

PhD Thesis

Development of Glycosyl *ortho*-[1-(*p*-MeOPhenyl) Vinyl]Benzoates (PMPVB) as Reactive Glycosyl Donors and Studies Toward the Synthesis of L-Sugars, non-ulosonic acids via Perlin Aldehydes

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June 2023



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to

Indian Institute of Technology Guwahati

for the award of the degree of

Doctor of Philosophy



**Department of Chemistry
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Statement

This thesis entitled “*Development of Glycosyl ortho-[1-(p-MeOPhenyl) Vinyl]Benzoates (PMPVB) as Reactive Glycosyl Donors and Studies Toward the Synthesis of L-Sugars, non-ulosonic acids via Perlin Aldehydes*” is a work of research and investigation carried out by me under the supervision of Dr. Pavan K. Kancharla, Department of Chemistry, Indian Institute of Technology Guwahati. This thesis has been submitted by me to the Department of Chemistry, Indian Institute of Technology Guwahati for the award of the degree of Doctor of Philosophy. I further declare that this work has not been submitted anywhere else for any degree, diploma, associateship or membership etc. of any Institute or University to the best of my knowledge.

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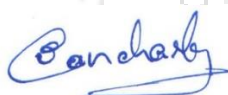
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Certificate

It is certified that the thesis entitled “*Development of Glycosyl ortho-/1-(p-MeOPhenyl) Vinyl/Benzoates (PMPVB) as Reactive Glycosyl Donors and Studies Toward the Synthesis of L-Sugars, non-ulosonic acids via Perlin Aldehydes*” being submitted to the Indian Institute of Technology Guwahati by Mr. Suwendu Halder (Roll. No. 176122101) for the award of the degree of Doctor of Philosophy in Chemistry is a bonafide record of research work carried out by him under my supervision. The information and data reported by him are solely the results of his original findings. He has meticulously carried out the investigations and followed the guidelines of the laboratory. This work has not been submitted elsewhere for any degree or diploma.



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Dedicated to my
Parents and Family members



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List of Publications and Conferences

Publications

1. **Halder, S.**; Addanki, R. B.; Kancharla, P. K.* “Regio- and Stereoselective C-Glycosylation of Indoles Using *Ortho*-[1-(*p*-MeO-Phenyl)vinyl]benzoates (PMPVB) as Glycosyl Donors under Brønsted Acid Catalysis” ***J. Org. Chem.* 2023, 88** 1844-1854.
2. **Halder, S.**; Addanki, R. B.; Moktan, S.; Kancharla, P. K.* “Glycosyl *Ortho*-[1-(*p*-MeOPhenyl)Vinyl]Benzoates (PMPVB) as Easily Accessible, Stable, and Reactive Glycosyl Donors for O-, S- and C-glycosylations Under Brønsted Acid Catalysis” ***J. Org. Chem.* 2022, 87(11)** 7033–7055.
3. **Halder, S.**; Addanki, R. B.; Kancharla, P. K.* “Catalytic stereoselective synthesis of 2-deoxy α -glycosides using glycosyl *ortho*-[1-(*p*-MeOPhenyl)Vinyl]Benzoate (PMPVB) donors” ***Org. & Biomol. Chem.* 2022, 20,** 1874-1878.
4. Addanki, R. B.; **Halder, S.**; Kancharla, P. K.* “TfO $\cdots$ H–O–H Interaction-Assisted Generation of a Silicon Cation from Allylsilanes: Access to Phenylallyl Ferrier Glycosides from Glycals” ***Org. Lett.* 2022, 24(7),** 1465-1470.
5. Mukherji, A.; Addanki, R. B.; **Halder, S.**; Kancharla, P. K.* “Sterically Strained Brønsted Pair Catalysis by Bulky Pyridinium Salts: Direct Stereoselective Synthesis of 2-Deoxy and 2,6-Dideoxy- β -thioglycosides from Glycals” ***J. Org. Chem.* 2021, 86,** 17226-17243.
6. **Halder, S.**; Addanki, R. B.; Kancharla, P. K.* "Three Step Synthesis of L-Altrose from D-galactose derived Perlin Aldehyde" ***JICS*, 2020, 97(2),** 243-250.

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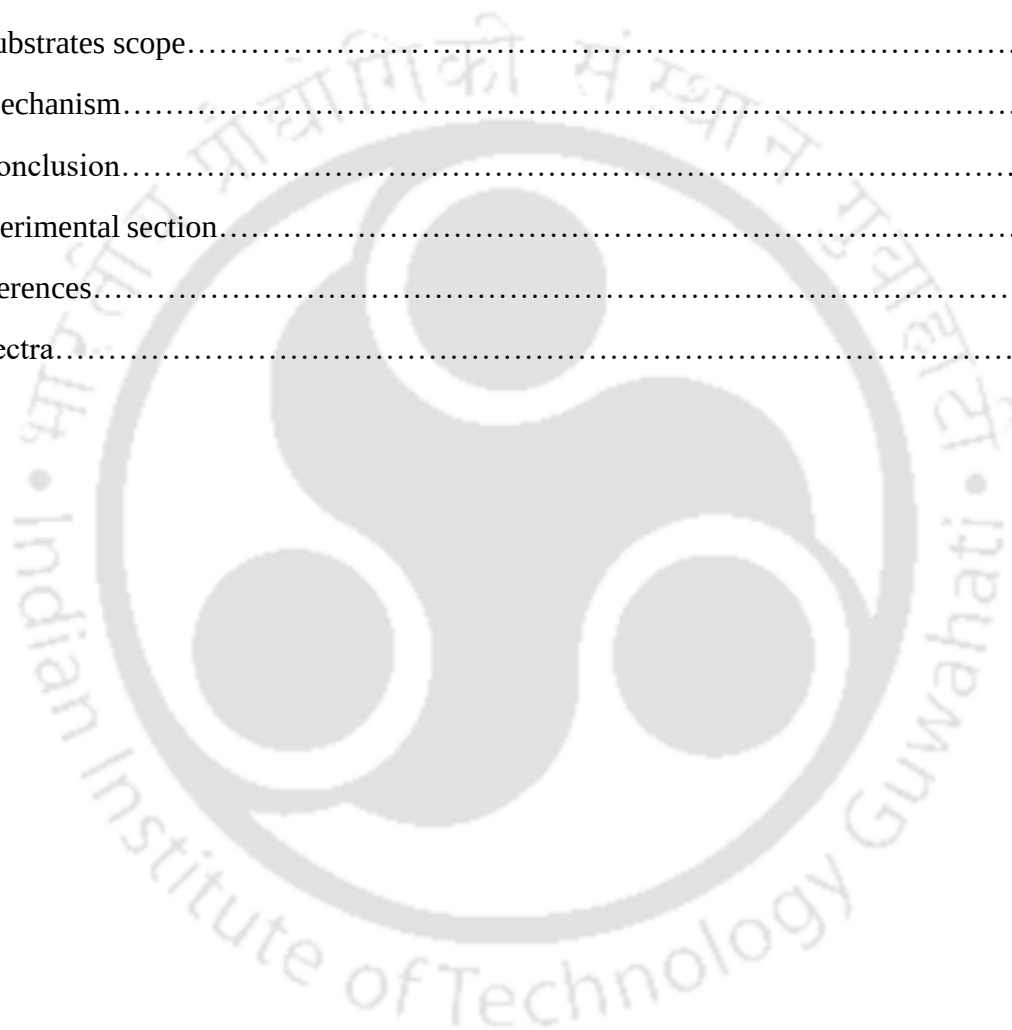
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Abbreviation

AcOH	Acetic acid
ACN	Acetonitrile
Ac	Acetyl
Å	Angstrom
α	Alpha
β	Beta
Ag ₂ O	Silver oxide
BF ₃	Boron trifluoride
BF ₄	Tetrafluoroborate
Bn	Benzyl
Bz	Benzoyl
BCl ₃	Boron trichloride
BSM	Bovine submaxillary mucin
Tf ₂ NH	Bis(trifluoromethane)sulfonimide
cat.	Catalytic/Catalyst
°C	Degree Celsius
CeCl ₃	Cerium(III) chloride
CH ₃	Methyl
CDCl ₃	Deuterated chloroform
C ₆ D ₆	Deuterated benzene
CBr ₄	Tetrabromomethane
Cbz	Carboxybenzyl
DCC	N,N'-Dicyclohexylcarbodiimide
DMAP	4-Dimethylaminopyridine
DNA	Deoxyribonucleic acid
DCM	Dichloromethane
DCE	1,2-Dichloroethane
DMF	N,N'-Dimethylformamide
DTBMP	2,6-Di- <i>tert</i> -butyl-4-methylpyridine
DIPEA	N,N'-Diisopropylethylamine
DFT	Density functional theory
DMSO	Dimethyl sulfoxide
δ	Delta
Et	Ethyl
Eq.	Equation
equiv	Equivalent
Et ₃ SiH	Triethylsilane
Fmoc	Fluorenylmethyloxycarbonyl
g	Gram
Hz	Hertz
h	Hour
HCl	Hydrochloric acid
HBr	Hydrobromic acid
HPLC	High performance liquid chromatography
HRMS	High-resolution mass spectroscopy
IPA	Isopropyl alcohol
KHMDS	Potassium bis(trimethylsilyl)amide
K ₂ CO ₃	Potassium carbonate

LiClO ₄	Lithium perchlorate
LiBr	Lithium bromide
Mm	Millimetre
MeI	Methyl iodide
MHz	Mega Hertz
Ms	Mesyl
min	Minute
Me	Methyl
ml	Millilitre
Mg	Milligram
μl	Microlitre
NOBF ₄	Nitrosyl tetrafluoroborate
NaHCO ₃	Sodium bicarbonate
Na ₂ S ₂ O ₄	Sodium dithionite
NIS	N-Iodosuccinimide
NaI	Sodium iodide
NaH	Sodium hydride
NMR	Nuclear magnetic resonance
nOe	Nuclear Overhauser effect
Nu	Nucleophile
Ph	Phenyl
PPh ₃	Triphenylphosphine
P(OPh) ₃	Triphenylphosphite
PCC	Pyridinium chlorochromate
ppm	Parts per million
RNA	Ribonucleic acid
rt	Room temperature
ROMP	Ring-opening metathesis polymerisation
SnCl ₄	Tin(IV) chloride
Tf	Triflate
Ts	Tosylate
TBAF	Tetra-n-butylammonium fluoride
TBAI	Tetra-n-butylammonium iodide
THF	Tetrahydrofuran
TTBP	2,4,6-Tri- <i>tert</i> -butylpyridine
TMS	Trimethylsilane
TBDPS	<i>tert</i> -Butyldiphenylsilyl
TIPS	Triisopropylsilane
TfOH	Triflic acid
TMSOTf	Trimethyltrifluoromethanesulfonate
TMSBr	Bromotrimethylsilane
TLC	Thin layer chromatography
UV	Ultraviolet
VT	Variable temperature
XRD	X-ray powder diffraction

Abstract

Carbohydrates are one of the essential classes of biomolecules playing crucial roles in agriculture and medicinal chemistry. The high density of stereochemical information and relative rigidity of carbohydrates provide a wonderful stage upon which a number of substitutions can be done to make biologically active target molecules. Carbohydrate scaffolds in bioactive molecules exhibit different roles in physiological events such as cell development, immune system, bacterial and viral infection, etc. The tremendous medicinal potential of glycomolecules has been evoked by worldwide chemists to synthesize these bioactive molecules.

The contents of the thesis entitled “***Development of Glycosyl ortho-[1-(p-MeOPhenyl) Vinyl]Benzoates (PMPVB) as Reactive Glycosyl Donors and Studies Toward the Synthesis of L-Sugars, non-ulosonic acids via Perlin Aldehydes***” have been divided into six chapters based on the experimental works, and results during the complete course of my research period. **Chapter I** of the thesis is entitled the literature review of *n*-Pentenyl glycosides (NPG's) and Perlin aldehyde. **Chapter IIA** deals with glycosyl *ortho*-[1-(*p*-MeOPhenyl)vinyl]benzoates (PMPVB) as easily accessible, stable, and reactive glycosyl donors for *O*-, *S*- and *C*-glycosylation reactions under Brønsted acid catalysis. **Chapter IIB** describes catalytic stereoselective synthesis of 2-deoxy α -glycosides using glycosyl *ortho*-[1-(*p*-MeOPhenyl)vinyl]benzoates (PMPVB) as glycosyl donors. In **Chapter III**, we disclosed regio and stereoselective *C*-glycosylation of indoles using *ortho*-[1-(*p*-MeOPhenyl)vinyl]benzoates (PMPVB) as glycosyl donors under Brønsted acid catalysis. **Chapter IV** focuses on three-step synthesis of protected L-altrose from D-galactose-derived Perlin aldehyde. **Chapter V** contains the synthesis of Aryl-Polyols from Perlin aldehyde.

Chapter I describes the literature survey of the importance of carbohydrates towards natural products, different types of *n*-pentenyl glycosyl (NPGs) donor-based glycosylation towards *C*-*O*, *C*-*S*, *C*-*C*, *C*-*N*, linkages, synthesis of δ -hydroxy α,β -unsaturated aldehyde (generally called Perlin aldehyde), and synthesis of different types of L-sugars.

Chapter IIA describes the synthesis and reactivity of Fraser-Reid type alkene donors (PMPVB) donors, that can be catalytically activated under Brønsted acidic conditions (30 mol % Tf₂NH) as well as NIS/TMSOTf conditions. All types of glycosylation (*O*-, *S*-, *C*-) are occurring in just 5 min at 0 °C, proving the high reactivity of the PMPVB donors. Comparative studies under both Brønsted acidic conditions (HNTf₂) and NIS/TMSOTf conditions with the PVB donor indicate the PMPVB donors are superior in reactivity compared to PVB donors.

Chapter IIB describes 2-deoxy *ortho*-[1-(*p*- MeOPhenyl)Vinyl]Benzoates (PMPVB) donors, Fraser-Reid type alkene donors as benchtop stable and reactive glycosyl donors for a protecting group independent stereoselective synthesis of 2-deoxy- α -glycosides under simple Brønsted acid catalysis which can be activated by using standard NIS/TMSOTf condition also. It was observed that the 2-deoxy PMPVB donors are reacting well with 1.2 equiv. of glycosyl acceptor in the presence of 30 mol % of triflic acid (TfOH) at 0 °C in DCM medium and provided α -selective *O*-glycosides with good to excellent yields.

Chapter III describes a practically useful synthetic protocol for the regio and stereoselective synthesis of indolyl glycosyl derivatives from the stable yet PMPVB glycosides. The

transformation can be achieved utilizing the simple Brønsted acid (Tf_2NH , 30 mol %) catalysis and does not require any metal catalysts or other expensive reagents.

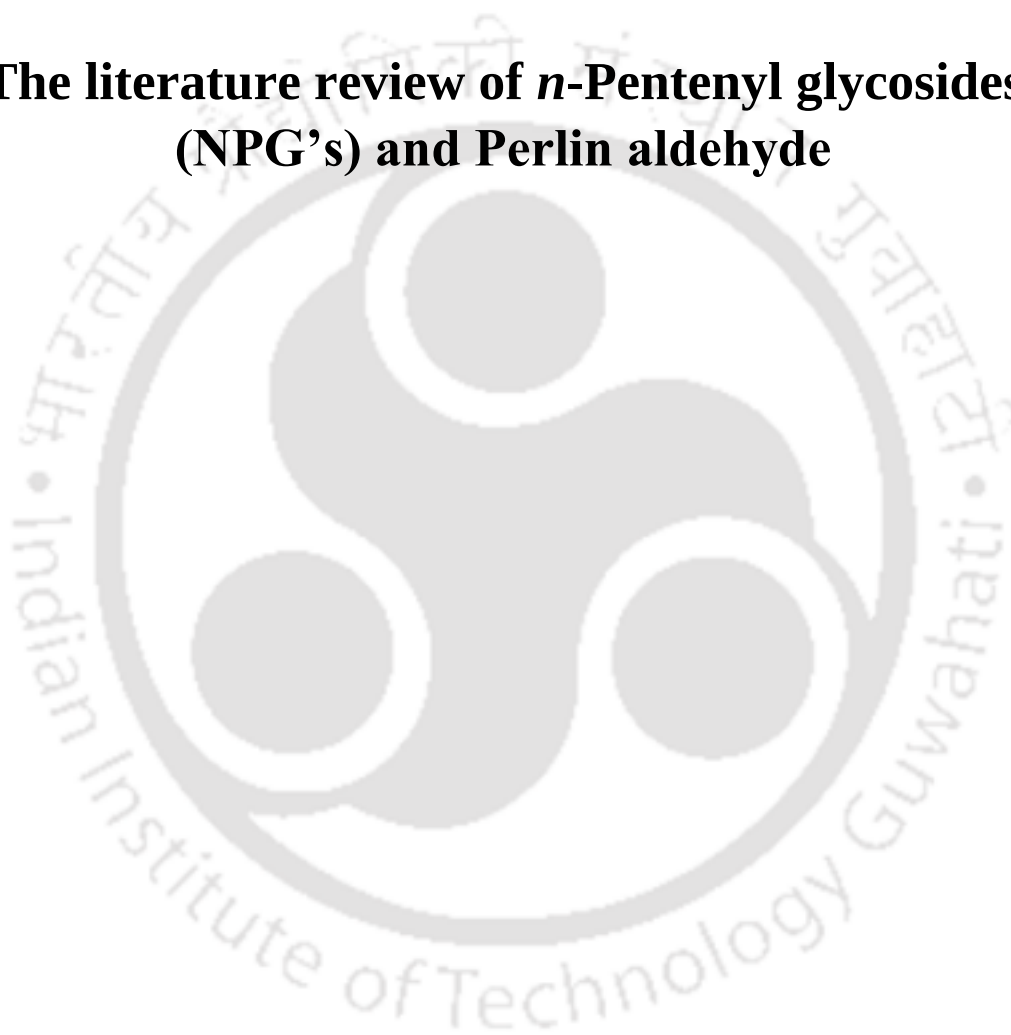
Chapter IV describes a very practical, short, three-step synthesis of protected L-altrose from Perlin aldehydes that are easily accessible from the commercially available galactal via the stereo-inversion of the Perlin aldehyde derived triflate followed by the dihydroxylation.

Chapter V describes the synthetic procedure for the synthesis of β -hydroxy- γ,δ -unsaturated aryl ketones and conjugated $\alpha,\beta,\gamma,\delta$ diene aryl ketones (*E*, *E*) easily. The regiospecific 1,2-addition of silyl enol ethers to saturated and unsaturated Perlin aldehydes has been achieved via the Mukaiyama aldol condition.



Chapter I

The literature review of *n*-Pentenyl glycosides (NPG's) and Perlin aldehyde

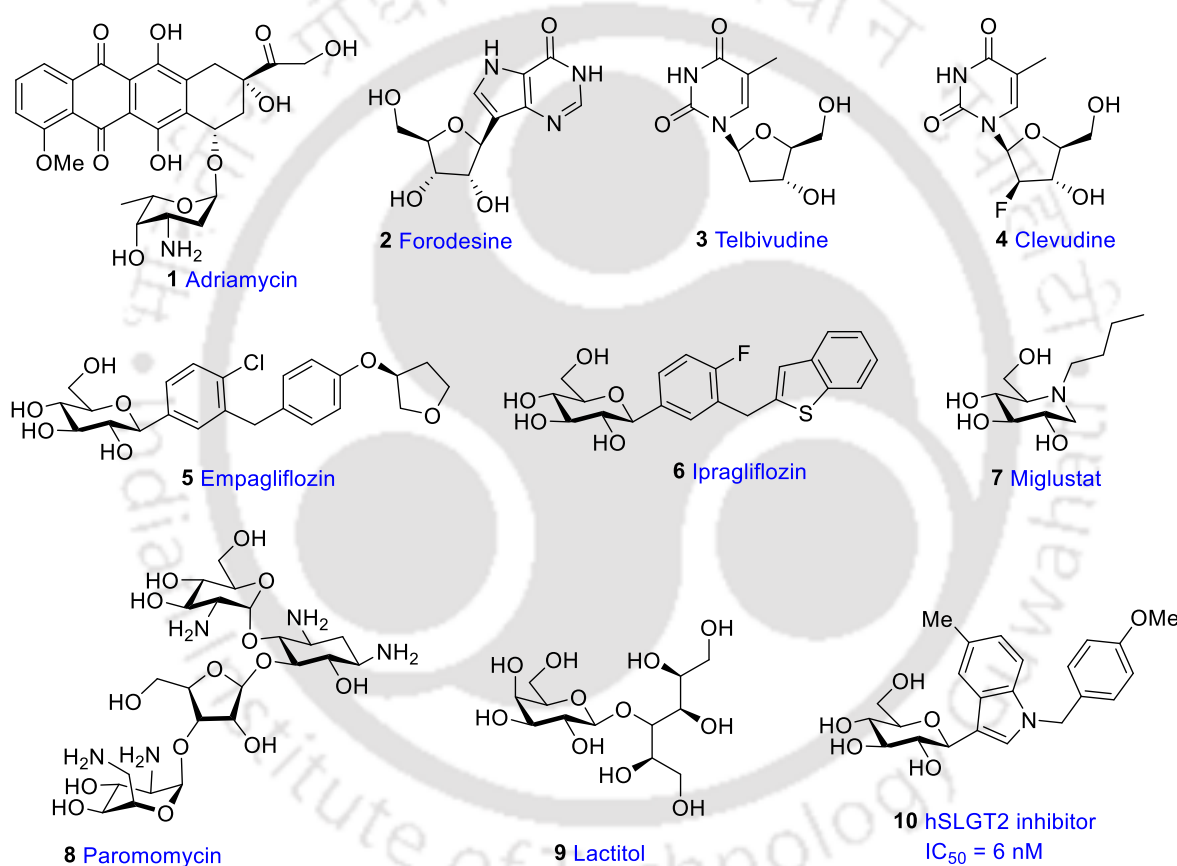




1.1. Introduction

Carbohydrates are essential molecules present in almost all aspects of life, performing different biological processes such as the formation of genetic and energy materials, and assist the structural formation of organisms¹. The biological importance of carbohydrate-based molecules has made chemists provide extra attention to the research area. The naturally occurring carbohydrates and their analogues have been examined as therapeutic agents for the treatment of different diseases². In recent times, many innovative carbohydrate-based drugs have been developed³.

It is reported that most of organisms get energy from D-glucose.⁴ D-Ribose and deoxyribose play a pivotal role in the synthesis of DNA, RNA, and energy-containing fabric, adenosine triphosphate (ATP).⁵

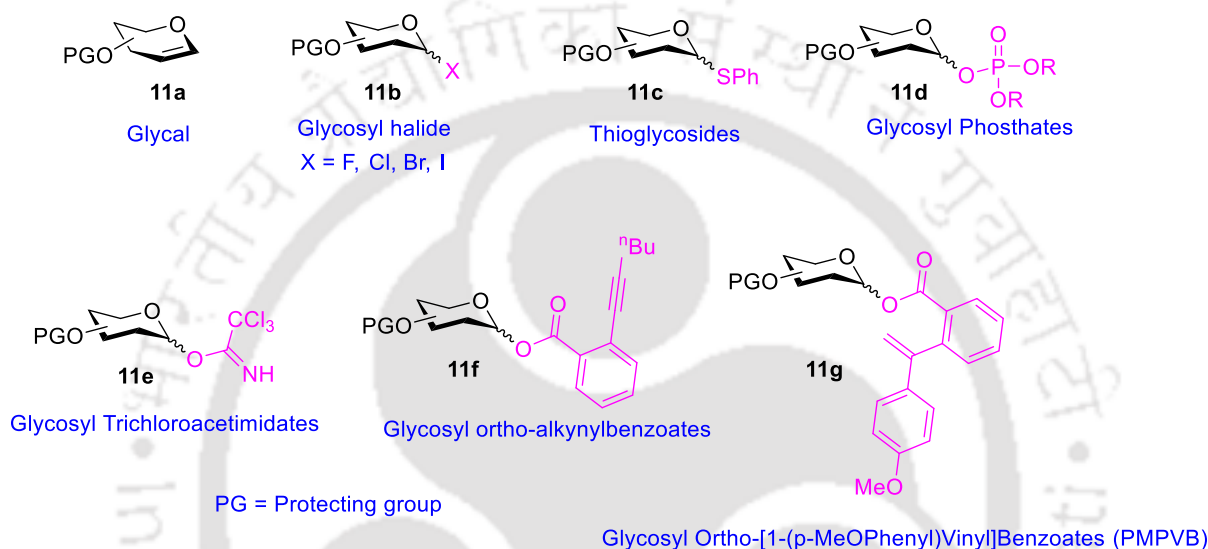


Scheme 1: Carbohydrate-based drug molecules

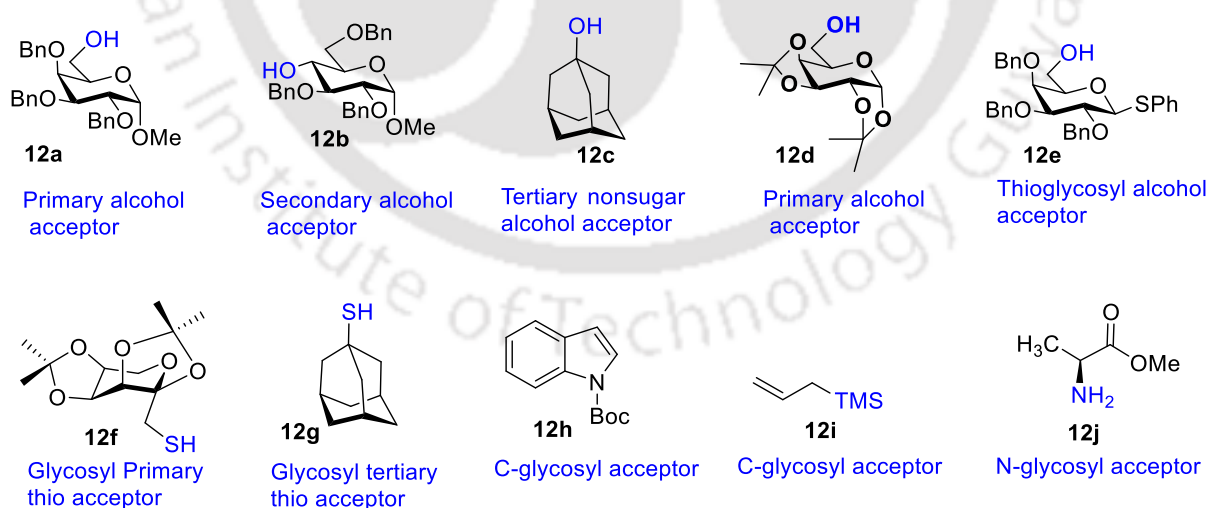
Some of the carbohydrate-based molecules have been discovered in the 1940s as antibiotics, including streptomycin, neomycin, and gentamycin; adriamycin (**1**), and forodesine (**2**) are the most widely prescribed anticancer drugs; for arthritis treatment, polysaccharide hyaluronic acid was prescribed; telbivudine (**3**), clevudine (**4**) was investigated as antiviral drugs; empagliflozin (**5**) and ipragliflozin (**6**) were treated as antidiabetic drugs; miglustat (**7**) is used to treat Gaucher's disease; in 2020, lactitol (**9**) was treated for Chronic idiopathic constipation; Paromomycin (**8**) is used as antiparasitic drugs.² For the treatment of type-2 diabetes, 3-indolyl-C-glycosides can be used as sodium-dependent glucose co-transporter 2 (sGLT2) (**10**) inhibitors.⁶

1.2. Glycosylation

Glycosylation is the attachment of one sugar moiety with other sugar moieties or other aglycons through the glycosidic linkage to form glycoconjugates at an anomeric center. Protein glycosylation is one of the major co-translational modifications (CTMs) and/or post-translational modifications (PTMs) observed, so far. Glycosylation is often a highly complex modification of proteins. It is reported that 70 % of human proteins are glycosylated.⁷ Glycosyl donor (Scheme 2) contains an electrophilic center at the anomeric position (C-1 carbon) to form a glycosidic bond with the glycosyl acceptor (Scheme 3) which has a nucleophilic center. Over the past decades, different types of glycosylations (C-O, C-S, C-N, C-C) have been achieved depending on the electronic nature of glycosyl acceptors.



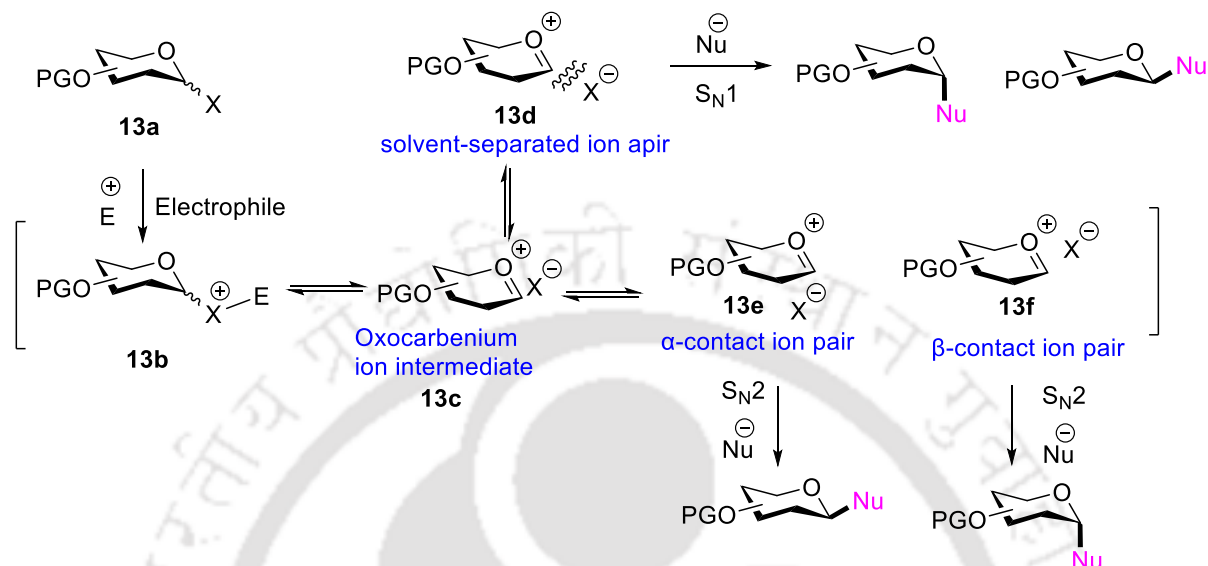
Scheme 2: Commonly used different glycosyl donors



Scheme 3: Commonly used different glycosyl acceptors

The glycosyl donor contains leaving moiety at the anomeric position which is activated in presence of an electrophilic promoter to make intermediate **13b** (Scheme 4). This intermediate **13b** can exist as reactive oxocarbenium ion intermediate **13c** after the liberation of the leaving moiety. Sp² hybridized naked oxocarbenium ion intermediate (**13c**), might exist solvent-

separated ion pairs (**13d**) or contact ion pair (**13e**, **13f**). The nucleophiles (glycosyl acceptors) present in the reaction medium will react at the anomeric position of unstable oxocarbenium ion intermediates to form glycoconjugate through glycosidic linkage (Scheme 4). The solvent-separated ion pair (**13d**) intermediate follow via an S_N1 -like pathway whereas contact ion pair (**13e**, **13f**) intermediates follow S_N2 mechanistic pathways.⁸



Scheme 4: General scheme for glycosylation

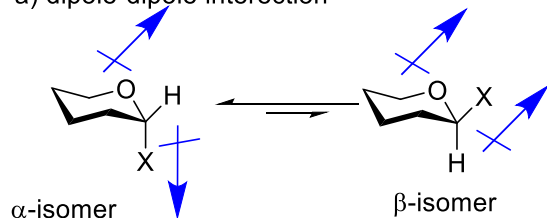
1.2.1. Factors affecting the glycosylation reactions.

a) Anomeric effect

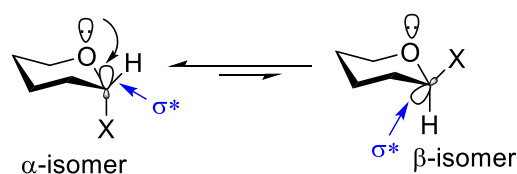
Generally, any electronegative substituent at the 2-position of the tetrahydropyran will preferentially orient itself in axial position. This effect is known as the **anomeric effect**. In 1955, J. T. Edward first observed this effect during studying carbohydrate chemistry. In 1958 **anomeric effect** term was introduced by Raymond Lemieux and that's why it is also familiar as **Edward-Lemieux effect**.⁹ The axial isomer (α -isomer) is more stable than the equatorial isomer (β -isomer) due to the anomeric effect, which can be explained by the following factors.

- dipole-dipole interaction,
- stereoelectronic $n-\sigma^*$ interaction, and
- $n-n$ repulsions coupled with C-H hydrogen bonding.

a) dipole-dipole interaction



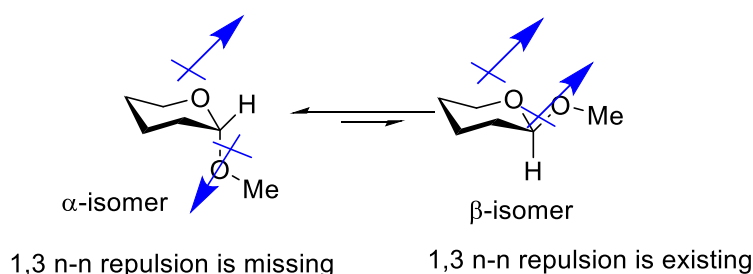
b) lone pair- σ^* of C-X bond overlap



Scheme 5: a) dipole-dipole interaction b) lone pair and σ^* of C-X bond overlap

There are two dipoles in the hereto atom containing pyranose sugar, directing in the same direction for the β -isomer whereas, in the α -isomer, the dipoles oppose each other. Hence, the

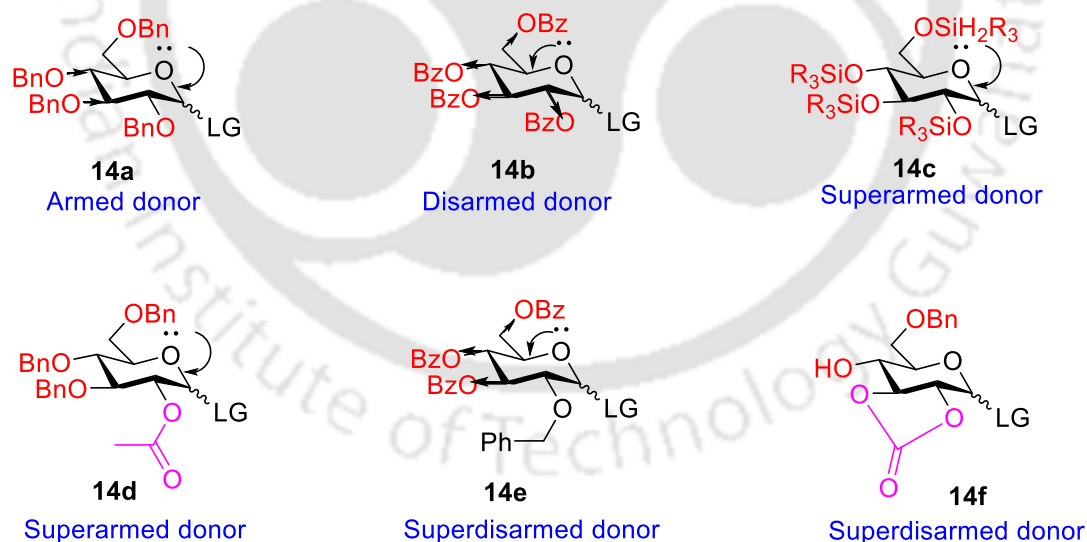
α -isomer is energetically more stable having a less net-dipole moment, compared to the β -isomer (Scheme 5a).



Scheme 6: *n-n* repulsion

The stereoelectronic effect reveals the hyperconjugation between the unshared electron pair of endocyclic ring oxygen and σ^* of the axial (exocyclic) C-X bond in 4C_1 conformation (Scheme 5b). In the case of the β -isomer of 2-methoxy pyran, two lone pairs of electrons are existing in eclipsed form, creating 1,3 *n-n* repulsion, resulting in higher energy whereas this type of repulsion is missing for α -isomer (Scheme 6). The existing *n-n* repulsion, coupled with the favorable hydrogen bonding between axial *H*-5 and lone pairs of electrons of the α -anomeric substituent (C-H/*n* hydrogen bonding), resulting more energy difference between the two isomers.¹⁰

b) Protecting group



Scheme 7: Classification of the glycosyl donors

In 1998 Fraser-Reid and co-workers disclosed the armed/disarmed strategy and how it affects the activation of glycosyl donors towards the glycosylation.¹¹ Conventionally, when the free hydroxyl groups are protected by electron-donating substituents like -OBn, -OMe, -O(*p*-MeBn), results in the stabilization of the in-situ generated oxocarbenium ion, thus increasing the reactivity of the glycosyl donors. Hence, the donors with the electron donating protecting groups are termed **Armed Donors** (Scheme 7, **14a**). Likewise, electron-

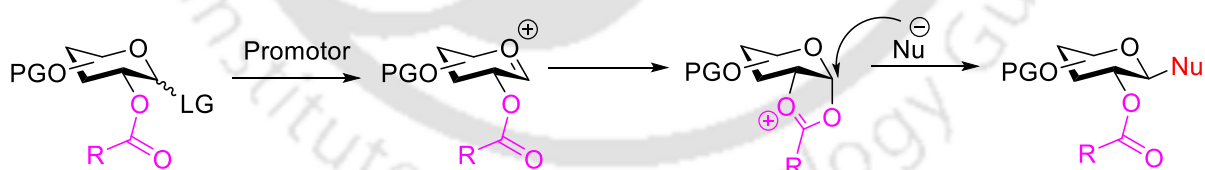
withdrawing protecting groups like -OAc, -OBz, destabilize the oxocarbenium ion intermediate, and thus make the donor less reactive towards glycosylation reactions. This type of protective group containing glycosyl donors are termed **Disarmed Donors** (Scheme 7, **14b**). In addition, there are another two types of familiar donors. The glycosyl donors that are more reactive than armed donors are known as **Superarmed Donors** and the donors that are less reactive relative to disarmed donors are known as **Superdisarmed Donors**.

In 2007, Mikael Bols and co-workers reported that the glycosyl donors having bulky silyl protection on 2, 3, 4 -hydroxyl groups e.g. *tert*-butyldiphenyl silyl (TBDPS), *tert*-butyldimethyl silyl (TBDMS), triisopropyl silyl (TIPS), show superior reactivity compared to perbenzylated armed donors.¹² The superior reactivity containing silyl-protected donors is familiar as **Superarmed Donors** (Scheme 7, **14c**). In 2011, Demchenko and coworkers disclosed the reactivity of the glycosyl donors having different protecting groups with different electronic environments.¹³ The glycosyl donors (Scheme 7, **14e**), having an electron-rich benzyl group at the C-2 position along with electron-deficient benzoyl or acetyl groups at the rest of the positions were found to be less reactive compared to perbenzoylated disarmed donors. These types of donors are familiar as **Superdisarmed Donors**. Boons and coworkers reported¹⁴ that the thio-glycosyl donors having trans-2,3-cyclic carbonate protecting group, both electronically and conformationally deactivate the anomeric center (Scheme 7, **14f**). This donor is also classified as **Superdisarmed Donor**.

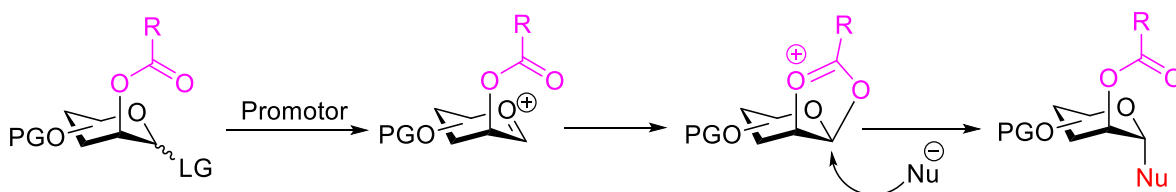
c) Neighbouring Group Participation:

The nucleophilicity of glycosyl acceptor plays a crucial role in getting stereoselective glycosylated products. Common oxygen nucleophiles, such as ethanol result in diastereomeric mixtures of products, regardless of the glycosyl donor whereas weaker nucleophiles, such as trifluoroethanol, resulted in stereoselective products because all nucleophilic substitution reactions undergo via kinetic control mechanism.¹⁵ It is generally conceived that the synthesis of β -isomer is difficult. One of the familiar approaches is to introduce ester (-OAc, -OBz)

a) C-2 group is equatorially oriented



b) C-2 group is axially oriented



Scheme 8: Schematic Presentation of Neighbouring Group Participation

linkage at the C-2 position. The C-2-ester protecting group not only assists the cleavage of the anomeric group but also results in the formation of a glycosyl dioxolenium ion thus stabilizing

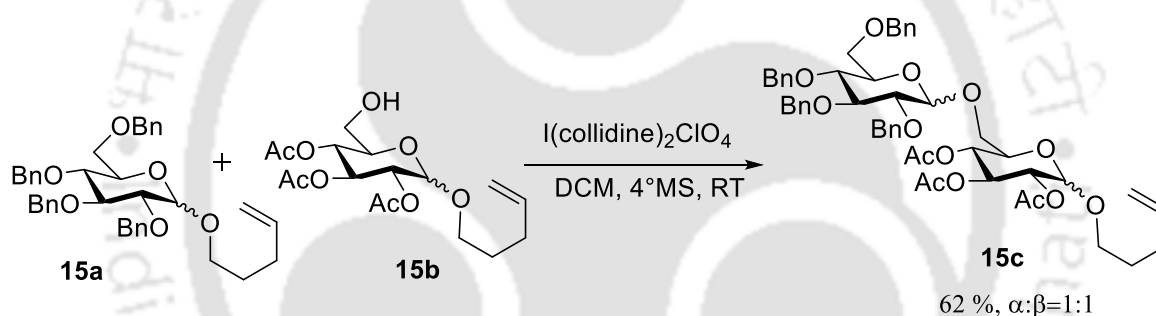
the oxocarbenium ion (Scheme 8a & b). Also, this allows the stereoselective construction of the anomeric bond based on the stereochemistry of the C-2 position.

d) Other Factors

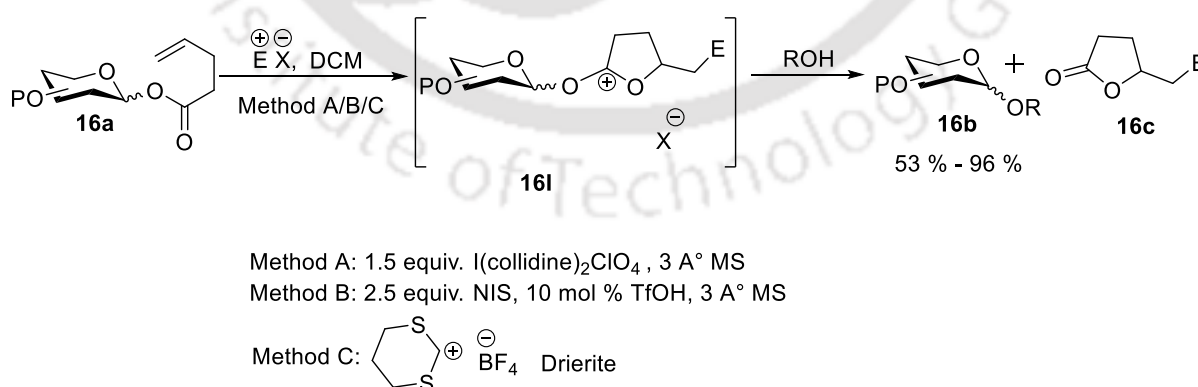
We have discussed the major factors which are controlling the stereochemistry of the newly generated glycosylated products. Other than these factors, reaction conditions e.g., temperature, solvent, dilution, reaction time, and promoters, etc. play a pivotal role, to get stereoselective products following different mechanistic pathways (S_N^1 , S_N^2 , S_N^i , etc.).

1.3 Literature Survey on Glycosylation:

In 1988, Fraser-Reid et.al. introduced *n*-pentenyl glycosides (NPGs), which were prepared from the corresponding sugar hemiacetals by treating with 4-penten-1-ol in presence of camphorsulfonic acid in DCM medium. They activated the *n*-pentenyl glycoside (NPGs) donor (**15a**) by using iodonium dicollidine perchlorate in a stoichiometric amount in DCM medium in the presence of activated 4Å MS and *n*-pentenyl glycoside-based acceptor (**15b**) at room temperature, which resulted in *n*-pentenyl-based disaccharide (**15c**) as a mixture of isomers (62%, $\alpha:\beta = 1:1$) (Scheme 9).¹¹



Scheme 9: Glycosylation of NPGs donor

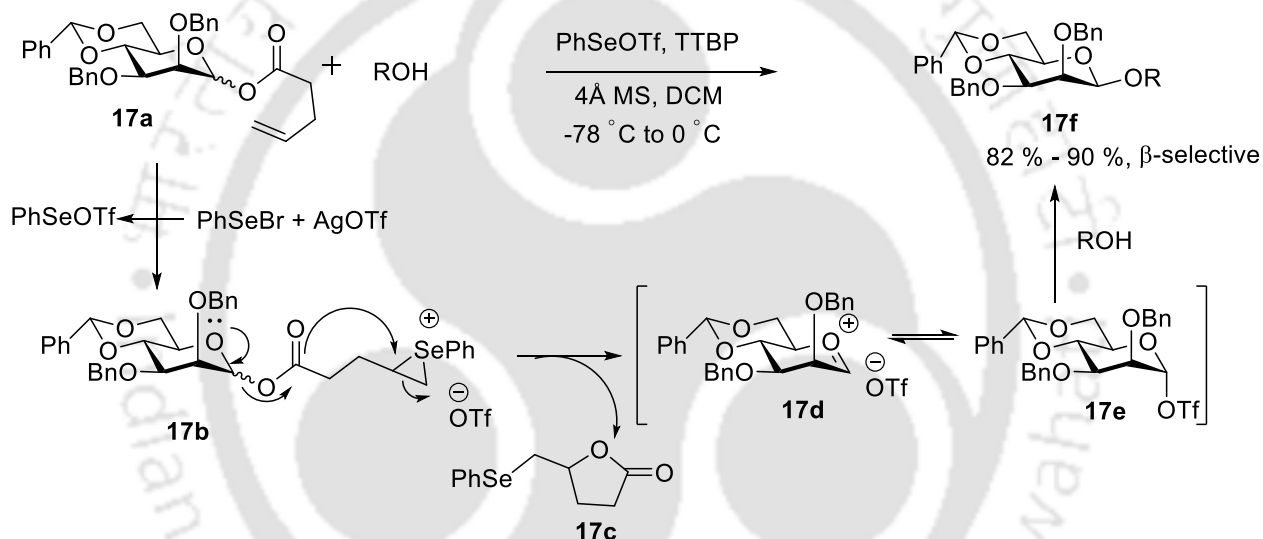


Scheme 10: Glycosylation of NPEs

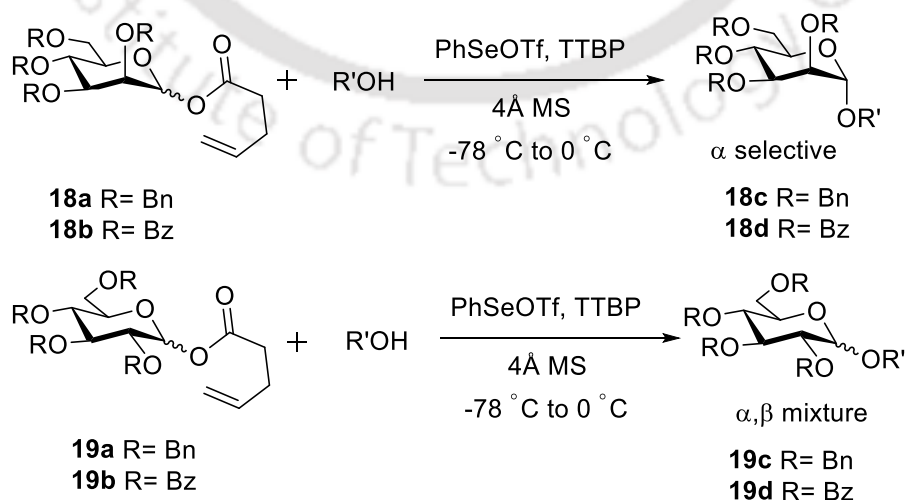
In 1990, Kunz and co-workers reported *n*-pentenyl esters (NPEs) which were prepared from the sugar hemiacetals by treating with 1.4 equiv. of economically cheap 4-pentenoic acid, 1.6 equiv. of 1,3-dicyclohexylcarbodiimide (DCC) and a catalytic amount of 4-dimethylaminopyridine (DMAP) in the DCM medium. This glycosylation reaction proceeds

based on an electrophile-induced lactonization via intermediate **16I**, with the liberation of expected glycosides (**16b**) along with γ -lactones (**16c**) (Scheme 10).¹⁶

In 2006, Kim and co-workers developed an innovative method for the β -mannopyranosylation applying 4,6-*O*-benzylidene mannosyl pentenoate (**17a**) as glycosyl donors and phenylselenenyl triflate (PhSeOTf) as a promoter. The promoter PhSeOTf can be readily generated in situ from commercially available PhSeBr and AgOTf (Scheme 11). The reaction was carried out in presence of 2,4,6-tri-*tert*-butylpyrimidine (TTBP)¹⁷ in DCM medium. This glycosylation proceeds via 3 member-based intermediate **17b** which is transformed to oxocarbenium ion (**17d**), which could be in equilibrium with α -triflate intermediate (**17e**) with the liberation of γ -phenylselenenylmethyl- γ -butyrolactone (**17c**) (Scheme 11). The nucleophilic attack by alcohol via S_N2 fashion of α -triflate intermediate **17e** resulted in β -mannopyranoside (**17f**).¹⁸



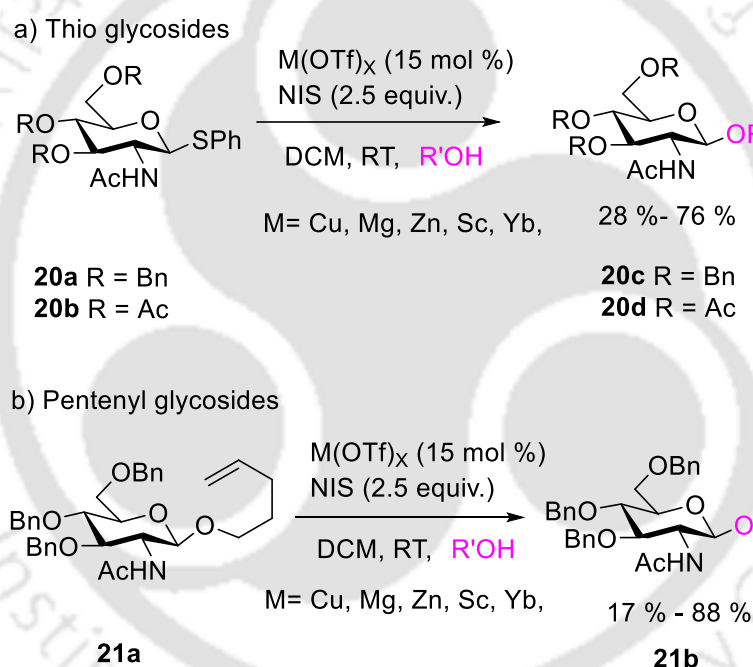
Scheme 11: Phenylselenenyl triflate promoted glycosylation



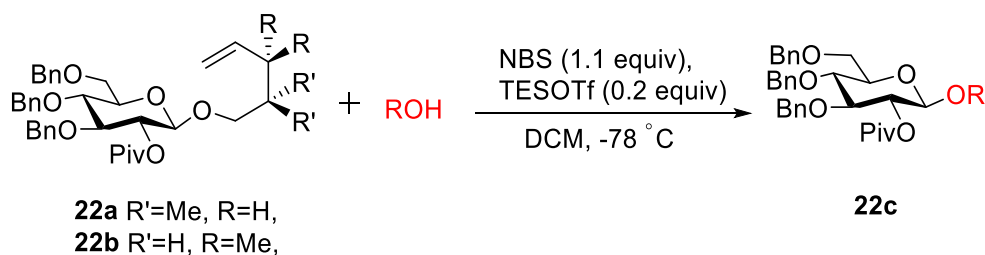
Scheme 12: Phenylselenenyl triflate promoted glycosylation

The same group later disclosed, PhSeOTf promoted glycosylations of mannosyl pentenoates and glucosyl pentenoates as a glycosyl *n*-pentenyl ester (NPEs) donors, devoid of the benzylidene protection, affording the corresponding glycoconjugates in high yields. The mannosyl donor provided completely α selective whereas the glucosyl donor resulted in a mixture of isomers (Scheme 12).¹⁹

Jensen et al. have developed the glycosylation of *N*-acetyl glucosamine utilizing *N*-iodosuccinimide (NIS) and metal triflates as activators in a DCM medium (Scheme 13).²⁰ They have used pentenyl glycosides and thioglycosides of *N*-acetylglucosamine (GlcNAc) as glycosyl donors for the preparation of *O*-glycosides of GlcNAc. In this method, they have investigated several rare earth metal triflates, to activate the donors in the presence of NIS. Both the donors resulted in good yields with both of the glycosyl acceptors 1-octanol as well as (-) menthol but pentenyl glycoside was superior in terms of yields. Both the donors resulted in poor to moderate yields during reaction with sugar acceptors.



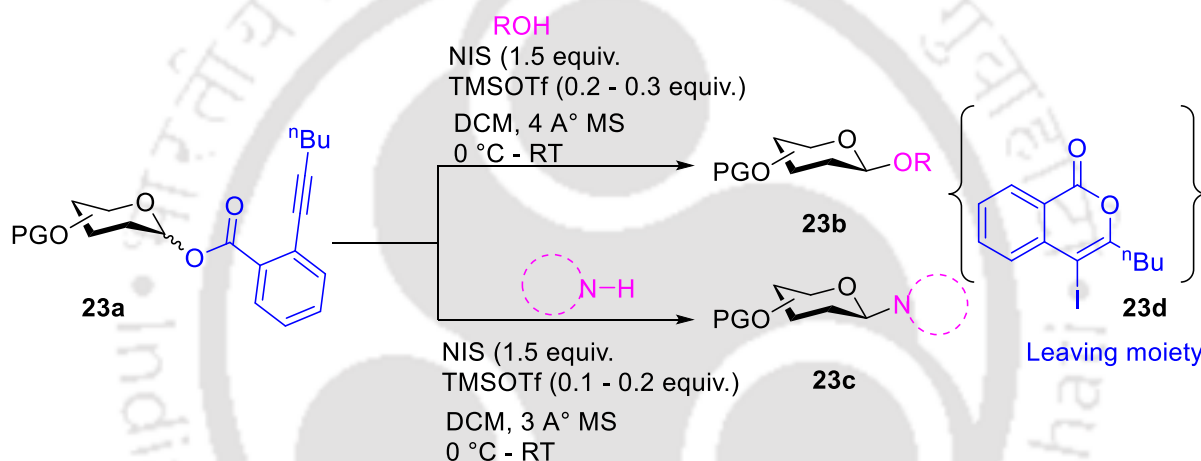
Scheme 13: Metal triflates mediated glycosylation



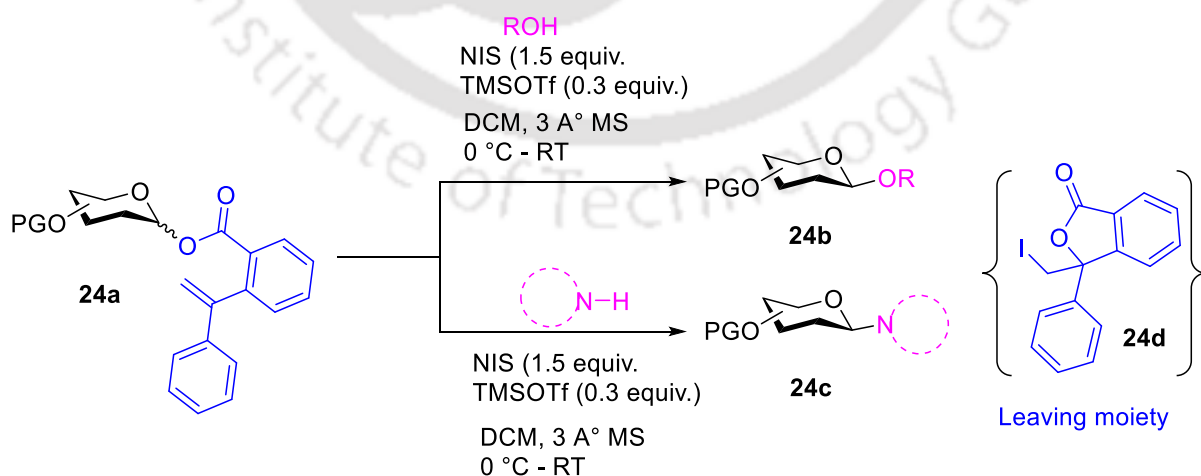
Scheme 14: Glycosylation of *gem*-Dimethyl 4-Pentenyl Glycosides.

Andrade and co-workers, developed,²¹ rigid and more reactive novel gem-dimethyl analogues of Fraser-Reid's 4-*n*-pentenyl glycosyl (NPGs) donors which can be prepared from 2,2-dimethyl-4-pentenol and 3,3-dimethyl-4-pentenol through DCC coupling with sugar hemiacetals. They have utilized NBS in a stoichiometric amount in the presence of TESOTf to activate the donor for glycosylation. The increased reactivity has been attributed to the gem-dimethyl effect (Scheme 14).

Yang and co-workers reported²² NIS/TMSOTf promoted *O*- and *N*-glycosylation to make *O*-glycosides (**23b**) and nucleosides (**23c**) by using glycosyl *ortho*-hexynylbenzoates (**23a**) as glycosyl donors (Scheme 15). They have done a comparative study with thio-glycoside to show the superior reactivity of glycosyl *ortho*-hexynylbenzoate. Taking this advantage, one-pot trisaccharide synthesis has been done. In this report, they also reported the stepwise synthesis of tetrasaccharides.



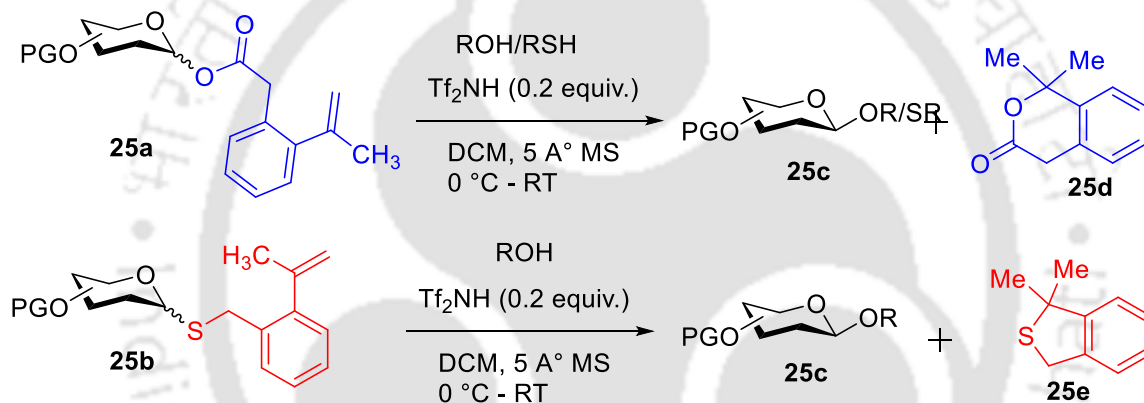
Scheme 15: Glycosylation of glycosyl *ortho*-hexynylbenzoate donors



Scheme 16: Glycosylation of glycosyl PVB donors

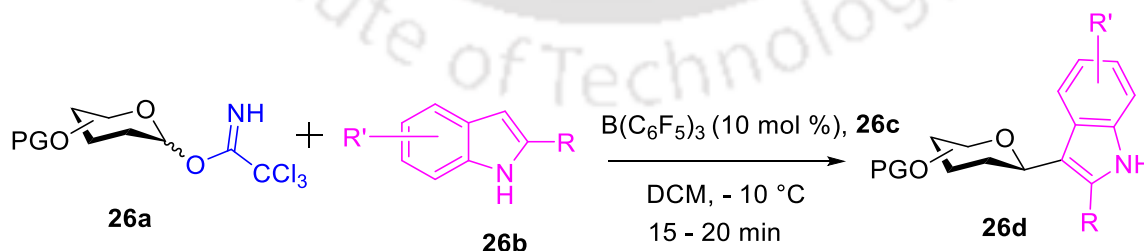
In 2020, Xiao, and co-workers developed²³ the synthesis of *O*-glycosides (**24b**) and nucleosides (**24c**) by using *ortho*-(1-phenylvinyl)benzoates (PVB) (**24a**) as a glycosyl donor and NIS/TMSOTf as a promoter (Scheme 16). They compared the reactivity of PVB donors with the thio glycosides as well as with simple Fraser Reid's *n*-pentenyl glycosides to show the superior reactivity of PVB donors. Utilizing these advantages, they have made some trisaccharides as well as tetrasaccharides applying a one-pot strategy.

In 2022, Li and co-workers, reported,²⁴ Brønsted acid (Tf₂NH)-Catalyzed glycosylation of *n*-pentenyl *O*-glycosides as well as thio-glycosides. The treatment of glycosyl *ortho*-isopropenylphenylacetates (GIPPAs) (**25a**) and *ortho*-isopropenylbenzyl thioglycosides (**25b**) with triflimide (Tf₂NH) in the presence of nucleophile, resulted in corresponding glycosides with the liberation of benzo-fused leaving moiety **25d** and **25e** respectively. This protocol has explored not only *O*-glycosides but also *S*- and *C*-glycosides synthesis. They have reported the different reactivity of the α -anomers as well as the β -anomers of GIPPAs towards glycosylation.



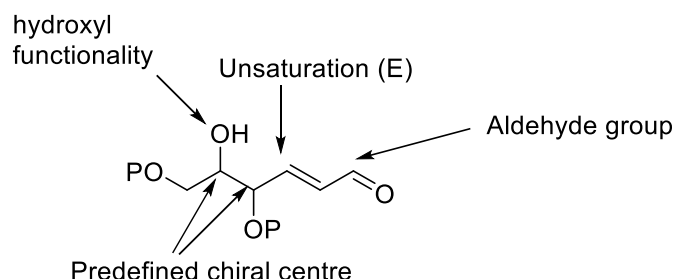
Scheme 17: Glycosylation of GIPPAs and *ortho*-isopropenylbenzyl thioglycosides donors

For the synthesis of *C*-glycosylation, a recent organo-catalyzed method developed by Mandal and co-workers utilizes tris(pentafluorophenyl) borane (B(C₆F₅)₃) (**26c**), an expensive catalyst to synthesize stereoselective (β -selective) 3-indolyl *C*-glycosides (**26d**) from the relatively unstable glycosyl trichloroacetimidate donors (**26a**) (Scheme 18).²⁵

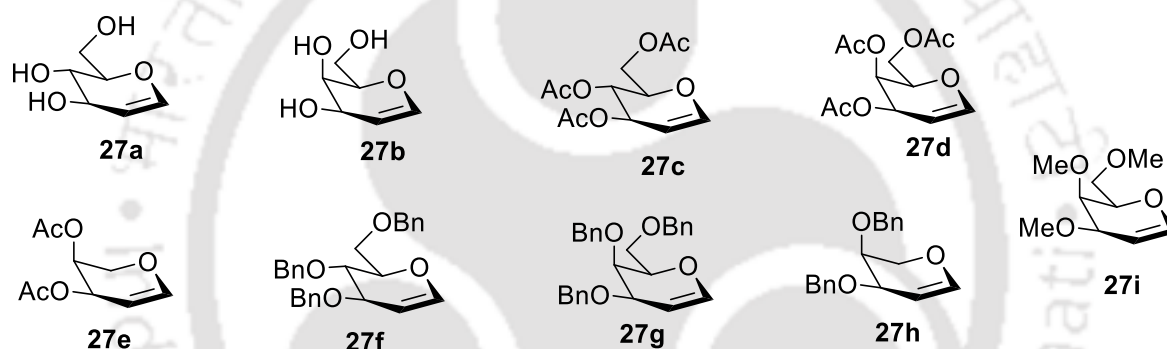


Scheme 18: Stereoselective *C*-glycosylation

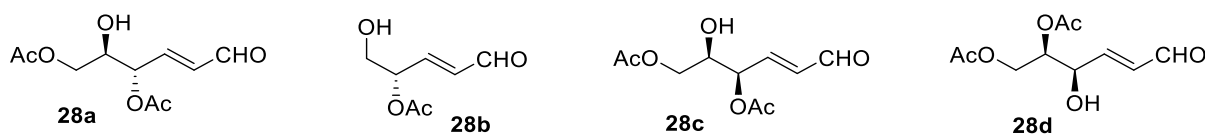
1.4 Synthesis of Perlin aldehyde

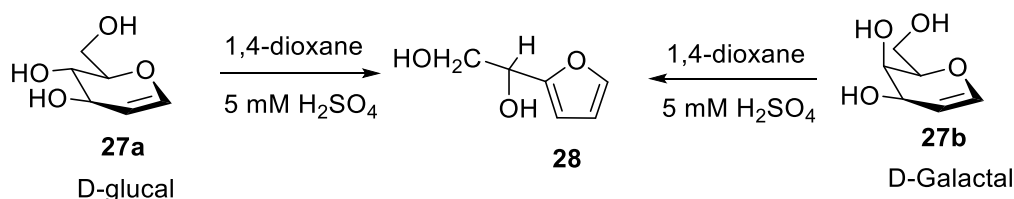
**Figure 1:** Perlin aldehyde

In 1975 A.S. Perlin first synthesized δ -hydroxy α,β -unsaturated aldehyde (generally called Perlin aldehyde) (figure 1) from commercially available glycals.²⁶ Due to the presence of (a) a high degree of functionality (free hydroxyl group, unsaturation (E) and aldehyde group (b) two predefined chiral centers (c) optically pure, the Perlin aldehyde, has been explored towards the synthesis of various natural products. Because of its high synthetic utility, the synthesis of Perlin aldehyde is highly desirable in carbohydrate chemistry. Over the last decades, so many synthetic procedures have been developed.²⁷

**Scheme 19:** Commonly used different glycals**a) Mercurial approach**

In 1975, A.S. Perlin reported, catalytic amount of mercuric sulfate mediated approach to synthesize Perlin aldehyde. In presence of 0.02 equiv. of mercuric sulfate in 1,4-dioxane and 5 mM sulfuric acid solvent system, acetylated glucal (**27c**) and arabinol (**27e**) were converted into their corresponding δ -hydroxy α,β -unsaturated aldehydes (**28a** & **28b** respectively, Scheme 20) in quantitative yields at room temperature whereas tri-acetylated galactal (**27d**) resulted in a mixture of 4,6- and 5,6-diacetates (**28c** & **28d** respectively). They have also disclosed that the unprotected free D-galactal (**27b**) and D-glucal (**27a**) in a similar fashion, resulted in 2-substituted furan (**28**) as the sole product (Scheme 21).²⁶

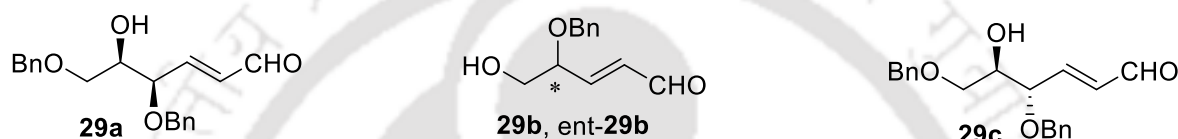
**Scheme 20:** Different Perlin aldehydes



Scheme 21: Synthesis of 2-substituted furan

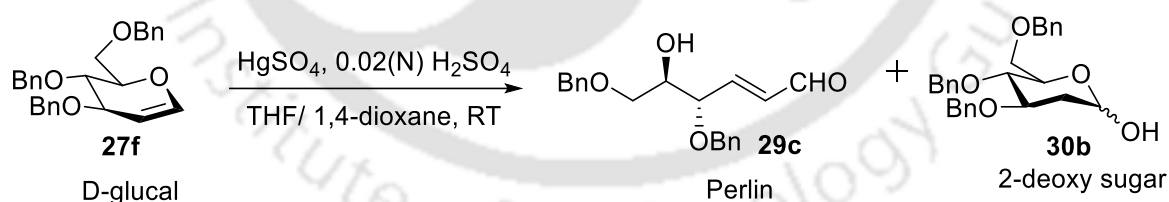
In 1991, Hirata et al. disclosed the another mercuric approach taking 10 mM sulfuric acid and catalytic amount of mercuric acid in THF, tribenzylated D-galactal (**27g**) resulted in corresponding δ -hydroxy α,β -unsaturated aldehydes (**29a**) in quantitative yield (Scheme 22) within 1h.²⁸

Tolstikov et al. described the synthesis of (E)-(4S)-4-benzyloxy-5-hydroxy-2-pentalenal **29b** and its enantiomer ent-**29b** (Scheme 22) in dioxane medium taking 5 mM H₂SO₄ and



Scheme 22: Structure of various Perlin aldehydes

catalytic amount of HgSO₄ from O-benzylated D- and L-arabinal at room temperature over 24 h.²⁹ In 1994 Lellouche and Quinton revealed the exclusive formation of glucose-derived Perlin aldehyde (**29c**, Scheme 22) from tri-benzylated D-glucal (**27f**) in dioxane medium by utilizing a catalytic amount of mercuric sulfate and 0.25 (M) aqueous sulfuric acid at room temperature in 68 h.³⁰

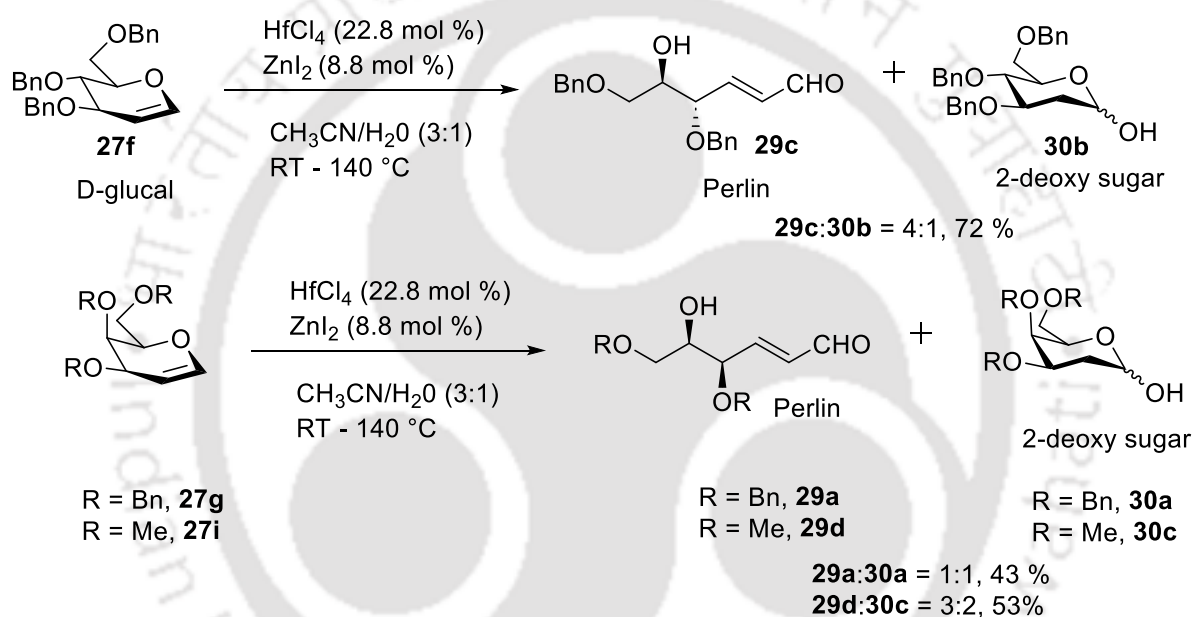
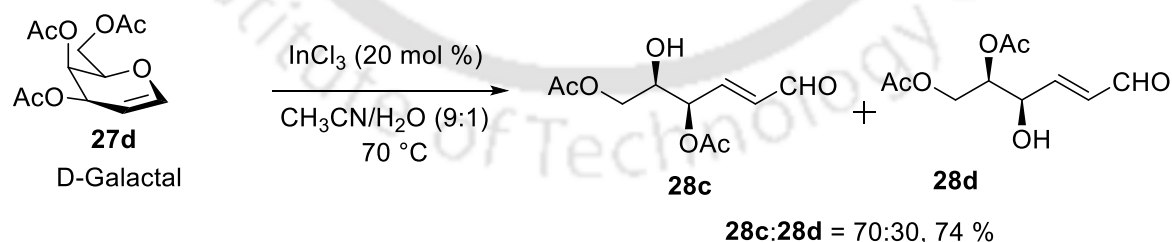


Scheme 23: Synthesis of Perlin aldehyde

Sathe et al. reported the solvent-dependent formation of Perlin aldehyde (**29c**) along with 2-deoxy sugar hemiacetal (**30b**) from benzyl-protected glucal (Scheme 23). They reported that in presence of a catalytic amount of mercuric sulfate and 10 mM H₂SO₄, benzyl-protected glucal (**27f**) in the 1,4-dioxane medium in refluxing conditions afforded 48 % of δ -hydroxy α,β -unsaturated aldehydes (**29c**) along with 24 % of 2-deoxy sugar hemiacetal (**30b**). Similarly, when they repeated the same reaction in the THF solvent system instead of 1,4-dioxane, they got 52 % 2-deoxy sugar hemiacetal (**30b**) as a major product and Perlin aldehyde (**29c**) as a minor product (24 %). On the contrary, in both THF or 1,4-dioxane solvent systems, benzyl-protected arabinal resulted in only α,β -unsaturated aldehyde exclusively in similar conditions.³¹

b) Nonmercurial approach

Due to the toxicity of Hg^{2+} , the pharmaceutical industry does not recommend the mercurial approach for the synthesis of Perlin aldehyde. So, the nonmercurial approach is highly desirable. Saquib et al. developed an alternative method to obtain Perlin aldehydes from protected glycals utilizing a combination of HfCl_4 and ZnI_2 . They have reported in presence of HfCl_4 and ZnI_2 , benzylated glucal (**27f**) resulted in Perlin aldehyde (**29c**) along with its 2-deoxy product (**30b**) in a 4:1 ratio, whereas benzylated and methylated galactal afforded a mixture of corresponding Perlin aldehyde and 2-deoxy product in 1:1 and 3:2 ratios, respectively (Scheme 24).³² Another nonmercurial approach have been developed by Ramesh and co-workers in $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ solvent system by utilizing InCl_3 as a catalyst, for the synthesis of Perlin aldehyde from different protected glycals (Scheme 25).³³

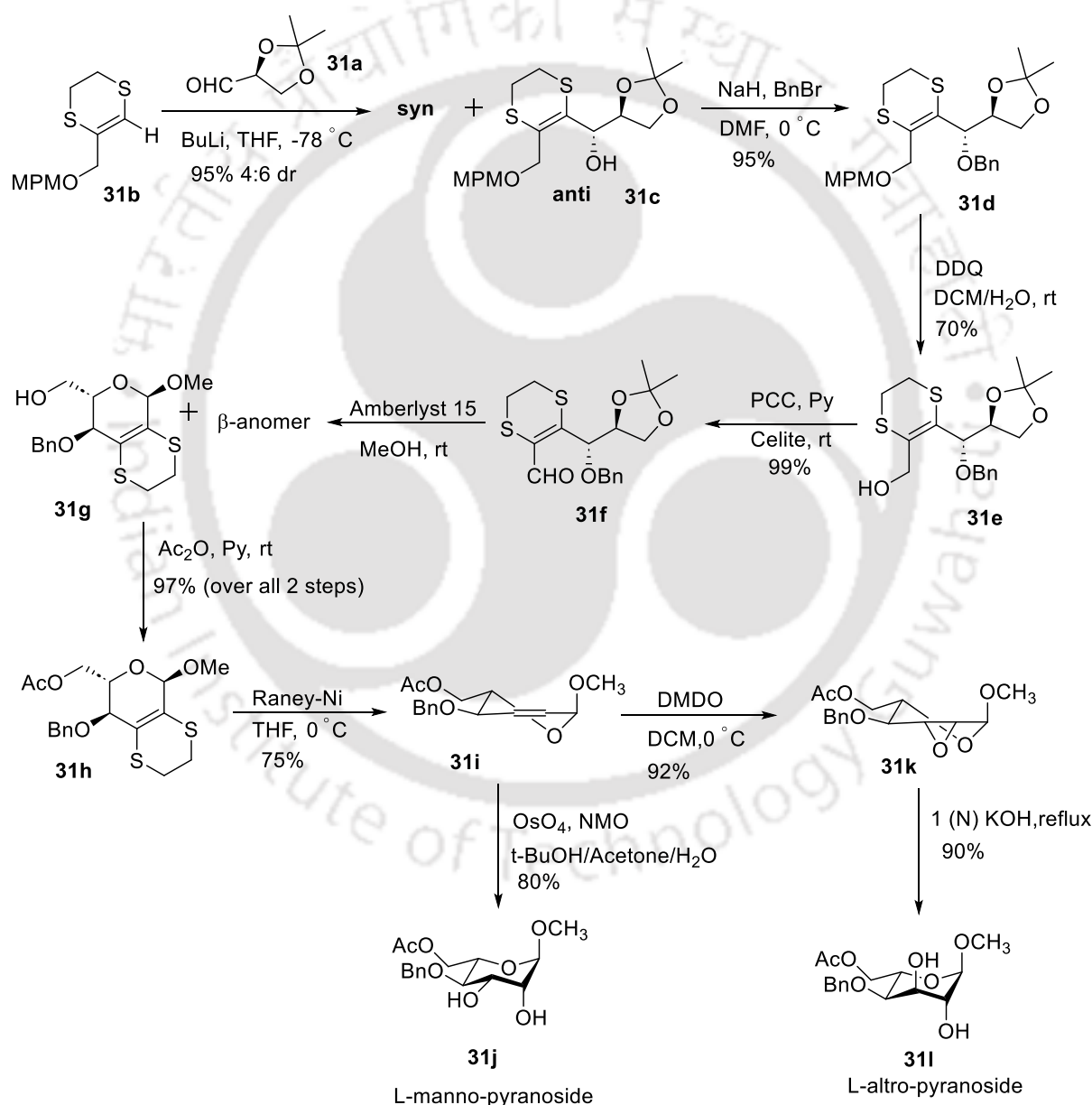
Scheme 24: HfCl_4 and ZnI_2 mediated hydrolysis of glycalsScheme 25: Hydrolysis of galactal utilizing InCl_3

1.5 Literature Survey on L-sugar:

L-Sugar,³⁴ an enantiomer of D-sugar is biologically important, playing a crucial role in nature. L-sugars are less common in nature compared to their enantiomer D-sugar, quite difficult to get from natural sources.³⁵ Some of the rare L-sugars have been discovered in many

clinically important bioactive oligosaccharides like heparin³⁶, antibiotics³⁷, glycopeptides, terpene glycosides, etc. Some of the bioactive natural products³⁸ have been synthesized from L-sugars, which are a natural chiral pool. Some of the L-sugars are commercially available, which are hugely expensive. For example, the cost of L-altrose, a constituent of the extracellular polysaccharides from *Butyrivibrio fibrisolvens* strain CF3³⁹ is \$11550 for 10 g. The research on the interconversion of the commercially available, cheap D-sugars to L-sugars has gained extra attention in carbohydrate chemistry.

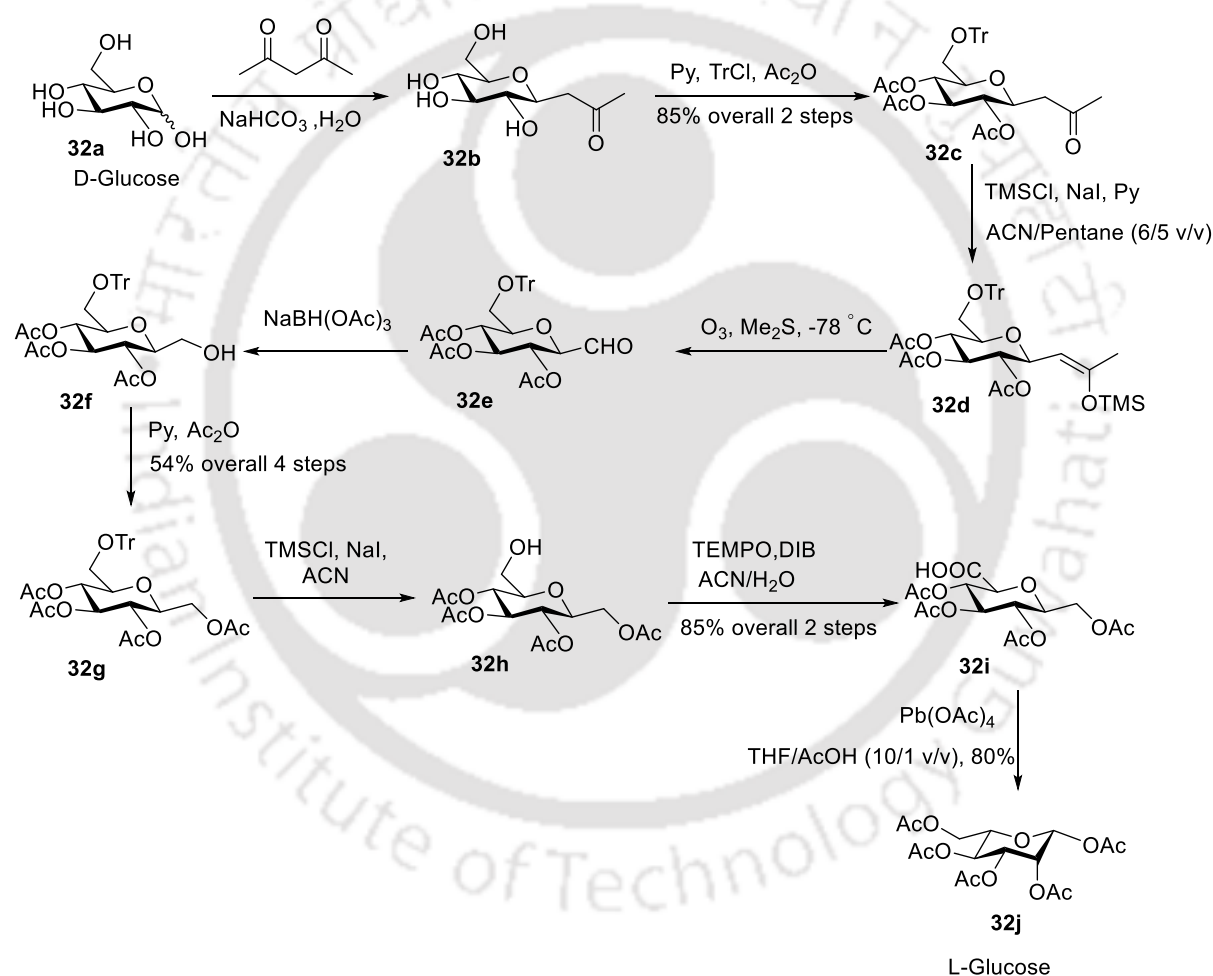
In 2006, Guaragna et al. reported³⁵ the synthesis of L-Mannose and L-Altrose, starting from 2,3-O-isopropylidene-L-glyceraldehyde (**31a**) and heterocyclic system (**31b**) (Scheme 26),



Scheme 26: Synthesis of L-Mannose and L-altrose

which can be prepared from commercially available methyl pyruvate after four steps. They started the coupling reaction between **31a** and **31b**, which resulted in a diastereomeric mixture

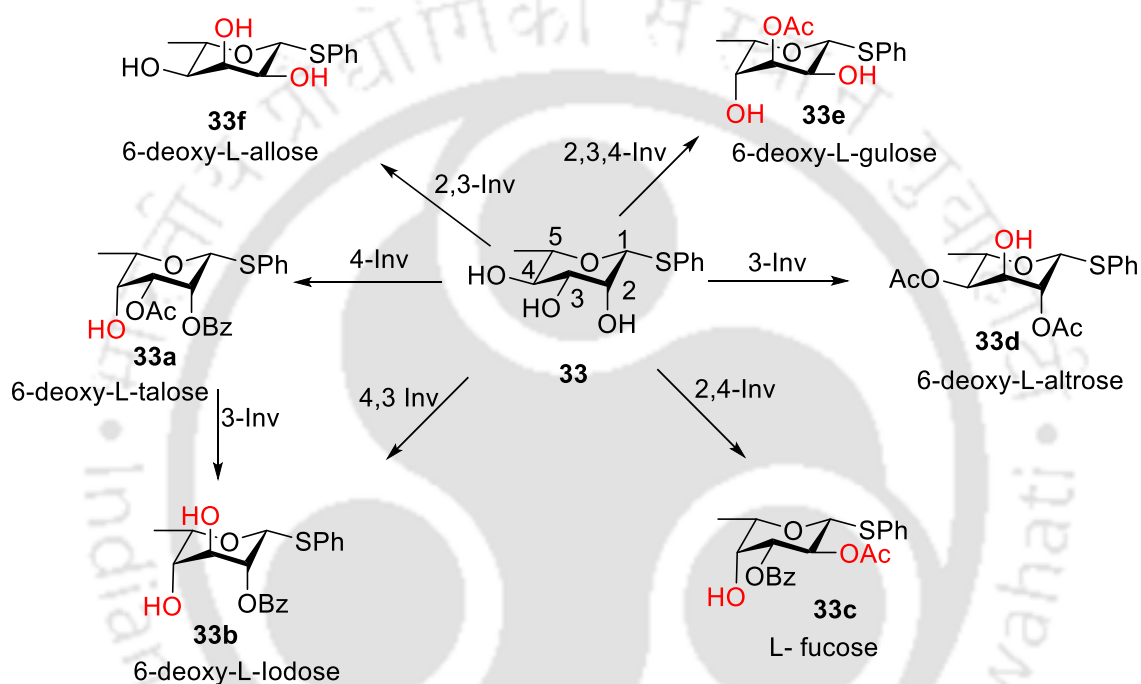
of secondary alcohol (**31c**). After successful separation through flash chromatography, the anti-diastereomer (**31c-anti**) has been decided as a model substrate for the entire synthetic pathway. Benzylation of the compound **31c-anti** with NaH & BnBr, afforded **31d** which was converted to hydroxyl compound **31e** by using DDQ in a DCM/H₂O medium. The compound **31e** was converted to aldehyde **31f** by utilizing the oxidizing agent PCC. Treatment of **31f** in presence of Amberlyst-15 in methanol resulted in a diastereomeric mixture of unstable bicyclic compound **31g** and its β -anomer. After acetylation of **31g**, the resulted isomeric mixture (**31h**) was separated by the recrystallization technique. Treatment of α -isomer of **31h** with Raney Ni in THF and consecutively desulfurization, resulted in pyranosyl derivative **31i**. The dihydroxylation of **31i** by using OsO₄/ NMO, resulted L-Manno-pyranoside (**31j**). To get other L-Sugar, they treated **31i** with DMDO, which resulted in anti-epoxide **31k**. After the base-catalyzed hydrolysis of **31k**, L-Altrose (**31l**) was prepared (Scheme 26).



Scheme 27: Synthesis of L-Glucose from D- Glucose

In 2014, Zhong-Jun Li et.al. reported the synthetic route to L-glucose⁴⁰ (**32j**) from D-glucose (**32a**) applying the strategy of head-to-tail inversion. The strategy was achieved by first incorporation of silyl enol ether at C-1 position (**32d**). Then they have conducted oxidation followed by reduction of the silyl enol ether at C-1 to afford (**32f**). Finally, oxidation of C-5 hydroxyl group followed by lead (IV) tetraacetate mediated oxidative decarboxylation of C-5, L-glucose (**32j**) have been achieved (Scheme 27).

Recently, Kulkarni et al. reported⁴¹ the synthesis of different 6-deoxy-L-hexoses from inexpensive L-rhamnose via nucleophilic attack on triflates intermediates in regio and stereoselective fashion (Scheme 28). They have synthesized 6-deoxy-L-talose (**33a**), 6-deoxy-L-idose (**33b**), L-fucose (**33c**), 6-deoxy-L-altrose (**33d**), 6-deoxy-L-gulose (**33e**), and 6-deoxy-L-allose (**33f**) thioglycosides via stereoselective displacements of L-thiorhamnosyl triflates. Regioselectively 2,3- *di-O*-benzoylated L-rhamnoside was treated with $\text{ Tf}_2\text{O}$ to make a C-4 triflate derivative which was subsequently treated with water resulted in 6-deoxy L-talose (**33a**). 6-deoxy L-iodose is structurally different from L-rhamnose at C-3 and C-4 stereochemistry. First, they made a C-4 inverted 6-deoxy L-talose derivative, and protect the C-3 position by $\text{ Tf}_2\text{O}$. Subsequent treatment of C-3 triflate derivative with TBANO_2 resulted



Scheme 28: Synthesis of L-hexoses from L-rhamnose

in 6-deoxy L-iodose (**33b**). The difference between L-Fucose from L-rhamnose is the stereochemistry at both C-2 and C-4 positions. They first made mono-benzoylated (C-3) L-rhamnose by using the reported procedure and protected the both C-2 and C-4 hydroxyl group with $\text{ Tf}_2\text{O}$ and treated with TBANO_2 in acetonitrile medium, resulting in L-fucose. To get the particular L-fucose derivative (**33c**), the C-2 hydroxyl group was protected by AcCl . To get the L-altrose derivative, they inverted the C-3 hydroxyl group of L-rhamnose. The C-3 hydroxyl group was first protected by $\text{ Tf}_2\text{O}$, followed by $\text{ Ac}_2\text{O}$ in one-pot to make an acetylated C-3 triflate derivative. The 3-*O*-triflyl-2,4-acetyl-L-rhamnoside was reacted with TBANO_2 in ACN medium at 80°C , resulting in 6-deoxy L-altroside (**33d**). The C-2, C-3, and C-4 positions of L-rhamnose were inverted to get 6-deoxy-L-guloside (**33e**). To achieve this, they first made 2-hydroxy-3,4-epoxy alcohol derivative by utilizing the cascade inversion protocol introduced by Ramström and co-workers.⁴² The treatment with Sc(OTf)_2 in acetic acid, resulted in 6-deoxy-L-gulose derivative (**33e**). To obtain the rare sugar 6-deoxy-L-allose (**33f**), C-2 and C-3 epimerization of L-rhamnose is required. They first made 4-benzoyl-2,3-dihydroxy L-

rhamnose derivative by the reported procedure.⁴³ The 2,3-hydroxyl groups were treated with Tf₂O to make 2,3-bistriflate intermediate which were subjected to inversion by using TBANO₂, provided 6-deoxy-L-alloside (**33f**) (Scheme 28).

1.6 Conclusion

As a summary of chapter I, the importance of carbohydrates towards natural products, biomolecules, and drug chemistry have been discussed. Types of glycosylations, different types of glycosyl donors, acceptors, and factors that affect the glycosylation have been discussed. Different types of *n*-pentenyl glycosyl (NPGs) donor-based glycosylation towards C-O, C-S, C-C, C-N, linkage have been discussed. The synthesis of δ -hydroxy α,β -unsaturated aldehyde (generally called Perlin aldehyde), and different types of L-sugars synthesis have been provided.

The upcoming chapters contain the exploration of Glycosyl *Ortho*-[1-(*p*-MeOPhenyl)Vinyl]Benzoates (PMPVB), Fraser-Reid's *n*-pentenyl glycoside (NPGs) type alkene donor towards the formation of stereo & regio-selective C-O, C-S, C-C glycoside linkages. Different types of polyols and L-sugars synthesis from Perlin aldehyde are discussed in detail.

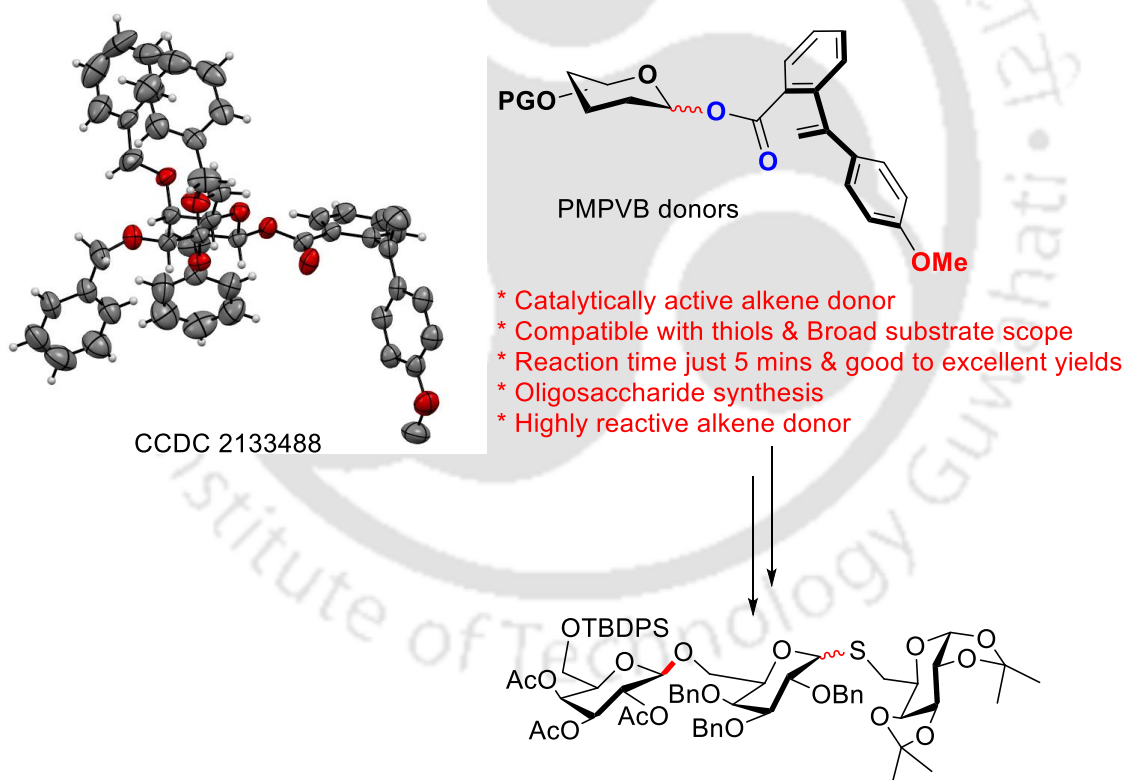
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Chapter IIA

Glycosyl *ortho*-[1-(*p*-MeOPhenyl)Vinyl]Benzoates (PMPVB) as Easily Accessible, Stable, and Reactive Glycosyl Donors for O-, S- and C-glycosylations Under Brønsted Acid Catalysis





2.1.1 INTRODUCTION

Carbohydrates are one of the important biomolecules^{1,2}, playing crucial roles in many biosynthetic process and pharmaceutical industry as well. In addition, due to the presence of inherent asymmetry of the sugar skeleton, glycolchemists are synthesizing various natural products utilizing it as an inexpensive chiral pool.^{3,4} Carbohydrate scaffolds in bioactive molecules exhibit different roles in physiological events such as cell development⁵, immune response⁶, bacterial and viral infection⁷, etc. During the time period, 2000 to 2021, 54 new carbohydrate-based drugs⁸ have been launched including molecules with antiviral, antibacterial, anticancer, antidiabetic, etc., properties. 1- α -C-nucleobase and 1- β -cyano-ribose scaffold containing Remdesivir (**1a**) proposed for the treatment of Ebola virus (IC₅₀ = 100 nmol/L) and MERS CoV (IC₅₀ = 340 nmol).⁹ Molnupiravir (**1b**), familiar as EIDD-2801, is a prodrug of ribonucleoside β -D-N-4-hydroxycytidine and is the first oral drug, approved in UK for the treatment of COVID-19.¹⁰ Human health is connected to bacterial infection in everyday life. It has been proven that human health is suffering from bacterial provoked pandemics including tuberculosis caused by Tubercle bacilli, cholera caused by *Vibrio cholera*, and anthrax

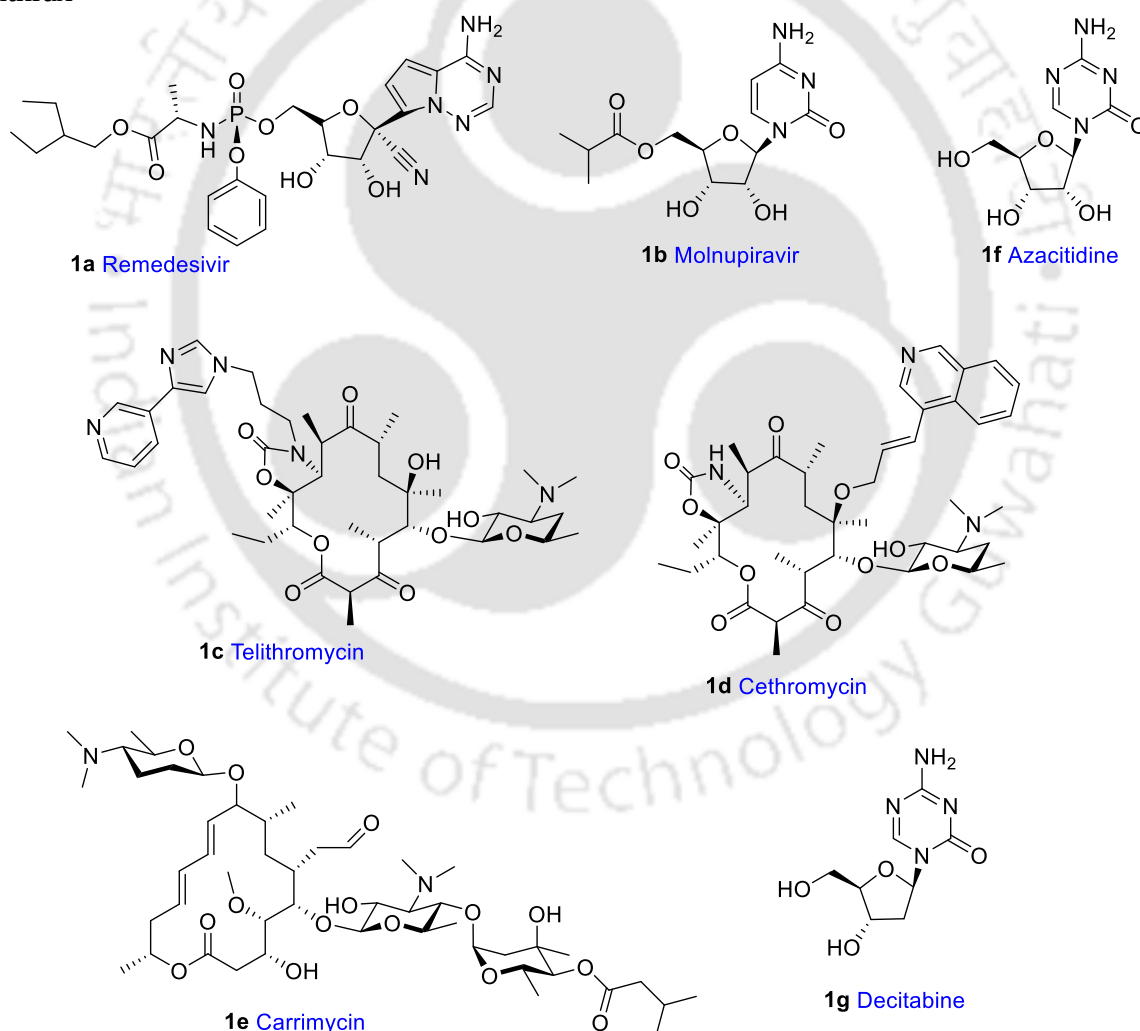


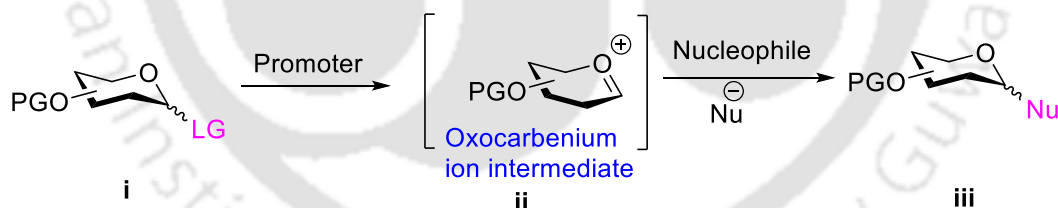
Figure 1: carbohydrate-based drugs

caused by *Bacillus anthracis*, etc. Nowadays, human health and life are facing severe threat by bacterial infections.¹¹ 3-Ketone, 5-O-desosamine, 11,12-cyclocarbamate, and butylimidazole-pyridine moieties containing, third-generation ketolide antibiotic, Telithromycin (**1c**)¹² is used

as an alternative for those patients who have an allergy to penicillins. Telithromycin (**1c**), derived from Erythromycin A, is used to prevent bacterial growth by interfering the bacterial peptide elongation. 4'-*O*-isovaleryl group containing 16-membered macrolide glycoside Carrimycin (**1e**) was approved by NMPA for the treatment of pneumonia in 2019. Carrimycin (**1e**) was derived from spiramycin I, which is more lipophilic and reactive compared to spiramycin I due to the presence of an additional 4'-*O*-isovaleryl group at sugar moiety. From the phase III clinical trial, it was reported that Carrimycin (**1e**) is superior to azithromycin.¹³ Carrimycin (**1e**) displays antiviral activity against the coronavirus.¹⁴ Over the past 20 years carbohydrate-based drugs have been developed for the different types of treatments of cancer including chemotherapy, radiotherapy, immunotherapy, etc.¹⁵⁻¹⁷ Azacitidine (**1f**), 5-*N* analogue of cytidine, and Decitabine (**1g**), 5-*N* analogue of 2-deoxycytidine, are carbohydrate-based drugs which infect the epigenetic gene regulation in different cancer cell utilizing cytotoxic reactivity.¹⁸

Glycosylation

Because of the heterogeneous character of carbohydrates, it is a difficult task for glyco-chemist to isolate pure glycan from natural sources. So, the chemical synthesis of carbohydrate derivatives receives significant attention in synthetic chemistry. Several efficient, reliable, and scalable glycosylation methods have been developed in the past century to synthesize these bioactive molecules. Among the various glycosylation methods, activation of leaving moiety of the glycosyl donor by using a promoter has attracted worldwide carbohydrate chemists for the synthesis of the carbohydrate-based precursor of bioactive molecules. Nowadays, glycosylation reactions have been categorized based on the leaving groups of glycosyl donors.¹⁹⁻²⁰ In the case of leaving group containing glycosyl donors (**i**), the promoters activate the leaving moiety which resulted in unstable, reactive oxocabenium intermediate (**ii**, Scheme 1) which is converted to glycoside (**iii**) (through the nucleophilic attack) at the anomeric position of oxocarbenium ion (this was discussed elaborately in chapter I, Scheme 4).



Scheme 1: General scheme for glycosylation

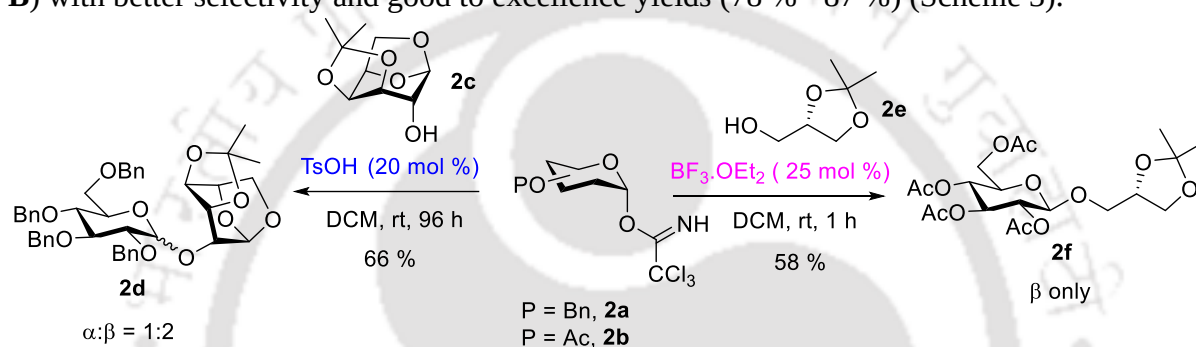
2.1.2 Literature review on glycosylation

Over one hundred and forty years, chemical glycosylation reactions are going on to synthesize oligosaccharides, since the glycosylation reaction done by Arthur Michael²¹ in 1879. After that researchers tried to develop new synthetic methods for glycosylation. In 1893, Fischer developed acid-catalyzed glycosylation, referred to as “Fischer glycosylation”. This method is rarely used for oligosaccharide synthesis. The oligosaccharide synthesis is quite challenging because of getting a mixture of isomers from every step. So, for this purpose purification and separation are needed for every step. To avoid this problem, new stereoselective and high-yielding synthetic methods have been developed.²¹⁻²⁵ Among the all catalytic glycosylation methods, the trichloroacetimidate method reported by Schmidt,²⁶ the glycosyl fluoride method introduced by Mukaiyama²⁷ and the *N*-(phenyl)trifluoroacetimidate

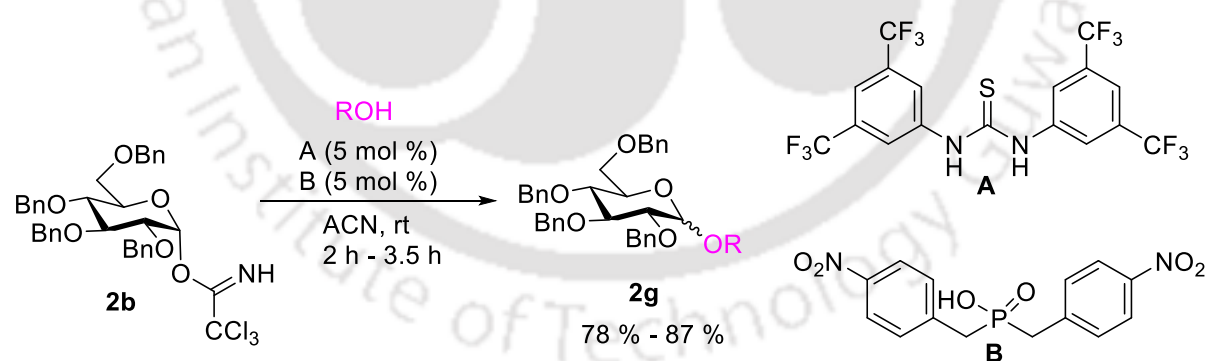
method developed by Yu²⁸ have occupied a significant place in glyco-chemistry over a long time.

Trichloroacetimidates

In 1976, Sinay and co-workers developed (N-methyl)acetimidate donors from glycosyl halide²⁹, and activated by using equivalent amount of *p*-toluenesulfonic acid (TsOH). This donor did not get much popularity due to the requirement of equivalent amount of acid. Inspired by this work, in 1980, Michel and Schmidt³⁰ developed trichloroacetimidate (TCA) donors. First, they activated the TCA donor by using catalytic amount of TsOH as well as BF₃·OEt₂ (Scheme 2). Later Grundler and Schmidt reported³¹ that the stereoselectivity of glycosylated products could be affected depending on the choice of catalyst. In 2013, Schmidt introduced thiourea and phosphoric acid co-catalyzed glycosylation of trichloroacetimidate donors.³² They have done the reaction in ACN medium in the presence of 5 mol % of both the catalyst (**A** & **B**) with better selectivity and good to excellence yields (78 % - 87 %) (Scheme 3).

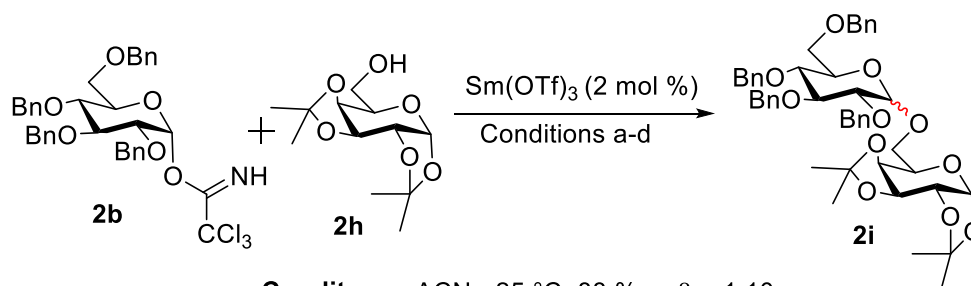


Scheme 2: Catalytic activation of Trichloroacetimidates



Scheme 3: Thiourea and Phosphoric acid co-catalyzed glycosylation

In 2000, Adinolfi et al. reported, Sm(OTf)₃ catalyzed glycosylation of perbenzylated glucose trichloroacetimidate donors. In this paper, they have studied solvent-dependent glycosylation. (Scheme 4).³³ Inspired by Pd-catalysed trans glycosylation, in 2016, Mukherjee et al. introduced FeCl₃-catalyzed trans glycosylation of 4,6-benzylidene protected perbenzylated gluco and galactosyl trichloroacetimidate donors. In presence of 10 mol % of FeCl₃, all the donors reacted well with glycosyl acceptors resulting in β -selectivity with excellent yields (Scheme 5).³⁴



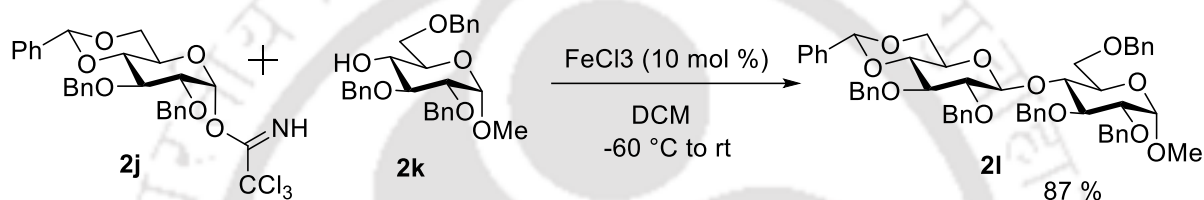
Condition a: ACN, -25°C , 88 %, $\alpha:\beta = 1:10$

Condition b: 4:1 = Toluene/THF, -25°C , 80 %, $\alpha:\beta = 1:2$

Condition c: 4:1 = Toluene/dioxane, -25°C , 73 %, $\alpha:\beta = 1:1$

Condition d: 4:1 $\text{Et}_2\text{O}/\text{THF}$, -25°C , 76 %, $\alpha:\beta = 1:1$

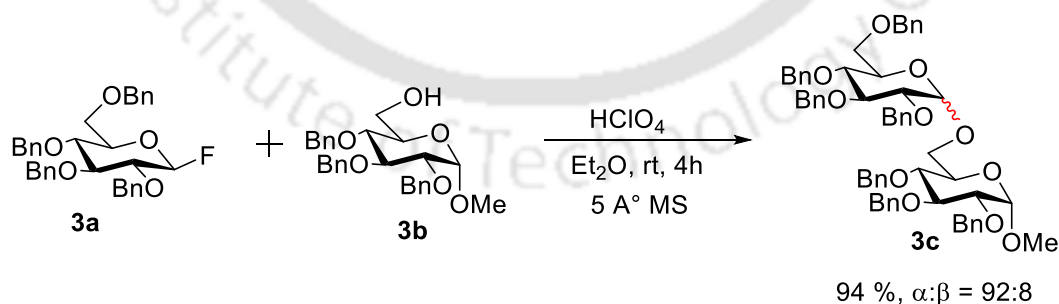
Scheme 4: $\text{Sm}(\text{OTf})_3$ catalyzed glycosylation of TCA donor



Scheme 5: FeCl_3 catalyzed glycosylation of TCA donors

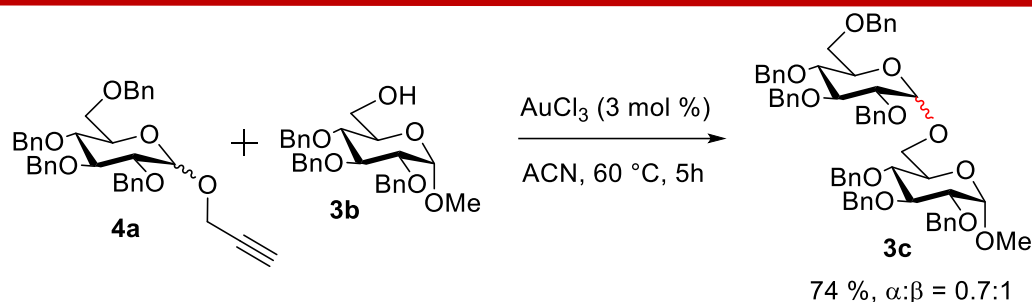
Glycosyl Fluoride

To overcome the stereoselectivity and yield problem of the glycosylation reaction, in 1981, Mukaiyama and co-workers introduced glycosyl fluoride.²⁷ Initially the stoichiometric amount of activator has been used to activate the glycosyl fluoride, resulting in high selectivity and yields also. Later they investigated various Lewis acids and Brønsted acids for activation of glycosyl fluoride donors. In 2001, the Mukaiyama group reported catalytic amounts of protic acids mediated stereoselective glycosylation of glycosyl fluoride (Scheme 6).³⁵



Scheme 6: Protic acids mediated glycosylation.

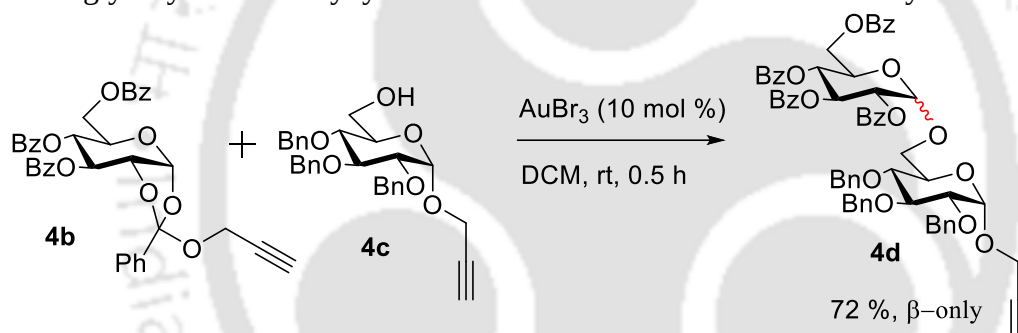
Alkyne-based glycosyl donor



Scheme 7: Activation of propargyl glycosyl donor by AuCl_3

In 2006, Hotha and co-workers first introduced alkyne-based glycosyl donors (propargyl glycosides), activated by using a catalytic amount of AuCl_3 .³⁶ It was observed that the selectivity and yields were poor for benzylated glucosyl, galactosyl as well as mannosyl donors in presence of 3 mol % of AuCl_3 in ACN medium (Scheme 7).

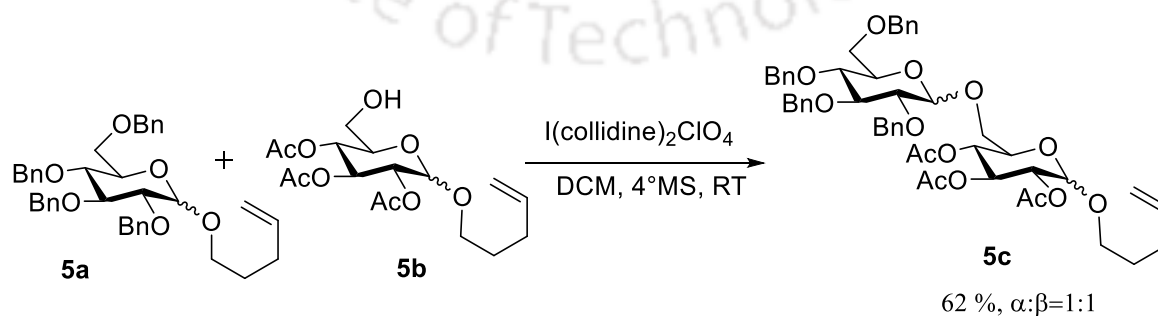
To improve the selectivity of the glycosylated products, in 2007, Hotha's group introduced propargyl 1,2-orthoester.³⁷ It was found that AuBr_3 was superior in 1,2 trans-glycosylation for oligosaccharide synthesis compared to AuCl_3 , AuCl , and Au_2O_3 in the DCM medium (Scheme 8). In 2008, the Yu group also introduced an efficient glycosylation protocol with glycosyl ortho-alkynylbenzoates as donors under the catalysis of Ph_3PAuOTf .³⁸



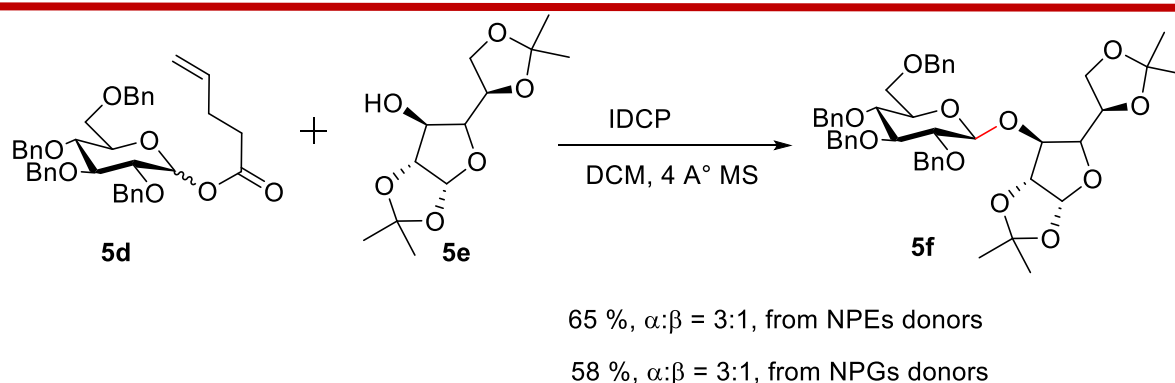
Scheme 8: Activation of propargyl orthoester.

Alkene-based glycosyl donors

In 1988, Fraser-Reid et al. first reported alkene-based donors, *n*-pentenyl glycosides (NPGs),³⁹ prepared by treatment with sugar hemiacetals and commercially available 4-penten-



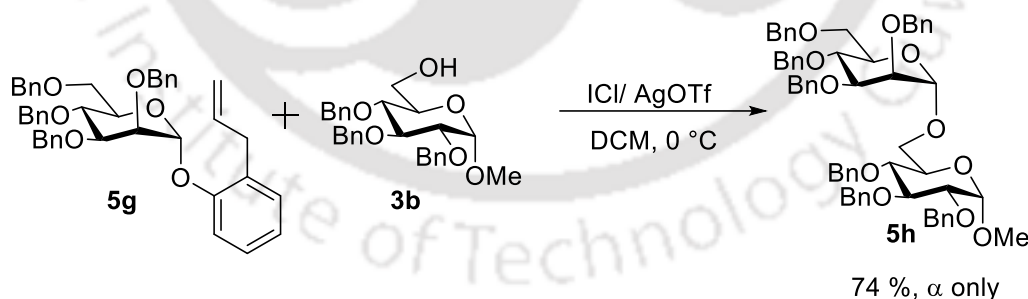
Scheme 9: Glycosylation of NPGs donor

**Scheme 10:** Glycosylation of NPEs donor

1-ol in presence of camphorsulfonic acid in DCM medium. The stoichiometric amount of iodonium dicollidine perchlorate has been used to activate the alkene-based donor (**5a**). It has been noticed that the selectivity and yields of this reaction were very poor in the case of perbenzylated alkene-based donor (Scheme 9).

In 1991, Fraser-Reid and co-workers developed *n*-pentenyl ester (NPEs)⁴⁰ by treatment with commercially available cheap 4-pentenoic acid and sugar hemiacetal utilizing DCC coupling protocol.⁴¹ They compared the reactivity of NPEs with previously reported NPGs³⁹ for glycosylation reaction (Scheme 10). Acetonide-protected glucose acceptor (**5e**) was reacted with *n*-pentenyl glycoside (NPGs) (**5a**), which resulted in a mixture of isomers ($\alpha:\beta=3:1$) with 58% yields whereas *n*-pentenyl ester (NPEs) (**5d**) afforded 65% yields with similar selectivity like NPGs (**5a**) (Scheme 10).

In 2012, Luo et al. developed a new NPGs-type glycosyl donor, 2-allylphenyl glycoside of mannose.⁴² They synthesized this donor by treatment with 2-allyl phenol and per-*O*-acetylated mannopyranoside by using $\text{BF}_3 \cdot \text{OEt}_2$, followed by deacetylation and benzylation in succession. It was reported that ICl/AgOTf is the best promoter to activate this donor among other alkenes activating promoters, resulting in good yields with completely α -selective (Scheme 11).

**Scheme 11:** Glycosylation of 2-Allylphenyl glycosides**2.2.1 Synthesis of PMPVB donors**

This work:

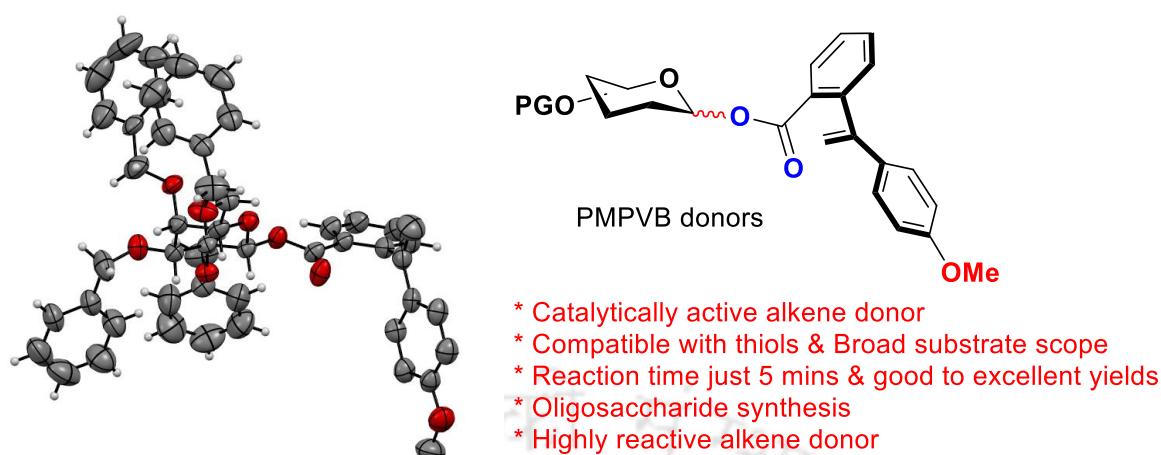
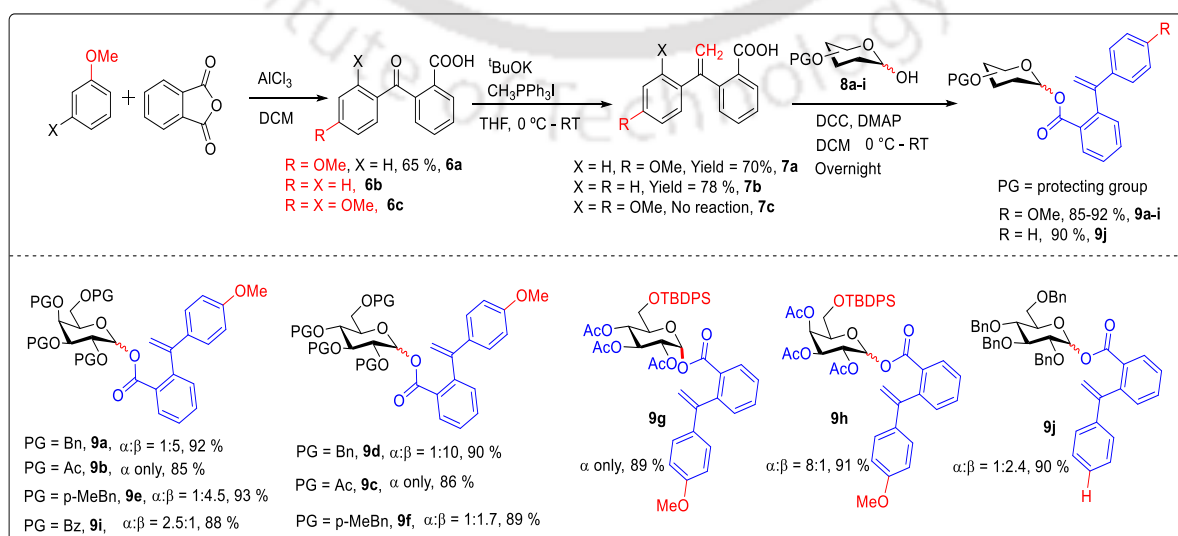
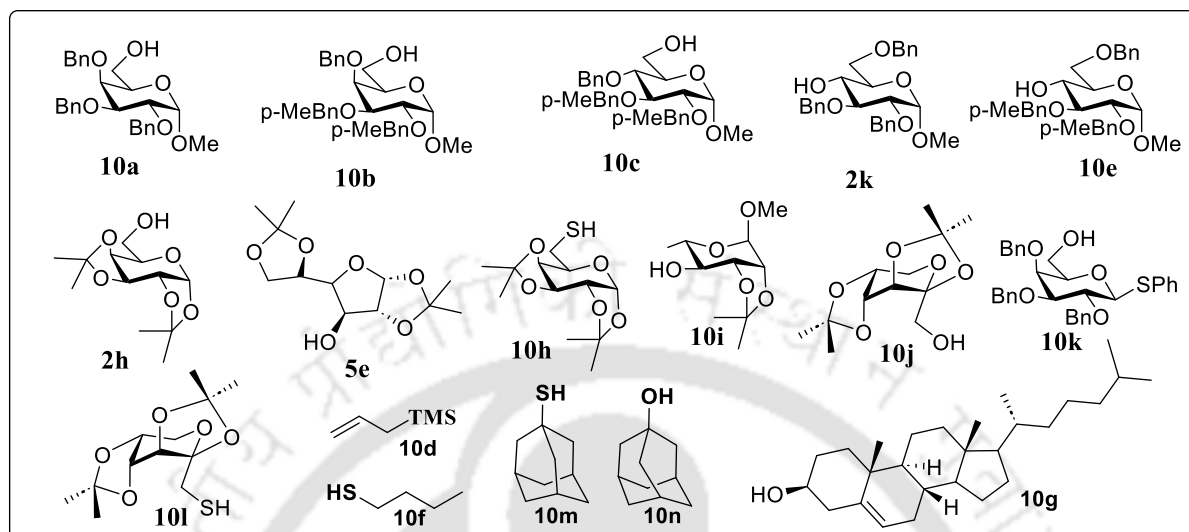


Fig. 2. Crystal structure of β -galactosyl PMPVB donor **2a** with 50 % ellipsoid contour probability (CCDC 2133488) and the structural depiction of general PMPVB donors.

The requirement of a stoichiometric amount of halonium ion is one of the vital disadvantages of the classic Fraser-Reid's stable and flexible *n*-pentenyl glycosides (NPGs)³⁹ to activate the glycosyl donors. So catalytic activation of the NPGs protocol is still desirable. Most of the alkene-type donors, activated by NIS/TMSOTf, are not capable of the synthesis of all kinds of glycosylation, particularly *S*-glycosylation.⁴³ Inspired by the reactivity difference between the benzyl group and the 4-methoxy benzyl (PMB) groups, we made *ortho*-(*p*-MeO)phenylvinylbenzoates (PMPVBs) as easily accessible, stable, and highly reactive alkene donors that can be activated under simple Brønsted acid conditions.

Our initial study was to prepare 4-methoxy as well as 2,4-dimethoxy substituted *ortho*-(1-phenylvinyl)benzoates (PVB)⁴⁴ donors. Successfully, we made *ortho*-(*p*-MeO) phenyl vinyl benzoates (PMPVBs) by DCC coupling with sugar hemiacetals (**8a-i**) and *ortho*-[1-(*p*-methoxyphenyl)vinyl]benzoic acid (**7a**) in presence of DCC and DMAP. The *ortho*-[1-(*p*-methoxyphenyl)vinyl]benzoic acid (**7a**) can be made easily from commercially available 2-(4-methoxy benzoyl)benzoic acid (**6a**) by simple Wittig methylation. We made 2-(4-methoxy benzoyl)benzoic acid (**6a**) from cheap and commercially available anisole and phthalic anhydride in quantitative yields. Unfortunately, we could not able to do Wittig methylation of 2-(2,4-dimethoxybenzoyl)benzoic acid (**6c**) due to steric hindrance.



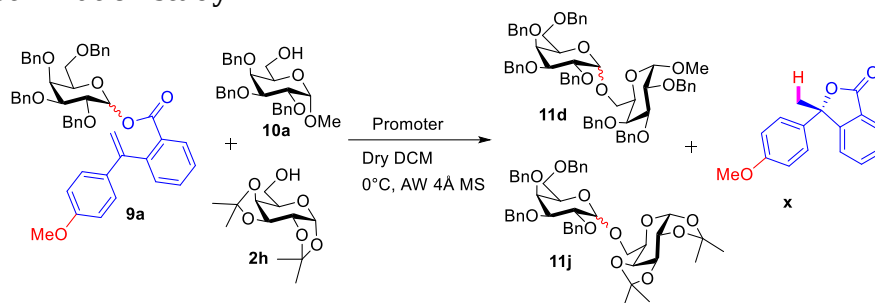
Scheme 12. Synthetic Route of PMPVB Donors**2.2.2 Synthesized of glycosyl acceptors used for this study****Scheme 13.** Glycosyl acceptors used for this study

After achieving the optimized conditions for the PMPVB donor synthesis, we made several PMPVB donors (**9a-i**) of glucose and galactose based having different protection (Scheme 12). It was found that all the donors are bench-stable after several months. All the donors were synthesized as an inseparable mixture of isomers except **9b**, **9c**, and **9g**. The peracetylated galactose donor **9b**, glucose donor **9c**, and 6-OTBDPS-protected triacetyl glucose-derived donor **9g** were synthesized as single α -isomers whereas 6-OTBDPS-protected triacetyl galactose-derived donor **9h** and benzoyl protected galactose donor **9i** were obtained as a mixture of isomers with ratio 8:1 and 2.5:1 (α : β) respectively. All the armed donors, perbenzylated and 4-methylbenzylated glucose and galactose based donors (**9a**, **9d**, **9e**, **9f**, **9j**) were obtained as a mixture of isomers from the ratio 1:1.7 to 1:10 (α : β).

2.2.3 Optimization study

After successfully synthesizing PMPVB donors, we investigated the glycosylation reaction by taking the per-benzyl galactosyl PMPVB donor (**9a**) with the galactose-derived 6-OH acceptor (**10a**) under various conditions (Table 1). For optimization of the reaction, a solution of glycosyl donor (**9a**) and acceptor (**10a**) in dry CH_2Cl_2 (0.03M) was stirred at room temperature for 60 min in the presence of activated acid-washed (AW) 4Å MS (0.9 g) under Ar atmosphere. Then the vessel was chilled to 0 °C, to which HNTf₂ was added. In the addition of catalyst up to 15 mol %, the PMPVB donor (**9a**) remained unaffected even after 24 h (Table 1, entries 1-3). After the addition of 20 mol % of the catalyst, a trace amount of product was formed after 24h (Table 1, entry 4). Then we increase the loading of the amount of catalyst up to 25 mol %, which resulted in 60 % product (**11d**) after 40 min (Table 1, entry 5). Again, we increase the amount of acceptor up to 2 equiv. instead of 1.2 equiv. which yielded 65 % (Table 1, entry 6). It was observed that in the presence of 30 mol % catalyst and 2 equiv. of the acceptor (**10a**), the reaction was completed within 5 min providing the desired disaccharide (**11d**) in 86 % yield (Table 1, entry 7). The reaction was also performed by taking TFA, *p*-TSA, and

Table 1: Optimization study



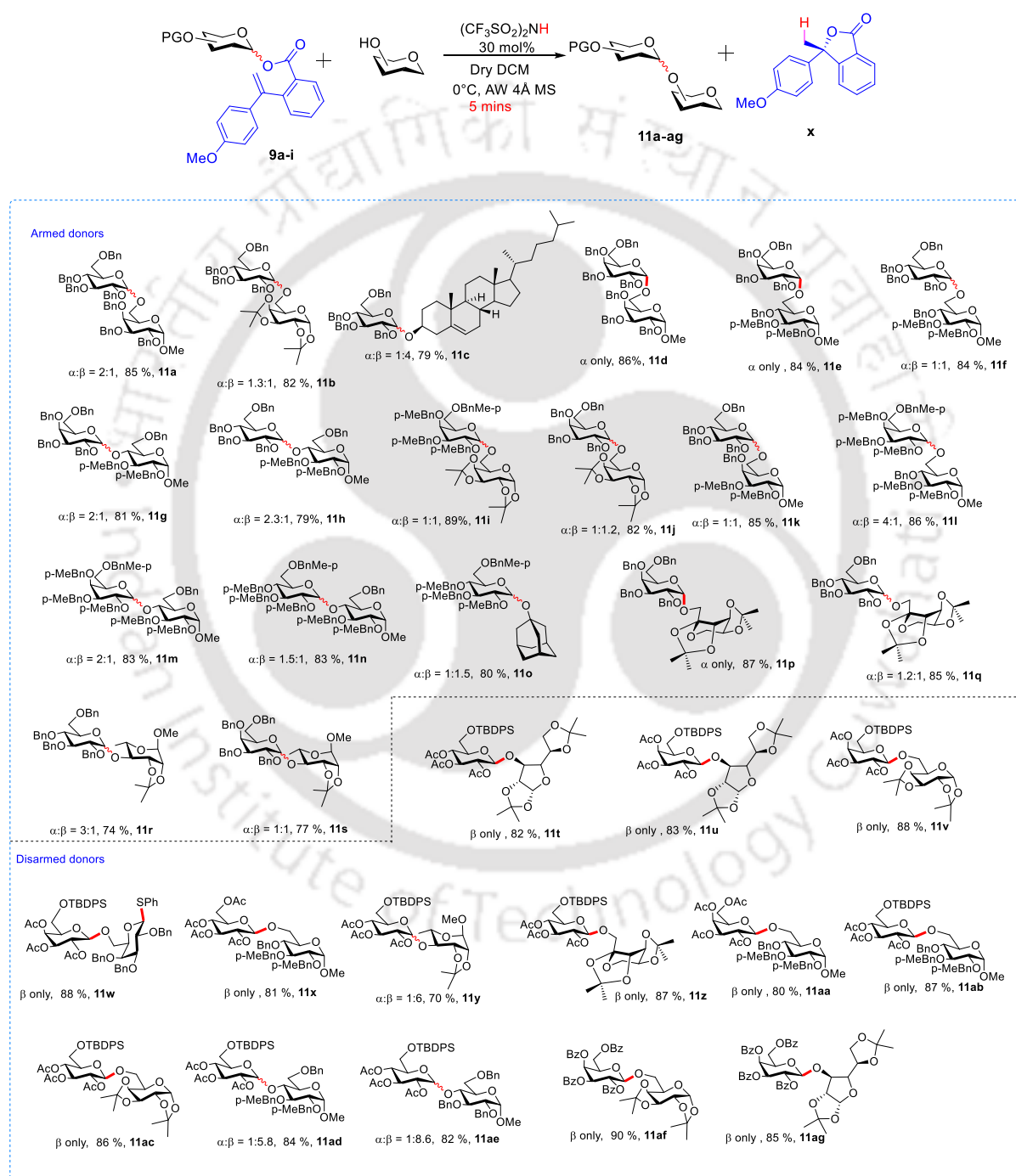
Entry	Promoter	Cat.(mol %)	acceptor (equiv.)	Time	Yield (%), $\alpha:\beta$
1	Tf ₂ NH	5	1.5	24 h	NR
2	Tf ₂ NH	10	1.5	24 h	NR
3	Tf ₂ NH	15	1.5	24 h	NR
4	Tf ₂ NH	20	1.5	24 h	trace
5	Tf ₂ NH	25	1.5	40 min	60, α only
6	Tf ₂ NH	25	2	40 min	65, α only
7	Tf ₂ NH	30	2	5 min	86, α only
8	TFA	30	2	24 h	NR
9	TMSOTf	30	2	24 h	NR
10	P-TSA	30	2	24 h	NR
11	TfOH	30	2	20 min	83, 8 : 1
12 ^a	Tf ₂ NH	30	2	5 min	83, α only
13 ^b	Tf ₂ NH	30	2	5 min	77, α only
14 ^c	*Tf ₂ NH	30	2	5 min	86, 1:1
15 ^d	*Tf ₂ NH	30	2	5 min	86, 1:1.2
16 ^e	*Tf ₂ NH	30	2	5 min	85, 1:1.2

Reaction conditions: Reactions were done at 0 °C in presence of activated acid-washed 4 Å MS in dry DCM medium (0.03M). *2h acceptor was used. a) reaction was done in Et₂O medium. b) Et₂O: DCM (1 :1) medium. c) reaction was performed using AW 3 Å MS d) AW 4 Å MS e) AW 5 Å MS.

TMSOTf as a catalyst which did not lead to any consumption of PMPVB donor (**9a**) even after 24 h (Table 1, entries 8-10). The reaction was done by using triflic acid (TfOH) as a catalyst (30 mol %), which provided 83 % of the desired product (**11d**) with selectivity 8:1 ($\alpha:\beta$) within 20 min (Table 1, entry 11). To check the solvent effect on the reaction we performed the reaction in a non-polar solvent diethyl ether, which resulted in 83 % yield with complete α selective whereas a mixture of solvent (DCM/Et₂O: 1:1) provided 77 % yield with the same selectivity (Table 1, entries 12-13). A comparative study has been performed by taking

different acid-washed molecular sieves along with the donor (**9a**) and acceptor (**2h**), which resulted in 86 % yields of the desired product (**11j**) with an anomeric selectivity of 1:1 ($\alpha:\beta$) for 3Å MS whereas 4Å MS provided 86 % yields with anomeric ratio 1:1.2 ($\alpha:\beta$) (Table 1, entries 14-15). The same experiment was done for 5Å MS, which yielded 85 % (1:1.2, $\alpha:\beta$) (Table 1, entry 16). So different molecular sieves did not alter the selectivity and yields much. The formation of cyclized by-product (**x**) is confirmed by ^1H and ^{13}C NMR studies.

2.2.4 The substrate scope of O-glycosylation

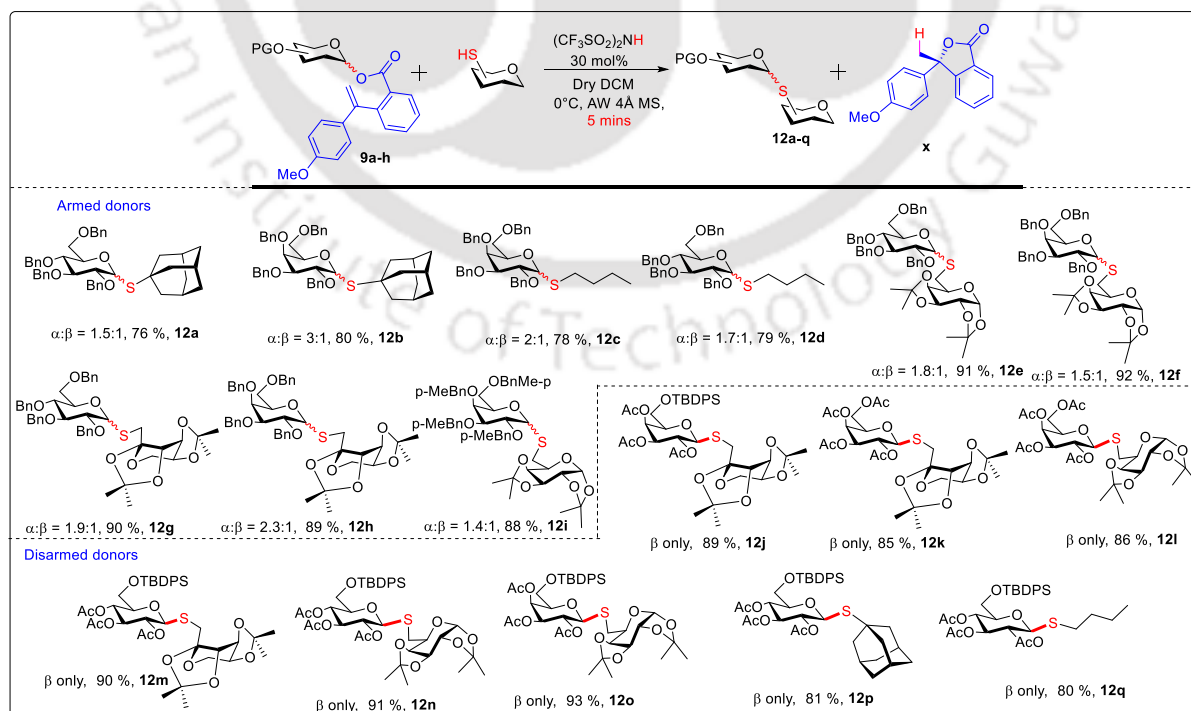


Scheme 14. Substrate scope for O-glycosylation

Taking the optimized condition, we focused on substrate scope for *O*-glycosylation varying different PMPVB donors and various acceptors (Scheme 14). The armed perbenzyl and per-4-Methyl-benzylated donors of glucose and galactose, resulted in the glycosylated products as a mixture of isomers (**11a-b**, **11f**, **11h**, **11k**, **11n**, **11q**, **11r**) and (**11d**, **11e**, **11g**, **11i-j**, **11l-m**, **11p**, **11s**), respectively, towards the α -anomer with good to excellent yields (74 % - 89 %) (Scheme 14). It was observed that the disarmed peracetylated donors (**11x**, **11aa**), perbenzoylated donors (**11af-ag**), and 6-*O*-silylated-peracetyl donors (**11t-w**, **11z**, **11ab-ac**) selectively resulted in β -isomer with good yields (80-90 %) due to the expected neighboring group participation (Scheme 14). The usually less reactive, hindered secondary acceptor also led to the products (Scheme 14, **11y**, **11ad-ae**) in just 5 mins, however, it resulted in a drop in the selectivity. The secondary and tertiary alcohols, cholesterol (**10g**), and adamantanol (**10n**) gave the corresponding products in 79 % and 80 % yields (Scheme 14, **11c**, and **11o**), respectively.

2.2.5 The substrate scope of thio-glycosylation

Compared to *O*-glycosides, thio-sugars are commonly rarely found in the living system. *S*-linked glycosides are biologically important as this class of compounds are not prone to enzymatic hydrolysis. Due to resistance properties towards hydrolysis, thio-glycosides are one of the important therapeutic targets. Common promoters like NIS/TfOH, AuCl₃ are incompatible with thiol acceptors for the thio-glycosylation.⁴³ Thio acceptors have a tendency for dimerization prone to coupling reaction.⁴⁵ Despite these difficulties, some synthetic protocols have been established for thio-glycosylation.⁴⁵⁻⁴⁸ So the development of a new synthetic procedure for thio-glycosylation is highly desirable. As we discussed earlier the acid-catalyzed activation of alkene-based donor PMPVB towards the synthesis of *O*-glycosidic linkage, taking advantage of this protocol, we investigated for *S*-glycosylation. We performed one reaction by taking a disarmed PMPVB donor (**9g**) and adamantane thiol (**10m**) as an acceptor in the presence of 30 mol % of Tf₂NH which resulted in expected thio-glycoside **12p**

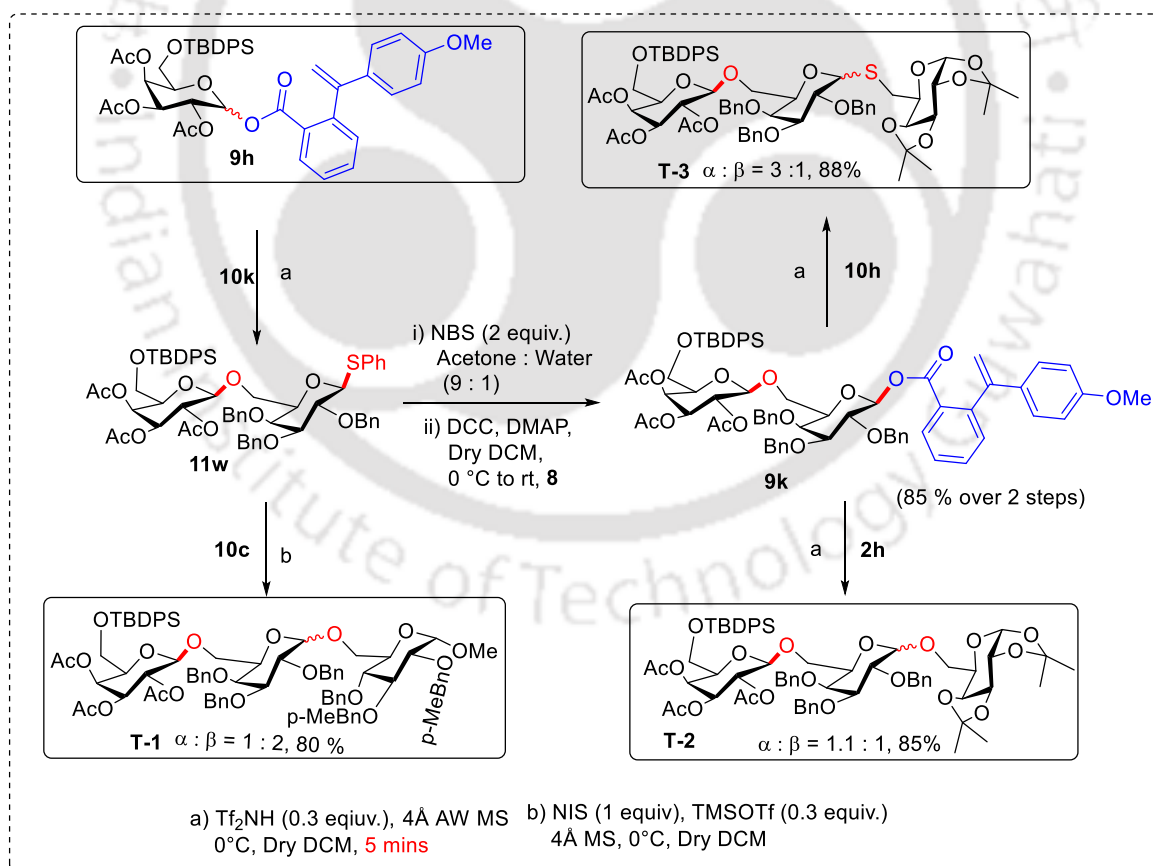


Scheme 15. Substrate scope for *S*-glycosylation

as a β -isomer with good yields (81 %) (Scheme 15). Excited by the result, we expanded the scope of thioglycosides (**12a-q**) (Scheme 15) varying the donors and acceptors. Luckily, all the glycosylation reactions led to good to excellent yields of the expected products (**12a-12q**). The disarmed donors are provided stereoselective β -glycosides (**12j-q**) due to neighboring group participation in good to excellent yields (80 % - 93 %) whereas the armed donor resulted in a mixture of isomer (**12a-i**) towards α -selective similar to *O*-glycosylation.

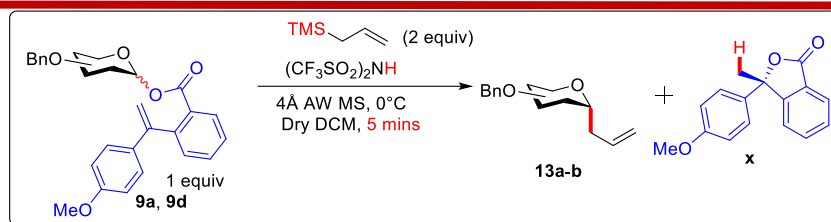
In order to showcase the orthogonality of the PMPVB donors with thioglycosides, we have utilized the thioglycoside derived 6-OH as the acceptor (**10k**) for *O*-disaccharide (**11w**, 88 %) as an exclusive β -isomer. The disaccharide **11w** was subjected to NIS/TMSOTf, which resulted in trisaccharide **T-1**. The trisaccharide **T-1** was obtained with an overall yield of 70 % as a 1:2, α : β mixture of isomers (Scheme 16). In order to showcase the efficiency of the current PMPVB donors towards the synthesis of oligosaccharides, the thioglycoside **11w** was converted to a disaccharide PMPVB donor **9k** in two steps (Scheme 16, 85 % over two steps, β only). The thus synthesized disaccharide-based PMPVB donor (**9k**) was successfully reacted with the acceptor **2h** under 30 mol % HNTf₂, which resulted in another trisaccharide **T-2** with a mixture of isomers (1.1:1, α : β) in excellent yields (85 %) (Scheme 16). As we discussed earlier, the PMPVB donor is capable to synthesize thio-disaccharide by using 30 mol % of Tf₂NH, the chemistry has also been utilized for the synthesis of a unique trisaccharide **T-3** containing both *O*- and *S*-linkages in 88 % yield with 3:1, α : β selectivity.

2.2.6 Synthesis of trisaccharides



Scheme 16: Synthesis of trisaccharides

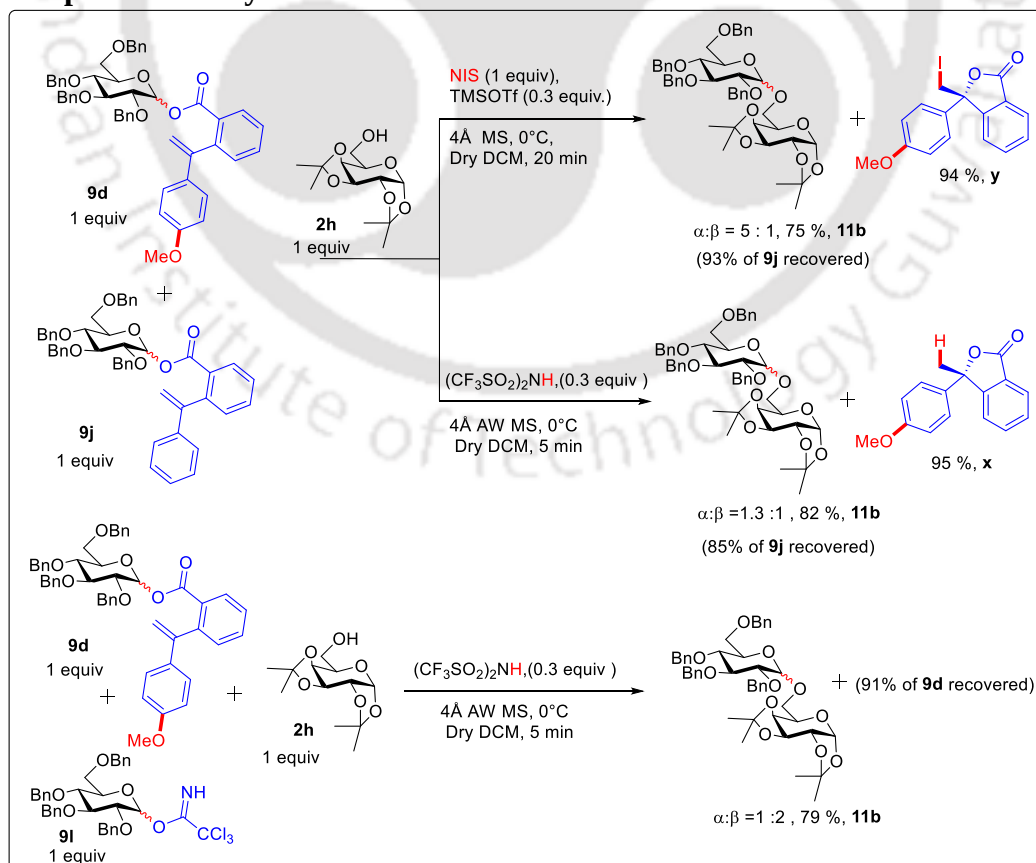
2.2.7 Table 2: Stereoselective C-glycosylation



Entry	Donor	Catalyst (equiv.)	Yields	$\alpha:\beta$	Products
1	9a	0.3	27 %	α only	13a
2	9a	1.0	82 %	α only	13a
3	9d	1.0	85 %	13:1	13b

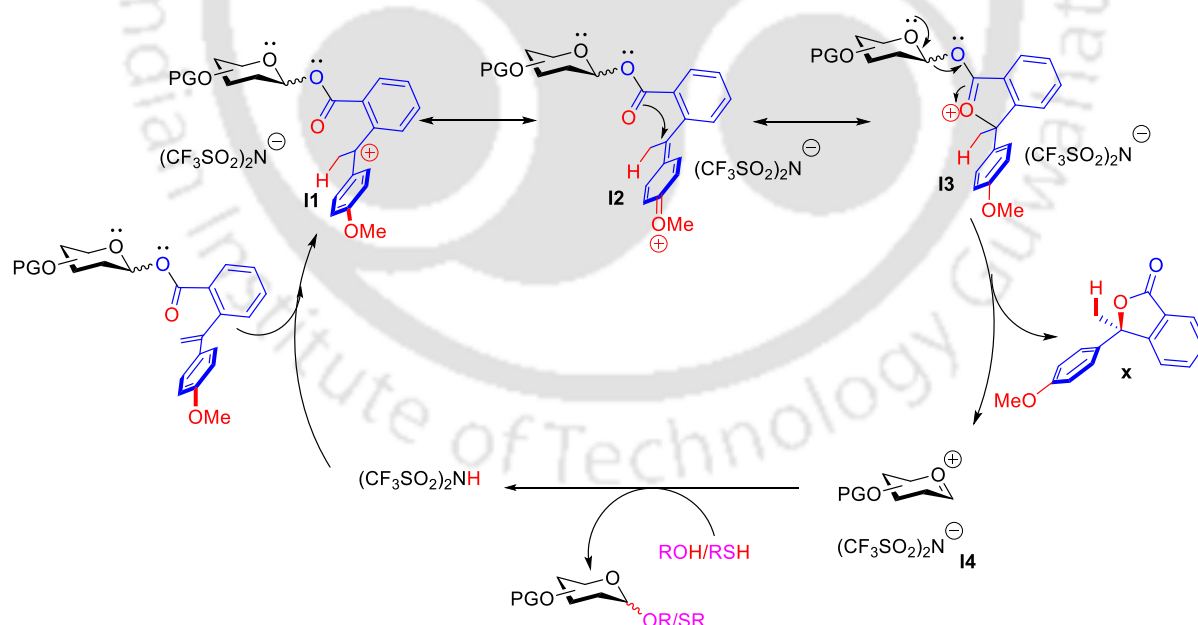
After successfully synthesis of O-glycosides and S-glycosides, we focused on C-glycosides. Intriguingly, the per-benzylated galactosyl donor **9a** reacted in a highly stereoselective fashion in the presence of 30 mol % Tf₂NH with allyltrimethylsilane (**10d**) and resulted in only the α -allylgalactoside **13a** exclusively with very low yields 27 % (Table 2, entry 1) as there is no source of H⁺ for regeneration of the catalyst. The same reaction was repeated with 1 equiv. of catalyst, which resulted in 82 % yields with α -selective (**13a**) (Table 2, entry 2). When the per-benzylated glucosyl donor **9d** was reacted with allyltrimethylsilane (**10d**) in the presence of 1 equiv. of Tf₂NH, resulted in alkyl glucoside **13b** in good yields (85 %) as a 13:1($\alpha:\beta$) mixture of anomers (Table 2, entry 3).

2.2.8 Comparative study.



Scheme 17: Comparative study

We compared the reactivity of PMPVB donors with PVB donors.⁴⁴ When a mixture of 1 equiv. of PMPVB donor **9d** and 1 equiv. of PVB donor **9j** were reacted in presence of 1 equiv. of NIS and 0.3 equiv. of TMSOTf, in the presence of 1 equiv. acceptor **2h**, in 20 mins, led to the complete conversion of **9d** into the expected disaccharide (**11b**), whereas 93 % of the PVB donor **9j** was recovered (Scheme 17). Also, 94 % of the *p*-methoxy substituted cyclized iodo-adduct (**y**) arising from donor **9d** has been isolated, suggesting the complete activation of the PMPVB donor **9d** in the presence of **9j**. Similarly, both the donors were also treated under the catalytic Brønsted acidic condition (30 mol % Tf₂NH), in which case 85 % of the donor **9j** has been recovered, indicating very little activation of the PVB donor **9j** in the presence of the PMPVB donor **9d** (Scheme 17). *p*-Methoxy substituted cyclized adduct (**x**) is isolated in 95 % yield, confirming the complete activation of the PMPVB donor **9d**. These studies suggest that the methoxy-substituted PMPVB donor **9d** is significantly more reactive than the PVB donor **9j** under both stoichiometric and catalytic activation conditions, and the PMPVB donor **9d** can selectively be activated in the presence of **9j**, indicating that PMPVB and PVB donors can be used for iterative oligosaccharide synthesis as well. We also compared the reactivity of PMPVB donor (**9d**) and acetimidate donor (**9l**) with acceptor **2h** under triflimide catalysis (Scheme 17) which resulted in 79 % of **11b** ($\alpha:\beta = 1:2$) along with recovery of **9d** (91 %). This experiment clearly demonstrates the superior reactivity of the acetimidate donor (**9l**) to the PMPVB donor (**9d**).

2.2.9 Plausible Mechanism**Scheme 18:** Plausible Mechanism

After successfully showcasing the catalytic activation of the newly synthesized PMPVB donors for the synthesis of O-, S- and C-linked glycosides, and based on the byproduct's observation, we propose the mechanism of the current protocol as showcased in scheme **18**. The Brønsted acid HNTf₂ protonates the alkene of the donor, resulting in a highly stable tertiary carbocation

intermediate **I1** that is further stabilized and can exist in resonance form **I2** due to the presence of the *p*-methoxyphenyl group which can exist as glycosyloxybenzofuranium intermediate **I3** (Scheme 18). The intermediate **I3** then undergoes expulsion of cyclized by-product (**x**) along with the generation of an oxo-carbenium ion **I4** that is trapped by the alcohol/thiol nucleophile. The newly generated oxocarbenium ion can exist as solvent-separated ion pairs or contact ion pairs (For details see Chapter I, Scheme 4).⁴⁹ The Brønsted acid HNTf₂ is regenerated following the deprotonation of the alcohol/thiol along with the liberation of the glycosylated products. Intriguingly, the crystal structure of the galactosyl donor **9a** (Fig 1, CCDC 2133488) reveals the perfect orthogonal orientation of the carbonyl group to alkene that could be the reason for the facile ring-closure to form the cyclic by-product under Brønsted acidic conditions.

2.2.10 Conclusion

In summary, we have synthesized Fraser-Reid type alkene donors that can be catalytically activated under Brønsted acidic conditions as well as NIS/TMSOTf conditions. All types of glycosylation (*O*-, *S*-, *C*-) are occurring just in 5 min at 0 °C, proven that the high reactivity of the PMPVB donors. Comparative studies under both Brønsted acidic conditions (HNTf₂) and NIS/TMSOTf conditions with the PVB donor indicate the PMPVB donors are superior in reactivity compared to PVB donors. The Brønsted acidic activation of the PMPVB donors has also been exploited in synthesizing *S*-linked glycosides that are not compatible with other alkene or alkyne-based donors due to the requirement of NIS activation or Gold catalysts that can react with thiol nucleophiles. The orthogonality and reactivity of the PMPVB donors have also been showcased by synthesizing trisaccharides containing *O*- and *S*-linkages. All the PMPVB donors are bench stable over several months. Overall, easily synthesizable and highly reactive PMPVB donors can be stable alternatives to the relatively unstable glycosylacetimidates and glycosylphosphates for the oligosaccharide synthesis under Brønsted acid catalysis. The utility of these donors to synthesize other polysaccharide natural products and improve the conditions towards substrate/protecting group independent stereoselective glycosylation reactions are under progress in our laboratory.

2.3 EXPERIMENTAL SECTION

General Information

All solvents purchased were of commercial grade and reagents were purchased from Sigma-Aldrich, Merck, Carbosynth, Spectrochem, Alfa Aesar, Avra and used without further purification for reactions.

Analysis

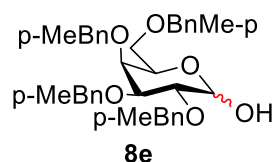
Reactions were monitored by TLC on Kieselgel 60 F254 (Merck). Detection was done by examination under UV light (254 nm) and by charring with 10% sulfuric acid in water. Purification was performed by both Ultra High-Performance Liquid Chromatography (UHPLC) using column [Particle size: (μ) 12, Dim: (mm) 250 x 10] in reverse phase and in normal phase using silica gel [Merck, 60-120 mesh] and Flash column chromatography (Combiflash^(R) NextGen 300). Extracts were concentrated in vacuo using both Büchi rotary evaporator (bath temperatures up to 40 °C) at a pressure of either 15 mmHg (diaphragm pump) and 0.7 mmHg (oil pump), at rt. ¹H- and ¹³C NMR were recorded on a Bruker 600 MHz, 500MHz, and 400 MHz spectrometers using CDCl₃ as solvent. Chemical shift values are

reported in ppm with the solvent as the internal standard (CDCl₃: δ 7.26 for ¹H, δ 77.16 for ¹³C). Data are reported as follows: chemical shifts (δ), multiplicity (s = singlet, d = doublet, dd = doublet of doublet, ddd = doublet of doublet of doublets, dt = doublet of triplet, t = triplet, td = triplet of doublet, q = quartet, m = multiplet) etc., coupling constants J (Hz), and integration. High-resolution mass measurements were performed using Agilent technologies mass spectrometer (QTOF-ESI mode). The diastereomeric ratios were calculated from crude NMR. Specific rotation was recorded in Autopol II S2, the units of the specific rotation is (deg·mL)/(g·dm) and concentration *c* is given in g/100 ml. The melting point range provided for the crystalline solids was recorded using Buchi B-545 melting point instrument. For heating purpose, silicon oil baths were used. Hemiacetals **8a-d**, **8h-i** were synthesized following literature procedures.⁵⁰⁻⁵¹ Compounds **7a-c**⁵²⁻⁵³ **9k**⁵⁴, **10a**, **2k**, **2h**, **5e**, **10h**, **10j** were synthesized by following literature procedures.⁵⁵⁻⁵⁸ Suitable crystals for single-crystal X-ray diffraction (SCXRD) analysis were obtained by dissolving “**9a β** ” in DCM and MeOH (3:1) followed by slow evaporation of solvent mixture at room temperature. The X-ray diffraction data were collected at 296 K with Mo K α radiation (λ = 0.71073 Å) using a Micro focused based Bruker D8 QUEST diffractometer equipped with a graphite monochromator. Apex IV software was used for data collection and also for indexing the reflections and determining the unit cell parameters; the collected data were integrated using Saint Software. The structures were solved by Intrinsic phasing and refined by full-matrix least-squares calculations using SHELXTL 2018 software. All the non-H atoms were refined in the anisotropic approximation.

General procedure 1

Sodium hydride (1.5 equiv. per OH group) was added to a stirring solution of the methylglycoside (1 mmol) in anhydrous DMF (10 mL) at 0 °C. After stirring it for 30 min, para methyl benzyl bromide (1.5 equiv. per OH group) was added at 0 °C, and the mixture was warmed to ambient temperature and stirred overnight. After completion of the reaction, the reaction mixture was quenched by the addition of methanol (5 mL), the solvents were removed under reduced pressure and the residue was taken up in H₂O/DCM (1:1). The product in the aqueous layer was extracted twice into DCM. The organic phase was washed with brine, dried (by Na₂SO₄), and concentrated under reduced pressure. The residue was purified by column chromatography [Hexane/Ethyl acetate] to yield the corresponding benzylated derivatives. The perbenzylated methyl glycoside (1 mmol) was dissolved in glacial acetic acid (10 mL) and 1N H₂SO₄ (5 mL) and stirred with heating at 90 °C for overnight. After cooling, the mixture was poured into ice water and extracted into DCM (3 × 40 ml). The organic layer was washed with saturated NaHCO₃ solution, dried over Na₂SO₄, and concentrated. The residue was purified by flash column chromatography (Hexane/Ethyl acetate).

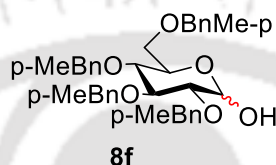
2,3,4,6-tetra-O-paramethylbenzyl- α/β -D-galactopyranose (**8e**).



Compound **8e** was synthesized according to General procedure 1 (white solid, 400.0 mg, 67 % yield over two steps, $\alpha:\beta$ = 2.4:1, *R_f* = 0.25 (Hexane/EtOAc, 3:1, v/v. m. p. 146–148). ¹H NMR (600 MHz, CDCl₃) δ 7.27 (t, *J* = 8.0 Hz, 4H), 7.25 – 7.22 (m, 3H), 7.18 – 7.10 (m, 14H), 7.09 (d, *J* = 7.7 Hz, 3H), 5.23 – 5.20 (m, 1H), 4.88 (d, *J* = 8.1 Hz, 1H), 4.85 (d, *J* = 10.9 Hz, 1H), 4.78 (d, *J* = 11.3 Hz, 1H), 4.74 (d, *J* = 8.7 Hz, 1H), 4.73 – 4.68 (m, 2H), 4.68 – 4.66 (m, 1H),

4.64 (d, $J = 11.5$ Hz, 1H), 4.63 – 4.59 (m, 1H), 4.54 (t, $J = 11.8$ Hz, 2H), 4.42 (d, $J = 11.7$ Hz, 2H), 4.32 (d, $J = 11.7$ Hz, 2H), 4.10 (t, $J = 6.3$ Hz, 1H), 3.98 (dd, $J = 9.8, 3.5$ Hz, 1H), 3.90 – 3.86 (m, 2H), 3.85 (d, $J = 2.5$ Hz, 1H), 3.82 (d, $J = 2.3$ Hz, 1H), 3.72 (dd, $J = 9.4, 7.7$ Hz, 1H), 3.57 – 3.53 (m, 1H), 3.53 – 3.50 (m, 1H), 3.48 (dd, $J = 9.2, 6.2$ Hz, 2H), 3.45 – 3.41 (m, 1H), 3.39 (dd, $J = 9.3, 6.5$ Hz, 1H), 3.21 (s, 1H), 2.36 (s, 5H), 2.33 (s, $J = 3.0$ Hz, 8H), 2.32 (s, 5H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 137.6, 137.5, 137.4, 137.3, 137.3, 135.6, 135.5, 135.5, 135.4, 135.4, 135.3, 134.8, 134.7, 129.1, 129.1, 129.1, 129.1, 129.1, 128.9, 128.9, 128.6, 128.5, 128.4, 128.2, 128.2, 128.2, 127.8, 127.7, 97.7, 92.0, 82.1, 80.6, 78.6, 76.3, 75.0, 74.3, 74.2, 74.2, 73.6, 73.4, 73.4, 73.3, 73.0, 72.8, 69.5, 69.0, 68.8, 21.3, 21.3. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{38}\text{H}_{48}\text{NO}_6$ 614.3482; found 614.3484. $[\alpha]_{\text{D}}^{35} = +0.38$ (c 0.01, CHCl_3).

2,3,4,6-tetra-O-paramethylbenzyl- α/β -D-glucopyranose (8f).

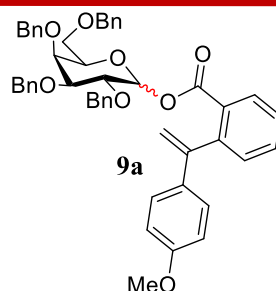


Compound **8f** was synthesized according to general procedure 1 (White solid, 406.0 mg, 68 % yield over two steps, $\alpha:\beta = 2.3:1$, $R_f = 0.25$ (Hexane/EtOAc, 3:1, v/v. m. p. 153–155 °C.). ^1H NMR (600 MHz, CDCl_3) δ 7.27 – 7.23 (m, 4H), 7.23 – 7.19 (m, 4H), 7.16 – 7.10 (m, 8H), 7.08 (d, $J = 7.7$ Hz, 3H), 6.99 (d, $J = 7.8$ Hz, 3H), 5.18–5.15 (m, 1H), 4.88 (t, $J = 8.4$ Hz, 2H), 4.79 (d, $J = 10.6$ Hz, 1H), 4.77 – 4.70 (m, 3H), 4.70 – 4.66 (m, 1H), 4.63 (d, $J = 11.6$ Hz, 1H), 4.56 (t, $J = 13.4$ Hz, 2H), 4.48 (d, $J = 12.0$ Hz, 1H), 4.44 – 4.39 (m, 2H), 4.38 (d, $J = 10.3$ Hz, 2H), 3.98 (d, $J = 8.9$ Hz, 1H), 3.91 (t, $J = 9.3$ Hz, 1H), 3.66 (dd, $J = 10.4, 4.0$ Hz, 2H), 3.63 – 3.60 (m, 1H), 3.59 (d, $J = 9.2$ Hz, 2H), 3.55 (d, $J = 10.1$ Hz, 2H), 3.54 – 3.50 (m, 1H), 3.49 (dd, $J = 10.8, 6.6$ Hz, 1H), 3.41–3.38 (m, 1H), 3.38 – 3.34 (m, 1H), 3.02 (s, 1H), 2.35 (s, 4H), 2.33 (d, $J = 2.7$ Hz, 5H), 2.32 (s, 4H), 2.31 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 137.8, 137.6, 137.5, 137.5, 137.5, 137.4, 137.4, 137.4, 135.7, 135.5, 135.2, 135.1, 134.9, 134.8, 134.7, 134.7, 129.2, 129.1, 129.1, 129.1, 129.0, 128.4, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 97.4, 91.4, 84.5, 82.9, 81.6, 79.7, 77.6, 77.4, 75.7, 74.9, 74.7, 73.4, 73.3, 73.2, 70.3, 68.5, 68.2, 21.3, 21.4, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{38}\text{H}_{48}\text{NO}_6$ 614.3482; found 614.3482. $[\alpha]_{\text{D}}^{35} = +0.32$ (c 0.01, CHCl_3).

General procedure 2

4-dimethylaminopyridine (DMAP) (0.2 equiv.) and N,N' -Dicyclohexylcarbodiimide (DCC) were added to a solution of sugar (1.0 equiv.) and Benzoic acid (**7a**, **7b**) (1.2 equiv.) in dry DCM at 0 °C. The resulting mixture was allowed to reach room temperature and stirred for overnight. After completion of the reaction, the mixture was diluted with CH_2Cl_2 , and washed with water and brine. The organic layer was dried over Na_2SO_4 , filtered, and concentrated in vacuo. The residue was purified by Flash column chromatography to afford the glycosyl donors (**9a-j**).⁵¹

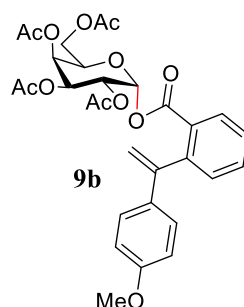
1-O-(2-(1-(4-methoxyphenyl)vinyl)benzoyl)-2,3,4,6-tetra-O-benzyl-D-galactopyranose (9a).



Compound **9a** was prepared from **8a** (540 mg, 1 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **9a** (715 mg, 92 %, $\alpha:\beta$ = 1:5) as a white solid, R_f = 0.50 (Hexane/EtOAc, 4:1, v/v. m. p. 95–97 °C.). The α anomer ^1H NMR (600 MHz, CDCl_3) δ 7.86 (d, J = 7.6 Hz, 1H), 7.48 (t, J = 7.2 Hz, 1H), 7.39 (t, J = 7.4 Hz, 1H), 7.35–7.30 (m, 6H), 7.30 – 7.28 (m, 3H), 7.28 – 7.25 (m, 6H), 7.25 – 7.22 (m, 4H), 7.21 (d, J = 8.8 Hz, 3H), 6.73 (d, J = 8.7 Hz, 2H), 6.49 (d, J = 3.5 Hz, 1H), 5.55 (s, 1H), 5.00 (s, 1H), 4.87 (d, J = 11.3 Hz, 1H), 4.66 (d, J = 11.5 Hz, 1H), 4.63 – 4.55 (m, 2H), 4.53 – 4.47 (m, 2H), 4.44 (d, J = 11.7 Hz, 1H), 4.36 (d, J = 11.7 Hz, 1H), 4.09 (dd, J = 10.1, 3.6 Hz, 1H), 3.79 (dd, J = 10.3, 6.9 Hz, 2H), 3.65 (s, 3H), 3.52 (dd, J = 10.1, 2.5 Hz, 1H), 3.48 (t, J = 8.4 Hz, 1H), 3.40 (dd, J = 9.0, 5.5 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 166.7, 160.4, 159.2, 147.4, 142.9, 138.8, 138.5, 138.3, 137.9, 132.7, 131.5, 131.2, 130.8, 130.4, 128.4, 128.3, 128.2, 128.2, 128.2, 128.1, 127.8, 127.8, 127.7, 127.5, 127.5, 127.4, 127.3, 127.2, 113.5, 112.8, 91.5, 78.5, 75.4, 74.9, 74.5, 73.4, 72.9, 72.8, 72.0, 68.2, 55.1. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{50}\text{H}_{52}\text{NO}_8$ 794.3693; found 794.3696. $[\alpha]_D^{35} = +0.30$ (c 0.015, CHCl_3).

The β anomer ^1H NMR (600 MHz, CDCl_3) δ 7.93 (d, J = 7.7 Hz, 1H), 7.52 (t, J = 7.2 Hz, 1H), 7.37 (t, J = 7.7 Hz, 1H), 7.34 (t, J = 5.9 Hz, 3H), 7.31–7.29 (m, 8H), 7.29–7.27 (m, 3H), 7.27 – 7.23 (m, 3H), 7.23 – 7.19 (m, 3H), 7.17 (d, J = 3.7 Hz, 2H), 7.14 (d, J = 8.7 Hz, 2H), 6.70 (d, J = 8.7 Hz, 2H), 5.58 (d, J = 8.1 Hz, 1H), 5.56 (s, 1H), 5.03 (s, 1H), 4.94 (d, J = 11.4 Hz, 1H), 4.72 – 4.65 (m, 3H), 4.62 (dd, J = 11.2, 6.5 Hz, 2H), 4.42 (d, J = 11.7 Hz, 1H), 4.37 (d, J = 11.7 Hz, 1H), 3.96 (t, J = 8.8 Hz, 2H), 3.68 (s, 3H), 3.66 – 3.62 (m, 1H), 3.60 – 3.56 (m, 2H), 3.47 (dd, J = 8.9, 5.0 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 164.9, 159.0, 148.6, 144.2, 138.7, 138.4, 138.3, 137.9, 133.4, 132.2, 131.5, 130.6, 129.4, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 113.6, 112.3, 94.8, 82.4, 78.1, 75.1, 74.8, 74.0, 73.5, 73.3, 72.9, 67.9, 55.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{50}\text{H}_{52}\text{NO}_8$ 794.3693; found 794.3694. $[\alpha]_D^{35} = +0.14$ (c 0.01, CHCl_3).

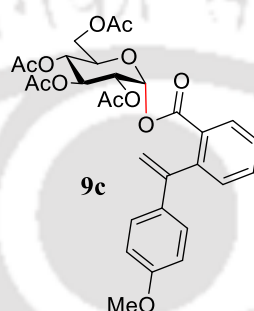
1-O-(2-(1-(4-methoxyphenyl)vinyl)benzoyl)-2,3,4,6-tetra-O-acetyl- α -D-galactopyranose (9b).



Compound **9b** was prepared from **8b** (350 mg, 1 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **9b** (497 mg, 85 %, $\alpha:\beta$ = 1:5) as a white solid, R_f = 0.50 (Hexane/EtOAc, 4:1, v/v. m. p. 95–97 °C.).

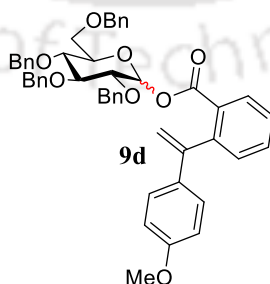
α only) as a colorless syrup, $R_f = 0.31$ (Hexane/EtOAc, 3:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.93 (d, $J = 7.8$ Hz, 1H), 7.55 (dd, $J = 10.8, 4.2$ Hz, 1H), 7.46 (t, $J = 7.6$ Hz, 1H), 7.31 (t, $J = 8.2$ Hz, 3H), 6.85 (d, $J = 8.8$ Hz, 2H), 6.47 (d, $J = 3.5$ Hz, 1H), 5.83 (s, 1H), 5.27 (dd, $J = 10.8, 3.5$ Hz, 1H), 5.20–5.14 (m, 2H), 5.06 (s, 1H), 3.87 (dd, $J = 11.2, 7.1$ Hz, 1H), 3.79 (dd, $J = 9.1, 4.2$ Hz, 1H), 3.77 (s, 3H), 3.46 (t, $J = 6.7$ Hz, 1H), 2.11 (s, 3H), 2.02 (s, 3H), 1.99 (s, 3H), 1.94 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.2, 170.1, 170.0, 170.0, 166.2, 159.5, 147.4, 143.1, 132.3, 132.1, 131.2, 130.7, 130.0, 128.0, 127.6, 113.8, 112.2, 90.7, 68.7, 67.5, 67.4, 66.6, 60.9, 55.2, 20.7, 20.6, 20.6, 20.5. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{30}\text{H}_{36}\text{NO}_{12}$ 602.2238; found 602.2238. $[\alpha]_D^{35} = +0.40$ (c 0.01, CHCl_3).

1-O-(2-(1-(4-methoxyphenyl)vinyl)benzoyl)-2,3,4,6-tetra-O-acetyl- α -D-glucopyranose (9c).



Compound **9c** was prepared from **8c** (540 mg, 1 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **9c** (503 mg, 86 %, α only) as a yellow syrup, $R_f = 0.30$ (Hexane/EtOAc, 3:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.90 (d, $J = 7.7$ Hz, 1H), 7.55 (t, $J = 7.1$ Hz, 1H), 7.46 (t, $J = 7.5$ Hz, 1H), 7.35–7.23 (m, 3H), 6.85 (d, $J = 8.8$ Hz, 2H), 6.42 (d, $J = 3.6$ Hz, 1H), 5.80 (s, 1H), 5.23 (t, $J = 9.9$ Hz, 1H), 5.07 (s, 1H), 5.04 (dd, $J = 10.2, 3.7$ Hz, 1H), 4.98 (t, $J = 9.9$ Hz, 1H), 3.96 (dd, $J = 12.6, 3.6$ Hz, 1H), 3.81–3.76 (m, 4H), 3.43 (d, $J = 10.2$ Hz, 1H), 2.06 (s, 3H), 2.00 (s, 3H), 1.97 (s, 3H), 1.94 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.6, 170.0, 169.7, 169.4, 166.2, 159.5, 147.3, 143.1, 132.3, 132.1, 131.0, 130.5, 130.2, 128.2, 127.6, 113.8, 112.7, 89.9, 70.0, 69.8, 69.4, 67.4, 61.0, 55.2, 20.7, 20.4. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{30}\text{H}_{36}\text{NO}_{12}$ 602.2238; found 602.2237. $[\alpha]_D^{35} = +0.48$ (c 0.01, CHCl_3).

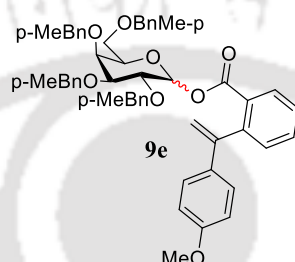
1-O-(2-(1-(4-methoxyphenyl)vinyl)benzoyl)-2,3,4,6-tetra-O-benzyl-D-glucopyranose (9d).



Compound **9d** was prepared from **8d** (540 mg, 1 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **9d** (699.2 mg, 90 %, $\alpha:\beta = 1:10$) as a white solid, $R_f = 0.50$ (Hexane/EtOAc, 4:1, v/v. m. p. 86–88 °C.). The β anomer ^1H NMR (600 MHz, CDCl_3) δ 7.95 (d, $J = 7.8$ Hz, 1H), 7.54 (td, $J = 7.5, 1.0$ Hz, 1H), 7.40 (t, $J = 7.6$ Hz, 1H), 7.32–7.30 (m, 4H), 7.29 (d, $J = 3.1$ Hz, 2H), 7.28 (d, $J = 3.8$ Hz, 3H),

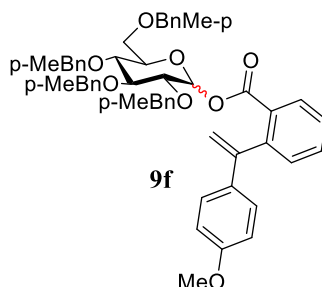
7.27-7.24 (m, $J = 6.8$ Hz, 5H), 7.23-7.20 (m, 3H), 7.18 (d, $J = 8.8$ Hz, 2H), 7.16-7.14 (m, 4H), 6.74 (d, $J = 8.8$ Hz, 2H), 5.65 (d, $J = 8.0$ Hz, 1H), 5.59 (s, 1H), 5.04 (s, 1H), 4.84 (d, $J = 10.9$ Hz, 1H), 4.79 (t, $J = 10.8$ Hz, 2H), 4.62 (t, $J = 9.5$ Hz, 2H), 4.60 – 4.57 (m, 1H), 4.55 (d, $J = 10.7$ Hz, 1H), 4.46 (d, $J = 12.1$ Hz, 1H), 3.73 (dd, $J = 11.6, 5.3$ Hz, 1H), 3.71 (s, 3H), 3.71 – 3.69 (m, 1H), 3.66 (m, 2H), 3.61 – 3.56 (m, 1H), 3.54 – 3.50 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 165.0, 159.1, 148.4, 144.2, 138.4, 138.1, 138.1, 138.0, 133.3, 132.2, 131.5, 130.5, 129.5, 128.4, 128.4, 128.4, 128.3, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 113.6, 112.5, 94.6, 84.8, 81.0, 75.7, 75.6, 75.0, 74.8, 73.5, 68.2, 55.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{50}\text{H}_{52}\text{NO}_8$ 794.3693; found 794.3695. $[\alpha]_{\text{D}}^{35} = +0.16$ (c 0.01, CHCl_3).

1-O-(2-(1-(4-methoxyphenyl)vinyl)benzoyl)-2,3,4,6-tetra-O-*p*-methyl-benzyl-D-galactopyranose (9e).

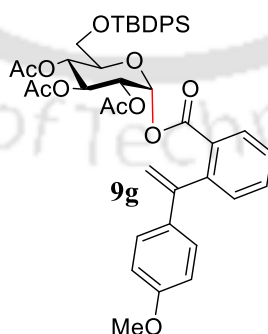


Compound **9e** was prepared from **8e** (597 mg, 1 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **9e** (774 mg, 93 %, $\alpha:\beta = 1:4.5$) as a white solid, $R_f = 0.50$ (Hexane/EtOAc, 4:1, v/v. m. p. 79–81 °C.). The α anomer, ^1H NMR (600 MHz, CDCl_3) δ 7.85 (d, $J = 7.8$ Hz, 1H), 7.46 (t, $J = 7.5$ Hz, 1H), 7.37 (t, $J = 7.6$ Hz, 1H), 7.23 (d, $J = 8.8$ Hz, 1H), 7.20 (d, $J = 8.5$ Hz, 5H), 7.17 – 7.13 (m, 5H), 7.11 (d, $J = 8.2$ Hz, 4H), 7.06 (d, $J = 6.4$ Hz, 4H), 6.73 (d, $J = 8.6$ Hz, 2H), 6.44 (d, $J = 3.5$ Hz, 1H), 5.55 (s, 1H), 4.99 (s, 1H), 4.81 (d, $J = 11.1$ Hz, 1H), 4.61 – 4.56 (m, 2H), 4.53 (d, $J = 12.1$ Hz, 1H), 4.47 – 4.42 (m, 2H), 4.39 (d, $J = 11.6$ Hz, 1H), 4.29 (d, $J = 11.5$ Hz, 1H), 4.05 (dd, $J = 10.0, 3.5$ Hz, 1H), 3.77 – 3.74 (m, 2H), 3.66 (s, 3H), 3.49 (dd, $J = 10.1, 2.1$ Hz, 1H), 3.44 (t, $J = 8.4$ Hz, 1H), 3.35 (dd, $J = 8.9, 5.5$ Hz, 1H), 2.35 (s, 3H), 2.34 (s, 3H), 2.32 (s, 3H), 2.30 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 166.7, 159.2, 147.5, 143.0, 137.4, 137.2, 137.1, 137.0, 135.9, 135.6, 135.3, 135.0, 132.9, 131.4, 131.3, 130.8, 130.5, 129.1, 129.0, 128.9, 128.9, 128.3, 128.3, 128.0, 128.0, 127.4, 127.3, 113.6, 112.9, 91.7, 78.6, 75.3, 74.6, 74.2, 73.3, 72.9, 72.8, 72.1, 68.2, 55.2, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{54}\text{H}_{60}\text{NO}_8$ 850.4319; found 850.4318. $[\alpha]_{\text{D}}^{35} = +0.18$ (c 0.01, CHCl_3).

The β anomer ^1H NMR (600 MHz, CDCl_3) δ 7.91 (d, $J = 7.8$ Hz, 1H), 7.51 (t, $J = 7.5$ Hz, 1H), 7.36 (t, $J = 7.6$ Hz, 1H), 7.30 (d, $J = 7.5$ Hz, 1H), 7.21 (t, $J = 7.3$ Hz, 4H), 7.16 – 7.09 (m, 10H), 7.05 (d, $J = 7.8$ Hz, 2H), 7.01 (d, $J = 7.8$ Hz, 2H), 6.70 (d, $J = 8.7$ Hz, 2H), 5.56 (s, 1H), 5.54 (d, $J = 8.0$ Hz, 1H), 5.02 (s, 1H), 4.88 (d, $J = 11.2$ Hz, 1H), 4.67 – 4.60 (m, 3H), 4.56 (dd, $J = 11.1, 3.6$ Hz, 2H), 4.36 (d, $J = 11.5$ Hz, 1H), 4.31 (d, $J = 11.5$ Hz, 1H), 3.94 – 3.89 (m, 2H), 3.69 (s, 3H), 3.60 – 3.57 (m, 1H), 3.56 – 3.51 (m, 2H), 3.43 (dd, $J = 8.7, 4.8$ Hz, 1H), 2.34 (s, 3H), 2.33 (s, 3H), 2.33 (s, 3H), 2.29 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 164.8, 159.0, 148.6, 144.2, 137.4, 137.3, 137.2, 137.1, 135.8, 135.4, 135.3, 134.9, 133.4, 132.0, 131.4, 130.6, 129.5, 129.1, 129.0, 128.9, 128.8, 128.4, 128.1, 128.0, 127.8, 127.7, 127.3, 113.6, 112.3, 94.8, 82.4, 77.9, 74.9, 74.5, 74.1, 73.3, 73.1, 72.8, 67.8, 55.1, 21.2, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{54}\text{H}_{60}\text{NO}_8$ 850.4319; found 850.4318. $[\alpha]_{\text{D}}^{35} = +0.50$ (c 0.025, CHCl_3).

1-O-(2-(1-(4-methoxyphenyl)vinyl)benzoyl)-2,3,4,6-tetra-O-p-methyl-benzyl-D-glucopyranose (9f).

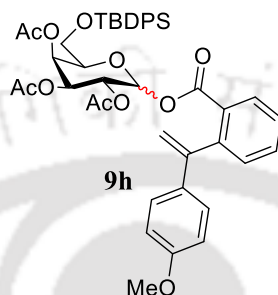
Compound **9f** was prepared from **8f** (597 mg, 1 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **9f** (741 mg, 89 %, $\alpha:\beta$ = 1:1.7) as a white solid, R_f = 0.50 (Hexane/EtOAc, 4:1, v/v. m. p. 83 – 85 °C.). ^1H NMR (600 MHz, CDCl_3) δ 7.94 (d, J = 7.8 Hz, 2H), 7.88 (d, J = 7.8 Hz, 1H), 7.53 (t, J = 7.5 Hz, 2H), 7.48 (t, J = 7.5 Hz, 1H), 7.39 (t, J = 7.5 Hz, 2H), 7.31 (d, J = 7.6 Hz, 2H), 7.27 (d, J = 7.6 Hz, 1H), 7.18 (m, 18H), 7.14 – 7.00 (m, 34H), 6.98 (d, J = 7.7 Hz, 2H), 6.74 (t, J = 7.9 Hz, 6H), 6.36 (d, J = 3.1 Hz, 1H), 5.62 (d, J = 8.0 Hz, 2H), 5.59 (s, 2H), 5.58 (s, 1H), 5.06 (s, 1H), 5.04 (s, 2H), 4.79 (d, J = 10.7 Hz, 2H), 4.74 (d, J = 10.5 Hz, 4H), 4.72 – 4.69 (m, 2H), 4.57 (m, 7H), 4.53 (d, J = 10.9 Hz, 2H), 4.50 (d, J = 11.4 Hz, 1H), 4.45 (d, J = 10.4 Hz, 2H), 4.40 (d, J = 11.9 Hz, 2H), 4.37 – 4.33 (m, 2H), 3.72 (s, 5H), 3.69 (d, J = 9.3 Hz, 2H), 3.66 (dd, J = 8.3, 3.3 Hz, 3H), 3.63 (m, 7H), 3.59 (d, J = 9.5 Hz, 3H), 3.57 – 3.53 (m, 4H), 3.47 (d, J = 9.4 Hz, 2H), 3.41 (d, J = 10.3 Hz, 1H), 2.33 (d, J = 3.9 Hz, 12H), 2.31 (t, J = 4.7 Hz, 18H), 2.29 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 166.2, 164.9, 159.2, 159.1, 148.4, 147.9, 144.2, 143.3, 137.5, 137.4, 137.4, 137.3, 137.3, 137.2, 137.2, 135.8, 135.5, 135.5, 135.1, 135.1, 135.1, 134.9, 134.8, 133.3, 133.1, 132.2, 131.7, 131.4, 131.0, 130.9, 130.6, 130.3, 129.5, 129.1, 129.0, 129.0, 129.0, 128.9, 128.2, 128.2, 128.1, 128.1, 128.1, 128.1, 128.0, 127.9, 127.8, 127.4, 127.4, 113.6, 113.6, 112.8, 112.4, 94.6, 90.8, 84.7, 80.8, 78.7, 77.1, 76.6, 75.6, 75.5, 75.4, 74.9, 74.8, 74.7, 73.4, 73.0, 72.7, 67.9, 67.7, 55.2, 55.1, 21.2, 21.2, 21.2, 21.2, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{54}\text{H}_{60}\text{NO}_8$ 850.4319; found 850.4319. $[\alpha]_D^{35} = +0.36$ (c 0.01, CHCl_3).

1-O-(2-(1-(4-methoxyphenyl)vinyl)benzoyl)-2,3,4-tri-O-acetyl-6-O-tert-butyldiphenylsilyl- α -D-glucopyranose (9g).

