CHAPTER 1

Gold Catalysis: Synthesis of O- and Carbamate- linked Amino Acid Glycoconjugates
Chapter 1: Introduction

Carbohydrates are like water, ubiquitously found on our planet. Carbohydrates are synthesised in plants and cyanobacteria by “photosynthesis” which is essential for all living beings on the earth. They are primary bio-molecules, which can get metabolized to monosaccharides, oligo- and polysaccharides. The photosynthetically produced sugar serves as energy source for photosynthesizing as well as for non-photosynthesizing organisms by direct consumption or indirect consumption, where the photosynthesis process is essentially reverses in very complex oxidative carbohydrate metabolism (Fig.1). Apart from source of energy to living organisms, carbohydrates are also present as major constituents of the shells of insects, crabs, and lobsters, and the supporting tissue of plants. Carbohydrates are present as part of all cell walls, spanning from the world of microbes to mammals.

Figure 1: - Carbohydrate Synthesis and Utilization

Synthetic carbohydrate chemistry is a challenging field for organic chemists because of the structural complexity associated with carbohydrates such as several hydroxyls per monosaccharide, branched and linear oligomers and carry different kinds of functional groups. Emil Fischer has made distinctive contribution in the area of carbohydrates,
nucleotide and peptide chemistry, who solved many problems of structure of carbohydrates and basic question about the stereochemistry. Many aspects of the roles played by the carbohydrates in the storage and supply of energy in biochemical system and the mechanism of biosynthesis and biodegradation of carbohydrates were understood in 1960. Further, the isolation of biologically active compounds from microorganisms, such as antibiotics, which contain unusual saccharides motivated organic chemists to learn the art of chemical transformation of monosaccharides & oligosaccharides.

**Diversity in Carbohydrates:-**

A unique kind of diversity embedded in the carbohydrates, which allows them to form very complex branched and linear oligomers compared to other two major classes of biologically important biopolymers, proteins and nucleic acids.\(^1\)\(^2\) Let us consider the oligomers of amino acids and nucleic acids, which have only two sides available to form polymers whereas in case of carbohydrates which have more than two functional groups participating in an oligomerization. In addition, the anomeric carbon can lead to two different stereoisomers, the \(\alpha\)-glycoside and \(\beta\)-glycoside. The carbohydrate oligomers diversity can be enhanced by derivatizations of the sugars rings such as \(O\)-methylation, \(O\)-acetylation, \(O\)-sulfatation, \(O\)-phosphorylation or oxidation.

![Sugar Structure](image)

<table>
<thead>
<tr>
<th>Pentamer</th>
<th>Nucleotide</th>
<th>Amino Acid</th>
<th>Carbohydrates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homooligomeric</td>
<td>1</td>
<td>1</td>
<td>17872</td>
</tr>
<tr>
<td>Heterooligomeric</td>
<td>120</td>
<td>120</td>
<td>2144640</td>
</tr>
</tbody>
</table>

**Figure 2:** Constitutional stereoisomers of Carbohydrate, Amino acid & Nucleotide

One more thing about the diversity of carbohydrates is that many more constitutional stereoisomers can be constructed from monosaccharides than from amino acids or nucleotide from which only linear oligomers can be designed (Fig.2).\(^3\) Modern glycosciences until now is not able understand, How is the extremely large structural diversity of
oligosaccharides utilized in nature is still a daunting question. Four monomeric building blocks are sufficient for DNA and RNA to form the molecular basis of the genomic information of an organism. DNA and RNA perform transformation of genetic code and the synthesis of many different proteins structures, which are required for the organism to function. Like nucleic acid, carbohydrates do not code the biological information in single monomer unit but in many oligosaccharides, three-dimensional structures and their molecular dynamics in water concludes its function.\(^4\) May be the biodiversity in carbohydrates is very vast because of which Nature has chosen them as protective wall and to differentiate between cells of different organism or within same.

**Glycoconjugates:**

Carbohydrates present on cell surfaces are frequently attached to other non-carbohydrates natural product of different kind, which are called “glycoconjugates”. The size of glycoconjugates varies from relatively small molecules to large biopolymers. Many small glycoconjugates possess antibiotic activity are glycosylated with oligosaccharides of varying complexity. These saccharides are important for biological storage and transport, for pharmacokinetics and pharmacodynamics and influence the properties of the molecule such as solubility, efficacy, and selectivity among the other.\(^1\)

On the other hand, even more complexity arises when carbohydrates are linked to proteins and lipids producing a large number of different glycoconjugates called glycoproteins, proteoglycans, glycolipds and GPI-anchors, respectively. Complex glycoconjugates are found in dissolved form or membrane bound and as part of a nano-dimensioned, macromolecular super-system, which is part of living cell surfaces and is called the ‘glycocalyx’. The biology of a complex carbohydrate ‘super-system’ is not fully understood until today and this forms the basis for a modern research field, named ‘glycobiology’ which requires an interdisciplinary endeavour to unravel the secrets of carbohydrates-based cellular communication and to eventually utilize this new knowledge and understanding in a novel therapeutic context.

Carbohydrate content in glycosylated proteins such as enzymes, antibodies, hormone, cytokines and receptor protein varies from 1% (in collagen) to 99% (in glycogen). Why carbohydrate content varies in nature? Consider glycogen stores glucose in animal livers and
muscles. Starch and glycogen serve as energy for plants and animals, respectively. Both these polymers are readily hydrolyzed into glucose monomer, which in turn can be further degraded to liberate their stored energy. But if it is glucose that is actually needed for fuel, why must it be stored as a polymer? The reason is that 1,000 glucose molecules would exert 1,000 times the osmotic pressure of a single glycogen molecule, causing water to enter the cell that eventually causes cell burst. The carbohydrate portion of the proteins can alter their biological and physicochemical properties such as their stability against protease or the activity of enzymes, and they can direct the folding of proteins towards certain three-dimensional structure.5-11

Glycoproteins are present in blood (on the basis blood group decided), in cytosol or in subcellular organelles and they are basic constituents of all cell membranes.12 In eukaryotic cell, they are integrated into the lipid bilayer, so that the biologically important carbohydrate moieties are exposed to extracellular matrix for biological process or event.13 Membrane bound glycoconjugates form the carbohydrate coat on cell surface, which called ‘glycocalyx’ is about more than 100nm size connected to extracellular matrix. The carbohydrate coat of particular cell is characteristic for its type and for its developmental, physiological and even pathological status. In embryonic cells or in cancer cells, the glyco-coat varies significantly, compared with adult or healthy cells, respectively. Thus, certain oligosaccharides can usually be associated with degenerative cell growth and used in cancer diagnostics as so-called tumor-associated antigens.14-19

Glycoproteins may contain one or several oligosaccharide side chains and most commonly three chemical linkages found in glycoproteins are 1) N-glycosidic (An aspargine of protein attached to N-acetyl glucosamine), 2) O-glycosidic (mostly serine and threonine via –OH side chain) and 3) via ethanolamine phosphate (anchors protein in cell membranes).

Figure 3:- Glycosidic linkages Generally Observed in Glycoproteins
Mucin or O-Glycan

Mucin-type glycans are the oligosaccharide components of glycoproteins initially found in mucus. Generally they are in the form of membrane-associated or secreted in gel form. Mucins form a major part of the protective biofilm on the surface of epithelial cells, where they provide a barrier to particulate matter bind microorganisms. In mucin type of glycoproteins mostly the serine and threonine residue of protein are linked through O-linkage of side chain hydroxyl and with different chain lengths leading to significant heterogeneity of these molecules. A characteristic feature of all mucins is the linkage of sugars portion to the protein backbone, which is always a α-O-glycosidic bond to N-acetyl-galactosamine (GalNAc). There is no common core of oligosaccharide present in O-glycoprotein as in case of N-glycans where a pentasaccharidic unit is common to all.

Glycoconjugates consist of very large diverse family of O-glycan. Apart from the above, there are several other structural patterns within O-glycan exist. Glycosylation may occur with different carbohydrates such as galactose, glucose, xylose and arabinose and even with mannose or L-fucose residue which are shown below (Fig.4).

![Glycoaminoacid Units Found in O-linked Glycoproteins](image)

**Figure 4**: Glycoaminoacid Units Found in O-linked Glycoproteins

Also O-glycosidic linkage is present in glycolipids where the hydrophobic part containing hydroxyl groups such as ceramide (Cer) are attached to hydrophilic carbohydrate moiety. Several hundred different glycosphingolipids structures are known. More complex glycosphingolipids are called gangliosides. Most gangliosides have common β-lactosyl moiety in the ceramide, the first two glycosylation steps in the biosynthesis of gangliosides are same for all members of this group.
**Enzymatic Glycosylation**

Before going to detailed study about the chemical glycosylation, it is better to briefly understand biosynthetic pathways of glycosylation work? The enzyme, which catalyzes the biosynthesis of oligosaccharides, is called ‘Leloir enzymes’ after the scientist who discovered their mechanism. They use nucleoside diphosphate or monophosphates for the stereo- and regiospecific transfer of the respective monosaccharide onto an acceptor saccharide (Fig.5).

Glycosyl transfer is facilitated by the superior leaving group properties of sugar nucleotides. The ester bond between the phosphate residue and the carbon atom in the sugar is a high-energy bond and thus transfer of the sugar residue to an acceptor hydroxyl group of another sugar or on a serine or threonine residue is energetically favored. Each glycosyltransferase is specific for both the donor sugar nucleotide and the acceptor molecule.

![Figure 5: Biosynthesis of UDP-Galactose and Enzyme Catalyzed Glycosylation in Nature](image)

Like the biosynthesis of protein guided by the genetic code, the structure of oligosaccharide is determined by the action of enzymes, and therefore oligosaccharides can be called as ‘secondary gene products’. If the glycoconjugates are synthesized in nature then why can’t it be isolated and used in medicinal chemistry and medicine. The problem is the ‘microheterogeneity’ associated with it, which arises because of the reaction conditions of specific enzymatic glycosylation and small differences in the biosynthesis of oligosaccharides. So, it is very difficult to isolate biologically important Leloir enzymes in single & pure form. Also we don’t have known universal enzyme, which will do the enzymatic glycosylation as they are very specific to every carbohydrate monomer. Here the carbohydrate chemist can play a very crucial role about the synthesis of glycoconjugates in laboratory and connect with the biology by checking its biological function in living organisms. This interconnection between the biology and carbohydrate chemistry opened new branch of chemistry called chemical glycobiology.
**O-Glycosidation**

21st century carbohydrate chemists have confronted with major challenge of synthesizing glycosides\(^{21-23}\) which deals with two main problems: 1) the regio- and stereoselective formation of glycosidic linkages for the synthesis of oligosaccharides and 2) the selective protection and deprotection of saccharide building blocks prior to and after the linkage step. Nature does all these things very selectively, without any protection-deprotection, efficiently and in an ecofriendly manner. Still the carbohydrate chemists are in search of a method, which will compete with nature. Very efficient method for oligosaccharide synthesis using robotics is not available. Many carbohydrate chemists have concentrated their research areas on the improvement in glycosylation methods and new reactions to get stereo- and regio- specific glycosidic linkage formation. The advances made in this sphere have been due to improvements made in recent years in the chemical, physical & enzymatic methods of structure analysis.

Our laboratory is involved in solving the problems of glycosylation reaction using Gold Catalysts, which will be discussed in detail later. The term glycoside here is referring normally to an O-glycoside. However, there are other glycosides such as N-, S- and C-glycosides present in nature but they are beyond scope of our work.

![Figure 6: General Terms in Glycosylation](image)

Glycosides in the carbohydrate chemistry can no longer be termed as a reducing sugar as the cyclic hemiacetal could be further functionalized at its anomeric center. The standard retro-synthetic analysis cleaves a glycoside at the glycosidic linkage into an electrophilic ‘glycosyl donor’ (glycon) synthon and a nucleophilic ‘glycosyl acceptor’ equivalent (aglycon) (Figure 6).

The aglycon part may a simple nucleophile such as methanol or ethanol, in case of methyl or ethyl glycoside respectively or it can be more complex hydroxylated natural product. When
a hydroxyl group of another monosaccharide is used to form glycoside with glycosyl donor, the product is called disaccharide and consequently glycoside, which consist of three, four or more monosaccharides unit are called tri-, tetra- and oligosaccharides respectively. Fischer glycosylation can be used for the synthesis of simple glycosides when the alcohol is not too much costly, complex and excess alcohol can be removed by evaporation after the reaction has been completed. To do the glycosylation efficiently one has to protect anomeric hydroxyl group by a better leaving group, which can be activated by a suitable catalyst and promoter, whereas the other hydroxyl groups of the sugar ring need to be protected. The beauty of nature is that it can do glycosylation in stereo- and regioselective manner without any protection of other hydroxyl group of monosaccharide by bringing both glycosyl donor and acceptor in close proximity by the use of enzymes.

![Figure 7: General Way of Glycoside Bond Formation](image)

The following are essential requirement for many glycosidation methodology 1) the derivatization of sugar into a sufficiently protected glycosyl donor equipped with a leaving group ‘LG’ at anomeric center; and 2) activation of this glycosyl donor by a suitable promoter, which activates the leaving group to allow coupling to a partially protected glycosyl acceptor leading to an glycosidic linkage (Figure 7). Now days many glycosylation methods are available, however it is difficult to predict which method is most suitable to synthesize a specific glycosidic linkage$^{24-25}$ (Figure 8). Here I want to quote words of Hans Paulsen$^1$ for this situation: “Each oligosaccharides 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 synthesis.”

