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**Functionalization of 3,4,6-tri-*O*-acetyl-D-glucal
via Click Chemistry and Palladium-Catalyzed
Cross-Coupling Reactions**

**Funcionalização de 3,4,6-tri-*O*-acetil-D-glucal
via *Click Chemistry* e Reações de
Acoplamento Cruzado Catalizado por Paládio**

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Click Chemistry and Palladium-Catalyzed Cross-
Coupling Reactions**

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RESUMO

Shamim, A. "**Funcionalização de 3,4,6-tri-*O*-acetil-D-glucal via *Click Chemistry* e Reações de Acoplamento Cruzado Catalizado por Paládio**" 2017. 277p. Tese de Doutorado - Pós-Graduação em Química, Instituto de Química, Universidade de São Paulo, SP - Brasil.

A funcionalização de 3,4,6-tri-*O*-acetil-D-glucal foi realizada utilizando reações de acoplamento cruzado (Sonogashira e Stille), ciclo-adições de azida-alcino (*Click chemistry*) e ciclização nucleófila promovida por eletrófilo. Utilizando estas reações juntamente com as já referidas transformações de grupos funcionais e reações de rearranjo de Ferrier, as bibliotecas de compostos à base de glucal foram sintetizadas e observadas em algumas moléculas fluorescência e outras foram disponibilizadas para avaliação de atividade biológica. Na primeira parte, foram sintetizadas bibliotecas de derivados de bis- e tris-triazolil-glicosila a partir de 3,4,6-tri-*O*-acetil-D-glucal utilizando as reações acima mencionadas.

A segunda parte deste trabalho consiste em sintetizar uma biblioteca de derivados glucal de 2-alquinilo usando um acoplamento de Sonogashira livre de cobre e ligante, seguido por aplicações sintéticas destes alquinos glucais. A hidrostanação regioselectiva catalisada por paládio destes glucanos 2-alquinilo foi realizada utilizando hidreto de tributilestanho para gerar uma biblioteca de derivados estanil regioisoméricos de glucal. Além disso, estes derivados de 2-alquinil-glucal sintetizados na primeira parte também foram utilizados na ciclização nucleofílica *5-endo-dig* promovida por eletrófilos para proporcionar derivados de glucal bicíclicos.

Na parte final, os derivados de estanho de glucal foram utilizados para sintetizar bibliotecas de derivados de 2-alcenil glucal substituído. Esta parte inclui também transformações de grupos funcionais e acoplamentos cruzados (Stille e Sonogashira), bem como "*click chemistry*" para gerar bibliotecas de derivados de 2-alquenil-D-glucal alquinilo e triazolilo substituídos. Na maioria dos casos os produtos foram obtidos em rendimentos muito bons a excelentes que foram analisados utilizando RMN, Infra vermelho, espectrometria de massas de alta resolução e outras técnicas analíticas quando aplicável.

Palavras-chave: D-glucal, *Click Chemistry*, 1,2,3-Triazois, Acoplamento de Sonogashira, Ciclização de *5-endo-dig*, Hidrostanação.

ABSTRACT

Shamim, A. “**Functionalization of 3,4,6-tri-*O*-acetyl-D-glucal via Click Chemistry and Palladium-Catalyzed Cross-Coupling Reactions**” 2017. 277p. Ph.D. Thesis – Postgraduate Program in Chemistry, Institute of Chemistry, University of São Paulo, São Paulo, SP-Brazil.

Functionalization of 3,4,6-tri-*O*-acetyl-D-glucal has been performed using cross-coupling (Sonogashira and Stille) reactions, azide-alkyne cycloadditions (Click chemistry) and electrophile-promoted nucleophilic alkyne cyclizations. Using these reactions along with the already reported functional group transformations (FGT) and Ferrier rearrangement reactions, libraries of glucal-based compounds were synthesized with members of characteristic photophysical and potential biological properties. In the first part, the synthesis of libraries of bis- and tris-triazolyl glycosyl derivatives is described starting from 3,4,6-tri-*O*-acetyl-D-glucal using the above-mentioned reactions.

In the second part of this work, the synthesis of a library of 2-alkynyl glucal derivatives using a copper and ligand-free Sonogashira coupling, followed by synthetic applications of these glucal alkynes is reported. Palladium-catalyzed regioselective hydrostannation of these 2-alkynyl glucals was performed using tributyltin hydride to generate a library of regioisomeric stannyl derivatives of glucal. Moreover, these 2-alkynyl glucal derivatives synthesized in the first part were also used in electrophile-promoted nucleophilic *5-endo-dig* cyclization to afford bicyclic glucal derivatives.

In the final part, the use of stannyl derivatives of glucal to synthesize libraries of substituted 2-alkenyl glucal derivatives is described. This part also includes certain functional group transformations and cross-couplings (Stille and Sonogashira) as well as click chemistry to generate libraries of alkynyl and triazolyl substituted 2-alkenyl-D-glucal derivatives. In most of the cases, the products were obtained in very good to excellent yields and were analyzed using ^1H NMR, ^{13}C NMR, FTIR, HRMS, and other analytic techniques where applicable.

Keywords: D-glucal, Click chemistry, 1,2,3-Triazoles, Sonogashira coupling, *5-endo-dig* Cyclization, Hydrostannation.

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1. INTRODUCTION

1.1. Carbohydrates

Carbohydrates can be broadly defined as polyhydroxy aldehydes or polyhydroxy ketones and their derivatives or compounds that yield one of them upon hydrolysis. They are mostly composed of carbon, oxygen, and hydrogen and got their name because of the earlier observation that they have the general formula $C_n(H_2O)_m$ and that is why they appeared to be “hydrates of carbon”. Being the most abundant of all organic compounds in nature and the most important source of chemical energy for living organisms, they also perform a variety of different functions such as cell-cell recognition, defense against pathogens and as important structural components.¹ Carbohydrates are synthesized in green plants by *photosynthesis* - a process that uses solar energy to reduce, carbon dioxide with water. The overall equation can be written as follows:²

Simple carbohydrates are also known as sugars or saccharides (Latin *Saccharum*, Greek *Sakcharon*, sugar). Based on hydrolysis, carbohydrates can be classified as *monosaccharides*—the simplest carbohydrates that cannot be hydrolyzed further, *disaccharides*—those that yield two monosaccharides upon hydrolysis, *oligosaccharides*—carbohydrates that yield 2-10 monosaccharides upon hydrolysis, and *polysaccharides*—are those carbohydrates that yield more than 10 monosaccharides upon hydrolysis.³

Monosaccharides also known as the simple sugars, are the building blocks of carbohydrate chemistry. They can be polyhydroxy aldehydes (known as *aldoses*) or polyhydroxy ketones (known as *ketoses*). Based on the number of carbon atoms Monosaccharides can be classified as trioses, tetroses, pentoses, hexoses and heptoses having three, four, five, six and seven carbon atoms respectively. Therefore, a six-carbon polyhydroxy aldehyde such as D-glucose is an aldohexose, while a six-carbon polyhydroxy ketone such as D-fructose is a ketohexose. Glucose is the most abundant monosaccharide known, it occurs in fruits, plants, honey and animals blood in free form and is also combined with other sugars or species in the form of glycosides, disaccharides,

and polysaccharides. The naturally occurring form of glucose is D-glucose also known as “grape sugar” and is an important building block in organic synthesis.^{1d}

D and L notations are most commonly used to denote the configuration of a monosaccharide, such as D-glyceraldehyde and L-glyceraldehyde as shown in the Fischer projection (Figure 1).

Figure 1. Fischer projections of D- and L-glyceraldehyde.

In a Fischer projection, the carbonyl carbon also called the anomeric carbon is always placed on the top or as close to the top as possible. Glyceraldehyde is considered as a standard and all the monosaccharides are described either D or L based on the configuration of the penultimate carbon atom (the last chiral carbon from the carbonyl group). Therefore, based on the D and L notations of the glyceraldehyde, if the hydroxyl group on the penultimate carbon of a sugar is on the right, then the compound is a D-sugar. On the other hand, if the hydroxyl group on the penultimate carbon is on the left, then the compound is an L-sugar (Figure 2).³

Figure 2. Representation of D- and L-hexoses in Fischer projection.

It is important to mention that the carbonyl groups of sugars are usually combined with one of the hydroxyl group within the same molecule resulting in the formation of a cyclic hemiacetal or hemiketal. Usually, five and six membered rings are formed and are named furanose (glucofuranose) and pyranose (glucopyranose) respectively. For D-glucose, the two possible six-membered (pyranose) cyclic forms along with the equilibrium ratio are represented both in the Fischer projections and Haworth projections.

In the Fischer projections, if the resulting hydroxyl group from the alcohol and carbonyl reaction is on the right side of the molecule then it is an α -sugar while if it is on the left side then it is a β -sugar. Similarly, in the Haworth projections if the resulting hydroxyl is pointed above the ring then it is a β form while if it is directed below compared to the ring then it is an α form (Figure 3).³

Figure 3. Fischer and Haworth projections and equilibrium between the cyclic and open-chain form of D-glucose.

1.1.1. Glycosides

Glycosides are compounds in which a carbohydrate moiety (glycone) is linked to another group usually a noncarbohydrate (aglycone) through a glycosidic bond.⁴ A glycosidic bond is a bond in which a sugar is attached via its anomeric carbon to another group. Based on the glycosidic bond, a glycoside could be an *O*-glycoside, an *S*-glycoside (thioglycoside) an *N*-glycoside (glycosylamine), or a *C*-glycoside (or *C*-glycosyl compound) having *O*-, *S*-, *N*-, or *C*- glycosidic bond respectively. Glycosides are very common in nature and many have also been synthesized by chemists.⁵ Some well-known naturally occurring glycosides include cardiac glycosides derived from the foxglove plant *Digitalis purpurea*, having steroid as the aglycone part. Cardiac glycosides are poisonous and act on the contractile force of cardiac muscle, disrupting the function of the heart. These glycosides are found to bind with specific amino acids in a protein responsible for the cellular transportation of sodium and potassium ions. By disturbing the concentrations of ions in cells, as a result, the contractility of the cells and muscle increases. Thus due to

these cardiotonic effects certain amounts of cardiac glycosides have been historically used and are still being clinically used for the treatment of chronic heart failure and arrhythmias.⁶ Some cardiac glycosides have shown neuroprotective activity against ischemic stroke and there are examples of cardiac glycosides used clinically for congestive heart failure (Figure 4).⁷

Figure 4. Selected biologically potent cardiac glycosides.

Glycosides are very important compounds and play key roles in living organisms for example food is stored in the form of glycosides, poisons usually are bound to a carbohydrate molecule to be eliminated from the body, they act as cellular adhesives and many others are used as medications.⁸ The aglycone part in a glycoside could be another natural or synthetic group and therefore there are many types of glycosides based on the aglycone moiety. Some well-known types of glycosides include saponin glycosides, flavonoid glycosides, anthracene glycosides, coumarin glycosides and phenolic glycosides. Some examples of biologically important C-, N-, S-, and O-glycosides are shown in Figure 5 below:⁹

Figure 5. Biologically important examples of C-, O-, N- and S-glycosides.

Many other glycosides are found to have potential anticancer, antifungal, antitubercular and enzyme inhibitory activities and some are being used as drugs in the market.¹⁰ Carbohydrates (glycone) are incorporated into many drugs and other potential compounds via glycosylation to introduce hydrophilicity, to lower toxicity, and to enhance bioactivity.¹¹ The glycone part could also facilitate the delivery of a drug or biologically important compound into the desired part of the cell and by hydrolysis of the glycosidic bond the drug could be released.¹² Some of the important glycoside-based drugs include Baicalin (a flavonoid glycoside) an active component of a “medical food” that is used as therapy for osteoarthritis, Morphine-6-glucuronide (morphine based glycoside) used as drug for postoperative pain relief, and Canagliflozin and Ipragliflozin are antidiabetic drugs currently in use (Figure 6).¹³

Figure 6. Examples of glycoside-based drugs currently in use.

1.1.2. Glycals

Glycals are the unsaturated enol ether derivatives of sugars having a double bond between carbon atom 1 and 2 of the cyclic monosaccharide. Glycals act as glycosyl donors and acceptors¹⁴ and thus are often used for the synthesis of different types of glycosides, oligosaccharides, and other glycoconjugates. In addition, glycals have various other synthetic applications including the synthesis of natural products,¹⁵ enzyme inhibitors,¹⁶ chiral ligands,¹⁷ L-sugars,¹⁸ and butyrolactones.¹⁹

The most well-known glycal is D-glucal which was first synthesized in 1913, by Hermann Emil Fischer from D-glucose.²⁰ His method involves the reductive elimination of a glycosyl halide with zinc. D-glucal has been used by many synthetic chemistry groups to synthesize numerous biologically as well as industrially important natural and synthetic compounds.²¹ Due to the presence of chiral centers, its comparatively low cost and easily modifiable functionalities it is considered as one of the most well-known building blocks for the synthesis of natural and synthetic products of potential applications. The hydroxyl groups are usually protected with an acetyl, benzyl or another group to modify its solubility and reactivity based on the designed conditions. One of the most common protected forms of D-glucal is the 3,4,6-tri-*O*-acetyl-D-glucal also called peracetylated D-glucal, D-glucal-triacetate or simply acetylated D-glucal, in which the

three hydroxyl group of D-glucal are acetylated. The acetylated derivative of D-glucal can be easily synthesized from D-glucose by acylation of the corresponding hydroxyl groups and converted back to D-glucose with transesterification using acid or base (Scheme 1).²²

Scheme 1. Interconversion of D-glucose, D-glucal, and 3,4,6-tri-*O*-acetyl-D-glucal.

Most of these protected derivatives of D-glucal are available commercially, are solids, easy to handle, soluble in common organic solvents and stable for comparatively longer times. To show the scope of these glucal derivatives in natural product synthesis, a summary of selected natural products synthesized from D-glucal or its derivatives is presented in Figure 7 below;²³

Figure 7. Sketch of selected natural products synthesized from D-glucal derivatives.

We used 3,4,6-tri-*O*-acetyl-D-glucal as starting material in most parts of this work that was purchased from Sigma-Aldrich with the product name “tri-*O*-acetyl-D-glucal” (CAS # 2873-29-2) 98 % pure, in a 25 gram light protected high-density polyethylene bottle as a white solid (m. p. 53-55 °C). Its molecular weight is 272.25 g/mol, and specific rotation $[\alpha]_D^{25} -12^\circ$ (c 2, EtOH).

1.2. Palladium-catalyzed cross-coupling reactions

Generally, a cross-coupling reaction is a reaction in which a new carbon-carbon or carbon-heteroatom bond is formed usually by coupling an organic halide or triflate (R-X) with an organometallic reagent (RM) using a transition metal catalyst. When palladium metal is used as the catalyst then it's called as palladium-catalyzed cross-coupling reaction. The organic halide or triflate is also termed as the electrophilic partner because of its electrophilic nature while the organometallic reagent due to its nucleophilic nature is called the nucleophilic partner. Richard F. Heck, Akira Suzuki, and Ei-ichi Negishi won the 2010 chemistry Noble prize for their work on palladium-catalyzed cross-coupling reactions. A general equation for palladium-catalyzed cross-coupling reaction can be written as below:

The importance of cross-coupling reactions is enormous and this class of reactions are very well-studied and have a lot of applications in industries and synthetic organic chemistry laboratories.²⁴ Based on the identity of halide (RX) and organometallic reagent (RM) some well-known palladium-catalyzed cross-coupling reactions are classified as;

Negishi Reaction - between an organohalide and organozinc compound

Heck Reaction - between aryl halides and alkenes

Suzuki Reaction - between organoboron species and an aryl halide

Stille Reaction - between organostannanes and organohalides

Sonogashira Reaction - between alkynes and aryl halides, usually with copper as co-catalyst

Hiyama Reaction - between organosilicon compounds and organohalides

Buchwald-Hartwig amination - between amine and an aryl halide/phenol or thiol.

The general mechanism of palladium-catalyzed cross-coupling reaction involves an “oxidative addition” step where the organic electrophile (organohalide or triflate, RX) adds to the palladium (0) catalyst to make a palladium (II) complex where both R and X species of organohalide are incorporated into the palladium metal. It is important to mention here that the active palladium catalyst in cross-coupling reactions is palladium in its zero oxidation state, that is palladium (0), and when other palladium catalysts such as palladium (II) are used they are converted by a ligand to the active palladium (0) species in the reaction. Now the palladium (II) intermediate complex that is generated after the oxidative addition step, is comparatively less stable and is followed by either a “transmetallation” or “migratory insertion” step. In the transmetallation step an organometallic species ($R'M$) replaces its organic part R' , with the halide (X) on palladium generating another palladium (II) intermediate with two organic species attached to the palladium metal which finally via a reductive elimination step leads to the reduced palladium (0) metal for more reaction, and the two organic moieties are coupled to make the product ($R-R'$). It is usually proposed that there is a *trans* to *cis* isomerization of the palladium intermediate before the reductive elimination step. In the migratory insertion pathway, the palladium inserts between the carbon-hydrogen bond of a nucleophile such as an alkene eventually leading to a palladium (II) intermediate with both hydrogen and alkene attached to the palladium atom which finally via reductive elimination leads to the palladium (0) catalyst and the product (substituted alkene). A base is mostly required in palladium-catalyzed cross-coupling reaction because it helps generate the organometallic partner in some cases and also it stabilizes the palladium intermediates involved. A generalized mechanistic cycle has been presented in Figure 8.²⁵

Figure 8. General mechanistic cycle for palladium-catalyzed cross-coupling reaction.

Among the palladium-catalyzed cross-coupling reactions, in our work, we mostly used the Sonogashira coupling with one case of Stille coupling to generate important glucal intermediates and final products. Therefore, we will briefly discuss Sonogashira and Stille coupling reactions with their importance in organic synthesis and their mechanistic studies.

1.2.1. Stille coupling

The palladium-catalyzed (or other transition metal-catalyzed) reaction of an organic electrophile (organohalide or triflate) with the organotin reagent is called Stille coupling. The reaction was named after Professor J. K. Stille who developed the comparatively mild and more applicable method (in 1978)²⁶ for this reaction although the ground work was done by Colin Eaborn, Toshihiko Migita, and Masanori Kosugi in 1976 and 1977.²⁷ Due to its mild reaction conditions, tolerance to a wide range of functionalities and easily preparable coupling partners, Stille coupling is one of the most widely used palladium-catalyzed C-C coupling reaction. Besides being an efficient intermolecular carbon-carbon bond forming reaction, the Stille reaction has been applied intramolecularly by various groups to generate carbocyclic and heterocyclic rings.²⁸ This intramolecular Stille coupling resulted in cyclic ring structures of medium to large sizes that are potential natural products and synthetically important compounds.²⁹ The mechanism consists of the same steps as described in the general mechanistic cycle

(Figure 8), where after the oxidative addition, organotin reagent replaces its organic moiety with a halide or triflate from the palladium complex in the transmetallation step. This is then followed by the same reductive elimination to generate the coupled product and recycle the palladium catalyst (Figure 9).

Figure 9. Generally proposed mechanistic cycle for Stille coupling.

Hydrostannation of alkynes is one of the widely used methods to generate vinyl stannane derivative that can subsequently be coupled with proper electrophilic species to make carbon-carbon bonds or they may be substituted by another easily replaceable groups or atoms (halide or triflate) that can then be further used in the next steps. Some selected examples of Stille coupling reaction to generate cyclic structure of potential natural products such as Dynemicin (an anticancer antibiotic) and Rapamycin (an antiaging and immunosuppressant) are presented in figure 10 below:³⁰

Figure 10. Synthetic steps involving Stille coupling in the total synthesis of selected natural products.

1.2.2. Sonogashira coupling

The Sonogashira coupling reaction was developed in 1975 by Kenkichi Sonogashira.³¹ It is currently one of the most widely used methods to synthesize substituted alkynes, especially in total synthesis, due to its versatility, ease, and broad applicability. It requires an organic electrophile (vinyl or aryl halide or triflate) to couple with a terminal alkyne in the presence of palladium catalyst, a base and usually a copper (I) salt as a cocatalyst.

The mechanistic cycle consists of the same oxidative addition, transmetalation and reductive elimination steps as mentioned in the general mechanism but here the organometallic reagent is an alkynyl cuprate that is generated by reaction of a copper (I) salt with the terminal alkyne in the presence of a base via a cyclic pathway also called as copper-catalyzed cycle. In this copper-catalyzed cycle, the copper makes a complex with the triple bond in order to make the terminal hydrogen more acidic for the base to remove it (Figure 11).

Figure 11. Proposed mechanistic cycles for Sonogashira coupling with copper as cocatalyst.

In the copper-free reaction after oxidative addition, the alkyne substitutes a ligand from the palladium (II) complex and the triple bond makes a kind of chelation with palladium metal. This chelation of the triple bond with palladium makes the terminal hydrogen of alkyne more acidic thus facilitates its removal by the base in the next step (Figure 12). The final step is the reductive elimination resulting in the production of substituted alkyne and the palladium (0) catalyst is recycled for more reaction.³²

Figure 12. Proposed mechanistic cycle for copper-free Sonogashira coupling.

The convenience of Sonogashira coupling coupled with the recent modifications such as copper and/or ligand-free conditions make it one of the most reliable route to

generate carbon-carbon bond in very complex and delicate systems. Many biologically important complex compounds such as Phorbaside A (a cytotoxic marine macrolide), Kedarcidin (a chromoprotein antitumor antibiotic), Calicheamicin (an enediyne antitumor antibiotic) and many others have been synthesized using Sonogashira reaction as one of the major steps (Figure 13).³³

Figure 13. Examples of selected natural products that are synthesized using Sonogashira coupling as one of the major steps.

1.3. Click chemistry

“Click chemistry” is a term used for a group of reactions that need simple reaction conditions, are fast, usually insensitive to water, generate minimal and inoffensive byproducts, have high yields, are commonly stereo- and regiospecific and versatile. These characteristics are common in reactions that usually occurs in living organisms where complex compounds are made in a simple and moderate way with minimal byproducts. The term “click chemistry” was first introduced by Barry Sharpless in 1999 at the 217th American Chemical Society national meeting, since then the term “click chemistry” or “click reaction” has become quite popular and has been used considerably in numerous publications.³⁴ This concept was used as a tactic by Sharpless to link the already available building blocks via click reactions, for quick drug development in order to avoid the slow

conventional drug discovery process. Click reactions include numerous powerful linking reactions but generally can be classified into the following major classes:

Cycloadditions - mainly 1,3-dipolar cycloadditions, but also include hetero-Diels-Alder cycloadditions.

Nucleophilic ring-openings - include the opening of strained heterocyclic rings (epoxides, aziridines, etc.).

Carbonyl chemistry (non-aldol type) - include the formation of aromatic heterocycles, ureas, thioureas, hydrazones, amides, etc.

Addition to C-C multiple bonds - examples include dihydroxylations, epoxidations, some Michael additions, etc.

Among the various types of click reactions, cycloadditions, especially Cu(I)-catalyzed Huisgen 1,3-dipolar cycloaddition of an azide with an alkyne to make 1,4-substituted, 1,2,3-triazoles, are the most used and well-studied.³⁵ These copper-catalyzed azide-alkyne cycloadditions (CuAAC) were first reported independently by the research groups of Sharpless³⁶ and of Meldal³⁷ in 2002, represents the catalyzed Huisgen 1,3-dipolar cycloadditions. The Huisgen 1,3-dipolar cycloadditions studied and investigated by Huisgen³⁸ in 1963, gives a mixture of the 1,4 and 1,5-disubstituted products. On the other hand, the CuAAC reaction is regiospecific generating only the 1,4-disubstituted triazole products and are thus in complete accordance with all the criteria of click chemistry (Figure 14). This reaction requires an azide (usually organic azide), an alkyne (most often a terminal), a Cu(I) species and a base or ligand in an organic or inorganic solvent.

Huisgen's 1,3-dipolar cycloaddition

CuAAC reaction

Figure 14. Representation of Huisgen's 1,3-dipolar cycloaddition and CuAAC reaction.

The proposed mechanism for this reaction involves the removal of the terminal alkyne hydrogen that is most probably made more acidic by the presence of a copper species, by a base to generate a copper acetylide intermediate. The copper acetylide intermediate then proceeds via the nucleophilic addition of the azide nitrogen to the copper atom to make another intermediate where both the alkyne and azide are attached to the same copper atom. Then a displacement of ligand from copper and cyclization of the azide nitrogen makes a cyclic intermediate which eventually rearranges and loses the copper nitrogen bond to generate copper substituted triazole ring. The final step is the displacement of the copper moiety to afford the copper catalyst and the 1,2,3-triazole product in the presence of a hydrogen source (Figure 15).³⁹

Figure 15. Proposed mechanistic cycle for CuAAC reaction.

A wide range of copper(I) salts (iodide, bromide, chloride, acetate etc.) and coordination complexes of copper(I) can be used as a catalyst for this reaction. With a copper(II) salt a mild reducing agent is commonly used to reduce the copper(II) to the active copper(I) species.³⁶ Copper(0) compounds (turnings, powder, nanoparticles, etc.) which usually forms copper(I) species on their surface have also been applied in this reaction.⁴⁰ Similarly, a wide range of ligands including nitrogen-based (usually polydentate) ligands, some phosphorous based ligands and carboxylates have been used under different circumstances but the amine ligands are usually found more effective.⁴¹ Another remarkable feature of the CuAAC reaction is the range of solvents that can be used in this reaction. This includes the non-polar aprotic solvents (toluene etc.), the polar aprotic solvents (acetonitrile, dichloromethane, THF, DMF, DMSO, etc.), the polar protic

solvents (alcohols and aqueous solvents) and mixtures of solvents.³⁷⁻⁴¹ The easy preparation of both the alkyne and azide and their stability in the wide reaction conditions along with the regiospecificity makes this reaction one of the most efficient processes in the synthesis of pharmaceutically, and industrially important compounds.

1.3.1. Triazoles

Triazoles are heterocyclic compounds with a five-membered ring having three nitrogen and two carbon atoms and a molecular formula $C_2H_3N_3$. They are aromatic heterocycles and can be classified into two types of isomers namely 1,2,3-triazoles and 1,2,4-triazoles depending on the relative positions of the three nitrogen atoms. The position of a proton on a nitrogen is sometimes denoted by the number of the nitrogen atom to which it is attached, followed by an italic symbol for hydrogen-like *1H*, *2H* etc. as shown in Figure 16 below:

Figure 16. Different isomeric forms of triazoles with chemical names.

Triazoles are used as antifungal drugs such as Voriconazole, Fluconazole, Pramiconazole, Ravuconazole, etc.⁴² Many substituted triazoles have been found to possess potential biological, photophysical and medicinal applications and are extensively studied in pharmaceutical, synthetic and material chemistry (Figure 17).⁴³ They are usually synthesized by the selective and mild reaction known as the azide-alkyne Huisgen cycloaddition as mentioned earlier in Section 1.3. Triazoles are very stable functional groups and mimic the properties of various other functional moieties that are present in biomolecules.⁴⁴ Here we will focus on the 1,4- substituted 1,2,3-triazoles that are among the most well-studied and widely used nitrogen heterocycles and can be easily obtained using the copper-catalyzed azide-alkyne cycloaddition reaction.

Figure 17. Selected biologically important triazole derivatives.

1.3.2. 1,4-substituted 1,2,3-triazoles

1,2,3-Triazoles represent the most widely studied triazoles having great potential in all the major areas of chemistry. Due to the bioisosteric potential of this ring, it is found to act like an amide bond due to its structural similarity to an amide moiety and thus mimics an amide group in its properties.⁴⁴⁻⁴⁶ Like the amide N-H bond, the polarized C(5)-H bond of triazole ring can act as a hydrogen bonding donor, on the other hand, the electrophilic C-4 shows somewhat similar electronic behavior like the carbonyl carbon. Moreover, the hydrogen bonding donor and acceptor properties of a triazole ring are comparatively higher than that of an amide group due to its comparatively larger overall dipolar moment.⁴⁵ Thus the potential of triazole rings as peptidomimetics is currently a hot topic in drug discovery and it has been observed that they are effective surrogates of dipeptides in α -helical structures and some derivatives closely mimic β -strands. Additionally, it is also predicted that triazole ring may mimic the acyl-phosphate, *trans*-olefinic moieties and other heterocyclic structures of drugs and other biologically important compounds (Figure 18).⁴⁶

Figure 18. Representation of the bioisosteric potential of triazole ring with important moieties of biomolecules.

Due to these structural similarities with potential biomolecules and other medicinal compounds, the triazole ring has been incorporated into many compounds and drugs to enhance their biological properties and interactions with cellular moieties, some selected examples of bioactive compounds and drugs having a triazole ring are presented in Figure 19.⁴⁷

Figure 19. Examples of 1,2,3-triazole-based drugs and bioactive compounds.

Besides, the triazole ring is also very often used as a linker or spacer to join two moieties to generate multi-target drugs and bidentate inhibitors such as HIV protease inhibitors, protein tyrosine phosphatase inhibitors, matrix metalloprotease inhibitors and inhibitors of inflammation-related enzymes.⁴⁸ Additionally, the triazole ring has been used by many groups to join various other moieties like lipids to proteins, fluorescent dyes to proteins, sugars to drugs, sugars to proteins, sugars to sugars and many others generating dimers, trimers, and polymers of both cyclic and open-chain structures having potential biological and photophysical applications (Figure 20).⁴⁹

Figure 20. Examples of selected compounds where triazole ring is used as a linker.

1.3.3. Glucal-derived 1,4-substituted 1,2,3-Triazoles

Click chemistry has been widely used and has a major impact on carbohydrate chemistry. Many examples can be found where a sugar moiety has been linked to a central core (peptide, drug, lipid, sugar, etc.) or any functional group is linked to a sugar via a triazole ring. This combination of a sugar with another moiety via a triazole ring can improve the hydrophilicity, bioavailability and the safety profile of the nonsugar moieties. Libraries of biologically potential compounds have thus been prepared using the simple click chemistry concept including potential antibiotics, antitumor, antimicrobials, antibacterial, anticancer and antitubercular agents as mentioned earlier. Besides, the triazole-crafted sugars moieties have also shown potential applications in

nanotechnology, and polymer, pharmaceutical and synthetic organic chemistry (Figure 21).⁵⁰

Figure 21. Selected examples of bioactive triazole-crafted glycoside derivatives.

Inspired by the biological and medicinal potential of glucal-based 1,4-substituted-1,2,3-triazole derivatives we explored different synthetic reactions to functionalize 3,4,6-tri-*O*-acetyl-D-glucal and generated libraries of mono-, bis- and tris-triazole derivatives of glucal.

1.4. Ferrier Rearrangement

Discovered by an English chemist Robert J. Ferrier in 1962,⁵¹ Ferrier rearrangement is generally a nucleophilic substitution reaction combined with allylic rearrangement usually in a glycal compound. This reaction involves the introduction of a nucleophile on the anomeric carbon of a glycal with allylic rearrangement. This reaction is not restricted only to glycals and can be used in any system having a heteroatom (with a lone pair of electrons) attached to a double bond and properly-positioned leaving group.⁵² It has been used mostly in glycals for the synthesis of glycosides by combining a nucleophile and a glycal in the presence of a Lewis acid.

The mechanism is proposed to start with the activation of the Leaving group LG (usually an acetyl or tosyl group) by the Lewis acid (LA) aided by the lone pair of electrons on the oxygen atom of the ring to generate an allylic oxocarbenium ion. This oxocarbenium ion species, because of their short life were believed to be hypothetical species until 2016 when A. Martin et al.⁵³ generated and stabilized such species using liquid superacid (HF/SbF₅) and analyzed them using NMR at low temperatures. The

oxocarbenium ion is then attacked by the nucleophile to afford usually the C-1 substituted product. There are however some complications present that can affect the diastereoselectivity and regioselectivity of the product, depending on the nature and stereochemistry of the LG, R₁, and R₂ as well as the nature of the nucleophile (Nu) (Figure 22).⁵⁴

Figure 22. The general mechanism of Ferrier rearrangement in glycols.

A wide range of Lewis acids including BF₃.OEt₂, SnCl₄, ZnCl₂, Yb (OTf)₃, FeCl₃, Sc (OTf)₃, InCl₃, BiCl₃, etc. with a variety of nucleophiles have been used to perform this reaction and generate glycoside products of great applications.⁵⁵ This is one the most used method in synthetic chemistry and specifically in carbohydrate chemistry to convert glycols to highly useful 2,3-unsaturated glycosides that can further be transformed into a variety of useful intermediates. Our group has previously used potassium salts of alkynyl trifluoroborate as nucleophiles with etherated boron trifluoride as Lewis acid in acetonitrile to perform highly stereoselective C-glycosylation (Ferrier rearrangement) on 3,4,6-tri-*O*-acetyl-D-glucal generating the major α-alkyne glycoside products with good yields (Scheme 2).⁵⁶

Scheme 2. Stereoselective C-glycosylation (C-alkynylation) of D-glucal with potassium alkynyltrifluoroborates.

In connection with this work and that of other groups on D-glucal derivatives, and inspired by the numerous applications of glycosyl-based triazole compounds we further

explored this area using 3,4,6-tri-*O*-acetyl and its derivatives as starting reagents. We were successful to obtain libraries of important triazolyl, alkynyl, alkenyl, and stannyl substituted glucal compounds as well as interesting and important glucal based intermediates, and bicyclic glucal compounds. Our work is mainly based on 3,4,6-tri-*O*-acetyl and its subsequent derivatives to functionalize them using click chemistry (CuAAC) reaction, Sonogashira coupling, hydrostannation, Stille coupling, nucleophilic *5-endo-dig* cyclization, Tsuji-Trost type azidation and functional group transformations. The details of the methodologies that we applied in our work are discussed in Section 3 (Results and Discussions) and the procedures that we used are mentioned in Section 7. The products were analyzed using the required and applicable analytical techniques (Section 6), structures of the synthesized compounds were elucidated (Section 7) using mostly ^1H NMR and ^{13}C NMR (Section 8), and other analytical techniques where applicable.

2. OBJECTIVES

The main objectives of our work can be categorized into two parts. First, the synthesis of glucal-based triazole derivatives using the main “Click reaction” i.e. CuAAC along with other reactions such as Ferrier rearrangement, Tsuji-Trost azidation, and functional group transformations. The second part is the synthesis of 2-alkynyl-D-glucal derivatives using copper- and ligand-free Sonogashira coupling, and the synthetic evaluations of these 2-alkynyl-D-glucal derivatives. These synthetic evaluations are 5-*endo-dig* cyclization, hydrostannation, Stille coupling, Sonogashira coupling and CuAAC reaction to obtain aryl, alkynyl and triazolyl substituted alkenyl derivatives of D-glucal, respectively.

First, we synthesized libraries of glucal-based triazoles using “Click chemistry” specifically the copper-catalyzed azide-alkyne cycloaddition (CuAAC) reactions (Scheme 3).

Scheme 3. Synthesis of 1,6-bis-triazolyl substituted glycosyl derivatives from 3,4,6-tri-*O*-acetyl-D-glucal.

This part includes the C-alkynylation (Ferrier rearrangement) and a Click (CuAAC) reaction starting with 3,4,6-tri-*O*-acetyl-D-glucal, followed by functional group transformations (FGT) and another Click reaction to obtain 1,6-bis-triazolyl glycosyl derivatives (Scheme 3). Similarly, the C-alkynylation and Click reaction of 3,4,6-tri-*O*-acetyl-D-glucal can also be followed by a Tsuji-Trost type allylic azidation and a subsequent Click reaction to generate regioisomeric 1,2- and 1,4-bis-triazolyl glycosyl derivatives (Scheme 4).

Scheme 4. Synthesis of 1,2- and 1,4-bis-triazolyl substituted glucal derivatives.

It also includes the functional group transformation of the bis-triazolyl glycosyl compounds synthesized in Scheme 4, and a third Click (CuAAC) reaction to afford the regioisomeric 1,2,6- and 1,4,6-tris-triazolyl glycosyl compounds (Scheme 5).

Scheme 5. Synthesis of 1,2,6- and 1,4,6-tris-triazolyl substituted glucal derivatives.

The second part was to perform a copper- and ligand-free Sonogashira coupling preceded by iodination of 3,4,6-tri-*O*-acetyl-D-glucal to synthesize 2-alkynyl glucal derivatives. This was then followed by synthetic evaluation of these synthesized 2-alkynyl-D-glucal derivatives that includes palladium-catalyzed hydrostannation and gold-catalyzed 5-*endo-dig* cyclization to obtain stannyl- and bicyclic glucal derivatives, respectively (Scheme 6).

Scheme 6. Synthesis of a stannyl-substituted alkenyl- and bicyclic glucal derivatives.

The stannyl derivatives of glucal prepared in Scheme 6 are intended to be used in Stille coupling, and iodination followed by Sonogashira coupling and CuAAC reaction to synthesize aryl and triazolyl substituted alkenyl derivatives of D-glucal, respectively (Scheme 7).

Scheme 7. Synthesis of triazolyl- and aryl substituted alkenyl derivatives of D-glucal.