Compound **9g** was prepared from **8g** (545 mg, 1 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **9g** (694 mg, 89 %, α only) as a colorless syrup, R_f = 0.30 (Hexane/EtOAc, 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.90 – 7.87 (m, 1H), 7.64 – 7.58 (m, 4H), 7.52 (td, J = 7.5, 1.2 Hz, 1H), 7.45 – 7.39 (m, 3H), 7.39 – 7.34 (m, 4H), 7.29 – 7.24 (m, 1H), 7.22 (d, J = 8.8 Hz, 2H), 6.71 (d, J = 8.8 Hz, 2H), 6.45 (d, J = 3.7 Hz, 1H), 5.74 (s, 1H), 5.28 – 5.15 (m, 2H), 5.05 (dd, J = 10.6, 4.5 Hz, 1H),

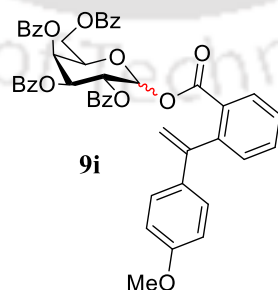
5.04 (s, 1H), 3.59 (s, 3H), 3.47 (dd, $J = 12.8, 3.0$ Hz, 1H), 3.37 (d, $J = 9.6$ Hz, 2H), 2.01 (s, 3H), 1.92 (s, 3H), 1.89 (s, 3H), 1.01 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.4, 169.9, 169.1, 166.2, 159.3, 147.4, 143.2, 135.7, 135.7, 133.1, 132.9, 132.4, 132.0, 131.0, 130.4, 130.4, 129.7, 129.7, 128.1, 127.7, 127.7, 127.5, 113.6, 112.7, 90.2, 72.3, 70.7, 69.7, 67.6, 61.3, 55.0, 26.7, 20.8, 20.4, 20.4, 19.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{44}\text{H}_{52}\text{NO}_{11}\text{Si}$ 798.3310; found 798.3310. $[\alpha]_{\text{D}}^{35} = +2.66$ (c 0.04, CHCl_3).

1-O-(2-(1-(4-methoxyphenyl)vinyl)benzoyl)-2,3,4-tri-O-acetyl-6-O-tert-butylidiphenylsilyl-D-galactopyranose (9h).



Compound **9h** was prepared from **8h** (545 mg, 1 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **9h** (725 mg, 91 %, $\alpha:\beta = 8:1$) as a colourless syrup, $R_f = 0.30$ (Hexane/EtOAc, 4:1, v/v). The α anomer, ^1H NMR (600 MHz, CDCl_3) δ 7.89 (d, $J = 7.5$ Hz, 1H), 7.58 (t, $J = 6.5$ Hz, 5H), 7.47 (t, $J = 7.2$ Hz, 1H), 7.44 – 7.40 (m, 2H), 7.36 (dd, $J = 14.0, 6.9$ Hz, 4H), 7.30 (d, $J = 7.5$ Hz, 1H), 7.23 (d, $J = 8.8$ Hz, 2H), 6.78 (d, $J = 8.8$ Hz, 2H), 6.39 (d, $J = 3.4$ Hz, 1H), 5.68 (s, 1H), 5.48 (d, $J = 1.8$ Hz, 1H), 5.24 (dd, $J = 10.9, 3.5$ Hz, 1H), 5.19 (dd, $J = 10.9, 3.0$ Hz, 1H), 5.05 (s, 1H), 3.92 (t, $J = 6.8$ Hz, 1H), 3.71 (s, 3H), 3.59 (dd, $J = 9.9, 5.9$ Hz, 1H), 3.51 – 3.47 (m, 1H), 1.98 (s, 3H), 1.96 (s, 3H), 1.86 (s, 3H), 1.01 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.1, 170.0, 169.9, 166.1, 159.4, 148.0, 143.2, 135.6, 135.6, 132.9, 132.8, 132.4, 132.1, 131.2, 130.4, 130.2, 129.9, 129.8, 128.0, 127.8, 127.7, 127.6, 113.8, 112.2, 90.6, 71.4, 67.9, 67.4, 66.9, 61.0, 55.2, 26.7, 20.7, 20.6, 20.4, 19.0. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{44}\text{H}_{52}\text{NO}_{11}\text{Si}$ 798.3310; found 798.3310. $[\alpha]_{\text{D}}^{35} = +2.80$ (c 0.04, CHCl_3).

1-O-(2-(1-(4-methoxyphenyl)vinyl)benzoyl)-2,3,4,6-tetra-O-benzoyl-D-galactopyranose (9i).

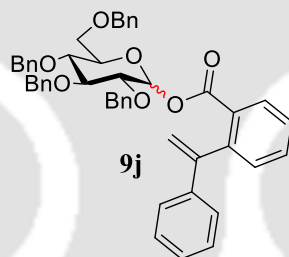


Compound **9i** was prepared from **8i** (596.59 mg, 1 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **9i** (732.92 mg, 88 %, $\alpha:\beta = 2.5:1$) as a colourless syrup, $R_f = 0.45$ (Hexane/EtOAc, 3:1, v/v). The α anomer ^1H NMR (500 CDCl_3) δ 8.02 (d, $J = 7.6$ Hz, 2H), 7.96 (d, $J = 7.7$ Hz, 2H), 7.89 – 7.83 (m, 3H), 7.78 (d, $J = 7.6$ Hz, 2H), 7.60 (t, $J = 7.4$ Hz, 1H), 7.55 (t, $J = 7.4$ Hz, 2H), 7.51 – 7.37 (m, 10H),

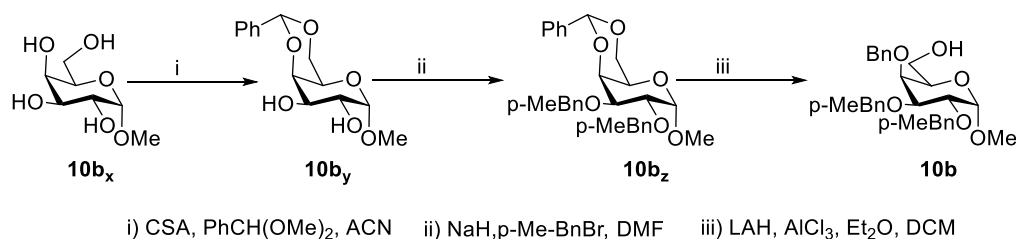
7.35 – 7.29 (m, 3H), 7.27 – 7.23 (m, 1H), 6.84 – 6.79 (m, 3H), 5.93 (s, 1H), 5.83 (dd, $J = 10.7$, 3.3 Hz, 1H), 5.79 (dd, $J = 10.7$, 2.9 Hz, 1H), 5.73 (s, 1H), 5.10 (s, 1H), 4.34 (dd, $J = 11.2$, 6.6 Hz, 1H), 4.09 (dd, $J = 11.2$, 7.1 Hz, 1H), 3.75 (t, $J = 6.6$ Hz, 1H), 3.59 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 166.4, 165.7, 165.6, 165.4, 165.4, 159.6, 147.5, 143.0, 133.6, 133.4, 133.3, 133.2, 132.2, 132.0, 131.1, 130.8, 130.2, 129.9, 129.8, 129.7, 129.5, 129.0, 129.0, 128.9, 128.7, 128.4, 128.3, 128.0, 127.6, 114.0, 112.4, 90.9, 69.2, 68.5, 68.3, 67.8, 61.5, 55.1. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{50}\text{H}_{44}\text{NO}_{12}$ 850.2858; found 850.2862. $[\alpha]_{\text{D}}^{35} = +1.02$ (c 0.02, CHCl_3).

The β anomer ^1H NMR (500 MHz, CDCl_3) δ 8.07 (d, $J = 7.3$ Hz, 2H), 7.99 (d, $J = 7.3$ Hz, 2H), 7.90 (d, $J = 7.8$ Hz, 1H), 7.87 (d, $J = 7.4$ Hz, 2H), 7.78 (d, $J = 7.3$ Hz, 2H), 7.63 (t, $J = 7.5$ Hz, 1H), 7.57 – 7.47 (m, 6H), 7.43 – 7.38 (m, 4H), 7.34 (t, $J = 7.7$ Hz, 2H), 7.28 – 7.22 (m, 2H), 7.13 (d, $J = 8.8$ Hz, 2H), 6.74 (d, $J = 8.8$ Hz, 2H), 6.10 (d, $J = 8.3$ Hz, 1H), 6.02 (d, $J = 3.0$ Hz, 1H), 5.99 – 5.91 (m, 1H), 5.63 (dd, $J = 10.3$, 3.4 Hz, 1H), 5.48 (d, $J = 12.1$ Hz, 1H), 4.93 (s, 1H), 4.56 (dd, $J = 11.0$, 6.1 Hz, 1H), 4.41 (t, $J = 6.5$ Hz, 1H), 4.34 (dd, $J = 11.0$, 7.1 Hz, 1H), 3.75 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 164.9, 164.4, 164.4, 164.1, 163.8, 158.1, 147.2, 143.1, 132.6, 132.4, 132.3, 132.2, 132.1, 131.3, 130.3, 129.3, 129.0, 128.8, 128.8, 128.7, 128.3, 128.0, 127.9, 127.9, 127.7, 127.6, 127.4, 127.4, 127.3, 126.8, 126.5, 112.5, 111.5, 91.7, 71.2, 70.7, 67.6, 66.8, 60.5, 54.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{50}\text{H}_{44}\text{NO}_{12}$ 850.2858; found 850.2861. $[\alpha]_{\text{D}}^{35} = +1.15$ (c 0.02, CHCl_3).

1-O-(2-(1-phenylvinyl)benzoyl)-2,3,4,6-tetra-O-benzyl-D-glucopyranose (**9j**).



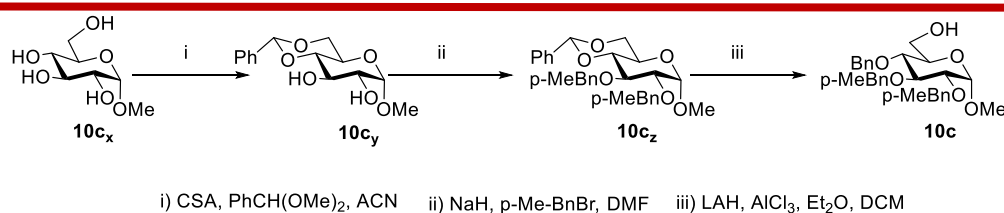
Compound **9j** was prepared from **8d** (540 mg, 1 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **9j** (699.2 mg, 90 %, $\alpha:\beta = 1:2.4$) as a white solid, $R_f = 0.50$ (Hexane/EtOAc, 4:1, v/v. m. p. 103–105 °C.). ^1H NMR (400 MHz, CDCl_3) δ 7.96 (dd, $J = 7.8$, 1.0 Hz, 1H), 7.90 (dd, $J = 7.7$, 1.1 Hz, 1H), 7.55 (td, $J = 7.5$, 1.3 Hz, 1H), 7.52 – 7.48 (m, 1H), 7.41 (td, $J = 7.6$, 1.1 Hz, 2H), 7.35 – 7.08 (m, 34H), 6.40 (d, $J = 3.4$ Hz, 1H), 5.69 (s, 1H), 5.69 (s, 1H), 5.63 (d, $J = 8.0$ Hz, 1H), 5.17 (s, 1H), 5.15 (s, 2H), 4.83 (t, $J = 7.5$ Hz, 2H), 4.77 (dd, $J = 11.6$, 2.0 Hz, 3H), 4.63 (d, $J = 6.9$ Hz, 1H), 4.62 – 4.58 (m, 3H), 4.55 (d, $J = 7.6$ Hz, 2H), 4.52 (d, $J = 8.6$ Hz, 1H), 4.47 (d, $J = 2.2$ Hz, 1H), 4.42 (d, $J = 13.3$ Hz, 1H), 3.75 (d, $J = 9.1$ Hz, 1H), 3.71 (t, $J = 4.5$ Hz, 1H), 3.68 (d, $J = 8.6$ Hz, 2H), 3.65 (d, $J = 3.9$ Hz, 2H), 3.62 (dd, $J = 5.6$, 2.8 Hz, 2H), 3.60 – 3.54 (m, 2H), 3.53–3.51 (m, 1H), 3.501–3.48 (s, 1H), 3.45 (dd, $J = 11.8$, 2.8 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 166.1, 164.9, 149.0, 148.5, 143.9, 143.1, 140.5, 140.3, 138.8, 138.4, 138.4, 138.1, 138.1, 138.0, 137.9, 137.9, 132.3, 131.8, 131.6, 131.1, 130.8, 130.6, 130.4, 129.4, 128.4, 128.4, 128.3, 128.3, 128.2, 127.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 127.5, 127.0, 126.6, 114.7, 114.2, 94.6, 90.7, 84.8, 81.6, 80.9, 78.9, 77.3, 75.7, 75.6, 75.5, 75.0, 74.9, 74.8, 73.6, 73.5, 73.1, 72.8, 68.2, 68.0. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{49}\text{H}_{50}\text{NO}_7$ 764.3587; found 764.3588. $[\alpha]_{\text{D}}^{35} = +1.22$ (c 0.02, CHCl_3).

Methyl 4-O-benzyl-2,3-di-O-p-methylbenzyl- α -D-galactopyranoside (10b).

A catalytic amount of camphorsulfonic acid (pH = 2) was added to a CH₃CN solution (100.0 mL) of methyl α -D-galactopyranoside (5.0 g, 25.7 mmol, **10b_x**) and PhCH(OMe)₂ (11.6 mL, 77.1 mmol). The resulting solution was stirred at rt for 48 h, then neutralized with TEA and concentrated *in vacuo*. The crude was washed with water, and brine, dried over Na₂SO₄, concentrated *in vacuo*. The crude reaction mixture, dissolved in DMF, was treated with NaH, followed by para methyl-benzyl bromide (p-Me-BnBr) at 0 °C. The resulting solution was stirred at room temperature for overnight. After completion of the reaction, MeOH was added to quench the excess NaH. The reaction mixture was concentrated *in vacuo*; then the crude was diluted with H₂O and extracted with CH₂Cl₂ (3 x 50.0 mL). The combined organic layers were washed with brine, dried over Na₂SO₄, concentrated *in vacuo*, and purified by flash column chromatography (hexane/AcOEt = 8:2) to get **10b_z** as a white solid (8.5 g, 67 % over two steps). ¹H NMR (600 MHz, CDCl₃) δ 7.51 (d, *J* = 6.5 Hz, 2H), 7.38 – 7.33 (m, 3H), 7.30 (d, *J* = 7.8 Hz, 2H), 7.26 (t, *J* = 6.8 Hz, 2H), 7.16 – 7.12 (m, 4H), 5.48 (s, 1H), 4.85 (d, *J* = 11.9 Hz, 1H), 4.80 (d, *J* = 12.2 Hz, 1H), 4.73 – 4.68 (m, 2H), 4.64 (d, *J* = 11.9 Hz, 1H), 4.19 (d, *J* = 12.3 Hz, 1H), 4.15 (d, *J* = 2.8 Hz, 1H), 4.03 (dd, *J* = 10.1, 3.5 Hz, 1H), 4.01 – 3.97 (m, 1H), 3.95 (dd, *J* = 10.1, 3.3 Hz, 1H), 3.56 (s, 1H), 3.37 (s, 3H), 2.34 (s, 3H), 2.34 (s, 3H). ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 137.8, 137.4, 137.3, 135.7, 135.5, 129.1, 129.0, 128.3, 128.2, 127.8, 126.4, 101.2, 99.6, 75.7, 75.1, 74.9, 73.7, 72.2, 69.4, 62.4, 55.6, 21.3, 21.3.

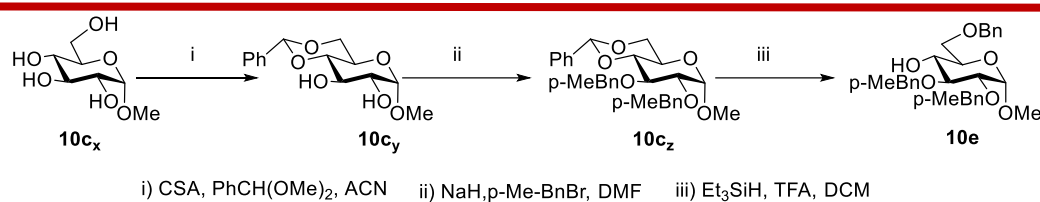
Methyl 2,3-di-paramethyl-O-benzyl-4,6-O-benzylidene- α -D-galactopyranoside (2 g, 4.08 mmol, **10b_z**) was dissolved in CH₂Cl₂/Et₂O (1:1, 20 mL) and stirred at rt under an N₂ atm. After 10 min., LiAlH₄ (1.08 g, 28.56 mmol) was added at 0 °C and the mixture was heated to reflux. After 10 min AlCl₃ (2.72 g, 20.40 mmol), dissolved in Et₂O (1.0 mL) was added at 0 °C and the mixture was heated to reflux. After 1.5 h, the mixture was removed from the heat and excess LiAlH₄ was quenched with EtOAc. The mixture was diluted with Et₂O and washed once with water. The water phase was extracted once with Et₂O and the combined organic phases were washed three times with water, dried over MgSO₄ and concentrated. The crude was purified by flash column chromatography (Hexane/AcOEt = 8:2) to yield compound **10b** as a white solid (1.65 g, 82 %. m. p. 72–74 °C.). ¹H NMR (600 MHz, CDCl₃) δ 7.34 – 7.33 (m, 2H), 7.32 – 7.28 (m, 5H), 7.26 (d, *J* = 7.9 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 7.13 (d, *J* = 7.8 Hz, 2H), 4.97 (d, *J* = 11.6 Hz, 1H), 4.85 (d, *J* = 11.5 Hz, 1H), 4.82 (d, *J* = 11.9 Hz, 1H), 4.70 (d, *J* = 11.5 Hz, 1H), 4.66 (d, *J* = 2.6 Hz, 1H), 4.64 (dd, *J* = 10.5, 8.7 Hz, 2H), 4.02 (dd, *J* = 10.1, 3.6 Hz, 1H), 3.91 (dd, *J* = 10.1, 2.8 Hz, 1H), 3.84 (d, *J* = 2.5 Hz, 1H), 3.72 – 3.66 (m, 2H), 3.46 (dd, *J* = 9.2, 6.7 Hz, 1H), 3.35 (s, 3H), 2.37 (s, 3H), 2.34 (s, 3H). ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 138.2, 137.4, 137.3, 135.7, 135.4, 129.1, 129.0, 128.7, 128.5, 128.2, 128.0, 127.7, 99.0, 79.0, 76.1, 75.1, 74.4, 73.6, 73.5, 70.2, 62.5, 55.4, 22.7, 21.2, 21.2. HRMS (ESI) *m/z*: [M + NH₄]⁺ calcd for C₃₀H₄₀NO₆ 510.2856; found 510.2850. [α]_D³⁵ = - 0.18 (c 0.01, CHCl₃).

Methyl 4-O-benzyl-2,3-di-O-p-methylbenzyl- α -D-glucopyranoside (10c).



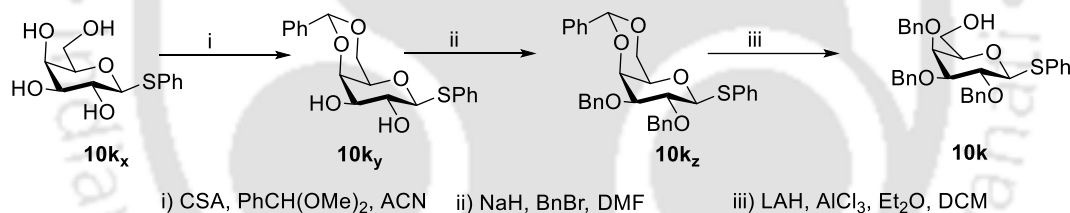
A catalytic amount of camphorsulfonic acid (pH = 2) was added to a CH₃CN solution (100.0 mL) of methyl α -D-glucopyranoside (5.0 g, 25.7 mmol, **10c_x**) and PhCH(OMe)₂ (11.6 mL, 77.1 mmol). The resulting solution was stirred at rt for 48 h, then neutralized with TEA and concentrated in vacuo. The crude was washed with water, brine, dried over Na₂SO₄, concentrated in vacuo. The crude reaction mixture, dissolved in DMF, was treated with NaH, followed by Para methyl-benzyl bromide (p-Me-BnBr) at 0 °C. The resulting solution was stirred at room temperature for overnight. After completion of the reaction, MeOH was added to quench excess NaH. The reaction mixture was concentrated in vacuo; then the crude was diluted with H₂O and extracted with CH₂Cl₂ (3 x 50.0 mL). The combined organic layers were washed with brine, dried over Na₂SO₄, concentrated in vacuo, and purified by flash column chromatography (hexane/AcOEt = 8:2) to get Methyl 2,3-di-paramethyl-O-benzyl-4,6-O-benzylidene- α -D-glucopyranoside (**10c_z**) as a white solid (8.2 g, 65 % yield over two steps). ¹H NMR (600 MHz, CDCl₃) δ 7.49 (d, J = 6.5 Hz, 2H), 7.41 – 7.36 (m, 3H), 7.29 – 7.24 (m, 4H), 7.13 (dd, J = 12.8, 7.8 Hz, 4H), 5.54 (s, 1H), 4.86 (d, J = 11.0 Hz, 1H), 4.83 (d, J = 12.1 Hz, 1H), 4.80 (d, J = 11.0 Hz, 1H), 4.66 (d, J = 12.1 Hz, 1H), 4.53 (d, J = 3.6 Hz, 1H), 4.26 (dd, J = 10.2, 4.8 Hz, 1H), 4.02 (t, J = 9.3 Hz, 1H), 3.81 (td, J = 10.0, 4.8 Hz, 1H), 3.70 (t, J = 10.3 Hz, 1H), 3.58 (t, J = 9.4 Hz, 1H), 3.52 (dd, J = 9.3, 3.7 Hz, 1H), 3.39 (s, 3H), 2.35 (s, 3H), 2.34 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 136.6, 136.5, 136.2, 134.7, 134.2, 128.1, 128.0, 127.9, 127.2, 127.2, 127.1, 125.0, 100.3, 98.4, 81.2, 77.9, 77.4, 74.2, 72.6, 68.1, 61.3, 54.3, 20.3. Methyl 2,3-di-p-methyl-O-benzyl-4,6-O-benzylidene- α -D-glucopyranoside (2g, 4.08 mmol, **10c_z**) was dissolved in CH₂Cl₂/Et₂O (1:1, 20 mL) and stirred at rt under a N₂ atm. After 10 min., LiAlH₄ (1.08 g, 28.56 mmol) was added at 0 °C and the mixture was heated to reflux. After 10 min, AlCl₃ (2.72 g, 20.40 mmol), dissolved in Et₂O (1.0 mL) at 0 °C and the mixture was heated to reflux. After 1.5 h, the mixture was removed from the heat and excess LiAlH₄ was quenched with EtOAc. The mixture was diluted with Et₂O and washed once with water. The water phase was extracted once with Et₂O and the combined organic phases were washed three times with water, dried over MgSO₄ and concentrated. The crude was purified by flash column chromatography (Hexane/AcOEt = 8:2) to yield compound **10c** as a white solid (1.65 g, 82 %. m. p. 62 – 64 °C.). ¹H NMR (600 MHz, CDCl₃) δ 7.35 – 7.31 (m, 2H), 7.29 (d, J = 6.0 Hz, 3H), 7.25 (dd, J = 7.9, 2.2 Hz, 4H), 7.14 (d, J = 7.4 Hz, 4H), 4.94 (d, J = 10.6 Hz, 1H), 4.88 (d, J = 11.0 Hz, 1H), 4.79 (d, J = 3.9 Hz, 1H), 4.77 (d, J = 5.4 Hz, 1H), 4.62 (d, J = 11.5 Hz, 2H), 4.51 (d, J = 3.5 Hz, 1H), 3.98 (t, J = 9.3 Hz, 1H), 3.77 – 3.72 (m, 1H), 3.67 (m, 1H), 3.65 – 3.61 (m, 1H), 3.50 (d, J = 9.4 Hz, 1H), 3.48 – 3.44 (m, 1H), 3.35 (s, 3H), 2.34 (s, 6H). ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 138.2, 137.7, 137.4, 135.7, 135.1, 129.2, 129.1, 128.5, 128.3, 128.2, 128.1, 127.9, 98.3, 81.8, 79.7, 77.4, 75.7, 75.0, 73.3, 70.6, 61.9, 55.2, 21.2. HRMS (ESI) m/z: [M + NH₄]⁺ calcd for C₃₀H₄₀NO₆ 510.2856; found 510.2855. [α]_D³⁵ = + 0.16 (c 0.01, CHCl₃).

Methyl 6-O-benzyl-2,3-di-O-p-methylbenzyl- α -D-glucopyranoside (3e).



To a cooled solution (0 °C) of **10cz** (2 g, 4.08 mmol) and Et₃SiH (3.26 mL, 20.4 mmol) in dry CH₂Cl₂ (40.0 mL), trifluoroacetic acid (1.56 mL, 20.4 mmol) was slowly added (15 min). The resulting solution was stirred at rt for three hours, and then the mixture was diluted with CH₂Cl₂ and neutralized with a saturated aqueous solution of NaHCO₃. The two phases were separated, and the organic layer was washed with a saturated aqueous solution of NaHCO₃ and brine, dried over Na₂SO₄, and concentrated *in vacuo*. The crude was purified by flash column chromatography (Hexane/AcOEt = 8:2) to yield compound **10e** as a white solid (1.53 g, 76 % m. p. 88 – 90 °C.). ¹H NMR (600 MHz, CDCl₃) δ 7.34 – 7.29 (m, 4H), 7.26 (t, *J* = 7.2 Hz, 5H), 7.16 (d, *J* = 7.8 Hz, 2H), 7.14 (d, *J* = 7.8 Hz, 2H), 4.96 (d, *J* = 11.3 Hz, 1H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.66 (d, *J* = 11.3 Hz, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.60 – 4.55 (m, 2H), 4.53 (d, *J* = 12.2 Hz, 1H), 3.74 (t, *J* = 9.2 Hz, 1H), 3.70–3.67 (m, 1H), 3.66 – 3.63 (m, 2H), 3.56 (t, *J* = 9.3 Hz, 1H), 3.50 (dd, *J* = 9.6, 3.5 Hz, 1H), 3.37 (s, 3H), 2.34 (s, 3H), 2.33 (s, 3H). ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 138.1, 137.7, 137.7, 135.8, 135.0, 129.4, 129.2, 128.4, 128.3, 128.2, 127.6, 98.3, 81.2, 79.3, 75.3, 73.6, 73.1, 70.5, 69.9, 69.4, 55.3, 21.3, 21.2. HRMS (ESI) *m/z*: [M + NH₄]⁺ calcd for C₃₀H₄₀NO₆ 510.2856; found 510.2856. [α]_D³⁵ = + 0.30 (*c* 0.015, CHCl₃).

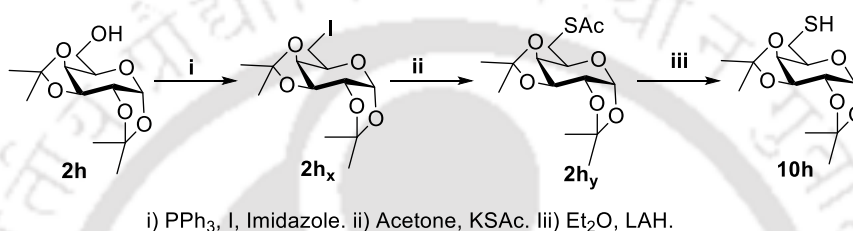
1-Phenyl mercapto-2,3,4-tri-*O*-benzyl-β-*D*-galactopyranoside (**10k**).



A catalytic amount of camphorsulfonic acid (pH = 2) was added to a CH₃CN solution (100.0 mL) of phenyl mercapto β-*D*-galactopyranoside (7.0 g, 25.7 mmol, **10kx**) and PhCH(OMe)₂ (11.6 mL, 77.1 mmol). The resulting solution was stirred at rt for 48 h, then neutralized with TEA and concentrated *in vacuo*. The crude was washed with water, and brine, dried over Na₂SO₄, concentrated *in vacuo*. The crude reaction mixture, dissolved in DMF, was treated with NaH, followed by benzyl bromide at 0 °C. The resulting solution was stirred at room temperature for overnight. After completion of the reaction, MeOH was added to quench excess NaH. The reaction mixture was concentrated *in vacuo*; then the crude was diluted with H₂O and extracted with CH₂Cl₂ (3 x 50.0 mL). The combined organic layers were washed with brine, dried over Na₂SO₄, concentrated *in vacuo*, and purified by flash column chromatography (hexane/AcOEt = 4:1) to get **10kz** as a white solid (9 g, 65 % yield over two steps). Phenyl mercapto 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-*D*-galactopyranoside (2.2 g, 4.07 mmol, **10kz**) was dissolved in CH₂Cl₂/Et₂O (1:1, 30 mL) and stirred at rt under an N₂ atmosphere. After 10 min., LiAlH₄ (1.08 g, 28.56 mmol) was added at 0 °C, and the mixture was heated to reflux. After an additional 10 min, AlCl₃ (2.72 g, 20.40 mmol) dissolved in Et₂O (1.0 mL) was added at 0 °C and the mixture was heated to reflux. After 1.5 h the mixture was removed from the heat and excess LiAlH₄ was quenched with EtOAc. The mixture was diluted with Et₂O and washed once with water. The water phase was extracted once with Et₂O and the combined organic phases were washed three times with water, dried over MgSO₄, and concentrated. The

crude was purified by flash column chromatography (Hexane/AcOEt = 4:1) to yield compound **10k** as a white solid (1.66 g, 75 % m. p. 89 - 91 °C.). ¹H NMR (600 MHz, CDCl₃) δ 7.54 (dd, *J* = 7.1, 2.1 Hz, 2H), 7.39 (d, *J* = 7.1 Hz, 2H), 7.37 – 7.27 (m, 13H), 7.24 – 7.19 (m, 3H), 4.97 (d, *J* = 11.6 Hz, 1H), 4.81 (d, *J* = 10.2 Hz, 1H), 4.75 (d, *J* = 10.3 Hz, 3H), 4.64 (t, *J* = 10.0 Hz, 2H), 3.95 (t, *J* = 9.4 Hz, 1H), 3.86 – 3.78 (m, 2H), 3.60 (dd, *J* = 9.2, 2.6 Hz, 1H), 3.54 – 3.47 (m, 1H), 3.45 – 3.42 (m, 1H). ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 138.4, 138.3, 138.2, 134.0, 131.6, 128.9, 128.5, 128.4, 128.4, 128.3, 128.2, 127.8, 127.8, 127.8, 127.7, 127.2, 87.7, 84.3, 78.9, 77.6, 75.7, 74.3, 73.5, 73.1, 62.3. HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₃₃H₃₄NaO₅S 565.2025; found 565.2028. [α]_D³⁵ = + 0.10 (c 0.01, CHCl₃).

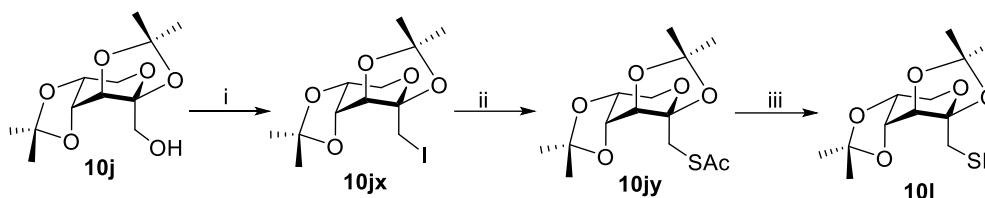
6-mercapto -1,2:3,4-di-O-isopropylidene- α -D-galactopyranose (**10h**).



1g of **2h** (3.84 mmol) was dissolved in 30 ml of toluene. 3g of triphenyl phosphine (11.52 mmol), 1.9 g of Iodine (7.68 mmol) and 1g of imidazole were added to the reaction mixture. Then the mixture was kept in refluxed condition for 5 h. After completion of reaction, solvent was evaporated, dissolved in DCM, worked up with water, dried with sodium sulfate and concentrated in rotavapour. The crude was purified by flash column chromatography (Hexane/AcOEt = 8:2) to yield compound **2hx** as a colorless liquid (1.38 g, 97 %). ¹H NMR (500 MHz, CDCl₃) δ 5.54 (d, *J* = 4.9 Hz, 1H), 4.61 (dd, *J* = 7.8, 1.9 Hz, 1H), 4.40 (d, *J* = 7.8 Hz, 1H), 4.30 (dd, *J* = 4.8, 2.3 Hz, 1H), 3.95 (t, *J* = 6.7 Hz, 1H), 3.32 (dd, *J* = 9.8, 7.0 Hz, 1H), 3.21 (dd, *J* = 9.8, 7.3 Hz, 1H), 1.54 (s, 3H), 1.45 (s, 3H), 1.35 (s, 3H), 1.34 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 107.2, 106.6, 94.4, 69.3, 68.8, 68.3, 66.7, 23.7, 23.7, 22.6, 22.2, 21.0. Compound **2hx** was dissolved in 30 ml of acetone. To the reaction mixture 1.7 g of potassium thioacetate were dissolved and the reaction mixture was kept at refluxed condition for 2 days. After completion of the reaction, acetone was evaporated, worked up with DCM, dried with sodium sulfate and concentrated in rotavapour. The crude was purified by flash column chromatography (Hexane/AcOEt = 8:2) to yield compound **2hy** as a colorless liquid (1.11 g, 94 %). ¹H NMR (500 MHz, CDCl₃) δ 5.51 (d, *J* = 4.5 Hz, 1H), 4.61 (d, *J* = 7.7 Hz, 1H), 4.31-4.23 (m, 2H), 3.85 (d, *J* = 3.9 Hz, 1H), 3.16 (dd, *J* = 13.7, 4.6 Hz, 1H), 3.04 (dd, *J* = 13.5, 8.8 Hz, 1H), 2.34 (s, 3H), 1.48 (s, 3H), 1.45 (s, 3H), 1.35 (s, 3H), 1.32 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 194.8, 108.5, 107.8, 95.5, 71.1, 70.0, 69.5, 65.8, 29.5, 28.7, 24.9, 24.9, 24.0, 23.4. Compound **2hy** was dissolved in 30 ml of diethyl ether. To the reaction mixture 140 mg of LAH were added at – 30 °C. Then the reaction mixture was kept at rt for 1 h. After completion of the reaction, saturated solution of ammonium chloride was added, filtered off, dried with sodium sulfate and concentrated in rotavapour. The crude was purified by flash column chromatography (Hexane/AcOEt = 8:1) to yield compound **10h** as a colorless liquid (809 mg, 84 %). ¹H NMR (500 MHz, CDCl₃) δ 5.53 (d, *J* = 5.0 Hz, 1H), 4.62 (dd, *J* = 7.9, 2.4 Hz, 1H), 4.35 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.32 (dd, *J* = 5.0, 2.4 Hz, 1H), 3.79 (td, *J* = 7.0, 1.6 Hz, 1H), 2.77 (dt, *J* = 14.5, 7.3 Hz, 1H), 2.67 (ddd, *J* = 13.5, 9.8, 6.7 Hz, 1H), 1.62 (dd, *J* = 9.8, 7.5 Hz, 1H), 1.55 (s, 3H), 1.44 (s, 3H), 1.35 (s, 3H), 1.34 (s, 3H). ¹³C{¹H} NMR (126 MHz, CDCl₃)

δ 108.3, 107.7, 95.6, 70.3, 69.9, 69.6, 68.9, 25.0, 24.0, 23.9, 23.5, 23.4. HRMS (ESI) m/z : $[M + Na]^+$ calcd for $C_{12}H_{20}O_5SNa$ 299.0924; found 299.0924. $[\alpha]_D^{35} = +0.70$ (c 0.015, $CHCl_3$).

1-mercapto-1-deoxy-2,3:4,5-di-O-isopropylidene- β -D-fructopyranose (**10l**)



i) PPh_3 , I, Imidazole. ii) DMF, KSAc. iii) Et_2O , LAH.

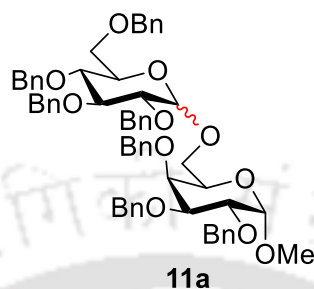
1 g of **10j** (3.84 mmol) was dissolved in 30 ml of toluene. 3 g of triphenyl phosphine (11.52 mmol), 1.9 g of Iodine (7.68 mmol) and 1 g of imidazole were added to the reaction mixture. Then the mixture was kept in refluxed condition for 5 h. After completion of reaction, solvent was evaporated, dissolved in DCM, worked up with water, dried with sodium sulfate and concentrated in rotavapour. The crude was purified by flash column chromatography (Hexane/ $AcOEt$ = 8:2) to yield compound **10j_x** as a colorless liquid (1.35 g, 95 %). 1H NMR (500 MHz, $CDCl_3$) δ 4.52 (dd, J = 7.9, 2.5 Hz, 1H), 4.24 (d, J = 2.6 Hz, 1H), 4.16 (d, J = 7.8 Hz, 1H), 3.83 (dd, J = 13.0, 1.6 Hz, 1H), 3.72 (d, J = 13.0 Hz, 1H), 3.46 (d, J = 10.7 Hz, 1H), 3.27 (d, J = 10.7 Hz, 1H), 1.47 (s, 3H), 1.41 (s, 3H), 1.36 (s, 3H), 1.28 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 108.2, 107.4, 99.3, 70.8, 69.7, 69.6, 61.0, 25.5, 25.0, 24.3, 23.2. Compound **10j_x** was dissolved in 30 ml of DMF. To the reaction mixture 1.7 g of potassium thioacetate were dissolved and the reaction mixture were kept at 90 °C for 5 h. After completion of the reaction, worked up with DCM, dried with sodium sulfate and concentrated in rota vapour. The crude was purified by flash column chromatography (Hexane/ $AcOEt$ = 8:2) to yield compound **10j_y** as a colorless liquid (1.07 g, 92 %). 1H NMR (500 MHz, $CDCl_3$) δ 4.57 (dd, J = 7.9, 2.3 Hz, 1H), 4.21 (t, J = 4.8 Hz, 2H), 3.84 (dd, J = 13.0, 1.3 Hz, 1H), 3.74 (d, J = 13.0 Hz, 1H), 3.41 – 3.33 (m, 2H), 2.36 (s, 3H), 1.53 (s, 3H), 1.51 (s, 3H), 1.41 (s, 3H), 1.34 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 193.5, 108.1, 107.4, 101.4, 72.0, 69.6, 69.3, 60.4, 36.6, 29.4, 25.3, 24.8, 23.9, 23.1. Compound **10j_y** was dissolved in 30 ml of diethyl ether. To the reaction mixture 140 mg of LAH were added at – 30 °C. Then the reaction mixture was kept at rt for 1 h. After completion of the reaction, saturated solution of ammonium chloride was added, filtered off, dried with sodium sulfate and concentrated in rota vapour. The crude was purified by flash column chromatography (Hexane/ $AcOEt$ = 8:1) to yield compound **10l** as a colorless liquid (743 mg, 80 %). 1H NMR (500 MHz, $CDCl_3$) δ 4.61 (dd, J = 7.9, 2.6 Hz, 1H), 4.33 (d, J = 2.6 Hz, 1H), 4.24 (d, J = 7.9 Hz, 1H), 3.93 (dd, J = 13.0, 1.6 Hz, 1H), 3.78 (d, J = 13.0 Hz, 1H), 3.06 (dd, J = 14.1, 6.9 Hz, 1H), 2.72 (dd, J = 14.1, 10.6 Hz, 1H), 1.69 (dd, J = 10.6, 6.9 Hz, 1H), 1.54 (s, 3H), 1.47 (s, 3H), 1.45 (s, 3H), 1.35 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 109.0, 108.4, 102.7, 71.9, 70.8, 70.4, 61.7, 32.7, 26.6, 25.9, 25.8, 24.0. HRMS (ESI) m/z : $[M + H]^+$ calcd for $C_{12}H_{21}O_5S$ 277.1099; found 277.1104. $[\alpha]_D^{35} = +0.18$ (c 0.01, $CHCl_3$).

General procedure 3

A solution of glycosyl donor **9a-i** (1.0 equiv.) and acceptor **2k**, **2h**, **5e**, **10a-g** (2.0 equiv.) in dry CH_2Cl_2 (0.03 M) was stirred at room temperature for 60 min in the presence of activated acid washed (AW) 4 Å MS (3.0 g/mmol) under Ar atmosphere. Then the vessel was chilled to 0 °C, to which triflimide ($(CF_3SO_2)_2NH$) (30 mol %) were added. The reaction mixture was stirred for 5 min and TLC was checked. After completion of the reaction within 5 min, the

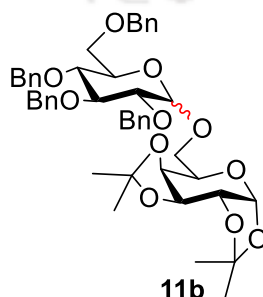
temperature gradually raised to room temperature. Then Et₃N was added to quench the reaction. The crude reaction mixture was worked up with water, washed with brine, dried by Na₂SO₄ and concentrated in rotavapor. The resulting crude reaction mixture was purified through Flash column chromatography to afford the glycosylated product.

Methyl 2,3,4-tri-O-benzyl-6-O-(2,3,4,6-tetra-O-benzyl-D-glucopyranosyl)- α -D-galactopyranoside (11a).



Glycosylation of **9d** (46.6 mg, 0.06 mmol) with **10a** (55.7 mg, 0.12 mmol) according to General procedure 3 afforded **11a** (50.3 mg, 85 %, $\alpha:\beta$ = 2:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.36 (Hexane/EtOAc = 4:1, v/v). ¹H NMR (600 MHz, CDCl₃) δ 7.40 – 7.33 (m, 19H), 7.33 – 7.21 (m, 80H), 7.15 – 7.09 (m, 6H), 4.96 – 4.91 (m, 5H), 4.90 (dd, J = 10.9, 2.4 Hz, 2H), 4.85 (d, J = 11.5 Hz, 3H), 4.81 (d, J = 12.3 Hz, 8H), 4.78 – 4.75 (m, 2H), 4.73 (d, J = 12.7 Hz, 3H), 4.70 (dd, J = 8.2, 3.3 Hz, 4H), 4.69 – 4.66 (m, 3H), 4.65 (dd, J = 9.4, 5.5 Hz, 4H), = 5.4 Hz, 1H), 4.59 (dd, J = 12.3, 2.9 Hz, 4H), 4.56 (d, J = 3.1 Hz, 1H), 4.53 – 4.47 (m, 2H), 4.46 (d, J = 4.5 Hz, 1H), 4.43 (d, J = 12.0 Hz, 3H), 4.38 (d, J = 7.8 Hz, 1H), 4.03 (dd, J = 10.1, 3.6 Hz, 1H), 4.00 (dd, J = 10.0, 3.6 Hz, 2H), 3.97 – 3.93 (m, 3H), 3.93 – 3.88 (m, 7H), 3.85 (t, J = 7.1 Hz, 2H), 3.83 – 3.81 (m, 1H), 3.79 (m, 2H), 3.73 – 3.68 (m, 7H), 3.66 (d, J = 9.7 Hz, 2H), 3.63 (d, J = 8.4 Hz, 1H), 3.61 – 3.58 (m, 2H), 3.53 (dd, J = 9.7, 3.5 Hz, 2H), 3.45 – 3.38 (m, 5H), 3.33 (s, 6H), 3.28 (s, 3H). ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 138.8, 138.8, 138.7, 138.6, 138.6, 138.48, 138.45, 138.3, 138.2, 138.1, 138.0, 137.9, 128.4, 128.4, 128.4, 128.3, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.5, 103.7, 98.8, 98.7, 97.3, 84.6, 82.4, 82.0, 79.7, 79.0, 77.7, 77.6, 76.4, 75.7, 75.6, 75.5, 75.4, 75.0, 75.0, 74.8, 74.7, 74.7, 74.7, 73.6, 73.5, 73.5, 73.5, 73.4, 73.4, 73.3, 70.3, 69.7, 69.3, 69.1, 68.7, 68.2, 67.1, 55.4, 55.4. HRMS (ESI) m/z : [M + NH₄]⁺ calcd for C₆₂H₇₀NO₁₁ 1004.4949; found 1004.4949. [α]_D³⁵ = + 0.20 (c 0.01, CHCl₃).

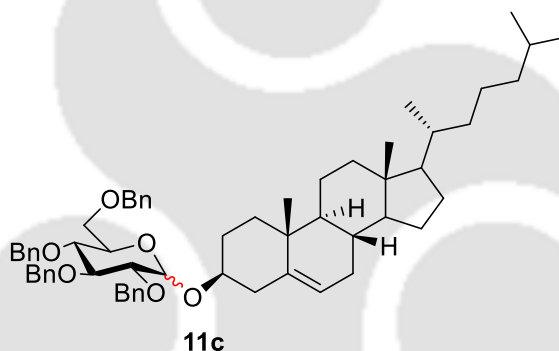
1,2;3,4-di-O-isopropylidene-6-O-(2,3,4,6-tetra-O-benzyl-D-glucopyranosyl)- α -D-galactopyranose (11b).



Glycosylation of **9d** (46.6 mg, 0.06mmol) with **2h** (31 mg, 0.12 mmol) according to General procedure 3 afforded **11b** (38.5 mg, 82 %, $\alpha:\beta$ = 1.3:1) as a colorless syrup. The crude product

was purified through flash column chromatography, $R_f = 0.35$ (Hexane: EtOAc = 4: 1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.43 (d, $J = 6.6$ Hz, 2H), 7.38 – 7.35 (m, 3H), 7.35 – 7.30 (m, 15H), 7.28 (dd, $J = 14.6, 7.2$ Hz, 15H), 7.14 – 7.11 (m, 4H), 5.58 (d, $J = 5.0$ Hz, 1H), 5.53 (d, $J = 5.0$ Hz, 1H), 5.06 (d, $J = 11.1$ Hz, 1H), 5.00 – 4.95 (m, 3H), 4.81 (t, $J = 9.6$ Hz, 3H), 4.79 – 4.75 (m, 1H), 4.74 – 4.68 (m, 3H), 4.65 – 4.63 (m, 1H), 4.62 – 4.58 (m, 3H), 4.55 – 4.49 (m, 2H), 4.46 (dd, $J = 10.5, 5.6$ Hz, 3H), 4.36 (dd, $J = 8.0, 1.3$ Hz, 1H), 4.34 – 4.30 (m, 2H), 4.25 (dd, $J = 8.0, 1.4$ Hz, 1H), 4.17 (dd, $J = 10.7, 3.4$ Hz, 1H), 4.11 – 4.07 (m, 1H), 4.03 (t, $J = 6.4$ Hz, 1H), 3.98 (t, $J = 9.3$ Hz, 1H), 3.82 (d, $J = 10.0$ Hz, 1H), 3.80 – 3.76 (m, 2H), 3.75 (t, $J = 3.0$ Hz, 1H), 3.73 (d, $J = 3.0$ Hz, 1H), 3.71 (dd, $J = 11.9, 4.6$ Hz, 2H), 3.69 – 3.66 (m, 1H), 3.66 – 3.61 (m, 3H), 3.59 (dd, $J = 9.6, 3.6$ Hz, 1H), 3.47 (d, $J = 8.1$ Hz, 1H), 3.46 – 3.42 (m, 1H), 1.53 (s, 3H), 1.50 (s, 3H), 1.45 (s, 6H), 1.33 (s, 3H), 1.32 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.9, 138.6, 138.3, 138.2, 138.1, 137.9, 128.7, 128.4, 128.4, 128.3, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 109.4, 109.2, 108.6, 108.6, 104.4, 97.0, 96.4, 96.3, 84.5, 82.0, 81.5, 79.7, 77.6, 77.5, 75.8, 75.7, 75.1, 75.1, 74.7, 74.4, 73.5, 73.4, 72.4, 71.4, 70.8, 70.7, 70.6, 70.4, 70.1, 69.8, 68.6, 68.2, 67.3, 66.1, 65.6, 26.2, 26.1, 26.0, 26.0, 25.1, 25.0, 24.6, 24.4. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{46}\text{H}_{58}\text{NO}_{11}$ 800.4004; found 800.4008. $[\alpha]_D^{35} = +0.67$ (c 0.01, CHCl_3).

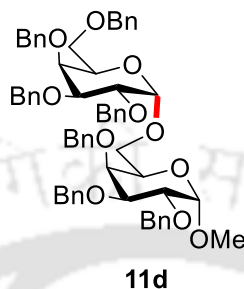
Cholesteryl 2, 3, 4, 6-tetra-O-benzyl-D-glucopyranoside (11c).



Glycosylation of **9d** (46.6 mg, 0.06 mmol) with cholesterol (**10g**) (46.4 mg, 0.12 mmol) according to General procedure 3 afforded **11c** (43 mg, 79 %, $\alpha:\beta = 1:4$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.6$ (Hexane: EtOAc = 7: 1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.35 (d, $J = 6.9$ Hz, 3H), 7.34 – 7.33 (m, 1H), 7.33 – 7.25 (m, 20H), 7.19 – 7.15 (m, 2H), 7.14 – 7.11 (m, 1H), 5.34 (d, $J = 2.1$ Hz, 1H), 5.28 (d, $J = 4.8$ Hz, 1H), 5.01 (d, $J = 10.8$ Hz, 1H), 4.98 (d, $J = 10.9$ Hz, 1H), 4.94 (d, $J = 2.5$ Hz, 1H), 4.92 (d, $J = 11.0$ Hz, 1H), 4.83 (d, $J = 8.2$ Hz, 1H), 4.81 (d, $J = 10.7$ Hz, 1H), 4.78 (d, $J = 6.8$ Hz, 1H), 4.76 (d, $J = 7.8$ Hz, 1H), 4.72 (d, $J = 10.9$ Hz, 1H), 4.65 (d, $J = 12.0$ Hz, 1H), 4.62 (d, $J = 6.9$ Hz, 1H), 4.60 (d, $J = 7.1$ Hz, 1H), 4.54 (dd, $J = 11.4, 8.6$ Hz, 2H), 4.50 (d, $J = 7.8$ Hz, 1H), 4.45 (dd, $J = 11.3, 7.7$ Hz, 1H), 4.03 – 3.99 (m, 1H), 3.88 (d, $J = 9.8$ Hz, 1H), 3.75 (d, $J = 7.0$ Hz, 1H), 3.73 (d, $J = 9.4$ Hz, 1H), 3.67 – 3.61 (m, 3H), 3.61 – 3.57 (m, 1H), 3.55 (t, $J = 9.4$ Hz, 1H), 3.50 – 3.46 (m, 1H), 3.46 – 3.42 (m, 2H), 2.43 – 2.39 (m, 1H), 2.33 (t, $J = 12.4$ Hz, 1H), 2.06 – 1.94 (m, 4H), 1.89 – 1.79 (m, 3H), 1.71 – 1.61 (m, 3H), 1.61 – 1.54 (m, 3H), 1.54 – 1.48 (m, 4H), 1.48 – 1.41 (m, 3H), 1.41 – 1.30 (m, 5H), 1.21 – 1.29 (m, 3H), 1.20 – 1.04 (m, 10H), 1.03 (s, 3H), 1.02 (s, 1H), 1.01 – 0.95 (m, 4H), 0.92 (d, $J = 6.4$ Hz, 4H), 0.87 (d, $J = 2.6$ Hz, 4H), 0.86 (d, $J = 2.6$ Hz, 4H), 0.68 (s, $J = 3.1$ Hz, 3H), 0.68 (s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 140.7, 140.6, 139.0, 138.7, 138.5, 138.3, 138.3, 138.2, 138.1, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 122.0, 121.8, 102.3, 94.6, 84.9, 82.4, 82.1, 79.9, 79.7, 78.0, 77.9, 76.5,

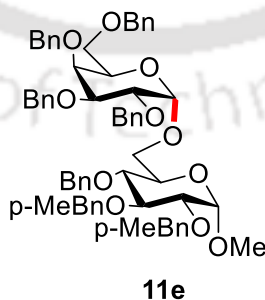
75.7, 75.2, 75.0, 75.0, 74.8, 73.5, 73.4, 73.1, 70.1, 69.2, 68.6, 56.8, 56.2, 50.2, 50.1, 42.4, 39.9, 39.8, 39.6, 39.2, 37.4, 37.1, 36.8, 36.8, 36.2, 35.8, 32.0, 31.9, 30.0, 29.8, 28.3, 28.1, 27.5, 24.3, 23.9, 22.9, 22.6, 21.1, 19.5, 19.4, 18.8, 11.9. . HRMS (ESI) m/z : $[M + NH_4]^+$ calcd for $C_{61}H_{84}NO_6$ 926.6293; found 926.6290. $[\alpha]_D^{35} = +0.37$ (c 0.01, $CHCl_3$).

Methyl 2,3,4-tri-O-benzyl-6-O-(2,3,4,6-tetra-O-benzyl- α -D-galactopyranosyl)- α -D-galactopyranoside (11d).



Glycosylation of **9a** (46.6 mg, 0.06 mmol) with **10a** (55.7 mg, 0.12 mmol) according to General procedure 3 afforded **11d** (50.9 mg, 86 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.37 (Hexane/EtOAc = 4:1, v/v). 1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.17 (m, 35H), 4.91 (t, J = 11.6 Hz, 2H), 4.83 (d, J = 4.8 Hz, 1H), 4.80 (dd, J = 8.6, 3.3 Hz, 2H), 4.75 (d, J = 8.4 Hz, 2H), 4.72 (d, J = 7.6 Hz, 1H), 4.67 (t, J = 11.8 Hz, 2H), 4.62 (dd, J = 7.8, 4.2 Hz, 2H), 4.55 (dd, J = 11.4, 7.3 Hz, 2H), 4.45 (d, J = 11.7 Hz, 1H), 4.37 (d, J = 11.7 Hz, 1H), 4.04 – 3.96 (m, 3H), 3.94 (d, J = 7.0 Hz, 1H), 3.93 – 3.90 (m, 1H), 3.88 (d, J = 1.9 Hz, 1H), 3.87 (d, J = 1.6 Hz, 1H), 3.70 (dd, J = 9.9, 6.3 Hz, 1H), 3.56 (d, J = 9.1 Hz, 1H), 3.54 – 3.46 (m, 2H), 3.44 – 3.38 (m, 1H), 3.26 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 137.8, 137.7, 137.6, 137.6, 137.5, 136.9, 127.4, 127.3, 127.3, 127.3, 127.3, 127.2, 127.1, 127.0, 126.8, 126.8, 126.7, 126.6, 126.6, 126.5, 126.5, 126.4, 97.7, 97.1, 78.0, 77.8, 76.2, 75.4, 75.2, 74.4, 73.8, 73.7, 73.6, 72.5, 72.5, 72.4, 72.2, 71.6, 68.3, 68.1, 67.6, 66.2, 54.2. HRMS (ESI) m/z : $[M + NH_4]^+$ calcd for $C_{62}H_{70}NO_{11}$ 1004.4949; found 1004.4948. $[\alpha]_D^{35} = +0.18$ (c 0.01, $CHCl_3$).

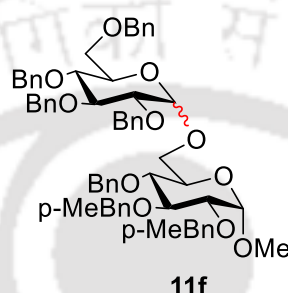
Methyl 4-O-benzyl-2,3-di-*p*-methyl-O-benzyl-6-O-(2,3,4,6-tetra-O-benzyl- α -D-galactopyranosyl)- α -D-glucopyranoside (11e).



Glycosylation of **9a** (46.6 mg, 0.06 mmol) with **10c** (59 mg, 0.12 mmol) according to General procedure 3 afforded **11e** (51.2 mg, 84 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.38 (Hexane/EtOAc = 4:1, v/v). 1H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 7H), 7.29 – 7.21 (m, 19H), 7.21 – 7.16 (m, 3H), 7.13 (d, J = 7.8 Hz, 2H), 7.08 (d, J = 7.8 Hz, 2H), 4.96 (d, J = 3.5 Hz, 1H), 4.92 (dd, J = 11.0, 5.9 Hz, 2H), 4.85 (d, J = 11.0 Hz, 1H), 4.79 (d, J = 12.0 Hz, 1H), 4.76 – 4.71 (m, 2H), 4.71 – 4.64 (m, 3H),

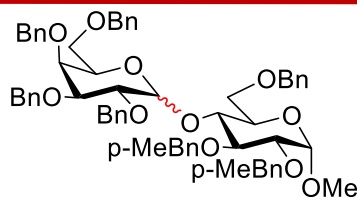
4.58 – 4.50 (m, 3H), 4.49 (d, $J = 3.5$ Hz, 1H), 4.42 (d, $J = 11.8$ Hz, 1H), 4.35 (d, $J = 11.8$ Hz, 1H), 4.01 (dd, $J = 9.3, 3.4$ Hz, 1H), 3.97 – 3.87 (m, 4H), 3.80 – 3.68 (m, 3H), 3.56 (d, $J = 9.2$ Hz, 1H), 3.53 – 3.47 (m, 2H), 3.39 (dd, $J = 9.6, 3.6$ Hz, 1H), 3.28 (s, 3H), 2.35 (s, 3H), 2.30 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.8, 138.8, 138.7, 138.5, 138.0, 137.5, 137.3, 135.9, 135.2, 129.1, 129.0, 128.4, 128.3, 128.2, 128.2, 128.2, 128.2, 128.1, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.4, 127.4, 98.0, 97.9, 82.0, 79.9, 78.3, 78.0, 76.4, 75.6, 75.1, 75.0, 74.8, 73.3, 73.2, 72.8, 72.5, 70.3, 69.4, 68.9, 66.5, 55.1, 21.2, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{64}\text{H}_{74}\text{NO}_{11}$ 1032.5262; found 1032.5260. $[\alpha]_{\text{D}}^{35} = +0.34$ (c 0.01, CHCl_3).

Methyl 4-O-benzyl-2,3-di-*p*-methyl-O-benzyl-6-O-(2,3,4,6-tetra-O-benzyl-D-glucopyranosyl)- α -D-glucopyranoside (11f).



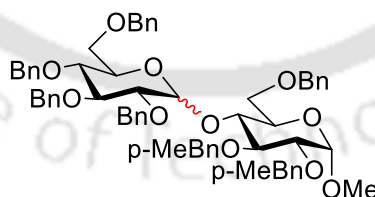
Glycosylation of **9d** (46.6 mg, 0.06 mmol) with **10c** (59 mg, 0.12 mmol) according to General procedure 3 afforded **11f** (51.2 mg, 84 %, $\alpha:\beta = 1:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.37$ (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.31 (d, $J = 3.1$ Hz, 9H), 7.30 – 7.25 (m, 26H), 7.23 (dd, $J = 8.2, 3.2$ Hz, 10H), 7.20 (d, $J = 7.5$ Hz, 6H), 7.16 (dd, $J = 6.6, 4.7$ Hz, 5H), 7.12 (dd, $J = 12.1, 6.6$ Hz, 8H), 7.08 (d, $J = 7.8$ Hz, 2H), 4.97 (d, $J = 11.5$ Hz, 1H), 4.95 (d, $J = 4.3$ Hz, 1H), 4.92 (d, $J = 8.1$ Hz, 2H), 4.90 (d, $J = 11.3$ Hz, 2H), 4.82 (d, $J = 7.6$ Hz, 1H), 4.79 (dd, $J = 9.4, 7.2$ Hz, 2H), 4.76 (dd, $J = 7.6, 4.9$ Hz, 2H), 4.75 – 4.73 (m, 2H), 4.71 (dd, $J = 12.1, 7.1$ Hz, 2H), 4.63 (d, $J = 5.4$ Hz, 2H), 4.61 (d, $J = 3.0$ Hz, 1H), 4.60 – 4.56 (m, 2H), 4.56 – 4.53 (m, 4H), 4.52 (d, $J = 2.9$ Hz, 1H), 4.51 – 4.48 (m, 2H), 4.43 (d, $J = 10.9$ Hz, 1H), 4.40 (d, $J = 12.1$ Hz, 1H), 4.34 (d, $J = 7.8$ Hz, 1H), 4.19 – 4.15 (m, 1H), 3.97 (dd, $J = 11.2, 7.5$ Hz, 2H), 3.94 (d, $J = 9.3$ Hz, 1H), 3.83 – 3.78 (m, 2H), 3.76 (dd, $J = 9.2, 5.5$ Hz, 2H), 3.73 – 3.66 (m, 3H), 3.66 – 3.64 (m, 1H), 3.63 (d, $J = 4.6$ Hz, 1H), 3.61 (dd, $J = 9.6, 4.6$ Hz, 3H), 3.57 (d, $J = 9.5$ Hz, 1H), 3.55 – 3.51 (m, 2H), 3.48 (dd, $J = 13.6, 5.4$ Hz, 3H), 3.43 (dt, $J = 7.6, 3.7$ Hz, 2H), 3.34 (s, $J = 10.9$ Hz, 3H), 3.31 (s, 3H), 2.35 (s, 3H), 2.34 (s, 3H), 2.33 (s, 3H), 2.29 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.8, 138.5, 138.5, 138.4, 138.4, 138.2, 138.1, 138.0, 137.7, 137.6, 137.3, 137.2, 135.8, 135.8, 135.2, 135.1, 129.2, 129.1, 129.1, 129.0, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.6, 127.6, 127.5, 103.8, 98.2, 98.1, 97.3, 84.8, 82.1, 82.0, 81.9, 81.7, 79.8, 79.5, 78.0, 77.9, 77.8, 77.6, 75.8, 75.7, 75.6, 75.5, 75.0, 75.0, 74.9, 74.9, 74.9, 73.5, 73.4, 73.3, 72.3, 70.3, 70.2, 69.9, 69.0, 68.6, 68.4, 66.1, 55.2, 55.2, 21.3, 21.2, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{64}\text{H}_{74}\text{NO}_{11}$ 1032.5262; found 1032.5262. $[\alpha]_{\text{D}}^{35} = +1.02$ (c 0.05, CHCl_3).

Methyl 6-O-benzyl-2,3-di-*p*-methyl-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-D-galactopyranosyl)- α -D-glucopyranoside (11g).

**11g**

Glycosylation of **9a** (46.6 mg, 0.06 mmol) with **10e** (59 mg, 0.12 mmol) according to General procedure 3 afforded **11g** (49.3 mg, 81 %, $\alpha:\beta = 2:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.40$ (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.36 – 7.23 (m, 30H), 7.23 – 7.19 (m, 8H), 7.17 (d, $J = 10.4$ Hz, 8H), 7.11 – 7.05 (m, 7H), 6.95 (d, $J = 7.7$ Hz, 1H), 5.77 (d, $J = 3.8$ Hz, 1H), 4.97 (dd, $J = 10.9$, 4.1 Hz, 1H), 4.94 (d, $J = 11.1$ Hz, 1H), 4.92 – 4.89 (m, 1H), 4.86 (d, $J = 11.4$ Hz, 1H), 4.79 (dd, $J = 17.0$, 7.3 Hz, 1H), 4.77 – 4.71 (m, 2H), 4.70 (d, $J = 5.2$ Hz, 1H), 4.69 – 4.67 (m, 2H), 4.67 – 4.61 (m, 3H), 4.61 – 4.57 (m, 2H), 4.58 – 4.53 (m, 2H), 4.51 (td, $J = 8.4$, 4.4 Hz, 4H), 4.41 (d, $J = 12.3$ Hz, 1H), 4.37 (d, $J = 11.8$ Hz, 1H), 4.32 (dd, $J = 14.4$, 2.4 Hz, 1H), 4.28 (d, $J = 11.7$ Hz, 2H), 4.25 (d, $J = 11.9$ Hz, 1H), 4.21 (d, $J = 11.6$ Hz, 1H), 4.04 (t, $J = 9.1$ Hz, 1H), 3.98 (dd, $J = 10.3$, 3.8 Hz, 1H), 3.95 – 3.89 (m, 3H), 3.88 – 3.77 (m, 5H), 3.73 (dd, $J = 9.6$, 7.8 Hz, 1H), 3.68 (dd, $J = 10.6$, 4.7 Hz, 1H), 3.63 (dd, $J = 10.5$, 2.0 Hz, 1H), 3.60 – 3.56 (m, 1H), 3.55 (d, $J = 4.2$ Hz, 1H), 3.52 (dd, $J = 9.6$, 3.5 Hz, 1H), 3.49 (m, 1H), 3.47 (d, $J = 8.6$ Hz, 1H), 3.46 – 3.44 (m, 1H), 3.42 (dd, $J = 5.9$, 2.9 Hz, 1H), 3.39 (dd, $J = 9.5$, 5.5 Hz, 1H), 3.36 (s, 3H), 3.35 (s, 1H), 3.34 – 3.30 (m, 1H), 2.32 (s, 4H), 2.31 (s, 4H), 2.28 (s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 139.1, 139.0, 138.6, 138.6, 138.6, 138.4, 138.3, 138.2, 138.1, 138.0, 137.6, 137.4, 136.6, 136.5, 136.4, 135.9, 135.5, 135.0, 129.1, 129.0, 128.9, 128.6, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5, 127.5, 127.4, 127.4, 126.9, 102.8, 98.5, 97.8, 97.3, 82.5, 82.0, 80.2, 80.1, 79.9, 79.2, 78.7, 76.6, 75.6, 75.4, 75.2, 74.8, 74.8, 74.6, 74.3, 73.8, 73.8, 73.6, 73.4, 73.4, 73.1, 73.1, 73.0, 72.8, 72.6, 72.5, 70.0, 69.8, 69.4, 69.4, 68.6, 68.3, 68.1, 55.3, 55.1, 21.3, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{64}\text{H}_{74}\text{NO}_{11}$ 1032.5262; found 1032.5261. $[\alpha]_{\text{D}}^{35} = -0.32$ (c 0.01, CHCl_3).

Methyl 6-O-benzyl-2,3-di-p-methyl-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-D-glucopyranosyl)- α -D-glucopyranoside (11h).

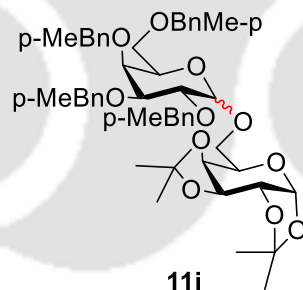
**11h**

Glycosylation of **9d** (46.6 mg, 0.06 mmol) with **10e** (59 mg, 0.12 mmol) according to General procedure 3 afforded **11h** (48.1 mg, 79 %, $\alpha:\beta = 2.3:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.41$ (Hexane/EtOAc = 4:1, v/v). The α anomer, ^1H NMR (600 MHz, CDCl_3) δ 7.29 – 7.21 (m, 17H), 7.20 – 7.17 (m, 7H), 7.13 – 7.05 (m, 9H), 5.71 (d, $J = 3.6$ Hz, 1H), 4.99 (d, $J = 11.2$ Hz, 1H), 4.87 (d, $J = 10.8$ Hz, 1H), 4.78 (d, $J = 7.5$ Hz, 1H), 4.75 (dd, $J = 12.8$, 9.5 Hz, 2H), 4.69 – 4.66 (m, 1H), 4.59 (d, $J = 11.9$ Hz, 1H), 4.55 (dd, $J = 10.7$, 7.5 Hz, 3H), 4.51 (d, $J = 6.7$ Hz, 1H), 4.49 (d, $J = 10.9$ Hz, 2H), 4.42 (d, $J = 10.8$ Hz, 1H), 4.27 (d, $J = 12.1$ Hz, 1H), 4.06 (t, $J = 9.0$ Hz, 1H), 4.02 (t, $J = 9.0$

Hz, 1H), 3.89 (t, $J = 9.3$ Hz, 1H), 3.84 (m, 1H), 3.81 (dd, $J = 10.7, 3.7$ Hz, 1H), 3.69 (d, $J = 9.9$ Hz, 1H), 3.66 – 3.62 (m, 2H), 3.56 (dd, $J = 9.2, 3.5$ Hz, 1H), 3.48 (td, $J = 10.1, 3.2$ Hz, 2H), 3.37 (d, $J = 10.5$ Hz, 1H), 3.36 (s, 3H), 2.32 (s, 3H), 2.32 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.8, 138.5, 138.2, 138.0, 138.0, 137.7, 136.7, 135.9, 135.0, 129.1, 128.9, 128.4, 128.3, 128.3, 128.3, 128.2, 128.0, 127.8, 127.8, 127.8, 127.6, 127.6, 127.5, 127.4, 127.3, 127.0, 97.9, 96.5, 82.0, 82.0, 80.0, 79.5, 77.7, 75.5, 74.9, 74.4, 73.5, 73.3, 73.2, 73.1, 72.1, 71.0, 69.5, 69.1, 68.2, 55.2, 21.2, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{64}\text{H}_{74}\text{NO}_{11}$ 1032.5262; found 1032.5265. $[\alpha]_{\text{D}}^{35} = +0.14$ (c 0.01, CHCl_3).

The β anomer, ^1H NMR (600 MHz, CDCl_3) δ 7.31 – 7.23 (m, 25H), 7.18 (dd, $J = 13.0, 5.0$ Hz, 4H), 7.07 (d, $J = 7.8$ Hz, 2H), 7.02 (d, $J = 7.8$ Hz, 2H), 5.01 (d, $J = 11.1$ Hz, 1H), 4.86 (d, $J = 10.9$ Hz, 1H), 4.82 – 4.74 (m, 4H), 4.73 (d, $J = 3.7$ Hz, 1H), 4.73 – 4.70 (m, 1H), 4.56 (dd, $J = 7.9, 4.3$ Hz, 2H), 4.54 (d, $J = 4.9$ Hz, 1H), 4.51 (d, $J = 3.7$ Hz, 1H), 4.47 – 4.44 (m, 1H), 4.41 – 4.37 (m, 1H), 4.37 (d, $J = 3.1$ Hz, 1H), 3.94 (t, $J = 9.5$ Hz, 1H), 3.84 – 3.79 (m, 2H), 3.73 – 3.70 (m, 1H), 3.61 – 3.53 (m, 3H), 3.50 – 3.45 (m, 2H), 3.43 (dd, $J = 9.4, 3.5$ Hz, 1H), 3.36 – 3.33 (m, 4H), 3.28 (dd, $J = 9.8, 3.0$ Hz, 1H), 2.31 (s, 3H), 2.28 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.6, 138.6, 138.6, 138.4, 137.9, 137.4, 136.6, 136.5, 135.4, 129.0, 128.7, 128.5, 128.4, 128.4, 128.3, 128.2, 128.0, 127.8, 127.8, 127.7, 127.6, 127.6, 127.5, 127.5, 127.3, 102.4, 98.6, 84.9, 82.8, 80.2, 78.6, 78.1, 76.5, 75.6, 75.3, 75.2, 74.9, 74.8, 73.5, 73.4, 73.3, 70.0, 69.0, 67.9, 55.3, 21.2, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{64}\text{H}_{74}\text{NO}_{11}$ 1032.5262; found 1032.5263. $[\alpha]_{\text{D}}^{35} = +0.4$ (c 0.015, CHCl_3).

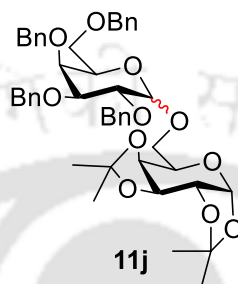
1,2;3,4-di-O-isopropylidene-6-O-(2,3,4,6-tetra-*p*-methyl-O-benzyl-D-galactopyranosyl)- α -D-galactopyranose (11i).



Glycosylation of **9e** (50 mg, 0.06 mmol) with **2h** (31 mg, 0.12 mmol) according to General procedure 3 afforded **11i** (44.8 mg, 89 %, $\alpha:\beta = 1:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.36$ (Hexane: EtOAc = 4: 1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.34 (d, $J = 7.9$ Hz, 2H), 7.28 – 7.23 (m, 6H), 7.18 – 7.11 (m, 16H), 7.11 – 7.06 (m, 8H), 5.56 (d, $J = 5.0$ Hz, 1H), 5.50 (d, $J = 5.0$ Hz, 1H), 4.98 (d, $J = 10.6$ Hz, 1H), 4.95 (d, $J = 3.7$ Hz, 1H), 4.86 (d, $J = 11.4$ Hz, 2H), 4.76 (d, $J = 11.4$ Hz, 1H), 4.72 (d, $J = 11.8$ Hz, 2H), 4.68 (dd, $J = 6.4, 4.1$ Hz, 2H), 4.65 (dd, $J = 10.8, 7.4$ Hz, 2H), 4.59 – 4.55 (m, 3H), 4.52 (d, $J = 11.3$ Hz, 1H), 4.43 – 4.37 (m, 2H), 4.36 – 4.34 (m, 2H), 4.33 (d, $J = 4.2$ Hz, 1H), 4.30 (ddd, $J = 7.3, 6.5, 2.2$ Hz, 3H), 4.22 (dd, $J = 7.9, 1.7$ Hz, 1H), 4.11 (dd, $J = 10.6, 3.7$ Hz, 1H), 4.08 – 4.04 (m, 1H), 4.03 – 3.98 (m, 2H), 3.96 (dd, $J = 13.9, 4.5$ Hz, 2H), 3.90 (dd, $J = 10.1, 2.7$ Hz, 1H), 3.82 (d, $J = 2.6$ Hz, 1H), 3.78 (dd, $J = 9.7, 7.8$ Hz, 1H), 3.76 – 3.73 (m, 1H), 3.71 (dd, $J = 10.4, 7.3$ Hz, 1H), 3.66 (dd, $J = 10.5, 7.4$ Hz, 1H), 3.51 (q, $J = 5.3$ Hz, 3H), 3.46 (dd, $J = 5.2, 2.7$ Hz, 2H), 3.44 (d, $J = 2.6$ Hz, 1H), 2.35 (s, 6H), 2.34 (s, 9H), 2.33 (s, 3H), 2.31 (s, 6H), 1.51 (s, 3H), 1.49 (s, 3H), 1.43 (s, 3H), 1.43 (s, 3H), 1.32 (d, $J = 4.0$ Hz, 3H), 1.31 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 137.4, 137.3, 137.1, 137.1, 137.1, 137.0,

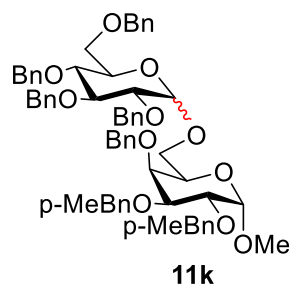
137.0, 136.9, 136.0, 136.0, 135.8, 135.7, 135.7, 135.1, 134.9, 129.1, 129.0, 129.0, 129.0, 128.9, 128.8, 128.8, 128.8, 128.7, 128.6, 128.4, 128.0, 128.0, 127.9, 127.7, 127.5, 109.3, 109.2, 108.6, 108.5, 104.6, 97.7, 96.4, 96.3, 81.9, 79.1, 78.9, 76.2, 74.7, 74.5, 74.5, 74.2, 73.3, 73.2, 73.1, 73.0, 72.9, 72.6, 71.5, 70.9, 70.8, 70.7, 70.5, 69.5, 69.2, 68.6, 68.5, 67.3, 66.3, 65.8, 26.1, 26.1, 26.0, 25.1, 24.9, 24.6, 24.5, 21.2. HRMS (ESI) m/z : $[M + NH_4]^+$ calcd for $C_{50}H_{66}NO_{11}$ 856.4630; found 856.4633. $[\alpha]_D^{35} = +0.19$ (c 0.01, $CHCl_3$).

1,2;3,4-di-O-isopropylidene-6-O-(2,3,4,6-tetra-O-benzyl-D-galactopyranosyl)- α -D-galactopyranose (11j).



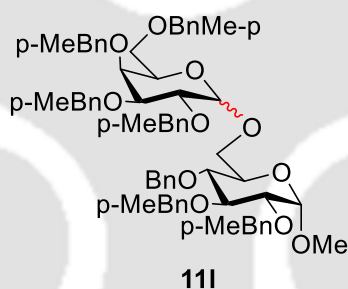
Glycosylation of **9a** (46.6 mg, 0.06 mmol) with **2h** (31 mg, 0.12 mmol) according to General procedure 3 afforded **11j** (38.5 mg, 82 %, $\alpha:\beta = 1:1.2$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.36$ (Hexane: EtOAc = 4: 1, v/v). 1H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, $J = 6.7$ Hz, 2H), 7.39 – 7.21 (m, 44H), 5.55 (d, $J = 5.0$ Hz, 1H), 5.50 (d, $J = 5.0$ Hz, 1H), 5.04 (d, $J = 11.1$ Hz, 1H), 5.00 (d, $J = 3.6$ Hz, 1H), 4.94 (d, $J = 3.0$ Hz, 1H), 4.91 (d, $J = 3.2$ Hz, 1H), 4.82 (d, $J = 11.7$ Hz, 1H), 4.78 (d, $J = 11.9$ Hz, 1H), 4 – 4.68 (m, 6H), 4.62 – 4.53 (m, 5H), 4.47 (d, $J = 11.8$ Hz, 1H), 4.45 – 4.38 (m, 6H), 4.33 – 4.27 (m, 3H), 4.21 (dd, $J = 7.9, 1.6$ Hz, 1H), 4.12 (dd, $J = 10.6, 3.6$ Hz, 1H), 4.09 – 3.98 (m, 6H), 3.95 (dd, $J = 10.0, 2.7$ Hz, 1H), 3.88 (d, $J = 2.5$ Hz, 1H), 3.82 (dd, $J = 9.7, 7.9$ Hz, 1H), 3.77 (dd, $J = 10.2, 3.8$ Hz, 1H), 3.73 (dd, $J = 10.6, 7.2$ Hz, 1H), 3.69 (dd, $J = 10.6, 7.4$ Hz, 1H), 3.61 – 3.54 (m, 4H), 3.54 – 3.48 (m, 4H), 1.51 (s, 3H), 1.48 (s, 4H), 1.43 (s, 3H), 1.42 (s, 3H), 1.32 (s, 3H), 1.31 – 1.28 (d, $J = 3.6$ Hz, 10H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 139.0, 138.9, 138.7, 138.7, 138.1, 137.9, 128.6, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.1, 127.9, 127.8, 127.8, 127.7, 127.7, 127.5, 127.4, 127.4, 127.3, 109.3, 109.2, 108.6, 108.5, 104.7, 97.6, 96.4, 96.3, 81.9, 79.1, 79.0, 76.4, 74.9, 74.8, 74.5, 73.5, 73.5, 73.4, 73.3, 73.1, 73.0, 72.7, 71.5, 70.9, 70.8, 70.7, 70.6, 70.5, 69.6, 69.1, 68.7, 68.6, 67.4, 66.3, 65.8, 26.1, 26.0, 26.0, 26.0, 25.1, 24.9, 24.6, 24.4. HRMS (ESI) m/z : $[M + NH_4]^+$ calcd for $C_{46}H_{58}NO_{11}$ 800.4004; found 800.4010. $[\alpha]_D^{35} = +2.62$ (c 0.04, $CHCl_3$).

Methyl 4-O-benzyl-2,3-di-*p*-methyl-O-benzyl-6-O-(2,3,4,6-tetra-O-benzyl-D-glucopyranosyl)- α -D-galactopyranoside (11k).



Glycosylation of **9d** (46.6 mg, 0.06 mmol) with **10b** (59 mg, 0.12 mmol) according to General procedure 3 afforded **11k** (51.8 mg, 85 %, $\alpha:\beta = 1:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.37$ (Hexane/EtOAc = 4:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.33 – 7.21 (m, 46H), 7.15 (dd, $J = 7.7, 3.0$ Hz, 4H), 7.13 – 7.09 (m, 6H), 4.95 (d, $J = 2.7$ Hz, 1H), 4.92 (m, 2H), 4.88 (dd, $J = 10.1, 7.5$ Hz, 2H), 4.81 (m, 2H), 4.79 (d, $J = 5.3$ Hz, 3H), 4.76 – 4.74 (m, 3H), 4.69 (dd, $J = 8.7, 5.2$ Hz, 3H), 4.64 (dd, $J = 5.3, 3.0$ Hz, 3H), 4.63 – 4.58 (m, 5H), 4.56 (d, $J = 3.4$ Hz, 2H), 4.53 (d, $J = 5.4$ Hz, 1H), 4.49 (d, $J = 3.4$ Hz, 1H), 4.45 (d, $J = 7.9$ Hz, 2H), 4.41 – 4.34 (m, 2H), 4.00 (dd, $J = 10.0, 3.3$ Hz, 1H), 3.98 – 3.94 (m, 1H), 3.94 – 3.91 (m, 2H), 3.91 – 3.85 (m, 4H), 3.80 (dd, $J = 10.8, 4.2$ Hz, 3H), 3.73 – 3.65 (m, 6H), 3.61 (dt, $J = 14.9, 6.0$ Hz, 3H), 3.53 (dd, $J = 9.6, 3.5$ Hz, 1H), 3.42 – 3.37 (m, 3H), 3.32 (s, 3H), 3.27 (s, 3H), 2.35 (s, 3H), 2.34 (s, 3H), 2.33 (s, 3H), 2.33 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.7, 138.6, 138.6, 138.5, 138.4, 138.2, 138.1, 138.1, 137.9, 137.3, 137.3, 137.2, 137.2, 135.8, 135.8, 135.5, 129.1, 129.0, 129.0, 129.0, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 127.4, 103.7, 98.9, 98.8, 97.2, 84.6, 82.4, 82.0, 79.7, 78.9, 76.1, 75.7, 75.6, 75.5, 75.0, 74.9, 74.7, 74.7, 74.6, 74.6, 73.5, 73.5, 73.4, 73.3, 73.3, 70.3, 69.7, 69.3, 69.2, 68.8, 68.3, 67.2, 55.4, 55.3, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{64}\text{H}_{70}\text{NaO}_{11}$ 1037.4816, found 1037.4817. $[\alpha]_D^{35} = +0.32$ (c 0.01, CHCl_3).

Methyl 4-O-benzyl-2,3-di-*p*-methyl-O-benzyl -6-O-(2,3,4,6-tetra-*p*-methyl-O-benzyl-D-galactopyranosyl)- α -D-glucopyranoside (11l**).**

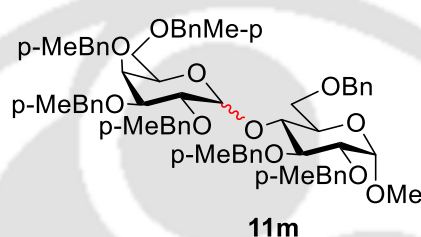


Glycosylation of **9e** (50 mg, 0.06 mmol) with **10c** (59 mg, 0.12 mmol) according to General procedure 3 afforded **11l** (55.3 mg, 86 %, $\alpha:\beta = 4:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.38$ (Hexane/EtOAc = 4:1, v/v). The α anomer, ^1H NMR (400 MHz, CDCl_3) δ 7.27 – 7.19 (m, 12H), 7.16 (d, $J = 7.6$ Hz, 4H), 7.12 (t, $J = 5.9$ Hz, 9H), 7.08 (d, $J = 7.9$ Hz, 2H), 6.99 (d, $J = 7.8$ Hz, 2H), 4.91 (d, $J = 10.6$ Hz, 1H), 4.88 – 4.83 (m, 2H), 4.75 (d, $J = 12.4$ Hz, 2H), 4.72 – 4.64 (m, 4H), 4.60 (d, $J = 12.1$ Hz, 1H), 4.54 – 4.46 (m, 3H), 4.35 (q, $J = 11.5$ Hz, 2H), 4.26 (d, $J = 7.7$ Hz, 1H), 4.11 (d, $J = 9.4$ Hz, 1H), 3.95 (t, $J = 9.2$ Hz, 1H), 3.85 – 3.76 (m, 3H), 3.58 (dd, $J = 10.7, 5.3$ Hz, 1H), 3.53 (d, $J = 7.4$ Hz, 1H), 3.51 – 3.41 (m, 5H), 3.28 (s, 3H), 2.35 (s, 3H), 2.34 (s, 3H), 2.33 (s, 3H), 2.32 (s, 6H), 2.28 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.5, 137.6, 137.5, 137.2, 137.0, 136.9, 135.9, 135.8, 135.8, 135.5, 135.2, 134.9, 129.1, 129.1, 129.0, 128.9, 128.8, 128.3, 128.3, 128.2, 128.2, 128.0, 127.7, 127.7, 127.5, 104.2, 98.0, 82.2, 81.9, 79.7, 79.2, 78.2, 75.6, 75.1, 74.8, 74.3, 73.4, 73.4, 73.2, 73.2, 72.8, 69.9, 68.6, 68.5, 55.2, 29.7, 21.2, 21.2, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{68}\text{H}_{82}\text{NO}_{11}$ 1088.5888, found 1088.5892. $[\alpha]_D^{35} = +0.26$ (c 0.01, CHCl_3).

The β anomer, ^1H NMR (600 MHz, CDCl_3) δ 7.29 – 7.25 (m, 7H), 7.25 – 7.21 (m, 7H), 7.19 (d, $J = 7.9$ Hz, 2H), 7.15 (d, $J = 8.2$ Hz, 3H), 7.14 – 7.07 (m, 9H), 7.04 (d, $J = 7.8$ Hz, 1H), 4.93 (d, $J = 3.5$ Hz, 1H), 4.90 (d, $J = 10.5$ Hz, 1H), 4.86 (dd, $J = 13.6, 11.2$ Hz, 2H), 4.76 –

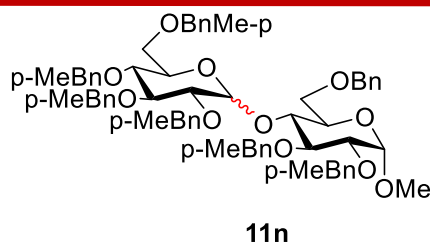
4.71 (m, 2H), 4.68 (d, $J = 6.4$ Hz, 1H), 4.66 (t, $J = 9.4$ Hz, 2H), 4.62 (d, $J = 11.8$ Hz, 1H), 4.55 (d, $J = 10.9$ Hz, 1H), 4.52 (d, $J = 8.7$ Hz, 1H), 4.50 (d, $J = 8.1$ Hz, 1H), 4.48 (d, $J = 3.5$ Hz, 1H), 4.37 (d, $J = 11.6$ Hz, 1H), 4.29 (d, $J = 11.6$ Hz, 1H), 3.97 (dd, $J = 10.1, 3.5$ Hz, 1H), 3.96 – 3.89 (m, 2H), 3.87 – 3.84 (m, 2H), 3.76 – 3.68 (m, 3H), 3.55 (t, $J = 9.2$ Hz, 1H), 3.47 – 3.41 (m, 2H), 3.38 (dd, $J = 9.6, 3.5$ Hz, 1H), 3.26 (s, 3H), 2.35 (s, 3H), 2.33 (s, 3H), 2.32 (s, 3H), 2.31 (s, 3H), 2.30 (s, 3H), 2.29 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.5, 137.5, 137.3, 137.2, 137.1, 137.0, 136.9, 135.9, 135.8, 135.8, 135.8, 135.2, 135.1, 129.1, 129.0, 129.0, 129.0, 128.9, 128.8, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.7, 127.6, 98.0, 97.9, 82.0, 80.0, 78.1, 78.0, 76.3, 75.6, 75.0, 74.8, 74.5, 73.3, 73.2, 72.6, 72.5, 70.3, 69.4, 68.9, 66.3, 65.2, 63.3, 55.0, 29.7, 21.2, 21.2, 21.1. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{68}\text{H}_{82}\text{NO}_{11}$ 1088.5888, found 1088.5886. $[\alpha]_{\text{D}}^{35} = +0.28$ (c 0.01, CHCl_3).

Methyl 6-O-benzyl-2,3-di-*p*-methyl-O-benzyl-4-O-(2,3,4,6-tetra-*p*-methyl-O-benzyl-D-galactopyranosyl)- α -D-glucopyranoside (11m).



Glycosylation of **9e** (50 mg, 0.06 mmol) with **10e** (59 mg, 0.12 mmol) according to General procedure 3 afforded **11m** (53.4 mg, 83 %, $\alpha:\beta = 2:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.38$ (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.29 – 7.19 (m, 26H), 7.17 (d, $J = 7.9$ Hz, 6H), 7.15 – 7.11 (m, 12H), 7.10 – 7.05 (m, 28H), 6.98 – 6.92 (m, 5H), 5.72 (d, $J = 3.8$ Hz, 2H), 4.96 (d, $J = 10.3$ Hz, 1H), 4.90 (t, $J = 10.9$ Hz, 3H), 4.81 (d, $J = 11.3$ Hz, 2H), 4.77 (d, $J = 9.2$ Hz, 1H), 4.73 (q, $J = 10.8$ Hz, 3H), 4.70 – 4.66 (m, 4H), 4.64 (dd, $J = 13.0, 5.8$ Hz, 3H), 4.59 (t, $J = 9.9$ Hz, 6H), 4.53 (d, $J = 11.4$ Hz, 2H), 4.49 (dd, $J = 11.3, 7.9$ Hz, 7H), 4.38 (d, $J = 12.3$ Hz, 2H), 4.32 (d, $J = 12.6$ Hz, 2H), 4.28 (d, $J = 7.7$ Hz, 1H), 4.23 (d, $J = 11.4$ Hz, 2H), 4.20 (d, $J = 11.6$ Hz, 1H), 4.15 (d, $J = 11.4$ Hz, 2H), 4.02 (t, $J = 9.1$ Hz, 2H), 3.96 (dd, $J = 10.3, 3.8$ Hz, 2H), 3.93 – 3.87 (m, 4H), 3.87 – 3.81 (m, 4H), 3.80 – 3.74 (m, 5H), 3.72 – 3.68 (m, 1H), 3.65 (dd, $J = 10.6, 4.6$ Hz, 2H), 3.62 – 3.59 (m, 2H), 3.55 – 3.48 (m, 4H), 3.43 (dd, $J = 13.5, 5.5$ Hz, 3H), 3.39 – 3.37 (m, 2H), 3.36 (s, 3H), 3.35 (s, 6H), 3.31 – 3.26 (m, 2H), 2.35 – 2.30 (m, 39H), 2.26 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.4, 138.2, 137.6, 137.3, 137.3, 137.2, 137.1, 137.0, 136.9, 136.9, 136.6, 136.4, 136.1, 136.0, 135.9, 135.7, 135.7, 135.5, 135.3, 135.2, 135.1, 135.0, 129.1, 129.0, 129.0, 129.0, 128.9, 128.8, 128.8, 128.8, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.7, 127.5, 127.5, 127.5, 127.3, 127.0, 102.9, 98.5, 97.8, 97.4, 82.5, 82.0, 80.2, 79.9, 79.2, 78.7, 75.4, 75.1, 74.6, 74.5, 74.3, 74.2, 73.8, 73.5, 73.3, 73.2, 73.1, 73.0, 72.6, 72.5, 70.1, 69.9, 69.5, 69.4, 68.6, 68.2, 55.3, 55.1, 21.2, 21.1. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{68}\text{H}_{82}\text{NO}_{11}$ 1088.5888; found 1088.5892. $[\alpha]_{\text{D}}^{35} = +0.30$ (c 0.01, CHCl_3).

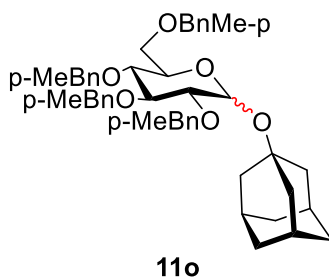
Methyl 6-O-benzyl-2,3-di-*p*-methyl-O-benzyl-4-O-(2,3,4,6-tetra-*p*-methyl-O-benzyl-D-glucopyranosyl)- α -D-glucopyranoside (11n).



Glycosylation of **9f** (50 mg, 0.06 mmol) with **10e** (59 mg, 0.12 mmol) according to General procedure 3 afforded **11n** (53.4 mg, 83 %, $\alpha:\beta = 1.5:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.38$ (Hexane/EtOAc = 4:1, v/v). The α anomer, ^1H NMR (600 MHz, CDCl_3) δ 7.26 – 7.20 (m, 6H), 7.18 (t, $J = 7.0$ Hz, 4H), 7.07 (m, 15H), 6.98 (d, $J = 7.7$ Hz, 2H), 6.94 (d, $J = 7.8$ Hz, 2H), 5.66 (d, $J = 3.5$ Hz, 1H), 4.96 (d, $J = 11.2$ Hz, 1H), 4.82 (d, $J = 10.5$ Hz, 1H), 4.73 – 4.66 (m, 4H), 4.57 (d, $J = 11.8$ Hz, 1H), 4.54 – 4.45 (m, 6H), 4.29 (d, $J = 10.5$ Hz, 1H), 4.19 (d, $J = 12.0$ Hz, 1H), 4.07 – 4.02 (m, 1H), 4.00 (m, 1H), 3.87 – 3.81 (m, 2H), 3.78 (dd, $J = 10.7, 3.7$ Hz, 1H), 3.65 – 3.57 (m, 3H), 3.55 (dd, $J = 9.2, 3.5$ Hz, 1H), 3.46 (dd, $J = 9.9, 3.6$ Hz, 1H), 3.43 (dd, $J = 10.6, 2.3$ Hz, 1H), 3.35 (s, 3H), 3.32 (d, $J = 10.4$ Hz, 1H), 2.33 (s, 12H), 2.28 (s, 3H), 2.26 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.2, 137.6, 137.3, 137.2, 137.2, 137.1, 136.7, 135.9, 135.9, 135.6, 135.0, 135.0, 134.9, 129.1, 129.0, 129.0, 128.9, 128.9, 128.4, 128.3, 128.2, 128.0, 127.3, 127.2, 127.1, 97.9, 96.5, 82.0, 82.0, 80.0, 79.2, 77.5, 75.4, 74.8, 74.4, 73.3, 73.3, 73.2, 73.1, 71.9, 70.9, 69.4, 69.0, 67.8, 55.1, 29.7, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{68}\text{H}_{82}\text{NO}_{11}$ 1088.5888; found 1088.5888. $[\alpha]_D^{35} = -0.40$ (c 0.01, CHCl_3).

For β anomer, ^1H NMR (600 MHz, CDCl_3) δ 7.31 – 7.28 (m, 3H), 7.27 – 7.23 (m, 5H), 7.18 – 7.11 (m, 8H), 7.07 (dt, $J = 13.6, 7.9$ Hz, 11H), 7.02 (d, $J = 7.7$ Hz, 2H), 5.02 (d, $J = 11.0$ Hz, 1H), 4.81 (d, $J = 10.7$ Hz, 1H), 4.76 – 4.66 (m, 6H), 4.56 – 4.50 (m, 3H), 4.46 (d, $J = 10.6$ Hz, 1H), 4.42 – 4.35 (m, 4H), 3.93 (t, $J = 9.5$ Hz, 1H), 3.85 – 3.80 (dd, $J = 16.6, 6.9$ Hz, 2H), 3.68 (d, $J = 10.5$ Hz, 1H), 3.62 (d, $J = 9.9$ Hz, 1H), 3.56 – 3.49 (m, 3H), 3.43 (m, 2H), 3.35 (s, 3H), 3.34 – 3.30 (m, 1H), 3.26 (dd, $J = 9.8, 3.5$ Hz, 1H), 2.33 (s, 6H), 2.31 (d, $J = 1.7$ Hz, 3H), 2.29 (s, 3H), 2.17 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 137.9, 137.4, 137.3, 137.2, 137.1, 136.9, 136.6, 136.5, 135.7, 135.6, 135.5, 135.4, 135.3, 129.0, 129.0, 128.9, 128.7, 128.4, 128.2, 128.2, 128.0, 127.9, 127.9, 127.9, 127.7, 127.7, 102.6, 98.6, 84.8, 82.7, 80.3, 78.6, 77.9, 76.8, 75.5, 75.2, 75.2, 75.1, 74.7, 74.6, 73.5, 73.3, 70.0, 68.8, 68.0, 55.3, 31.0, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{68}\text{H}_{82}\text{NO}_{11}$ 1088.5888; found 1088.5886. $[\alpha]_D^{35} = -0.28$ (c 0.01, CHCl_3).

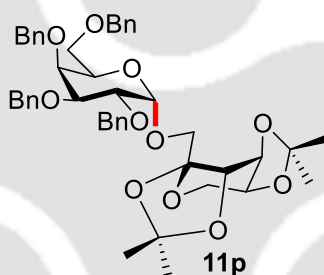
1-Adamantanyl-2,3,4,6-tetra-*p*-methyl-O-benzyl -D-glucopyranoside (**4o**).



Glycosylation of **9f** (50 mg, 0.06 mmol) with 1-adamantanol (**10n**) (18.3 mg, 0.12 mmol) according to General procedure 3 afforded **11o** (35.1 mg, 80 %, $\alpha:\beta = 1:1.5$) as a colorless

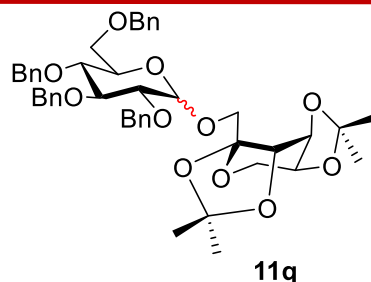
symp. The crude product was purified through flash column chromatography, R_f = 0.6 (Hexane: EtOAc = 7: 1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.24 (m, 6H), 7.21 (d, J = 7.7 Hz, 4H), 7.17 (d, J = 7.9 Hz, 2H), 7.15 – 7.08 (m, 11H), 7.08 – 7.05 (m, 5H), 6.99 (d, J = 7.8 Hz, 2H), 5.23 (d, J = 3.6 Hz, 1H), 4.94 (t, J = 11.0 Hz, 2H), 4.85 (d, J = 10.6 Hz, 1H), 4.78 – 4.73 (m, 3H), 4.71 (d, J = 10.6 Hz, 1H), 4.67 (d, J = 3.5 Hz, 1H), 4.65 (d, J = 4.8 Hz, 2H), 4.62 (d, J = 8.1 Hz, 1H), 4.60 (d, J = 8.4 Hz, 1H), 4.54 (d, J = 11.9 Hz, 1H), 4.49 (d, J = 11.9 Hz, 1H), 4.45 (d, J = 10.6 Hz, 1H), 4.37 (dd, J = 19.6, 11.2 Hz, 2H), 3.98 – 3.94 (m, 2H), 3.74 – 3.67 (m, 2H), 3.58 (m, 4H), 3.49 (dd, J = 9.7, 3.6 Hz, 1H), 3.47 – 3.43 (m, 1H), 3.43 (d, J = 4.3 Hz, 1H), 3.41 – 3.37 (m, 1H), 2.34 (s, 3H), 2.33 (s, 6H), 2.32 (s, 6H), 2.31 (s, 3H), 2.30 (s, 3H), 2.15 (s, 3H), 2.12 (s, 3H), 1.94 (s, 2H), 1.92 (s, 2H), 1.86 – 1.81 (m, 6H), 1.79 (d, J = 11.4 Hz, 3H), 1.67 – 1.59 (m, 11H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 137.4, 137.3, 137.3, 137.2, 137.2, 137.1, 136.1, 135.8, 135.6, 135.4, 135.3, 135.2, 135.0, 129.0, 129.02, 129.0, 129.0, 129.0, 128.4, 128.3, 128.1, 128.1, 128.1, 127.8, 96.2, 89.9, 85.0, 82.2, 82.0, 79.8, 78.1, 77.9, 75.6, 75.4, 75.2, 74.9, 74.8, 74.6, 74.5, 73.3, 73.2, 72.8, 69.6, 69.3, 68.4, 42.8, 42.4, 36.3, 30.7, 30.7, 21.2, 21.2, 21.2, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{48}\text{H}_{62}\text{NO}_6$ 748.4577; found 748.4576. $[\alpha]_{\text{D}}^{35} = +0.24$ (c 0.01, CHCl_3).

2,3;4,5-di-O-isopropylidene-1-O- (2,3,4,6-tetra-O-benzyl- α -D-galactopyranosyl)- β -D-fructopyranose (11p).



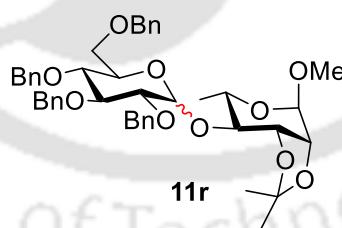
Glycosylation of **9a** (46.6 mg, 0.06 mmol) with **10j** (31.2 mg, 0.12 mmol) according to General procedure 3 afforded **11p** (40.7 mg, 87 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.36 (Hexane: EtOAc = 3: 1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.37 (d, J = 7.2 Hz, 2H), 7.30 (m, 18H), 4.95 (d, J = 11.4 Hz, 1H), 4.90 (d, J = 3.5 Hz, 1H), 4.81 (d, J = 11.7 Hz, 1H), 4.75 (d, J = 12.2 Hz, 1H), 4.68 (dd, J = 11.9, 6.6 Hz, 2H), 4.59 (d, J = 11.5 Hz, 1H), 4.56 (d, J = 2.6 Hz, 1H), 4.53 (dd, J = 7.8, 2.5 Hz, 1H), 4.46 (d, J = 11.7 Hz, 1H), 4.39 (d, J = 11.7 Hz, 1H), 4.21 (d, J = 7.7 Hz, 1H), 4.04 (dd, J = 10.0, 3.5 Hz, 1H), 4.00 (t, J = 6.6 Hz, 1H), 3.97 (s, 1H), 3.93 – 3.88 (m, 3H), 3.71 (d, J = 12.9 Hz, 1H), 3.55 (t, J = 8.4 Hz, 1H), 3.49 (dd, J = 9.1, 5.7 Hz, 1H), 3.39 (d, J = 10.7 Hz, 1H), 1.49 (s, 3H), 1.47 (s, 3H), 1.36 (s, 3H), 1.34 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.8, 138.7, 137.9, 128.4, 128.3, 128.2, 127.9, 127.7, 127.7, 127.6, 127.5, 127.4, 108.9, 108.6, 102.3, 98.8, 78.4, 76.9, 74.9, 74.8, 73.4, 73.2, 72.7, 71.1, 70.1, 69.5, 69.4, 69.3, 68.6, 61.1, 26.6, 26.0, 25.5, 24.1. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{46}\text{H}_{58}\text{NO}_{11}$ 800.4004; found 800.4007. $[\alpha]_{\text{D}}^{35} = +0.28$ (c 0.01, CHCl_3).

2,3;4,5-di-O-isopropylidene-1-O- (2,3,4,6-tetra-O-benzyl-D-glucopyranosyl)- β -D-fructopyranose (11q).



Glycosylation of **9d** (46.6 mg, 0.06 mmol) with **10j** (31.2 mg, 0.12 mmol) according to General procedure 3 afforded **11q** (40 mg, 85 %, $\alpha:\beta = 1.2:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.35$ (Hexane: EtOAc = 3: 1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.38 – 7.23 (m, 35H), 7.21 – 7.16 (m, 2H), 7.15 – 7.11 (m, 3H), 5.01 (d, $J = 10.7$ Hz, 1H), 4.91 (d, $J = 10.9$ Hz, 1H), 4.88 (d, $J = 10.9$ Hz, 1H), 4.85 (d, $J = 3.4$ Hz, 1H), 4.82 (d, $J = 10.9$ Hz, 2H), 4.79 (d, $J = 11.0$ Hz, 1H), 4.76 (d, $J = 7.8$ Hz, 1H), 4.74 (d, $J = 8.5$ Hz, 1H), 4.68 (d, $J = 10.8$ Hz, 1H), 4.65 (d, $J = 12.2$ Hz, 2H), 4.60 (dd, $J = 11.1$, 7.5 Hz, 2H), 4.58 (d, $J = 2.5$ Hz, 2H), 4.57 – 4.53 (m, 2H), 4.52 – 4.46 (m, 3H), 4.44 (d, $J = 12.1$ Hz, 1H), 4.25 – 4.20 (m, 2H), 3.98 – 3.95 (m, 1H), 3.95 – 3.91 (m, 3H), 3.90 (dd, $J = 11.5$, 6.2 Hz, 2H), 3.84 (d, $J = 9.9$ Hz, 1H), 3.79 – 3.74 (m, 2H), 3.73 (dd, $J = 5.8$, 2.9 Hz, 2H), 3.70 (d, $J = 6.7$ Hz, 1H), 3.69 – 3.63 (m, 3H), 3.62 (dd, $J = 10.7$, 1.8 Hz, 1H), 3.57 (dd, $J = 9.6$, 3.4 Hz, 1H), 3.49 (dd, $J = 10.0$, 6.4 Hz, 1H), 3.46 – 3.42 (m, 1H), 3.40 (d, $J = 10.7$ Hz, 1H), 1.61 (s, 3H), 1.52 (s, 3H), 1.48 (s, 6H), 1.44 (s, 3H), 1.42 (s, 3H), 1.37 (s, 3H), 1.31 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.7, 138.7, 138.5, 138.4, 138.4, 138.2, 137.9, 128.4, 128.4, 128.4, 128.3, 128.3, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 108.9, 108.8, 108.7, 103.2, 102.3, 102.2, 98.2, 84.8, 82.5, 81.9, 80.3, 77.8, 77.5, 75.7, 75.5, 75.1, 75.0, 74.9, 73.7, 73.5, 73.1, 71.1, 71.0, 70.4, 70.3, 70.2, 70.2, 70.1, 69.5, 69.4, 68.9, 68.3, 61.1, 61.1, 26.7, 26.6, 26.0, 26.0, 25.7, 25.5, 24.1, 24.1. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{46}\text{H}_{58}\text{NO}_{11}$ 800.4004; found 800.4006. $[\alpha]_{\text{D}}^{35} = +0.48$ (c 0.01, CHCl_3).

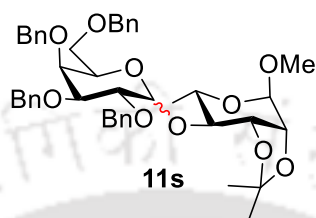
Methyl 6-deoxy-4-O-(2,3,4,6-tetra-O-benzyl-D-glucopyranosyl)-2,3-O-isopropylidene- α -L-pneumopyranoside (11r).



Glycosylation of **9d** (46.6 mg, 0.06 mmol) with **10i** (26.2 mg, 0.12 mmol) according to General procedure 3 afforded **11r** (32.7 mg, 74 %, $\alpha:\beta = 3:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.29$ (Hexane: EtOAc = 4: 1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.37 – 7.22 (m, 36H), 7.17 (t, $J = 8.0$ Hz, 4H), 4.96 (d, $J = 2.9$ Hz, 2H), 4.96 (d, $J = 8.6$ Hz, 1H), 4.88 – 4.84 (m, 2H), 4.84 – 4.81 (m, 3H), 4.79 (dd, $J = 14.1$, 6.4 Hz, 2H), 4.74 – 4.72 (m, 1H), 4.71 (d, $J = 11.6$ Hz, 1H), 4.66 (d, $J = 11.9$ Hz, 1H), 4.61 (t, $J = 13.1$ Hz, 2H), 4.54 – 4.50 (m, 2H), 4.49 (d, $J = 12.1$ Hz, 2H), 4.45 (d, $J = 12.1$ Hz, 1H), 4.21 – 4.16 (m, 1H), 4.09 (dd, $J = 13.8$, 6.7 Hz, 2H), 4.05 (d, $J = 5.4$ Hz, 2H), 3.98 (t, $J = 9.4$ Hz, 2H), 3.92 (t, $J = 9.4$ Hz, 1H), 3.86 (dd, $J = 9.0$, 3.2 Hz, 1H), 3.79 (t, $J = 9.7$ Hz, 3H), 3.76 – 3.70 (m, 3H), 3.65 – 3.62 (m, 1H), 3.60 (dd, $J = 9.8$, 3.4 Hz, 2H), 3.33 (s, 3H), 3.32 (m, 1H), 3.31 (s, 1H), 3.29 (s, 1H), 1.43 (s, 3H), 1.35 (s, 1H), 1.31 (d, $J = 6.3$ Hz, 6H), 1.25 (s, 3H), 1.20

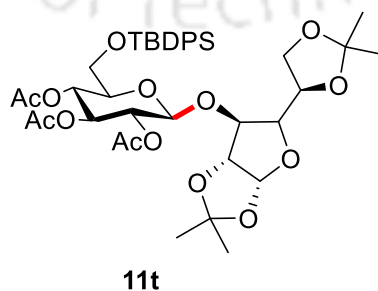
(s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.8, 138.3, 138.0, 137.9, 128.5, 128.4, 128.4, 128.3, 128.3, 128.0, 128.0, 127.8, 127.8, 127.7, 127.7, 127.6, 109.0, 98.3, 97.8, 82.2, 80.9, 79.8, 77.9, 77.3, 75.9, 75.6, 75.2, 74.3, 73.6, 70.3, 68.0, 64.8, 28.2, 26.4, 17.4. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{44}\text{H}_{56}\text{NO}_{10}$ 758.3899; found 758.3895. $[\alpha]_{\text{D}}^{35} = +0.36$ (c 0.01, CHCl_3).

Methyl 6-deoxy-4-O-(2,3,4,6-tetra-O-benzyl-D-galactopyranosyl)-2,3-O-isopropylidene- α -L-pneumopyranoside (11s).



Glycosylation of **9a** (46.6 mg, 0.06 mmol) with **10i** (26.2 mg, 0.12 mmol) according to General procedure 3 afforded **11s** (34 mg, 77 %, $\alpha:\beta = 1:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.3$ (Hexane: EtOAc = 4: 1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.42 – 7.29 (m, 40H), 4.97 (d, $J = 5.3$ Hz, 1H), 4.96 (d, $J = 2.4$ Hz, 2H), 4.93 (d, $J = 11.1$ Hz, 1H), 4.87 (d, $J = 6.7$ Hz, 1H), 4.86 (d, $J = 2.4$ Hz, 1H), 4.84 (d, $J = 2.6$ Hz, 1H), 4.78 (d, $J = 12.9$ Hz, 3H), 4.75 – 4.72 (m, 3H), 4.63 (d, $J = 11.8$ Hz, 1H), 4.61 (d, $J = 11.6$ Hz, 1H), 4.51 (d, $J = 11.9$ Hz, 1H), 4.45 (d, $J = 3.6$ Hz, 2H), 4.43 – 4.40 (m, 1H), 4.28 – 4.22 (m, 2H), 4.14 – 4.16 (m, 1H), 4.09 (t, $J = 5.6$ Hz, 3H), 3.99 (dd, $J = 10.2, 2.6$ Hz, 1H), 3.91 (d, $J = 2.2$ Hz, 1H), 3.75 (dt, $J = 13.4, 6.6$ Hz, 2H), 3.69 – 3.67 (m, 1H), 3.66 – 3.61 (m, 4H), 3.58 – 3.57 (m, 1H), 3.56 (d, $J = 4.0$ Hz, 1H), 3.54 (d, $J = 7.8$ Hz, 1H), 3.52 – 3.50 (m, 1H), 3.40 (s, 3H), 3.35 (s, 3H), 3.34 – 3.32 (m, 1H), 3.31 (d, $J = 6.3$ Hz, 1H), 1.47 (s, 3H), 1.39 (s, 3H), 1.34 (s, 3H), 1.32 (d, $J = 6.5$ Hz, 6H), 1.27 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 139.0, 139.0, 138.8, 138.7, 138.7, 138.3, 138.1, 137.9, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 127.8, 127.8, 127.7, 127.6, 127.5, 127.5, 127.5, 127.4, 127.4, 127.4, 109.2, 109.0, 102.1, 98.8, 98.0, 97.8, 82.3, 80.2, 79.7, 79.4, 78.6, 78.2, 76.1, 75.9, 75.9, 75.1, 74.9, 74.6, 74.5, 74.4, 74.0, 73.5, 73.5, 73.3, 73.2, 72.5, 68.8, 68.7, 67.7, 64.9, 64.4, 54.9, 54.6, 28.0, 27.8, 26.4, 26.3, 17.9, 17.3. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{44}\text{H}_{52}\text{NaO}_{10}$ 763.3453; found 763.3450. $[\alpha]_{\text{D}}^{35} = +0.26$ (c 0.01, CHCl_3).

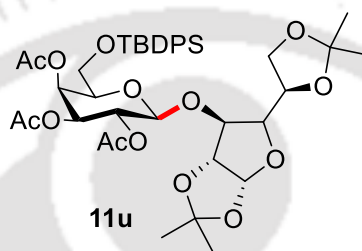
1,2;4,6-di-O-isopropylidene-3-O-(2,3,4-tri-O-acetyl-6-O-tert-butylbiphenylsilyl)- β -D-glucopyranosyl)- α -D-glucofuranose (11t).



Glycosylation of **9g** (46.9 mg, 0.06 mmol) with **10g** (31.2 mg, 0.12 mmol) according to General procedure 3 afforded **11t** (38.7 mg, 82 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.32$ (Hexane: EtOAc = 3:1, v/v). ^1H

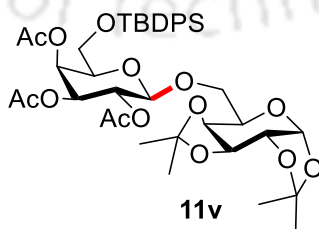
NMR (600 MHz, CDCl₃) δ 7.71 – 7.67 (m, 2H), 7.67 – 7.64 (m, 2H), 7.44 – 7.36 (m, 6H), 5.98 (d, J = 3.7 Hz, 1H), 5.17 (t, J = 9.3 Hz, 1H), 5.13 (t, J = 9.4 Hz, 1H), 5.03 – 4.99 (m, 1H), 4.59 (d, J = 8.0 Hz, 1H), 4.57 (d, J = 3.7 Hz, 1H), 4.22 (dd, J = 7.2, 3.8 Hz, 1H), 4.19 (d, J = 3.8 Hz, 1H), 4.00 (dd, J = 11.4, 2.5 Hz, 1H), 3.76 (td, J = 7.3, 2.5 Hz, 1H), 3.73 (d, J = 3.4 Hz, 2H), 3.64 (dd, J = 11.4, 7.4 Hz, 1H), 3.54 (dt, J = 9.4, 3.4 Hz, 1H), 2.03 (s, 3H), 2.00 (s, 3H), 1.90 (s, 3H), 1.49 (s, 3H), 1.36 (s, 3H), 1.36 (s, 3H), 1.33 (s, 3H), 1.04 (s, 9H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 170.6, 169.3, 169.3, 135.8, 135.6, 133.3, 133.0, 129.7, 127.7, 127.7, 112.2, 106.4, 100.9, 100.9, 84.0, 79.1, 75.0, 74.6, 73.3, 71.7, 71.4, 69.4, 68.7, 62.6, 27.2, 26.7, 26.5, 24.1, 24.0, 20.7, 20.7, 20.6, 19.2. HRMS (ESI) m/z : [M + NH₄]⁺ calcd for C₄₀H₅₈NO₁₄Si 804.3627; found 804.3628. $[\alpha]_D^{35}$ = + 0.40 (c 0.01, CHCl₃).

1,2;4,6-di-O-isopropylidene-3-O-(2,3,4-tri-O-acetyl-6-O-tert-butylbiphenylsilyl)- β -D-galactopyranosyl)- α -D-glucofuranose (11u).



Glycosylation of **9h** (46.9 mg, 0.06 mmol) with **10g** (31.2 mg, 0.12 mmol) according to General procedure 3 afforded **11u** (39.3 mg, 83 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.33 (Hexane: Ethyl acetate = 3:1, v/v). ¹H NMR (600 MHz, CDCl₃) δ 7.64 – 7.57 (m, 4H), 7.47 – 7.35 (m, 6H), 5.95 (d, J = 3.7 Hz, 1H), 5.56 (d, J = 2.9 Hz, 1H), 5.18 (dd, J = 10.4, 8.0 Hz, 1H), 5.03 (dd, J = 10.5, 3.4 Hz, 1H), 4.57 – 4.50 (m, 2H), 4.18 (m, 2H), 3.97 (dd, J = 11.3, 2.4 Hz, 1H), 3.79 – 3.72 (m, 2H), 3.70 (td, J = 7.4, 2.4 Hz, 1H), 3.65 (dd, J = 9.4, 8.1 Hz, 1H), 3.60 (dd, J = 11.3, 7.6 Hz, 1H), 2.04 (s, 3H), 2.00 (s, 3H), 1.99 (s, 3H), 1.46 (s, 3H), 1.34 (s, 3H), 1.31 (s, 6H), 1.02 (s, 9H). ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 170.3, 170.2, 169.4, 135.6, 135.6, 133.0, 132.7, 129.9, 129.8, 127.8, 112.2, 106.4, 101.3, 100.9, 83.9, 79.1, 74.9, 73.3, 71.6, 71.2, 69.4, 69.1, 67.0, 61.0, 27.2, 26.7, 26.5, 24.1, 24.0, 20.8, 20.7, 20.7, 19.0. HRMS (ESI) m/z : [M + NH₄]⁺ calcd for C₄₀H₅₈NO₁₄Si 804.3627; found 804.3626. $[\alpha]_D^{35}$ = - 0.38 (c 0.01, CHCl₃).

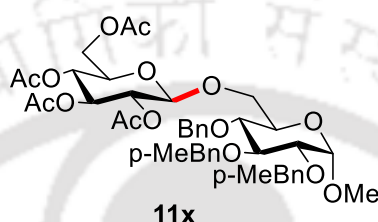
1,2;3,4-di-O-isopropylidene-6-O-(2,3,4-tri-O-acetyl-6-O-tert-butylbiphenylsilyl)- β -D-galactopyranosyl)- α -D-galactopyranose (11v).



Glycosylation of **9h** (46.9 mg, 0.06 mmol) with **2h** (31.2 mg, 0.12 mmol) according to General procedure 3 afforded **11v** (41.6 mg, 88 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.31 (Hexane/EtOAc = 3:1, v/v). ¹H NMR (600 MHz, CDCl₃) δ 7.63 – 7.58 (m, 4H), 7.47 – 7.35 (m, 6H), 5.58 (d, J = 2.8 Hz, 1H), 5.50 (d, J = 4.9 Hz, 1H), 5.18 (dd, J = 10.4, 8.1 Hz, 1H), 5.05 (dd, J = 10.5, 3.3 Hz, 1H), 4.56 (dd,

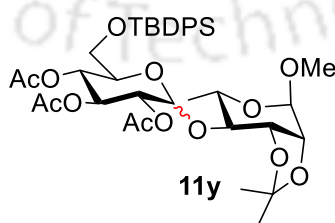
$J = 7.9, 2.1$ Hz, 1H), 4.53 (d, $J = 8.0$ Hz, 1H), 4.28 (dd, $J = 4.8, 2.3$ Hz, 1H), 4.13 (dd, $J = 8.0, 1.3$ Hz, 1H), 3.99 (dd, $J = 11.5, 3.1$ Hz, 1H), 3.90 (d, $J = 6.5$ Hz, 1H), 3.80 – 3.76 (m, 1H), 3.74 (dd, $J = 9.7, 5.7$ Hz, 1H), 3.66 – 3.59 (m, 2H), 2.09 (s, 3H), 2.00 (s, 3H), 1.99 (s, 3H), 1.49 (s, 3H), 1.42 (s, 3H), 1.31 (s, 3H), 1.29 (s, 3H), 1.02 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.3, 170.2, 169.9, 135.6, 135.6, 132.9, 132.7, 129.9, 129.8, 127.8, 127.8, 109.3, 108.7, 102.0, 96.2, 73.1, 71.2, 71.1, 70.6, 70.4, 69.6, 68.9, 67.8, 67.0, 60.9, 26.7, 26.1, 25.9, 25.1, 24.2, 20.9, 20.8, 20.7, 19.0. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{40}\text{H}_{58}\text{NO}_{14}\text{Si}$ 804.3627; found 804.3628. $[\alpha]_{\text{D}}^{35} = -0.62$ (c 0.015, CHCl_3).

Methyl 4-O-benzyl-2,3-di-*p*-methyl-O-benzyl-6-O-(2,3,4,6-tetra-O-acetyl- β -D-glucopyranosyl)- α -D-glucopyranoside (11x).



Glycosylation of **9c** (41 mg, 0.07 mmol) with **10c** (69 mg, 0.14 mmol) according to General procedure 3 afforded **11x** (46.7 mg, 81 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.3$ (Hexane/EtOAc = 3:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.37 – 7.29 (m, 3H), 7.26 – 7.20 (m, 6H), 7.13 (dd, $J = 7.5, 5.4$ Hz, 4H), 5.17 (t, $J = 9.4$ Hz, 1H), 5.11 – 5.01 (m, 2H), 4.93 (d, $J = 10.6$ Hz, 1H), 4.86 (d, $J = 10.9$ Hz, 1H), 4.75 (dd, $J = 11.1, 9.4$ Hz, 2H), 4.60 (d, $J = 12.0$ Hz, 1H), 4.51 (dd, $J = 9.9, 5.1$ Hz, 3H), 4.23 (dd, $J = 12.3, 4.7$ Hz, 1H), 4.11 (dd, $J = 12.3, 2.4$ Hz, 1H), 4.04 (dd, $J = 10.6, 1.4$ Hz, 1H), 3.94 (t, $J = 9.3$ Hz, 1H), 3.75 (dd, $J = 9.9, 3.3$ Hz, 1H), 3.70 – 3.61 (m, 2H), 3.48 (dd, $J = 9.6, 3.6$ Hz, 1H), 3.42 – 3.36 (m, 1H), 3.35 (s, 3H), 2.34 (s, 3H), 2.34 (s, 3H), 2.05 (s, 3H), 2.02 (s, 3H), 1.99 (s, 3H), 1.95 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.7, 170.4, 169.4, 169.1, 138.2, 137.7, 137.3, 135.7, 135.0, 129.2, 129.1, 128.5, 128.3, 128.1, 127.9, 127.7, 100.7, 98.2, 81.8, 79.5, 77.6, 75.6, 74.9, 73.3, 73.0, 71.8, 71.3, 69.6, 68.3, 68.2, 61.9, 55.2, 21.2, 20.7, 20.7, 20.6, 20.6. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{44}\text{H}_{58}\text{NO}_{15}$ 840.3806; found 840.3807. $[\alpha]_{\text{D}}^{35} = +0.14$ (c 0.01, CHCl_3).

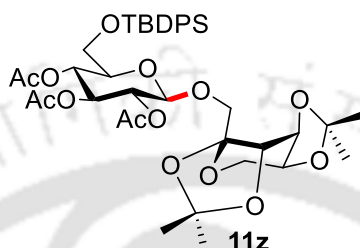
Methyl 6-deoxy-4-O-(2,3,4-tri-O-acetyl-6-O-*tert*-butylbiphenylsilyl)-D-glucopyranosyl)-2,3-O-isopropylidene- α -L-pneumopyranoside (11y).



Glycosylation of **9g** (46.9 mg, 0.06 mmol) with **10i** (26.2 mg, 0.12 mmol) according to General procedure 3 afforded **11y** (31.5 mg, 70 %, $\alpha:\beta = 1:6$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.32$ (Hexane: EtOAc = 3:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.68 – 7.66 (m, 2H), 7.65 – 7.62 (m, 2H), 7.45 – 7.40 (m, 3H), 7.39 – 7.35 (m, 3H), 5.26 – 5.22 (m, 2H), 4.99 (dd, $J = 12.7, 5.5$ Hz, 2H), 4.87 (s, 1H), 4.07 (q, $J = 5.6$ Hz, 2H), 3.73 (d, $J = 11.4$ Hz, 1H), 3.69 (dd, $J = 11.4, 3.9$ Hz, 1H), 3.62 (d, $J = 5.1$ Hz,

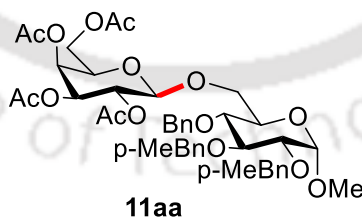
2H), 3.55 – 3.51 (m, 1H), 3.37 (s, 3H), 2.07 (s, 3H), 2.01 (s, 3H), 1.92 (s, 3H), 1.60 (s, 3H), 1.42 (s, 3H), 1.33 (d, $J = 4.8$ Hz, 3H), 1.04 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.6, 169.7, 169.2, 135.6, 135.5, 133.1, 132.8, 129.8, 129.7, 127.8, 127.7, 109.3, 99.6, 97.8, 79.3, 78.3, 76.0, 74.4, 73.4, 71.8, 68.6, 63.9, 62.0, 54.8, 29.7, 28.0, 26.6, 26.4, 20.8, 20.7, 20.6, 19.2, 17.5. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{38}\text{H}_{52}\text{NaO}_{13}\text{Si}$ 767.3069; found 767.3068. $[\alpha]_{\text{D}}^{35} = +0.12$ (c 0.01, CHCl_3).

2,3,4,5-di-O-isopropylidene-1-O- (2,3,4-tri-O-acetyl-6-O-tert-butylbiphenylsilyl)- β -D-glucopyranosyl)- β -D-fructopyranose (11z).



Glycosylation of **9g** (46.9 mg, 0.06 mmol) with **10j** (31.2 mg, 0.12 mmol) according to General procedure 3 afforded **11z** (41 mg, 87 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.3$ (Hexane: EtOAc = 3:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.67 – 7.61 (m, 4H), 7.44 – 7.35 (m, 6H), 5.18 – 5.13 (m, 2H), 5.04 (td, $J = 7.9, 1.9$ Hz, 1H), 4.64 (d, $J = 7.9$ Hz, 1H), 4.59 (dd, $J = 7.8, 2.6$ Hz, 1H), 4.45 (d, $J = 2.7$ Hz, 1H), 4.22 (d, $J = 7.9$ Hz, 1H), 3.95 (d, $J = 10.7$ Hz, 1H), 3.92 (dd, $J = 12.9, 1.6$ Hz, 1H), 3.73 (t, $J = 11.1$ Hz, 4H), 3.55 (dd, $J = 6.0, 3.3$ Hz, 1H), 2.02 (s, 3H), 1.99 (s, 3H), 1.86 (s, 3H), 1.54 (s, 3H), 1.37 (s, 3H), 1.36 (s, 3H), 1.30 (s, 3H), 1.04 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.5, 169.4, 169.3, 135.6, 133.1, 133.0, 129.8, 129.7, 127.8, 127.7, 109.0, 108.7, 102.0, 100.5, 74.7, 73.6, 71.6, 71.0, 70.2, 69.9, 69.8, 68.7, 62.6, 61.3, 26.7, 26.6, 25.9, 25.5, 24.1, 20.8, 20.7, 20.6, 19.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{40}\text{H}_{58}\text{NO}_{14}\text{Si}$ 804.3621; found 804.3621. $[\alpha]_{\text{D}}^{35} = +0.32$ (c 0.01, CHCl_3).

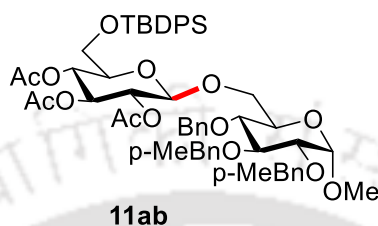
Methyl 4-O-benzyl-2,3-di-p-methyl-O-benzyl-6-O-(2,3,4,6-tetra-O-acetyl- β -D-galactopyranosyl)- α -D-glucopyranoside (11aa).



Glycosylation of **9b** (41 mg, 0.07 mmol) with **10c** (69 mg, 0.14 mmol) according to General procedure 3 afforded **11aa** (46 mg, 80 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.31$ (Hexane/EtOAc = 3:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.37 – 7.29 (m, 3H), 7.24 (dd, $J = 10.1, 7.8$ Hz, 6H), 7.13 (dd, $J = 7.6, 4.7$ Hz, 4H), 5.36 (d, $J = 2.7$ Hz, 1H), 5.25 (dd, $J = 10.4, 8.0$ Hz, 1H), 4.98 (dd, $J = 10.4, 3.4$ Hz, 1H), 4.93 (d, $J = 10.7$ Hz, 1H), 4.86 (d, $J = 10.9$ Hz, 1H), 4.75 (dd, $J = 11.2, 8.6$ Hz, 2H), 4.61 (d, $J = 12.0$ Hz, 1H), 4.54 – 4.49 (m, 2H), 4.47 (d, $J = 8.0$ Hz, 1H), 4.17 – 4.10 (m, 2H), 4.09 – 4.05 (m, 1H), 3.95 (t, $J = 9.3$ Hz, 1H), 3.85 (t, $J = 6.7$ Hz, 1H), 3.76 (dd, $J = 10.0, 3.4$ Hz, 1H), 3.65 (dd, $J = 10.7, 5.0$ Hz, 1H), 3.48 (dd, $J = 9.6, 3.5$ Hz, 1H), 3.39 (d, $J = 9.1$ Hz,

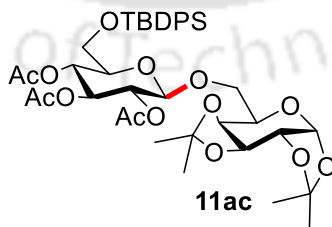
1H), 3.35 (s, 3H), 2.34 (s, 6H), 2.12 (s, 3H), 2.02 (s, 3H), 1.97 (s, 3H), 1.96 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 169.4, 169.3, 169.2, 168.1, 137.2, 136.6, 136.3, 134.7, 134.1, 128.1, 128.0, 127.5, 127.3, 127.1, 126.8, 126.7, 100.3, 97.1, 80.8, 78.6, 76.7, 76.2, 74.6, 73.8, 72.3, 70.1, 69.6, 68.7, 67.8, 67.3, 66.0, 60.1, 54.2, 20.2, 19.8, 19.6, 19.6. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{44}\text{H}_{58}\text{NO}_{15}$ 840.3806; found 840.3804. $[\alpha]_{\text{D}}^{35} = -0.24$ (c 0.01, CHCl_3).

Methyl 4-O-benzyl-2,3-di-*p*-methyl-O-benzyl-6-O-(2,3,4-tri-O-acetyl-6-O-*tert*-butyldiphenylsilyl)- β -D-glucopyranosyl)- α -D-glucopyranoside (11ab).



Glycosylation of **9g** (46.9 mg, 0.06 mmol) with **10c** (59 mg, 0.12 mmol) according to General procedure 3 afforded **11ab** (53.3 mg, 87 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.31$ (Hexane/EtOAc = 3:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.67 (dd, $J = 7.3, 1.8$ Hz, 2H), 7.65 – 7.62 (m, 2H), 7.41 – 7.31 (m, 8H), 7.29 (d, $J = 7.1$ Hz, 1H), 7.27–7.24 (m, 4H), 7.22 (d, $J = 7.9$ Hz, 2H), 7.13 (t, $J = 8.3$ Hz, 4H), 5.15 (t, $J = 9.4$ Hz, 1H), 5.09 – 5.05 (m, 1H), 5.04 (dd, $J = 7.1, 5.9$ Hz, 1H), 4.93 (d, $J = 10.6$ Hz, 1H), 4.86 (d, $J = 10.8$ Hz, 1H), 4.76 (t, $J = 12.4$ Hz, 2H), 4.61 (d, $J = 12.0$ Hz, 1H), 4.55 (d, $J = 3.5$ Hz, 1H), 4.51 (d, $J = 10.8$ Hz, 1H), 4.48 (d, $J = 8.0$ Hz, 1H), 4.09 (d, $J = 9.5$ Hz, 1H), 3.96 (t, $J = 9.3$ Hz, 1H), 3.72 (dd, $J = 11.6, 5.5$ Hz, 2H), 3.68 (ddd, $J = 10.6, 5.6, 3.1$ Hz, 2H), 3.51 (ddd, $J = 13.1, 7.5, 2.8$ Hz, 2H), 3.43 (t, $J = 9.5$ Hz, 1H), 3.34 (s, 3H), 2.35 (s, 3H), 2.34 (s, 3H), 1.98 (s, 3H), 1.93 (s, 3H), 1.90 (s, 3H), 1.02 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.6, 169.3, 169.1, 138.3, 137.7, 137.3, 135.7, 135.7, 135.6, 135.1, 133.2, 133.1, 129.7, 129.7, 129.2, 129.1, 128.5, 128.3, 128.2, 127.8, 127.7, 127.7, 127.7, 100.7, 98.2, 81.9, 79.6, 77.6, 75.7, 74.9, 74.8, 73.5, 73.3, 71.6, 69.7, 68.7, 67.9, 62.7, 55.1, 26.7, 21.2, 20.7, 20.7, 20.6, 19.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{58}\text{H}_{74}\text{NO}_{14}$ Si 1036.4879; found 1036.4876. $[\alpha]_{\text{D}}^{35} = +0.16$ (c 0.01, CHCl_3).

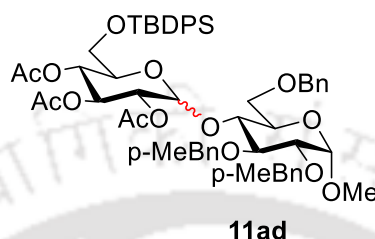
1,2,3,4-di-O-isopropylidene-6-O-(2,3,4-tri-O-acetyl-6-O-*tert*-butyldiphenylsilyl)- β -D-glucopyranosyl)- α -D-galactopyranose (11ac).



Glycosylation of **9g** (46.9 mg, 0.06 mmol) with **2h** (31.2 mg, 0.12 mmol) according to General procedure 3 afforded **11ac** (40.6 mg, 86 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.31$ (Hexane/EtOAc = 3:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.68 (ddd, $J = 13.5, 7.5, 1.5$ Hz, 4H), 7.45 – 7.35 (m, 6H), 5.52 (d, $J = 4.9$ Hz, 1H), 5.17 (p, $J = 9.3$ Hz, 2H), 5.01 (t, $J = 8.6$ Hz, 1H), 4.61 – 4.57 (m, 2H), 4.30 (dd, $J = 4.9, 2.4$ Hz, 1H), 4.20 (dd, $J = 7.9, 1.7$ Hz, 1H), 4.07 (dd, $J = 11.4, 3.5$ Hz, 1H), 3.95 (m, 1H), 3.75 – 3.68 (m, 3H), 3.54 (m, 1H), 2.08 (s, 3H), 2.00 (s, 3H), 1.90 (s, 3H), 1.52 (s, 3H),

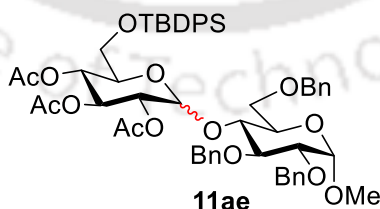
1.43 (s, 3H), 1.33 (s, 3H), 1.31 (s, 3H), 1.04 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.5, 169.7, 169.3, 135.7, 135.6, 133.2, 133.2, 129.7, 129.7, 127.7, 127.7, 109.4, 108.6, 101.4, 96.3, 74.5, 73.2, 71.3, 71.3, 70.7, 70.5, 69.2, 68.8, 67.9, 62.5, 26.7, 26.1, 26.0, 25.1, 24.3, 20.8, 20.7, 20.6, 19.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{40}\text{H}_{58}\text{NO}_{14}\text{Si}$ 804.3627; found 804.3626. $[\alpha]_{\text{D}}^{35} = -0.84$ (c 0.025, CHCl_3).

Methyl 6-O-benzyl-2,3-di-*p*-methyl-O-benzyl-4-O-(2,3,4-tri-O-acetyl-6-O-tert-butyl-diphenylsilyl-D-glucopyranosyl)- α -D-glucopyranoside (11ad).



Glycosylation of **9g** (46.9 mg, 0.06 mmol) with **10e** (59 mg, 0.12 mmol) according to General procedure 3 afforded **11ad** (51.4 mg, 84 %, $\alpha:\beta = 1:5.8$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.32$ (Hexane/EtOAc = 3:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.69 – 7.65 (m, 2H), 7.63 – 7.60 (m, 2H), 7.43 – 7.38 (m, 4H), 7.37 – 7.29 (m, 7H), 7.16 (dd, $J = 9.6, 8.3$ Hz, 4H), 7.07 (d, $J = 7.7$ Hz, 2H), 7.00 (d, $J = 7.7$ Hz, 2H), 5.04 (t, $J = 9.6$ Hz, 1H), 4.92 (t, $J = 9.4$ Hz, 1H), 4.86 – 4.79 (m, 2H), 4.75 (d, $J = 11.8$ Hz, 1H), 4.70 (t, $J = 12.5$ Hz, 2H), 4.55 (d, $J = 12.2$ Hz, 1H), 4.52 (d, $J = 3.5$ Hz, 1H), 4.49 (d, $J = 8.0$ Hz, 1H), 4.43 (t, $J = 10.8$ Hz, 1H), 3.87 (t, $J = 9.4$ Hz, 1H), 3.82 (t, $J = 9.2$ Hz, 1H), 3.72 (dd, $J = 10.7, 3.0$ Hz, 1H), 3.63 (d, $J = 9.5$ Hz, 1H), 3.58 (td, $J = 12.4, 3.2$ Hz, 3H), 3.42 (dd, $J = 9.4, 3.6$ Hz, 1H), 3.34 (s, 3H), 3.22 – 3.17 (m, 1H), 2.31 (s, 3H), 2.28 (s, 3H), 1.97 (s, 3H), 1.93 (s, 3H), 1.86 (s, 3H), 1.02 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.5, 169.3, 169.2, 137.6, 137.4, 136.5, 136.2, 135.7, 135.7, 135.3, 133.2, 133.1, 129.7, 129.7, 129.0, 128.7, 128.6, 128.3, 128.2, 128.1, 127.8, 127.8, 127.7, 99.5, 98.6, 79.3, 78.5, 76.4, 74.7, 74.4, 73.7, 73.4, 72.3, 69.8, 68.9, 67.8, 62.6, 55.3, 26.8, 21.2, 20.8, 20.7, 20.6, 19.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{58}\text{H}_{74}\text{NO}_{14}\text{Si}$ 1036.4879; found 1036.4879. $[\alpha]_{\text{D}}^{35} = -0.34$ (c 0.01, CHCl_3).

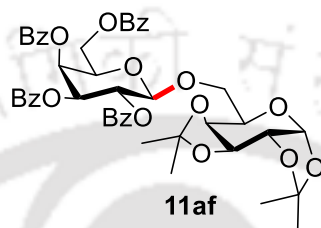
Methyl 2,3,6-tri-O-benzyl-4-O-(2,3,4-tri-O-acetyl-6-O-tert-butyl-diphenylsilyl-D-glucopyranosyl)- α -D-glucopyranoside (11ae).



Glycosylation of **9g** (46.9 mg, 0.06 mmol) with **2k** (55.7 mg, 0.12 mmol) according to General procedure 3 afforded **11ae** (48.8 mg, 82 %, $\alpha:\beta = 1:8.6$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.33$ (Hexane/EtOAc, 3:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.67 (dd, $J = 7.5, 1.5$ Hz, 2H), 7.63 – 7.60 (m, 2H), 7.43 – 7.37 (m, 4H), 7.37 – 7.30 (m, 7H), 7.30 – 7.23 (m, 7H), 7.20 – 7.15 (m, 3H), 5.04 (t, $J = 9.6$ Hz, 1H), 4.93 (t, $J = 9.3$ Hz, 1H), 4.90 – 4.84 (m, 1H), 4.79 (d, $J = 12.1$ Hz, 1H), 4.74 – 4.70 (m, 2H), 4.59 (dd, $J = 10.5, 8.0$ Hz, 2H), 4.50 (d, $J = 7.9$ Hz, 1H), 4.43 (d, $J = 12.1$ Hz, 1H), 3.90 (t, $J = 9.4$ Hz, 1H), 3.85 (t, $J = 9.2$ Hz, 1H), 3.74 (dd, $J = 10.7, 3.1$ Hz, 1H), 3.63 – 5.61 (m, 1H), 3.60

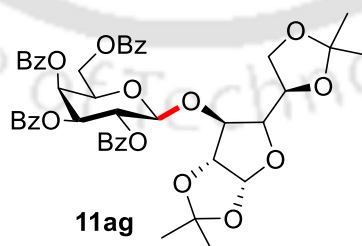
– 3.54 (m, 2H), 3.52 (dd, $J = 11.5, 4.8$ Hz, 1H), 3.46 (dt, $J = 9.4, 4.6$ Hz, 1H), 3.36 (s, 3H), 3.19 (ddd, $J = 9.9, 4.7, 2.6$ Hz, 1H), 1.98 (s, 3H), 1.93 (s, 3H), 1.86 (s, 3H), 1.02 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.5, 169.3, 169.2, 139.3, 138.3, 137.6, 135.7, 135.7, 133.2, 133.1, 129.7, 129.7, 128.6, 128.4, 128.3, 128.2, 128.0, 127.8, 127.8, 127.5, 127.0, 99.7, 98.5, 79.6, 78.8, 76.5, 74.8, 74.5, 73.8, 73.7, 73.6, 72.3, 69.8, 68.9, 67.8, 62.6, 55.3, 26.8, 20.8, 20.7, 20.6, 19.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{56}\text{H}_{70}\text{NO}_{14}$ Si 1008.4566; found 1008.4565. $[\alpha]_{\text{D}}^{35} = +0.08$ (c 0.01, CHCl_3).

1,2;3,4-di-O-isopropylidene-6-O-(2,3,4,6-tetra-O-benzoyl- β -D-galactopyranosyl)- α -D-galactopyranose (11af).



Glycosylation of **9i** (50 mg, 0.06 mmol) with **2h** (31 mg, 0.12 mmol) according to General procedure 3 afforded **11af** (45.3 mg, 90 %, β only) as a colorless syrup. ^1H NMR (500 MHz, CDCl_3) δ 8.09 (d, $J = 7.4$ Hz, 2H), 8.03 (d, $J = 7.4$ Hz, 2H), 7.97 (d, $J = 7.4$ Hz, 2H), 7.78 (d, $J = 7.4$ Hz, 2H), 7.61 (t, $J = 7.4$ Hz, 1H), 7.55 (t, $J = 7.4$ Hz, 1H), 7.48 (q, $J = 7.7$ Hz, 3H), 7.42 (td, $J = 7.7, 3.0$ Hz, 3H), 7.36 (t, $J = 7.8$ Hz, 2H), 7.24 (dd, $J = 14.4, 6.7$ Hz, 2H), 5.99 (d, $J = 3.1$ Hz, 1H), 5.81 (dd, $J = 10.3, 8.1$ Hz, 1H), 5.61 (dd, $J = 10.4, 3.4$ Hz, 1H), 5.41 (d, $J = 5.0$ Hz, 1H), 5.02 (d, $J = 8.0$ Hz, 1H), 4.67 (dd, $J = 11.2, 6.6$ Hz, 1H), 4.46 – 4.39 (m, 2H), 4.34 (t, $J = 6.6$ Hz, 1H), 4.21 (dd, $J = 5.0, 2.3$ Hz, 1H), 4.11 (d, $J = 7.9$ Hz, 1H), 4.06 (q, $J = 9.3$ Hz, 1H), 3.95 – 3.88 (m, 2H), 1.39 (s, 3H), 1.24 (s, 3H), 1.22 (s, 3H), 1.20 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 165.0, 164.6, 164.5, 164.3, 132.5, 132.2, 132.0, 129.0, 128.9, 128.8, 128.8, 128.4, 128.1, 127.8, 127.6, 127.4, 127.2, 127.2, 108.3, 107.4, 100.7, 95.2, 70.8, 70.3, 70.0, 69.5, 69.3, 68.7, 67.4, 67.2, 66.4, 61.0, 24.9, 24.8, 23.8, 23.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{46}\text{H}_{50}\text{NO}_{15}$ 856.3175; found 856.3178. $[\alpha]_{\text{D}}^{35} = +0.18$ (c 0.01, CHCl_3).

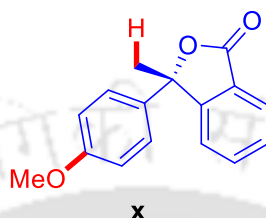
1,2;4,6-di-O-isopropylidene-3-O-(2,3,4,6-tetra-O-benzoyl- β -D-galactopyranosyl)- α -D-glucopyranose (11ag).



Glycosylation of **9i** (50 mg, 0.06 mmol) with **5e** (31.2 mg, 0.12 mmol) according to General procedure 3 afforded **11ag** (42.8 mg, 85 %, β only) as a colorless syrup. ^1H NMR (500 MHz, CDCl_3) δ 8.09 (d, $J = 7.3$ Hz, 2H), 8.03 (d, $J = 7.3$ Hz, 2H), 7.95 (d, $J = 7.4$ Hz, 2H), 7.78 (d, $J = 7.3$ Hz, 2H), 7.62 (t, $J = 7.4$ Hz, 1H), 7.56 (t, $J = 7.4$ Hz, 1H), 7.49 (q, $J = 7.6$ Hz, 3H), 7.46 – 7.40 (m, 3H), 7.36 (t, $J = 7.8$ Hz, 2H), 7.27 – 7.22 (m, 2H), 5.99 (d, $J = 3.1$ Hz, 1H), 5.89 (d, $J = 3.7$ Hz, 1H), 5.81 (dd, $J = 10.4, 8.0$ Hz, 1H), 5.60 (dd, $J = 10.4, 3.4$ Hz, 1H), 4.93 (d, $J = 7.9$ Hz, 1H), 4.67 (dd, $J = 11.3, 6.4$ Hz, 1H), 4.49 (d, $J = 3.6$ Hz, 1H), 4.43 (dd, $J = 11.3, 6.8$

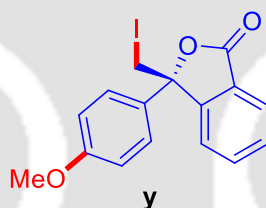
Hz, 1H), 4.32 (t, $J = 6.6$ Hz, 1H), 4.17 – 4.13 (m, 2H), 4.08 (d, $J = 3.8$ Hz, 1H), 3.77 – 3.69 (m, 2H), 1.40 (s, 3H), 1.29 (s, 3H), 1.13 (s, 3H), 1.10 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 165.1, 164.6, 164.6, 164.1, 132.5, 132.2, 132.2, 132.1, 129.0, 128.8, 128.8, 128.5, 128.4, 128.0, 127.8, 127.6, 127.4, 127.3, 127.2, 111.1, 105.3, 101.1, 99.9, 83.0, 78.2, 73.9, 70.6, 70.3, 69.4, 68.8, 67.1, 61.0, 26.1, 25.5, 22.7, 22.6. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{46}\text{H}_{50}\text{NO}_{15}$ 856.3175; found 856.3180. $[\alpha]_{\text{D}}^{35} = +0.26$ (c 0.01, CHCl_3).

3-(4-methoxyphenyl)-3-methylisobenzofuran-1(3H)-one (x).



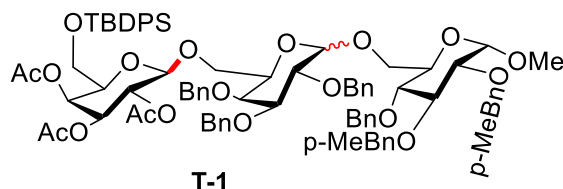
^1H NMR (400 MHz, CDCl_3) δ 7.91 (d, $J = 7.7$ Hz, 1H), 7.66 (td, $J = 7.6, 1.0$ Hz, 1H), 7.52 (td, $J = 7.6, 0.7$ Hz, 1H), 7.42 (d, $J = 7.7$ Hz, 1H), 7.36 – 7.31 (m, 2H), 6.89 – 6.84 (m, 2H), 3.79 (s, 3H), 2.02 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.0, 159.5, 154.4, 134.3, 132.6, 129.1, 126.7, 125.9, 125.2, 122.1, 114.0, 87.6, 55.3, 27.2. HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{16}\text{H}_{15}\text{O}_3$ 255.1021; found 255.1025. $[\alpha]_{\text{D}}^{35} = -0.60$ (c 0.01, CHCl_3).

3-(iodomethyl)-3-(4-methoxyphenyl)isobenzofuran-1(3H)-one (y).



^1H NMR (600 MHz, CDCl_3) δ 7.93 (d, $J = 7.6$ Hz, 1H), 7.74 (t, $J = 7.5$ Hz, 1H), 7.61 – 7.57 (m, 2H), 7.46 (d, $J = 8.7$ Hz, 2H), 6.90 (d, $J = 8.6$ Hz, 2H), 4.03 (d, $J = 11.2$ Hz, 1H), 3.94 (d, $J = 11.2$ Hz, 1H), 3.80 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 168.9, 160.0, 150.9, 134.3, 129.9, 129.5, 126.9, 126.6, 126.0, 122.3, 114.3, 86.9, 55.4, 13.1. HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{16}\text{H}_{14}\text{IO}_3$ 380.9988; found 380.9988. $[\alpha]_{\text{D}}^{35} = +0.36$ (c 0.01, CHCl_3).

Trisaccharide (T-1).

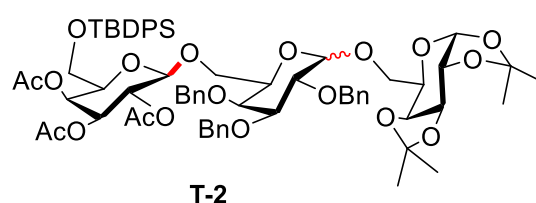


Glycosylation of **9h** (46.9 mg, 0.06 mmol) with **10k** (65.1 mg, 0.12 mmol) according to General procedure 3 afforded **11w** (56.5 mg, 88 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.31$ (Hexane/EtOAc = 3:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.64 – 7.57 (m, 4H), 7.52 (dd, $J = 7.4, 1.8$ Hz, 2H), 7.44 (dt, $J = 6.9, 5.8$ Hz, 2H), 7.41 (d, $J = 7.3$ Hz, 2H), 7.40 – 7.38 (m, 1H), 7.37 (d, $J = 4.8$ Hz, 3H), 7.34 – 7.26

(m, 8H), 7.25-7.21 (m, 5H), 7.19 (t, $J = 7.2$ Hz, 2H), 7.14 (t, $J = 7.2$ Hz, 1H), 5.57 (d, $J = 3.1$ Hz, 1H), 5.11 (dd, $J = 10.3, 8.0$ Hz, 1H), 4.99 (dd, $J = 10.4, 3.4$ Hz, 1H), 4.90 (d, $J = 11.4$ Hz, 1H), 4.81 (d, $J = 10.2$ Hz, 1H), 4.74 (d, $J = 10.2$ Hz, 1H), 4.71 (s, 2H), 4.61 (d, $J = 9.7$ Hz, 1H), 4.58 (d, $J = 11.4$ Hz, 1H), 4.45 (d, $J = 7.9$ Hz, 1H), 3.88 (t, $J = 9.4$ Hz, 1H), 3.79 (d, $J = 2.0$ Hz, 1H), 3.75 – 3.72 (m, 2H), 3.69 (q, $J = 5.5$ Hz, 2H), 3.58 (t, $J = 10.8$ Hz, 1H), 3.54 (dd, $J = 9.2, 2.6$ Hz, 1H), 3.51 (t, $J = 5.6$ Hz, 1H), 1.99 (s, 3H), 1.98 (s, 3H), 1.91 (s, 3H), 1.02 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 169.1, 169.0, 168.6, 137.4, 137.3, 137.1, 134.6, 134.5, 133.3, 131.9, 131.8, 130.4, 128.9, 128.0, 127.4, 127.3, 127.3, 127.1, 127.0, 126.8, 126.8, 126.7, 126.6, 126.5, 126.2, 100.0, 87.0, 82.9, 76.9, 76.2, 74.7, 73.3, 72.8, 72.0, 71.9, 70.2, 68.3, 67.7, 65.9, 59.7, 25.7, 19.7, 19.6, 19.6, 18.0. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{61}\text{H}_{72}\text{NO}_{13}\text{Si}$ 1086.4494; found 1086.4493. $[\alpha]_{\text{D}}^{35} = +0.24$ (c 0.01, CHCl_3).

A solution of glycosyl donor **11w** (64.2 mg, 0.06 mmol) and acceptor **10c** (59 mg, 0.06 mmol) in dry CH_2Cl_2 (0.03 M) was stirred at room temperature for 60 min in the presence of activated 4Å MS (200 mg) under Ar atmosphere. Then the vessel was chilled to 0 °C, to which NIS (13.5 mg, 0.06 mmol) and TMSOTf (4 μL , 30 mol %) were added. The reaction mixture was stirred for 20 min at 0 °C. Then, Et_3N was added to quench the reaction. The crude reaction mixture was worked up with water, washed with brine, dried by Na_2SO_4 , concentrated in rotavapor. The resulting crude reaction mixture was purified through Flash column chromatography to afford the trisaccharide **T-1** (69.7 mg, 80 %, $\alpha:\beta = 1:2$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.27$ (Hexane/ $\text{EtOAc} = 3:1$, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.63 – 7.58 (m, 12H), 7.46 – 7.35 (m, 19H), 7.35 – 7.27 (m, 20H), 7.22 (m, 39H), 7.17 – 7.07 (m, 24H), 5.57 (t, $J = 4.0$ Hz, 3H), 5.11 (ddd, $J = 10.8, 8.0, 3.0$ Hz, 3H), 4.98 (dq, $J = 10.5, 3.4$ Hz, 5H), 4.91 (d, $J = 10.6$ Hz, 4H), 4.88 (d, $J = 5.5$ Hz, 2H), 4.85 (t, $J = 8.5$ Hz, 3H), 4.78 (d, $J = 12.0$ Hz, 1H), 4.74 (d, $J = 10.8$ Hz, 1H), 4.73 – 4.68 (m, 4H), 4.67 (t, $J = 8.0$ Hz, 8H), 4.62 – 4.58 (m, 3H), 4.54 – 4.48 (m, 9H), 4.44 (d, $J = 7.9$ Hz, 1H), 4.37 (d, $J = 7.9$ Hz, 2H), 4.26 (d, $J = 7.7$ Hz, 1H), 4.10 (d, $J = 10.7$ Hz, 1H), 3.95 (dt, $J = 12.3, 6.4$ Hz, 5H), 3.85 – 3.81 (m, 2H), 3.81 – 3.76 (m, 6H), 3.74 (dd, $J = 9.9, 4.7$ Hz, 3H), 3.72 – 3.68 (m, 8H), 3.67 (d, $J = 4.7$ Hz, 2H), 3.64 (d, $J = 6.6$ Hz, 4H), 3.63 (d, $J = 7.5$ Hz, 3H), 3.58 (dd, $J = 14.9, 6.7$ Hz, 3H), 3.52 – 3.47 (m, 3H), 3.47 – 3.41 (m, 2H), 3.40 (dd, $J = 9.5, 3.5$ Hz, 3H), 3.30 (s, 6H), 3.28 (s, 3H), 2.34 (d, $J = 9.2$ Hz, 9H), 2.33 (s, 3H), 2.30 (s, 6H), 1.98 (s, 9H), 1.98 (s, 9H), 1.93 (s, 3H), 1.90 (s, 6H), 1.02 (s, 27H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.2, 170.1, 170.1, 170.0, 169.4, 169.3, 138.8, 138.7, 138.6, 138.5, 138.4, 138.3, 137.6, 137.5, 137.2, 137.2, 135.9, 135.9, 135.7, 135.6, 135.6, 135.5, 135.2, 135.1, 132.9, 132.9, 132.7, 132.7, 129.9, 129.9, 129.1, 129.1, 129.0, 129.0, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 127.8, 127.8, 127.8, 127.6, 127.5, 127.5, 127.4, 104.1, 101.2, 101.1, 98.1, 98.1, 97.7, 82.1, 82.0, 81.9, 79.9, 79.5, 79.0, 77.9, 77.9, 77.8, 76.4, 75.6, 75.5, 75.4, 75.2, 74.9, 74.8, 74.7, 74.5, 73.8, 73.7, 73.3, 73.2, 73.0, 73.0, 72.9, 72.4, 71.2, 71.2, 70.6, 70.0, 69.6, 69.4, 69.3, 68.9, 68.3, 68.2, 66.8, 65.9, 60.7, 55.3, 55.0, 26.7, 21.2, 21.2, 21.2, 20.8, 20.8, 20.7, 20.7, 20.6, 19.0. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{85}\text{H}_{102}\text{NO}_{19}\text{Si}$ 1468.6815; found 1468.6815. $[\alpha]_{\text{D}}^{35} = +0.44$ (c 0.01, CHCl_3).

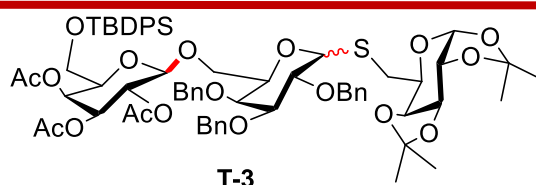
Trisaccharide (T-2).



A solution of glycosyl donor **11w** (64.2 mg, 0.06 mmol) in a mixture of acetone and water (acetone: water = 9:1) (4 mL) was treated with NBS (21.4 mg, 0.12 mmol). After completion of the reaction, acetone was evaporated in rotavapor. The crude reaction mixture was worked up with water, washed with brine, dried by Na₂SO₄ and concentrated in rotavapor. The resulting crude reaction mixture was treated with 2-(1-(4-methoxyphenyl)vinyl)benzoic acid according to general procedure 2 to afford **9k** as a glycosyl donor which was purified through flash column chromatography (61.9 mg, 85 % overall two steps, β only) as colorless syrup. R_f = 0.35 (Hexane/EtOAc = 3:1, v/v). ¹H NMR (600 MHz, CDCl₃) δ 7.91 (d, J = 7.8 Hz, 1H), 7.61 – 7.56 (m, 4H), 7.53 (t, J = 7.5 Hz, 1H), 7.42 (dd, J = 7.0, 4.8 Hz, 2H), 7.40 – 7.34 (m, 5H), 7.33 – 7.24 (m, 8H), 7.23 – 7.19 (m, 3H), 7.17 – 7.12 (m, 7H), 6.68 (d, J = 8.8 Hz, 2H), 5.59 (d, J = 2.9 Hz, 1H), 5.57 (s, 1H), 5.53 (d, J = 8.0 Hz, 1H), 5.10 (dd, J = 10.3, 8.0 Hz, 1H), 5.02 (s, 1H), 5.00 (d, J = 3.3 Hz, 1H), 4.87 (d, J = 11.1 Hz, 1H), 4.67 (t, J = 5.5 Hz, 3H), 4.59 (dd, J = 11.1, 6.6 Hz, 2H), 4.43 (d, J = 7.9 Hz, 1H), 3.93 – 3.89 (m, 1H), 3.83 – 3.78 (m, 2H), 3.73 (dd, J = 8.3, 5.8 Hz, 1H), 3.68 (dd, J = 9.0, 4.7 Hz, 1H), 3.66 (s, 3H), 3.58 (t, J = 9.3 Hz, 1H), 3.55 – 3.51 (m, 3H), 1.99 (s, 3H), 1.99 (s, 3H), 1.95 (s, 3H), 1.01 (s, 9H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 169.1, 169.0, 168.7, 163.8, 158.0, 147.6, 143.1, 137.4, 137.3, 137.1, 134.6, 134.5, 132.4, 131.8, 131.7, 131.7, 130.5, 129.5, 128.9, 128.8, 128.4, 127.4, 127.2, 127.2, 127.1, 126.8, 126.8, 126.7, 126.6, 126.6, 126.5, 126.4, 112.5, 111.3, 100.0, 93.7, 81.0, 76.9, 76.2, 74.0, 73.7, 73.2, 72.4, 71.9, 70.2, 68.2, 66.3, 65.8, 59.6, 54.1, 25.7, 19.7, 19.6, 19.6, 18.0. HRMS (ESI) m/z : [M + NH₄]⁺ calcd for C₇₁H₈₀NO₁₆Si 1230.5246; found 1230.5246. [α]_D³⁵ = - 0.88 (c 0.02, CHCl₃).

Glycosylation of **9k** (48.5 mg, 0.04 mmol) with **2h** (20.8 mg, 0.08 mmol) according to General procedure 3 afforded **T-2** (41.4 mg, 85 %, α : β = 1.1:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.26 (Hexane/EtOAc = 3:1, v/v). ¹H NMR (600 MHz, CDCl₃) δ 7.63 – 7.57 (m, 8H), 7.47 – 7.40 (m, 9H), 7.40 – 7.34 (m, 11H), 7.31 (m, 12H), 7.21 (dd, J = 15.1, 7.0 Hz, 4H), 7.15 – 7.08 (m, 6H), 5.59 (m, 2H), 5.56 (d, J = 4.9 Hz, 1H), 5.52 (d, J = 4.9 Hz, 1H), 5.14 (ddd, J = 13.2, 10.4, 8.1 Hz, 2H), 5.05 (d, J = 9.3 Hz, 1H), 5.04 – 4.99 (m, 3H), 4.88 – 4.85 (m, 2H), 4.85 – 4.75 (m, 3H), 4.73 (d, J = 8.8 Hz, 2H), 4.72 – 4.65 (m, 3H), 4.59 (d, J = 7.9 Hz, 2H), 4.56 (dd, J = 9.8, 5.1 Hz, 2H), 4.52 (d, J = 8.2 Hz, 2H), 4.36 (d, J = 7.7 Hz, 1H), 4.34 (d, J = 9.4 Hz, 1H), 4.32 – 4.29 (m, 2H), 4.21 (d, J = 8.0 Hz, 1H), 4.13 (dd, J = 10.6, 3.0 Hz, 1H), 4.08 (d, J = 6.9 Hz, 1H), 4.04 – 3.99 (m, 2H), 3.91 (dd, J = 12.5, 4.6 Hz, 2H), 3.84 – 3.82 (m, 1H), 3.81 – 3.73 (m, 5H), 3.69 (m, 4H), 3.65 (dd, J = 11.6, 6.8 Hz, 3H), 3.63 – 3.57 (m, 4H), 3.44 (dt, J = 9.8, 4.8 Hz, 2H), 2.02 (s, 3H), 2.02 (s, 3H), 2.00 (s, 3H), 2.00 (s, 3H), 1.98 (s, 3H), 1.97 (s, 3H), 1.51 (s, 3H), 1.49 (s, 3H), 1.44 (s, 3H), 1.41 (s, 3H), 1.33 (s, 3H), 1.31 (s, 3H), 1.30 (s, 6H), 1.02 (s, 18H). ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 170.2, 170.1, 170.1, 170.0, 169.5, 169.5, 138.9, 138.8, 138.6, 138.5, 138.4, 138.2, 135.6, 135.6, 135.5, 132.9, 132.8, 132.7, 132.7, 129.9, 129.9, 128.7, 128.5, 128.4, 128.3, 128.3, 128.1, 128.1, 127.9, 127.8, 127.8, 127.8, 127.7, 127.6, 127.6, 127.6, 127.5, 127.5, 127.4, 127.4, 127.4, 109.3, 109.2, 108.6, 108.5, 104.7, 101.1, 100.9, 97.1, 96.4, 96.3, 81.6, 78.8, 78.7, 76.2, 75.1, 74.8, 74.7, 74.4, 74.2, 73.7, 73.4, 73.2, 73.0, 72.9, 72.5, 71.4, 71.3, 71.3, 70.9, 70.8, 70.7, 70.5, 69.8, 69.4, 69.3, 69.3, 68.5, 67.9, 67.4, 66.9, 66.9, 66.1, 65.7, 60.7, 60.6, 26.7, 26.2, 26.1, 26.0, 26.0, 25.1, 24.9, 24.6, 24.3, 20.9, 20.8, 20.7, 20.6, 19.0. HRMS (ESI) m/z : [M + NH₄]⁺ calcd for C₆₇H₈₆NO₁₉Si 1236.5563; found 1236.5567. [α]_D³⁵ = + 0.26 (c 0.01, CHCl₃).

Trisaccharide (T-3).

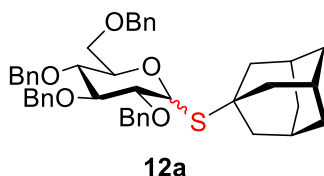


Glycosylation of **9k** (48.5 mg, 0.04 mmol) with **10h** (22.1 mg, 0.08 mmol) according to General procedure 4 afforded **T-3** (43.5 mg, 88 %, $\alpha:\beta$ = 3:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.27 (Hexane/EtOAc = 3:1, v/v). For α anomer, ^1H NMR (600 MHz, CDCl_3) δ 7.63 – 7.56 (m, 4H), 7.45 – 7.20 (m, 18H), 7.14 – 7.09 (m, 3H), 5.59 (d, J = 3.0 Hz, 1H), 5.58 (d, J = 5.4 Hz, 1H), 5.53 (d, J = 5.0 Hz, 1H), 5.14 (dd, J = 10.4, 7.9 Hz, 1H), 5.03 (dd, J = 10.5, 3.4 Hz, 1H), 4.86 (d, J = 11.0 Hz, 1H), 4.80 (d, J = 11.9 Hz, 1H), 4.77 (d, J = 11.7 Hz, 1H), 4.66 (d, J = 11.9 Hz, 1H), 4.63–4.59 (m, 2H), 4.54 (d, J = 11.0 Hz, 1H), 4.45 (d, J = 7.9 Hz, 1H), 4.36 (dd, J = 7.9, 1.6 Hz, 1H), 4.30 (dd, J = 5.0, 2.4 Hz, 1H), 4.24 (dd, J = 10.0, 5.4 Hz, 1H), 4.21 (t, J = 6.5 Hz, 1H), 3.89 (td, J = 7.3, 1.3 Hz, 1H), 3.86–3.81 (m, 2H), 3.75 (dd, J = 8.3, 5.8 Hz, 1H), 3.73 – 3.69 (m, 2H), 3.63 – 3.59 (m, 1H), 3.55 (dd, J = 10.2, 6.2 Hz, 1H), 2.78 (dd, J = 13.7, 7.7 Hz, 1H), 2.74 (dd, J = 13.7, 7.3 Hz, 1H), 2.03 (s, 3H), 1.99 (s, 3H), 1.98 (s, 3H), 1.48 (s, 3H), 1.43 (s, 3H), 1.32 (s, 3H), 1.31 (s, 3H), 1.02 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.2, 170.1, 169.5, 138.7, 138.4, 138.2, 135.6, 135.5, 132.9, 132.7, 129.9, 129.9, 128.4, 128.3, 128.3, 128.1, 127.9, 127.8, 127.8, 127.6, 127.5, 127.4, 127.4, 109.3, 108.5, 101.1, 96.7, 84.3, 79.0, 75.9, 75.0, 75.0, 73.3, 73.0, 72.0, 71.5, 71.3, 71.0, 70.5, 69.8, 69.3, 67.6, 66.9, 66.5, 60.7, 29.2, 26.7, 26.2, 26.0, 24.9, 24.6, 20.9, 20.7, 20.6. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{67}\text{H}_{86}\text{NO}_{18}$ SSi 1252.5329; found 1252.5332. $[\alpha]_{\text{D}}^{35} = +0.52$ (c 0.01, CHCl_3).

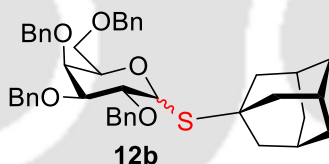
For β anomer, ^1H NMR (500 MHz, CDCl_3) δ 7.59 (t, J = 8.4 Hz, 4H), 7.45 – 7.34 (m, 8H), 7.34 – 7.25 (m, 8H), 7.22 (d, J = 6.9 Hz, 2H), 7.13 (dd, J = 15.3, 7.6 Hz, 3H), 5.59 (d, J = 2.9 Hz, 1H), 5.50 (d, J = 4.9 Hz, 1H), 5.15 – 5.09 (m, 1H), 5.03 (dd, J = 10.4, 3.2 Hz, 1H), 4.87 (dd, J = 10.7, 7.5 Hz, 2H), 4.79 (d, J = 10.3 Hz, 1H), 4.71 – 4.65 (m, 2H), 4.59 – 4.54 (m, 2H), 4.48 (d, J = 7.9 Hz, 1H), 4.38 – 4.33 (m, 2H), 4.28 (dd, J = 4.9, 2.2 Hz, 1H), 3.93 (t, J = 6.9 Hz, 1H), 3.80 – 3.73 (m, 4H), 3.70 – 3.63 (m, 2H), 3.58 (t, J = 9.3 Hz, 1H), 3.49 – 3.43 (m, 2H), 2.97 (dd, J = 13.3, 6.3 Hz, 1H), 2.90 (dd, J = 13.2, 8.1 Hz, 1H), 2.04 (s, 3H), 2.00 (s, 3H), 1.98 (s, 3H), 1.46 (s, 3H), 1.42 (s, 3H), 1.30 (s, 6H), 1.02 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.1, 170.0, 169.6, 138.4, 138.3, 138.2, 135.6, 135.5, 132.8, 132.7, 129.9, 128.4, 128.3, 128.2, 128.1, 128.1, 127.8, 127.8, 127.7, 127.6, 127.5, 109.1, 108.6, 101.2, 96.6, 85.7, 83.8, 78.1, 77.7, 75.7, 74.4, 73.6, 72.9, 72.8, 71.2, 71.1, 70.8, 70.6, 69.4, 68.4, 67.8, 66.9, 60.6, 31.9, 26.7, 26.1, 26.0, 25.0, 24.4, 20.9, 20.7, 20.6. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{67}\text{H}_{82}\text{O}_{18}\text{SSiNa}$ 1257.4883; found 1257.4873. $[\alpha]_{\text{D}}^{35} = +0.48$ (c 0.01, CHCl_3).

General Procedure 4.

A solution of glycosyl PMPVB donor **9a-h** (1 equiv.) and acceptor **10h-j** (2.0 equiv.) in dry CH_2Cl_2 (0.03 M) was stirred at room temperature for 60 min in the presence of activated acid washed (AW) 4 Å MS (3.0 g/mmol) under Ar atmosphere. Then the vessel was chilled to 0 °C, to which triflimide (30 mol %) was added. After completion of the reaction within 5 min, the temperature gradually raised to room temperature. Then Et_3N was added to quench the reaction. The crude reaction mixture was worked up with water, washed with brine, dried by Na_2SO_4 , concentrated in rotavapor. The resulting crude reaction mixture was purified through flash column chromatography to afford the glycosylated product.

1-Adamantanyl 2,3,4,6-tetra-O-benzyl-1-thio-D-glucopyranoside (12a).

Glycosylation of **9d** (46.6 mg, 0.06 mmol) with 1-adamanthiol (**10m**) (20.2 mg, 0.12 mmol) according to General procedure 4 afforded **12a** (31.5 mg, 76 %, $\alpha:\beta = 1.5:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.6$ (Hexane: EtOAc = 7: 1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.40 – 7.11 (m, 60H), 5.63 (d, $J = 4.9$ Hz, 2H), 4.99 – 4.95 (m, 3H), 4.91 (d, $J = 10.9$ Hz, 1H), 4.83 (d, $J = 1.3$ Hz, 2H), 4.81 (d, $J = 3.1$ Hz, 2H), 4.75 (d, $J = 10.7$ Hz, 2H), 4.72 (d, $J = 11.9$ Hz, 2H), 4.68 (d, $J = 4.8$ Hz, 2H), 4.66 (d, $J = 7.8$ Hz, 2H), 4.65 – 4.61 (m, 2H), 4.56 (dd, $J = 11.4, 3.9$ Hz, 2H), 4.53 (d, $J = 12.0$ Hz, 1H), 4.44 (d, $J = 10.9$ Hz, 2H), 4.42 (d, $J = 12.1$ Hz, 2H), 4.34 – 4.30 (m, 2H), 3.79 (dd, $J = 9.6, 5.6$ Hz, 3H), 3.77 (d, $J = 3.5$ Hz, 2H), 3.75 – 3.71 (m, 2H), 3.69 (d, $J = 8.6$ Hz, 1H), 3.68 – 3.63 (m, 2H), 3.63 – 3.62 (m, 1H), 3.61 (d, $J = 4.6$ Hz, 1H), 3.60 – 3.58 (m, 1H), 3.55 – 3.51 (m, 1H), 3.51 – 3.47 (m, 1H), 3.39 (t, $J = 9.3$ Hz, 1H), 2.02 (s, 10H), 2.00 (s, 3H), 1.97 (s, 3H), 1.95 (d, $J = 1.8$ Hz, 11H), 1.68 (s, 18H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.8, 138.6, 138.4, 138.3, 138.2, 138.1, 138.0, 137.9, 128.4, 128.4, 128.3, 128.3, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6, 127.5, 87.0, 82.9, 81.7, 81.6, 79.7, 79.3, 78.6, 78.1, 77.6, 75.9, 75.8, 75.5, 75.0, 75.0, 73.4, 73.4, 72.3, 70.3, 69.6, 68.5, 46.6, 46.1, 44.3, 44.0, 36.3, 36.3, 29.9, 29.8. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{44}\text{H}_{54}\text{NO}_5\text{S}$ 708.3723; found 708.3723. $[\alpha]_D^{35} = +0.70$ (c 0.02, CHCl_3).

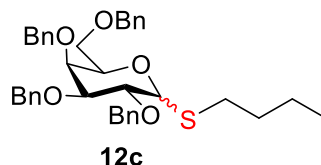
1-Adamantanyl 2,3,4,6-tetra-O-benzyl-1-thio-D-galactopyranoside (12b).

Glycosylation of donor **9a** (46.6 mg, 0.06 mmol) with 1-adamanthiol (**9m**) (20.2 mg, 0.12 mmol) according to General procedure 4 afforded **12b** (33.2 mg, 80 %, $\alpha:\beta = 3:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.61$ (Hexane: EtOAc = 7: 1, v/v). The α anomer, ^1H NMR (600 MHz, CDCl_3) δ 5.69 (d, $J = 5.7$ Hz, 1H), 4.96 (d, $J = 11.4$ Hz, 1H), 4.85 (d, $J = 11.8$ Hz, 1H), 4.70 (dt, $J = 11.8, 10.8$ Hz, 3H), 4.55 (d, $J = 11.4$ Hz, 1H), 4.43 (dt, $J = 16.1, 11.8$ Hz, 3H), 4.26 (dd, $J = 10.2, 5.7$ Hz, 1H), 3.95 (d, $J = 1.8$ Hz, 1H), 3.69 (dd, $J = 10.2, 2.8$ Hz, 1H), 3.57 (dd, $J = 9.2, 7.3$ Hz, 1H), 3.50 (dd, $J = 9.3, 5.9$ Hz, 1H), 1.99 (s, 3H), 1.94 (s, 6H), 1.66 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.9, 138.8, 138.3, 138.1, 128.4, 128.3, 128.2, 128.1, 127.6, 127.5, 80.4, 79.9, 76.0, 75.4, 74.8, 73.5, 73.3, 72.4, 69.4, 68.7, 45.8, 44.0, 36.3, 29.8. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{44}\text{H}_{54}\text{NO}_5\text{S}$ 708.3723; found 708.3723. $[\alpha]_D^{35} = -0.22$ (c 0.01, CHCl_3).

The β anomer, ^1H NMR (600 MHz, CDCl_3) δ 7.41 – 7.23 (m, 20H), 4.95 – 4.90 (m, 2H), 4.75 – 4.69 (m, 2H), 4.60 (dd, $J = 10.8, 3.7$ Hz, 2H), 4.45 (d, $J = 11.5$ Hz, 1H), 4.37 (d, $J = 11.5$ Hz, 1H), 3.92 (d, $J = 2.7$ Hz, 1H), 3.74 (t, $J = 9.5$ Hz, 1H), 3.61 – 3.54 (m, 4H), 2.02 (s, 3H), 2.00 (s, 1H), 1.98 (s, 2H), 1.93 (s, 2H), 1.91 (s, 1H), 1.67 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3)

δ 138.8, 138.5, 138.5, 138.0, 128.4, 128.3, 128.2, 127.9, 127.8, 127.6, 127.6, 127.5, 84.4, 81.9, 78.3, 75.8, 74.4, 73.6, 72.9, 69.3, 46.3, 44.2, 36.3, 29.8. HRMS (ESI) m/z : $[M + NH_4]^+$ calcd for $C_{44}H_{54}NO_5S$ 708.3723; found 708.3723. $[\alpha]_D^{35} = +0.26$ (c 0.01, $CHCl_3$).

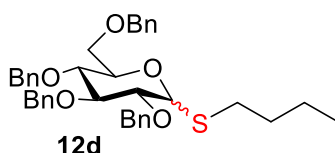
Butyl 2,3,4,6-tetra-O-benzyl-1-thio-D-galactopyranoside (12c).



Glycosylation of **9a** (46.6 mg, 0.06 mmol) with 1-butanethiol (**10f**) (13 μ l, 0.12 mmol) according to General procedure 4 afforded **12c** (28.7 mg, 78 %, $\alpha:\beta = 2:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.62$ (Hexane: EtOAc = 7: 1, v/v). For α anomer, 1H NMR (600 MHz, $CDCl_3$) δ 7.39 (d, $J = 7.2$ Hz, 2H), 7.36 (d, $J = 7.2$ Hz, 2H), 7.34 – 7.29 (m, 8H), 7.27 – 7.26 (m, 5H), 7.25 (t, $J = 6.0$ Hz, 3H), 5.45 (d, $J = 5.5$ Hz, 1H), 4.94 (d, $J = 11.5$ Hz, 1H), 4.83 (d, $J = 11.8$ Hz, 1H), 4.74 (d, $J = 11.7$ Hz, 1H), 4.69 (t, $J = 11.5$ Hz, 2H), 4.59 – 4.55 (m, 1H), 4.46 (d, $J = 11.8$ Hz, 1H), 4.40 (d, $J = 11.8$ Hz, 1H), 4.32 – 4.26 (m, 2H), 3.93 (d, $J = 1.7$ Hz, 1H), 3.80 (dd, $J = 9.9, 2.7$ Hz, 1H), 3.53 (d, $J = 6.3$ Hz, 2H), 2.60 – 2.52 (m, 1H), 2.47 (dt, $J = 12.7, 7.6$ Hz, 1H), 1.55 (dd, $J = 13.7, 5.9$ Hz, 2H), 1.42 – 1.33 (m, 2H), 0.88 (t, $J = 7.4$ Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 138.8, 138.7, 138.3, 138.1, 128.4, 128.4, 128.3, 128.3, 128.2, 128.0, 127.7, 127.6, 127.6, 127.5, 127.5, 83.7, 79.6, 76.3, 75.2, 74.8, 73.4, 73.4, 72.5, 69.6, 69.1, 31.5, 29.1, 22.1, 13.7. HRMS (ESI) m/z : $[M + NH_4]^+$ calcd for $C_{38}H_{48}NO_5S$ 630.3253; found 630.3255. $[\alpha]_D^{35} = +1.56$ (c 0.04, $CHCl_3$).

For β anomer, 1H NMR (600 MHz, $CDCl_3$) δ 7.39 (d, $J = 7.0$ Hz, 2H), 7.35 (t, $J = 7.4$ Hz, 3H), 7.33 – 7.29 (m, 10H), 7.29 – 7.26 (m, 5H), 4.97 – 4.93 (m, 1H), 4.88 (d, $J = 10.1$ Hz, 1H), 4.79 (d, $J = 10.1$ Hz, 1H), 4.72 (d, $J = 7.3$ Hz, 2H), 4.61 (d, $J = 11.7$ Hz, 1H), 4.45 (d, $J = 11.7$ Hz, 1H), 4.42 – 4.38 (m, 2H), 3.95 (d, $J = 2.3$ Hz, 1H), 3.81 (t, $J = 9.5$ Hz, 1H), 3.61 – 3.54 (m, 4H), 2.77 – 2.71 (m, 1H), 2.67 (dt, $J = 12.6, 7.6$ Hz, 1H), 1.64 – 1.59 (m, 2H), 1.40 (qd, $J = 14.2, 6.9$ Hz, 2H), 0.89 (t, $J = 7.4$ Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 138.8, 138.4, 138.3, 137.9, 128.5, 128.4, 128.3, 128.2, 128.0, 128.0, 127.8, 127.8, 127.7, 127.6, 127.5, 85.5, 84.1, 78.5, 77.2, 75.8, 74.4, 73.6, 72.7, 68.8, 32.0, 30.4, 22.1, 13.7. HRMS (ESI) m/z : $[M + NH_4]^+$ calcd for $C_{38}H_{48}NO_5S$ 630.3253; found 630.3254. $[\alpha]_D^{35} = +1.34$ (c 0.04, $CHCl_3$).

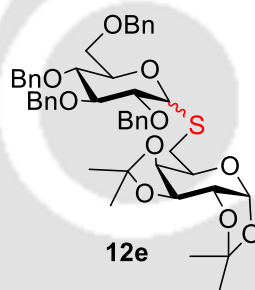
Butyl 2,3,4,6-tetra-O-benzyl-1-thio-D-glucopyranoside (12d).



Glycosylation of **9c** (46.6 mg, 0.06 mmol) with 1-butanethiol (**10f**) (13 μ l, 0.12 mmol) according to General procedure 4 afforded **12d** (29 mg, 79 %, $\alpha:\beta = 1.7:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.61$ (Hexane: EtOAc = 7: 1, v/v). 1H NMR (600 MHz, $CDCl_3$) δ 7.38 (d, $J = 7.3$ Hz, 4H), 7.35 – 7.22 (m, 42H), 7.19 – 7.15 (m, 2H), 7.14 (d, $J = 6.2$ Hz, 4H), 5.37 (d, $J = 5.1$ Hz, 2H), 4.95 (d, $J = 10.8$

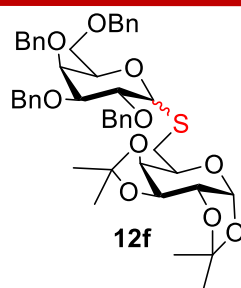
Hz, 2H), 4.92 (dd, $J = 10.6, 4.7$ Hz, 2H), 4.84 (d, $J = 11.7$ Hz, 2H), 4.81 (t, $J = 5.4$ Hz, 2H), 4.76 (d, $J = 10.8$ Hz, 2H), 4.75 – 4.69 (m, 3H), 4.66 (d, $J = 11.8$ Hz, 2H), 4.60 (dd, $J = 12.2, 2.6$ Hz, 3H), 4.56 (t, $J = 11.2$ Hz, 3H), 4.48 – 4.45 (m, 3H), 4.44 (d, $J = 8.3$ Hz, 2H), 4.19 (d, $J = 9.9$ Hz, 2H), 3.89 – 3.84 (m, 2H), 3.82 (dd, $J = 9.5, 5.2$ Hz, 2H), 3.78 – 3.72 (m, 3H), 3.70 – 3.65 (m, 1H), 3.65 – 3.59 (m, 5H), 3.48 – 3.41 (m, 2H), 2.80 – 2.74 (m, 1H), 2.71 (dt, $J = 12.5, 7.5$ Hz, 1H), 2.60 – 2.54 (m, 2H), 2.48 (dt, $J = 12.8, 7.5$ Hz, 2H), 1.68 – 1.62 (m, 2H), 1.62 – 1.56 (m, 4H), 1.46 – 1.35 (m, 6H), 0.91 (td, $J = 7.3, 2.2$ Hz, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.8, 138.5, 138.3, 138.2, 138.1, 138.0, 137.9, 137.9, 128.5, 128.4, 128.4, 128.4, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7, 127.6, 86.7, 85.3, 83.5, 82.6, 81.9, 79.6, 79.1, 78.0, 77.5, 75.8, 75.7, 75.5, 75.1, 75.0, 73.5, 72.4, 70.5, 69.2, 68.6, 32.0, 31.6, 30.6, 29.5, 22.1, 22.0, 13.7. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{38}\text{H}_{48}\text{NO}_5\text{S}$ 630.3253; found 630.3257. $[\alpha]_{\text{D}}^{35} = +0.26$ (c 0.01, CHCl_3).

1,2;3,4-di-O-isopropylidene-6-thio-(2,3,4,6-tetra-O-benzyl-D-galactopyranosyl)- α -D-galactopyranose (12e).



Glycosylation of **9d** (46.6 mg, 0.06 mmol) with **10h** (33.2 mg, 0.12 mmol) according to General procedure 4 afforded **12e** (43.6 mg, 91 %, $\alpha:\beta = 1.8:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.37$ (Hexane: EtOAc = 4:1, v/v) ^1H NMR (600 MHz, CDCl_3) δ 7.40 – 7.24 (m, 48H), 7.17 – 7.11 (m, 6H), 5.56 (d, $J = 4.1$ Hz, 2H), 5.54 (d, $J = 5.1$ Hz, 2H), 5.51 (d, $J = 5.0$ Hz, 1H), 4.94 (d, $J = 10.8$ Hz, 3H), 4.91 (d, $J = 11.0$ Hz, 1H), 4.83 (d, $J = 10.0$ Hz, 2H), 4.80 (dd, $J = 13.5, 5.6$ Hz, 3H), 4.75 (dd, $J = 10.8, 3.6$ Hz, 4H), 4.62 – 4.57 (m, 6H), 4.56 – 4.50 (m, 3H), 4.48 – 4.42 (m, 5H), 4.36 (dd, $J = 7.9, 1.5$ Hz, 1H), 4.32 – 4.29 (m, 4H), 4.27 (dd, $J = 5.0, 2.3$ Hz, 1H), 4.18 (d, $J = 9.8$ Hz, 2H), 3.99 – 3.92 (m, 3H), 3.86 – 3.82 (m, 3H), 3.77 (dd, $J = 10.6, 3.3$ Hz, 2H), 3.73 (dd, $J = 10.7, 1.4$ Hz, 1H), 3.69 – 3.63 (m, 5H), 3.63 – 3.57 (m, 2H), 3.46 – 3.40 (m, 1H), 3.02 (dd, $J = 13.6, 6.3$ Hz, 1H), 2.92 (dd, $J = 13.6, 7.7$ Hz, 1H), 2.86 (dd, $J = 13.5, 7.9$ Hz, 2H), 2.75 (dd, $J = 13.5, 7.0$ Hz, 2H), 1.53 (s, 3H), 1.51 (s, 6H), 1.45 (s, 6H), 1.41 (s, 3H), 1.35 – 1.30 (m, 14H), 1.28 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.7, 138.5, 138.3, 138.1, 138.1, 137.0, 137.9, 137.8, 128.5, 128.4, 128.4, 128.4, 128.4, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 109.3, 109.2, 108.7, 108.6, 96.7, 96.6, 86.6, 85.6, 84.2, 82.4, 81.9, 79.3, 79.1, 78.0, 75.8, 75.7, 75.4, 75.1, 75.1, 73.5, 71.9, 71.5, 71.2, 71.0, 70.9, 70.8, 70.6, 70.5, 69.1, 68.4, 66.4, 30.7, 29.8, 26.2, 26.1, 26.0, 26.0, 25.0, 25.0, 24.6, 24.5. HRMS (ESI) m/z : $[\text{M} + \text{K}]^+$ calcd for $\text{C}_{46}\text{H}_{54}\text{KO}_{10}\text{S}$ 837.3069; found 837.3066. $[\alpha]_{\text{D}}^{35} = +0.42$ (c 0.01, CHCl_3).

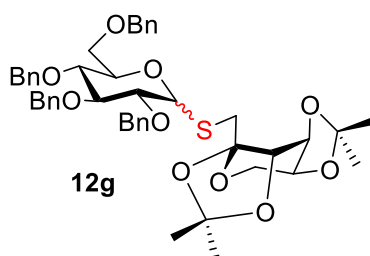
1,2;3,4-di-O-isopropylidene-6-thio-(2,3,4,6-tetra-O-benzyl-D-galactopyranosyl)- α -D-galactopyranose (12f).



Glycosylation of **9a** (46.6 mg, 0.06 mmol) with **10h** (33.2 mg, 0.12 mmol) according to General procedure 4 afforded **12f** (44 mg, 92 %, $\alpha:\beta = 1.5:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.37$ (Hexane: EtOAc = 4:1, v/v). For α anomer ^1H NMR (600 MHz, CDCl_3) δ 7.39 (d, $J = 7.1$ Hz, 2H), 7.33 (dd, $J = 13.6, 7.1$ Hz, 6H), 7.31 – 7.24 (m, 12H), 5.58 (d, $J = 5.5$ Hz, 1H), 5.52 (d, $J = 5.0$ Hz, 1H), 4.92 (d, $J = 11.4$ Hz, 1H), 4.82 (d, $J = 11.8$ Hz, 1H), 4.78 (d, $J = 11.7$ Hz, 1H), 4.69 (d, $J = 11.8$ Hz, 1H), 4.64 (d, $J = 11.7$ Hz, 1H), 4.57 (d, $J = 11.4$ Hz, 1H), 4.52 (dd, $J = 7.9, 2.3$ Hz, 1H), 4.45 (d, $J = 11.8$ Hz, 1H), 4.40 (d, $J = 11.8$ Hz, 1H), 4.32 – 4.26 (m, 4H), 3.96 (d, $J = 1.9$ Hz, 1H), 3.95 – 3.92 (m, 1H), 3.77 (dd, $J = 10.0, 2.8$ Hz, 1H), 3.56 (dd, $J = 9.1, 7.5$ Hz, 1H), 3.50 (dd, $J = 9.2, 5.8$ Hz, 1H), 2.84 (dd, $J = 13.6, 7.9$ Hz, 1H), 2.74 (dd, $J = 13.6, 6.9$ Hz, 1H), 1.48 (s, 3H), 1.41 (d, $J = 9.0$ Hz, 3H), 1.31 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.8, 138.6, 138.2, 138.0, 128.4, 128.3, 128.3, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 127.6, 127.5, 127.5, 109.2, 108.6, 96.7, 84.8, 79.3, 76.1, 75.0, 74.9, 73.4, 73.3, 72.1, 71.4, 71.0, 70.5, 69.8, 68.6, 66.6, 29.7, 26.2, 26.0, 24.9, 24.6. HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{46}\text{H}_{55}\text{O}_{10}\text{S}$ 799.3510 found; 799.3510. $[\alpha]_{\text{D}}^{35} = +0.36$ (c 0.01, CHCl_3).

For β anomer ^1H NMR (600 MHz, CDCl_3) δ 7.39 – 7.24 (m, 20H), 5.50 (d, $J = 5.0$ Hz, 1H), 4.94 (d, $J = 11.7$ Hz, 1H), 4.89 (d, $J = 10.3$ Hz, 1H), 4.79 (d, $J = 10.2$ Hz, 1H), 4.71 (s, 2H), 4.60 (d, $J = 11.7$ Hz, 1H), 4.49 – 4.42 (m, 3H), 4.39 (d, $J = 11.7$ Hz, 1H), 4.35 (dd, $J = 7.9, 1.7$ Hz, 1H), 4.26 (dd, $J = 5.0, 2.4$ Hz, 1H), 3.94 (t, $J = 4.8$ Hz, 2H), 3.80 (t, $J = 9.5$ Hz, 1H), 3.57 (d, $J = 6.0$ Hz, 2H), 3.54 (dt, $J = 12.5, 4.4$ Hz, 2H), 2.98 (dd, $J = 13.6, 6.2$ Hz, 1H), 2.90 (dd, $J = 13.6, 7.9$ Hz, 1H), 1.48 (s, 3H), 1.41 (s, 3H), 1.31 (s, 3H), 1.27 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.7, 138.4, 138.4, 137.8, 128.4, 128.4, 128.3, 128.2, 128.0, 128.0, 127.8, 127.6, 127.5, 127.5, 109.1, 108.6, 96.6, 85.9, 84.0, 78.6, 75.7, 74.5, 73.6, 73.6, 72.7, 71.2, 70.8, 70.6, 68.7, 68.2, 30.6, 26.1, 26.0, 25.0, 24.4. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{46}\text{H}_{58}\text{NO}_{10}\text{S}$ 816.3776; found 816.3779. $[\alpha]_{\text{D}}^{35} = +0.50$ (c 0.01, CHCl_3).

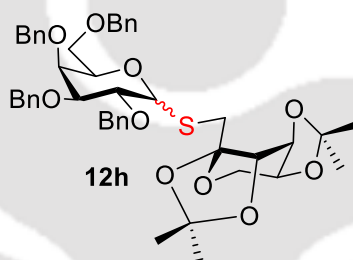
2,3;4,5-di-O-isopropylidene-1-thio- (2,3,4,6-tetra-O-benzyl-D-glucopyranosyl)- β -D-fructopyranose (12g).



