Utility of Sterically Strained Brønsted Salts as Organocatalysts in Glycosylation Reactions

A Thesis Submitted

in Partial Fulfilment of the Requirements

for the Degree of

DOCTOR OF PHILOSOPHY

by

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STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati, India under the supervision of Dr. Pavan K. Kancharla.

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

Guwahati — Ananya Mukherji

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CERTIFICATE

This is to certify that Ms. Ananya Mukherji has been working under my supervision since January 2017. I am forwarding her thesis entitled "**Utility of Sterically Strained Brønsted Salts as Organocatalysts in Glycosylation Reaction**" being submitted for the Ph.D. degree of this institute. I certify that she has fulfilled all the requirements according to the rules of this institute, and regarding the investigations embodied in her thesis and this work has not been submitted elsewhere for a degree.

Guwahati — Dr. Pavan K. Kancharla

August 2022 — Thesis Supervisor

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Ananya Mukherji

List of Publications and Presentations

Publications:

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2. Ghosh, T.; **Mukherji, A**.; Kancharla, P. K. *Org. Lett.* **2019**, *21*, 3490–3495.

3. Ghosh, T.; **Mukherji, A.**; Kancharla, P. K. *Eur. J. Org. Chem.* **2019**, *2019*, 7488-7498.

4. **Mukherji, A**.; Kancharla, P. K. *Org. Lett.* **2020**, *22*, 2191–2195.

5. Ghosh, T.; **Mukherji, A.**; Kancharla, P. K. *J. Org. Chem.* **2021**, 86, 1253–1261.

6**. Mukherji, A.**; Addanki, R. B.; Halder, S.; Kancharla, P. K. *J. Org. Chem.* **2021**, *86*, 17226–17243.

7. **Mukherji, A.**; Kancharla, P. K. *Synlett.* **2022** (Accepted Manuscript).

Conferences Attended:

1. Presented a Poster Presentation in FICS - 2018, held at Indian Institute of Technology, Guwahati, India.

2. Presented a Poster Presentation in OMSRI - 2019, held at Indian Institute of Technology, Roorkee, India.

3. Presented a Poster Presentation in NFCFA – 2019, held at BITS Pilani, Goa, India.

4. Presented an Oral Presentation at First Virtual JNOST Conference - 2020, Organised by IISc, Bangalore, India.

5. Attended lectures in NERC-2022.

Members of the Doctoral Committee

Dr. Pavan K. Kancharla (Thesis supervisor)

Dr. Anil Kumar Saikia (Chairman)

Dr. Aditya Narayan Panda (Member)

Dr. Dipankar Srimani (Member)

Abbreviation

AcOH	Acetic acid
ACN	Acetonitrile
Ac	Acetyl
Å	Angstrom
α	Alpha
β	Beta
BF_3	Boron trifluoride
BF_4	Tetrafluoroborate
Bn	Benzyl
Bz	Benzoyl
BAr^F_4	Tetrakis(3,5-bis(trifluoromethyl)phenyl)borate
cat.	Catalytic/Catalyst
°C	Degree Celsius
CH_3	Methyl
$CDCl_3$	Deuterated chloroform
DNA	Deoxyribonucleic acid
DCM	Dichloromethane
DCE	1,2-Dichloroethane
DMF	N,N'-Dimethylformamide
DTBP	2,6-Di-*tert*-butylpyridine
DTBMP	2,6-Di-*tert*-butyl-4-methylpyridine
DIPEA	N,N'-Diisopropylethylamine
DMSO	Dimethyl sulfoxide
δ	Delta
Et	Ethyl
Eq.	Equation
Equiv	Equivalent
Et_3SiH	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
K_2CO_3	Potassium carbonate
LiBr	Lithium bromide
Mm	Millimetre
MeI	Methyl iodide
MHz	Mega hertz
min	Minute
Me	Methyl
ml	Millilitre
mg	Milligram
µl	Microlitre
$NaHCO_3$	Sodium bicarbonate
NIS	N-Iodosuccinimide
NaI	Sodium iodide
NaH	Sodium hydride
NMR	Nuclear magnetic resonance
nOe	Nuclear Overhauser effect
Nu	Nucleophile
Ph	Phenyl
PPh_3	Triphenylphosphine
ppm	Parts per million

RNA	Ribonucleic acid
rt	Room temperature
Tf	Triflate
Ts	Tosylate
TBAI	Tetra-n-butylammonium iodide
THF	Tetrahydrofuran
TTBP	2,4,6-Tri-butylpyrimidine
TTBPy	2,4,6-Tri-*tert*-butylpyridine
TES	Triethylsilyl
TMS	Trimethylsilane
TBDMS	*tert*-Butyldimethylsilyl
TBDPS	*tert*-Butyldiphenylsilyl
TIPS	Triisopropylsilane
TIPDS	Tetraisopropyl disiloxane
TfOH	Triflic acid
TMSOTf	Trimethyltrifluoromethanesulfonate
TLC	Thin layer chromatography
UV	Ultraviolet
XRD	X-ray powder diffraction

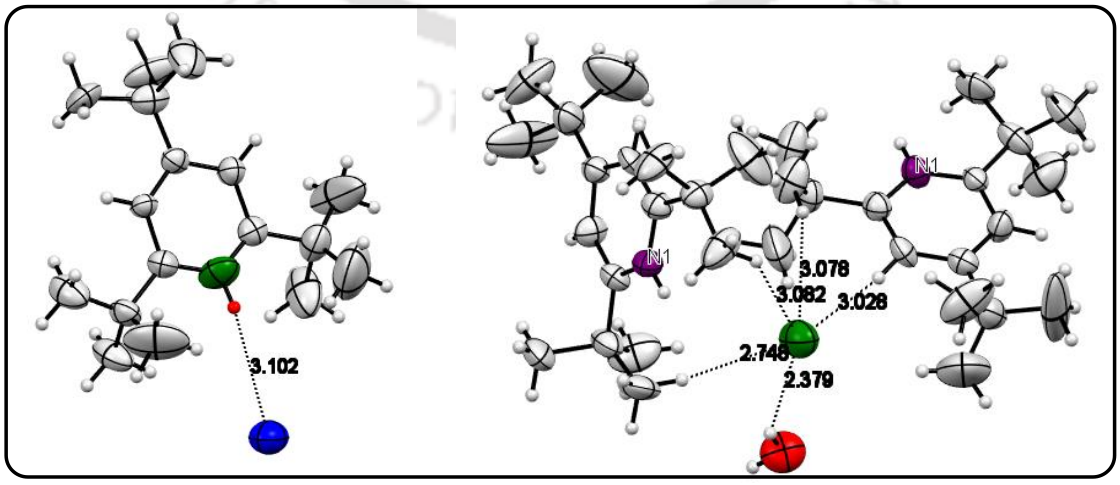
Abstract

The contents of the thesis titled as "Utility of Sterically Strained Brønsted Salts as organocatalysts in Glycosylation Reaction" is divided into five chapters. The first chapter describes the literature review on sterically strained Brønsted Salts like protonated pyridine derivatives substituted with bulky alkyl groups. Their utility in various organic reactions as well as in glycosylation reactions was discussed. The second chapter deals with the hydration of glycals by sterically hindered 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst. The third chapter demonstrates direct stereoselective synthesis of 2-deoxy and 2,6-dideoxy-β-thioglycosides from glycals. Chapter four reveals us that 2,4,6-tri-*tert*-butylpyridinium (TTBPy) salts can catalyze the sulfonamidoglycosylation of 2-deoxy and 2,6-dideoxy Sugars. The fifth chapter focuses on the effect of various silyl protecting groups on the stereoselectivity of rhamnosylation and TBDPS protected α-rhamnosides were synthesized stereoselectively.

Chapter I. Sterically Strained Brønsted Salts and Their Utility

2,4,6-Tri-*tert*-butylpyridine (TTBPy) and other sterically strained pyridine analogues 2,6-di-*tert*-butylpyridine (DTBP), 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) and 2,4,6-tri-*tert*-butylpyrimidine (TTBP) are known for their unique reactivity in various organic reactions. Considering the inductive effects caused by the presence of *tert*-butyl groups present in these molecules, these are expected to be more basic than pyridine and lutidine. In contrast, the observed aqueous *pKa* of DTBP and TTBPy is about ~2 units lesser (*pKa* of TTBPy = 3.4) as the sterically bulky conjugate acid corresponding to these molecules are poorly soluble in aqueous solutions. These molecules are sufficiently bulky that they are unable to form an adduct with boron trifluoride or CH_3^+ but can get protonated.

The hydrochloride salt of TTBPy shows unusual reactivity due to the complete shielding of the cationic $[N\text{-}H]^+$ by the bulky ortho-*tert*-butyl groups and the $[NH]^+\cdots Cl^-$ distance is unusually longer (3.10 Å) compared to H-bonding distance, resulting in strained/frustrated electrostatic interactions between the ion-pair. Throughout this thesis, we have successfully showcased the utility of the poor electrostatic interactions arising due to steric strain in the ion-pair involving the sterically bulky $TTBPyH^+$ cation in activating a third molecule like water, alcohol (ROH), thiol (RSH) or sulfonamide (RSO_2NH_2) to perform respective glycosylation on glycal donors.

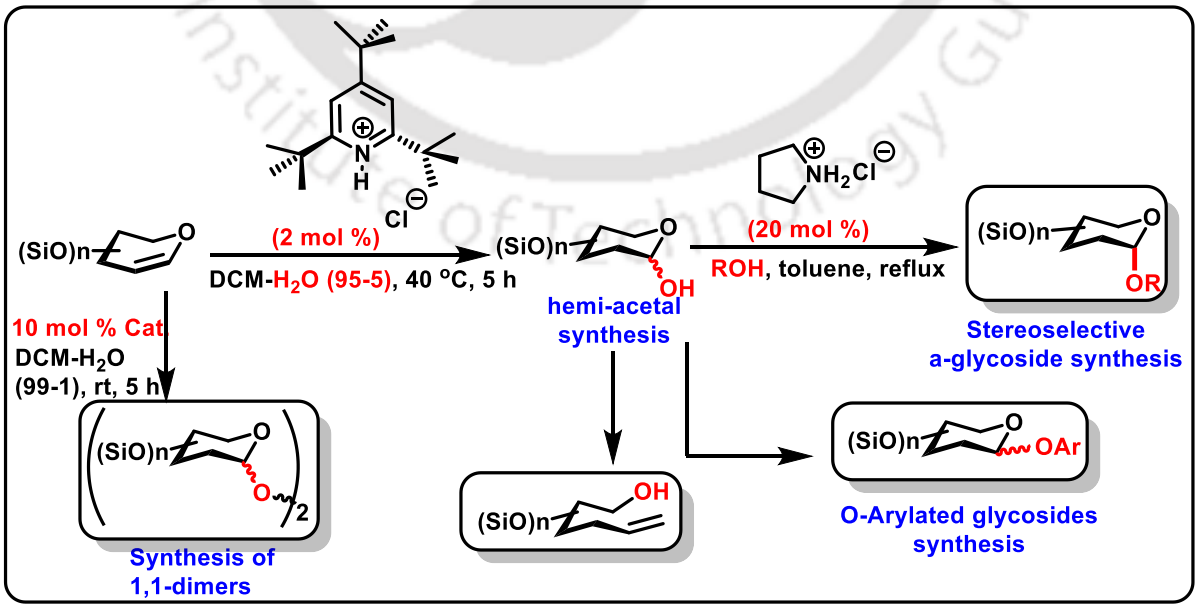


Scheme 1. *XRD Structure of TTBPy·HCl and TTBPy·HCl, $3H_2O$*

The cavity of protonated $[TTBPy\text{-}H]^+$ is around ~3.27 Å as evidenced from the XRD structure, that can accommodate either a water molecule or a chloride anion within the hydrogen bonding distance. The poor coordination ability of $[TTBPy\text{-}H]^+$ could explain its utility as a proton trapping reagent.

Chapter II. C–H···Anion Interactions Assisted Addition of Water to Glycals by Sterically Hindered 2,4,6-Tri-*tert*-butylpyridinium Hydrochloride

2-deoxy glycosides have huge biological importance. 2-deoxy-D-ribose is the main constituent of deoxyribonucleic acid (DNA). Furthermore, 2-deoxy, 2,6-dideoxy, and 2,3,6-trideoxy sugars are present in naturally available and biologically important molecules. Moreover, rhamnose or 6-deoxy-L-mannose is a 2,6-dideoxy sugar and is commonly, found in plant glycosides. There are several literature methods to synthesize 2-deoxy sugar hemiacetals from their corresponding glycal molecule. The current methods for the synthesis of sugar lactols from glycals involve the use of highly acidic conditions like 4–8 M HCl or triphenylphosphine/HBr, under which some of the silyl protecting groups are usually unstable and lead to reduced yields or the decomposition of starting materials. In this chapter, we have displayed the utility of the bulky TTBPy·HCl as a highly efficient organocatalyst that can convert the acid-sensitive silyl-protected glycals to the respective hemiacetals and their dimerized products in high yields via a unique C–H···Cl– interaction assisted hydration. The criticality of the concentration of water in the reaction outcome is indicative of a unique mechanistic pathway by the bulky pyridine salt and not via the general Brønsted acid mechanism. The various silyl protected hemiacetals thus synthesized were successfully utilized in the stereoselective synthesis of both α and β glycosides. Also, the anomeric hemiacetals have been successfully utilized in the synthesis of *O*-arylated glycosides via a copper catalyzed addition of phenylboronic acids. The organocatalytic hydration of glycals presented here in combination with the iminiumcatalyzed stereoselective glycosylation provides a practically simple approach for the synthesis of oligosaccharides and various other carbohydrate synthons. These novel concepts have the potential to be applicable to various other synthetic transformations, as well.



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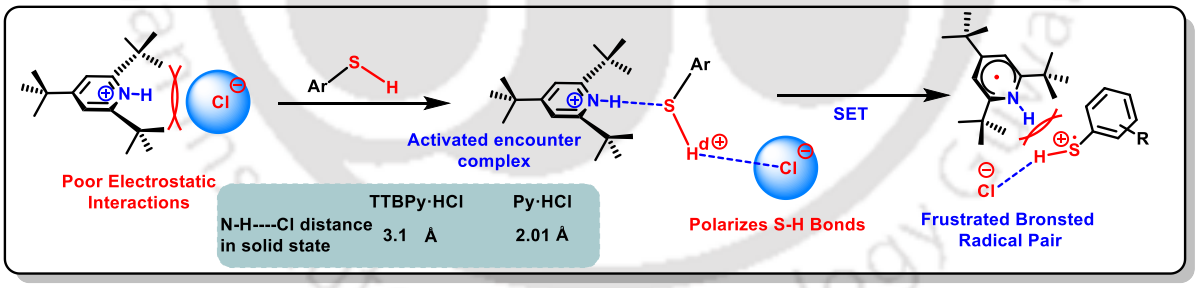
Scheme 2. *Hydration of Glycals by Sterically Hindered TTBPy·HCl and Further Applications*

Chapter III. Sterically Strained Brønsted Pair Catalysis by Bulky Pyridinium Salts: Direct Stereoselective Synthesis of 2-Deoxy and 2,6-Dideoxy-β-thioglycosides from Glycals

2-Deoxythioglycosides (anomeric oxygen atom is replaced by sulfur atom), besides their utility as stable glycosyl donors, are a stable class of alternatives for the structure and function study of 2-deoxy *O*-linked glycosides as these compounds retain their biological activity and also are resistant towards enzymatic cleavage. Hence, these compounds form prime candidates as therapeutic agents as well. Despite the advantages and their significance, the synthesis of 2-deoxythioglycosides remains an underdeveloped area with only a few methods available for the synthesis of 2-deoxythioglycosides and is limited to the usage of simple thiol nucleophiles. In this chapter, we report organocatalytic synthesis of 2-deoxy-*S*-glycosides synthesis directly from glycals. we have successfully showcased the utility of the poor electrostatic interactions arising due to steric strain in the ion-pair involving the sterically bulky 2,4,6-tri-*tert*-butylpyridinium cation in activating sugar thiols, thus synthesizing the biologically important class of compounds, 2-deoxy-thioglycosides, the synthesis of which otherwise require Rhenium catalysis or multistep synthesis. Also, this organocatalytic protocol allows us to access β-thioglycosides, unlike the general glycal activation methods. Spectroscopic studies (1H NMR, IR) reveal the reaction is driven by acceptor (thiol) activation. ESR studies provided evidence for the potential involvement of the intriguing frustrated radical pair intermediates in the current protocol. The influence of coordinating versus weakly coordinating anions on the observed reactivity and selectivity has also been investigated, reflecting the necessity of coordinating anion like chloride. The concept of increased reactivity imbued upon the anion when bound with the sterically bulky pyridinium resulting from the frustrated interactions has a huge potential in organic synthesis.



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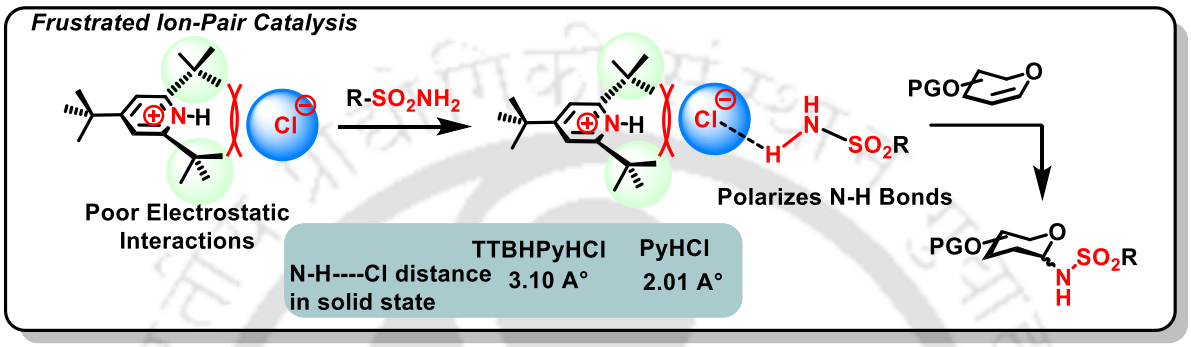
Scheme 3. *Sterically Strained TTBPy·HCl Catalyzed Direct Stereoselective Synthesis of 2-Deoxy and 2,6-dideoxy-β thioglycosides from Glycals*

Chapter IV. Cl-…H-N Interactions Assisted Addition of Sulfonamides to Enol Ethers: Synthesis of 2-Deoxy and 2,6-Dideoxy Sulfonamido Glycosides

In this chapter, we have successfully showcased the utility of the poor electrostatic interactions arising due to steric strain in the ion-pair involving the sterically bulky $TTBPyH^+$ cation in activating aliphatic and aromatic sulfonamides to perform sulfonamidoglycosylation on glycal donors. Sulfonamides are known to possess a broad spectrum of biological activities. Several sulfonamides have appeared as useful therapeutics for the treatment of cancer and chemotherapy. This chapter describes a strategy for the stereoselective synthesis

of both α and β sulfonamidoglycosides. The preparation is high yielding and effective for gram scale synthesis. There are very few literature reports on sulfonamidoglycosylation and all of the synthesized molecules are previously not known in the literature. IR studies reiterate the fact that the sterically protected N-H proton is not involved in any exchange process. ESR studies provided evidence for the potential involvement of the frustrated radical pair intermediates in the current protocol. Interestingly, the observed catalytic activity also seems to be influenced by the catalyst counter anion. Besides, the thus synthesized sulfonamidoglycosides have been converted to corresponding N-methylated product as an application.



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Scheme 4. *Sulfonamidoglycosylation of 2-Deoxy and 2,6-Dideoxy Sugars*

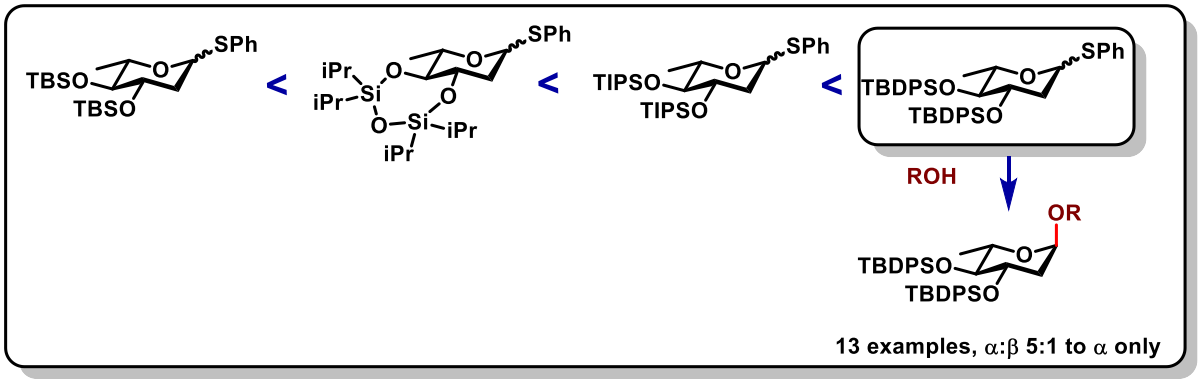
Chapter V. Influence of Various Silyl Protecting Groups on the Stereo-Selectivity of Rhamnosylation: Stereoselective Synthesis of OTBDPS Protected α-Rhamnosides

After further deoxygenation on 2-deoxy sugars (mostly at C-3 and/or C-6 position), we can get its di/trideoxy analogues. These dideoxy or trideoxy sugar units are found in many natural products like angucycline jadomycin, digitoxin, landomycin (angucycline) and mithramycin (anthracycline) etc. Several research groups have developed new methods for controlling stereo selectivity in glycosylation reactions using 2-deoxy and 2,6-dideoxy sugar donors.

Reactions with glucal substrates gave products with higher stereocontrol than rhamnals, which can be attributed to the conformational preference of the C6-side chain present in glucal donors, which is lacking in the rhamnal moieties. Hence, getting a stereoselective glycosylated product derived from rhamnal donors is more challenging.

In this chapter, we have studied the effect of silylethers on the 3,4-positions of the L-rhamnose ring, several well-known literature methods of glycosylation have been employed on various silyl protected L-rhamnose derived glycosyl donors and the stereoselectivity of their related products has been observed. Four different silyl protecting groups were chosen to perform this study on L-rhamnose sugar. The stereoselectivity of *O*-, *C*- and *S*-glycoside was monitored in this study.

It is observed that OTBDPS protecting group provided better α-stereo selectivity than OTIPS, cyclic OTIPDS and OTBDMS group on L-rhamnose donors. As an application of this study, stereoselective OTBDPS protected 2, 6- dideoxy L-rhamnosides were synthesized with various glycosyl acceptors with excellent yields. Moreover, a trisaccharide was also synthesized. It is observed that α-stereo preference was retained in that case also.



Manuscript under Progress.

***Scheme 5**. Stereoselectivity Preference in Glycosylation*

Contents

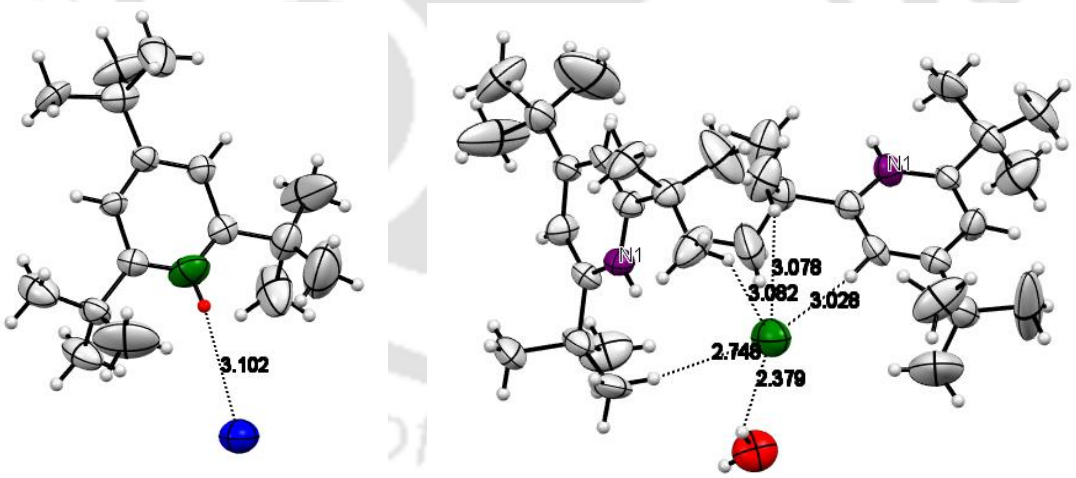
5.8 References

5.9 Spectra

5.10 nOe Experiments

Chapter I

Sterically Strained Brønsted Salts and Their Utility in Glycosylation Reaction

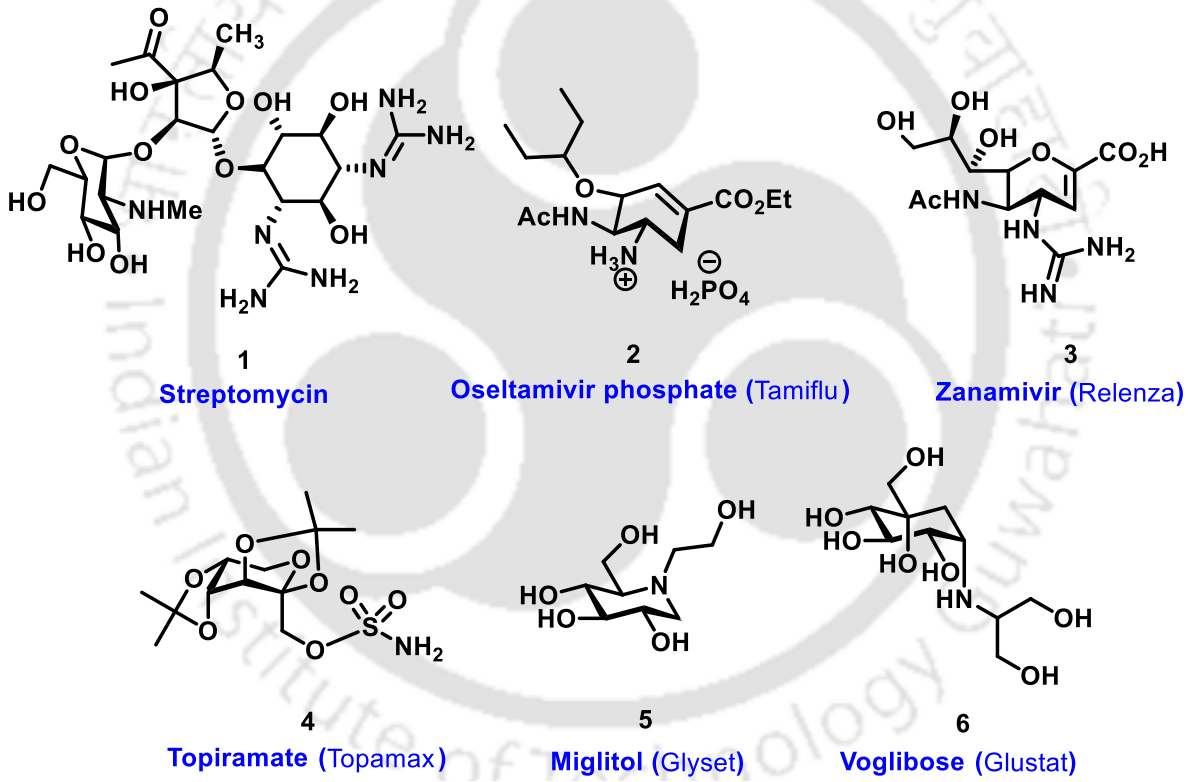


1.1 Literature Survey on Glycosylation Reaction

1.1.1 Carbohydrates:

Carbohydrates are generally available as an immediate energy source and it is one of the most abundant molecules on earth occupying up to 75% of the biomass. It plays role in avoiding amino acid degradation to restore energy and also circumvents ketosis process to prevent the breakdown of fatty acids.

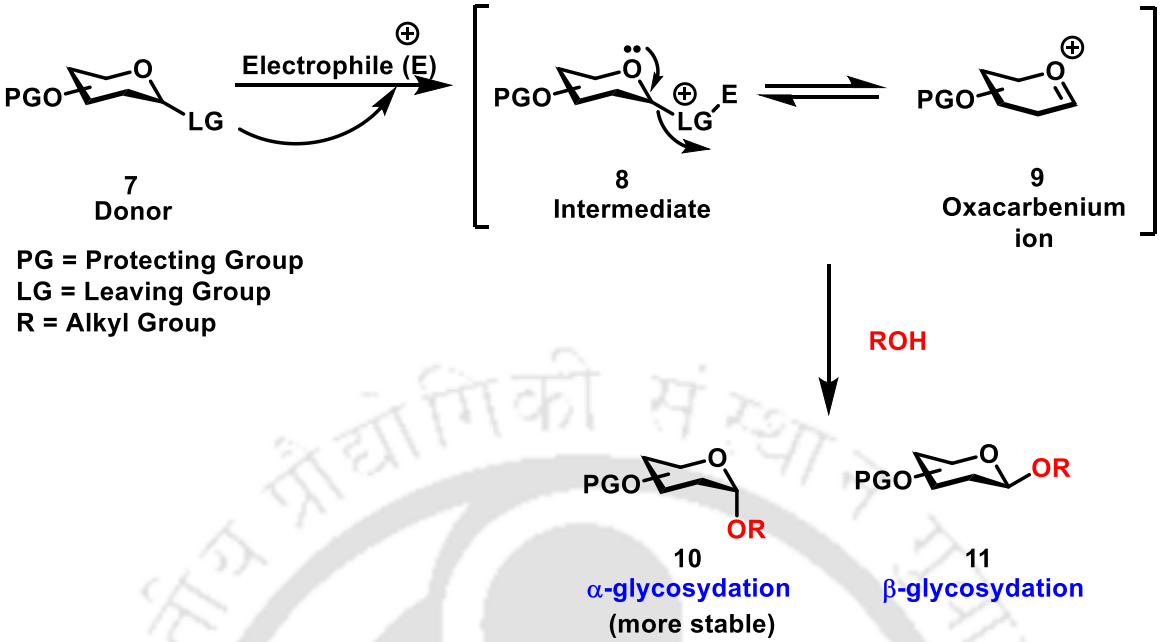
A huge number of medically important antibiotics e.g. Streptomycin (to treat a number of bacterial infections, including tuberculosis), Acarbose (for treating diabetes), Tamiflu (for treating influenza), Zanamivir (helps to decrease flu symptoms), Topiramate (to treat epilepsy and migraine), Miglitol (to treat type 2 diabetes), Voglibose (to treat diabetes), etc are carbohydrate derivatives (scheme 1, molecule **1**-**6**).[1]



Scheme 1: *Carbohydrate-Based Molecules in Medicinal Chemistry*

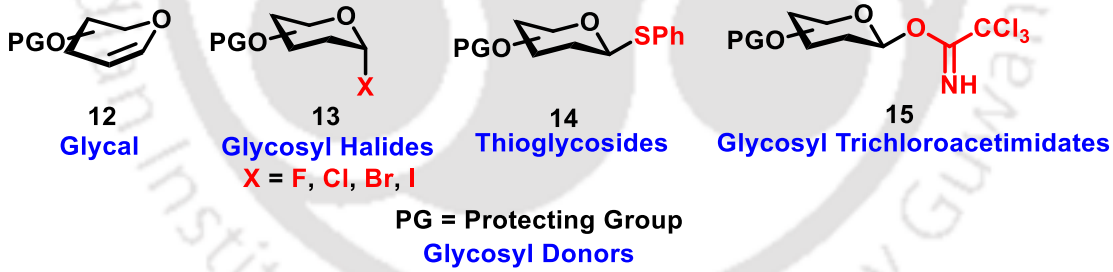
1.1.2 Basics of Chemical Glycosylation:

Carbohydrates are found in nature as oligosaccharides like cellulose, chitin etc., or glycoconjugates such as glycopeptides and glycolipids in which each carbohydrate (saccharide) units are connected through glycosidic linkages, formed via glycosylation reaction. Glycosylation is the reaction between a sugar moiety having an electrophilic center (or **glycosyl donor**) and another sugar or nonsugar nucleophile (**glycosyl acceptor**).



Scheme 2: *General Scheme for O-Glycosylation*

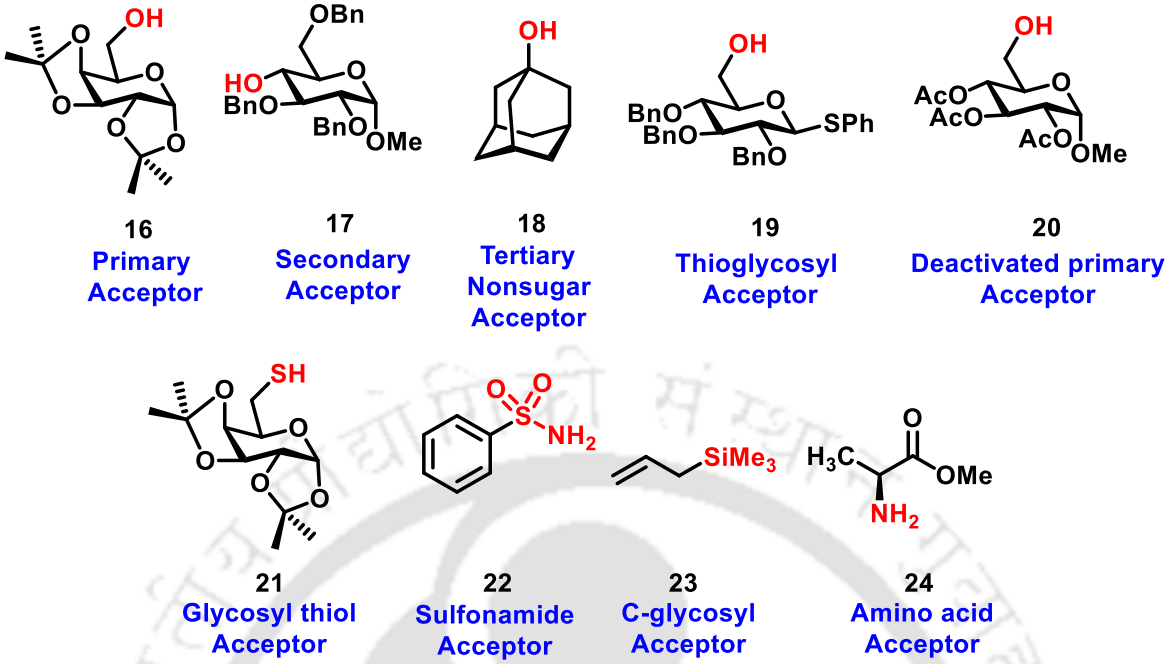
As shown in the above scheme (scheme 2), Glycosyl donor 7**,** having a leaving group at C1 or anomeric carbon, reacts with glycosyl acceptor **ROH,** which can be any sugar or non-carbohydrate molecule having a free hydroxyl group to provide *O*-glycosylated compound **10** or **11**.



Scheme 3: *Commonly Used Glycosyl Donors*

Some commonly used glycosyl donors are glycals (having a double bond between C1 and C2), glycosyl halides, anomeric thioglycosides, glycosyl trichloroacetimidates, etc (scheme 3, molecule **12-15**).

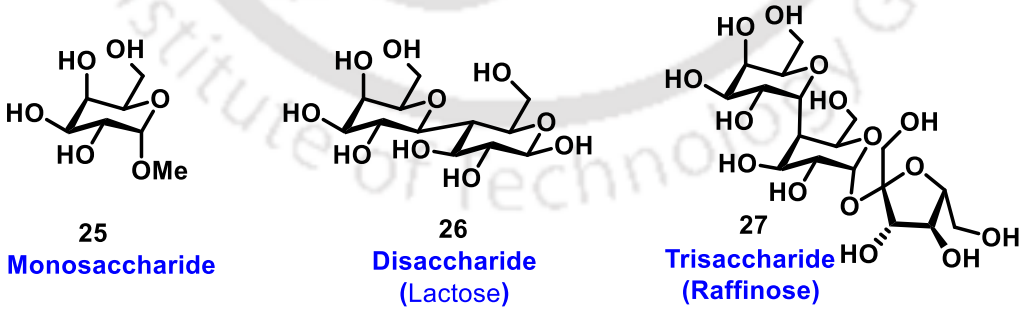
Scheme 4 shows some examples of frequently used glycosyl acceptors. Compounds **16**, **17,** and **18** represent glycosyl acceptors having primary, secondary, and tertiary hydroxyl groups respectively. Compound **19** is a phenyl thio glycoside that can be used as an acceptor in an **orthogonal glycosylation** process to synthesize a polysaccharide**.** Molecule **20** is an example of a deactivated primary sugar acceptor, having electron-withdrawing acetyl protecting group.



Scheme 4: *Glycosyl Acceptors*

Similarly, in literature thio glycosylation, sulfonamido glycosylation, *C*-glycosylation, and *N*- glycosylation are also studied frequently. The acceptors which can be used in such processes are also shown in scheme 4 (compound **21**-**24**).

When a sugar molecule is attached to a non-sugar nucleophile (*O*-, *S*- or, *N*- based nucleophiles) then such saccharide residues are called monosaccharides and similarly, structures containing more than one monosaccharide are known as oligosaccharides (scheme 5). The syntheses of complex oligosaccharides via the formation of glycosidic bonds play important roles in several biological processes.



Scheme 5: *Monosaccharide and Oligosaccharide*

1.1.3 Factors Affecting Glycosylation Reaction:

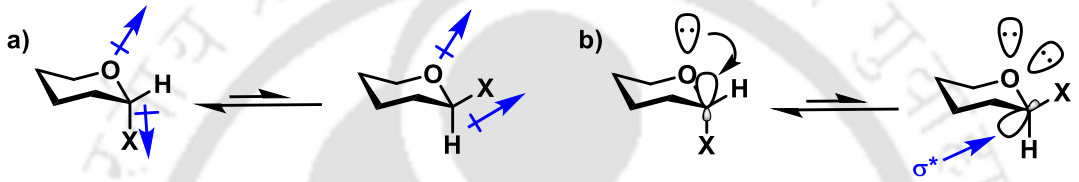
- **Anomeric Effect:**

In general, equatorial substituents of cyclohexanes are energetically more stable, as substituents in axial positions have 1,3-diaxial interactions. Although, it is observed that both axial and equatorial isomers i.e. α- and β-isomers of D-glucopyranose exist in aqueous solution and also α-isomers predominate when the anomeric –OH group is replaced by halides, -OR, -SR etc. This is due to the "**Anomeric Effect**" discovered by Raymond Lemieux in 1958 and also named as **Edward-Lemieux effect**.[2] This is a stereoelectronic effect that defines the influence of heteroatomic polar substituents at the anomeric center of the pyranose ring are more stable in axial orientation than in the sterically less hindered equatorial orientation which means α-isomer is more stable than β. This effect is dependent on three major factors:

a) dipole-dipole interaction,

b) stereoelectronic n-σ* interaction, and

c) n-n repulsions coupled with C-H hydrogen bonding (Scheme 6).[3]



Scheme 6: *a) Dipole-dipole interaction and b) Lone pair and σ* orbitals in α- and β-anomers.*

There are two dipoles generated in a sugar pyranose ring, one directed towards outside from the two nonbonding electron pairs located on endocyclic i.e. in exocyclic direction and another dipole directing from anomeric carbon towards the heteroatom attached to it. In α-anomer, these two dipoles are directed in opposite directions and hence, dipole-dipole interaction is small and energetically favorable. On the other hand, in the case of β-anomer, these two dipoles are acting in the same direction i.e. parallel to each other and hence, the dipole-dipole interaction is more and energetically unfavorable. This makes the α-anomer more stable than the β-anomer.

The stereoelectronic effect reveals that in α-anomer, the non-bonding electronic orbital of the ring oxygen atom is synperiplanar to the anti-bonding orbital of the anomeric carbon substituent which is axially oriented in $^4C_1$ conformation. The resulting n-σ* interactions help in the shortening and elongation of O-C1 bond and C1-heteroatom bonds respectively. This type n-σ* interaction is not possible in β-anomer as these two orbitals are antiperiplanar to each other when the substituent at anomeric carbon is in equatorial position and hence, such stabilization is absent in β-anomer, making it less stable anomer.

In the case of β-anomer, the lone pairs of electrons on the oxygen are coplanar with the heteroatom attached at the anomeric center, giving rise to 1,3-interaction. These eclipsing lone pairs result in an unfavorable n-n interactions and generates high energy. The stabilizing interactions in α-isomer along with the destabilizing interactions in β-anomer results in an energetic difference between the anomers.[4,5]

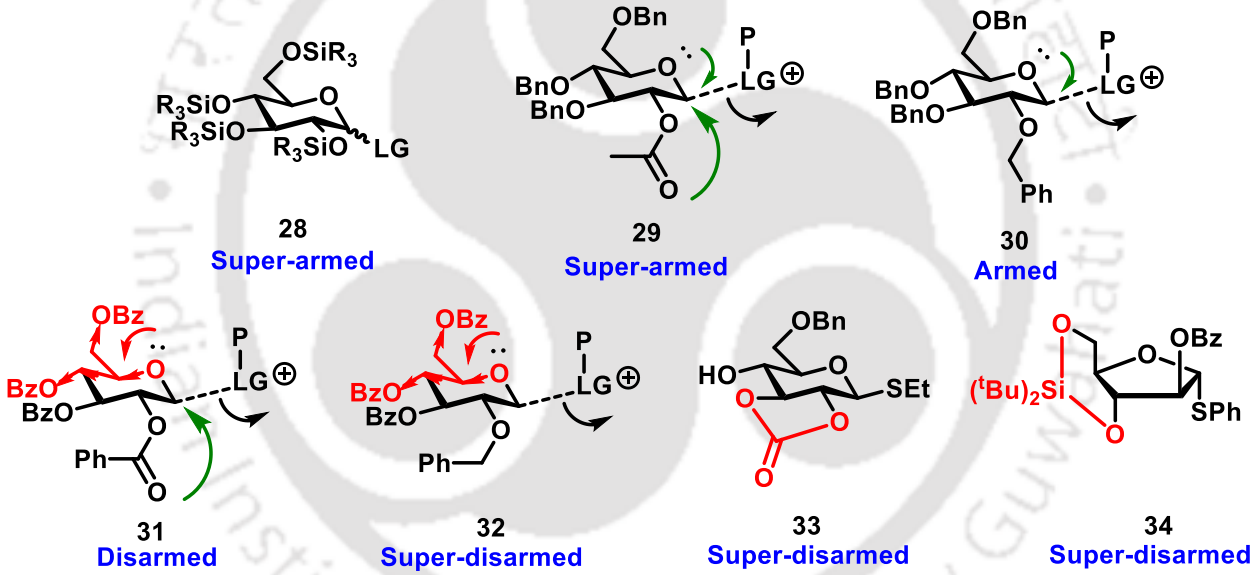
❖ Protecting Group Effect:

Fraser-Reid and co-workers have discovered armed-disarmed glycosylation.[6,7] This strategy describes that the hydroxyl protecting groups in the sugar moiety can influence the reactivity outcome of substrates towards glycosylation reaction.

Conventionally, when electron rich substituents such as $–OCH_2C_6H_5$ (–OBn), –OMe, -Op-MeBn, -Op-OMeBn (-OPMB) group etc are present as hydroxyl protecting groups then the electron density of the glycosyl done increases and hence, the generated oxocarbenium ion becomes more stable and efficient to react with a glycosyl acceptor and thus favours glycosylation reaction. Such donors containing electron donating substituents are known as **Armed Donors** (scheme 7, compound **30**).

On the other hand, the electron withdrawing substituents such as $–OCOCH_3$ (–OAc), $–OCOC_6H_5$ (–OBz) group etc. decrease the electron density on the glycosyl donor and thus, destabilizes the resultant oxocarbenium ion and become less reactive in glycosylation. Such donors containing electron withdrawing substituents are known as **Disarmed Donors** (scheme 7, compound **31**).

There are some more categories of glycosyl donors e.g. sugar building blocks having more reactivity than armed donors are termed as **superarmed** donors and less reactivity than disarmed donors are **superdisarmed** donors. Different authors have described this superarmed-superdisarmed concept in their own way.



Scheme 7: *Classification of Glycosyl Donor in terms of Reactivity*

In general, according to recent studies the class of donors where the hydroxyl protecting groups are protected with highly reactive bulky silyl substituents e.g. *tert*-butyldiphenyl silyl (TBDPS), *tert*-butyldimethyl silyl (TBDMS), triisopropyl silyl (TIPS) etc are found to be more reactive as glycosyl donors than per-benzylated armed donors. Due to the superior reactivity of such donors these are termed as **Superarmed Donors** (scheme 7, compound **28**, **29**).[8]

Demchenko et al. have reported that a mixed protecting group present in a sugar building block can unexpectedly affect the glycosyl donor reactivity.[9] The presence of "arming" benzyl group at C-2 and "disarming" acetyl or benzoyl groups at the remaining hydroxyls (scheme 7, compound **32**), can make the donor less reactive than traditional per-benzoylated disarmed donors.

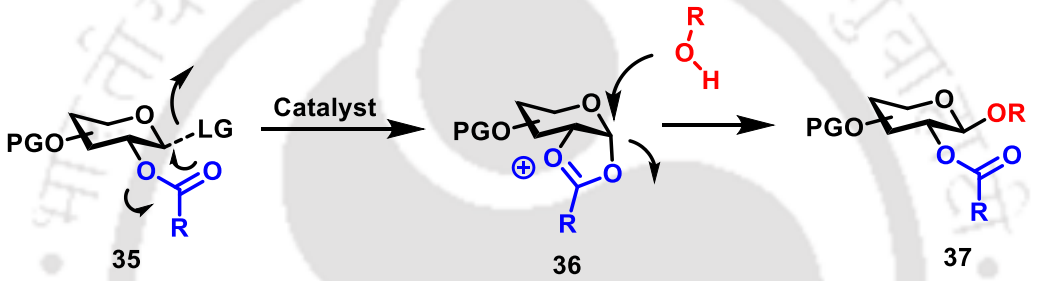
Recent studies by Boons and coworkers[10] shows that anomeric thioglycosides having cyclic 2,3-carbonate protecting group could be even less reactive (superdisarmed) than

traditional disarmed per-acylated thioglycosyl donors. They have reported that trans-2,3-cyclic carbonates deactivate the anomeric center of thioglycoside donors both electronically and conformationally (scheme 7, compound **33**).

Yang's group has studied the armed- disarmed concept on ribose sugar. They have concluded that this concept is also applicable in ribo-furanose reactivity towards glycosylation. Additionally, they have showcased that 3,4-di-*tert*-butyl-disiloxane protected donor shows disarming effect (scheme 7, compound **34**).[11]

❖ **Neighboring Group Participation:**

As we know, α-glycosides are more stable than β-glycosides due to the anomeric effect. Hence, the synthesis of β-isomer in glycosylation reaction is relatively difficult and more challenging.[12]



Scheme 8: *General Representation of Neighbouring Group Participation*

Hence, several approaches have been discovered to overcome this challenge and one of the most well-known way is to introduce an ester protecting group (-OAc or –OBz etc) in the C2 position. If the C2 position is axially oriented then it blocks the β-phase and the attack of the acceptor occurs from the bottom phase, resulting in the formation of α-glycoside. Alternatively, if the C2 participating group is at the equatorial position then it gives β-glycosides as the major product. This phenomenon has been termed as **Neighboring Group Participation** (scheme 8).

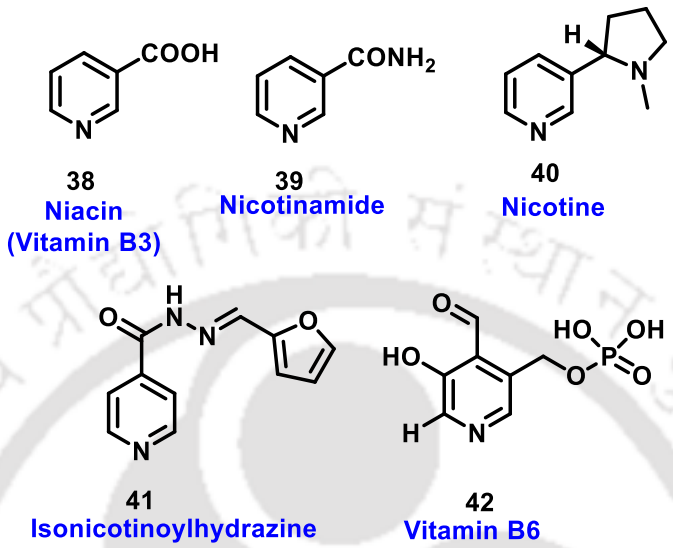
❖ **Other Factors:**

The major factors which affect the stereoselective outcome of any glycosylation reaction e.g. leaving group present at the anomeric center, anomeric effect, protecting group effect, neighbouring group participation have been discussed but there are several other factors to control the stereoselectivity. The reaction condition employed plays a crucial role e.g. temperature, solvent (polar/ nonpolar), dilution, reaction time and most importantly catalyst system which decides the reaction pathway (S_N1 reaction via oxocarbenium ion provides a mixture of α and β isomer whereas via S_N2 displacement one can get stereoselective product formation).

1.2 Literature Survey on Bulky Pyridine Derivatives:

Pyridines are benzenes with one nitrogen atom replacing one ring carbon atom. The presence of one nitrogen atom in the ring imparts electron-deficient nature to the N-heterocycles

due to the inherent electron-withdrawing inductive (-I) and mesomeric (-M) effects of the nitrogen atom. Pyridine ring exists in many important organic compounds e.g agrochemicals, pharmaceuticals and vitamins etc. Several organic reactions are known to synthesize pyridine derivatives for example Chichibabin synthesis,[13] Bönnemann cyclization[14] and Kröhnke pyridine synthesis[15] etc.



Scheme 9: *Drugs Containing Pyridine Ring*

The important pyridine derivatives include niacin, nicotinamide (to treat pellagra), isonicotinoylhydrazine (medication for tuberculosis), nicotine (helps to treat addiction or dependence on smoking cigarettes), strychnine, and vitamin B6 (scheme 9).

Some of the well-studied hindered pyridine derivatives are TTBP (2,4,6-tri-*tert*-butylpyrimidine), TTBPy (2,4,6-tri-*tert*-butylpyridine), DTBP (2,6-di-*tert*-butylpyridine),

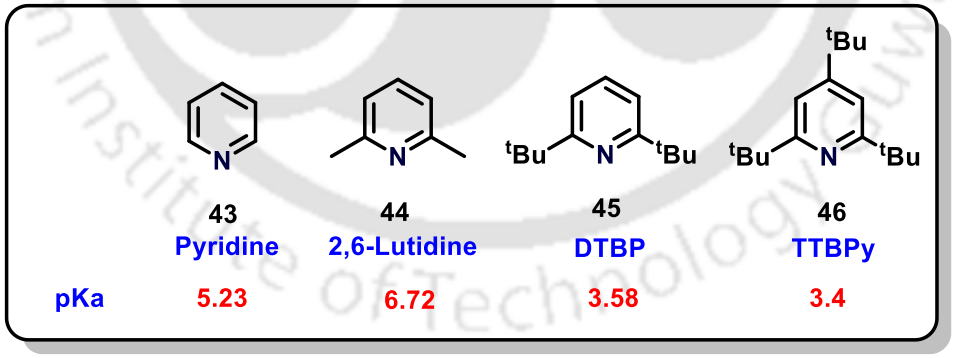


Figure 1*: pKa Trend of Pyridine Derivatives*

DTBMP (2,6-di-*tert*-butyl-4-methylpyridine) etc. All these molecules are known for their unique reactivity. The hindered non-nucleophilic base 2,4,6-tri-*tert*-butylpyridine (TTBPy) is usually utilized as a proton scavenger.

However, there are detailed studies on the ability of these hindered pyridine and pyrimidine compounds as bases. Steric factors are known to control the reactivity in organic transformations.[16]

The extraordinary ability of tri-*tert*-butylpyridine to differentiate the Bronsted and Lewis acids is one of the classic examples on the influence of sterics in altering the reactivity. 2,4,6-Tri-*tert*-butylpyridine (TTBPy),[17] considering the inductive effects, is anticipated to be more basic than pyridine and lutidine. However, the observed aqueous p*K*a value of TTBPy is lower (p*K*a of TTBPy = 3.4) than expected. This effect can only be explained by considering the poor solvation of the protonated pyridinium cation. The bulky *tert*-butyl groups at ortho positions of the pyridines, hinder the solvation process of the cationic site that results in an electronically unstable species,[18,19] and hence the lower p*K*a values. This effect can be felt more in DMSO (pK_{DMSO} of DTBP is 0.81) suggesting an extremely weak hydrogen bonding of DTBPH with a large DMSO molecule (relative to H_2O). It is evident that the reactivity of $TTBPyH^+$ in various organic reactions depends extensively on the hydrogen bonding character of the reaction solvent. Typically, the cavity size of the $TTBPyH^+$ does not allow any hydrogen bonding interaction (Figure 2) of the anions with the cationic N-H^+ site.[20]

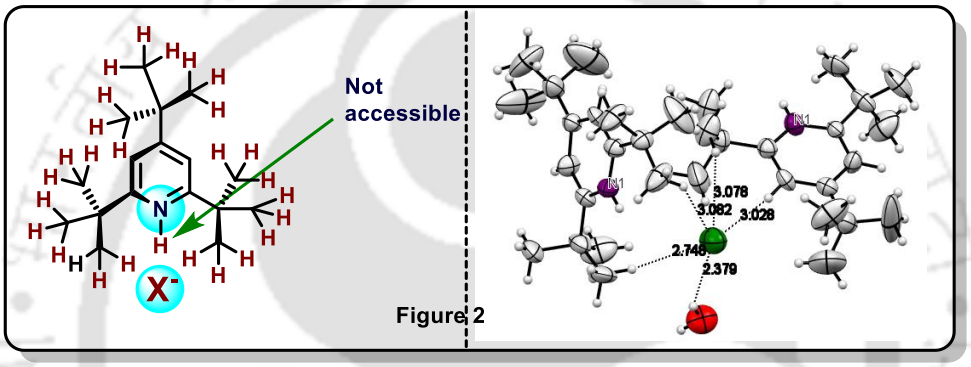
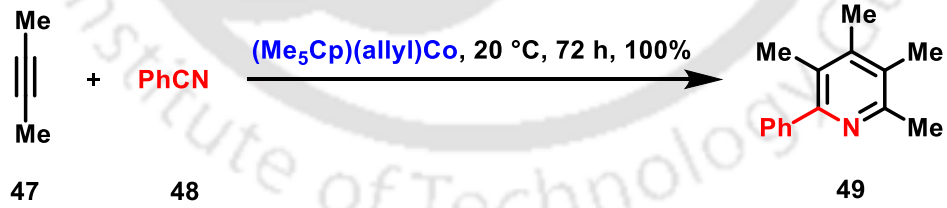


Figure 2: *XRD Structure of TTBPy·HCl, 3H_2O*

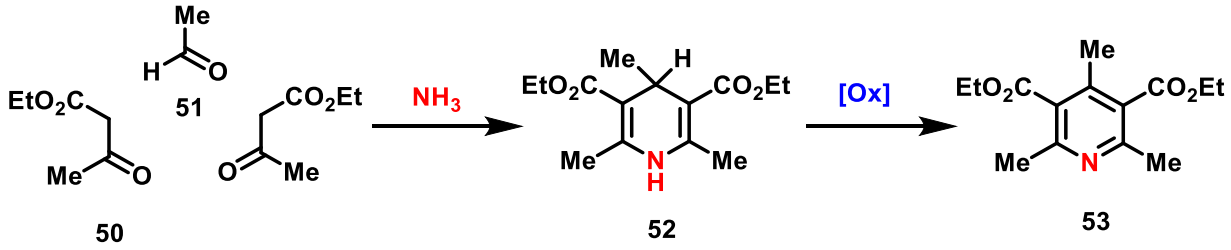
1.3 Synthesis of Substituted Pyridines:

Selective cyclo-trimerization of alkynes with nitriles leads to the formation of penta-substituted pyridines (scheme 10).



Scheme 10: *Cyclo-trimerization of Alkynes*

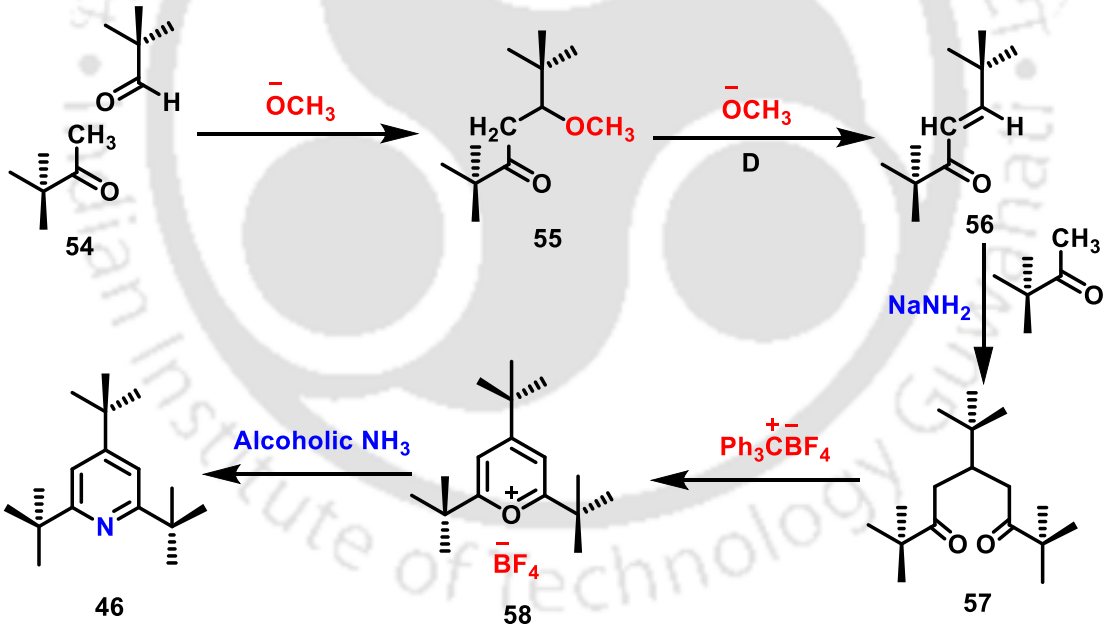
Anderson and coworkers first introduced pyridines in 1840s.[21] They have obtained 2-methylpyridine or β-picoline from the distillation of bone oil and subsequently using the same method they have synthesized pyridine and some dimethylpyridines (lutidine derivatives).[22] The well-known Hantzsch synthesis was discovered in 1882 (scheme 11),[23] and later a vapour-phase synthesis was also established by Chichibabin in 1906.[24]



Scheme 11: *Hantzsch Pyridine Synthesis*

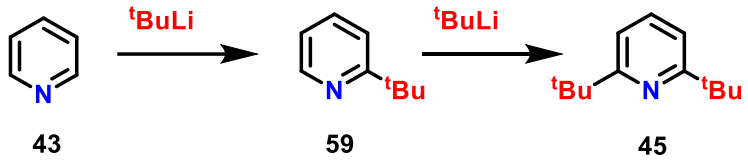
2,4,6-tri-*tert*-butylpyridine (TTBPy), a highly hindered pyridine derivative was first introduced and synthesized by Mach and Dimroth in 1968 starting from pinacolone via the formation of oxonium salts (scheme 12).[17]

They have synthesized 2,4,6-tri-*tert*-butylpyrylium tetrafluoroborate as shown in the following scheme. The methoxy ketone was converted into the unsaturated ketone when boiled in a basic medium, whereas acids convert it into a cyclic carboxonium salt. Finally, 2,4,6-tri-*tert*-butylpyridine is formed quantitatively by the action of alcoholic ammonia on the pyrylium salt.



Scheme 12: *Synthesis of TTBP*

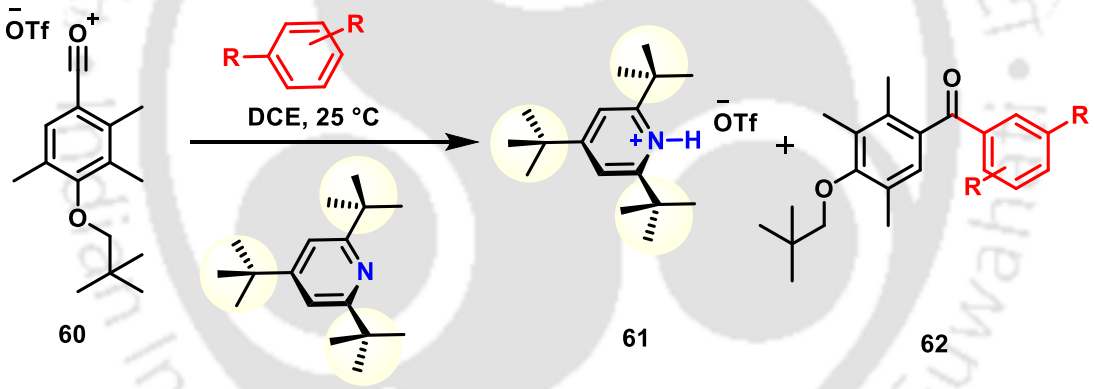
Brown and Kanner successfully synthesized 2,6-di-*tert*-butylpyridine by reacting *tert*-butyllithium with 2-*tert*-butylpyridine at -78° (Scheme 13). They have demonstrated the feasibility of the synthesis through a two-stage subsequent alkylation of pyridine.[25]



Scheme 13: *Synthesis of DTBP*

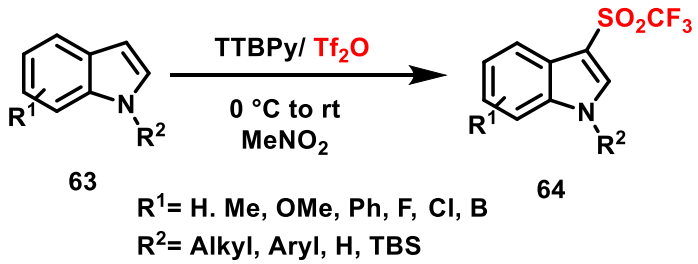
1.4 Utility of Sterically Strained Pyridine Derivatives in Various Organic Reactions:

TTBPy and one of its much well-studied analogues, 2,6-di-*tert*-butylpyridine (DTBP) are only capable of coordinating with a proton and not with any other Lewis acids like CH_3^+ or BF_3 etc.[25,26] These molecules have been exploited in various reactions for their unique property as non-nucleophilic bases. TTBPy can act as an acid scavenger in organic reactions where excess proton is generated during the reaction or, it can also be used as a buffering agent in studies of reactions of metal ions in aqueous solutions.[26] The inability of the hindered base TTBPy to behave as a nucleophile has been exploited in various organic transformations for example in characterizing the concentration of acylium ions in aromatic acylation reactions (Scheme 14).[27]



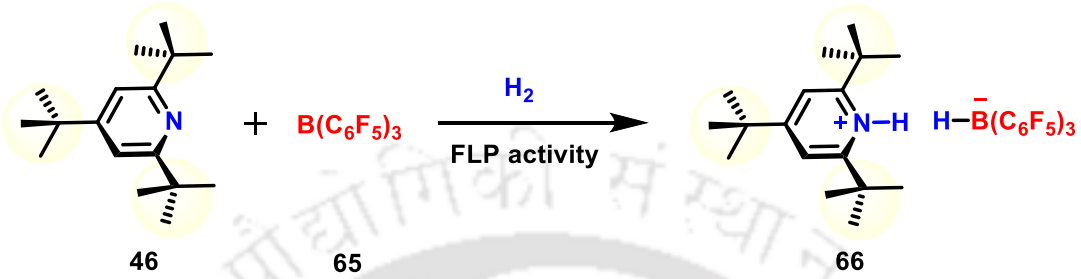
Scheme 14: *Acylation of an Aromatic Compound in the Presence of TTBPy*

Shibata and coworkers used TTBPy/Tf_2O combination to synthesize indole triflones (Scheme 15).[28] *N*-Alkyl, aryl and *N*-H indole triflones were synthesized by this method along with biindolyl triflones efficiently without any use of organometallic chemistry.



Scheme 15: *Synthesis of Indole triflones in the Presence of TTBPy/Tf_2O System*

According to a recent observation by Berke and coworkers, the bulky TTBPy can show frustrated Lewis pair (FLP) reactivity in the presence of $B(C_6F_5)_3$ or $[(acridine)BCl_2][AlCl_4]$ and can heterolytically cleave H_2 (Scheme 16).[29,30] Intriguingly, Ingleson and coworkers observed that the position of the hydride from H_2 has been found to be the C9 position of acridine unlike on the usually expected boron.

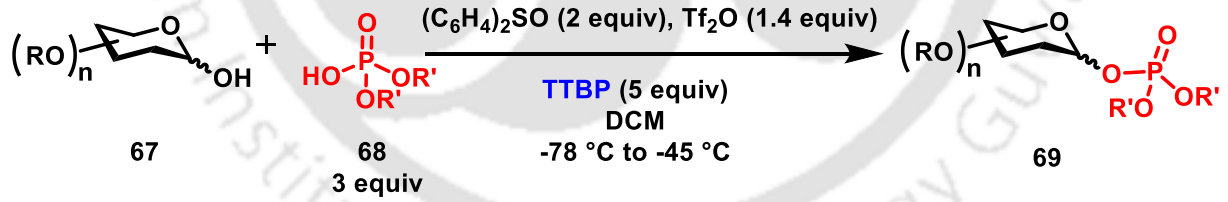


Scheme 16: *Heterolytic Cleavage of Hydrogen by FLP*

1.5 Utility of Sterically Strained Pyridine Derivatives in Glycosylation Reactions:

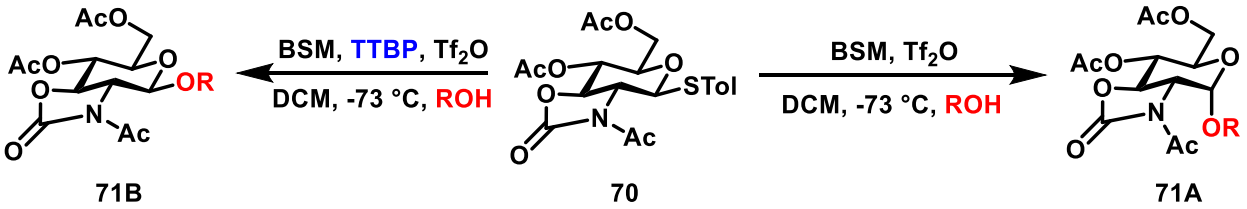
Sterically bulky pyridine derivative 2,4,6-tri-*tert*-butylpyridine (TTBPy) along with other hindered bases, 2,4,6-tri-*tert*-butylpyrimidine (TTBP), 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) and 2,6-di-*tert*-butylpyridine (DTBP) were used in glycosylation reactions as proton trapping agents to capture the strong acid released during the reaction as a byproduct.[31]

Gin and coworkers have developed a method to synthesize glycosyl-1-phosphates from anomeric hemi-acetals using diphenyl sulfoxide as the catalyst and in this method, they have used an excess of TTBPy (5 equivalents) to neutralize the unwanted excess acid (Scheme 17).[32]



Scheme 17: *Activation of Hemiacetal in the Presence of TTBPy/sulfoxide Catalytic System*

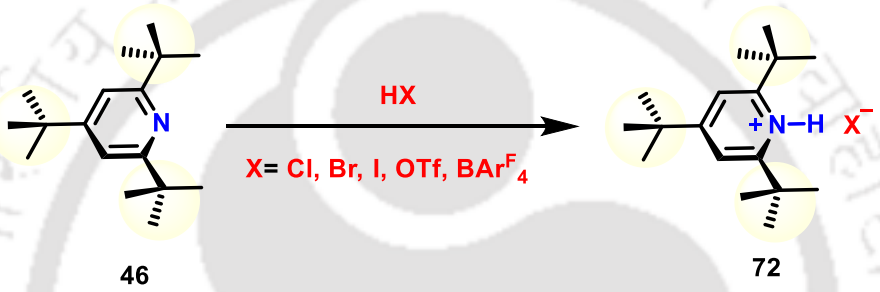
However, Crich later introduced 2,4,6- tri-*tert*-butylpyrimidine (TTBP) as a potential alternative to TTBPy because TTBP is non-hygroscopic, stable and easy to handle, white crystalline powder, unlike the other hindered pyridine derivatives.[33] Ye and coworkers introduced stereoselective glycosylation of 2,3-oxazolidinone thioglycoside as a donor (Scheme 18).[34] Though the mechanism is not precise, the authors observed an intriguing stereo-switch in glycosylation reaction outcome of glucosamine-derived glycosides in the presence and absence of 2,4,6-tri-*tert*-butylpyrimidine.



Scheme 18: *Activation of Thioglycosides in the presence of BSM/ TTBP/ Tf_2O Catalytic System*

1.6 Sterically Strained Pyridinium Salts and Their Utility as Organocatalyst in Various Glycosylation Reactions:

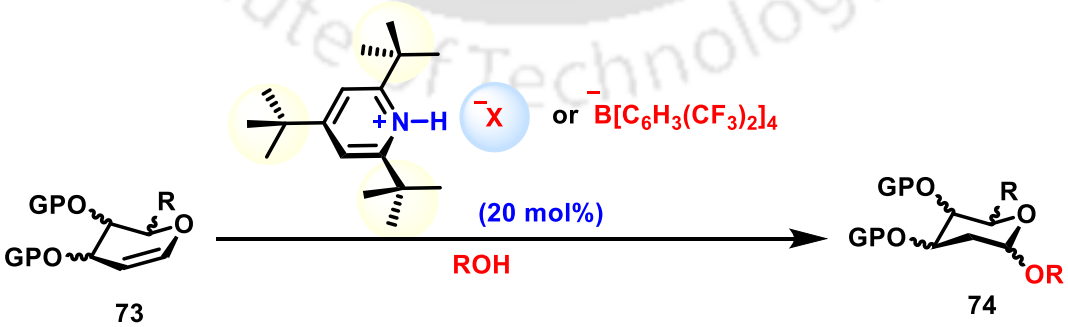
TTBPy salts were synthesized with different counter anions like hydrochloride, hydrobromide, iodide, triflate and $BAr^F{}_4$ as shown in the general scheme (scheme 19).



Scheme 19: *Catalyst Synthesis*

So far in literature the utility of TTBPy and similar sterically bulky pyridine derivatives in glycosylation reactions were showcased only as proton scavengers to trap the excess proton released during the course of reaction.

In 2019, for the first time, the conjugate acid of TTBPy was used to carry out glycosylation reaction on glycal donors to synthesize deoxy sugars by our group.[20] Kancharla and coworkers have reported that the conjugate acid of bulky base 2,4,6-tri-*tert*-butylpyridine can activate glycals towards stereoselective *O*-glycosylation and from the optimization studies varying the counter-anions, it was observed that with chloride anion the catalyst gives best results, in terms of yield and selectivity.



Scheme 20: *O-Glycosylation using TTBPy·HX Catalysis*

It has been reported by our group that TTBPy salts are able to catalyze the glycosylation of glycal donors efficiently with 20 mol % of catalyst loading in a highly stereoselective fashion leading to the synthesis of various α-selective deoxy glycosides (Scheme 20).[20] Mechanistic studies (control experiments including spectroscopic studies) performed in this work reveal that TTBPyH catalyzes the reaction *via* a unique hydrogen bonding assisted activation (HB) and not *via* the traditional Brønsted acid mechanism (BA).[35] Besides, the catalytic activity of TTBPyH can be also controlled by the nature of the counter-ion.

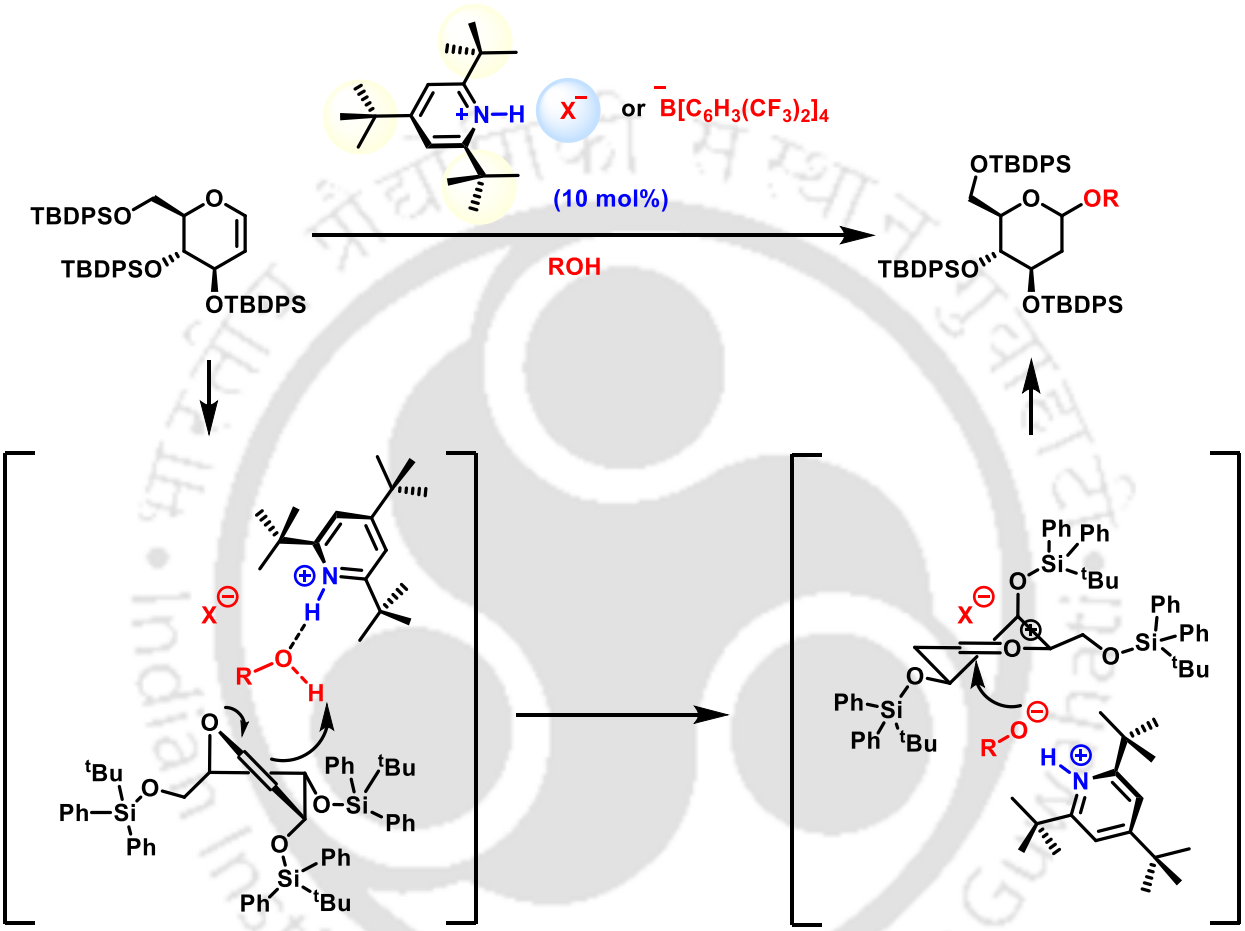


***Figure 4**: Mechanistic Pathway for O-Glycosylation using TTBPy·HX Catalysis*

In this study, a hydrogen-bond assisted mechanism (HB mechanism) was proposed for the observed catalysis as depicted in Figure 4 (α-stereoselectivity was explained using tri-TBDPS protected glucal). The increased acidity of the alcoholic hydrogen due to its hydrogen bonding interaction with the catalyst TTBPyH helps in protonating the glycals. This results in the formation of the oxocarbenium ion that is then trapped by the alkoxide ion bound to TTBPyH giving rise to the observed product and also the regeneration of the catalyst.

1.7 Conclusion and Summary:

As a summary of chapter I, the importance of carbohydrates have been discussed as natural products, biologically important molecules and also as drugs in medicinal chemistry.

From the general discussion on glycosylation chemistry, we have understood that several factors can affect the stereochemical outcome of any glycosylation reaction.

In literature, 2,4,6-tri-*tert*-butylpyridine (TTBPy) and other sterically strained pyridine derivatives DTBP, DTBMP and TTBP etc are known for their use as proton scavengers to trap H^+. The utility of these hindered bases arising from their non-nucleophilic basic character in various organic transformations has been thoroughly discussed. On the other hand, the studied p*K*a values of these bulky pyridines suggest that these are not as strong bases as are generally conceived that stands in contrary to their general usage as proton trapping agents. However, in 2019, Kancharla and coworkers have utilized such bulky TTBPy salts as organocatalysts for the first time and have showcased the potential of these salts in catalyzing the stereoselective glycosylation reaction of glycals.

The upcoming chapters in this thesis also rely on the exploration of the bulky 2,4,6-tri-*tert*-butylpyridinium salts as organocatalyts for C-O, C-S and C-N bond forming reactions in carbohydrate chemistry. The poor electrostatic interactions within the ion-pair specifically in relatively non-polar organic solvents like dichloromethane resulting in frustrated Bronsted pair interactions have been exploited in the development of new glycosylation protocols.

1.8 References:

1. Gorelik, E.; Galili, U.; Raz, A. *Cancer Metastasis Rev.* **2001**, *20*, 245–77.

2. Lemieux, R. U.; Kullnig, R. K.; Bernstein, H. J.; Schneider, W. G. *J. Am. Chem. Soc.* **1958**, *80*, 6098–105.

3. Lemieux, R. U. *Pure Appl. Chem.* **1971**, *25*, 527–48.

4. Vila, A.; Mosquera, R. A. *J. Comput. Chem.* **2007**, *28*, 1516–30.

5. Box, V. G. S. *Heterocycles.* **1990**, *31*, 1157–81.

6. Mootoo, D. R.; Konradsson, P.; Udodong, U.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1988**, *110*, 5583–84.

7. Fraser-Reid, B.; Wu, Z.; Udodong, U. E.; Ottosson, H. *J. Org. Chem.* **1990**, *55*, 6068–70.

8. Pedersen, C. M.; Nordstrøm, L. U.; Bols, M. *J. Am. Chem. Soc.* **2007**, *129*, 9222–35.

9. Premathilake, H. D.; Demchenko, A. V. *Top Curr Chem.* **2011**, *301*, 189–221.

10. Zhu, T.; Boons G. J. *Org. Lett.* **2001**, *3*, 4201–03.

11. Liang, X. Y.; Bin, H. C.; Yang J. S. *Org. Lett.* **2013**, *15*, 2834-37.

12. Hou, D.; Lowary, T. L. *Carbohydr. Res.* **2009,** *344*, 1911–40.

13. Tschitschibabin, A. E. *Adv. Synth. Catal.* **1924**, *107*, 122-28.

14. Helmut Bönnemann, H. *Angew. Chem. Int. Ed.* **1978**, *17*, 505-15.

15. Zecher, W.; Kröhnke, F. *Eur. J. Inorg. Chem.* **1961**, *94*, 690-97.

16. Eglinton, G. *Nature* **1959,** *184*, 1522-1522.

17. Dimroth, K.; Mach, W. *Angew. Chem., Int. Ed.* **1968,** *7*, 460-61.

18. Vanderplas, H. C.; Koudijs, A. *Recl Trav Chim Pay B* **1978**, *97*, 159-61.

19. Houriet, R.; Rolli, E. *New J Chem* **1987**, *11*, 221-24.

20. Ghosh, T.; Mukherji, A.; Kancharla, P. K. *Org. Lett.* **2019**, *21*, 3490-95.

21. Anderson, T. *Liebigs Ann.* **1846**, *60*, 86-103.

22. Anderson, T. *Liebigs Ann.* **1851**, *80*, 44-55.

23. Hantzsch, A. *Liebigs Ann.* **1882**, *215*, 72.

24. Tschitschibabin, A. E. *Russ. J. Phys. Chem.* **1905**, *37*, 1229-53.

25. Brown, H. C.; Kanner, B. *J. Am. Chem. Soc.* **1966,** *88*, 986–92.

26. Deutsch, E.; Cheung, N. K. V. *J. Org. Chem.* **1973**, *38*, 1123-26.

27. Effenberger, F.; Eberhard, J. K.; Maier, A. H. *J. Am. Chem. Soc.* **1996,** *118*, 12572–79.

28. Xu, X. H.; Liu, G. K.; Azuma, A.; Tokunaga, E.; Shibata, N. *Org. Lett.* **2011,** *13*, 4854–57.

29. Jiang, C.; Blacque, O.; Fox T.; Berke, H. *Organometallics* **2011**, *30*, 2117–24.

30. Clark, E. R.; Ingleson, M. J. *Organometallics* **2013,** *32*, 6712–17.

31. Boebel, T. A.; Gin, D. Y. *Angew. Chem., Int. Ed.* **2003,** *42*, 5874–77.

32. Garcia, B. A.; Gin, D. Y. *Org. Lett.* **2000,** *2*, 2135–38.

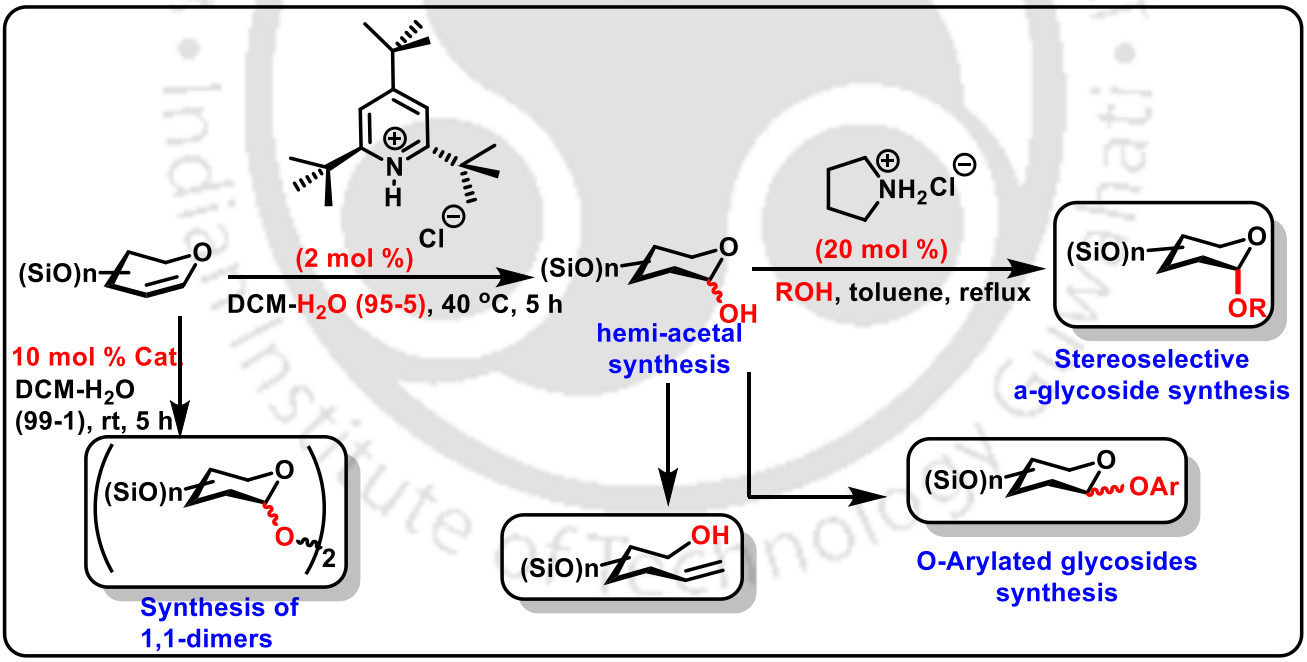
33. Crich, D.; Dudkin, V. *J. Am. Chem. Soc.* **2001,** *123*, 6819–25.

34. Geng, Y.; Zhang, L. H.; Ye, X. S. *Chem. Commun.* **2008**, 597–99.

35. Farcasiu, D.; Lezcano, M.; Vinslava, A. *New J. Chem.* **2000**, *24*, 199-201.

Chapter II

C–H···Anion Interactions Assisted Addition of Water to Glycals by Sterically Hindered 2,4,6-Tri-tert-butylpyridinium Hydrochloride

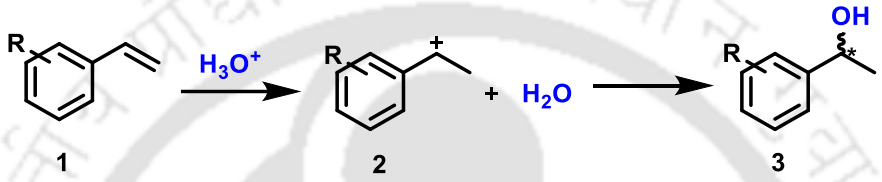


Mukherji, A.; Kancharla, P. K. *Org. Lett.* **2020**, *22*, 2191–2195.

C−H···Anion Interactions Assisted Addition of Water to Glycals by Sterically Hindered 2,4,6-Tri-*tert*-butylpyridinium Hydrochloride

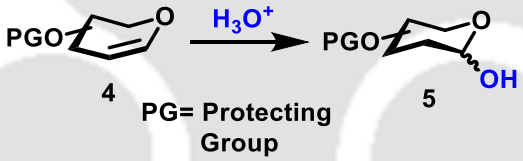
2.1 Introduction:

There are sufficient studies on the hydration of terminal olefin styrene and substituted styrene and from the evidences it was demonstrated that the reaction is carried out in the presence of an acid catalyst and the carbonium ion intermediate generated in situ forms the Markovnikov addition product irreversibly (scheme 1).[1] The hydration mechanism of styrene reveals that the proton transfer from H_3O^+ to styrene, which is also the rate determining step, results in the formation of the carbonium ion which is followed by the formation of corresponding (substituted) phenylethan-1-ol.[2]



Scheme 1: *Hydration on Styrene*

Hydration on the olefinic carbon of glycal, i.e. sugars having a double bond between C1 and C2, has also been well studied in the literature (scheme 2).



Scheme 2: *Hydration on Glycal*

Hydration on any glycal molecule provides corresponding 2-deoxy sugars, i.e. C-2 hydroxyl group is replaced by H atom.

2.1.1 Deoxy Sugars:

These 2-deoxy glycosides (Figure 1) have huge biological importance. 2-deoxy-D-ribose is the main constituent of deoxyribonucleic acid (DNA). Furthermore, 2-deoxy, 2,6-dideoxy, and 2,3,6-

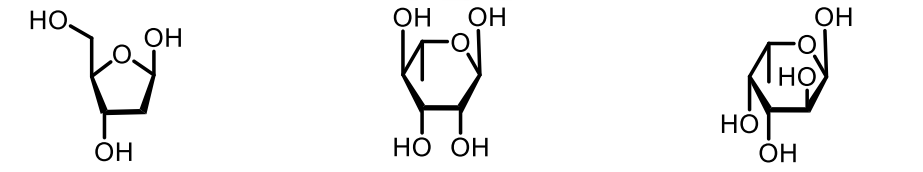


Figure 1: *Deoxy Sugars*

trideoxy sugars are present in naturally available and biologically important molecules.[3] Fucose or 6-deoxy-L-galactose is the main component of fucoidan of brown algae and is found in N-linked glycans. Moreover, rhamnose or 6-deoxy-L-mannose is a 2,6-dideoxy sugar and is commonly found in plant glycosides.

2-Deoxy Sugars: One of the most important 2-deoxy sugar is 2-deoxy-D-erythro-pentose (2-deoxyribose) which is the main constituent of deoxyribonucleic acids (DNA). Moreover, 2-deoxy- D-arabino-hexose (2-deoxyglucose) is known as an energy restriction mimetic agent.[4] Besides, synthesis of 2-deoxy glycosides are also challenging as they are very tough to handle, sensitive towards hydrolysis and prone to 1,2-elimination reaction.

2.1.2 2,6-Dideoxy Sugars:

These are one of the most highly abundant carbohydrates in nature and they have antibiotic and antitumor activity. Among them, 2,6-dideoxy-3-methoxy-hexopyranoses and 2,6-dideoxy-3-amino-hexopyranoses are found as components of various natural products in medicinal chemistry. D-Boivinose, which can be isolated from the seeds of Corchorus olitorius L, was found as a component of a cardenolide glycoside.[5] L-boivinose is the least abundant of the three and is found in corn (Zea mays).[6] D-digitoxose is the main constituents of plant cardiac and other steroidal glycosides[7] whereas L-digitoxose has been found in actinomycetes, particularly as a unique family of antibiotics, the jadomycins. L-olivose is the main constituent of the trisaccharide chain of the anthracycline Aclacinomycin A. Interestingly, L-olivose is not available in nature but its 3-methoxy derivative, i.e. L-oleandrose has been isolated in oleandomycin which is a macrolide antibiotic produced by Streptomyces antibioticus (Figure 2).[7]

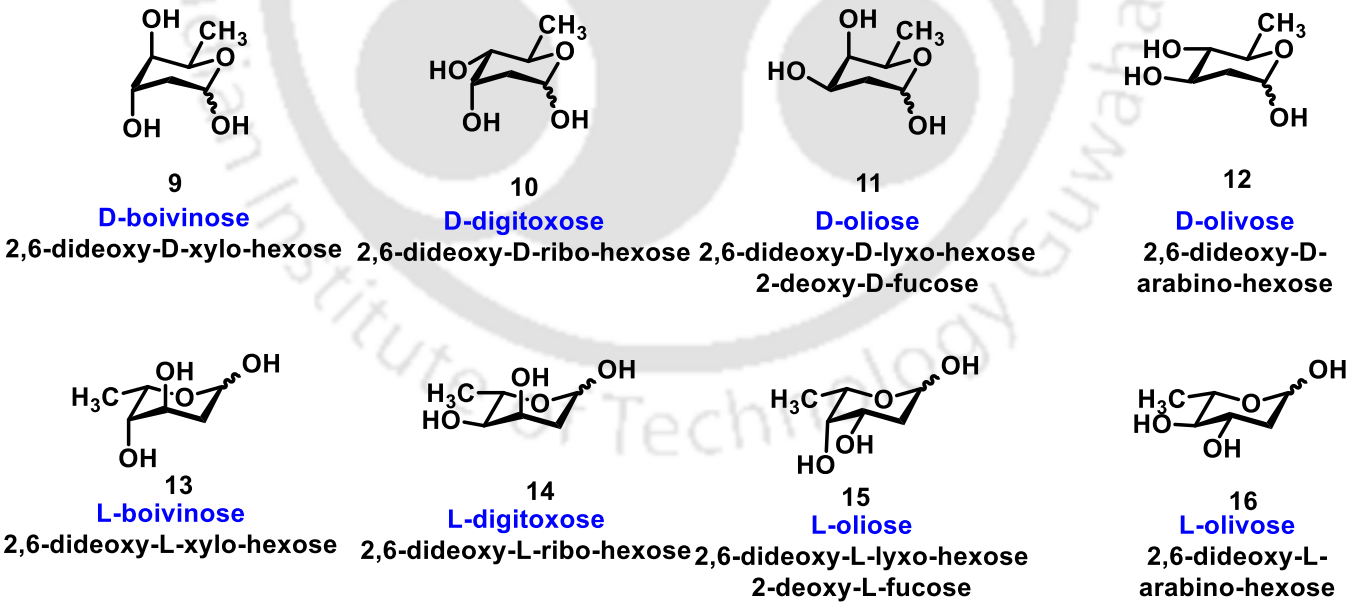


Figure 2: *Naturally Occurring 2,6-Dideoxy Sugars*

2.1.3 Biological Importance of Deoxy Sugars:

Deoxysugars are found in various natural products and also as structural components in several glycoproteins, bacterial endotoxins and secondary metabolites etc. Deoxy sugars are found to be involved with intercellular communications, immunogenic responses to pathogenic bacteria and also in many biologically important antibiotics.[8] The change in the number or structure of the deoxysugar unit present in these natural products can affect their activity. Also, by modifying the sugar unit one can enhance the activity of antibiotics. Thus, to develop useful drugs or to design new and effective therapeutic strategies, it is crucial to understand both the genetic and mechanistic aspects of deoxysugar biosynthesis. Thus, developing new biologically important medicinal products containing deoxy sugar units as well as studying the mechanistic information are always areas of interest to organic chemists.

Naturally, 2-deoxy sugars are found in biologically active molecules. Most of them have antitumor and anticancer activities.[8] Deoxysugar plasmids were exploited to synthesize the clinically relevant aureolic acid anticancer drug derivatives i.e. mithramycin analogues (Figure 3).[9-13]

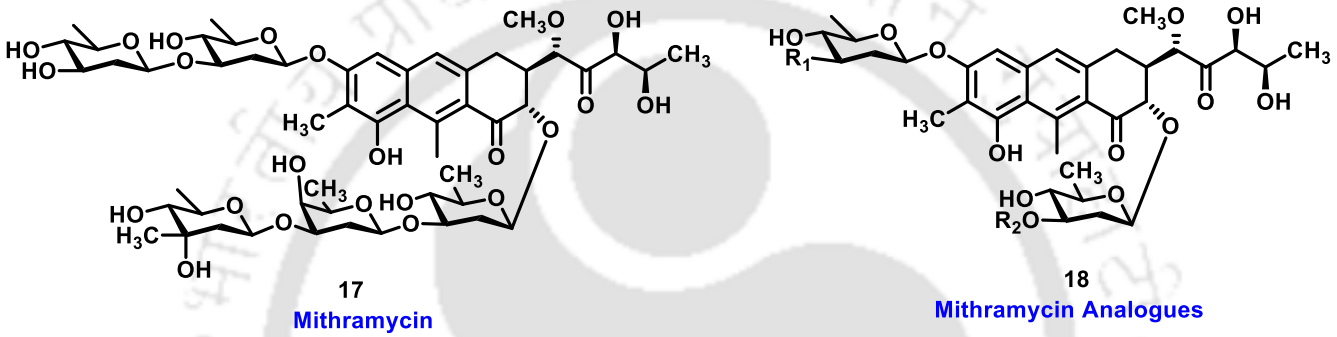


Figure 3: *Anticancer Drug Mithramycin*

In addition, deoxysugars also seem to play a significant role in the DNA-binding properties of antitumor anthracycline antibiotics (Figure 4). Hutchison and coworkers exploited the same and attempted to synthesize various deoxyaminosugars to attach them anthracycline-type aglycones in pursuit of developing new antitumor drugs.[14] Antitumor antibiotics such as Anthracycline are a class of natural products containing tetracyclic aglycone units linked to the 2-deoxy sugar. Daunomycin, Adriamycin and Robumycin form noncovalent complexes with DNA through intercalation and inhibit DNA replication and RNA transcription.[11,12]

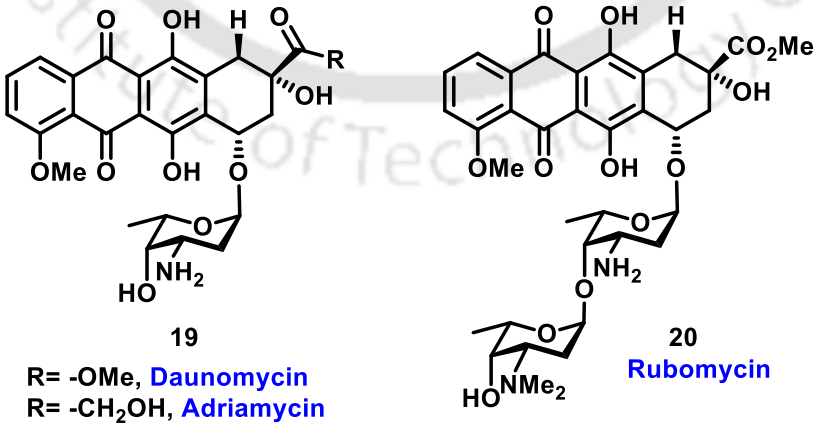


Figure 4: *Antitumor Antibiotics*

Doxorubicin is a well-known drug for antitumor activity. Anthracycline derivatives (Figure 5), e.g. Marcellomycin and Aclacinomycin A containing long carbohydrate chains are known for their lower toxicity.[14]

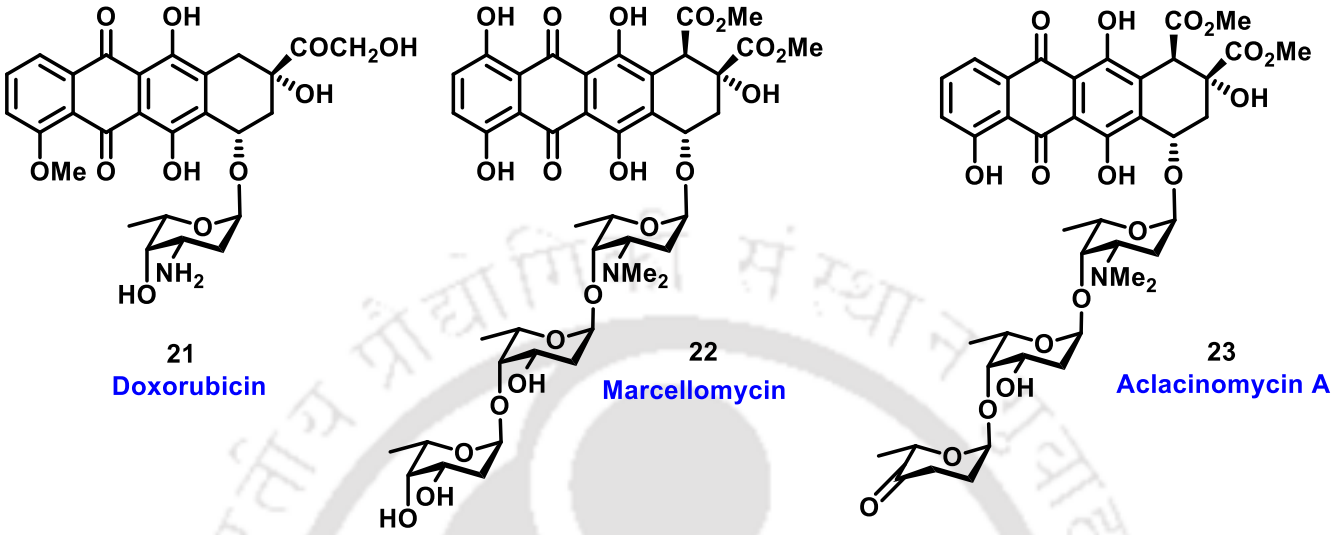


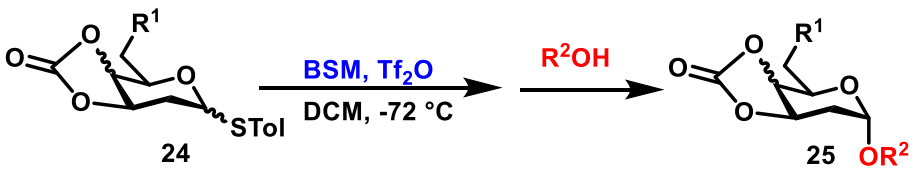
Figure 5: *Naturally Occurred Anthracycline Antitumor Drugs*

2.2 Literature Reports

2.2.1 Literature Preview on Organocatalytic Stereoselective Synthesis of 2-Deoxy Glycosides

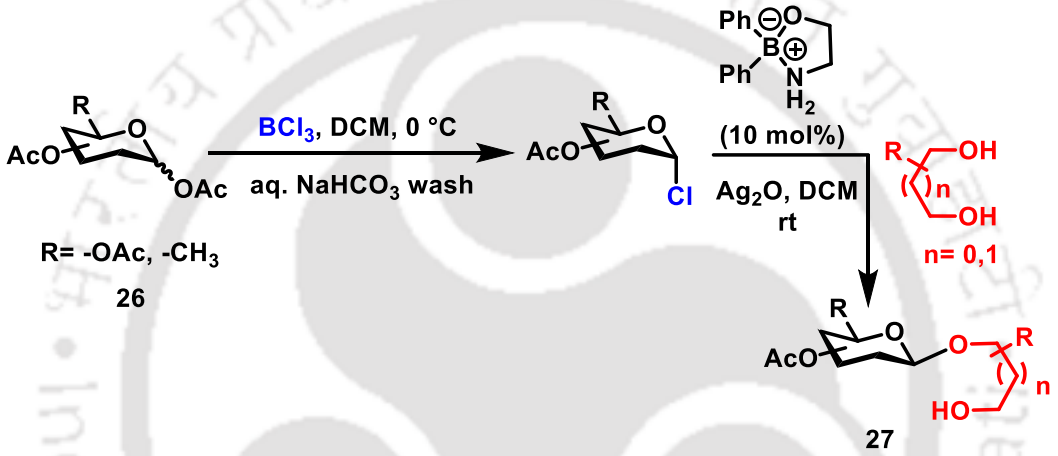
Catalysis in which the rate of the chemical reaction is increased by an organic molecule is termed as **organocatalysis**. These molecules consist of carbon, hydrogen, sulfur and other non-metal elements that are found in organic compounds. Enantioselective organocatalysis is a most established synthetic method to catalyze challenging transformations in synthetic organic chemistry. It is critical in the development of methods to synthesize chiral molecules with exclusive regio-, chemo-, and stereoselectivity. Organocatalysis is known for its easy to handle and simple operational purpose. These catalysts are readily commercially available, easy to prepare, and have low toxicity. These important features make organocatalysis an attractive method to synthesize complex organic molecules, including oligosaccharides, in a stereoselective fashion.

In literature, there are various reports on the synthesis of 2-deoxy α-glycosides. Xin-Shan Ye and coworkers explored an efficient pre-activation method to activate anomeric thioglycosides towards the formation of highly α-selective glycosylation of deoxysugars (Scheme 3).[15] They have used 2-deoxy- and 2,6-dideoxythioglycosides as glycosyl donors. They have shown a variety of glycosyl acceptors and donors can be used in this method. The presence of a 3,4-*O*-carbonate group in glycosyl donors enhances the α-selectivity in the product outcome. The above mentioned donor is activated in the presence of 4 Å MS in DCM solvent with a combination of triflic anhydride and benzenesulfinyl morpholine (BSM) at -72 °C. This pre-activated donor when treated with any glycosyl acceptor provides the corresponding α-glycoside.



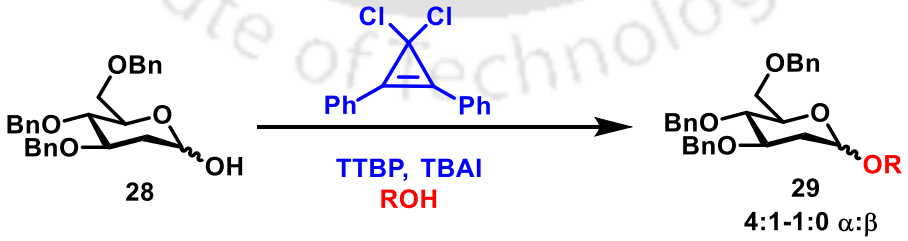
Scheme 3: *α-Selective Glycosylation of 3,4-O-Carbonate-Protected Deoxythioglycosides*

Taylor and coworkers have showcased regio- and stereo-selective synthesis of β-deoxy glycosides. They have chosen gluco-, galacto- and rhamno- based per-acetate donors and converted them into anomeric chloride. The thus obtained anomeric chloride was then reacted with *cis*-1,2- and 1,3-diol acceptors using an organo-boron catalyst in presence of Ag_2O (scheme 4).[16] In this method, they were able to synthesize partially protected disaccharides with regio- and β-stereoselectivity.



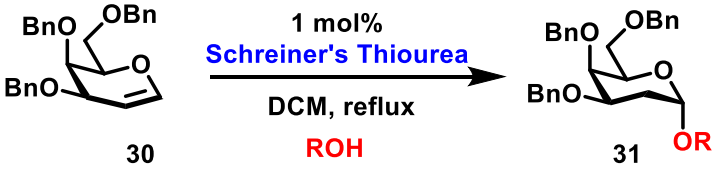
Scheme 4: *Organoboron-Catalyzed Synthesis of β-2-Deoxyglycosides*

Bennett and coworkers have proposed dehydrative glycosylation reactions using 2-deoxy and 2,6-dideoxy-sugar hemiacetals as donors and by using a catalyst combination of 3,3-dichloro-1,2-diphenylcyclopropene and tetrabutylammonium iodide (TBAI) (Scheme 5).[17] The reactions are performed under mild conditions at room temperature and resulted into α-selective glycosylated products. The authors have shown that the method is compatible with a variety of glycosyl acceptors, including those containing acid and base sensitive protecting groups.



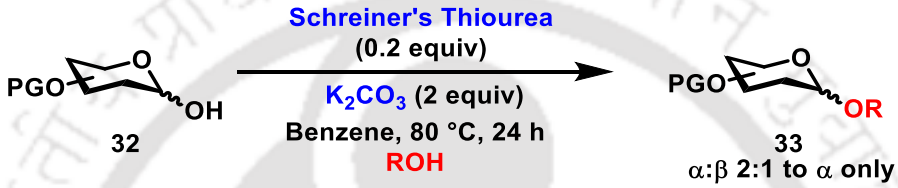
Scheme 5: *Cyclopropenium Cation Promoted Dehydrative Glycosylations*

Galan, McGarrigle, and Balmond reported the reaction of glycals with Schreiner's thiourea to synthesize α-stereoselective 2-deoxygalactosides (Scheme 6).[18] They have showcased that this method is tolerant to a wide range of protecting groups, e.g., ethyl, allyl, benzyl, methoxymethyl ether (MOM) and silyl ether.



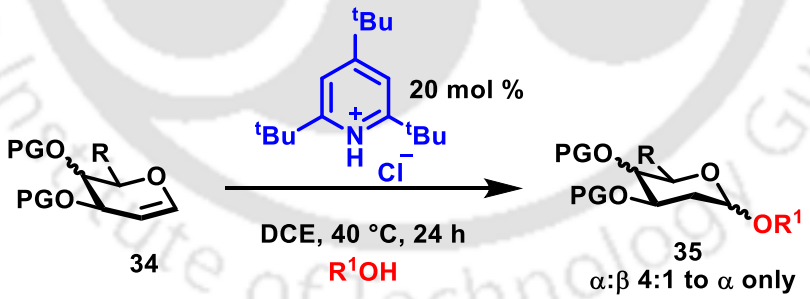
Scheme 6: *Schreiner's Thiourea Catalysed Glycosylation*

Another report by Ye and coworkers shows that protected glycosyl chloride can be activated by Koenigs−Knorr activation method to afford deoxyglycosides with high yields and more towards α-selectivity (Scheme 7).[19] They have reported that the combination of thiourea catalyst with K_2CO_3 provides the desired disaccharides in 24 h at 80 °C.



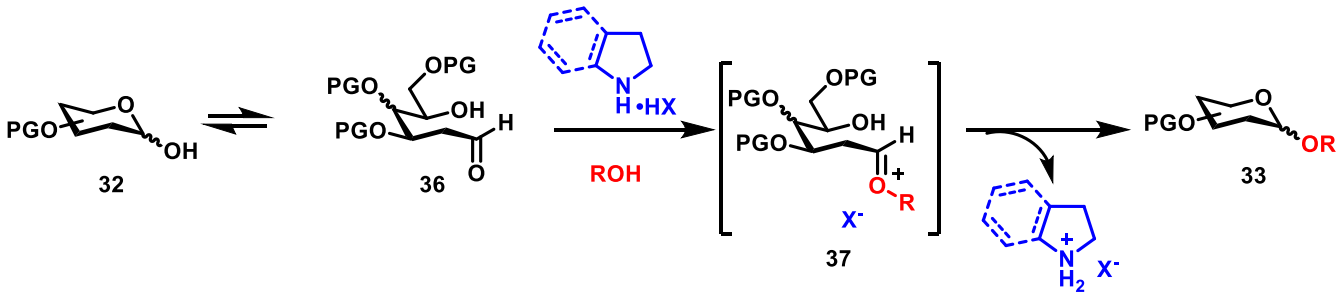
Scheme 7: *Koenigs−Knorr activation of Glycosyl Chlorides*

In 2019, an organocatalyzed glycosylation method was developed by our group where we have demonstrated that the strained and bulky protonated 2,4,6-tri-*tert*-butylpyridine salts with various counteranions can be used as efficient catalysts to carryout highly α-selective glycosylation reactions of various glycals (Scheme 8).[20] The mechanism proposed for this transformation states that a single hydrogen bond mediated protonation occurs on glycals and it is not *via* the traditional Brønsted acid pathway. The counteranion of the $TTBPyH^+$ catalyst also plays a role in the reactivity and stereochemical outcome of the reaction.



Scheme 8: *TTBPy·HCl Catalysed Glycosylation*

An organocatalytic glycosylation method has been showcased by our group exploiting the lactol functionality (Scheme 9).[21] This method proceeds *via* catalytic generation of glycosyl oxocarbenium ions from lactols under forcible conditions. Weakly Brønsted-acidic and readily available secondary amine salts were used as organocatalysts to obtain the diastereoselective glycosides containing 2-deoxypyranoses and furanoses. This operationally simple iminium catalyzed glycosylation method of deoxy sugar hemiacetals is known as a potentially alternative method to the existing literature methods which require an inert and moisture free atmosphere and/or expensive metal catalysts.

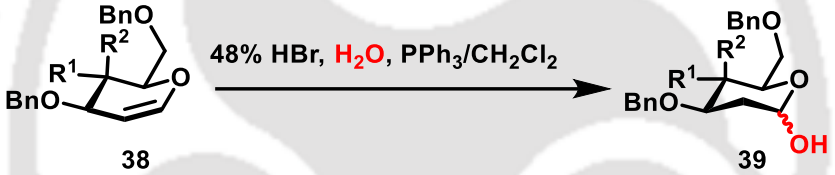


Scheme 9: *Secondary Amine Salts Catalysed Glycosylation*

2.2.2 Initial Studies on Deoxy Sugar Hemi-acetal Synthesis:

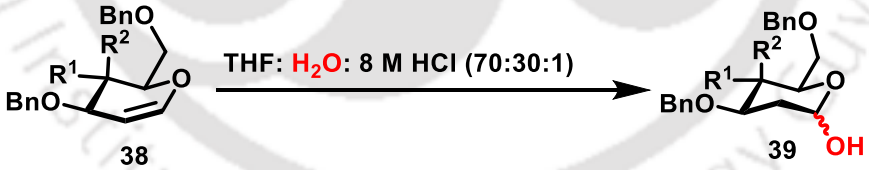
When a glycal molecule is reacted with water instead of an acceptor molecule, then it generates sugar hemiacetal (which have free hydroxyl group at the C1 position). There are several literature methods to synthesize 2-deoxy sugar hemiacetals from their corresponding glycal molecules. They are discussed below.

Tri-O-benzyl protected glycal can be activated by triphenyl phosphine in the presence of 48% HBr in CH_2Cl_2 leading to the formation of corresponding 2-deoxysugar (Scheme 10).[22]



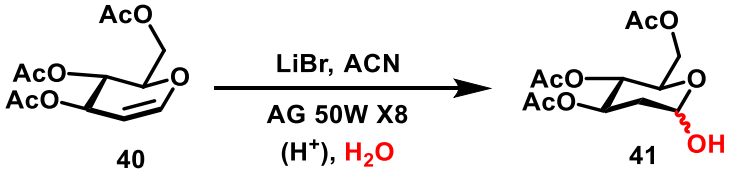
Scheme 10: *Synthesis of 2-Deoxysugar from Glycal in the Presence of Ph_3P-HBr*

Another well-known procedure for the synthesis of 2-deoxy sugar is activation of the glycal by 90:10:1 tetrahydrofuran/ H_2O /8 (M) hydrochloric acid mixtures (Scheme 11).[23]



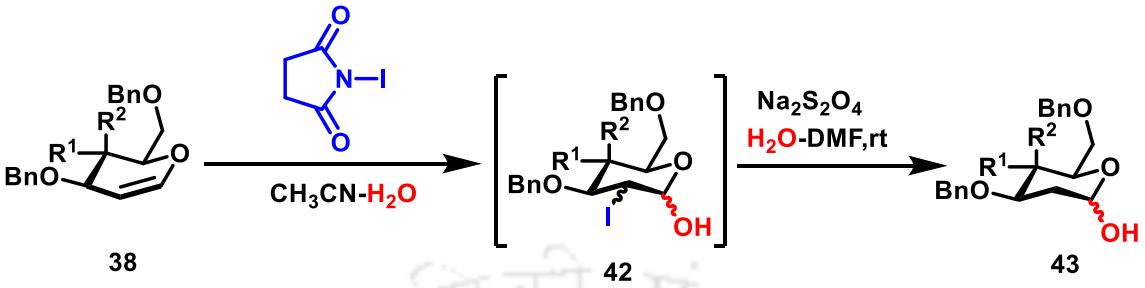
Scheme 11: *Synthesis of 2-Deoxysugar in the Presence of 8 M HCl*

To convert acetyl protected glucal into corresponding deoxy sugar, a mixture of acid resin and lithium bromide is used (Scheme 12).[24]



Scheme 12: *Synthesis of 2-Deoxysugar in the Presence of Acid-resin and LiBr*

N-iodosuccinimide in the presence of aqueous acetonitrile activates galactal to transform corresponding 2-iodo pyranoside (Scheme 13).[25a] This method is relatively mild however it requires an extra step to remove the unwanted 2-iodo substituent.



Scheme 13: *Synthesis of 2-Deoxy Hemiacetals via 2-Iodopyranoside Using NIS*

Another mild process to synthesize 2-deoxy pyranoses is a reaction of glycal with lanthanide salts (Scheme 14).[25b] It was found that glycal can be activated by $CeCl_3.7H_2O$– NaI system to form corresponding 2-deoxy glycosides in stereoselective fashion with high yields. Although, in absence of NaI formation of Ferrier product was observed.

Scheme 14: *Synthesis of 2-Deoxy Pyranose from Glycal in Presence of $CeCl_3.7H_2O$–NaI*

2.3 2-Deoxy Trehalose Sugar:

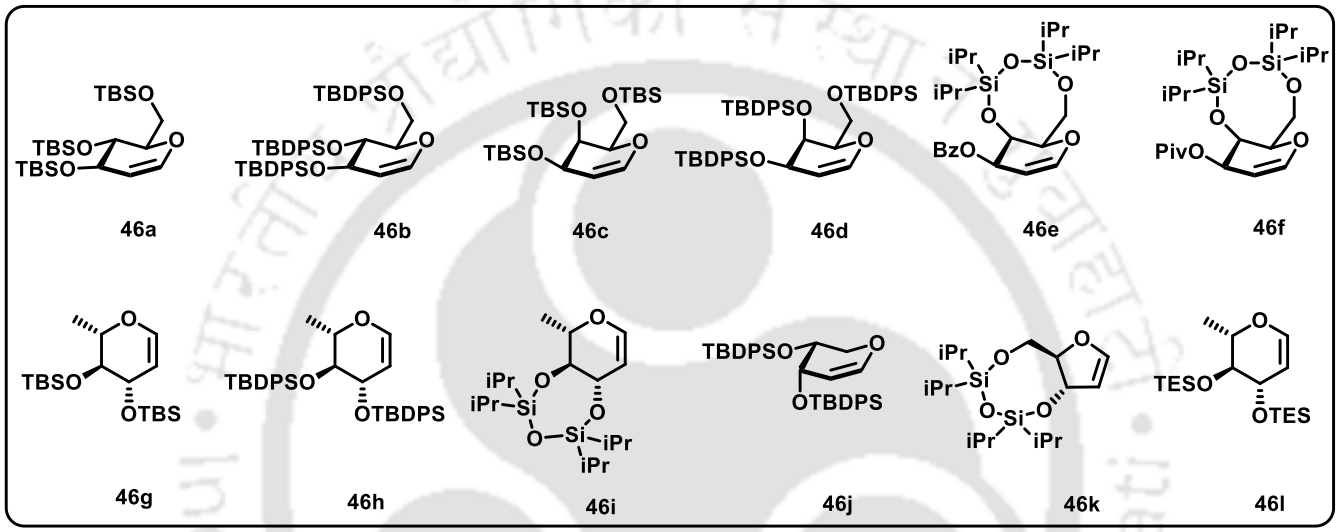
Trehalose sugars are a type of non-reducing disaccharide in which the two sugar units are linked in a 1,1-glycosidic linkage which can generate either symmetrical (αβ) or unsymmetrical (αα or ββ) dimer. These molecules are present in various organisms e.g. bacteria, yeast, fungi, insects, invertebrates, and plants etc, where they are utilized to serve as a source of energy and carbon. It can also serve as a signaling molecule in yeast and plants to control specific metabolic pathways and also affect their growth. Additionally, trehalose molecules can also protect proteins and cellular membranes from inactivation or denaturation due to several stress conditions e.g. desiccation, dehydration, heat, cold, and oxidation. Moreover, trehalose is found as an integral component in glycolipids present in mycobacteria and corynebacteria which are essential for cell wall structures.

Biao Yu and co-workers proposed a dehydrative glycosylation method that explains the activation of glycosyl hemiacetals using nonafluorobutanesulfonyl fluoride (NfF) as a catalyst.[26] They have shown that, in the absence of any acceptor, self-condensation of the glycosyl hemiacetal takes place which provides the corresponding symmetrical 1,1′-dimer or trehalose molecules in high yields. This present glycosylation reaction proceeds under mild basic conditions. Self-condensation product or dimerized product is a very common expected by-product in the dehydrative glycosylation method as 2-deoxy lactols show a high tendency towards self-condensation of the substrates. So far, there are very few literature reports to synthesize these trehalose compounds as the primary reaction outcome and not as a by-product. Trehalose compounds containing silyl protected sugar units have not been studied so far; hence their synthesis is also unexplored.

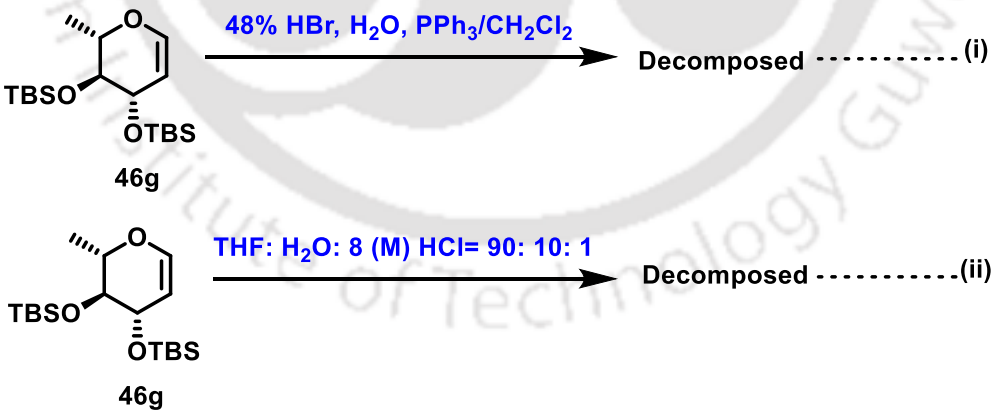
2.4 Silyl Protected Deoxy Sugar Synthesis:

Silyl protecting groups occupy a significant position in synthetic organic chemistry[27] and more so in carbohydrate chemistry.[28,29] It is well established that the silyl protecting groups that, in general, demand a huge steric space, and hence impose a conformational restriction, offer better anomeric selectivities in glycosylation reactions.[28,20] However, the influence of silyl protecting groups in the chemistry of 2-deoxysugars, versatile intermediates in carbohydrate chemistry, has been under-explored because of the difficulty in synthesizing the 2-deoxy-hemiacetal precursors.

Glycals Used in this Study:



The current methods for the synthesis of sugar lactols from glycals involve the use of highly acidic

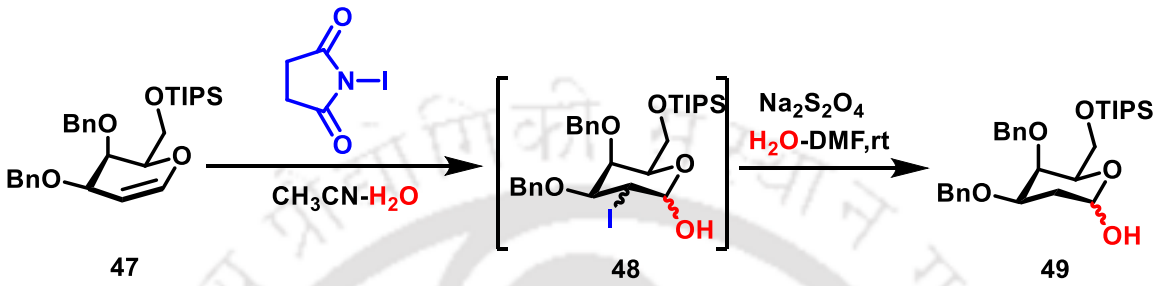


Scheme 15: *Application of Literature Methods of Hemiacetal Synthesis*

conditions like 4−8 M HCl[23] or triphenylphosphine/HBr,[22] under which some of the silyl protecting groups are usually unstable and lead to reduced yields or the decomposition of starting materials (Scheme 15).

TBS-protected L-rhamnal **26g** was subjected to literature methods[22,23] to synthesize the corresponding 2-deoxy hemiacetal but, both the above mentioned method gave decomposed reaction mixture at room temperature within 2 h.

The NIS-ACN method[25a] can provide the sugar lactols in presence of acid sensitive silyl protecting groups also, however, with an unwanted 2-iodo substitution that requires an extra step for removal (Scheme 16).



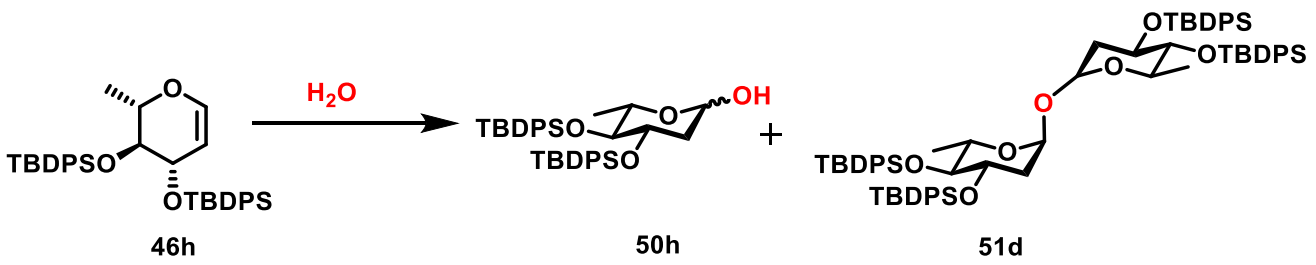
Scheme 16: *NIS-ACN Method of Hemiacetal Synthesis*

Hence, most studies of 2-deoxy and 2,6-dideoxy-hemiacetals are restricted to the stable benzyl and benzoyl/acetyl protecting groups.[30–33] In the study presented here, we show that TTBPy salts can catalyze the formation of hemiacetals from glycals effectively with as little as 2 mol % catalyst. In addition, the biologically important 2-deoxy trehalose analogues[34] are synthesized directly from glycals for the first time, with variations in the concentrations of water. In addition, the utility of various silylprotected hemiacetals has been showcased in the stereoselective glycosylation reactions via the distinctive secondary amine catalysis.

2.5 Optimisation Study:

We then swiftly shifted our focus to optimize our reaction condition to selectively synthesize more numbers of silyl protected hemiacetals and trehalose derivatives. We have chosen di-*O*-TBDPS-protected rhamnal to perform initial optimization studies. First, we reacted rhamnal **46h** with 2 mol % TTBPy·HCl in dry DCM and found it unreactive under these conditions (Table 1A, entry 1). When we performed the reaction with a different solvent system (THF: H_2O= 95: 5), hemiacetal **50h** was only obtained as a product in 42% yield and moreover, we didn't observe the formation of dimerized compound **51d** (Table 1A, entry 2). Although both hemiacetal and dimer formation was achieved by using pyridinium hydrochloride salt as a catalyst but in that case, no product selectivity was observed, i.e. mixture of **50h** and **51d** were formed irrespective of the solvent to water ratio (Table 1A, entry 3-5).

Table 1A. Optimization Studies.

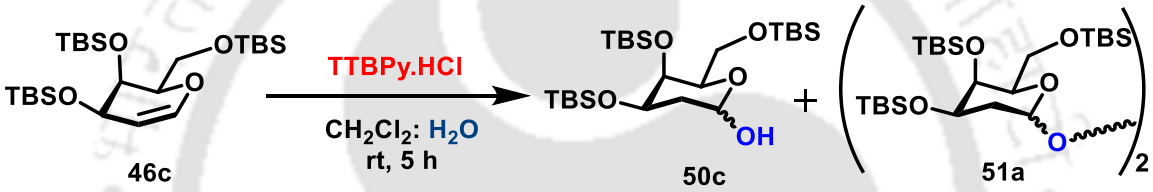


Entry	Catalyst	Cat. ([mol%])	Solvent	Isolated Yield of **50h**[%]	Isolated Yield of **51d**[%]
1	TTBPy.HCl	2	CH_2Cl_2	-	-
2	TTBPy.HCl	2	THF:H_2O (95:5)	42	-
3[a]	Py.HCl	2	CH_2Cl_2	36	-
4	Py.HCl	2	CH_2Cl_2 : H_2O (95:5)	20	42
5[b]	Py.HCl	10	CH_2Cl_2 : H_2O (99:1)	18	52

Reaction conditions: Reactions were done at 40°C, time 24 h. [a]Yield was determined using crude ^{1}H-NMR analysis. [b]Reaction was done at room temperature.

Next, we have chosen tri-*O*-TBDMS-protected galactal to perform the optimization studies.

Table 1B. Optimization Studies.



Entry	Cat. ([mol %])	Solvent (CH_2Cl_2: H_2O)	Isolated Yield of **50c**[%]	Isolated Yield of **51a**[%]
1	20	95:5	65	12
2	10	95:5	54	20
3	5	95:5	50	22
4[a]	2	95:5	80	-
5[b]	1	95:5	-	-
6	5	99:1	14	40
7	10	99:1	-	88

Reaction conditions: [a]Reaction was done at 40°C, time 24 h. [b]Reaction was kept at 60°C, solvent DCE: H_2O= 95:5, monitored for 2 days.

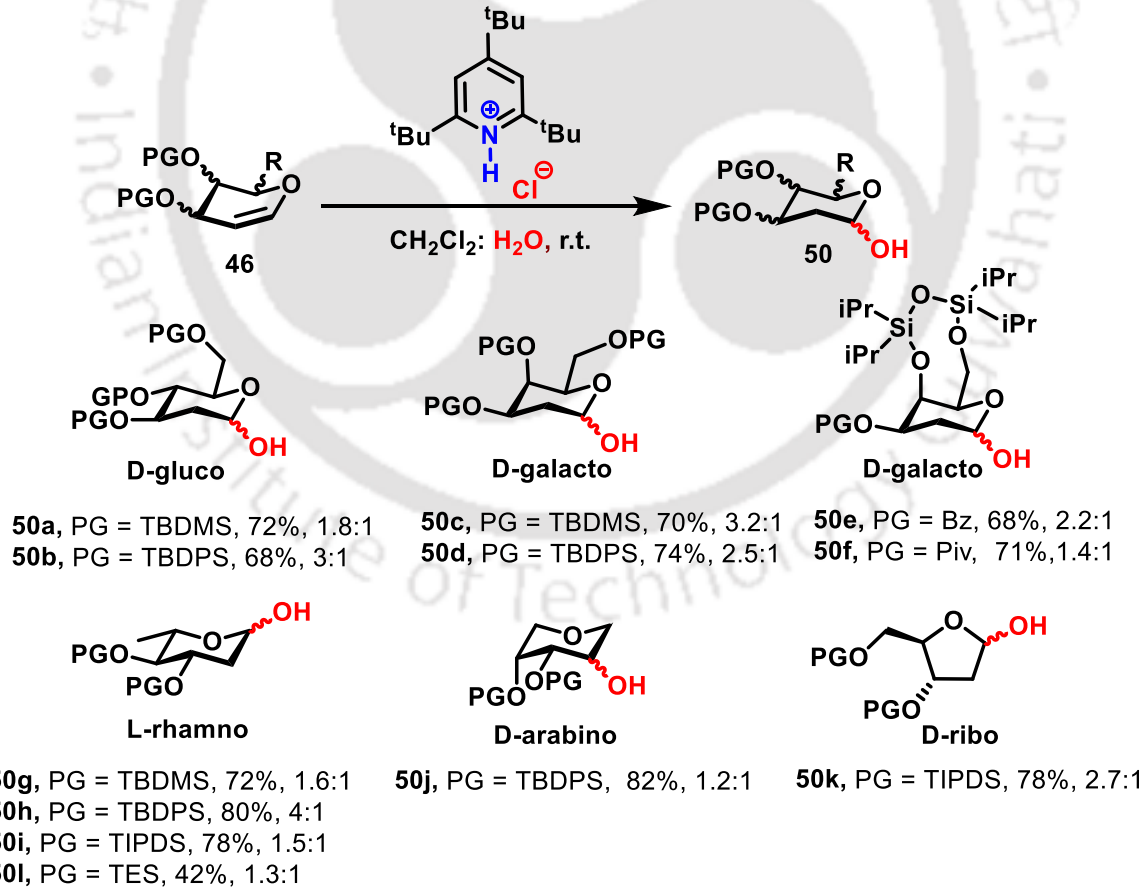
First, we reacted TBS-protected galactal with 20 mol % TTBPy·HCl in dry DCM and found that it is unreactive under these conditions. This suggests that the bulky pyridine derivative, though it has a

low p*K*a in aqueous solution, as expected, cannot behave as a cationic Brønsted acid to protonate glycals in halogenated nonpolar organic solvents. However, when we deliberately used a DCM/H_2O solvent system (95:5) under the same conditions, this allowed the conversion of the galactal into the respective hemiacetal **50c** in 65% yield (Table 1B, entry 1). Also surprisingly, we have isolated the 2-deoxygalactose-derived trehalose analogue **51a** in 12% yield. When the catalytic loading was decreased to 10 and 5 mol % (Table 1B, entries 2 and 3, respectively), the percentage conversion to the hemiacetal **50c** also dropped to 54% and 50%, respectively, and an eventual increase in the percentage of 2-deoxy trehalose **51a** was observed. Interestingly, when the reaction was performed at 40 °C with a decrease in catalyst loading to 2 mol %, exclusive formation of hemiacetal **50c** in high yield was achieved (Table 1B, entry 4). A further decrease in catalyst loading to 1 mol %, even with an increase in temperature, did not lead to the formation of the product (Table 1B, entry 5). On the contrary with a catalytic loading of 10 mol % at rt and with reduced water content in the solvent mixture of 99:1, we were able to switch the product distribution to provide 88% of the 2-deoxy trehalose derivative **51a** (Table 1B, entry 7).

2.6 Results and Discussion

2.6.1 Scope of Various 2-Deoxysugar and 2-Deoxy Trehalose Derivatives with Different Glycosyl Donors:

Scheme 17. Silylated 2-deoxysugars from glycals.



50a, PG = TBDMS, 72%, 1.8:1
50b, PG = TBDPS, 68%, 3:1

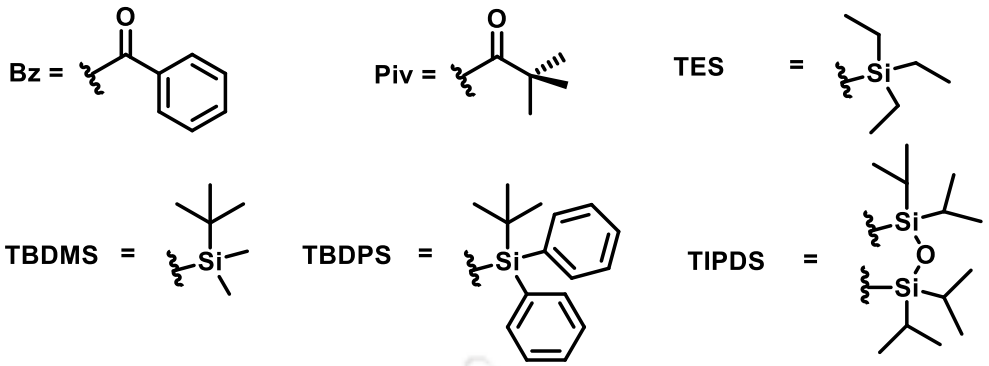
50c, PG = TBDMS, 70%, 3.2:1
50d, PG = TBDPS, 74%, 2.5:1

50e, PG = Bz, 68%, 2.2:1
50f, PG = Piv, 71%,1.4:1

50g, PG = TBDMS, 72%, 1.6:1
50h, PG = TBDPS, 80%, 4:1
50i, PG = TIPDS, 78%, 1.5:1
50l, PG = TES, 42%, 1.3:1

50j, PG = TBDPS, 82%, 1.2:1

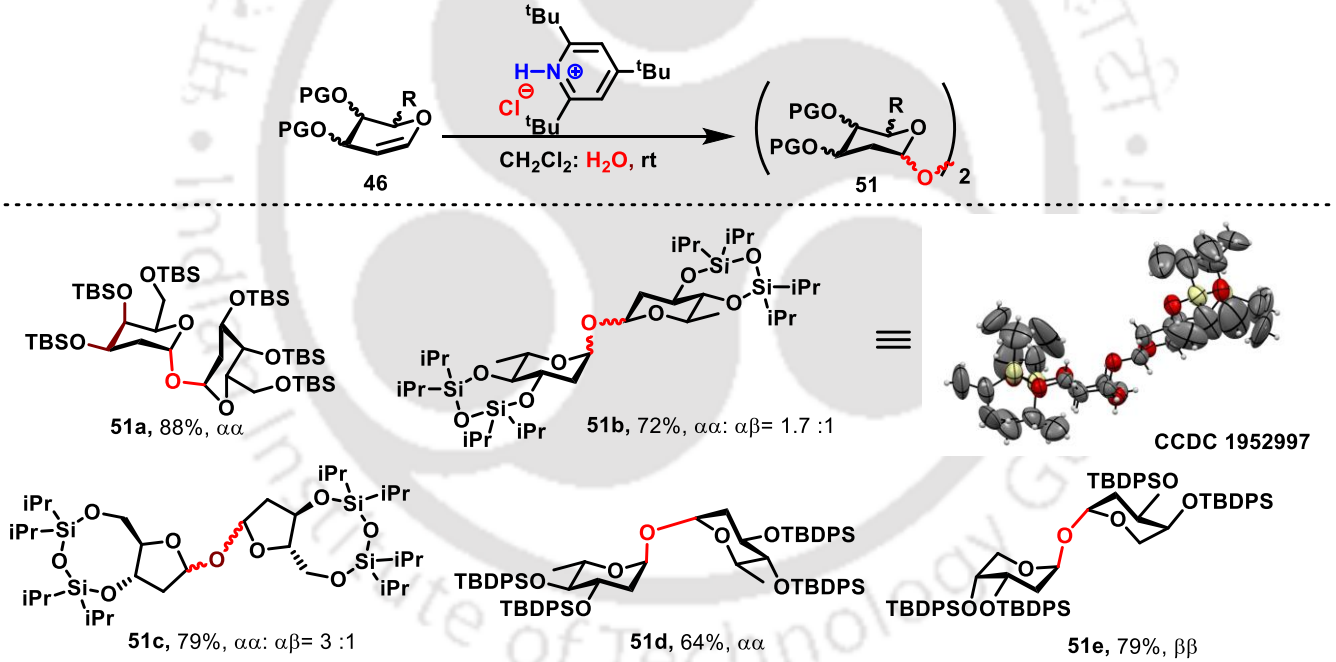
50k, PG = TIPDS, 78%, 2.7:1



Reaction conditions**:** Solvent DCM: H_2O= 95:5, Catalyst- 2 mol %, 40°C.

With the optimized conditions in hand, for both the synthesis of silyl-protected hemiacetals and the 2-deoxy trehalose derivatives, we tested the substrate scope with various silyl-protected glycals. Gluco-, galacto-, rhamno-, arabino-, and ribo-glycals were synthesized, and OTBDMS, OTBDPS, OTIPDS, and OTES protecting groups were chosen for our study (scheme 17).

Scheme 18. Silylated 2-Deoxysugar Dimers from Their Respective Glycals



Reaction conditions: Solvent DCM: H_2O= 99:1, Catalyst- 10 mol %, rt.

All of the hemiacetals were obtained in good to excellent yields (Scheme 17, **50a**–**50k**). Even the highly acid sensitive OTES-protected L-rhamnal has been converted to the corresponding hemiacetals **50l** in 42% yield. Despite the presence of bulky and cyclic silyl protecting groups, none of the sugar derivatives existed in open-chain form (**50e**, **50f**, **50i**, and **50k**).

Similarly, a few of the glycals were also subjected to the conditions of obtaining the trehalose derivatives and were successfully converted into the respective products (Scheme 18, **51a**–**51e**).

2.6.2 Control Experiments:

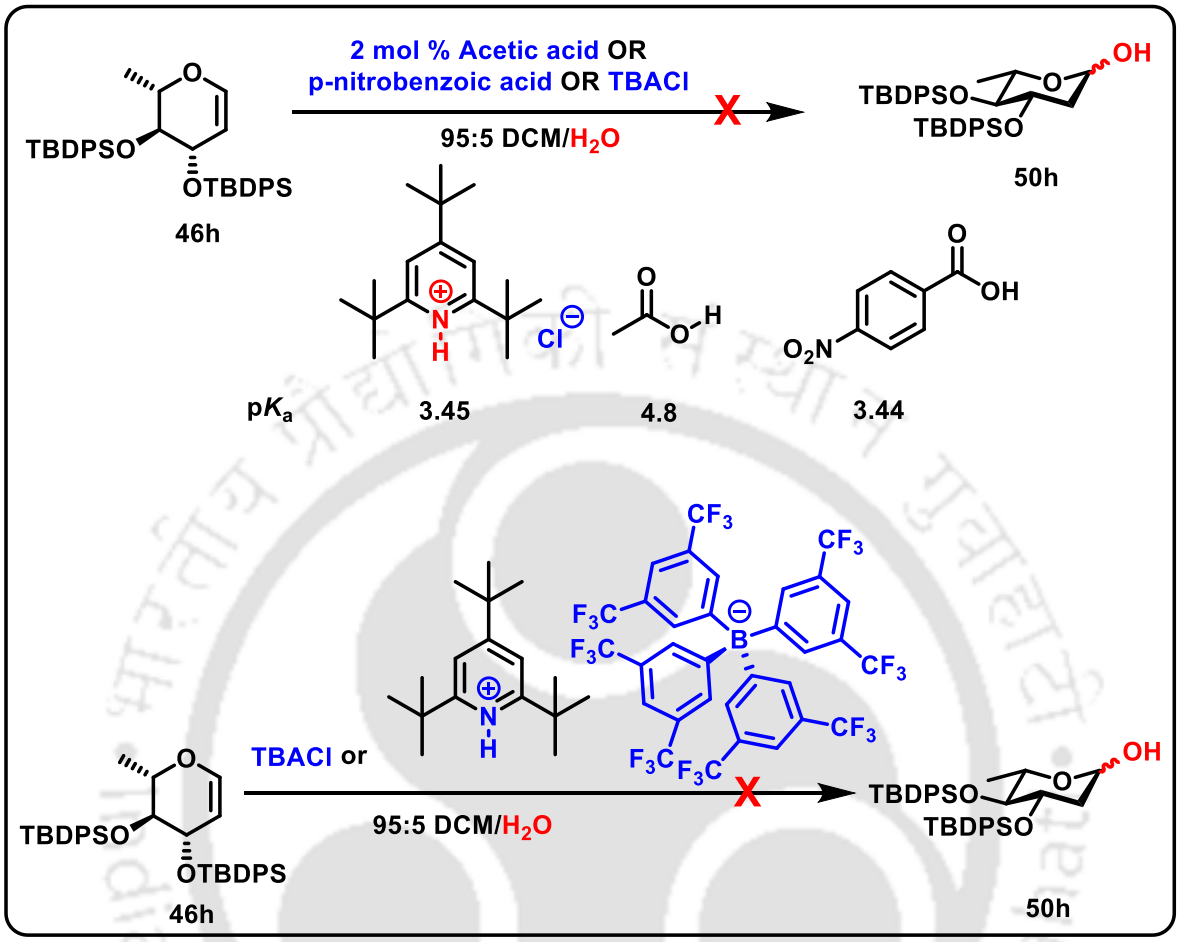


Figure 6: *Control Experiments*

To understand the mechanism, the reaction was performed with acids with similar p*K*a values (Figure 6). The inability of *p*-nitrobenzoic acid (p*K*a = 3.4) and acetic acid (p*K*a = 4.7) to catalyze the synthesis of hemiacetals confirms that the rate-determining step is not the proton transfer from the cationic Brønsted $[TTBPyH]^+$ to the glycals (Figure 6). Also, the reaction with a quaternary ammonium salt TBACl (Figure 6) led to only trace amounts of product, which further demonstrates the uniqueness of TTBPy·HCl catalysis.

2.6.3 NMR Experiments:

However, it is suggestive of a unique mechanism where, presumably, water activation via hydrogen bonding with TTBPy·HCl has been achieved. The increased acidity of the protons of the water molecule allows the protonation of glycals. ^{1}H NMR spectra of TTBPy·HCl at different concentrations of H_2O were recorded (Figure 7). It has been observed that the chemical shifts of the signals of the non-exchangeable ring protons of the pyridine as well as alkyl group signals were affected by increasing concentrations of water. The NH peak of the catalyst H_A shifted downfield (from δ 14.20 to 14.45), whereas the aromatic protons H_B shifted upfield (from δ 7.58 to 7.53); there is also a slight upfield shift

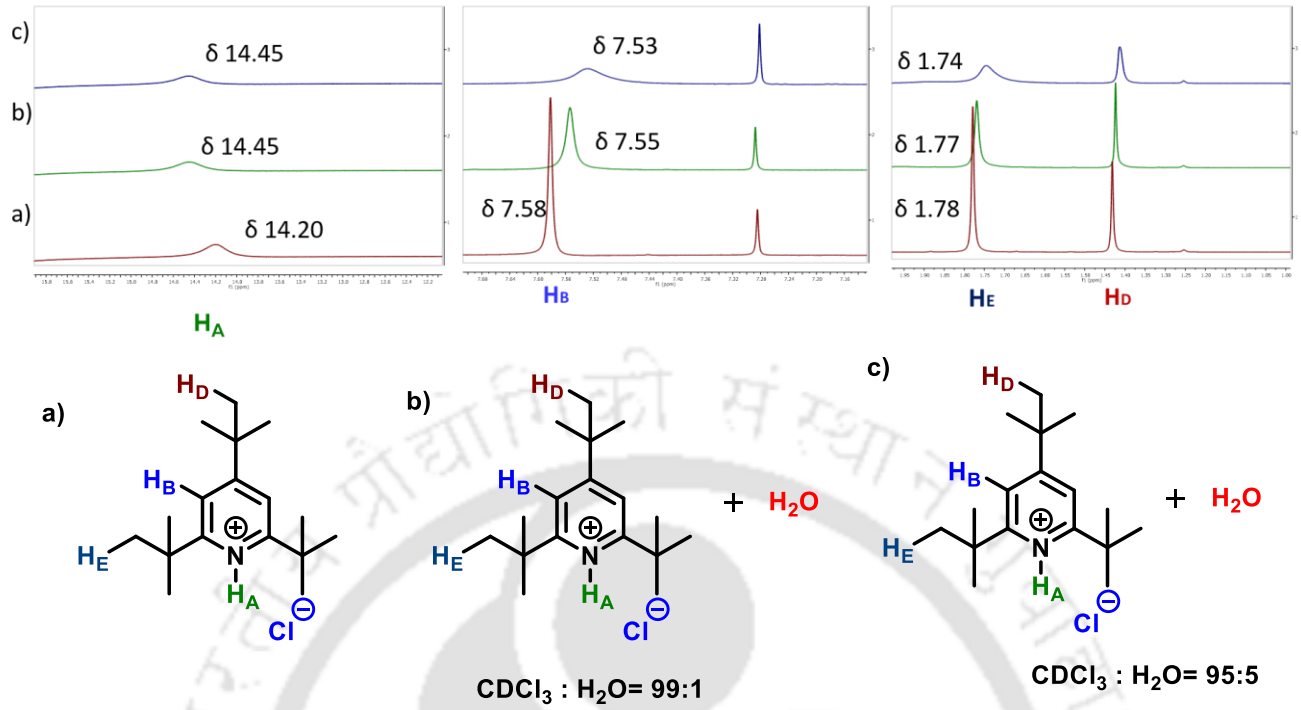


Figure 7: *a) 0.035 mmol of TTBPy.HCl b) 0.035 mmol of TTBPy.HCl and water (99:1 ratio) c) 0.035 mmol of TTBPy.HCl and water (95:5 ratio).*

in the ^{t}Bu protons H_E and H_D (from δ 1.78 to 1.74 and from δ 1.43 to 1.41 respectively). Also, with increasing concentrations of water, the signals of the pyridine protons are broadened, which is indicative of some interaction between the water molecules and salt.[35] The observed shifts and the broadening increase with an increase in the amount of water (95:5 $CHCl_3$: H_2O).