3. RESULTS AND DISCUSSION

3.1. Synthesis of 1,6-bis-triazolyl glycoside derivatives

Inspired by the methods developed in our laboratory for the diastereoselective synthesis of *C*-alkynyl glycosides, followed by some functionalizations,^{56, 57} we further evaluated the synthetic applications of the synthesized glycosyl derivatives. These methods utilize 3,4,6-tri-*O*-acetyl-D-glucal **1** as the glycosyl reagent and include Ferrier rearrangement using potassium salts of alkynyl-trifluoroborate as nucleophiles, etherated boron trifluoride as the Lewis acid in acetonitrile at -45 to 0 °C for 10-30 minutes to generate *C*-alkynyl glycoside derivatives. The diastereoselectivity of this reaction is very high and the ratio of **α** diastereomer to that of the **β** is up to 98:2. Further reactions performed previously include the click reactions of the trimethylsilyl-protected alkynyl glycoside derivative **2a** to generate 1-triazolyl glycoside derivatives **3**.⁵⁷ This was then followed by functional group manipulations to afford the product of interest, the 6-mesylate derivative of the triazolyl glycoside **4**.⁵⁸ We followed all the above-mentioned reactions starting with trimethylsilyl protected potassium salt of ethynyl trifluoroborate and 3,4,6-tri-*O*-acetyl-D-glucal to generate the corresponding alkynyl glycosides **2a** and **2b**. Then the **α** diastereomer **2a** (the major one) was isolated via flash chromatography and as mentioned was used in the CuAAC reaction using phenyl azide to synthesize the corresponding triazolyl derivative **3**, followed by the functional group transformations (base catalyzed transesterification and mesylation) to generate the mesylate **4** (Scheme 8).

Scheme 8. Synthesis of Glycosyl mesylate derivative **4** starting from 3,4,6-tri-*O*-acetyl-D-glucal.

Having obtained the mesylate, we performed the nucleophilic substitution reaction to convert this mesylate into the corresponding glycosyl azide **5** using sodium azide in THF and water (2:1) under microwave irradiation. The reaction was performed at 180 °C for 30 minutes to afford the product with 85 % yield (Scheme 9).

Scheme 9. Synthesis of glycosyl azide **5** from the corresponding glycosyl mesylate **4**.

In the next step, different terminal alkynes were treated with the glycosyl azide **5** to synthesize a library of 1,6-bis-triazolyl glycoside derivatives **6a-o** using the copper-catalyzed azide-alkyne cycloaddition (CuAAC) reaction.⁵⁹ Copper iodide (10 mol%) was used as the catalyst with PMDETA (*N, N, N', N'', N'''*-pentamethyldiethylenetriamine (1 eq.) as a base at 100 °C, under microwave irradiation for 10-20 minutes (Table 1).

Table 1. Synthesis of 1,6-bis-triazolyl glycoside derivative via CuAAC reaction

Entry	Alkyne	Product	Yield (%)
1			93
2			96
3			85

4		6d	94
5		6e	90
6		6f	87
7		6g	92
8		6h	90
9		6i	90
10		6j	92
11		6k	94
12		6l	95

13		6m	70
14 ^{a,b}		6n	45 ^c
15		6o	87

a = the temperature used was 150 °C. b = Reaction time = 40 min. c = Monomer (**6m**) = 20%

The formation of the bis-triazole product was indicated by the presence of a second peak around 8 ppm in ^1H NMR due to the hydrogen of the second triazole ring and by the presence of hydrogens of the alkyne moiety that is now incorporated into the product. This is also supported by the corresponding peaks of carbon atoms in ^{13}C NMR (Section 8) and by the m/z value in HRMS (Section 7). To discuss briefly, here we selected the region of interest (6-8.4 ppm) of ^1H NMR spectra of compound **5** (the azide) and **6j** (the triazole product from azide **5** with 4-ethynylaniline) for comparative study. In the ^1H NMR spectrum of **5** in Figure 23-A, the peak for the hydrogen of triazole ring can be observed as a singlet at 8.00 ppm (1H), that of the phenyl ring are between 7.7-7.3 ppm (5H), and the hydrogens of the double bond of glycosyl rings are at 6.15-5.95 ppm (2H).

Figure 23. ^1H NMR spectra of Compound **5** (A) and Compound **6j** (B).

When we performed the ^1H NMR for product **6j** and compare it with the spectrum of azide **5** (Figure 23-A), two singlets were observed at 8.17 ppm (1H) and 8.10 ppm (1H) (Figure 23-B) indicating the presence of two triazole rings. We also observed two doublets with an integration of two hydrogens each, at 7.71 ppm and 6.2 ppm,

respectively that shows the presence of the aniline ring. The hydrogens of the phenyl ring and those of the double bond of glycosyl ring can be observed at around 7.5 ppm and 6.2-5.95 ppm, respectively. The complete (^1H NMR and ^{13}C NMR) spectra of these two compounds and all the bis-triazolyl glycosyl compounds shown in Table 1 are given in Section 8 (p. 127-141) and are interpreted in Section 7 (p. 74-80).

3.2. Photophysical studies of the fluorescent compounds (6g and 6h)

Thin layer chromatography of compounds **6g** and **6h**, when analyzed using the 365 nm UV light, showed blue fluorescence, which was then confirmed and further investigated by analysis on a fluorescence spectrophotometer. In the absorbance spectra of compounds **6g** and **6h**, we observed broadband absorption in the UV range (Figures 24-A and 24-B, respectively). For compound **6g**, the UV absorption ranged from 250 nm to 360 nm and for compound **6h** from 260 nm to 330 nm. Compound **6g** clearly showed an absorption peak (λ_{max}) at 262 nm with two small peaks at around 290 nm and 306 nm, while compound **6h** showed a broad band with two peaks at around 266 nm and 302 nm. As the peak of maximum absorption for compound **6g** is at 262 nm and as the difference of the two absorption peaks for compound **6h** is minimal, we decided to fix the excitation wavelength of the emission spectra at 260 nm.

Figure 24. The UV absorption spectra of compounds **6g** (A) and **6h** (B) in comparison with a blank spectrum (DMSO).

From the emission spectra (Figure 25), both compounds showed a single long band (λ_{em}) at 336 nm and 367 nm (**6g** and **6h**, respectively). Here, the results are shown only for the most diluted solutions because both compounds showed overload measurements in the emission band from 10⁻² M to 10⁻⁴ M concentrations, indicating a high-intensity fluorescence emission. These results suggest that these compounds can be

applied as chemical sensors in *in vitro* assays due their fluorescent characteristics at low concentrations.⁶⁰

Figure 25. Fluorescence spectra for compounds **6g** and **6h**.

In general, fluorescent molecules have been considered suitable to be employed as fluorescent sensors due to their capacity to respond to external stimuli and to be distinguishable at a specific wavelength.⁶¹ From these results, we expect that the triazole derived glycosyl compounds **6g** and **6h** could be applied as biosensors since triazole derived fluorescent compounds have already been found as chemosensors for metal ions and proteins.^{60, 62} This idea of linking fluorescent alkynes with glucal-based azides to synthesize fluorescent glucal-derived triazoles could be of potential significance in biochemistry and analytical chemistry for developing potential compounds that can be analyzed by fluorescence spectroscopy.

3.3. Synthesis of 1,2- and 1,4-bis-triazolyl glycoside derivatives

Bis-triazole derivatives of D-glucal were synthesized starting from 3,4,6-tri-*O*-acetyl-D-glucal **1**. This was then followed by the synthesis of tris-triazolyl glycoside derivatives using functional group modifications and the click (CuAAC) reaction. The synthesis of glucal-based bis-triazole derivatives includes Ferrier rearrangement (to obtain glucal alkynes **2** and click reaction to obtain the glycosyl-triazoles **3** as already mentioned in Scheme 13. The *C*-alkynyl glycoside derivatives **2a** and **2b** are separable by flash chromatography and the major diastereomer **a** (ratio α : β up to 98:2) was used in the next step with different organic azides to afford glycosyl triazoles **3**. The glycosyl triazoles **3**, were then used in palladium-catalyzed Tsuji-Trost type allylic azidation of

the corresponding allylic acetates to obtain regioisomeric glucal-based allylic azides **7a** and **7b** (Scheme 10).

Scheme 10. Synthesis of glucal-based allylic azide regioisomers from 3,4,6-tri-*O*-acetyl-D-glucal.

Isolation of the two regioisomeric azides **7a** and **7b** using flash chromatography was not successful and we were also unable to find out the ratio of each pair of regioisomers using gas chromatography. Therefore, we used both the regioisomeric azides in the next step that is the copper-catalyzed azide-alkyne cycloaddition reaction. It was found that the pair of regioisomeric bis-triazolyl glycosyl derivatives **8a** and **8b** were, however, separable through flash chromatography. Thus, a library of 1,2- and 1,4-bis-triazolyl glycosyl derivatives was synthesized, the products were purified using flash chromatography and were analyzed using NMR, IR, and HRMS. A range of terminal alkynes including alkyl, cycloalkyl, and aryl alkynes was used with different glycosyl azides in the presence of copper iodide (7 mol%) as catalyst, PMDETA (1.2 eq.) as the base in DMF, at 60 °C for 2 to 4 hours to obtain a library of bis-triazolyl glycosyl derivatives (Table 2).

Table 2. Synthesis of bis-triazole glycosyl derivatives via click reaction of glucal azides

Entry	Glucal Azide (R)	Alkyne	Product (a: b: c)	Yield ^a (%)
1			 60 : 40	79
2			 60 : 40	77
3			 69 : 31	81
4			 58 : 42	78

5			76
		70 : 30	
6			75
		68 : 32	
7			82
		61 : 39	
8			80 ^b
		24 : 42 : 34	

a = isolated combined yield of the regioisomers, b = reflux conditions (in the azidation step) and 2.5 equivalents of sodium azide were used.

The stereoselectivity of the palladium catalyzed allylic substitution reactions is well-studied and elaborated by many groups and is found to be affected by the palladium catalyst used, the solvent system, substituents on the allylic system, the nature of the leaving group (LG), the nature and concentration of the nucleophile (Nu) and temperature.⁶³ Under normal reaction conditions, the commonly observed products are the allylic regioisomers with the new nucleophile added from the same side as the leaving group was attached. Here, in most cases for the bis-triazolyl glycosyl products (entries 1-7, Table 2) we also observed the same stereoselectivity that is the azide adds from the same side where the acetate was attached. However, in one case (entry 8, Table 2) where higher temperatures (reflux conditions) and comparatively higher concentrations of sodium azide (2.5 equivalents) were used in the azidation step, it was observed that the products also contain one compound with inversion of configuration at C-4 as confirmed by the single-crystal X-ray diffraction analysis (Figure 26, Orthorhombic with $P2_12_12_1$

space group). It is important to mention here that as we could not isolate the allylic glucal azides so we rely our observations on the corresponding triazole derivatives and therefore the stereochemistry is also based on the triazole products **8**.

Figure 26. ORTEP diagram of the tris-triazolyl glycosyl compound **8c-8**.

The compound **8c-8** (entry 8, Table 2) is an epimer of **8a-8** with the opposite (inversion of) configuration at C-4 of the glycosyl ring. This indicates that higher temperatures and a higher concentration of sodium azide in the Tsuji-Trost type azidation of allylic acetates effect the stereoselectivity of the reaction. To avoid this complication the temperature was kept at 50 °C in the azidation step and lesser quantities of sodium azide (1.2 eq.) were used and the reaction was quenched as soon as the starting material disappeared (TLC monitoring). On the other hand, this could be used as an opportunity to make the epimers of such compounds using temperature and/or concentration variations. From the isolated yields of the bis-triazolyl glycosyl products the ratio of regioisomer **a** to **b** was roughly 3:2 and was in accordance to the one reported in the literature.⁶³ As we were interested in both the regioisomers of bis-triazolyl glycosyl compounds so we did not use other palladium catalysts or ligands to improve the regioselectivity as reported by many groups.⁶⁴

The structures of bis-triazolyl glycosides were confirmed by the COSY-NMR analysis of both or one of the regioisomers of each pair and with the XRD analysis of

8c- 8. Although the complete ^1H NMR, ^{13}C NMR and COSY-NMR spectra are given for these regioisomeric bis- triazolyl glycoside derivatives in Section 8 (p.142-167), here, we will compare the COSY-NMR spectrum of the two selected regioisomers **8a-2** and **8b-2** in details and confirm the structure of each regioisomer. As it is obvious if hydrogens couple in COSY-NMR it means they are attached to the adjacent carbon atoms. The region of interest of COSY-NMR (4-8 ppm) for both regioisomers that is **8a-2** and **8b-2**, is presented in Figure 27. In Figure 27-A the COSY spectrum of **8a-2** is shown in which the lower most rectangle A shows the coupling of the phenyl ring hydrogens H -10 and H -14 (at around 7.75 ppm) with H -11, 12 and 13 (around 7.52 ppm). The coupling of the hydrogen on sp^2 carbons of the glucal ring i.e. H -2 and H -3 are represented by rectangle B. The hydrogen on anomeric carbon (H -1, at around 5.75 ppm) shows coupling with the hydrogen on the sp^2 carbon (H -2, at around 6.5 ppm) of the ring as represented by rectangle C. Similarly, rectangle D shows the coupling between hydrogen on the other sp^2 carbon (H -3, at around 6.15 ppm) of the glycosyl ring with the hydrogen on carbon attached to the triazole nitrogen (H -4, at around 5.35 ppm), while rectangle E shows the coupling of hydrogens on C -4 with the one on C -5 (H -5, 4.2 ppm) of the ring.

(A)

Figure 27. COSY-NMR Spectra of compound **8a-2** (A) and **8b-2** (B).

Figure 27-B shows the COSY spectrum of compound **8b-2**, and it can be observed that here the phenyl hydrogens *H*-10 and 14 are coupling with *H*-12, 13 and 14 (rectangle F, Figure 27-B) just like those in the case of compound **8a-2** (rectangle A, Figure 27-A). The coupling of the hydrogens on the sp^2 carbons (*H*-3 and *H*-4) is shown by rectangle G. The characteristic couplings of *H*-2 (5.73) with *H*-3 (6.3 ppm) and *H*-1 (5.38 ppm) are represented by rectangle H and I, respectively. Similarly, the couplings of *H*-5 (4.5 ppm) with the two hydrogens on *C*-6 *H*-6a (4.59 ppm) and *H*-6b (4.2 ppm) are shown by rectangle J and K, respectively. By these coupling correlations, we can confirm the relative positions of the hydrogen atoms and thus can elucidate the structure of the regioisomers.

3.4. Synthesis of 1,2,6- and 1,4,6-tris-triazolyl glycoside derivatives

The synthetic scope of these bis-triazolyl glycosyl derivatives was explored using **8a-1** and **8b-1** as representative compounds to synthesize tris-triazolyl glycosyl compounds **12**. This process consists of functional group transformations including base-catalyzed transesterification, mesylation, and nucleophilic azidation. In the first step, we used base-catalyzed transesterification of the acetate group of **8a-1** and **8b-1** to synthesize the corresponding hydroxyl derivatives **9a** and **9b** respectively. Mesylation of the hydroxyl group of each of the two products **9a** and **9b** were performed, generating the

corresponding mesylate derivatives **10a** and **10b** respectively, followed by azidation of the mesyl group in each case to afford the azide products **11a** and **11b** (Scheme 11). For simplicity, in Scheme 11 these steps have been represented only for **8b-1** but the same was performed for **8a-1**. The yields of these reactions were excellent and the products in most of the cases did not need purification via chromatography.

Note. The same steps were performed for compound **8a-1** to obtain the corresponding products **9a**, **10a** and **11a** respectively.

Scheme 11. Synthesis of glycosyl azides **11a** and **11b** from the corresponding glycosyl acetates **8a-1** and **8b-1** via functional group transformations.

Although the azides **11a** and **11b** were analyzed by NMR spectroscopy and HRMS (Section 7 and 8) it is interesting and an easy way to perform the FTIR to observe a medium to strong peak at around 2100 cm^{-1} for the stretching vibrations of the azide group. In Figure 28 the FTIR Spectrum of the Azide **11b** is shown with a strong peak at 2099 cm^{-1} for the absorption of stretching vibrations of the azide group.

Figure 28. FTIR Spectrum of Compound **11b**.

Once the two glycosyl azides **11a** and **11b** were synthesized, they were used in another CuAAC reaction using different alkynes to synthesize a small library of tri-
triazolyl glycosyl derivatives **12a-d** (Table 3).

Table 3. Synthesis of tris-triazolyl glycosyl derivatives using CuAAC reaction

Entry	Glucal azide	Alkyne	Product	Yield (%) ^a
1	11b			85
2	11b			94
3	11b ^b			92
4	11a			89

a = isolated yields, b = 1.2 equivalents of tetrabutyl ammonium fluoride (TBAF) was used to deprotect the TMS group.

3.5. Synthesis of 2-alkynyl D-glucal derivatives

Starting from 3,4,6-tri-*O*-acetyl-D-glucal **1**, 2-iodo-3,4,6-tri-*O*-acetyl-D-glucal **13** was synthesized using the procedure from literature.⁶⁵ This involves the use of *N*-iodosuccinimide (NIS) as the iodine source and AgNO₃ as the Lewis acid in acetonitrile at reflux for 4 h (Scheme 12).

Scheme 12. Synthesis of 2-iodo-3,4,6-tri-*O*-acetyl-D-glucal from 3,4,6-tri-*O*-acetyl-D-glucal.

It was possible to crystallize compound **13** by keeping its concentrated solution in ethyl acetate at 4 °C for 48 hours.⁶⁶ The crystal system of this compound was found to be orthorhombic with $P2_12_12_1$ space group (Figure 29).

Figure 29. ORTEP diagram of 2-iodo-3,4,6-tri-*O*-acetyl-D-glucal.

In the crystal, molecules are linked into a supramolecular chain along the *a* axis through two *C*—*H*...*O* interactions to the same acceptor carbonyl *O* atom (Figure 30).

Figure 30. A view of the supramolecular chain mediated by C-H...O interactions.

Compound **13** was then subjected to the copper and ligand-free Sonogashira reaction conditions to afford 2-alkynyl-3,4,6-tri-*O*-acetyl-D-glucal derivatives. First, we tried different catalysts using phenyl acetylene as the standard alkyne, Cs_2CO_3 as base and DMF as solvent at room temperature under nitrogen. It was found that palladium

acetate showed the best result with 96 % yield of the corresponding alkynyl-3,4,6-tri-*O*-acetyl-D-glucal derivative **14a** (entry 2, Table 4).

Catalysts other than palladium did not lead to the product (entries 4-6, Table 4), same was the case when no catalyst was used (entry 7, Table 4). The concentration of catalyst also has an effect as 2 mol% of palladium acetate showed lower yields but using higher than 5 mol% did not increase the yield further (entries 8 and 9 respectively, Table 4). Similarly, different solvents were screened to check the efficiency of the reaction and it was found that DMF was the best among the solvents used with 96 % yield and completion of the reaction in only 20 minutes. Other polar aprotic solvents also showed comparable results but it took comparatively longer times for the reactions to complete (entries 10-13, Table 4).

Table 4. Optimization of reaction conditions for Sonogashira coupling of 2-iodo-3,4,6-tri-*O*-acetyl-D-glucal

Entry	Catalyst (5 mol %)	Base ^c	Solvent	Time (h)	Yield(%)
1	Pd (dppf)Cl ₂ ·CH ₂ Cl ₂	Cs ₂ CO ₃	DMF	2	90
2	Pd (OAc)₂	Cs₂CO₃	DMF	0.3	96
3	PdCl ₂	Cs ₂ CO ₃	DMF	2	94
4	Yb(OTf) ₃	Cs ₂ CO ₃	DMF	3	NR
5	Ag OTf	Cs ₂ CO ₃	DMF	3	NR
6	Rh(III) acetylacetonate	Cs ₂ CO ₃	DMF	3	NR
7	-----	Cs ₂ CO ₃	DMF	5	NR
8	Pd (OAc) ₂ ^a	Cs ₂ CO ₃	DMF	5	80
9	Pd (OAc) ₂ ^b	Cs ₂ CO ₃	DMF	0.3	96
10	Pd (OAc) ₂	Cs ₂ CO ₃	ACN	2	93
11	Pd (OAc) ₂	Cs ₂ CO ₃	DMSO	1.5	87
12	Pd (OAc) ₂	Cs ₂ CO ₃	THF	2.5	75
13	Pd (OAc) ₂	Cs ₂ CO ₃	DCM	2	80
14	Pd (OAc) ₂	K ₂ CO ₃	DMF	1	93
15	Pd (OAc) ₂	Na ₂ CO ₃	DMF	2	75
16	Pd (OAc) ₂	CaCO ₃	DMF	2	5
17	Pd (OAc) ₂	CsF	DMF	1.5	65
18	Pd (OAc) ₂	TBAF	DMF	1	80
19	Pd (OAc) ₂	PMDETA	DMF	3	5
20	Pd (OAc) ₂	KOH	DMF	1.5	30
21	Pd (OAc) ₂	DIPEA	DMF	1.5	50
22	Pd (OAc) ₂	-----	DMF	3	Trace

a = 2 mol % of Pd (OAc)₂, b = 10 mol % Pd(OAc)₂, c = 1.5 eq., NR = no reaction.

Different bases were then screened and Cs_2CO_3 was found to be the most effective followed by potassium carbonate and sodium carbonate (entry 2, 14 and 15, Table 4). CsF and TBAF (tetrabutylammonium fluoride) also showed good yields (entry 17 and 18 respectively, Table 4). KOH , CaCO_3 , and organic bases i.e. PMDETA and DIPEA (*N,N*-diisopropylethylamine) were not very effective and showed lower yields (entries 16, 19, 20 and 21, Table 4) while using no base resulted in only traces of the product (entry 22, Table 4).

Once the conditions were optimized i.e. using palladium acetate (5 mol%) as catalyst and Cs_2CO_3 (1.5 eq.) as a base in DMF at room temperature under nitrogen, different terminal alkynes were then used to check the versatility of this reaction. A series of 2-alkynyl 3,4,6-tri-*O*-acetyl-D-glucal derivatives (**14a-p**) were synthesized with very good to excellent yields using the optimized reaction conditions. The reaction was found to tolerate electron withdrawing, electron donating, aryl and heteroaryl, alkyl and cycloalkyl groups. The presence of amines or hydroxyl groups, as well as double bonds, did not affect the yields of the reaction (Table 5).⁶⁷

Table 5. Synthesis of a library of 2-alkynyl-3,4,6-tri-*O*-acetyl-D-glucal derivatives from 2-iodo-3,4,6-tri-*O*-acetyl-D-glucal via Sonogashira reaction

Entry	Alkyne	Time(h)	Product	Yield (%) ^a
1		0.3		96
2		0.3		94
3		0.4		94
4		6.0		83
5		6.0		77

6		1.0		91
7		6.0		80
8		6.0		84
9		0.5		92
10		1.0		80
11		0.7		95
12		0.5		94
13		0.7		90
14		1.5		90
15		1.5		93
16		1.0		95

a = isolated yields.

3.6. Synthesis of bicyclic D-glucal derivatives

To check the application of the products of copper-free Sonogashira coupling, they were used in a cyclization reaction to afford bicyclic D-glucal derivatives **16a-g** (Scheme 13). First, the acetyl groups were converted into alcohols using potassium carbonate (20 mol %) as a base in methanol for 5 hours at room temperature to afford the corresponding 2-alkynyl-D-glucal derivatives **15a-g**, followed by an electrophile promoted nucleophilic alkyne (*5-endo-dig*) cyclization reaction (Scheme 13).

Scheme 13. Transesterification followed by cyclization of the 2-alkynyl-3,4,6-tri-*O*-acetyl-D-glucal derivatives.

Various electrophiles were used to promote the cyclization but only gold (III) chloride showed appreciable results (entries 1-5, Table 6). The reaction was optimized using 10 mol % of AuCl₃ as higher concentrations did not increase the yields (entry 10, Table 6). Similarly, 1,4-dioxane was found to be the most effective among the solvents used (entry 1, Table 6).

Table 6. Optimization of reaction conditions for Gold (III) chloride promoted nucleophilic 5-*endo-dig* cyclization of 2-alkynyl-3,4,6-tri-*O*-acetyl-D-glucal **14a**

Entry	Catalyst	Solvent	Time (h)	Yield (%)
1	AuCl ₃	1,4-Dioxane	5	40
2	AgOTf ^a	1,4-Dioxane	1	Decomposed
3	Ru(C ₅ H ₇ O ₂) ₃ ^a	1,4-Dioxane	12	NR
4	CuI ^a	1,4-Dioxane	12	NR
5	Pd(OAc) ₂	1,4-Dioxane	12	Decomposed
6	AuCl ₃	THF	12	10
7	AuCl ₃	DCM	12	12
8	AuCl ₃	MeOH	12	10
9	AuCl ₃	DMF	12	5
10	AuCl ₃ ^a	1,4-Dioxane	5	40
11	AuCl ₃ ^b	1,4-Dioxane	22	10
12	AuCl ₃ ^c	1,4-Dioxane	20	11

a = 20 mol% of catalyst was used, b = 10 mol % of PPh₃, c = 2 eq. of NaHCO₃ were used, NR = no reaction.

Using triphenylphosphine and sodium bicarbonate as bases also lowered the yields of cyclization (entries 11 and 12, respectively; Table 6). The optimized conditions according to Table 6 were achieved using gold (III) chloride in 1,4-dioxane at reflux for 5 hours. The probable reason for the lowered yields could be the electronic factors as the

alkyne is attached to a carbon, which has a comparatively high electron density while the hydroxyl group is on a carbon with comparatively low electron density. A similar effect of lowered nucleophilicity due to electronic mismatch was also previously reported by groups performing cyclization reactions.⁶⁸ Another possible reason could be the rigidity of the molecule due to its cyclic nature and presence of the double bond of the glucal ring. The enyne system of the glucal alkyne is quite rigid as obvious from the planar sp^2 and linear sp hybridization of the double and triple bonds, respectively. Therefore, the orientation of the hydroxyl group and the alkyne may not favor efficient cyclization.

Once the reaction conditions for *5-endo-dig* cyclization were optimized (Table 6, entry 1), glucal alkynes having different substituents on the alkyne were tried in order to synthesize a class of bicyclic glucal derivatives (**16a-g**) as shown in Table 7. The presence of an -OH group on the benzene and using electron deficient hetero-aromatic compounds did not lead to the formation of the product (entries 2 and 3, Table 7). Alkynes having alkyl and electron rich aromatic substituents were found to proceed to the cyclic products (entries 1, and 4-7, Table 7). The cyclization showed excellent regioselectivity for the *5-endo-dig* product compared to that of the *4-exo-dig* cyclization. The likely reason for *5-endo-dig* regioselectivity is the comparatively strained product in case of *4-exo-dig* cyclization and the use of electrophile ($AuCl_3$) and higher temperatures. That is why we only observed the *5-endo-dig* products in our reactions.

Table 7. Gold (III) Chloride promoted nucleophilic *5-endo-dig* cyclization to afford hydro-furan fused D-glucal derivatives

Entry	-R	Time (h)	Product	Yield (%) ^a
1		5	16a	40
2		24	16b	NR
3		24	16c	NR

4		5		45
5		5		38
6		5		52
7		5		35

a = isolated yields.

3.7. Synthesis of Stannyl substituted 2-alkenyl-D-glucal derivatives

Based on the above-mentioned results to generate *C*-2 alkynyl-substituted glucal derivatives **14a-j**, we developed a regioselective palladium-catalyzed hydrostannation of these alkynes to achieve stannyl derivatives of glucals in good yields. Starting from 3,4,6-tri-*O*-acetyl-D-glucal **1**, the corresponding 2-iodo-D-glucal derivative **13** was synthesized, followed by a ligand- and copper-free Sonogashira coupling reaction to obtain 2-alkynyl-3,4,6-tri-*O*-acetyl-D-glucal derivatives **14a-j** according to the procedures described earlier in Section 3.5 and as summarized in Scheme 14.

Scheme 14. Synthesis of 2-alkynyl-D-glucal derivatives from 3,4,6-tri-*O*-acetyl-D-glucal.

These 2-alkynyl-3,4,6-tri-*O*-acetyl-D-glucal derivatives were then screened under hydrostannation conditions using different catalysts, solvents, and temperatures (Table 8). It was observed that the use of bis(triphenylphosphine)palladium(II) chloride (2 mol%) as catalyst, and 1.2 equivalents of tributyltin hydride in tetrahydrofuran at room temperature for one hour, gave the best results among the conditions used (entry 8, Table 8).⁶⁹

Table 8. Optimization of reaction conditions for palladium-catalyzed hydrostannation of glucal alkynes

Entry	Catalyst (mol%) ^a	Solvent	Temperature (°C)	Time	Yield (%) ^b
1	Pd(PPh ₃) ₄ (5)	THF	−78–rt	18 h	50
2	Pd(PPh ₃) ₄ (5)	Toluene	−78–rt	22 h	56
3	Pd(PPh ₃) ₄ (5)	DCM	−78–rt	22 h	53
4	Pd(PPh ₃) ₄ (5) ^c	Toluene	−78–rt	22 h	60
5	Pd(PPh ₃) ₄ (5) ^c	THF	−78–rt	22 h	68
6	Pd(PPh ₃) ₄ (10) ^{c,d}	THF	rt	48 h	74
7	Pd(OAc) ₂ (6)	Toluene	−78–rt	22 h	NR
8	PdCl₂(PPh₃)₂ (2)	THF	rt	1 h	85

a = 1.2 eq. of HSnBu₃ were used. b = combined isolated yields, c = 1.5 eq. of HSnBu₃ were used. d = reaction was performed using ultrasound.

Tributyltin hydride was added dropwise to minimize the homocoupling reaction in which two tributyltin hydride molecules couple to make a di-stannane derivative and liberate hydrogen. The color of the reaction mixture changed from light yellow or light orange to dark orange or reddish brown, respectively, as the tributyltin hydride was added, and the evolution of hydrogen gas was observed because of homocoupling of excess tributyltin hydride. The use of higher concentrations of tributyltin hydride and palladium catalyst did not affect the yields of the reaction (entries 4–6, Table 8). Among the catalysts applied, bis-(triphenylphosphine)palladium(II) chloride showed the best results, followed by tetrakis(triphenylphosphine)palladium(0), while with palladium acetate the reaction did not work.

With the optimized conditions achieved, a series of 2-alkynyl-3,4,6-tri-*O*-acetyl-D-glucals were used to obtain a library of stannane derivatives of glucal with good to excellent regioselectivity (Table 9). The regioselectivity of this hydrostannation was found to be dependent on the nature of the substituent group on the alkyne. Here we use **α** and **β** terminology to denote whether the stannyl group is attached to the carbon adjacent to the glucal ring (**α** regioisomer) or to the other carbon (**β** regioisomer). When a glucal alkyne having an alkyl substituent was used, the major product was found to be **α** regioisomer, while with glucal alkynes having aryl substituents, the regioselectivity

depended on the electronic nature of the aromatic ring. In electron-rich aryl-substituted alkynes **α** selectivity was observed (entries 2 and 3, Table 9), while with electron-neutral and electron-deficient aryl-substituted alkynes the selectivity shifted in favor of the **β** regioisomer (entries 1, 4-5, and 10, Table 9). This effect could be explained by the polarization of alkyne due to the presence of different groups and thus the H-Sn (with electronegative hydrogen) bond of tributyltin hydride adds to the alkyne accordingly as explained in the next paragraph. The utility of this process was demonstrated by performing this reaction on a gram-scale to prepare **17a** (2.2 gram, both regioisomers) using **14a** (1.5 gram) with the same regioselectivity (2:3) and comparative yields (entry 1, Table 9).

Table 9. Synthesis of a library of glucal-derived vinyl stannanes from 2-alkynyl glucal derivatives

$R' = \text{H or Ac}$

Entry	Glucal alkyne (14a-l)	Yield (%) ^a	Ratio $\alpha:\beta$ ^b
1		85(83) ^c	 2 : 3
2		68	 8.8 : NI
3		63	 3 : 2
4		67	 1.2 : 8.8
5		60	 1 : 9
6		72	 9.9 : traces
7		60	 9.5 : traces

8		64	
	14h		17h 9.2 : NI
9		63	
	14i		17i 9.6 : traces
10		70	
	14j		17j 4 : NI
11		60	
	14i unprotected		17k 9.9 : traces
12		70	
	14a Unprotected		17l 1 : 1
13		60	
	14j Unprotected		17m 4.5 : 5.5

a = combined isolated yields of both the regioisomers, b = the ratio was obtained either through isolated yields of each regioisomer or through ^{119}Sn NMR in cases of mixtures that were not isolated. c = yields on a gram scale. NI = not isolated (from the mixture it was possible to isolate only one regioisomer.)

The probable reason for the regioselectivity in electron-deficient and electron-neutral aryl alkynes for the formation of the β product is the polarization of the triple bond caused by the aromatic ring creating a slightly positive charge on the α -carbon to the glucal ring. Now, as proposed in the mechanism (Figure 31),⁷⁰ the slightly negative charge on hydrogen in the metal complex (complex C, Figure 31) will add preferentially to this comparatively positive carbon of the alkyne. In the case of alkyl and electron-rich aryl-substituted alkynes, we need to focus on both the complex C (the polarization of alkyne is different) and the hydrometallation step, in which a vinyl palladium species is formed (complex D, Figure 31). The presence of an acetyl group in the vicinity could be responsible for the stability of the vinyl palladium species and thus lead to the corresponding regioselectivity of this reaction (Figure 31).

Figure 31. Proposed mechanism for palladium-catalyzed hydrostannation of alkynes.

To further explore this latter fact of oxygen chelation with palladium, we performed hydrostannation reactions using glucal stannanes having hydroxyl groups instead of acetyl, to check the possible role of the oxygen atoms in stabilizing the vinyl palladium intermediate in this reaction. It was observed that when these glucal alkynes with hydroxyl groups were used, the regioselectivity of hydrostannation was slightly enhanced in favor of the **β** product compared with the corresponding acetylated glucal alkynes (entries 11 and 13, Table 9). This indicates the enhanced role of the oxygen atom, which now is probably more involved in the stabilization of the palladium intermediate in the mechanism.

It was possible in most of the cases to purify each regioisomer of the pair by flash chromatography (except for **17j** where only the **α** isomer was isolated) and to characterize the structure of each regioisomer using ^1H NMR (entries 6–9, 12 and 13, Table 9), DEPT-135 and HMBC (entries 1–4, Table 9) analysis. For regioisomeric pairs that could not be isolated by flash chromatography, ^{119}Sn NMR analysis was performed using SnCl_4 as the internal standard, to check the regioisomeric ratio (entries 4 and 5, Table 9). ^{119}Sn NMR spectra also confirmed the regioselectivity of this reaction as shown for compound **17d** (Figure 32).

Figure 32-A is the ^{119}Sn NMR Spectrum of the pure **17d α** single peak at -31.63 ppm (as the quantity isolated was very small so we could not perform the ^1H NMR and ^{13}C NMR spectra), while Figure 32-B is the ^{119}Sn NMR Spectrum of the pure **17d β** with

a triplet at -30.63 (t, $J = 11.5$ Hz). The triplet observed is probably a 4J coupling of the fluorine atom on the aromatic ring with the Sn atom of tributyltin group. The ^{119}Sn NMR Spectrum of the mixture of diastereomers **17d** α and **17d** β is shown in Figure 32-C and the integration of the two peaks shows a ratio of 1:9 of the α diastereomer to that of the β . ^{119}Sn NMR analysis was performed in all those cases where the regioisomeric pairs could not be isolated by flash chromatography (Section 8).

Figure 32. ^{119}Sn NMR spectra of β isomer (A), α isomer (B) and a mixture of the two (C) of **17d**.

3.8. Synthesis of Aryl substituted 2-alkenyl glucal derivatives

To check the application of these glucal-derived stannanes they were used under Stille reaction conditions to couple with aryl halides. Different reaction conditions were applied to achieve this coupling, but in most of the cases, the reaction did not work efficiently (Table 10).⁷¹ Copper iodide (10 mol %) as a catalyst was used with *N*-methylpyrrolidone and dimethyl formamide as solvents at 110 °C for 4 hours (entry 1, Table 10). The use of other reaction conditions either did not lead to the products (entries 4 and 5, Table 10), resulted in decomposition of the starting reagent (entries 2, 6 and 9, Table 10), or the yields were not very good (entries 3 and 8, Table 10).

Table 10. Optimization of Stille coupling of vinyl stannane derivatives of glucal with phenyl iodide

Entry	Catalyst (mol%)	Solvent	Temperature (°C)	Time	Yield (%)
1	CuI (10) ^a	DMF:NMP 1:1	100–110	12 h	70
2	PdCl ₂ (PPh ₃) ₂ (3)	DMF	100	48 h	Decomposed
3	Pd ₂ (dba) ₃ (4) ^b	DMF	100	48 h	30
4	Pd ₂ (dba) ₃ (5) ^c	THF	rt	24 h	NR
5	PdCl ₂ (PPh ₃) ₂ (5) ^d	DMF	120	5 h	NR
6	PdCl ₂ (PPh ₃) ₂ (10) ^e	DMF	90–100	12 h	Decomposed
7	Pd(PPh ₃) ₄ (10) ^f	DMF	rt	12 h	Decomposed
8	PdCl ₂ (PPh ₃) ₂ (5) ^g	DMF	130	20 min	50

a = NaCl (1 eq.) b = AsPh₃ (16 mol%) and CsF (2 eq.) were used. c = Butylated hydroxytoluene BHT (1 eq.) and AsPh₃ (0.2 eq.) were used. d = CuI (10 mol%) and AsPh₃ (5 mol%) were used. e = AsPh₃ (20 mol%) and CuI (20 mol%) were used. f = AsPh₃ (20 mol%), CuI (20 mol%) and CsF (2 eq.) were used. g = CuI (10 mol%) and AsPh₃ (5 mol%) were used and reaction was performed under microwaves.