Glycosylation of **9d** (46.6 mg, 0.06 mmol) with **10i** (33.2 mg, 0.12 mmol) according to General procedure 4 afforded **12g** (43.1 mg, 90 %, $\alpha:\beta = 1.9:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.36$ (Hexane: EtOAc = 3: 1, v/v). ^1H

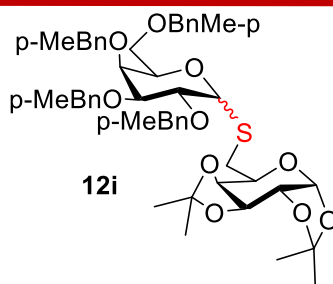
NMR (600 MHz, CDCl₃) δ 7.38 (d, J = 7.1 Hz, 2H), 7.36 - 7.23 (m, 25H), 7.16 (dd, J = 10.4, 4.4 Hz, 3H), 5.53 (d, J = 5.3 Hz, 1H), 4.91 (t, J = 10.5 Hz, 2H), 4.84 (t, J = 5.5 Hz, 1H), 4.82 - 4.75 (m, 3H), 4.73 (d, J = 8.8 Hz, 1H), 4.64 (d, J = 11.8 Hz, 1H), 4.62 - 4.59 (m, 1H), 4.59 - 4.56 (m, 3H), 4.53 (dd, J = 7.3, 4.6 Hz, 1H), 4.49 (d, J = 11.0 Hz, 1H), 4.43 (d, J = 12.1 Hz, 1H), 4.28 (d, J = 2.5 Hz, 1H), 4.24 - 4.18 (m, 3H), 3.95 (dd, J = 12.9, 1.5 Hz, 1H), 3.93 - 3.90 (m, 1H), 3.89 (d, J = 9.1 Hz, 1H), 3.84 (dd, J = 9.5, 5.3 Hz, 1H), 3.78 - 3.72 (m, 4H), 3.69 (dd, J = 13.7, 7.8 Hz, 1H), 3.65 (dd, J = 9.1, 5.0 Hz, 1H), 3.62 (dd, J = 10.6, 1.6 Hz, 1H), 3.45-3.41 (m, 2H), 3.00 (d, J = 14.0 Hz, 1H), 2.94 (d, J = 14.7 Hz, 1H), 2.91 (d, J = 14.0 Hz, 1H), 1.52 (s, 5H), 1.48 (s, 3H), 1.46 (s, 2H), 1.45 (s, 2H), 1.43 (s, 3H), 1.34 (s, 3H), 1.31 (s, 2H). ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 138.8, 138.6, 138.5, 138.2, 138.1, 138.1, 138.0, 138.0, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 109.1, 109.0, 108.8, 108.4, 103.5, 103.1, 86.8, 85.6, 84.0, 82.4, 82.3, 79.6, 79.0, 77.9, 77.4, 75.73, 75.70, 75.5, 75.1, 74.9, 73.6, 73.5, 72.4, 72.2, 71.5, 71.0, 70.9, 70.7, 70.4, 70.4, 68.7, 68.4, 61.8, 61.6, 37.1, 26.8, 26.7, 26.03, 26.01, 26.0, 25.7, 24.2, 24.1 HRMS (ESI) m/z : [M + NH₄]⁺ calcd for C₄₆H₅₈NO₁₀S 816.3776; found 816.3774. [α]_D³⁵ = + 0.28 (c 0.01, CHCl₃).

2,3,4,5-di-O-isopropylidene-1-thio- (2,3,4,6-tetra-O-benzyl-D-galactopyranosyl)- β -D-fructopyranose(12h).



Glycosylation of **9a** (46.6 mg, 0.06 mmol) with **10l** (33.2 mg, 0.12 mmol) according to General procedure 4 afforded **12h** (42.6 mg, 89 %, α : β = 2.3:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.38 (Hexane: EtOAc = 3: 1, v/v). ¹H NMR (600 MHz, CDCl₃) δ 7.39 (d, J = 7.1 Hz, 2H), 7.36 - 7.23 (m, 28H), 5.60 (d, J = 5.4 Hz, 1H), 4.92 (d, J = 11.4 Hz, 2H), 4.87 (d, J = 10.4 Hz, 1H), 4.79 (dd, J = 15.9, 7.7 Hz, 3H), 4.71 (d, J = 2.7 Hz, 1H), 4.68 (dd, J = 11.7, 7.5 Hz, 2H), 4.60 (d, J = 11.6 Hz, 1H), 4.59 - 4.57 (m, 1H), 4.57 - 4.55 (m, 2H), 4.46 - 4.43 (m, 1H), 4.42 (d, J = 2.6 Hz, 1H), 4.41 (d, J = 4.7 Hz, 1H), 4.40 - 4.37 (m, 1H), 4.32 (t, J = 6.5 Hz, 1H), 4.28 (dd, J = 9.9, 5.4 Hz, 1H), 4.24 (d, J = 2.6 Hz, 1H), 4.21 (d, J = 7.9 Hz, 2H), 4.00 - 3.93 (m, 2H), 3.90 (dd, J = 13.1, 1.7 Hz, 2H), 3.84 (dd, J = 9.9, 2.8 Hz, 1H), 3.80 (t, J = 9.5 Hz, 1H), 3.75 (dd, J = 12.9, 4.2 Hz, 2H), 3.62 (dd, J = 11.5, 8.2 Hz, 1H), 3.58 - 3.50 (m, 4H), 3.38 (d, J = 14.7 Hz, 1H), 2.99 - 2.91 (m, 3H), 2.90 (d, J = 9.1 Hz, 1H), 1.50 (s, 3H), 1.49 (s, 2H), 1.44 (s, 3H), 1.42 (s, 2H), 1.40 (s, 5H), 1.32 (s, 3H), 1.31 (s, 2H). ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 138.8, 138.8, 138.6, 138.4, 138.1, 137.8, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.6, 127.6, 127.5, 127.5, 127.4, 109.1, 109.1, 108.8, 108.3, 103.5, 103.2, 85.2, 84.3, 84.2, 79.3, 79.0, 76.3, 75.7, 75.0, 74.9, 74.6, 73.6, 73.5, 73.4, 73.3, 72.7, 72.5, 72.4, 71.7, 70.9, 70.9, 70.4, 70.3, 69.6, 68.7, 68.2, 61.7, 61.5, 36.9, 36.3, 29.7, 26.7, 26.6, 26.0, 25.9, 25.6, 24.2, 24.1. HRMS (ESI) m/z : [M + NH₄]⁺ calcd for C₄₆H₅₈NO₁₀S 816.3776; found 816.3779. [α]_D³⁵ = + 0.32 (c 0.01, CHCl₃).

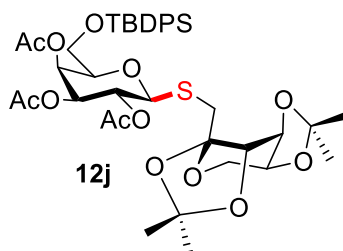
1,2,3,4-di-O-isopropylidene-6-thio-(2,3,4,6-tetra-*p*-methyl-O-benzyl-D-galactopyranosyl)- α -D-galactopyranose (12i).



Glycosylation of **9e** (50 mg, 0.06 mmol) with **10h** (33.2 mg, 0.12 mmol) according to General procedure 4 afforded **12i** (45.2 mg, 88 %, $\alpha:\beta = 1.4:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.37$ (Hexane/EtOAc = 4:1, v/v). For α anomer, ^1H NMR (600 MHz, CDCl_3) δ 7.27 (d, $J = 7.9$ Hz, 2H), 7.16 – 7.10 (m, 10H), 7.08 (d, $J = 7.8$ Hz, 2H), 5.53 – 5.50 (m, 2H), 4.86 (d, $J = 11.2$ Hz, 1H), 4.75 (d, $J = 11.6$ Hz, 1H), 4.71 (d, $J = 11.5$ Hz, 1H), 4.63 (d, $J = 11.7$ Hz, 1H), 4.60 (d, $J = 11.6$ Hz, 1H), 4.52 (dd, $J = 6.7, 4.3$ Hz, 2H), 4.39 (d, $J = 11.6$ Hz, 1H), 4.33 (d, $J = 11.6$ Hz, 1H), 4.30 (dd, $J = 7.9, 1.6$ Hz, 1H), 4.27 (dd, $J = 5.0, 2.3$ Hz, 1H), 4.26 – 4.21 (m, 2H), 3.94 – 3.89 (m, 2H), 3.72 (dd, $J = 10.0, 2.8$ Hz, 1H), 3.51 (dd, $J = 8.7, 7.2$ Hz, 1H), 3.44 (dd, $J = 9.2, 5.7$ Hz, 1H), 2.83 (dd, $J = 13.6, 8.2$ Hz, 1H), 2.72 (dd, $J = 13.6, 6.8$ Hz, 1H), 2.35 (s, 3H), 2.34 (s, 6H), 2.31 (s, 3H), 1.48 (s, 3H), 1.42 (s, 3H), 1.31 (s, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 137.3, 137.2, 137.2, 137.1, 135.8, 135.6, 135.3, 135.0, 129.1, 129.0, 129.0, 128.9, 128.5, 128.0, 127.9, 127.6, 109.2, 108.6, 96.7, 85.0, 79.3, 75.8, 74.6, 74.6, 73.3, 73.2, 72.1, 71.4, 71.0, 70.6, 69.9, 68.4, 66.6, 29.8, 26.2, 26.0, 25.0, 24.5, 21.2, 21.2, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{50}\text{H}_{66}\text{NO}_{10}\text{S}$ 872.4402; found 872.4406. $[\alpha]_{\text{D}}^{35} = +0.28$ (c 0.01, CHCl_3).

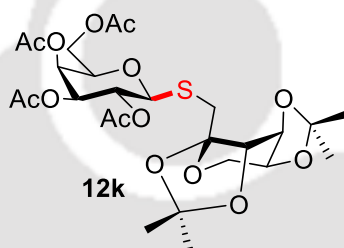
For β anomer, ^1H NMR (600 MHz, CDCl_3) δ 7.26 (d, $J = 7.2$ Hz, 2H), 7.23 (d, $J = 7.9$ Hz, 2H), 7.18 (d, $J = 7.9$ Hz, 2H), 7.16 – 7.08 (m, 10H), 5.50 (d, $J = 5.0$ Hz, 1H), 4.87 (d, $J = 11.5$ Hz, 1H), 4.81 (d, $J = 10.0$ Hz, 1H), 4.74 (d, $J = 10.0$ Hz, 1H), 4.65 (s, 2H), 4.54 (d, $J = 11.5$ Hz, 1H), 4.48 (dd, $J = 7.9, 2.3$ Hz, 1H), 4.42 (d, $J = 9.7$ Hz, 1H), 4.39 – 4.35 (m, 2H), 4.33 (d, $J = 11.5$ Hz, 1H), 4.26 (dd, $J = 5.0, 2.3$ Hz, 1H), 3.95 – 3.91 (m, 1H), 3.89 (d, $J = 2.5$ Hz, 1H), 3.76 (t, $J = 9.5$ Hz, 1H), 3.54 – 3.51 (m, 2H), 3.49 (dt, $J = 10.8, 5.0$ Hz, 2H), 2.96 (dd, $J = 13.6, 6.1$ Hz, 1H), 2.88 (dd, $J = 13.6, 8.0$ Hz, 1H), 2.35 (s, 3H), 2.34 – 2.30 (m, 9H), 1.48 (s, 3H), 1.41 (s, 3H), 1.31 (s, 3H), 1.28 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 137.5, 137.3, 137.3, 137.1, 135.7, 135.4, 134.8, 129.1, 129.1, 128.9, 128.8, 128.4, 128.2, 128.1, 127.7, 109.0, 108.6, 96.6, 85.7, 83.9, 78.5, 75.6, 74.2, 73.4, 73.2, 73.0, 71.1, 70.8, 70.6, 68.6, 68.2, 30.4, 26.1, 26.0, 25.0, 24.4, 21.2, 21.2, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{50}\text{H}_{66}\text{NO}_{10}\text{S}$ 872.4402; found 872.4407. $[\alpha]_{\text{D}}^{35} = +0.26$ (c 0.01, CHCl_3).

2,3;4,5-di-O-isopropylidene-1-thio- (2,3,4-tri-O-acetyl-6-O-tert-butylbiphenylsilyl)- β -D-galactopyranosyl)- β -D-fructopyranose (12j).



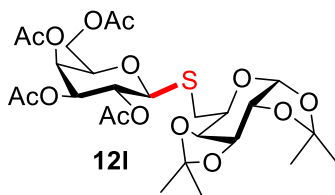
Glycosylation of **9h** (46.9 mg, 0.06 mmol) with **10l** (33.2 mg, 0.12 mmol) according to General procedure 4 afforded **12j** (42.9 mg, 89 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.32 (Hexane: EtOAc = 3:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.60 – 7.55 (m, 4H), 7.46 – 7.34 (m, 6H), 5.65 (d, J = 2.8 Hz, 1H), 5.16 (t, J = 10.0 Hz, 1H), 5.08 (dd, J = 10.0, 3.3 Hz, 1H), 4.76 (d, J = 10.0 Hz, 1H), 4.56 (dd, J = 7.9, 2.7 Hz, 1H), 4.30 (d, J = 2.7 Hz, 1H), 4.20 (d, J = 8.3 Hz, 1H), 3.92 (dd, J = 12.9, 1.6 Hz, 1H), 3.81 (dd, J = 8.6, 5.8 Hz, 1H), 3.76 – 3.71 (m, 2H), 3.60 (t, J = 9.3 Hz, 1H), 3.26 (d, J = 14.8 Hz, 1H), 2.81 (d, J = 14.8 Hz, 1H), 2.01 (s, 3H), 1.99 (s, 3H), 1.99 (s, 3H), 1.53 (s, 3H), 1.44 (s, 3H), 1.36 (s, 3H), 1.28 (s, 3H), 1.02 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.2, 170.1, 169.5, 135.7, 135.6, 132.8, 132.7, 129.9, 129.8, 127.8, 127.8, 109.1, 108.8, 103.3, 83.7, 76.6, 72.3, 71.7, 70.8, 70.2, 68.4, 67.1, 61.7, 60.5, 35.7, 26.7, 26.7, 25.9, 25.8, 24.0, 20.7, 20.7, 20.7, 19.0. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{40}\text{H}_{58}\text{NO}_{13}\text{SSi}$ 820.3393; found 820.3396. $[\alpha]_{\text{D}}^{35}$ = - 0.34 (c 0.01, CHCl_3).

2,3;4,5-di-O-isopropylidene-1-thio- (2,3,4,6-tetra-O-acetyl- β -D-galactopyranosyl)- β -D-fructopyranose (12k).



Glycosylation of **9b** (35 mg, 0.06 mmol) with **10l** (33.2 mg, 0.12 mmol) according to General procedure 4 afforded **12k** (30.9 mg, 85 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.29 (Hexane: EtOAc = 3:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 5.42 (d, J = 2.8 Hz, 1H), 5.20 (t, J = 10.0 Hz, 1H), 5.04 (dd, J = 10.0, 3.4 Hz, 1H), 4.77 (d, J = 10.1 Hz, 1H), 4.61 (dd, J = 7.9, 2.7 Hz, 1H), 4.37 (t, J = 4.8 Hz, 1H), 4.24 (d, J = 8.3 Hz, 1H), 4.16 (dd, J = 11.3, 6.6 Hz, 1H), 4.12 (dd, J = 11.4, 6.8 Hz, 1H), 3.93 (td, J = 13.5, 4.5 Hz, 2H), 3.77 (d, J = 12.9 Hz, 1H), 3.32 (t, J = 15.9 Hz, 1H), 2.88 (d, J = 14.8 Hz, 1H), 2.16 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 1.98 (s, 3H), 1.55 (s, 3H), 1.48 (s, 3H), 1.47 (s, 3H), 1.34 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.4, 170.3, 170.1, 169.4, 109.1, 108.8, 103.2, 84.2, 74.3, 71.9, 71.6, 70.8, 70.2, 68.0, 67.3, 61.7, 61.2, 36.3, 26.7, 25.88, 25.86, 24.0, 20.72, 20.69, 20.67, 20.6. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{26}\text{H}_{38}\text{NaO}_{14}\text{S}$ 629.1874, found 629.1863. $[\alpha]_{\text{D}}^{35}$ = - 0.22 (c 0.01, CHCl_3).

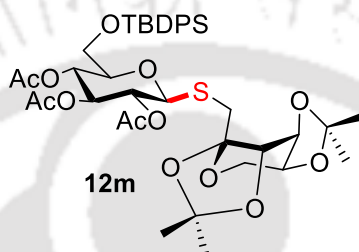
1,2;3,4-di-O-isopropylidene-6-thio-(2,3,4,6-tetra-O-acetyl- β -D-galactopyranosyl)- α -D-galactopyranose (12l).



Glycosylation of **9b** (35 mg, 0.06 mmol) with **10h** (33.2 mg, 0.12 mmol) according to General procedure 4 afforded **12l** (31.2 mg, 86 %, β only) as a colorless syrup. The crude product was

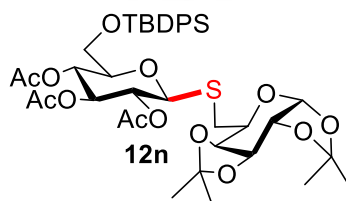
purified through flash column chromatography, $R_f = 0.29$ (Hexane: EtOAc = 3:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 5.51 (d, $J = 5.0$ Hz, 1H), 5.43 (d, $J = 3.3$ Hz, 1H), 5.21 (t, $J = 10.0$ Hz, 1H), 5.05 (dd, $J = 10.0, 3.4$ Hz, 1H), 4.70 (d, $J = 10.0$ Hz, 1H), 4.61 (dd, $J = 7.9, 2.4$ Hz, 1H), 4.32 – 4.28 (m, 2H), 4.13 (dd, $J = 6.6, 5.2$ Hz, 2H), 3.92 (dd, $J = 7.0, 6.1$ Hz, 2H), 2.98 (dd, $J = 13.9, 7.4$ Hz, 1H), 2.81 (dd, $J = 13.9, 5.9$ Hz, 1H), 2.16 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 1.98 (s, 3H), 1.54 (s, 3H), 1.45 (s, 3H), 1.35 (s, 3H), 1.33 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.4, 170.3, 170.1, 169.6, 109.4, 108.7, 96.5, 84.3, 74.4, 72.0, 71.8, 70.9, 70.4, 69.1, 67.5, 67.3, 61.5, 30.2, 26.1, 26.0, 24.9, 24.5, 20.8, 20.7, 20.7, 20.6. HRMS (ESI) m/z : $[\text{M} + \text{K}]^+$ calcd for $\text{C}_{26}\text{H}_{38}\text{KO}_{14}\text{S}$ 645.1614; found 645.1604. $[\alpha]_D^{35} = +0.60$ (c 0.01, CHCl_3).

2,3,4,5-di-O-isopropylidene-1-thio- (2,3,4-tri-O-acetyl-6-O-tert-butylbiphenylsilyl)- β -D-glucopyranosyl)- β -D-fructopyranose (12m).



Glycosylation of **9g** (46.9 mg, 0.06 mmol) with **10l** (33.2 mg, 0.12 mmol) according to General procedure 4 afforded **12m** (43.4 mg, 90 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.31$ (Hexane: EtOAc = 3:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.69 (dd, $J = 7.8, 1.4$ Hz, 2H), 7.66 – 7.63 (m, 2H), 7.43 – 7.35 (m, 6H), 5.30 (t, $J = 9.7$ Hz, 1H), 5.19 (t, $J = 9.3$ Hz, 1H), 5.03 (t, $J = 9.7$ Hz, 1H), 4.75 (d, $J = 10.1$ Hz, 1H), 4.54 (dd, $J = 7.9, 2.7$ Hz, 1H), 4.41 (d, $J = 2.7$ Hz, 1H), 4.20 (d, $J = 7.9$ Hz, 1H), 3.93 (dd, $J = 12.9, 1.7$ Hz, 1H), 3.79 (dd, $J = 11.6, 1.9$ Hz, 1H), 3.74 (d, $J = 12.9$ Hz, 1H), 3.70 (dd, $J = 11.7, 3.9$ Hz, 1H), 3.52 (ddd, $J = 10.0, 3.7, 2.1$ Hz, 1H), 3.34 (d, $J = 15.0$ Hz, 1H), 2.88 (d, $J = 15.0$ Hz, 1H), 2.02 (s, 3H), 2.01 (s, 3H), 1.92 (s, 3H), 1.53 (d, $J = 10.4$ Hz, 3H), 1.48 (s, 3H), 1.44 (s, 3H), 1.29 (s, 3H), 1.05 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.6, 169.3, 169.2, 135.8, 135.6, 133.2, 133.0, 129.7, 129.6, 127.7, 127.7, 109.1, 108.8, 103.4, 83.8, 78.2, 74.6, 71.5, 71.0, 70.9, 70.3, 68.4, 62.2, 61.8, 36.3, 26.7, 26.7, 25.9, 24.1, 20.7, 20.7, 20.6, 19.2. HRMS (ESI) m/z : $[\text{M} + \text{K}]^+$ calcd for $\text{C}_{40}\text{H}_{54}\text{KO}_{13}\text{SSi}$ 841.2686, found 841.2680 $[\alpha]_D^{35} = +0.38$ (c 0.01, CHCl_3).

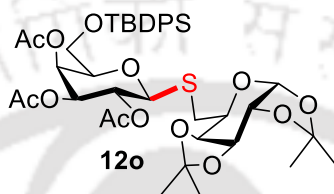
1,2,3,4-di-O-isopropylidene-6-thio-(2,3,4-tri-O-acetyl-6-O-tert-butylbiphenylsilyl)- β -D-glucopyranosyl)- α -D-galactopyranose (12n).



Glycosylation of **9g** (46.9 mg, 0.06 mmol) with **10h** (33.2 mg, 0.12 mmol) according to General procedure 4 afforded **12n** (43.9 mg, 91 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.31$ (Hexane/EtOAc = 3:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.70 (dd, $J = 7.7, 1.5$ Hz, 2H), 7.66 (dd, $J = 7.8, 1.3$ Hz, 2H), 7.44 – 7.36 (m, 6H), 5.51 (d, $J = 5.0$ Hz, 1H), 5.21–5.14 (m, 2H), 5.02 (t, $J = 9.6$ Hz, 1H), 4.63 (d, $J = 10.1$

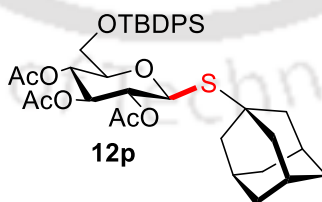
Hz, 1H), 4.54 (dd, $J = 7.9, 2.3$ Hz, 1H), 4.29 (dd, $J = 5.0, 2.4$ Hz, 1H), 4.26 (dd, $J = 7.9, 1.7$ Hz, 1H), 3.94 – 3.90 (m, 1H), 3.72 (d, $J = 3.4$ Hz, 2H), 3.54 (dt, $J = 9.3, 3.4$ Hz, 1H), 3.02 (dd, $J = 13.6, 7.8$ Hz, 1H), 2.85 (dd, $J = 13.6, 5.6$ Hz, 1H), 2.05 (s, 3H), 2.00 (s, 3H), 1.90 (s, 3H), 1.55 (s, 3H), 1.40 (s, 3H), 1.33 (s, 3H), 1.28 (s, 3H), 1.05 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.4, 169.5, 169.2, 135.7, 135.6, 133.2, 133.0, 129.7, 129.7, 127.7, 127.7, 109.3, 108.7, 96.5, 83.6, 78.7, 74.4, 71.8, 70.8, 70.4, 70.3, 68.8, 68.6, 62.7, 30.1, 26.7, 26.1, 26.0, 25.0, 24.5, 20.8, 20.7, 20.6, 19.2. HRMS (ESI) m/z : $[\text{M} + \text{K}]^+$ calcd for $\text{C}_{40}\text{H}_{54}\text{KO}_{13}\text{SSi}$ 841.2686 found 841.2688. $[\alpha]_{\text{D}}^{35} = +0.42$ (c 0.01, CHCl_3).

1,2;3,4-di-O-isopropylidene-6-thio-(2,3,4-tri-O-acetyl-6-O-tert-butylbiphenylsilyl)- β -D-galactopyranosyl)- α -D-galactopyranose (12o).



Glycosylation of **9h** (46.9 mg, 0.06 mmol) with **10h** (33.2 mg, 0.12 mmol) according to General procedure 4 afforded **12o** (44.8 mg, 93 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.32$ (Hexane/EtOAc = 3:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.62 – 7.57 (m, 4H), 7.46 – 7.35 (m, 6H), 5.63 (d, $J = 2.9$ Hz, 1H), 5.48 (d, $J = 5.0$ Hz, 1H), 5.17 (t, $J = 10.0$ Hz, 1H), 5.08 (dd, $J = 10.0, 3.4$ Hz, 1H), 4.60 (d, $J = 10.0$ Hz, 1H), 4.54 (dd, $J = 7.9, 2.4$ Hz, 1H), 4.27 (dd, $J = 5.0, 2.4$ Hz, 1H), 4.23 (dd, $J = 7.9, 1.7$ Hz, 1H), 3.87 – 3.83 (m, 1H), 3.79 (dd, $J = 8.0, 6.1$ Hz, 1H), 3.73 (dd, $J = 9.9, 5.6$ Hz, 1H), 3.60 (dd, $J = 9.6, 8.7$ Hz, 1H), 2.91 (dd, $J = 13.6, 7.3$ Hz, 1H), 2.80 (dd, $J = 13.6, 6.3$ Hz, 1H), 2.06 (s, 3H), 2.02 (s, 3H), 1.99 (s, 3H), 1.45 (s, 3H), 1.41 (s, 3H), 1.31 (s, 3H), 1.29 (s, 3H), 1.02 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.2, 170.1, 169.7, 135.6, 135.5, 132.8, 132.7, 129.9, 129.8, 127.8, 109.3, 108.6, 96.5, 84.5, 72.3, 71.6, 70.8, 70.4, 68.7, 67.8, 67.1, 60.9, 30.2, 26.7, 26.1, 26.0, 24.9, 24.5, 20.8, 20.7, 19.0. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{40}\text{H}_{58}\text{NO}_{13}\text{SSi}$ 820.3393; found 820.3383. $[\alpha]_{\text{D}}^{35} = +0.36$ (c 0.01, CHCl_3).

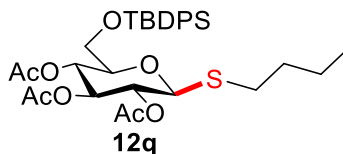
1-Adamantanyl 2,3,4-tri-O-acetyl-6-O-tert-butylbiphenylsilyl-1-thio- β -D-glucopyranoside (12p).



Glycosylation of **9g** (46.9 mg, 0.06 mmol) with 1-adamantylthiol (**10m**) (20.2 mg, 0.12 mmol) according to General procedure 4 afforded **12p** (33.8 mg, 81 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.59$ (Hexane: EtOAc = 3: 1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.67 (td, $J = 8.1, 1.5$ Hz, 4H), 7.45 – 7.34 (m, 6H), 5.24 (t, $J = 9.3$ Hz, 1H), 4.99 (t, $J = 9.6$ Hz, 1H), 4.93 (t, $J = 9.7$ Hz, 1H), 4.73 (d, $J = 10.2$ Hz, 1H), 3.73 (dd, $J = 11.7, 6.3$ Hz, 1H), 3.65 – 3.58 (m, 2H), 2.04 (s, 6H), 1.99 (s, 4H), 1.96 (s, 2H), 1.88 (d, $J = 12.2$ Hz, 3H), 1.84 (s, 3H), 1.68 (s, $J = 9.2$ Hz, 5H), 1.64 (s, 1H), 1.03 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.4, 169.4, 169.3, 135.7, 135.6, 133.1, 133.0,

129.7, 127.7, 127.7, 79.8, 78.9, 74.4, 70.3, 68.8, 63.2, 46.3, 44.1, 36.1, 29.7, 26.6, 20.9, 20.7, 20.5, 19.1. HRMS (ESI) m/z : $[M + Na]^+$ calcd for $C_{38}H_{50}NaO_8SSi$ 717.2893; found 717.2893. $[\alpha]_D^{35} = +0.50$ (c 0.01, $CHCl_3$).

Butyl 2,3,4-tri-O-acetyl-6-O-tert-butyldiphenylsilyl-1-thio- β -D-glucopyranoside (12q).

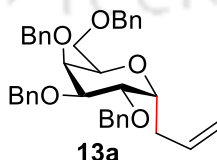


Glycosylation of **9g** (46.9 mg, 0.06 mmol) with 1-butanethiol (**10f**) (13 μ l, 0.12 mmol) according to General procedure 4 afforded **12q** (29.6 mg, 80 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.6 (Hexane: EtOAc = 3: 1, v/v). 1H NMR (600 MHz, $CDCl_3$) δ 7.71 – 7.68 (m, 2H), 7.67 – 7.64 (m, 2H), 7.42 (dd, J = 7.4, 5.0 Hz, 2H), 7.38 (dt, J = 11.4, 5.7 Hz, 4H), 5.22 – 5.16 (m, 2H), 5.06 (t, J = 9.5 Hz, 1H), 4.47 (d, J = 10.0 Hz, 1H), 3.75 (dd, J = 11.6, 2.0 Hz, 1H), 3.71 (dd, J = 11.6, 4.5 Hz, 1H), 3.59 – 3.54 (m, 1H), 2.74 (ddd, J = 12.2, 8.3, 6.6 Hz, 1H), 2.70 – 2.64 (m, 1H), 2.06 (s, 3H), 2.01 (s, 3H), 1.90 (s, 3H), 1.65 – 1.54 (m, 2H), 1.43 – 1.34 (m, 2H), 1.04 (s, 9H), 0.89 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 170.4, 169.5, 169.2, 135.7, 135.6, 133.1, 133.0, 129.7, 129.7, 127.7, 127.7, 83.0, 78.8, 74.4, 70.0, 68.5, 62.6, 31.7, 29.0, 26.7, 22.0, 20.8, 20.7, 20.6, 19.2, 13.6. HRMS (ESI) m/z : $[M + NH_4]^+$ calcd for $C_{32}H_{48}NO_8SSi$ 634.2870; found 634.2870. $[\alpha]_D^{35} = +0.18$ (c 0.01, $CHCl_3$).

General procedure 5.

A solution of glycosyl donor **9a**, **9d** (46.6 mg, 0.06 mmol), and allylTMS (**10d**) (19.1 μ l, 0.12 mmol) in dry CH_2Cl_2 (0.03 M) was stirred at room temperature for 60 min in the presence of activated acid-washed (AW) 4 Å MS (180 mg) under Ar atmosphere. Then the vessel was chilled to 0 °C, to which triflimide (16.9 mg, 0.06 mmol) was added. The reaction mixture was stirred for 5 min and TLC was checked. After completion of the reaction within 5 min, the temperature gradually raised to room temperature. Then Et_3N was added to quench the reaction. The crude reaction mixture was worked up with water, washed with brine, dried by Na_2SO_4 , and concentrated in rotavapor. The resulting crude reaction mixture was purified through Flash column chromatography to afford the C-glycosylated product (**13a**, **13b**).

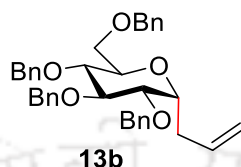
3-(tetra-O-benzyl- α -D-galactopyranosyl)propene (13a).



The compound **13a** was synthesized according to General procedure 5 (28.1 mg, 82 %, α only), R_f = 0.8 (Hexane/EtOAc = 4:1, v/v). When this reaction was performed in presence of 30 mol % of catalyst (triflimide), we got 27 % of the desired product (**17**). Spectral data were matched with reported values.⁵⁵ 1H NMR (600 MHz, $CDCl_3$) δ 7.36 -7.22 (m, 20H), 5.78 -5.70 (m, 1H), 5.07 (d, J = 17.1 Hz, 1H), 5.02 (d, J = 10.1 Hz, 1H), 4.69 (d, J = 11.9 Hz, 2H), 4.60-4.55 (m, 3H), 4.52 (dd, J = 11.8, 6.9 Hz, 2H), 4.49 (d, J = 12.0 Hz, 1H), 4.08 -3.97 (m, 3H), 3.84 (t, J =

8.4 H, 1H), 3.77 – 3.69 (m, 2H), 3.66 (dd, $J = 10.5, 4.6$ Hz, 1H), 2.46 – 2.39 (m, 1H), 2.37 – 2.30 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.6, 138.5, 138.4, 138.3, 135.1, 128.4, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.5, 116.8, 76.4, 74.2, 73.2, 73.1, 73.0, 72.6, 67.2, 32.2. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{37}\text{H}_{40}\text{NaO}_5$ 587.2773; found 587.2774. $[\alpha]_{\text{D}}^{35} = +0.43$ (c 0.01, CHCl_3).

3-(tetra-O-benzyl- α -D-glucopyranosyl)propene (**13b**).



The compound **13b** was synthesized according to General procedure 5 (28.8 mg, 85 %, $\alpha:\beta = 13.2:1$), $R_f = 0.81$ (Hexane/EtOAc = 4:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 7.35 – 7.22 (m, 18H), 7.15 – 7.11 (m, 2H), 5.86 – 5.76 (m, 1H), 5.10 (d, $J = 17.3$ Hz, 1H), 5.06 (d, $J = 10.2$ Hz, 1H), 4.92 (d, $J = 11.0$ Hz, 1H), 4.81 (d, $J = 5.0$ Hz, 1H), 4.79 (d, $J = 5.3$ Hz, 1H), 4.68 (d, $J = 11.6$ Hz, 1H), 4.63 (d, $J = 4.3$ Hz, 1H), 4.60 (d, $J = 4.9$ Hz, 1H), 4.49 (d, $J = 5.6$ Hz, 1H), 4.46 (d, $J = 7.0$ Hz, 1H), 4.12 (dt, $J = 10.3, 5.0$ Hz, 1H), 3.82 – 3.73 (m, 2H), 3.70 (dd, $J = 10.1, 2.0$ Hz, 1H), 3.66 – 3.59 (m, 3H), 2.54 – 2.42 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 137.8, 137.3, 137.1, 133.8, 127.4, 127.4, 127.3, 126.9, 126.9, 126.8, 126.8, 126.7, 126.7, 126.6, 126.5, 115.8, 81.4, 79.1, 77.2, 74.4, 74.0, 72.7, 72.5, 72.1, 70.2, 68.0, 28.8. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{37}\text{H}_{44}\text{NO}_5$ 582.3214; found 582.3216. $[\alpha]_{\text{D}}^{35} = +0.54$ (c 0.01, CHCl_3).

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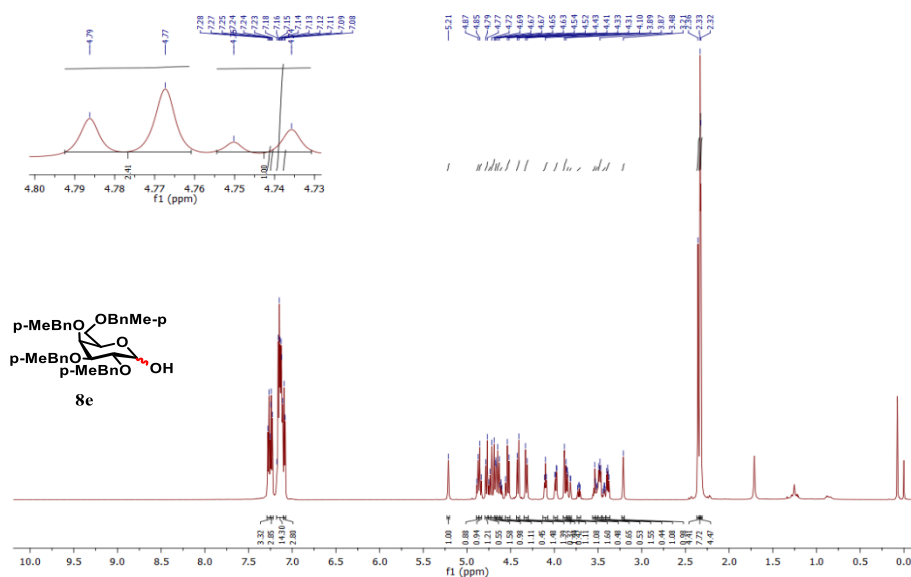
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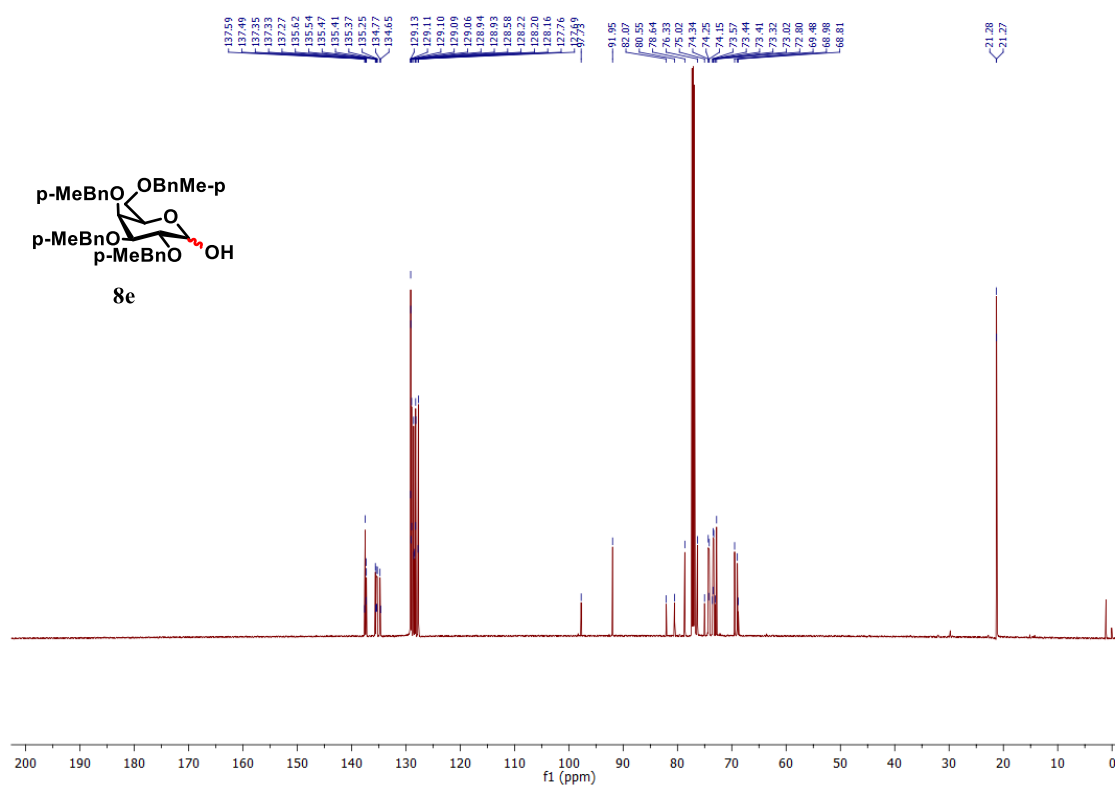


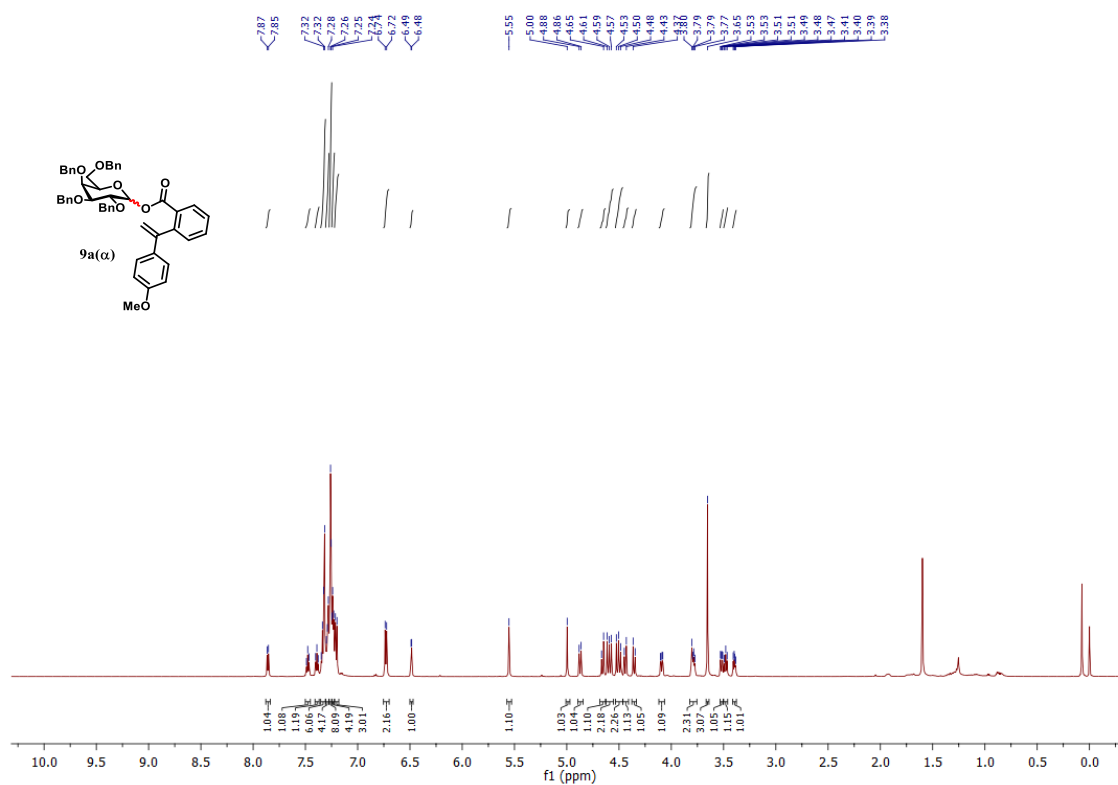
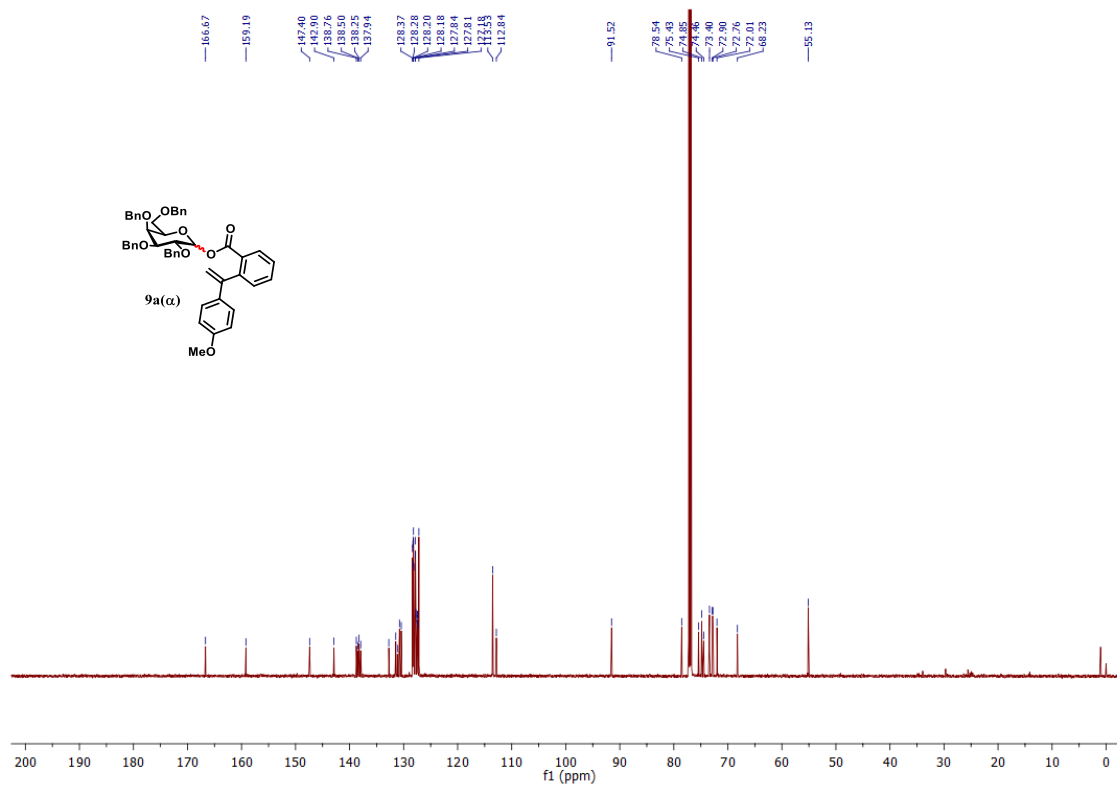
2.5 Spectra

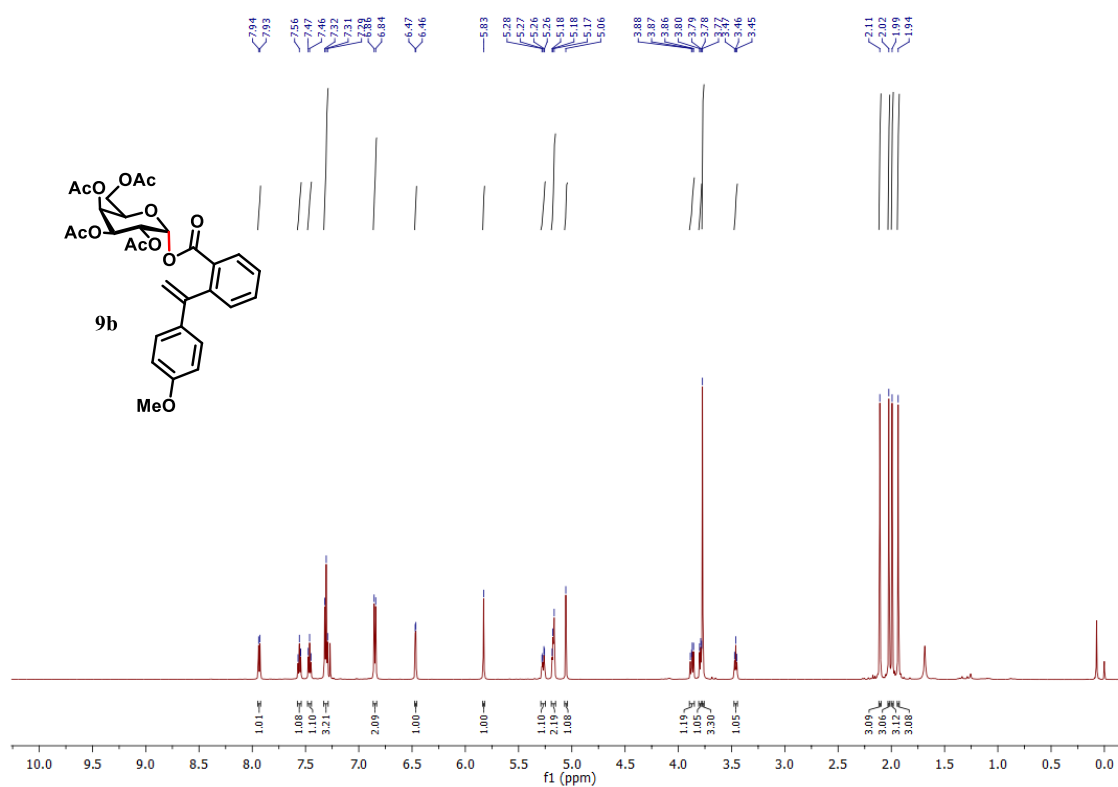
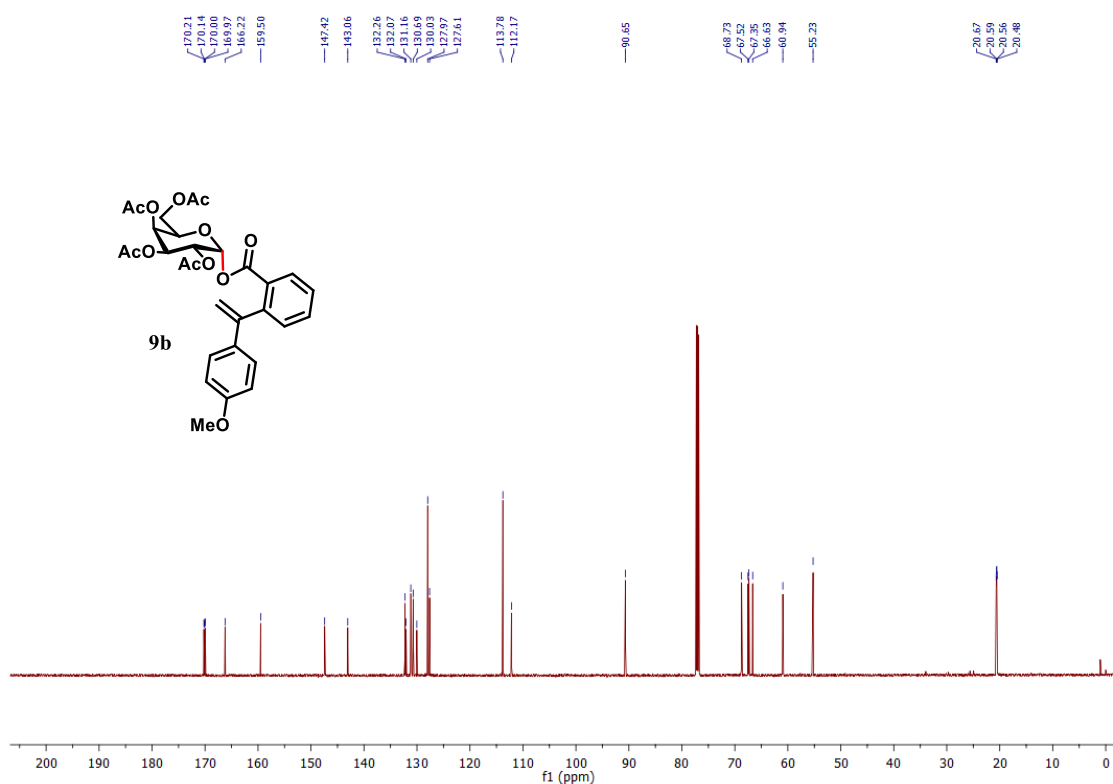
^1H NMR spectrum of compound **8e** (600 MHz, CDCl_3):



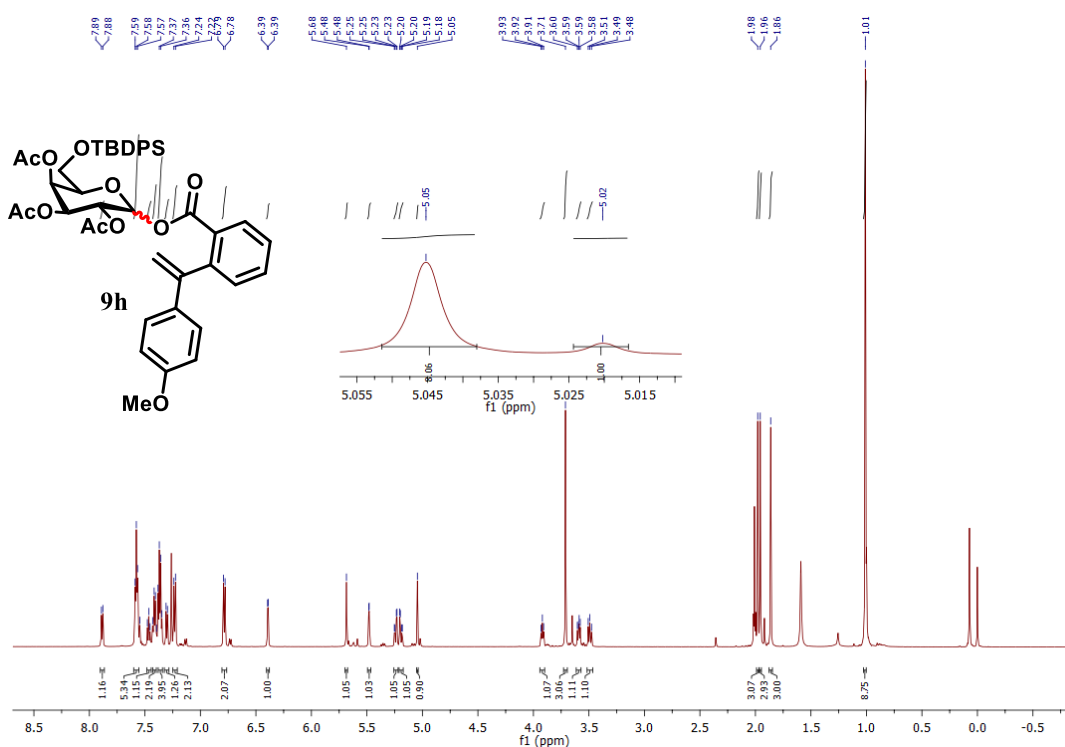
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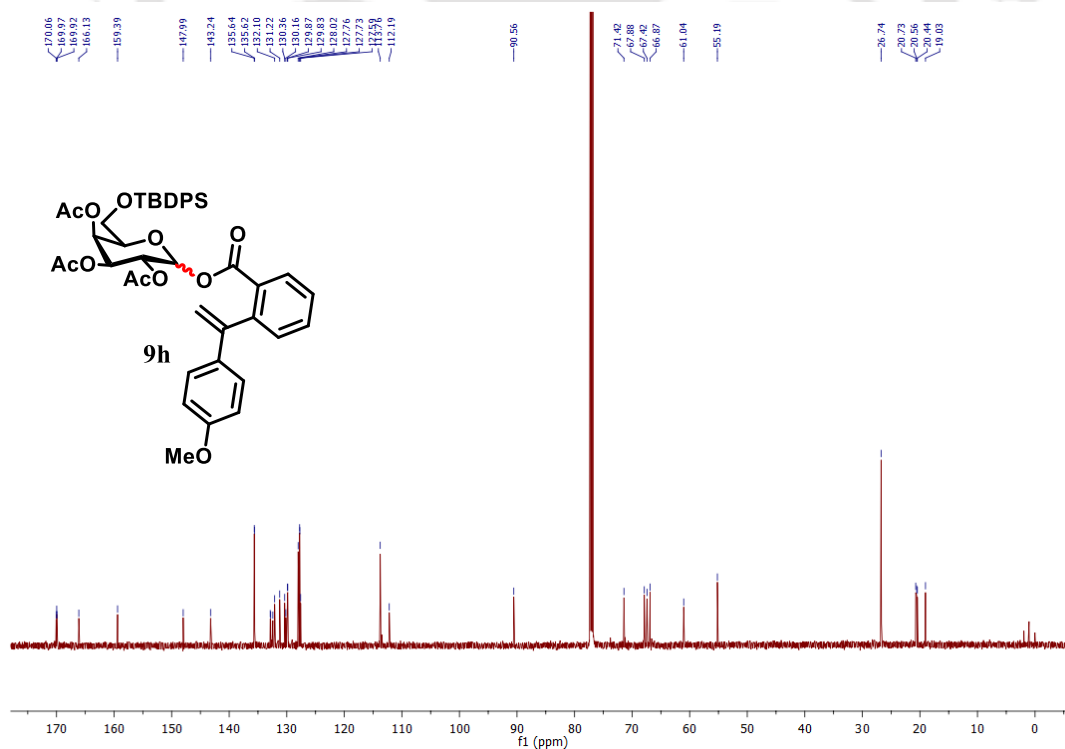
^1H NMR spectrum of compound 9a(α) (600 MHz, CDCl_3): **$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 9a(α) (600 MHz, CDCl_3):**

^1H NMR spectrum of compound 9b (600 MHz, CDCl_3): **$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 9b (600 MHz, CDCl_3):**

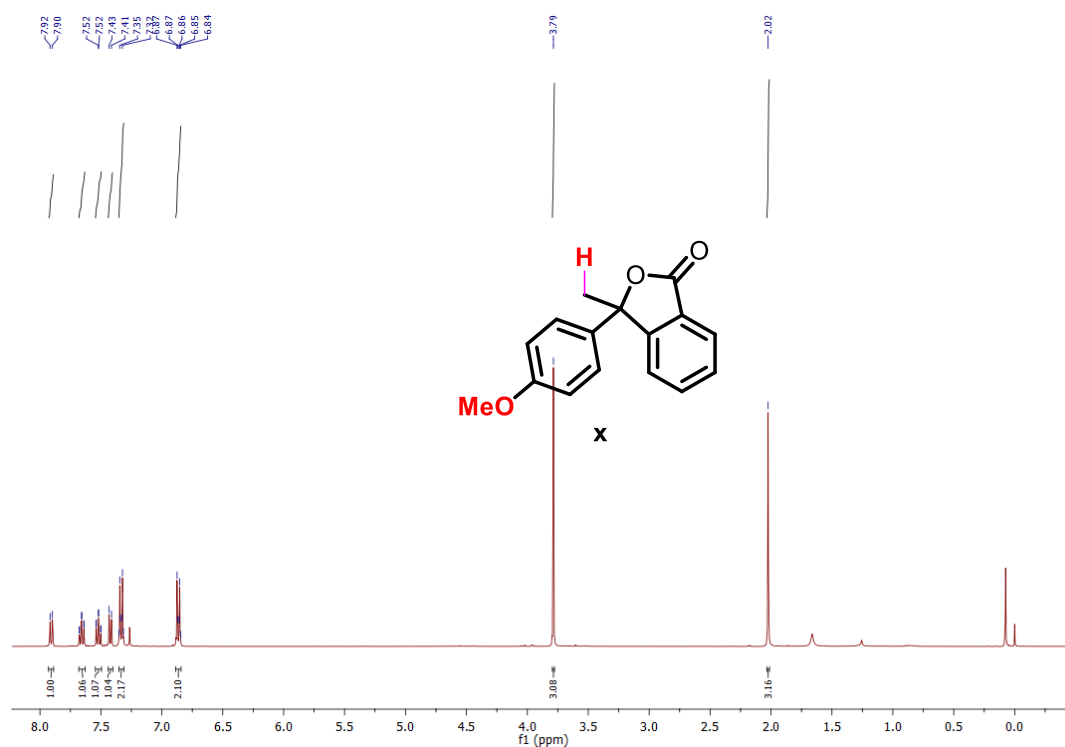
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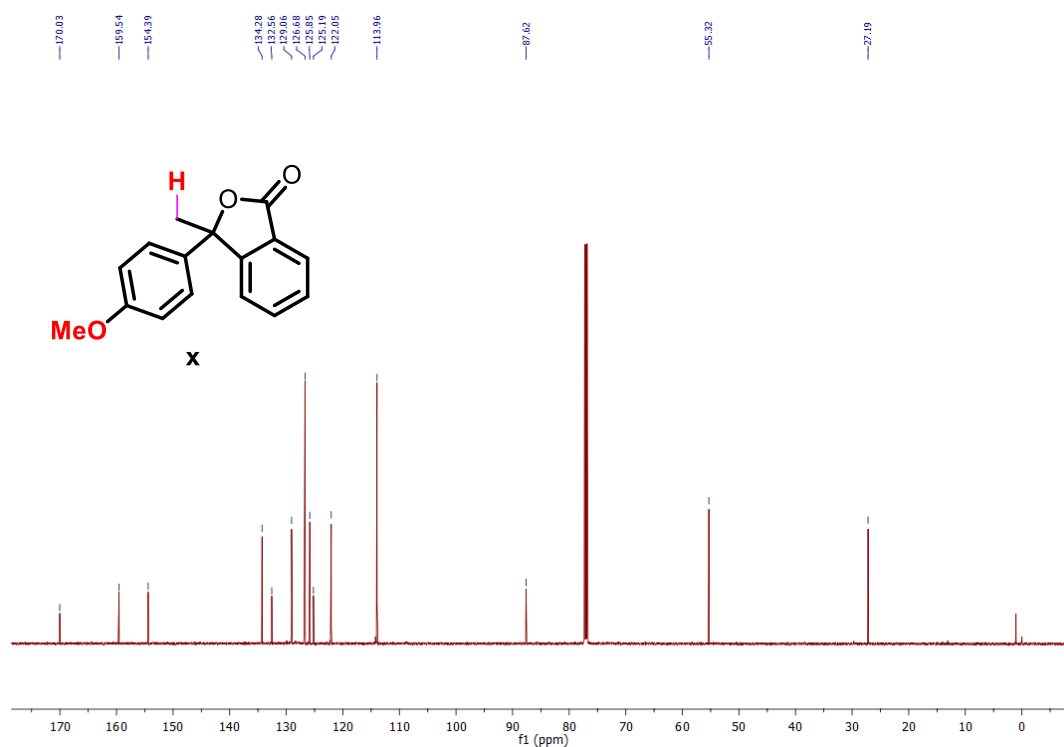
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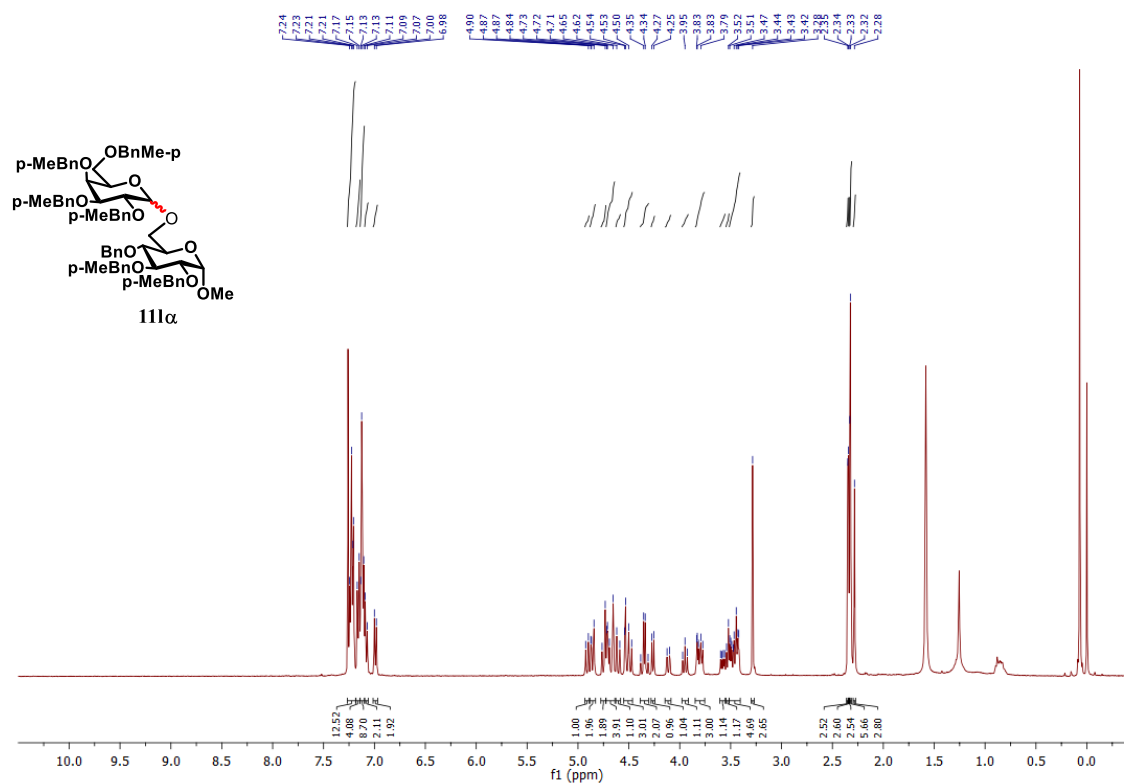
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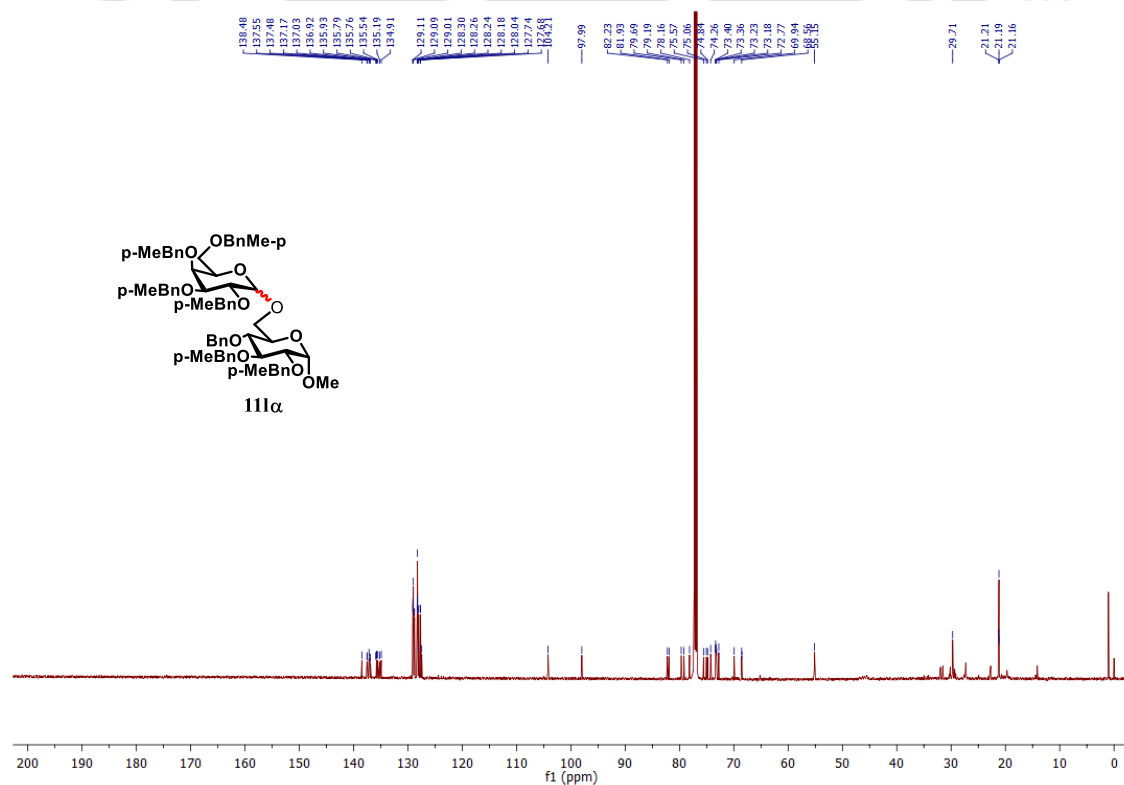
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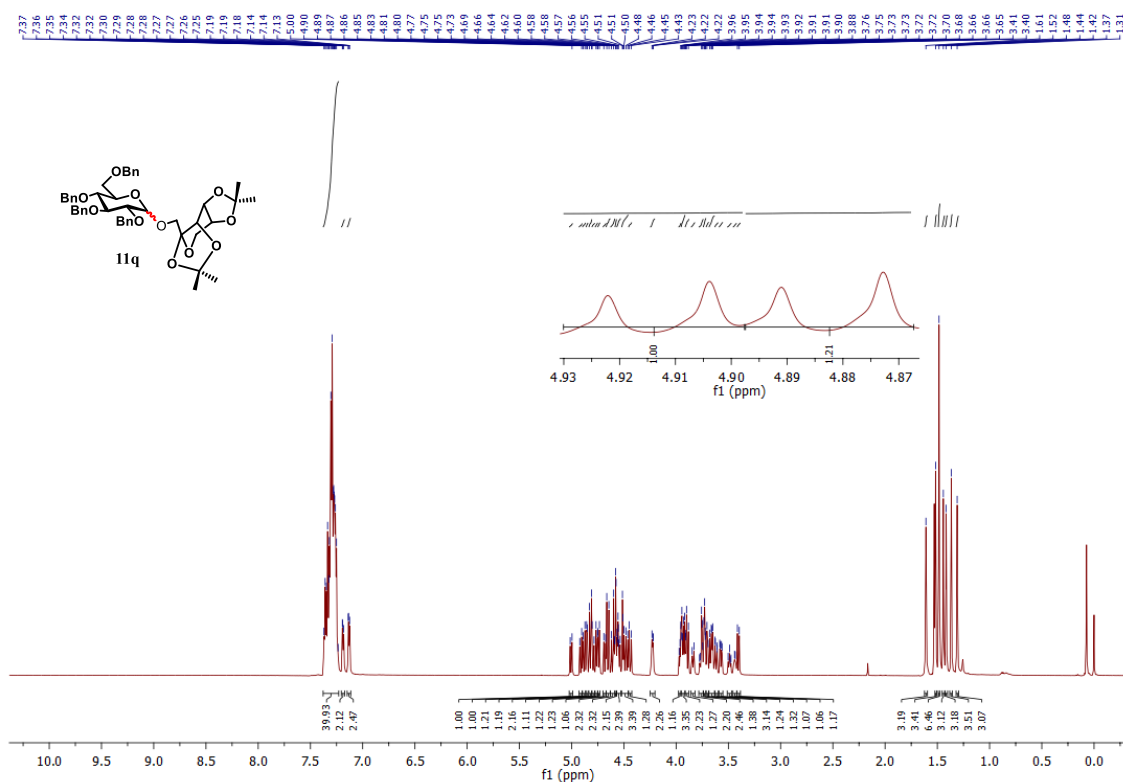
^1H NMR spectrum of compound 11l(α) (400 MHz, CDCl_3):



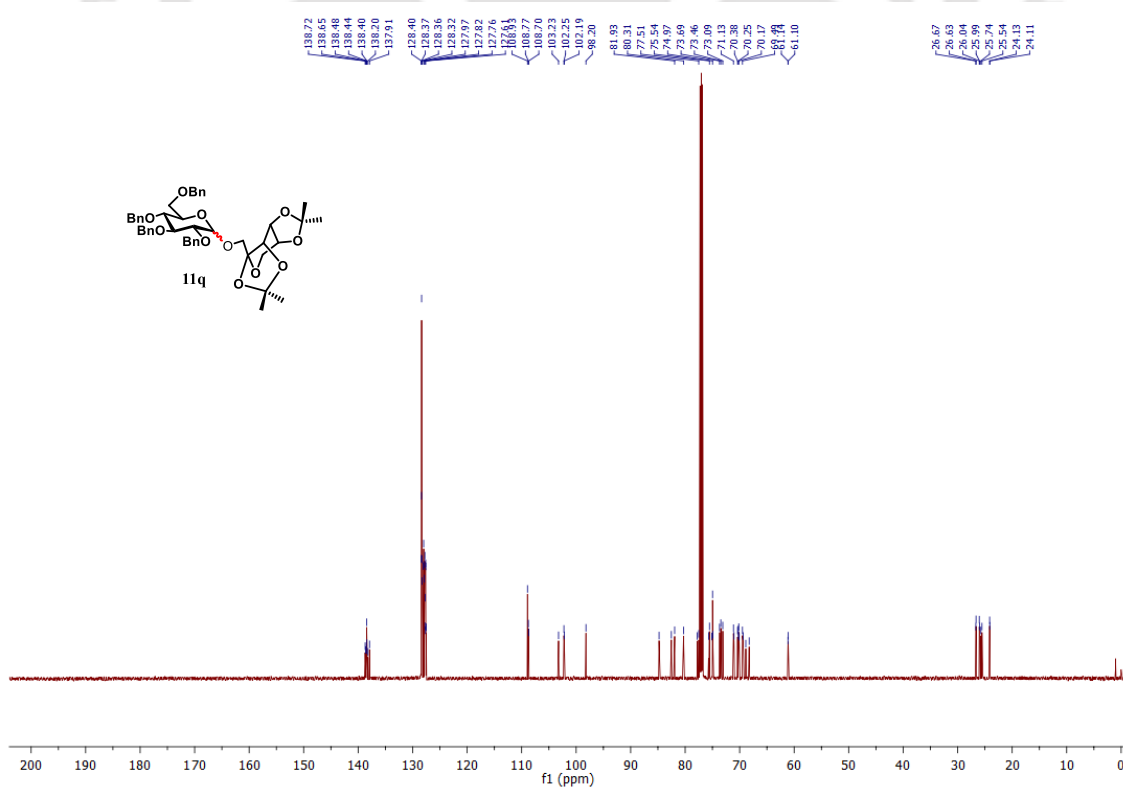
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 11l(α) (600 MHz, CDCl_3):



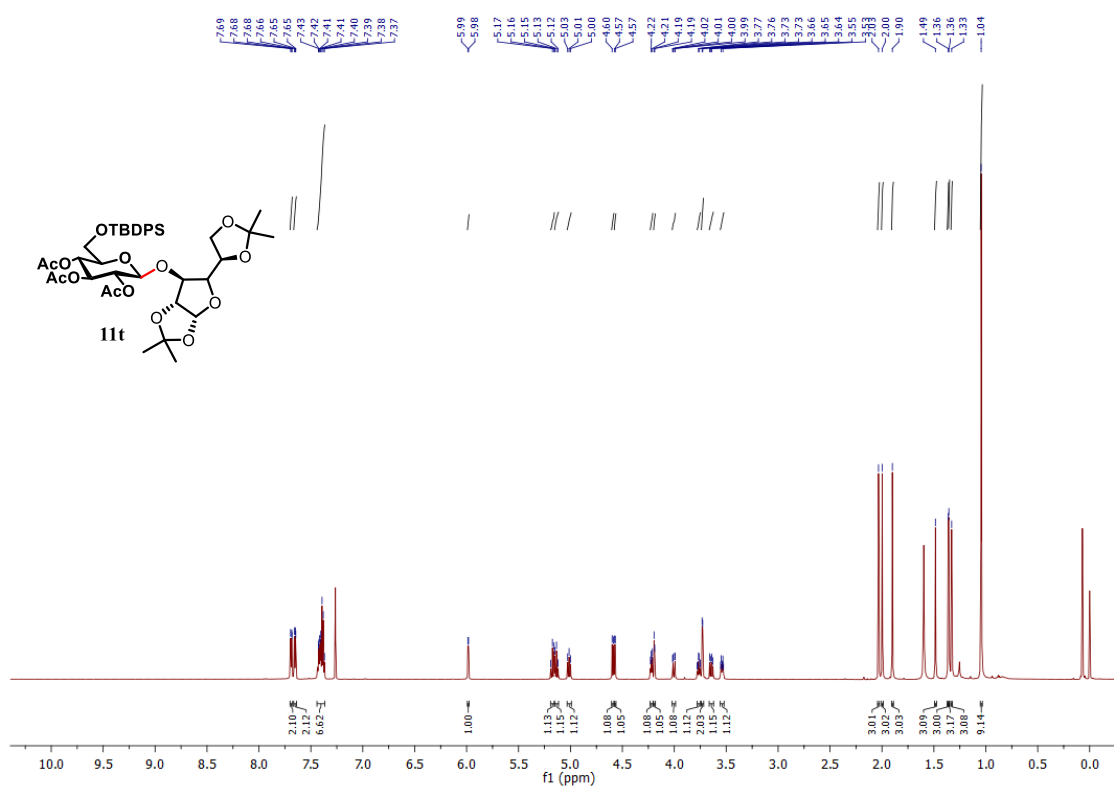
^1H NMR spectrum of compound 11q (600 MHz, CDCl_3):



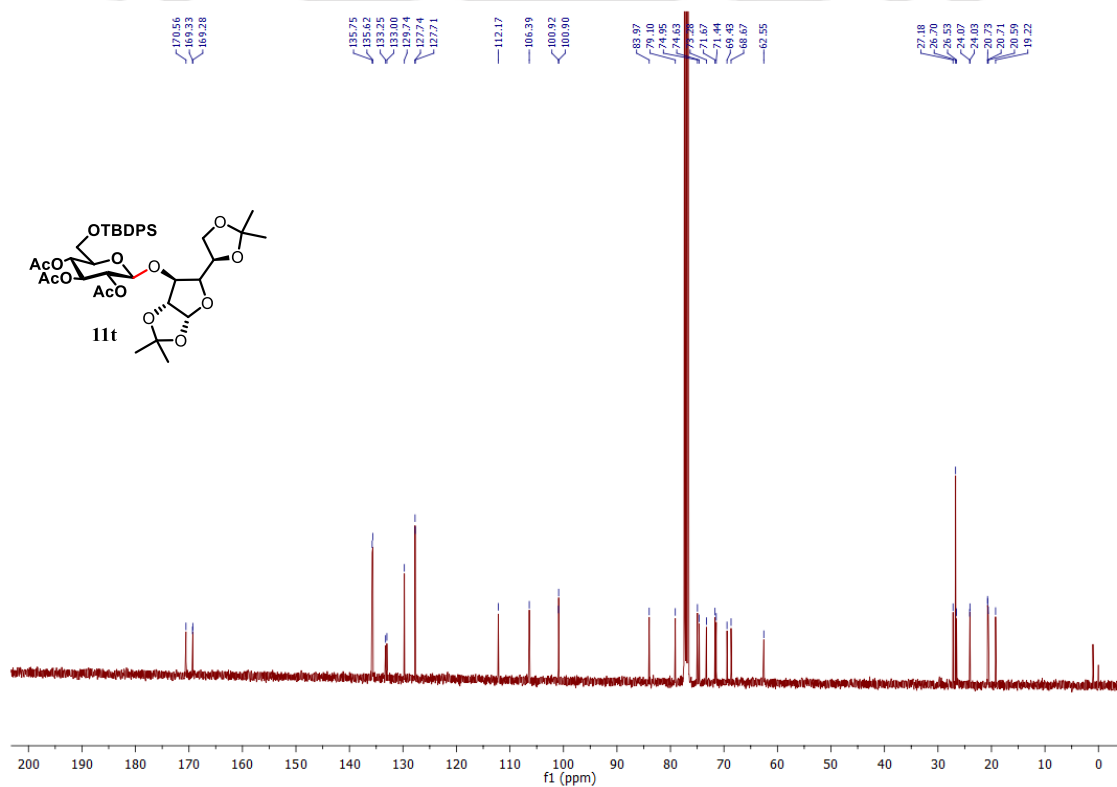
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 11q (600 MHz, CDCl_3):



^1H NMR spectrum of compound 11t (600 MHz, CDCl_3):



$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 11t (400 MHz, CDCl_3):



Chemical structure of **11w** is shown above the spectrum. The structure is a disaccharide derivative with various protecting groups: OTBDPS, AcO, BnO, and SPh.

¹H NMR spectrum (CDCl₃) of compound **11w**. The x-axis represents the chemical shift in ppm (f1 (ppm)), ranging from 0.0 to 10.0. The spectrum shows several multiplets and a large singlet at 1.0 ppm. Integration values are provided below the baseline.

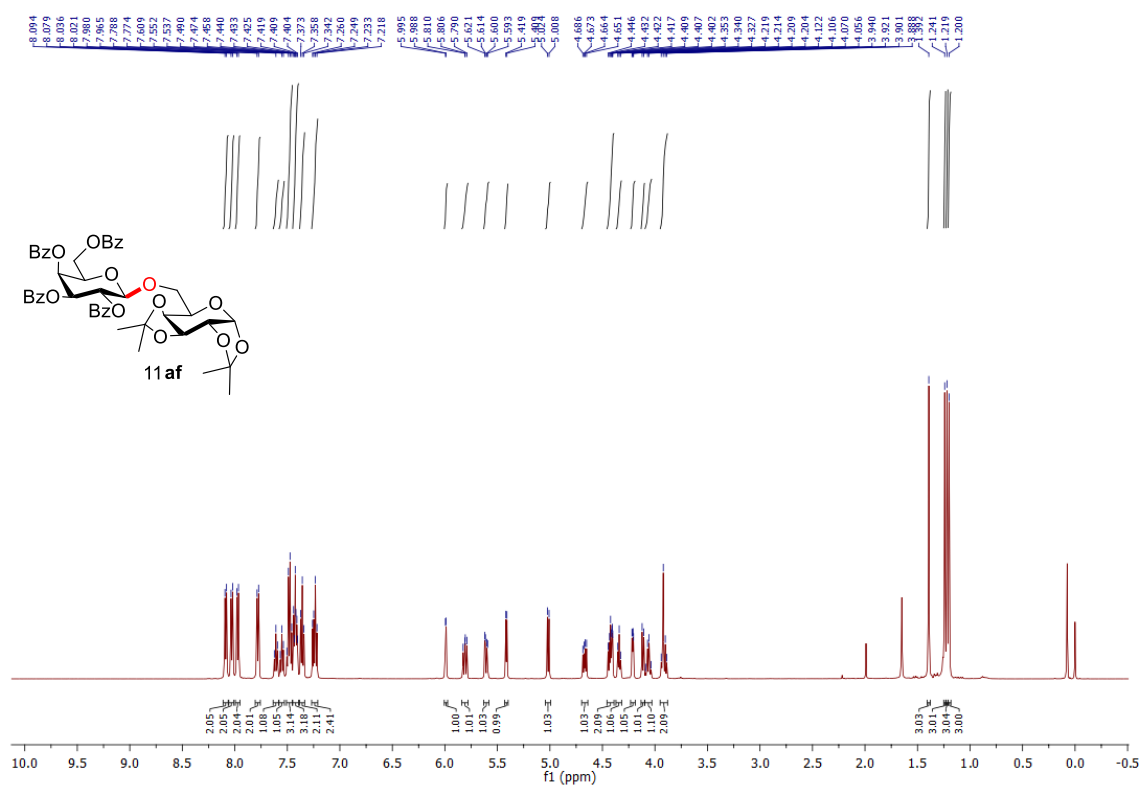
Integration values (from left to right): 4.27, 2.06, 2.06, 1.25, 1.25, 8.24, 4.83, 2.09, 0.99, 1.00, 1.06, 1.08, 1.10, 1.10, 1.10, 1.08, 1.08, 1.01, 1.11, 1.06, 1.99, 2.09, 2.09, 1.08, 1.09, 2.90, 2.93, 2.90, 8.94.

Chemical structure of **11w** is shown above the spectrum. The structure is a dimeric sugar derivative with various protecting groups (AcO, BnO, OTBDPS, SPh).

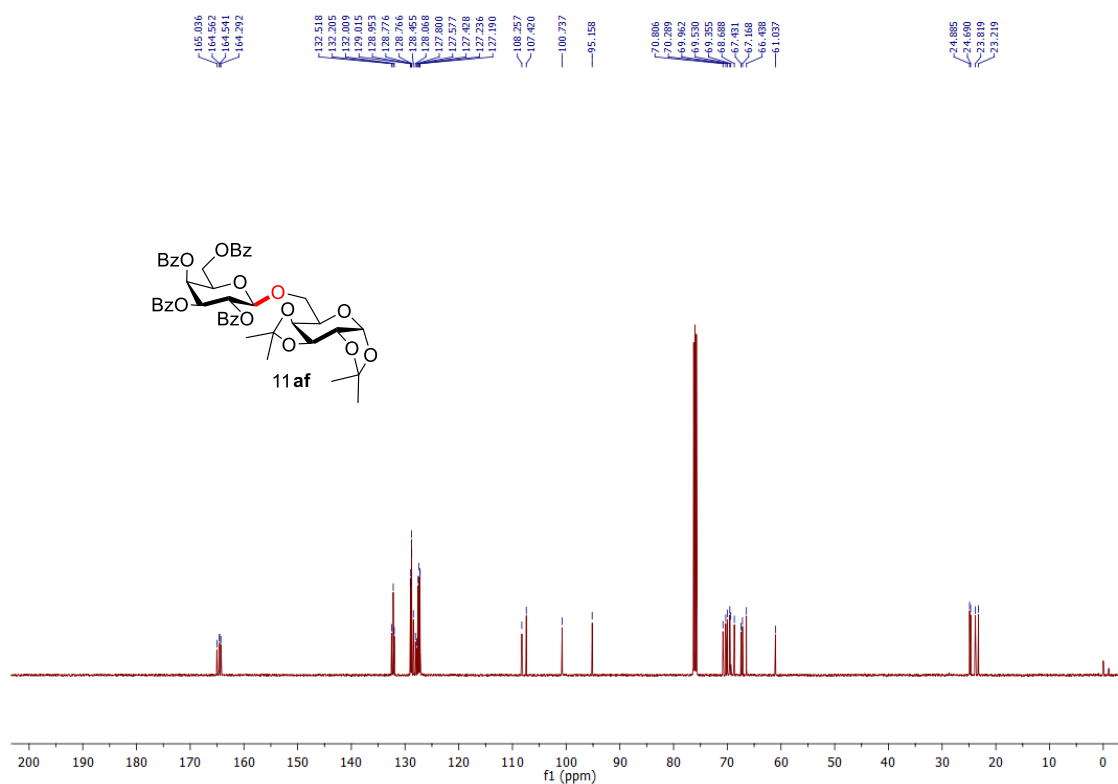
13C NMR Spectrum (ppm):

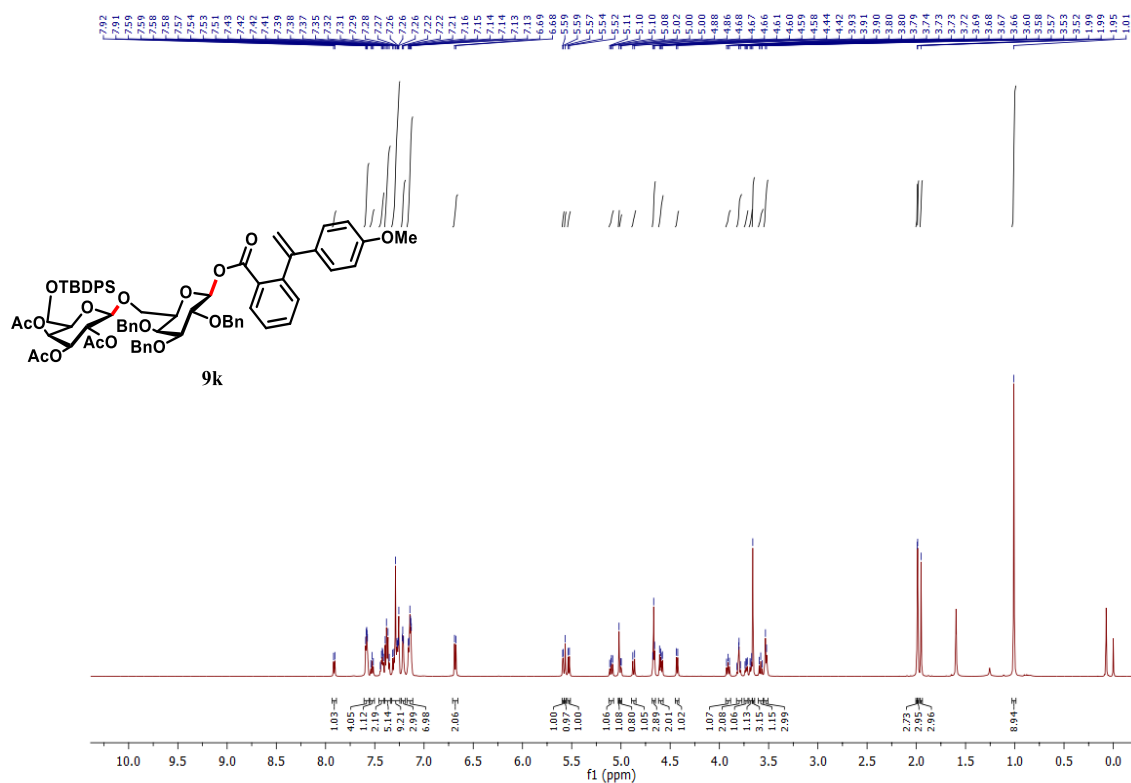
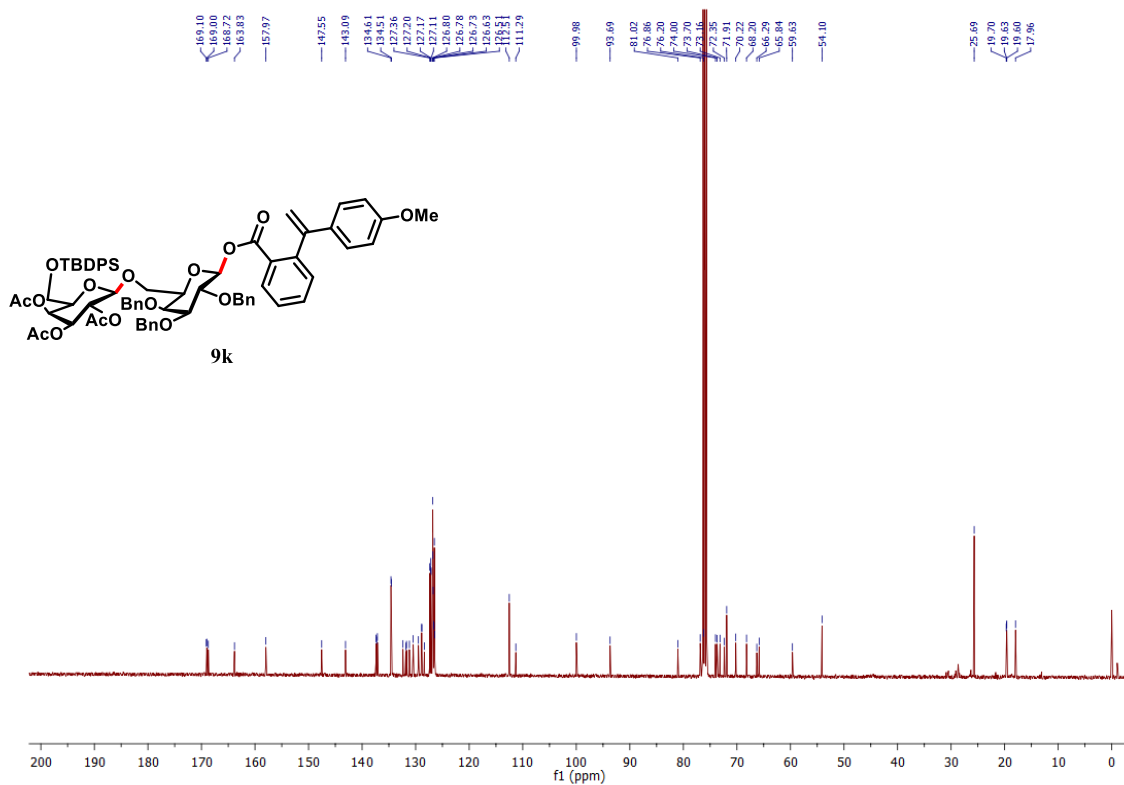
- 169.08, 168.98, 168.56
- 137.41, 137.26, 137.12, 134.62, 134.54, 133.72, 133.57, 131.80, 131.75, 130.35, 128.89, 127.95, 127.74, 127.61, 127.30, 127.13, 126.95, 126.83, 126.79, 126.52, 126.57, 126.50, 126.16
- 99.97
- 87.01, 82.92, 76.93, 76.86, 76.80, 72.77, 72.01, 71.87, 70.20
- 25.71, 19.74, 19.61, 19.59, 17.99

^1H NMR spectrum of compound 11af (500 MHz, CDCl_3):

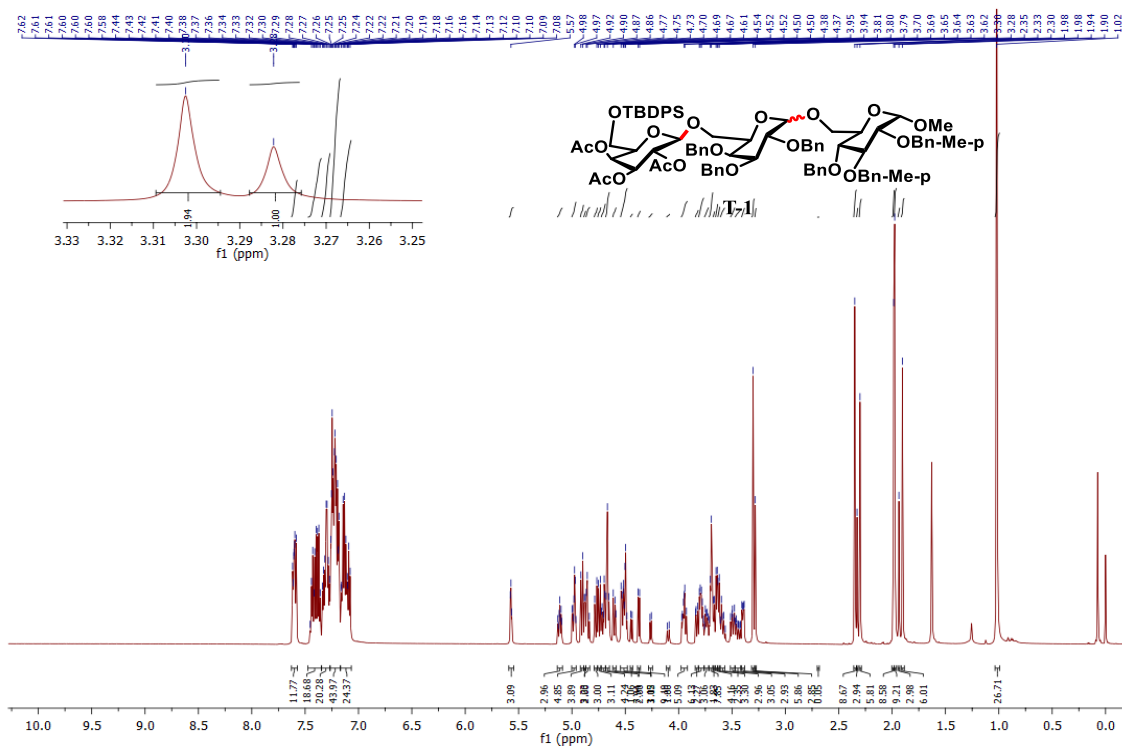


$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 11af (500 MHz, CDCl_3):

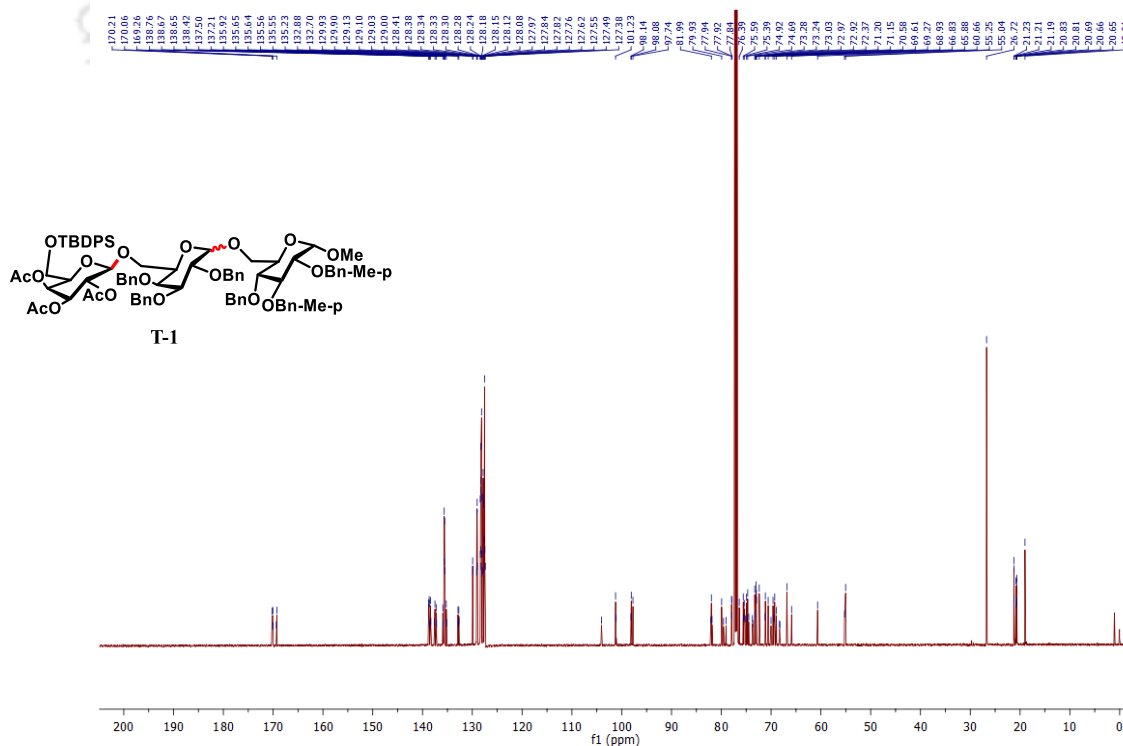


^1H NMR spectrum of compound 9k (600 MHz, CDCl_3): **$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 9k (400 MHz, CDCl_3):**

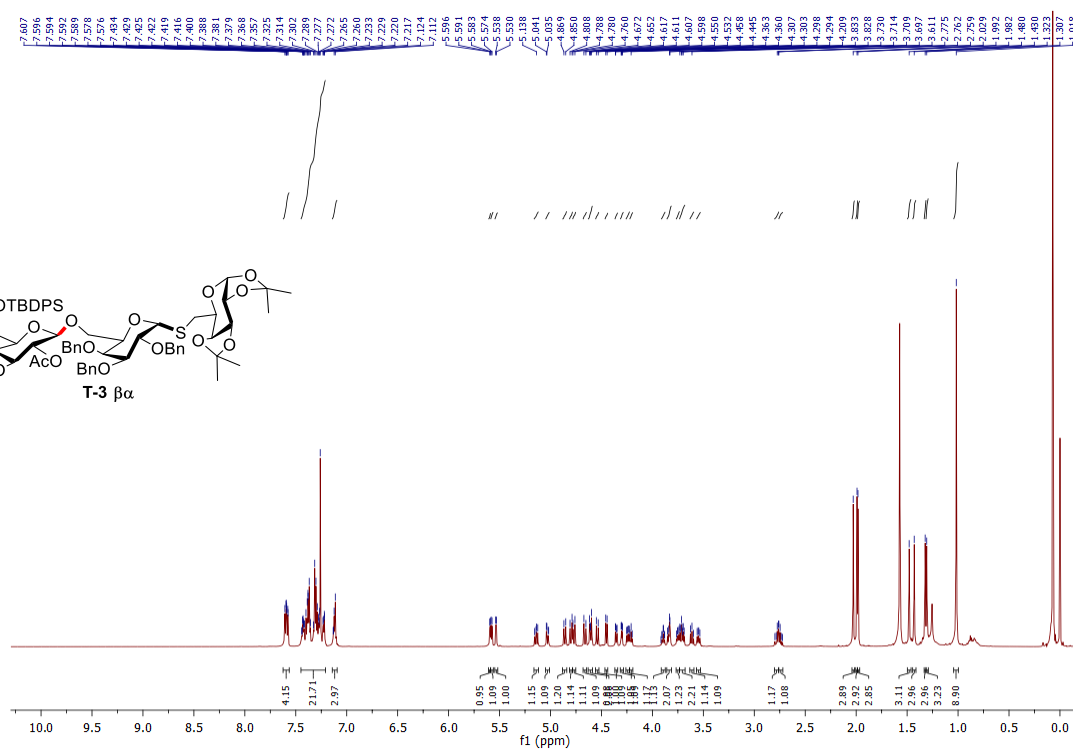
^1H NMR spectrum of compound T-1 (600 MHz, CDCl_3):



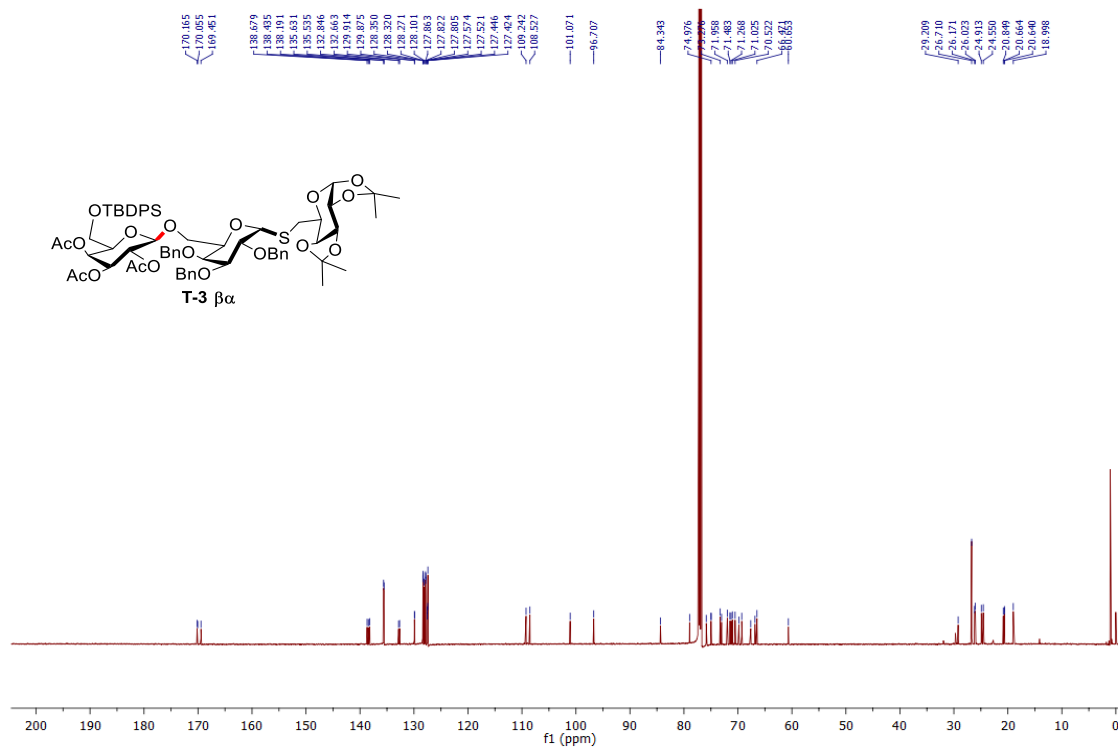
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound T-1 (600 MHz, CDCl_3):



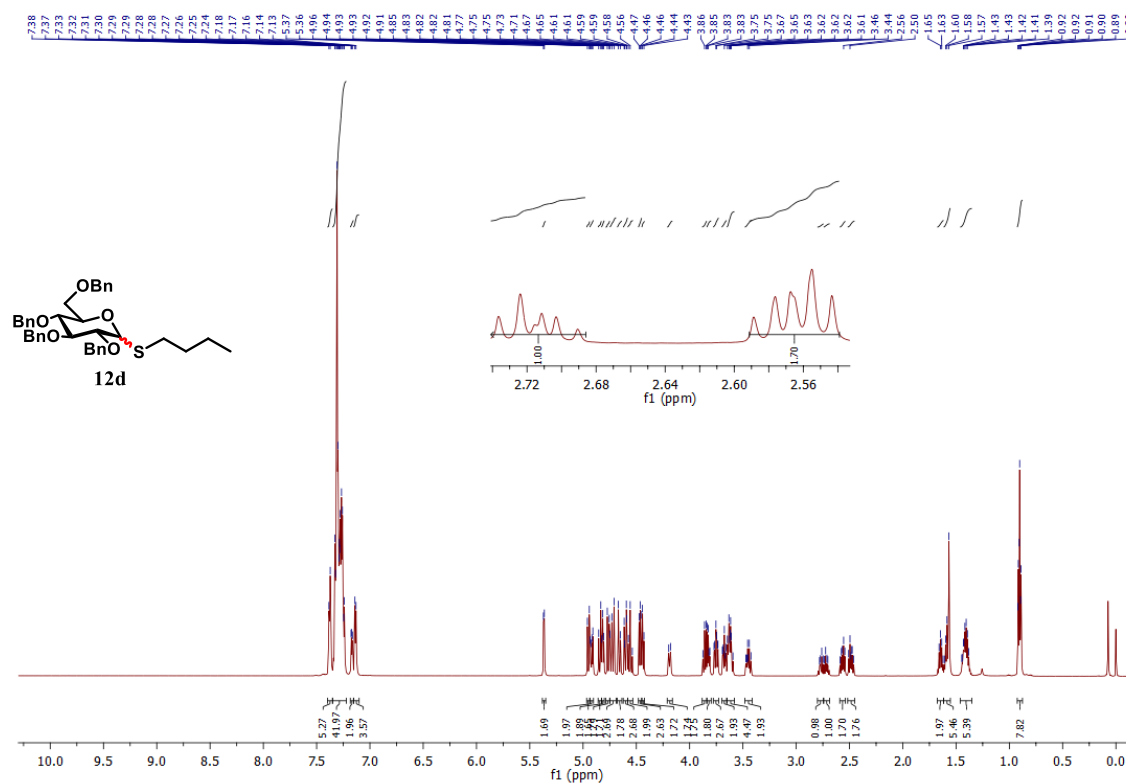
T-3 $\beta\alpha$



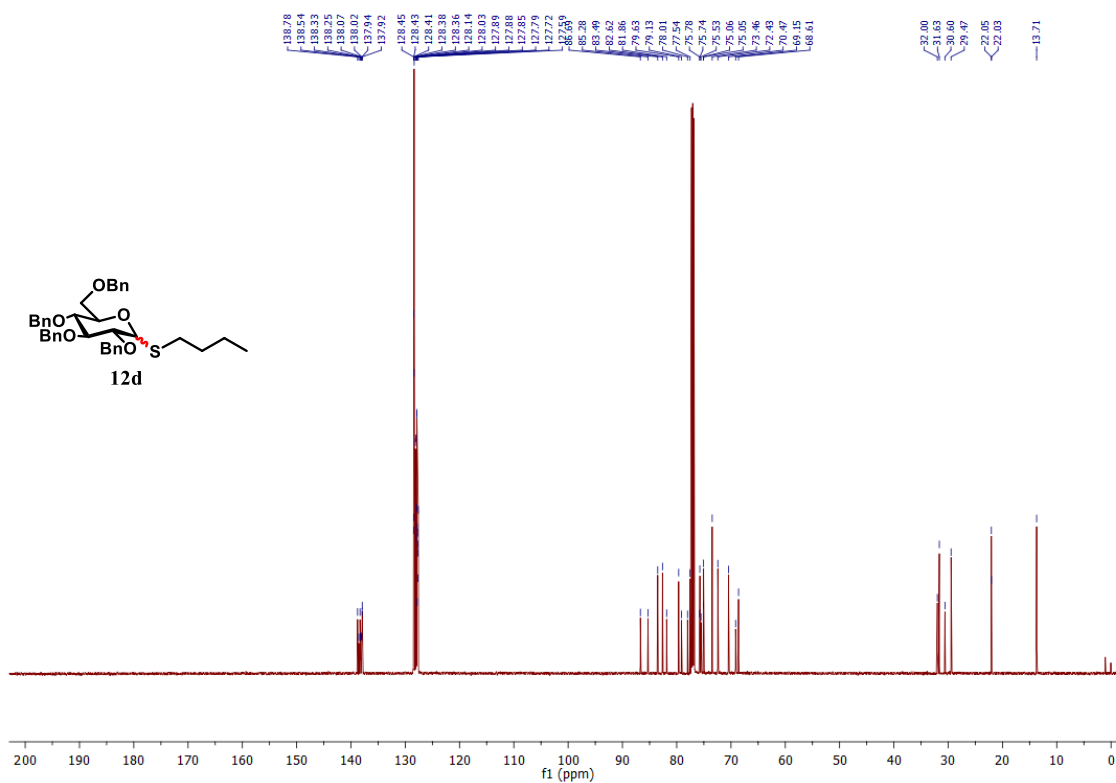
T-3 β



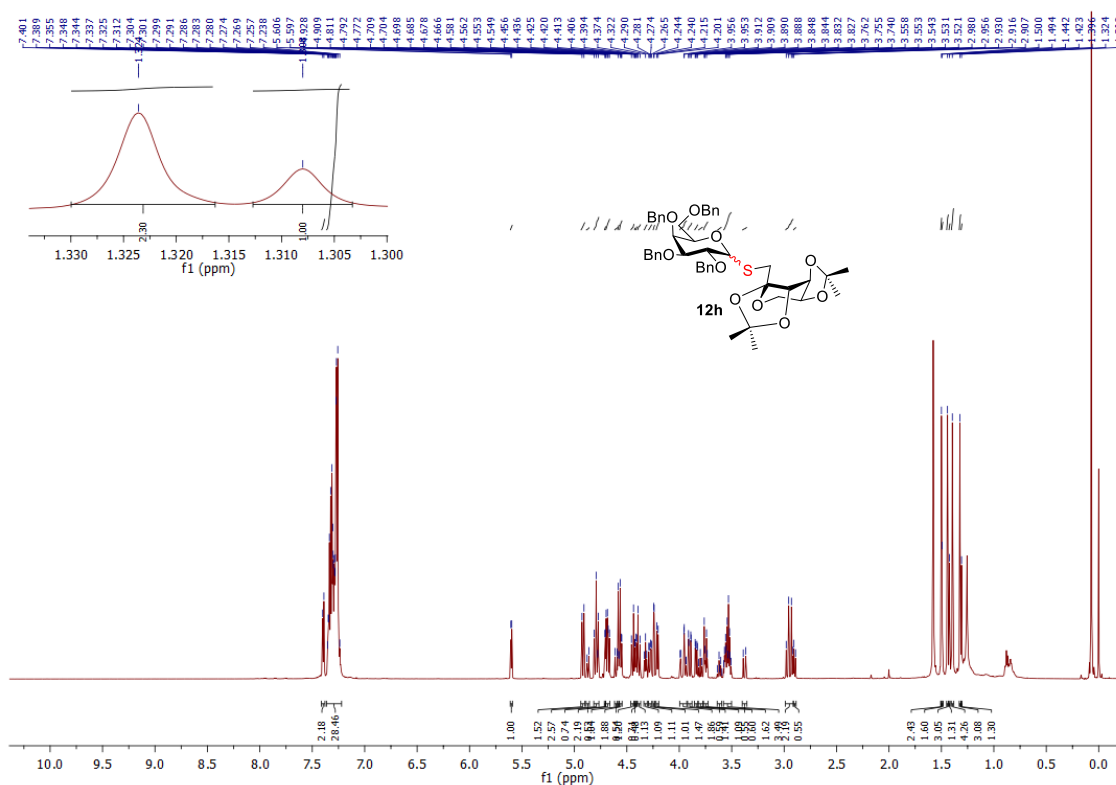
^1H NMR spectrum of compound 12d (600 MHz, CDCl_3):



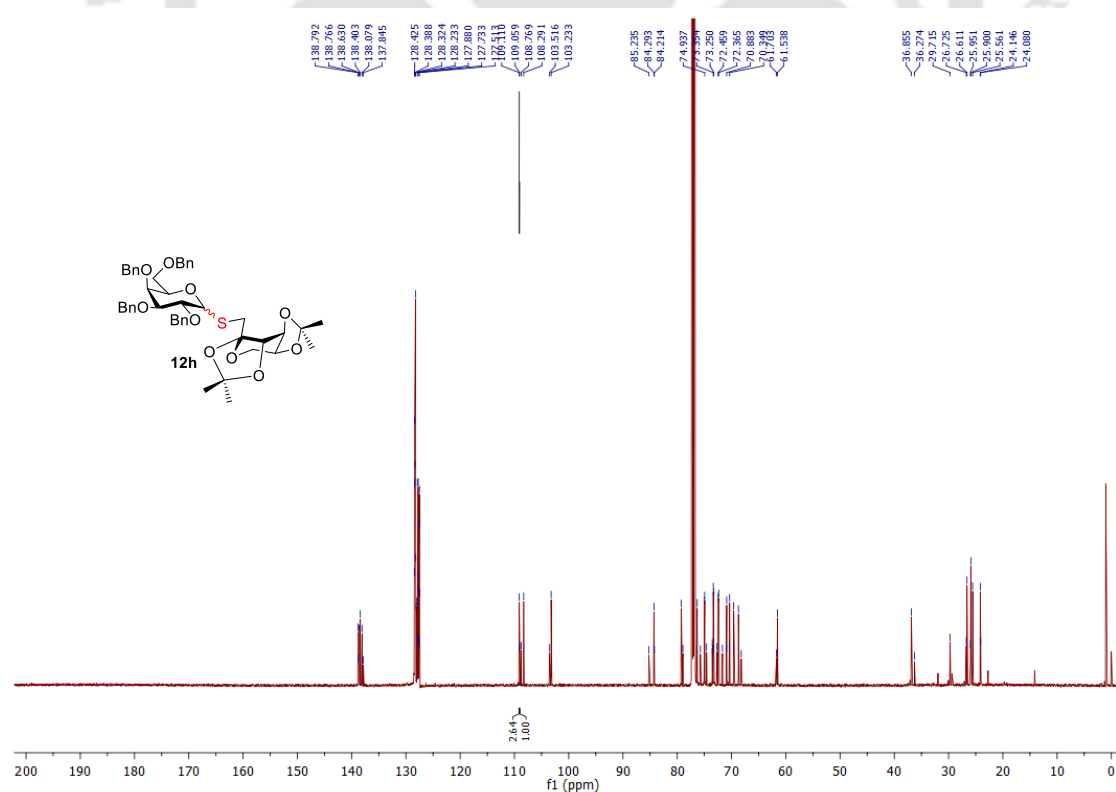
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 12d (600 MHz, CDCl_3):

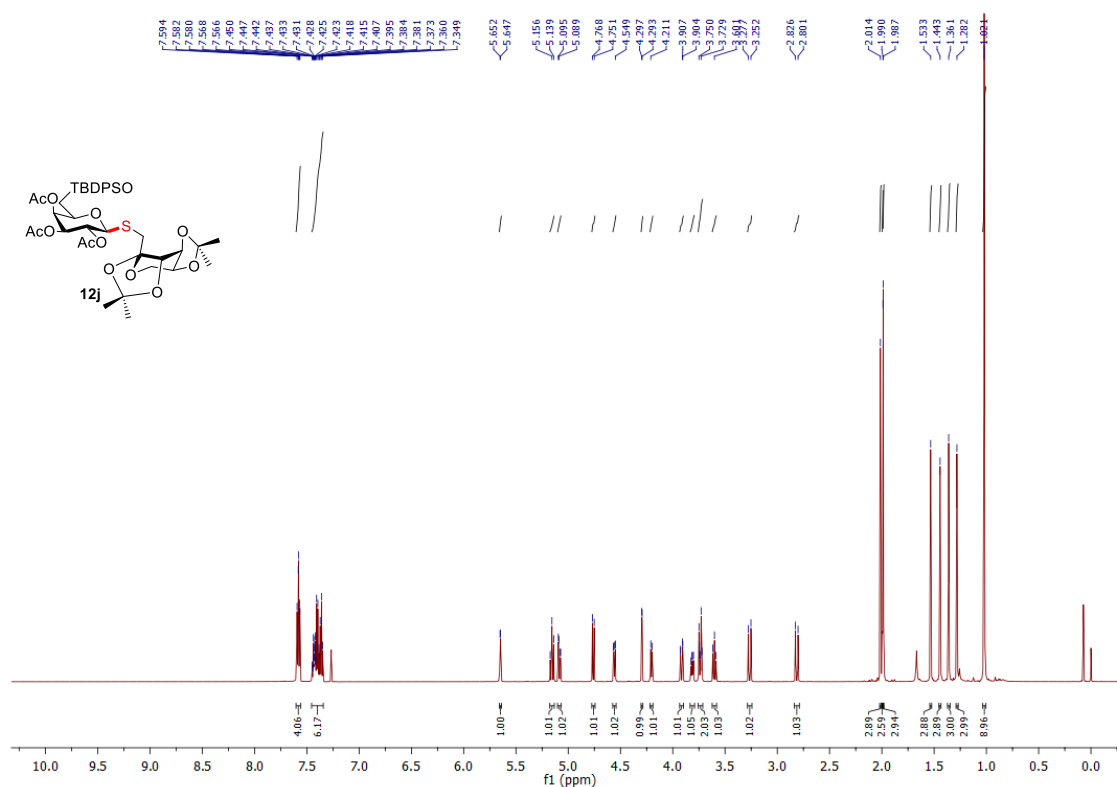
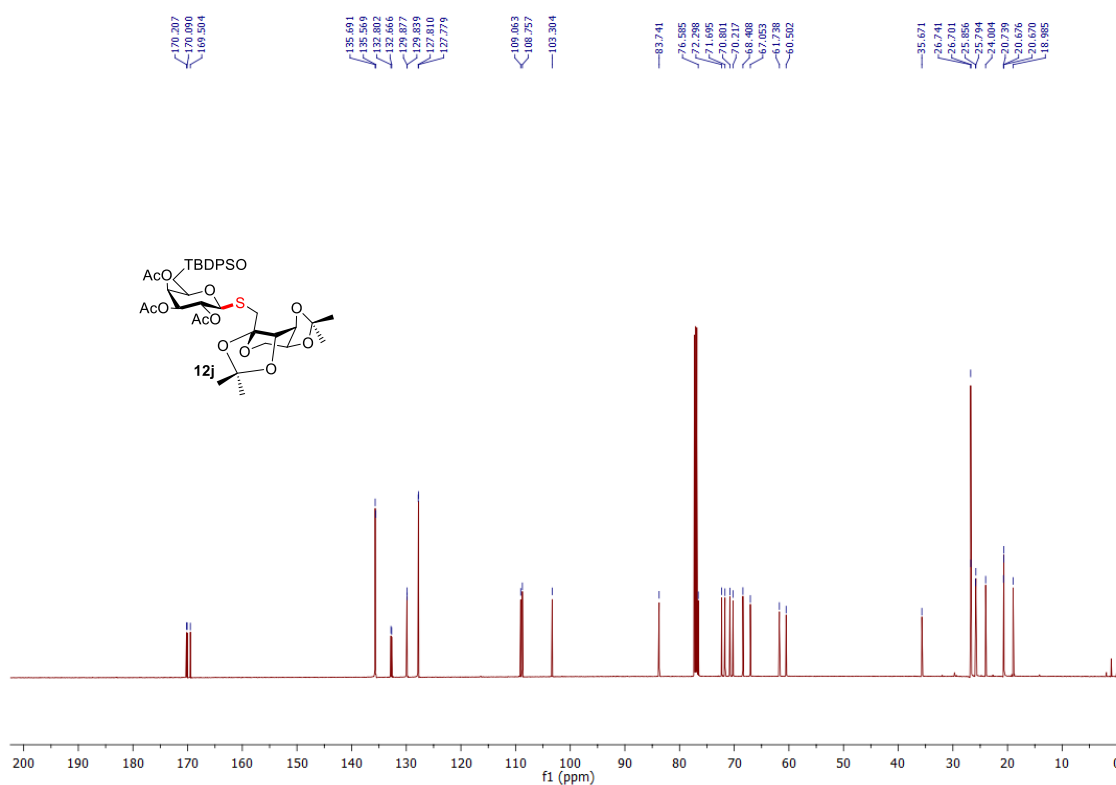


^1H NMR spectrum of compound 12h (600 MHz, CDCl_3):

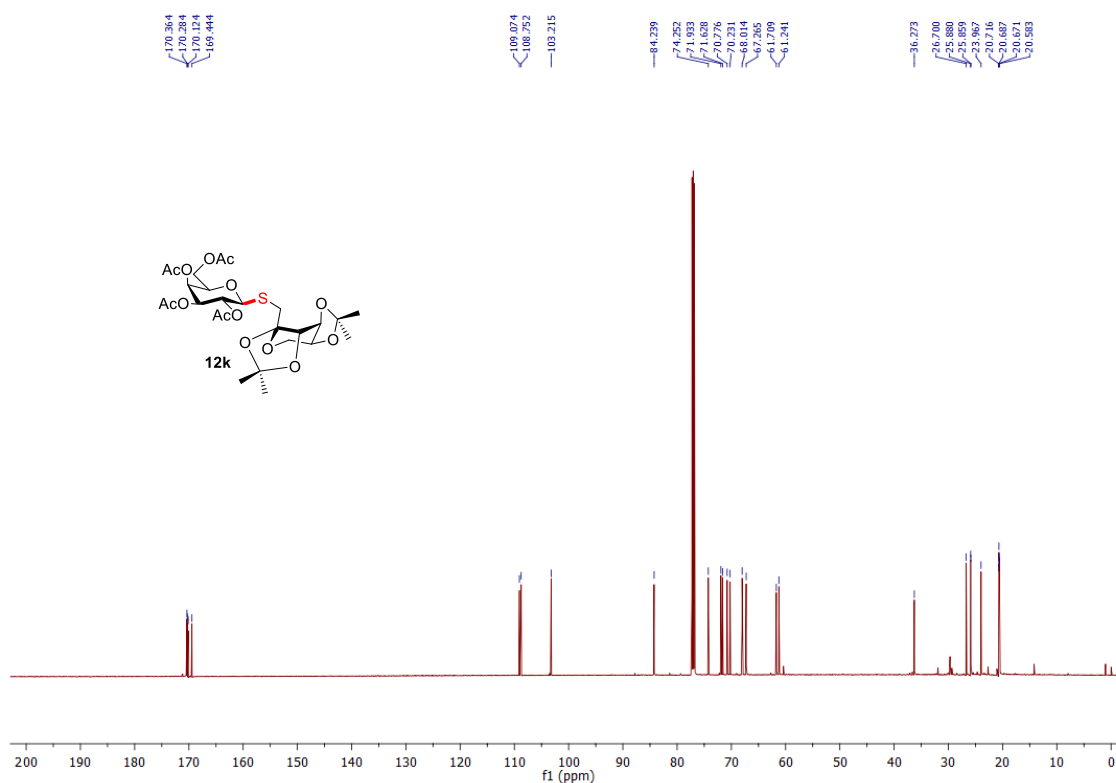


$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 12h (600 MHz, CDCl_3):

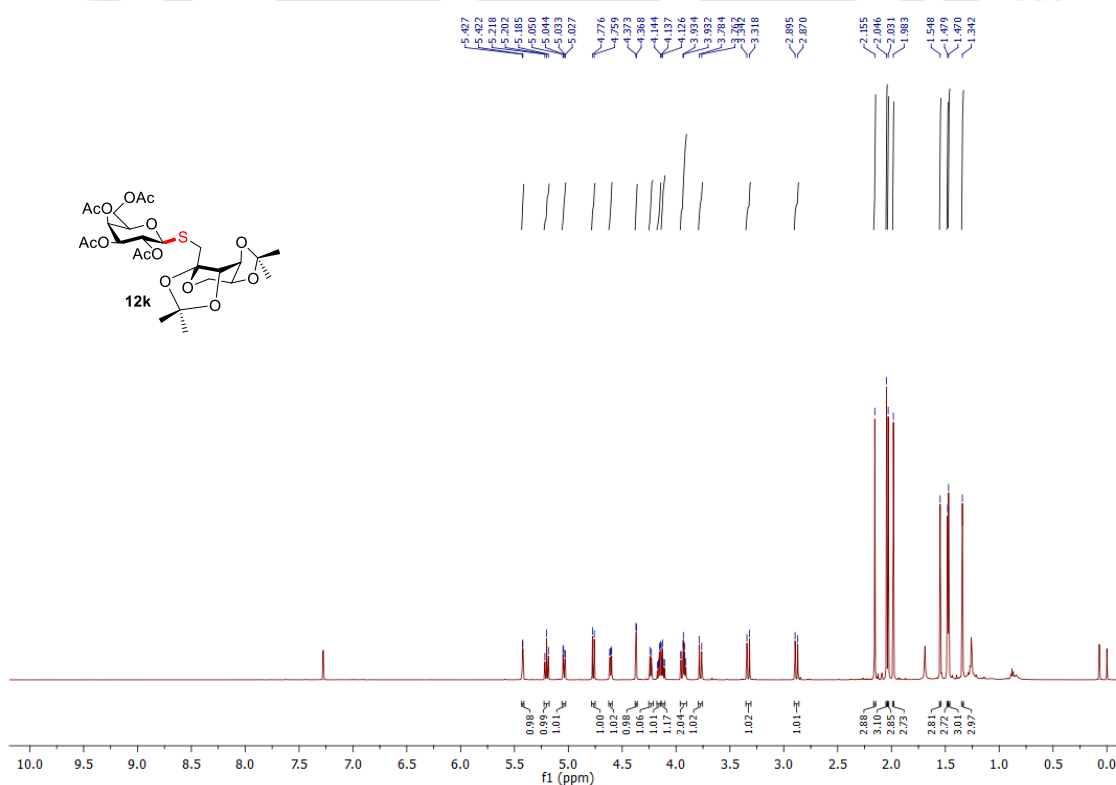


^1H NMR spectrum of compound 12j (600 MHz, CDCl_3): **$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 12j (600 MHz, CDCl_3):**

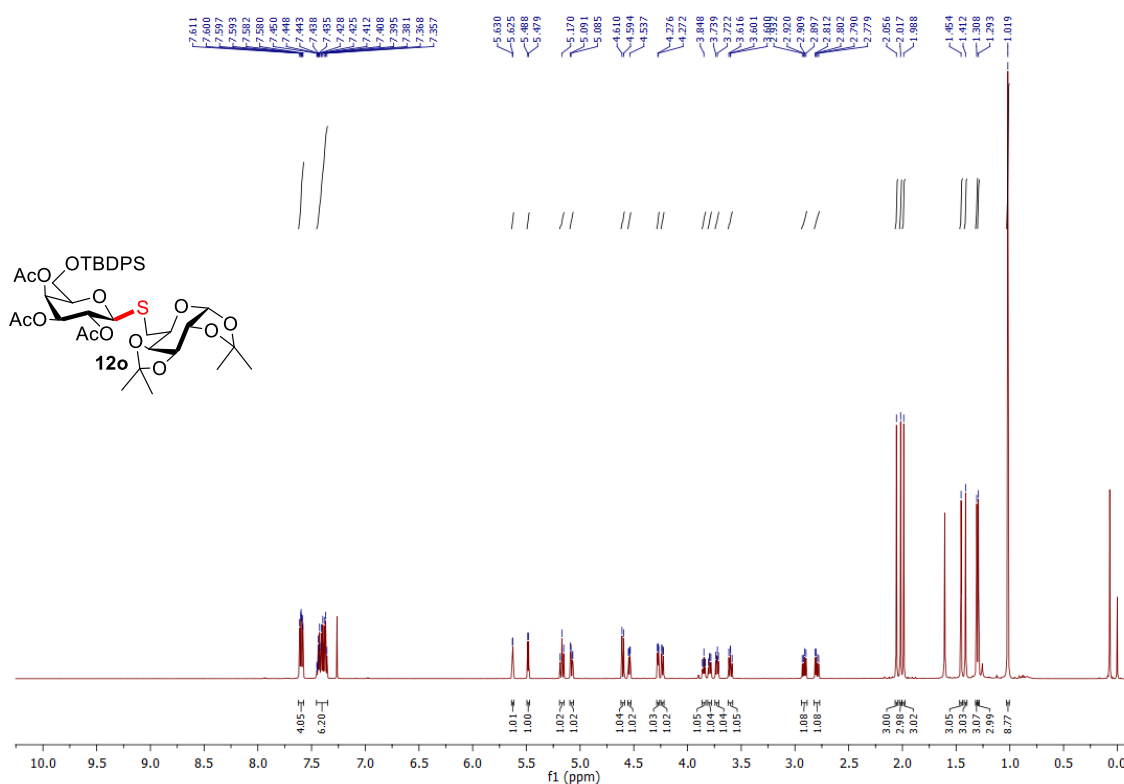
^1H NMR spectrum of compound 12k (600 MHz, CDCl_3):



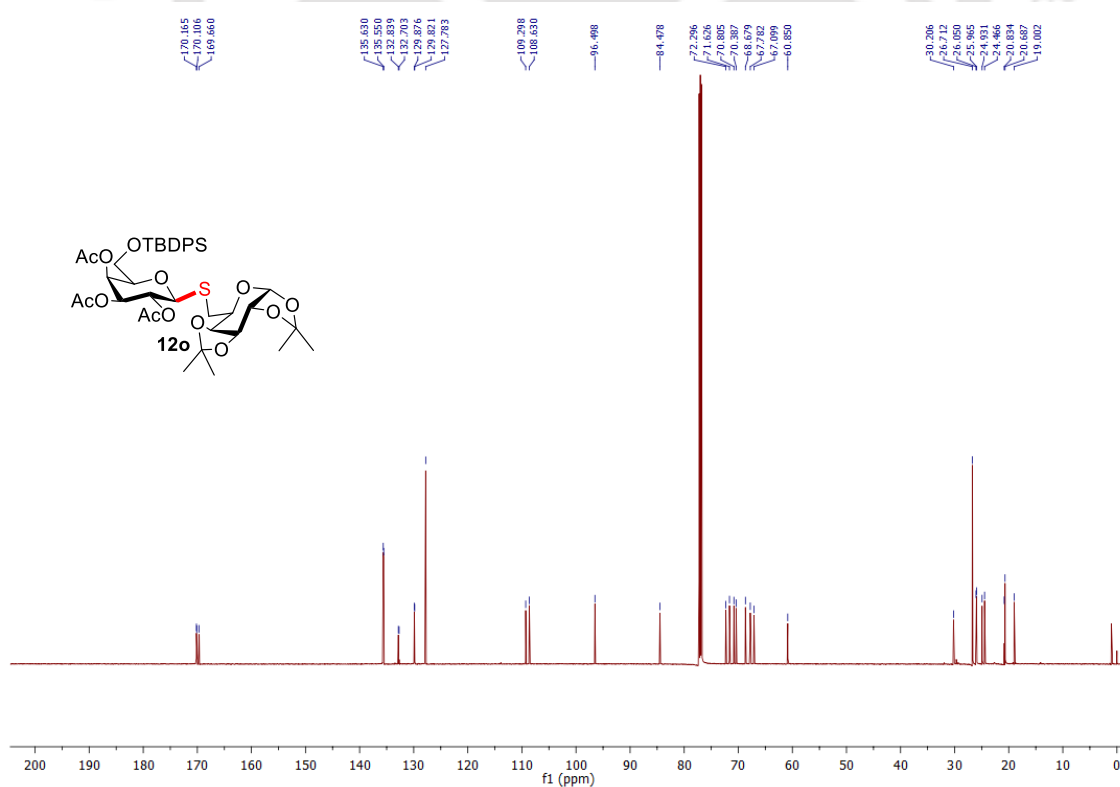
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 12k (600 MHz, CDCl_3):

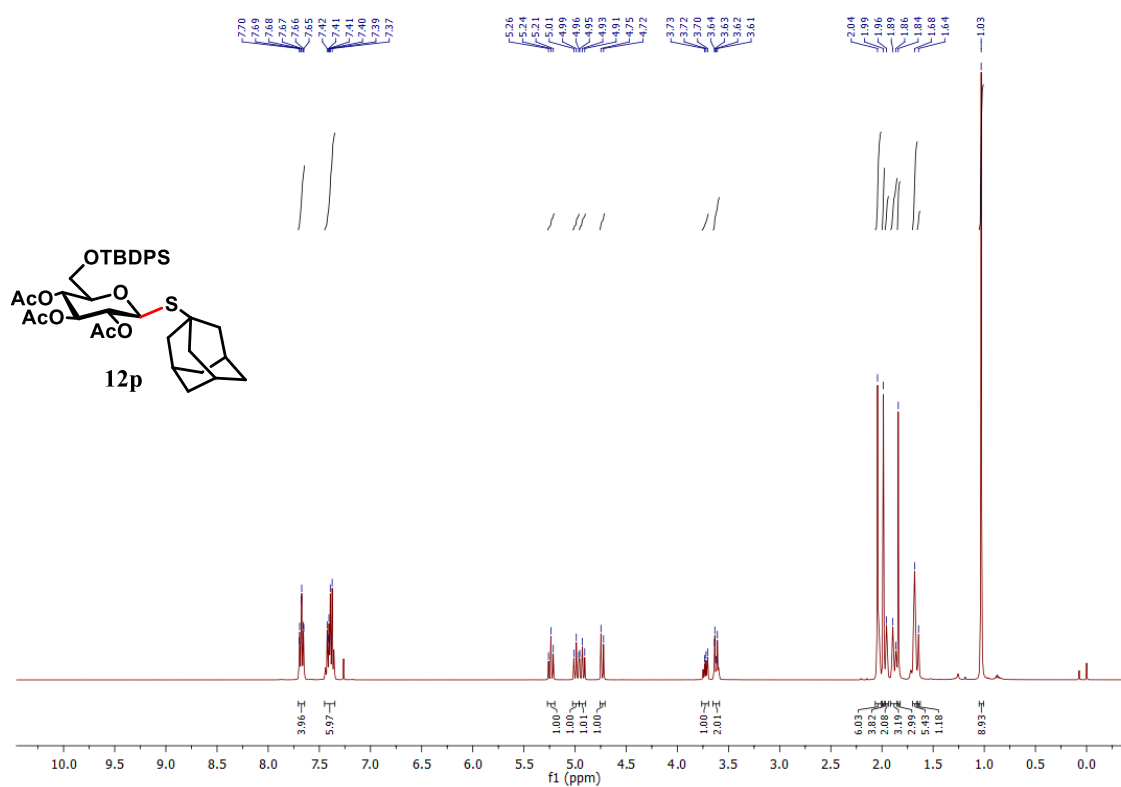
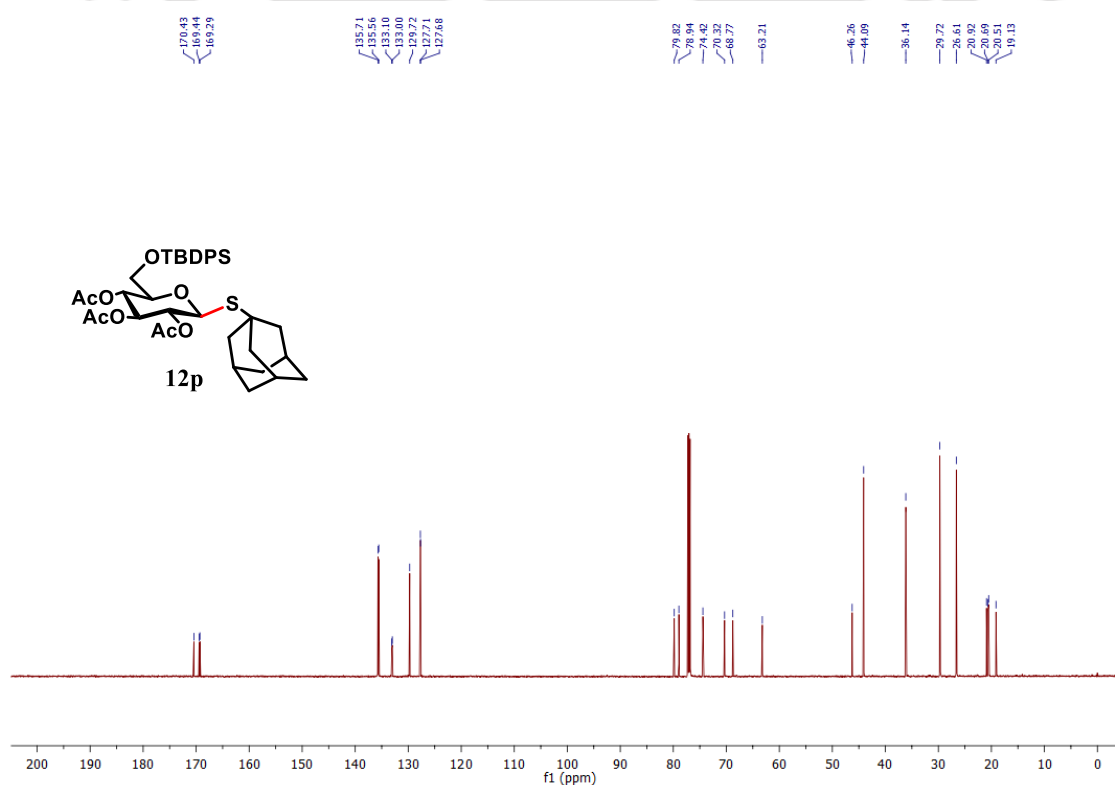


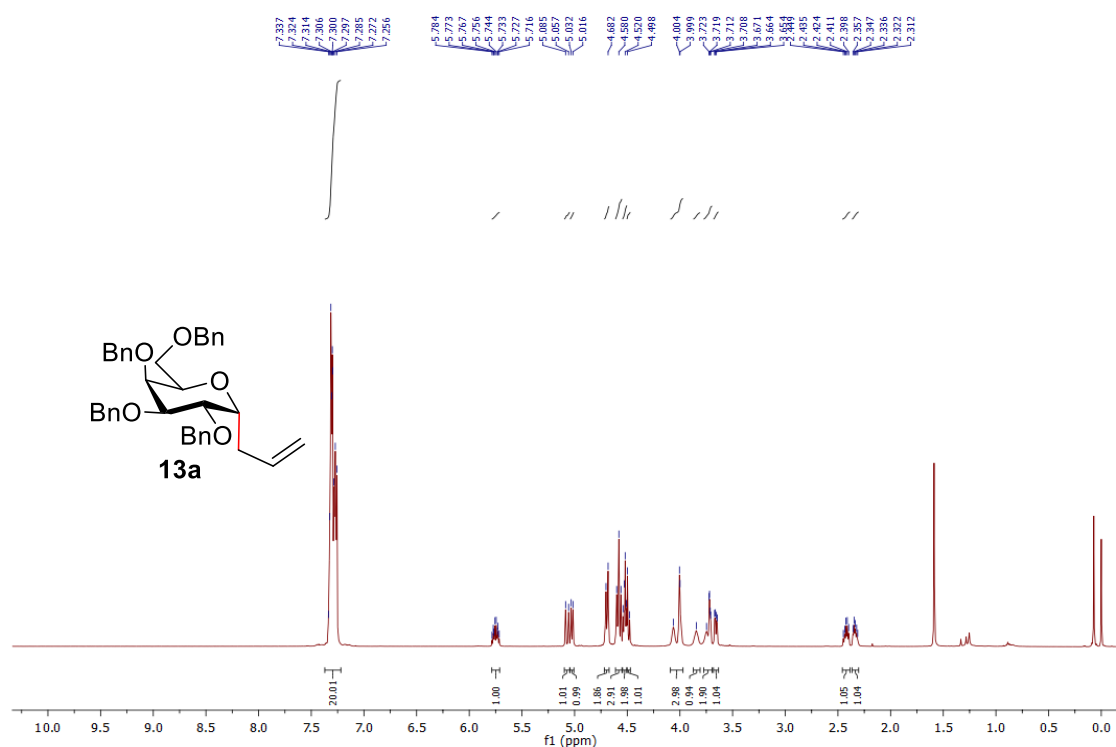
^1H NMR spectrum of compound 12o (600 MHz, CDCl_3):



$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 12o (600 MHz, CDCl_3):



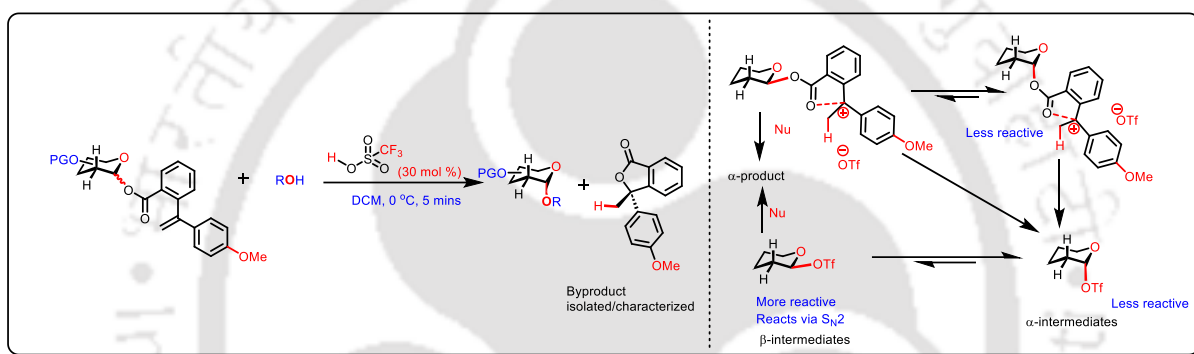
^1H NMR spectrum of compound 12p (400 MHz, CDCl_3): **$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 12p (600 MHz, CDCl_3):**

^1H NMR spectrum of compound 13a (600 MHz, CDCl_3):

The Supporting Information for chapter IIA is available at
<https://pubs.acs.org/doi/10.1021/acs.joc.2c00093>

Chapter IIB

Catalytic Stereoselective Synthesis of 2-Deoxy α -glycosides Using Glycosyl *Ortho*-[1-(*p*-MeOPhenyl)Vinyl]Benzoates (PMPVB) Donors





3.1.1 Introduction

2-deoxy sugars, having lack of any functionality at the C-2 position, are an important class of compounds present in various natural products.¹ It has been observed that some of the 2-deoxy sugar-containing molecules play a crucial role in different biological processes.² Over the past years, 2-deoxy-containing glycoconjugates received extra attention from chemical, medicinal, and pharmaceutical research.³⁻⁵ Most of the naturally occurring 2-deoxy sugar-containing bioactive molecules have anticancer, antiviral, antibacterial, and antitumor properties.⁶ 2-deoxy ribose is present in deoxyribonucleic acids (DNA) as a sugar skeleton. It was found that 2-deoxy ribose or 2,6 dideoxy hexoses influence the reactivity of bioactive molecules to which they are attached. 2,6-dideoxy hexoses are commonly observed in antibiotics and anti-cancer agents.⁷ Anthracycline containing Doxorubicin and Daunorubicin and their derivatives are strong neoplastic agents which are connected to 2-deoxy amino sugar through a glycosidic bond. All of them bind to DNA between nucleotide base pairs with the DNA double helix through specific intercalation of the planar anthracycline nucleus. These molecules are blocking the ligation-religation reaction through the stabilization of the DNA-topoisomerase II complex. These 2-deoxy sugars are frequently modified at different positions e.g., oxidation at the C-6 position, and replacement of the hydroxy group with amines at the C-3 position, etc. The number of sugar units is varied in different drugs from one sugar unit such as jadomycin to a longer oligosaccharide chain unit such as digitoxin.⁸

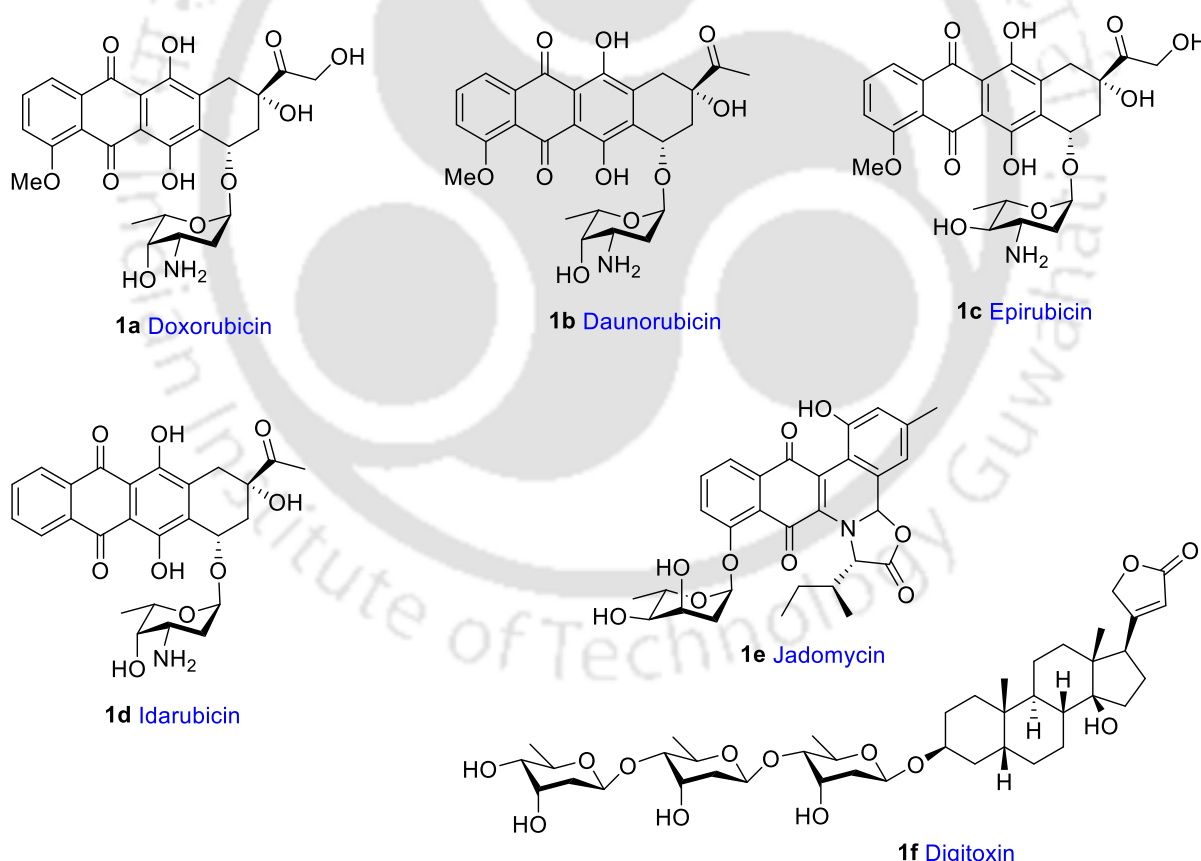


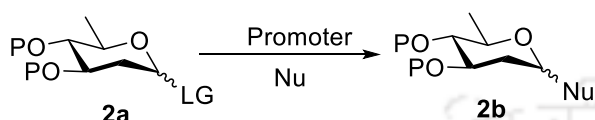
Figure 1: 2-deoxy sugar-based drugs

3.1.2 Literature review on 2-deoxy glycosylation

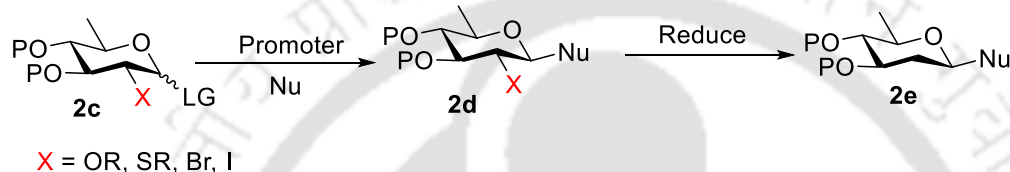
Due to the biological importance of 2-deoxy sugars, researchers are always involved in developing new synthetic procedures to make these valuable compounds. The

stereoselective synthesis of both α - and β -glycosides of 2-deoxy sugars face some challenges like a) the formation of Ferrier by-products, b) the lack of functionality at the C-2 position that can control the stereoselective synthesis of glycosides. Several research groups are developing a new direct synthetic procedure to control the stereochemistry of glycosylated products. All the approaches have been classified into five categories depending on the class of reactivity: direct synthesis, indirect synthesis, addition to glycals, de novo synthesis, and anomeric alkylation-based approaches.⁸

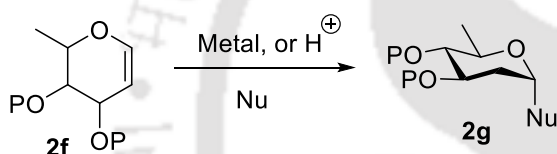
Direct method



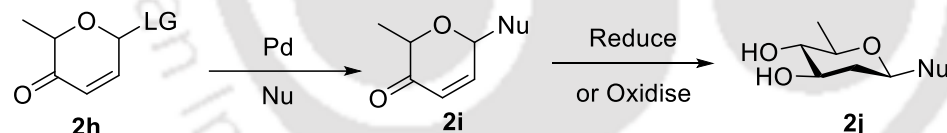
Indirect method



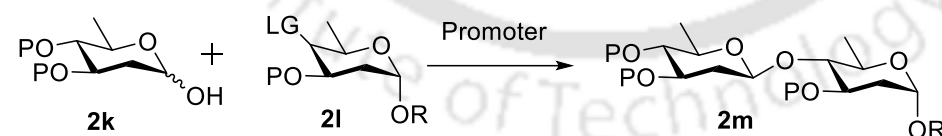
Addition to glycals



de novo synthesis



Anomeric alkylation-based approaches



Scheme 1: Different approaches to deoxy-sugar synthesis.

3.1.2.1 Direct synthesis

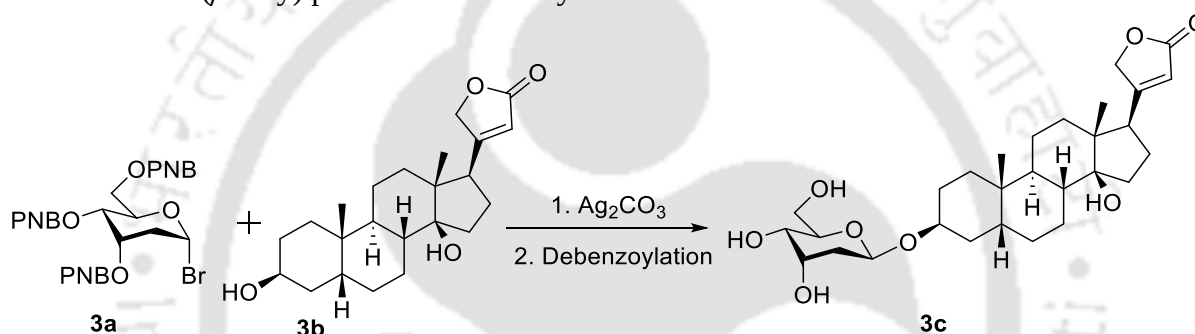
Generally, an activated 2-deoxy donor and nucleophiles (referred to as an acceptor) are involved in the glycosylation reaction. So, it is a difficult task to control stereoselectivity in this type of reaction. In recent times various approaches are developed to control stereoselectivity by choosing appropriate promoters, solvent systems, protecting group study, etc.⁹⁻¹⁴

Glycosyl halide

One of the approaches for direct synthesis is the activation of the glycosyl halides. Except for the glycosyl fluoride, all the glycosyl halides are too unstable. It is very difficult to handle it. Generally, it has to be synthesized *in-situ* during the progress of the reaction or it has to be utilized immediately after the synthesis. The selectivity and reactivity of the reaction depend on the nature of leaving moiety and the promoters used as well.

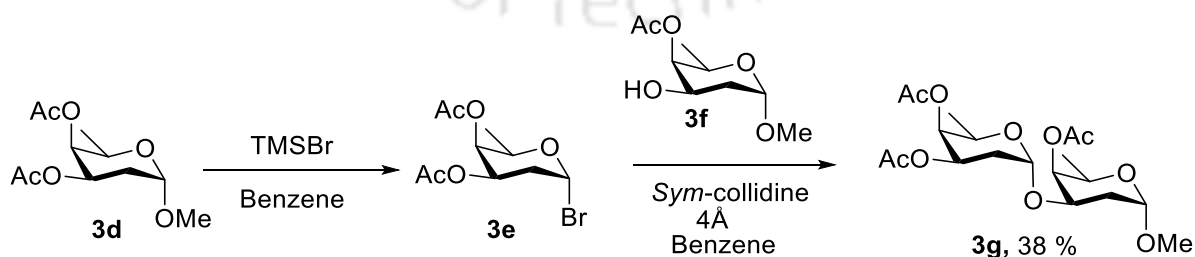
Glycosyl bromide

In 1923, Bergmann et al. first reported the formation of anomeric bromide by utilizing HBr/AcOH from anomeric benzoate.¹⁵ Later, Levene and Cortese reported the synthesis of glycosyl nucleoside by utilizing glycosyl bromide.¹⁶ In 1963, Zorbach and co-workers reported the synthetic route of digitoxin derivative **3c** from 1-bromo-2-deoxy-3,4,6-*tri-O-p*-nitrobenzoyl ribopyranose **3a** along with digitoxigenin **3b**, followed by deprotection of *p*-nitrobenzoyl group (Scheme 2).¹⁷ They used Ag₂CO₃ as a promoter, which resulted in a stereoselective (β only) product with 46 % yields.



Scheme 2: Synthesis of digitoxin derivative

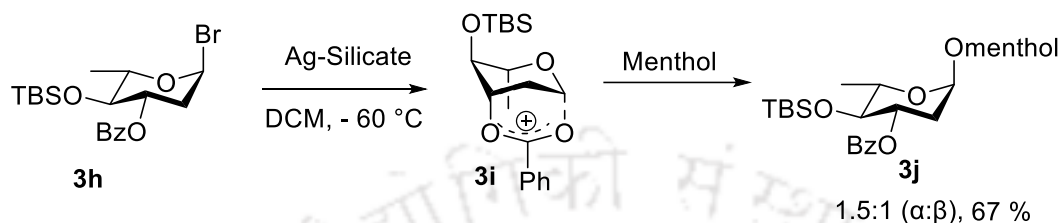
In 1980, Thiem and Meyer, disclosed the synthesis of glycosyl bromide and glycosyl iodide by using TMSBr and TMSI respectively from the corresponding methyl- and acetoxyglycosides.¹⁸ Later, the same group applied this protocol for the synthesis of deoxy-sugar-based disaccharide containing a fragment of Chromomycin A₃.¹⁹ In this procedure, they converted the acetylated methyl glycoside (**3d**) to bromoglycoside (**3e**) by using TMSBr in benzene followed by freeze-drying with benzene. Later the bromoglycoside (**3e**) was treated with a glycosyl acceptor (**3f**) in presence of *sym*-collidine and 4Å molecular sieves (MS), which resulted in the corresponding disaccharide **3g** (38 % yields) (Scheme 3).



Scheme 3: Thiem's synthesis of the Chromomycin A₃ Disaccharide

Most of the studies on the use of Ag-silicate for the activation of deoxy-sugar bromides were limited to particular cases;²⁰⁻²¹ However, in 2014, Kaneko and Herzon explored the scope

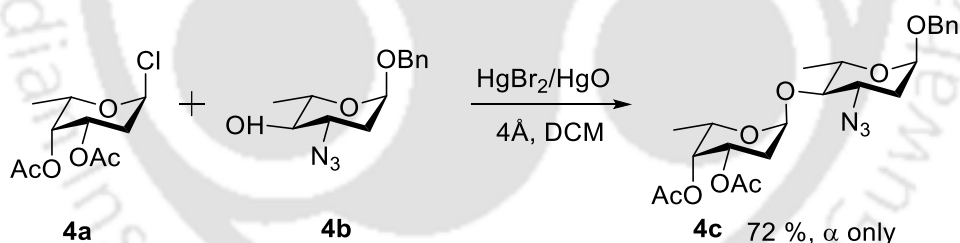
of this chemistry with a number of donor/acceptor pairs.²² They made a series of deoxyglycosyl bromides by using trimethylsilyl bromide. They found that glycosyl bromides reacted well with different acceptors in the presence of Ag-silicate in good to excellent yields (72–94%) with moderate to high levels of β -selectivity (1:3.4 α : β to β -only). The exception was to use benzoate protection in the C-3 position. The benzoate-protected glycosyl bromide (**3h**) was reacted with menthol in the presence of Ag-silicate, which resulted in 67% yields with a mixture of anomers 1.5:1 (α : β) (**3j**) (Scheme 3a).



Scheme 3a: Herzon's Explanation for β -Selectivity

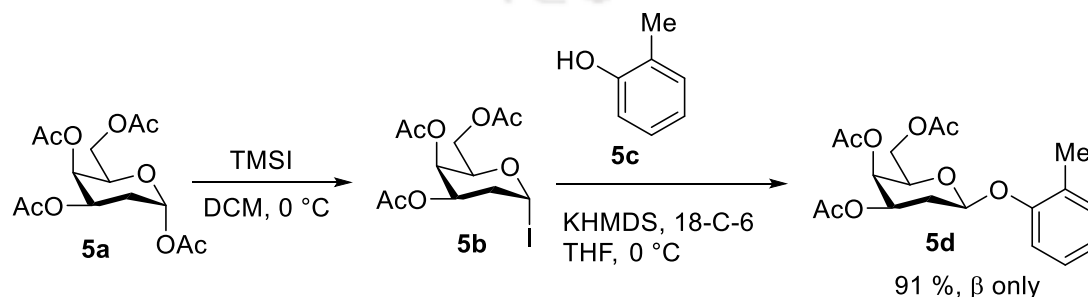
Glycosyl chloride

Glycosyl chloride is less reactive compare to glycosyl bromide and is more moisture sensitive as well.²³ Zorbach and Payne reported the synthesis of A Monodigitoxoside of Digitoxigenin from the corresponding deoxy glycosyl chloride.²⁴ In most of the cases, Helferich conditions were applied to activate the glycosyl chloride donors, where basically toxic mercury salts were used.²⁵⁻²⁶ In 1989, Ramilarison and Monneret disclosed the synthesis of disaccharide of musettamycine by the treatment of 2-deoxy-3,4-*di*-O-acetylfucosyl chloride (**4a**) with azide-protected rhodosamine acceptor (**4b**) in presence of toxic HgBr_2/HgO and 4Å molecular sieves (MS) in DCM medium, which resulted in stereoselective (α only) disaccharide (**4c**) in 73 % yield (Scheme 4).²⁷



Scheme 4: Synthesis of the Disaccharide of musettamycine under Helferich Conditions

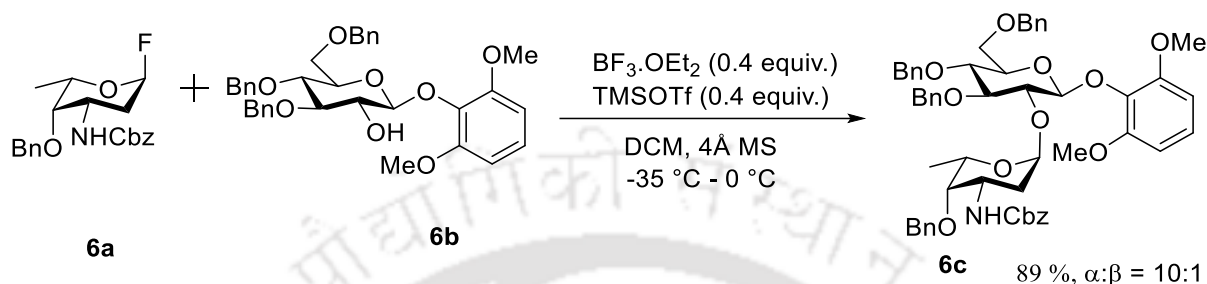
Glycosyl Iodide



Scheme 5: Synthesis of Aryl 2-deoxyglycosides

In 2003, Lam et al. disclosed the synthesis of glycosyl iodide from the corresponding 2-deoxy galactose tetraacetate (**5a**) by using TMSI in a DCM medium at 0 °C. The α -galactosyl iodide (**5b**) was reacted with *ortho*-cresol (**5c**) in the presence of KHMDS, 18-crown-6, resulting in complete 2-deoxy β -glycoside (**5d**) via an S_N2 displacement fashion with excellent yields (91 %) (Scheme 5).²⁸

Glycosyl Fluoride

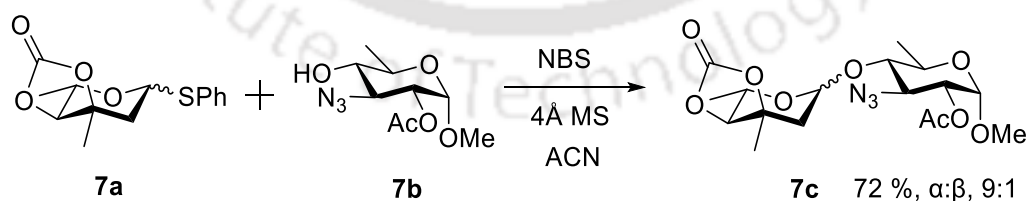


Scheme 6: Activation of a glycosyl Fluoride

The glycosyl fluorides are stable glycosyl donors compared to other glycosyl halides. In 1984, Papahatjis and co-workers reported the formation of glycosyl fluorides from corresponding thioglycosides by utilizing dimethylaminosulfur trifluoride (DAST) or HF-pyridine with *N*-bromosuccinimide (NBS).²⁹ Same group later disclosed the Lewis acid-mediated activation of glycosyl fluoride. The glycosyl fluoride (**6a**) was treated with orthogonally protected C-2 -OH glucose acceptor (**6b**) in the presence of BF₃.OEt₂ and TMSOTf, which resulted in an (α : β =10:1) mixture of anomers (**6c**) in excellent yields (89 %) (Scheme 6).³⁰

Thioglycosides

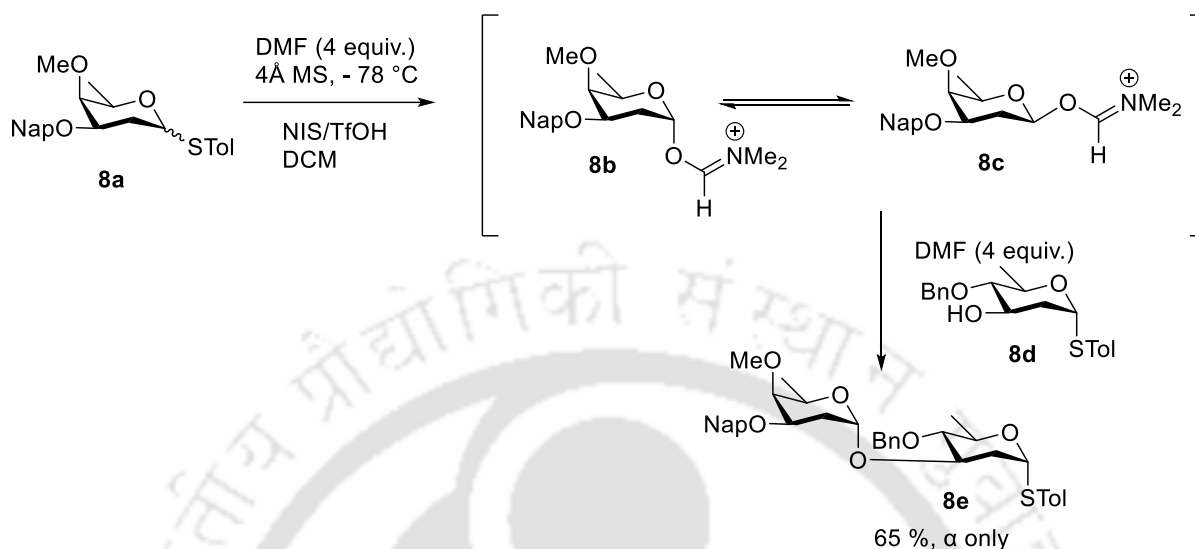
Thioglycosyl donors made their own place in synthetic chemistry due to their stability and ease of activation under mild conditions. In 1983, the Nicolaou group disclosed the activation of phenylthioglycoside by using NBS as a promoter. The treatment of deoxythioglycoside (**7a**) with hindered secondary sugar acceptor (**7b**) in the presence of NBS (1.1 equiv.) and 4Å MS in acetonitrile medium, resulted in the desired coupled product (**7c**) with good yields (72 %) as a mixture of isomers ($\alpha:\beta$ = 9:1) (Scheme 7).³¹



Scheme 7: NBS activation of 2-deoxy thioglycoside

Mong and co-workers demonstrate the solvent effect on the activation of thioglycosides by using DMF as a solvent modulator.³² The activation of 2-deoxy glycosides (**8a**) by utilizing NIS/TfOH as an activator in the presence of DMF, afforded glycosyl imidate (**8b**, **8c**) (Scheme 8). These two imidates (**8b**, **8c**) exist in equilibrium between themselves (more stable α -imidate **8b** and more reactive β -imidate **8c**). The nucleophilic attack is happening on the more reactive β -imidate (**8c**), which resulted in α -glycosides (**8e**) with excellent yields of 65 % for the thio

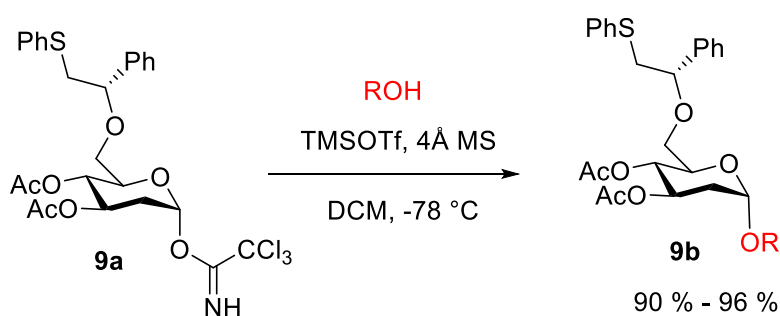
acceptor **8d**. Depending on the reactivity of thioglycosides, 4 equiv. to 12 equiv. of DMF is needed for the activation of donors. Additional DMF is needed before the addition of the acceptor. So preactivation method is applied here.



Scheme 8: NIS/TfOH activation of thioglycosides

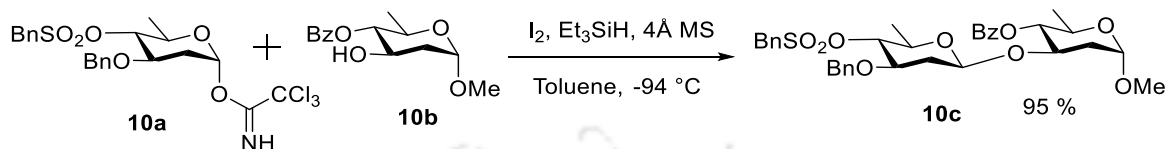
Trichloroacetimidates

In 1986, Schmidt first developed highly reactive 2-deoxy trichloroacetimidate donors for the construction of glycosidic linkage under mild conditions.³³ The usually high reactivity of the trichloroacetimidate donor is further assisted by the lack of the electron-withdrawing oxygen at the 2-position and hence the 2-deoxy trichloroacetimidate donors are more reactive and moisture sensitive as well. These donors can be activated under very mildly acidic conditions also. So, it is quite difficult to handle these highly reactive unstable donors. Most of cases, Lewis acid activators (TMSOTf, $\text{BF}_3 \cdot \text{OEt}_2$, AgOTf, etc) have been used to activate these donors which provided unselective glycosides.³⁴⁻³⁷ There is a role of protecting groups to control the selectivity of 2-deoxy trichloroacetimidate donors toward the synthesis of the stereoselective glycosidic linkage. Boons and co-workers reported a chiral auxiliary-based approach toward the synthesis of the stereoselective glycosidic bonds.³⁸ They have installed thio based auxiliary at the C-6 position of 2-deoxy glucosyl trichloroacetimidate donors (**9a**) and activated by using TMSOTf, which resulted in good to excellent α -selectivity (**9b**) with excellent yields (Scheme 9). From the observed results it was clear that the chirality of the auxiliary did not affect the stereochemical outcome of the reaction.

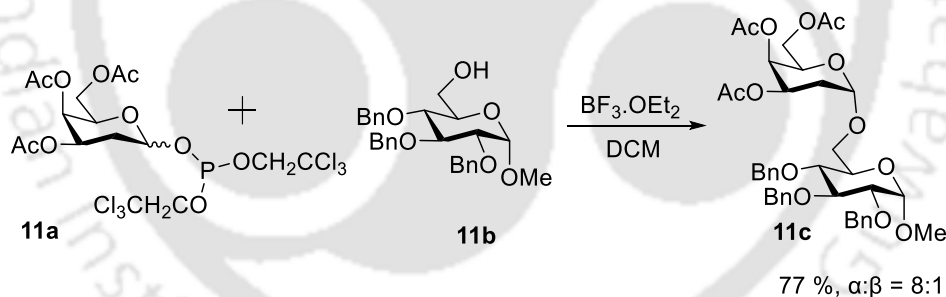
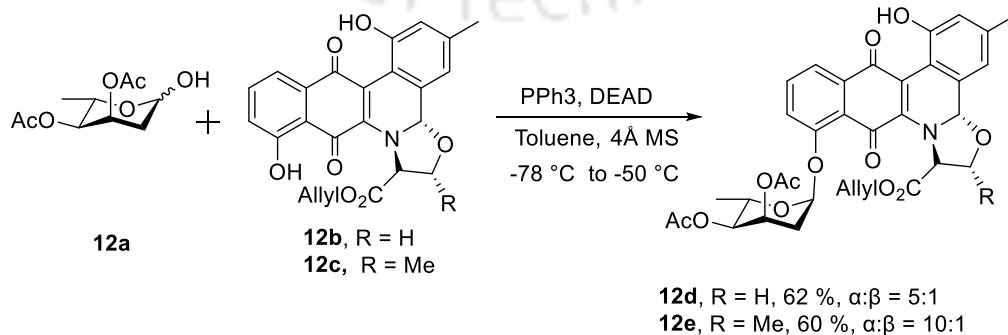


Scheme 9: TMSOTf mediated activation of auxiliary-based-trichloroacetimidate donors

Takahashi and co-workers reported I_2 and Et_3SiH mediated activation of trichloroacetimidates donors (**10a**) having an *O*-benzylsulfonate group at the C-4 position, which resulted in highly β -selective glycosides (**10c**) with 95 % yields (Scheme 10).³⁹ They examined the same reaction by taking the C-4 benzyl-protected trichloroacetimidate donor, which failed to provide stereoselective glycosides.³⁹

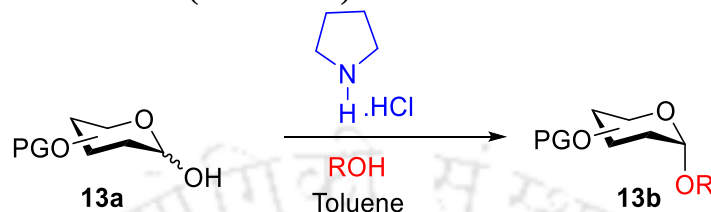
**Scheme 10:** I_2 and Et_3SiH mediated activation of trichloroacetimidate**Phosphites**

As we discussed earlier, the instability of 2-deoxyglycosyl trichloroacetimidate donor in moisture and column purification in normal silica gel, in contrast, the 2-deoxy glycosyl phosphite donor doesn't have this purification problem.⁴⁰ In 1994, the Schmidt group demonstrated the stability of 2-deoxy glycosyl phosphite donors towards the synthesis of glycoconjugate bonds.⁴¹ The 2-deoxy glycosyl phosphite donors (**11a**) were activated by using $BF_3 \cdot OEt_2$ in the presence of primary glycosyl acceptor (**11b**), which resulted in the expected disaccharide (**11c**) with good α -selectivity in 77 % yields (Scheme 11). For the secondary acceptors, they used $SnCl_4$ as an activating agent instead of $BF_3 \cdot OEt_2$.

**Scheme 11:** Schmidt's activation of 2-deoxy glycosyl phosphite donors**Hemiacetals****Scheme 12:** Synthesis of Jadomycin family

Hemiacetals are self-stable donors which do not have purification problems as well as moisture sensitivity problems like trichloroacetimidates donors. In 1991, Roush's group reported the synthesis of aryl 2-deoxy β -glycosides via Mitsunobu reaction from corresponding 2-deoxy sugar hemiacetals.⁴² Yang and Yu reported the synthesis of the jadomycin family of natural products from sugar hemiacetals (Scheme 12).⁴³

In 2018, Kancharla and co-workers developed the secondary amine-catalyzed (Pyrrolidine hydrochloride, 20 mol %) stereoselective 2-deoxy α -glycosides from corresponding sugar hemiacetals (Scheme 13).⁴⁴



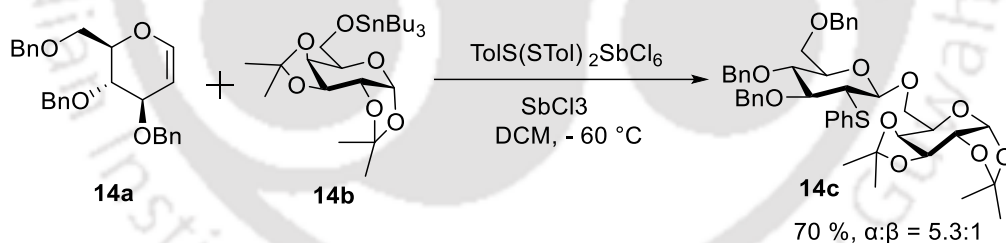
Scheme 13: Stereoselective glycosylation

3.1.2.2 Indirect methods

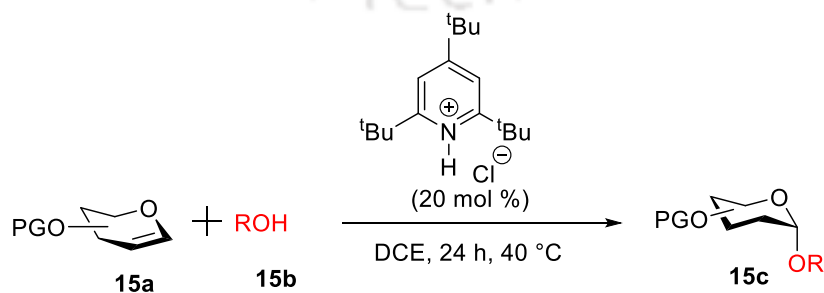
For indirect approaches, extra steps are needed to install and remove an extra auxiliary at C-2 position to control the stereochemistry of glycosylated products.⁴⁵⁻⁴⁷

3.1.2.3 Addition to glycals

Numerous synthetic procedures have been developed to synthesize the stereoselective 2-deoxy glycosides by nucleophilic addition to glycals. Many of the classic approaches involved mild acidic conditions such as sulfonic acids,⁴⁸ triphenylphosphine



Scheme 14: TolS(STol)₂SbCl₆ catalysed glycosylation

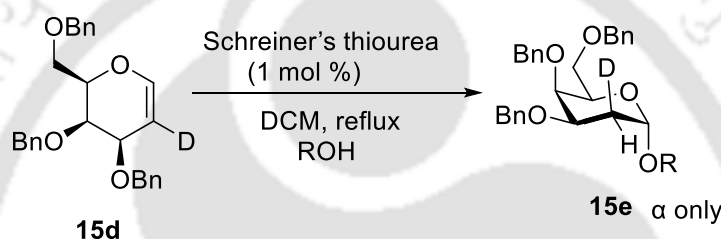


Scheme 15: Stereoselective glycosylation of glycals

hydrobromide,⁴⁹ acidic resin AG50W-X2/LiBr for the synthesis of stereoselective glycosides.⁵⁰ Franck and co-workers developed an updated method by using arylbis(arylthio)sulfonium salts to activate glycols for 2-deoxy glycosylation reactions (Scheme 14).⁵¹ In 2019, Kancharla and co-worker developed 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyzed stereoselective (α -selective) glycosylation from corresponding glycols (Scheme 15).⁵²

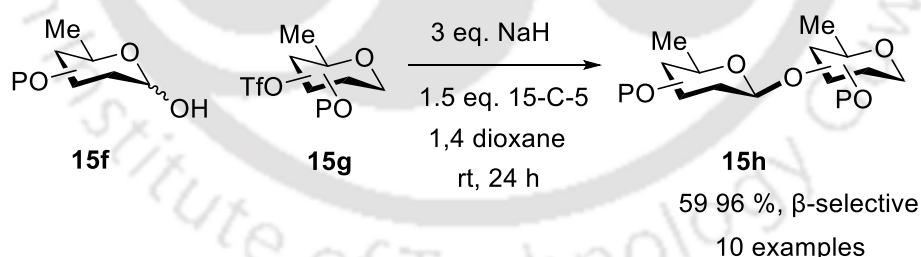
3.1.3 Organocatalysis applied to deoxyglycoside synthesis

Recent years have seen an emergence in the application of thioureas as small-molecule catalysts in a myriad of synthetic transformations.⁵³⁻⁵⁵ Inspired by enzymatic active sites, thioureas have been designed to catalyze glycosylation reactions. Taking inspiration from the work of Kotke and Schreiner,⁵⁶ in 2012, Galan, McGarrigle, and co-workers reported the α -stereoselective synthesis of 2-deoxyglycosides from glycol. The reaction proceeds with excellent yields and high selectivity for the α -anomer in the presence of 1.2 equiv of the galactal donor (Scheme 15a).⁵⁷



Scheme 15a: Galan and McGarrigle's Thiourea-Catalyzed Glycosylation of Galactals

A more recent report by Zhu et al. describes the direct synthesis of 2-deoxy- β -glycosides involving anomeric *O*-alkylation with triflates as a secondary electrophile. For this method a free hydroxy group is required at the C-3 position, to avoid the side products. According to the report, the best result was obtained when the corresponding lactol in 1,4-dioxane was reacted

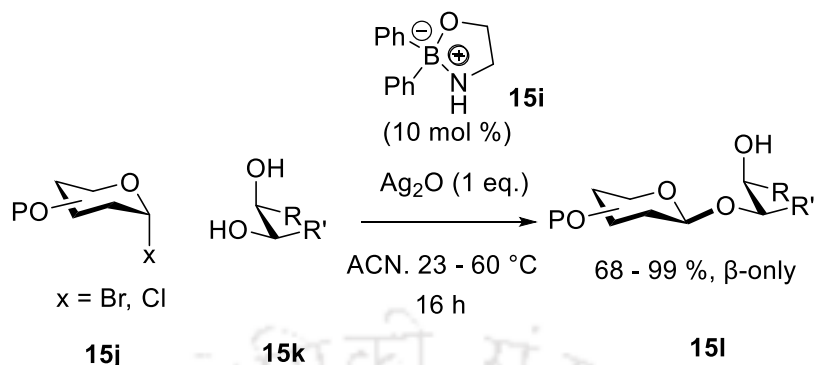


Scheme 15b: Anomeric Alkylation Involving Triflates as Leaving Groups

with sodium hydride followed by the addition of triflate and a sodium chelating agent (15-crown-5). The lactols having C-3 hydroxy group were reacted with sugar-derived primary and secondary triflate as a nucleophile which resulted in different oligosaccharides with good to excellent yields in a β -selective fashion (Scheme 15b).⁵⁸

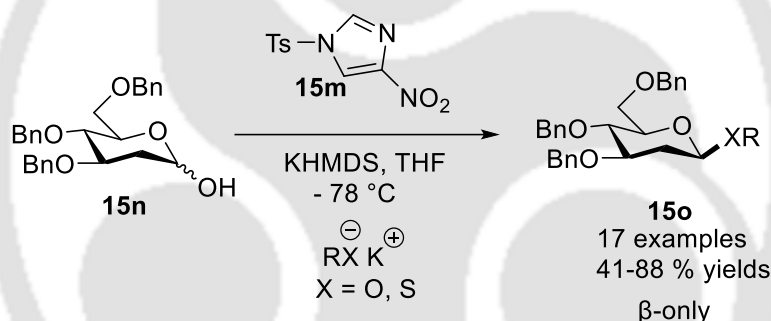
Taylor and co-workers reported in 2011 a very elegant example of the application of organoboron catalysis in Koenigs–Knorr glycosylations. A diphenylborinic acid-derived catalyst (**15i**) was used in the presence of stoichiometric silver(I) oxide to activate partially protected (at C-1 and C-6) glycosyl acceptors **15k**. Taking advantage of the presence of a 1,2-

cis-diol moiety in the glycoside acceptor, completely regioselective glycosylations could be achieved (Scheme 15c).⁵⁹



Scheme 15c: Regioselective Glycosylation Using Diphenylborinic-Derived Ethanolamine Adduct

In 2013, Bennett Group disclosed a strategy for the synthesis of β -selective 2-deoxy glycosides based on anomeric *O*-sulfonation followed by nucleophilic displacement. In this method 2-deoxy hemiacetals were reacted with *N*-sulfonyl imidazoles to generate a reactive electrophilic species in situ, presumably a glycosyl sulfonate, which can react with different nucleophiles in an $\text{S}_{\text{N}}2$ fashion, resulting in β -selective glycosides (Scheme 15d).⁶⁰

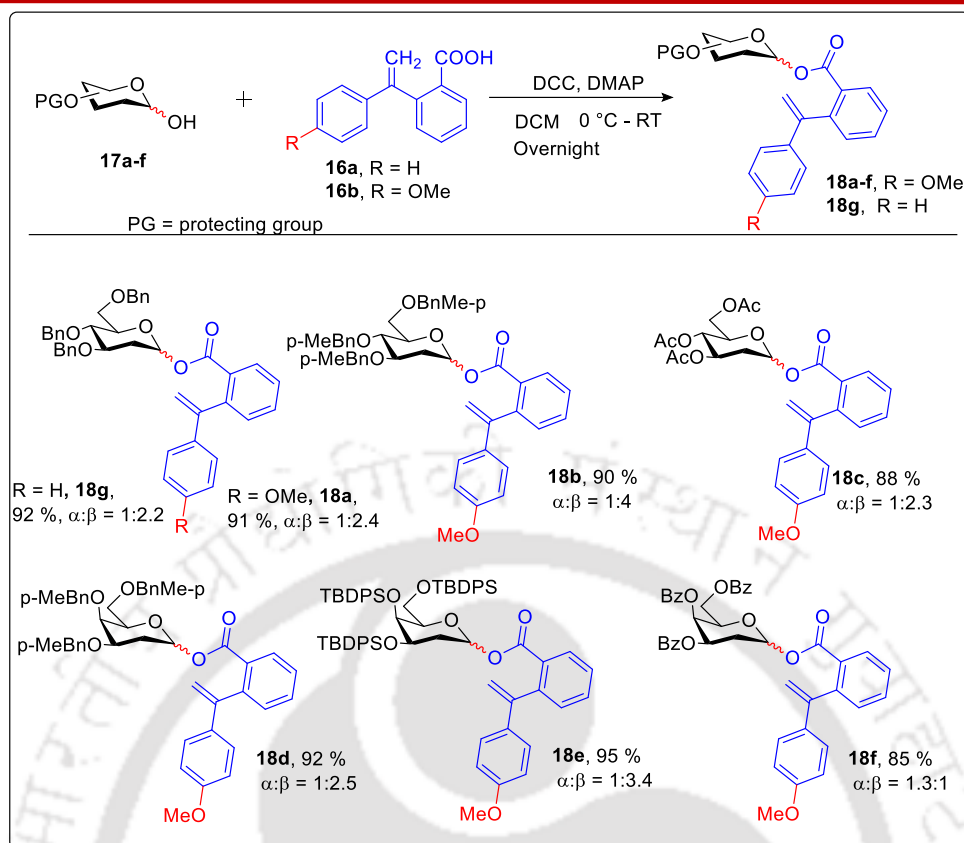


Scheme 15d: *N*-Sulfonylimidazole-Catalyzed Synthesis of 2-Deoxy- β -glycosides

Recently so many glycal activation methods are developed. Some of them are not compatible with less reactive acetyl/benzoyl substrates⁶¹⁻⁶² and in some cases, metals⁶³⁻⁶⁴ have been used to catalyse glycals that are prone to provide the undesired Ferrier byproducts.⁶⁵⁻⁶⁶

3.2 This work

From the above discussion, a general catalytic user-friendly method for the stereoselective construction of the 2-deoxyglycosidic bond remains a challenge. We present here 2-deoxy *ortho*-[1-(*p*-MeOPhenyl) Vinyl]Benzoates (PMPVB) donors as stable and reactive glycosyl donors for a protecting group independent stereoselective synthesis of α -2-deoxyglycosides under simple Brønsted acid catalysis. These alkene donors by virtue of their rigidity and 1,1-diphenyl substitutions⁶⁷⁻⁶⁸ along with a *p*-methoxy group can easily react with not only strong electrophilic reagents like NIS but also can be activated under simple Brønsted acidic conditions. The ability of these donors to react with Brønsted acid makes them the Fraser-Reid type alkene donors⁶⁹⁻⁷⁰ that can be catalytically activated. Along with stability and reactivity, PMPVB donors allow the construction of the 2-deoxy *O*-glycosidic linkage in a highly stereoselective fashion.



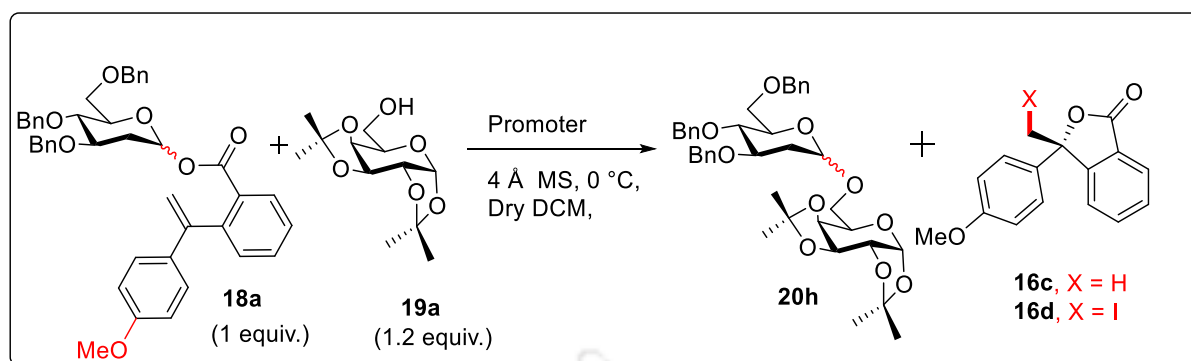
Scheme 16: Synthesis of PMPVB donors

3.2.1 Synthesis of PMPVB donors

2-Deoxy PMPVB donors are readily prepared by DCC coupling of the corresponding acid with 2-deoxy hemiacetals in excellent yields.⁷¹ 2-deoxyglucose (**18a-c**, **18g**) and 2-deoxygalactose (**18d-f**) donors with various protecting groups have been made, as shown in Scheme 16. All the donors (**18a-e**, **18g**) with various protecting groups have been obtained as a mixture of isomers with β as the dominant donor except for the 2-deoxy *tri*-O-benzoyl protected galactose derived donor (**18f**) that is obtained with α isomer as the major product.

3.2.2 Optimization study

After successfully synthesizing PMPVB donors, we investigated the glycosylation reaction by taking the per-benzyl 2-deoxyglucoosyl PMPVB donor (**18a**) with the galactose-derived 6-OH acceptor (**19a**) under various conditions (Table 1). When donor **18a** (0.06 mmol) was reacted with acceptor **19a** (0.072 mmol) in dry CH_2Cl_2 (1.5 mL) at 0°C under bistriflimide ($(\text{CF}_3\text{SO}_3)_2\text{NH}$) as the Brønsted acid catalyst (30 mol %), the reaction went to completion in just 5 min, yielding 83 % of the desired disaccharide product (**20h**) in 1.7:1 ($\alpha:\beta$) ratio (Table 1, entry 1). Since this is an alkene-based donor and can be activated under NIS/TMSOTf conditions, the same has been tried to see if the yield or selectivity could be improved. However, under NIS (1.1 equiv) and TMSOTf (30 mol %), the reaction was slower relative to the Brønsted acidic conditions (20 min), and the yield dropped to 79 % yield (1.7:1, $\alpha:\beta$) (Table 1, entry 2). Also, the release of succinimide as another byproduct could also interfere in the reaction leading to poor selectivity. Intriguingly enough, when the reaction was tried with another strong acid, trifluoromethane sulfonic acid (TfOH), instead of bistriflamide, as a promoter (30 mol %), it led to an 85 % yield of the product (**20h**) with an improved anomeric

Table 1: Optimization study

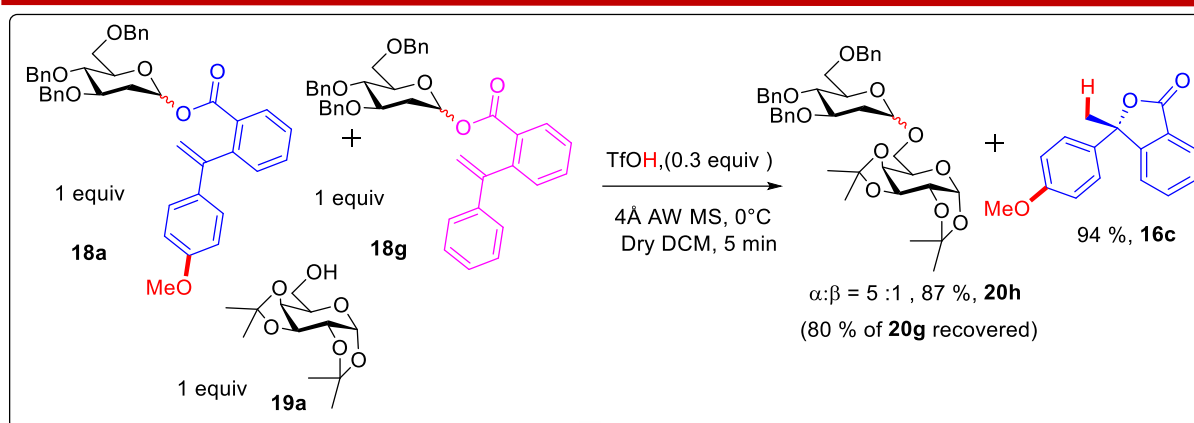
Entry	Catalyst	Amount (mol %)	Time	Yield (%)	Anomeric Ratio ($\alpha:\beta$)
1	(CF ₃ SO ₂) ₂ NH	30	5 min	83	1.7:1
2	NIS (1.1 equiv.), TMSOTf	30	20 min	79	1.7:1
3	TfOH	30	5 min	85	5.4:1
4	TfOH	5	24 h	-	
5	TfOH	10	24 h	-	
6 ^a	TfOH	15	5 h	64	2.7:1
7	TfOH	20	30 min	80	3.6:1
8	TfOH	25	15 min	81	4.5:1
9 ^b	TfOH	30	12 h	18	2:1

Reaction conditions: Reactions were done at 0 °C in presence of activated acid-washed 4 Å MS in dry DCM medium. ^a Based-on recovery of starting material. ^b **18g** donor was used.

ratio of 5.4:1 ($\alpha:\beta$) of the product (Table 1. entry 3). The reaction was tried at various catalytic loadings to evaluate the influence of catalyst concentration on the selectivities. The donor could not be activated at 5 and 10 mol % of the triflic acid (Table 1. entries 4, 5) even after 24 h. There is a gradual increase in the yields and selectivities when the catalytic mol % was increased from 15 to 25 (Table 1. entries 6-8) also with a drastic decrease in reaction time as well. In order to understand the influence of the –OMe group of the PMPVB donor on the outcome of the glycosylation reaction, we did another experiment taking a PVB donor (**18g**) that is devoid of the methoxy group, which resulted in only 18 % yield of the product with an anomeric ratio of 2.2:1 ($\alpha:\beta$) after 12 h (Table 1, entry 9).

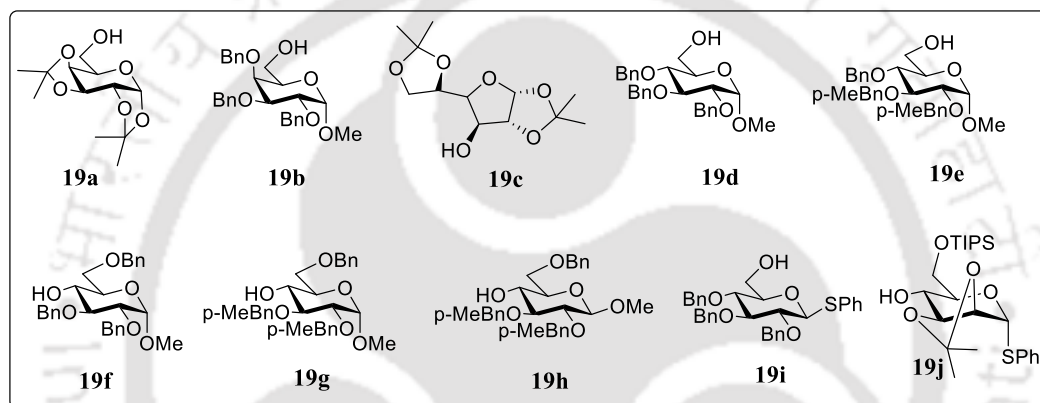
3.2.3 Comparative study

We performed a comparative study between PMPVB and PVB donors to know the reactivity difference. A mixture of 1 equiv. of PMPVB donor (**18a**) and 1 equiv. of donor PVB⁶⁷ (**18g**) in the presence of 1 equiv. of glycosyl acceptor (**19a**), were reacted under the catalytic Brønsted acidic condition. After 5 min, we quenched the reaction and isolated the products. Where 80 % of the PVB donor (**18g**) has been recovered, indicating little activation of the PVB donor (**18g**) in the presence of the PMPVB donor (**18a**) with 87 % yield of the desired product (**20h**) ($\alpha:\beta$, 5:1) along with *p*-methoxy substituted cyclized adduct (**16c**) in 94 % (Scheme 17).