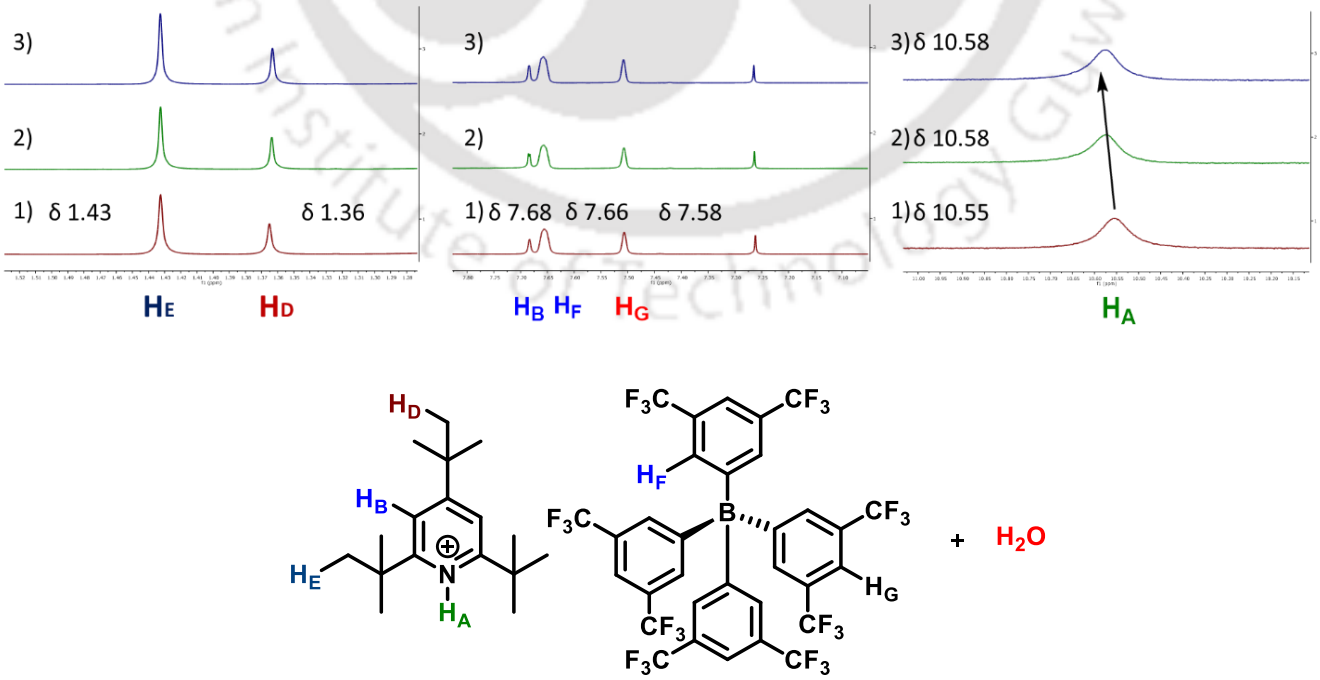


Figure 8: *1) 0.012 mmol of TTBPy.BAR$^{F}_{4}$ 2) 0.012 mmol of TTBPy. BAR$^{F}_{4}$ and water (99:1 ratio) 3) 0.012 mmol of TTBPy. BAR$^{F}_{4}$ and water (95:5 ratio).*

Intriguingly, when the ^{1}H NMR spectra were recorded with TTBPy·BAR$^{F}_{4}$ salt, no such change in the signals of TTBPy was observed (Figure 8). Also, TTBPy·BAR$^{F}_{4}$ salt failed to catalyze the synthesis of hemiacetals or the trehalose derivatives under the optimized conditions. This suggests that the observed phenomenon is anion specific.

2.6.4 IR Studies:

The infrared hydrogen bonding band for the TTBPy·HCl salt is unusually sharp at 3350 cm^{-1} (Figure 9) unlike the other pyridinium salts, in line with the observations of Arnett and Chawla for DTBP.[36] In addition, the IR stretching frequency was not affected when recorded in the presence of moisture [3350 cm^{-1} (Figure 9)], indicating further that the hindered protonated pyridine is not involved in any exchange processes.

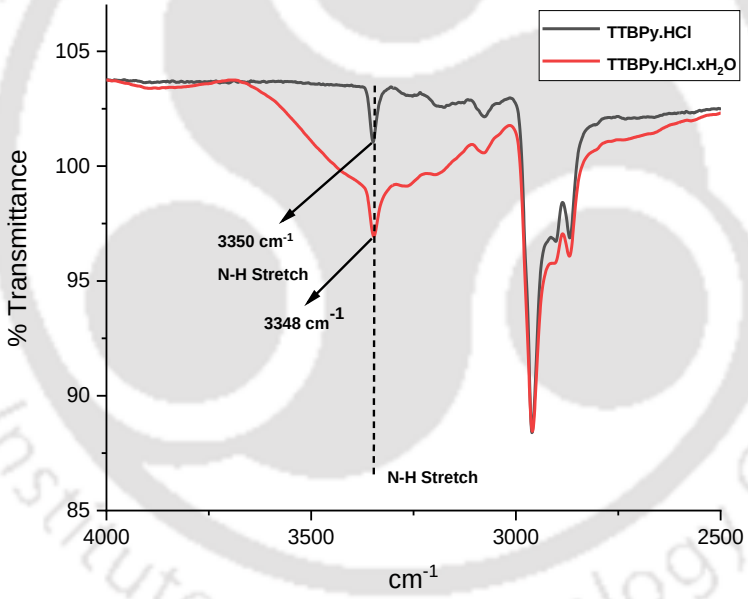
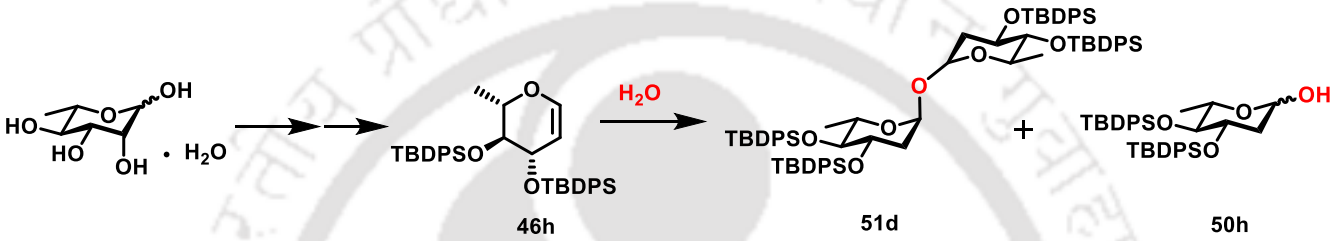


Figure 9: *Plot of Transmittance vs Wavelength.*

We were curious to understand the behavior of the cationic [TTBPyH]$^{+}$ in solvents with poor coordination ability like chloroform or dichloromethane with a few molecules of water where the anion can be solvated. We envisaged that the structural differences between ion pairs that are in contact and solvent separated ion pairs[37–40] can be achieved by varying the concentrations of water in a nonpolar organic solvent like dichloromethane, and the variation in the hydrogen bond induced acidity on the water molecule could be exploited in the hydration of the activated alkenes,[41,2] i.e., glycals under mild conditions.

A closer look at the crystal structure of TTBPy·HCl revealed that the ion pair is not stabilized by N−H···Cl interactions but rather is stabilized by several C−H···Cl− interactions.[42] Also, the halide is observed to be in a hydrogen bonding network with water molecules. The thus activated water molecule reacts with the glycal to provide the hemiacetals. The broadening of the signals in the ^{1}H NMR spectra corresponding to the aromatic protons along with the ortho *tert*-butyl protons in solution state could be arising due to the strong C−H···Cl−···H−O−H interactions that can be perceived even in the solid state. To the best of our knowledge, this is a unique mechanism by which the enol ethers can be hydrated and this kind of catalysis has not yet been reported. All of these observations also reiterate the fact that the sterically protected N−H proton is not involved in any exchange process or the transfer of a proton to a water molecule giving rise to the hydronium ions.[43-45]

2.6.5 Gram Scale Synthesis of Compound 50h



Scheme 19: *Gram Scale Synthesis*

3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **46h** was synthesized from commercially available L-rhamnose monohydrate following the previously reported method.[20] Glycal **46h** (1.1 gm, 1.81 mmol, 1.0 equiv) was taken in a round bottomed flask and the flask was then filled with dry DCM and water in 95:5 ratios (20 ml) under continuous stirring condition. 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (10 mg, 0.036 mmol, 2 mol%) was added and heated at 40 °C (using oil bath) in the sealed flask until the reaction was determined to be complete by TLC (after 18 h glycal was consumed). The reaction mixture was quenched by water (62 ml) and it was extracted with DCM (3x47 ml), dried over Na_2SO_4 and concentrated then concentrated in vacuo and purified by silica gel column chromatography (Merck 60-120 mesh, 40 gm). The crude product was purified by column chromatography on silica gel eluted with hexane/EA to give compound **51d** (eluent 3% EA in hexane, amount 13 mg, yield 6%) as a colourless liquid and compound **50h** (eluent 10% EA in hexane, amount 0.88 gm, yield 78%) as a colourless crystalline solid.

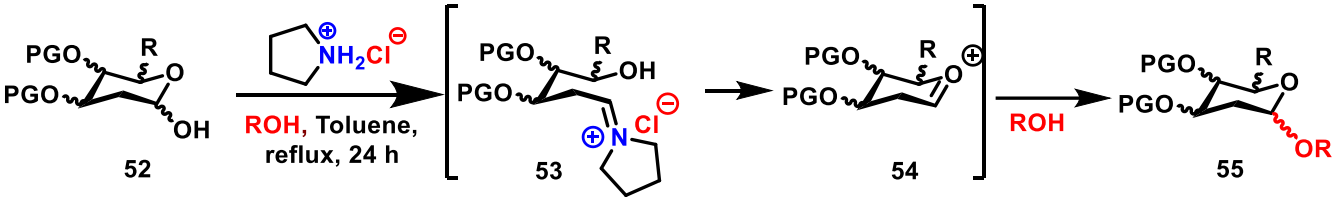
2.7 Application of Synthesized 2-Deoxyhemiacetals in Several Other Reactions

2-Deoxyhemiacetals synthesized using the above organocatalytic method were further utilized in several other reactions like glycosylation, aryl-glycosylation or Chan-Lam coupling, Wittig reaction etc.

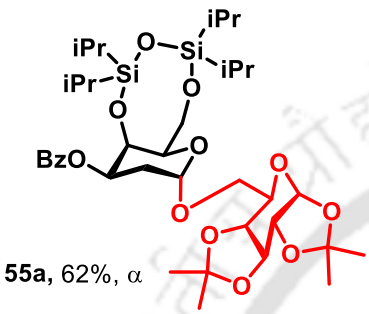
2.7.1 Stereoselective Glycosylations of Silyl-Protected Hemiacetals via Secondary Amine Catalysis

The synthetic utility of the thus synthesized hemiacetals was showcased in accessing α-selective disaccharides via a unique secondary amine catalysis[46] (Scheme 18, **55a**−**55k**) in decent to good yields. Pyrrolidinium hydrochloride forms an iminium ion with the open-chain aldehydic form of the

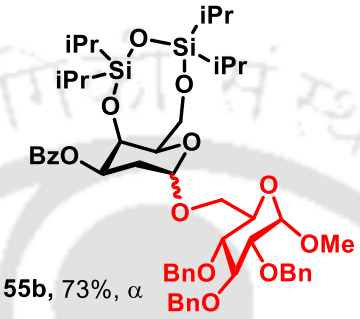
Scheme 20:



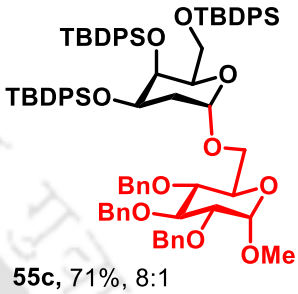
2-deoxy-galactose



55a, 62%, α



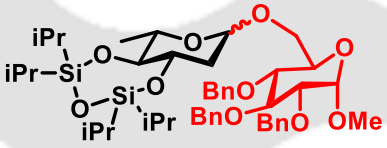
55b, 73%, α



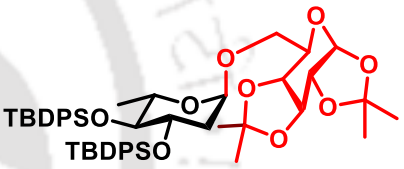
55c, 71%, 8:1

2-deoxy-rhamnose

55d, 57%, α

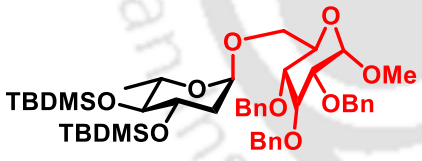


55e, 59%, 8.5:1

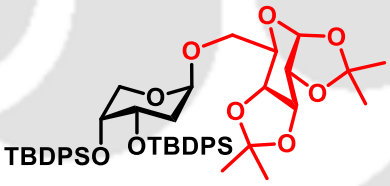


55f, 62%, 8:1

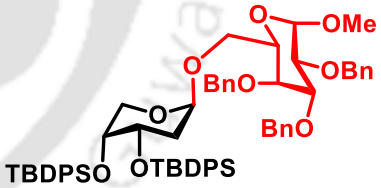
2-deoxy-arabinose



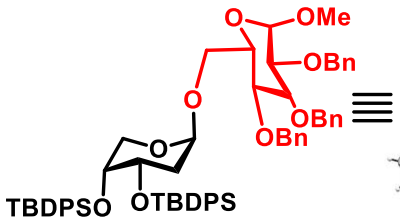
55g, 55%, 7:1



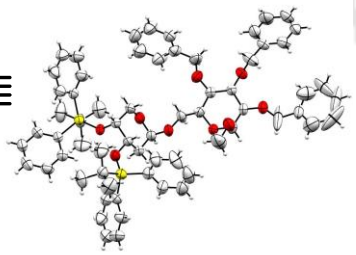
55h, 65%, β



55i, 72%, 10:1



55j, 59%, 6:1



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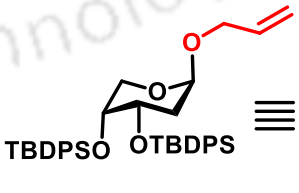
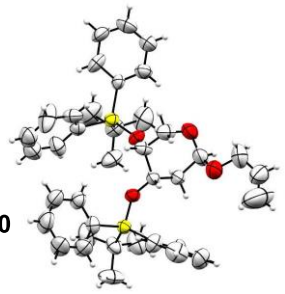


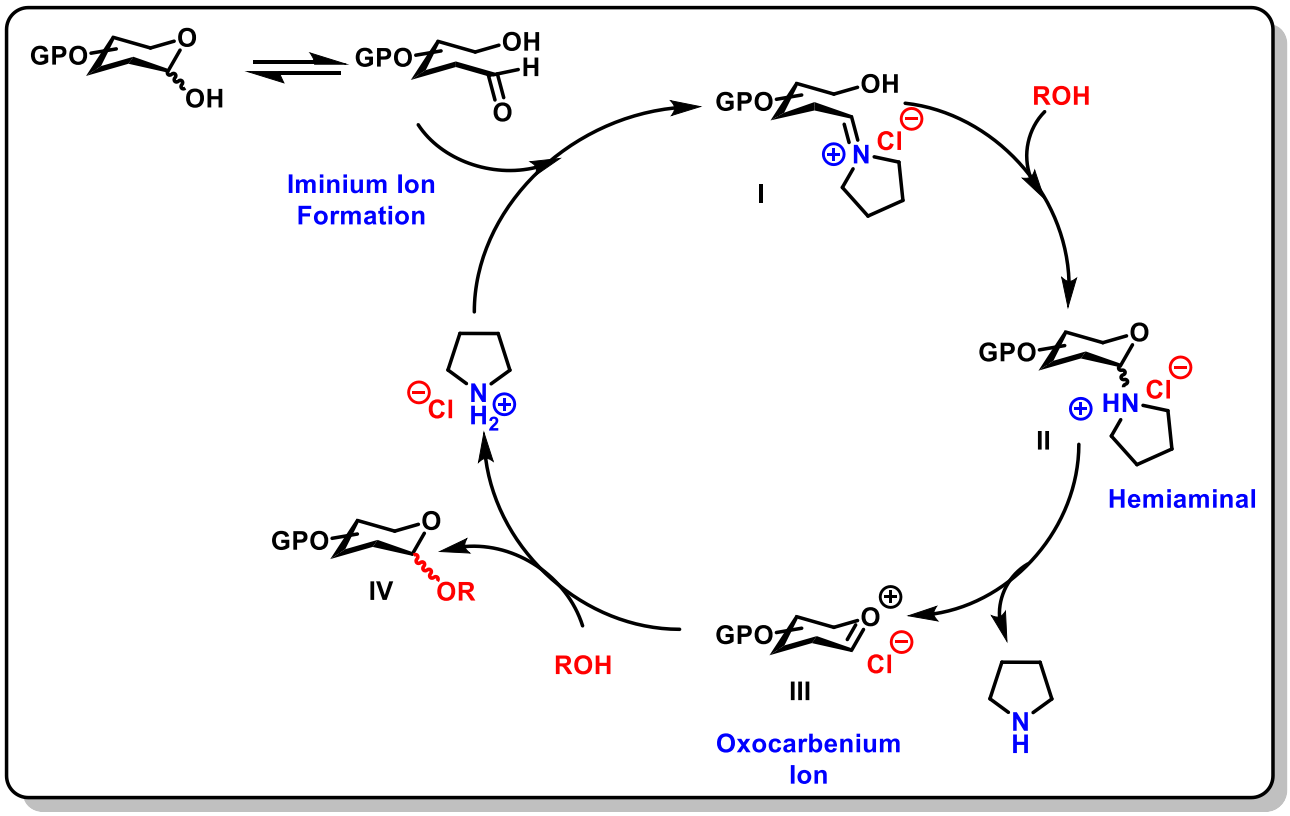
55k, 83%, 3:1



CCDC 1952990

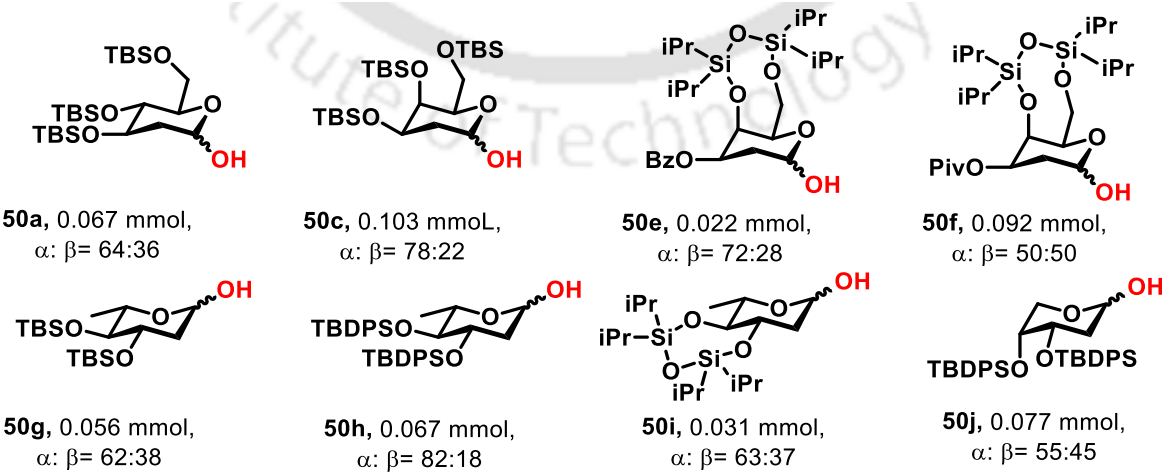
Reaction condition: 1.1 equivalents of acceptor were used in the case of monosaccharide (**55k**) and 1.5 equivalents of the acceptor (**57a-d**) were used in the case of disaccharides (**55a-j**) synthesis. Anomeric selectivity was determined either from ^{1}H-NMR spectrum (in case of compound **(55a-j**) or from HPLC chromatogram (in case of **55k**).

Scheme 20: *Stereoselective Glycosylations of Silyl-Protected Hemiacetals via Secondary Amine Catalysis*



Scheme 21: *Proposed Mechanistic Pathway for Glycosylation Reaction*

2.7.2 Equilibrium Anomeric Ratio of Various Donors.

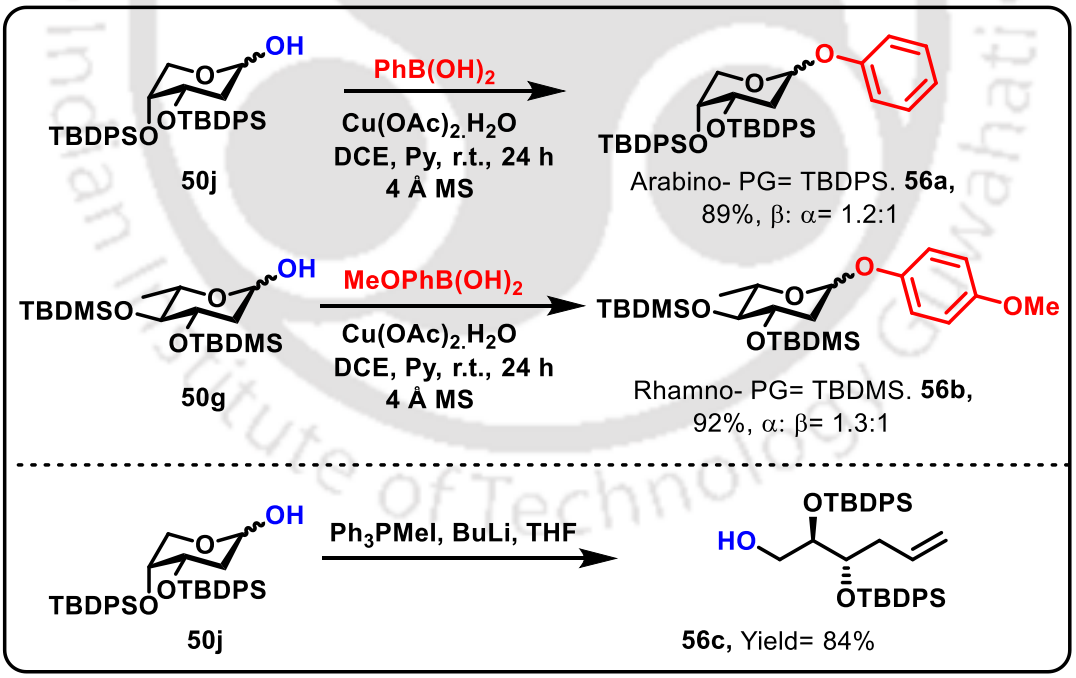


Reaction conditions: 0.022 mmol to 0.103 mmol of 2-deoxy hemiacetal (**50a**, **50c**, **50e-j**) was dissolved in 0.6 mL $CDCl_3$ and heated to 55°C. Change in the anomeric ratio was monitored by ^{1}H-NMR at an interval of 5 h and then 3 h.

Table 2: *Equilibrium Anomeric Ratio of Various Donors.*

hemiacetal. The thus formed iminium species undergo a ring closure forming a hemiaminal species that upon further expulsion of ammonium species results in the formation of an oxocarbenium ion.[46] The attack of the sugar alcohol on the variously bulky silylprotected oxocarbenium ions resulted in the stereoselective bond formation leading to the α-selective glycosylations (Scheme 22, **55a**–**f**). The observed selectivities in disaccharide formation were higher than in the case of benzyl-protected donors and acceptors under similar reaction conditions.[22] This signifies the conformational restriction imposed by the various sterically bulky silyl protecting groups on the oxocarbenium ions of the respective sugars. The thermodynamic equilibrium ratios of various silylprotected hemiacetals[47] were estimated through NMR experiments to understand the electronic effect of these bulky silyl protecting groups on the anomeric equilibrium of 2-deoxygluco-, galacto-, rhamno-, and arabinopyranoses (Table 2). The ^{1}H NMR spectra of the hemiacetals in $CDCl_3$ were monitored until the equilibrium was achieved, and the anomeric ratios presented reflect the change in the equilibrium position with the change in protecting group. In addition, the mismatch of the anomeric selectivities obtained in the secondary amine catalysis with the thermodynamic anomeric equilibrium ratios of hemiacetals is indicative of the kinetic origins of the products under the present catalysis.

2.7.3 Other Reactions of Anomeric Hemiacetals



Scheme 22: *Other Reactions of Anomeric Hemiacetals*

In addition, the utility of the silyl-protected hemiacetals has also been shown in the synthesis of *O*-aryl glycosides[48] (Scheme 22). Compounds **50j** and **50g** were converted to the respective *O*-aryl glycosides **56a** and **56b** via a copper-catalyzed addition of the phenylboronic acid in 89% and 92%

yields, respectively. In addition, compound **50j** has also been converted to a terminal olefin containing chiral polyol **56c** in 84% yield via a simple Wittig reaction. These substrates are synthetically important as these silyl-protected olefins can undergo a ring closure leading to interesting carbocycles under boron catalysis.

2.8 Conclusion:

In conclusion, we have displayed the utility of the bulky TTBPy·HCl as a highly efficient organocatalyst that can convert the acid sensitive silyl-protected glycals to the respective hemiacetals in high yields via a unique C−H···Cl− interaction assisted hydration. The reactivity difference of the organocatalyst depending on the concentration of water, thus determining the product outcome, has been showcased. In addition, the thus synthesized hemiacetals have been utilized again in mechanistically distinct secondary amine catalysis for the stereoselective synthesis of various glycosides. Also, the anomeric hemiacetals have been successfully utilized in the synthesis of *O*-arylated glycosides via a copper catalyzed addition of phenylboronic acids. The organocatalytic hydration of glycals presented here in combination with the iminiumcatalyzed stereoselective glycosylation provides a practically simple approach for the synthesis of oligosaccharides and various other carbohydrate synthons. These novel concepts have the potential to be applicable to various other synthetic transformations, as well.

2.9 Experimental Section

General Information

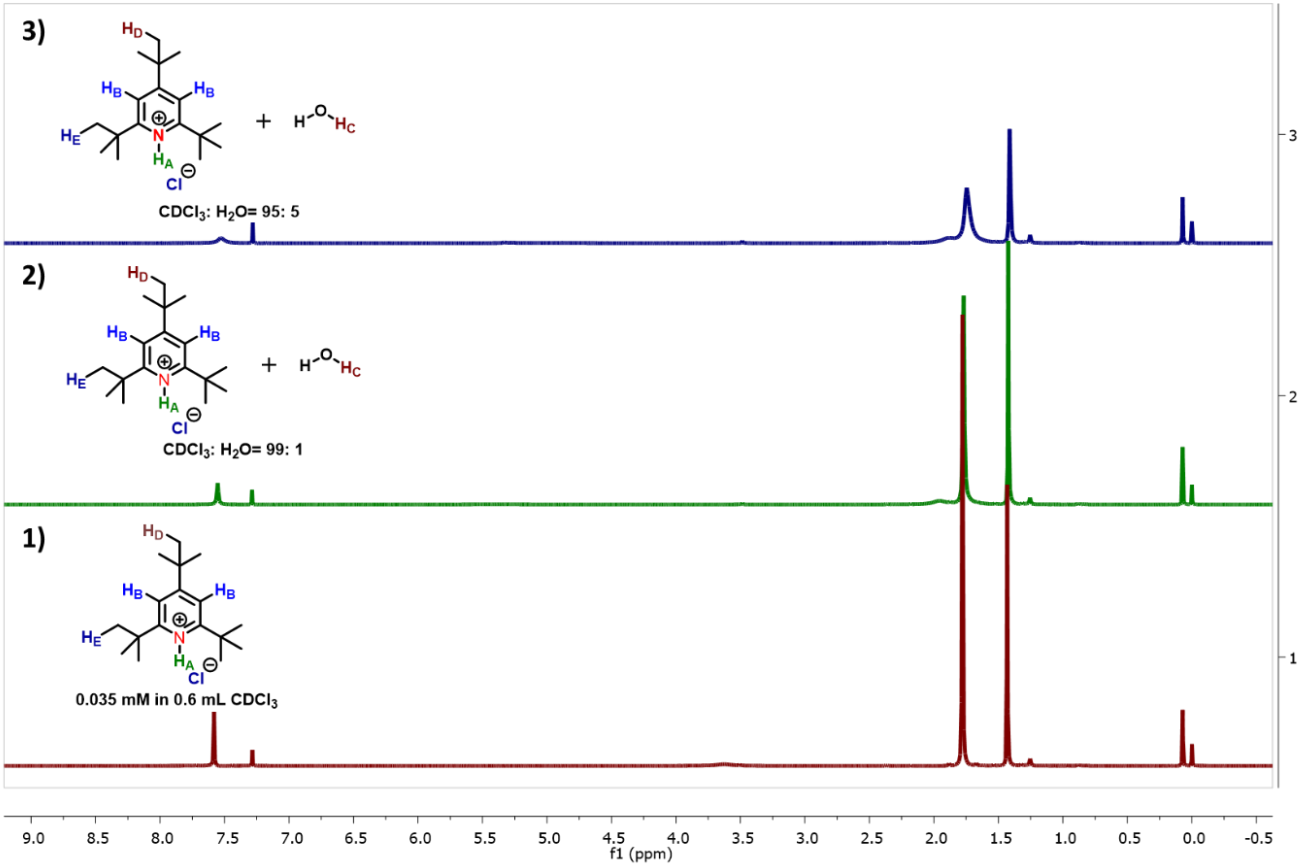
All solvents used were in commercial grade for reaction without further purification. Reagents purchased from Sigma-Aldrich, Merck, Spectrochem, Alfa Aesar, Loba and used without further purification.

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]. 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 room temperature. ^{1}H- and ^{13}C- NMR were recorded on a Bruker 600MHz and 400MHz 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 13C). Data are reported as follows: chemical shifts (δ), multiplicity (s = singlet, d = doublet, dd = double 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 High Resolution Mass spectrometer QTOF 6520. The diastereomeric ratio was calculated from crude NMR. Specific rotation was recorded in Rudolph Research Analytical Polarimeter, the units of the specific rotation is (deg·mL)/(g·dm) and concentration *c* is given in g/100 ml. IR was recorded in PerkinElmer FT-IR spectrometer for solid sample or sample solution without using KBr pellet. Melting point range provided for the crystalline solids were recorded using Digital Melting Point Apparatus of Optics Technology.

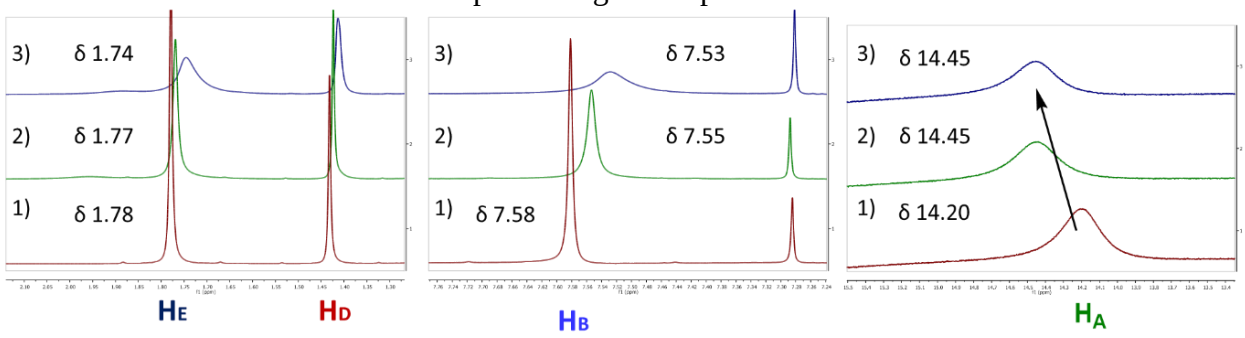
NMR Titration Experiments:

^{1}H NMR titration of TTBPy.HCl with water in 0.6 ml solution of $CDCl_3$

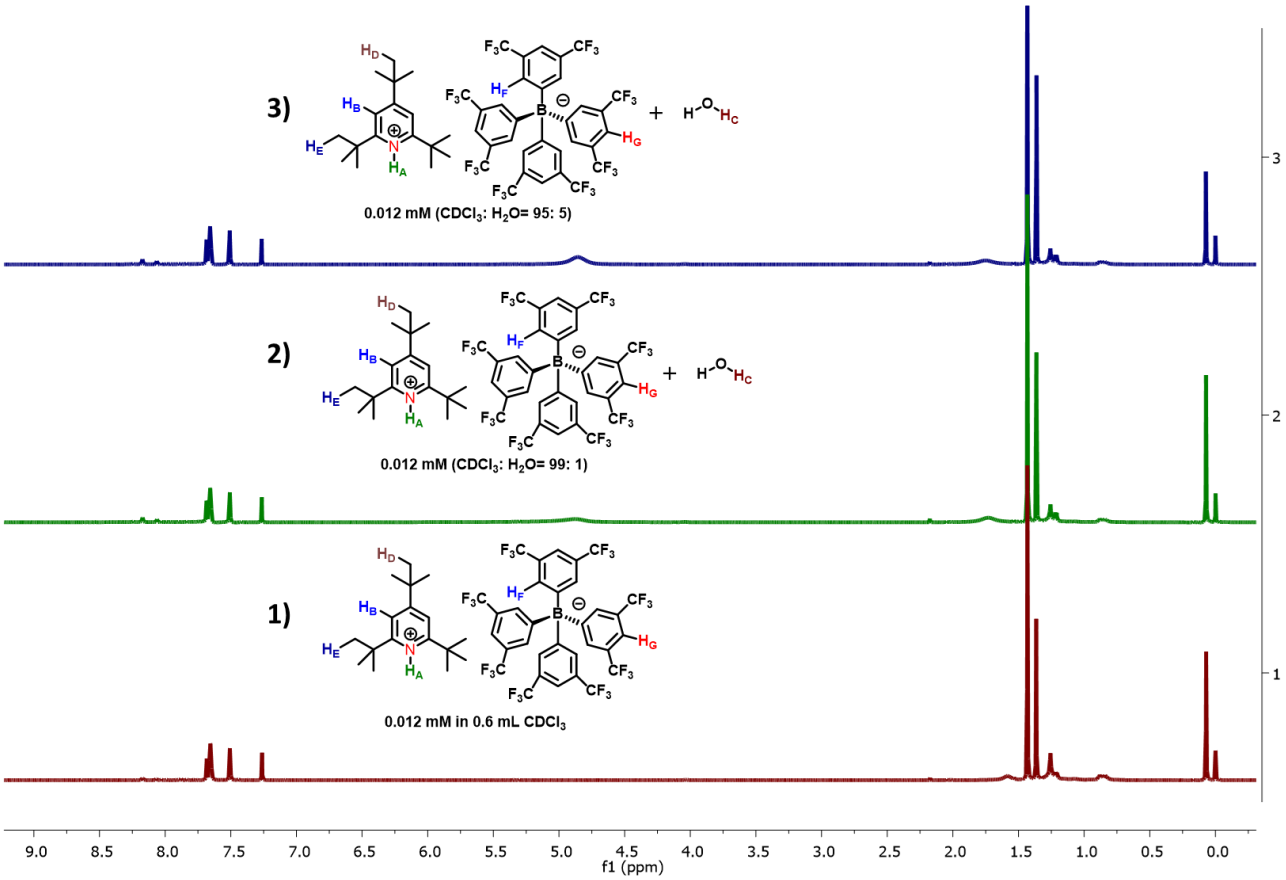


1) 0.035 mmol of TTBPy.HCl 2) 0.035 mmol of TTBPy.HCl and water (99:1 ratio) 3) 0.035 mmol of TTBPy.HCl and water (95:5 ratio).

Specific regions expanded

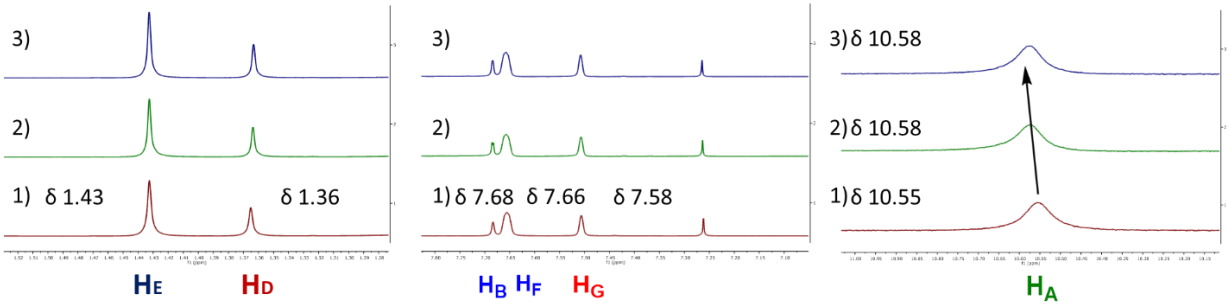


^{1}H NMR titration of TTBPy.BAR$^{F}_{4}$ with water in 0.6 ml solution of $CDCl_3$



1) 0.012 mmol of TTBPy.BAR$^F_4$ 2) 0.012 mmol of TTBPy.BAR$^F_4$ and water (99:1 ratio) 3) 0.012 mmol of TTBPy.BAR$^F_4$ and water (95:5 ratio).

Specific regions expanded



Study of the N-H Stretching Frequency of TTBPy·HCl from IR Spectroscopy:

Preparation of TTBPy.HCl.xH_2O: Catalyst TTBPy.HCl was dissolved in 0.5 ml of 99:1 CH_2Cl_2: H_2O solution and IR spectrum was recorded. It was compared with the IR spectrum of the dry solid catalyst sample.

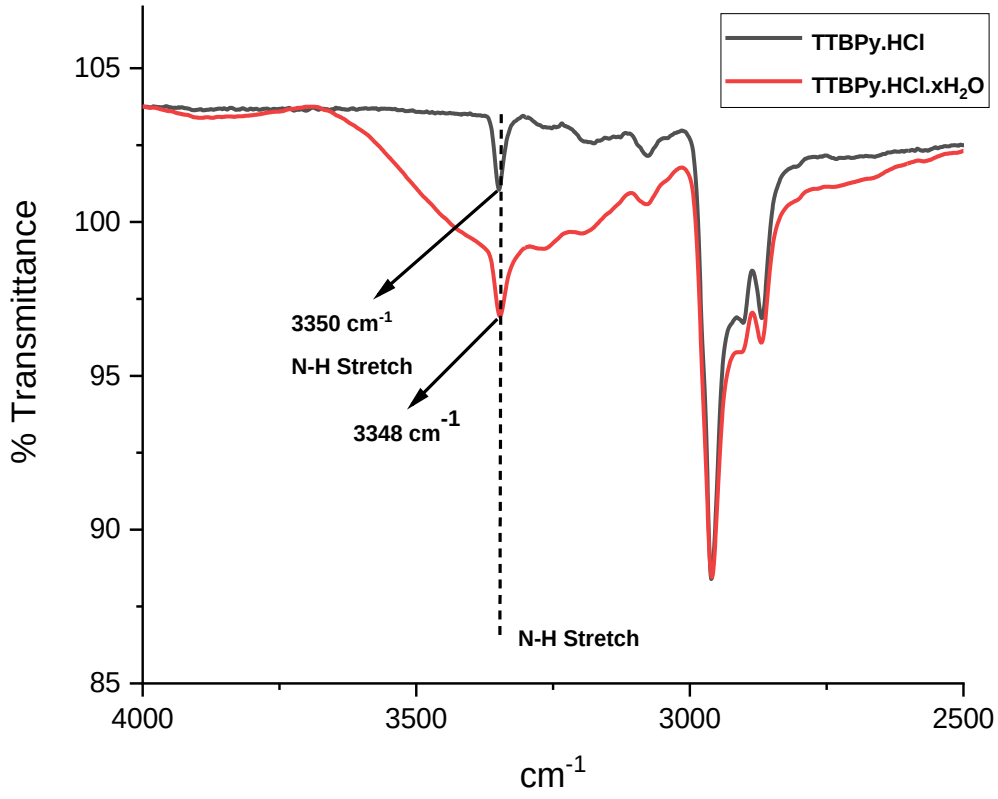
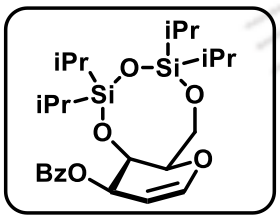


Figure S1: Plot of Transmittance vs Wavelength.

Synthesis of 2,6-anhydro-5-deoxy-4-O-benzoyl-1,3-O-(tetraiso-propyldisiloxane-1,3-diyl)-d-arabino-hex-5-enitol (46e):



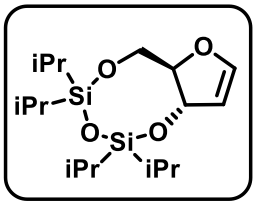
D-Galactal (500 mg, 3.42 mmol, 1.0 equiv) was dissolved in 20 ml pyridine. Then, $TIPDSCl_2$ (1.65 ml, 5.13 mmol, 1.5 equiv) was added into it and this solution was stirred for 5h. The reaction mixture was then concentrated and extracted with ethyl acetate (3x30 ml). The organic phase was washed with 1 (N) HCl (100 ml) followed by brine (100 ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude was purified by column chromatography in ethyl acetate/hexane solvent system to give the product as a white solid. R_f- 0.9 (10% ethyl acetate in hexane), amount- 1.2 g, yield- 92%. The product obtained (1.2 g, 3.09 mmol, 1 equiv) was dissolved in DCM. Then, pyridine (0.40 ml, 4.63 mmol, 1.5 equiv) and benzoyl Chloride (0.60 ml, 4.63 mmol, 1.5 equiv) was added into it, maintaining ice cold condition and the reaction mixture was allowed to stir for overnight at room temperature. Upon completion of the reaction, the reaction mixture was extracted with DCM (3x30 ml). The organic phase was washed with 1 (N) HCl (100 ml) followed by brine (100

ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude was purified by silica gel column chromatography (Merck 60-120 mesh, 20 gm) in ethyl acetate/hexane solvent system to give the product as a colourless liquid. R_f- 0.6 in 10% EA/ hexane, eluent 3% EA in hexane, amount- 1.3 g, yield- 88%. Re-purification was done using HPLC (retention time- 6 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 8.07 (m, 2H), 7.58 – 7.55 (m, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 6.43 (dd, *J* = 6.2, 2.1 Hz, 1H), 5.74 (d, *J* = 1.3 Hz, 1H), 4.74 (dt, *J* = 6.2, 1.8 Hz, 1H), 4.64 (d, *J* = 2.3 Hz, 1H), 4.14 – 4.10 (m, 1H), 3.90 (d, *J* = 3.2 Hz, 1H), 3.88 (d, *J* = 1.0 Hz, 1H), 1.10 – 1.03 (m, 22H), 0.89 (d, *J* = 7.1 Hz, 3H), 0.68 (d, *J* = 6.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.6, 144.8, 133.0, 130.1, 129.8, 128.2, 99.1, 75.3, 68.4, 61.4, 59.0, 17.4, 17.4, 17.3, 17.2, 17.2, 17.1, 17.1, 17.1, 13.7, 13.3, 12.7, 12.6. HRMS (ESI-QTOF) $C_{25}H_{40}O_6Si_2NH_4$ $[M+NH_4]^+$- calculated- 510.2707; found- 510.2698. $[\alpha]_D^{22}$= 6 (*c* 0.4, $CHCl_3$).

Synthesis of 3,4-di-*O-tert*-butyldiphenylsilyl-D-arabinal (46j):

D-Arabinal (500 mg, 4.30 mmol, 1.0 equiv) was dissolved 20 ml DMF. Then, imidazole (878 mg, 12.91 mmol, 3.0 equiv) followed by TBDPSCl (3.4 ml, 12.91 mmol, 3.0 equiv) were added into it and allowed to stir for overnight. The reaction mixture was then concentrated and extracted with ethyl acetate (3x30 ml). The organic phase was washed with brine (100 ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude was purified by column chromatography (Merck 60-120 mesh, 20 gm) in ethyl acetate/hexane solvent system to give the product as a colourless oil. R_f- 0.5 in 10% EA/hexane, eluent 4% EA in hexane, amount- 2.1 g, yield- 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 6.8 Hz, 2H), 7.73 – 7.68 (m, 4H), 7.62 (d, *J* = 6.9 Hz, 2H), 7.41 – 7.26 (m, 12H), 6.01 (d, *J* = 5.9 Hz, 1H), 4.31 (t, *J* = 5.8 Hz, 1H), 4.23 – 4.21 (m, 1H), 4.10 (t, *J* = 10.3 Hz, 1H), 3.91 (dt, *J* = 10.6, 3.5 Hz, 1H), 3.54 (dd, *J* = 10.0, 2.3 Hz, 1H), 1.11 (s, 9H), 1.09 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.8, 136.2, 136.1, 135.8, 135.8, 134.9, 134.2, 133.8, 133.6, 129.9, 129.7, 129.5, 127.7, 127.6, 127.5, 127.3, 101.9, 69.4, 64.8, 64.3, 27.1, 27.1, 26.9, 19.4, 19.2. HRMS (ESI-QTOF) $C_{37}H_{44}O_3Si_2Na$ $[M+Na]^+$- calculated- 615.2727; found- 615.2743. $[\alpha]_D^{22}$= 65 (*c* 1.0, $CHCl_3$).

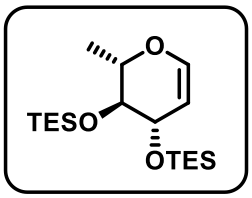
Synthesis of 1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyl-disiloxane-1,3-diyl)-D-erythro-pent-1-entiol (46k):



D-Ribal (500 mg, 4.30 mmol, 1.0 equiv) was dissolved 20 ml DMF. Then, imidazole (878 mg, 12.91 mmol, 3.0 equiv) followed by $TIPDSiCl_2$ (2.1 ml, 6.45 mmol, 1.5 equiv) were added into it and allowed to stir for overnight. The reaction mixture was then concentrated and extracted with ethyl acetate (3x30 ml). The organic phase was washed with brine (100 ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude was purified by column chromatography (Merck 60-120 mesh, 20 gm) in ethyl acetate/hexane solvent system to give the product as a colourless oil. R_f-

0.5 in 10% EA/ hexane, eluent 3% EA in hexane, amount- 1.2 g, yield- 80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.40 (d, *J* = 5.9 Hz, 1H), 4.84 (t, *J* = 5.8 Hz, 1H), 4.44 (t, *J* = 4.0 Hz, 1H), 4.12 (dt, *J* = 10.9, 3.9 Hz, 1H), 3.88 (ddd, *J* = 9.9, 4.0, 1.4 Hz, 1H), 3.81 – 3.75 (m, 1H), 1.10 – 0.96 (m, 28H). HRMS (ESI-QTOF) $C_{17}H_{35}O_4Si_2$ $[M+H]^+$- calculated- 359.2074; found- 359.2079.

Synthesis of 3,4-di-O-triethylsilyl-L-Rhamnal (46l):



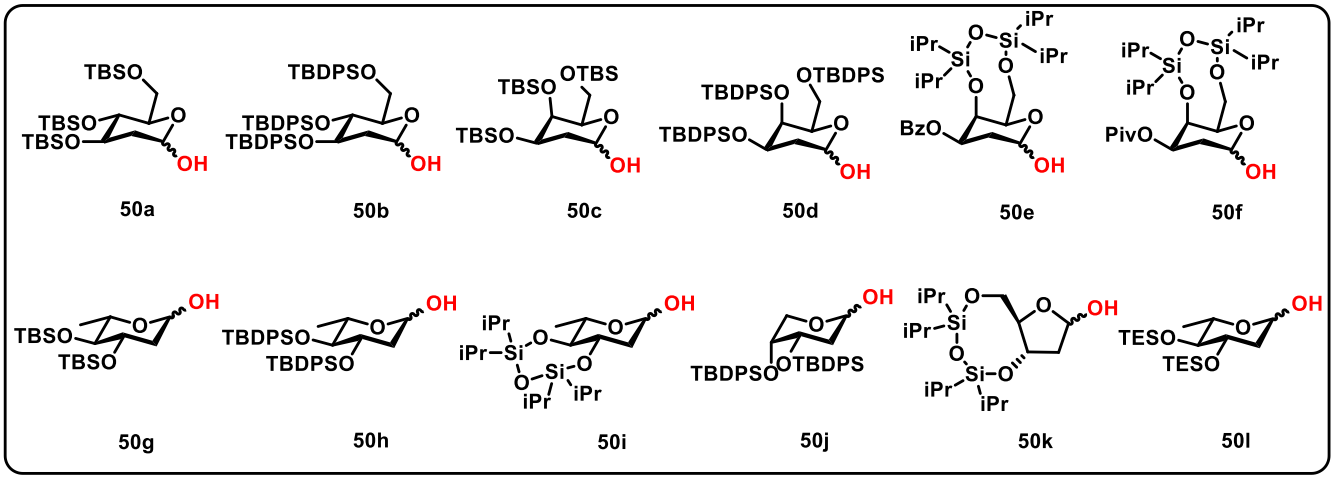
L-Rhamnal (500 mg, 3.84 mmol, 1.0 equiv) was dissolved 20 ml DMF. Then, imidazole (785 mg, 11.53 mmol, 3.0 equiv) followed by Et_3SiCl (1.9 ml, 11.53 mmol, 3.0 equiv) were added into it and allowed to stir for overnight. The reaction mixture was then concentrated and extracted with ethyl acetate (3x30 ml). The organic phase was washed with brine (100 ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude was purified by column chromatography (Merck 60-120 mesh, 20 gm) using hexane as solvent to give the product as a colourless oil. R_f- 0.5 in hexane, amount- 1.1 g, yield- 79%. ^{1}H NMR (400 MHz, CDCl3) δ 6.27 (dd, J = 6.1, 0.8 Hz, 1H), 4.67 (dd, J = 6.1, 2.8 Hz, 1H), 4.14 (dd, J = 4.6, 2.5 Hz, 1H), 3.90 – 3.83 (m, 1H), 3.54 (dd, J = 7.7, 5.7 Hz, 1H), 1.32 (d, J = 6.6 Hz, 3H), 0.97 (t, J = 7.9 Hz, 18H), 0.65 (dq, J = 16.0, 7.9 Hz, 12H). ^{13}C NMR (101 MHz, CDCl3) δ 143.4, 103.2, 75.6, 75.3, 70.3, 17.3, 6.9, 5.4, 5.2. HRMS (ESI-QTOF) $C_{18}H_{38}O_3Si_2Na$ $[M+Na]^+$- calculated- 381.2257; found- 381.2263. $[\alpha]_D^{22}$= 10 (*c* 0.5, $CHCl_3$).

Glycal **46a-d** and **46f-i** was prepared following previously reported procedures. Spectroscopic data were in agreement with the reported data. [18,20,49-52]

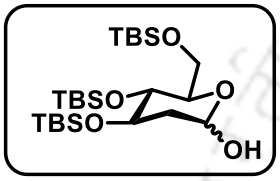
General Method to Synthesize Hemiacetals from Glycals:

Glycal (0.58-1.39 mmol, 1.0 equiv) and catalyst TTBPy·HCl (2 mol%) was taken in a round bottomed flask and the flask was then filled with dry DCM and water in 95:5 ratios (10 ml for 0.58 mmol). The mixtures were stirred and heated at 40 °C (using oil bath) in the sealed flask until the reaction was determined to be complete by either TLC or NMR analysis of the crude material. The reaction mixture was quenched by water (20 ml for 0.58 mmol) and it was extracted with DCM (3x15 ml for 0.58 mmol), dried over Na_2SO_4 and concentrated then concentrated in vacuo and purified by silica gel column chromatography (Merck 60-120 mesh, 20 gm).

2-Deoxy and 2,6-Dideoxy Hemiacetals Synthesized in this Method:

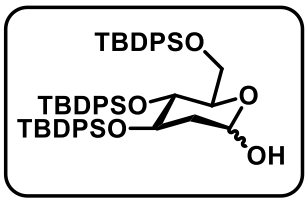


Synthesis of 3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-glucopyranose (50a):



General procedure was followed by taking 3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-glucal **46a** (500 mg, 1.0 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (6 mg, 0.0212 mmol, 2 mol%) in DCM: Water solvent (95:5, 10ml) for 24 h at 40°C to get the product as a colourless liquid. R_f- 0.9 in 20% EA/hexane, eluent 7% EA in hexane, amount- 373 mg, yield- 72%. α: β=1.8:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.26 (d, *J* = 2.8 Hz, 1.8H), 4.95 (dd, *J* = 9.4, 3.8 Hz, 1H), 4.31 (d, *J* = 7.7 Hz, 1H), 4.05 – 3.97 (m, 3H), 3.92 – 3.70 (m, 8.5H), 3.63 (t, *J* = 5.7 Hz, 1H), 3.44 (dt, *J* = 14.3, 6.4 Hz, 3H), 3.20 (s, 1.7H), 2.25 – 2.20 (m, 1H), 2.04 (dt, *J* = 13.0, 3.6 Hz, 2H), 1.62 (dd, *J* = 13.1, 6.3 Hz, 3.5H), 0.91 – 0.89 (m, 81H), 0.08 (td, *J* = 9.1, 3.2 Hz, 67H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 92.8, 91.1, 78.1, 75.4, 72.1, 70.6, 70.0, 63.9, 63.1, 38.5, 37.1, 30.9, 30.3, 29.7, 26.2, 26.08, 26.1, 26.0, 25.9, 25.6, 18.5, 18.3, 18.3, 18.2, 18.0, 18.0, -3.3, -3.4, -3.6, -3.7, -3.8, -4.3, -4.5, -4.6, -4.6, -5.1, -5.1, -5.2. HRMS (ESI-QTOF) $C_{24}H_{54}O_5Si_3Na$ $[M+Na]^+$- calculated- 529.3177; found- 529.3182. $[\alpha]_D^{22}$ = -19 (*c* 1.7, $CHCl_3$).

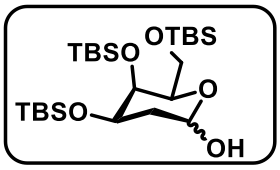
Synthesis of 3,4,6-tri-*O*-*tert*-butyldiphenylsilyl-D-glucopyranose (50b):



General procedure was followed by taking 3,4,6-tri-*O*-*tert*-butyldiphenylsilyl-D-glucal **46b** (500 mg, 0.58 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (4 mg, 0.0116 mmol, 2 mol%) in DCM: Water solvent (95:5, 10ml) for 24 h at 40°C to get the product as a colourless liquid. R_f- 0.9 in 20% EA/hexane, eluent 6% EA in hexane, amount- 347 mg, yield- 68%. α: β=3:1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 – 7.63 (m, 6H), 7.58 – 7.50 (m, 18H), 7.44 – 7.20 (m, 87H), 7.18 – 7.14 (m, 15H), 5.13 (d, *J* = 8.8 Hz, 1H), 5.01 (t, *J* = 6.4 Hz, 3H), 4.38 (d, *J* = 9.5 Hz, 1H), 4.25 (d, *J* = 3.3 Hz, 1H), 4.13 – 4.11 (m, 3H), 4.08 (d, *J* = 6.4 Hz, 1H), 4.02 (dd, *J* = 11.0, 8.0 Hz, 3H), 3.96 (d, *J* =

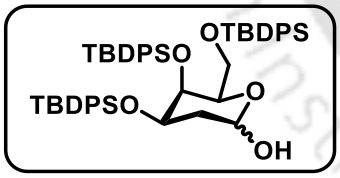
4.8 Hz, 1H), 3.90 (d, *J* = 2.5 Hz, 3H), 3.70 (s, 3H), 3.62 (dd, *J* = 11.1, 4.7 Hz, 3H), 2.46 (d, *J* = 6.2 Hz, 1H), 2.13 – 2.10 (m, 1H), 1.76 – 1.72 (m, 3H), 1.51 (dd, *J* = 10.4, 2.9 Hz, 3.8H), 0.99 (s, 26H), 0.98 (s, 9H), 0.93 (s, 26H), 0.93 (s, 9H), 0.87 (s, 9H), 0.79 (s, 26H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 135.8, 135.7, 135.7, 135.7, 135.6, 135.6, 135.6, 133.8, 133.6, 133.4, 133.2, 133.0, 133.0, 129.8, 129.6, 129.6, 129.6, 129.5, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5, 88.3, 80.9, 71.1, 70.2, 68.7, 62.6, 34.9, 29.7, 26.9, 26.9, 26.8, 26.8, 22.7, 19.1, 18.8, 14.1. HRMS (ESI-QTOF) $C_{54}H_{66}O_5Si_3Na$ $[M+Na]^+$- calculated- 901.4116; found- 901.4114. $[\alpha]_D^{22}$= -18 (*c* 1.2, $CHCl_3$).

Synthesis of 3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-galactopyranose (50c):



General procedure was followed by taking 3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-galactal **46c** (500 mg, 1.0 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (6 mg, 0.0212 mmol, 2 mol%) in DCM: Water solvent (95:5, 10ml) for 24 h at 40°C to get the product as a colourless liquid. R_f- 0.9 in 20% EA/hexane, eluent 8% EA in hexane, amount- 415 mg, yield- 80%. α: β=3.2:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (s, 3.2H), 4.76 – 4.71 (m, 1H), 4.11 (ddd, *J* = 11.6, 4.0, 2.3 Hz, 3.2H), 3.88 – 3.84 (m, 6.5H), 3.80 (s, 1H), 3.74 (dd, *J* = 10.0, 7.5 Hz, 1H), 3.69 – 3.62 (m, 3.2H), 3.47 (d, *J* = 7.7 Hz, 1H), 3.31 (t, *J* = 6.6 Hz, 1H), 3.00 (s, 3.2H), 2.12 – 2.05 (m, 3.3H), 1.96 – 1.88 (m, 1H), 1.83 (d, *J* = 2.9 Hz, 1H), 1.64 (dd, *J* = 12.5, 4.2 Hz, 3.4H), 0.92 – 0.89 (m, 112H), 0.12 – 0.06 (m, 75H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 94.6, 92.7, 76.5, 72.9, 71.4, 70.3, 68.8, 67.8, 62.8, 61.9, 37.3, 33.7, 30.9, 29.7, 26.2, 26.2, 26.2, 26.1, 25.9, 25.9, 18.6, 18.5, 18.3, 18.2, -3.9, -4.0, -4.4, -4.4, -4.7, -4.7, -4.9, -4.9, -5.3, -5.3. HRMS (ESI-QTOF) $C_{24}H_{54}O_5Si_3Na$ $[M+Na]^+$- calculated- 529.3177; found- 529.3182. $[\alpha]_D^{22}$= -19 (*c* 2.6, $CHCl_3$).

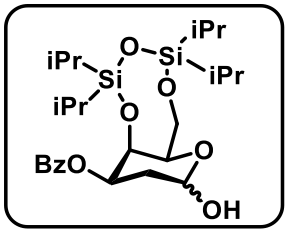
Synthesis of 3,4,6-tri-*O*-*tert*-butyldiphenylsilyl-D-galactopyranose (50d):



General procedure was followed by taking 3,4,6-tri-*O*-*tert*-butyldiphenylsilyl-D-galactal **46d** (500 mg, 0.58 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (4 mg, 0.0116 mmol, 2 mol%) in DCM: Water solvent (95:5, 10ml) for 24 h at 40°C to get the product as a colourless liquid. R_f- 0.9 in 20% EA/hexane, eluent 7% EA in hexane, amount- 378 mg, yield- 74%. Re-purification was done using HPLC (retention time- 7 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). α: β=2.5:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.50 (m, 24H), 7.37 – 7.09 (m, 92H), 4.18 (d, *J* = 7.5 Hz, 1H), 3.97 (d, *J* = 9.1 Hz, 2.6H), 3.84 (s, 2.6H), 3.60 – 3.43 (m, 7.2H), 3.27 (dd, *J* = 10.8, 4.0 Hz, 1H), 3.12 (s, 2.5H), 2.89 – 2.86 (m, 1H), 2.26 (s, 2.4H), 1.47 (d, *J* = 11.9 Hz, 2.4H), 0.96 (s, 9H), 0.94 (s, 27H), 0.91 (s, 9H), 0.82 (s, 23H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.5, 136.3, 136.2, 136.0, 136.0, 136.0, 135.8, 135.6, 135.5, 134.0, 133.7, 133.6, 133.5, 132.9, 132.8, 129.8, 129.6, 129.6, 129.5, 129.4, 129.4, 129.2, 127.6, 127.6, 127.5, 127.5, 127.5, 127.4, 127.2, 94.3, 77.6, 77.2, 72.6, 70.9,

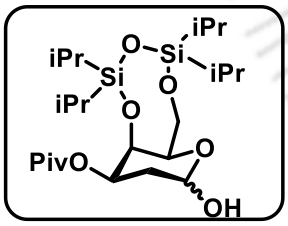
64.6, 36.9, 29.7, 27.2, 27.2, 27.2, 27.1, 26.9, 20.0, 19.0, 19.0, 18.9. HRMS (ESI-QTOF) $C_{54}H_{66}O_5Si_3NH_4$ $[M+NH_4]^+$- calculated- 896.4562; found- 896.4566. $[\alpha]_D^{22}$= -2 (*c* 0.5, $CHCl_3$).

Synthesis of 2-Deoxy-3-O-benzoyl-1,3-O-(tetraisopropyldisiloxane-1,3-diyl)-D-galactopyranose (50e):



General procedure was followed by taking 2,6-anhydro-5-deoxy-4-O-benzoyl-1,3-O-(tetraiso-propyldisiloxane-1,3-diyl)-D-arabino-hex-5-enitol **46e** (500 mg, 1.01 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (6 mg, 0.02 mmol, 2 mol%) in DCM: Water solvent (95:5, 10ml) for 24 h at 40°C to get the product as a colourless liquid. R_f- 0.5 in 20% EA/hexane, eluent 11% EA in hexane, amount- 352 mg, yield- 68%. Re-purification was done using HPLC (retention time- 6.5 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). α: β=2.2:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 5.5, 3.8 Hz, 6H), 7.57 (dd, *J* = 14.6, 7.3 Hz, 3.3H), 7.44 (dd, *J* = 14.3, 6.6 Hz, 6.2H), 5.56 – 5.51 (m, 2.2H), 5.45 (d, *J* = 2.7 Hz, 2.2H), 5.17 – 5.12 (m, 1H), 4.93 (d, *J* = 7.2 Hz, 1H), 4.50 (s, 2.2H), 4.40 (s, 1H), 4.19 (dd, *J* = 10.0, 5.7 Hz, 2.2H), 3.87 – 3.72 (m, 6.6H), 3.67 (dd, *J* = 9.5, 5.9 Hz, 1H), 2.41 (td, *J* = 12.4, 3.5 Hz, 2.2H), 2.24 – 2.15 (m, 1H), 2.10 (d, *J* = 10.3 Hz, 1H), 1.92 (dd, *J* = 12.3, 4.4 Hz, 2.3H), 1.12 – 1.03 (m, 67H), 0.97 – 0.83 (m, 18H), 0.77 (t, *J* = 7.7 Hz, 11H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 133.1, 132.9, 130.3, 130.0, 129.8, 129.8, 128.2, 128.1, 94.5, 92.5, 74.5, 71.9, 69.9, 69.5, 65.5, 64.3, 59.7, 59.4, 33.4, 30.0, 17.4, 17.4, 17.3, 17.3, 17.3, 17.1, 17.1, 13.6, 13.3, 13.3, 13.2, 13.2, 12.7. HRMS (ESI-QTOF) $C_{25}H_{42}O_7Si_2NH_4$ $[M+NH_4]^+$- calculated- 528.2813; found- 528.2826. $[\alpha]_D^{22}$= -54 (*c* 0.55, $CHCl_3$).

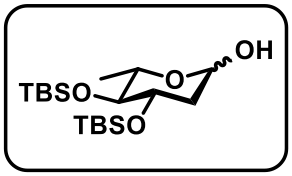
Synthesis of 2-Deoxy-3-O-pivaloyl-1,3-O-(tetraisopropyldisiloxane-1,3-diyl)-D-galactopyranose (50f):



General procedure was followed by taking 2,6-anhydro-5-deoxy-4-O-pivaloyl-1,3-O-(tetraiso-propyldisiloxane-1,3-diyl)-D-arabino-hex-5-enitol **46f** (500 mg, 1.06 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (6 mg, 0.0212 mmol, 2 mol%) in DCM: Water solvent (95:5, 10ml) for 24 h at 40°C to get the product as a colourless liquid. R_f- 0.5 in 20% EA/hexane, eluent 12% EA in hexane, amount- 369 mg, yield- 71%. α: β=1.4:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.30 (d, *J* = 2.8 Hz, 1.4H), 5.23 – 5.18 (m, 1.4H), 4.81 – 4.78 (m, 1H), 4.23 (s, 1.4H), 4.13 (d, *J* = 2.0 Hz, 1H), 4.03 (dd, *J* = 9.8, 5.9 Hz, 1.4H), 3.76 – 3.63 (m, 4.4H), 3.53 – 3.48 (m, 1H), 2.15 – 2.08 (m, 1.5H), 1.92 – 1.87 (m, 1H), 1.73 (dd, *J* = 12.2, 4.2 Hz, 2.2H), 1.19 – 1.13 (m, 22H), 1.03 – 0.85 (m, 74H).^{13}C NMR (101 MHz, $CDCl_3$) δ 178.3, 94.3, 92.4, 74.7, 71.7, 70.3, 69.2, 66.1, 64.9, 59.6, 59.4, 38.8, 33.2, 29.9, 27.1, 27.1, 17.8, 17.8, 17.7, 17.4, 17.4, 17.4, 17.3, 17.1, 17.1, 17.0, 13.6, 13.6, 13.4, 13.3, 13.2, 13.0, 12.8.

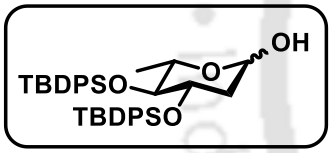
HRMS (ESI-QTOF) $C_{23}H_{46}O_7Si_2NH_4$ $[M+NH_4]^+$- calculated- 508.3126; found- 508.3118. $[\alpha]_D^{22}$= +17 (*c* 2.3, $CHCl_3$).

Synthesis of 3,4-di-*O*-*tert*-butyldimethylsilyl-L-rhamnopyranose (50g):



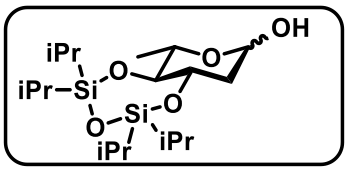
General procedure was followed by taking 3,4-di-*O*-*tert*-butyldimethylsilyl-L-rhamnal **46g** (500 mg, 1.39 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (8 mg, 0.0276 mmol, 2 mol%) in DCM: Water solvent (95:5, 10ml) for 16 h at 40°C to get the product as a colourless liquid. R_f- 0.5 in 20% EA/hexane, eluent 10% EA in hexane, amount- 378 mg, yield- 72%. α: β=1.6:1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.28 (d, *J* = 2.5 Hz, 1.6H), 4.86 – 4.83 (m, 1H), 4.01 (ddd, *J* = 10.4, 7.6, 4.5 Hz, 1.6H), 3.91 – 3.87 (m, 1.8H), 3.69 (ddd, *J* = 11.1, 7.7, 4.6 Hz, 1H), 3.40 (d, *J* = 6.7 Hz, 1H), 3.34 (dq, *J* = 12.8, 6.4 Hz, 1H), 3.19 (td, *J* = 8.1, 2.4 Hz, 2.6H), 2.24 (ddd, *J* = 12.7, 4.4, 2.0 Hz, 1H), 2.09 (ddd, *J* = 13.2, 4.2, 2.4 Hz, 1.6H), 1.67 (d, *J* = 8.0 Hz, 1.8H), 1.57 (ddd, *J* = 12.5, 10.9, 9.4 Hz, 1H), 1.30 (d, *J* = 6.4 Hz, 3H), 1.25 (d, *J* = 6.5 Hz, 4.8H), 0.93 – 0.91 (m, 36H), 0.11 (dt, *J* = 9.6, 5.1 Hz, 28H). Other spectroscopic data were in agreement with the reported data. [53]

Synthesis of 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnopyranose (50h):



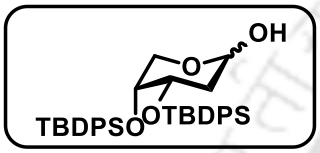
General procedure was followed by taking 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **46h** (500 mg, 0.82 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (5 mg, 0.0164 mmol, 2 mol%) in DCM: Water solvent (95:5, 10ml) for 16 h at 40°C to get the product as a colourless crystalline solid. R_f- 0.5 in 20% EA/hexane, eluent 10% EA in hexane, amount- 412 mg, yield- 80%. Re-purification was done using HPLC (retention time- 4.8 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). m. p. 98.5–100.2 °C. α: β=4:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.22 (m, 104H), 5.37 (s, 4H), 5.18 (d, *J* = 9.7 Hz, 1H), 4.50 (d, *J* = 9.8 Hz, 1H), 4.20 (d, *J* = 3.5 Hz, 1H), 4.09 (d, *J* = 2.6 Hz, 4H), 4.00 (q, *J* = 6.4 Hz, 4H), 3.73 (q, *J* = 7.2 Hz, 1H), 3.61 (s, 1H), 3.52 (s, 4H), 2.92 (s, 4H), 2.21 (dt, *J* = 14.0, 3.4 Hz, 1H), 1.85 – 1.78 (m, 4H), 1.77 – 1.72 (m, 4H), 1.20 (t, *J* = 6.8 Hz, 16H), 0.98 (s, 9H), 0.95 (s, 36H), 0.93 (s, 36H), 0.92 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.8, 135.7, 135.7, 135.7, 133.7, 133.6, 133.4, 133.3, 133.3, 132.6, 132.6, 130.0, 129.9, 129.8, 129.7, 129.6, 127.8, 127.8, 127.6, 127.6, 127.6, 92.4, 88.2, 74.7, 73.5, 72.4, 72.3, 72.0, 71.4, 35.6, 32.8, 29.7, 26.9, 26.8, 21.5, 19.1, 19.0, 18.9, 17.6. HRMS (ESI-QTOF) $C_{38}H_{48}O_4Si_2Na$ $[M+Na]^+$- calculated- 647.2989; found- 647.2994. $[\alpha]_D^{22}$= -8 (*c* 2.1, $CHCl_3$).

Synthesis of 2,6-Deoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranose (50i):



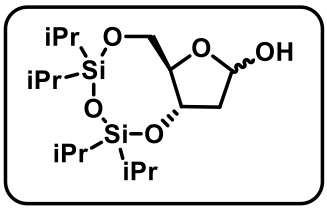
General procedure was followed by taking 3,4-O-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-1,2,6-trideoxy-L-arabino-1-hexenopyranose **46i** (500 mg, 1.34 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (8 mg, 0.0268 mmol, 2 mol%) in DCM: Water solvent (95:5, 10ml) for 16 h at 40°C to get the product as a colourless liquid. R_f- 0.5 in 20% EA/hexane, eluent 10% EA in hexane, amount- 409 mg, yield- 78%. α: β=1.5:1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.31 (s, 1.5H), 4.84 – 4.82 (m, 1H), 4.08 – 4.04 (m, 1.5H), 3.90 (dq, *J* = 12.6, 6.2 Hz, 1.5H), 3.79 (d, *J* = 6.4 Hz, 1H), 3.74 – 3.70 (m, 1H), 3.33 (td, *J* = 12.4, 6.1 Hz, 1H), 3.25 (t, *J* = 9.0 Hz, 2.5H), 3.06 (d, *J* = 1.8 Hz, 1H), 2.24 (dd, *J* = 12.8, 5.0 Hz, 1H), 2.13 (dd, *J* = 13.4, 5.2 Hz, 1.5H), 1.70 (t, *J* = 12.4 Hz, 1.7H), 1.61 (dd, *J* = 22.7, 11.6 Hz, 1.2H), 1.33 (d, *J* = 6.1 Hz, 3H), 1.28 (d, *J* = 6.2 Hz, 5H), 1.09 – 0.94 (m, 74H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 93.0, 91.1, 79.1, 78.2, 72.7, 71.5, 69.9, 67.1, 40.3, 37.5, 17.1, 17.1, 16.6, 16.4, 16.4, 16.4, 16.4, 16.3, 16.3, 16.2, 12.0, 11.9, 11.9, 11.3, 11.2. HRMS (ESI-QTOF) $C_{18}H_{39}O_5Si_2$ $[M+H]^+$- calculated- 391.2336; found- 391.2374. $[\alpha]_D^{22}$= -7 (*c* 0.6, $CHCl_3$).

Synthesis of 3,4-di-*O*-*tert*-butyldiphenylsilyl-D-arabinopyranose (50j):



General procedure was followed by taking 3,4-di-*O*-*tert*-butyldiphenylsilyl-D-arabinal **46j** (500 mg, 0.84 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (5 mg, 0.0168 mmol, 2 mol%) in DCM: Water solvent (95:5) for 16 h at 40°C to get the product as a colourless liquid. R_f- 0.5 in 20% EA/hexane, eluent 10% EA in hexane, amount- 422 mg, yield- 82%. α: β=1.2:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.60 (m, 15H), 7.45 – 7.22 (m, 28H), 5.21 (d, *J* = 2.9 Hz, 1.2H), 4.71 (d, *J* = 9.5 Hz, 1H), 4.18 (d, *J* = 8.1 Hz, 2H), 3.99 (dd, *J* = 11.5, 8.2 Hz, 1H), 3.80 – 3.79 (m, 1.2H), 3.67 (dt, *J* = 7.7, 3.1 Hz, 1H), 3.58 (dd, *J* = 11.3, 5.6 Hz, 1.2H), 3.44 (dd, *J* = 11.6, 2.2 Hz, 1.2H), 3.10 (dd, *J* = 11.6, 3.4 Hz, 1H), 2.14 – 2.09 (m, 1.2H), 2.00 (ddd, *J* = 13.4, 6.4, 4.0 Hz, 1H), 1.54 – 1.52 (m, 1H), 1.37 – 1.32 (m, 1.6H), 1.10 (s, 8H), 1.10 (s, 10H), 1.07 (s, 10H), 0.99 (s, 8H).^{13}C NMR (101 MHz, $CDCl_3$) δ 136.1, 136.0, 136.0, 135.9, 135.9, 135.8, 134.3, 134.2, 133.9, 133.8, 133.5, 133.3, 133.0, 132.8, 130.0, 129.8, 129.7, 129.7, 129.6, 129.5, 127.8, 127.7, 127.6, 127.6, 127.6, 127.5, 92.6, 71.7, 70.9, 70.1, 68.7, 63.8, 36.5, 31.9, 30.88, 29.3, 27.1, 27.1, 27.0, 27.0, 19.3, 19.3, 19.1, 14.1. HRMS (ESI-QTOF) $C_{37}H_{46}O_4Si_2Na$ $[M+Na]^+$- calculated- 633.2832; found- 633.2821. $[\alpha]_D^{22}$= -13 (*c* 2.4, $CHCl_3$).

Synthesis of 1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyl-disiloxane-1,3-diyl)-D-ribofuranose (50k):



General procedure was followed by taking 1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyl-disiloxane-1,3-diyl)-D-erythro-pent-1-entiol **46k** (500 mg, 1.39 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (8 mg, 0.0276 mmol, 2 mol%) in DCM: Water solvent (95:5) for 16 h at 40°C to get the product as a colourless liquid. R_f- 0.5 in 20% EA/hexane, eluent 10% EA in hexane, amount- 367 mg, yield- 70%. α: β=2.7:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (d, *J* = 10.4 Hz,

2.7H), 5.25 (s, 1H), 5.07 (dd, *J* = 10.4, 1.5 Hz, 2.7H), 4.55 (s, 2.7H), 4.44 – 4.41 (m, 1H), 4.09 – 4.01 (m, 3.8H), 3.96 (t, *J* = 10.5 Hz, 2.9H), 3.89 (dd, *J* = 11.4, 3.3 Hz, 1H), 3.71 (dd, *J* = 11.4, 6.9 Hz, 1H), 3.61 (dd, *J* = 10.7, 4.0 Hz, 2.9H), 3.55 (d, *J* = 4.9 Hz, 2.6H), 2.14 – 2.06 (m, 3.9H), 1.95 – 1.90 (m, 2.9H), 1.78 – 1.75 (m, 1H), 1.41 – 1.26 (m, 16H), 1.08 – 0.88 (m, 103H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 92.7, 91.6, 71.0, 70.9, 70.7, 68.9, 65.3, 64.2, 58.8, 42.0, 36.9, 35.7, 30.1, 29.1, 23.4, 23.1, 17.6, 17.5, 17.5, 17.5, 17.4, 17.3, 17.2, 17.2, 17.2, 17.1, 17.1, 14.1, 14.0, 13.7, 13.6, 13.3, 13.1, 12.9, 12.7, 11.1. HRMS (ESI-QTOF) $C_{17}H_{36}O_5Si_2Na$ $[M+Na]^+$- calculated- 399.1999; found- 399.1973. $[\alpha]_D^{22}$= -8 (*c* 2.1, $CHCl_3$).

Synthesis of 3,4-di-O-triethylsilyl-L-Rhammopyranose (50l):

3,4-di-O-triethylsilyl-L-Rhamnal **46l** (500 mg, 1.39 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (8 mg, 0.0268 mmol, 5 mol%) in DCM: Water solvent (95:5, 10ml) was taken in a round bottom flask and was stirred at room temperature. After 15 min, the starting material was consumed (monitored by TLC). The reaction was quenched by Et_3N (2 mL) and purified through neutral alumina column chromatography to get the product as a colourless liquid. R_f- 0.8 in 20% EA/hexane, eluent 8% EA in hexane, amount- 220 mg, yield- 42%. α: β=1.3:1. ^{1}H NMR (400 MHz, CDCl3) δ 5.26 (bs, 1.3H), 4.82 – 4.78 (m, 1H), 3.96 (ddd, J = 11.0, 8.1, 4.8 Hz, 1.3H), 3.85 (dq, J = 12.7, 6.3 Hz, 1.3H), 3.63 (ddd, J = 11.4, 8.0, 4.9 Hz, 1H), 3.33 – 3.26 (m, 1.8H), 3.16 (t, J = 8.4 Hz, 2.3H), 2.62 (s, 1H), 2.23 (ddd, J = 12.5, 4.8, 2.0 Hz, 1H), 2.09 (ddd, J = 13.0, 4.8, 1.6 Hz, 1.3H), 1.60 (d, J = 2.4 Hz, 1H), 1.58 – 1.50 (m, 1.3H), 1.29 (d, J = 6.2 Hz, 3H), 1.23 (d, J = 6.4 Hz, 4H), 0.97 (td, J = 7.8, 2.3 Hz, 41H), 0.69 – 0.61 (m, 28H). ^{13}C NMR (101 MHz, CDCl3) δ 93.6, 91.8, 78.7, 78.1, 77.2, 72.7, 72.7, 70.1, 69.1, 41.8, 39.1, 29.7, 18.5, 18.4, 7.0, 7.0, 6.9, 6.9, 5.3, 5.3, 5.3. HRMS (ESI-QTOF) $C_{18}H_{40}O_4Si_2Na$ $[M+Na]^+$- calculated- 399.2363; found- 399.2375. $[\alpha]_D^{22}$= -10 (*c* 1.8, $CHCl_3$).

Equilibrium Anomeric Ratios of Various Silyl Protected 2-Deoxy Glycosyl Hemiacetals

General Procedure: 0.022- 0.103 mmol of 2-deoxy hemiacetals (**50a**, **50c**, **50e-j**) were dissolved in 0.6 mL $CDCl_3$ respectively in NMR tubes under inert conditions and were sealed using the NMR septa. Each sample was subjected to heating at 55° C with periodical monitoring of their ^{1}H NMR spectra until the equilibrium has been achieved.

Equilibrium Anomeric Ratio of various Donors:

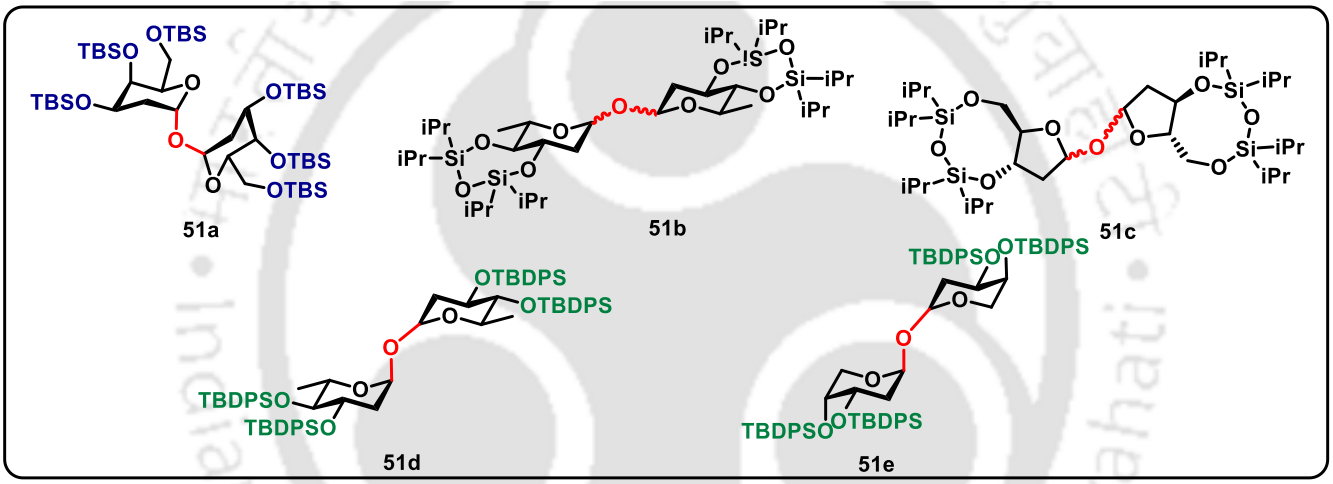
2-Deoxy Glycosyl Hemiacetals	Concentration	Equilibrium Anomeric Ratio
50a	0.067 mmol	64:36
50c	0.103 mmol	78:22
50e	0.022 mmol	72:28
50f	0.092 mmol	50:50
50g	0.056 mmol	62:38
50h	0.067 mmol	82:18

50i	0.031 mmol	63:37
50j	0.077 mmol	55:45

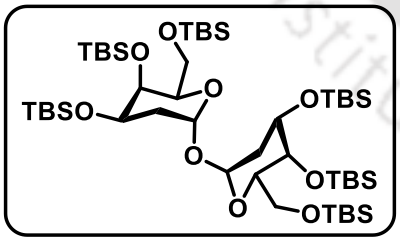
General Method to Synthesize 2-deoxy trehalose from Glycals:

Glycal (0.82-1.39 mmol, 1.0 equiv) and catalyst TTBPy·HCl (10 mol%) was taken in a round bottomed flask and the flask was then filled with dry DCM and water in 99:1 ratio (10 ml for 0.82 mmol). The mixtures were stirred at room temperature in the sealed flask until the reaction was determined to be complete by either TLC or NMR analysis of the crude material. The reaction mixture was quenched by water (20 ml for 0.82 mmol) and it was extracted with DCM (3x15 ml for 0.82 mmol), dried over Na_2SO_4 and concentrated then concentrated in vacuo and purified by column chromatography (Merck 60-120 mesh, 20 gm).

2-deoxy trehalose Synthesized in this Method:



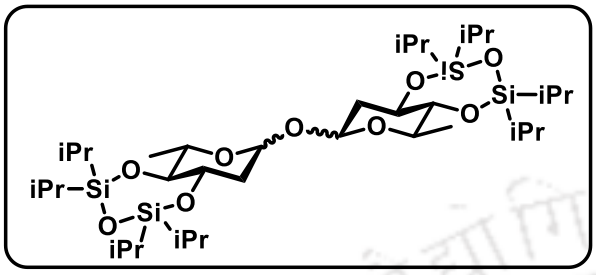
Synthesis of (3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-galactopyranosyl)-(1→1)-3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-galactopyranoside (51a):



General procedure was followed by taking 3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-galactal **46c** (500 mg, 1.0 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (29 mg, 0.102 mmol, 10 mol%) in DCM: Water solvent (99:1) for 5 h to get the product as a colourless liquid. R_f- 0.8 in 10% EA/hexane, eluent 2% EA in hexane, amount- 845 mg, yield- 83%. αα isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.16 (d, *J* = 2.6 Hz, 1H), 4.05 – 4.00 (m, 1H), 3.84 (s, 1H), 3.68 – 3.58 (m, 3H), 2.14 (td, *J* = 12.2, 3.4 Hz, 1H), 1.53 (dd, *J* = 12.2, 4.0 Hz, 1H), 0.92 (s, 9H), 0.90 (s, 9H), 0.88 (s, 9H), 0.11 (s, 3H), 0.08 – 0.07 (m, 9H), 0.04 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 93.7, 73.1, 70.2, 68.3, 62.4,

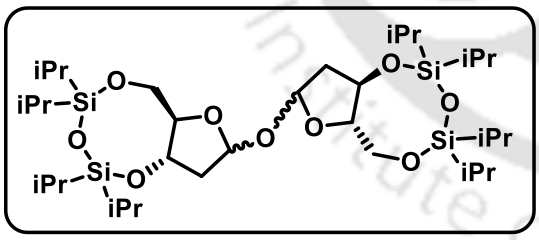
26.9, 26.2, 26.1, 25.8, 18.6, 18.2, -4.0, -4.5, -4.8, -4.9, -5.2, -5.3. HRMS (ESI-QTOF) $C_{48}H_{106}O_9Si_6Na$ $[M+Na]^+$- calculated- 1017.6350; found- 1017.6392. $[\alpha]_D^{22}$= +34 (*c* 3.4, $CHCl_3$).

Synthesis of (2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranosyl) -(1→1)-2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranoside (51b):



General procedure was followed by taking 3,4-O-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-1,2,6-trideoxy-L-arabino-1-hexenopyranose **46i** (500 mg, 1.34 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (38 mg, 0.134 mmol, 10 mol%) in DCM: Water solvent (99:1) for 5 h to get the product as a colourless crystalline solid. R_f- 0.5 in 10% EA/hexane, eluent 3% EA in hexane, amount- 809 mg, yield- 79%. m. p. 164.8–166.4 °C. αα: αβ= 1.7:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.11 (d, *J* = 2.6 Hz, 1.7H), 5.08 (d, *J* = 3.3 Hz, 1H), 4.66 (dd, *J* = 10.0, 1.7 Hz, 1H), 4.04 – 3.96 (m, 2.8H), 3.92 (dt, *J* = 12.4, 6.2 Hz, 1H), 3.72 – 3.66 (m, 1H), 3.60 (dt, *J* = 15.1, 6.2 Hz, 1.8H), 3.28 – 3.22 (m, 5H), 2.17 – 2.11 (m, 1.7H), 2.09 – 2.02 (m, 2H), 1.79 – 1.64 (m, 4H), 1.32 (d, *J* = 5.4 Hz, 3H), 1.26 (dd, *J* = 11.1, 6.4 Hz, 10H), 1.08 – 0.91 (m, 104H).^{13}C NMR (101 MHz, $CDCl_3$) δ 99.2, 97.9, 92.5, 80.0, 79.8, 79.2, 74.0, 72.5, 71.3, 71.2, 68.7, 68.5, 40.0, 38.5, 38.1, 18.1, 17.6, 17.5, 17.4, 17.4, 17.3, 17.3, 17.3, 17.2, 13.0, 12.9, 12.9, 12.6, 12.3, 12.3, 12.2, 12.2, 12.2. 18.9. HRMS (ESI-QTOF) $C_{36}H_{74}O_9Si_4NH_4$ $[M+NH_4]^+$- calculated- 780.4754; found- 780.4758. $[\alpha]_D^{22}$= +52 (*c* 1.3, $CHCl_3$).

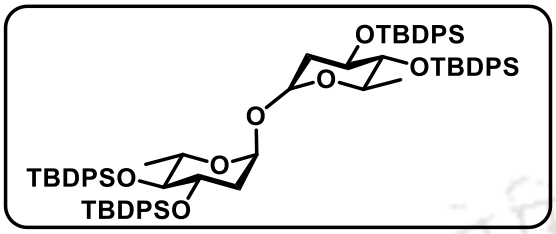
Synthesis of (1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyld-isiloxane-1,3-diyl)-D-ribofuranosyl) -(1→1)-1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyld-isiloxane-1,3-diyl)-D-ribofuranoside (51c):



General procedure was followed by taking 1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyl-disiloxane-1,3-diyl)-D-erythro-pent-1-entiol **46k** (500 mg, 1.39 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (40 mg, 0.138 mmol, 10 mol%) in DCM: Water solvent (99:1) for 5 h to get the product as a colourless liquid. R_f- 0.5 in 10% EA/hexane, eluent 2% EA in hexane, amount- 810 mg, yield- 79%. αα: αβ= 3:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 – 5.76 (m, 1H), 5.74 – 5.71 (m, 1H), 5.43 (dd, *J* = 5.1, 2.4 Hz, 3H), 4.88 (s, 4H), 4.42 – 4.39 (m, 3H), 4.09 – 4.08 (m, 3H), 3.93 – 3.92 (m, 1H), 3.90 (d, *J* = 3.0 Hz, 1H), 3.73 – 3.70 (m, 3H), 3.67 (dd, *J* = 8.6, 1.7 Hz, 3H), 2.66 (d, *J* = 8.1 Hz, 1H), 2.08 (ddd, *J* = 12.8, 8.0, 2.5 Hz, 4H), 1.81 – 1.75 (m, 3H), 1.07 – 0.93 (m, 185H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 128.2, 126.9, 126.4, 125.9, 125.5, 92.5, 70.7, 69.1, 64.4, 64.3, 38.1, 29.7, 17.6, 17.5, 17.5, 17.5, 17.3, 17.3, 17.3, 17.2, 17.1, 17.1, 17.1, 13.6, 13.4, 13.3, 13.2, 13.1, 13.0, 12.9.

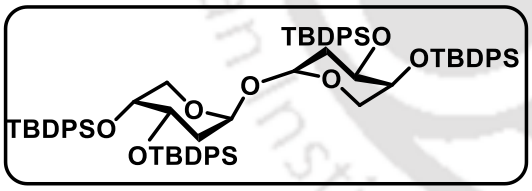
HRMS (ESI-QTOF) $C_{34}H_{74}O_9Si_4N$ $[M+NH_4]^+$- calculated- 752.4441; found- 752.4445. $[\alpha]_D^{22}$= -19 (*c* 0.5, $CHCl_3$).

Synthesis of (3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnopyranosyl) -(1→1)-3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnopyranoside (51d):



General procedure was followed by taking 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **46h** (500 mg, 0.82 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (25 mg, 0.082 mmol, 10 mol%) in DCM: Water solvent (99:1) for 5 h to get the product as a colourless liquid. R_f- 0.5 in 10% EA/hexane, eluent 3% EA in hexane, amount- 650 mg, yield- 64%. Re-purification was done using HPLC (retention time- 8 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). αα isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 6.7 Hz, 2H), 7.50 (t, *J* = 8.0 Hz, 6H), 7.39 – 7.34 (m, 6H), 7.31 – 7.21 (m, 10H), 5.31 (dd, *J* = 7.8, 3.5 Hz, 1H), 4.11 (d, *J* = 2.7 Hz, 1H), 3.86 – 3.80 (m, 1H), 3.55 (t, *J* = 3.4 Hz, 1H), 1.92 (d, *J* = 2.6 Hz, 1H), 1.72 (dt, *J* = 13.5, 3.7 Hz, 1H), 1.10 (d, *J* = 6.9 Hz, 3H), 0.94 (s, 9H), 0.94 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.0, 135.8, 135.8, 135.7, 135.5, 134.0, 133.8, 133.8, 133.6, 129.6, 129.6, 129.5, 129.4, 127.5, 127.5, 127.5, 127.4, 91.0, 74.9, 72.8, 72.5, 34.3, 27.2, 27.0, 26.9, 26.9, 19.3, 19.1, 18.2. HRMS (ESI-QTOF) $C_{76}H_{94}O_7Si_4NH_4$ $[M+NH_4]^+$- calculated- 1248.6420; found- 1248.6423. $[\alpha]_D^{22}$= -5 (*c* 0.5, $CHCl_3$).

Synthesis of (3,4-di-*O*-*tert*-butyldiphenylsilyl-D-arabinopyranosyl) -(1→1)-3,4-di-*O*-*tert*-butyldiphenylsilyl-D-arabinopyranoside (51e):

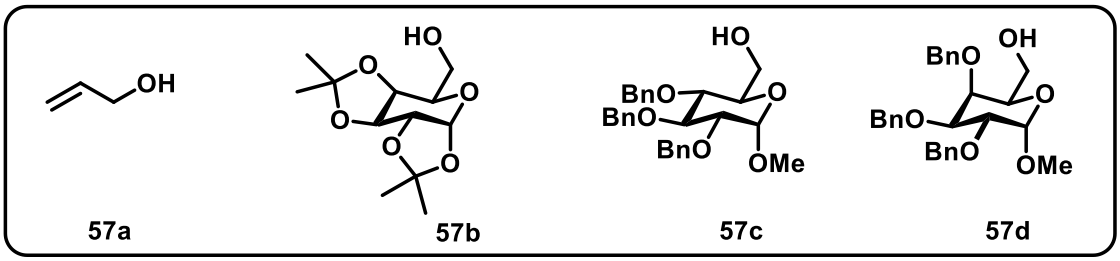


General procedure was followed by taking 3,4-di-*O*-*tert*-butyldiphenylsilyl-D-arabinal **46j** (500 mg, 0.84 mmol, 1.0 equiv) and 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (24 mg, 0.084 mmol, 10 mol%) in DCM: Water solvent (99:1) for 5 h to get the product as a colourless liquid. R_f- 0.5 in 10% EA/hexane, eluent 3% EA in hexane, amount- 761 mg, yield- 75%. Re-purification was done using HPLC (retention time- 9 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). Selectivity ββ: αα= 6:1. ββ isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.0 Hz, 2H), 7.76 (d, *J* = 6.6 Hz, 2H), 7.56 – 7.28 (m, 11H), 7.21 – 7.167(m, 1H), 7.11 (t, *J* = 7.2 Hz, 2H), 6.93 (d, *J* = 7.0 Hz, 2H), 4.77 (s, 1H), 3.77 (s, 1H), 3.52 (d, *J* = 9.4 Hz, 1H), 3.00 (d, *J* = 11.5 Hz, 1H), 2.62 (d, *J* = 11.9 Hz, 1H), 2.09 (t, *J* = 10.8 Hz, 1H), 1.11 (s, 9H), 1.06 (d, *J* = 5.1 Hz, 1H), 0.98 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.3, 136.1, 135.9, 135.8, 135.7, 135.7, 135.6, 134.8, 134.8, 134.1, 133.9, 133.7, 129.6, 129.6, 129.5, 129.4, 127.7, 127.6, 127.5, 127.4, 127.3, 95.2, 77.2, 70.8, 67.2, 63.4, 33.8, 29.7, 27.1, 27.0, 26.9, 26.7, 26.6, 19.5, 18.9. HRMS (ESI-QTOF) $C_{74}H_{90}O_7Si_4NH_4$ $[M+NH_4]^+$- calculated- 1220.6107; found- 1220.6112. $[\alpha]_D^{22}$= -34 (*c* 1.3, $CHCl_3$).

General Method for Glycosylation:

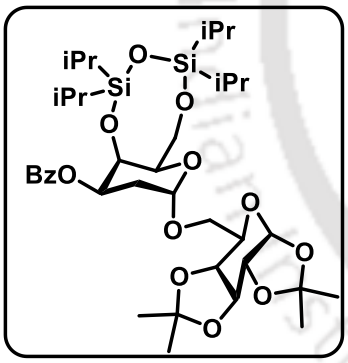
Hemi acetal donor (0.06-0.13 mmol, 1.0 equiv), glycosyl acceptor (0.09-0.20 mmol, 1.1-1.5 equiv) and catalyst pyrrolidine.HCl (20 mol%) was taken in a round bottomed flask and the flask was then filled with dry toluene (0.5 ml for 0.06 mmol donor). The mixtures were stirred and refluxed at 100 °C (using oil bath) in the sealed flask until the reaction was determined to be complete by either TLC or NMR analysis of the crude material. The reaction mixture was quenched by water (20 ml for 0.06 mmol donor) and it was extracted with DCM (3x15 ml for 0.06 mmol donor), dried over Na_2SO_4 and concentrated then concentrated in vacuo and purified by column chromatography (Merck 60-120 mesh, 7 gm) and HPLC (using HPLC-grade acetonitrile solvent, flow rate- 5 ml/min).

Acceptors Used in this Method:



57a 57b 57c 57d

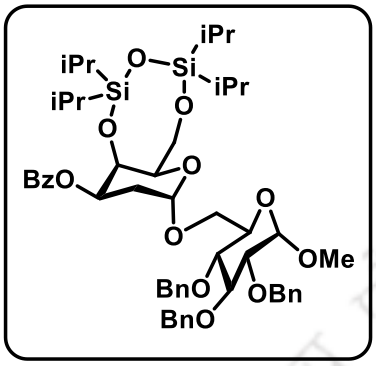
Synthesis of (4,6-di-O-tetraisopropyldisiloxane-1,3-diyl-3-O-benzoyl-2-deoxy-α-D-galactosyl) -(1→6)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranoside (55a):



General procedure was followed by adding glycosyl donor **50e** (50 mg, 0.10 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst (2 mg, 0.019 mmol, 20 mol%) and glycosyl acceptor **57b** (36 mg, 0.15 mmol, 1.5 equiv) at 100°C for 24 h to get the product as a colourless liquid **55a**. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 45 mg, yield- 62%. Re-purification was done using HPLC (retention time- 8 min). Selectivity α. α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.95 (m, 2H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 2H), 5.46 (d, *J* = 5.0 Hz, 1H), 5.41 – 5.36 (m, 1H), 4.96 (d, *J* = 2.9 Hz, 1H), 4.55 (dd, *J* = 7.9, 2.3 Hz, 1H), 4.42 (s, 1H), 4.24 (dd, *J* = 5.0, 2.4 Hz, 1H), 4.21 (dd, *J* = 7.9, 1.8 Hz, 1H), 3.90 (dt, *J* = 7.1, 4.0 Hz, 2H), 3.77 – 3.66 (m, 3H), 3.58 (dd, *J* = 9.9, 7.8 Hz, 1H), 2.34 (td, *J* = 12.4, 3.6 Hz, 1H), 1.86 (dd, *J* = 12.1, 4.5 Hz, 1H), 1.50 (s, 3H), 1.37 (s, 3H), 1.27 (s, 6H), 0.99 (ddd, *J* = 15.6, 11.5, 6.4 Hz, 21H), 0.89 – 0.80 (m, 4H), 0.67 (bs, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ 166.3, 132.9, 130.3, 129.7, 128.1, 109.2, 108.6, 97.8, 96.3, 70.8, 70.6, 70.6, 70.0, 69.9, 65.9, 65.5, 65.3, 59.6, 29.9, 26.1, 26.0, 24.9, 24.5, 17.4, 17.4, 17.4, 17.3, 17.3, 17.3, 17.1, 17.1, 13.6, 13.3,

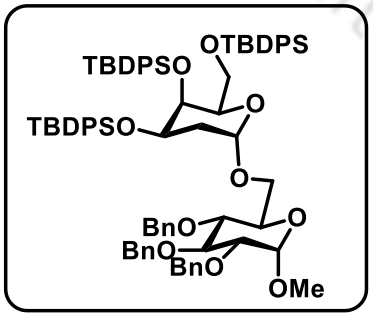
13.1, 12.7. HRMS (ESI-QTOF) $C_{37}H_{60}O_{12}Si_2NH_4$ $[M+NH_4]^+$- calculated- 770.3967; found- 770.3978. $[\alpha]_D^{22}$= 11 (*c* 2.0, $CHCl_3$).

Synthesis of Methyl 2,3,4-tri-O-benzyl-6-O-(4,6-di-O-tetraisopropyldisiloxane-1,3-diyl-3-O-benzoyl-2-deoxy-α-D-galactosyl)-α-D-glucopyranoside (55b):



General procedure was followed by adding glycosyl donor **50e** (50 mg, 0.10 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst (2 mg, 0.019 mmol, 20 mol%) and glycosyl acceptor **57c** (36 mg, 0.15 mmol, 1.5 equiv) at 100°C for 24 h to get the product as a colourless liquid **55b**. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 68 mg, yield- 73%. Re-purification was done using HPLC (retention time- 11 min). Selectivity α. α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.2 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.37 – 7.26 (m, 15H), 5.44 – 5.40 (m, 1H), 5.03 – 4.95 (m, 2H), 4.81 (dd, *J* = 14.2, 11.6 Hz, 2H), 4.68 – 4.60 (m, 1H), 4.48 (s, 1H), 4.00 (t, *J* = 9.2 Hz, 1H), 3.94 (dd, *J* = 9.9, 5.5 Hz, 1H), 3.82 – 3.74 (m, 3H), 3.70 – 3.65 (m, 2H), 3.56 – 3.49 (m, 2H), 3.38 (s, 3H), 2.40 (td, *J* = 12.3, 3.4 Hz, 1H), 1.91 (dd, *J* = 12.3, 4.3 Hz, 1H), 1.09 – 1.01(m, 19H), 0.95 – 0.72 (m, 10H).^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 138.7, 138.2, 132.9, 130.4, 129.7, 128.4, 128.4, 128.4, 128.3, 128.1, 128.1, 127.9, 127.9, 127.7, 127.5, 104.6, 97.9, 82.2, 80.1, 78.0, 77.9, 77.2, 75.7, 75.6, 75.0, 75.0, 74.7, 74.6, 73.4, 70.0, 69.9, 69.8, 65.9, 65.8, 65.4, 65.3, 59.5, 57.1, 55.2, 29.9, 17.4, 17.4, 17.3, 17.3, 17.1, 17.1, 13.6, 13.3, 13.1, 12.7. HRMS (ESI-QTOF) $C_{53}H_{72}O_{12}Si_2NH_4$ $[M+NH_4]^+$- calculated- 974.4906; found- 974.4921. $[\alpha]_D^{22}$= 63 (*c* 0.4, $CHCl_3$).

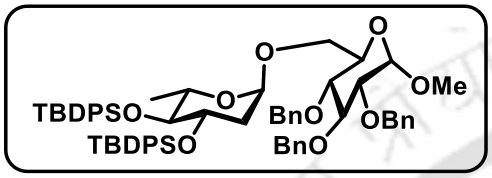
Synthesis of Methyl 2,3,4-tri-O-benzyl-6-O-(3,4,6-tri-O-*tert*-butyldiphenylsilyl-2-deoxy-α-D-galactopyranosyl)-α-D-glucopyranoside (55c):



General procedure was followed by adding glycosyl donor **50d** (50 mg, 0.06 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst (2 mg, 0.012 mmol, 20 mol%) and glycosyl acceptor **57c** (26 mg, 0.09 mmol, 1.5 equiv) at 100°C for 24 h to get the product as a colourless liquid **55c**. R_f- 0.9 in 10% EA/hexane, eluent 2% EA in hexane, amount- 54 mg, yield- 71%. Re-purification was done using

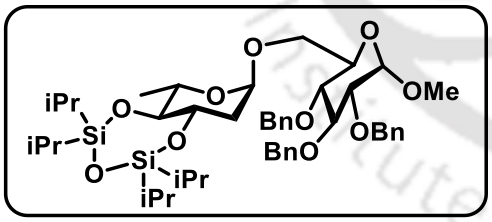
HPLC (retention time- 15 min). Selectivity α:β= 8:1. α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.60 (m, 2H), 7.53 – 7.51 (m, 2H), 7.30 (qdd, *J* = 9.7, 8.4, 5.7 Hz, 40H), 7.14 – 7.03 (m, 6H), 5.06 (dd, *J* = 8.8, 2.7 Hz, 1H), 4.96 (d, *J* = 10.9 Hz, 1H), 4.88 (dd, *J* = 10.6, 4.1 Hz, 2H), 4.78 (dd, *J* = 14.3, 11.1 Hz, 2H), 4.67 (d, *J* = 12.2 Hz, 1H), 4.62 (d, *J* = 3.5 Hz, 1H), 4.37 (d, *J* = 9.8 Hz, 1H), 4.00 – 3.96 (m, 4H), 3.70 (d, *J* = 6.8 Hz, 2H), 3.61 (d, *J* = 10.4 Hz, 2H), 3.54 – 3.51 (m, 1H), 3.39 (d, *J* = 7.6 Hz, 1H), 3.36 (s, 3H), 1.92 – 1.86 (m, 1H), 1.68 – 1.64 (m, 1H), 0.98 (s, 9H), 0.82 (s, 9H), 0.77 (s, 9H). Other Spectroscopic data is in agreement with the reported data. [20]

Synthesis of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α-L-rhamnosyl)-α-D-glucopyranoside (55d):



General procedure was followed by adding glycosyl donor **50h** (50 mg, 0.08 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst (2 mg, 0.016 mmol, 20 mol%) and glycosyl acceptor **57c** (56 mg, 0.12 mmol, 1.5 equiv) at 100°C for 24 h to get the product as a colourless liquid **55d**. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 49 mg, yield- 57%. Re-purification was done using HPLC (retention time- 12 min). Selectivity α. α-anomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 6.8 Hz, 2H), 7.44 (dd, *J* = 11.7, 7.1 Hz, 5H), 7.38 – 7.18 (m, 30H), 4.99 (d, *J* = 10.9 Hz, 1H), 4.96 (dd, *J* = 7.9, 3.6 Hz, 1H), 4.83 – 4.79 (m, 3H), 4.67 (d, *J* = 12.2 Hz, 1H), 4.61 (d, *J* = 3.5 Hz, 1H), 4.49 (d, *J* = 10.7 Hz, 1H), 4.11 (d, *J* = 3.6 Hz, 1H), 4.01 – 3.98 (m, 2H), 3.88 – 3.84 (m, 1H), 3.77 (dd, *J* = 10.0, 3.3 Hz, 1H), 3.61 (dd, *J* = 11.1, 4.9 Hz, 1H), 3.54 (ddd, *J* = 14.3, 6.9, 3.5 Hz, 1H), 3.50 – 3.47 (m, 1H), 3.35 (s, 3H), 1.90 (ddd, *J* = 13.3, 8.0, 2.7 Hz, 1H), 1.68 – 1.64 (m, 1H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.86 (s, 9H). Other Spectroscopic data is in agreement with the reported data. [20]

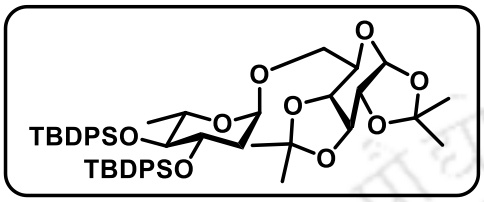
Synthesis of Methyl 2,3,4-tri-O-benzyl-6-O-(2,6-deoxy-3,4-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-α-L-erythro-hexapyranosyl)-α-D-glucopyranoside (55e):



General procedure was followed by adding glycosyl donor **50i** (50 mg, 0.13 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst (3 mg, 0.027 mmol, 20 mol%) and glycosyl acceptor **57c** (89 mg, 0.20 mmol, 1.5 equiv) at 100°C for 24 h to get the product as a colourless liquid **55e**. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 63 mg, yield- 59%. Re-purification was done using HPLC (retention time- 11 min). Selectivity α:β= 8.5:1. α-anomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 – 7.18 (m, 17H), 4.93 – 4.70 (m, 6H), 4.61 (dd, *J* = 25.4, 11.5 Hz, 1H), 4.51 – 4.45 (m, 2H), 3.91 (ddd, *J* = 14.4, 13.0, 7.3 Hz, 2H), 3.81 (t, *J* = 9.9 Hz, 1H), 3.65 – 3.52 (m, 2H), 3.43 (dt, *J* = 7.8, 4.8 Hz, 1H), 3.33 (dt, *J* = 9.0, 5.8 Hz, 1H), 3.29 (s, 3H), 3.15 (q, *J* = 8.8 Hz, 1H), 2.01 (dd, *J* = 13.1, 5.1 Hz, 1H), 1.63 – 1.56 (m, 1H), 1.18 (dd, *J* = 14.3, 6.3 Hz, 3H), 1.01 – 0.81 (m, 35H).^{13}C NMR (151 MHz, $CDCl_3$) δ 138.7, 138.6, 138.5, 138.1, 138.1, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0,

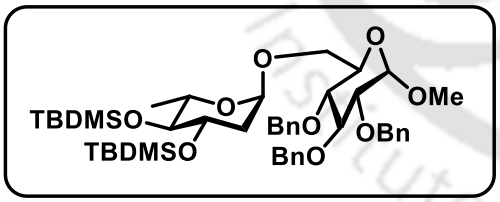
127.9, 127.9, 127.8, 127.8, 127.8, 127.6, 104.5, 99.5, 98.3, 98.0, 97.8, 97.5, 84.7, 82.4, 82.1, 82.0, 80.1, 80.0, 78.4, 78.4, 75.8, 75.6, 75.0, 75.0, 74.7, 74.5, 73.9, 73.4, 72.3, 71.4, 71.3, 70.3, 68.0, 67.9, 66.8, 66.2, 56.7, 55.1, 54.8, 39.8, 38.5, 38.4, 18.1, 18.0, 18.0, 17.6, 17.5, 17.5, 17.5, 17.4, 17.4, 17.3, 17.3, 17.3, 17.2, 14.0, 13.6, 13.0, 12.9, 12.9, 12.4, 12.3. HRMS (ESI-QTOF) $C_{46}H_{68}O_{10}Si_2NH_4$ $[M+NH_4]^+$- calculated- 854.4695; found- 854.4695. $[\alpha]_D^{22}$= -13 (*c* 2.0, $CHCl_3$).

Synthesis of (3,4-di-*O*-*tert*-butyldiphenylsilyl-2-deoxy-α-L-rhamnosyl)-(1→6)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranoside (55f):



General procedure was followed by adding glycosyl donor **50h** (50 mg, 0.08 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst (2 mg, 0.016 mmol, 20 mol%) and glycosyl acceptor **57b** (31 mg, 0.12 mmol, 1.5 equiv) at 100°C for 24 h to get the product as a colourless liquid **55f**. R_f- 0.4 in 10% EA/hexane, eluent 6% EA in hexane, amount- 43 mg, yield- 62%. Re-purification was done using HPLC (retention time- 11 min). Selectivity α:β= 8:1. α-anomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.0 Hz, 2H), 7.49 – 7.44 (m, 6H), 7.39 – 7.3 (m, 4H), 7.29 (dd, *J* = 15.1, 7.6 Hz, 4H), 7.23 (dt, *J* = 11.1, 7.6 Hz, 4H), 5.53 (d, *J* = 5.0 Hz, 1H), 4.99 (dd, *J* = 7.8, 3.6 Hz, 1H), 4.61 (dd, *J* = 7.9, 2.2 Hz, 1H), 4.31 (dd, *J* = 4.9, 2.3 Hz, 1H), 4.25 (dd, *J* = 8.0, 1.4 Hz, 1H), 4.09 (d, *J* = 3.0 Hz, 1H), 3.97 (t, *J* = 5.4 Hz, 1H), 3.91 (dd, *J* = 10.5, 5.5 Hz, 1H), 3.85 (dd, *J* = 6.7, 4.3 Hz, 1H), 3.63 (dd, *J* = 10.4, 6.8 Hz, 1H), 3.53 (t, *J* = 3.2 Hz, 1H), 1.87 (ddd, *J* = 13.3, 8.0, 2.6 Hz, 1H), 1.75 – 1.71 (m, 1H), 1.54 (s, 3H), 1.45 (s, 3H), 1.34 (s, 6H), 1.10 (d, *J* = 6.9 Hz, 3H), 0.93 (s, 9H), 0.91 (s, 9H). Other Spectroscopic data is in agreement with the reported data. [20]

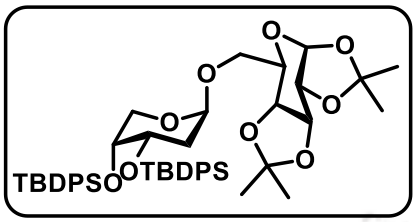
Synthesis of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α-L-rhamnosyl)-α-D-glucopyranoside (55g):



General procedure was followed by adding glycosyl donor **50g** (50 mg, 0.13 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst (3 mg, 0.027 mmol, 20 mol%) and glycosyl acceptor **57c** (92 mg, 0.20 mmol, 1.5 equiv) at 100°C for 24 h to get the product as a colourless liquid **55g**. R_f- 0.4 in 10% EA/hexane, eluent 6% EA in hexane, amount- 60 mg, yield- 55%. Re-purification was done using HPLC (retention time- 10.8 min). Selectivity α:β= 7:1. α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.24 (m, 19H), 4.99 (d, *J* = 10.8 Hz, 1H), 4.88 (d, *J* = 11.0 Hz, 1H), 4.81 (dd, *J* = 11.5, 5.8 Hz, 2H), 4.71 (s, 1H), 4.66 (d, *J* = 12.1 Hz, 1H), 4.57 (d, *J* = 3.5 Hz, 1H), 4.53 (d, *J* = 11.0 Hz, 1H), 4.00 (t, *J* = 9.2 Hz, 1H), 3.93 – 3.88 (m, 1H), 3.85 (d, *J* = 12.2 Hz, 1H), 3.879– 3.76 (m, 1H), 3.60 (dd, *J* = 8.7, 6.5 Hz, 1H), 3.50 (dd, *J* = 9.6, 3.5 Hz, 1H), 3.38 (t, *J* = 5.4 Hz, 1H), 3.36 (s, 3H), 3.12 (t, *J* = 8.5 Hz, 1H), 2.04 (ddd, *J* = 13.2, 4.7, 1.2 Hz, 1H), 1.61 – 1.57 (m, 1H), 1.17 (d, *J* = 6.4 Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.10 – 0.05 (m, 14H).^{13}C NMR (101 MHz, $CDCl_3$) δ 138.7, 138.1, 128.5, 128.4, 128.4, 128.2, 128.0,

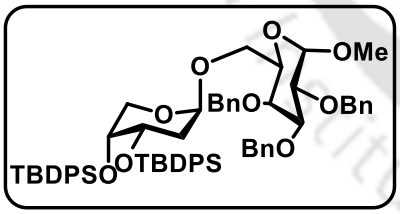
128.0, 127.8, 127.6, 97.7, 97.5, 82.1, 80.0, 78.3, 78.2, 77.2, 75.8, 75.1, 73.4, 70.6, 70.2, 69.0, 66.4, 54.8, 39.3, 26.2, 26.1, 18.6, 18.3, 18.1, -2.8, -3.08, -4.1, -4.4. HRMS (ESI-QTOF) $C_{46}H_{70}O_9Si_2NH_4$ $[M+NH_4]^+$- calculated- 840.4902; found- 840.5110. $[\alpha]_D^{22}$= -7 (*c* 2.5, $CHCl_3$).

Synthesis of (3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosyl) -(1→6)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranoside (55h):



General procedure was followed by adding glycosyl donor **50j** (50 mg, 0.08 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst (2 mg, 0.016 mmol, 20 mol%) and glycosyl acceptor **57b** (32 mg, 0.12 mmol, 1.5 equiv) at 100°C for 24 h to get the product as a colourless liquid **55h**. R_f- 0.4 in 10% EA/hexane, eluent 6% EA in hexane, amount- 45 mg, yield- 65%. Re-purification was done using HPLC (retention time- 9 min). Selectivity β. β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 9.8, 3.4 Hz, 4H), 7.65 – 7.63 (m, 2H), 7.57 (d, *J* = 7.0 Hz, 2H), 7.41 – 7.24 (m, 12H), 5.46 (d, *J* = 5.0 Hz, 1H), 4.84 (t, *J* = 2.5 Hz, 1H), 4.49 (dd, *J* = 7.9, 2.2 Hz, 1H), 4.25 (dd, *J* = 5.0, 2.3 Hz, 1H), 4.07 (d, *J* = 9.8 Hz, 1H), 3.85 (d, *J* = 6.9 Hz, 2H), 3.74 (t, *J* = 6.0 Hz, 1H), 3.59 (dd, *J* = 9.7, 7.0 Hz, 1H), 3.38 (dt, *J* = 9.8, 8.9 Hz, 3H), 2.29 (t, *J* = 10.9 Hz, 1H), 1.47 (s, 3H), 1.34 (s, 3H), 1.31 (s, 3H), 1.19 (s, 3H), 1.10 (s, 9H), 1.07 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.1, 136.0, 135.9, 135.9, 134.6, 134.2, 134.0, 133.7, 129.6, 129.5, 129.5, 129.4, 127.5, 127.5, 127.5, 127.4, 108.9, 108.4, 98.4, 96.2, 71.1, 70.8, 70.6, 70.4, 68.5, 66.5, 65.6, 63.9, 27.1, 27.0, 26.1, 25.9, 24.9, 24.4, 19.5, 19.1. HRMS (ESI-QTOF) $C_{49}H_{64}O_9Si_2NH_4$ $[M+NH_4]^+$- calculated- 870.4433; found- 870.4448. $[\alpha]_D^{22}$= -38 (*c* 3.4, $CHCl_3$).

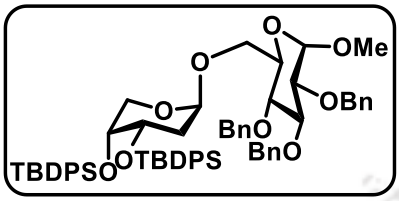
Synthesis of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosyl)-α-D-galactopyranoside (55i):



General procedure was followed by adding glycosyl donor **50j** (50 mg, 0.08 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst (2 mg, 0.016 mmol, 20 mol%) and glycosyl acceptor **57d** (38 mg, 0.12 mmol, 1.5 equiv) at 100°C for 24 h to get the product as a colourless liquid **55i**. R_f- 0.4 in 10% EA/hexane, eluent 6% EA in hexane, amount- 62 mg, yield- 72%. Re-purification was done using HPLC (retention time- 10 min). Selectivity β:α=10:1. β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 6.8 Hz, 4H), 7.62 (d, *J* = 6.8 Hz, 2H), 7.56 (d, *J* = 7.0 Hz, 2H), 7.43 – 7.22 (m, 23H), 7.16 – 7.14 (m, 4H), 4.88 – 4.77 (m, 4H), 4.68 (dd, *J* = 25.3, 11.9 Hz, 2H), 4.61 (d, *J* = 3.6 Hz, 1H), 4.30 (d, *J* = 11.4 Hz, 1H), 4.03 (d, *J* = 9.0 Hz, 1H), 3.98 (dd, *J* = 10.0, 3.6 Hz, 1H), 3.86 (dd, *J* = 10.1, 2.7 Hz, 1H), 3.75 (s, 1H), 3.64 – 3.60 (m, 2H), 3.45 (dd, *J* = 10.3, 6.5 Hz, 1H), 3.31 (dd, *J* = 10.1, 6.3 Hz, 2H), 3.24 (s, 3H), 3.10 (d, *J* = 11.6 Hz, 1H), 2.22 (d, *J* = 8.0 Hz, 1H), 1.48 (d, *J* = 12.8 Hz, 1H), 1.09 (s, 9H), 1.05 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 138.6, 138.5, 136.1, 136.0, 135.9, 135.9, 134.5, 134.2,

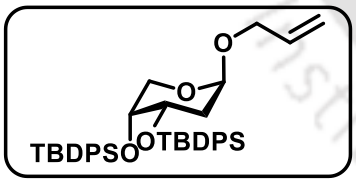
133.9, 133.6, 129.6, 129.5, 129.5, 128.4, 128.3, 128.1, 127.8, 127.7, 127.5, 127.5, 127.5, 127.5, 127.4, 127.3, 98.6, 98.6, 79.1, 76.5, 75.6, 74.7, 73.5, 73.4, 70.9, 69.2, 63.7, 55.2, 29.7, 27.1, 27.0, 19.4, 19.2. HRMS (ESI-QTOF) $C_{65}H_{76}O_9Si_2NH_4$ $[M+NH_4]^+$- calculated-1074.5372; found1074.5374-. $[\alpha]_D^{22}$= -17 (*c* 0.8, $CHCl_3$).

Synthesis of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosyl)-α-D-glucopyranoside (55j):



General procedure was followed by adding glycosyl donor **50j** (50 mg, 0.08 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst (2 mg, 0.016 mmol, 20 mol%) and glycosyl acceptor **57c** (38 mg, 0.12 mmol, 1.5 equiv) at 100°C for 24 h to get the product as a colourless crystalline solid **55j**. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 51 mg, yield- 59%. Re-purification was done using HPLC (retention time- 12 min). m. p. 162.6–164.6 °C. Selectivity β:α=6:1. β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.72 (m, 3H), 7.64 – 7.62 (m, 2H), 7.54 (d, *J* = 7.1 Hz, 2H), 7.39 – 7.27 (m, 29H), 7.15 – 7.13 (m, 2H), 4.99 (d, *J* = 11.0 Hz, 1H), 4.80 (d, *J* = 11.0 Hz, 1H), 4.74 (d, *J* = 12.4 Hz, 1H), 4.69 – 4.66 (m, 3H), 4.51 (d, *J* = 3.5 Hz, 1H), 4.24 (dd, *J* = 10.9, 6.4 Hz, 1H), 4.08 (d, *J* = 9.7 Hz, 1H), 3.91 – 3.86 (m, 2H), 3.64 (d, *J* = 10.6 Hz, 1H), 3.52 (d, *J* = 8.6 Hz, 1H), 3.41 – 3.36 (m, 4H), 3.22 (s, 3H), 2.21 (t, *J* = 11.3 Hz, 1H), 1.40 – 1.36 (m, 1H), 1.10 (s, 9H), 1.03 (s, 9H).^{13}C NMR (101 MHz, $CDCl_3$) δ 139.2, 138.4, 138.2, 136.1, 136.0, 136.0, 135.8, 134.1, 134.0, 133.7, 129.9, 129.6, 129.6, 129.5, 128.4, 128.4, 128.3, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5, 127.5, 127.5, 98.1, 97.7, 82.0, 79.6, 75.6, 74.9, 73.0, 70.9, 69.6, 54.9, 29.7, 27.1, 27.0, 19.5, 19.1. HRMS (ESI-QTOF) $C_{65}H_{76}O_9Si_2NH_4$ $[M+NH_4]^+$- calculated- 1074.5372; found- 1074.5374. $[\alpha]_D^{22}$= -24 (*c* 0.9, $CHCl_3$).

Synthesis of Allyl 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinopyranoside (55k):

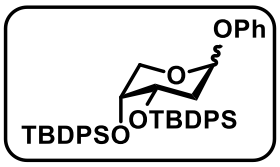


General procedure was followed by adding glycosyl donor **50j** (50 mg, 0.08 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst (2 mg, 0.016 mmol, 20 mol%) and glycosyl acceptor **57a** (6 µL, 5 mg, 0.09 mmol, 1.1 equiv) at 100°C for 24 h to get the product as a colourless crystalline solid **55k**. R_f- 0.4 in 10% EA/hexane, eluent 6% EA in hexane, amount- 44 mg, yield- 83%. Re-purification was done using HPLC (retention time- 8 min). m. p. 156.2–158.5 °C. Selectivity β:α=3:1. β-anomer:^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 6.9 Hz, 4H), 7.69 (d, *J* = 6.9 Hz, 2H), 7.62 (d, *J* = 7.0 Hz, 2H), 7.39 (ddt, *J* = 26.9, 12.4, 7.3 Hz, 8H), 7.31 – 7.28 (m, 5H), 5.74 (ddd, *J* = 16.3, 9.9, 4.9 Hz, 1H), 5.06 – 5.04 (m, 2H), 4.84 (t, *J* = 3.1 Hz, 1H), 4.18 (d, *J* = 9.3 Hz, 1H), 3.99 (d, *J* = 13.5 Hz, 1H), 3.86 (s, 1H), 3.78 (dd, *J* = 13.5, 4.7 Hz, 1H), 3.46 (bs, 1H), 3.38 – 3.36 (m, 1H), 2.21 (d, *J* = 10.1 Hz, 1H), 1.45 (d, *J* = 12.6 Hz, 1H), 1.12 (s, 9H), 1.11 (s, 9H).^{13}C NMR (151 MHz, $CDCl_3$) δ 136.1, 136.0, 135.9, 135.9, 134.5, 134.4, 134.2, 133.9, 133.6, 129.6, 129.6, 129.5, 129.4, 127.6, 127.5, 127.5, 127.5, 115.5, 97.5,

70.9, 68.6, 67.7, 63.8, 27.1, 27.0, 19.4, 19.2. HRMS (ESI-QTOF) $C_{40}H_{50}O_4Si_2Na$ $[M+Na]^+$- calculated- 673.3145; found- 673.3145. $[\alpha]_D^{22}$= -19 (*c* 0.5, $CHCl_3$).

Aryl Glycoside Synthesis:

Synthesis of Phenyl 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α, β-D-arabinopyranoside (56aαβ):

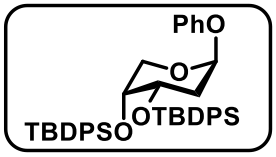


General procedure was followed as mentioned in literature [36] by taking monohydrated copper(II) acetate (6 mg, 0.03 mmol) and pyridine (11µL, 0.14 mmol) in a round-bottom flask and were added on activated 4 Å molecular sieves (50 mg). Dichloroethane (100 µL) was added, and the resulting suspension was stirred for 5 min. Phenylboronicacid (0.42 mmol) was then introduced, and the reaction medium was stirred again for 5 min. Finally, the hemi-acetal **50j** (0.14 mmol) was added and the resulting mixture was stirred at room temperature and under an air atmosphere for 24 h (the round-bottom flask was capped to prevent the evaporation of dichloromethane). The medium was then diluted with dichloromethane and filtered over celite. Purification by silica gel chromatography (cyclohexane/EtOAc) afforded the desired compound. R_f- 0.6 in 10% EA/hexane, eluent 4% EA in hexane, amount- 50 mg, yield- 89%. α and β anomers were isolated in HPLC. Selectivity α: β= 1:1.2.

Synthesis of Phenyl 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α-D-arabinopyranoside (56aα):

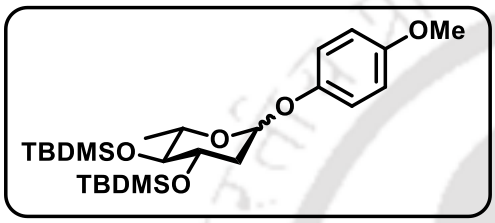
Re-purification was done using HPLC (retention time- 7 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was a colourless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.0 Hz, 2H), 7.70 (d, *J* = 6.9 Hz, 2H), 7.67 (d, *J* = 7.1 Hz, 2H), 7.62 (d, *J* = 7.1 Hz, 2H), 7.41 (dd, *J* = 16.2, 7.4 Hz, 4H), 7.34 (q, *J* = 7.6 Hz, 4H), 7.29 (td, *J* = 7.5, 2.7 Hz, 4H), 7.23 (t, *J* = 7.9 Hz, 2H), 6.96 (t, *J* = 8.6 Hz, 1H), 4.92 (bt, 1H), 4.01 – 4.00 (m, 1H), 3.95 (dd, *J* = 11.3, 6.2 Hz, 1H), 3.78 – 3.77 (m, 1H), 3.04 (dd, *J* = 11.4, 1.7 Hz, 1H), 2.33 – 2.28 (m, 1H), 1.66 (dd, *J* = 8.9, 3.5 Hz, 1H), 1.13 (s, 9H), 1.07 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 136.2, 136.1, 136.0, 134.3, 134.2, 133.7, 133.6, 129.7, 129.6, 129.5, 129.3, 127.6, 127.6, 127.5, 121.7, 116.6, 96.4, 70.2, 70.1, 35.6, 27.1, 27.0, 19.3, 19.3. HRMS (ESI-QTOF) $C_{43}H_{50}O_4Si_2NH_4$ $[M+NH_4]^+$- calculated- 704.3586; found- 704.3597. $[\alpha]_D^{22}$= 16 (*c* 1.1, $CHCl_3$).

Synthesis of Phenyl 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosepyranoside (56aβ):



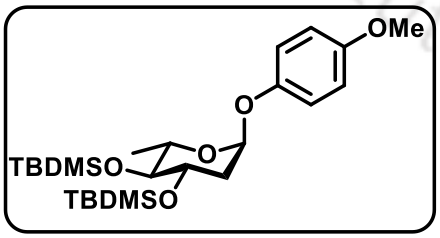
Re-purification was done using HPLC (retention time- 8 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was a colourless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.1 Hz, 2H), 7.74 (d, *J* = 7.1 Hz, 2H), 7.71 (d, *J* = 7.1 Hz, 2H), 7.59 (d, *J* = 7.2 Hz, 2H), 7.41 (t, *J* = 7.4 Hz, 4H), 7.36 (t, *J* = 7.3 Hz, 4H), 7.30 (dd, *J* = 13.3, 7.0 Hz, 4H), 7.18 (t, *J* = 7.8 Hz, 2H), 6.90 (t, *J* = 7.3 Hz, 1H), 6.80 (d, *J* = 8.1 Hz, 2H), 5.49 (bt, 1H), 4.26 (d, *J* = 10.2 Hz, 1H), 3.94 (s, 1H), 3.43 (bs, 2H), 2.41 (t, *J* = 10.2 Hz, 1H), 1.58 (bs, 1H), 1.14 (s, 9H), 1.10 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 136.2, 136.0, 135.9, 135.9, 134.5, 134.1, 133.9, 133.6, 129.7, 129.6, 129.6, 129.5, 129.2, 127.6, 127.6, 127.5, 121.5, 116.2, 96.7, 70.9, 68.2, 64.6, 34.2, 27.1, 27.1, 19.5, 19.1. HRMS (ESI-QTOF) $C_{43}H_{50}O_4Si_2Na$ $[M+Na]^+$- calculated- 709.3140; found- 709.3143. $[\alpha]_D^{22}$= -112 (*c* 1.0, $CHCl_3$).

Synthesis of p-Methoxybenzyl 3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α, β-L-rhamnopyranoside (56bαβ):



General procedure was followed as mentioned in literature [48] by taking monohydrated copper(II) acetate (7 mg, 0.027 mmol) and pyridine (12μL, 0.13 mmol) in a round-bottom flask and were added on activated 4 Å molecular sieves (50 mg). Dichloroethane (100 μL) was added, and the resulting suspension was stirred for 5 min. 4-methoxyphenylboronicacid (0.40 mmol) was then introduced, and the reaction medium was stirred again for 5 min. Finally, the hemi-acetal **50j** (0.13 mmol) was added and the resulting mixture was stirred at room temperature and under an air atmosphere for 24 h (the round-bottom flask was capped to prevent the evaporation of dichloromethane). The medium was then diluted with dichloromethane and filtered over celite. Purification by silica gel chromatography (cyclohexane/EtOAc) afforded the desired compound. R_f- 0.6 in 10% EA/hexane, eluent 4% EA in hexane, amount- 57 mg, yield- 92%. α and β anomers were isolated in HPLC. Selectivity α: β= 1.3:1.

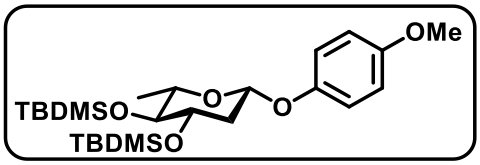
Synthesis of p-Methoxybenzyl 3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α-L-rhamnopyranoside (56bα):



Re-purification was done using HPLC (retention time- 8 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 – 6.95 (m, 2H), 6.83 – 6.79 (m, 2H), 5.38 (d, *J* = 1.5 Hz, 1H), 4.11 (ddd, *J* = 11.0, 8.0, 4.6 Hz, 1H), 3.80 – 3.73 (m, 4H), 3.22 (t, *J* = 8.4 Hz, 1H), 2.26 (ddd, *J* = 13.2, 4.6, 1.7 Hz, 1H), 1.78 (ddd, *J* = 14.2, 10.9, 3.6 Hz, 1H), 1.20 (d, *J* = 6.4 Hz, 3H), 0.93 (s, 9H), 0.90 (s, 9H), 0.15 – 0.07 (m, 13H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 154.6, 151.1, 117.8, 114.5, 96.7, 78.2, 70.6, 69.7, 55.6, 39.4, 26.3, 26.1, 18.7, 18.3,

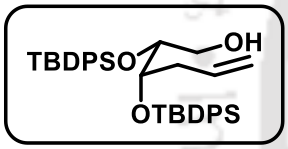
18.1, -2.8, -3.1, -4.0, -4.3. HRMS (ESI-QTOF) $C_{25}H_{46}O_4Si_2Na$ $[M+Na]^+$- calculated- 505.2781; found- 505.2780. $[\alpha]_D^{22}$= -55 (*c* 1.1, $CHCl_3$).

Synthesis of p-Methoxybenzyl 3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-β-L-rhamnopyranoside (56bβ):



Re-purification was done using HPLC (retention time- 7 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 – 6.93 (m, 2H), 6.83 – 6.79 (m, 2H), 5.00 (dd, *J* = 9.7, 2.1 Hz, 1H), 3.76 (s, 3H), 3.71 (ddd, *J* = 11.5, 8.0, 4.8 Hz, 1H), 3.36 (tt, *J* = 12.6, 6.3 Hz, 1H), 3.22 (t, *J* = 8.3 Hz, 1H), 2.29 (ddd, *J* = 12.6, 4.7, 2.1 Hz, 1H), 1.85 (td, *J* = 11.5, 9.9 Hz, 1H), 1.31 (d, *J* = 6.3 Hz, 3H), 0.92 (s, 9H), 0.91 (s, 9H), 0.12 – 0.07 (m, 13H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.9, 151.3, 117.6, 114.5, 97.8, 77.7, 72.9, 72.9, 55.7, 40.6, 26.3, 26.1, 18.9, 18.3, 18.1, -2.8, -3.0, -3.9, -4.1. HRMS (ESI-QTOF) $C_{25}H_{46}O_4Si_2Na$ $[M+Na]^+$- calculated- 505.2781; found- 505.2790. $[\alpha]_D^{22}$= 31 (*c* 1.0, $CHCl_3$).

Synthesis of 4,5-Di-*O*-*tert*-butyldiphenylsilyl-1,2,3,6-tetradeoxy-D-arabino-pent-1-enitol (56c):



To a solution of methyltriphenylphosphonium iodide (0.325 g, 0.911 mmol) in THF (2 mL) was added dropwise at 0°C 1.6 M BuLi in hexane (0.47 mL,0.757 mmol). The reaction was stirred for 30 min at 0°C and then for 30 min at room temperature. In another flask, a solution of BuLi in hexane (1.6 M, 0.133 mL,0.217 mmol) was added dropwise at 0°C to a solution of 2-deoxy sugar **50j** (100 mg, 0.164 mmol) in THF (1 mL) and stirred for 30 min. The resulting solution was then cannulated into the THF solution of phosphorane. The reaction mixture was stirred for 24 h at room temperature, then quenched with a saturated aqueous solution of NH_4Cl (5 mL) and extracted with AcOEt (5 mL). The combined organic layers were dried over $MgSO_4$, evaporated under reduced pressure and the residue was purified by column chromatography to give the desired compound **56c** as a colourless oil. R_f- 0.5 in 20% EA/hexane, eluent 8% EA in hexane, amount 84 mg, yield 85%. Re-purification was done using HPLC (retention time- 6.5 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.49 (m, 8H), 7.42 – 7.25 (m, 12H), 5.78 – 5.66 (m, 1H), 5.02 – 4.86 (m, 2H), 3.85 – 3.50 (m, 4H), 2.56 (d, *J* = 77.9 Hz, 1H), 2.30 – 2.15 (m, 2H), 1.00 (dd, *J* = 13.1, 5.7 Hz, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.0, 135.9, 135.9, 135.8, 135.6, 135.5, 135.4, 134.5, 133.8, 133.7, 133.5, 133.3, 133.2, 133.1, 132.9, 132.8, 129.8, 129.7, 129.7, 129.7, 129.6, 127.7, 127.7, 127.7, 127.5, 127.5, 127.5, 117.1, 116.9, 77.3, 77.0, 76.7, 75.2, 73.7, 73.7, 73.6, 65.5, 65.0, 37.1, 37.0, 27.0, 27.0, 26.8, 26.8, 19.4, 19.3, 19.1, 19.1. HRMS (ESI-QTOF) $C_{38}H_{48}O_3Si_2NH_4$ $[M+NH_4]^+$- calculated- 626.3486; found- 626.3478. $[\alpha]_D^{22}$= 1 (*c* 0.9, $CHCl_3$).

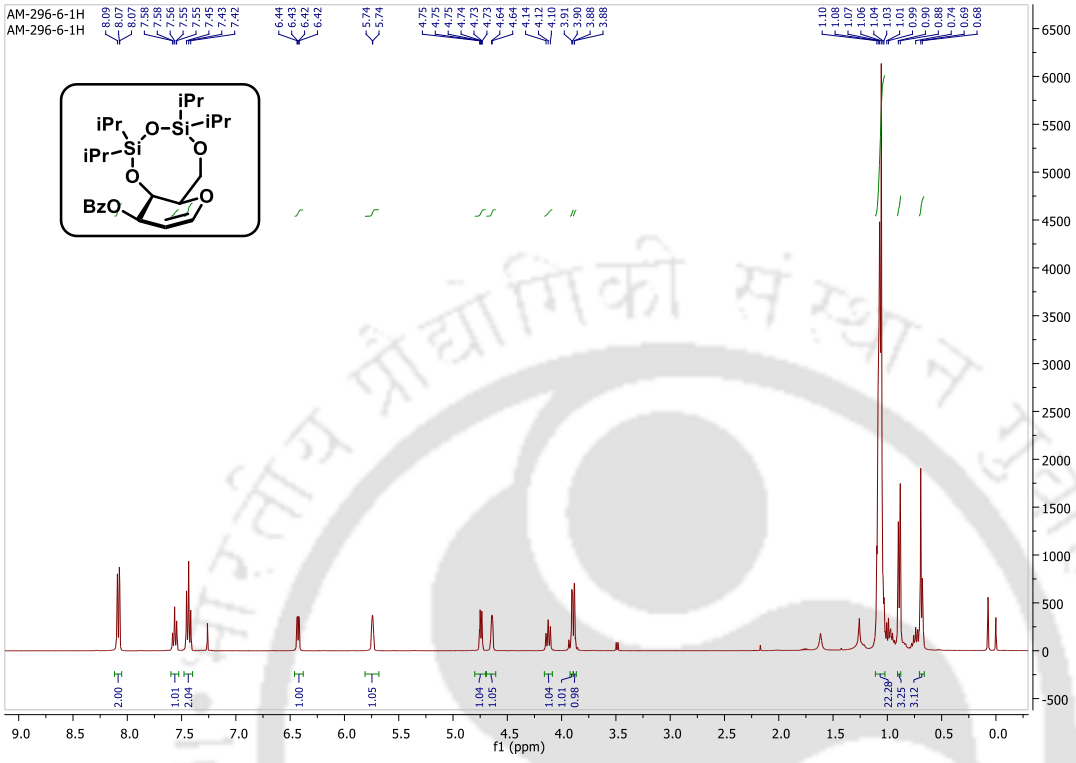
2.10 References:

1. Schubert, W. M.; Lamm, B.; Keeffe, J. R. *J. Am. Chem. Soc.***1964**, *86*, 4727-29.
2. Schnapperelle, I.; Hummel, W.; Gröger, H. *Chem. Eur. J.* **2012**, *18*, 1073-76.
3. De Lederkremer, D.; R. M.; Marino, C. *Adv. Carbohydr. Chem. Biochem.* **2008**, *61*, 143–216.
4. Zhu, Z.; Jiang, W.; McGinley, J. N.; Thompson, H. J. *Cancer Res.* **2005,** *65*, 7023–30.
5. Nakamura, T.; Goda, Y.; Sakai, S.; Kondo, K.; Akiyama, H.; Toyoda, M. *Phytochemistry*, **1998,** *49*, 2097–102.
6. Suzuki, R.; Okada, Y.; Okuyama, T. *J. Nat. Prod.* **2003**, *66*, 564–65.
7. Reichstein, T.; Weiss, E. *Adv. Carbohydr. Chem.* **1962**, *17*, 65–120.
8. Weymouth-Wilson, A. C. *Nat. Prod. Rep.* **1997**, *14*, 99–110.
9. Williama Lown, J. *Chem. Soc. Rev.* **1993**, *22*, 165–76.
10. Lombo, F.; Menendez, N.; Salas, J. A.; Mendez, C. *Appl. Microbiol. Biotechnol.* **2006**, *73*, 1–14.
11. Krohn, K.; Rohr, J. *Springer* **1997**, 127–95.
12. Rohr, J.; Thiericke, R. *Nat. Prod. Rep.* **1992**, *9*, 103–37.
13. Davies, H.; Green, R. *Nat. Prod. Rep.* **1986**, *3*, 87–121.
14. Madduri, K.; Kennedy, J.; Rivola, G.; Solari, A. I.; Filippini, S.; Zanuso, G.; Colombo, A. L.; Gewain, K. M.; Occi, J. L.; MacNeil D. J.; Hutchinson C. R. *Nat. Biotechnol.* **1998**, *16*, 69–74.
15. Lu, Y. S.; Li, Q.; Zhang, L. H.; Ye. X. S. *Org. Lett.* **2008**, *10*, 3445–48.
16. Beale, T. M.; Moon, P. J.; Taylor, M. S. *Org. Lett.* **2014**, *16*, 3604–07.
17. Nogueira, J. M.; Nguyen, S. H.; Bennett, C. S. *Org. Lett.* **2011**, *13*, 2814–17.
18. Balmond, E. I.; Coe, D. M.; Galan, M. C.; McGarrigle, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 9152−55.
19. Sun, L.; Wu, X.; Xiong, D. C.; Ye, X. S. *Angew. Chem., Int. Ed.* **2016**, *55*, 8041−44.
20. Ghosh, T.; Mukherji, A.; Kancharla, P. K. *Org. Lett.* **2019**, *21*, 3490-95.
21. Ghosh, T.; Mukherji, A.; Srivastava, H. K.; Kancharla, P. K. *Org. Biomol. Chem.* **2018,** *16*, 2870–75.
22. Niu, Y.; Cao, X.; Ye, X. S. *Helv. Chim. Acta* **2008**, *91*, 746-52.
23. Page, P. C. B.; Chan, Y.; Liddle, J.; Elsegood, M. R. J. *Tetrahedron* **2014**, *70*, 7283-305.
24. Sabesan, S.; Neira, S. *J. Org. Chem.* **1991**, *56*, 5468–72.
25.a) Costantino, V.; Imperatore, C.; Fattorusso, E.; Mangoni, A. *Tetrahedron Lett.* **2000**, *41*, 9177-80.
b) Yadav, J. S.; Reddy, B. V. S.; Reddy, K. B.; Satyanarayana, M. *Tetrahedron Lett.* **2002**, *43*, 7009–12.
26. Tang, Y.; Reddy, D. P.; Yu, B. *Tetrahedron* **2021**, *78*, 131800.
27. Liang, H.; Hu, L.; Corey, E. J., *Org. Lett.* **2011,** *13*, 4120-23.
28. Manzoni, L. *Chem. Commun.* **2003**, *23*, 2930-31.
29. Balmond, E. I.; Benito-Alifonso, D.; Coe, D. M.; Alder, R. W.; McGarrigle, E. M.; Galan, M. C. *Angew. Chem.* **2014**, *126*, 8329-33.
30. Morris, W. J.; Shair, M. D. *Org. Lett.* **2009**, *11*, 9-12.
31. Issa, J. P.; Bennett, C. S. *J. Am. Chem. Soc.* **2014**, *136*, 5740-44.
32. Zhu, D.; Baryal, K. N.; Adhikari, S.; Zhu, J. *J. Am. Chem. Soc.* **2014**, *136*, 3172-75.
33. Bennett, C. S.; Galan, M. C. *Chem. Rev.* **2018**, *118*, 7931-85.
34. a) Backus, K. M.; Boshoff, H. I.; Barry, C. S.; Boutureira, O.; Patel, M. K.; D'Hooge, F.; Lee, S. S.; Via, L. E.; Tahlan, K.; Barry, C. E., 3rd; Davis, B. G. *Nat. Chem. Biol.* **2011**, *7*, 228-35.
b) Elbein, A. D.; Pan, Y. T.; Pastuszak, I.; Carroll, D. *Glycobiology* **2003,** *13* (4), 17R-27R.
35. Andreeva, D. V.; Ip, B.; Gurinov, A. A.; Tolstoy, P. M.; Denisov, G. S.; Shenderovich, I. G.; Limbach, H. H. *J. Phys. Chem. A.* **2006**, *110*, 10872-79.
36. Arnett, E. M.; Chawla, B. *J. Am. Chem. Soc.* **1979**, *101*, 7141-46.