When the optimized reaction conditions were achieved (entry 1, Table 10), different vinyl stannanes and aryl halides were used to synthesize the corresponding aryl-substituted alkenyl glucal derivatives. When the products were analyzed by NMR and HRMS it was found that in most of the cases the reduction of the vinyl stannanes to the corresponding alkenes occurred (entries 3–6, Table 11), along with some cases of coupling (entries 1 and 2, Table 11).⁷²

Table 11. Synthesis of aryl-substituted alkenyl derivatives of glucal via Stille coupling

Entry	Glucal Stannane	R'-X (1.2 eq.)	Product ^a	
			A (% Yield)	B (% Yield%)
1			 18a 65	Not Observed
2			 18a 70	Not Observed
2			 19a 73 Not Observed	
3			 19a 70 Not Observed	
4			 19b 67 Traces	
5			 19c 79 Not Observed	

a = isolated yields.

3.9. Synthesis of alkynyl substituted 2-alkenyl glucal derivatives

To further explore the synthetic applications of these vinyl stannane derivatives of glucal, the stannane group was converted to iodide using iodine (1.2 eq.) in dichloromethane at room temperature for 2 hours (Table 12).⁷³ These vinyl iodide derivatives were then subjected to the Sonogashira coupling⁷⁴ to form the corresponding alkynyl-substituted 2-alkenyl glucal derivatives using bis(triphenylphosphine) palladium(II) chloride (5 mol%) as catalyst with CuI (5 mol%) in triethylamine (2 mL) at room temperature for 2 to 8 hours.

Table 12. Synthesis of alkynyl-substituted 2-alkenyl derivatives of glucal via a Sonogashira coupling

Entry	Starting Material	Alkyne	Time (h)	Product	Yield (%) ^a
1 ^b			3		87
2			3		85
3			3		80
4			3		80
5			4		88
6			8		86
7 ^b			3		84

a = isolated yields, b = transesterification of acetyl groups was performed using conditions from Table 6.

This reaction was found to tolerate electron-withdrawing, electron-donating, aryl, heteroaryl, alkyl, and cycloalkyl groups, giving products in very good yields at room temperature.

3.10. Synthesis of triazolyl substituted 2-alkenyl-D-glucal derivatives

Using the reaction conditions and procedures discussed in Section 3.7 and 3.9 TMS-protected alkynyl substituted 2-alkenyl derivatives of glucal **21h-n** were synthesized as summarized in Scheme 15. This includes the synthesis of 2-iodo-3,4,6-tri-*O*-acetyl-D-glucal **13** starting from compound **1**, followed by the copper and ligand-free Sonogashira coupling and regioselective palladium-catalyzed hydrostannation to obtain the corresponding alkynyl derivatives **14** and stannyl derivatives **17** of D-glucal, respectively. These stannyl derivatives **17** were then subjected to iodination to afford **20** and Sonogashira coupling to get the desired starting materials **21** for the click reaction (Scheme 15).

Scheme 15. Synthesis of TMS-protected alkyne derivatives of glucal from 3,4,6-tri-*O*-acetyl-D-glucal.

Based on above scheme eight trimethylsilyl protected alkyne substituted 2-alkenyl derivatives of glucal (**21h-n**) were synthesized having different R groups as summarized below (Table 13):

Table 13. Synthesis of TMS-protected glugal derived alkynes from the corresponding iodo compounds

Entry	Starting Material (20)	Product (21h-n)	Yield (%) ^a
1			95
2			94
3			91
4			93
5			92
6			93
7			91

a = isolated yields.

Synthetic Applications of these TMS-protected glugal alkyne derivatives were evaluated by using them in a copper-catalyzed azide-alkyne cycloaddition reaction to synthesize the corresponding triazolyl substituted 2-alkenyl glugal derivatives **22**. To optimize reaction conditions for the synthesis of glugal-based triazoles the TMS-protected alkynyl glugal **21h** was used under the reaction conditions summarized in Table 14, with

phenyl azide as the standard azide and tetrabutylammonium fluoride (TBAF, 1.2 eq.) to remove the TMS- group.

Table 14. Optimization of glucal-derived triazole synthesis from the corresponding TMS-protected glucal derivative

Entry	Catalyst (5 mol %)	Base (1.2 eq.)	Solvent (2 mL)	Yield (%)
1	CuI	PMDETA	DMF	93
2	CuI	Cs ₂ CO ₃	DMF	Decomposed
3	CuI	TMEDA*	DMF	90
4	CuI	NEt ₃	DMF	80
5	CuI	NaAsc.	DMF	83
6	CuI	PMDETA	MeOH	Decomposed
7	CuI	PMDETA	THF	91
8	CuI	PMDETA	ACN	Decomposed
9	CuI	PMDETA	DCM	80
10	CuSO ₄ ·5H ₂ O	PMDETA	DMF	12
11	Cu(OAc) ₂	PMDETA	DMF	65
12	CuCO ₃	PMDETA	DMF	16

* TMEDA = Tetramethylethylenediamine

In these conditions different bases, solvents, and copper catalysts were screened and it was observed that this cyclization reaction gives better yields when copper iodide (5 mol %) is used as catalyst, *N,N,N',N'',N'''*-pentamethyldiethylenetriamine (PMDETA) (1.2 eq.) was used as the base, TBAF (tetrabutylammonium fluoride) (1.1 eq.) as deprotecting agent for TMS- group, and DMF as solvent at room temperature for 12 hours (entry 1, Table 14).

As the conditions have been optimized according to Table 14, different azides and glucal alkynes with different R groups were then used to synthesize a library of glucal-derived triazoles as summarized below (Table 15);⁷⁵

Table 15. Synthesis of a library of glucal-derived triazole compounds

<p> $\text{21h-n} \xrightarrow[\text{TBAF (1.1 eq.), DMF, rt, 12 h}]{\text{R'N}_3 \text{ (1.2 eq.)}, \text{CuI (5\%)}, \text{PMDETA (1.2 eq.)}} \text{22a-o}$ </p> <p>75-95 %</p>				
Entry	Starting Material	Azide	Product	Yield ^a (%)
1				93
2				90
3				95
4				84
5				75
6				80

7	21j		22g	75
8	21k		22h	77
9	21l		22i	84
10	21m		22j	78
11	21n		22k	91
12	21o		22l	83
14	21p		22m	89
15 ^b	21q (unprotected)		22n	88

a = isolated yields, b = the acetyl groups were transesterified before the Sonogashira step.

This copper-catalyzed azide-alkyne cycloaddition reaction to generate triazolyl substituted 2-alkenyl glucal derivatives were well tolerated by electron withdrawing,

electron donating and neutral moieties including aromatic, heteroaromatic, alkyl, and cycloalkyl groups. The yields of reactions vary from very good to excellent depending on the groups attached to both the azide and alkyne. The products were easy to purify and in some cases did not need chromatographic purification. These products can be tested for biological applications especially those having sulfur containing rings can be tested as proteasome inhibitors, antioxidants and in metal sensing.

4. CONCLUSION

The conclusion of this work can be divided into two major parts; first, *the synthesis of glucal-based triazoles using mainly the CuAAC reaction* and second, *palladium-catalyzed cross-coupling reactions to synthesize glucal-based alkynes followed by their synthetic applications.*

In the first part, libraries of 1,6-substituted bis-triazolyl glycosides derivatives have been synthesized using CuAAC (click chemistry) reaction, functional group transformations, and Ferrier rearrangement starting from 3,4,6-tri-*O*-acetyl-D-glucal. Photophysical studies of some fluorescent compounds have been performed. Similarly, libraries of regioisomeric 1,2- and 1,4-substituted bis-triazolyl glycoside derivatives have been synthesized using palladium-catalyzed Tsuji-Trost azidation and CuAAC reactions. Functional group transformations and another CuAAC reaction of these 1,2- and 1,4-substituted bis-triazolyl glycoside derivatives were performed to afford a small library of regioisomer 1,2,6- and 1,4,6-substituted tris-triazolyl glycoside derivatives.

In the second part, palladium-catalyzed copper- and ligand-free Sonogashira coupling was used to afford important glucal-based alkynes. These glucal-alkyne derivatives synthesized via Sonogashira reaction have further been synthetically evaluated using gold-catalyzed *5-endo-dig* cyclization and palladium-catalyzed hydrostannation to synthesize libraries of bicyclic glucal derivatives and stannyl derivatives of glucal, respectively. The stannyl derivatives of glucal were further used in Stille coupling and in iodination followed by Sonogashira coupling and CuAAC reaction to obtain libraries of aryl-, alkynyl- and triazolyl-substituted 2-alkenyl-D-glucal derivatives. In *5-endo-dig* cyclization and especially Stille coupling we were only successful in achieving moderate yields and a small libraries of five and one compounds were obtained, respectively.

Literature survey of related glucal-based triazoles implies that the synthesized glucal triazole derivatives could have potential biological significance as enzyme inhibitors, peptidomimetics, antitubercular, and antidiabetic agents. Similarly, glucal-based alkynes, triazoles and alkenes can have a potential role as antibiotics, chemosensors for metals ions and proteins, and in the synthesis of synthetic vaccines, as well as potential ligands in metal catalysis and nanochemistry. Structures of all the synthesized products were elucidated through NMR, FTIR, HRMS, X-ray diffraction and other analytical techniques where applicable.

5. PERSPECTIVES

The perspective of this work can be summarized as:

- Glucal-based triazoles can have potential biological applications as antitubercular agents, antidiabetic agents, peptidomimetics and enzyme inhibitors.
- Glucal-based alkynyl, aryl, triazolyl and alkenyl derivatives can also have potential applications for developing antibiotics, synthetic vaccines, and chemosensors for metals and biomolecules.
- Synthesis and photophysical studies of fluorescent glucal derivatives by linking a fluorescent group with glucal moiety via a triazole ring.
- Triazole-crafted glycosyl dimers can further be used to synthesize polymeric compounds with alternative glycosyl and triazole moieties.
- The presence of stereogenic centers, heterocyclic ring systems, and functional groups make the synthesized compounds useful as potential ligands in metal-catalyzed reactions.
- These libraries of compounds can also be used to chelate noble metals (Ag, Au, etc.) and can have potential applications in nanochemistry and material chemistry.
- Computational studies of the concerned compounds can be performed to further explore the kinetics and other physical phenomena of various reaction steps and compounds.

6. MATERIALS AND METHODS

Proton nuclear magnetic resonance spectra (^1H NMR) were obtained at 300 MHz using Bruker DPX 300 instrument. Spectra were recorded in CDCl_3 solutions, some of them in DMSO-*d*6, methanol-*d*4, $(\text{CD}_3)_2\text{CO}$. Chemical shifts are reported in ppm, referenced to the solvent peak or tetramethylsilane (TMS) as the external reference. Data are reported as follows: chemical shift (δ), multiplicity, coupling constant (J) in Hertz and integrated intensity. Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained at 75 MHz. Spectra were recorded in CDCl_3 solutions, some of them in methanol-*d*4, DMSO-*d*6, and $(\text{CD}_3)_2\text{CO}$. Chemical shifts are reported in ppm, referenced to the solvent peak or tetramethylsilane (TMS) as the external standard. Abbreviations to denote the multiplicity of a particular signal are s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sex (sextet) and m (multiplet). X-Ray analysis was done using Bruker APEX II CCD diffractometer. Microwave synthesis was performed by Anton Paar Monowave 300 Synthesizer. Column chromatography was performed using silica gel (230-400 mesh). High-resolution mass spectrometry was performed with high-resolution ESI-TOF mass spectrometer Shimadzu LCMS-IT-TOF using methanol as solvent, the analysis was done in ESI+ and ESI- modes and in some cases APCI (atmospheric-pressure chemical ionization) mode, with 50% solution of acetonitrile/ H_2O and 0.1% formic. FTIR analysis was performed using Cary 630 FTIR Agilent Technologies. The melting points were observed using Buchi Melting Point B – 545. Thin layer chromatography (TLC) was performed using silica gel UV_{254} , 0.20 mm thickness. For visualization, TLC plates were either placed under ultraviolet light, or stained with iodine, and/or acidic vanillin solution. Tetrahydrofuran was dried and purified by distillation from sodium with a benzophenone indicator. All other solvents were ACS or HPLC grade unless otherwise noted. Air and moisture-sensitive reactions were conducted in flame-dried or oven dried glassware equipped with tightly fitted rubber septa and under a positive atmosphere of dry nitrogen. Reagents and solvents were handled using standard syringe techniques.

7. EXPERIMENTAL

General Procedure 1 (GP1); Synthesis of Azide 5:

The mesylate (1 mmol, 351 mg) in THF (1 mL) and sodium azide (2.5 mmol, 163 mg) in H_2O (2 mL) were placed in a 10 mL SiC vial, sealed with a PTFE-coated silicon septum and closed with a snap cap made of PEEK (polyether ether ketone). A stir bar coated with PTFE (Polytetrafluoroethylene) was placed inside the vial for proper homogenization. The reaction tube was placed inside the cavity of Anton Paar monowave synthesis system, operated at $180\text{ }^\circ\text{C}$ (temperature monitored by a built-in IR sensor), a power of 100W and a pressure of 10bar for 30 min. After completion of the reaction, ethyl acetate was added to extract the azide (5), the organic phase was dried over MgSO_4 and concentrated under vacuum. The product was purified by flash chromatography and eluted with ethyl acetate/hexane. The product was obtained as a yellow oil in 85% yield.

(2*R*,3*S*,6*S*)-2-(azidomethyl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-ol (5);

The product was obtained as yellow oil in 85% (254 mg) yield. ^1H NMR (300 MHz, CDCl_3) δ 8.00 (s, 1H), 7.72 (d, $J = 7.2$ Hz, 2H), 7.49 – 7.28 (m, 3H), 6.18 – 5.91 (m, 2H), 5.56 – 5.35 (d, $J = 2.1$ Hz, 1H), 4.11 (dd, $J = 7.8, 6.7$ Hz, 1H), 3.74 (d, $J = 8.2$ Hz, 1H), 3.68 – 3.56 (m, 1H), 3.45 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 146.91; 136.80; 130.41; 129.80 (2C); 129.01; 127.25; 120.91; 120.59 (2C); 73.47; 67.31; 64.16; 51.79; IR: 3352, 2924, 2097, 1600, 1503, 1277, 1229, 1192, 1035, 760 cm^{-1} . HRMS calculated for $\text{C}_{14}\text{H}_{14}\text{N}_6\text{O}_2$ [$\text{M}^+ + \text{H}$] = 298.1178, found: 298.1162.

General Procedure 2 (GP2); Synthesis of compounds 6a-n:

The azide 5 (1 mmol, 298 mg), terminal alkyne (1.2 eq.), CuI (10 mol %), PMDETA (1 eq.) and THF (3 mL) were taken in 10 mL SiC vial, sealed with a PTFE-coated silicon septum and closed with a snap cap made of PEEK (polyether ether ketone). A stir bar coated with PTFE (Polytetrafluoroethylene) was placed

inside the vial for proper homogenization. The reaction tube was placed inside the cavity of Anton Paar monowave synthesis system, operated at 100°C (temperature monitored by a built-in IR sensor) for 10-20 min. After the completion of the reaction by TLC analysis concentrated aqueous solution of NH₄Cl (20 mL) was added to the reaction mixture and extracted with ethyl acetate (3x25 mL). The organic phase was dried over MgSO₄, filtered, and concentrated under vacuum. The product was purified by flash chromatography and eluted with ethyl acetate/hexane.

(2*R*,3*S*,6*S*)-2-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-ol (**6a**):

The product was obtained as white solid in 93% (373 mg) yield. IR (film, cm⁻¹): 3440, 3120, 3100, 1610, 1509, 1057, 1027, 1004, 765 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 7.91 (s, 1H), 7.69 (d, *J* = 7.1 Hz, 2H), 7.49 (s, 1H), 7.40 (dd, *J* = 6.6, 2.9 Hz, 2H), 7.33 – 7.14 (m, 6H), 6.03 (q, *J* = 10.4 Hz, 2H), 5.43 (s, 1H), 4.74 (dd, *J* = 14.2, 1.9 Hz, 1H), 4.49 (dd, *J* = 14.3, 7.4 Hz, 1H), 4.02 (d, *J* = 8.8 Hz, 1H), 3.75 (t, *J* = 7.1 Hz, 1H). ¹³C NMR(CDCl₃, 75 MHz) δ (ppm): 147.61; 146.87; 136.54; 131.03; 130.34; 129.65 (2C); 128.89 (2C); 128.76; 128.19; 126.89; 125.65 (2C); 121.53; 120.30; 120.26 (2C); 73.04; 68.06; 64.00; 51.45. The compound decomposed above 175 °C. HRMS calculated for C₂₂H₂₀N₆O₂ [M + H]⁺ = 400.1648, found: 400.1671.

(2*R*,3*S*,6*S*)-2-((4-cyclopropyl-1*H*-1,2,3-triazol-1-yl)methyl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-ol (**6b**)

The product was obtained as light yellow oil in 96% (351 mg) yield. IR (film, cm⁻¹): 3347, 3156, 3120, 3100, 3010, 2978, 1647, 1613, 1509, 1470, 1430, 1323, 1040, 1010, 823, 760. ¹H NMR (300 MHz, CDCl₃) δ 7.73 – 7.50 (m, 3H), 7.26-7.48 (m, 4H), 6.11 – 5.93 (m, 2H), 5.43 (s, 1H), 4.61 (dd, *J* = 14.3, 1.9 Hz, 1H), 4.37 (dd, *J* = 14.3, 7.2 Hz, 1H), 3.96 (d, *J* = 8.4 Hz, 1H), 3.67 (dd, *J* = 11.2, 4.4 Hz, 1H), 1.89 – 1.71 (m, 1H), 0.89 – 0.72 (m, 2H), 0.71 – 0.62 (m, 2H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 150.10; 146.85; 136.71; 131.12; 129.73 (2C); 128.84; 126.77; 121.62; 120.38 (2C); 120.34; 72.95; 68.01; 63.79; 51.20; 7.86; 7.71; 6.60. HRMS calculated for C₁₉H₂₀N₆O₂ [M + H]⁺ = 364.1648. Found: 364.1656.

(2*R*,3*S*,6*S*)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-2-((4-(thiophen-3-yl)-1*H*-1,2,3-triazol-1-yl)methyl)-3,6-dihydro-2*H*-pyran-3-ol (**6c**)

The product was obtained as a yellow gummy solid in 85 % (345 mg) yield. IR (film, cm^{-1}): 3436, 3144, 3123, 1600, 1505, 1065, 1048, 1028, 998, 780, 763 cm^{-1} . ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 8.29 (s, 1H), 8.08 (s, 1H), 7.78 (dd, $J = 2.9, 1.2$ Hz, 1H), 7.69 – 7.54 (m, 3H), 7.53 – 7.38 (m, 4H), 6.17 – 5.92 (m, 2H), 5.48 (d, $J = 2.3$ Hz, 1H), 4.77 (dd, $J = 14.3, 2.1$ Hz, 1H), 4.50 (dd, $J = 14.4, 8.4$ Hz, 1H), 3.96 (1H), 3.67 (1H) these last two peaks are merged in the broad peak of moisture present in the DMSO solvent. ^{13}C NMR ($\text{DMSO}-d_6$, 75 MHz) δ (ppm): 146.80, 142.72, 136.14, 131.60, 130.80, 129.83 (2C), 128.81, 127.11, 126.58, 125.61, 121.84, 120.84, 120.79, 119.86 (2C), 72.97, 67.22, 63.18, 50.82. HRMS calculated for $\text{C}_{20}\text{H}_{18}\text{N}_6\text{O}_2\text{S}$ $[\text{M} + \text{H}]^+ = 406.1212$, found: 406.1290.

(2*R*,3*S*,6*S*)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-2-((4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)methyl)-3,6-dihydro-2*H*-pyran-3-ol (**6d**):

The product was obtained as a white solid in 94% (391 mg) yield. IR (film, cm^{-1}): 3430, 3117, 3101, 2957, 2867, 1610, 1509, 1270, 1057, 1032, 1012, 823, 761. ^1H NMR (300 MHz, CDCl_3) δ 7.86 (s, 1H), 7.58 (d, $J = 7.8$ Hz, 2H), 7.45 (m, 3H), 7.26 (dd, $J = 3.2, 2.5$ Hz, 3H), 7.11 (d, $J = 7.9$ Hz, 2H), 6.13 – 5.85 (m, 2H), 5.45 (s, 1H), 4.82 – 4.63 (m, 1H), 4.50 (dd, $J = 14.2, 7.2$ Hz, 1H), 3.98 (s, 2H), 3.74 (d, $J = 8.2$ Hz, 1H), 2.28 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 147.73, 146.88, 138.02, 136.60, 129.65 (2C), 129.55 (2C), 128.73, 127.54, 127.01, 125.58 (2C), 121.17, 120.31 (2C), 120.20, 73.06, 68.14, 64.11, 51.41, 21.26. The compound decomposed above 180 $^{\circ}\text{C}$. HRMS calcd for $\text{C}_{23}\text{H}_{22}\text{N}_6\text{O}_2$ $[\text{M} + \text{H}]^+ = 414.1804$, found 414.1834.

(2*R*,3*S*,6*S*)-2-((4-pentyl-1*H*-1,2,3-triazol-1-yl)methyl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-ol (**6e**):

7. Experimental

The product was obtained as light yellow oil in 90% (355 mg) yield. IR (film, cm^{-1}): 3403, 3132, 3110, 2921, 2867, 1605, 1508, 1475, 1270, 1050, 1022, 997, 763. ^1H NMR (300 MHz, CDCl_3) δ 7.69 – 7.48 (m, 3H), 7.50 – 7.26 (m, 4H), 6.19 – 5.85 (m, 2H), 5.46 (s, 1H), 4.63 (dd, $J = 14.3, 2.4$ Hz, 1H), 4.44 (dd, $J = 14.4, 6.8$ Hz, 1H), 4.31 (s, 1H), 3.95 (d, $J = 7.4$ Hz, 1H), 3.78 – 3.62 (m, 1H), 2.56 (dd, $J = 8.7, 7.0$ Hz, 2H), 1.63 – 1.39 (m, 2H), 1.20 (m, 4H), 0.77 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR(CDCl_3 , 75 MHz) δ (ppm): 148.32, 146.80, 136.76, 131.02, 129.74 (2C), 128.85, 126.90, 122.70, 120.40 (2C), 120.31, 72.90, 68.06, 63.81, 51.16, 31.39, 29.04, 25.54, 22.29, 13.92. HRMS calcd for $\text{C}_{21}\text{H}_{26}\text{N}_6\text{O}_2$ $[\text{M} + \text{H}]^+ = 394.2117$, Found: 394.2121.

(2*R*,3*S*,6*S*)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-2-((4-(pyridin-3-yl)-1*H*-1,2,3-triazol-1-yl)methyl)-3,6-dihydro-2*H*-pyran-3-ol (**6f**):

The product was obtained as a light yellow solid in 87% (349 mg) yield. IR (film, cm^{-1}): 3405, 3132, 3110, 2921, 2867, 1605, 1508, 1475, 1270, 1050, 1022, 997, 763. ^1H NMR (300 MHz, $\text{DMSO}-d_6$) ^1H NMR (300 MHz, DMSO) δ 9.07 (s, 1H), 8.64 (s, 1H), 8.55 (d, $J = 3.8$ Hz, 1H), 8.32 – 8.13 (m, 2H), 7.73 (dd, $J = 8.2, 1.5$ Hz, 2H), 7.49 (tdd, $J = 12.4, 6.9, 3.9$ Hz, 4H), 6.15 (dd, $J = 10.3, 3.1$ Hz, 1H), 6.01 (dd, $J = 12.0, 1.7$ Hz, 1H), 5.52 (d, $J = 5.6$ Hz, 2H), 4.85 (dd, $J = 14.3, 2.2$ Hz, 1H), 4.60 (dd, $J = 14.3, 8.2$ Hz, 1H), 4.11 – 4.00 (m, 1H), 3.75 (td, $J = 8.3, 2.0$ Hz, 1H). ^{13}C NMR ($\text{DMSO}-d_6$, 75 MHz) δ (ppm): 148.77, 146.83, 146.31, 143.36, 136.34, 132.29, 131.05, 129.73 (2C), 128.64, 126.57 (2C), 123.91, 122.77, 120.94, 119.88 (2C), 72.92, 67.36, 63.22, 51.02. The compound decomposed at 198°C. HRMS calculated for $\text{C}_{21}\text{H}_{19}\text{N}_7\text{O}_2$ $[\text{M} + \text{H}]^+ = 401.160$, found: 401.1671.

(2*R*,3*S*,6*S*)-2-((4-([1,1'-biphenyl]-4-yl)-1*H*-1,2,3-triazol-1-yl)methyl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-ol (**6g**)

The product was obtained as a white solid in 92% (439 mg) yield. IR (film, cm^{-1}): 3222, 3160, 3144, 3051, 2837, 1603, 1508, 1378, 1305, 1195, 1117, 1050, 1035, 767, 754. ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 8.52 (s, 1H), 8.22 (s, 1H), 7.92 (d, $J = 8.2$ Hz, 2H), 7.73 (t, $J = 7.2$ Hz, 6H), 7.57 – 7.33 (m, 6H), 6.08 (dd, $J = 43.0, 10.3$ Hz, 2H), 5.51 (d, $J = 6.6$ Hz, 1H), 4.84 (d, $J = 14.1$ Hz, 1H), 4.57 (dd, $J = 14.3, 8.3$ Hz, 1H), 4.05

(t, $J = 6.6$ Hz, 1H), 3.76 (t, $J = 7.5$ Hz, 1H). ^{13}C NMR (DMSO- d_6 , 75 MHz) δ (ppm): 146.92, 145.83, 139.60, 139.41, 136.36, 131.07, 129.76 (3C), 128.96 (2C), 128.61, 127.51, 127.06 (2C), 126.59, 126.48 (2C), 125.63 (2C), 122.10, 120.81, 119.89 (2C), 73.02, 67.38, 63.28, 50.97. The compound decomposed above 220 °C. HRMS calculated for $\text{C}_{28}\text{H}_{24}\text{N}_6\text{O}_2$ $[\text{M} + \text{H}]^+ = 476.1961$, found: 476.2001.

(2*R*,3*S*)-2-((4-(6-methoxynaphthalen-2-yl)-1*H*-1,2,3-triazol-1-yl)methyl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-ol (**6h**)

The product was obtained as a white solid in 90% (433 mg) yield. IR (film, cm^{-1}): 3384, 3250, 2900, 2870, 1657, 1510, 1270, 1026, 994, 827, 765. ^1H NMR (300 MHz, DMSO- d_6) δ 8.53 (s, 1H), 8.30 (s, 1H), 8.22 (s, 1H), 8.02 – 7.77 (m, 3H), 7.74 – 7.68 (m, 2H), 7.48 – 7.28 (m, 4H), 7.20 (dd, $J = 8.9, 2.5$ Hz, 1H), 6.14 (dd, $J = 10.3, 3.1$ Hz, 1H), 5.53 (d, $J = 2.1$ Hz, 1H), 4.84 (dd, $J = 14.3, 1.9$ Hz, 1H), 4.58 (dd, $J = 14.3, 8.3$ Hz, 1H), 4.13 – 3.98 (m, 1H), 3.90 (s, 3H), 3.75 (dd, $J = 8.3, 6.6$ Hz, 1H). ^{13}C NMR (DMSO- d_6 , 75 MHz) δ (ppm): 157.43, 146.90, 146.37, 136.33, 133.85, 131.06, 129.70 (2C), 129.45, 128.59, 128.53, 127.29, 126.58, 125.87, 124.01, 123.38, 121.93, 120.83, 119.87 (2C), 119.05, 106.04, 73.03, 67.37, 63.25, 55.22, 50.93. The compound decomposed above 195 °C. HRMS calcd for $\text{C}_{27}\text{H}_{24}\text{N}_6\text{O}_3$ $[\text{M} + \text{H}]^+ = 480.1910$ found 480.1946.

(2*R*,3*S*)-2-((4-(2,4-difluorophenyl)-1*H*-1,2,3-triazol-1-yl)methyl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-ol (**6i**)

The product was obtained as yellow solid in 85% (371 mg) yield. IR (film, cm^{-1}): 3443, 3140, 3120, 1650, 1512, 1033, 1005, 820, 766. ^1H NMR (300 MHz, DMSO- d_6) δ 8.35 – 8.19 (m, 2H), 8.13 (m, 1H), 7.83 – 7.70 (m, 2H), 7.60 – 7.44 (m, 3H), 7.40 – 7.11 (m, 2H), 6.14 (dd, $J = 10.4, 1.9$ Hz, 1H), 6.01 (d, $J = 10.3$ Hz, 1H), 5.61 – 5.42 (m, 1H), 4.87 (dd, $J = 14.2, 2.1$ Hz, 1H), 4.64 (dd, $J = 14.3, 8.2$ Hz, 1H), 4.05 (dd, $J = 10.8, 4.2$ Hz, 1H), 3.88 – 3.74 (m, 1H). ^{13}C NMR (DMSO- d_6 , 75 MHz) δ (ppm) 160, 146.77, 138.94, 136.40, 130.97 (3C), 128.60, 128.48, 128.42, 126.61, 123.98 (d, $J = 10.8$ Hz), 120.88, 119.88 (2C), 115.09 (d, $J = 9.8$ Hz), 112.16 (d, $J = 21.5$ Hz), 104.39 (t, $J = 26.1$ Hz), 72.79; 67.32, 63.29, 50.87. The compound decomposed at 152 °C. HRMS calculated for $\text{C}_{22}\text{H}_{18}\text{F}_2\text{N}_6\text{O}_2$ $[\text{M} + \text{H}]^+ = 436.1459$, found: 436.1493.

(2*R*,3*S*)-2-((4-(4-aminophenyl)-1*H*-1,2,3-triazol-1-yl)methyl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-ol (**6j**)

The product was obtained as a yellow solid in 92% (382 mg) yield. IR (film, cm^{-1}): 3440, 3420, 3335, 3110, 3100, 1640, 1603, 1502, 1030, 1010, 760. ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 8.17 (s, 1H), 8.10 (s, 1H), 7.71 (d, $J = 7.0$ Hz, 2H), 7.60 – 7.42 (m, 5H), 6.62 (d, $J = 8.4$ Hz, 2H), 6.21 – 6.07 (m, 1H), 5.98 (d, $J = 10.3$ Hz, 1H), 5.52 (dd, $J = 7.1, 4.7$ Hz, 1H), 5.21 (s, 1H), 4.84 – 4.70 (m, 1H), 4.49 (dd, $J = 14.3, 8.4$ Hz, 1H), 4.02 (t, $J = 6.8$ Hz, 1H), 3.70 (t, $J = 7.7$ Hz, 1H). ^{13}C NMR ($\text{DMSO-}d_6$, 75 MHz) δ (ppm): 148.53, 147.15, 146.97, 136.30, 130.98, 129.80 (2C), 128.67, 126.60, 126.13 (2C), 120.64, 119.89 (2C), 119.84, 118.32, 113.99 (2C), 73.10, 67.35, 63.25, 50.77. m.p. 103.5–104.5 $^{\circ}\text{C}$. HRMS calculated for $\text{C}_{22}\text{H}_{21}\text{N}_7\text{O}_2$ $[\text{M} + \text{H}]^+ = 415.1757$, found: 415.1783.

(2*R*,3*S*,6*S*)-2-((4-(4-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)methyl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-ol (**6-k**)

The product was obtained as light yellow gummy solid in 94% (404 mg) yield. IR (film, cm^{-1}): 3391, 3280, 3166, 3127, 2957, 2920, 2874, 2853, 1620, 1601, 1562, 1501, 1251, 1235, 1227, 1030, 819, 808, 754. ^1H NMR (300 MHz, CDCl_3) δ 7.82 (s, 1H), 7.62 (d, $J = 8.7$ Hz, 2H), 7.50 (s, 1H), 7.45 – 7.40 (m, 2H), 7.32 – 7.21 (m, 3H), 6.82 (d, $J = 8.7$ Hz, 2H), 6.17 – 5.90 (m, 2H), 5.44 (d, $J = 1.9$ Hz, 1H), 4.71 (dd, $J = 14.3, 2.2$ Hz, 1H), 4.49 (dd, $J = 14.3, 7.3$ Hz, 1H), 4.02 (dd, $J = 8.6, 1.6$ Hz, 1H). ^{13}C NMR (CDCl_3 , 75 MHz) δ (ppm): 159.64, 147.51, 146.85, 136.59, 131.01, 129.66 (3C), 128.76, 126.97 (2C), 123.06, 120.72, 120.30 (3C), 114.32 (2C), 73.03, 68.09, 64.05, 55.33, 51.38. HRMS calculated for $\text{C}_{23}\text{H}_{22}\text{N}_6\text{O}_3$ $[\text{M} + \text{H}]^+ = 430.1753$, found: 430.1784.

(2*R*,3*S*,6*S*)-2-((4-(4-(hydroxymethyl)phenyl)-1*H*-1,2,3-triazol-1-yl)methyl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-ol (**6l**)

The product was obtained as yellow oil in 95% (409 mg) yield. IR (film, cm^{-1}): 3430, 3395, 3220, 3150, 2920, 2870, 1621, 1603, 1557, 1503, 1495, 1035, 825, 807, 757. ^1H NMR (300 MHz, CDCl_3) δ 7.98 (s, 1H), 7.64 (s, 1H), 7.53 – 7.36 (m, 3H), 7.35 – 7.10 (m, 6H), 6.02 (m, 2H), 5.44 (d, $J = 1.7$ Hz, 1H), 4.75 (dd, $J = 14.3, 2.1$ Hz, 1H), 4.60 – 4.41 (m, 3H), 4.42 – 4.18 (m, 1H), 4.07 – 3.92 (m, 1H), 3.81 – 3.69 (m, 1H), 2.23 (d, $J = 23.7$ Hz, 1H). ^{13}C NMR (CDCl_3 , 75 MHz) δ (ppm): 147.38, 146.64, 138.62, 136.52, 131.04, 130.82, 129.72, 129.60 (2C), 128.88, 128.75, 128.64, 128.29, 126.81, 123.51, 120.56, 120.25 (2C), 72.80, 67.88, 64.34, 63.94, 51.58. HRMS calculated for $\text{C}_{23}\text{H}_{22}\text{N}_6\text{O}_3$ $[\text{M} + \text{H}]^+ = 430.1753$, found: 430.1787.

(2*R*,3*S*,6*S*)-2-((4-(4-ethynylphenyl)-1*H*-1,2,3-triazol-1-yl)methyl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-ol (**6m**)

The product was obtained as a yellow solid in 70% (297 mg) yield. IR (film, cm^{-1}): 3429, 3293, 3146, 2903, 2106 (characteristic alkyne C-C stretch), 1613, 1600, 1501, 1469, 1231, 1073, 1035, 799, 761. ^1H NMR (300 MHz, CDCl_3) δ 7.94 (s, 1H), 7.65 (d, $J = 8.1$ Hz, 2H), 7.52 (s, 1H), 7.47 – 7.35 (m, 4H), 7.31 – 7.21 (m, 3H), 6.04 (q, $J = 10.6$ Hz, 2H), 5.44 (d, $J = 18.2$ Hz, 1H), 4.73 (d, $J = 12.9$ Hz, 1H), 4.52 (dd, $J = 14.3, 7.3$ Hz, 1H), 4.02 (d, $J = 8.5$ Hz, 1H), 3.75 (t, $J = 7.1$ Hz, 1H), 3.06 (s, 1H). ^{13}C NMR (CDCl_3 , 75 MHz) δ (ppm): 146.84, 146.70, 136.55, 133.08 (2C), 130.98, 130.65, 129.70 (2C), 128.89, 126.96, 125.46 (2C), 121.89, 121.82, 120.39, 120.30 (2C), 83.42, 78.03, 72.89, 68.03, 64.06, 51.46. The compound decomposed at 170 $^\circ\text{C}$. HRMS calculated for $\text{C}_{24}\text{H}_{20}\text{N}_6\text{O}_2$ $[\text{M} + \text{H}]^+ = 424.1648$, found: 424.1671.