Scheme 17: Comparative study

3.2.4 Synthesized of glycosyl acceptors used for this study

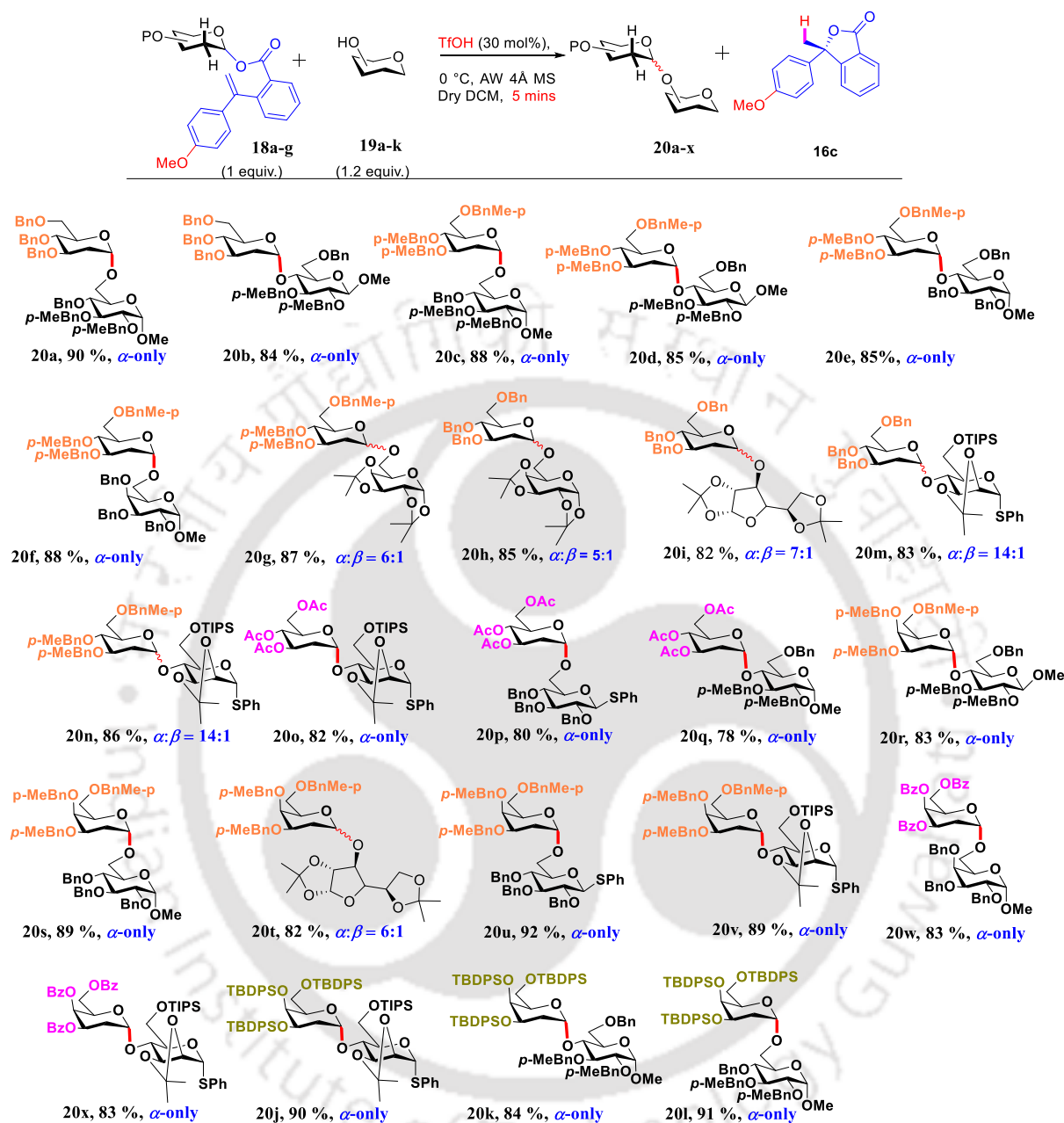


Scheme 18: Synthesized acceptors

3.2.5 Substrate scope O-glycosylation

With the optimized conditions in hand, we have decided to test the protocol on other 2-deoxy PMPVB donors synthesized with variously protected acceptors (Scheme 19). It was interesting to note that the glycosylation of armed perbenzylated and per-*p*-methylbenzylated 2-deoxy galactosyl and glucosyl donors reacted in a highly stereoselective fashion giving rise to α isomer exclusively with good to excellent yields (20a–f, 20r–s, 20u–v, 83–92 %). The high selectivities were retained even in the case of hindered and less reactive secondary acceptors as well (20b, 20d–e, 20r, 20v). The super armed silylated 2-deoxygalactosyl donor also resulted in the glycosyl products as single isomers (α only) in excellent yields (20j–l; 84–91 %). The peracetylated glucosyl and perbenzoylated 2-deoxygalactosyl donors also resulted selectively in α isomer with good yields (20o–q, 20w–x, 80–85 %) even in the case of less reactive secondary 4-OH of mannosyl acceptor (19j). The highly hindered mannosyl acceptor (19j), when reacted with perbenzylated and per-*p*-methylbenzyl protected glucosyl donors, provided the disaccharides in excellent selectivities of 14:1 and 14:1 respectively (20m & 20n). A drop in selectivities was observed when acetonide-protected acceptors 19a & 19c were used as acceptors (20g–i, 20t; 5:1 to 7:1, $\alpha:\beta$) in their coupling reactions with perbenzylated and per-*p*-methylbenzylated 2-deoxygalactosyl as well as glucosyl donors. Unlike the other alkene-based donors, these PMPVB donors can be activated in the presence of thioglycoside

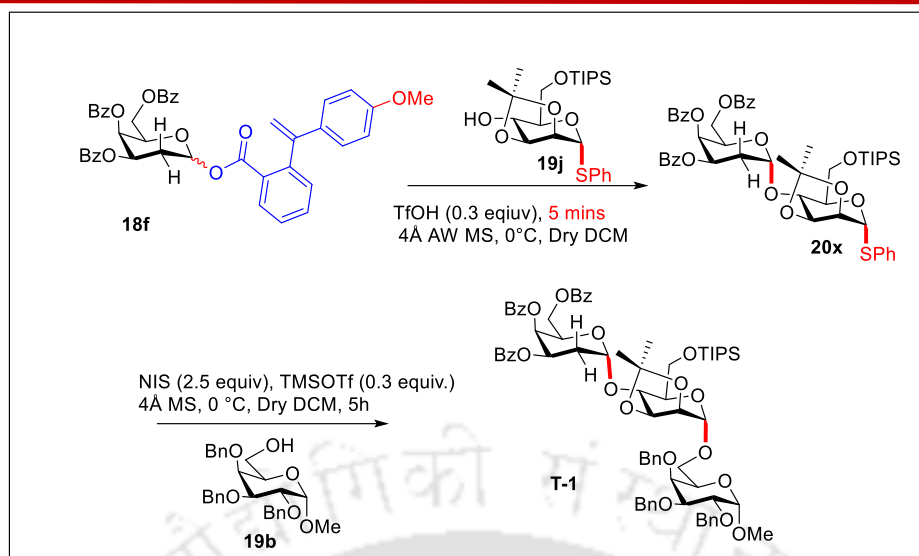
donors and the successful coupling reactions with thiomannopyranoside (**19j**) stands as evidence for the same.



Scheme 19: Substrate scope of 2-deoxy sugars

3.2.6 Synthesis of trisaccharide

One of the disaccharides (**20x**) thus synthesized has also been converted to the trisaccharide **T-1** using standard NIS/TMSOTf protocol in presence of acceptor (**19b**), where trisaccharide **T-1** was also obtained as a single isomer (α only) in 76 % yield (brsm) (Scheme 20).

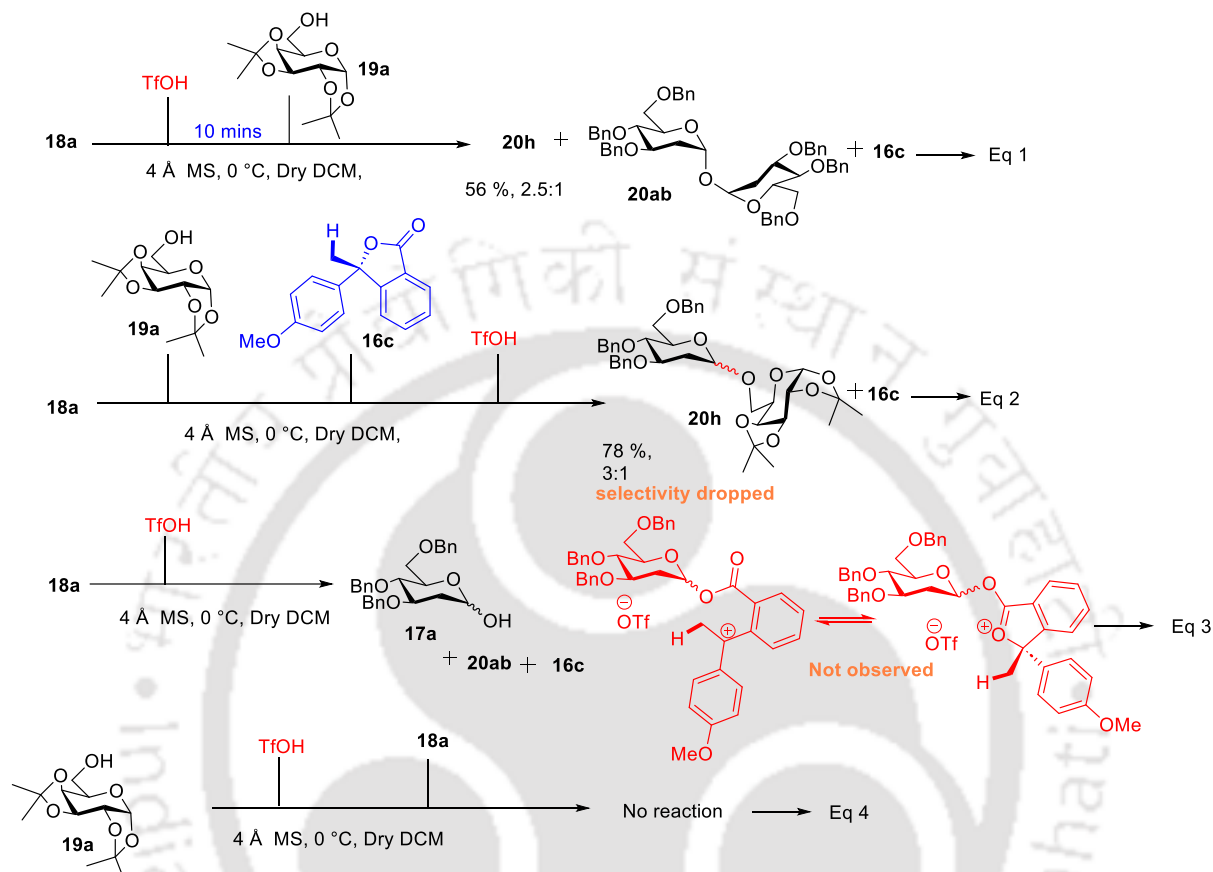


Scheme 20: Synthesis of **Gal-Man-Gal** Trisaccharide **T-1**.

3.2.7 Control experiments

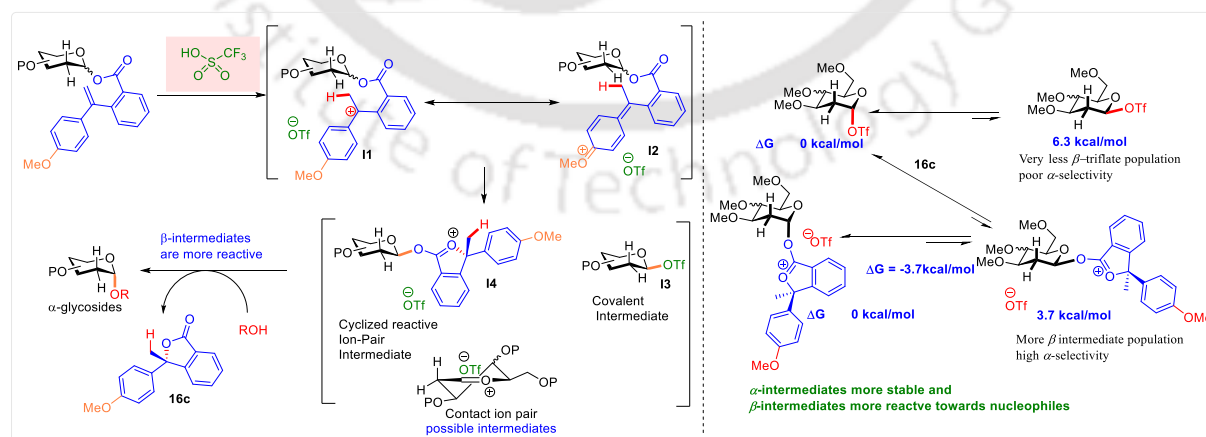
A variety of control experiments have been performed to understand the reasons behind the observed high α -selectivity. Usually, the α -selectivity in 2-deoxyglycosides is explained via the corresponding oxocarbenium ions that are inherently α -directing; however, the facial selectivity usually is dependent on the protecting groups on the donor. The protecting group independent high α -selectivities observed in the current protocol could arise from a possible S_N2 attack as well. With the growing body of evidence for the involvement of β -glycosyl triflates in α -selective glycosylation reactions,^{72–74} invoking the naked oxocarbenium ion may no longer be a valid explanation for the anomeric selectivity. We ran a few control experiments and theoretical studies to decipher the mechanism and the possible intermediates giving rise to the observed high α -selectivities. For better comparisons, we have chosen the acetonide acceptor **19a** for the control experiments (same as the optimization studies) as this is one of the very few acceptors where the α -selectivity is relatively low. The preactivation method where the acceptor **19a** is added 10 minutes later to the addition of the catalyst led to only 56 % of the product **20h** with a drop in α selectivity to 5.4:1 to 2.5:1 (Scheme 21, eqn (1)). While this experiment does not rule out the possibility of the involvement of β -glycosyl triflates as potential intermediates, this experiment suggests that it may not be the only reason for the observed high α -selectivity. The reaction, when performed with an excess amount of the cyclic byproduct **16c** (1.5 equiv.) in the reaction mixture, led to a drop in the anomeric selectivity from 5.4:1 to 3:1 (α : β) and the yield from 85 % to 78 % (Scheme 21, eqn (2)). The drop-in selectivity and the yield could be the resultant of a slight decrease in the rate of reaction due to the shift in the equilibrium because of the presence of **16c**. Also, this experiment not only demonstrates that the by-product can react back with the oxocarbenium ion but also suggests that the cyclic intermediate **14** (Scheme 22) could be the potential intermediate affecting the stereochemical outcome of the glycosylation. The experiment performed in the absence of acceptor alcohol in order to observe the protonated intermediate only resulted in the formation of the hydrolyzed product **17a** (38 %) and dimerized product **20ab** (24 %) along with the byproduct **16c** (91 %) (Scheme 21, eqn (3)). This shows that the alkene donor once protonated is a highly unstable species and undergoes rapid cyclization followed by elimination leading to oxocarbenium ion. Surprisingly, the reaction in which the donor was added after the

prior mixing of the acceptor alcohol (**19a**) and the catalyst did not lead to the coupled product even after 5 h (Scheme 21, eqn (4)). Presumably, the Brønsted acid catalyst is sequestered by the acceptor alcohol via multiple hydrogen-bonding networks.



Scheme 21: Control experiments

3.2.8 Proposed mechanism



Scheme 22: Proposed mechanism and the minimum energy structures of the intermediates

The above experiments suggest that the observed high selectivities could be arising from the S_N2 attack of the alcohol onto the more reactive protonated β -glycosylbenzofuranium

intermediate (**I4**) or/and β -glycosyltriflate (**I3**) or/and the β -contact ion-pair. DFT calculations were performed using the B3LYP/6-31 g(d) level of theory on methylprotected donors to understand the relative energy differences between α and β intermediates, which revealed that the α -glycosyloxybenzofuranium intermediate is more stable by 3.7 kcal/mol. In contrast, the difference in free energies between α and β -glycosyltriflates is 6.3 kcal/mol. These calculations according to Curtin-Hammett principle suggest that the β -intermediates could be significantly unstable and hence could be more reactive than their α counterparts, and the preferential attack of the *O*-nucleophiles on β -intermediates leads to the observed high α -selectivities. Based on all these observations and Lemieux's seminal studies on glycosyl bromides,⁷⁵ we propose the mechanism of the current protocol as depicted in Scheme 22.

3.2.9 Conclusion

In summary, we have demonstrated the utility of the new PMPVB donors towards the stereoselective synthesis of 2-deoxy α -glycosides. The method provides the coupled product in excellent diastereoselectivities arising from the difference in energies of the reactive intermediates. The relatively less energy difference between the α/β glycosyl benzofuranium intermediate results in an increase in the β -intermediate population that is also significantly more reactive towards nucleophiles could be the reason for the observed high α -selectivity. The high selectivities observed are independent of the protecting groups and showcased on both 2-deoxyglucosyl and 2-deoxygalactosyl donors. Extending the PMPVB donor protocol towards the synthesis of 2-deoxysugar based natural products is under progress in our laboratory.

3.3 Experimental section

General Information

All solvents purchased were of commercial grade and reagents were purchased from Sigma-Aldrich, Merck, Carbosynth, Spectrochem, Alfa Aesar, Avra and used without further purification for reactions.

Analysis

Reactions were monitored by TLC on Kieselgel 60 F254 (Merck). Detection was done by examination under UV light (254 nm) and by charring with 10 % sulfuric acid in water. Purification was performed by both Ultra High-Performance Liquid Chromatography (UHPLC) using column [Particle size: (μ) 12, Dim: (mm) 250 x 10] in reverse phase and in normal phase using silica gel [Merck, 60-120 mesh] and Flash column chromatography (Combiflash^(R) NextGen 300). Extracts were concentrated in vacuo using both Büchi rotary evaporator (bath temperatures up to 40 °C) at a pressure of either 15 mmHg (diaphragm pump) and 0.7 mmHg (oil pump), at rt. ¹H- and ¹³C NMR were recorded on a Bruker 600 MHz, 500 MHz, and 400 MHz spectrometer using CDCl₃ as solvent. Chemical shift values are reported in ppm with the solvent as the internal standard (CDCl₃: δ 7.26 for ¹H, δ 77.16 for ¹³C). Data are reported as follows: chemical shifts (δ), multiplicity (s = singlet, d = doublet, dd = doublet of doublet, ddd = doublet of doublet of doublets, dt = doublet of triplet, t = triplet, td = triplet of doublet, q = quartet, m = multiplet) etc., coupling constants *J* (Hz), and integration. High-resolution mass measurements were performed using Agilent technologies mass spectrometer (QTOF-ESI mode). The diastereomeric ratios were calculated from crude NMR. Specific

rotation was recorded in Autopol II S2, the units of the specific rotation is (deg·mL)/(g·dm) and concentration c is given in g/100 ml.

Hemiacetals used in this study

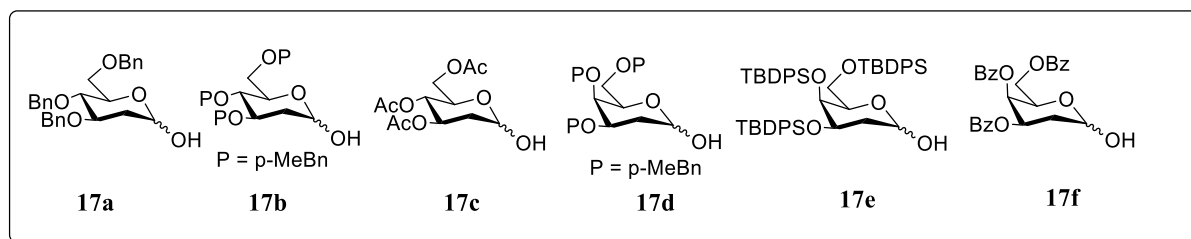


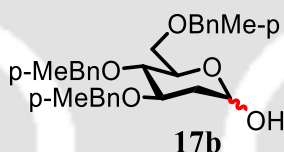
Figure 2: Synthesized hemiacetals

1a, 1c, 1e, 1f were synthesized following literature procedures.^{52,75}

General procedure 1

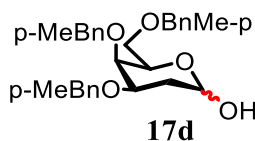
3,4,6-*tri-para*-methyl-*O*-benzyl-*D*-glycal (110 mg, 0.24 mmol, 1eqv.) was dissolved in 2 ml of 90:10:1 THF: water: 8(M) HCl and was stirred for 24 h.⁵² The reaction mixture was then concentrated and extracted with DCM three times. The organic phase was washed with brine, dried over anhydrous Na₂SO₄ and concentrated. The crude was purified by Flash column chromatography in Ethyl acetate/Hexane solvent system.

Synthesis of 3,4,6-*tri- p*-methyl-*O*-benzyl-2-deoxy- α/β -*D*-glucopyranose (17b)



17b was synthesized according to general procedure 1 (white solid, 85.7 mg, 75 %, $\alpha:\beta$ = 2.6:1, R_f = 0.30 (Hexane/EtOAc, 3:2, v/v). ¹H NMR (500 MHz, CDCl₃) δ 7.25 – 7.02 (m, 15H), 5.39 (s, 1H), 4.88 – 4.72 (m, 2H), 4.67 – 4.53 (m, 4H), 4.50–4.42 (m, 3H), 4.04–3.96 (m, 2H), 3.70–3.60 (m, 3H), 3.50 – 3.41 (m, 2H), 3.21 (s, 1H), 2.64 (s, 1H), 2.43 – 2.35 (m, 1H), 2.33 (s, 12H), 2.26 (dd, J = 12.8, 4.1 Hz, 1H), 1.71 – 1.63 (m, 1H), 1.53 (d, J = 11.9 Hz, 1H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 136.3, 136.2, 134.7, 134.5, 134.3, 134.3, 134.0, 128.1, 128.0, 128.0, 127.9, 127.1, 127.1, 126.8, 126.8, 93.2, 91.2, 78.0, 77.4, 76.6, 75.9, 74.0, 73.7, 72.3, 70.7, 70.4, 69.9, 68.1, 68.0, 37.0, 34.5, 20.1. HRMS (ESI) calcd for C₃₀H₄₀NO₅ [M+NH₄]⁺ 494.2906, found 494.2910. $[\alpha]_D^{35}$ = 0.32 (c 0.01, CHCl₃).

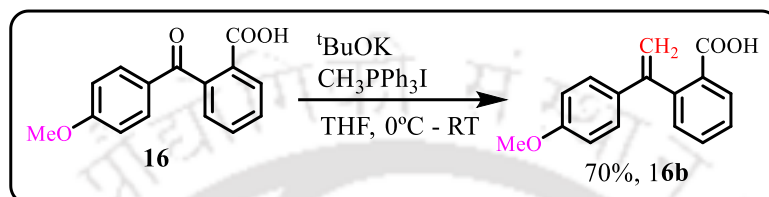
Synthesis of 3,4,6-*tri- p*-methyl-*O*-benzyl-2-deoxy- α/β -*D*-galactopyranose (17d)



17d was synthesized according to general procedure 1 (White solid, 86.9 mg, 76 %, $\alpha:\beta$ = 3.3:1, R_f = 0.31 (Hexane/EtOAc, 3:2, v/v). ¹H NMR (500 MHz, CDCl₃) δ 7.24 – 7.06 (m, 12H), 5.39

(s, 1H), 4.85 (d, J = 11.5 Hz, 1H), 4.57 – 4.51 (m, 3H), 4.44 (d, J = 11.8 Hz, 1H), 4.34 (d, J = 11.7 Hz, 1H), 4.07 (t, J = 5.8 Hz, 1H), 3.93 (d, J = 10.8 Hz, 1H), 3.78 (s, 1H), 3.53 (t, J = 8.2 Hz, 1H), 3.39 (dd, J = 9.1, 5.7 Hz, 1H), 3.27 (s, 1H), 2.33 (s, 6H), 2.31 (s, 3H), 2.16 (t, J = 12.4 Hz, 1H), 1.94 (d, J = 12.4 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 136.3, 136.1, 136.1, 134.8, 134.5, 133.9, 128.0, 128.0, 127.8, 127.4, 127.1, 126.4, 91.6, 73.2, 72.9, 72.3, 71.8, 69.3, 69.1, 69.0, 30.1, 20.1, 20.1. HRMS (ESI) calcd for $\text{C}_{30}\text{H}_{40}\text{NO}_5$ $[\text{M}+\text{NH}_4]^+$ 494.2906, found 494.2906. $[\alpha]_{\text{D}}^{35} = 0.66$ (c 0.016, CHCl_3).

Synthesis of *ortho*-[1-(*p*-methoxy phenyl)vinyl]benzoic acid (**16b**)



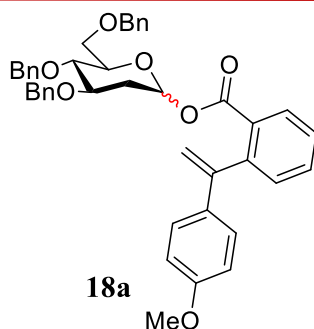
Scheme 23: Synthesis of *ortho*-[1-(*p*-methoxy phenyl)vinyl]benzoic acid

To a suspension of methyl triphenylphosphonium iodide (7.14 g, 20.0 mmol) in THF (100 mL) was added potassium *tert*-butoxide (3.36 g, 30.0 mmol) at 0°C . The mixture was then stirred for 30 min. Then 2-(4-methoxybenzoyl) benzoic acid (**16**) (10.0 mmol) was added to the reaction mixture at 0°C . The mixture was allowed to warm to room temperature, and stirred for 24 h. After completion of the reaction, THF was evaporated and the mixture was treated with 10 % NaOH (100 mL). The aqueous layer was washed with DCM (50 mL) and acidified with 1N HCl to make the pH reach 6. The aqueous layer was extracted with ethyl acetate (350 mL). The combined extracts were washed with brine (100 mL), dried over Na_2SO_4 , and evaporated *in vacuo*. The residue was purified by recrystallization from petroleum ether/ethyl acetate to give the product as a white solid, *ortho*-[1-(*p*-methoxy phenyl) vinyl]benzoic acid (**16b**).⁷⁷ The compound **16a** were synthesized by following literature procedures.⁷⁷

General procedure 2

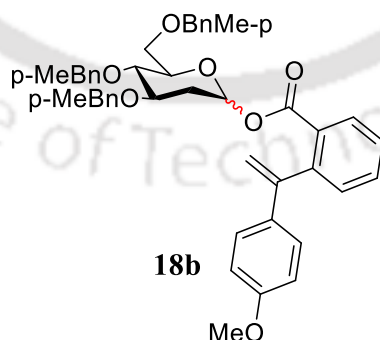
4-dimethylaminopyridine (DMAP) (0.2 equiv.) and *N,N*-dicyclohexylcarbodiimide (DCC) were added to a solution of **Sugar** (1.0 equiv. **17a-f**) and benzoic acid (**16a**, **16b**) (1.2 equiv.) in dry DCM at 0°C . The resulting mixture was allowed to reach room temperature and stirred for overnight. After completion of the reaction, the mixture was diluted with CH_2Cl_2 , and washed with water and brine. The organic layer was dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. The residue was purified by Flash column chromatography to afford the glycosyl donors (**18a-g**).⁷¹

Synthesis of 3,4,6-*tri-O*-benzyl-2-deoxy-D-glucopyranosyl-2-(1-(4-methoxyphenyl)vinyl)benzoate (**18a**)



Compound **18a** was prepared from **17a** (434.5 mg, 1 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **18a** (610.4 mg, 91 %, $\alpha:\beta = 1:2.4$) as a white solid, $R_f = 0.52$ (Hexane/EtOAc, 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.90 (d, $J = 7.7$ Hz, 1H), 7.82 (d, $J = 7.7$ Hz, 1H), 7.51 (dd, $J = 10.8, 4.2$ Hz, 1H), 7.50 – 7.46 (m, 1H), 7.42 – 7.37 (m, 2H), 7.35 – 7.22 (m, 19H), 7.17 (t, $J = 8.9$ Hz, 6H), 6.79 (d, $J = 8.7$ Hz, 2H), 6.75 (d, $J = 8.7$ Hz, 1H), 6.24 (d, $J = 2.0$ Hz, 1H), 5.61 (s, 1H), 5.59 (d, $J = 1.7$ Hz, 1H), 5.57 (s, 1H), 5.12 (s, 1H), 5.02 (s, 1H), 4.86 (d, $J = 10.8$ Hz, 1H), 4.82 (d, $J = 10.9$ Hz, 1H), 4.63 – 4.57 (m, 3H), 4.53 (d, $J = 3.0$ Hz, 1H), 4.52 (d, $J = 1.9$ Hz, 1H), 4.49 (d, $J = 12.1$ Hz, 2H), 4.45 (d, $J = 12.1$ Hz, 1H), 4.39 (q, 11.6 Hz, 1H), 3.74 (d, $J = 4.0$ Hz, 1H), 3.72 (s, 4H), 3.70 (d, $J = 1.4$ Hz, 1H), 3.68 (dd, $J = 6.1, 2.4$ Hz, 1H), 3.65 (dd, $J = 9.0, 3.9$ Hz, 1H), 3.63 (d, $J = 4.4$ Hz, 1H), 3.61 (s, $J = 5.8$ Hz, 2H), 3.59 (d, $J = 9.2$ Hz, 1H), 3.56 (d, $J = 9.6$ Hz, 1H), 3.51 (dd, $J = 10.8, 1.2$ Hz, 1H), 3.48 – 3.44 (m, 1H), 2.14 (dd, $J = 13.1, 3.3$ Hz, 1H), 2.12 – 2.07 (m, 1H), 1.77 – 1.70 (m, 1H), 1.55 (q, $J = 11.4$ Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 166.5, 165.5, 159.4, 159.2, 148.5, 148.3, 143.4, 142.8, 138.7, 138.6, 138.3, 138.2, 138.2, 138.1, 133.3, 132.7, 132.1, 131.7, 131.3, 131.0, 131.0, 130.2, 130.2, 130.1, 128.5, 128.4, 128.4, 128.4, 128.3, 128.1, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 127.5, 113.7, 113.6, 112.6, 112.1, 93.1, 93.0, 78.9, 77.5, 75.9, 75.0, 74.8, 73.6, 73.5, 73.5, 71.7, 71.5, 68.7, 68.4, 55.2, 55.1, 34.9, 34.3. HRMS (ESI) calcd for $\text{C}_{43}\text{H}_{46}\text{NO}_7$ $[\text{M}+\text{NH}_4]^+$ 688.3274, found 688.3274. $[\alpha]_D^{35} = 0.88$ (c 0.015, CHCl_3)

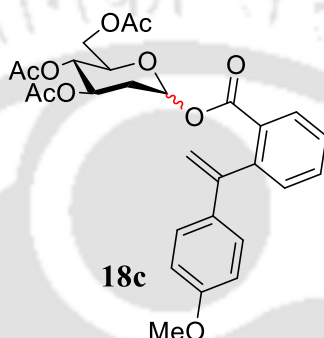
Synthesis of 3,4,6-tri- *p*-methyl- *O*-benzyl-2-deoxy-D-glucopyranosyl-2-(1-(4-methoxyphenyl)vinyl)benzoate (**18b**)



Compound **18b** was prepared from **17b** (476.6 mg, 1 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **18b** (641.6 mg, 90 %, $\alpha:\beta = 1:4$) as a colourless syrup, $R_f = 0.52$ (Hexane/EtOAc, 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.90 (d, $J = 7.7$ Hz, 1H), 7.52 (t, $J = 7.4$ Hz, 1H), 7.40 (t, $J = 7.7$ Hz, 1H), 7.33 (d, $J = 7.5$ Hz, 1H), 7.21 (dd, $J = 7.3, 3.8$ Hz, 4H), 7.18 (d, $J = 8.6$ Hz, 2H), 7.14 (d, $J = 7.6$ Hz, 2H), 7.10 (d, $J = 7.7$ Hz, 2H), 7.08 (d, $J = 7.5$ Hz, 2H), 7.03 (d, $J = 7.8$ Hz, 2H), 6.79 (d, $J = 8.6$ Hz,

2H), 5.61 (s, 1H), 5.55 (d, $J = 8.8$ Hz, 1H), 5.11 (s, 1H), 4.79 (d, $J = 10.5$ Hz, 1H), 4.59 – 4.54 (m, 2H), 4.49 (d, $J = 11.4$ Hz, 1H), 4.43 (d, $J = 11.2$ Hz, 2H), 3.74 (s, 3H), 3.69 (dd, $J = 10.8$, 3.8 Hz, 1H), 3.65 (d, $J = 10.0$ Hz, 1H), 3.57 (dd, $J = 11.2$, 4.8 Hz, 1H), 3.53 (t, $J = 9.0$ Hz, 1H), 3.42 (d, $J = 9.0$ Hz, 1H), 2.35 (s, 3H), 2.32 (s, 3H), 2.32 (s, 3H), 2.07 (dd, $J = 11.4$, 3.8 Hz, 1H), 1.56 – 1.49 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 165.4, 159.2, 148.5, 143.4, 137.4, 137.4, 137.3, 135.3, 135.2, 135.0, 133.3, 132.0, 131.3, 130.2, 130.1, 129.1, 129.0, 129.0, 128.1, 127.9, 127.8, 127.5, 113.5, 112.5, 92.9, 78.7, 77.1, 75.9, 74.8, 73.3, 71.4, 68.3, 55.2, 34.9, 21.2, 21.2. HRMS (ESI) calcd for $\text{C}_{46}\text{H}_{52}\text{NO}_7$ $[\text{M}+\text{NH}_4]^+$ 730.3744, found 730.3746. $[\alpha]_{\text{D}}^{35} = 0.86$ (c 0.014, CHCl_3).

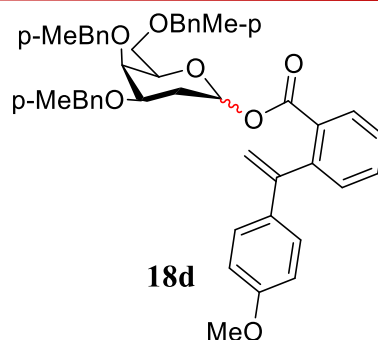
Synthesis of 3,4,6-tri-*O*-acetyl-2-deoxy-D-glucopyranosyl-2-(1-(4-methoxyphenyl)vinyl)benzoate (**18c**)



Compound **18c** was prepared from **17c** (290.3 mg, 1 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **18c** (463.4 mg, 88 %, $\alpha:\beta = 1:2.3$) as a yellow syrup, $R_f = 0.4$ (Hexane/EtOAc, 3:1, v/v). The α anomer, ^1H NMR (600 MHz, CDCl_3) δ 7.88 (d, $J = 7.7$ Hz, 1H), 7.54 (t, $J = 7.5$ Hz, 1H), 7.45 (t, $J = 7.6$ Hz, 1H), 7.32 (d, $J = 7.6$ Hz, 1H), 7.28 – 7.25 (m, 2H), 6.82 (d, $J = 8.6$ Hz, 2H), 6.25 (d, $J = 2.7$ Hz, 1H), 5.77 (s, 1H), 5.11 (s, 1H), 5.06–5.00 (m, 1H), 4.93 (t, $J = 9.8$ Hz, 1H), 4.08 (dd, $J = 12.5$, 3.7 Hz, 1H), 3.80 (dd, $J = 12.8$, 1.4 Hz, 1H), 3.78 (s, 3H), 3.51 (d, $J = 10.1$ Hz, 1H), 2.10 (dd, $J = 13.3$, 5.3 Hz, 1H), 2.05 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.89 – 1.83 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 169.7, 169.0, 168.7, 165.2, 158.4, 146.9, 141.8, 131.4, 131.0, 130.0, 129.6, 129.2, 127., 126.6, 112.8, 111.5, 90.8, 69.2, 67.6, 67.5, 60.6, 54.2, 32.8, 19.9, 19.7, 19.5. HRMS (ESI) calcd for $\text{C}_{28}\text{H}_{34}\text{NO}_{10}$ $[\text{M}+\text{NH}_4]^+$ 544.2183, found 544.2184. $[\alpha]_{\text{D}}^{35} = 0.18$ (c 0.01, CHCl_3).

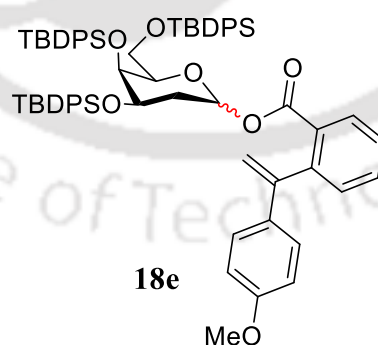
The β anomer, ^1H NMR (600 MHz, CDCl_3) δ 7.88 (d, $J = 7.4$ Hz, 1H), 7.54 (t, $J = 7.1$ Hz, 1H), 7.41 (t, $J = 7.3$ Hz, 1H), 7.35 (d, $J = 7.3$ Hz, 1H), 7.17 (d, $J = 8.2$ Hz, 2H), 6.80 (d, $J = 8.2$ Hz, 2H), 5.68 (d, $J = 9.2$ Hz, 1H), 5.62 (s, 1H), 5.11 (s, 1H), 4.97 (d, $J = 5.1$ Hz, 2H), 4.27 (dd, $J = 12.0$, 3.9 Hz, 1H), 4.04 (d, $J = 12.2$ Hz, 1H), 3.78 (s, 3H), 3.67 (s, 1H), 2.14–2.08 (m, 1H), 2.06 (s, 3H), 2.03 (s, 6H), 1.69 – 1.62 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.7, 170.0, 169.8, 165.1, 159.2, 148.4, 143.5, 133.2, 132.2, 131.3, 130.1, 129.6, 127.9, 127.5, 113.5, 112.6, 91.8, 91.7, 91.7, 72.8, 70.1, 68.3, 62.0, 55.2, 34.3, 20.8, 20.7, 20.7. HRMS (ESI) calcd for $\text{C}_{28}\text{H}_{34}\text{NO}_{10}$ $[\text{M}+\text{NH}_4]^+$ 544.2183, found 544.2177. $[\alpha]_{\text{D}}^{35} = 0.50$ (c 0.014, CHCl_3).

Synthesis of 3,4,6-tri-*p*-methyl-*O*-benzyl-2-deoxy-D-galactopyranosyl-2-(1-(4-methoxyphenyl)vinyl)benzoate (**18d**)



Compound **18d** was prepared from **17d** (476.6 mg, 1 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **18d** (655.8 mg, 92 %, $\alpha:\beta = 1:2.5$) as a white solid, $R_f = 0.55$ (Hexane/EtOAc, 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.89 (d, $J = 7.6$ Hz, 1H), 7.83 (d, $J = 7.6$ Hz, 1H), 7.50 (dt, $J = 14.6, 7.4$ Hz, 2H), 7.42 – 7.36 (m, 2H), 7.33 (d, $J = 7.5$ Hz, 1H), 7.25 – 7.05 (m, 21H), 6.77 (dd, $J = 8.4, 4.4$ Hz, 3H), 6.28 (d, $J = 2.0$ Hz, 1H), 5.60 (s, 1H), 5.55 (s, 1H), 5.52 (d, $J = 6.0$ Hz, 1H), 5.12 (s, 1H), 5.00 (s, 1H), 4.85 (d, $J = 11.4$ Hz, 1H), 4.79 (d, $J = 11.3$ Hz, 1H), 4.57 (d, $J = 11.5$ Hz, 1H), 4.48 (d, $J = 10.6$ Hz, 3H), 4.43 – 4.37 (m, 2H), 4.33 (d, $J = 6.0$ Hz, 1H), 4.31 (d, $J = 6.0$ Hz, 1H), 4.30–4.29 (m, 1H), 4.22 (d, $J = 11.5$ Hz, 1H), 3.79 (d, $J = 10.8$ Hz, 2H), 3.74 – 3.71 (m, 4H), 3.69 (s, 1H), 3.56 (t, $J = 9.8$ Hz, 1H), 3.51 (d, $J = 2.5$ Hz, 2H), 3.50 (d, $J = 5.2$ Hz, 2H), 3.47 (d, $J = 8.0$ Hz, 1H), 3.41 (dd, $J = 9.0, 5.5$ Hz, 1H), 2.37 – 2.29 (m, 13H), 2.25 – 2.19 (m, 1H), 2.06 – 1.98 (m, 1H), 1.80 (d, $J = 11.5$ Hz, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 166.8, 165.4, 159.3, 159.1, 148.6, 148.1, 143.4, 142.6, 137.5, 137.4, 137.4, 137.3, 137.2, 137.2, 135.7, 135.6, 135.3, 135.0, 134.9, 134.8, 133.3, 132.7, 132.1, 131.6, 131.3, 131.3, 130.8, 130.3, 130.3, 129.9, 129.2, 129.1, 129.1, 128.9, 128.9, 128.5, 128.3, 128.2, 128.1, 128.1, 127.9, 127.5, 127.3, 113.6, 113.5, 112.5, 112.1, 93.7, 93.3, 76.5, 74.8, 74.2, 74.1, 74.1, 73.3, 73.3, 72.5, 71.9, 70.9, 70.1, 70.1, 68.6, 68.3, 55.2, 55.2, 31.1, 29.9, 21.2. HRMS (ESI) calcd for $\text{C}_{46}\text{H}_{52}\text{NO}_7$ [$\text{M}+\text{NH}_4$] $^+$ 730.3744, found 730.3743. $[\alpha]_{\text{D}}^{35} = -1.479$ (c 0.02, CHCl_3).

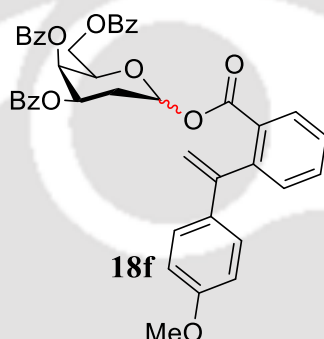
Synthesis of 3,4,6-*tri-O-tert*-butyldiphenylsilyl-2-deoxy-D-galactopyranosyl-2-(1-(4-methoxyphenyl)vinyl)benzoate (**18e**)



Compound **18e** was prepared from **17e** (439.7 mg, 0.5 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **18e** (530 mg, 95 %, $\alpha:\beta = 1:3.4$) as a white solid, $R_f = 0.8$ (Hexane/EtOAc, 5:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.95 (d, $J = 7.6$ Hz, 1H), 7.66 (d, $J = 6.9$ Hz, 1H), 7.60 (d, $J = 7.2$ Hz, 1H), 7.57 (d, $J = 7.1$ Hz, 3H), 7.55 – 7.49 (m, 6H), 7.47 – 7.37 (m, 8H), 7.36 – 7.31 (m, 6H), 7.31 – 7.26 (m, 5H), 7.25 – 7.18 (m, 9H), 7.18 – 7.13 (m, 8H), 7.05 (t, $J = 7.4$ Hz, 2H), 7.01 (d, $J = 8.5$ Hz, 1H), 6.71 (d, $J = 8.7$ Hz, 2H), 6.63 (d, $J = 8.7$ Hz, 1H), 6.06 (bs, 1H), 5.53 (s, 1H), 5.44 (s, 1H), 5.25 (d, $J = 9.1$ Hz, 1H), 5.03 (s, 1H), 4.92 (s, 1H), 4.06 (s, 1H), 3.96 (d, $J = 9.8$ Hz, 1H), 3.81 (s,

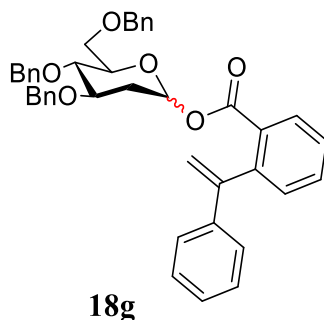
1H), 3.70 (s, 3H), 3.69 (s, 1H), 3.56 (m, 1H), 3.50 (m, 2H), 3.45 (m, 1H), 3.22 (d, $J = 6.8$ Hz, 1H), 3.10 (d, $J = 7.1$ Hz, 1H), 3.03 (bs, 1H), 2.50 (t, $J = 11.1$ Hz, 1H), 2.19 (dd, $J = 11.3, 9.1$ Hz, 1H), 1.46 (d, $J = 10.8$ Hz, 1H), 1.34 – 1.27 (m, 1H), 1.04 (s, 3H), 1.00 (s, 9H), 0.98 (s, 12H), 0.85 (s, 9H), 0.80 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 165.9, 164.6, 159.0, 158.9, 148.4, 148.4, 143.6, 143.2, 136.5, 136.5, 136.2, 135.9, 135.9, 135.8, 135.8, 135.7, 135.6, 135.5, 135.4, 133.8, 133.7, 133.7, 133.6, 133.5, 133.4, 133.3, 133.3, 133.1, 132.5, 131.8, 131.5, 131.2, 131.1, 130.7, 130.3, 128.0, 129.9, 129.8, 129.6, 129.6, 129.4, 129.3, 129.2, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.5, 127.5, 127.4, 127.3, 127.2, 127.1, 113.4, 113.3, 112.6, 112.3, 92.8, 92.5, 78.1, 76.4, 72.3, 71.6, 70.8, 69.9, 64.4, 64.3, 55.2, 55.1, 33.2, 32.4, 29.8, 27.2, 27.2, 27.1, 26.8, 26.7, 20.0, 18.9, 18.9. HRMS (ESI) calcd for $\text{C}_{70}\text{H}_{82}\text{NO}_7\text{Si}_3$ $[\text{M}+\text{NH}_4]^+$ 1132.5399, found 1132.5415. $[\alpha]_{\text{D}}^{35} = +0.40$ (c 0.01, CHCl_3).

Synthesis of 3,4,6-tri-O-benzoyl-2-deoxy-D-galactopyranosyl-2-(1-(4-methoxyphenyl)vinyl)benzoate (18f)



Compound **18f** was prepared from **17f** (476.5 mg, 1 mmol) according to General procedure 2. The crude product was purified Flash column chromatography to afford **18f** (605.8 mg, 85 %, $\alpha:\beta = 1.3:1$) as a white solid, $R_f = 0.45$ (Hexane/EtOAc, 3:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 8.09 – 8.06 (m, 2H), 8.04 – 7.95 (m, 6H), 7.95 – 7.91 (m, 2H), 7.85 – 7.82 (m, 4H), 7.64 – 7.35 (m, 19H), 7.34 – 7.27 (m, 7H), 7.23 – 7.17 (m, 2H), 6.80 – 6.74 (m, 4H), 6.50 (d, $J = 2.5$ Hz, 1H), 5.89 – 5.85 (m, 2H), 5.78 (d, $J = 2.7$ Hz, 1H), 5.65 (d, $J = 6$ Hz, 1H), 5.63 (s, 1H), 5.40 – 5.36 (m, 1H), 5.36 – 5.32 (m, 1H), 5.15 (s, 1H), 5.13 (s, 1H), 4.55 (dd, $J = 11.3, 6.5$ Hz, 1H), 4.40 – 4.37 (m, 1H), 4.36 – 4.33 (m, 1H), 4.22 (dd, $J = 6.9, 6.4$ Hz, 1H), 4.17 (dd, $J = 11.2, 6.9$ Hz, 1H), 4.00 (t, $J = 6.7$ Hz, 1H), 3.67 (s, 3H), 3.55 (s, 3H), 2.36 (td, $J = 12.9, 3.6$ Hz, 1H), 2.09 (m, 2H), 2.00 – 1.95 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 164.7, 164.2, 164.1, 163.7, 163.7, 163.5, 163.5, 163.4, 157.7, 157.5, 146.6, 146.2, 141.6, 141.0, 131.6, 131.6, 131.4, 131.4, 131.3, 131.3, 131.3, 130.4, 130.3, 130.2, 129.5, 129.3, 128.9, 128.6, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 126.8, 126.7, 126.6, 126.5, 126.5, 126.2, 126.1, 125.8, 125.8, 112.0, 111.8, 111.0, 110.5, 90.9, 90.7, 70.5, 67.7, 67.1, 65.0, 65.0, 64.3, 60.4, 60.4, 53.3, 53.2, 29.0, 27.7. HRMS (ESI) calcd for $\text{C}_{43}\text{H}_{40}\text{NO}_{10}$ $[\text{M}+\text{NH}_4]^+$ 730.2652, found 730.2653. $[\alpha]_{\text{D}}^{35} = +0.26$ (c 0.01, CHCl_3).

Synthesis of 3,4,6-tri-O-benzyl-2-deoxy-D-glucopyranosyl-2-(1-phenyl)vinyl)benzoate (18g)

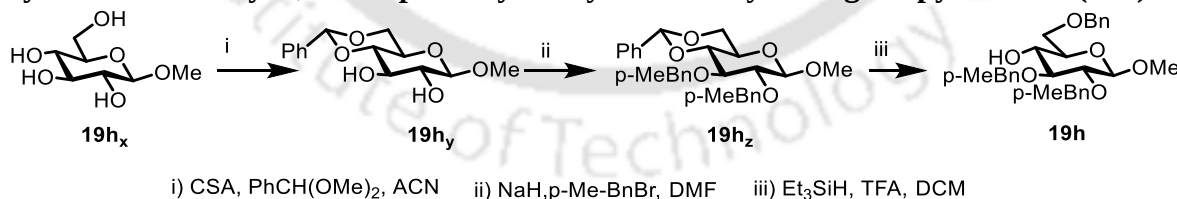


Compound **18g** was prepared from **17a** (434.5 mg, 1 mmol) according to General procedure 2. The crude product was purified by Flash column chromatography to afford **18a** (589.5 mg, 92 %, $\alpha:\beta$ = 1:2.2) as a colorless syrup, R_f = 0.53 (Hexane/EtOAc, 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.92 (dd, J = 7.8, 0.8 Hz, H), 7.82 (dd, J = 7.8, 0.9 Hz, 1H), 7.54 (td, J = 7.5, 1.2 Hz, 1H), 7.50 (td, J = 7.5, 1.2 Hz, 1H), 7.43 – 7.38 (m, 1H), 7.37 – 7.19 (m, 29H), 7.19 – 7.15 (m, 4H), 6.21 (d, J = 2.2 Hz, 1H), 5.72 (s, 1H), 5.68 (s, 1H), 5.54 (dd, J = 9.9, 2.0 Hz, 1H), 5.23 (s, 1H), 5.15 (s, 1H), 4.85 (d, J = 10.8 Hz, 1H), 4.83 (d, J = 11.0 Hz, 1H), 4.61 – 4.56 (m, 3H), 4.54 – 4.49 (m, 3H), 4.48 (d, J = 4.5 Hz, 1H), 4.45 (d, J = 12.1 Hz, 1H), 4.40 (q, J = 11.6 Hz, 1H), 3.72 (dd, J = 10.9, 4.0 Hz, 1H), 3.69 (d, J = 1.9 Hz, 1H), 3.66 (dt, J = 6.3, 2.7 Hz, 1H), 3.64 – 3.60 (m, 2H), 3.57 (dd, J = 16.7, 7.5 Hz, 2H), 3.51 (dd, J = 10.8, 1.4 Hz, 1H), 3.45 (ddd, J = 9.1, 3.7, 2.0 Hz, 1H), 2.13 – 2.09 (m, 1H), 2.05 (ddd, J = 12.5, 4.6, 2.1 Hz, 1H), 1.76 – 1.70 (m, 1H), 1.52 (dd, J = 22.6, 10.9 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 166.2, 165.3, 149.1, 148.9, 143.1, 142.6, 140.5, 140.1, 138.6, 138.5, 138.3, 138.2, 138.1, 138.1, 132.1, 131.8, 131.5, 131.1, 130.9, 130.3, 130.2, 130.0, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5, 126.9, 126.7, 114.4, 114.1, 93.1, 93.0, 78.9, 77.4, 75.9, 75.0, 74.8, 73.6, 73.5, 73.5, 71.7, 71.5, 68.7, 68.4, 34.8, 34.2. HRMS (ESI) calcd for $\text{C}_{42}\text{H}_{44}\text{NO}_6$ $[\text{M}+\text{NH}_4]^+$ 658.3163, found 658.3167. $[\alpha]_{\text{D}}^{35} = +0.38$ (c 0.01, CHCl_3).

Synthesis of acceptors

19a-g, 19i, were synthesized by following literature procedures.⁷¹

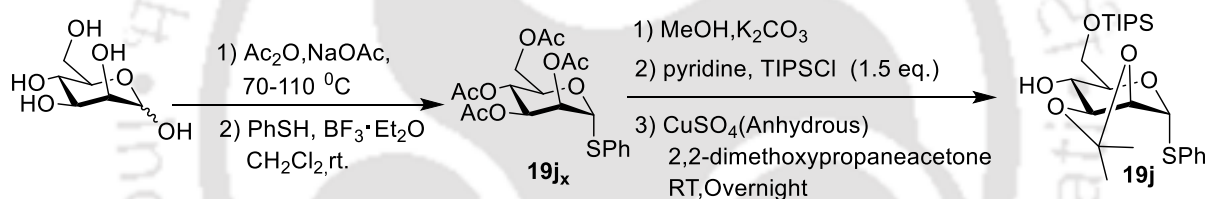
Synthesis of Methyl 2,3-di-*O*-*p*-methylbenzyl-6-*O*-benzyl- α -D-glucopyranoside (**19h**)



A catalytic amount of camphorsulfonic acid ($\text{pH} = 2$) was added to a CH_3CN solution (100.0 mL) of methyl β -D-glucopyranoside (5.0 g, 25.7 mmol, **19hx**) and $\text{PhCH}(\text{OMe})_2$ (11.6 mL, 77.1 mmol). The resulting solution was stirred at rt for 48 h, then neutralized with TEA and concentrated *in vacuo*. The crude was washed with water, brine, dried over Na_2SO_4 , concentrated *in vacuo*. The crude reaction mixture, dissolved in DMF, was treated with NaH, followed by *p*-methyl-benzyl bromide (*p*-Me-BnBr) at 0 °C. The resulting solution was stirred at room temperature overnight. After completion of the reaction, MeOH was added to quench excess NaH. The reaction mixture was concentrated *in vacuo*; then the crude was diluted with H_2O and extracted with CH_2Cl_2 (3 x 50.0 mL). The combined organic layers were washed with

brine, dried over Na_2SO_4 , concentrated *in vacuo*, and purified by flash column chromatography (hexane/AcOEt = 8:2) to get Methyl 2,3-di-paramethyl-O-benzyl-4,6-O-benzylidene- α -D-glucopyranoside (**19h_z**) as a white solid (7.85 g, 60 % over two steps). To a cooled solution (0 °C) of **19h_z** (2 g, 4.08 mmol) and Et_3SiH (3.26 mL, 20.4 mmol) in dry CH_2Cl_2 (40.0 mL), trifluoroacetic acid (1.56 mL, 20.4 mmol) was slowly added (15 min). The resulting solution was stirred at rt for 3 h, and then the mixture was diluted with CH_2Cl_2 and neutralized with a saturated aqueous solution of NaHCO_3 . The two phases were separated, the organic layer was washed with a saturated aqueous solution of NaHCO_3 and brine, dried over Na_2SO_4 , and concentrated *in vacuo*. The crude was purified by flash column chromatography (Hexane/AcOEt = 8:2) to yield compound **19h** as a white solid (1.46 g, 73 %). ^1H NMR (600 MHz, CDCl_3) δ 7.33 (d, J = 4.3 Hz, 4H), 7.30-7.24 (m, 3H), 7.21 (d, J = 7.8 Hz, 2H), 7.14 (d, J = 7.7 Hz, 4H), 4.90 – 4.85 (m, 2H, benzylic), 4.67 (d, J = 8.6 Hz, 1H), 4.65 (d, J = 9.3 Hz, 1H), 4.60 (d, J = 12.1 Hz, 1H), 4.57 (d, J = 12.1 Hz, 1H), 4.31 (d, J = 7.3 Hz, 1H), 3.77 (dd, J = 10.5, 3.4 Hz, 1H), 3.68 (dd, J = 10.5, 5.5 Hz, 1H), 3.57 (s, 3H), 3.54 (t, J = 9.0 Hz, 1H), 3.45 – 3.36 (m, 3H), 2.46 (s, 1H), 2.34 (s, 3H), 2.33 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.1, 137.7, 137.7, 135.8, 135.0, 129.3, 129.2, 128.4, 128.3, 128.2, 127.6, 98.3, 81.2, 79.3, 75.3, 73.6, 73.0, 70.5, 69.9, 69.4, 55.3, 21.2, 21.2. HRMS (ESI) calcd for $\text{C}_{30}\text{H}_{40}\text{NO}_6$ $[\text{M}+\text{NH}_4]^+$ 510.2856, found 510.2850. $[\alpha]_D^{35} = +0.1$ (c 0.01, CHCl_3).

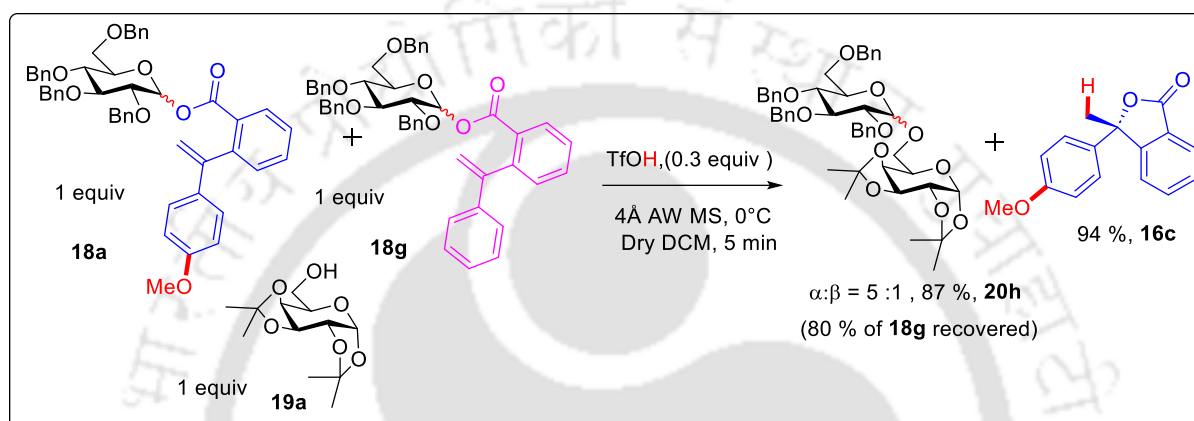
Phenyl 2,3-O-isopropylidene-6-O-triisopropylsilyl-1-thio- α -D-mannopyranoside (**19j**)



Ac_2O (20 mL) was added to a 100 mL flask, followed by the addition of anhydrous NaOAc (5.0 g). The mixture was stirred at 70 °C for 30 min. After that D-mannose (5.0 g, 2.7 mmol) was added into the flask portion-wise over 30 minutes. After vigorously stirring at 70 °C for another 30 min then the reaction mixture was heated at 110 °C for 6 h. After cooling down to room temperature, the mixture was poured into ice water (30 mL) and stirred vigorously for 1 hour. The resulting mixture was extracted by CH_2Cl_2 (40 mL $\times$ 3). The combined CH_2Cl_2 layer was washed with saturated NaHCO_3 solution and brine, dried over anhydrous Na_2SO_4 , filtered and concentrated. The residue was dried under a vacuum before being dissolved by anhydrous CH_2Cl_2 (80 mL). To the solution was added thiophenol (3.8 g), followed by the addition of $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (5.2 mL). The mixture was stirred at ambient temperature overnight and quenched by a saturated NaHCO_3 solution (20 mL). The organic layer was washed with saturated Na_2CO_3 aqueous solution and brine, dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated and purified by flash column chromatography to give compound **19j_x**. K_2CO_3 (100 mg) was added to a solution of **19j_x** (4.7 g, 10.6 mmol) in methanol (20 mL). After stirring at room temperature for 3 h, the mixture was filtered and the filtrate was concentrated. The residue was dissolved in anhydrous pyridine (20 mL), followed by the addition of TIPSCl (2.2 mL). The reaction mixture was stirred for 6 h after completion of reaction the mixture was diluted with CH_2Cl_2 (200 mL) and washed by 1M HCl solution, saturated NaHCO_3 solution and brine sequentially. The organic layer was dried over anhydrous Na_2SO_4 and concentrated and the residue was dissolved in anhydrous acetone (100 mL), followed by the addition of

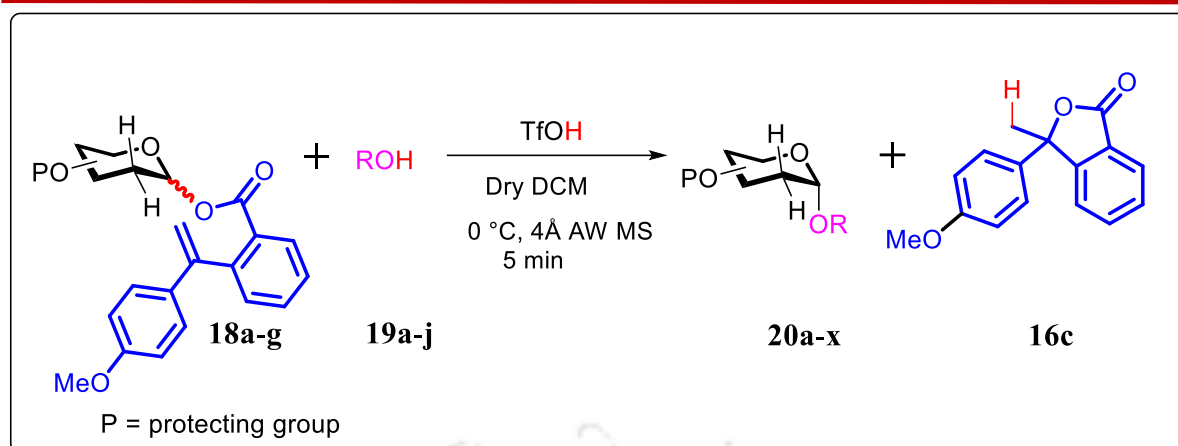
anhydrous CuSO_4 (10.0 g) and 2,2-dimethoxypropane. The mixture was stirred overnight and then filtered. The filtrate was concentrated and purified by flash column chromatography to give **19j** (3.5 g, 7.56 mmol, 70 %) as colorless syrup. $R_f = 0.6$ (Hexane/EtOAc = 5/1). ^1H NMR (500 MHz, CDCl_3) δ 7.47 (dd, $J = 8.0, 1.4$ Hz, 2H), 7.32 – 7.24 (m, 3H), 5.75 (s, 1H), 4.33 (dd, $J = 5.8, 0.6$ Hz, 1H), 4.21 – 4.17 (m, 1H), 4.03 (ddd, $J = 10.1, 5.8, 4.7$ Hz, 1H), 3.92 – 3.85 (m, 2H), 3.82 (dd, $J = 10.3, 6.1$ Hz, 1H), 3.32 (d, $J = 1.5$ Hz, 1H), 1.54 (s, 3H), 1.37 (s, 3H), 1.09 – 1.02 (m, 21H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 132.3, 130.8, 128.0, 126.5, 108.8, 82.8, 77.1, 74.9, 71.5, 68.6, 64.0, 27.0, 25.4, 16.9, 16.8, 10.8. HRMS (ESI) calcd for $\text{C}_{24}\text{H}_{40}\text{NaO}_5\text{Si}$ $[\text{M}+\text{NH}_4]^+$ 491.2263, found 491.2273. $[\alpha]_D^{35} = +0.68$ (c 0.025, CHCl_3).

Comparative study



Scheme 17: Comparative study

A solution of glycosyl donor **18a** (40.2 mg, 0.06 mmol) and **18g** (38.5 mg, 0.06 mmol), and acceptor **19a** (15.6 mg, 0.06 mmol) in dry CH_2Cl_2 (0.03 M) was stirred at room temperature for 60 min in the presence of activated acid washed (AW) 4Å MS (250 mg) under Ar atmosphere. Then the vessel was chilled to 0°C , to which TfOH (1.6 μl , 30 mol %) were added. The reaction mixture was stirred for 5 min at 0°C . Then, Et_3N was added to quench the reaction. The crude reaction mixture was worked up with water, washed with brine, dried by Na_2SO_4 , and concentrated in rotavapor. The resulting crude reaction mixture was purified through Flash column chromatography to afford the glycosylated products **20h** (35.3 mg, 87 %, $\alpha:\beta = 5:1$), **18g** (30.8 mg, 80 % recovered), and cyclized adduct **16c** (14.3 mg, 94 %). Spectral data for **16c**, ^1H NMR (400 MHz, CDCl_3) δ 7.91 (d, $J = 7.7$ Hz, 1H), 7.66 (td, $J = 7.6, 1.0$ Hz, 1H), 7.52 (td, $J = 7.6, 0.7$ Hz, 1H), 7.42 (d, $J = 7.7$ Hz, 1H), 7.36 – 7.31 (m, 2H), 6.89 – 6.84 (m, 2H), 3.79 (s, 3H), 2.02 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.0, 159.5, 154.4, 134.3, 132.6, 129.1, 126.8, 125.8, 125.2, 122.0, 114.0, 87.6, 55.3, 27.2. HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{15}\text{O}_3$ $[\text{M}+\text{H}]^+$ 255.1021, found 255.1025. $[\alpha]_D^{35} = -0.60$ (c 0.01, CHCl_3).

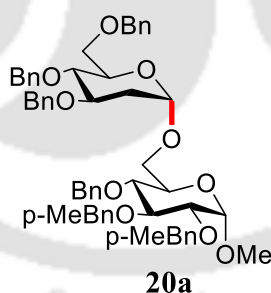


Scheme 24: General scheme for O-glycosylation

General procedure 3

A solution of glycosyl donor **18a-g** (1 equiv.) and acceptor **19a-j** (1.2 equiv.) in dry CH_2Cl_2 (0.03 M) was stirred at room temperature for 60 min in the presence of activated acid washed (AW) 4 Å MS (3.0 g/mmol) under Ar atmosphere. Then the vessel was chilled to 0 °C, to which triflic acid (30 mol %) were added. The reaction mixture was stirred for 5 min and TLC were checked. After completion of the reaction within 5 min, the temperature gradually rises to room temperature. Then Et_3N was added to quench the reaction. The crude reaction mixture was worked up with water, washed with brine, dried by Na_2SO_4 , and concentrated in rotavapor. The resulting crude reaction mixture was purified through Flash column chromatography to afford the glycosylated product.

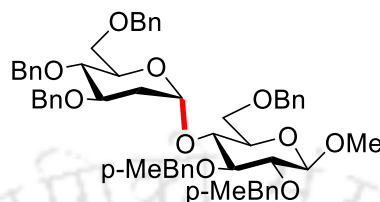
Synthesis of Methyl 2,3-di-*p*-methyl-O-benzyl-4-O-benzyl-6-O-(3,4,6-tri-O-benzyl-2-deoxy- α -D-glucopyranosyl)- α -D-glucopyranoside (**20a**)



Glycosylation of **18a** (40.2 mg, 0.06 mmol) with **19e** (35.5 mg, 0.072 mmol) according to General procedure 3 afforded **20a** (49 mg, 90 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.55 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.31 (t, J = 8.2 Hz, 3H), 7.29 - 7.20 (m, 19H), 7.13 (dd, J = 10.9, 8.0 Hz, 6H), 4.99 (d, J = 2.2 Hz, 1H), 4.93 (t, J = 11.8 Hz, 2H), 4.87 (d, J = 11.0 Hz, 1H), 4.75 (dd, J = 10.9, 8.8 Hz, 2H), 4.64 (dd, J = 11.7, 8.2 Hz, 2H), 4.60 (d, J = 11.5 Hz, 1H), 4.56 (d, J = 7.4 Hz, 1H), 4.56 - 4.51 (m, 2H), 4.47 (d, J = 11.0 Hz, 1H), 4.39 (d, J = 12.1 Hz, 1H), 3.96 (t, J = 9.1 Hz, 1H), 3.94 - 3.90 (m, 1H), 3.80 (dd, J = 11.3, 4.3 Hz, 1H), 3.72 (dd, J = 9.9, 3.3 Hz, 1H), 3.66 (d, J = 9.7 Hz, 1H), 3.59 (t, J = 9.2 Hz, 2H), 3.55 (d, J = 11.2 Hz, 1H), 3.51 - 3.44 (m, 3H), 3.33 (s, 3H), 2.34 (s, 3H), 2.33 (s, 3H), 2.29 (dd, J = 12.9, 4.9 Hz, 1H), 1.68 (td, J = 12.7, 3.2 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 137.7, 137.6, 137.4, 137.1, 136.6,

136.3, 134.7, 134.1, 128.1, 128.0, 127.3, 127.3, 127.3, 127.2, 127.2, 127.1, 126.8, 126.7, 126.7, 126.5, 126.5, 126.4, 97.0, 96.7, 81.1, 78.8, 77.1, 76.7, 76.2, 74.6, 73.8, 73.8, 72.4, 72.1, 70.7, 69.9, 68.7, 67.7, 64.7, 54.0, 34.3, 20.2. HRMS (ESI) calcd for $C_{57}H_{68}NO_{10}$ $[M+NH_4]^+$ 926.4843, found 926.4842. $[\alpha]_D^{35} = +0.30$ (c 0.01, $CHCl_3$).

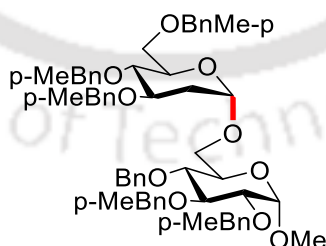
Synthesis of Methyl 2,3-di-*p*-methyl-*O*-benzyl-6-*O*-benzyl -4-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy- α -D-glucopyranosyl)- β -D-glucopyranoside (20b)



20b

Glycosylation of **18a** (40.2 mg, 0.06 mmol) with **19h** (35.5 mg, 0.072 mmol) according to General procedure 3 afforded **20b** (45.8 mg, 84 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.6$ (Hexane/EtOAc = 4:1, v/v). 1H NMR (600 MHz, $CDCl_3$) δ 7.32 – 7.24 (m, 18H), 7.20 (t, $J = 8.4$ Hz, 3H), 7.16 (d, $J = 6.9$ Hz, 2H), 7.13 – 7.09 (m, 5H), 5.40 (d, $J = 2.6$ Hz, 1H), 4.92 (d, $J = 10.9$ Hz, 1H), 4.88 – 4.81 (m, 2H), 4.61 (d, $J = 10.7$ Hz, 1H), 4.56 (d, $J = 12.4$ Hz, 2H), 4.54 – 4.50 (m, 3H), 4.48 (dd, $J = 11.4, 6.9$ Hz, 2H), 4.38 (d, $J = 12.2$ Hz, 1H), 4.29 (d, $J = 7.7$ Hz, 1H), 3.84 – 3.79 (m, 1H), 3.77 (d, $J = 10.3$ Hz, 1H), 3.67 (d, $J = 9.6$ Hz, 1H), 3.61 (dd, $J = 10.2, 5.8$ Hz, 3H), 3.57 (s, 3H), 3.56 – 3.49 (m, 2H), 3.43 (d, $J = 10.2$ Hz, 2H), 3.41 – 3.37 (m, 1H), 2.32 (s, 3H), 2.32 (s, 3H), 2.04 (dd, $J = 12.8, 4.5$ Hz, 1H), 1.53 (d, $J = 3.7$ Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 137.8, 137.7, 137.5, 137.3, 136.3, 136.2, 134.5, 134.5, 128.0, 127.3, 127.3, 127.3, 127.2, 126.9, 126.8, 126.6, 126.5, 126.5, 126.4, 103.6, 98.1, 83.8, 81.3, 77.2, 74.9, 74.1, 73.8, 73.8, 73.4, 72.5, 72.4, 70.8, 70.6, 69.0, 67.8, 56.0, 34.7, 20.1, 20.1. HRMS (ESI) calcd for $C_{57}H_{68}NO_{10}$ $[M+NH_4]^+$ 926.4843, found 926.4843. $[\alpha]_D^{35} = +0.4$ (c 0.01, $CHCl_3$).

Synthesis of Methyl 2,3-di-*p*-methyl-*O*-benzyl-4-*O*-benzyl -6-*O*-(3,4,6-tri-*p*-methyl-*O*-benzyl-2-deoxy- α -D-glucopyranosyl)- α -D-glucopyranoside (20c)

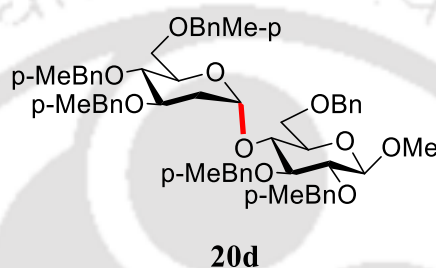


20c

Glycosylation of **18b** (42.8 mg, 0.06 mmol) with acceptor **19e** (35.5 mg, 0.072 mmol) according to General procedure 3 afforded **20c** (50.2 mg, 88 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.5.6$ (Hexane: EtOAc = 4: 1, v/v). 1H NMR (600 MHz, $CDCl_3$) δ 7.27 – 7.19 (m, 11H), 7.17 (d, $J = 7.7$ Hz, 2H), 7.12 (dd, $J = 11.1, 8.0$ Hz, 4H), 7.10 – 7.05 (m, 6H), 7.01 (d, $J = 7.7$ Hz, 2H), 4.98 (d, $J = 2.2$ Hz, 1H), 4.94 (d, $J = 10.5$ Hz, 1H), 4.91 (d, $J = 11.1$ Hz, 1H), 4.80 (d, $J = 10.7$ Hz, 1H), 4.76 (d, $J = 5.1$ Hz, 1H), 4.74 (d, $J = 3.4$ Hz, 1H), 4.63 (d, $J = 12.0$ Hz, 1H), 4.58 (q, $J = 11.6$

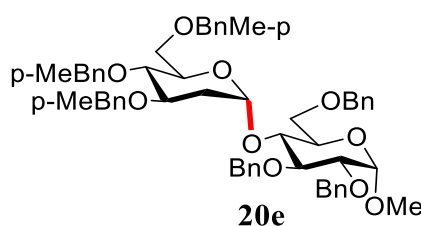
Hz, 2H), 4.53 (dd, $J = 11.1, 7.9$ Hz, 3H), 4.39 (d, $J = 10.7$ Hz, 1H), 4.34 (d, $J = 12.0$ Hz, 1H), 3.96 (t, $J = 9.2$ Hz, 1H), 3.92 – 3.87 (m, 1H), 3.78 (dd, $J = 11.3, 4.4$ Hz, 1H), 3.71 (dd, $J = 9.9, 3.5$ Hz, 1H), 3.63 (d, $J = 9.7$ Hz, 1H), 3.58 (dd, $J = 10.7, 3.4$ Hz, 1H), 3.57 – 3.53 (m, 2H), 3.48 (dd, $J = 9.9, 3.7$ Hz, 1H), 3.45 (d, $J = 9.7$ Hz, 2H), 3.32 (s, 3H), 2.34 (s, 3H), 2.33 (s, 6H), 2.30 (s, 3H), 2.29 (s, 3H), 2.26 (dd, $J = 12.9, 4.9$ Hz, 1H), 1.65 (td, $J = 12.8, 3.3$ Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 137.4, 136.6, 136.2, 136.2, 136.1, 136.0, 134.7, 134.7, 134.6, 134.2, 134.1, 128.1, 128.0, 128.0, 127.9, 127.8, 127.3, 127.2, 127.1, 127.0, 126.9, 126.8, 126.5, 97.0, 96.8, 81.1, 78.9, 77.0, 76.8, 74.6, 73.8, 73.6, 72.2, 72.1, 70.6, 69.9, 68.7, 67.4, 64.7, 54.0, 34.3, 20.1, 20.1, 20.1. HRMS (ESI) calcd for $\text{C}_{60}\text{H}_{74}\text{NO}_{10}$ $[\text{M}+\text{NH}_4]^+$ 968.5313, found 968.5313. $[\alpha]_{\text{D}}^{35} = +0.28$ (c 0.01, CHCl_3).

Synthesis of Methyl 2,3-di-*p*-methyl-*O*-benzyl-6-*O*-benzyl-4-*O*-(3,4,6-tri-*p*-methyl-*O*-benzyl-2-deoxy- α -D-glucopyranosyl)- β -D-glucopyranoside (20d)



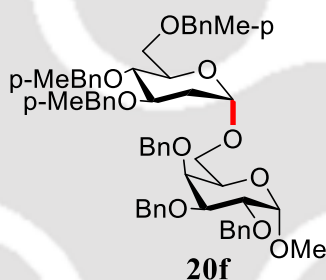
Glycosylation of **18b** (42.8 mg, 0.06 mmol) with acceptor **19h** (35.5 mg, 0.072 mmol) according to General procedure 3 afforded **20d** (48.5 mg, 85 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.59$ (Hexane/EtOAc = 4:1, v/v) ^1H NMR (600 MHz, CDCl_3) δ 7.28 (dt, $J = 12.7, 6.2$ Hz, 4H), 7.25 (d, $J = 13.2$ Hz, 1H), 7.21 (d, $J = 7.4$ Hz, 3H), 7.18 (t, $J = 7.0$ Hz, 4H), 7.13 – 7.07 (m, 11H), 7.03 (d, $J = 7.6$ Hz, 2H), 5.38 (d, $J = 1.3$ Hz, 1H), 4.91 (d, $J = 10.8$ Hz, 1H), 4.85 (d, $J = 10.7$ Hz, 1H), 4.77 (d, $J = 10.5$ Hz, 1H), 4.61 (d, $J = 10.7$ Hz, 1H), 4.54 (d, $J = 11.7$ Hz, 2H), 4.51 (dd, $J = 10.5, 3.8$ Hz, 3H), 4.49 – 4.46 (m, 1H), 4.38 (d, $J = 10.5$ Hz, 1H), 4.33 (d, $J = 12.0$ Hz, 1H), 4.29 (d, $J = 7.6$ Hz, 1H), 3.82 – 3.75 (m, 2H), 3.65 (d, $J = 9.6$ Hz, 1H), 3.62 – 3.58 (m, 3H), 3.57 (s, 3H), 3.50 (t, $J = 8.2$ Hz, 2H), 3.41 (dd, $J = 11.9, 6.8$ Hz, 2H), 3.38 (d, $J = 9.2$ Hz, 1H), 2.32 (s, 9H), 2.31 (s, 3H), 2.30 (s, 3H), 2.02 (dd, $J = 12.9, 4.3$ Hz, 1H), 1.54 (td, $J = 12.9, 3.3$ Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 137.5, 136.3, 136.2, 136.2, 136.2, 136.1, 134.7, 134.6, 134.4, 134.4, 134.1, 128.0, 128.0, 128.0, 127.9, 127.3, 127.2, 127.1, 127.1, 126.7, 126.6, 126.5, 126.4, 103.5, 98.1, 83.7, 81.2, 76.9, 76.1, 74.9, 74.1, 73.6, 73.4, 72.3, 72.3, 70.8, 70.6, 68.9, 67.4, 56.0, 34.7, 20.1, 20.1, 20.1. HRMS (ESI) calcd for $\text{C}_{60}\text{H}_{74}\text{NO}_{10}$ $[\text{M}+\text{NH}_4]^+$ 968.5313, found 968.5312. $[\alpha]_{\text{D}}^{35} = +0.48$ (c 0.01, CHCl_3).

Synthesis of Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(3,4,6-tri-*p*-methyl-*O*-benzyl-2-deoxy- α -D-glucopyranosyl)- α -D-glucopyranoside (20e)



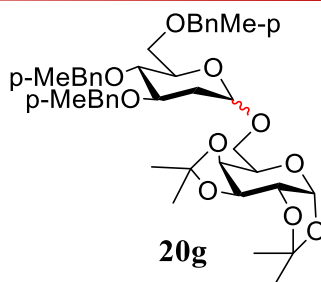
Glycosylation of **18b** (42.8 mg, 0.06 mmol) with **19f** (33.5 mg, 0.072 mmol) according to General procedure 3 afforded **20e** (47.11 mg, 85 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.6 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.31 (dd, J = 13.4, 6.1 Hz, 5H), 7.29–7.24 (m, 9H), 7.22 – 7.20 (m, 1H), 7.18 (d, J = 7.8 Hz, 2H), 7.15 (d, J = 7.7 Hz, 2H), 7.12 – 7.05 (m, 6H), 7.02 (d, J = 7.7 Hz, 2H), 5.40 (d, J = 2.3 Hz, 1H), 5.01 (d, J = 11.1 Hz, 1H), 4.78 (d, J = 10.6 Hz, 1H), 4.73 (d, J = 12.0 Hz, 1H), 4.61 (dd, J = 9.6, 2.7 Hz, 3H), 4.54 – 4.46 (m, 4H), 4.43 (d, J = 12.1 Hz, 1H), 4.38 (d, J = 10.6 Hz, 1H), 4.29 (d, J = 12.0 Hz, 1H), 3.86 (t, J = 9.1 Hz, 1H), 3.84 – 3.79 (m, 1H), 3.71 – 3.61 (m, 5H), 3.57 (dd, J = 10.4, 3.0 Hz, 1H), 3.53 – 3.48 (m, 2H), 3.38 (s, 3H), 3.37 (s, 1H), 2.33 (s, 3H), 2.31 (s, 3H), 2.29 (s, 3H), 2.05 (dd, J = 12.8, 4.5 Hz, 1H), 1.57 – 1.52 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.6, 138.3, 138.0, 137.2, 137.2, 137.2, 135.7, 135.6, 135.0, 129.0, 129.0, 128.9, 128.5, 128.4, 128.3, 128.1, 128.1, 128.1, 127.9, 127.7, 127.6, 127.5, 127.4, 127.4, 99.5, 97.7, 82.1, 80.1, 77.9, 77.1, 76.2, 75.4, 74.7, 73.3, 73.2, 73.2, 71.8, 71.7, 69.8, 69.5, 68.3, 55.2, 35.9, 21.2, 21.2, 21.2. HRMS (ESI) calcd for $\text{C}_{58}\text{H}_{70}\text{NO}_{10}$ $[\text{M}+\text{NH}_4]^+$ 940.5000, found 940.4990. $[\alpha]_{\text{D}}^{35} = +0.52$ (c 0.015, CHCl_3).

Synthesis of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4,6-tri-*para*-methyl-*O*-benzyl-2-deoxy- α -D-glucopyranosyl)- α -D-galactopyranoside (**20f**)



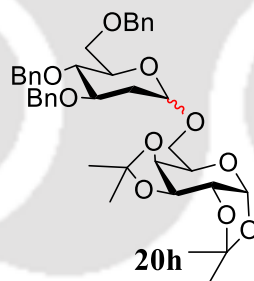
Glycosylation of **18b** (42.8 mg, 0.06 mmol) with **19b** (33.5 mg, 0.072 mmol) according to General procedure 3 afforded **20f** (48.8 mg, 88 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.5 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.41 (d, J = 7.4 Hz, 2H), 7.38 – 7.34 (m, 4H), 7.33 – 7.24 (m, 9H), 7.22 (d, J = 7.6 Hz, 4H), 7.11 (t, J = 7.7 Hz, 4H), 7.08 (d, J = 7.6 Hz, 2H), 7.00 (d, J = 7.8 Hz, 2H), 4.95 – 4.92 (m, 1H), 4.89 (d, J = 11.7 Hz, 1H), 4.85 – 4.81 (m, 1H), 4.79 (d, J = 10.5 Hz, 1H), 4.76 (d, J = 11.7 Hz, 1H), 4.68 (d, J = 12.1 Hz, 1H), 4.64 (d, J = 3.7 Hz, 2H), 4.61 (d, J = 12.1 Hz, 1H), 4.58 (t, J = 5.6 Hz, 3H), 4.41 (d, J = 12.0 Hz, 1H), 4.38 (d, J = 10.4 Hz, 1H), 4.02 (dd, J = 10.0, 3.5 Hz, 1H), 3.92 (dd, J = 10.0, 2.4 Hz, 1H), 3.86 – 3.80 (m, 2H), 3.76 – 3.70 (m, 2H), 3.63 (d, J = 9.9 Hz, 1H), 3.61 – 3.53 (m, 3H), 3.34 – 3.30 (m, 1H), 3.29 (s, 3H), 2.32 (s, 3H), 2.31 (s, 6H), 2.01 (dd, J = 12.7, 4.7 Hz, 1H), 1.61 – 1.56 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.8, 138.4, 137.4, 137.3, 137.3, 135.6, 135.4, 134.9, 129.1, 129.1, 129.0, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 127.8, 127.8, 127.6, 127.5, 98.6, 97.2, 79.2, 77.8, 77.1, 76.5, 74.9, 74.6, 74.5, 73.6, 73.5, 73.3, 71.7, 70.7, 68.6, 68.1, 65.5, 55.3, 55.2, 35.40, 21.2, 21.2. HRMS (ESI) calcd for $\text{C}_{58}\text{H}_{70}\text{NO}_{10}$ $[\text{M}+\text{NH}_4]^+$ 940.5000, found 940.4993. $[\alpha]_{\text{D}}^{35} = +0.40$ (c 0.01, CHCl_3).

Synthesis of 1,2;3,4-*di*-*O*-isopropylidene-6-*O*-(3,4,6-tri-*p*-methyl-*O*-benzyl-2-deoxy-D-glucopyranosyl)- α -D-galactopyranose (**20g**)

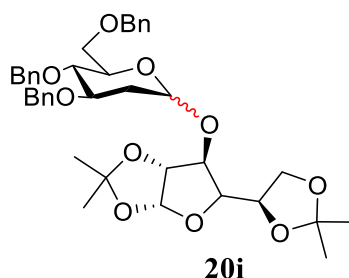


Glycosylation of **18b** (42.8 mg, 0.06 mmol) with **19a** (18.7 mg, 0.072 mmol) according to General procedure 3 afforded **20g** (37.5 mg, 87 %, $\alpha:\beta$ = 6:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.54 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.23 (d, J = 7.7 Hz, 4H), 7.12 (t, J = 7.4 Hz, 4H), 7.07 (d, J = 7.6 Hz, 2H), 7.03 (d, J = 7.8 Hz, 2H), 5.51 (d, J = 4.9 Hz, 1H), 5.00 (d, J = 2.3 Hz, 1H), 4.81 (d, J = 10.6 Hz, 1H), 4.60 (q, J = 12.4 Hz, 4H), 4.43 (t, J = 11.5 Hz, 2H), 4.30 (dd, J = 4.6, 1.9 Hz, 1H), 4.21 (d, J = 7.9 Hz, 1H), 3.98 – 3.91 (m, 2H), 3.79 – 3.68 (m, 3H), 3.65 (dd, J = 10.3, 7.1 Hz, 1H), 3.61 (d, J = 9.4 Hz, 2H), 2.33 (s, 3H), 2.32 (s, 3H), 2.32 (s, 3H), 2.30 – 2.27 (m, 1H), 1.73 – 1.67 (m, 1H), 1.51 (s, 3H), 1.43 (s, 3H), 1.34 (s, 3H), 1.32 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 137.3, 137.2, 137.1, 135.8, 135.5, 135.1, 129.0, 129.0, 128.9, 128.1, 128.1, 127.7, 109.3, 108.5, 97.3, 96.3, 78.0, 77.4, 74.8, 73.3, 71.7, 71.0, 70.9, 70.7, 70.6, 68.4, 65.6, 65.3, 35.4, 26.2, 26.0, 24.9, 24.6, 21.2. HRMS (ESI) calcd for $\text{C}_{42}\text{H}_{58}\text{NO}_{10}$ $[\text{M}+\text{NH}_4]^+$ 736.4061, found 736.4069. $[\alpha]_D^{35}$ = + 0.30 (c 0.01, CHCl_3).

Synthesis of 1,2;3,4-di-*O*-isopropylidene-6-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranosyl)- α -D-galactopyranose (**20h**)

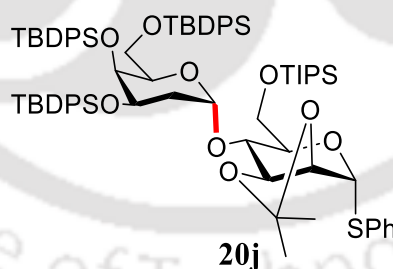


Glycosylation of **18a** (40.2 mg, 0.06 mmol) with **19a** (18.7 mg, 0.072 mmol) according to General procedure 3 afforded **20h** (34.4 mg, 85 %, $\alpha:\beta$ = 5:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.55 (Hexane/EtOAc = 4:1, v/v). For α anomer, ^1H NMR (500 MHz, CDCl_3) δ 7.36 – 7.28 (m, 10H), 7.28 – 7.24 (m, 3H), 7.18 (d, J = 7.4 Hz, 2H), 5.51 (d, J = 4.9 Hz, 1H), 5.02 (d, J = 2.4 Hz, 1H), 4.88 (d, J = 10.8 Hz, 1H), 4.69 – 4.62 (m, 3H), 4.59 (dd, J = 11.7, 3.5 Hz, 1H), 4.56 – 4.47 (m, 2H), 4.32 – 4.28 (m, 1H), 4.22 (d, J = 7.9 Hz, 1H), 4.03 – 3.97 (m, 1H), 3.95 (dd, J = 11.7, 4.9 Hz, 1H), 3.79 (dd, J = 7.3, 3.4 Hz, 2H), 3.74 – 3.71 (m, 1H), 3.66 (dd, J = 11.6, 5.2 Hz, 3H), 2.32 (dd, J = 13.0, 4.9 Hz, 1H), 1.72 (td, J = 13.0, 3.3 Hz, 1H), 1.51 (s, 3H), 1.43 (s, 3H), 1.33 (s, 3H), 1.32 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 137.8, 137.6, 137.2, 127.3, 127.3, 127.3, 126.9, 126.9, 126.7, 126.5, 126.5, 126.5, 108.3, 107.5, 96.3, 95.3, 77.2, 76.5, 73.9, 72.5, 70.8, 70.0, 69.7, 67.8, 64.7, 64.4, 34.4, 25.1, 25.0, 23.9, 23.6. HRMS (ESI) calcd for $\text{C}_{39}\text{H}_{52}\text{NO}_{10}$ $[\text{M}+\text{NH}_4]^+$ 694.3591, found 694.3587. $[\alpha]_D^{35}$ = + 0.36 (c 0.01, CHCl_3).

Synthesis of 1,2;4,6-di-*O*-isopropylidene-3-*O*-(2,3,4-*tri-O*-benzyl-*D*-glucopyranosyl)- α -*D*-glucofuranose (20i)


Glycosylation of **18a** (40.2 mg, 0.06 mmol) with **19c** (18.7 mg, 0.072 mmol) according to General procedure 3 afforded **20i** (33.3 mg, 82 %, α/β = 7:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.57 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.33 (dt, J = 12.1, 7.5 Hz, 10H), 7.27 (dd, J = 13.7, 7.8 Hz, 3H), 7.18 (d, J = 6.7 Hz, 2H), 5.82 (d, J = 3.3 Hz, 1H), 5.24 (d, J = 2.3 Hz, 1H), 4.89 (d, J = 10.6 Hz, 1H), 4.64 (dd, J = 12.4, 5.1 Hz, 4H), 4.52 (dd, J = 11.1, 8.7 Hz, 2H), 4.24 (d, J = 2.1 Hz, 1H), 4.14 (dd, J = 13.9, 5.7 Hz, 1H), 4.11 – 4.08 (m, 1H), 4.06 (dd, J = 8.4, 2.2 Hz, 1H), 3.97 (dd, J = 8.4, 5.8 Hz, 1H), 3.95 – 3.91 (m, 1H), 3.81 – 3.76 (m, 2H), 3.73 (d, J = 8.9 Hz, 1H), 3.60 (t, J = 9.2 Hz, 1H), 2.27 (dd, J = 12.8, 4.7 Hz, 1H), 1.75 – 1.69 (m, 1H), 1.47 (s, 3H), 1.40 (s, 3H), 1.32 (s, 3H), 1.23 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.5, 138.2, 138.0, 128.4, 128.4, 128.4, 128.1, 127.9, 127.8, 127.7, 127.7, 111.8, 109.2, 105.3, 98.7, 83.7, 81.3, 80.2, 78.1, 77.2, 75.2, 73.6, 72.5, 71.9, 71.7, 68.9, 67.7, 35.2, 26.8, 26.1, 25.4. HRMS (ESI) calcd for $\text{C}_{39}\text{H}_{52}\text{NO}_{10}$ $[\text{M}+\text{NH}_4]^+$ 694.3591, found 694.3589.

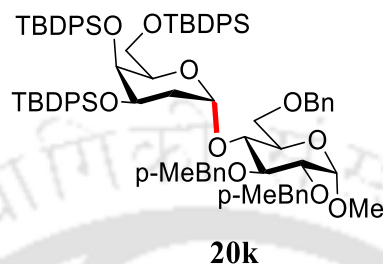
$[\alpha]_D^{35} = +0.12$ (c 0.01, CHCl_3).

Phenyl 2,3-*O*-isopropylidene-6-*O*-triisopropylsilyl-4-(3,4,6-*tri-O*-*tert*-butyldiphenylsilyl-2-deoxy- α -*D*-galactopyranosyl)- α -*D*-thiomannopyranoside (20j)


Glycosylation of **18e** (55.8 mg, 0.05 mmol) with **19j** (27.9 mg, 0.06 mmol) according to General procedure 3 afforded **20j** (59.9 mg, 90 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.8 (Hexane/EtOAc = 7:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.65 (d, J = 7.2 Hz, 2H), 7.60 (d, J = 7.2 Hz, 2H), 7.53 – 7.47 (m, 7H), 7.42 – 7.29 (m, 11H), 7.28 – 7.22 (m, 5H), 7.19 (dd, J = 13.5, 6.4 Hz, 4H), 7.15 (t, J = 7.5 Hz, 2H), 6.95 (t, J = 7.3 Hz, 2H), 5.69 (s, 1H), 5.43 (bs, 1H), 4.26 (d, J = 5.4 Hz, 1H), 3.98 – 3.94 (m, 1H), 3.93 (d, J = 8.6 Hz, 1H), 3.87–3.82 (m, 2H), 3.72 (d, J = 10.0 Hz, 1H), 3.68 – 3.56 (m, 3H), 3.45 (d, J = 6.5 Hz, 1H), 2.93 (d, J = 9.3 Hz, 1H), 2.34 (dt, J = 11.7, 9.3 Hz, 1H), 1.42 (s, 3H), 1.32 (s, 3H), 1.29 – 1.26 (m, 1H), 1.03 (s, 9H), 0.99 (s, 9H), 0.89 – 0.81 (m, 30H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 136.5, 136.2, 136.1, 135.8, 135.8, 135.5, 134.5, 133.8, 133.8, 133.7, 133.5, 133.4, 132.3, 131.5, 129.7, 129.5, 129.5, 129.3, 129.2, 129.0,

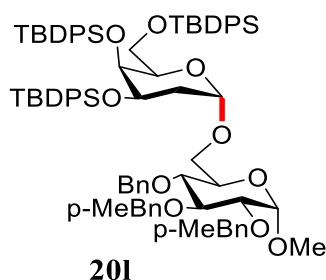
128.8, 127.7, 127.6, 127.5, 127.4, 127.2, 127.0, 109.4, 95.9, 84.3, 78.6, 76.5, 74.8, 72.6, 71.9, 71.5, 69.5, 65.5, 64.0, 33.5, 27.9, 27.2, 26.7, 26.5, 20.0, 18.8, 18.8, 17.9, 17.9, 11.7. HRMS (ESI) calcd for $C_{78}H_{108}NO_9SSi_4$ $[M+NH_4]^+$ 1346.6822, found 1346.6822. $[\alpha]_D^{35} = +0.84$ (c 0.025, $CHCl_3$).

Synthesis of Methyl 2,3-di-*p*-methyl-*O*-benzyl-6-*O*-benzyl-4-*O*-(3,4,6-tri-*O*-tert-butyldiphenylsilyl-2-deoxy- α -D-galactopyranosyl)- α -D-glucopyranoside (20k)



Glycosylation of **18e** (55.8 mg, 0.05 mmol) with **19g** (29.6 mg, 0.06 mmol) according to General procedure 3 afforded **20k** (56.9 mg, 84 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.75$ (Hexane/EtOAc = 7:1, v/v). 1H NMR (600 MHz, $CDCl_3$) δ 7.60 (d, $J = 7.2$ Hz, 2H), 7.50 – 7.44 (m, 9H), 7.43 – 7.37 (m, 4H), 7.35 (t, $J = 7.5$ Hz, 2H), 7.31 (t, $J = 7.4$ Hz, 2H), 7.27 (d, $J = 7.5$ Hz, 2H), 7.24 – 7.17 (m, 13H), 7.09 – 7.06 (m, 4H), 6.94 (t, $J = 7.4$ Hz, 2H), 6.89 (t, $J = 7.2$ Hz, 2H), 6.86 – 6.82 (m, 1H), 5.39 (d, $J = 2.5$ Hz, 1H), 4.86 (d, $J = 10.7$ Hz, 1H), 4.70 (d, $J = 12.0$ Hz, 1H), 4.54 (d, $J = 12.0$ Hz, 1H), 4.45 (d, $J = 3.3$ Hz, 1H), 4.34 (d, $J = 10.0$ Hz, 1H), 4.32 (d, $J = 8.3$ Hz, 1H), 4.15 (d, $J = 12.1$ Hz, 1H), 3.68 (d, $J = 10.9$ Hz, 1H), 3.60 – 3.54 (m, 3H), 3.45 (s, 3H), 3.40 – 3.32 (m, 3H), 3.31 (d, $J = 9.5$ Hz, 1H), 3.17 (dd, $J = 10.1, 8.1$ Hz, 1H), 3.01 (d, $J = 6.9$ Hz, 1H), 2.75 (d, $J = 9.3$ Hz, 1H), 2.38 (s, 3H), 2.31 (s, 3H), 2.22 (td, $J = 12.2, 3.3$ Hz, 1H), 1.32 – 1.28 (m, 1H), 1.03 (s, 9H), 0.98 (s, 9H), 0.86 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 138.1, 137.6, 137.2, 136.6, 136.2, 136.1, 135.9, 135.6, 135.6, 134.9, 133.9, 133.8, 133.5, 133.4, 132.4, 129.8, 129.6, 129.3, 129.3, 129.1, 129.1, 129.0, 128.4, 128.0, 128.0, 127.8, 127.6, 127.5, 127.5, 127.3, 127.0, 97.7, 82.2, 79.6, 75.0, 74.3, 73.2, 73.1, 72.6, 72.4, 69.8, 69.7, 69.6, 65.5, 55.0, 33.8, 27.2, 27.2, 26.9, 21.3, 21.2, 20.0, 18.8, 18.8. HRMS (ESI) calcd for $C_{84}H_{104}NO_{10}Si_3$ $[M+NH_4]^+$ 1370.6968, found 1370.6963. $[\alpha]_D^{35} = +1.14$ (c 0.04, $CHCl_3$).

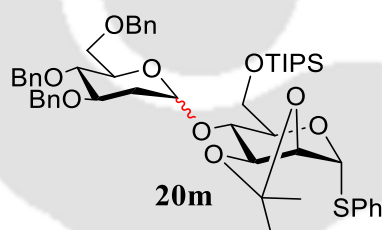
Synthesis of Methyl 2,3-di-*p*-methyl-*O*-benzyl-4-*O*-benzyl-6-*O*-(3,4,6-tri-*O*-tert-butyldiphenylsilyl-2-deoxy- α -D-galactopyranosyl)- α -D-glucopyranoside (20l)



Glycosylation of **18e** (55.8 mg, 0.05 mmol) with **19e** (29.6 mg, 0.06 mmol) according to General procedure 3 afforded **20l** (61.5 mg, 91 %, α only) as a colorless syrup. The crude

product was purified through flash column chromatography, $R_f = 0.7$ (Hexane/EtOAc = 7:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.55 – 7.51 (m, 4H), 7.46 (d, $J = 6.5$ Hz, 4H), 7.42 – 7.34 (m, 5H), 7.32 – 7.25 (m, 9H), 7.23–7.18 (m, 7H), 7.17 – 7.06 (m, 12H), 7.02 (t, $J = 7.4$ Hz, 2H), 4.98 (d, $J = 2.3$ Hz, 1H), 4.94 (d, $J = 10.7$ Hz, 1H), 4.74 (merge d, 2H), 4.68 (d, $J = 12.2$ Hz, 1H), 4.61 (d, $J = 10.9$ Hz, 1H), 4.51 (d, $J = 3.2$ Hz, 1H), 4.18 (d, $J = 10.9$ Hz, 1H), 4.00 (d, $J = 10.0$ Hz, 1H), 3.88 (t, $J = 9.3$ Hz, 1H), 3.75 (s, 1H), 3.71 (dd, $J = 11.6, 3.9$ Hz, 1H), 3.58 – 3.54 (m, 1H), 3.52 (dd, $J = 9.8, 3.0$ Hz, 1H), 3.46 (d, $J = 11.5$ Hz, 1H), 3.39 (dd, $J = 9.6, 3.3$ Hz, 1H), 3.36 (d, $J = 5.2$ Hz, 1H), 3.20 (s, 3H), 3.16 (t, $J = 9.5$ Hz, 1H), 2.86 (dd, $J = 10.4, 2.3$ Hz, 1H), 2.41 – 2.36 (m, 1H), 2.35 (s, 3H), 2.33 (s, 3H), 1.69 – 1.63 (m, 1H), 1.00 (s, 9H), 0.97 (s, 9H), 0.84 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 137.5, 136.5, 136.0, 135.4, 135.1, 135.1, 134.9, 134.8, 134.7, 134.5, 134.2, 132.9, 132.6, 131.7, 128.8, 128.6, 128.4, 128.2, 128.1, 128.0, 127.9, 127.2, 127.1, 126.9, 126.5, 126.4, 126.4, 126.3, 126.1, 97.0, 96.8, 80.9, 78.4, 76.8, 74.4, 73.9, 72.7, 71.9, 71.2, 69.2, 69.1, 64.1, 53.8, 32.5, 26.3, 26.2, 25.8, 20.2, 19.0, 18.0, 17.8. HRMS (ESI) calcd for $\text{C}_{84}\text{H}_{104}\text{NO}_{10}\text{Si}_3$ $[\text{M}+\text{NH}_4]^+$ 1370.6968, found 1370.6974. $[\alpha]_{\text{D}}^{35} = +0.50$ (c 0.01, CHCl_3).

Phenyl 2,3-O-isopropylidene-6-O-triisopropylsilyl-4-(3,4,6-tri-O-benzyl-2-deoxy-D-glucopyranosyl)- α -D-thiomannopyranoside (20m)

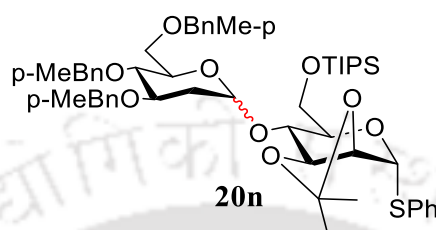


Glycosylation of **18a** (40.2 mg, 0.06 mmol) with **19j** (33.8 mg, 0.072 mmol) according to General procedure 3 afforded **20m** (44 mg, 83 %, $\alpha:\beta = 14:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.7$ (Hexane/EtOAc = 4:1, v/v). The α anomer, ^1H NMR (600 MHz, CDCl_3) δ 7.51 (d, $J = 6.8$ Hz, 2H), 7.35 – 7.23 (m, 16H), 7.18 (d, $J = 6.9$ Hz, 2H), 5.77 (s, 1H), 5.59 (d, $J = 1.8$ Hz, 1H), 4.90 (d, $J = 11.2$ Hz, 1H), 4.66 (d, $J = 11.5$ Hz, 1H), 4.62 (dd, $J = 11.9, 6.0$ Hz, 2H), 4.54 (d, $J = 11.2$ Hz, 1H), 4.48 (d, $J = 12.2$ Hz, 1H), 4.31 (d, $J = 5.5$ Hz, 1H), 4.27 – 4.24 (m, 1H), 4.06 – 4.02 (m, 1H), 3.94 – 3.88 (m, 2H), 3.86 – 3.80 (m, 2H), 3.77 – 3.72 (m, 2H), 3.72 – 3.68 (m, 1H), 3.58 (d, $J = 9.1$ Hz, 1H), 2.31 (dd, $J = 12.8, 4.4$ Hz, 1H), 1.76 (td, $J = 12.9, 3.3$ Hz, 1H), 1.52 (s, 3H), 1.33 (s, 3H), 1.00 – 0.93 (m, 21H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.9, 138.7, 138.0, 133.7, 131.6, 128.9, 128.4, 128.3, 128.1, 128.0, 127.6, 127.6, 127.6, 127.5, 127.4, 127.3, 109.7, 95.7, 83.9, 78.6, 77.9, 77.5, 76.4, 74.6, 73.5, 71.9, 71.5, 70.8, 70.6, 68.5, 62.7, 35.6, 27.9, 26.7, 18.0, 18.0, 11.9. HRMS (ESI) calcd for $\text{C}_{51}\text{H}_{72}\text{NO}_9\text{SSi}$ $[\text{M}+\text{NH}_4]^+$ 902.4697, found 902.4698. $[\alpha]_{\text{D}}^{35} = +0.38$ (c 0.01, CHCl_3).

The β anomer ^1H NMR (600 MHz, CDCl_3) δ 7.44 (d, $J = 7.2$ Hz, 2H), 7.36 – 7.22 (m, 16H), 7.20 – 7.17 (m, 2H), 5.77 (s, 1H), 4.87 (d, $J = 10.7$ Hz, 1H), 4.76 (d, $J = 8.6$ Hz, 1H), 4.66 (d, $J = 11.7$ Hz, 1H), 4.62 (d, $J = 12.2$ Hz, 1H), 4.59 (d, $J = 11.7$ Hz, 1H), 4.54 (d, $J = 10.7$ Hz, 1H), 4.50 (d, $J = 12.2$ Hz, 1H), 4.36 – 4.32 (m, 1H), 4.30 (d, $J = 5.5$ Hz, 1H), 4.08 (dd, $J = 9.5, 7.6$ Hz, 1H), 3.94 (d, $J = 9.6$ Hz, 1H), 3.82 (dd, $J = 11.4, 2.5$ Hz, 1H), 3.75 (dd, $J = 10.7, 4.4$ Hz, 1H), 3.72 (dd, $J = 11.6, 1.8$ Hz, 1H), 3.67 (dd, $J = 10.4, 1.3$ Hz, 1H), 3.60 (dd, $J = 10.6, 4.8$ Hz, 2H), 3.36 (d, $J = 3.0$ Hz, 1H), 2.30 (dd, $J = 12.4, 1.9$ Hz, 1H), 1.73 – 1.68 (m, 1H), 1.46

(s, 3H), 1.33 (s, 3H), 1.08 – 0.96 (m, 21H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 138.3, 138.3, 133.9, 131.1, 128.9, 128.4, 128.4, 128.3, 128.2, 127.9, 127.7, 127.7, 127.5, 127.2, 109.4, 99.3, 83.9, 79.6, 77.9, 76.8, 76.4, 75.0, 74.4, 73.3, 71.5, 71.0, 69.1, 61.8, 36.9, 27.9, 26.5, 18.0, 17.9, 11.8. HRMS (ESI) calcd for $\text{C}_{51}\text{H}_{72}\text{NO}_9\text{SSi}$ $[\text{M}+\text{NH}_4]^+$ 902.4697, found 902.4698. $[\alpha]_{\text{D}}^{35} = +0.28$ (c 0.01, CHCl_3).

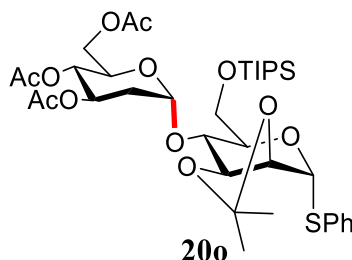
Phenyl 2,3-*O*-isopropylidene-6-*O*-triisopropylsilyl-4-(3,4,6-*tri-p*-methyl-*O*-benzyl-2-deoxy- D -glucopyranosyl)- α - D -thiomannopyranoside (20n).



Glycosylation of **18b** (42.8 mg, 0.06 mmol) with **19j** (33.8 mg, 0.072 mmol) according to General procedure 3 afforded **20n** (47.9 mg, 86 %, $\alpha:\beta = 14:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.71$ (Hexane/EtOAc = 4:1, v/v). The α anomer ^1H NMR (600 MHz, CDCl_3) δ 7.51 (d, $J = 6.9$ Hz, 2H), 7.26 (m, 3H), 7.22 (d, $J = 7.8$ Hz, 2H), 7.19 (d, $J = 7.8$ Hz, 2H), 7.12 (d, $J = 7.7$ Hz, 2H), 7.08 (d, $J = 8.2$ Hz, 4H), 7.04 (d, $J = 7.9$ Hz, 2H), 5.77 (s, 1H), 5.57 (d, $J = 2.1$ Hz, 1H), 4.83 (d, $J = 10.9$ Hz, 1H), 4.59 (m, 3H), 4.45 (d, $J = 10.9$ Hz, 1H), 4.42 (d, $J = 12.1$ Hz, 1H), 4.30 (d, $J = 5.4$ Hz, 1H), 4.25 (t, $J = 6.2$ Hz, 1H), 4.06 – 4.01 (m, 1H), 3.91 – 3.86 (m, 2H), 3.84 (dd, $J = 11.2, 1.7$ Hz, 1H), 3.81 (dd, $J = 11.2, 4.7$ Hz, 1H), 3.72 – 3.69 (m, 2H), 3.65 (t, $J = 9.3$ Hz, 1H), 3.53 (d, $J = 9.0$ Hz, 1H), 2.33 (s, 6H), 2.30 (s, 3H), 2.29 – 2.25 (m, 1H), 1.74 (td, $J = 12.9, 3.4$ Hz, 1H), 1.52 (s, 3H), 1.34 (s, 3H), 1.00 – 0.94 (m, 21H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 136.1, 136.1, 135.7, 135.0, 134.8, 134.1, 132.9, 130.6, 128.0, 127.9, 127.8, 127.7, 127.0, 126.7, 126.5, 126.3, 108.6, 94.8, 83.0, 77.6, 76.9, 76.4, 75.4, 73.4, 72.4, 70.8, 70.7, 70.1, 69.9, 67.4, 61.8, 34.7, 26.8, 25.58, 20.1, 20.1, 17.0, 16.9, 11.0. HRMS (ESI) calcd for $\text{C}_{54}\text{H}_{78}\text{NO}_9\text{SSi}$ $[\text{M}+\text{NH}_4]^+$ 944.5167, found 944.5167. $[\alpha]_{\text{D}}^{35} = +1.88$ (c 0.035, CHCl_3).

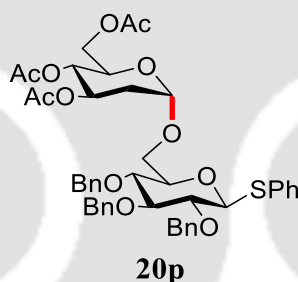
For β anomer, ^1H NMR (600 MHz, CDCl_3) δ 7.44 (d, $J = 7.2$ Hz, 2H), 7.29 – 7.24 (m, 3H), 7.23 (d, $J = 8.0$ Hz, 4H), 7.13 (t, $J = 8.5$ Hz, 4H), 7.09 (d, $J = 7.8$ Hz, 2H), 7.04 (d, $J = 7.9$ Hz, 2H), 5.76 (s, 1H), 4.80 (d, $J = 10.4$ Hz, 1H), 4.73 (d, $J = 8.7$ Hz, 1H), 4.60 (t, $J = 11.9$ Hz, 2H), 4.55 (d, $J = 11.5$ Hz, 1H), 4.44 (t, $J = 10.4$ Hz, 2H), 4.35 – 4.31 (m, 1H), 4.29 (d, $J = 5.5$ Hz, 1H), 4.06 (dd, $J = 9.5, 7.5$ Hz, 1H), 3.93 (d, $J = 9.6$ Hz, 1H), 3.81 (dd, $J = 11.4, 2.5$ Hz, 1H), 3.71 (dd, $J = 10.3, 3.9$ Hz, 2H), 3.64 – 3.60 (m, 1H), 3.58 – 3.53 (m, 2H), 3.31 (d, $J = 3.4$ Hz, 1H), 2.34 (s, 3H), 2.33 (s, 6H), 2.29 – 2.24 (m, 1H), 1.71 – 1.64 (m, 1H), 1.45 (s, 3H), 1.31 (s, 3H), 1.04 – 0.95 (m, 21H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 136.3, 136.1, 134.5, 134.4, 134.4, 133.0, 130.2, 128.1, 127.9, 127.9, 127.8, 127.2, 127.0, 126.8, 126.1, 108.3, 98.4, 83.1, 78.4, 76.9, 75.8, 75.4, 74.2, 73.8, 73.5, 72.2, 70.4, 70.2, 68.0, 61.0, 35.9, 28.7, 26.8, 25.4, 20.1, 16.9, 16.9, 10.9. HRMS (ESI) calcd for $\text{C}_{54}\text{H}_{78}\text{NO}_9\text{SSi}$ $[\text{M}+\text{NH}_4]^+$ 944.5167, found 944.5171. $[\alpha]_{\text{D}}^{35} = +0.40$ (c 0.01, CHCl_3).

Phenyl 2,3-*O*-isopropylidene-6-*O*-triisopropylsilyl-4-(3,4,6-*tri-O*-acetyl-2-deoxy- α - D -glucopyranosyl)- α - D -thiomannopyranoside (20o).



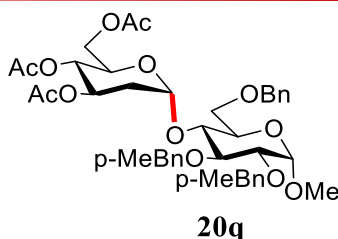
Glycosylation of **18c** (31.6 mg, 0.06 mmol) with **19j** (33.8 mg, 0.072 mmol) according to General procedure 3 afforded **20o** (36.5 mg, 82 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.45 (Hexane: EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.49 (d, J = 6.9 Hz, 2H), 7.31 – 7.26 (m, 3H), 5.82 (s, 1H), 5.64 (d, J = 2.0 Hz, 1H), 5.29 – 5.24 (m, 1H), 5.05 (t, J = 9.8 Hz, 1H), 4.32 (dd, J = 12.2, 4.3 Hz, 2H), 4.30 – 4.28 (m, 1H), 4.08 – 4.03 (m, 2H), 4.02 – 3.95 (m, 2H), 3.93 (dd, J = 11.3, 3.4 Hz, 1H), 3.80 (dd, J = 11.2, 1.3 Hz, 1H), 2.27 (dd, J = 12.6, 4.9 Hz, 1H), 1.84 (td, J = 12.8, 3.4 Hz, 1H), 1.53 (s, 3H), 1.35 (s, 3H), 1.03–0.99 (m, 21H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.9, 170.3, 169.9, 133.3, 131.7, 129.0, 127.5, 109.8, 94.4, 83.7, 78.4, 76.3, 70.0, 70.0, 69.1, 68.9, 68.2, 62.3, 62.2, 35.0, 27.9, 26.6, 21.1, 20.9, 20.7, 18.0, 17.9, 12.0. HRMS (ESI) calcd for $\text{C}_{36}\text{H}_{60}\text{NO}_{12}\text{SSi}$ $[\text{M}+\text{NH}_4]^+$ 758.3605, found 758.3608. $[\alpha]_D^{35}$ = + 0.60 (c 0.01, CHCl_3).

Phenyl 2,3,4-tri-O-benzyl-6-(3,4,6-tri-O-acetyl-2-deoxy- α -D-glucopyranosyl)- β -D-thioglucopyranoside (20p).



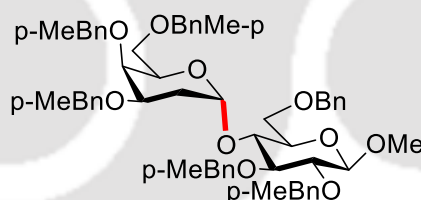
Glycosylation of **18c** (31.6 mg, 0.06 mmol) with **19i** (39 mg, 0.072 mmol) according to General procedure 3 afforded **20p** (41.6 mg, 85 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.38 (Hexane/EtOAc = 4:1, v/v) ^1H NMR (500 MHz, CDCl_3) δ 7.52 (d, J = 7.7 Hz, 2H), 7.38 (d, J = 7.3 Hz, 2H), 7.36–7.24 (m, 16H), 5.34–5.27 (m, 1H), 5.02 – 4.97 (m, 2H), 4.95 – 4.90 (m, 3H), 4.83 (d, J = 10.9 Hz, 1H), 4.75 (d, J = 10.3 Hz, 1H), 4.65 (t, J = 11.8 Hz, 2H), 4.20 (d, J = 8.9 Hz, 1H), 3.97 (d, J = 11.1 Hz, 2H), 3.78 (d, J = 11.7 Hz, 1H), 3.72 (d, J = 10.8 Hz, 2H), 3.54 – 3.47 (m, 3H), 2.29 (dd, J = 12.9, 5.1 Hz, 1H), 2.05 (s, 3H), 2.03 (s, 3H), 1.94 (s, 3H), 1.84 – 1.77 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 169.7, 169.1, 168.8, 137.3, 137.0, 137.0, 133.0, 130.5, 128.0, 127.4, 127.4, 127.2, 126.9, 126.8, 126.8, 126.7, 126.6, 126.4, 96.4, 86.6, 85.7, 79.9, 77.3, 76.8, 74.8, 74.4, 74.0, 68.1, 66.8, 65.6, 61.1, 33.9, 20.0, 19.7, 19.6. HRMS (ESI) calcd for $\text{C}_{45}\text{H}_{54}\text{NO}_{12}\text{S}$ $[\text{M}+\text{NH}_4]^+$ 832.3367, found 832.3369. $[\alpha]_D^{35}$ = + 1.0 (c 0.015, CHCl_3).

Synthesis of Methyl 2,3-di-*p*-methyl-O-benzyl-6-O-benzyl-4-O-(3,4,6-tri-O-acetyl-2-deoxy- α -D-glucopyranosyl)- α -D-glucopyranoside (20q)



Glycosylation of **18c** (31.6 mg, 0.06 mmol) with **19g** (35.5 mg, 0.072 mmol) according to General procedure 3 afforded **20q** (36.7 mg, 80 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.45 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.36 – 7.31 (m, 4H), 7.29 – 7.25 (m, 1H), 7.23 (d, J = 7.8 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 7.12 (dd, J = 8.1, 1.8 Hz, 4H), 5.42 (d, J = 2.8 Hz, 1H), 5.22 – 5.17 (m, 1H), 4.99 (d, J = 10.9 Hz, 1H), 4.90 (t, J = 9.8 Hz, 1H), 4.72 (d, J = 12.0 Hz, 1H), 4.62 (d, J = 12.3 Hz, 1H), 4.60–4.56 (m, 2H), 4.55 (d, J = 3.3 Hz, 1H), 4.52 (d, J = 12.2 Hz, 1H), 4.11 (dd, J = 12.3, 3.9 Hz, 1H), 3.90 (t, J = 9.2 Hz, 1H), 3.84–3.80 (m, 1H), 3.79 – 3.75 (m, 1H), 3.74 (dd, J = 12.3, 1.6 Hz, 1H), 3.66 (dd, J = 9.7, 7.4 Hz, 2H), 3.64 – 3.60 (m, 1H), 3.49 (dd, J = 9.7, 3.4 Hz, 1H), 3.41 (s, 3H), 2.34 (s, 3H), 2.33 (s, 3H), 2.04–2.01 (m, 7H), 2.00 (s, 3H), 1.63 – 1.59 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 169.6, 169.1, 168.7, 137.1, 136.7, 136.2, 134.6, 133.9, 128.1, 128.0, 127.4, 127.2, 126.7, 126.6, 126.4, 97.5, 96.8, 80.7, 78.9, 75.3, 74.2, 72.3, 72.1, 68.6, 68.3, 68.3, 67.9, 67.6, 61.2, 54.3, 34.2, 20.1, 20.1, 19.9, 19.7. HRMS (ESI) calcd for $\text{C}_{42}\text{H}_{56}\text{NO}_{13}$ $[\text{M}+\text{NH}_4]^+$ 782.3752, found 782.3752. $[\alpha]_{\text{D}}^{35}$ = + 0.26 (c 0.01, CHCl_3).

Synthesis of Methyl 2,3-di-*p*-methyl-*O*-benzyl-6-*O*-benzyl-4-*O*-(3,4,6-tri-*p*-methyl-*O*-benzyl-2-deoxy- α -D-galactopyranosyl)- β -D-glucopyranoside (**20r**)

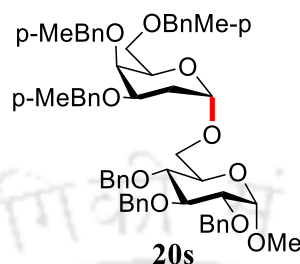


Glycosylation of **20d** (42.8 mg, 0.06 mmol) with **19h** (35.5 mg, 0.072 mmol) according to General procedure 3 afforded **20r** (47.4 mg, 83 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.60 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.27 (d, J = 4.3 Hz, 4H), 7.24 – 7.17 (m, 7H), 7.16 – 7.08 (m, 14H), 5.45 (d, J = 2.9 Hz, 1H), 4.89 (d, J = 10.5 Hz, 1H), 4.85 (d, J = 10.7 Hz, 1H), 4.82 (d, J = 11.5 Hz, 1H), 4.62 (d, J = 10.7 Hz, 1H), 4.54 (d, J = 11.3 Hz, 2H), 4.50 (d, J = 12.4 Hz, 2H), 4.43 (d, J = 11.7 Hz, 1H), 4.40 (d, J = 12.1 Hz, 1H), 4.35 (d, J = 11.5 Hz, 1H), 4.28 (t, J = 9.9 Hz, 2H), 3.81 (bs, 1H), 3.78 (d, J = 7.2 Hz, 1H), 3.76 (d, J = 10.8 Hz, 1H), 3.74 – 3.70 (m, 1H), 3.60 – 3.55 (m, 5H), 3.52 (t, J = 9.0 Hz, 1H), 3.45– 3.41 (m, 3H), 3.38 (t, J = 8.4 Hz, 1H), 2.34 (s, 3H), 2.33 (s, 3H), 2.31 (merged s, 9H), 2.11 (td, J = 12.5, 3.7 Hz, 1H), 1.82 (dd, J = 12.3, 3.5 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 137.6, 136.3, 136.3, 136.2, 136.1, 136.09, 134.8, 134.5, 134.5, 134.2, 134.1, 128.1, 128.0, 128.0, 127.8, 127.4, 127.2, 127.2, 126.9, 126.7, 126.6, 126.4, 126.3, 103.5, 98.3, 83.7, 81.2, 74.5, 74.2, 73.8, 73.5, 73.4, 72.9,

72.3, 72.2, 71.4, 69.8, 69.2, 69.2, 68.5, 56.0, 30.5, 20.1, 20.1. HRMS (ESI) calcd for $C_{60}H_{74}NO_{10}$ $[M+NH_4]^+$ 968.5313, found 968.5310.

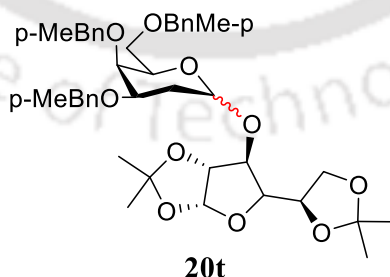
$[\alpha]_D^{35} = +0.5$ (c 0.01, $CHCl_3$).

Synthesis of Methyl 2,3,4-*tri*-O-benzyl-6-O-(3,4,6-*tri*-*p*-methyl-O-benzyl-2-deoxy- α -D-galactopyranosyl)- α -D-glucopyranoside (20s)



Glycosylation of **18d** (42.8 mg, 0.06 mmol) with **19d** (33.5 mg, 0.072 mmol) according to General procedure 3 afforded **20s** (49.33 mg, 89 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.6$ (Hexane/EtOAc = 4:1, v/v). 1H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.17 (m, 20H), 7.13 – 7.07 (m, 7H), 5.01 (d, $J = 2.5$ Hz, 1H), 4.98 (d, $J = 10.7$ Hz, 1H), 4.85 (d, $J = 6.0$ Hz, 1H), 4.83 (d, $J = 5.3$ Hz, 1H), 4.81 (d, $J = 6.4$ Hz, 1H), 4.79 (d, $J = 7.8$ Hz, 1H), 4.68 (d, $J = 12.1$ Hz, 1H), 4.58 (d, $J = 3.4$ Hz, 1H), 4.55 (d, $J = 11.3$ Hz, 1H), 4.53–4.49 (m, 3H), 4.36 (d, $J = 11.6$ Hz, 1H), 4.28 (d, $J = 11.5$ Hz, 1H), 3.98 (t, $J = 9.3$ Hz, 1H), 3.86 – 3.78 (m, 4H), 3.71 (dd, $J = 9.9, 3.1$ Hz, 1H), 3.60 (d, $J = 10.4$ Hz, 1H), 3.52 (dd, $J = 9.6, 3.4$ Hz, 1H), 3.50 – 3.44 (m, 3H), 3.30 (s, 3H), 2.33 (s, 3H), 2.31 (s, 3H), 2.28 (s, 3H), 2.18 (td, $J = 12.3, 3.0$ Hz, 1H), 1.98 (dd, $J = 12.4, 3.8$ Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 137.8, 137.3, 137.2, 136.2, 136.2, 136.0, 134.9, 134.4, 134.1, 128.0, 128.0, 127.8, 127.4, 127.4, 127.3, 127.0, 126.9, 126.8, 126.7, 126.6, 126.6, 126.5, 97.3, 96.8, 81.1, 79.1, 77.0, 74.8, 74.0, 73.0, 73.0, 72.3, 72.2, 71.6, 69.1, 69.0, 68.9, 68.3, 65.0, 53.9, 30.0, 20.1, 20.1. HRMS (ESI) calcd for $C_{58}H_{70}NO_{10}$ $[M+NH_4]^+$ 940.5000, found 940.5003. $[\alpha]_D^{35} = +0.34$ (c 0.01, $CHCl_3$).

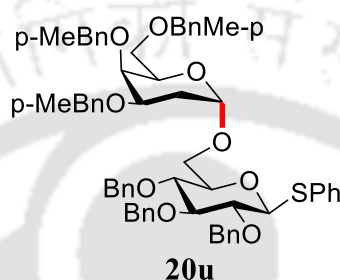
Synthesis of 1,2;4,6-*di*-O-isopropylidene-3-O-(3,4,6-*tri*-*p*-methyl-2-deoxy-D-galactopyranosyl)- α -D-glucofuranose (20t)



Glycosylation of **18d** (42.8 mg, 0.06 mmol) with **19c** (18.7 mg, 0.072 mmol) according to General procedure 3 afforded **20t** (35.4 mg, 82 %, $\alpha:\beta = 6:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.58$ (Hexane/EtOAc = 4:1, v/v). 1H NMR (600 MHz, $CDCl_3$) δ 7.24 – 7.09 (m, 12H), 5.82 (d, $J = 3.4$ Hz, 1H), 5.22 (d, $J = 2.8$ Hz, 1H), 4.87 (d, $J = 11.4$ Hz, 1H), 4.69 (d, $J = 3.4$ Hz, 1H), 4.57 (d, $J = 4.9$ Hz, 1H), 4.56 – 4.53 (m, 2H), 4.46 (d, $J = 11.6$ Hz, 1H), 4.37 (d, $J = 11.5$ Hz, 1H), 4.20 (d, $J = 2.5$ Hz, 1H),

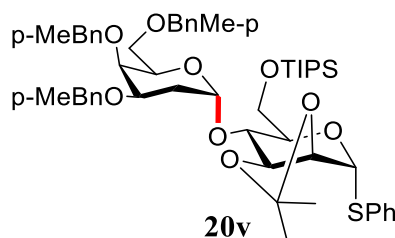
4.19 – 4.14 (m, 1H), 4.10 – 4.05 (m, 2H), 3.95 (dd, $J = 8.4, 5.7$ Hz, 1H), 3.89 – 3.85 (m, 2H), 3.84 – 3.80 (m, 1H), 3.57 (dd, $J = 9.4, 6.4$ Hz, 1H), 3.49 (dd, $J = 9.4, 6.1$ Hz, 1H), 2.35 (s, 3H), 2.34 (s, 3H), 2.32 (s, 3H), 2.21 (td, $J = 12.4, 3.6$ Hz, 1H), 1.96 (dd, $J = 12.5, 3.9$ Hz, 1H), 1.47 (s, 3H), 1.39 (s, 3H), 1.32 (s, 3H), 1.20 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 136.3, 136.3, 136.2, 134.8, 134.3, 134.0, 128.1, 128.0, 127.9, 127.3, 126.9, 126.4, 110.8, 108.0, 104.3, 98.6, 82.5, 80.3, 80.0, 73.3, 73.0, 72.4, 71.7, 71.6, 70.0, 69.3, 68.9, 66.6, 30.1, 25.8, 25.7, 25.1, 24.37, 20.1. HRMS (ESI) calcd for $\text{C}_{42}\text{H}_{58}\text{NO}_{10}$ $[\text{M}+\text{NH}_4]^+$ 736.4061, found 736.4061. $[\alpha]_{\text{D}}^{35} = +0.48$ (c 0.01, CHCl_3).

Phenyl 2,3,4-tri-*O*-benzyl-6-(3,4,6-tri-*p*-methyl-*O*-benzyl-2-deoxy- α -D-galactopyranosyl)- β -D-thioglucopyranoside (20u)



Glycosylation of **18d** (42.8 mg, 0.06 mmol) with **19i** (39 mg, 0.072 mmol) according to General procedure 3 afforded **20u** (55.3 mg, 92 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.61$ (Hexane: EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 7.55 (d, $J = 7.2$ Hz, 2H), 7.40 (d, $J = 7.2$ Hz, 2H), 7.37–7.29 (m, 8H), 7.29 – 7.19 (m, 12H), 7.16 – 7.08 (m, 8H), 5.07 (d, $J = 2.6$ Hz, 1H), 4.91 (d, $J = 10.4$ Hz, 1H), 4.88 (d, $J = 8.9$ Hz, 1H), 4.84 (d, $J = 10.2$ Hz, 2H), 4.80 (d, $J = 10.7$ Hz, 1H), 4.74 (d, $J = 10.2$ Hz, 1H), 4.64 (d, $J = 9.8$ Hz, 1H), 4.56 (d, $J = 11.1$ Hz, 1H), 4.55 – 4.52 (m, 2H), 4.51 (d, $J = 11.5$ Hz, 1H), 4.41 (d, $J = 11.6$ Hz, 1H), 4.34 (d, $J = 11.6$ Hz, 1H), 3.88 (t, $J = 6.4$ Hz, 1H), 3.86 – 3.82 (m, 2H), 3.80 (dd, $J = 11.5, 4.9$ Hz, 1H), 3.74 – 3.71 (m, 1H), 3.70 (d, $J = 8.8$ Hz, 1H), 3.52 (dd, $J = 11.1, 7.6$ Hz, 2H), 3.50 – 3.44 (m, 3H), 2.33 (s, 3H), 2.32 (s, 3H), 2.29 (s, 3H), 2.22 (td, $J = 12.3, 3.3$ Hz, 1H), 1.99 – 2.23 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 137.4, 137.0, 136.2, 136.2, 136.0, 134.9, 134.5, 134.2, 132.7, 131.0, 128.1, 128.0, 127.8, 127.4, 127.4, 127.3, 127.2, 126.8, 126.7, 126.5, 126.4, 97.4, 86.1, 85.7, 79.9, 77.5, 77.1, 74.8, 74.4, 74.0, 73.4, 73.0, 72.1, 71.7, 69.2, 69.0, 68.4, 65.1, 30.1, 29.9, 20.1, 20.1. HRMS (ESI) calcd for $\text{C}_{63}\text{H}_{72}\text{NO}_9\text{S}$ $[\text{M}+\text{NH}_4]^+$ 1018.4928, found 1018.4933. $[\alpha]_{\text{D}}^{35} = +0.38$ (c 0.01, CHCl_3).

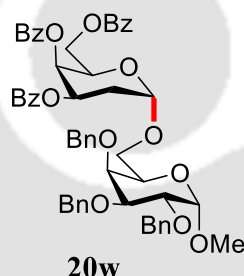
Phenyl 2,3-*O*-isopropylidene-6-*O*-triisopropylsilyl-4-(3,4,6-tri-*p*-methyl-*O*-benzyl-2-deoxy- α -D-glucopyranosyl)- α -D-thiomannopyranoside (20v)



Glycosylation of **18d** (42.8 mg, 0.06 mmol) with **19j** (33.8 mg, 0.072 mmol) according to General procedure 3 afforded **20v** (49.6 mg, 89 %, α only) as a colorless syrup. The crude

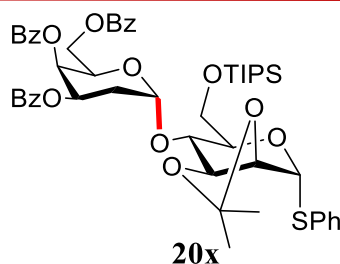
product was purified through flash column chromatography, $R_f = 0.71$ (Hexane/EtOAc = 4:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 7.53 (d, $J = 7.5$ Hz, 2H), 7.28 – 7.20 (m, 5H), 7.18 (d, $J = 7.5$ Hz, 2H), 7.14 (d, $J = 7.9$ Hz, 4H), 7.11 (d, $J = 7.8$ Hz, 2H), 7.06 (d, $J = 7.6$ Hz, 2H), 5.76 (s, 1H), 5.56 (d, $J = 2.6$ Hz, 1H), 4.84 (d, $J = 11.3$ Hz, 1H), 4.57 – 4.49 (m, 3H), 4.42 (d, $J = 11.5$ Hz, 1H), 4.34 – 4.29 (m, 2H), 4.24 (t, $J = 6.3$ Hz, 1H), 4.09 – 4.03 (m, 1H), 3.92 (s, 1H), 3.89 (d, $J = 6.8$ Hz, 1H), 3.84 (d, $J = 11.1$ Hz, 3H), 3.80 (dd, $J = 10.9, 5.6$ Hz, 1H), 3.60 (t, $J = 8.3$ Hz, 1H), 3.45 (dd, $J = 8.4, 5.5$ Hz, 1H), 2.34 (s, 3H), 2.33 (s, 3H), 2.30 (s, 3H), 2.28 – 2.22 (m, 1H), 1.98 (dd, $J = 12.3, 4.0$ Hz, 1H), 1.48 (s, 3H), 1.32 (s, 3H), 1.01 – 0.96 (m, 21H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 136.1, 135.9, 135.0, 134.5, 134.2, 133.1, 130.5, 128.0, 127.9, 127.8, 127.8, 127.2, 126.8, 126.4, 126.2, 108.6, 95.1, 83.1, 77.5, 75.5, 73.5, 73.1, 72.3, 71.7, 70.3, 70.0, 69.5, 69.3, 67.9, 62.1, 30.2, 28.7, 26.8, 25.6, 20.1, 17.0, 16.9, 10.9. HRMS (ESI) calcd for $\text{C}_{54}\text{H}_{78}\text{NO}_9\text{SSi}$ $[\text{M}+\text{NH}_4]^+$ 944.5167, found 944.5165. $[\alpha]_{\text{D}}^{35} = -0.34$ (c 0.01, CHCl_3).

Phenyl 2,3,4-tri-*O*-benzyl-6-(3,4,6-tri-*O*-benzoyl-2-deoxy- α -D-galactopyranosyl)- α -D-galactopyranoside (20w)

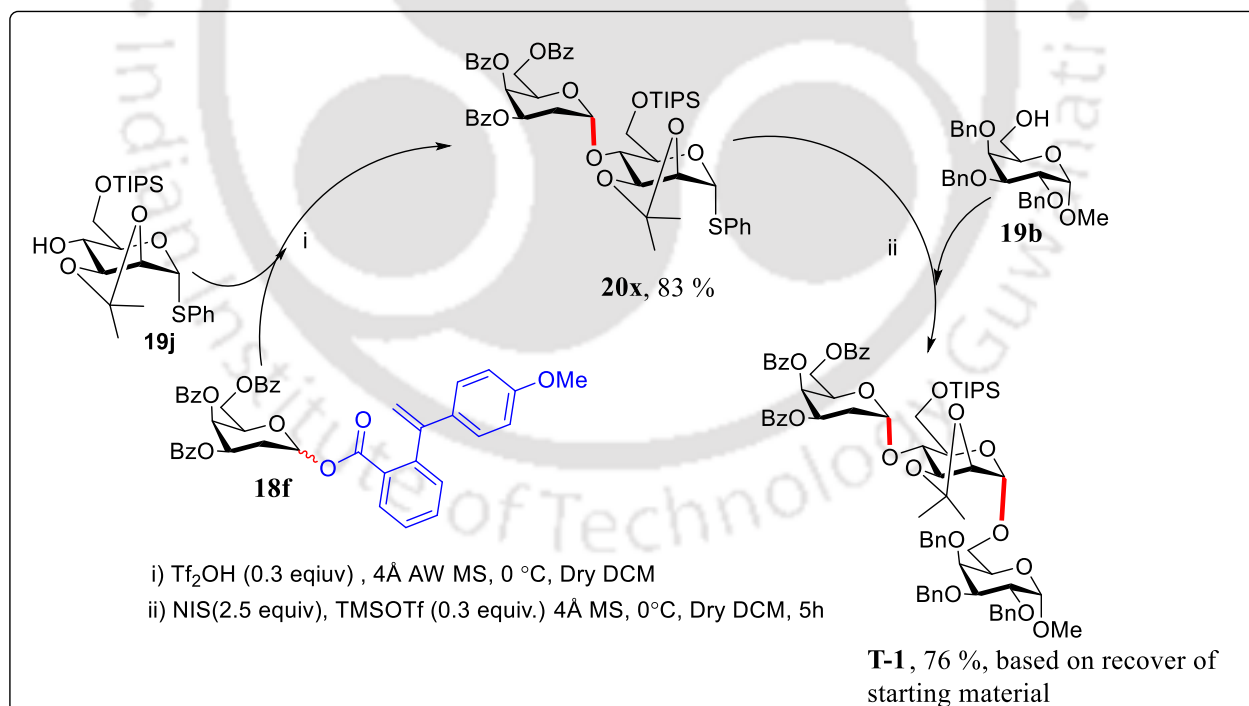


Glycosylation of **18f** (42.9 mg, 0.06 mmol) with **19b** (33.5 mg, 0.072 mmol) according to General procedure 3 afforded **20w** (46.1 mg, 83 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.49$ (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 8.08 (d, $J = 7.3$ Hz, 2H), 8.00 (d, $J = 7.3$ Hz, 2H), 7.84 (d, $J = 7.3$ Hz, 2H), 7.62 (t, $J = 7.4$ Hz, 1H), 7.52 – 7.46 (m, 4H), 7.43 (d, $J = 7.4$ Hz, 2H), 7.40 – 7.27 (m, 13H), 5.79 (d, $J = 1.9$ Hz, 1H), 5.62 – 5.57 (m, 1H), 4.95 (d, $J = 11.9$ Hz, 1H), 4.91 (d, $J = 11.6$ Hz, 1H), 4.82 (d, $J = 8.7$ Hz, 2H), 4.80 (d, $J = 8.7$ Hz, 1H), 4.69 – 4.65 (m, 2H), 4.62 (d, $J = 11.9$ Hz, 1H), 4.52 – 4.49 (m, 1H), 4.46 (dd, $J = 11.0, 7.5$ Hz, 1H), 4.38 (dd, $J = 11.1, 5.0$ Hz, 1H), 4.01 – 3.97 (m, 2H), 3.93 (bs, 1H), 3.86 (t, $J = 6.2$ Hz, 1H), 3.78 (dd, $J = 9.1, 6.1$ Hz, 1H), 3.38 (dd, $J = 9.1, 6.8$ Hz, 1H), 3.36 (s, 3H), 2.23 (td, $J = 12.5, 3.3$ Hz, 1H), 1.93 (dd, $J = 12.5, 4.9$ Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 165.1, 164.6, 164.5, 137.8, 137.6, 137.5, 132.3, 132.0, 132.0, 128.8, 128.7, 128.7, 128.6, 127.5, 127.5, 127.4, 127.3, 127.3, 127.3, 127.0, 126.7, 126.6, 126.5, 97.7, 96.2, 78.2, 75.6, 73.7, 73.5, 72.6, 72.5, 67.9, 66.6, 66.4, 66.1, 65.3, 62.4, 54.3, 29.6. HRMS (ESI) calcd for $\text{C}_{55}\text{H}_{58}\text{NO}_{13}$ $[\text{M}+\text{NH}_4]^+$ 940.3908, found 940.3906. $[\alpha]_{\text{D}}^{35} = +0.42$ (c 0.01, CHCl_3).

Phenyl 2,3-*O*-isopropylidene-6-*O*-triisopropylsilyl-4-(3,4,6-tri-*O*-benzoyl-2-deoxy- α -D-galactopyranosyl)- α -D-thiomannopyranoside (20x)



Glycosylation of **18f** (42.9 mg, 0.06 mmol) with **19j** (33.8 mg, 0.072 mmol) according to General procedure 3 afforded **20x** (46.3 mg, 83 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.51 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 8.09 (d, J = 7.4 Hz, 2H), 7.98 (d, J = 7.4 Hz, 2H), 7.85 (d, J = 7.4 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.54 – 7.50 (m, 3H), 7.47 (dd, J = 15.6, 7.7 Hz, 3H), 7.39 (t, J = 7.7 Hz, 2H), 7.34 – 7.25 (m, 5H), 5.91 (bs, 1H), 5.86 (d, J = 1.8 Hz, 1H), 5.84 (s, 1H), 5.70 – 5.66 (m, 1H), 4.59 (t, J = 7.0 Hz, 1H), 4.49 (dd, J = 11.0, 6.1 Hz, 1H), 4.38–4.34 (m, 2H), 4.33 (dd, J = 10.9, 8.3 Hz, 1H), 4.16 – 4.08 (m, 2H), 4.00 (dd, J = 11.2, 3.8 Hz, 1H), 3.88 (d, J = 10.4 Hz, 1H), 2.41 (td, J = 12.5, 3.3 Hz, 1H), 2.22 (dd, J = 12.5, 4.7 Hz, 1H), 1.53 (s, 3H), 1.38 (s, 3H), 1.00 – 0.93 (m, 21H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 166.0, 165.7, 165.4, 133.5, 133.4, 133.1, 133.1, 131.7, 129.9, 129.7, 129.6, 129.6, 129.4, 129.0, 128.6, 128.4, 128.3, 127.5, 109.8, 95.3, 83.8, 78.5, 76.4, 70.8, 70.4, 67.5, 67.2, 67.0, 62.6, 62.4, 30.9, 27.9, 26.6, 17.9, 17.8, 12.0. HRMS (ESI) calcd for $\text{C}_{51}\text{H}_{66}\text{NO}_{12}\text{SSi}$ $[\text{M}+\text{NH}_4]^+$ 944.4075, found 944.4071. $[\alpha]_D^{35}$ = + 0.18 (c 0.01, CHCl_3).



Scheme 5. Synthesis of trisaccharide (T-1).

A solution of glycosyl donor **20x** (27.8 mg, 0.03 mmol) and acceptor **19b** (16.7 mg, 0.036 mmol) in dry CH_2Cl_2 (0.03 M) was stirred at room temperature for 60 min in the presence of activated 4Å MS (80 mg) under Ar atmosphere. Then the vessel was chilled to 0 °C, to which NIS (16.9 mg, 0.075 mmol) and TMSOTf (1.6 μL , 30 mol%) were added. The reaction mixture

was stirred for 5h min at 0 °C. Then, Et₃N was added to quench the reaction. The crude reaction mixture was worked up with water, washed with brine, dried by Na₂SO₄, concentrated in rotavapor. The resulting crude reaction mixture was purified through Flash column chromatography to afford the trisaccharide **T-1** (18.7 mg, 76 %, based on recovered donor **20x**, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.25 (Hexane/EtOAc = 3:1, v/v). ¹H NMR (500 MHz, CDCl₃) δ 8.10 – 8.05 (m, 2H), 8.00 – 7.96 (m, 2H), 7.85 – 7.82 (m, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.4 Hz, 1H), 7.49 – 7.44 (m, 3H), 7.43 – 7.34 (m, 8H), 7.33 – 7.26 (m, 11H), 5.86 (d, J = 2.4 Hz, 1H), 5.80 (d, J = 2.6 Hz, 1H), 5.65 – 5.60 (m, 1H), 4.96 (d, J = 11.7 Hz, 1H), 4.90 (d, J = 11.7 Hz, 1H), 4.83 (d, J = 12.1 Hz, 1H), 4.78 (d, J = 11.7 Hz, 1H), 4.75 (s, 1H), 4.70 (d, J = 6.4 Hz, 1H), 4.69 (d, J = 1.7 Hz, 1H), 4.65 (d, J = 11.7 Hz, 1H), 4.48 (q, J = 6.4 Hz, 2H), 4.33 (dd, J = 13.2, 9.4 Hz, 1H), 4.23 – 4.19 (m, 1H), 4.07 (dd, J = 10.0, 3.6 Hz, 1H), 4.00 (d, J = 9.3 Hz, 1H), 3.97 (dd, J = 10.1, 2.7 Hz, 1H), 3.92 – 3.87 (m, 2H), 3.87 – 3.83 (m, 2H), 3.82 (d, J = 6.8 Hz, 1H), 3.78 (dd, J = 9.1, 5.5 Hz, 1H), 3.64 – 3.59 (m, 1H), 3.44 – 3.39 (m, 1H), 3.37 (s, 3H), 2.37 (td, J = 12.5, 3.6 Hz, 1H), 2.17 (dd, J = 12.0, 5.6 Hz, 1H), 1.49 (s, 3H), 1.35 (s, 3H), 1.04 – 0.97 (m, 21H). ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 165.9, 165.7, 165.4, 138.8, 138.5, 138.4, 133.3, 133.1, 133.0, 129.9, 129.7, 129.7, 129.7, 129.4, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.1, 127.9, 127.7, 127.5, 127.5, 109.6, 98.8, 96.5, 95.3, 79.4, 78.7, 76.5, 75.6, 74.3, 74.0, 73.6, 73.5, 71.1, 69.1, 68.5, 67.7, 67.3, 67.0, 65.1, 63.2, 62.6, 55.5, 30.9, 29.7, 27.9, 26.5, 17.9, 17.9, 12.0. HRMS (ESI) calcd for C₇₃H₉₂NO₁₈Si [M+NH₄]⁺ 1298.6084, found 1298.6082. $[\alpha]_D^{35}$ = + 0.18 (c 0.01, CHCl₃).



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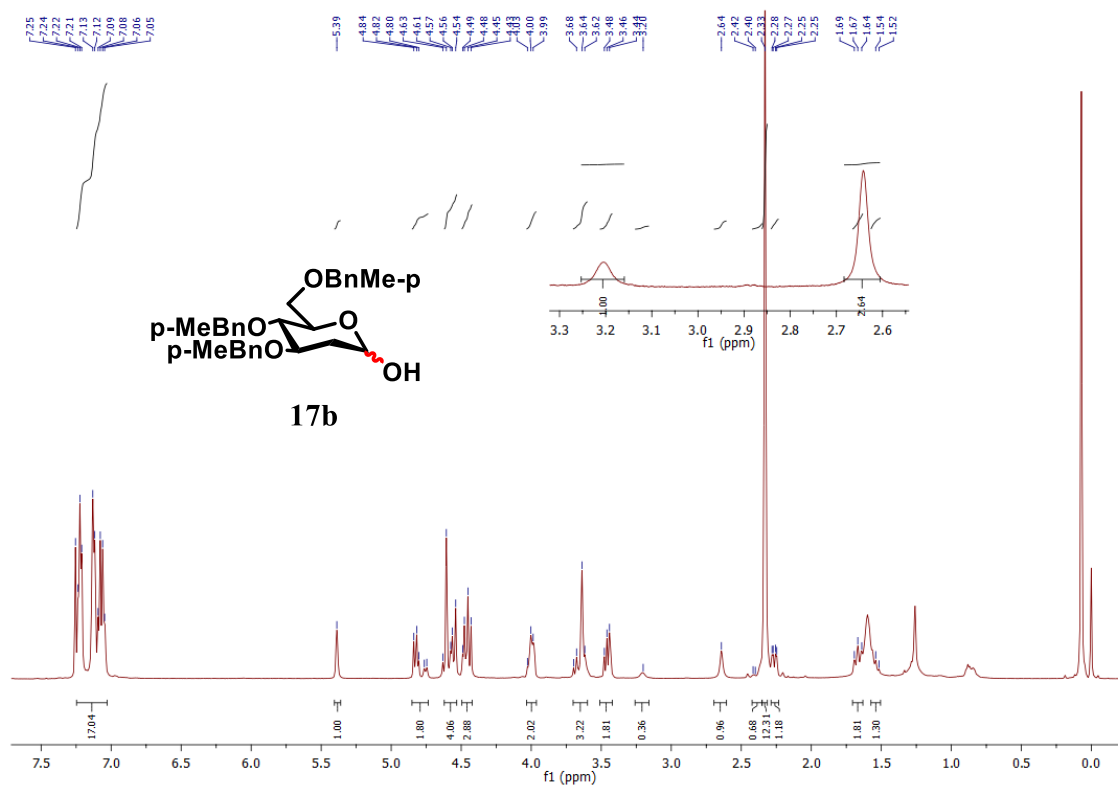
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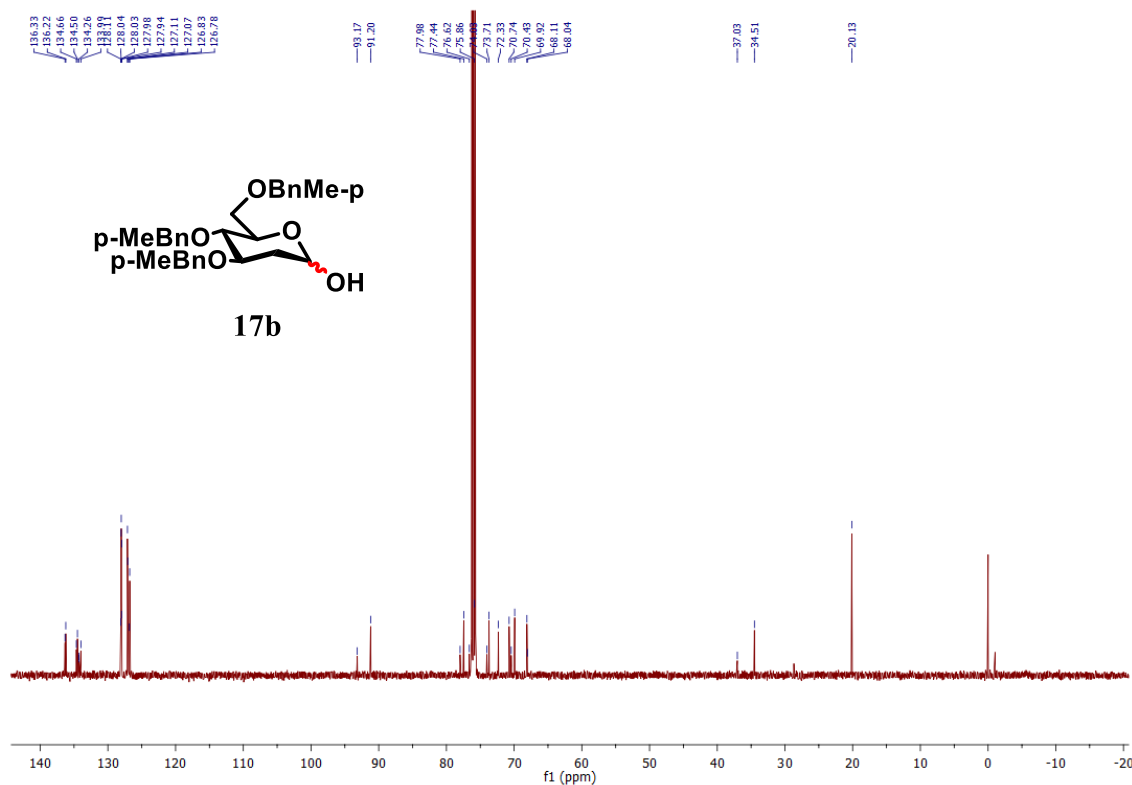
3.5

Spectra

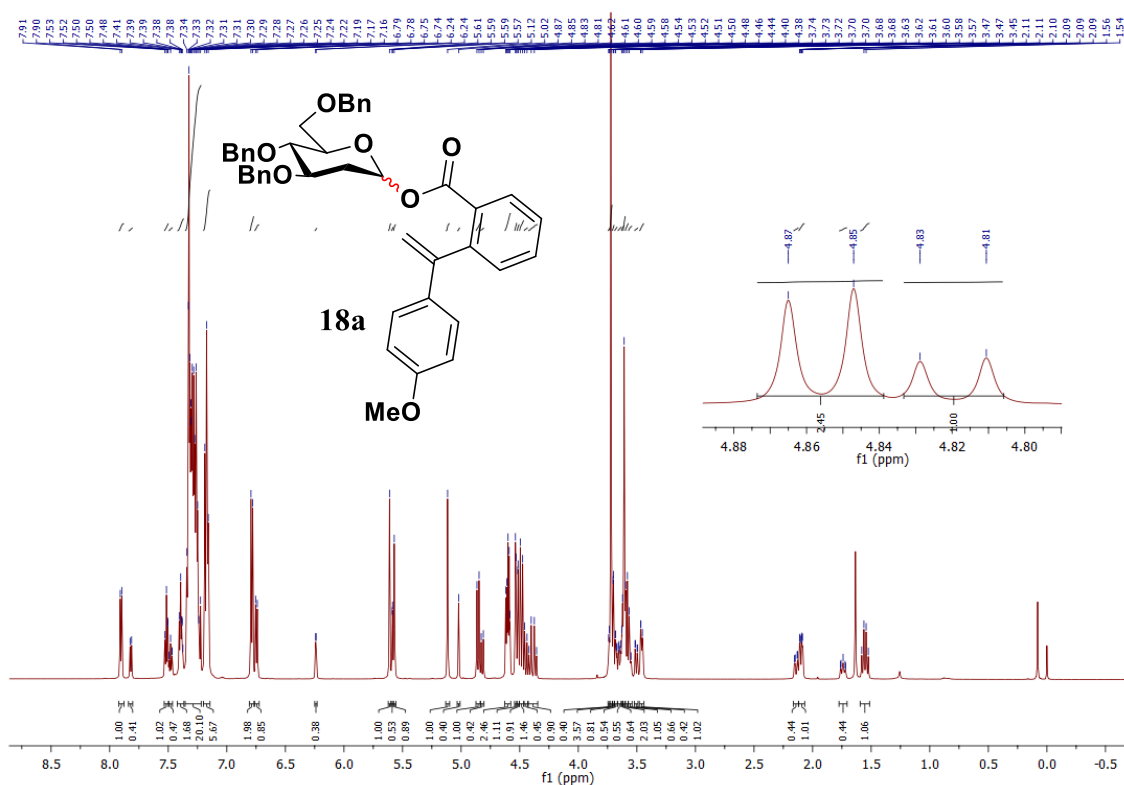
^1H NMR spectrum of compound 17b (500 MHz, CDCl_3):



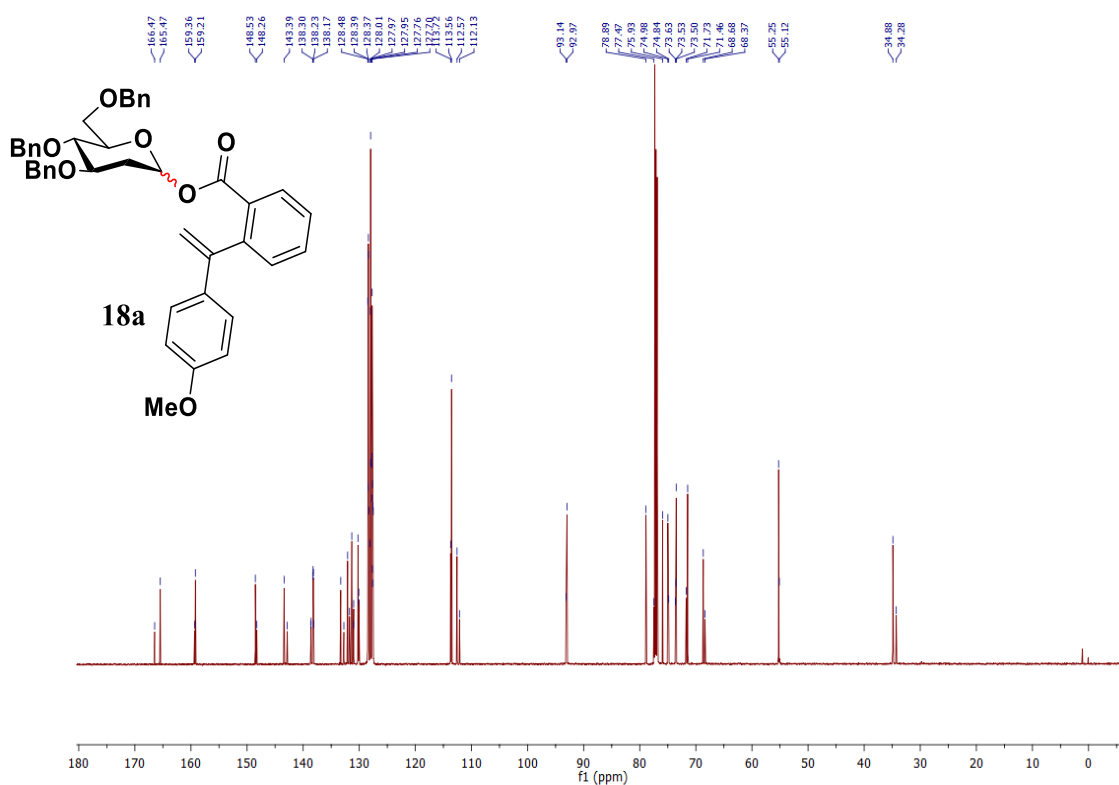
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 17b (500 MHz, CDCl_3):



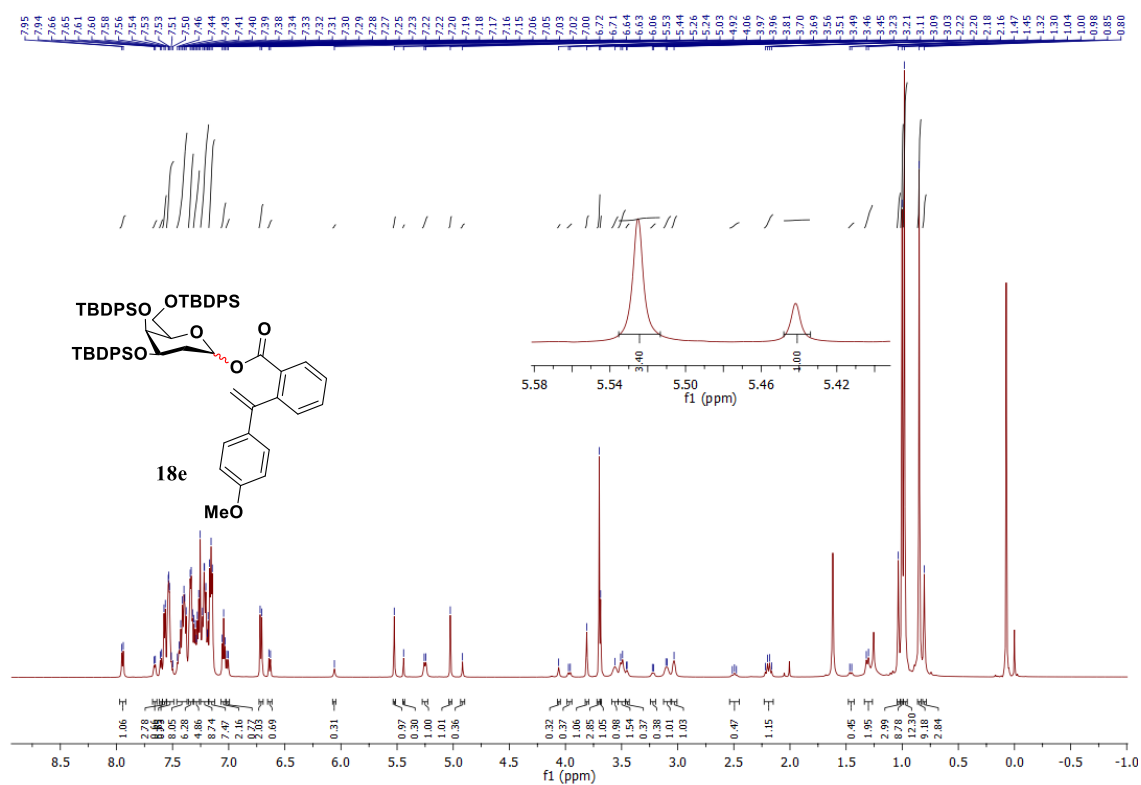
^1H NMR spectrum of compound 18a (600 MHz, CDCl_3):



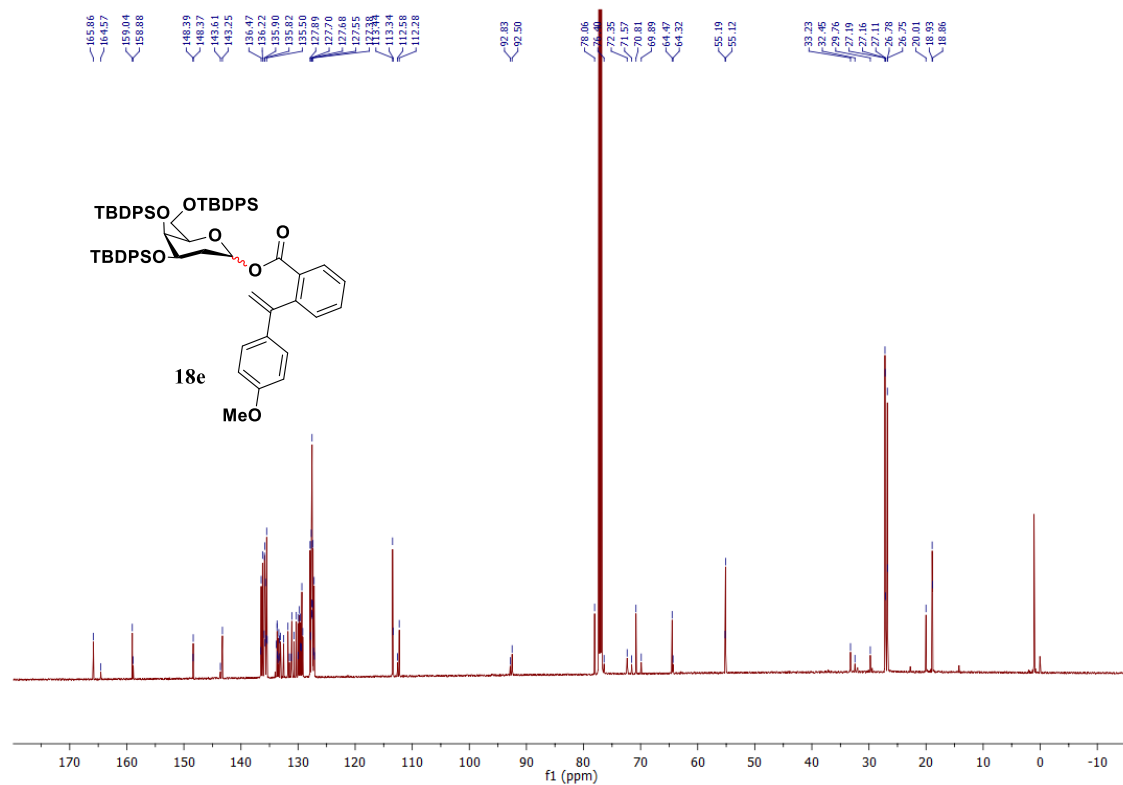
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 18a (600 MHz, CDCl_3):



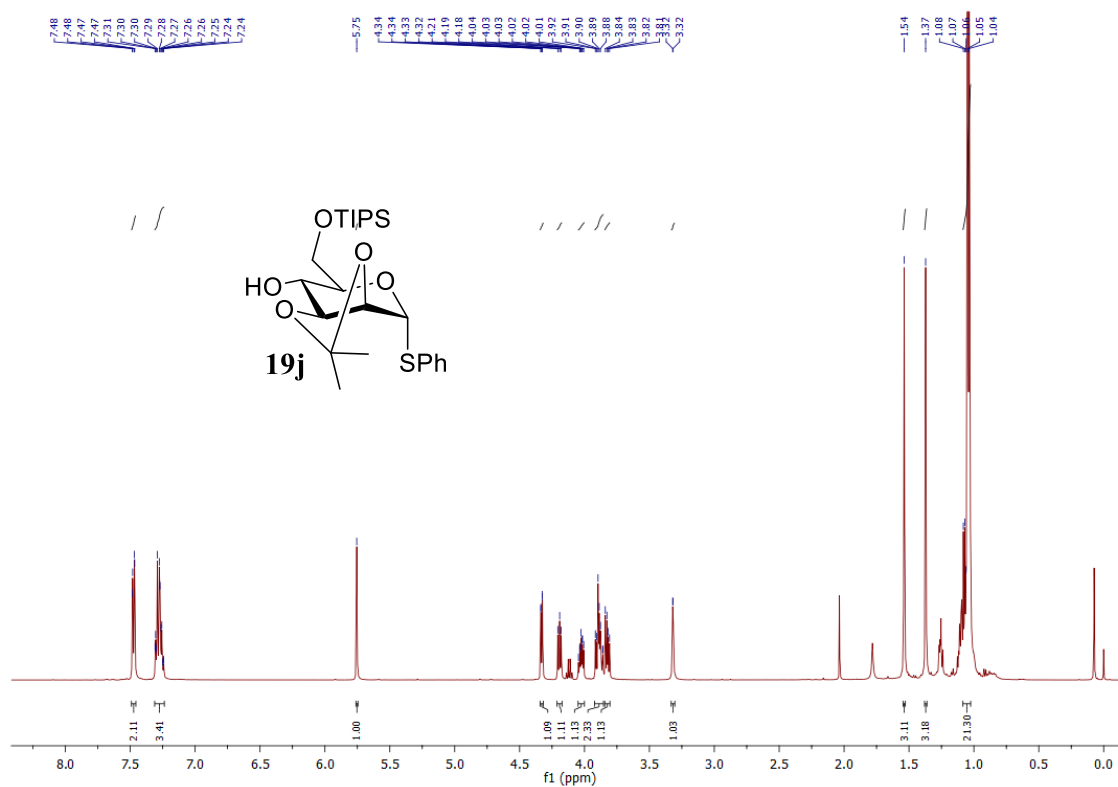
^1H NMR spectrum of compound 18e (600 MHz, CDCl_3):



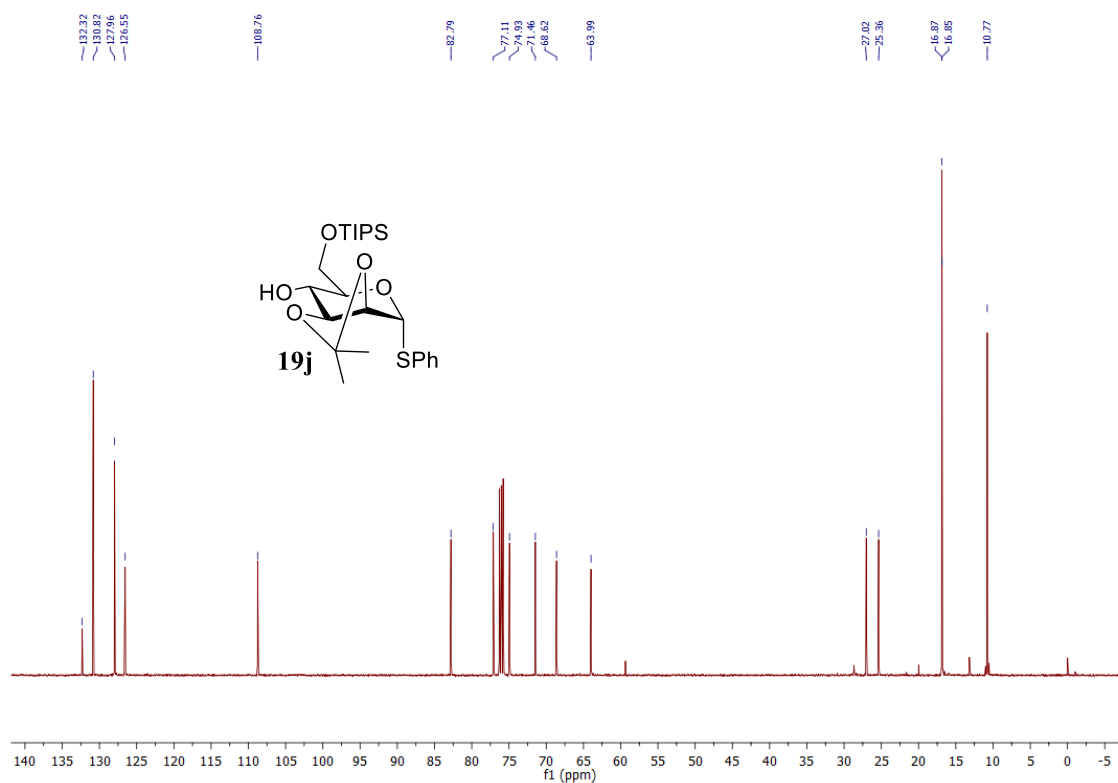
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 18e (600 MHz, CDCl_3):



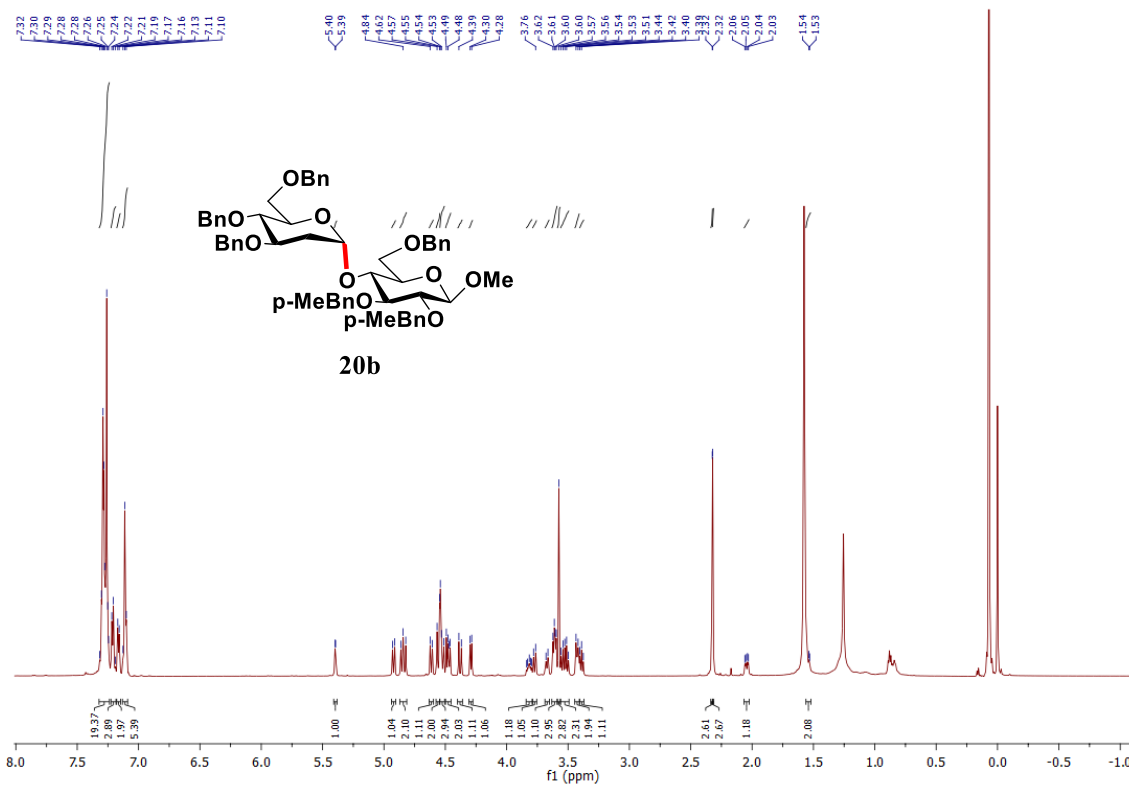
^1H NMR spectrum of compound 19j (500 MHz, CDCl_3):



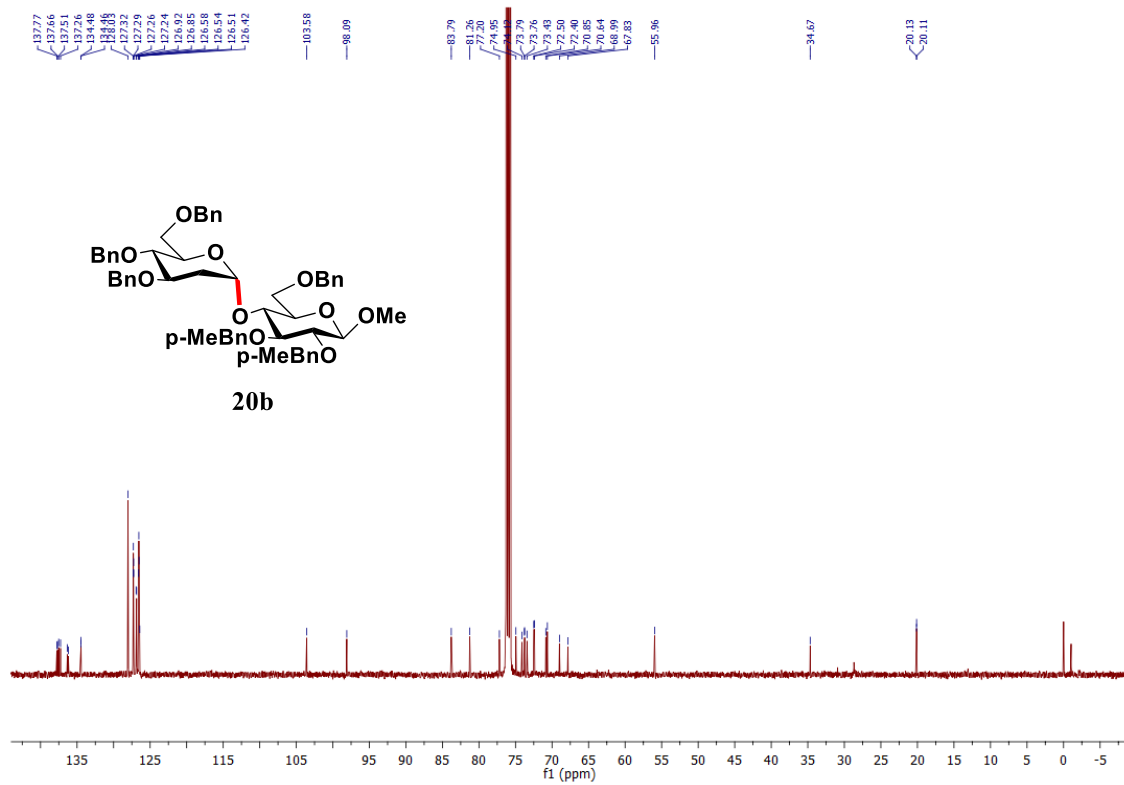
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 19j (500 MHz, CDCl_3):



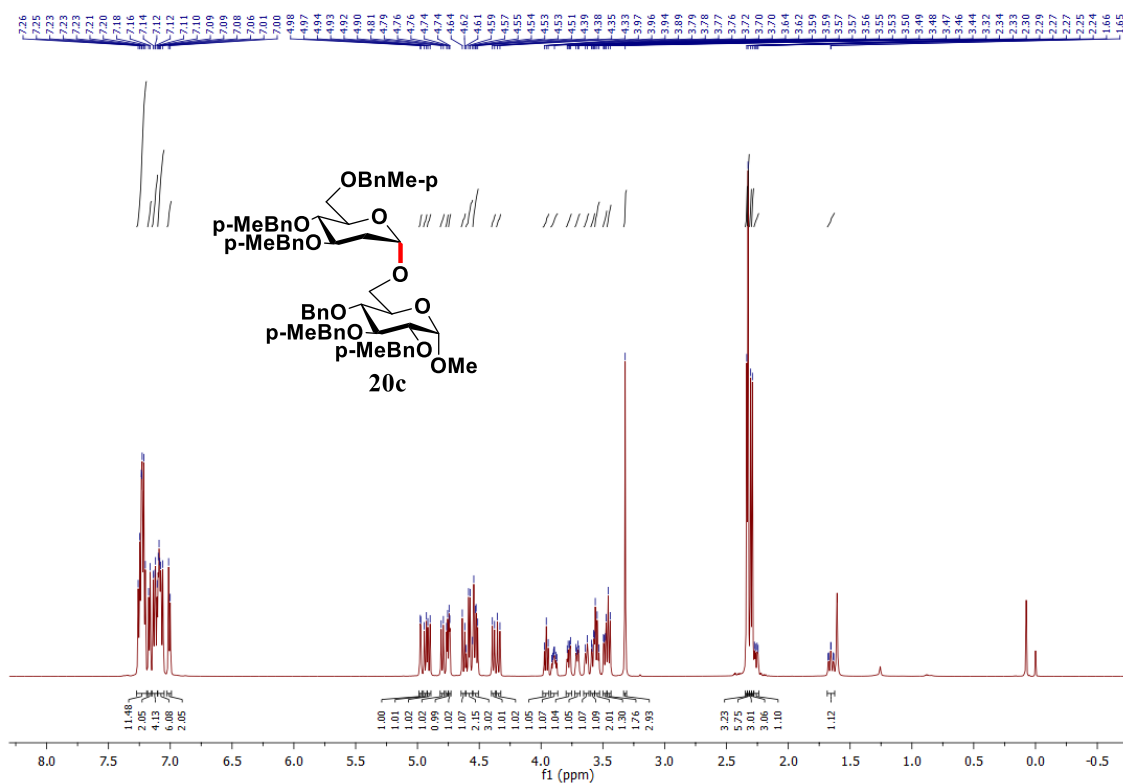
¹H NMR spectrum of compound 20b (600 MHz, CDCl₃):



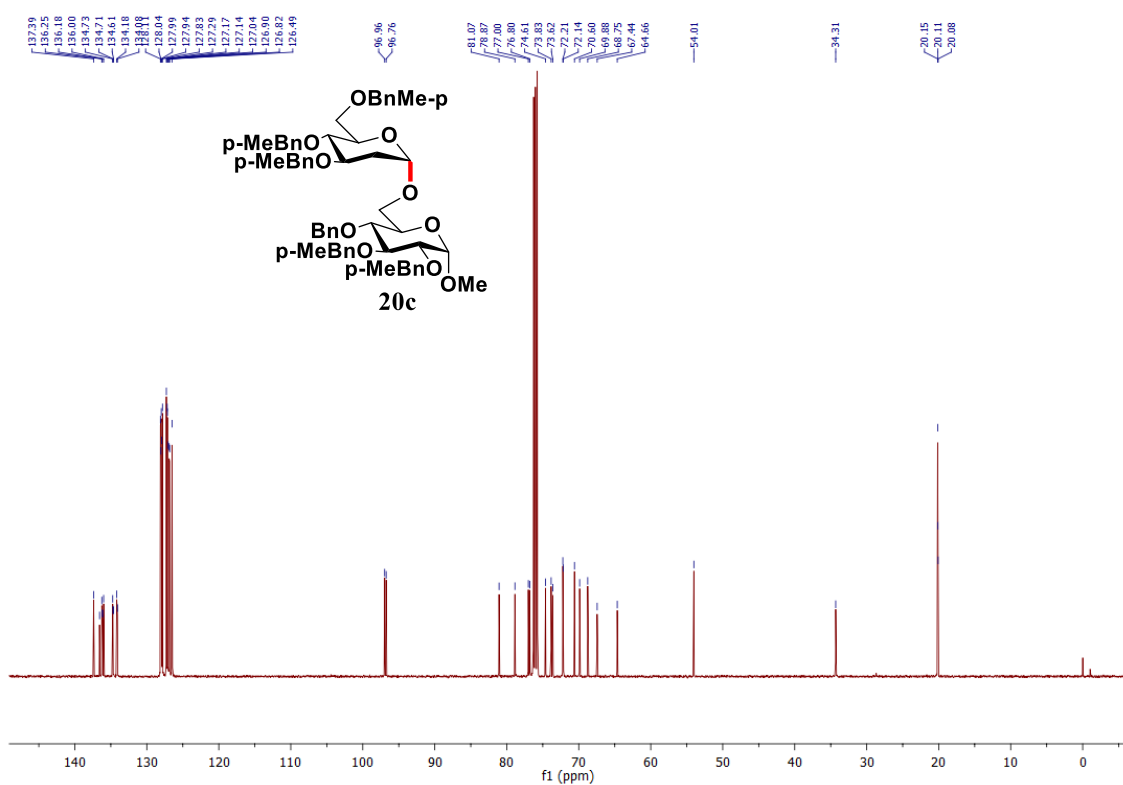
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 20b (500 MHz, CDCl_3):



^1H NMR spectrum of compound 20c (600 MHz, CDCl_3):



$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 20c (500 MHz, CDCl_3):

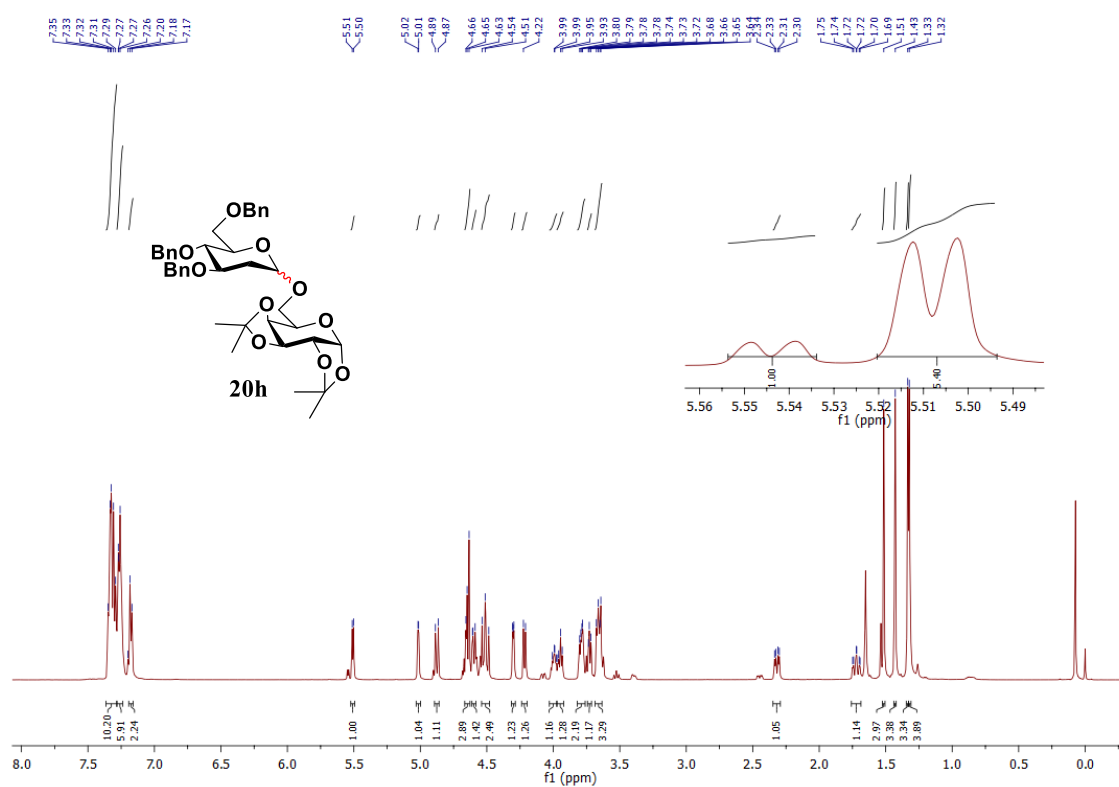


Chemical structure of compound 20f is shown above the spectrum. The structure is a dimeric glycoside with two pyranose rings. The left ring has a p-MeBnO group at C2 and a p-MeBnO group at C4. The right ring has a BnO group at C2, a BnO group at C4, and a BnOMe group at C6. The label "20f" is below the structure.

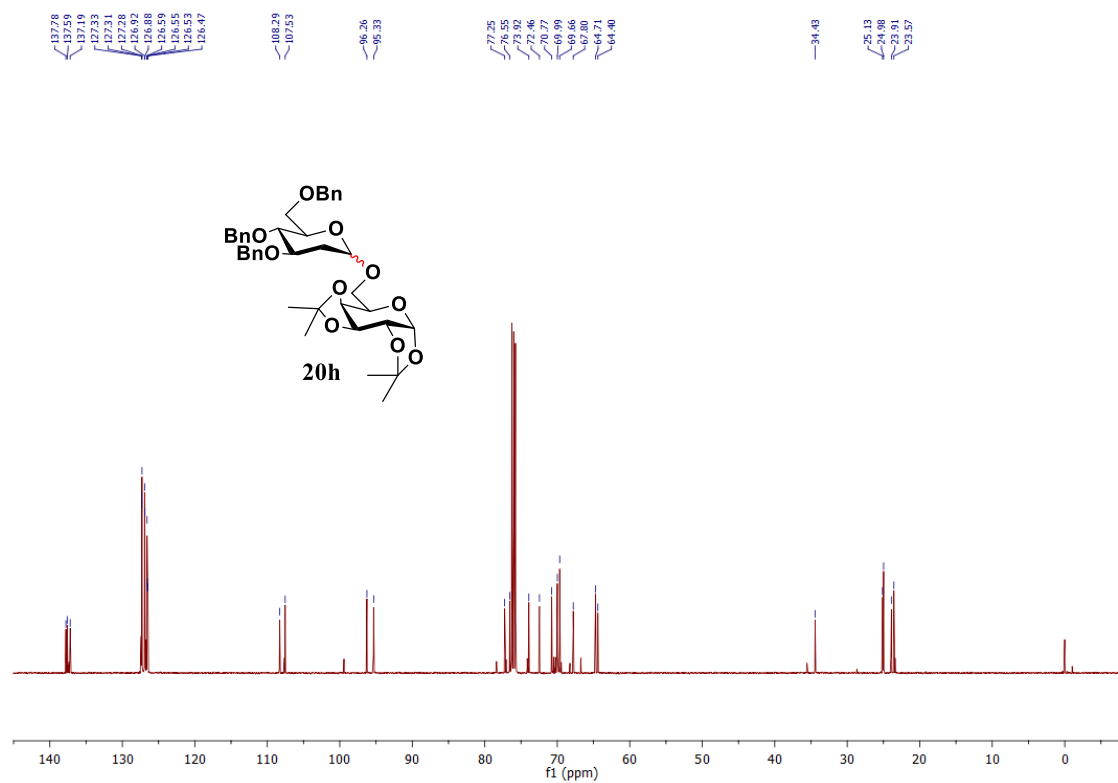
Chemical structure of compound 20f is shown above the spectrum. The structure is a complex molecule with a central pyranose ring. Substituents include p-MeBnO, OBnMe-p, and a 2f group. The spectrum shows peaks corresponding to these groups, with the following chemical shifts (ppm) labeled above the peaks:

- 138.83, 138.45, 137.39, 137.35, 136.63, 135.63, 135.41, 134.91, 129.06, 128.96, 128.54, 128.46, 128.39, 128.34, 128.23, 128.22, 127.77, 127.76, 127.59, 127.53, 98.62, 97.24, 79.25, 77.81, 77.41, 76.53, 74.88, 74.57, 74.54, 73.61, 73.55, 73.32, 71.70, 70.70, 68.62, 68.15, 65.51, 55.31, 55.24, 35.40, 21.25, 21.23.

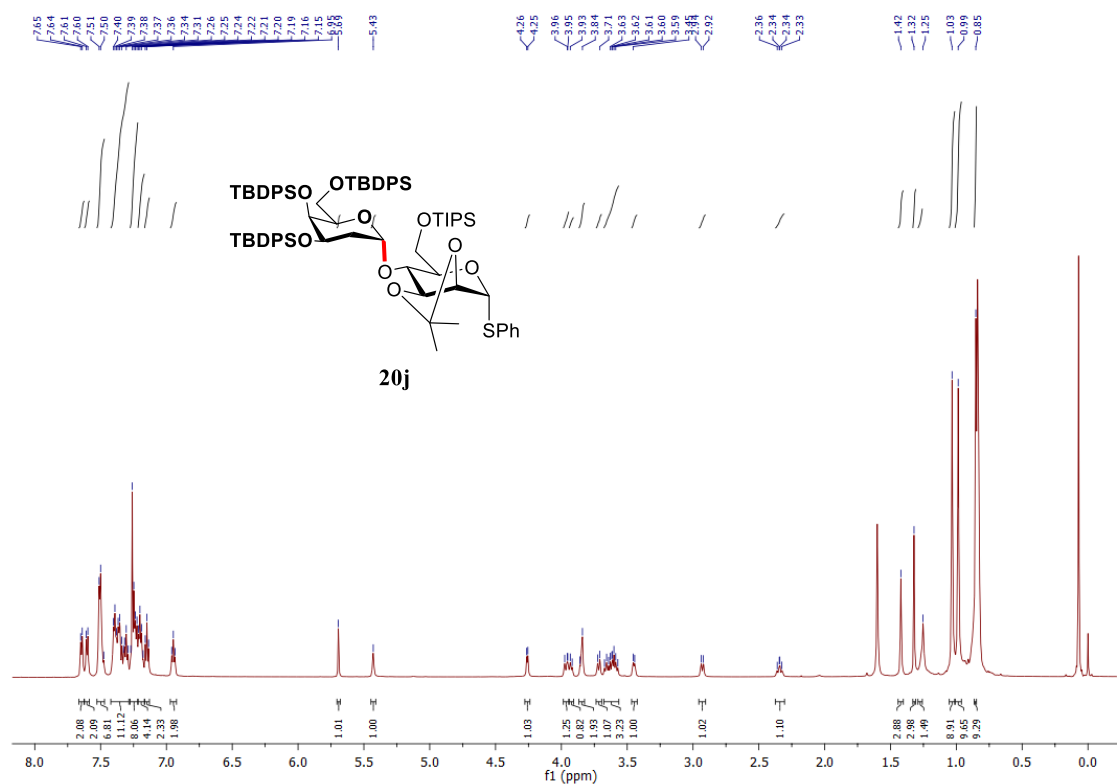
^1H NMR spectrum of compound 20h (500 MHz, CDCl_3):



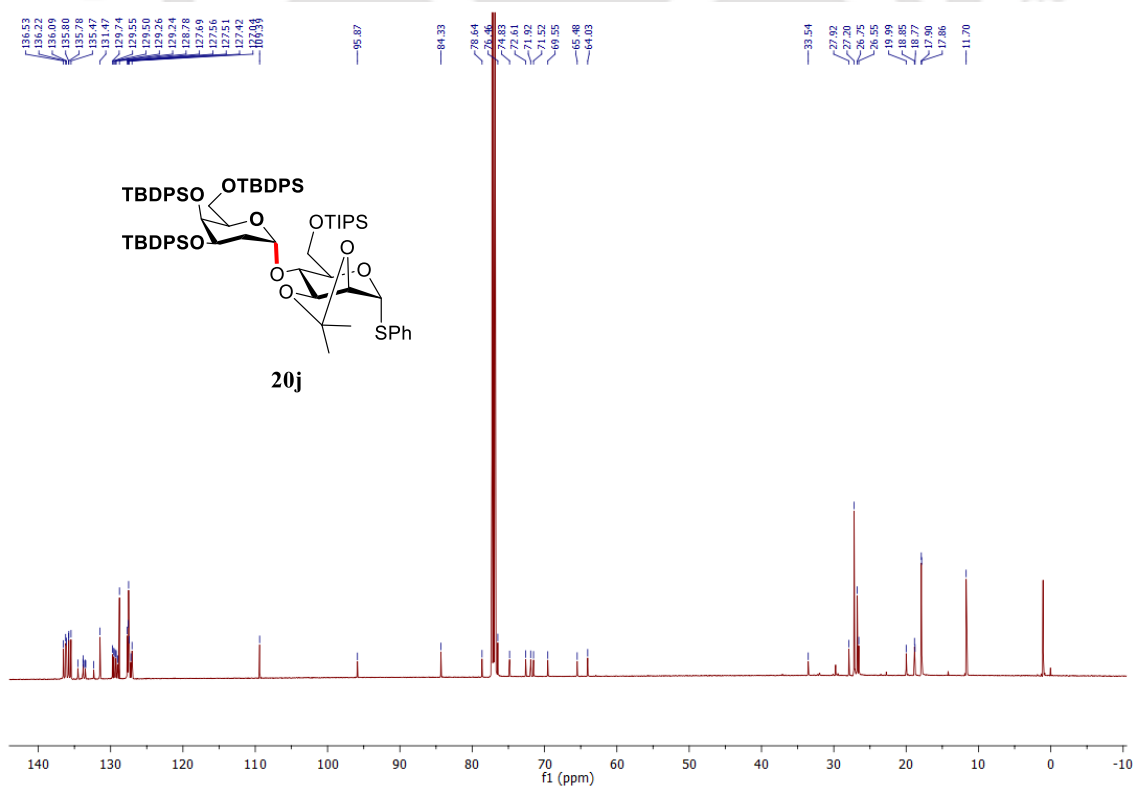
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 20h (500 MHz, CDCl_3):



^1H NMR spectrum of compound 20j (600 MHz, CDCl_3):



$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 20j (600 MHz, CDCl_3):



[illegible]

Chemical structure of compound 20k is shown above the spectrum. The structure is a complex glycoside with multiple protecting groups: TBDSO, OTBDPS, OBn, and p-MeBnO.