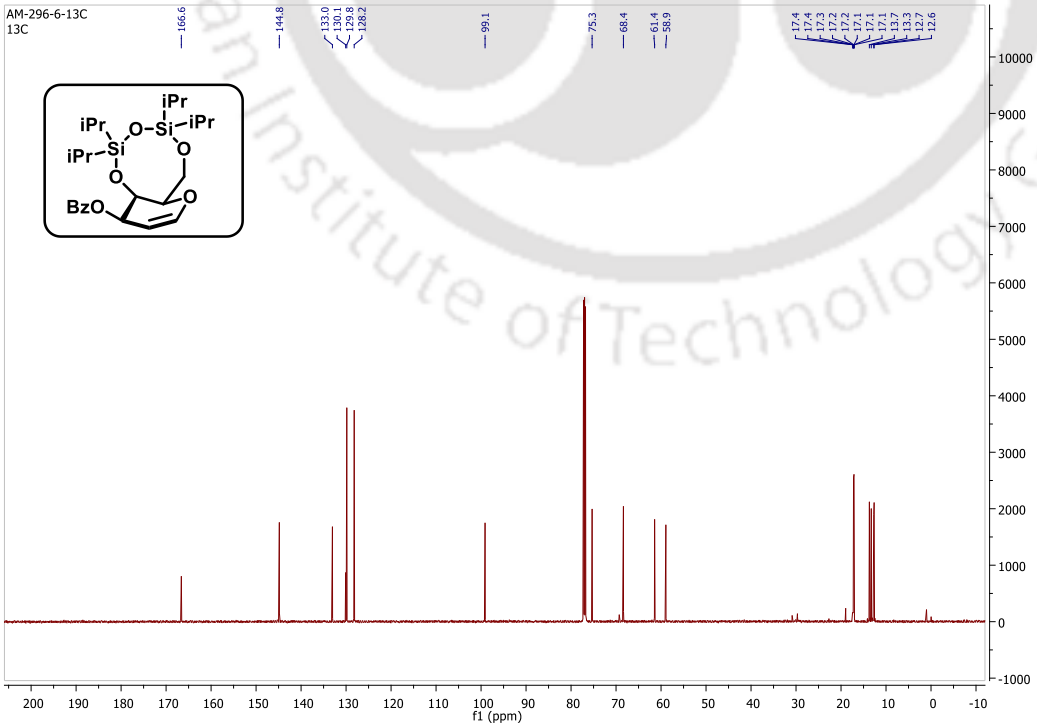
37. Mahoney, J. M.; Beatty, A. M.; Smith, B. D. *J. Am. Chem. Soc.* **2001**, *123*, 5847-48.
38. Lu, J. M.; Rosokha, S. V.; Lindeman, S. V.; Neretin, I. S.; Kochi, J. K. *J. Am. Chem. Soc.* **2005**, *127*, 1797-809.
39. Antonio, M. R.; Nyman, M.; Anderson, T. M. *Angew. Chem.,Int. Ed.* **2009**, *48*, 6136-40.
40. Ciardi, M.; Tancini, F.; Gil-Ramirez, G.; Escudero Adan, E. C.; Massera, C.; Dalcanale, E.; Ballester, P. *J. Am. Chem. Soc.* **2012**, *134*, 13121-32.
41. Jensen, C. M.; Trogler, W. C. *Science* **1986**, *233*, 1069-71.
42. Shi, G.; Tehrani, Z. A.; Kim, D.; Cho, W. J.; Youn, Il-S.; Lee, H. M.; Yousuf, M.; Ahmed, N.; Shirinfar, B.; Teator, A. J.; Lastovickova, D. M.; Rasheed, L.; Lah, M. S.; Bielawski, C. W.; Kim, K. S.; *Sci. Rep.* **2016**, *6*, 30123.
43. Bernasconi, C. F.; Carre, D. J. *J. Am. Chem. Soc.* **1979,** *101*, 2707-09.
44. Gold, V.; Lee, R. A. *J. Chem. Soc., Chem. Commum.* **1984,** *15*, 1032-34.
45. Houriet, R.; Rolli, E. *New J. Chem.* **1987,** *11*, 221-24.
46. Ghosh, T.; Mukherji, A.; Kancharla, P. K. *Eur. J. Org. Chem.* **2019**, *2019*, 7488-98.
47. Moume-Pymbock, M.; Furukawa, T.; Mondal, S.; Crich, D. *J. Am. Chem. Soc.* **2013**, *135*, 14249-55.
48. Verdelet, T.; Benmahdjoub, S.; Benmerad, B.; Alami, M.; Messaoudi, S. *J. Org. Chem.* **2019**, *84*, 9226-38.
49. Levecque, P.; Gammon, D. W.; Kinfe, H. H.; Jacobs, P.; Vos, D. D.; Sels, B. *Adv. Synth. Catal*. **2008**, *350*, 1557–68.
50. Balmond, E. I.; Alifonso, D. B.; Coe, D. M.; Alder, R. W.; McGarrigle, E. M.; Galan, M. C. *Angew. Chem.* **2014**, 53, 8190-94.
51. Li, H. H.; Ye, X. S.*Org. Biomol. Chem*. **2009**, *7*, 3855–61.
52. Gonzalez, C. C.; Kennedy, A. R.; Leon, E. I.; Fagundo, C. R.; Suarez, E. *Chem. Eur. J.* **2003**, *9*, 5800-09.
53. Kunst, E.; Gallier, F.; Dujardin, G.; Yusubov, M. S., Kirschning, A. *Org. Lett.* **2007**, *9*, 5199-202.

2.11 Spectra:

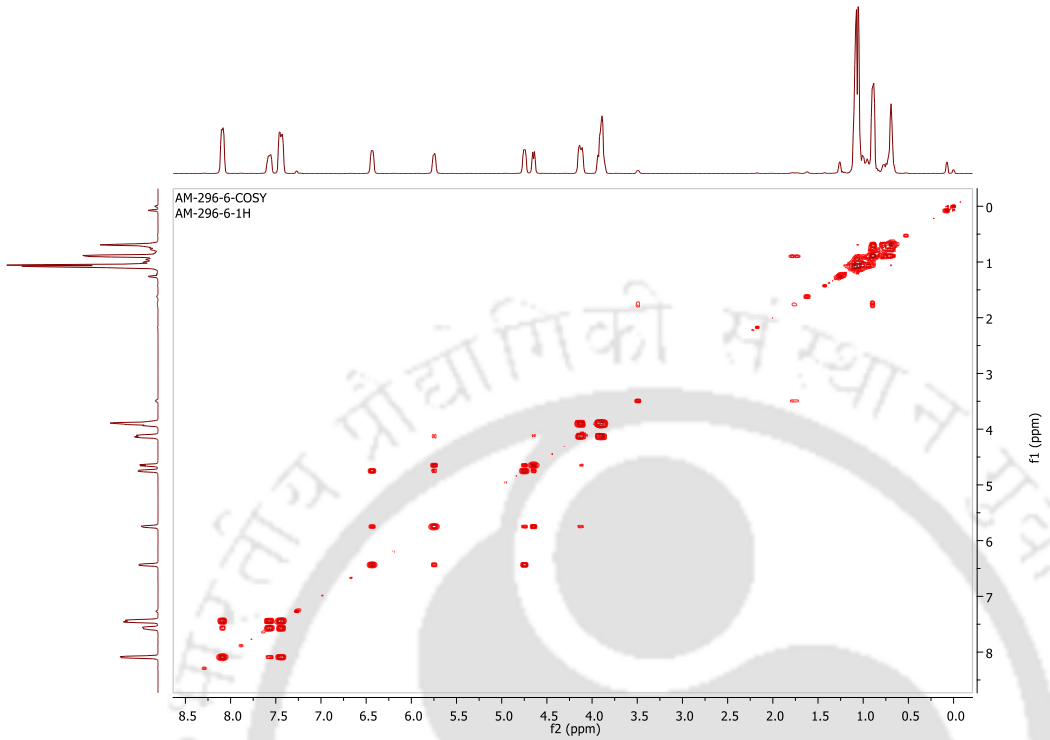
^{1}H NMR of 2,6-anhydro-5-deoxy-4-O-benzoyl-1,3-O-(tetraiso-propyldisiloxane-1,3-diyl)-D-arabino-hex-5-enitol 46e (400 MHz, $CDCl_3$)



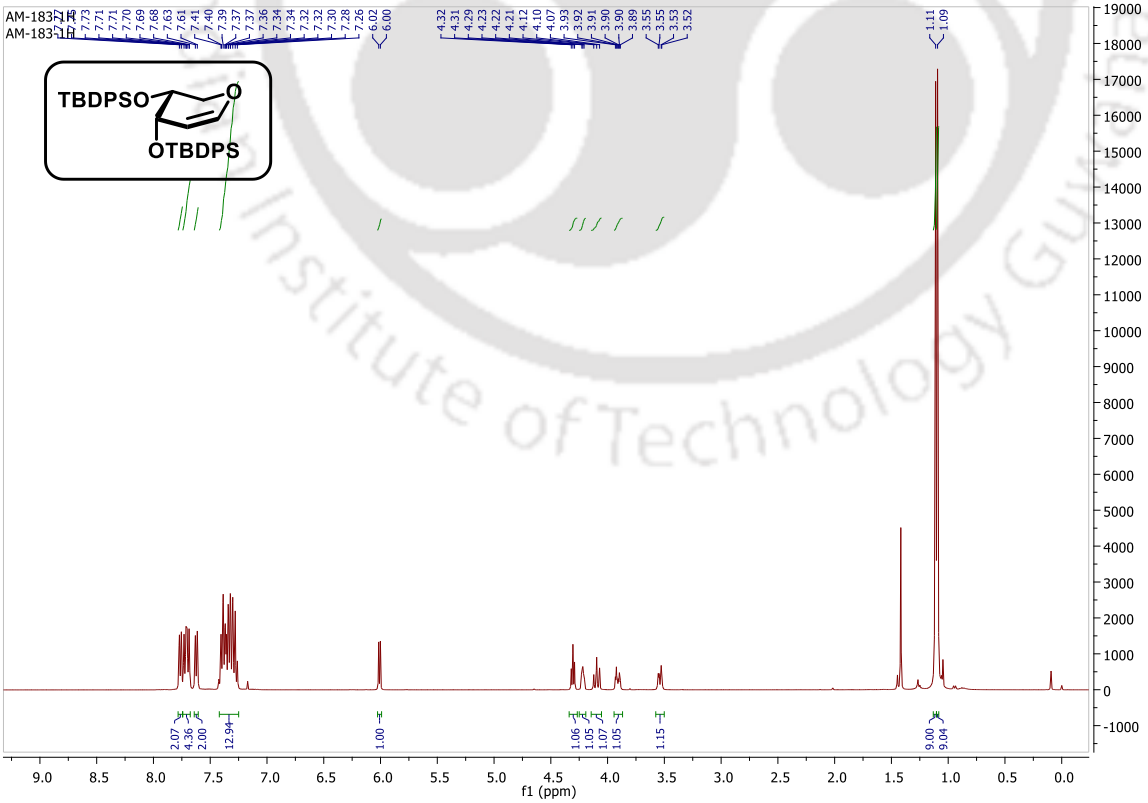
^{13}C NMR of 2,6-anhydro-5-deoxy-4-O-benzoyl-1,3-O-(tetraiso-propyldisiloxane-1,3-diyl)-D-arabino-hex-5-enitol 46e (400 MHz, $CDCl_3$)



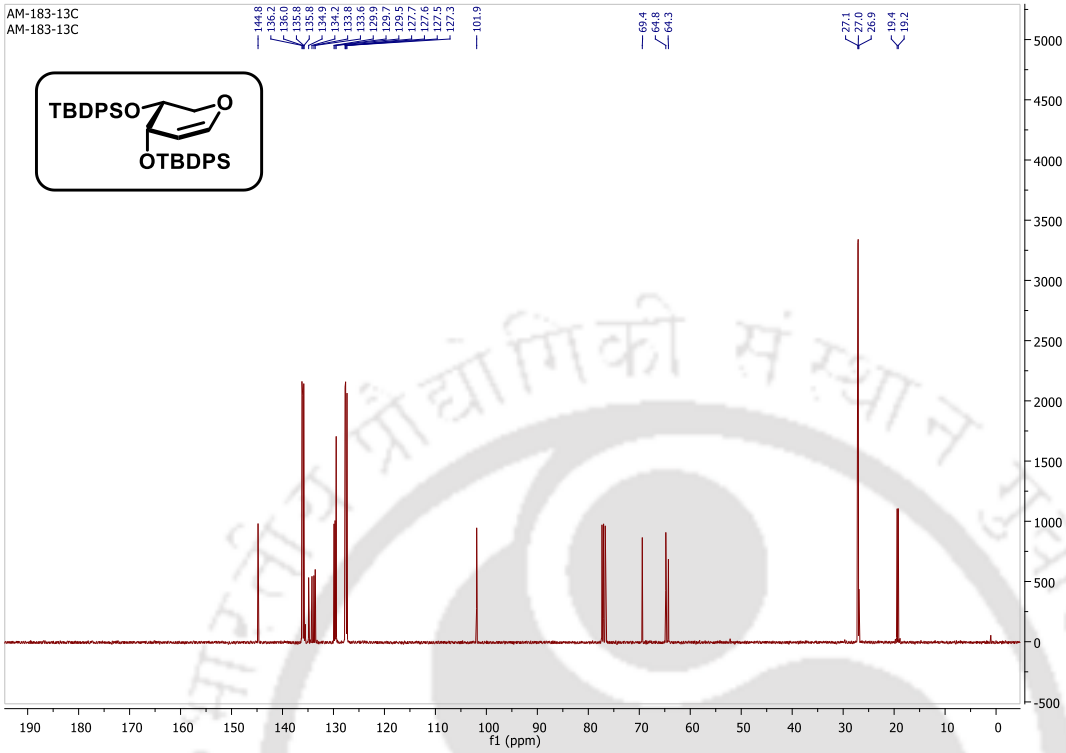
COSY NMR of 2,6-anhydro-5-deoxy-4-O-benzoyl-1,3-O-(tetraiso-propyldisiloxane-1,3-diyl)-D-arabino-hex-5-enitol 46e (400 MHz, $CDCl_3$)



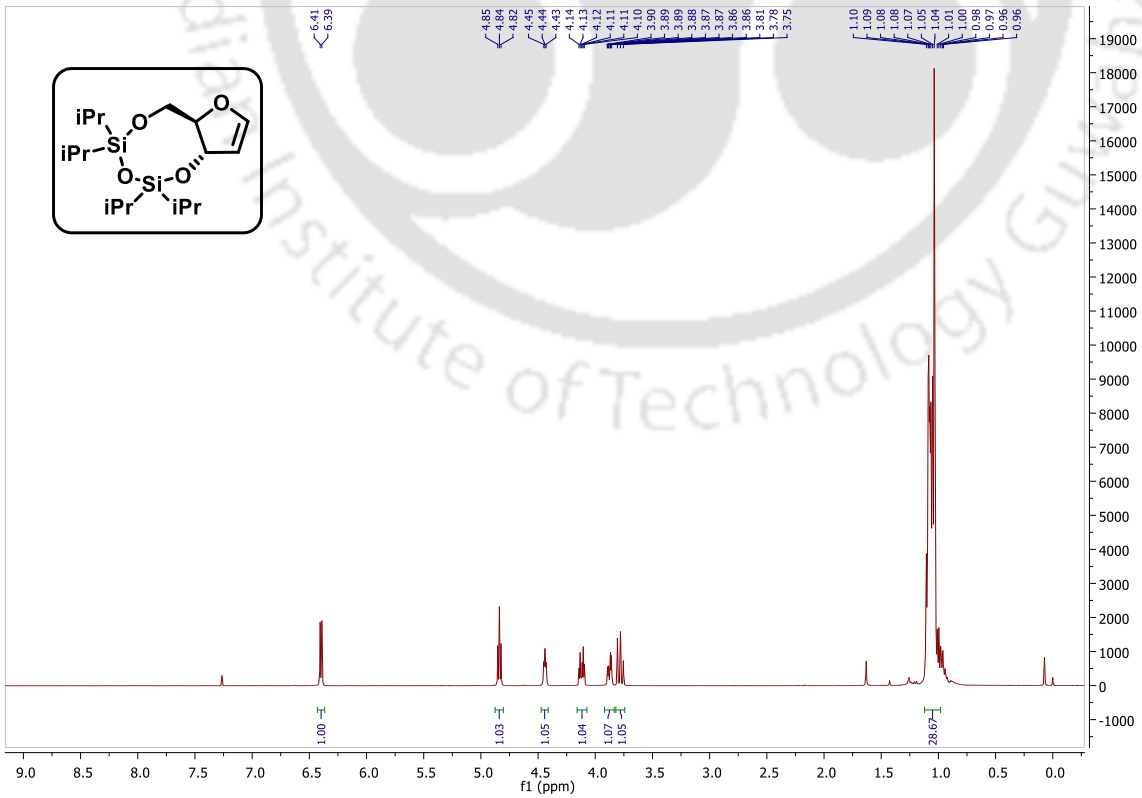
^{1}H NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-D-arabinal 46j (400 MHz, $CDCl_3$)



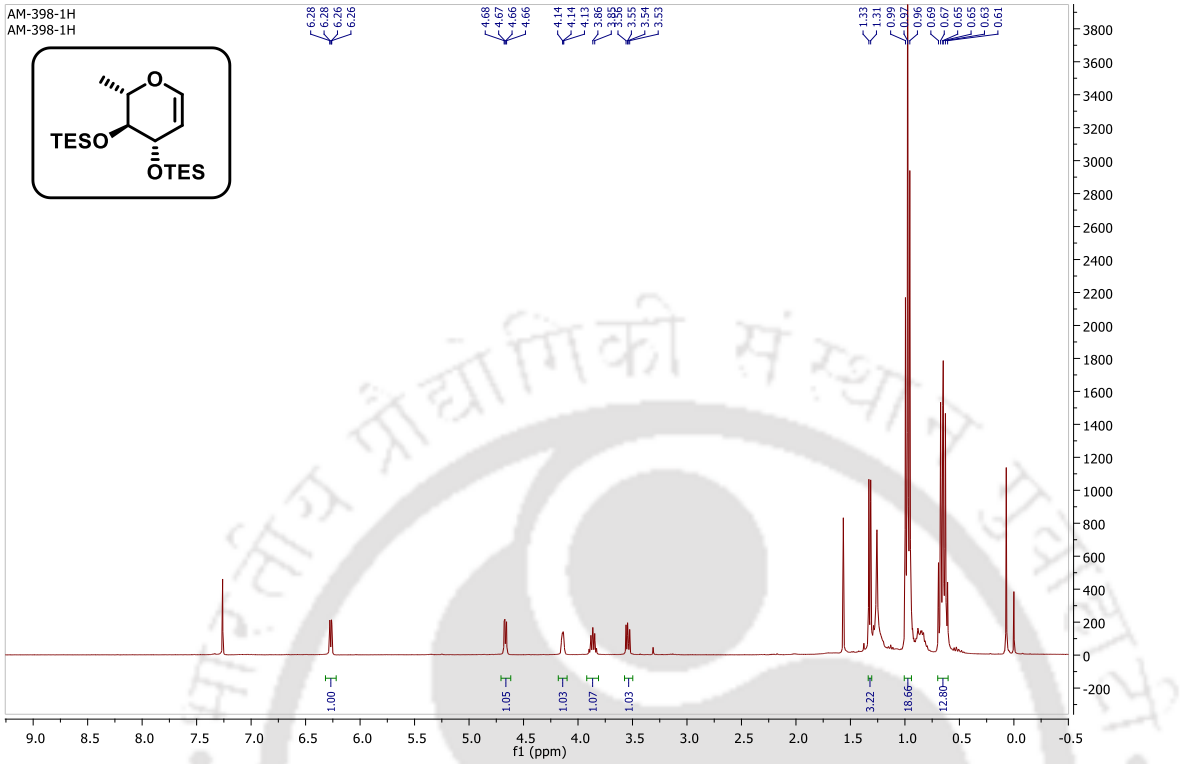
^{13}C NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-D-arabinal 46j (400 MHz, $CDCl_3$)



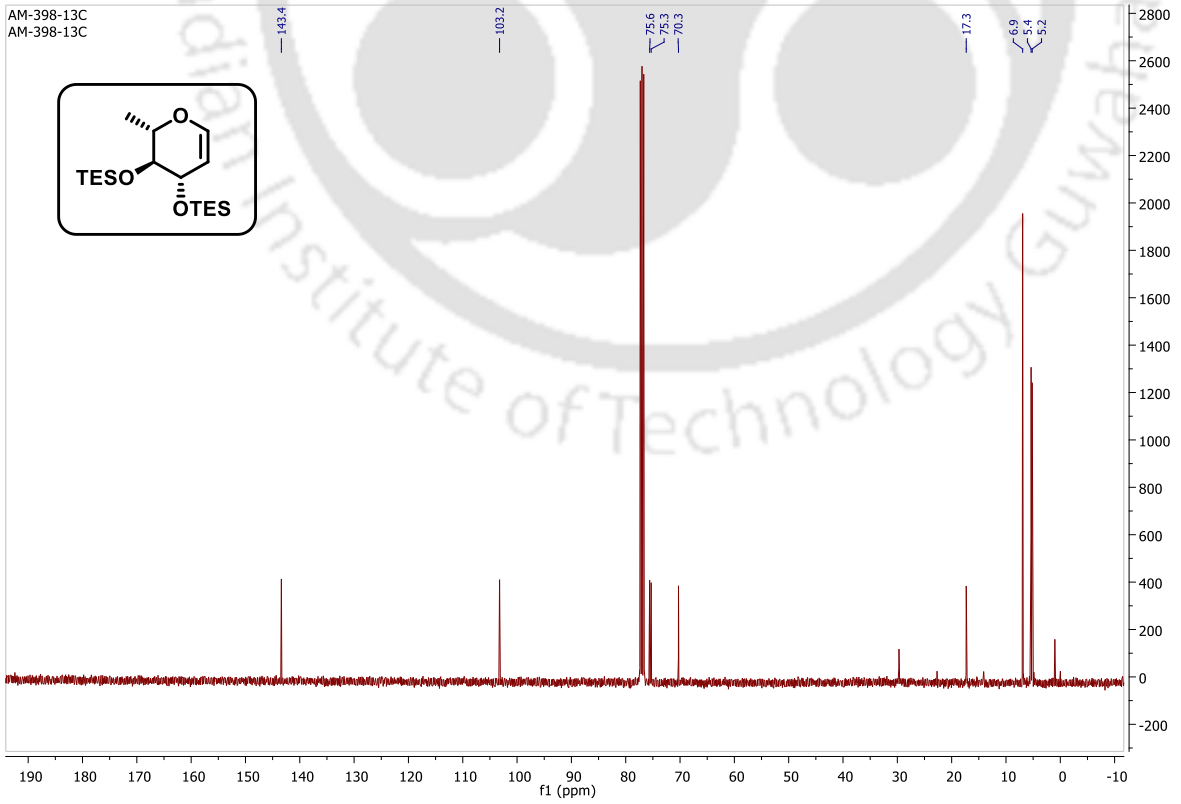
^{1}H NMR of 1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyl-disiloxane-1,3-diyl)-D-erythro-pent-1-entiol 46k (400 MHz, $CDCl_3$)



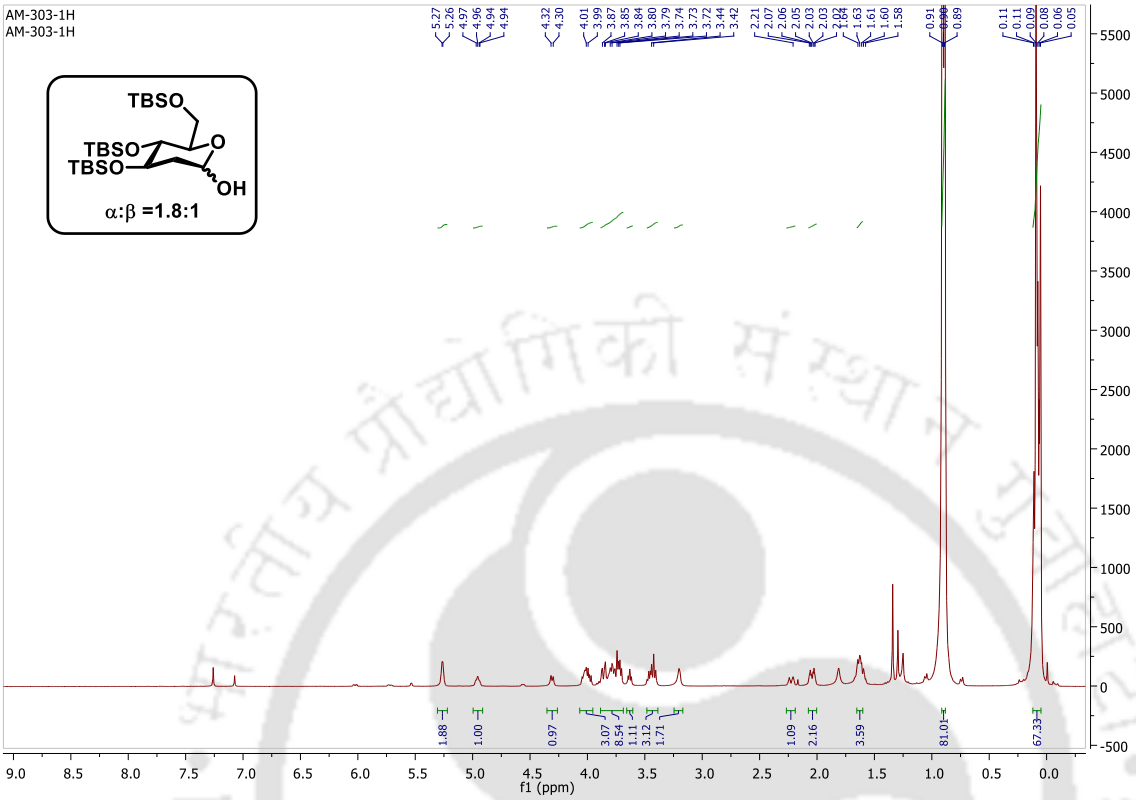
^{1}H NMR of 3,4-di-O-triethylsilyl-L-Rhamnal 46l (400 MHz, $CDCl_3$)



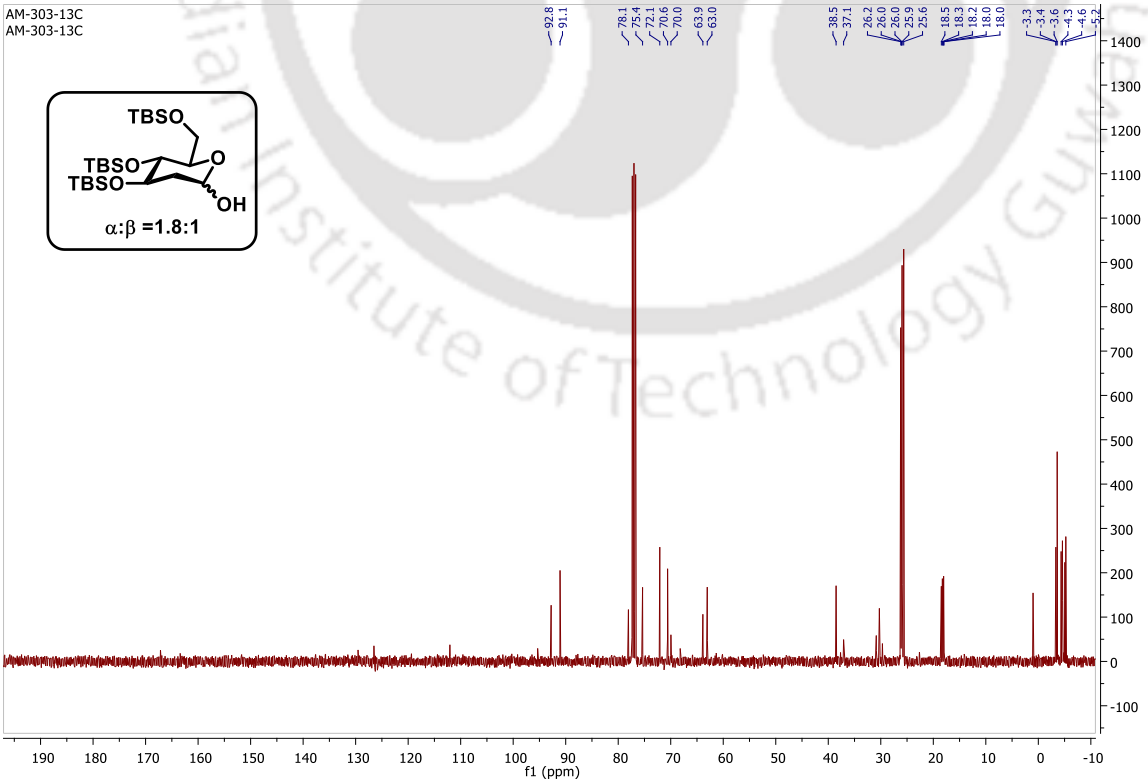
^{13}C NMR of 3,4-di-O-triethylsilyl-L-Rhamnal 46l (400 MHz, $CDCl_3$)



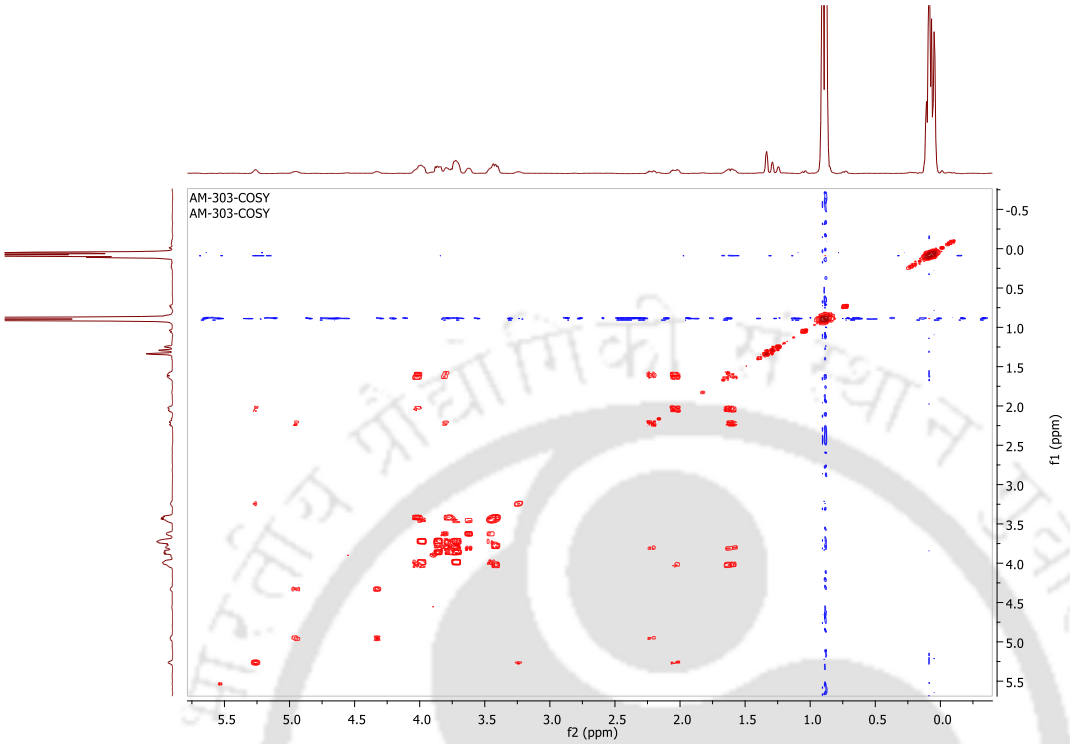
^{1}H NMR of 3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-glucopyranose 50a (400 MHz, $CDCl_3$)



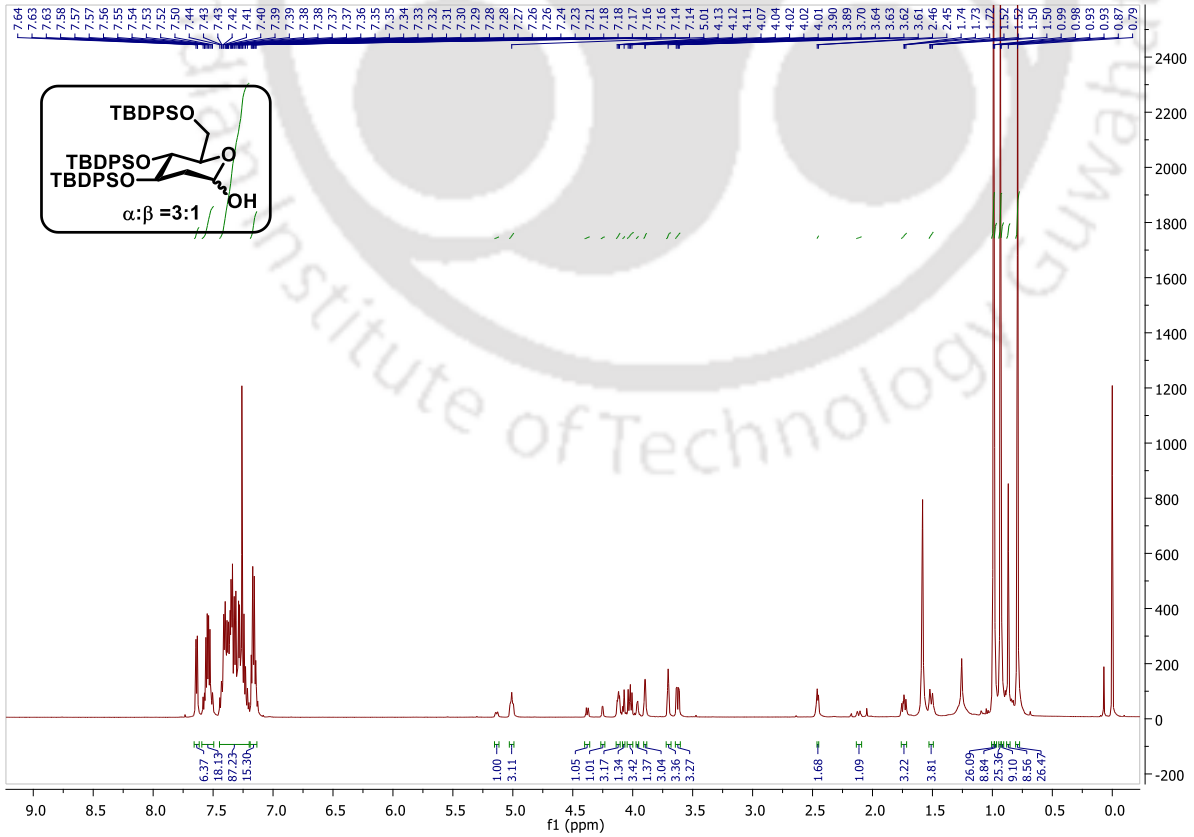
^{13}C NMR of 3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-glucopyranose 50a (400 MHz, $CDCl_3$)



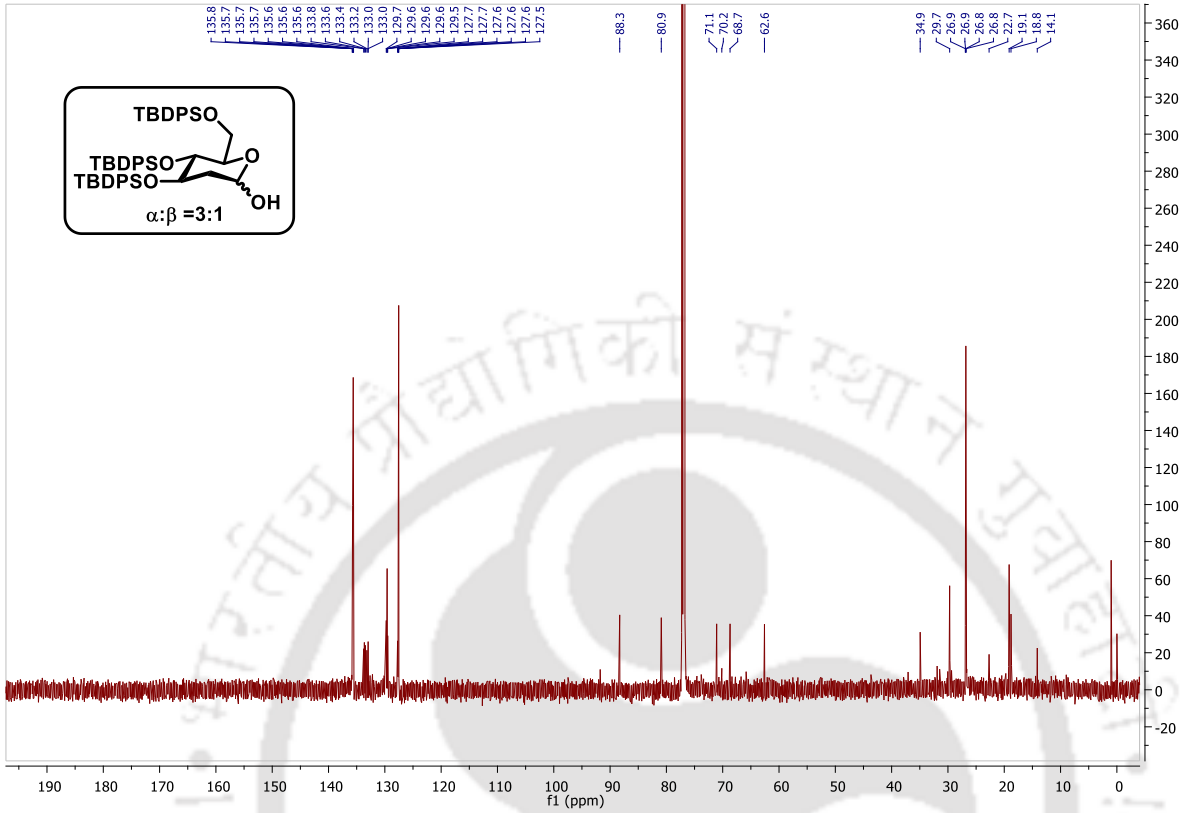
COSY NMR of 3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-glucopyranose 50a (400 MHz, $CDCl_3$)



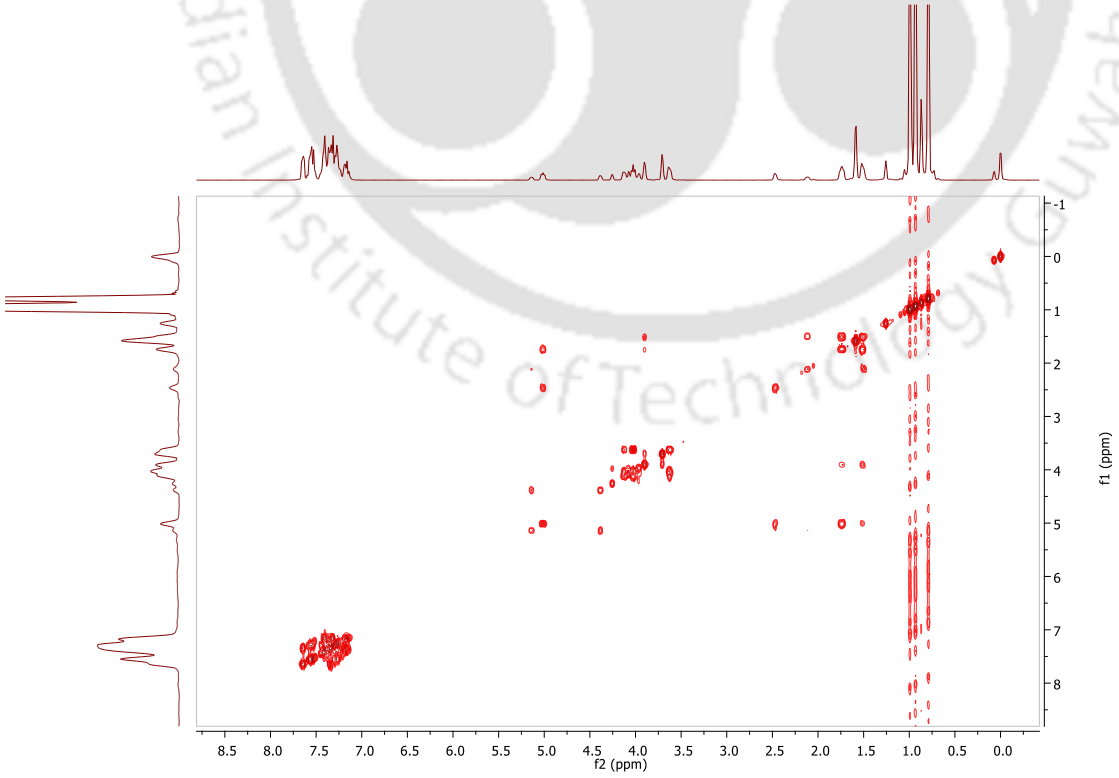
^{1}H NMR of 3,4,6-tri-*O*-*tert*-butyldiphenylsilyl-D-glucopyranose 50b (600 MHz, $CDCl_3$)



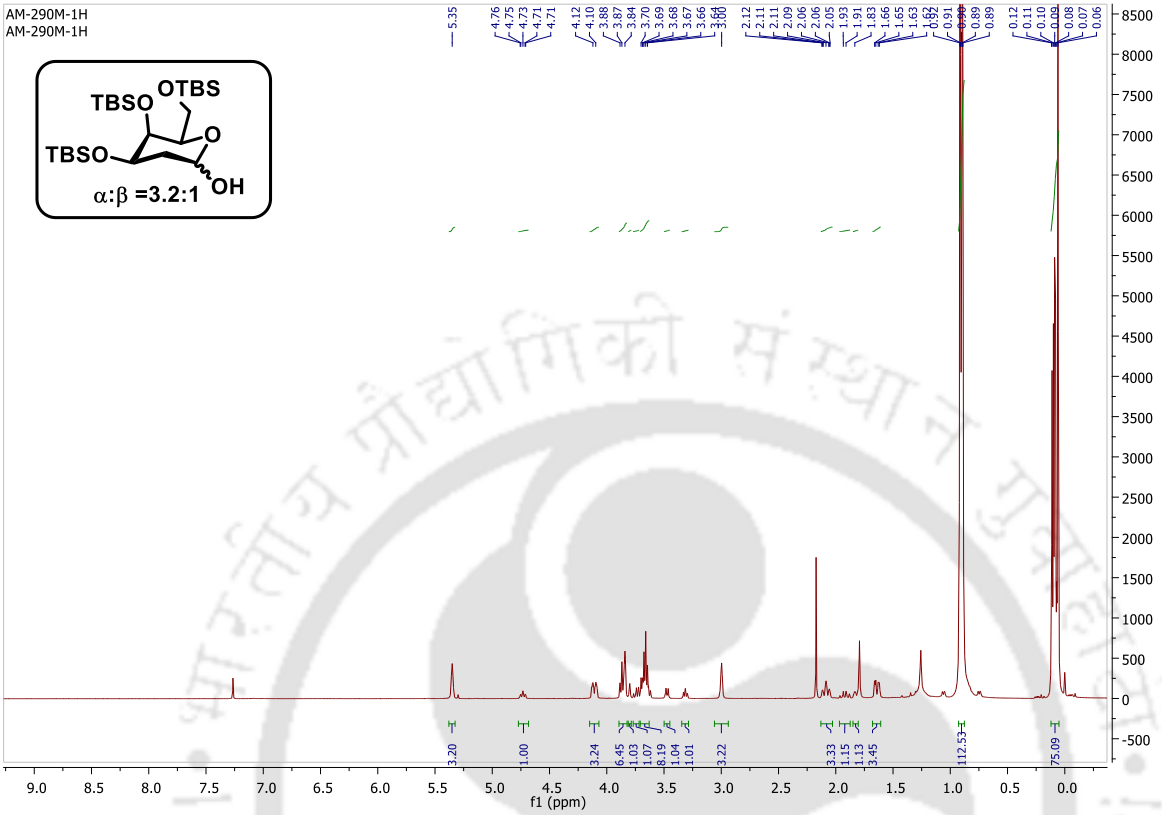
^{13}C NMR of 3,4,6-tri-*O*-*tert*-butyldiphenylsilyl-D-glucopyranose 50b (600 MHz, $CDCl_3$)



COSY NMR of 3,4,6-tri-*O*-*tert*-butyldiphenylsilyl-D-glucopyranose 50b (600 MHz, $CDCl_3$)



^{1}H NMR of 3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-galactopyranose 50c (400 MHz, $CDCl_3$)



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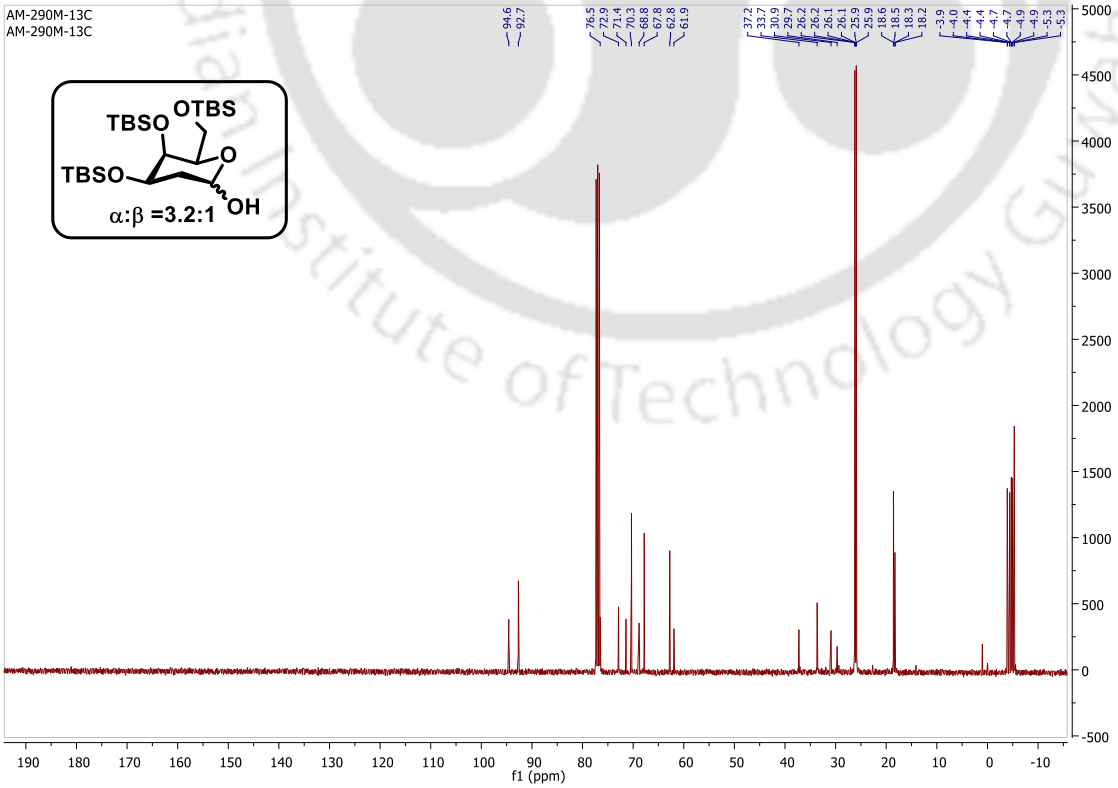
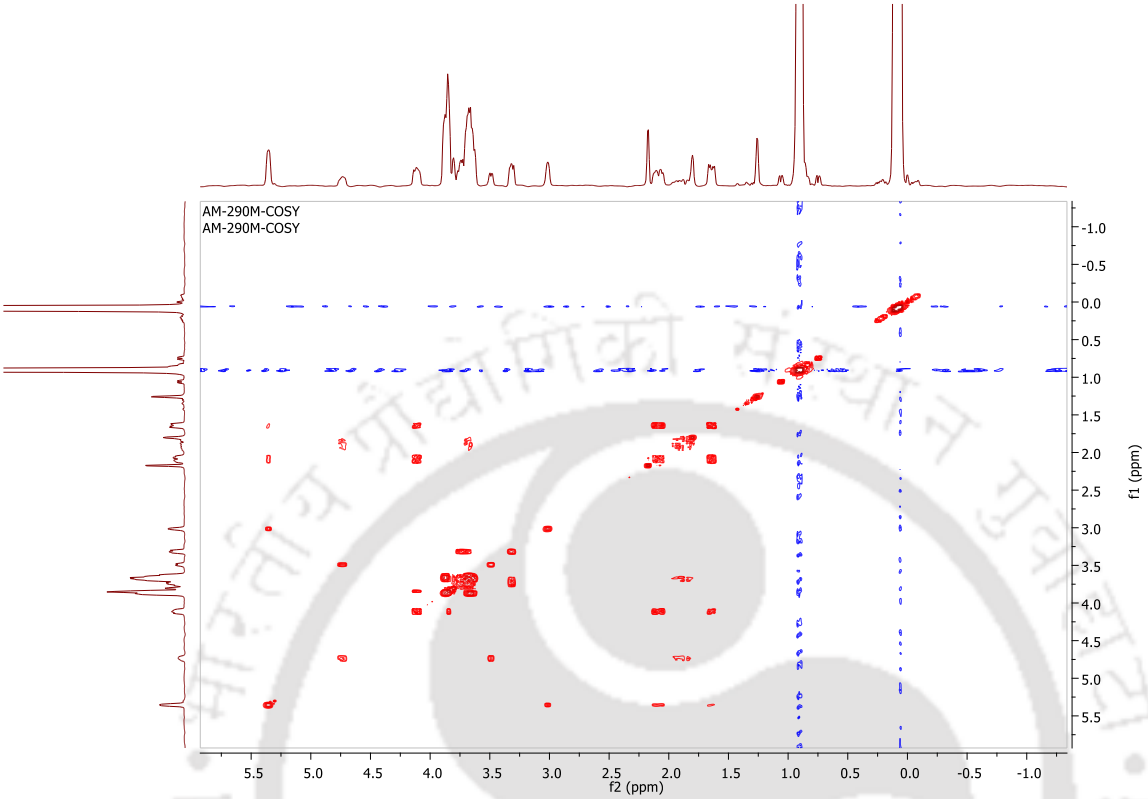
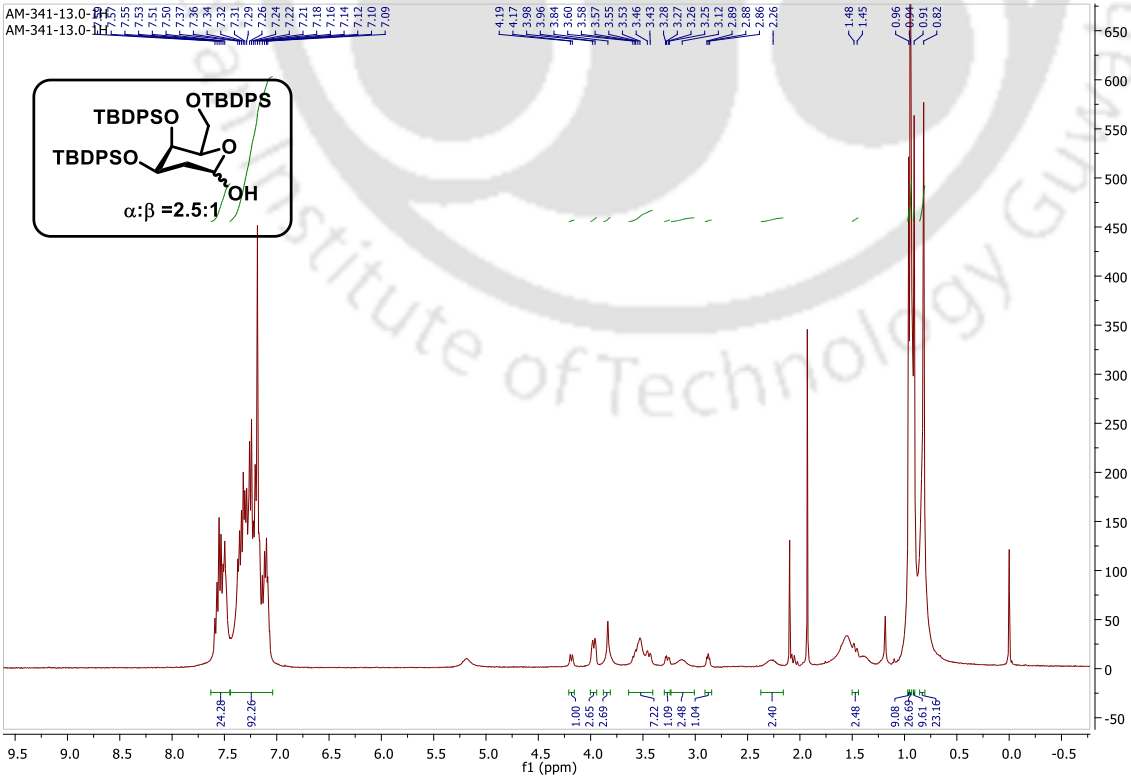


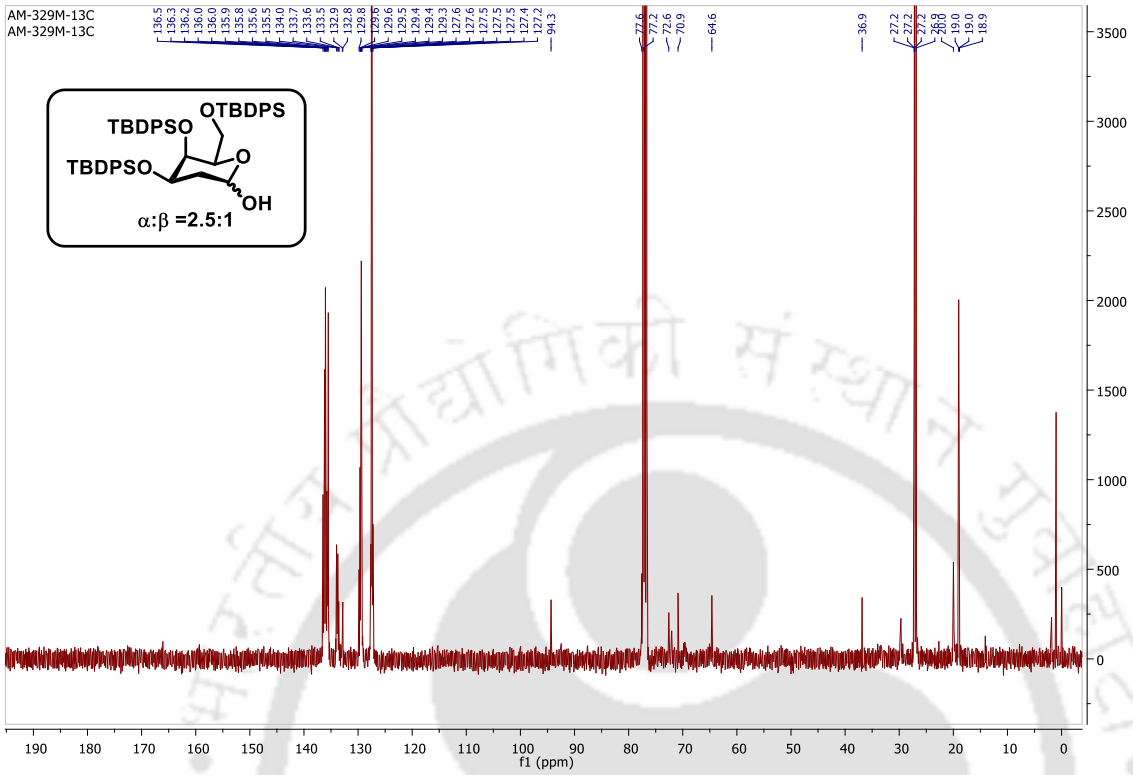
COSY NMR of 3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-galactopyranose 50c (400 MHz, $CDCl_3$)



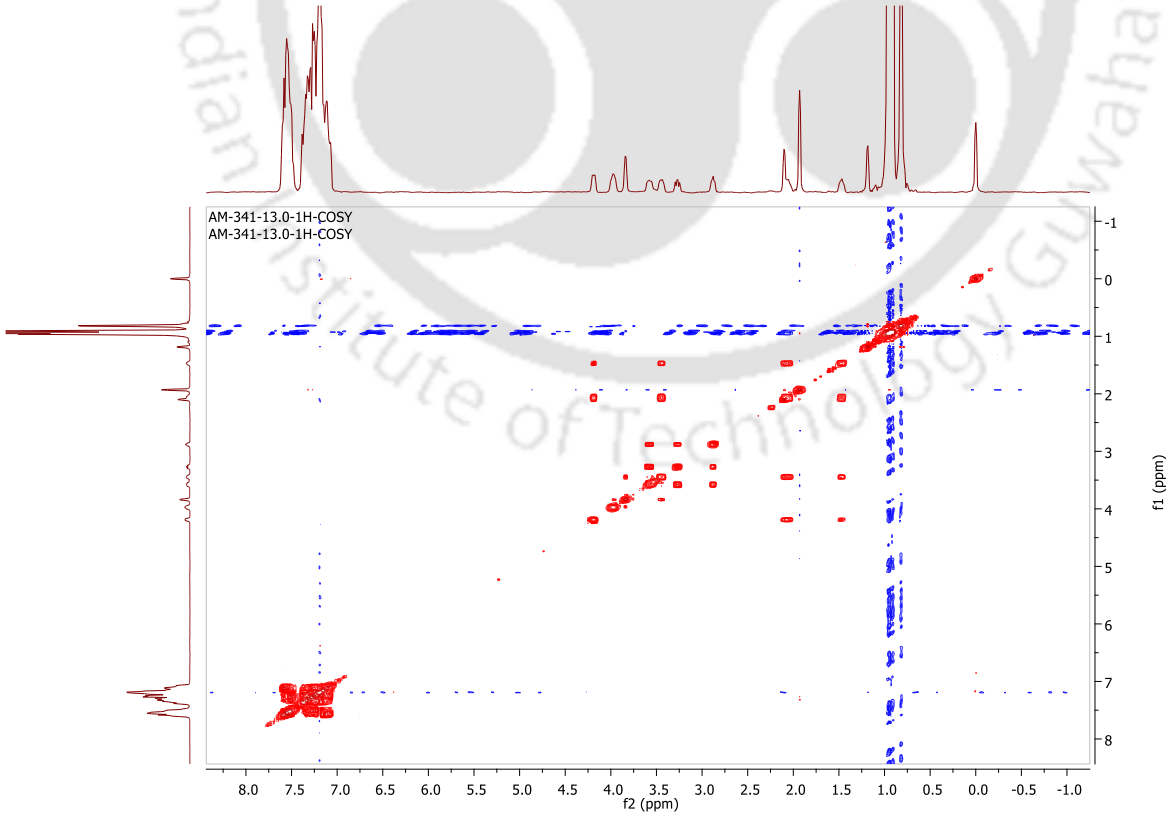
^{1}H NMR of 3,4,6-tri-*O*-*tert*-butyldiphenylsilyl-D-galactopyranose 50d (400 MHz, $CDCl_3$)



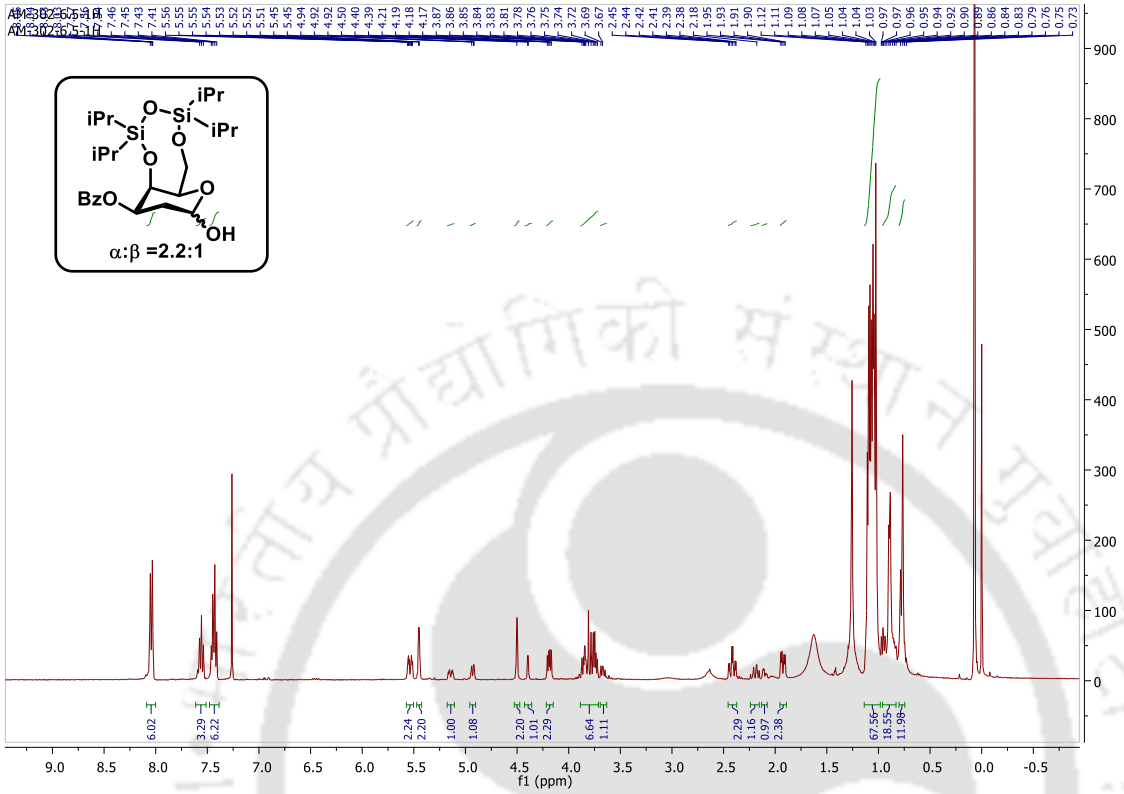
^{13}C NMR of 3,4,6-tri-*O*-*tert*-butyldiphenylsilyl-D-galactopyranose 50d (400 MHz, $CDCl_3$)



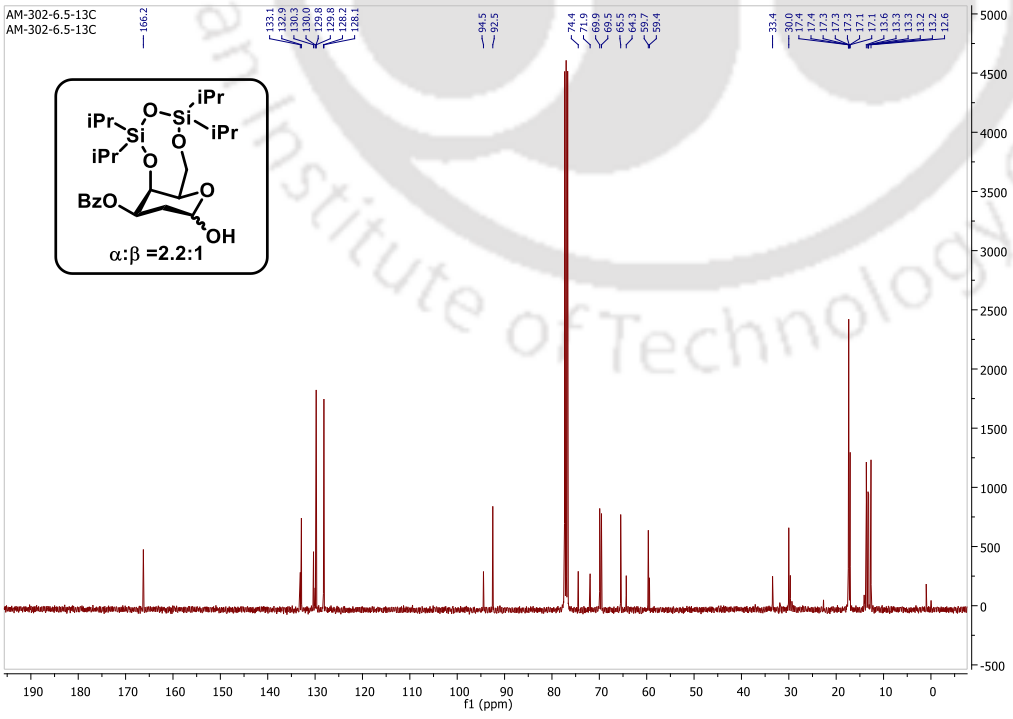
COSY NMR of 3,4,6-tri-*O*-*tert*-butyldiphenylsilyl-D-galactopyranose 50d (400 MHz, $CDCl_3$)



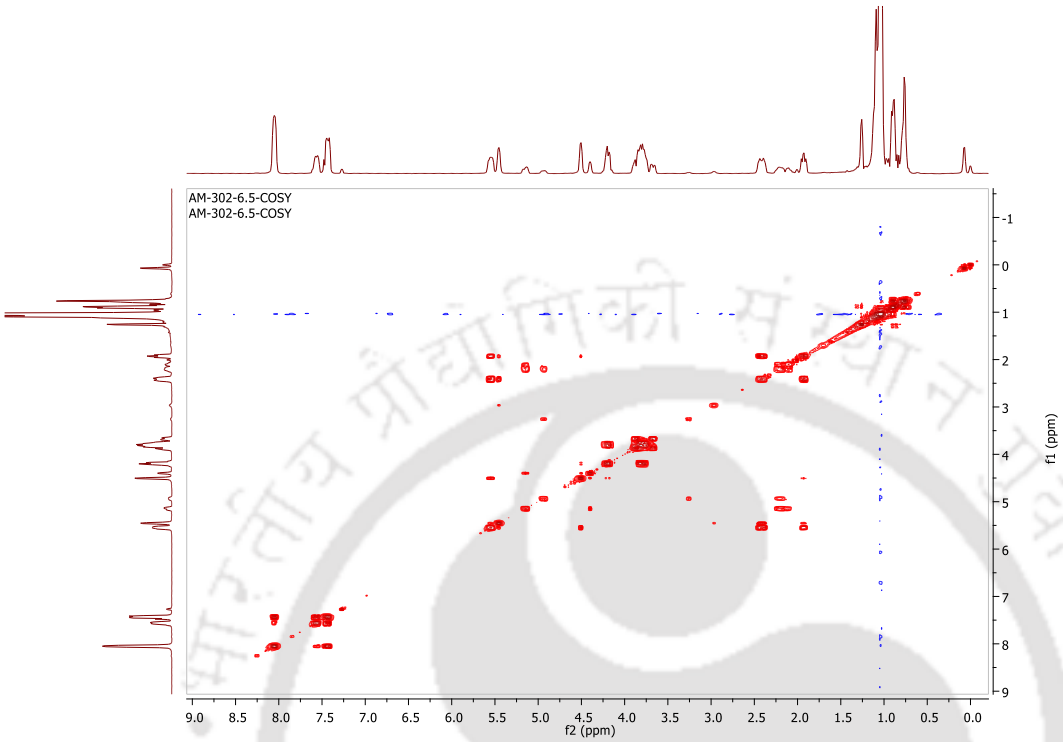
^{1}H NMR of 2-Deoxy-3-O-benzoyl-1,3-O-(tetraisopropyldisiloxane-1,3-diyl)-D-galactopyranose 50e (400 MHz, $CDCl_3$)



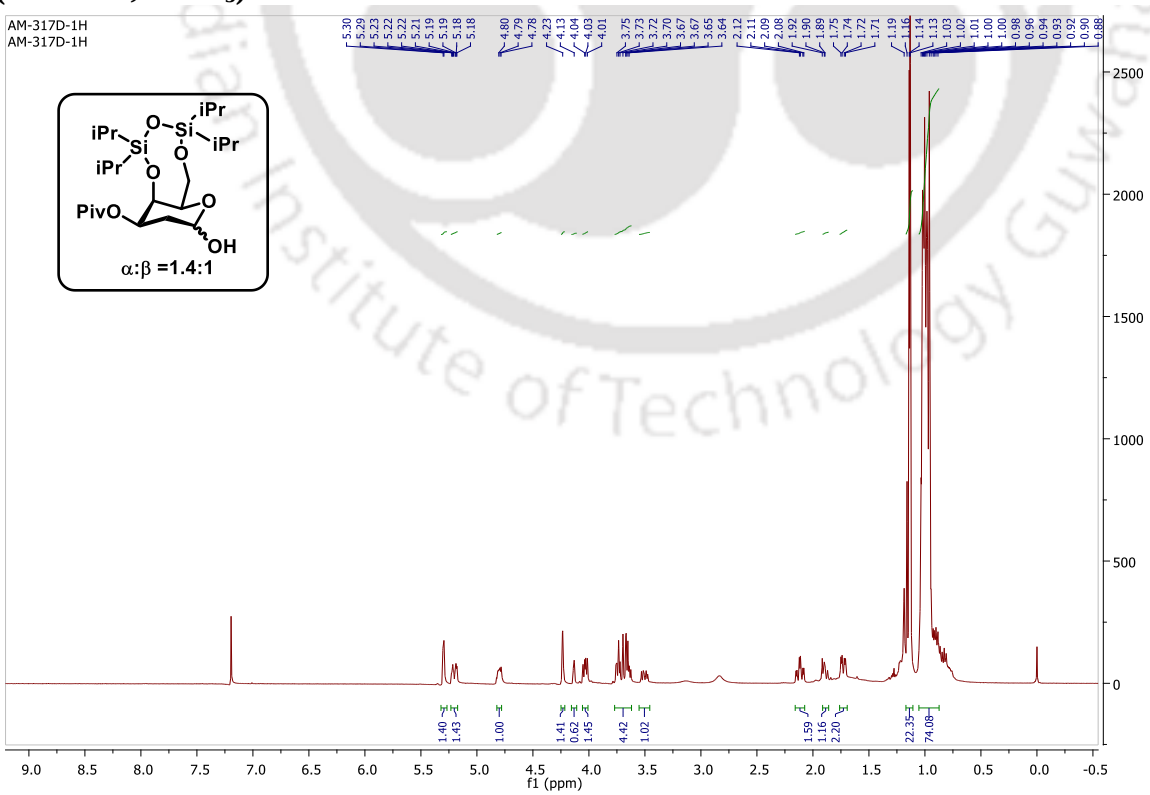
^{13}C NMR of 2-Deoxy-3-O-benzoyl-1,3-O-(tetraisopropyldisiloxane-1,3-diyl)-D-galactopyranose 50e (400 MHz, $CDCl_3$)



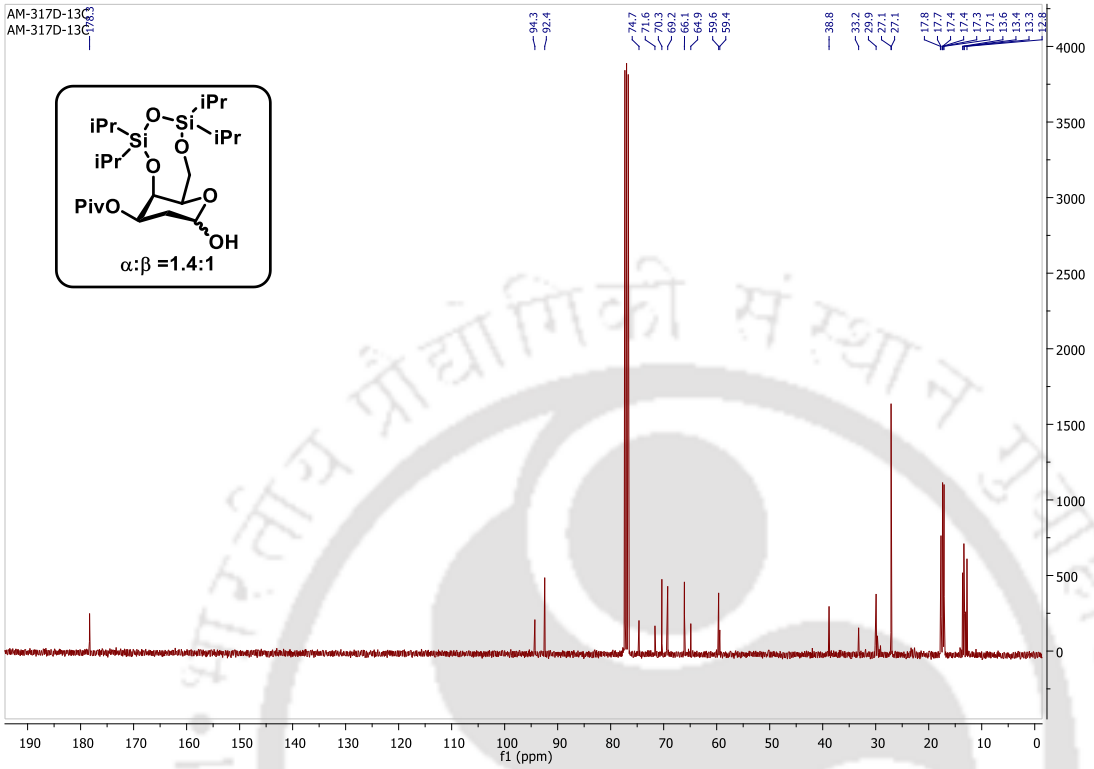
COSY NMR of 2-Deoxy-3-O-benzoyl-1,3-O-(tetraisopropyldisiloxane-1,3-diyl)-D-galactopyranose 50e (400 MHz, $CDCl_3$)



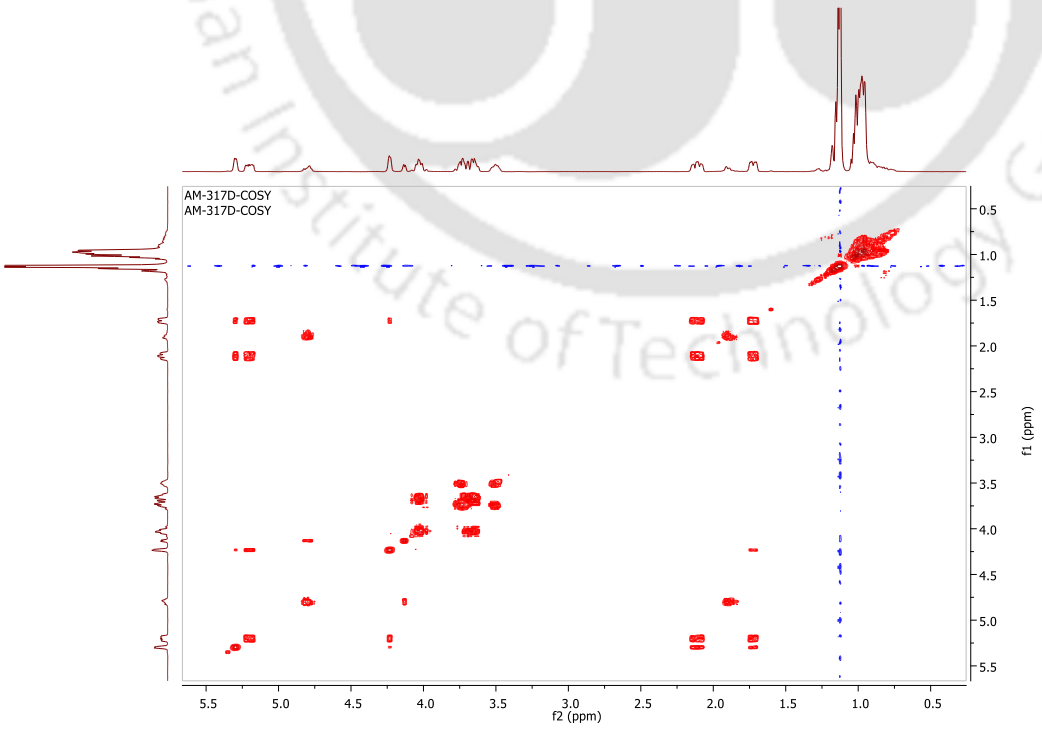
^{1}H NMR of 2-Deoxy-3-O-pivaloyl-1,3-O-(tetraisopropyldisiloxane-1,3-diyl)-D-galactopyranose 50f (400 MHz, $CDCl_3$)



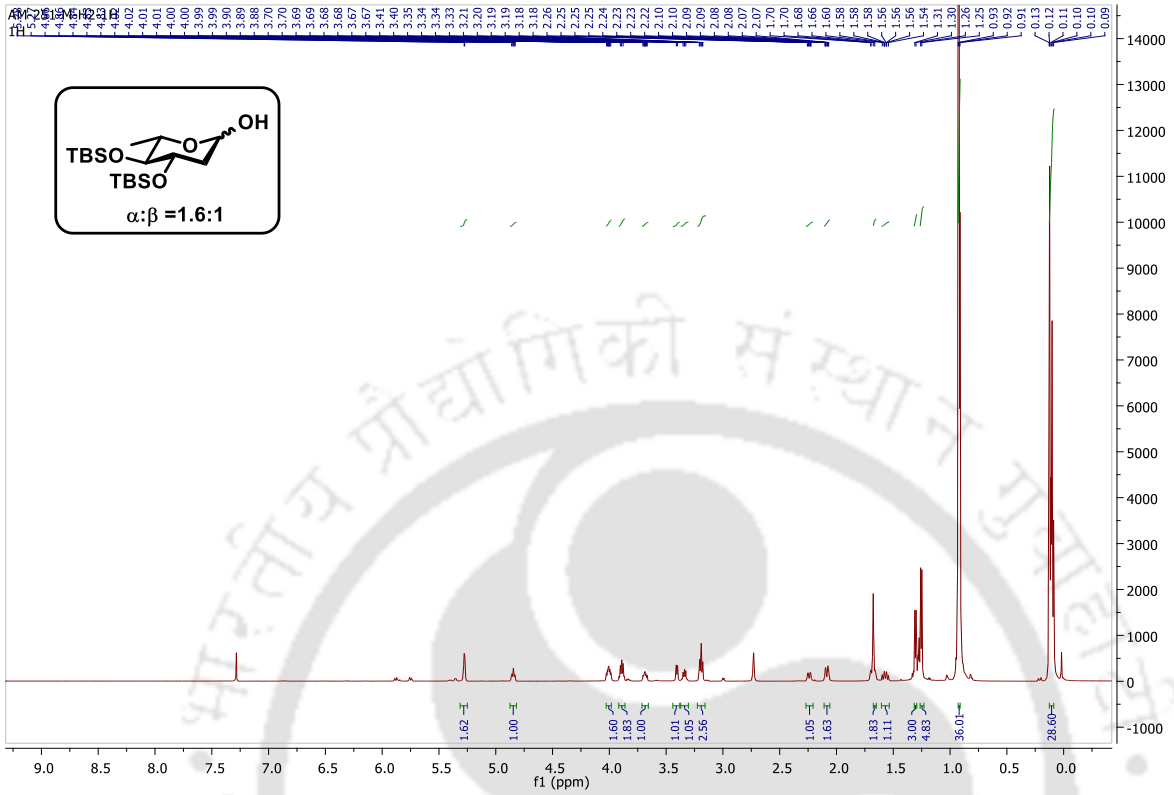
^{13}C NMR of 2-Deoxy-3-O-pivaloyl-1,3-O-(tetraisopropyldisiloxane-1,3-diyl)-D-galactopyranose 50f (400 MHz, $CDCl_3$)



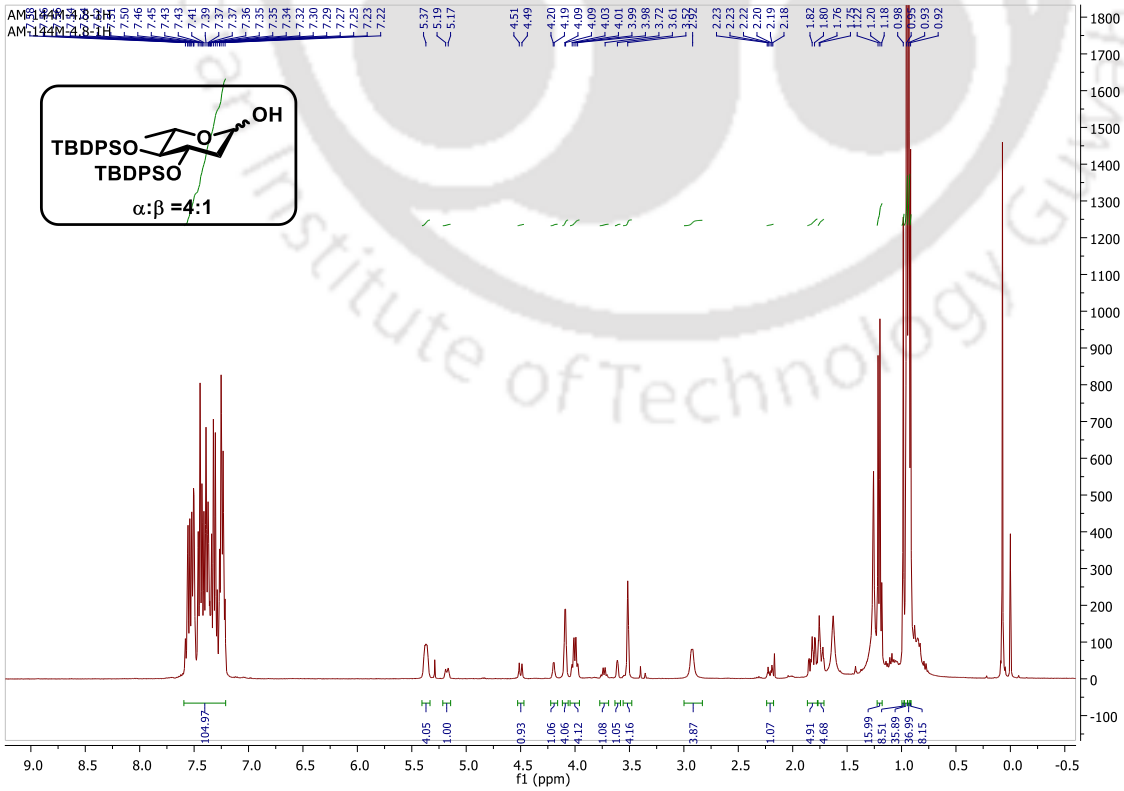
COSY NMR of 2-Deoxy-3-O-pivaloyl-1,3-O-(tetraisopropyldisiloxane-1,3-diyl)-D-galactopyranose 50f (400 MHz, $CDCl_3$)



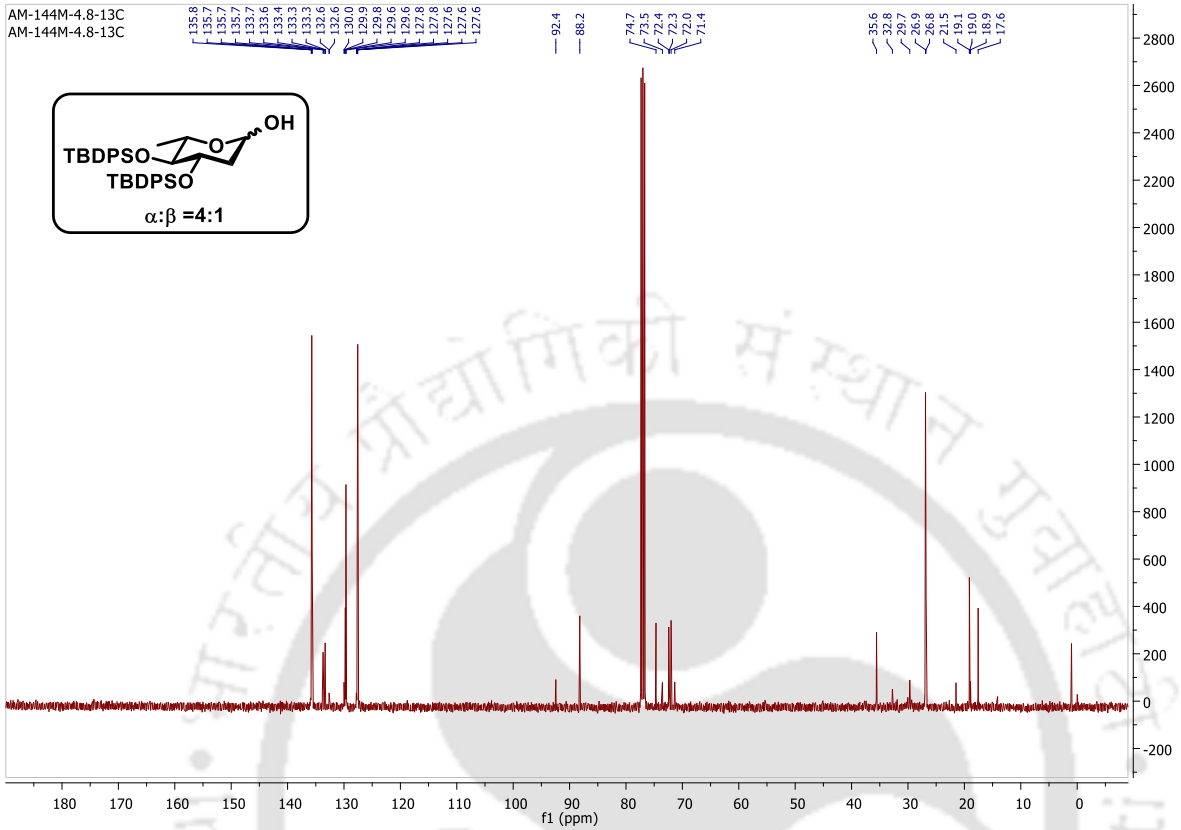
^{1}H NMR of 3,4-di-*O*-*tert*-butyldimethylsilyl-L-rhamnopyranose 50g (600 MHz, $CDCl_3$)



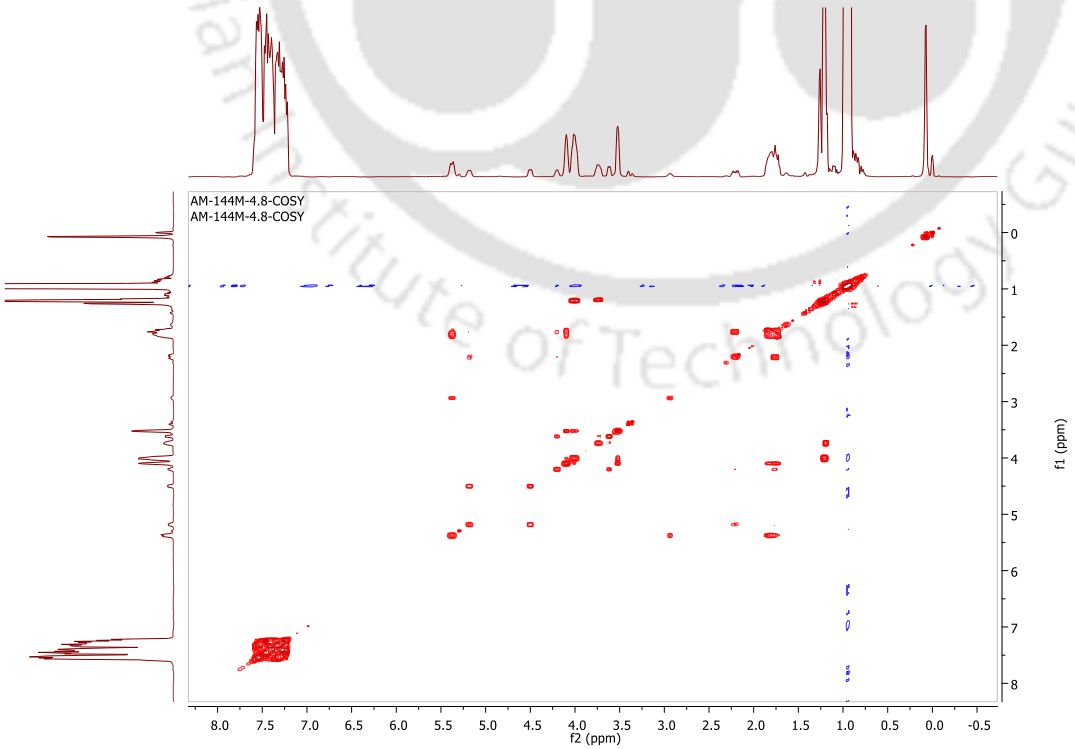
^{1}H NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnopyranose 50h (400 MHz, $CDCl_3$)



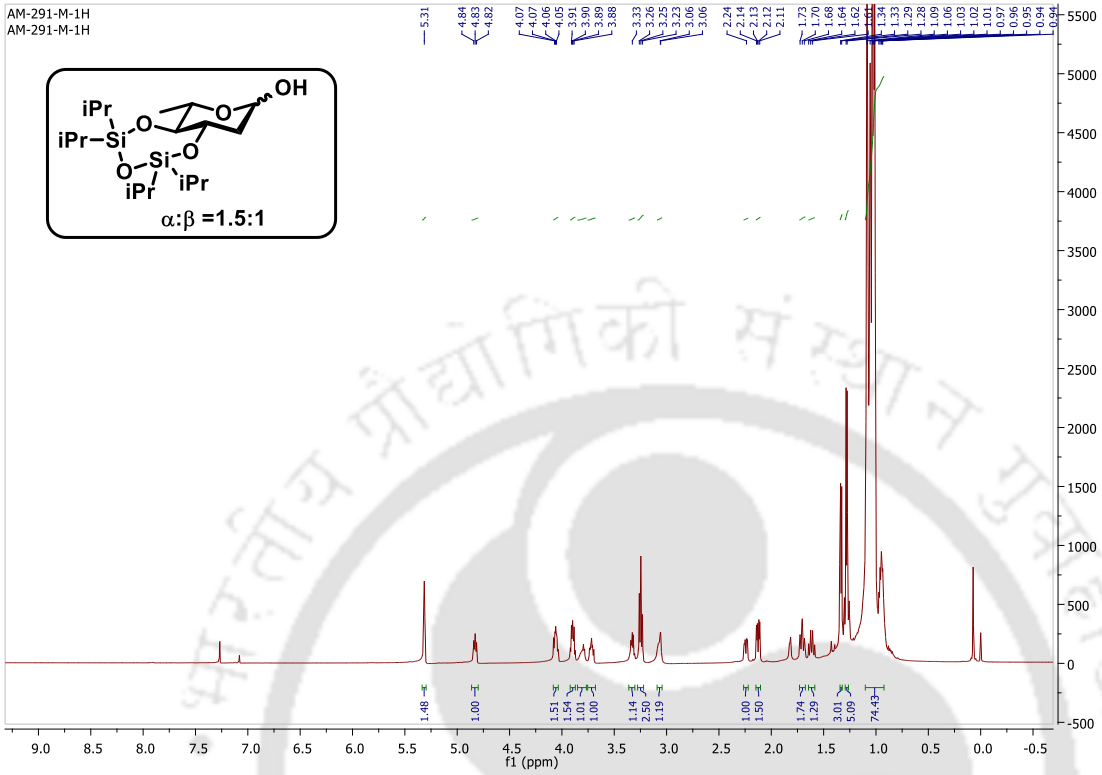
^{13}C NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnopyranose 50h (400 MHz, $CDCl_3$)



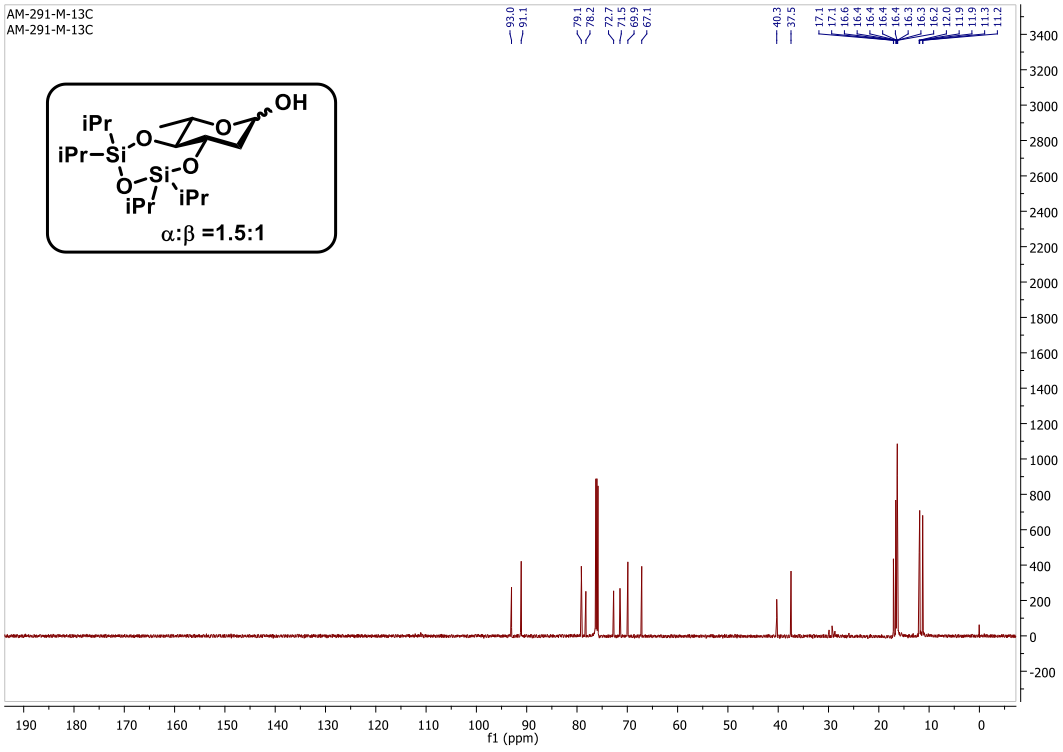
COSY NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnopyranose 50h (400 MHz, $CDCl_3$)



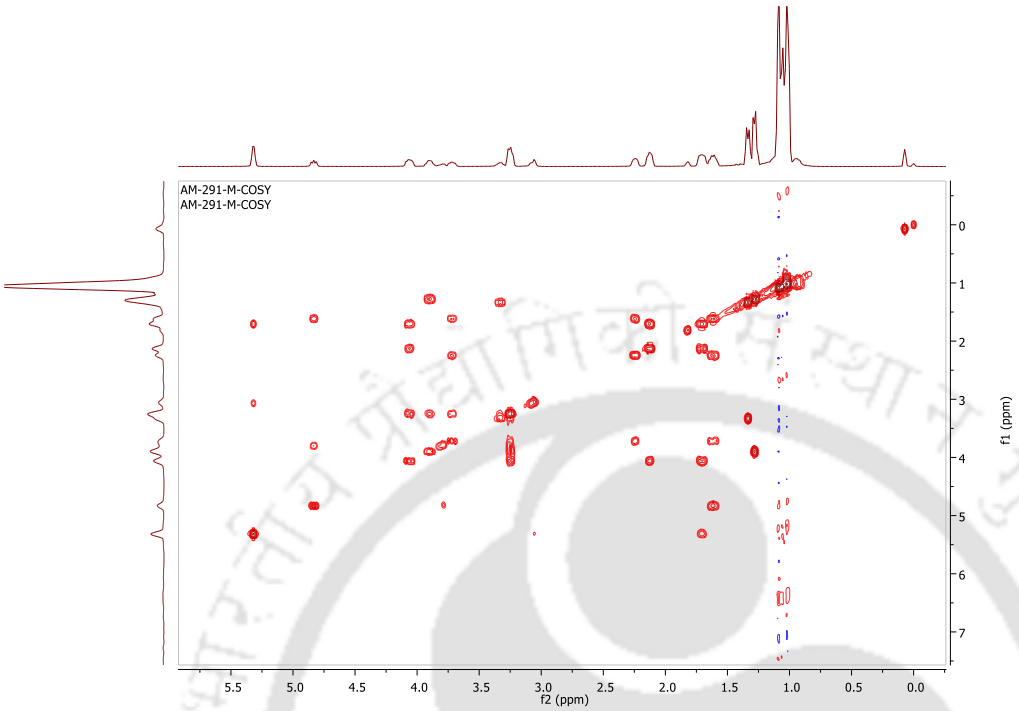
^{1}H NMR of 2,6-Deoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranose 50i (600 MHz, $CDCl_3$)



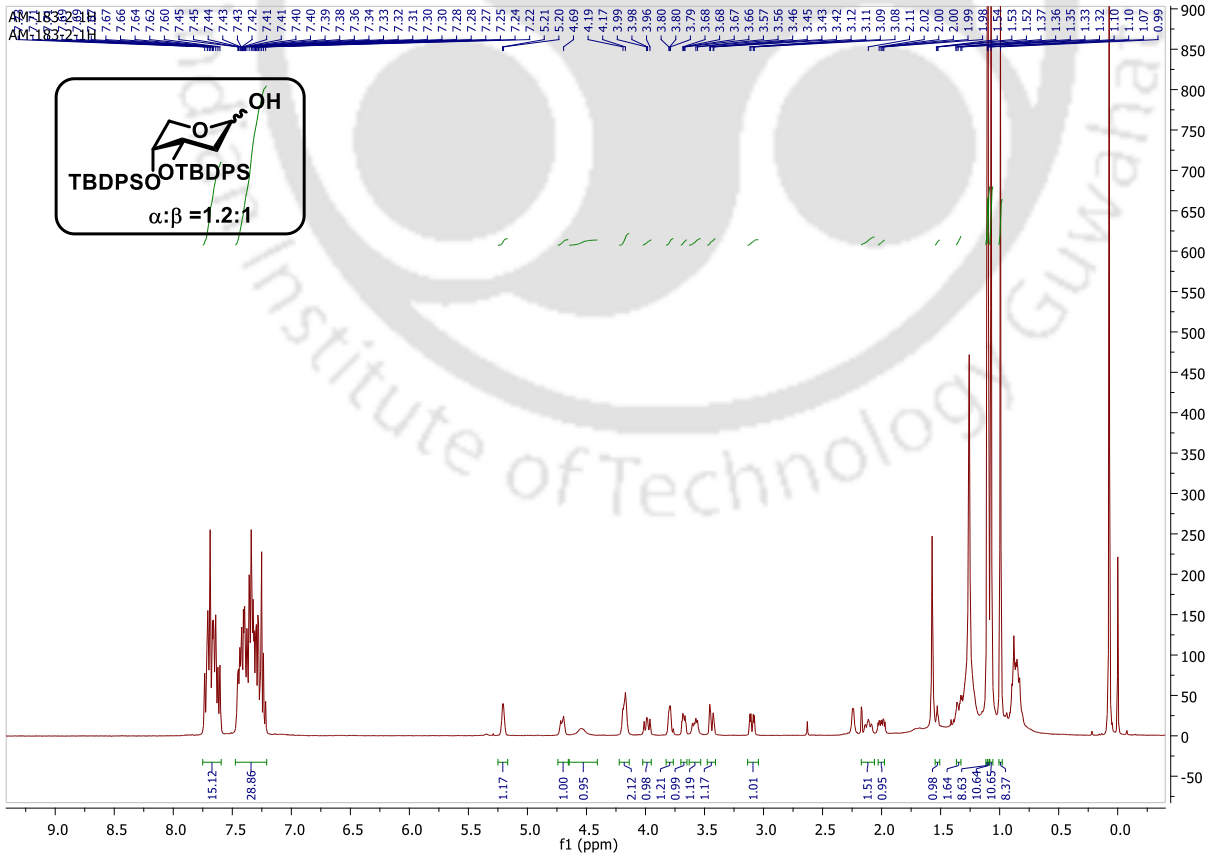
^{13}C NMR of 2,6-Deoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranose 50i (600 MHz, $CDCl_3$)



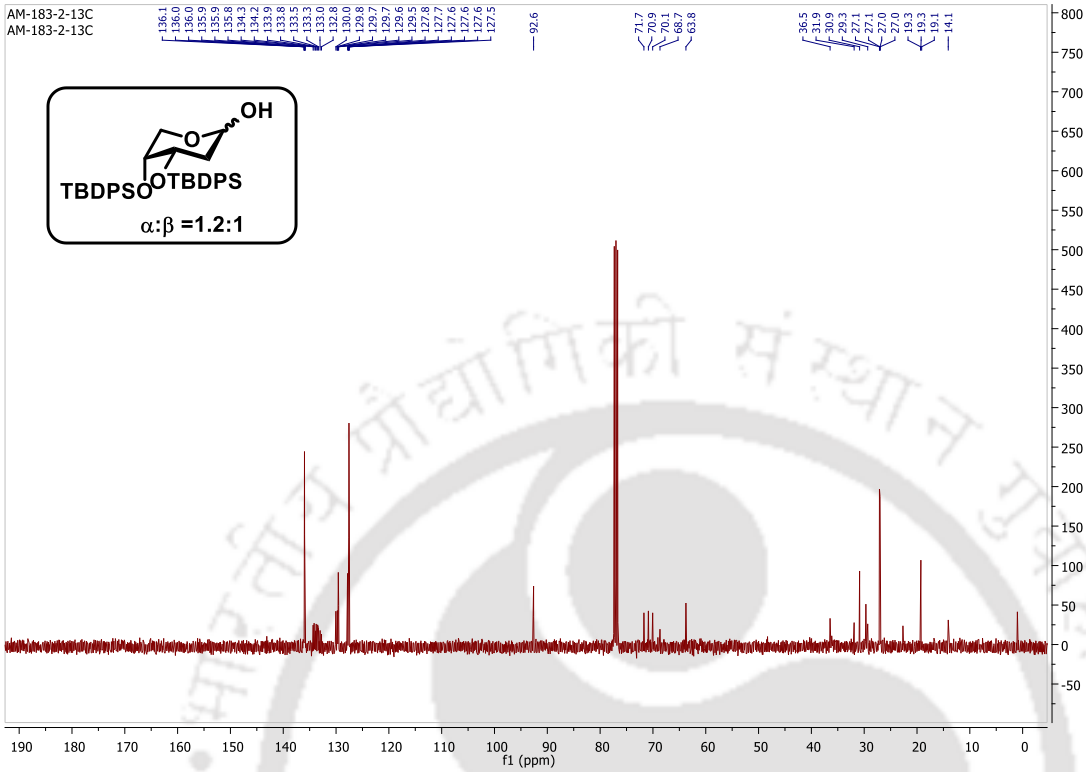
COSY NMR of 2,6-Deoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranose 50i (600 MHz, $CDCl_3$)



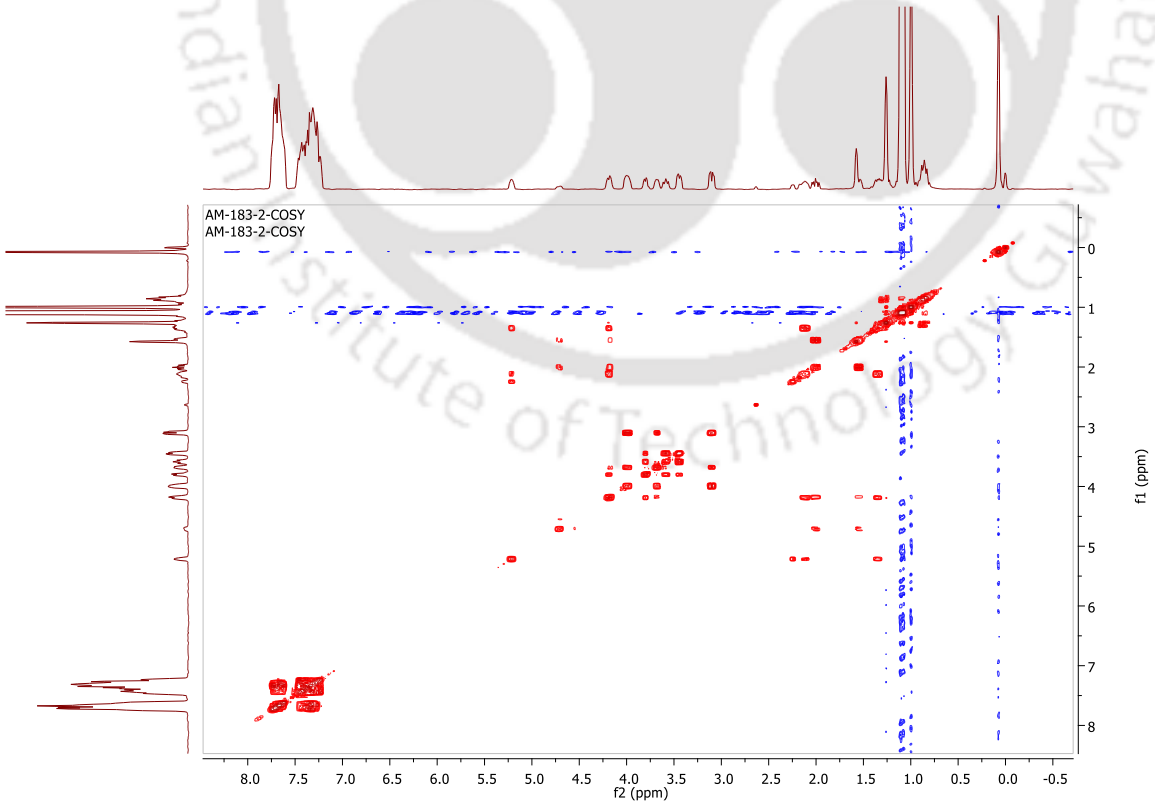
^{1}H NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-D-arabinopyranose 50j (400 MHz, $CDCl_3$)



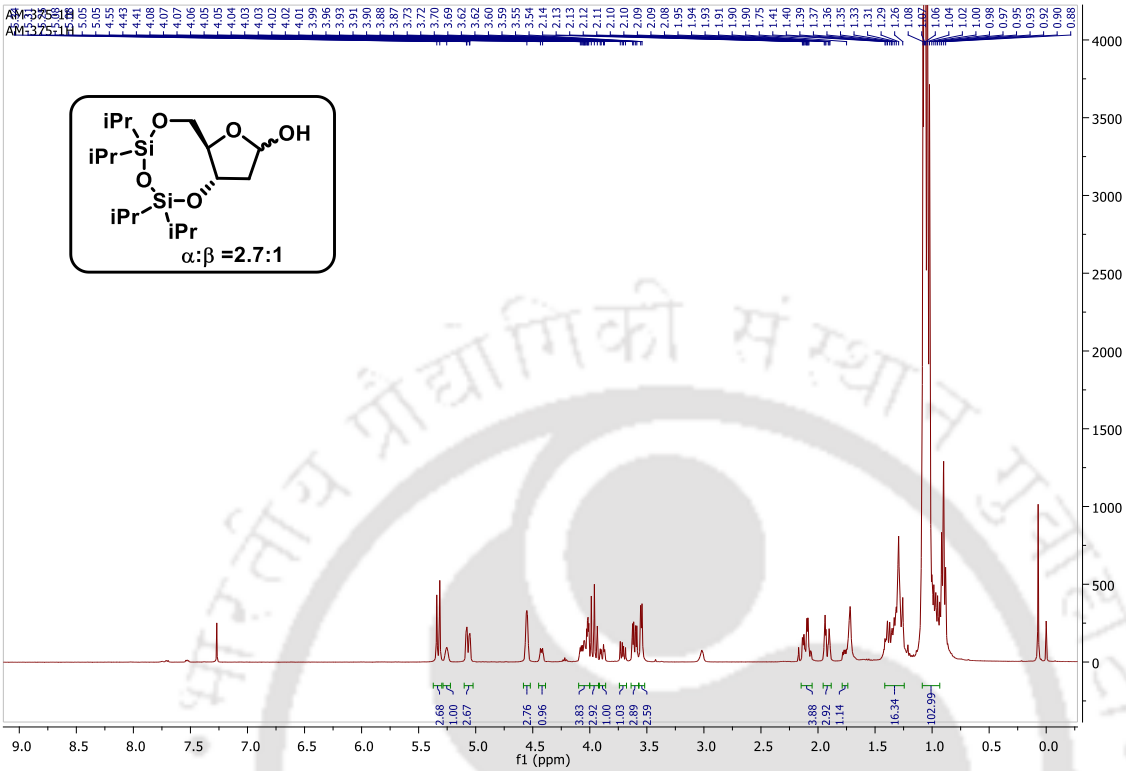
^{13}C NMR of 3,4-di-*O-tert*-butyldiphenylsilyl-D-arabinopyranose 50j (400 MHz, $CDCl_3$)



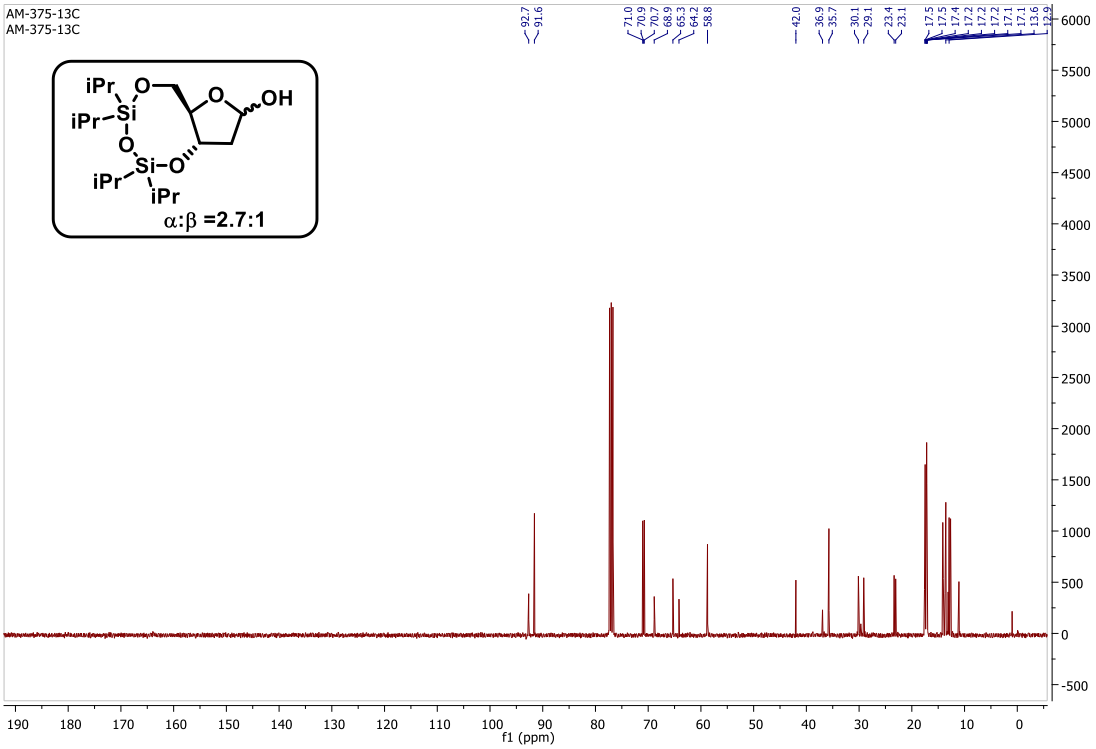
COSY NMR of 3,4-di-*O-tert*-butyldiphenylsilyl-D-arabinopyranose 50j (400 MHz, $CDCl_3$)



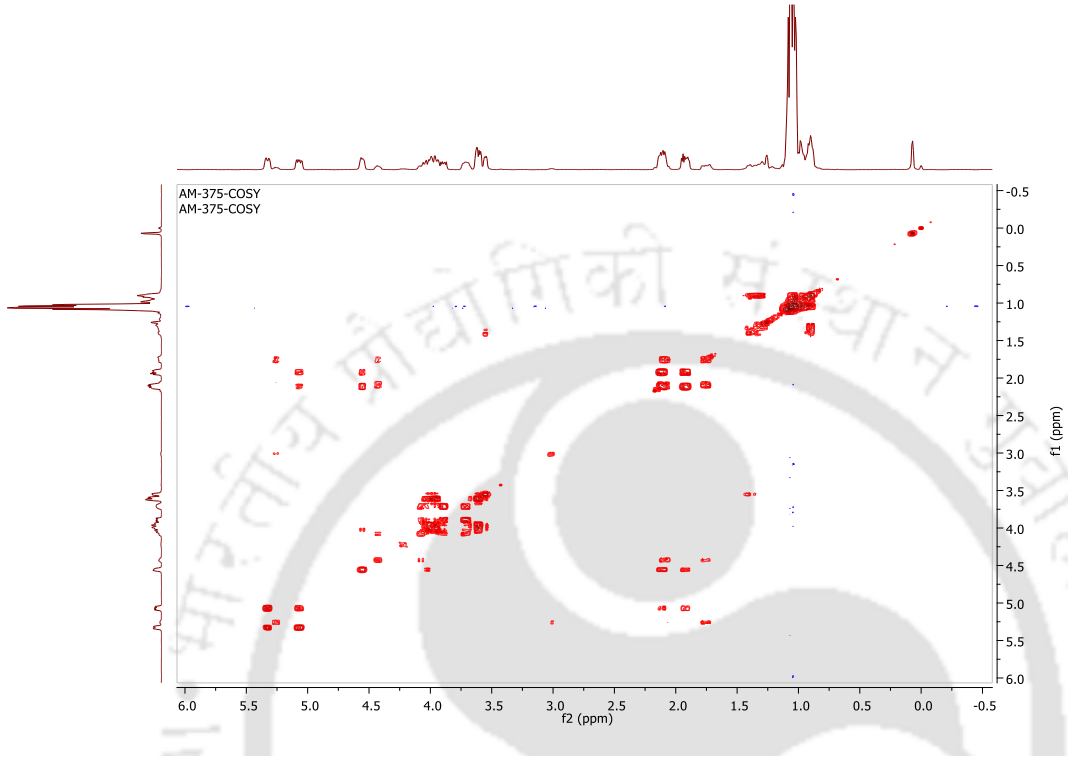
^{1}H NMR of 1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyl-disiloxane-1,3-diyl)-D-ribofuranoside 50k (400 MHz, $CDCl_3$)



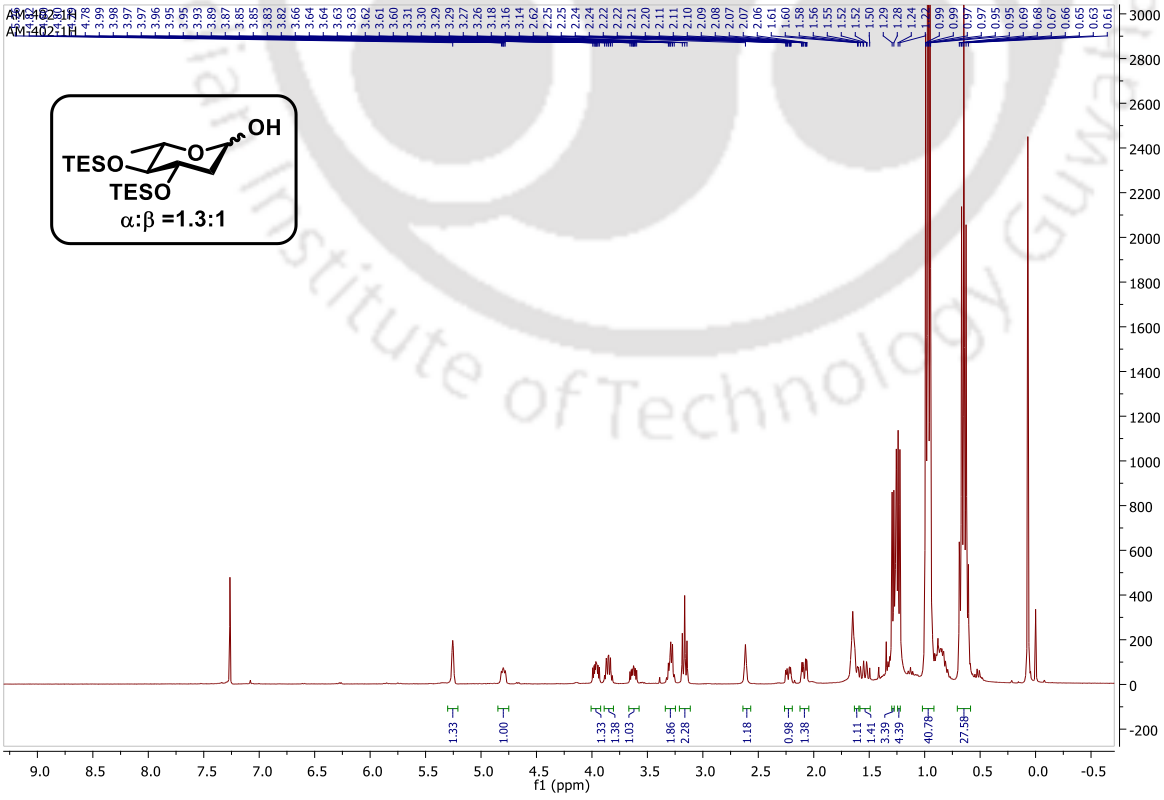
^{13}C NMR of 1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyl-disiloxane-1,3-diyl)-D-ribofuranose 50k (400 MHz, $CDCl_3$)



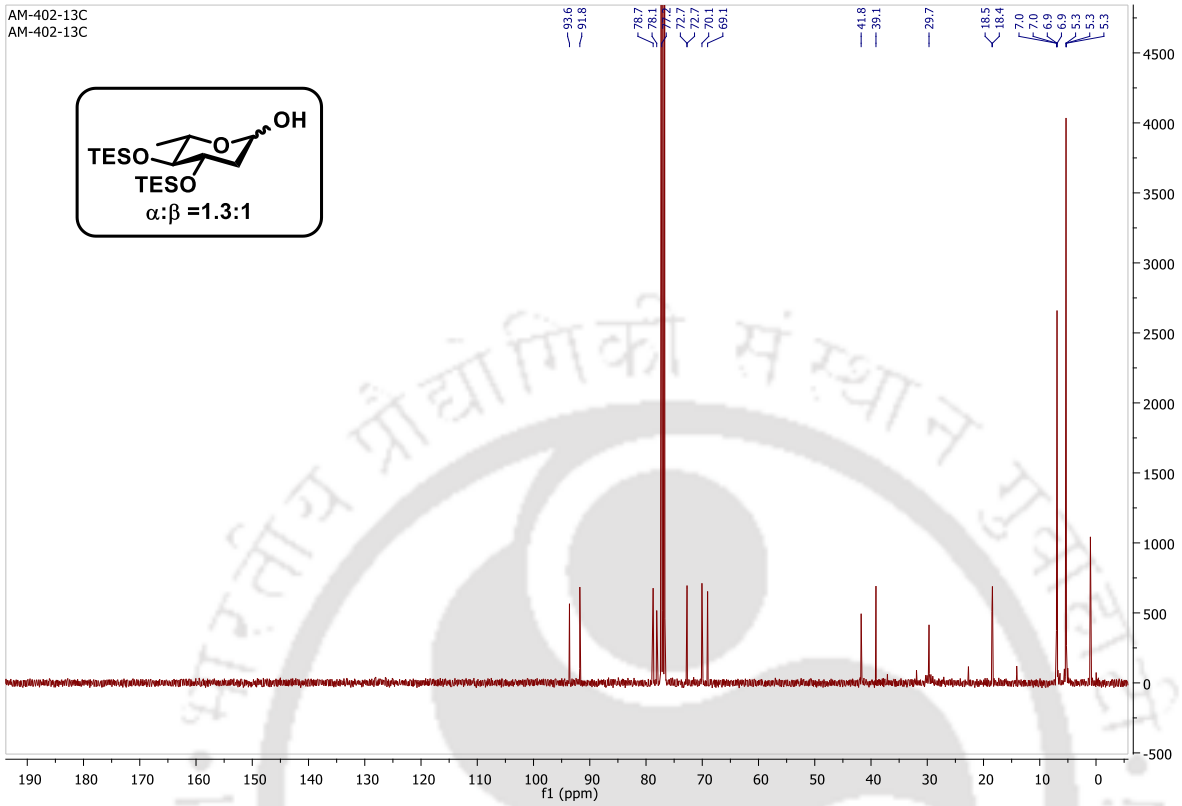
COSY NMR of 1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyl-disiloxane-1,3-diyl)-D-ribofuranoside 50k (400 MHz, $CDCl_3$)



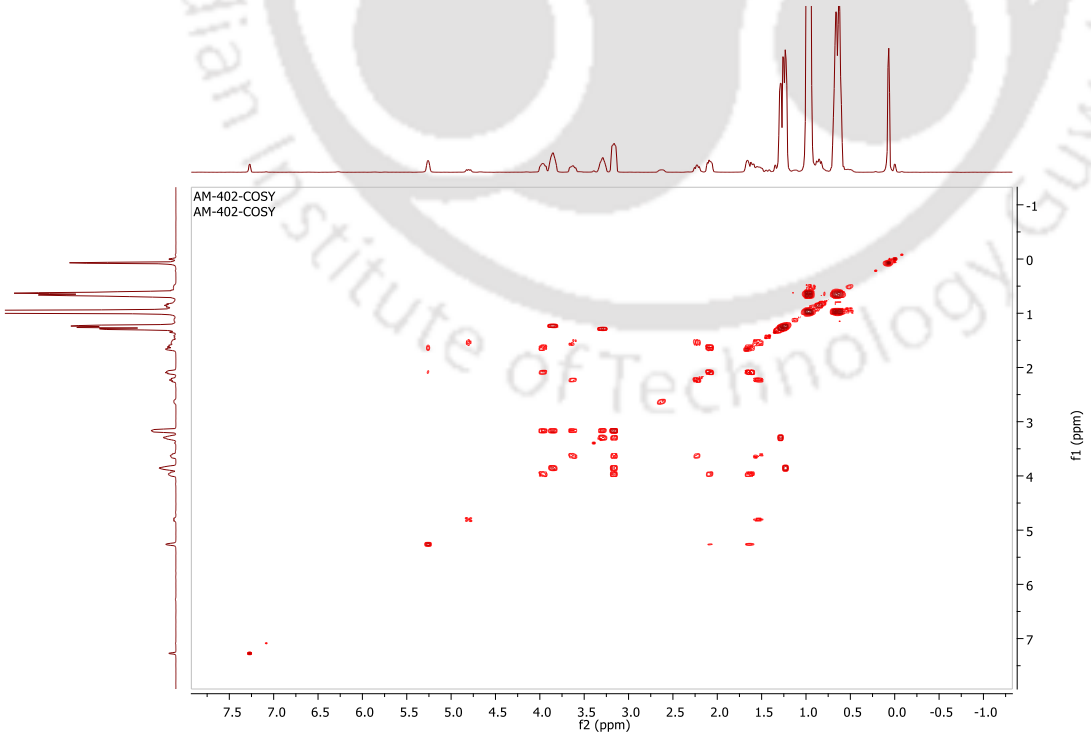
^{1}H NMR of 3,4-di-O-triethylsilyl-L-Rhammopyranose 50l (400 MHz, $CDCl_3$)



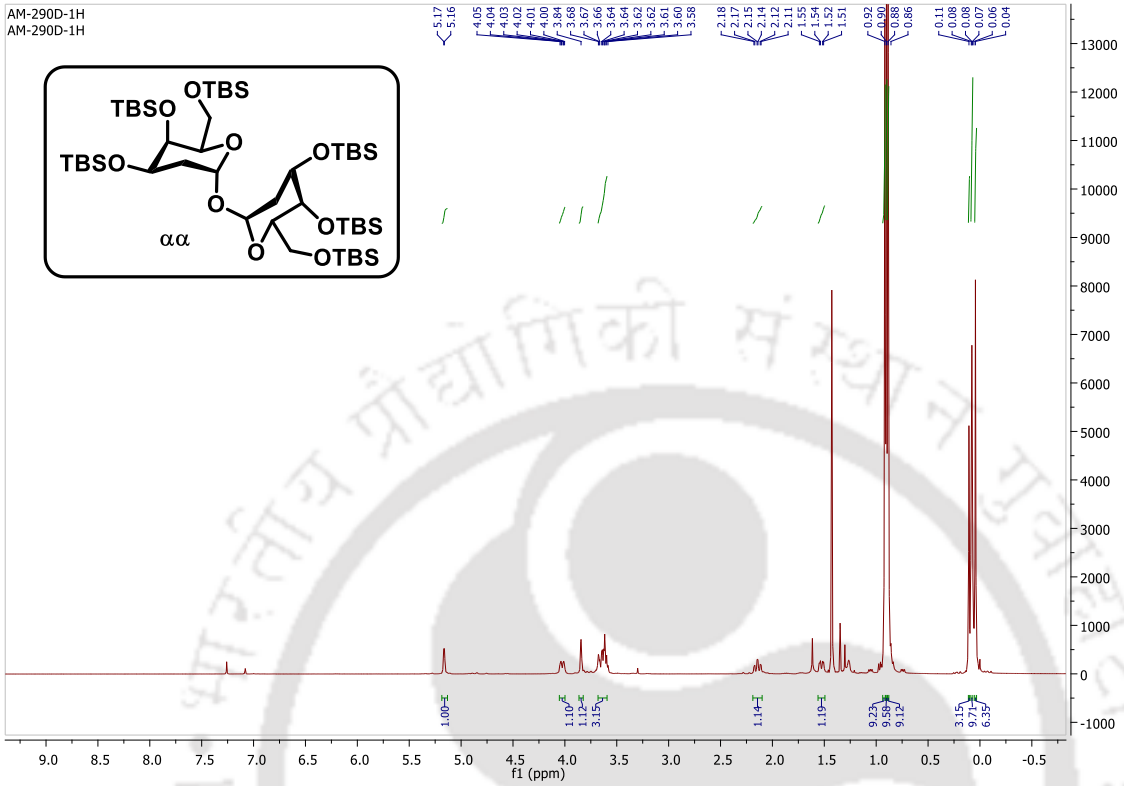
^{13}C NMR of 3,4-di-O-triethylsilyl-L-Rhammopyranose 50l (400 MHz, $CDCl_3$)



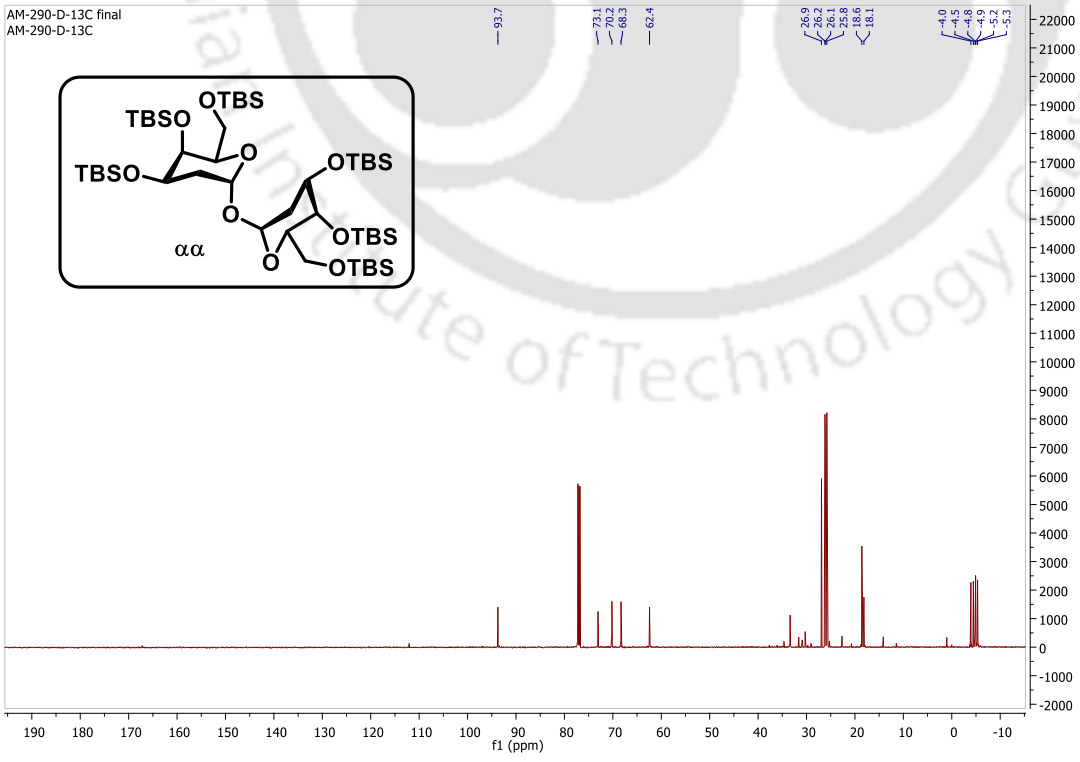
COSY NMR of 3,4-di-O-triethylsilyl-L-Rhammopyranose 50l (400 MHz, $CDCl_3$)



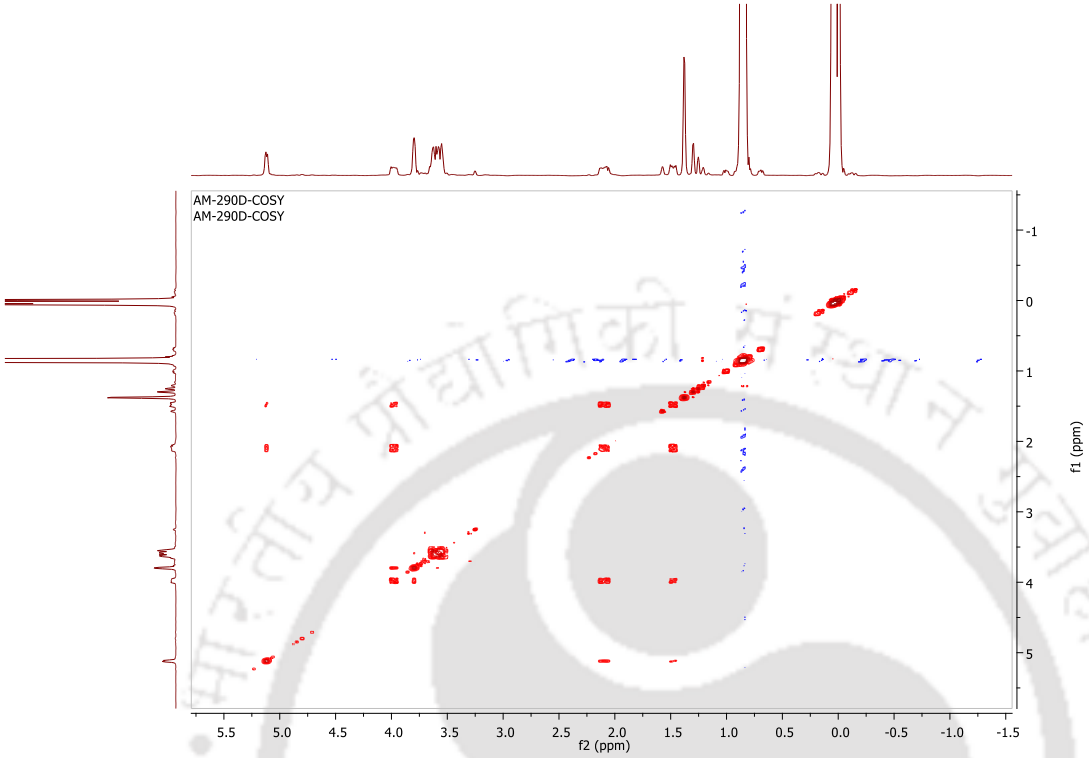
^{1}H NMR of (3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-galactopyranosyl)-(1→1)-3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-galactopyranoside 51a (400 MHz, $CDCl_3$)



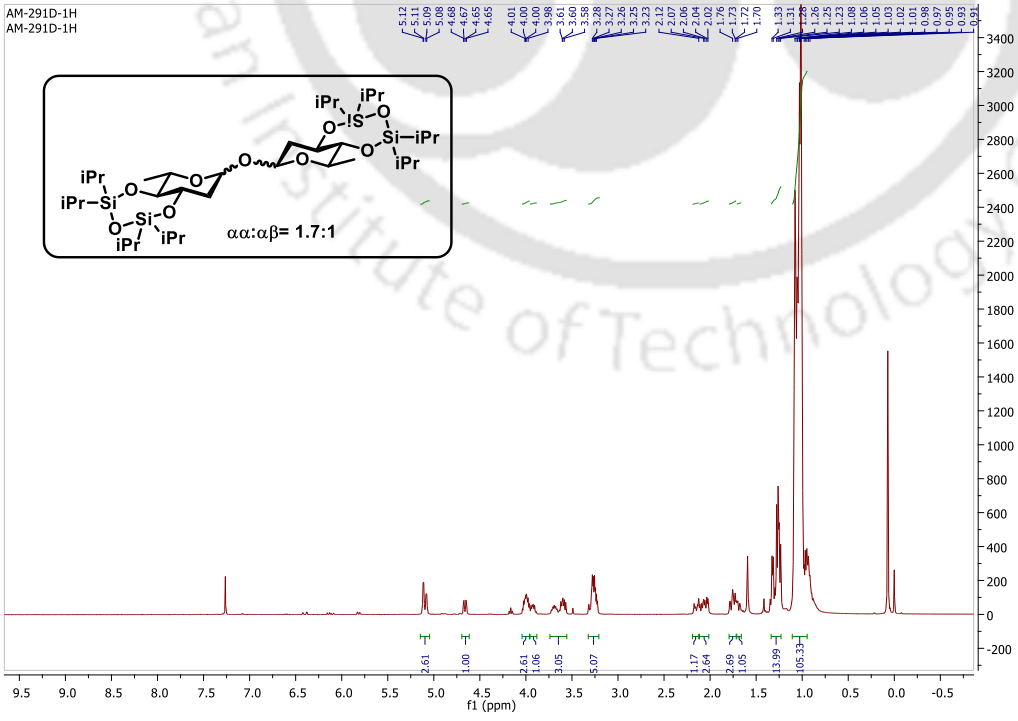
^{13}C NMR of (3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-galactopyranosyl)-(1→1)-3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-galactopyranoside 51a (400 MHz, $CDCl_3$)



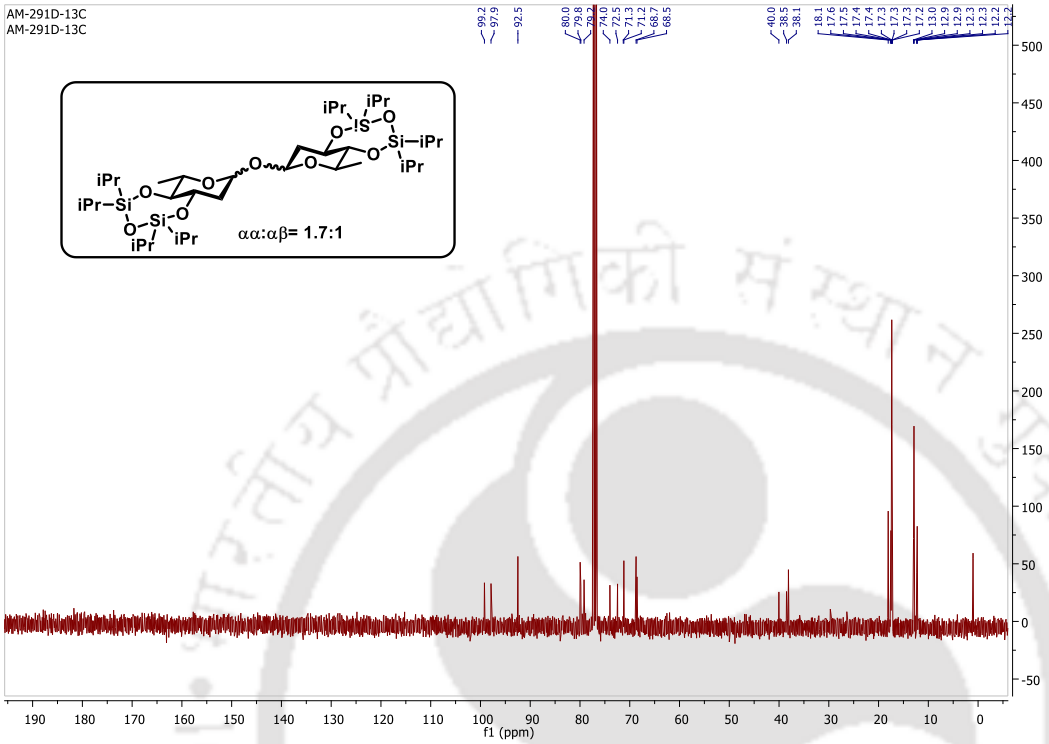
COSY NMR of (3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-galactopyranosyl)-(1→1)-3,4,6-tri-*O*-*tert*-butyldimethylsilyl-D-galactopyranoside 51a (400 MHz, $CDCl_3$)



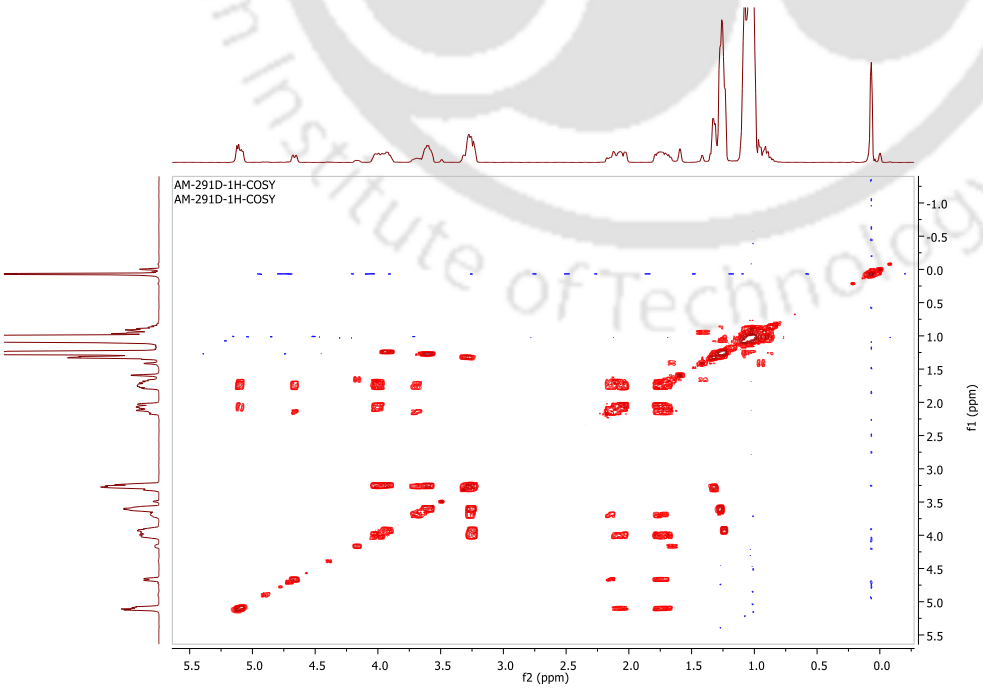
^{1}H NMR of (2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranosyl)-(1→1)-2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranoside 51b (400 MHz, $CDCl_3$)



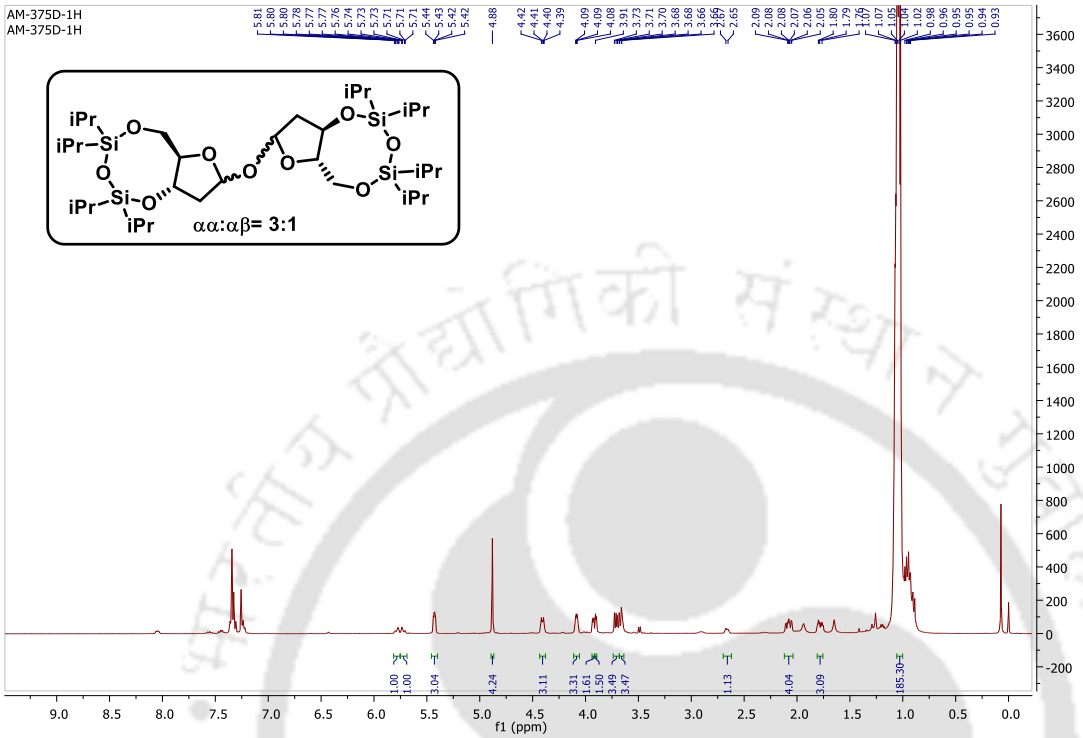
^{13}C NMR of (2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranosyl) -(1→1)-2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranoside 51b (400 MHz, $CDCl_3$)



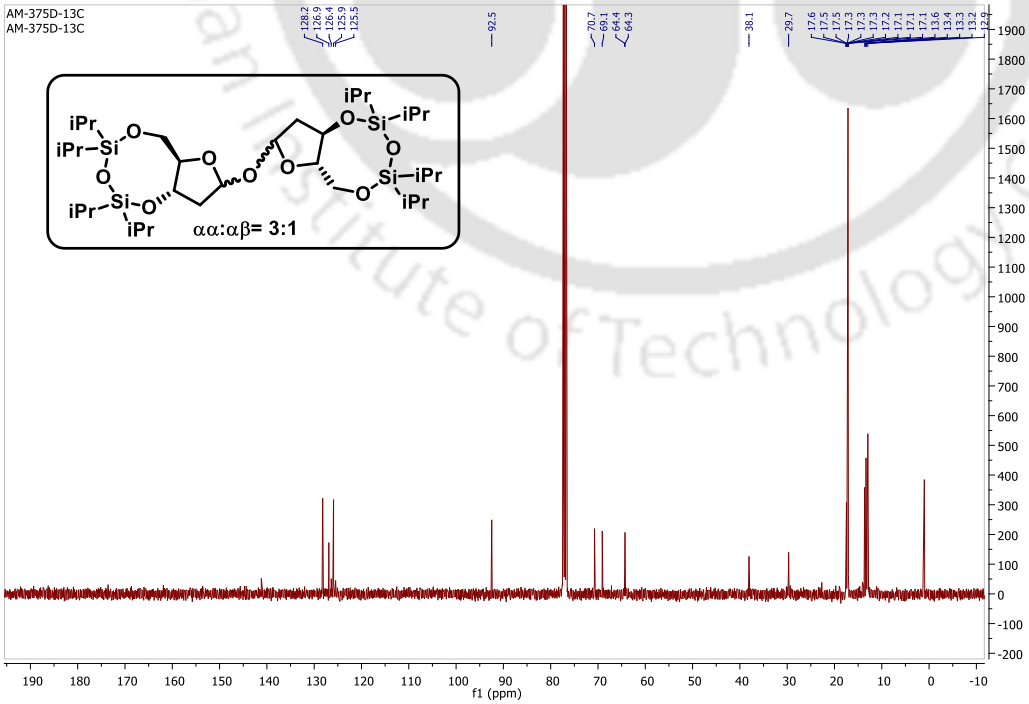
COSY NMR of (2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranosyl) -(1→1)-2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranoside 51b (400 MHz, $CDCl_3$)