(2*R*,2'*R*,3*S*,3'*S*,6*S*,6'*S*)-2,2'-((4,4'-(1,4-phenylene)bis(1*H*-1,2,3-triazole-4,1-diyl))bis(methylene))bis(6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-ol) (**6n**)

7. Experimental

The compound was obtained as light yellow solid in 45% (325 mg) yield. IR (film, cm^{-1}): 3321, 3041, 2950, 2840, 1641, 1465, 1400, 1115, 1017. ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 8.53 (s, 2H), 8.20 (s, 2H), 7.88 (s, 4H), 7.71 (d, $J = 7.6$ Hz, 4H), 7.57 – 7.31 (m, 6H), 6.29 – 5.86 (m, 4H), 5.53 (d, $J = 2.0$ Hz, 2H), 4.83 (d, $J = 12.5$ Hz, 2H), 4.57 (dd, $J = 14.3, 8.2$ Hz, 2H), 4.04 (d, $J = 7.0$ Hz, 2H), 3.75 (t, $J = 7.4$ Hz, 2H). ^{13}C NMR ($\text{DMSO-}d_6$, 75 MHz) δ (ppm): 146.91 (2C), 146.84 (2C), 136.33 (2C), 131.04 (2C), 130.03 (2C), 129.72 (4C), 128.58 (2C), 126.60 (2C), 125.54 (4C), 122.18 (2C), 120.80 (2C), 119.86 (4C), 72.99 (2C), 67.38 (2C), 63.24 (2C), 50.95 (2C). m.p. 107-109 °C. HRMS calculated for $\text{C}_{38}\text{H}_{34}\text{N}_{12}\text{O}_4$ $[\text{M} + \text{H}]^+ = 722.2826$, found: 722.2993.

(2*R*,3*S*,6*S*)-2-((4-(cyclohex-1-en-1-yl)-1*H*-1,2,3-triazol-1-yl)methyl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-ol (**6o**)

The compound was obtained as light yellow oil in 87% yield (353 mg); IR (film, cm^{-1}): 3358, 3138, 2929, 2861, 1600, 1505, 1374, 1229, 1074, 1045, 845, 804, 761; ^1H NMR (300 MHz, CDCl_3) δ 7.59 – 7.46 (m, 4H), 7.46 – 7.13 (m, 3H), 6.38 (s, 1H), 6.10 – 5.87 (m, 2H), 5.43 (s, 1H), 4.67 (dd, $J = 14.3, 2.4$ Hz, 1H), 4.41 (dd, $J = 14.3, 7.3$ Hz, 1H), 4.07 – 3.92 (m, 1H), 3.70 (m, 1H), 2.32 – 2.15 (m, 2H), 2.16 – 1.98 (m, 2H), 1.71 – 1.20 (m, 4H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 149.19, 146.90, 136.69, 131.11, 129.69 (2C), 128.76, 127.02, 126.79, 125.17, 120.38, 120.32 (2C), 120.26, 73.05, 68.09, 63.92, 51.29, 26.27, 25.24, 22.37, 22.12; HRMS calculated for $\text{C}_{22}\text{H}_{24}\text{N}_6\text{O}_2$ $[\text{M} + \text{H}]^+ = 404.1961$, found: 404.11881.

General Procedure 3 (GP3); Synthesis of compounds **8a**, **8b**, and **8c**;

To a mixture of tetrakis(triphenylphosphine)palladium(0) (5 mol%), allylic acetate **3** (0.5 mM) in $\text{THF}:\text{H}_2\text{O}$ (7:3) was added sodium azide (1.1 eq.) and the reaction mixture was stirred at 50 °C for 1-2 hours. The color of the reaction mixture was observed to change from yellow to brown as the reaction completed (TLC monitoring). After completion of the reaction, the reaction mixture was extracted with a saturated solution of ammonium chloride (25 mL) and ethyl acetate (3x20 mL). The organic phases were combined, dried

over magnesium sulfate, filtered, and concentrated under vacuum. The mixture of the two products was passed through the chromatographic column to remove any residual ligands and side products. This was then followed by the next step where the mixture of azides **7** was taken in a two neck round bottom flask and the terminal alkyne (1.2 eq.), and copper iodide (7 mol %) were added in dimethylformamide (5 mL). This reaction mixture was stirred at 60 °C for 2-5 hours and on completion (TLC monitoring) the saturated solution of ammonium chloride (25 mL) was added. The reaction was extracted with ethyl acetate (3x20 mL), the organic phases were combined, dried over magnesium sulfate, filtered and evaporated under vacuum. The products were purified by flash chromatography using hexane and ethyl acetate as eluents.

((2*S*,3*S*,6*S*)-3-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8a-1**);

White solid. IR (film, cm^{-1}); 1737, 1600, 1505, 1367, 1229, 1045, 910, 761, 728, 693. ^1H NMR (300 MHz, CDCl_3) δ 8.16 (s, 1H), 8.11 (s, 1H), 7.83 (d, $J = 8.8$ Hz, 2H), 7.75 (d, $J = 9.1$ Hz, 2H), 7.53 (t, $J = 7.5$ Hz, 2H), 7.48 – 7.37 (m, 3H), 7.31 (t, 1H), 6.50 (d, $J = 10.2$ Hz, 1H), 6.15 (d, $J = 10.3$ Hz, 1H), 5.73 (s, 1H), 5.45 (d, $J = 7.6$ Hz, 1H), 4.32 (dt, $J = 7.8, 4.4$ Hz, 1H), 4.21 (d, $J = 4.4$ Hz, 2H), 2.04 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.53, 148.08, 146.11, 136.78, 130.92, 130.32, 129.88, 129.86, 129.08, 128.84 (2C), 128.27, 125.73 (2C), 124.00, 121.06, 120.59, 120.54, 119.15, 71.27, 67.09, 62.80, 54.67, 20.74. m. p. 60.4 °C. HRMS (ESI+), calcd. for $\text{C}_{24}\text{H}_{23}\text{N}_6\text{O}_3$ $[\text{M} + \text{H}]^+ = 443.1832$; found: 443.1795.

((2*S*,5*R*,6*S*)-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-5,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8b-1**);

Yellow solid. IR (film, cm^{-1}); 1737, 1601, 1505, 1439, 1367, 1231, 1078, 1046, 909, 728, 703, 693. ^1H NMR (300 MHz, CDCl_3) δ 8.12 (s, 1H), 8.08 (s, 1H), 7.81 (d, $J = 7.8$ Hz, 2H), 7.71 (d, $J = 8.7$ Hz, 2H), 7.55 – 7.27 (m, 6H), 6.32 (d, $J = 10.5$ Hz, 1H), 6.15 (d, $J = 10.4$ Hz, 1H), 5.98 (s, 1H), 5.46 (d, $J = 4.1$ Hz, 1H), 4.59 (dd, $J = 11.8, 5.8$ Hz, 1H), 4.49 (dd, $J = 5.7, 2.9$ Hz, 1H), 4.22 (dd, $J = 11.8, 3.2$ Hz, 1H), 2.11 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.70, 147.59, 143.98, 136.71, 130.55, 130.35, 129.80 (2C), 129.06, 128.81 (2C), 128.17, 125.71 (2C), 124.75, 121.74, 120.59 (2C), 119.93, 69.74 (2C), 64.41, 55.22, 20.94. m. p. 65.5 °C. HRMS (ESI+), calcd. for $\text{C}_{24}\text{H}_{23}\text{N}_6\text{O}_3$ $[\text{M} + \text{H}]^+ = 443.1832$; found: 443.1792.

((2*S*,3*S*,6*S*)-3-(4-butyl-1*H*-1,2,3-triazol-1-yl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8a-2**);

Colorless oil. IR (film, cm^{-1}); 3134, 3077, 2933, 2959, 1739, 1601, 1506, 1374, 1235, 1048, 763, 735. ^1H NMR (300 MHz, CDCl_3) δ 8.11 (s, 1H), 7.76 (d, $J = 8.1$ Hz, 2H), 7.59 – 7.45 (m, 4H), 6.46 (dt, $J = 10.2$, 2.8 Hz, 1H), 6.10 (dt, $J = 10.2$, 2.5 Hz, 1H), 5.71 (d, $J = 2.7$ Hz, 1H), 5.36 (dt, $J = 7.8$, 2.5 Hz, 1H), 4.24 (dt, $J = 8.0$, 4.2 Hz, 1H), 4.15 (d, $J = 5.4$ Hz, 2H), 2.71 (t, $J = 7.8$ Hz, 3H), 2.06 (s, 3H), 1.65 (p, $J = 7.6$ Hz, 3H), 1.38 (h, $J = 7.3$ Hz, 3H), 0.92 (t, $J = 7.3$ Hz, 4H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.57, 148.91, 146.21, 136.83, 130.42, 129.89 (2C), 129.10, 124.41, 120.92, 120.60 (2C), 119.90, 71.13, 67.18, 62.82, 54.39, 31.51, 25.42, 22.36, 20.77, 13.80. HRMS (ESI+), calcd. for $\text{C}_{24}\text{H}_{23}\text{N}_6\text{O}_3$ $[\text{M} + \text{H}]^+ = 423.2145$; found: 423.2105.

((2*S*,5*R*,6*S*)-5-(4-butyl-1*H*-1,2,3-triazol-1-yl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-5,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8b-2**);

Light yellow oil. IR (film, cm^{-1}); 3146, 2952, 2935, 2874, 1737, 1601, 1506, 1378, 1235, 1086, 1046, 763, 735, 694. ^1H NMR (300 MHz, CDCl_3) δ 8.04 (s, 1H), 7.72 (d, $J = 7.8$ Hz, 2H), 7.60 – 7.41 (m, 4H), 6.28 (dd, $J = 8.5$, 1.7 Hz, 1H), 6.12 (d, $J = 10.4$ Hz, 1H), 5.86 (s, 1H), 5.37 (d, $J = 4.2$ Hz, 1H), 4.57 (dd, $J = 11.6$, 6.0 Hz, 1H), 4.49 (s, 1H), 4.20 (dd, $J = 11.7$, 2.8 Hz, 1H), 2.69 (t, $J = 7.6$ Hz, 2H), 2.12 (s, 3H), 1.63 (p, $J = 7.6$ Hz, 2H), 1.34 (h, $J = 7.2$ Hz, 3H), 0.90 (t, $J = 7.4$ Hz, 4H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.68, 148.21, 144.14, 136.74, 129.91, 129.82 (2C), 129.08, 125.05, 121.59, 120.77, 120.60 (2C), 69.84, 69.68, 64.41, 55.12, 31.52, 25.42, 22.29, 20.90, 13.78. HRMS (ESI+), calcd. for $\text{C}_{24}\text{H}_{23}\text{N}_6\text{O}_3$ $[\text{M} + \text{H}]^+ = 423.2145$; found: 423.2098.

((2*S*,5*R*,6*S*)-5-(4-(2,4-difluorophenyl)-1*H*-1,2,3-triazol-1-yl)-6-(1-(4-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)-5,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8b-3**);

Light brown oil. IR (film, cm^{-1}); 3144, 2956, 1739, 1601, 1562, 1520, 1493, 1229, 1039, 834, 734. ^1H NMR (300 MHz, CDCl_3) δ 8.36 – 8.18 (m, 1H), 8.12 (s, 1H), 8.02 (s, 1H), 7.65 (d, J = 8.6 Hz, 2H), 7.04 (d, J = 7.7 Hz, 3H), 6.89 (t, J = 9.0 Hz, 1H), 6.52 (d, J = 9.9 Hz, 1H), 6.16 (d, J = 10.2 Hz, 1H), 5.74 (s, 1H), 5.45 (dd, J = 4.8, 2.2 Hz, 1H), 4.32 (d, J = 4.1 Hz, 1H), 4.22 (d, J = 3.6 Hz, 2H), 3.88 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.52, 160.06, 145.94, 140.87, 132.69, 131.25, 130.27, 128.83, 123.66, 122.99, 122.29, 121.71, 121.55, 120.89, 120.71, 114.90, 114.86, 112.19, 112.15, 111.91, 111.86, 104.48, 104.14, 103.80, 71.31, 67.29, 62.73, 55.66, 54.71, 20.73. HRMS (ESI+), calcd. for $\text{C}_{25}\text{H}_{23}\text{F}_2\text{N}_6\text{O}_4$ $[\text{M} + \text{H}]^+ = 509.1749$; found: 509.1708.

((2*S*,3*S*,6*S*)-3-(4-(2,4-difluorophenyl)-1*H*-1,2,3-triazol-1-yl)-6-(1-(4-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8a-3**).

Pale yellow oil. IR (film, cm^{-1}); 3153, 3082, 2963, 1743, 1628, 1601, 1521, 1493, 1257, 1235, 1041, 808, 737. ^1H NMR (300 MHz, CDCl_3) δ 8.16 (dd, J = 15.2, 8.4 Hz, 1H), 7.90 (d, J = 3.5 Hz, 1H), 7.39 (d, J = 8.8 Hz, 2H), 7.16 (s, 1H), 7.07 – 6.80 (m, 4H), 6.49 – 6.36 (m, 1H), 6.32 (d, J = 10.3 Hz, 1H), 5.71 (s, 1H), 5.56 (s, 1H), 4.91 (d, J = 2.9 Hz, 1H), 4.54 (dd, J = 12.0, 7.1 Hz, 1H), 4.30 (dd, J = 12.1, 3.2 Hz, 1H), 3.81 (s, 3H), 2.12 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 171.35, 170.72, 159.86, 131.12, 130.19, 128.81, 124.38, 122.32, 120.14, 114.64, 112.14, 112.07, 111.84, 111.80, 104.43, 104.08, 103.75, 72.43, 68.55, 63.57, 55.72, 55.58, 20.88. HRMS (ESI+), calcd. for $\text{C}_{25}\text{H}_{23}\text{F}_2\text{N}_6\text{O}_4$ $[\text{M} + \text{H}]^+ = 509.1749$; found: 509.1697.

((2*S*,3*S*,6*S*)-3-(4-cyclopropyl-1*H*-1,2,3-triazol-1-yl)-6-(1-(4-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8a-4**).

Pale yellow oil. IR (film, cm^{-1}); 3144, 3088, 2959, 1739, 1520, 1443, 1255, 1231, 1041, 836, 732. ^1H NMR (300 MHz, CDCl_3) δ 7.96 (s, 1H), 7.61 (d, J = 8.6 Hz, 2H), 7.53 (s, 1H), 7.01 (d, J = 8.5 Hz, 2H), 6.25 (d, J = 10.1 Hz, 1H), 6.10 (d, J = 10.4 Hz, 1H), 5.82 (s, 1H), 5.35 (d, J = 2.8 Hz, 1H), 4.54 (dd, J = 11.5, 5.8 Hz, 1H), 4.46 (s, 1H), 4.21 (d, J = 11.5 Hz, 1H), 3.86 (s, 3H), 2.13 (s, 3H), 2.01 – 1.84 (m, 1H), 0.92 (d, J = 8.2 Hz, 2H), 0.82 (s, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.62, 160.05, 143.89, 130.18, 130.14, 124.83, 122.23(3C), 121.65, 119.91, 114.83(2C), 69.84, 69.57, 64.50, 55.64, 55.02, 20.87, 7.63, 7.57, 6.72. HRMS (ESI+), calcd. for $\text{C}_{22}\text{H}_{25}\text{N}_6\text{O}_4$ $[\text{M} + \text{H}]^+ = 437.1937$; found: 437.1687.

((2*S*,5*R*,6*S*)-5-(4-cyclopropyl-1*H*-1,2,3-triazol-1-yl)-6-(1-(4-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)-5,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8b-4**);

Colourless oil. IR (film, cm^{-1}); 3138, 3088, 2941, 1739, 1520, 1441, 1253, 1229, 1082, 1039, 836, 728. ^1H NMR (300 MHz, CDCl_3) δ 7.94 (s, 1H), 7.57 (d, $J = 9.0$ Hz, 2H), 7.42 (s, 1H), 6.96 (d, $J = 9.0$ Hz, 2H), 6.44 – 6.29 (m, 1H), 5.99 (dd, $J = 10.2, 2.2$ Hz, 1H), 5.60 (d, $J = 2.3$ Hz, 1H), 5.25 (dd, $J = 7.7, 2.4$ Hz, 1H), 4.17 – 4.10 (m, 1H), 4.10 – 4.02 (m, 2H), 3.80 (s, 3H), 1.97 (s, 3H), 1.92 – 1.76 (m, 1H), 0.92 – 0.81 (m, 2H), 0.84 – 0.61 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.50, 160.07, 145.97, 132.09, 130.53, 130.25, 124.27, 122.23, 121.04, 114.90, 71.05, 67.18, 62.85, 55.65, 54.46, 20.71, 7.76, 7.72, 6.73. HRMS (ESI+), calcd. for $\text{C}_{22}\text{H}_{25}\text{N}_6\text{O}_4$ $[\text{M} + \text{H}]^+ = 437.1937$; found: 437.1693.

((2*S*,3*S*,6*S*)-6-(1-(benzo[d]thiazol-7-yl)-1*H*-1,2,3-triazol-4-yl)-3-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-3,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8a-5**);

White solid. IR (film, cm^{-1}); 3136, 3080, 2954, 1739, 1609, 1486, 1369, 1233, 1046, 816, 698. ^1H NMR (300 MHz, CDCl_3) δ 9.08 (s, 1H), 8.36 (s, 1H), 8.23 (dd, $J = 16.4, 8.8$ Hz, 2H), 8.09 (s, 1H), 7.89 – 7.76 (m, 3H), 7.42 – 7.28 (m, 3H), 6.40 – 6.27 (m, 1H), 6.21 – 6.11 (m, 1H), 5.99 (s, 1H), 5.49 (d, $J = 4.1$ Hz, 1H), 4.61 (dd, $J = 11.7, 5.9$ Hz, 1H), 4.53 (s, 1H), 4.23 (d, $J = 11.1$ Hz, 1H), 2.10 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 175.37, 161.30, 157.88, 152.11, 149.02, 139.82, 139.04, 135.60, 135.34, 133.60 (3C), 132.93, 130.39 (2C), 129.20, 129.07, 127.26, 124.78, 124.03, 119.01, 74.70, 74.26, 69.26, 60.08, 25.66. m. p. 190 °C. HRMS (ESI+), calcd. for $\text{C}_{25}\text{H}_{22}\text{N}_7\text{O}_3\text{S}$ $[\text{M} + \text{H}]^+ = 500.1505$; found: 500.1453.

((2*S*,5*R*,6*S*)-6-(1-(benzo[d]thiazol-7-yl)-1*H*-1,2,3-triazol-4-yl)-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-5,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8b-5**);

Pale yellow gummy solid. IR (film, cm^{-1}); 3136, 3069, 2965, 1739, 1480, 1439, 1372, 1233, 1046, 767, 698. ^1H NMR (300 MHz, CDCl_3) δ 8.37 (s, 1H), 8.20 (d, $J = 8.8$ Hz, 1H), 8.09 (s, 1H), 7.91 (s, 1H), 7.80 (dd, $J = 11.5, 4.3$ Hz, 3H), 7.41 – 7.17 (m, 4H), 6.62 (dd, $J = 10.0, 3.1$ Hz, 1H), 6.36 – 6.21 (m, 1H), 5.79

(s, 1H), 5.29 (d, $J = 3.6$ Hz, 1H), 4.59 (dd, $J = 11.7, 5.9$ Hz, 1H), 4.50 (s, 1H), 4.22 (dd, $J = 11.7, 2.7$ Hz, 1H), 1.87 (s, 4H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.18, 155.98, 147.90, 146.14, 134.34, 132.31, 130.50, 128.83 (2C), 128.23, 125.75 (2C), 124.76, 123.45, 121.02, 119.61, 119.19, 114.32, 69.18, 68.33, 62.71, 53.65, 20.64. HRMS (ESI+), calcd. for $\text{C}_{25}\text{H}_{22}\text{N}_7\text{O}_3\text{S}$ $[\text{M} + \text{H}]^+ = 500.1505$; found: 500.1461.

((2*R*,3*S*,6*S*)-3-acetoxy-6-(1-((2*S*,3*S*,6*S*)-2-(acetoxymethyl)-6-(1-(benzo[d]thiazol-7-yl)-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-yl)-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8a-6**);

Light yellow gummy solid. IR (film, cm^{-1}): 3140, 3115, 2957, 1739, 1600, 1503, 1372, 1231, 1045, 762, 690. ^1H NMR (300 MHz, CDCl_3) δ 7.94 (s, 1H), 7.76 (s, 1H), 7.64 (d, $J = 8.0$ Hz, 2H), 7.05 (d, $J = 8.8$ Hz, 2H), 6.67 (dd, $J = 10.0, 3.4$ Hz, 1H), 6.42 – 6.21 (m, 2H), 5.99 (d, $J = 8.6$ Hz, 1H), 5.78 (s, 1H), 5.53 (s, 1H), 5.34 (d, $J = 4.2$ Hz, 2H), 4.43 (s, 1H), 4.31 – 4.05 (m, 4H), 3.95 – 3.80 (m, 4H), 2.09 (s, 6H), 1.97 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.78, 170.34, 170.06, 160.15, 146.33, 145.47, 132.56, 130.20, 129.52, 125.85, 123.12, 122.24 (2C), 122.01, 120.61, 114.92 (2C), 69.64, 69.01, 68.33, 67.69, 64.97, 63.06, 62.55, 55.65, 53.63, 21.02, 20.72, 20.62. HRMS (ESI+), calcd. for $\text{C}_{28}\text{H}_{31}\text{N}_6\text{O}_8$ $[\text{M} + \text{H}]^+ = 579.2203$; found: 579.2181.

((2*R*,3*S*,6*S*)-3-acetoxy-6-(1-((2*S*,3*R*,6*S*)-6-(acetoxymethyl)-2-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-yl)-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8b-6**);

Light yellow oil. IR (film, cm^{-1}): 3142, 3118, 1745, 1600, 1503, 1372, 1231, 1046, 765, 693. ^1H NMR (300 MHz, CDCl_3) δ 7.90 (s, 1H), 7.77 (s, 1H), 7.54 (d, $J = 9.0$ Hz, 2H), 6.95 (d, $J = 8.9$ Hz, 2H), 6.28 – 5.98 (m, 3H), 5.95 – 5.79 (m, 2H), 5.41 (s, 1H), 5.30 (d, $J = 3.7$ Hz, 1H), 5.28 – 5.17 (m, 1H), 4.51 – 4.35 (m, 2H), 4.10 (ddd, $J = 14.8, 10.9, 2.7$ Hz, 3H), 3.89 – 3.72 (m, 4H), 2.05 (s, 3H), 1.99 (d, $J = 3.6$ Hz, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.72, 170.65, 170.31, 160.10, 145.96, 143.68, 132.13, 132.00, 130.70, 130.12, 129.71, 128.56, 128.40, 125.54, 124.36, 122.35, 122.20 (2C), 121.64, 114.87 (2C), 69.96, 69.69, 69.59, 67.51, 64.84, 64.40, 62.86, 55.64, 55.25, 20.96, 20.87, 20.74. HRMS (ESI+), calcd. for $\text{C}_{28}\text{H}_{31}\text{N}_6\text{O}_8$ $[\text{M} + \text{H}]^+ = 579.2203$; found: 579.2187.

((2*S*,3*S*,6*S*)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)-3,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8a-7**);

White solid. IR (film, cm^{-1}); 3140, 2924, 1737, 1600, 1501, 1229, 1045, 761, 732, 693. ^1H NMR (300 MHz, CDCl_3) δ 8.07 (s, 1H), 8.01 (s, 1H), 7.70 (t, $J = 6.4$ Hz, 4H), 7.57 – 7.42 (m, 3H), 7.20 (d, $J = 7.8$ Hz, 2H), 6.32 (d, $J = 8.9$ Hz, 1H), 6.15 (d, $J = 10.3$ Hz, 1H), 5.95 (s, 1H), 5.45 (d, $J = 4.1$ Hz, 1H), 4.60 (dd, $J = 11.7, 5.9$ Hz, 1H), 4.50 (s, 1H), 4.22 (dd, $J = 11.8, 3.0$ Hz, 1H), 2.36 (s, 3H), 2.11 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 170.78, 170.34, 170.06, 160.15, 146.33, 145.47, 132.56, 130.20, 129.52, 125.85, 123.12, 122.24 (2C), 122.01, 120.61, 114.92 (2C), 69.64, 69.01, 67.69, 64.97, 63.06, 62.55, 55.65, 53.63, 21.02, 20.72, 20.62. m. p. 182.7 °C. HRMS (ESI+), calcd. for $\text{C}_{25}\text{H}_{25}\text{N}_6\text{O}_3$ $[\text{M} + \text{H}]^+ = 457.1988$; found: 457.2019.

((2*S*,5*R*,6*S*)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-5-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)-5,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8b-7**);

White solid. IR (film, cm^{-1}); 3140, 2926, 1737, 1600, 1501, 1229, 1045, 909, 728, 693. ^1H NMR (300 MHz, CDCl_3) δ 8.07 (s, 1H), 7.94 (s, 1H), 7.73 (t, $J = 9.0$ Hz, 4H), 7.61 – 7.41 (m, 3H), 7.22 (t, $J = 6.9$ Hz, 2H), 6.68 (dd, $J = 10.0, 2.9$ Hz, 1H), 6.32 (dd, $J = 9.8, 5.6$ Hz, 1H), 5.83 (s, 1H), 5.33 (d, $J = 3.2$ Hz, 1H), 4.43 (s, 1H), 4.31 (dd, $J = 7.3, 4.3$ Hz, 1H), 4.21 (d, $J = 4.2$ Hz, 1H), 2.37 (s, 3H), 1.93 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.16, 147.95, 145.85, 138.03, 136.84, 132.36, 129.88 (2C), 129.51 (2C), 129.11, 129.07, 127.72, 125.66 (2C), 123.36, 120.62, 120.58 (2C), 119.25, 69.17, 68.36, 62.79, 53.64, 21.26. m. p. 184.4 °C. HRMS (ESI+), calcd. for $\text{C}_{25}\text{H}_{25}\text{N}_6\text{O}_3$ $[\text{M} + \text{H}]^+ = 457.1988$; found: 457.2011.

((2*S*,3*S*,6*S*)-3-(4-cyclopropyl-1*H*-1,2,3-triazol-1-yl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8a-8**);

White solid. IR (film, cm^{-1}); 3144, 3006, 2956, 1739, 1600, 1505, 1233, 1043, 763, 693. ^1H NMR (300 MHz, CDCl_3) δ 8.04 (s, 1H), 7.72 (d, $J = 8.1$ Hz, 2H), 7.53 (t, $J = 7.5$ Hz, 3H), 7.49 – 7.37 (m, 1H), 6.25 (d, $J = 10.3$ Hz, 1H), 6.11 (d, $J = 10.4$ Hz, 1H), 5.84 (s, 1H), 5.37 (d, $J = 3.9$ Hz, 1H), 4.55 (dd, $J = 11.7, 5.9$ Hz, 1H), 4.47 (s, 1H), 4.21 (dd, $J = 11.6, 2.8$ Hz, 1H), 2.13 (s, 3H), 1.97 – 1.86 (m, 1H), 0.92 (d, $J =$

8.3 Hz, 2H), 0.88 – 0.72 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3): δ 170.16, 150.33, 145.94, 136.85, 132.01, 129.88 (2C), 129.11, 123.46, 120.58 (2C), 120.45, 119.57, 69.21, 68.30, 62.80, 53.40, 20.63, 7.77, 7.72, 6.79. m. p. 82.7 °C. HRMS (ESI+), calcd. for $\text{C}_{21}\text{H}_{23}\text{N}_6\text{O}_3$ $[\text{M} + \text{H}]^+ = 407.1832$; found: 407.1801.

((2*S*,5*R*,6*S*)-5-(4-cyclopropyl-1*H*-1,2,3-triazol-1-yl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-5,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8b-8**);

Light yellow gummy solid. IR (film, cm^{-1}): 3142, 3118, 1743, 1600, 1503, 1372, 1231, 1046, 763, 692. ^1H NMR (300 MHz, CDCl_3) δ 8.03 (s, 1H), 7.76 (d, $J = 7.7$ Hz, 2H), 7.63 – 7.36 (m, 4H), 6.63 (dd, $J = 10.0$, 2.6 Hz, 1H), 6.37 – 6.18 (m, 1H), 5.78 (s, 1H), 5.25 (d, $J = 2.9$ Hz, 1H), 4.37 (dd, $J = 9.9$, 4.5 Hz, 1H), 4.28 – 4.11 (m, 2H), 2.01 – 1.86 (m, 4H), 1.07 – 0.80 (m, 4H). ^{13}C NMR (75 MHz, CDCl_3): δ 170.59, 149.90, 144.12, 136.76, 130.13, 129.79 (2C), 129.03, 124.82, 121.55, 120.58 (2C), 119.89, 69.81, 69.59, 64.46, 55.00, 20.86, 7.63, 7.57, 6.72. HRMS (ESI+), calcd. for $\text{C}_{21}\text{H}_{23}\text{N}_6\text{O}_3$ $[\text{M} + \text{H}]^+ = 407.1832$; found: 407.1811.

((2*S*,3*R*,6*S*)-3-(4-cyclopropyl-1*H*-1,2,3-triazol-1-yl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**8c-8**);

White solid. IR (film, cm^{-1}): 3142, 3118, 1739, 1600, 1503, 1372, 1231, 1046, 765, 693. ^1H NMR (300 MHz, CDCl_3) δ 8.04 (s, 1H), 7.75 (d, $J = 7.4$ Hz, 2H), 7.60 – 7.44 (m, 4H), 6.63 (dd, $J = 10.1$, 3.5 Hz, 1H), 6.27 (ddd, $J = 9.9$, 5.7, 1.9 Hz, 1H), 5.79 (s, 1H), 5.32 – 5.20 (m, 1H), 4.45 – 4.31 (m, 1H), 3.83 (dd, $J = 11.8$, 5.4 Hz, 1H), 3.70 (dd, $J = 11.8$, 6.8 Hz, 1H), 2.05 – 1.90 (m, 4H), 1.02 – 0.92 (m, 2H), 0.92 – 0.84 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.16, 150.33, 145.94, 136.85, 132.01, 129.88 (2C), 129.11, 123.46, 120.58 (2C), 120.45, 119.57, 69.21, 68.30, 62.80, 53.40, 20.63, 7.77, 7.72, 6.79. m. p. 85.2 °C. HRMS (ESI+), calcd. for $\text{C}_{21}\text{H}_{23}\text{N}_6\text{O}_3$ $[\text{M} + \text{H}]^+ = 407.1832$; found: 407.1803.

((2*S*,3*S*,6*S*)-3-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-2-yl)methanol (**9a**);

7. Experimental

Pale yellow solid. IR (film, cm^{-1}); 3342, 3118, 2975, 1600, 1503, 1372, 1231, 1046, 765, 693. ^1H NMR (300 MHz, CDCl_3) δ 8.05 (s, 1H), 7.94 (s, 1H), 7.86 (d, $J = 6.9$ Hz, 2H), 7.75 (d, $J = 7.2$ Hz, 2H), 7.61 – 7.29 (m, 6H), 6.74 (d, $J = 9.9$ Hz, 1H), 6.47 – 6.26 (m, 1H), 5.81 (s, 1H), 5.35 (s, 1H), 4.29 (d, $J = 6.3$ Hz, 1H), 3.24 (d, $J = 17.4$ Hz, 2H), 2.65 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 136.83, 133.28, 130.40, 129.85, 129.11, 128.87, 128.31, 125.76, 122.76, 120.69, 120.61, 119.90, 71.36, 68.25, 61.29, 53.34. m. p. 201 °C. HRMS (ESI+), calcd. for $\text{C}_{22}\text{H}_{21}\text{N}_6\text{O}_2$ $[\text{M} + \text{H}]^+ = 401.1726$; found: 401.1731.

((2*S*,5*R*,6*S*)-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-5,6-dihydro-2*H*-pyran-2-yl)methanol (**9b**):

Light yellow solid. IR (film, cm^{-1}); 3340, 3118, 2970, 1603, 1505, 1372, 1231, 1045, 765, 693. ^1H NMR (300 MHz, CDCl_3) δ 8.13 (s, 1H), 8.08 (s, 1H), 7.85 (d, $J = 7.8$ Hz, 2H), 7.74 (d, $J = 8.0$ Hz, 2H), 7.62 – 7.30 (m, 6H), 6.35 (d, $J = 10.6$ Hz, 1H), 6.23 (d, $J = 10.2$ Hz, 1H), 5.94 (s, 1H), 5.49 (s, 1H), 4.36 (s, 1H), 3.94 (s, 2H), 2.36 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 136.83, 133.28, 130.40, 129.85 (2C), 129.11, 128.87 (2C), 128.31, 125.76 (2C), 122.76, 120.69 (2C), 120.61, 119.90, 71.36, 68.25, 61.29, 53.34. m. p. 195.0 °C. HRMS (ESI+), calcd. for $\text{C}_{22}\text{H}_{21}\text{N}_6\text{O}_2$ $[\text{M} + \text{H}]^+ = 401.1726$; found: 401.1743.

((2*S*,3*S*,6*S*)-3-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-2-yl)methyl methanesulfonate (**10a**):

Light yellow solid. IR (film, cm^{-1}); 3130, 3118, 2970, 1601, 1503, 1372, 1231, 1045, 763, 692. ^1H NMR (300 MHz, CDCl_3) δ 8.18 (s, 1H), 8.05 – 7.73 (m, 5H), 7.66 – 7.31 (m, 6H), 6.84 (dd, $J = 10.1$, 3.6 Hz, 1H), 6.34 (ddd, $J = 10.0$, 5.8, 2.1 Hz, 1H), 5.88 (d, $J = 2.2$ Hz, 1H), 5.34 (d, $J = 5.5$ Hz, 1H), 4.56 – 4.39 (m, 1H), 4.28 – 4.05 (m, 1H), 3.75 (dd, $J = 11.4$, 7.7 Hz, 1H), 2.96 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 148.08, 145.59, 133.21, 130.25, 129.84 (2C), 129.04, 128.90 (2C), 128.82, 128.42, 125.79 (2C), 122.33, 120.60 (3C), 119.67, 69.87, 68.90, 68.81, 53.28, 37.84. m. p. 129 °C. HRMS (ESI+), calcd. for $\text{C}_{23}\text{H}_{23}\text{N}_6\text{O}_4\text{S}$ $[\text{M} + \text{H}]^+ = 479.1501$; found: 479.1491.

((2*S*,5*R*,6*S*)-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-5,6-dihydro-2*H*-pyran-2-yl)methyl methanesulfonate (**10b**);

Light yellow solid. IR (film, cm^{-1}); 3130, 3118, 2970, 1601, 1503, 1372, 1231, 1045, 763, 692. ^1H NMR (300 MHz, DMSO) δ 8.98 (s, 1H), 8.54 (s, 1H), 8.00 – 7.80 (m, 4H), 7.61 (t, $J = 7.6$ Hz, 2H), 7.56 – 7.39 (m, 3H), 7.34 (t, $J = 7.1$ Hz, 1H), 6.42 – 6.21 (m, 2H), 5.84 (s, 1H), 5.44 (d, $J = 3.7$ Hz, 1H), 4.69 – 4.56 (m, 2H), 4.51 (d, $J = 9.3$ Hz, 1H), 3.26 (s, 3H). ^{13}C NMR (75 MHz, DMSO) δ 146.89, 144.61, 136.96, 131.03, 130.58, 130.39 (2C), 129.34 (3C), 128.44, 125.66 (2C), 124.98, 122.89, 120.89, 120.64 (2C), 70.60, 69.95, 69.64, 55.79, 37.35. m. p. 225.3 $^{\circ}\text{C}$. HRMS (ESI+), calcd. for $\text{C}_{23}\text{H}_{23}\text{N}_6\text{O}_4\text{S}$ $[\text{M} + \text{H}]^+ = 409.1501$; found: 409.1483.

4-((2*S*,5*S*,6*R*)-6-(azidomethyl)-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-5,6-dihydro-2*H*-pyran-2-yl)-1-phenyl-1*H*-1,2,3-triazole (**11a**);

Light yellow gummy solid. IR (film, cm^{-1}); 3132, 3099, 2924, 2121, 1600, 1506, 1233, 1046, 763, 694. ^1H NMR (300 MHz, CDCl_3) δ 7.88 (s, 1H), 7.78 (d, $J = 8.1$ Hz, 2H), 7.43 (ddd, $J = 19.8, 16.6, 9.2$ Hz, 9H), 6.55 (dd, $J = 10.3, 1.9$ Hz, 1H), 6.10 (dd, $J = 10.3, 2.2$ Hz, 1H), 5.65 (d, $J = 2.2$ Hz, 1H), 4.87 – 4.68 (m, 2H), 4.25 (td, $J = 7.6, 3.9$ Hz, 1H), 3.91 (dd, $J = 5.0, 2.4$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 148.31, 147.10, 136.80, 131.26 (2C), 130.04, 129.62 (2C), 128.97 (2C), 128.64 (2C), 125.92 (2C), 123.12, 120.37 (2C), 119.46, 72.18, 67.99, 55.82, 54.83. HRMS (ESI+), calcd. for $\text{C}_{22}\text{H}_{20}\text{N}_9\text{O}$ $[\text{M} + \text{H}]^+ = 426.1791$; found: 426.1734.

1-((2*S*,3*R*,6*S*)-6-(azidomethyl)-2-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-3-yl)-4-phenyl-1*H*-1,2,3-triazole (**11b**);

Light yellow gummy solid. IR (film, cm^{-1}); 3132, 3099, 2924, 2099, 1600, 1506, 1233, 1046, 763, 694. ^1H NMR (300 MHz, CDCl_3) δ 8.16 (s, 1H), 8.08 (s, 1H), 7.84 (d, $J = 7.1$ Hz, 2H), 7.72 (d, $J = 7.2$ Hz, 2H),

7.58 – 7.28 (m, 6H), 6.41 – 6.29 (m, 1H), 6.16 (d, $J = 10.3$ Hz, 1H), 5.97 (d, $J = 1.3$ Hz, 1H), 5.46 (d, $J = 2.8$ Hz, 1H), 4.42 (s, 1H), 3.68 – 3.54 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 147.77, 143.94, 136.73, 131.48, 130.61, 129.85 (2C), 129.15, 128.83 (2C), 128.15, 125.74 (2C), 124.30, 121.44, 120.65 (2C), 119.79, 70.37, 69.86, 54.89, 53.58. HRMS (ESI+), calcd. for $\text{C}_{22}\text{H}_{20}\text{N}_9\text{O}$ $[\text{M} + \text{H}]^+ = 426.1791$; found: 426.1751.

