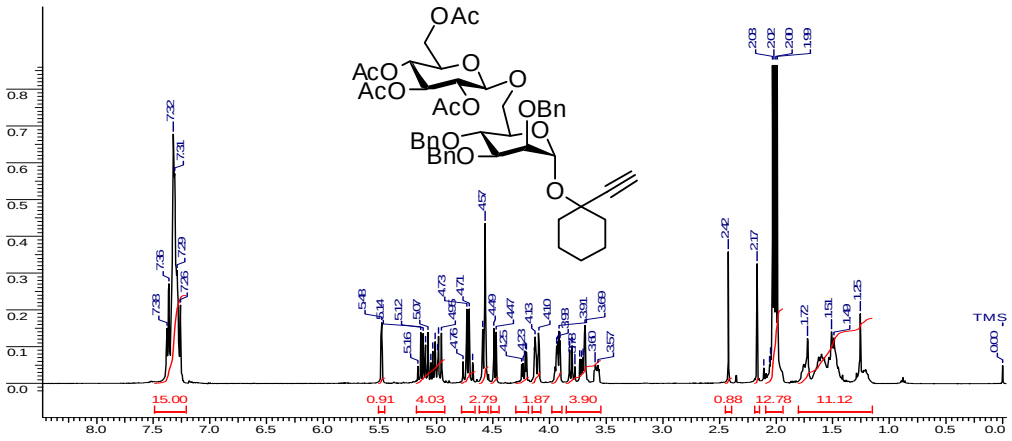
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **40**



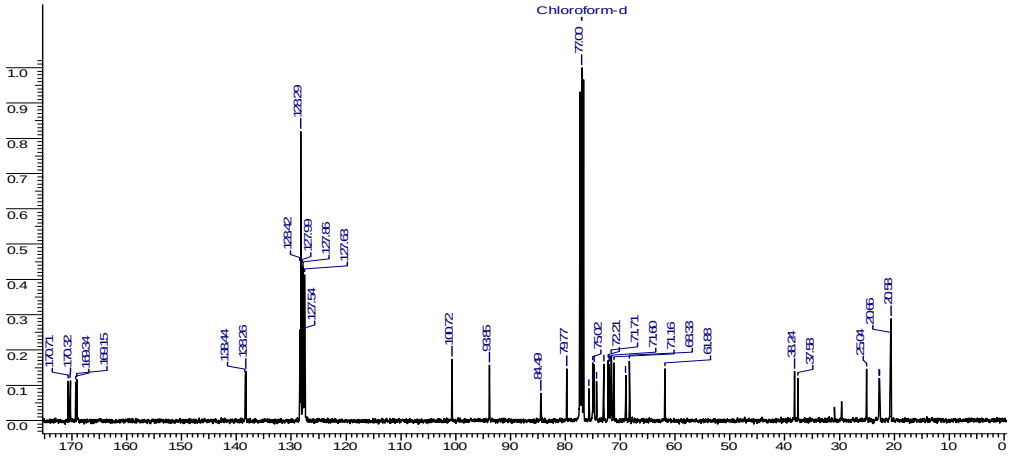
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of Compound **40**



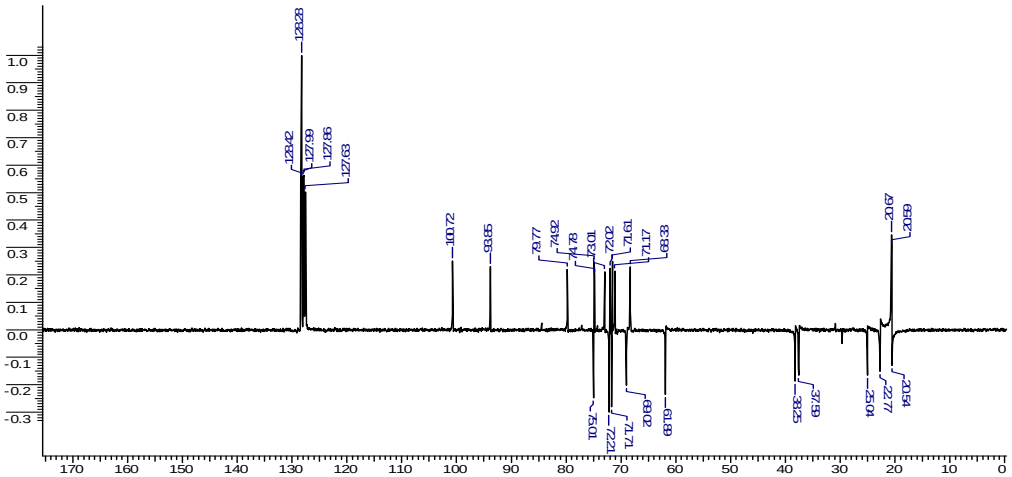
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **41**