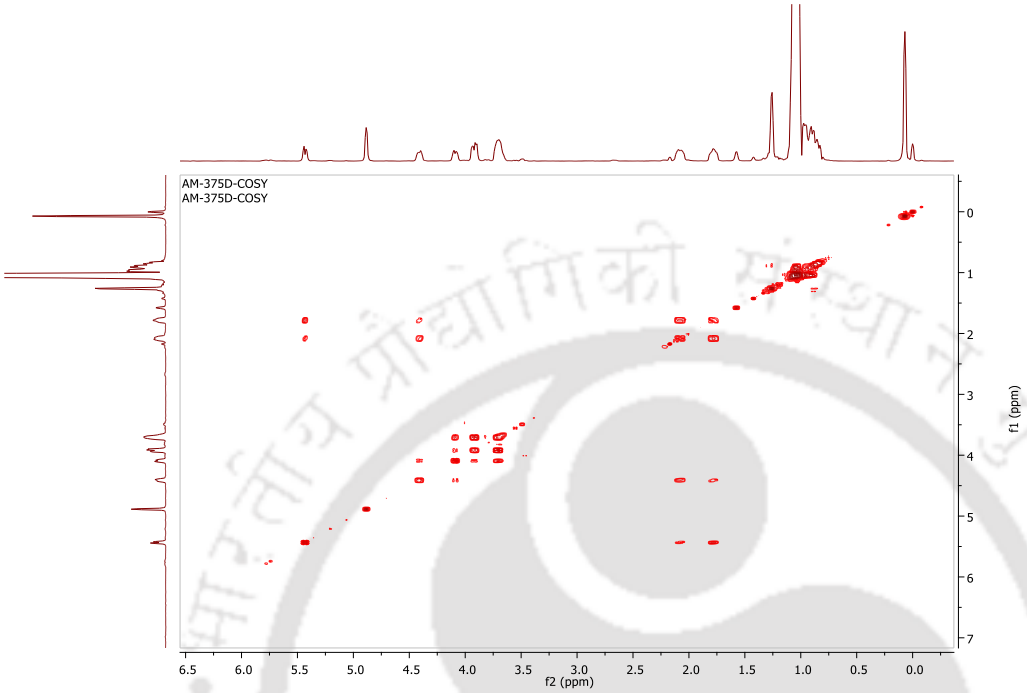
^{1}H NMR of (1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyld-isiloxane-1,3-diyl)-D-ribofuranosyl) -(1→1)-1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyld-isiloxane-1,3-diyl)-D-ribofuranoside 51c (400 MHz, $CDCl_3$)



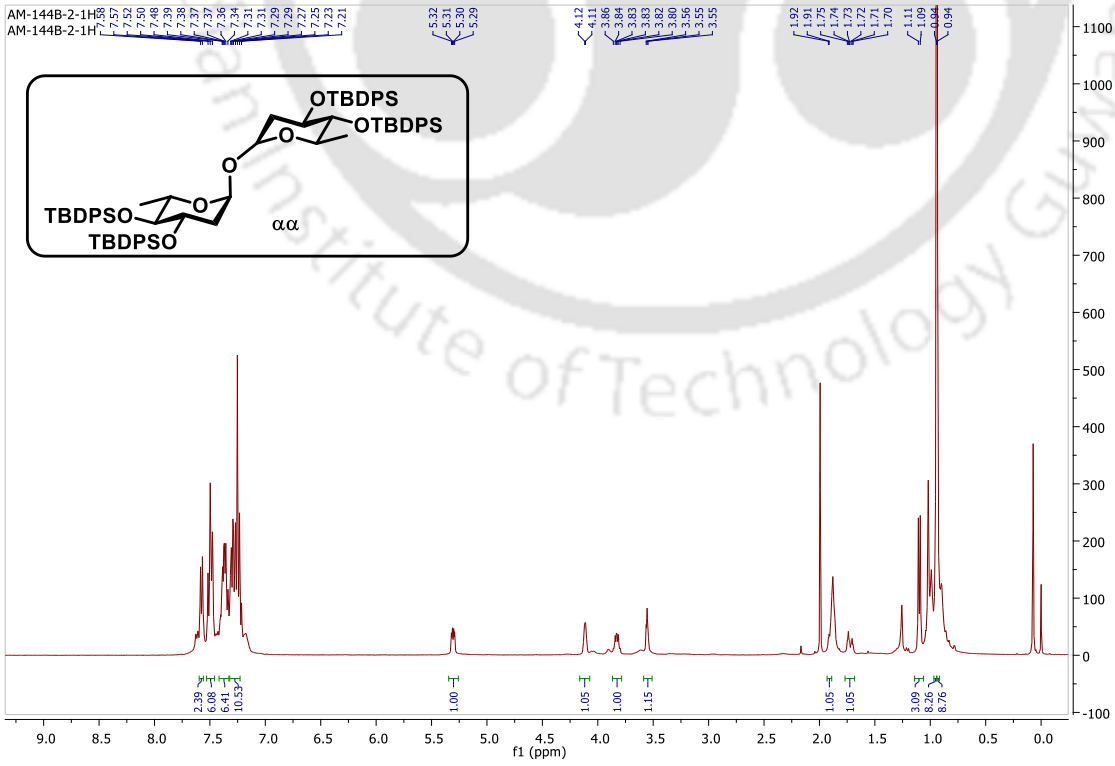
^{13}C NMR of (1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyld-isiloxane-1,3-diyl)-D-ribofuranosyl) -(1→1)-1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyld-isiloxane-1,3-diyl)-D-ribofuranoside 51c (400 MHz, $CDCl_3$)



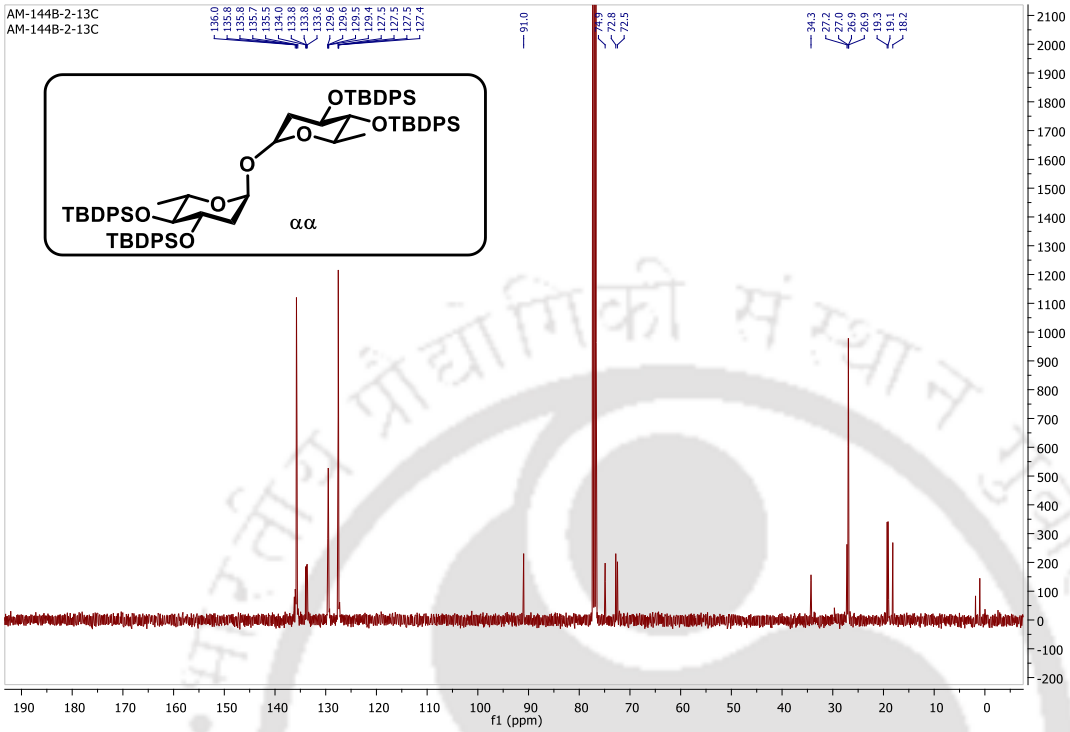
COSY NMR of (1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyld-isiloxane-1,3-diyl)-D-ribofuranosyl) -(1→1)-1,4-Anhydro-2-deoxy-3,5-O-(1,1,3,3-tetraisopropyld-isiloxane-1,3-diyl)-D-ribofuranoside 51c (400 MHz, $CDCl_3$)



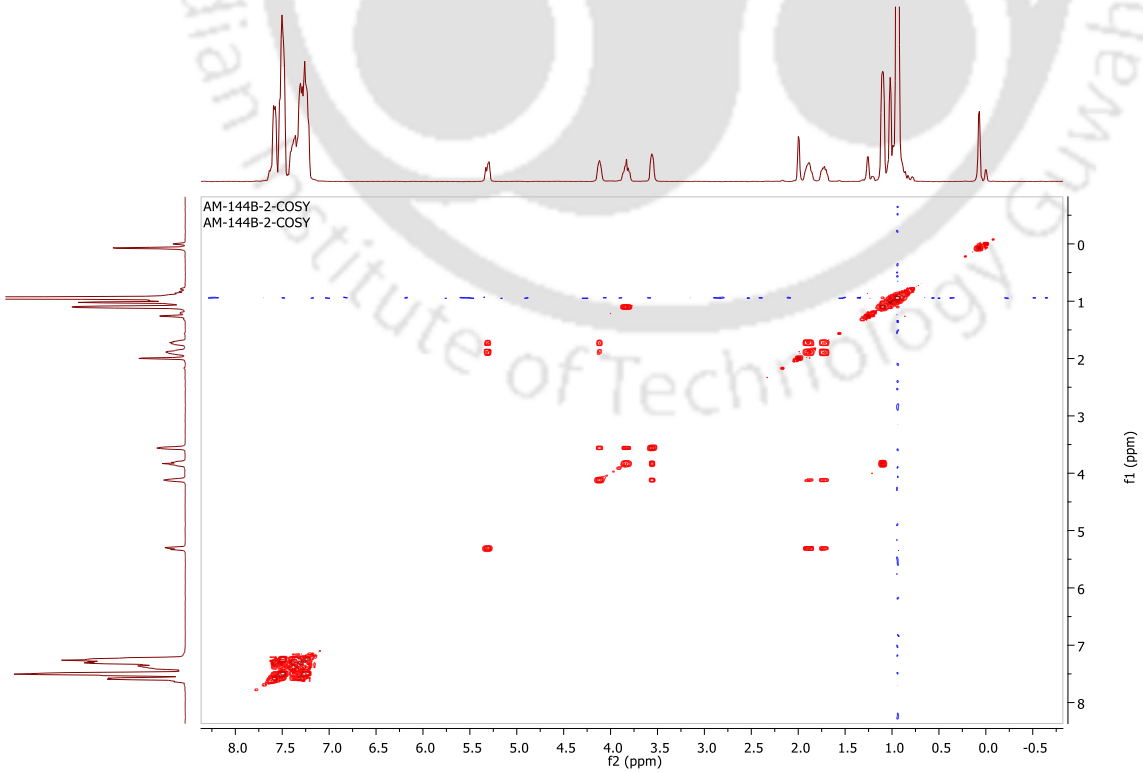
^{1}H NMR of (3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnopyranosyl) -(1→1)-3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnopyranoside 51d (400 MHz, $CDCl_3$)



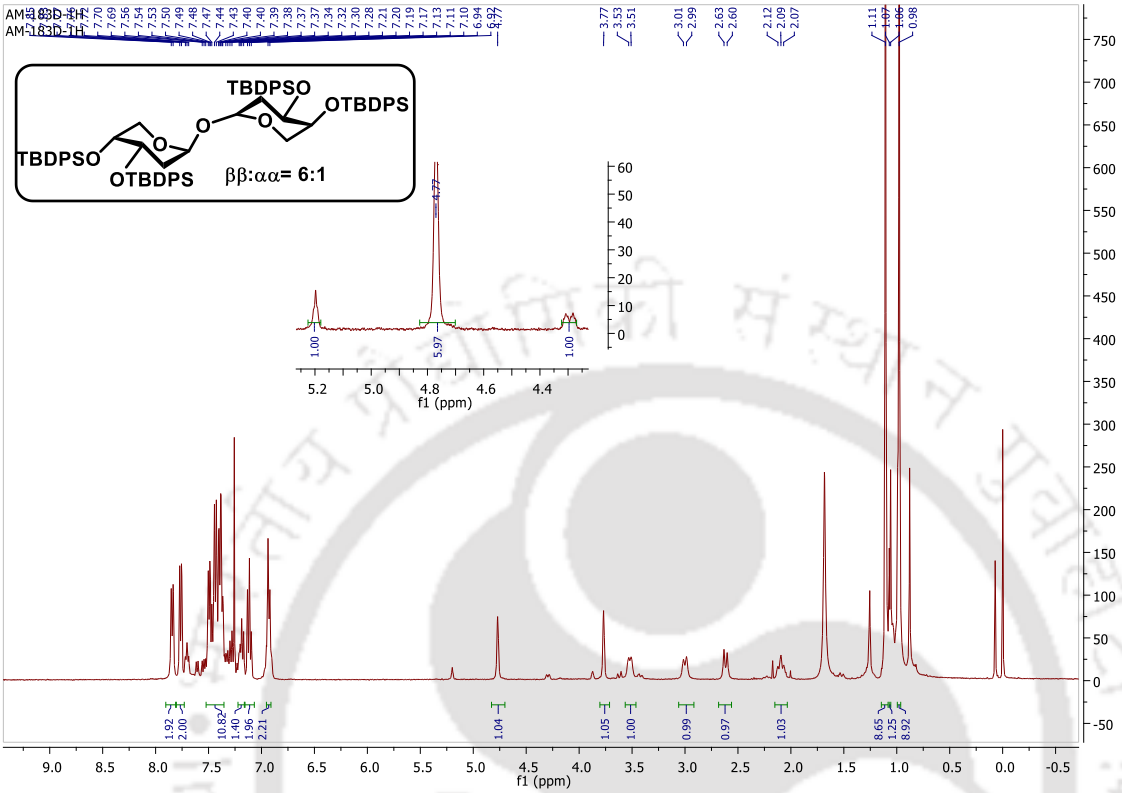
^{13}C NMR of (3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnopyranosyl) -(1→1)-3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnopyranoside 51d (400 MHz, $CDCl_3$)



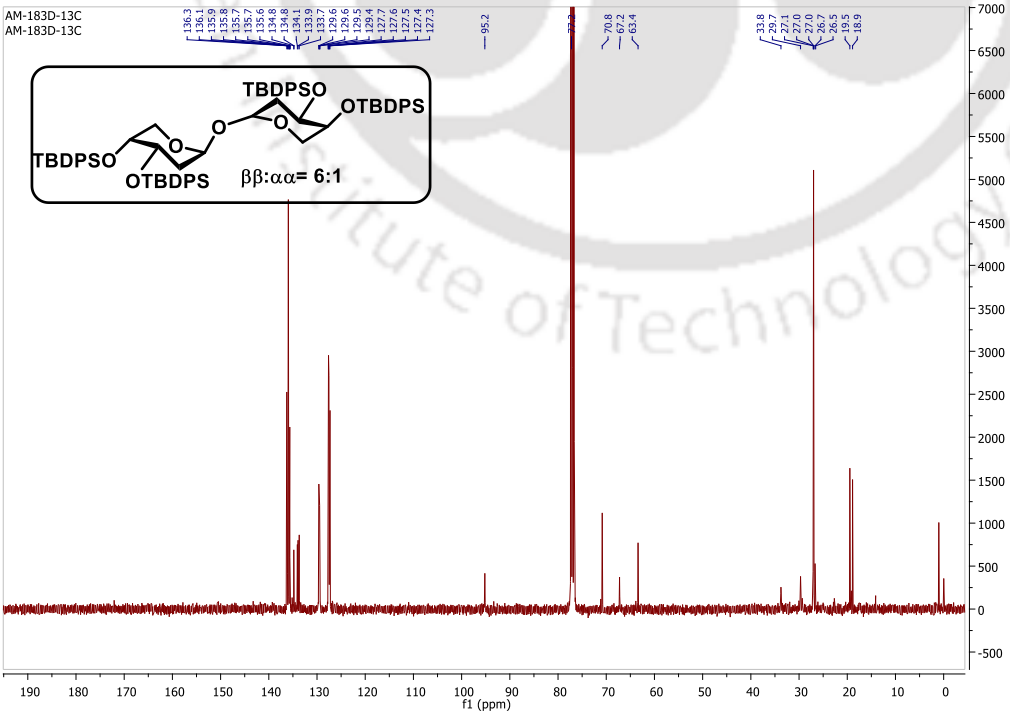
COSY NMR of (3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnopyranosyl) -(1→1)-3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnopyranoside 51d (400 MHz, $CDCl_3$)



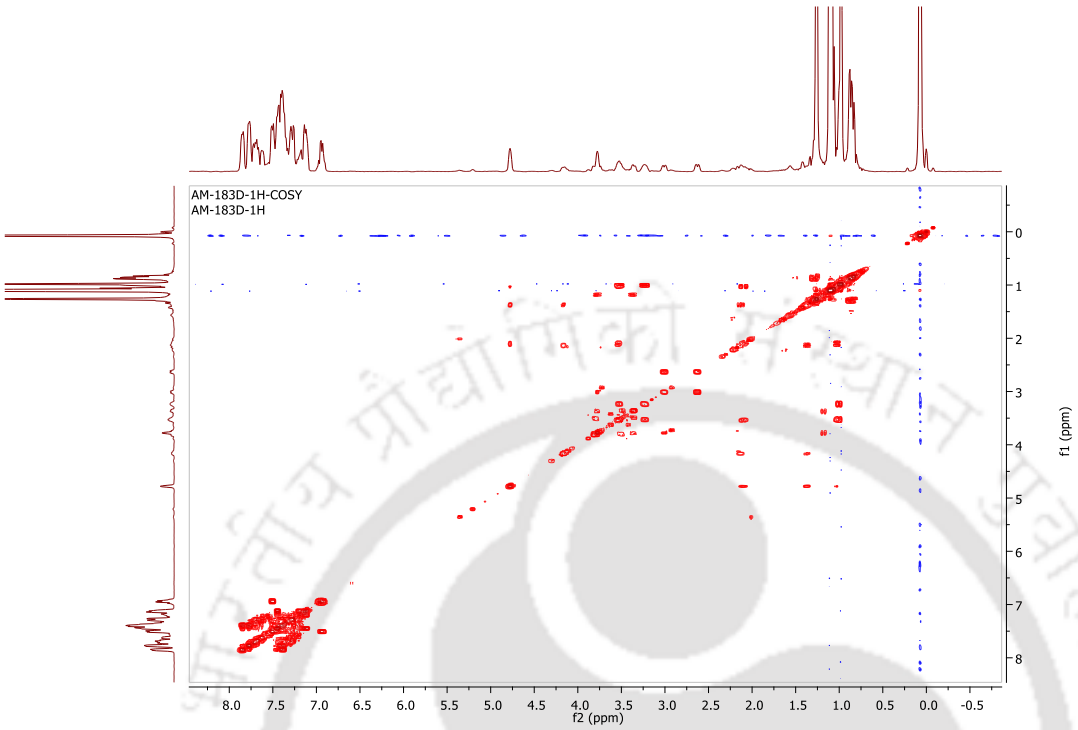
^{1}H NMR of (3,4-di-*O*-*tert*-butyldiphenylsilyl-D-arabinopyranosyl) -(1→1)-3,4-di-*O*-*tert*-butyldiphenylsilyl-D-arabinopyranoside 51e (600 MHz, $CDCl_3$)



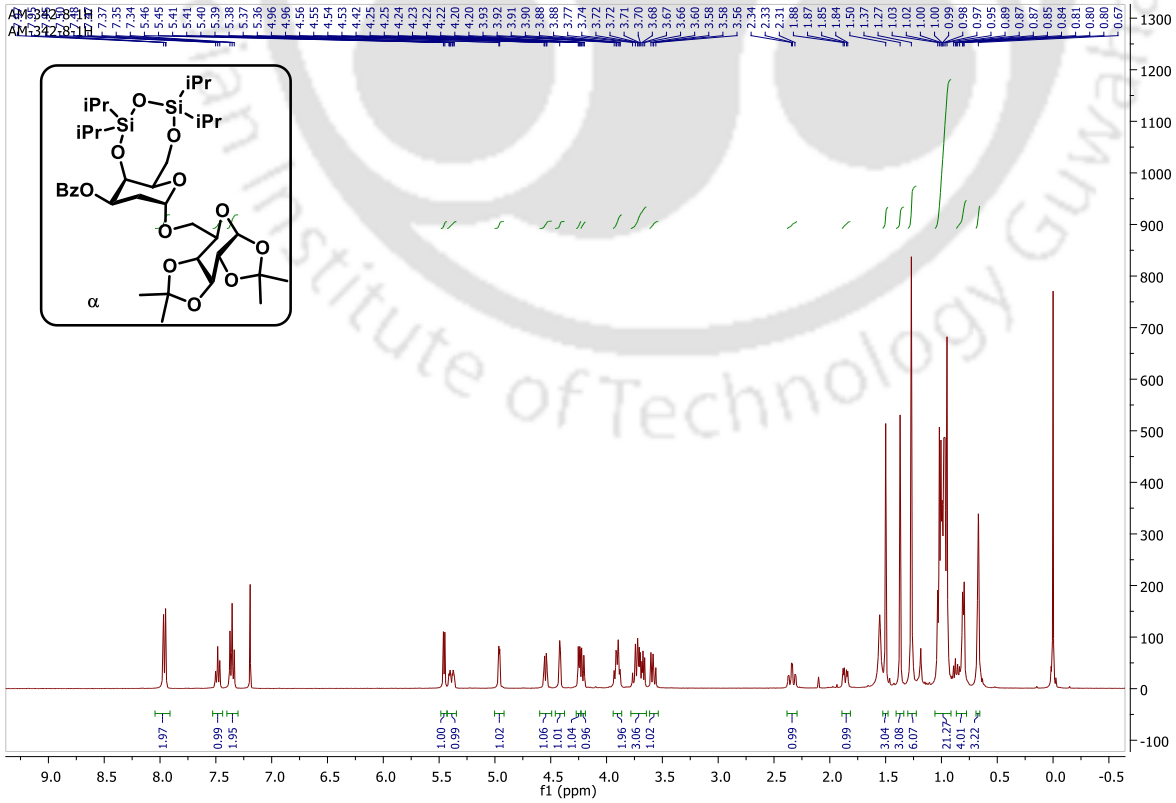
^{13}C NMR of (3,4-di-*O*-*tert*-butyldiphenylsilyl-D-arabinopyranosyl) -(1→1)-3,4-di-*O*-*tert*-butyldiphenylsilyl-D-arabinopyranoside 51e (600 MHz, $CDCl_3$)



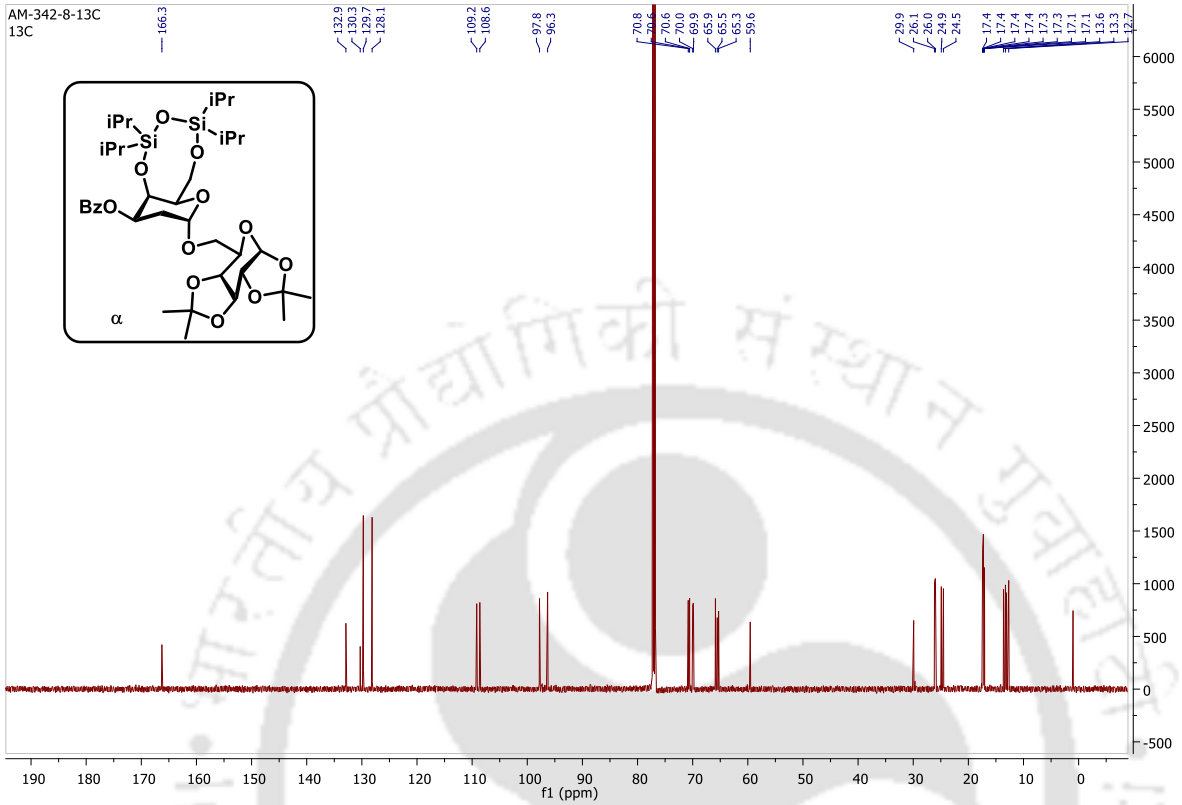
COSY NMR of (3,4-di-*O-tert*-butyldiphenylsilyl-D-arabinopyranosyl)-(1→1)-3,4-di-*O-tert*-butyldiphenylsilyl-D-arabinopyranoside 51e (600 MHz, $CDCl_3$)



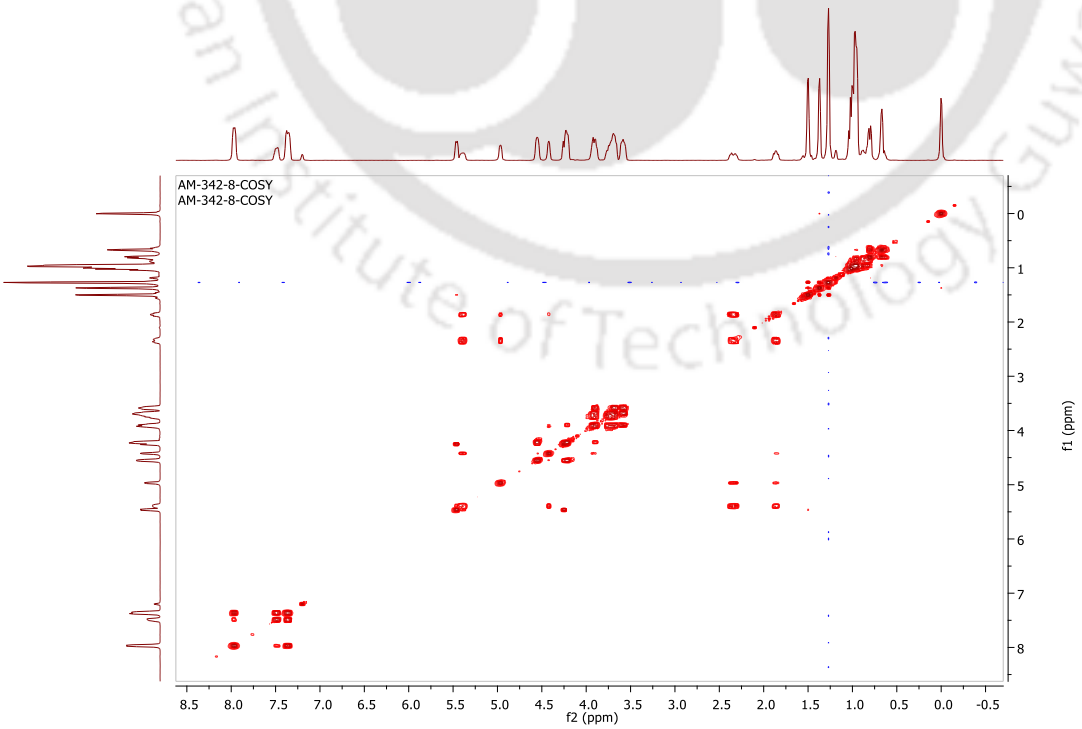
^{1}H NMR of (4,6-di-O-tetraisopropyldisiloxane-1,3-diyl-3-O-benzoyl-2-deoxy-α-D- galactosyl) -(1→6)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranoside 55a (400 MHz, $CDCl_3$)



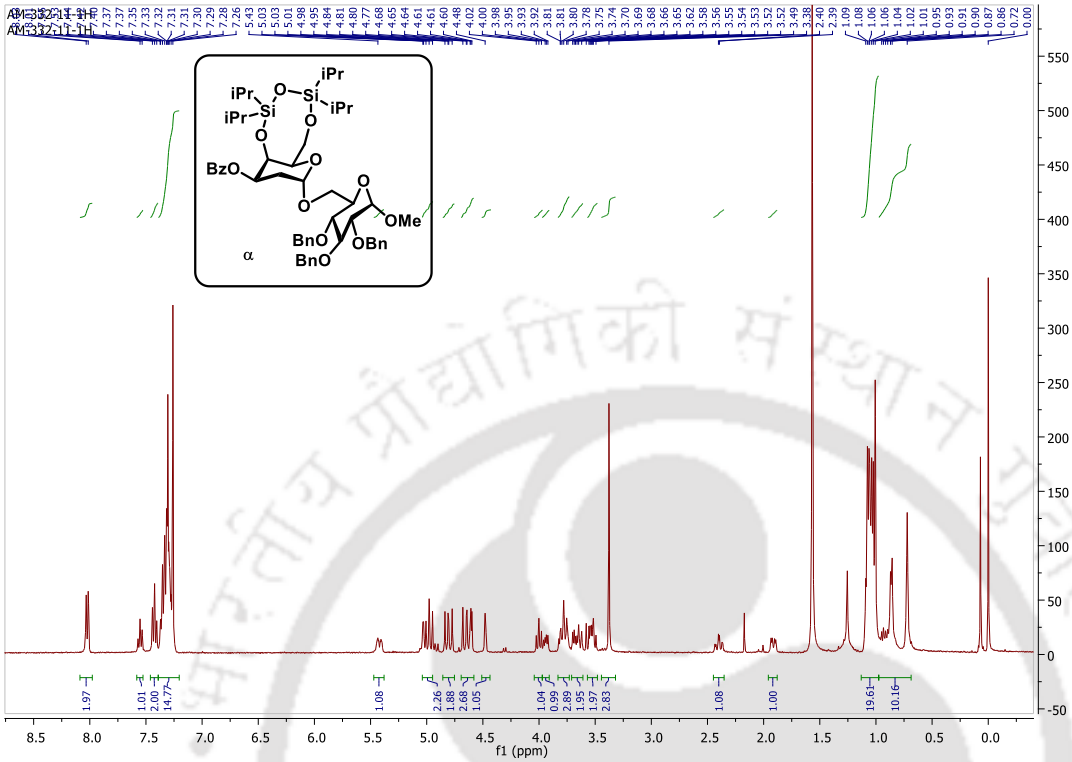
^{13}C NMR of (4,6-di-O-tetraisopropyldisiloxane-1,3-diyl-3-O-benzoyl-2-deoxy-α-D- galactosyl)-(1→6)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranoside 55a (400 MHz, $CDCl_3$)



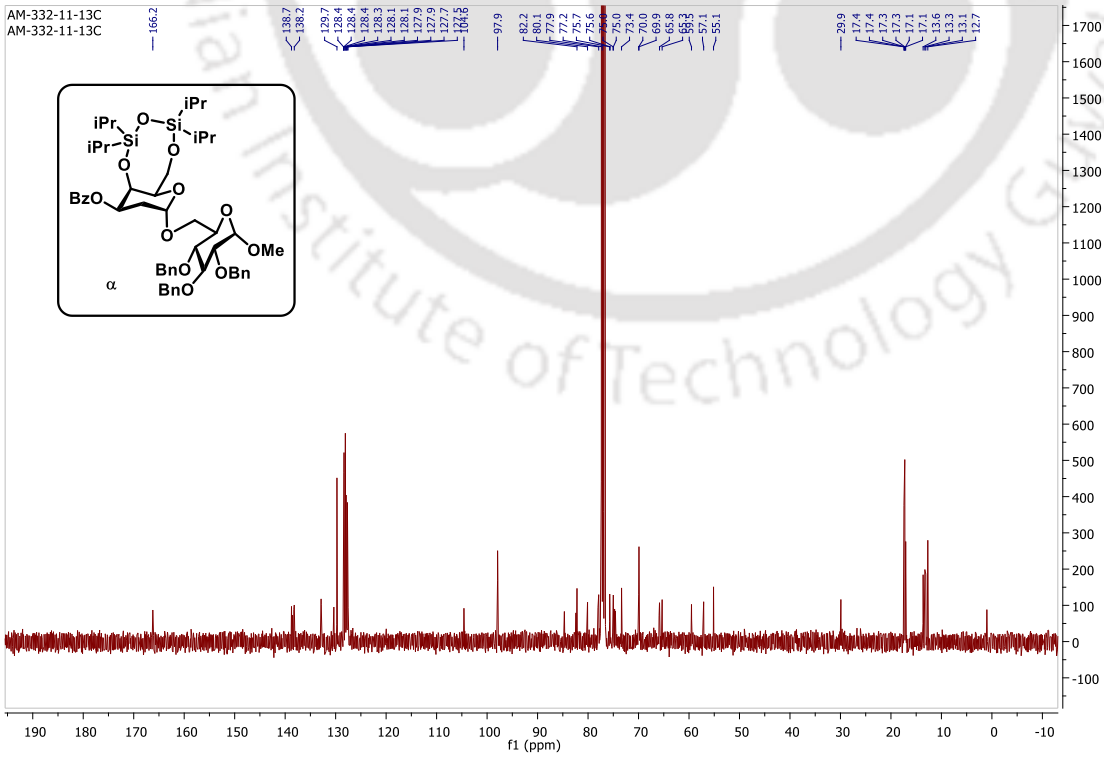
COSY NMR of (4,6-di-O-tetraisopropyldisiloxane-1,3-diyl-3-O-benzoyl-2-deoxy-α-D-galactosyl)-(1→6)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranoside 55a (400 MHz, $CDCl_3$)



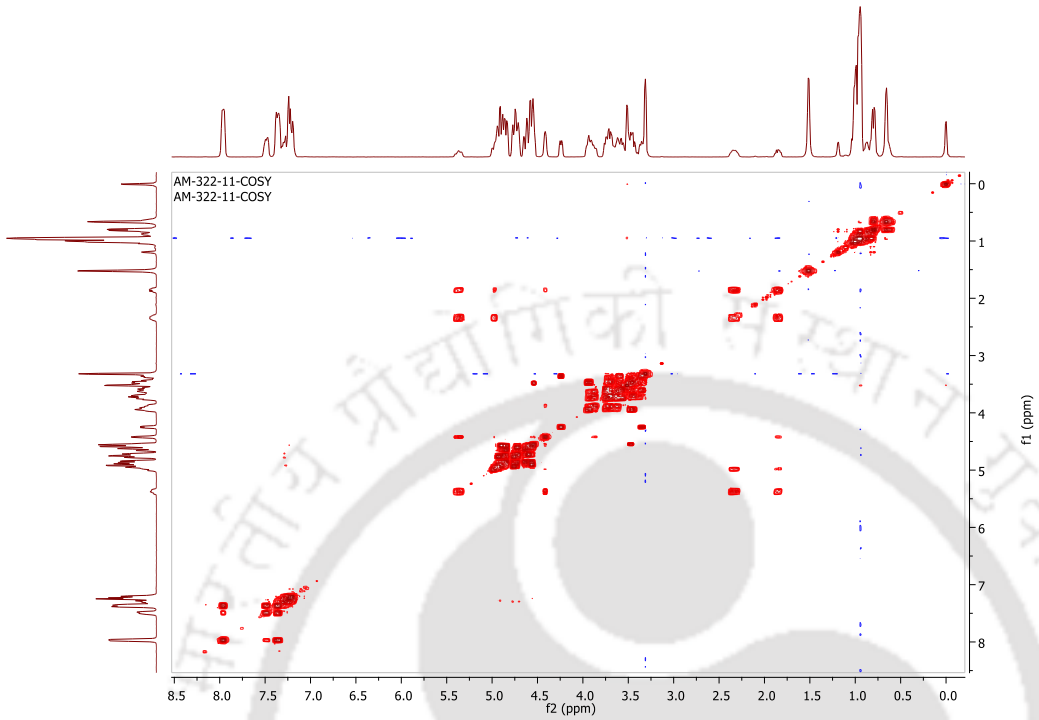
^{1}H NMR of Methyl 2,3,4-tri-O-benzyl-6-O-(4,6-di-O-tetraisopropyldisiloxane-1,3-diyl-3-O-benzoyl-2-deoxy-α-D-galactosyl)-α-D-glucopyranoside 55b (400 MHz, $CDCl_3$)



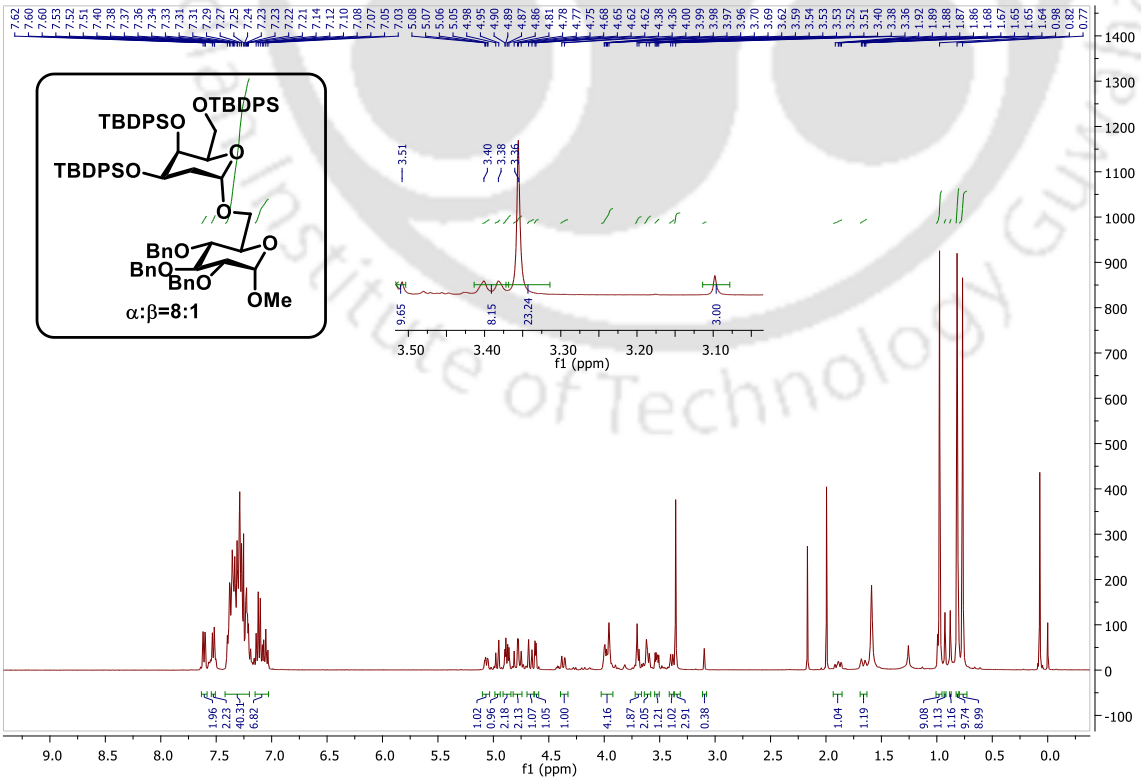
^{13}C NMR of Methyl 2,3,4-tri-O-benzyl-6-O-(4,6-di-O-tetraisopropyldisiloxane-1,3-diyl-3-O-benzoyl-2-deoxy-α-D-galactosyl)-α-D-glucopyranoside 55b (400 MHz, $CDCl_3$)



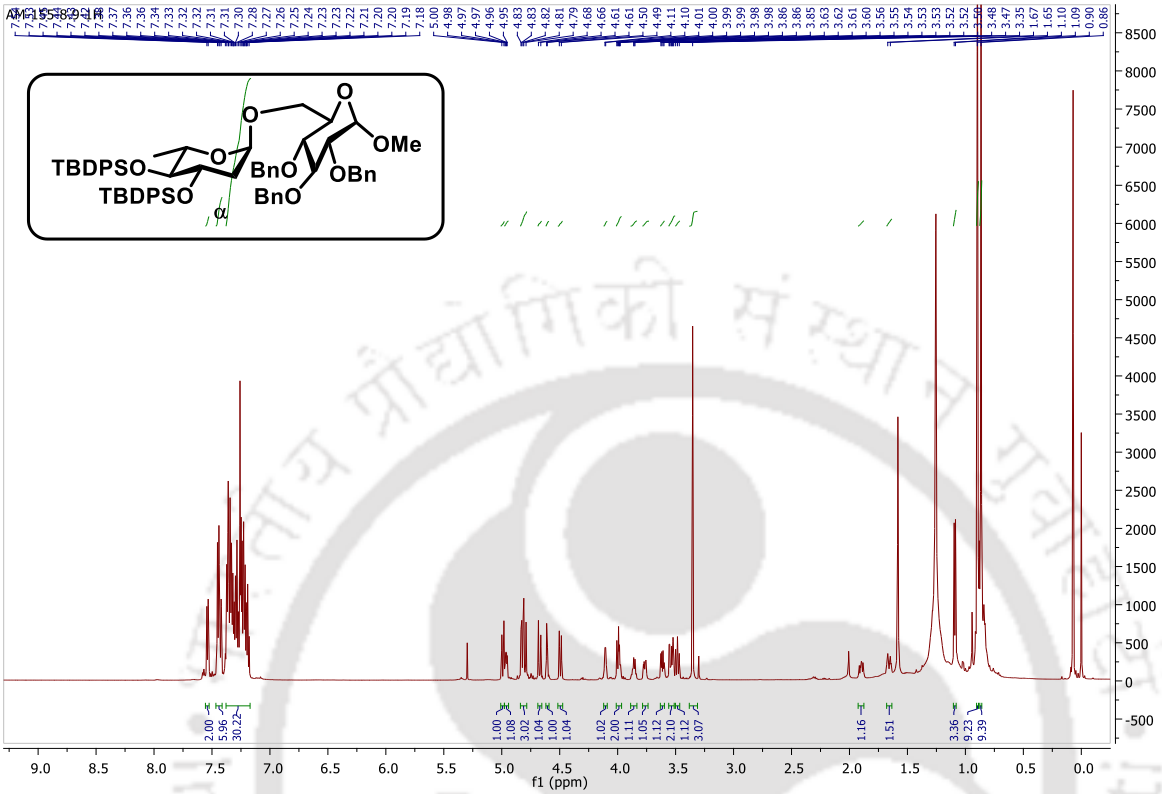
COSY NMR of Methyl 2,3,4-tri-O-benzyl-6-O-(4,6-di-O-tetraisopropyldisiloxane-1,3-diyl-3-O-benzoyl-2-deoxy-α-D-galactosyl)-α-D-glucopyranoside 55b (400 MHz, $CDCl_3$)



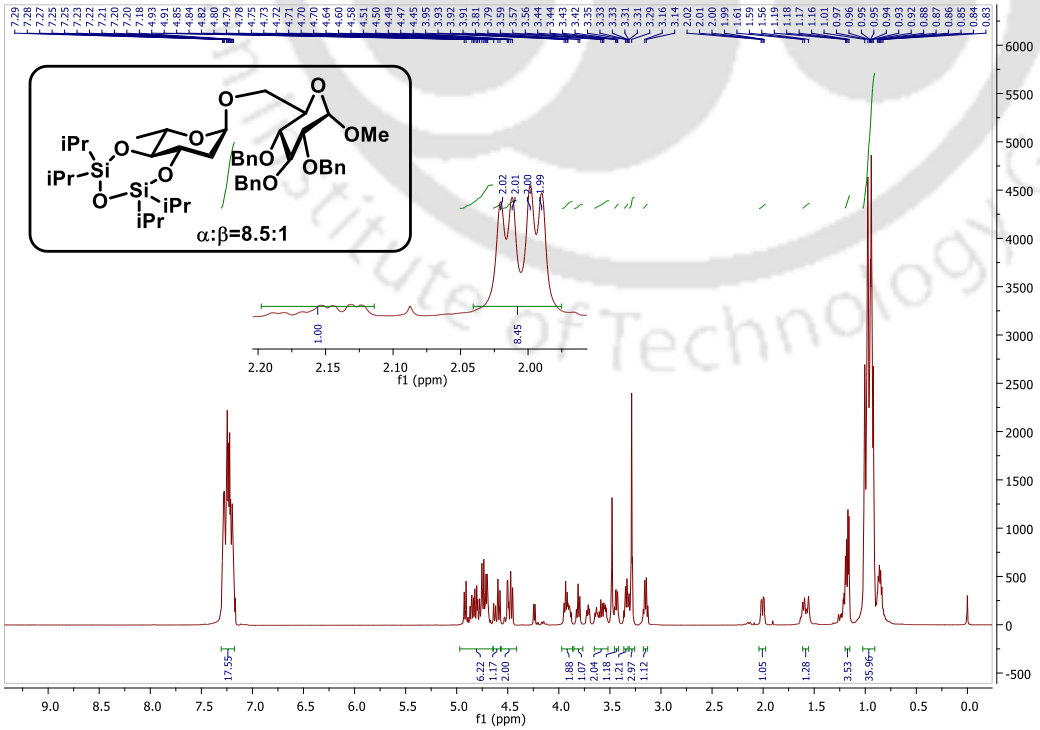
^{1}H NMR of Methyl 2,3,4-tri-O-benzyl-6-O-(3,4,6-tri-O-*tert*-butyldiphenylsilyl-2-deoxy-α-D-galactopyranosyl)-α-D-glucopyranoside 55c (400 MHz, $CDCl_3$)



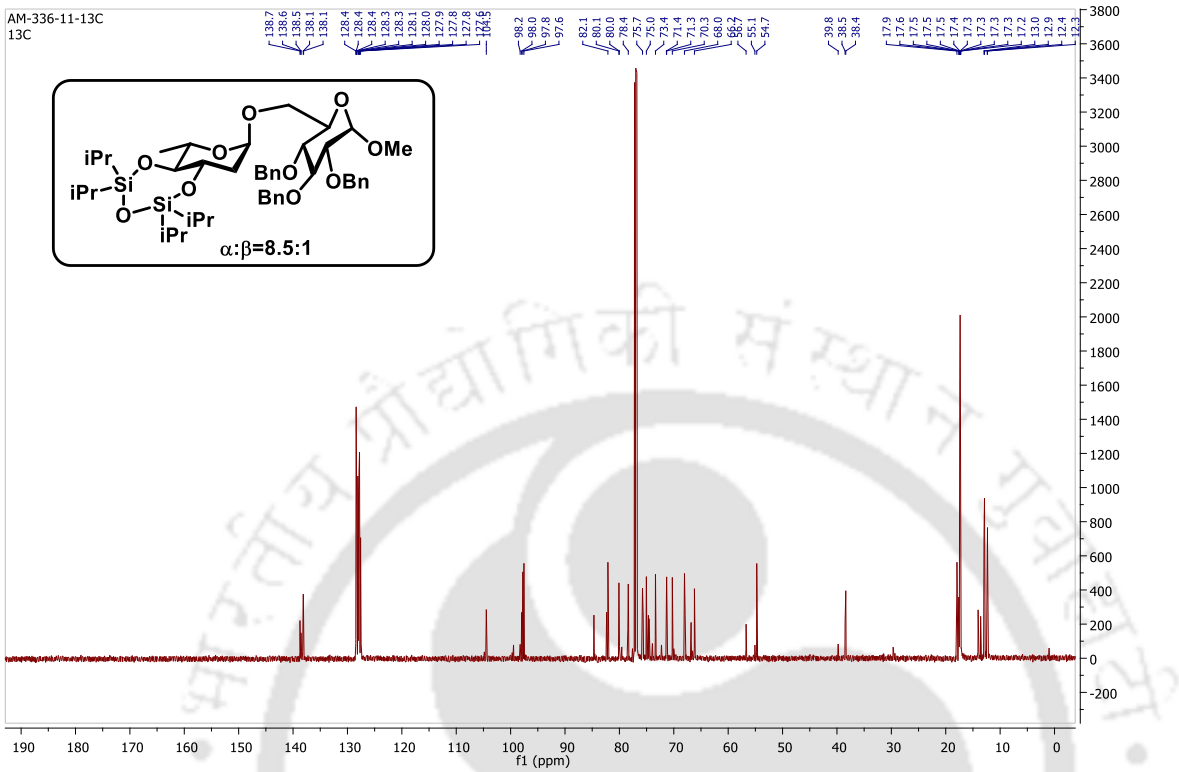
^{1}H NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α-L-rhamnosyl)-α-D-glucopyranoside 55d (600 MHz, $CDCl_3$)



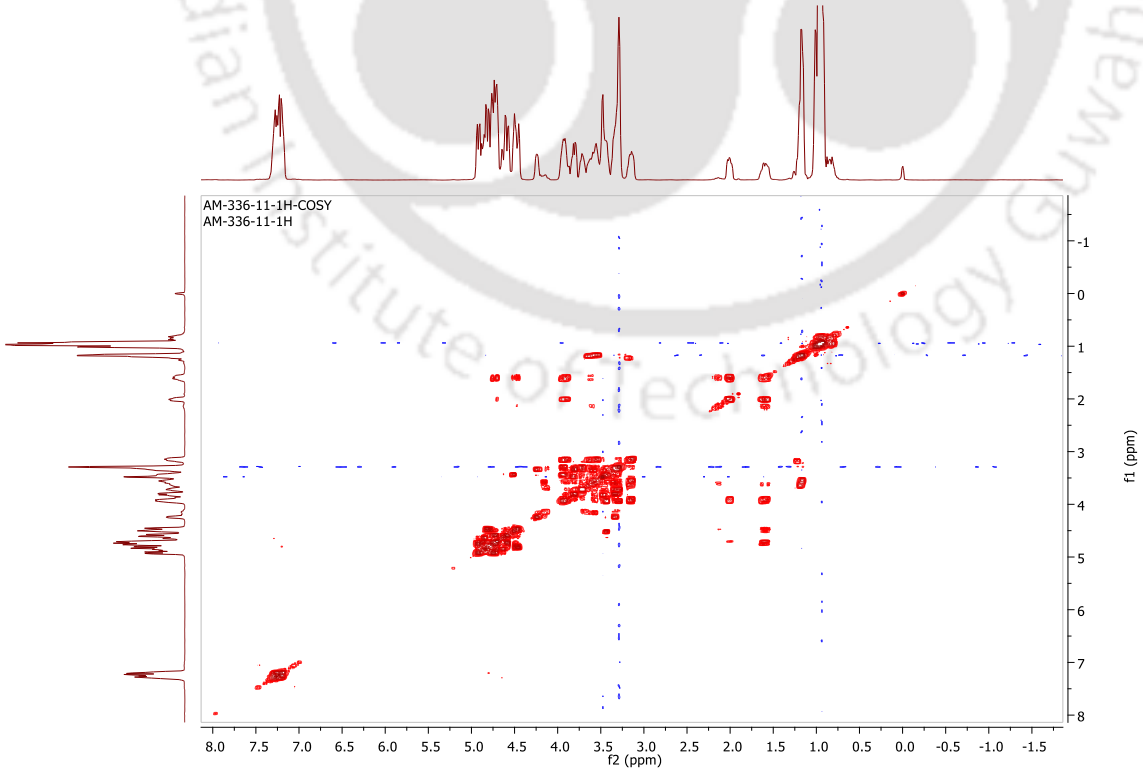
^{1}H NMR of Methyl 2,3,4-tri-O-benzyl-6-O-(2,6-deoxy-3,4-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-α-L-erythro-hexapyranosyl)-α-D-glucopyranoside 55e (600 MHz, $CDCl_3$)



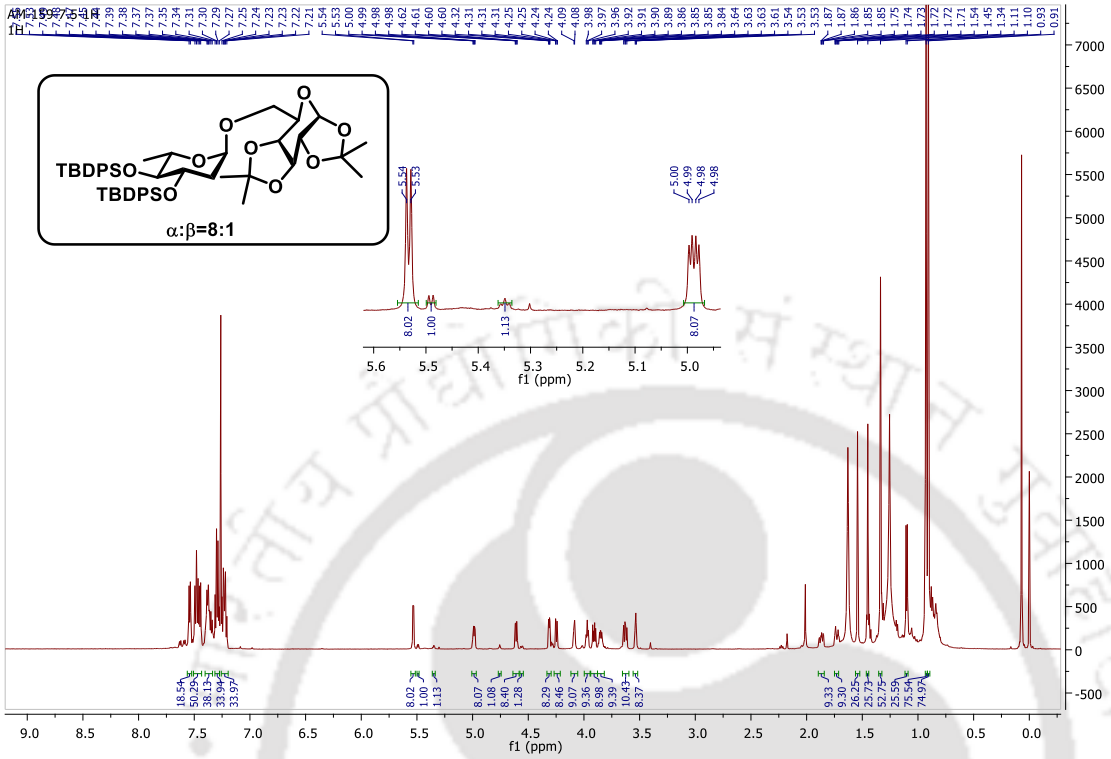
^{13}C NMR of Methyl 2,3,4-tri-O-benzyl-6-O-(2,6-deoxy-3,4-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-α-L-erythro-hexapyranosyl)-α-D-glucopyranoside 55e (600 MHz, $CDCl_3$)



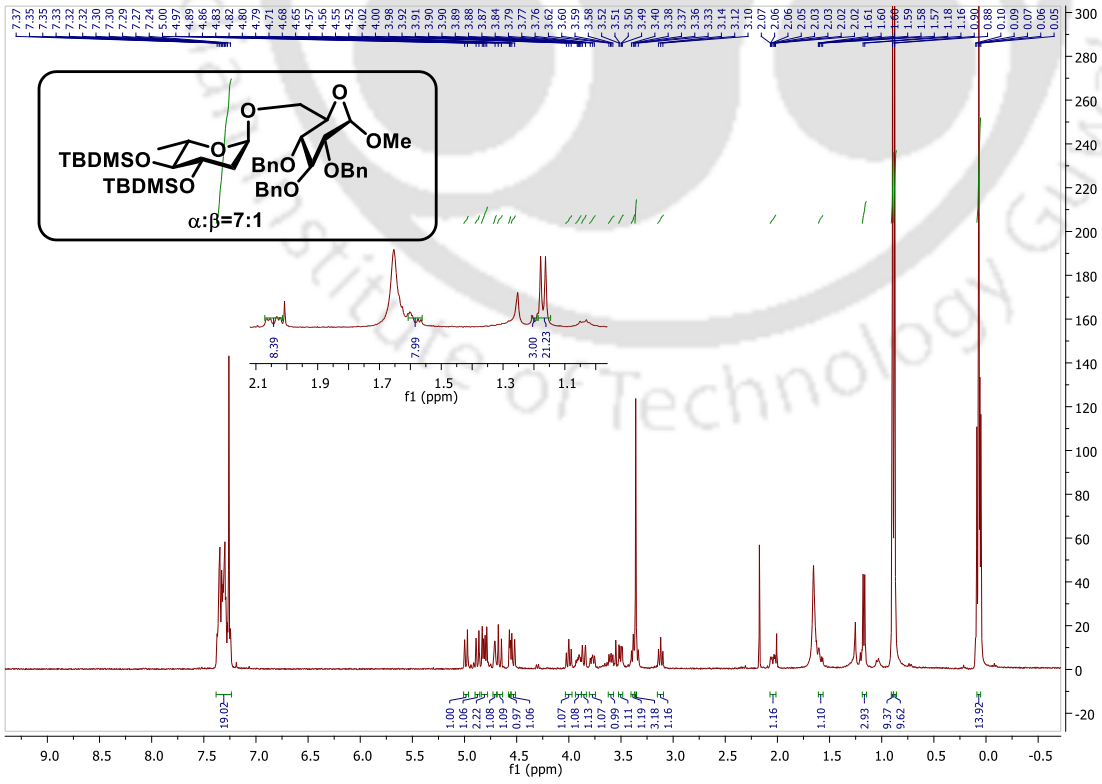
COSY NMR of Methyl 2,3,4-tri-O-benzyl-6-O-(2,6-deoxy-3,4-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-α-L-erythro-hexapyranosyl)-α-D-glucopyranoside 55e (600 MHz, $CDCl_3$)



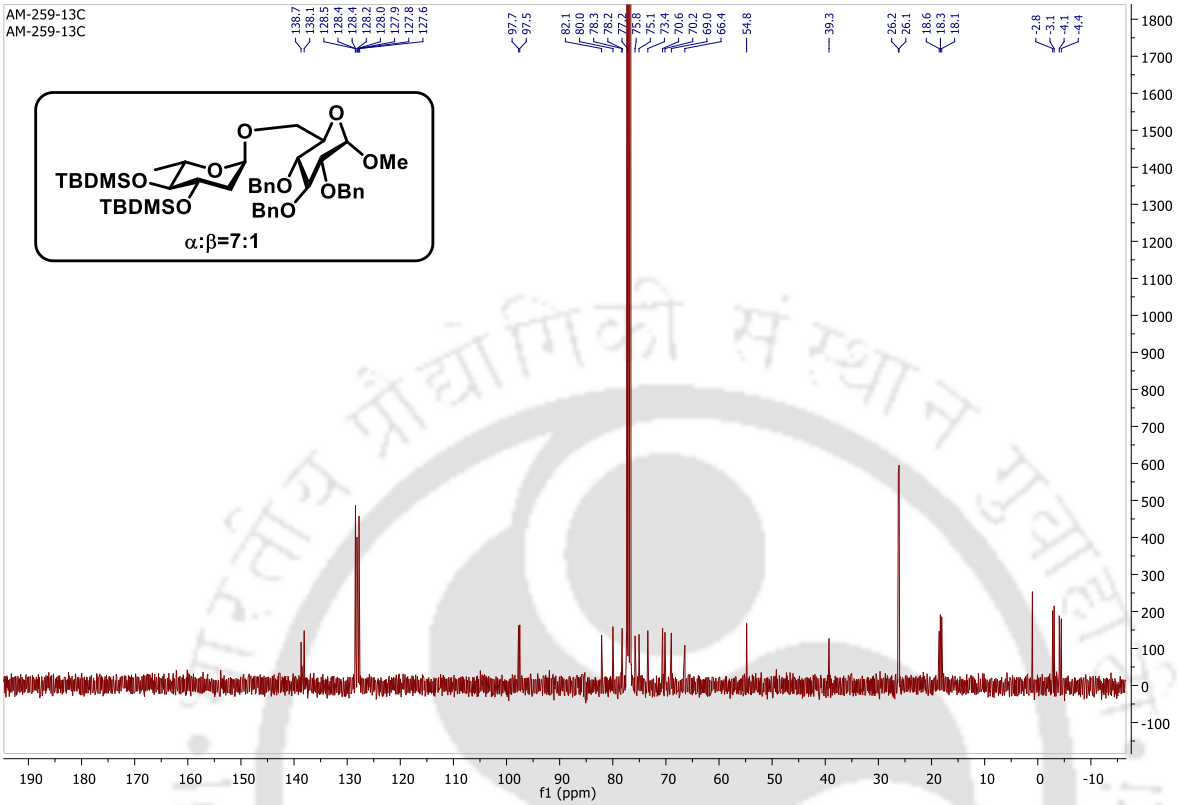
^{1}H NMR of (3,4-di-O-*tert*-butyldiphenylsilyl-2-deoxy-α-L-rhamnosyl)-(1→6)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranoside 55f (600 MHz, $CDCl_3$)



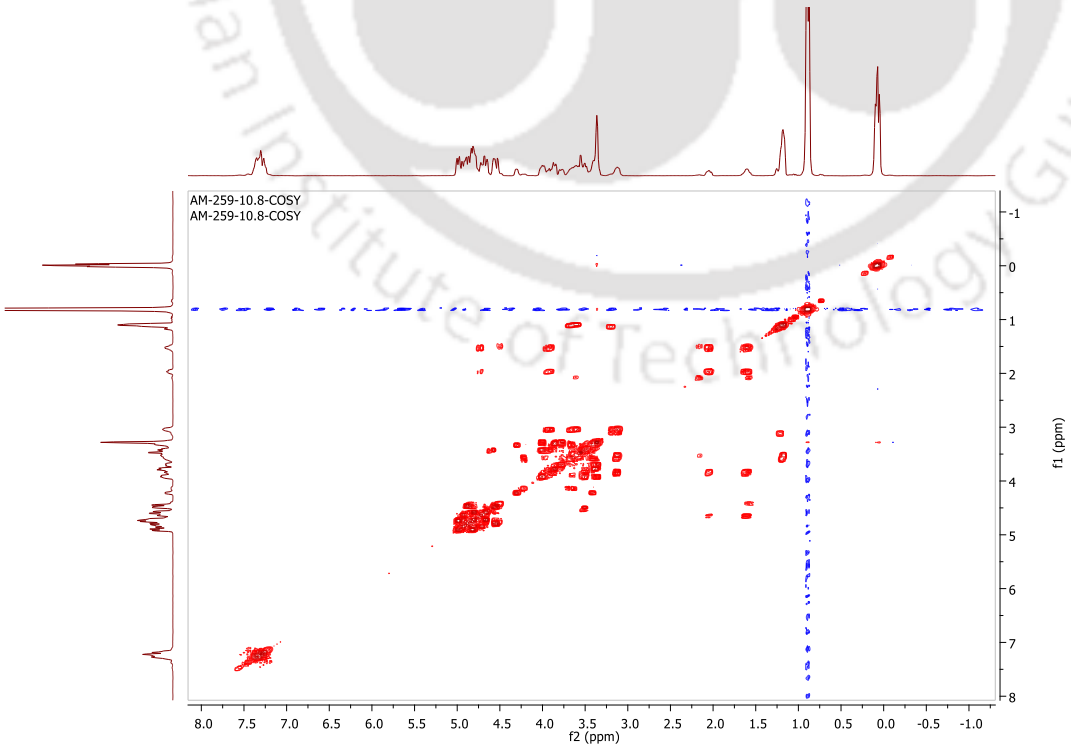
^{1}H NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α-L-rhamnosyl)-α-D-glucopyranoside 55g (400 MHz, $CDCl_3$)



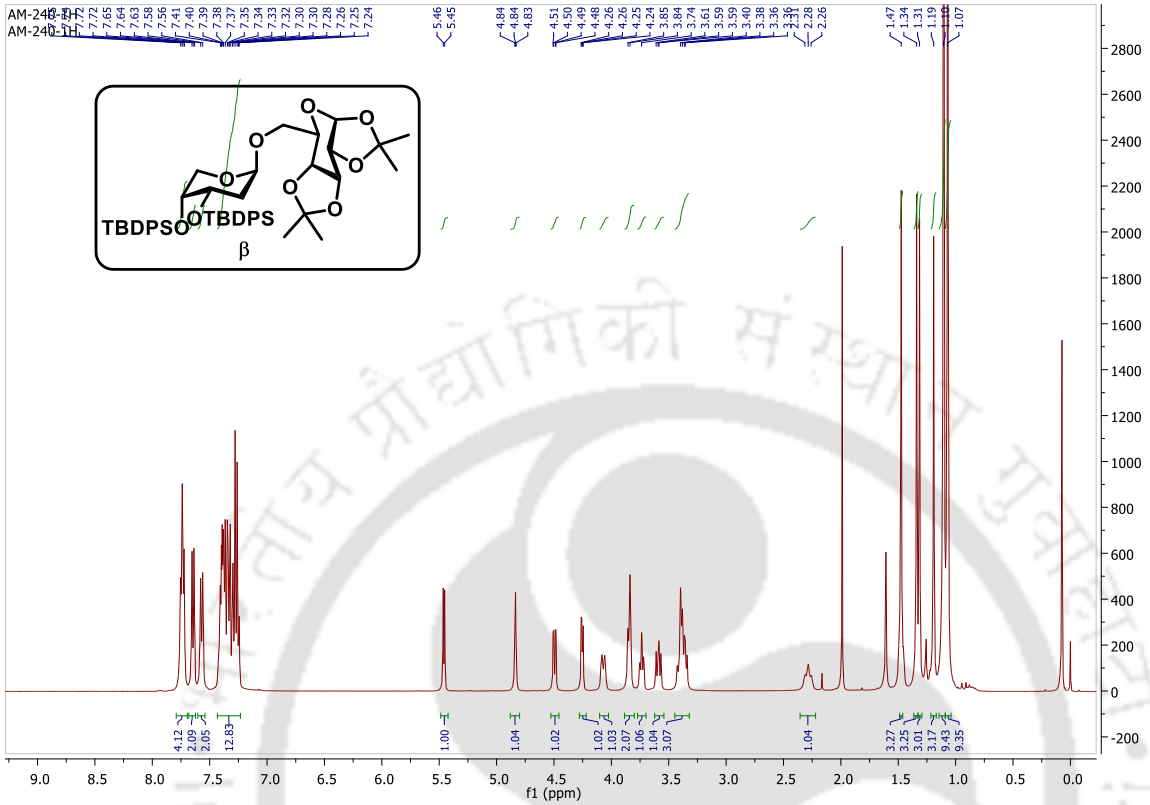
^{13}C NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α-L-rhamnosyl)-α-D-glucopyranoside 55g (400 MHz, $CDCl_3$)



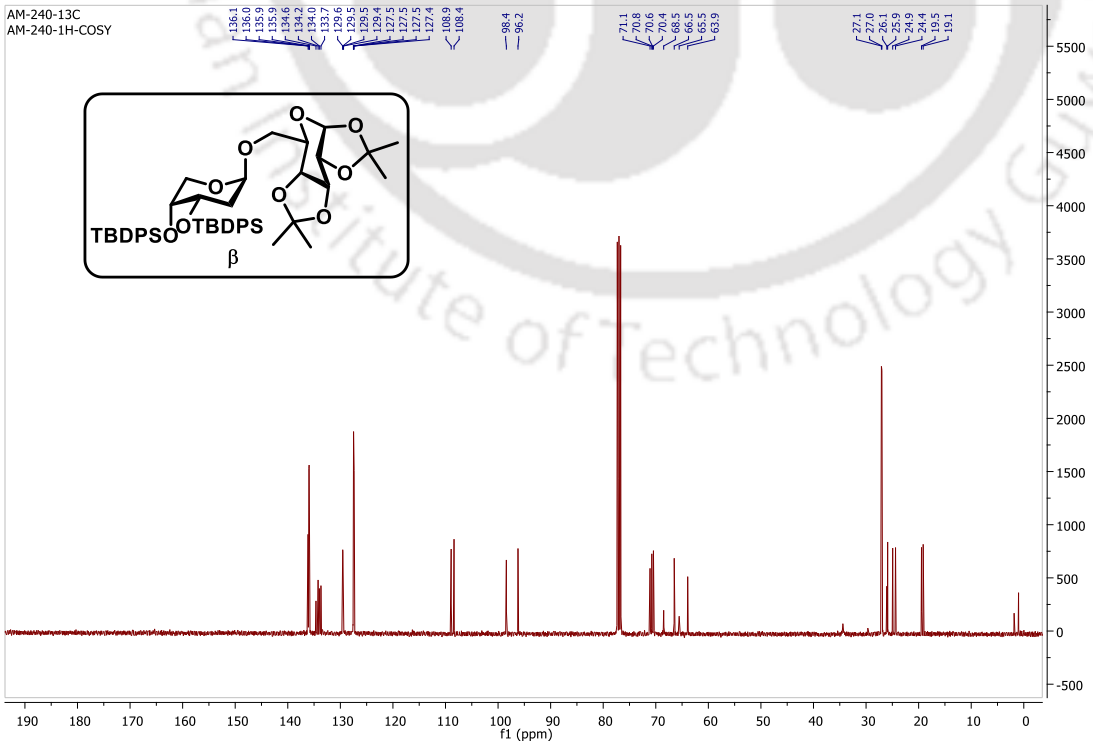
COSY NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α-L-rhamnosyl)-α-D-glucopyranoside 55g (400 MHz, $CDCl_3$)



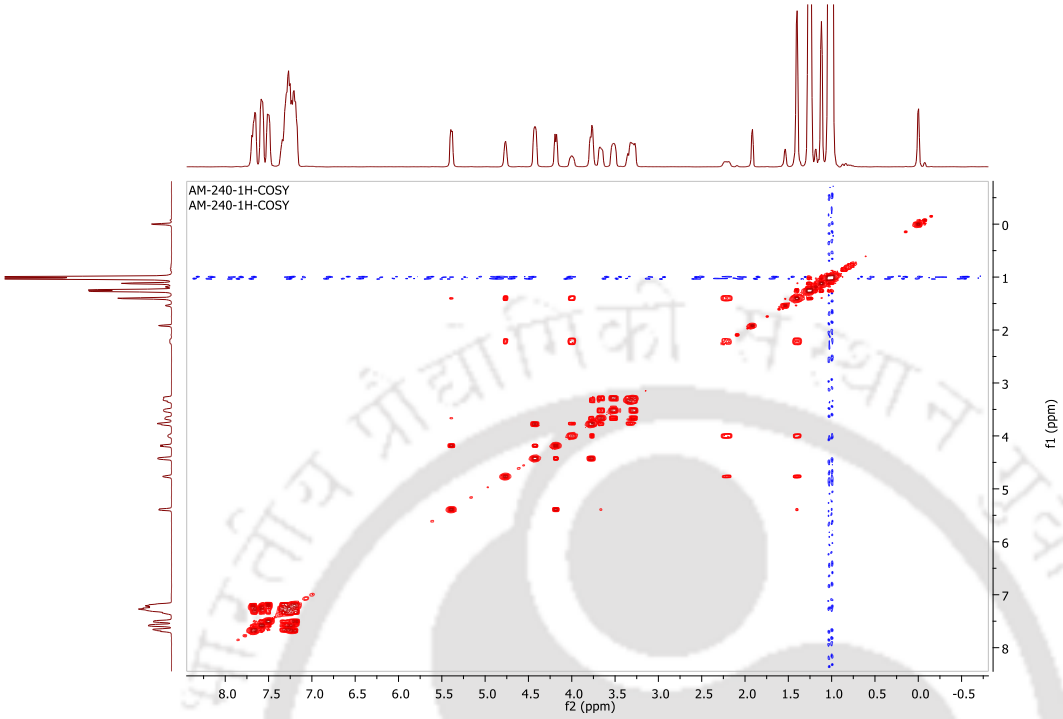
^{1}H NMR of (3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosyl)-(1→6)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranoside 55h (400 MHz, $CDCl_3$)



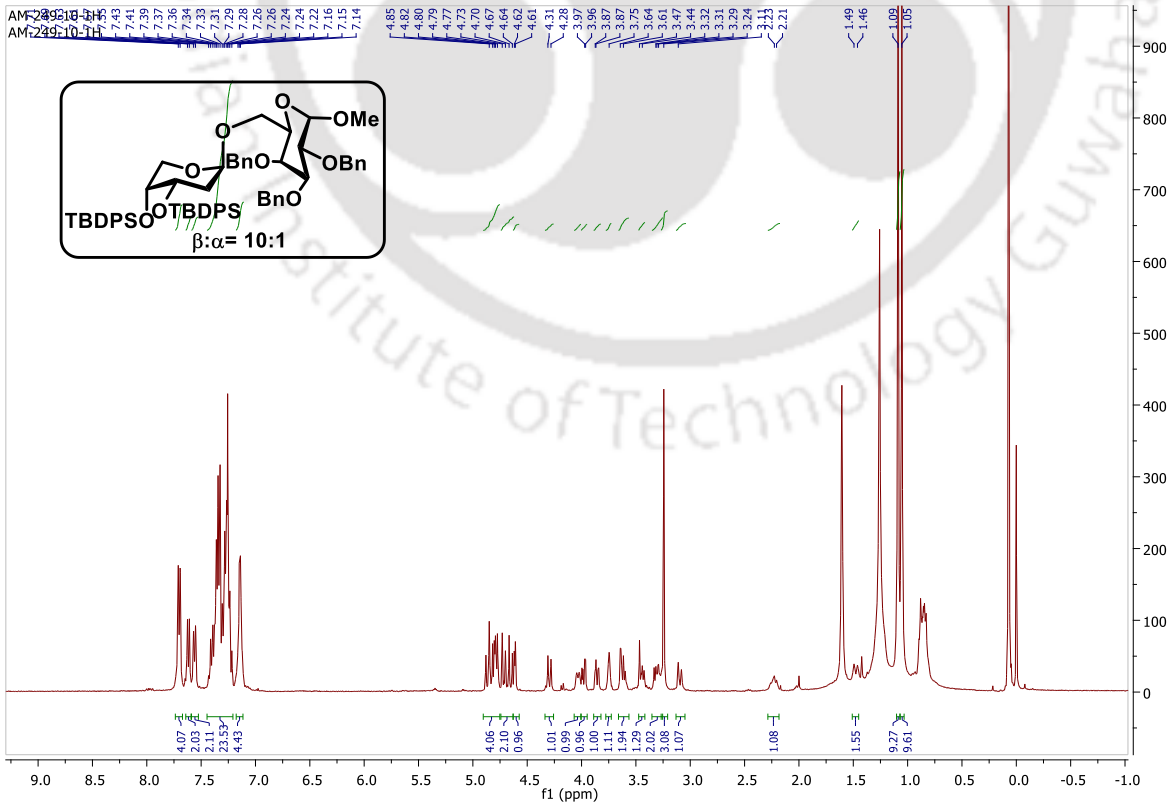
^{13}C NMR of (3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosyl)-(1→6)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranoside 55h (400 MHz, $CDCl_3$)



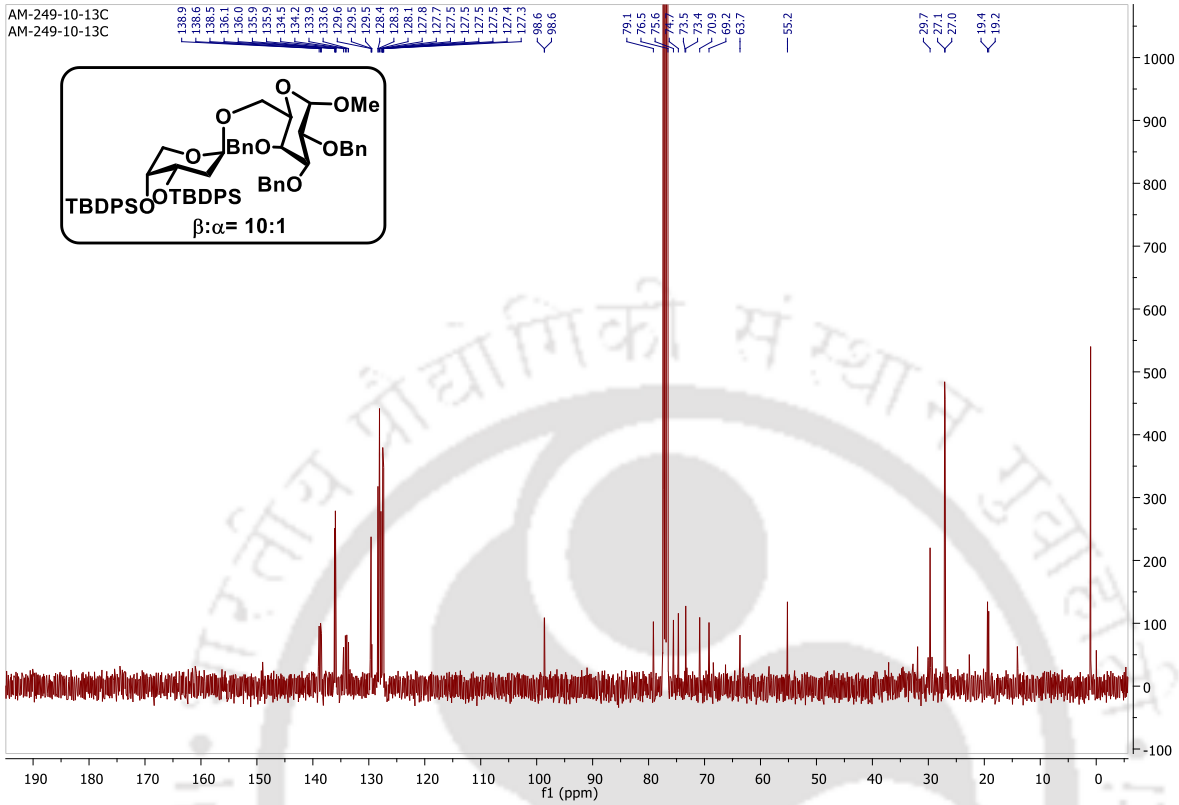
COSY NMR of (3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosyl) -(1→6)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranoside 55h (400 MHz, $CDCl_3$)



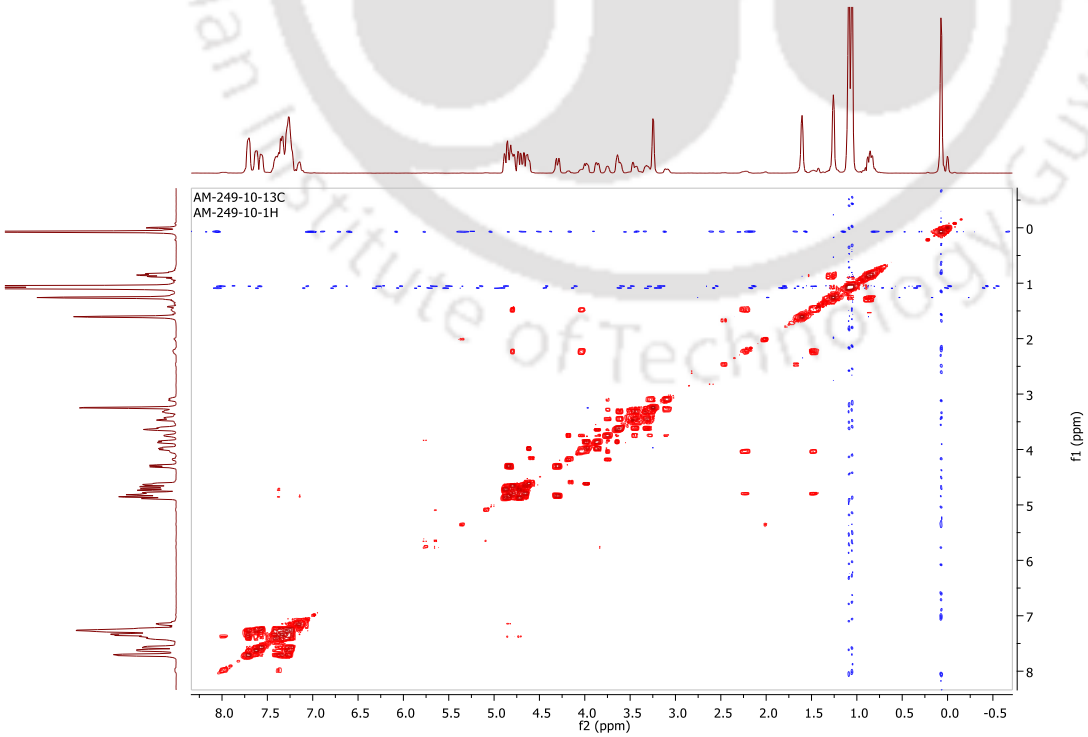
^{1}H NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosyl)-α-D-galactopyranoside 55i (400 MHz, $CDCl_3$)



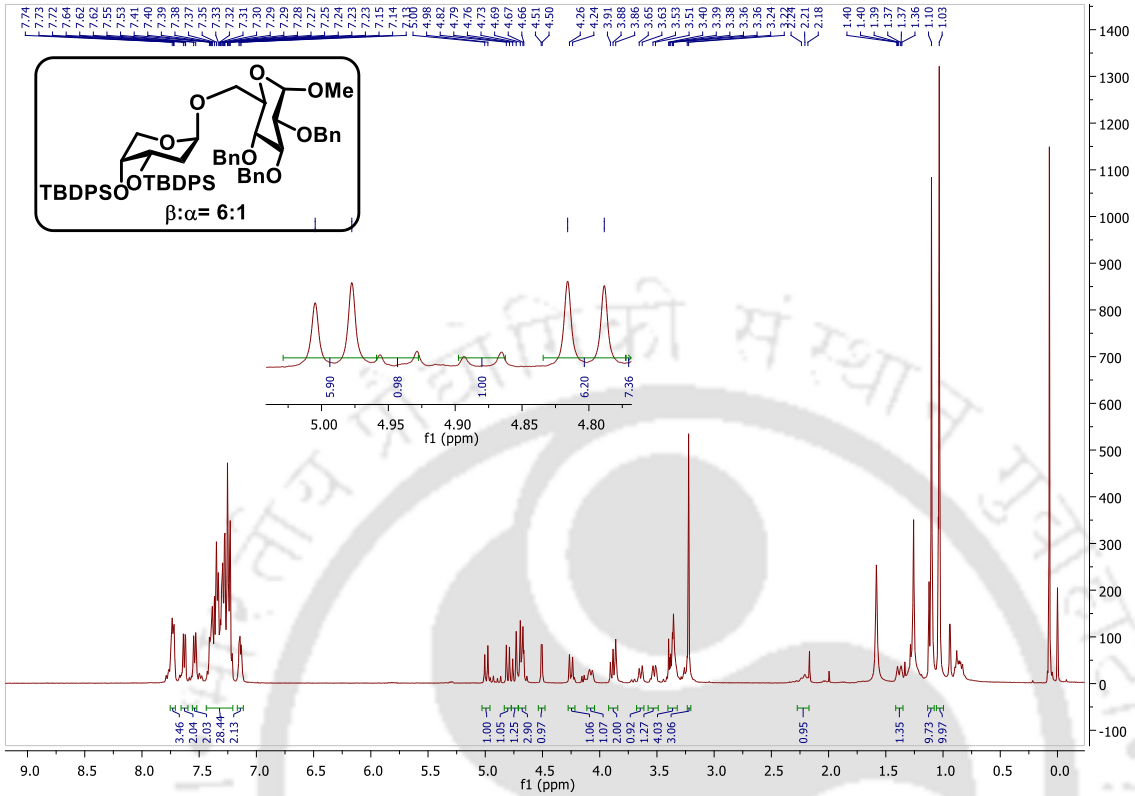
^{13}C NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosyl)-α-D-galactopyranoside 55i (400 MHz, $CDCl_3$)



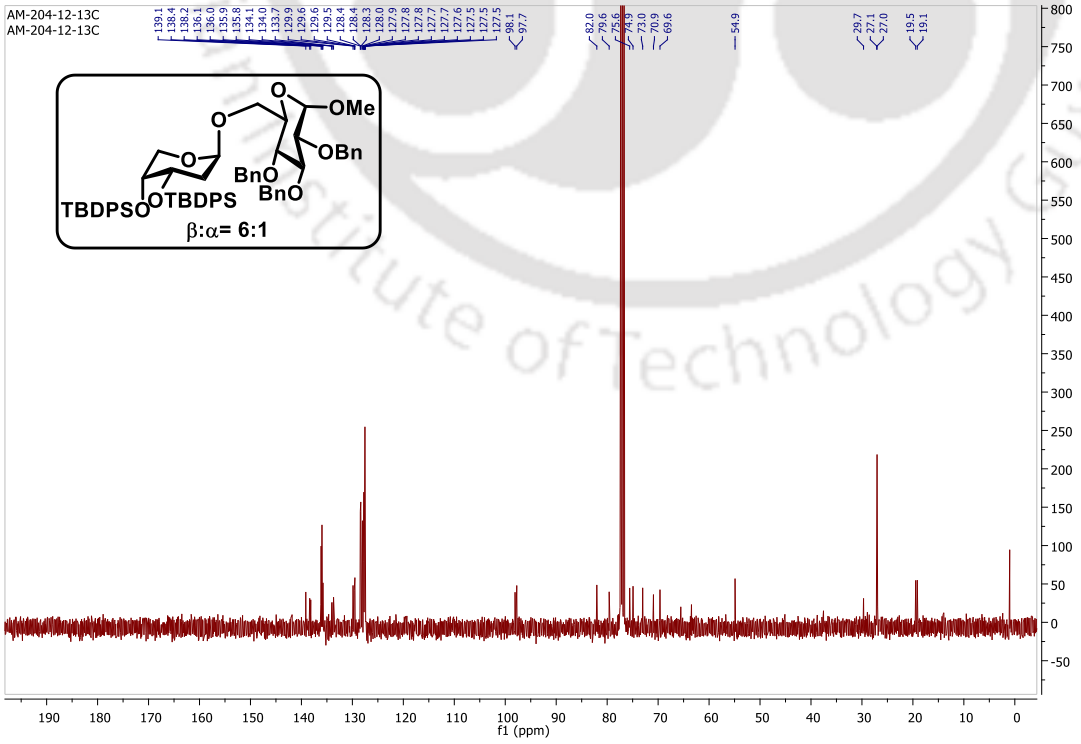
COSY NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosyl)-α-D-galactopyranoside 55i (400 MHz, $CDCl_3$)



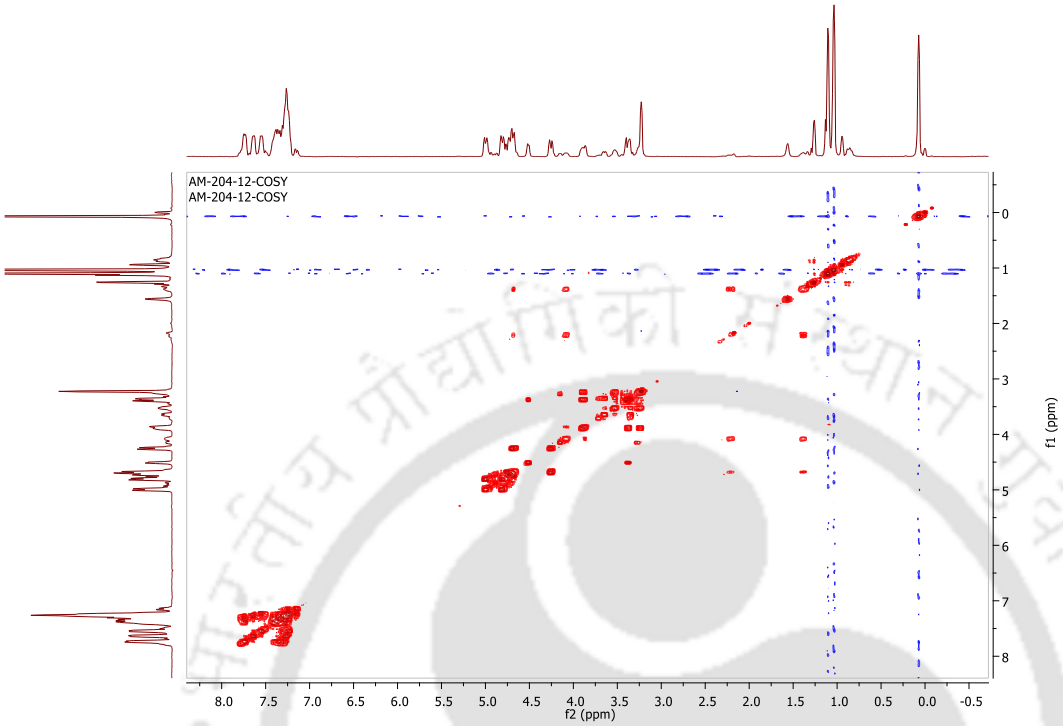
^{1}H NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosyl)-α-D-glucopyranoside 55j (400 MHz, $CDCl_3$)



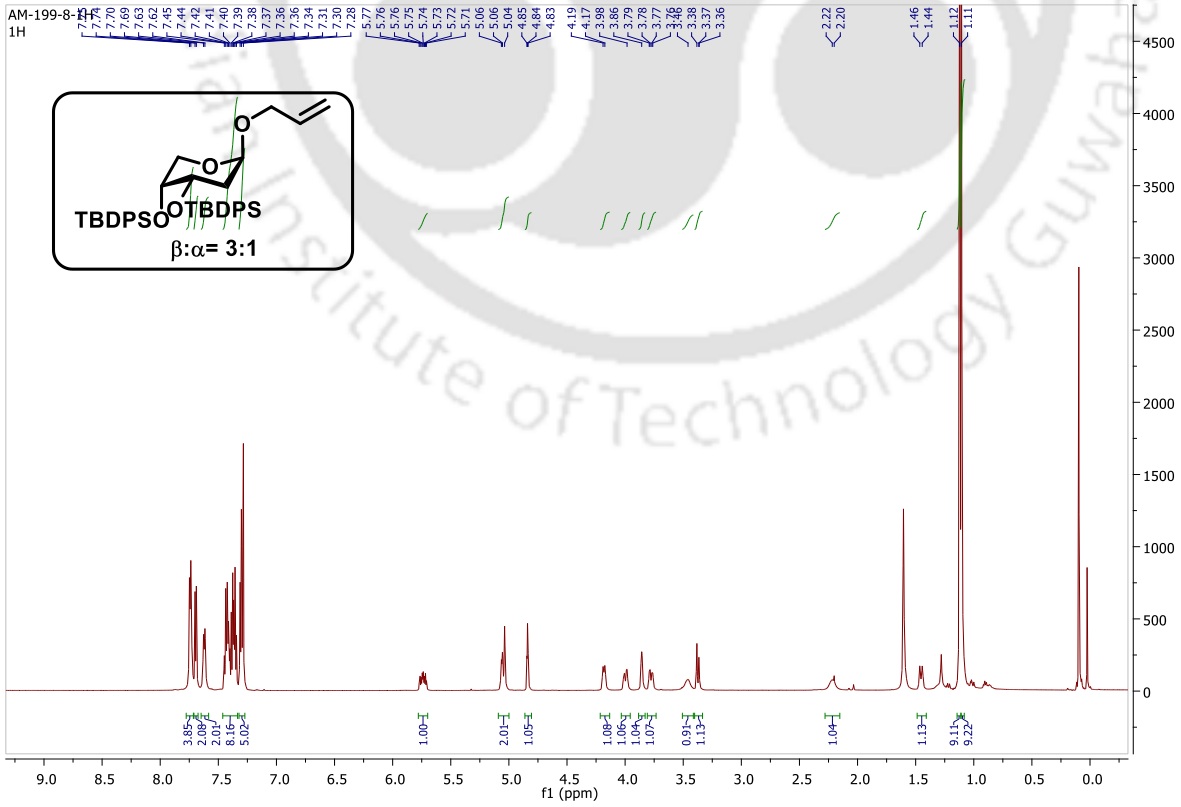
^{13}C NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosyl)-α-D-glucopyranoside 55j (400 MHz, $CDCl_3$)



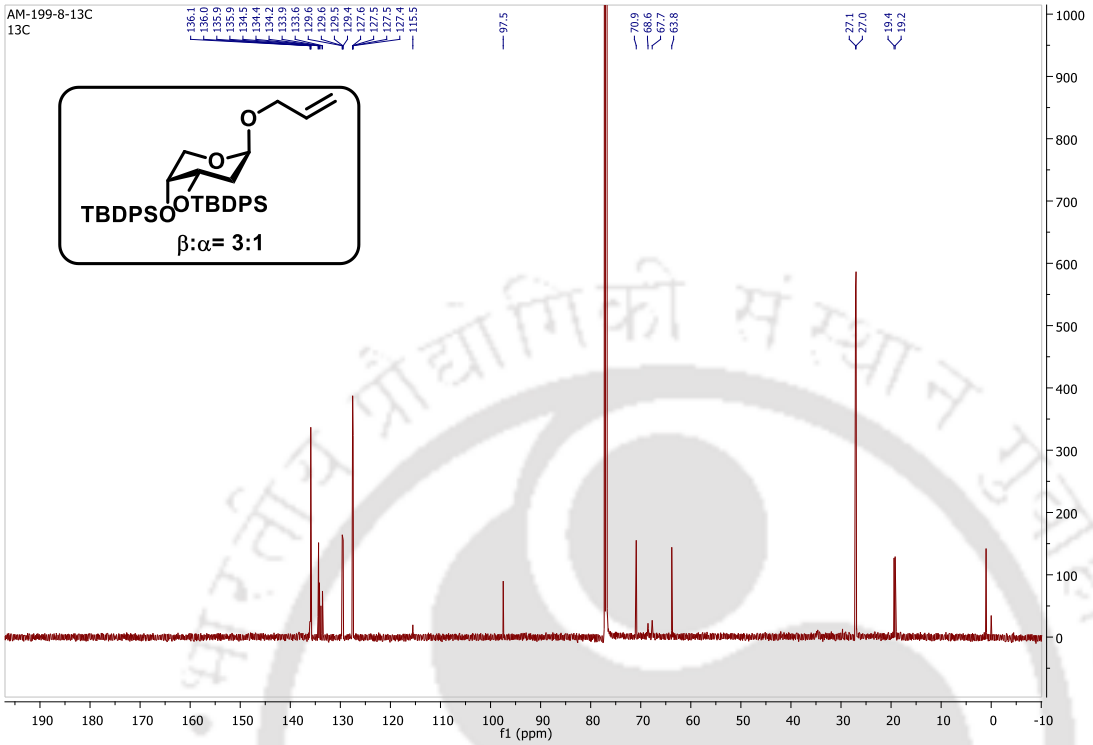
COSY NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosyl)-α-D-glucopyranoside 55j (400 MHz, $CDCl_3$)



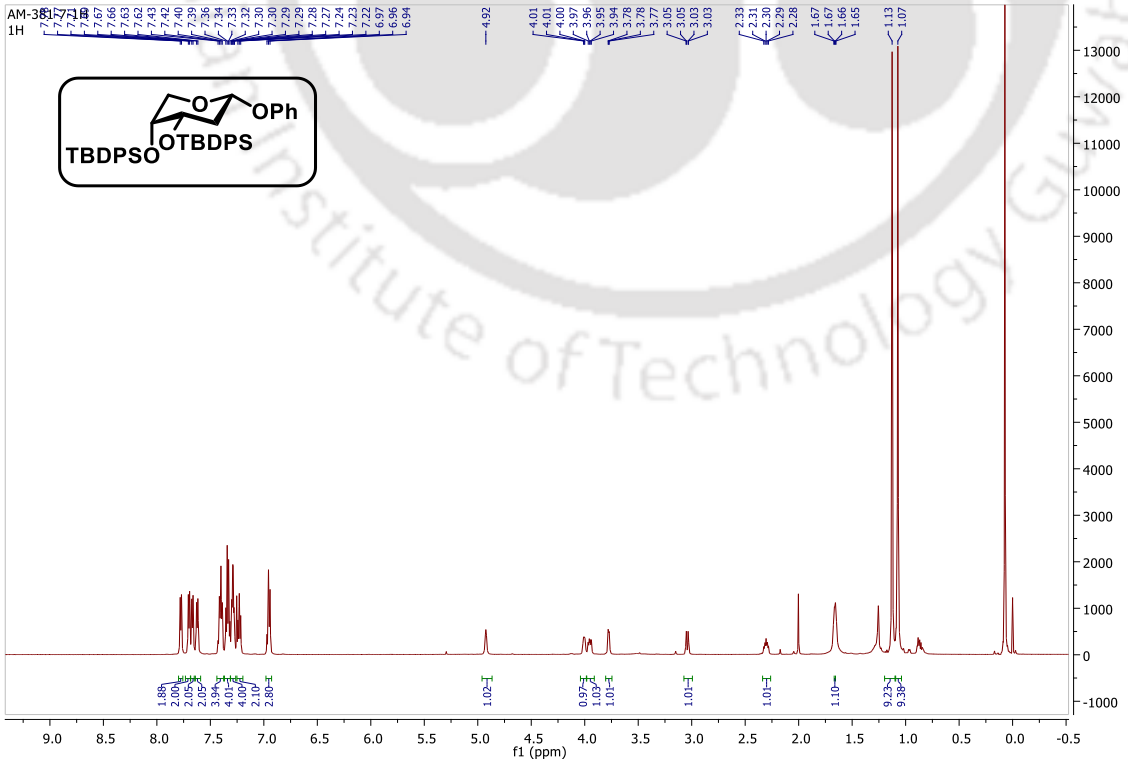
^{1}H NMR of Allyl 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosepyranoside 55k (600 MHz, $CDCl_3$)



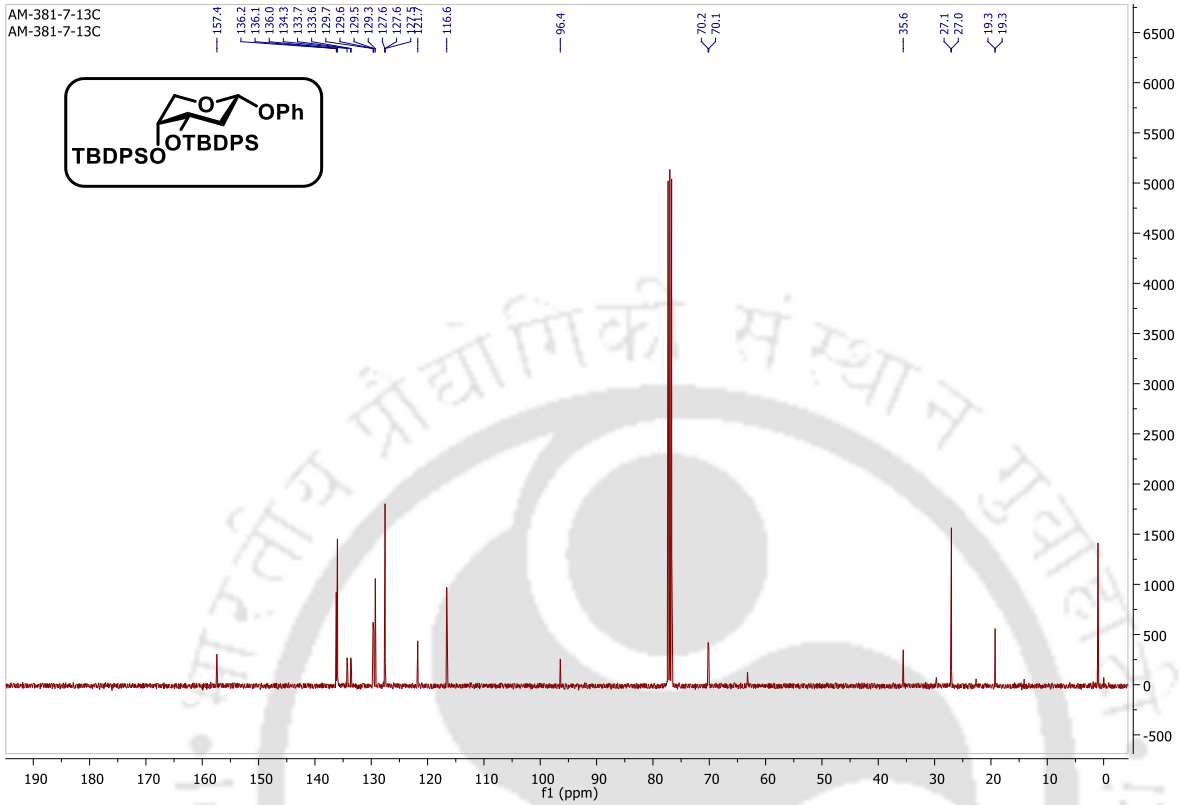
^{13}C NMR of Allyl 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosepyranoside 55k (600 MHz, $CDCl_3$)



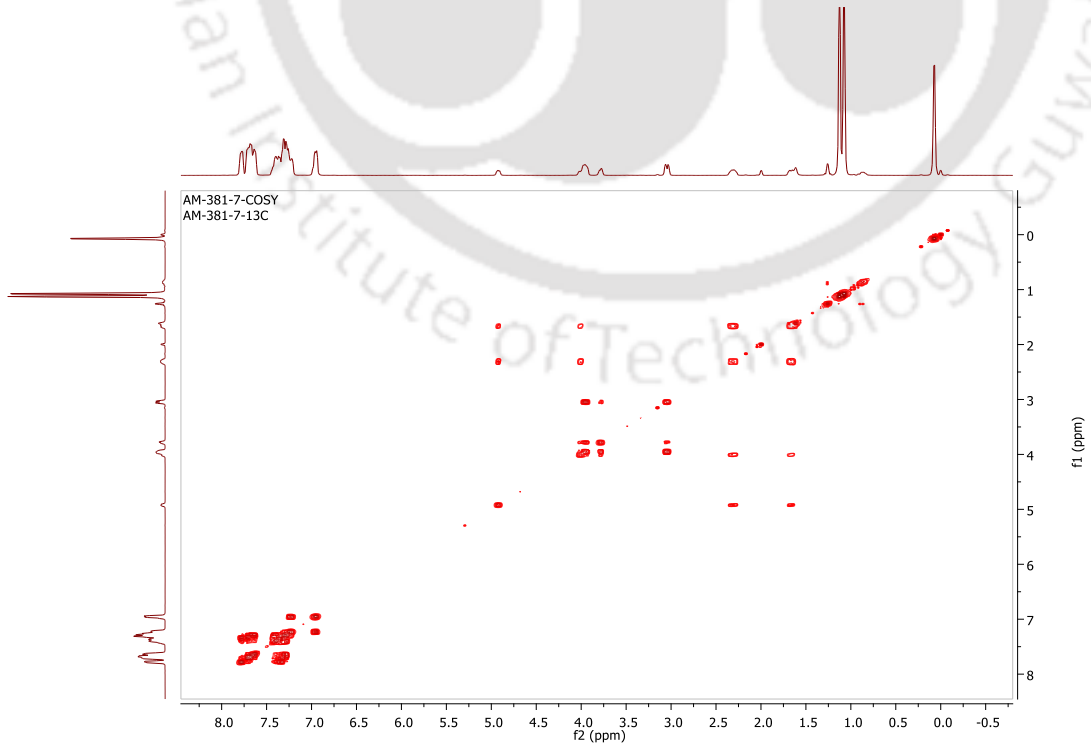
^{1}H NMR of Phenyl 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α-D-arabinopyranoside 56a*α* (600 MHz, $CDCl_3$)



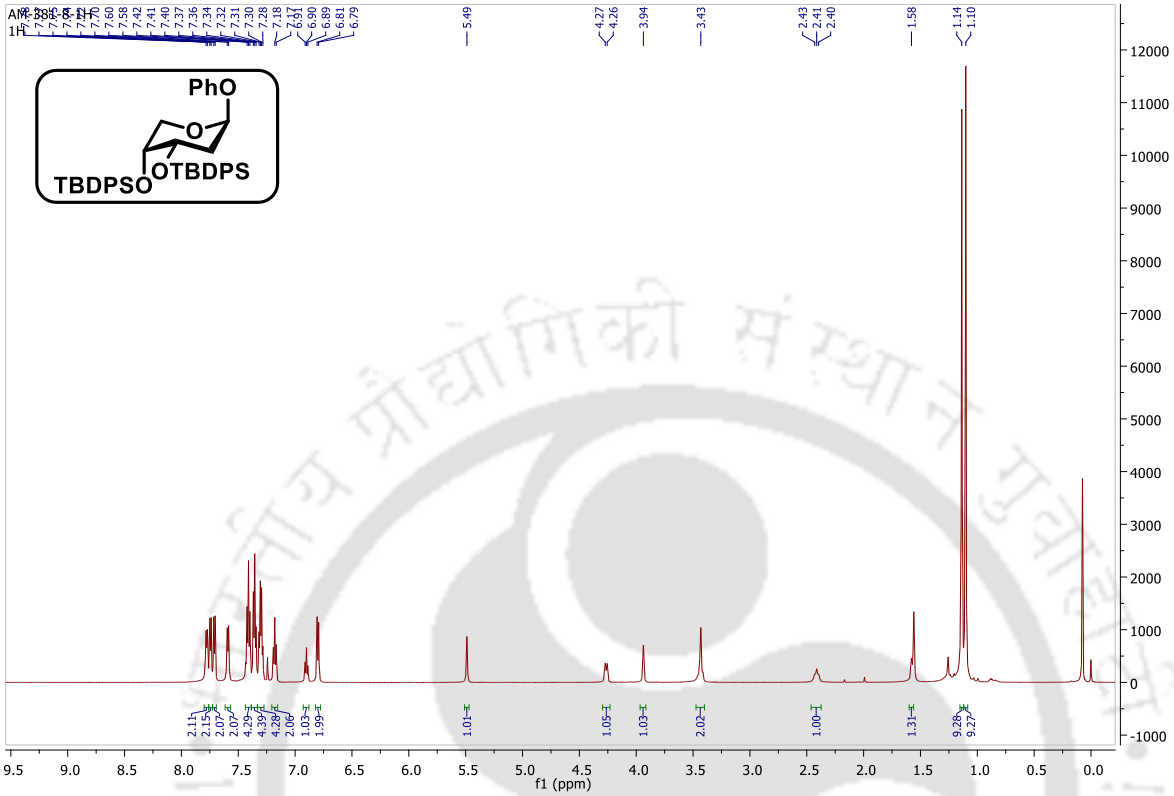
^{13}C NMR of Phenyl 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α-D-arabinopyranoside 56aα (600 MHz, $CDCl_3$)



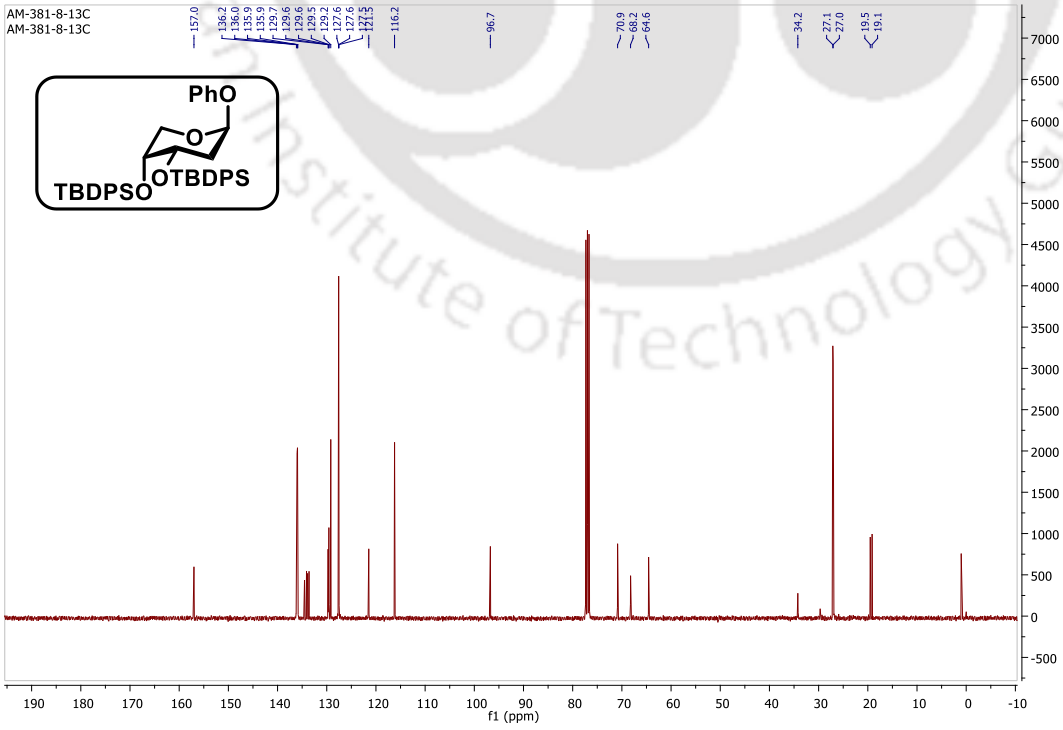
COSY NMR of Phenyl 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α-D-arabinopyranoside 56aα (600 MHz, $CDCl_3$)



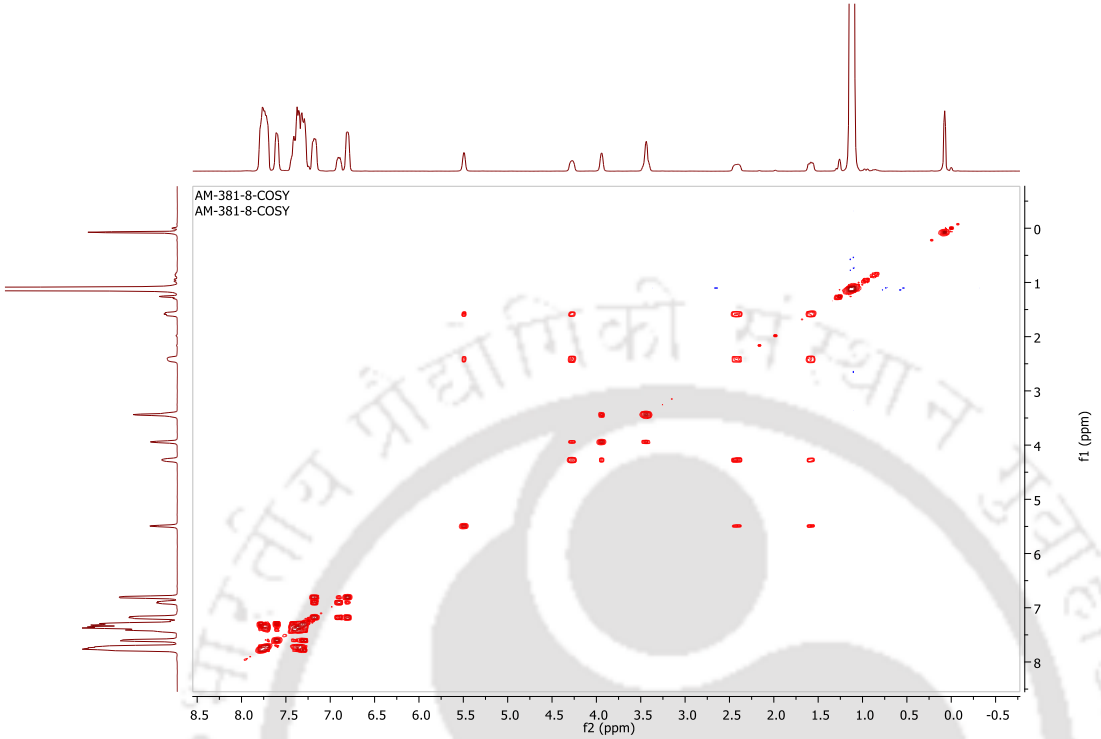
^{1}H NMR of Phenyl 3,4-di-*O-tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosepyranoside 56aβ (600 MHz, $CDCl_3$)



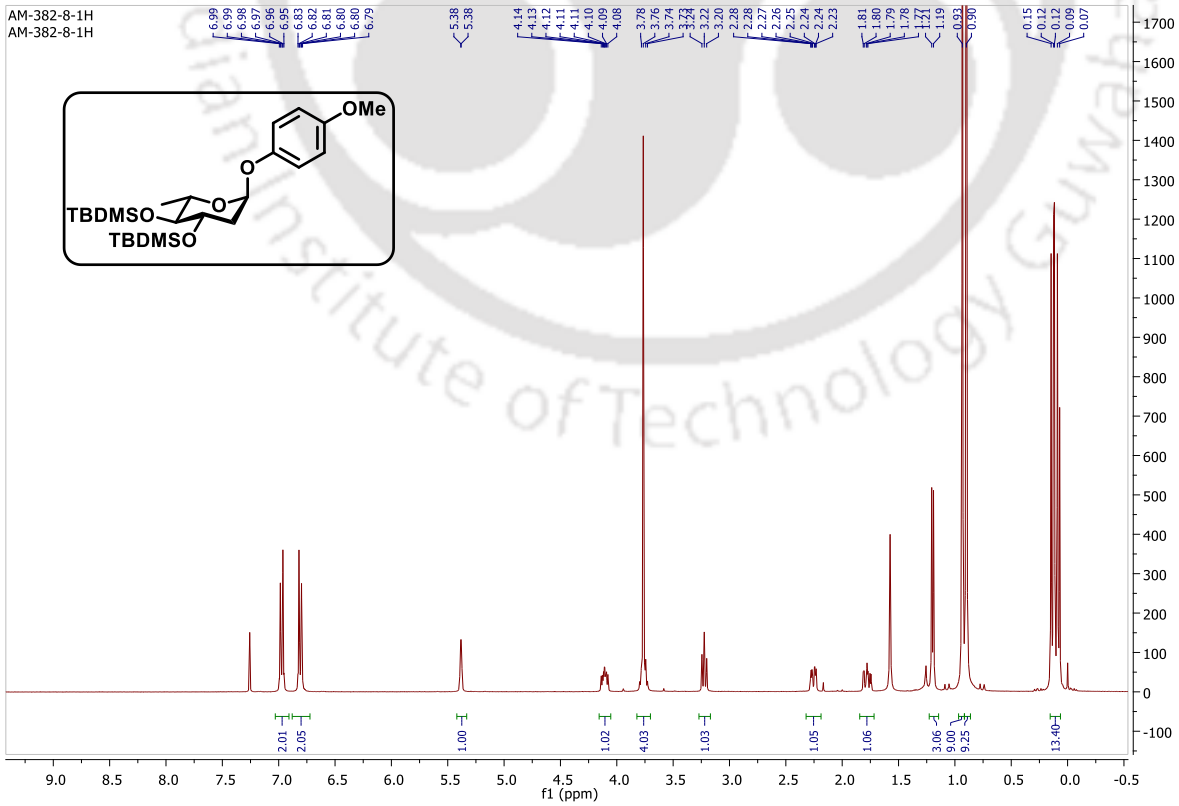
^{13}C NMR of Phenyl-3,4-di-*O-tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosepyranoside 49aβ (600 MHz, $CDCl_3$)



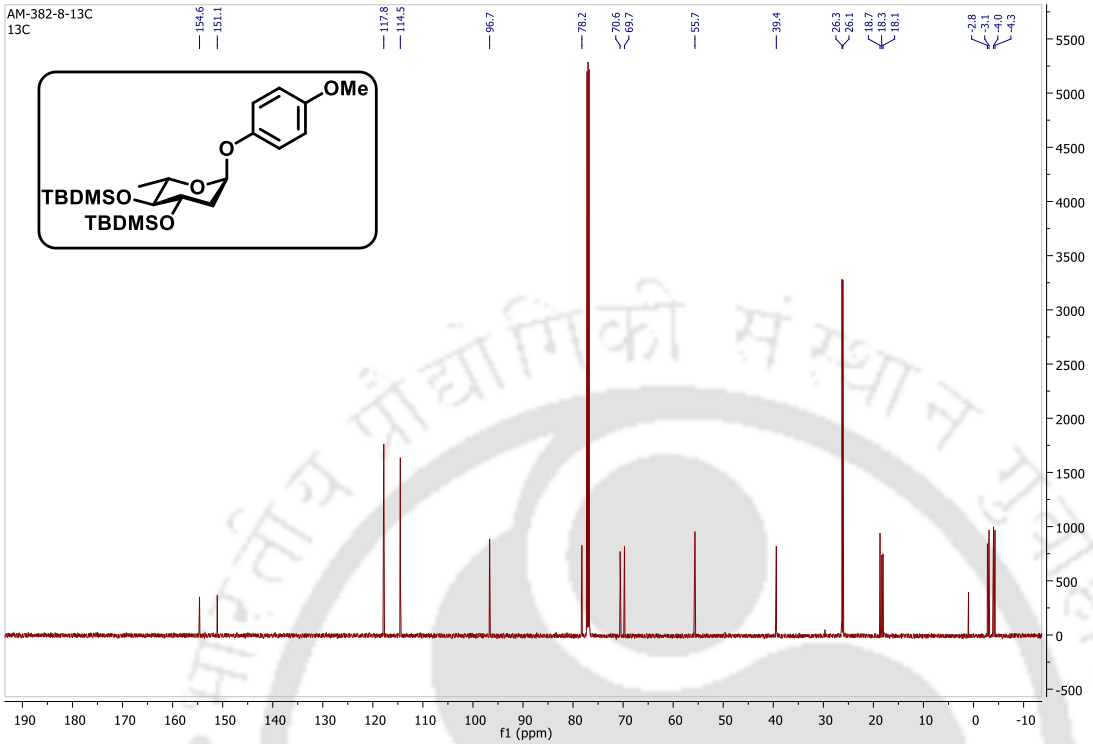
COSY NMR of Phenyl 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-D-arabinosepyranoside 56aβ (600 MHz, $CDCl_3$)



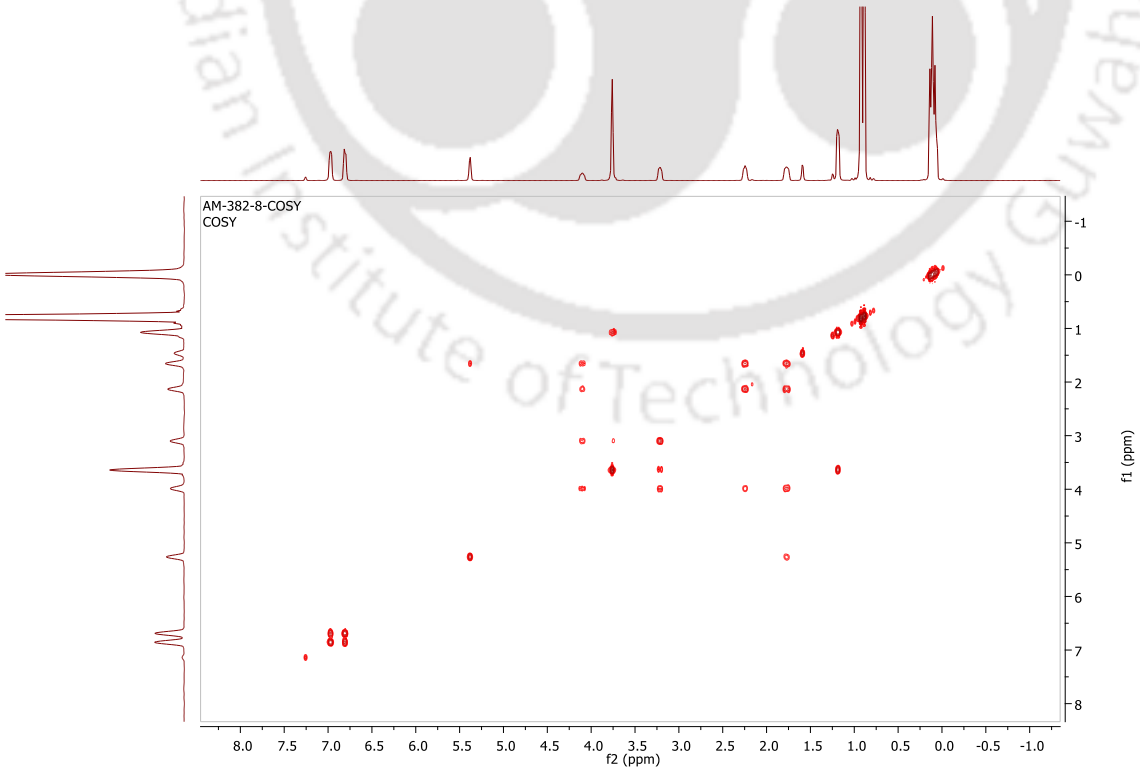
^{1}H NMR p-Methoxybenzyl 3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α-L-rhamnopyranoside 56b*α* (400 MHz, $CDCl_3$)



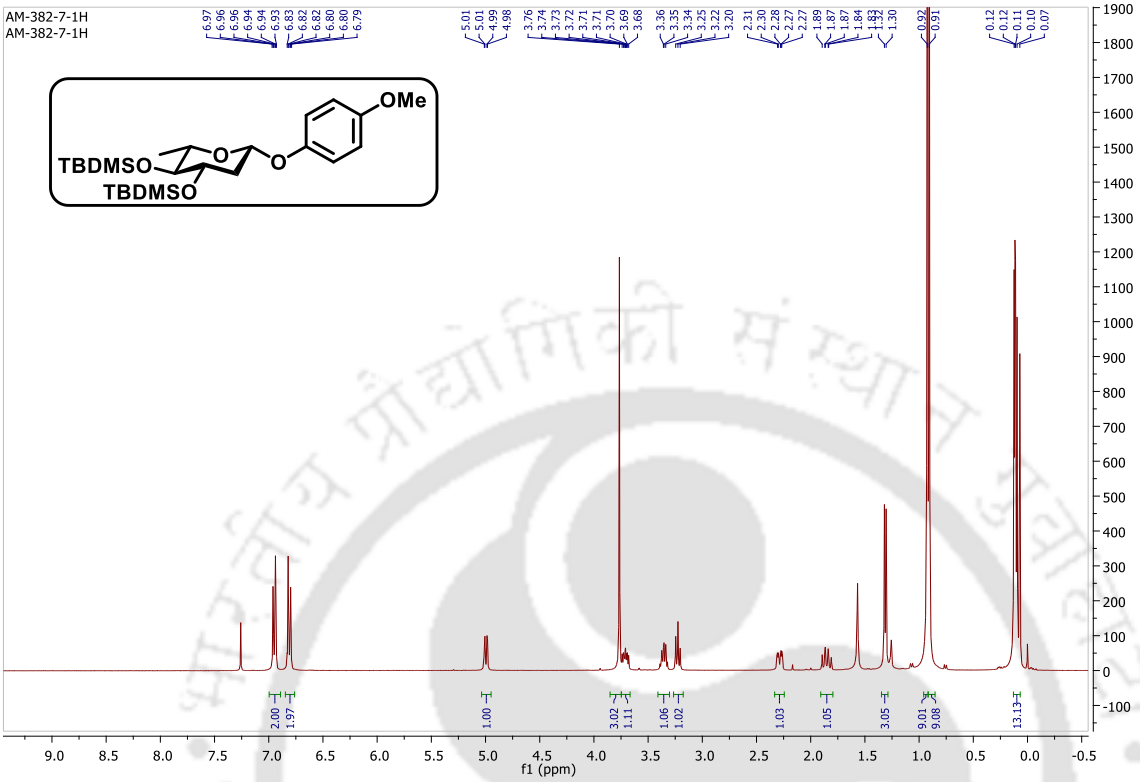
^{13}C NMR p-Methoxybenzyl 3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α-L-rhamnopyranoside 56bα (400 MHz, $CDCl_3$)



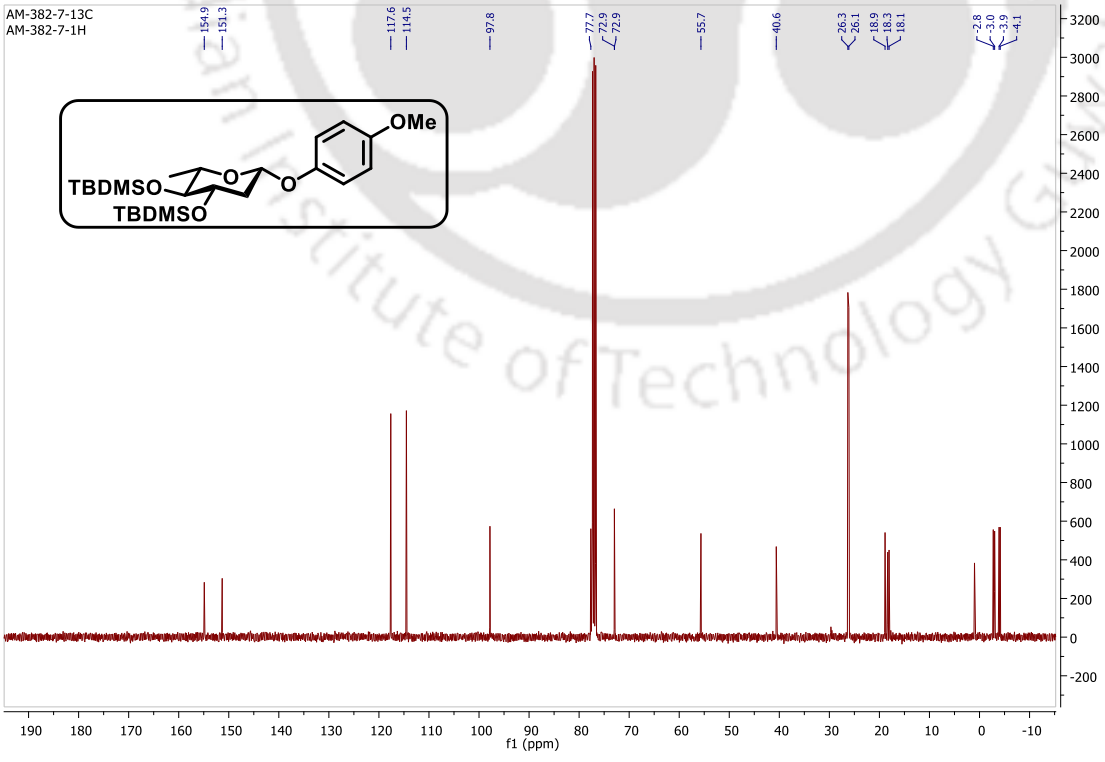
COSY NMR p-Methoxybenzyl 3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α-L-rhamnopyranoside 56bα (400 MHz, $CDCl_3$)



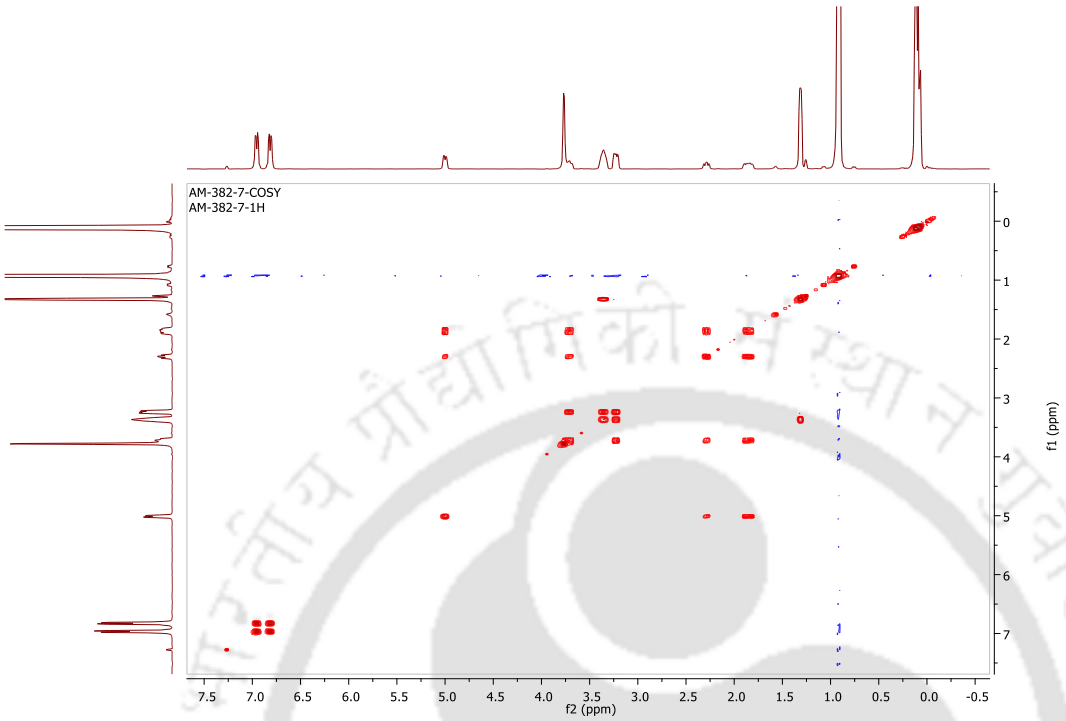
^{1}H NMR of p-Methoxybenzyl 3,4-di-*O-tert*-butyldimethylsilyl-2,6-dideoxy-β-L-rhamnopyranoside 56bβ (400 MHz, $CDCl_3$)



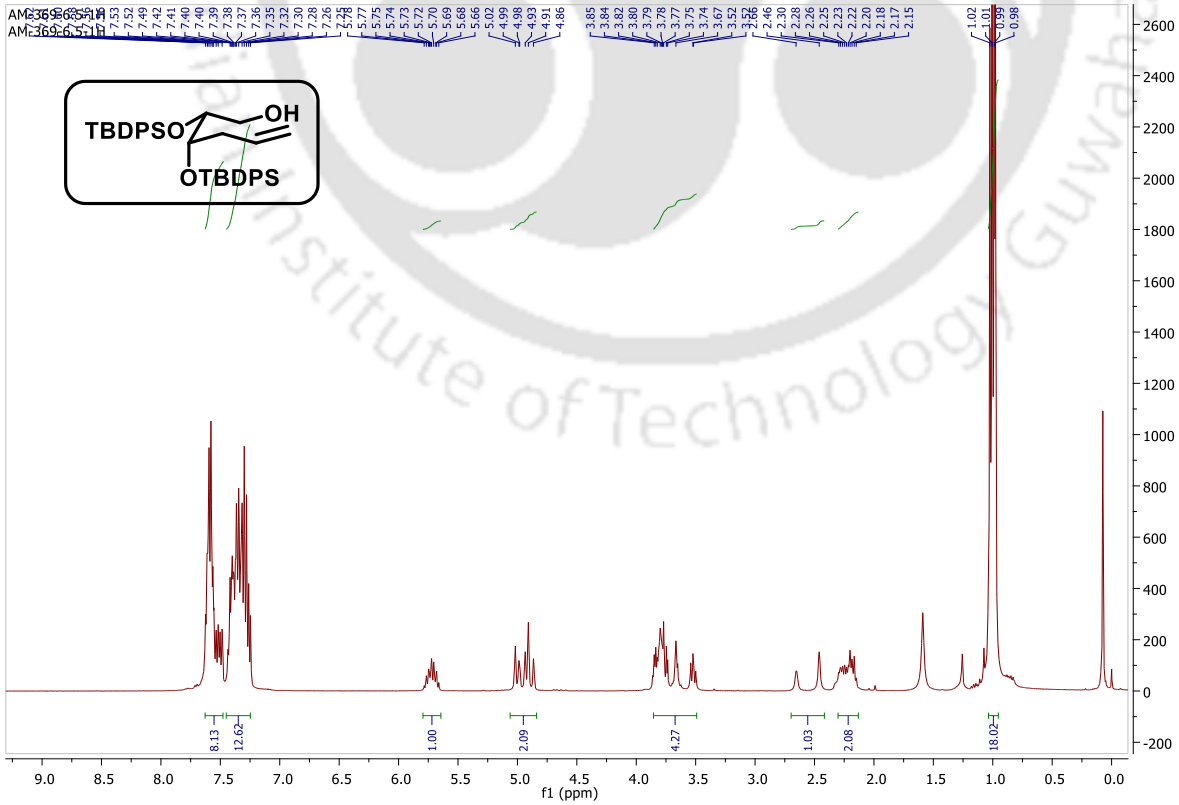
^{13}C NMR of p-Methoxybenzyl 3,4-di-*O-tert*-butyldimethylsilyl-2,6-dideoxy-β-L-rhamnopyranoside 56bβ (400 MHz, $CDCl_3$)



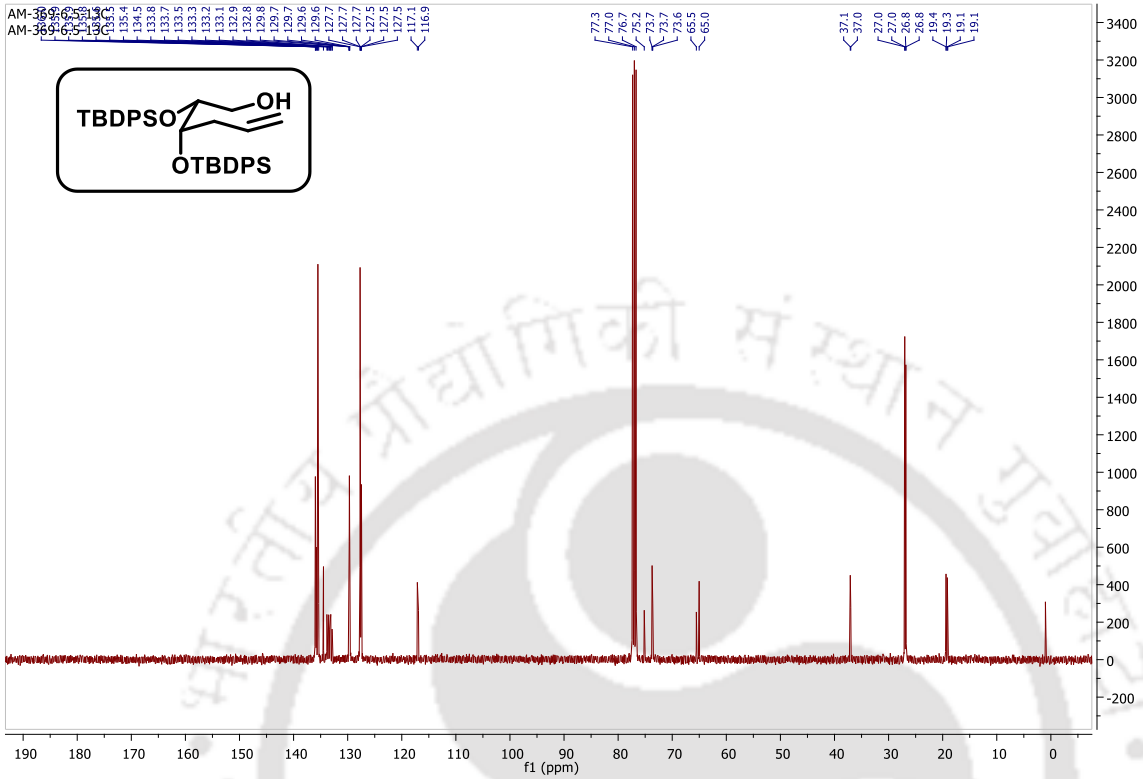
COSY NMR of p-Methoxybenzyl 3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-β-L-rhamnopyranoside 56bβ (400 MHz, $CDCl_3$)



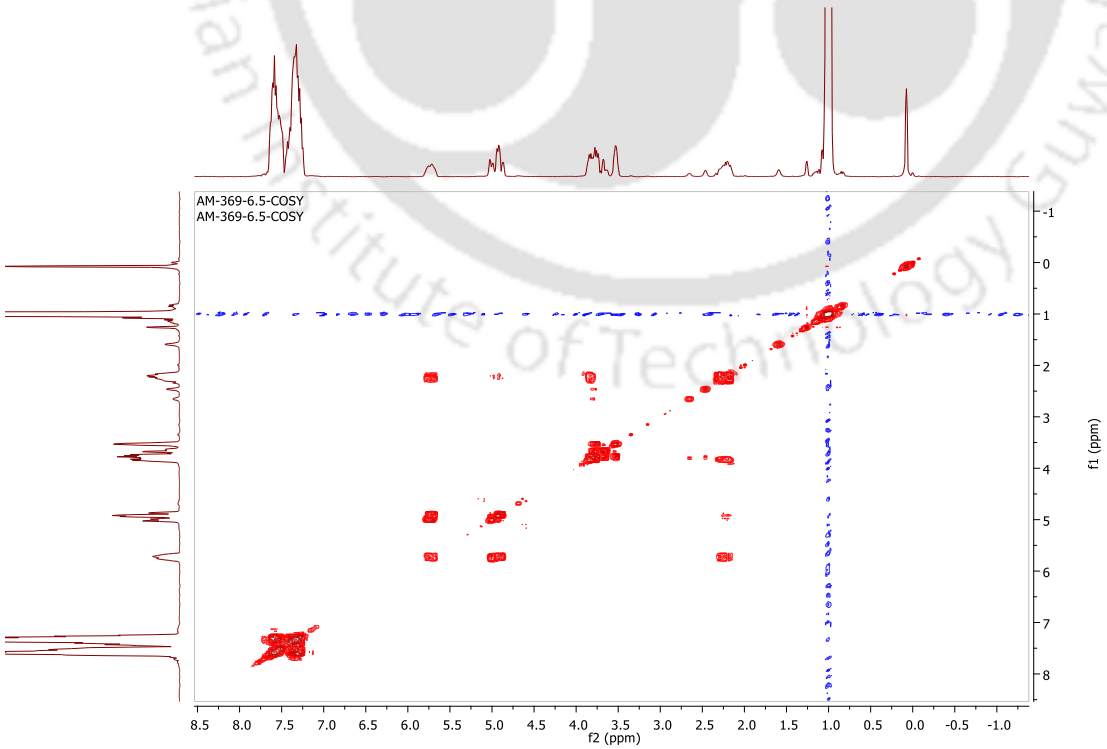
^{1}H NMR of 4,5-Di-*O*-*tert*-butyldiphenylsilyl-1,2,3,6-tetradeoxy-D-arabino-pent-1-enitol 56c (400 MHz, $CDCl_3$)



^{3}C NMR of 4,5-Di-*O*-*tert*-butyldiphenylsilyl-1,2,3,6-tetradeoxy-D-arabino-pent-1-enitol 56c (400 MHz, $CDCl_3$)

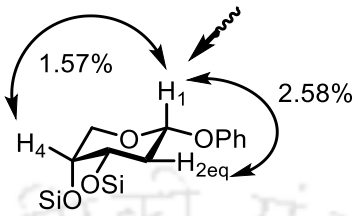


COSY NMR of 4,5-Di-*O*-*tert*-butyldiphenylsilyl-1,2,3,6-tetradeoxy-D-arabino-pent-1-enitol 56c (400 MHz, $CDCl_3$)

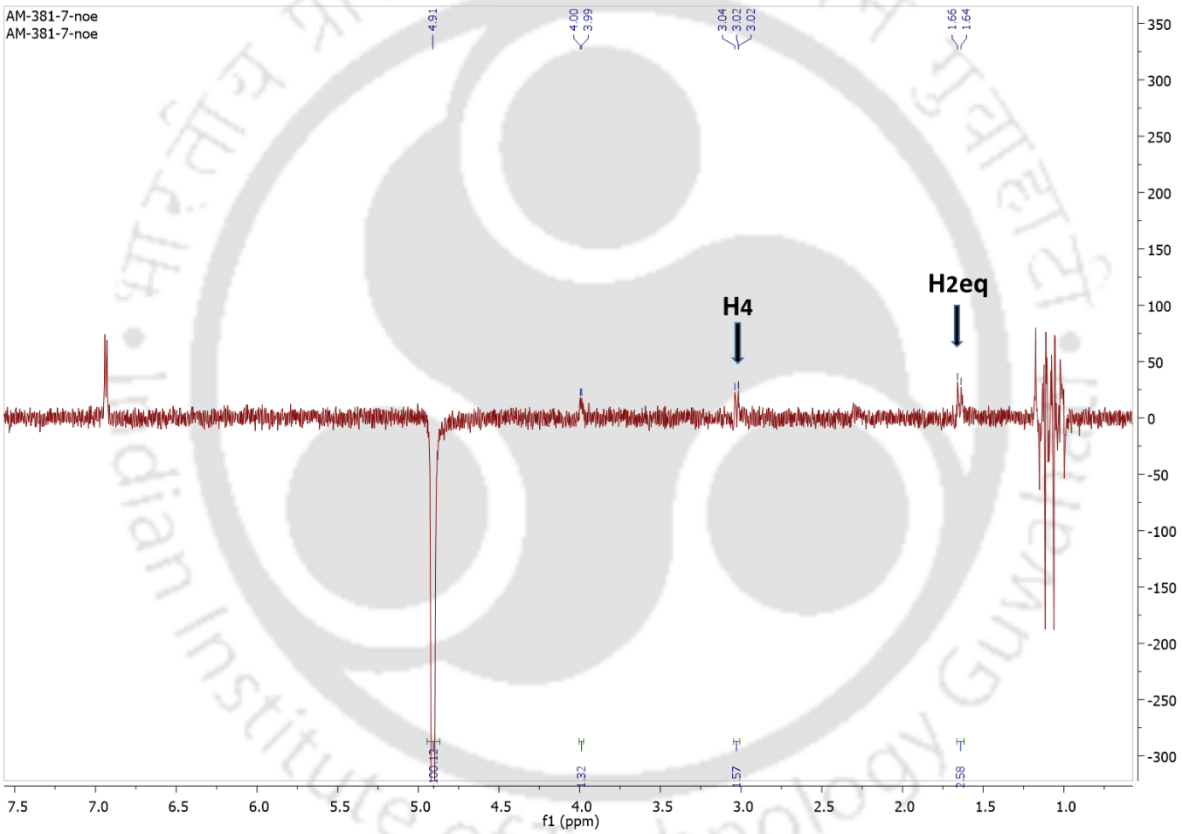


2.12 nOe Experiment of 56a*α*

Irradiation of H_1: Upon irradiation of $\mathbf{H_1}$ the enhancement on the equatorial 2-deoxy proton (appearing at 1.65 ppm) is found 2.58%. In addition, $\mathbf{H_4}$ which is appearing at 3.03 is also enhanced by 1.57%. Hence, $\mathbf{H_1}$ is cis to both $\mathbf{H_4}$ and as well as $\mathbf{H_{2ax}}$. Thus, the compound is in alpha configuration.