Despite the availability of a variety of glycosyl donors, glycosylation methods used to date can be classified into three sub-catergories:

1) ‘Koenigs-Knorr’ type reaction using glycosyl halide
2) Trichloroacetimidate method employing ‘Glycosyl Trichloroacetimidates’, and
3) Use of stable glycoside such as Thioglycosides and n-Pentenyl Glycosides as glycosyl donors.
Figure 8: Glycosyl Donors Used in Glycosylation Reaction

Two major principal problems are frequently associated with the stereochemical outcome of glycoside synthesis. These are 1) the regiochemistry of the glycosidic linkage, which is formed and 2) the conformation of the new glycosidic bond. Regiochemistry problem can be halted with by placing the appropriate protecting group on the glycosyl acceptor, leaving only one hydroxyl group unprotected. The stereochemical course of a glycosidation procedure determines whether a β- or α-glycoside will be the product of this reaction which was found to be highly dependent on the neighboring group at C-2. Participating neighboring group at C-2 leads normally to a 1,2-trans glycoside in a stereospecific reaction, whereas glycosylation with non-participating C-2 substituent will result in the formation of both 1,2-trans as well as 1,2-cis glycosides with more or less stereoselectivity. The recent observations on the neighboring group from Demchenko\textsuperscript{26} group showed that sometimes C-3, C-4 and C-5 group can also participate and gives raise to stereoselective glycoside products. The detailed mechanism and factors affecting of formation of 1,2-trans and 1,2-cis glycoside will be discussed in the following section.
Anomeric Effect

Two stereogenic isomers are generally possible at anomeric center for any monosaccharide. They are termed as α- and β-isomers or 1,2-cis and 1,2-trans isomers. In general the equatorial substituent of cyclohexyl chair rings are most energetically favoured as compared to their axial counterparts because of steric reasons and 1,3-diaxial interactions. However, in D-pyranosides especially carbohydrate derivatives with electronegative group at anomeric center, axial isomers are often more stable than equatorial ones. The unusual preference of sterically unfavoured axial position over equatorial position at C-1 carbon has been termed as “anomeric effect”. The anomeric effect is explained by R U Leimeux on the basis of intramolecular electrostatic interaction of two dipoles next to the anomeric center (Figure 9).

The anomeric effect was discovered in the case of carbohydrates but has been found to be of general importance for molecules where two heteroatoms are bound to a tetrahedral center. So, the essential group for the appearance of an anomeric effect is -C-Y-C-X- where Y= N, O, S and X= Br, Cl, F, N, O, S. Anomeric configuration, where the two nearly perpendicular dipoles partially neutralize each other (an energetically more stable arrangement as in axial substituent) are favoured over the diastereomers where the anomeric configuration leads to intramolecular addition of the two parallel dipoles (an energetically unfavourable arrangement as in equatorial substituent). The anomeric effect is different for each case and strongly influenced by the substituent at C-2 position. When the substituent is an equatorial position as in the case of glucose and galactose, the anomeric effect is weakened, whereas the anomeric effect is enhanced in C-2 axial substituent of mannose.
The nature of group at C-1 has crucial influence for the anomeric effect, as it is directly depends upon the electronegativity. Solvents also influence the anomeric effect, increased polarity of the solvent decreases the influence of the anomeric effect on the equilibration of the two alternative conformers in solution. If the substituent at the anomeric center is clearly electropositive then, it leads to the stabilization of the anomer with the equatorially positioned anomeric group (Figure 10). This effect is not different from the anomeric effect, and hence been termed as the “reverse anomeric effect”.29-30

![Figure 10:- Reverse Anomeric Effect](image)

**Neighbouring Group Participation of the C-2 Ester Functionality**

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

**Effect of Solvent**

Solvent has also an effect on the anomeric outcome of glycosidations.31 The influence of ether and acetonitrile on the anomeric outcome of glycosylation reactions under S_N1-type
conditions that is without a participating neighboring group, has been extensively invistigated.\textsuperscript{32} Ethers such as diethyl ether or THF favor the formation of 1, 2-cis glycosides, where as 1, 2-trans glycosides are the major products of glycosylation in acetonitrile in the absence of a neighboring group at C-2 (Figure 11).

\textbf{1,2-trans Glycosidation}

1,2-trans glycoside can be obtained by using suitable glycosyl donor which is activated in presence of a which initiates departure of the anomic leaving group leaving behind a cation, which is stabilized as oxocarbenium ion. The ester group bound at C-2 will exert an anchimeric effect leading to an acyloxonium intermediate which is formed initially from the oxocarbenium ion. Nucleophilic attack on dioxolane ring at C-1 leads to trans-cleavage yielding 1, 2-trans oriented O-glycosidic linkage (Figure 12).

\textbf{Figure 12:- 1,2 trans-Glycosylation with Neighbouring Group Participation}

Sometimes we can observe formation of orthoesters when the nucleophilic attack took place at the dioxolane ring carbon instead of C-1. Orthoester formation can be main reaction when neutral or basic reaction conditions are applied. Using benzoates or pivaloates as protecting groups in C-2 strongly reduces the tendency for orthoester formation compared to that when acetyl groups are used.

\textbf{Figure 13:- 1,2 trans-Glycosylation Without Neighbouring Group Participation}
1,2-trans glycosidation product are observed in some cases which are shown below (Figure 13). When glycosyl halides are treated with insoluble silver salts and no neighboring group participation group present, we could get the 1,2-trans glycoside as major product. Solvent also play role important role when no NGP group present and polar solvent such as acetonitrile gives trans glycosidation product. Nucleophilic 2,3-glycosyl epoxide opening also gives trans glycoside. These are some cases where no NGP present and other reaction condition favours trans glycosidation.

1,2-cis Glycosidation

Synthesis of 1,2-cis glycoside is much more difficult than 1,2-trans glycosides. For this one has to choose suitable group at C-2 as a non-neighboring group such as an O-alkyl ether. This can direct an SN2 reaction at the anomeric center of β-glycosyl bromide that eventually would furnish α-glycoside. However this is not practical since β-pyranosyl halide, especially bromides are greatly destabilized by the anomeric effect. R. Lemeuix and co-workers\(^3\), showed that α-pyranosyl bromides reacted in the presence of tetraalkylammonium bromide with anion to produce the β-pyranosyl bromide in situ. The highly reactive β-pyranosyl

![Diagram](image)

**Figure 14:** 1,2-cis-Glycosylation as Major product by in situ Anomerization bromide reacts much faster than its α-analog to give the α-glycoside in large proportions in a kinetically-controlled reaction.\(^1\)\(^,\)\(^3\)\(^4\) This method is called ‘in situ anomerization’ (Figure 14). Which works well with galactose or fucose as donor, it is less effective for glucose and β-mannoside synthesis. Acceptor hydroxyl also plays important role in the proportion of α-glycoside as it decreases with lower donor activity or diminished reactivity of hydroxyl group. Also one can take advantage of “reverse anomeric effect” for the synthesis of 1,2-cis O-glycosides.\(^3\)\(^5\) Very few methods were forced to be suitable for the synthesis of glycosyl amino acid and reported methods for the synthesis O-linked glycoaminoacid are:
The Koenigs-Knorr method\textsuperscript{36-38}

In 1901 Wilhelm Koenigs and the Eduard Knorr from the University of Munich introduced a very classical method for the synthesis of 1,2-\textit{trans} glycosides using glycosyl halide as glycosyl donor. This very old method of glycosylation, generally glycosyl bromide and glycosyl chlorides are used in the presence of a halide ion acceptor (promoter) usually a silver\textsuperscript{23} or mercury salts as both insoluble Ag\textsubscript{2}O, Ag\textsubscript{2}CO\textsubscript{3} as well as soluble silver triflate (AgOTf)\textsuperscript{39} and silver perchlorate (AgClO\textsubscript{4})\textsuperscript{40} are employed. Later on Helferich introduced modification to the promoter by using mixture of mercury salts such as HgBr\textsubscript{2} and Hg(CN)\textsubscript{2}.\textsuperscript{41}

Koenigs-Knorr reaction normally leads to the formation of 1,2-\textit{trans} glycosides with participating group at the C-2 position, especially when insoluble silver salts are used as promoter. The reason for this is that silver salts provide surface for glycosidation thereby assisting the formation of the \textit{trans} glycoside by shielding the \textit{α}-face of the sugar. During the course of reaction, silver bromide formed as byproduct which is precipitated out of the reaction mixture.

Sometimes base used in combination with silver salts plays a major role in glycosylation reaction such as combination of silver trifluoromethanesulfonate (AgOTf) and 2,4,6-collidine which leads to the formation of glycosyl orthoester. When it is replaced by N,N,N',N'-tetramethylurea the course of the reaction is different and goes through 1,2-orthoester intermediate leading to 1,2-\textit{trans} glycoside as a major product.

However the reaction suffers from two disadvantages: first is the lability of glycosyl halides, with the \textit{β}-glycosyl bromide being unstable due to anomeric effect, and the second the use of heavy metals salts in the range of equimolar amounts. Sometimes mixture of 1,2-\textit{cis} and \textit{trans} glycoside products observed using glycosyl halide as donor.\textsuperscript{42-43}
The trichloroacetimidate method\textsuperscript{22,41,44-46}

R.R. Schmidt and co-workers have developed the most widely used glycosylation method in oligosaccharides synthesis by employing trichloroacetimidate as glycosyl donors, that is superior to the Koenigs-Knorr method.\textsuperscript{41} The general significance lies in their ability to act as strong glycosyl donors (armed donor) under relatively mild acid catalysis. This reaction is very simple to carry out and amount of Lewis acid varies from case to case. This may happen because of the formation of orthoester as intermediate, thus more catalyst is required in this case to isomerize orthoester to corresponding direct glycoside. For the synthesis of glycosyl donor, one has to selectively deprotect the anomeric-protecting group and base treatment (K\textsubscript{2}CO\textsubscript{3}, NaH or DBU) with trichloroacetonitrile to form glycosyl trichloroacetimidate.

![Chemical structure](image)

Glycosyl trichloroacetimidates give very good yields in small as well as large scales. Frequently glycosyl trichloroacetimidate are more stable than respective glycosyl bromides and can be stored at lower temperatures for many months. Ether protected trichloroacetimidate are more reactive than their ester protected counterparts, as ether groups stabilize the oxonium ion, which occurs as intermediate of the glycosylation reaction. Reactive donors are handled at lower temperature because the high reactivity leads to side reaction or even decomposition of the glycosyl donor before the glycosylation happens. When the acceptor alcohol is very unreactive, the donor may rearrange to the corresponding glycosyl trichloroacetamide, which is reported to have no donor activity leading to lower glycoside yields. In such cases Inverse glycosylation procedure will be used to improve the yields and stereocontrol, where the glycosyl acceptor and the catalyst are first dissolved together and the glycosyl donor is then added.

Neighboring group participation effect of C-2 protecting group in trichloroacetimidate method is dominating the anomeric stereocontrol during glycosylation, giving rise to 1,2-trans glycosides. When non-participating protecting groups are selected, $S_{N}2$-type reaction can be carried out by use of non-polar solvents, low reaction temperature, and weak Lewis acid catalyst (BF\textsubscript{3}.Et\textsubscript{2}O). Strong acid catalyst (TMSOTf, TfOH), higher temperature and more
polar solvents support the formation of the thermodynamically more stable glycosylation products, which are the α-manno and β-gluco type. One can perform one-pot tri- or oligosaccharide synthesis by employing different glycosyl donors with tuned donor activities to allow multiple glycosylation in a single pot.

**Thioglycosides**

Thioglycosides as glycosyl donors was first introduced by Lonn and coworkers in 1980’s wherein, the promoter activates the sulphur of thioglycosides producing an intermediate sulfonium ion which in turn forms oxocarbenium ion and subsequently, trapped with the glycosyl acceptor to offer glycosides. Promoters used for such reaction are MeOTf, DMTST, Iodinium dicollidine perchlorate, and NIS-TfOH. The advantages of using thioglycosides are their stability under a wide range of reaction conditions. Additionally, thioglycosides act as temporary protecting groups at the anomeric position that helps to synthesize both glycosyl donor as well as glycosyl acceptor for the synthesis of oligosaccharides. But the unpleasant odour of thiols and its effect on health limits use of them as glycosyl donors.