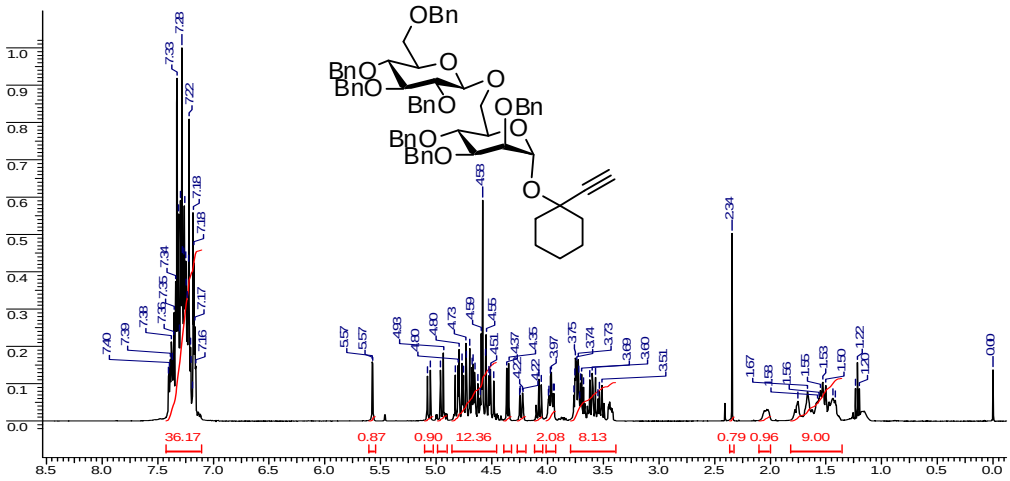
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **41**



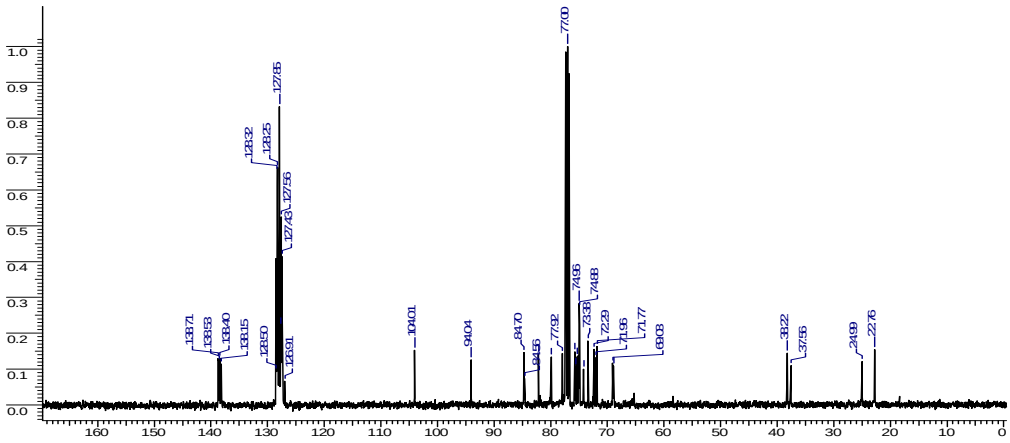
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **41**