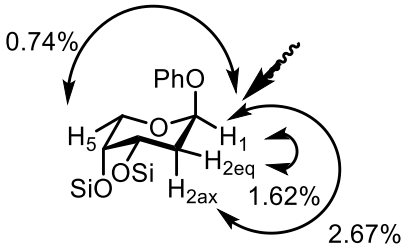


The **α** configuration of **56a**



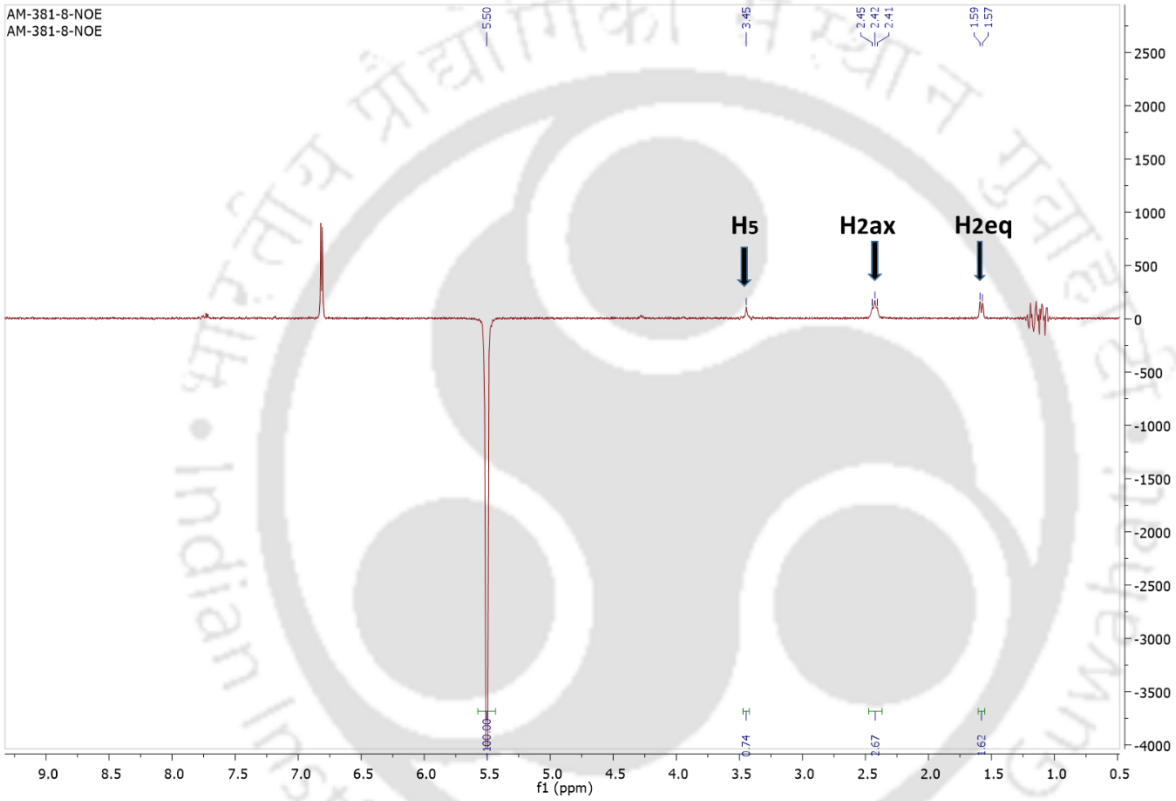
nOe Experiment of 56aβ

Irradiation of H_1: Upon irradiation of anomeric proton $\mathbf{H_1}$ (at 5.50 ppm), the enhancement on the axial 2-deoxy proton (appearing at 2.42 ppm) is found 2.67% which is greater than that of the equatorial 2-deoxy proton (appearing at 1.58 ppm) which is 1.62%. Hence, $\mathbf{H_1}$ is cis to $\mathbf{H_{2eq}}$ and trans to $\mathbf{H_{2ax}}$. From the above observation it can be concluded that the compound is beta isomer.



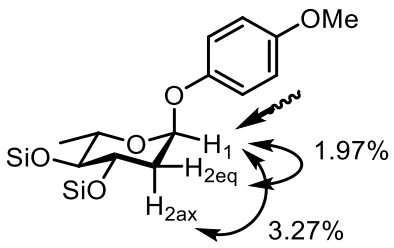
The **β** configuration of **56a**

Irradiation of H_1 of 56aβ:



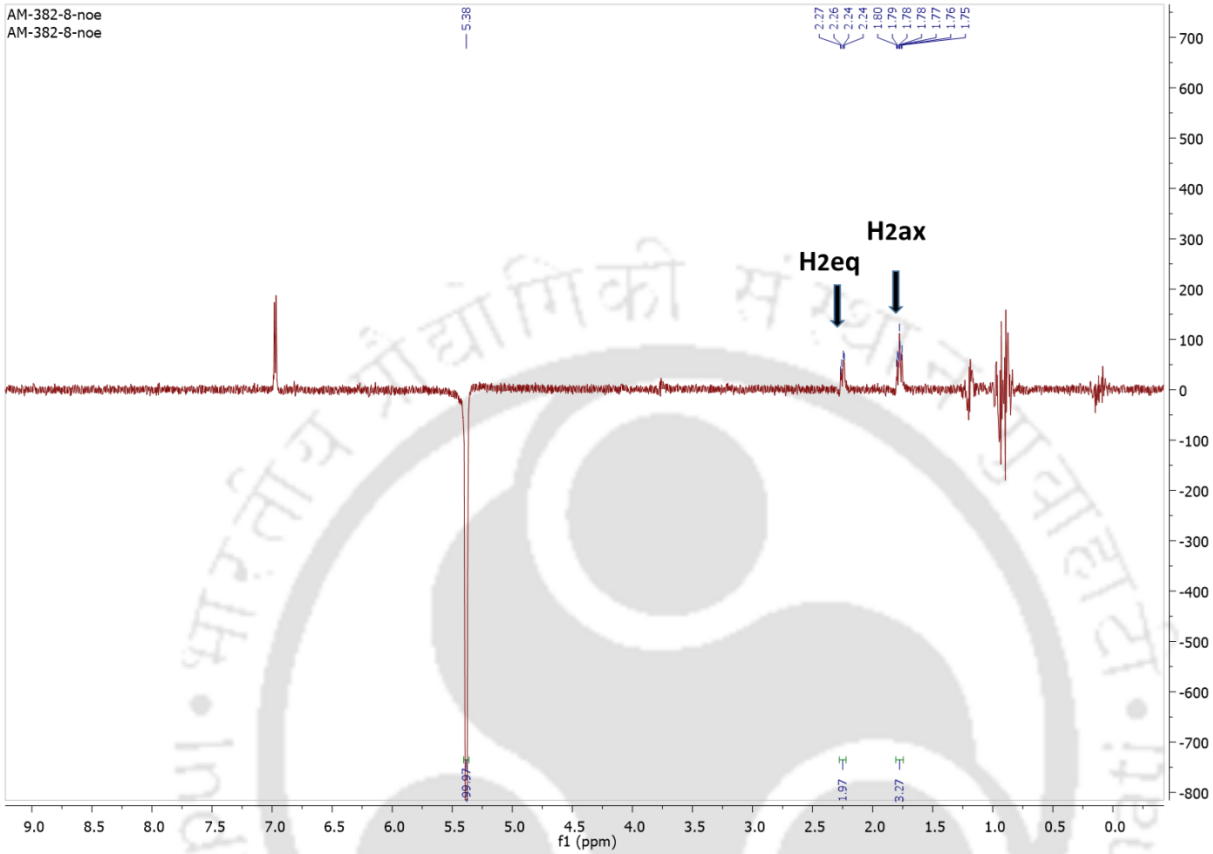
nOe Experiment of 56b*α*

Irradiation of H_1: Upon irradiation of anomeric proton $\mathbf{H_1}$ (at 5.38 ppm), the enhancement on the equatorial 2-deoxy proton (appearing at 2.25 ppm) is found 1.97% which is less than that of the axial 2-deoxy proton (appearing at 1.78 ppm) which is 3.27%. Hence, $\mathbf{H_1}$ is cis to $\mathbf{H_{2eq}}$ and trans to $\mathbf{H_{2ax}}$. From the above observation it can be concluded that the compound is alpha isomer.



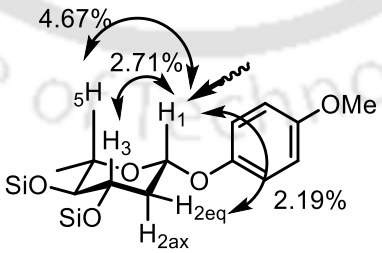
The ***α*** configuration of **56b**

Irradiation of H_1 of 56b*α*:



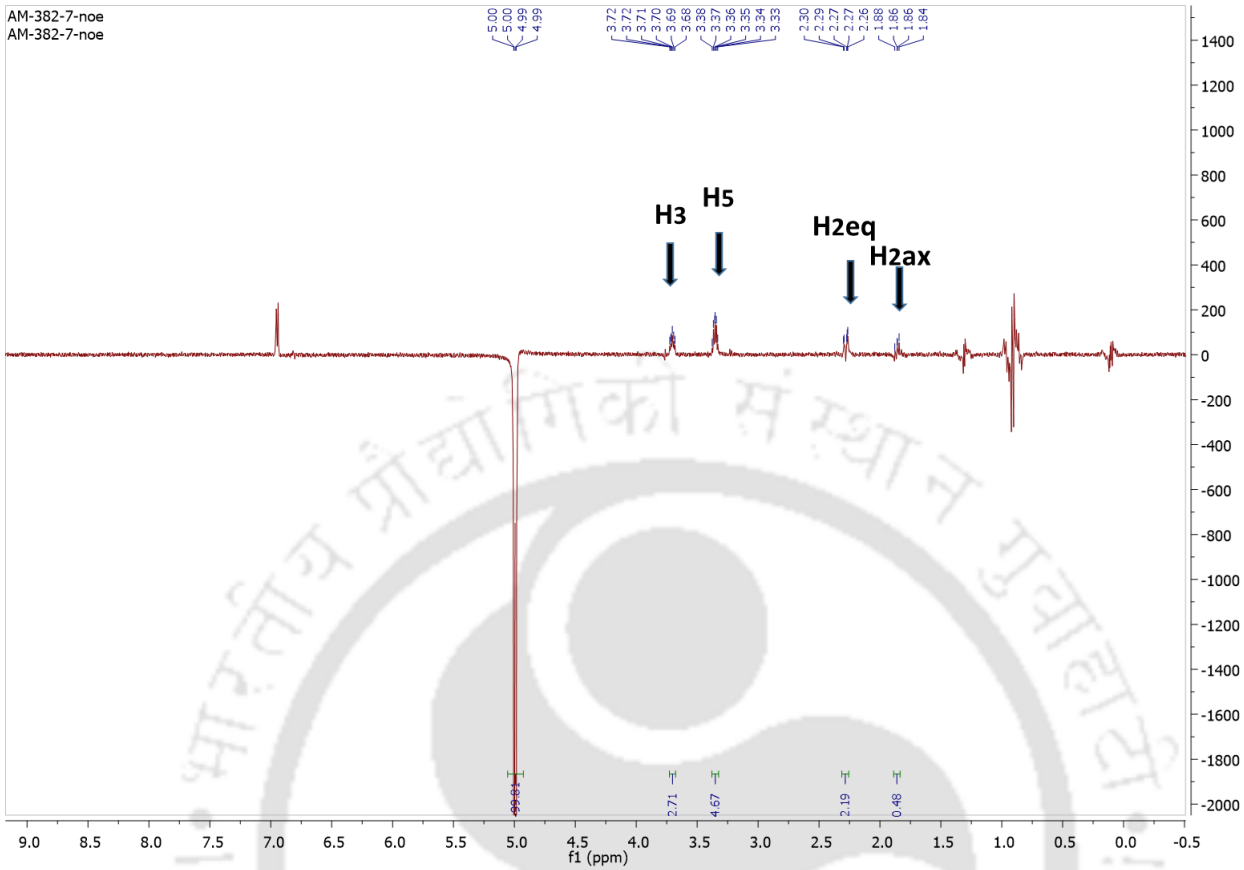
nOe Experiment of 56bβ

Irradiation of H_1: Upon irradiation of anomeric proton H_1 (at 5.00 ppm), the enhancement on the equatorial 2-deoxy proton (appearing at 2.28 ppm) is found 2.19%. In addition, H_3 and H_5 which are appearing at 3.70 and 3.36 respectively are also enhanced by 2.71% and 4.67%. Hence, H_1 is cis to both H_3 and H_5 and as well as H_{2eq}. Thus, the compound is in beta configuration.



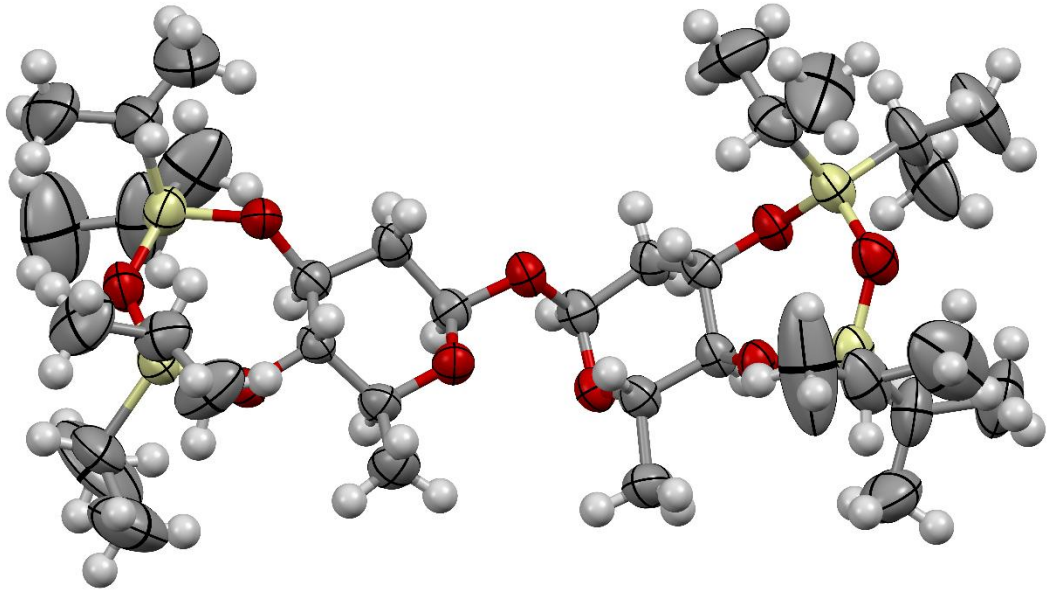
The **β** configuration of **56b**

Irradiation of H_1 of 56bβ:



2.13 XRD Data:

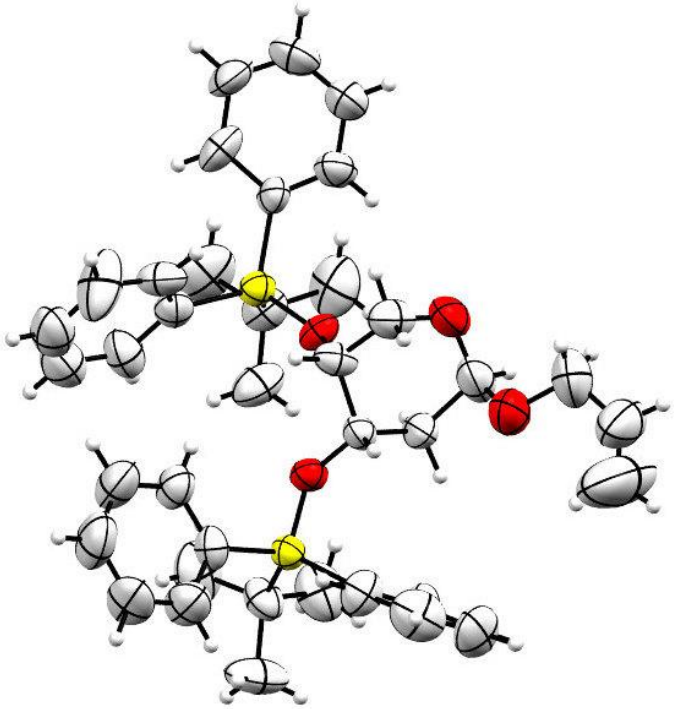
XRD Data of **51b:**



Crystal system	= monoclinic

Bond precision:	C-C = 0.0169 Å	
Wavelength	= 0.71073	
Cell:	a = 29.443(9) Å	
	b = 10.166(3) Å	
	c = 16.882(5) Å	
	α = 90°	
	β = 106.187(11)°	
	γ = 90°	
Temperature:	296 K	
	Calculated	Reported
Volume:	4853(3) $Å^3$	4853(3) $Å^3$
Space group:	C 2	
Hall group:	C 2y	
Moiety formula:	C35 H71 O10 Si4	
Sum formula:	C35 H71 O10 Si4	C18 H28 O5 Si2
Mr:	763.32	763.32
Dx:	1.046 g cm^{-3}	1.042 g cm^{-3}
Z:	4	4
Mu:	0.166 mm^{-1}	0.166 mm^{-1}
F(000):	1668.0	1632.0
F(000'):	1670.01	
Ranges (h,k,l)max:	35,12,20	35,12,20
Nref:	8968[4757]	8890
Data completeness	= 1.87/ 0.99	
Theta(max)	= 25.41	
R(reflections)	= 0.0825(3628)	
wR2(reflections)	= 0.2479(8890)	
S	= 0.979	
Npar	= 458	

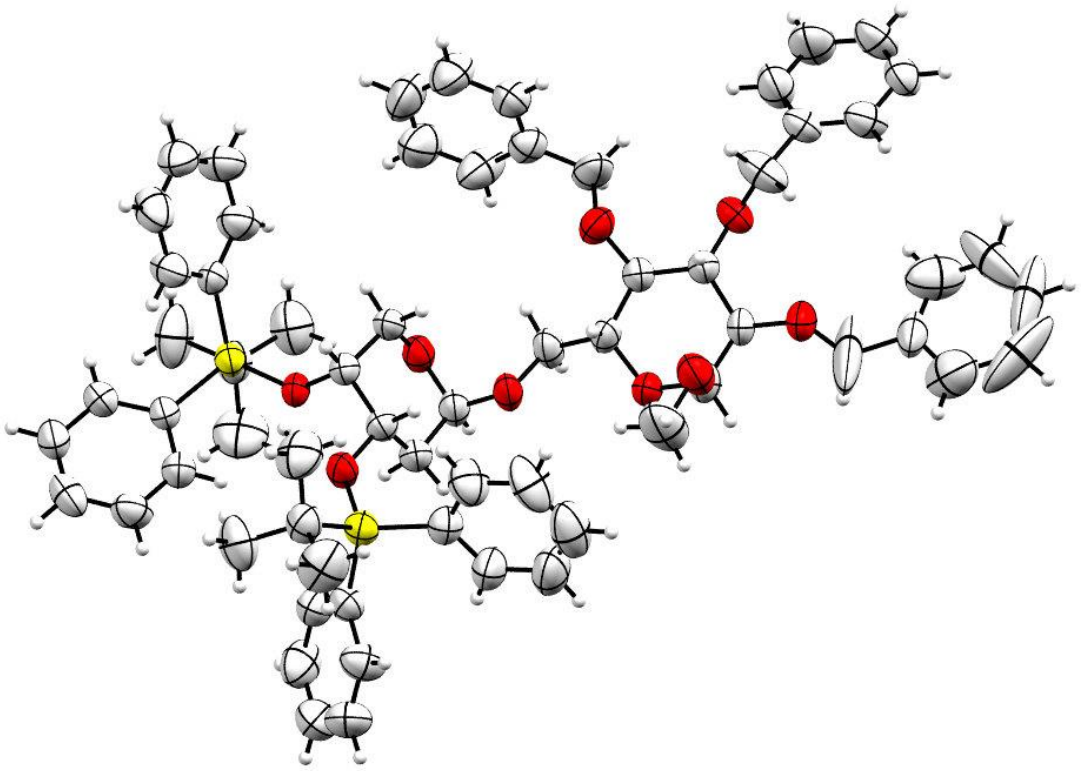
XRD Data of **55k**:



Crystal system	= Monoclinic	
Bond precision:	C-C = 0.0192 Å	
Wavelength	= 0.71073	
Cell:	a = 10.5387(15) Å	
	b = 33.130(5) Å	
	c = 11.6786(16) Å	
	α = 90°	
	β = 109.235(5) °	
	γ = 90°	
Temperature:	296 K	
	Calculated	Reported
Volume:	3849.9(10) $Å^3$	3849.9(9) $Å^3$
Space group:	P 21	P21
Hall group:	P 2yb	
Moiety formula:	C40 H50 O4 Si2	
Sum formula:	C40 H50 O4 Si2	C40 H50 O4 Si2
Mr:	650.98	650.98
Dx:	1.123 g cm^{-3}	1.123 g cm^{-3}
Z:	4	4

Mu:	0.129 mm^{-1}	0.129 mm^{-1}
F(000):	1400.0	1400.0
F(000'):	1401.18	
Ranges (h,k,l)max:	12,39,13	12,39,13
Nref:	13583[6921]	13583
Tmin,Tmax:	0.977,0.985	
Tmin':	0.973	
Data completeness	= 0.988/1.00	
Theta(max)	= 25.000	
R(reflections)	= 0.1128(8665)	
wR2(reflections)	= 0.3540(13583)	
S	= 1.080	
Npar	= 841	

XRD Data of 55j:

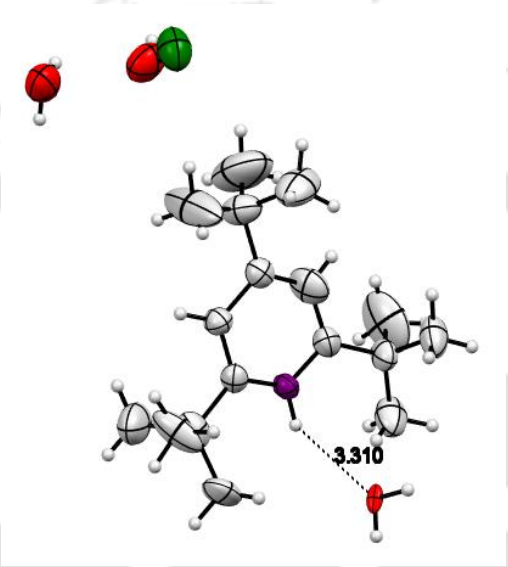


Crystal system	= Orthorhombic

Bond precision:	C-C = 0.0130 Å	
Wavelength	= 0.71073	
Cell:	a = 10.031(7) Å	
	b = 29.69(2) Å	
	c = 20.267(14) Å	
	α = 90°	
	β = 90°	
	γ = 90°	
Temperature:	298 K	
	Calculated	Reported
Volume:	6036(7) $Å^3$	6036(7) $Å^3$
Space group:	P 21 21 21	P 21 21 21
Hall group:	P 2ac 2ab	P 2ac 2ab
Moiety formula:	C65 H76 O9 Si2	C65 H76 O9 Si2
Sum formula:	C65 H76 O9 Si2	C65 H76 O9 Si2
Mr:	1057.44	1057.44
Dx:	1.164 g cm^{-3}	1.164 g cm^{-3}
Z:	4	4
Mu:	0.113 mm^{-1}	0.113 mm^{-1}
F(000):	2264.0	2264.0
F(000'):	2265.63	
Ranges (h,k,l)max:	13,39,26	13,39,26
Nref:	14760[8122]	14602
Tmin,Tmax:	0.971,0.979	0.971,0.979
Tmin':	0.969	
Correction method	= # Reported	
T Limits:	Tmin = 0.971	
	Tmax = 0.979	
AbsCorr	= Multi-scan	
Data completeness	= 1.00/1.00	
Theta(max)	= 28.122	
R(reflections)	= 0.0791(6002)	
wR2(reflections)	= 0.2142(14602)	
S	= 1.019	

Npar	= 692

XRD Data of TTBPy.HCl, $3H_2O$:

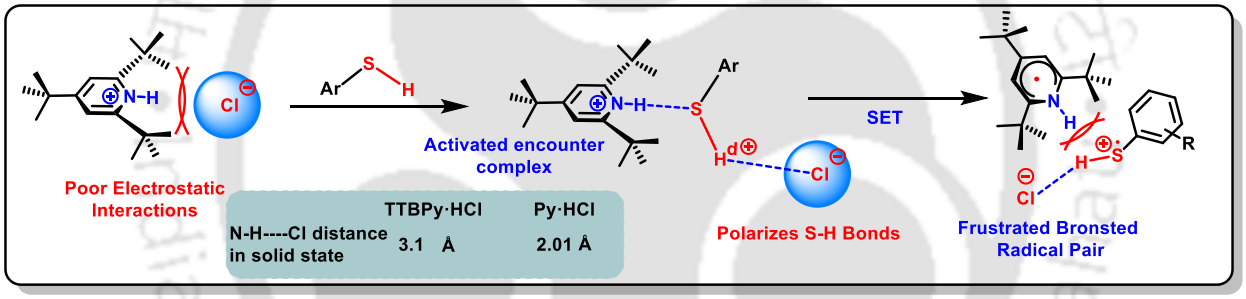


Crystal system	=	
Bond precision:	C-C = 0.0152 Å	
Wavelength	= 0.71073	
Cell:	a = 18.8335 (13) Å	
	b = 10.1093 (7) Å	
	c = 11.3681 (7) Å	
	α = 90°	
	β = 90°	
	γ = 90°	
Temperature:	293 K	
	Calculated	Reported
Volume:	2164.4 (3) $Å^3$	2164.4 (3) $Å^3$
Space group:	P c a 21	P c a 21
Hall group:	P 2c -2ac	P 2c -2ac
Moiety formula:	C17 H30 N, Cl, 2(H20), O	

Sum formula:	C17 H34 Cl N O3	C17 H34 Cl N O3
Mr:	335.90	335.90
Dx:	1.031 g cm^{-3}	1.031 g cm^{-3}
Z:	4	4
Mu:	0.187 mm^{-1}	0.187 mm^{-1}
F(000):	736.0	736.0
F(000'):	736.88	
Ranges (h,k,l)max:	22,12,13	22,12,13
Nref:	3811[2014]	3022
Tmin,Tmax:	0.960,0.978	
Tmin':	0.949	
T Limits:	Tmin = 0.960	
	Tmax = 0.978	
Data completeness	= 1.50/0.79	
Theta(max)	= 24.981	
R(reflections)	= 0.1054(2258)	
wR2(reflections)	= 0.3370(3022)	
S	= 1.222	
Npar	= 205	

Chapter III

Sterically Strained Brønsted Pair Catalysis by Bulky Pyridinium Salts: Direct Stereoselective Synthesis of 2-Deoxy and 2,6-Dideoxy-β-thioglycosides from Glycals



Mukherji, A.; Addanki, R. B.; Halder, S.; Kancharla, P. K. *J. Org. Chem.* **2021**, *86*, 17226–17243.

Sterically Strained Brønsted Pair Catalysis by Bulky Pyridinium Salts: Direct Stereoselective Synthesis of 2-Deoxy and 2,6-Dideoxy-β-thioglycosides from Glycals

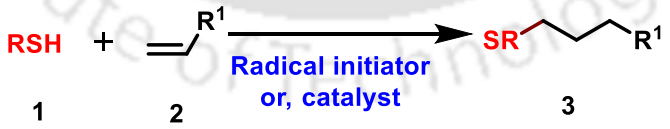
3.1 Introduction:

3.1.1 Thiolation on Terminal Olefin:

Organic compounds containing sulfur atoms are known as organosulfur compounds. They can be identified from their physical characteristics e.g. foul odors, but some sweet-smelling compounds are also known, e.g., saccharin. Nature is rich with organosulfur compounds as sulfur is one of the essential components in living organisms. Among the 20 common amino acids, there are two organosulfur compounds, which are cysteine and methionine. Penicillin and other antibiotics containing the sulfanilamide moiety (sulfa drugs) contain sulfur atoms. Sulfur is present in several lifesaving antibiotics and drugs; on the other hand, sulfur mustard or mustard gas is a life-threatening chemical warfare agent used in terrorism. In addition, sulfur is an essential component in many of the nonrenewable fuel natural resources e.g. fossil fuels, coal, petroleum, and natural gas, the removal of such resources is a significant target of the oil refineries.

Oxygen and selenium are present in the same group in the periodic table with sulfur which is group 16 or the chalcogen group and hence all of them have the same valance electron configuration which leads to similar chemical and physical properties. Hence organosulfur compounds are expected to have similarities with carbon–oxygen, carbon–selenium, and carbon-tellurium compounds as these are structural isosteres (atoms, molecules, or ions having similar size due to having the same number of atoms and valence electrons).

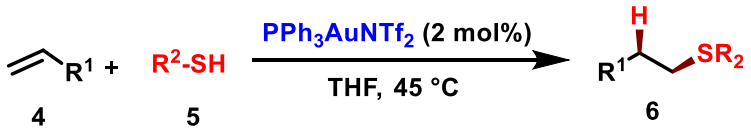
The thiol-ene reaction or hydrothiolation in alkene as described below in scheme 1, is an organic reaction between any molecule containing a free thiol group and an alkene to form a thioether compound. Thiol-ene reaction was first introduced by Posner in 1905[1] but due to its wide range of applications, it gained importance in later times. This reaction provides a Markovnikov or an anti-Markovnikov addition of a thiol moiety to a terminal alkene. This reaction can be included in a click chemistry reaction due to its high yield, stereoselectivity, and thermodynamic driving force.



Scheme 1: *Thiol-ene Reaction*

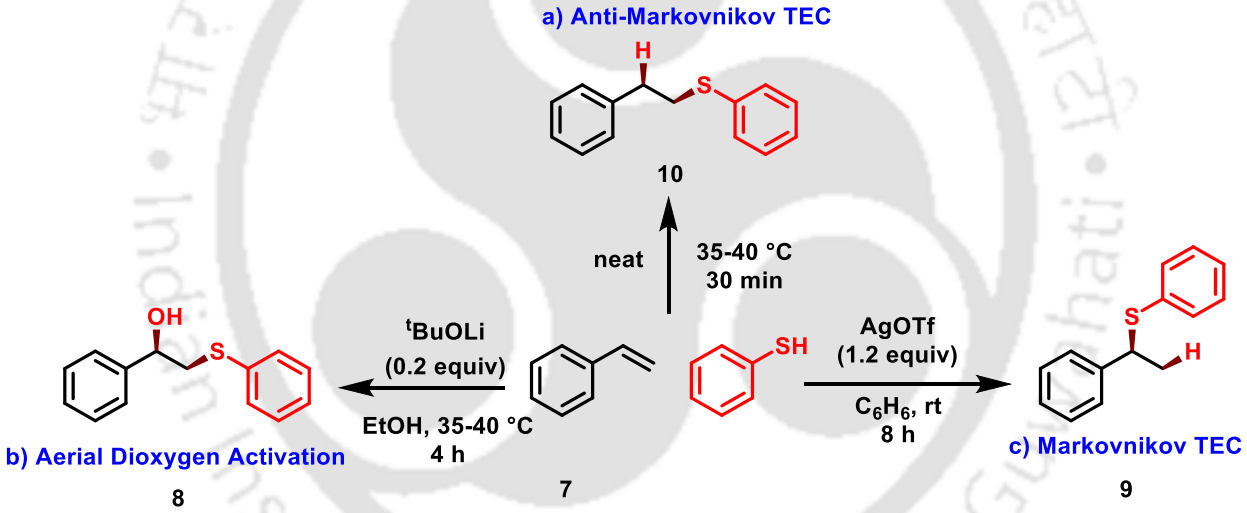
Ogawa and co-workers have shown anti-Markovnikov addition of organosulfur compounds, to alkenes which doesn't contain any activating protecting group, using transition-metal-catalyst. In 2016, they have reported a gold-catalyzed hydrothiolation method of deactivated alkenes, which provides the anti-Markovnikov addition products in good yields and

regioselectivity (scheme 2).[2] They have used 2 mol% of PPh_3AuNTf_2 as a gold-based catalyst to perform hydrothiolation on several unactivated alkenes.



Scheme 2: *Gold-Catalyzed Anti-Markovnikov Selective Hydrothiolation*

Markovnikov and anti-Markovnikov thiol–ene click (TEC) reactions and the synthesis of β-hydroxysulfides are well-known C–S bond-forming reactions between styrenes and thiols. In 2018, Mal and co-workers have reported that with varying reaction conditions like solvents, additives, temperature etc., any of these above mentioned three reactions could be achieved exclusively in excellent yields (scheme 3).[3] The described anti-Markovnikov TEC reaction is one of the most straightforward approaches to synthesizing several organosulfur compounds. Similarly, the aerial dioxygen activation reaction (to synthesize compound **8**) was performed under metal-free conditions in one pot.



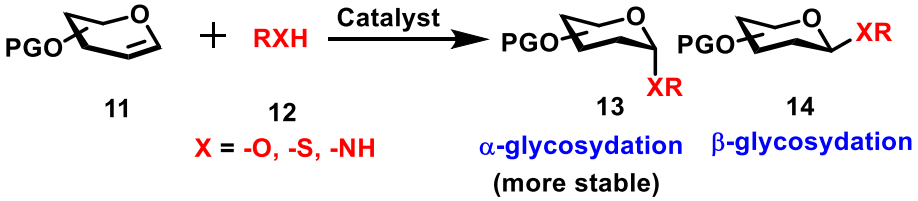
Scheme 3:*Thio-ene Click Reaction*

3.1.2 Thioglycosides:

A carbohydrate mono- or oligosaccharide is synthesized when a glycosyl donor reacts with any suitable glycosyl acceptor to form a glycosidic bond at the C1 or anomeric position of the donor, and this process is called glycosylation. When the acceptor is an aryl or alkyl thiol molecule (i.e., **X**= -**S**), this process is referred to as thio-glycosylation (scheme 4).

Thioglycosides (anomeric oxygen atom is replaced by sulfur atom) have been extensively used as glycosyl donors in glycosylation process e.g. anomeric phenyl/ tolyl/ ethyl thioglycosides are very frequently used donors in carbohydrate chemistry due to their high stability. Also, these

are useful building blocks for orthogonal glycosylation, as thioglycosides can be activated only under specific reaction conditions.



Scheme 4: *Glycosylation with Glycal Donor*

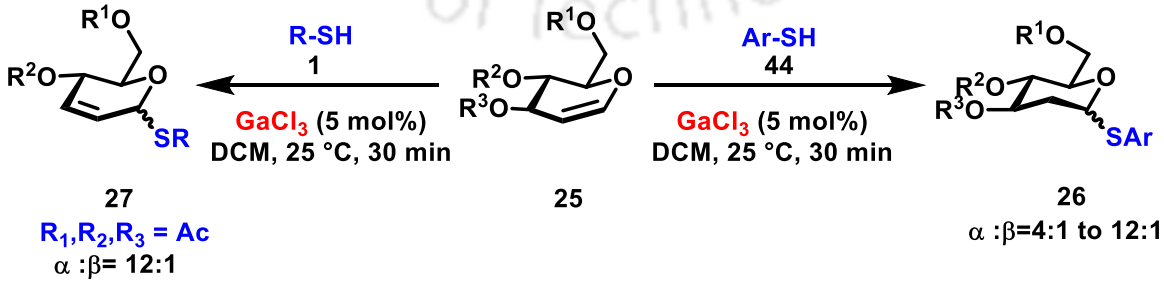
These molecules can serve as both glycosyl donor and acceptor in orthogonal glycosylation methods to synthesize polysaccharides.

There are limited studies in the field of thiolation on the olefinic carbon of glycal.

3.1.3 2-Deoxythioglycosides:

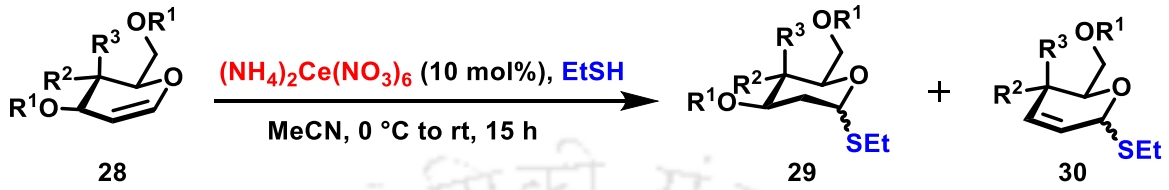
2-Deoxy and 2,6-dideoxysugars are an important class of carbohydrates and form a part of several biologically important natural products,[4] and the synthesis of these classes of compounds has received significant attention in recent times.[5] However, owing to the lack of any stereodirecting group at the C-2 position, the stereoselective synthesis of this class of compounds has been a challenging task. Despite the significance, 2-deoxyglycosides remain labile and are sensitive to enzymatic hydrolysis which hampers our understanding of the influence of these biomolecules. 2-Deoxythioglycosides (anomeric oxygen atom is replaced by sulfur atom), besides their utility as stable glycosyl donors, are a stable class of alternatives for the structure and function study of 2-deoxy *O*- linked glycosides as these compounds retain their biological activity and also are resistant towards enzymatic cleavage. Hence, these compounds form prime candidates as therapeutic agents as well. Despite the advantages and their significance, the synthesis of 2-deoxythioglycosides remains an underdeveloped area with only a few methods available for the synthesis of 2- deoxythioglycosides and are limited to the usage of simple thiol nucleophiles.[6,7]

Yadav and co-workers have reported $GaCl_3$-catalysed addition of aromatic thiols on glycals to synthesize 2-deoxy thioglycosides. They have observed the formation of Ferrier rearrangement product when aliphatic thiols are used as acceptors (Scheme 5).[6b]



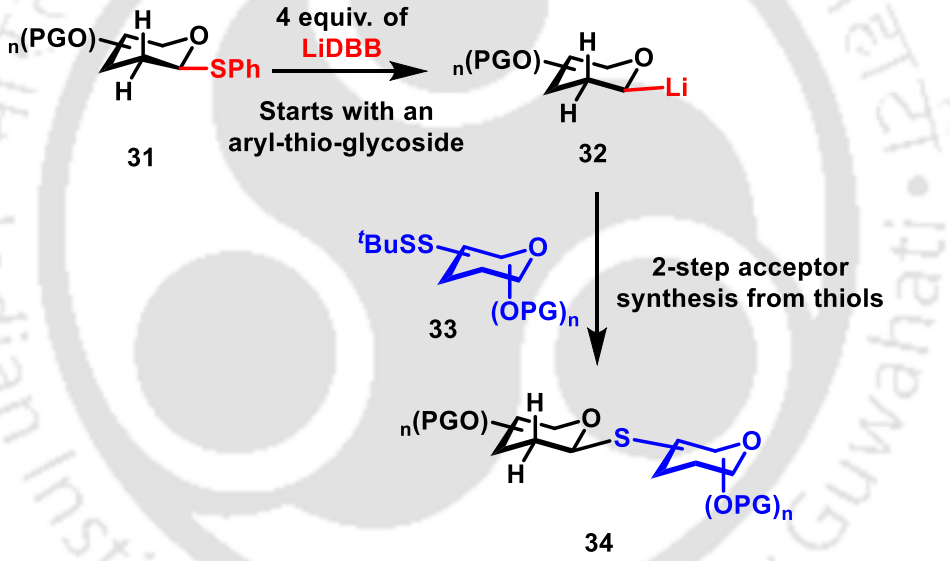
Scheme 5: *$GaCl_3$-Catalyzed Addition of Thiols to Glycals*

Jayaraman and co-workers developed a novel method to synthesize 2-deoxy-1-thioglycosides from glycals using ceric ammonium nitrate as a catalyst. They have proposed that the reaction proceeds *via* radical oxocarbenium ion formation and also predicted that the process is mediated by thiolate intermediates (Scheme 6).[7]



Scheme 6: *Ceric Ammonium Nitrate Mediated Synthesis of 2-Deoxy-1-Thioglycosides*

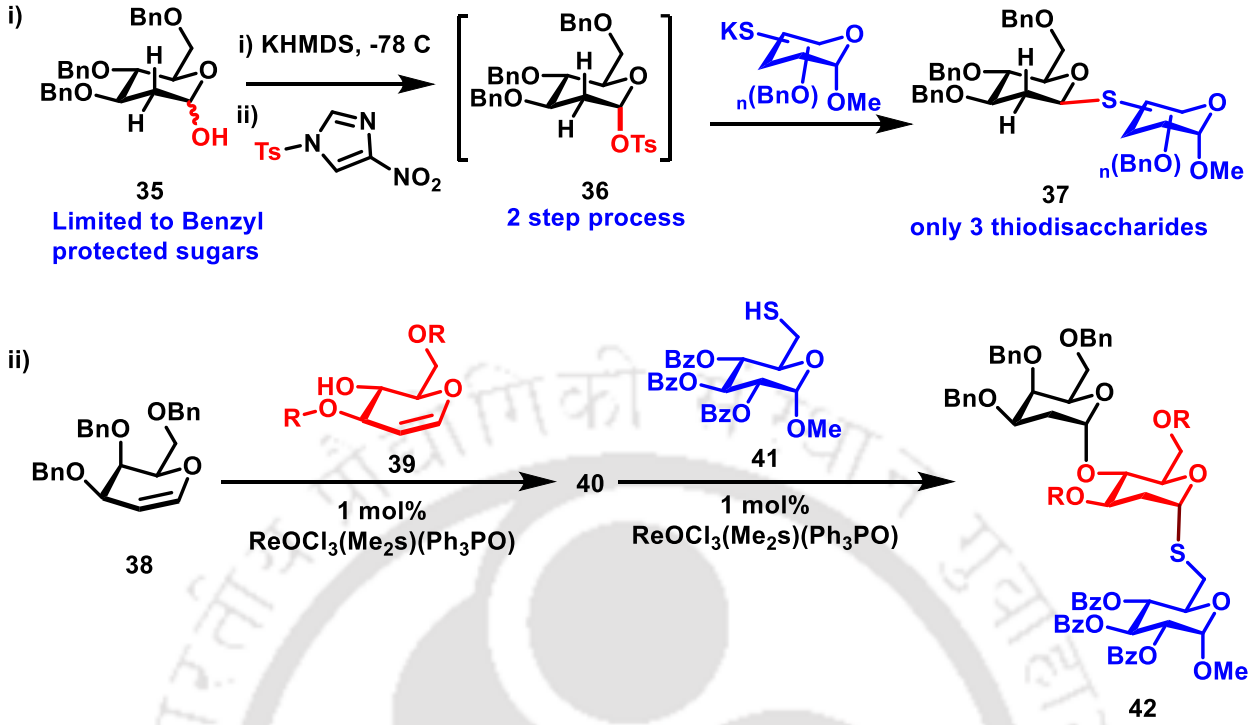
Zhu and co-workers have developed an exquisite procedure to synthesize both α and β thioglycosides in a stereoselective fashion, albeit in a multi-step sequence (Scheme 7).[8]



Scheme 7: *Stereoselective Synthesis of S-Linked 2-Deoxy Sugars*

Bennett and co-workers have shown the activation of 2-deoxy-sugar hemiacetals for glycosylation reaction using N-sulfonyl imidazoles *via* generation of glycosyl sulfonate intermediates. They have obtained β-specific glycosides under these reaction conditions (Scheme 8, i).[9a]

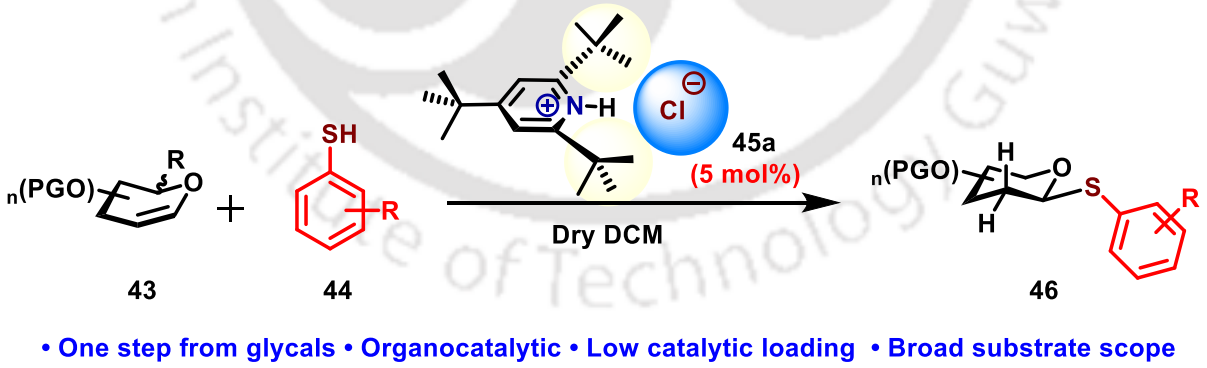
Toste and co-workers showcased the rhenium catalyzed synthesis of 2-deoxy-α-thioglycosides with only one example. However, it was later adopted by other groups proving the efficiency of the protocol.[9a] Bennett and co-workers also have employed their S_N2 displacement strategy for the synthesis of 2-deoxythiodisaccharides (Scheme 8, ii).[9b]



Scheme 8: *2-Deoxy Thio-disaccharide Synthesis*

3.2 This Work:

After successfully utilizing the bulky ion-pair catalysis in the synthesis of 2-deoxy *O*-glycosides in **chapter-II**,[10] herein we report the first organocatalytic synthesis of 2-deoxy-thioglycoside directly from glycals. Also, evidence has been found for the involvement of frustrated radical pair for the first time in Brønsted pair catalysis (scheme 9).



Scheme 9: *This Work*

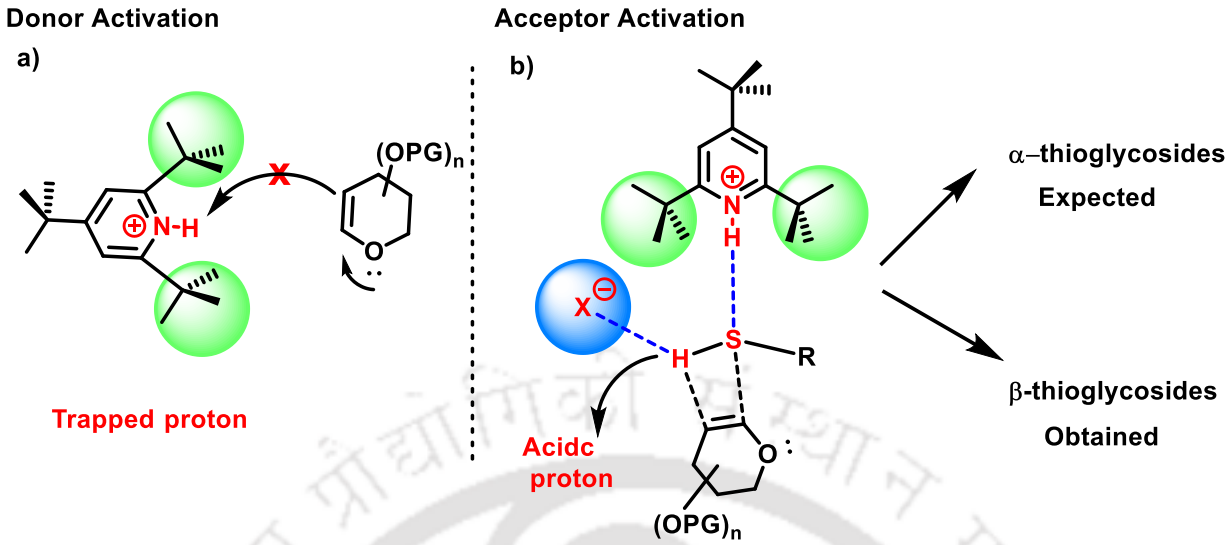
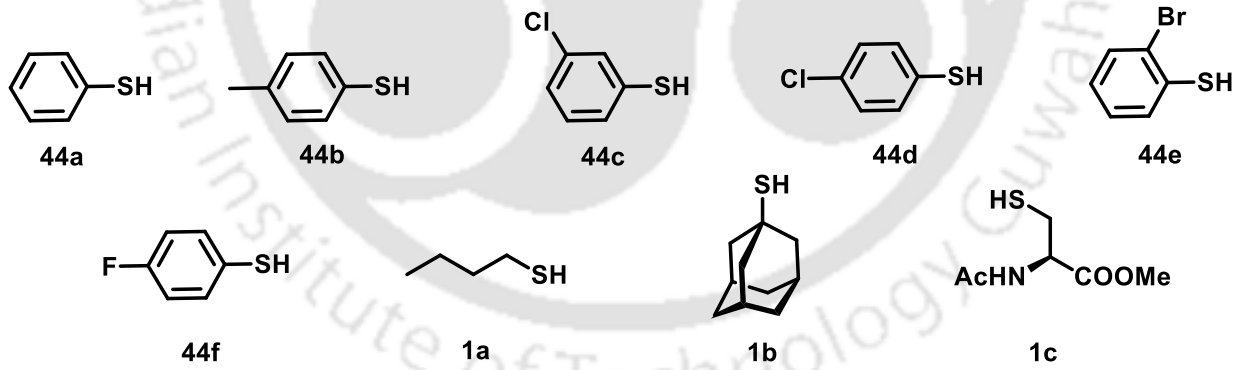


Figure 1: *Present Work*

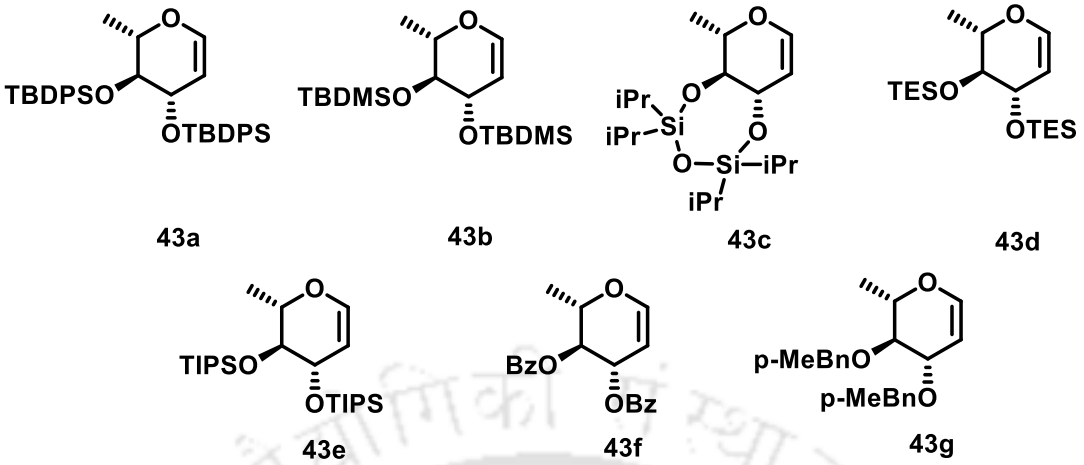
As depicted in Figure 1, we envisioned that the frustrated ion-pair interactions would help the ion-pair catalyst polarize the thiol, thus leading to the addition of thiol onto enol ethers under mild conditions.

3.3 Results and Discussion

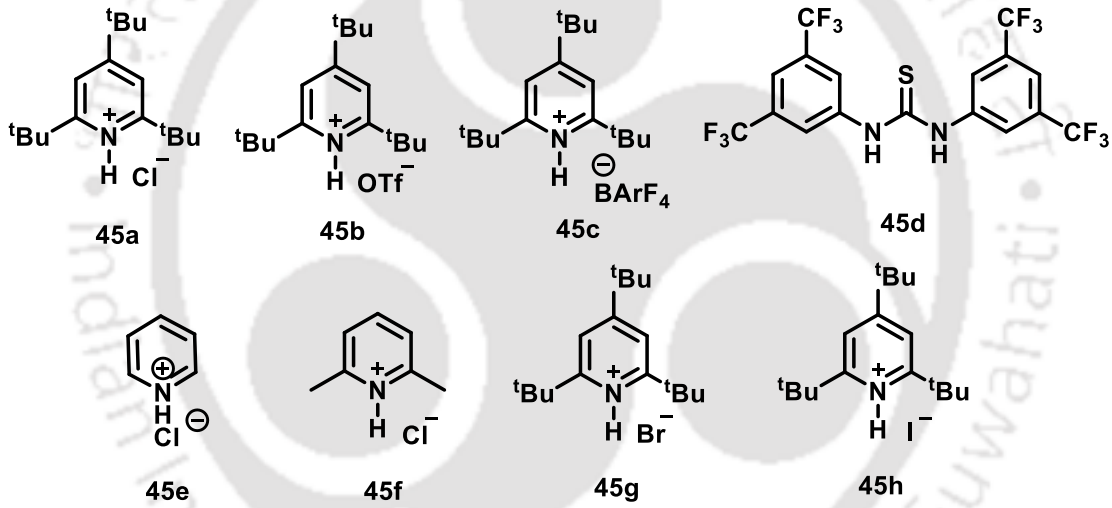
Thio-acceptors Used in this Method:



Glycals Used in this Method:



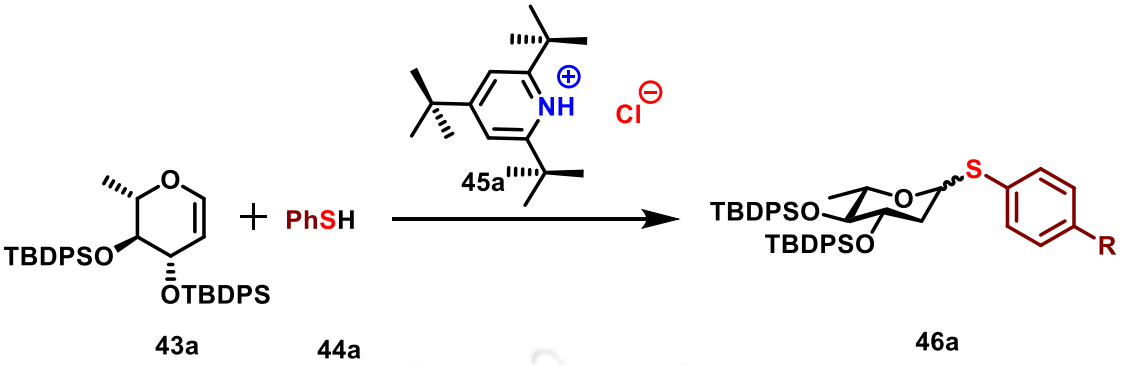
Catalysts Used in this Method:



3.3.1 Optimization Studies:

Rhamnal **1a** has been reacted with 1.2 equiv of thiophenol in the presence of 20 mol% of TTBPy·HCl catalyst (Table 1, entry 1). To our pleasant surprise, the reaction went to completion in just 30 mins giving rise to the expected 2-deoxythioglycoside product **4a** in 72% yield. We found that the reaction proceeds exceedingly well with 5 mol% of the catalyst giving rise to the product in 79% yield in 3 h (Table 1, entry 2), and the change in catalytic mol% did not affect the selectivity.

Table 1. Optimization Studies.



43a 44a 46a

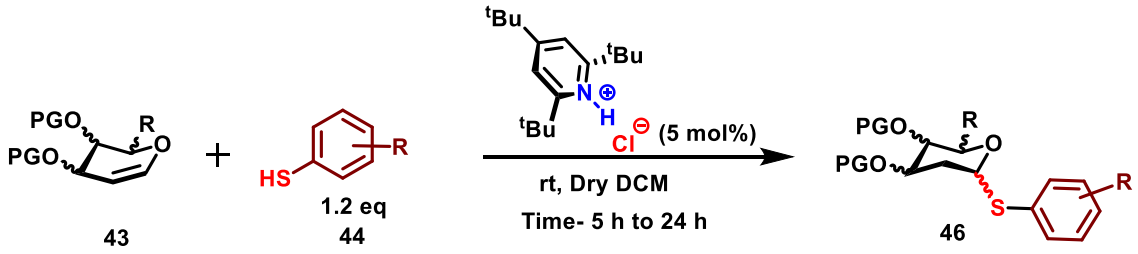
Entry	Acceptor	Cat. ([mol%])	Time	Product (α:β)
1	**44a**	20	30 min	**46a,** 72%, (1: 1.5)
2	**44a**	5	3 h	**46a**, 79%, (1: 1.5)

Reaction condition: 1.2 equiv of acceptor thiophenol **44a** was used in DCM at rt. Yield was determined using crude ^{1}H-NMR analysis. Anomeric selectivity was determined from ^{1}H-NMR spectra.

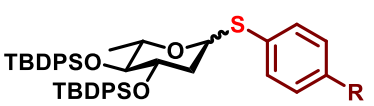
3.3.2 Scope of Derivatives:

With the optimized conditions in hand, the protocol has been tested with various substituted thiophenols with OTBDPS, OTBDMS, OTIPDS, OTES and OTIPS protected rhamnal derivatives where the products **46a-f** and **46j-p** are obtained in good yields (Table 2). Less reactive benzoyl rhamnal also gave thioglycoside product **46p** in 53% yield. However, in all the cases, the thioglycosides have been obtained in poor anomeric selectivity, albeit surprisingly more towards β-selectivity. Interestingly, the selectivity shifted to *α* when Galan's disiloxane-protected rhamnal donor **43c** was used.

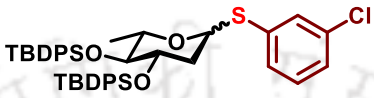
Table 2. Synthesis of 2,6-Di-deoxyarylthioglycosides.



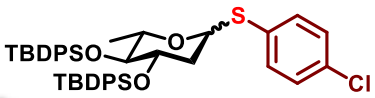
Aromatic thiols as acceptors



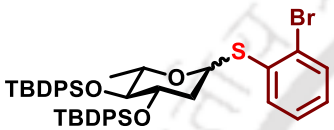
R= H, 46a, 79%, α: β= 1: 1.5
R= CH_3, 46b, 67%, α: β= 1: 1.3



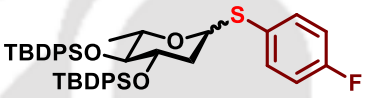
46c, 79%, α: β= 1: 1.6



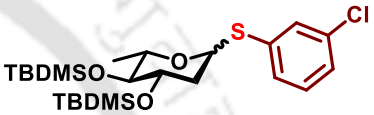
46d, 82%, α: β= 1: 1.5



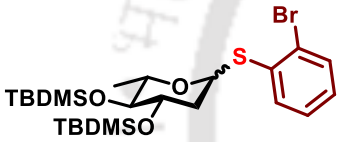
46e, 69%, α: β= 1: 1.1



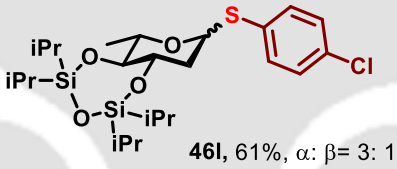
46f, 65%, α: β= 1: 1.5



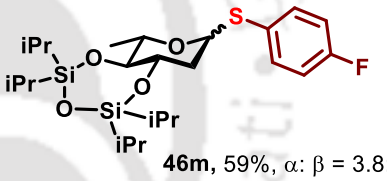
46j, 80%, α: β= 1: 2



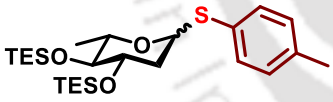
46k, 72%, α: β = 1: 1.4



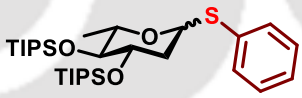
46l, 61%, α: β= 3: 1



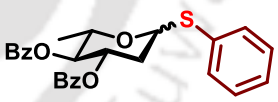
46m, 59%, α: β = 3.8: 1



46n, 65%, α: β= 1: 1.2



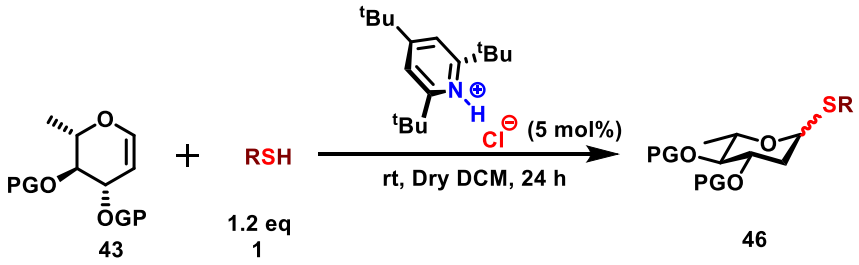
46o, 72%, α: β= 1: 1.5

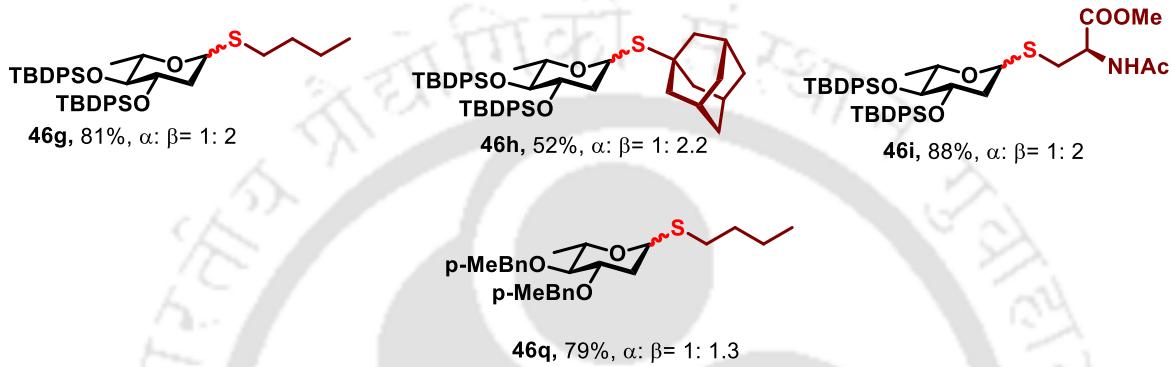


46p, 53%, α: β= 1: 2

The variously protected rhamnal derivatives with various alkyl thiol acceptors led to the 2,6-dideoxy-alkyl-thio-monosaccharides **46g-i** and **46q** in good yields with β-isomers as the major products (Table 3). The glycosylation method worked well with tertiary thiol like adamantane thiol **1b** too, giving the product **46h** in 79% yield in 4:1 selectivity favoring β (Table 3). Also, we were able to synthesize the glycosyl cysteine derivative **1c** in 88% yield and 2:1 (β:α) selectivity. However, the sterically highly bulky OTBDPS protected galactal failed to give any glycosylated product under the current bulky catalysis, which also signifies the steric bulk constraints and the limitation of the current protocol.

Table 3. Synthesis of 2,6-Di-deoxyalkylthioglycosides.

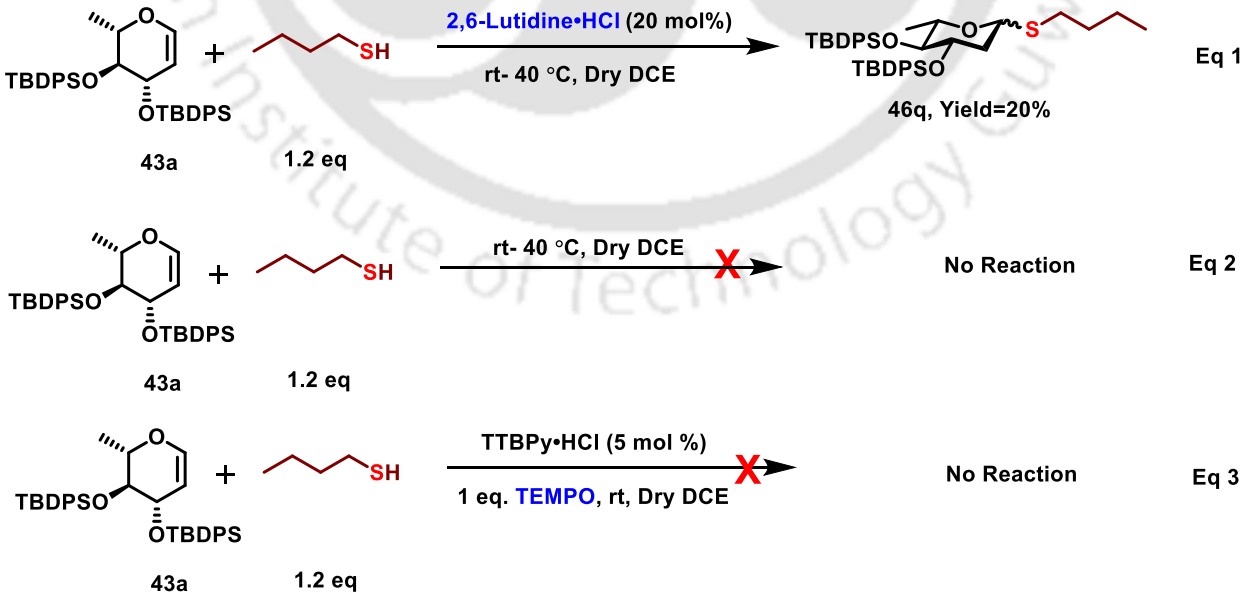


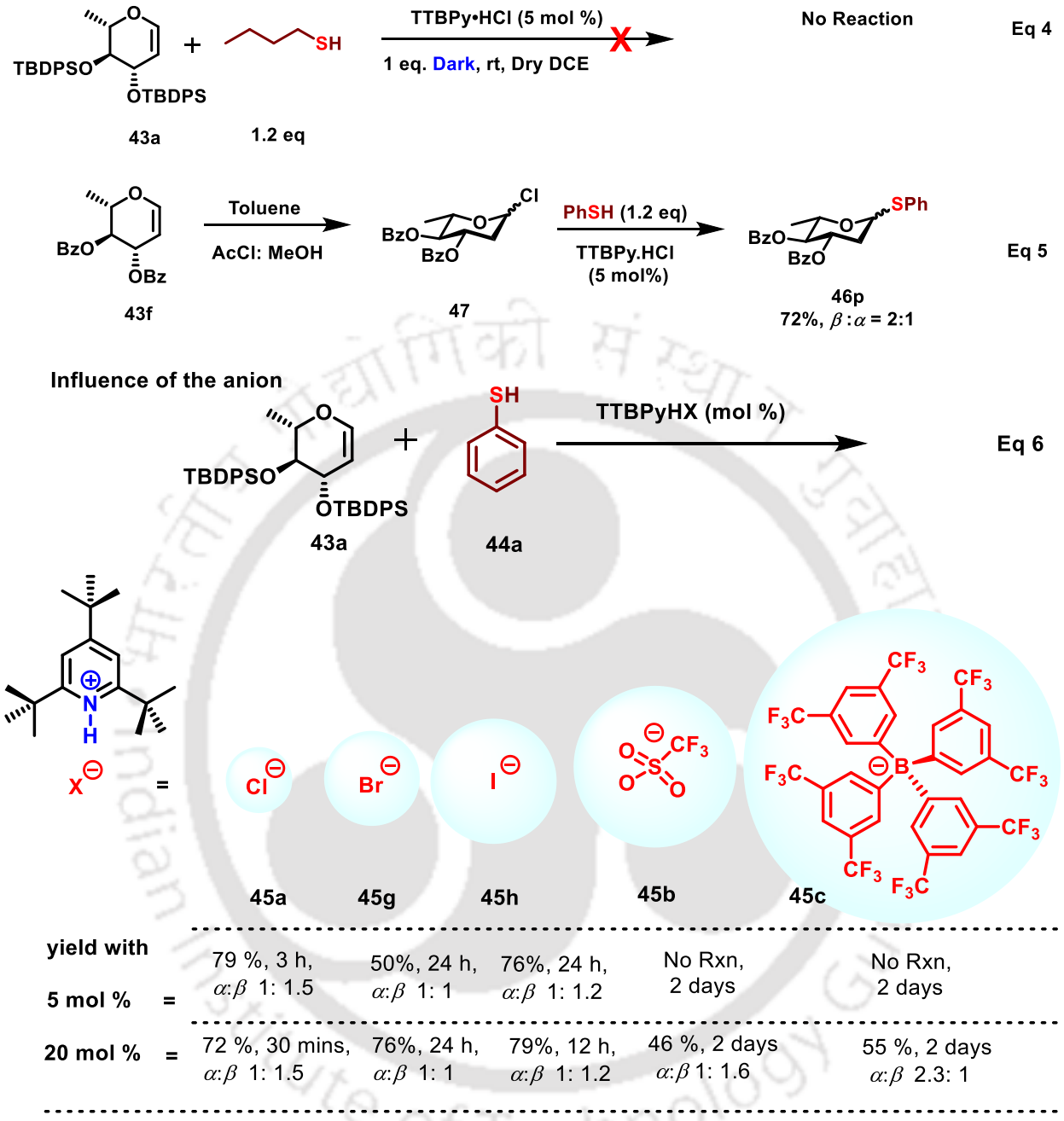


3.3.3 Control Experiments:

Several control experiments were performed to reveal the nature of the mechanism of the current unique transformation. As expected, the reaction without any catalyst did not lead to any product (Scheme 10, eq 2). The sterically less bulky lutidine·HCl led to only 20% of product formation after two days, revealing ortho *tert*-butyl groups' significance in the observed catalysis (Scheme 10, eq 1).

Scheme 10:





Scheme 10: *Control Experiments and Studies on the Influence of Anions*

3.3.4 Mechanistic Studies:

In order to understand the mode of activation of the reaction, NMR studies were performed where ^{1}H NMR spectra of butanethiol was recorded with varying concentrations of the organocatalyst. Interestingly, the signal for the non-exchangeable α-protons of the butanethiol, which in the absence of the catalyst appears as an apparent quartet at δ 2.52 ppm has

slowly converted into a triplet with increasing concentrations of the catalyst (Figure 2, a). Also, the signal for the S-H proton slowly disappears, suggesting a strong H-bonding interaction between the catalyst and the alkyl thiol (Figure 2, a). When a similar study was performed with the less sterically bulky lutidine·HCl, no such change was observed. Besides, the N-H proton, which appears at δ 14.54 ppm when the ratio of catalyst *vs* thiol is 1:5, has slowly moved upfield to δ 14.32 ppm when the ratio is increased to 1:1. Also, broadening has been observed in the signal H_B that corresponds to the ring protons of TTBPy (Figure 2, a). All these changes clearly demonstrate a very strong H-bonding network between the catalyst and the acceptor thiol. With the recent seminal studies on the photo-redox catalysis by the pyridinium salts,[11] and the understanding that frustration can lead to radical behavior,[12] we suspected the involvement of frustrated radical pair[13] intermediates under the present conditions where thiols are involved.

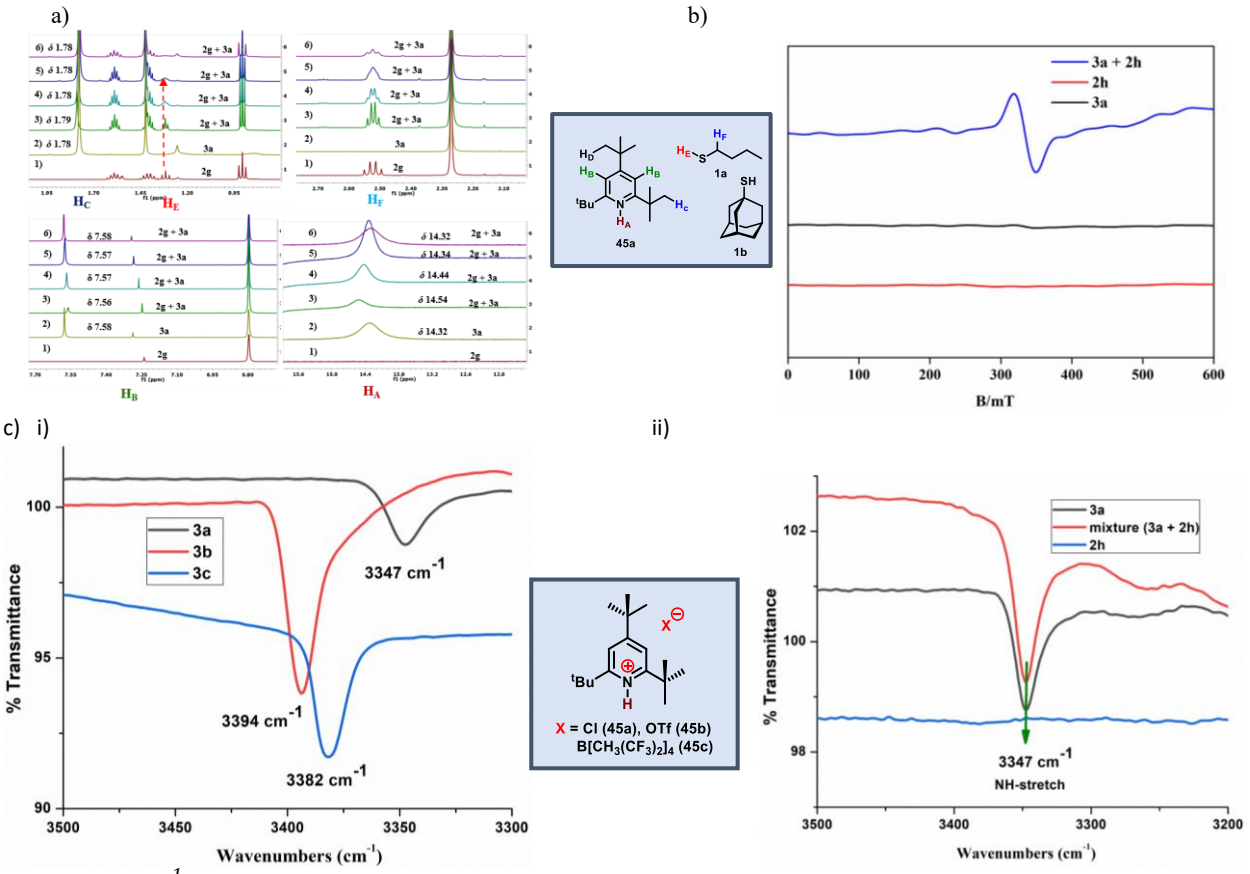


Figure 2: *a) ^{1}H NMR studies between **45a** and **1a** (1-butanethiol) in 0.6 ml solution of $CDCl_3$. b) EPR studies between **45a** and **1a** (adamantanethiol). c) i) The N-H IR stretching frequency in various TTBPy salts and ii) mixture of **45a** and **1a**.*

It is not surprising to assume that the bulky pyridinium $[TTBPyH]^+$ with three *tert*-butyl groups that can stabilize an α-radical can be easily reduced, under frustration by a thiol, resulting in the formation of a neutral pyridyl radical/sulfur radical pair (Figure 3, **III**). Intriguingly, the

ESR analysis of an equimolar mixture of TTBPy·HCl and adamantane thiol showed the spontaneous generation of a radical intermediate (Figure 2, b & Figure 3, **III**). Though the signal with a *g*-value of 2.02 can be attributed to the sulfur radical, the broad signal may also overlap with the carbon-centered radical as well. Also, the reaction did not proceed when performed in the presence of a radical trapping agent TEMPO (Scheme 10, eq 3). More intriguingly, less than 10% conversion was observed when the reaction was performed in the dark (Scheme 10, eq 4). These experiments suggest the possible involvement of a frustrated radical pair (FRP) species in the current transformation. In addition, IR studies are performed to understand the catalyst and the thiol interactions. Unlike other pyridines, the protonated $[TTBPyH]^+$ gives a sharp signal at 3347 cm^{-1} for the N- H stretch that indicates that the N-H proton does not involve in H-bonding (Figure 2, c-ii). Also, the N-H stretch is barely affected in the presence of adamantane thiol. This IR experiment, along with the ^1H NMR studies, points to an anion-directed activation. Experiments were conducted with TTBPy salts with bromide, iodide, triflate, and $BAr^F{}_4$ as anions to further assess the influence of anion on the catalysis (Scheme 10, eq 6). When rhamnal **1a** was treated with thiophenol in the presence of 5 mol% of various salts, it has been observed that the bromide salt gave the product in 50% yield after 24 h, whereas the same reaction with the chloride salt goes to completion in just 3 h (Scheme 10, eq 6). The iodide salt worked better than the bromide salt presumably due to the increased frustration due to the larger ionic size, however, the strongly coordinating chloride salt is still more reactive (Scheme 10, eq 6). When the pre-synthesized glycosyl chloride from the corresponding benzoate rhamnal was subjected to the reaction conditions, it formed the product **46p** in similar selectivities (β:α 2:1), further strengthening glycosyl chlorides as possible intermediates under the current protocol (Scheme 10, eq 5). The triflate and the $BAr^F{}_4$ salts fail to catalyze the reaction at 5 mol% catalytic loading (Scheme 10, eq 6). However, with an increase in catalytic loading to 20 mol%, these triflate and $BAr^F{}_4$ salts led to product conversion of 46% and 55% after two days. These experiments suggest the significance of a small coordinating anion like chloride for the observed catalysis where the frustration is likely higher. However, it can also be argued that the H-bonding ability of cationic $[TTBPyH]^+$ is further diminished in the presence of the bulky anions. The hypsochromic shift of the N-H stretching frequency in the IR spectroscopy when the coordinating chloride ion is replaced by triflate and $BAr^F{}_4$ anions (Figure 2, c-i) suggests the strengthening and thus shortening of the N-H bond that can make it inaccessible for any possible H-bonding interaction with thiols.

3.4 Proposed Mechanism:

Based on all the above observations and studies (^1H NMR, ESR, and IR), we propose the mechanism as depicted in Figure 5. The acceptor is activated by the frustrated ion-pair, either by S-H...Cl^- interactions or via N-H^+.....S-H...Cl^- interactions, forming an activated "encounter complex." The increased acidity of the thiol proton in the activated encounter complex can protonate glycals generating the oxocarbenium ion that may lead to the product formation via glycosyl chloride (Figure 3, double-electron pathway). However, a single-electron pathway cannot be ruled out based on the ESR experiments. The activated encounter complex (Figure 3, **II**) can undergo single electron transfer (SET from the thiol to the pyridinium giving rise to a sulfur radical cation (Figure 3, **III**) which upon spontaneous evolution of HCl may form a frustrated radical pair (Figure 3, **IV**). The thus released HCl reacts with the glycal leading to the

formation of the glycosyl chloride or the oxocarbenium ion intermediate. The frustrated neutral radical pair that can exist in equilibrium with its ion-pair (Figure 3, **V**) may react with the glycosyl chloride giving rise to the observed product, thus regenerating the catalyst TTBPy·HCl (Figure 3, **I**). Thiols being soft nucleophiles, react on the glycosyl chlorides in an S_N2 fashion than on oxocarbenium ions, providing the β-thioglycosides. The aromatic thiols react directly with the oxocarbenium ions, presumably via cation pi-interactions leading to a diminished anomeric selectivity.

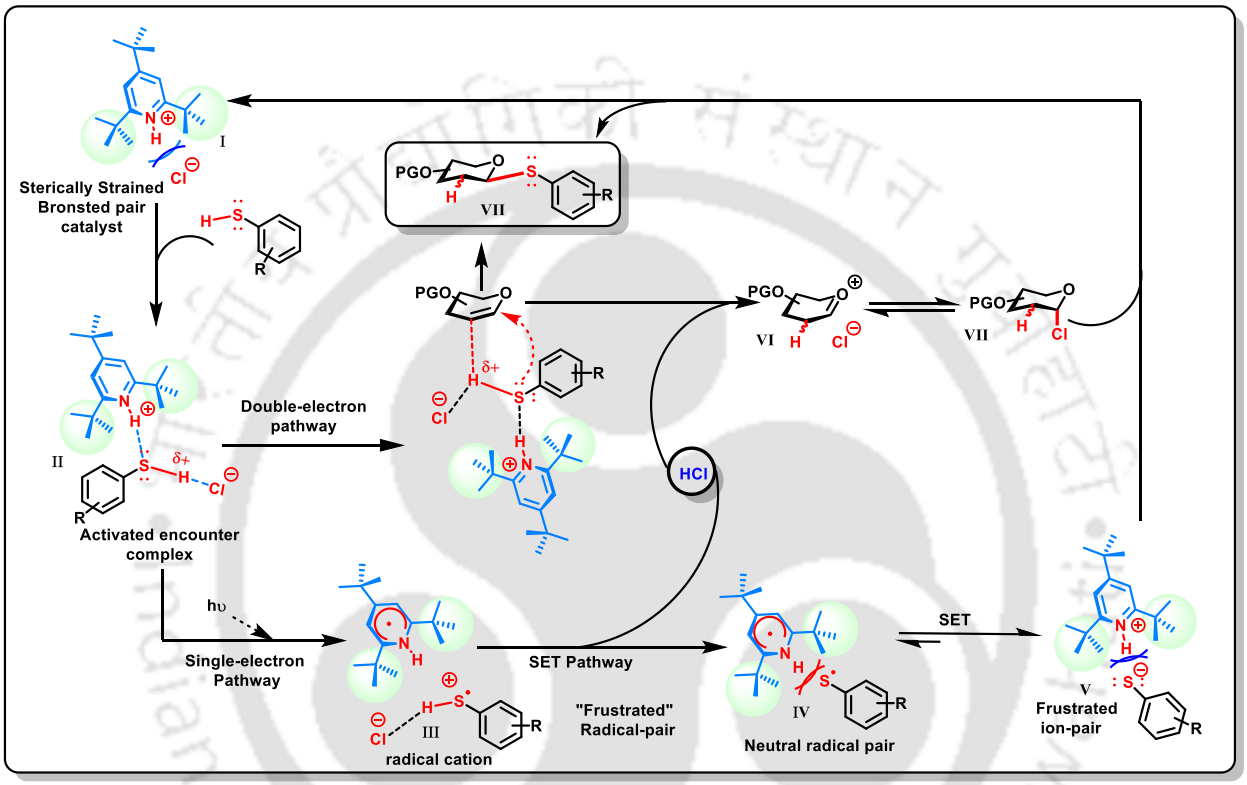


Figure 3: *Proposed Mechanism*

3.5 Conclusion

In conclusion, we have successfully showcased the utility of the poor electrostatic interactions arising due to steric strain in the ion-pair involving the sterically bulky 2,4,6-tri-*tert*-butylpyridinium cation in activating sugar thiols, thus synthesizing the biologically important class of compounds, 2-deoxy-thioglycosides, the synthesis of which otherwise require Rhenium catalysis or multi-step synthesis. Also, this organocatalytic protocol allows us to access β-thioglycosides, unlike the general glycal activation methods. Spectroscopic studies (^{1}H NMR, IR) reveal the reaction is driven by acceptor (thiol) activation. ESR studies provided evidence for the potential involvement of the intriguing frustrated radical pair intermediates in the current protocol. The influence of coordinating versus weakly coordinating anions on the observed reactivity and selectivity has also been investigated, reflecting the necessity of coordinating anion like chloride. The concept of increased reactivity imbued upon the anion when bound with

the sterically bulky pyridinium resulting from the frustrated interactions has a huge potential in organic synthesis.

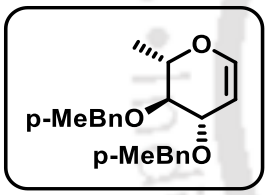
3.6 Experimental Section:

General Information and Analysis:

The general information and analysis section for chapter-III is same as mentioned in chapter-II. The additional details are given below.

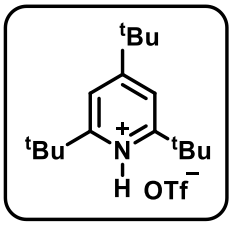
^{1}H- and ^{13}C{^{1}H}- NMR were recorded on a Bruker 600MHz, 500 MHz and 400MHz spectrometer using $CDCl_3$ as solvent. The α and β stereochemistry of the separated products has been established using NOE technique for some representative examples. Further, analyzing and matching of the chemical shifts and couplings constants analysis of the rest of the compounds with the representative compounds has been undertaken. In addition, some of the known compounds stereochemistry has also been matched with the literature reports as well. ESR Spectrum of sample solution was recorded in JEOL JES-FA200 Electron Spin Resonance Spectrometer. 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.

Synthesis of 3,4-di-O-para-methylbenzyl-L-rhamnal (43g):



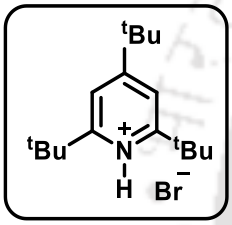
L-Rhamnal (500 mg, 3.84 mmol, 1.0 equiv) was dissolved in 20 ml DMF. Then, to it NaH (461 mg, 19.2 mmol, 3 equiv considering 60% dispersion in mineral oil) was added slowly. Then, 4-methyl benzyl bromide (2.2 g, 11.5 mmol, 3 equiv) was added portion wise slowly and it was stirred for 24 h. Then, it was quenched with MeOH (5 ml). Now, the solvent was concentrated and extracted with DCM (3x30 ml). The organic phase was washed with brine (100 ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Then, it was purified by column chromatography in ethyl acetate/hexane solvent system to afford the white solid **43g**. R_f- 0.5 in 10% EA in hexane, amount- 1.0 g, yield- 77%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 – 7.24 (m, 2H), 7.22 (d, *J* = 7.8 Hz, 2H), 7.15 (d, *J* = 7.7 Hz, 4H), 6.34 (d, *J* = 6.1 Hz, 1H), 4.85 – 4.83 (m, 2H), 4.65 – 4.59 (m, 2H), 4.54 (d, *J* = 11.4 Hz, 1H), 4.50 (d, *J* = 5.6 Hz, 1H), 4.18 (d, *J* = 6.4 Hz, 1H), 3.93 (dq, *J* = 12.9, 6.4 Hz, 1H), 3.47 – 3.44 (m, 1H), 2.34 (s, 6H), 1.36 (d, *J* = 6.4 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 144.8, 137.6, 137.5, 137.4, 135.5, 135.4, 135.4, 129.2, 129.2, 128.3, 128.0, 100.4, 79.4, 76.4, 74.1, 74.1, 71.9, 70.6, 21.3, 17.6. HRMS (ESI) m/z: $[M + NH_4]^+$ calcd for $C_{22}H_{30}NO_3$ 356.2226; found 356.2218. $[\alpha]_D^{22}$ = +5.17 (*c* 0.3, $CHCl_3$).

Synthesis of 2,4,6-tri-*tert*-butylpyridinium trifluoromethanesulfonate salt (45b):



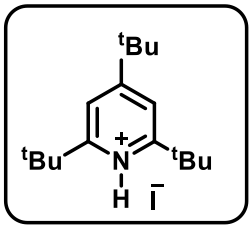
2,4,6-tri-*tert*-butylpyridine (100 mg, 0.404 mmol, 1.0 equiv) was dissolved in 2 ml of diethyl ether and triflic acid (60 mg, 36 µL, 0.404 mmol, 1.0 equiv) was added to it dropwise keeping it in ice bath. After that, it was stirred at 0 °C for 1 h and immediately a white precipitate of **3f** was observed. Then, the solution was allowed to settle down for few min and after decant the solution, the solid part was then concentrated under reduced pressure and washed with ether to get a white solid **45b** in quantitative yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.03 (s, 1H), 7.64 (s, 2H), 1.59 (s, 18H), 1.43 (s, 9H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 173.2, 164.3, 118.5, 37.1, 37.1, 30.2, 29.1. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{31}N$ 249.2451; found 249.2444.

Synthesis of 2,4,6-tri-*tert*-butylpyridinium hydrobromide salt (45g):



2 ml of acetyl bromide was added dropwise to 2 ml of methanol in ice bath. After few min, ether (1 ml) solution of 2,4,6-tri-*tert*-butylpyridine (500 mg, 2.020 mmol) was added dropwise to it which readily resulted in a turbid solution and the reaction mixture was stirred at 0 °C for 1 h. The solution was then concentrated under reduced pressure to get a white solid. The solid was washed with ether (5x5 ml) to afford **45g** in quantitative yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 13.15 (s, 1H), 7.60 (s, 2H), 1.81 (s, 18H), 1.45 (s, 9H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 172.2, 165.4, 118.5, 37.7, 36.9, 30.7, 30.6. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{31}N$ 249.2451; found 249.2449.

Synthesis of 2,4,6-tri-*tert*-butylpyridinium hydroiodide salt (45h):



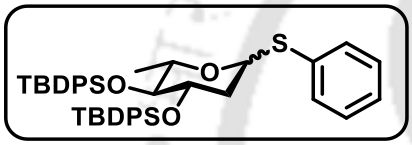
2,4,6-tri-*tert*-butylpyridine (100 mg, 0.404 mmol, 1.0 equiv) was dissolved in 2 ml of toluene and 57% w/w aq. solution of hydriodic acid (0.404 mmol, 1.0 equiv) was added to it dropwise keeping it in ice bath. After that, it was stirred at 0 °C for 1 h and pale yellow colored solution of **45h** was observed. Then, the solution was concentrated under reduced pressure, co-

evaporated with toluene and washed with ether to get a brown solid **45h** in quantitative yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.37 (s, 1H), 7.71 (d, *J* = 1.4 Hz, 2H), 1.73 (s, 18H), 1.47 (s, 9H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 173.0, 163.3, 118.9, 37.2, 37.0, 30.2, 29.8. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{30}N$ 248.2378; found 248.2368.

General Method to Synthesize Thio-glycosides from Glycals:

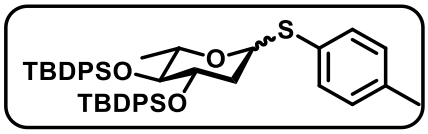
Glycal (0.082- 0.148 mmol, 1.0 equiv) and thio glycosyl acceptor (0.098- 0.178 mmol, 1.2 equiv) was taken in a round bottomed flask (10 mL). The flask was then filled with dry DCM and catalyst TTBPy·HCl (5 mol%) was added to it. The mixtures were stirred in the sealed flask until the reaction was determined to be complete by either TLC or NMR analysis of the crude material. The reaction mixture was quenched by water (20 ml for 0.082 mmol) and it was extracted with DCM (3x15 ml for 0.082 mmol), dried over Na_2SO_4 and concentrated in vacuo and purified by silica gel column chromatography (Merck 60-120 mesh, 7 gm) followed by HPLC purification (using HPLC-grade acetonitrile solvent, flow rate- 5 ml/min).

Synthesis of Phenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexopyranoside (46a):



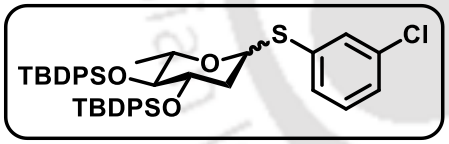
According to general method, a solution of glycosyl donor 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **43a** (50 mg, 0.082 mmol, 1.0 equiv) and glycosyl acceptor thiophenol **44a** (11 mg, 10 µL, 0.098 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (1.2 mg, 0.0041 mmol, 5 mol%) and stirred for 4 h to get the product **46a** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 47 mg, yield- 79%. Re-purification was done using HPLC (Hypersil Gold C18, water/acetonitrile = 0/100, flow rate = 5.0 mL/min, I = 214 nm) tR = 9 min. Selectivity α: β=1:1.5. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 – 7.53 (m, 15.5H), 7.49 – 7.47 (m, 2H), 7.44 (d, *J* = 6.8 Hz, 2H), 7.42 – 7.18 (m, 42H), 5.47 (dd, *J* = 11.2, 2.8 Hz, 1H), 5.00 (dd, *J* = 9.4, 4.2 Hz, 1.5H), 4.15 (q, *J* = 5.5 Hz, 1.5H), 4.04 – 3.98 (m, 2H), 3.68 – 3.65 (m, 3H), 3.50 (bt, 1H), 2.12 (ddd, *J* = 19.0, 11.9, 3.7 Hz, 2.5H), 1.77 – 1.72 (m, 1.5H), 1.69 (dt, *J* = 13.5, 2.6 Hz, 1H), 1.23 (d, *J* = 7.2 Hz, 3H), 1.10 (d, *J* = 6.3 Hz, 4.4H), 0.96 (s, 13H), 0.95 (s, 22H), 0.91 (s, 9H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 136.0, 135.9, 135.9, 135.9, 135.8, 135.8, 135.7, 134.5, 134.4, 134.1, 134.0, 133.8, 133.7, 133.5, 133.4, 133.3, 131.5, 130.5, 129.9, 129.8, 129.8, 129.8, 129.7, 129.7, 129.7, 128.9, 128.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.0, 126.7, 80.1, 78.1, 75.8, 75.4, 75.2, 72.6, 72.4, 71.7, 37.4, 34.0, 27.2, 27.1, 27.1, 26.9, 20.5, 19.5, 19.3, 19.2, 19.2, 17.1. HRMS (ESI) m/z: $[M + NH_4]^+$ calcd for $C_{44}H_{52}O_3Si_2SNH_4$ 734.3519; found 734.3521. $[\alpha]_D^{22}$ = +11.2 (*c* 0.09, $CHCl_3$).

Synthesis of Tolyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexopyranoside (46b):



According to general method, a solution of glycosyl donor 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **43a** (50 mg, 0.082 mmol, 1.0 equiv) and glycosyl acceptor 4-methylbenzenethiol **44b** (12 mg, 0.098 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (1.2 mg, 0.0041 mmol, 5 mol%) and stirred for 4 h to get the product **46b** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 40 mg, yield- 67%. Re-purification was done using HPLC (Hypersil Gold C18, water/acetonitrile = 0/100, flow rate = 5.0 mL/min, I = 214 nm) tR = 10 min. Selectivity α: β=1:1.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.09 (m, 51.3H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.92 (d, *J* = 8.0 Hz, 2.5H), 5.29 (dd, *J* = 11.2, 2.8 Hz, 1H), 4.78 (dd, *J* = 9.6, 4.0 Hz, 1.3H), 4.03 (q, *J* = 5.7 Hz, 1.3H), 3.88 (dd, *J* = 15.6, 4.3 Hz, 2H), 3.51 (tt, *J* = 11.0, 5.5 Hz, 2.6H), 3.37 (s, 1H), 2.20 (merged, 6.6H), 1.97 (tdd, *J* = 11.4, 7.1, 4.0 Hz, 2.3H), 1.63 – 1.55 (m, 2.3H), 1.11 (d, *J* = 7.1 Hz, 3H), 0.98 (d, *J* = 6.4 Hz, 4H), 0.85 – 0.83 (m, 30H), 0.79 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.2, 137.0, 136.0, 135.9, 135.9, 135.9, 135.8, 135.8, 134.5, 134.1, 134.1, 133.8, 133.8, 133.5, 133.5, 133.4, 132.4, 131.5, 131.5, 130.4, 129.9, 129.8, 129.8, 129.8, 129.7, 129.7, 129.6, 129.6, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7, 80.6, 78.1, 77.4, 76.1, 75.6, 75.2, 73.0, 72.4, 71.8, 37.6, 34.0, 27.2, 27.1, 27.1, 26.9, 21.2, 21.2, 20.5, 19.5, 19.2, 19.2, 17.1. HRMS (ESI) m/z: $[M + NH_4]^+$ calcd for $C_{45}H_{54}O_3Si_2SNH_4$ 748.3676; found 748.3683. $[\alpha]_D^{22}$ = +12.1 (*c* 0.08, $CHCl_3$).

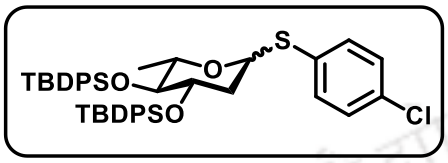
Synthesis of 3-Chlorophenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexopyranoside (46c):



According to general method, a solution of glycosyl donor 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **43a** (50 mg, 0.082 mmol, 1.0 equiv) and glycosyl acceptor 3-chlorobenzenethiol **44c** (14 mg, 0.098 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (1.2 mg, 0.0041 mmol, 5 mol%) and stirred for 2 h to get the product **46c** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 49 mg, yield- 79%. Re-purification was done using HPLC (Hypersil Gold C18, water/acetonitrile = 0/100, flow rate = 5.0 mL/min, I = 214 nm) tR = 10 min. Selectivity α: β=1:1.6. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60 – 7.15 (m, 77H), 5.48 (dd, *J* = 11.2, 2.8 Hz, 1H), 5.10 (dd, *J* = 8.6, 4.5 Hz, 1.6H), 4.16 (q, *J* = 5.2 Hz, 1.6H), 4.04 (d, *J* = 2.5 Hz, 1H), 4.00 (dd, *J* = 13.3, 6.3 Hz, 1H), 3.70 (dd, *J* = 6.7, 3.7 Hz, 1.7H), 3.65 – 3.64 (m, 1.7H), 3.53 (bt, 1H), 2.18 (dt, *J* = 13.7, 4.9 Hz, 2H), 2.10 (ddd, *J* = 13.6, 11.5, 2.5 Hz, 1H), 1.75 (ddd, *J* = 13.8, 8.6, 5.4 Hz, 2H), 1.69 (d, *J* = 13.5 Hz, 1H), 1.25 (d, *J* = 7.2 Hz, 3H), 1.14 (d, *J* = 6.7 Hz, 5H), 0.96 (d, *J* = 5.2 Hz, 37H), 0.93 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 138.0, 136.8, 135.9, 135.8, 135.7, 135.7, 135.7, 134.3, 134.0, 133.8, 133.7, 133.6, 133.4, 133.3, 133.3, 133.1, 130.5, 129.8, 129.7,

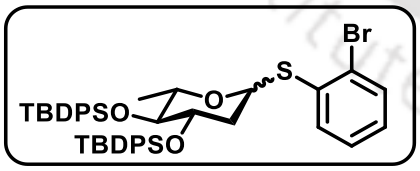
129.7, 129.7, 129.6, 128.9, 128.1, 127.7, 127.6, 127.6, 127.6, 126.8, 126.6, 79.7, 77.8, 75.3, 75.1, 75.0, 72.4, 71.9, 71.5, 36.6, 33.7, 27.0, 27.0, 26.9, 26.8, 20.3, 19.3, 19.1, 19.1, 19.1, 17.0. HRMS (ESI) m/z: $[M + NH_4]^+$ calcd for $C_{44}H_{51}O_3Si_2SClNH_4$ 768.3130; found 768.3134. $[\alpha]_D^{22}$= +14.5 (*c* 0.08, $CHCl_3$).

Synthesis of 4-Chlorophenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexopyranoside (46d):



According to general method, a solution of glycosyl donor 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **43a** (50 mg, 0.082 mmol, 1.0 equiv) and glycosyl acceptor 4-chlorothiophenol **44d** (14 mg, 0.098 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (1.2 mg, 0.0041 mmol, 5 mol%) and stirred for 2 h to get the product **46d** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 51 mg, yield- 82%. Re-purification was done using HPLC (Hypersil Gold C18, water/acetonitrile = 0/100, flow rate = 5.0 mL/min, I = 214 nm) tR = 10 min. Selectivity α: β=1:1.6. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.17 (m, 64H), 5.41 (dd, *J* = 11.2, 2.8 Hz, 1H), 4.98 (dd, *J* = 9.0, 4.4 Hz, 1.6H), 4.15 (q, *J* = 5.3 Hz, 1.6H), 4.02 – 3.96 (m, 2H), 3.69 – 3.62 (m, 3H), 3.51 (t, *J* = 2.0 Hz, 1H), 2.17 – 2.04 (m, 2.7H), 1.74 – 1.63 (m, 2.7H), 1.22 (d, *J* = 7.1 Hz, 3H), 1.11 (d, *J* = 6.4 Hz, 5H), 0.96 – 0.94 (m, 36H), 0.91 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 136.0, 135.9, 135.9, 135.9, 135.8, 135.8, 134.3, 134.0, 133.9, 133.9, 133.7, 133.6, 133.4, 133.4, 133.2, 133.2, 133.1, 132.9, 132.8, 132.2, 129.9, 129.9, 129.8, 129.8, 129.8, 129.7, 128.9, 127.8, 127.8, 127.7, 127.7, 127.7, 80.0, 78.1, 75.5, 75.4, 75.3, 72.3, 72.3, 71.6, 37.0, 33.9, 27.2, 27.1, 27.0, 26.9, 20.4, 19.5, 19.2, 19.2, 19.2, 17.1. HRMS (ESI) m/z: $[M + NH_4]^+$ calcd for $C_{44}H_{51}O_3Si_2SClNH_4$ 768.3130; found 768.3165. $[\alpha]_D^{22}$= +18.2 (*c* 0.08, $CHCl_3$).

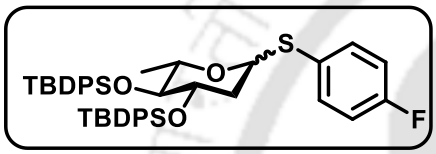
Synthesis of 2-Bromophenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexopyranoside (46e):



According to general method, a solution of glycosyl donor 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **43a** (50 mg, 0.082 mmol, 1.0 equiv) and glycosyl acceptor 2-bromothiophenol **44e** (19 mg, 0.098 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (1.2 mg, 0.0041 mmol, 5 mol%) and stirred for 1.5 h to get the product **46e** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 45 mg, yield- 69%. Re-purification was done using HPLC (Hypersil Gold C18, water/acetonitrile = 0/100, flow rate = 5.0 mL/min, I = 214 nm) tR = 10 min. Selectivity α:

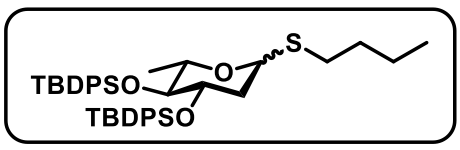
β=1:1.2. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.62 (d, *J* = 6.8 Hz, 2.2H), 7.57 – 7.22 (m, 47H), 7.05 – 6.99 (m, 2.2H), 5.60 (dd, *J* = 11.1, 3.2 Hz, 1H), 5.26 (dd, *J* = 8.0, 4.9 Hz, 1.2H), 4.17 (q, *J* = 4.7 Hz, 1.2H), 4.07 (d, *J* = 2.6 Hz, 1H), 4.00 – 3.96 (m, 1H), 3.77 – 3.75 (m, 1.2H), 3.65 (dd, *J* = 4.4, 3.2 Hz, 1.2H), 3.56 (bt, 1H), 2.31 (dt, *J* = 13.8, 5.0 Hz, 1H), 2.21 – 2.16 (m, 1.2H), 1.91 – 1.87 (m, 1.2H), 1.79 (dt, *J* = 13.4, 3.0 Hz, 1H), 1.23 (d, *J* = 7.1 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3.4H), 0.99 (s, 9H), 0.95 (s, 18H), 0.93 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 138.4, 137.2, 136.1, 135.9, 135.9, 135.9, 135.8, 135.8, 133.9, 133.9, 133.7, 133.7, 133.5, 133.5, 133.3, 132.9, 132.8, 130.1, 130.0, 129.9, 129.9, 129.8, 129.7, 129.1, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 127.3, 126.9, 123.8, 123.2, 78.4, 78.1, 75.1, 74.8, 74.4, 73.1, 71.6, 71.3, 35.8, 33.3, 27.2, 27.1, 27.0, 20.4, 19.4, 19.3, 19.3, 19.2, 17.4. HRMS (ESI) m/z: $[M + NH_4]^+$ calcd for $C_{44}H_{51}O_3Si_2SBrNH_4$ 812.2625; found 812.2627. $[\alpha]_D^{22}$= +22.6 (*c* 0.08, $CHCl_3$).

Synthesis of 4-Fluorophenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexopyranoside (46f):



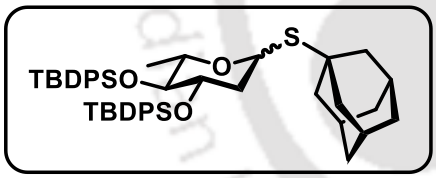
According to general method, a solution of glycosyl donor 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **43a** (50 mg, 0.082 mmol, 1.0 equiv) and glycosyl acceptor 4-fluorothiophenol **44f** (13 mg, 11 µL, 0.098 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (1.2 mg, 0.0041 mmol, 5 mol%) and stirred for 2.5 h to get the product **46f** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 39 mg, yield- 65%. Re-purification was done using HPLC (Hypersil Gold C18, water/acetonitrile = 0/100, flow rate = 5.0 mL/min, I = 214 nm) tR = 8.5 min. Selectivity α: β=1:1.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 – 7.20 (m, 57H), 6.97 (t, *J* = 8.7 Hz, 1H), 6.91 (t, *J* = 8.7 Hz, 2H), 5.34 (dd, *J* = 11.1, 2.9 Hz, 3H), 4.89 (dd, *J* = 9.2, 4.2 Hz, 1.5H), 4.14 (q, *J* = 5.4 Hz, 1.5H), 4.01 (d, *J* = 2.5 Hz, 1H), 3.97 (dd, *J* = 14.3, 7.2 Hz, 1H), 3.64 – 3.60 (m, 3H), 3.50 (s, 1H), 2.10 (dt, *J* = 13.8, 4.8 Hz, 1.5H), 2.06 – 2.00 (m, 1H), 1.67 (ddd, *J* = 12.5, 9.2, 4.4 Hz, 2.5H), 1.20 (d, *J* = 7.1 Hz, 3H), 1.10 (d, *J* = 6.3 Hz, 4.5H), 0.95 (s, 13H), 0.94 (s, 9H), 0.93 (s, 13H), 0.90 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 136.0, 136.0, 135.9, 135.9, 135.9, 135.8, 134.7, 134.7, 134.4, 134.1, 134.1, 133.9, 133.9, 133.8, 129.9, 129.8, 129.8, 129.7, 127.8, 127.8, 127.8, 127.7, 127.7, 116.0, 115.8, 80.6, 78.2, 76.0, 75.8, 75.2, 72.7, 72.5, 71.8, 37.3, 34.0, 29.9, 27.2, 27.2, 27.1, 27.0, 20.5, 19.5, 19.2, 17.2. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{44}H_{51}O_3Si_2SFNa$ 757.2979; found 757.3019. $[\alpha]_D^{22}$= +13.9 (*c* 0.08, $CHCl_3$).

Synthesis of Butyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexopyranoside (46g):



According to general method, a solution of glycosyl donor 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **43a** (50 mg, 0.082 mmol, 1.0 equiv) and glycosyl acceptor 1-butanethiol **1a** (9 mg, 11 µL, 0.098 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (1.2 mg, 0.0041 mmol, 5 mol%) and stirred for 1.5 h to get the product **46g** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 47 mg, yield- 81%. Re-purification was done using HPLC (Hypersil Gold C18, water/acetonitrile = 0/100, flow rate = 5.0 mL/min, I = 214 nm) tR = 11 min. Selectivity α: β=1:2.2. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65 (t, *J* = 6.1 Hz, 8.6H), 7.59 (dd, *J* = 6.3, 1.3 Hz, 8.5H), 7.56 – 7.54 (m, 2.2H), 7.51 – 7.50 (m, 2H), 7.47 – 7.21 (m, 43.5H), 5.19 (dd, *J* = 11.2, 2.6 Hz, 1H), 4.55 (dd, *J* = 10.5, 3.5 Hz, 2.2H), 4.15 (dd, *J* = 12.4, 6.1 Hz, 2.2H), 4.02 (d, *J* = 2.6 Hz, 1H), 3.96 – 3.92 (m, 1H), 3.67 (t, *J* = 5.6 Hz,2.21H), 3.54 (p, *J* = 6.5 Hz, 3H), 2.74 (ddd, *J* = 12.8, 8.5, 6.3 Hz, 1H), 2.62 (ddd, *J* = 12.7, 8.6, 6.8 Hz, 1H), 2.57 – 2.53 (m, 2.2H), 2.50 – 2.45 (m, 2.2H), 2.09 (ddd, *J* = 13.6, 9.7, 2.5 Hz, 1H), 1.95 (ddd, *J* = 13.5, 5.6, 3.6 Hz, 2.2H), 1.66 – 1.58 (m, 6.5H), 1.53 – 1.39 (m, 6.5H), 1.36 – 1.29 (m, 4.5H), 1.22 (d, *J* = 7.2 Hz, 3H), 1.03 (d, *J* = 6.5 Hz, 6.6H), 0.99 (s, 18H), 0.97 (s, 10H), 0.94 (s, 30H), 0.87 (t, *J* = 7.4 Hz, 7H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 135.9, 135.9, 135.9, 135.8, 135.8, 135.7, 134.7, 134.2, 134.2, 133.8, 133.8, 133.5, 133.4, 133.4, 129.9, 129.8, 129.7, 129.7, 129.7, 129.7, 129.6, 127.7, 127.7, 127.7, 127.7, 127.6, 127.6, 127.6, 78.2, 78.0, 77.0, 74.7, 73.7, 72.5, 71.6, 38.5, 34.3, 32.3, 32.0, 30.3, 29.4, 27.2, 27.1, 27.0, 26.9, 22.2, 22.1, 20.4, 19.6, 19.3, 19.2, 19.2, 17.1, 13.8, 13.8, 2.0. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{42}H_{56}O_3Si_2SNa$ 719.3386; found 719.3380. $[\alpha]_D^{22}$= +26.1 (*c* 0.08, $CHCl_3$).

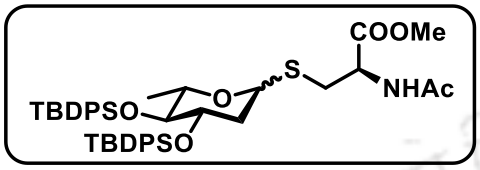
Synthesis of 1-Adamantanyl-2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexopyranoside (46h):



According to general method, a solution of glycosyl donor 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **43a** (50 mg, 0.082 mmol, 1.0 equiv) and glycosyl acceptor 1-adamantanethiol **1b** (17 mg, 0.098 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (1.2 mg, 0.0041 mmol, 5 mol%) and stirred for 5 h to get the product **46h** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 33 mg, yield- 52%. Re-purification was done using HPLC (Hypersil Gold C18, water/acetonitrile = 0/100, flow rate = 5.0 mL/min, I = 214 nm) tR = 15 min. Selectivity α: β=1:2. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 – 7.63 (m, 6H), 7.58 – 7.54 (m, 8H), 7.49 (d, *J* = 6.9 Hz, 2H), 7.45 – 7.28 (m, 29H), 7.26 – 7.20 (m, 3H), 5.47 (dd, *J* = 11.4, 2.4 Hz, 1H), 4.76 (dd, *J* = 11.2, 3.3 Hz, 2H), 4.13 (q, *J* = 6.2 Hz, 2H), 3.96 – 3.93 (m, 2H), 3.66 (t, *J* = 5.5 Hz, 2H), 3.58 – 3.54 (m, 2H), 3.52 (s, 1H), 2.05 – 1.92 (m, 16H), 1.87 (ddd, *J* = 13.6, 5.9, 3.4 Hz, 2H), 1.81 (q, *J* = 12.4 Hz, 10H), 1.70 – 1.61 (m, 17H), 1.54 (d, *J* = 13.6 Hz, 1H), 0.98 (dd, *J* = 12.2, 9.3 Hz, 25H), 0.92 (d, *J* = 2.1 Hz, 21H), 0.89 (d, *J* = 3.3 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 136.0, 136.0, 135.9, 135.9, 135.9, 135.8, 135.8, 134.7, 134.3, 134.3, 134.0, 133.9, 133.7, 133.6, 129.9, 129.8, 129.8, 129.7, 129.7, 129.6, 129.6, 129.6, 127.7, 127.7, 127.7, 78.4, 78.0, 74.8, 73.8,

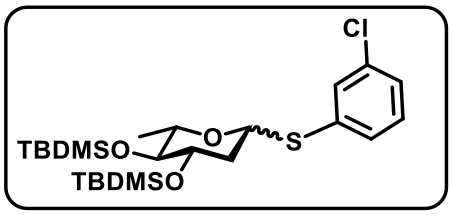
72.7, 72.0, 68.7, 45.8, 44.3, 44.1, 39.6, 36.5, 36.4, 30.0, 29.9, 27.3, 27.2, 27.1, 27.0, 20.6, 19.7, 19.3, 19.2, 17.3. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{48}H_{62}O_3Si_2SNa$ 797.3856; found 797.3855. $[\alpha]_D^{22}$= +22.5 (*c* 0.08, $CHCl_3$).

Synthesis of Methyl N-acetyl-L-cysteine-2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexopyranoside (46i):



According to general method, a solution of glycosyl donor 3,4-di-*O-tert*-butyldiphenylsilyl-L-rhamnal **43a** (50 mg, 0.082 mmol, 1.0 equiv) and glycosyl acceptor N-acetyl-L-cysteine methyl ester **1c** (18 mg, 0.098 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (1.2 mg, 0.0041 mmol, 5 mol%) and stirred for 5 h to get the product **46i** as a colourless oil. R_f- 0.4 in 40% EA/hexane, eluent 22% EA in hexane, amount- 58 mg, yield- 88%. Re-purification was done using HPLC (Hypersil Gold C18, water/acetonitrile = 5/95, flow rate = 5.0 mL/min, I = 214 nm) tR = 8 min. Selectivity α: β=1:2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.21 (m, 74H), 5.14 (dd, *J* = 11.5, 2.1 Hz, 1H), 4.81 (dt, *J* = 8.1, 4.1 Hz, 2.3H), 4.69 (dd, *J* = 8.7, 4.8 Hz, 2.3H), 4.56 (td, *J* = 7.2, 4.2 Hz, 1H), 4.12 (q, *J* = 5.1 Hz, 2.3H), 4.03 (d, *J* = 2.4 Hz, 1H), 3.90 (q, *J* = 7.2 Hz, 1H), 3.73 (s, 3H), 3.70 (s, 6.8H), 3.67 (dd, *J* = 6.7, 3.5 Hz, 2H), 3.64 – 3.62 (m, 2.3H), 3.54 (s, 1H), 3.34 (dd, *J* = 14.6, 4.4 Hz, 2.3H), 3.23 (dd, *J* = 14.5, 4.2 Hz, 1H), 2.96 (dd, *J* = 14.5, 7.4 Hz, 1H), 2.77 (dd, *J* = 14.6, 3.9 Hz, 2.3H), 2.17 – 2.05 (m, 3.3H), 1.97 (s, 7H), 1.92 (s, 3H), 1.68 – 1.57 (m, 3.3H), 1.25 (d, *J* = 7.2 Hz, 3H), 1.11 (d, *J* = 6.6 Hz, 6.9H), 0.98 – 0.96 (m, 50H), 0.93 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 171.4, 170.9, 170.6, 170.4, 136.0, 135.8, 135.8, 135.8, 135.7, 135.7, 134.1, 133.8, 133.7, 133.5, 133.3, 133.2, 133.1, 133.1, 130.1, 129.9, 129.9, 129.9, 129.8, 129.8, 127.9, 127.8, 127.8, 127.7, 127.7, 79.6, 78.5, 76.3, 74.9, 72.7, 71.7, 71.4, 71.0, 52.9, 52.6, 52.5, 52.3, 36.7, 35.3, 33.9, 32.0, 27.1, 27.0, 26.9, 23.1, 23.0, 20.6, 19.4, 19.2, 19.2, 19.2, 16.9. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{44}H_{57}O_6NSi_2SNa$ 806.3343; found 806.3344. $[\alpha]_D^{22}$= +18.9 (*c* 0.08, $CHCl_3$).

Synthesis of 3-Chlorophenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-α,β-L-arabino-hexopyranoside (46jαβ):



According to general method, a solution of glycosyl donor 3,4-di-*O-tert*-butyldimethylsilyl-L-rhamnal **43b** (50 mg, 0.139 mmol, 1.0 equiv) and glycosyl acceptor 3-chlorobenzenethiol (24 mg, 0.167 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-

tert-butylpyridinium hydrochloride catalyst (2 mg, 0.0069 mmol, 5 mol%) and stirred for 10 h to get the product **46jαβ** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 61 mg, yield- 80%. α and β anomers were isolated using HPLC (Hypersil Gold C18, water/acetonitrile = 0/100, flow rate = 5.0 mL/min, I = 214 nm) tR = 11 min (major), 13 min (minor). Selectivity ratio obtained from HPLC curve α: β= 1:2.

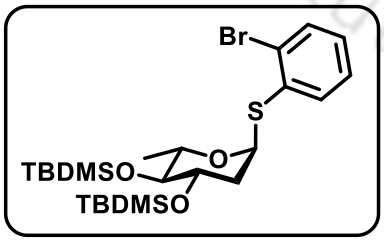
Synthesis of 3-Chlorophenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-β-L-arabino-hexopyranoside (46jβ):

HPLC retention time of the **β** isomer- 11 min (solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 2.0, 1.1 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.21 (dd, *J* = 3.8, 1.7 Hz, 2H), 4.81 (dd, *J* = 12.0, 1.9 Hz, 1H), 3.67 (ddd, *J* = 10.9, 8.1, 4.9 Hz, 1H), 3.32 (dq, *J* = 8.7, 6.2 Hz, 1H), 3.17 (t, *J* = 8.5 Hz, 1H), 2.23 (ddd, *J* = 12.8, 4.9, 1.9 Hz, 1H), 1.76 (dd, *J* = 23.7, 12.1 Hz, 1H), 1.31 (d, *J* = 6.3 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.10 – 0.07 (m, 12H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 136.8, 134.6, 130.1, 129.9, 128.5, 127.2, 81.4, 77.6, 77.3, 74.5, 41.0, 26.4, 26.2, 19.1, 18.5, 18.2, -2.6, -2.8, -3.7, -4.1. HRMS (ESI) m/z: $[M + NH_4]^+$ calcd for $C_{24}H_{43}O_3Si_2SClNH_4$ 520.2504; found 520.2553. $[\alpha]_D^{22}$= +33.8 (*c* 0.08, $CHCl_3$).

Synthesis of 3-Chlorophenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-α-L-arabino-hexopyranoside (46jα):

HPLC retention time of the **α** isomer- 13 min (solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was colourless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48 (d, *J* = 1.8 Hz, 1H), 7.35 (dt, *J* = 7.0, 1.8 Hz, 1H), 7.24 – 7.20 (m, 2H), 5.55 (dd, *J* = 5.2, 2.4 Hz, 1H), 4.06 (dq, *J* = 13.1, 6.5 Hz, 1H), 3.93 – 3.90 (m, 1H), 3.23 (t, *J* = 7.9 Hz, 1H), 2.27 (ddd, *J* = 13.6, 4.2, 2.6 Hz, 1H), 2.06 (ddd, *J* = 13.7, 10.6, 5.4 Hz, 1H), 1.28 (d, *J* = 6.4 Hz, 3H), 0.94 (s, 9H), 0.93 (s, 9H), 0.15 – 0.05 (m, 12H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 137.7, 134.6, 130.5, 130.0, 128.8, 127.1, 83.0, 77.9, 71.4, 70.9, 39.6, 26.4, 26.2, 25.8, 18.5, 18.4, 18.2, 18.2, 1.3, 1.2, -2.8, -2.9, -3.1, -3.9, -4.3. HRMS (ESI) m/z: $[M + NH_4]^+$ calcd for $C_{24}H_{43}O_3Si_2SClNH_4$ 520.2504; found 520.2551. $[\alpha]_D^{22}$= -2.6 (*c* 0.08, $CHCl_3$).

Synthesis of 2-Bromophenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-α,β-L-arabino-hexopyranoside (46kαβ):



According to general method, a solution of glycosyl donor 3,4-di-*O*-*tert*-butyldimethylsilyl-L-rhamnal **43b** (50 mg, 0.139 mmol, 1.0 equiv) and glycosyl acceptor 2-bromothiophenol (32 mg, 0.167 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (2 mg, 0.0069 mmol, 5 mol%) and stirred for 10 h to

get the product **46kαβ** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 55 mg, yield- 72%. α and β anomers were isolated using HPLC (Hypersil Gold C18, water/acetonitrile = 0/100, flow rate = 5.0 mL/min, I = 214 nm) tR = 9.5 min (major), 11.5 min (minor). Selectivity α: β= 1:1.4.

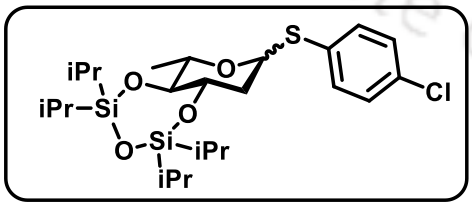
Synthesis of 2-Bromophenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-α-L-arabino-hexopyranoside (46kα):

Re-purification was done using HPLC (retention time- 11.5 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.55 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.26 (dd, *J* = 15.3, 1.3 Hz, 1H), 7.06 (td, *J* = 7.8, 1.5 Hz, 1H), 5.61 (dd, *J* = 5.4, 2.5 Hz, 1H), 4.04 (dq, *J* = 12.9, 6.4 Hz, 1H), 3.98 – 3.92 (m, 1H), 3.21 (t, *J* = 7.9 Hz, 1H), 2.30 (ddd, *J* = 13.7, 4.3, 2.7 Hz, 1H), 2.07 (ddd, *J* = 13.7, 10.4, 5.5 Hz, 1H), 1.23 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.2, 133.0, 131.1, 128.0, 127.7, 124.8, 82.0, 78.0, 77.4, 71.5, 71.1, 39.5, 26.5, 26.4, 26.2, 26.2, 18.6, 18.4, 18.2, 1.2, -2.8, -3.2, -3.9, -4.3. HRMS (ESI) m/z: $[M + NH_4]^+$ $C_{24}H_{43}O_3Si_2SBrNH_4$ 564.1999; found 564.2038. $[\alpha]_D^{22}$= -3.9 (c 0.04, $CHCl_3$).

Synthesis of 2-Bromophenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-β-L-arabino-hexopyranoside (46kβ):

Re-purification was done using HPLC (retention time- 9.5 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.47 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.28 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.06 (td, *J* = 7.8, 1.5 Hz, 1H), 4.90 (dd, *J* = 11.9, 1.9 Hz, 1H), 3.71 (ddd, *J* = 10.9, 8.1, 5.0 Hz, 1H), 3.37 (tt, *J* = 12.5, 6.3 Hz, 1H), 3.21 (t, *J* = 8.5 Hz, 1H), 2.30 (ddd, *J* = 12.8, 4.9, 1.9 Hz, 1H), 1.86 (dd, *J* = 23.7, 12.1 Hz, 1H), 1.31 (d, *J* = 6.3 Hz, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.10 (dd, *J* = 5.4, 4.1 Hz, 10H), 0.07 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 136.9, 133.0, 129.4, 128.4, 128.1, 127.5, 123.4, 80.2, 77.7, 77.2, 74.5, 40.7, 26.4, 26.2, 19.2, 18.5, 18.2, 1.2, -2.6, -2.8, -3.7, -4.0. HRMS (ESI) m/z: $[M + NH_4]^+$ calcd for $C_{24}H_{43}O_3Si_2SBrNH_4$ 564.1999; found 564.2038. $[\alpha]_D^{22}$= +28.9 (*c* 0.08, $CHCl_3$).

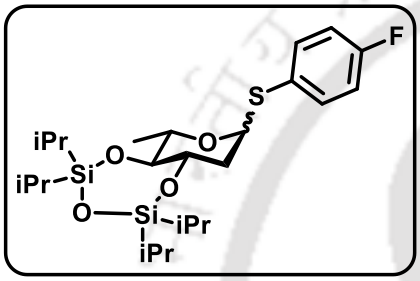
Synthesis of 4-Chlorophenyl 2,6-dideoxy-3,4-O-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-α,β-L-arabino-hexopyranoside (46l):



According to general method, a solution of glycosyl donor 3,4-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-1,2,6-trideoxy-L-arabino-1-hexenopyranose **43c** (50 mg, 0.134 mmol, 1.0 equiv) and glycosyl acceptor 4-chlorothiophenol (23 mg, 0.161 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (1.9 mg,

0.0067 mmol, 5 mol%) and stirred for 24 h to get the product **46l** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 42 mg, yield- 61%. Re-purification was done using HPLC (Hypersil Gold C18, water/acetonitrile = 0/100, flow rate = 5.0 mL/min, I = 214 nm) tR = 13 min. Selectivity α: β=3:1. α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.37 (m, 2H), 7.28 – 7.25 (m, 2H), 5.54 (d, *J* = 5.5 Hz, 1H), 4.11 (tt, *J* = 12.5, 6.2 Hz, 1H), 3.97 (ddd, *J* = 11.7, 8.3, 5.2 Hz, 1H), 3.28 (t, *J* = 8.7 Hz, 1H), 2.28 (dd, *J* = 13.7, 5.2 Hz, 1H), 2.13 (ddd, *J* = 13.8, 11.7, 5.8 Hz, 1H), 1.29 (d, *J* = 6.2 Hz, 3H), 1.11 – 0.92 (m, 28H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 134.0, 133.2, 132.5, 129.2, 84.2, 80.2, 72.0, 69.4, 39.2, 18.0, 17.8, 17.6, 17.5, 17.5, 17.4, 17.4, 13.1, 13.0, 12.4, 12.4, 1.2. HRMS (ESI) m/z: $[M + NH_4]^+$ calcd for $C_{24}H_{41}O_4Si_2SClNH_4$ 534.2296; found 534.2303. $[\alpha]_D^{22}$= +19.0 (*c* 0.08, $CHCl_3$).

Synthesis of 4-Fluorophenyl 2,6-dideoxy-3,4-O-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-α,β-L-arabino-hexopyranoside (46mαβ):



According to general method, a solution of glycosyl donor 3,4-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-1,2,6-trideoxy-L-arabino-1-hexenopyranose **43c** (50 mg, 0.134 mmol, 1.0 equiv) and glycosyl acceptor 4-fluorothiophenol (21 mg, 17 µL, 0.167 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (1.9 mg, 0.0067 mmol, 5 mol%) and stirred for 24 h to get the product **46mαβ** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 40 mg, yield- 59%. α and β anomers were isolated using HPLC (Hypersil Gold C18, water/acetonitrile = 0/100, flow rate = 5.0 mL/min, I = 214 nm) tR = 7.5 min (major), 6.5 min (minor). Selectivity α: β= 3.8:1.

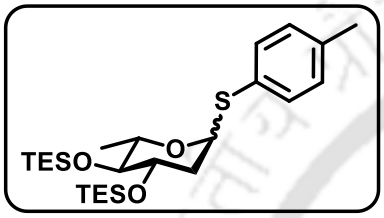
Synthesis of 4-Fluorophenyl 2,6-dideoxy-3,4-O-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-α-L-arabino-hexopyranoside (46mα):

Re-purification was done using HPLC (retention time- 7.5 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 2H), 7.03 – 6.97 (m, 2H), 5.46 (d, *J* = 5.5 Hz, 1H), 4.14 (dq, *J* = 9.0, 6.2 Hz, 1H), 3.98 (ddd, *J* = 11.7, 8.3, 5.2 Hz, 1H), 3.28 (t, *J* = 8.7 Hz, 1H), 2.29 (dd, *J* = 13.5, 5.0 Hz, 1H), 2.18 – 2.08 (m, 1H), 1.30 (d, *J* = 6.2 Hz, 3H), 1.11 – 0.94 (m, 28H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 134.1, 134.0, 116.2, 116.1, 84.8, 80.3, 72.0, 69.3, 39.2, 18.0, 17.8, 17.6, 17.6, 17.5, 17.5, 17.5, 17.4, 17.4, 13.1, 13.0, 12.4, 12.4. HRMS (ESI) m/z: $[M + K]^+$ calcd for $C_{24}H_{41}O_4Si_2SFK$ 539.1885; found 539.2120. $[\alpha]_D^{22}$= -5.9 (*c* 0.08, $CHCl_3$).

Synthesis of 4-Fluorophenyl 2,6-dideoxy-3,4-O-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-β-L-arabino-hexopyranoside (46mβ):

Re-purification was done using HPLC (retention time- 6.5 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.48 (m, 2H), 7.01 (t, *J* = 8.7 Hz, 2H), 4.70 (dd, *J* = 12.0, 1.8 Hz, 1H), 3.75 – 3.69 (m, 1H), 3.32 – 3.22 (m, 2H), 2.27 (ddd, *J* = 13.1, 5.3, 1.8 Hz, 1H), 1.78 (dd, *J* = 24.2, 12.1 Hz, 1H), 1.35 (d, *J* = 5.8 Hz, 3H), 1.07 – 0.90 (m, 28H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 134.3, 134.2, 116.1, 116.0, 82.5, 79.3, 76.6, 75.2, 39.9, 18.5, 17.8, 17.5, 17.5, 17.5, 17.4, 17.4, 17.4, 13.0, 13.0, 12.4, 12.3, 1.2. HRMS (ESI) m/z: $[M + K]^+$ calcd for $C_{24}H_{41}O_4Si_2SFK$ 539.1885; found 539.2120. $[\alpha]_D^{22}$= +22.4 (*c* 0.04, $CHCl_3$).

Synthesis of Tolyl 2,6-dideoxy-3,4-bis-O-[triethylsilyl]-1-thio-α,β-L-arabino-hexopyranoside (46nαβ):



According to general method, a solution of glycosyl donor 3,4-di-O-triethylsilyl-L-rhamnal **43d** (50 mg, 0.139 mmol, 1.0 equiv) and glycosyl acceptor 4-methylbenzenethiol (21 mg, 0.167 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (2 mg, 0.0069 mmol, 5 mol%) and stirred for 16 h to get the product **46nαβ** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 44 mg, yield- 65%. α and β anomers were isolated using HPLC (Hypersil Gold C18, water/acetonitrile = 0/100, flow rate = 5.0 mL/min, I = 214 nm) tR = 12 min (major), 10 min (minor). Selectivity α: β= 1:1.2.

Synthesis of Tolyl 2,6-dideoxy-3,4-bis-O-[triethylsilyl]-1-thio-α-L-arabino-hexopyranoside (46nα):

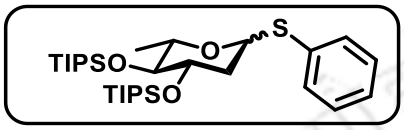
Re-purification was done using HPLC (retention time- 12 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.1 Hz, 2H), 7.10 (d, *J* = 7.9 Hz, 2H), 5.44 (d, *J* = 4.3 Hz, 1H), 4.10 (dq, *J* = 12.6, 6.3 Hz, 1H), 3.94 – 3.88 (m, 1H), 3.19 (t, *J* = 8.5 Hz, 1H), 2.32 (s, 3H), 2.27 (ddd, *J* = 13.4, 4.6, 1.4 Hz, 1H), 2.02 (ddd, *J* = 13.4, 11.3, 5.6 Hz, 1H), 1.24 (d, *J* = 6.4 Hz, 3H), 0.98 (td, *J* = 7.9, 3.1 Hz, 18H), 0.69 – 0.62 (m, 12H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 137.3, 132.0, 131.7, 129.8, 84.2, 79.1, 71.3, 69.9, 39.9, 21.3, 18.4, 7.2, 7.1, 5.5, 5.4, 1.12. HRMS (ESI) m/z: $[M + K]^+$ calcd for $C_{25}H_{46}O_3Si_2SK$ 521.2343; found 521.2386. $[\alpha]_D^{22}$= -2.4 (*c* 0.03, $CHCl_3$).

Synthesis of Tolyl 2,6-dideoxy-3,4-bis-O-[triethylsilyl]-1-thio-β-L-arabino-hexopyranoside (46nβ):

Re-purification was done using HPLC (retention time- 10 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 7.9 Hz, 2H), 4.70 (dd, *J* = 11.9, 1.8 Hz,

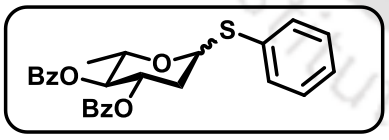
1H), 3.62 (ddd, *J* = 11.0, 8.0, 5.1 Hz, 1H), 3.25 (dt, *J* = 14.9, 6.1 Hz, 1H), 3.17 – 3.13 (m, 1H), 2.34 (s, 3H), 2.23 (ddd, *J* = 12.7, 5.1, 1.8 Hz, 1H), 1.72 (dd, *J* = 23.7, 12.1 Hz, 1H), 1.29 (d, *J* = 6.1 Hz, 3H), 0.95 (dd, *J* = 8.5, 7.6 Hz, 18H), 0.62 (tt, *J* = 9.7, 4.7 Hz, 12H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 137.6, 132.0, 130.6, 129.7, 82.2, 78.4, 77.4, 77.0, 74.5, 40.9, 21.3, 18.8, 7.2, 7.1, 5.5, 1.2. HRMS (ESI) m/z: $[M + K]^+$ calcd for $C_{25}H_{46}O_3Si_2SK$ 521.2343; found 521.2386. $[\alpha]_D^{22}$ = +36.2 (*c* 0.08, $CHCl_3$).

Synthesis of Phenyl 2,6-dideoxy-3,4-bis-O-[triisopropylsilyl]-1-thio-α,β-L-arabino-hexopyranoside (46o):



According to general method, a solution of glycosyl donor 3,4-bis-(triisopropylsilyl)-L-rhamnal **43e** (50 mg, 0.113 mmol, 1.0 equiv) and glycosyl acceptor thiophenol (15 mg, 14 µL, 0.135 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (1.6 mg, 0.0056 mmol, 5 mol%) and stirred for 10 h to get the product **46o** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 45 mg, yield- 72%. Re-purification was done using HPLC (Hypersil Gold C18, water/acetonitrile = 0/100, flow rate = 5.0 mL/min, I = 214 nm) tR = 16 min. Selectivity α: β=1:1.5. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.8 Hz, 2H), 7.49 (d, *J* = 7.8 Hz, 2.5H), 7.33 – 7.22 (m, 8H), 5.47 (d, *J* = 10.1 Hz, 1H), 4.91 (d, *J* = 11.1 Hz, 1.5H), 4.15 (d, *J* = 6.9 Hz, 1H), 4.09 (s, 1H), 3.90 (s, 1.5H), 3.60 (s, 1H), 3.47 (d, *J* = 4.0 Hz, 3H), 2.40 – 2.38 (m, 1.5H), 2.31 (t, *J* = 11.8 Hz, 1H), 1.89 – 1.84 (m, 2.5H), 1.47 (d, *J* = 7.0 Hz, 3H), 1.41 (d, *J* = 4.4 Hz, 4.5H), 1.20 – 1.07 (m, 104H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 134.9, 134.7, 131.2, 130.9, 128.9, 128.8, 127.1, 126.8, 81.1, 77.7, 77.6, 75.7, 75.6, 74.6, 72.8, 71.6, 39.9, 35.2, 19.4, 18.6, 18.5, 18.5, 18.4, 18.3, 18.3, 18.3, 18.3, 17.2, 13.8, 12.7, 12.6. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{30}H_{56}O_3Si_2SNa$ 575.3386; found 575.3423. $[\alpha]_D^{22}$ = +29.4 (*c* 0.09, $CHCl_3$).

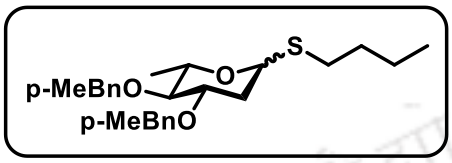
Synthesis of Phenyl 3,4-di-O-benzoyl-2,6-dideoxy-1-thio-L-rhamnopyranoside (46p):



According to general method, a solution of glycosyl donor 3,4-Di-O-benzoyl-L-rhamnal **43f** (50 mg, 0.148 mmol, 1.0 equiv) and glycosyl acceptor thiophenol (20 mg, 18 µL, 0.178 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (8.4 mg, 0.030 mmol, 20 mol%) and stirred for 24 h to get the product **46p** as a colourless oil. R_f- 0.5 in 20% EA/hexane, eluent 10% EA in hexane, amount- 35 mg, yield- 53%. Selectivity α: β=1:2. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 – 8.01 (m, 2H), 7.98 – 7.97 (m, 2H), 7.63 – 7.58 (m, 2H), 7.49 – 7.41 (m, 6H), 7.37 (dd, *J* = 7.7, 1.5 Hz, 2H), 6.09 (ddd, *J* = 9.4, 3.5, 1.8 Hz, 1H), 5.09 (dd, *J* = 8.5, 1.7 Hz, 1H), 4.38 (dd, *J* = 9.3, 5.2 Hz, 1H), 3.81 – 3.75 (m, 1H), 2.37 (ddd, *J* = 14.8, 9.5, 5.2 Hz, 1H), 2.12 (ddd, *J* = 14.9, 9.3, 3.7 Hz, 1H), 1.17 (d, *J* = 6.2 Hz,

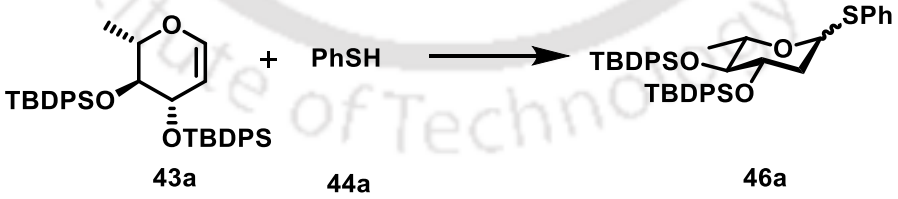
3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 167.5, 165.9, 133.9, 133.7, 133.6, 133.5, 133.4, 132.9, 130.1, 130.0, 129.5, 129.2, 129.1, 129.1, 128.7, 128.6, 128.4, 128.2, 78.0, 77.4, 77.2, 76.9, 70.8, 65.5, 55.2, 37.6, 29.8, 19.0, 14.3, 14.2. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{26}H_{24}O_5SH$ 449.1423; found 449.1426. $[\alpha]_D^{22}$= -5.8 (*c* 0.09, $CHCl_3$).

Synthesis of Butyl 2,6-dideoxy-3,4-di-O-para-methylbenzyl-1-thio-α,β-L-arabino-hexopyranoside (46q):



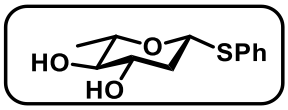
According to general method, a solution of glycosyl donor 3,4-di-O-para-methylbenzyl-L-rhamnal **43g** (50 mg, 0.148 mmol, 1.0 equiv) and glycosyl acceptor **1a** (16 mg, 20 µL, 0.177 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (2.1 mg, 0.0074 mmol, 5 mol%) and stirred for 24 h to get the product **46q** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 50 mg, yield- 79%. Selectivity β: α= 1.3: 1. ^1H NMR (500 MHz, $CDCl_3$) δ 7.22 (dd, *J* = 12.2, 5.2 Hz, 9H), 7.13 (d, *J* = 7.7 Hz, 9H), 5.29 (d, *J* = 5.5 Hz, 1.3H), 4.89 (dd, *J* = 10.7, 5.0 Hz, 2.3H), 4.65 – 4.55 (m, 6.8H), 4.46 (d, *J* = 11.6 Hz, 1H), 4.06 (dq, *J* = 12.4, 6.1 Hz, 1.3H), 3.88 – 3.83 (m, 1.3H), 3.62 – 3.58 (m, 1H), 3.31 (dq, *J* = 12.2, 6.1 Hz, 1H), 3.09 (dt, *J* = 15.4, 9.0 Hz, 2.3H), 2.72 – 2.62 (m, 2H), 2.57 (dt, *J* = 14.3, 7.3 Hz, 1.3H), 2.52 – 2.46 (m, 1.3H), 2.34 (s, 14H), 2.27 (dd, *J* = 13.3, 4.8 Hz, 1.3H), 2.01 – 1.95 (m, 1.3H), 1.70 (dd, *J* = 23.9, 11.8 Hz, 1.2H), 1.60 (dd, *J* = 14.6, 7.3 Hz, 6H), 1.39 (dt, *J* = 14.8, 7.4 Hz, 5H), 1.31 (d, *J* = 6.1 Hz, 3H), 1.27 (d, *J* = 6.4 Hz, 5H), 0.90 (dd, *J* = 12.5, 7.3 Hz, 7H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 137.6, 137.5, 137.4, 135.8, 135.7, 135.7, 135.5, 129.3, 129.2, 129.2, 129.2, 128.4, 128.2, 128.0, 128.0, 84.6, 83.6, 80.6, 80.5, 79.8, 77.9, 75.9, 75.4, 75.1, 71.9, 71.6, 67.7, 37.6, 36.5, 32.1, 32.0, 30.9, 30.6, 29.9, 22.1, 22.1, 21.3, 18.6, 18.2, 13.8. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{26}H_{36}O_3SNa$ 541.2283; found 541.2289. $[\alpha]_D^{22}$= +16.8 (*c* 0.03, $CHCl_3$).

Large Scale Synthesis of 46a:



A solution of glycosyl donor 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **43a** (1.1 g, 1.812 mmol, 1.0 equiv) and glycosyl acceptor thiophenol **44a** (0.242 g, 220 µL, 2.17 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (26 mg, 0.0906 mmol, 5 mol%) and stirred for 24 h at rt to get the product **46a** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 936 mg, yield- 72%. Selectivity was determined from crude NMR analysis α: β=1:1.5.

Synthesis of Phenyl 2,6-dideoxy-1-thio-L-rhamnopyranoside (46r):



Phenyl 3,4-di-O-benzoyl-2,6-dideoxy-1-thio-L-rhamnopyranoside **46p** (50 mg, 0.111 mmol, 1.0 equiv) was taken in MeOH and to it catalytic amount of NaOMe was added and the reaction was stirred at rt until starting material was completely consumed. After that the reaction mixture was evaporated to dry and the crude material purified via column chromatography on silica to afford the pure product **46r** as a colourless syrup. R_f- 0.4 in EA, eluent 50% EA in hexane, amount- 22 mg, yield- 82%. Selectivity β: α= 2.5: 1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 7.1 Hz, 2H), 7.45 (d, *J* = 7.4 Hz, 4.5H), 7.31 – 7.22 (m, 11.5H), 5.58 (d, *J* = 5.6 Hz, 2.5H), 4.81 (dd, *J* = 11.8, 1.7 Hz, 1H), 4.16 (td, *J* = 12.4, 6.2 Hz, 2.5H), 3.97 – 3.92 (m, 2.5H), 3.65 (ddd, *J* = 11.4, 8.8, 5.2 Hz, 1H), 3.35 (tt, *J* = 12.2, 6.1 Hz, 1H), 3.14 (dt, *J* = 14.3, 9.0 Hz, 3.5H), 2.38 – 2.31 (m, 3.5H), 2.14 – 2.08 (m, 2.5H), 1.78 (dd, *J* = 24.0, 11.8 Hz, 1H), 1.37 (d, *J* = 6.1 Hz, 3H), 1.30 (d, *J* = 6.2 Hz, 7.5H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 135.3, 131.7, 131.4, 129.1, 129.0, 127.6, 127.3, 84.1, 82.1, 78.6, 77.6, 76.0, 73.1, 70.1, 68.7, 39.4, 38.7, 29.8, 18.1, 17.7. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{12}H_{16}O_3SH$ 241.0898; found 241.0895. $[\alpha]_D^{22}$= +3.4 (*c* 0.09, $CHCl_3$).

3.7 References:

1. Posner, T. *Eur. J. Inorg. Chem.* **1905**, *38*, 646-57.

2. Tamai, T.; Fujiwara, K.; Higashimae, S.; Nomoto, A.; Ogawa, A. *Org. Lett.* **2016**, *18*, 2114−17.

3. Choudhuri, K.; Mandala, A.; Mal, P. *Chem.Commun.* **2018**, *54*, 3759-62.

4. (a) He, X. M.; Liu, H. W. *Curr. Opin. Chem. Biol.* **2002**, 6, 590-97. (b) Sastry, M.; Patel, D. *J. Biochemistry-Us* **1993**, *32*, 6588-604. (c) Rohr, J.; Thiericke, R. *Nat. Prod. Rep.* **1992**, *9*, 103-37. (d) Crow, R. T.; Rosenbaum, B.; Smith, R.; Guo, Y.; Ramos, K. S.; Sulikowski, G. A. Bioorg. *Med. Chem. Lett.* **1999**, *9*, 1663-66.

5. (a) Guo, Y.; Sulikowski, G. A. *J. Am. Chem. Soc.* **1998**, *120*, 1392-97. (b) Balmond, E. I.; Coe, D. M.; Galan, M. C.; McGarrigle, E. M. *Angew. Chem. Int. Ed.* **2012**, *51*, 9152-55. (c) Sun, L. F.; Wu, X. W.; Xiong, D. C.; Ye, X. S. *Angew. Chem. Int. Ed*. **2016**, *55*, 8041-44. (d) Bennett, C. S.; Galan, M. C. *Chem. Rev.* **2018**, *118*, 7931-85.

6. (a) Crich D.; Ritchie T. *J. Carbohydr. Res.* **1989**, *190*, C3–C6. (b) Yadav J. S.; Reddy B. V. S.; Bhaskar E. V.; Raghavendra S.; Narsaiah A. V. *Tetrahedron Lett.* **2007**, *48*, 677-80.

7. Paul S.; Jayaraman N. *Carbohydr. Res.* **2004**, *339*, 2197-204.

8. Baryal, K. N.; Zhu, J. L. *Synlett* **2014**, *25*, 308-12.

9. (a) Issa, J. P.; Lioyd D.; Steliotes, E.; Bennett C. S. *Org. Lett.* **2013**, *15*, 4170-73.

(b) Sherry, B. D.; Loy, R. N.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 4510-11.

10. . Ghosh, T.; Mukherji, A.; Kancharla, P. K. *Org. Lett.* **2019**, *21*, 3490-95.