**n-Pentenyl glycosides**

Fraser-Reid and coworkers introduced pentenyl glycoside as stable glycosyl donor in which the pentenyl group is activated by an electrophilic addition of the iodinium ion to double bond of the glycosyl donor followed by an intramolecular displacement through an oxygen atom present at the anomeric center and the simultaneous removal of cyclized product to form an oxocarbenium ion which is then trapped by glycosyl acceptor. The s used for these reactions are NIS alone or NIS/Et₃SiOTf, NIS/TfOH and NIS/Yb(OTf)₃. Later pentenyl 1,2-orthoesters was also employed for the synthesis of oligosaccharides by Fraser-Reid. But the major limitation is the excess use of N-iodosuccinimide (NIS).
The potential of the n-peteny1 glycoside methodology is further increased by the observation that acyl and ether protected n-pentenyl glycosides displays different reactivities. This finding leads to new concept in glycosylation known as the armed-disarmed glycosylation.51

1,2-Orthoesters55-63

Kochetkov and coworkers systematically studied 1,2-orthoester and applied for the stereoselective synthesis of 1,2-trans glycosides. In 1964 they published first paper on glycoside synthesis using 1,2-methyl orthoester as glycosyl donor and cholesterol as acceptor55 and they have also studied leaving ability of different orthoesters such as ethyl, isopropyl, tert-butyl and cyano 1,2-orthoester. Taking advantage from pentenyl glycoside as glycosyl donor Fraser-Reid and coworkers introduced the pentenyl 1,2-orthoesters as glycosyl donor in the presence of NIS/Yb(OTf)3 to get 1,2-trans glycosides.64-66

When the orthoester is reacted in the presence of suitable catalyst, there are two possibilities. One is the formation of trans orthoester or the direct glycoside which depends upon the ratio of catalyst to orthoester, i.e the critical ratio.56 Glycosylation predominates above the critical ratio, and trans- esterification below. At high catalyst concentration (H+A-) its anion mask the positive charge of the acyloxonium, thus hindering nucleophilic attack of glycosyl acceptor which then takes place at the glycoside C-1. For a reaction without addition of co-catalyst, dichloromethane as solvent and addition catalyst of HgBr[sub2] minor amount (0.001moles) results in formation of transorthoester product. On the other hand use of polar solvent nitromethane and high catalyst ratio of HgBr[sub2] (0.008-0.1 moles) gives
trans glycoside as major product. In presence of co-catalyst such as p-toluenesulfonic acid (TsOH, 0.00025 mole), HgBr₂ (0.001-0.008 mole) per mole of orthoester & nitromethane as solvent gives trans glycoside whereas less than above ratio gives either mixture of trans orthoester & trans glycoside or trans orthoester as major product. At low concentration direct attack and fresh orthoester formation becomes more likely. However, at higher catalyst concentration the formation of other by products such as the acetate of glycosyl acceptor and dialkyl ether becomes very pronounced cis and trans glycosides can also result. Even solvent-catalyst combination has characteristic critical value. In polar solvents, like nitromethane, HgCl₂ and HgBr₂ are examples of suitable catalysts, whereas in nonpolar solvents like chlorobenzene and dichloromethane, the perchlorates of pyridine and lutidine represent better choice. Actually the last combination gives best yields. The orthoester method has been successfully applied to numerous glycoside syntheses.

With this brief introduction to O-glycoside synthesis we will discuss the present work on the synthesis of amino acid glycoconjugates using Gold Catalyst and Propargyl 1,2-orthoesters as glycosyl donor and hydroxyl group containing amino acid such as serine, threonine etc. Also the interesting result we got when the t-Boc protected amino acid reacted with Propargyl 1,2-orthoester in presence of Gold catalyst.

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Chapter 1: Present Work

Carbohydrates are easily available from natural resources, which are one of the starting building blocks in current research work. Availability of carbohydrates in bulk quantity as well as low price makes carbohydrates as very good starting material to carry out research work in carbohydrate field. As carbohydrates are available from nature, they are embedded with chirality, because nature only synthesizing one isomer of any biological important biomolecule such as in case of amino acid, carbohydrates, alkaloids and other natural products.\textsuperscript{67-69} Apart from the configuration at C-1 carbon, stereochemistry of the all chiral centers in carbohydrates are fixed, which is very good source of chirality. Selective protection and deprotection strategies are heart of synthetic carbohydrate chemistry. Many research groups are involved in control stereochemistry and regioselectivity of the glycosidic bond of carbohydrates. Controlling only single carbon stereochemistry is very difficult; one could imagine what will be the situation if one has to controlled stereochemistry at rest of carbon, which will much more difficult. But nature can do this entire thing very easily with taking care of stereochemistry at each center and ecofriendly by taking the help of enzymes. Isolation of most of the biological important complex carbohydrates is difficult as they are present in small quantities as well as in micro-heterogeneous form. So it is desirable to have synthetic route, which will give access to synthesize these materials in large quantities and study its biological properties.

Biological importance of the glycosylated amino acids in glycoprotein, antifreeze compounds\textsuperscript{70-74} & in glycopoly peptide chemistry\textsuperscript{75-76} makes synthesis of glycosylated amino acids one of the challenging research areas for synthetic chemists. We thought to use gold catalyzed glycosylation methodology developed in our laboratory using gold salts as Lewis acid catalyst to attach hydroxyl group containing amino acid to carbohydrates. For this we have chosen the side chain hydroxyl group containing amino acids as other starting biomolecule of our research work, both these are available from Nature very easily and commercially very cheap. There are different methods for attachment of amino acid to carbohydrates, which we discussed in introduction part of this chapter, but each method has its own advantages and disadvantages. So carbohydrate community always associated with solving the major problem of stereo- and regio- selectivity in glycosylation using
different leaving group varying Lewis acid catalyst combination & by different protecting group on carbohydrates.

To begin our current work, I would like to give brief introduction about how we arrive at point where one could do glycosylation by using gold salts. Gold is known for very long time as precious metal and has unique properties (malleable, corrosion resistance, excellent electrical conductance & biologically not hazardous), which are well documented. Such as very classical example of nanotechnology in ancient days is the Lycurgus Cup 1400 year old was coloured with colloidal gold and silver. It was also used by Ethruscan peoples in seventh century BC to secure substitute teeth. Michael Faraday’s 1857 report conjectured that gold could exist in solution as finely ‘divided metallic state’ rather than as an oxide, and exactly 100 years ago the Nobel prize winner Ernest Rutherford published date on ‘gold foil’ experiment proof of the existence of the nucleus and hence structure of the atom. Gold has become extremely important in science and technology because of the pioneering work done by Faraday and Rutherford. In 1960s firstly Bell Laboratories developed the first gold-bonded microchips followed by NASAs use of gold to protect sensitive instrument from radiation in space. These applications highlight bulk properties of gold. In 1970s Geoff Bond and colleagues published breakthrough describing gold having some catalytic activity n certain reactions. Up to 1980s researchers showed both theoretically and experimentally that gold can acts as superior catalyst in a range of reaction including acetylene hydrochlorination and CO oxidation. Gold is active in the form of its halide salts or complex. Gold is used in various applications such as monetary exchange, investment, jewelary, medicine, food and drinks, industry, electronics etc. Most often it occurs as a native metal, typically metal solid solution with silver i.e. gold silver alloy.

Recently nanotechnology has been benefitted because of gold’s unique properties.77-79 Also numerous applications of gold catalysis has been shown in field of key reaction in total synthesis and synthesis of diverse library of molecule for high-throughput screening.80-82 Organic chemists believe that as gold is precious metal and its use in organic synthesis may be more expensive. But if one considers the organometallic complexes of Ru, Pt, Ir and Rh are actually more expensive than gold complexes. So gold compounds can be used in organic synthesis by taking advantage of catalytic activity of gold complex.
O-glycoconjugates plays important role in various biological processes. As evident from introduction part, which we have discussed problems associated with the synthesis and isolation of single & pure form of glycoconjugates. This led to us think about new method for the synthesis of O-linked glycoconjugates.

Last five year’s gold catalyzed glycosidations have gained attention was foremost goal is the glycosidation. While synthesizing the diverse library of molecules for biological activity from our group, propargyl group was found to behave as leaving group in the presence of AuCl₃. Generally Diels-Alder reaction is used for diverse library of compounds, when the 1,2:5,6-bis-O-(1-methylethyldiene)-3-C-(5-methyl-2-furanyl)-3-O-prop-2-ynyl-allofuranose 1 is reacted to get Diels-Alder product between the propargyl and the furan substituent at C-3 in presence of 3 mole% of AuCl₃ in acetonitrile as solvent. However, the required Diels-Alder product 2 along with the 5 % of propargyl ether hydrolyzed product 3 at C-3 carbon were observed (Figure 15).⁸³ To check leaving group ability of propargyl group, 3-O-prop-2-ynyl-4,6-di-O-benzyl-1,2-glucal 4 was treated with methanol in the presence of 3 mole % of AuCl₃ in acetonitrile and found an unexpected methyl 2,3-dideoxy glucoside 5 (Scheme 15).⁸⁴-⁸⁵ The initial coordination of gold with the triple bond of alkyne assist the cleavage of propargyloxy moiety and simultaneous attack of alcohols from α-face lead to stereoselective formation of α-glycoside. Further AuCl₃ mediated activation of propargyloxy moiety was utilized for the synthesis of C-2 methylene glycoside 7 using per-O-benzylated C-2 propargyloxy methyl glycal 6 as glycosyl donors.⁸⁵

Deprotection of propargyl ether in carbohydrates was already reported by different groups using samarium iodide and water,⁸⁶ dicobaltoctacarbonyl followed by treatment with trifluoroactic acid,⁸⁷ titanium and metal catalyzed isomerization.⁸⁸ Unfortunately they have never explored these methods for glycosidation and oligosaccharide synthesis. Beyond that, propargyl glycosides can used in Husigen’s 1, 3-dipolar azide-alkyne cycloaddition (Click Chemistry) to synthesize bioconjugates or surface modification of polymer or nanoparticle.⁸⁹-⁹⁰

For the first time, propargyl glycosides were activated in the presence of AuCl₃ for the synthesis of glycosides and disaccharides. In this approach, initial treatment of armed prop-2-ynyl 2,3,4,6-tetra-O-benzyl-α:β-D-glucopyranosides 8 with water in presence of 3 mole %
AuCl₃ in acetonitrile for 12 h at room temperature gave a mixture of per-O-benzylated lactols 9 (Figure 15). Encouraging results prompted to use other nucleophilic alcohols in place of water to facilitate transglycosylation for the synthesis of glycosides and disaccharides. The glycosylation performed between the propargyl glycoside 8 and menthol 10 in the presence of 3 mole % AuCl₃/CH₃CN/60°C/6 h resulted into a mixture of α,β-
menthyl glucosides 11 in 68 % yield.91 The glycosylation was failed when other alkyne activators namely PtCl₂, Cu(OAc)₂, Co₂(CO)₈ and RuCl₃ catalyst were employed. Further, glycosylation failed to give 1,2-trans glycosides, when the glycosylation was attempted with disarmed C-2 ester functionalized propargyl per-O-benzoylated or per-O-acetylated glucosides and an aglycon in the presence of 3 mole % AuCl₃/CH₃CN/60°C. This experimental study confirms that AuCl₃ will work well with armed glycosides and thus was applied for other monosaccharides such as mannose, galactose and glucose with various aglycons to get corresponding glycosides or disaccharides respectively.51 In case of glucoside and galactoside we get mixture of α,β-glycosides were observed. Whereas mannosyl donor provided the α-isomer due to strong anomeric effect as well as bulky substituent at C-2 position.

The common advantage of propargyl glycosides are 1) stable towards the environmental conditions and protecting group manipulations, 2) glycosyl donor which required 3 mole % of AuCl₃ for the activation of propargyloxy group, 3) easily accessible and 4) widely useful in bioconjugation or functionalization via copper catalyzed cycloaddition reaction with azide derived from peptides, lipids, proteins and polymers.

Unfortunately, a mixture of products formed during glycosylation, when a propargyl glucoside and galactoside were used in presence of AuCl₃ in acetonitrile at higher temperature. In order to get stereoselective 1,2-trans glycosylation, propargyl 1,2-orthoester can be used as glycosyl donor in which the C-2 ester group will be participated to stabilize the oxonium ion and nucleophilic attack will give rise to a 1,2-trans glycoside. Already orthoesters are explored to give stereoselective 1,2-trans glycoside product as we discussed in introductory part by Kochetkov & Bert-Fraser-Reid groups, who showed its

Scheme 1:- Application of Gold Complexes for Stereoselective 1,2-trans Glycoside Formation

application to 1,2-trans glycoside synthesis using different orthoesters. Gold Catalysis repature was found to be suitable for the synthesis of 1,2-trans glycosides from orthoester.
Accordingly propargyl 1,2-orthoester 12a are used for synthesis of 1,2-trans glycosides and disaccharides 14 (Scheme 1).92-93 Controlled study on glycosylation has been done using different Lewis catalyst in combination with Brønsted acid & base, which confirms that gold salts are required to get glycosidation reaction happen; addition of bases such as triethylamine or pyridine doesn’t give any glycosidic product due to quenching of acidic reaction medium.

![Glycosylated Proteins](image1)

**Figure : Glycoproteins and Importance of Glycoaminoacid Derivatives in Glycopeptide Synthesis**

Thus, we thought of applying glycosylation methodology for the synthesis of glycosylated amino acid glycoconjugates, which are important class of building blocks for glycopolypeptide synthesis and solid phase glycopeptide synthesis. For this we have chosen side chain hydroxyl group containing amino acids such as serine or threonine in place of simple alcohol or carbohydrate to get glycosylated amino acid glycoconjugates. Synthesis starts with propargyl 1,2-Orthoester, which has been synthesized from per-O-benzyolated monosaccharide such as glucose, galactose and mannose in two steps.