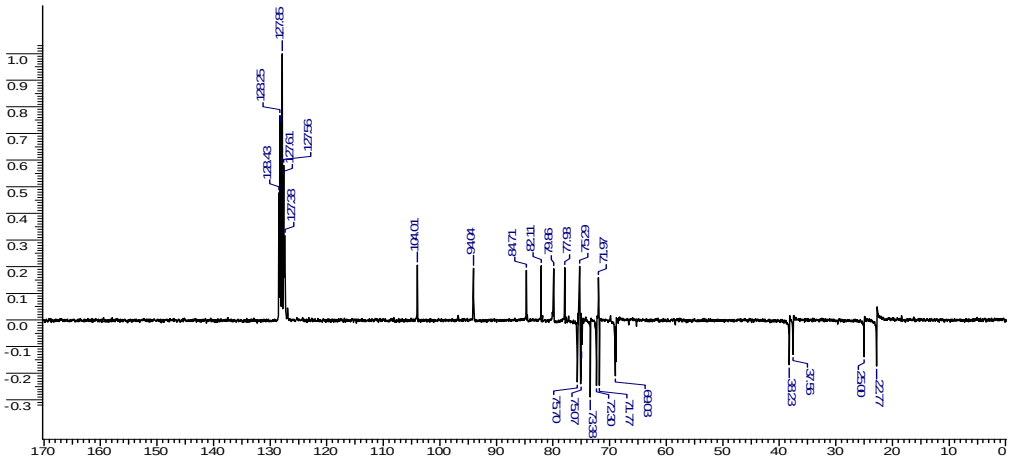
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **42**



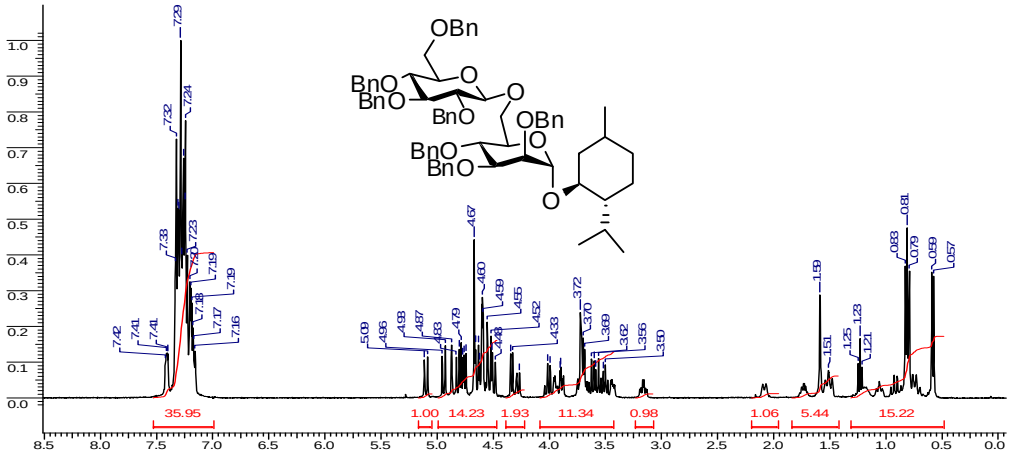
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **42**



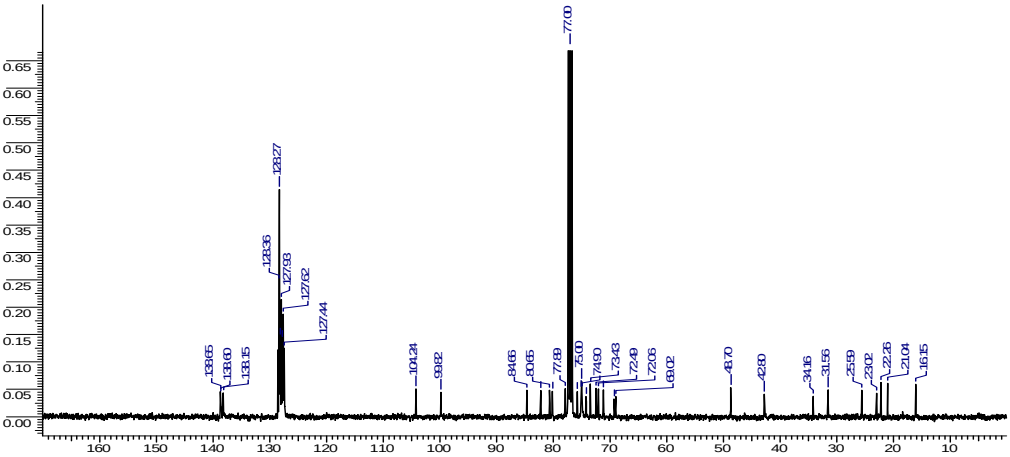
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **42**