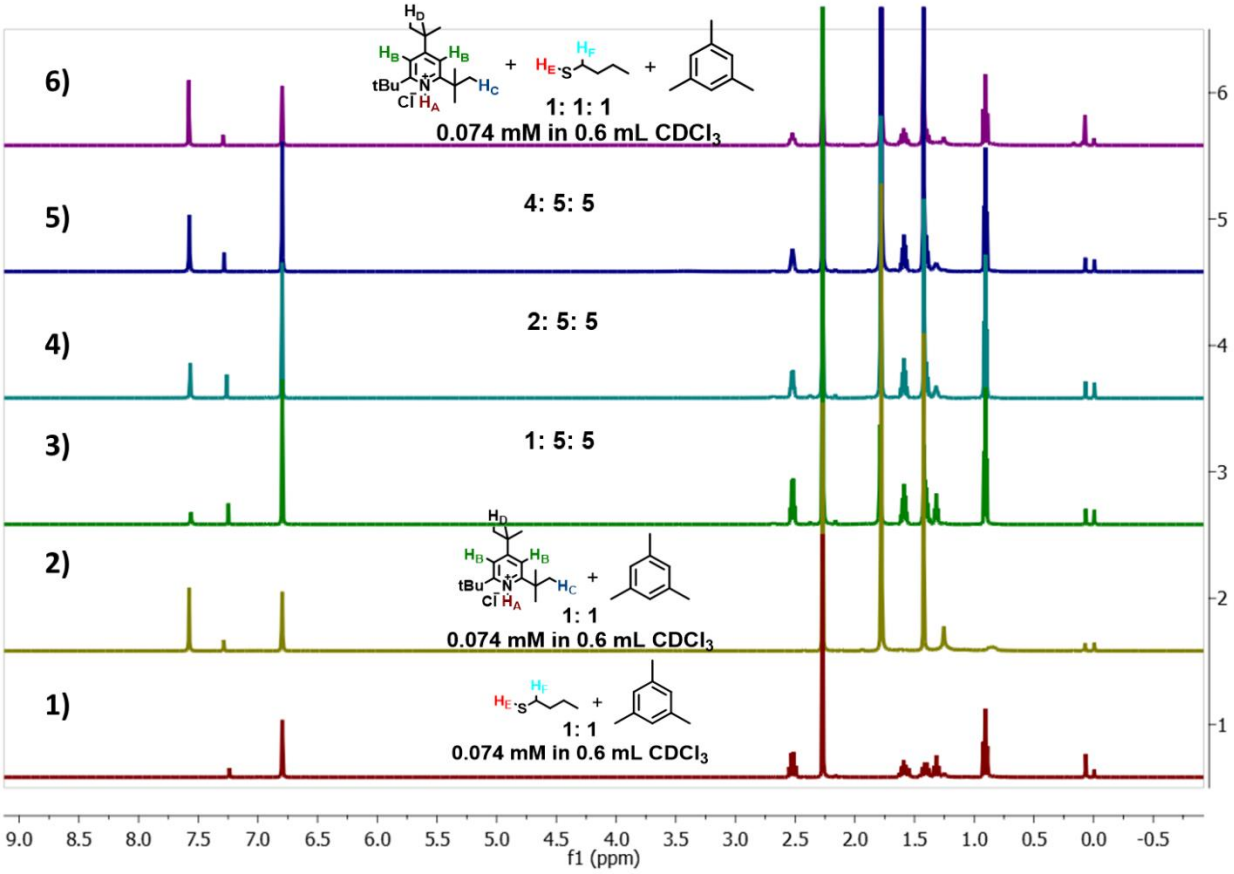
11. Rossler, S. L.; Jelier, B. J.; Magnier, E.; Dagousset, G.; Carreira, E. M.; Togni, A. Angew. Chem. Int. Edit. **2020**, 59, 9264-80.

12. Schilter, D. Frustration leads to radical behaviour. Nat. Rev. Chem. **2018**, 2, 255-255.

13. Dasgupta, A.; Richards, E.; Melen, R. L. Frustrated Radical Pairs: Insights From EPR Spectroscopy. Angew. Chem. Int. Ed. **2020**, 60, 53-65.

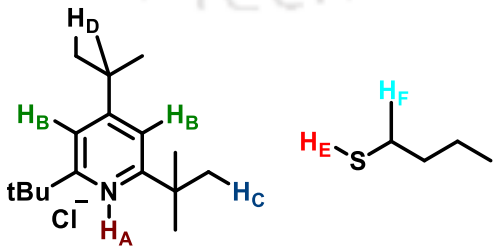
3.8 NMR, IR, ESR Studies:
3.8.1 NMR Titration Experiments:

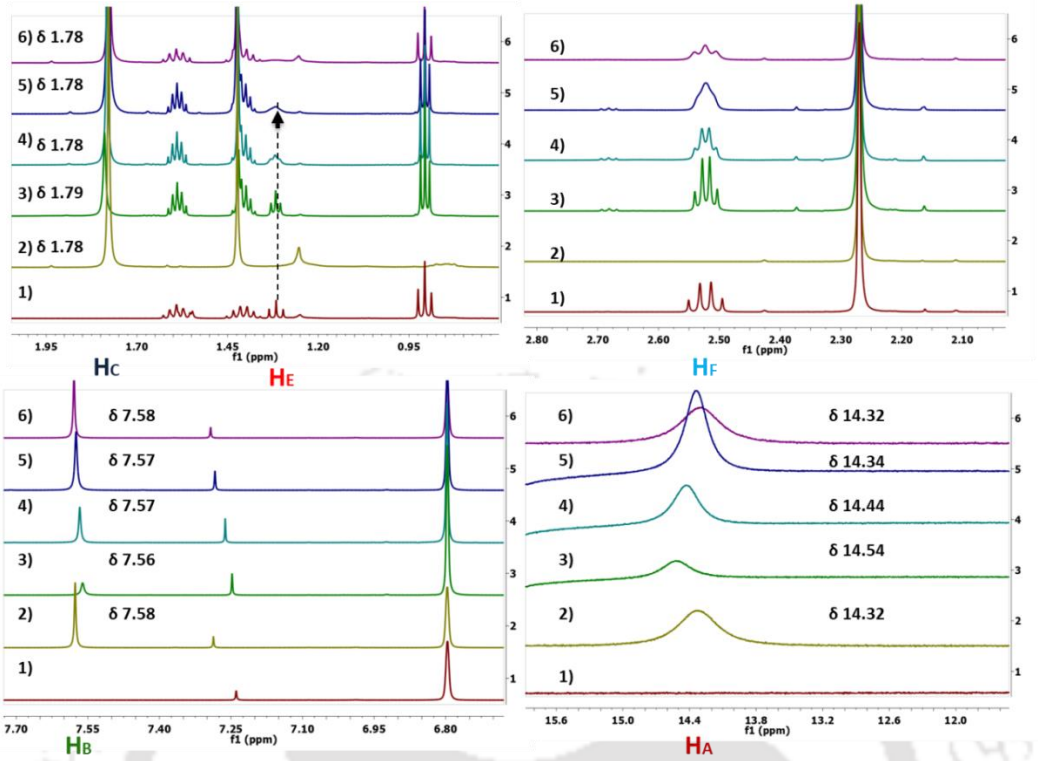
^{1}H NMR titration of TTBPy·HCl with 1-butanethiol in 0.6 ml solution of $CDCl_3$



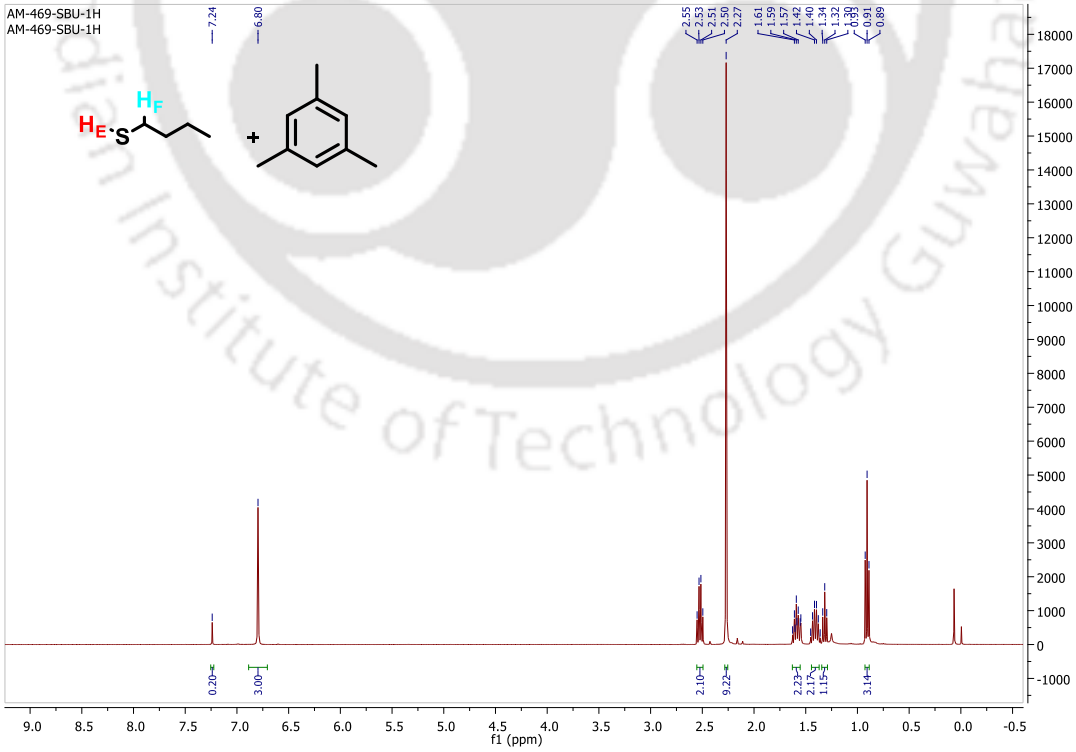
1) 0.074 mmol of 1-butanethiol 2) 0.074 mmol of TTBPy·HCl 3) 0.074 mmol of 1-butanethiol and 0.0148 mmol of TTBPy·HCl 4) 0.074 mmol of 1-butanethiol and 0.0296 mmol of TTBPy·HCl 5) 0.074 mmol of 1-butanethiol and 0.0592 mmol of TTBPy.HCl 6) 0.074 mmol of 1-butanethiol and 0.074 mmol of TTBPy·HCl. 0.074 mmol of mesitylene is used as an internal standard in all the experiments for the purpose of calibration.

Specific regions expanded

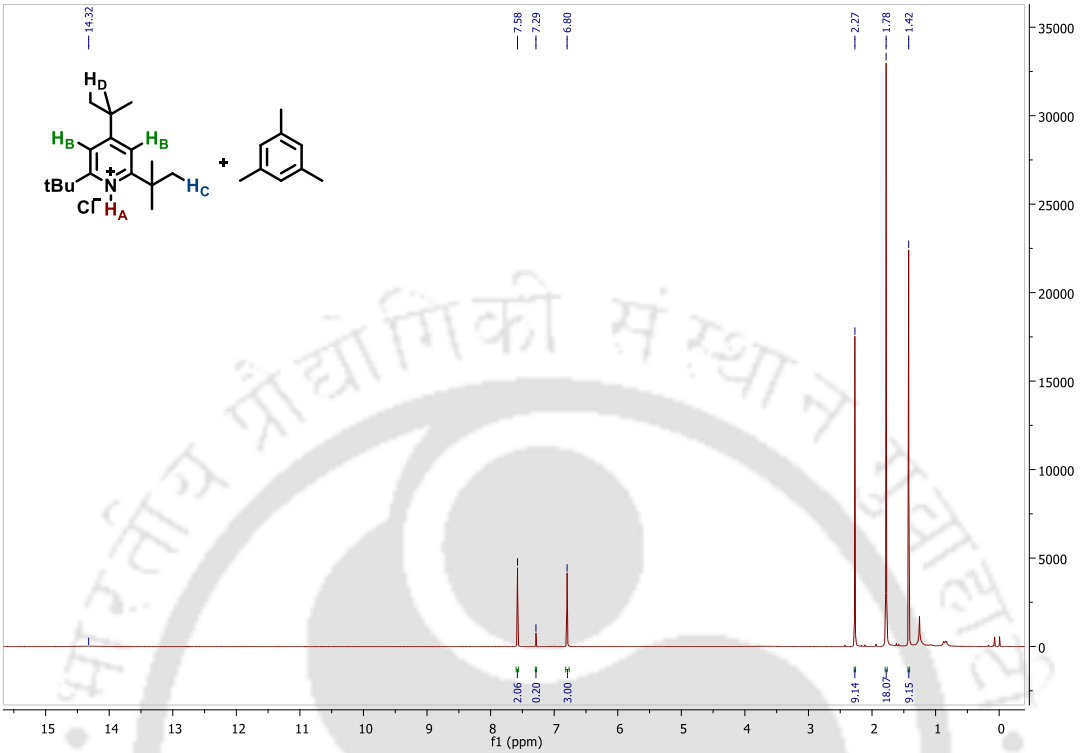




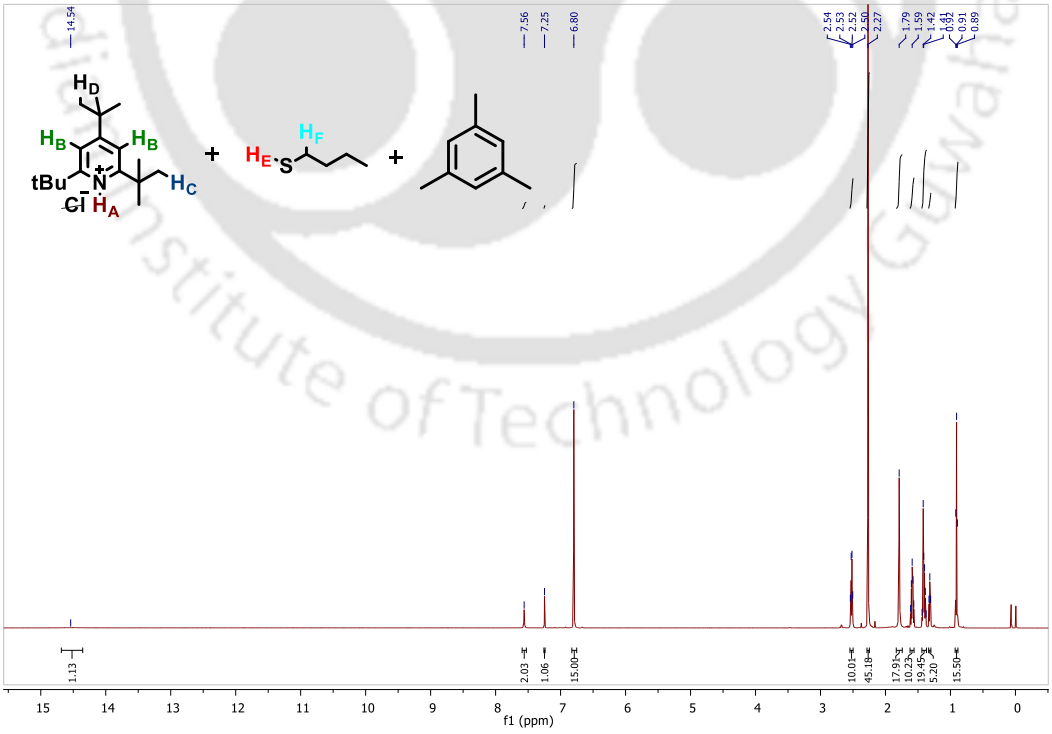
1:1 mixture of 1-butanethiol and mesitylene (0.074 mmol of each component in 0.6 mL of $CDCl_3$)



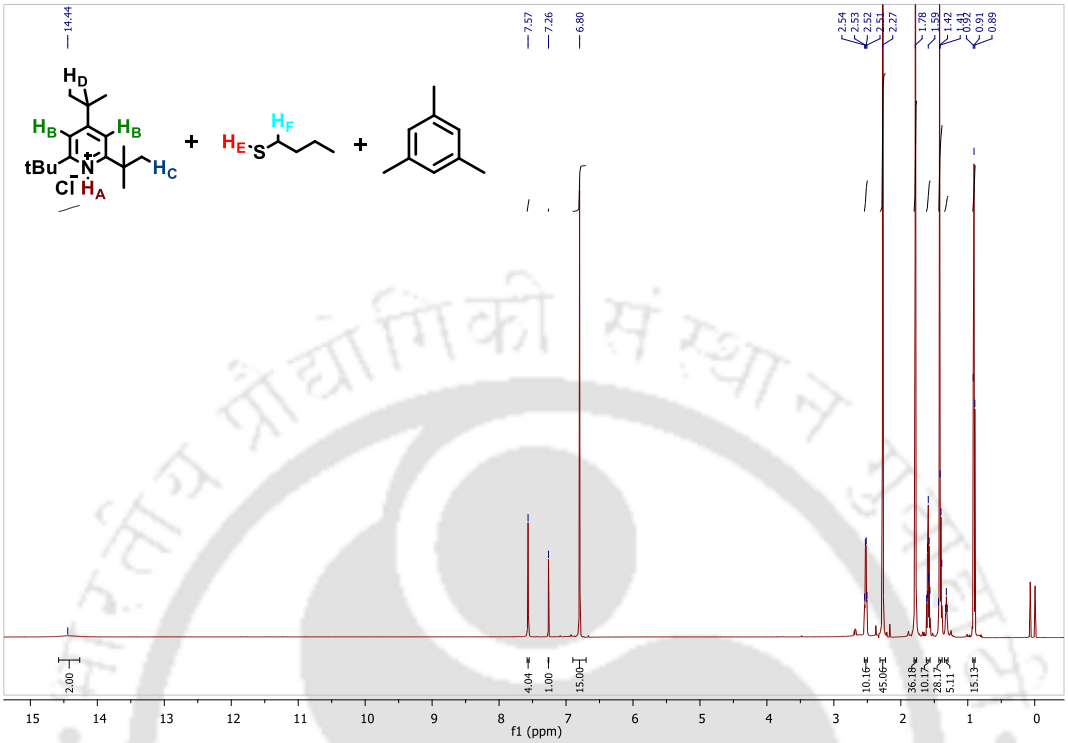
1:1 mixture of TTBPy·HCl and mesitylene (0.074 mmol of each component in 0.6 mL of $CDCl_3$)



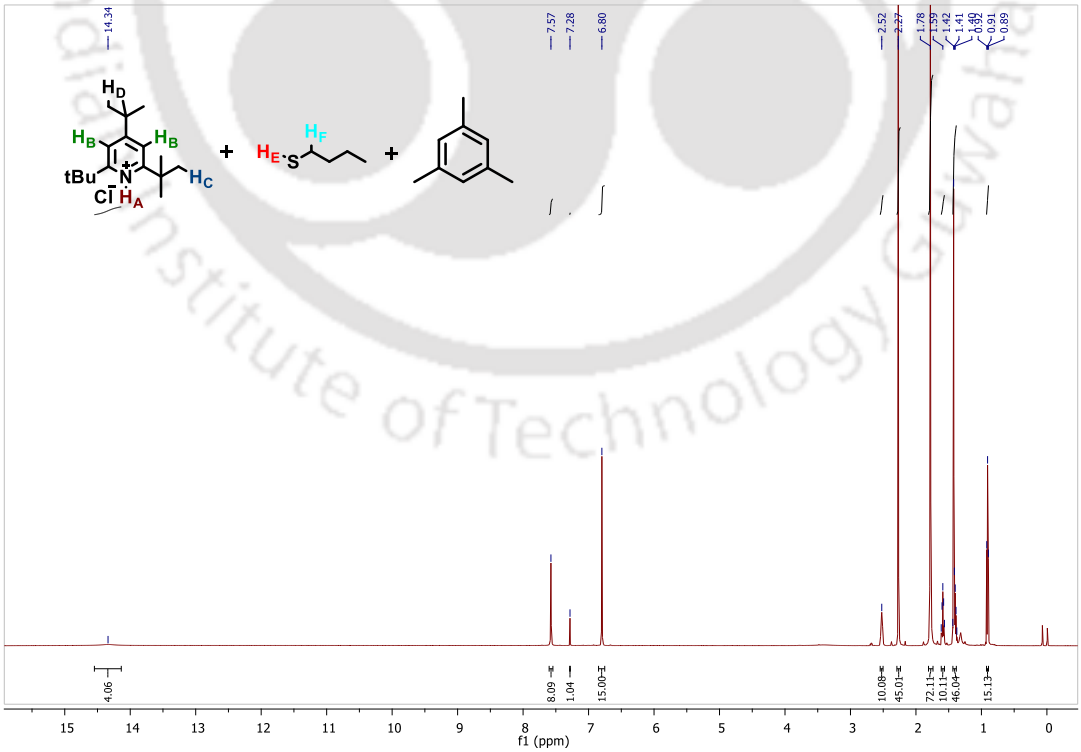
5:1:5 mixture of 1-butanethiol, TTBPy·HCl and mesitylene (0.074 mmol of mesitylene in 0.6 mL of $CDCl_3$)



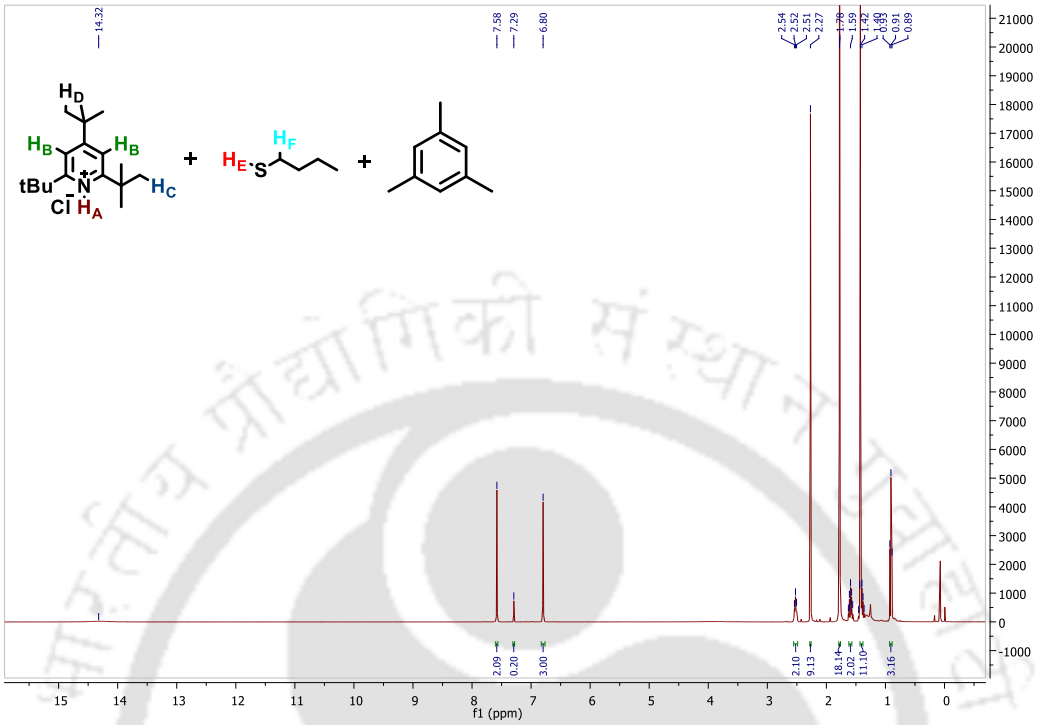
5:2:5 mixture of 1-butanethiol, TTBPy·HCl and mesitylene (0.074 mmol of mesitylene in 0.6 mL of $CDCl_3$)



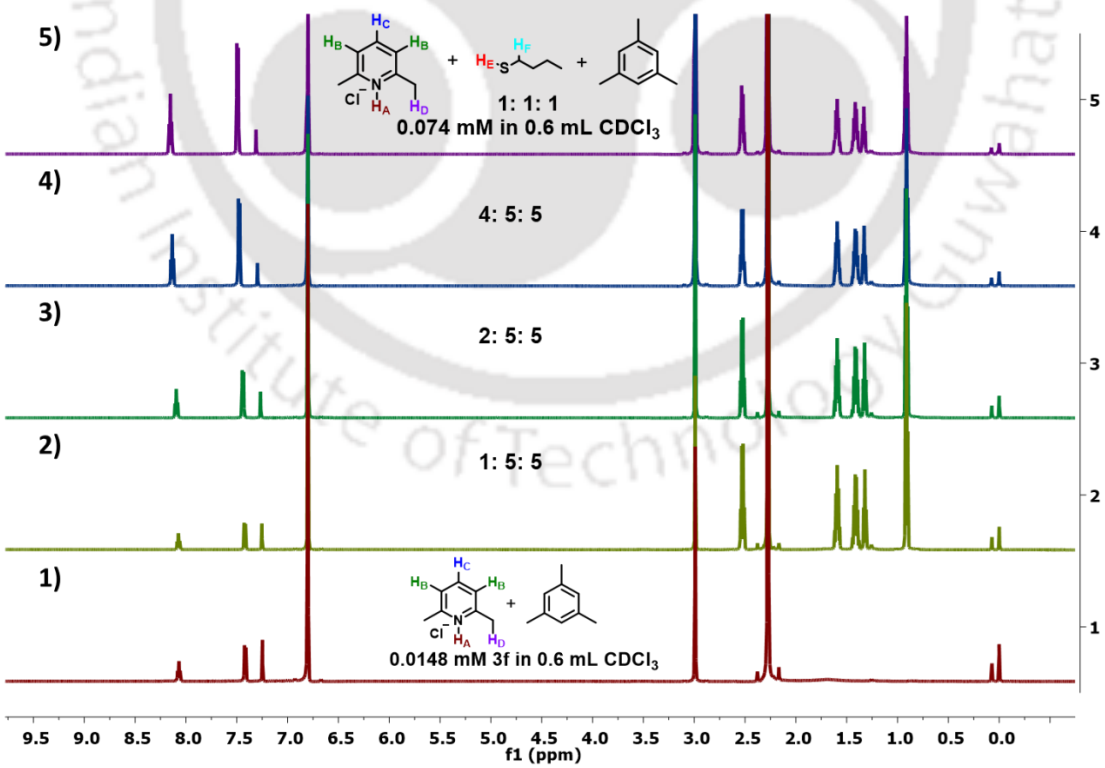
5:4:5 mixture of 1-butanethiol, TTBPy·HCl and mesitylene (0.074 mmol of mesitylene in 0.6 mL of $CDCl_3$)



1:1:1 mixture of 1-butanethiol, TTBPy·HCl and mesitylene (0.074 mmol of mesitylene in 0.6 mL of $CDCl_3$)

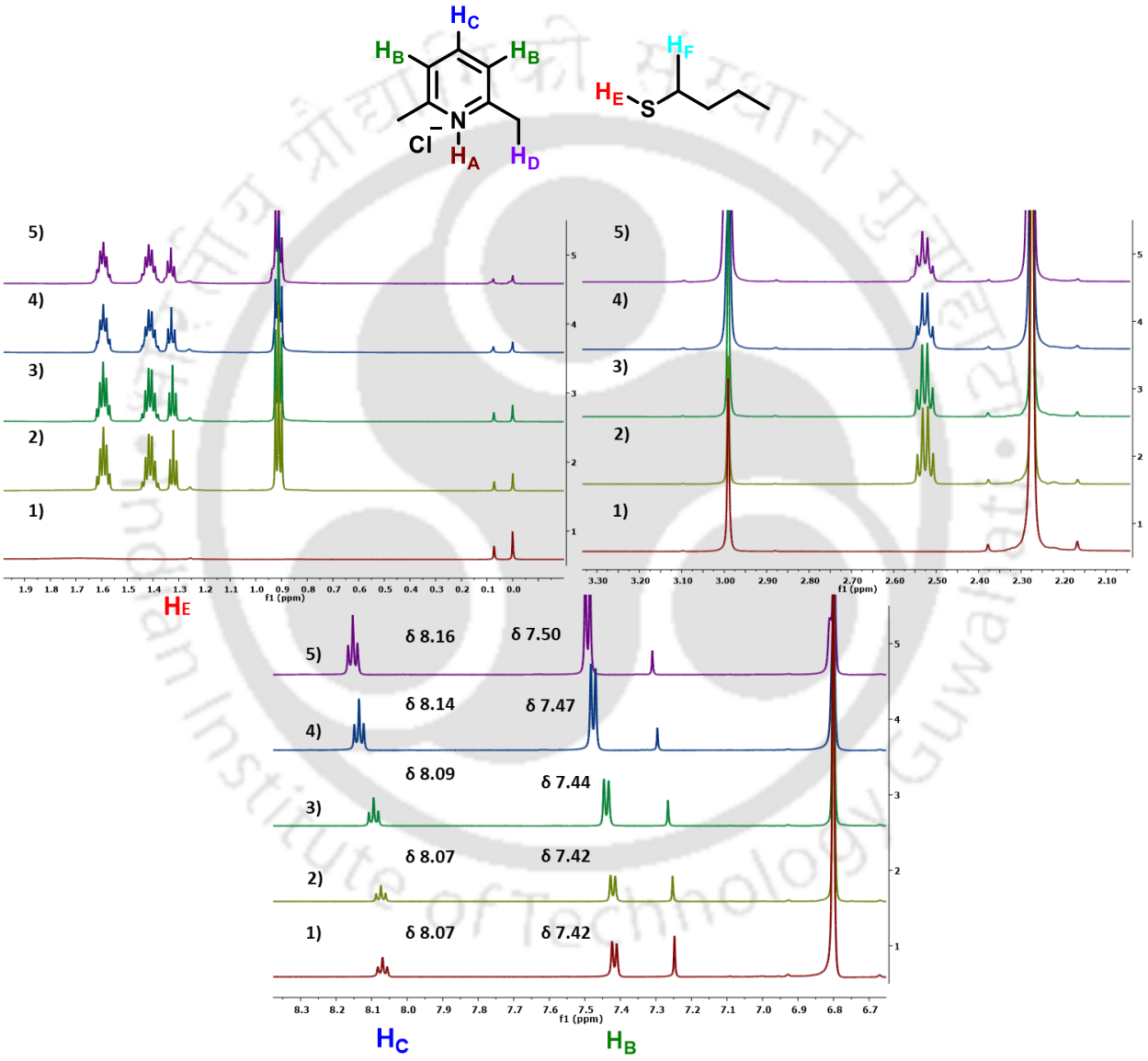


^{1}H NMR titration of lutidine.HCl with 1-butanethiol in 0.6 ml solution of $CDCl_3$

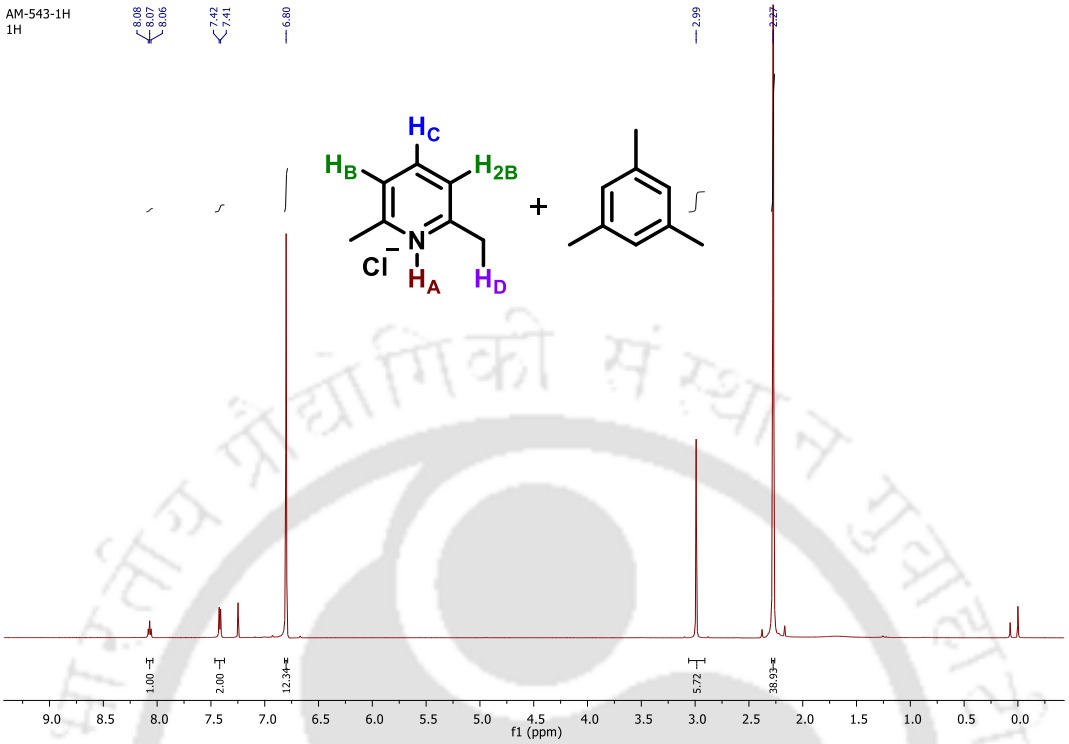


1) 0.0148 mmol of lutidine.HCl 2) 0.074 mmol of 1-butanethiol and 0.0148 mmol of lutidine.HCl 3) 0.074 mmol of 1-butanethiol and 0.0296 mmol of lutidine.HCl 4) 0.074 mmol of 1-butanethiol and 0.0592 mmol of lutidine.HCl 5) 0.074 mmol of 1-butanethiol and 0.074 mmol of lutidine.HCl. 0.074 mmol of mesitylene is used as an internal standard in all the experiments for the purpose of calibration.

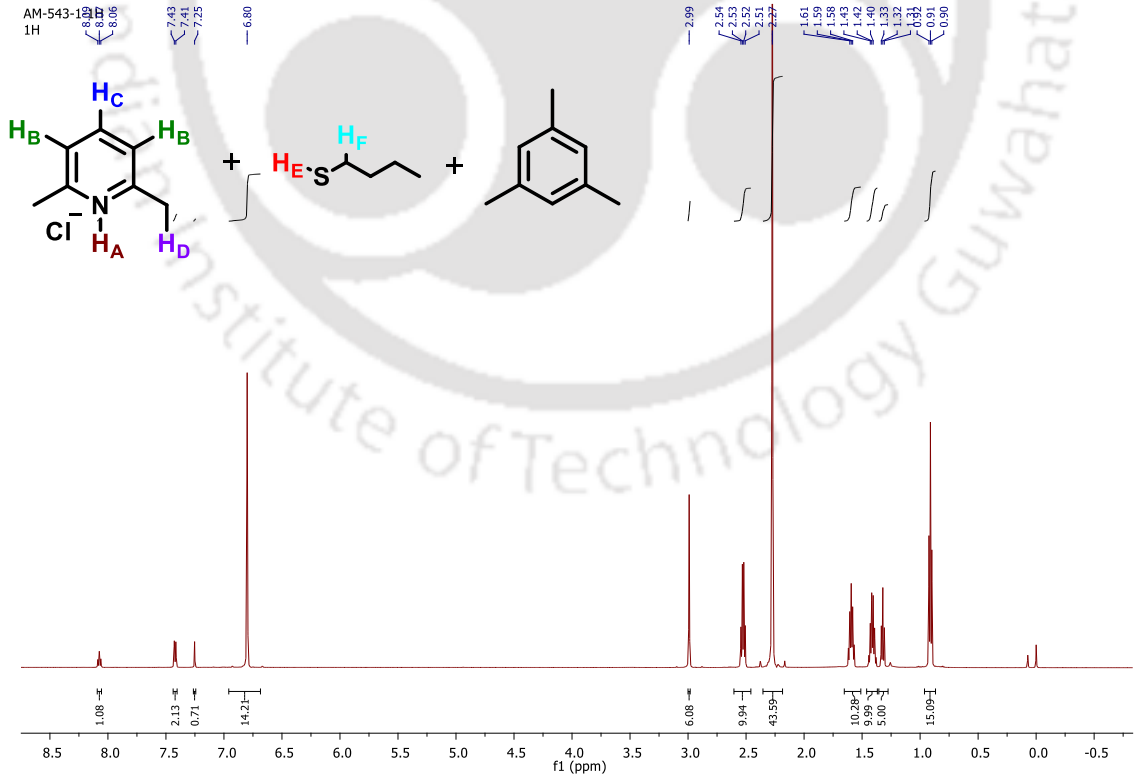
Specific regions expanded



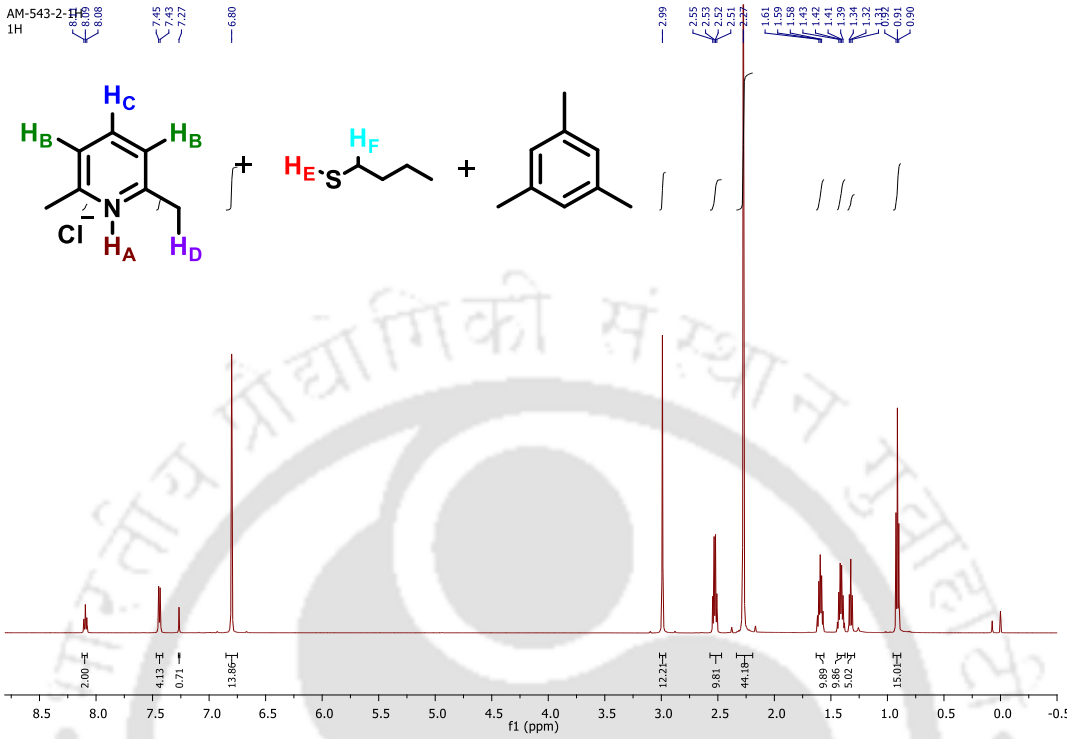
^{1}H NMR titration of 0.0148 mmol of lutidine.HCl and mesitylene (in 0.6 mL of $CDCl_3$)



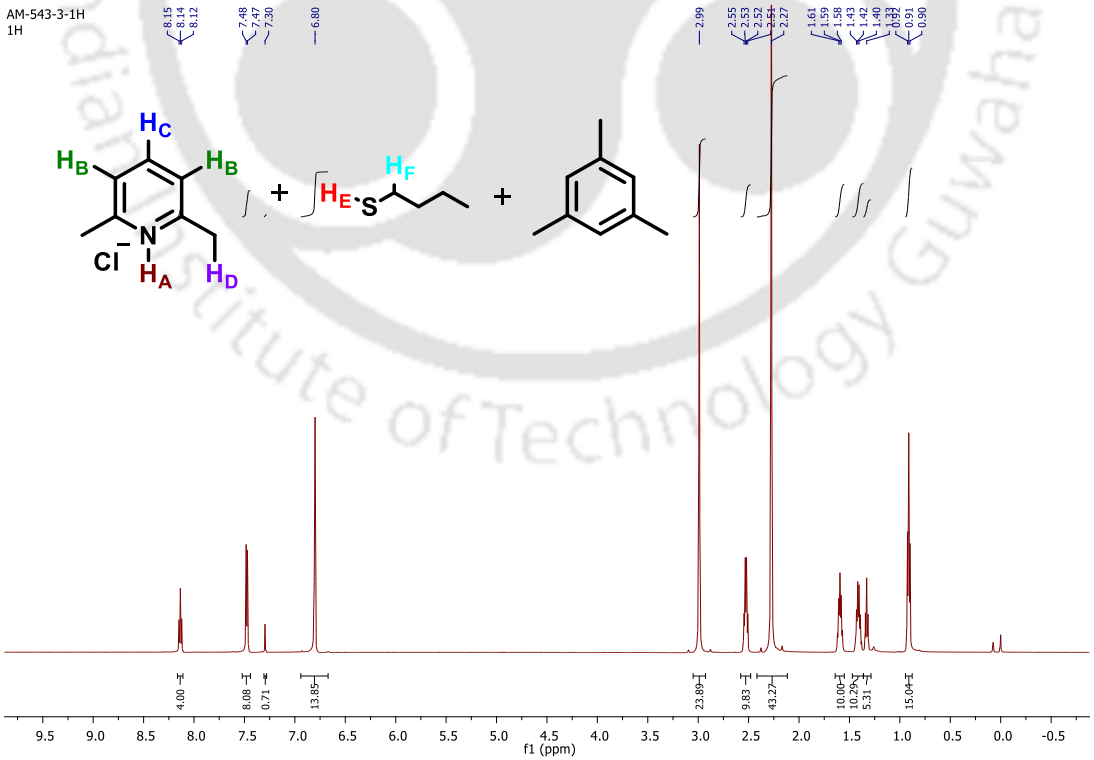
5:1:5 mixture of 1-butanethiol, lutidine.HCl and mesitylene (0.074 mmol of mesitylene in 0.6 mL of $CDCl_3$)



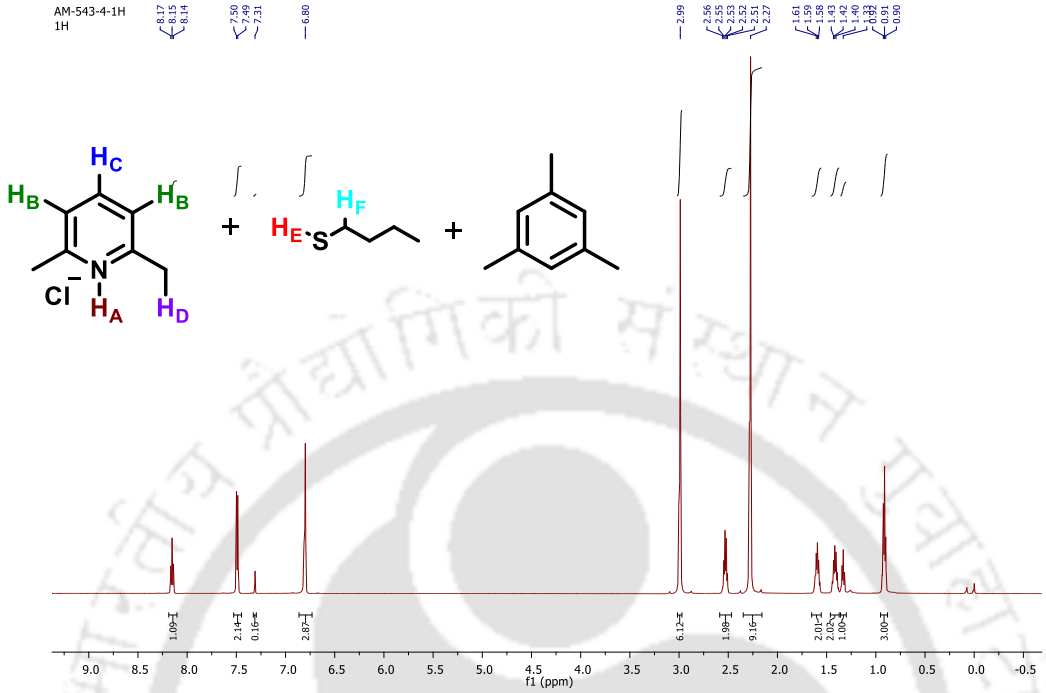
5:2:5 mixture of 1-butanethiol, lutidine.HCl and mesitylene (0.074 mmol of mesitylene in 0.6 mL of $CDCl_3$)



5:4:5 mixture of 1-butanethiol, lutidine.HCl and mesitylene (0.074 mmol of mesitylene in 0.6 mL of $CDCl_3$)

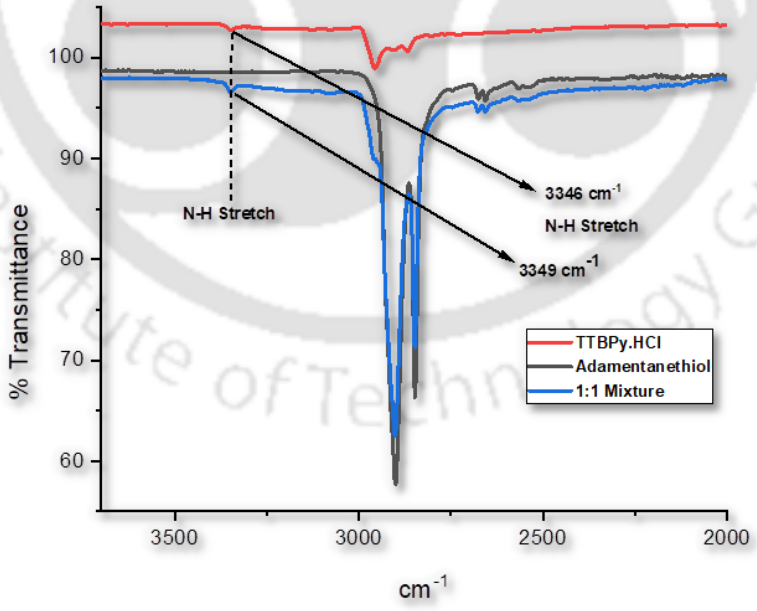


1:1:1 mixture of 1-butanethiol, lutidine.HCl and mesitylene (0.074 mmol of mesitylene in 0.6 mL of $CDCl_3$)

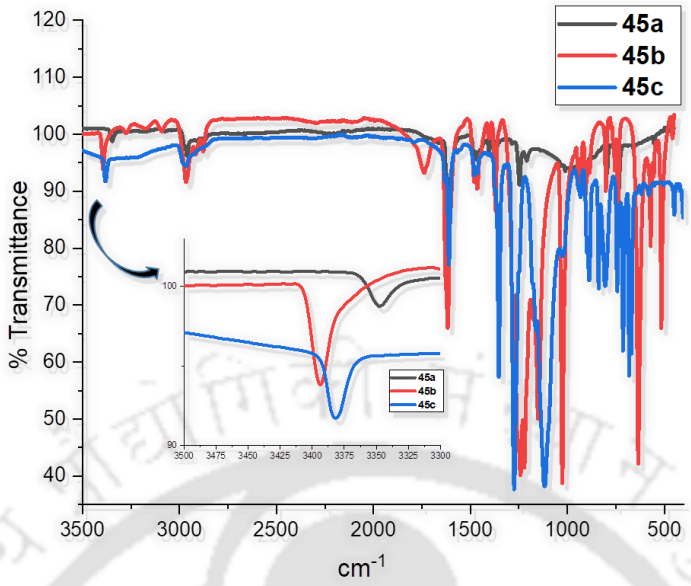


3.8.2 Study of the N-H Stretching Frequency of TTBPy·HCl from IR Spectroscopy:

IR spectrum of TTBPy·HCl catalyst, adamentanethiol and mixture of these two were recorded and their merged spectrum was presented below. The N-H stretching frequency of TTBPy·HCl was not affected in presence of adamentanethiol.



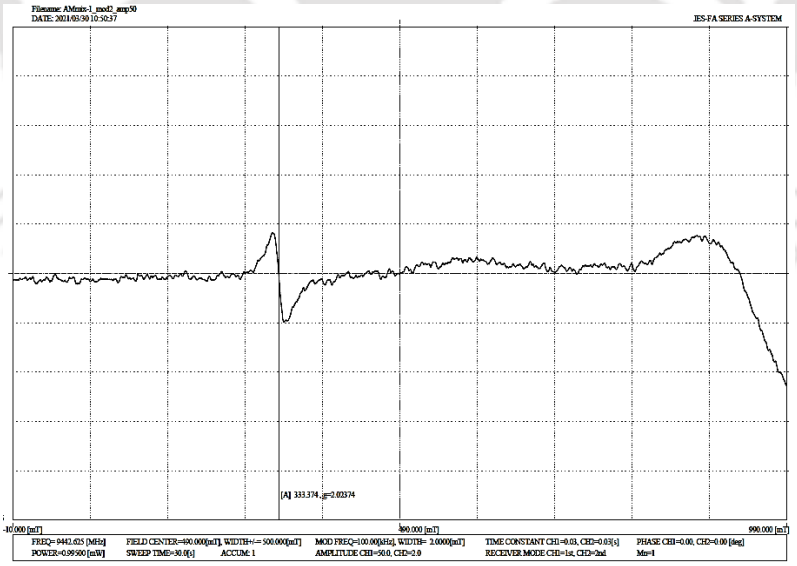
IR spectrum of TTBPy catalysts with different counter anions were merged and a hypsochromic shift of the N-H stretch with weakly coordinating anions has been observed.



3.8.3 ESR Study:

ESR spectrum of TTBPy·HCl catalyst (**45a,** 3 mg in 0.3 ml DCM) and adamentane thiol (**1b,** 1.8 mg in 0.3 ml DCM) was recorded at room temperature and both of them didn't show any signal. 1:1 mixture of **45a** and **1b** (3 mg of **45a** and 1.8 mg of **1b** in 0.3 ml DCM) gave rise to a spontaneous ESR signal at rt having g value 2.02374.

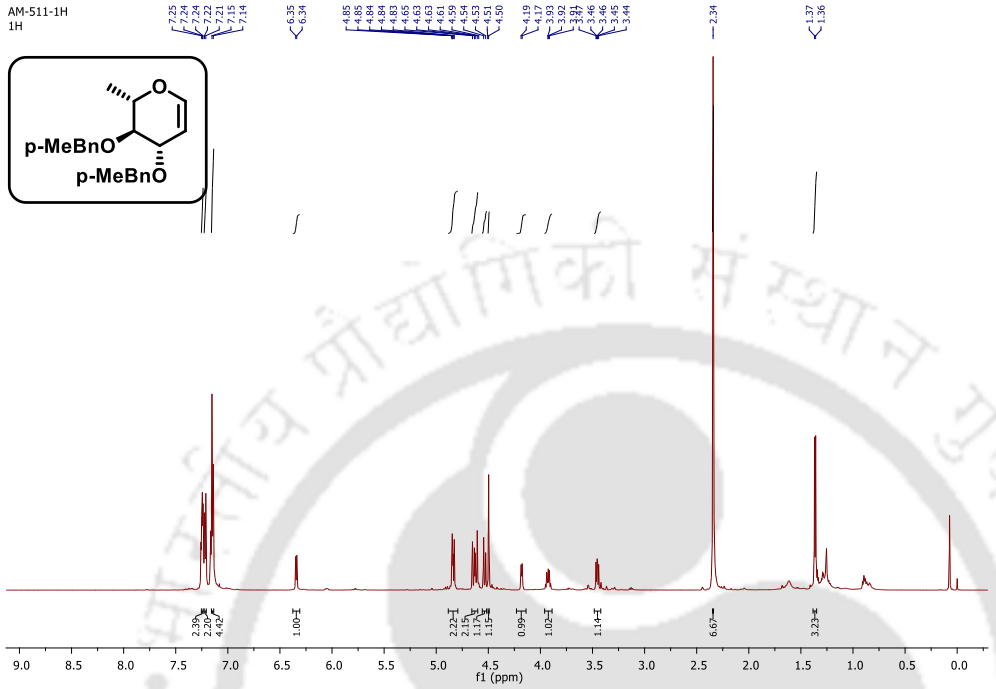
ESR Spectrum of 45a + 1b:



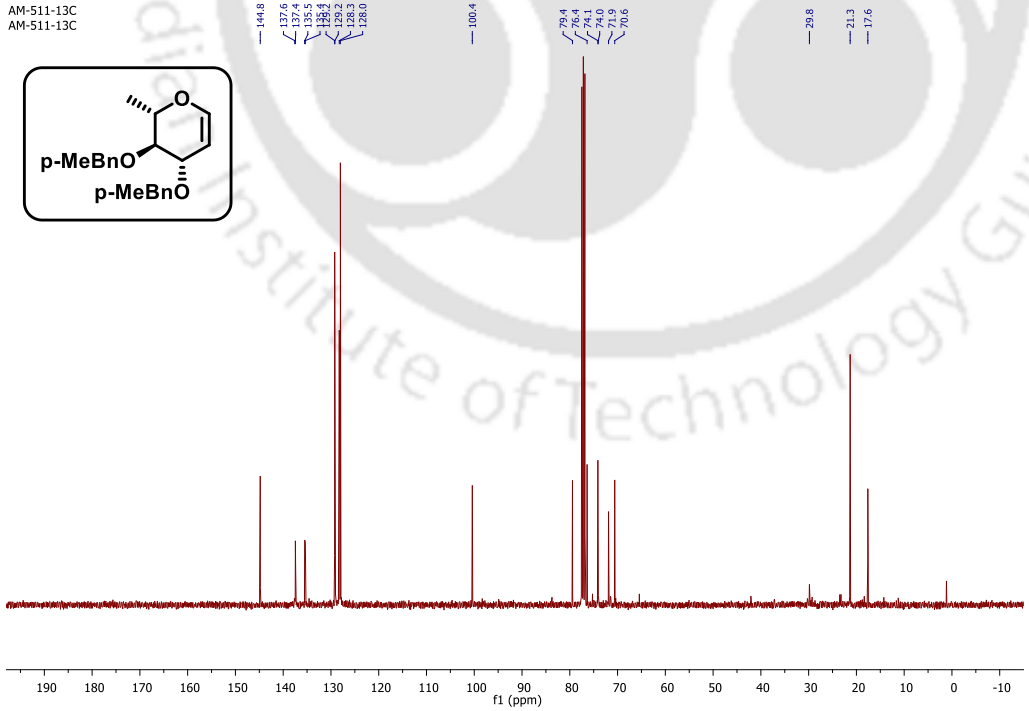
FREQ= 9442.625 mHz, FIELD CENTER=490.000 mT, WIDTH+/-= 500.000 mT, MOD FREQ=100.00 kHz, WIDTH= 2.0000 mT, TIME CONSTANT CH1=0.03, CH2=0.03 s, PHASE CH1=0.00, CH2=0.00 [deg], POWER=0.99500 mW, SWEEP TIME=30.0 s, ACCUM: 1, AMPLITUDE CH1=50.0, CH2=2.0, RECEIVER MODE CH1=1st, CH2=2nd, Mn= 1.

3.9 Spectra:

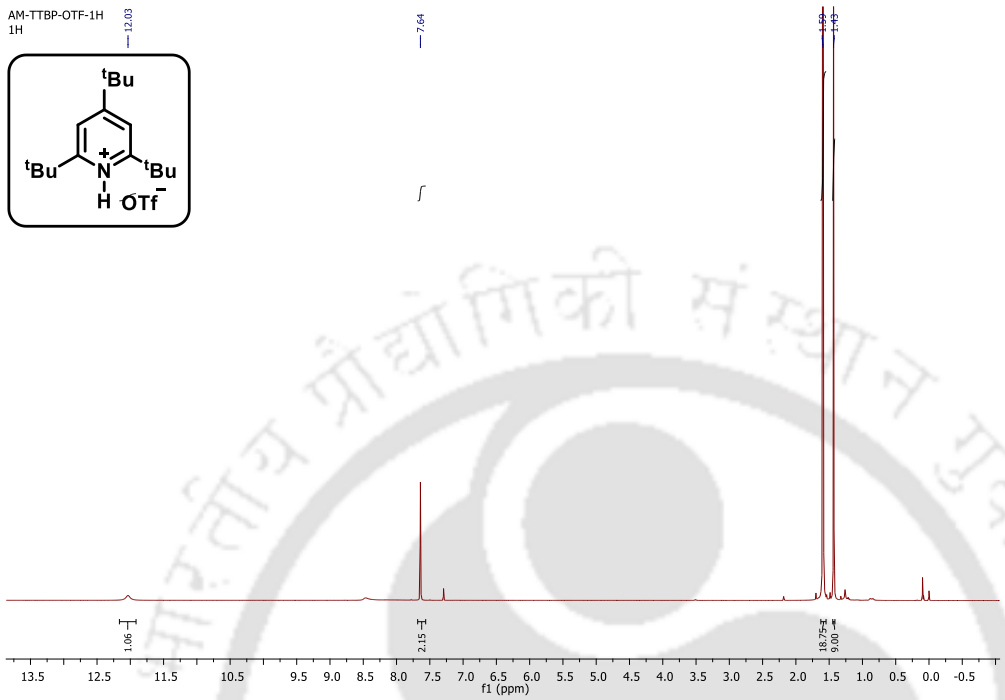
^{1}H NMR of 3,4-di-*O*-para-methylbenzyl-L-rhamnal (43g, 600 MHz, $CDCl_3$):



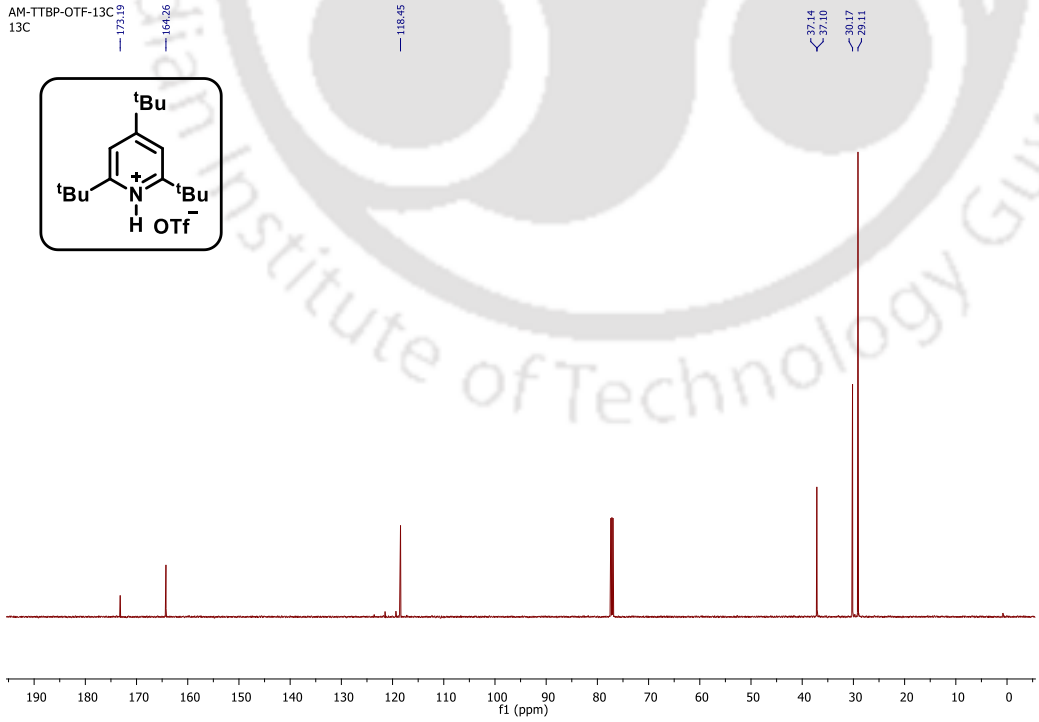
^{13}C{^{1}H} NMR of 3,4-di-*O*-para-methylbenzyl-L-rhamnal (43g, 400 MHz, $CDCl_3$):



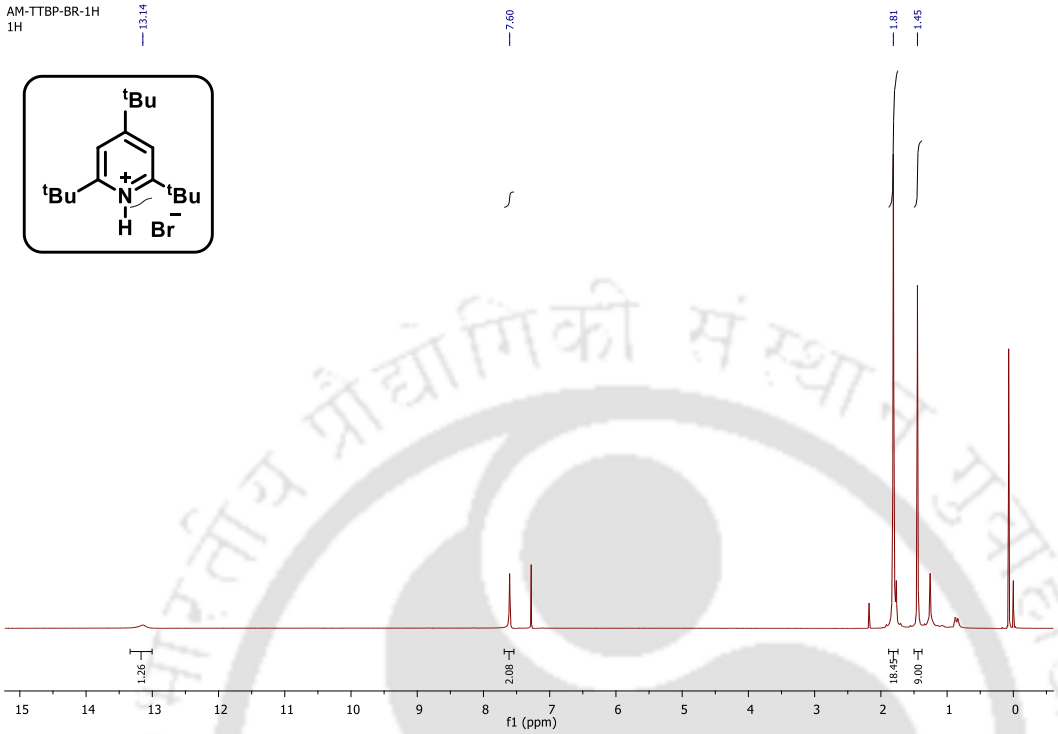
^{1}H NMR of 2,4,6-tri-tertiary-butylpyridinium trifluoromethanesulfonate salt (45b, 600 MHz, $CDCl_3$):



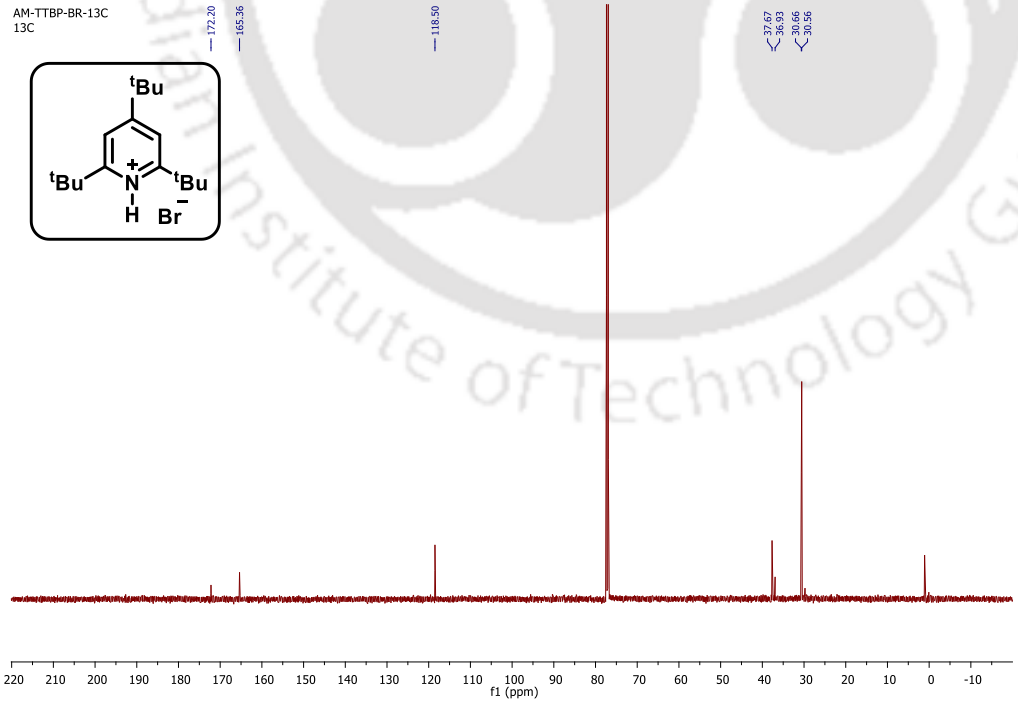
^{13}C{^{1}H} NMR of 2,4,6-tri-tertiary-butylpyridinium trifluoromethanesulfonate salt (45b, 600 MHz, $CDCl_3$):



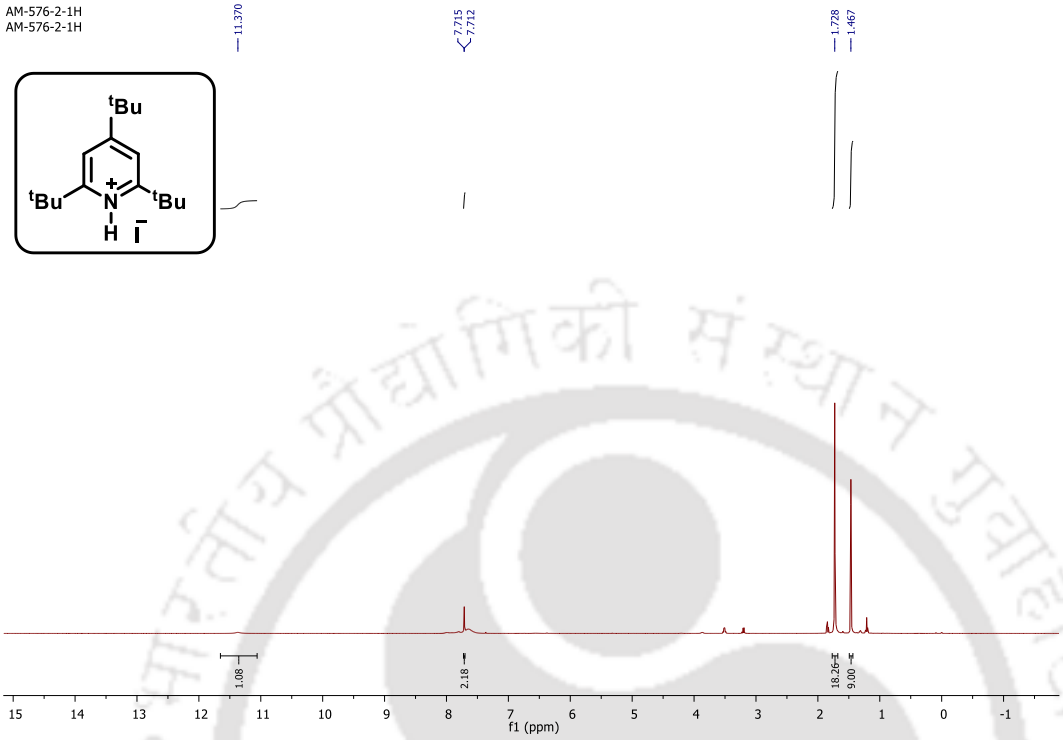
^{1}H NMR of 2,4,6-tri-tertiary-butylpyridinium hydrobromide salt (45g, 600 MHz, $CDCl_3$):



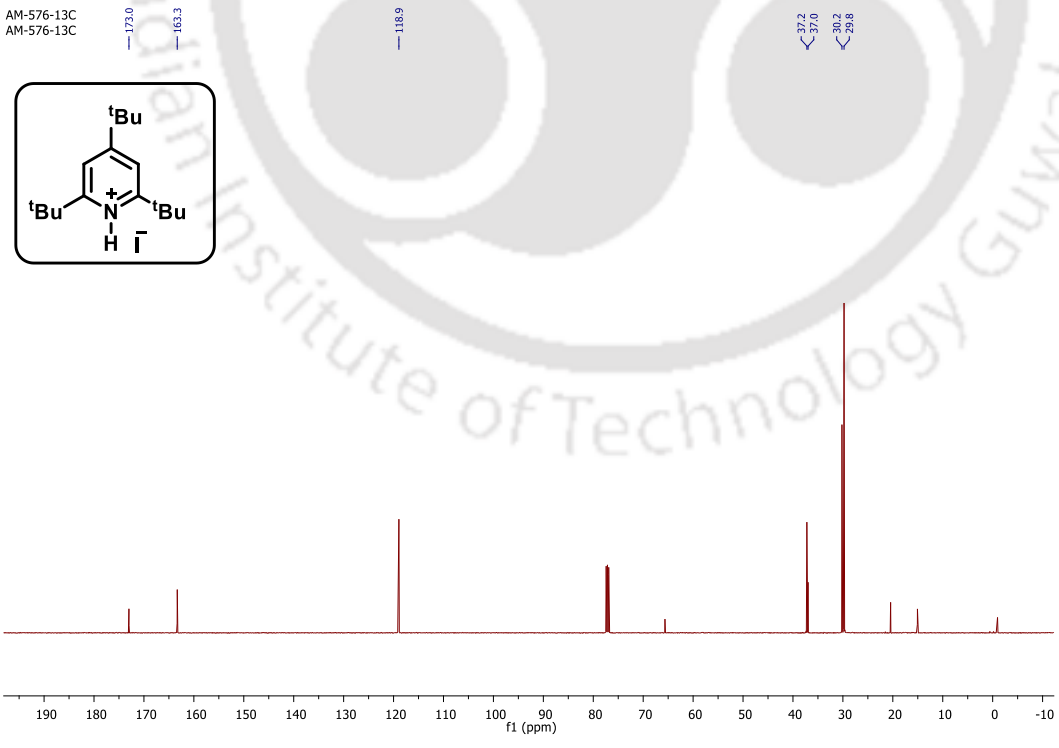
^{13}C{^{1}H} NMR of 2,4,6-tri-tertiary-butylpyridinium hydrobromide salt (45g, 600 MHz, $CDCl_3$):



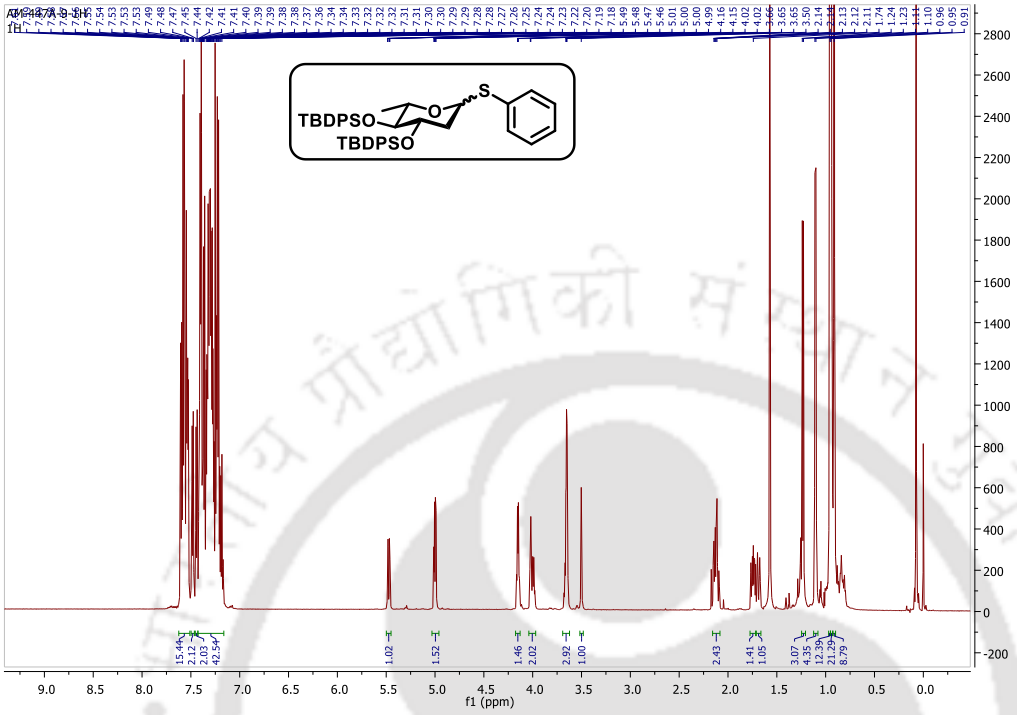
^{1}H NMR of 2,4,6-tri-tertiary-butylpyridinium hydriodide salt (45h, 500 MHz, $CDCl_3$):



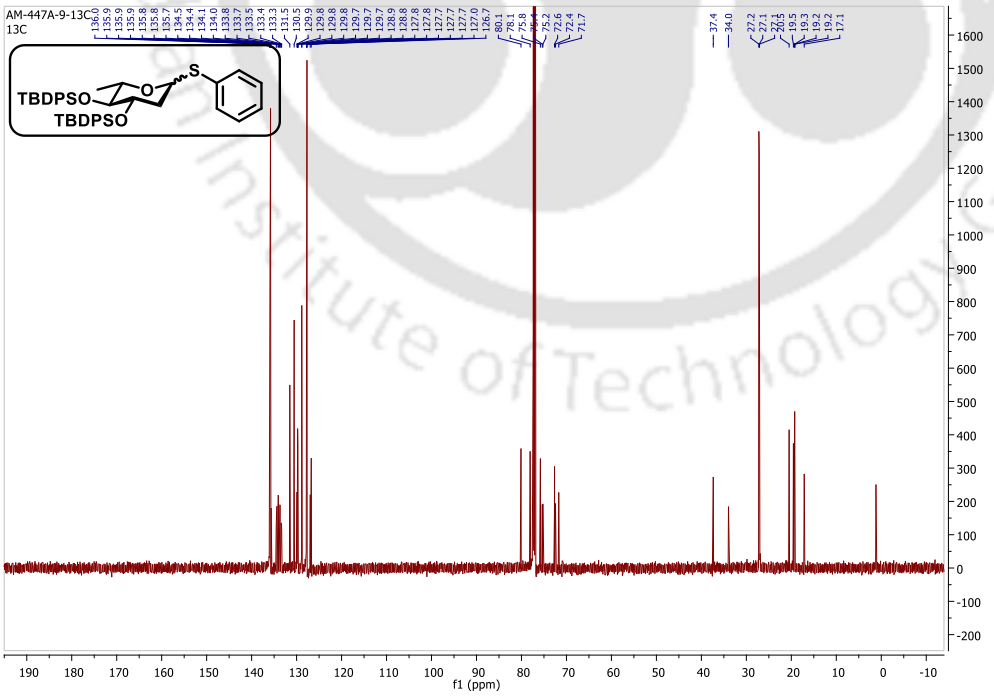
^{13}C{^{1}H} NMR of 2,4,6-tri-tertiary-butylpyridinium hydriodide salt (45h, 500 MHz, $CDCl_3$):



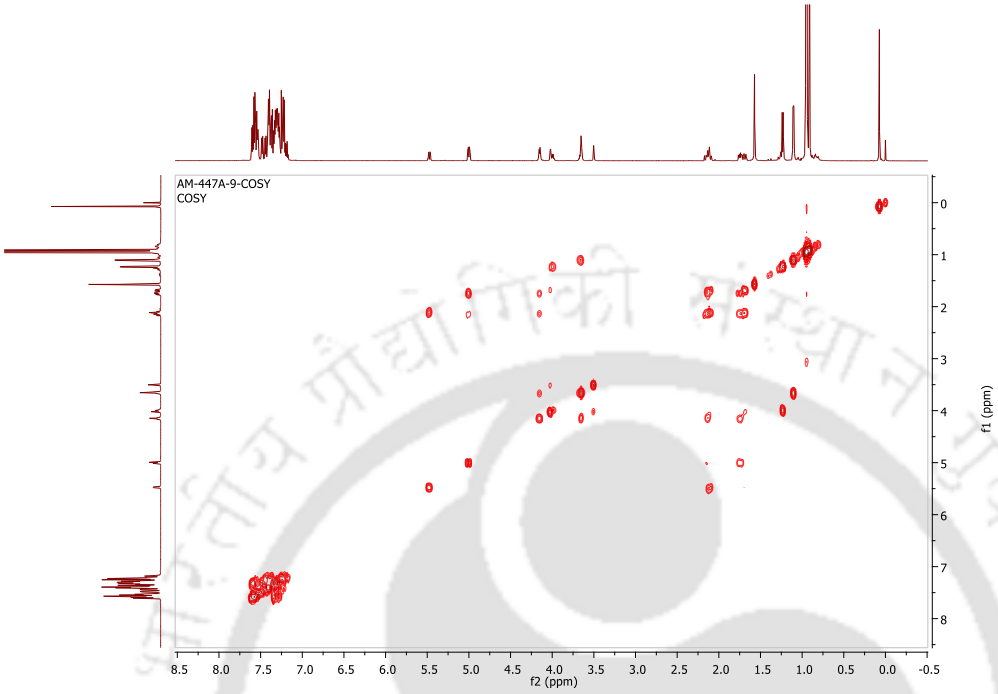
^{1}H NMR of Phenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46a, 600 MHz, $CDCl_3$):



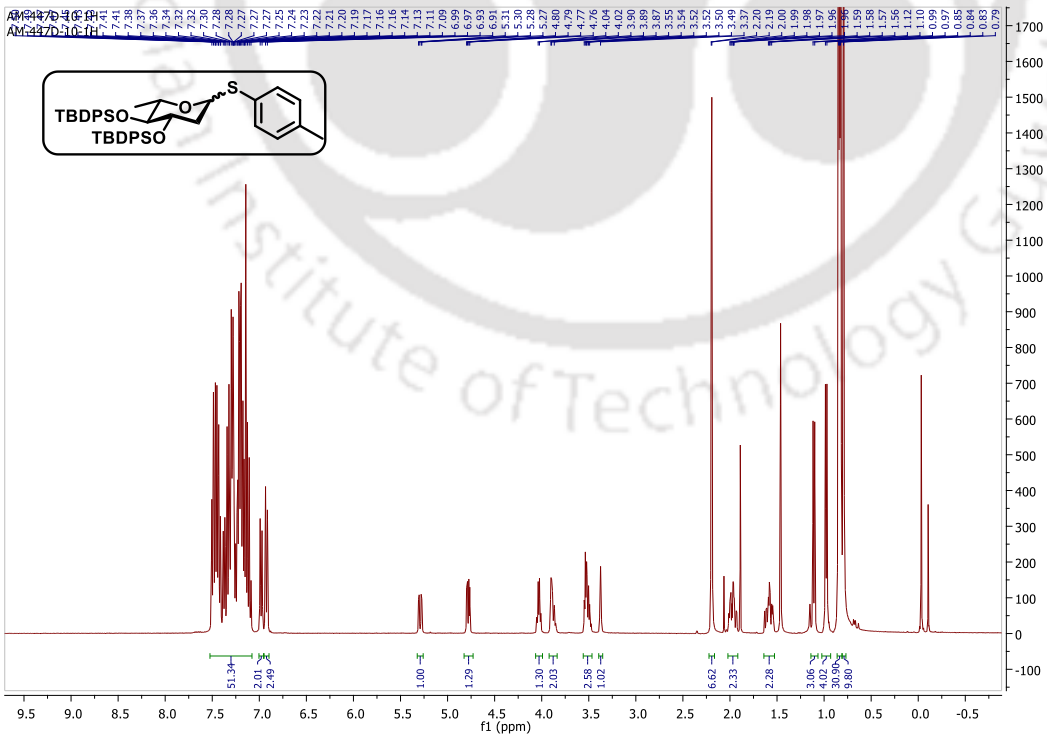
^{13}C{^{1}H} NMR of Phenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46a, 600 MHz, $CDCl_3$):



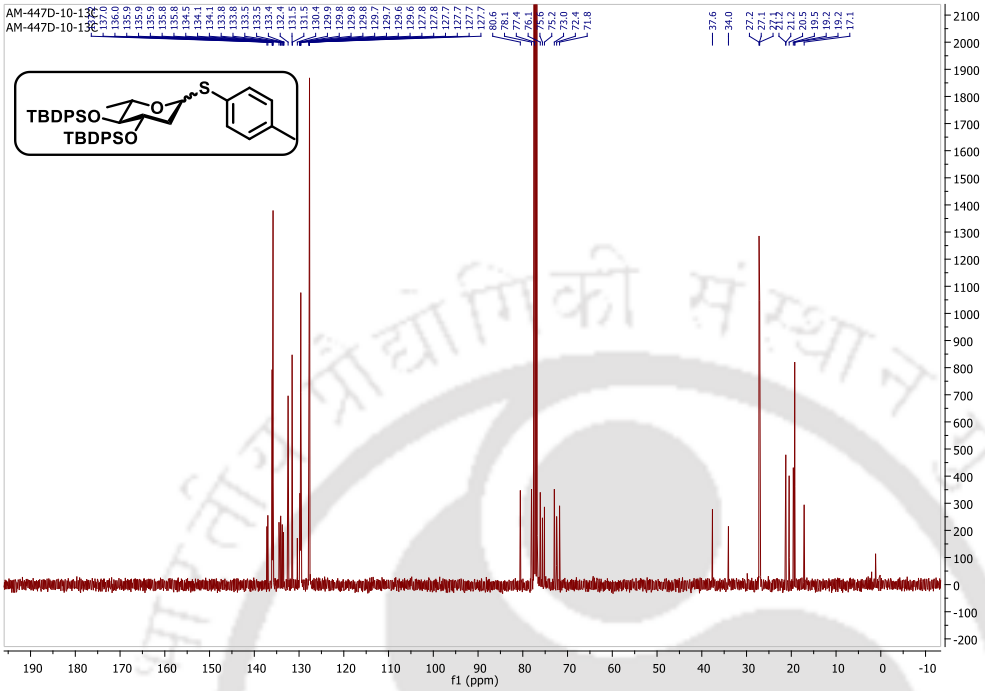
COSY NMR of Phenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46a, 600 MHz, $CDCl_3$):



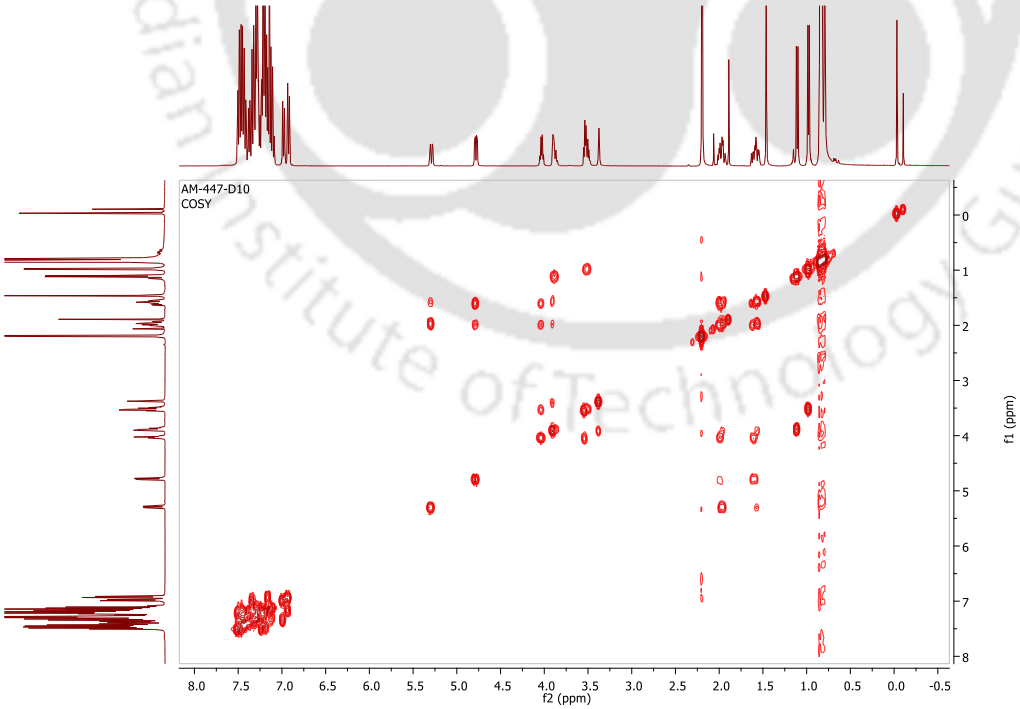
^{1}H NMR of Tolyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46b, 400 MHz, $CDCl_3$):



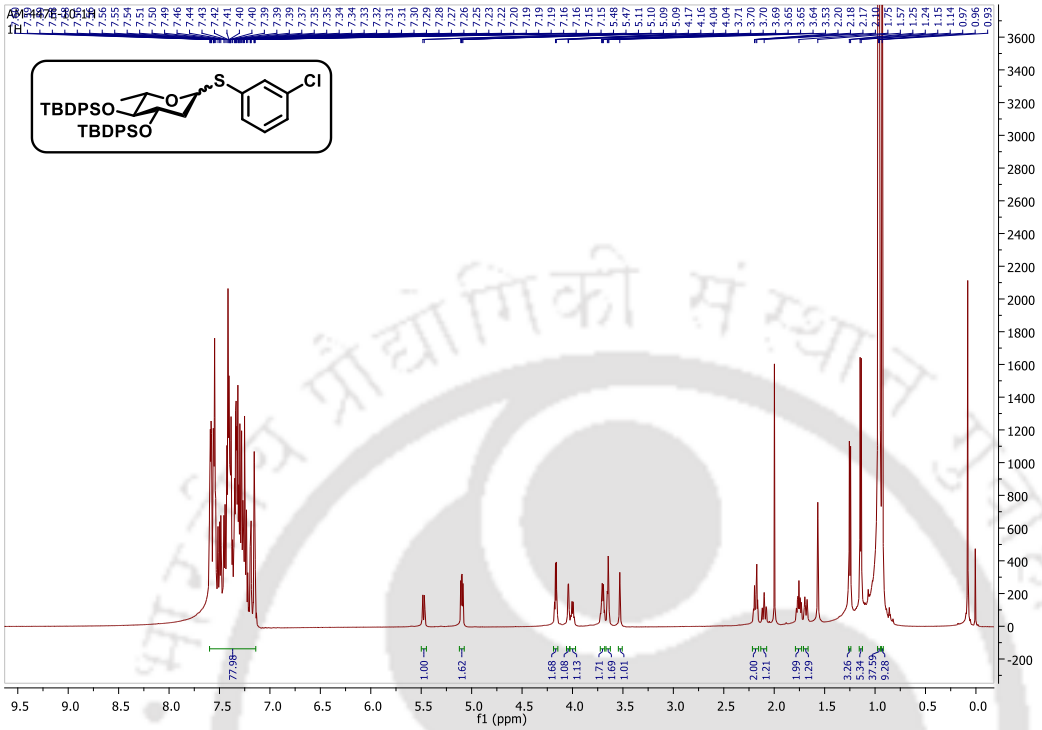
$^{13}C\{^{1}H\}$ NMR of Tolyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46b, 400 MHz, $CDCl_3$):



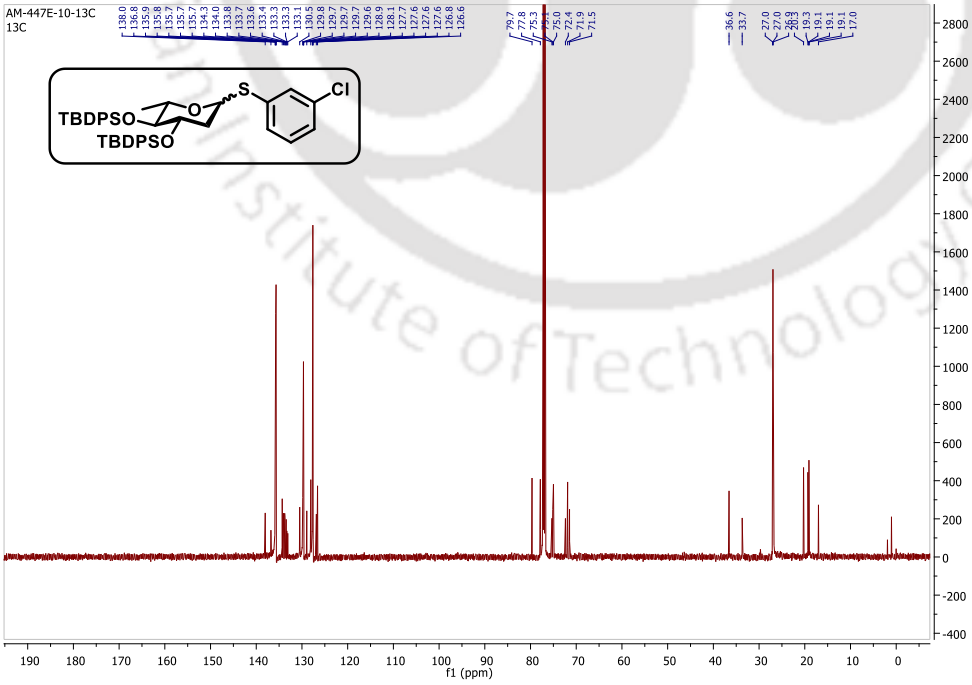
COSY NMR of Tolyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46b, 400 MHz, $CDCl_3$):



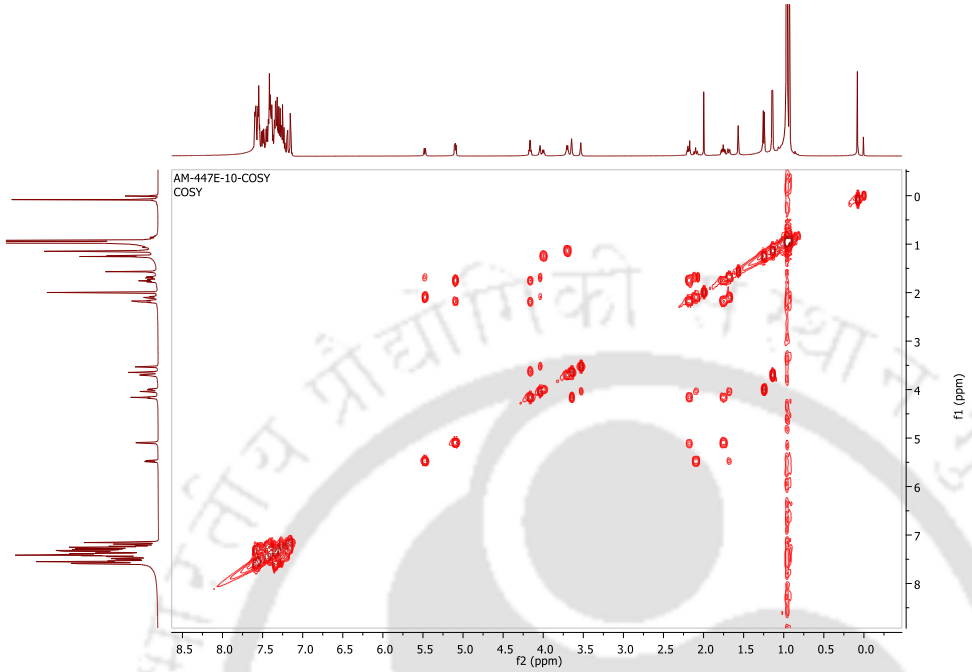
^{1}H NMR of 3-Chlorophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46c, 600 MHz, $CDCl_3$):



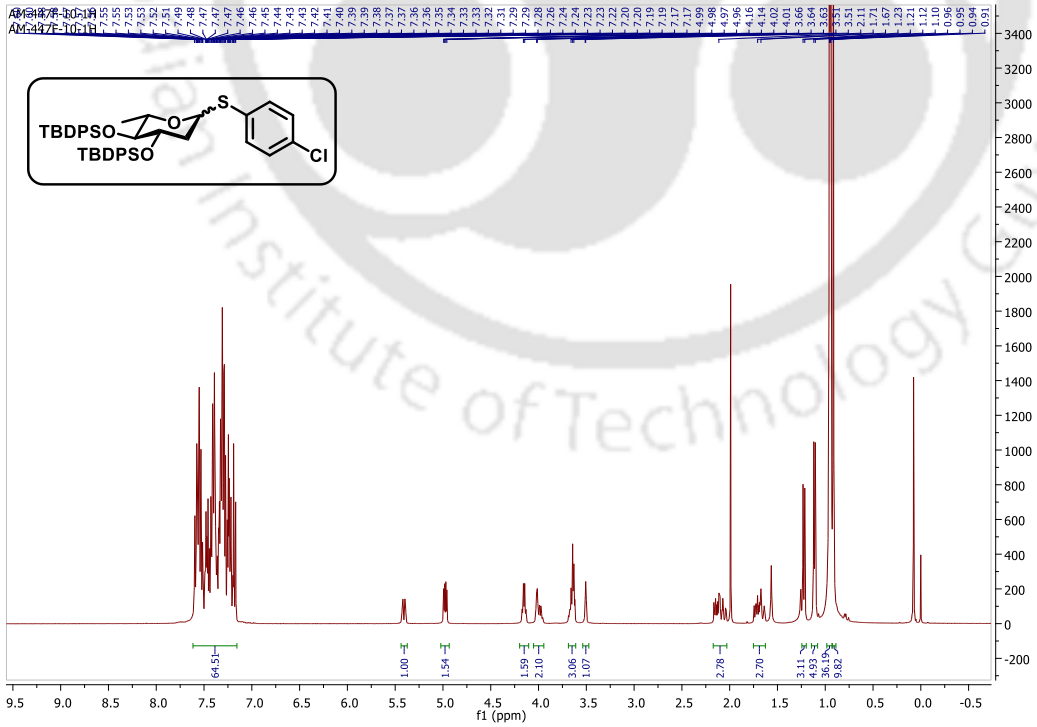
^{13}C{^{1}H} NMR of 3-Chlorophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46c, 600 MHz, $CDCl_3$):



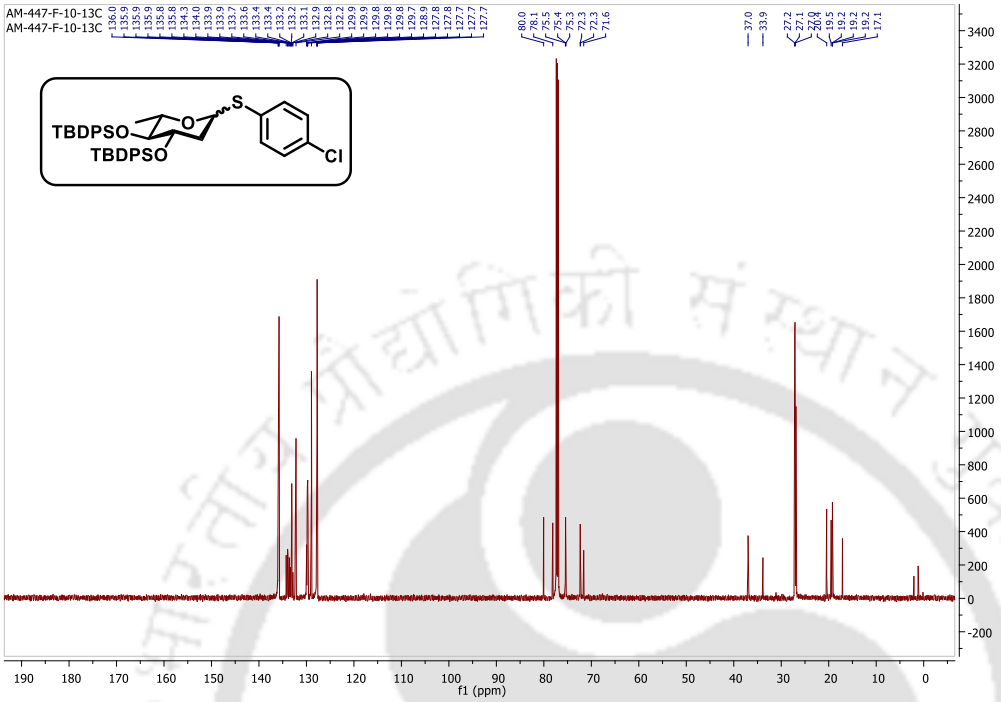
COSY NMR of 3-Chlorophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46c, 600 MHz, $CDCl_3$):



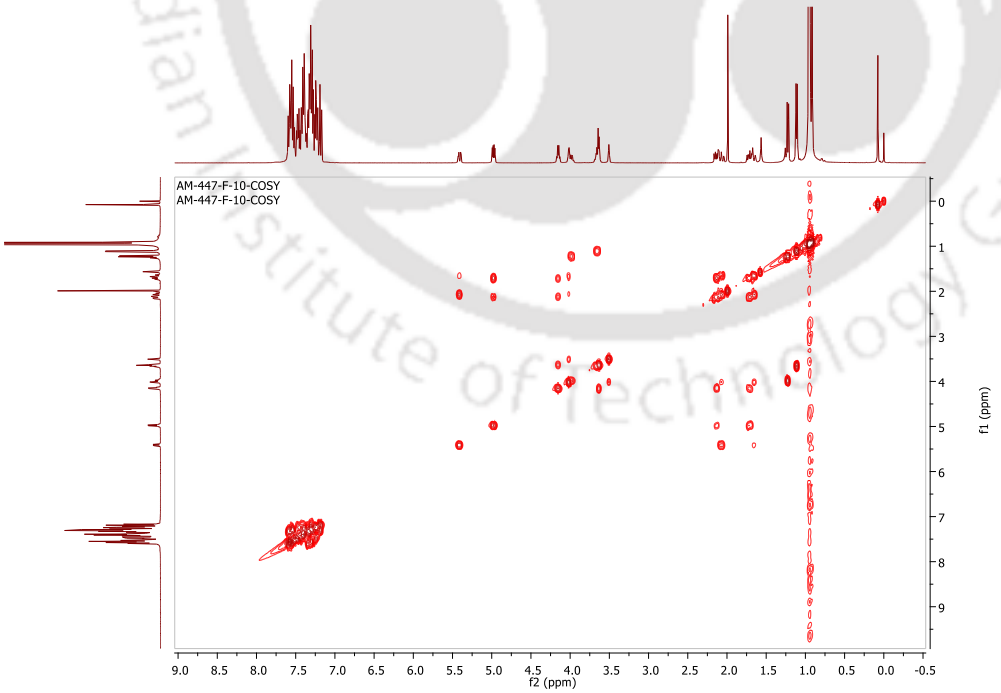
^{1}H NMR of 4-Chlorophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46d, 400 MHz, $CDCl_3$):



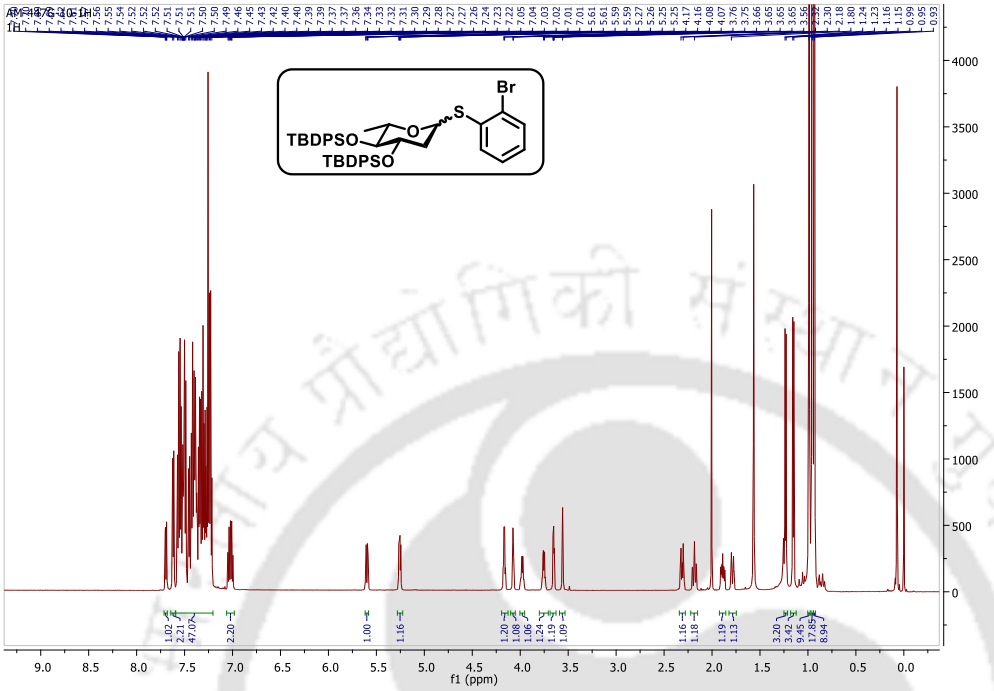
$^{13}C\{^{1}H\}$ NMR of 4-Chlorophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46d, 600 MHz, $CDCl_3$):



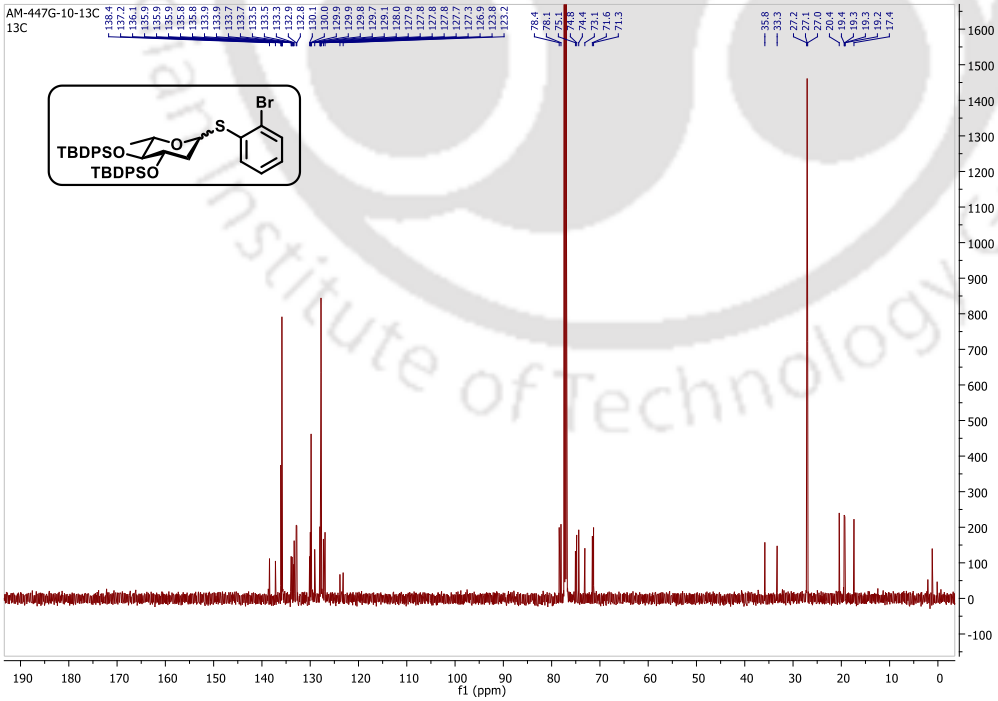
COSY NMR of 4-Chlorophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46d, 400 MHz, $CDCl_3$):



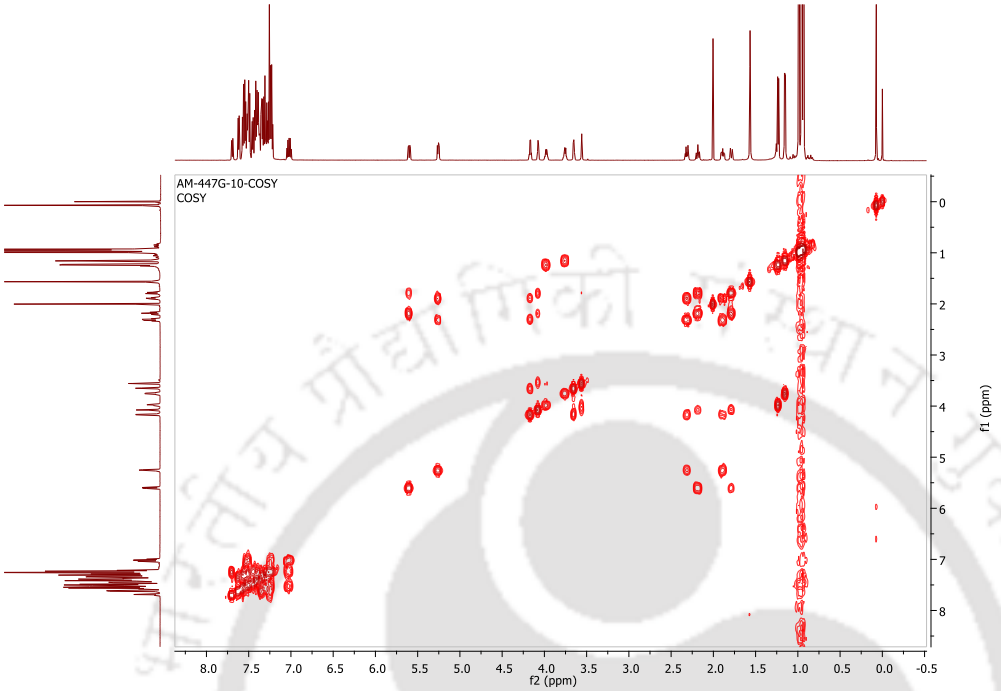
^{1}H NMR of 2-Bromophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46e, 600 MHz, $CDCl_3$):



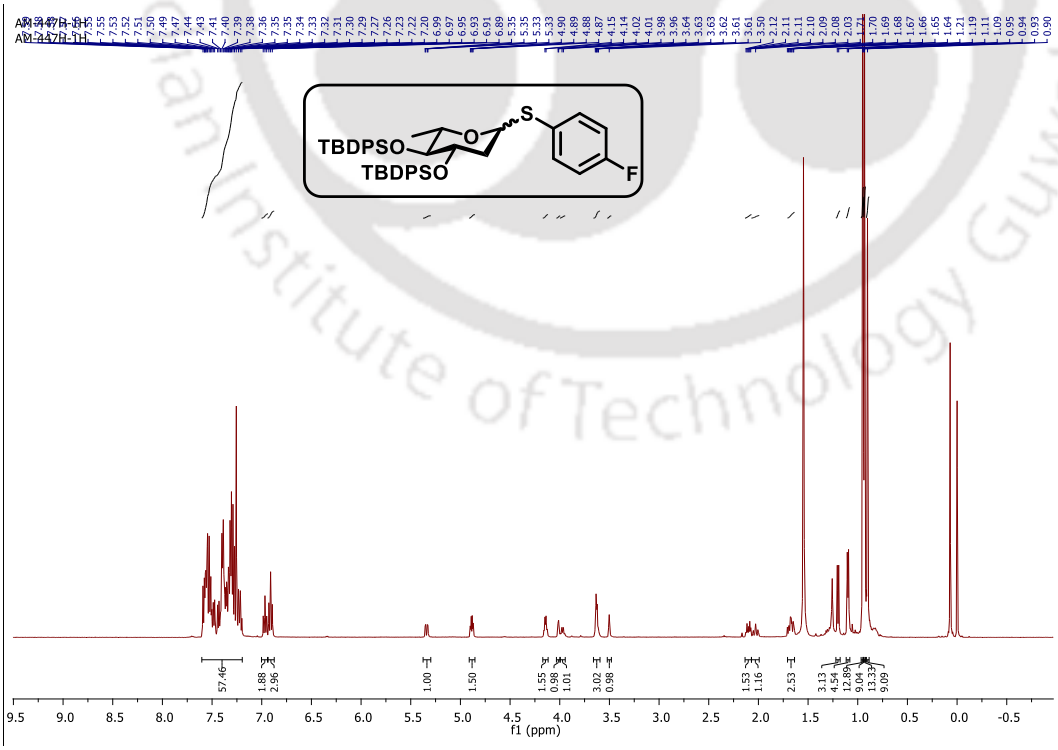
^{13}C{^{1}H} NMR of 2-Bromophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46e, 600 MHz, $CDCl_3$):



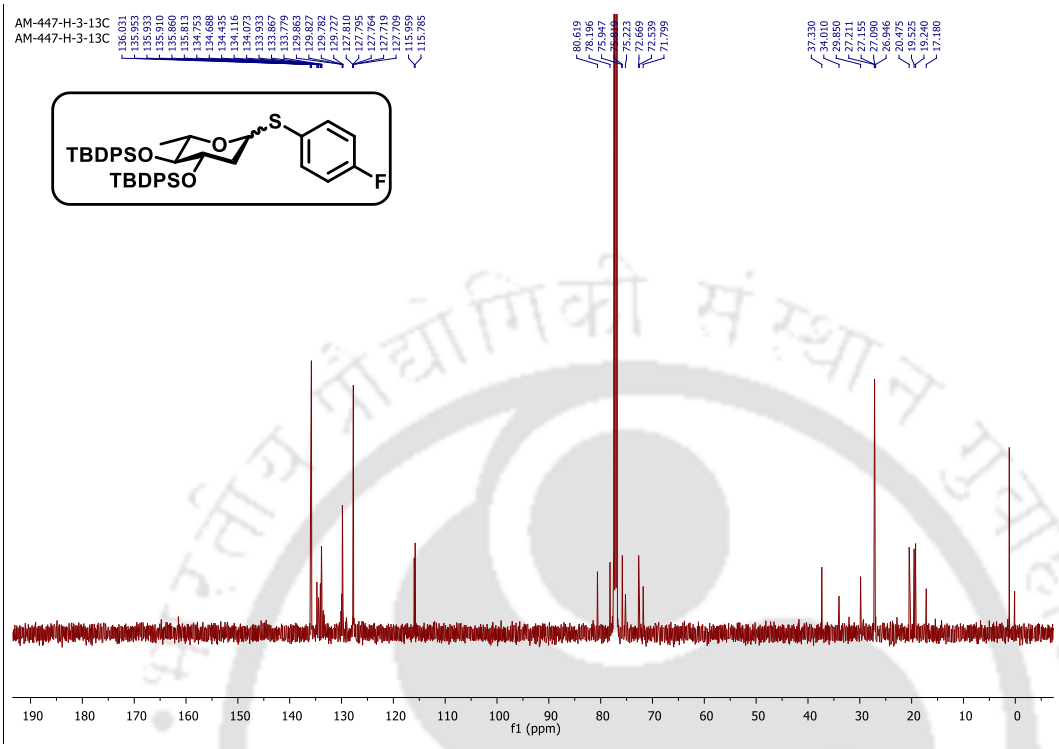
COSY NMR of 2-Bromophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46e, 600 MHz, $CDCl_3$):



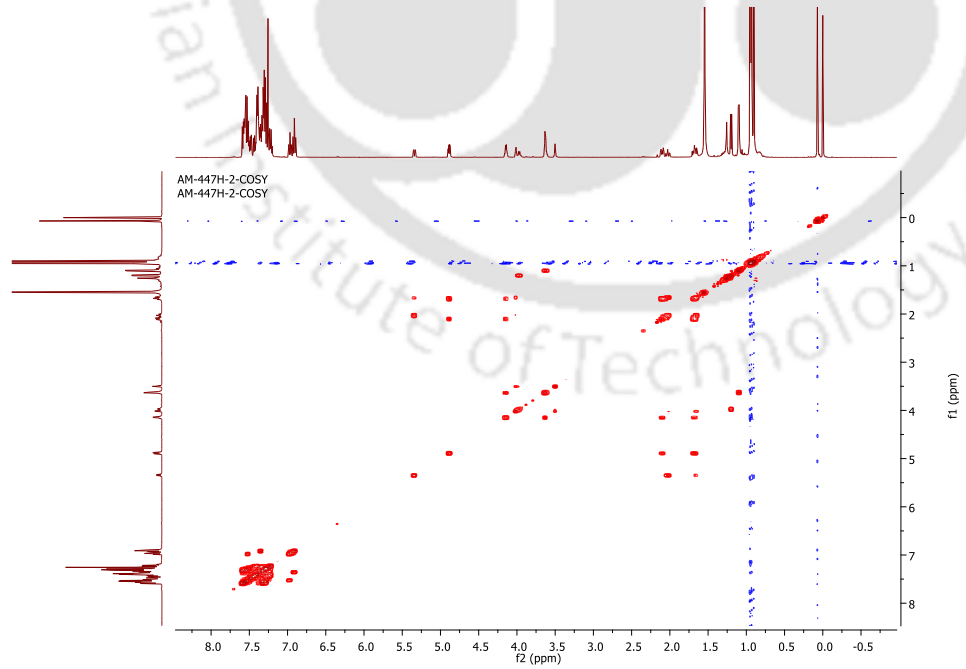
^{1}H NMR of 4-Fluorophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46f, 500 MHz, $CDCl_3$):



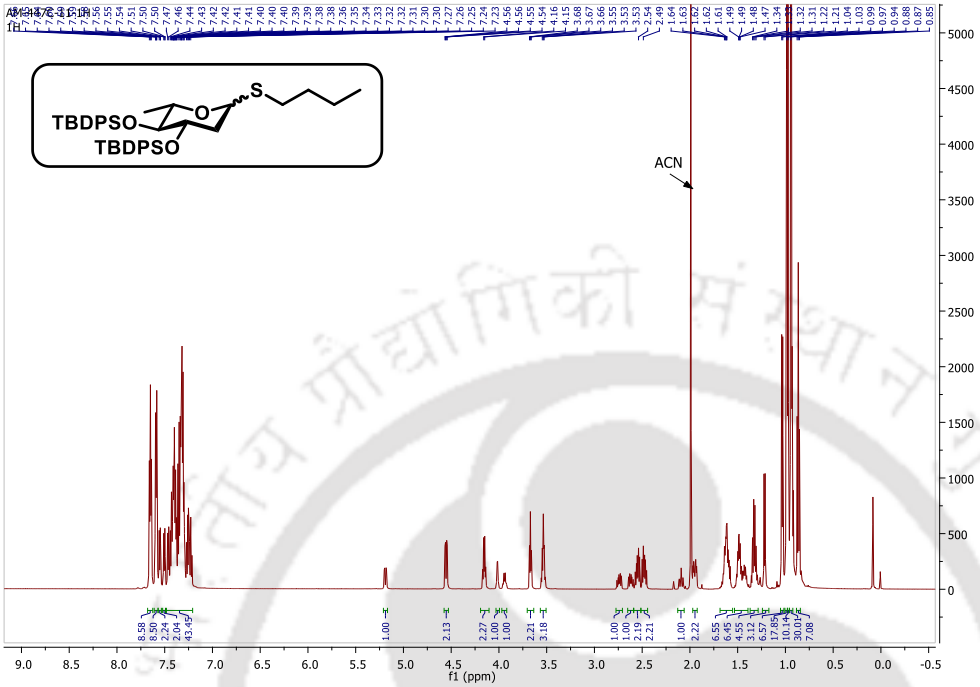
$^{13}C\{^{1}H\}$ NMR of 4-Fluorophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46f, 500 MHz, $CDCl_3$):



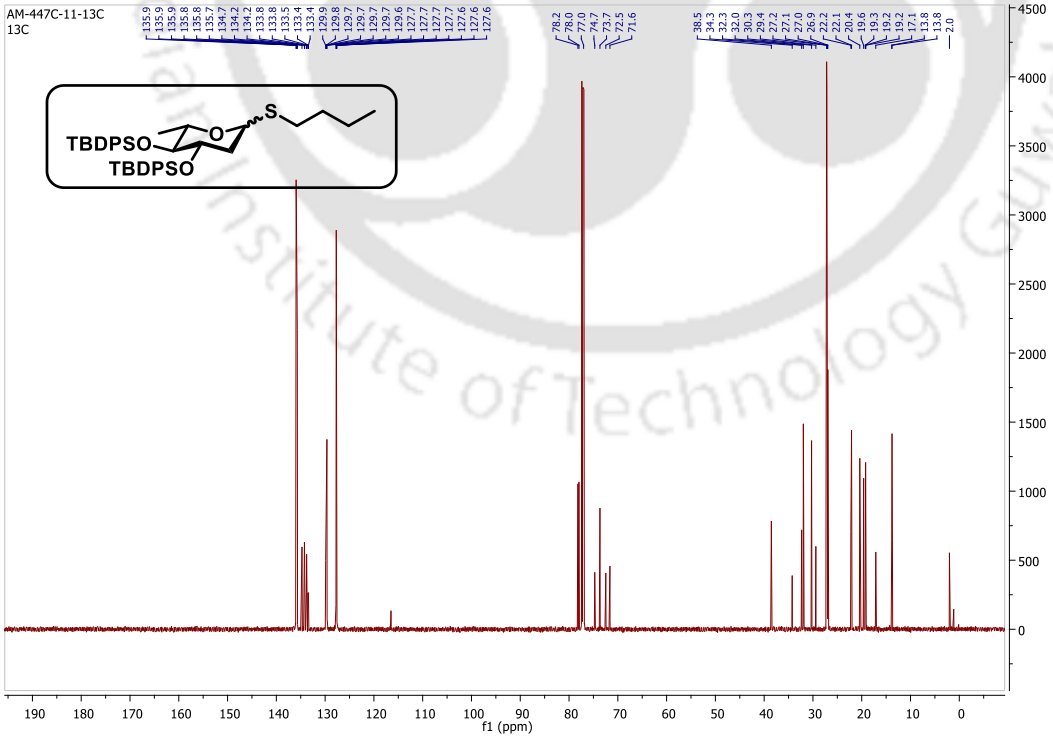
COSY NMR of 4-Fluorophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46f, 500 MHz, $CDCl_3$):



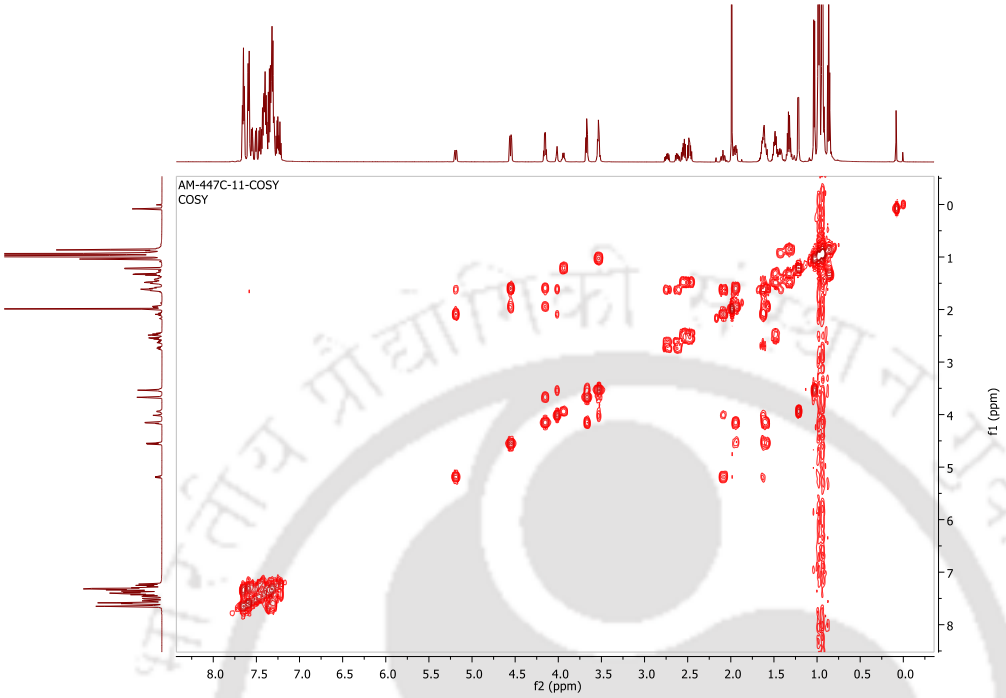
^{1}H NMR of Butyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46g, 600 MHz, $CDCl_3$):



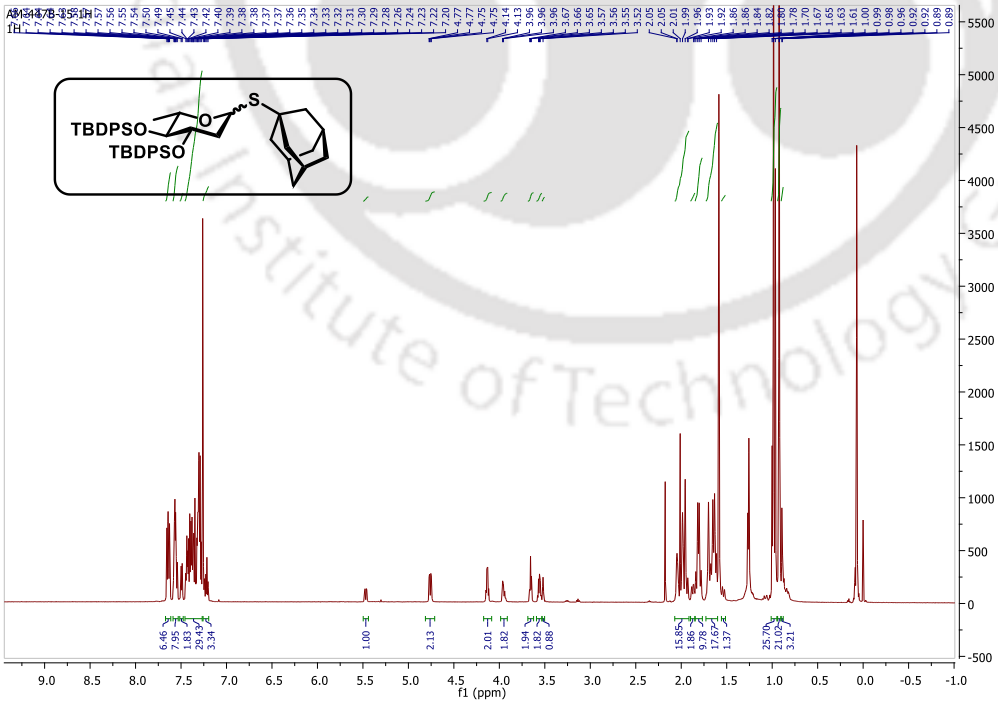
^{13}C{^{1}H} NMR of Butyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46g, 600 MHz, $CDCl_3$):



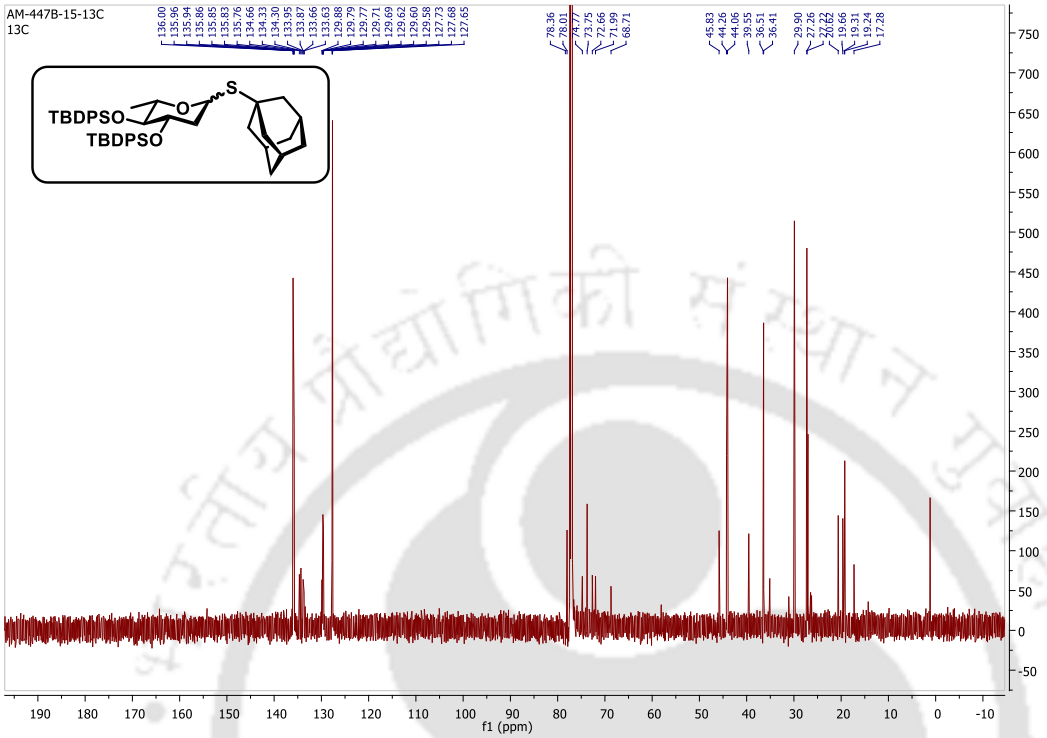
COSY NMR of Butyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46g, 600 MHz, $CDCl_3$):



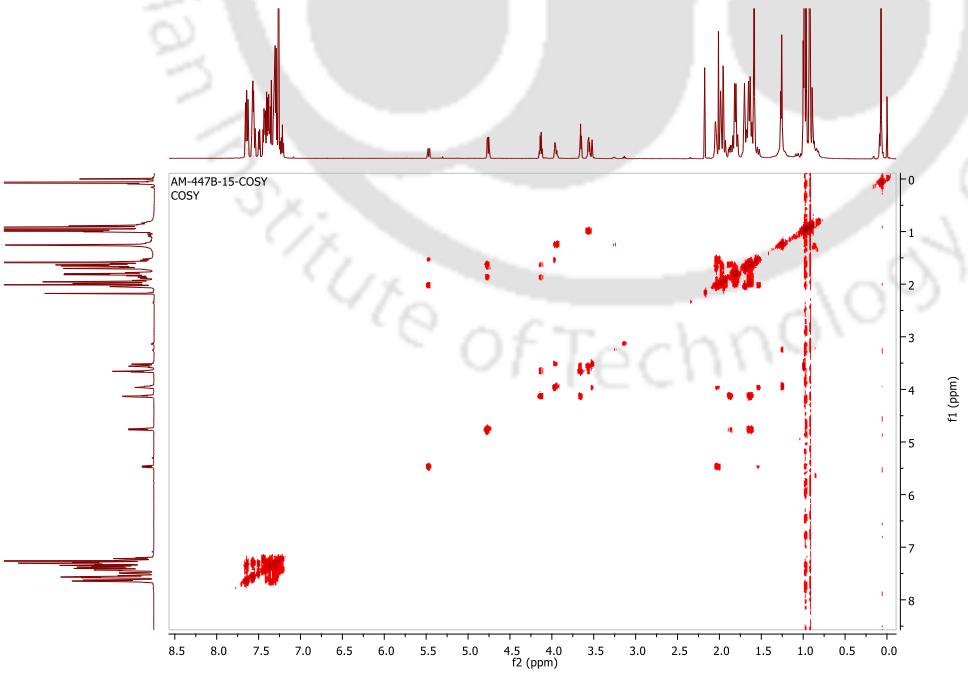
^{1}H NMR of 1-Adamantanyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46h, 600 MHz, $CDCl_3$):



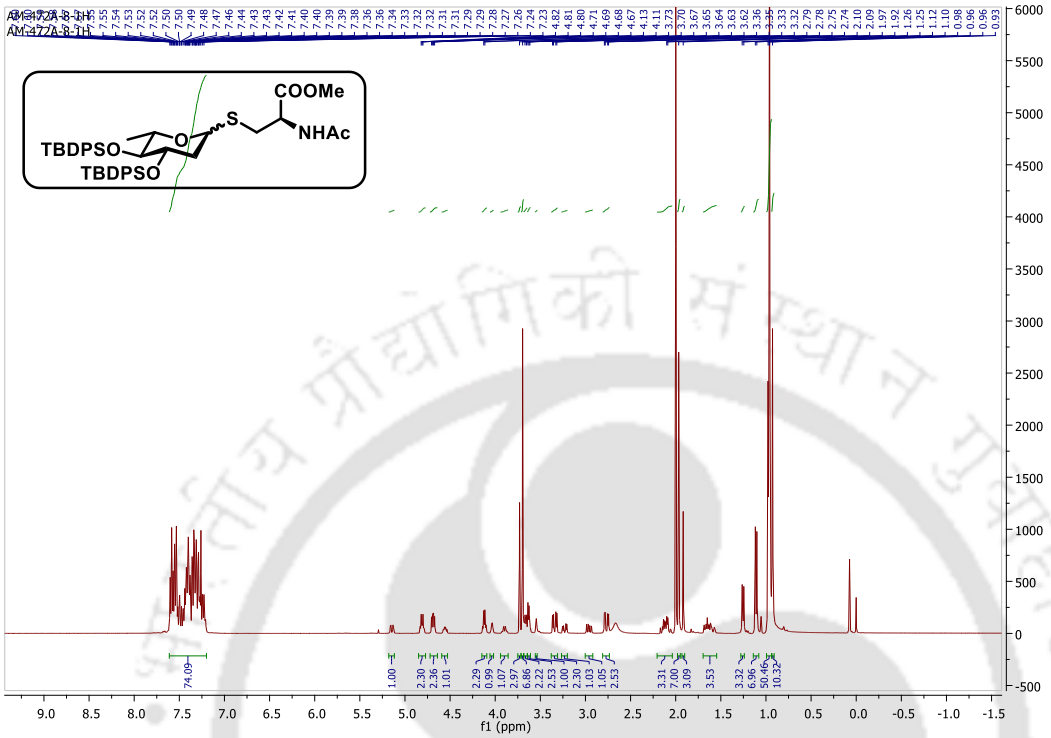
$^{13}C\{^{1}H\}$ NMR of 1-Adamantanyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46h, 600 MHz, $CDCl_3$):



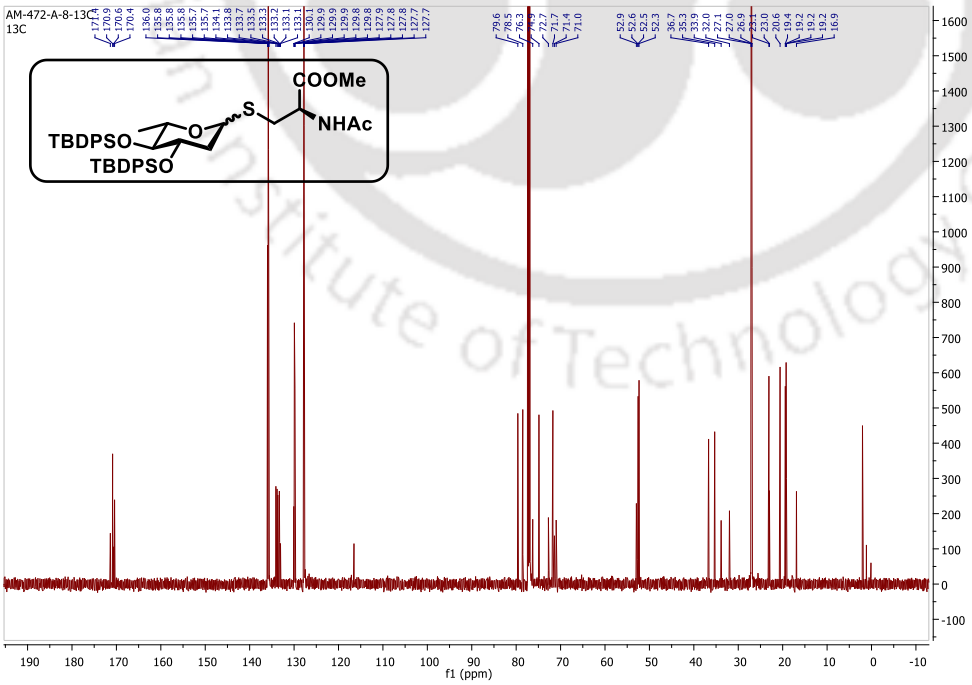
COSY NMR of 1-Adamantanyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46h, 600 MHz, $CDCl_3$):



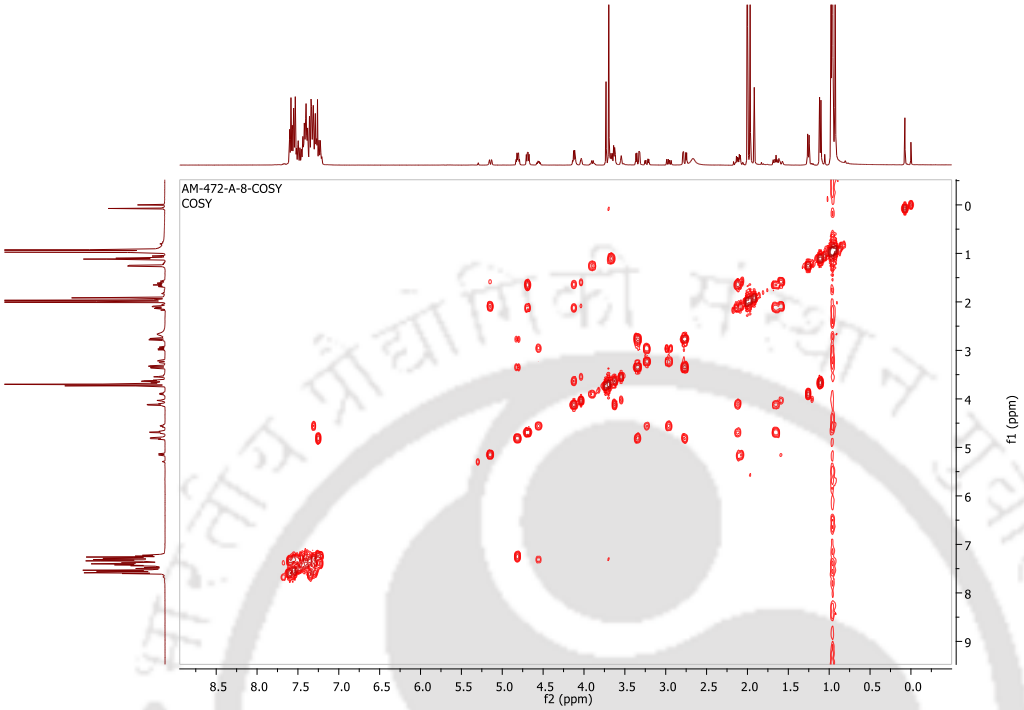
^{1}H NMR of Methyl N-acetyl-L-cysteine-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46i, 400 MHz, $CDCl_3$):



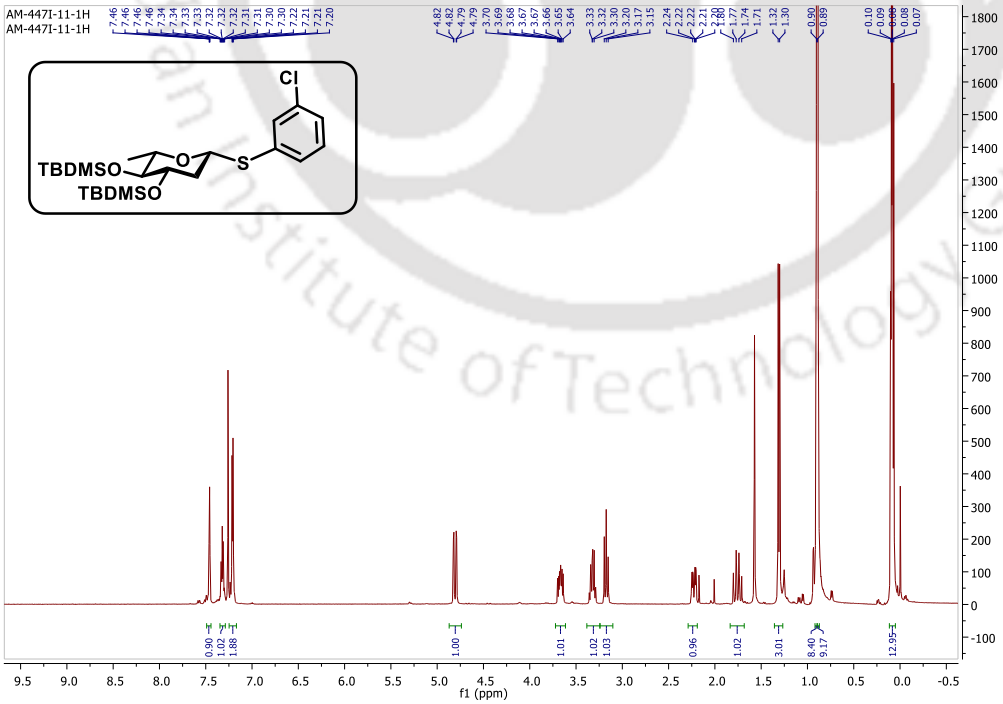
^{13}C{^{1}H} NMR of Methyl N-acetyl-L-cysteine-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46i, 600 MHz, $CDCl_3$):



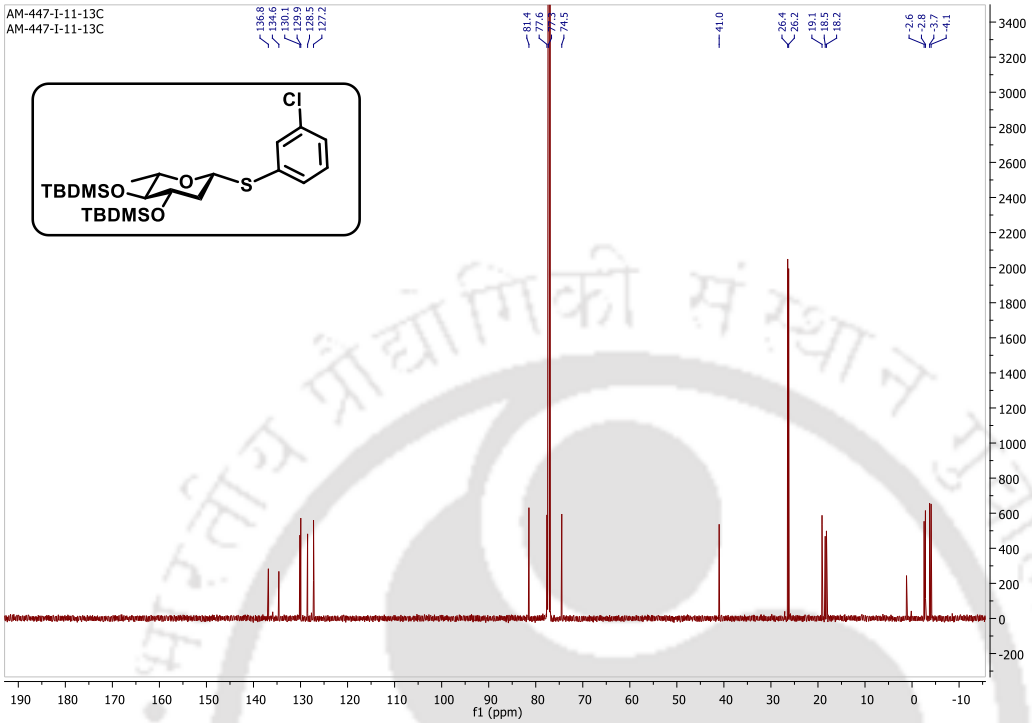
COSY NMR of Methyl N-acetyl-L-cysteine-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46i, 400 MHz, $CDCl_3$):



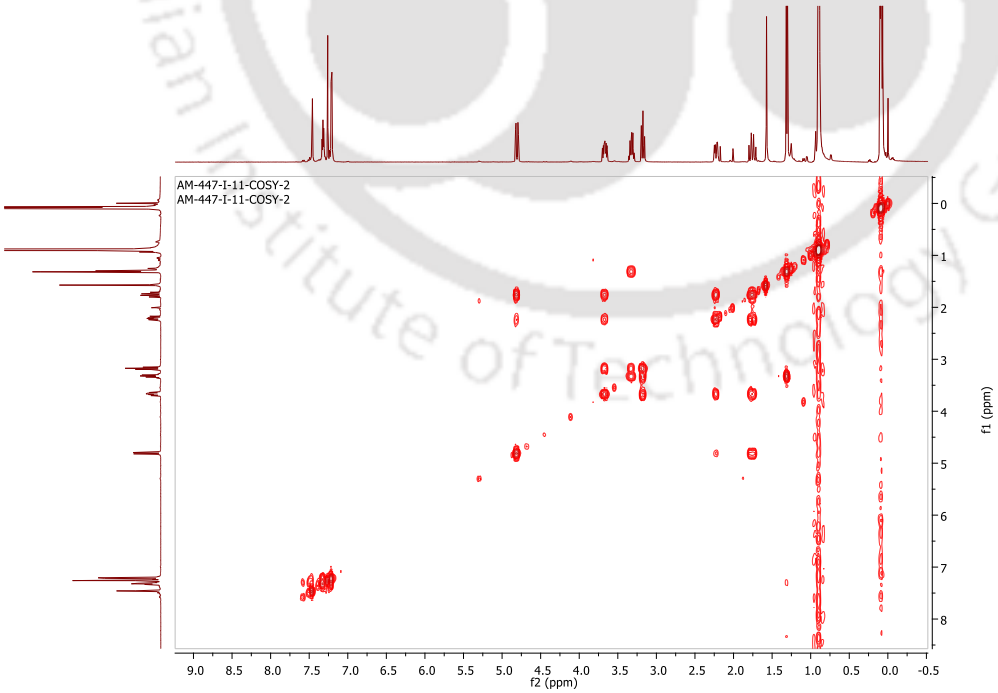
^{1}H NMR of 3-Chlorophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-β-L-arabino-hexapyranoside (46jβ, 400 MHz, $CDCl_3$):



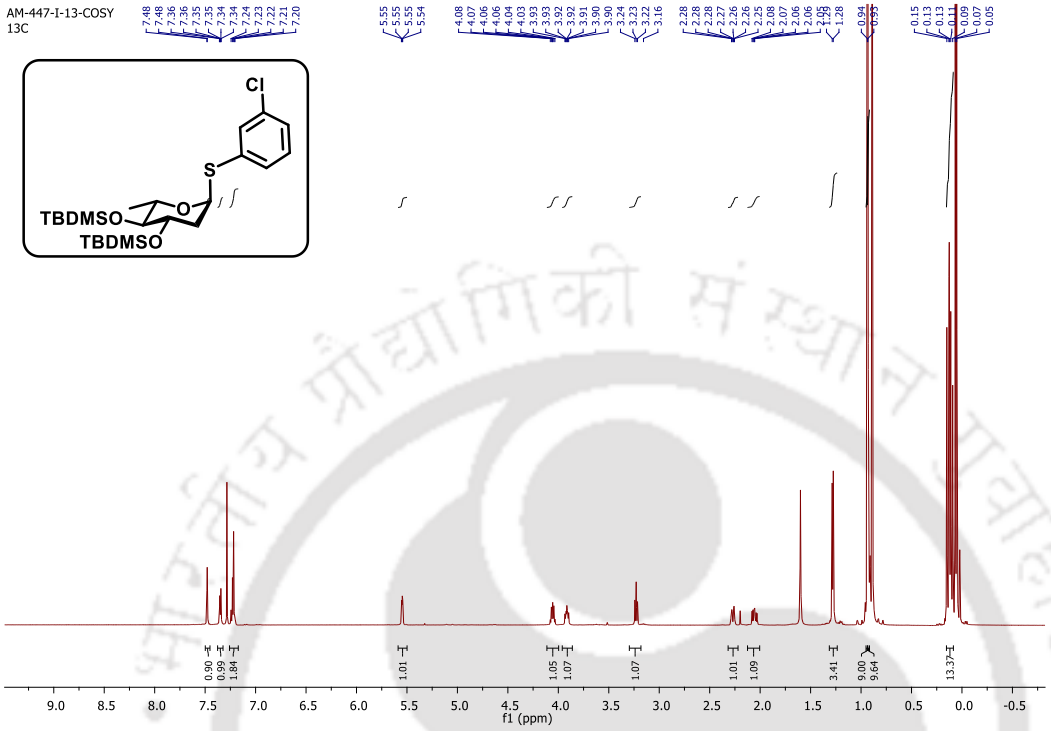
$^{13}C\{^{1}H\}$ NMR of 3-Chlorophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-β-L-arabino-hexapyranoside (46jβ, 600 MHz, $CDCl_3$):



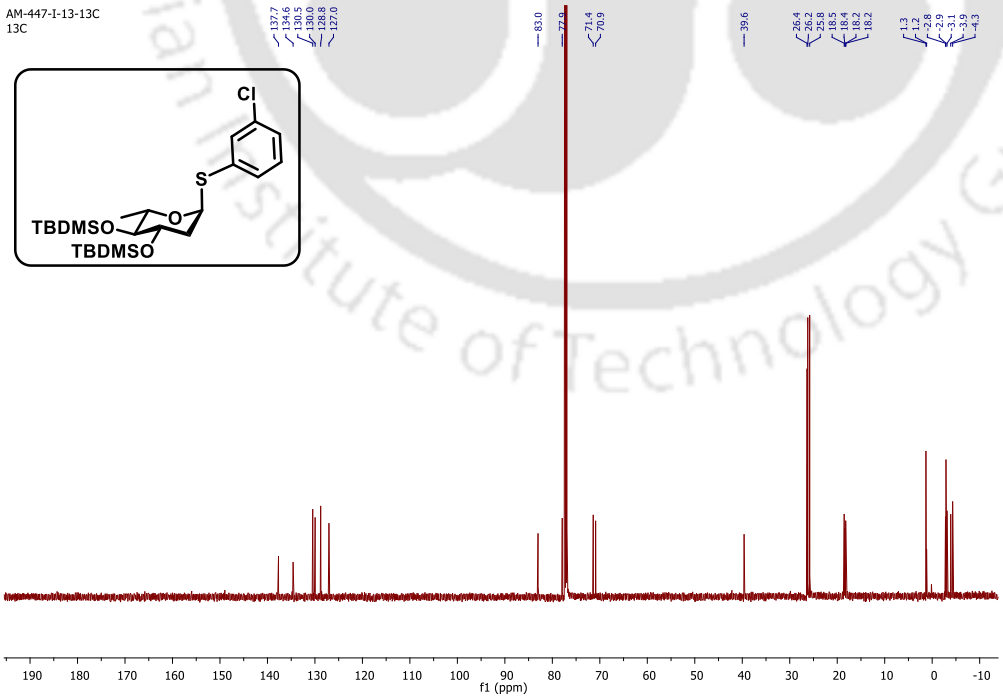
COSY NMR of 3-Chlorophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-β-L-arabino-hexapyranoside (46jβ, 400 MHz, $CDCl_3$):