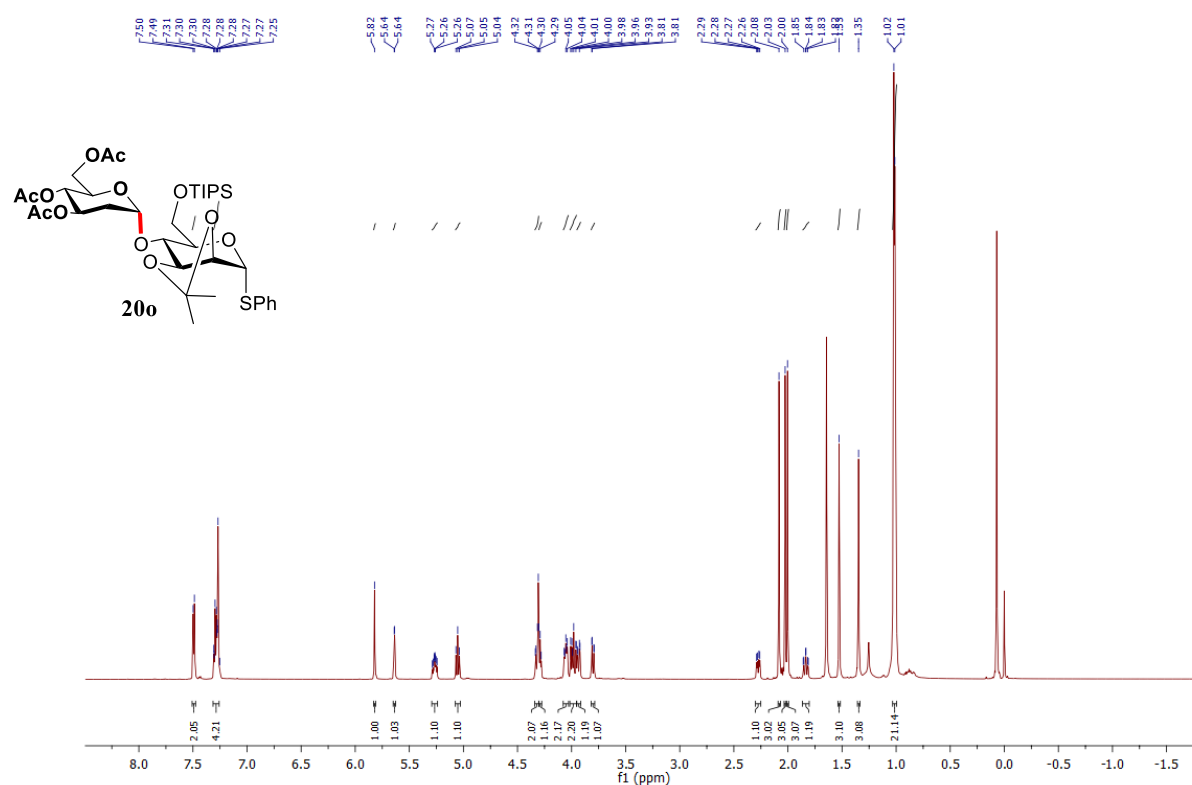
1H NMR peaks (ppm):

- 137.65, 137.53, 136.16, 136.06, 135.92, 135.63, 135.61, 135.59, 133.89, 129.77, 129.59, 129.29, 129.26, 129.24, 129.08, 128.37, 127.98, 127.96, 127.82, 127.80, 127.55, 127.46, 127.35, 127.14
- 82.22, 79.56, 77.56, 77.36, 72.59, 71.38, 69.82, 69.70, 66.56, 66.36
- 55.03
- 33.78
- 27.23, 27.18, 26.91, 26.86, 21.21, 20.02, 18.85, 18.82

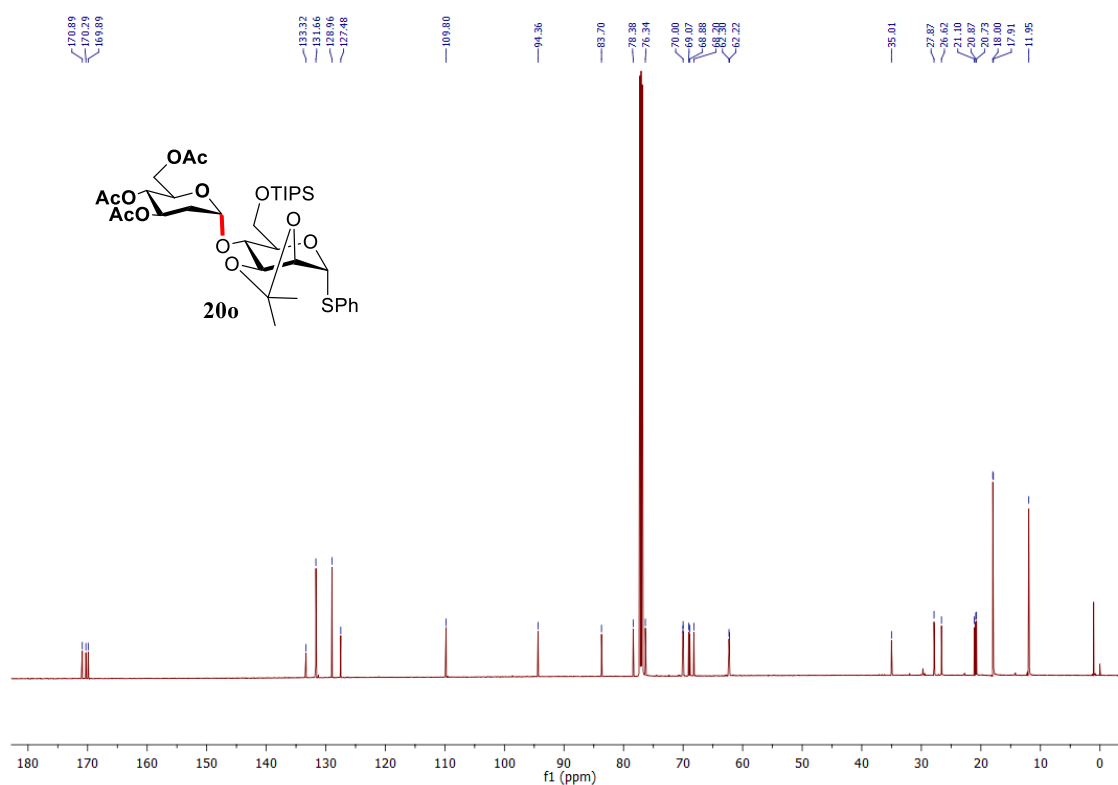
Chemical structure of **20m β** is shown, featuring a benzylidene-protected sugar derivative with an OTIPS group and a SPh group.

¹H NMR spectrum (CDCl₃) of **20m β** is displayed, showing peaks from 0 to 140 ppm. The spectrum includes a large solvent peak at 7.26 ppm. Key peaks are labeled with their chemical shifts: 138.33, 138.31, 133.89, 131.15, 128.90, 128.86, 128.30, 128.19, 127.91, 127.73, 127.70, 127.65, 127.17, 109.4, 99.30, 83.89, 79.59, 77.95, 76.76, 76.37, 75.04, 74.22, 73.51, 71.51, 70.99, 69.08, 61.78, 36.86, 27.86, 26.52, 17.99, 17.93, and 11.84.

^1H NMR spectrum of compound 20o (600 MHz, CDCl_3):



$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 20o (600 MHz, CDCl_3):



Chemical structure of compound 20p is shown above the spectrum. The structure is a dimer of a substituted sugar derivative. The top sugar unit is a pyranose ring with an OAc group at C1, an AcO group at C2, and an OAc group at C3. The bottom sugar unit is a pyranose ring with a BnO group at C1, a BnO group at C2, a BnO group at C3, and an SPh group at C4. The two units are linked by an ether bond between the C4 of the top unit and the C1 of the bottom unit.

1H NMR spectrum (CDCl₃):

- Chemical shift range: 0.0 to 8.0 ppm.
- Integration values: 1.95, 2.05, 18.02, 1.00, 2.13, 3.18, 1.05, 2.09, 1.02, 1.98, 1.03, 2.02, 3.05, 1.01, 2.82, 3.18, 2.05, 1.06.

Chemical structure of compound **20p** is shown above the spectrum. The structure is a dimer of a substituted furanose derivative. The top furanose ring has an OAc group at C2, an AcO group at C3, and an O-CH₂- group at C4. The bottom furanose ring has a BnO group at C2, a BnO group at C3, a BnO group at C4, and an SPh group at C5. The label **20p** is below the structure.

¹H NMR spectrum (CDCl₃) of compound **20p**. The x-axis is labeled f1 (ppm) and ranges from 180 to -10. The spectrum shows several peaks, with the following chemical shifts (ppm) labeled above the peaks:

- 169.69, 169.07, 168.83
- 132.26, 132.06, 131.97, 130.48, 128.05, 127.45, 127.44, 127.19, 126.86, 126.83, 126.77, 126.71, 126.59, 126.44
- 96.37
- 88.64, 85.73, 79.95, 77.22, 76.79, 74.79, 74.46, 73.96, 73.98, 68.15, 66.85, 65.59, 61.15
- 33.87
- 19.97, 19.73, 19.63

Chemical structure of **20r** is shown above the spectrum. The structure is a dimer of a substituted furan derivative. The peaks are labeled with their chemical shifts in ppm: 7.28, 7.26, 7.24, 7.23, 7.21, 7.19, 7.18, 7.15, 7.14, 7.13, 7.10, 7.09, 5.45, 5.44, 4.84, 4.81, 4.62, 4.60, 4.58, 4.57, 4.51, 4.49, 4.44, 4.41, 4.39, 4.38, 4.28, 3.81, 3.78, 3.77, 3.76, 3.59, 3.57, 3.52, 3.43, 3.42, 3.39, 3.38, 2.34, 2.33, 2.32, 2.31, 2.11, 2.10, 1.88, 1.83, 1.82, 1.81. Integration values are shown below the peaks: 3.81, 6.87, 14.08, 1.00, 1.00, 1.04, 1.02, 1.06, 1.06, 1.71, 1.03, 2.10, 1.03, 0.92, 1.12, 1.07, 5.12, 1.13, 3.05, 1.12, 2.72, 2.88, 8.84, 1.09, 1.06.

Chemical structure of compound **20r** is shown above the spectrum. The structure is a trimeric sugar derivative with p-methoxybenzyl (p-MeBnO) and benzyl (OBn) protecting groups. The anomeric carbons are labeled with 'p-MeBnO' and 'OBnMe-p'.

13C NMR spectrum (CDCl₃) data:

Chemical Shift (ppm)
137.59
137.00
136.23
136.23
136.15
136.09
134.51
134.48
134.22
134.12
128.06
128.00
127.84
127.39
127.22
127.20
126.75
126.75
126.59
126.35
103.54
98.31
83.75
81.24
74.54
74.24
73.79
73.47
73.38
72.85
72.35
72.21
71.41
69.77
69.25
55.56
30.53
20.13
20.12

Chemical structure of **20u** is shown above the spectrum. The structure is a complex molecule with multiple stereocenters and functional groups, including a p-methoxybenzyl (p-MeBn) group, a benzyl (Bn) group, and a phenyl (Ph) group.

¹H NMR spectrum (CDCl₃) of compound **20u**. The x-axis represents the chemical shift (f1) in ppm, ranging from -0.5 to 8.0. The spectrum shows several multiplets and singlets, with integration values indicated below the peaks.

Integration values (from left to right): 2.02, 8.06, 13.45, 8.38, 1.00, 1.08, 1.06, 1.00, 0.97, 1.24, 1.78, 1.06, 1.01, 1.05, 2.06, 1.17, 1.19, 0.86, 3.23, 2.62, 2.97, 2.98, 1.39.

Peak positions (f1 in ppm) listed on the right side of the spectrum: 7.56, 7.54, 7.41, 7.36, 7.34, 7.33, 7.32, 7.31, 7.28, 7.27, 7.25, 7.24, 7.22, 7.21, 7.20, 7.15, 7.14, 7.12, 7.10, 7.09, 5.07, 5.07, 4.92, 4.90, 4.88, 4.87, 4.85, 4.83, 4.81, 4.79, 4.75, 4.72, 4.65, 4.63, 4.57, 4.55, 4.54, 4.52, 4.52, 4.50, 4.42, 4.40, 4.35, 4.33, 3.89, 3.88, 3.87, 3.85, 3.85, 3.82, 3.82, 3.81, 3.79, 3.79, 3.73, 3.72, 3.72, 3.69, 3.69, 3.52, 3.51, 3.51, 3.48, 3.48, 3.47, 3.45, 3.45, 2.33, 2.32, 2.29, 2.29, 2.22, 2.22, 2.20, 2.20, 2.02, 2.02, 1.99, 1.99.

Chemical structure of compound 20u is shown above the spectrum. The structure is a dimer of a substituted furanose derivative. The top furanose ring has a p-MeBnO group at C2, an OBnMe-p group at C3, and a p-MeBnO group at C4. The bottom furanose ring has a BnO group at C2, a BnO group at C3, and a SPh group at C4. The x-axis is labeled 'f1 (ppm)' and ranges from 0 to 140. The y-axis is labeled 'Intensity'.

Chemical structure of compound **20x** is shown above the ^1H NMR spectrum. The structure features a central core with various substituents, including BzO, OBz, OTIPS, and SPh.

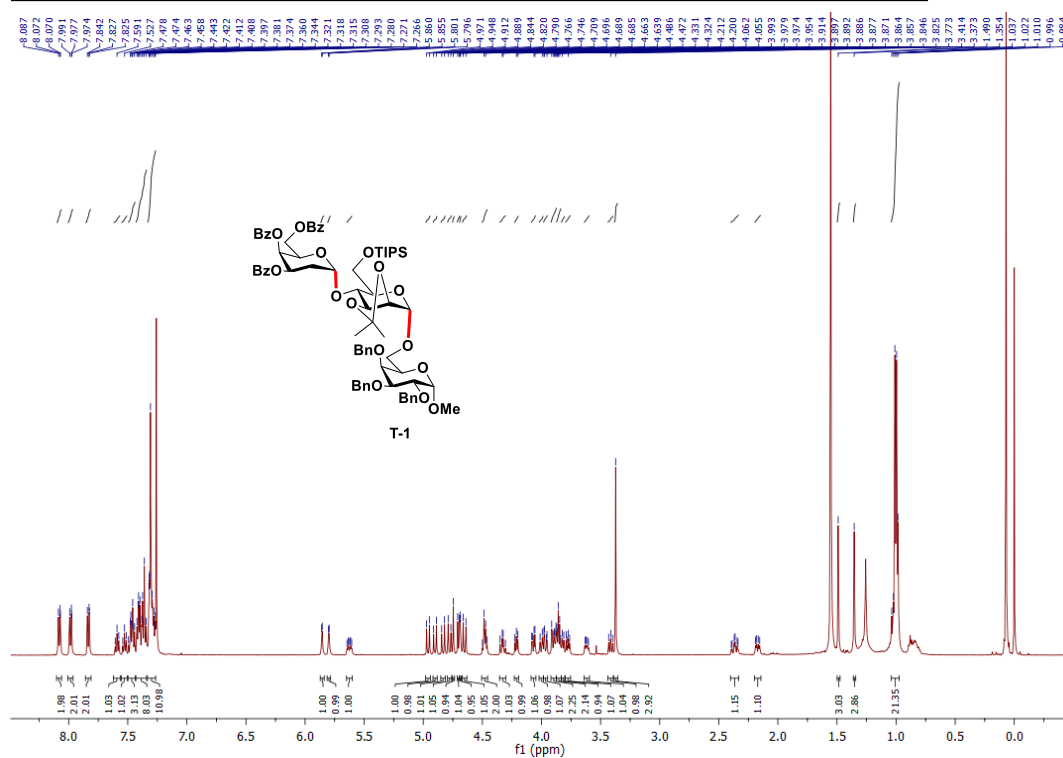
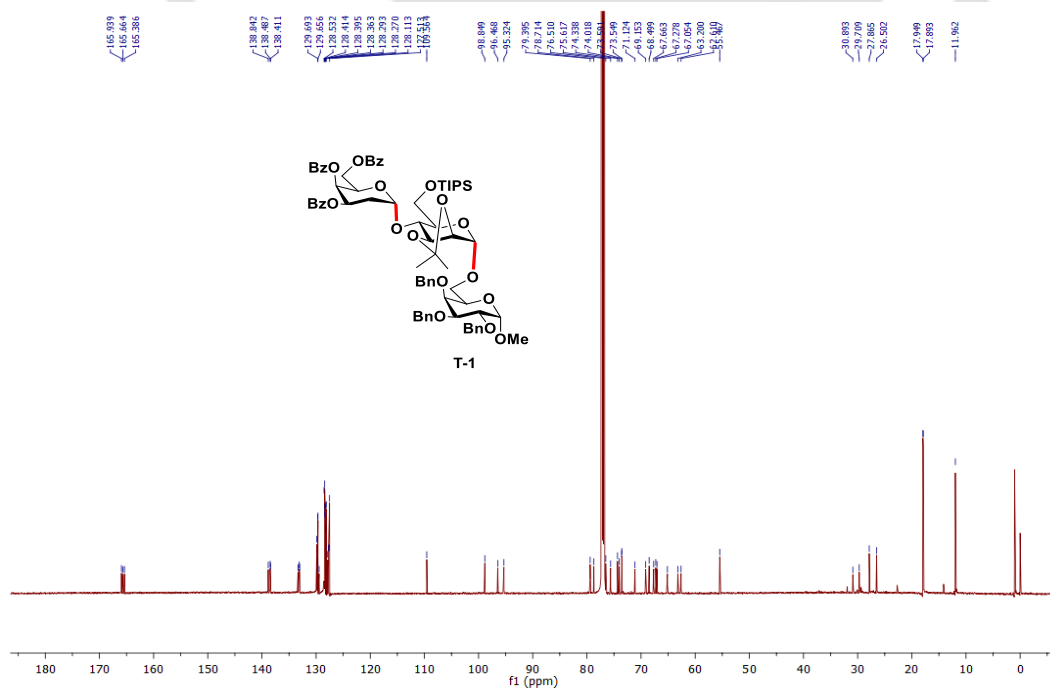
The ^1H NMR spectrum (CDCl₃) displays peaks corresponding to the structure. The x-axis represents the chemical shift in ppm, ranging from 0 to 8.5. The y-axis represents the intensity of the signal.

Integration values are provided below the peaks, indicating the relative areas under the curves:

- 8.00, 8.08, 7.99, 7.98, 7.86, 7.85, 7.53, 7.52, 7.52, 7.48, 7.46, 7.41, 7.39, 7.32, 7.31, 7.30, 7.29, 7.28, 7.27, 7.26, 7.25, 7.24, 7.23, 7.22, 7.21, 7.20, 7.19, 7.18, 7.17, 7.16, 7.15, 7.14, 7.13, 7.12, 7.11, 7.10, 7.09, 7.08, 7.07, 7.06, 7.05, 7.04, 7.03, 7.02, 7.01, 7.00, 6.99, 6.98, 6.97, 6.96, 6.95, 6.94, 6.93, 6.92, 6.91, 6.90, 6.89, 6.88, 6.87, 6.86, 6.85, 6.84, 6.83, 6.82, 6.81, 6.80, 6.79, 6.78, 6.77, 6.76, 6.75, 6.74, 6.73, 6.72, 6.71, 6.70, 6.69, 6.68, 6.67, 6.66, 6.65, 6.64, 6.63, 6.62, 6.61, 6.60, 6.59, 6.58, 6.57, 6.56, 6.55, 6.54, 6.53, 6.52, 6.51, 6.50, 6.49, 6.48, 6.47, 6.46, 6.45, 6.44, 6.43, 6.42, 6.41, 6.40, 6.39, 6.38, 6.37, 6.36, 6.35, 6.34, 6.33, 6.32, 6.31, 6.30, 6.29, 6.28, 6.27, 6.26, 6.25, 6.24, 6.23, 6.22, 6.21, 6.20, 6.19, 6.18, 6.17, 6.16, 6.15, 6.14, 6.13, 6.12, 6.11, 6.10, 6.09, 6.08, 6.07, 6.06, 6.05, 6.04, 6.03, 6.02, 6.01, 6.00, 5.99, 5.98, 5.97, 5.96, 5.95, 5.94, 5.93, 5.92, 5.91, 5.90, 5.89, 5.88, 5.87, 5.86, 5.85, 5.84, 5.83, 5.82, 5.81, 5.80, 5.79, 5.78, 5.77, 5.76, 5.75, 5.74, 5.73, 5.72, 5.71, 5.70, 5.69, 5.68, 5.67, 5.66, 5.65, 5.64, 5.63, 5.62, 5.61, 5.60, 5.59, 5.58, 5.57, 5.56, 5.55, 5.54, 5.53, 5.52, 5.51, 5.50, 5.49, 5.48, 5.47, 5.46, 5.45, 5.44, 5.43, 5.42, 5.41, 5.40, 5.39, 5.38, 5.37, 5.36, 5.35, 5.34, 5.33, 5.32, 5.31, 5.30, 5.29, 5.28, 5.27, 5.26, 5.25, 5.24, 5.23, 5.22, 5.21, 5.20, 5.19, 5.18, 5.17, 5.16, 5.15, 5.14, 5.13, 5.12, 5.11, 5.10, 5.09, 5.08, 5.07, 5.06, 5.05, 5.04, 5.03, 5.02, 5.01, 5.00, 4.99, 4.98, 4.97, 4.96, 4.95, 4.94, 4.93, 4.92, 4.91, 4.90, 4.89, 4.88, 4.87, 4.86, 4.85, 4.84, 4.83, 4.82, 4.81, 4.80, 4.79, 4.78, 4.77, 4.76, 4.75, 4.74, 4.73, 4.72, 4.71, 4.70, 4.69, 4.68, 4.67, 4.66, 4.65, 4.64, 4.63, 4.62, 4.61, 4.60, 4.59, 4.58, 4.57, 4.56, 4.55, 4.54, 4.53, 4.52, 4.51, 4.50, 4.49, 4.48, 4.47, 4.46, 4.45, 4.44, 4.43, 4.42, 4.41, 4.40, 4.39, 4.38, 4.37, 4.36, 4.35, 4.34, 4.33, 4.32, 4.31, 4.30, 4.29, 4.28, 4.27, 4.26, 4.25, 4.24, 4.23, 4.22, 4.21, 4.20, 4.19, 4.18, 4.17, 4.16, 4.15, 4.14, 4.13, 4.12, 4.11, 4.10, 4.09, 4.08, 4.07, 4.06, 4.05, 4.04, 4.03, 4.02, 4.01, 4.00, 3.99, 3.98, 3.97, 3.96, 3.95, 3.94, 3.93, 3.92, 3.91, 3.90, 3.89, 3.88, 3.87, 3.86, 3.85, 3.84, 3.83, 3.82, 3.81, 3.80, 3.79, 3.78, 3.77, 3.76, 3.75, 3.74, 3.73, 3.72, 3.71, 3.70, 3.69, 3.68, 3.67, 3.66, 3.65, 3.64, 3.63, 3.62, 3.61, 3.60, 3.59, 3.58, 3.57, 3.56, 3.55, 3.54, 3.53, 3.52, 3.51, 3.50, 3.49, 3.48, 3.47, 3.46, 3.45, 3.44, 3.43, 3.42, 3.41, 3.40, 3.39, 3.38, 3.37, 3.36, 3.35, 3.34, 3.33, 3.32, 3.31, 3.30, 3.29, 3.28, 3.27, 3.26, 3.25, 3.24, 3.23, 3.22, 3.21, 3.20, 3.19, 3.18, 3.17, 3.16, 3.15, 3.14, 3.13, 3.12, 3.11, 3.10, 3.09, 3.08, 3.07, 3.06, 3.05, 3.04, 3.03, 3.02, 3.01, 3.00, 2.99, 2.98, 2.97, 2.96, 2.95, 2.94, 2.93, 2.92, 2.91, 2.90, 2.89, 2.88, 2.87, 2.86, 2.85, 2.84, 2.83, 2.82, 2.81, 2.80, 2.79, 2.78, 2.77, 2.76, 2.75, 2.74, 2.73, 2.72, 2.71, 2.70, 2.69, 2.68, 2.67, 2.66, 2.65, 2.64, 2.63, 2.62, 2.61, 2.60, 2.59, 2.58, 2.57, 2.56, 2.55, 2.54, 2.53, 2.52, 2.51, 2.50, 2.49, 2.48, 2.47, 2.46, 2.45, 2.44, 2.43, 2.42, 2.41, 2.40, 2.39, 2.38, 2.37, 2.36, 2.35, 2.34, 2.33, 2.32, 2.31, 2.30, 2.29, 2.28, 2.27, 2.26, 2.25, 2.24, 2.23, 2.22, 2.21, 2.20, 2.19, 2.18, 2.17, 2.16, 2.15, 2.14, 2.13, 2.12, 2.11, 2.10, 2.09, 2.08, 2.07, 2.06, 2.05, 2.04, 2.03, 2.02, 2.01, 2.00, 1.99, 1.98, 1.97, 1.96, 1.95, 1.94, 1.93, 1.92, 1.91, 1.90, 1.89, 1.88, 1.87, 1.86, 1.85, 1.84, 1.83, 1.82, 1.81, 1.80, 1.79, 1.78, 1.77, 1.76, 1.75, 1.74, 1.73, 1.72, 1.71, 1.70, 1.69, 1.68, 1.67, 1.66, 1.65, 1.64, 1.63, 1.62, 1.61, 1.60, 1.59, 1.58, 1.57, 1.56, 1.55, 1.54, 1.53, 1.52, 1.51, 1.50, 1.49, 1.48, 1.47, 1.46, 1.45, 1.44, 1.43, 1.42, 1.41, 1.40, 1.39, 1.38, 1.37, 1.36, 1.35, 1.34, 1.33, 1.32, 1.31, 1.30, 1.29, 1.28, 1.27, 1.26, 1.25, 1.24, 1.23, 1.22, 1.21, 1.20, 1.19, 1.18, 1.17, 1.16, 1.15, 1.14, 1.13, 1.12, 1.11, 1.10, 1.09, 1.08, 1.07, 1.06, 1.05, 1.04, 1.03,

Chemical structure of **20x** is shown above the spectrum. The structure is a complex molecule with a central core and various substituents. The peaks are labeled with their corresponding chemical shifts in ppm.

Chemical Shift (ppm)
165.96
165.98
165.44
133.49
133.38
133.15
133.08
131.71
129.89
129.82
129.65
129.47
128.97
128.56
128.41
128.34
127.49
109.84
95.26
83.85
79.52
76.46
70.90
70.43
67.53
67.20
67.03
62.60
62.43
30.86
27.89
26.62
17.93
17.85
11.95

^1H NMR spectrum of compound T-1 (500 MHz, CDCl_3): **$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound T-1 (600 MHz, CDCl_3):**

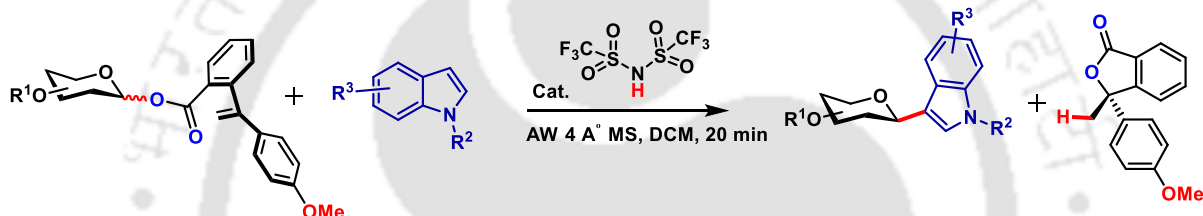
The Supporting Information of Chapter IIB is available at

The supporting information of Chapter IIB is available at

<https://www.rsc.org/suppdata/d1/ob/d1ob02502c/d1ob02502c1.pdf>

Chapter III

Regio and Stereoselective C-Glycosylation of Indoles Using *ortho*-[1-(*p*-MeO-Phenyl)vinyl]benzoates (PMPVB) as Glycosyl Donors Under Brønsted acid Catalysis





4.1.1 Introduction

C-glycosides having the C-C linkage are one of the significant compounds for glycochemists due to the resistance towards enzymatic hydrolysis along with the presence of numerous bioactive natural products.¹ Among the numerous modification strategies for the development of bioactive C-glycosides, one of the classical approaches is glycosylation, a nucleophilic attack at the anomeric center of the carbohydrate. One of the important factors in C-glycosylation reaction is stereoselectivity with high yields which is quite difficult due to the poor nucleophilicity of C-nucleophiles. Indoles and substituted indoles are π -nucleophiles having better nucleophilicity parameters compared to other π -nucleophiles.² Indole scaffold is frequently present in many natural products, agrochemicals, and pharmaceuticals and imparts anti-inflammatory and anti-cancer properties.³

Indole and its derivative are found in different kinds of plants, animals, and marine organisms.⁴ Indole is the core substance of different bioactive natural products (Figure 1). Indoles are one of widely distributed the heterocyclic compounds having biological importance. Generally, indole and its simple alkyl-derivatives are found as a colorless crystalline solid having a range of odours.⁵ Tryptophan (2-amino-3-(3'-indolyl)propionic acid) (**1a**, Figure1) an essential naturally occurring amino acid, participates in many biological processes.⁶ Naturally occurring indole-3-acetic acid (IAA) (**1b**, Figure1) is an auxin class of plant hormone.⁷ Hydroxy group containing tryptamine (5-hydroxytryptamine, Serotonin) (**1c**, Figure1) biochemically derived from tryptophan, found in all bilateral animals which is a vasoconstrictor hormone that plays a crucial role in conducting impulses to the brain.⁸ Melatonin (**1d**, Figure1) is a hormone found in animals, plants, and microbes, which is thought to control the diurnal rhythm of physiological functions.⁹ Sumatriptan (**1f**, Figure1) a derivative of tryptamine is commonly used for the treatment of migraine.¹⁰ Indole-3-carbinol (I3C) (**1h**, Figure1) and 3,3'-diindolyl-methane (DIM) (**1e**, Figure1) are found in cruciferous vegetables such as broccoli, brussels sprouts, cabbage, and kale, having anticarcinogenic, antioxidant, and antiatherogenic properties.¹¹ Indole alkaloid containing an antihypertensive drug, Ajmalicine (**1g**, Figure1) is naturally found in numerous plants and is used in the treatment of high blood pressure.¹²

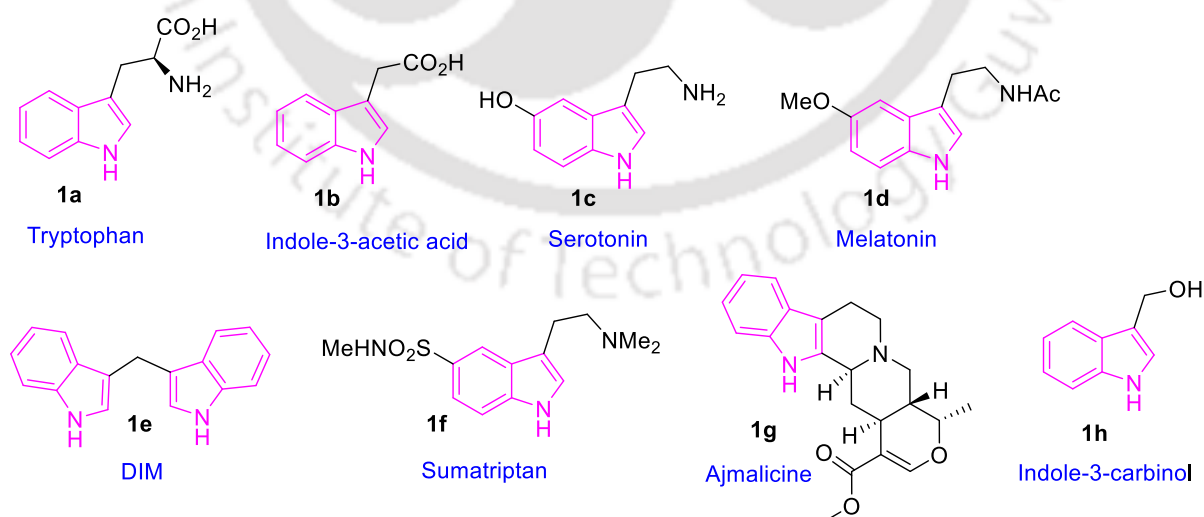


Figure 1: Indole-containing natural products and drugs

Recently some C-indolyl glycosides have been isolated from natural sources having *anti-viral* and *anti-cancer* properties along with other anti-disease properties (figure 2).¹³ The α -C

-mannosyltryptophan (**2a**) is the first naturally occurring C-glycosyl amino acid which was discovered from the tryptophan residue of human RNase. The C-2 position of tryptophan moiety is connected to the mannose sugar at the anomeric position through the C-C glycosidic linkage.¹⁴ Recently, 3-indolyl-C-glycosides (**2b** & **2c**) (Figure 2) have also been approved as sodium-dependent glucose cotransporter 2 (SGLT2) inhibitors for the treatment of type-2 diabetes mellitus (T2DM) patients.¹⁵ 2-Indolyl-C-glycosides named *N*-methoxy-indole-3-acetonitrile-2-*C*- β -D-glucopyranoside (**2d**) and indole-3-acetonitrile-4-methoxy-2-*C*- β -D-glucopyranoside (**2e**) were the first isolated alkaloids C-glycosides from *Isatis* which exhibit cytotoxic activities against human myeloid leukemia HL-60 cells, human liver cancer HepG2 cells, and human myeloid leukemia Mata cells.¹³

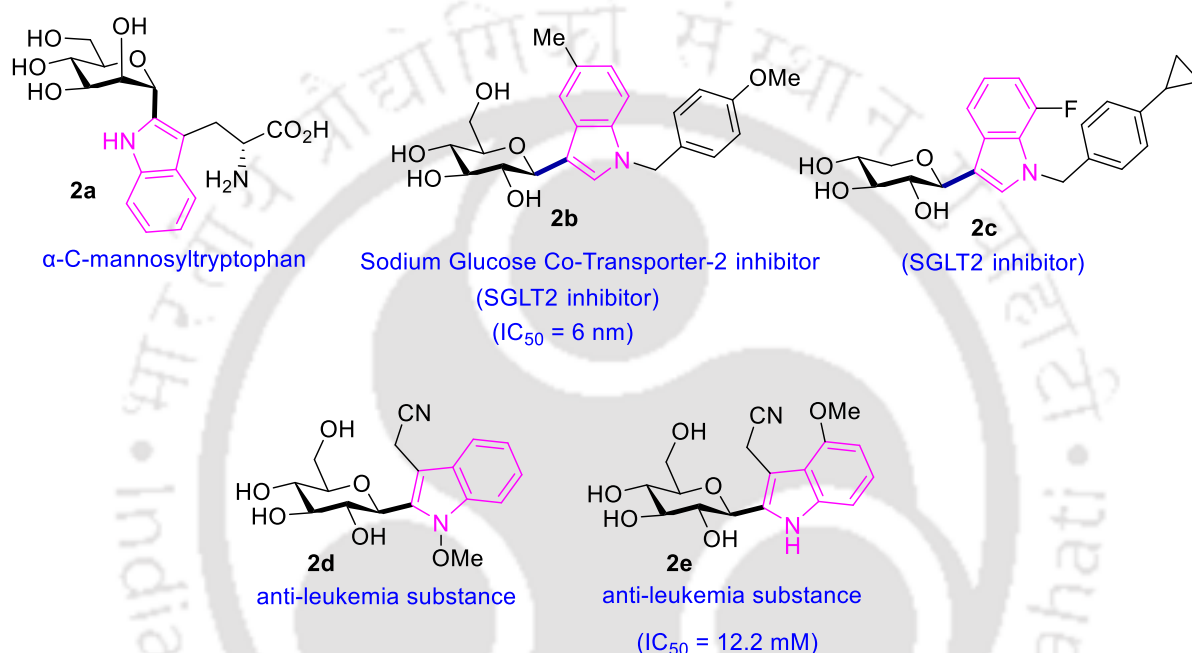


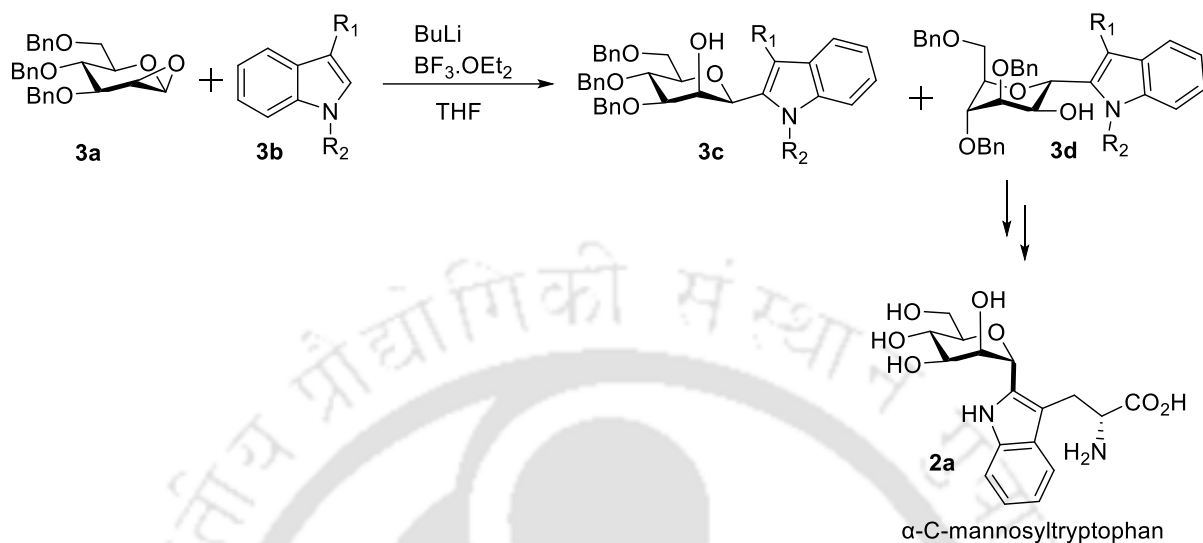
Figure 2: Bioactive molecules containing indole C-glycosides.

4.1.2 Literature survey of indolyl C-glycosides

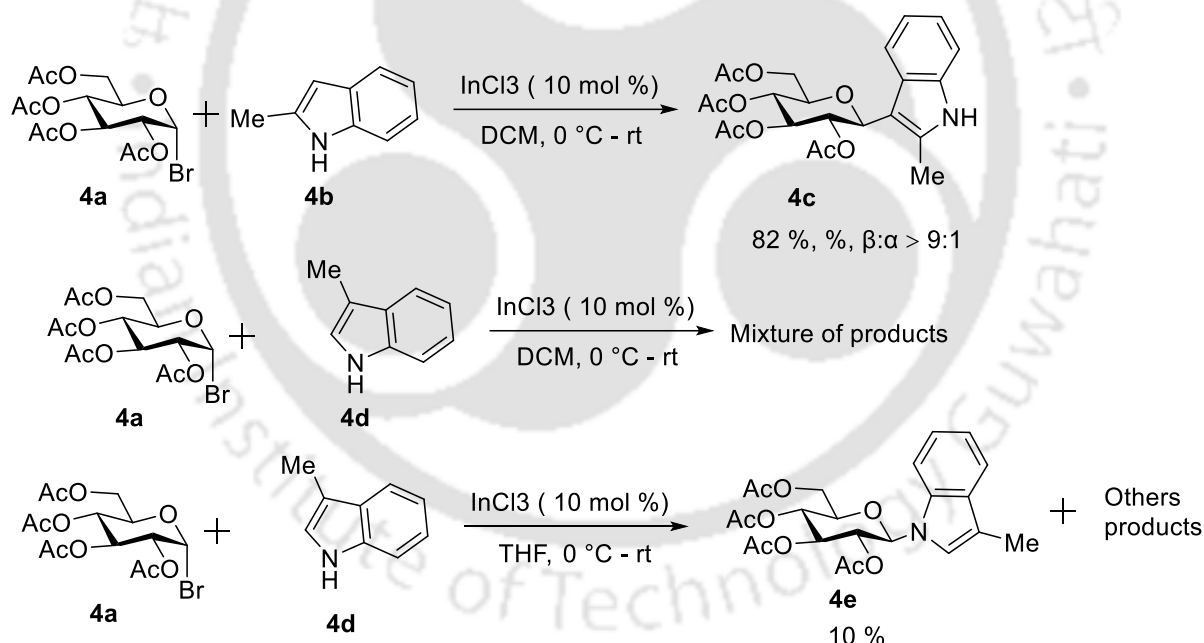
Compared to O-glycosylation and N-glycosylation, C-glycosylations are less developed which can be attributed to the poor nucleophilicity of the C-nucleophiles relative to the O-nucleophiles. The development of C-glycosylation approaches is more sluggish compared to other glycosylation methods. Organometallic reagents with increased nucleophilicities have been introduced to react with the glycosyl donor to overcome the poor nucleophilicity of C-nucleophiles.¹⁶⁻¹⁷ There is a recent surge in the development of synthetic methods, particularly toward the stereoselective synthesis of C-aryl and C-heteroaryl glycosides.¹⁸ Among the C-glycosylation procedures, some methods involve expensive metal-catalyzed C-H activation protocols,¹⁹ and some other methods involve metallated nucleophiles based on Grignard, tin, lithium and other reagents with glycosyl donors.²⁰ Certain methods also involve the usage of carboanionic reactivity at the anomeric center.²¹ However, these reagents are difficult to handle due to their inherent air and moisture sensitivity or involve multistep synthesis.

The incorporation of a higher-order structure of the parent protein influences the biological activity of the protein. After discovering the C-glycosyl amino acid, namely, C₂- α -

D-C-mannosylpyranosyl-L-tryptophan, Ito, and coworkers, developed the synthetic procedure of Mannosyl Tryptophan and Its derivatives from benzyl-protected 1,2-anhydro-mannose and lithiated indole derivative through a few steps (protection, functional group interconversion, deprotection) (Scheme 1).²²



Scheme 1: Total Synthesis of Mannosyl Tryptophan

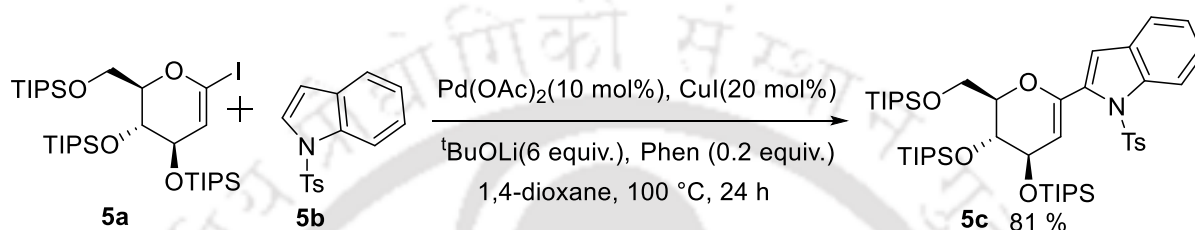


Scheme 2: InCl₃ catalyzed glycosylation of glycosyl bromide

In 2007, Taneja and co-workers reported InCl₃ catalyzed 3-indolyl C-glycosylation by using glycosyl bromide as a potential glycosyl donor (Scheme 2).²³ It was reported that 2-substituted indoles afforded good yields compared to other substituted indoles whereas the unsubstituted indoles provided very low yields. *N*-methyl indole having a nitro substitution at the aromatic ring failed to provide glycosylated products. They also performed a reaction taking 3-methyl indole (4d) with similar optimized conditions which resulted in an inseparable mixture of products. Later repetition of the reaction in THF medium instead of

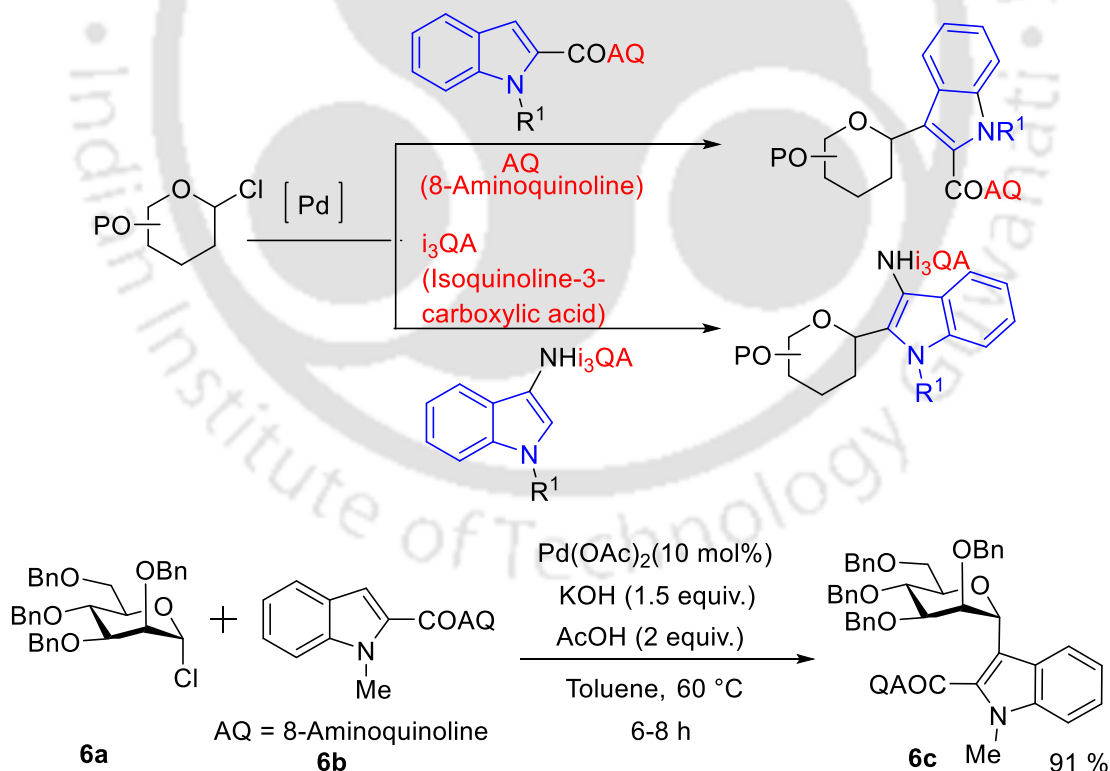
DCM provided 10 % of *N*-glycosylate product (**4e**) along with other mixture of products (Scheme 2).

In 2017, Zhang et al. reported a palladium/copper co-catalyzed direct cross-coupling reaction of 1-iodoglycals with *N*-substituted indoles in a regioselective *C*–*H* functionalization manner (Scheme 3).²⁴ In this report only silyl-protected 1-iodoglycals (glucal, galactal, rhamnal) and *N*-tosyl-protected substituted indoles have been used for this study. They also investigated the reaction by taking a strong electron-withdrawing group (nitro group) containing indole which failed to react with tri-isopropyl silyl-protected 1-iodoglucal under similar optimized conditions.



Scheme 3: palladium/copper co-catalyzed *C*-glycosylation

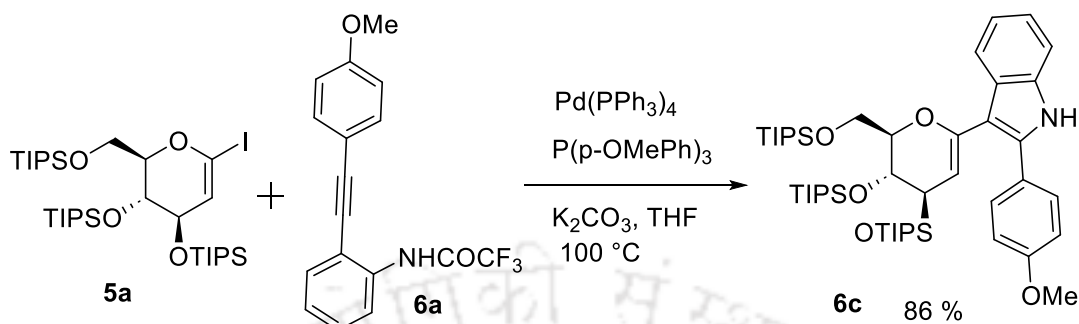
Chen and co-workers also developed elegant palladium-catalyzed ortho-directed *C*–*H* glycosylation of indoles with glycosyl chloride donors (Scheme 4).^{19a}



Scheme 4: palladium-catalyzed glycosylation of mannosyl chloride

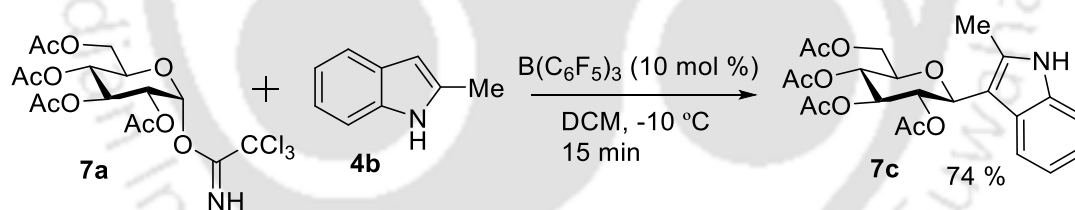
In 2020, Sun and co-workers reported a sequential heterocyclization and *C*-glycosylation sequence of *O*-alkynyl anilines with 1-iodoglycals to construct 3-indolyl-*C*-glycosides (Scheme 5).²⁵ They investigated the reaction of taking substituted *O*-

alkynyltrifluoroacetanilides with tri-isopropyl silyl-protected 1-iodoglycals (glucal & rhamnal). They performed the reaction with different protection of *N*-group of *O*-alkynyl anilines where acetyl, benzyl, and benzoyl protection failed to provide the expected C-glycosides whereas tosyl protection did well.



Scheme 5: Palladium-catalysed glycosylation of 1-Iodo-glycals

Nishikawa et al. also reported synthesis of β -analogue of *C*-mannosyltryptophan, a multi-step sequence involving *C*-2 substituted sugar indoles utilizing a Castro indole synthesis.²⁶ While the existing methods are dominated by the metal-catalyzed *C-H* activation protocols, a recent method developed by Mandal and co-workers utilizes tris(pentafluorophenyl)borane ($\text{B(C}_6\text{F}_5)_3$), an expensive catalyst to synthesize indolyl glycosides from the relatively unstable glycosyl trichloroacetimidate donors (Scheme 6).²⁶ It was reported that in the presence of 10 mol % of ($\text{B(C}_6\text{F}_5)_3$) at -10°C Schmidt's donor α -trichloroacetimidates react well with substituted indoles in DCM medium within 15 min via Friedel–Crafts-type glycosylation pathway which resulted in the stereoselective synthesis of 3-indolyl- β -*C*-glycosides.



Scheme 6: $\text{B(C}_6\text{F}_5)_3$ -Catalyzed 3-Indolyl-*C*- Glycosylation

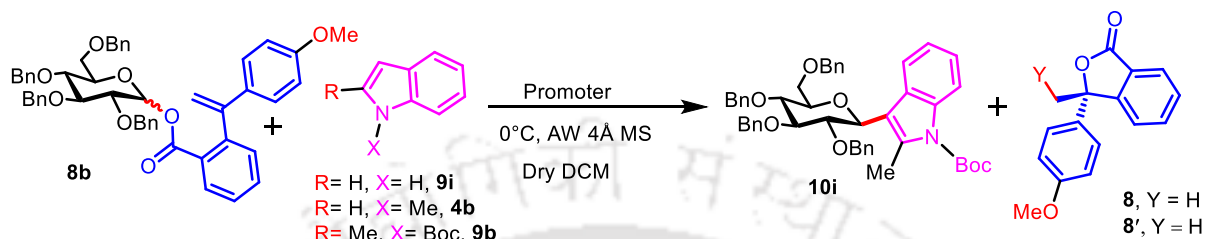
4.2 This Work

Most of these methods suffer from the drawbacks of metal catalysis, multi-step reaction sequences, usage of auxiliaries, and delicate reaction conditions. Also, all of these methods utilize unprotected indoles that might have a tendency to lead to a competing *N*-glycosylation reaction, resulting in lower product yields. On the other hand, the usual protecting groups on indole, like the *N*-acetyl and *N*-Boc protecting groups, reduce the nucleophilicity of the indole derivatives, which may result in poor coupling reactions. In order to have broad applicability, it is important to develop methods where these *N*-protected indoles can be coupled to provide the indolyl glycosides. In this chapter, following our interest in the synthesis of *C*-glycosyl derivatives,²⁷ we describe the utility of our recently introduced highly reactive yet stable PMPVB donors²⁸ that can be activated under simple catalytic Brønsted acidic conditions, without the need of any metal catalysis, toward the regio and stereoselective synthesis of *C*-linked indolyl glycosides in excellent yields. The mechanism leading to such

stereoselective glycosylations are discussed in detail.

4.2.1 Table1: Optimization of the Reaction Conditions

From our recent works, PMPVB donors are extremely reactive donors that can provide O- and S-glycosides in just 5 minutes using 30 mol % of Brønsted acid (TfOH, Tf₂NH).²⁸ However, the nucleophilicity of indoles is not comparable to alcohols/thiols. We anticipated that the high reactivity of the PMPVB donors might allow us to use indoles as nucleophiles.

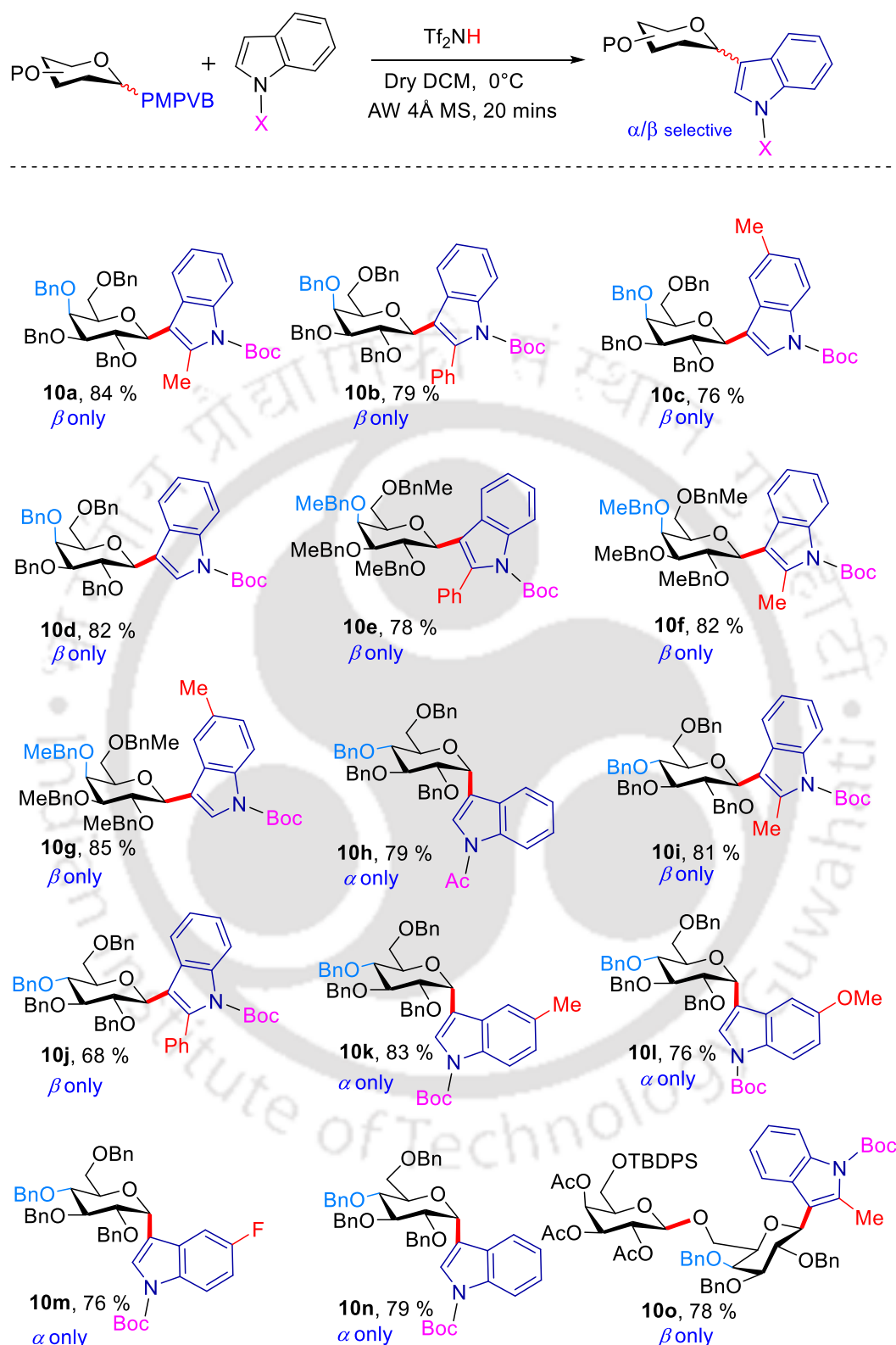


Entry	Cat. (mol %)	acceptor	D/A	Time	Yield (%), $\alpha:\beta$
1	Tf ₂ NH (30)	9b	1/2	20 min	82, β only
2 ^a	NIS/ TMSOTf	9b	1/2	20 min	11, β only
3	TfOH (30)	9b	1/2	20 min	72, β only
4	Tf ₂ NH (30)	9i	1/2	24 h	NR
5	Tf ₂ NH (30)	4b	1/2	24 h	NR
6	Tf ₂ NH (30)	9b	1/1.2	20 min	81, β only

Reaction conditions: Reactions were done at 0 °C in the presence of activated acid-washed 4 Å MS in dry DCM medium (0.03M). a) 1.2 equiv. of NIS and 30 mol % of TMSOTf were used. D/A: Donor/Acceptor ratio. NR: No reaction. The reaction scale was 0.06 - 0.07 mmol.

Our studies commenced by reacting the PMPVB donor **8b** with the *N*-Boc protected indole acceptor **9b** (2 equiv.) in dry CH₂Cl₂ in the presence of 30 mol % of Tf₂NH (Table 1, entry 1). To our pleasant surprise, the reaction resulted in an excellent 82 % yield of the expected product **10i** as an exclusive β -isomer within 20 min. The regiochemistry of the product was confirmed from ¹H NMR analysis where the indole 3-H signal was found missing whereas the stereochemistry was confirmed by the presence of anomeric proton at δ 4.57 with coupling constant $J_{1,2}$ = 9.4 Hz, along with the nOe analysis. The same reaction under 30 mol % of triflic acid (TfOH) as the Brønsted acid catalyst instead of triflimide (Tf₂NH), led to a slight decrease in the yield (72 %) albeit again only as a β -isomer (Table 1, entry 3). As we know that the alkene donors can be activated using NIS/TMSOTf as a promoter system,^{28a} we tested those conditions for indolyl glycoside synthesis. However, it only led to 11 % of the desired product (Table 1, entry 2). Also, when the reaction was performed with unprotected indole **9i** and *N*-methyl indole **4b**, it did not lead to the activation of the donor, presumably due to the protonation of the indole nitrogen under the strongly acidic conditions, thereby quenching the Brønsted acid catalyst (Table 1, entries 4 & 5). The reaction with *N*-Boc acceptor **9b** led to a clean conversion under 30 % of Tf₂NH to the C-indolyl glycoside **10i**, even when the

Scheme 7: Substrate scope for gluco and galacto derived donors



Reaction conditions: Donor (1.0 equiv.), acceptor (1.2 equiv.), Ti_2NH (30 mol %). Reactions were done at 0 °C in the presence of activated acid-washed 4 Å MS in dry DCM medium (0.03M)

stoichiometry of the acceptor is reduced to just 1.2 equiv. and provided the product with an 81 % yield also, with no loss in selectivity (Table 1, entry 6).

4.2.2 The substrate scope of 2-oxy sugars

Taking these as the optimized conditions, we proceeded to test the scope of the glycosylation reaction (Scheme 7). The benzyl and para methyl benzyl-protected galactose donors gave 3-indolyl C-glycosides (**10a - g**) with various C-2 & C-5 substituted indoles in moderate to good yields (76 - 85 %) (Scheme 7) as exclusive β - anomers. Similarly, benzyl-protected glucose donor resulted in exclusively β -anomers when 2-substituted *N*-Boc indoles (**10i** & **10j**) were used, whereas, interestingly, the *N*-Boc indoles devoid of 2-substitution, resulted in a complete stereo-switch providing α -glycosides as the only products (**10k-n**) irrespective of the electronic nature of the C-5 substitution (Scheme 7). The reaction led to very similar results even when the protecting group is changed from *N*-Boc to *N*-acetyl protecting group and gave the α -glycoside **10h**. Also, even a more complex disaccharide-based donor (**8i**) with an additional O-glycosidic linkage too provided the expected product **10o** in 78 % yield and maintained the stereoselectivity (β), reiterating the efficacy of the current protocol (Scheme 7).

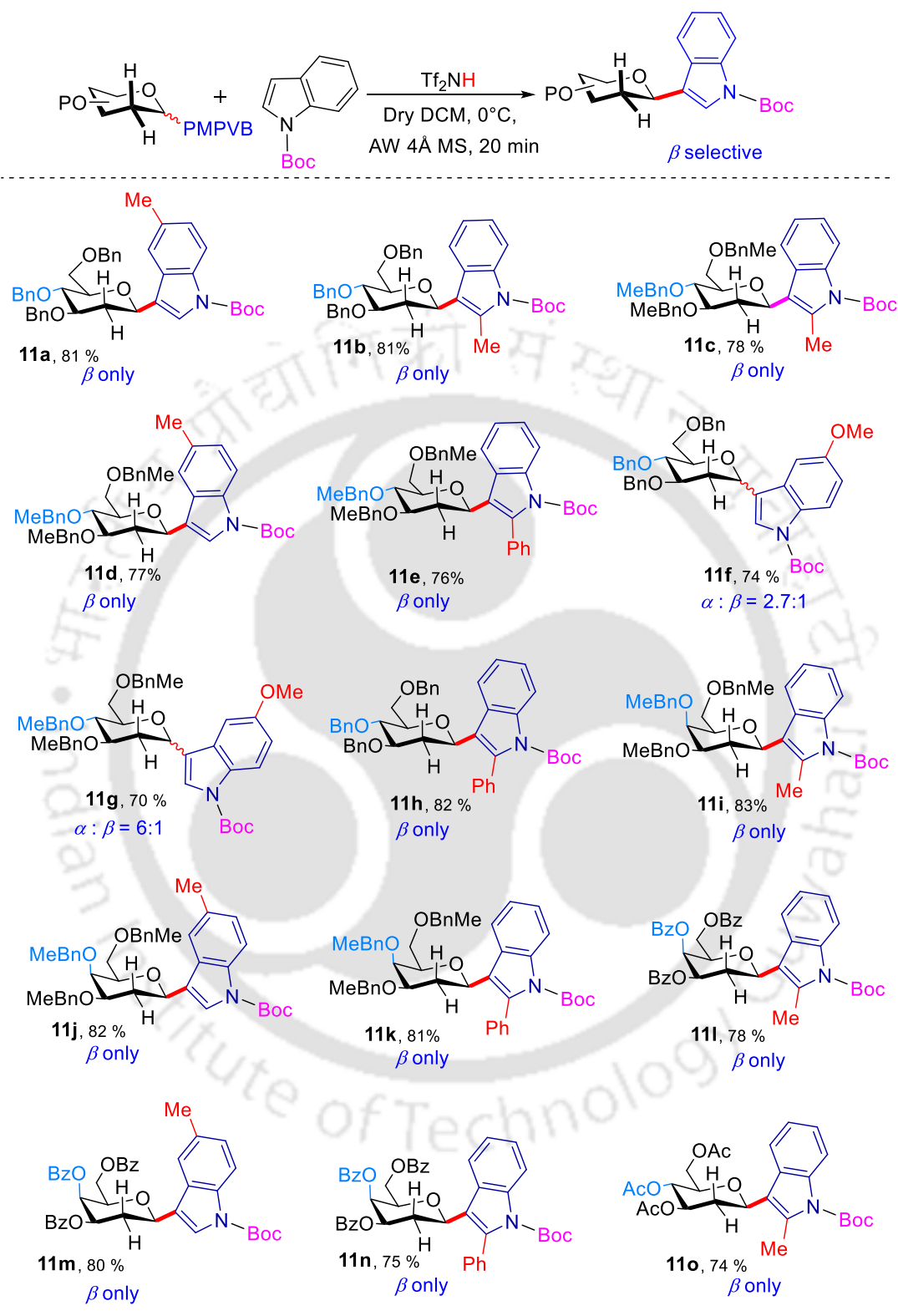
4.2.3 The substrate scope of 2-deoxy sugars

Next, we decided to test the efficacy of the method on the relatively more reactive 2-deoxy donors. As in-general attaining high stereoselectivities in the case of 2-deoxy glycosylations is challenging, we were curious to test the efficiency of the current protocol on 2-deoxy glucose and galactose-derived donors. Pleasingly, this method, under similar optimized conditions, gave several of the coupling products, 3-indolyl C- glycosyl derivatives, irrespective of the protecting groups on the 2-deoxy sugar (**11a-o**, Scheme 8) in a highly stereoselective fashion. The benzyl, *p*-methyl benzyl, and acetyl-protected glucose donors gave exclusive β -selective indolyl C- glycosyl derivatives (**11a-e**, **11h**, **11o**) in good yields (74 - 81 %) with *N*-Boc indoles (Scheme 8). Surprisingly, when C-5 methoxy substituted indole was used as a coupling partner, the products **11f** and **11g** were obtained as a mixture of anomers ($\alpha:\beta = 2.7:1$, $\alpha:\beta = 6:1$ respectively) presumably due to the increased nucleophilicity of indole (Scheme 8). The benzoyl and *p*-methyl benzyl protected galactose donors resulted in exclusive β -selective indolyl C-glycosyl derivatives (**11i-n**, 75-83 %), with *N*-Boc indoles (Scheme 8). Extensive coupling constants and nOe analysis has been done to establish the stereoselectivities.

4.2.4 Control experiments & Mechanism

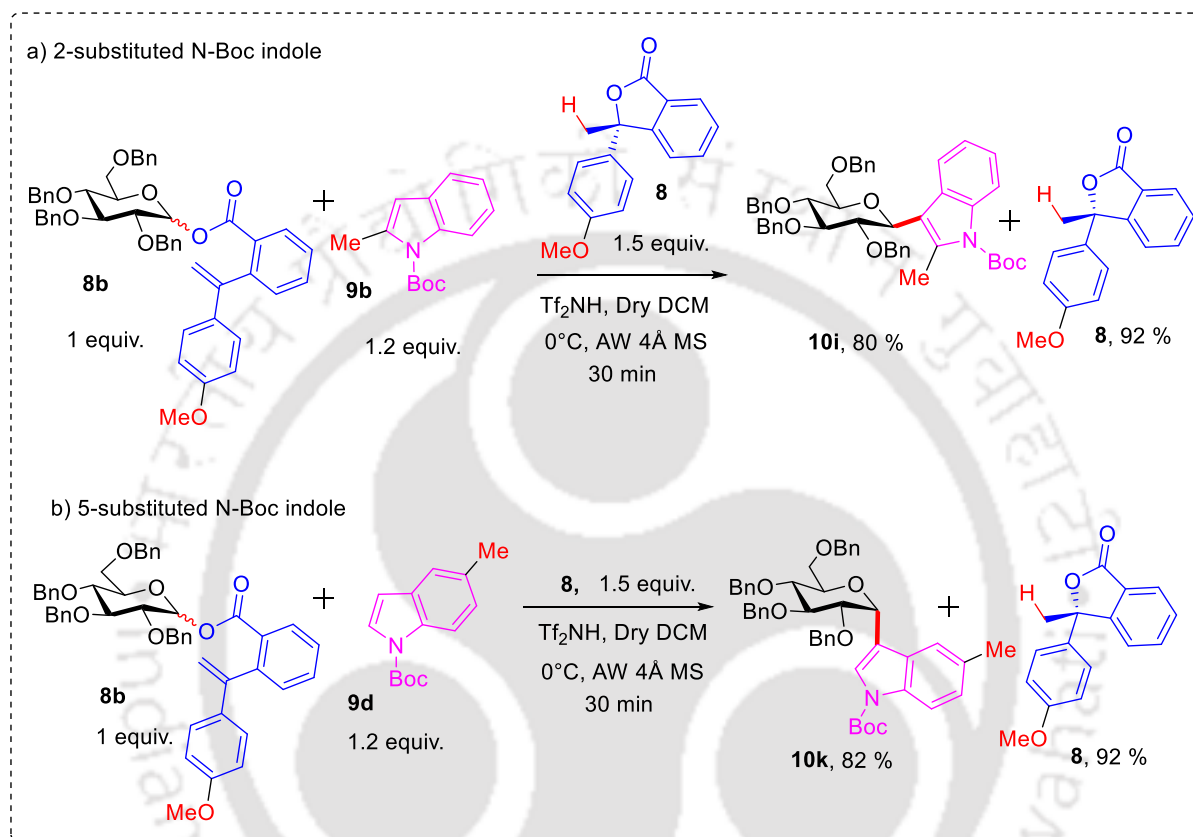
A couple of control experiments were performed to get insights into the mechanism and identify the possible intermediates. An experiment was performed with the pre-addition of 1.5 equiv. of cyclized by-product **8** along with the donor (**8b**) and the C-2 substituted acceptor (**9b**) (Scheme 9). We anticipated that the presence of an excess amount of the leaving moiety (**8**) would inflict a change in the anomeric selectivity if **I1** is the possible intermediate (Scheme 10a), as observed in the case of O-glycosylation reactions.^{28b} However, no change in the anomeric selectivity was observed in this reaction providing the product in 80 % yield as a β -isomer, which eliminates **I1** as the possible intermediate. A similar reaction with C-2 unsubstituted indole **9d** also led to no change in selectivity. The presence of excess by-product **8** with nucleophilic oxygens could also influence the anomeric ratio of the contact ion-pairs **I2**

Scheme 8: Substrate scope for 2-deoxy sugar derived donors.



Reaction conditions: Donor (1.0 equiv.), acceptor (1.2 equiv.), Tf_2NH (30 mol %). Reactions were done at 0°C in the presence of activated acid-washed 4Å MS in dry DCM medium (0.03M)

and could in turn affect the anomeric selectivity (Scheme 10a). Clearly, this experiment provides evidence that, presumably, the indoles could be reacting via dissociative mechanisms involving the putative oxocarbenium ion **13** as the potential intermediate (Scheme 10a). The nucleophilic attack might be happening on the pseudoaxial conformer of the oxocarbenium ion as predicted by Woerpel for the heteroatom containing oxocarbenium ions²⁹ giving rise to the observed β -selectivity. Based on the observations, the mechanism is proposed, as shown in Scheme 10b. The PMPVB donor, after the protonation of the remote alkene group, leading to



Scheme 9: Control experiments

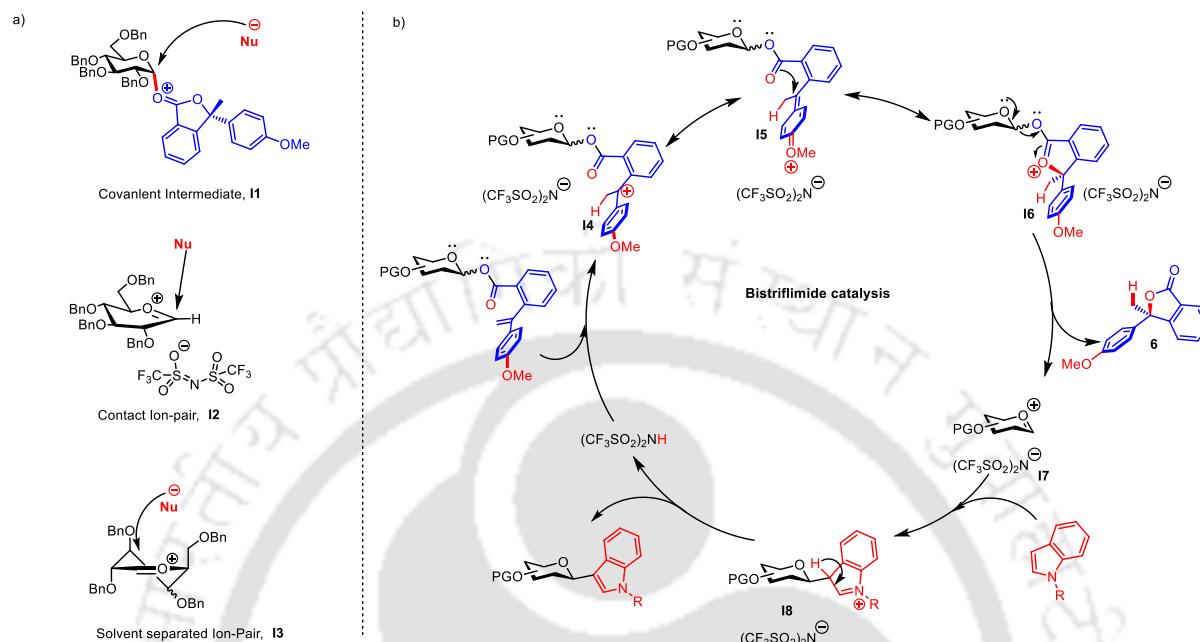
a stabilized carbocation (**14**, **15**), undergoes 5-exo-trig cyclization (**16**) followed by the expulsion of the cyclized product (**8**), leading to the formation of a naked oxocarbenium ion **17** (Scheme 10b). This, after the Friedel-Craft's alkylation, followed by the aromatization-driven deprotonation, gives rise to the indolyl glycosyl derivatives along with the regeneration of the bistriflimide catalyst (Scheme 10b).

In addition, we were also able to recycle the cyclic byproduct **8** under TMSOTf/DIPEA conditions (Scheme 11) and convert it back to the benzoic acid derivative (**8r**) that could again be utilized for the synthesis of the donors.

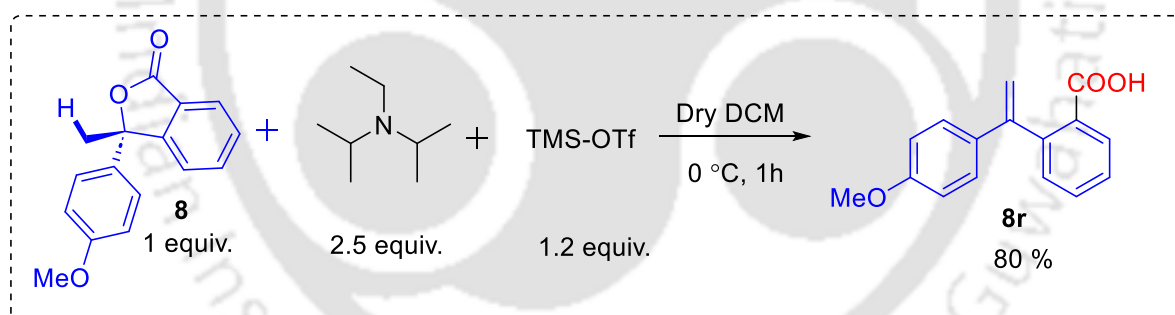
4.2.5 Conclusion

In conclusion, we developed a practically useful synthetic protocol for the regio and stereoselective synthesis of indolyl glycosyl derivatives from the stable yet PMPVB glycosides. The transformation can be achieved utilizing the simple Brønsted acid catalysis and does not require any metal catalysts or other expensive reagents. The non-participating nature

of the leaving moiety plays a crucial role in achieving the observed high selectivities. The Brønsted acid catalyzed transformation using the highly reactive PMPVB donors could open up pathways for many other C-glycoside containing natural products.



Scheme 10: a) Possible intermediates b) Probable mechanism



Scheme 11: Recycling the by-product

4.3 Experimental section

General Information

All solvents purchased were of commercial grade and reagents were purchased from Sigma-Aldrich, Merck, TCI, Carbosynth, Spectrochem, Alfa Aesar, Avra and used without further purification for reactions.

Analysis

Reactions were monitored by TLC on Kieselgel 60 F254 (Merck). Detection was done by examination under UV light (254 nm) and by charring with 10 % sulfuric acid in water. Purification was performed by both Ultra High-Performance Liquid Chromatography (UHPLC) using column [Particle size: (μ) 12, Dim: (mm) 250 x 10] in reverse phase and in normal phase using silica gel [Merck, 60-120 mesh] and Flash column chromatography (Combiflash (R) NextGen 300). Extracts were concentrated in vacuo using both Büchi rotary evaporator (bath temperatures up to 40 °C) at a pressure of either 15 mmHg (diaphragm pump) and 0.7 mmHg (oil pump), at rt. ^1H and ^{13}C NMR were recorded on a Bruker 600 MHz, 500 MHz and 400 MHz spectrometer using CDCl_3 as solvent. Chemical shift values are reported in ppm with the solvent as the internal standard (CDCl_3 : δ 7.26 for ^1H , δ 77.16 for ^{13}C). Data are reported as follows: chemical shifts (δ), multiplicity (s = singlet, d = doublet, dd = doublet of doublet, ddd = doublet of doublets, dt = doublet of triplet, t = triplet, q = quartet, m = multiplet, bs = broad singlet) etc., coupling constants J (Hz), and integration. High-resolution mass measurements were performed using Agilent technologies mass spectrometer (QTOF-ESI mode). Specific rotation was recorded in Autopol II S2, the units of the specific rotation is (deg·mL)/(g·dm) and concentration c is given in g/100 ml. For heating purpose, silicon oil baths were used. The diastereomeric ratio was calculated from crude ^1H NMR. The α and β stereochemistries of the separated products were established using the NOE technique for some representative examples. Structural assignments were made with additional information from gCOSY, gHSQC experiments. Utilized all PMPVB donors (**8a-i**), and N-protected indoles (**9a-h**) are known in the literature. PMPVB donors (**8a-i**) were synthesized following reported procedures.²⁸ **9a-g** were synthesized according to the literature procedure.³⁰⁻³³

General procedure 1

A solution of glycosyl donors (**8a-i**) (1 equiv.) and acceptors (**9a-g**) (1.2 equiv.) in dry CH_2Cl_2 (0.03 M) was stirred at room temperature for 60 min in the presence of activated acid washed (AW) 4 Å MS (3.0 g/mmol) under Ar atmosphere. Then the vessel was chilled to 0 °C, to which triflamide (30 mol %) was added. The reaction mixture was stirred for 20 min and TLC was checked. After completion of the reaction within 20 min, the temperature gradually rises to room temperature. Then Et_3N was added to quench the reaction. The crude reaction mixture was worked up with water, washed with brine, dried by Na_2SO_4 , and concentrated in rotavapor. The resulting crude reaction mixture was purified through Flash column chromatography to afford the glycosylated product.

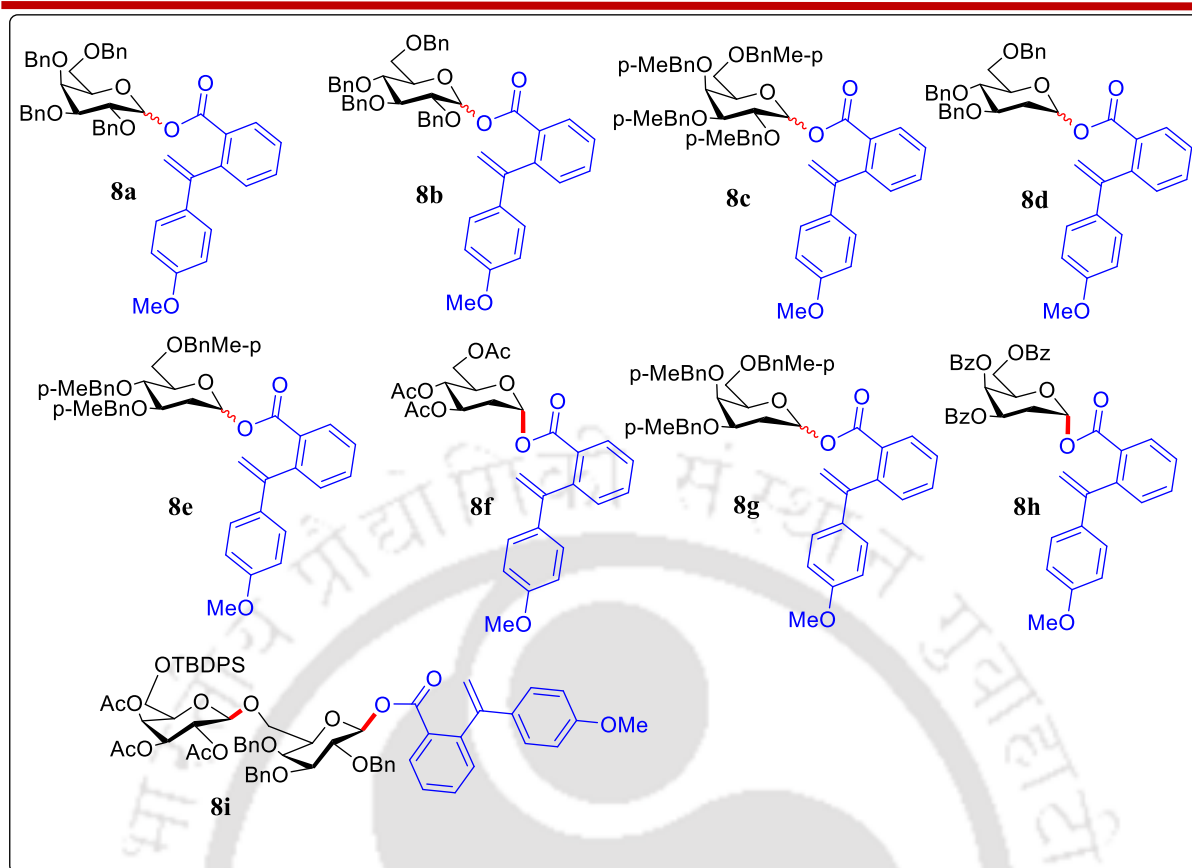


Figure 3: Synthesized PMPVB donors

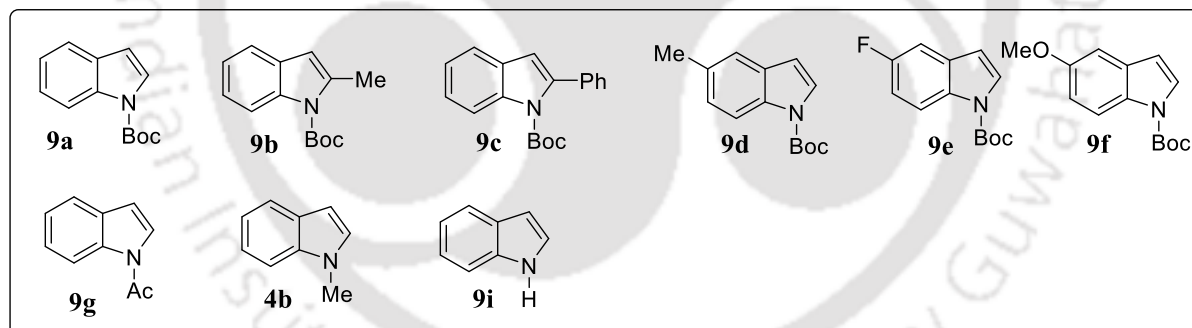
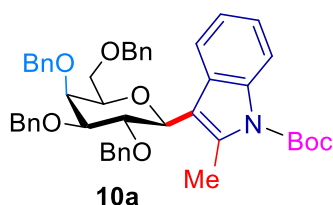


Figure 4: Indoles are used in this study

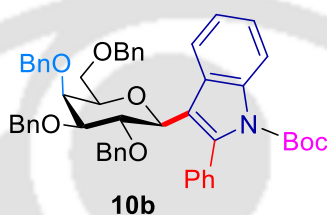
Synthesis of 3-(2,3,4,6-tetra-O-benzyl- β -D-galactopyranosyl)-2-methyl-1-tert-butyloxycarbonyl-indole (10a).



Glycosylation of **8a** (54.0 mg, 0.069 mmol) with **9b** (19.0 mg, 0.083 mmol) according to General procedure 1 afforded **10a** (44 mg, 84 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.58 (Hexane/EtOAc = 4:1, v/v). ^1H

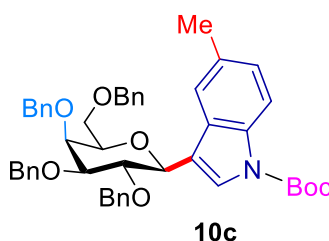
NMR (500 MHz, CDCl₃) δ 8.07 – 7.86 (m, 2H), 7.47 – 7.23 (m, 15H), 7.18 (t, J = 7.6 Hz, 1H), 7.14 – 6.97 (m, 4H), 6.94 (bs, 2H), 5.13 (d, J = 11.3 Hz, 1H, -CH₂-Ph), 4.83 (d, J = 11.7 Hz, 1H, -CH₂-Ph), 4.79 (d, J = 11.7 Hz, 1H, -CH₂-Ph), 4.67 (d, J = 11.3 Hz, 1H, -CH₂-Ph), 4.53 (d, J = 7.9 Hz, 1H, H-1), 4.50 – 4.41 (m, 3H, -CH₂-Ph), 4.40 – 4.31 (m, 1H, H-2), 4.15 (s, 1H, H-4), 3.92 (d, J = 7.8 Hz, 1H, -CH₂-Ph), 3.78 – 3.67 (m, 3H, together merged of H-3, H-6, & H-6'), 3.64 – 3.57 (m, 1H, H-5), 2.48 (s, 3H), 1.70 – 1.66 (m, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 149.7, 138.2, 137.7, 136.9, 127.4{2}, 127.2, 126.9{2}, 126.7, 126.5{2}, 126.4{2}, 126.3, 122.3, 121.4, 115.6, 114.1, 83.5, 82.5, 77.6, 74.3, 73.5, 73.3, 72.5, 71.5, 67.7, 27.3, 13.5. HRMS (ESI) m/z : [M + NH₄]⁺ calcd for C₄₈H₅₅N₂O₇ 771.4004; found 771.4005. $[\alpha]_D^{35}$ = + 0.31 (c 0.01, CHCl₃).

Synthesis of 3-(2,3,4,6-tetra-*O*-benzyl- β -D-galactopyranosyl)-2-phenyl-1-*tert*-butyloxycarbonyl-indole (10b).



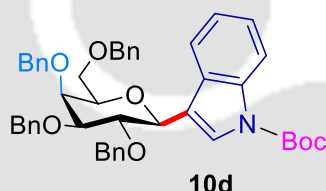
Glycosylation of **8a** (59.0 mg, 0.076 mmol) with **9c** (27.0 mg, 0.092 mmol) according to General procedure 1 afforded **10b** (49 mg, 79 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.57 (Hexane/EtOAc = 4:1, v/v). ¹H NMR (500 MHz, CDCl₃) δ 8.17 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 7.6 Hz, 1H), 7.44 (d, J = 7.2 Hz, 2H), 7.41 – 7.21 (m, 19H), 7.11 – 7.02 (m, 4H), 6.91 (d, J = 6.3 Hz, 2H), 5.10 (d, J = 11.1 Hz, 1H, -CH₂-Ph), 4.80 (d, J = 11.7 Hz, 1H, -CH₂-Ph), 4.74 (d, J = 11.7 Hz, 1H, -CH₂-Ph), 4.65 (d, J = 11.2 Hz, 1H, -CH₂-Ph), 4.60 – 4.50 (m, 2H, H-2 & -CH₂-Ph merged), 4.43 (d, J = 11.8 Hz, 1H, -CH₂-Ph), 4.39 (d, J = 11.8 Hz, 1H, -CH₂-Ph), 4.26 (d, J = 9.0 Hz, 1H, H-1), 4.15 – 4.06 (m, 2H, H-4 & -CH₂-Ph merged), 3.67 (t, J = 8.1 Hz, 1H, H-5), 3.63 (dd, J = 9.4, 2.4 Hz, 1H, H-3), 3.59 – 3.55 (m, 1H, H-6'), 3.53 (dd, J = 8.3, 5.0 Hz, 1H, H-6), 1.20 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 150.2, 139.3, 138.7, 138.2, 137.9, 137.7, 137.0, 133.4, 130.2, 128.4{2}, 128.2, 128.0, 127.8, 127.7, 127.6, 127.5{2}, 127.4, 127.3, 124.5, 122.8, 121.6, 118.3, 114.9, 84.5, 83.0, 78.0, 76.3, 75.2, 74.8, 74.6, 74.1, 73.5, 72.3, 68.6, 27.5. HRMS (ESI) m/z : [M + NH₄]⁺ calcd for C₅₃H₅₇N₂O₇ 833.4160; found 833.4156. $[\alpha]_D^{35}$ = + 0.23 (c 0.01, CHCl₃).

Synthesis of 3-(2,3,4,6-tetra-*O*-benzyl- β -D-galactopyranosyl)-5-methyl-1-*tert*-butyloxycarbonyl-indole (10c).



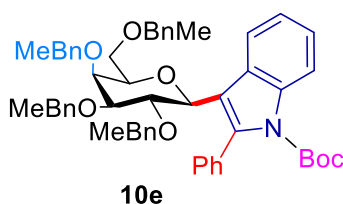
Glycosylation of **8a** (57.0 mg, 0.073 mmol) with **9d** (20.0 mg, 0.086 mmol) according to General procedure 1 afforded **10c** (42 mg, 76 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.58 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 7.97 (d, J = 6.9 Hz, 1H), 7.60 (s, 1H), 7.55 (s, 1H), 7.43 (d, J = 7.2 Hz, 2H), 7.40 (d, J = 7.2 Hz, 2H), 7.37 – 7.24 (m, 11H), 7.15 – 7.04 (m, 4H), 6.90 – 6.84 (m, 2H), 5.12 (d, J = 11.4 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.83 (d, J = 11.8 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.79 (d, J = 11.8 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.66 (d, J = 11.4 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.48 (dd, J = 12.1, 9.1 Hz, 3H, $-\text{CH}_2\text{-Ph}$ merged), 4.42 (d, J = 9.5 Hz, 1H, H-1), 4.27 (t, J = 9.4 Hz, 1H, H-2), 4.14 (d, J = 2.5 Hz, 1H, H-4), 3.94 (d, J = 10.4 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 3.76 – 3.68 (m, 3H, H-3, H-5, & H-6' merged), 3.66 – 3.59 (m, 1H, H-6), 2.25 (s, 3H), 1.64 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 148.6, 138.3, 137.6, 136.9, 133.1, 131.1, 128.0, 127.4, 127.3, 127.2, 127.0, 126.9, 126.7, 126.6, 126.5, 126.4, 126.3, 124.8, 123.5, 120.1, 117.6, 113.7, 83.1, 82.3, 77.6, 75.9, 75.3, 74.2, 73.7, 73.5, 72.5, 71.5, 67.7, 27.2, 20.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{48}\text{H}_{55}\text{N}_2\text{O}_7$ 771.4004; found 771.4010. $[\alpha]_{\text{D}}^{35} = +0.35$ (c 0.01, CHCl_3).

Synthesis of 3-(2,3,4,6-tetra-*O*-benzyl- β -D-galactopyranosyl)-1-*tert*-butyloxycarbonyl-indole (10d).



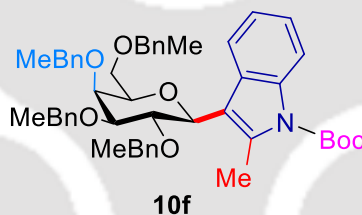
Glycosylation of **8a** (50.0 mg, 0.064 mmol) with **9a** (17.0 mg, 0.078 mmol) according to General procedure 1 afforded **10d** (39 mg, 82 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.60 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 8.11 (s, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.59 (s, 1H), 7.43 (d, J = 7.3 Hz, 2H), 7.40–7.31 (m, 7H), 7.30 (d, J = 7.0 Hz, 3H), 7.28 – 7.25 (m, 4H), 7.15 – 7.07 (m, 4H), 6.88 (d, J = 6.8 Hz, 2H), 5.10 (d, J = 11.4 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.80 (q, J = 11.8 Hz, 2H, $-\text{CH}_2\text{-Ph}$ merged), 4.68 (d, J = 11.4 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.51 (d, J = 10.5 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.49 – 4.42 (m, 3H, H-1 & $-\text{CH}_2\text{-Ph}$ merged), 4.27 (t, J = 9.4 Hz, 1H, H-2), 4.13 (d, J = 2.4 Hz, 1H, H-4), 3.96 (d, J = 10.5 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 3.75 – 3.71 (m, 2H, H-3 & H-5 merged), 3.70 – 3.67 (m, 1H, H-6'), 3.61 (dd, J = 8.7, 5.2 Hz, 1H, H-6), 1.65 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 149.6, 139.1, 138.6, 137.9, 137.8, 135.8, 128.4, 128.4, 128.3, 128.2, 128.0{2}, 127.8, 127.6{2}, 127.5{2}, 127.4, 124.4, 122.6, 121.3, 118.9, 115.1, 84.2, 83.5, 78.6, 76.9, 76.1, 75.3, 74.5, 74.2, 73.5, 72.4, 68.7, 28.2. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{47}\text{H}_{53}\text{N}_2\text{O}_7$ 757.3853; found 757.3853. $[\alpha]_{\text{D}}^{35} = +0.29$ (c 0.01, CHCl_3).

Synthesis of 3-(2,3,4,6-tetra-*O*-(4-methylbenzyl)- β -D-galactopyranosyl)-2-phenyl-1-*tert*-butyloxycarbonyl-indole (10e).



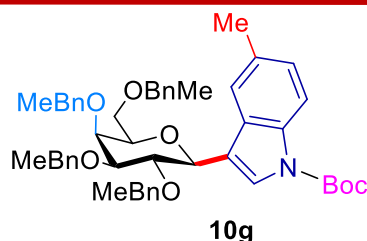
Glycosylation of **8c** (50.0 mg, 0.06 mmol) with **9c** (21.0 mg, 0.072 mmol) according to General procedure 1 afforded **10e** (41 mg, 78 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.60 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 8.14 (d, J = 8.3 Hz, 1H), 7.96 (d, J = 7.6 Hz, 1H), 7.38 – 7.28 (d, J = 6.5 Hz, 7H), 7.28 – 7.23 (m, 3H), 7.19 (d, J = 7.8 Hz, 2H), 7.13 (dd, J = 8.1, 3.1 Hz, 4H), 7.08 (d, J = 7.9 Hz, 2H), 7.02 (t, J = 7.4 Hz, 1H), 6.82 (d, J = 7.8 Hz, 2H), 6.78 (d, J = 7.5 Hz, 2H), 5.05 (d, J = 11.0 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.75 (d, J = 11.4 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.69 (d, J = 11.4 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.59 (d, J = 11.1 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.54 – 4.46 (m, 2H, H-2 & $-\text{CH}_2\text{-Ph}$ merged), 4.38 (d, J = 11.6 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.33 (d, J = 11.6 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.22 (d, J = 9.3 Hz, 1H, H-1), 4.12 – 4.05 (m, 2H, H-4 & $-\text{CH}_2\text{-Ph}$ merged), 3.64 – 3.57 (m, 2H, H-3 & H-5 merged), 3.54 – 3.49 (m, 1H, H-6'), 3.47 (dd, J = 8.4, 5.0 Hz, 1H, H-6), 2.40 (s, 3H, -4-methyl of Ph), 2.34 (s, 3H, -4-methyl of Ph), 2.30 (s, 3H, -4-methyl of Ph), 2.21 (s, 3H, -4-methyl of Ph), 1.22 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 150.3, 137.5, 137.4, 137.1, 136.9, 136.8, 136.4, 135.8, 135.0, 134.9, 133.5, 130.3, 129.0{2}, 128.9, 128.5, 128.4, 128.1, 127.6, 127.5, 124.3, 122.7, 121.7, 118.5, 114.8, 84.6, 82.9, 77.4, 76.3, 75.0, 74.8, 74.4, 73.8, 73.3, 72.1, 68.4, 27.5, 21.2{2}, 21.1. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{57}\text{H}_{65}\text{N}_2\text{O}_7$ 889.4786; found 889.4781. $[\alpha]_{\text{D}}^{35} = +0.41$ (c 0.01, CHCl_3).

Synthesis of 3-(2,3,4,6-tetra-O-(4-methylbenzyl)- β -D-galactopyranosyl)-2-methyl-1-tert-butyloxycarbonyl-indole (10f).



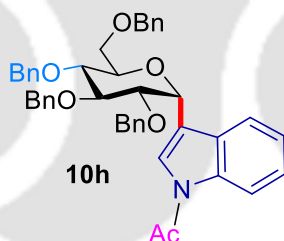
Glycosylation of **8c** (56.0 mg, 0.067 mmol) with **9b** (19.0 mg, 0.082 mmol) according to General procedure 1 afforded **10f** (45 mg, 82 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.61 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 8.02 (d, J = 8.2 Hz, 1H), 7.91 (s, 1H), 7.31 (d, J = 6.4 Hz, 2H), 7.28 (d, J = 7.9 Hz, 2H), 7.21 – 7.13 (m, 7H), 7.10 (d, J = 7.8 Hz, 2H), 7.00 (s, 1H), 6.87 (d, J = 5.8 Hz, 2H), 6.76 (bs, 2H), 5.08 (d, J = 11.0 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.77 (d, J = 11.5 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.72 (d, J = 11.5 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.61 (d, J = 11.1 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.48 (d, J = 7.2 Hz, 1H, H-1), 4.42 (d, J = 11.3 Hz, 2H, $-\text{CH}_2\text{-Ph}$ merged), 4.37 (d, J = 11.7 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.33 (bs, 1H, H-2), 4.11 (s, 1H, H-4), 3.88 (d, J = 10.0 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 3.72 – 3.63 (m, 3H, H-3, H-5, & H-6' merged), 3.55 (dd, J = 8.4, 4.8 Hz, 1H, H-6), 2.48 (s, 3H), 2.39 (s, 3H), 2.35 (s, 3H), 2.32 (s, 3H), 2.23 (s, 3H), 1.68 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 150.7, 137.4, 137.2, 137.0, 136.8, 136.3, 135.7, 134.9, 129.1, 129.0, 128.8, 128.5, 128.3, 128.1, 127.6, 127.5, 123.2, 122.4, 121.0, 116.6, 115.0, 84.4, 83.5, 78.0, 76.7, 75.2, 75.0, 74.3, 74.0, 73.4, 72.3, 68.6, 28.3, 21.2{3}, 14.1. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{52}\text{H}_{63}\text{N}_2\text{O}_7$ 827.4630; found 827.4632. $[\alpha]_{\text{D}}^{35} = +0.47$ (c 0.01, CHCl_3).

Synthesis of 3-(2,3,4,6-tetra-O-(4-methylbenzyl)- β -D-galactopyranosyl)-5-methyl-1-tert-butyloxycarbonyl-indole (10g).

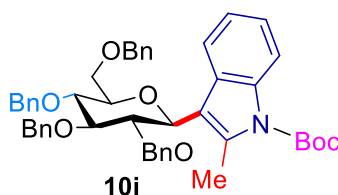


Glycosylation of **8c** (57.0 mg, 0.068 mmol) with **9d** (19.0 mg, 0.082 mmol) according to General procedure 1 afforded **10g** (47 mg, 85 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.61 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 7.95 (d, J = 7.0 Hz, 1H), 7.55 (s, 1H), 7.53 (s, 1H), 7.29 (t, J = 7.2 Hz, 4H), 7.15 (t, J = 6.4 Hz, 6H), 7.10 (d, J = 7.8 Hz, 2H), 7.06 (d, J = 8.6 Hz, 1H), 6.88 (d, J = 7.8 Hz, 2H), 6.75 (d, J = 7.9 Hz, 2H), 5.05 (d, J = 11.1 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.78 (d, J = 11.6 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.73 (d, J = 11.6 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.59 (d, J = 11.1 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.44 (dd, J = 10.9, 7.3 Hz, 2H, $-\text{CH}_2\text{-Ph}$, merged), 4.39 (d, J = 9.2 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.37 (d, J = 7.2 Hz, 1H, H-1), 4.22 (t, J = 9.4 Hz, 1H, H-2), 4.09 (d, J = 2.4 Hz, 1H, H-4), 3.91 (d, J = 10.3 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 3.70 – 3.64 (m, 3H, H-3, H-5, & H-6' merged), 3.58 (q, J = 9.2 Hz, 1H, H-6), 2.36 (s, 3H), 2.35 (s, 3H), 2.32 (s, 3H), 2.23 (s, 6H), 1.64 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 149.7, 137.5, 137.2, 137.1, 136.9, 136.3, 135.6, 134.9, 134.8, 132.0, 129.1, 129.0, 128.9, 128.6, 128.5, 128.1, 127.6, 125.7, 124.5, 121.2, 118.7, 114.6, 84.0, 83.2, 78.1, 76.2, 75.0, 74.5, 74.1, 73.4, 72.3, 68.5, 28.2, 21.2{2}, 21.1. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{52}\text{H}_{59}\text{NO}_7\text{Na}$ 832.4184; found 832.4190. $[\alpha]_D^{35} = -0.33$ (c 0.01, CHCl_3).

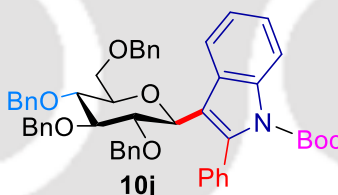
Synthesis of 3-(2,3,4,6-tetra-O-benzyl- α -D-glucopyranosyl)-1-acetyl-indole (**10h**).



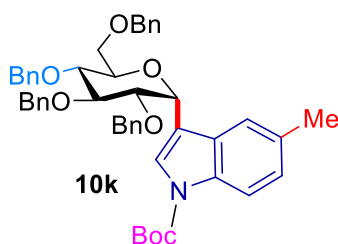
Glycosylation of **8b** (49.0 mg, 0.063 mmol) with **9g** (12.0 mg, 0.075 mmol) according to General procedure 1 afforded **10h** (34 mg, 79 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.52 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 8.41 (d, J = 8.1 Hz, 1H), 7.87 (d, J = 7.8 Hz, 1H), 7.83 (s, 1H), 7.40 – 7.20 (m, 20H), 7.11 – 7.07 (m, 2H), 5.57 (d, J = 4.5 Hz, 1H, H-1), 5.03 (d, J = 11.0 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.90 (d, J = 11.0 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.82 (d, J = 10.7 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.75 (d, J = 11.4 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.70 (d, J = 11.4 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.64 (d, J = 12.1 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.48 (d, J = 10.8 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.43 (d, J = 12.0 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.17 – 4.08 (m, 2H, H-2 & H-3 merged), 3.82 – 3.78 (m, 1H, H-4), 3.65 (dd, J = 10.6, 3.2 Hz, 1H, H-6), 3.57 (dd, J = 10.5, 1.4 Hz, 1H, H-6'), 3.32 (d, J = 9.8 Hz, 1H, H-5), 2.50 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 168.5, 138.6, 138.2, 138.0, 137.9, 135.6, 129.8, 128.5, 128.4{2}, 128.2, 128.0, 127.9, 127.8, 127.7{2}, 125.5, 125.2, 123.8, 120.8, 117.3, 116.4, 81.8, 80.4, 78.2, 75.2, 75.0, 73.5, 72.7, 72.4, 70.3, 68.7, 23.9. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{44}\text{H}_{43}\text{NO}_6\text{Na}$ 704.2983; found 704.2992. $[\alpha]_D^{35} = +0.52$ (c 0.01, CHCl_3).

Synthesis of 3-(2,3,4,6-tetra-O-benzyl- β -D-glucopyranosyl)-2-methyl-1-tert-butyloxycarbonyl-indole (10i).


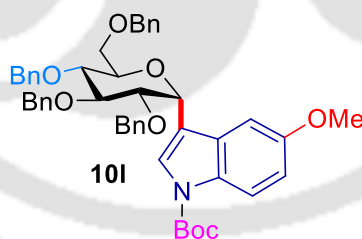
Glycosylation of **8b** (52.0 mg, 0.067 mmol) with **9b** (18.0 mg, 0.078 mmol) according to General procedure 1 afforded **10i** (41 mg, 81 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.58 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 8.09 (d, J = 8.3 Hz, 1H), 7.77 (s, 1H), 7.36 – 7.21 (m, 16H), 7.11 (dd, J = 12.4, 6.4 Hz, 4H), 6.82 (s, 2H), 4.98 – 4.89 (m, 3H, $-\text{CH}_2\text{-Ph}$, merged), 4.71 (d, J = 10.7 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.62 (d, J = 12.1 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.57 (d, J = 9.4 Hz, 1H, H-1), 4.53 (dd, J = 12.2, 4.2 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.44 – 4.37 (m, 1H, $-\text{CH}_2\text{-Ph}$), 3.97 – 3.90 (m, 2H, H-2 & H-4), 3.89 – 3.80 (m, 3H, H-6, H-6' & $-\text{CH}_2\text{-Ph}$, merged), 3.76 (d, J = 10.9 Hz, 1H, H-5), 3.61 (d, J = 8.1 Hz, 1H, H-3), 2.49 (s, 3H), 1.69 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 150.6, 138.8, 138.6, 138.4, 137.8, 136.1, 135.5, 128.4{2}, 128.3, 128.1, 128.0, 127.8{2}, 127.6, 127.5, 127.4, 123.5, 122.5, 115.8, 115.4, 87.0, 83.7, 81.9, 79.4, 78.3, 75.8, 75.2, 75.0, 73.4, 69.2, 28.3, 14.6. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{51}\text{NO}_7\text{Na}$ 776.3558; found 776.3556. $[\alpha]_{\text{D}}^{35}$ = - 0.28 (c 0.01, CHCl_3).

Synthesis of 3-(2,3,4,6-tetra-O-benzyl- β -D-glucopyranosyl)-2-phenyl-1-tert-butyloxycarbonyl-indole (10j).


Glycosylation of **8b** (52.0 mg, 0.067 mmol) with **9c** (24.0 mg, 0.082 mmol) according to General procedure 1 afforded **10j** (37 mg, 68 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.59 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 8.23 (d, J = 8.4 Hz, 1H), 7.85 (d, J = 7.8 Hz, 1H), 7.39 – 7.27 (m, 17H), 7.21 (dd, J = 18.6, 7.5 Hz, 4H), 7.14 – 7.04 (m, 4H), 6.89 (d, J = 5.7 Hz, 2H), 4.94 (d, J = 10.8 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.88 (t, J = 10.6 Hz, 2H, $-\text{CH}_2\text{-Ph}$, merged), 4.67 (d, J = 10.9 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.61 (d, J = 12.1 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.49 – 4.42 (m, 2H, $-\text{CH}_2\text{-Ph}$, merged), 4.30 (d, J = 9.4 Hz, 1H, H-1), 4.10 – 4.01 (m, 2H, H-2 & $-\text{CH}_2\text{-Ph}$, merged), 3.96 – 3.86 (m, 1H, H-4), 3.80 (dd, J = 11.1, 3.1 Hz, 1H, H-6), 3.72 – 3.67 (m, 2H, H-5 & H-6', merged), 3.42 (dd, J = 9.5, 0.9 Hz, 1H, H-3), 1.21 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 150.1, 138.7, 138.6, 138.4, 138.0, 137.8, 137.0, 133.3, 130.2, 128.4{2}, 128.3{2}, 127.9, 127.8{2}, 127.7, 127.6{2}, 127.5, 127.4{2}, 124.6, 122.8, 121.1, 117.5, 115.1, 86.9, 83.1, 81.4, 79.1, 78.3, 75.7, 75.0, 74.9, 73.3, 69.0, 27.4. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{53}\text{H}_{57}\text{N}_2\text{O}_7$ 833.4160; found 833.4145. $[\alpha]_{\text{D}}^{35}$ = - 0.54 (c 0.01, CHCl_3).

Synthesis of 3-(2,3,4,6-tetra-O-benzyl- α -D-glucopyranosyl)-5-methyl-1-tert-butylloxycarbonyl-indole (10k).


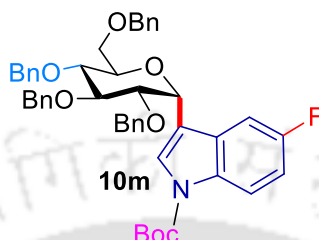
Glycosylation of **8b** (58.0 mg, 0.075 mmol) with **9d** (21.0 mg, 0.091 mmol) according to General procedure 1 afforded **10k** (47 mg, 83 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.60 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 8.05 (s, 1H), 7.96 (d, J = 6.8 Hz, 1H), 7.64 (s, 1H), 7.36 (d, J = 6.7 Hz, 2H), 7.35 – 7.19 (m, 16H), 7.11 (d, J = 7.5 Hz, 1H), 7.10 – 7.04 (m, 2H), 5.53 (d, J = 5.4 Hz, 1H, H-1), 5.06 (d, J = 10.8 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.87 (d, J = 10.8 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.80 (d, J = 10.7 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.73 (d, J = 11.8 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.70 (d, J = 11.8 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.61 (d, J = 12.1 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.46 (d, J = 10.8 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.43 (d, J = 12.2 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.23 (t, J = 9.2 Hz, 1H, H-3), 4.08 (dd, J = 9.7, 5.9 Hz, 1H, H-2), 3.82 – 3.73 (m, 1H, H-4), 3.64 (dd, J = 10.6, 3.3 Hz, 1H, H-6), 3.54 (dd, J = 10.6, 1.8 Hz, 1H, H-6'), 3.32 (d, J = 9.8 Hz, 1H, H-5), 2.37 (s, 3H), 1.65 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 149.7, 138.8, 138.2, 137.9, 133.3, 132.2, 130.2, 128.4{2}, 128.3{2}, 128.1, 127.9{2}, 127.6{2}, 126.1, 125.9, 120.7, 114.8, 114.6, 83.5, 82.7, 80.5, 78.1, 75.7, 75.1, 73.4, 72.4, 71.9, 70.3, 68.7, 28.2, 21.4. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{51}\text{NO}_7\text{Na}$ 776.3558; found 776.3572. $[\alpha]_D^{35}$ = -0.28 (c 0.01, CHCl_3).

Synthesis of 3-(2,3,4,6-tetra-O-benzyl- α -D-glucopyranosyl)-5-methoxy-1-tert-butylloxycarbonyl-indole (10l).


Glycosylation of **8b** (48.0 mg, 0.062 mmol) with **9f** (18.0 mg, 0.073 mmol) according to General procedure 1 afforded **10l** (36 mg, 76 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.52 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 8.08 (s, 1H), 7.97 (s, 1H), 7.38 – 7.21 (m, 19H), 7.09 – 7.06 (m, 2H), 6.91 (dd, J = 9.0, 2.5 Hz, 1H), 5.52 (d, J = 5.4 Hz, 1H, H-1), 5.06 (d, J = 10.7 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.87 (d, J = 10.7 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.81 (d, J = 10.7 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.75 (d, J = 11.7 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.72 (d, J = 11.8 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.58 (d, J = 12.2 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.46 (d, J = 10.8 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.44 (d, J = 12.2 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.23 (t, J = 9.2 Hz, 1H, H-3), 4.08 (dd, J = 9.7, 5.8 Hz, 1H, H-2), 3.81 – 3.76 (m, 1H, H-4), 3.73 (s, 3H), 3.64 (dd, J = 10.6, 3.1 Hz, 1H, H-6), 3.55 (dd, J = 10.5, 1.5 Hz, 1H, H-6'), 3.31 (d, J = 9.8 Hz, 1H, H-5), 1.65 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 155.8, 149.6, 138.7, 138.2{2}, 137.8,

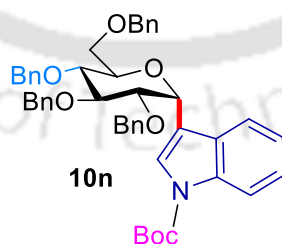
130.8, 129.8, 128.4{3}, 128.3, 128.1, 128.0, 127.9, 127.7, 127.6, 126.6, 115.7, 114.9, 113.7, 102.9, 83.6, 82.6, 80.5, 78.1, 75.7, 75.1, 73.5, 72.5, 72.0, 70.4, 68.7, 55.6, 28.2. HRMS (ESI) m/z : $[M + NH_4]^+$ calcd for $C_{48}H_{55}N_2O_8$ 787.3953; found 787.3949. $[\alpha]_D^{35} = -0.39$ (c 0.01, $CHCl_3$).

Synthesis of 3-(2,3,4,6-tetra-O-benzyl- α -D-glucopyranosyl)-5-fluoro-1-tert-butylloxycarbonyl-indole (10m).



Glycosylation of **8b** (50.0 mg, 0.064 mmol) with **9e** (18.0 mg, 0.076 mmol) according to General procedure 1 afforded **10m** (37 mg, 76 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.56$ (Hexane/EtOAc = 4:1, v/v). 1H NMR (600 MHz, $CDCl_3$) δ 8.12 (s, 1H), 8.04 (s, 1H), 7.53 (dd, $J = 9.2, 2.3$ Hz, 1H), 7.36 (d, $J = 6.9$ Hz, 2H), 7.34 – 7.24 (m, 13H), 7.24 – 7.20 (m, 3H), 7.04 (ddd, $J = 11.3, 8.2, 2.6$ Hz, 3H), 5.48 (d, $J = 5.3$ Hz, 1H, H-1), 5.05 (d, $J = 10.8$ Hz, 1H, $-CH_2$ -Ph), 4.87 (d, $J = 10.8$ Hz, 1H, $-CH_2$ -Ph), 4.79 (d, $J = 10.6$ Hz, 1H, $-CH_2$ -Ph), 4.74 (s, 2H, $-CH_2$ -Ph, merged), 4.66 (d, $J = 12.1$ Hz, 1H, $-CH_2$ -Ph), 4.43 (t, $J = 10.5$ Hz, 2H, $-CH_2$ -Ph, merged), 4.19 (t, $J = 9.2$ Hz, 1H, H-3), 4.08 (dd, $J = 9.7, 5.8$ Hz, 1H, H-2), 3.77 (t, $J = 9.3$ Hz, 1H, H-4), 3.65 (dd, $J = 10.6, 3.1$ Hz, 1H, H-6), 3.56 (dd, $J = 10.8, 1.2$ Hz, 1H, H-6'), 3.27 (d, $J = 9.8$ Hz, 1H, H-5), 1.65 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 160.0, 158.4, 149.3, 138.7, 138.1{2}, 137.8, 128.4{2}, 128.3, 128.1, 128.0, 127.9, 127.7{2}, 127.6, 115.9, 115.8, 115.1{2}, 112.4, 112.3, 106.5, 106.4, 84.0, 82.5, 80.4, 78.0, 75.7, 75.1, 73.5, 72.6, 72.2, 70.2, 68.6, 28.2. HRMS (ESI) m/z : $[M + NH_4]^+$ calcd for $C_{47}H_{52}FN_2O_7$ 775.3759; found 775.3762. $[\alpha]_D^{35} = -0.43$ (c 0.01, $CHCl_3$).

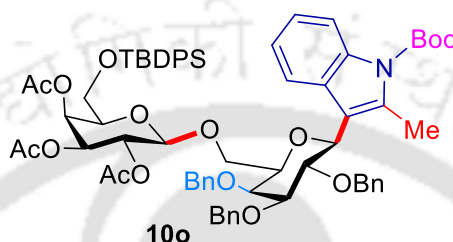
Synthesis of 3-(2,3,4,6-tetra-O-benzyl- α -D-glucopyranosyl)-1-tert-butylloxycarbonyl-indole (10n).



Glycosylation of **8b** (53.0 mg, 0.068 mmol) with **9a** (18.0 mg, 0.083 mmol) according to General procedure 1 afforded **10n** (40 mg, 79 %, α only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.58$ (Hexane/EtOAc = 4:1, v/v). 1H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.85 (d, $J = 7.8$ Hz, 1H), 7.36 (d, $J = 6.7$ Hz, 2H), 7.34 – 7.15 (m, 19H), 7.07 (dd, $J = 7.0, 2.2$ Hz, 2H), 5.56 (d, $J = 5.6$ Hz, 1H, H-1), 5.06 (d, $J = 10.8$ Hz, 1H, $-CH_2$ -Ph), 4.87 (d, $J = 10.8$ Hz, 1H, $-CH_2$ -Ph), 4.80 (d, $J = 10.7$ Hz, 1H, $-CH_2$ -Ph), 4.77 – 4.70 (m, 2H, $-CH_2$ -Ph, merged), 4.62 (d, $J = 12.1$ Hz, 1H, $-CH_2$ -Ph), 4.46 (d, $J = 10.7$

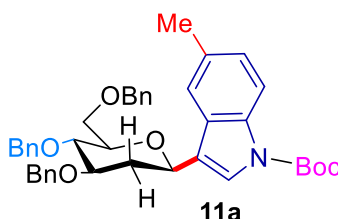
Hz, 1H, -CH₂-Ph), 4.41 (d, *J* = 12.1 Hz, 1H, -CH₂-Ph), 4.23 (t, *J* = 9.2 Hz, 1H, H-3), 4.09 (dd, *J* = 9.7, 5.8 Hz, 1H, H-2), 3.80 – 3.74 (m, 1H, H-4), 3.64 (dd, *J* = 10.3, 3.0 Hz, 1H, H-6), 3.55 (dd, *J* = 10.6, 1.8 Hz, 1H, H-6'), 3.32 (d, *J* = 9.8 Hz, 1H, H-5), 1.66 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 148.6, 137.8, 137.3, 137.2, 137.0, 134.2, 129.0, 127.4, 127.3{2}, 127.1, 126.9, 126.8, 126.6{2}, 125.1, 123.5, 121.7, 119.8, 114.2, 114.0, 82.7, 81.6, 79.6, 77.2, 74.6, 74.0, 72.5, 71.5, 71.1, 69.3, 67.9, 27.2. HRMS (ESI) *m/z*: [M + NH₄]⁺ calcd for C₄₇H₅₃N₂O₇ 757.3853; found 757.3845. [α]_D³⁵ = -0.35 (c 0.01, CHCl₃).

Synthesis of 3-(2,3,4-*tri*-O-benzyl-6-O-(2,3,4-*tri*-O-acetyl-6-O-*tert*-butyldiphenylsilyl)-β-D-galactopyranosyl)-β-D-galactopyranosyl)-2-methyl-1-*tert*-butyloxycarbonyl-indole (10o).



Glycosylation of **8i** (50 mg, 0.041 mmol) with **9b** (12 mg, 0.051 mmol) according to General procedure 1 afforded **10o** (38 mg, 78 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, *R_f* = 0.49 (Hexane/EtOAc = 4:1, v/v). ¹H NMR (500 MHz, CDCl₃) δ 8.04 (d, *J* = 8.3 Hz, 1H), 7.96 – 7.83 (m, 1H), 7.58 (dd, *J* = 6.4, 4.6 Hz, 4H), 7.46 – 7.16 (m, 17H), 7.15 – 7.06 (m, 3H), 6.99 (d, *J* = 2.4 Hz, 1H), 6.86 (d, *J* = 1.0 Hz, 1H), 5.55 (d, *J* = 3.1 Hz, 1H), 5.11 (dd, *J* = 10.0, 8.3 Hz, 1H), 5.06 (d, *J* = 11.1 Hz, 1H), 4.97 (dd, *J* = 10.4, 3.0 Hz, 1H), 4.80 (d, *J* = 11.8 Hz, 1H), 4.76 (d, *J* = 11.8 Hz, 1H), 4.66 (d, *J* = 11.1 Hz, 1H), 4.51 – 4.42 (m, 2H), 4.41 – 4.30 (m, 2H), 4.04 – 3.96 (m, 2H), 3.93 – 3.83 (m, 1H), 3.70 – 3.60 (m, 5H), 3.56 (dd, *J* = 13.9, 6.2 Hz, 1H), 2.46 (s, 3H), 1.99 (s, 3H), 1.96 (s, 3H), 1.85 (s, 3H), 1.69 (s, 9H), 1.58 (s, 9H). ¹³C NMR (126 MHz, CDCl₃) δ 170.2, 170.0, 169.7, 150.7, 139.1, 138.6, 135.6, 135.5, 132.9, 132.7, 129.9{2}, 128.4, 128.1, 127.9, 127.8{2}, 127.5, 127.4, 127.3, 123.3, 122.5, 116.5, 115.2, 101.4, 84.2, 83.6, 78.4, 75.3, 74.4, 74.1, 73.0, 72.5, 71.2, 69.3, 68.7, 66.8, 60.7, 28.3, 26.7, 20.6{3}, 19.0, 14.4. HRMS (ESI) *m/z*: [M + NH₄]⁺ calcd for C₆₉H₈₃N₂O₁₅ Si 1207.5557; found 1207.5570. [α]_D³⁵ = +0.49 (c 0.01, CHCl₃).

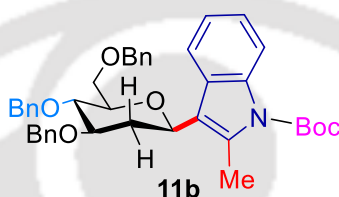
Synthesis of 3-(3,4,6-*tri*-O-benzyl-2-deoxy-β-D-glucopyranosyl)-5-methyl-1-*tert*-butyloxycarbonyl-indole (11a).



Glycosylation of **8d** (51.0 mg, 0.076 mmol) with **9d** (21.0 mg, 0.09 mmol) according to General procedure 1 afforded **11a** (40 mg, 81 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, *R_f* = 0.62 (Hexane/EtOAc = 4:1, v/v). ¹H NMR

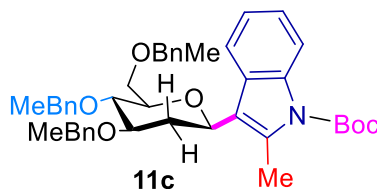
(500 MHz, CDCl₃) δ 7.98 (d, J = 7.0 Hz, 1H), 7.50 (s, 1H), 7.44 (s, 1H), 7.39 – 7.23 (m, 15H), 7.12 (d, J = 8.4 Hz, 1H), 4.97 (d, J = 10.8 Hz, 1H, -CH₂-Ph), 4.74 (d, J = 11.6 Hz, 1H, -CH₂-Ph), 4.68 (d, J = 12.5 Hz, 2H, -CH₂-Ph), 4.64 (d, J = 11.5 Hz, 2H, H-1, merged with -CH₂-Ph), 4.56 (d, J = 12.2 Hz, 1H, -CH₂-Ph), 3.88 – 3.83 (m, 1H, H-3), 3.83 – 3.80 (m, 2H), 3.72 – 3.67 (m, 1H), 3.65 (dt, J = 9.6, 3.0 Hz, 1H), 2.46 (ddd, J = 13.0, 4.9, 1.7 Hz, 1H, H-2'), 2.39 (s, 3H), 2.06 – 1.98 (m, 1H, H-2), 1.65 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 149.8, 138.6{2}, 138.5, 134.0, 132.1, 128.9, 128.5, 128.4, 128.3, 128.0, 127.7{2}, 127.6, 127.4, 125.9, 122.7, 120.7, 120.1, 114.9, 83.5, 81.1, 79.7, 78.6, 75.1, 73.4, 71.7, 71.5, 69.7, 37.1, 28.2, 21.4. HRMS (ESI) m/z : [M + Na]⁺ calcd for C₄₁H₄₅NO₆Na 670.3139; found 670.3145. $[\alpha]_D^{35}$ = + 0.29 (c 0.01, CHCl₃).

Synthesis of 3-(3,4,6-tri-*O*-benzyl-2-deoxy- β -D-glucopyranosyl)-2-methyl-1-*tert*-butyloxycarbonyl-indole (11b).



Glycosylation of **8d** (51.0 mg, 0.076 mmol) with **9b** (21.0 mg, 0.09 mmol) according to General procedure 1 afforded **11b** (40 mg, 81 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.62 (Hexane/EtOAc = 4:1, v/v). ¹H NMR (600 MHz, CDCl₃) δ 8.07 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.36 – 7.25 (m, 15H), 7.22 (t, J = 7.8 Hz, 1H), 7.13 (t, J = 7.5 Hz, 1H), 4.99 (d, J = 10.8 Hz, 1H, -CH₂-Ph), 4.76 (dd, J = 10.7, 3.4 Hz, 1H, H-1), 4.70 (dd, J = 11.2, 4.3 Hz, 2H, -CH₂-Ph, merged), 4.64 (d, J = 11.8 Hz, 2H, -CH₂-Ph, merged), 4.54 (d, J = 12.2 Hz, 1H, -CH₂-Ph), 3.89 (dd, J = 10.9, 3.9 Hz, 1H, H-6), 3.84 – 3.79 (m, 2H, H-3 & H-4 merged), 3.78 (dd, J = 10.8, 1.3 Hz, 1H, H-6'), 3.60 – 3.57 (m, 1H, H-5), 2.58 (s, 3H), 2.23 – 2.14 (m, 2H, H-2 & H-2' merged), 1.67 (s, 9H). ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 150.8, 138.7, 138.6, 138.5, 136.0, 133.2, 128.4{2}, 128.3, 128.1, 127.8, 127.7, 127.6{2}, 127.4, 127.3, 123.4, 122.4, 120.1, 118.1, 115.3, 83.7, 81.1, 79.5, 78.4, 75.2, 73.3, 71.9, 71.4, 69.5, 37.1, 28.3, 14.4. HRMS (ESI) m/z : [M + NH₄]⁺ calcd for C₄₁H₄₉N₂O₆ 665.3585; found 665.3589. $[\alpha]_D^{35}$ = - 0.43 (c 0.01, CHCl₃).

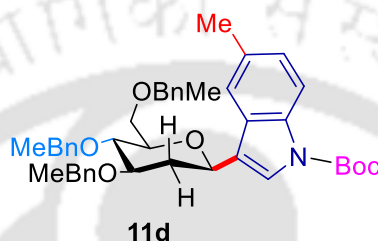
Synthesis of 3-(3,4,6-tri-*O*-(4-methylbenzyl)-2-deoxy- β -D-glucopyranosyl)-2-methyl-1-*tert*-butyloxycarbonyl-indole (11c).



Glycosylation of **8e** (50.0 mg, 0.070 mmol) with **9b** (19.0 mg, 0.082 mmol) according to General procedure 1 afforded **11c** (38 mg, 78 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.63 (Hexane/EtOAc = 4:1, v/v). ¹H NMR (500 MHz, CDCl₃) δ 8.07 (d, J = 8.3 Hz, 1H), 7.78 (d, J = 7.8 Hz, 1H), 7.24 – 7.08 (m,

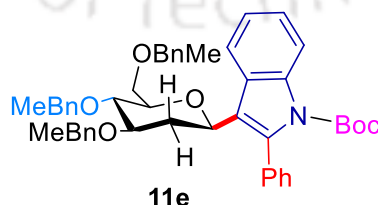
14H), 4.92 (d, $J = 10.6$ Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.73 (dd, $J = 10.6, 3.5$ Hz, 1H, H-1), 4.67 – 4.57 (m, 4H, $-\text{CH}_2\text{-Ph}$, merged), 4.48 (d, $J = 12.0$ Hz, 1H, $-\text{CH}_2\text{-Ph}$), 3.83 (dd, $J = 10.8, 4.0$ Hz, 1H, H-6), 3.81 – 3.72 (m, 3H, H-3, H-4 & H-6' merged), 3.55 (dd, $J = 9.0, 2.3$ Hz, 1H, H-5), 2.57 (s, 3H), 2.35 (s, 3H), 2.33 (s, 3H), 2.32 (s, 3H), 2.20 – 2.08 (m, 2H, H-2 & H-2' merged), 1.67 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 150.8, 137.3{2}, 137.0, 136.0, 135.6, 135.5, 133.2, 129.1, 129.0{2}, 128.2, 127.8, 127.7, 127.6, 123.4, 122.4, 120.2, 118.2, 115.3, 83.7, 81.0, 79.6, 78.2, 75.0, 73.2, 71.8, 71.3, 69.3, 37.2, 28.3, 21.2{2}, 14.4. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{44}\text{H}_{51}\text{NO}_6\text{Na}$ 712.3609; found 712.3599. $[\alpha]_{\text{D}}^{35} = +0.51$ (c 0.01, CHCl_3).

Synthesis of 3-(3,4,6-tri-*O*-(4-methylbenzyl)-2-deoxy- β -D-glucopyranosyl)-5-methyl-1-*tert*-butyloxycarbonyl-indole (11d).



Glycosylation of **8e** (58.0 mg, 0.081 mmol) with **9d** (22.0 mg, 0.095 mmol) according to General procedure 1 afforded **11d** (43 mg, 77 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.63$ (Hexane/EtOAc = 4:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 7.98 (d, $J = 6.7$ Hz, 1H), 7.49 (s, 1H), 7.44 (s, 1H), 7.28 – 7.24 (m, 2H), 7.22 (d, $J = 7.8$ Hz, 2H), 7.17 – 7.07 (m, 9H), 4.90 (d, $J = 10.6$ Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.69 (d, $J = 11.4$ Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.64 (dd, $J = 11.4, 5.7$ Hz, 2H, H-1, merged with $-\text{CH}_2\text{-Ph}$), 4.60 (d, $J = 9.9$ Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.58 (d, $J = 8.2$ Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.51 (d, $J = 12.0$ Hz, 1H, $-\text{CH}_2\text{-Ph}$), 3.84 – 3.79 (m, 1H, H-3), 3.79 – 3.74 (m, 2H), 3.67 – 3.59 (m, 2H), 2.46 – 2.41 (m, 1H, H-2'), 2.39 (s, 3H), 2.34 (2s, 6H), 2.32 (s, 3H), 2.00 (dd, $J = 24.2, 11.8$ Hz, 1H, H-2), 1.65 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 149.8, 137.3{2}, 137.0, 135.6, 135.5{2}, 134.0, 132.0, 129.1, 129.0{2}, 128.2, 127.8{2}, 125.9, 122.7, 120.8, 120.1, 114.9, 83.5, 80.9, 79.7, 78.5, 75.0, 73.3, 71.6, 71.5, 69.5, 37.1, 28.2, 21.4, 21.2{2}, 21.1. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{44}\text{H}_{55}\text{N}_2\text{O}_6$ 707.4055; found 707.4051. $[\alpha]_{\text{D}}^{35} = +0.45$ (c 0.01, CHCl_3).

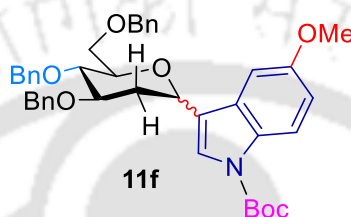
Synthesis of 3-(3,4,6-tri-*O*-(4-methylbenzyl)-2-deoxy- β -D-glucopyranosyl)-2-phenyl-1-*tert*-butyloxycarbonyl-indole (11e).



Glycosylation of **8e** (50.0 mg, 0.070 mmol) with **9c** (25.0 mg, 0.085 mmol) according to General procedure 1 afforded **11e** (40 mg, 76 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.62$ (Hexane/EtOAc = 4:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 8.22 (d, $J = 8.4$ Hz, 1H), 7.95 (d, $J = 7.8$ Hz, 1H), 7.42 – 7.36 (m, 3H), 7.35 – 7.25 (m, 3H), 7.24 – 7.16 (m, 5H), 7.15 – 7.08 (m, 8H), 4.87 (d, $J = 10.7$ Hz, 1H,

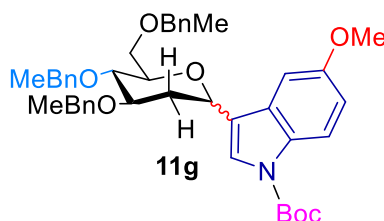
-CH₂-Ph), 4.62 – 4.54 (m, 4H, -CH₂-Ph, merged), 4.45 (d, *J* = 11.9 Hz, 1H, -CH₂-Ph), 4.33 (dd, *J* = 11.7, 2.1 Hz, 1H, H-1), 3.78 (dd, *J* = 10.8, 3.9 Hz, 1H, H-6), 3.74 – 3.67 (m, 2H, H-4 & H-6' merged), 3.63 – 3.56 (m, 1H, H-3), 3.36 (dd, *J* = 9.5, 2.0 Hz, 1H, H-5), 2.34 (s, 3H), 2.33 (s, 6H), 2.19 (dd, *J* = 24.4, 11.6 Hz, 1H, H-2), 2.08 (ddd, *J* = 13.0, 4.9, 2.1 Hz, 1H, H-2'), 1.20 (s, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 150.1, 137.2{2}, 136.9, 135.8, 135.7, 135.5, 135.4, 133.8, 129.7, 129.1, 129.0, 128.9, 128.1, 127.9, 127.6, 127.4, 124.5, 122.7, 121.6, 120.3, 115.1, 83.1, 80.8, 79.3, 78.1, 74.9, 73.2, 71.9, 71.4, 69.4, 37.4, 27.5, 21.2{2}. HRMS (ESI) *m/z*: [M + NH₄]⁺ calcd for C₄₉H₅₇N₂O₆ 769.4211; found 769.4206. [α]_D³⁵ = + 0.47 (c 0.01, CHCl₃).

Synthesis of 3-(3,4,6-*tri*-*O*-benzyl-2-deoxy-D-glucopyranosyl)-5-methoxy-1-*tert*-butyloxycarbonyl-indole (11f).



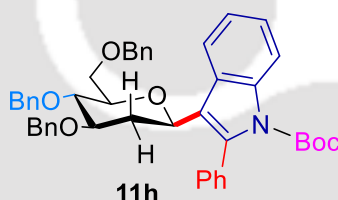
Glycosylation of **8d** (53.0 mg, 0.079 mmol) with **9f** (23.0 mg, 0.093 mmol) according to General procedure 1 afforded **11f** (39 mg, 74 %, α:β = 2.7:1) as a colorless syrup. The crude product was purified through flash column chromatography, *R_f* = 0.55 (Hexane/EtOAc = 4:1, v/v). ¹H NMR (500 MHz, CDCl₃) δ 8.30 (s, 1H), 8.02 (d, *J* = 7.0 Hz, 1H), 7.58 – 7.42 (m, 2H), 7.42 – 7.21 (m, 25H), 7.15 (d, *J* = 2.4 Hz, 1H), 7.06 (d, *J* = 3.7 Hz, 1H), 6.97 (s, 1H), 6.93 – 6.87 (m, 2H), 6.47 (d, *J* = 3.6 Hz, 1H), 5.18 (dd, *J* = 11.5, 1.8 Hz, 1H, H-1), 5.01 – 4.94 (m, 2H), 4.87 (d, *J* = 10.3 Hz, 1H), 4.73 (dd, *J* = 13.8, 11.2 Hz, 1H), 4.69 (d, *J* = 5.9 Hz, 2H), 4.68 – 4.65 (m, 2H), 4.65 – 4.59 (m, 4H), 4.54 (dd, *J* = 12.2, 3.4 Hz, 2H), 3.91 – 3.87 (m, 2H), 3.87 – 3.82 (m, 7H, H-3 & H-4 merged), 3.81 (dd, *J* = 5.4, 3.9 Hz, 1H), 3.78 (dd, *J* = 10.6, 1.5 Hz, 1H), 3.72 – 3.62 (m, 3H), 3.62 – 3.58 (m, 1H, H-5), 2.54 – 2.45 (m, 1H), 2.35 – 2.29 (m, 1H, H-2'), 2.06 – 1.97 (m, 1H), 1.91 (dd, *J* = 23.9, 11.5 Hz, 1H, H-2), 1.65 (d, *J* = 3.4 Hz, 12H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 155.8, 152.2, 151.3, 149.8, 138.8{3}, 138.7, 138.6, 138.5{2}, 131.2, 130.1, 129.5, 128.5, 128.4, 128.3{3}, 128.0, 127.7{2}, 127.6{2}, 127.5{2}, 127.4, 127.3, 126.3, 126.1, 123.1, 121.1, 120.7, 116.0, 114.7, 113.4, 113.3, 108.8, 108.4, 106.9, 103.1, 101.5, 83.3, 81.5, 81.4, 81.1, 79.5, 79.2, 78.7, 78.6, 78.4, 75.1, 75.0, 73.5, 73.4{2}, 72.3, 72.0, 71.7, 71.5, 71.3{2}, 70.0, 69.7, 69.6, 56.7, 55.7, 37.2, 36.8, 28.2{2}. HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₄₁H₄₅NO₇Na 686.3088; found 686.3092. [α]_D³⁵ = + 0.37 (c 0.01, CHCl₃).

Synthesis of 3-(3,4,6-*tri*-*O*-(4-methylbenzyl)-2-deoxy-D-glucopyranosyl)-5-methoxy-1-*tert*-butyloxycarbonyl-indole (11g).



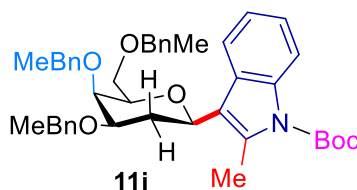
Glycosylation of **8e** (55.0 mg, 0.077 mmol) with **9f** (23.0 mg, 0.093 mmol) according to General procedure 1 afforded **11g** (38 mg, 70 %, $\alpha:\beta = 6:1$) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.54$ (Hexane/EtOAc = 4:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 8.01 (d, $J = 7.8$ Hz, 1H), 7.46 (d, $J = 0.9$ Hz, 1H), 7.23 (dd, $J = 10.9, 8.1$ Hz, 4H), 7.17 (d, $J = 7.9$ Hz, 2H), 7.14 – 7.08 (m, 7H), 7.05 (d, $J = 3.7$ Hz, 1H), 6.89 (d, $J = 9.0$ Hz, 1H), 5.16 (dd, $J = 11.4, 1.6$ Hz, 1H, H-1), 4.92 (d, $J = 10.7$ Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.67 – 4.57 (m, 4H, $-\text{CH}_2\text{-Ph}$, merged), 4.48 (d, $J = 11.9$ Hz, 1H, $-\text{CH}_2\text{-Ph}$), 3.85 (s, 4H, H-3, merged with $-\text{OMe}$ of indole), 3.82 (dd, $J = 12.6, 5.7$ Hz, 2H, H-4, merged with H-6), 3.79 – 3.72 (m, 2H, H-6', merged), 3.56 (d, $J = 9.4$ Hz, 1H, H-5), 2.36 – 2.31 (m, 10H), 2.30 – 2.27 (m, 1H, H-2), 1.88 (dd, $J = 24.1, 11.6$ Hz, 1H, H-2'), 1.66 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 151.3, 149.8, 137.2{2}, 137.0, 135.8, 135.7, 129.0{3}, 128.2, 127.8, 127.7, 126.1, 121.2, 114.6, 108.8, 108.4, 83.2, 81.2, 79.2, 78.3, 75.0, 73.2, 72.0, 71.2, 69.4, 56.7, 37.2, 28.2, 21.2{2}, 21.1. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{44}\text{H}_{55}\text{N}_2\text{O}_7$ 723.4004; found 723.4006. $[\alpha]_{\text{D}}^{35} = +0.53$ (c 0.01, CHCl_3).

Synthesis of 3-(3,4,6-tri-O-benzyl-2-deoxy- β -D-glucopyranosyl)-2-phenyl-1-tert-butyloxycarbonyl-indole (11h).



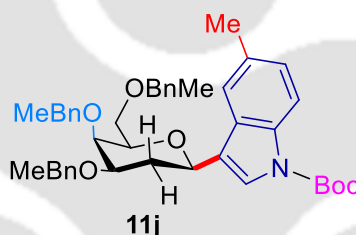
Glycosylation of **8d** (47.0 mg, 0.07 mmol) with **9c** (25.0 mg, 0.085 mmol) according to General procedure 1 afforded **11h** (41 mg, 82 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.54$ (Hexane/EtOAc = 4:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 8.23 (d, $J = 8.4$ Hz, 1H), 7.95 (d, $J = 7.8$ Hz, 1H), 7.42 – 7.38 (m, 3H), 7.37 – 7.23 (m, 18H), 7.19 (t, $J = 7.5$ Hz, 1H), 4.94 (d, $J = 10.9$ Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.68 – 4.56 (m, 4H, $-\text{CH}_2\text{-Ph}$, merged), 4.51 (d, $J = 12.1$ Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.36 (dd, $J = 11.6, 2.2$ Hz, 1H, H-1), 3.83 (dd, $J = 10.8, 3.8$ Hz, 1H, H-6), 3.77 (t, $J = 9.2$ Hz, 1H, H-4), 3.72 (dd, $J = 10.8, 1.5$ Hz, 1H, H-6'), 3.68 – 3.60 (m, 1H, H-3), 3.44 – 3.37 (m, 1H, H-5), 2.22 (dd, $J = 24.3, 11.6$ Hz, 1H, H-2), 2.12 (ddd, $J = 13.0, 5.0, 2.3$ Hz, 1H, H-2'), 1.20 (s, 9H). ^{13}C NMR (126 MHz, CDCl_3) δ 150.1, 138.7, 138.5, 136.9, 135.4, 133.8, 129.7, 128.4, 128.3{2}, 127.9, 127.7, 127.6{2}, 127.4, 127.3, 124.6, 122.7, 121.5, 120.2, 115.1, 83.1, 80.9, 79.2, 78.2, 75.0, 73.3, 71.9, 71.5, 69.5, 37.4, 27.5. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{46}\text{H}_{47}\text{NO}_6\text{Na}$ 732.3296; found 732.3300. $[\alpha]_{\text{D}}^{35} = -0.23$ (c 0.01, CHCl_3).

Synthesis of 3-(3,4,6-tri-O-(4-methylbenzyl)-2-deoxy- β -D-galactopyranosyl)-2-methyl-1-tert-butyloxycarbonyl-indole (11i).



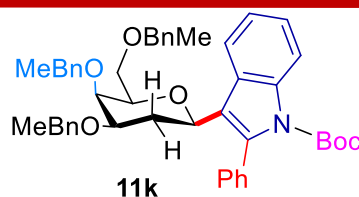
Glycosylation of **8g** (52.0 mg, 0.073 mmol) with **9b** (20.0 mg, 0.086 mmol) according to General procedure 1 afforded **11i** (42 mg, 83 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.57 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 8.03 (d, J = 8.4 Hz, 1H), 7.90 (t, J = 9.2 Hz, 1H), 7.32 (d, J = 7.8 Hz, 2H), 7.22 (d, J = 7.9 Hz, 2H), 7.20 – 7.12 (m, 7H), 7.10 (d, J = 7.7 Hz, 2H), 7.06 (t, J = 7.3 Hz, 1H), 5.04 (d, J = 11.3 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.73 (dd, J = 11.9, 2.6 Hz, 1H, H-1), 4.62 (d, J = 11.3 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.60 – 4.55 (m, 2H, $-\text{CH}_2\text{-Ph}$, merged), 4.44 (d, J = 11.7 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.39 (d, J = 11.7 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.01 (s, 1H, H-4), 3.75 – 3.71 (m, 1H, H-3), 3.70 (d, J = 8.3 Hz, 1H, H-5), 3.67 – 3.64 (m, 1H, H-6), 3.58 (dd, J = 8.5, 4.9 Hz, 1H, H-6'), 2.67 (q, J = 12.1 Hz, 1H, H-2), 2.56 (s, 3H), 2.37 (s, 3H), 2.34 (s, 3H), 2.32 (s, 3H), 1.85 – 1.80 (m, 1H, H-2'), 1.66 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 150.8, 137.3, 137.2, 136.7, 136.5, 135.9, 135.5, 135.0, 133.1, 129.1, 129.0, 128.8, 128.1, 127.5, 127.4, 123.3, 122.4, 120.5, 118.8, 115.1, 83.5, 78.3, 77.4, 74.0, 73.3, 72.4, 71.8, 69.8, 69.1, 32.5, 28.3, 21.2{2}, 14.3. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{44}\text{H}_{51}\text{NO}_6\text{Na}$ 712.3609; found 712.3602. $[\alpha]_{\text{D}}^{35} = +0.18$ (c 0.01, CHCl_3).

Synthesis of 3-(3,4,6-tri-O-(4-methylbenzyl)-2-deoxy- β -D-galactopyranosyl)-5-methyl-1-tert-butyloxycarbonyl-indole (11j).



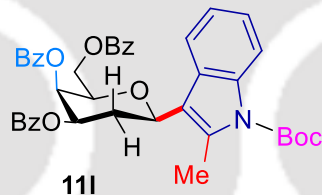
Glycosylation of **8g** (54.0 mg, 0.076 mmol) with **9d** (21.0 mg, 0.091 mmol) according to General procedure 1 afforded **11j** (43 mg, 82 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.57 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 7.96 (d, J = 7.2 Hz, 1H), 7.48 (s, 2H), 7.29 – 7.22 (m, 4H), 7.17 (dd, J = 10.3, 8.1 Hz, 4H), 7.13 – 7.06 (m, 5H), 4.96 (d, J = 11.4 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.66 – 4.58 (m, 4H, H-1, merged with $-\text{CH}_2\text{-Ph}$), 4.46 (d, J = 11.6 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.39 (d, J = 11.6 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 3.97 (s, 1H, H-4), 3.75 – 3.71 (m, 1H, H-3), 3.70 (d, J = 6.1 Hz, 1H, H-6), 3.67 (t, J = 7.9 Hz, 1H, H-5), 3.62 (dd, J = 8.9, 5.5 Hz, 1H, H-6'), 2.54 (q, J = 12.0 Hz, 1H, H-2), 2.35 (s, 3H), 2.33 (s, 6H), 2.32 (s, 3H), 2.12 – 2.06 (m, 1H, H-2'), 1.63 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 149.8, 137.4, 137.3, 136.9, 136.3, 135.5, 135.2, 134.1, 132.0, 129.1{2}, 128.8, 128.1, 127.5, 125.8, 122.9, 120.9, 120.4, 114.8, 83.3, 78.5, 77.9, 77.3, 77.0, 76.8, 74.1, 73.4, 72.4, 71.9, 70.0, 69.5, 32.3, 28.2, 21.3, 21.2. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{44}\text{H}_{51}\text{NO}_6\text{Na}$ 712.3609; found 712.3612. $[\alpha]_{\text{D}}^{35} = +0.27$ (c 0.01, CHCl_3).

Synthesis of 3-(3,4,6-tri-O-(4-methylbenzyl)-2-deoxy- β -D-galactopyranosyl)-2-phenyl-1-tert-butyloxycarbonyl-indole (11k).



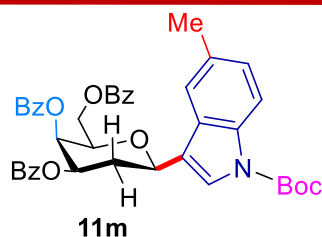
Glycosylation of **8g** (49.0 mg, 0.069 mmol) with **9c** (24.0 mg, 0.082 mmol) according to General procedure 1 afforded **11k** (42 mg, 81 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.58 (Hexane/EtOAc = 4:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 8.17 (d, J = 8.4 Hz, 1H), 8.09 (d, J = 7.8 Hz, 1H), 7.42 – 7.36 (m, 3H), 7.35 – 7.26 (m, 5H), 7.22 – 7.06 (m, 11H), 5.02 (d, J = 11.2 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.60 (d, J = 11.2 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.56 (d, J = 11.8 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.51 (d, J = 11.8 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.41 (d, J = 11.7 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.37 (d, J = 6.9 Hz, 1H, $-\text{CH}_2\text{-Ph}$), 4.34 (dd, J = 9.5, 2.0 Hz, 1H, H-1), 3.94 (s, 1H, H-4), 3.68 (t, J = 8.3 Hz, 1H, H-6), 3.58 – 3.52 (m, 2H, H-3 & H-5 merged), 3.51 – 3.47 (m, 1H, H-6'), 2.75 (q, J = 12.1 Hz, 1H, H-2), 2.38 (s, 3H), 2.33 (s, 3H), 2.31 (s, 3H), 1.79 (d, J = 12.7 Hz, 1H, H-2'), 1.20 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 150.2, 137.3, 137.1, 136.9, 136.7, 136.6, 135.5, 135.1, 135.0, 133.9, 129.8, 129.0, 128.8, 128.1, 127.9, 127.7, 127.6, 127.4, 124.5, 122.7, 122.1, 121.0, 114.9, 83.0, 78.3, 74.0, 73.3, 72.4, 71.9, 69.9, 69.1, 32.7, 27.5, 21.2, 21.1. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{49}\text{H}_{57}\text{N}_2\text{O}_6$ 769.4211; found 769.4206. $[\alpha]_D^{35} = -0.36$ (c 0.01, CHCl_3).

Synthesis of 3-(3,4,6-tri -O-benzoyl-2-deoxy- β -D-galactopyranosyl)-2-methyl-1-tert-butylloxycarbonyl-indole (11l).



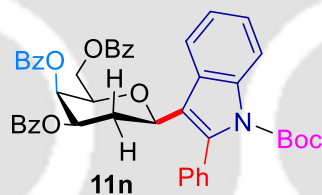
Glycosylation of **8h** (52.0 mg, 0.073 mmol) with **9b** (20.0 mg, 0.086 mmol) according to General procedure 1 afforded **11l** (39 mg, 78 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.45 (Hexane/EtOAc = 3:1, v/v). ^1H NMR (600 MHz, CDCl_3) δ 8.24 (d, J = 7.3 Hz, 2H), 8.12 (d, J = 8.2 Hz, 1H), 8.08 (d, J = 7.7 Hz, 1H), 8.01 (d, J = 7.3 Hz, 2H), 7.84 (d, J = 7.4 Hz, 2H), 7.66 (t, J = 7.4 Hz, 1H), 7.57 – 7.50 (m, 3H), 7.48 (t, J = 7.4 Hz, 1H), 7.39 (t, J = 7.7 Hz, 2H), 7.33 – 7.26 (m, 3H), 7.23 (t, J = 7.3 Hz, 1H), 5.98 (d, J = 1.7 Hz, 1H, H-4), 5.63 – 5.54 (m, 1H, H-3), 5.10 (dd, J = 11.8, 2.2 Hz, 1H, H-1), 4.65 (dd, J = 11.3, 5.9 Hz, 1H, H-6), 4.47 (dd, J = 11.3, 6.9 Hz, 1H, H-6'), 4.32 (t, J = 6.3 Hz, 1H, H-5), 2.81 (q, J = 12.2 Hz, 1H, H-2), 2.67 (s, 3H), 2.13 (d, J = 13.0 Hz, 1H, H-2'), 1.69 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 166.2, 165.9, 165.6, 150.7, 136.1, 133.7, 133.4, 133.1{2}, 129.9{2}, 129.8, 129.7, 129.6{2}, 128.7, 128.3{2}, 127.7, 123.6, 122.4, 119.8, 117.5, 115.6, 84.0, 75.0, 72.3, 70.7, 67.4, 63.0, 32.2, 28.3, 14.4. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{41}\text{H}_{39}\text{NO}_9\text{Na}$ 712.2517; found 712.2525. $[\alpha]_D^{35} = +0.52$ (c 0.01, CHCl_3).

Synthesis of 3-(3,4,6-tri -O-benzoyl-2-deoxy- β -D-galactopyranosyl)-5-methyl-1-tert-butylloxycarbonyl-indole (11m).



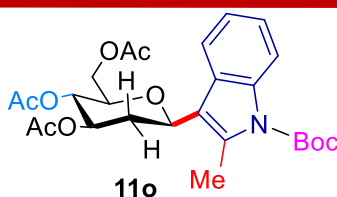
Glycosylation of **8h** (59.0 mg, 0.083 mmol) with **9d** (23.0 mg, 0.099 mmol) according to General procedure 1 afforded **11m** (46 mg, 80 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.45 (Hexane/EtOAc = 3:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 8.22 – 8.15 (m, 2H), 8.07 – 8.03 (m, 2H), 8.01 (d, J = 7.6 Hz, 1H), 7.90 – 7.84 (m, 2H), 7.62 (dd, J = 16.0, 8.9 Hz, 3H), 7.55 (t, J = 7.4 Hz, 1H), 7.52 – 7.47 (m, 3H), 7.42 (t, J = 7.8 Hz, 2H), 7.32 (t, J = 7.8 Hz, 2H), 7.15 (d, J = 8.4 Hz, 1H), 5.94 (d, J = 2.8 Hz, 1H, H-4), 5.64 – 5.55 (m, 1H, H-3), 5.01 (d, J = 10.2 Hz, 1H, H-1), 4.64 (dd, J = 11.3, 6.8 Hz, 1H, H-6), 4.48 (dd, J = 11.3, 6.1 Hz, 1H, H-6'), 4.40 (t, J = 6.3 Hz, 1H, H-5), 2.68 (q, J = 12.1 Hz, 1H, H-2), 2.44 – 2.37 (m, 4H, H-2', merged with $-\text{CH}_3$ of C-5 indole), 1.67 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 165.2, 164.8, 164.6, 148.7, 132.4, 132.1, 131.2, 128.9, 128.8, 128.7, 128.6, 127.8, 127.6, 127.4, 127.3, 125.1, 122.0, 119.1, 118.9, 114.1, 82.7, 74.3, 71.2, 69.8, 66.3, 62.3, 30.9, 27.2, 20.4. HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{41}\text{H}_{43}\text{N}_2\text{O}_9$ 707.2963; found 707.2957. $[\alpha]_D^{35} = -0.26$ (c 0.01, CHCl_3).

Synthesis of 3-(3,4,6-tri-O-benzoyl-2-deoxy- β -D-galactopyranosyl)-2-phenyl-1-tert-butyloxycarbonyl-indole (**11n**).



Glycosylation of **8h** (57.0 mg, 0.080 mmol) with **9c** (28.0 mg, 0.095 mmol) according to General procedure 1 afforded **11n** (45 mg, 75 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.44 (Hexane/EtOAc = 3:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 8.29 (d, J = 8.4 Hz, 1H), 8.24 (t, J = 7.3 Hz, 3H), 7.98 (d, J = 7.6 Hz, 2H), 7.82 (d, J = 7.6 Hz, 2H), 7.67 (t, J = 7.4 Hz, 1H), 7.58 – 7.50 (m, 3H), 7.47 (dd, J = 11.7, 6.0 Hz, 4H), 7.42 – 7.27 (m, 8H), 5.88 (d, J = 2.1 Hz, 1H, H-4), 5.43 – 5.38 (m, 1H, H-3), 4.70 (dd, J = 11.8, 2.1 Hz, 1H, H-1), 4.61 (dd, J = 11.3, 5.8 Hz, 1H, H-6), 4.42 (dd, J = 11.3, 7.0 Hz, 1H, H-6'), 4.14 (t, J = 6.4 Hz, 1H, H-5), 2.89 (q, J = 12.3 Hz, 1H, H-2), 2.10 – 2.05 (m, 1H, H-2'), 1.22 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 166.1, 165.9, 165.6, 150.0, 137.0, 136.2, 133.4, 133.1{2}, 130.0, 129.9, 129.8, 129.7{2}, 128.7, 128.3{2}, 128.2{2}, 127.3, 124.8, 122.7, 121.0 119.4, 115.5, 83.4, 74.7, 72.5, 70.5, 67.3, 62.9, 32.2, 27.5. HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{46}\text{H}_{42}\text{NO}_9$ 752.2854; found 752.2858. $[\alpha]_D^{35} = +0.45$ (c 0.01, CHCl_3).

Synthesis of 3-(3,4,6-tri-O-acetyl-2-deoxy- β -D-glucopyranosyl)-2-methyl-1-tert-butyloxycarbonyl-indole (**11o**).



Glycosylation of **8f** (48.0 mg, 0.091 mmol) with **9b** (25.0 mg, 0.11 mmol) according to General procedure 1 afforded **11o** (34 mg, 74 %, β only) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.48 (Hexane/EtOAc = 3:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 8.08 (d, J = 8.1 Hz, 1H), 7.72 (d, J = 7.5 Hz, 1H), 7.25 – 7.21 (m, 1H), 7.19 (t, J = 7.1 Hz, 1H), 5.25 – 5.16 (m, 2H, H-3 & H-4 merged), 4.88 (dd, J = 11.7, 2.4 Hz, 1H, H-1), 4.28 (dd, J = 12.2, 4.2 Hz, 1H, H-6), 4.20 (dd, J = 12.2, 2.1 Hz, 1H, H-6'), 3.78 (dd, J = 5.4, 2.5 Hz, 1H, H-5), 2.58 (s, 3H), 2.29 (dd, J = 24.1, 11.6 Hz, 1H, H-2), 2.23 – 2.17 (m, 1H, H-2'), 2.10 (s, 3H), 2.09 (s, 3H), 2.02 (s, 3H), 1.67 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 170.8, 170.4, 170.0, 150.6, 136.0, 133.7, 127.4, 123.6, 122.5, 119.6, 116.8, 115.5, 84.0, 76.2, 72.4, 72.0, 69.4, 62.8, 36.5, 28.3, 20.9, 20.8, 14.3. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{26}\text{H}_{33}\text{NO}_9\text{Na}$ 526.2048; found 526.2053. $[\alpha]_{\text{D}}^{35}$ = - 0.33 (c 0.01, CHCl_3).

Procedure to recycle the cyclized by-product (**8**)

The by-product (**8**) (46 mg, 0.18 mmol) was taken in an oven-dried round bottom flask, and dissolved in dry DCM. To the reaction vessel, 1.2 equiv. of TMS-OTf (40 μl , 0.22 mmol) was added in an inert condition, followed by *N,N*-Diisopropylethylamine (2.5 equiv.) (78 μl , 0.45 mmol) at 0 $^\circ\text{C}$. The reaction was left at the same temperature for 1h. After completion of the reaction ice cold water was added to quench the reaction. The aqueous part was separated and acidified with 1(N) HCl to make the pH at 6. The white color aqueous part was extracted with ethyl acetate (20 ml X 3). The extracted part was washed with brine, dried over Na_2SO_4 , and concentrated (37 mg, 80 %). The NMR data were recorded from the crude product (**8r**) without purification and matched with the reported data.²⁸

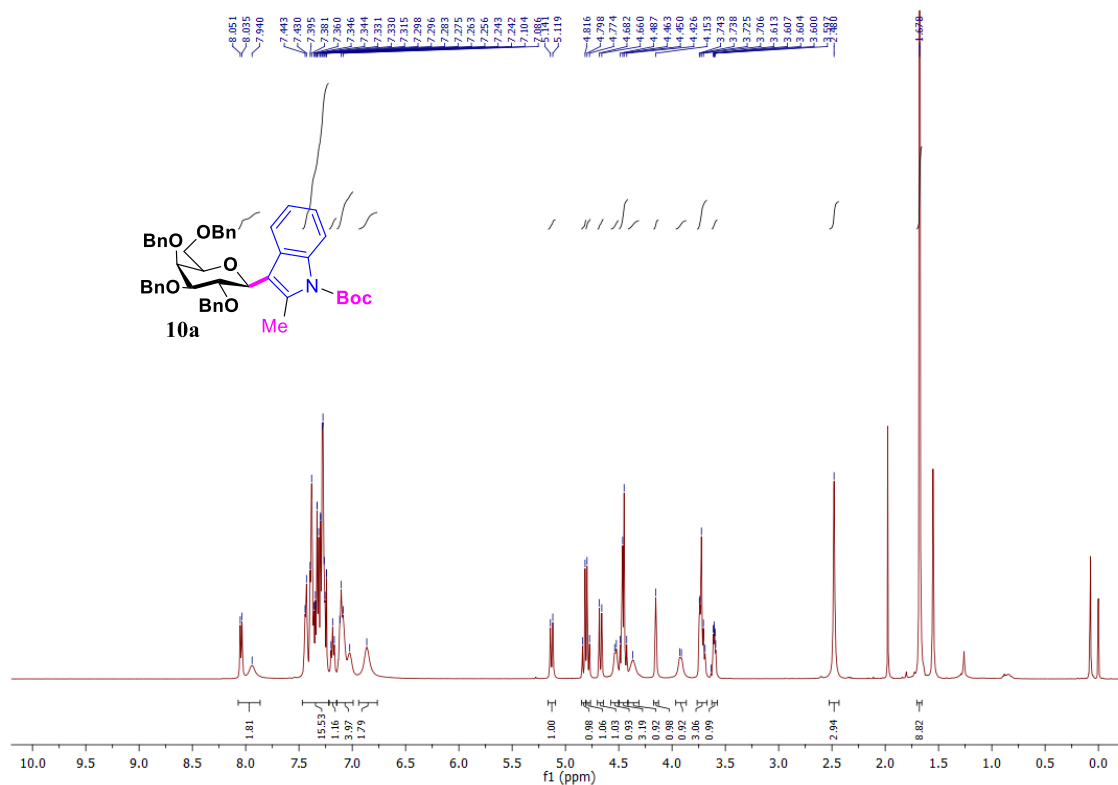
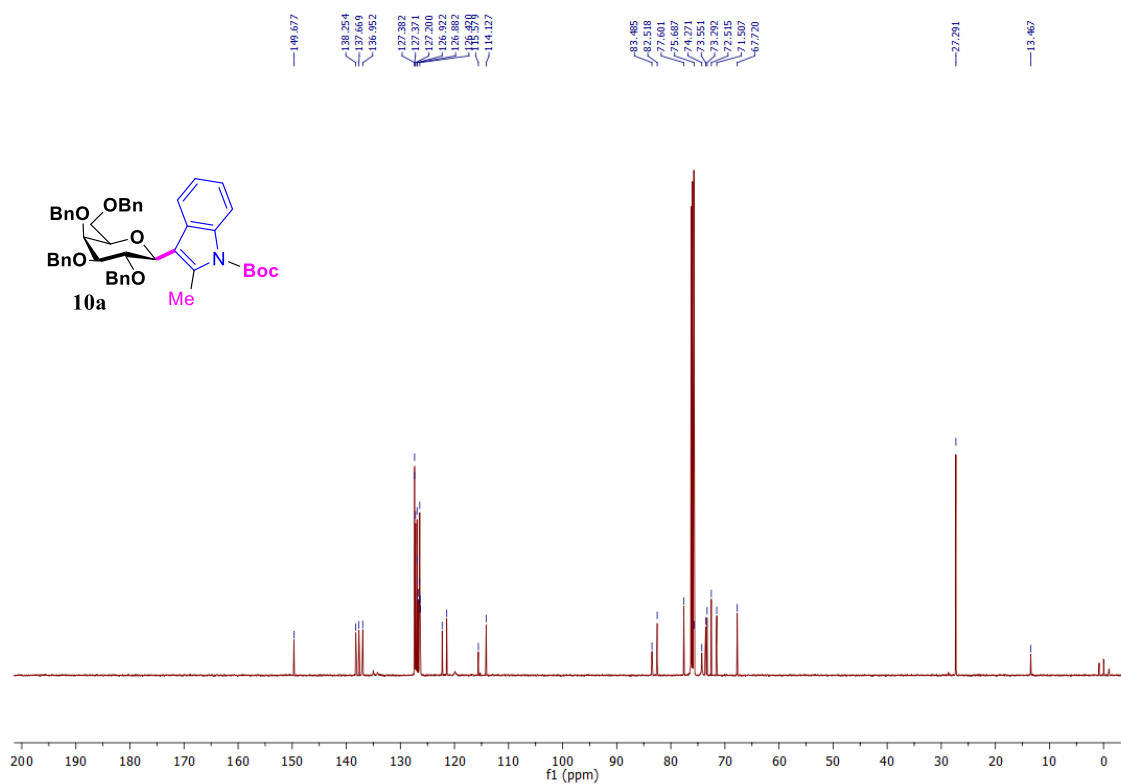
4.4 References

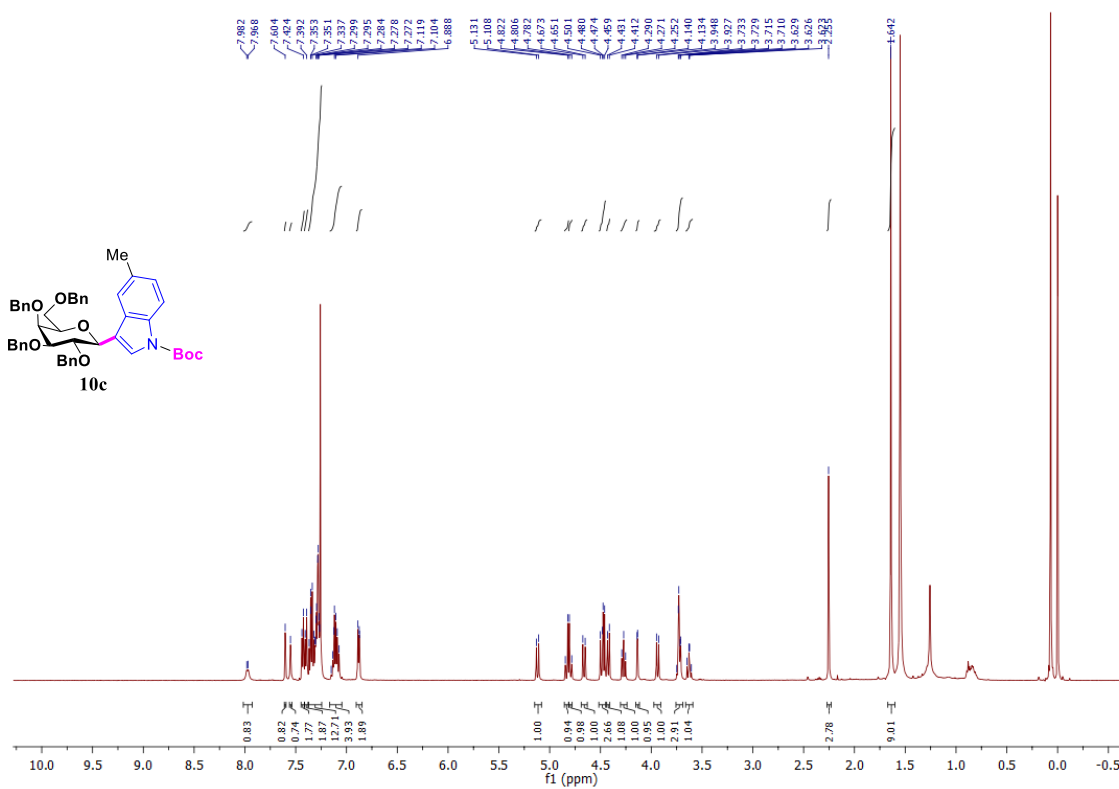
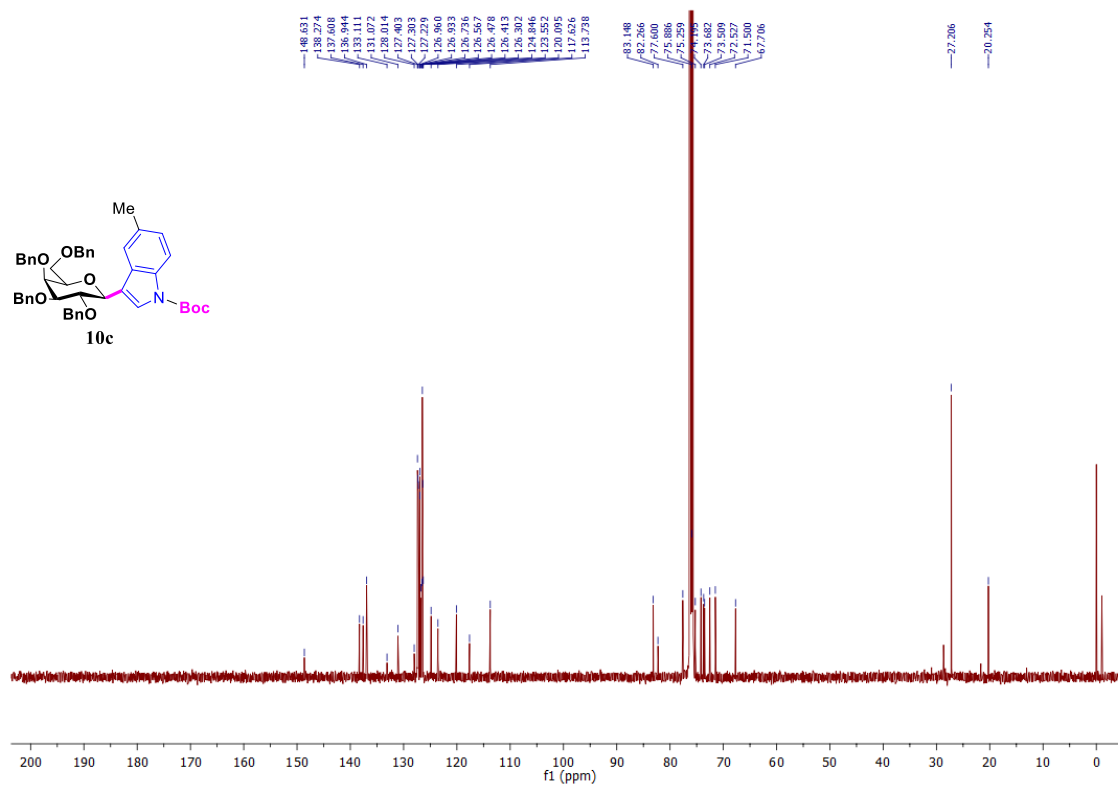
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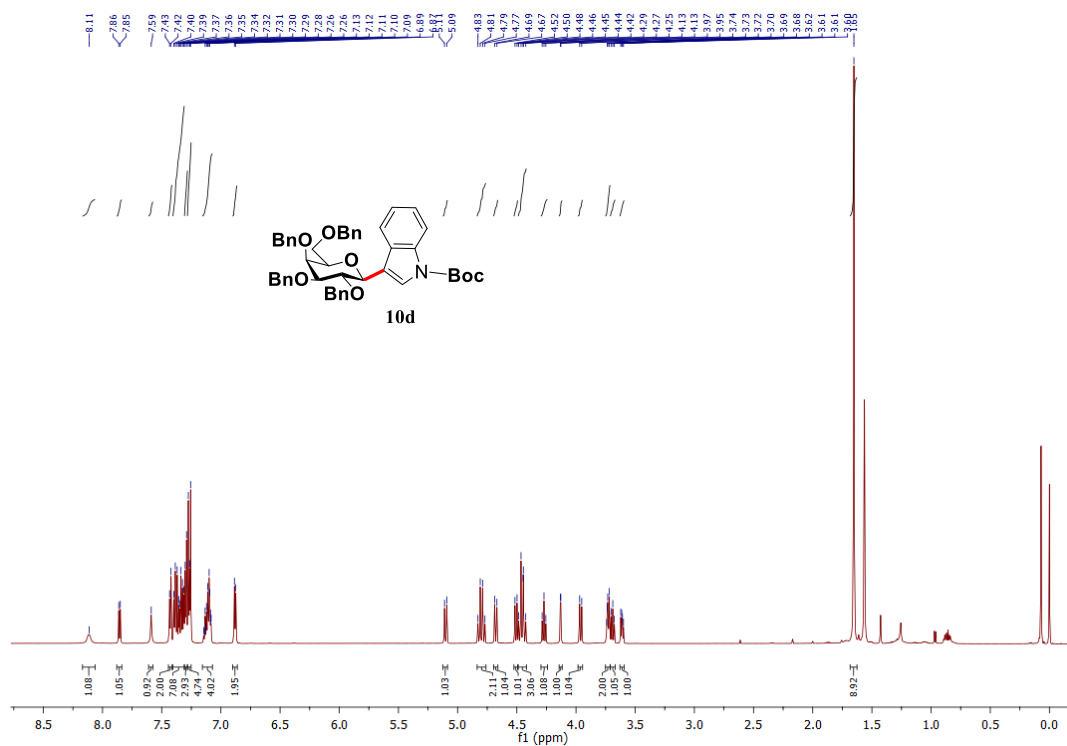
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- (b). Halder, S.; Addanki, R. B.; Sarmah, B.; Kancharla, P. K. *Org. Biomol. Chem.* **2022**, 20, 1874.
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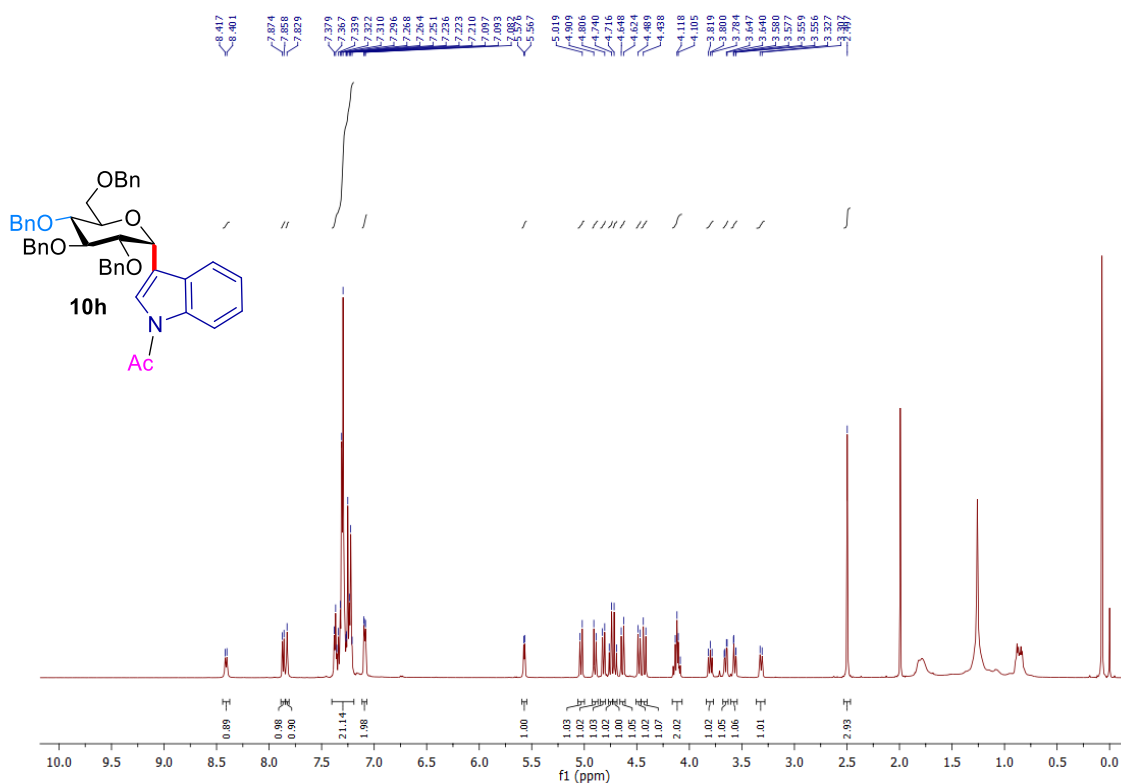
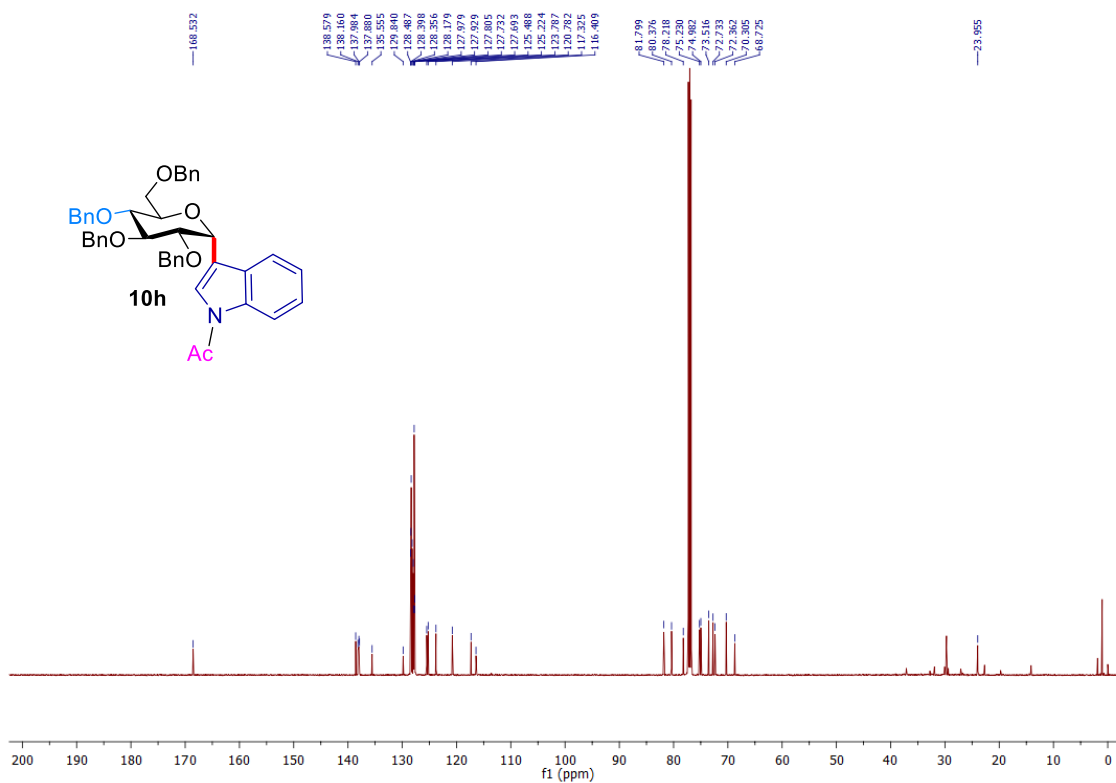
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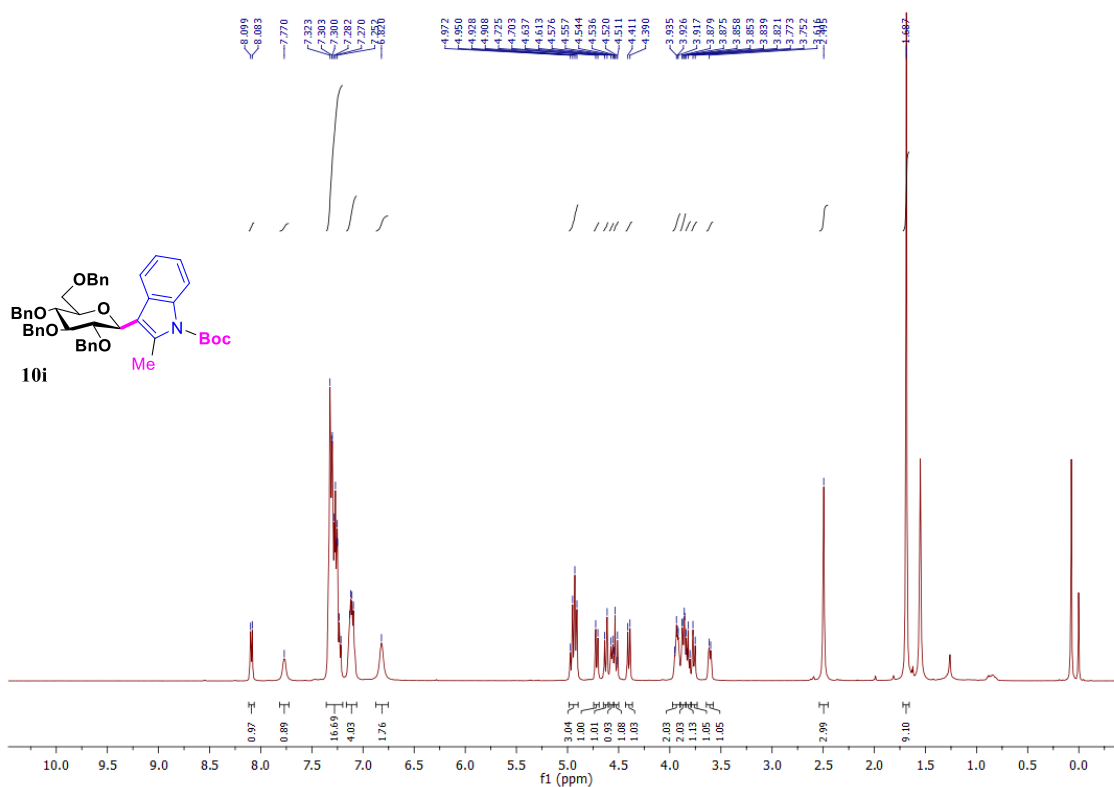
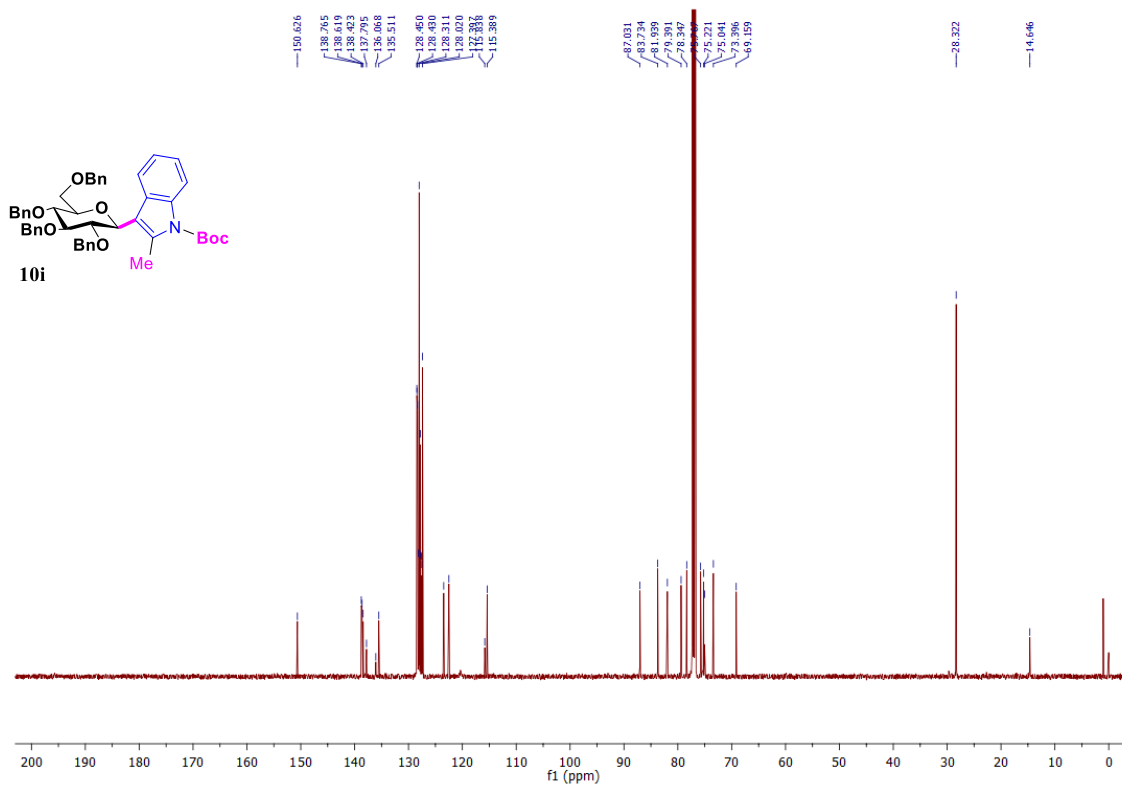
Spectra

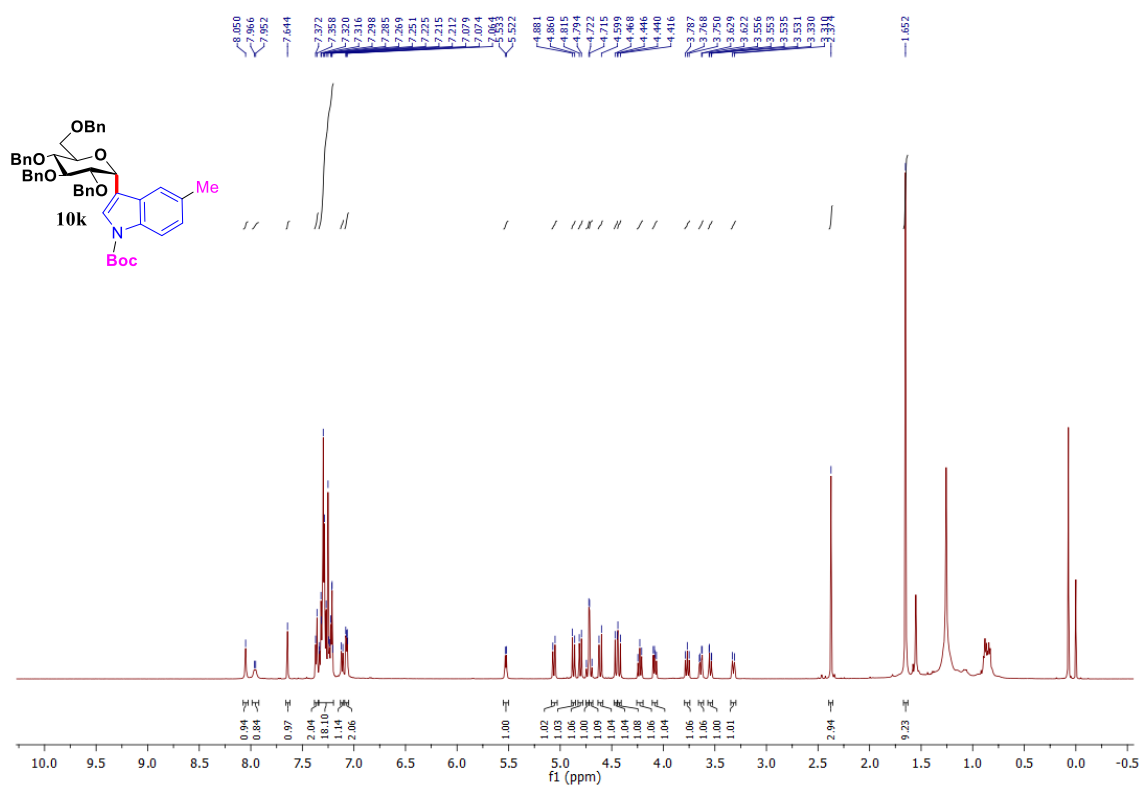
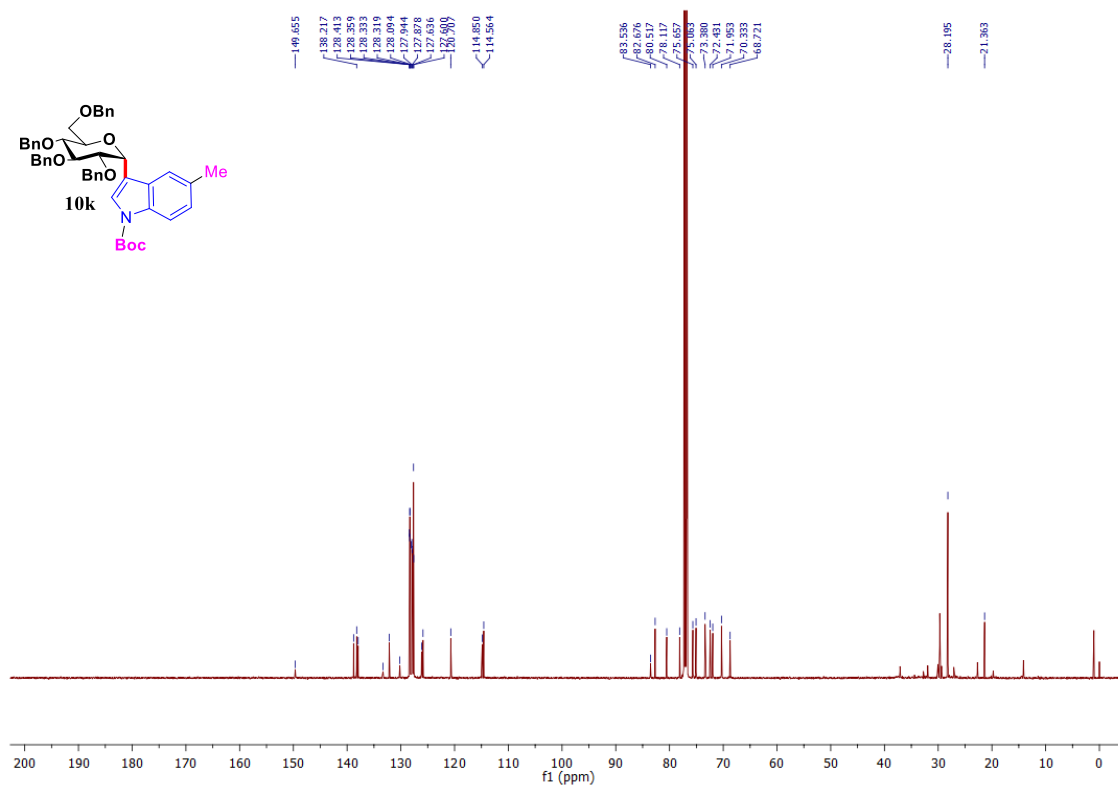
 ^1H NMR spectrum of compound 10a (500 MHz, CDCl_3): **$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 10a (500 MHz, CDCl_3):**

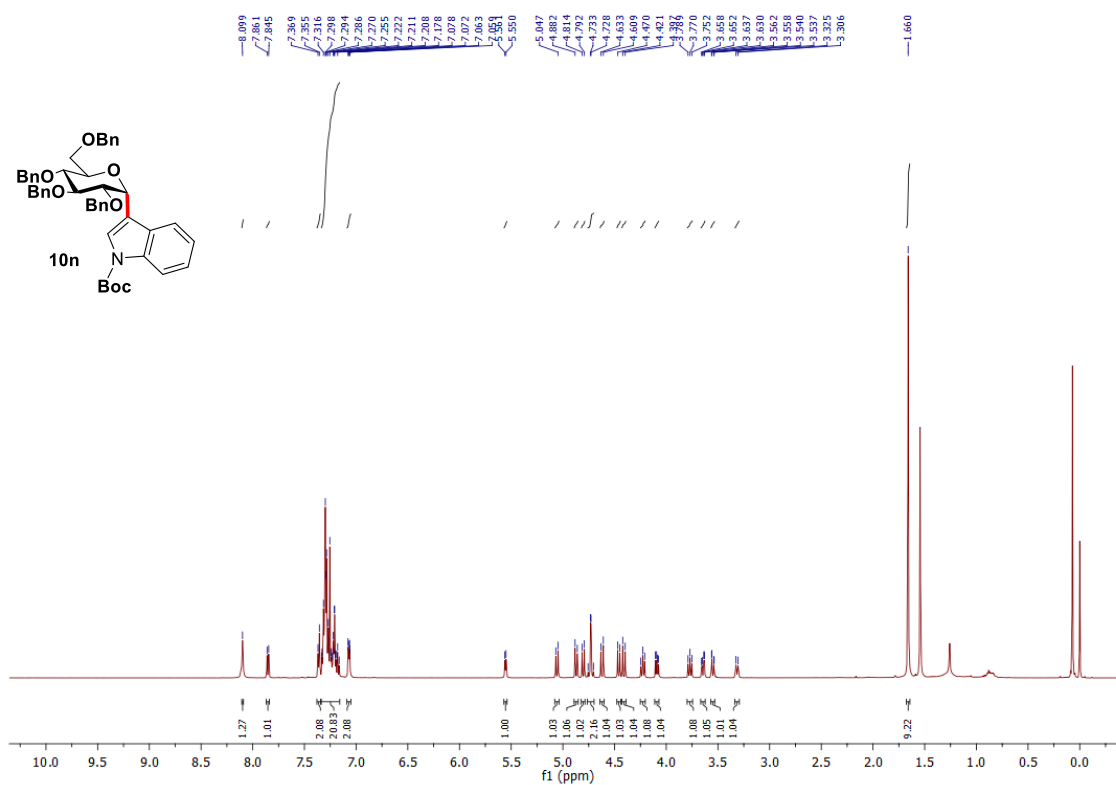
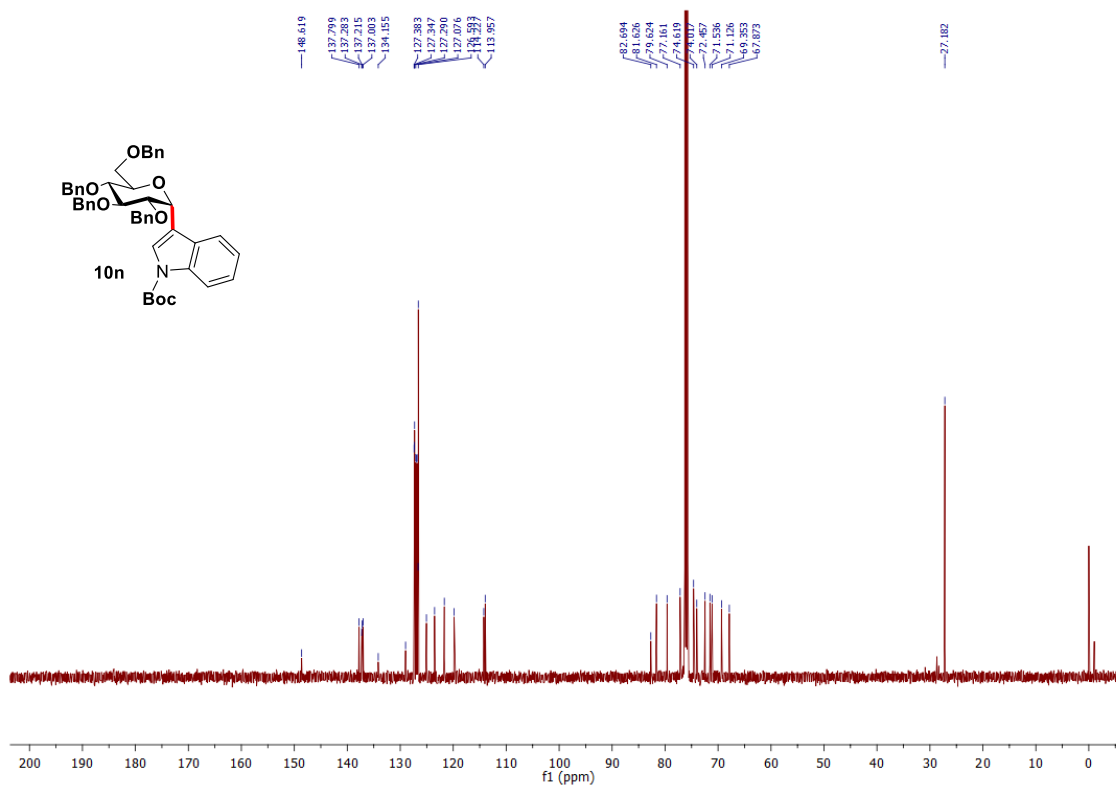
^1H NMR spectrum of compound 10c (500 MHz, CDCl_3): **$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 10c (500 MHz, CDCl_3):**

^1H NMR spectrum of compound 10d (600 MHz, CDCl_3):

^1H NMR spectrum of compound 10h (500 MHz, CDCl_3): **$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 10h (500 MHz, CDCl_3):**

^1H NMR spectrum of compound 10i (500 MHz, CDCl_3): **$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 10i (500 MHz, CDCl_3):**

^1H NMR spectrum of compound 10k (500 MHz, CDCl_3): **$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 10k (500 MHz, CDCl_3):**

^1H NMR spectrum of compound 10n (500 MHz, CDCl_3): **$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 10n (500 MHz, CDCl_3):**

[illegible]

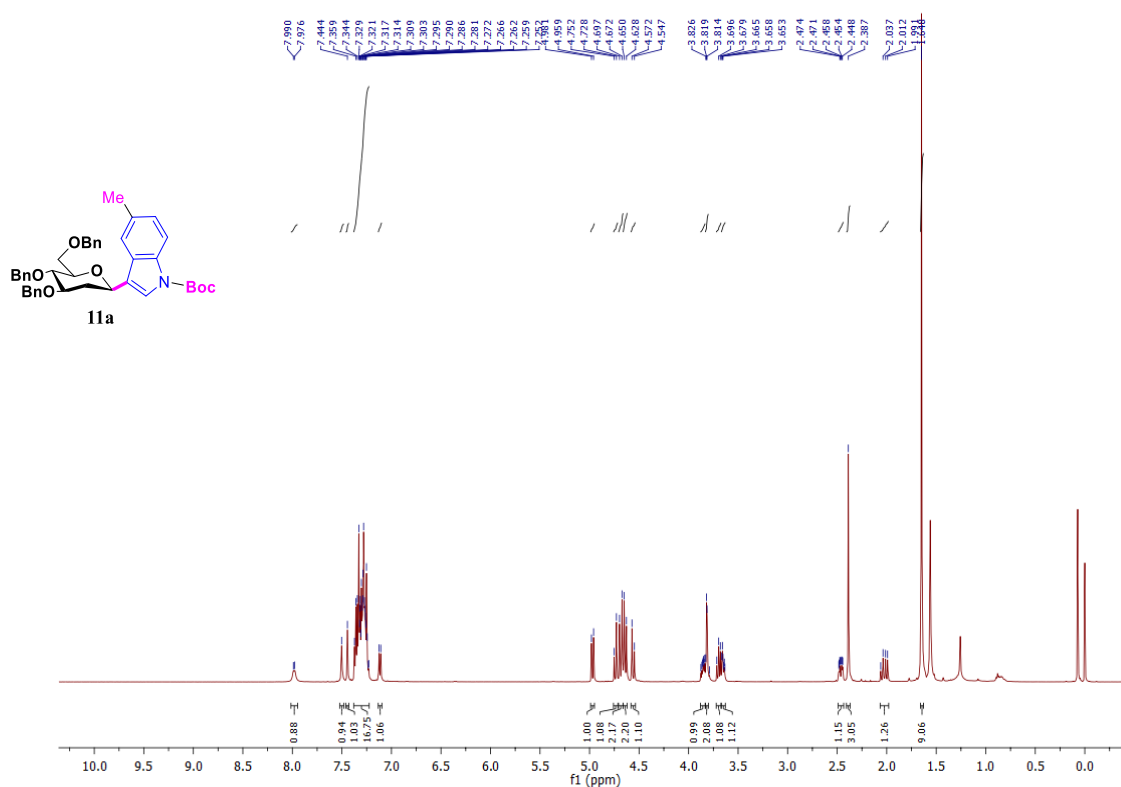
Chemical structure of compound **10o** is shown above the spectrum. The structure features a central sugar moiety (likely a derivative of D-glucose) substituted with various groups: a tert-butyldimethylsilyl (OTBDPS) group, an acetoxy (AcO) group, a benzoyloxy (OBn) group, and a 1-methyl-2-(4-methylphenyl)-1H-imidazole-5-yl group (labeled with Me and Boc).