1-phenyl-4-((2S,3R,6S)-3-(4-phenyl-1H-1,2,3-triazol-1-yl)-6-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)-3,6-dihydro-2H-pyran-2-yl)-1H-1,2,3-triazole (12a);

Light yellow gummy solid. IR (film, cm^{-1}): 3130, 2957, 2931, 1600, 1505, 1462, 1231, 1076, 1046, 765, 694. ^1H NMR (300 MHz, DMSO) δ 8.98 (s, 1H), 8.63 (s, 1H), 8.04 (s, 1H), 7.87 (dd, $J = 15.7, 7.4$ Hz, 4H), 7.75 (d, $J = 6.9$ Hz, 2H), 7.61 (t, $J = 7.5$ Hz, 2H), 7.43 (ddd, $J = 24.3, 15.4, 7.1$ Hz, 7H), 6.47 (d, $J = 10.2$ Hz, 1H), 6.29 (d, $J = 9.1$ Hz, 1H), 5.82 (s, 1H), 5.50 (d, $J = 3.6$ Hz, 1H), 4.92 (ddd, $J = 17.2, 14.4, 5.0$ Hz, 2H), 4.72 (s, 1H). ^{13}C NMR (75 MHz, DMSO) δ 146.38, 146.24, 144.01, 136.43, 131.24, 130.58, 130.31, 129.90 (3C), 128.85 (3C), 128.76 (2C), 127.86, 127.83, 125.12 (3C), 123.96, 122.54, 122.49, 120.15 (2C), 119.86, 69.54, 69.29, 55.14, 51.42. HRMS (ESI+), calcd. for $\text{C}_{30}\text{H}_{26}\text{N}_9\text{O}$ $[\text{M} + \text{H}]^+ = 528.2260$; found: 528.2234.

4-butyl-1-(((2S,5R,6S)-5-(4-phenyl-1H-1,2,3-triazol-1-yl)-6-(1-phenyl-1H-1,2,3-triazol-4-yl)-5,6-dihydro-2H-pyran-2-yl)methyl)-1H-1,2,3-triazole (12b);

Light yellow gummy solid. IR (film, cm^{-1}): 3136, 2957, 2931, 1601, 1505, 1462, 1231, 1076, 1046, 765, 696. ^1H NMR (300 MHz, CDCl_3) δ 8.07 (s, 1H), 7.82 (d, $J = 7.1$ Hz, 2H), 7.73 (d, $J = 7.2$ Hz, 2H), 7.59 – 7.38 (m, 5H), 7.35 (d, $J = 5.3$ Hz, 3H), 6.43 – 6.24 (m, 2H), 5.83 (d, $J = 1.4$ Hz, 1H), 5.47 (d, $J = 2.7$ Hz, 1H), 4.72 (dd, $J = 14.9, 5.9$ Hz, 1H), 4.65 – 4.56 (m, 2H), 2.65 – 2.40 (m, 2H), 1.50 (tq, $J = 13.1, 6.4$ Hz, 2H), 1.22 (dq, $J = 14.8, 7.3$ Hz, 2H), 0.81 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 148.69, 147.57, 143.77, 136.69, 131.80, 130.37 (2C), 129.86, 129.20, 128.80 (2C), 128.22, 125.84 (2C), 123.74, 122.52, 121.35, 120.67 (2C), 119.36, 70.71, 69.06, 54.54, 52.22, 31.29, 25.26, 22.25, 13.67. HRMS (ESI+), calcd. for $\text{C}_{28}\text{H}_{30}\text{N}_9\text{O}$ $[\text{M} + \text{H}]^+ = 508.2573$; found: 508.2554.

((2*R*,3*S*,6*S*)-3-acetoxy-6-(1-(((2*S*,5*R*,6*S*)-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-5,6-dihydro-2*H*-pyran-2-yl)methyl)-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-2-yl)methyl acetate (**12c**);

Light yellow solid. IR (film, cm^{-1}); 1657, 1236, 1052, 1026, 1002, 763, 665. ^1H NMR (300 MHz, DMSO) δ 8.93 (s, 1H), 8.26 (s, 1H), 8.14 (s, 1H), 7.88 (t, $J = 6.8$ Hz, 4H), 7.62 (t, $J = 7.6$ Hz, 2H), 7.56 – 7.42 (m, 3H), 7.36 (t, $J = 7.3$ Hz, 1H), 6.40 (d, $J = 10.4$ Hz, 1H), 6.28 (d, $J = 10.5$ Hz, 1H), 6.10 (d, $J = 10.3$ Hz, 1H), 5.79 (d, $J = 10.4$ Hz, 2H), 5.52 (d, $J = 4.9$ Hz, 1H), 5.39 (s, 1H), 5.15 (d, $J = 7.9$ Hz, 1H), 4.97 (dd, $J = 14.3, 7.5$ Hz, 1H), 4.90 – 4.78 (m, 1H), 4.74 (s, 1H), 4.09 (dd, $J = 12.0, 5.4$ Hz, 1H), 4.04 – 3.94 (m, 1H), 3.78 (dd, $J = 5.0, 2.3$ Hz, 1H), 1.98 (s, 3H), 1.93 (s, 3H). ^{13}C NMR (75 MHz, DMSO): δ 170.02, 169.85, 146.38, 144.94, 144.24, 136.42, 130.58, 130.47, 130.22, 129.89 (3C), 128.84 (2C), 127.96, 125.23 (2C), 124.78, 124.53, 122.33, 120.29, 120.09 (3C), 70.25, 68.68, 68.60, 66.72, 64.31, 62.44, 55.61, 51.00, 20.64, 20.39. m. p. 120 $^{\circ}\text{C}$. HRMS (ESI+), calcd. for $\text{C}_{34}\text{H}_{34}\text{N}_9\text{O}_6$ $[\text{M} + \text{H}]^+ = 664.2632$; found: 664.2601.

4-butyl-1-(((2*R*,3*S*,6*S*)-3-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-6-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-3,6-dihydro-2*H*-pyran-2-yl)methyl)-1*H*-1,2,3-triazole (**12d**);

Yellowish green gummy solid. IR (film, cm^{-1}); 3136, 2957, 2931, 1601, 1505, 1462, 1231, 1076, 1046, 765, 696. ^1H NMR (300 MHz, CDCl_3) δ 7.83 (s, 1H), 7.76 – 7.68 (m, 2H), 7.64 (s, 1H), 7.58 – 7.48 (m, 3H), 7.42 – 7.32 (m, 6H), 6.62 (dd, $J = 10.3, 2.9$ Hz, 1H), 6.10 (dd, $J = 12.4, 2.1$ Hz, 1H), 5.73 (d, $J = 2.0$ Hz, 1H), 5.44 (dd, $J = 7.9, 2.3$ Hz, 1H), 4.72 (dd, $J = 14.2, 8.3$ Hz, 1H), 4.58 (dd, $J = 14.2, 3.0$ Hz, 1H), 4.50 (td, $J = 8.1, 3.0$ Hz, 1H), 2.72 (t, 2H), 1.66 (dt, $J = 15.4, 7.5$ Hz, 2H), 1.38 (dq, $J = 14.5, 7.3$ Hz, 2H), 0.92 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 149.04, 148.17, 146.51, 136.68, 131.18, 130.97, 129.94, 129.67 (2C), 128.94 (2C), 128.77, 128.63, 125.83, 123.83 (2C), 120.33 (2C), 120.08, 119.85, 72.13, 67.70, 55.47, 55.39, 31.40, 25.44, 22.34, 13.78. HRMS (ESI+), calculated for $\text{C}_{28}\text{H}_{30}\text{N}_9\text{O}$ $[\text{M} + \text{H}]^+ = 508.2573$; found: 508.2601.

General Procedure 4 (GP4); Synthesis of compounds 14a-o and 15a-g:

To a mixture of 2-iodo-3,4,6-tri-*O*-acetyl-D-glucal **13** (398 mg, 1 mmol) and DMF (5 mL) in a two neck round bottom flask under nitrogen was added palladium acetate (11.2 mg, 5 mol%) and cesium carbonate (488.7 mg, 1.5 eq.). This was then followed by the dropwise addition of the terminal alkyne (1.2 eq.) while stirring, at room temperature for 0.3-5 hours. The color of the reaction mixture changes from a yellowish to dark brown as the catalyst and base are added. After completion of reaction (TLC monitoring) concentrated aqueous solution of ammonium chloride (20 mL) was added to the reaction mixture and was extracted with ethyl acetate (3x25 mL). The organic phases were combined and extracted with deionized/distilled water (1x40 mL). The resulting organic phase was dried over magnesium sulfate, filtered and concentrated under vacuum. The product was purified by flash chromatography using ethyl acetate and hexane as eluents.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-(phenylethynyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (14a):

Light brown oil. IR (cm⁻¹, film); 3067, 2961, 1745, 1631, 1598, 1492, 145, 1371, 1223, 1186, 1048, 1028, 912, 760, 694; ¹H NMR (300 MHz, CDCl₃) δ 7.32 – 7.25 (m, 2H), 7.20 (dd, *J* = 4.9, 2.0 Hz, 3H), 6.86 (s, 1H), 5.56-5.54 (d, *J* = 5.4 Hz, 1H), 5.17 (dd, *J* = 7.0, 5.5 Hz, 1H), 4.36 (dd, *J* = 11.8, 5.9 Hz, 1H), 4.28 (m, 1H), 4.14 (dd, *J* = 11.8, 3.0 Hz, 1H), 2.05 – 1.97 (m, 9H). ¹³C NMR (75 MHz, CDCl₃) δ 170.41, 170.09, 169.37, 150.52, 131.19, 128.29, 128.04, 123.13, 97.26, 90.17, 83.41, 74.42, 67.35, 66.51, 61.11, 20.79, 20.73, 20.65. HRMS calculated for C₂₀H₂₀NaO₇ [M+Na]⁺ = 395.1107, found 395.0949.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-(*p*-tolylethynyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (14b):

Light yellow oil. IR (cm⁻¹, film) 3030, 1743, 1631, 1512, 1434, 1371, 1216, 1181, 1046, 1028, 957, 910, 819. ¹H NMR (300 MHz, CDCl₃) δ 7.18 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 7.8 Hz, 2H), 6.84 (s, 1H), 5.55 (d, *J* = 5.5 Hz, 1H), 5.24 – 5.10 (m, 1H), 4.35 (dd, *J* = 11.9, 5.9 Hz, 1H), 4.28 (dd, *J* = 10.0, 5.4 Hz, 1H), 4.14 (dd, *J* = 11.9, 2.8 Hz, 1H), 2.25 (s, 3H), 2.02 (d, *J* = 3.3 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 170.40, 170.09, 169.36, 150.22, 138.16, 131.09 (2C), 129.05 (2C), 120.05, 97.40, 90.30, 82.64, 74.38, 67.43, 66.54, 61.12, 21.41, 20.76, 20.70, 20.62. HRMS calculated for C₂₁H₂₂O₇ [M+Na]⁺ = 409.1263, found 409.0964.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-(cyclopropylethynyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**14c**):

Light yellow oil. IR (cm⁻¹, film) 2982, 2257, 1737, 1633, 1430, 1374, 1222, 1046, 1030, 912, 730. ¹H NMR (300 MHz, CDCl₃) δ 6.69 (s, 1H), 5.40 (d, *J* = 5.6 Hz, 1H), 5.10 (dd, *J* = 7.1, 5.5 Hz, 1H), 4.31 (dd, *J* = 11.8, 5.8 Hz, 1H), 4.23-4.18 (m, 1H), 4.11 (dd, *J* = 11.9, 3.2 Hz, 1H), 2.05 – 1.98 (m, 9H), 1.27 – 1.17 (m, 1H), 0.74 – 0.67 (m, 2H), 0.61-0.56 (m, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 170.38, 170.05, 169.34, 149.76, 97.34, 93.98, 74.11, 69.16, 67.60, 66.57, 61.13, 20.71, 20.69, 20.60, 8.45, 8.40, -0.00. HRMS calculated for C₁₇H₂₀O₇ [M+Na]⁺ = 359.1107, found 359.1005.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((4-aminophenyl)ethynyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**14d**):

Light brown gummy solid. IR (cm⁻¹, film) 3369, 2930, 1737, 1629, 1600, 1512, 1371, 1220, 1181, 1022, 909, 832. ¹H NMR (300 MHz, CDCl₃) δ 7.10 (d, *J* = 8.5 Hz, 2H), 6.81 (s, 1H), 6.50 (d, *J* = 8.5 Hz, 2H), 5.53 (dd, *J* = 5.6, 1.0 Hz, 1H), 5.16 (dd, *J* = 7.1, 5.5 Hz, 1H), 4.35 (dd, *J* = 11.9, 5.8 Hz, 1H), 4.26 (td, *J* = 6.6, 2.9 Hz, 1H), 4.14 (dd, *J* = 11.9, 3.1 Hz, 1H), 2.04 – 2.00 (m, 9H). ¹³C NMR (75 MHz, CDCl₃) δ 170.48, 170.20, 169.43, 149.56, 146.60, 132.60, 114.67, 112.40, 97.67, 90.75, 80.91, 74.28, 67.59, 66.64, 61.18, 20.81, 20.73, 20.65. HRMS calculated for C₂₀H₂₁NO₇ [M+H]⁺ = 388.1318, found 388.1114.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-(pyridin-3-ylethynyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**14e**):

Colorless oil. IR (cm⁻¹, film) 3078, 3034, 2976, 2211, 1749, 1631, 1583, 1479, 1410, 1372, 1227, 1186, 1052, 1025, 957, 912, 810, 707. ¹H NMR (300 MHz, CDCl₃) δ 8.71 (s, 1H), 8.50 (d, *J* = 28.6 Hz, 1H), 7.81 – 7.55 (m, 1H), 7.29 – 7.17 (m, 1H), 6.93 (s, 1H), 5.54 (d, *J* = 5.6 Hz, 1H), 5.18 (dd, *J* = 6.4, 5.2 Hz, 1H), 4.46 – 4.26 (m, 2H), 4.27 – 4.09 (m, 1H), 2.15-1.98 (m, 9H). ¹³C NMR (75 MHz, CDCl₃) δ 170.37, 169.98, 169.32, 152.96, 151.60, 151.02, 149.33, 147.51, 139.49, 138.65, 123.29, 96.56, 87.65, 86.43, 74.54, 66.90, 66.31, 60.99, 20.74, 20.70, 20.62. HRMS calculated for C₂₀H₂₁NO₇ [M+H]⁺ = 374.1240, found 374.1074.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((2,4-difluorophenyl)ethynyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**14f**):

Light yellow oil. IR (cm⁻¹, film) 3085, 2970, 2218, 1747, 1633, 1506, 1430, 1372, 1225, 1186, 1147, 1052, 1033, 970, 912, 855, 819. ¹H NMR (300 MHz, CDCl₃) δ 7.33 – 7.15 (m, 1H), 6.90 (d, *J* = 1.1 Hz, 1H), 6.82 – 6.67 (m, 2H), 5.57 (d, *J* = 5.6 Hz, 1H), 5.18 (dd, *J* = 7.1, 5.7 Hz, 1H), 4.43 – 4.23 (m, 2H), 4.16 (dd, *J* = 11.8, 2.8 Hz, 1H), 2.11 – 1.91 (m, 9H). ¹³C NMR (75 MHz, CDCl₃) δ 170.41, 170.11, 169.35, 164.28 (dd, *J* = 17.8, 11.2 Hz), 160.93 (dd, *J* = 16.6, 11.9 Hz), 151.06, 133.77 (dd, *J* = 9.7, 2.6 Hz), 111.50 (dd, *J* = 21.8, 3.6 Hz), 108.13 (dd, *J* = 15.9, 4.2 Hz), 104.19 (t, *J* = 25.4 Hz), 97.02, 88.30, 82.44, 74.55, 67.16, 66.43, 61.06, 20.70, 20.66, 20.63. HRMS calculated for C₂₀H₁₈F₂O₇ [M+H]⁺ = 431.0918, found 431.0757.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-(hex-1-yn-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**14g**):

Colorless oil. IR (cm⁻¹, film) 2959, 2935, 2875, 1749, 1635, 1458, 1436, 1371, 1227, 1182, 1052, 1032, 912. ¹H NMR (300 MHz, CDCl₃) δ 6.69 (s, 1H), 5.43 (d, *J* = 5.5 Hz, 1H), 5.11 (dd, *J* = 7.2, 5.5 Hz, 1H), 4.32 (dd, *J* = 11.9, 5.8 Hz, 1H), 4.21 (td, *J* = 6.6, 3.1 Hz, 1H), 4.12 (dd, *J* = 12.0, 3.2 Hz, 1H), 2.19 (t, *J* = 6.8 Hz, 2H), 2.01 (d, *J* = 3.7 Hz, 9H), 1.45 – 1.25 (m, 4H), 0.83 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 170.40, 170.06, 169.37, 149.48, 97.46, 90.81, 74.11, 73.96, 67.66, 66.70, 61.14, 30.70, 21.81, 20.71, 20.65, 20.61, 18.94, 13.50. HRMS calculated for C₁₈H₂₄O₇ [M+Na]⁺ = 375.3687, found 375.3576.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((6-methoxynaphthalen-2-yl)ethynyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**14h**):

Light yellow oil. IR (cm⁻¹, film) 3084, 2970, 2956, 2942, 1736, 1628, 1601, 1503, 1488, 1387, 1378, 1251, 1238, 1227, 1208, 1179, 1166, 1132, 1052, 1032, 905, 886, 853. ¹H NMR (300 MHz, CDCl₃) δ 7.72 (s, 1H), 7.57 (t, *J* = 8.4 Hz, 2H), 7.30 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.10 – 6.96 (m, 2H), 6.89 (s, 1H), 5.58 (d, *J* = 5.6 Hz, 1H), 5.18 (dd, *J* = 6.9, 5.5 Hz, 2H), 4.41 – 4.24 (m, 2H), 4.15 (dd, *J* = 11.8, 3.0 Hz, 1H), 3.81 (s, 3H), 2.09 – 1.94 (m, 9H). ¹³C NMR (75 MHz, CDCl₃) δ 170.42, 170.15, 169.40, 158.30, 150.39, 134.01, 130.73, 129.24, 128.68, 128.47, 126.80, 119.39, 118.03, 105.87, 97.42, 90.72, 83.05, 74.42, 67.41, 66.56, 61.15, 55.30, 20.84, 20.74, 20.65. HRMS calculated for C₂₅H₂₄O₈ [M+Na]⁺ = 475.1369, found 475.1224.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-(thiophen-3-ylethynyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**14i**):

Light yellow oil. IR (cm⁻¹, film) 3110, 2960, 2930, 1743, 1629, 1523, 1434, 1371, 1220, 1182, 1048, 1030, 955, 912, 786. ¹H NMR (300 MHz, CDCl₃) δ 7.30 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.17 (dd, *J* = 5.0, 3.0 Hz, 1H), 6.98 (dd, *J* = 5.0, 1.2 Hz, 1H), 6.85 (d, *J* = 1.1 Hz, 1H), 5.52 (d, *J* = 5.5 Hz, 1H), 5.16 (dd, *J* = 6.8, 5.4 Hz, 1H), 4.36 (dd, *J* = 11.8, 6.0 Hz, 1H), 4.28 (td, *J* = 6.4, 2.9 Hz, 4H), 4.14 (dd, *J* = 11.8, 3.0 Hz, 1H), 2.04 – 2.00 (m, 9H). ¹³C NMR (75 MHz, CDCl₃) δ 170.40, 170.07, 169.36, 150.47, 129.63, 128.18, 125.32, 122.11, 97.09, 85.19, 82.88, 74.36, 67.27, 66.48, 61.10, 20.78, 20.72, 20.64. HRMS calculated for C₁₈H₁₈O₇S [M+H]⁺ = 379.0843, found 379.0340.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-(4-hydroxybut-1-yn-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**14j**):

Colorless oil. IR (cm⁻¹, film) 2965, 2840, 1745, 1631, 1607, 1512, 1462, 1445, 1371, 1223, 1184, 1032, 959, 912, 836. ¹H NMR (300 MHz, CDCl₃) δ 6.73 (s, 1H), 5.44 (d, *J* = 5.4 Hz, 1H), 5.12 (dd, *J* = 6.8, 5.3 Hz, 1H), 4.33 (dd, *J* = 11.8, 6.0 Hz, 1H), 4.24 (td, *J* = 6.4, 3.0 Hz, 1H), 4.13 (dd, *J* = 11.9, 3.2 Hz, 1H), 3.65 (dt, *J* = 12.3, 6.0 Hz, 2H), 2.51 – 2.42 (m, 2H), 2.08 – 1.99 (m, 9H). ¹³C NMR (75 MHz, CDCl₃) δ 170.63, 170.44, 169.36, 150.02, 96.91, 87.52, 74.22, 67.54, 66.47, 61.11, 23.85, 23.58, 20.85, 20.72, 20.65. HRMS calculated for C₁₆H₂₀O₈ [M-H]⁻ = 339.1158, found 339.1067.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((4-methoxyphenyl)ethynyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**14k**):

Brown oil. IR (cm⁻¹, film) 3391, 2944, 2840, 1745, 1633, 1607, 1514, 1372, 1223, 1182, 1145, 1026, 836. ¹H NMR (300 MHz, CDCl₃) δ 7.23 (d, *J* = 8.5 Hz, 2H), 6.83 (s, 1H), 6.74 (d, *J* = 8.6 Hz, 2H), 5.54 (d, *J* = 5.6 Hz, 1H), 5.16 (dd, *J* = 7.0, 5.5 Hz, 1H), 4.35 (dd, *J* = 11.9, 5.9 Hz, 1H), 4.27 (td, *J* = 6.5, 2.9 Hz, 1H), 4.14 (dd, *J* = 11.9, 3.1 Hz, 1H), 3.71 (s, 3H), 2.11 – 1.95 (m, 9H). ¹³C NMR (75 MHz, CDCl₃) δ 170.39, 170.09, 169.36, 159.50, 149.97, 132.66, 115.24, 113.97, 97.44, 90.03, 81.88, 74.34, 67.46, 66.55, 61.13, 55.23, 20.77, 20.70, 20.62. HRMS calculated for C₂₁H₂₂O₈ [M+H]⁺ = 403.1400, found 403.1305.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((4-pentylphenyl)ethynyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**14l**):

Yellowish brown oil. IR (cm⁻¹, film) 2959, 2931, 2859, 1747, 1631, 1512, 1439, 1371, 1223, 1184, 1143, 1050, 1030, 959, 912, 843. ¹H NMR (300 MHz, CDCl₃) δ 7.20 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 8.2 Hz, 2H), 6.85 (s, 1H), 5.55 (d, *J* = 5.7 Hz, 1H), 5.17 (dd, *J* = 7.0, 5.5 Hz, 1H), 4.36 (dd, *J* = 11.9, 5.9 Hz, 1H), 4.27 (td, *J* = 6.5, 2.9 Hz, 1H), 4.15 (dd, *J* = 11.9, 3.0 Hz, 1H), 2.50 (t, *J* = 7.7 Hz, 2H), 2.07 – 1.98 (m, 9H), 1.60 – 1.43 (m, 2H), 1.24 (tt, *J* = 5.8, 3.2 Hz, 4H), 0.81 (t, *J* = 6.8 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 170.41, 170.10, 169.37, 150.21, 143.23, 131.12 (2C), 128.40 (2C), 120.24, 97.43, 90.34, 82.61, 74.38, 67.44, 66.56, 61.14, 35.81, 31.39, 30.86, 22.47, 20.78, 20.72, 20.64, 13.96. HRMS calculated for C₂₅H₃₀O₇ [M-H]⁻ = 441.1992, found 441.0016.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((4-phenethylphenyl)ethynyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**14m**):

Colorless oil. IR (cm⁻¹, film) 3065, 3030, 2940, 1743, 1633, 1499, 1456, 1371, 1218, 1179, 1048, 1030, 909, 752, 702. ¹H NMR (300 MHz, CDCl₃) δ 7.25 – 7.17 (m, 2H), 7.13 (dd, *J* = 6.9, 4.4 Hz, 3H), 6.68 (s, 1H), 5.40 (d, *J* = 5.4 Hz, 1H), 5.09 (dd, *J* = 6.8, 5.5 Hz, 1H), 4.31 (dd, *J* = 11.9, 5.9 Hz, 1H), 4.25 – 4.17 (m, 1H), 4.10 (dd, *J* = 11.9, 3.1 Hz, 1H), 2.73 (t, *J* = 7.4 Hz, 2H), 2.48 (t, *J* = 7.5 Hz, 2H), 2.00 (d, *J* = 3.7 Hz, 6H), 1.96 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 170.41, 170.09, 169.39, 149.85, 140.54, 128.50, 128.37 (2C), 126.27, 97.19, 89.85, 74.88, 74.12, 67.49, 66.65, 61.14, 35.05, 21.45, 20.75, 20.72, 20.63. HRMS calculated for C₂₂H₂₄O₇ [M+H]⁺ = 401.1689, found 401.1601.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((3-hydroxyphenyl)ethynyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**14n**):

Yellow oil. IR (cm⁻¹, film) 3410, 3085, 2980, 2935, 1745, 1663, 1631, 1609, 1592, 1579, 1484, 1448, 1371, 1220, 1181, 1046, 1030, 955, 912, 873, 786, 761, 689. ¹H NMR (300 MHz, CDCl₃) δ 7.06 (t, *J* = 7.9 Hz, 1H), 6.89 – 6.80 (m, 2H), 6.78 (dd, *J* = 2.5, 1.5 Hz, 1H), 6.75 – 6.68 (m, 1H), 6.58 (s, 1H), 5.55 (d, *J* = 5.6, 1H), 5.17 (dd, *J* = 7.0, 5.6 Hz, 1H), 4.36 (dd, *J* = 11.9, 5.8 Hz, 1H), 4.28 (td, *J* = 6.5, 2.8 Hz, 1H), 4.15 (dd, *J* = 11.9, 2.9 Hz, 1H), 2.05 – 2.00 (m, 9H). ¹³C NMR (75 MHz, CDCl₃) δ 170.73, 170.44, 169.60, 155.98, 150.58, 129.54, 124.13, 123.41, 117.87, 115.73, 97.20, 90.12, 83.15, 74.38, 67.47, 66.53, 61.18, 20.80, 20.72, 20.66. HRMS calculated for C₂₀H₂₀O₈ [M-H]⁻ = 387.1158, found 387.1075.

(2*R*,3*S*,4*R*)-5-([1,1'-biphenyl]-4-ylethynyl)-2-(acetoxymethyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**14o**):

Yellow gummy solid. IR (cm⁻¹, film) 3060, 3032, 2950, 1739, 1629, 1488, 1371, 1218, 1181, 1046, 1026, 957, 912, 843, 767, 726, 700. ¹H NMR (300 MHz, CDCl₃) δ 7.65 – 7.51 (m, 4H), 7.46 (dd, *J* = 7.7, 5.9 Hz, 4H), 7.37 (t, *J* = 7.3 Hz, 1H), 6.99 (s, 1H), 5.68 (d, *J* = 5.4 Hz, 1H), 5.29 (dd, *J* = 6.9, 5.5 Hz, 1H), 4.47 (dd, *J* = 11.8, 5.9 Hz, 1H), 4.40 (td, *J* = 6.5, 2.9 Hz, 1H), 4.26 (dd, *J* = 11.9, 3.0 Hz, 1H), 2.17 – 2.09 (m, 9H). ¹³C NMR (75 MHz, CDCl₃) δ 170.42, 170.12, 169.39, 150.57, 140.81, 140.32, 131.61, 128.85, 127.61, 126.99, 122.05, 97.34, 90.12, 84.14, 74.46, 67.36, 66.53, 61.13, 20.82, 20.74, 20.66. HRMS calculated for C₂₆H₂₄O₇ [M-H]⁻ = 447.1522, found 447.1479.

(2*R*,3*S*,4*R*)-2-(hydroxymethyl)-5-(phenylethynyl)-3,4-dihydro-2*H*-pyran-3,4-diol (**15a**):

Light yellow gummy solid. IR (cm⁻¹, film) 3391, 2940, 2203, 1726, 1678, 1495, 1447, 1078, 1045, 765, 698. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.35 (ddd, *J* = 13.9, 9.7, 6.1 Hz, 1H), 6.90 (s, 1H), 3.93 (d, *J* = 5.9 Hz, 1H), 3.88 – 3.78 (m, 1H), 3.75 – 3.59 (m, 1H), 3.54 (dd, *J* = 7.6, 6.2 Hz, 1H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 149.74, 130.79 (2C), 128.51 (2C), 127.62, 123.62, 100.33, 87.98, 87.88, 80.37, 78.00, 73.11, 68.44, 67.93, 59.94. HRMS calculated for C₁₄H₁₄O₄ [M-H]⁻ = 246.0892, found 245.0818.

(2*R*,3*S*,4*R*)-2-(hydroxymethyl)-5-((3-hydroxyphenyl)ethynyl)-3,4-dihydro-2*H*-pyran-3,4-diol (**15b**):

Yellow oil. IR (cm⁻¹, film) 3336, 2921, 2841, 1633, 1512, 1287, 1254, 1143, 1072, 1050, 830. ¹H NMR (300 MHz, methanol-*d*₄) δ 6.96 (t, *J* = 7.9 Hz, 1H), 6.84 – 6.65 (m, 3H), 6.59 (ddd, *J* = 8.2, 2.4, 0.8 Hz, 1H), 4.00 (d, *J* = 6.5 Hz, 1H), 3.84 – 3.66 (m, 3H), 3.57 (dd, *J* = 10.8, 4.0 Hz, 2H). ¹³C NMR (75 MHz, methanol-*d*₄) δ 157.23, 150.06, 129.49, 125.27, 122.77, 117.76, 115.25, 101.03, 89.12, 85.18, 80.12, 69.91, 68.89, 60.97. HRMS calculated for C₁₄H₁₄O₅ [M-H]⁻ = 261.0841, found 261.0788.

(2*R*,3*S*,4*R*)-2-(hydroxymethyl)-5-(pyridin-3-ylethynyl)-3,4-dihydro-2*H*-pyran-3,4-diol (**15c**):

Yellow gummy solid. IR (cm⁻¹, film) 3351, 2952, 1640, 1633, 1443, 1421, 1390, 1181, 1107, 1025, 667. ¹H NMR (300 MHz, methanol-*d*₄) δ 8.59 (s, 1H), 8.43 (d, *J* = 4.8 Hz, 1H), 7.85 (d, *J* = 7.9 Hz, 1H), 7.39 (dd, *J* = 7.9, 5.0 Hz, 1H), 6.96 (s, 1H), 4.17 (d, *J* = 6.6 Hz, 1H), 4.01 – 3.84 (m, 3H), 3.74 (dd, *J* = 8.3, 6.7 Hz, 1H). ¹³C NMR (75 MHz, methanol-*d*₄) δ 152.21, 152.05, 148.27, 139.99, 124.91, 123.25, 101.61, 91.14, 86.17, 81.46, 70.72, 69.75, 61.92. HRMS calculated for C₁₃H₁₃NO₄ [M-H]⁻ = 246.0845, found 246.0734.

(2*R*,3*S*,4*R*)-2-(hydroxymethyl)-5-((4-pentylphenyl)ethynyl)-3,4-dihydro-2*H*-pyran-3,4-diol (**15d**):

White solid. IR (cm⁻¹, film) 3290, 2959, 2933, 2858, 1626, 1514, 1413, 1197, 1074, 1019, 914. ¹H NMR (300 MHz, MeOD) δ 7.28 (d, *J* = 7.9 Hz, 2H), 7.08 (d, *J* = 7.8 Hz, 2H), 6.81 (s, 1H), 4.10 (d, *J* = 6.4 Hz, 1H), 4.00 – 3.74 (m, 3H), 3.69 (d, *J* = 6.8 Hz, 1H), 2.68 – 2.45 (m, 2H), 1.58 (d, *J* = 6.8 Hz, 2H), 1.30 (s, 4H), 0.86 (t, *J* = 6.6 Hz, 3H). ¹³C NMR (75 MHz, MeOD) δ 150.73, 143.89, 132.17 (2C), 129.43 (2C), 122.67, 102.29, 90.11, 85.89, 81.21, 71.01, 69.97, 62.02, 36.76, 32.58, 32.19, 23.56, 14.38. m. p. 182.6 °C. HRMS calculated for C₁₉H₂₄O₄ [M-H]⁻ = 315.675, found 315.1611.

(2*R*,3*S*,4*R*)-5-([1,1'-biphenyl]-4-ylethynyl)-2-(hydroxymethyl)-3,4-dihydro-2*H*-pyran-3,4-diol (**15e**):

Light yellow solid. IR (cm⁻¹, film) 3275, 2929, 1633, 1488, 1451, 1194, 1078, 1052, 1037, 844, 769, 702. ¹H NMR (300 MHz, MeOD) δ 7.68 – 7.28 (m, 9H), 6.89 (s, 1H), 4.20 (d, *J* = 5.6 Hz, 1H), 3.91 (s, 3H), 3.76 (d, *J* = 6.5 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 150.86, 141.30, 132.42 (3C), 129.64 (2C), 128.34, 127.65(4C), 123.91, 101.69, 89.80, 86.94, 80.66, 70.59, 69.67, 61.83. m. p. 204.1 °C. HRMS calculated for C₂₀H₁₈O₄ [M-H]⁻ = 321.1105, found 321.1158.

(2*R*,3*S*,4*R*)-2-(hydroxymethyl)-5-((4-methoxyphenyl)ethynyl)-3,4-dihydro-2*H*-pyran-3,4-diol (**15f**):

Light yellow gummy solid. IR (cm⁻¹, film) 3286, 2921, 2843, 1633, 1514, 1290, 1253, 1194, 1141, 1074, 1052, 1030, 933, 870, 832. ¹H NMR (300 MHz, methanol-*d*₄) δ 7.30 (d, *J* = 8.9 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 2H), 6.79 (s, 1H), 4.08 (d, *J* = 6.5 Hz, 1H), 3.89 – 3.80 (m, 3H), 3.75 (s, 3H), 3.70 – 3.63 (m, 1H). ¹³C NMR (75 MHz, methanol-*d*₄) δ 160.88, 150.51, 133.74 (2C), 117.65, 115.09 (2C), 102.47, 89.88, 84.99, 81.28, 71.15, 70.10, 62.13, 55.88. HRMS calculated for C₁₅H₁₆O₅ [M-H]⁻ = 275.0998, found 275.0890.

(2*R*,3*S*,4*R*)-5-(hex-1-yn-1-yl)-2-(hydroxymethyl)-3,4-dihydro-2*H*-pyran-3,4-diol (**15g**);

Light yellow pasty solid. IR (cm⁻¹, film) 3326, 2921, 2843, 1630, 1510, 1290, 1253, 1194, 1141, 1074, 1052, 1030, 932, 870, 832. ¹H NMR (300 MHz, methanol-*d*₄) δ 6.66 (s, 1H), 4.02 (d, *J* = 6.6 Hz, 1H), 3.92 – 3.76 (m, 3H), 3.70 – 3.56 (m, 1H), 2.32 (t, *J* = 6.7 Hz, 2H), 1.60 – 1.38 (m, 4H), 0.94 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (75 MHz, methanol-*d*₄) δ 148.18, 100.97, 88.78, 79.39, 75.44, 69.77, 68.62, 60.60, 30.81, 21.55, 18.49, 12.59. HRMS calculated for C₁₂H₁₈O₄ [M-H]⁻ = 225.1205, found 225.0890.

General Procedure 5 (GP5); Synthesis of compounds 16a-g:

In a round bottom two-neck flask, under nitrogen containing the 2-alkynyl-D-glucal (0.5 mM) and 1,4-dioxane (15 mL) was added gold (III) chloride (30 mg, 10 mol %) and was refluxed for 5-24 hours. The reaction was then quenched by adding saturated solution of ammonium hydroxide (15 mL) and was extracted with ethyl acetate (3x20 mL). The organic phase was then dried over magnesium sulfate, filtered and saturated under vacuum. The product was purified by flash chromatography using ethyl acetate and hexane as eluents (10-20 % ethyl acetate/hexane).

(6*R*,7*S*,7*aR*)-6-(hydroxymethyl)-2-phenyl-7,7*a*-dihydro-6*H*-furo[3,2-*c*]pyran-7-ol (**16a**):

Light yellow oil. IR (cm⁻¹, film) 3420, 3063, 2929, 2903, 1681, 1629, 1495, 1451, 1402, 1134, 1108, 1078, 1015, 762, 698. ¹H NMR (300 MHz, CDCl₃) δ 7.38 (dd, *J* = 6.7, 2.9 Hz, 2H), 7.25 (dd, *J* = 5.0, 1.7 Hz, 3H), 6.07 (d, *J* = 4.5 Hz, 1H), 5.52 (s, 1H), 4.64 (dd, *J* = 6.4, 1.3 Hz, 1H), 3.97 – 3.84 (m, 1H), 3.70 (d, *J* = 4.3 Hz, 1H), 3.45 (dd, *J* = 8.0, 1.9 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 170.88, 137.79, 133.25, 131.72, 128.34, 122.33, 97.95, 90.39, 84.86, 66.51, 65.05, 62.82. HRMS (APCI negative mode M-1-H₂O) calculated for C₁₄H₁₄O₄: 227.0786, found 227.0727.