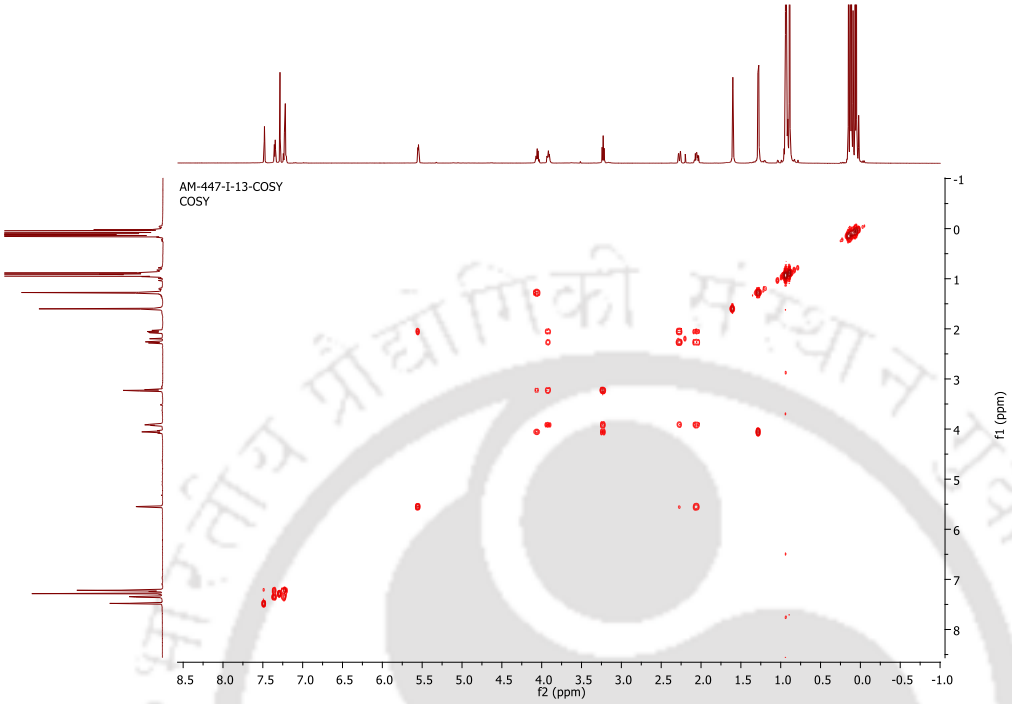
^{1}H NMR of 3-Chlorophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-α-L-arabino-hexapyranoside (46jα, 600 MHz, $CDCl_3$):



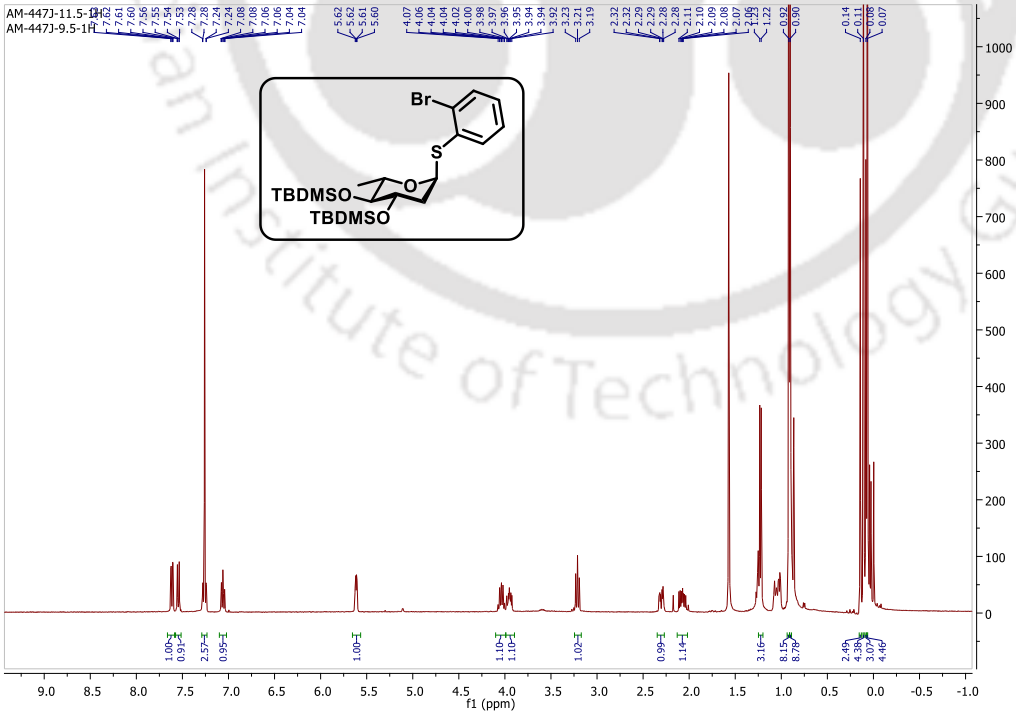
^{13}C{^{1}H} NMR of 3-Chlorophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-α-L-arabino-hexapyranoside (46jα, 600 MHz, $CDCl_3$):



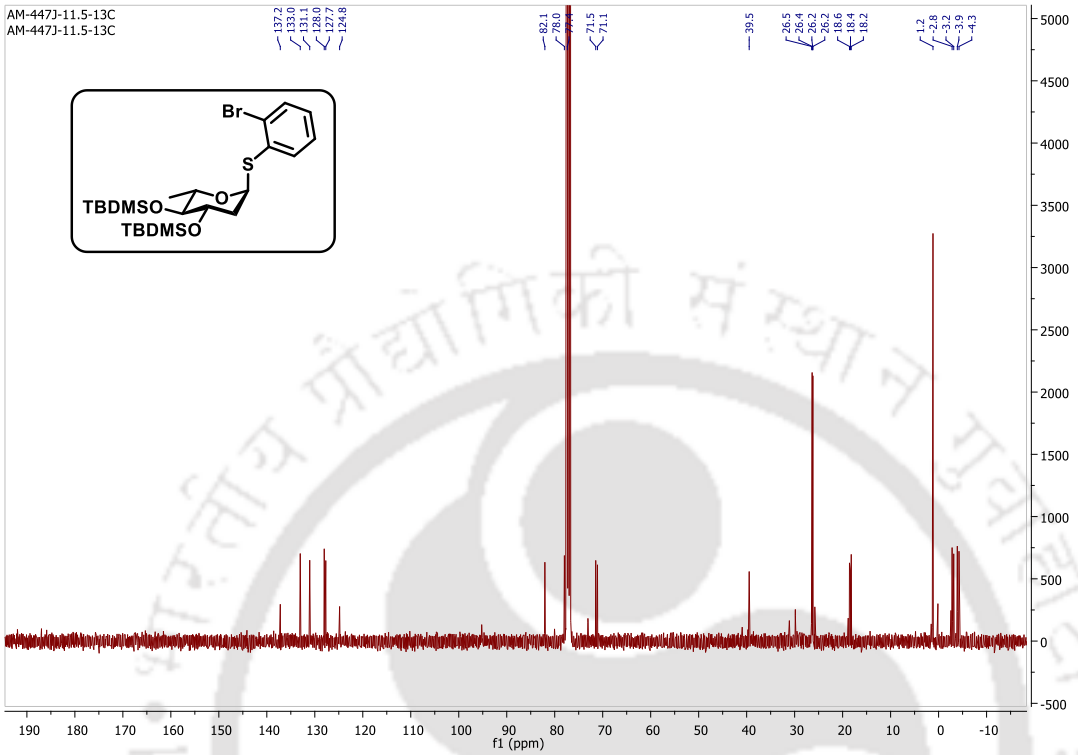
COSY NMR of 3-Chlorophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-*α*-L-arabino-hexapyranoside (46j*α*, 600 MHz, $CDCl_3$):



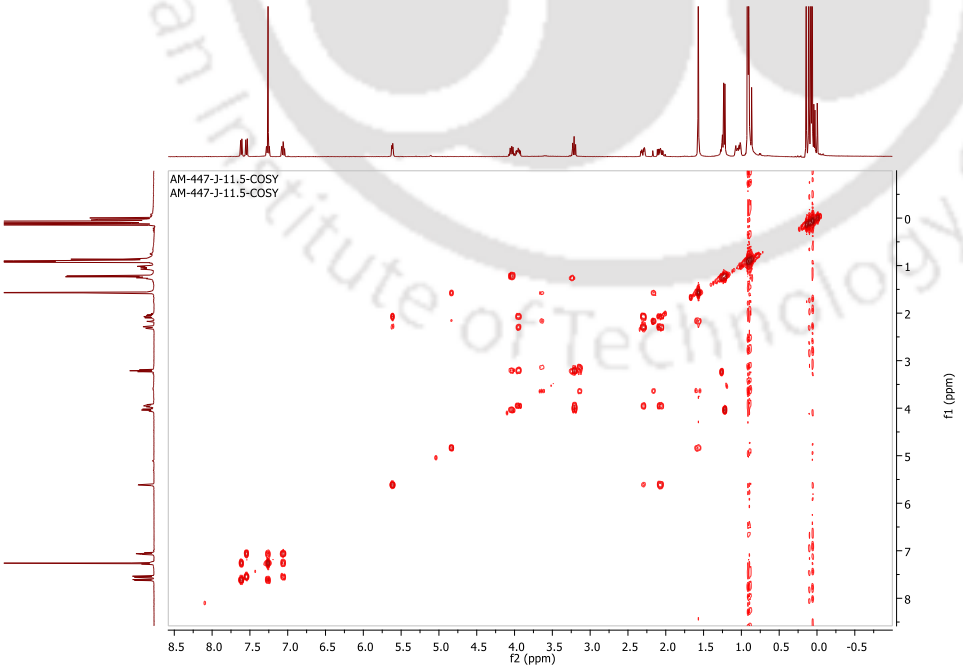
^{1}H NMR of 2-Bromophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-*α*-L-arabino-hexapyranoside (46k*α*, 400 MHz, $CDCl_3$):



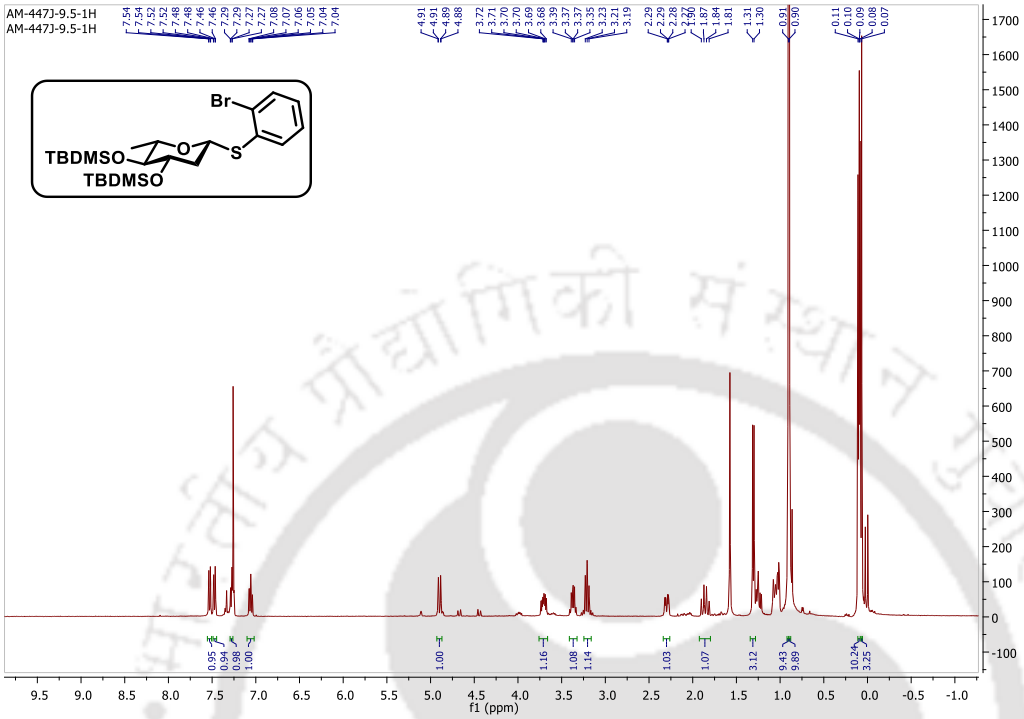
$^{13}C\{^{1}H\}$ NMR of 2-Bromophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-α-L-arabino-hexapyranoside (46kα, 400 MHz, $CDCl_3$):



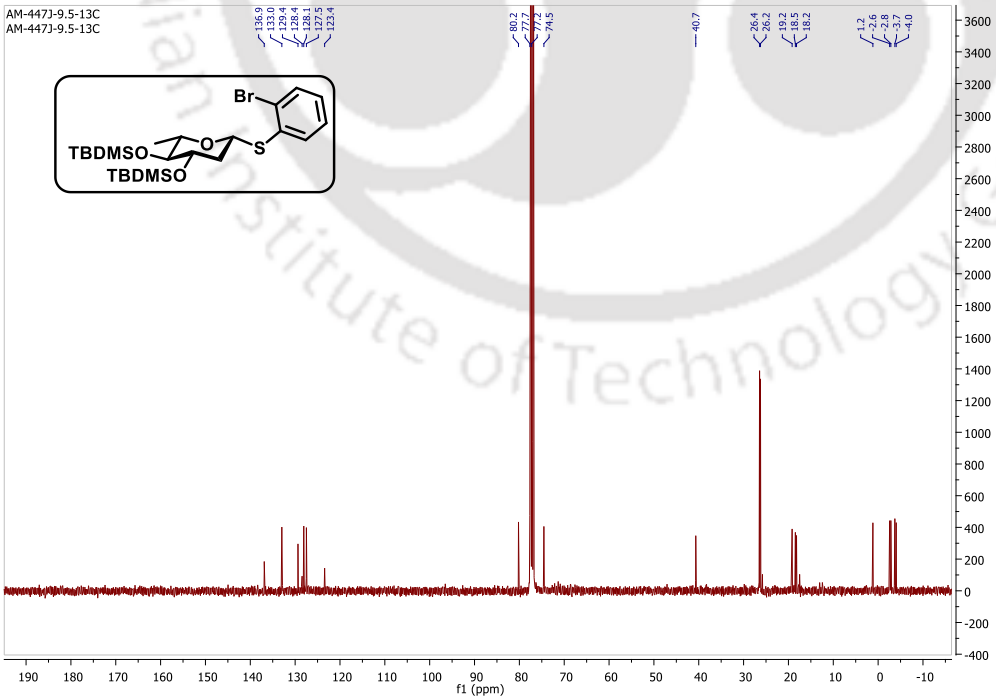
COSY NMR of 2-Bromophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-α-L-arabino-hexapyranoside (46kα, 400 MHz, $CDCl_3$):



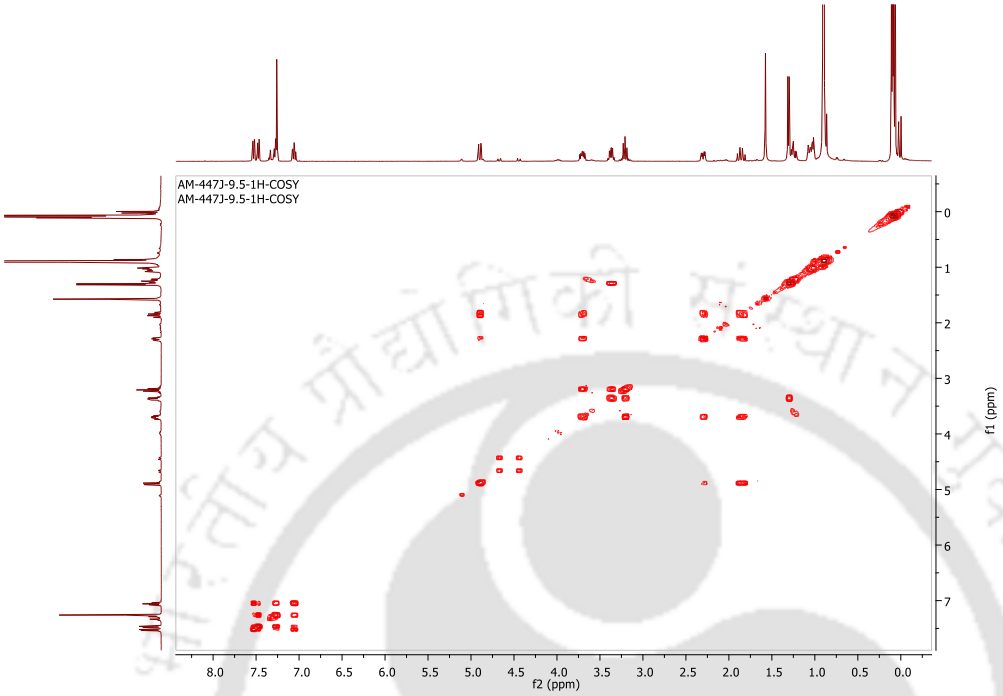
^{1}H NMR of 2-Bromophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-β-L-arabino-hexapyranoside (46kβ, 400 MHz, $CDCl_3$):



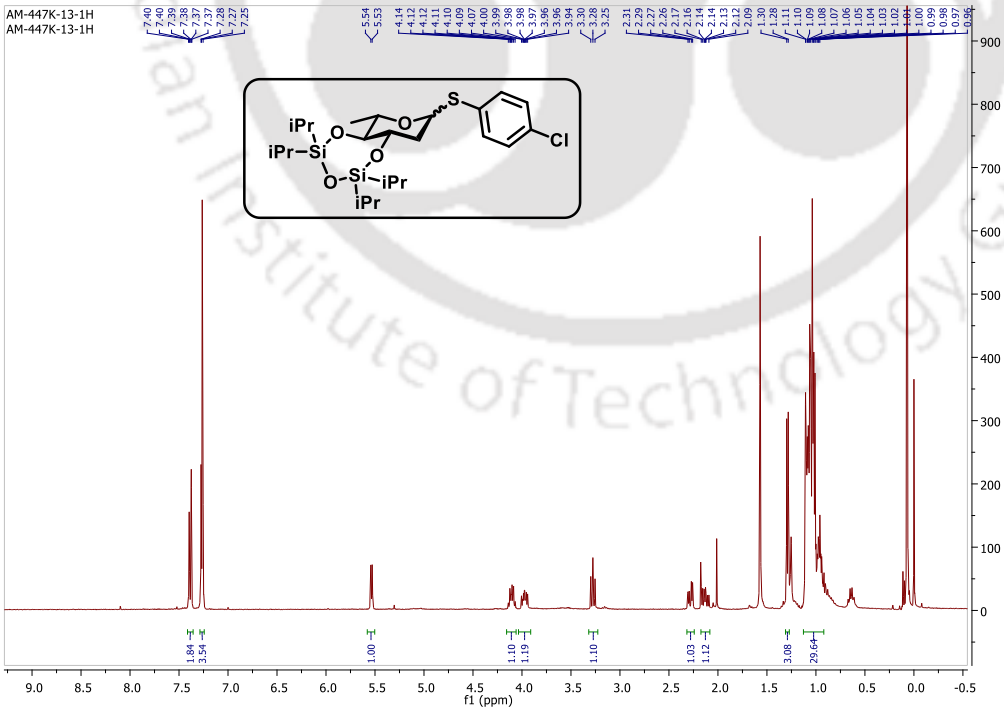
^{13}C{^{1}H} NMR of 2-Bromophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-β-L-arabino-hexapyranoside (46kβ, 400 MHz, $CDCl_3$):



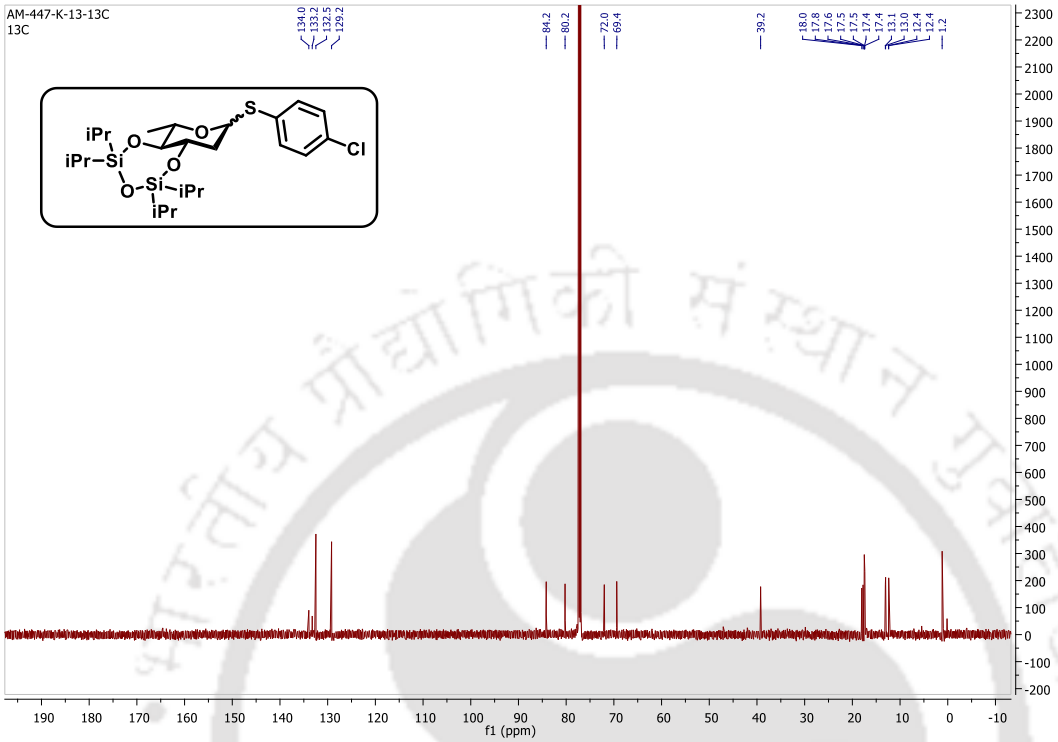
COSY NMR of 2-Bromophenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-β-L-arabino-hexapyranoside (46kβ, 400 MHz, $CDCl_3$):



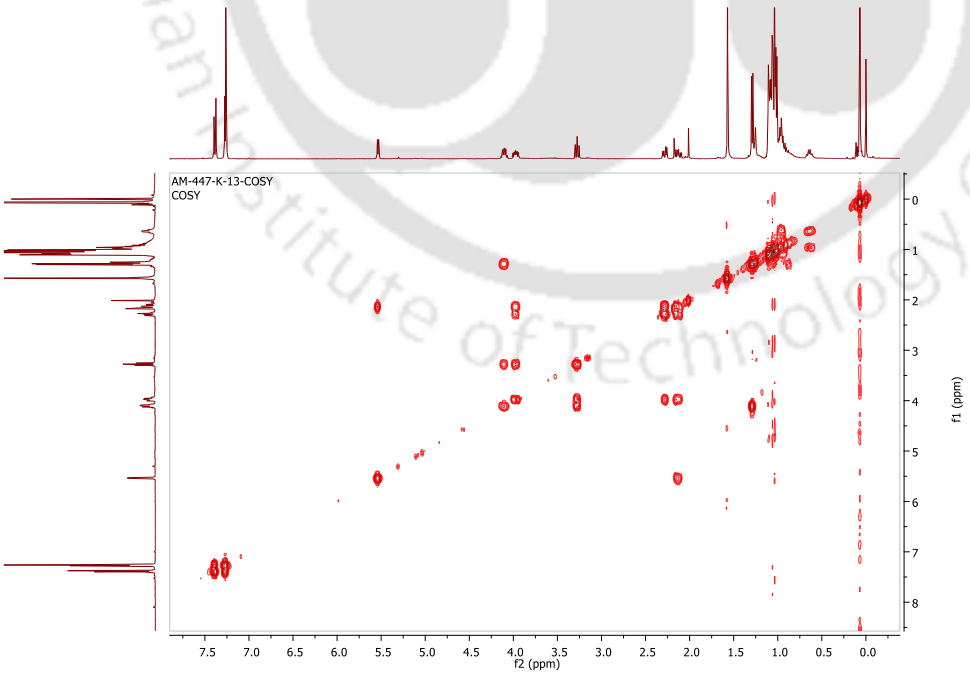
^{1}H NMR of 4-Chlorophenyl 2,6-dideoxy-3,4-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-α,β-L-arabino-hexapyranoside (46l, 400 MHz, $CDCl_3$):



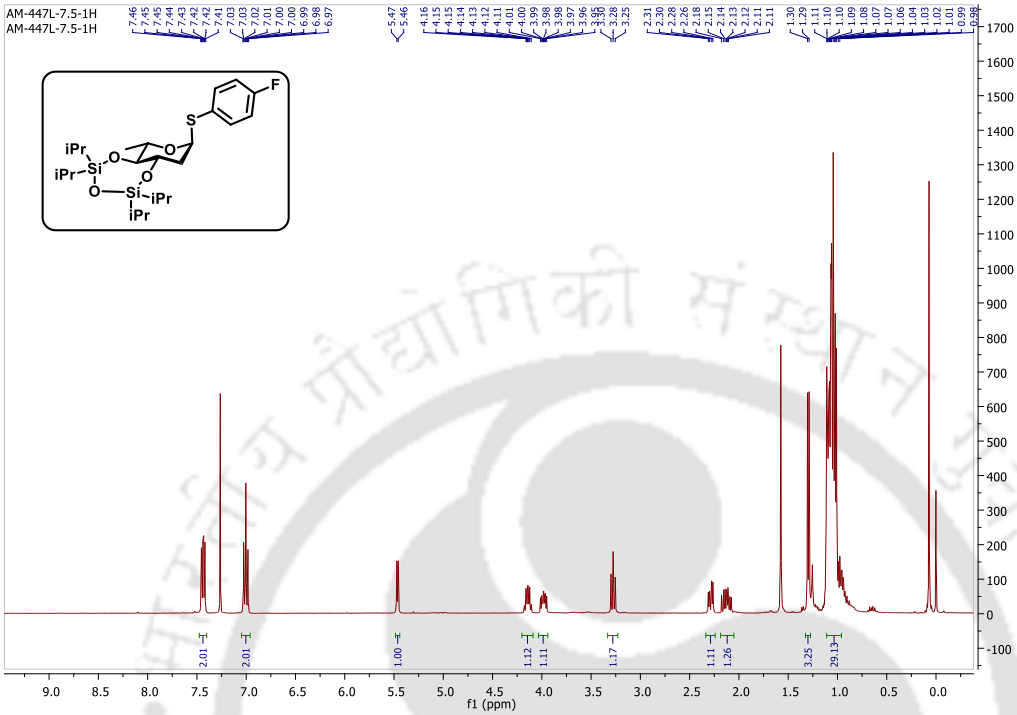
$^{13}C\{^{1}H\}$ NMR of 4-Chlorophenyl 2,6-dideoxy-3,4-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-α,β-L-arabino-hexapyranoside (46l, 600 MHz, $CDCl_3$):



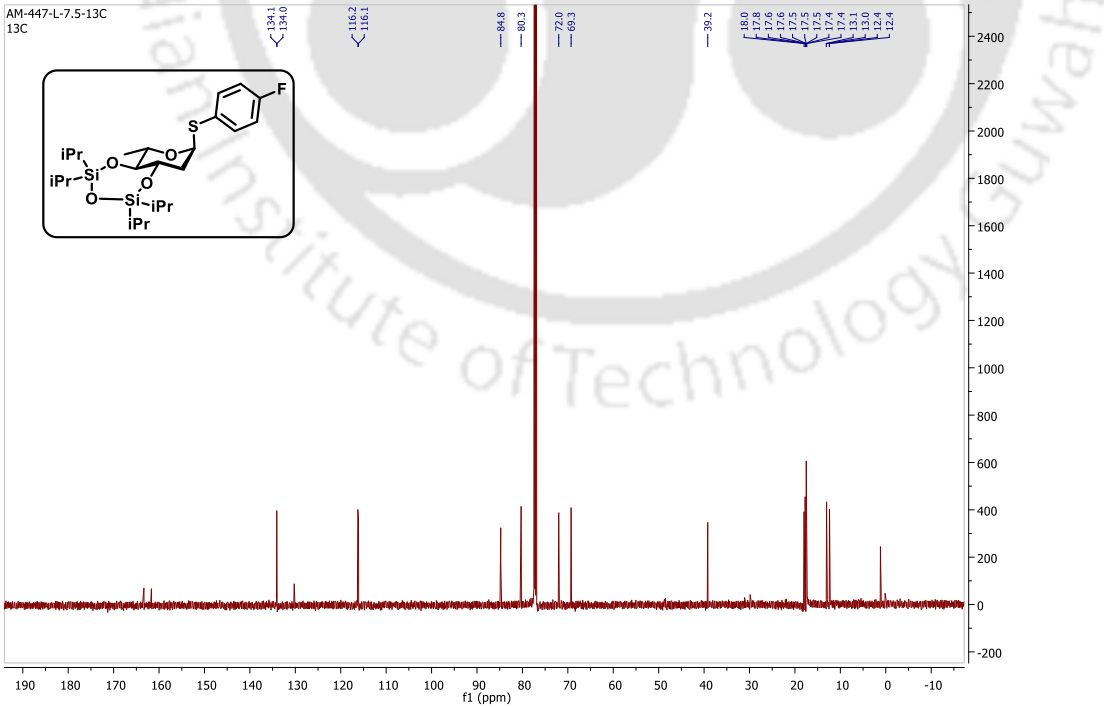
COSY NMR of 4-Chlorophenyl 2,6-dideoxy-3,4-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-α,β-L-arabino-hexapyranoside (46l, 400 MHz, $CDCl_3$):



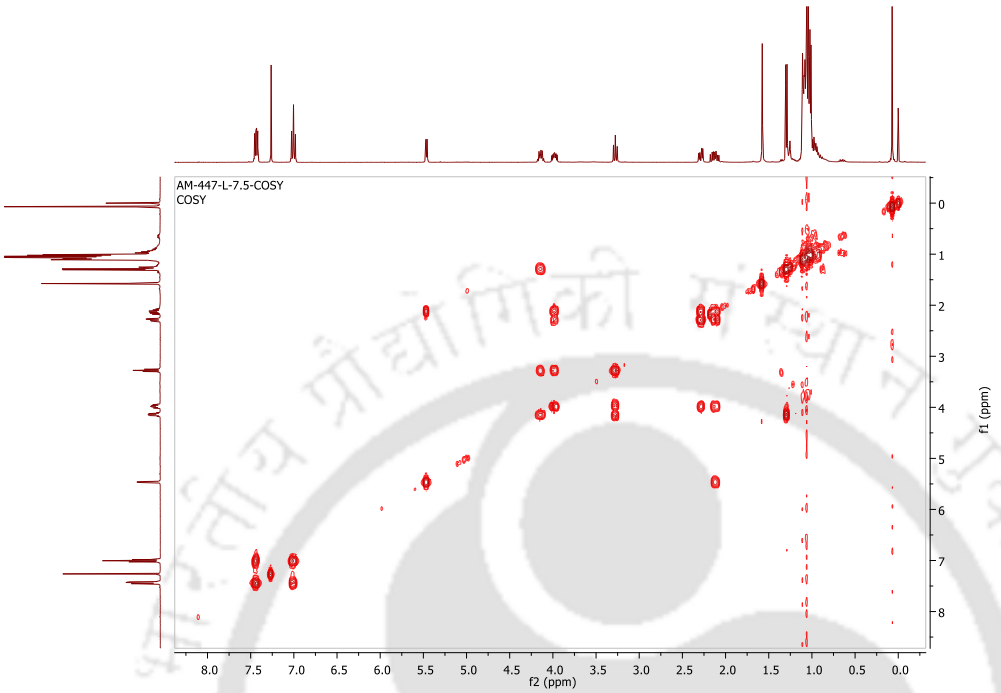
^{1}H NMR of 4-Fluorophenyl 2,6-dideoxy-3,4-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-α-L-arabino-hexapyranoside (46m*a*, 400 MHz, $CDCl_3$):



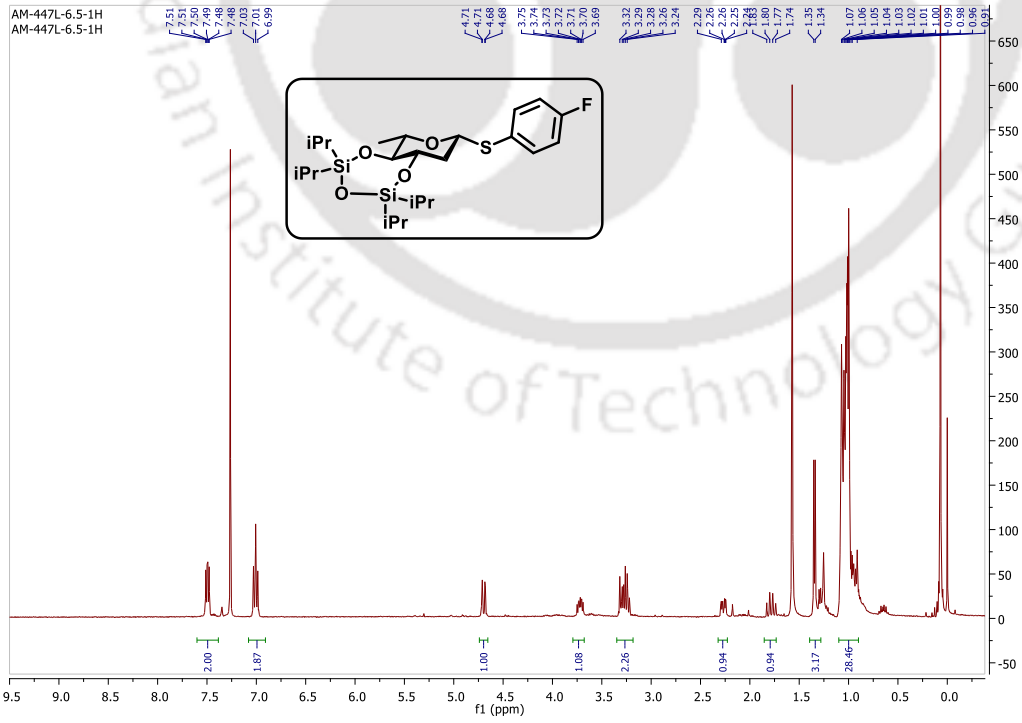
^{13}C{^{1}H} NMR of 4-Fluorophenyl 2,6-dideoxy-3,4-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-α-L-arabino-hexapyranoside (46m*a*, 600 MHz, $CDCl_3$):



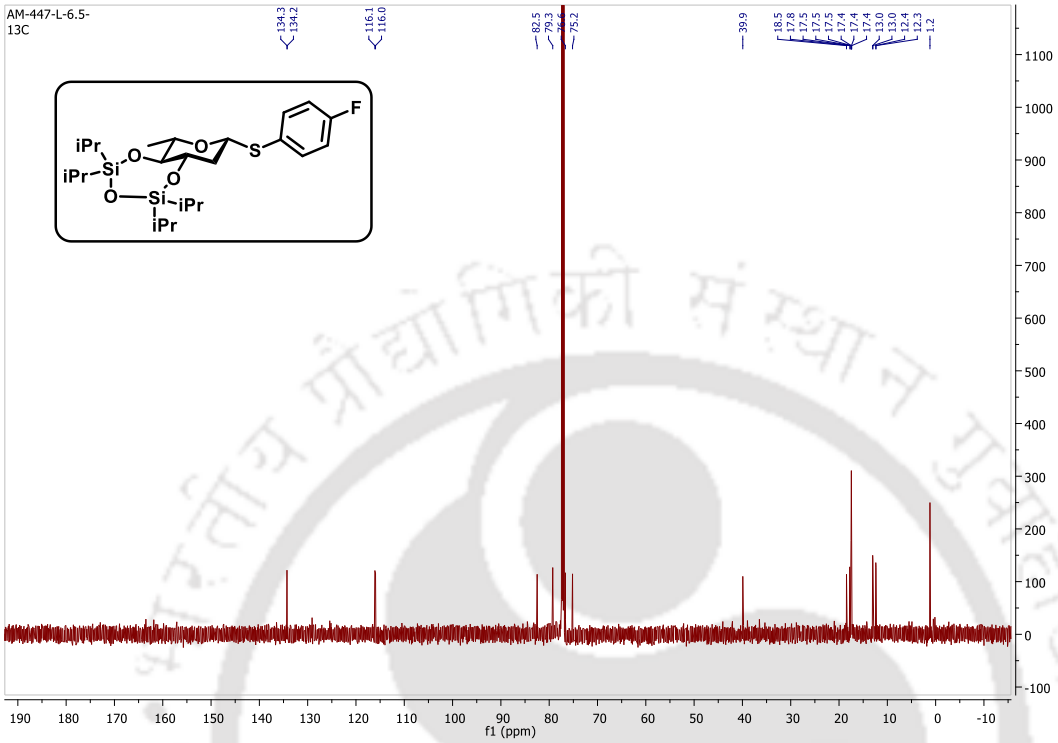
COSY NMR of 4-Fluorophenyl 2,6-dideoxy-3,4-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-α-L-arabino-hexapyranoside (46m*α*, 400 MHz, $CDCl_3$):



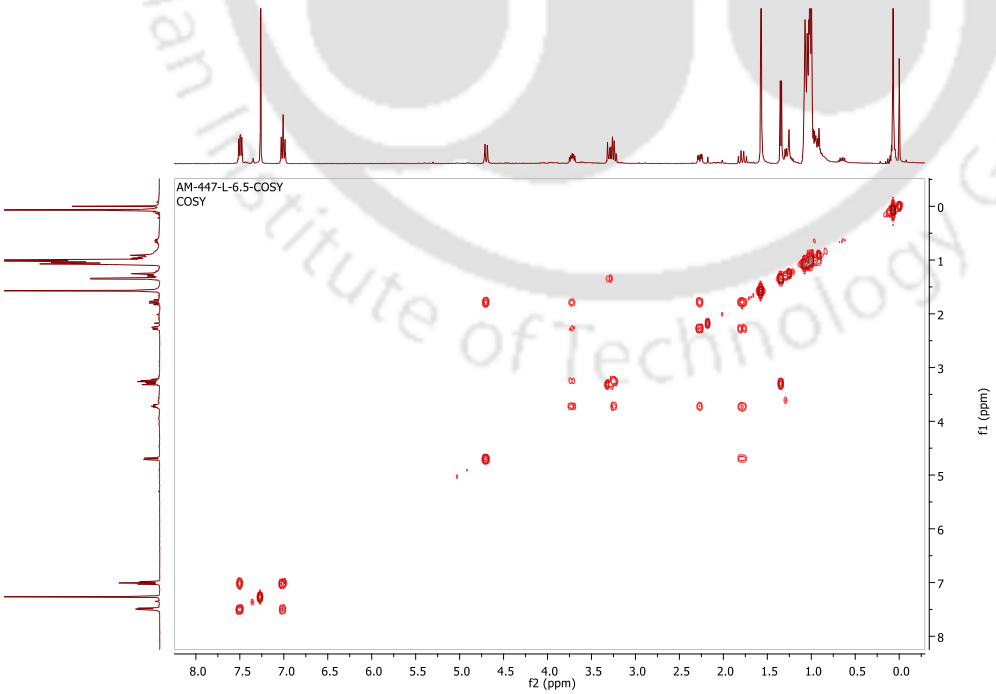
^{1}H NMR of 4-Fluorophenyl 2,6-dideoxy-3,4-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-β-L-arabino-hexapyranoside (46mβ, 400 MHz, $CDCl_3$):



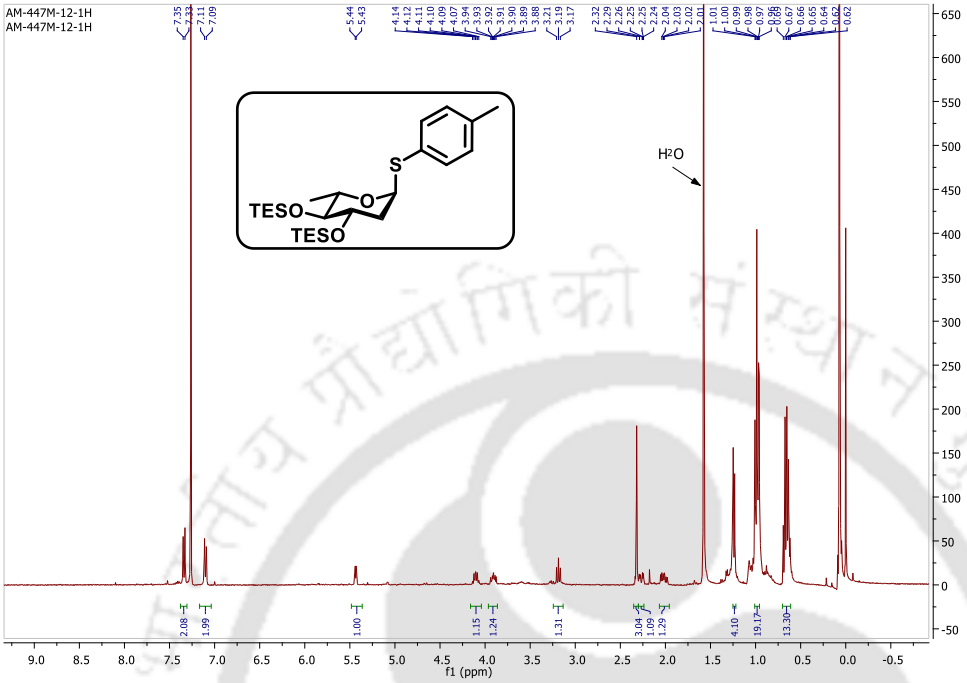
$^{13}C\{^{1}H\}$ NMR of 4-Fluorophenyl 2,6-dideoxy-3,4-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-β-L-arabino-hexapyranoside (46mβ, 600 MHz, $CDCl_3$):



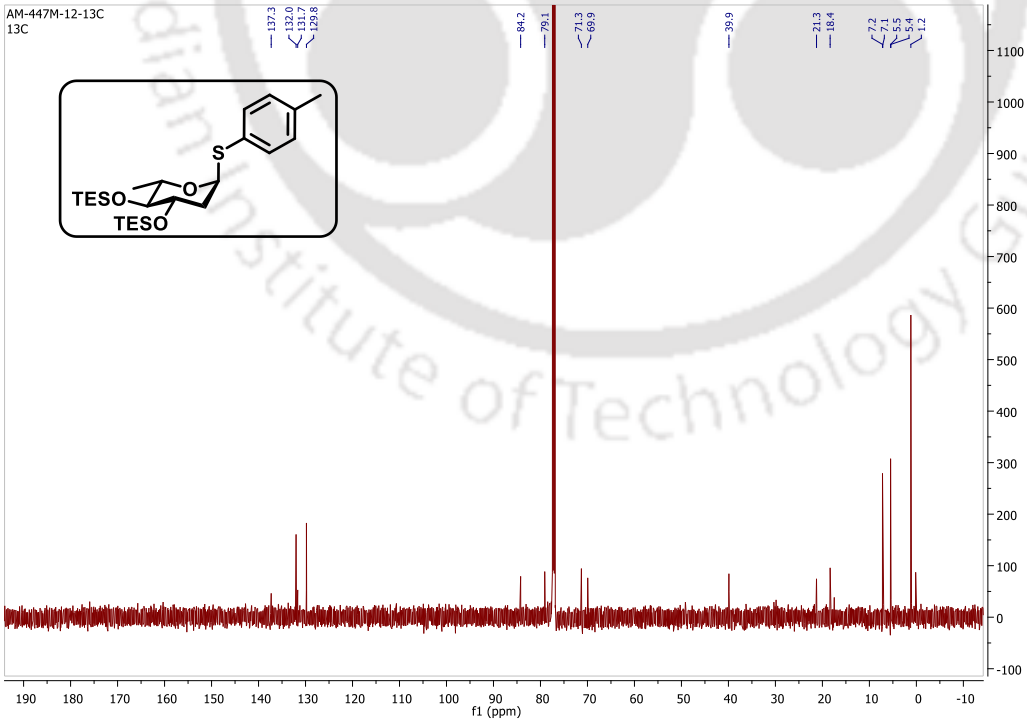
COSY NMR of 4-Fluorophenyl 2,6-dideoxy-3,4-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-β-L-arabino-hexapyranoside (46mβ, 400 MHz, $CDCl_3$):



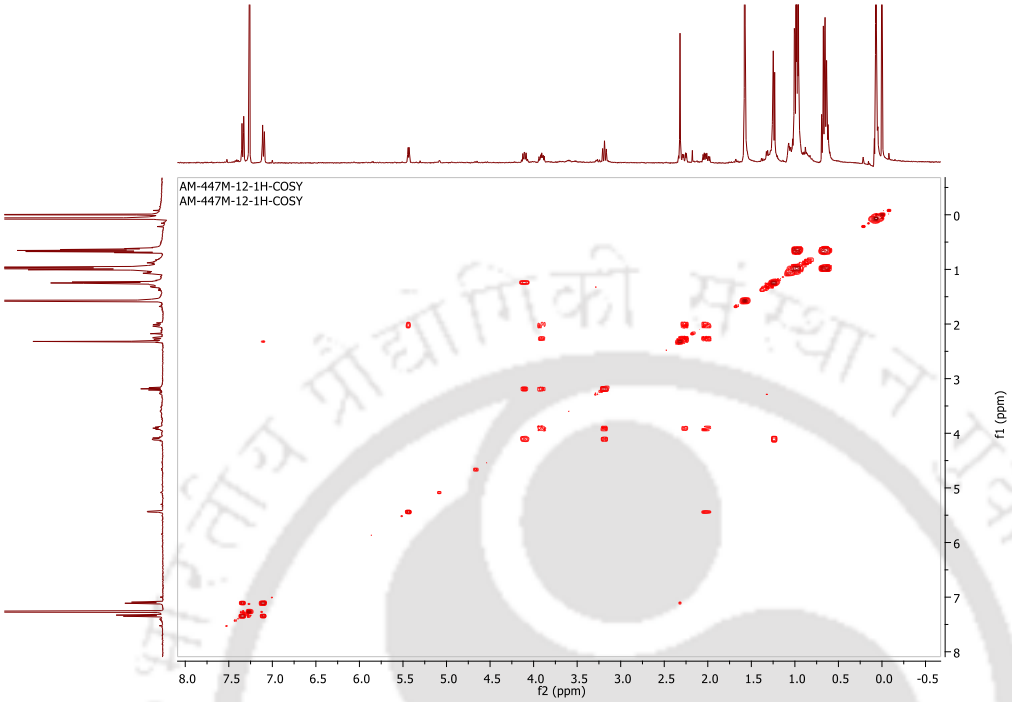
^{1}H NMR of Tolyl 2,6-dideoxy-3,4-bis-*O*-[triethylsilyl]-1-thio-α-L-arabino-hexapyranoside (46nα, 400 MHz, $CDCl_3$):



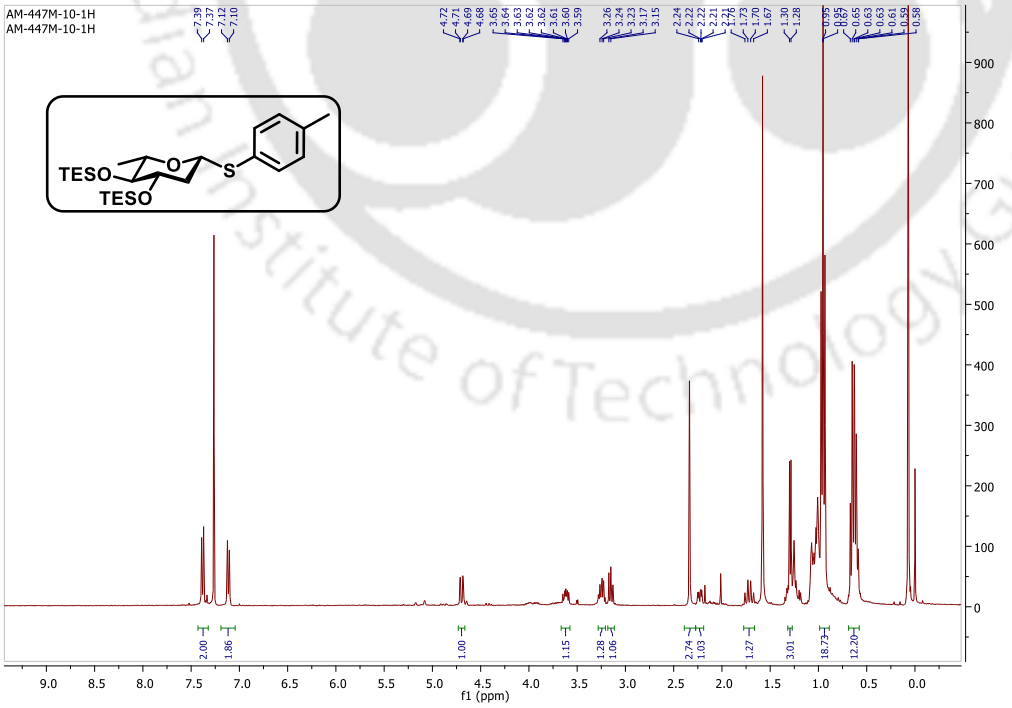
^{13}C{^{1}H} NMR of Tolyl 2,6-dideoxy-3,4-bis-*O*-[triethylsilyl]-1-thio-α-L-arabino-hexapyranoside (46nα, 600 MHz, $CDCl_3$):



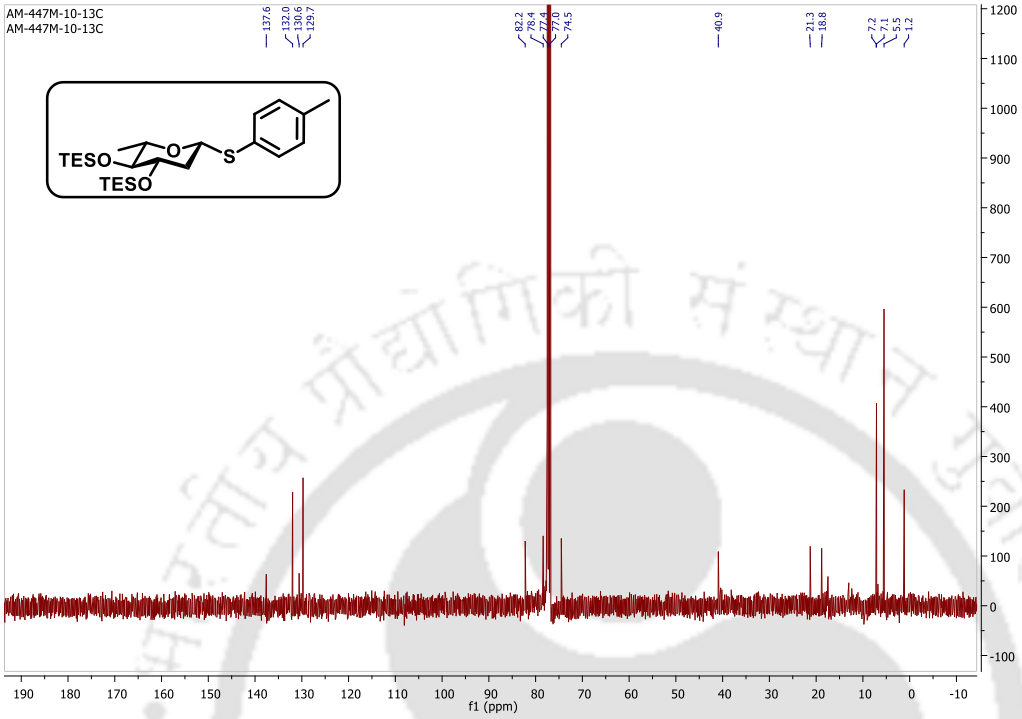
COSY NMR of Tolyl 2,6-dideoxy-3,4-bis-*O*-[triethylsilyl]-1-thio-α-L-arabino-hexapyranoside (46nα, 400 MHz, $CDCl_3$):



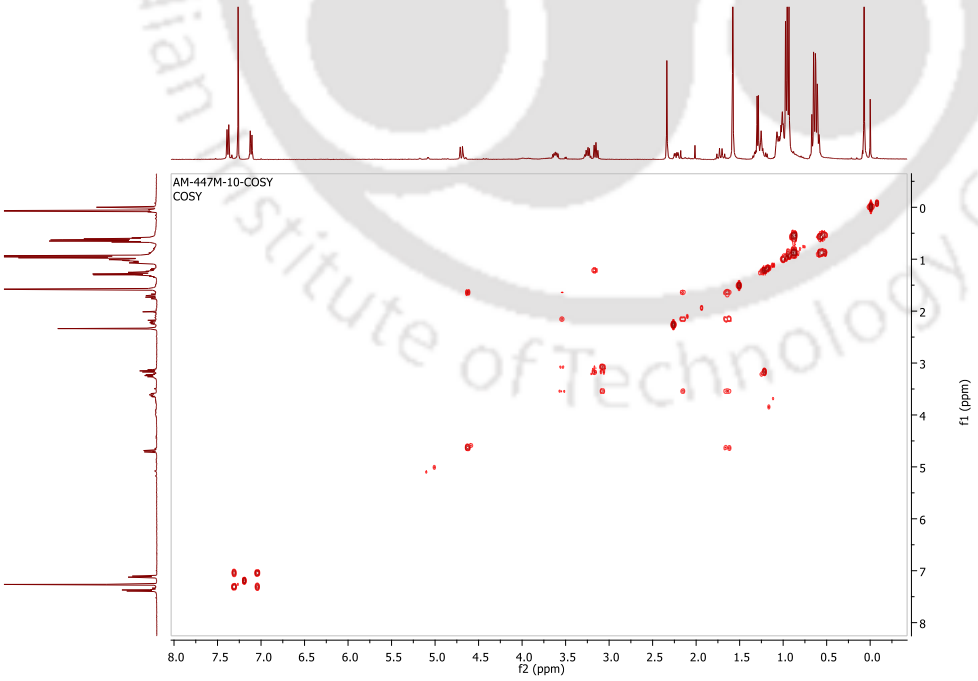
^{1}H NMR of Tolyl 2,6-dideoxy-3,4-bis-*O*-[triethylsilyl]-1-thio-β-L-arabino-hexapyranoside (46nβ, 400 MHz, $CDCl_3$):



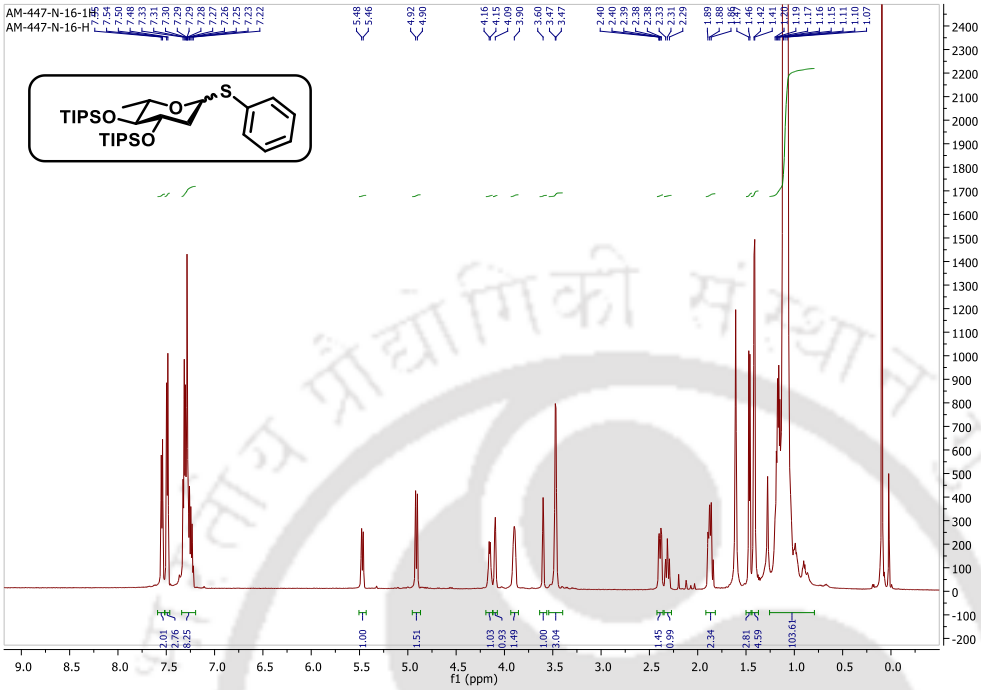
$^{13}C\{^{1}H\}$ NMR of Tolyl 2,6-dideoxy-3,4-bis-*O*-[triethylsilyl]-1-thio-β-L-arabino-hexapyranoside (46nβ, 400 MHz, $CDCl_3$):



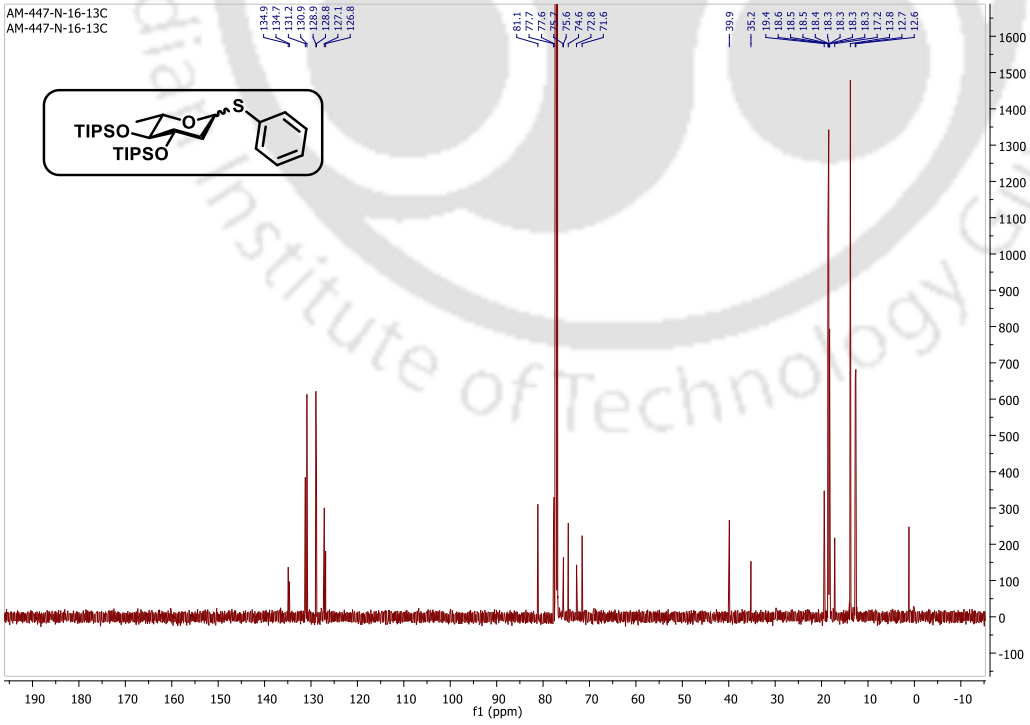
COSY NMR of Tolyl 2,6-dideoxy-3,4-bis-*O*-[triethylsilyl]-1-thio-β-L-arabino-hexapyranoside (46nβ, 400 MHz, $CDCl_3$):



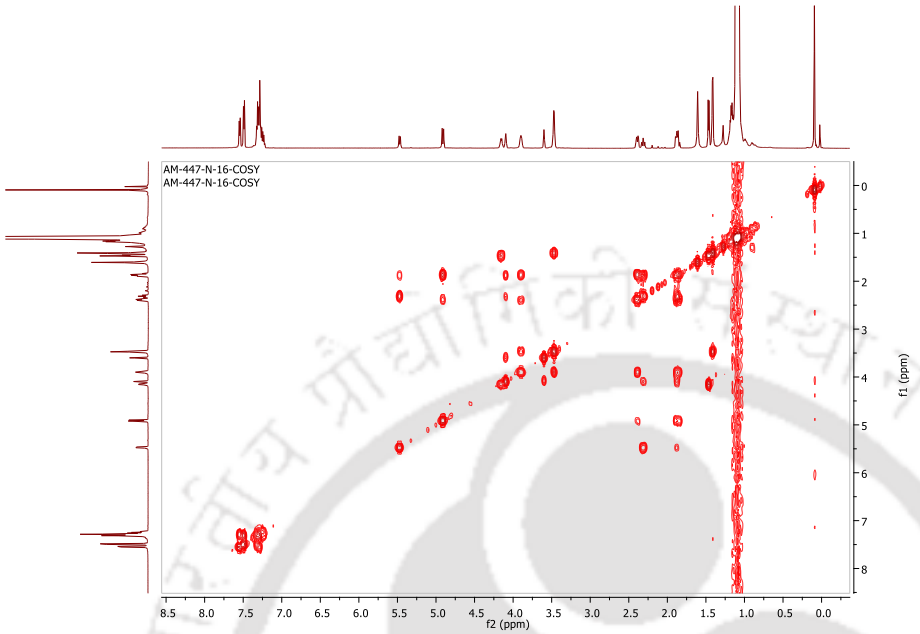
^{1}H NMR of Phenyl 2,6-dideoxy-3,4-bis-*O*-[triisopropylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46o, 600 MHz, $CDCl_3$):



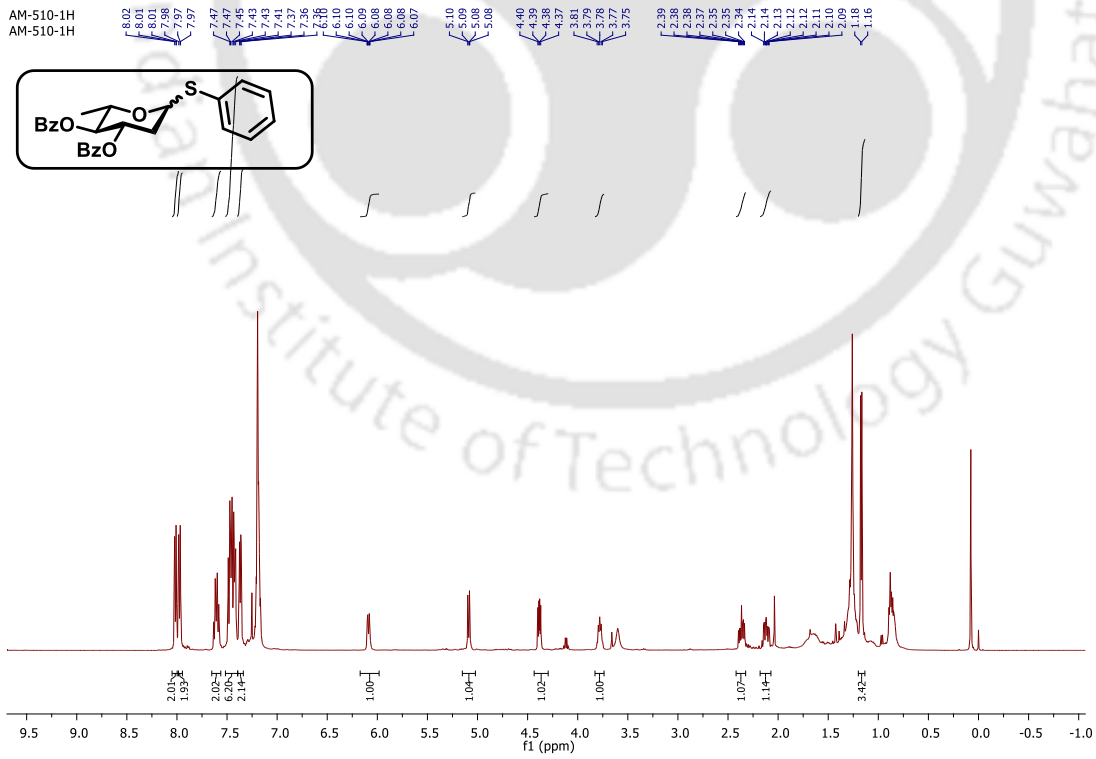
^{13}C{^{1}H} NMR of Phenyl 2,6-dideoxy-3,4-bis-*O*-[triisopropylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46o, 600 MHz, $CDCl_3$):



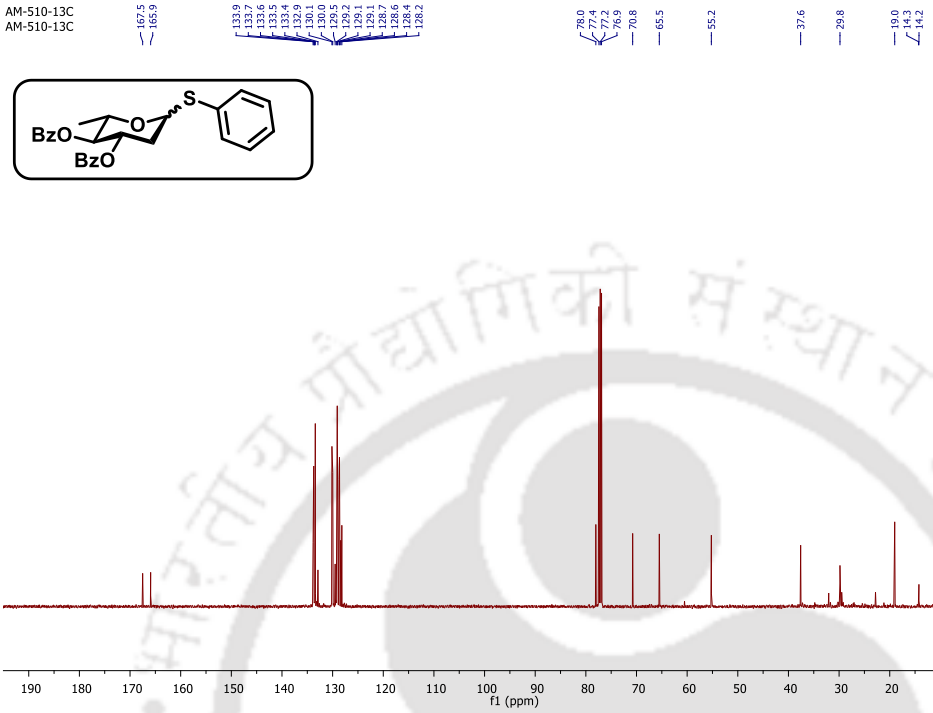
COSY NMR of Phenyl 2,6-dideoxy-3,4-bis-*O*-[triisopropylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (46o, 600 MHz, $CDCl_3$):



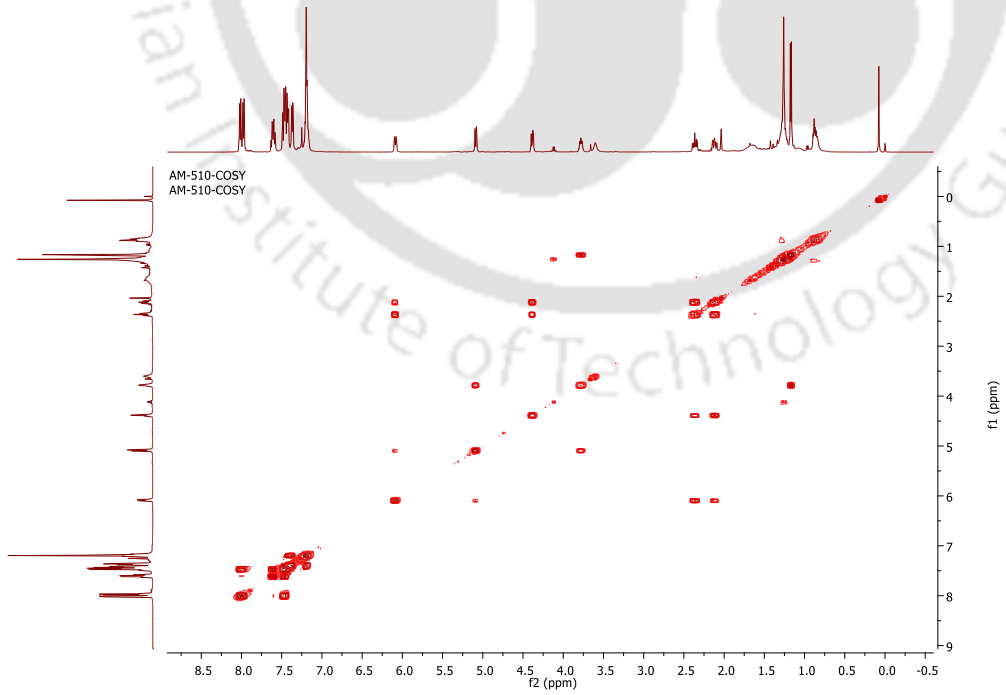
^{1}H NMR of Phenyl 3,4-di-*O*-benzoyl-2,6-dideoxy-1-thio-L-rhamnopyranoside (46p, 500 MHz, $CDCl_3$):



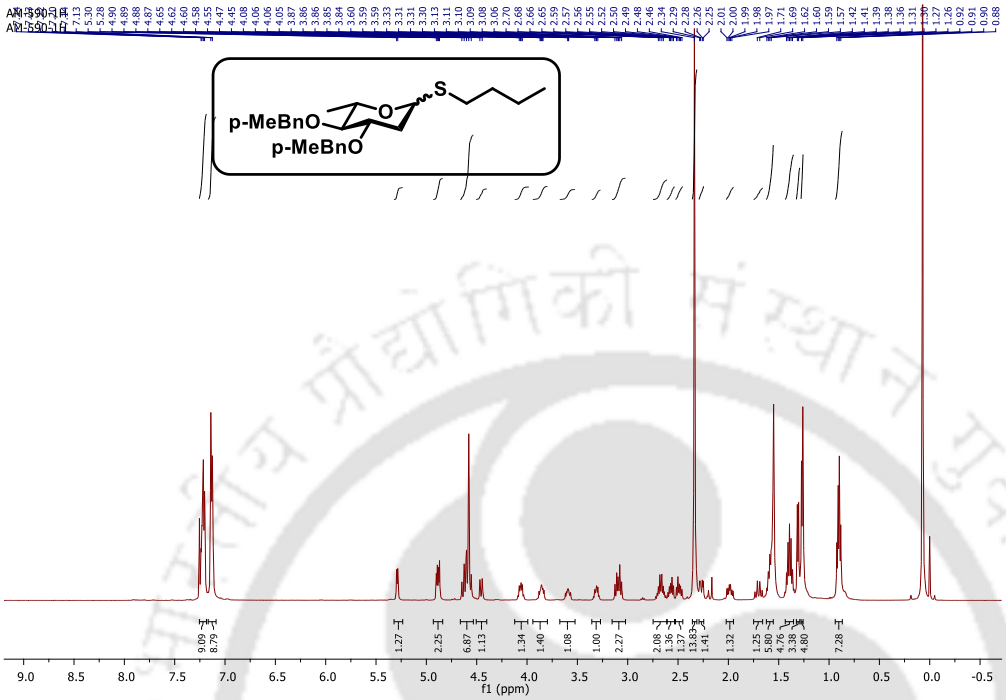
$^{13}C\{^{1}H\}$ NMR of Phenyl 3,4-di-*O*-benzoyl-2,6-dideoxy-1-thio-L-rhamnopyranoside (46p, 500 MHz, $CDCl_3$):



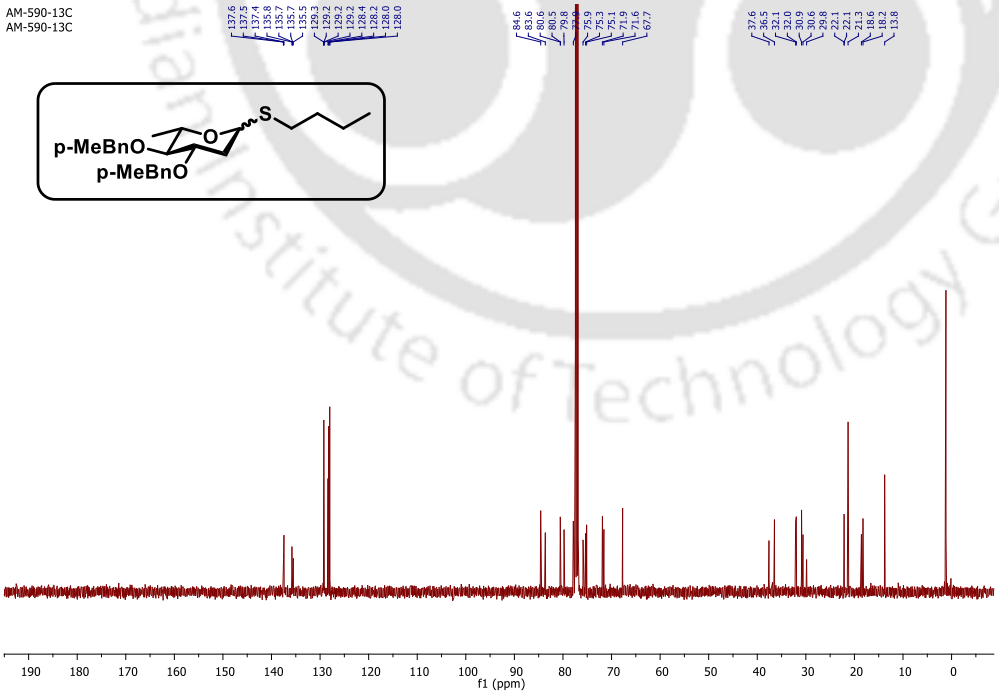
COSY NMR of Phenyl 3,4-di-*O*-benzoyl-2,6-dideoxy-1-thio-L-rhamnopyranoside (46p, 500 MHz, $CDCl_3$):



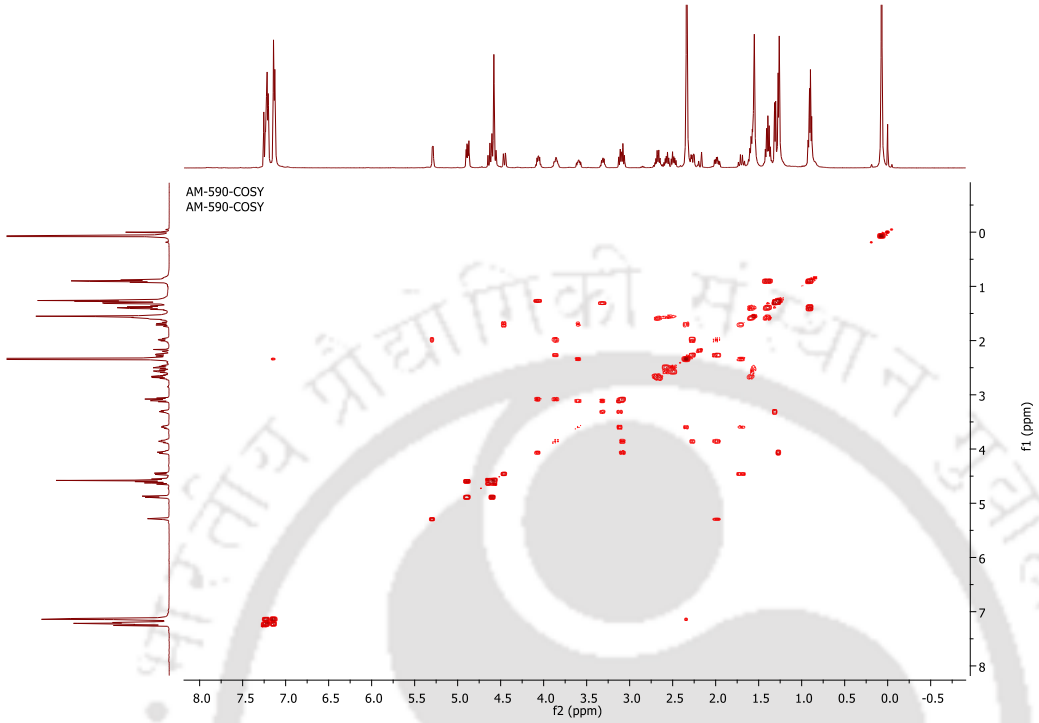
^{1}H NMR of Butyl 2,6-dideoxy-3,4-di-O-para-methylbenzyl-1-thio-α,β-L-arabino-hexopyranoside (46g, 600 MHz, $CDCl_3$):



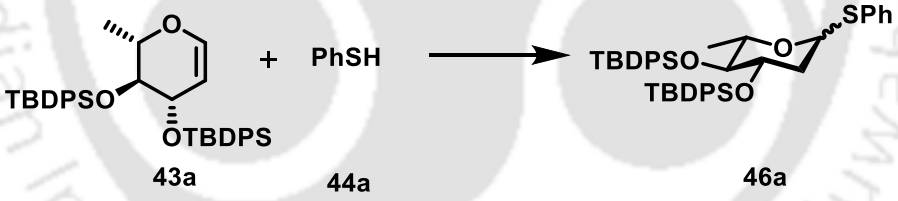
^{13}C{^{1}H} NMR of Butyl 2,6-dideoxy-3,4-di-O-para-methylbenzyl-1-thio-α,β-L-arabino-hexopyranoside (46g, 600 MHz, $CDCl_3$):



COSY NMR of Butyl 2,6-dideoxy-3,4-di-O-para-methylbenzyl-1-thio-α,β-L-arabino-hexopyranoside (46g, 600 MHz, $CDCl_3$):

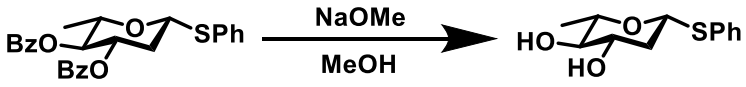


3.10 Large Scale Synthesis of 46a:



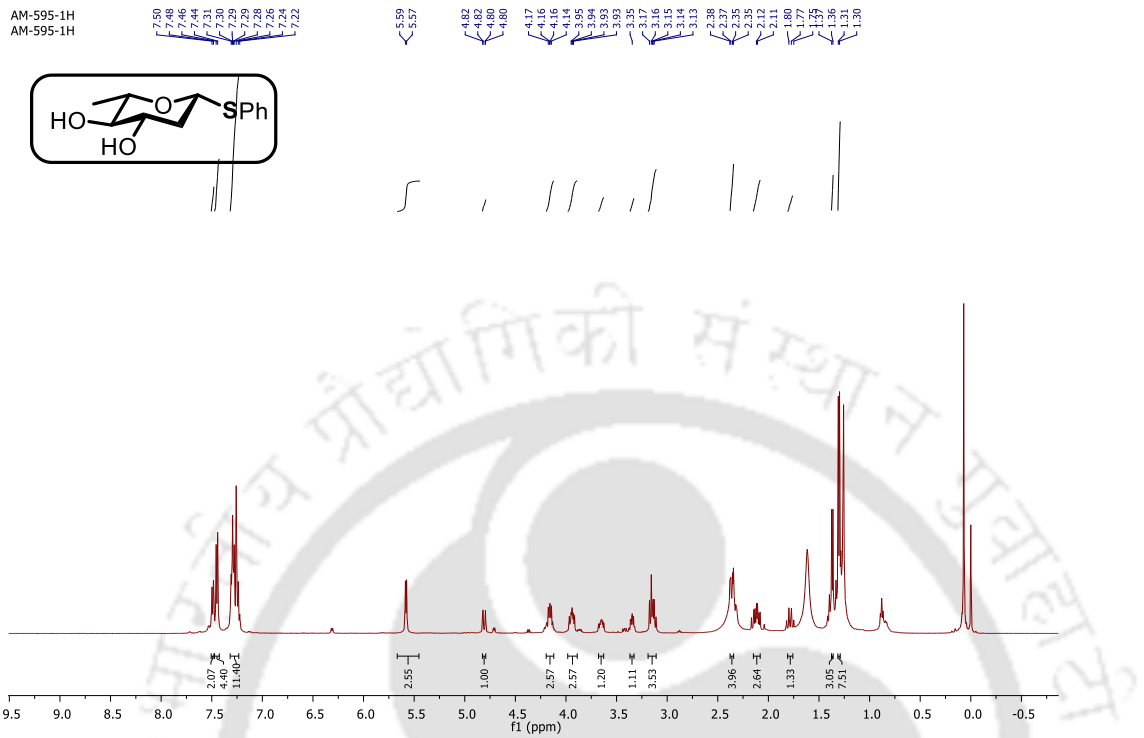
A solution of glycosyl donor 3,4-di-*O*-tertiary-butyldiphenylsilyl-L-rhamnal **43a** (1.1 g, 1.812 mmol, 1.0 equiv) and glycosyl acceptor thiophenol **44a** (0.242 g, 220 µL, 2.17 mmol, 1.2 equiv) in dry DCM at rt was treated with 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst (26 mg, 0.0906 mmol, 5 mol%) and stirred for 24 h at rt to get the product **46a** as a colourless oil. R_f- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 936 mg, yield- 72%. Selectivity was determined from crude NMR analysis α: β=1:1.5.

3.11 Synthesis of Unprotected Thioglycosides:

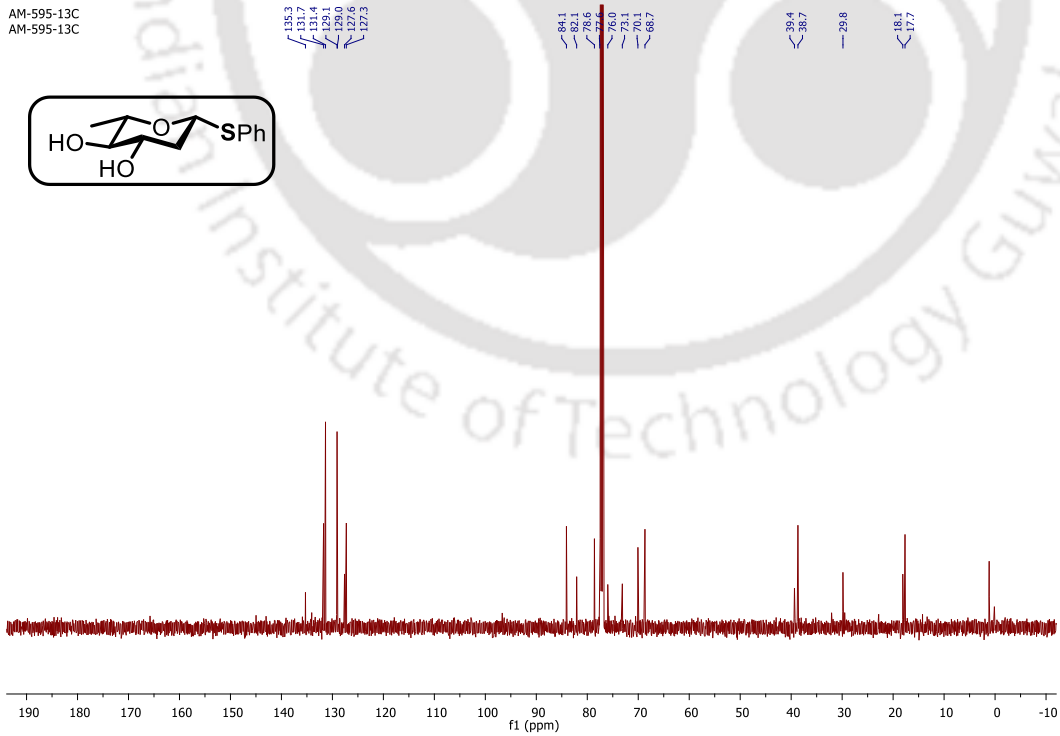


46r, 82%, 2.5:1

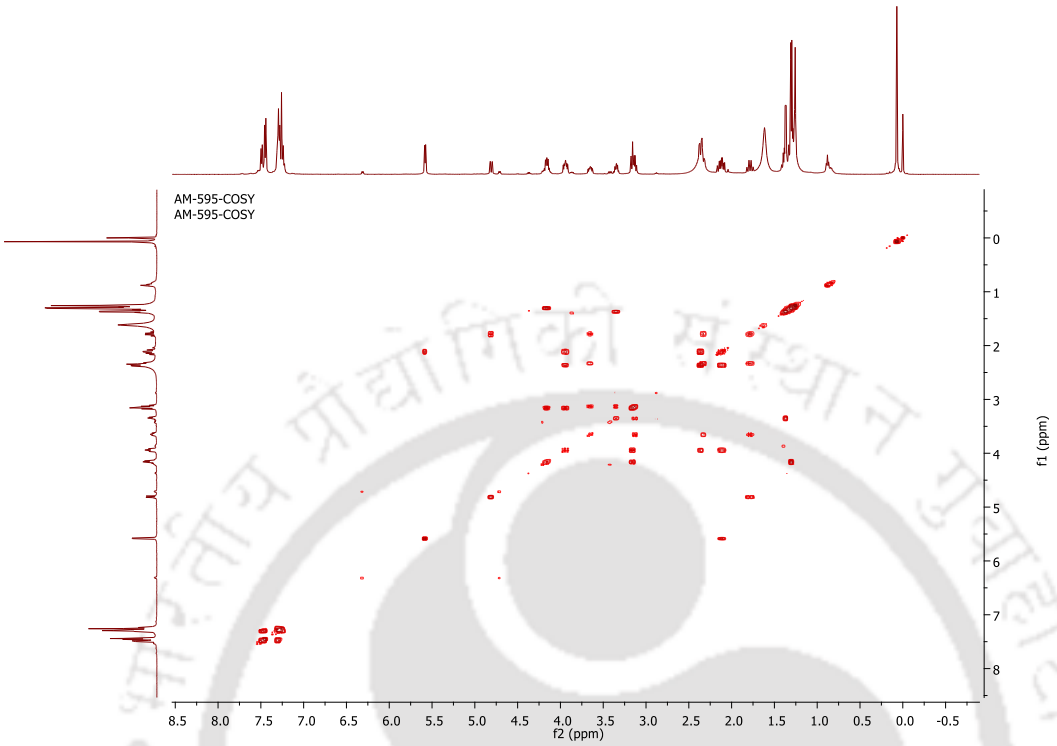
^{1}H NMR of Phenyl 2,6-dideoxy-1-thio-L-rhamnopyranoside (46r, 500 MHz, $CDCl_3$):



^{13}C{^{1}H} NMR of Phenyl 2,6-dideoxy-1-thio-L-rhamnopyranoside (46r, 500 MHz, $CDCl_3$):



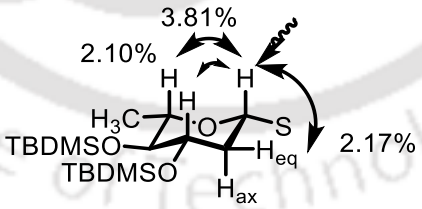
COSY NMR of Phenyl 2,6-dideoxy-1-thio-L-rhamnopyranoside (46r, 500 MHz, $CDCl_3$):



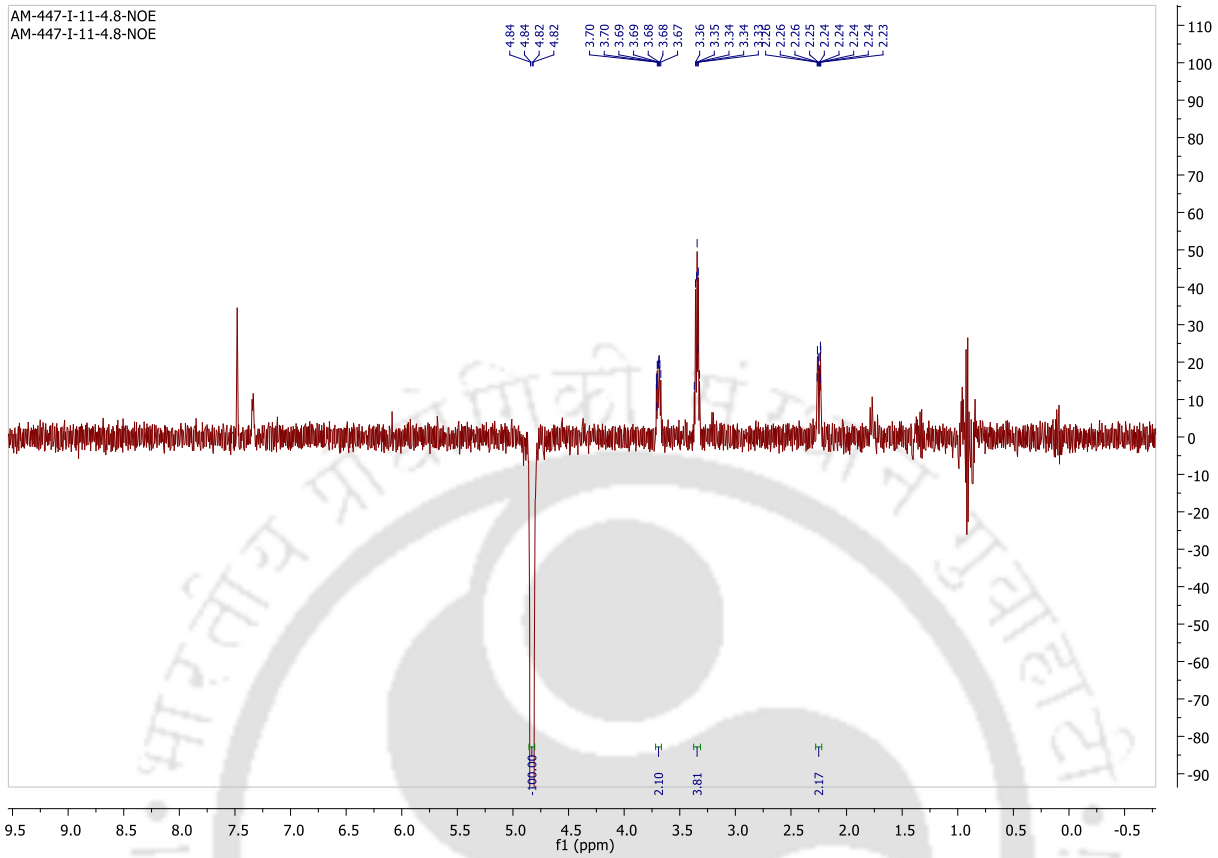
3.12 nOe Experiments:

nOe Experiment of 46jβ

Irradiation of H_1: Upon irradiation of H_1 (at 4.84 ppm), the enhancement on the equatorial 2-deoxy proton (appearing at 2.25 ppm) is found 2.17%. In addition, H_3 (appearing at 3.70 ppm) and H_5 (appearing at 3.35 ppm) also enhanced by 2.10% and 3.81% respectively. Hence, H_1 is cis to both H_3, H_5 and as well as H_{2eq}. Thus, the compound is in beta configuration.

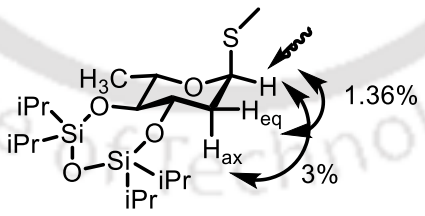


β configuration of **46j**

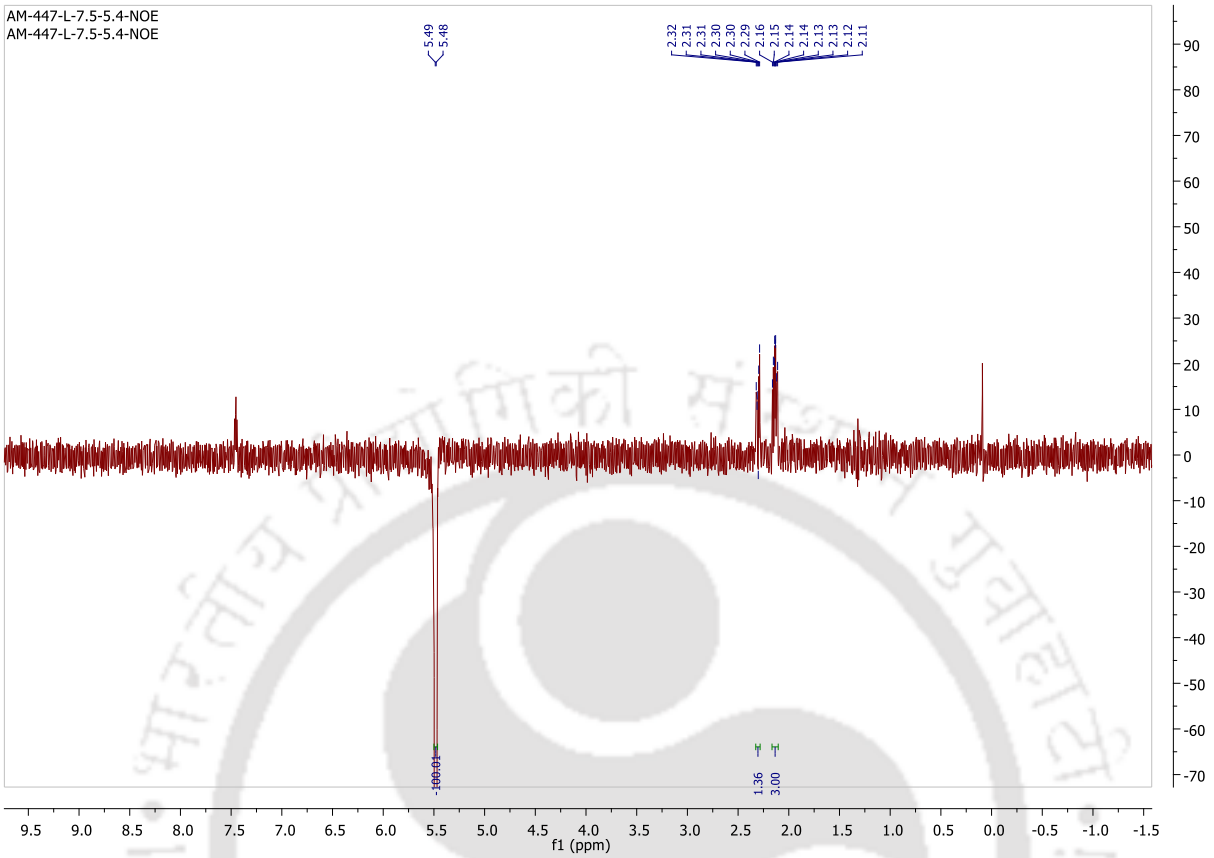


nOe Experiment of 46mα

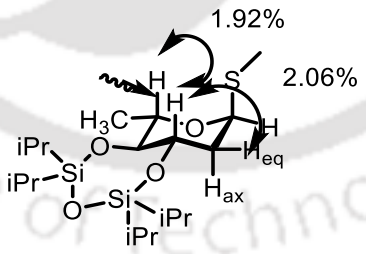
Irradiation of H_1: Upon irradiation of anomeric proton **H_1** (at 5.48 ppm), the enhancement on the axial 2-deoxy proton (appearing at 2.14 ppm) is found 3.00% which is greater than that of the equatorial 2-deoxy proton (appearing at 2.30 ppm) which is 1.36%. Hence, **H_1** is cis to **H_{2ax}** and trans to **H_{2eq}.** From the above observation it can be concluded that the compound is alpha isomer.



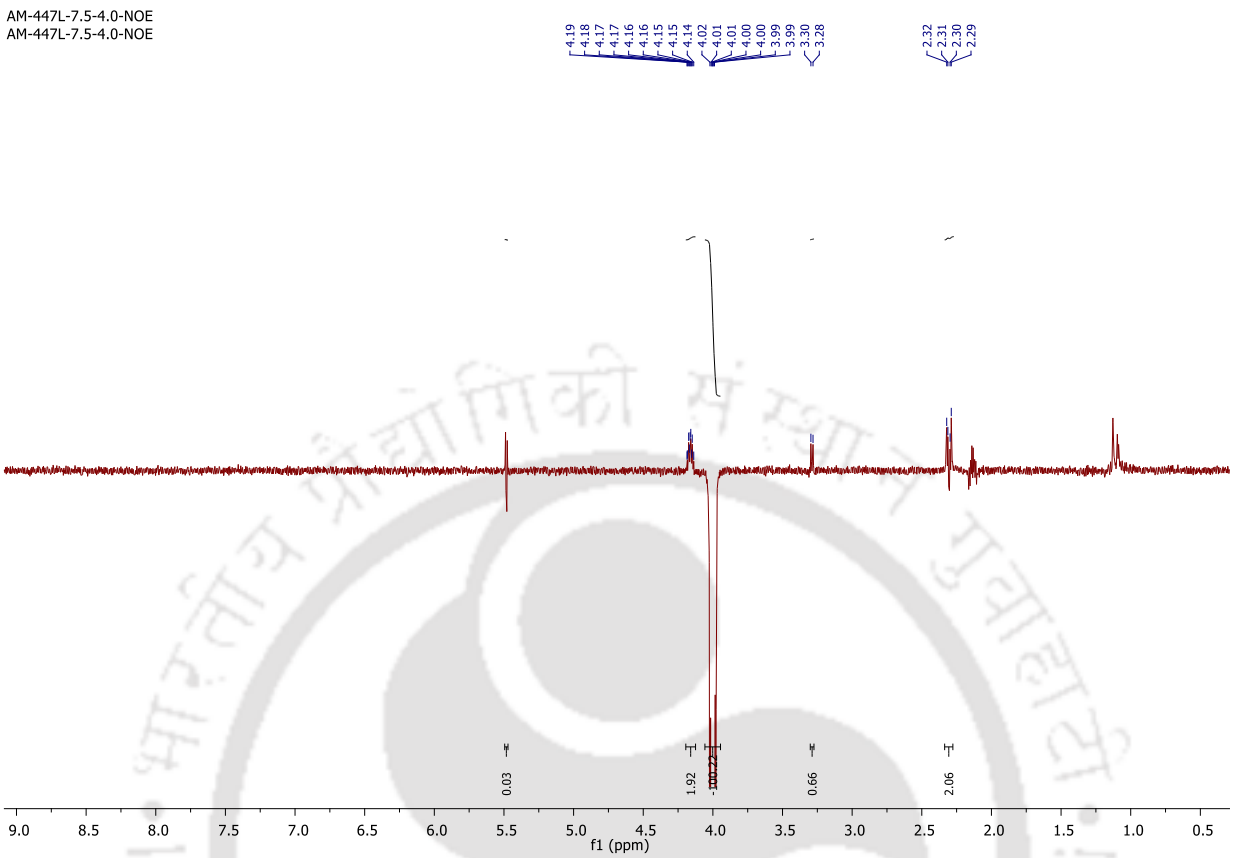
α configuration of **46m**



Irradiation of H_3: Upon irradiation of **H_3** (appearing at 4.00 ppm) the enhancement on the equatorial 2-deoxy proton (appearing at 2.30 ppm) is found 2.06%. In addition, **H_4** (appearing at 3.30 ppm) and **H_5** (appearing at 4.16 ppm) also enhanced by 0.66% and 1.92% respectively. There is no enhancement of anomeric proton **H_1**. Hence, **H_3** is cis to both **H_5** and **H_{2eq}** and trans to **H_1**. Thus, the compound is in alpha configuration.



α configuration of **46m**



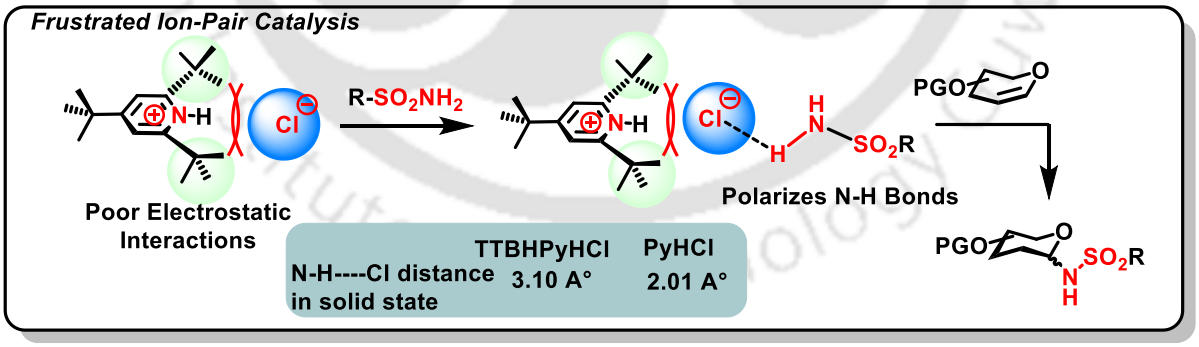
3.13 Assignment of Stereochemistry:

The α and β stereochemistry of the separated products has been established using nOe technique for some representative examples as shown. Further, analyzing and matching of the chemical shifts and couplings constants analysis of the rest of the compounds with the representative compounds has been undertaken. The stereochemistry has been carefully assigned for all the compounds. In addition, some of the known compounds stereochemistry has also been matched with the literature reports as well. Some of the analysis is provided below.

Phenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-1-thio-α,β-L-arabino-hexopyranoside is known in literature (*Angew. Chem. Int. Ed.* **2013**, *52*, 8012 –8016) and all aryl thiol gave similar ^{1}H NMR and based on that aryl thiol derivatives were analysed.

Chapter IV

Cl⁻…H-N Interactions Assisted Addition of Sulfonamides to Enol Ethers: Synthesis of 2-Deoxy and 2,6-Dideoxy Sulfonamido Glycosides



Mukherji, A.; Kancharla, P. K. *Synlett*. **2022**, DOI: 10.1055/a-1892-4608.

Cl^-…H-N Interactions Assisted Addition of Sulfonamides to Enol Ethers: Synthesis of 2-Deoxy and 2,6-Dideoxy Sulfonamido Glycosides

4.1 Introduction:

Sulfonamides or sulfa drugs are prepared by reacting sulfonyl chloride with ammonia or an amine and the functional group present in such drugs, having the general chemical formula $–SO_2NH_2$, is called sulfonamide group.

Sulfonamides have antifungal and antimalarial functions and it can also be used as antiallergic and to treat coughs. The moiety is also present in thiazide diuretic drugs (hydrochlorothiazide, metolazone, and indapamide) to treat high blood pressure and also in loop diuretic medicines (furosemide, bumetanide, and torsemide) to prevent heart failure, hypertension etc. In addition, several other drugs e.g. acetazolamide, sulfonylureas (glipizide, glyburide), and some COX-2 inhibitors (e.g., celecoxib) also contain sulfonamide functional group.

Sulfonamides are known to possess a broad spectrum of biological activities. Several sulfonamides have appeared for cancer and chemotherapy treatment. E7010, E7070, T138067 and ABT-751 (structures shown in Fig 1) can function as inhibitors of tumour cell proliferation. Some of these drugs are under clinical testing and are going to be used as antitumor medicines in the future.[1] The mechanism of antitumor activity of these sulfonamide-containing drugs has been studied in detail. It was concluded that they bind to tubulin at the colchicine binding site and inhibit the assembly of microtubule.[2] Sulfonamides having a terminal or free sulfonamido group e.g. E7070 behaves as a strong carbonic anhydrase inhibitor.[3]

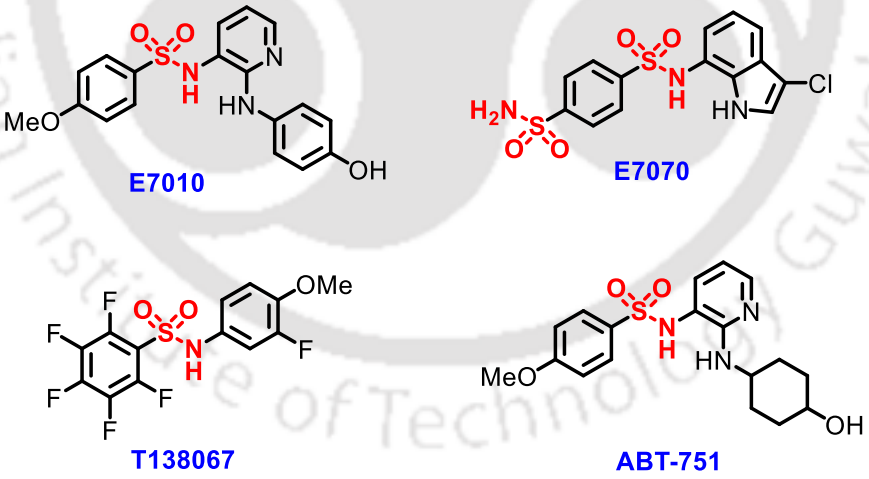


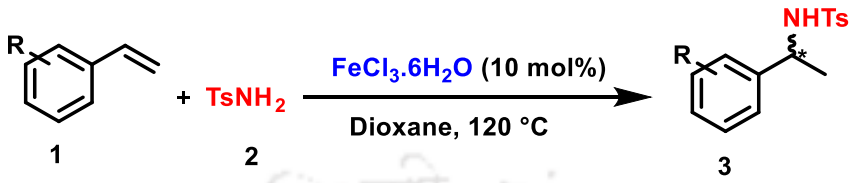
Fig 1*: Antimitotic Sulfonamides*

The aromatic and heterocyclic sulfonamides show strong inhibition of growth against many cancer cell lines. Moreover, sulfonamides that are present in zinc containing enzyme carbonic anhydrase inhibitor drugs can also be used as diuretic, antiglaucoma and antiepileptic drugs. In addition, hypoglycemic sulfonamides are useful in diabetes treatments as well.[4,5]

4.2 Literature Reports

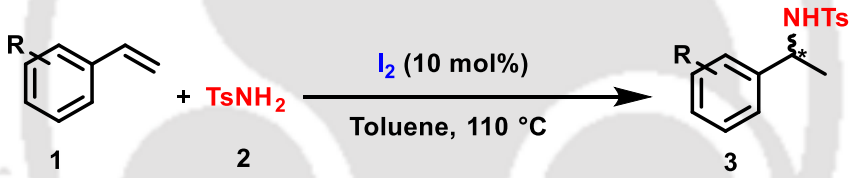
5.2.1 Addition of Sulfonamides to Terminal Alkenes

Intermolecular Markovnikov addition of sulfonamides and 1,3-dicarbonyl compounds to alkenes like styrenes, 1,3-dienes and enol-ethers etc was showcased by Zotto et al. using green and inexpensive $FeCl_3$ catalyst in the absence of any promoters (scheme 1).[6]



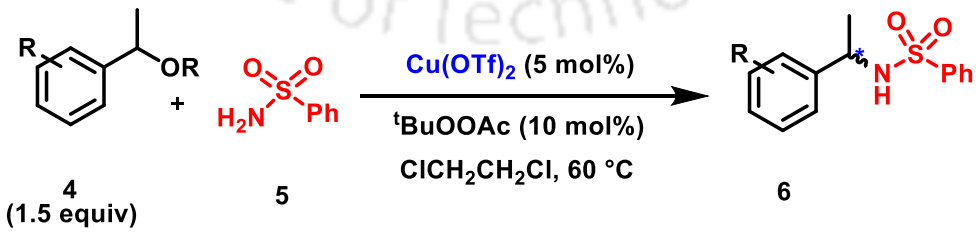
Scheme 1: *Addition of Sulfonamides using Fe(III) Catalyst*

Yadav and coworkers have demonstrated the intermolecular hydroamination reaction of vinyl arenes with sulfonamides using 10 mol% of iodine as a catalyst to synthesize tosyl and mesyl-protected secondary amines (scheme 2). The method invented by them was simple, practical, and inexpensive and the molecular iodine used as a catalyst was also commercially available and cheap. The experiments carried out using this method were high yielding and have a high reaction rate.[7]



Scheme 2: *Addition of Sulfonamides using Molecular Iodine*

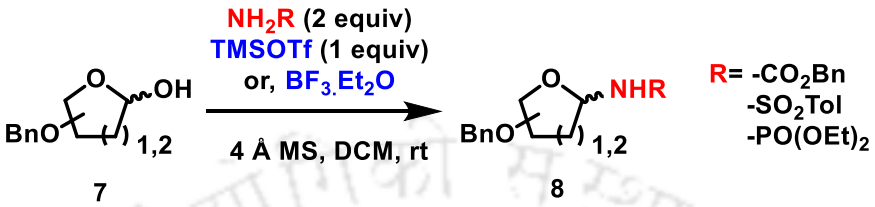
Powell and coworkers have developed amidation reaction of allylic and benzylic acetates using copper triflate/t-BuOOAc-catalyst system to couple substituted sulfonamides with acetate electrophiles to convert C-O bond into C-N bond (scheme 3). In this work, they performed the amidation reaction in the benzylic position, using allylic or benzylic acetates as substrates that any other unsaturated compounds cannot further activate.[8]



Scheme 3: *Addition of Sulfonamides using Copper triflate/t-BuOOAc Catalyst System*

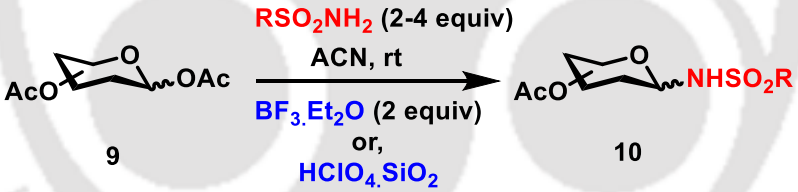
4.2.2 Sulfonamidoglycosylation

V. Liautard et al. have shown that benzyl protected aldose hemiacetal sugars react with deactivated amines having alkoxycarbonyl, tosyl or phosphoryl group using Lewis acids as catalysts (e.g. TMSOTf or $BF_3.OEt_2$) to provide the corresponding glycosylamines (scheme 4).[9] These glycosylamine derivatives are found to be present in some useful nitrogen containing natural products. Moreover, N-glycosylated sulfamides are known to exhibit activities such as inhibiting zinc containing enzyme carbonic anhydrase.[10]



Scheme 4: *Sulfonamidoglycosylation on Ribose*

Colinas and co-workers have invented a method for sulfonamidoglycosylation of readily available per-*O*-acetylated sugars using boron trifluoride–diethyl ether as a promoter.[11] They have synthesized β-glycosyl sulfonamides in good yields and with excellent stereoselectivity. even with per-*O*-acetylated D-mannose (scheme 5). The sulfonamide functional group, present in the anomeric position of the products obtained in this method, enables them to react with the active sites of carbohydrate-processing enzymes and they can function as enzyme inhibitors. In addition, the sulfonamidoglycosylation of D-mannose provided glycosides with the β-configuration which is an important finding.

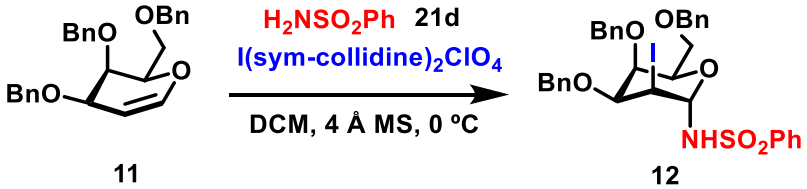


Scheme 5: *Sulfonamidoglycosylation of Per-O-acetylated Sugars*

4.2.3 Sulfonamidoglycosylation on Deoxy Sugars

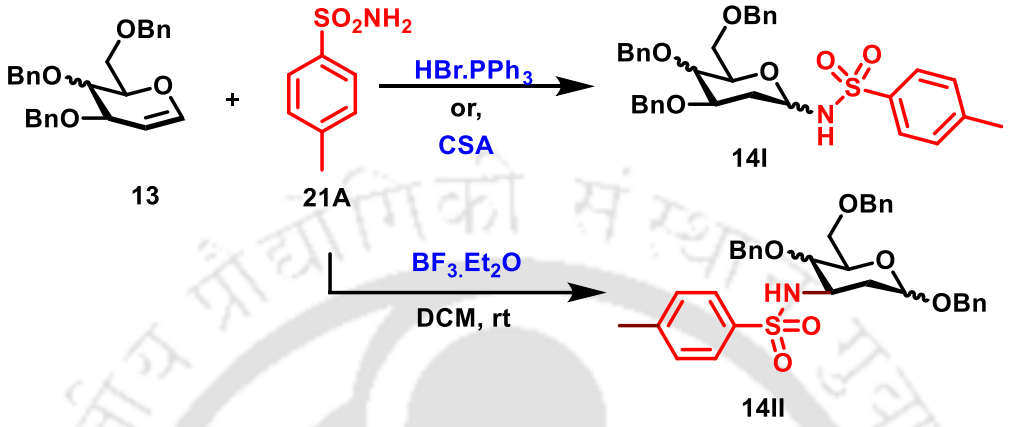
There is only a few sulfonamidoglycosylation reported in the literature so far. Danishefsky's group synthesized 2-iodo substituted sulfonamides by reacting glycals with iodonium disym-collidine perchlorate and benzenesulfonamide (scheme 6).[12]

They have performed these reactions using D-glucal, D-galactal, and D-allal donors. They have further treated these products under alkaline conditions to generate a C_1-C_2 sulfonylaziridine. A 2-iodo-α-sulfonamidoglycoside was obtained when they carried out this reaction with a sulfonamide glycosyl acceptor in the presence of a strong base.



Scheme 6: *Sulfonamidoglycosylation using I(sym-collidine)$_2$ClO$_4$*

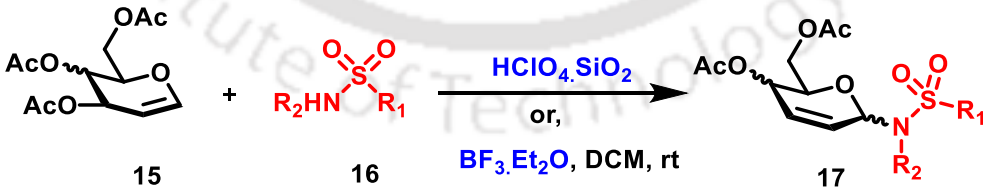
The reaction of sulfonamides with benzyl protected glucal and galactal has been shown by P. A. Colinas et al., where sulfonamidoglycosylation was achieved by using a catalytic amount of triphenylphosphine hydrobromide with high α-stereoselectivity (Scheme 7).[13] They have shown some of these new glycosylsulfonamides can be utilized as inhibitors of hepatocellular carcinoma cell lines.



Scheme 7: *Sulfonamidoglycosylation using HBr.PPh$_3$ Catalyst*

In this same work, the authors have showcased that using CSA as a catalyst gives the corresponding glycosylsulfonamide with lesser yield. In presence of boron trifluoride etherate catalyst compound **14II** was obtained in better yield. They have proposed that the formation of compound **14II** could be due to the reaction of sulfonamide with the C3-carbenium ion followed by the addition of the benzyl alcohol in the anomeric position.

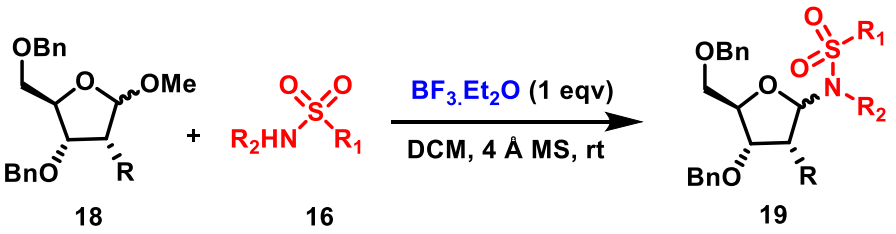
Ferrier sulfonamidoglycosylation was reported in the presence of $BF_3.Et_2O$[14] and $HClO_4.SiO_2$[15] to synthesize 2,3-unsaturated n-glycosylsulfonamides (Scheme 8) with α-stereoselectivity. Colinas et al. have studied the reaction of acetylated glycals and sulfonamides using $HClO_4.SiO_2$ where they have observed the formation of Ferrier sulfonamidoglycosylation. Using 1 mol% $BF_3.Et_2O$ as a catalyst shows similar reactivity and had little influence on the stereoselectivity outcome.



Scheme 8: *Ferrier Sulfonamidoglycosylation*

Colinas et al. have synthesized ribofuranosyl sulfonamides by reacting methoxy ribo-furanosides with sulfonamide acceptors using borontrifluoride ethyletherate as a catalyst (scheme 9).[16] The same group has showcased previously, that the sulfonamidoglycosylation of methyl glycosides of ribose using perchloric acid immobilized on silica gel can afford the corresponding sulfonamido glycosides.[1] In this work, they have shown that the sulfonamidoglycosylation of benzylated methyl ribofuranosides using Lewis acid catalyzed

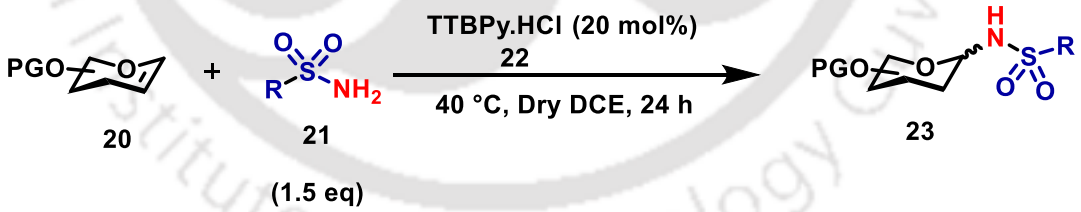
method, provides sulfonamidofuranosides efficiently. Also, side product such as ribofuranoid glycal formation was not observed in this method.



Scheme 9: *Sulfonamidoglycosylation on Ribose Sugar*

This Work:

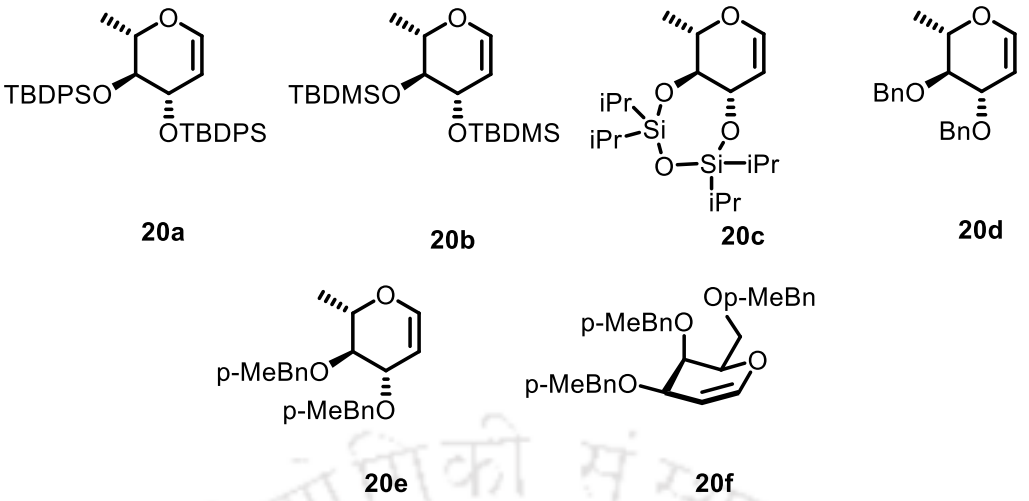
Several methods of glycosylation of glycals have been reported in the literature to synthesize 2-deoxy and 2,6-dideoxy glycosides. Preparation of 2-deoxyglycosides from glycals using the conjugate acid of the bulky base 2,4,6-tri-*tert*-butylpyridine have been previously reported by our group in 2019.[17] In this method, the deoxy glycosides were obtained with good yield and α-stereoselectivity. Later, we have reported glycals' hydration using the same catalyst system (as discussed in **chapter II**).[18] The method afforded the deoxy hemiacetals and trehalose derivatives corresponding to various silyl protected (OTBDPS, OTBS, cyclic OTIPDS, OTES etc) glycals under varying concentrations of water in high yields. In presence of other acid catalysts, such as hydrochloric, hydrofluoric acids, boron trifluoride etherate, Amberlyst H-15 resin, p-toluensulfonic acid, etc glycosylation of glycals gives a complex reaction mixture due to the formation of unwanted Ferrier glycosides resulting in 2,3- unsaturated glycosides.[19] In **chapter III** we have showcased further utilization of our catalyst TTBPyHCl to carry out thio-glycosylation on glycal donors.[20] Here in, we are reporting sulfonamidoglycosylation of glycals using TTBPy-catalysis.



Scheme 10: *This Work*

4.3 Results and Discussion

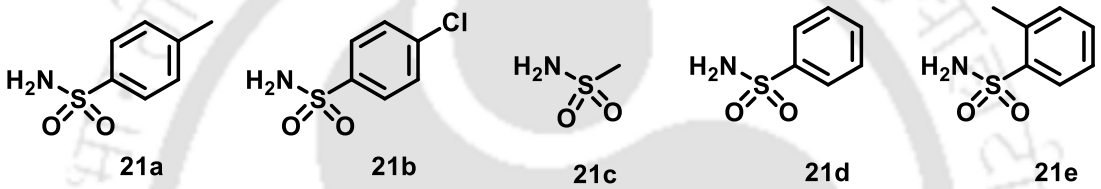
Glycals Used in this Method:



20a **20b** **20c** **20d**

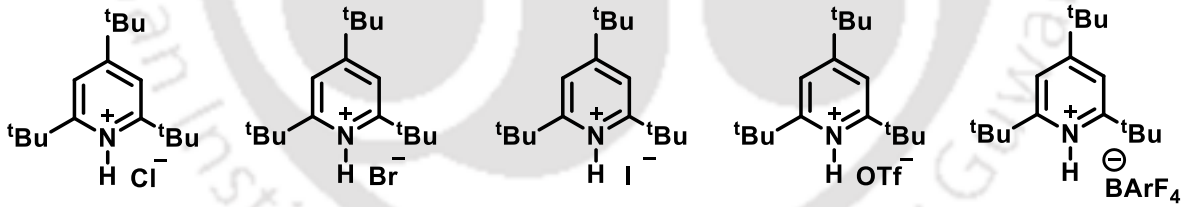
20e **20f**

Sulfonamide Acceptors Used in this Method:



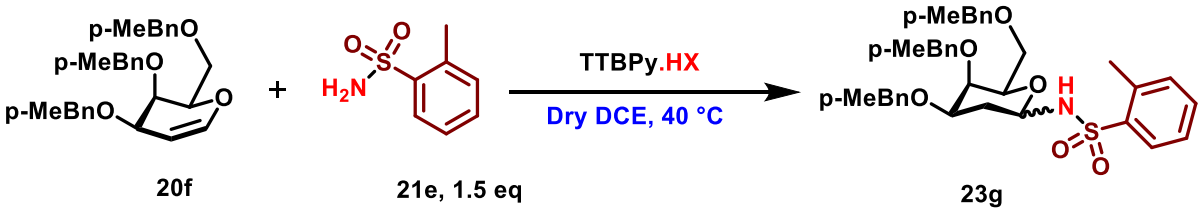
21a **21b** **21c** **21d** **21e**

Catalysts Used in this Method:



22a **22b** **22c** **22d** **22e**

4.3.1 Optimization Studies:



20f **21e, 1.5 eq** **23g**

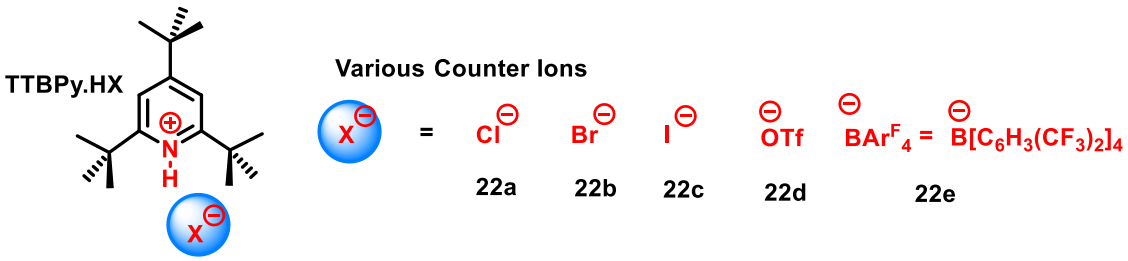


Table 1. Optimization Table

Sl No.	Catalyst, mol %	Time	Yield	Selectivity (α: β)[a]
1.	**22a,** 5 mol%	24 h	-	-
2.	**22a**, 20 mol%	24 h	75 %	1: 3.4
3.[b]	**22a**, 20 mol%	24 h	-	-
4.[c]	**22a**, 20 mol%	24 h	-	-
5.	**22b**, 20 mol%	24 h	66 %	1: 3
6.	**22c**, 20 mol%	2 d	41 %	1: 3
7.	**22d**, 20 mol%	2 d	46 %	1: 3
8.	**22e**, 20 mol%	2 d	-	-

Reaction condition: [a]Anomeric selectivities were determined by ^{1}H-NMR analysis. [b]Reaction was performed in DMF as solvent. [c]Reaction was performed in DMSO as solvent.

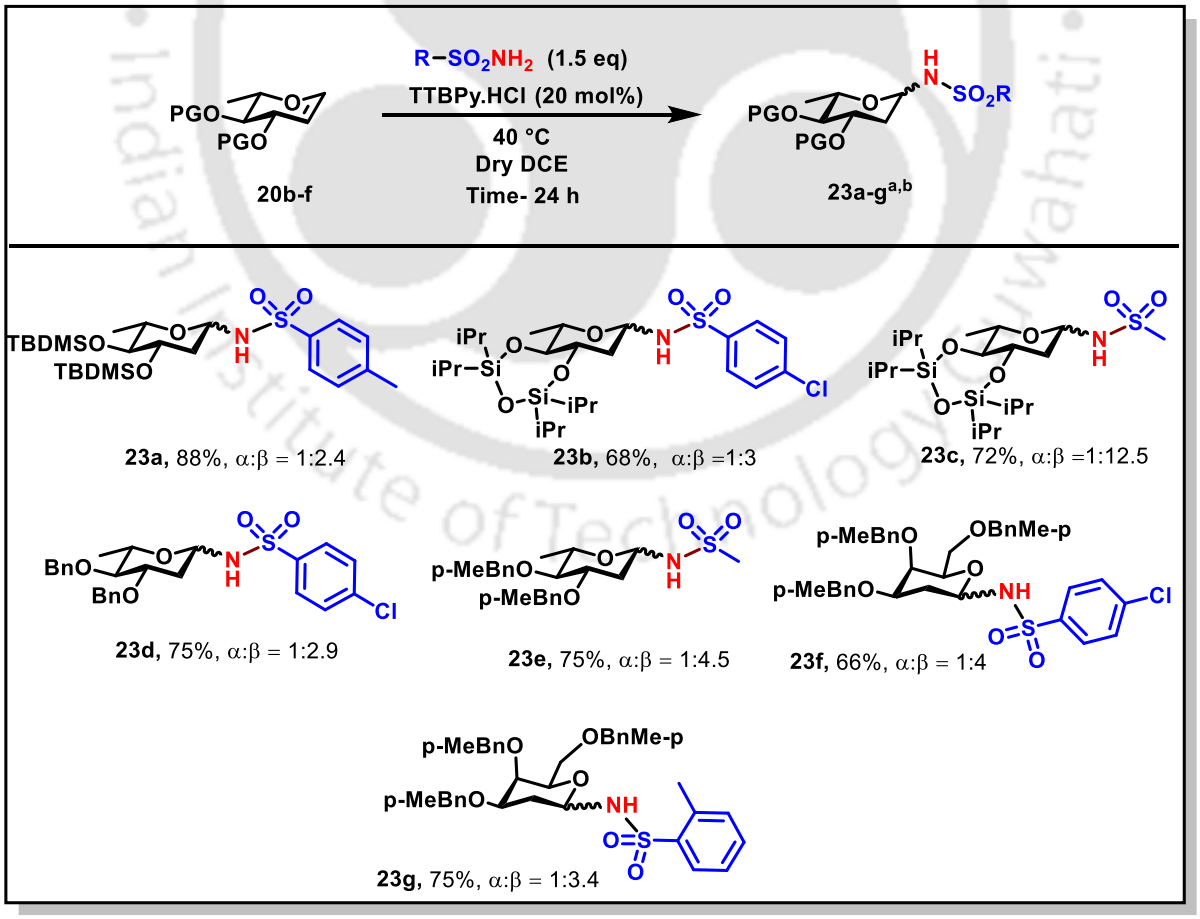
Our attempts started by using 3,4,6-tri-O-(*p*-methylbenzyl)-D-galactal **20f** and ortho-toluenesulfonamide as starting materials and the chloride salt **22a** as the catalyst in dichloroethane as the solvent. The reaction between **20f** and **21e** led to no conversion under 5 mol% of the catalyst even at 40 °C. However, we found that the sulfonamidoglycosylation proceeded smoothly at 40 °C when 20 mol% of the catalyst **22a** was used along with 1.5 equiv of the sulfonamide. The product product **23g** was obtained in 75% yield and with anomericc ratio 3.4:1 in favour of β-isomer. To decipher the roles of cation and anion in the current bulky pyridinium catalysis, we then performed the experiments by varying the anions of the catalyst. The reactions were performed with TTBPy salts of bromide, iodide, triflate, and BArF as anions, tabulated in Table 1. When Galactal **20f** was treated with *o*-toluenesulfonamide in the presence of 20 mol% of various salts, it was observed that the bromide salt gave the product in 66% yield after 24 h. In contrast, the same reaction with the chloride salt gave 75% yield (Table 1, entry 2). Whereas, a further drop in product yields was observed with iodide and triflate salts under the same reaction conditions. (41% and 46% respectively, Table 1, Entries 6, 7). Intriguingly, no conversion is observed when the anion is switched to a weakly coordinating BArF. These studies clearly demonstrate the criticality of anions under the current transformation.

Furthermore, no reaction was observed when polar solvents like DMF or DMSO were used (Table 1, Entries 3 & 4 respectively). Again, these experiments showcase the significance of the non-polar solvents in the current transformation. The polar solvents in which the individual ions are stabilized would remove any kind of strain or frustration within the ion-pair and hence cannot catalyze the transformation. With the optimized conditions in hand, various sugar glycals have been subjected to the conditions to provide the corresponding 2-deoxysulfonamides.

4.3.2 Scope of Derivatives:

The protocol has been tested with various substituted benzene sulfonamides **21a-e** by reacting them with OTBDMS, OTIPDS, OBn and O-pMeBn protected rhamnal and galactal donors **20b-f** where products **23a-g** are obtained in good yields and moderate to good stereoselectivity (Table 2). No significant change in stereoselectivity was observed when the protecting group is changed from silyl to benzyl and *p*-methylbenzyl on rhamnose based donrs **20b-e**. To our surprise, methanesulfonamide reacted with silyl protected rhamnose donor **20c** to provide expected compund **23c** with high β-selectivity (β: α= 12.5: 1). *p*-Methylbenzyl protected galactal donor reacted with sulfonamide acceptor **21b** and **21e** to provide respective glycosylated compound **23f** and **23g** with 66% and 75% yield respectively. Aliphatic sulfonamide **21c** also smoothly coupled to **20c** and **20e** to give expected products **23c** and **23e**, with 72% and 75% yield respectively, in favour of β-stereoselectivity. All of these donors gave β-glycosylsulfonamide irrespective of the sulfonamide acceptor used. The stereochemistry of the products have been confirmed by nOe analysis and also the coupling constants. When the signal for the anomeric proton of **23c** at 4.80 ppm was irradiated, an enhancement in the signal at 3.35 ppm corresponding to H-5 is observed suggesting the cis relation between the sulfonamide group and the C5-methyl group.

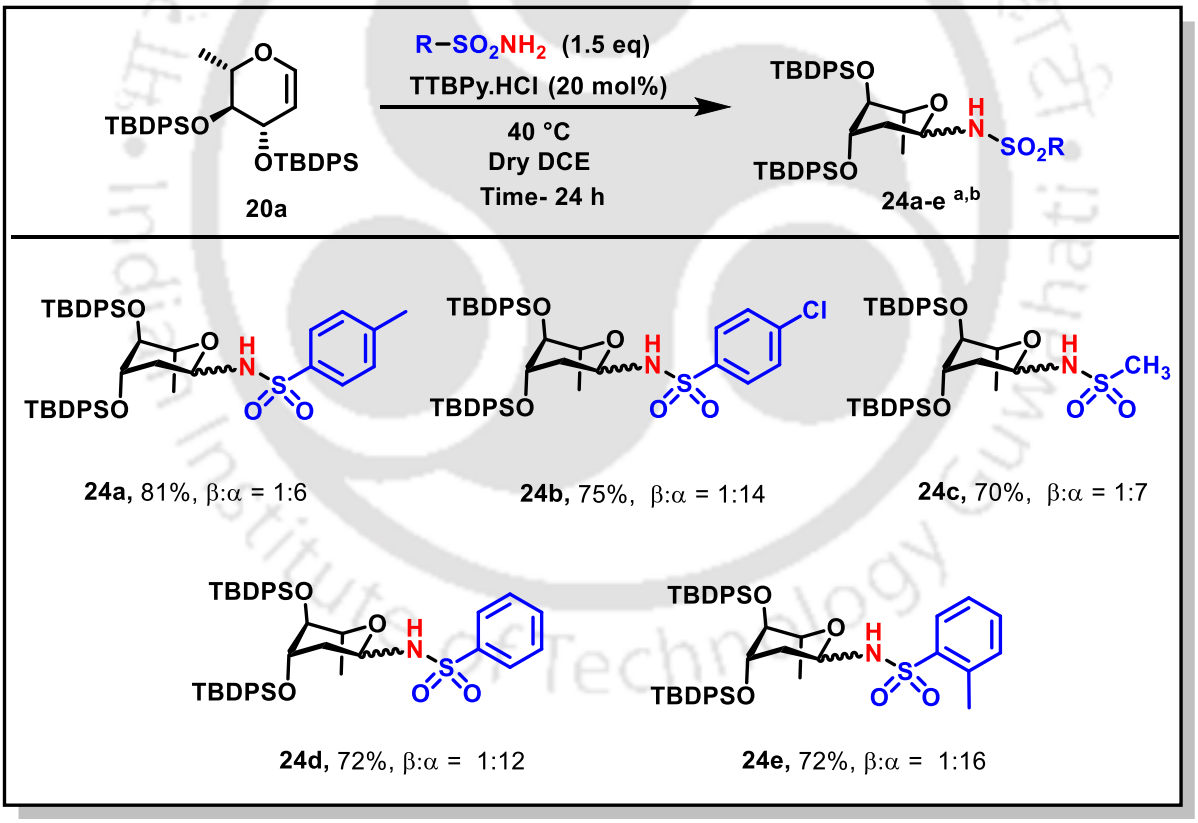
Table 2. Glycosylation of OTBDMS-, Cyclic OTIPDS-, Benzyl- and p-Methylbenzyl-Protected Glycals with Various Sulfonamide Acceptors



Reaction condition: [a]Anomeric selectivities were determined by [1]H-NMR analysis. [b]Isomer analysis was done by nOe experiment.

Interestingly, when 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **20a** was reacted with toulylsulfonamide under the reaction conditions, it surprisingly lead to stereo-switch and gave the α-product as the major anomer (α:β = 6:1). Later, the coupled products of **20a** with other sulfonamides have also been prepared (Table 3). In all the cases, the sulfonamidoglycosides **24a-e** were obtained with excellent stereoselectivity ratios ranging from 6:1 to 16: 1 favouring α-isomer. The stereochemistry of the products has been confirmed by nOe analysis. The irradiation of the signal for H1 at 5.40 ppm led to an enhancement of the signal for the C-5 methyl doublet at 1.31 ppm confirming the cis-relation of the anomeric proton and there by the β-sulfonide. However, this also confirms the $^4C_1$ conformation of the di-O-TBDPS protected products. A variety of sulfonamides **21a-e** were reacted with 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **20a** to show the versatility of the reaction.

Table 3. Sulfonamidoglycosylation of di-OTBDPS-Protected L-Rhamnal with Various Acceptors

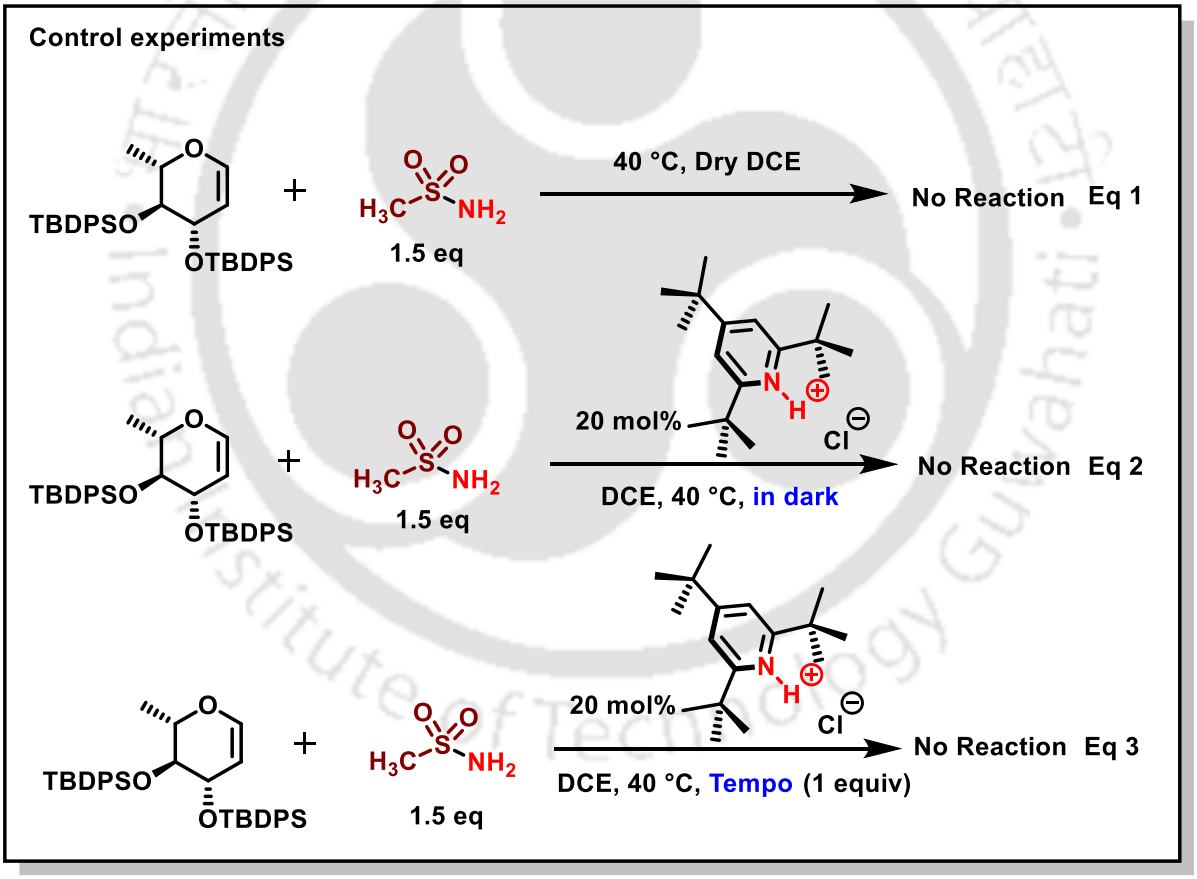


Reaction condition: [a]Anomeric selectivities are determined from [1]H-NMR analysis. [b]Isomer analysis was done by nOe experiment.

4.3.3 Control Experiments:

In order to understand the mechanism, a few control experiments were performed. Firstly, the reaction between the rhamnal and the methylsulfonamide when performed in the absence of the catalyst did not lead to any conversion, suggesting the importance of the catalyst (Scheme 11, Eq 1). Also, a few solid state IR studies were performed. Unlike other pyridines, the protonated $[TTBPyH]^+$ gives a sharp signal at 3346 cm^{-1} for the N- H stretch in the IR spectrum indidicating the inability of the N-H proton to involve in any H-bonding. When the IR spectrum was recorded with a 1:1 mixture of TTBPy·HCl with p-toluenesulfonamide and methanesulfonamide (**21a** and **21c**), no change was observed for the N-H stretch of the bulky pyridinium species demonstrating the sulfonamide is not involved in any interaction with the cationic species. However, the intensity of the stretch corresponding to the NH_2 doublet of the sulfonamide is significantly decreased indicating some interaction with the bulky pyridine salt. Also, the reaction did not proceed under the same optimized condition when performed in dark conditions (Scheme 11, eq 2). Also, no product formation was observed in the presence of a radical trapping agent TEMPO (Scheme 11, eq 3). These experiments suggest the possible involvement of a frustrated radical pair (FRP) species in the current transformation.

Scheme 10. Various Control Experiments with TTBPy.HCl Catalyst



Scheme 11: *Control Experiments*

4.4 IR and EPR Studies:

4.4.1 Study of the N-H Stretching Frequency of TTBPy·HCl from IR Spectroscopy

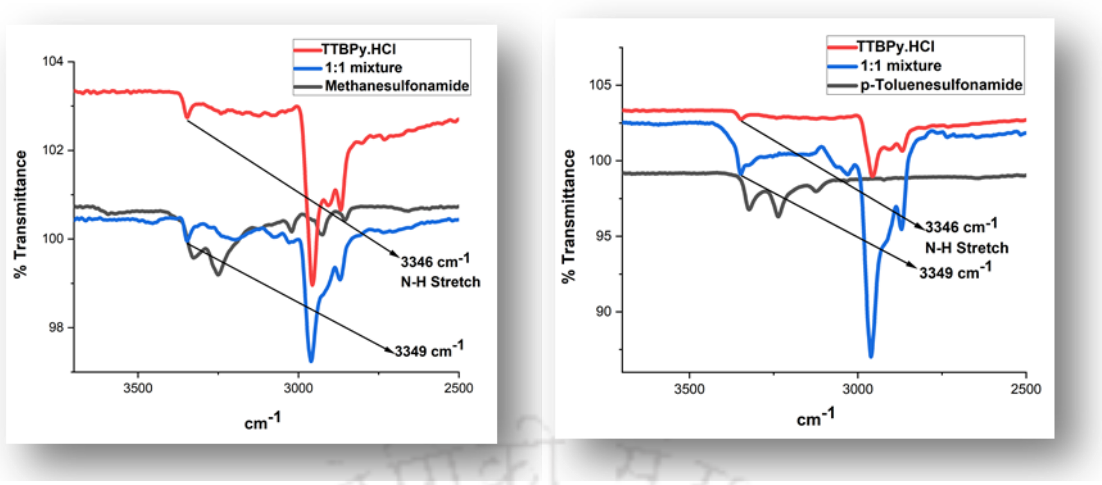


***Fig 2**: Study of the N-H Stretching frequency from IR Spectroscopy*

IR studies are performed to understand the catalyst and the sulfonamide interactions. IR spectrum of TTBPy·HCl catalyst, sulfonamide (**2a** and **2c**) and mixture of these two were recorded and their merged spectrum was shown. Unlike other pyridines, the protonated $[TTBPyH]^+$ gives a sharp signal at 3346 cm^{-1} for the N- H stretch that indicates that the N-H proton does not involve in H-bonding (Figure 2). Also, the N-H stretch is barely affected in the presence of both methane sulfonamide and p-toluene sulfonamide.