The ¹³C NMR spectrum (CDCl₃) displays peaks corresponding to the structure, with the following chemical shifts (ppm) labeled above the spectrum:

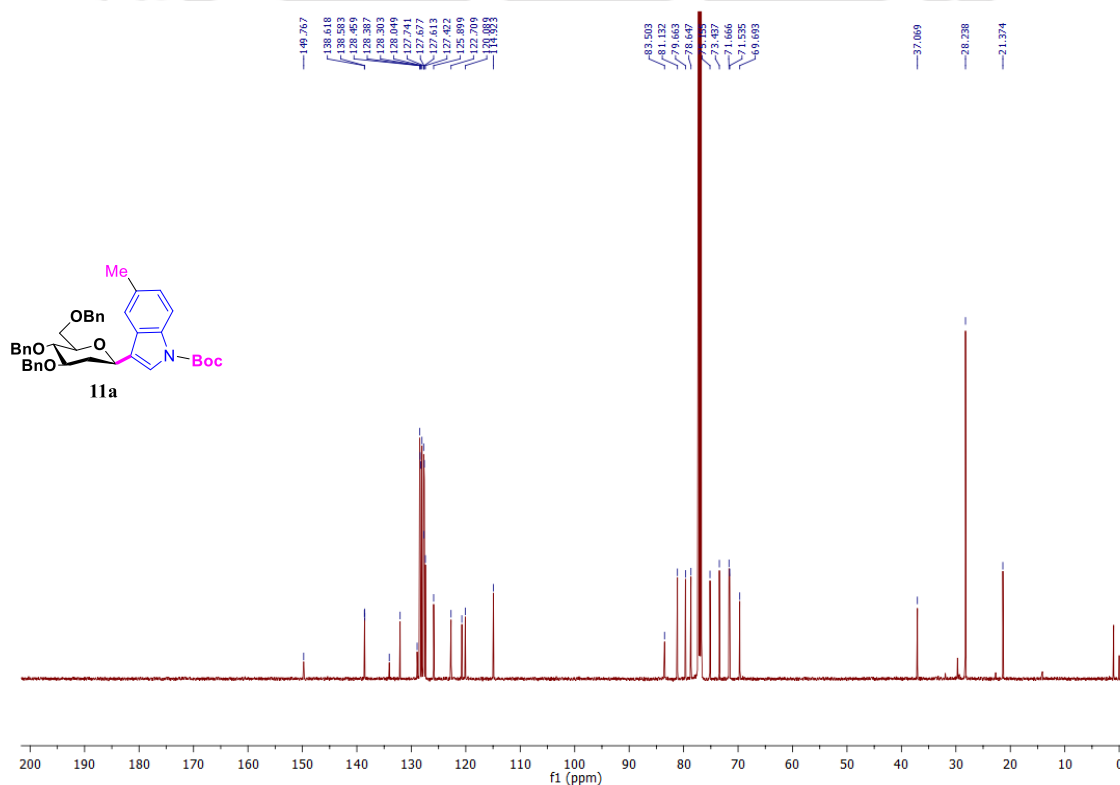
- 170.159, 169.660, 150.680, 135.627, 132.528, 129.889, 129.855, 128.400, 128.121, 127.812, 127.413, 127.382, 127.549, 127.394, 127.200, 115.159, 101.446, 84.245, 83.630, 79.629, 74.152, 73.000, 72.460, 71.159, 69.309, 68.888, 28.316, 26.690, 20.655, 20.633, 20.576, 18.975, 14.488.

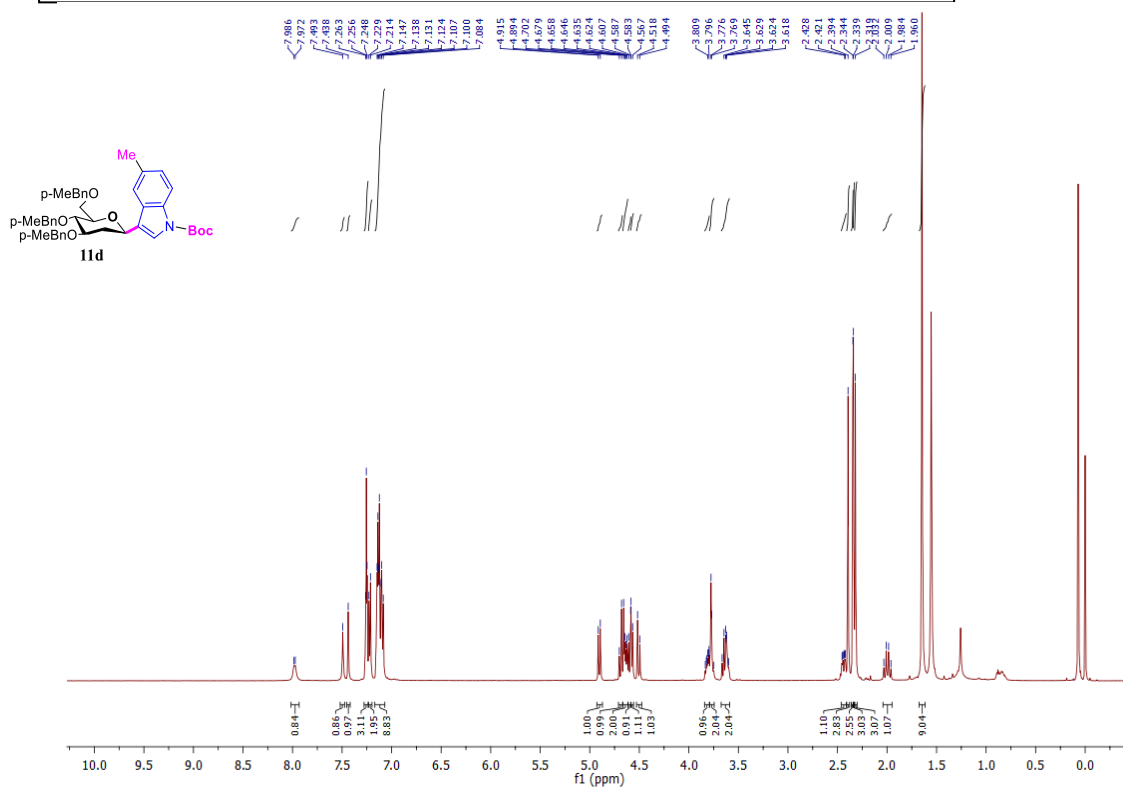
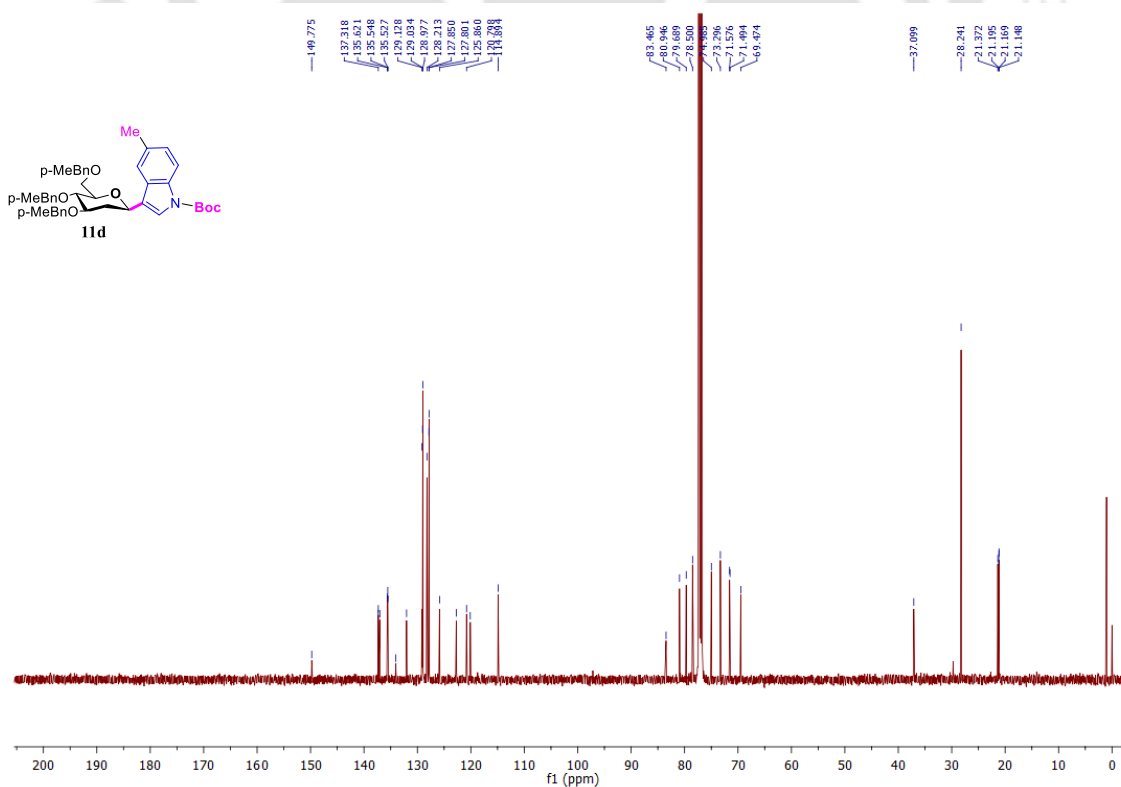
The spectrum shows a complex pattern of peaks, with a prominent cluster of signals between 120 and 140 ppm, and a distinct set of signals in the aliphatic region (10-30 ppm).

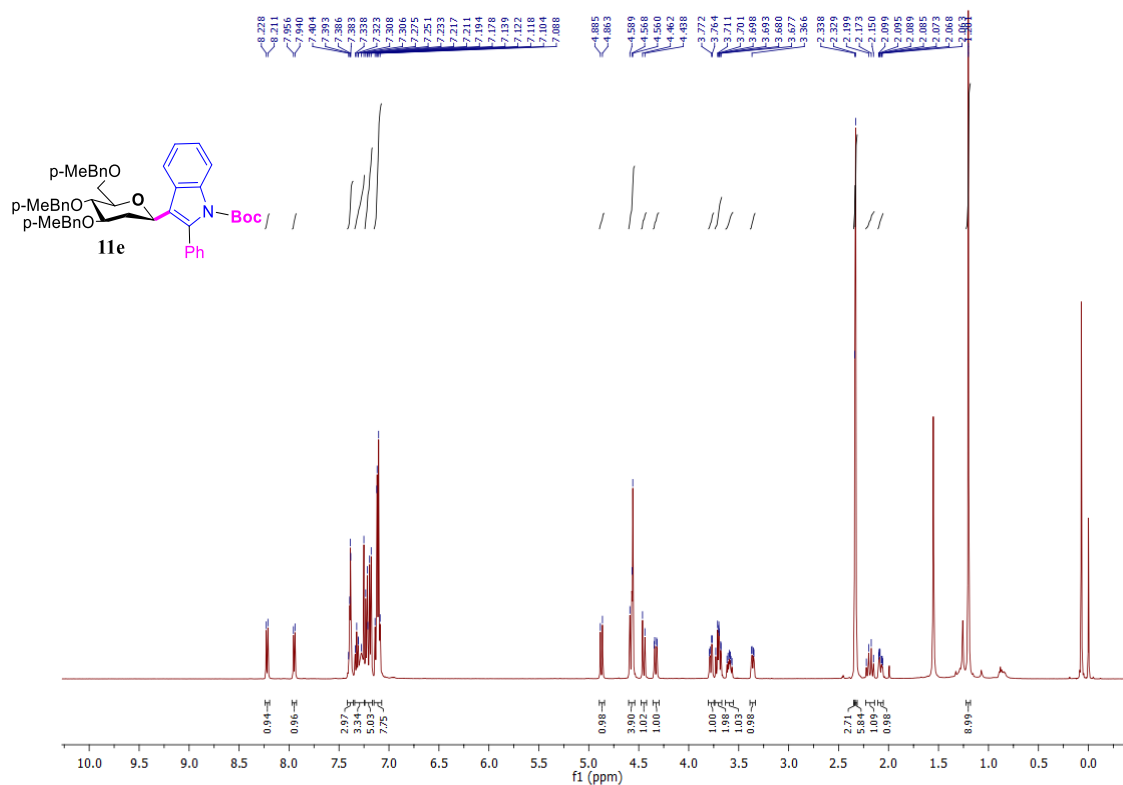
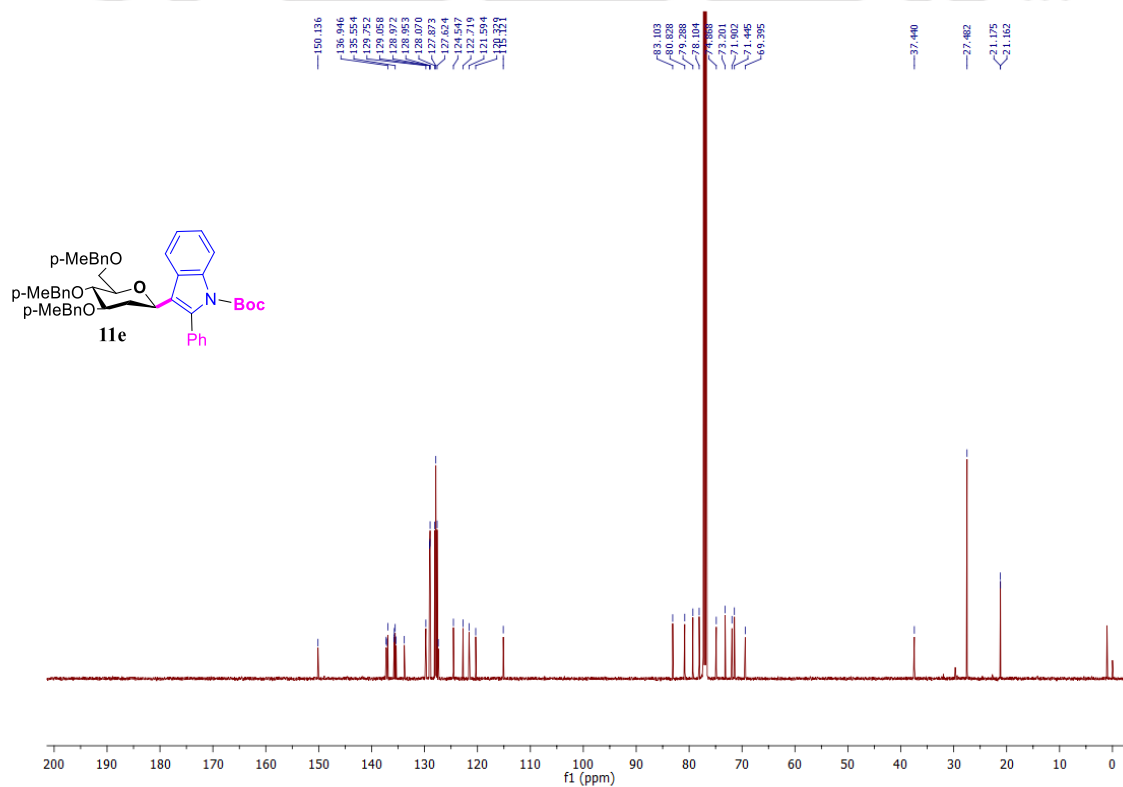
¹H NMR spectrum of compound 11a (500 MHz, CDCl₃):



$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 11a (500 MHz, CDCl_3):



^1H NMR spectrum of compound 11d (500 MHz, CDCl_3): **$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 11d (500 MHz, CDCl_3):**

^1H NMR spectrum of compound 11e (500 MHz, CDCl_3): **$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 11e (500 MHz, CDCl_3):**

Chemical structure of 11f: COc1ccc2c(c1)c(c3ccccc3O[C@H]2C(=O)OC(=O)c4ccccc4)OC(=O)c5ccccc5

¹H NMR spectrum (CDCl₃):

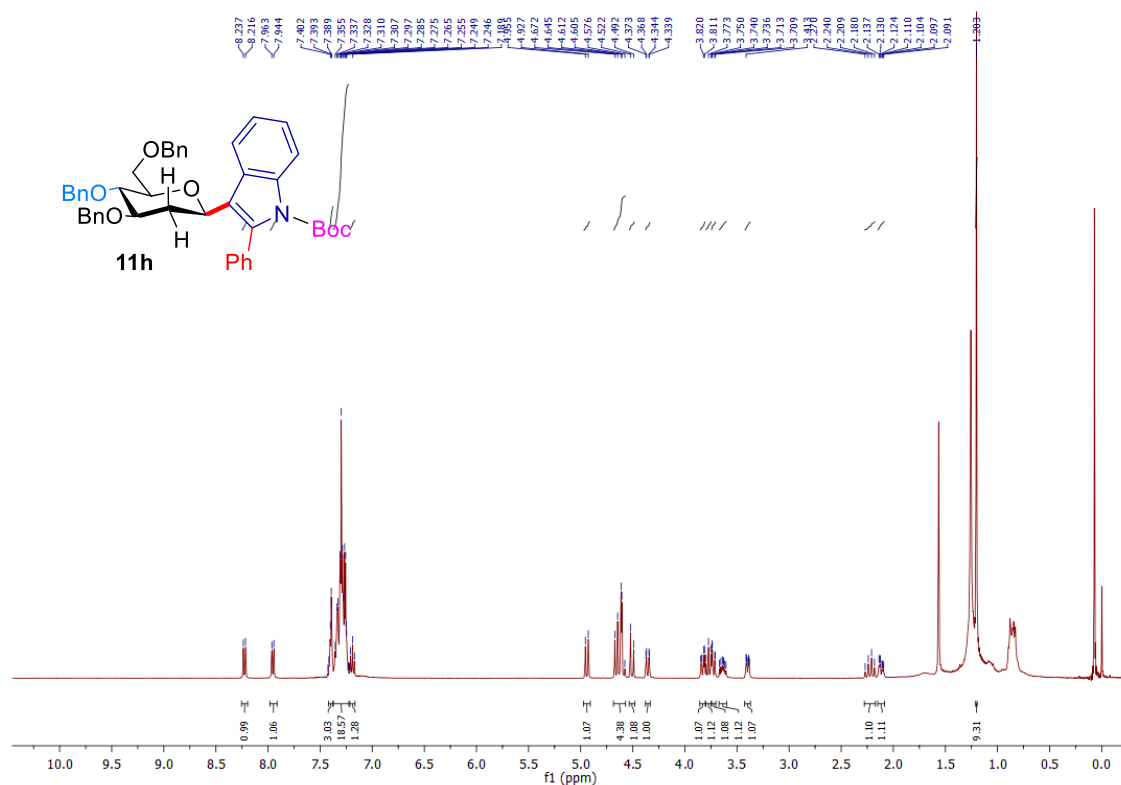
- Chemical shifts (ppm):** 8.023, 7.462, 7.385, 7.366, 7.355, 7.340, 7.334, 7.320, 7.306, 7.288, 7.280, 7.269, 7.255, 7.155, 7.151, 7.081, 6.969, 6.909, 6.891, 6.891, 6.878, 6.878, 5.193, 5.173, 5.170, 4.998, 4.976, 4.956, 4.954, 4.954, 4.859, 4.733, 4.728, 4.706, 4.684, 4.684, 4.674, 4.663, 4.659, 4.646, 4.623, 4.597, 4.556, 4.549, 4.531, 4.515, 3.993, 3.983, 3.887, 3.872, 3.855, 3.855, 3.852, 3.852, 3.834, 3.816, 3.807, 3.798, 3.798, 3.788, 3.769, 3.766, 3.714, 3.682, 3.658, 3.658, 3.648, 3.607, 3.591, 3.591, 2.338, 2.334, 2.324, 2.317, 2.313, 2.313, 2.307, 1.995, 1.973, 1.893, 1.655, 1.648.
- Integration values:** 0.34, 1.16, 1.74, 26.92, 0.46, 0.03, 0.03, 0.43, 1.41, 0.42, 1.00, 1.71, 0.41, 1.15, 1.43, 3.52, 1.39, 1.01, 6.73, 0.92, 1.10, 2.43, 1.05, 0.77, 1.06, 0.97, 1.13, 11.20.

11f

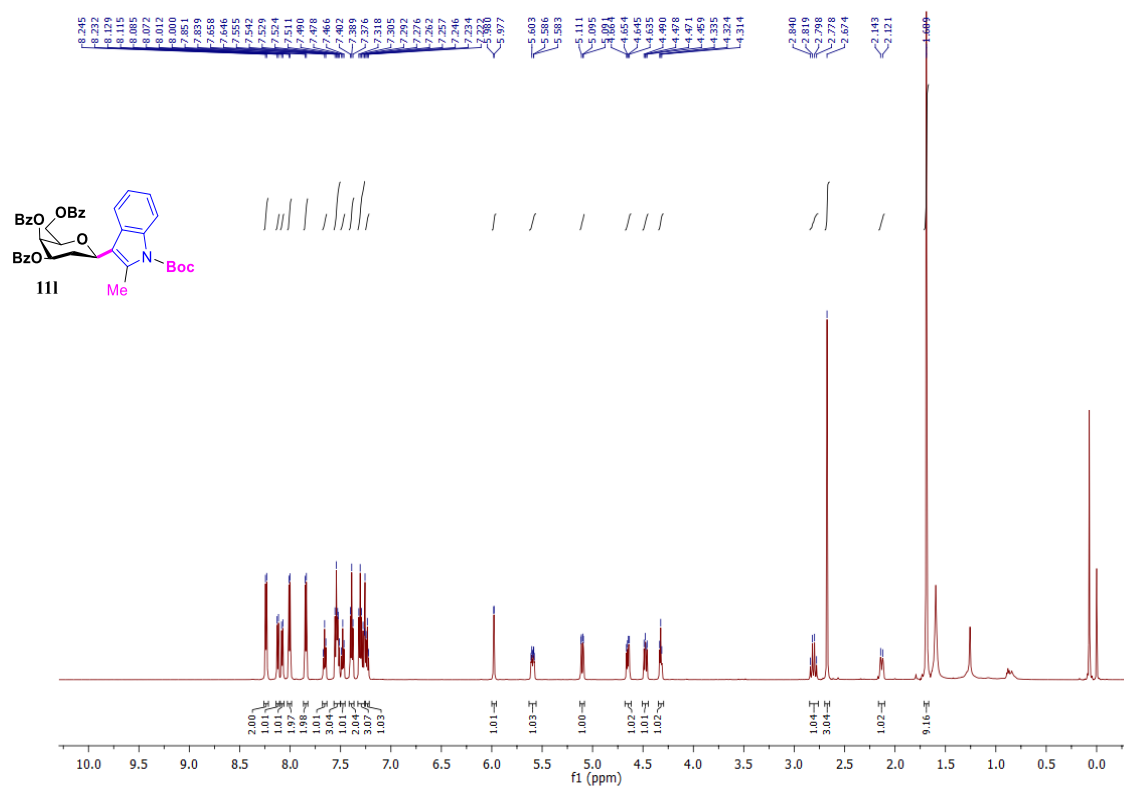
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127.553
127.522
127.383
127.372
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108.798
108.371
81.404
79.209
78.734
78.646
75.146
75.136
73.414
73.356
73.346
72.095
71.345
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55.748
37.164
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28.251
28.179

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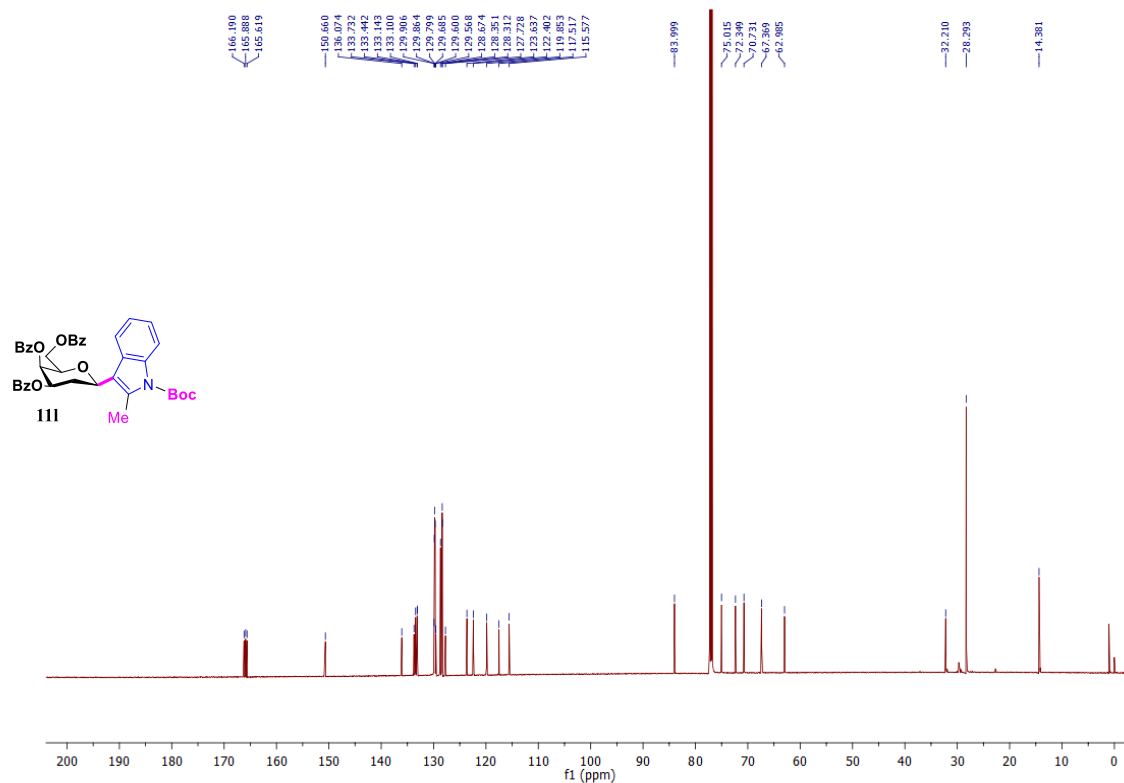
f1 (ppm)

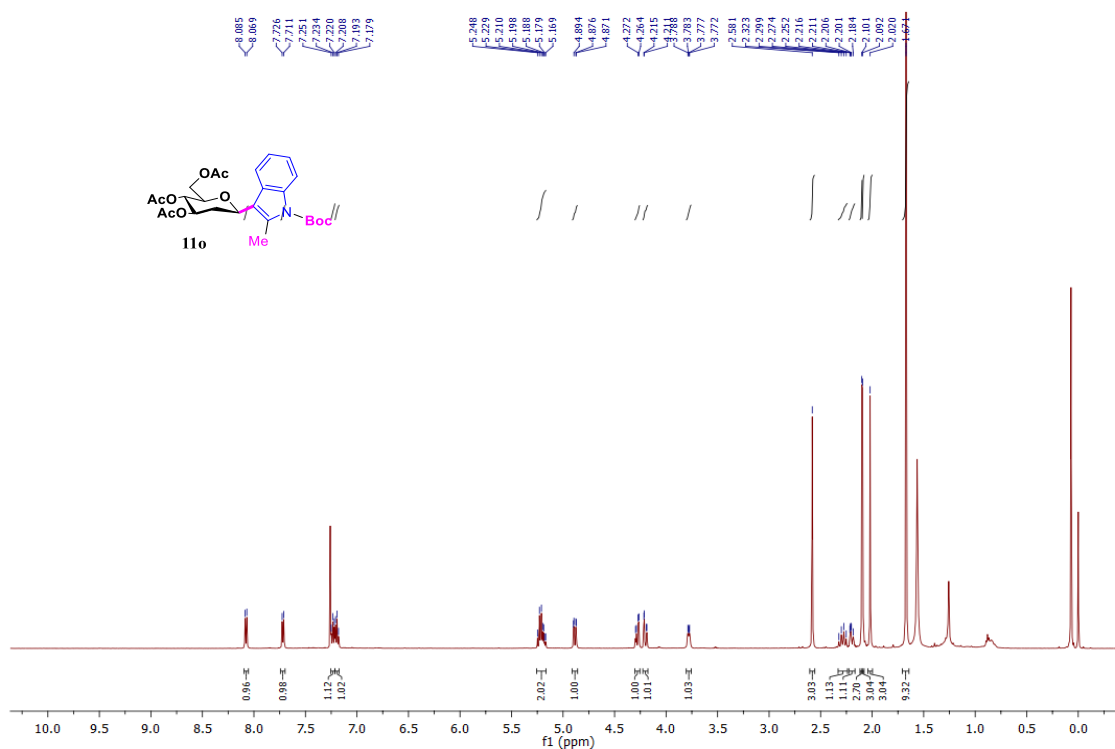
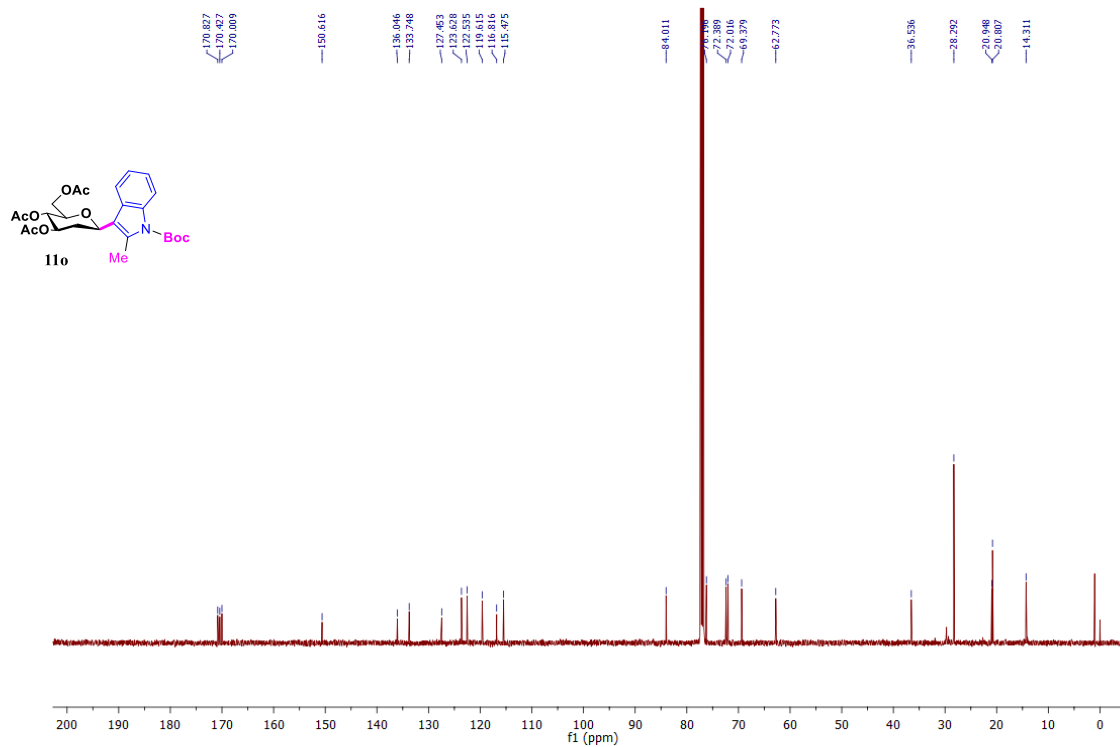
^1H NMR spectrum of compound 11h (400 MHz, CDCl_3):

¹H NMR spectrum of compound 11l (600 MHz, CDCl₃):



$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 11l (600 MHz, CDCl_3):

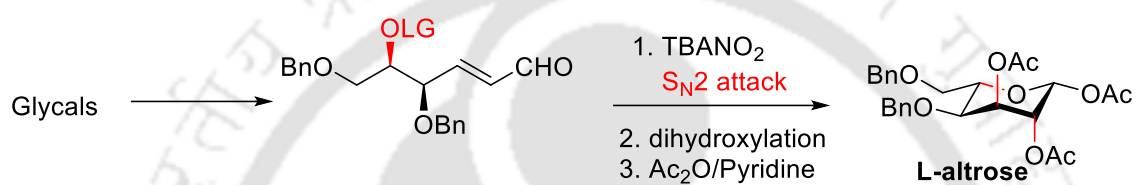


^1H NMR spectrum of compound 11o (500 MHz, CDCl_3): **$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 11o (500 MHz, CDCl_3):**

The Supporting Information of Chapter III is available at
<https://pubs.acs.org/doi/10.1021/acs.joc.2c02426>

Chapter IV

Three Step Synthesis of Protected L-Altrose from D-Galactose Derived Perlin Aldehyde





5.1.1 Introduction

L-Sugars,¹ unlike their enantiomers, the D-sugars, are rare² but are biologically important and play significant roles in nature. Some of these rare L-sugars find their use in the synthesis of low-calorie sweeteners,³ immunosuppressive agents,⁴ antiviral^{5,6} compounds, and also as chiral building blocks in the synthesis of natural products.^{7,8} Some of these L-hexoses are a part of various antibiotics,^{9,10} terpene glycosides, and also clinically important oligosaccharides like heparin (**1c**, figure 1).¹¹ L-Guluronic acid containing anionic polysaccharide alginates **1a** was discovered in the cell walls of brown algae, and some bacterial species.¹² Due to the presence of acid functionality in alginates, it can bind to metal, resulting in gels that can be used for multiple purposes e.g. healthcare (wound gels) and the food industry (beer foam), etc.

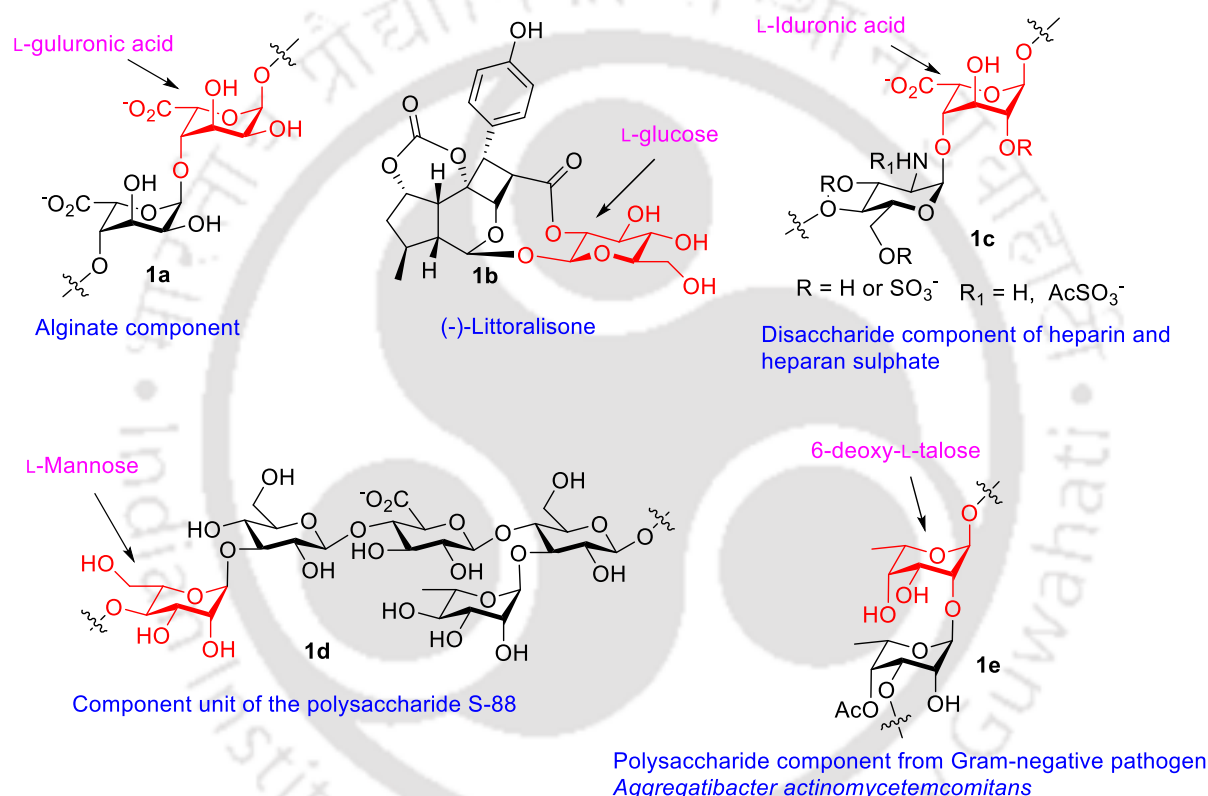


Figure 1: L-sugar containing bioactive molecules

L-glucoside containing Littoralisone **1b** (Figure 1) has been found in *Verbena littoralis*. Generally, it is used as a folk medicine^{13,14} and it actively participates to increase nerve growth factor (NGF) induced neurite outgrowth from PC12D cells. L-Mannose containing capsular polysaccharides S-88 (**1d**, Figure 1) from *Sphingomonas* are used in the industry as gelling agents.¹⁵ It has been discovered that the lipopolysaccharide of the Gram-negative bacteria *Actinobacillus actinomycetemcomitans* serotype c contains the 6-deoxy-L-talose (**1e**, Figure 1).¹⁶

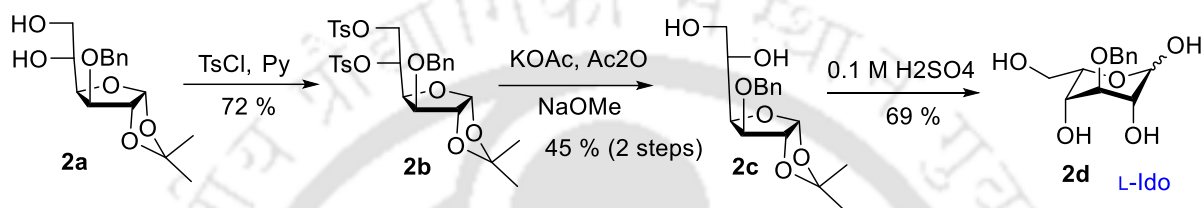
5.1.2 Literature review on L-Sugar

Commercially available L-sugars are hugely expensive. For example, the cost of L-altrose,¹ a constituent of the extracellular polysaccharides from *Butyrivibrio fibrisolvens* strain CF3 is

\$11550 for 10 g and hence, the research on the interconversion of the commercially cheap D-sugars to L-sugars has gained continuous attention in carbohydrate chemistry.

5.1.2.1 C-5 Epimerizations

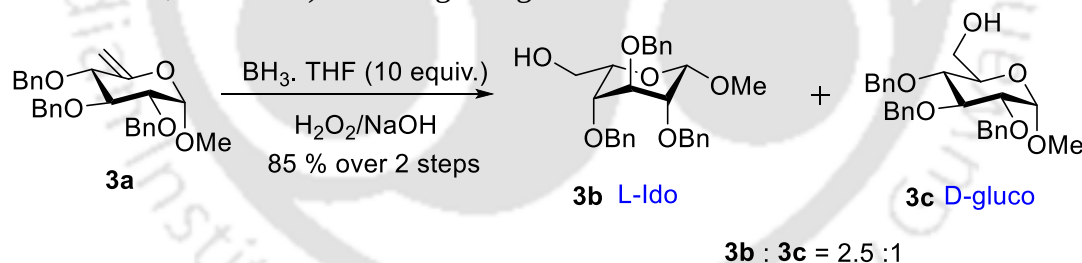
One of the oldest methods is C-5 epimerization technique for L-sugars synthesis. Generally, D-sugars have been utilized as a starting material for L-sugars synthesis. It was reported that D-glucose and D-mannose were converted to L-idose¹⁷⁻²⁰ and L-gulose²¹⁻²², respectively through C-5 epimerization. In 1976, Wyss and co-workers developed the synthetic procedure of L-iodose from D-glucose.¹⁹ The 5,6-di-O-sulfonyl D-glucofuranose **2b** was converted to the compound **2c** via acetate mediated double substitution which was converted to L-iodose (**2d**) after acid hydrolysis (Scheme 1).



Scheme 1: Synthesis of L-Idose

5.1.2.2 L-Sugars from Alkene-based Carbohydrates

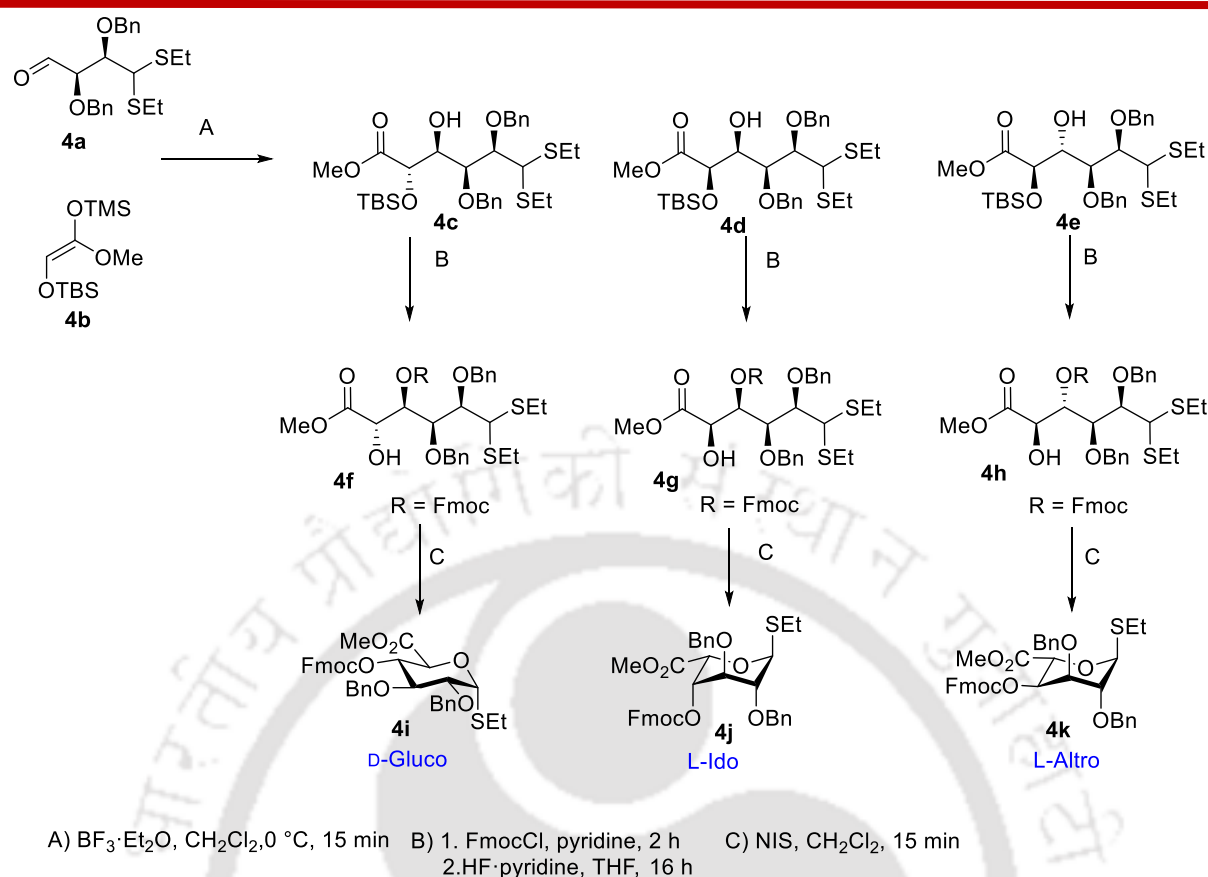
One of the alternative methods is the stereoselective hydroboration of exocyclic alkenes for L-sugars synthesis. The treatment of 6-deoxyhalo compounds with silver fluoride in pyridine leads to the corresponding exocyclic alkenes derivatives.²³ Interestingly, diborane addition to an exocyclic alkene **3a** afforded a mixture of methyl L-idoside **3b** and D-glucoside **3c** (**3b**:**3c** = 2.5:1, Scheme 2) favouring L-sugar.



Scheme 2: Hydroboration of Exocyclic Alkenes

5.1.2.3 Addition to Carbohydrate Aldehydes

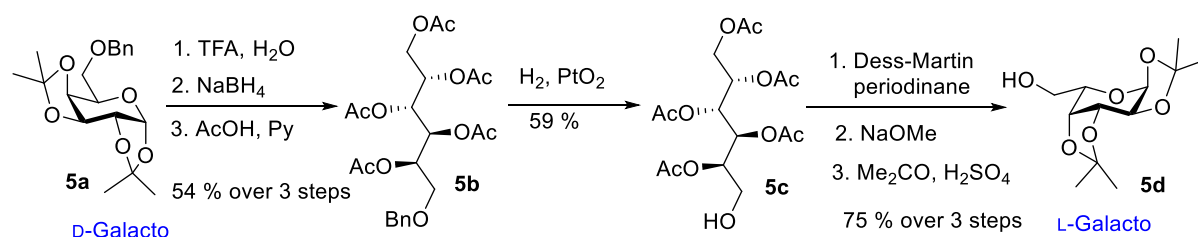
Chain elongation technology have been applied to synthesize L-hexoses. Seeberger and co-workers performed Mukaiyama-type aldol reaction by utilizing $\text{BF}_3 \cdot \text{OEt}_2$ as a Lewis acid taking L-arabinose derived dithioacetal-containing aldehyde (**4a**) and silyl enol ether (**4b**), afforded a mixture of D-glucuronic acid (**4c**), L-idouronic acid (**4d**), and L-altouronic acid (**4e**) with the ratio 1:1:1. After that, the treatment with FmocCl in pyridine followed by HF-Pyridine resulted in the compounds **4f**, **4g** and **4h** respectively. Finally, NIS promoted cyclization resulted in thioacetalated D-glucose (**4i**), L-idose (**4j**) and L-altrose (**4k**) (Scheme 3).²⁴



Scheme 3: Mukaiyama Aldol Addition

5.1.2.4 Head-to-Tail Inversion

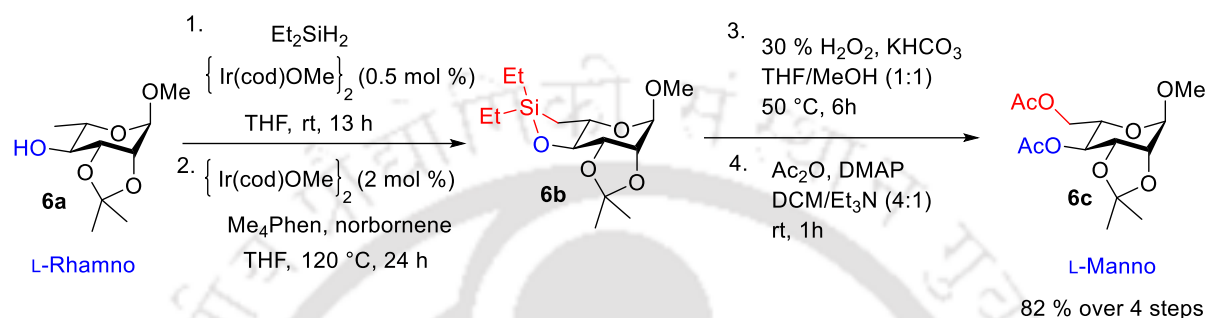
One of the familiar methods for the synthesis of L-sugars is Head-to-Tail Inversion. Traditionally in Fischer projection D-hexoses contain C-2 -OH at right hand side. There is an exchange of oxidation state between C-1 & C-6 that will turn C-2 into new C-5 for L-hexoses. During the conversion of D-hexoses to L-hexoses, the anomeric C-1 will be converted to alcohol by reduction and C-6 will be transformed to aldehyde by oxidation. Galactose derived compound **5a** was converted to galactitol derivative **5b** by the removal of isopropylidene groups followed by reduction and peracetylation of the remaining free -OH groups. Then debenzoylation protocol was applied utilizing Adam's catalyst to synthesize alcoholic compound **5c**. The alcoholic compound **5c** was converted to L-Galactose derivative **5d**, via Dess–Martin oxidation of the 6-OH group, subsequent deacetylation followed by acetonide protection (Scheme 4).²⁵



Scheme 4: Synthesis of L-galacto from D-galacto utilizing Head-to-Tail Inversion method

5.1.2.5 Synthesis of L-sugars using C–H Activation method

It was reported that commercially available 6-deoxy-L-sugars can be converted to L-hexoses utilizing C–H activation method.²⁶ Bols and co-workers applied this methodology for the synthesis of methyl L-mannoside (**6c**) from L-rhamnoside (**6a**). Silylation followed by C–H activation of the L-rhamnoside **6a** by using iridium catalyst afforded oxasiloxane **6b**. The compound **6b** was converted to methyl L-mannoside **6c** via Fleming–Tamao oxidation followed by acetylation with 82 % yields over 4 steps (Scheme 5).²⁷



Scheme 5: Synthesis of Methyl L-Mannoside using C–H Activation method

5.2 This work

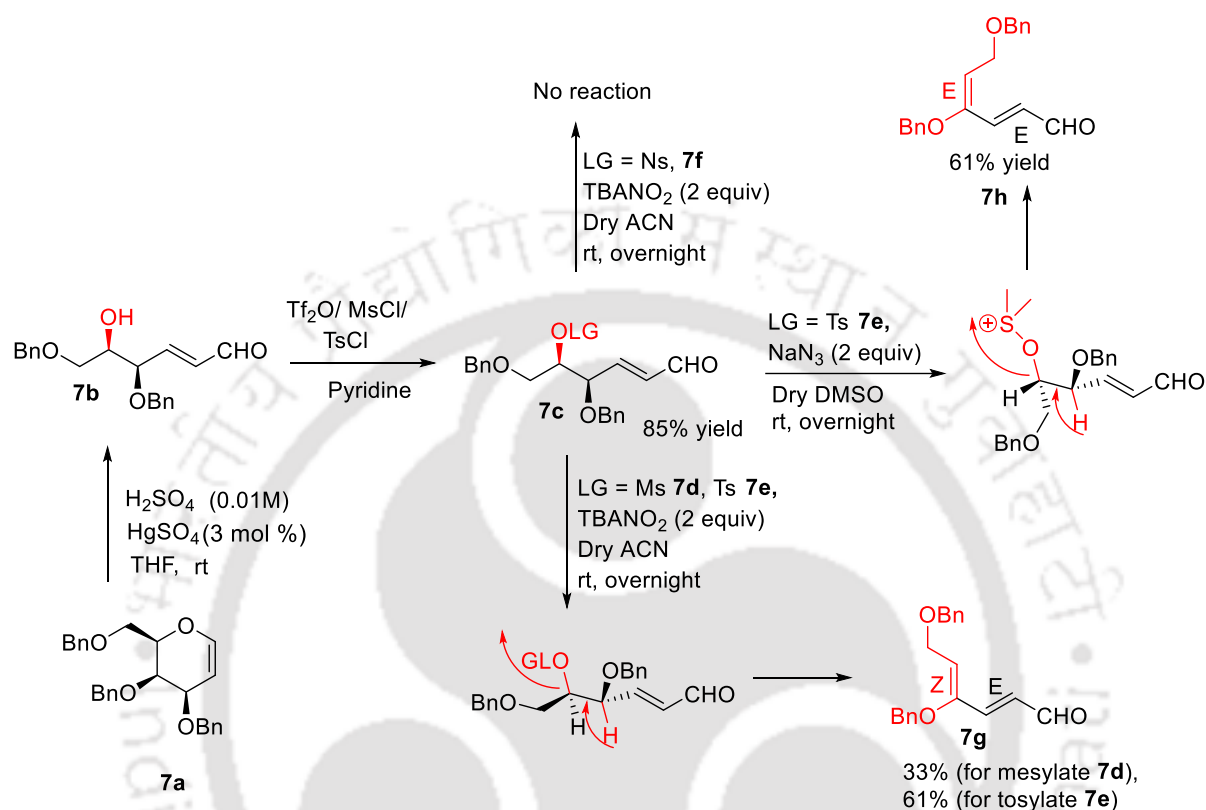
Most of these methods suffer from the drawbacks of metal catalysis, multi-step reaction sequences, usage of auxiliaries and delicate reaction conditions. Herein, we report a proof of concept for a short synthetic route towards the synthesis of L-sugars via the synthesis of L-altrose,^{28–30} one of the most expensive L-sugars. The synthesis has been achieved via Perlin aldehyde, an easily accessible synthetic intermediate from commercially available glycals.

Perlin aldehydes with a high degree of functionality a) two well defined chiral centers, b) an unprotected alcohol and c) an α,β -unsaturated system for further functionalization, have been attractive chiral pool synthons in organic chemistry. Ever since its first discovery by A.S. Perlin in 1975,³¹ these Perlin aldehydes have been used in the total synthesis of several natural products. Perlin aldehydes are easily accessible from the corresponding glycals in a single step. Treatment of the glycals with Hg_2SO_4 in THF and 0.01(M) H_2SO_4 at room temperature provides the corresponding Perlin aldehydes in almost quantitative yields. Non-mercurial Lewis acids have also been employed for the synthesis of these aldehydes although at elevated temperatures. Though Perlin aldehydes have been utilized in the synthesis of various natural products, the synthetic potential of these chirally rich synthons has not been utilized for the synthesis of L-sugars. We envisaged that the stereo-inversion of the free hydroxyl group followed by simple dihydroxylation would lead to the synthesis of L-sugars. However, the approach poses a significant synthetic challenge as these compounds can undergo an E2 elimination process leading to a stable conjugate double bond with the already existing α,β -unsaturated aldehyde.

Here in this report, we present our initial reports of this three-step strategy towards the synthesis of protected L-sugars from Perlin-aldehydes **7b** and also some of the interesting observations that were made in the process of achieving the target.

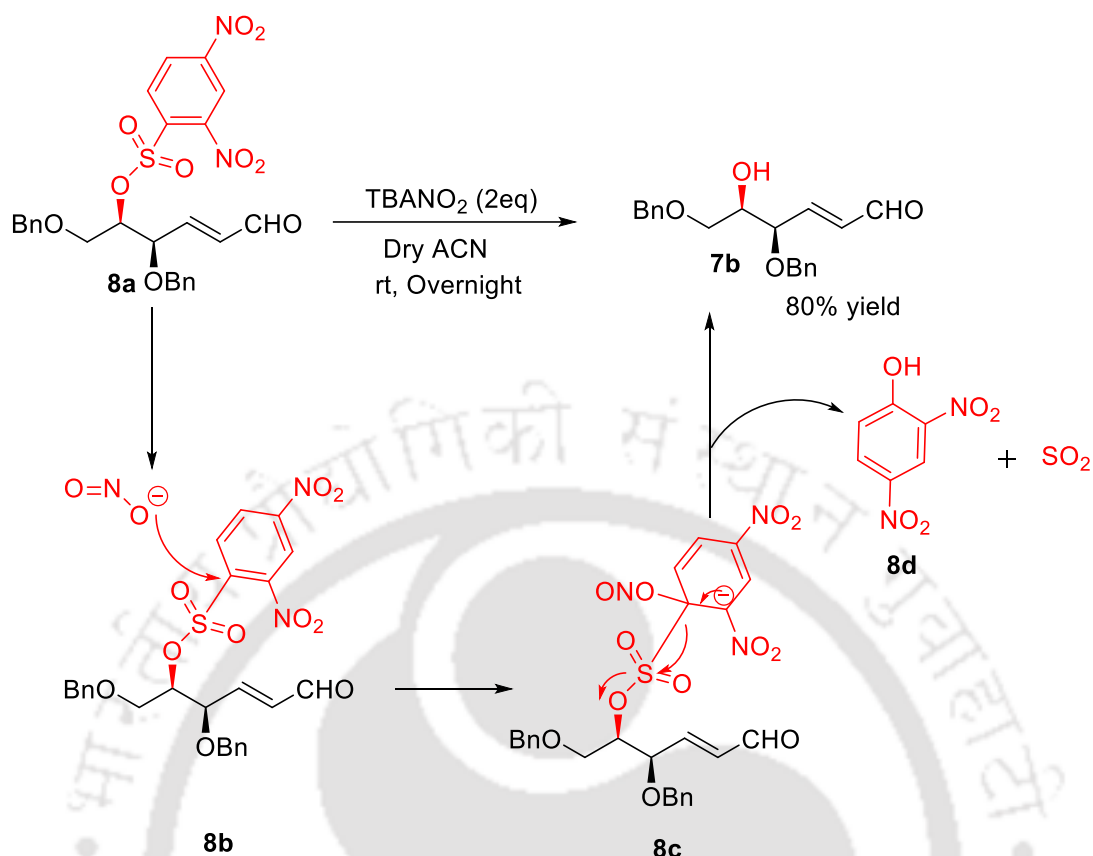
5.2.1 Initial approach

Our initial attempts started with the synthesis of Perlin aldehydes **7b** with various leaving groups at the C-5 position. The D-galactose derived Perlin aldehyde **7b** was chosen for this study.

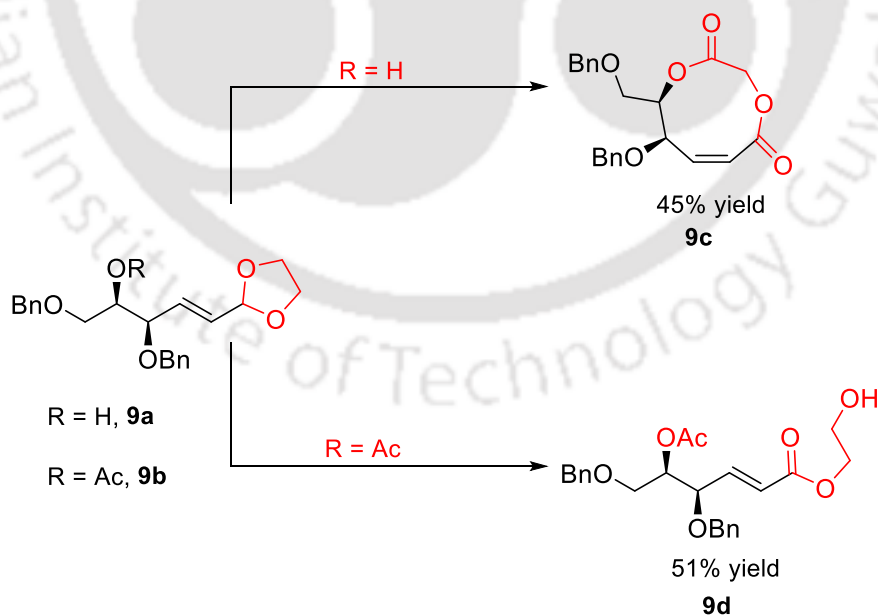


Scheme 6. Synthesis of Perlin aldehyde derivatives

Hence, the galactose derived Perlin aldehyde **7b** has been treated with mesyl chloride in the presence of pyridine that led to the formation of the corresponding mesylate **7d** in 73 % yield. Similarly, the corresponding tosylate **7e**, nosylate **7f**, 2,4-dinitrotosylate **8a** and triflate **10a** compounds have also been successfully synthesized by treating the alcohol **7b** under the respective conditions (refer to the *experimental section* for details). We then subjected the mesylate compound **7d** for the stereo-inversion by reacting with tetrabutylammonium nitrite (TBANO₂) nucleophile in order to obtain the inverted alcoholic group. However, to our surprise, the isolated compound was observed to be an *E,Z*-dienal **7g**, promoted via the E2 elimination in 33 % (Scheme 6). Similarly, the tosylate compound **7e**, when subjected to similar reaction conditions, also led to the formation of the eliminated compound **7g** in moderate yield of 61 % (Scheme 6). Interestingly, when the reaction was performed in DMSO as a solvent instead of acetonitrile and NaN₃ as nucleophile, *E,E*-diene **7h** has been obtained (Scheme 6). The change in stereochemistry of the olefinic product obtained can be attributed to the S_N2 attack of DMSO followed by E2 elimination reaction. The nosylated compound **7f**, when treated with TBANO₂, did not lead to any conversion. An intriguing observation has been made when 2,4-dinitrobenzenesulfonyl group has been used as a possible sulfonate **8a** and treated with TBANO₂ as a nucleophile, we have obtained the alcohol **7b** as the product, however,



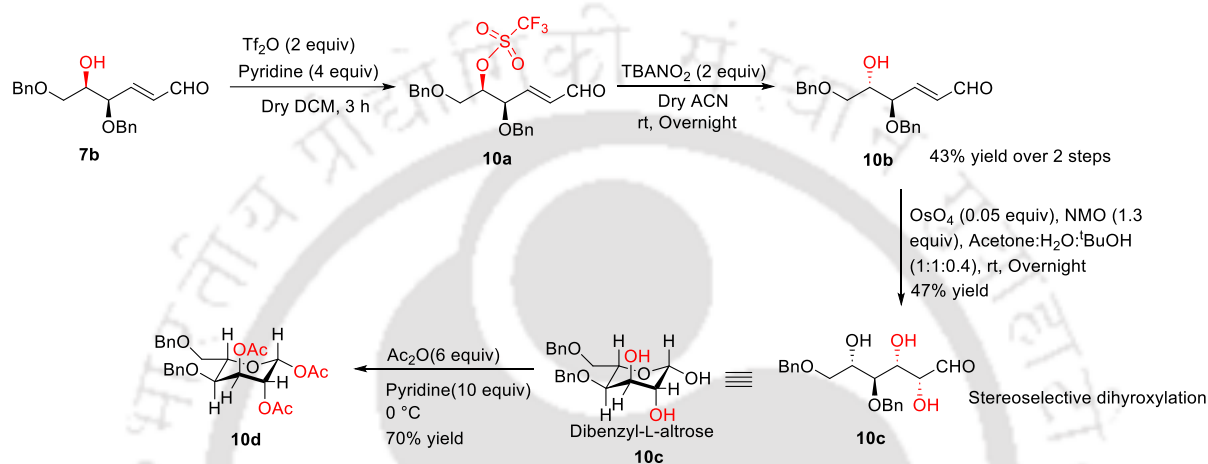
Scheme 7: Unusual behaviour of 2,4-dinitrosulfonate.



Scheme 8: Oxone mediated oxidation

surprisingly with a stereo-retention instead of stereo-inversion. This phenomenon can be explained by an *ipso* attack of the nucleophile at the C-S bond followed by the elimination of sulfur dioxide giving rise to the stereo-retentive alcoholic product **7b** along with 2,4-dinitrophenol **8d** as a byproduct (Scheme 7). This observation is in accordance with a recent observation reported by Mandal and coworkers³² and has been explored in a C-N bond forming reaction. Attempts to form an epoxide utilising oxone on the acetal-protected aldehydes **9a** and **9b** gave rise to allylic oxidation products **9c** and **9d** respectively (Scheme 8).

5.2.2 Synthesis of L-altrose

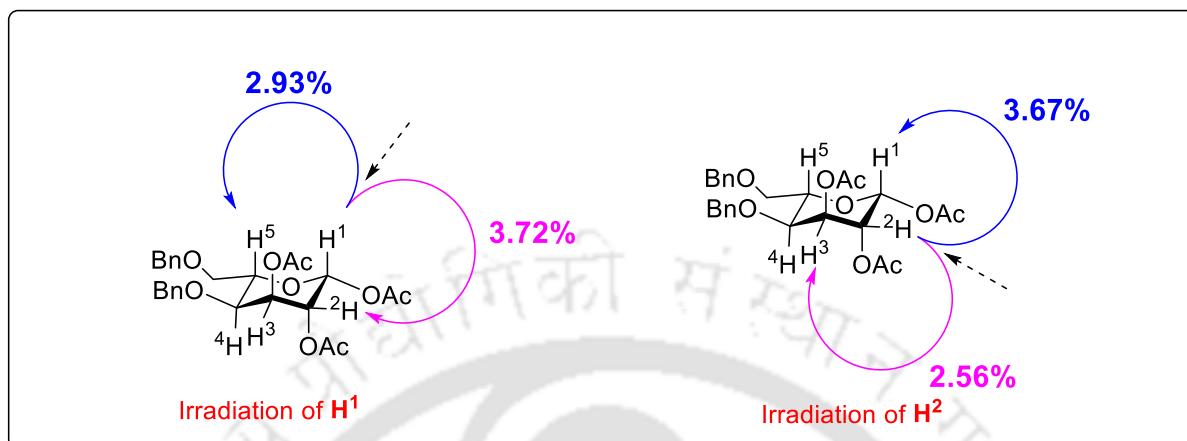


Scheme 9: Synthetic route of L-altrose

After many failed attempts with various leaving groups, we decided to test trifluoromethanesulfonate (triflate) as a leaving group having greater nucleofugal ability for the current desired transformation. Hence, the corresponding triflate has been made by treating the alcohol **7b** under Tf_2O /pyridine conditions that led to the formation of the desired compound **10a**. The crude triflate compound **10a** when treated with TBANO_2 , underwent a smooth $\text{S}_{\text{N}}2$ inversion and yielded the compound **10b**, a precursor of L-sugars in 43 % overall yield over two steps. The product was confirmed by the disappearance of signals corresponding to the H-4 & H-5 at 4.29 and 3.87 ppm respectively in the D-isomer (**7b**) and appearance of signals at 4.12 and 3.84 ppm respectively for the L-isomer (**10b**) in ^1H NMR spectrum indicating the inversion of the stereocenter. The unique nature of the triflate group, despite being a better nucleofuge than the tosylate **7e** and mesylate **7d** did not undergo the competitive E2 elimination but provided the desired inversion of the stereocenter leading to the L-sugars **10b**. Next, treatment of the resultant unprotected alcohol **10b** with OsO_4 resulted in a stereoselective dihydroxylation reaction presumably controlled by the C-4 O-benzyl protecting group giving rise to L-altrose **10c**. The compound **10c** has also been characterized as a triacetate **10d**, after the acetylation under the standard conditions of Ac_2O /pyridine (Scheme 9).

From nOe experiment, upon irradiation of anomeric proton (α -isomer) H^1 , enhancement was observed in the signals corresponding to H^2 (3.72 % w.r.t. H^1) and H^5 (2.93 % w.r.t. H^1) which indicates that H^1 is in *cis* relation with both H^2 and H^5 . Similarly, irradiation of H^2 led to a substantial enhancement of H^1 (3.67 % w.r.t. H^2) and weak enhancement of H^3

(2.56 % w.r.t. H^2) thus confirming the di-equatorial relation of H^2 & H^3 . Besides, the coupling constants of H^1 ($J = 1.6$ Hz), H^2 ($J = 1.6$ Hz, 4.7 Hz), H^3 ($J = 4.5$ Hz, 3.3 Hz), and H^4 ($J = 8.9$ Hz, 3.1 Hz), also reveal the stereochemical relation of these protons. Based on these experiments, the structure has been identified as L-altrose (Scheme 10).



Scheme 10: nOe experiment

5.2.3 Conclusion

In conclusion, we have developed a very practical, short, three-step synthesis of L-altrose from Perlin aldehydes that are easily accessible from the commercially available glycals via the stereo-inversion of the Perlin aldehyde derived triflate followed by the dihydroxylation. Also, the ability of various leaving groups towards the stereo-inversion has been discussed. An interesting observation of the 2,4-dinitrosulfonate esters undergoing *ipso* substitution has also been discussed. The strategy has the potential for the synthesis of all the possible eight L-sugars and will be pursued in due course.

5.3 Experimental Section

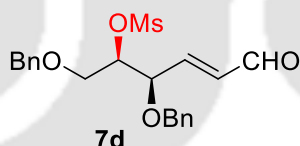
General Information

All solvents purchased were of commercial grade and reagents were purchased from Sigma-Aldrich, Merck, TCI, Carbosynth, Spectrochem, Alfa Aesar, Avra and used without further purification for reactions.

Analysis

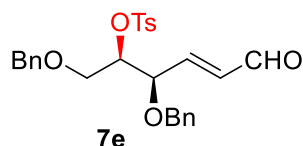
Reactions were monitored by TLC on Kieselgel 60 F254 (Merck). Detection was done by examination under UV light (254 nm) and by charring with 10 % sulfuric acid in water. Purification was performed by both Ultra High-Performance Liquid Chromatography (UHPLC) using column [Particle size: (μ) 12, Dim: (mm) 250 x 10] in reverse phase and in normal phase using silica gel [Merck, 60-120 mesh] and Flash column chromatography (Combiflash (R) NextGen 300). Extracts were concentrated in vacuo using both Büchi rotary evaporator (bath temperatures up to 40 °C) at a pressure of either 15 mmHg (diaphragm pump) and 0.7 mmHg (oil pump), at rt. ^1H and ^{13}C NMR were recorded on a Bruker 600 MHz, and 400 MHz spectrometer using CDCl_3 as solvent. Chemical shift values are reported in ppm with the solvent as the internal standard (CDCl_3 : δ 7.26 for ^1H , δ 77.16 for ^{13}C). Data are reported as follows: chemical shifts (δ), multiplicity (s = singlet, d = doublet, dd = doublet of doublet, ddd = doublet of doublet of doublets, dt = doublet of triplet, t = triplet, q = quartet, m = multiplet, bs = broad singlet) etc., coupling constants J (Hz), and integration. High-resolution mass measurements were performed using Agilent technologies mass spectrometer (QTOF-ESI mode). For heating purpose, silicon oil baths were used. Compound **7b** were synthesized following reported procedure.³¹

Synthesis of (2R,3R,E)-1,3-bis(benzyloxy)-6-oxohex-4-en-2-yl methane sulfonate (**7d**)



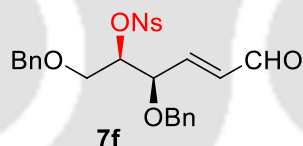
To a solution of benzyl-protected perlin (0.2 g, 0.61 mmol) in dry DCM, pyridine (98 μl , 1.22 mmol) was added followed by mesyl chloride (0.12 ml, 1.22 mmol) at 0 °C. The mixture was stirred for 3 h at room temperature under nitrogen atmosphere. After completion, ice cooled water was added to freeze the reaction, extracted with ethyl acetate (3 x 40 ml). The combined organic layers were washed with brine, dried over Na_2SO_4 , concentrated under reduced pressure. The crude residue was purified through flash chromatography to afford white solid **7d**. R_f = 0.6 (40 % ethyl acetate in hexane), yield = 73 %. Spectroscopic data were matched with reported value.³³ ^1H NMR (600 MHz, CDCl_3) δ 9.48 (d, J = 7.8 Hz, 1H), 7.35 – 7.15 (m, 10H), 6.65 (dd, J = 15.8, 5.3 Hz, 1H), 6.32 (ddd, J = 15.8, 7.8, 1.2 Hz, 1H), 4.75 (td, J = 6.3, 3.0 Hz, 1H), 4.55 (d, J = 11.6 Hz, 1H), 4.47 (d, J = 11.7 Hz, 1H), 4.41 – 4.37 (m, 3H), 3.65 (dd, J = 11.1, 3.0 Hz, 1H), 3.55 (dd, J = 11.1, 6.6 Hz, 1H), 2.90 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 193.3, 153.1, 147.7, 137.8, 136.4, 129.0, 128.7, 128.5, 128.3, 128.2, 128.0, 126.3, 74.7, 72.8, 64.6, 31.6.

Synthesis of (2R,3R,E)-1,3-bis(benzyloxy)-6-oxohex-4-en-2-yl 4-methylbenzenesulfonate (7e)



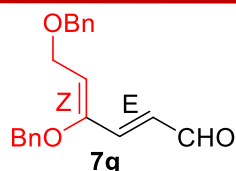
To a solution of benzyl-protected perlin (0.2 g, 0.61 mmol) in dry DCM, pyridine (98 μ l, 1.22 mmol) was added followed by tosyl chloride (0.35 g, 1.82 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 4 h under nitrogen atmosphere. After completion of the reaction, ice cooled water was added to freeze the reaction. The reaction mixture was extracted with DCM (3x40 ml). The combined organic layers were washed with brine, dried over Na_2SO_4 , concentrated under reduced pressure. The crude reaction mixture was purified by Flash chromatography to afford colourless liquid **7e**. R_f = 0.6 (30 % ethyl acetate in hexane), yield = 78 %. ^1H NMR (600 MHz, CDCl_3) δ 9.38 (d, J = 7.9 Hz, 1H), 7.72 (d, J = 8.2 Hz, 2H), 7.34 – 7.26 (m, 6H), 7.23 – 7.16 (m, 6H), 6.59 (dd, J = 15.8, 5.4 Hz, 1H), 6.27 – 6.22 (m, 1H), 4.67 (q, J = 5.0 Hz, 1H), 4.55 (d, J = 11.7 Hz, 1H), 4.44 (dd, J = 7.1, 2.9 Hz, 1H), 4.41 (d, J = 3.8 Hz, 1H), 4.39 (d, J = 3.9 Hz, 1H), 4.34 (d, J = 11.8 Hz, 1H), 3.73 (dd, J = 10.6, 4.8 Hz, 1H), 3.56 (dd, J = 10.6, 5.6 Hz, 1H), 2.37 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 192.7, 151.1, 144.0, 137.2, 136.8, 133.9, 133.2, 129.7, 128.5, 128.4, 128.1, 128.0, 127.9, 127.9, 127.8, 80.4, 76.3, 73.4, 72.4, 67.8, 21.6.

Synthesis of (2R,3R,E)-1,3-bis(benzyloxy)-6-oxohex-4-en-2-yl 4-nitrobenzenesulfonate (7f)



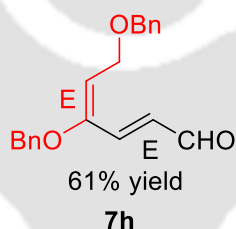
To a solution of benzyl-protected perlin (0.2 g, 0.61 mmol) in dry DCM, pyridine (98 μ l, 1.22 mmol) was added, followed by 4-nitrobenzenesulfonyl chloride (0.27 g, 1.22 mmol) at 0 °C. The reaction mixture was stirred for 5 h at room temperature under nitrogen atmosphere. After completion of the reaction, ice cooled water was added to freeze the reaction. The reaction mixture was extracted by DCM (3x40 ml). The combined organic layers were washed with brine, concentrated under reduced pressure. The crude mixture was purified by Flash chromatography to afford colourless liquid **7f**. R_f = 0.45 (20 % ethyl acetate in hexane), yield = 75 %. ^1H NMR (600 MHz, CDCl_3) δ 9.55 (d, J = 7.7 Hz, 1H), 8.01 (d, J = 8.9 Hz, 2H), 7.94 (d, J = 8.9 Hz, 2H), 7.34 – 7.30 (m, 6H), 7.22 – 7.19 (m, 2H), 7.14 – 7.11 (m, 2H), 6.70 (dd, J = 15.8, 5.4 Hz, 1H), 6.38 (ddd, J = 15.8, 7.7, 1.1 Hz, 1H), 4.79 (td, J = 6.1, 3.0 Hz, 1H), 4.58 (d, J = 11.5 Hz, 1H), 4.48 (dd, J = 7.8, 3.3 Hz, 1H), 4.38 (dd, J = 22.1, 11.4 Hz, 2H), 4.26 (d, J = 11.4 Hz, 1H), 3.71 (dd, J = 11.2, 2.9 Hz, 1H), 3.54 (dd, J = 11.2, 6.3 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 192.5, 150.4, 149.7, 141.9, 136.7, 136.5, 134.6, 129.2, 128.6, 128.5, 128.4, 128.3, 127.9, 127.9, 123.9, 82.5, 76.8, 73.6, 72.5, 68.3.

Synthesis of (2E,4Z)-4,6-bis(benzyloxy)hexa-2,4-dienal (7g)



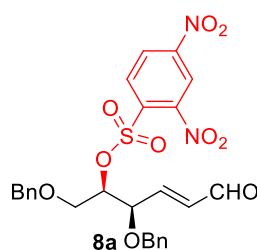
To a solution of compound **7d**, **7e** (0.1 g, 0.25 mmol) in dry ACN, TBANO₂ was added at rt. The mixture was stirred for overnight under nitrogen atmosphere. After completion, water was added to freeze the reaction, extracted with ethyl acetate (3 x 40 ml). The combined organic layers were washed with brine, dried over Na₂SO₄, concentrated under reduced pressure. The crude residue was purified through flash chromatography to afford colorless liquid **7g**. *R*_f = 0.7 (30 % ethyl acetate in hexane), yield = 33 %. Spectroscopic data were matched with reported value.³³ ¹H NMR (600 MHz, CDCl₃) δ 9.64 (d, *J* = 7.9 Hz, 1H), 7.38 – 7.28 (m, 11H), 6.92 (d, *J* = 15.5 Hz, 1H), 6.39 (dd, *J* = 15.5, 7.9 Hz, 1H), 5.77 (t, *J* = 6.6 Hz, 1H), 4.75 (s, 2H), 4.46 (s, 2H), 4.13 (d, *J* = 6.6 Hz, 2H). ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 193.3, 153.1, 147.6, 137.7, 136.3, 129.0, 128.6, 128.5, 128.2, 127.9, 127.9, 127.0, 126.3, 74.7, 72.8, 64.6. HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₀H₂₀O₃Na 331.1310; found 331.1322.

Synthesis of (2E,4E)-4,6-bis(benzyloxy)hexa-2,4-dienal (**7h**)



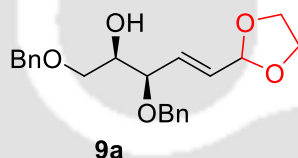
To a solution of compound **7e** (0.1 g, 0.21 mmol) in dry DMSO, sodium azide (0.041 g, 0.63 mmol) was added at rt. The mixture was stirred for overnight under nitrogen atmosphere. After completion, water was added to freeze the reaction and extracted with ethyl acetate (3x40 ml). The combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated under reduced pressure. The crude residue was purified through flash chromatography to afford colourless liquid **7h**. *R*_f = 0.7 (30 % ethyl acetate in hexane), yield = 61 %. Spectroscopic data were matched with reported value.³³ ¹H NMR (600 MHz, CDCl₃) δ 9.59 (d, *J* = 8.0 Hz, 1H), 7.40 – 7.30 (m, 11H), 7.19 (d, *J* = 15.3 Hz, 1H), 6.62 (dd, *J* = 15.3, 8.0 Hz, 1H), 5.36 (t, *J* = 7.6 Hz, 1H), 4.88 (s, 2H), 4.54 (s, 2H), 4.23 (d, *J* = 7.6 Hz, 2H). HRMS (ESI) *m/z*: [M + Na]⁺ calcd for C₂₀H₂₀O₃Na 331.1310; found 331.1318.

Synthesis of (2R,3R,E)-1,3-bis(benzyloxy)-6-oxohex-4-en-2-yl 2,4-dinitrobenzenesulfonate (**8a**)



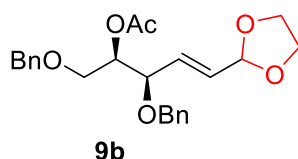
To a solution of benzyl-protected perlin (0.2 g, 0.61 mmol) in dry DCM, pyridine (98 μ l, 1.22 mmol) was added, followed by 2,4-dinitrobenzenesulfonyl chloride (0.325 g, 1.22 mmol) at 0 °C. The reaction mixture was stirred for 5 h at room temperature under nitrogen atmosphere. After completion, ice cooled water was added to freeze the reaction. The reaction mixture was extracted by DCM (3x40 ml). The combined organic layers were washed with brine, concentrated under reduced pressure. The crude mixture was purified by Flash chromatography to afford colourless liquid **8a**, R_f = 0.4 (30 % ethyl acetate in hexane), yield = 69 %. ^1H NMR (600 MHz, CDCl_3) δ 9.59 (d, J = 7.7 Hz, 1H), 8.10 (dd, J = 14.9, 5.3 Hz, 2H), 8.04 (dd, J = 8.6, 2.0 Hz, 1H), 7.30 – 7.26 (m, 6H), 7.17 – 7.15 (m, 2H), 7.12 – 7.09 (m, 2H), 6.72 (dd, J = 15.8, 5.4 Hz, 1H), 6.42 (dd, J = 15.9, 7.7 Hz, 1H), 4.91 (td, J = 6.4, 2.3 Hz, 1H), 4.59 – 4.56 (m, 1H), 4.52 (t, J = 5.6 Hz, 1H), 4.43 (d, J = 11.1 Hz, 1H), 4.37 (d, J = 11.4 Hz, 1H), 4.25 (d, J = 11.1 Hz, 1H), 3.75 (dd, J = 11.4, 2.2 Hz, 1H), 3.65 (dd, J = 11.4, 6.6 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 192.5, 149.7, 149.0, 136.6, 136.4, 135.2, 134.8, 132.4, 128.5, 128.4, 128.4, 127.9, 127.8, 127.7, 126.0, 119.9, 84.7, 76.8, 73.6, 72.3, 68.5.

Synthesis of (2R,3R,E)-1,3-bis(benzyloxy)-5-(1,3-dioxolan-2-yl)pent-4-en-2-ol (**9a**)



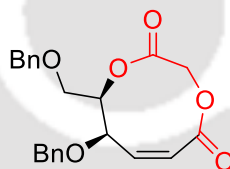
To an oven dried RB, benzyl-protected perlin aldehyde (0.2 g, 0.61 mmol) was added, dissolved in dry benzene. 2,3,5-collidine (11 μ l, 15 mol %) and D(+)-10-camphorsulfonic acid (0.021 g, 0.09 mmol, 15 mol %), excess ethylene glycol (171 μ l, 3.05 mmol) was added to it. The reaction mixture was refluxed under nitrogen for 3 h. After cooling down to rt, water (50 ml) and trimethylamine (0.1mL) was added, extracted with ether (3 x 40 ml), dried over Na_2SO_4 , concentrated under reduced pressure. The crude residue was purified through Flash chromatography to afford colourless liquid **9a**, R_f = 0.3 (30 % ethyl acetate in hexane), yield = 80 %. Spectroscopic data were matched with reported value.³⁴ ^1H NMR (400 MHz, CDCl_3) δ 7.36 – 7.23 (m, 10H), 5.90 (dd, J = 15.8, 7.3 Hz, 1H), 5.79 (dd, J = 15.8, 5.6 Hz, 1H), 5.29 (d, J = 5.7 Hz, 1H), 4.64 (d, J = 11.6 Hz, 1H), 4.51 (q, J = 12.0 Hz, 2H), 4.36 (d, J = 11.6 Hz, 1H), 4.04 – 3.95 (m, 3H), 3.93 – 3.88 (m, 2H), 3.78 (dd, J = 9.7, 5.1 Hz, 1H), 3.57 (dd, J = 10.0, 4.0 Hz, 1H), 3.49 (dd, J = 10.0, 5.4 Hz, 1H), 2.73 (s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 138.1, 137.9, 132.6, 131.2, 128.4, 128.4, 128.0, 127.8, 127.8, 127.7, 102.9, 79.3, 73.5, 72.9, 71.0, 70.5, 65.0.

Synthesis of (2R,3R,E)-1,3-bis(benzyloxy)-5-(1,3-dioxolan-2-yl) pent-4-en-2-yl acetate (**9b**)



To a solution of compound **9a** (0.2 g, 0.54 mmol) in dry DCM, pyridine (87 μ l, 1.08 mmol) was added, followed by acetic anhydride (102 μ l, 1.08 mmol) at 0 °C. The reaction mixture was stirred for 3h at room temperature under nitrogen atmosphere. After completion of the reaction ice cooled water was added to freeze the reaction. The reaction mixture was extracted by DCM (3x40 ml). The combined organic layers were washed with brine, concentrated under reduced pressure. The crude mixture was purified by Flash chromatography to afford colourless liquid **9b**, R_f = 0.6 (40 % ethyl acetate in hexane), yield = 70 %. ^1H NMR (600 MHz, CDCl_3) δ 7.35 – 7.25 (m, 10H), 5.82 (t, J = 5.1 Hz, 2H), 5.28 (d, J = 4.6 Hz, 1H), 5.15 (dd, J = 10.0, 5.3 Hz, 1H), 4.65 (d, J = 12.0 Hz, 1H), 4.50 (d, J = 12.0 Hz, 1H), 4.43 (d, J = 12.0 Hz, 1H), 4.38 (d, J = 12.0 Hz, 1H), 4.16 (t, J = 5.3 Hz, 1H), 3.99 – 3.94 (m, 2H), 3.93 – 3.88 (m, 2H), 3.63 (dd, J = 10.5, 4.3 Hz, 1H), 3.57 (dd, J = 10.5, 5.7 Hz, 1H), 2.08 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.5, 144.5, 137.9, 131.6, 130.9, 128.4, 128.4, 128.4, 127.8, 127.7, 127.7, 102.8, 76.9, 73.5, 73.2, 71.1, 68.3, 65.0, 21.1.

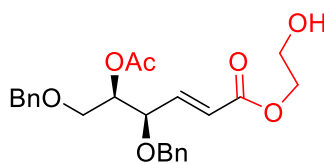
Synthesis of (8R,9R,Z)-8-(benzyloxy)-9-((benzyloxy)methyl)-8,9-dihydro-5H-1,4-dioxonine-2,5(3H)-dione (**9c**)



9c

To a solution of compound **9a** (0.05 g, 0.13 mmol) in acetone (0.3ml), NaHCO_3 (0.022 g, 0.26 mmol) was added at 0 °C. After that, a solution of oxone (0.1 g, 0.16 mmol) in water (165 μ l) was added dropwise. The mixture was stirred for 24 h. Upon completion of the reaction, acetone was removed under reduced pressure. The reaction mixture was extracted with ethyl acetate (3x40 ml). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified through flash chromatography to afford colourless liquid **9c**. R_f = 0.4 (50 % ethyl acetate in hexane), yield = 45 %. ^1H NMR (400 MHz, CDCl_3) δ 7.39 – 7.27 (m, 10H), 6.98 (ddd, J = 19.4, 15.8, 6.3 Hz, 1H), 6.12 (dd, J = 15.5, 12.6 Hz, 1H), 4.64 (d, J = 11.5 Hz, 1H), 4.59 – 4.46 (m, 2H), 4.40 (dd, J = 11.5, 2.4 Hz, 1H), 4.29 (dd, J = 5.1, 2.7 Hz, 1H), 4.19 (dd, J = 11.5, 5.5 Hz, 1H), 3.85 (dt, J = 9.7, 4.6 Hz, 2H), 3.58 (dd, J = 9.8, 4.4 Hz, 1H), 3.50 (dd, J = 9.9, 5.4 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 168.9, 165.1, 145.9, 144.3, 136.7, 136.3, 127.5, 127.4, 127.1, 127.0, 127.0, 126.8, 122.3, 77.5, 72.5, 71.3, 70.9, 70.9, 69.1, 65.3, 60.2.

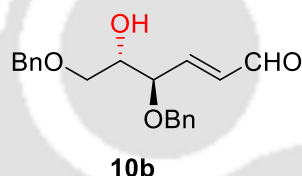
Synthesis of 2-hydroxyethyl (4R,5R,E)-5-acetoxy-4,6-bis(benzyloxy)hex-2-enoate (**9d**)



9d

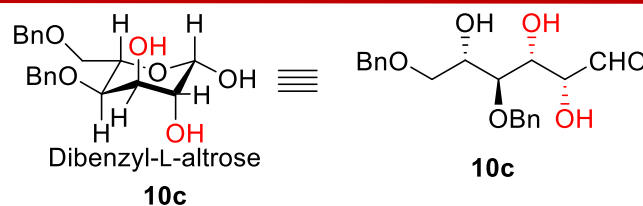
To a solution of compound **9b** (0.05 g, 0.12 mmol) in acetone (0.24 ml), NaHCO₃ (0.02 g, 0.24 mmol) was added at 0 °C. After that, a solution of oxone (0.09 g, 0.14 mmol) in water (145 µl) was added dropwise. The mixture was stirred for 1 d. After completion of the reaction, acetone was removed under reduced pressure. The reaction mixture was extracted with ethyl acetate (3x40 ml). The combined organic layers were washed with brine, dried over Na₂SO₄, concentrated under reduced pressure. The crude residue was purified through flash chromatography to afford colourless liquid **9d**. *R_f* = 0.6 (40 % ethyl acetate in hexane), yield = 51 %. ¹H NMR (400 MHz, CDCl₃) δ 7.34 – 7.27 (m, 10H), 6.90 (dd, *J* = 15.7, 5.6 Hz, 1H), 6.15 (dd, *J* = 15.7, 1.0 Hz, 1H), 5.17 (dd, *J* = 10.1, 5.0 Hz, 1H), 4.64 (d, *J* = 11.9 Hz, 1H), 4.52 – 4.41 (m, 3H), 4.33 – 4.27 (m, 3H), 3.87 – 3.83 (m, 2H), 3.65 (dd, *J* = 10.5, 4.5 Hz, 1H), 3.55 (dd, *J* = 10.4, 5.7 Hz, 1H), 2.07 (s, 3H). ¹³C{¹H}NMR (151 MHz, CDCl₃) δ 170.5, 166.1, 144.6, 137.6, 137.4, 128.5, 128.4, 128.0, 127.9, 127.8, 127.7, 123.2, 76.4, 73.3, 73.0, 72.0, 68.0, 66.3, 61.2, 21.1.

Synthesis of (4R,5S,E)-4,6-bis(benzyloxy)-5-hydroxyhex-2-enal (**10b**)



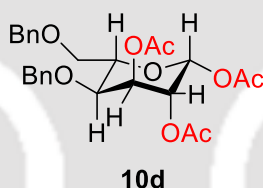
To a solution of benzyl-protected perlin aldehyde **7b** (0.1 g, 0.31 mmol) in dry DCM, pyridine (0.1 ml, 4 equiv) was added, followed by Trifluoromethanesulfonic anhydride (0.1 ml, 0.62 mmol) at 0 °C. The reaction mixture was stirred for 3 h at room temperature under nitrogen atmosphere. After completion of the reaction, ice water was added to freeze the reaction. The product was extracted by ethyl acetate (3 x 40 ml). The organic layer was washed with 2(N) HCl (30 ml), saturated solution of NaHCO₃ (2 x 50 ml), brine solution and dried over Na₂SO₄. The crude triflate **10a** was dissolved in dry acetonitrile, to this solution TBANO₂ (0.13 g, 0.44 mmol) was added at rt under nitrogen atmosphere, allowed for stirring overnight. After completion, water was added to freeze the reaction, extracted with ethyl acetate (3x40 ml). The combined organic layers were washed with brine solution, concentrated, purified through Flash chromatography to afford compound **10b**, as a colourless liquid. *R_f* = 0.3 (30 % ethyl acetate in hexane). The overall yield was 43 % over 2 steps. ¹H NMR (400 MHz, CDCl₃) δ 9.59 (d, *J* = 7.9 Hz, 1H), 7.38 – 7.23 (m, 10H), 6.88 (dd, *J* = 15.9, 6.0 Hz, 1H), 6.34 (ddd, *J* = 15.9, 7.9, 1.0 Hz, 1H), 4.60 (d, *J* = 11.5 Hz, 1H), 4.50 (d, *J* = 7.3 Hz, 2H), 4.43 – 4.39 (m, 1H), 4.12 (dd, *J* = 6.1, 0.9 Hz, 1H), 3.84 (dd, *J* = 10.6, 5.3 Hz, 1H), 3.59 (qd, *J* = 9.6, 4.9 Hz, 2H), 2.42 (s, 1H). ¹³C{¹H} NMR (151 MHz, CDCl₃) δ 193.4, 153.8, 137.5, 137.2, 133.9, 128.6, 128.5, 128.1, 128.0, 128.0, 127.9, 78.5, 73.5, 72.3, 72.0, 70.1. HRMS (ESI) *m/z*: [M + NH₄]⁺ calcd for C₂₀H₂₆NO₄ 344.1862; found 344.1860.

Synthesis of 4,6-di-O-benzyl L-altropyranose (**10c**)



To a stirred solution of compound **10b** (0.1 g, 0.31 mmol) in 5 ml mixture of acetone:water:butanol (1:1:0.4) at rt was added NMO.H₂O (48 μ l 0.4 mmol) followed by catalytic amount by 2 % aqueous solution of OsO₄ (0.2 ml, 0.016 mmol). The reaction mixture was stirred for overnight. After completion of the reaction, it was treated with Na₂S₂O₅. The reaction mixture was further stirred for another 1 h and extracted with ethyl acetate (3 x 50 ml), washed with 1(N) HCl (50 ml), water and finally brine solution dried over Na₂SO₄, concentrated under reduced pressure, purified by column chromatography (ethyl acetate:hexane = 3:1) to afford colourless liquid **10c**. R_f = 0.6 (100 % ethyl acetate); Yield = 47%. ¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.12 (m, 10H), 5.04 (d, J = 15.0 Hz, 1H), 4.68 – 4.40 (m, 5H), 4.19 (d, J = 12.7 Hz, 1H), 3.99 – 3.78 (m, 3H), 3.68 (d, J = 24.2 Hz, 3H), 2.41 (s, 1H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 136.7, 136.4, 127.6, 127.4, 127.2, 127.1, 127.0, 126.9, 93.9, 91.8, 72.6, 70.9, 69.6, 68.2, 67.0, 64.8. HRMS (ESI) m/z : [M + K]⁺ calcd for C₂₀H₂₄KO₆ 399.1210; found 399.1249.

Synthesis of 4,6-di-O-benzyl 1,2,3-tri-O-acetyl-L-altropyranose (**10d**)



To a solution of compound **10c** (0.1 g, 0.28 mmol) in dry DCM, pyridine (0.09 ml, 1.12 mmol) was added followed by acetic anhydride (0.11 ml, 1.12 mmol) at 0 °C. The reaction mixture was stirred for 3 h at room temperature under nitrogen atmosphere. After completion of the reaction, ice water was added to freeze the reaction, extracted by ethyl acetate (3x40 ml). The combined organic layers were washed with saturated NaHCO₃ to remove excess acid, brine solution and dried over Na₂SO₄, concentrated under reduced pressure. The crude residue was purified by Flash chromatography (ethyl acetate:hexane = 1:2) to afford colourless liquid **10d**. R_f = 0.5 (40 % ethyl acetate in hexane); Yield = 70 %. ¹H NMR (400 MHz, CDCl₃) δ 7.34 – 7.17 (m, 10H), 6.09 (d, J = 1.6 Hz, 1H), 5.51 (dd, J = 4.5, 3.3 Hz, 1H), 5.17 (dd, J = 4.7, 1.6 Hz, 1H), 4.64 (dd, J = 9.3, 5.8 Hz, 1H), 4.59 (d, J = 5.3 Hz, 1H), 4.52 – 4.49 (m, 1H), 4.37 (d, J = 10.8 Hz, 1H), 4.06 (dd, J = 8.0, 4.3 Hz, 1H), 3.94 (dd, J = 8.9, 3.1 Hz, 1H), 3.73 – 3.70 (m, 2H), 2.15 (s, 3H), 2.11 (s, 3H), 2.07 (s, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 169.5, 169.4, 168.8, 138.0, 137.2, 128.4, 128.4, 128.3, 128.2, 128.0, 127.7, 90.3, 74.4, 73.6, 72.1, 70.7, 68.9, 67.9, 66.3, 29.7, 21.0, 20.9. HRMS (ESI) m/z : [M + NH₄]⁺ calcd for C₂₆H₃₄NO₉ 504.2234; found 504.2234.

5.4 References

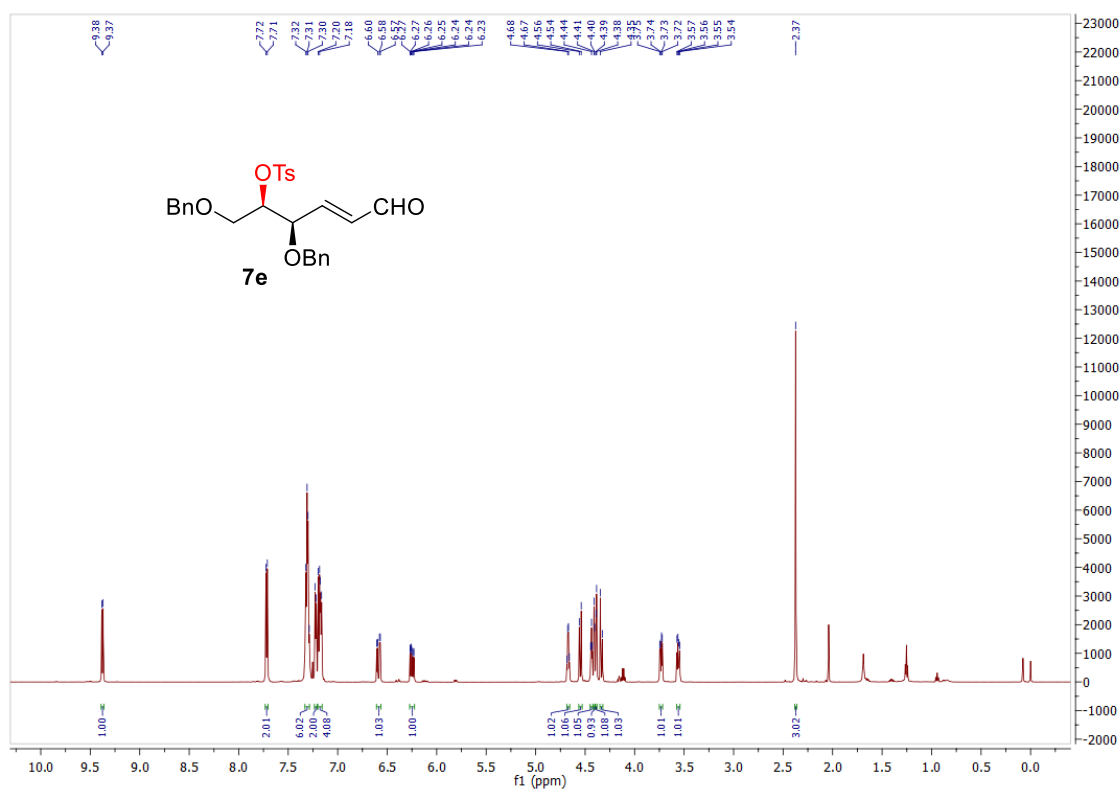
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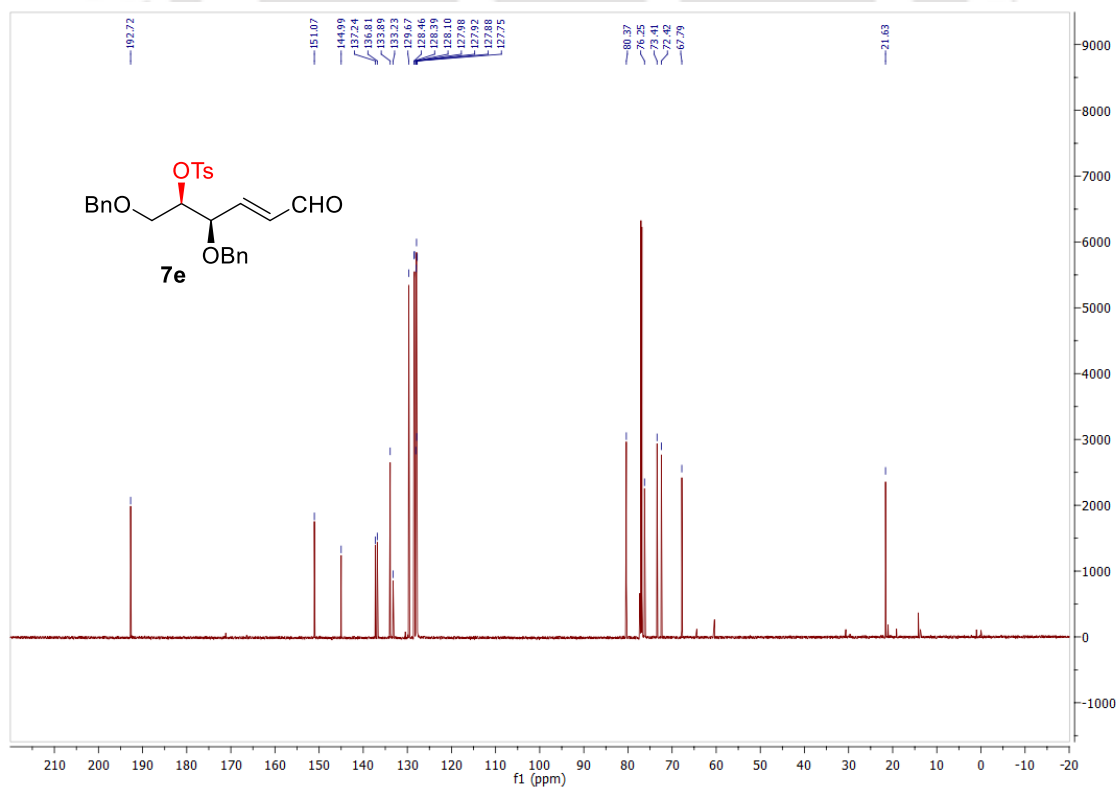
5.5

Spectra

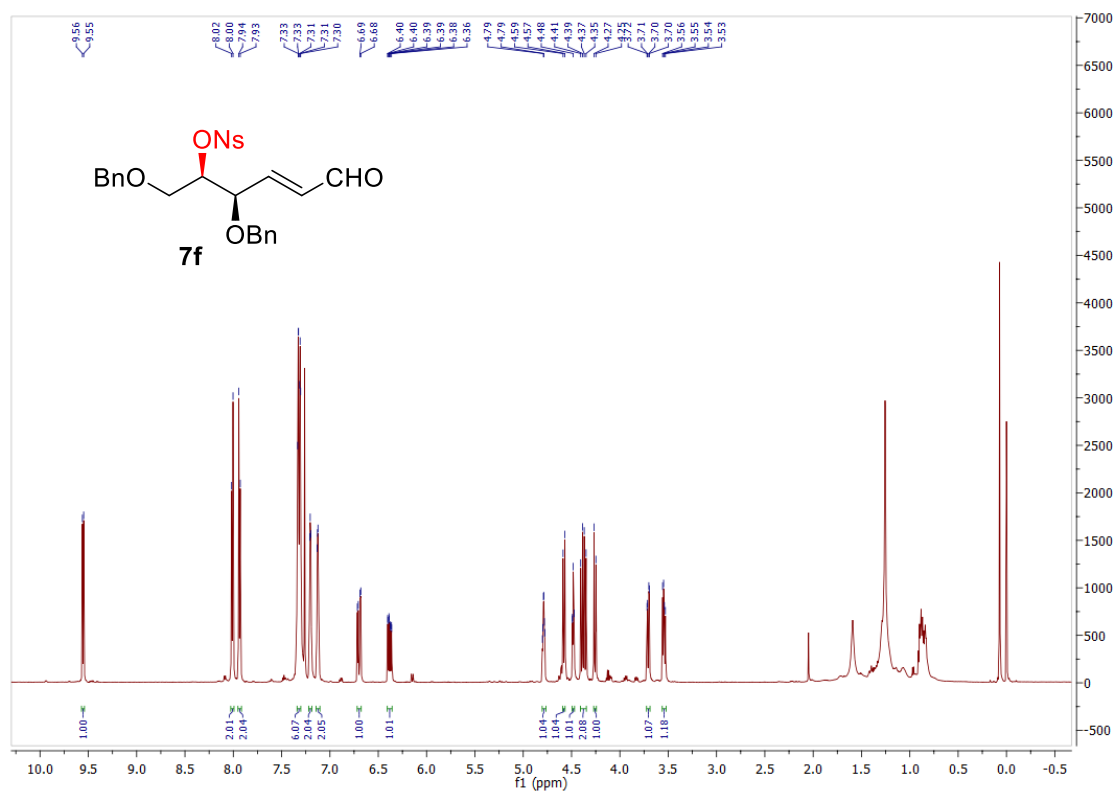
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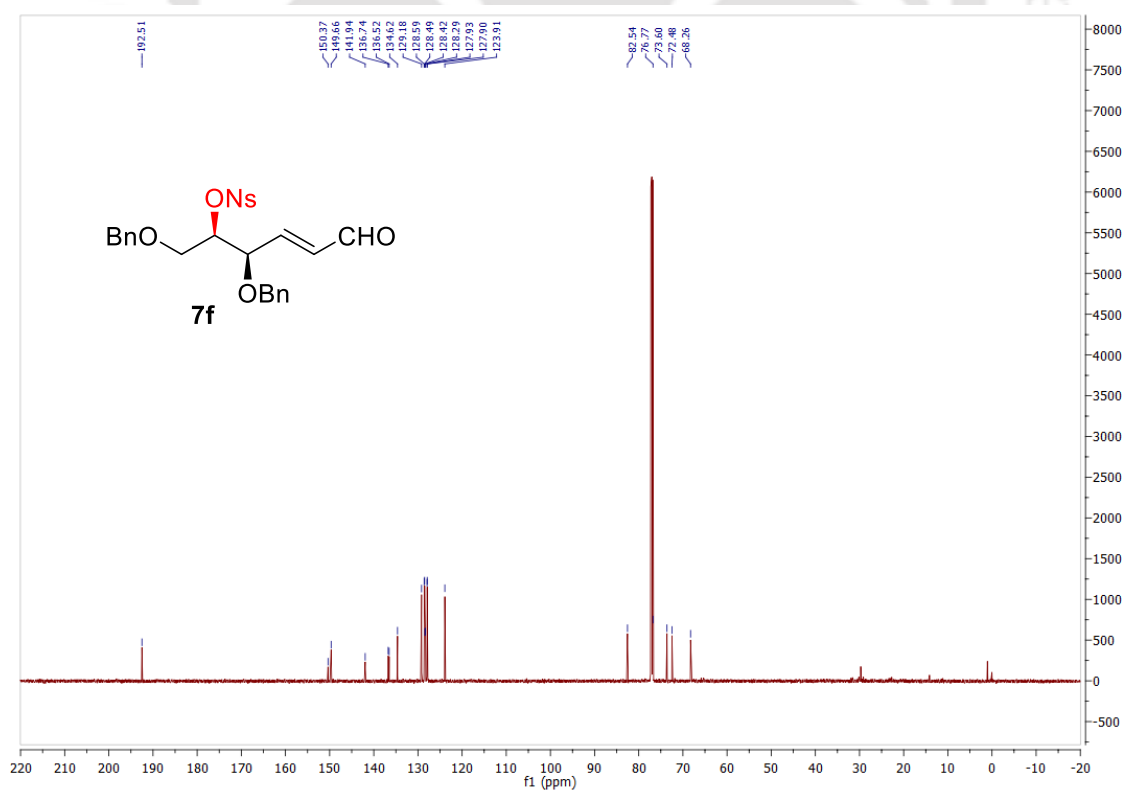
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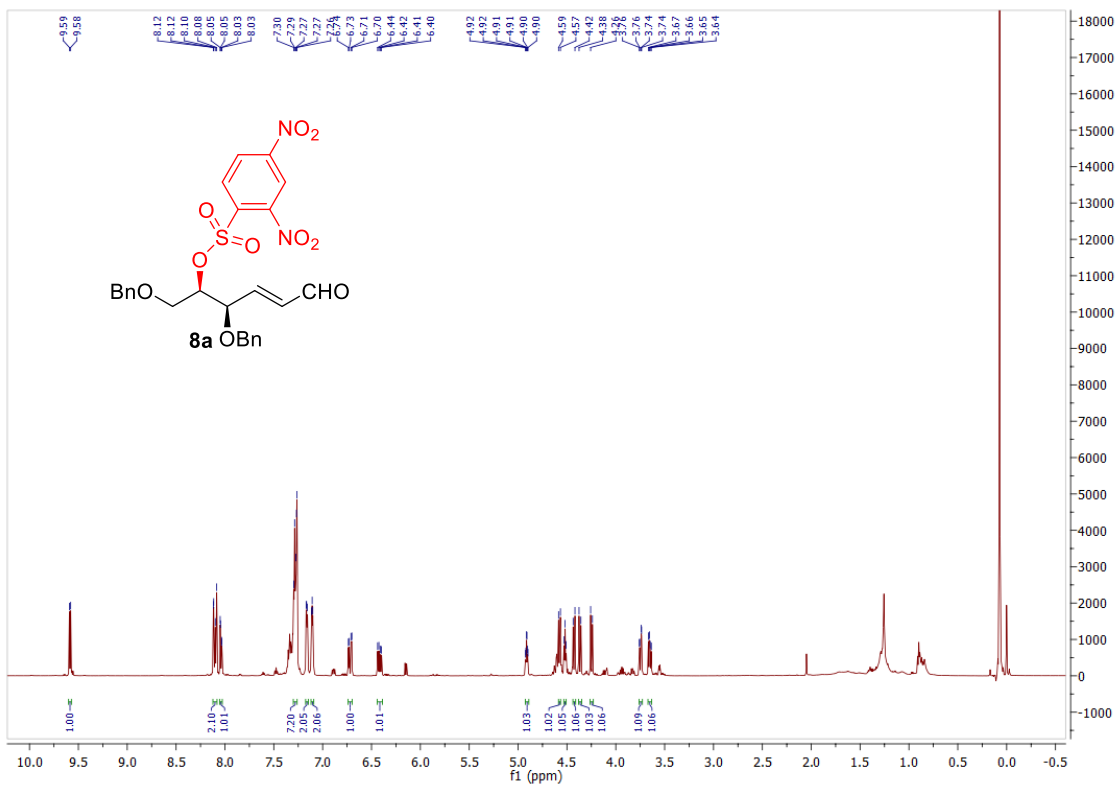
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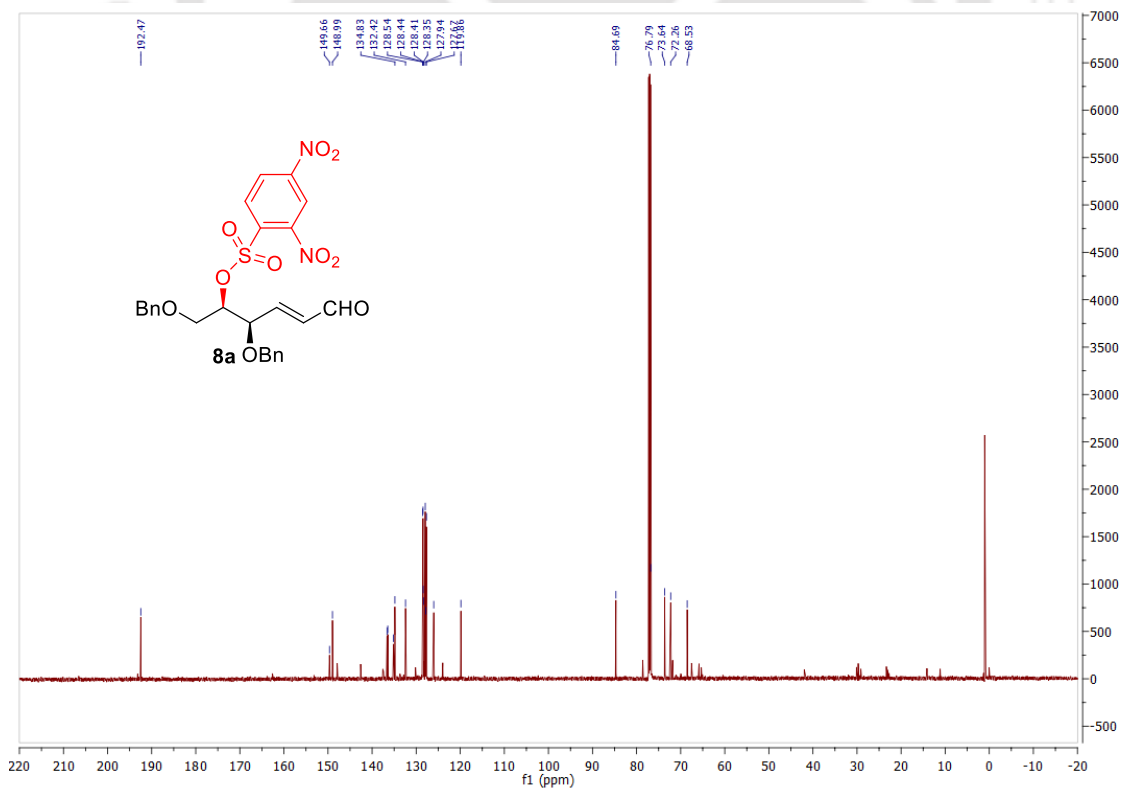
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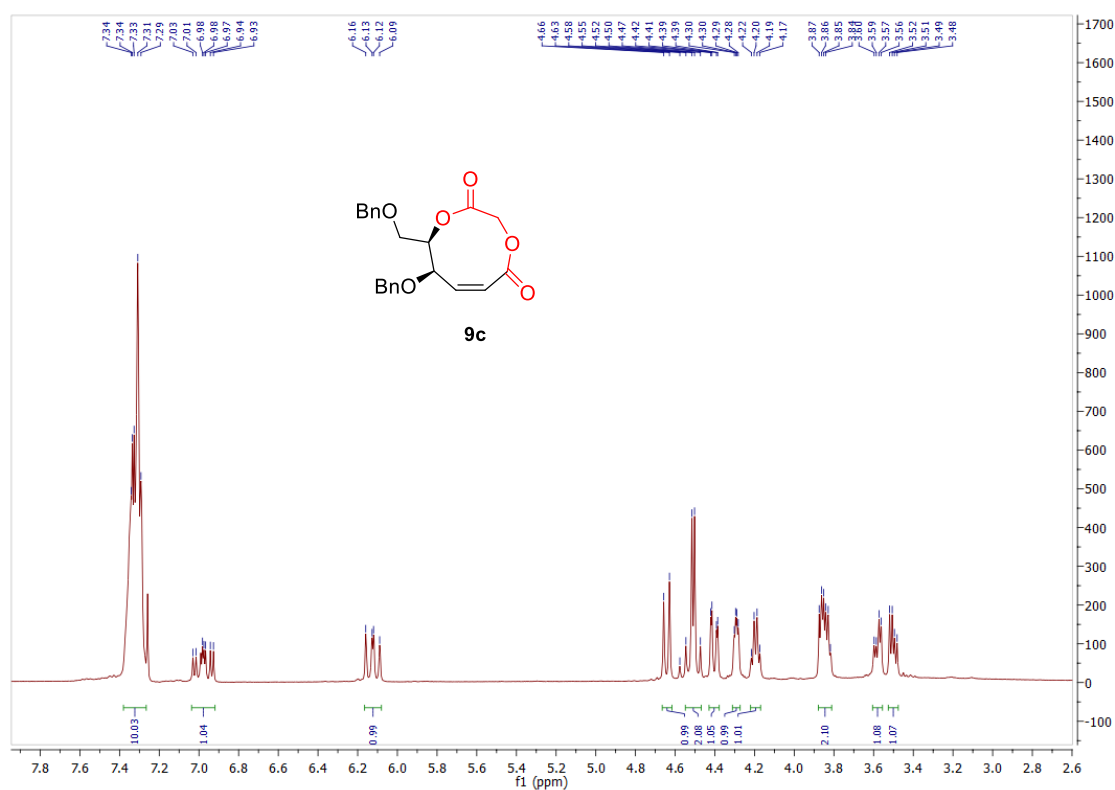
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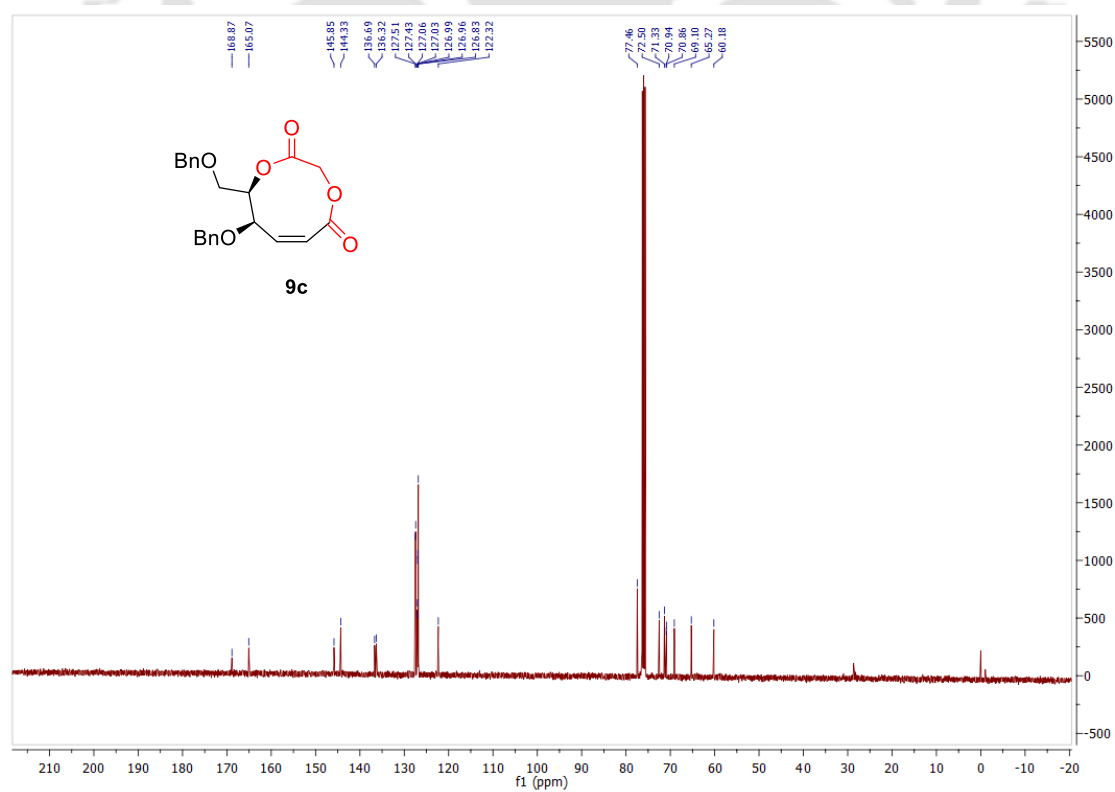
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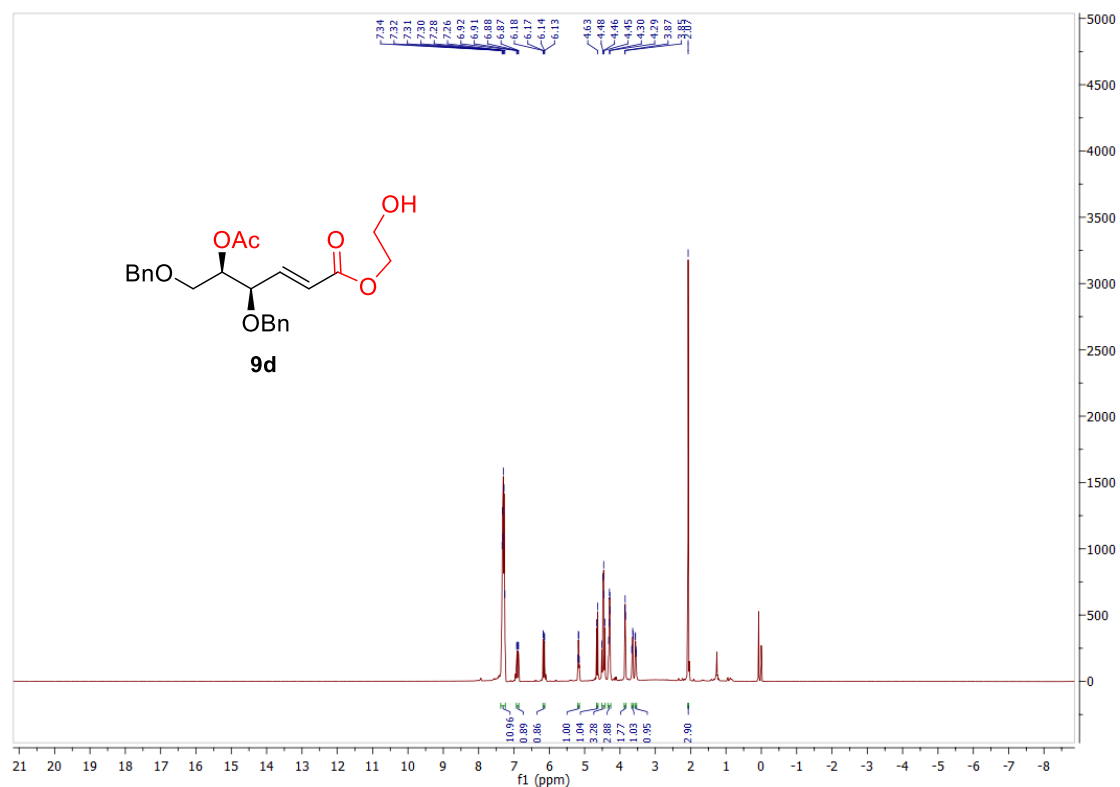
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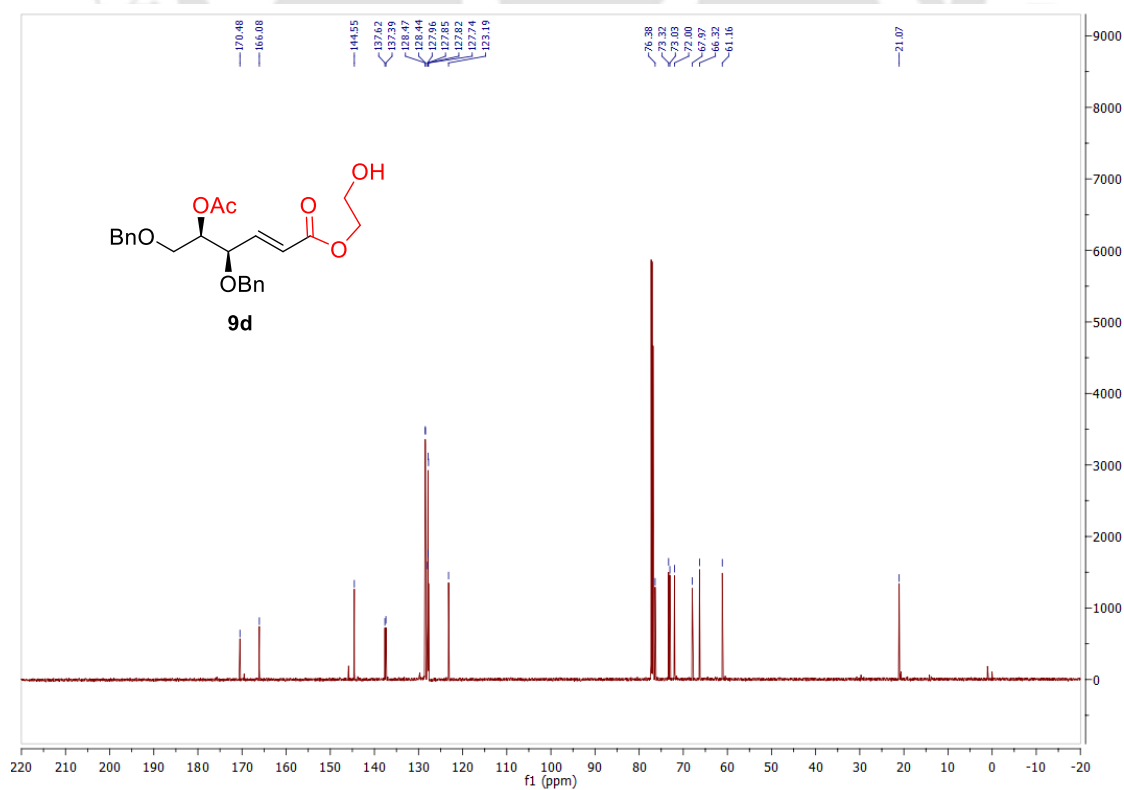
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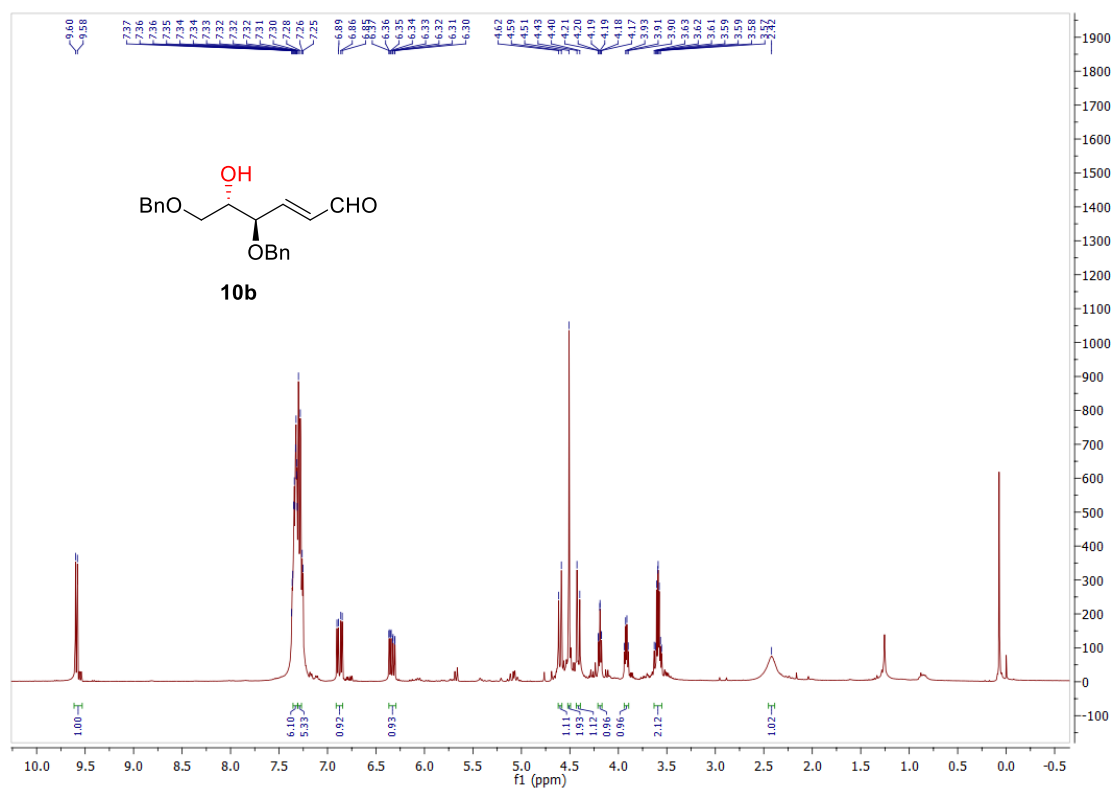
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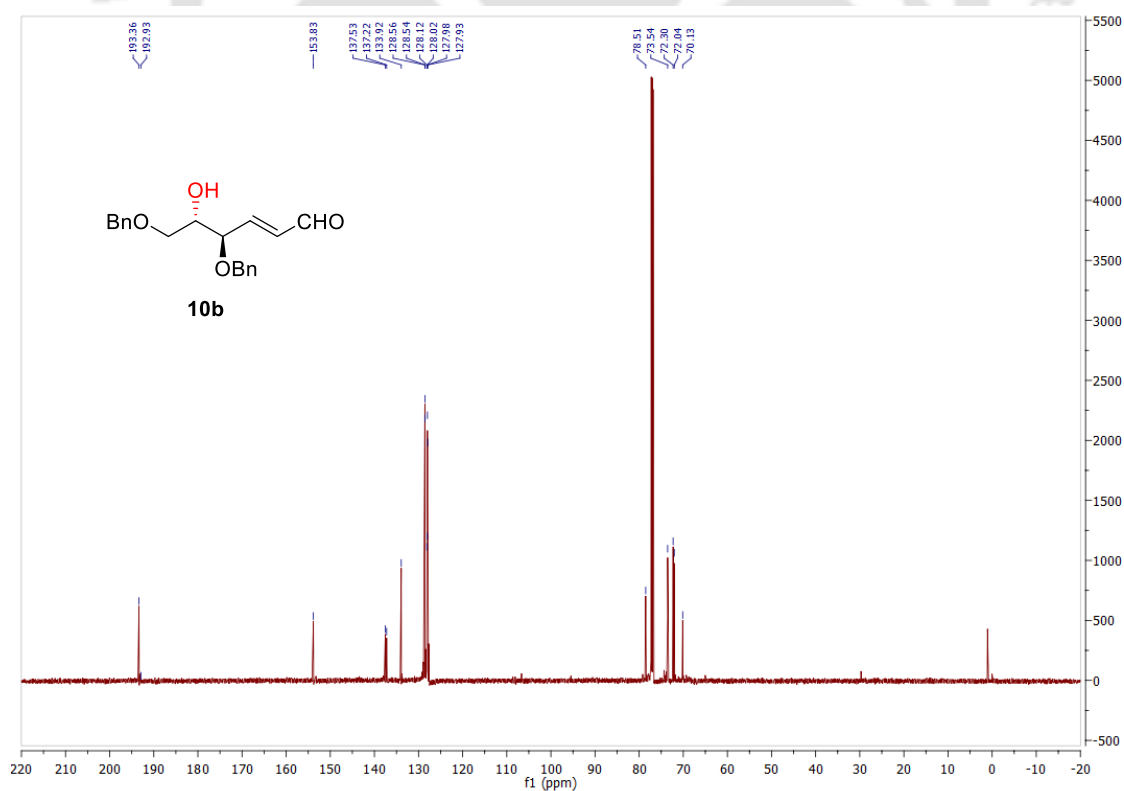
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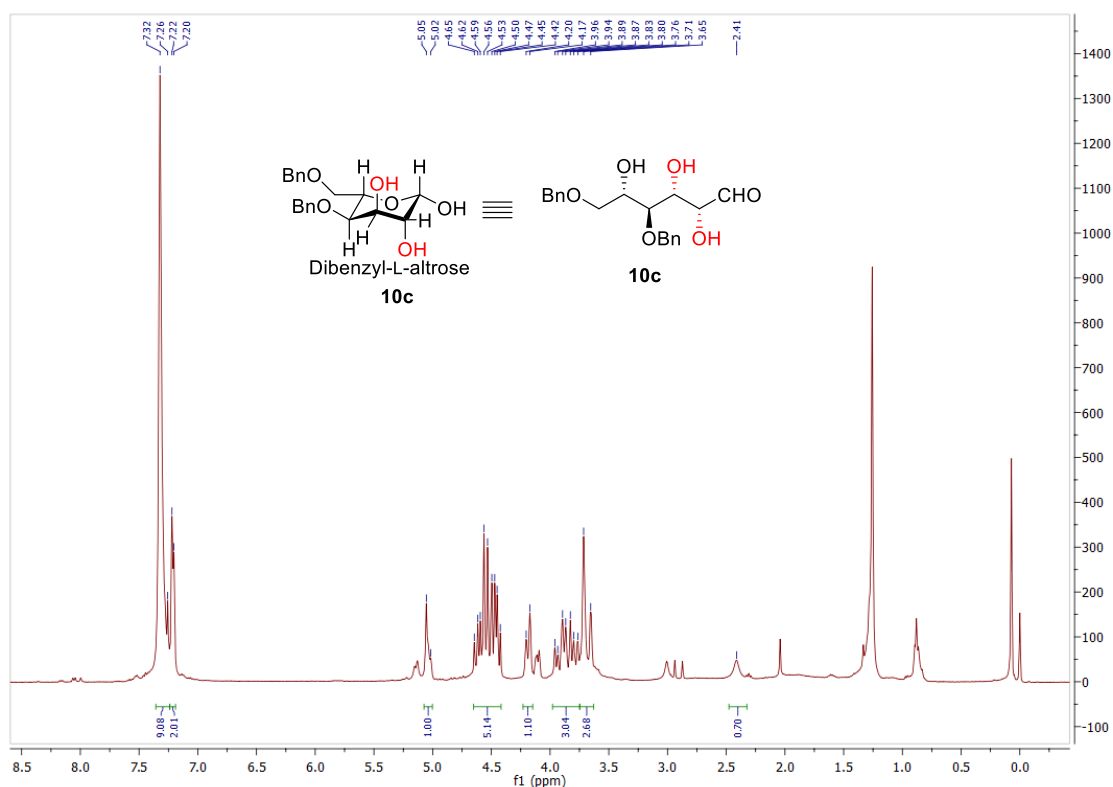
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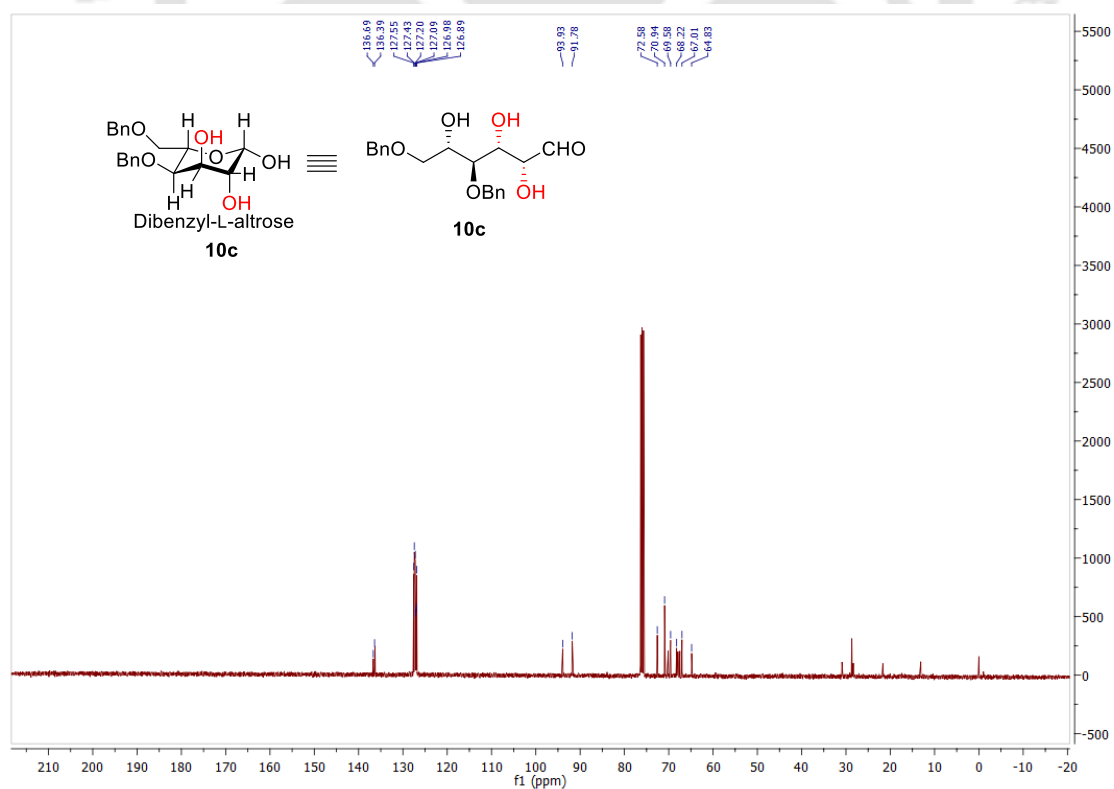
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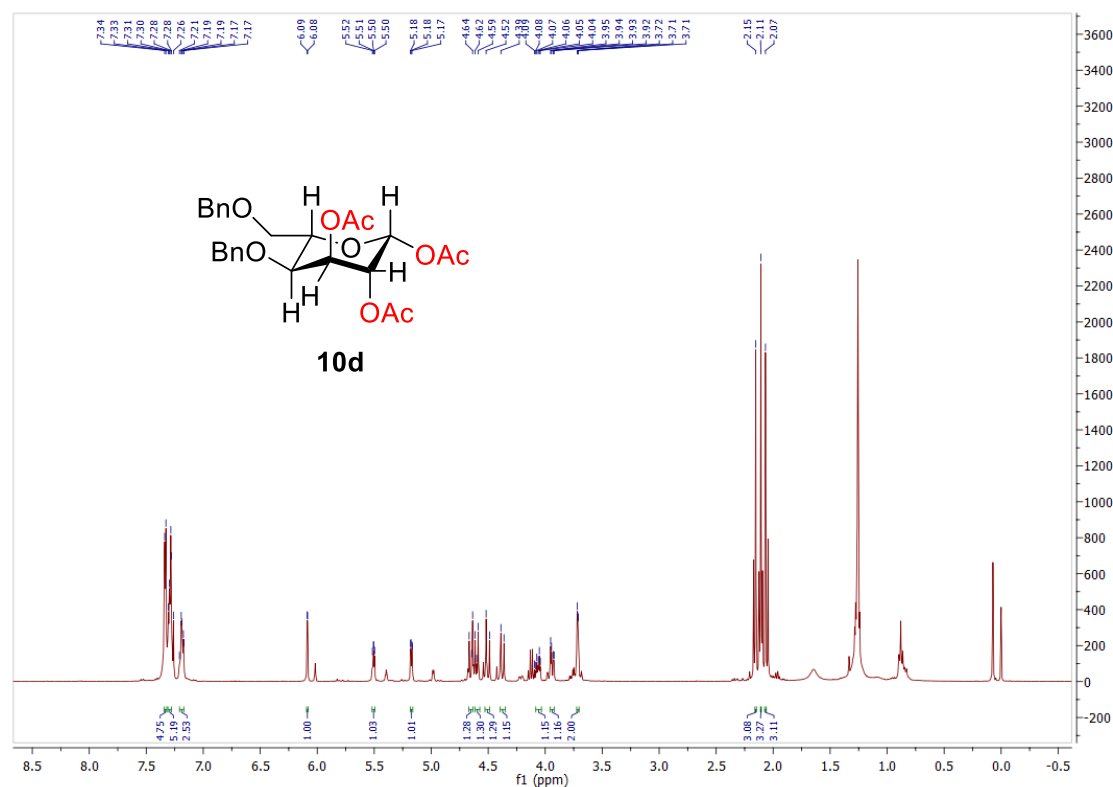
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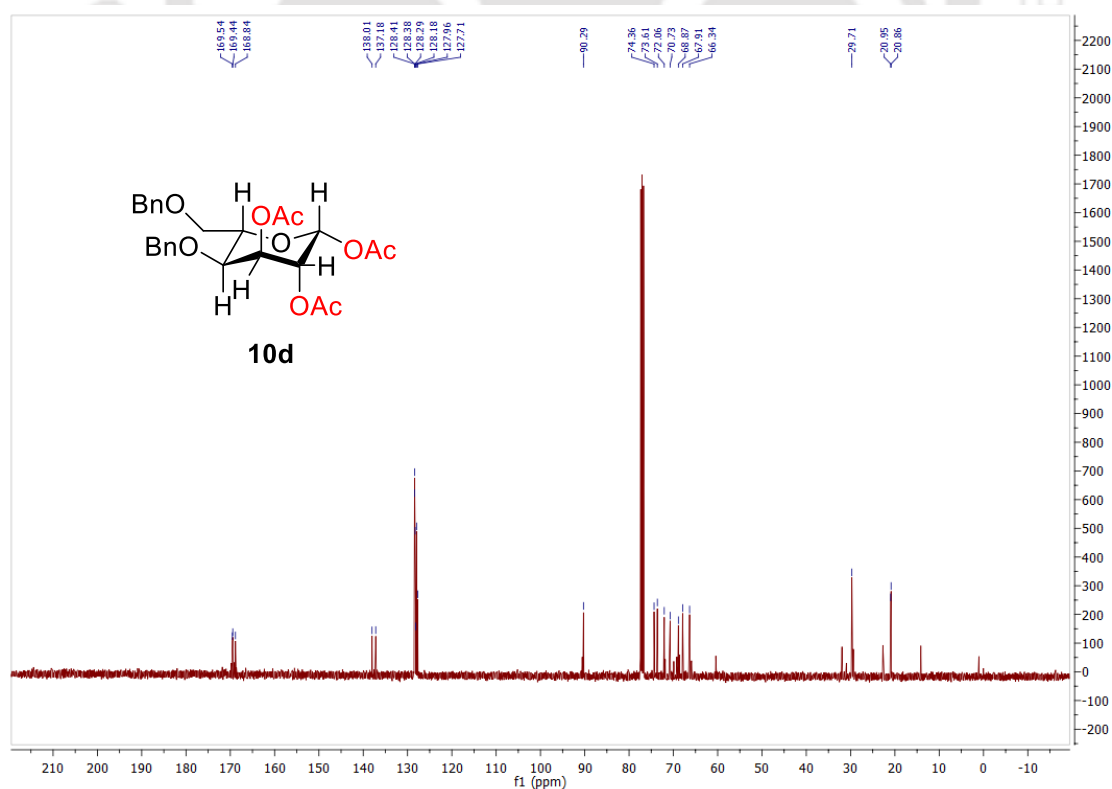
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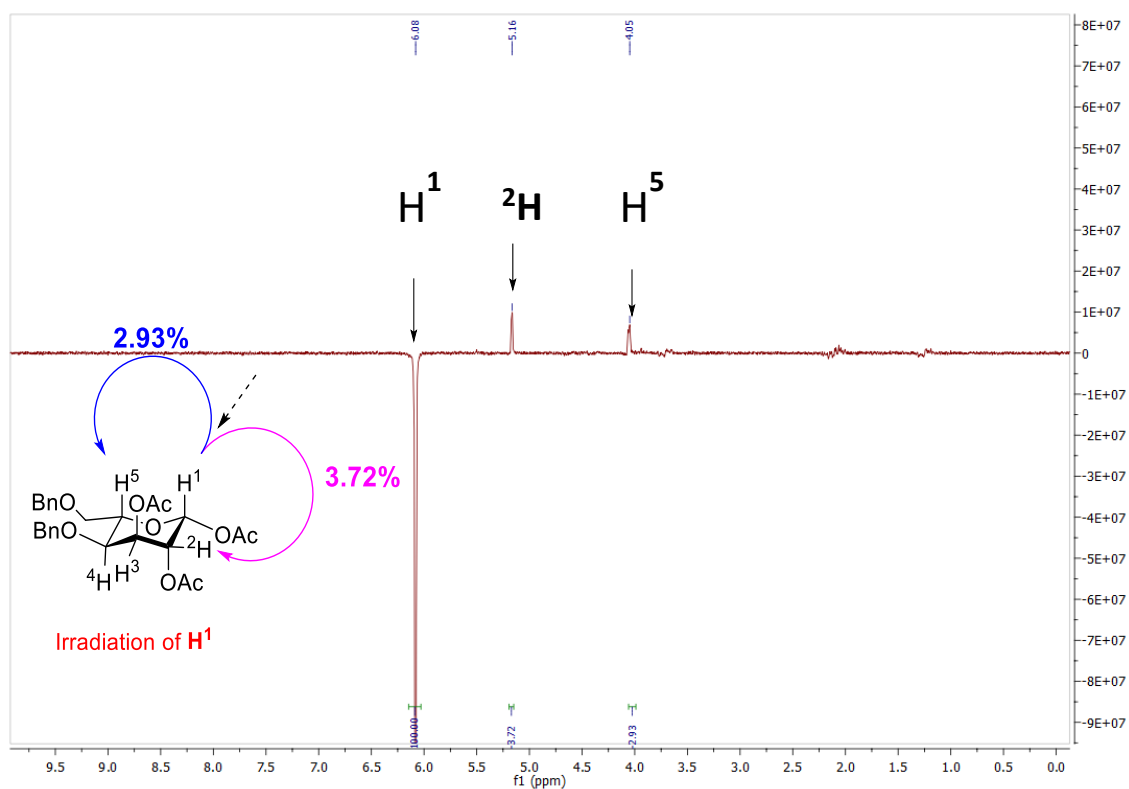
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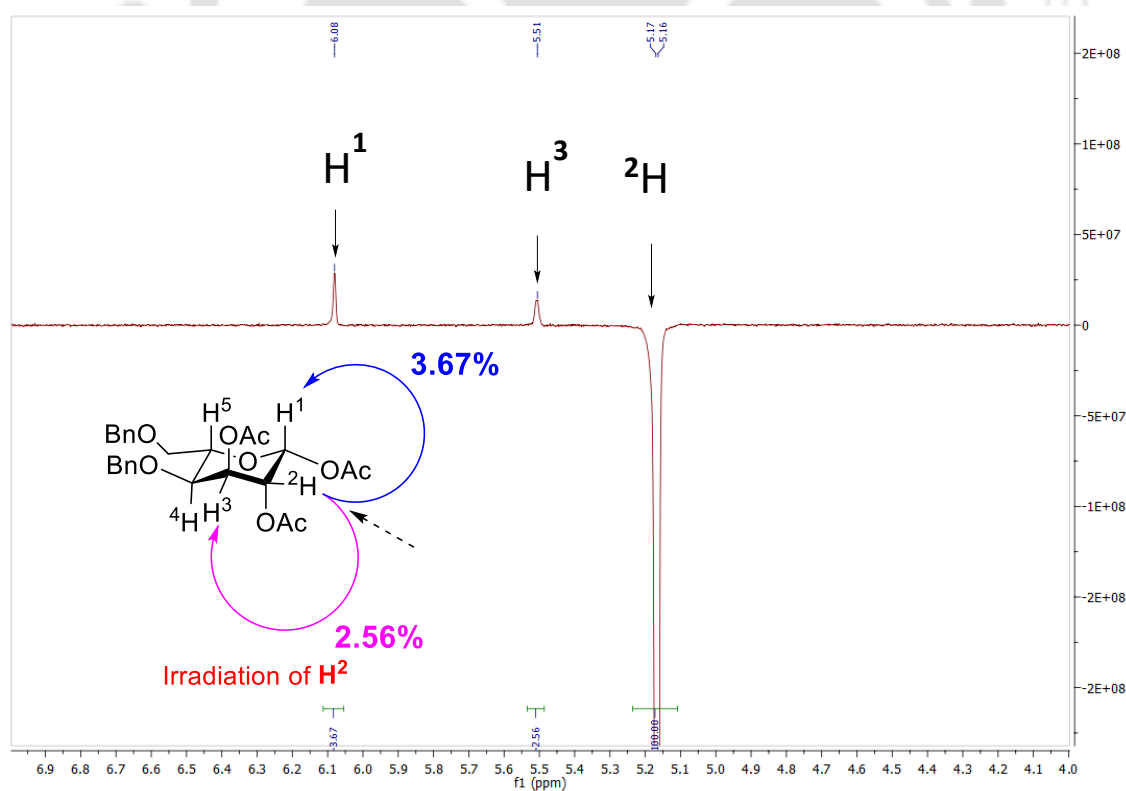
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 10d



Irradiation of anomeric proton (α -isomer) H^1 of compound 10d

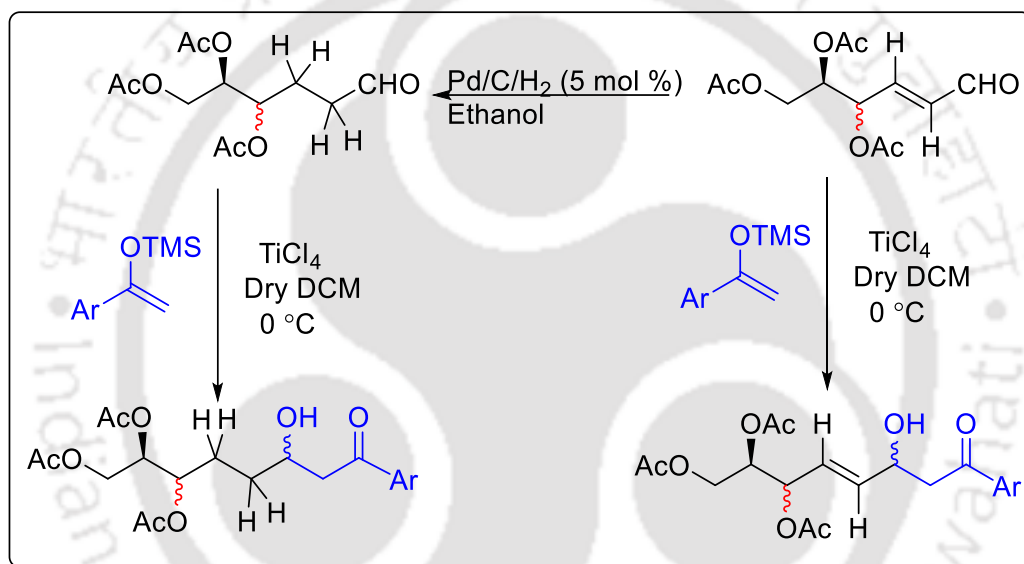


Irradiation of anomeric proton (α -isomer) H^2 of compound 10d



Chapter V

Synthesis of aryl-polyols from Perlin aldehyde





6.1.1 Introduction

Chiral polyols with well-defined chiral centers are a part of several natural products and are of particular interest to organic chemists.¹ Perlin aldehydes, that are easily accessible from the corresponding glycals¹ are attractive synthons to synthesize various cyclic² and acyclic³ sugar derivatives and other natural products having biological functionalities. The presence of conjugated double bonds along with carbonyl functionality of Perlin aldehyde have been exploited as a chiral pool⁴ for the synthesis of natural products, e.g. optically pure triacetoxymethylene⁵ derivative obtained from Perlin aldehyde. There are several synthetic strategies available in the literature to synthesize long-chain acyclic sugar derivatives of biological importance⁶. In synthetic chemistry, the formation of the new chiral center along with stereoselective C-C bond formation has played a crucial role. The design and execution of stereo and regioselective strategies for the synthesis of bioactive molecules from commercially inexpensive precursors are of high interest. The synthesis of a β -hydroxy- γ,δ -unsaturated keto sugar maintaining stereoselectivity is highly desirable for carbohydrate chemists. As discussed in the chapter I, A.S. Perlin first synthesized δ -hydroxy- α,β -unsaturated aldehyde (generally called Perlin aldehyde) in 1975 from commercially available glycals.⁷ Due to the presence of (a) a high degree of functionality (free hydroxyl group, unsaturation (E) and aldehyde group (b) two predefined chiral centers (c) optically pure, the Perlin aldehyde, has been explored towards the synthesis of various natural products. Over the last decades, so many synthetic procedures have been developed for the synthesis of bioactive molecules (Figure 1).¹

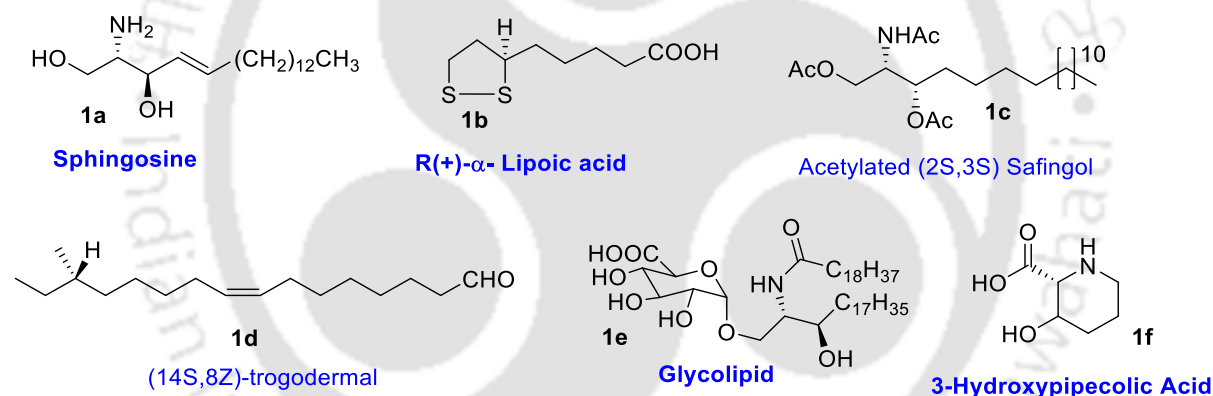
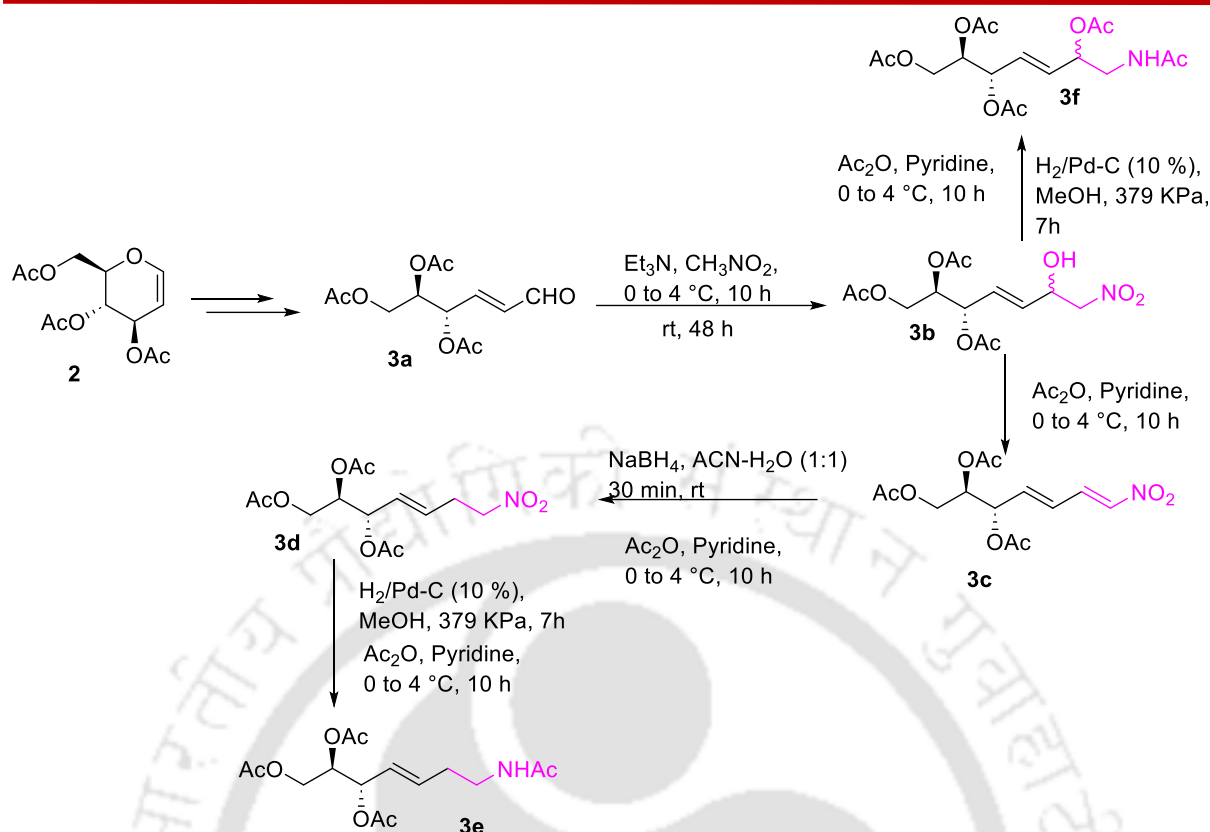


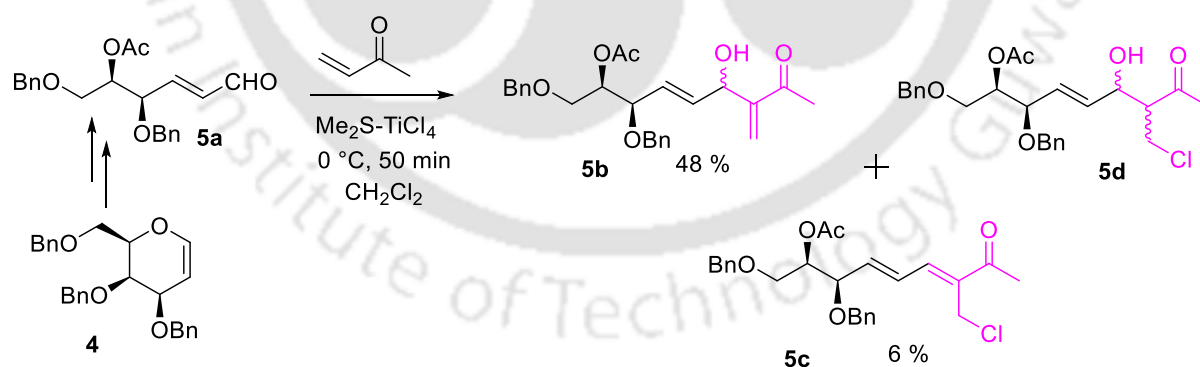
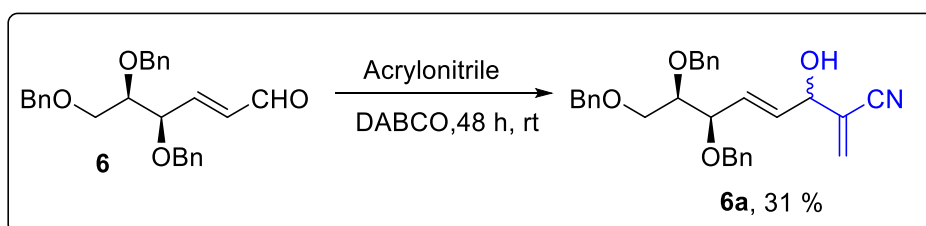
Figure 1: Perlin-derived bio-important compounds

6.1.2 Literature reviews

In 2000, Bhaduri and co-workers reported polyhydroxy nitro and amino sugar via Henry reaction from α,β -unsaturated aldehyde sugar with nitromethane (Scheme 1).⁸ Addition of nitromethane in the presence of triethyl amine to the reaction mixture of **3a**, resulted in inseparable diastereomeric mixture **3b**. Dehydration of compound **3b** was carried out in the presence of acetic anhydride and pyridine which resulted in dialkene product **3c**. The regioselective reduction of the C1-C2 double bond was achieved by NaBH₄. The terminal nitro group was converted to an amine by using 10 % of H₂/Pd-C which was later converted to N-acetyl derivative **3e**. Similarly, compound **3b** was converted to N-acetyl derivative **3f** (Scheme 1). In 2002, Bhaduri and co-workers first disclosed the Morita–Baylis–Hillman reaction on Perlin aldehyde where it acts as an electrophile in the presence of methylvinyl ketone and Me₂S-TiCl₄ (Scheme 2).⁹ They have reported that the distribution of product formation depends on the reaction time. While the reaction was run for 15 min, the chloro-product (**5d**) was the major one, however, olefin product (**5b**) forms as the major product if the reaction is run for 50 min.

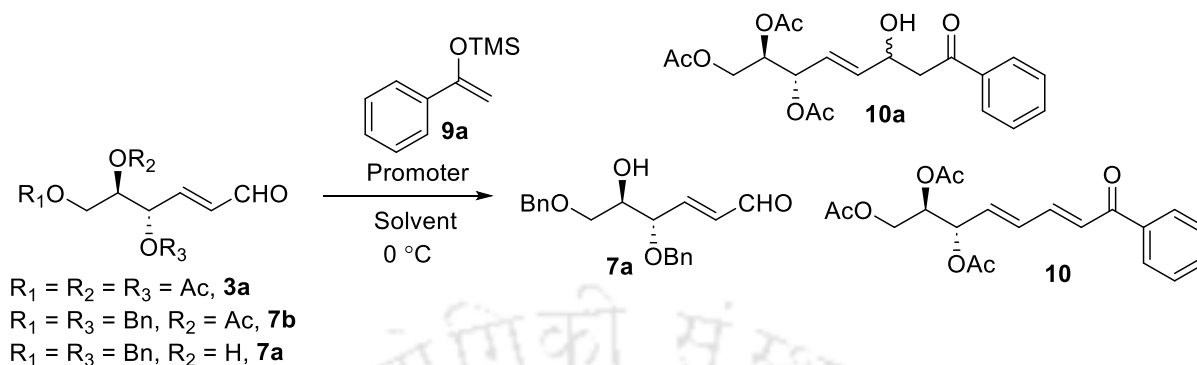
**Scheme 1:** Synthesis of polyhydroxy nitro and amino sugar

They also allowed the reaction for a longer time. After 6 h, all products were converted to the dialkene chloro product **5c** (Scheme 2). The same group later performed the same reaction taking acrylonitrile and DABCO instead of methylvinyl ketone and $\text{Me}_2\text{S-TiCl}_4$ respectively, which resulted in only one coupled product **6a** (Scheme 3).¹⁰

**Scheme 2:** MVK and $\text{Me}_2\text{S-TiCl}_4$ mediated Baylis-Hillman reaction on Perlin aldehyde**Scheme 3:** Acrylonitrile and DABCO mediated Baylis-Hillman reaction on Perlin aldehyde

6.2 This work

6.2.1 Table 1: Optimization studies



Entry	Aldehyde	Promoter	Solvent	Time	Products		
					7a	10a	10
1	7a	TiCl ₄	DCM	24 h	NR	-	-
2	7b	TiCl ₄	DCM	2 h	95 %	-	-
3	3a	TiCl ₄	DCM	1 h	-	82 %	8 %
4	3a	TiCl ₄	THF	1 h	-	65 %	19 %
5	3a	TiCl ₄	Toluene	1 h	-	76 %	12 %
6	3a	TiCl ₄	ACN	24	-	-	15 %
7	3a	BF ₃ .OEt ₂	DCM	1 h	-	32 %	61 %
8	3a	TMSOTf	DCM	24 h	-	-	23 %
9	3a	Cu(OTf) ₂	ACN	24 h	NR	-	-
10	3a	TiCl ₄	DCM	40 min	-	74 %	-
11	3a	TiCl ₄	DCM	50 min	-	87 %	-
12*	3a	TiCl ₄	DCM	3 h	-	76 %	
13	3a	TiCl ₄	DCM	12 h	-	-	85 %

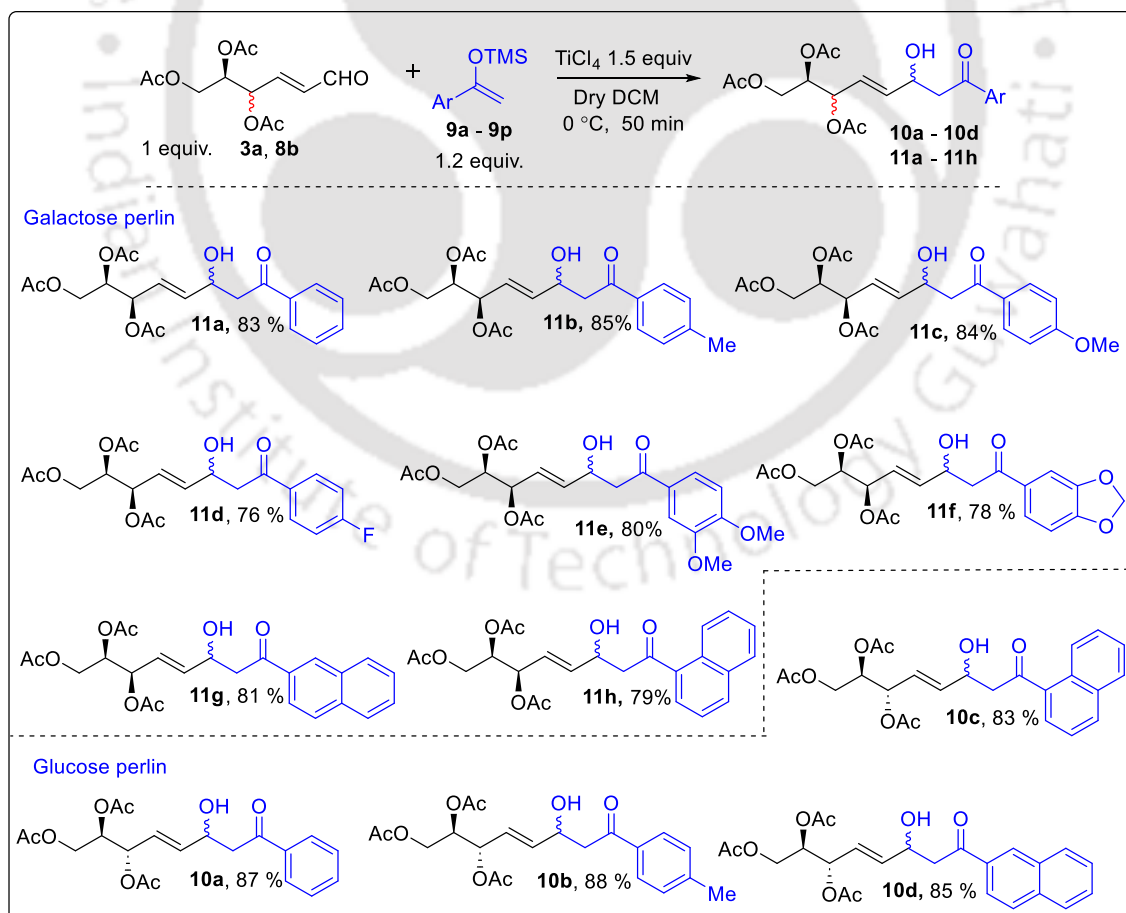
Reaction conditions: Perlin aldehyde (1 equiv.), silyl enol ether (1.2 equiv), Promoter (1.5 equiv.), All the reactions were performed at 0 °C, and * reaction was performed at – 30 °C.

In 1973, Mukaiyama et al. reported an innovative cross-aldol reaction by using silyl enol ethers with aldehydes (ketones) in the presence of the Lewis acid, titanium tetrachloride.¹¹ Mukaiyama aldol reaction provides a great platform to functionalize aldehydes with silyl-based carbon nucleophiles under Lewis acidic conditions. Activation of a carbonyl group by a Lewis acid assists the attack of a carbon nucleophile providing a new carbon-carbon bond under acidic

conditions.¹² In this chapter, we report the Mukaiyama cross aldol condensation on α,β -unsaturated aldehyde sugar with silyl enol ether towards the synthesis of long-chain sugars with a generation of the new chiral center.

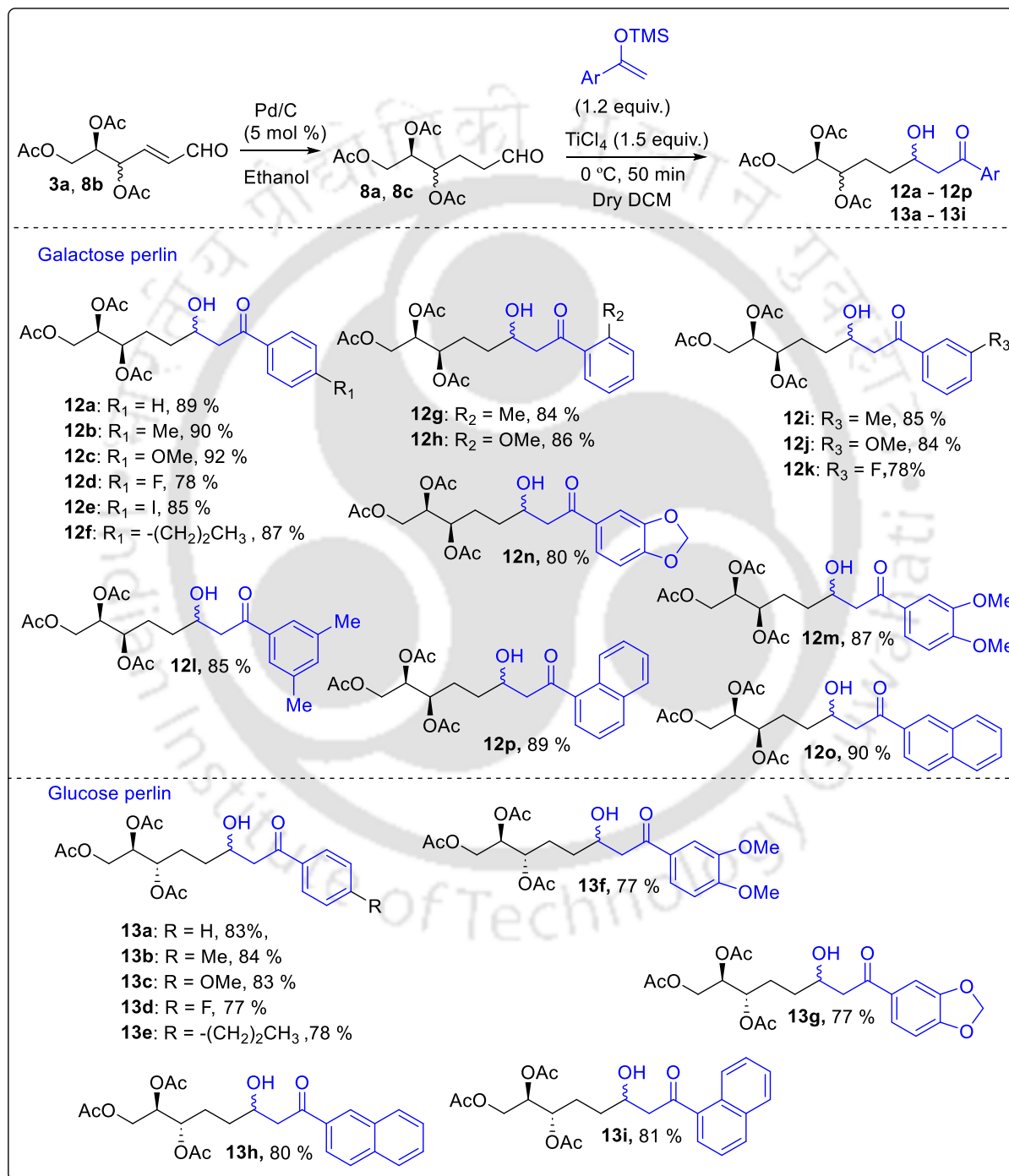
Our initial approach was to investigate the reaction of the δ -hydroxy- α,β -unsaturated aldehyde sugar (**7a**) with silyl enol ether (**9a**) in the presence of 1.5 equiv. of TiCl_4 in the DCM medium which did not lead to any consumption of starting material (Table 1, entry 1) presumably due to the reaction of the free hydroxyl group with TiCl_4 , thus quenching the reagent. Then we protect the free hydroxyl group by using Ac_2O (**7b**) and performed the same reaction which resulted in δ -hydroxy α,β -unsaturated aldehyde sugar (**7a**) (Table 1, entry 2) because the keto center is more electrophilic than aldehyde center. After that, we change the protecting group of sugar to acetyl from benzyl and performed the same reaction taking (2E)-4,5,6-*tri-O*-acetyl-2,3-dideoxy-aldehyde-threo-hex-2-enose (**3a**) with silyl enol ether (**9a**) which resulted in 82 % desired inseparable diastereomeric mixture product (**10a**) along with eliminated conjugated $\alpha,\beta,\gamma,\delta$ diene (**10**)⁴ in 8 % within 1h (Table 1, entry 3). To check the reactivity of our protocol in a polar aprotic solvent, we performed the same reaction in THF which resulted in the desired product (**10a**) in 65 % along with 19 % dienone product (**10**) (Table 1, entry 4) whereas in acetonitrile medium resulted in only 15 % the dienone product (**10**) (Table 1, entry 6). However, changing the solvent to toluene resulted in an increase in the product **10a** (76 %) and a decrease in the formation of the dienone by-product **10** (12 %) (Table 1, entry 5). Changing the Lewis acids to $\text{BF}_3\cdot\text{OEt}_2$ and TMS-OTf led to a significant increase in the

6.2.2 Substrates scope



Scheme 4: Substrate scope for (2E)-4,5,6-*tri-O*-acetyl-2,3-dideoxy-aldehyde-hex-2-enose (**3a**, **8b**)

formation of the dienone product (Table 1, entry 7 & Table 1, entry 8). Interestingly, no reaction was observed even after 24 h, when copper triflate, a metal-based Lewis acid was used (Table 1, entry 9). Later, we investigated the influence of time on the alcohol/diene ratio. When we decreased the reaction time from 1 h to 40 min & 50 min, surprisingly, eliminated the formation of any diene product and provided the desired alcohol product (**10a**) in 74 % and 87 % respectively (Table 1, entry 10, 11). To check the reactivity of aldehyde at lower temperatures, we performed the reaction at $-30\text{ }^{\circ}\text{C}$ which resulted in only desired product (**10a**) in 76 % after 3h without any diene product (**10**) (table 1, entry 12).

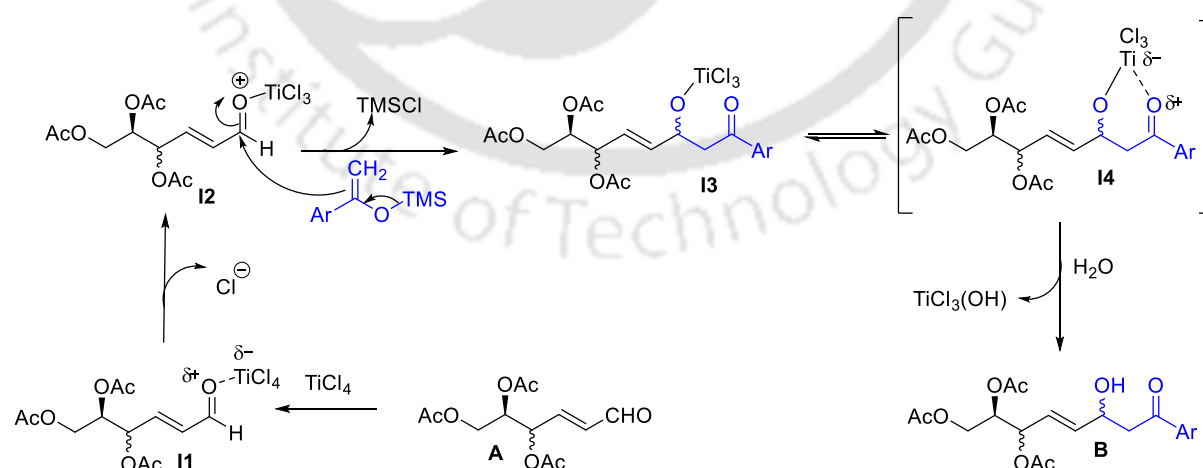


Scheme 5: Substrate scope for 4,5,6- tri-O-acetyl-2,3-dideoxy-aldehyde-hexose (**8a**, **8c**)

After the successful optimization of the reaction conditions, we focused on studying the reactivity of the (2E)-4,5,6-*tri*-O-acetyl-2,3-dideoxy-aldehyde-threo-hex-2-enose (**3a**) and (2E)-4,5,6-*tri*-O-acetyl-2,3-dideoxy-aldehyde-erythro-hex-2-enose (**8b**) with variously substituted silyl enol ethers (**9a**–**9p**) (Scheme 4). All the reactions completed smoothly in 50 min, giving the desired inseparable diastereomeric mixture of products (**10a**–**10d**, **11a**–**11h**) with good to excellent yields. It was observed that the nature of the electronic substitution of the silyl enol ether does not play any role in the yield of the desired products. (2E)-4,5,6-*tri*-O-acetyl-2,3-dideoxy-aldehyde-erythro-hex-2-enose (**8b**) resulted in good to excellent yields (76 % - 85 %) with *para*-substituted phenyl silyl enol ether (**11b** – **11d**), disubstituted silyl enol ether (**11e** - **11f**), and with simple phenyl silyl enol ether (**11a**). Similarly, naphthalene-based silyl enol ether provided good yields (79 % - 81 %) (**11g** – **11h**). The glucal-derived (2E)-4,5,6-*tri*-O-acetyl-2,3-dideoxy-aldehyde-threo-hex-2-enose (**3a**) also provided an inseparable diastereomeric mixture of products (**10a** - **10d**) with good to excellent yields (83 % - 87 %).

We performed a reaction taking (2E)-4,5,6-*tri*-O-acetyl-2,3-dideoxy-aldehyde-threo-hex-2-enose (**3a**) and silyl enol ether (**9a**) in the presence of 1.5 equiv. of TiCl_4 in DCM medium for 12 h which resulted in only eliminated conjugated $\alpha,\beta,\gamma,\delta$ diene (**10**) in 85 % (Table 1, entry 13). From this experiment, it is clear that β -hydroxy- γ,δ -unsaturated keto compound (**10a**) is too reactive and is prone to elimination under the reaction conditions to form the conjugated $\alpha,\beta,\gamma,\delta$ diene (**10**). We reduced the unsaturated double by using 5 mol % Pd/C in ethanol¹⁰ to make 4,5,6-*tri*-O-acetyl-2,3-dideoxy-aldehyde-hexose (**8a**, **8c**). Taking the same optimized condition, we made several cross-aldol products (Scheme 5) (**12a** – **12p** & **13a** – **13i**) by taking 4,5,6-*tri*-O-acetyl-2,3-dideoxy-aldehyde –hexose (**8b**, **8c**) with different silyl enol ether (**9a** – **9p**). When the current protocol was examined taking the 4,5,6-*tri*-O-acetyl-2,3-dideoxy-aldehyde-erythro-hexose (**8c**), it was observed that all the reactions have completed within 50 min with excellent yields (Scheme 5) (**12a** – **12p**) (78 % - 92 %), independent of the electronic nature of the substituent on the aromatic ring. Similarly, we also made several examples (Scheme 5) (**13a** – **13i**) (76 % - 84 %) from 4,5,6-*tri*-O-acetyl-2,3-dideoxy-aldehyde-threo-hexose (**8a**). It was noticed that, generally, the galactose-based derivative (**8c**) gives better yields than the glucose-based derivate (**8a**).

6.2.3 Mechanism



Scheme 6: Plausible mechanism

The mechanism is based on the well-established Mukayama-aldol reaction mechanism. The strong Lewis acid, titanium tetrachloride activates the α,β -unsaturated carbonyl carbon (**I1**) onto which the nucleophilic silyl enol ether attacks resulting in the formation of

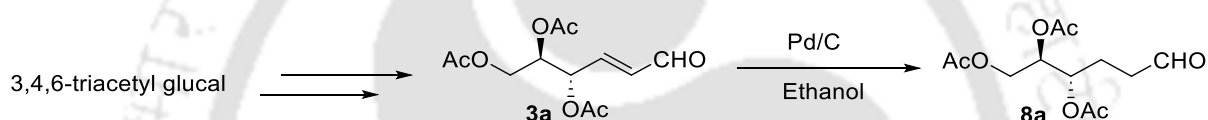
intermediate¹³ **I4**, with the expulsion of TMSCl. **I4** upon hydrolysis would lead to the observed product (Scheme 6). After hydrolysis, desired products (**B**) are forming along with water-soluble $\text{TiCl}_3(\text{OH})$. However, **I4** can also undergo elimination to provide the thermodynamically more stable dienone product upon longer reaction times.

6.2.4 Conclusion

In conclusion, we developed the synthetic procedure for the synthesis of β -hydroxy- γ,δ -unsaturated aryl ketones and conjugated $\alpha,\beta,\gamma,\delta$ diene aryl ketones (E, E) (**10**) easily. The regioselective 1,2-addition of silyl enol ethers to saturated and unsaturated Perlin aldehydes has been achieved via Mukayama aldol conditions. The influence of solvent, Lewis acids and time on the outcome of the reaction has been well-studied. These functionally rich arylpolyols could be of very high significance for the organic chemists and can be useful synthons for the synthesis of a variety of natural products. Further exploration of the synthetic utility of this interesting class of compounds is under progress in our laboratory.

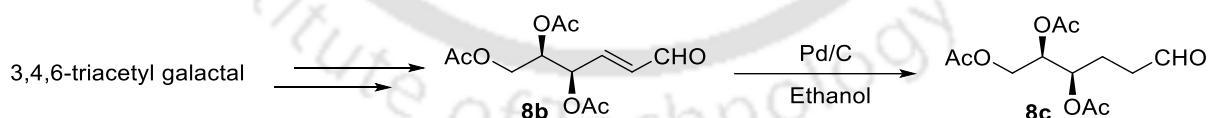
6.3 Experimental section

Preparation of 4,5,6- tri-O-acetyl-2,3-dideoxy-aldehyde-threo-hexose (**8a**).



(2E)-4,5,6-*tri-O*-acetyl-2,3-dideoxy-aldehyde-threo-hex-2-enose (**3a**) was prepared from commercially available 3,4,6-triacetyl glugal according to the reported procedure.¹⁴ Hydrogenation of **3a** with 5 mole % Pd/C led to its dihydro derivative 4,5,6- *tri-O*-acetyl-2,3-dideoxy-aldehyde-threo-hexose (**8a**) as a colorless syrup according to the reported procedure.¹⁵ ¹H NMR (400 MHz, CDCl_3) δ 9.76 (s, 1H), 5.19 – 5.13 (m, 1H), 5.13 – 5.07 (m, 1H), 4.30 (dd, J = 12.2, 3.4 Hz, 1H), 4.16 (dd, J = 12.2, 6.6 Hz, 1H), 2.53 (t, J = 7.3 Hz, 2H), 2.09 (s, 3H), 2.06 (s, 6H), 2.03 – 1.85 (m, 2H). ¹³C{¹H} NMR (101 MHz, CDCl_3) δ 200.5, 170.5, 170.1, 170.0, 71.4, 70.9, 61.8, 39.5, 22.3, 20.7, 20.7, 20.6.

Preparation of 4, 5, 6 – tri -o-acetyl-2,3-dideoxy- aldehyde-erythro-hexose (**8c**).



(2E)-4,5,6-*tri-O*-acetyl-2,3-dideoxy-aldehyde-erythro-hex-2-enose (**8b**) was prepared from commercially available 3,4,6-triacetyl galactal according to the reported procedure.¹⁴ Hydrogenation of **8b** with 5 mole % Pd/C led to its dihydro derivative 4,5,6-*tri-O*-acetyl-2,3-dideoxy-aldehyde-erythro-hexose (**8c**) as a colorless syrup according to the reported procedure.¹⁵ ¹H NMR (400 MHz, CDCl_3) δ 9.75 (s, 1H), 5.23 – 5.18 (m, 1H), 5.16 – 5.11 (m, 1H), 4.29 (dd, J = 11.9, 4.3 Hz, 1H), 4.04 (dd, J = 11.9, 6.7 Hz, 1H), 2.52 (dd, J = 15.0, 7.6 Hz, 2H), 2.11 (s, 3H), 2.08 (s, 3H), 2.06 (s, 3H), 1.96 – 1.86 (m, 2H). ¹³C{¹H} NMR (101 MHz, CDCl_3) δ 200.3, 170.5, 170.3, 170.2, 71.1, 70.6, 62.2, 39.5, 22.9, 20.7, 20.6.

General procedure A

To a solution of acetophenone in dry DCM, trimethylamine (3 equiv.) was added at 0 °C followed by TMSOTf (1.2 equiv.) at the same temperature. Upon completion of the reaction after 1h, a saturated solution of NaHCO₃ was added to quench the reaction. The crude reaction mixture was diluted with DCM, workup with water, brine, dried over Na₂SO₄, and concentrated in a rotaevaporator (bath temperature 10 °C). The crude reaction mixture was used for the next step without further purification.

Silyl enol ethers were used for this study.

All the silyl enol ether (**9a – 9p**), used for this study were made according to **general procedure A**. The spectroscopic data of the compounds (**9a -9l**)¹⁶, **9m**¹⁷, **9n**¹⁸, **9o**¹⁹ were matched with the reported data.

Synthesis of trimethyl((1-(4-propyl phenyl)vinyl)oxy)silane (**9p**)

The silyl enol ether (**9p**) was synthesized according to General procedure A.