![Synthesis Diagram](image2)

We have chosen benzoyl as protecting group for carbohydrates because it is easily available in comparison to acetic anhydride which comes under narcotic drug act. Benzoylation of all the monosaccharides used in present work was carried out by using benzoyl chloride and pyridine as the reaction solvent. The treatment of per-O-benzyolated glucose with 33% HBr
in AcOH formed 2,3,4,6-tetra-O-benzoyl-α-D-glucopyranosyl bromide that was subsequently reacted with propargyl alcohol, 2,6-lutidine and a catalytic amount of TBAI in dichloromethane at 65°C for 2 days to give propargyl 1,2-orthoester 12a. In the $^1$H NMR spectrum of compound 12a, resonances at $\delta_H$ 2.40 ppm as triplet and $\delta_H$ 3.99 ppm as a doublet clearly indicate the presence of propargyl group and a doublet at $\delta_H$ 6.11 ppm ($J=5.31$ Hz) which is a characteristic for β-configured anomeric proton of orthoester were noticed. Rest of signals in spectrum were in complete agreement with the assigned structure 12a. In addition, $^{13}$C NMR spectrum revealed the characteristic signals corresponding to α-anomeric carbon and the quaternary carbon at δ 97.7 (C1) and 121.1 ppm respectively while rest of the other signals were in accordance to the assigned structure 3,4,6-tri-O-benzoyl-α-D-glucopyranose-1,2(prop-2-ynyl orthobenzoate) 12a. The structure was further supported by mass spectroscopic analysis (Mol.Wt.Calcd. 634.62, Found: 656.21(M$^+$+Na)).

Only a limited number of approaches are available for the attachment of a serine/threonine.$^{94-104}$ For example, one of the earliest and widely used methods couples the CbzSer(OH)Bn and an acetobromo sugar by means of environmentally detrimental mercury salts. A notable and significant improvement was reported by Cameron’s group$^{94}$ taking advantage of reaction conditions developed by Field et al.$^{106}$ In this premise, methods that enable preparation of amino acid glycosides from stable glycosyl donors using catalytic and eco-friendly reagents are essential.$^{105}$

In continuation of the programme on gold catalyzed glycosylations, we got interested in the exploitation of propargyl 1,2-orthoesters$^{57,92-93}$ for the synthesis of amino acid glycoconjugates. To begin our investigation, initially propargyl 1,2-orthoesters, Fmoc- and Cbz-protected serine/threonine were considered. Selective protection of amino acid was done by following literature procedure$^{106-107}$ to get desired hydroxyl containing amino acid

![Scheme 2: Gold catalyzed Glycosidation for Glycoaminoacid derivatives](image)
derivative for glycosidation reaction. Accordingly, per-O-benzyolated glucose 1,2-O-orthoester 12a was allowed to react with serine derived aglycon. Among various naturally occurring amino acids, hydroxyl containing serine and threonine and their Fmoc-, Cbz- and Boc-protected derivatives are the most widely used in peptide synthesis. Thus, CbzSer(OH)Bn 13a reacted with 3,4,6-tri-O-benzoyl-α-D-glucopyranose-1,2(prop-2-ynyl orthobenzoate) 12a in the presence of 7 mol% of AuBr3 as catalyst and 4 Å MS powder to make sure anhydrous medium in dry dichloromethane at room temperature for 30 min to afford Benzyl N-(benzyloxycarbonyl)-O-(2,3,4,6-tetra-O-benzoyl-b-D-glucopyranosyl)-L-serinate 15a (Scheme 2).108

The literature indicated that several attempts have been made to synthesize amino acid glycosides that included use of toxic Hg salts, very extensive and laborious purification protocols, which led to a poor overall yield of the resulting glycoconjugate.94,97,109 However, AuBr3 catalyzed glycosylation resulted in the isolation of Benzyl N-(benzyloxycarbonyl)-O-(2,3,4,6-tetra-O-benzoyl-b-D-glucopyranosyl)-L-serinate 15a in 76% yield. Simple gravity flow and conventional silica gel column chromatography would be sufficient to separate propargyl 2,3,4,6-tetra-O-benzoyl-β-D-glucopyranoside (sole byproduct)92-93 from the required serine glucoside 15a. 1,2-trans Glycosidic linkage was confirmed by NMR spectral studies wherein the anomeric proton was noticed at δH 4.78 ppm (d, 1H, J = 7.6 Hz) and the anomeric carbon was observed at the δc 101.3 ppm.108

We then continued our synthesis endeavour with 1,2-orthoester 12a that was allowed to react with FmocThr(OH)OMe 13b to give the threoninyl glucoside 15b in good yield.
Furthermore, CbzThr(OH)Bn 13c reacted with the glucosyl orthoester donor 12a resulting in the formation of threoninyl glucoside 15c (Scheme 3). It is interesting to note that the N-

<table>
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<tr>
<th>Propargyl 1,2-orthoesters</th>
<th>Glycosyl acceptors</th>
<th>1,2-trans glycoaminoacid</th>
<th>Time &amp; Yield</th>
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<tr>
<td></td>
<td></td>
<td></td>
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Reagents and Conditions: AuBr₃ (10 mol %)/CH₂Cl₂/4 Å MS powder/rt, 30 min
Cbz- or N-Fmoc-groups and benzyl/methyl esters were intact during the gold catalyzed glycosylation.\textsuperscript{108}

Versatility of the glycosylation methodology with gold reagents was further extended to the other glycosyl donors to get glycoamino acids. For example, galactosyl (12b), mannosyl (12c) and lactosyl (12d) 1,2-orthoesters were allowed to react with serine and threonine derived aglycons (13a–13d) to obtain corresponding galactosides (16a–16c), mannosides (17a–17c) and lactosides (18a–18c) respectively in good yields (Table 1). In all the cases, we identified formation of 1,2-\textit{trans} selective glycosides only.\textsuperscript{108}

Glycosylated amino acids are very useful in the synthesis of carbohydrate modified peptides. These glycopeptides shows antifreeze properties\textsuperscript{73-74} and carbohydrate moiety gives extra stability to helical conformation of peptide backbone.\textsuperscript{110} Only few methods are reported for synthesis of glycoaminoacid derivatives, which can be used in solid peptide phase synthesis. Here, we are reporting gold catalyzed method for synthesis of glycoaminoacid. For this, we synthesized amino acid derivatives, which can be selectively deprotected to get amino or acid group using suitable condition. This kind of selectively

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**Scheme 4:** Orthogonal Deprotection of Glycoaminoacid for Solid Phase Peptide Synthesis
deprotected compounds are useful for amide coupling or to attach resin in case of solid phase synthesis. Amino and the acid groups are protected as Fmoc and allyl respectively, so that they can be orthogonally deprotected.

Synthesis of glycopeptides demands the use of differentially and orthogonally protected glyco-serine/threonine conjugates. In order to synthesize a free carboxylic acid or amine, aglycon FmocSer(OH)COOAllyl ester was designed and reacted with the glucosyl propargyl 1,2-orthoester to obtain the desired amino acid glycoside in 70%. Orthogonal deprotection of amino and acid group was carried out by Rh-mediated isomerization of the double bond using Wilkinson's catalyst followed by hydrolysis led to the amino acid glycoside as a free carboxylic acid in 85% yield whereas the deprotection of 9-fluorenylethoxycarbonyl (Fmoc-) group by the use of diethylamine afforded the free amine (Scheme 4).

tert-Butoxy carbamates (t-Boc) of serine/threonine are also frequently used in the glycopeptide synthesis. Thus a model gold catalyzed glycosylation was performed between 1,2-orthoester and BocSer(OH)OMe using standard condition. The required amino acid glucoside was not observed and instead, surprisingly an orthoester A was obtained in 27% yield; the major compound being a O-linked glucosyl carbamate.

The structures of orthoester A and carbamate were assigned after thorough characterization using $^1$H & $^{13}$C NMR and LC-MS spectral analysis (Scheme 5). For example,
anomic proton of compound A was noticed at δ_H 6.01 ppm as a doublet (J = 5.2 Hz) along with anomeric and quaternary carbons at δ_C 97.6 and 121.1 ppm respectively. Structural integrity of compound 24 was confirmed as the 1,2-trans O-carbamate, since the anomeric proton was identified in a more deshielded region at δ_C 6.06 ppm as a doublet (J = 8.4 Hz) and concurrently the anomeric carbon was noticed at δ_C 93.5 ppm.117 This unexpected set back was attributed to acidic reaction conditions and hence it has been envisioned that strong Lewis and Brønsted acids would facilitate the glycoside formation.93 But the presence of the acid labile t-Boc group posed a serious hurdle in this direction.

Activation of propargyl orthoesters led to the formation of oxocarbenium ion which is in equilibrium with dioxolenium ion intermediate. These intermediates were trapped with protected amino acid derivatives in different ways. Such as if the aglycon amino acid was protected with acid compatible group the gives β-O-glycoaminoacid, direct attack of t-Boc protected amino acid on dioxolenium ion gives transorthoester product A in case of low Lewis acid catalyst addition, whereas if catalyst contains both Lewis and Brønsted acid then
preferentially 1,2-trans carbamate linked glycoaminoacid derivatives formation was observed. Possible mechanism for formation of high yielding carbamate linked glycoside are direct trapping of oxocarbenium ion by carbonyl group of t-Boc and then cleavage of t-Boc into isobutylene group led to formation of carbamate linked glycoside 24. Other possibility of formation of glucosyl carbamate was the reaction conditions that facilitated the cleavage of the tertiary butyl group thereby producing a reactive carbamic acid. Usually carbamic acids liberate carbon dioxide to afford corresponding amines; however, in this situation, carbamic acid trapped the in situ generated oxocarbenium ion from to give 12a.

This peculiar observation was further corroborated, as the t-Boc protected phenylalanine has also reacted with the glycosyl donor 12a to give glucosyl carbamate 26a in 65% yield. In previous case (Scheme 5), there was competition between the aglycon because of which mixture of product formation was observed to overcome this aglycon 25a was designed and reacted with 12a. Less Brønsted acidic and alkynophilic AuCl₃ did not improve the performance of the reaction as the release of HCl will not be facile in an aprotic medium; nevertheless, near quantitative yield of compound 26a was obtained in 2 h with a catalytic amount of HAuCl₄·3H₂O was used (Scheme 6). Similar cleavage of the t-butyl group and intramolecular cyclization was observed, when N-Boc protected alkynylamines were treated with gold reagents to give alkylidene 2-oxazolidinones.

![Scheme 6: Optimization of Glycosyl Carbamate formation using different Gold Complexes](image)

The unusual formation of the carbamate linkage needs a special mention. Glycosyl carbamates are important because of their stability to alkaline conditions and some of them are reported to act as glycosyl donors. In addition, glycosyl carbamates are studied as dopamine prodrugs (Parkinson’s), nitric oxide (NO) donors for biomedical research and surfactants. Recently, carbamate linkages were explored for studying carbohydrate-protein interactions and also for ligation. Glycosyl carbamates
can be prepared by a reaction of corresponding lactol and an isocyanate\textsuperscript{128} in the presence of a base\textsuperscript{120} or from glycosyl carbonates.\textsuperscript{129} TMSOTf catalyzed reaction of glycosyl trichloroacetimidates perhaps gives easy access but in moderate to good yields depending on the type of substrate.\textsuperscript{117} Recently Markus Oberthür and coworker showed the synthesis of glycosyl carbamate under non-acid conditions.\textsuperscript{130}

Thus, methods that enable easy synthesis of glycosyl carbamates without the use of toxic isocyanates from stable glycosyl donors are invaluable. The foregoing discussion clearly highlights the merit of HAuCl\textsubscript{4}.3H\textsubscript{2}O catalyzed synthesis of glucosyl carbamate from stable propargyl 1,2-orthoester as a glycosyl donor. This reaction works very well when the t-Boc protected primary amine were used whereas t-Boc protected secondary or tertiary amines could not gives desired glycosyl carbamates. The generality of the methodology has been verified by using a panel of t-Boc protected amines and propargyl 1,2-orthoesters. t-Boc protected amino compounds of alicyclic (25b), aliphatic (25c, 25d) and aromatic (25e,25f) reacted with glucose 1,2-orthoester 12a to afford their respective carbamates 26b–26f (Table 2). Furthermore, galactosyl- (12b), mannosyl- (12c) and lactosyl- (12d) derived propargyl 1,2-orthoesters also participated successfully in the glycosylation reaction to afford the corresponding 1,2-trans glycosides 27a–b, 28a–b and 29a–b in near quantitative yields (Table 2).
Reagents and Conditions: HAuCl₄ (7 mol %)/CH₂Cl₂/4 Å MS powder/rt, 30 min

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<th>1,2-trans Glycosyl carbamate</th>
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| 12b                      | ![Image](image1) | ![Image](image2)               | 97 %  |
|                         | 25a               | ![Image](image3)               | 98 %  |

| 12c                      | 25b               | ![Image](image4)               | 95 %  |

| 13d                      | 25b               | ![Image](image5)               | 96 %  |
In conclusion, a new method for the synthesis of aminoacid glycoconjugates was described which is more applicable to Cbz- and Fmoc-protected amino acid Me/benzyl esters. t-Boc protected serine derivative was found to give serine 1,2-orthoester in poor yield and the major compound was found to be the glycosyl carbamate. Optimized reaction conditions showed HAuCl₄·3H₂O gives glycosyl carbamates in excellent yields. The generality of this methodology was evaluated using various glycosyl donors, aglycons and building blocks. Gold salts are found to be of immense benefit to synthesize diverse glycosidic linkages and glycoaminoacid derivatives. Transformation of these glycoaminoacid derivatives to polymerizable monomers and their application to glycopolypeptide synthesis can be envisioned.