(6*R*,7*S*,7*aR*)-6-(hydroxymethyl)-2-(4-pentylphenyl)-7,7*a*-dihydro-6*H*-furo[3,2-*c*]pyran-7-ol (**16d**):

Light yellow oil. IR (cm⁻¹, film) 3387, 2959, 2929, 2858, 1629, 1611, 1510, 1462, 1439, 1417, 1383, 1365, 1298, 1134, 1082, 1060, 1015, 937, 919, 870. ¹H NMR (300 MHz, CDCl₃) δ 7.35 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 6.10 (d, *J* = 3.9 Hz, 1H), 5.57 (s, 1H), 4.76 – 4.64 (m, 1H), 3.97 (t, *J* = 7.3 Hz, 1H), 3.76 (d, *J* = 4.0 Hz, 1H), 3.50 (dd, *J* = 8.0, 1.8 Hz, 1H), 2.59 (t, *J* = 7.6 Hz, 2H), 1.68 – 1.55 (m, 2H), 1.40 – 1.24 (m, 4H), 0.88 (t, *J* = 6.4 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 177.83, 144.16, 131.65, 129.02, 128.80, 128.50, 126.45, 124.02, 119.46, 98.44, 84.62, 76.42, 66.67, 63.12, 35.89, 31.43, 30.84, 22.50, 14.00. HRMS (APCI negative mode M-1-H₂O) calculated for C₁₉H₂₄O₄: 297.1569, found 297.1505.

(6*R*,7*S*,7*aR*)-2-([1,1'-biphenyl]-4-yl)-6-(hydroxymethyl)-7,7*a*-dihydro-6*H*-furo[3,2-*c*]pyran-7-ol (**16e**):

Light yellow oil. IR (cm⁻¹, film) 3573, 3335, 3033, 3992, 2907, 2854, 103, 1488, 1410, 1365, 1331, 1264, 1246, 1074, 1007, 970, 933, 899, 847, 769. ¹H NMR (300 MHz, CDCl₃) δ 7.76 – 7.24 (m, 9H), 6.15 (d, *J* = 4.5 Hz, 1H), 5.61 (s, 1H), 4.72 (d, *J* = 6.3 Hz, 1H), 4.11 – 3.91 (m, 1H), 3.78 (d, *J* = 4.0 Hz, 1H), 3.52 (dd, *J* = 8.0, 1.8 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 177.84, 141.60, 140.14, 132.15 (2C), 129.49, 128.88 (2C), 128.85, 127.78, 127.04 (3C), 126.90, 121.18, 98.38, 85.84, 76.42, 66.65, 63.14. HRMS (APCI negative mode M-1-H₂O) calculated for C₂₀H₁₈O₄: 303.1099, found 303.1044.

(6*R*,7*S*,7*aR*)-6-(hydroxymethyl)-2-(4-methoxyphenyl)-7,7*a*-dihydro-6*H*-furo[3,2-*c*]pyran-7-ol (**16f**):

Light yellow oil. IR (cm⁻¹, film) 3391, 2966, 2936, 2899, 2840, 1730, 1607, 1573, 1514, 1465, 1447, 1421, 1369, 1290, 1249, 1179, 1078, 1011, 978, 937, 836. ¹H NMR (300 MHz, CDCl₃) δ 7.37 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 4.5 Hz, 2H), 6.09 (s, 1H), 5.57 (s, 1H), 4.70 (dd, *J* = 4.8, 1.6 Hz, 1H), 3.97 (dd, *J* = 7.8, 6.6 Hz, 1H), 3.80 (t, *J* = 4.2 Hz, 4H), 3.66 (d, *J* = 2.2 Hz, 1H), 3.50 (dd, *J* = 8.0, 2.0 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 160.08, 159.41, 133.25, 129.85, 128.68, 114.08, 98.43, 84.10, 76.43, 66.65, 63.15, 55.30. HRMS (APCI negative mode M-1-H₂O) calculated for C₁₅H₁₆O₅: 257.0892, found 257.0843.

(6*R*,7*S*,7*aR*)-2-butyl-6-(hydroxymethyl)-7,7*a*-dihydro-6*H*-furo[3,2-*c*]pyran-7-ol (**16g**):

Colorless oil. IR (cm⁻¹, film) 3312, 2933, 1663, 1592, 1454, 139, 1313, 1104, 1082, 907, 881, 791. ¹H NMR (300 MHz, CDCl₃) δ 5.88 (d, *J* = 4.6 Hz, 1H), 5.36 (s, 1H), 4.59 (d, *J* = 6.5 Hz, 1H), 3.94 – 3.81 (m, 1H), 3.63 (d, *J* = 4.6 Hz, 1H), 3.45 – 3.35 (m, 1H), 2.27 (t, *J* = 6.9 Hz, 2H), 1.59 – 1.23 (m, 4H), 0.85 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 177.83, 144.16, 119.46, 98.44, 84.62, 78.50, 66.67, 63.12, 35.89, 31.43, 30.84, 14.00. HRMS (APCI negative mode M-H) calculated for C₁₂H₁₈O₄: 226.1205, found 225.1153.

General Procedure 6 (GP6); Synthesis of compounds **17a-m**:

To a solution of the glucal alkyne (**14-j**, 0.5 mM) in dry tetrahydrofuran (5 mL) at room temperature under nitrogen was added bis-(triphenylphosphine)palladium(II) chloride (2 mol%) while stirring. Tributyltin hydride (1.2 eq.) was added dropwise over a period of 10 minutes and the reaction mixture was stirred for two hours at room temperature. After completion of reaction according to thin layer chromatography (TLC) monitoring the product was extracted with ethyl acetate (3x20 mL) and a saturated solution of ammonium chloride (20 mL). The organic phases were combined, dried over magnesium sulfate, filtered and evaporated *in vacuo*. The products were isolated via flash chromatography using hexane and ethyl acetate as eluent systems.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-phenyl-1-(tributylstannyl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**17a α**):

Light yellow oil. IR (film, cm⁻¹); 2959, 2873, 2854, 1748, 1637, 1464, 1372, 1220, 1179, 1149, 1048, 918, 698. ¹H NMR (300 MHz, CDCl₃) δ 7.44 (d, *J* = 7.2 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.18 (t, *J* = 7.3 Hz, 1H), 6.64 (s, 1H), 6.16 (s, 1H), 5.37 (d, *J* = 4.1 Hz, 1H), 5.15 (t, *J* = 4.8 Hz, 1H), 4.39 (dd, *J* = 11.6, 6.6 Hz, 1H), 4.33 – 4.23 (m, 1H), 4.19 (dd, *J* = 11.6, 3.6 Hz, 1H), 2.08 (d, *J* = 4.4 Hz, 6H), 1.87 (s, 3H), 1.53 (q, *J* = 8.3 Hz, 6H), 1.35 (q, *J* = 7.2 Hz, 6H), 0.96 (dt, *J* = 27.7, 7.8 Hz, 15H). ¹³C NMR (75 MHz, CDCl₃) δ 170.38, 169.68, 169.42, 142.65, 141.96, 140.11, 137.80, 128.73, 128.06, 126.98, 113.90, 73.07, 67.84,

67.45, 61.71, 29.00, 27.36, 20.81, 20.66, 20.58, 13.67, 10.36. ^{119}Sn NMR (112 MHz, CDCl_3) δ -33.91 (s). HRMS (ESI), calculated. for $\text{C}_{32}\text{H}_{48}\text{NaO}_7\text{Sn}$ $[\text{M} + \text{Na}]^+ = 687.2320$; found: 687.2298.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-phenyl-2-(tributylstannyl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**17a** β):

Light yellow oil. IR (film, cm^{-1}); 2959, 2925, 2873, 2854, 1748, 1644, 1629, 1462, 1372, 1223, 1182, 1052, 1025, 963, 918, 702; ^1H NMR (300 MHz, CDCl_3) δ 7.24 (t, $J = 7.7$ Hz, 2H), 7.08 (t, $J = 7.4$ Hz, 1H), 6.93 (dd, $J = 8.0, 1.2$ Hz, 2H), 6.24 (s, 1H), 5.87 (s, 1H), 5.36 (d, $J = 4.6$ Hz, 1H), 5.08 (dd, $J = 5.9, 4.6$ Hz, 1H), 4.27 (dd, $J = 11.5, 6.4$ Hz, 1H), 4.23 – 4.15 (m, 1H), 4.12 (q, $J = 7.1$ Hz, 1H), 2.03 (s, 6H), 2.01 (s, 3H), 1.46 – 1.34 (m, 6H), 1.32 – 1.20 (m, 6H), 0.95 – 0.81 (m, 15H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.35, 169.79, 169.49, 148.32, 146.24, 145.20, 131.95, 128.39, 126.20, 125.05, 109.58, 73.22, 67.34 (2C), 60.30, 28.86 (3C), 27.22 (3C), 20.94, 20.77, 20.58, 13.58 (3C), 10.05 (3C). ^{119}Sn NMR (112 MHz, CDCl_3) δ -34.15 (s). HRMS (ESI), calculated for $\text{C}_{32}\text{H}_{48}\text{NaO}_7\text{Sn}$ $[\text{M} + \text{Na}]^+ = 687.2320$; found: 687.2299.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(4-aminophenyl)-1-(tributylstannyl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**17b** α):

Yellow oil. IR (film, cm^{-1}); 3473, 3379, 2959, 2929, 2873, 2854, 1748, 1629, 1514, 1372, 1231, 1182, 1052, 1026; ^1H NMR (300 MHz, CDCl_3) δ 7.29 (d, $J = 8.1$ Hz, 2H), 6.59 (d, $J = 8.1$ Hz, 2H), 6.49 (s, 1H), 6.18 (s, 1H), 5.40 (d, $J = 3.7$ Hz, 1H), 5.17 (t, $J = 5.0$ Hz, 1H), 4.44 (dd, $J = 11.7, 6.6$ Hz, 1H), 4.30 (dd, $J = 10.1, 5.9$ Hz, 1H), 4.20 (dd, $J = 11.6, 3.5$ Hz, 1H), 2.08 (d, $J = 5.2$ Hz, 6H), 1.84 (s, 3H), 1.60 – 1.45 (m, 4H), 1.34 (dq, $J = 14.1, 7.1$ Hz, 8H), 1.03 – 0.83 (m, 15H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.48, 169.78, 169.49, 145.62, 142.72, 139.70, 137.32, 130.07 (2C), 128.41, 114.48 (2C), 114.41, 73.10, 68.01, 67.63, 61.81, 29.02 (3C), 27.37 (3C), 20.83, 20.70, 20.58, 13.67 (3C), 10.28 (3C). HRMS (ESI), calculated for $\text{C}_{32}\text{H}_{49}\text{NNaO}_7\text{Sn}$ $[\text{M} + \text{Na}]^+ = 702.2429$; found: 702.2401.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(3-hydroxyphenyl)-1-(tributylstannyl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**17c** α):

Colorless oil. IR (film, cm^{-1}); 3408, 2959, 2925, 2873, 2854, 1748, 1629, 1581, 1372, 1223, 1171, 1052, 1026, 698; ^1H NMR (300 MHz, CDCl_3) δ 7.32 (d, $J = 2.0$ Hz, 1H), 7.16 (t, $J = 7.8$ Hz, 1H), 6.82 – 6.68 (m, 2H), 6.66 (s, 1H), 6.58 (s, 1H), 6.18 (s, 1H), 5.23 (t, $J = 2.1$ Hz, 1H), 5.05 (t, $J = 2.9$ Hz, 1H), 4.79 (dd, $J = 11.9, 8.3$ Hz, 1H), 4.44 (ddd, $J = 8.4, 4.1, 2.6$ Hz, 1H), 4.08 (dd, $J = 11.9, 4.4$ Hz, 1H), 2.15 (s, 3H), 2.11 (s, 6H), 1.73 (s, 3H), 1.57 – 1.46 (m, 6H), 1.44 – 1.21 (m, 6H), 1.02 – 0.97 (m, 6H) 0.95 – 0.88 (m, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 171.76, 169.51, 169.42, 155.93, 142.63, 142.56, 139.34, 139.10, 129.37, 121.76, 114.73, 114.60, 112.71, 72.29, 67.24, 65.70, 61.33, 28.98 (3C), 27.37 (3C), 20.91, 20.83, 20.26, 13.67 (3C), 10.25 (3C). HRMS (ESI), calculated for $\text{C}_{32}\text{H}_{48}\text{NaO}_8\text{Sn}$ $[\text{M} + \text{Na}]^+ = 703.2269$; found: 703.2233.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(3-hydroxyphenyl)-2-(tributylstannyl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**17c** β):

Colorless oil. IR (film, cm^{-1}); 3408, 2959, 2925, 2873, 2854, 1748, 1629, 1581, 1372, 1223, 1171, 1052, 1026, 698; ^1H NMR (300 MHz, CDCl_3) δ 7.11 (t, $J = 7.9$ Hz, 1H), 6.57 (dd, $J = 7.1, 2.2$ Hz, 1H), 6.48 (s, 2H), 6.28 (s, 1H), 5.91 (s, 1H), 5.85 (s, 1H), 5.33 (d, $J = 3.9$ Hz, 1H), 5.08 (t, $J = 4.4$ Hz, 1H), 4.35 (dd, $J = 11.4, 6.8$ Hz, 1H), 4.30 – 4.21 (m, 1H), 4.11 (dd, $J = 11.4, 3.9$ Hz, 1H), 2.07 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 1.48 – 1.37 (m, 6H), 1.28 (m, 6H), 0.93 – 0.83 (m, 15H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.97, 170.05, 169.69, 156.08, 148.29, 146.73, 146.10, 132.11, 129.58, 118.86, 112.97, 112.47, 109.45, 72.86, 67.39, 66.78, 61.21, 28.88 (3C), 27.23 (3C), 20.79, 20.78, 20.69, 13.61 (3C), 10.12 (3C). HRMS (ESI), calculated for $\text{C}_{32}\text{H}_{48}\text{NaO}_8\text{Sn}$ $[\text{M} + \text{Na}]^+ = 703.2269$; found: 703.2231.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(2,4-difluorophenyl)-2-(tributylstannyl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**17d** β):

Brown oil. IR (film, cm^{-1}); 2959, 2929, 2877, 2854, 1748, 1626, 1588, 1499, 1372, 1223, 1179, 1052, 1026, 970, 851; ^1H NMR (300 MHz, CDCl_3) δ 6.96 – 6.67 (m, 3H), 6.28 (s, 1H), 6.03 (s, 1H), 5.31 (d, $J = 4.5$ Hz, 1H), 5.08 (t, $J = 5.0$ Hz, 1H), 4.36 – 4.16 (m, 2H), 4.08 (dd, $J = 11.4, 3.1$ Hz, 1H), 2.04 (s, 6H), 2.01 (s, 3H), 1.46 – 1.35 (m, 6H), 1.32 – 1.22 (m, 6H), 0.94 – 0.83 (m, 16H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.22, 169.68, 169.36, 159.45 (dd, $J = 246.75, 235$ Hz), 159.37 (dd, $J = 11.5, 4.1$ Hz), 156.15, 156.00, 145.87, 139.98, 135.28, 129.06, 128.98 (dd, $J = 8.9, 5.4$ Hz), 128.32 (dd, $J = 16.9, 3.8$ Hz), 111.20 (dd, $J = 21.0, 3.4$ Hz), 103.79 (t, $J = 25.7$ Hz), 109.89, 104.12, 103.78, 103.44, 73.34, 67.20, 66.83, 61.18, 28.72,

27.16, 20.65, 20.56, 20.48, 13.51, 10.15. HRMS (ESI), calculated for $C_{32}H_{46}F_2NaO_7Sn$ $[M + Na]^+ = 723.2131$; found: 723.2096.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(pyridin-3-yl)-2-(tributylstannyl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**17e β**):

Yellow oil. IR (film, cm^{-1}); 2959, 2929, 2873, 2854, 1748, 1644, 1626, 1465, 1372, 1220, 1182, 1052, 1026, 914, 881, 717; 1H NMR (300 MHz, $CDCl_3$) δ 8.36 (d, $J = 3.9$ Hz, 1H), 8.25 (s, 1H), 7.37 – 7.09 (m, 2H), 6.25 (s, 1H), 6.02 (s, 1H), 5.30 (d, $J = 4.4$ Hz, 1H), 5.08 (t, $J = 5.1$ Hz, 1H), 4.37 – 4.16 (m, 2H), 4.08 (dd, $J = 11.5, 2.8$ Hz, 1H), 2.05 (t, $J = 9.4$ Hz, 9H), 1.56 – 1.17 (m, 12H), 0.99 – 0.77 (m, 15H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.20, 169.66, 169.33, 147.40, 146.90, 146.27, 143.77, 140.89, 134.38, 133.64, 123.11, 109.36, 73.36, 66.97 (2C), 61.14, 28.77 (3C), 27.12 (3C), 20.66 (2C), 20.49, 13.50 (3C), 10.08 (3C). ^{119}Sn NMR (112 MHz, $CDCl_3$) δ -27.43 (s). HRMS (ESI), calculated for $C_{31}H_{47}NNaO_7Sn$ $[M + Na]^+ = 688.2272$; found: 688.2258.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-cyclopropyl-1-(tributylstannyl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**17f α**):

Light yellow oil. IR (film, cm^{-1}); 3003, 2959, 2929, 2873, 2854, 1748, 1644, 1599, 1462, 1372, 1223, 1175, 1048, 1022, 914, 736; 1H NMR (300 MHz, $CDCl_3$) δ 6.14 (s, 1H), 5.34 (d, $J = 4.8$ Hz, 1H), 5.13 (dd, $J = 6.4, 4.9$ Hz, 1H), 4.90 (d, $J = 9.5$ Hz, 1H), 4.39 (dd, $J = 11.9, 6.1$ Hz, 1H), 4.18 (dt, $J = 9.7, 4.9$ Hz, 1H), 4.10 (dd, $J = 11.9, 3.5$ Hz, 1H), 1.99 (s, 3H), 1.98 (s, 3H), 1.91 (s, 3H), 1.72 (td, $J = 8.2, 3.4$ Hz, 1H), 1.46 – 1.13 (m, 12H), 0.81 (dd, $J = 12.4, 5.1$ Hz, 15H), 0.72 – 0.58 (m, 2H), 0.26 (d, $J = 3.3$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.16, 169.74, 169.23, 150.52, 139.39, 133.87, 114.32, 73.27, 68.37, 67.85, 61.29, 28.86 (3C), 27.18 (3C), 20.59, 20.56, 20.45, 13.50 (3C), 12.33, 9.86 (3C), 7.50, 7.19. HRMS (ESI), calculated for $C_{29}H_{48}NaO_7Sn$ $[M + Na]^+ = 651.2320$; found: 651.2304.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-4-hydroxy-1-(tributylstannyl)but-1-en-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**17g α**):

Light yellow oil. IR (film, cm^{-1}); 3555, 2929, 2873, 2854, 1748, 1644, 1462, 1372, 1220, 1182, 1156, 1048, 1022, 918, 881; ^1H NMR (300 MHz, CDCl_3) δ 6.10 (d, $J = 1.0$ Hz, 1H), 5.73 (t, $J = 7.0$ Hz, 1H), 5.35 – 5.24 (m, 1H), 5.16 (dd, $J = 5.8, 4.3$ Hz, 1H), 4.63 (dd, $J = 12.1, 7.0$ Hz, 1H), 4.29 (dt, $J = 6.7, 3.3$ Hz, 1H), 4.08 (dd, $J = 12.1, 3.3$ Hz, 1H), 3.69 – 3.55 (m, 2H), 2.51 (q, $J = 6.9$ Hz, 2H), 2.10 (s, 3H), 2.08 (s, 3H), 1.99 (s, 3H), 1.48 (ddd, $J = 12.2, 5.6, 3.3$ Hz, 6H), 1.31 (q, $J = 7.3$ Hz, 6H), 0.90 (q, $J = 8.1, 7.2$ Hz, 15H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.64, 169.85, 169.46, 141.89, 140.83, 138.99, 113.39, 73.22, 67.98, 67.74, 62.40, 61.00, 33.88, 28.93 (3C), 27.26 (3C), 20.71, 20.68, 20.65, 13.60 (3C), 10.04 (3C). HRMS (ESI), calculated for $\text{C}_{28}\text{H}_{49}\text{O}_8\text{Sn}$ $[\text{M} + \text{H}]^+ = 633.2449$; found: 633.2461.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-4-phenyl-1-(tributylstannyl)but-1-en-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**17h** α):

Yellow oil. IR (film, cm^{-1}); 3029, 2959, 2925, 2873, 2854, 1748, 1644, 1629, 1458, 1372, 1223, 1179, 1052, 1026, 702; ^1H NMR (300 MHz, CDCl_3) δ 7.26 (t, $J = 7.3$ Hz, 2H), 7.16 (d, $J = 7.7$ Hz, 3H), 5.79 (s, 1H), 5.73 (t, $J = 6.8$ Hz, 1H), 5.31 (d, $J = 4.6$ Hz, 1H), 5.26 – 5.10 (m, 1H), 4.43 (dd, $J = 11.6, 6.1$ Hz, 1H), 4.31 – 4.12 (m, 2H), 2.74 – 2.59 (m, 2H), 2.52 (t, $J = 7.1$ Hz, 2H), 2.09 (s, 3H), 2.04 (s, 3H), 1.95 (s, 3H), 1.45 (q, $J = 8.1$ Hz, 6H), 1.38 – 1.23 (m, 6H), 1.05 – 0.75 (m, 15H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.40, 169.89, 169.45, 145.48, 141.73, 138.99, 138.00, 128.57 (2C), 128.27 (2C), 125.82, 113.52, 73.18, 68.31, 67.88, 61.40, 36.20, 32.19, 28.98 (3C), 27.35 (3C), 20.74 (2C), 20.67, 13.66 (3C), 10.05 (3C). HRMS (ESI), calculated for $\text{C}_{34}\text{H}_{53}\text{O}_7\text{Sn}$ $[\text{M} + \text{H}]^+ = 693.2813$; found: 693.2801.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-1-(tributylstannyl)hex-1-en-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**17i** α):

Yellow oil. IR (film, cm^{-1}); 2957, 2924, 2874, 2855, 177, 1448, 1371, 1222, 1160, 1048, 1020, 696, 668; ^1H NMR (300 MHz, CDCl_3) δ 6.09 (s, 1H), 5.69 (t, $J = 6.9$ Hz, 1H), 5.34 (d, $J = 4.6$ Hz, 1H), 5.18 (dd, $J = 6.2, 4.7$ Hz, 1H), 4.46 (dd, $J = 11.8, 6.2$ Hz, 1H), 4.27 (td, $J = 6.2, 3.5$ Hz, 1H), 4.19 (dd, $J = 11.8, 3.6$ Hz, 1H), 2.20 (d, $J = 5.8$ Hz, 1H), 2.09 (s, 3H), 2.07 (s, 3H), 1.97 (s, 3H), 1.53 – 1.40 (m, 6H), 1.40 – 1.23 (m, 10H), 0.95 – 0.85 (m, 18H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.35, 169.85, 169.42, 146.96, 139.02, 136.66, 113.82, 73.21, 68.33, 67.90, 61.37, 32.07, 29.88, 28.96 (3C), 27.28 (3C), 22.31, 20.70, 20.66, 20.61, 13.93, 13.60 (3C), 10.01 (3C). HRMS (ESI), calculated for $\text{C}_{30}\text{H}_{52}\text{NaO}_7\text{Sn}$ $[\text{M} + \text{Na}]^+ = 667.2633$; found: 667.2629.

(2*R*,3*S*,4*R*)-5-((*E*)-2-([1,1'-biphenyl]-4-yl)-1-(tributylstannyl)vinyl)-2-(acetoxymethyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**17j** α):

Yellow oil. IR (film, cm^{-1}); 2957, 2924, 2874, 2855, 1750, 1642, 1488, 1371, 1222, 1160, 1048, 1020, 696, 668; ^1H NMR (300 MHz, CDCl_3) δ 7.53 (d, $J = 7.1$ Hz, 2H), 7.47 (s, 4H), 7.35 (t, $J = 7.4$ Hz, 2H), 7.24 (t, $J = 7.3$ Hz, 1H), 6.59 (s, 1H), 6.11 (s, 1H), 5.34 (d, $J = 4.1$ Hz, 1H), 5.11 (dd, $J = 5.2, 4.4$ Hz, 1H), 4.35 (dd, $J = 11.6, 6.7$ Hz, 1H), 4.24 (dd, $J = 10.1, 5.0$ Hz, 1H), 4.14 (dd, $J = 11.6, 3.6$ Hz, 1H), 2.00 (s, 6H), 1.81 (s, 3H), 1.56 – 1.18 (m, 12H), 0.89 (dt, $J = 14.5, 7.7$ Hz, 15H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.44, 169.77, 169.47, 142.51, 142.26, 140.72, 140.01, 139.64, 136.78, 129.25 (2C), 128.76 (2C), 127.25, 126.92 (2C), 126.74 (2C), 114.02, 73.13, 67.89, 67.59, 61.76, 29.04 (3C), 27.40 (3C), 20.85, 20.69, 20.64, 13.71 (3C), 10.41 (3C). HRMS (ESI), calculated for $\text{C}_{38}\text{H}_{52}\text{NaO}_7\text{Sn}$ $[\text{M} + \text{Na}]^+ = 763.2633$; found: 763.2613.

(2*R*,3*S*,4*R*)-2-(hydroxymethyl)-5-((*E*)-1-(tributylstannyl)hex-1-en-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diol (**17k** α):

Light yellow oil. IR (film, cm^{-1}); 3430, 2959, 2924, 2874, 1492, 1445, 1179, 1030, 914, 758, 702, 697; ^1H NMR (300 MHz, CDCl_3) δ 5.88 (s, 1H), 5.74 (t, $J = 6.8$ Hz, 1H), 4.10 (d, $J = 3.0$ Hz, 1H), 3.84 (d, $J = 16.9$ Hz, 3H), 3.79 – 3.70 (m, 1H), 3.42 (s, 1H), 2.46 (s, 1H), 2.21 – 2.03 (m, 3H), 1.97 (s, 1H), 1.65 – 1.36 (m, 6H), 1.27 (td, $J = 14.7, 7.6$ Hz, 10H), 0.90 – 0.78 (m, 18H). ^{13}C NMR (75 MHz, CDCl_3) δ 147.24, 137.37, 136.30, 117.36, 77.48, 71.75, 70.67, 62.01, 32.22, 30.16, 29.05 (3C), 27.33 (3C), 22.40, 13.99, 13.66 (3C), 10.16 (3C). HRMS (ESI), calculated for $\text{C}_{24}\text{H}_{46}\text{NaO}_4\text{Sn}$ $[\text{M} + \text{Na}]^+ = 541.2316$; found: 541.2256.

(2*R*,3*S*,4*R*)-2-(hydroxymethyl)-5-((*E*)-2-phenyl-1-(tributylstannyl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diol (**17l** α):

Light yellow oil. IR (film, cm^{-1}); 3430, 2957, 2923, 2873, 1611, 1600, 1492, 1445, 1179, 1030, 915, 758, 697; ^1H NMR (300 MHz, CDCl_3) δ 7.36 (d, $J = 7.6$ Hz, 2H), 7.20 (t, $J = 7.4$ Hz, 2H), 7.10 (t, $J = 7.3$ Hz, 1H), 6.63 (s, 1H), 5.96 (s, 1H), 4.15 (dd, $J = 7.3, 3.2$ Hz, 1H), 3.80 (q, $J = 5.2, 4.7$ Hz, 3H), 3.73 (dd, $J =$

8.6, 4.8 Hz, 1H), 3.28 (d, $J = 3.3$ Hz, 1H), 2.37 (s, 1H), 2.14 (d, $J = 3.6$ Hz, 1H), 1.96 (s, 1H), 1.69 – 1.38 (m, 6H), 1.37 – 1.12 (m, 12H), 0.92 – 0.72 (m, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 146.59, 145.91, 144.39, 133.33 (2C), 128.61 (2C), 126.43, 125.47, 114.91, 77.87, 69.45, 69.32, 61.48, 28.91 (3C), 27.25 (3C), 13.61 (3C), 10.16 (3C). HRMS (ESI), calculated for $\text{C}_{26}\text{H}_{42}\text{NaO}_4\text{Sn}$ $[\text{M} + \text{Na}]^+ = 561.2002$; found: 561.1972.

(2*R*,3*S*,4*R*)-2-(hydroxymethyl)-5-((*E*)-2-phenyl-2-(tributylstannyl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diol (**17l** β):

Light yellow oil. IR (film, cm^{-1}); 3434, 2959, 2927, 2874, 1617, 1604, 1492, 1445, 1179, 1032, 914, 758, 694; ^1H NMR (300 MHz, CDCl_3) δ 7.28 (d, $J = 7.1$ Hz, 2H), 7.15 (d, $J = 6.4$ Hz, 1H), 7.07 – 7.03 (m, 2H), 6.38 (s, 1H), 6.07 (d, $J = 2.6$ Hz, 1H), 3.89 (s, 1H), 3.81 – 3.62 (m, 5H), 3.00 (s, 1H), 2.28 (s, 1H), 1.50 – 1.21 (m, 12H), 0.95 – 0.83 (m, 15H). ^{13}C NMR (75 MHz, CDCl_3) δ 146.59, 145.91, 144.39, 133.33, 128.61 (2C), 126.43 (2C), 125.47, 114.91, 77.87, 69.45, 69.32, 61.48, 28.91 (3C), 27.25 (3C), 13.61 (3C), 10.16 (3C). HRMS (ESI), calculated for $\text{C}_{26}\text{H}_{42}\text{NaO}_4\text{Sn}$ $[\text{M} + \text{Na}]^+ = 561.2002$; found: 561.1972.

(2*R*,3*S*,4*R*)-5-((*E*)-2-([1,1'-biphenyl]-4-yl)-1-(tributylstannyl)vinyl)-2-(hydroxymethyl)-3,4-dihydro-2*H*-pyran-3,4-diol (**17m** α):

Yellow oil. IR (film, cm^{-1}); 3437, 2959, 2927, 2874, 1615, 1602, 1492, 1445, 1179, 1030, 916, 752, 698; ^1H NMR (300 MHz, CDCl_3) δ 7.57 – 7.41 (m, 6H), 7.35 (t, $J = 7.5$ Hz, 2H), 7.25 (t, $J = 7.2$ Hz, 1H), 6.67 (s, 1H), 6.02 (s, 1H), 4.24 (dd, $J = 7.2, 3.2$ Hz, 1H), 3.89 – 3.75 (m, 3H), 3.40 (s, 2H), 2.95 (d, $J = 3.3$ Hz, 1H), 2.18 (s, 1H), 2.06 (d, $J = 3.5$ Hz, 1H), 1.53 – 1.41 (m, 6H), 1.21 (dd, $J = 14.0, 6.3$ Hz, 6H), 0.85 (td, $J = 7.3, 2.0$ Hz, 15H). ^{13}C NMR (75 MHz, CDCl_3) δ 142.21, 141.55, 140.57, 139.87, 138.62, 136.38, 129.23 (2C), 128.76 (2C), 127.32, 127.04, 126.92 (2C), 126.86, 118.27, 71.16, 70.83, 62.22, 60.40, 29.07 (3C), 27.38 (3C), 13.56 (3C), 10.53 (3C). HRMS (ESI), calculated for $\text{C}_{32}\text{H}_{47}\text{O}_4\text{Sn}$ $[\text{M} + \text{H}]^+ = 615.2496$; found: 615.2420.

(2*R*,3*S*,4*R*)-5-((*E*)-2-([1,1'-biphenyl]-4-yl)-2-(tributylstannyl)vinyl)-2-(hydroxymethyl)-3,4-dihydro-2*H*-pyran-3,4-diol (**17m β**):

Yellow oil. IR (film, cm^{-1}); 3432, 2959, 2928, 2874, 1614, 1601, 1492, 1445, 1179, 1030, 914, 736, 698; ^1H NMR (300 MHz, CDCl_3) δ 7.51 (dd, $J = 15.3, 7.8$ Hz, 3H), 7.35 (t, $J = 7.6$ Hz, 2H), 7.27 – 7.22 (m, 1H), 7.04 (d, $J = 8.0$ Hz, 2H), 6.38 (s, 1H), 6.01 (s, 1H), 3.90 (d, $J = 5.9$ Hz, 1H), 3.73 (dt, $J = 23.8, 12.3$ Hz, 4H), 1.44 – 1.11 (m, 12H), 0.82 (dt, $J = 19.7, 7.2$ Hz, 15H). ^{13}C NMR (75 MHz, CDCl_3) δ 142.21, 141.55, 140.57, 139.87, 138.62, 129.23 (2C), 128.76 (2C), 127.32, 126.92 (3C), 126.86, 118.27, 71.16, 70.83, 62.22, 60.40, 27.84 (3C), 26.82 (3C), 13.69 (3C), 10.53 (3C). HRMS (ESI), calculated for $\text{C}_{32}\text{H}_{47}\text{O}_4\text{Sn} [\text{M} + \text{H}]^+ = 615.2496$; found: 615.2421.

General Procedure 7 (GP7); Synthesis of compounds **18a**, **19a-c**:

To a stirred solution of the vinylstannane **17** (0.5 mM) and NaCl (29 mg, 0.5 mM) in DMF: NMP (4:1, 5 mL) solvent system was added CuI (9.5 mg, 10 mol %) and heated to 80 °C. The aryl halide (1.2 eq.) was then added dropwise and the reaction mixture was stirred at 110 °C for 4 hours. The reaction mixture was cooled to room temperature and a saturated solution of NH_4Cl (15 mL) was added. The reaction mixture was extracted with ethyl acetate (3 x 15 mL) and the organic phases were combined, dried with anhydrous MgSO_4 , filtered and evaporated under reduced pressure. The products were isolated by flash chromatography using ethyl acetate and n-hexane (3:7 to 1:1) solvent system.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*Z*)-2-(2,4-difluorophenyl)-2-phenylvinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**18a**):

Light brown oil. IR (film, cm^{-1}); 3077, 2959, 2928, 2874, 2857, 1743, 1620, 1505, 1371, 1222, 1179, 1141, 1050, 1026, 970, 853, 698; ^1H NMR (300 MHz, CDCl_3) δ 7.21 (dt, $J = 11.8, 5.8$ Hz, 3H), 7.14 – 7.00 (m, 2H), 6.75 (ddd, $J = 33.7, 17.4, 10.4$ Hz, 3H), 6.27 (d, $J = 6.9$ Hz, 2H), 5.28 (d, $J = 4.3$ Hz, 1H), 5.04 (t, $J = 4.8$ Hz, 1H), 4.38 – 4.17 (m, 2H), 4.05 (t, $J = 9.9$ Hz, 1H), 1.98 (s, 6H), 1.93 (s, 3H). ^{13}C NMR (75 MHz,

CDCl_3) δ 170.38, 169.98, 169.49, 164.21, 158.33, 146.27, 145.63, 141.47, 141.02, 140.90, 134.55, 132.76 (dd, $J = 9.3, 5.4$ Hz), 128.36 (2C), 127.64, 126.59 (2C), 124.85, 123.75, 123.69, 123.53, 123.48, 111.66 (dd, $J = 21.2, 3.5$ Hz), 109.56, 104.51 (t, $J = 25.6$ Hz), 73.46, 67.29, 66.97, 61.20, 20.77 (2C), 20.62. HRMS (ESI), calculated for $\text{C}_{26}\text{H}_{24}\text{F}_2\text{NaO}_7$ $[\text{M} + \text{Na}]^+ = 509.1388$; found: 509.1416.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*Z*)-styryl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**19a**);

Light yellow oil. IR (film, cm^{-1}); 3060, 2957, 2924, 2874, 2855, 1749, 1646, 1495, 1460, 1371, 1225, 1181, 1024, 683; ^1H NMR (300 MHz, CDCl_3) δ 7.36 – 7.26 (m, 4H), 7.25 – 7.19 (m, 1H), 6.44 (d, $J = 9.6$ Hz, 2H), 5.81 (d, $J = 12.0$ Hz, 1H), 5.51 (d, $J = 4.8$ Hz, 1H), 5.25 – 5.12 (m, 1H), 4.41 (dd, $J = 11.9, 6.3$ Hz, 1H), 4.33 – 4.25 (m, 1H), 4.17 (dd, $J = 11.9, 3.3$ Hz, 1H), 2.07 (s, 6H), 1.97 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.42, 170.18, 169.51, 146.41, 145.31, 137.40, 128.60, 127.11, 125.94, 123.97, 110.82, 73.82, 67.51, 67.16, 63.78, 20.81, 20.71, 20.68. HRMS (ESI), calculated. for $\text{C}_{20}\text{H}_{22}\text{NaO}_7$ $[\text{M} + \text{Na}]^+ = 397.1263$; found: 397.1291.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*Z*)-2-(pyridin-2-yl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**19b**):

Yellow oil. IR (film, cm^{-1}); 3017, 2957, 2874, 1739, 1693, 1639, 1439, 1371, 1222, 1179, 1050, 1028, 916, 722; ^1H NMR (300 MHz, CDCl_3) δ 8.51 (s, 1H), 7.62 (d, $J = 8.1$ Hz, 1H), 7.43 (dd, $J = 18.9, 5.3$ Hz, 1H), 7.18 (d, $J = 8.3$ Hz, 1H), 6.38 (s, 1H), 6.32 (d, $J = 12.0$ Hz, 1H), 5.88 (d, $J = 11.9$ Hz, 1H), 5.41 (d, $J = 4.3$ Hz, 1H), 5.12 (dd, $J = 6.2, 5.0$ Hz, 1H), 4.34 (dd, $J = 11.9, 6.3$ Hz, 1H), 4.26 – 4.16 (m, 1H), 4.09 (dd, $J = 11.9, 3.3$ Hz, 1H), 2.01 (s, 6H), 1.93 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.42, 170.00, 169.51, 149.72, 148.09, 145.76, 135.47, 128.40, 126.77, 126.50, 123.23, 108.10, 73.74, 67.36, 67.23, 61.28, 20.77, 20.71, 20.66. HRMS (ESI), calculated for $\text{C}_{19}\text{H}_{22}\text{NO}_7$ $[\text{M} + \text{Na}]^+ = 376.1396$; found: 376.1364.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*Z*)-4-hydroxybut-1-en-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**19c**):

Yellow oil. IR (film, cm^{-1}); 3583, 2959, 2924, 2875, 1745, 1650, 1372, 1225, 1048, 1026, 916; ^1H NMR (300 MHz, CDCl_3) δ 6.48 (s, 1H), 5.66 (d, $J = 11.4$ Hz, 1H), 5.53 – 5.43 (m, 1H), 5.41 (d, $J = 5.1$ Hz, 1H), 5.13 (dd, $J = 6.2, 5.0$ Hz, 1H), 4.44 (dd, $J = 12.1, 6.5$ Hz, 1H), 4.24 (td, $J = 6.4, 3.3$ Hz, 1H), 4.08 (dd, $J = 12.1, 3.2$ Hz, 1H), 3.60 (dd, $J = 12.1, 6.1$ Hz, 2H), 2.47 – 2.29 (m, 2H), 2.03 (s, 3H), 2.01 (s, 3H), 1.97 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.59, 170.38, 169.57, 144.00, 128.90, 125.18, 108.21, 73.60, 68.05, 67.42, 62.31, 61.15, 27.82, 20.87, 20.79, 20.70. HRMS (ESI), calculated for $\text{C}_{16}\text{H}_{22}\text{NaO}_8$ $[\text{M} + \text{Na}]^+ = 365.1212$; found: 365.1194.