¹H NMR (400 MHz, CDCl₃) δ 7.49 (d, *J* = 8.2 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 2H), 4.86 (d, *J* = 1.5 Hz, 1H), 4.37 (d, *J* = 1.4 Hz, 1H), 2.58 (t, *J* = 7.6 Hz 2H), 1.66 - 1.60 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H), 0.26 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 155.9, 143.0, 135.2, 128.3, 125.3, 90.4, 37.9, 24.6, 13.9, 0.2.

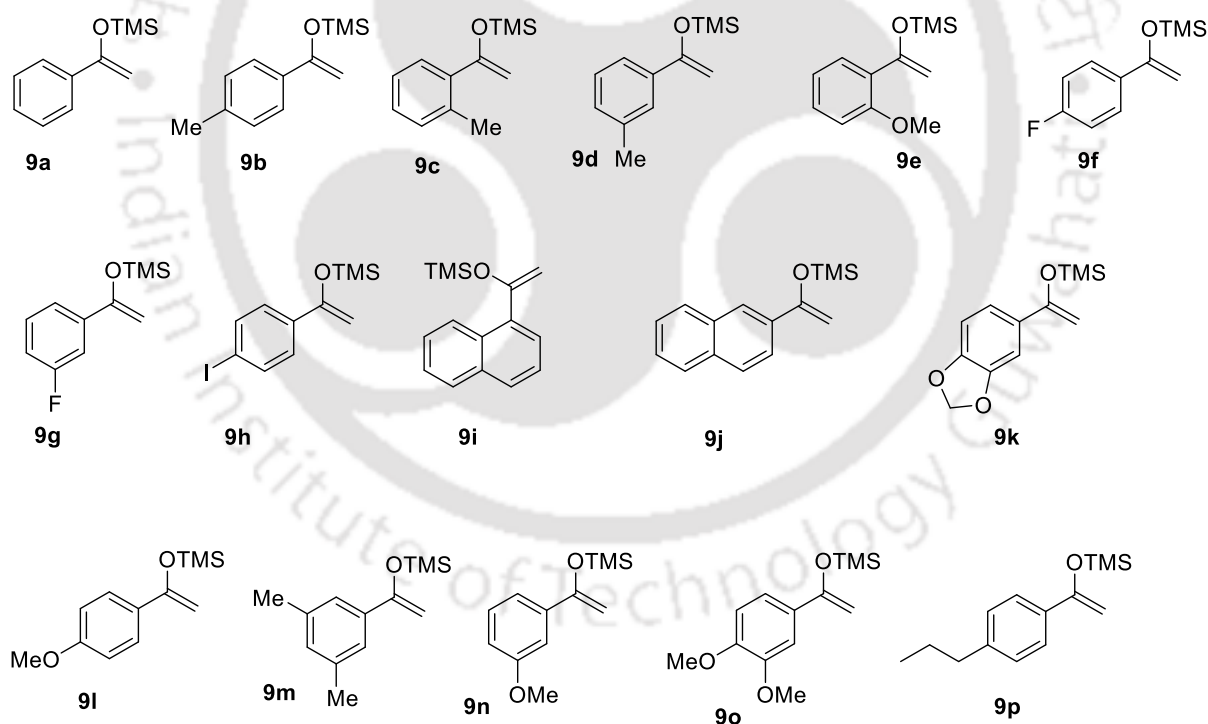


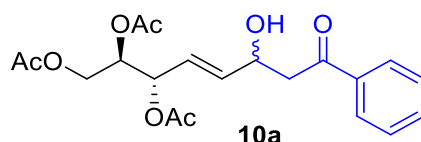
Figure 2: Synthesized silyl enol ether

General procedure B

A solution of (2E)-4,5,6-*tri-O*-acetyl-2,3-dideoxy-aldehyde-hex-2-enose **3a**, **8b** (1 equiv.) and silyl enol ether **9a-9p** (1.2 equiv.) in dry CH₂Cl₂ (0.04 M) was stirred at room temperature for 5 min under Ar atmosphere. Then the vessel was chilled to 0 °C, to which TiCl₄ (1.5 equiv.) was added. The reaction mixture was stirred for 50 min and TLC was checked. After completion of the reaction within 50 min, the temperature gradually rises to room temperature.

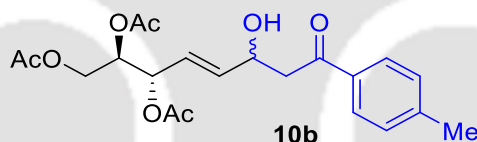
Then saturated NaHCO_3 solution was added to quench the reaction. The crude reaction mixture was worked up with water, washed with brine, dried by Na_2SO_4 , and concentrated in rotavapor. The resulting crude reaction mixture was purified through Flash column chromatography to afford the glycosylated product.

Synthesis of (2R,3S,E)-6-hydroxy-8-oxo-8-phenyloct-4-ene-1,2,3-triyl triacetate (10a)



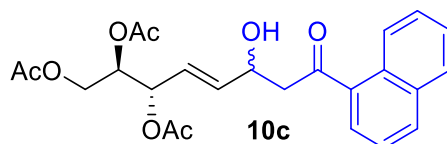
Mukaiyama aldol condensation of **3a** (55 mg, 0.20 mmol) with **9a** (48 mg, 0.25 mmol) according to General procedure B afforded **10a** (70 mg, 88 %, d.r.: 1.8:1) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.46$ (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.98 – 7.90 (m, 6H), 7.60 (t, $J = 7.4$ Hz, 3H), 7.48 (t, $J = 7.7$ Hz, 6H), 5.95 (t, $J = 4.3$ Hz, 1H), 5.92 (t, $J = 4.4$ Hz, 2H), 5.84 (d, $J = 6.8$ Hz, 2H), 5.80 (d, $J = 6.8$ Hz, 1H), 5.52 (dd, $J = 6.7, 4.6$ Hz, 3H), 5.26 – 5.17 (m, 3H), 4.84 – 4.77 (m, 3H), 4.28 (dd, $J = 3.5, 1.9$ Hz, 1H), 4.25 (dd, $J = 3.5, 1.9$ Hz, 2H), 4.19 (d, $J = 7.1$ Hz, 2H), 4.16 (d, $J = 7.1$ Hz, 1H), 3.43 (s, 2H), 3.24 – 3.10 (m, 6H), 2.09 – 2.07 (m, 18H), 2.06 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 198.7, 169.6, 169.2, 169.1, 168.7, 135.7, 135.6, 135.5, 132.7, 127.7, 127.1, 123.0, 122.9, 71.0, 70.7, 70.6, 66.4, 66.3, 60.8, 43.7, 20.0, 19.9, 19.7. $[\alpha]_D^{35} = +0.40$ (c 0.02, CHCl_3).

Synthesis of (2R,3S,E)-6-hydroxy-8-oxo-8-(p-tolyl)oct-4-ene-1,2,3-triyl triacetate (10b).



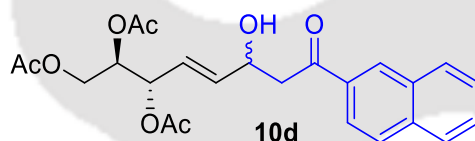
Mukaiyama aldol condensation of **3a** (48 mg, 0.18 mmol) with **9b** (44 mg, 0.21 mmol) according to General Procedure B afforded **10b** (63 mg, 88 %, d.r.: 1.9:1) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.48$ (Hexane/EtOAc = 2:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 7.84 (d, $J = 8.0$ Hz, 6H), 7.27 (d, $J = 7.0$ Hz, 6H), 5.94 (t, $J = 4.9$ Hz, 1H), 5.91 (t, $J = 4.9$ Hz, 2H), 5.83 (d, $J = 6.9$ Hz, 2H), 5.80 (d, $J = 6.9$ Hz, 1H), 5.54 – 5.49 (m, 3H), 5.25 – 5.18 (m, 3H), 4.75 – 4.81 (m, 3H), 4.26 (d, $J = 11.9$ Hz, 3H), 4.18 (d, $J = 7.1$ Hz, 2H), 4.16 (d, $J = 7.1$ Hz, 1H), 3.45 (s, 3H), 3.20 (d, $J = 3.0$ Hz, 1H), 3.17 (d, $J = 3.0$ Hz, 2H), 3.12 (d, $J = 8.6$ Hz, 2H), 3.08 (d, $J = 8.7$ Hz, 1H), 2.42 (s, 9H), 2.08 (s, 17H), 2.06 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 198.4, 169.6, 169.1, 169.1, 168.7, 143.7, 135.8, 135.7, 133.1, 128.4, 127.3, 122.9, 122.8, 71.1, 70.7, 70.7, 66.5, 66.4, 60.8, 43.5, 20.7, 20.0, 19.9, 19.7. $[\alpha]_D^{35} = +0.54$ (c 0.03, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{26}\text{O}_8\text{Na}$ 429.1520; found 429.1527.

Synthesis of (2R,3S,E)-6-hydroxy-8-(naphthalen-1-yl)-8-oxooct-4-ene-1,2,3-triyl triacetate (10c)



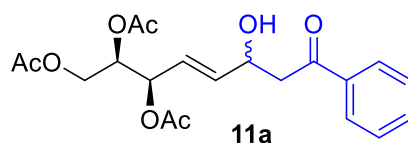
Mukaiyama aldol condensation of **3a** (55 mg, 0.20 mmol) with **9i** (60 mg, 0.25 mmol) according to General Procedure B afforded **10c** (74 mg, 83 %, d.r.: 1.8:1) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.47$ (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 8.66 (d, $J = 8.6$ Hz, 3H), 8.00 (d, $J = 8.2$ Hz, 3H), 7.88 (t, $J = 8.5$ Hz, 5H), 7.60 (t, $J = 7.3$ Hz, 3H), 7.56 – 7.47 (m, 5H), 5.99 – 5.96 (m, 1H), 5.95 – 5.92 (m, 2H), 5.85 (d, $J = 6.8$ Hz, 2H), 5.81 (d, $J = 6.8$ Hz, 1H), 5.52 (dd, $J = 6.5, 4.7$ Hz, 3H), 5.26 – 5.20 (m, 3H), 4.86 (q, $J = 5.4$ Hz, 3H), 4.28 (d, $J = 3.4$ Hz, 1H), 4.25 (d, $J = 3.4$ Hz, 2H), 4.18 (d, $J = 7.1$ Hz, 2H), 4.15 (d, $J = 7.1$ Hz, 1H), 3.48 (s, 2H), 3.26 (d, $J = 6.0$ Hz, 6H), 2.06 (dd, $J = 5.2, 2.8$ Hz, 24H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 202.5, 169.6, 169.2, 168.7, 135.9, 135.7, 134.0, 134.0, 133.0, 132.4, 129.0, 127.5, 127.4, 127.4, 127.2, 125.6, 124.6, 123.3, 123.0, 122.9, 71.0, 70.7, 70.6, 66.9, 66.8, 60.8, 47.0, 46.9, 19.9, 19.8, 19.7. $[\alpha]_D^{35} = +3.86$ (c 0.4, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{24}\text{H}_{26}\text{O}_8\text{Na}$ 465,1520; found 465.1520.

Synthesis of (2R,3S,E)-6-hydroxy-8-(naphthalen-2-yl)-8-oxooct-4-ene-1,2,3-triyl triacetate (**10d**)



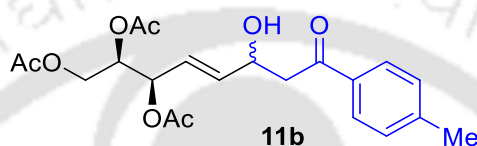
Mukaiyama aldol condensation of **3a** (53 mg, 0.19 mmol) with **9j** (58 mg, 0.24 mmol) according to General Procedure B afforded **10d** (69 mg, 80 %, d.r.: 1.9:1) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.47$ (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 8.47 (s, 3H), 8.03 – 7.96 (m, 6H), 7.92 – 7.87 (m, 6H), 7.65 – 7.54 (m, 6H), 6.00 (t, $J = 4.3$ Hz, 1H), 5.96 (t, $J = 4.3$ Hz, 2H), 5.87 (d, $J = 6.4$ Hz, 2H), 5.83 (d, $J = 6.9$ Hz, 1H), 5.55 (dd, $J = 6.6, 4.6$ Hz, 3H), 5.27 – 5.22 (m, 3H), 4.89 – 4.82 (m, 3H), 4.30 (dd, $J = 3.3, 2.4$ Hz, 1H), 4.27 (dd, $J = 3.2, 2.5$ Hz, 2H), 4.20 (d, $J = 7.1$ Hz, 2H), 4.17 (d, $J = 7.1$ Hz, 1H), 3.38 – 3.24 (m, 6H), 2.10 – 2.07 (m, 18H), 2.06 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 198.6, 169.6, 169.2, 169.2, 168.7, 135.8, 135.7, 134.8, 132.8, 131.4, 129.2, 128.7, 127.8, 127.6, 126.8, 126.0, 123.0, 122.9, 122.5, 71.1, 70.7, 70.7, 66.5, 66.4, 60.8, 43.8, 20.0, 19.9, 19.7. $[\alpha]_D^{35} = +2.67$ (c 0.2, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{24}\text{H}_{26}\text{O}_8\text{Na}$ 465,1520; found 465.1531.

Synthesis of (2R,3R,E)-6-hydroxy-8-oxo-8-phenyloct-4-ene-1,2,3-triyl triacetate (**11a**)



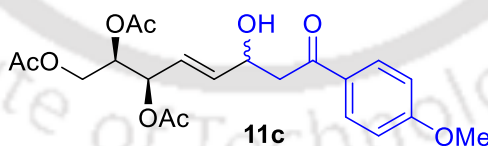
Mukaiyama aldol condensation of **8b** (50 mg, 0.18 mmol) with **9a** (44 mg, 0.23 mmol) according to General procedure B afforded **11a** (60 mg, 83 %, d.r.: 1.6:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.47 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.95 (d, J = 7.5 Hz, 5H), 7.60 (t, J = 7.3 Hz, 3H), 7.48 (t, J = 7.7 Hz, 5H), 5.95 (t, J = 4.5 Hz, 1H), 5.91 (t, J = 4.5 Hz, 2H), 5.79 (d, J = 6.9 Hz, 2H), 5.76 (d, J = 6.8 Hz, 1H), 5.53 (t, J = 6.1 Hz, 3H), 5.25 – 5.19 (m, 3H), 4.82 – 54.79 (m, 3H), 4.34 (t, J = 3.8 Hz, 1H), 4.31 (t, J = 3.8 Hz, 2H), 4.10 – 4.02 (m, 3H), 3.37 (s, 2H), 3.19 – 3.09 (m, 6H), 2.10 – 2.05 (m, 24H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 198.7, 198.6, 169.5, 169.1, 168.7, 135.8, 135.6, 135.5, 132.7, 127.7, 127.1, 123.0, 70.8, 70.7, 70.4, 70.4, 66.4, 66.4, 61.2, 43.7, 43.6, 19.9, 19.8, 19.7. $[\alpha]_D^{35} = +2.20$ (c 0.3, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{24}\text{O}_8\text{Na}$ 415.1363; found 415.1358.

Synthesis of (2R,3R,E)-6-hydroxy-8-oxo-8-(p-tolyl)oct-4-ene-1,2,3-triyl triacetate (**11b**).



Mukaiyama aldol condensation of **8b** (52 mg, 0.19 mmol) with **9b** (48 mg, 0.23 mmol) according to General Procedure B afforded **11b** (66 mg, 85 %, d.r.: 1.6:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.48 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.84 (d, J = 8.2 Hz, 5H), 7.29 – 7.25 (m, 5H), 5.96 – 5.93 (m, 1H), 5.92 – 5.89 (m, 2H), 5.79 (dt, J = 6.8, 1.7 Hz, 2H), 5.76 – 5.73 (m, 1H), 5.52 (t, J = 6.0 Hz, 3H), 5.22 (td, J = 6.1, 3.9 Hz, 3H), 4.80 – 4.72 (m, 3H), 4.34 (t, J = 3.8 Hz, 1H), 4.31 (t, J = 3.8 Hz, 2H), 4.10 – 4.02 (m, 3H), 3.43 (s, 2H), 3.22 – 3.04 (m, 6H), 2.42 (s, 8H), 2.08 (s, 15H), 2.06 (s, 7H, merged). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 198.4, 198.3, 169.5, 169.1, 168.7, 168.7, 143.7, 135.8, 135.7, 133.1, 128.4, 127.3, 122.9, 70.8, 70.8, 70.4, 70.4, 66.5, 66.4, 61.2, 43.5, 43.4, 20.7, 19.9, 19.8, 19.7. $[\alpha]_D^{35} = -1.2$ (c 0.1, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{26}\text{O}_8\text{Na}$ 429.1520; found 429.1521.

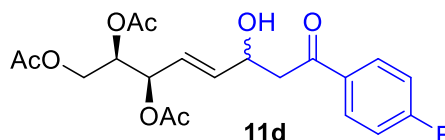
Synthesis of (2R,3R,E)-6-hydroxy-8-(4-methoxyphenyl)-8-oxooct-4-ene-1,2,3-triyl triacetate (**11c**)



Mukaiyama aldol condensation of **8b** (51 mg, 0.19 mmol) with **9l** (51 mg, 0.23 mmol) according to General Procedure B afforded **11c** (66 mg, 83 %, d.r.: 1.6:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.42 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.92 (d, J = 8.9 Hz, 5H), 6.94 (d, J = 8.9 Hz, 5H), 5.96 – 5.93 (m, 1H), 5.93 – 5.89 (m, 2H), 5.80 – 5.77 (m, 2H), 5.76 – 5.73 (m, 1H), 5.52 (t, J = 6.4 Hz, 3H), 5.22 (td, J = 6.1, 3.9 Hz, 3H), 4.80 – 4.72 (m, 3H), 4.34 (t, J = 3.9 Hz, 1H), 4.31 (t, J = 3.8 Hz, 2H), 4.06 (ddd, J = 11.9, 6.1, 4.5 Hz, 3H), 3.88 (s, 8H), 3.53 (s, 2H), 3.19 – 3.02 (m, 6H), 2.10 – 2.04 (m, 24H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 197.3, 197.2, 169.5, 169.1, 168.7, 168.7, 163.0, 135.9, 135.8, 129.4, 128.6, 122.8, 112.9, 70.8, 70.8,

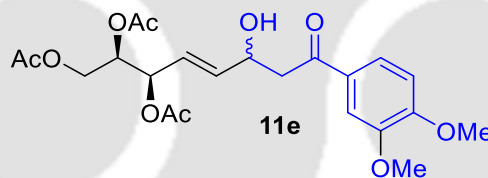
70.5, 70.4, 66.5, 66.5, 61.2, 54.5, 43.2, 43.1, 19.9, 19.8, 19.7. $[\alpha]_D^{35} = -0.93$ (c 0.06, CHCl₃). HRMS (ESI) m/z: $[M + Na]^+$ calcd for C₂₁H₂₆O₉Na 445.1469; found 445.1468.

Synthesis of (2R,3R,E)-8-(4-fluorophenyl)-6-hydroxy-8-oxooct-4-ene-1,2,3-triyl triacetate (11d)



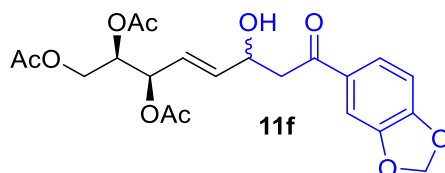
Mukaiyama aldol condensation of **8b** (53 mg, 0.19 mmol) with **9f** (50 mg, 0.24 mmol) according to General Procedure B afforded **11d** (56 mg, 70 %, d.r.: 1.6:1) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.45$ (Hexane/EtOAc = 2:1, v/v). ¹H NMR (500 MHz, CDCl₃) δ 7.98 (dd, $J = 8.6, 5.4$ Hz, 5H), 7.15 (t, $J = 8.5$ Hz, 5H), 5.94 (t, $J = 4.7$ Hz, 1H), 5.91 (t, $J = 4.7$ Hz, 2H), 5.80 – 5.77 (m, 2H), 5.77 – 5.74 (m, 1H), 5.55 – 5.49 (m, 3H), 5.23 (dd, $J = 9.9, 6.0$ Hz, 3H), 4.81 – 4.74 (m, 3H), 4.32 (ddd, $J = 11.8, 5.5, 4.0$ Hz, 3H), 4.07 (ddd, $J = 12.1, 8.1, 6.4$ Hz, 3H), 3.31 (s, 2H), 3.19 – 3.07 (m, 6H), 2.09 (s, 16H), 2.06 (s, 8H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 197.0, 196.9, 169.5, 169.1, 168.7, 168.7, 166.1, 164.1, 135.7, 135.5, 132.0, 132.0, 129.9, 129.8, 123.1, 115.0, 114.8, 70.8, 70.7, 70.4, 70.4, 66.4, 66.3, 61.2, 43.7, 43.6, 19.9, 19.8, 19.7. $[\alpha]_D^{35} = +0.47$ (c 0.05, CHCl₃). HRMS (ESI) m/z: $[M + Na]^+$ calcd for C₂₀H₂₃FO₈Na 433.1269; found 433.1268.

Synthesis of (2R, 3R, E)-8-(3,4-dimethoxyphenyl)-6-hydroxy-8-oxooct-4-ene-1,2,3-triyl triacetate (11e)



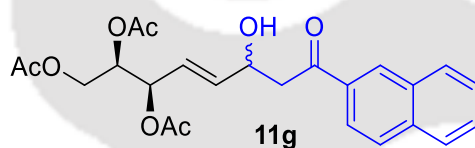
Mukaiyama aldol condensation of **8b** (49 mg, 0.18 mmol) with **9o** (55 mg, 0.22 mmol) according to General Procedure B afforded **11e** (65 mg, 80 %, d.r.: 1.6:1) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.39$ (Hexane/EtOAc = 2:1, v/v). ¹H NMR (500 MHz, CDCl₃) δ 7.57 (d, $J = 8.3$ Hz, 3H), 7.51 (s, 3H), 6.90 (d, $J = 8.4$ Hz, 3H), 5.95 (t, $J = 4.9$ Hz, 1H), 5.92 (t, $J = 4.9$ Hz, 2H), 5.81 – 5.74 (m, 3H), 5.53 (t, $J = 6.2$ Hz, 3H), 5.22 (dd, $J = 9.8, 5.9$ Hz, 3H), 4.80 – 4.72 (m, 3H), 4.32 (ddd, $J = 10.8, 6.5, 3.9$ Hz, 3H), 4.10 – 4.03 (m, 3H), 3.96 (s, 8H), 3.94 (s, 9H), 3.52 (s, 2H), 3.19 – 3.04 (m, 6H), 2.10 – 2.05 (m, 24H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 197.3, 197.2, 169.5, 169.1, 168.7, 168.7, 152.9, 148.2, 135.9, 135.8, 128.8, 128.8, 122.9, 122.1, 109.1, 109.0, 70.8, 70.8, 70.4, 66.6, 66.5, 61.2, 55.1, 55.0, 43.1, 43.1, 19.9, 19.8, 19.7. $[\alpha]_D^{35} = +0.33$ (c 0.03, CHCl₃).

Synthesis of (2R,3R,E)-8-(benzo[δ][1,3]dioxol-5-yl)-6-hydroxy-8-oxooct-4-ene-1,2,3-triyl triacetate (11f)



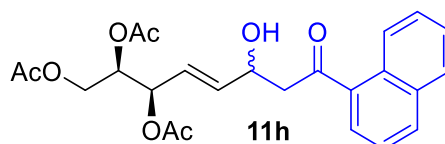
Mukaiyama aldol condensation of **8b** (47 mg, 0.17 mmol) with **9k** (50 mg, 0.21 mmol) according to General Procedure B afforded **11f** (59 mg, 78 %, d.r.: 1.6:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.42 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.54 (d, J = 8.1 Hz, 3H), 7.41 (s, 2H), 6.86 (d, J = 8.2 Hz, 2H), 6.06 (s, 5H), 5.94 (t, J = 4.4 Hz, 1H), 5.90 (t, J = 4.4 Hz, 2H), 5.78 (d, J = 6.7 Hz, 2H), 5.74 (d, J = 6.7 Hz, 1H), 5.52 (t, J = 6.1 Hz, 3H), 5.22 (dd, J = 9.9, 6.0 Hz, 3H), 4.79 – 4.71 (m, 3H), 4.33 (t, J = 3.9 Hz, 1H), 4.30 (t, J = 3.9 Hz, 2H), 4.10 – 4.02 (m, 3H), 3.45 (s, 2H), 3.16 – 2.99 (m, 6H), 2.09 (s, 15H), 2.06 (s, 8H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 196.7, 196.6, 169.5, 169.1, 168.7, 151.3, 147.3, 135.8, 135.7, 130.4, 123.7, 122.9, 107.0, 106.7, 101.0, 70.8, 70.7, 70.4, 70.4, 66.5, 66.4, 61.2, 43.4, 43.3, 19.9, 19.7, 19.7. $[\alpha]_{\text{D}}^{35}$ = - 0.73 (c 0.03, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{24}\text{O}_{10}\text{Na}$ 459.1262; found 459.1262.

Synthesis of (2R,3R,E)-6-hydroxy-8-(naphthalen-2-yl)-8-oxooct-4-ene-1,2,3-triyl triacetate (**11g**)



Mukaiyama aldol condensation of **8b** (53 mg, 0.19 mmol) with **9j** (58 mg, 0.24 mmol) according to General Procedure B afforded **11g** (70 mg, 81 %, d.r.: 1.5:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.48 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 8.46 (s, 3H), 8.03 – 7.95 (m, 5H), 7.93 – 7.85 (m, 5H), 7.66 – 7.54 (m, 5H), 6.00 (t, J = 4.2 Hz, 1H), 5.96 (t, J = 4.2 Hz, 2H), 5.83 (dt, J = 6.8, 1.5 Hz, 2H), 5.79 (dt, J = 6.8, 1.5 Hz, 1H), 5.54 (t, J = 6.4 Hz, 3H), 5.24 (td, J = 6.1, 3.9 Hz, 3H), 4.88 – 4.80 (m, 3H), 4.35 (t, J = 3.9 Hz, 1H), 4.32 (t, J = 3.9 Hz, 2H), 4.12 – 4.04 (m, 3H), 3.48 (s, 2H), 3.38 – 3.22 (m, 6H), 2.11 – 2.02 (m, 24H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 198.6, 198.5, 169.5, 169.1, 168.7, 135.8, 135.7, 134.8, 132.9, 132.9, 131.4, 129.2, 128.7, 127.8, 127.6, 126.8, 126.0, 123.0, 123.0, 122.5, 70.8, 70.8, 70.5, 70.4, 66.5, 66.5, 61.2, 43.8, 43.7, 19.9, 19.8, 19.7. $[\alpha]_{\text{D}}^{35}$ = + 0.22 (c 0.01, CHCl_3).

Synthesis of (2R,3R,E)-6-hydroxy-8-(naphthalen-1-yl)-8-oxooct-4-ene-1,2,3-triyl triacetate (**11h**)



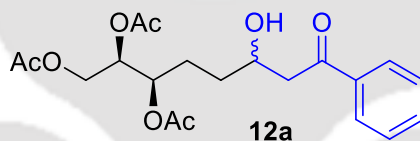
Mukaiyama aldol condensation of **8b** (58 mg, 0.21 mmol) with **9i** (63 mg, 0.26 mmol) according to General Procedure B afforded **11h** (74 mg, 79 %, d.r.:1.6:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.47

(Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 8.66 (d, J = 8.6 Hz, 3H), 8.01 (d, J = 8.2 Hz, 3H), 7.89 (t, J = 7.8 Hz, 5H), 7.65 – 7.58 (m, 3H), 7.57 – 7.46 (m, 6H), 5.98 (t, J = 4.1 Hz, 1H), 5.94 (t, J = 4.2 Hz, 2H), 5.81 (dd, J = 6.8, 1.3 Hz, 2H), 5.77 (dd, J = 6.8, 1.3 Hz, 1H), 5.55 – 5.49 (m, 3H), 5.23 (td, J = 6.1, 4.0 Hz, 3H), 4.89 – 4.80 (m, 3H), 4.34 (t, J = 4.1 Hz, 1H), 4.31 (t, J = 4.1 Hz, 2H), 4.11 – 4.02 (m, 3H), 3.42 (s, 2H), 3.29 – 3.22 (m, 6H), 2.09 – 2.04 (m, 24H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 202.5, 202.4, 169.5, 169.1, 168.7, 135.8, 135.7, 134.0, 134.0, 133.0, 132.4, 129.0, 127.5, 127.4, 127.2, 125.6, 124.6, 123.3, 123.0, 70.7, 70.7, 70.4, 70.4, 66.9, 66.8, 61.1, 46.8, 46.8, 19.9, 19.8, 19.7. $[\alpha]_{\text{D}}^{35} = +3.20$ (c 0.2, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{24}\text{H}_{26}\text{O}_8\text{Na}$ 465.1520; found 464.1219.

General Procedure C

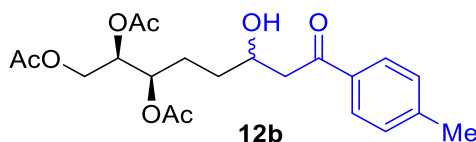
A solution of glycosyl donor **8a**, **8c** (1 equiv.) and silyl enol ether **5a-5p** (1.2 equiv.) in dry CH_2Cl_2 (0.03 M) was stirred at room temperature for 5 min under Ar atmosphere. Then the vessel was chilled to 0 °C, to which TiCl_4 (1.8 equiv.) was added. The reaction mixture was stirred for 50 min and TLC were checked. After completion of the reaction within 50 min, the temperature gradually rises to room temperature. Then saturated NaHCO_3 solution was added to quench the reaction. The crude reaction mixture was worked up with water, washed with brine, dried by Na_2SO_4 , concentrated in rotavapor. The resulting crude reaction mixture was purified through Flash column chromatography to afford the glycosylated product.

Synthesis of (2R,3R)-6-hydroxy-8-oxo-8-phenyloctane-1,2,3-triyl triacetate (**12a**)



Mukaiyama aldol condensation of **8c** (62 mg, 0.23 mmol) with **9a** (53 mg, 0.28 mmol) according to General Procedure C afforded **12a** (79 mg, 89 %, d.r.: 1.3:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.42 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.94 (d, J = 7.7 Hz, 5H), 7.59 (t, J = 7.4 Hz, 2H), 7.47 (t, J = 7.7 Hz, 5H), 5.28 – 5.15 (m, 6H), 4.32 (d, J = 4.2 Hz, 1H), 4.29 (d, J = 4.2 Hz, 1H), 4.25 – 4.15 (m, 2H), 4.05 (ddd, J = 11.6, 6.8, 3.0 Hz, 2H), 3.38 (d, J = 12.5 Hz, 2H), 3.18 – 3.00 (m, 5H), 2.11 (s, 7H), 2.09 (s, 7H), 2.05 (s, 7H), 1.97 – 1.81 (m, 3H), 1.76 – 1.66 (m, 2H), 1.66 – 1.47 (m, 5H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 199.5, 199.4, 169.6, 169.4, 169.4, 169.2, 169.2, 135.7, 132.6, 127.7, 127.1, 70.7, 70.2, 70.1, 66.3, 66.0, 61.4, 61.4, 44.1, 44.1, 31.1, 30.8, 25.7, 25.6, 19.8, 19.8, 19.7. $[\alpha]_{\text{D}}^{35} = +9.97$ (c 0.8, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{26}\text{O}_8\text{Na}$ 417.1520; found 417.1529.

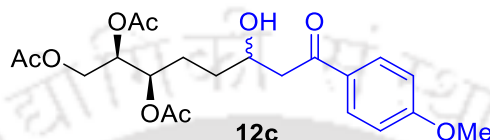
Synthesis of (2R,3R)-6-hydroxy-8-oxo-8-(*p*-tolyl)octane-1,2,3-triyl triacetate (**12b**)



Mukaiyama aldol condensation of **8c** (55 mg, 0.20 mmol) with **9b** (50 mg, 0.24 mmol) according to General Procedure C afforded **12b** (74 mg, 90 %, d.r.: 1.3:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.43 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 7.84 (d, J = 7.8 Hz, 5H), 7.27 (d, J

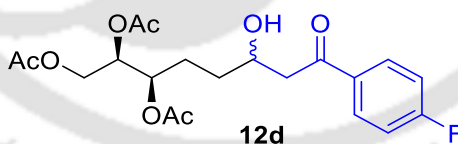
= 7.9 Hz, 5H), 5.28 – 5.14 (m, 5H), 4.32 (d, J = 4.0 Hz, 1H), 4.30 (d, J = 4.0 Hz, 1H), 4.23 – 4.15 (m, 2H), 4.09 – 3.99 (m, 2H), 3.40 (s, 2H), 3.12 (d, J = 17.7 Hz, 2H), 3.06 – 2.96 (m, 2H), 2.42 (s, 7H), 2.11 (s, 7H), 2.09 (s, 7H), 2.05 (s, 7H), 1.95 – 1.82 (m, 3H), 1.75 – 1.65 (m, 2H), 1.64 – 1.47 (m, 5H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 199.3, 199.1, 169.6, 169.4, 169.4, 169.2, 169.2, 143.5, 133.2, 128.4, 127.2, 70.7, 70.3, 70.2, 70.1, 66.4, 66.1, 61.4, 61.4, 43.9, 43.9, 31.1, 30.8, 25.7, 25.7, 20.7, 19.8, 19.8, 19.7. $[\alpha]_{\text{D}}^{35} = -1.99$ (c 0.1, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{21}\text{H}_{32}\text{NO}_8$ 426.2122; found 426.2126.

Synthesis of (2R,3R)-6-hydroxy-8-(4-methoxyphenyl)-8-oxooctane-1,2,3-triyl triacetate (12c)



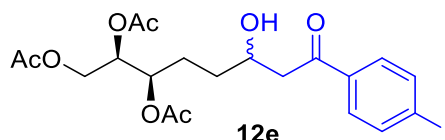
Mukaiyama aldol condensation of **8c** (50 mg, 0.18 mmol) with **9l** (49 mg, 0.22 mmol) according to General Procedure C afforded **12c** (71 mg, 92 %, d.r.: 1.3:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.39 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.92 (d, J = 8.7 Hz, 4H), 6.94 (d, J = 8.8 Hz, 4H), 5.28 – 5.13 (m, 5H), 4.32 (d, J = 4.2 Hz, 1H), 4.29 (d, J = 4.2 Hz, 1H), 4.22 – 4.12 (m, 2H), 4.04 (ddd, J = 11.5, 6.7, 2.8 Hz, 2H), 3.88 (s, 7H), 3.46 (d, J = 17.3 Hz, 2H), 3.10 (dt, J = 17.5, 2.5 Hz, 2H), 3.03 – 2.92 (m, 2H), 2.11 (s, 6H), 2.09 (s, 7H), 2.05 (s, 7H), 1.95 – 1.81 (m, 3H), 1.76 – 1.65 (m, 2H), 1.55 – 1.45 (m, 5H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 198.1, 198.0, 169.6, 169.4, 169.4, 169.2, 169.2, 162.9, 129.4, 128.8, 112.9, 70.7, 70.3, 70.2, 70.1, 66.5, 66.2, 61.4, 61.4, 54.5, 43.6, 43.5, 31.1, 30.9, 25.7, 25.7, 19.8, 19.8, 19.7. $[\alpha]_{\text{D}}^{35} = +13.99$ (c 0.6, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{21}\text{H}_{32}\text{NO}_9$ 442.2072; found 442.2078.

Synthesis of (2R,3R)-8-(4-fluorophenyl)-6-hydroxy-8-oxooctane-1,2,3-triyl triacetate (12d)



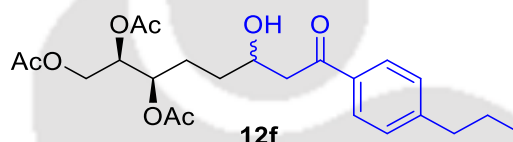
Mukaiyama aldol condensation of **8c** (51 mg, 0.19 mmol) with **9f** (48 mg, 0.23 mmol) according to General Procedure C afforded **12d** (60 mg, 78 %, d.r.: 1.3:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.43 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 8.04 – 7.89 (m, 5H), 7.14 (t, J = 8.4 Hz, 5H), 5.28 – 5.14 (m, 5H), 4.32 (d, J = 4.0 Hz, 1H), 4.29 (d, J = 4.0 Hz, 1H), 4.24 – 4.15 (m, 2H), 4.07 – 4.01 (m, 2H), 3.30 (s, 2H), 3.13 – 2.98 (m, 5H), 2.11 (s, 7H), 2.09 (s, 7H), 2.05 (s, 7H), 1.95 – 1.82 (m, 3H), 1.76 – 1.65 (m, 2H), 1.64 – 1.48 (m, 5H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 197.8, 197.7, 169.6, 169.4, 169.4, 169.2, 169.2, 166.1, 164.0, 129.8, 129.7, 114.9, 114.8, 70.7, 70.2, 70.1, 66.3, 66.0, 61.4, 61.4, 44.1, 44.0, 31.0, 30.8, 25.7, 25.6, 19.8, 19.8, 19.7. $[\alpha]_{\text{D}}^{35} = +5.69$ (c 0.4, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{25}\text{FO}_8\text{Na}$ 435.1426; found 435.1435.

Synthesis of (2R,3R)-6-hydroxy-8-(4-iodophenyl)-8-oxooctane-1,2,3-triyl triacetate (12e)



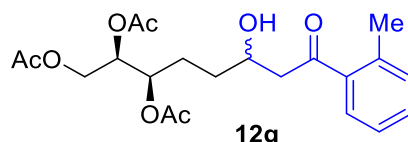
Mukaiyama aldol condensation of **8c** (52 mg, 0.19 mmol) with **9h** (74 mg, 0.23 mmol) according to General Procedure C afforded **12e** (84 mg, 85 %, d.r.:1.3:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.42 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.84 (d, J = 8.4 Hz, 4H), 7.64 (d, J = 8.3 Hz, 4H), 5.28 – 5.13 (m, 5H), 4.32 (d, J = 4.2 Hz, 1H), 4.29 (d, J = 4.2 Hz, 1H), 4.24 – 4.15 (m, 2H), 4.04 (ddd, J = 11.5, 6.8, 2.8 Hz, 2H), 3.23 (s, 2H), 3.12 – 2.94 (m, 5H), 2.11 (s, 6H), 2.09 (s, 6H), 2.05 (s, 6H), 1.94 – 1.81 (m, 3H), 1.76 – 1.65 (m, 3H), 1.64 – 1.45 (m, 5H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 198.8, 198.6, 169.6, 169.4, 169.4, 169.2, 169.2, 137.1, 134.9, 128.4, 100.7, 70.7, 70.2, 70.1, 66.2, 65.9, 61.4, 61.4, 44.1, 44.0, 31.0, 30.8, 25.7, 25.6, 19.9, 19.8, 19.7. $[\alpha]_D^{35} = +2.99$ (c 0.3, CHCl_3).

Synthesis of (2R,3R)-6-hydroxy-8-oxo-8-(4-propylphenyl)octane-1,2,3-triyl triacetate (**12f**)



Mukaiyama aldol condensation of **8c** (53 mg, 0.19 mmol) with **9p** (54 mg, 0.23 mmol) according to General Procedure C afforded **12f** (73 mg, 87 %, d.r.: 1.3:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.46 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.86 (d, J = 8.1 Hz, 5H), 7.31 – 7.22 (m, 5H), 5.28 – 5.15 (m, 5H), 4.32 (d, J = 4.2 Hz, 1H), 4.29 (d, J = 4.2 Hz, 1H), 4.25 – 4.14 (m, 2H), 4.05 (ddd, J = 11.7, 6.8, 2.9 Hz, 2H), 3.42 (d, J = 17.3 Hz, 2H), 3.12 (dt, J = 17.6, 2.6 Hz, 2H), 3.02 (dt, J = 17.6, 8.8 Hz, 2H), 2.68 – 2.61 (m, 5H), 2.11 (s, 7H), 2.09 (s, 7H), 2.05 (s, 7H), 1.90 – 1.82 (m, 4H), 1.77 – 1.47 (m, 12H), 0.95 (t, J = 7.3 Hz, 7H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 199.3, 199.2, 169.6, 169.4, 169.4, 169.2, 169.2, 148.2, 133.4, 127.8, 127.2, 70.7, 70.3, 70.3, 70.1, 66.4, 66.1, 61.4, 61.4, 43.9, 43.9, 37.0, 31.1, 30.9, 25.8, 25.7, 23.1, 19.8, 19.8, 19.7, 12.7. $[\alpha]_D^{35} = +3.13$ (c 0.3, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{33}\text{O}_8$ 437.2170; found 437.2157.

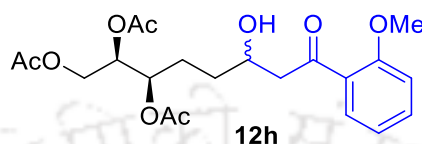
Synthesis of (2R,3R)-6-hydroxy-8-oxo-8-(o-tolyl)octane-1,2,3-triyl triacetate (**12g**)



Mukaiyama aldol condensation of **8c** (49 mg, 0.18 mmol) with **9c** (46 mg, 0.22 mmol) according to General Procedure C afforded **12g** (61 mg, 84 %, d.r.:1.3:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.43 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 7.64 (d, J = 7.6 Hz, 2H), 7.39 (t, J = 7.4 Hz, 2H), 7.30 – 7.23 (m, 4H), 5.27 – 5.14 (m, 5H), 4.32 (d, J = 4.1 Hz, 1H), 4.29 (d, J = 4.1 Hz, 1H), 4.21 – 4.14 (m, 2H), 4.08 – 4.02 (m, 2H), 3.36 (s, 2H), 3.10 – 2.93 (m, 5H), 2.11

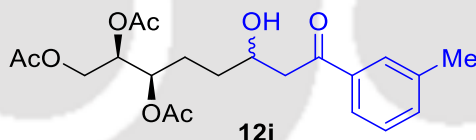
(s, 7H), 2.08 (s, 7H), 2.05 (s, 8H), 1.93 – 1.81 (m, 3H), 1.75 – 1.64 (m, 2H), 1.62 – 1.46 (m, 5H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 203.4, 203.3, 169.6, 169.4, 169.4, 169.2, 137.5, 137.4, 136.3, 136.2, 131.2, 130.8, 130.8, 127.8, 127.8, 124.8, 70.7, 70.3, 70.2, 70.1, 66.6, 66.3, 61.4, 61.4, 46.8, 46.8, 31.1, 30.8, 25.7, 25.6, 20.4, 20.4, 19.8, 19.8, 19.7. $[\alpha]_{\text{D}}^{35} = +5.99$ (c 0.4, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{21}\text{H}_{32}\text{NO}_8$ 426.2122; found 426.2124.

Synthesis of (2R,3R)-6-hydroxy-8-(2-methoxyphenyl)-8-oxooctane-1,2,3-triyl triacetate (12h)



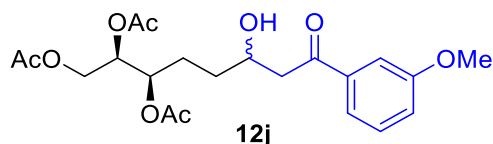
Mukaiyama aldol condensation of **8c** (49 mg, 0.18 mmol) with **9n** (49 mg, 0.22 mmol) according to General Procedure C afforded **12h** (65 mg, 86 %, d.r.: 1.5:1) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.39$ (Hexane/ $\text{EtOAc} = 2:1$, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.73 (d, $J = 7.6$ Hz, 2H), 7.49 (t, $J = 7.5$ Hz, 2H), 7.06 – 6.93 (m, 4H), 5.27 – 5.14 (m, 5H), 4.32 (d, $J = 4.1$ Hz, 1H), 4.29 (d, $J = 4.2$ Hz, 2H), 4.17 – 4.01 (m, 5H), 3.92 (s, 6H), 3.34 (d, $J = 22.9$ Hz, 2H), 3.20 (dt, $J = 18.1, 2.2$ Hz, 2H), 3.09 – 2.98 (m, 2H), 2.11 (s, 7H), 2.09 (s, 7H), 2.05 (s, 7H), 1.95 – 1.81 (m, 4H), 1.74 – 1.45 (m, 12H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 201.7, 201.5, 169.6, 169.4, 169.4, 169.2, 169.2, 158.0, 158.0, 133.2, 133.2, 129.4, 126.6, 126.6, 119.8, 110.7, 70.8, 70.4, 70.3, 70.1, 66.7, 66.5, 61.4, 61.4, 54.5, 49.5, 49.4, 31.0, 30.9, 25.8, 19.9, 19.8, 19.7. $[\alpha]_{\text{D}}^{35} = +5.19$ (c 0.3, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{29}\text{O}_9$ 425.1806; found 425.1796.

Synthesis of (2R,3R)-6-hydroxy-8-oxo-8-(m-tolyl)octane-1,2,3-triyl triacetate (12i)



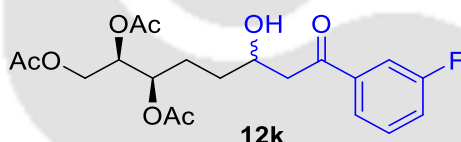
Mukaiyama aldol condensation of **8c** (57 mg, 0.21 mmol) with **9d** (52 mg, 0.25 mmol) according to General Procedure C afforded **12i** (73 mg, 86 %, d.r.:1.2:1) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.44$ (Hexane/ $\text{EtOAc} = 2:1$, v/v). ^1H NMR (500 MHz, CDCl_3) δ 7.73 (d, $J = 11.9$ Hz, 4H), 7.40 (d, $J = 7.4$ Hz, 2H), 7.35 (t, $J = 7.5$ Hz, 2H), 5.27 – 5.15 (m, 5H), 4.32 (d, $J = 4.1$ Hz, 1H), 4.30 (d, $J = 4.1$ Hz, 1H), 4.23 – 4.15 (m, 2H), 4.08 – 4.01 (m, 2H), 3.36 (d, $J = 21.4$ Hz, 2H), 3.13 (d, $J = 17.9$ Hz, 2H), 3.09 – 2.98 (m, 2H), 2.42 (s, 7H), 2.11 (s, 7H), 2.09 (s, 7H), 2.05 (s, 7H), 1.96 – 1.83 (m, 3H), 1.75 – 1.65 (m, 3H), 1.65 – 1.47 (m, 5H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 199.8, 199.7, 169.6, 169.4, 169.4, 169.2, 169.2, 137.5, 135.7, 133.4, 127.6, 124.3, 70.7, 70.3, 70.3, 70.1, 66.4, 66.1, 61.4, 61.4, 44.1, 44.1, 31.1, 30.8, 25.7, 25.6, 20.3, 19.9, 19.8, 19.8, 19.7. $[\alpha]_{\text{D}}^{35} = +2.53$ (c 0.3, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{29}\text{O}_8$ 409.1857; found 409.1847.

Synthesis of (2R,3R)-6-hydroxy-8-(3-methoxyphenyl)-8-oxooctane-1,2,3-triyl triacetate (12j)



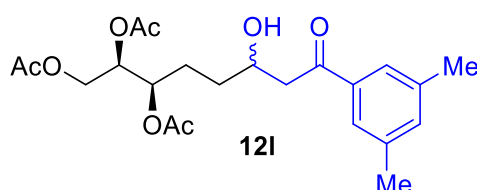
Mukaiyama aldol condensation of **8c** (52 mg, 0.19 mmol) with **9n** (51 mg, 0.23 mmol) according to General Procedure C afforded **12j** (68 mg, 84 %, d.r.:1.3:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.39 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 7.51 (d, J = 7.6 Hz, 2H), 7.46 (s, 2H), 7.38 (t, J = 7.9 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 5.28 – 5.15 (m, 5H), 4.32 (d, J = 4.1 Hz, 1H), 4.30 (d, J = 4.1 Hz, 1H), 4.24 – 4.15 (m, 2H), 4.08 – 4.02 (m, 2H), 3.86 (s, 7H), 3.31 (s, 2H), 3.16 – 2.98 (m, 5H), 2.11 (s, 7H), 2.09 (s, 7H), 2.05 (s, 7H), 1.95 – 1.82 (m, 3H), 1.75 – 1.65 (m, 3H), 1.64 – 1.47 (m, 5H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 199.4, 199.3, 169.6, 169.4, 169.4, 169.2, 169.2, 158.9, 137.0, 128.7, 119.7, 119.1, 111.3, 70.7, 70.3, 70.1, 66.4, 66.1, 61.4, 61.4, 54.5, 44.2, 44.2, 31.0, 30.8, 25.8, 25.7, 19.8, 19.8, 19.7. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{28}\text{O}_9\text{Na}$ 447.1626; found 447.1629. $[\alpha]_D^{35} = +0.93$ (c 0.07, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{28}\text{O}_9\text{Na}$ 447.1626; found 447.1629.

Synthesis of (2R,3R)-8-(3-fluorophenyl)-6-hydroxy-8-oxooctane-1,2,3-triyl triacetate (**12k**)



Mukaiyama aldol condensation of **8c** (55 mg, 0.20 mmol) with **9g** (51 mg, 0.24 mmol) according to General Procedure C afforded **12k** (63 mg, 76 %, d.r.:1.3:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.42 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.72 (d, J = 7.7 Hz, 2H), 7.62 (d, J = 9.3 Hz, 2H), 7.46 (td, J = 7.9, 5.6 Hz, 2H), 7.29 (td, J = 8.0, 2.3 Hz, 2H), 5.28 – 5.14 (m, 5H), 4.32 (d, J = 4.2 Hz, 1H), 4.29 (d, J = 4.2 Hz, 1H), 4.25 – 4.16 (m, 2H), 4.05 (ddd, J = 11.4, 6.8, 2.8 Hz, 2H), 3.25 (s, 2H), 3.14 – 2.99 (m, 5H), 2.11 (s, 6H), 2.09 (s, 7H), 2.05 (s, 7H), 1.97 – 1.81 (m, 4H), 1.77 – 1.66 (m, 2H), 1.65 – 1.49 (m, 5H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 198.2, 198.1, 169.6, 169.5, 169.4, 169.3, 169.2, 162.9, 160.9, 137.7, 137.7, 129.4, 129.4, 122.9, 122.9, 119.7, 119.5, 113.9, 113.7, 70.7, 70.2, 70.1, 66.2, 65.9, 61.4, 61.4, 44.4, 44.4, 31.0, 30.8, 25.7, 25.6, 19.8, 19.8, 19.7. $[\alpha]_D^{35} = +0.1$ (c 0.3, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{25}\text{FO}_8\text{Na}$ 435.1426; found 435.1432.

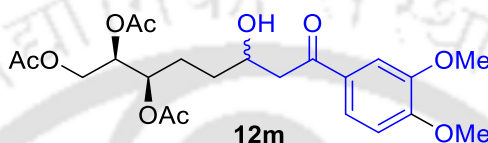
Synthesis of (2R,3R)-8-(3,5-dimethylphenyl)-6-hydroxy-8-oxooctane-1,2,3-triyl triacetate (**12l**)



Mukaiyama aldol condensation of **8c** (56 mg, 0.20 mmol) with **9m** (54 mg, 0.24 mmol) according to General Procedure C afforded **12l** (73 mg, 85 %, d.r.:1.2:1) as a colorless syrup.

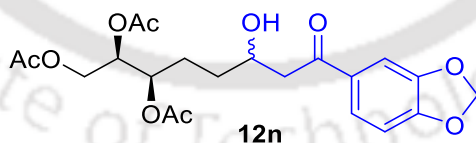
The crude product was purified through flash column chromatography, $R_f = 0.48$ (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.54 (s, 4H), 7.22 (s, 2H), 5.28 – 5.14 (m, 5H), 4.32 (d, $J = 4.2$ Hz, 1H), 4.29 (d, $J = 4.2$ Hz, 1H), 4.22 – 4.14 (m, 2H), 4.09 – 4.01 (m, 2H), 3.36 (d, $J = 18.6$ Hz, 2H), 3.12 (dt, $J = 17.6, 2.7$ Hz, 2H), 3.00 (dt, $J = 17.8, 9.0$ Hz, 2H), 2.37 (s, 12H), 2.11 (s, 6H), 2.09 (s, 6H), 2.05 (s, 6H), 1.96 – 1.82 (m, 3H), 1.76 – 1.49 (m, 10H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 200.1, 200.0, 169.6, 169.4, 169.4, 169.2, 169.2, 137.4, 135.8, 134.3, 124.9, 70.7, 70.3, 70.3, 70.1, 66.4, 66.1, 61.4, 61.4, 44.1, 44.1, 31.1, 30.8, 25.8, 25.7, 20.2, 19.8, 19.8, 19.7. $[\alpha]_{\text{D}}^{35} = +0.31$ (c 0.01, CHCl_3). $[\alpha]_{\text{D}}^{35} = +1.00$ (c 0.09, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{22}\text{H}_{34}\text{NO}_8$ 440.2879; found 440.2880.

Synthesis of (2R,3R)-8-(3,4-dimethoxyphenyl)-6-hydroxy-8-oxooctane-1,2,3-triyl triacetate (12m)



Mukaiyama aldol condensation of **8c** (48 mg, 0.18 mmol) with **9o** (55 mg, 0.22 mmol) according to General Procedure C afforded **12m** (70 mg, 87 %, d.r.:1.4:1) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.36$ (Hexane/EtOAc = 2:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 7.56 (d, $J = 8.3$ Hz, 2H), 7.50 (s, 2H), 6.90 (d, $J = 8.4$ Hz, 2H), 5.28 – 5.15 (m, 5H), 4.32 (d, $J = 3.8$ Hz, 1H), 4.30 (d, $J = 3.8$ Hz, 1H), 4.22 – 4.14 (m, 2H), 4.08 – 4.02 (m, 2H), 3.96 (s, 6H), 3.94 (s, 7H), 3.41 (d, $J = 21.1$ Hz, 2H), 3.15 – 3.08 (m, 2H), 3.05 – 2.94 (m, 2H), 2.11 (s, 7H), 2.09 (s, 7H), 2.05 (s, 7H), 1.94 – 1.83 (m, 3H), 1.76 – 1.65 (m, 3H), 1.65 – 1.47 (m, 5H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 198.2, 198.1, 169.6, 169.4, 169.4, 169.2, 169.2, 152.8, 148.2, 128.9, 122.0, 109.1, 109.0, 70.8, 70.3, 70.2, 70.1, 66.6, 66.3, 61.4, 61.4, 55.1, 55.0, 43.5, 43.45, 31.1, 30.9, 25.8, 25.7, 19.9, 19.8, 19.8, 19.7. $[\alpha]_{\text{D}}^{35} = +5.80$ (c 0.2, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{30}\text{O}_{10}\text{Na}$ 477.1731; found 477.1733.

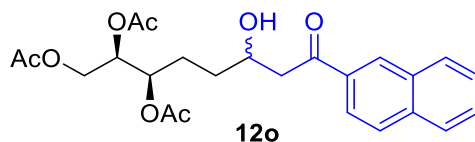
Synthesis of (2R,3R)-8-(benzo[δ][1,3]dioxol-5-yl)-6-hydroxy-8-oxooctane-1,2,3-triyl triacetate (12n)



Mukaiyama aldol condensation of **8c** (57 mg, 0.21 mmol) with **9k** (60 mg, 0.25 mmol) according to General Procedure C afforded **12n** (73 mg, 80 %, d.r.: 1.4:1) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.37$ (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.54 (d, $J = 8.1$ Hz, 2H), 7.41 (s, 2H), 6.85 (d, $J = 8.2$ Hz, 2H), 6.05 (s, 5H), 5.28 – 5.13 (m, 5H), 4.32 (d, $J = 4.2$ Hz, 1H), 4.29 (d, $J = 4.2$ Hz, 1H), 4.21 – 4.11 (m, 2H), 4.09 – 4.00 (m, 3H), 3.38 (d, $J = 17.0$ Hz, 2H), 3.11 – 2.89 (m, 5H), 2.11 (s, 6H), 2.09 (s, 7H), 2.05 (s, 7H), 1.95 – 1.80 (m, 3H), 1.76 – 1.64 (m, 3H), 1.63 – 1.45 (m, 5H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 197.6, 197.4, 169.6, 169.4, 169.4, 169.2, 169.2, 151.2, 147.3, 130.6, 123.6, 106.9, 106.7, 101.0, 70.7, 70.2, 70.1, 66.5,

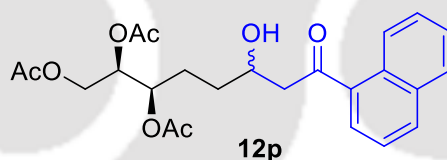
66.1, 61.4, 61.4, 43.8, 43.7, 31.0, 30.8, 25.7, 25.7, 19.8, 19.8, 19.7. $[\alpha]_D^{35} = -0.53$ (c 0.01, CHCl₃). HRMS (ESI) m/z: $[M + NH_4]^+$ calcd for C₂₁H₃₀NO₁₀ 456.1864; found 456.1870.

Synthesis of (2R,3R)-6-hydroxy-8-(naphthalen-2-yl)-8-oxooctane-1,2,3-triyl triacetate (12o)



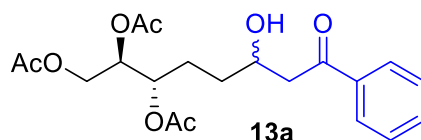
Mukaiyama aldol condensation of **8c** (53 mg, 0.19 mmol) with **9j** (56 mg, 0.23 mmol) according to General Procedure C afforded **12o** (77 mg, 90 %, d.r.: 1.3:1) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.44$ (Hexane/EtOAc = 2:1, v/v). ¹H NMR (500 MHz, CDCl₃) δ 8.46 (s, 2H), 7.99 (dd, $J = 15.4, 8.3$ Hz, 5H), 7.93 – 7.85 (m, 5H), 7.62 (t, $J = 7.3$ Hz, 2H), 7.57 (t, $J = 7.3$ Hz, 2H), 5.30 – 5.17 (m, 5H), 4.33 (d, $J = 3.1$ Hz, 1H), 4.31 (d, $J = 3.1$ Hz, 1H), 4.29 – 4.21 (m, 2H), 4.09 – 4.03 (m, 2H), 3.46 – 3.10 (m, 7H), 2.12 (s, 7H), 2.10 (s, 7H), 2.06 (s, 7H), 2.01 – 1.86 (m, 3H), 1.79 – 1.53 (m, 9H). ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 199.5, 199.4, 169.6, 169.4, 169.4, 169.2, 169.2, 134.8, 133.0, 133.0, 131.5, 129.1, 128.6, 127.8, 127.6, 126.8, 125.9, 122.5, 70.7, 70.3, 70.3, 70.1, 66.5, 66.2, 61.4, 61.4, 44.2, 44.1, 31.1, 30.9, 25.8, 25.7, 19.9, 19.8, 19.7. $[\alpha]_D^{35} = -7.99$ (c 0.5, CHCl₃). HRMS (ESI) m/z: $[M + Na]^+$ calcd for C₂₄H₂₈O₈Na 467.1676; found 467.1689.

Synthesis of (2R,3R)-6-hydroxy-8-(naphthalen-2-yl)-8-oxooctane-1,2,3-triyl triacetate (12p)



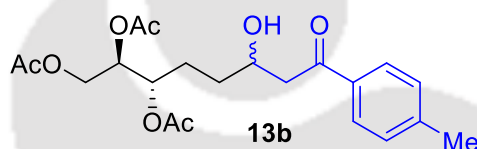
Mukaiyama aldol condensation of **8c** (56 mg, 0.20 mmol) with **9i** (58 mg, 0.24 mmol) according to General Procedure C afforded **12p** (81 mg, 89 %) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.44$ (Hexane/EtOAc = 2:1, v/v). ¹H NMR (400 MHz, CDCl₃) δ 8.57 (d, $J = 8.5$ Hz, 1H), 7.93 (d, $J = 8.2$ Hz, 1H), 7.83 – 7.76 (m, 2H), 7.53 (t, $J = 7.5$ Hz, 1H), 7.49 – 7.39 (m, 2H), 5.21 – 5.07 (m, 2H), 4.27 – 4.14 (m, 2H), 4.01 – 3.93 (m, 1H), 3.29 (d, $J = 16.1$ Hz, 1H), 3.18 – 3.02 (m, 2H), 2.03 (s, 3H), 2.01 (s, 3H), 1.97 (s, 3H), 1.88 – 1.74 (m, 1H), 1.70 – 1.59 (m, 1H), 1.58 – 1.44 (m, 2H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 203.6, 203.5, 169.5, 169.4, 169.4, 169.2, 169.2, 134.2, 134.2, 133.0, 132.3, 132.3, 129.0, 127.5, 127.2, 127.2, 125.6, 124.6, 123.3, 70.7, 70.2, 70.1, 66.8, 66.5, 61.4, 61.4, 47.4, 47.3, 31.1, 30.9, 25.8, 25.6, 19.8, 19.8, 19.7. $[\alpha]_D^{35} = +4.79$ (c 0.3, CHCl₃). HRMS (ESI) m/z: $[M + Na]^+$ calcd for C₂₄H₂₈O₈Na 467.1676; found 467.1690.

Synthesis of (2R,3S)-6-hydroxy-8-oxo-8-phenyloctane-1,2,3-triyl triacetate (13a)



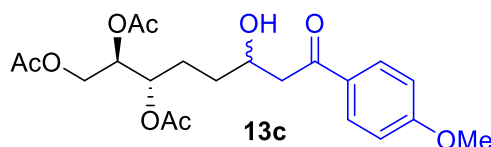
Mukaiyama aldol condensation of **8a** (50 mg, 0.18 mmol) with **9a** (43 mg, 0.22 mmol) according to General Procedure C afforded **13a** (60 mg, 83 %, d.r.:1.5:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.43 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.95 (d, J = 7.8 Hz, 5H), 7.59 (t, J = 7.4 Hz, 3H), 7.48 (t, J = 7.7 Hz, 5H), 5.22 – 5.12 (m, 5H), 4.34 (t, J = 2.9 Hz, 1H), 4.31 (t, J = 3.0 Hz, 2H), 4.26 – 4.14 (m, 5H), 3.37 (s, 2H), 3.16 (dt, J = 17.7, 2.3 Hz, 3H), 3.05 (ddd, J = 17.8, 8.8, 6.2 Hz, 3H), 2.09 (s, 7H), 2.08 (s, 7H), 2.06 (s, 7H), 1.98 – 1.85 (m, 3H), 1.84 – 1.47 (m, 10H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 199.6, 199.5, 169.7, 169.4, 169.3, 169.2, 135.6, 132.6, 127.7, 127.1, 71.1, 70.9, 70.8, 70.6, 66.4, 65.9, 61.0, 44.1, 44.1, 31.2, 31.0, 25.6, 25.3, 19.9, 19.7. $[\alpha]_D^{35}$ = + 3.26 (c 0.1, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{20}\text{H}_{30}\text{NO}_8$ 412.1966; found 412.1974.

Synthesis of (2R,3S)-6-hydroxy-8-oxo-8-(p-tolyl)octane-1,2,3-triyl triacetate (**13b**)



Mukaiyama aldol condensation of **8a** (56 mg, 0.20 mmol) with **9b** (52 mg, 0.25 mmol) according to General Procedure C afforded **13b** (70 mg, 84 %, d.r.: 1.5:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.47 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.84 (d, J = 8.1 Hz, 5H), 7.29 – 7.23 (m, 5H), 5.22 – 5.12 (m, 5H), 4.34 (t, J = 2.9 Hz, 1H), 4.31 (t, J = 2.9 Hz, 2H), 4.25 – 4.13 (m, 5H), 3.44 (s, 2H), 3.16 – 3.13 (m, 1H), 3.12 – 3.08 (m, 2H), 3.01 (ddd, J = 17.6, 8.9, 6.0 Hz, 3H), 2.42 (s, 8H), 2.09 – 2.07 (m, 15H), 2.06 (s, 8H), 1.99 – 1.84 (m, 5H), 1.81 – 1.48 (m, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 199.2, 199.2, 169.7, 169.4, 169.3, 169.2, 143.5, 133.2, 128.4, 127.2, 71.2, 70.9, 70.9, 70.6, 66.5, 66.0, 61.0, 43.9, 43.9, 31.2, 31.0, 25.6, 25.3, 20.7, 19.9, 19.7. $[\alpha]_D^{35}$ = - 0.40 (c 0.01, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{21}\text{H}_{32}\text{NO}_8$ 426.2122; found 426.4128.

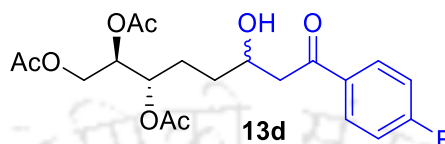
Synthesis of (2R,3S)-6-hydroxy-8-(4-methoxyphenyl)-8-oxooctane-1,2,3-triyl triacetate (**13c**)



Mukaiyama aldol condensation of **8a** (56 mg, 0.20 mmol) with **9l** (55 mg, 0.25 mmol) according to General Procedure C afforded **13c** (72 mg, 83 %, d.r.:1.6:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.40 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.92 (d, J = 8.7 Hz, 5H), 6.94 (d, J = 8.9 Hz, 5H), 5.22 – 5.11 (m, 5H), 4.34 (t, J = 2.9 Hz, 1H), 4.31 (t, J = 3.0 Hz, 2H), 4.24 – 4.13 (m, 5H), 3.88 (s, 8H), 3.49 (s, 2H), 3.14 – 3.12 (m, 1H), 3.08 (d, J = 2.2 Hz, 2H), 3.03 –

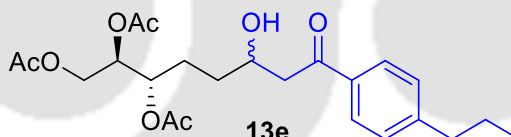
2.92 (m, 3H), 2.08 (s, 8H), 2.07 (s, 8H), 2.06 (s, 8H), 1.96 – 1.82 (m, 4H), 1.80 – 1.46 (m, 10H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 198.1, 198.1, 169.7, 169.4, 169.3, 169.2, 162.9, 129.4, 128.7, 112.9, 71.2, 70.9, 70.8, 70.6, 66.6, 66.1, 61.0, 54.5, 43.6, 43.6, 31.3, 31.0, 25.6, 25.3, 19.9, 19.7. $[\alpha]_{\text{D}}^{35} = +2.73$ (c 0.2, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{28}\text{O}_9\text{Na}$ 447.1626; found 447.1632.

Synthesis of (2R,3S)-8-(4-fluorophenyl)-6-hydroxy-8-oxooctane-1,2,3-triyl triacetate (13d)



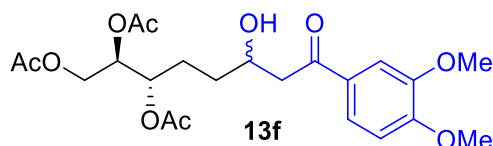
Mukaiyama aldol condensation of **8a** (50 mg, 0.18 mmol) with **9f** (47 mg, 0.22 mmol) according to General Procedure C afforded **13d** (54 mg, 72 %, d.r.:1.5:1) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.42$ (Hexane/ $\text{EtOAc} = 2:1$, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.98 (dd, $J = 8.6, 5.5$ Hz, 5H), 7.14 (dd, $J = 14.0, 5.4$ Hz, 5H), 5.22 – 5.12 (m, 5H), 4.34 (t, $J = 2.6$ Hz, 1H), 4.31 (t, $J = 2.7$ Hz, 2H), 4.26 – 4.14 (m, 5H), 3.29 (s, 2H), 3.15 – 2.99 (m, 6H), 2.08 (s, 7H), 2.08 (s, 7H), 2.06 (s, 7H), 1.98 – 1.84 (m, 3H), 1.82 – 1.47 (m, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 198.8, 198.8, 170.7, 170.3, 170.2, 167.0, 165.0, 133.2, 130.8, 130.7, 115.9, 115.7, 72.1, 71.9, 71.8, 71.6, 67.4, 66.8, 62.0, 45.1, 32.2, 32.0, 26.6, 26.3, 20.9, 20.7. $[\alpha]_{\text{D}}^{35} = +1.20$ (c 0.09, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{25}\text{FO}_8\text{Na}$ 435.1426; found 435.1433.

Synthesis of (2R,3S)-6-hydroxy-8-oxo-8-(4-propylphenyl)octane-1,2,3-triyl triacetate (13e)



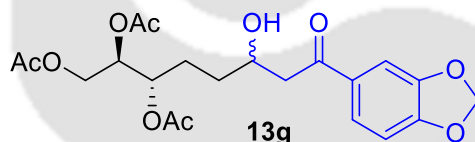
Mukaiyama aldol condensation of **8a** (53 mg, 0.19 mmol) with **9p** (54 mg, 0.23 mmol) according to General Procedure C afforded **13e** (66 mg, 78 %, d.r.:1.8:1) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.46$ (Hexane/ $\text{EtOAc} = 2:1$, v/v). ^1H NMR (500 MHz, CDCl_3) δ 7.86 (d, $J = 7.9$ Hz, 6H), 7.27 (d, $J = 8.0$ Hz, 6H), 5.21 – 5.12 (m, 6H), 4.32 (d, $J = 12.3$ Hz, 3H), 4.24 – 4.13 (m, 6H), 3.44 (s, 2H), 3.15 (s, 1H), 3.11 (s, 2H), 3.06 – 2.98 (m, 3H), 2.65 (t, $J = 7.6$ Hz, 6H), 2.08 (s, 8H), 2.07 (s, 8H), 2.06 (s, 9H), 1.99 – 1.82 (m, 6H), 1.81 – 1.48 (m, 16H), 0.95 (t, $J = 7.3$ Hz, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 199.3, 199.2, 169.7, 169.4, 169.3, 169.2, 148.2, 133.4, 127.8, 127.2, 71.2, 70.9, 70.9, 70.6, 66.5, 66.0, 61.0, 43.9, 43.9, 37.0, 31.3, 31.0, 25.6, 25.3, 23.1, 19.9, 19.7, 12.7. $[\alpha]_{\text{D}}^{35} = +2.67$ (c 0.3, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{23}\text{H}_{32}\text{O}_8\text{Na}$ 459.1989; found 459.1997.

Synthesis of (2R,3S)-8-(3,4-dimethoxyphenyl)-6-hydroxy-8-oxooctane-1,2,3-triyl triacetate (13f)



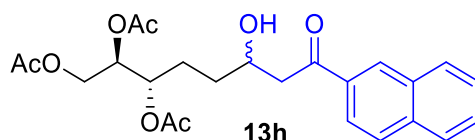
Mukaiyama aldol condensation of **8a** (48 mg, 0.18 mmol) with **9o** (55 mg, 0.22 mmol) according to General Procedure C afforded **13f** (61 mg, 77 %, d.r.:1.5:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.37 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 7.57 (dd, J = 8.4, 1.3 Hz, 3H), 7.51 (d, J = 1.8 Hz, 3H), 6.90 (d, J = 8.4 Hz, 3H), 5.23 – 5.12 (m, 5H), 4.34 (t, J = 2.9 Hz, 1H), 4.31 (t, J = 3.0 Hz, 2H), 4.25 – 4.11 (m, 6H), 3.96 (s, 8H), 3.94 (s, 8H), 3.46 (s, 2H), 3.15 (d, J = 2.6 Hz, 1H), 3.10 (d, J = 2.6 Hz, 2H), 3.05 – 2.94 (m, 3H), 2.09 (s, 8H), 2.08 (s, 8H), 2.06 (s, 8H), 1.97 – 1.83 (m, 4H), 1.82 – 1.47 (m, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 199.1, 199.1, 170.7, 170.4, 170.3, 170.2, 153.8, 149.1, 129.9, 123.0, 110.1, 110.0, 72.2, 71.9, 71.8, 71.6, 67.6, 67.1, 62.0, 56.1, 56.0, 44.5, 44.5, 32.3, 32.1, 26.6, 26.3, 20.9, 20.7. $[\alpha]_{\text{D}}^{35}$ = + 0.47 (c 0.02, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{30}\text{O}_{10}\text{Na}$ 477.1731; found 477.1739.

Synthesis of (2R,3S)-8-(benzo[δ][1,3]dioxol-5-yl)-6-hydroxy-8-oxooctane-1,2,3-triyl triacetate (**13g**)



Mukaiyama aldol condensation of **8a** (57 mg, 0.21 mmol) with **9k** (60 mg, 0.25 mmol) according to General Procedure C afforded **13g** (70 mg, 77 %, d.r.:1.8:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.38 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 7.54 (d, J = 8.1 Hz, 3H), 7.41 (s, 3H), 6.86 (d, J = 8.1 Hz, 3H), 6.06 (s, 6H), 5.21 – 5.12 (m, 6H), 4.32 (d, J = 12.4 Hz, 3H), 4.24 – 4.12 (m, 6H), 3.39 (s, 2H), 3.09 (s, 1H), 3.05 (s, 2H), 2.95 (dt, J = 17.4, 8.6 Hz, 3H), 2.08 (s, 8H), 2.07 (s, 8H), 2.06 (s, 9H), 1.99 – 1.83 (m, 4H), 1.80 – 1.54 (m, 12H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 197.6, 197.5, 169.7, 169.4, 169.3, 169.2, 151.2, 147.3, 130.6, 123.6, 107.0, 106.7, 101.0, 71.2, 70.9, 70.9, 70.6, 66.5, 66.0, 61.0, 43.8, 43.8, 31.2, 31.0, 25.6, 25.3, 19.9, 19.7. $[\alpha]_{\text{D}}^{35}$ = + 2.46 (c 0.4, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{26}\text{O}_{10}\text{Na}$ 461.1418; found 461.1421.

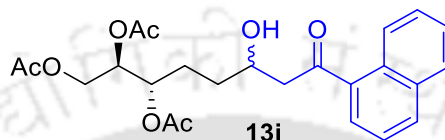
Synthesis of (2R,3S)-6-hydroxy-8-(naphthalen-2-yl)-8-oxooctane-1,2,3-triyl triacetate (**13h**)



Mukaiyama aldol condensation of **8a** (51 mg, 0.19 mmol) with **9j** (56 mg, 0.23 mmol) according to General Procedure C afforded **13h** (67 mg, 81 %, d.r.:1.3:1) as a colorless syrup. The crude product was purified through flash column chromatography, R_f = 0.45 (Hexane/EtOAc = 2:1, v/v). ^1H NMR (500 MHz, CDCl_3) δ 8.45 (s, 2H), 7.98 (dd, J = 17.3, 8.3

Hz, 5H), 7.88 (t, $J = 8.6$ Hz, 5H), 7.61 (t, $J = 7.4$ Hz, 2H), 7.56 (t, $J = 7.4$ Hz, 2H), 5.24 – 5.15 (m, 5H), 4.35 (s, 1H), 4.33 (s, 1H), 4.31 – 4.17 (m, 5H), 3.44 (s, 2H), 3.29 (s, 1H), 3.26 (s, 2H), 3.23 – 3.13 (m, 3H), 2.08 (s, 14H), 2.06 (s, 7H), 1.99 – 1.87 (m, 3H), 1.84 – 1.53 (m, 8H). $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 199.5, 199.4, 169.7, 169.4, 169.3, 169.2, 134.8, 133.0, 131.5, 129.1, 128.6, 127.7, 127.6, 126.8, 125.9, 122.5, 71.2, 70.9, 70.9, 70.6, 66.5, 66.0, 61.0, 44.2, 44.2, 31.3, 31.1, 25.6, 25.3, 19.9, 19.7. $[\alpha]_{\text{D}}^{35} = +2.73$ (c 0.3, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{24}\text{H}_{32}\text{NO}_8$ 462.2122; found 462.2128.

Synthesis of (2R,3S)-6-hydroxy-8-(naphthalen-1-yl)-8-oxooctane-1,2,3-triyl triacetate (13i)



Mukaiyama aldol condensation of **8a** (47 mg, 0.17 mmol) with **9i** (50 mg, 0.21 mmol) according to General Procedure C afforded **13i** (61 mg, 80 %) as a colorless syrup. The crude product was purified through flash column chromatography, $R_f = 0.45$ (Hexane/EtOAc = 2:1, v/v). ^1H NMR (400 MHz, CDCl_3) δ 8.65 (d, $J = 8.5$ Hz, 1H), 8.00 (d, $J = 8.2$ Hz, 1H), 7.88 (dd, $J = 7.3, 4.6$ Hz, 2H), 7.63 – 7.57 (m, 1H), 7.56 – 7.46 (m, 2H), 5.22 – 5.12 (m, 2H), 4.36 – 4.22 (m, 2H), 4.18 (ddd, $J = 12.1, 6.8, 2.4$ Hz, 1H), 3.42 (s, 1H), 3.25 – 3.11 (m, 2H), 2.10 – 2.03 (m, 9H), 1.98 – 1.85 (m, 1H), 1.82 – 1.49 (m, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 204.6, 204.6, 170.7, 170.4, 170.4, 170.3, 135.2, 135.2, 134.0, 133.4, 130.0, 128.6, 128.3, 128.2, 126.6, 125.7, 124.3, 72.1, 71.9, 71.8, 71.6, 67.9, 67.4, 62.0, 62.0, 48.4, 48.3, 32.3, 32.0, 26.6, 26.2, 20.9, 20.8. $[\alpha]_{\text{D}}^{35} = +0.73$ (c 0.02, CHCl_3). HRMS (ESI) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{24}\text{H}_{32}\text{NO}_8$ 462.2122; found 462.2127.

6.4 References

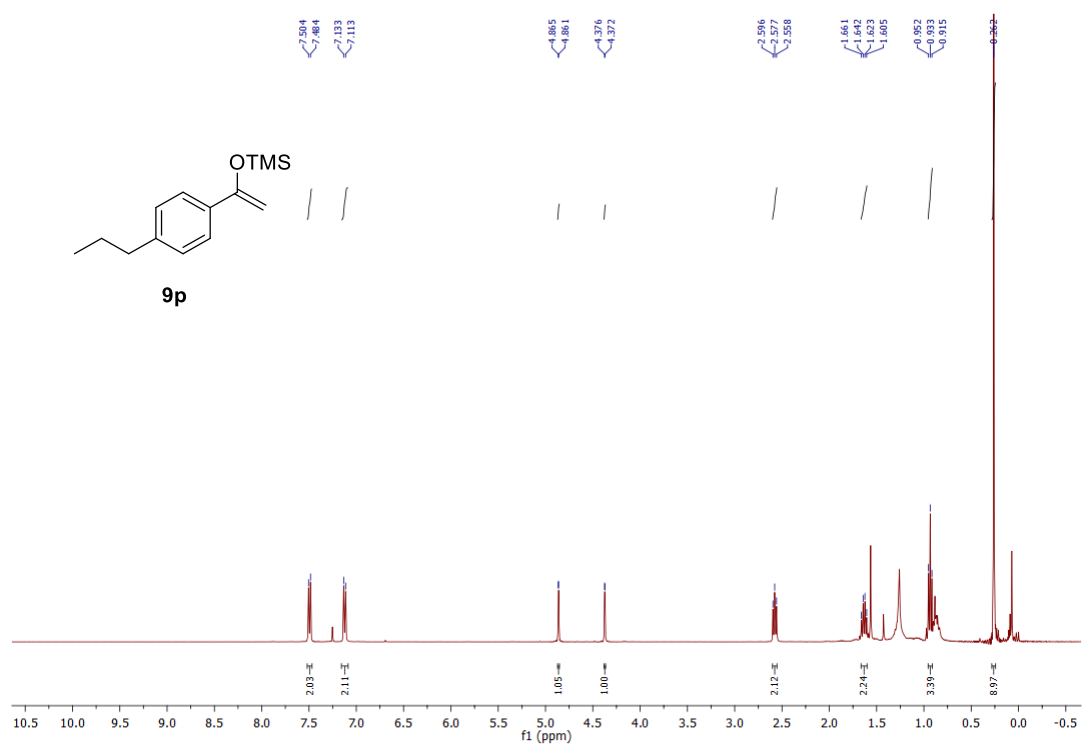
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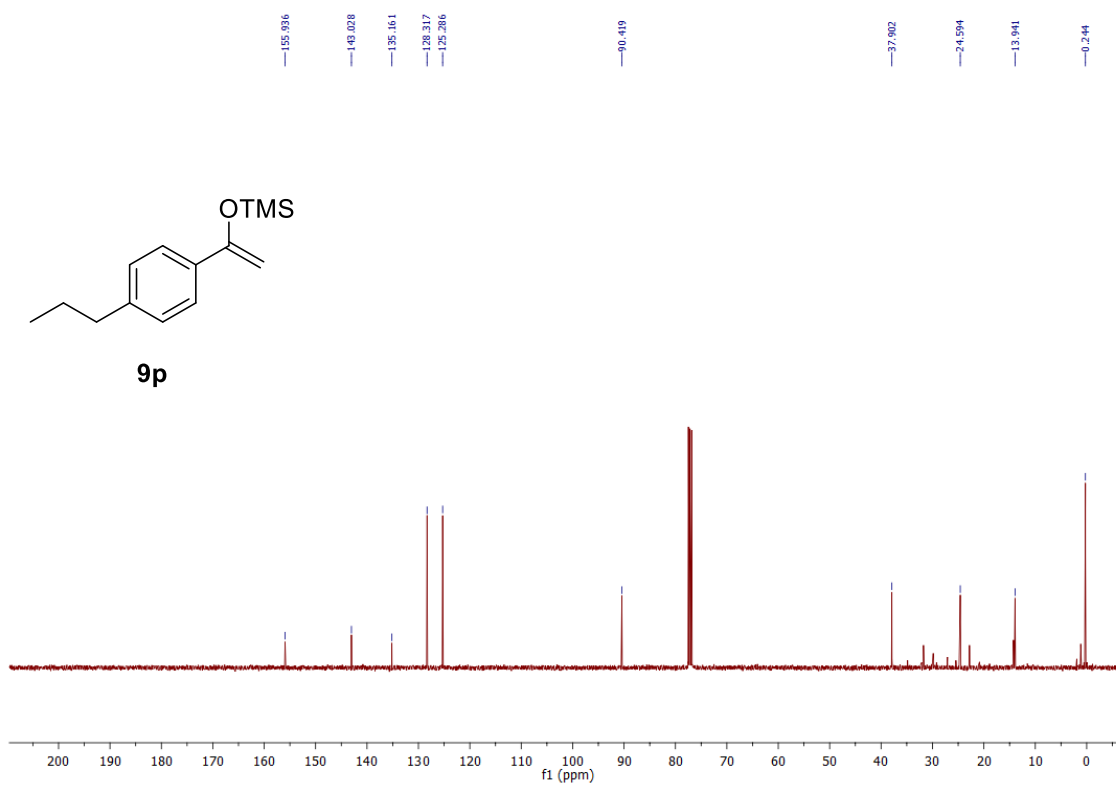
6.5

Spectra

^1H NMR spectrum of compound 9p (400 MHz, CDCl_3):

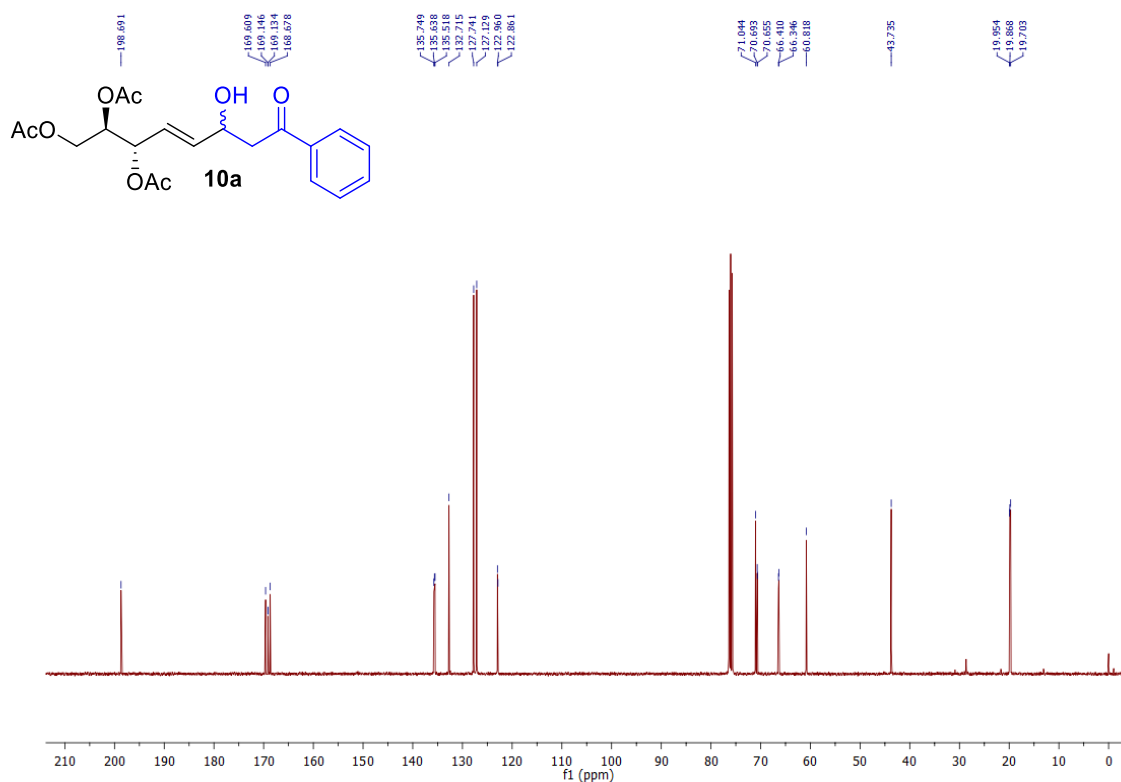
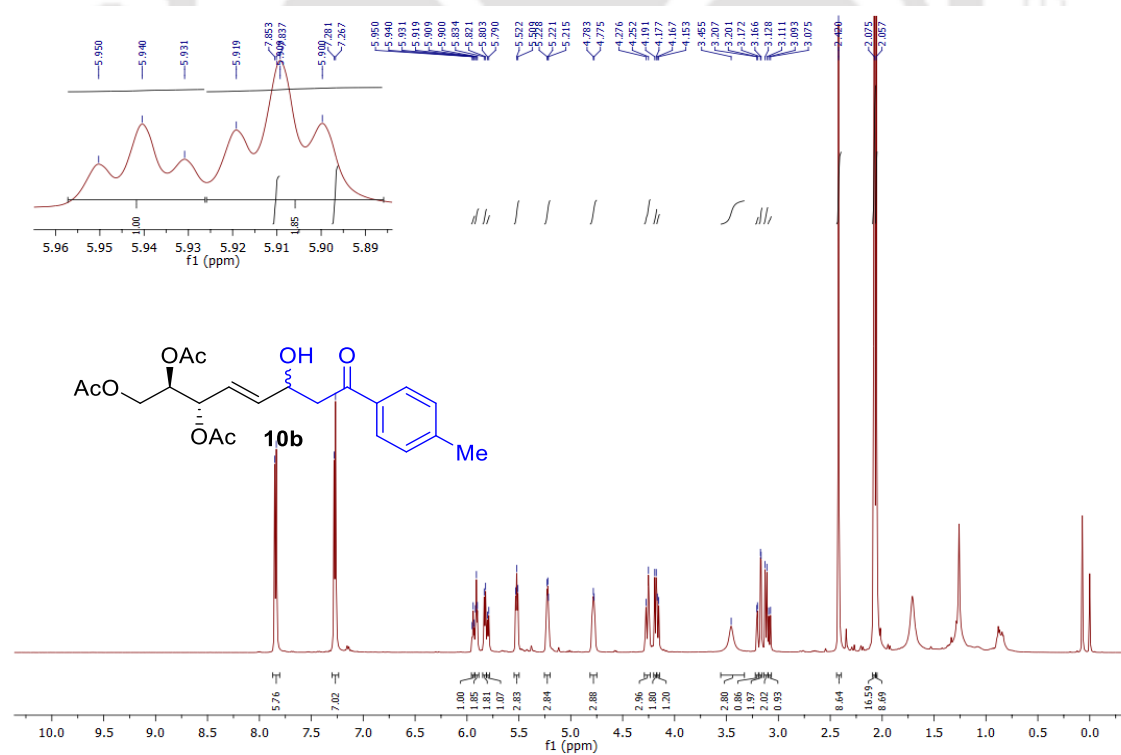


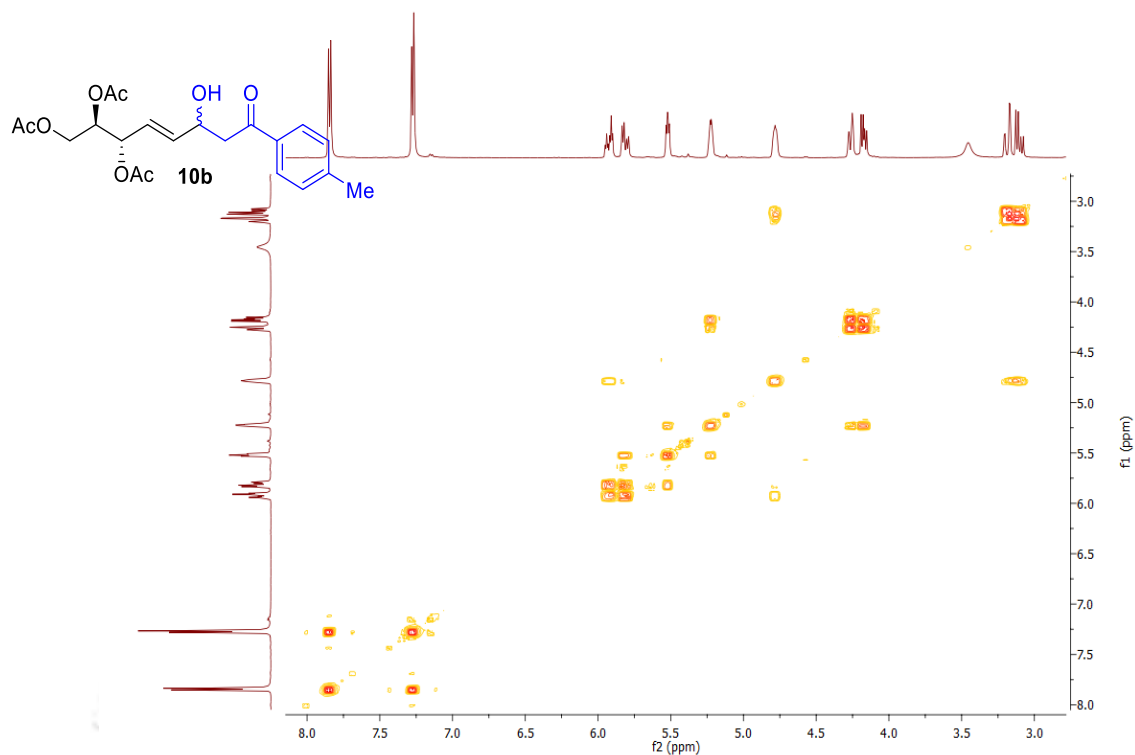
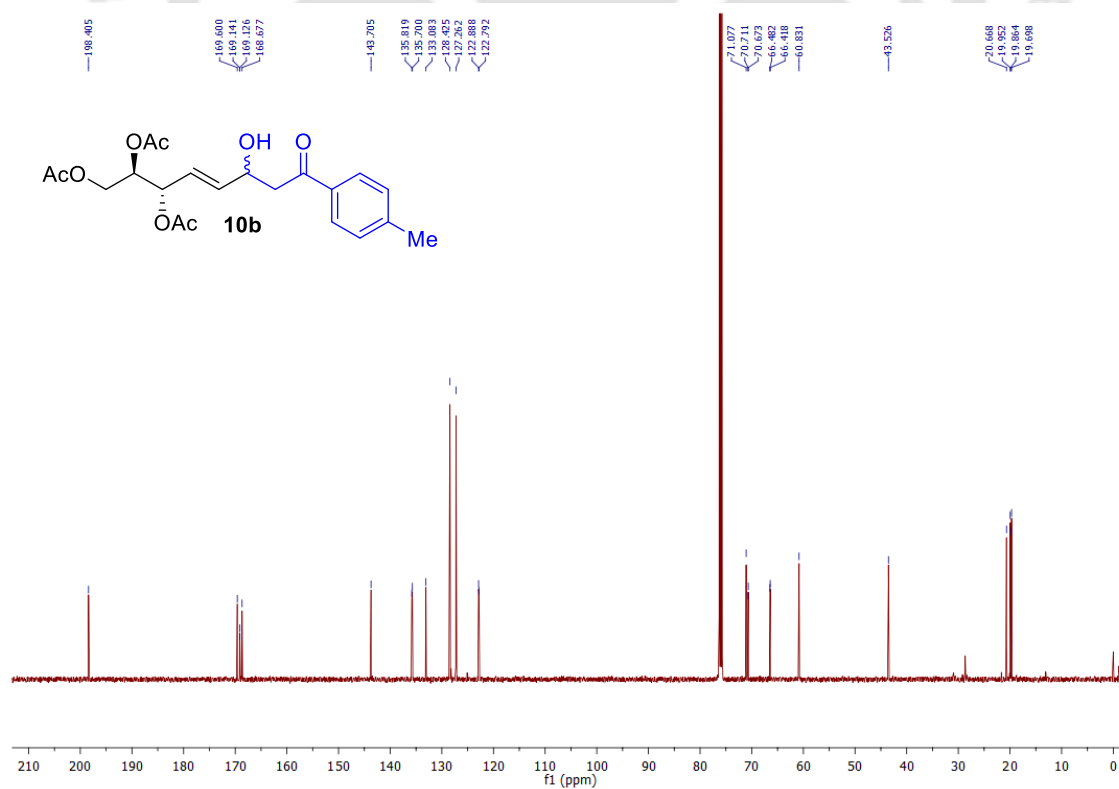
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 9p (400 MHz, CDCl_3):

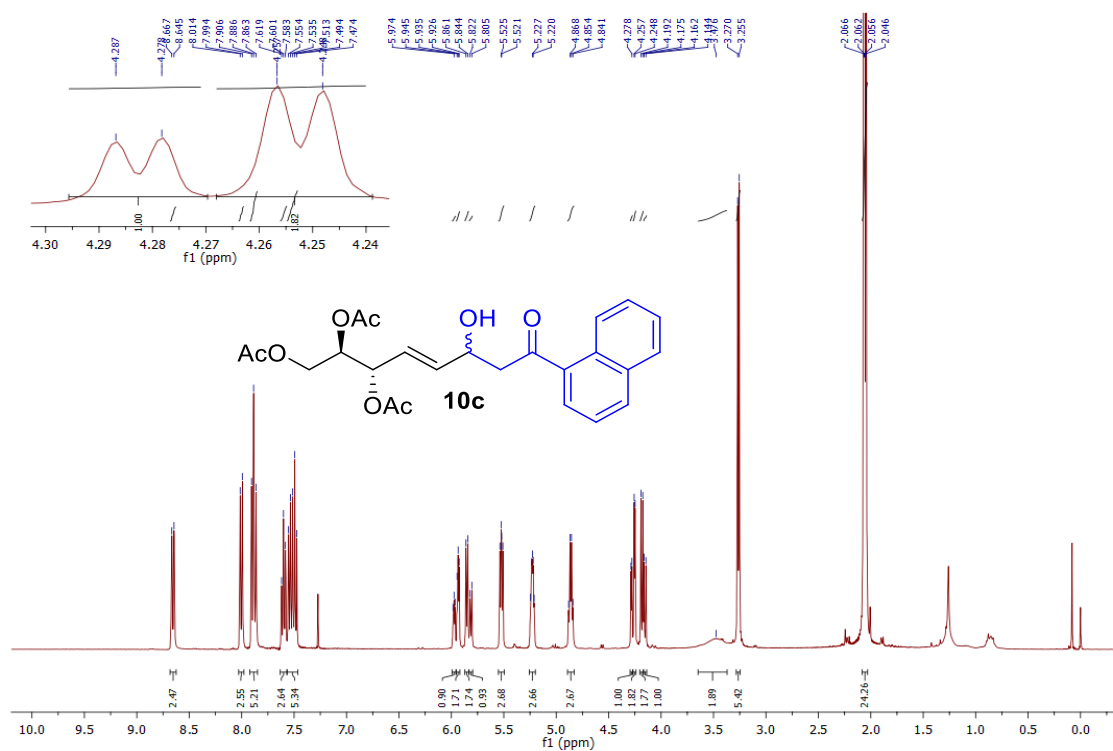
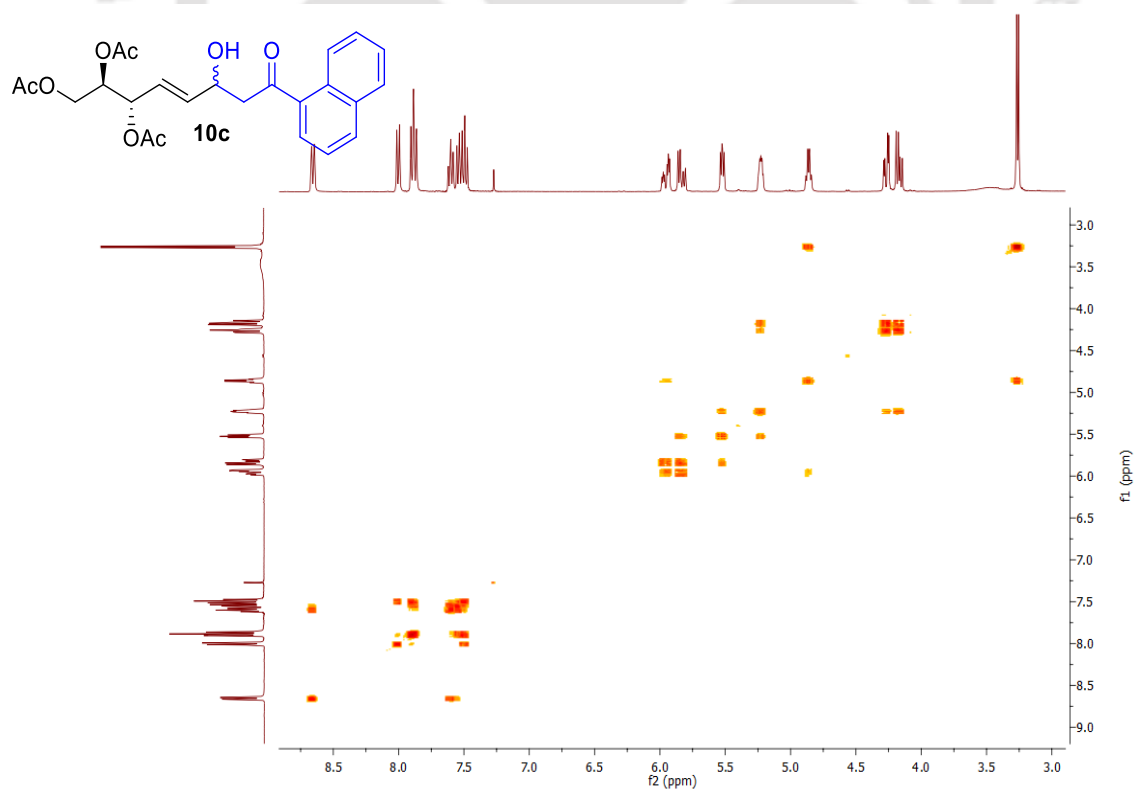


[illegible]

Chemical structure of compound **10a** is shown above the NMR spectrum. The structure is (E)-1-(benzoyloxymethyl)-2-acetoxy-3-(acetoxy(methyl)oxy)but-2-ene. The spectrum displays the ¹H and ¹³C NMR data, with the 2D plot showing correlations between the two dimensions. The x-axis represents the ¹H chemical shift (f2) in ppm, ranging from 8.0 to 3.0. The y-axis represents the ¹³C chemical shift (f1) in ppm, ranging from 2.5 to 8.5. The 1D ¹H NMR spectrum is projected along the top, and the 1D ¹³C NMR spectrum is projected along the left side of the 2D plot. The 2D plot shows several cross-peaks, including correlations between the benzoyl carbonyl carbon (166 ppm) and its corresponding protons (7.8 ppm), and between the acetoxy methyl groups (3.0-4.0 ppm) and their corresponding carbons (17-20 ppm).

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 10a (400 MHz, CDCl_3): **^1H NMR spectrum of compound 10b (500 MHz, CDCl_3):**

COSY NMR spectrum of compound 10b (500 MHz, CDCl₃):**¹³C{¹H} NMR spectrum of compound 10b (500 MHz, CDCl₃):**

^1H NMR spectrum of compound 10c (400 MHz, CDCl_3):**COSY NMR spectrum of compound 10c (400 MHz, CDCl_3):**

Chemical structure of **10c** is shown above the spectrum. The structure is a substituted cyclohexene derivative. It features a cyclohexene ring with a double bond between carbons 1 and 2. Carbon 1 is substituted with an acetoxy group (OAc). Carbon 2 is substituted with a hydroxyl group (OH). Carbon 3 is substituted with an acetoxy group (OAc). Carbon 4 is substituted with a 2-phenylacetyl group (CH₂COPh). The spectrum shows peaks corresponding to these functional groups and the aromatic ring.

Chemical structure of 10c:

CC(=O)OC[C@H]1C=C[C@@H](OC(=O)C)C[C@H]1CC(=O)Cc2ccccc2

10c

13C NMR spectrum (CDCl₃):

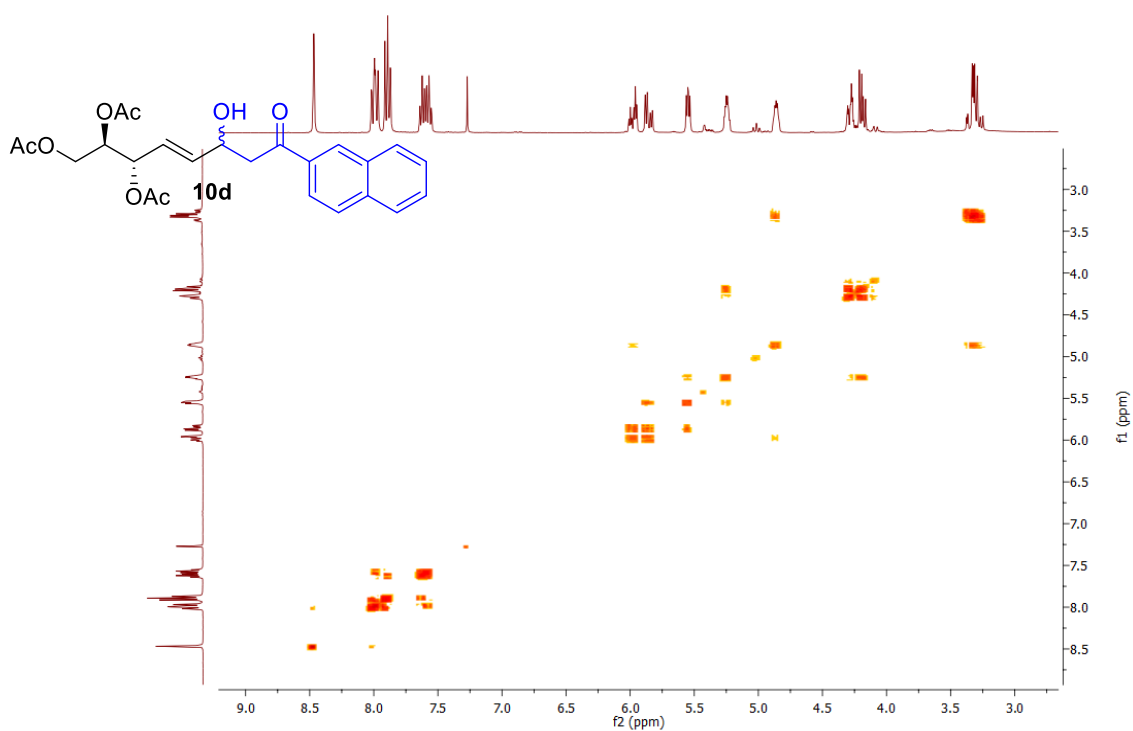
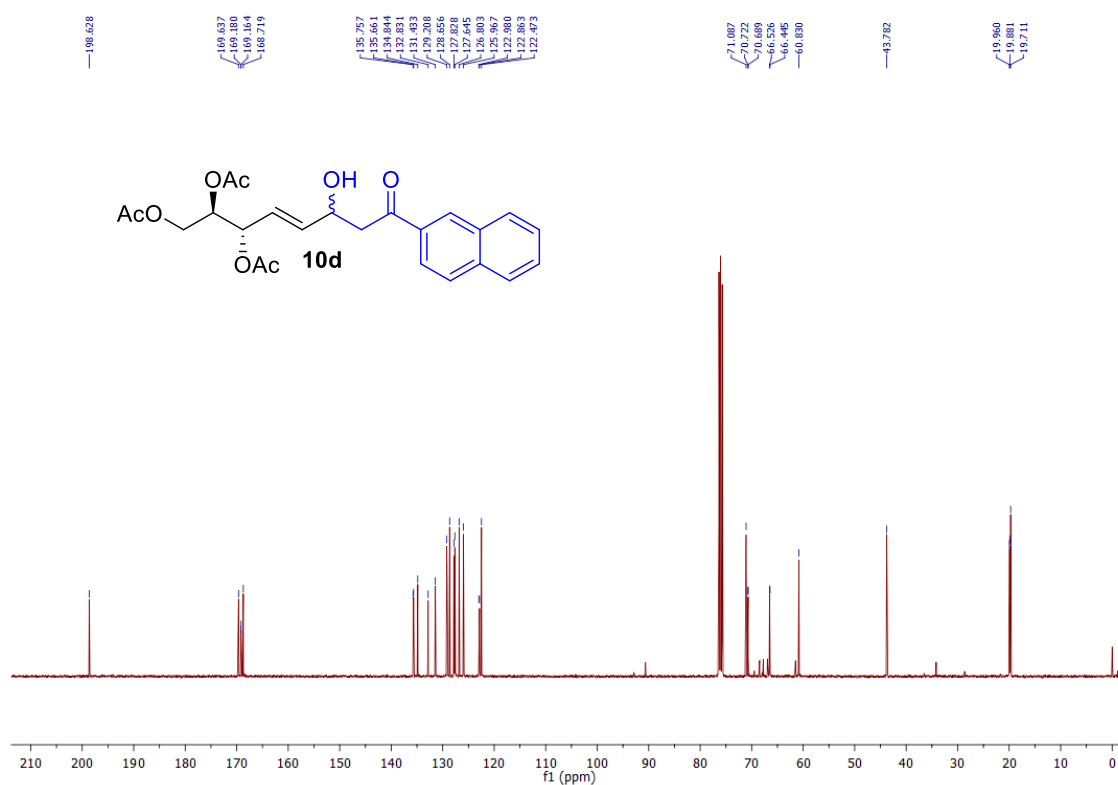
The spectrum displays peaks in the following regions (ppm):

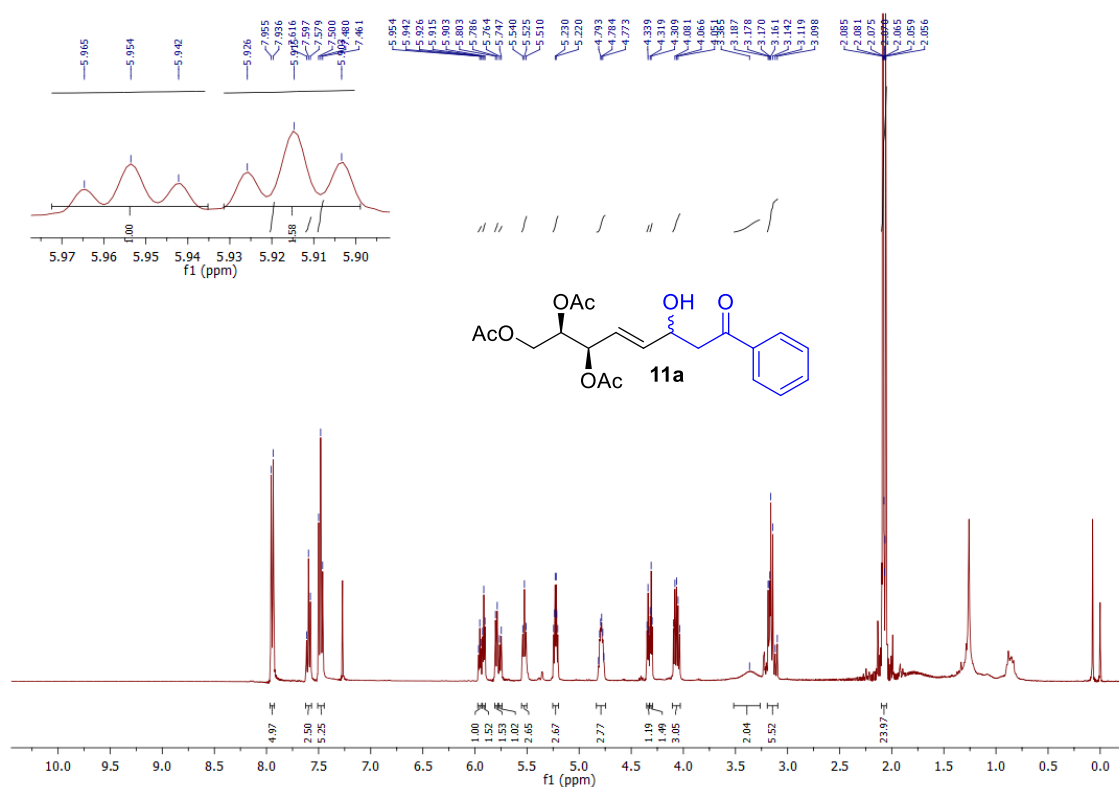
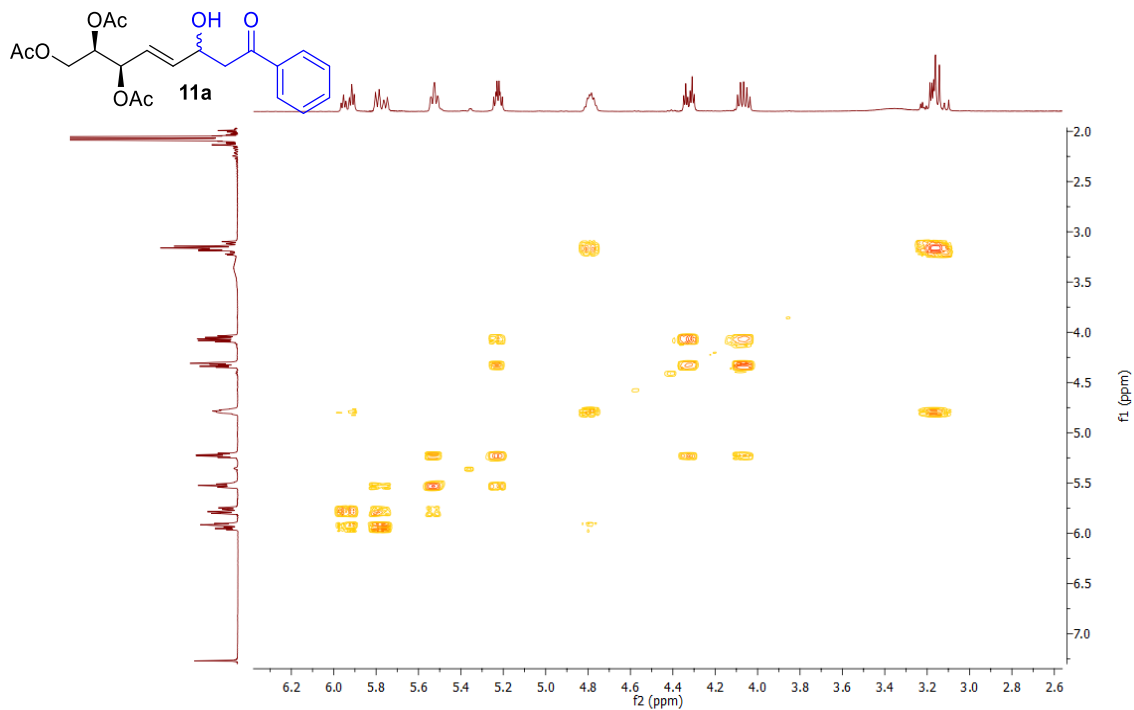
- Carbonyl region: ~202.46, ~169.61, ~169.14, ~168.62.
- Aromatic region: ~135.86, ~135.75, ~135.54, ~134.51, ~134.07, ~132.96, ~132.41, ~129.03, ~127.51, ~127.39, ~127.27, ~125.59, ~124.64, ~123.33, ~123.15, ~122.89.
- Aliphatic region: ~71.05, ~70.61, ~70.60, ~66.85, ~66.84, ~60.81, ~46.94, ~46.90.
- Reference peak: ~19.52, ~19.68, ~19.88.

¹H NMR spectrum of compound 10d in CDCl₃.

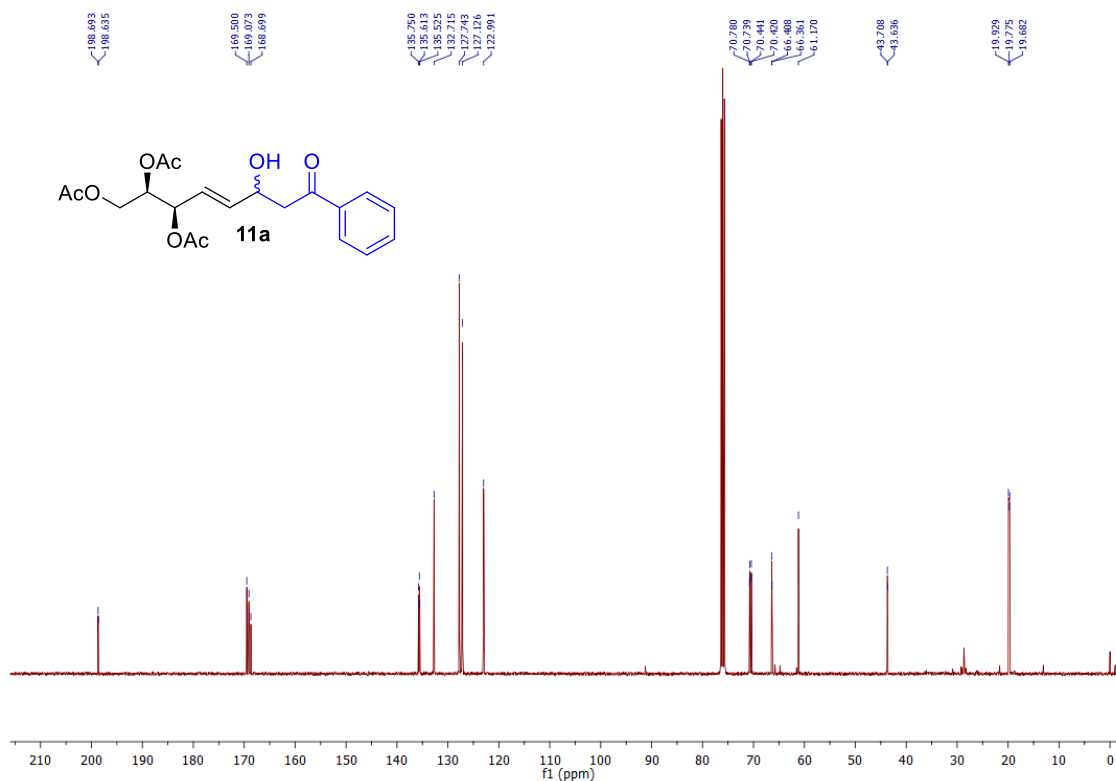
Chemical structure of 10d: CC(=O)OC[C@H](OC(=O)C)C/C=C/C(O)CC(=O)c1ccc2ccccc2c1

Peak list (ppm): 8.509, 8.488, 8.468, 7.998, 7.994, 7.988, 7.987, 7.913, 7.912, 7.911, 7.910, 7.909, 7.908, 7.907, 7.906, 7.905, 7.904, 7.903, 7.902, 7.901, 7.900, 7.899, 7.898, 7.897, 7.896, 7.895, 7.894, 7.893, 7.892, 7.891, 7.890, 7.889, 7.888, 7.887, 7.886, 7.885, 7.884, 7.883, 7.882, 7.881, 7.880, 7.879, 7.878, 7.877, 7.876, 7.875, 7.874, 7.873, 7.872, 7.871, 7.870, 7.869, 7.868, 7.867, 7.866, 7.865, 7.864, 7.863, 7.862, 7.861, 7.860, 7.859, 7.858, 7.857, 7.856, 7.855, 7.854, 7.853, 7.852, 7.851, 7.850, 7.849, 7.848, 7.847, 7.846, 7.845, 7.844, 7.843, 7.842, 7.841, 7.840, 7.839, 7.838, 7.837, 7.836, 7.835, 7.834, 7.833, 7.832, 7.831, 7.830, 7.829, 7.828, 7.827, 7.826, 7.825, 7.824, 7.823, 7.822, 7.821, 7.820, 7.819, 7.818, 7.817, 7.816, 7.815, 7.814, 7.813, 7.812, 7.811, 7.810, 7.809, 7.808, 7.807, 7.806, 7.805, 7.804, 7.803, 7.802, 7.801, 7.800, 7.799, 7.798, 7.797, 7.796, 7.795, 7.794, 7.793, 7.792, 7.791, 7.790, 7.789, 7.788, 7.787, 7.786, 7.785, 7.784, 7.783, 7.782, 7.781, 7.780, 7.779, 7.778, 7.777, 7.776, 7.775, 7.774, 7.773, 7.772, 7.771, 7.770, 7.769, 7.768, 7.767, 7.766, 7.765, 7.764, 7.763, 7.762, 7.761, 7.760, 7.759, 7.758, 7.757, 7.756, 7.755, 7.754, 7.753, 7.752, 7.751, 7.750, 7.749, 7.748, 7.747, 7.746, 7.745, 7.744, 7.743, 7.742, 7.741, 7.740, 7.739, 7.738, 7.737, 7.736, 7.735, 7.734, 7.733, 7.732, 7.731, 7.730, 7.729, 7.728, 7.727, 7.726, 7.725, 7.724, 7.723, 7.722, 7.721, 7.720, 7.719, 7.718, 7.717, 7.716, 7.715, 7.714, 7.713, 7.712, 7.711, 7.710, 7.709, 7.708, 7.707, 7.706, 7.705, 7.704, 7.703, 7.702, 7.701, 7.700, 7.699, 7.698, 7.697, 7.696, 7.695, 7.694, 7.693, 7.692, 7.691, 7.690, 7.689, 7.688, 7.687, 7.686, 7.685, 7.684, 7.683, 7.682, 7.681, 7.680, 7.679, 7.678, 7.677, 7.676, 7.675, 7.674, 7.673, 7.672, 7.671, 7.670, 7.669, 7.668, 7.667, 7.666, 7.665, 7.664, 7.663, 7.662, 7.661, 7.660, 7.659, 7.658, 7.657, 7.656, 7.655, 7.654, 7.653, 7.652, 7.651, 7.650, 7.649, 7.648, 7.647, 7.646, 7.645, 7.644, 7.643, 7.642, 7.641, 7.640, 7.639, 7.638, 7.637, 7.636, 7.635, 7.634, 7.633, 7.632, 7.631, 7.630, 7.629, 7.628, 7.627, 7.626, 7.625, 7.624, 7.623, 7.622, 7.621, 7.620, 7.619, 7.618, 7.617, 7.616, 7.615, 7.614, 7.613, 7.612, 7.611, 7.610, 7.609, 7.608, 7.607, 7.606, 7.605, 7.604, 7.603, 7.602, 7.601, 7.600, 7.599, 7.598, 7.597, 7.596, 7.595, 7.594, 7.593, 7.592, 7.591, 7.590, 7.589, 7.588, 7.587, 7.586, 7.585, 7.584, 7.583, 7.582, 7.581, 7.580, 7.579, 7.578, 7.577, 7.576, 7.575, 7.574, 7.573, 7.572, 7.571, 7.570, 7.569, 7.568, 7.567, 7.566, 7.565, 7.564, 7.563, 7.562, 7.561, 7.560, 7.559, 7.558, 7.557, 7.556, 7.555, 7.554, 7.553, 7.552, 7.551, 7.550, 7.549, 7.548, 7.547, 7.546, 7.545, 7.544, 7.543, 7.542, 7.541, 7.540, 7.539, 7.538, 7.537, 7.536, 7.535, 7.534, 7.533, 7.532, 7.531, 7.530, 7.529, 7.528, 7.527, 7.526, 7.525, 7.524, 7.523, 7.522, 7.521, 7.520, 7.519, 7.518, 7.517, 7.516, 7.515, 7.514, 7.513, 7.512, 7.511, 7.510, 7.509, 7.508, 7.507, 7.506, 7.505, 7.504, 7.503, 7.502, 7.501, 7.500, 7.499, 7.498, 7.497, 7.496, 7.495, 7.494, 7.493, 7.492, 7.491, 7.490, 7.489, 7.488, 7.487, 7.486, 7.485, 7.484, 7.483, 7.482, 7.481, 7.480, 7.479, 7.478, 7.477, 7.476, 7.475, 7.474, 7.473, 7.472, 7.471, 7.470, 7.469, 7.468, 7.467, 7.466, 7.465, 7.464, 7.463, 7.462, 7.461, 7.460, 7.459, 7.458, 7.457, 7.456, 7.455, 7.454, 7.453, 7.452, 7.451, 7.450, 7.449, 7.448, 7.447, 7.446, 7.445, 7.444, 7.443, 7.442, 7.441, 7.440, 7.439, 7.438, 7.437, 7.436, 7.435, 7.434, 7.433, 7.432, 7.431, 7.430, 7.429, 7.428, 7.427, 7.426, 7.425, 7.424, 7.423, 7.422, 7.421, 7.420, 7.419, 7.418, 7.417, 7.416, 7.415, 7.414, 7.413, 7.412, 7.411, 7.410, 7.409, 7.408, 7.407, 7.406, 7.405, 7.404, 7.403, 7.402, 7.401, 7.400, 7.399, 7.398, 7.397, 7.396, 7.395, 7.394, 7.393, 7.392, 7.391, 7.390, 7.389, 7.388, 7.387, 7.386, 7.385, 7.384, 7.383, 7.382, 7.381, 7.380, 7.379, 7.378, 7.377, 7.376, 7.375, 7.374, 7.373, 7.372, 7.371

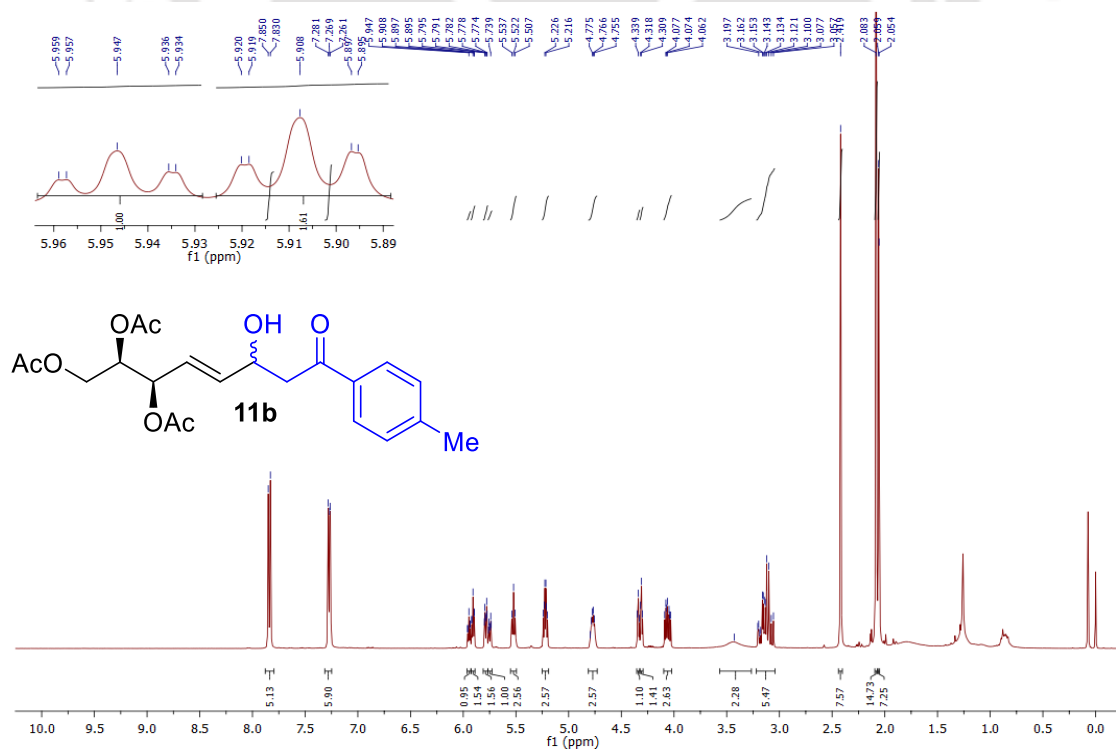
COSY NMR spectrum of compound 10d (400 MHz, CDCl₃):**¹³C{¹H} NMR spectrum of compound 10d (400 MHz, CDCl₃):**

^1H NMR spectrum of compound 11a (400 MHz, CDCl_3):**COSY NMR spectrum of compound 11a (400 MHz, CDCl_3):**

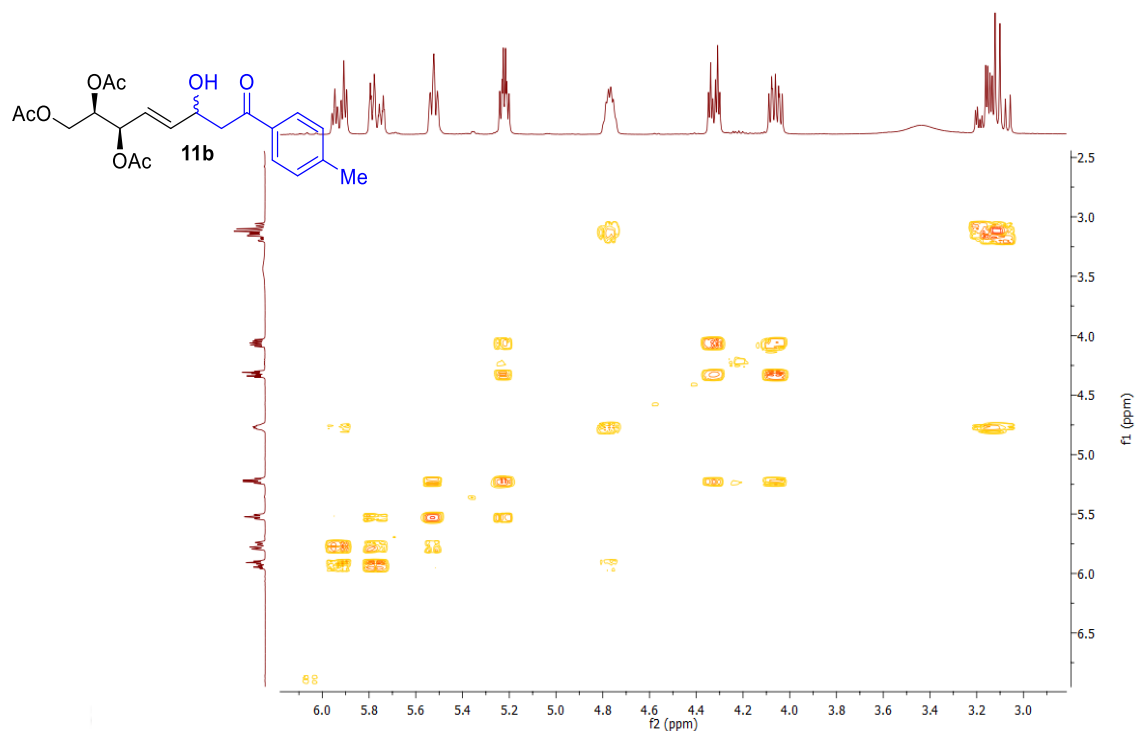
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 11a (400 MHz, CDCl_3):



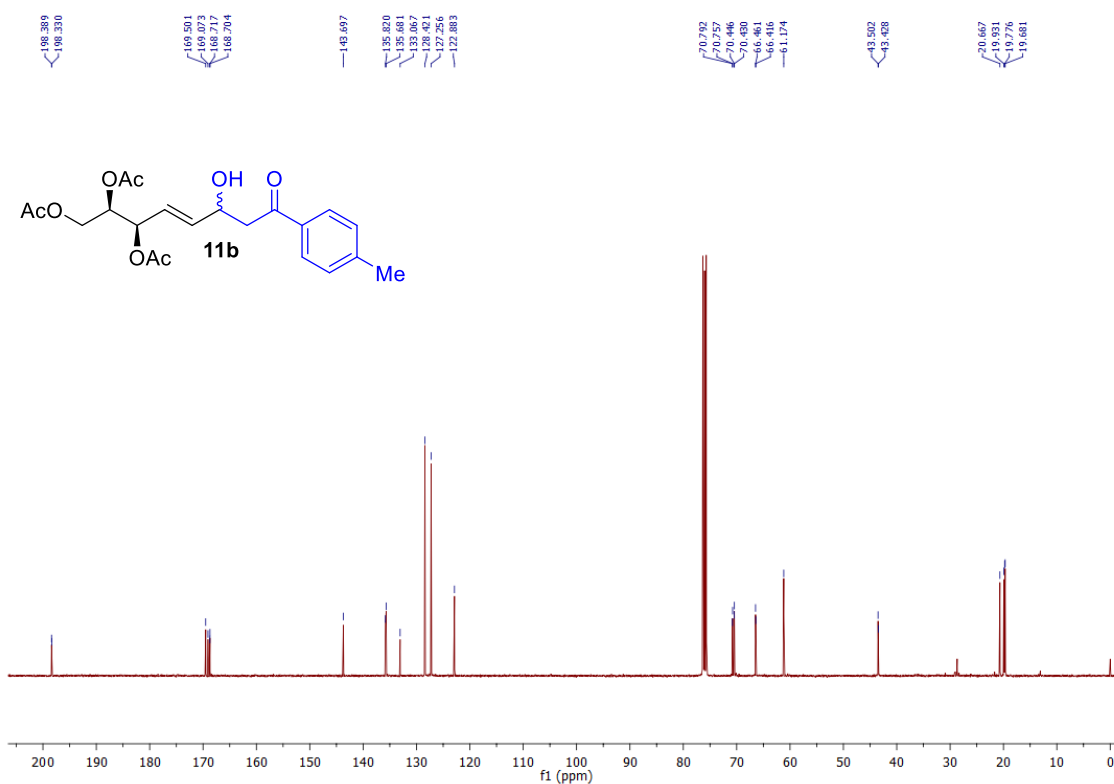
^1H NMR spectrum of compound 11b (400 MHz, CDCl_3):

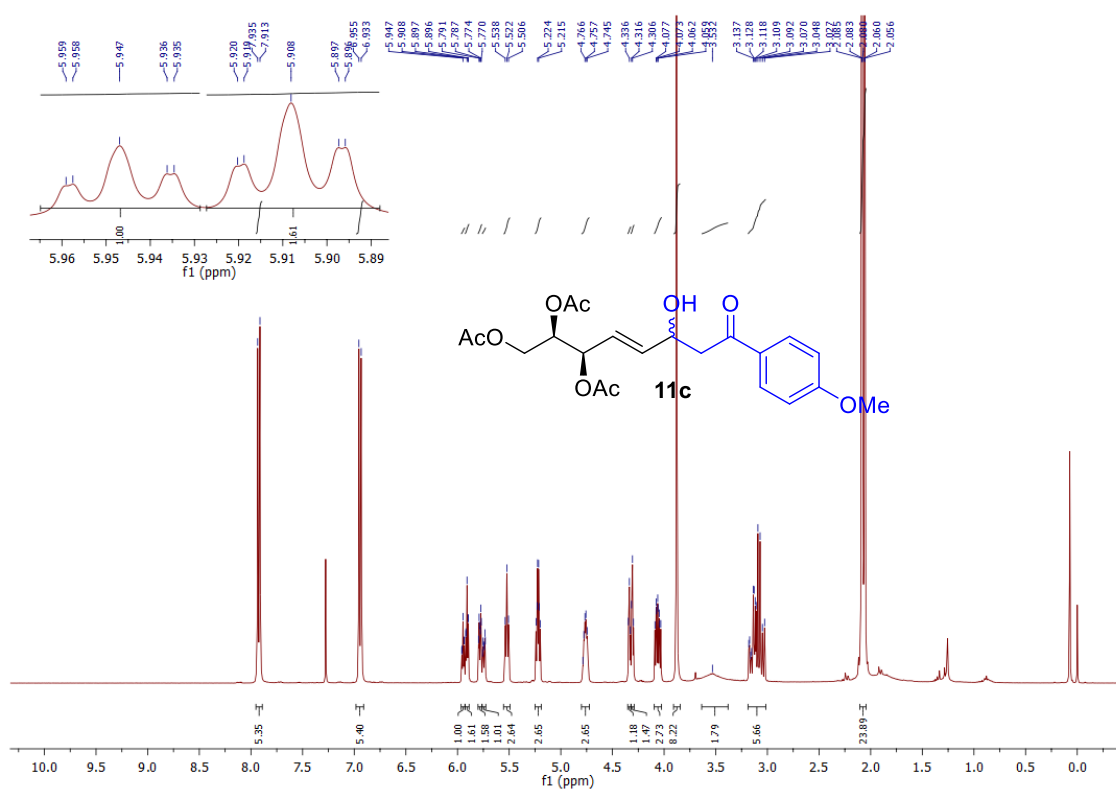
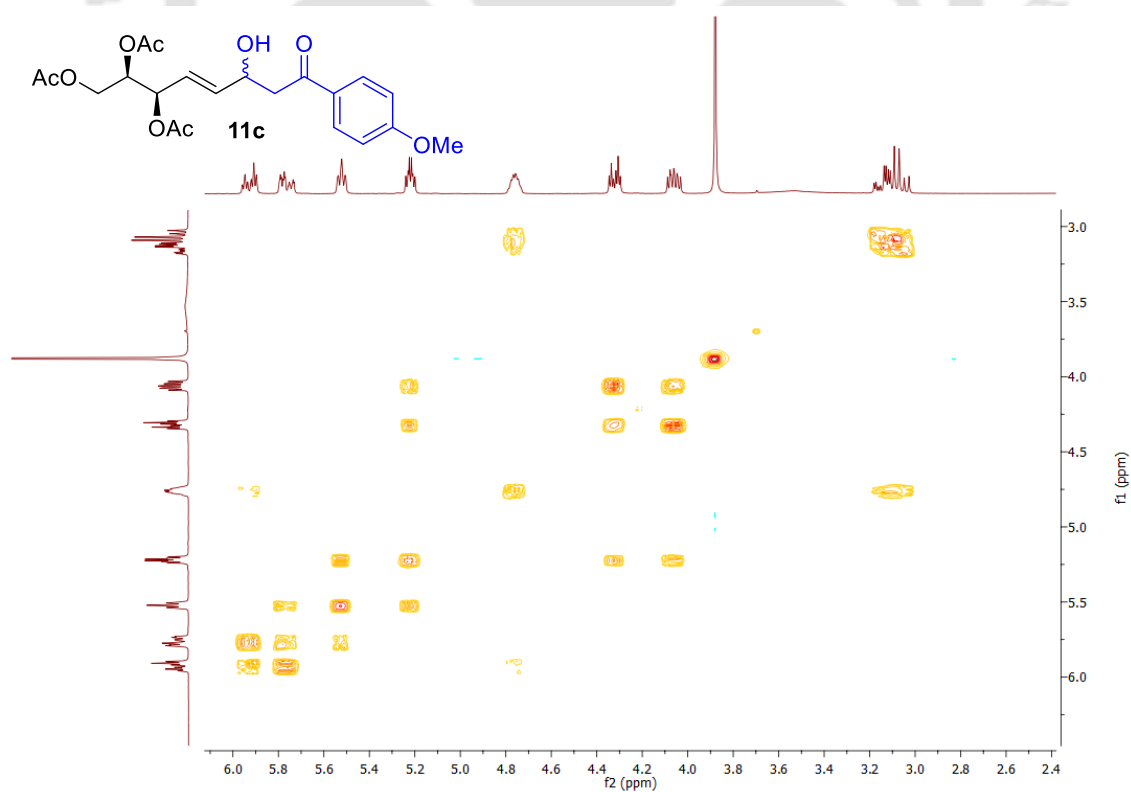


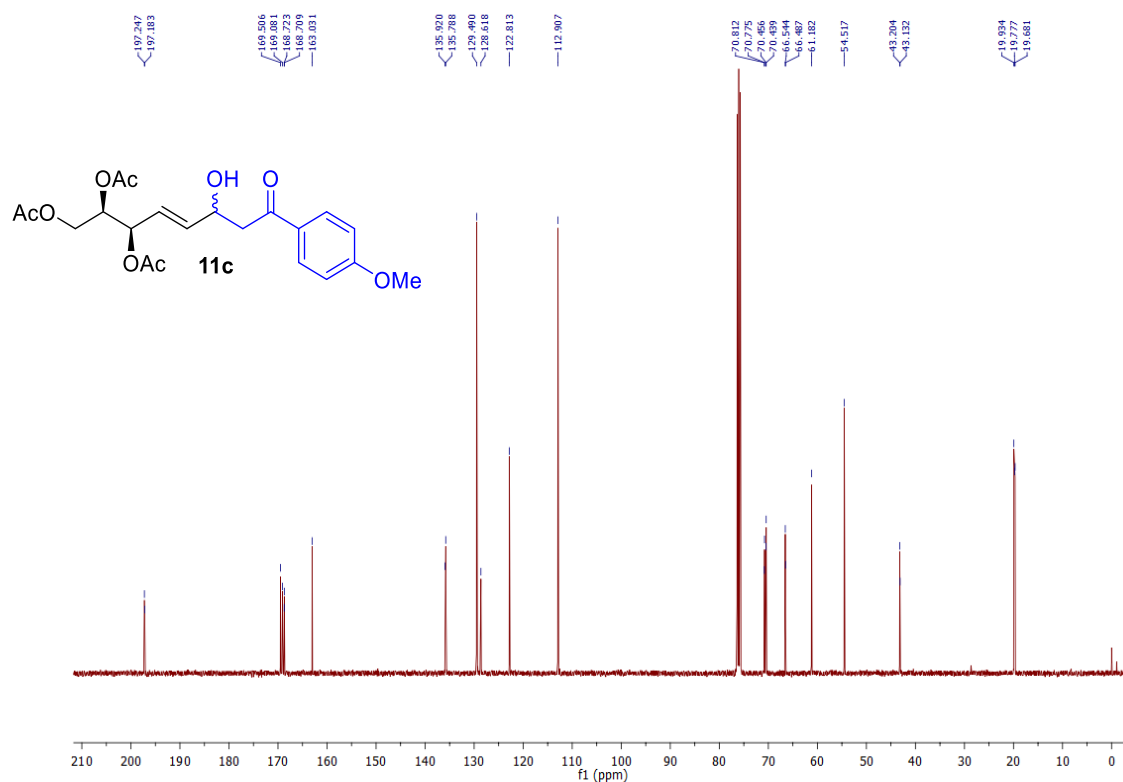
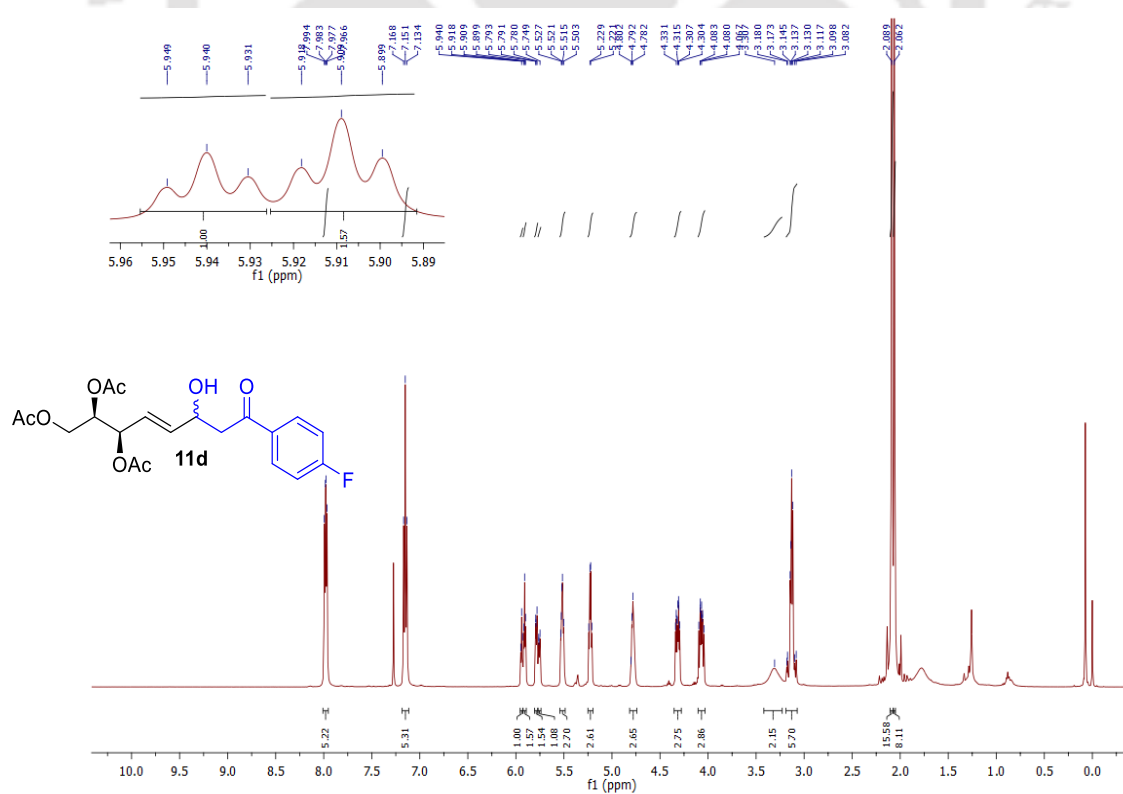
COSY NMR spectrum of compound 11b (400 MHz, CDCl₃):



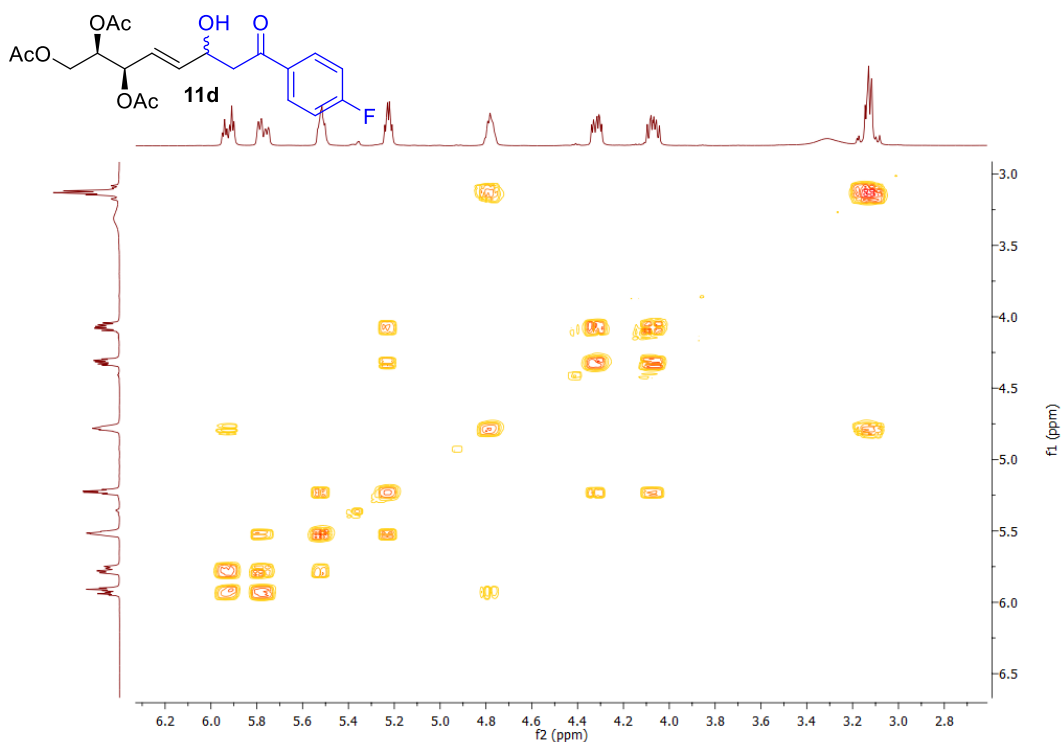
¹³C{¹H} NMR spectrum of compound 11b (400 MHz, CDCl₃):



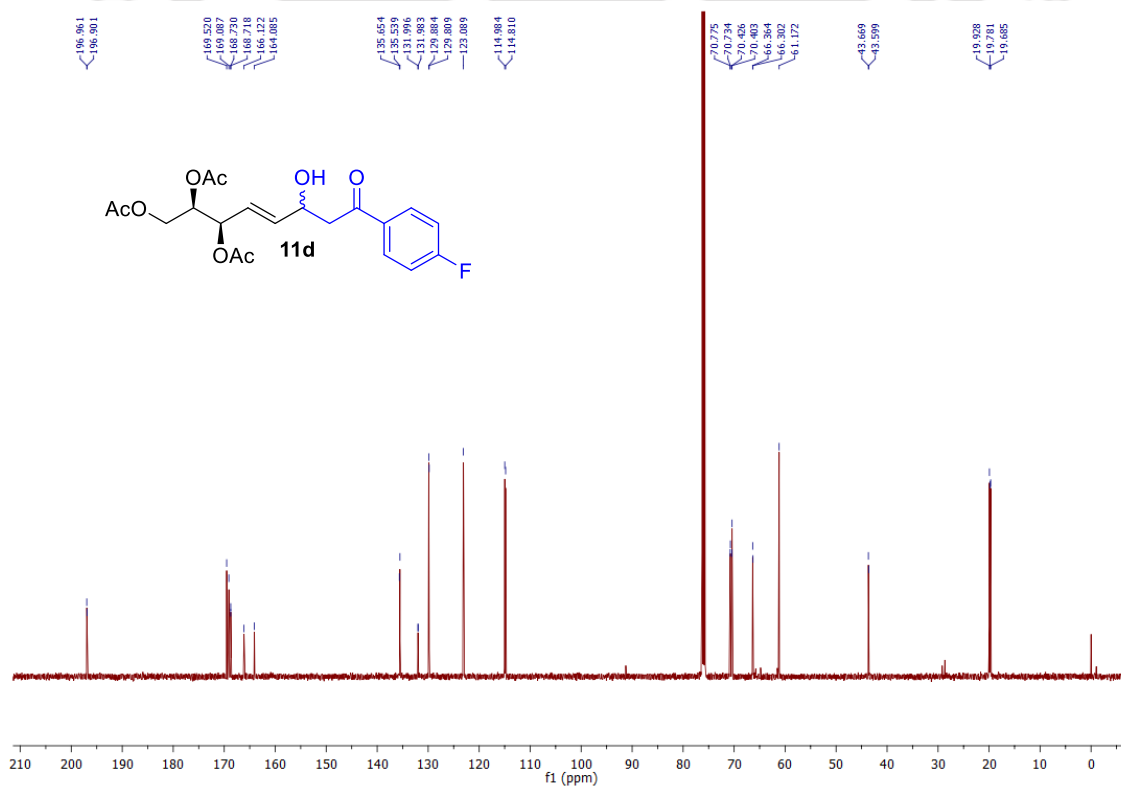
^1H NMR spectrum of compound 11c (400 MHz, CDCl_3):**COSY NMR spectrum of compound 11c (400 MHz, CDCl_3):**

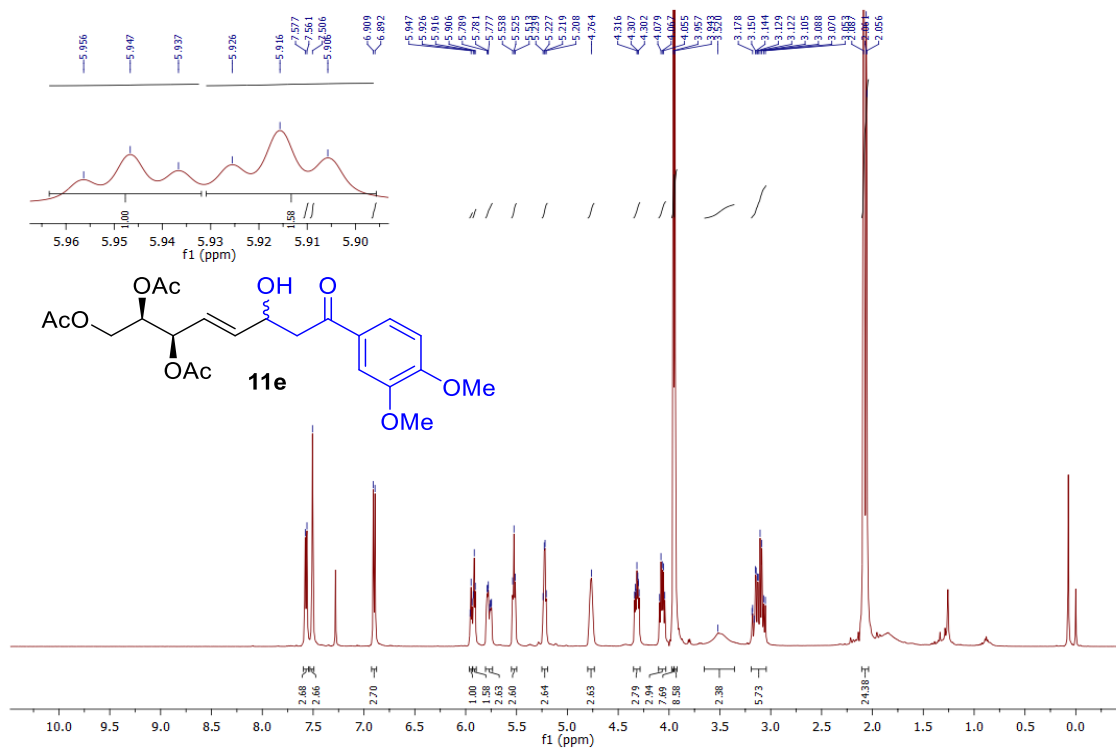
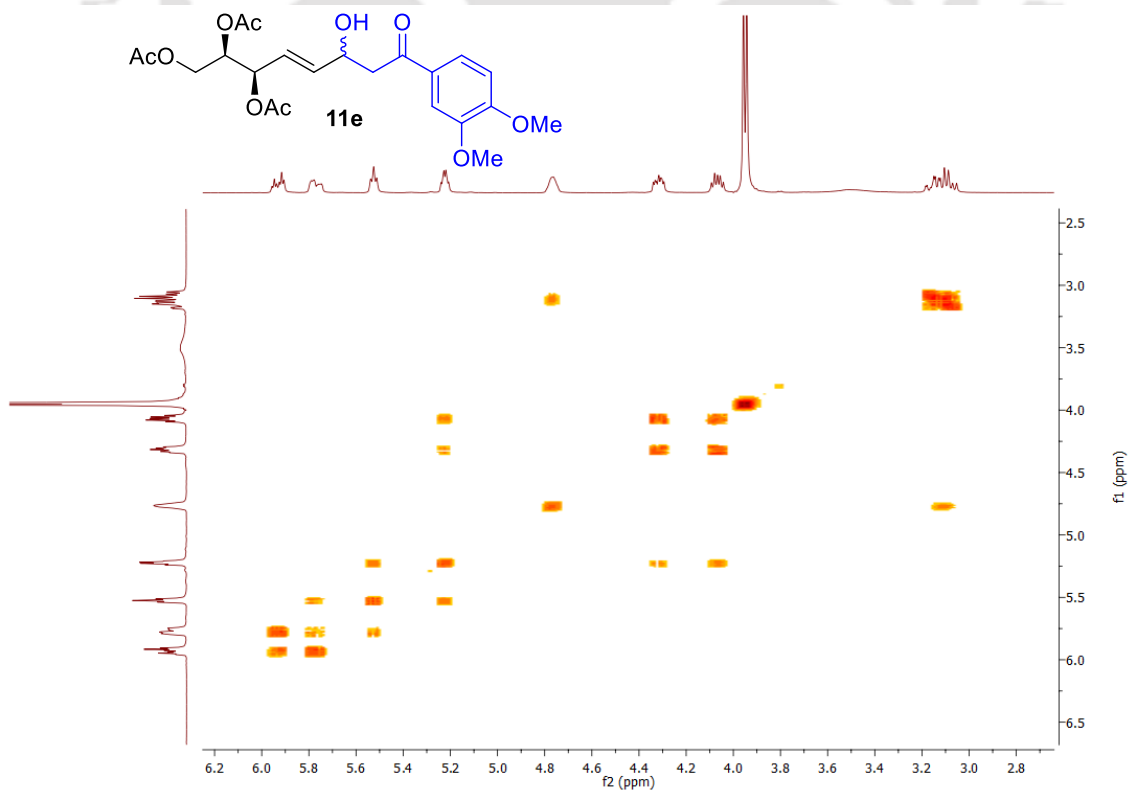
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 11c (400 MHz, CDCl_3):

 ^1H NMR spectrum of compound 11d (500 MHz, CDCl_3):


COSY NMR spectrum of compound 11d (500 MHz, CDCl₃):

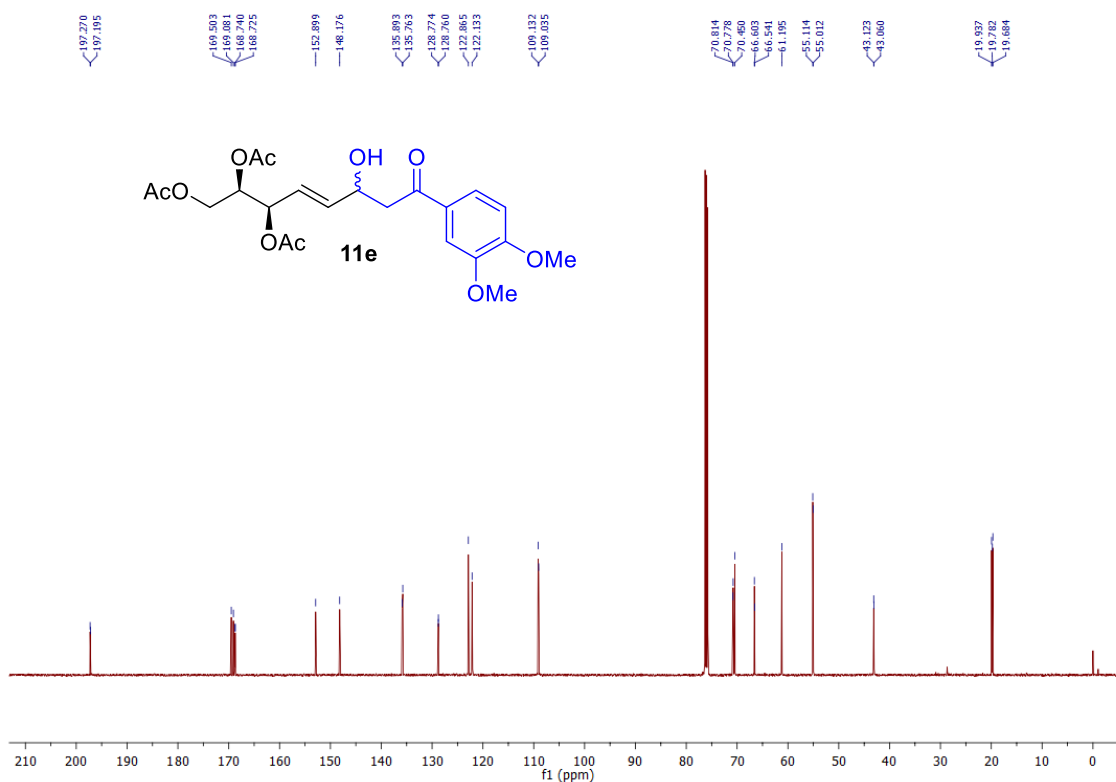


¹³C{¹H} NMR spectrum of compound 11d (500 MHz, CDCl₃):

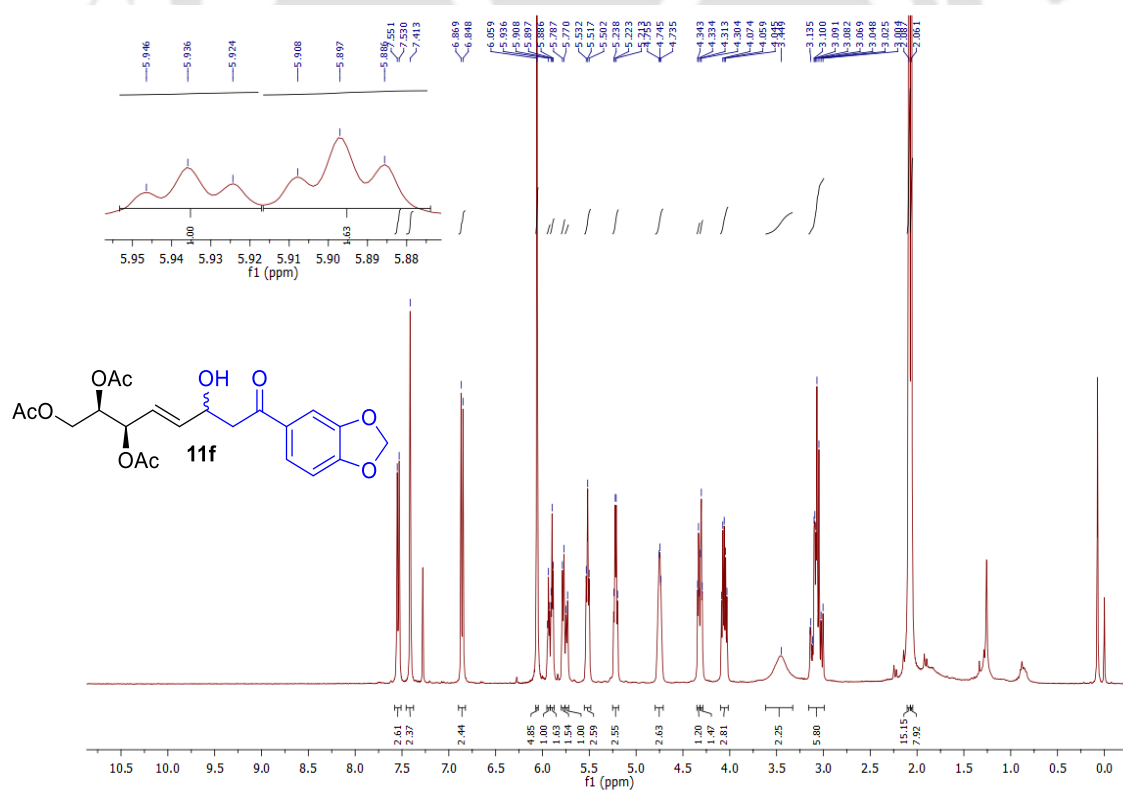


^1H NMR spectrum of compound 11e (500 MHz, CDCl_3):**COSY NMR spectrum of compound 11e (500 MHz, CDCl_3):**

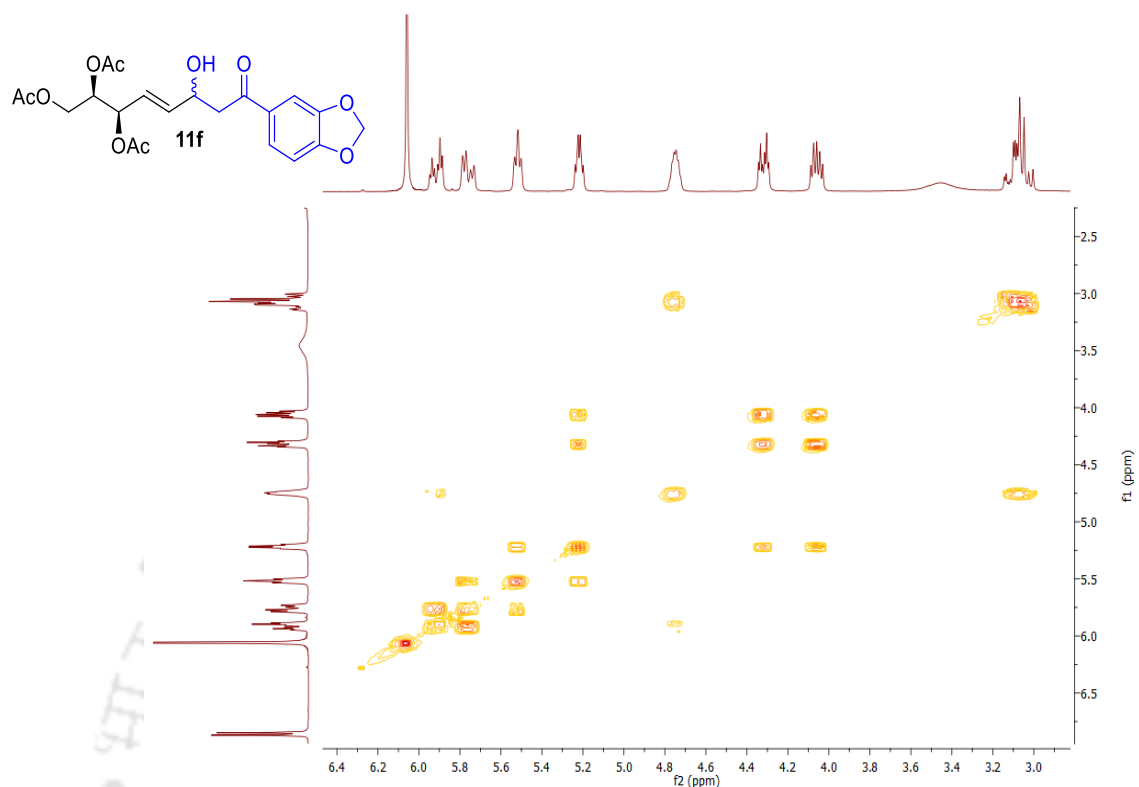
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 11e (500 MHz, CDCl_3):



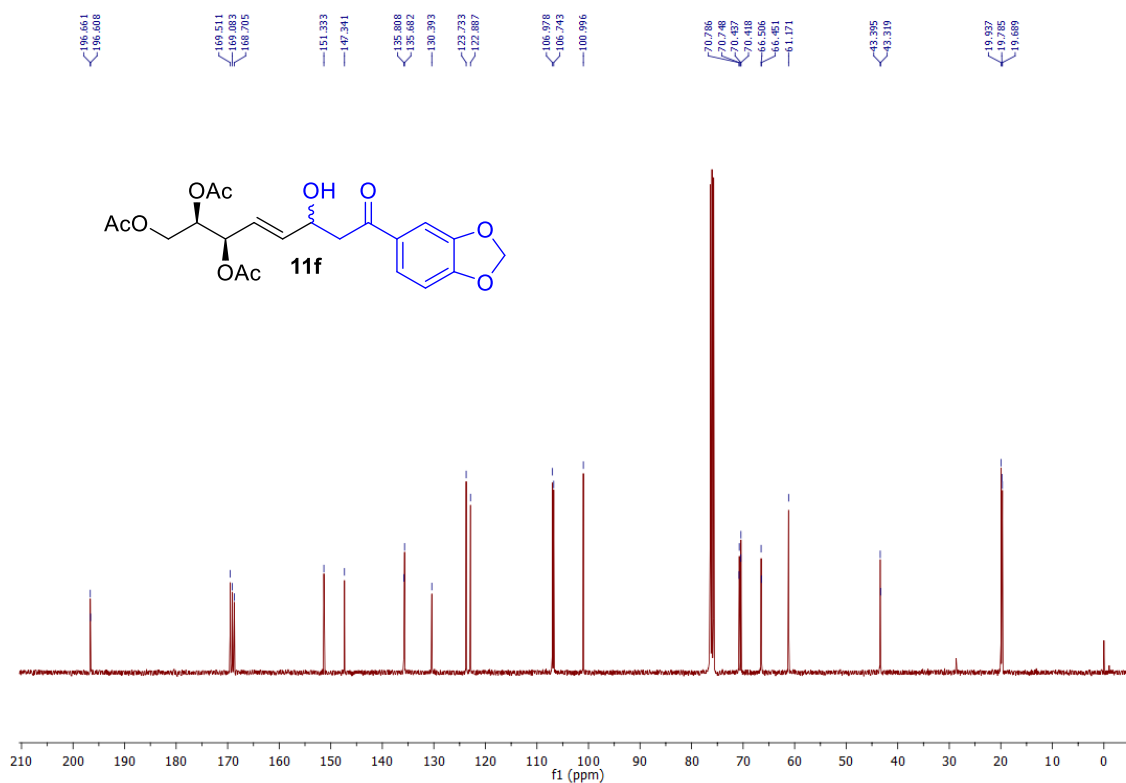
¹H NMR spectrum of compound 11f (400 MHz, CDCl₃):

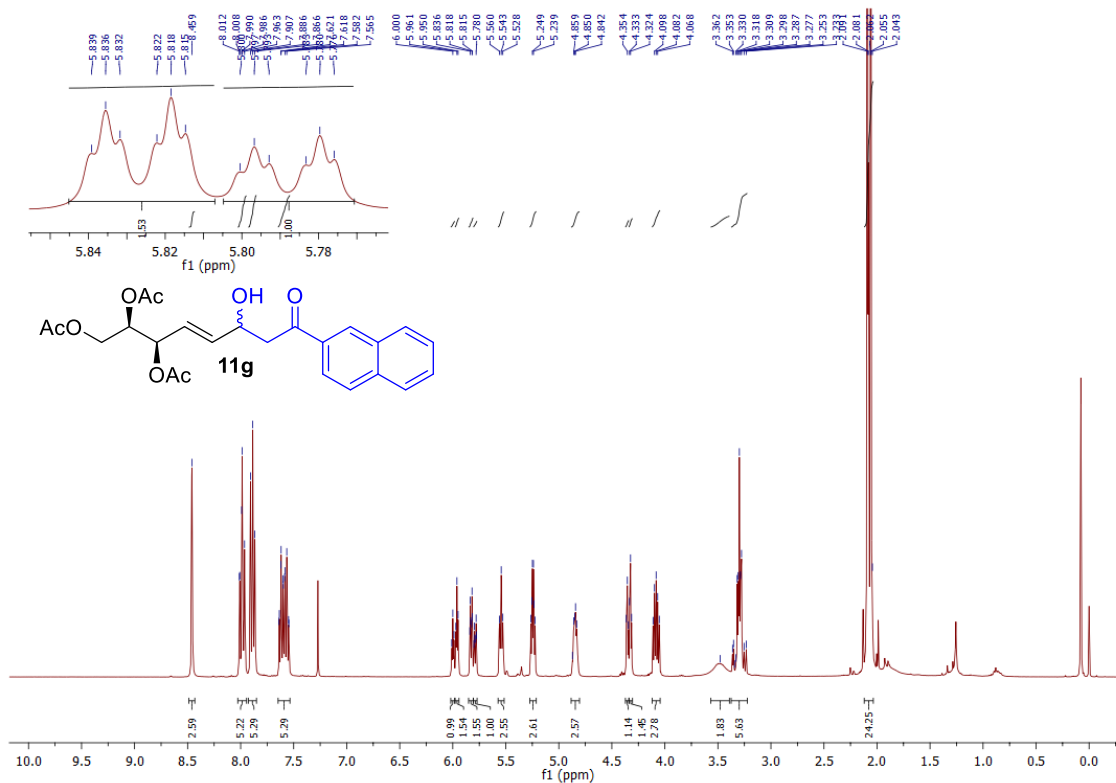
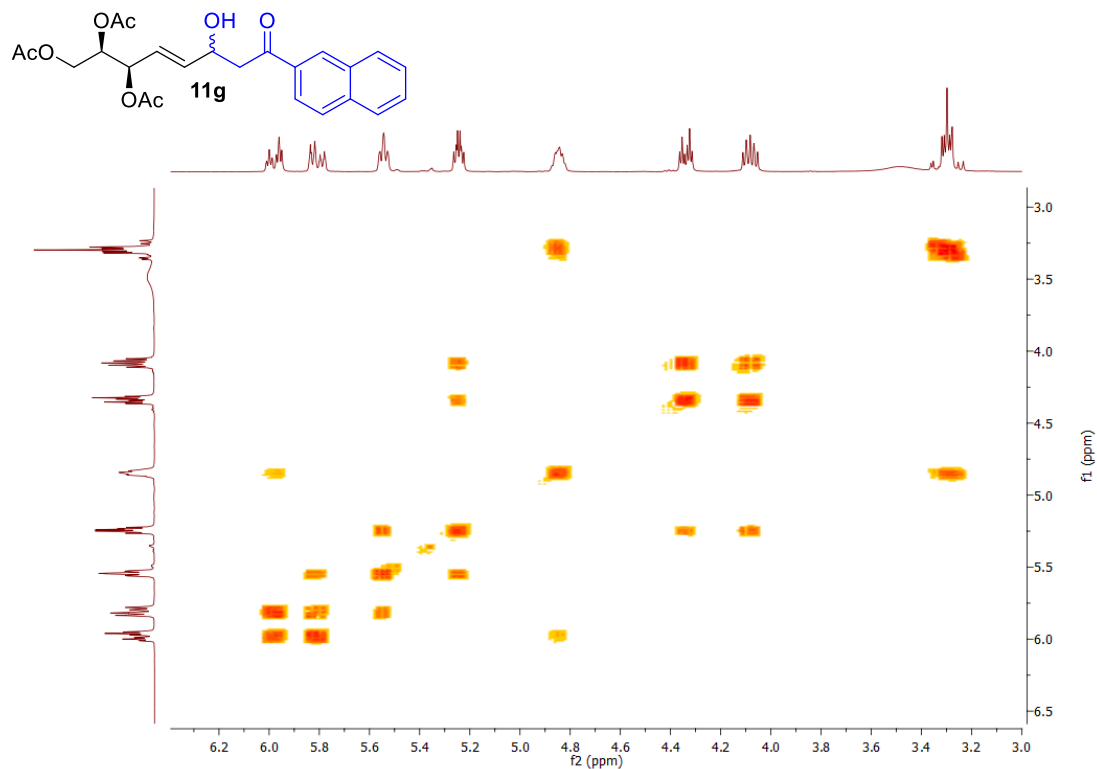


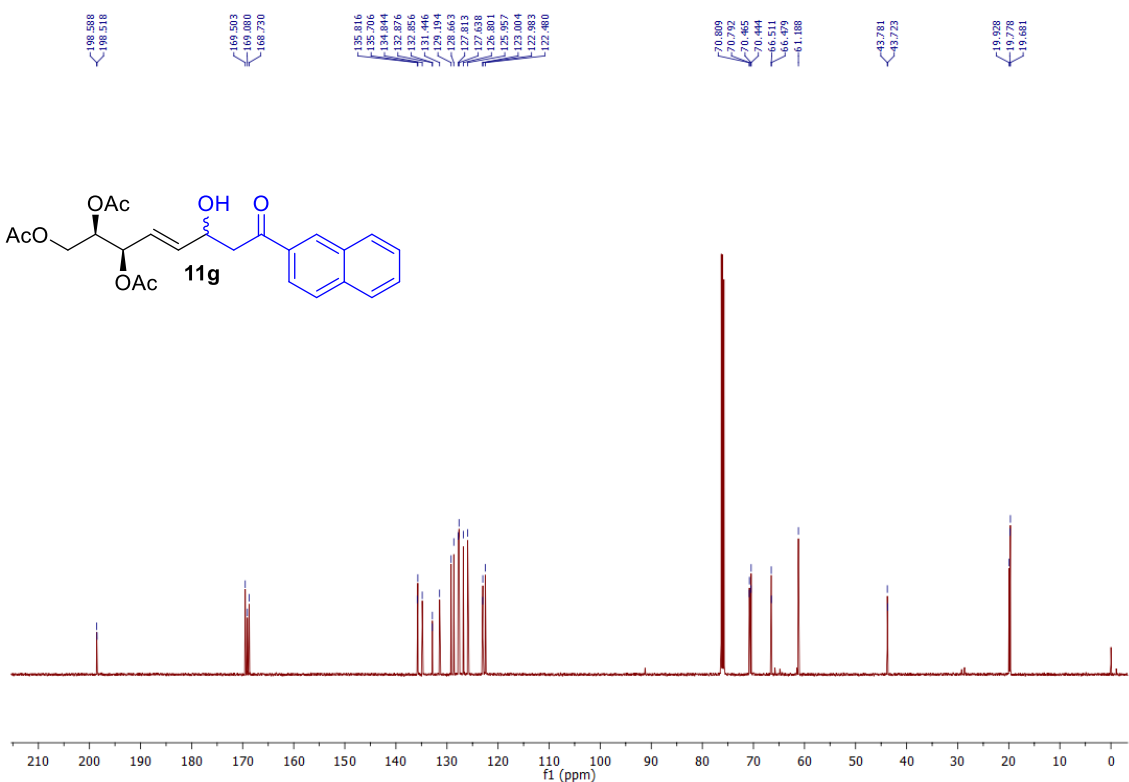
COSY NMR spectrum of compound 11f (400 MHz, CDCl₃):



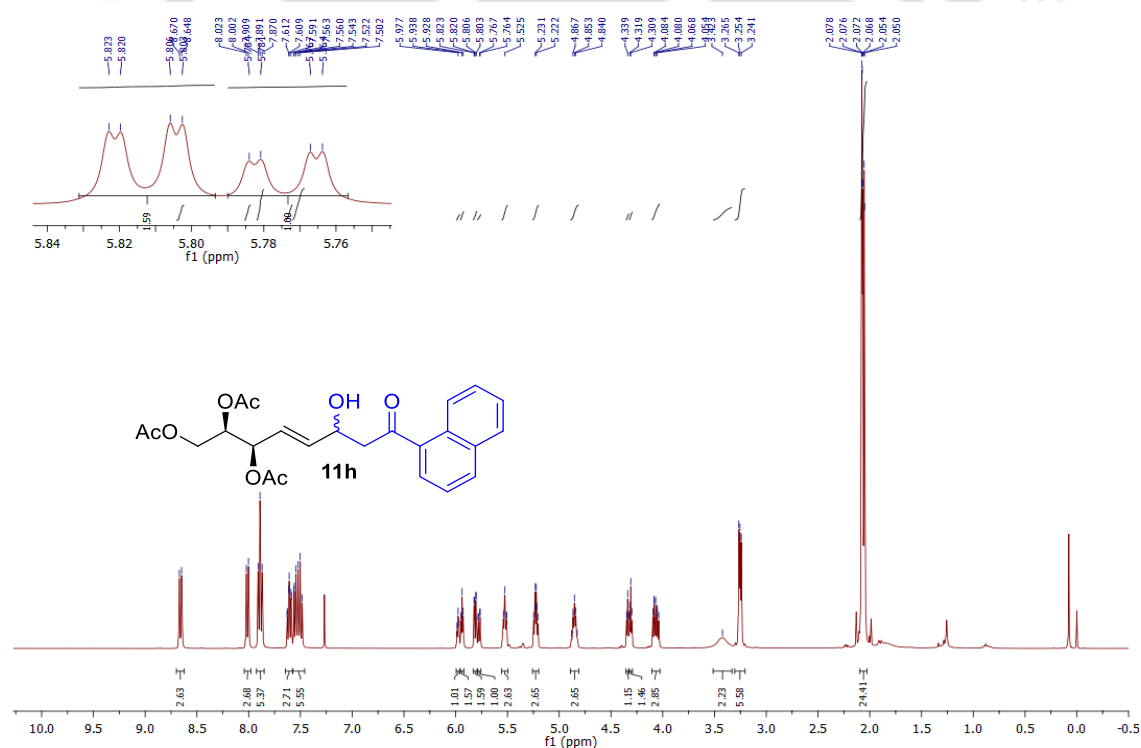
¹³C{¹H} NMR spectrum of compound 11f (400 MHz, CDCl₃):

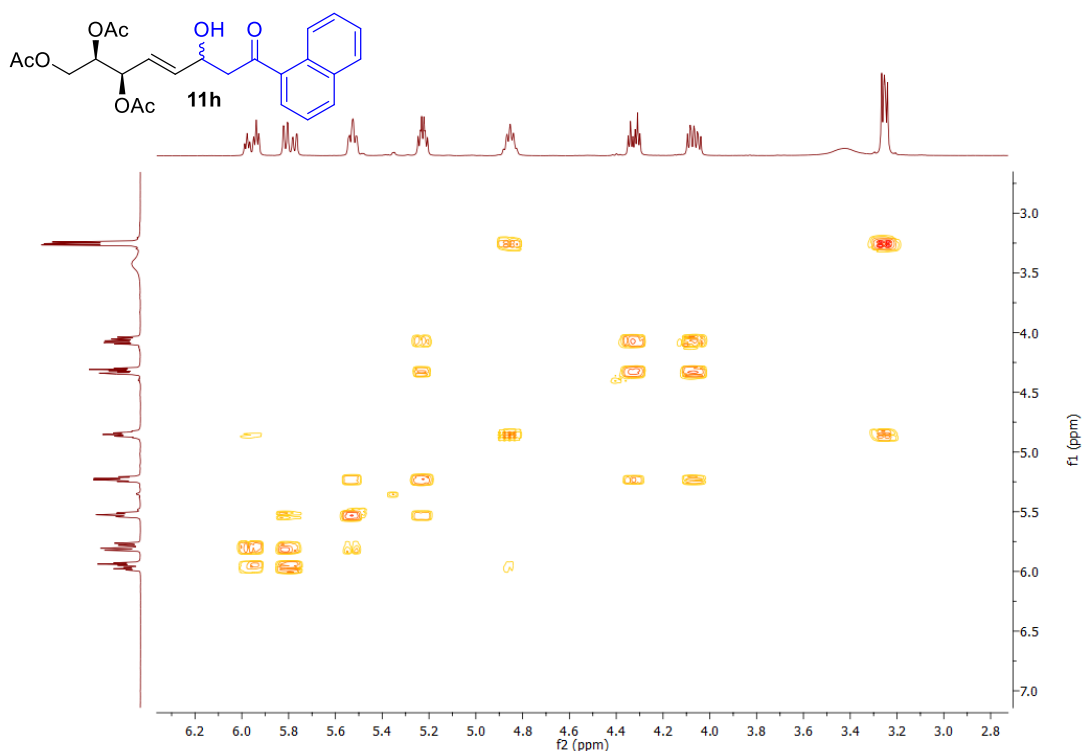
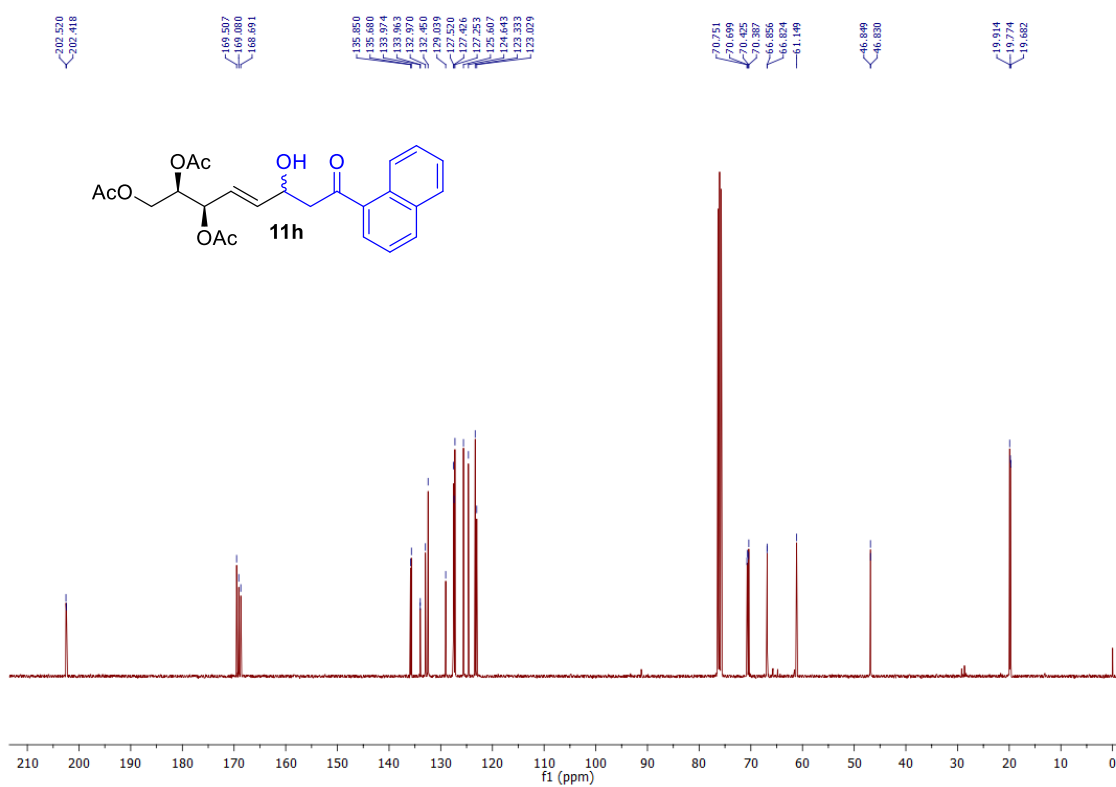


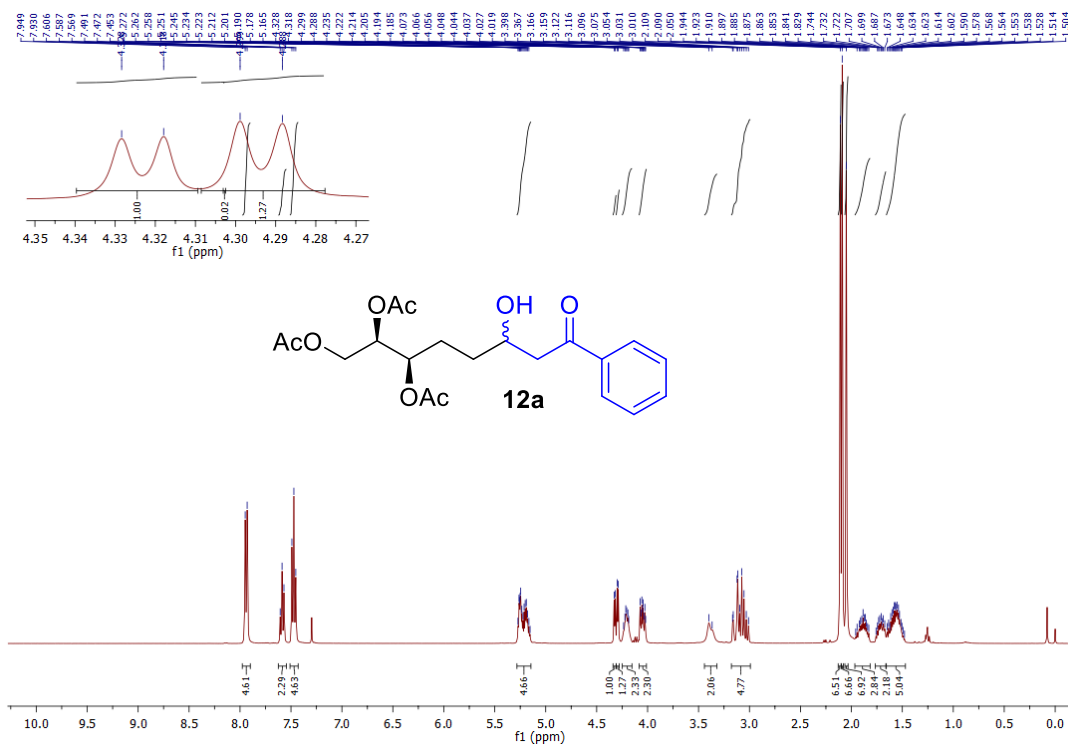
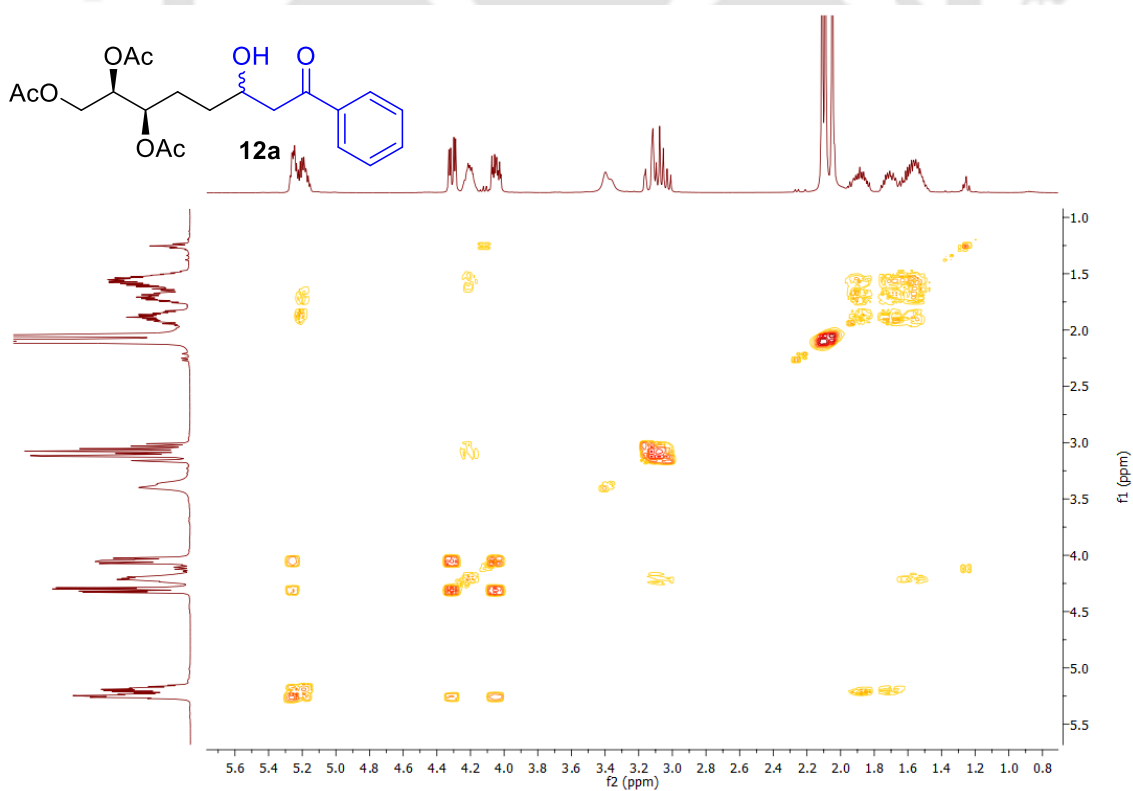
^1H NMR spectrum of compound 11g (400 MHz, CDCl_3):**COSY NMR spectrum of compound 11g (400 MHz, CDCl_3):**

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 11g (500 MHz, CDCl_3):

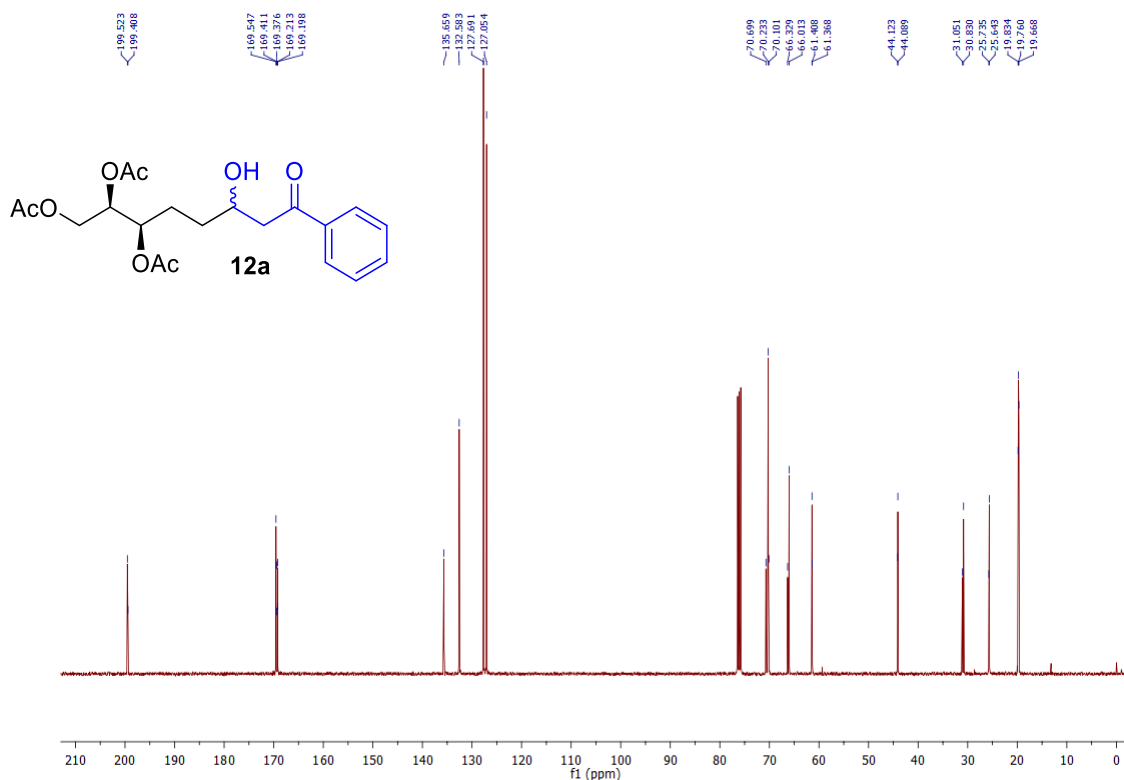
¹H NMR spectrum of compound 11h (400 MHz, CDCl₃):



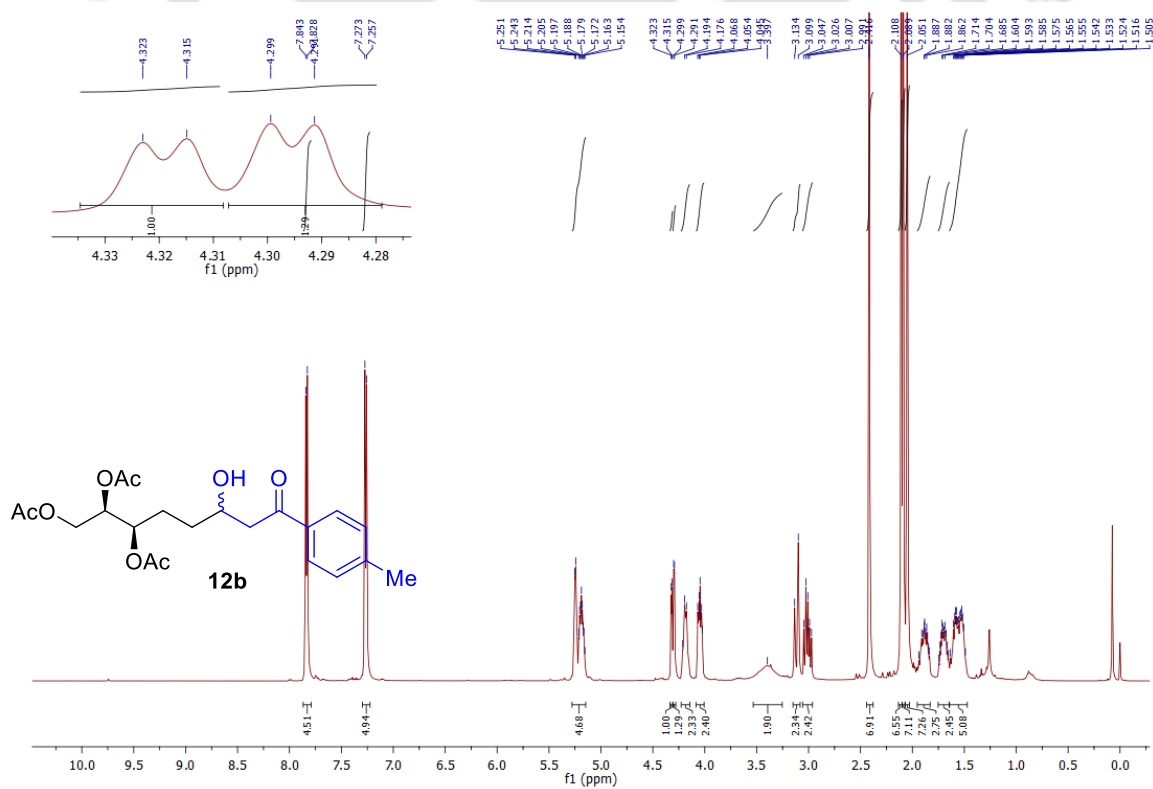
COSY NMR spectrum of compound 11h (400 MHz, CDCl₃):