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General Procedure for Propargyl 1,2-Orthoester:

In 500mL round bottom flask α-D-Glucose (10 g, 0.056mol) and DMAP (0.05g, 0.4mmol) were dissolved in pyridine (125mL) and to this solution benzoyl chloride (100mL) was added slowly added using dropping funnel. The resultant reaction mixture was stirred for 24 h at room temperature and then evaporated to dryness. The solid residue was dissolved in CH₂Cl₂ and water was carefully added with cooling and vigorous stirring to decompose the excess of benzyol chloride. Then solvent was removed on rota vap to give crude pentabenzoate glucose (35.0 g, 90 % yield). The crude per-O-benzyolated glucose was dissolved in CH₂Cl₂ and acetic anhydride was added to maintain anhydrous conditions. The reaction mixture was cooled to 0°C for 1 h. Then temperature of reaction mixture was raised to room temperature and stirred for 12 h. The reaction mixture was then diluted with cold CH₂Cl₂ and cold water. After this organic layer was washed 3-4 times with cold water and then with saturated NaHCO₃ to remove acetic acid. Organic layer was kept on anhydrous Na₂SO₄ and then solvent was evaporated on rotavap to get the crude glycosyl bromide 2,3,4,6-tetra-O-benzoyl-α-D-glucopyranosyl bromide (32.3 g, 98 % yield). To a solution of per-benzoylated glucosyl bromide (20 g, 30.3mmol) in anhydrous CH₂Cl₂ (100mL) was added 2,6-lutidine (15mL), propargyl alcohol (9mL, 15.2mmol) followed by a catalytic amount of tetra-n-butylammonium iodide (50mg) at room temperature under argon atmosphere. Then, the reaction mixture was refluxed at 65°C for 48 h, diluted with aqueous oxalic acid solution and extracted with CH₂Cl₂ (2X100). A combined organic layer was washed with water, brine, dried over anhydrous sodium sulfate and concentrated in vacuo. The resulting brownish black residue was purified by silica gel column chromatography using petroleum ether-ethyl acetate as the mobile phase to afford corresponding 3,4,6-tri-O-benzoyl-a-D-glucopyranose-1,2-(pro-2-ynyl orthobenzoate) 12a (16.3g, 85%) as white solid. Exactly similar procedure was used for synthesis of propargyl 1,2-orthoester of D-galactose, D-mannose and Lactose

General procedure for the Gold Catalyzed Glycosylations:
To a solution of 1,2-orthoester (0.1 mmol), glycosyl acceptor (0.11 mmol) and activated 4Å molecular sieves powder (50 mg) in anhydrous CH₂Cl₂ (5 mL) was added AuBr₃ (7 mol%) under argon atmosphere at room temperature. The reaction mixture was stirred at room temperature for the specified time and the reaction mixture was filtered and the filtrate was concentrated in vacuo. The resulting residue was purified by silica gel column chromatography using ethyl acetate-petroleum ether as the mobile phase.

**General procedure for the synthesis of glycosyl carbamates from propargyl 1,2-orthoesters:**

To a solution of glycosyl donor (0.1 mmole) and t-Boc protected amine (0.1 mmole) in anhydrous CH₂Cl₂ (5 mL) was added 4 Å MS powder (50 mg 0.1 mmol-1) and 5 mol% of HAuCl₄·3H₂O under argon atmosphere at room temperature. The resulting mixture was stirred till the completion of the reaction as judged by TLC analysis (2 h). 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.

**Benzyl N-(benzyloxycarbonyl)-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-L-serinate (15a):**

\[ \{ \alpha \}^{25}_{D} +14.0^{o} (c 1.0, \text{CHCl}_3); ^1H \text{NMR} (200.13 \text{ MHz, CDCl}_3): \delta 3.91(\text{dd}, J = 3.4, 10.3 \text{ Hz, 1H}), 4.01(\text{ddd}, J = 3.3, 4.9, 8.3 \text{ Hz, 1H}), 4.32-4.56(\text{m, 3H}), 4.61(\text{dd}, J = 3.2, 12.2 \text{ Hz, 1H}), 4.78(\text{d}, J = 7.6 \text{ Hz, 1H}), 4.99(\text{dd}, J = 12.3, 19.4 \text{ Hz, 2H}), 5.13(\text{dd}, J = 12.3, 14.3 \text{ Hz, 2H}), 5.45(\text{dd}, J = 7.8, 9.5 \text{ Hz, 1H}), 5.61(\text{m, 2H}), 5.86(\text{t, J = 9.6 Hz, 1H}), 7.20-7.58(\text{m, 22H}), 7.78-8.05(\text{m, 8H}); ^13C \text{NMR} (50.32 \text{ MHz, CDCl}_3): \delta 54.2, 62.9, 66.9, 67.4, 69.3, 69.4, 71.7, 72.2, 72.5, 101.3, 128.0-129.8, 133.1, 133.2, 133.3, 133.4, 135.2, 136.2, 155.8, 165.1, 165.1, 165.7, 166.1, 169.2; \text{Anal. calcd for } C_{52}H_{43}NO_{14}: C, 68.79; H, 5.00; N, 1.54; \text{found: C, 67.87; H, 5.21; N, 1.66; MS (ESI) calcd for } C_{52}H_{43}NO_{14} [M+Na]^+, 930.902; \text{found, 930.671.}

**Methyl N-(9-Fluorenlymethoxycarbonyl)-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-L-threoninate (15b):**

\[ \{ \alpha \}^{25}_{D} +12.0^{o}(c 1.0, \text{CHCl}_3); ^1H \text{NMR} (200.13 \text{ MHz, CDCl}_3): \delta 1.14(\text{d,} \cdots \]
3H, \(J = 6.3\) Hz), 3.71(s, 3H), 4.05-4.58(m, 7H), 4.65(dd, \(J = 3.3, 12.2\) Hz, 1H), 4.87(d, \(J = 7.7\) Hz, 1H), 5.48(dd, \(J = 8.0, 9.7\) Hz, 1H), 5.69(m, 2H), 5.91(t, \(J = 9.7\) Hz, 1H), 7.20-7.65(m, 20H), 7.72-8.06(m, 8H); \(^{13}\)C NMR (50.32 MHz, CDCl\(_3\)): \(\delta\) 16.9, 47.0, 52.5, 58.4, 62.8, 67.3, 69.4, 71.8, 72.1, 72.6, 75.1, 99.3, 119.9, 125.2, 127.0-128.8, 133.2, 133.3, 133.3, 133.4, 141.1, 141.2, 143.6, 143.9, 156.7, 165.1, 165.7, 166.1, 170.5; Anal. calcd for C\(_{54}\)H\(_{47}\)NO\(_{14}\): C, 69.44; H, 5.07; N, 1.50; found: C, 69.18; H, 5.22; N, 1.80; MS (ESI) calcd for C\(_{54}\)H\(_{47}\)NO\(_{14}\) [M+Na]+, 956.939; found, 956.694.

**Benzyl N-(benzyloxy carbonyl)-O-(2,3,4,6-tetra-O-benzoyl-\(\beta\)-D-glucopyranosyl)-L-threoninate (15c):** \([\alpha]_{D}^{25} +4.0^\circ\) (c 1.0, CHCl\(_3\));

\(^1\)H NMR (200.13 MHz, CDCl\(_3\)): \(\delta\) 1.11(d, \(J = 6.3\) Hz, 3H), 3.86(td, \(J = 3.5, 4.1, 9.4\) Hz, 1H), 4.30-4.59(m, 4H), 4.74(d, \(J = 8.0\) Hz, 1H), 5.04(s, 2H), 5.18(s, 2H), 5.38(dd, \(J = 8.0\) Hz, 1H), 5.62(m, 2H), 5.80(t, \(J = 9.5\) Hz, 1H), 7.20-7.58(m, 22H), 7.79-8.05(m, 8H); \(^{13}\)C NMR (50.32 MHz, CDCl\(_3\)): \(\delta\) 17.0, 58.4, 62.6, 66.9, 67.2, 69.2, 71.9, 72.0, 72.5, 75.0, 99.0, 127.8-129.7, 133.1, 133.2, 133.3, 133.4, 135.4, 136.2, 156.7, 165.0, 165.0, 165.7, 166.0, 169.8; Anal. calcd for C\(_{55}\)H\(_{49}\)NO\(_{14}\): C, 69.05; H, 5.14; N, 1.52; found: C, 68.64; H, 5.76; N, 1.77; MS (ESI) calcd for C\(_{55}\)H\(_{49}\)NO\(_{14}\) [M+Na]+, 944.928; found, 944.722.

**Benzyl N-(benzyloxy carbonyl)-O-(2,3,4,6-tetra-O-benzoyl-\(\beta\)-D-galactopyranosyl)-L-serinate (16a):** \([\alpha]_{D}^{25} +58.0^\circ\) (c 1.0, CHCl\(_3\));

\(^1\)H NMR (200.13 MHz, CDCl\(_3\)): \(\delta\) 3.98(dd, \(J = 3.2, 10.4\) Hz), 4.19(m, 2H), 4.32-4.80(m, 4H), 5.00(q, 2H, \(J = 12.3, 17.7\) Hz), 5.17(q, 2H, \(J = 12.4, 17.3\) Hz), 5.56(m, 1H), 5.73(m, 2H), 5.96(m, 1H), 7.20-7.68(m, 22H), 7.74-8.11(m, 8H); \(^{13}\)C NMR (50.32 MHz, CDCl\(_3\)): \(\delta\) 54.3, 61.8, 66.9, 67.0, 67.4, 67.9, 69.4, 69.5, 71.4, 101.8, 127.9-130.0, 133.2, 133.3, 133.6, 135.2, 136.1, 155.8, 165.2, 165.4, 165.5, 166.0, 169.3; Anal. calcd for C\(_{52}\)H\(_{45}\)NO\(_{14}\): C, 68.79; H, 5.00; N, 1.54; found: C, 67.86; H, 5.18; N, 1.62; MS (ESI) calcd for C\(_{52}\)H\(_{45}\)NO\(_{14}\) [M+Na]+, 930.902; found, 930.671.

**Methyl N-(9-Fluorenylmethoxycarbonyl)-O-(2,3,4,6-tetra-O-benzoyl-\(\beta\)-D-galactopyranosyl)-L-serinate (16b):** \([\alpha]_{D}^{25} +66.0^\circ\) (c 1.0, CHCl\(_3\)); \(^1\)H NMR (200.13 MHz, CDCl\(_3\)): \(\delta\) 3.68(s, 3H), 3.94(dd, \(J = 3.4, 10.4\) Hz, 1H), 4.14(t, \(J = 6.9\) Hz, 1H), 4.25-4.52(m, 6H), 4.63(dd, \(J = 6.5, 11.1\) Hz, 1H), 4.73(d, \(J = 7.6\) Hz, 1H), 5.52(d, \(J = 8.1\) Hz, 1H), 5.60(dd, \(J = 3.3, 10.2\) Hz, 1H), 5.75(dd,
$J = 7.8, 10.2 \text{ Hz}, 1H), 6.00(d, J = 3.3 \text{ Hz}, 1H), 7.20-7.66(m, 20H), 7.75-8.11(m, 8H); ^{13}C \text{ NMR (50.32 MHz, CDCl}_3\text{): } \delta 47.1, 52.7, 54.3, 61.9, 66.7, 67.9, 69.4, 69.4, 71.4, 71.4, 101.8, 119.9-130.0, 133.2, 133.3, 133.6, 141.3, 141.3, 143.7, 143.8, 155.7, 165.2, 165.5, 165.5, 166.0, 169.8; \text{Anal. calcd for } C_{53}H_{45}NO_{14}: C, 69.20; H, 4.93; N, 1.52; \text{found: C, 67.94; H, 4.02; N, 1.66; MS (ESI) calcd for } C_{53}H_{45}NO_{14} [M+Na]^+, 942.913; \text{found, 942.643}.$

**Benzyl \ N-(benzoylcarbonyl)-O-(2,3,4,6-tetra-O-benzoyl-\beta-D-galactopyranosyl)-L-threoninate (16c): [\alpha]_{25}^{D} +36.0^\circ (c 1.0, CHCl}_3\text{): } ^{1}H \text{ NMR (200.13 MHz, CDCl}_3\text{): } \delta 1.14(d, J = 6.4 \text{ Hz}, 3H), 4.06(t, J = 6.4 \text{ Hz}, 1H), 4.31(dd, J = 7.1, 11.3 \text{ Hz}, 1H), 4.43(dd, J = 2.2, 9.3 \text{ Hz}, 1H), 4.48-4.61(m, 2H), 4.71(d, J = 7.8 \text{ Hz}, 1H), 5.07(s, 2H), 5.24(s, 2H), 5.51(dd, J = 3.3, 10.4 \text{ Hz}, 1H), 5.61-5.75(m, 2H), 5.92(d, J = 3.8 \text{ Hz}, 1H), 7.19-7.66(m, 22H), 7.75-8.08(m, 8H); ^{13}C \text{ NMR (50.32 MHz, CDCl}_3\text{): } \delta 17.4, 58.5, 61.6, 67.0, 67.3, 67.8, 69.8, 71.1, 71.3, 75.6, 99.9, 127.8-130.0, 133.2, 133.3, 133.3, 133.5, 135.4, 136.2, 156.7, 165.2, 165.5, 165.5, 165.9, 169.9; \text{Anal. calcd for } C_{53}H_{47}NO_{14}: C, 69.05; H, 5.14; N, 1.52; \text{found: C, 66.49; H, 4.95; N, 1.35; MS (ESI) calcd for } C_{53}H_{47}NO_{14} [M+Na]^+, 944.289; \text{found, 944.785}.$