(2*R*,3*S*,4*R*)-2-(hydroxymethyl)-5-((*E*)-1-iodo-2-phenylvinyl)-3,4-dihydro-2*H*-pyran-3,4-diol (**20a**);

Yellow liquid. IR (film, cm^{-1}); 3440, 3027, 3064, 2962, 2259, 1630, 1370, 1220, 1182, 1022, 914, 761, 732, 696. ^1H NMR (300 MHz, methanol- d_4) δ 7.31 (ddd, $J = 21.0, 12.8, 7.2$ Hz, 6H), 6.57 (s, 1H), 3.98 (d, $J = 6.3$ Hz, 1H), 3.82 – 3.65 (m, 2H), 3.57 (t, $J = 6.8$ Hz, 1H), 3.31 (d, $J = 1.2$ Hz, 1H). ^{13}C NMR (75 MHz, methanol- d_4) δ 146.13, 139.94, 131.11, 128.97 (2C), 128.38 (2C), 127.29, 122.53, 113.01, 79.69, 70.10, 69.77, 61.25. HRMS (ESI), calculated for $\text{C}_{14}\text{H}_{16}\text{IO}_4$ $[\text{M} + \text{H}]^+ = 375.0093$; found: 375.0104.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-iodo-2-phenylvinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**20b**);

Light brown liquid. IR (film, cm^{-1}); 3023, 2963, 1741, 1629, 1447, 1372, 1220, 1182, 1052, 1022, 914, 709. ^1H NMR (300 MHz, CDCl_3) δ 8.14 (s, 1H), 7.84 (d, $J = 9$ Hz, 2H), 7.68 – 7.50 (m, 5H), 7.46 (d, $J = 9$ Hz, 1H), 7.34 (t, $J = 7$ Hz, 2H), 7.23 (q, $J = 4.0$ Hz, 1H), 6.67 (s, 1H), 5.57 (d, $J = 4.4$ Hz, 1H), 5.21 (t, $J = 4.8$ Hz, 1H), 4.82 (dd, $J = 9.0$ Hz, 6.0 Hz, 1H), 4.34 – 4.09 (m, 1H), 2.15 (s, 6H), 1.83 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.25, 169.40, 150.44, 146.11, 137.09, 136.24, 130.68, 129.72, 129.31, 128.60, 128.26, 127.67, 124.27, 120.29, 119.15, 108.29, 73.62, 67.47, 66.08, 60.95, 20.87, 20.79, 20.52. HRMS (ESI +) calculated for $\text{C}_{20}\text{H}_{22}\text{IO}_7$ $[\text{M} + \text{H}]^+ = 501.0410$ found; 501.0239.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-1-iodo-2-phenylvinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**20c**);

Light brown liquid. IR (film, cm^{-1}); 3027, 3064, 2962, 2259, 1745, 1637, 1372, 1216, 1182, 1022, 914, 762, 732, 698. ^1H NMR (300 MHz, CDCl_3) δ 7.45 – 7.13 (m, 6H), 6.57 (s, 1H), 5.76 (d, $J = 4.5$ Hz, 1H), 5.26 (t, $J = 5.0$ Hz, 1H), 4.52 – 4.28 (m, 2H), 4.20 (d, $J = 8.8$ Hz, 1H), 2.11 (s, 3H), 2.08 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.30, 169.66, 169.47, 145.28, 145.26, 144.29, 136.99, 128.42, 128.20, 127.83, 113.49, 95.39, 73.96, 66.98, 66.79, 61.44, 20.78, 20.75, 20.66. HRMS (ESI +) calculated for $\text{C}_{20}\text{H}_{22}\text{IO}_7$ $[\text{M}+\text{H}]^+ = 501.0410$ found; 501.0298.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(4-aminophenyl)-1-iodovinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**20d**);

Brown liquid. IR (film, cm^{-1}); 3473, 3382, 2959, 1739, 1626, 1516, 1371, 1218, 1179, 1048, 1022, 909, 829, 730. ^1H NMR (300 MHz, CDCl_3) δ 7.19 (d, $J = 8.4$ Hz, 3H), 6.71 – 6.46 (m, 3H), 5.74 (d, $J = 4.5$ Hz, 1H), 5.32 – 5.11 (m, 1H), 4.51 – 4.28 (m, 2H), 4.19 (dd, $J = 11.6, 3.3$ Hz, 1H), 2.09 (s, 6H), 1.97 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.40, 169.73, 169.53, 146.24, 145.15, 144.36, 129.63 (2C), 127.35, 114.69 (2C), 113.96, 90.65, 73.89, 67.07, 66.72, 61.54, 20.76, 20.71 (2C). HRMS (ESI +) calculated for $\text{C}_{20}\text{H}_{23}\text{INO}_7$ $[\text{M}+\text{H}]^+ = 516.0519$ found; 516.0497.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-iodo-2-(pyridin-3-yl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**20e**);

Light brown liquid. IR (film, cm^{-1}); 2959, 1743, 1639, 1628, 1371, 1220, 1181, 1050, 1024, 909, 728. ^1H NMR (300 MHz, CDCl_3) δ 8.49 (s, 1H), 8.38 (d, $J = 3.9$ Hz, 1H), 7.56 (d, $J = 7.6$ Hz, 1H), 7.18 (t, $J = 6.4$ Hz, 1H), 6.74 (s, 1H), 6.29 (s, 1H), 5.10 (d, $J = 4.4$ Hz, 1H), 5.04 – 4.91 (m, 1H), 4.22 (d, $J = 10.2$ Hz, 2H), 4.05 – 3.90 (m, 1H), 1.95 (d, $J = 6.7$ Hz, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 171.50, 170.90, 170.63, 149.97, 149.83, 137.16, 134.60, 120.79, 109.60, 107.59, 75.08, 68.07, 67.63, 62.36, 21.96, 21.83. HRMS (ESI +) calculated for $\text{C}_{19}\text{H}_{21}\text{INO}_7$ $[\text{M}+\text{H}]^+ = 502.0363$ found; 502.0538.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(2,4-difluorophenyl)-2-iodovinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**20f**);

Dark brown liquid. IR (film, cm^{-1}); 2958, 1743, 1618, 1600, 1499, 1426, 1371, 1222, 1179, 1143, 1095, 1050, 1024, 909, 853, 732. ^1H NMR (300 MHz, CDCl_3) δ 7.24 (q, $J = 7.9$ Hz, 1H), 6.82 (h, $J = 9.6, 9.0$ Hz, 3H), 6.38 (s, 1H), 5.13 (d, $J = 4.1$ Hz, 1H), 5.04 (t, $J = 3.5$ Hz, 1H), 4.29 (m, 2H), 4.06 (dd, $J = 7.3$ Hz, 1H), 2.03 (s, 6H), 2.01 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.13, 169.52, 169.22, 162.78 (dd, $J = 251.4, 11.5$ Hz), 147.52, 139.23, 131.64 (d, $J = 7.7$ Hz), 126.42 (dd, $J = 15.5, 4.1$ Hz), 111.74 (dd, $J = 21.7, 3.6$ Hz), 110.08, 104.58 (t, $J = 25.5$ Hz), 83.43, 73.52, 66.50, 65.33, 60.92, 20.64, 20.59, 20.49. HRMS (ESI +) calculated for $\text{C}_{20}\text{H}_{19}\text{F}_2\text{IO}_7$ $[\text{M}+\text{Na}]^+ = 559.0041$ found; 559.0171.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-1-iodohex-1-en-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**20g**);

Light brown liquid. IR (film, cm^{-1}); 2959, 2931, 2859, 1745, 1628, 1436, 1371, 1218, 1181, 1050, 1022, 912, 732. ^1H NMR (300 MHz, CDCl_3) δ 6.58 (s, 1H), 6.37 (t, $J = 7.6$ Hz, 1H), 5.66 (d, $J = 4.9$ Hz, 1H), 5.24 (t, $J = 5.6$ Hz, 1H), 4.47 (dd, $J = 11.9, 6.2$ Hz, 1H), 4.36 (dt, $J = 9.7, 6.6$ Hz, 1H), 4.18 (dd, $J = 12.2, 3.2$ Hz, 1H), 2.27 – 2.09 (m, 8H), 2.03 (s, 3H), 1.43 – 1.26 (m, 4H), 0.92 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.25, 169.80, 169.40, 145.81, 137.21, 115.36, 99.34, 73.90, 66.94, 66.46, 61.07, 36.36, 30.32, 22.08, 20.69, 20.65, 20.62, 20.58, 13.53. HRMS (ESI +) calculated for $\text{C}_{18}\text{H}_{26}\text{IO}_7$ $[\text{M}+\text{H}]^+ = 481.0723$ found; 481.1120.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-cyclopropyl-1-iodovinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**20h**);

Yellow liquid. IR (film, cm^{-1}); 2957, 2929, 1745, 1641, 1432, 1369, 1218, 1179, 1050, 1022, 912, 734. ^1H NMR (300 MHz, CDCl_3) δ 6.74 (s, 1H), 5.69 (t, $J = 7.8$ Hz, 2H), 5.27 (t, $J = 5.8$ Hz, 1H), 4.48 (dd, $J = 12.1, 6.3$ Hz, 1H), 4.34 (td, $J = 6.5, 3.0$ Hz, 1H), 4.18 (dd, $J = 12.2, 3.0$ Hz, 1H), 2.09 (s, 6H), 2.06 (s, 3H), 1.72 (tt, $J = 8.8, 4.6$ Hz, 1H), 0.78 (p, $J = 9.3, 8.8$ Hz, 2H), 0.47 (d, $J = 5.0$ Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.16, 169.62, 169.33, 149.83, 144.43, 113.26, 86.23, 74.04, 66.92, 66.89, 60.99, 20.69, 20.64, 20.57, 14.24, 7.36, 7.30. HRMS (ESI -) calculated for $\text{C}_{17}\text{H}_{22}\text{IO}_7$ $[\text{M}-\text{H}]^- = 465.0410$ found; 465.0509.

General Procedure 8 (GP8); Synthesis of compounds 21a-m:

To a stirred solution of the vinyl iodide **20** (0.3 mM), bis(triphenylphosphine)palladium(II) chloride (5 mol %) and copper iodide (5 mol %) in a 1:1 mixture of DMF and triethylamine was added dropwise the acetylene (1.2 eq.). The reaction mixture was stirred for 3 to 8 hours at room temperature under nitrogen. A saturated solution of NH_4Cl (15 mL) was added to the reaction mixture after completion of reaction (monitored by TLC). The mixture was extracted with ethyl acetate (3 x 15 mL) and the organic phases were combined, dried over anhydrous MgSO_4 , filtered, and evaporated *in vacuo*. The products were isolated by flash chromatography using ethyl acetate and hexane solvent system.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-4-cyclopropyl-2-phenylbut-1-en-3-yn-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**21a**):

Reddish brown gummy solid. IR (film, cm^{-1}); 3430, 2959, 2924, 2874, 1613, 1600, 1492, 1445, 1179, 1030, 914, 758, 694. ^1H NMR (300 MHz, methanol- d_4) δ 7.45 – 7.29 (m, 2H), 7.34 – 7.13 (m, 3H), 6.34 (s, 1H), 6.14 (s, 1H), 3.98 (d, J = 6.4 Hz, 1H), 3.73 (dd, J = 13.4, 7.3 Hz, 2H), 3.58 (t, J = 6.9 Hz, 1H), 3.40 – 3.25 (m, 1H), 1.50 – 1.28 (m, 1H), 0.85 – 0.67 (m, 2H), 0.61 (dd, J = 4.9, 2.4 Hz, 2H). ^{13}C NMR (75 MHz, methanol- d_4) δ 146.13, 139.94, 131.11, 128.97 (2C), 128.38 (2C), 127.29, 122.53, 113.01, 92.57, 79.69, 78.95, 70.10, 69.77, 61.25, 8.07 (2C), 0.00. HRMS (ESI), calculated for $\text{C}_{19}\text{H}_{21}\text{O}_4$ $[\text{M}+\text{H}]^+$ = 313.1440; found: 313.1411.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2,6-diphenylhex-1-en-3-yn-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**21b**):

Brown oil. IR (film, cm^{-1}); 3062, 3028, 2941, 2259, 1743, 1639, 1371, 1220, 1177, 1048, 1024, 910, 730, 700. ^1H NMR (300 MHz, CDCl_3) δ 7.48 – 7.03 (m, 10H), 6.35 (s, 1H), 6.21 (s, 1H), 5.39 (d, J = 4.7 Hz, 1H), 5.14 (t, J = 5.3 Hz, 1H), 4.46 – 4.21 (m, 2H), 4.19 – 4.03 (m, 1H), 2.87 (t, J = 7.4 Hz, 2H), 2.64 (t, J = 7.4 Hz, 2H), 2.07 (d, J = 2.8 Hz, 1H), 2.01 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.38, 169.79, 169.52, 147.27, 140.63, 138.29, 129.47, 128.57 (2C), 128.52 (2C), 128.41 (2C), 128.33 (2C), 127.66, 126.25,

123.82, 108.66, 89.72, 83.86, 73.53, 67.27, 66.95, 61.33, 35.08, 21.70, 20.79, 20.77, 20.62. HRMS (ESI), calculated for $C_{30}H_{30}NaO_7$ $[M+Na]^+ = 525.1889$; found: 525.1834.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-4-(3-hydroxyphenyl)-2-phenylbut-1-en-3-yn-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**21c**):

Yellowish brown oil. IR (film, cm^{-1}); 3373, 2255, 1743, 1579, 1445, 1371, 1220, 1181, 1153, 1048, 1026, 909, 730. 1H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.29 (m, 2H), 7.28 – 7.17 (m, 3H), 7.05 (t, $J = 7.9$ Hz, 1H), 6.88 (d, $J = 7.9$ Hz, 1H), 6.80 (d, $J = 2.1$ Hz, 1H), 6.69 (dd, $J = 8.0, 2.4$ Hz, 1H), 6.37 (s, 1H), 6.30 (s, 1H), 5.31 (d, $J = 4.8$ Hz, 1H), 5.04 (t, $J = 5.3$ Hz, 1H), 4.32 – 4.15 (m, 2H), 4.13 – 4.00 (m, 1H), 1.96 (d, $J = 6.8$ Hz, 6H), 1.89 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.73, 170.13, 169.80, 155.85, 148.12, 137.85, 130.81, 129.50, 128.62 (2C), 128.59 (2C), 127.98, 124.37, 123.84, 123.03, 118.15, 115.78, 108.86, 91.90, 89.31, 73.61, 67.26, 66.89, 61.37, 20.82, 20.77, 20.65. HRMS (ESI), calculated for $C_{28}H_{26}NaO_8$ $[M+Na]^+ = 513.1525$; found: 513.1499.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-phenyl-4-(pyridin-3-yl)but-1-en-3-yn-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**21d**):

Yellowish brown oil. IR (film, cm^{-1}); 3056, 3026, 2251, 1743, 1615, 1477, 1218, 1168, 1022, 909, 730, 702. 1H NMR (300 MHz, $CDCl_3$) δ 8.65 (s, 1H), 8.49 (d, $J = 4.9$ Hz, 1H), 7.69 (d, $J = 7.8$ Hz, 1H), 7.45 – 7.39 (m, 2H), 7.38 – 7.27 (m, 3H), 7.22 (dd, $J = 8.0, 4.9$ Hz, 1H), 6.49 (s, 1H), 6.44 (s, 1H), 5.39 (d, $J = 4.8$ Hz, 1H), 5.13 (t, $J = 5.2$ Hz, 1H), 4.41 – 4.28 (m, 2H), 4.14 (d, $J = 8.8$ Hz, 1H), 2.06 (d, $J = 2.9$ Hz, 6H), 1.99 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.33, 169.67, 169.46, 152.08, 148.49, 148.33, 138.24, 131.97, 128.68 (2C), 128.56 (2C), 128.08, 122.93, 122.26, 108.76, 95.29, 85.84, 73.71, 67.08, 66.58, 61.24, 20.79, 20.76, 20.61. HRMS (ESI), calculated for $C_{27}H_{25}NNaO_7$ $[M+Na]^+ = 498.1528$; found: 498.1521.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*Z*)-4-(4-aminophenyl)-1-phenylbut-1-en-3-yn-2-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**21e**):

Brown oil. IR (film, cm^{-1}); 3473, 3379, 2959, 2929, 1740, 1650, 1371, 1232, 1182, 1052, 1026, 690. ^1H NMR (300 MHz, CDCl_3) δ 7.46 (d, $J = 7.1$ Hz, 2H), 7.38 – 7.17 (m, 6H), 6.93 (s, 1H), 6.60 (t, $J = 8.6$ Hz, 3H), 6.52 (s, 1H), 5.85 (d, $J = 4.9$ Hz, 1H), 5.29 (dd, $J = 6.0, 4.8$ Hz, 1H), 4.46 (dd, $J = 11.4, 6.3$ Hz, 1H), 4.40 (dd, $J = 6.1, 3.1$ Hz, 1H), 4.25 (dd, $J = 11.5, 3.1$ Hz, 1H), 2.11 (s, 6H), 2.02 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.51, 170.02, 169.67, 146.94, 145.86, 136.51, 136.36, 133.90, 132.95 (2C), 128.89 (2C), 128.38 (2C), 127.52, 118.83, 114.71 (2C), 114.62, 112.20, 108.41, 90.95, 88.06, 73.64, 67.64, 66.71, 61.60, 20.83, 20.80, 20.69. HRMS (ESI), calculated for $\text{C}_{28}\text{H}_{26}\text{NO}_7$ $[\text{M}-\text{H}]^- = 488.1709$; found: 488.1731.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*Z*)-6-hydroxy-1-phenylhex-1-en-3-yn-2-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**21f**):

Yellow oil. IR (film, cm^{-1}); 3490, 3023, 2944, 1739, 1650, 1371, 1218, 1177, 1024, 916, 700. ^1H NMR (300 MHz, CDCl_3) δ 7.31 (d, $J = 6.5$ Hz, 2H), 7.27 – 7.19 (m, 2H), 7.14 (t, $J = 7.2$ Hz, 1H), 6.76 (s, 1H), 6.31 (s, 1H), 5.80 (d, $J = 5.0$ Hz, 1H), 5.23 – 5.07 (m, 1H), 4.37 – 4.22 (m, 2H), 4.13 (dd, $J = 11.6, 3.0$ Hz, 1H), 3.85 – 3.44 (m, 2H), 2.45 (t, $J = 6.1$ Hz, 2H), 2.02 (s, 3H), 2.01 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.57, 170.50, 169.67, 145.79, 137.25, 136.03, 128.76 (2C), 128.40 (2C), 127.59, 118.19, 108.55, 88.04, 82.47, 73.77, 67.66, 66.99, 61.52, 61.03, 24.03, 20.87, 20.77, 20.66. HRMS (ESI), calculated for $\text{C}_{24}\text{H}_{26}\text{NaO}_8$ $[\text{M}+\text{Na}]^+ = 465.1525$; found: 465.1498.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2,4-diphenylbut-1-en-3-yn-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**21g**):

Brown oil. IR (film, cm^{-1}); 3473, 3432, 3058, 2959, 2924, 2874, 1613, 1600, 1492, 1445, 1179, 1030, 914, 758, 694. ^1H NMR (300 MHz, CDCl_3) δ 7.47 – 7.13 (m, 10H), 6.35 (s, 1H), 6.21 (s, 1H), 5.39 (d, J = 4.3 Hz, 1H), 5.21 – 5.06 (m, 1H), 4.48 – 4.23 (m, 2H), 4.15 (dd, J = 11.3, 2.9 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 148.14, 138.40, 132.20, 131.45 (2C), 128.83 (2C), 128.72 (2C), 128.50, 128.32, 128.25 (2C), 127.99, 125.99, 113.99, 99.06, 96.98, 77.94, 69.72, 69.43, 61.87. HRMS (ESI), calculated for $\text{C}_{22}\text{H}_{19}\text{O}_4$ $[\text{M}-\text{H}]^-$ = 347.1281; found: 347.1269.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-1-phenyl-4-(trimethylsilyl)but-1-en-3-yn-2-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**21h**);

Light yellow liquid. IR (film, cm^{-1}); 2961, 2902, 2130, 1745, 1618, 1371, 1216, 1177, 1024, 912, 843, 732. ^1H NMR (300 MHz, CDCl_3) δ 7.18 (d, J = 7.4 Hz, 2H), 7.08 (t, J = 7.4 Hz, 2H), 7.00 (t, J = 7.2 Hz, 1H), 6.70 (s, 1H), 6.23 (s, 1H), 5.51 (d, J = 4.7 Hz, 1H), 5.01 (t, J = 5.4 Hz, 1H), 4.21 (dd, J = 11.0, 4.5 Hz, 1H), 4.14 (dd, J = 10.0, 6.9 Hz, 1H), 3.99 (dd, J = 11.2, 2.7 Hz, 1H), 1.87 (s, 6H), 1.80 (s, 3H), 0.00 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.52, 169.79, 169.67, 146.16, 138.51, 136.03, 128.97 (2C), 128.49 (2C), 127.92, 118.47, 108.02, 105.55, 94.95, 73.73, 67.61, 66.59, 61.68, 20.86, 20.77, 0.00 (3C). HRMS (ESI +) calculated for $\text{C}_{25}\text{H}_{31}\text{O}_7\text{Si}$ $[\text{M}+\text{H}]^+$ = 471.1839 found; 471.1769.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-phenyl-4-(trimethylsilyl)but-1-en-3-yn-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**21i**);

Light yellow liquid. IR (film, cm^{-1}); 3062, 2961, 2902, 2129, 1745, 1618, 1495, 1447, 1371, 1216, 1177, 1050, 1024, 912, 843, 732, 702. ^1H NMR (300 MHz, CDCl_3) δ 7.45 – 7.08 (m, 5H), 6.22 (s, 1H), 6.16 (s, 1H), 5.17 (d, J = 4.7 Hz, 1H), 4.92 (t, J = 5.2 Hz, 1H), 4.22 – 4.05 (m, 2H), 3.94 (dd, J = 11.2, 2.9 Hz, 1H), 1.86 (d, J = 6 Hz, 1H), 1.79 (s, 3H), 0.00 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.35, 169.71, 169.49, 148.09, 137.58, 131.77, 128.64, 128.54, 128.50, 127.87, 123.11, 108.70, 107.44, 94.07, 73.65, 67.19, 66.68, 61.30, 20.83, 20.79, 20.65, 0.00. HRMS (ESI +) calculated for $\text{C}_{25}\text{H}_{31}\text{O}_7\text{Si}$ $[\text{M}+\text{H}]^+$ = 471.1839 found; 471.1754.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-1-(4-aminophenyl)-4-(trimethylsilyl)but-1-en-3-yn-2-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**21j**);

Light yellow liquid. IR (film, cm^{-1}); 3473, 3384, 2951, 2132, 1739, 1609, 1514, 1371, 1222, 1177, 1022, 910, 845, 730. ^1H NMR (300 MHz, CDCl_3) δ 7.00 (d, $J = 8.2$ Hz, 2H), 6.55 (s, 1H), 6.33 (d, $J = 8.1$ Hz, 2H), 6.25 (s, 1H), 5.46 (d, $J = 4.8$ Hz, 1H), 5.07 – 4.88 (m, 1H), 4.20 (dd, $J = 11.7, 6.4$ Hz, 1H), 4.11 (dt, $J = 9.6, 4.7$ Hz, 1H), 3.96 (dd, $J = 11.7, 3.3$ Hz, 1H), 1.84 (s, 6H), 1.73 (s, 3H), -0.00 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.46, 169.74, 169.57, 146.50, 145.43, 139.10, 130.44, 125.96, 114.62, 114.36, 108.25, 106.63, 93.24, 73.57, 67.62, 66.61, 61.66, 20.79, 20.75, 20.71, -0.00. HRMS (ESI +) calculated for $\text{C}_{25}\text{H}_{32}\text{NO}_7\text{Si}$ $[\text{M}+\text{H}]^+ = 486.1948$ found; 486.1781.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(pyridin-3-yl)-4-(trimethylsilyl)but-1-en-3-yn-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**21k**);

Yellowish liquid. IR (film, cm^{-1}); 2960, 1744, 1639, 1628, 1372, 1222, 1181, 1050, 1024, 909, 845, 728. ^1H NMR (300 MHz, CDCl_3) δ 8.43 (d, $J = 35.6$ Hz, 2H), 7.55 (d, $J = 7.8$ Hz, 1H), 7.16 – 7.10 (m, $J = 5.0$ Hz, 1H), 6.29 (d, $J = 4.1$ Hz, 2H), 5.17 (d, $J = 4.6$ Hz, 1H), 4.96 (t, $J = 5.1$ Hz, 1H), 4.29 – 4.10 (m, 2H), 4.01 – 3.87 (m, 1H), 1.90 (d, $J = 2.6$ Hz, 6H), 1.84 (s, 3H), 0.00 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.60, 170.00, 169.73, 149.96, 148.93, 146.68, 136.26, 134.60, 133.70, 121.19, 119.89, 108.71, 106.69, 95.38, 74.18, 67.17, 66.73, 61.46, 21.06, 20.93, 0.20. HRMS (ESI +) calculated for $\text{C}_{24}\text{H}_{30}\text{NO}_7\text{Si}$ $[\text{M}+\text{H}]^+ = 472.1792$ found; 472.161.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(2,4-difluorophenyl)-4-(trimethylsilyl)but-1-en-3-yn-1-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**21l**);

Light brown liquid. IR (film, cm^{-1}); 2959, 1744, 1620, 1600, 1499, 1426, 1372, 1221, 1177, 1143, 1095, 1050, 1023, 909, 853, 732. ^1H NMR (300 MHz, CDCl_3) δ 7.21 – 7.03 (m, 1H), 6.67 (ddd, $J = 20.7, 10.0, 7.5$ Hz, 2H), 6.29 (s, 1H), 6.25 (s, 1H), 5.08 (d, $J = 4.4$ Hz, 1H), 4.91 (t, $J = 4.8$ Hz, 1H), 4.17 (q, $J = 8.3$,

7.6 Hz, 2H), 3.94 (dd, $J = 11.0, 2.5$ Hz, 1H), 1.88 (s, 6H), 1.82 (s, 3H), -0.00 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.40, 169.79, 169.52, 165.53 – 153.75 (m), 148.10, 135.05, 131.80 (dd, $J = 9.6, 4.7$ Hz), 121.55 (dd, $J = 15.8, 3.9$ Hz), 114.72, 111.80 (dd, $J = 21.4, 3.7$ Hz), 109.26, 106.35, 104.63 (t, $J = 25.6$ Hz), 94.10, 73.87, 67.02, 66.14, 61.22, 20.84, 20.82, 20.70, -0.00. HRMS (ESI +) calculated for $\text{C}_{25}\text{H}_{29}\text{F}_2\text{O}_7\text{Si}$ $[\text{M}+\text{H}]^+ = 507.1651$ found; 507.1587.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-1-(trimethylsilyl)oct-3-en-1-yn-3-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**21m**);

Light yellow liquid. IR (film, cm^{-1}); 2961, 2875, 2259, 1745, 1371, 1220, 1033, 910, 845, 832. ^1H NMR (300 MHz, CDCl_3) δ 6.58 (s, 1H), 6.37 (t, $J = 7.6$ Hz, 1H), 5.66 (d, $J = 4.9$ Hz, 1H), 5.24 (t, $J = 5.6$ Hz, 1H), 4.47 (dd, $J = 11.9, 6.2$ Hz, 1H), 4.36 (dt, $J = 9.7, 6.6$ Hz, 1H), 4.18 (dd, $J = 12.2, 3.2$ Hz, 2H), 2.27 – 2.10 (m, 8H), 2.09 (s, 3H), 1.43 – 1.26 (m, 4H), 0.92 (t, $J = 7.1$ Hz, 3H), 0.00 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.16, 169.59, 169.36, 146.71, 143.84, 115.31, 112.85, 99.38, 90.68, 74.02, 66.91, 66.86, 60.98, 31.80, 31.31, 22.04, 20.64, 20.58, 13.78, 0.00 (3C). HRMS (ESI +) calculated for $\text{C}_{23}\text{H}_{35}\text{O}_7\text{Si}$ $[\text{M}+\text{H}]^+ = 451.2152$ found; 451.198.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-1-cyclopropyl-4-(trimethylsilyl)but-1-en-3-yn-2-yl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**21n**);

Light yellowish green liquid. IR (film, cm^{-1}); 2961, 2142, 1745, 1650, 1371, 1220, 1181, 1024, 912, 843, 732. ^1H NMR (300 MHz, CDCl_3) δ 6.53 (s, 1H), 5.59 (d, $J = 5.3$ Hz, 1H), 5.29 (d, $J = 10.1$ Hz, 1H), 5.09 (t, $J = 6.0$ Hz, 1H), 4.33 (dd, $J = 12.0, 6.0$ Hz, 1H), 4.21 (tt, $J = 6.5, 3.4$ Hz, 1H), 4.03 (dd, $J = 12.0, 3.2$ Hz, 1H), 1.93 (d, $J = 4.4$ Hz, 6H), 1.88 (s, 3H), 1.60 (dh, $J = 12.8, 4.5$ Hz, 1H), 0.70 (td, $J = 6.7, 3.1$ Hz, 2H), 0.34 (q, $J = 4.2$ Hz, 2H), 0.00 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.58, 170.11, 169.73, 146.50, 145.04, 115.30, 108.57, 104.92, 92.13, 73.94, 67.61, 67.32, 61.39, 20.88, 20.81, 20.74, 12.45, 9.08, 8.00, 0.00. HRMS (ESI +) calculated for $\text{C}_{22}\text{H}_{31}\text{O}_7\text{Si}$ $[\text{M}+\text{H}]^+ = 435.1839$ found; 435.1745.