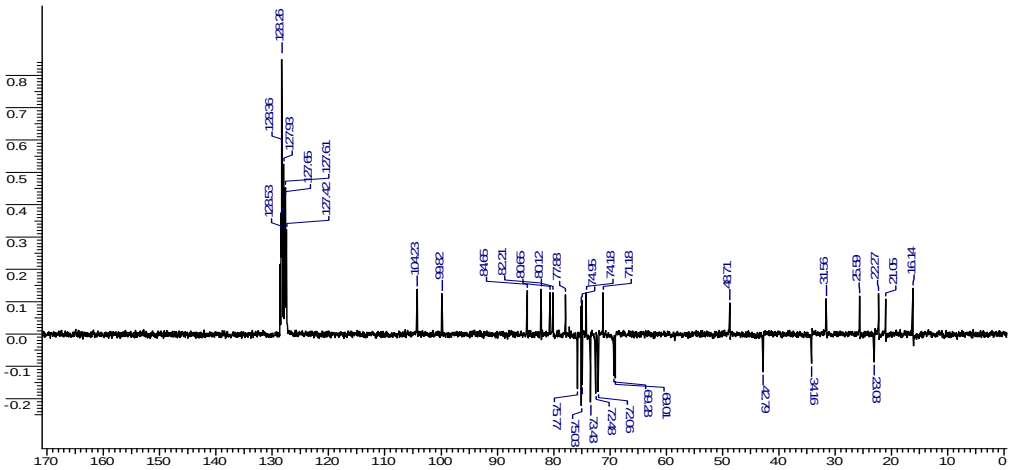
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **43**



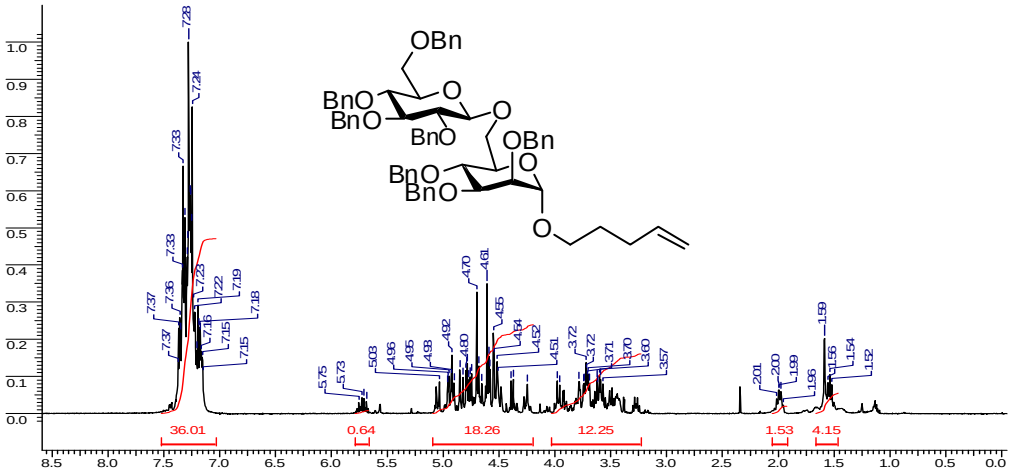
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **43**