**Benzyl \ N-(benzoylcarbonyl)-O-(2,3,4,6-tetra-O-benzoyl-\alpha-D-mannopyranosyl)-L-serinate (17a): [\alpha]_{25}^{D} -42.0^\circ (c 1.0, CHCl}_3\text{): } ^{1}H \text{ NMR (200.13 MHz, CDCl}_3\text{): } \delta 4.14(d, J = 2.7 \text{ Hz}, 2H), 4.32-4.68(m, 4H), 4.99(d, J = 1.6 \text{ Hz}, 1H), 5.14(d, J = 1.5 \text{ Hz}, 2H), 5.32(dd, J = 12.1, 20.5 \text{ Hz}, 2H), 5.59(dd, J = 1.8, 3.2 \text{ Hz}, 1H), 5.79(dd, J = 3.2, 10.1 \text{ Hz}, 1H), 5.96(d, J = 7.9 \text{ Hz}, 1H), 6.09(t, J = 10.1 \text{ Hz}, 1H), 7.20-7.65(m, 22H), 7.81-8.14(m, 8H); ^{13}C \text{ NMR (50.32 MHz, CDCl}_3\text{): } \delta 54.5, 62.6, 66.5, 67.2, 67.8, 67.9, 69.4, 69.7, 70.1, 98.4, 128.1-129.9, 133.0, 133.1, 133.4, 133.5, 135.0, 136.0, 155.9, 165.2, 165.3, 165.4, 166.1, 169.5; \text{Anal. calcd for } C_{52}H_{45}NO_{14}: C, 68.79; H, 5.00; N, 1.54; \text{found: C, 68.21; H, 5.58; N, 1.49; MS (ESI) calcd for } C_{52}H_{45}NO_{14} [M+Na]^+, 930.902; \text{found, 930.671}.$

**Methyl \ N-(9-Fluorenylemethoxycarbonyl)-O-(2,3,4,6-tetra-O-benzoyl-\alpha-D-mannopyranosyl)-L-threoninate (17b): [\alpha]_{25}^{D} -30.0^\circ (c 1.0, CHCl}_3\text{): } ^{1}H \text{ NMR (200.13 MHz, CDCl}_3\text{): } \delta 1.43(d, J = 6.2 \text{ Hz}, 3H), 3.90(s, 3H), 4.33(dd, J = 7.1, 14.4 \text{ Hz}, 2H), 4.28-4.75(m, 6H), 5.17(d, J = 1.5 \text{ Hz}, 1H), 5.50(dd, J = 1.8, 3.1 \text{ Hz}, 1H), 5.75-5.95(m, 2H), 6.10(t, \text{ found, 930.671}.$
9.6 Hz, 1H), 7.20-8.10(m, 28H); $^{13}$C NMR (50.32 MHz, CDCl$_3$): δ 18.2, 47.1, 53.0, 58.6, 62.9, 66.9, 67.5, 69.4, 69.6, 70.5, 77.8, 99.0, 119.9, 125.2, 127.1-129.8, 133.1, 133.2, 133.5, 133.5, 141.3, 141.3, 143.7, 143.8, 156.7, 165.3, 165.5, 166.1, 170.5; Anal. calcd for C$_{54}$H$_{47}$NO$_{14}$: C, 69.44; H, 5.07; N, 1.50; found: C, 66.42; H, 4.20; N, 1.34; MS (ESI) calcd for C$_{54}$H$_{47}$NO$_{14}$ [M+Na]$^+$, 956.289; found, 956.820.

**Benzyl**  $N$-(benzyloxy carbonyl)-O-(2,3,4,6-tetra-O-benzoyl-α-D-mannopyranosyl)-L-threoninate (17c): [α]$_{25}$D –40.0° (c 1.0, CHCl$_3$); 

$^1$H NMR (200.13 MHz, CDCl$_3$): δ 1.42(d, J = 6.2 Hz, 3H), 4.42-4.55(m, 3H), 4.57-4.71(m, 2H), 5.07(d, J = 1.8 Hz, 1H), 5.19(s, 2H), 5.31(s, 2H), 5.45(dd, J 1.8, 3.1 Hz, 1H), 5.72-5.85(m, 2H), 6.06(t, J = 9.9 Hz, 1H), 7.21-7.68(m, 22H), 7.82-8.10(m, 8H); $^{13}$C NMR (50.32 MHz, CDCl$_3$): δ 18.3, 58.8, 62.9, 66.8, 67.3, 67.9, 69.6, 69.7, 70.5, 77.9, 99.0, 128.1-129.9, 133.1, 133.1, 133.5, 133.5, 135.0, 136.1, 156.7, 165.2, 165.4, 166.1, 169.9; Anal. calcd for C$_{53}$H$_{47}$NO$_{14}$: C, 69.05; H, 5.14; N, 1.52; found: C, 69.51; H, 4.67; N, 1.02; MS (ESI) calcd for C$_{53}$H$_{47}$NO$_{14}$ [M+Na]$^+$, 944.928; found, 944.785.

**Benzyl**  $N$-(benzyloxy carbonyl)-O-[2,3,6-tri-O-benzoyl-4-O-(2,3,4,6-tetra-O-benzoyl-β-D-galactopyranosyl)-β-D-glucopyranosyl]-L-serinate (18a): [α]$_{25}$D +46.0° (c 1.0, CHCl$_3$); $^1$H NMR (200.13 MHz, CDCl$_3$): δ 3.59(d, J = 9.7 Hz, 1H), 3.70(d, J = 6.5 Hz, 2H), 3.78-3.92(m, 2H), 4.18(t, J = 9.7 Hz, 1H), 4.26(dd, J = 2.6, 10.4 Hz, 1H), 4.36-4.59(m, 4H), 4.81-4.98(m, 3H), 5.06(s, 2H), 5.32-5.45(m, 2H), 5.52(d, J = 8.0 Hz, 1H), 5.69(d, J = 9.2 Hz, 2H), 5.75(d, J = 6.2 Hz, 1H), 7.11-7.64(m, 31H), 7.69-8.02(m, 14H); $^{13}$C NMR (100.61 MHz, CDCl$_3$): δ 54.2, 61.0, 62.1, 66.9, 67.3, 67.5, 69.4, 69.8, 71.3, 71.5, 71.7, 72.5, 73.0, 75.6, 100.9, 101.3, 128.0-130.0, 133.1, 133.2, 133.3, 133.4, 133.5, 133.5, 135.1, 136.2, 155.8, 164.8, 165.1, 165.2, 165.3, 165.4, 165.6, 165.8, 169.2; Anal. calcd for C$_{79}$H$_{67}$NO$_{22}$: C, 68.64; H, 4.89; N, 1.01; found: C, 68.36; H, 4.38; N, 1.12; MS (ESI) calcd for C$_{79}$H$_{67}$NO$_{22}$ [M+Na]$^+$, 1405.361; found, 1404.813 (M$^+$+1).

**Methyl**  $N$-(9-Fluorenylmethoxycarbonyl)-O-[2,3,6-tri-O-benzoyl-4-O-(2,3,4,6-tetra-O-benzoyl-β-D-galactopyranosyl)-β-D-glucopyranosyl]-L-serinate (18b): [α]$_{25}$D +48.0° (c 1.0,
**Methyl N-(9-Fluorenylethoxycarbonyl)-O-[2,3,6-tri-O-benzoyl-4-O-(2,3,4,6-tetra-O-benzoyl-β-D-galactopyranosyl)-β-D-glucopyranosyl]-L-threoninate (18c):**  \([\alpha]^D_{25} +42.0^\circ\) (c 1.0, CHCl₃); \(^1\)H NMR (400.13 MHz, CDCl₃): \(\delta\) 1.11(d, \(J = 6.4\) Hz, 3H), 3.57(s, 3H), 3.70-3.86(m, 3H), 3.94(t, \(J = 6.6\) Hz, 1H), 4.13-4.45(m, 6H), 4.52(dt, \(J = 3.9, 12.9\) Hz, 1H), 4.61(ABq, \(J = 14.9\)Hz, 1H), 4.85(ABq, \(J = 8\) Hz, 2H), 5.44(m, 2H), 5.69(d, \(J = 9.3\) Hz, 1H), 5.73-5.87(m, 3H), 7.12-8.13(m, 43H); \(^13\)C NMR (100.61 MHz, CDCl₃): \(\delta\) 16.8, 47.0, 52.3, 58.4, 61.0, 62.1, 67.3, 67.5, 69.9, 71.4, 71.7, 72.6, 73.0, 74.9, 75.7, 77.2, 99.0, 101.0, 119.9, 125.2, 127.0-129.9, 133.2, 133.3, 133.4, 133.5, 133.5, 141.1, 141.2, 143.6, 143.9, 156.7, 164.8, 165.2, 165.3, 165.4, 165.5, 165.8, 170.4; Anal. calcd for C₈₀H₆₇NO₂₂ [M+Na]⁺, 1431.400; found, 1431.034.

**Allyl N-(9-Fluorenylethoxycarbonyl)-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-L-Serinate (20):**  \([\alpha]^D_{25} +15.0^\circ\) (c 1.0, CHCl₃); \(^1\)H NMR (200.13 MHz, CDCl₃): \(\delta\) 3.91(dd, \(J = 3.2, 10.1\) Hz, 1H), 4.13(m, 2H), 4.08-4.70(m, 8H), 4.79(d, \(J = 7.7\) Hz, 1H), 5.13-5.33(m, 2H), 5.43-5.98(m, 5H), 7.20-8.08(m, 28H); \(^13\)C NMR (50.32 MHz, CDCl₃): \(\delta\) 47.1, 54.3, 62.9, 66.3, 66.9, 69.5, 71.7, 72.3, 72.6, 101.4, 118.7, 120.0, 120.1, 125.1, 125.2, 127.0-129.8, 131.3, 133.2, 133.3, 133.4, 133.5, 141.2, 141.3, 143.7,
143.8, 155.8, 165.0, 165.1, 165.7, 166.1, 169.0; Anal. calcd for C_{55}H_{47}NO_{14}: C, 69.83; H, 5.01; N, 1.48; found: C, 69.50; H, 4.97; N, 1.51; MS (ESI) calcd for C_{55}H_{47}NO_{14} [M+Na]^+; 968.289; found, 968.196.

**Allyl O-2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl-L-Serinate (22):** [α]_{D}^{25} +13.3° (c 1.0, CHCl_3); ^1H NMR (200.13 MHz, CDCl_3): δ 3.47(bs, 1H), 3.71(dd, J = 3.5, 9.3 Hz, 1H), 4.02(m, 2H), 4.14-4.34(m, 1H), 4.36(m, 2H), 4.49(dd, J = 2.8, 11.8 Hz, 1H), 4.77(d, J = 7.8 Hz, 1H), 4.93-5.14(m, 2H), 5.37(dd, J = 7.9, 9.5 Hz, 1H), 5.53(t, J = 9.6 Hz, 1H), 5.66(m, 1H), 5.75(t, J = 9.6 Hz, 1H), 7.08-7.45(m, 12H), 7.68(d, J = 7.6 Hz, 2H), 7.75(d, J = 7.5 Hz, 2H), 7.81(d, J = 7.6 Hz, 2H), 7.88(d, J = 7.2 Hz, 2H); ^13C NMR (100.61 MHz, CDCl_3): δ 54.6, 63.0, 65.7, 69.5, 71.7, 71.7, 72.3, 72.8, 101.3, 118.5, 128.2-129.9, 131.7, 133.1, 133.2, 133.3, 133.4, 165.0, 165.1, 165.8, 166.1, 172.6; MS (ESI) calcd for C_{46}H_{37}NO_{12} [M+Na]^+, 746.221; found, 746.306.

**N-(9-Fluorenylmethoxycarbonyl)-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-L-Serine (21):** [α]_{D}^{25} +8.3° (c 1.0, CHCl_3); ^1H NMR (200.13 MHz, CDCl_3): δ 4.08(m, 3H), 4.25(m, 2H), 4.39(dd, J = 4.9, 8.7 Hz, 2H), 4.53(dd, J = 4.3, 12.1 Hz, 1H), 4.66(dd, J = 2.6, 12.1 Hz, 1H), 5.10(d, J = 8.0 Hz, 1H), 5.50(t, J = 8.1 Hz, 1H), 5.72(t, J = 9.8 Hz, 1H), 6.02(t, J = 9.5 Hz, 1H), 7.23-8.84(m, 28H); ^13C NMR (100.61 MHz, CDCl_3): δ 56.0, 64.2, 67.8, 70.4, 71.1, 73.1, 73.3, 74.6, 79.5, 102.0, 120.9, 121.0, 126.3, 126.4, 128.1-130.9, 134.4, 134.4, 134.5, 134.7, 142.5, 142.6, 145.1, 145.3, 158.1, 166.7, 166.7, 166.7, 167.0, 167.5; MS (ESI) calcd for C_{52}H_{43}NO_{14} [M+Na]^+, 928.886; found, 928.480.