General Procedure 9 (GP9); Synthesis of compounds 22a-o:

To a stirred solution of **21h** (470 mg, 1 mM), copper iodide (9.5 mg, 5 mol %) and PMDTA (251 μL , 1.2 eq.) in DMF (3 mL) under nitrogen was added dropwise Phenyl azide (134 μL , 1.2 eq.), followed by addition of Tetrabutylammonium fluoride (347 μL , 1.2 eq.). The mixture was stirred at room temperature and monitored via thin layer chromatography unless the disappearance of starting material. After reaction completion, the mixture was extracted using saturated ammonium chloride solution (15 mL) and ethyl acetate (15 mL x 3). The organic phases were combined, dried over magnesium sulfate, filtered and evaporated under vacuum. The product was isolated by flash chromatography using hexane: ethyl acetate eluent system.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-phenyl-1-(1-phenyl-1*H*-1,2,3-triazol-4-yl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**22a**);

Yellow oil. IR (film, cm^{-1}); 3146, 3061, 2957, 1739, 1652, 1600, 1503, 1369, 1220, 1181, 1043, 914, 734. ^1H NMR (300 MHz, CDCl_3) δ 8.14 (s, 1H), 7.84 (d, $J = 8.8$ Hz, 2H), 7.63 (d, $J = 7.8$ Hz, 3H), 7.55 (t, $J = 7.6$ Hz, 2H), 7.47 (d, $J = 7.4$ Hz, 1H), 7.37 (t, $J = 7.4$ Hz, 2H), 7.32 – 7.21 (m, 1H), 6.64 (s, 1H), 5.56 (d, $J = 4.0$ Hz, 1H), 5.23 (t, $J = 4.4$ Hz, 1H), 4.82 (dd, $J = 12.1, 7.7$ Hz, 1H), 4.52 (dd, $J = 8.3, 4.1$ Hz, 1H), 4.19 – 3.99 (m, 1H), 2.15 (s, 6H), 1.83 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.60, 169.40, 150.44, 146.11, 137.09, 136.24, 130.68, 129.72, 129.31, 128.60, 128.26, 127.67, 124.27, 120.29, 119.15, 108.29, 73.62, 67.47, 66.08, 60.95, 20.87, 20.79, 20.52. HRMS (ESI +) calculated for $\text{C}_{28}\text{H}_{28}\text{N}_3\text{O}_7$ $[\text{M}+\text{H}]^+ = 518.1927$ found; 518.1219.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-phenyl-2-(1-phenyl-1*H*-1,2,3-triazol-4-yl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**22b**);

Yellow oil. IR (film, cm^{-1}); 3060, 1739, 1613, 1600, 1503, 1371, 1220, 1177, 1022, 910, 761, 728, 693. ^1H NMR (300 MHz, CDCl_3) δ 7.55 (d, $J = 7.8$ Hz, 2H), 7.49 – 7.19 (m, 9H), 7.01 (s, 1H), 6.39 (s, 1H), 5.22 (d, $J = 4.5$ Hz, 1H), 5.03 (t, $J = 4.8$ Hz, 1H), 4.36 – 4.16 (m, 2H), 4.04 (t, $J = 7.3$ Hz, 1H), 1.97 (s, 6H), 1.90 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.33, 169.70, 169.46, 150.76, 147.84, 138.59, 136.93, 129.61, 129.25, 128.99, 128.92, 128.53, 128.00, 122.53, 120.26, 119.05, 108.61, 73.35, 66.97, 66.66, 61.34, 20.88, 20.80, 20.62. HRMS (ESI +) calculated for $\text{C}_{28}\text{H}_{28}\text{N}_3\text{O}_7$ $[\text{M}+\text{H}]^+ = 518.1927$ found; 518.1129.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(1-(3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)-2-phenylvinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**22c**);

Bright yellow oil. IR (film, cm^{-1}); 3147, 3050, 2960, 1739, 1620, 1534, 1371, 1352, 1222, 1179, 1048, 1024, 909, 728. ^1H NMR (300 MHz, CDCl_3) δ 8.39 (s, 0H), 8.17 (d, $J = 8.2$ Hz, 1H), 8.04 (d, $J = 8.2$ Hz, 1H), 7.62 (t, $J = 8.2$ Hz, 1H), 7.39 – 7.29 (m, 3H), 7.26 (d, $J = 7.4$ Hz, 2H), 7.06 (s, 1H), 6.43 (s, 1H), 5.22 (d, $J = 4.3$ Hz, 1H), 5.04 (t, $J = 4.6$ Hz, 1H), 4.34 – 4.20 (m, 2H), 4.05 (td, $J = 8.2, 7.7, 2.5$ Hz, 1H), 1.99 (s, 6H), 1.92 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.36, 169.68, 169.46, 151.58, 148.89, 148.26, 138.26, 137.66, 130.86, 129.19, 129.12, 128.25, 125.67, 123.52, 122.91, 118.60, 114.84, 108.51, 73.44, 66.89, 66.52, 61.33, 20.89, 20.82, 20.64. HRMS (ESI +) calculated for $\text{C}_{28}\text{H}_{27}\text{N}_4\text{O}_9$ $[\text{M}+\text{H}]^+ = 563.1778$ found; 563.2008.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(1-(naphthalen-2-yl)-1*H*-1,2,3-triazol-4-yl)-2-phenylvinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**22d**);

Yellow oil. IR (film, cm^{-1}); 3138, 3058, 2963, 1739, 1631, 1600, 1432, 1371, 1220, 1175, 1020, 912, 730. ^1H NMR (300 MHz, CDCl_3) δ 7.87 (dd, $J = 14.6, 8.1$ Hz, 2H), 7.67 – 7.38 (m, 5H), 7.35 – 7.13 (m, 6H), 7.10 (s, 1H), 6.43 (s, 1H), 5.26 (d, $J = 4.3$ Hz, 1H), 5.06 (t, $J = 4.2$ Hz, 1H), 4.26 (d, $J = 8.3$ Hz, 2H), 4.13 – 3.87 (m, 1H), 1.99 (s, 6H), 1.94 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.39, 169.78, 169.51, 150.16, 147.86, 138.66, 134.13, 133.65, 130.29, 129.26, 129.09, 128.91, 128.49, 128.22, 127.99, 127.81, 127.01, 124.88, 123.81, 123.37, 122.49, 122.37, 108.68, 73.39, 67.04, 66.73, 61.40, 20.95, 20.85, 20.66. HRMS (ESI +) calculated for $\text{C}_{32}\text{H}_{30}\text{N}_3\text{O}_7$ $[\text{M}+\text{H}]^+ = 568.2084$ found; 568.1898.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(1-(4-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)-2-phenylvinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**22e**);

Yellow oil. IR (film, cm^{-1}); 3142, 3058, 2961, 2840, 1739, 1631, 1613, 1518, 1371, 1222, 1173, 1024, 910, 728. ^1H NMR (300 MHz, CDCl_3) δ 7.45 (d, $J = 9.0$ Hz, 2H), 7.29 (td, $J = 11.3, 10.4, 6.2$ Hz, 5H), 7.17 (s, 1H), 6.99 (s, 1H), 6.87 (d, $J = 9.0$ Hz, 2H), 6.38 (s, 1H), 5.22 (d, $J = 4.3$ Hz, 1H), 5.03 (t, $J = 4.8$ Hz, 1H), 4.24 (q, $J = 11.6, 8.9$ Hz, 2H), 4.12 – 3.93 (m, 1H), 3.75 (s, 2H), 1.98 (s, 6H), 1.91 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.34, 169.72, 169.47, 159.69, 150.56, 147.75, 138.67, 130.42, 129.27, 129.17, 128.88, 127.95, 122.31, 121.92, 119.30, 114.67, 108.63, 73.34, 67.00, 66.71, 61.36, 55.57, 20.88, 20.81, 20.63. HRMS (ESI +) calculated for $\text{C}_{29}\text{H}_{30}\text{N}_3\text{O}_8$ $[\text{M}+\text{H}]^+ = 548.2033$ found; 548. 1858.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(4-aminophenyl)-1-(1-(benzo[d]thiazol-7-yl)-1*H*-1,2,3-triazol-4-yl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**22f**);

Yellow gummy solid. IR (film, cm^{-1}); 3471, 3373, 1739, 1628, 1605, 1371, 1222, 1181, 1147, 1022, 912, 732. ^1H NMR (300 MHz, CDCl_3) δ 9.08 (s, 1H), 8.50 (s, 1H), 8.26 (d, $J = 8.8$ Hz, 1H), 8.20 (s, 1H), 7.98 (dd, $J = 8.8, 2.1$ Hz, 1H), 7.52 (s, 1H), 7.46 (d, $J = 8.1$ Hz, 2H), 6.75 – 6.45 (m, 4H), 5.59 (d, $J = 3.8$ Hz, 1H), 5.23 (t, $J = 4.4$ Hz, 1H), 4.92 (dd, $J = 12.2, 7.9$ Hz, 1H), 4.54 – 4.44 (m, 1H), 4.10 (td, $J = 13.3, 12.2, 5.2$ Hz, 2H), 2.16 (s, 6H), 1.80 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.75, 169.46, 169.42, 155.45, 152.91, 151.56, 146.39, 145.77, 135.06, 134.73, 130.96, 130.82, 126.39, 124.52, 120.18, 118.91, 118.83, 114.66, 113.68, 108.81, 73.59, 67.64, 66.02, 60.89, 20.90, 20.85, 20.56. HRMS (ESI +) calculated for $\text{C}_{29}\text{H}_{28}\text{N}_5\text{O}_7\text{S}$ $[\text{M}+\text{H}]^+ = 590.1709$ found; 590.2045.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(4-aminophenyl)-1-(1-(2-fluorophenyl)-1*H*-1,2,3-triazol-4-yl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**22g**);

Yellow liquid. IR (film, cm^{-1}); 3471, 3373, 1739, 1628, 1605, 1371, 1222, 1181, 1147, 1022, 912, 732. ^1H NMR (300 MHz, CDCl_3) δ 8.12 – 7.88 (m, 2H), 7.56 – 7.37 (m, 4H), 7.38 – 7.24 (m, 2H), 6.74 – 6.52 (m, 3H), 5.58 (d, $J = 4.0$ Hz, 1H), 5.27 (t, $J = 4.5$ Hz, 1H), 4.65 (dd, $J = 11.9, 7.3$ Hz, 1H), 4.51 (dt, $J = 7.4, 4.2$ Hz, 1H), 4.22 (dd, $J = 12.0, 3.8$ Hz, 1H), 2.13 (d, $J = 4.0$ Hz, 6H), 1.81 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.50, 169.55, 169.48, 154.83, 151.52, 150.57, 146.38, 145.84, 131.47, 130.77, 130.02, 129.92, 126.40, 125.30, 124.74, 121.50, 121.39, 120.42, 117.08, 116.82, 114.64, 108.11, 73.47, 67.48, 66.27, 61.47, 20.80, 20.74, 20.46. HRMS (ESI +) calculated for $\text{C}_{28}\text{H}_{28}\text{FN}_4\text{O}_7$ $[\text{M}+\text{H}]^+ = 551.1942$ found; 551.084.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-1-(1-(benzo[d]thiazol-7-yl)-1*H*-1,2,3-triazol-4-yl)-2-(pyridin-3-yl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**22h**);

Light brown liquid. IR (film, cm^{-1}); 3063, 2959, 1745, 1488, 1371, 1225, 1184, 1045, 1028, 735. ^1H NMR (300 MHz, CDCl_3) δ 9.10 (s, 1H), 8.86 (s, 1H), 8.54 (d, $J = 2.1$ Hz, 1H), 8.34 (s, 1H), 8.29 (d, $J = 8.8$ Hz, 1H), 8.06 – 7.97 (m, 2H), 7.93 (d, $J = 8.0$ Hz, 1H), 7.60 (s, 1H), 7.42 – 7.17 (m, 2H), 6.67 (s, 1H), 5.49 (d, $J = 3.8$ Hz, 1H), 5.19 (t, $J = 4.4$ Hz, 1H), 4.96 (dd, $J = 12.3, 8.2$ Hz, 1H), 4.60 – 4.40 (m, 1H), 4.02 (dd, $J = 12.2, 3.2$ Hz, 1H), 2.17 (s, 6H), 1.84 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.75, 169.46, 169.42, 155.45, 152.91, 151.56, 148.73, 146.39, 145.77, 135.06, 134.73, 130.96, 130.82, 126.39, 124.52, 120.18, 118.91, 118.83, 114.66, 113.68, 108.81, 73.59, 67.64, 66.02, 60.89, 20.90, 20.85, 20.56. HRMS (ESI +) calculated for $\text{C}_{28}\text{H}_{26}\text{N}_5\text{O}_7\text{S}$ $[\text{M}+\text{H}]^+ = 576.1553$ found; 576.1941.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(2,4-difluorophenyl)-2-(1-(3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**22i**);

Bright yellow oil. IR (film, cm^{-1}); 3136, 3105, 2967, 1743, 1620, 1536, 1506, 1354, 1225, 1181, 1048, 1030, 970, 739; ^1H NMR (300 MHz, CDCl_3) δ 8.41 (s, 1H), 8.19 (d, $J = 8.1$ Hz, 1H), 8.07 (d, $J = 8.2$ Hz, 1H), 7.64 (t, $J = 8.2$ Hz, 1H), 7.44 (s, 1H), 7.28 – 7.16 (m, 1H), 7.14 (s, 1H), 6.88 (tdd, $J = 11.7, 8.4, 2.5$ Hz, 2H), 6.49 (s, 1H), 5.19 (d, $J = 4.2$ Hz, 1H), 5.04 (t, $J = 4.3$ Hz, 1H), 4.29 (dd, $J = 9.0, 5.7$ Hz, 2H), 4.04 (q, $J = 7.1$ Hz, 1H), 2.00 (s, 6H), 1.93 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.32, 169.71, 169.40, 164.80, 164.63, 161.54 (ddd, $J = 249.4, 227.6, 12.0$ Hz), 158.45, 158.30, 150.30, 148.89, 148.24, 137.58, 132.31 (dd, $J = 9.1, 4.9$ Hz), 130.91, 126.60, 125.75, 123.02, 121.22 (d, $J = 45.4$ Hz), 118.02, 114.87, 112.23 (d, $J = 24.7$ Hz), 108.59, 105.29, 104.95 (t, $J = 25.7$ Hz), 73.61, 66.74, 66.01, 61.17, 20.78, 20.71, 20.61. HRMS (ESI +) calculated for $\text{C}_{28}\text{H}_{25}\text{F}_2\text{N}_4\text{O}_9$ $[\text{M}+\text{H}]^+ = 599.1590$ found; 599.1553.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(1-(benzo[d]thiazol-7-yl)-1*H*-1,2,3-triazol-4-yl)-2-(2,4-difluorophenyl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**22j**);

Light brown oil. IR (film, cm^{-1}); 3075, 2983, 2112, 1737, 1611, 1505, 1486, 1223, 1179, 1046, 1026, 916, 849, 732. ^1H NMR (300 MHz, CDCl_3) δ 9.07 (s, 1H), 8.33 (s, 1H), 8.20 (d, $J = 8.8$ Hz, 1H), 7.80 (d, $J = 8.9$ Hz, 1H), 7.52 (s, 1H), 7.32 (q, $J = 7.9$ Hz, 1H), 7.21 (s, 1H), 7.03 – 6.81 (m, 2H), 6.56 (s, 1H), 5.28 (d, $J = 4.1$ Hz, 1H), 5.13 (t, $J = 4.3$ Hz, 1H), 4.35 (q, $J = 7.0, 5.5$ Hz, 2H), 4.20 – 4.12 (m, 1H), 2.07 (s, 6H), 2.01 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.31, 169.73, 169.40, 166.58 – 156.80 (m), 153.01, 149.83, 147.96, 135.00, 134.40, 132.37 (dd, $J = 9.4, 5.2$ Hz), 125.94, 124.51, 121.63 (dd, $J = 16.7, 3.8$ Hz), 119.00, 118.67, 113.80, 112.08 (dd, $J = 21.1, 3.6$ Hz), 108.66, 104.83 (t, $J = 25.3$ Hz), 73.55, 66.78, 66.08, 61.18, 20.77, 20.72, 20.60. HRMS (ESI +) calculated for $\text{C}_{29}\text{H}_{25}\text{F}_2\text{N}_4\text{O}_7\text{S}$ $[\text{M}+\text{H}]^+ = 611.1412$ found; 611.1196.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-(2,4-difluorophenyl)-2-(1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazol-4-yl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**22k**);

Light yellow oil. IR (film, cm^{-1}); 3071, 2981, 1743, 1618, 1506, 1372, 1326, 1223, 1173, 1048, 1022, 912, 847, 732. ^1H NMR (300 MHz, CDCl_3) δ 7.83 (d, $J = 8.4$ Hz, 2H), 7.75 (d, $J = 8.2$ Hz, 2H), 7.47 (s, 1H), 7.30 (q, $J = 7.7$ Hz, 1H), 7.20 (s, 1H), 6.94 (ddd, $J = 17.3, 10.0, 7.4$ Hz, 2H), 6.56 (s, 1H), 5.27 (d, $J = 4.1$ Hz, 1H), 5.11 (t, $J = 4.4$ Hz, 1H), 4.35 (q, $J = 6.5, 5.5$ Hz, 2H), 4.12 (q, $J = 7.1$ Hz, 1H), 2.07 (s, 6H), 2.00 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.34, 169.75, 169.42, 150.05, 148.09, 139.26, 132.25, 130.82, 130.38, 127.03, 126.98, 126.33, 125.18, 121.70, 121.38, 120.19, 118.01, 112.30, 111.97, 108.62, 105.21, 104.87, 104.53, 73.59, 66.77, 66.08, 61.17, 20.75, 20.69, 20.58. HRMS (ESI +) calculated for $\text{C}_{29}\text{H}_{25}\text{F}_5\text{N}_3\text{O}_7$ $[\text{M}+\text{H}]^+ = 622.1613$ found; 622.0991.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-cyclopropyl-1-(1-phenyl-1*H*-1,2,3-triazol-4-yl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**22l**);

Light yellow liquid. IR (film, cm^{-1}); 1745, 1506, 1372, 1227, 1043, 939, 765. ^1H NMR (300 MHz, CDCl_3) δ 7.82 (s, 1H), 7.73 (d, $J = 7.1$ Hz, 2H), 7.63 – 7.32 (m, 3H), 6.66 (s, 1H), 6.02 (d, $J = 10.2$ Hz, 1H), 5.71 (d, $J = 5.0$ Hz, 1H), 5.32 (t, $J = 5.7$ Hz, 1H), 4.63 (dd, $J = 12.1, 6.5$ Hz, 1H), 4.54 – 4.42 (m, 1H), 4.21 (dd, $J = 12.1, 3.3$ Hz, 1H), 2.12 (s, 3H), 2.10 (s, 3H), 1.92 (s, 3H), 1.83 (tt, $J = 7.9, 4.2$ Hz, 1H), 0.89 (qd, $J = 8.7, 5.7, 3.6$ Hz, 2H), 0.74 – 0.38 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.51, 169.80, 169.45, 149.24, 145.30, 138.64, 137.09, 129.64, 128.46, 121.44, 120.47, 120.27, 117.46, 108.40, 73.85, 67.59, 67.52, 61.22, 20.78, 20.72, 20.65, 11.79, 8.10, 7.72. HRMS (ESI +) calculated for $\text{C}_{25}\text{H}_{28}\text{N}_3\text{O}_7$ $[\text{M}+\text{H}]^+ = 482.1927$ found; 482.182.

(2*R*,3*S*,4*R*)-2-(acetoxymethyl)-5-((*E*)-2-cyclopropyl-1-(1-(2-fluorophenyl)-1*H*-1,2,3-triazol-4-yl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diyl diacetate (**22m**);

Pale yellow gummy solid. IR (film, cm^{-1}); 1743, 1504, 1371, 1225, 1043, 939, 765. ^1H NMR (300 MHz, CDCl_3) δ 7.97 (td, $J = 7.8, 1.7$ Hz, 1H), 7.88 (s, 1H), 7.50 – 7.35 (m, 1H), 7.38 – 7.16 (m, 2H), 6.67 (s, 1H), 6.04 (d, $J = 10.2$ Hz, 1H), 5.63 (d, $J = 4.6$ Hz, 1H), 5.50 – 5.12 (m, 1H), 4.71 – 4.38 (m, 2H), 4.24 (dd, $J = 11.9, 3.4$ Hz, 1H), 2.12 (s, 6H), 1.95 (s, 3H), 1.92 – 1.77 (m, 1H), 1.02 – 0.78 (m, 2H), 0.61 (tt, $J = 5.1, 2.2$ Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.50, 169.78, 169.49, 153.06 (d, $J = 250.0$ Hz), 148.89, 145.29, 138.87, 129.89 (d, $J = 7.8$ Hz), 125.49 – 125.10 (m), 124.67, 121.39, 120.44 (d, $J = 8.6$ Hz), 117.03, 116.76, 107.92, 73.67, 67.36, 67.01, 61.29, 20.73 (2C), 20.64, 11.79, 8.07, 7.74. HRMS (ESI +) calculated for $\text{C}_{25}\text{H}_{27}\text{FN}_3\text{O}_7$ $[\text{M}+\text{H}]^+ = 500.1833$ found; 500.1697.

(2*R*,3*S*,4*R*)-2-(hydroxymethyl)-5-((*E*)-2-phenyl-2-(1-phenyl-1*H*-1,2,3-triazol-4-yl)vinyl)-3,4-dihydro-2*H*-pyran-3,4-diol (**22n**);

Light yellow gummy solid. IR (film, cm^{-1}); 3430, 3060, 1615, 1600, 1503, 1361, 1220, 1170, 1022, 910, 761, 728, 696. ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 8.72 (s, 1H), 7.94 (d, $J = 7.8$ Hz, 2H), 7.73 (d, $J = 7.5$ Hz, 2H), 7.61 (t, $J = 7.4$ Hz, 2H), 7.55 – 7.45 (m, 1H), 7.42 (s, 1H), 7.32 (t, $J = 7.1$ Hz, 2H), 7.27 – 7.14 (m, 1H), 6.24 (s, 1H), 5.25 (d, $J = 4.4$ Hz, 1H), 5.07 (d, $J = 4.7$ Hz, 1H), 4.69 (t, $J = 4.9$ Hz, 1H), 4.33 (t, $J = 4.9$ Hz, 1H), 3.99 (s, 1H). ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$) δ 149.74, 142.77, 136.82, 136.65, 129.81, 129.38, 128.49, 127.93, 127.31, 126.78, 120.38, 119.90, 111.96, 79.70, 69.07, 68.36, 60.60. HRMS (ESI +) calculated for $\text{C}_{22}\text{H}_{22}\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+ = 392.1610$ found; 392.1219.

8. NMR SPECTRA

Compound 5 (¹H NMR spectrum)

Compound 5 (¹³C NMR spectrum)

Compound 6a (^1H NMR spectrum) Compound 6a (^{13}C NMR spectrum)

Compound 6b (^1H NMR spectrum) Compound 6b (^{13}C NMR spectrum)

Compound 6c (¹H NMR spectrum)

Compound 6c (¹³C NMR spectrum)

Compound 6d (^1H NMR spectrum) Compound 6d (^{13}C NMR spectrum)

Compound 6e (^1H NMR spectrum) Compound 6e (^{13}C NMR spectrum)

Compound 6f (¹H NMR spectrum) Compound 6f (¹³C NMR spectrum)

Compound 6g (^1H NMR spectrum) Compound 6g (^{13}C NMR spectrum)

Compound 6h (^1H NMR spectrum) Compound 6h (^{13}C NMR spectrum)

Compound 6i (¹H NMR spectrum) Compound 6i (¹³C NMR spectrum)

Compound 6j (^1H NMR spectrum) Compound 6j (^{13}C NMR spectrum)

Compound 6k (^1H NMR spectrum) Compound 6k (^{13}C NMR spectrum)

Compound 6l (¹H NMR spectrum) Compound 6l (¹³C NMR spectrum)

Compound 6m (¹H NMR spectrum) Compound 6m (¹³C NMR spectrum)

Compound 6n (^1H NMR spectrum) Compound 6n (^{13}C NMR spectrum)

Compound 6o (¹H NMR spectrum) Compound 6o (¹³C NMR spectrum)

Compound 8a-1 (^1H NMR spectrum) Compound 8a-1 (^{13}C NMR spectrum)

Compound 8a-1 (^1H - ^1H COSY spectrum)

Compound 8b-1 (^1H NMR spectrum) Compound 8b-1 (^{13}C NMR spectrum)

Compound 8b-1 (^1H - ^1H COSY spectrum)

Compound 8a-2 (^1H NMR spectrum) Compound 8a-2 (^{13}C NMR spectrum)

Compound 8a-2 (^1H - ^1H COSY spectrum)

Compound 8b-2 (¹H NMR spectrum) Compound 8b-2 (¹³C NMR spectrum)

Compound 8b-2 (^1H - ^1H COSY spectrum)

Compound 8a-3 (^1H NMR spectrum) Compound 8a-3 (^{13}C NMR spectrum)

Compound 8a-3 (^1H - ^1H COSY spectrum)

Compound 8b-3 (^1H NMR spectrum) Compound 8b-3 (^{13}C NMR spectrum)

Compound 8a-4 (¹H NMR spectrum) Compound 8a-4 (¹³C NMR spectrum)

Compound 8b-4 (^1H NMR spectrum) Compound 8b-4 (^{13}C NMR spectrum)

Compound 8b-4 (^1H - ^1H COSY spectrum)

Compound 8a-5 (^1H NMR spectrum) Compound 8a-5 (^{13}C NMR spectrum)

Compound 8b-5 (¹H NMR spectrum)

Compound 8b-5 (¹³C NMR spectrum)

Compound 8b-5 (^1H - ^1H COSY spectrum)

Compound 8a-6 (^1H NMR spectrum) Compound 8a-6 (^{13}C NMR spectrum)

Compound 8b-6 (^1H NMR spectrum) Compound 8b-6 (^{13}C NMR spectrum)

Compound 8b-6 (^1H - ^1H COSY spectrum)

Compound 8a-7 (¹H NMR spectrum) Compound 8a-7 (¹³C NMR spectrum)

Compound 8b-7 (^1H NMR spectrum) Compound 8b-7 (^{13}C NMR spectrum)

Compound 8b-7 (^1H - ^1H COSY spectrum)

Compound 8a-8 (^1H NMR spectrum)

Compound 8b-8 (^1H NMR spectrum) Compound 8b-8 (^{13}C NMR spectrum)

Compound 8c-8 (^1H NMR spectrum) Compound 8c-8 (^{13}C NMR spectrum)

Compound 9a (^1H NMR spectrum) Compound 9a (^{13}C NMR spectrum)

Compound 9b (^1H NMR spectrum) Compound 9b (^{13}C NMR spectrum)

Compound 10a (¹H NMR spectrum) Compound 10a (¹³C NMR spectrum)

Compound 10b (¹H NMR spectrum) Compound 10b (¹³C NMR spectrum)

Compound 11a (^1H NMR spectrum) Compound 11a (^{13}C NMR spectrum)

Compound 11b (¹H NMR spectrum) Compound 11b (¹³C NMR spectrum)

Compound 12a (^1H NMR spectrum) Compound 12a (^{13}C NMR spectrum)

Compound 12b (¹H NMR spectrum)

Compound 12b (¹³C NMR spectrum)

Compound 12c (¹H NMR spectrum) Compound 12c (¹³C NMR spectrum)

Compound 12d (^1H NMR spectrum) Compound 12d (^{13}C NMR spectrum)

Compound 14a (^1H NMR spectrum) Compound 14a (^{13}C NMR spectrum)

Compound 14b (¹H NMR spectrum) Compound 14b (¹³C NMR spectrum)

Compound 14c (¹H NMR spectrum) Compound 14c (¹³C NMR spectrum)

Compound 14d (¹H NMR spectrum) Compound 14d (¹³C NMR spectrum)

Compound 14e (¹H NMR spectrum) Compound 14e (¹³C NMR spectrum)

Compound 14f (¹H NMR spectrum) Compound 14f (¹³C NMR spectrum)

Compound 14g (¹H NMR spectrum) Compound 14g (¹³C NMR spectrum)

Compound 14h (¹H NMR spectrum) Compound 14h (¹³C NMR spectrum)

Compound 14i (¹H NMR spectrum) Compound 14i (¹³C NMR spectrum)

Compound 14j (¹H NMR spectrum) Compound 14j (¹³C NMR spectrum)

Compound 14k (¹H NMR spectrum) Compound 14k (¹³C NMR spectrum)

Compound 14l (¹H NMR spectrum) Compound 14l (¹³C NMR spectrum)

Compound 14m (¹H NMR spectrum) Compound 14m (¹³C NMR spectrum)

Compound 14n (^1H NMR spectrum) Compound 14n (^{13}C NMR spectrum)

Compound 14o (¹H NMR spectrum) Compound 14o (¹³C NMR spectrum)

Compound 15a (¹H NMR spectrum)

Compound 15a (¹³C NMR spectrum)

Compound 15b (^1H NMR spectrum) Compound 15b (^{13}C NMR spectrum)

Compound 15c (¹H NMR spectrum) Compound 15c (¹³C NMR spectrum)

Compound 15d (¹H NMR spectrum) Compound 15d (¹³C NMR spectrum)

Compound 15e (^1H NMR spectrum) Compound 15e (^{13}C NMR spectrum)

Compound 15f (¹H NMR spectrum)

Compound 15f (¹³C NMR spectrum)

Compound 15g (^1H NMR spectrum) Compound 15g (^{13}C NMR spectrum)

Compound 16a (^1H NMR spectrum) Compound 16a (^{13}C NMR spectrum)

Compound 16d (¹H NMR spectrum) Compound 16d (¹³C NMR spectrum)

Compound 16e (^1H NMR spectrum) Compound 16e (^{13}C NMR spectrum)

Compound 16f (^1H NMR spectrum) Compound 16f (^{13}C NMR spectrum)

Compound 16g (^1H NMR spectrum) Compound 16g (^{13}C NMR spectrum)

Compound 17a- α (^1H NMR spectrum)

Compound 17a- α (^{13}C NMR spectrum)

Compound 17a- β (^1H NMR spectrum) Compound 17a- β (^{13}C NMR spectrum)

Compound 17a- β (HSQC spectrum) ^{119}Sn NMR spectra of compound 17a α (B) and 17a β (A) Compound 17a α and 17a β (^{119}Sn NMR spectra)

Compound 17b- α (^1H NMR spectrum) Compound 17b- α (^{13}C NMR spectrum)

Compound 17b- α (HMBC spectrum)

Compound 17c- α (^1H NMR spectrum) Compound 17c- α (^{13}C NMR spectrum)

Compound 17c- α (HMBC spectrum)

Compound 17c- β (^1H NMR spectrum) Compound 17c- β (^{13}C NMR spectrum)

Compound 17c- β (HMBC spectrum)

Compound 17d- β (^1H NMR spectrum) Compound 17d- β (^{13}C NMR spectrum)

Compound 17d- β (DEPT-135 spectrum) Compound 17d- β (HMBC spectrum)

Compound 17e- β (^1H NMR spectrum) Compound 17e- β (^{13}C NMR spectrum)

Compound 17e- β (^{119}Sn NMR spectrum) Compound 17e- β and 17e- α (^{119}Sn NMR spectrum)

Compound 17f- α (^1H NMR spectrum) Compound 17f- α (^{13}C NMR spectrum)

Compound 17g- α (^1H NMR spectrum) Compound 17g- α (^{13}C NMR spectrum)

Compound 17h- α (^1H NMR spectrum) Compound 17h- α (^{13}C NMR spectrum)

Compound 17i- α (^1H NMR spectrum) Compound 17i- α (^{13}C NMR spectrum)

Compound 17j- α (^1H NMR spectrum) Compound 17j- α (^{13}C NMR spectrum)

Compound 17k- α (^1H NMR spectrum) Compound 17k- α (^{13}C NMR spectrum)

Compound 17l-β (¹H NMR spectrum)

Compound 17I-β (¹³C NMR spectrum)

Compound 17m- α (^1H NMR spectrum) Compound 17m- α (^{13}C NMR spectrum)

Compound 17m- β (^1H NMR spectrum) Compound 17m- β (^{13}C NMR spectrum)

Compound 18a (^1H NMR spectrum) Compound 18a (^{13}C NMR spectrum)

Compound 19a (^1H NMR spectrum) Compound 19a (^{13}C NMR spectrum)

Compound 19b (^1H NMR spectrum) Compound 19b (^{13}C NMR spectrum)

Compound 20a (^1H NMR spectrum) Compound 20a (^{13}C NMR spectrum)

Compound 20c (^1H NMR spectrum) Compound 20c (^{13}C NMR spectrum)

Compound 20d (¹H NMR spectrum) Compound 20d (¹³C NMR spectrum)

Compound 20e (^1H NMR spectrum) Compound 20e (^{13}C NMR spectrum)

Compound 20g (^1H NMR spectrum) Compound 20g (^{13}C NMR spectrum)

Compound 20h (^1H NMR spectrum) Compound 20h (^{13}C NMR spectrum)

Compound 21a (^1H NMR spectrum) Compound 21a (^{13}C NMR spectrum)

Compound 21b (¹H NMR spectrum) Compound 21b (¹³C NMR spectrum)

Compound 21c (¹H NMR spectrum) Compound 21c (¹³C NMR spectrum)

Compound 21d (¹H NMR spectrum) Compound 21d (¹³C NMR spectrum)

Compound 21e (¹H NMR spectrum) Compound 21e (¹³C NMR spectrum)

Compound 21g (^1H NMR spectrum) Compound 21g (^{13}C NMR spectrum)

Compound 21h (¹H NMR spectrum) Compound 21h (¹³C NMR spectrum)

Compound 21i (¹H NMR spectrum) Compound 21i (¹³C NMR spectrum)

Compound 21j (¹H NMR spectrum) Compound 21j (¹³C NMR spectrum)

Compound 21k (^1H NMR spectrum) Compound 21k (^{13}C NMR spectrum)

Compound 211 (^1H NMR spectrum) Compound 211 (^{13}C NMR spectrum)

Compound 21m (¹H NMR spectrum) Compound 21m (¹³C NMR spectrum)

Compound 21n (¹H NMR spectrum) Compound 21n (¹³C NMR spectrum)

Compound 22a (^1H NMR spectrum) Compound 22a (^{13}C NMR spectrum)

Compound 22d (¹H NMR spectrum) Compound 22d (¹³C NMR spectrum)

Compound 22e (^1H NMR spectrum) Compound 22e (^{13}C NMR spectrum)

Compound 22g (^1H NMR spectrum) Compound 22g (^{13}C NMR spectrum)

Compound 22j (¹H NMR spectrum) Compound 22j (¹³C NMR spectrum)

Compound 22k (¹H NMR spectrum) Compound 22k (¹³C NMR spectrum)

Compound 22n (^1H NMR spectrum) Compound 22n (^{13}C NMR spectrum)

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10. Curriculum Vitae

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08/2013-present

PhD student in Organic Chemistry

Instituto de Química, Universidade de São Paulo, SP – Brasil.

Advisor: Prof. Dr. Helio A. Stefani

Research: Functionalization of 3,4,5-tri-*O*-acetyl-D-glucal via Click Chemistry and palladium-catalyzed cross coupling Reactions

07/2011-02/2013

Junior Research Fellow

HEJ – Research Institute of Chemistry, ICCBS, University of Karachi, Karachi-75270, Sindh, Pakistan.

Supervisor: Prof. Dr. Muhammad Raza Shah

Research: Synthesis, and Photophysical and Biological Applications of Natural Product-Based Gold Nanoparticle

2005-2008

Masters: M.Sc Chemistry (Organic Chemistry)

Institute of Chemical Sciences (ICS), University of Peshawar, Peshawar – KP, Pakistan.

Supervisor: Prof. Dr. Gias-Uddin

Research: Studies on the Chemical Constituents of *Ruellia Tuberosa* Linn.

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Graduation: B.Sc (Chemistry and Biology),

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Work Experience:

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Teaching Assistant:

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QFL4320 – Reatividade de Compostos Orgânicos I

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Teaching Chemistry to undergraduates

Postgraduate College Nowshera, KP – Pakistan

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Work in Industry:

Executive Production:

Qarshi Industries Pvt. Ltd. Hattar, Haripur, KP – Pakistan.

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Quality Control Analyst:

Shazeb Pharmaceutical Industries, Pvt. Ltd. Haripur, KP – Pakistan.

Publications:

(A) Publications from the Thesis:

1. **Shamim, A.;** Souza, F. B. Vasconcelos, S. N. S. Stefani, H. A. "Synthesis of a library of glucal-derived triazoles copper-catalyzed azide-alkyne cyclization" *Tetrahedron Lett.* **2017**, 58, 884-888.
2. **Shamim, A.;** Barbeiro, C. S.; Ali, B.; Stefani, H. A. "Synthesis of Stannyl-Substituted d-Glucal Derivatives via Palladium-Catalyzed Regioselective Hydrostannation and Their Synthetic Applications" *ChemistrySelect*, **2016**, 18, 5653-5659.
3. **Shamim, A.;** Souza, F. B.; Trossini, G. H. G.; Gatti, F. M. Stefani, H. A. "Synthesis of C-glycosyl-bis-1,2,3-triazole derivatives from 3,4,6-tri-O-acetyl-D-glucal" *Mol. Divers.*, **2015**, 19, 423-434.
4. **Shamim, A.;** Vasconcelos, S. N. S.; Ali, B.; Madureira, L. S.; Zukerman-Schpector, J.; Stefani, H. A. "Ligand and copper-free Sonogashira coupling to achieve 2-alkynyl d-glucal derivatives: regioselective electrophile promoted nucleophilic 5-endo-dig cyclization" *Tetrahedron Lett.*, **2015**, 43, 5836-5842.
5. **Shamim, A.;** Vasconcelos, S. N. S.; De Oliveira, I. M.; Reis, J. S.; Pimenta, D. C.; Zukerman-Schpector, J.; Stefani, H. A. "Synthesis of Glycosyl Azides and Their Applications using Click Chemistry to Generate bis- and Tris-triazolyl Glycosyl Derivatives." *Synthesis* **2017**, 00, 000-000. (SS-2017-05-0353-OP).
6. Zukerman-Schpector, J.; Caracelli, I.; Stefani, H. A.; **Shamim, A.;** Tiekink, E. R.T "Crystal structure of [(2*R*, 3*R*, 4*S*)-3,4-bis(acetyloxy)-5-iodo-3,4-dihydro-2 *H* -pyran-2-yl]methyl acetate," *Acta Cryst. E.*, **2015**, 71, o53-o54.

(B) Publications from collaboration with Lab colleagues and from previous work:

7. Ali, B.; Vasconcelos, S. N. S.; Shamim, A.; Zukerman-Schpector, J.; Stefani, H. A. "Synthesis of 1-((4-methoxyphenyl)-3-alkynes)-1*H*-pyrrole-2,5-diones and functionalization to triazoles" *Arabian J. Chem.*, **2017**, 10, 500-508.
8. Vasconcelos, S. N. S. Shamim A.; Ali B.; Oliveira I. M.; Stefani, H. A. "Functionalization of protected tyrosine via Sonogashira reaction: Synthesis of 3-(1,2,3-triazolyl)-tyrosine" *Mol. Divers.*, **2016**, 20, 469-481.
9. Ali, B.; Zukerman-Schpector, J.; Ferreira, F. P.; Shamim, A.; Pimenta, D. C.; Stefani, H. A. "Lewis-acid catalyzed N-acyliminium ion cyclodimerization: synthesis of symmetrical 1,4-dioxanes" *Tetrahedron Lett.*, **2015**, 9, 1153-1158.
10. Shah, M. R.; Shamim, A.; White, L. S.; Bertino, M. F.; Mesaik, M. A.; Soomro S. "The anti-inflammatory properties of Au-scopoletin nanoconjugates" *New J. Chem.*, **2014**, 38, 5566-5572.
11. Ali, B.; Shamim, A.; Vasconcelos, S. N. S.; Stefani, H. A. "Synthesis and applications of 4-substituted 1-(4-iodophenyl)pyrrolidine-2,5-diones" *Tetrahedron Lett.*, **2015**, 28, 4234-4241.

12. Souza, F. B. Shamim, A.; Argomedo, L. M. Z. Pimenta, D. C.; Stefani, H. A. "Synthesis of enyne and aryl vinyl sulfoxides: functionalization via Pummerer rearrangement" *Mol. Divers.*, **2015**, *19*, 773-785.
13. De Oliveira, I. M.; Vasconcelos, S. N. S.; Barbeiro, C. S.; Correra, T. S.; Shamim, A.; Pimenta, D. C.; Caracelli, I.; Zukerman-Schpector, J.; Manarin F.; Stefani, H. A. *New J. Chem.* **2017**, *00*, 000-000 (NJ-ART-05-2017-001803).

Participation in Chemistry Conferences:

08/2016	252 nd American Chemical Society, National Meeting - Philadelphia, PA, USA.
11/2015	16 th Brazilian Meeting on Organic Synthesis (BMOS) - Buzios, Brazil.
06/2015	16 th Tetrahedron Symposium - Berlin, Germany, June 16-19, 2015.
08/2014	248 th American Chemical Society, National Meeting - San Francisco, CA, USA.
01/2013	4 th International Symposium-cum-Training course on Molecular Medicine and Drug Research - HEJRIC, Karachi, Pakistan.
06/2012	Regional Workshop on Chemical Laboratory Safety and Security - ICCBS, University of Karachi, Pakistan.
05/2012	Pak-US Workshop on Applications of Nanotechnology - ICCBS, Karachi, Pakistan.
04/2012	Workshop on Developing skills for interpretation of 1D and 2D NMR Spectral Data for Structure Determination of Organic Compounds - LEJ (HEC), Pakistan.

Awards and Scholarships:

06/2013	Won "Bolsa de Internacionalização" Instituto de Química, Universidade de São Paulo, São Paulo, SP – Brasil.
08/2012	Scored 98 percentile (920/990) in ETS-Subject Chemistry GRE International Test, USA.
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