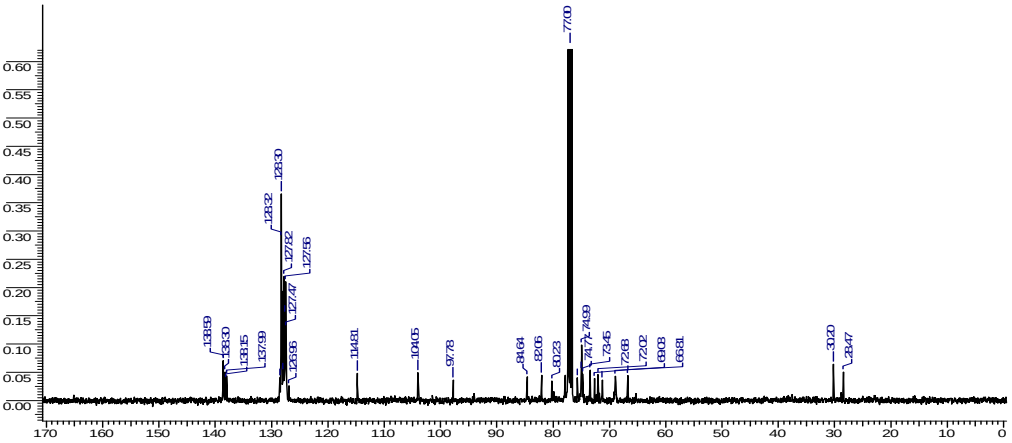
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **43**



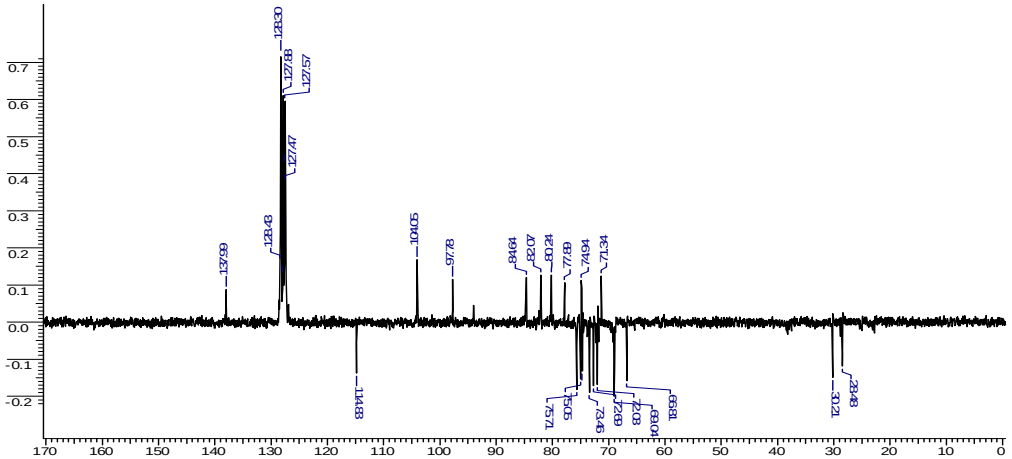
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **45**



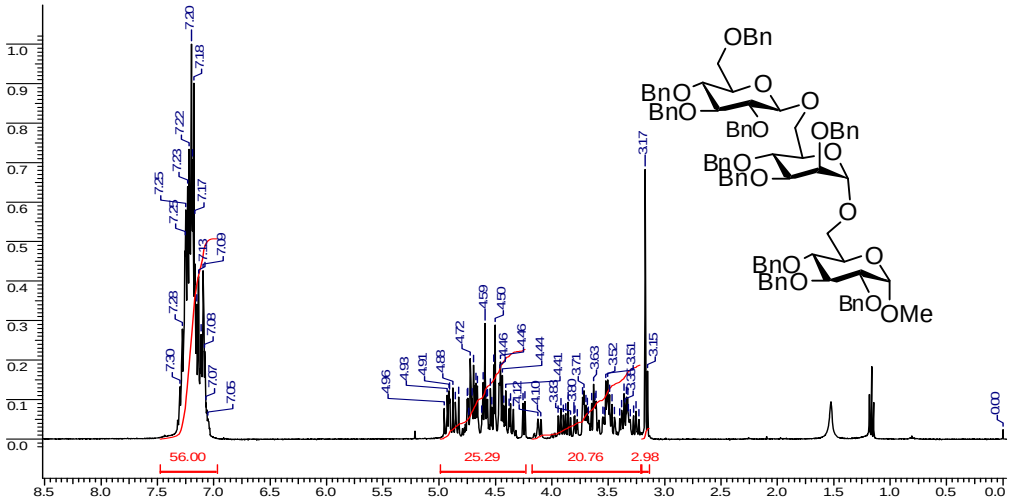
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **45**