**3,4,6-tri-O-Benzoyl-1,2-O-[(2S-(2-tert-butoxy carbonylamino)-3-methoxy-3-oxopropoxy) phenylmethylene] -α-D-glucopyranoside (A):** [α]_{D}^{25} = +3.8 (c = 1.0, CHCl_3); ^1H NMR (400.13 MHz, CDCl_3): δ 1.41(s, 9 H), 3.60(dd, J = 3.2, 9.9 Hz, 1 H), 3.69(m, 1 H), 3.71(s, 3 H), 4.09(ddd, J = 3.1, 4.9, 7.9 Hz, 1 H), 4.37(dd, J = 5.0, 11.7 Hz, 2 H), 4.52(dd, J = 2.8, 11.7 Hz, 1 H), 4.74(t, J = 4.2 Hz, 1 H), 5.31(d, J = 8.8 Hz, 1 H), 5.47(d, J = 8.8 Hz, 1 H), 5.73(bs, 1 H), 6.01(d, J = 5.2 Hz, 1 H), 7.21-7.66(m, 12 H), 7.70(d, J = 7.3 Hz, 2 H), 7.91(d, J = 7.8 Hz, 2 H), 7.94(d, J = 8.2 Hz, 2 H), 8.08(d, J = 7.3 Hz,
2 H); $^{13}$C NMR (100.61 MHz, CDCl$_3$): $\delta =$ 28.2(3C), 52.5, 53.4, 63.9, 64.2, 67.6, 68.3, 69.0, 72.2, 80.1, 97.6, 121.1, 126.2, 128.2-130.1, 133.0, 133.5, 133.7, 134.5, 155.3, 164.5, 165.1, 166.0, 170.7; HRMS (MALDI-TOF): m/z Calcd for C$_{43}$H$_{43}$NO$_{13}$+Na, 820.2581; Found, 820.2577.

**Methyl N-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyloxycarbonyl)-L-serinate (24):** $[\alpha]_D^{25} = +32.9$ (c = 1.0, CHCl$_3$); $^1$H NMR (400.13 MHz, CDCl$_3$): $\delta =$ 2.44(bs, 1 H), 3.61(s, 3 H), 3.94(ddd, J = 3.2, 11.4, 14.8 Hz, 2 H), 4.29-4.38(m, 2 H), 4.51(dd, J = 4.8, 12.3 Hz, 1 H), 4.65(dd, J = 2.9, 12.3 Hz, 1 H), 5.68(dd, J = 8.3, 9.5 Hz, 1 H), 5.77(t, J = 9.5 Hz, 1 H), 5.97(m, 2 H), 6.06(d, J = 8.4 Hz, 1 H), 7.25-7.61(m, 12 H), 7.85(d, J = 7.4 Hz, 2 H), 7.91(d, J = 7.4 Hz, 2 H), 7.96(d, J = 7.4 Hz, 2 H), 8.05(d, J = 7.4 Hz, 2 H); $^{13}$C NMR (100.61 MHz, CDCl$_3$): $\delta =$ 52.6, 56.0, 62.6, 62.6, 68.9, 70.7, 72.8, 73.0, 93.5, 128.3-130.0, 133.2, 133.3, 133.5, 153.5, 155.1, 165.2, 165.6, 166.2, 170.2; HRMS (MALDI-TOF): m/z Calcd for C$_{39}$H$_{33}$NO$_{14}$+Na, 764.1955; Found, 764.1960.

**Methyl N-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyloxycarbonyl)-L-phenylalaninate (26a):** $[\alpha]_D^{25} = +46.5$ (c = 1.0, CHCl$_3$); $^1$H NMR (200.13 MHz, CDCl$_3$): $\delta =$ 3.07(ddd, J = 5.6, 13.8, 19.4 Hz, 2 H), 3.54(s, 3 H), 4.29(ddd, J = 3.2, 4.5, 7.6 Hz, 1 H), 4.44-4.71(m, 3 H), 5.44(d, J = 8.3 Hz, 1 H), 5.63(dd, J = 8.3, 9.5 Hz, 1 H), 5.74(t, J = 9.5 Hz, 1 H), 5.92(t, J = 9.6 Hz, 1 H), 6.02(d, J = 8.2 Hz, 1 H), 6.98-7.61(m, 17 H), 7.76-8.10(m, 8 H); $^{13}$C NMR (50.32 MHz, CDCl$_3$): $\delta =$ 37.8, 52.2, 55.0, 62.7, 69.1, 70.6, 72.9, 72.9, 93.3, 127.2, 128.3-130.0, 133.1, 133.3, 133.4, 133.5, 135.2, 153.1, 165.1, 165.1, 166.6, 171.0; HRMS (MALDI-TOF): m/z Calcd for C$_{45}$H$_{39}$NO$_{13}$+Na, 824.2319; Found, 824.2320.

**N-(2,3,4,6-tetra-O-Benzoyl-β-D-glucopyranosyloxycarbonyl)-adamantylamine (26b):** $[\alpha]_D^{25} = +34.6$ (c = 1.0, CHCl$_3$); $^1$H NMR (200.13 MHz, CDCl$_3$): $\delta =$ 1.61(m, 6 H), 1.82(m, 6 H), 2.01(m, 3 H), 4.26(qd, J = 3.1, 4.7, 8.0 Hz, 1 H), 4.48(dd, J = 4.9, 12.3 Hz, 1 H), 4.62(dd, J = 3.0, 12.3 Hz, 1 H), 4.75(s, 1 H), 5.61(dd, J = 8.6, 9.4 Hz, 1 H), 5.72(t, J = 9.5 Hz, 1 H), 5.88-6.03(m, 2 H), 7.23-7.61(m, 12 H), 7.78-8.08(m, 8 H); $^{13}$C NMR (50.32 MHz, CDCl$_3$): $\delta =$ 29.3(3C), 36.1(3C), 41.3(3C), 51.2, 62.7, 69.2, 70.9, 72.8, 73.0, 92.6, 128.2-
130.0, 133.0, 133.2, 133.4, 133.5, 151.2, 165.1, 165.3, 165.6, 166.1; HRMS (MALDI-TOF): m/z Calcd for C_{45}H_{43}NO_{11}^+Na, 796.2734; Found, 796.2730.

**N-(2,3,4,6-tetra-O-Benzoyl-β-D-glucopyranosyloxycarbonyl)-methylamine (10c):** [$\alpha$]_D^{25} = +47.6 (c = 1.0, CHCl₃); $^1$H NMR (200.13 MHz, CDCl₃): δ = 2.74(d, J = 4.9 Hz, 3 H), 4.31(qd, J = 3.0, 4.3, 7.3 Hz, 1 H), 4.48(dd, J = 4.4, 12.3 Hz, 1 H), 4.64(dd, J = 2.8, 12.3 Hz, 1 H), 4.92(q, J = 4.7, 9.6 Hz, 1 H), 5.66(dd, J = 8.3, 9.6 Hz, 1 H), 5.76(t, J = 9.6 Hz, 1 H), 5.97(t, J = 9.6 Hz, 1 H), 6.05(d, J = 8.1 Hz, 1 H), 7.24-7.61(m, 12 H), 7.79-8.01(m, 8 H); $^{13}$C NMR (50.32 MHz, CDCl₃): δ = 27.4, 62.6, 69.0, 70.8, 72.7, 72.9, 93.1, 128.2-130.0, 133.1, 133.2, 133.4, 133.5, 154.3, 165.1, 165.2, 165.6, 166.1; HRMS (MALDI-TOF): m/z Calcd for C_{36}H_{31}NO_{11}^+Na, 676.1795; Found, 676.1790.

**N-(2,3,4,6-tetra-O-Benzoyl-β-D-glucopyranosyloxycarbonyl)-dodecylamine (26d):** [$\alpha$]_D^{25} = +34.4 (c = 1.0, CHCl₃); $^1$H NMR (200.13 MHz, CDCl₃): δ = 0.88(t, J = 6.1 Hz, 3 H), 1.15-1.45(m, 20 H), 3.10(ddd, J = 1.4, 6.8, 8.7 Hz, 2 H), 4.30(qd, J = 3.0, 4.1, 7.2 Hz, 1 H), 4.48(dd, J = 4.5, 12.3 Hz, 1 H), 4.65(dd, J = 2.9, 12.4 Hz, 1 H), 4.92(t, J = 5.9 Hz, 1 H), 5.64(dd, J = 8.3, 9.6 Hz, 1 H), 5.75(t, J = 9.6 Hz, 1 H), 5.96(t, J = 9.6 Hz, 1 H), 6.05(d, J = 8.3 Hz, 1 H), 7.23-7.68(m, 12 H), 7.79-8.08(m, 8 H); $^{13}$C NMR (50.32 MHz, CDCl₃): δ = 14.1, 22.6, 26.6, 29.1, 29.3, 29.4, 29.5, 29.6, 29.6, 31.9, 41.1, 62.7, 69.1, 70.9, 72.8, 72.9, 93.1, 128.2-130.0, 133.1, 133.2, 133.4, 133.4, 153.6, 165.1, 165.2, 165.6, 166.1; HRMS (MALDI-TOF): m/z Calcd for C_{47}H_{33}NO_{11}^+Na, 830.3516; Found, 830.3520.

**N-(2,3,4,6-tetra-O-Benzoyl-β-D-glucopyranosyloxycarbonyl)-2-(3,4-dimethoxyphenyl) ethylamine (26e):** [$\alpha$]_D^{25} = +30.2 (c = 1.0, CHCl₃); $^1$H NMR (200.13 MHz, CDCl₃): δ = 2.66(t, J = 7.1 Hz, 2 H), 3.35(ddd, J = 1.5, 6.1, 8.6 Hz, 2 H), 3.79, 3.82(2s, 6 H), 4.31(qd, J = 2.9, 4.2, 7.9 Hz, 1 H), 4.48(dd, J = 4.6, 12.4 Hz, 1 H), 4.65(dd, J = 2.9, 12.4 Hz, 1 H), 4.97(t, J = 6.0 Hz, 1 H), 5.62(dd, J = 8.4, 9.6 Hz, 1 H), 5.75(t, J = 9.6 Hz, 1 H), 5.96(t, J = 9.6 Hz, 1 H), 6.05(d, J = 8.4 Hz, 1 H), 6.55-6.74(m, 3 H), 7.23-7.61(m, 12 H), 7.75-8.08(m, 8 H); $^{13}$C NMR (50.32 MHz, CDCl₃): δ = 35.1, 42.3, 55.6, 55.7, 62.6, 69.0, 70.8, 72.7, 72.9, 93.1, 111.2, 111.6, 120.5, 128.2-129.8, 130.7, 133.0, 133.2, 133.4, 133.4, 147.5, 148.8, 153.6,
N-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyloxy carbonyl)-aniline (26f): \([\alpha]_D^{25} = +29.2\) (c = 1.0, CHCl₃); \(^1\)H NMR (200.13 MHz, CDCl₃): \(\delta = 4.35(qd, J = 3.1, 4.7, 7.7\) Hz, 1 H), 4.50(dd, \(J = 4.7, 12.3\) Hz, 1 H), 4.65(dd, \(J = 3.1, 12.3\) Hz, 1 H), 5.72(dd, \(J = 8.2, 9.6\) Hz, 1 H), 5.77(t, \(J = 9.7\) Hz, 1 H), 6.00(t, \(J = 9.7\) Hz, 1 H), 6.12(d, \(J = 8.2\) Hz, 1 H), 6.92-7.20(m, 2 H), 7.23-7.61(m, 16 H), 7.80-8.08(m, 8 H); \(^13\)C NMR (50.32 MHz, CDCl₃): \(\delta = 62.6, 69.0, 70.8, 72.9, 73.0, 93.2, 118.9, 124.1, 128.2-130.0, 133.1, 133.3, 133.5, 133.6, 136.8, 150.7, 165.1, 165.3, 165.6, 166.1; HRMS (MALDI-TOF): m/z Calcd for C₄₅H₄₃NO₁₁+Na, 738.1951; Found, 738.1950.

Methyl N-(2,3,4,6-tetra-O-benzoyl-β-D-galactopyranosyloxy carbonyl)-L-phenylalaninate (27a): \([\alpha]_D^{25} = +96.6\) (c = 1.0, CHCl₃); \(^1\)H NMR (200.13 MHz, CDCl₃): 4.35-4.78(m, 4 H), 5.46(d, \(J = 8.2\) Hz, 1 H), 5.65(dd, \(J = 3.3, 10.2\) Hz, 1 H), 5.90(dd, \(J = 8.3, 10.2\) Hz, 1 H), 6.01-6.08(m, 2 H), 7.09(m, 2 H), 7.18-7.70(m, 15 H), 7.73-8.15(m, 8 H); \(^13\)C NMR (50.32 MHz, CDCl₃): \(\delta = 37.7, 52.1, 54.9, 61.7, 67.8, 68.6, 71.7, 72.0, 93.6, 127.2, 128.2-130.0, 133.2, 133.3, 133.6, 135.2, 153.1, 165.2, 165.4, 165.9, 171.0; HRMS (MALDI-TOF): m/z Calcd for C₄₅H₄₃NO₁₁+Na, 824.2319; Found, 824.2320.