¹³C{¹H} NMR spectrum of compound 11h (400 MHz, CDCl₃):


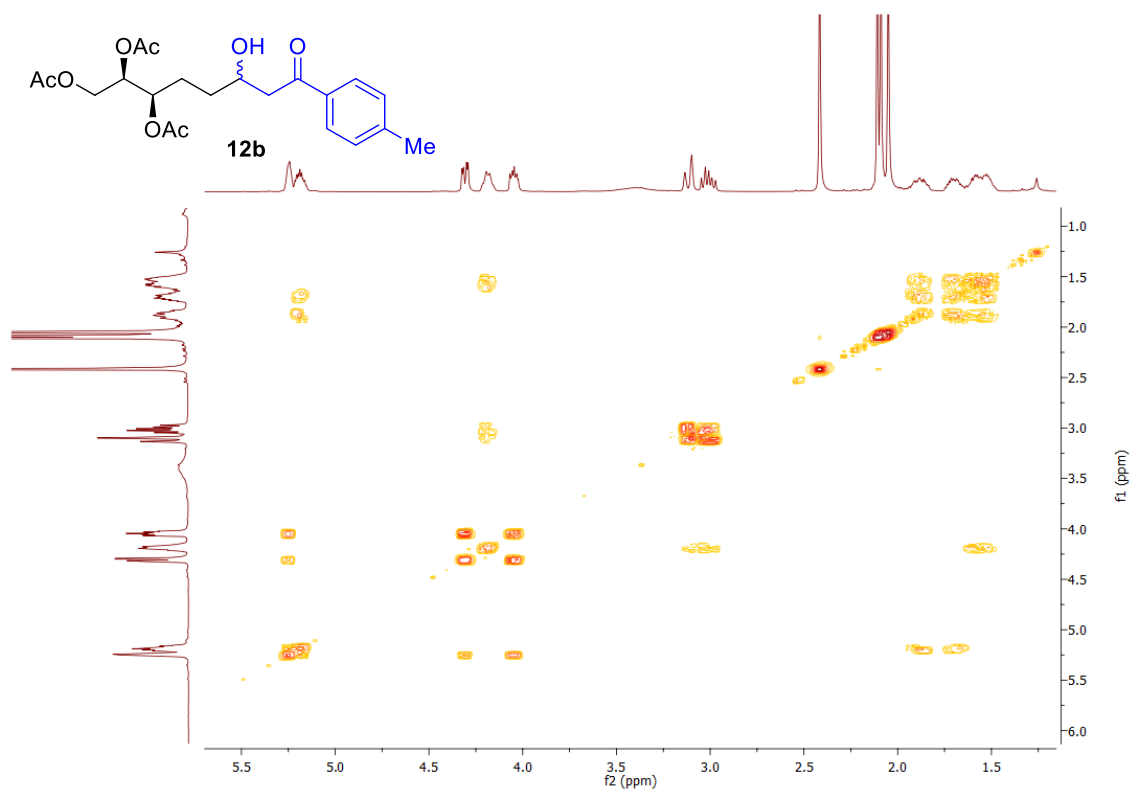
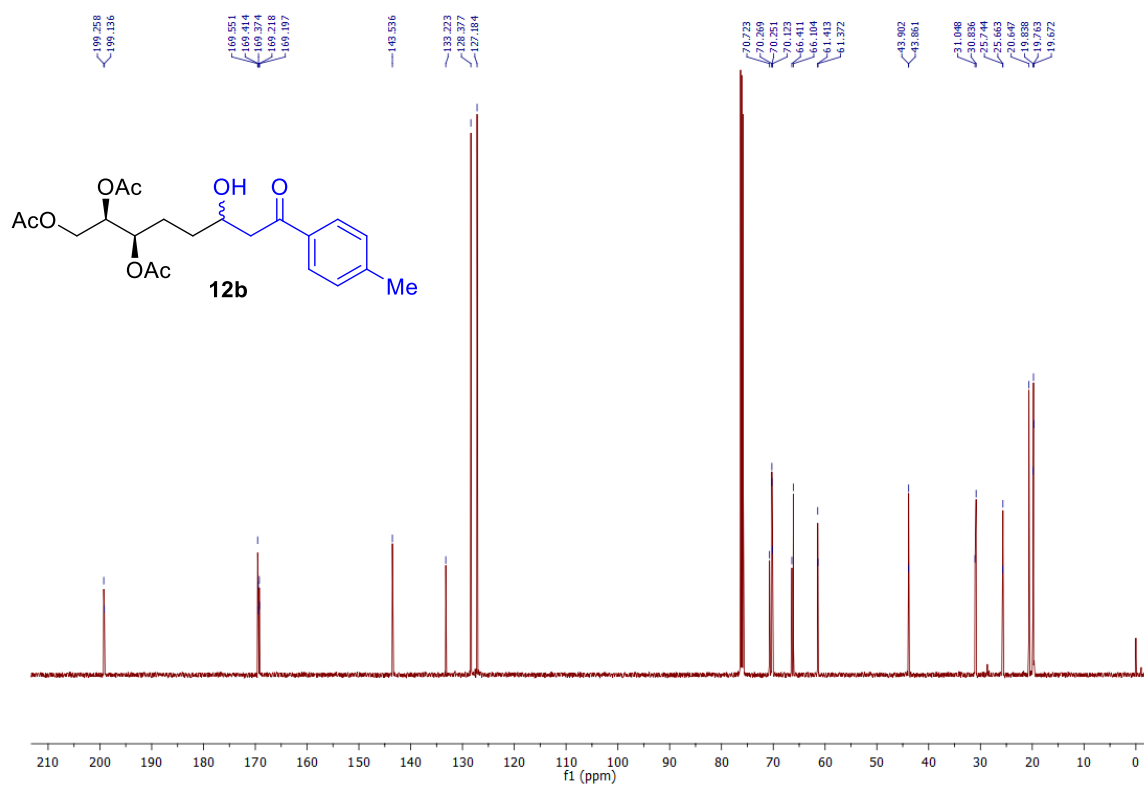
^1H NMR spectrum of compound 12a (400 MHz, CDCl_3):**COSY NMR spectrum of compound 12a (400 MHz, CDCl_3):**

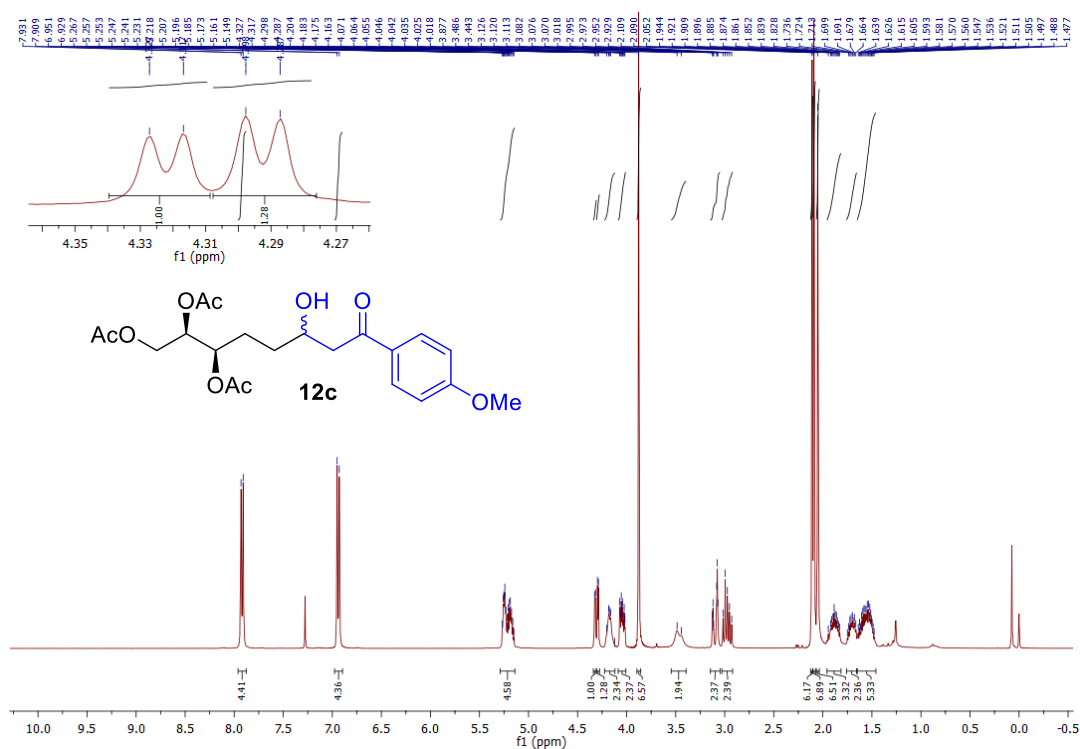
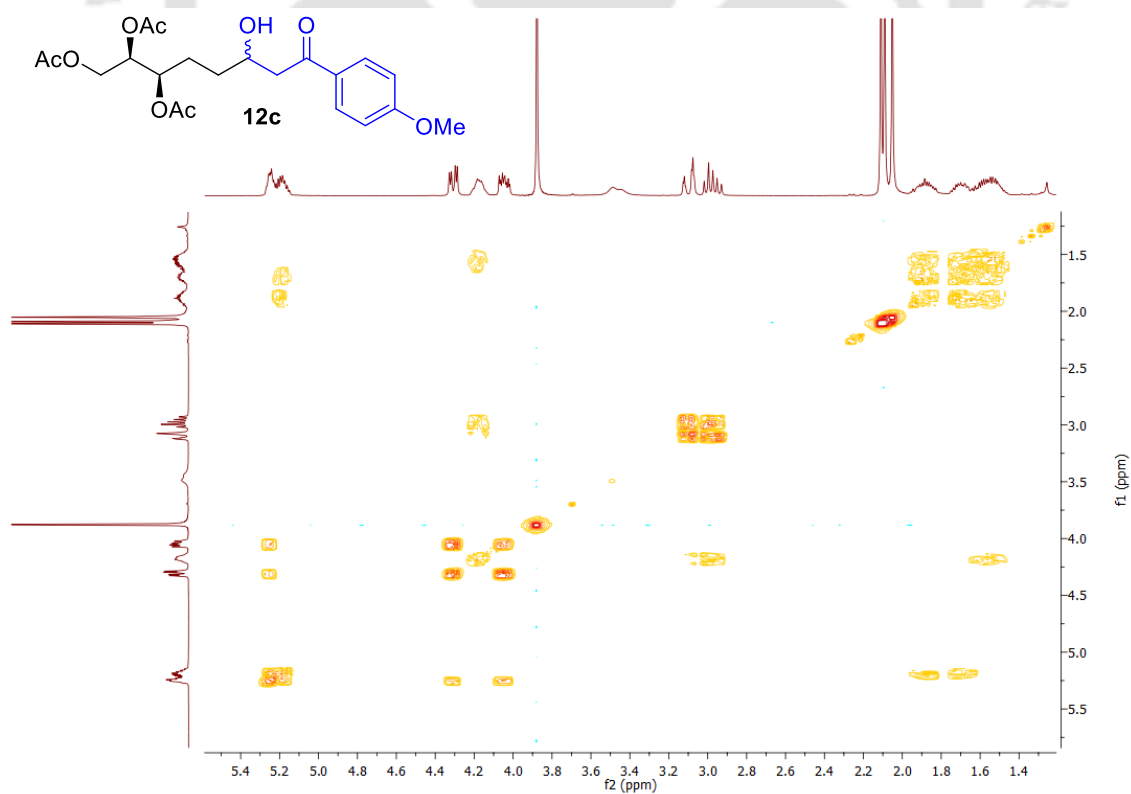
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 12a (400 MHz, CDCl_3):

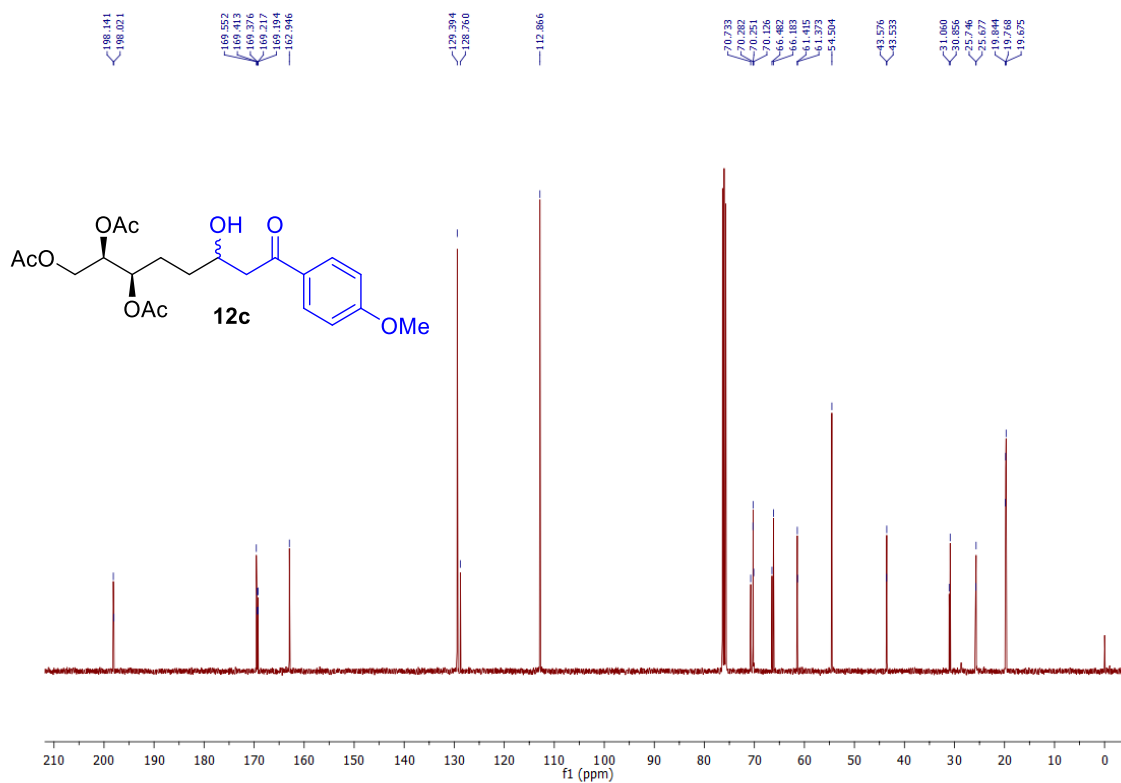
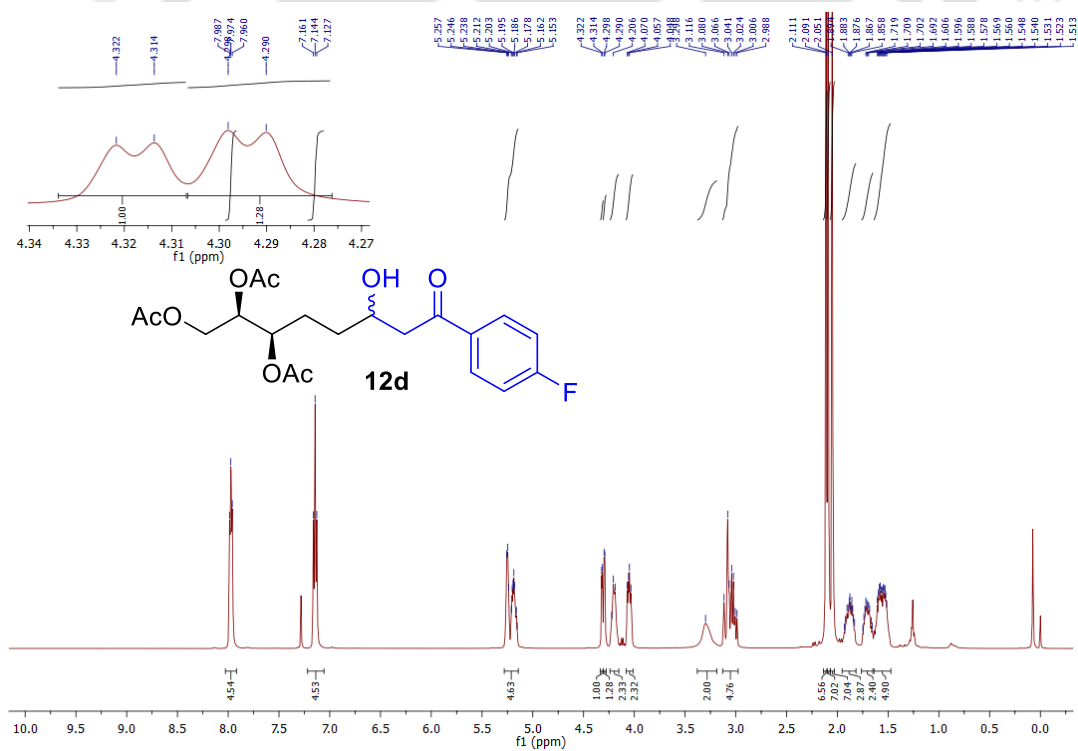


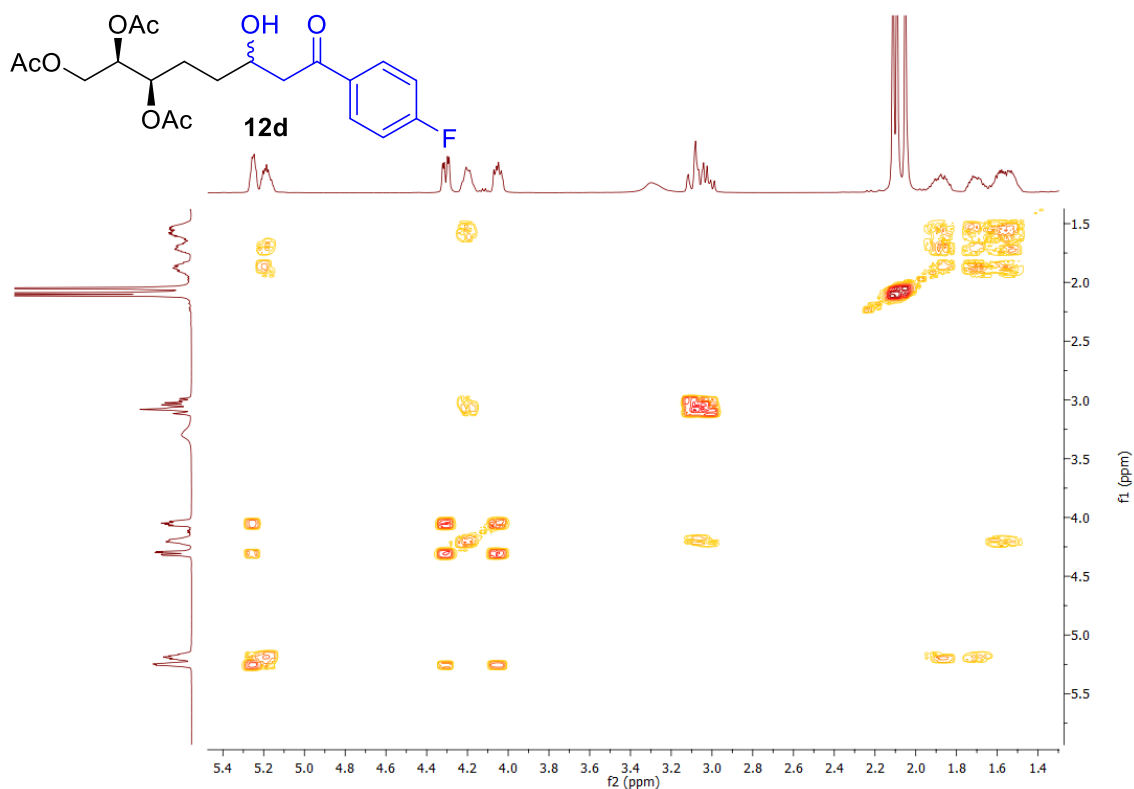
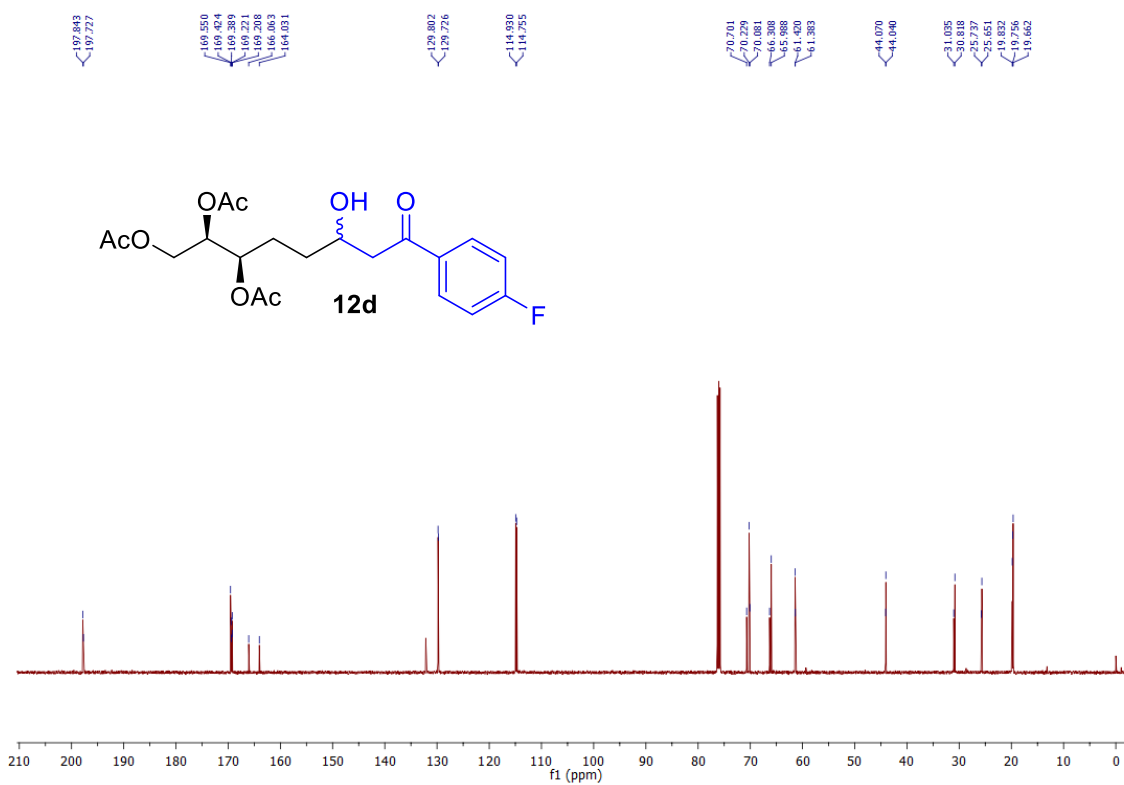
^1H NMR spectrum of compound 12b (500 MHz, CDCl_3):

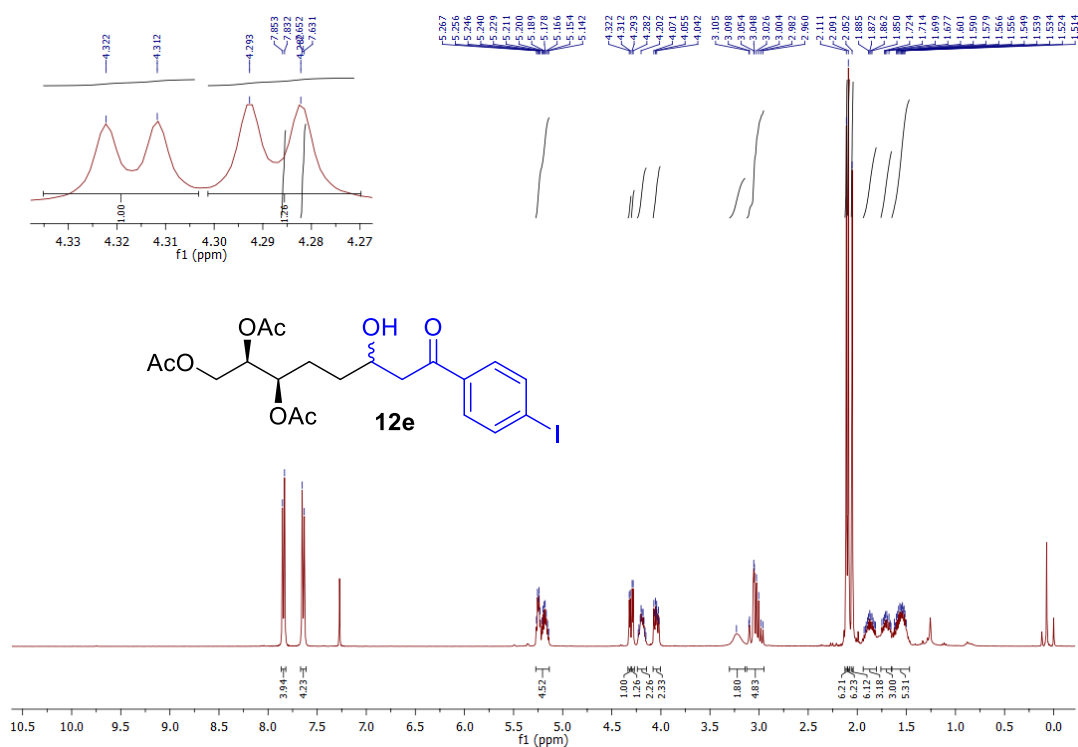
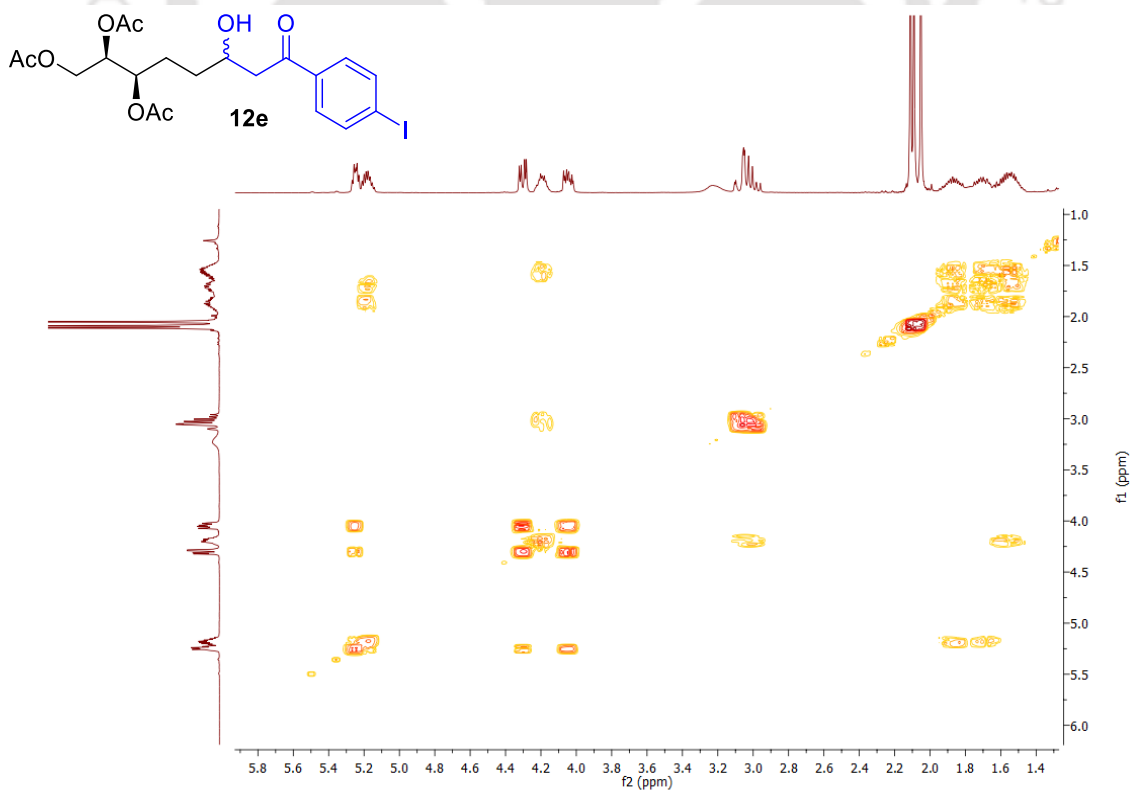


COSY NMR spectrum of compound 12b (500 MHz, CDCl₃):**¹³C{¹H} NMR spectrum of compound 12b (500 MHz, CDCl₃):**

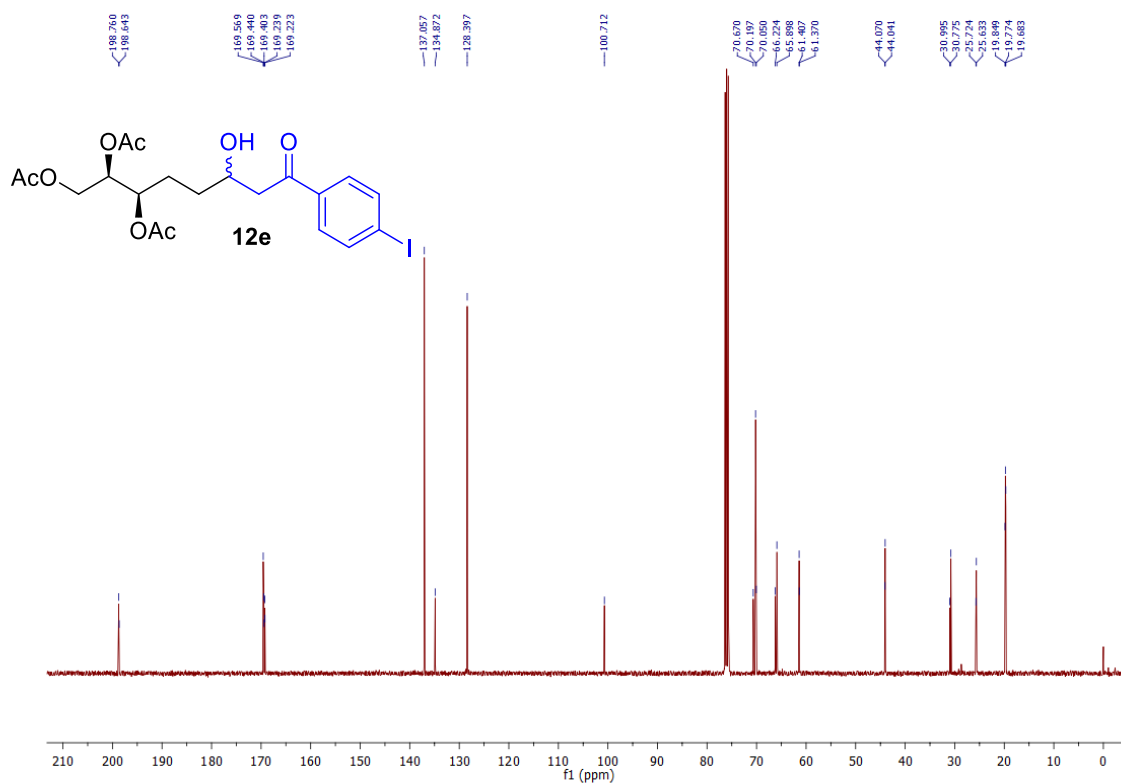
^1H NMR spectrum of compound 12c (400 MHz, CDCl_3):**COSY NMR spectrum of compound 12c (400 MHz, CDCl_3):**

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 12c (400 MHz, CDCl_3): **^1H NMR spectrum of compound 12d (500 MHz, CDCl_3):**

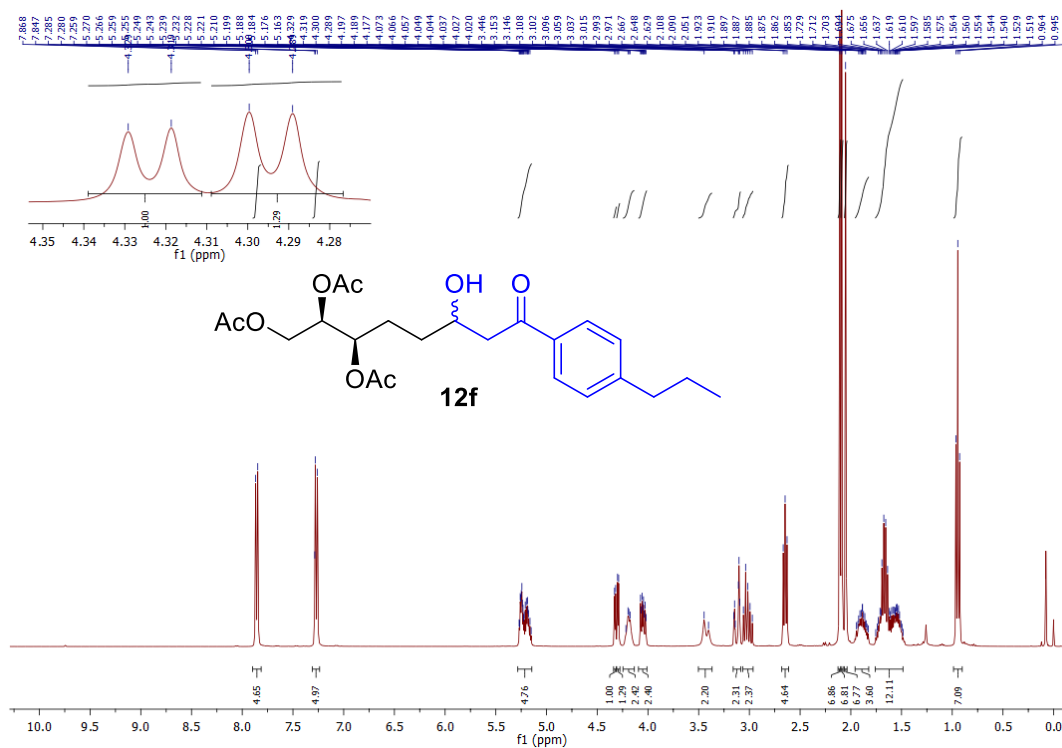
COSY NMR spectrum of compound 12d (500 MHz, CDCl₃):**¹³C{¹H} NMR spectrum of compound 12d (500 MHz, CDCl₃):**

^1H NMR spectrum of compound 12e (400 MHz, CDCl_3):**COSY NMR spectrum of compound 12e (400 MHz, CDCl_3):**

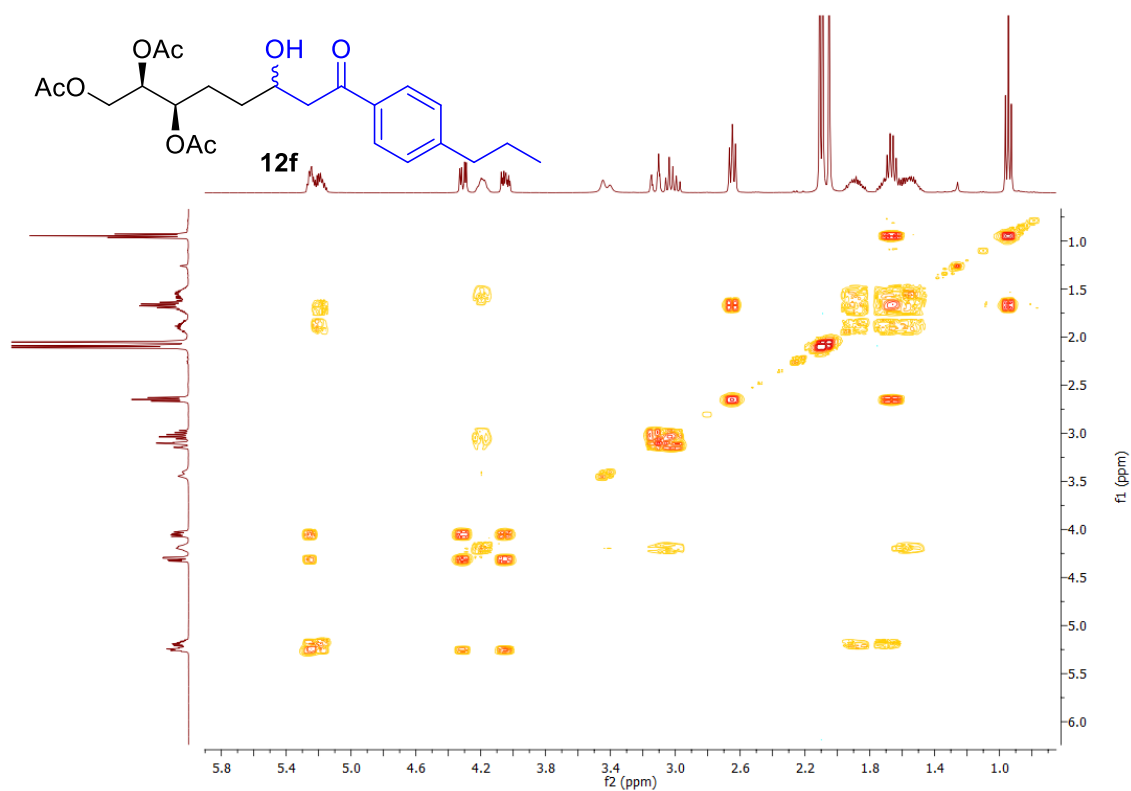
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 12e (400 MHz, CDCl_3):



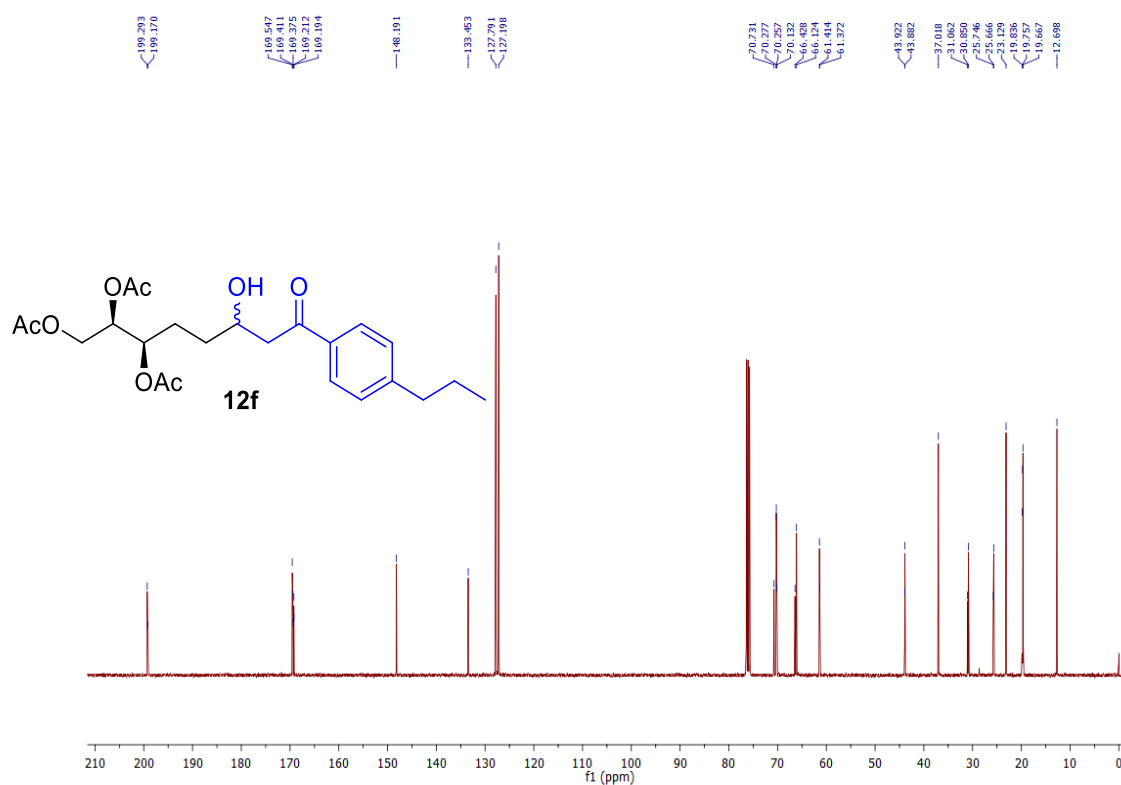
¹H NMR spectrum of compound 12f (400 MHz, CDCl₃):

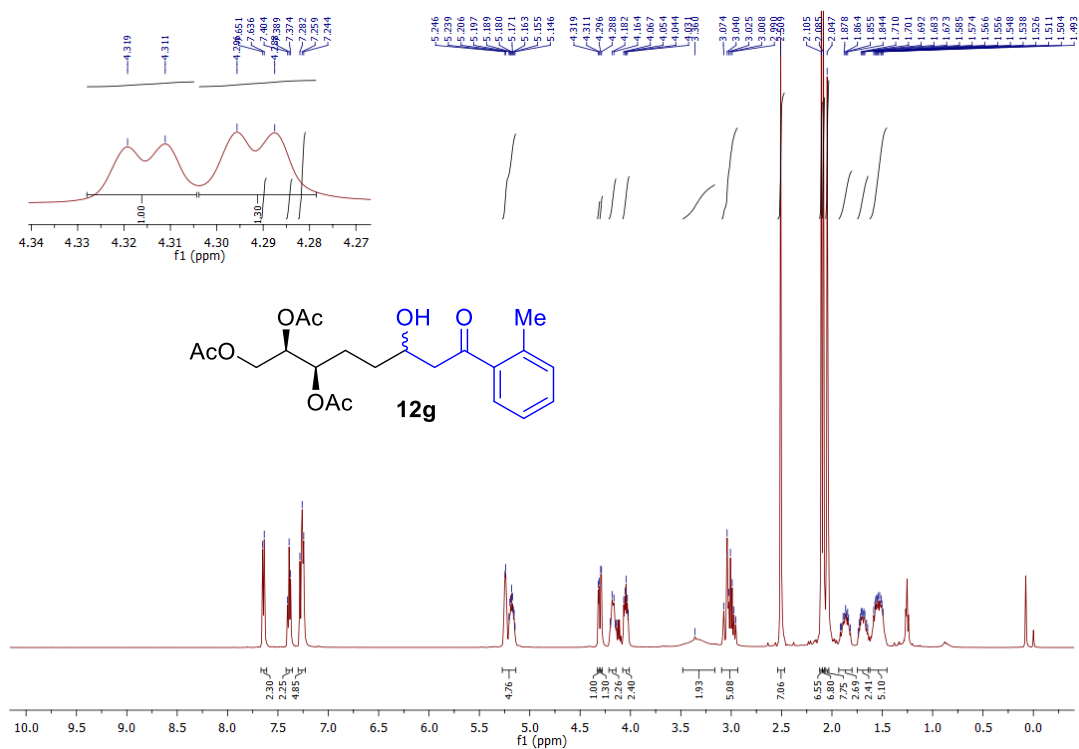
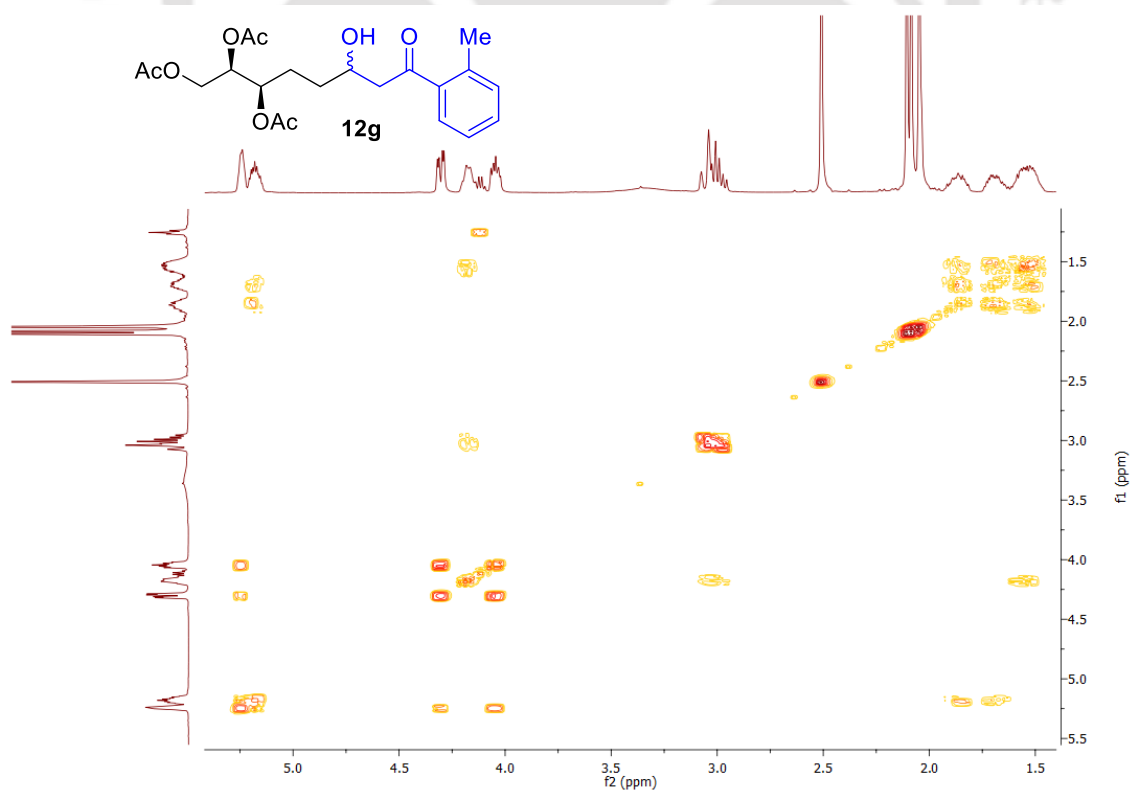


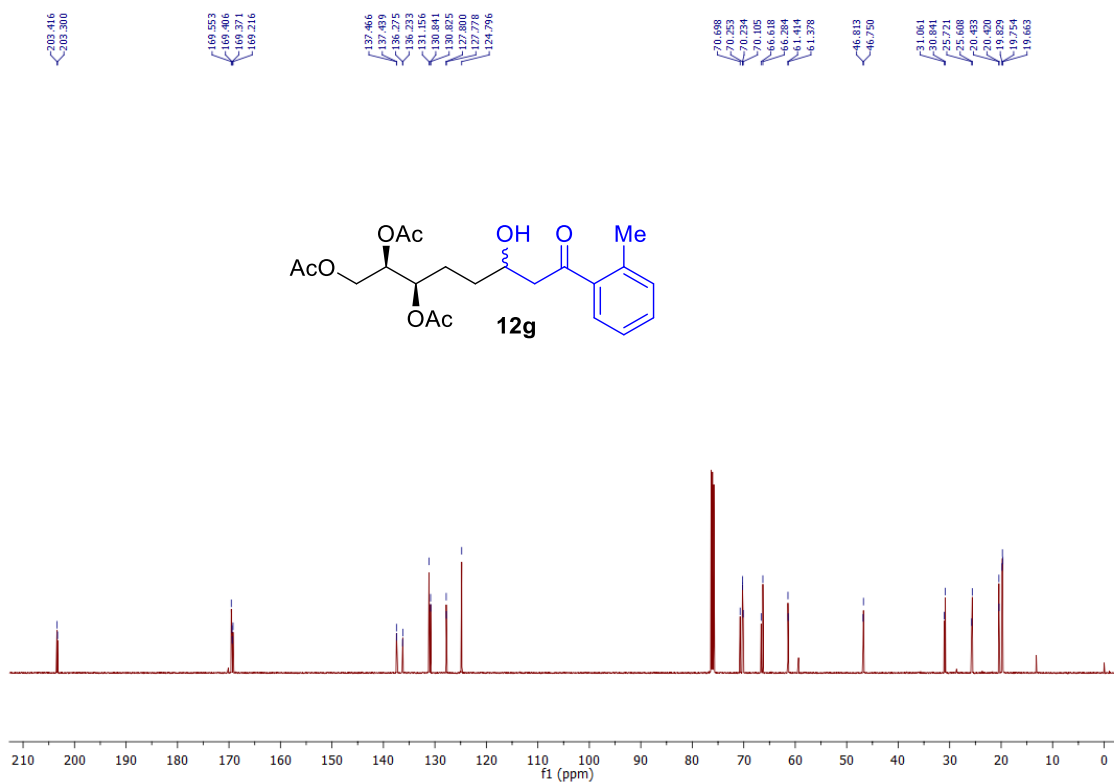
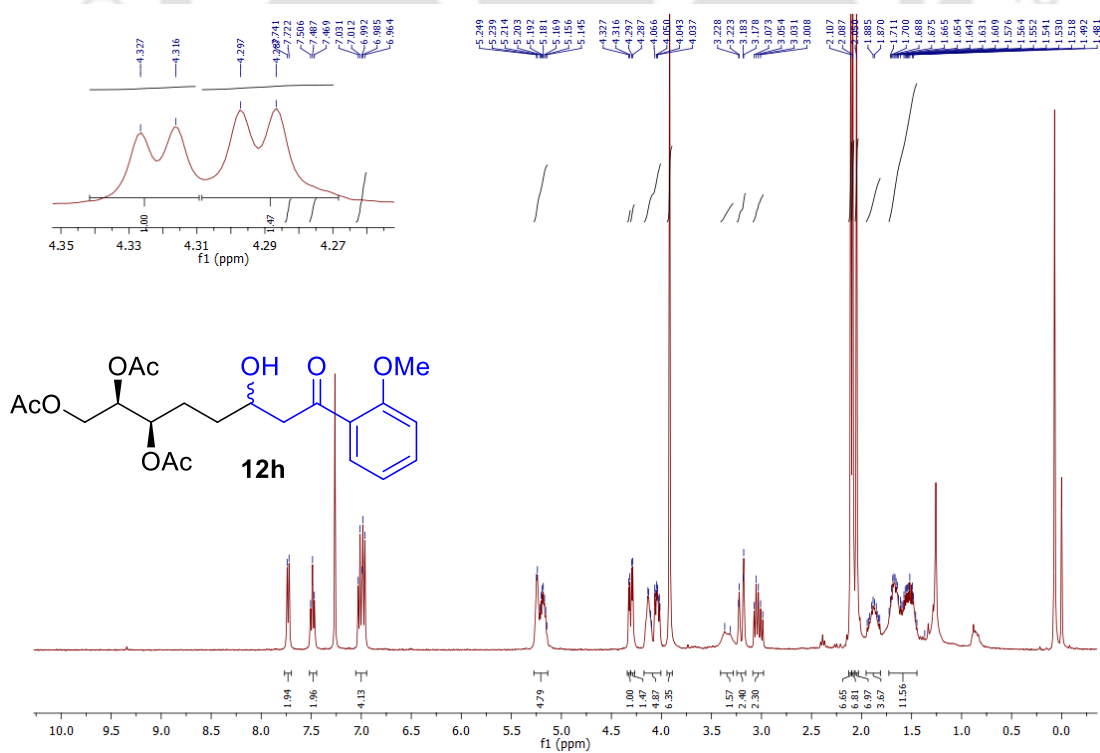
COSY NMR spectrum of compound 12f (400 MHz, CDCl₃):

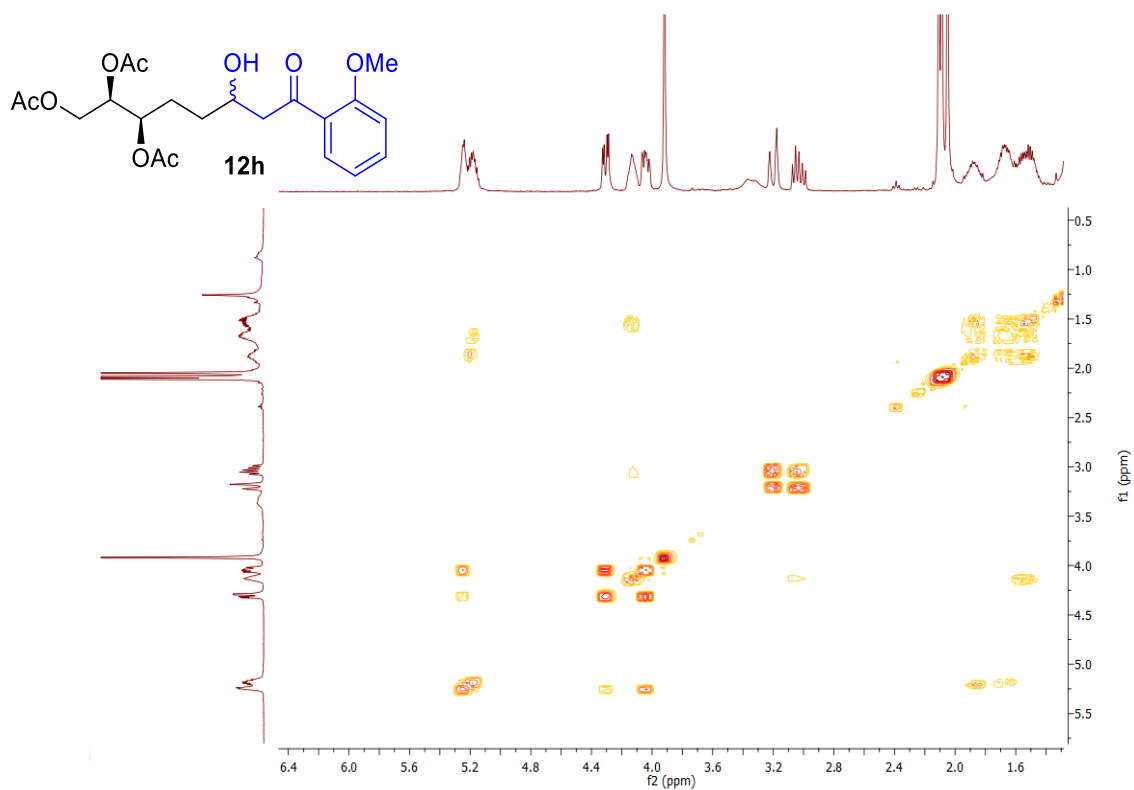
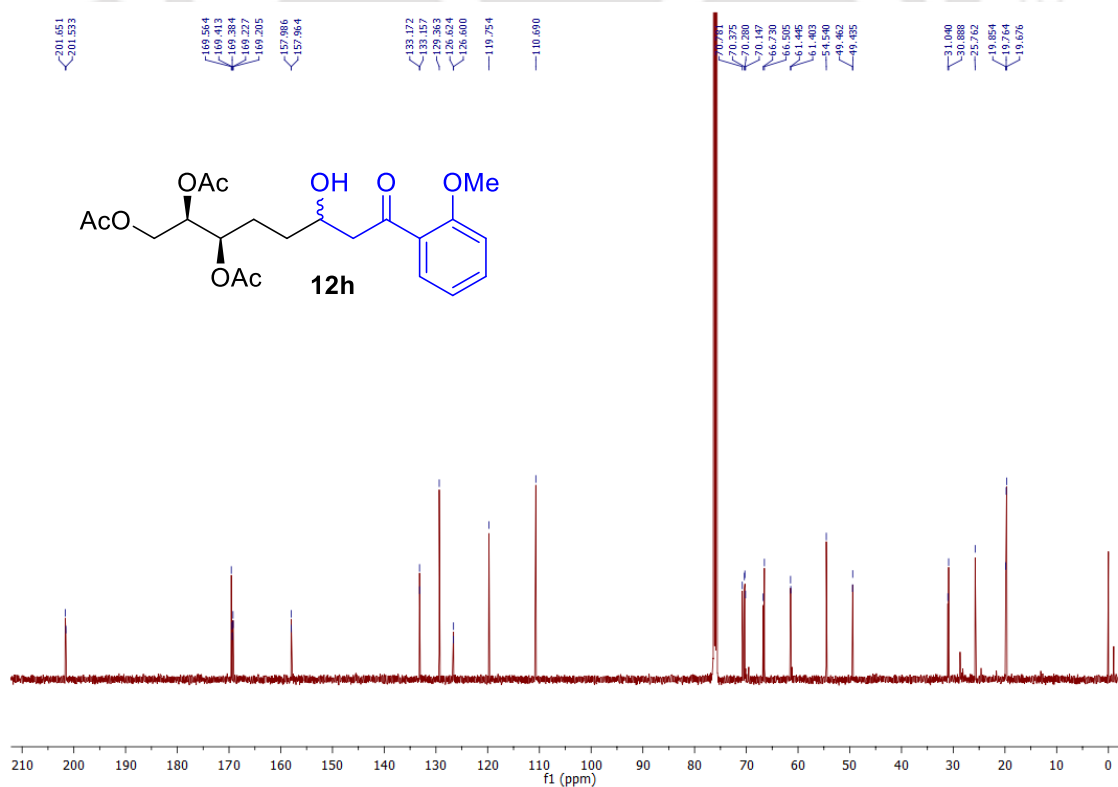


¹³C{¹H} NMR spectrum of compound 12f (400 MHz, CDCl₃):

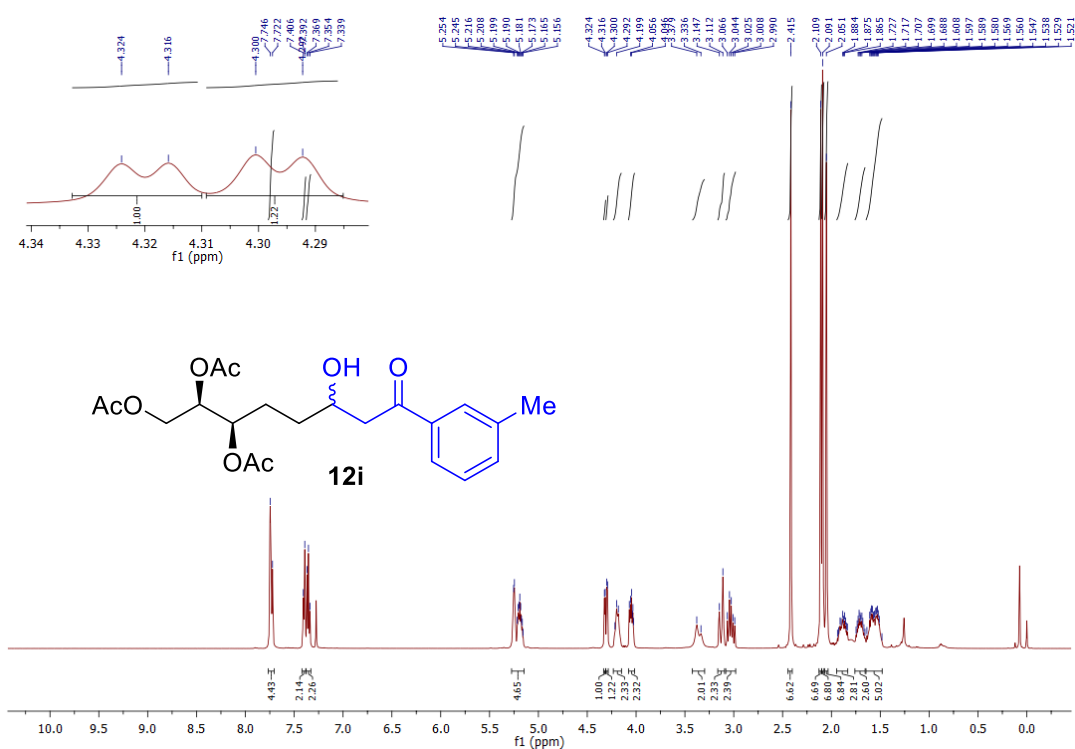


^1H NMR spectrum of compound 12g (500 MHz, CDCl_3):**COSY NMR spectrum of compound 12g (500 MHz, CDCl_3):**

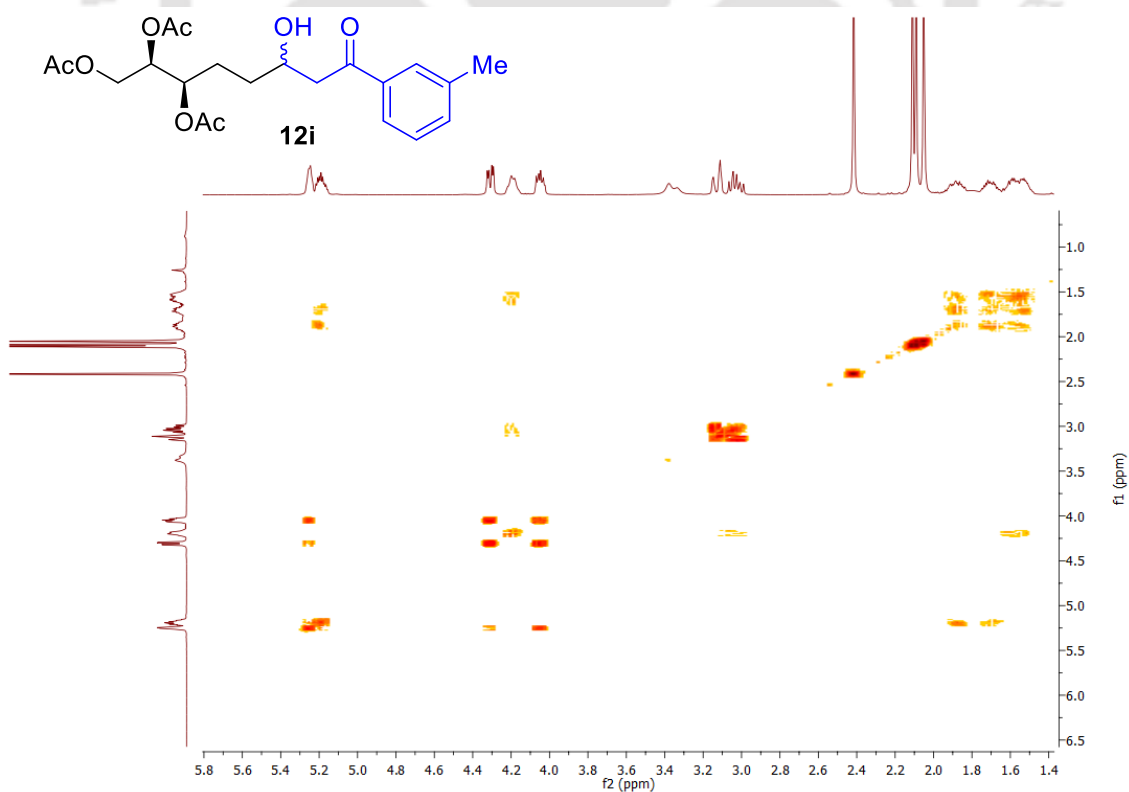
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 12g (500 MHz, CDCl_3): **^1H NMR spectrum of compound 12h (400 MHz, CDCl_3):**

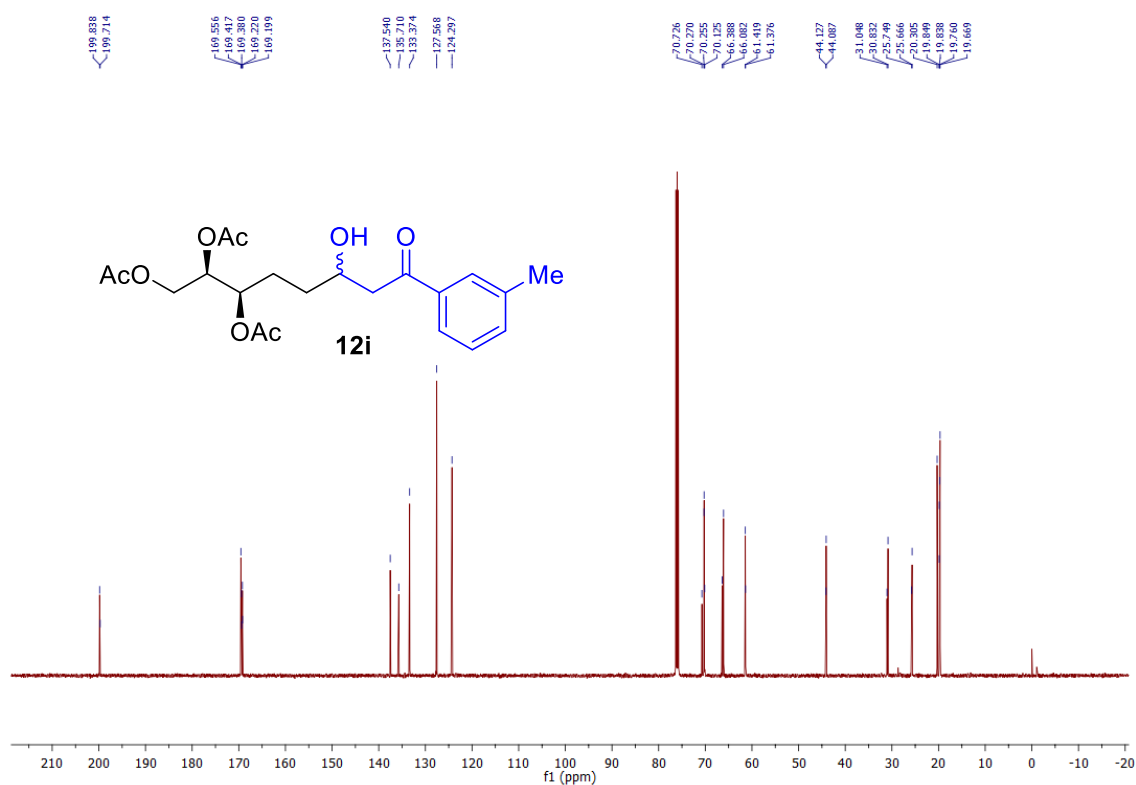
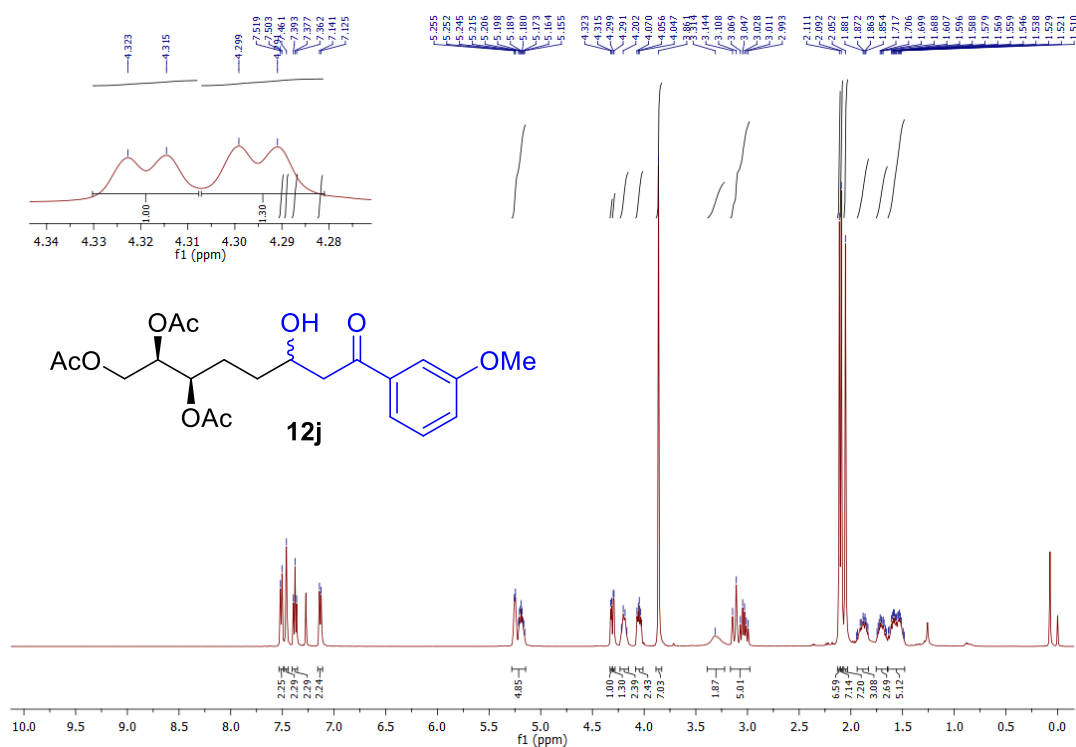
COSY NMR spectrum of compound 12h (400 MHz, CDCl₃):**¹³C{¹H} NMR spectrum of compound 12h (500 MHz, CDCl₃):**

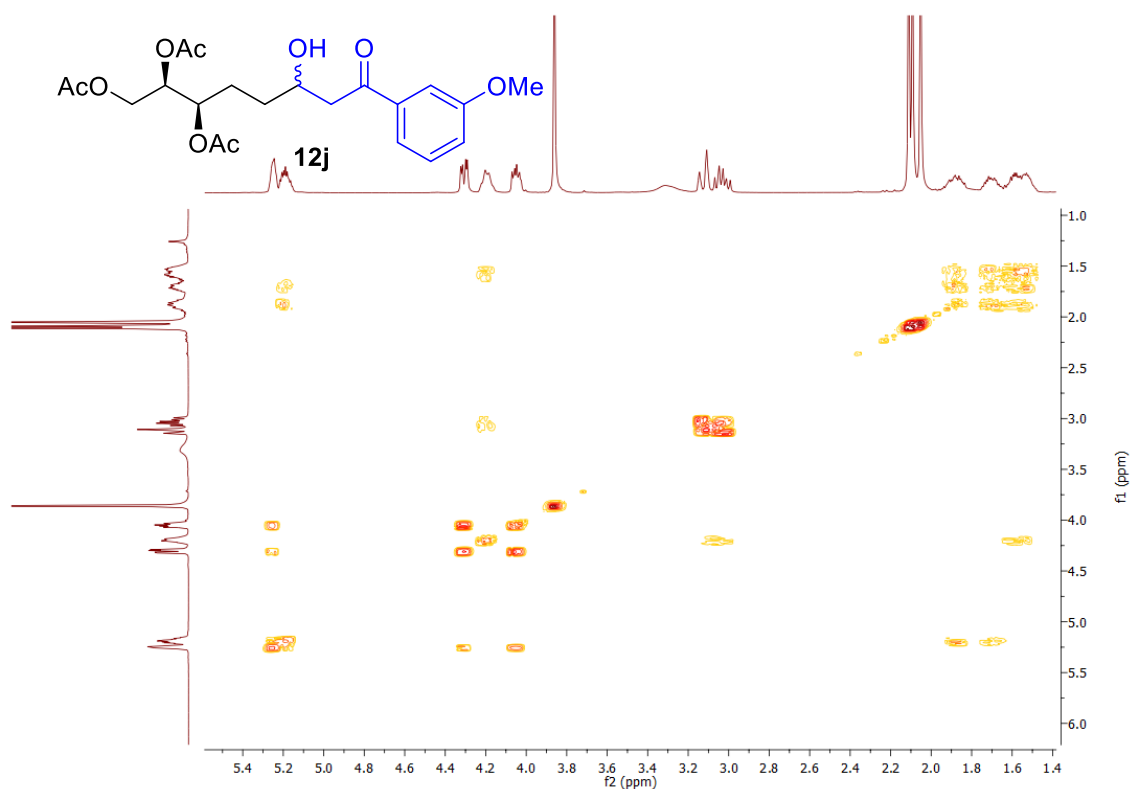
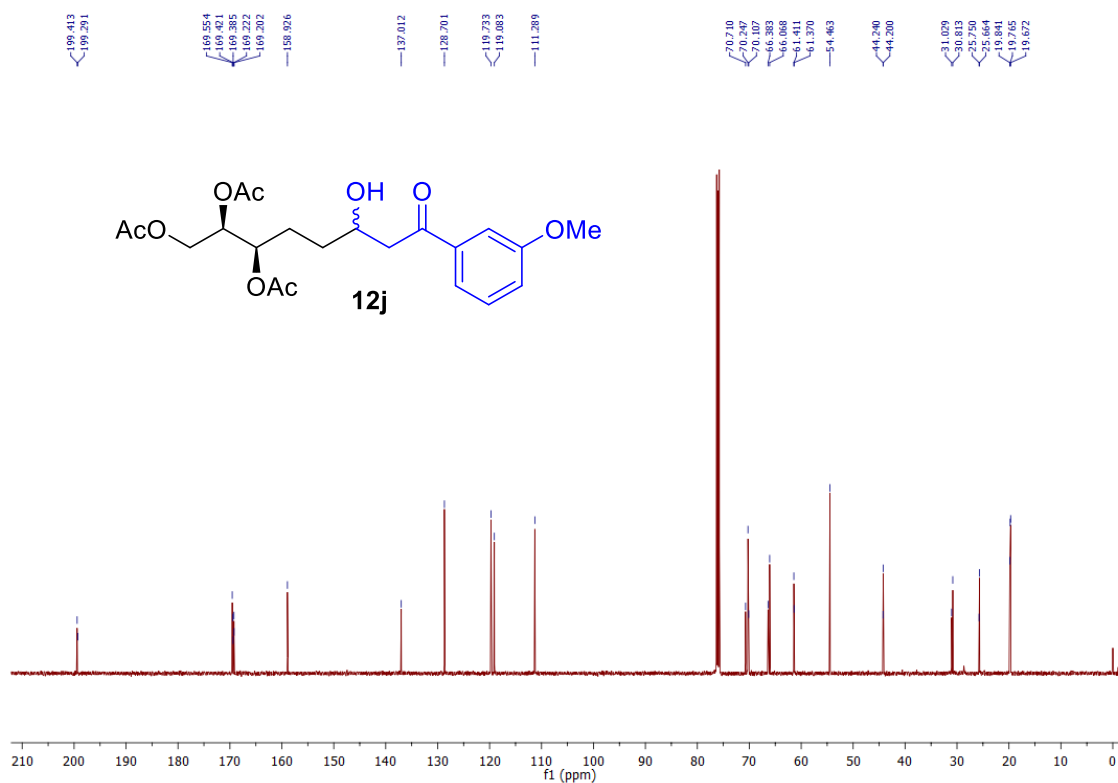
¹H NMR spectrum of compound 12i (500 MHz, CDCl₃):

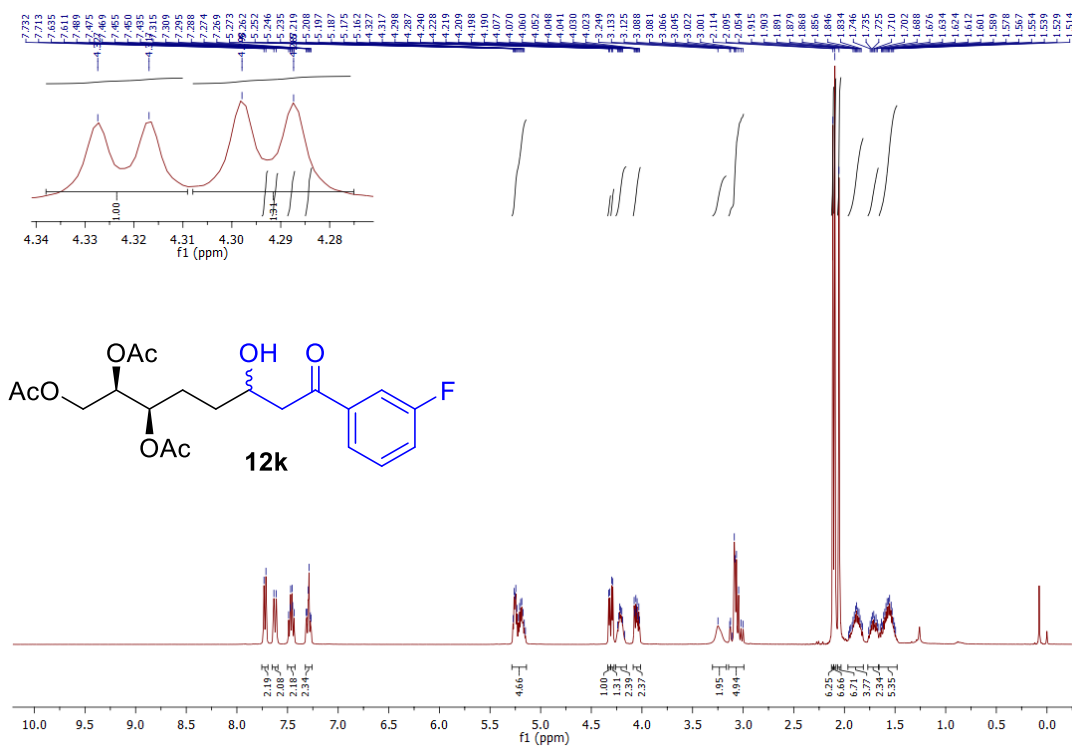
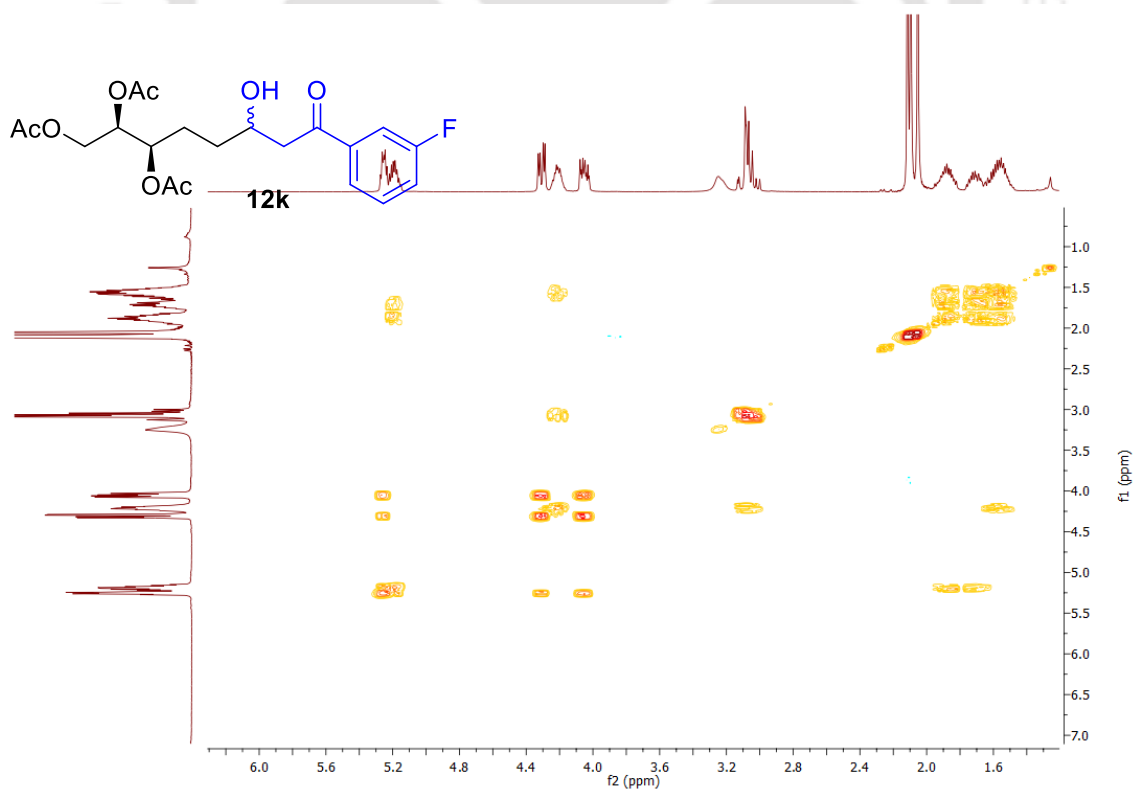


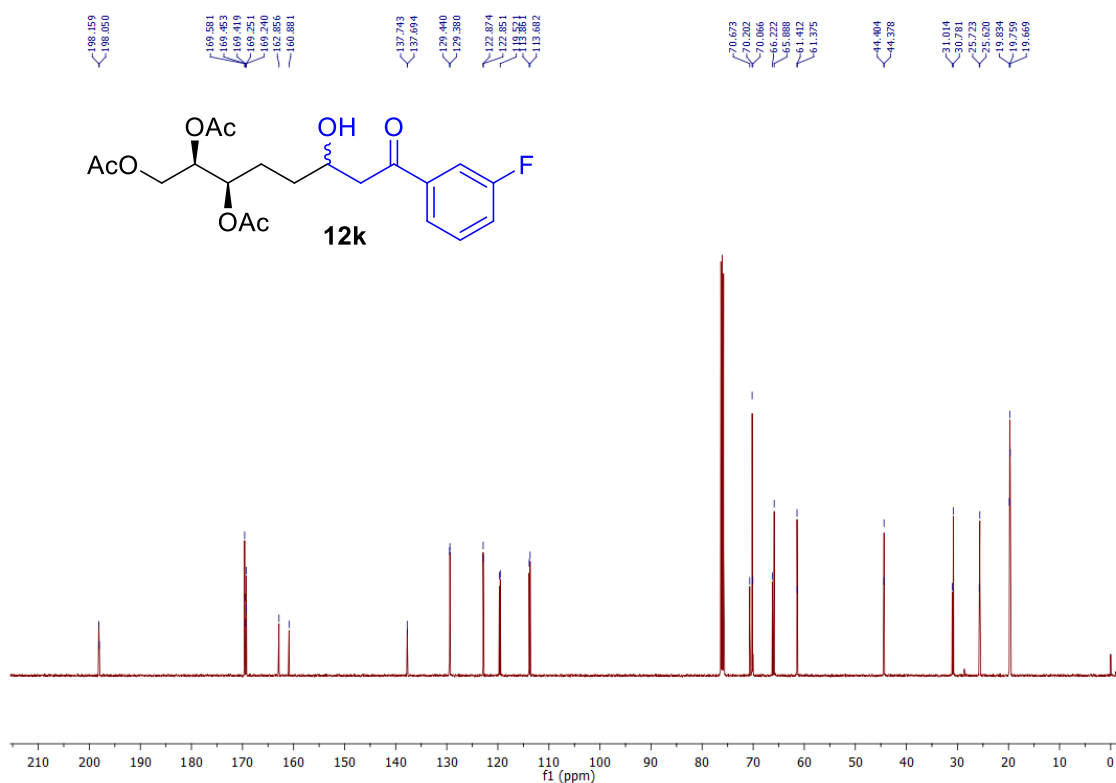
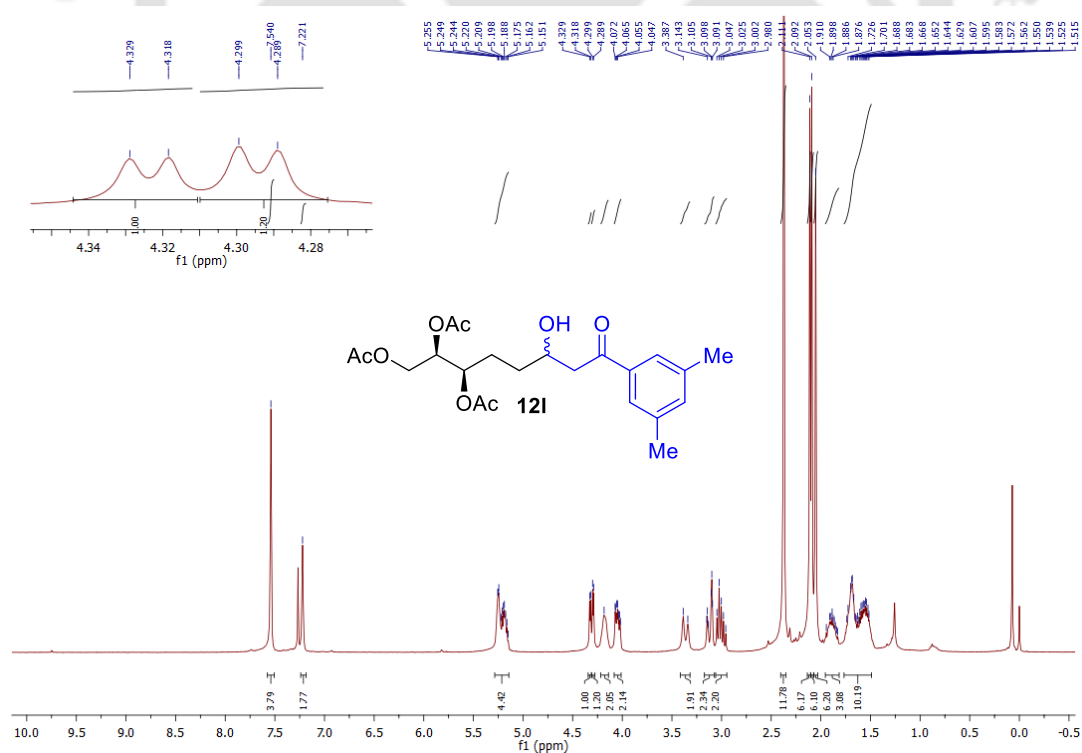
COSY NMR spectrum of compound 12i (500 MHz, CDCl₃):

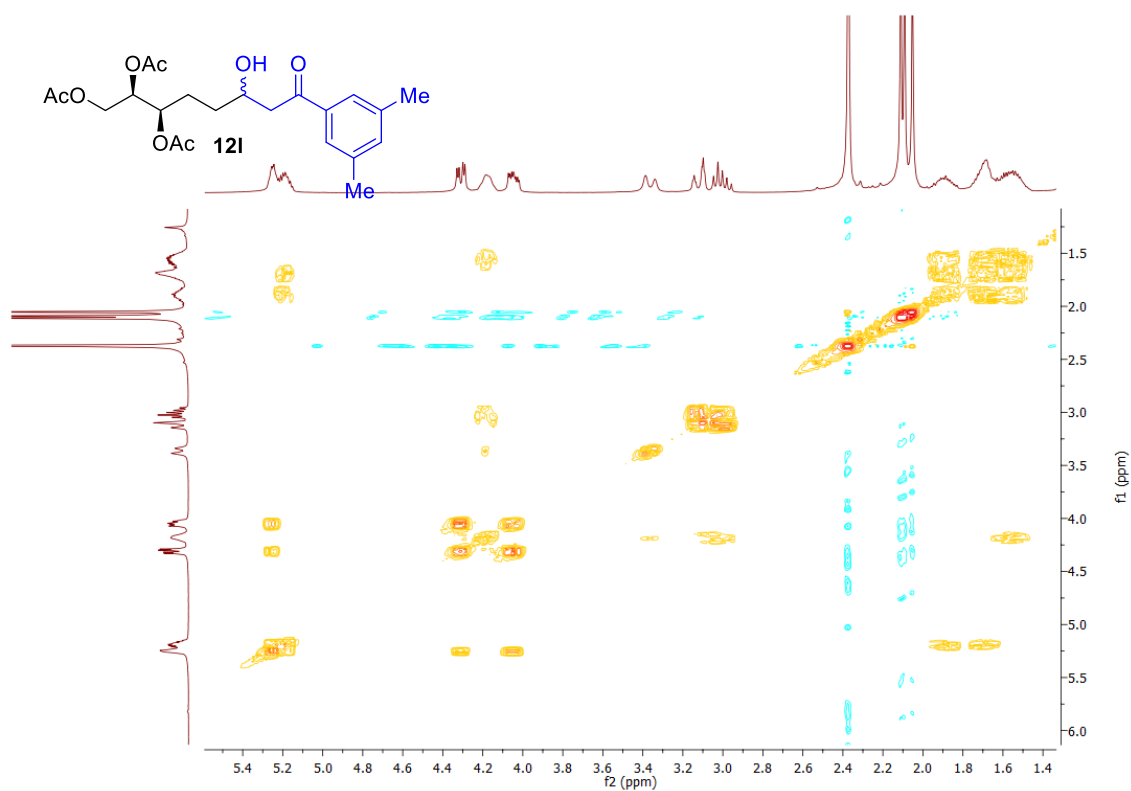
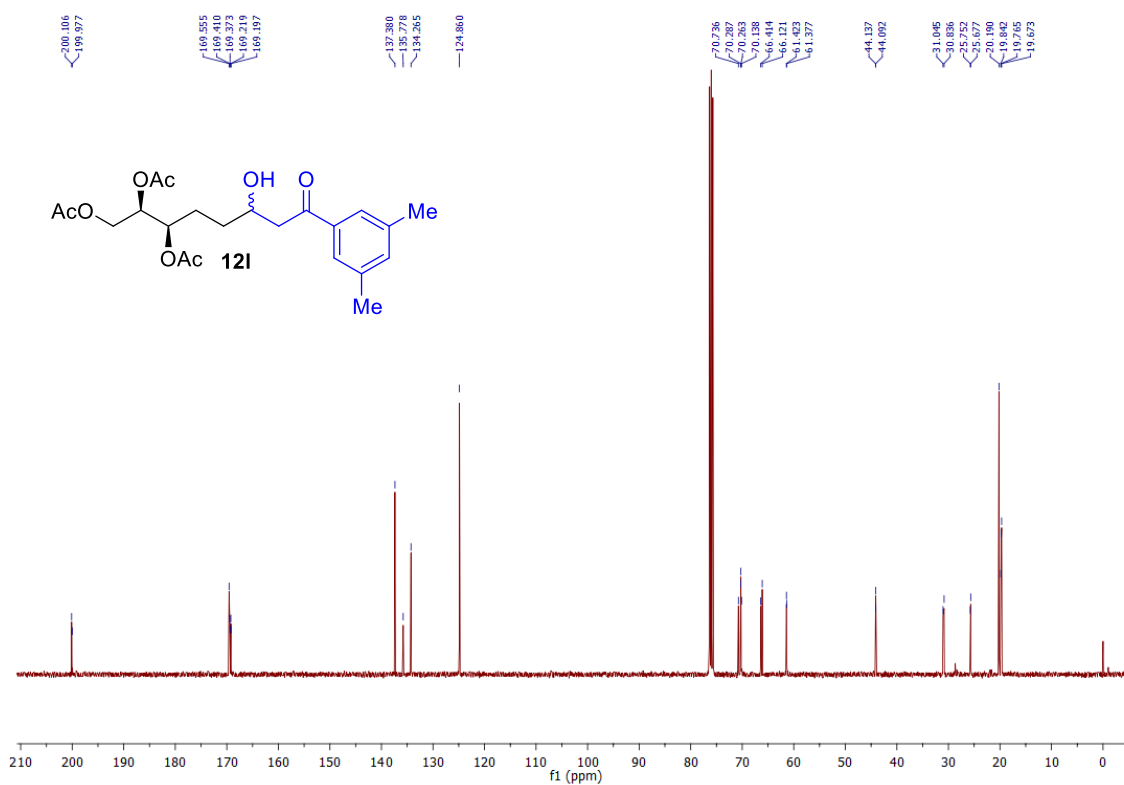


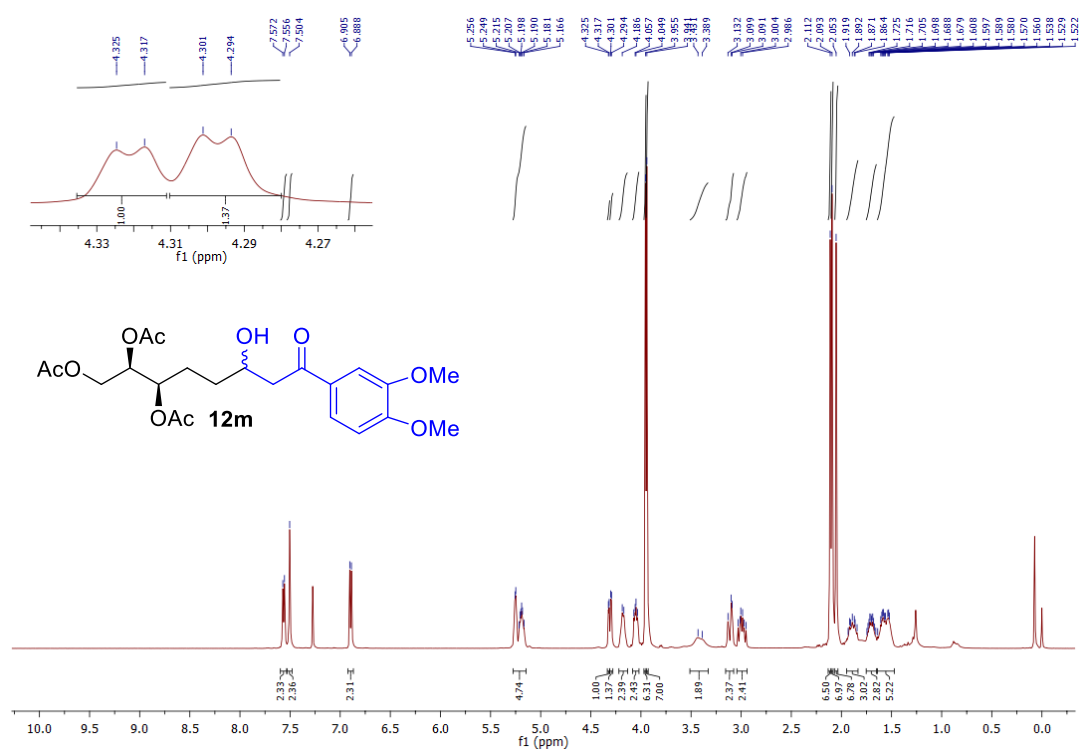
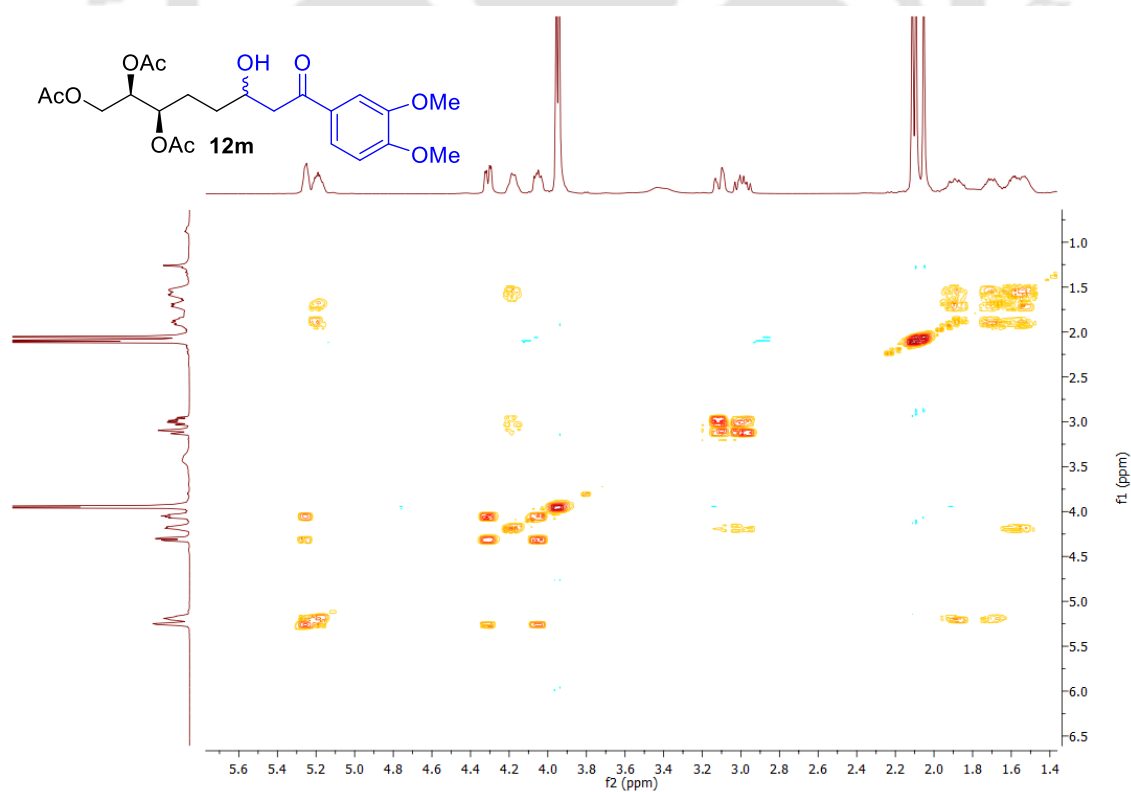
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 12i (500 MHz, CDCl_3): **^1H NMR spectrum of compound 12j (500 MHz, CDCl_3):**

COSY NMR spectrum of compound 12j (500 MHz, CDCl₃):**¹³C{¹H} NMR spectrum of compound 12j (500 MHz, CDCl₃):**

^1H NMR spectrum of compound 12k (400 MHz, CDCl_3):**COSY NMR spectrum of compound 12k (400 MHz, CDCl_3):**

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 12k (500 MHz, CDCl_3): **^1H NMR spectrum of compound 12l (400 MHz, CDCl_3):**

COSY NMR spectrum of compound 12l (400 MHz, CDCl₃):**¹³C{¹H} NMR spectrum of compound 12l (400 MHz, CDCl₃):**

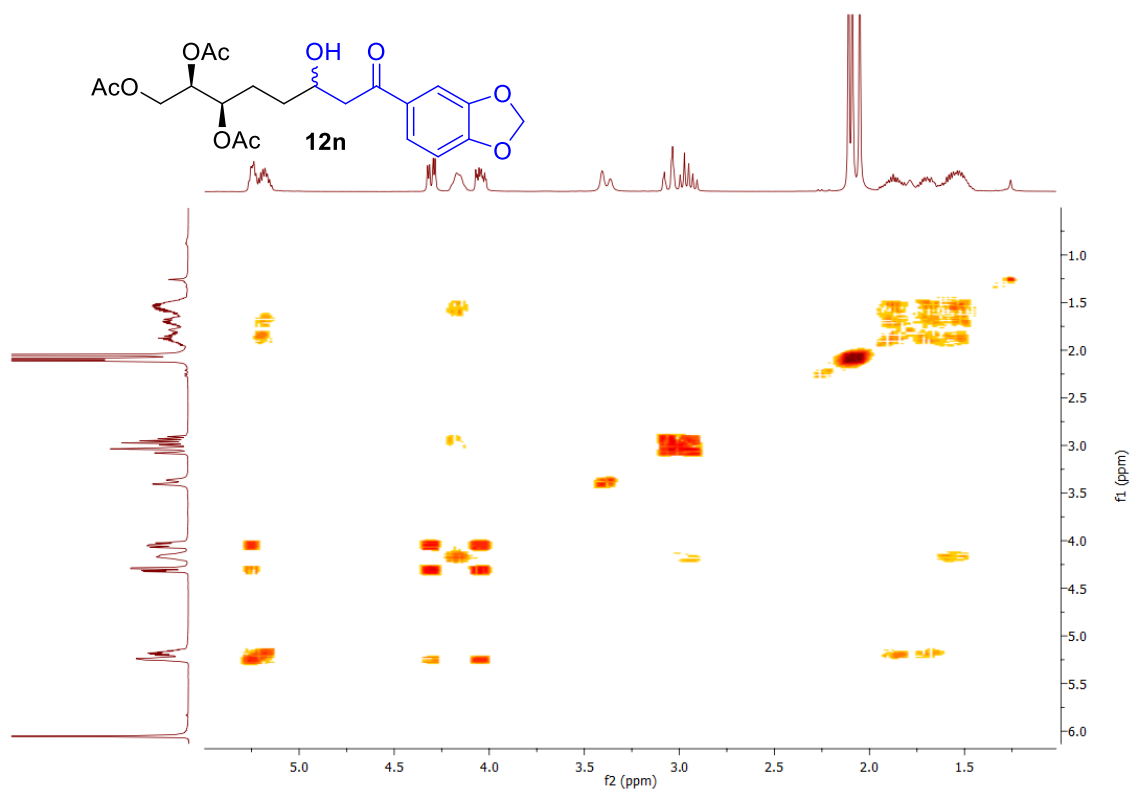
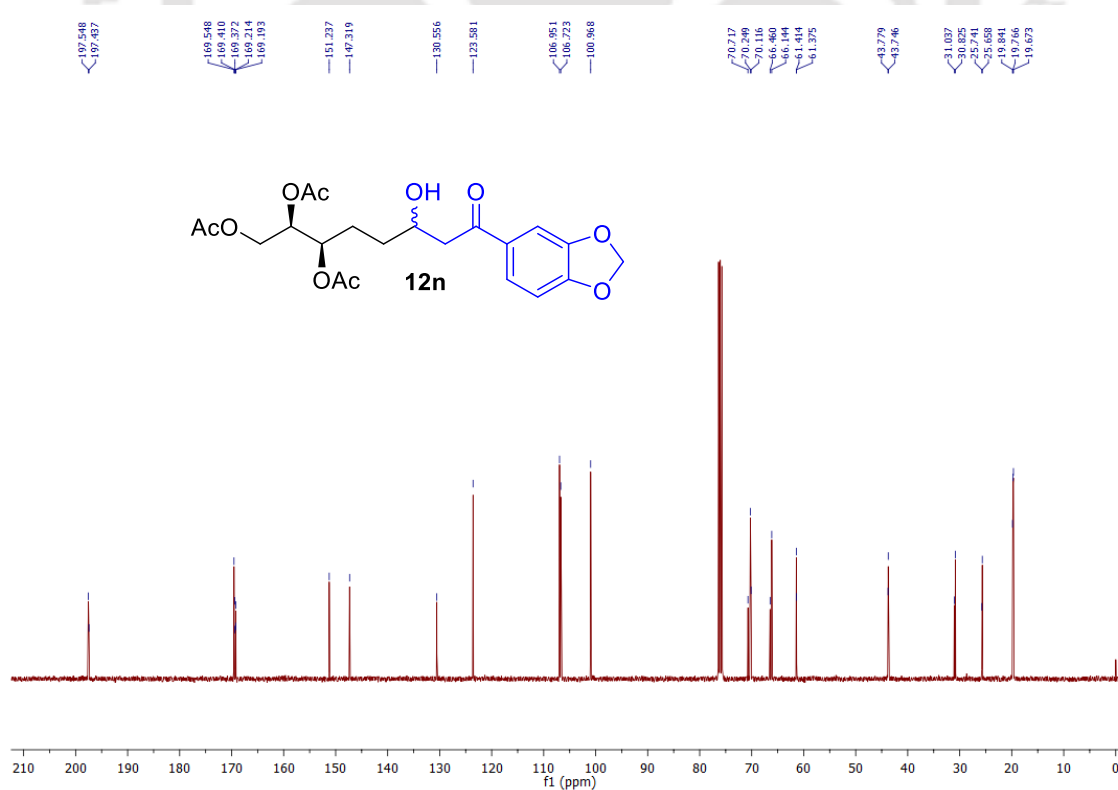
^1H NMR spectrum of compound 12m (500 MHz, CDCl_3):**COSY NMR spectrum of compound 12m (500 MHz, CDCl_3):**

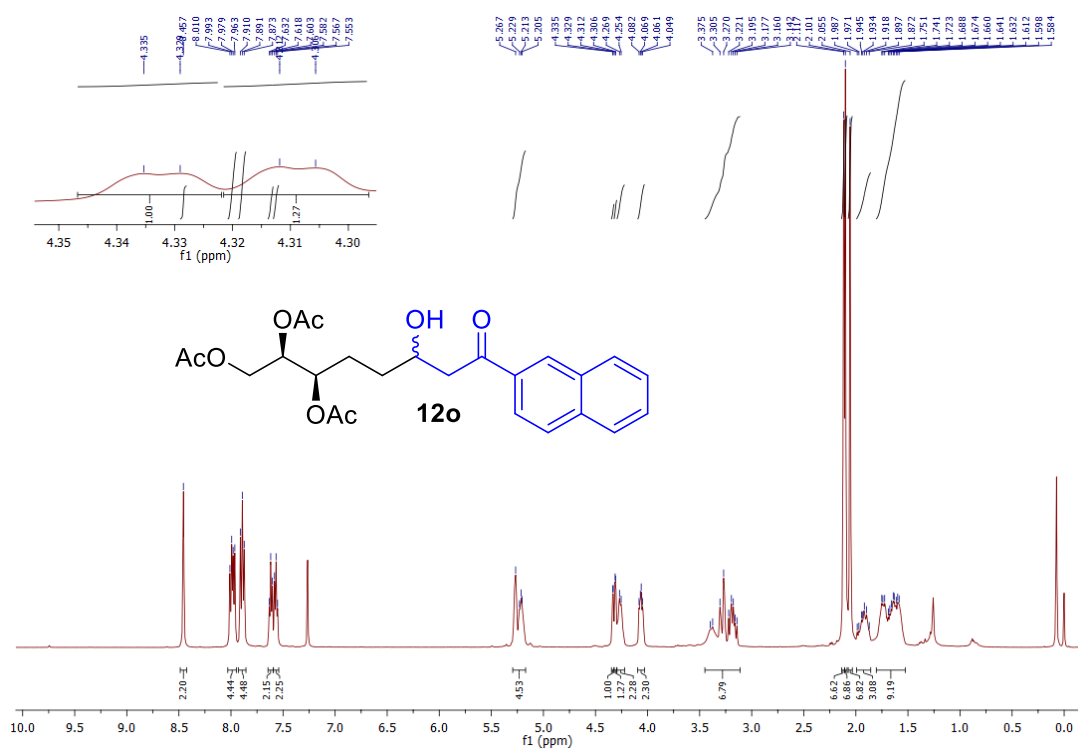
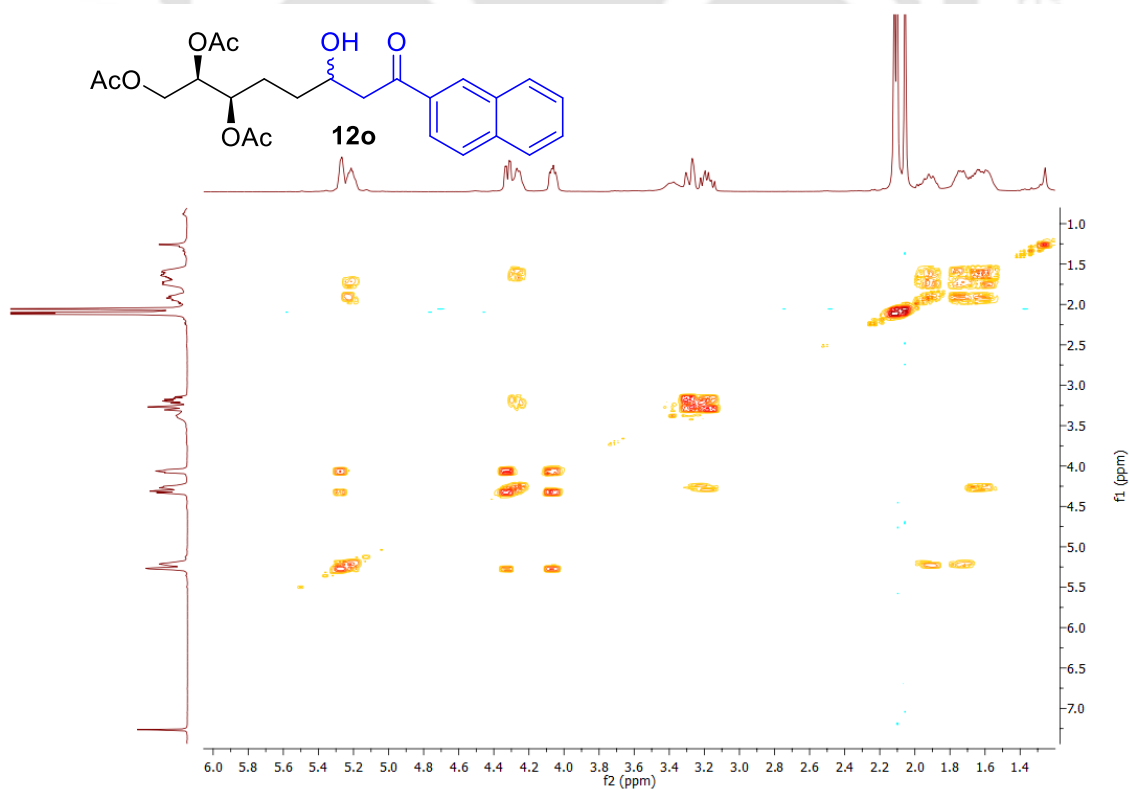
Chemical structure of compound **12m** is shown above the spectrum. The structure is a substituted pentane derivative with two acetoxy (OAc) groups, a hydroxyl (OH) group, and a 3,4-dimethoxybenzoyl group.

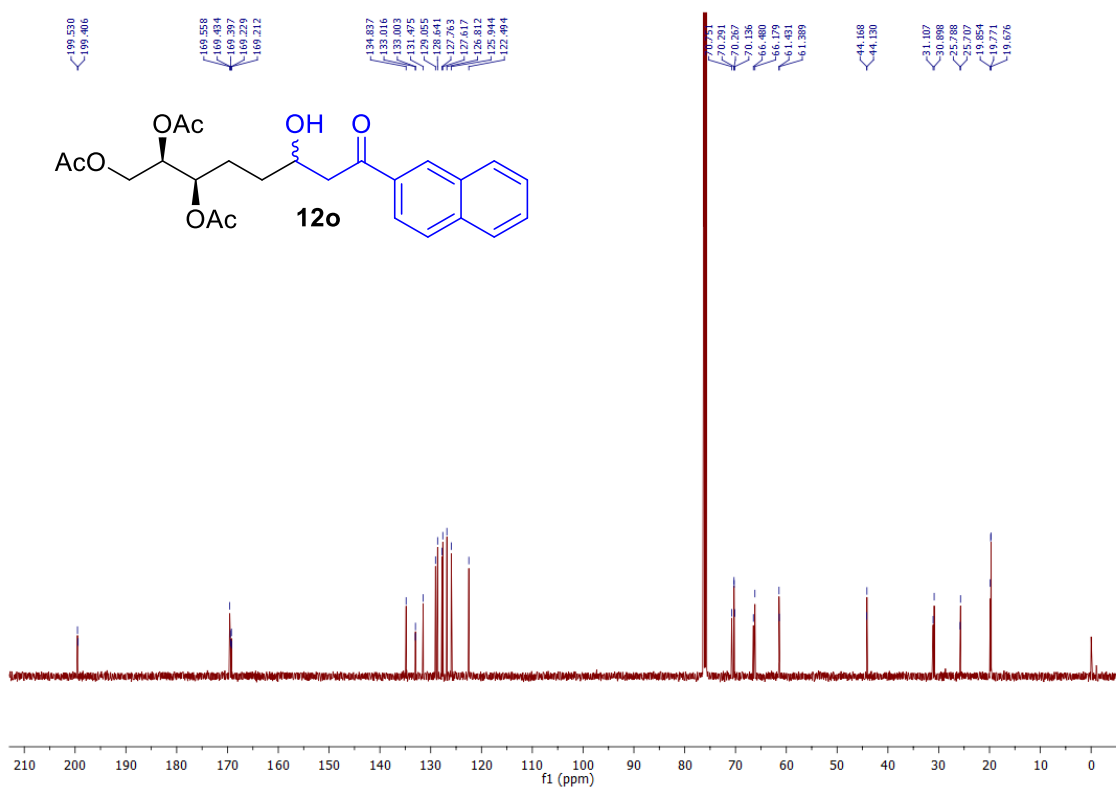
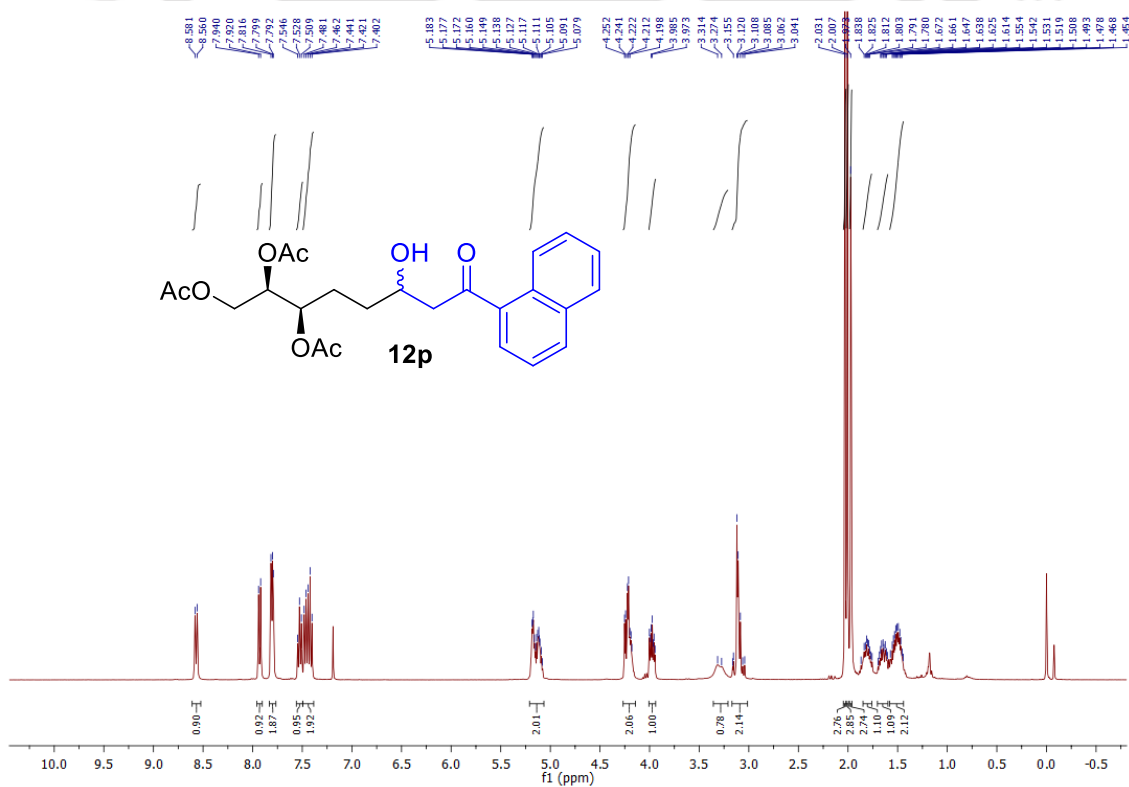
The ¹³C NMR spectrum (CDCl₃) displays the following chemical shifts (ppm):

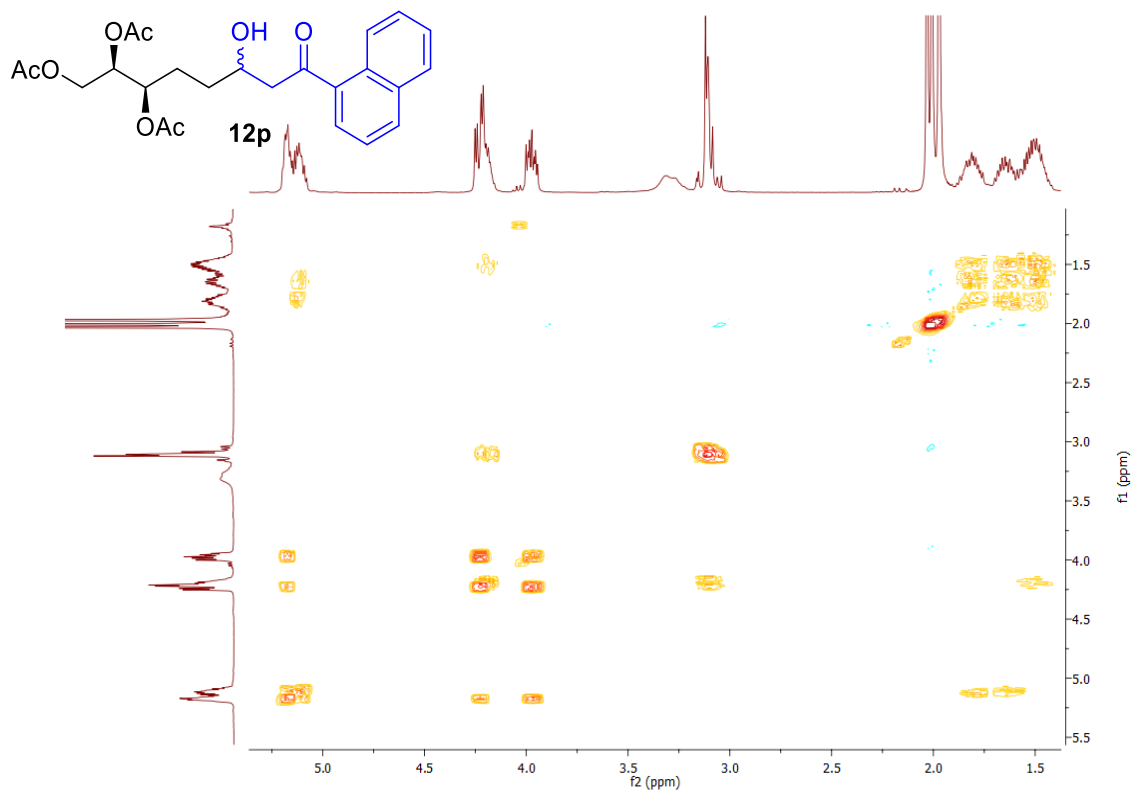
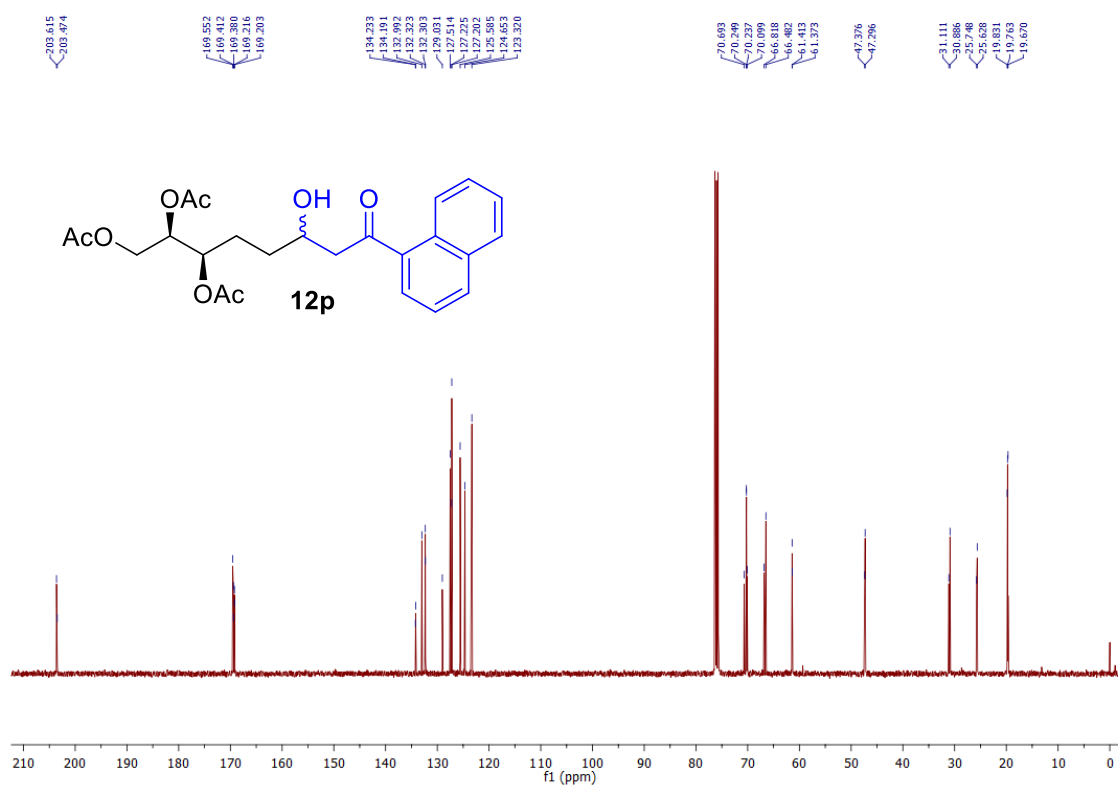
- 200.53
- 198.048
- 169.549
- 169.425
- 169.389
- 169.221
- 169.199
- 152.838
- 148.184
- 128.827
- 121.997
- 109.138
- 109.052
- 70.553
- 70.345
- 70.244
- 70.110
- 66.550
- 66.267
- 61.407
- 56.352
- 55.100
- 55.021
- 43.524
- 43.476
- 31.079
- 30.895
- 25.764
- 25.718
- 19.852
- 19.766
- 19.673

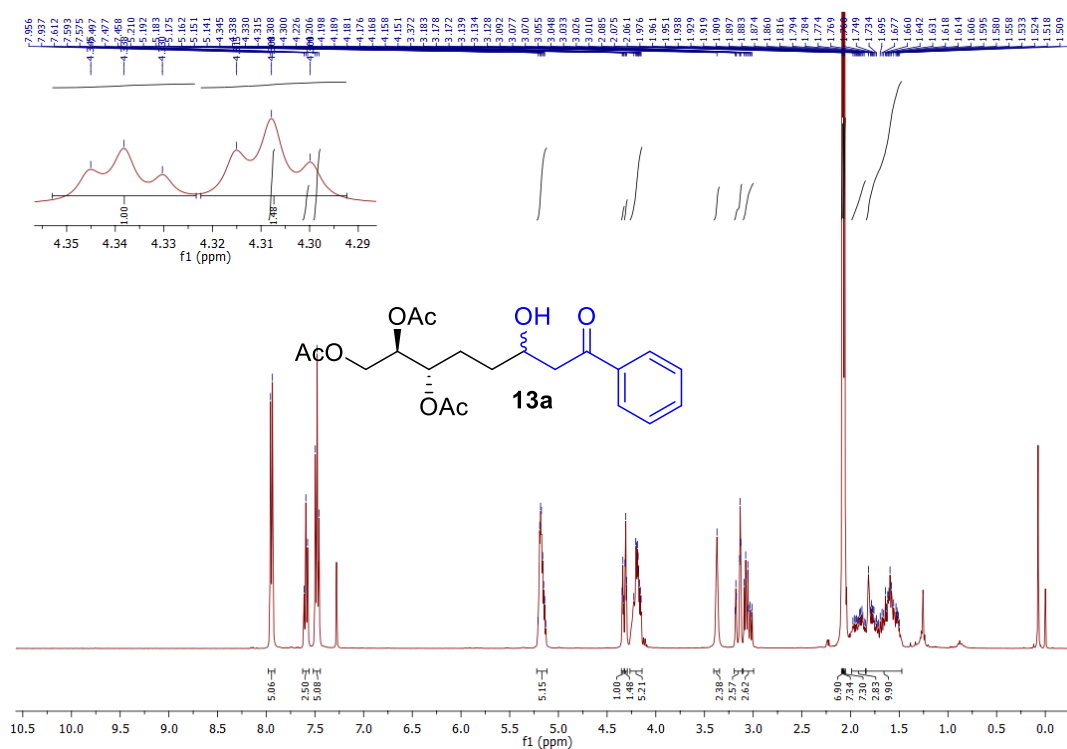
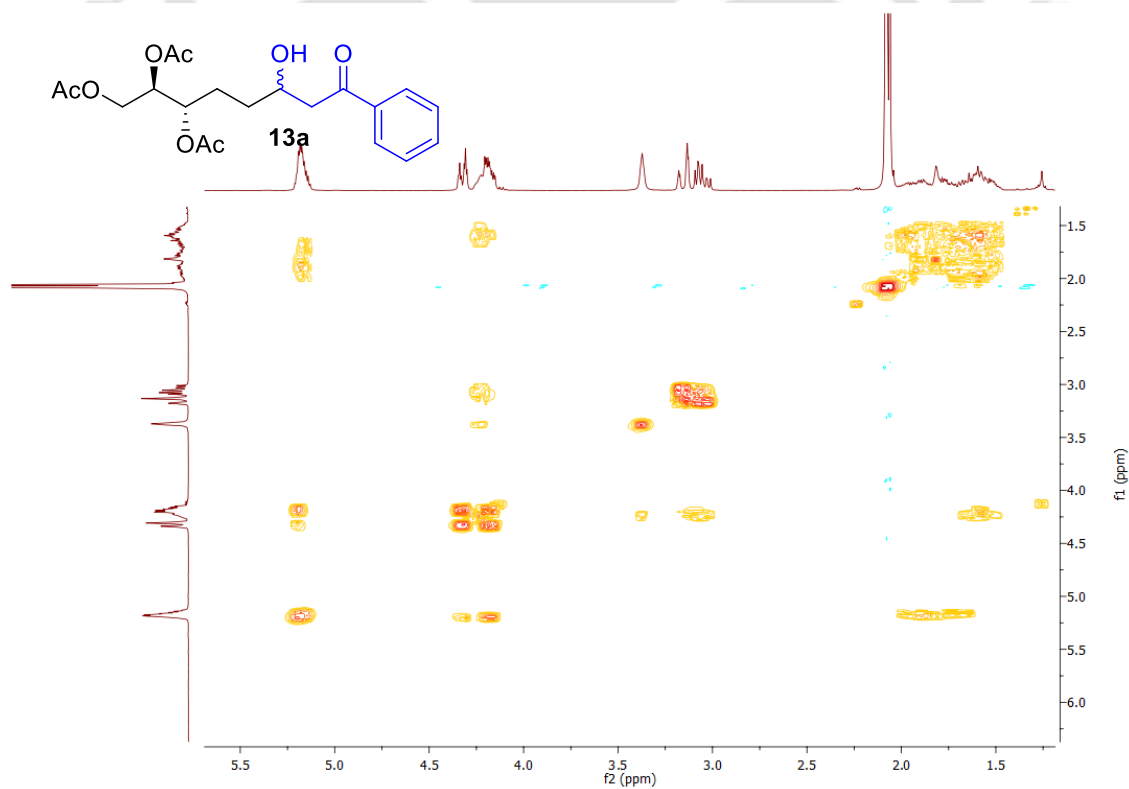
Chemical structure of **12n** is shown above the spectrum. The spectrum displays peaks from -0.5 to 10.0 ppm. Key features include a broad singlet at ~7.4 ppm (OH), aromatic signals between 6.5-7.5 ppm, a singlet at ~4.47 ppm (CH), and aliphatic signals between 1.5-3.5 ppm. Integration values are provided below the baseline, and a list of peak chemical shifts is on the right.

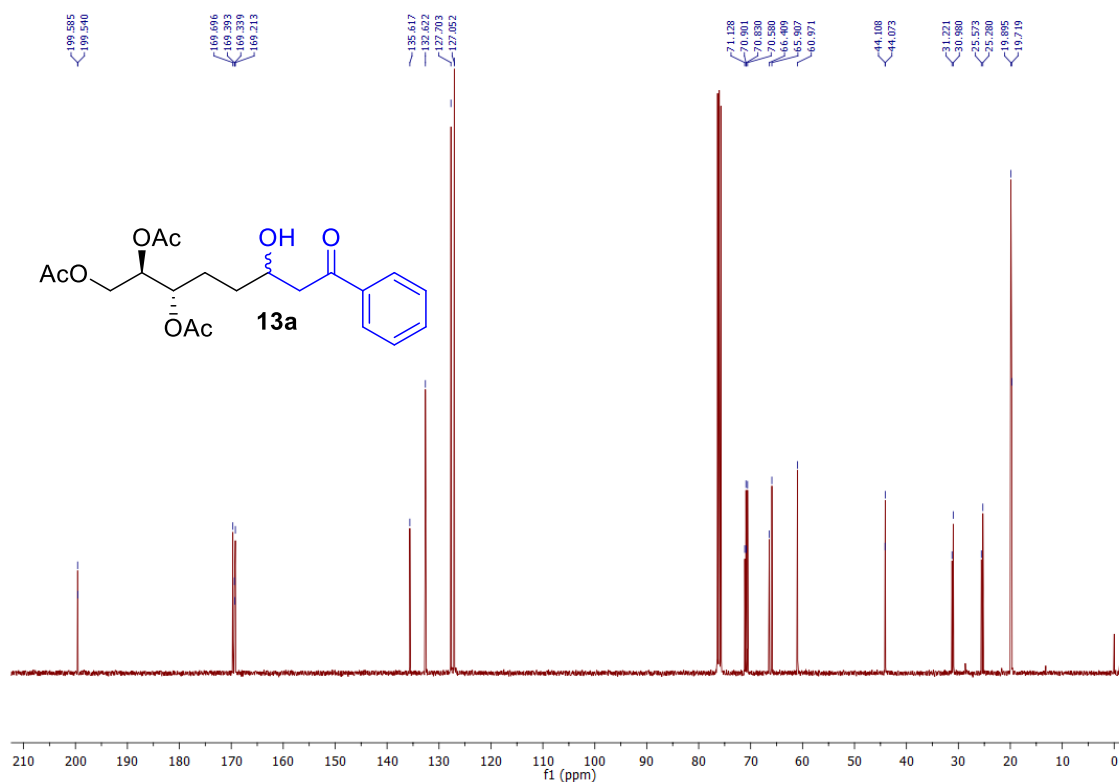
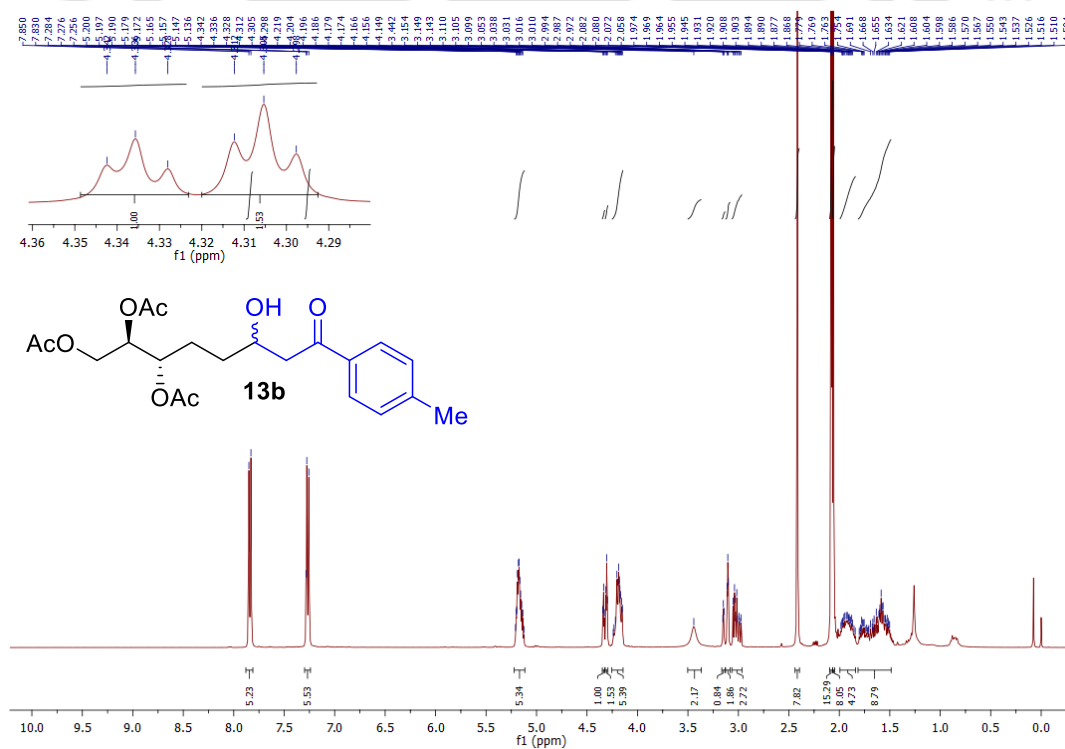
COSY NMR spectrum of compound 12n (400 MHz, CDCl₃):**¹³C{¹H} NMR spectrum of compound 12n (400 MHz, CDCl₃):**

^1H NMR spectrum of compound 12o (500 MHz, CDCl_3):**COSY NMR spectrum of compound 12o (500 MHz, CDCl_3):**

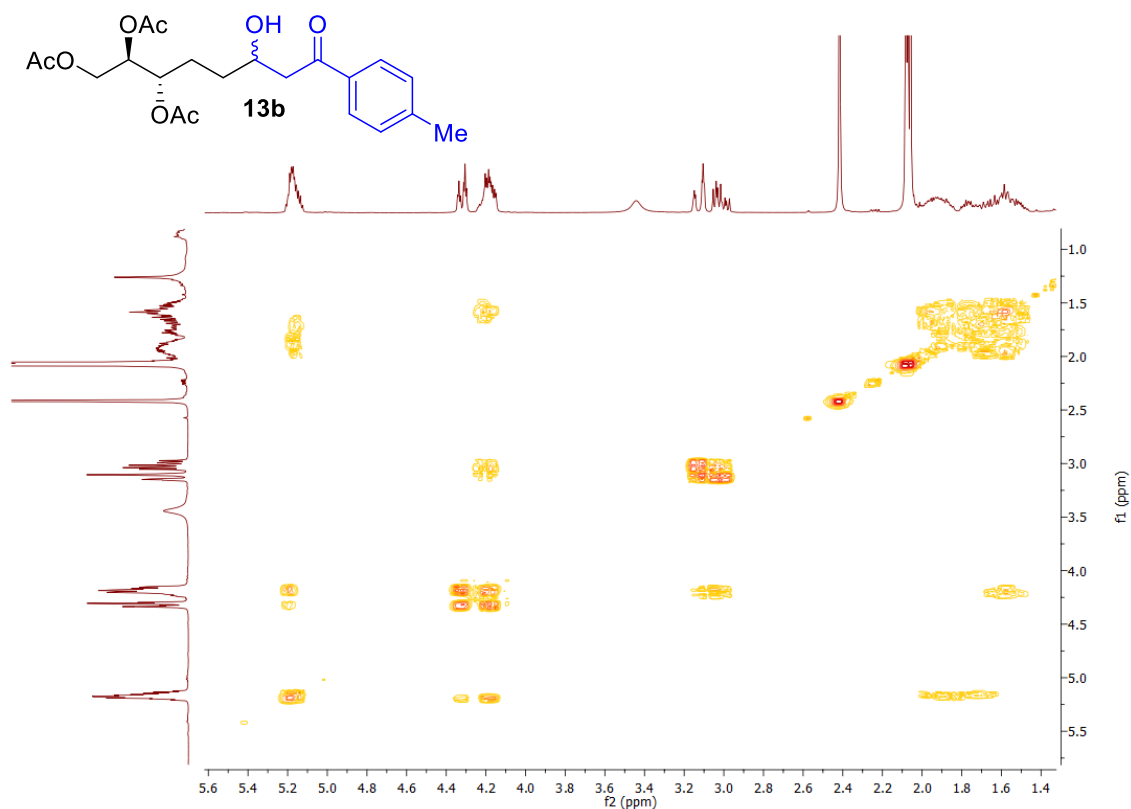
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 12o (500 MHz, CDCl_3): **^1H NMR spectrum of compound 12p (400 MHz, CDCl_3):**

COSY NMR spectrum of compound 12p (400 MHz, CDCl₃):**¹³C{¹H} NMR spectrum of compound 12p (400 MHz, CDCl₃):**

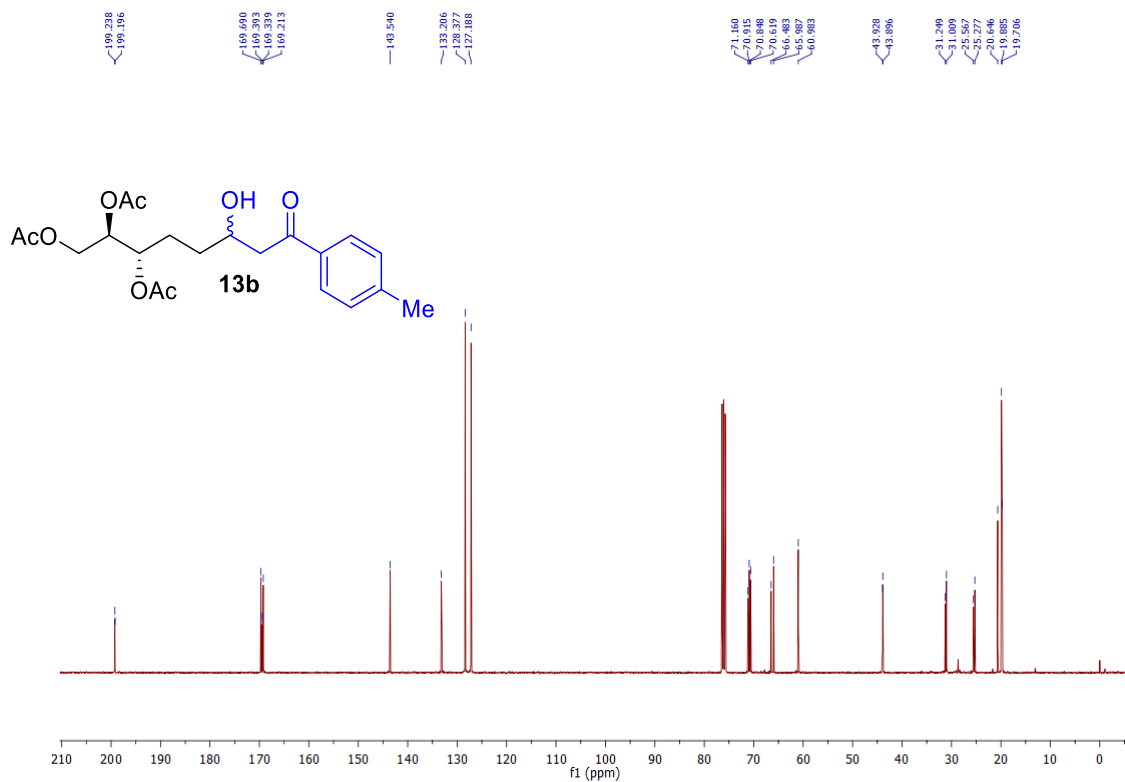
^1H NMR spectrum of compound 13a (400 MHz, CDCl_3):**COSY NMR spectrum of compound 13a (400 MHz, CDCl_3):**

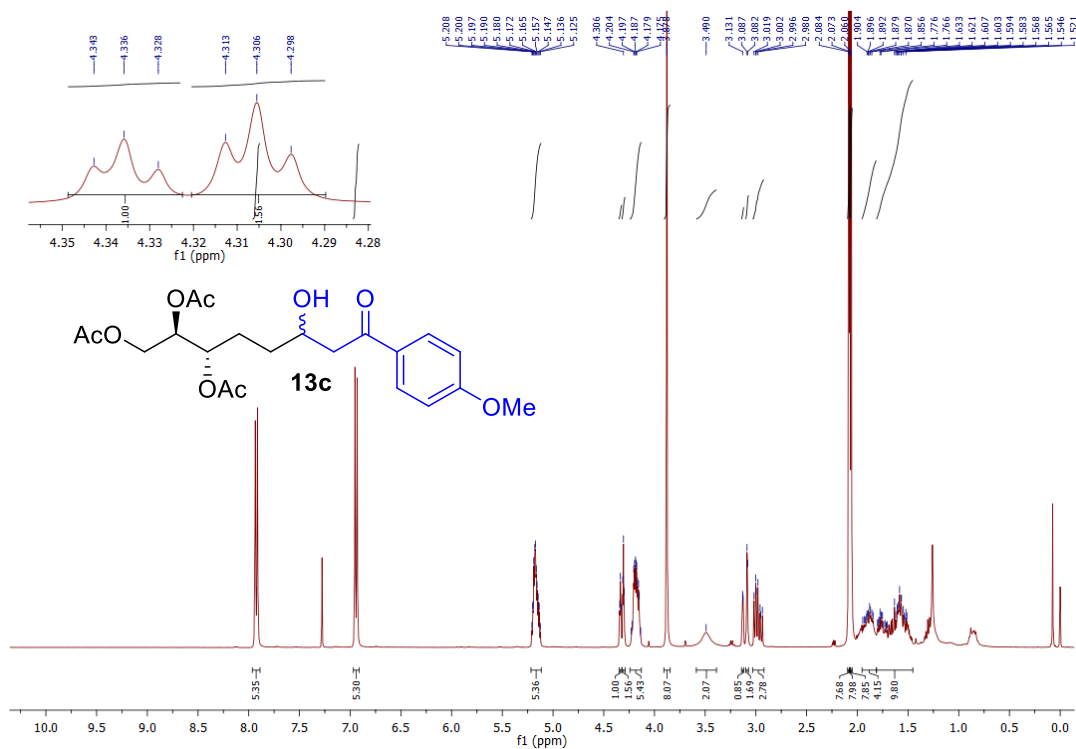
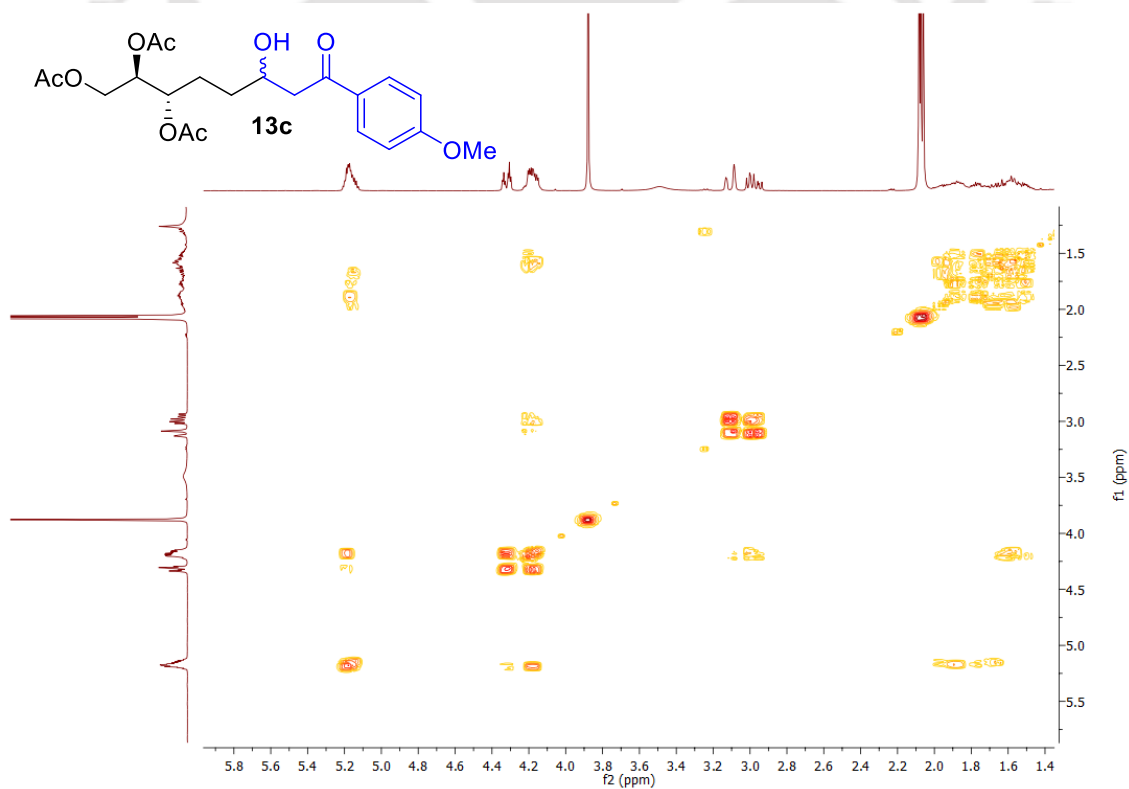
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 13a (400 MHz, CDCl_3): **^1H NMR spectrum of compound 13b (400 MHz, CDCl_3):**

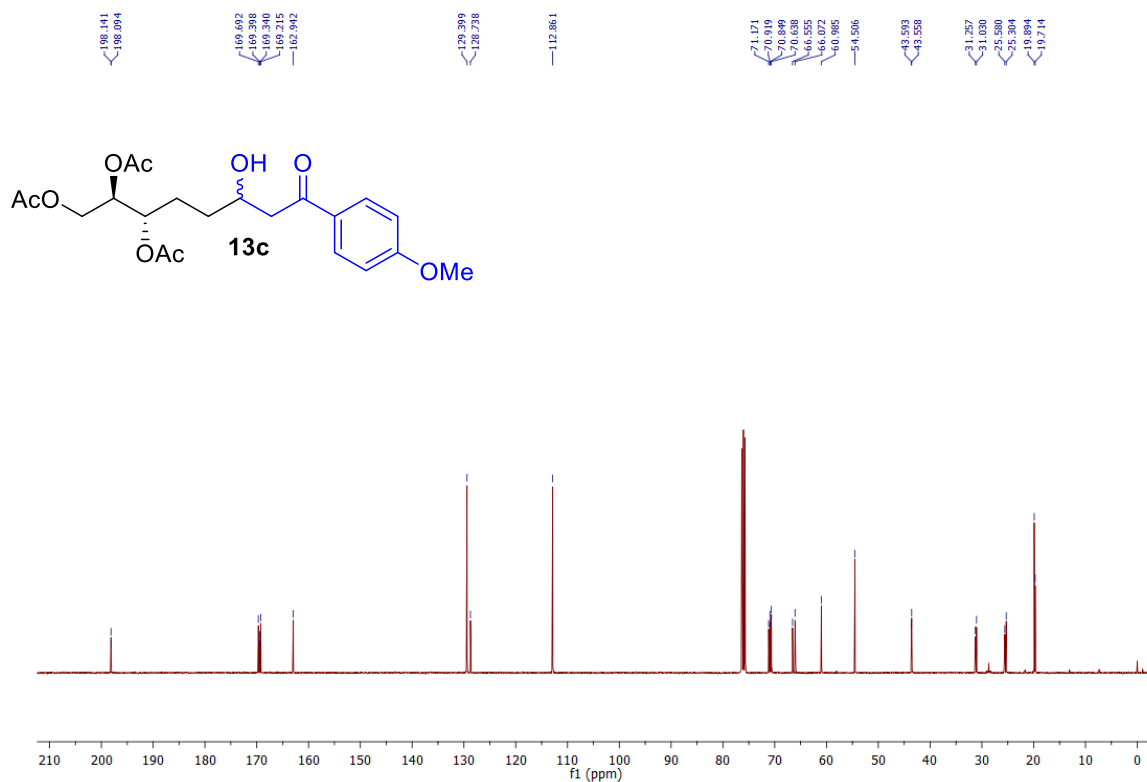
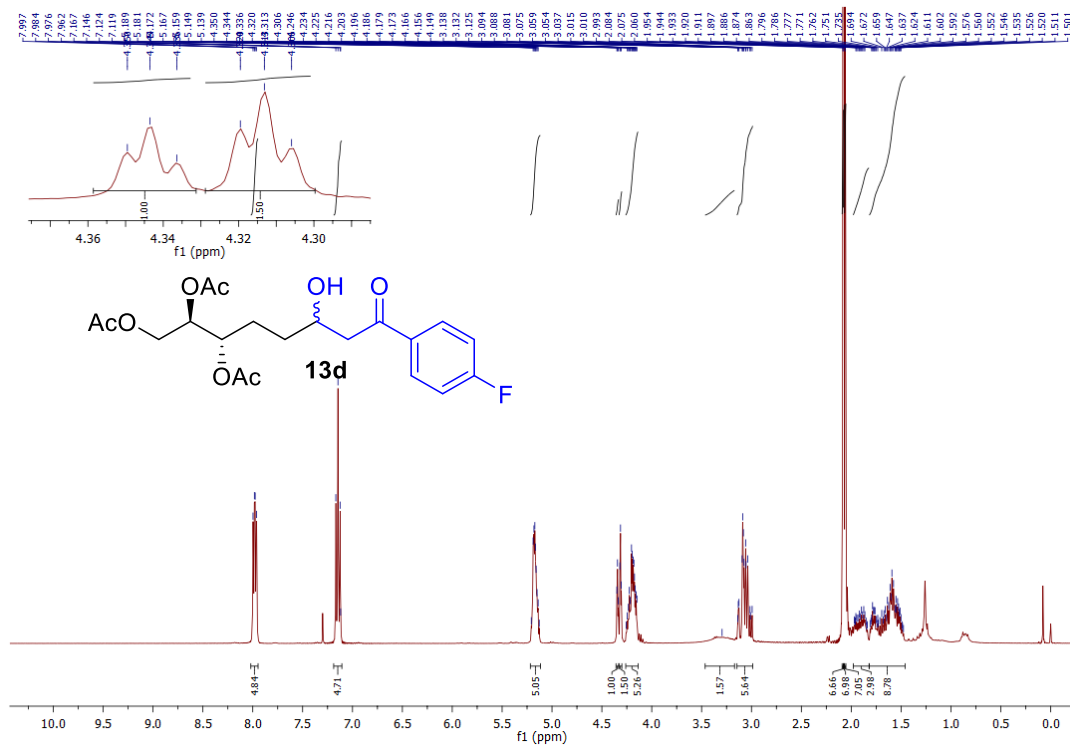
COSY NMR spectrum of compound 13b (400 MHz, CDCl₃):

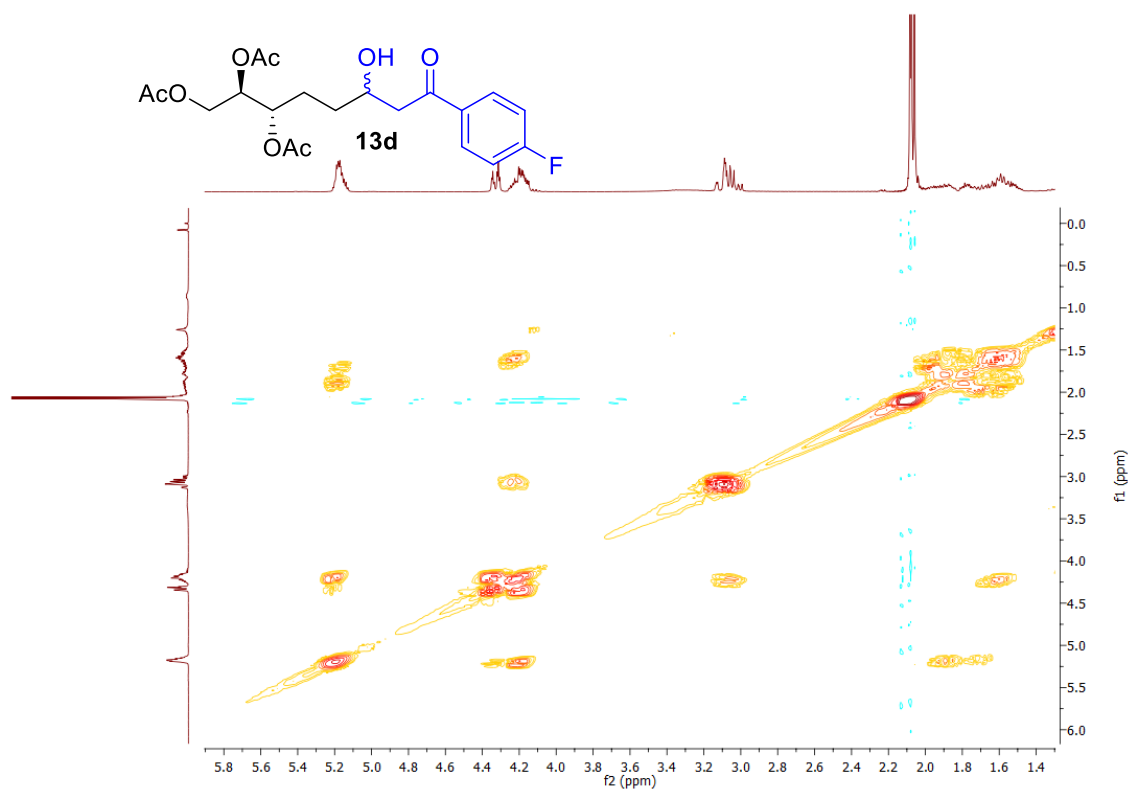
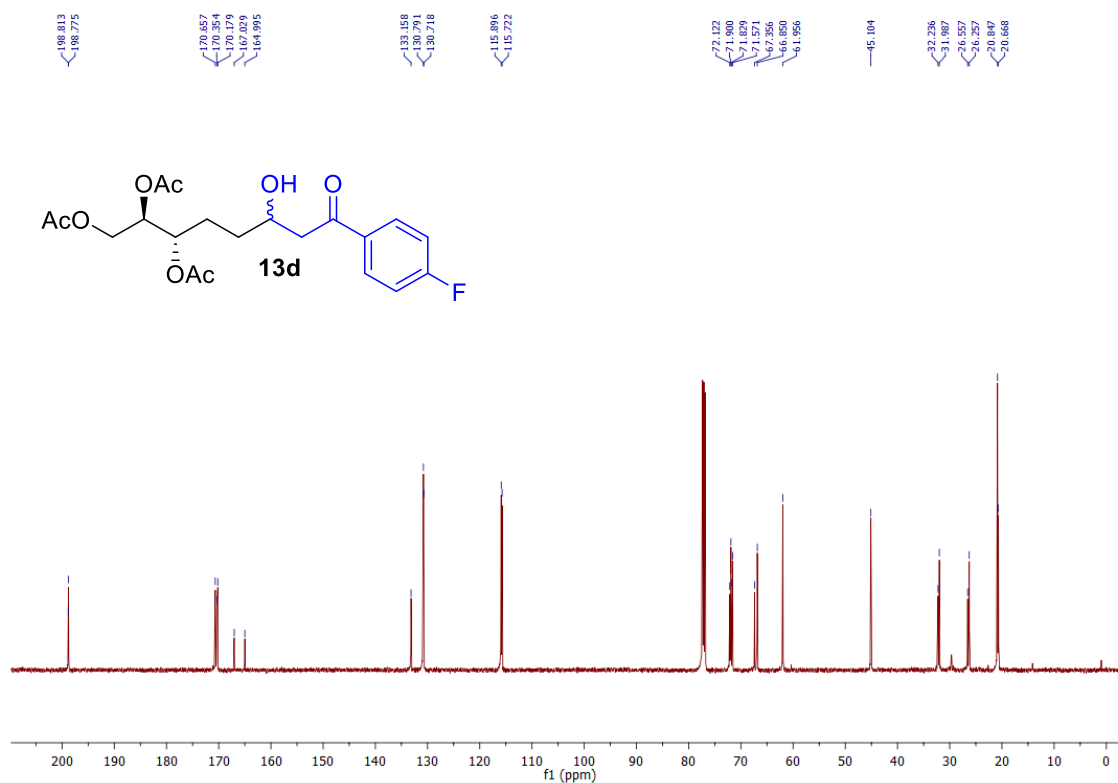


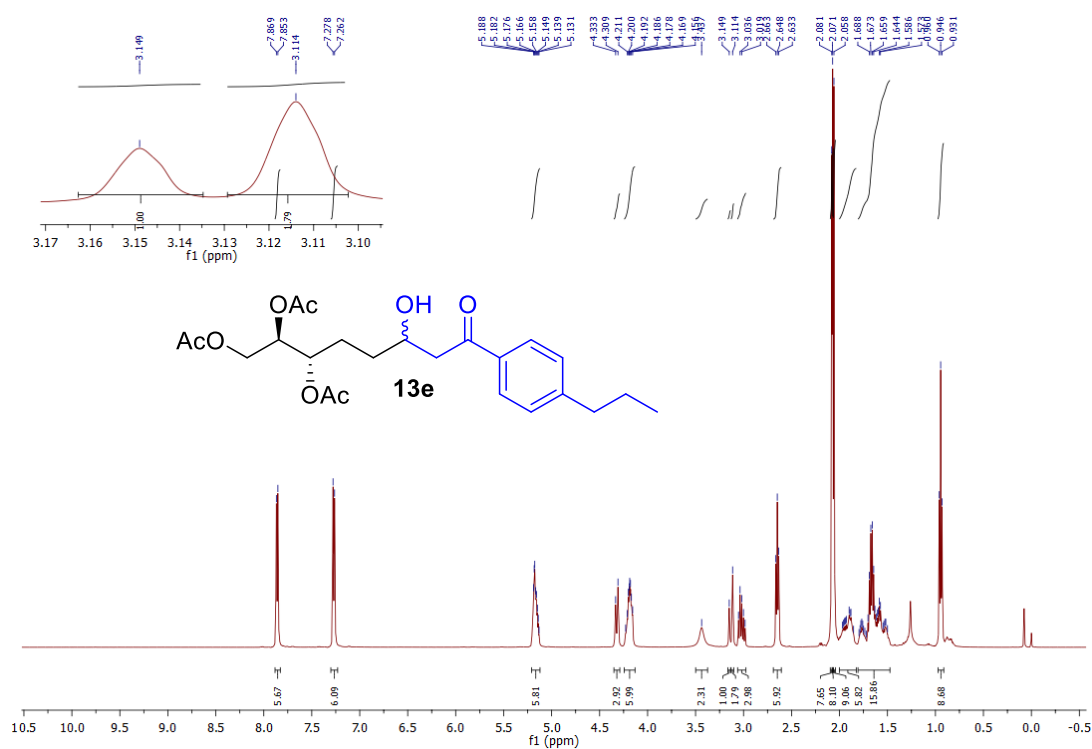
¹³C{¹H} NMR spectrum of compound 13b (400 MHz, CDCl₃):

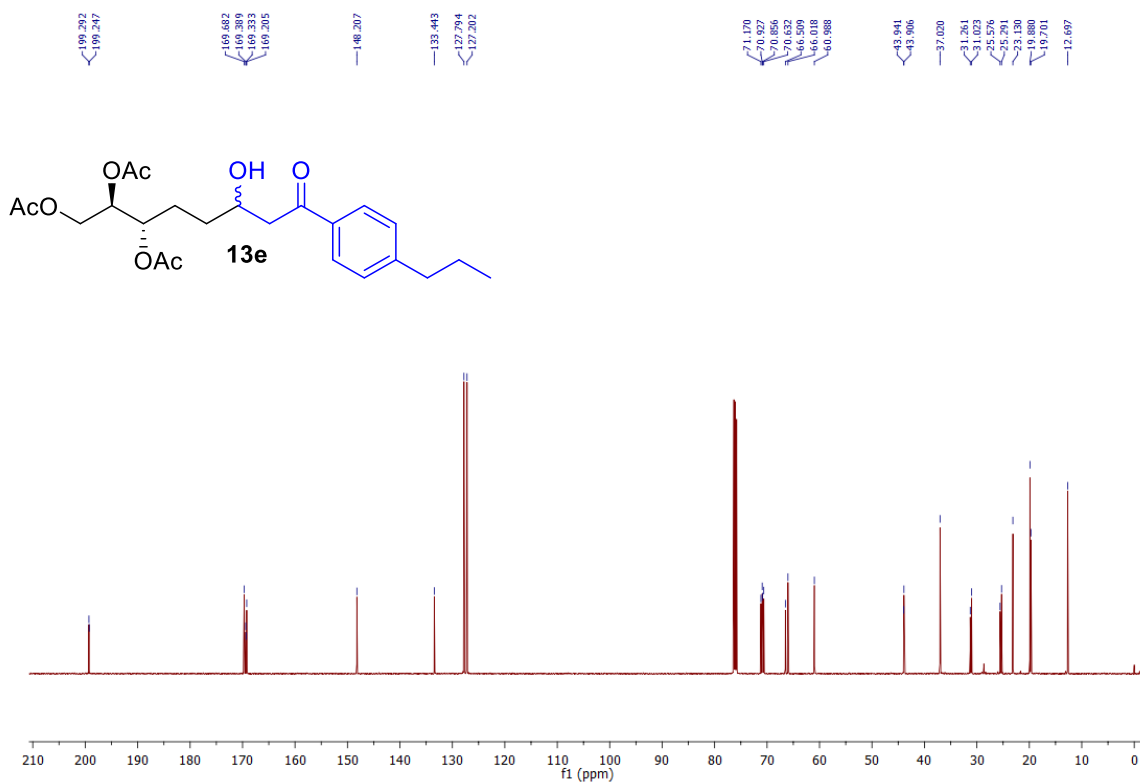
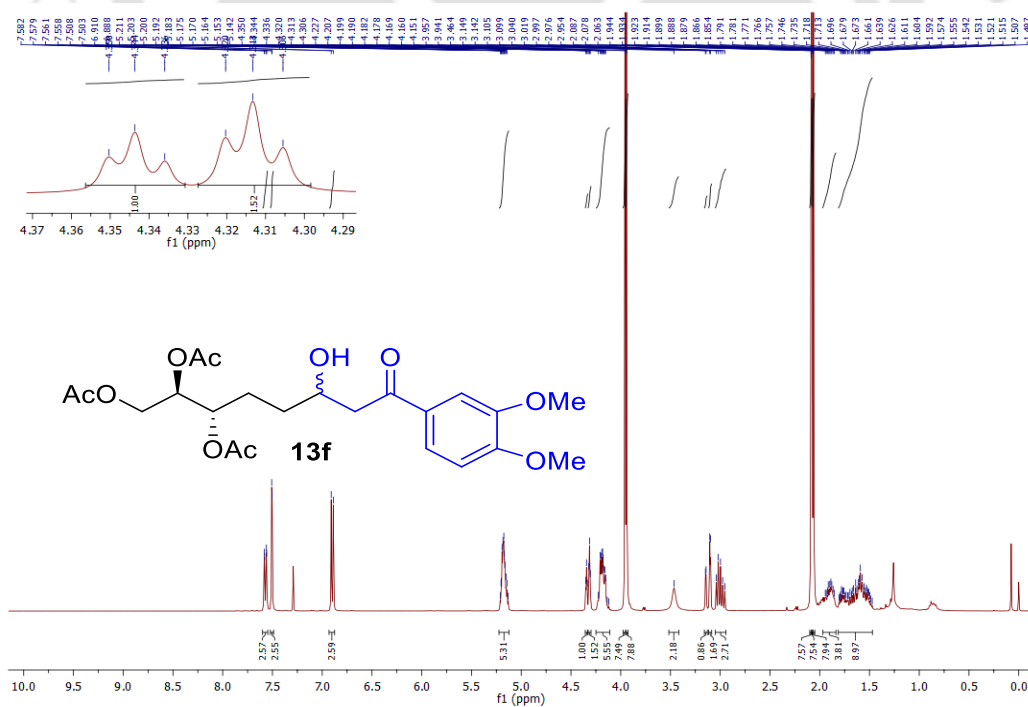


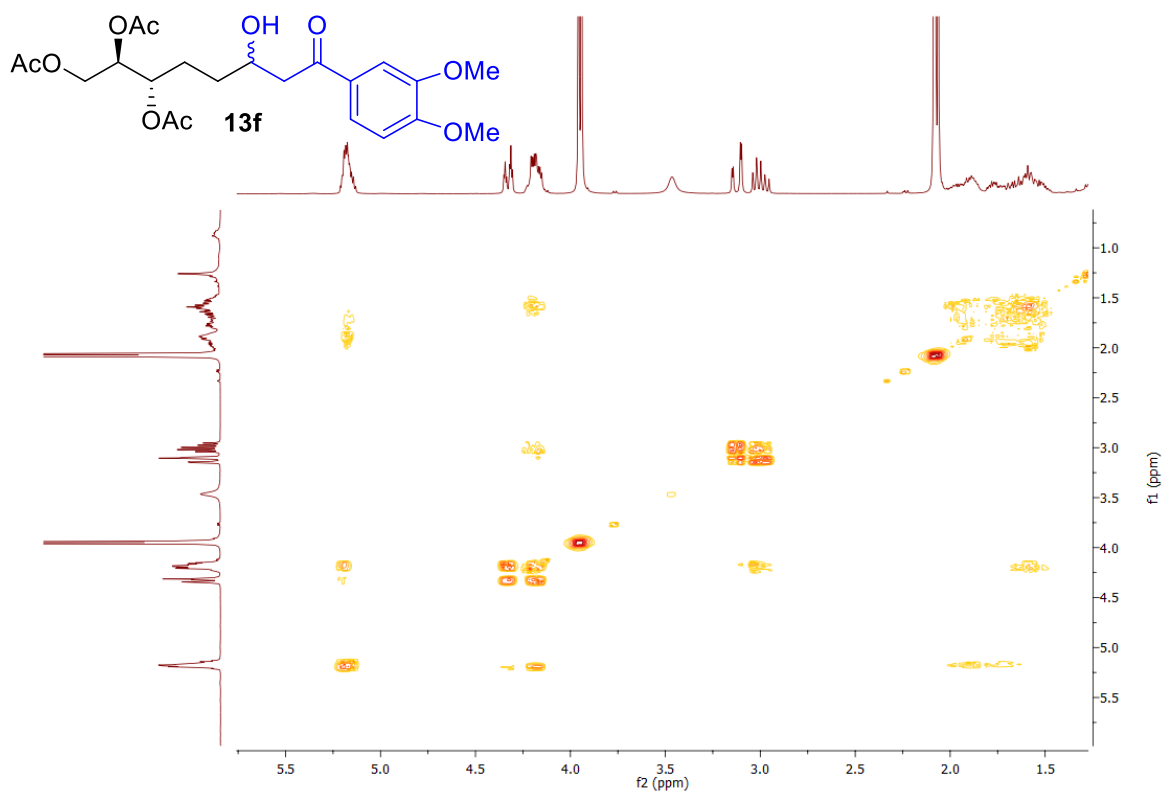
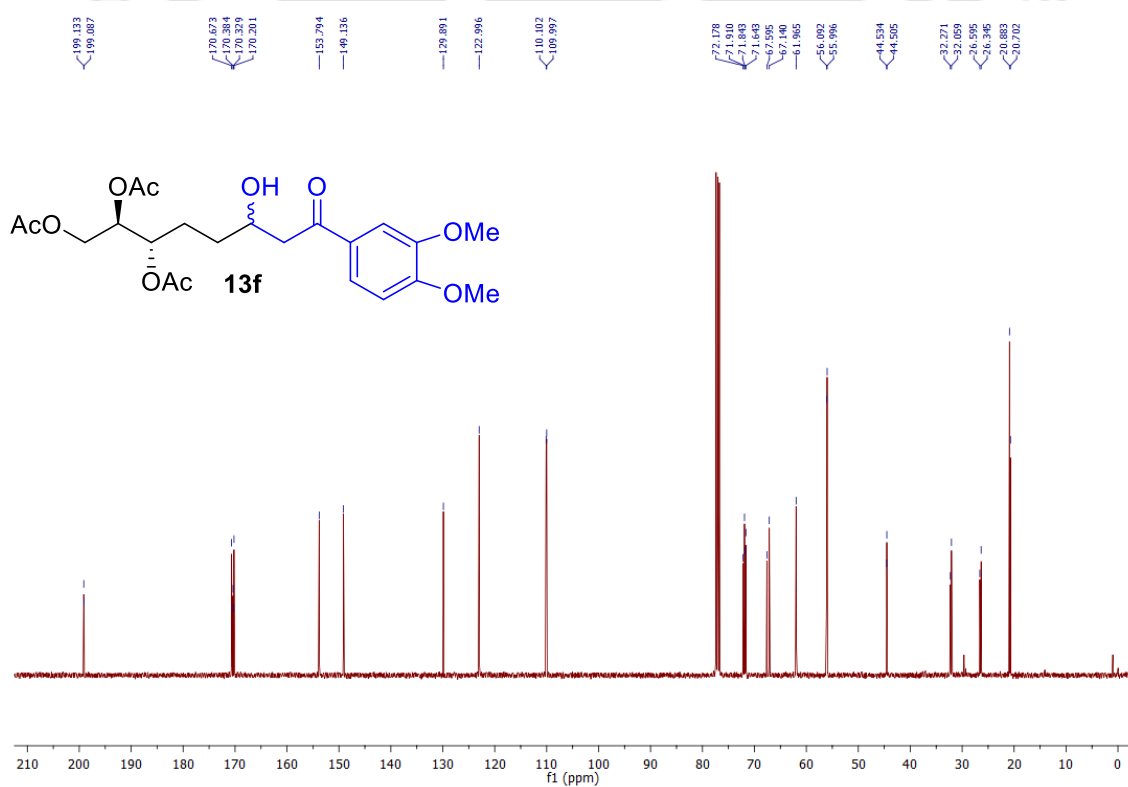
^1H NMR spectrum of compound 13c (400 MHz, CDCl_3):**COSY NMR spectrum of compound 13c (400 MHz, CDCl_3):**

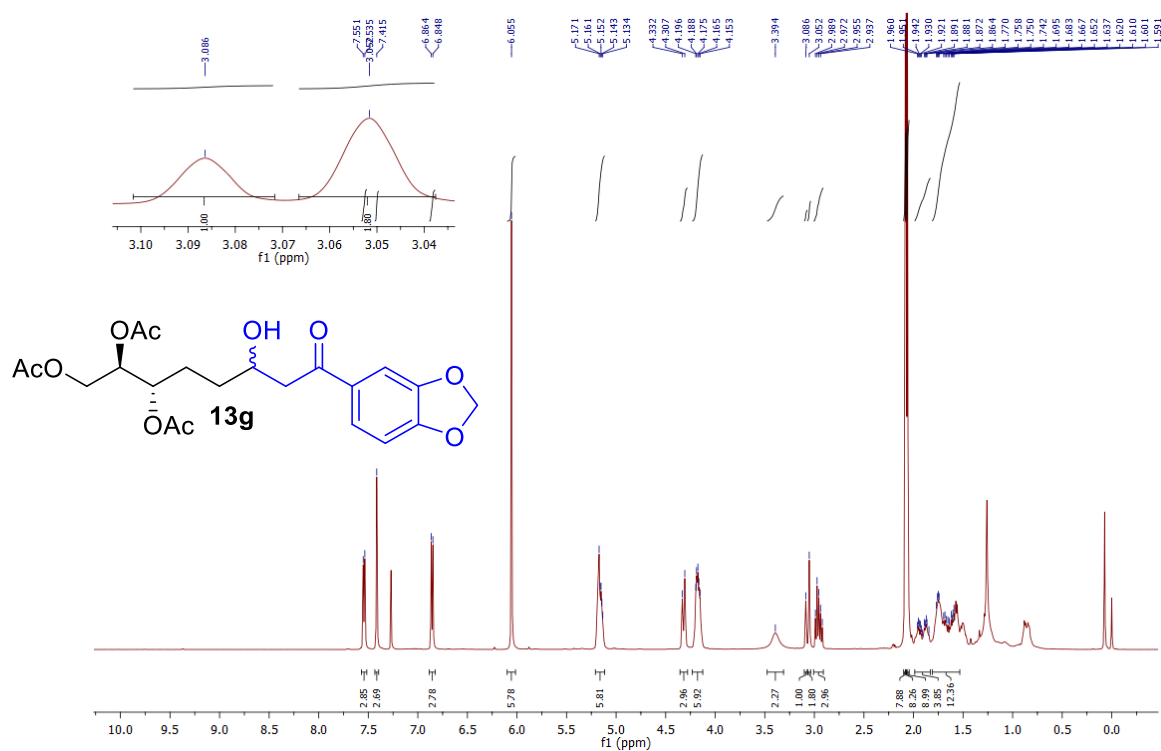
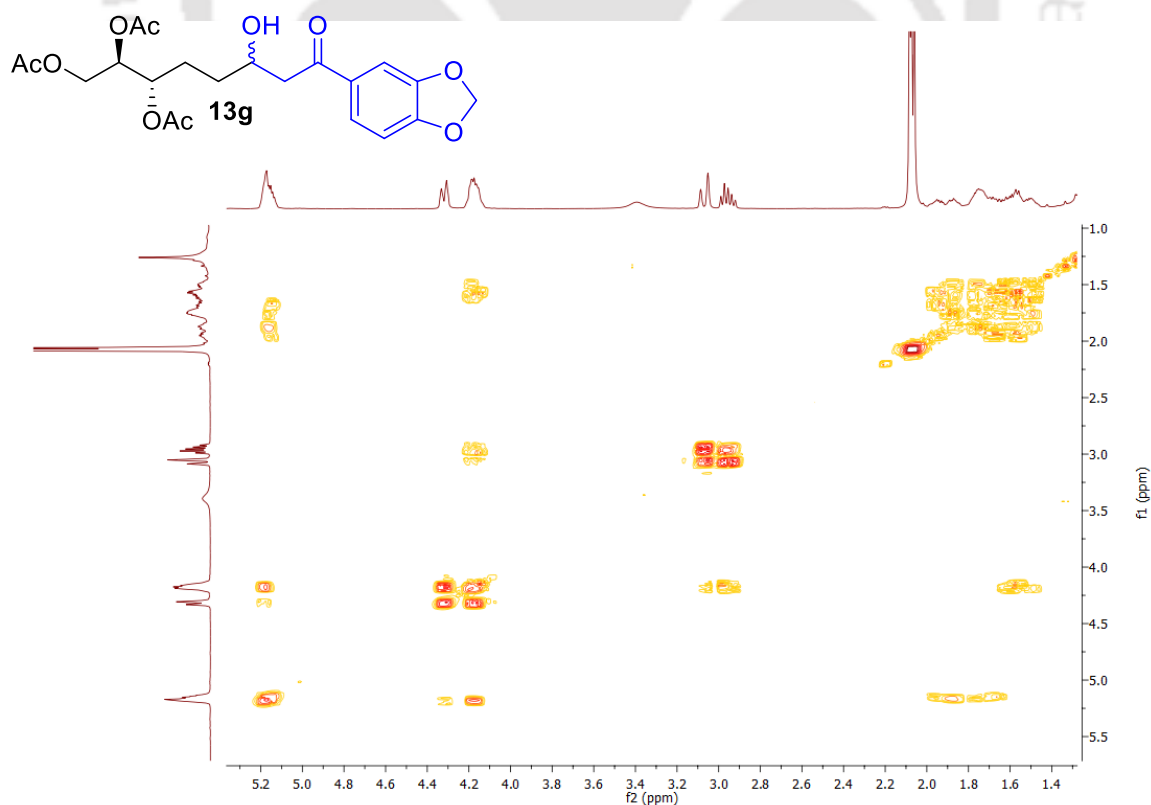
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 13c (400 MHz, CDCl_3): **^1H NMR spectrum of compound 13d (400 MHz, CDCl_3):**

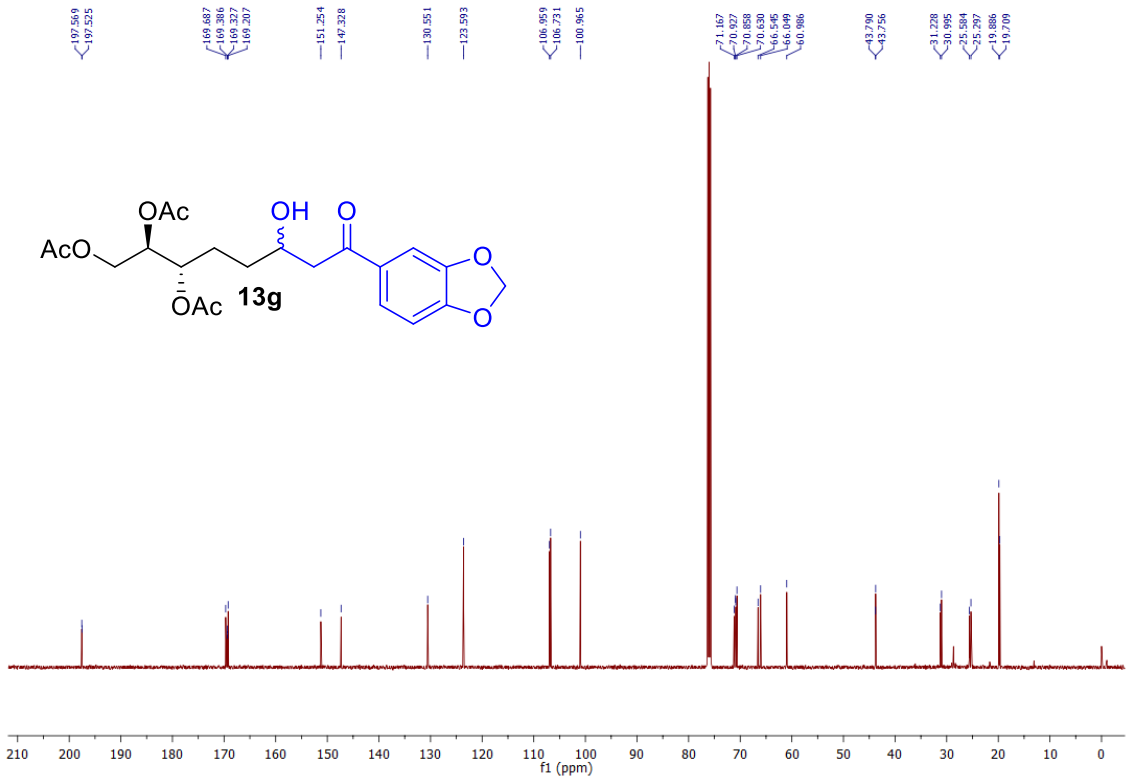
COSY NMR spectrum of compound 13d (400 MHz, CDCl₃):**¹³C{¹H} NMR spectrum of compound 13d (500 MHz, CDCl₃):**

^1H NMR spectrum of compound 13e (500 MHz, CDCl_3):

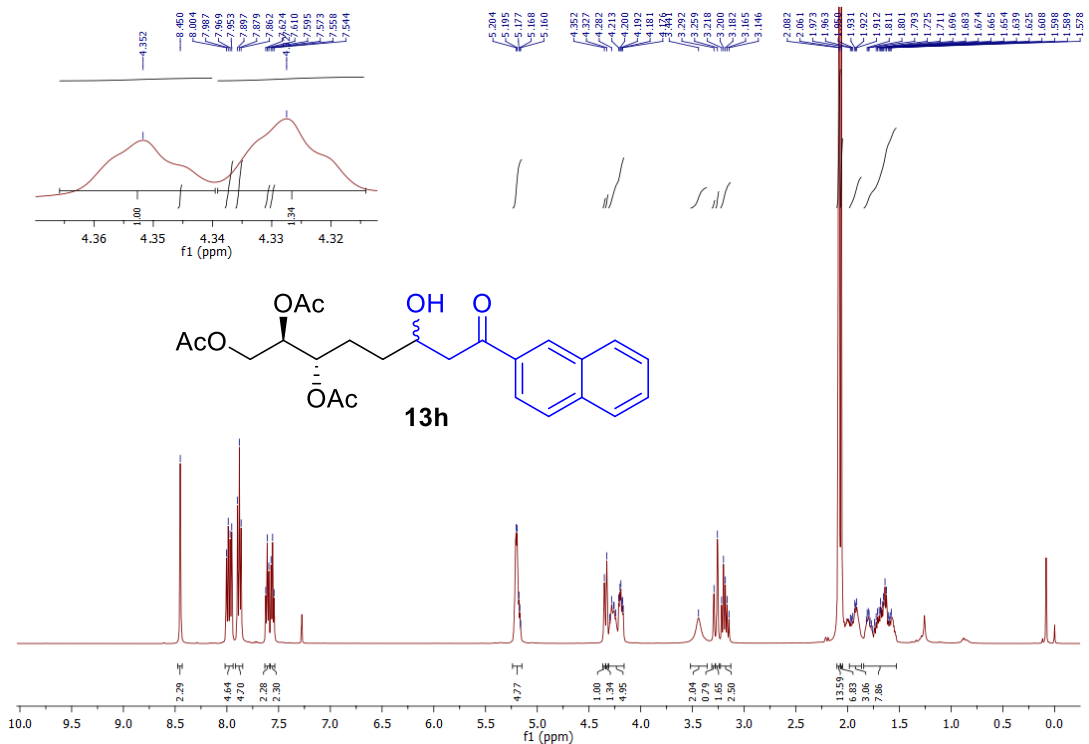
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 13e (500 MHz, CDCl_3): **^1H NMR spectrum of compound 13f (400 MHz, CDCl_3):**

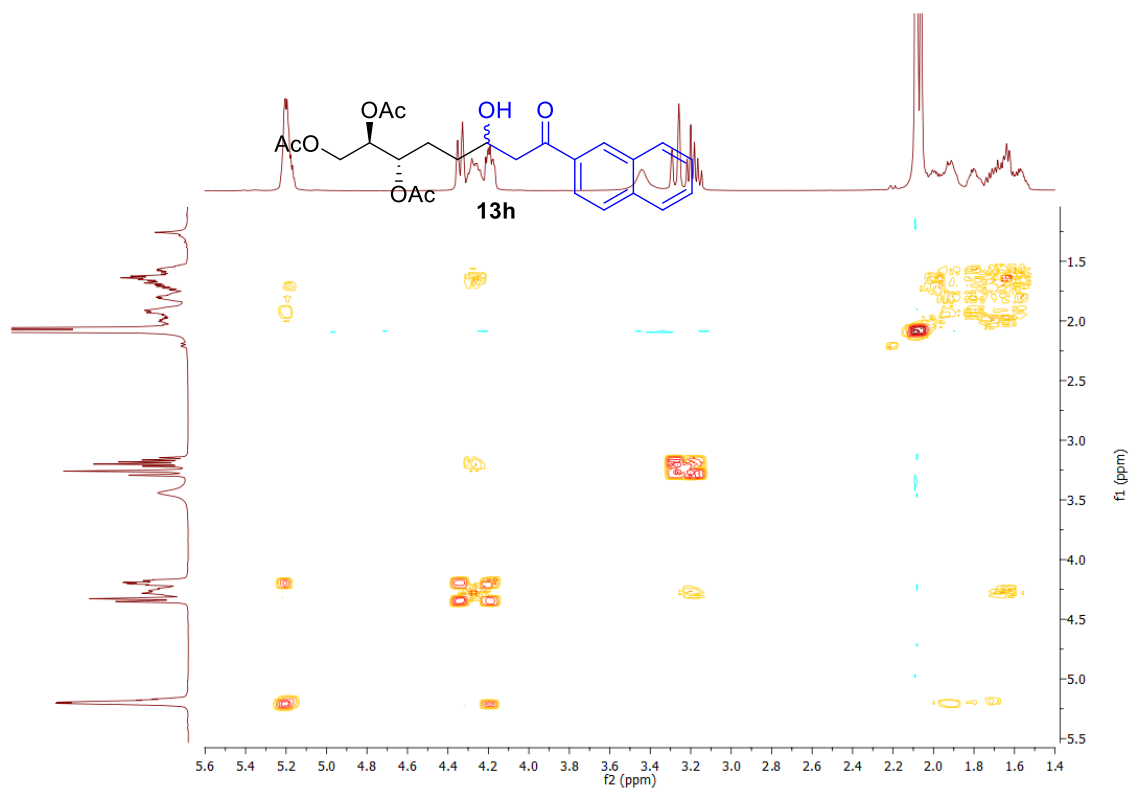
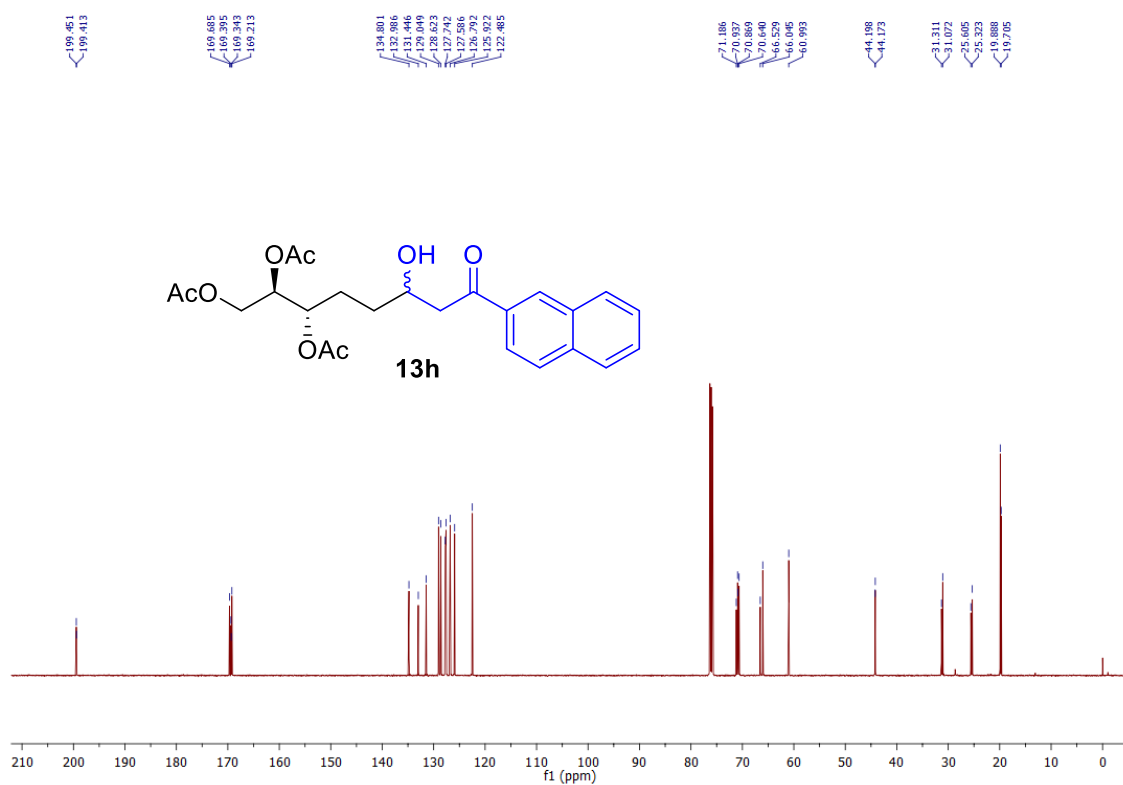
COSY NMR spectrum of compound 13f (400 MHz, CDCl₃):**¹³C{¹H} NMR spectrum of compound 13f (400 MHz, CDCl₃):**

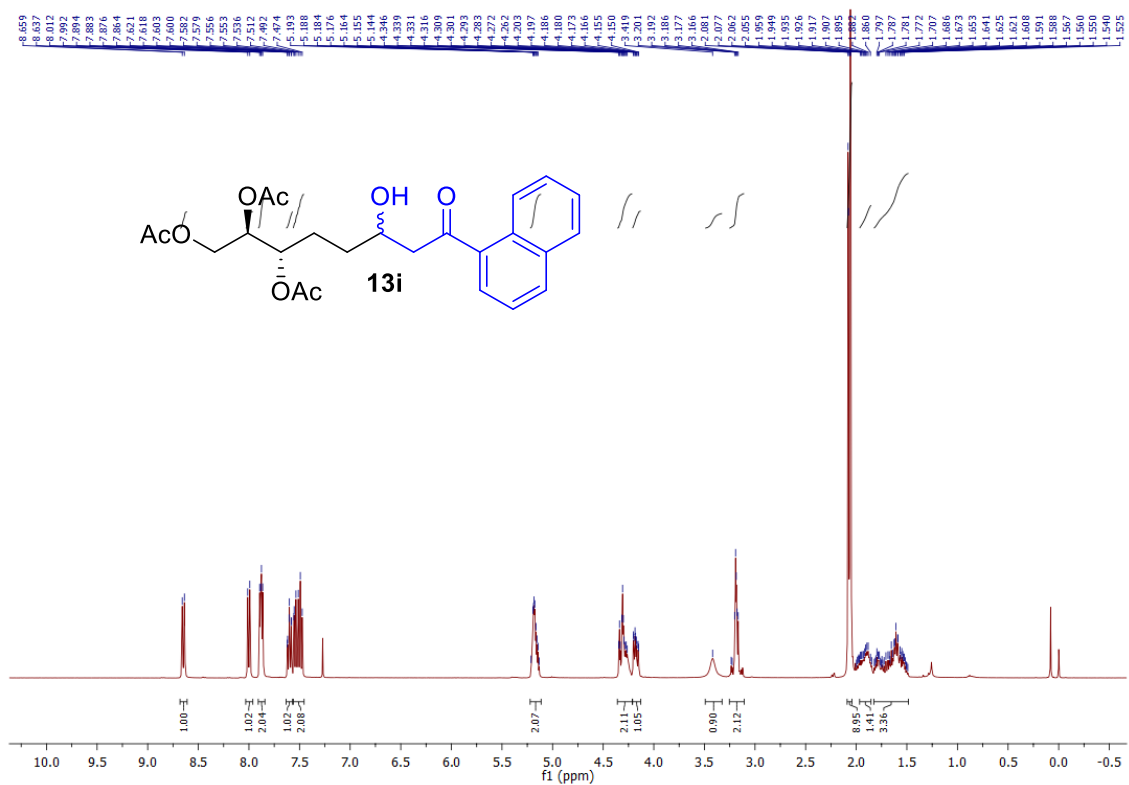
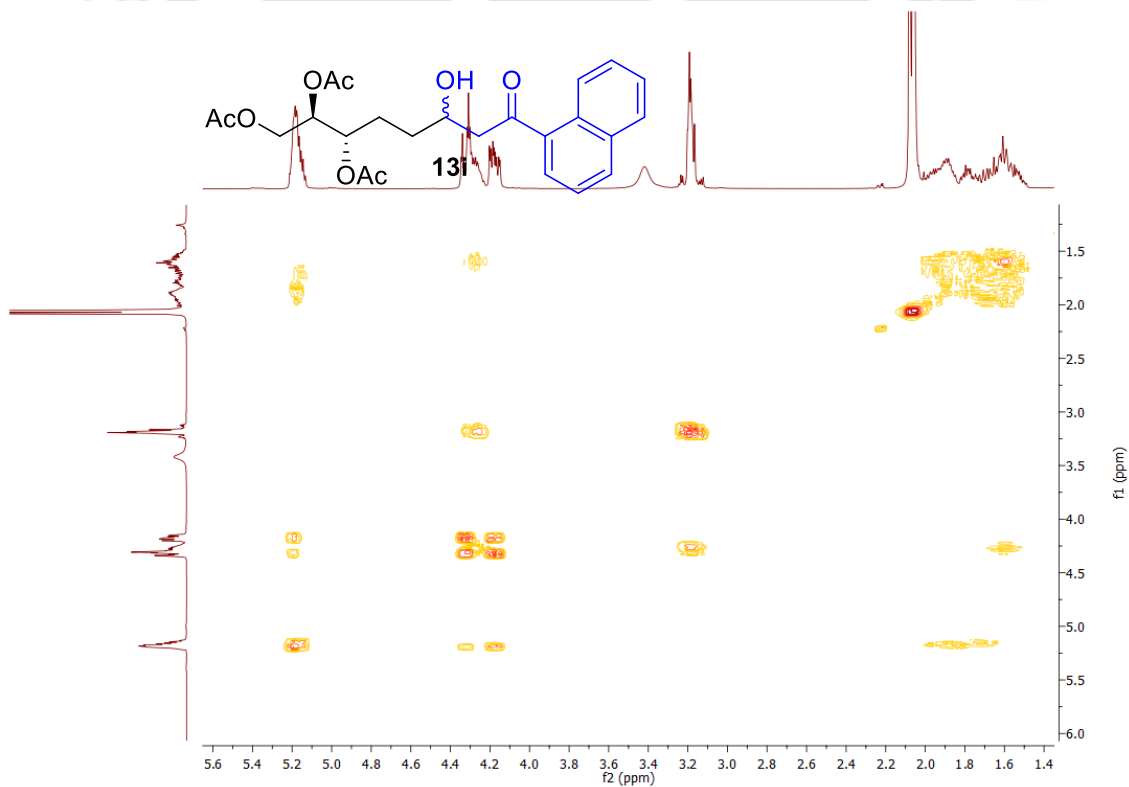
^1H NMR spectrum of compound 13g (500 MHz, CDCl_3):**COSY NMR spectrum of compound 13g (500 MHz, CDCl_3):**

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 13g (500 MHz, CDCl_3):

¹H NMR spectrum of compound 13h (500 MHz, CDCl₃):



COSY NMR spectrum of compound 13h (500 MHz, CDCl₃):¹³C{¹H} NMR spectrum of compound 13h (500 MHz, CDCl₃):

^1H NMR spectrum of compound 13i (400 MHz, CDCl_3):**COSY NMR spectrum of compound 13i (400 MHz, CDCl_3):**

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 13i (500 MHz, CDCl_3):