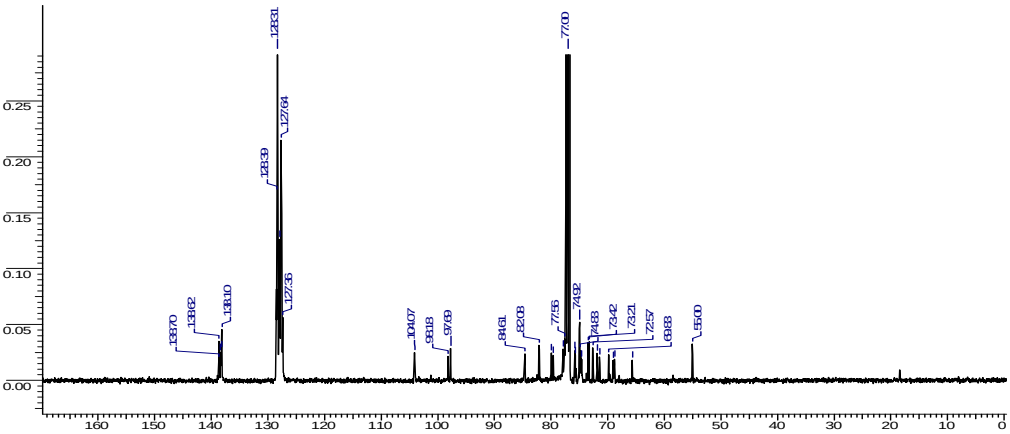
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **45**



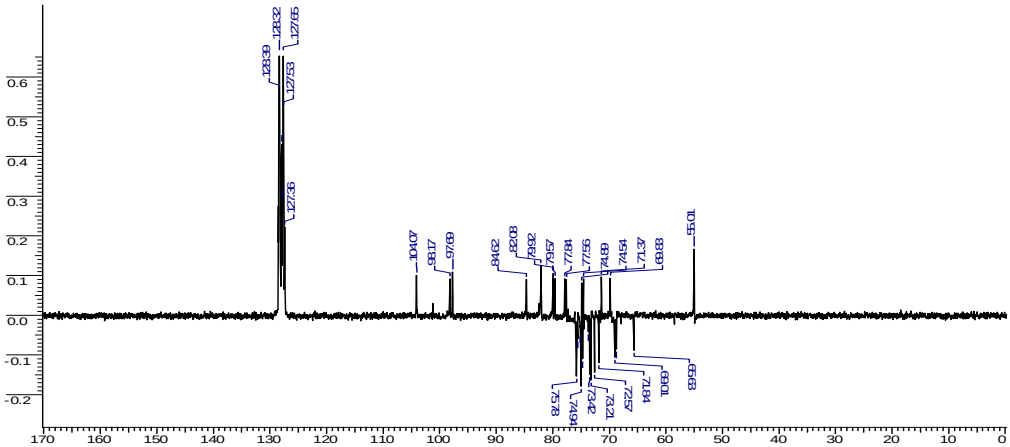
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **47**