N-(2,3,4,6-tetra-O-Benzoyl-β-D-galactopyranosyloxy carbonyl)-adamantylamine (27b): \([\alpha]_D^{25} = +97.3\) (c = 1.0, CHCl₃); \(^1\)H NMR (200.13 MHz, CDCl₃): \(\delta = 1.61(m, 6 H), 1.83(m, 6 H), 2.01(m, 3 H), 4.34-4.52(m, 2 H), 4.67(dd, \(J = 4.2, 8.6\) Hz, 1 H), 4.79(s, 1 H), 5.66(dd, \(J = 3.4, 10.1\) Hz, 1 H), 5.87(t, \(J = 8.3\) Hz, 1 H), 5.95-6.07(m, 2 H), 7.20-7.68(m, 12 H), 7.75-8.16(m, 8 H); \(^13\)C NMR (50.32 MHz, CDCl₃): \(\delta = 29.2(3C), 36.0(3C), 41.3(3C), 51.2, 61.7, 67.9, 68.9, 71.7, 71.9, 92.9, 128.2-130.0, 133.1, 133.3, 133.4, 133.5, 151.2, 165.3, 165.4, 165.5, 165.9; HRMS (MALDI-TOF): m/z Calcd for C₄₅H₄₃NO₁₁+Na, 796.2734; Found, 796.2730.
Methyl N-(2,3,4,6-tetra-O-benzoyl-α-D-mannopyranosyloxycarbonyl)-L-phenylalaninate (28a): [α]$_D^{25}$ = -17.8 (c = 1.0, CHCl$_3$); $^1$H NMR (200.13 MHz, CDCl$_3$): δ 3.19 (d, J = 5.9 Hz, 2 H), 3.75(s, 3 H), 4.45(dd, J = 3.6, 9.7 Hz, 1 H), 4.50(m, 1 H), 4.61-4.82(m, 2 H), 5.60(d, J = 8.3 Hz, 1 H), 5.77(dd, J = 2.0, 3.3 Hz, 1 H), 5.89(dd, J = 3.3, 10.2 Hz, 1 H), 6.10 (t, J = 10.2 Hz, 1 H), 6.29(d, J = 2.0 Hz, 1 H), 7.15-7.63(m, 17 H), 7.80-8.14(m, 8 H); $^{13}$C NMR (50.32 MHz, CDCl$_3$): δ = 38.1, 52.4, 54.9, 62.3, 66.1, 69.2, 69.8, 70.5, 91.7, 127.3, 128.2-130.0, 133.0, 133.3, 133.4, 133.6, 135.3, 152.5, 165.1, 165.2, 165.6, 166.0, 171.6; HRMS (MALDI-TOF): m/z Calcd for C$_{45}$H$_{39}$NO$_{13}$+Na, 824.2319; Found, 824.2320.

N-(2,3,4,6-tetra-O-Benzoyl-α-D-mannopyranosyloxycarbonyl)-adamantylamine (28b):

[α]$_D^{25}$ = -41.7 (c = 1.0, CHCl$_3$); $^1$H NMR (200.13 MHz, CDCl$_3$): δ = 1.61(m, 6 H), 1.83(m, 6 H), 2.01(m, 3 H), 4.34-4.52(m, 2 H), 4.67(dd, J = 4.2, 8.6 Hz, 1 H), 4.79(s, 1 H), 5.66(dd, J = 3.4, 10.1 Hz, 1 H), 5.87(t, J = 8.3 Hz, 1 H), 5.95-6.07(m, 2 H), 7.20-7.68(m, 12 H), 7.75-8.16(m, 8 H); $^{13}$C NMR (50.32 MHz, CDCl$_3$): δ = 29.4(3C), 36.2(3C), 41.5(3C), 51.4, 62.7, 66.4, 69.6, 70.0, 70.3, 90.7, 128.3-130.0, 133.0, 133.3, 133.5, 133.6, 150.5, 165.2, 165.3, 165.7, 166.1; HRMS (MALDI-TOF): m/z Calcd for C$_{45}$H$_{43}$NO$_{11}$+Na, 796.2734; Found, 796.2730.

Methyl N-(2,3,6-tri-O-benzoyl-4-O-(2,3,4,6-tetra-O-benzoyl-β-D-galactopyranosyloxycarbonyl)-β-D-glucopyranosyloxycarbonyl)-L-phenylalaninate (29a): [α]$_D^{25}$ = +54.5 (c = 1.0, CHCl$_3$); $^1$H NMR (200.13 MHz, CDCl$_3$): δ = 3.04(ddd, J = 5.8, 13.9, 19.4 Hz, 2 H), 3.52(s, 3 H), 3.58-4.05(m, 4 H), 4.29(t, J = 9.6 Hz, 1 H), 4.43-4.65(m, 3 H), 4.85(d, J = 7.9 Hz, 1 H), 5.35(dd, J = 3.4, 6.5 Hz, 1 H), 5.39(s, 1 H), 5.56(dd, J = 8.4, 9.7 Hz, 1 H), 5.72(dd, J = 7.9, 10.3 Hz, 2 H), 5.83(t, J = 9.4 Hz, 1 H), 5.87(d, J = 8.4 Hz, 1 H), 6.95-7.78(m, 26 H), 7.86-8.07(m, 14 H); $^{13}$C NMR (50.32 MHz, CDCl$_3$): δ = 37.8, 52.2, 54.9, 60.9, 62.0, 67.4, 69.7, 70.4, 71.3, 71.7, 72.9, 73.5, 75.6, 93.2, 101.0, 127.1, 128.2-130.0, 133.1, 133.2, 133.3, 133.4, 133.6, 133.8, 135.2, 153.0, 164.7, 165.2, 165.2, 165.3, 165.4, 165.5, 165.8, 171.0; HRMS (MALDI-TOF): m/z Calcd for C$_{72}$H$_{63}$NO$_{21}$+Na, 1298.3634; Found, 1298.3630.
N-(2,3,6-tri-O-Benzoyl-4-O-(2,3,4,6-tetra-O-benzoyl-β-D-galactopyranosyl)-β-D-glucopyranosyloxycarbonyl)-L-adamantylamine (29b): \([\alpha]_D^{25} = +48.0 \ (c = 1.0, \text{CHCl}_3)\); \(^1\text{H}\) NMR (200.13 MHz, CDCl\(_3\)): \(\delta = 1.58 (m, \ 6 \ H),\) 1.78 (m, 6 H), 1.99 (m, 3 H), 3.60-3.98 (m, 4 H), 4.29 (t, \(J = 9.6 \ \text{Hz}, \ 1 \ H\)), 4.48 (dd, \(J = 3.7, \ 12.4 \ \text{Hz}, \ 1 \ H\)), 4.59 (dd, \(J = 1.7, \ 12.4 \ \text{Hz}, \ 1 \ H\)), 4.71 (s, 1 H), 4.84 (d, \(J = 7.9 \ \text{Hz}, \ 1 \ H\)), 5.35 (dd, \(J = 3.3, \ 10.2 \ \text{Hz}, \ 1 \ H\)), 5.54 (t, \(J = 9.0 \ \text{Hz}, \ 1 \ H\)), 5.72 (dd, \(J = 7.8, \ 10.2 \ \text{Hz}, \ 2 \ H\)), 5.79-5.95 (m, 2 H), 7.06-7.80 (m, 21 H), 7.75-8.06 (m, 14 H); \(^{13}\text{C}\) NMR (50.32 MHz, CDCl\(_3\)): \(\delta = 29.2(3\text{C}), \ 36.0(3\text{C}), \ 41.3(3\text{C}), \ 51.1, \ 60.9, \ 62.2, \ 67.4, \ 69.7, \ 70.8, \ 71.3, \ 71.7, \ 72.9, \ 73.5, \ 75.7, \ 92.5, \ 101.0, \ 128.2-130.0, \ 133.1, \ 133.2, \ 133.3, \ 133.4, \ 133.5, \ 133.6, \ 133.6, \ 151.1, \ 164.8, \ 165.2, \ 165.2, \ 165.4, \ 165.4, \ 165.5, \ 165.8; \) HRMS (MALDI-TOF): \(m/z \ \text{Calcd for C}_{72}\text{H}_{65}\text{NO}_{19}^+\text{Na}, \ 1270.4048; \) Found, 1270.4050.

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1H NMR (CDCl₃, 200.13 MHz) Spectrum of Compound 12a

13C NMR (CDCl₃, 50.32 MHz) Spectrum of Compound 12a

DEPT NMR (CDCl₃, 50.32 MHz) Spectrum of Compound 12a
$^1$H NMR (CDCl$_3$, 200.13MHz) Spectrum of Compound 15a

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 15a

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 15a
$^1$H NMR (CDCl$_3$, 200.13MHz) Spectrum of Compound 15b

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 15b

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 15b
$^1$H NMR (CDCl$_3$, 200.13MHz) Spectrum of Compound 15c

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 15c

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 15c
$^1$H NMR (CDCl$_3$, 200.13MHz) Spectrum of Compound 16a

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 1a

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 16a
$^1$H NMR (CDCl$_3$, 200.13MHz) Spectrum of Compound 16b

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 16b

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 16b
$^1$H NMR (CDCl$_3$, 200.13 MHz) Spectrum of Compound 16c

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 16c
$^1$H NMR (CDCl$_3$, 200.13MHz) Spectrum of Compound 17a

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 17a

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 17a
$^1$H NMR (CDCl$_3$, 200.13MHz) Spectrum of Compound 17b

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 17b

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 17b
$^1$H NMR (CDCl$_3$, 200.13 MHz) Spectrum of Compound 17c

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 17c

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 17c
\( ^1\text{H NMR (CDCl}_3, 200.13\text{MHz)} \) Spectrum of Compound 18a

\( ^{13}\text{C NMR (CDCl}_3, 100.61\text{MHz)} \) Spectrum of Compound 18a

DEPT NMR (CDCl\textsubscript{3}, 100.61 MHz) Spectrum of Compound 18a
$^1$H NMR (CDCl$_3$, 500.13MHz) Spectrum of Compound 18b

$^{13}$C NMR (CDCl$_3$, 125.76 MHz) Spectrum of Compound 18b

DEPT NMR (CDCl$_3$, 125.76 MHz) Spectrum of Compound 18b
$^1$H NMR (CDCl$_3$, 400.13MHz) Spectrum of Compound 18c

$^{13}$C NMR (CDCl$_3$, 100.61 MHz) Spectrum of Compound 18c

DEPT NMR (CDCl$_3$, 100.61 MHz) Spectrum of Compound 18c
$^1$H NMR (CDCl$_3$, 200.13MHz) Spectrum of Compound 20

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 20

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 20
$^1$H NMR (CD$_3$OD, 200.13MHz) Spectrum of Compound 21

$^{13}$C NMR (CD$_3$OD, 100.61 MHz) Spectrum of Compound 21

DEPT NMR (CD$_3$OD, 100.61 MHz) Spectrum of Compound 21
$^1$H NMR (CDCl$_3$, 400.13MHz) Spectrum of Compound A

$^{13}$C NMR (CDCl$_3$, 100.61 MHz) Spectrum of Compound A

DEPT NMR (CDCl$_3$, 100.61 MHz) Spectrum of Compound A
$^1$H NMR (CDCl$_3$, 400.13MHz) Spectrum of Compound 24

$^{13}$C NMR (CDCl$_3$, 100.61 MHz) Spectrum of Compound 24

DEPT NMR (CDCl$_3$, 100.61 MHz) Spectrum of Compound 24
$^1$H NMR (CDCl$_3$, 200.12 MHz) Spectrum of Compound 26a

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 26a

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 26a
$^{1}$H NMR (CDCl$_3$, 200.12 MHz) Spectrum of Compound 26b

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 26b

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 26b
$^1$H NMR (CDCl$_3$, 200.12MHz) Spectrum of Compound 26c

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 26c

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 26c
\(^1\)H NMR (CDCl\(_3\), 200.12MHz) Spectrum of Compound 26d

\(^1\)C NMR (CDCl\(_3\), 50.32 MHz) Spectrum of Compound 26d

DEPT NMR (CDCl\(_3\), 50.32 MHz) Spectrum of Compound 26d
$^1$H NMR (CDCl$_3$, 200.12 MHz) Spectrum of Compound 26e

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 26e

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 26e
$^1$H NMR (CDCl$_3$, 200.12 MHz) Spectrum of Compound 26f

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 26f

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 26f
$^1$H NMR (CDCl$_3$, 200.12MHz) Spectrum of Compound 27a

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 27a

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 27a
$^1$H NMR (CDCl$_3$, 200.12 MHz) Spectrum of Compound 27b

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 27b

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 27b
$^1$H NMR (CDCl$_3$, 200.12 MHz) Spectrum of Compound 28a

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 28a

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 28a
$^1$H NMR (CDCl$_3$, 200.12 MHz) Spectrum of Compound 28b

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 28b

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 28b
$^1$H NMR (CDCl$_3$, 200.12MHz) Spectrum of Compound 29a

$^{13}$C NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 29a

DEPT NMR (CDCl$_3$, 50.32 MHz) Spectrum of Compound 29a
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