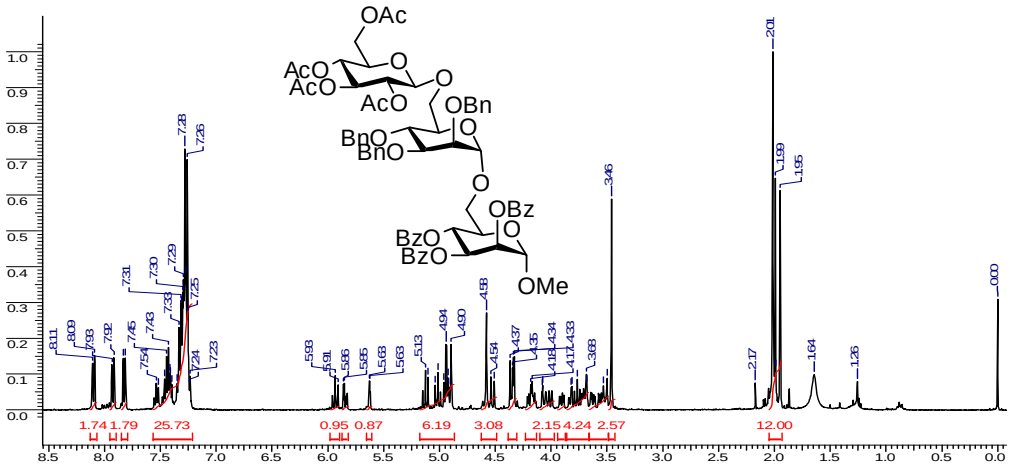
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **47**



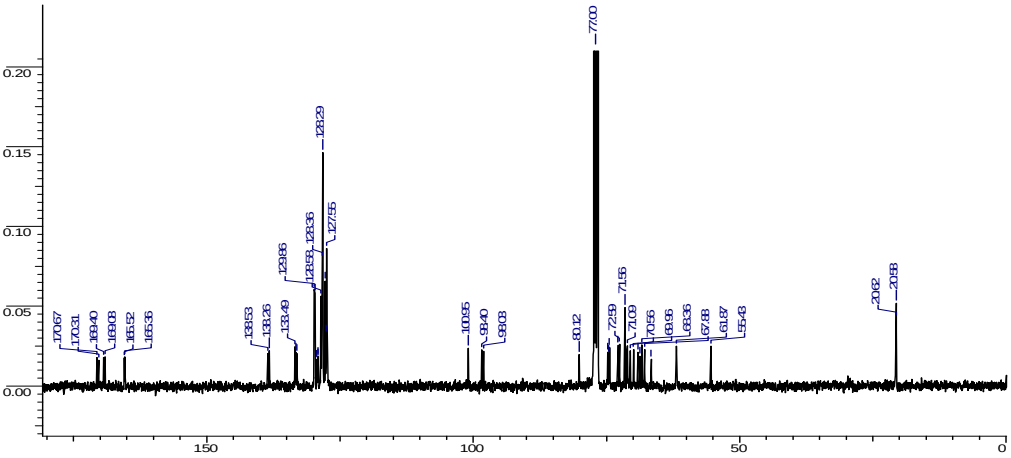
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **47**



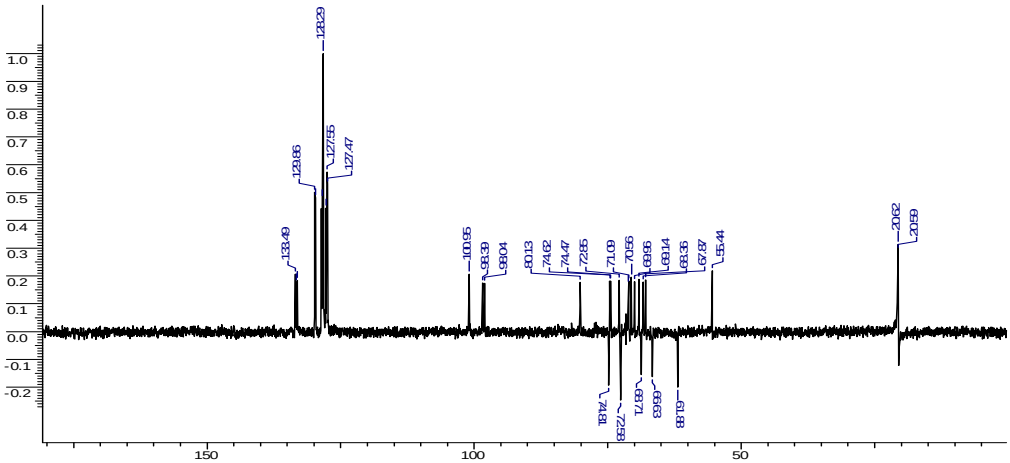
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **48**



^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **48**



DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **48**



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