4.4.2 ESR Study:

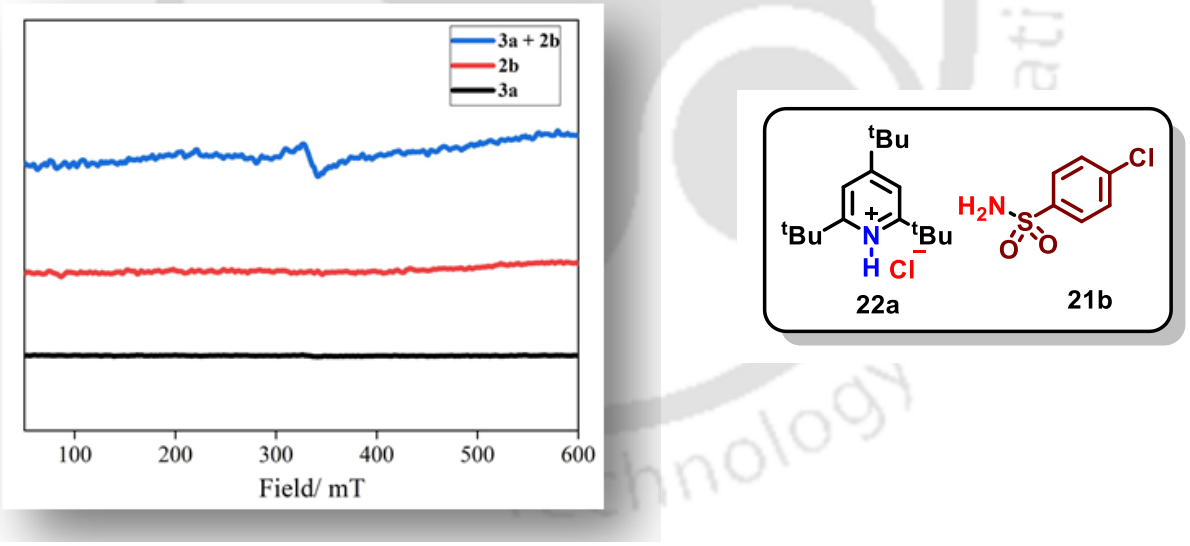
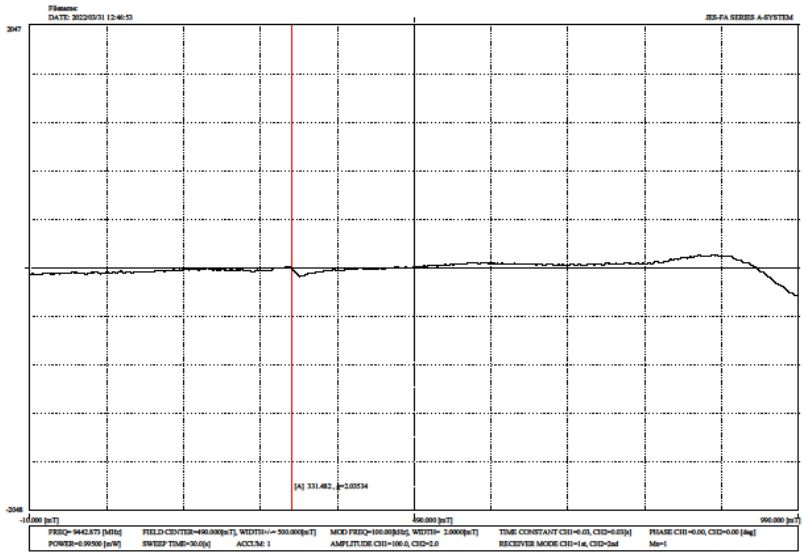


***Fig 3**: ESR Study*

ESR spectrum of TTBPy·HCl catalyst (**22a,** 3 mg in 0.3 ml DCM) and 4-Chlorobenzenesulfonamide (**21b,** 2 mg in 0.3 ml DCM) was recorded at room temperature and both of them didn't show any signal. 1:1 mixture of **22a** and **21b** (3 mg of **22a** and 2 mg of **21b** in 0.3 ml DCM) gave rise to a spontaneous ESR signal at rt having g value 2.03534.

ESR Spectrum of 22a + 21b:



FREQ= 9442.873 mHz, FIELD CENTER=490.000 mT, WIDTH+/-= 500.000 mT, MOD FREQ=100.00 kHz, WIDTH= 2.0000 mT, TIME CONSTANT CH1=0.03, CH2=0.03 s, PHASE CH1=0.00, CH2=0.00 [deg], POWER=0.99500 mW, SWEEP TIME=30.0 s, ACCUM: 1, AMPLITUDE CH1=100.0, CH2=2.0, RECEIVER MODE CH1=1st, CH2=2nd, Mn= 1.

The EPR signal is not conclusive provides only little evidence towards the involvement of any radical species under the reaction conditions. However, the IR experiments, along with the control experiments and the optimization studies with various salts, point to an anion-directed activation similar to the *O*- and *S*-glycosylation reactions.

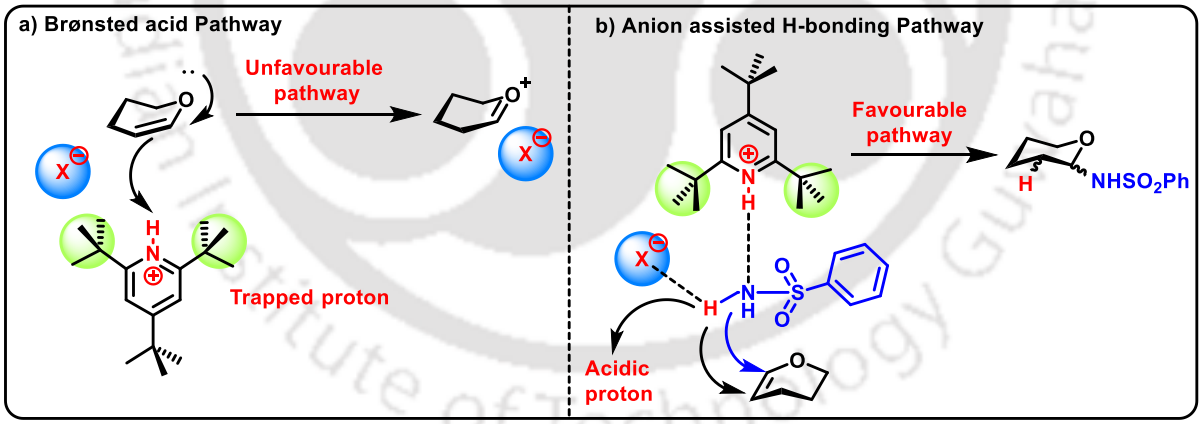
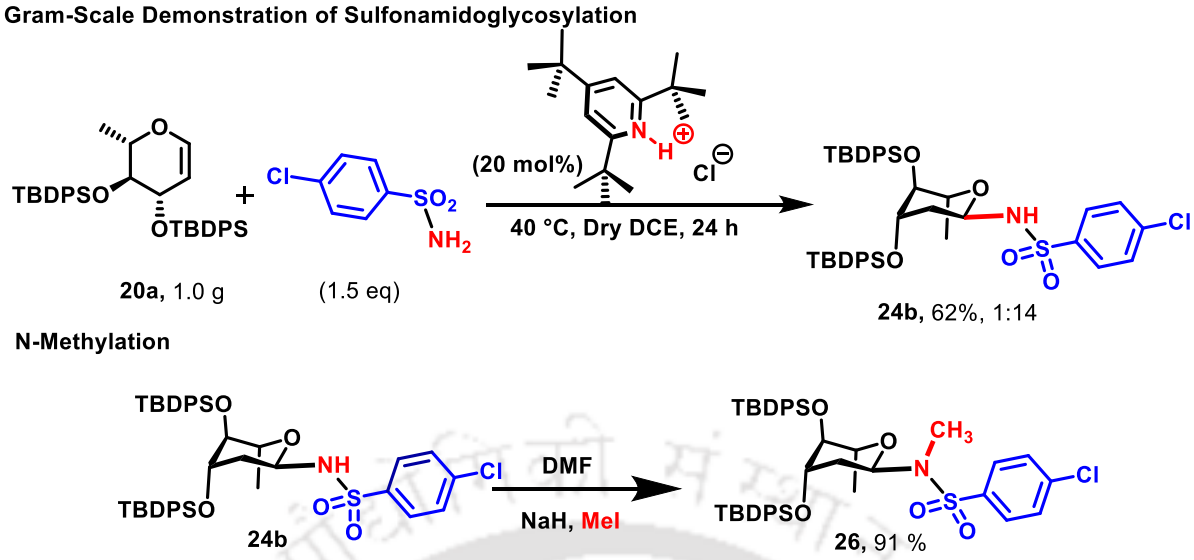


Fig 4: *Proposed Mechanism*

The anions associate with the sterically bulky 2,4,6-tri-*tert*-pyridinium, due to the strain within the ion-pair is imparted with unsual reactivity and can polarize the N-H bond of the sulfonamido group. The thus mildly acidic N-H proton protonates the glycals which undergoes a nucleophilic addtion onto the glycosyloxacarbenium ion leading to the observed N-glycosylated products (Figure 4, b).

4.5 Applications:

Scheme 11. Further Reactions of Sulfonamidoglycosylation.

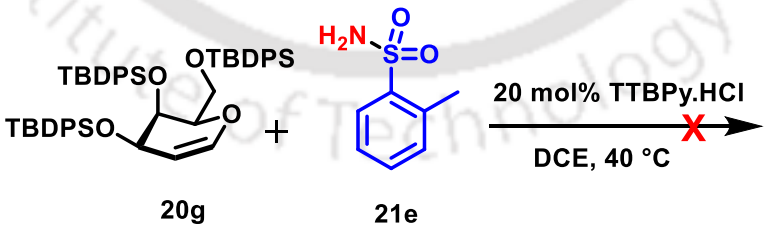


Scheme 12: *Application*

The applicability of current mild catalysis for the sulfonamidoglycosylation protocol towards large scale synthesis was also investigated. We were delighted to find that 1 gm of di-*O*-TBDPS protected L-rhamnal **20a** was reacted with glycosyl sulfonamide acceptor **21b** in the presence of 20 mol % of **22a** in DCE at 40 °C, afforded the corresponding sulfonamidoglycoside **24b** in 62% yield with α selectivity (Scheme 12). Also, N-alkylation of the one of the derivatives (**24b**) has been performed to showcase the utility of these sulfonamidoglycosides for the further transformations. The compound **24b** when reacted with iodomethane in the presence of sodium hydride in DMF as a solvent provided the corresponding N-methyl adduct in an excellent 91% yield.

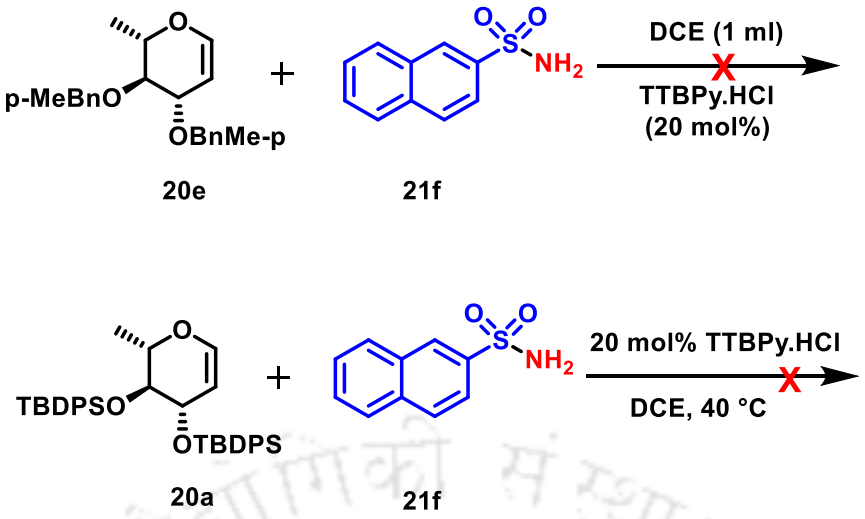
4.6 Failures:

The sterically highly bulky OTBDPS protected galactal **20g** reacted with sulfonamide **21e**. It failed to give any glycosylated product under the optimized conditions (Scheme 13), which signifies the steric bulk constraints and the limitation of the current protocol.



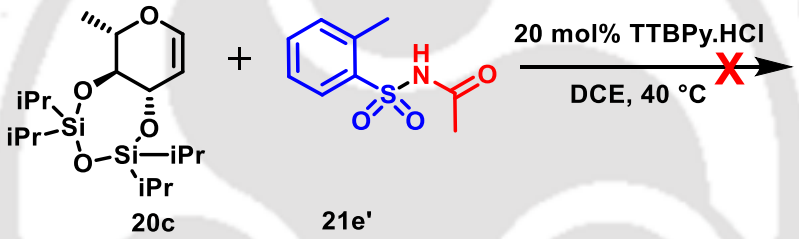
Scheme 13: *Sulfonamidoglycosylation with tri-O-TBDPS-Galactal*

The steric bulk was increased in the sulfonamide acceptor part and naphthalene-2-sulfonamide was used and this reaction also failed to give the expected products with donors **20a** and **20e** (Scheme 14), under the same optimized conditions.



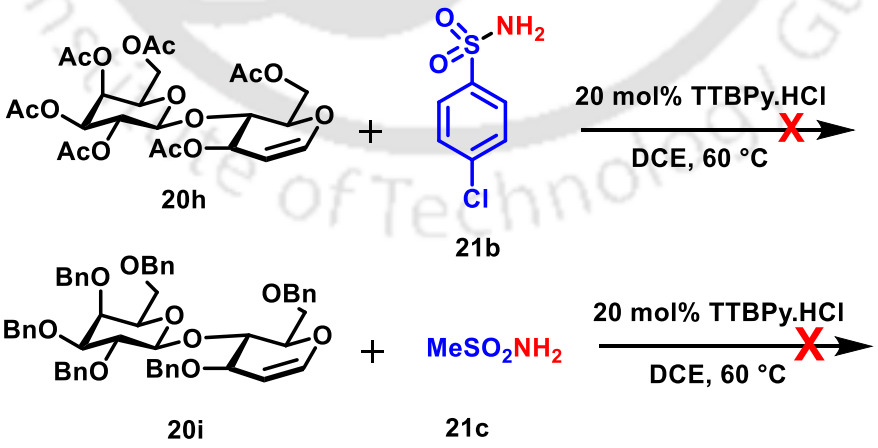
Scheme 14: *Sulfonamidoglycosylation with Naphthalene-2-sulfonamide*

We attempted to synthesize N-acetylated Glycosyl Sulfonamide and for that purpose, acetylation was performed on acceptor **2e**. Further reaction with acetylated sulfonamide acceptor **2e'** didn't precede with the optimized reaction conditions (Scheme 15).



Scheme 15: *Sulfonamidoglycosylation with N-acetylated Sulfonamide*

To synthesize disaccharide-based sulfonamidoglycoside, acetylated and benzylated lactal were synthesized. Both didn't react in the presence of the catalyst **3a** even at elevated temperatures (Scheme 16).



Scheme 16: *Sulfonamidoglycosylation with D-Lactal*

4.7 Conclusion:

In conclusion, the work described here provides a strategy for the stereoselective synthesis of both α and β sulfonamidoglycosides. The preparation is high yielding and

effective for gram scale synthesis. We have successfully showcased the utility of the sterically bulky 2,4,6-tri-*tert*-butylpyridinium salts in activating sulfonamides, thus synthesizing the biologically important class of compounds, 2-deoxy and 2,6-dideoxy sulfonamidoglycosides. IR studies reiterate the fact that the sterically protected N-H proton is not involved in H-bonding interactions. Interestingly, the observed catalytic activity also seems to be influenced by the catalyst counterion. Besides, the application of the sulfonamidoglycosides has been shown by synthesizing the corresponding N-alkylated product.

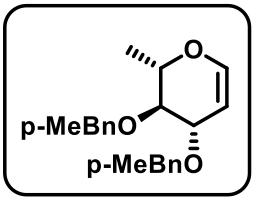
4.8 Experimental Section:

General Information and Analysis:

The general information and analysis section for chapter-IV is same as mentioned in **chapter-III**.

Synthesis of Donors and Catalysts Used in this Method:

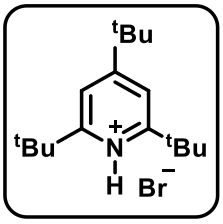
Synthesis of 3,4-di-O-para-methylbenzyl-L-rhamnal (20e):



L-Rhamnal (500 mg, 3.84 mmol, 1.0 equiv) was dissolved in 20 ml DMF. Then, to it NaH (461 mg, 19.2 mmol, 3 equiv considering 60% dispersion in mineral oil) was added slowly. Then, 4-methyl benzyl bromide (2.2 g, 11.5 mmol, 3 equiv) was added portion wise slowly and it was stirred for 24 h. Then, it was quenched with MeOH (5 ml). Now, the solvent was concentrated and extracted with DCM (3x30 ml). The organic phase was washed with brine (100 ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Then, it was purified by column chromatography in ethyl acetate/hexane solvent system to afford the white solid **20e**. R_f- 0.5 in 10% EA in hexane, amount- 1.0 g, yield- 77%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 – 7.24 (m, 2H), 7.22 (d, *J* = 7.8 Hz, 2H), 7.15 (d, *J* = 7.7 Hz, 4H), 6.34 (d, *J* = 6.1 Hz, 1H), 4.85 – 4.83 (m, 2H), 4.65 – 4.59 (m, 2H), 4.54 (d, *J* = 11.4 Hz, 1H), 4.50 (d, *J* = 5.6 Hz, 1H), 4.18 (d, *J* = 6.4 Hz, 1H), 3.93 (dq, *J* = 12.9, 6.4 Hz, 1H), 3.47 – 3.44 (m, 1H), 2.34 (s, 6H), 1.36 (d, *J* = 6.4 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 144.8, 137.6, 137.5, 137.4, 135.5, 135.4, 135.4, 129.2, 129.2, 128.3, 128.0, 100.4, 79.4, 76.4, 74.1, 74.1, 71.9, 70.6, 21.3, 17.6. HRMS (ESI) m/z: $[M + NH_4]^+$ calcd for $C_{22}H_{30}NO_3$ 356.2226; found 356.2218. $[\alpha]_D^{22}$= +5.17 (*c* 0.3, $CHCl_3$).

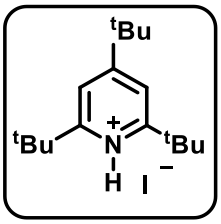
Glycal **20a-20d** and **20f** was prepared following previously reported procedures. Spectroscopic data were in agreement with the reported data. [17, 21-23]

Synthesis of 2,4,6-tri-*tert*-butylpyridinium hydrobromide salt (22b):



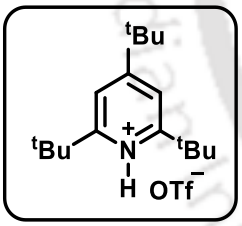
2 ml of acetyl bromide was added dropwise to 2 ml of methanol in ice bath. After few min, ether (1 ml) solution of 2,4,6-tri-*tert*-butylpyridine (500 mg, 2.020 mmol) was added dropwise to it which readily resulted in a turbid solution and the reaction mixture was stirred at 0 °C for 1 h. The solution was then concentrated under reduced pressure to get a white solid. The solid was washed with ether (5x5 ml) to afford **22b** in quantitative yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 13.15 (s, 1H), 7.60 (s, 2H), 1.81 (s, 18H), 1.45 (s, 9H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 172.2, 165.4, 118.5, 37.7, 36.9, 30.7, 30.6. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{30}N$ 248.2378; found 248.2351.

Synthesis of 2,4,6-tri-*tert*-butylpyridinium hydroiodide salt (22c):



2,4,6-tri-*tert*-butylpyridine (100 mg, 0.404 mmol, 1.0 equiv) was dissolved in 2 ml of toluene and 57% w/w aq. solution of hydriodic acid (0.404 mmol, 1.0 equiv) was added to it dropwise keeping it in ice bath. After that, it was stirred at 0 °C for 1 h and pale yellow colored solution of **22c** was observed. Then, the solution was concentrated under reduced pressure, co-evaporated with toluene and washed with ether to get a brown solid **3c** in quantitative yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.37 (s, 1H), 7.71 (d, J = 1.4 Hz, 2H), 1.73 (s, 18H), 1.47 (s, 9H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 173.0, 163.3, 118.9, 37.2, 37.0, 30.2, 29.8. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{30}N$ 248.2378; found 248.2368.

Synthesis of 2,4,6-tri-*tert*-butylpyridinium trifluoromethanesulfonate salt (22d):



2,4,6-tri-*tert*-butylpyridine (100 mg, 0.404 mmol, 1.0 equiv) was dissolved in 2 ml of diethyl ether and triflic acid (60 mg, 36 µL, 0.404 mmol, 1.0 equiv) was added to it dropwise keeping it in ice bath. After that, it was stirred at 0 °C for 1 h and immediately a white precipitate of **22d** was observed. Then, the solution was allowed to settle down for few min and after decant the solution, the solid part was then concentrated under reduced pressure and washed with ether to get a white solid **3d** in quantitative yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.03 (s, 1H), 7.64 (s, 2H), 1.59 (s, 18H), 1.43 (s, 9H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 173.2, 164.3, 118.5, 37.1, 37.1, 30.2, 29.1. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{30}N$ 248.2378; found 248.2351.

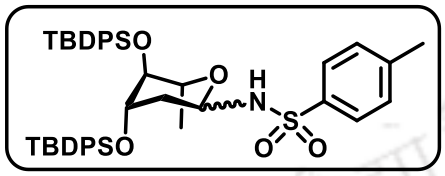
Catalyst **3a** and **3e** was prepared following previously reported procedures. Spectroscopic data were in agreement with the reported data. [17]

General Method to Synthesize Sulfonamido-glycosides from Glycals:

Glycal (0.082- 0.161 mmol, 1.0 equiv) and glycosyl sulfonamide acceptor (0.123-0.240 mmol, 1.5 equiv) was taken in a round bottomed flask (10 mL). The flask was then filled with dry DCE and catalyst TTBPy·HCl (20 mol%) was added to it. The mixtures were

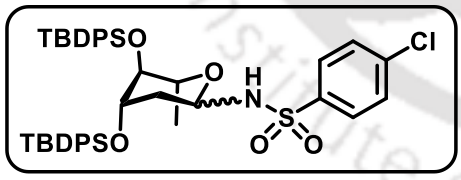
stirred at 40 °C in a sealed flask until the reaction was determined to be complete by either TLC or NMR analysis of the crude material. The reaction mixture was quenched by water (20 ml for 0.082 mmol) and it was extracted with DCM (3x15 ml for 0.082 mmol), dried over Na_2SO_4 and concentrated in vacuo and purified by silica gel column chromatography (Merck 60-120 mesh, 7 gm) followed by HPLC purification (using HPLC-grade acetonitrile solvent, flow rate- 5 ml/min) for some of the compounds.

3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β−L-rhamnopyranosyl p-toluenesulfonamide (24a)



According to general method, a solution of glycosyl donor 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **20a** (50 mg, 0.082 mmol, 1.0 equiv) and glycosyl sulfonamide acceptor **21a** (21 mg, 0.123 mmol, 1.5 equiv) in dry DCE at 40 °C was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (5 mg, 0.0164 mmol, 20 mol%) and stirred for 24 h to get the product **24a** as a colourless oil. R_f- 0.4 in 20% EA/hexane, eluent 7% EA in hexane, amount- 52 mg, yield- 81%. Selectivity α: β=6: 1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.2 Hz, 2H), 7.49 – 7.33 (m, 14H), 7.26 – 7.19 (m, 8H), 5.36 (td, *J* = 10.4, 1.9 Hz, 1H), 5.12 (d, *J* = 10.2 Hz, 1H), 3.95 (d, *J* = 1.7 Hz, 1H), 3.75 (q, *J* = 7.3 Hz, 1H), 3.42 (d, *J* = 2.7 Hz, 1H), 2.42 (s, 3H), 1.81 (ddd, *J* = 13.2, 10.8, 2.6 Hz, 1H), 1.53 (d, *J* = 13.1 Hz, 1H), 1.13 (d, *J* = 7.4 Hz, 3H), 0.96 (s, 9H), 0.88 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.3, 138.6, 135.9, 135.8, 135.7, 133.7, 133.2, 133.1, 133.0, 130.1, 129.9, 129.8, 129.5, 127.9, 127.8, 127.8, 127.7, 127.5, 75.8, 73.2, 71.3, 70.8, 34.9, 27.0, 26.9, 21.7, 19.2, 19.1, 16.5. HRMS (ESI-QTOF) $C_{45}H_{54}O_5NSSi_2NH_4$ $[M+NH_4]^+$- calculated- 795.3683; found- 795.3681. $[\alpha]_D^{22}$= -20 (*c* 0.70, $CHCl_3$).

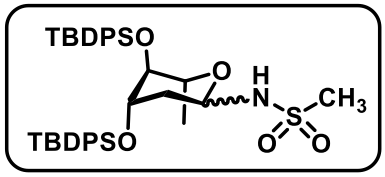
3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-chlorobenzene sulfonamide (24b)



According to general method, a solution of glycosyl donor 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **20a** (50 mg, 0.082 mmol, 1.0 equiv) and glycosyl sulfonamide acceptor **21b** (24 mg, 0.125 mmol, 1.5 equiv) in dry DCE at 40 °C was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (5 mg, 0.0164 mmol, 20 mol%) and stirred for 24 h to get the product **24b** as a colourless oil. R_f- 0.4 in 20% EA/hexane, eluent 7% EA in hexane, amount- 49 mg, yield- 75%. Selectivity α: β=14: 1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.6 Hz, 2H), 7.42 (m, 16H), 7.24 (m, 6H), 5.36 (td, *J* = 10.3, 1.9 Hz, 1H), 5.21 (d, *J* = 10.2 Hz, 1H), 3.98 (d, *J* = 1.6 Hz, 1H), 3.72 (q, *J* = 7.2 Hz, 1H), 3.43 (d, *J* = 2.6 Hz, 1H), 1.99 (s, 3H), 1.85 – 1.79 (m, 1H), 1.55 (d, *J* = 13.3 Hz, 1H), 1.11 (d, *J* = 7.3 Hz, 3H), 0.97 (s, 9H), 0.89 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.4, 139.0, 135.9, 135.8, 135.7, 133.7, 133.2, 133.1, 133.1, 130.1, 129.9, 129.9, 129.8, 129.1, 129.0, 128.9, 128.0, 127.9, 127.8,

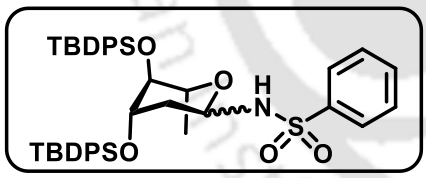
127.8, 127.7, 75.7, 73.3, 71.3, 70.9, 34.8, 27.0, 26.9, 19.2, 19.1, 16.6. $[\alpha]_D^{22}$= -22 (*c* 0.70, $CHCl_3$).

3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl methanesulfonamide (24c)



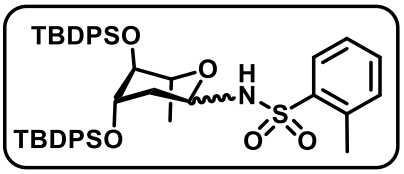
According to general method, a solution of glycosyl donor 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **20a** (50 mg, 0.082 mmol, 1.0 equiv) and glycosyl sulfonamide acceptor **21c** (12 mg, 0.126 mmol, 1.5 equiv) in dry DCE at 40 °C was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (5 mg, 0.0164 mmol, 20 mol%) and stirred for 24 h to get the product **24c** as a colourless oil. R_f- 0.4 in 20% EA/hexane, eluent 7% EA in hexane, amount- 41 mg, yield- 70%. Selectivity α: β=7: 1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 11.7, 4.6 Hz, 4H), 7.46 – 7.45 (m, 1H), 7.43 – 7.34 (m, 8H), 7.31 – 7.23 (m, 6H), 5.38 (td, *J* = 10.7, 1.6 Hz, 1H), 4.90 (d, *J* = 10.6 Hz, 1H), 4.03 (d, *J* = 1.6 Hz, 1H), 3.92 (q, *J* = 7.3 Hz, 1H), 3.49 (d, *J* = 2.8 Hz, 1H), 3.10 (s, 3H), 1.87 – 1.83 (m, 1H), 1.60 (d, *J* = 13.1 Hz, 1H), 1.29 (d, *J* = 7.4 Hz, 3H), 0.98 (s, 9H), 0.93 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 135.9, 135.8, 135.7, 135.7, 133.8, 133.2, 133.1, 133.0, 130.1, 129.9, 129.9, 128.0, 127.9, 127.8, 127.8, 127.7, 76.0, 73.1, 71.3, 70.7, 43.6, 34.3, 27.0, 26.9, 19.3, 19.1, 16.8. HRMS (ESI-QTOF) $C_{39}H_{51}O_5NSSi_2NH_4$ $[M+NH_4]^+$- calculated- 719.3370; found- 719.3374. $[\alpha]_D^{22}$= -29 (*c* 0.80, $CHCl_3$).

3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl benzene sulfonamide (24d)



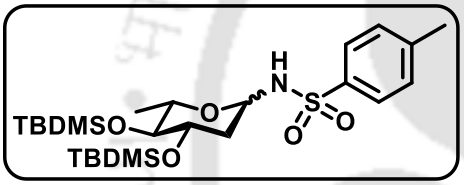
According to general method, a solution of glycosyl donor 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **20a** (50 mg, 0.082 mmol, 1.0 equiv) and glycosyl sulfonamide acceptor **21d** (20 mg, 0.127 mmol, 1.5 equiv) in dry DCE at 40 °C was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (5 mg, 0.0164 mmol, 20 mol%) and stirred for 24 h to get the product **24d** as a colourless oil. R_f- 0.4 in 20% EA/hexane, eluent 7% EA in hexane, amount- 45 mg, yield- 72%. Selectivity α: β=12: 1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.7 Hz, 2H), 7.56 – 7.33 (m, 18H), 7.26 - 7.19 (m, 5H), 5.36 (t, *J* = 10.2 Hz, 1H), 5.15 (d, *J* = 10.1 Hz, 1H), 3.97 (s, 1H), 3.71 (q, *J* = 7.1 Hz, 1H), 3.42 (s, 1H), 1.84 – 1.79 (m, 1H), 1.56 (d, *J* = 13.3 Hz, 1H), 1.09 (d, *J* = 7.3 Hz, 3H), 0.96 (s, 9H), 0.89 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.7, 135.9, 135.8, 135.7, 133.8, 133.2, 133.1, 133.1, 132.6, 130.1, 129.9, 129.8, 128.8, 127.9, 127.8, 127.8, 127.7, 127.5, 75.7, 73.3, 71.4, 70.9, 34.9, 27.0, 26.9, 19.2, 19.1, 16.5. $[\alpha]_D^{22}$= -15 (*c* 0.60, $CHCl_3$).

3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl o-toluenesulfonamide (24e)



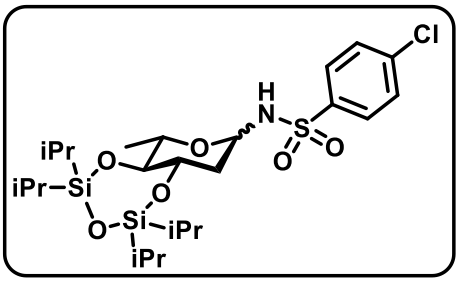
According to general method, a solution of glycosyl donor 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal **20a** (50 mg, 0.082 mmol, 1.0 equiv) and glycosyl sulfonamide acceptor **21e** (21 mg, 0.123 mmol, 1.5 equiv) in dry DCE at 40 °C was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (5 mg, 0.0164 mmol, 20 mol%) and stirred for 24 h to get the product **24e** as a colourless oil. R_f- 0.4 in 20% EA/hexane, eluent 7% EA in hexane, amount- 46 mg, yield- 72%. Selectivity α: β=16: 1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.8 Hz, 1H), 7.48 (dd, *J* = 6.4, 4.8 Hz, 3H), 7.44 – 7.20 (m, 20H), 5.19 (t, *J* = 9.9 Hz, 1H), 5.10 (d, *J* = 10.4 Hz, 1H), 3.98 (s, 1H), 3.70 (q, *J* = 7.3 Hz, 1H), 3.39 (d, *J* = 2.1 Hz, 1H), 2.68 (s, 3H), 1.87 – 1.82 (m, 1H), 1.53 (d, *J* = 13.2 Hz, 1H), 0.94 (s, 9H), 0.90 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.2, 137.5, 135.9, 135.8, 135.7, 133.9, 133.3, 133.1, 133.1, 132.7, 132.3, 130.1, 129.9, 129.8, 129.5, 127.9, 127.8, 127.8, 127.7, 126.0, 75.8, 72.9, 71.4, 70.7, 35.0, 27.0, 26.9, 20.5, 19.3, 19.1, 16.1. $[\alpha]_D^{22}$= -04 (*c* 0.20, $CHCl_3$).

3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-toluenesulfonamide (23a)



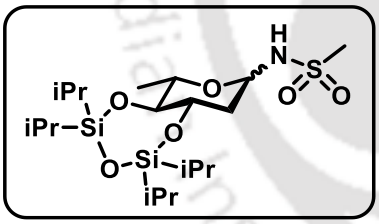
According to general method, a solution of glycosyl donor 3,4-di-*O*-*tert*-butyldimethylsilyl-L-rhamnal **20b** (50 mg, 0.139 mmol, 1.0 equiv) and glycosyl sulfonamide acceptor **21a** (36 mg, 0.210 mmol, 1.5 equiv) in dry DCE at 40 °C was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (8 mg, 0.0276 mmol, 20 mol%) and stirred for 24 h to get the product **23a** as a colourless oil. R_f- 0.4 in 20% EA/hexane, eluent 7% EA in hexane, amount- 65 mg, yield- 88%. Selectivity α: β= 1: 2.4. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 14.0, 8.3 Hz, 7H), 7.29 (dd, *J* = 9.0, 4.6 Hz, 7.2H), 5.50 (d, *J* = 9.3 Hz, 1H), 5.29 – 5.26 (m, 1H), 5.19 (d, *J* = 10.3 Hz, 2.4H), 4.82 (td, *J* = 10.4, 2.0 Hz, 2.4H), 3.80 – 3.76 (m, 1H), 3.64 (ddd, *J* = 10.9, 7.9, 4.7 Hz, 2.4H), 3.46 – 3.42 (m, 1H), 3.19 – 3.14 (m, 3.4H), 3.00 (t, *J* = 8.3 Hz, 2.4H), 2.43 (s, 3H), 2.43 (s, 7H), 2.15 (ddd, *J* = 12.6, 4.5, 2.1 Hz, 2.4H), 1.97 (ddd, *J* = 13.4, 6.2, 3.6 Hz, 1H), 1.75 (ddd, *J* = 13.3, 7.2, 4.0 Hz, 1H), 1.46 (dd, *J* = 23.4, 10.8 Hz, 2.4H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.3 Hz, 7.2H), 0.93 – 0.87 (m, 62H), 0.11 – 0.07 (m, 31H), 0.02 (s, 10H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.6, 143.4, 138.6, 138.5, 129.5, 129.4, 127.5, 127.5, 80.1, 77.3, 75.9, 74.4, 74.3, 73.3, 73.0, 70.8, 40.9, 36.9, 26.4, 26.2, 26.2, 26.1, 26.0, 21.7, 18.5, 18.4, 18.2, 18.1, 17.3, 1.2, -2.7, -3.0, -3.8, -3.9, -4.0, -4.1, -4.4, -4.5. HRMS (ESI-QTOF) $C_{25}H_{47}O_5NSSi_2Na$ $[M+Na]^+$- calculated- 552.2611; found- 552.2647. $[\alpha]_D^{22}$= -20 (*c* 0.80, $CHCl_3$).

3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranosyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-chlorobenzene sulfonamide (23b)



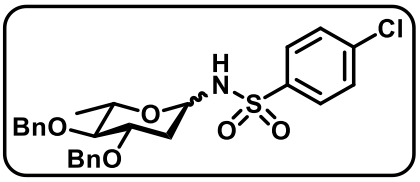
According to general method, a solution of glycosyl donor 3,4-O-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-1,2,6-trideoxy-L-arabino-1-hexenopyranose **20c** (50 mg, 0.134 mmol, 1.0 equiv) and glycosyl sulfonamide acceptor **21b** (39 mg, 0.204 mmol, 1.5 equiv) in dry DCE at 40 °C was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (8 mg, 0.0268 mmol, 20 mol%) and stirred for 24 h to get the product **23b** as a colourless oil. R_f- 0.4 in 20% EA/hexane, eluent 7% EA in hexane, amount- 52 mg, yield- 68%. Selectivity α: β=1: 3. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.6 Hz, 5.4H), 7.84 (d, *J* = 8.6 Hz, 2H), 7.49 (d, *J* = 8.6 Hz, 5.4H), 7.45 (d, *J* = 8.6 Hz, 2H), 5.92 (d, *J* = 7.6 Hz, 3H), 5.34 (dd, *J* = 13.3, 6.9 Hz, 3H), 5.26 (d, *J* = 10.2 Hz, 1H), 4.81 (t, *J* = 9.8 Hz, 1H), 3.71 (dt, *J* = 7.9, 6.7 Hz, 4H), 3.13 (ddt, *J* = 39.9, 15.5, 7.6 Hz, 7.5H), 2.20 (dd, *J* = 12.8, 3.6 Hz, 1H), 2.03 (dd, *J* = 13.9, 5.2 Hz, 3H), 1.95 – 1.89 (m, 3H), 1.53 (dd, *J* = 23.8, 11.3 Hz, 1H), 1.27 (d, *J* = 6.3 Hz, 3H), 1.08 – 0.82 (m, 108H), 0.83 (d, *J* = 5.8 Hz, 8H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.3, 139.8, 139.4, 139.3, 129.3, 129.1, 129.0, 128.9, 80.4, 79.7, 79.1, 79.1, 74.2, 74.0, 71.3, 68.5, 40.0, 37.8, 17.8, 17.8, 17.7, 17.5, 17.5, 17.4, 17.4, 17.3, 13.0, 13.0, 12.9, 12.4, 12.4, 12.3. $[\alpha]_D^{22}$= -20 (*c* 0.70, $CHCl_3$).

3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranosyl-2,6-dideoxy-α,β-L-rhamnopyranosyl methanesulfonamide (23c)



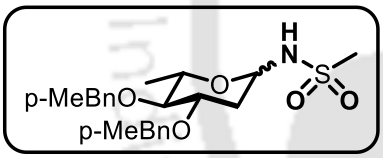
According to general method, a solution of glycosyl donor 3,4-O-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-1,2,6-trideoxy-L-arabino-1-hexenopyranose **20c** (50 mg, 0.134 mmol, 1.0 equiv) and glycosyl sulfonamide acceptor **21c** (19 mg, 0.200 mmol, 1.5 equiv) in dry DCE at 40 °C was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (8 mg, 0.0268 mmol, 20 mol%) and stirred for 24 h to get the product **23c** as a colourless oil. R_f- 0.4 in 20% EA/hexane, eluent 7% EA in hexane, amount- 45 mg, yield- 72%. Selectivity α: β=1: 12.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (dd, *J* = 9.2, 3.3 Hz, 1H), 4.79 (td, *J* = 11.1, 1.9 Hz, 1H), 3.74 (ddd, *J* = 11.2, 8.1, 5.3 Hz, 1H), 3.34 (dq, *J* = 12.3, 6.1 Hz, 1H), 3.19 (t, *J* = 8.5 Hz, 1H), 3.10 (s, 3H), 2.22 (ddd, *J* = 12.8, 5.2, 1.9 Hz, 1H), 1.58 (dd, *J* = 23.9, 11.3 Hz, 1H), 1.29 (d, *J* = 5.8 Hz, 3H), 1.08 – 0.92 (m, 28H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 80.3, 79.2, 74.1, 73.9, 43.5, 39.7, 31.0, 30.4, 29.8, 18.2, 17.7, 17.5, 17.4, 17.4, 17.4, 17.3, 17.2, 17.2, 13.2, 13.0, 12.9, 12.4, 12.3. HRMS (ESI-QTOF) $C_{19}H_{41}O_6NSSi_2Na$ $[M+Na]^+$- calculated- 490.2091; found- 490.2099. $[\alpha]_D^{22}$= -10 (*c* 0.40, $CHCl_3$).

3,4-di-*O*-benzyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-chlorobenzene sulfonamide (23d)



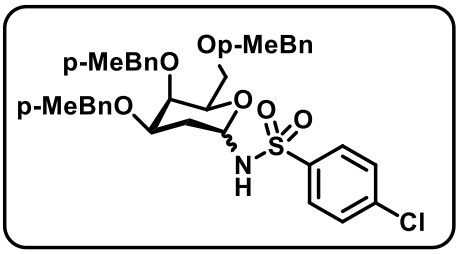
According to general method, a solution of glycosyl donor 3,4-di-O-benzyl-L-rhamnal **20d** (50 mg, 0.161 mmol, 1.0 equiv) and glycosyl sulfonamide acceptor **21b** (46 mg, 0.240 mmol, 1.5 equiv) in dry DCE at 40 °C was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (9.1 mg, 0.0322 mmol, 20 mol%) and stirred for 24 h to get the product **23d** as a colourless oil. R_f- 0.4 in 20% EA/hexane, eluent 7% EA in hexane, amount- 61 mg, yield- 75%. Selectivity α: β=1: 2.9. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 – 7.80 (m, 7.6H), 7.43 (d, *J* = 8.5 Hz, 7.6H), 7.34 – 7.23 (m, 37H), 5.94 (d, *J* = 7.7 Hz, 1H), 5.38 (dd, *J* = 19.0, 7.9 Hz, 3.8H), 4.88 (d, *J* = 11.0 Hz, 2.8H), 4.82 (d, *J* = 10.9 Hz, 1H), 4.76 (dd, *J* = 15.2, 5.6 Hz, 2.8H), 4.66 – 4.53 (m, 11.4H), 3.69 – 3.64 (m, 1H), 3.61 (ddd, *J* = 11.1, 8.8, 5.0 Hz, 2.8H), 3.23 (dq, *J* = 12.2, 6.1 Hz, 2.8H), 3.14 (td, *J* = 12.4, 6.1 Hz, 1H), 3.02 (t, *J* = 8.6 Hz, 1H), 2.95 (t, *J* = 8.9 Hz, 2.7H), 2.36 – 2.33 (m, 2.8H), 2.20 – 2.16 (m, 1H), 1.91 – 1.85 (m, 1H), 1.47 (dd, *J* = 23.3, 11.4 Hz, 2.9H), 0.99 (d, *J* = 6.1 Hz, 8.4H), 0.81 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.1, 139.3, 138.3, 138.1, 129.2, 129.1, 129.0, 128.9, 128.6, 128.6, 128.5, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 82.9, 80.3, 79.4, 75.3, 73.1, 72.0, 71.8, 68.0, 37.3, 34.6, 17.9, 17.5. $[\alpha]_D^{22}$= -26 (*c* 0.70, $CHCl_3$).

3,4-di-*O*-*para*-methylbenzyl-2,6-dideoxy-α,β-L-rhamnopyranosyl methanesulfonamide (23e)



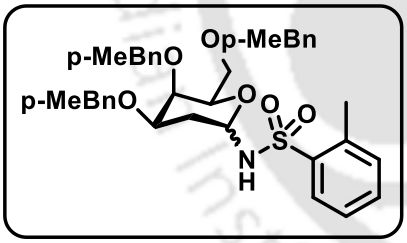
According to general method, a solution of glycosyl donor 3,4-di-O-para-methylbenzyl-L-rhamnal **20e** (50 mg, 0.148 mmol, 1.0 equiv) and glycosyl sulfonamide acceptor **21c** (21 mg, 0.221 mmol, 1.5 equiv) in dry DCE at 40 °C was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (8.4 mg, 0.0296 mmol, 20 mol%) and stirred for 24 h to get the product **23e** as a colourless oil. R_f- 0.4 in 20% EA/hexane, eluent 7% EA in hexane, amount- 48 mg, yield- 75%. Selectivity α: β=1: 4.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (t, *J* = 8.4 Hz, 4H), 7.15 (d, *J* = 7.7 Hz, 4H), 5.03 (d, *J* = 10.1 Hz, 1H), 4.88 (d, *J* = 10.7 Hz, 1H), 4.72 (dd, *J* = 15.0, 5.9 Hz, 1H), 4.59 (dd, *J* = 16.4, 6.0 Hz, 3H), 3.62 (ddd, *J* = 11.2, 8.8, 5.0 Hz, 1H), 3.37 (dq, *J* = 12.3, 6.1 Hz, 1H), 3.07 (s, 3H), 3.04 (t, *J* = 9.0 Hz, 1H), 2.35 (s, 6H), 2.32 – 2.31 (m, 1H), 1.48 (dd, *J* = 23.4, 11.3 Hz, 1H), 1.26 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.8, 137.7, 135.3, 135.1, 129.4, 129.2, 128.4, 128.1, 83.1, 80.2, 79.2, 75.3, 73.1, 72.0, 43.5, 37.2, 21.3, 18.3. $[\alpha]_D^{22}$= +06 (*c* 0.20, $CHCl_3$).

3,4,6-Tri-O-*para*-methylbenzyl-2-deoxy-α,β−D-galactopyranosyl p-chlorobenzene sulfonamide (23f)



According to general method, a solution of glycosyl 3,4,6-tri-O-para-methylbenzyl-D-galactal **20f** (50 mg, 0.109 mmol, 1.0 equiv) and glycosyl sulfonamide acceptor **21b** (31 mg, 0.162 mmol, 1.5 equiv) in dry DCE at 40 °C was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (6.2 mg, 0.0218 mmol, 20 mol%) and stirred for 24 h to get the product **23f** as a colourless oil. R_f- 0.4 in 20% EA/hexane, eluent 7% EA in hexane, amount- 47 mg, yield- 66%. Selectivity α: β=1: 4. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 – 7.76 (m, 8H), 7.32 – 7.07 (m, 72H), 5.51 (d, *J* = 7.1 Hz, 1H), 5.45 – 5.42 (m, 1H), 5.31 (d, *J* = 10.3 Hz, 4H), 4.77 (dd, *J* = 19.4, 10.4 Hz, 9H), 4.54 (d, *J* = 9.9 Hz, 9H), 4.48 (dd, *J* = 16.9, 8.1 Hz, 6H), 4.30 (d, *J* = 12.0 Hz, 7H), 4.23 (dd, *J* = 20.0, 11.4 Hz, 3H), 3.77 (s, 1H), 3.73 (s, 4H), 3.58 (d, *J* = 11.4 Hz, 1H), 3.53 (d, *J* = 11.6 Hz, 4H), 3.41 – 3.37 (m, 6H), 3.28 – 3.25 (m, 4H), 3.11 (dd, *J* = 9.2, 5.7 Hz, 4H), 2.84 (q, *J* = 8.9 Hz, 1H), 2.36 (d, *J* = 2.2 Hz, 30H), 2.30 (s, 15H), 2.05 (d, *J* = 11.8 Hz, 4H), 1.94 (dd, *J* = 23.2, 11.6 Hz, 4H), 1.78 (d, *J* = 12.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.2, 139.8, 139.2, 139.0, 137.8, 137.6, 137.4, 135.6, 135.4, 135.1, 135.0, 134.9, 134.9, 129.4, 129.3, 129.2, 129.2, 129.1, 129.1, 129.0, 128.9, 128.8, 128.3, 128.3, 128.1, 127.7, 127.6, 81.2, 79.2, 77.3, 75.5, 74.4, 74.0, 73.5, 73.4, 72.2, 71.2, 70.8, 70.5, 68.7, 68.1, 32.9, 21.3. $[\alpha]_D^{22}$= +09 (*c* 0.20, $CHCl_3$).

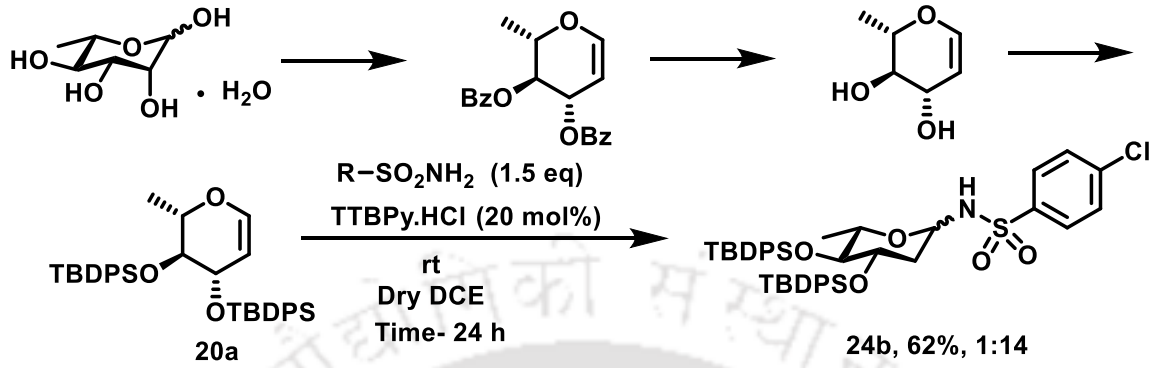
3,4,6-Tri-O-*para*-methylbenzyl-2-deoxy-α,β−D-galactopyranosyl o-toluenesulfonamide (23g)



According to general method, a solution of glycosyl 3,4,6-tri-O-para-methylbenzyl-D-galactal **20f** (50 mg, 0.109 mmol, 1.0 equiv) and glycosyl sulfonamide acceptor **21a** (28 mg, 0.164 mmol, 1.5 equiv) in dry DCE at 40 °C was treated with 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (6.2 mg, 0.0218 mmol, 20 mol%) and stirred for 24 h to get the product **23g** as a colourless oil. R_f- 0.4 in 20% EA/hexane, eluent 7% EA in hexane, amount- 52 mg, yield- 75%. Selectivity α: β=1: 3.4. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.7 Hz, 4H), 7.31 (t, *J* = 7.3 Hz, 4H), 7.23 – 7.05 (m, 62H), 5.36 (t, *J* = 5.0 Hz, 1H), 5.30 (d, *J* = 10.5 Hz, 4H), 4.80 (d, *J* = 11.2 Hz, 3.4H), 4.76 (d, *J* = 11.4 Hz, 1H), 4.63 (td, *J* = 10.5, 2.0 Hz, 3.4H), 4.56 – 4.47 (m, 12H), 4.44 (t, *J* = 9.5 Hz, 2H), 4.22 (s, 7H), 4.16 (dd, *J* = 22.5, 11.6 Hz, 2H), 3.81 (s, 1H), 3.74 (s, 3.4H), 3.58 – 3.55 (m, 1H), 3.51 – 3.48 (m, 3.4H), 3.33 (t, *J* = 8.3 Hz, 5.4H), 3.27 (dd, *J* = 12.7, 7.7 Hz, 3.4H), 3.00 (dd, *J* = 8.9, 4.9 Hz, 3.4H), 2.59 (s, 14H), 2.35 (s, 26H), 2.31 (s, 12H), 2.05 (dd, *J* = 8.9, 3.1 Hz, 3.4H), 1.97 (dd, *J* = 21.9, 10.4 Hz, 5H), 1.79 (dd, *J* = 13.2, 3.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.7, 137.7, 137.6, 137.5, 137.4, 135.7, 135.0, 135.0, 132.9, 132.6, 132.4, 132.3, 129.9, 129.3, 129.2, 129.1, 129.0, 128.7, 128.4, 128.2, 128.1, 127.7, 126.4, 126.0, 80.9, 79.6, 77.3, 75.5, 74.5, 74.2, 73.6,

73.3, 71.2, 70.7, 70.5, 70.4, 68.3, 67.7, 33.4, 29.8, 21.3, 20.7, 20.6. [α] $^{22}_{D}$= -22 (*c* 0.70, $CHCl_3$).

Large Scale synthesis of 24b:



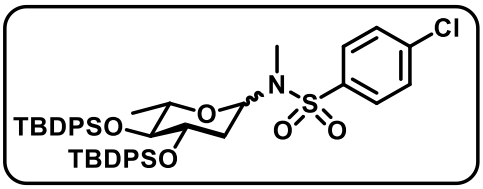
*Large Scale Synthesis of **24b***

3,4-di-*O*-benzoyl-L-rhamnal was synthesized from commercially available L-rhamnose monohydrate following previously reported method.[17] 3,4-di-*O*-benzoyl-L-rhamnal (3 g, 8.85 mmol) was stirred in MeOH (50 mL) at 0 °C and then NaOMe (48 mg, 0.89 mmol) and catalytic amount of Na-metal was added. The resulting mixture was stirred for 6 h at room temperature and the solvent was evaporated to dryness. The crude was purified by silica gel column chromatography (Merck, 60-120 mesh) using 50% EA in hexane as eluent to obtain L-rhamnal in quantitative yield.

L-Rhamnal (1 gm, 7.68 mmol, 1.0 equiv) was dissolved in 50 ml of anhydrous DMF. Then, imidazole (1.6 gm, 23.04 mmol, 3.0 equiv) followed by TBDPSCl (3.3 ml, 23.04 mmol, 3.0 equiv) were added into it and allowed to stir for overnight. The reaction mixture was then concentrated and extracted with ethyl acetate (3x30 ml). The organic phase was washed with brine (100 ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude was purified by column chromatography using hexane as solvent to give the product **20a** as a white solid. R_f- 0.3 (in hexane), amount- 3.6 g, yield- 76%.

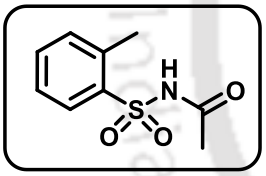
Glycal **20a** (1.0 gm, 1.65 mmol, 1.0 equiv) and glycosyl sulfonamide acceptor **21b** (474 mg, 2.48 mmol, 1.5 equiv) was taken in a round bottomed flask and the flask was then filled with dry DCE under continuous stirring condition. 2,4,6-tri-*tert*-butylpyridinium hydrochloride catalyst (18 mg, 0.327 mmol, 20 mol%) was added and the reaction mixture was heated at 40 °C (using oil bath) in the sealed flask until the reaction was determined to be complete by TLC (after 18 h glycal was consumed). The reaction mixture was quenched by water (62 ml) and it was extracted with DCM (3x47 ml), dried over Na_2SO_4 and concentrated then concentrated in vacuo and purified by silica gel column chromatography (Merck 60-120 mesh, 40 gm). The crude product was purified by column chromatography on silica gel eluted with hexane/EA to give compound **24b** (eluent 7% EA in hexane, amount 855 mg, yield 62%) as a colourless liquid.

3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α-L-rhamnopyranosyl N-methyl-p-chlorobenzene sulfonamide (26)



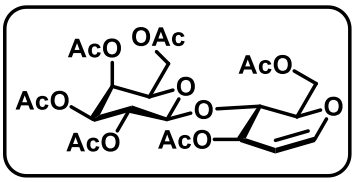
3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-β-L-rhamnopyranosyl p-chlorobenzene sulfonamide **24b** (50 mg, 0.063 mmol, 1.0 equiv) was dissolved in 2 ml DMF. Then, to it NaH (4 mg, 0.157 mmol, 1.5 equiv considering 60% dispersion in mineral oil) was added slowly at 0 °C. Then, methyl iodide (6 µL, 0.157 mmol, 1.5 equiv) was added portion wise slowly and it was stirred for 2 h at rt. Then, it was quenched with MeOH (0.5 ml). Now, the solvent was concentrated and extracted with DCM (3x10 ml). The organic phase was washed with brine (50 ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Then, it was purified by column chromatography in ethyl acetate/hexane solvent system to afford the white solid **26**. R_f- 0.5 in 10% EA in hexane, amount- 46 g, yield- 91%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.6 Hz, 2H), 7.56 (d, *J* = 6.8 Hz, 2H), 7.49 – 7.37 (m, 14H), 7.25 (ddd, *J* = 24.5, 13.6, 7.8 Hz, 6H), 5.91 (d, *J* = 9.9 Hz, 1H), 4.06 (s, 1H), 3.80 (q, *J* = 7.2 Hz, 1H), 3.46 (d, *J* = 2.8 Hz, 1H), 2.80 (s, 3H), 2.15 – 2.10 (m, 1H), 1.37 (d, *J* = 13.0 Hz, 1H), 1.23 (d, *J* = 7.4 Hz, 3H), 1.02 (s, 9H), 0.90 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9, 138.1, 136.0, 135.8, 135.7, 135.7, 133.8, 133.3, 133.2, 133.1, 130.1, 129.9, 129.9, 129.8, 129.4, 129.1, 128.0, 127.8, 127.8, 127.7, 76.0, 75.2, 71.6, 70.5, 31.8, 28.4, 27.1, 26.9, 19.3, 19.2, 16.6. $[\alpha]_D^{22}$= -20 (*c* 0.70, $CHCl_3$).

Synthesis of N-(o-tolylsulfonyl)acetamide (21e'):



Free sulfonamide (200 mg, 1.17 mmol), anhydrous $ZnCl_2$ (16 mg, 0.117 mmol, 0.10 equiv) and Ac_2O (0.22 mL, 2.34 mmol, 2 equiv) were mixed and stirred at rt for 1 h and then poured into a mixture of EtOAc (10.0 mL) and H_2O (50.0 mL). The layers were separated and the aqueous was extracted with EtOAc. Combined organic layers were dried over Na_2SO_4 and concentrated in vacuo to afford white solid N-(o-tolylsulfonyl)acetamide quantitatively. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.14 (d, *J* = 7.9 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 7.7 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 2.67 (s, 3H), 2.08 (s, 3H). Other spectroscopic data were in agreement with the reported data. [24]

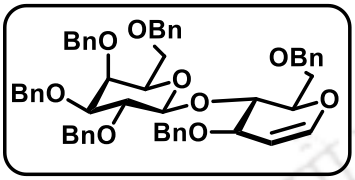
Synthesis of 3,6,2',3',4',6'-Hexa-O-acetyl-D-lactal (20h):



D-Lactal (200 mg, 0.65 mmol, 1.0 equiv) was taken in DCM (20 ml). Then, pyridine (0.472 ml, 5.85 mmol, 9 equiv) and Ac_2O (0.552 ml, 5.85 mmol, 9 equiv) was added to it and the mixture was allowed to stir at rt for overnight. Now, the solvent was concentrated and extracted with DCM (3x30 ml). The organic phase was washed with brine (100 ml), dried

over anhydrous Na_2SO_4 and concentrated under reduced pressure. Then, it was purified by column chromatography in ethyl acetate/hexane solvent system to afford 3,6,2',3',4',6'-Hexa-O-acetyl-D-lactal. R_f- 0.5 in 40% EA in hexane, amount- 298 mg, yield- 82%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.42 (d, *J* = 6.1 Hz, 1H), 5.45 – 5.31 (m, 1H), 5.20 (dd, *J* = 10.4, 8.1 Hz, 1H), 5.01 (dd, *J* = 10.5, 3.3 Hz, 1H), 4.84 (dd, *J* = 6.0, 3.4 Hz, 1H), 4.67 (d, *J* = 8.0 Hz, 1H), 4.44 (dd, *J* = 11.7, 2.3 Hz, 1H), 4.23 – 4.06 (m, 2H), 4.00 (dd, *J* = 7.2, 5.7 Hz, 1H), 3.92 (t, *J* = 6.7 Hz, 1H), 2.16 (s, 1H), 2.12 (s, 1H), 2.09 (s, 1H), 2.06 (d, *J* = 5.0 Hz, 2H), 1.98 (s, 1H). Other spectroscopic data were in agreement with the reported data. [25]

Synthesis of 3,6,2',3',4',6'-Hexa-O-benzyl-D-lactal (20i):



D-Lactal (200 mg, 0.65 mmol, 1.0 equiv) was dissolved in 20 ml DMF. Then, to it NaH (234 mg, 9.73 mmol, 9 equiv considering 60% dispersion in mineral oil) was added slowly. Then, benzyl bromide (0.69 ml, 5.85 mmol, 9 equiv) was added portion wise slowly and it was stirred for 24 h. Then, it was quenched with MeOH (5 ml). Now, the solvent was concentrated and extracted with DCM (3x30 ml). The organic phase was washed with brine (100 ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Then, it was purified by column chromatography in ethyl acetate/hexane solvent system to afford 3,6,2',3',4',6'-hexa-O-benzyl-D-lactal. R_f- 0.5 in 40% EA in hexane, amount- 430 mg, yield- 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.21 (m, 30H), 6.43 (d, *J* = 6.2 Hz, 1H), 4.93 (d, *J* = 11.6 Hz, 1H), 4.87 (dd, *J* = 5.8, 3.6 Hz, 1H), 4.83 (d, *J* = 10.8 Hz, 1H), 4.74 – 4.68 (m, 3H), 4.60 (s, 2H), 4.57 – 4.54 (m, 2H), 4.47 (s, 2H), 4.35 (q, *J* = 11.7 Hz, 2H), 4.26 (dd, *J* = 8.9, 5.2 Hz, 1H), 4.14 (dd, *J* = 10.5, 4.5 Hz, 2H), 3.87 (d, *J* = 2.4 Hz, 1H), 3.84 (dd, *J* = 10.7, 6.3 Hz, 1H), 3.78 (dd, *J* = 9.5, 8.0 Hz, 1H), 3.67 (dd, *J* = 10.7, 3.4 Hz, 1H), 3.57 – 3.43 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.6, 138.9, 138.9, 138.8, 138.6, 138.2, 138.0, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 127.7, 127.5, 102.9, 99.9, 82.4, 79.6, 76.0, 75.3, 74.7, 73.7, 73.6, 73.4, 73.3, 73.1, 72.4, 70.5, 68.7, 68.1.

4.9 Reference:

1. Colinas, P. A.; Núñez N. A.; Bravo. R.D. *J. Carbohydr. Chem.* **2008**, *27*, 141-47.

2. (a) Jordan, M. A.; Wilson, L. *Nat. Rev. Cancer* **2004**, *4*, 253–65; (b) Yoshimatsu, K.; Yamaguchi, A.; Yoshino, H.; Koyagi, N.; Kitoh, K. *Cancer Res.* **1997**, *57*, 3208-13.

3. Abbate, F.; Casini, A.; Owa, T.; Scozzafava, A.; Supuran, C.T. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 217–23.

4. Supuran, C. T.; Briganti, F.; Tilli, S.; Chegwidde, W. R.; Scozzafava, A. *Bioorg. Med. Chem.* **2001**, *9*, 703-14.

5. Supuran, C. T.; Scozzafava, A.; Menabuoni, L.; Mincione, F.; Briganti, F.; Mincione, G. *Eur. J. Pharm. Sci.* **1999**, *8*, 317-28.

6. Zotto, C. D.; Michaux, J.; Ruiz, A. Z.; Gayon, E.; Virieux, D.; Campagne, J. M.; Terrasson, V.; Pieters, G.; Gaucher, A.; Prim, D. *J. Organomet. Chem* **2011**, *696*, 296-304.

7. Yadav, J. S.; Reddy, B. V. S.; Rao, T. S.; Krishna, B. B. M. *Tetrahedron Lett.* **2009**, *50*, 5351–53.

8. Wang, H.Y.; Xiao-Qiu Pu, X. Q.; Yang, X. J. *J. Org. Chem.* **2018**, *83*, 13103−10.

9. Liautard, V.; Pillard, C.; Desvergnes, V.; Martin O. R. *Carbohydr. Res.* **2008**, *343*, 2111–17.

10. Colinas, P. A.; Bravo, R. D.; Vullo, D.; Scozzafava, A.; Supuran, C. T. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5086–90.

11. Colinas, P. A.; Témpera, C. A.; Rodríguez, O. M.; Bravo, R. D.; *Synthesis* **2009**, *24*, 4143–48.

12. Griffith, D. A.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1990**, *112*, 5811–19.

13. Colinas, P. A.; Bravo, R. D. *Org. Lett.* **2003**, *5*, 4509–11.

14. Colinas, P. A.; Bravo, R. D. Carbohydr. Res. **2007**, 342, 2297–302.

15. Colinas, P. A.; Bravo, R. D. *Mol. Med. Chem.* **2007**, 62-66.

16. Colinas, P. A.; Bravo, R. D. *Tetrahedron Lett*. **2005**, *46*, 1687–89.

17. Ghosh, T.; Mukherji, A.; Kancharla, P. K. *Org. Lett.* **2019**, *21*, 3490-95.

18. Mukherji, A.; Kancharla, P. K. *Org. Lett.* **2020**, *22*, 2191–95.

19. Ferrier, R. J. *Top. Curr. Chem.* **2001**, *215*, 153-75.

20. Mukherji, A.; Addanki, R. B.; Halder, S.; Kancharla, P. K. *J. Org. Chem.* **2021**, *86*, 17226-43.

21. Balmond, E. I.; Alifonso, D. B.; Coe, D. M.; Alder, R. W.; McGarrigle, E. M.; Galan, M. C. *Angew. Chem.* **2014**, *53*, 8190-94.

22. Li, H. H.; Ye, X. S. *Org. Biomol. Chem.* **2009**, *7*, 3855-61.

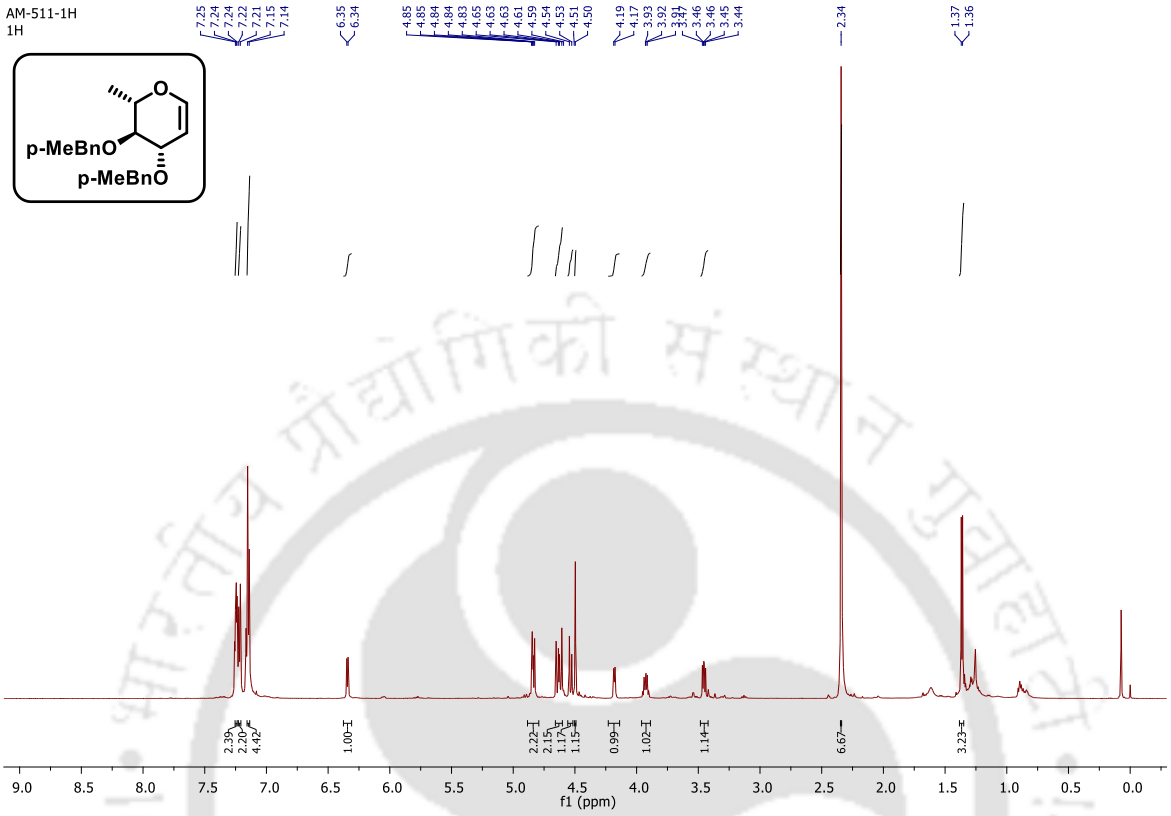
23. Singha, A. K.; Kandasamy, J. *Org. Biomol. Chem.* **2018**, *16*, 5107-12.

24. Dong, Y.; Chen, J.; Xu, H. *Chem. Commun.* **2019**, *55*, 2027-30.

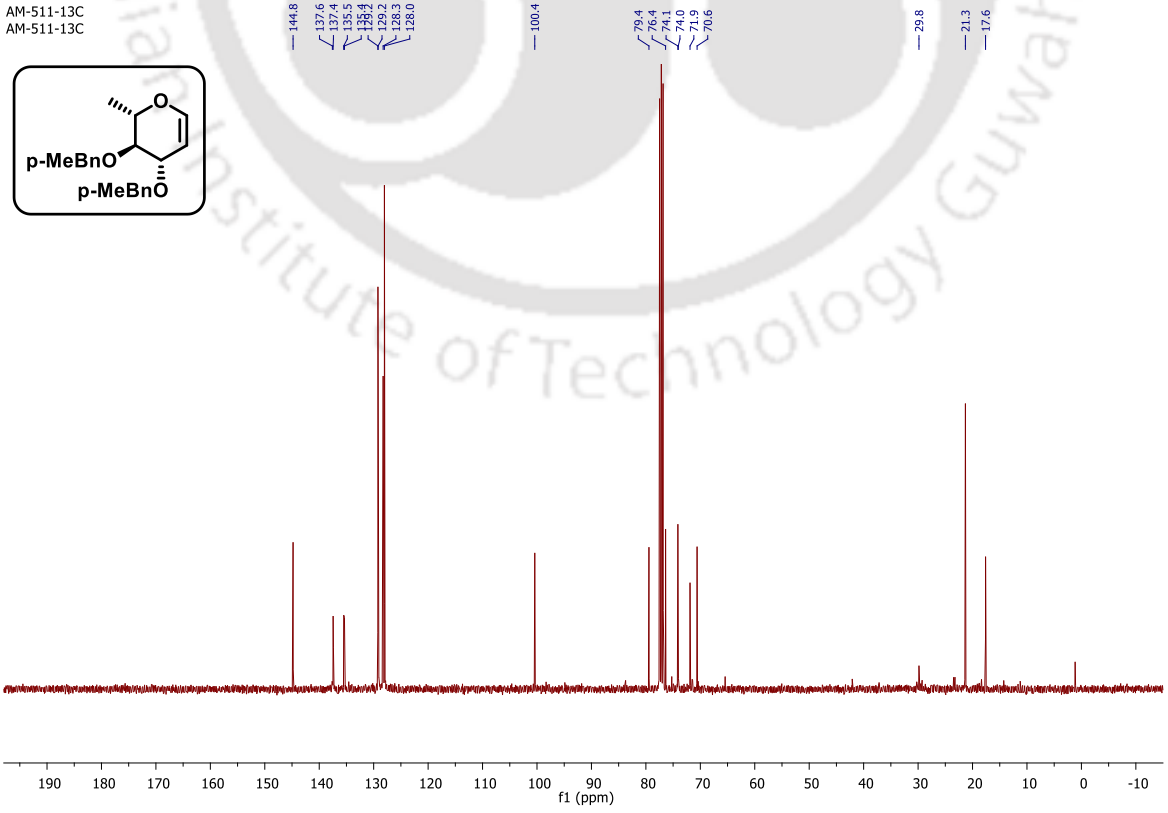
25. Chen, H.; Xian, T.; Zhang, W.; Si, W.; Luo, X.; Zhang, B.; Zhang, M.; Wang, Z.; Zhang, J. *Carbohydr. Res.* **2016**, *431*, 42-46.

4.10 Spectra:

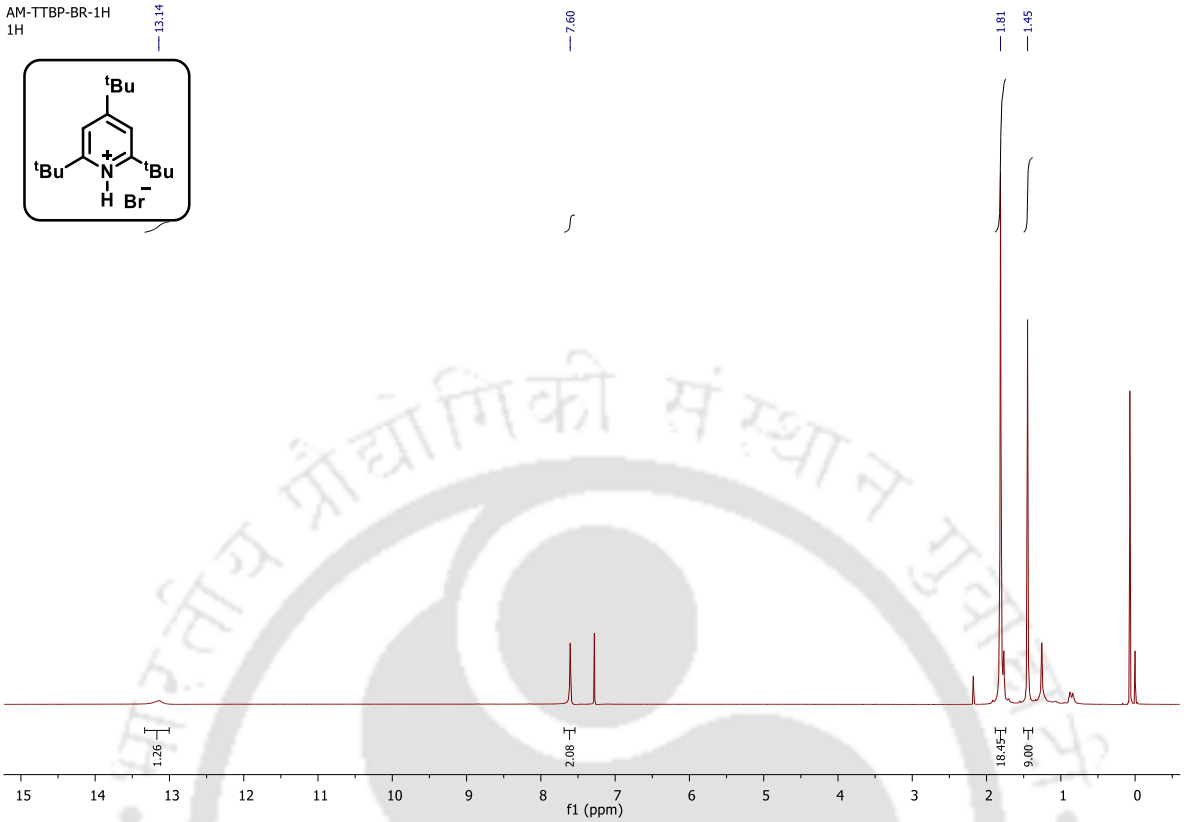
^{1}H NMR of 3,4-di-*O*-para-methylbenzyl-L-rhamnal (20e, 600 MHz, $CDCl_3$):



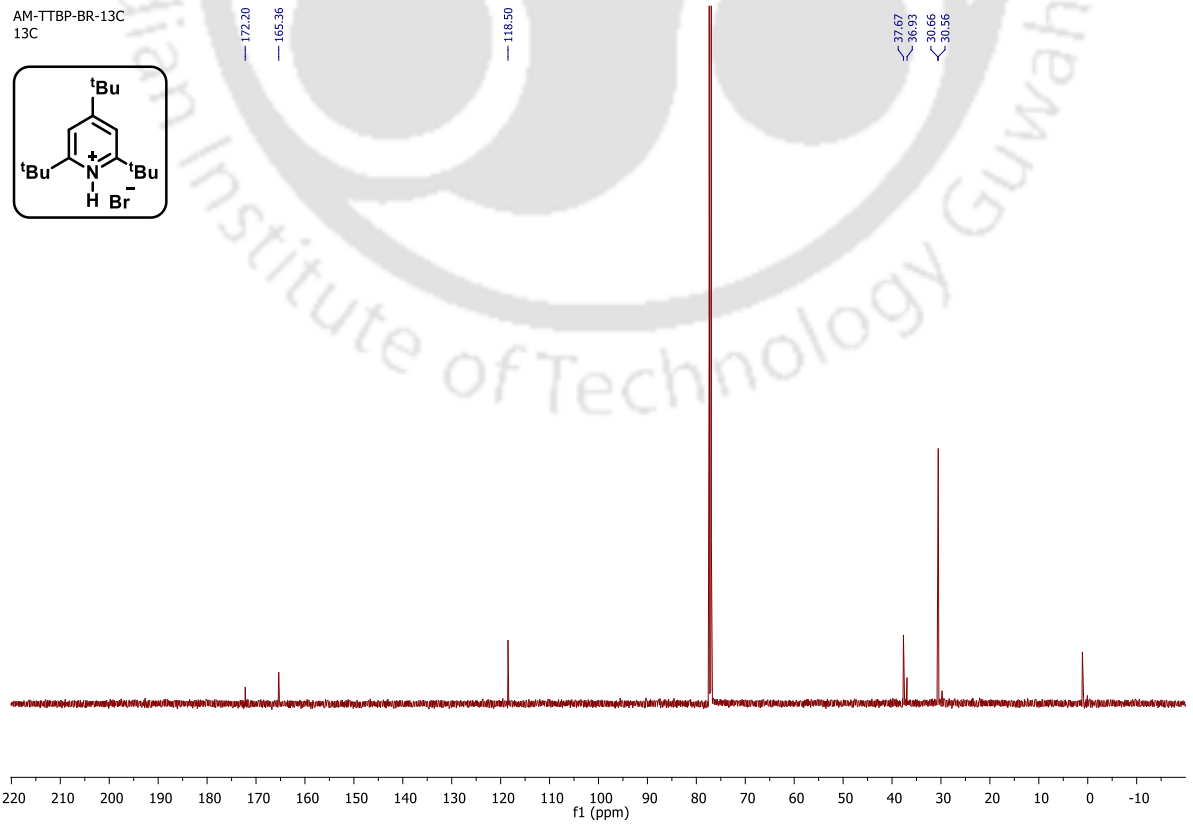
^{13}C{^{1}H} NMR of 3,4-di-*O*-para-methylbenzyl-L-rhamnal (20e, 400 MHz, $CDCl_3$):



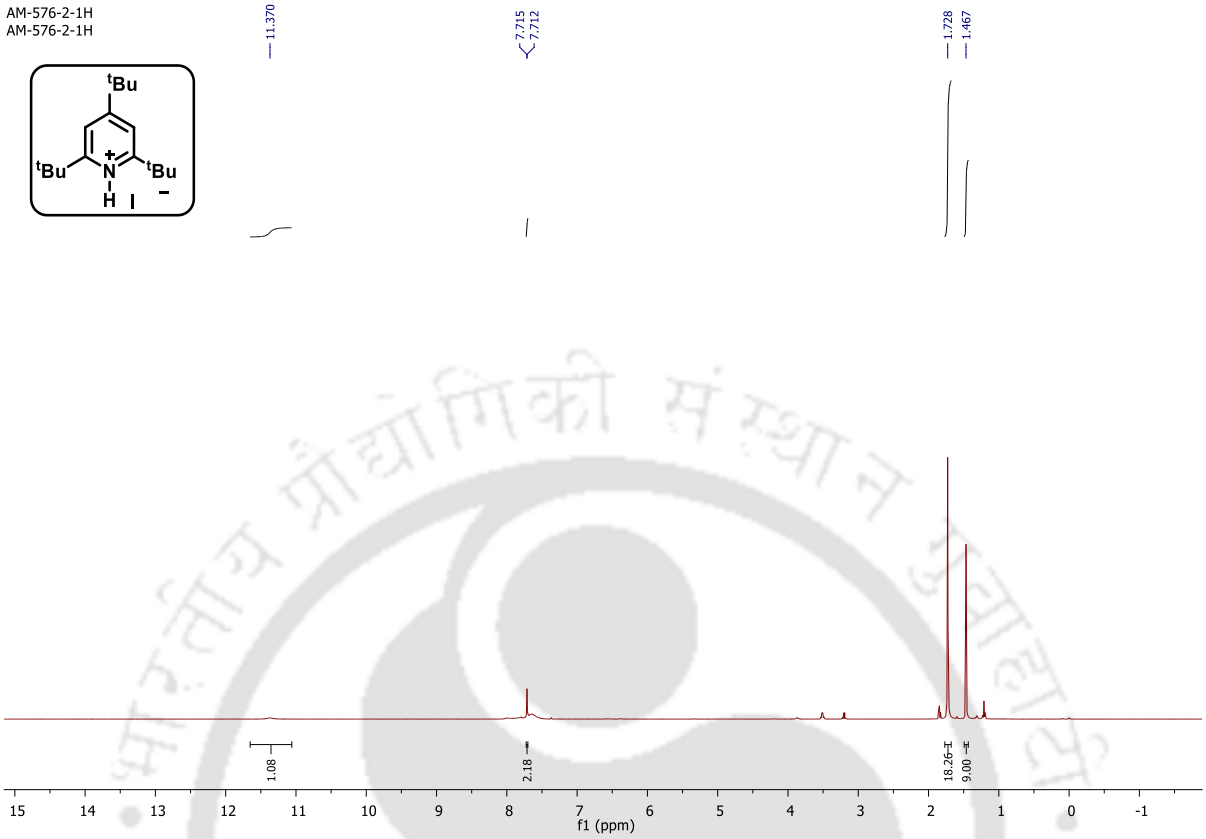
^{1}H NMR of 2,4,6-tri-*tert*-butylpyridinium hydrobromide salt (22b, 600 MHz, $CDCl_3$):



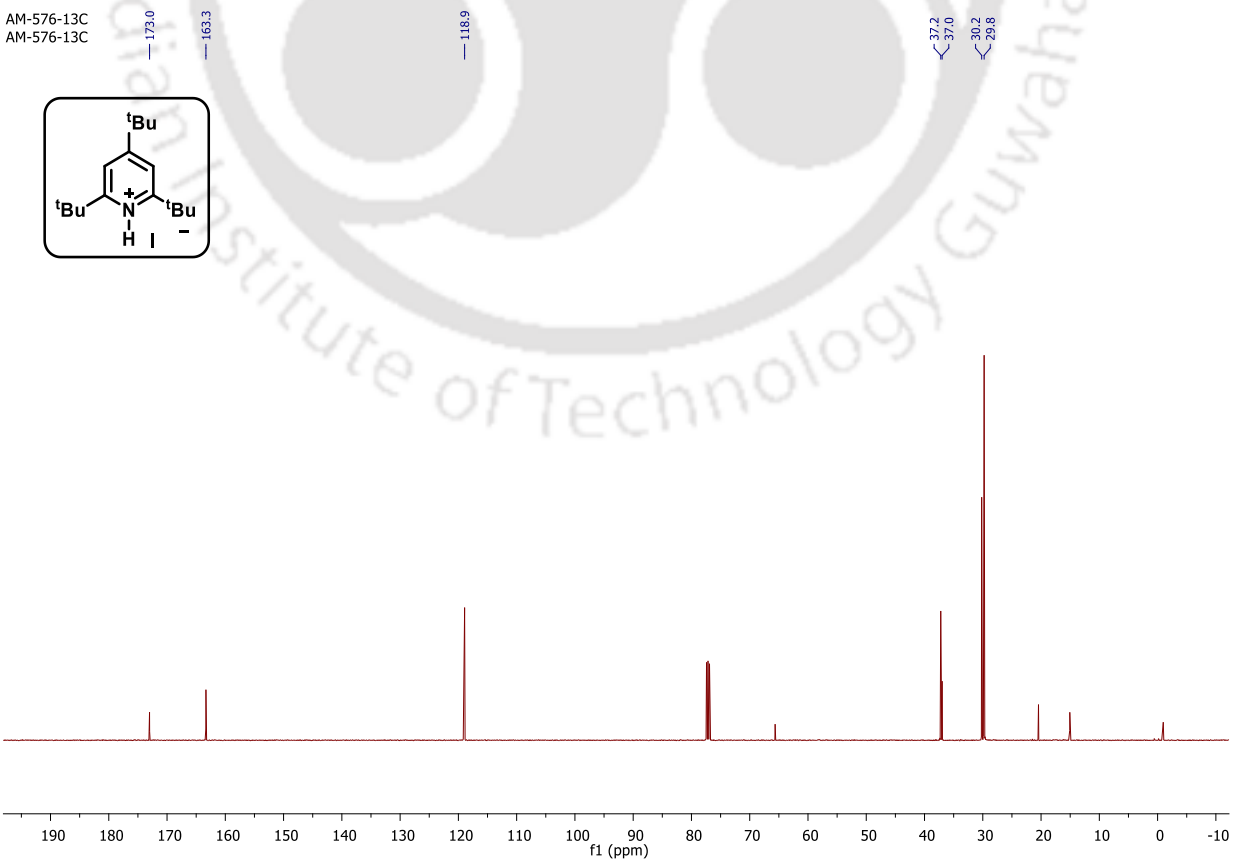
^{13}C{^{1}H} NMR of 2,4,6-tri-*tert*-butylpyridinium hydrobromide salt (22b, 600 MHz, $CDCl_3$):



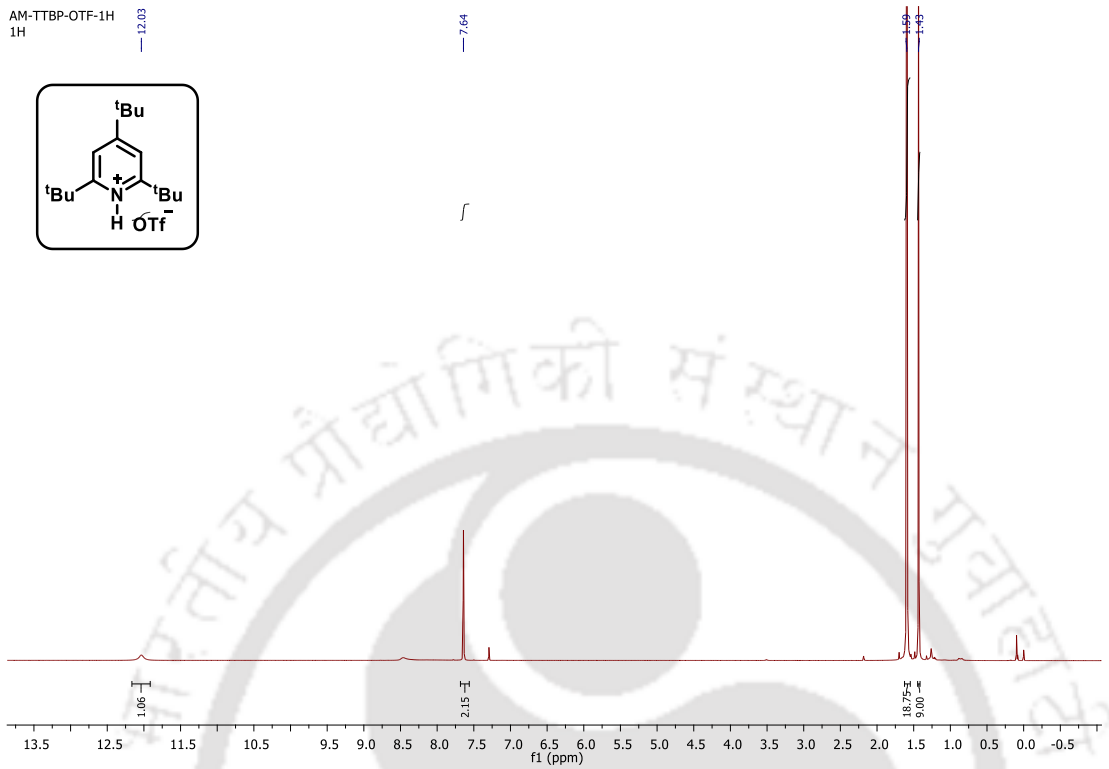
^{1}H NMR of 2,4,6-tri-*tert*-butylpyridinium hydriodide salt (22c, 500 MHz, $CDCl_3$):



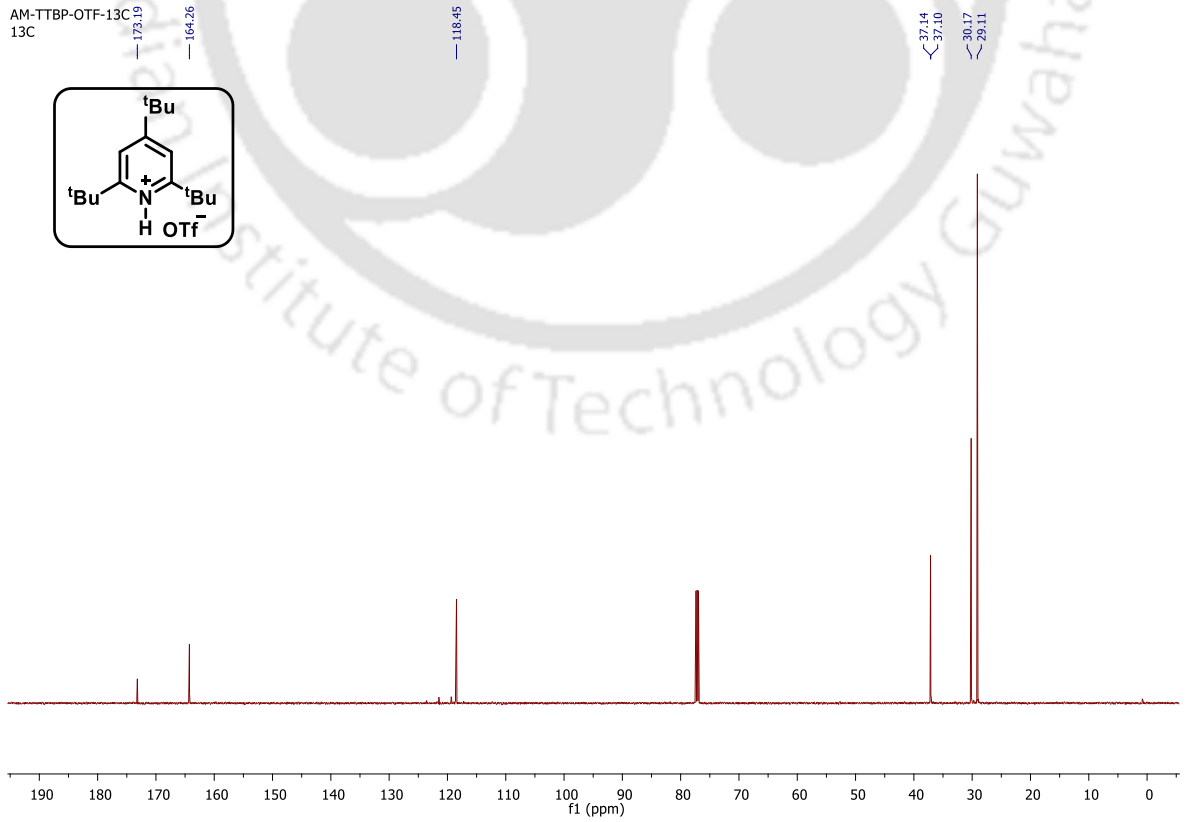
^{13}C{^{1}H} NMR of 2,4,6-tri-*tert*-butylpyridinium hydriodide salt (22c, 500 MHz, $CDCl_3$):



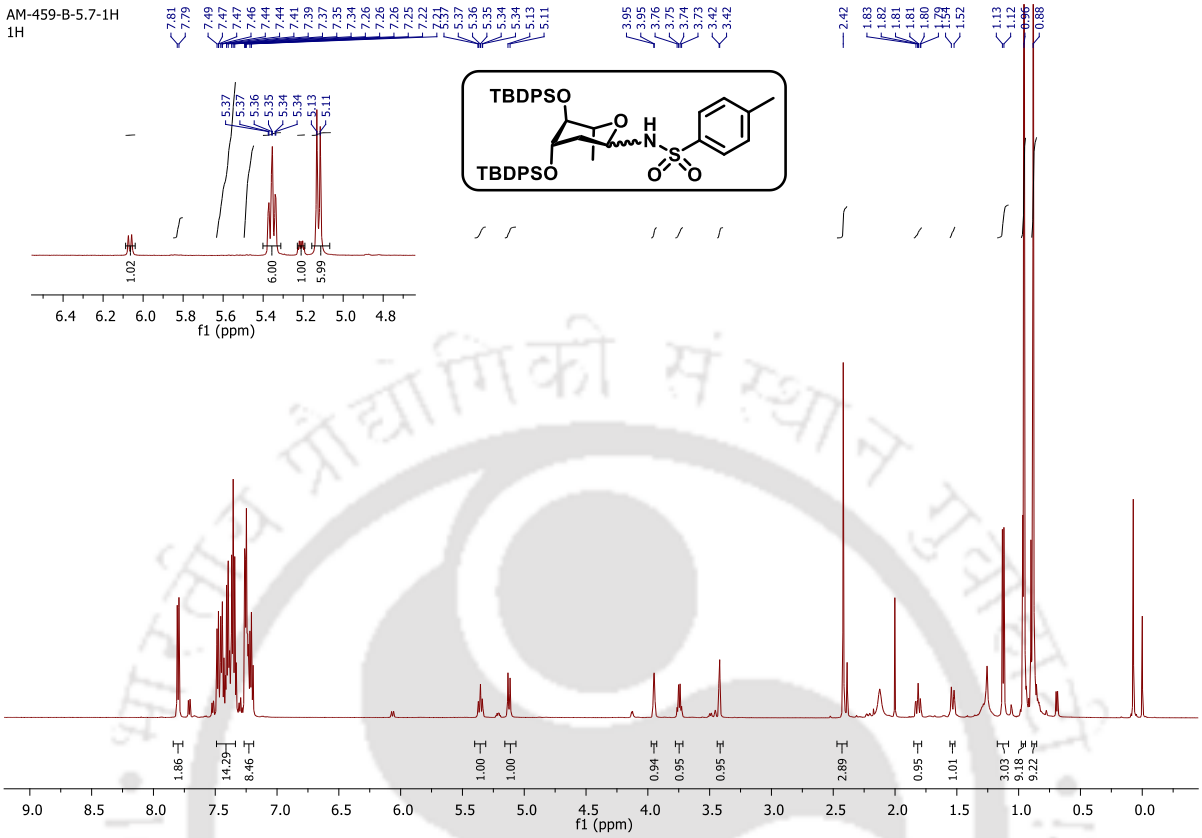
^{1}H NMR of 2,4,6-tri-*tert*-butylpyridinium trifluoromethanesulfonate salt (22d, 600 MHz, $CDCl_3$):



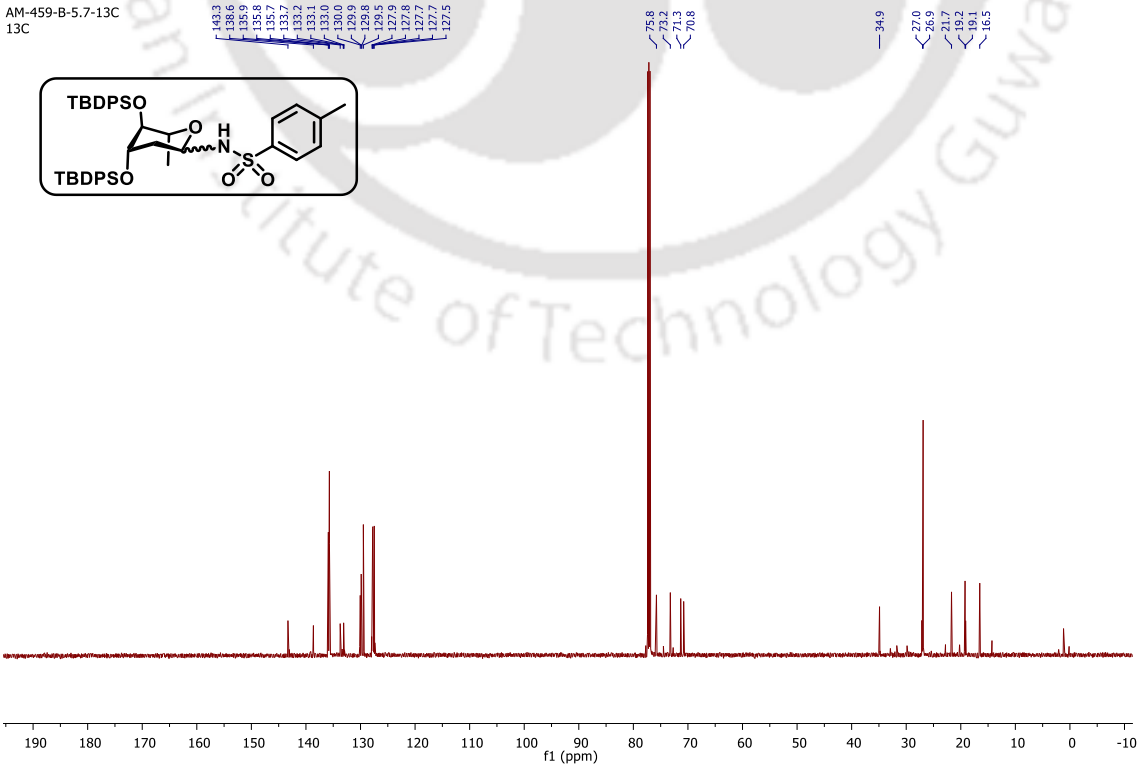
^{13}C{^{1}H} NMR of 2,4,6-tri-*tert*-butylpyridinium trifluoromethanesulfonate salt (22d, 600 MHz, $CDCl_3$):



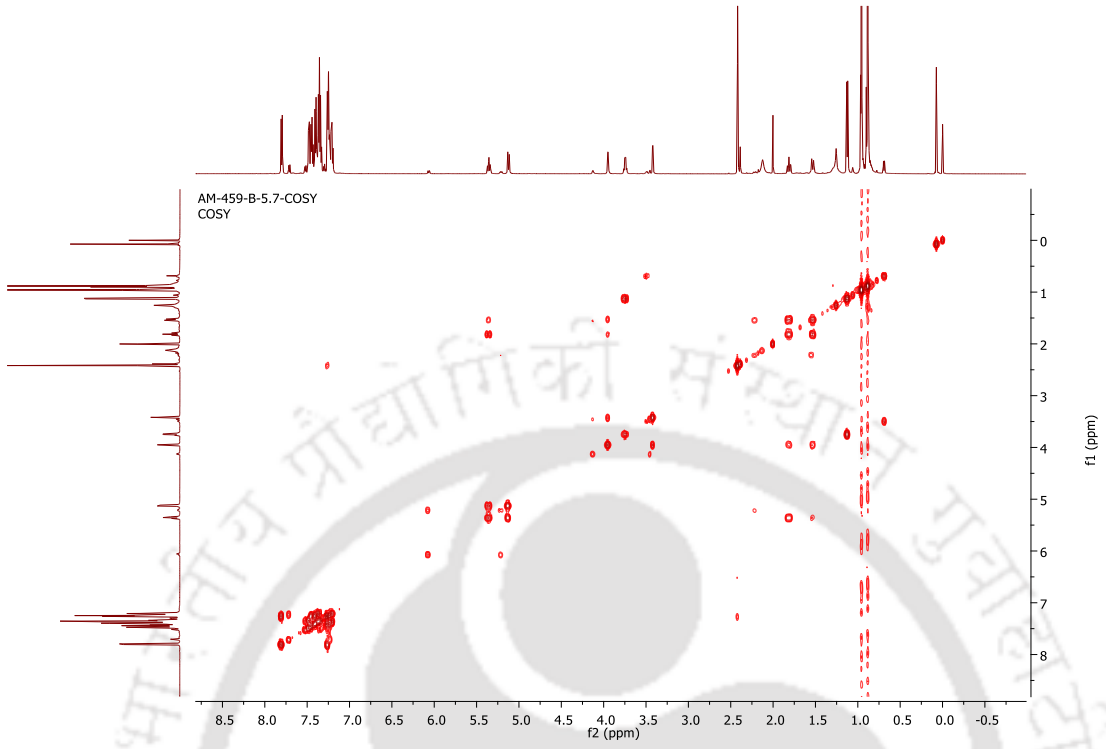
^{1}H NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β−L-rhamnopyranosyl p-toluenesulfonamide (24a, 600 MHz, $CDCl_3$):



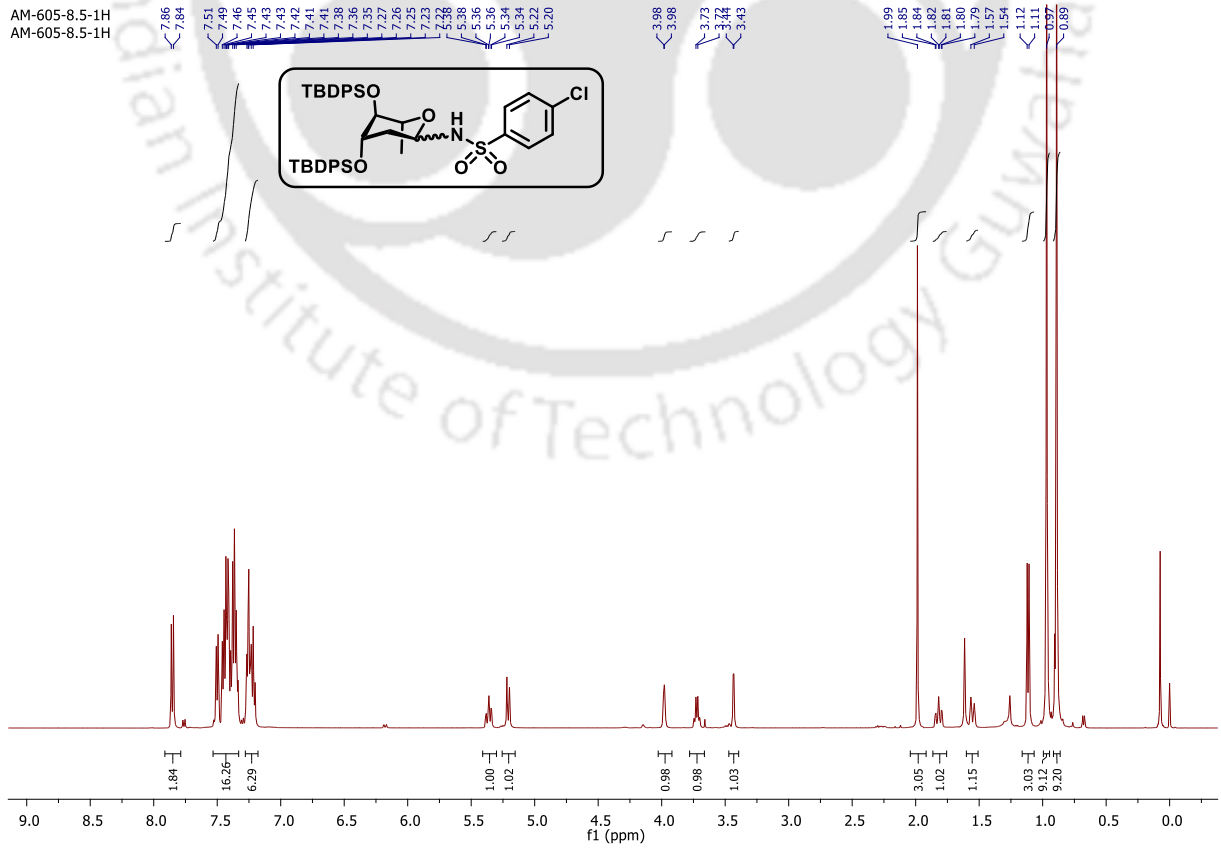
^{13}C NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β−L-rhamnopyranosyl p-toluenesulfonamide (24a, 600 MHz, $CDCl_3$):



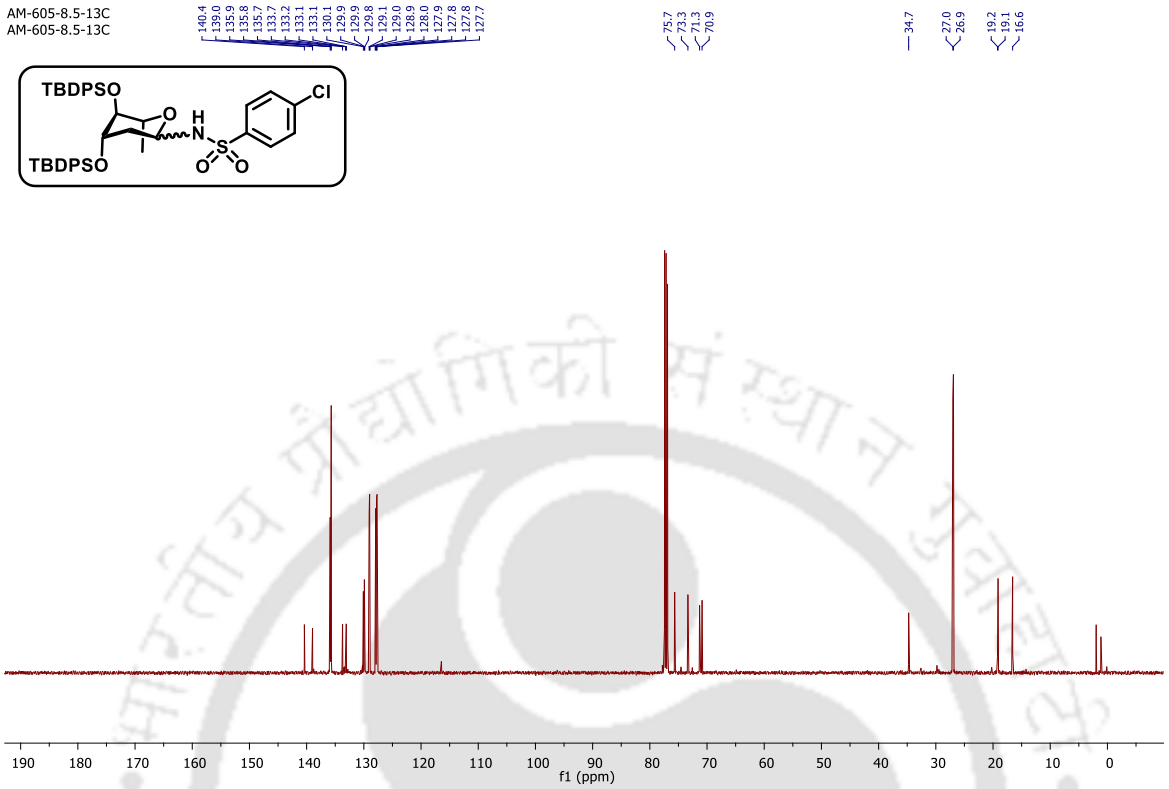
COSY NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β−L-rhamnopyranosyl p-toluenesulfonamide (24a, 600 MHz, $CDCl_3$):



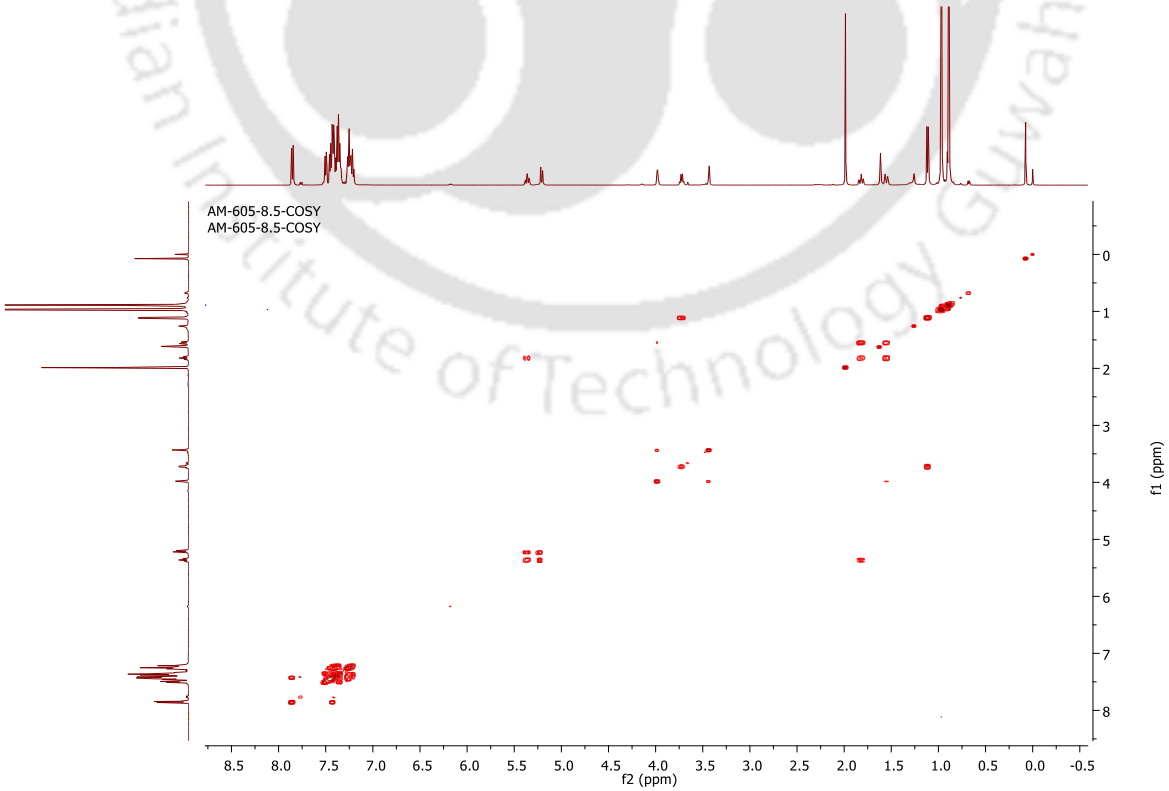
^{1}H NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-chlorobenzene sulfonamide (24b, 500 MHz, $CDCl_3$):



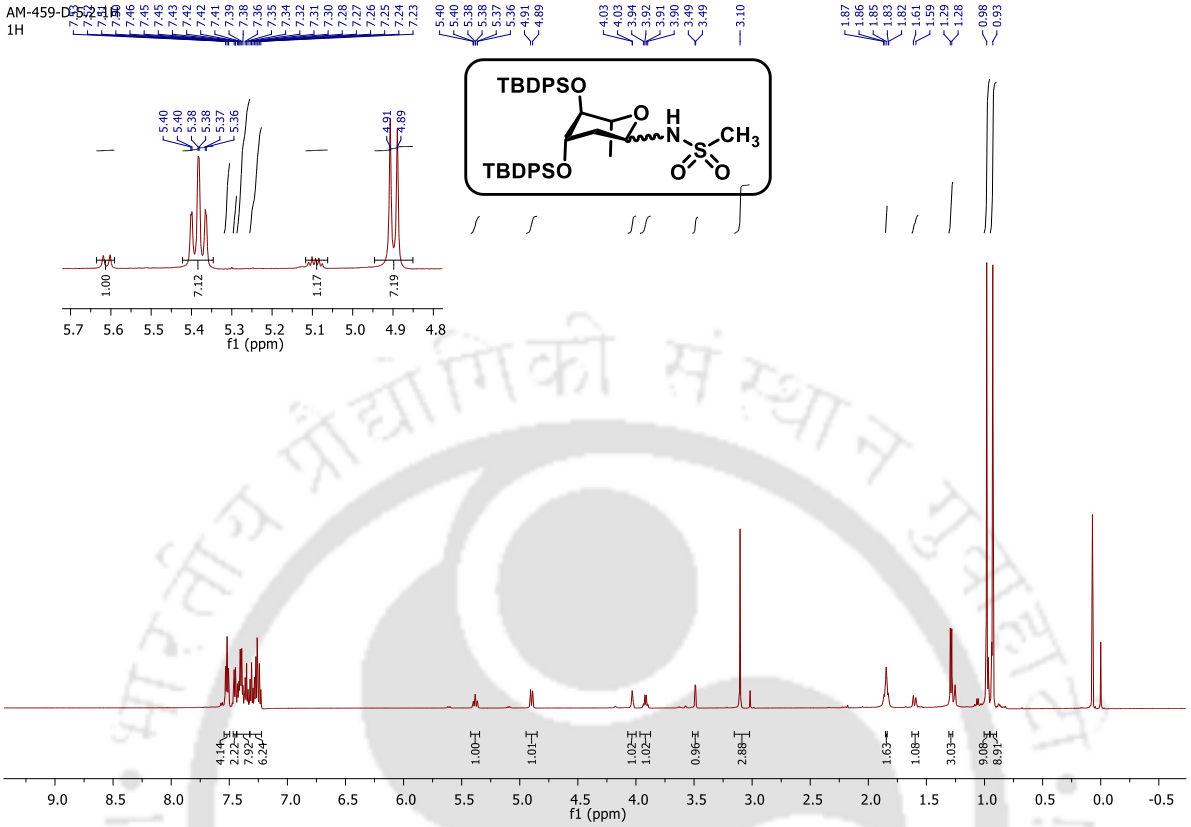
^{13}C NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-chlorobenzene sulfonamide (24b, 500 MHz, $CDCl_3$):



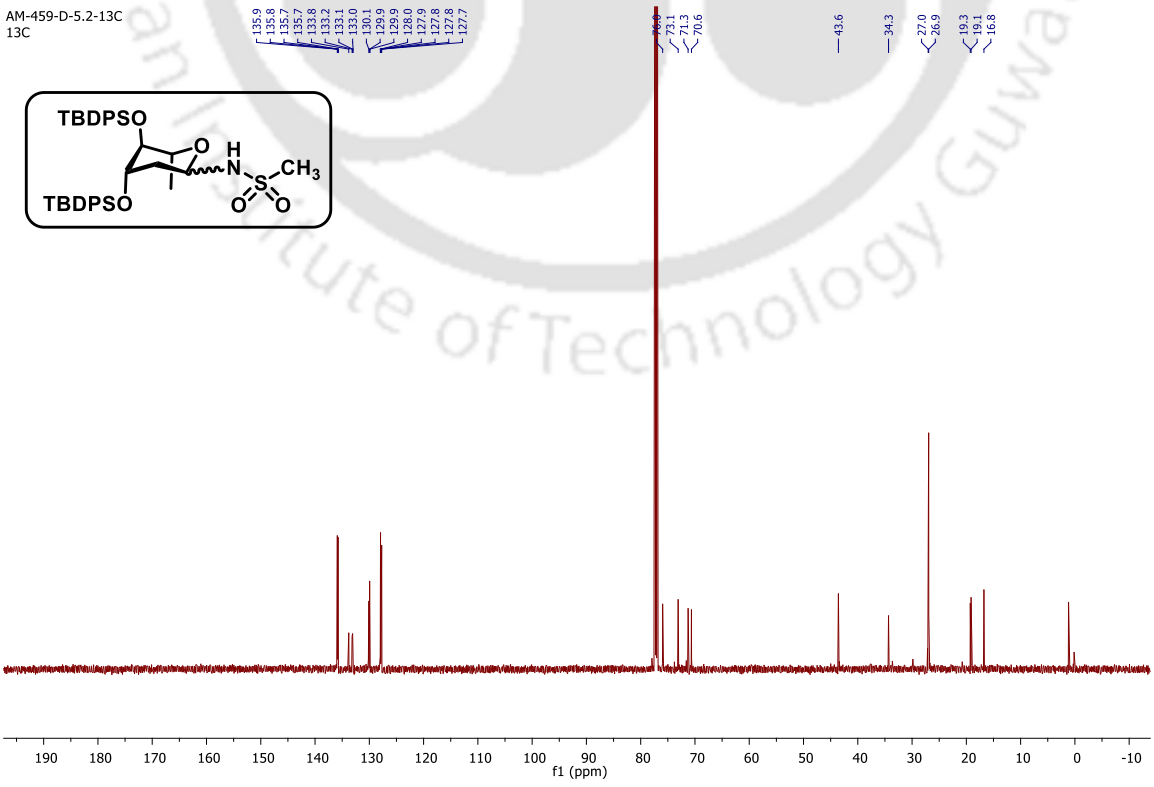
COSY NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-chlorobenzene sulfonamide (24b, 500 MHz, $CDCl_3$):



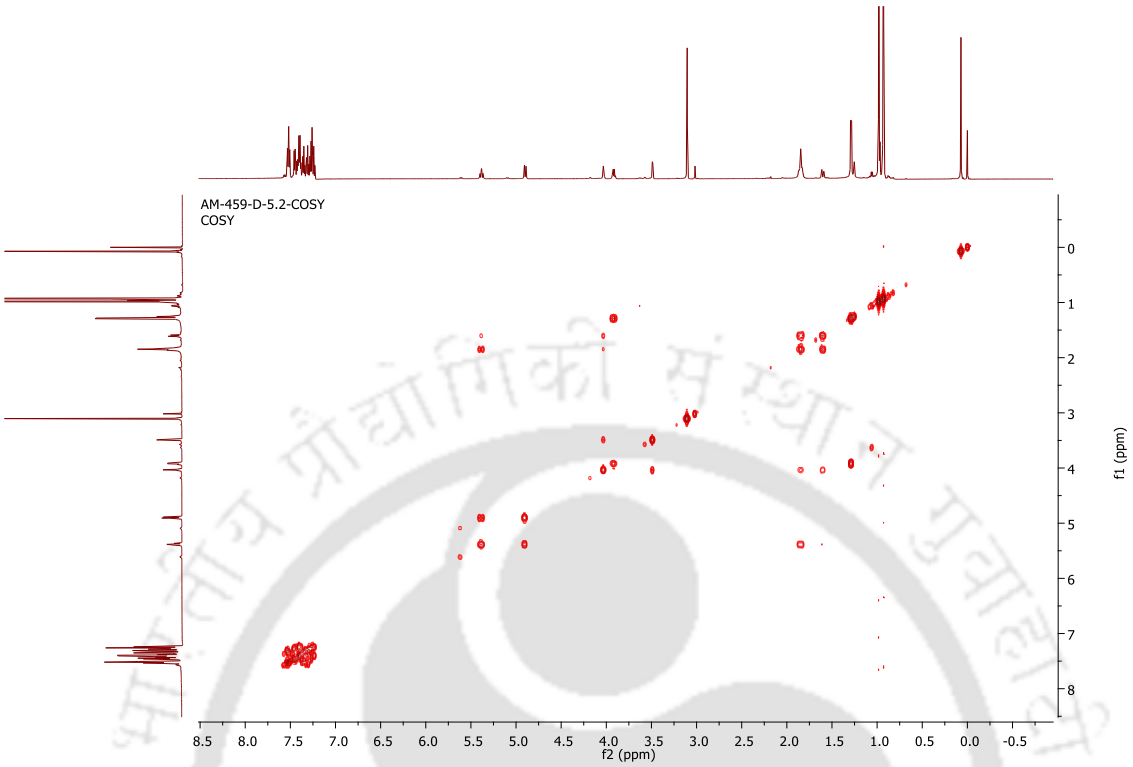
^{1}H NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl methanesulfonamide (24c, 600 MHz, $CDCl_3$):



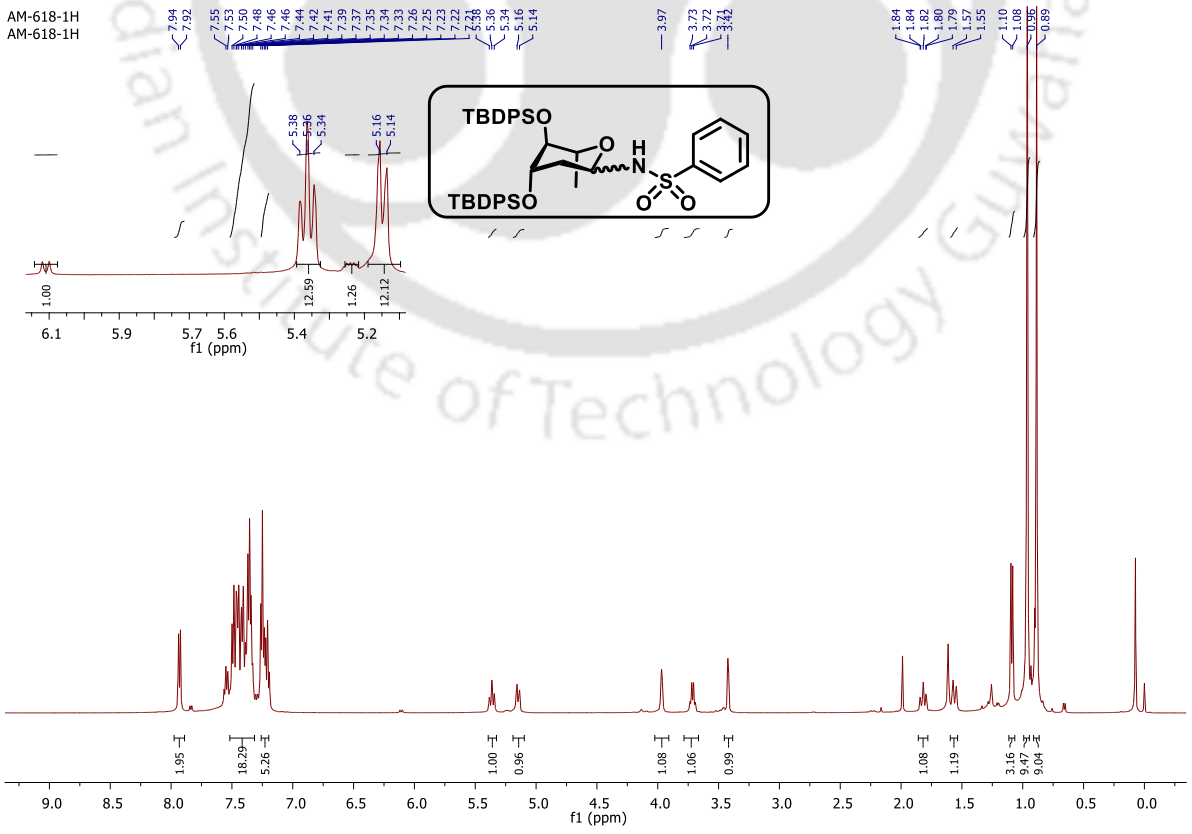
^{13}C NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl methanesulfonamide (24c, 600 MHz, $CDCl_3$):



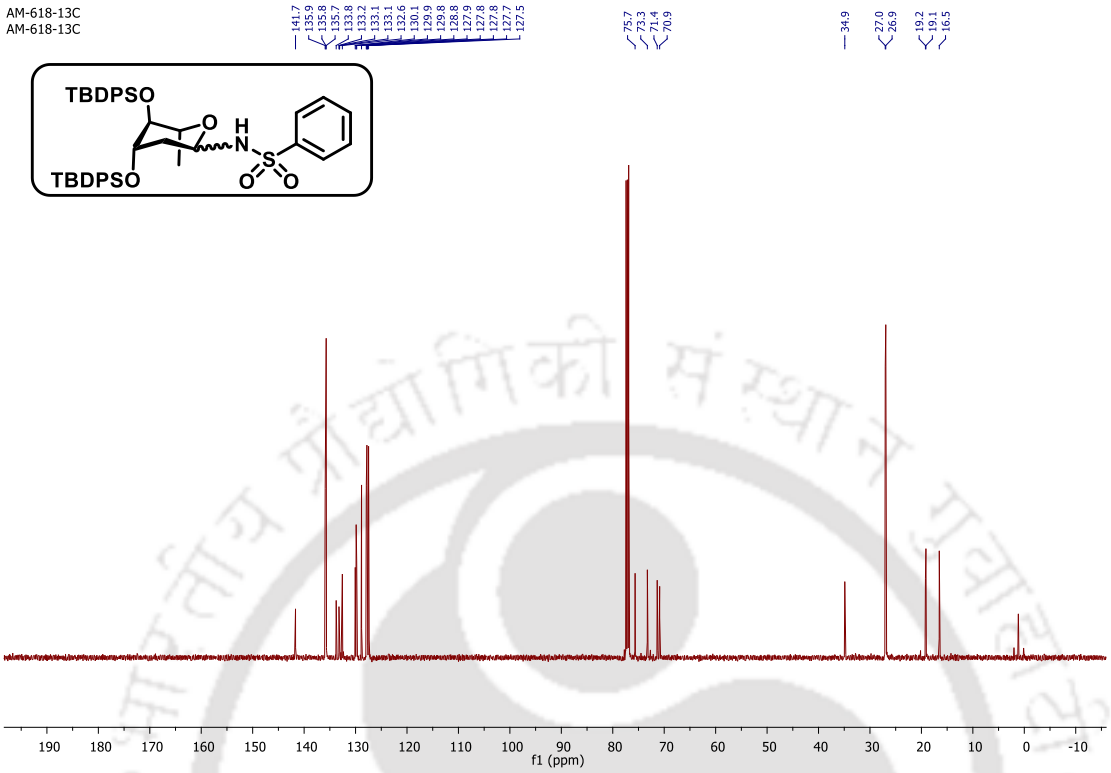
COSY NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl methanesulfonamide (24c, 600 MHz, $CDCl_3$):



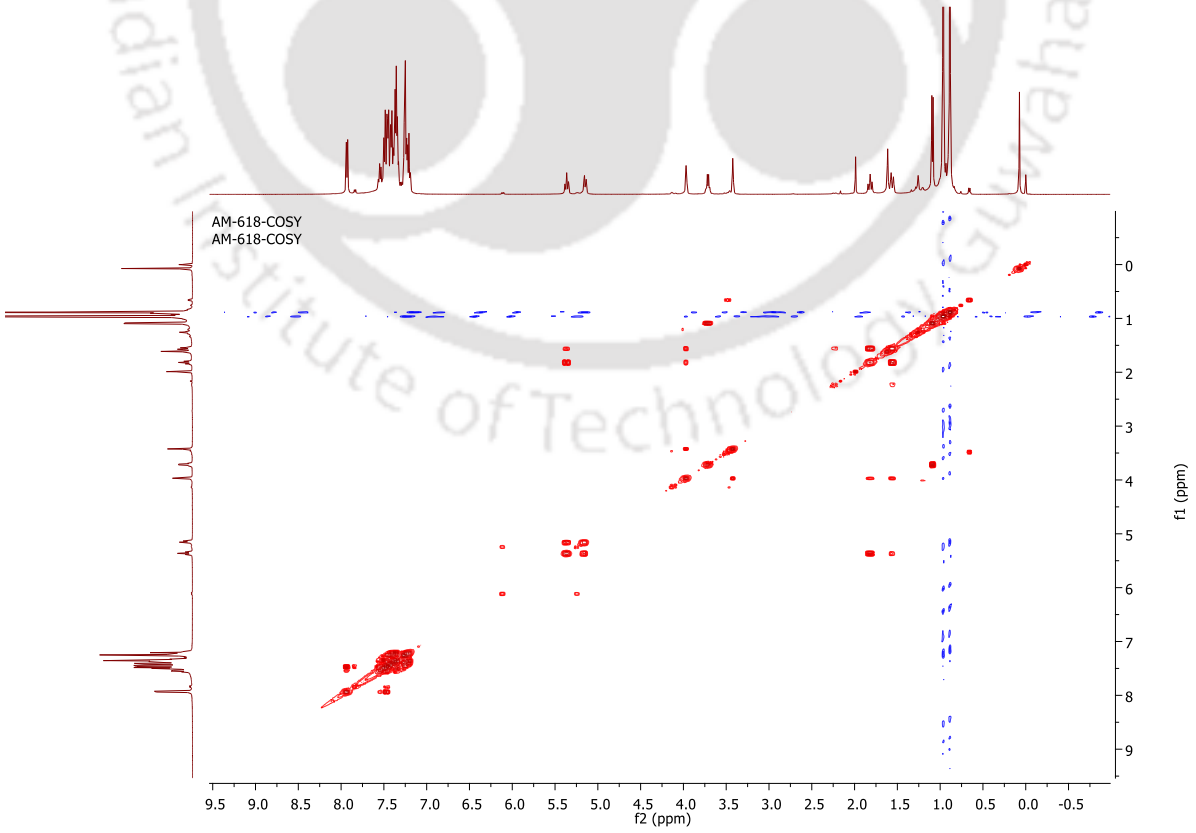
^{1}H NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl benzene sulfonamide (24d, 500 MHz, $CDCl_3$):



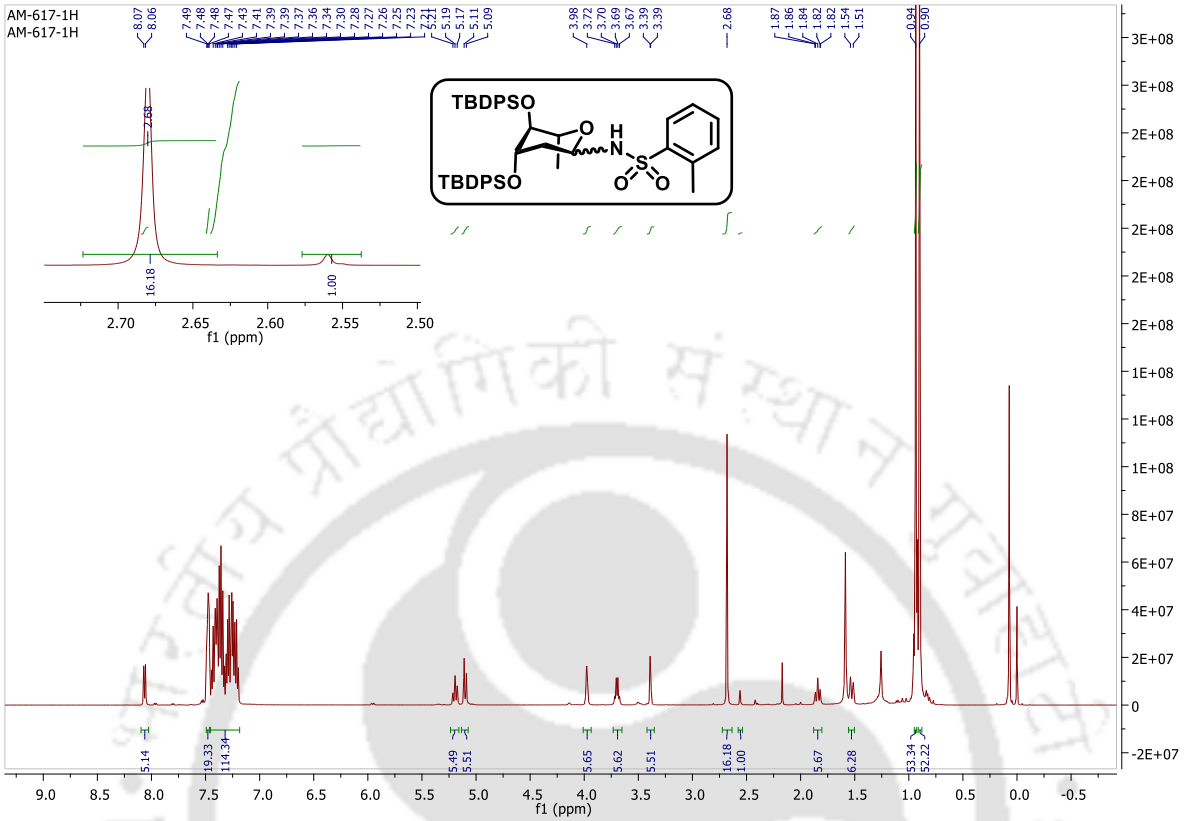
^{13}C NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl benzene sulfonamide (24d, 500 MHz, $CDCl_3$):



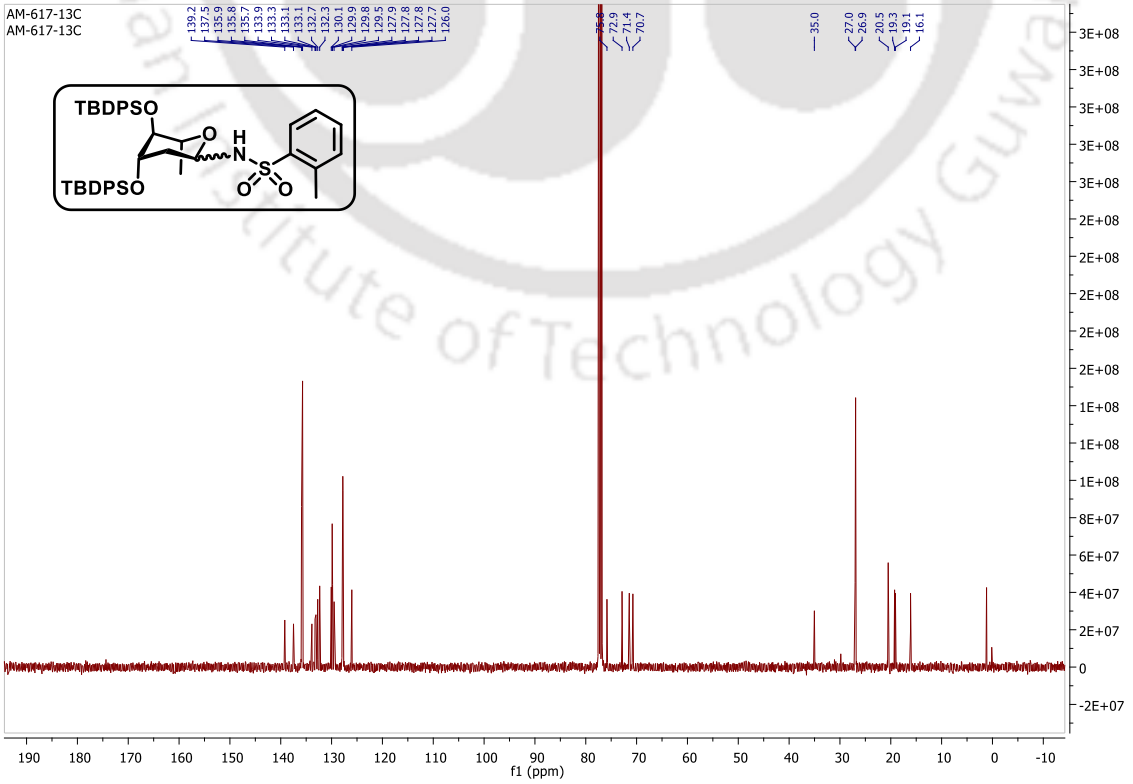
COSY NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl benzene sulfonamide (24d, 500 MHz, $CDCl_3$):



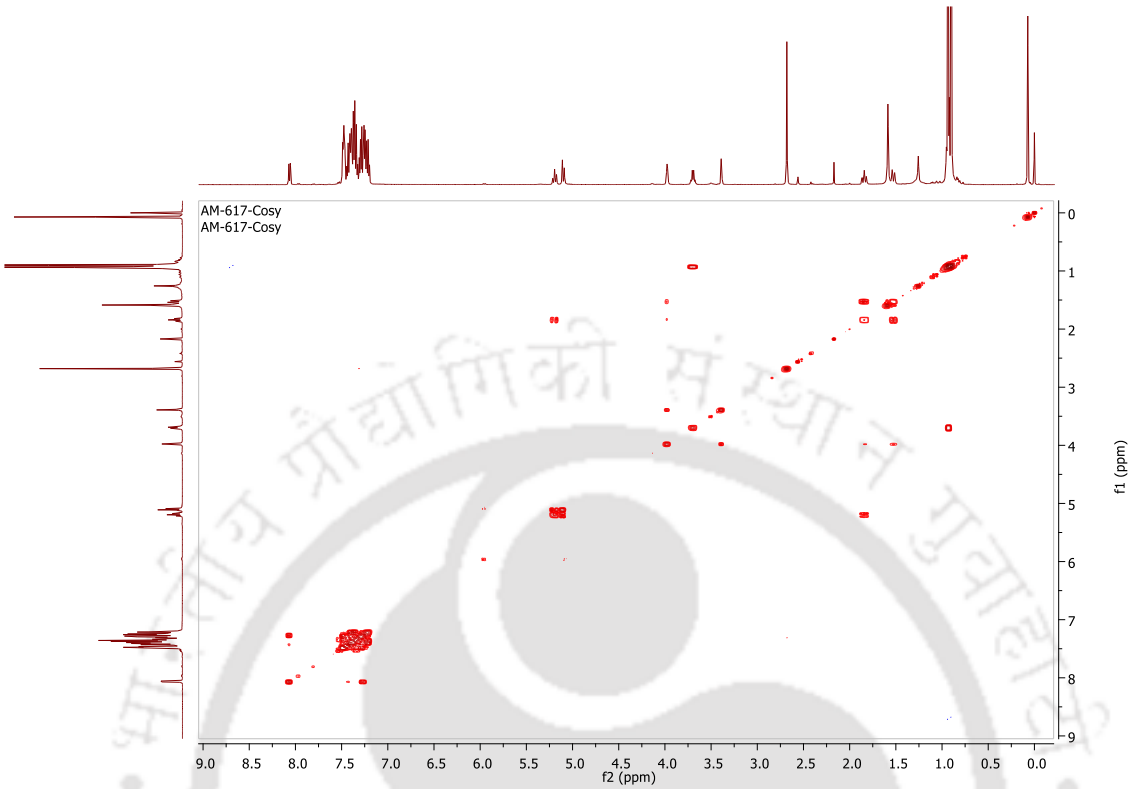
^{1}H NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl o-toluenesulfonamide (24e, 500 MHz, $CDCl_3$):



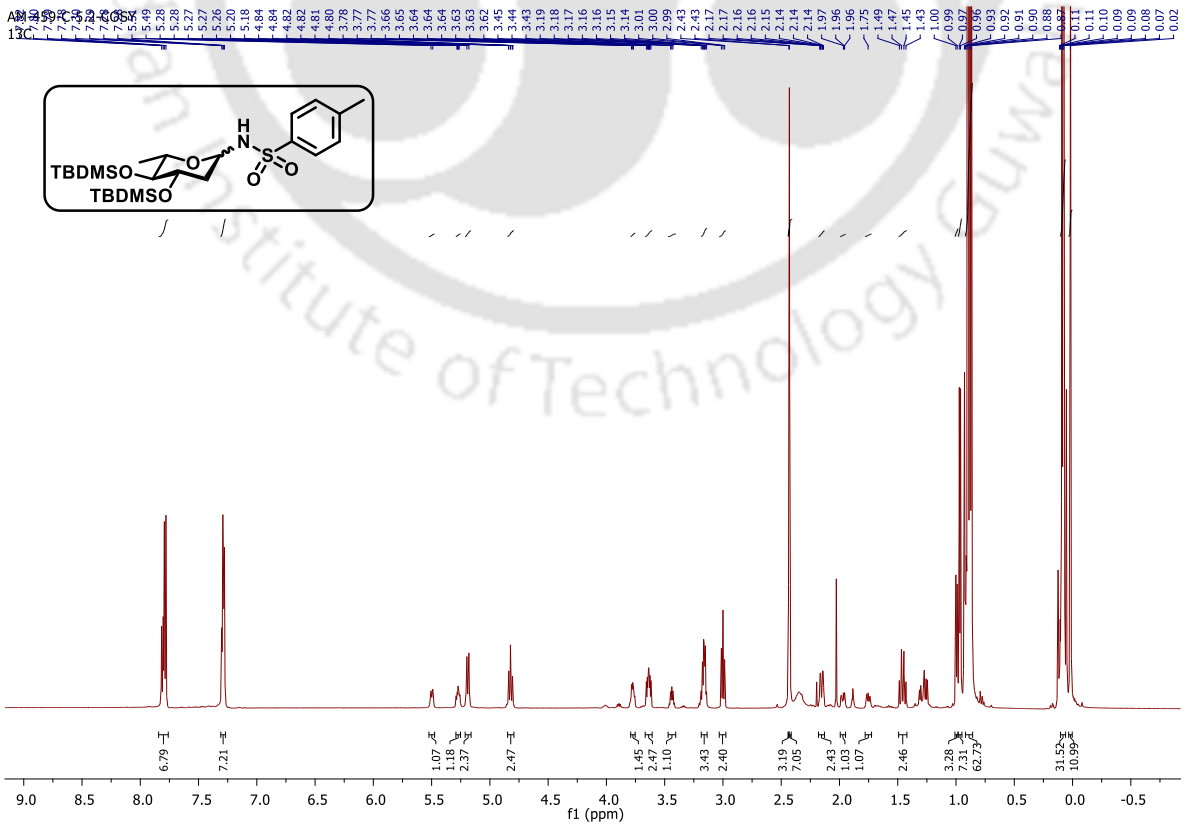
^{13}C NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl o-toluenesulfonamide (24e, 400 MHz, $CDCl_3$):



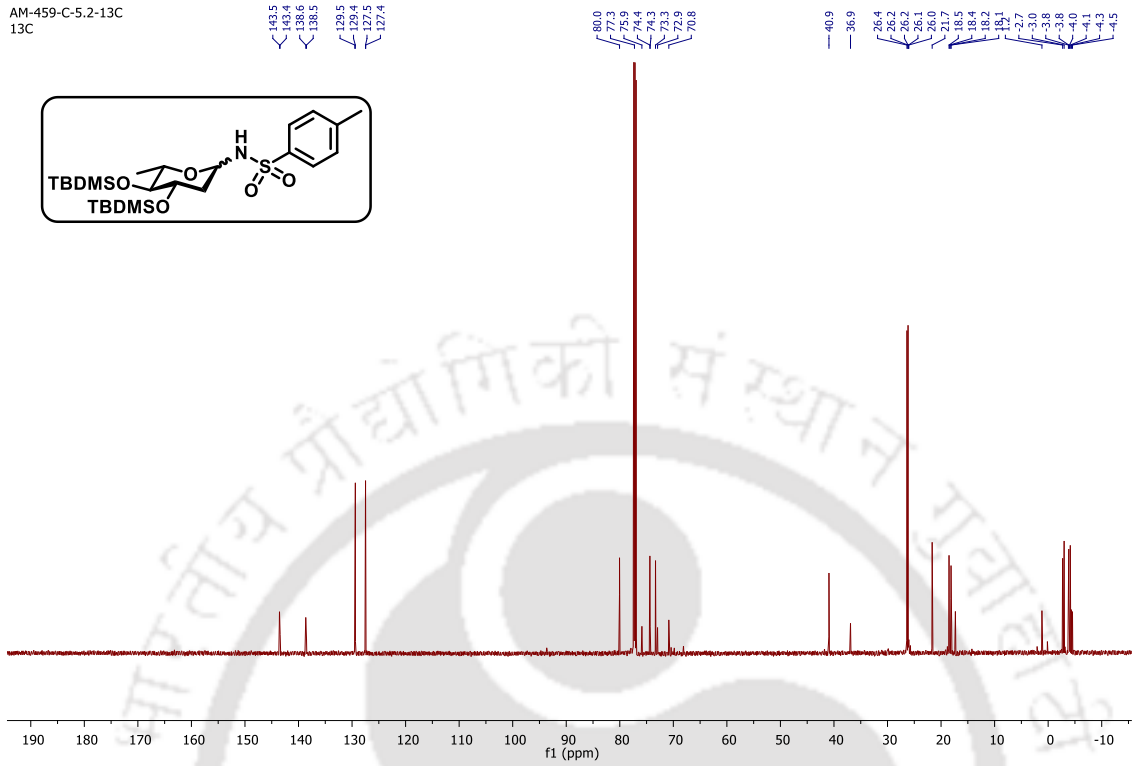
COSY NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl o-toluenesulfonamide (24e, 500 MHz, $CDCl_3$):



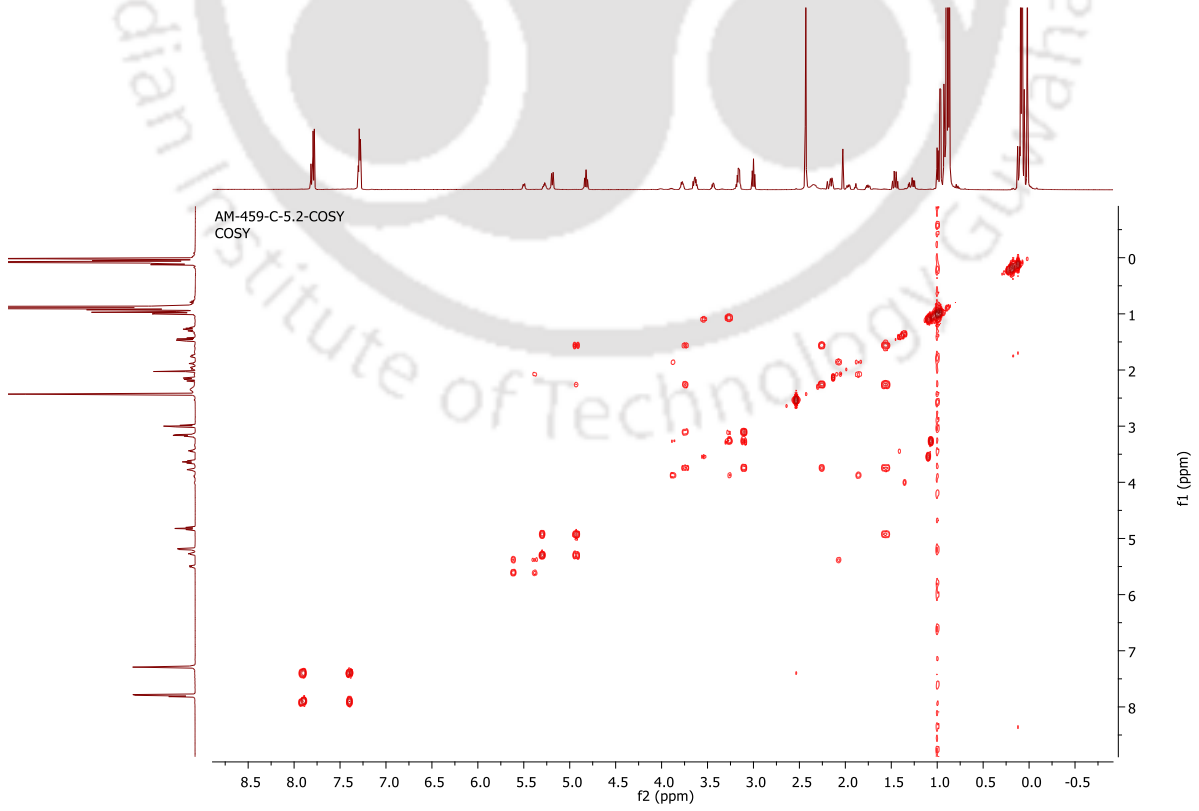
^{1}H NMR of 3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-toluenesulfonamide (23a, 600 MHz, $CDCl_3$):



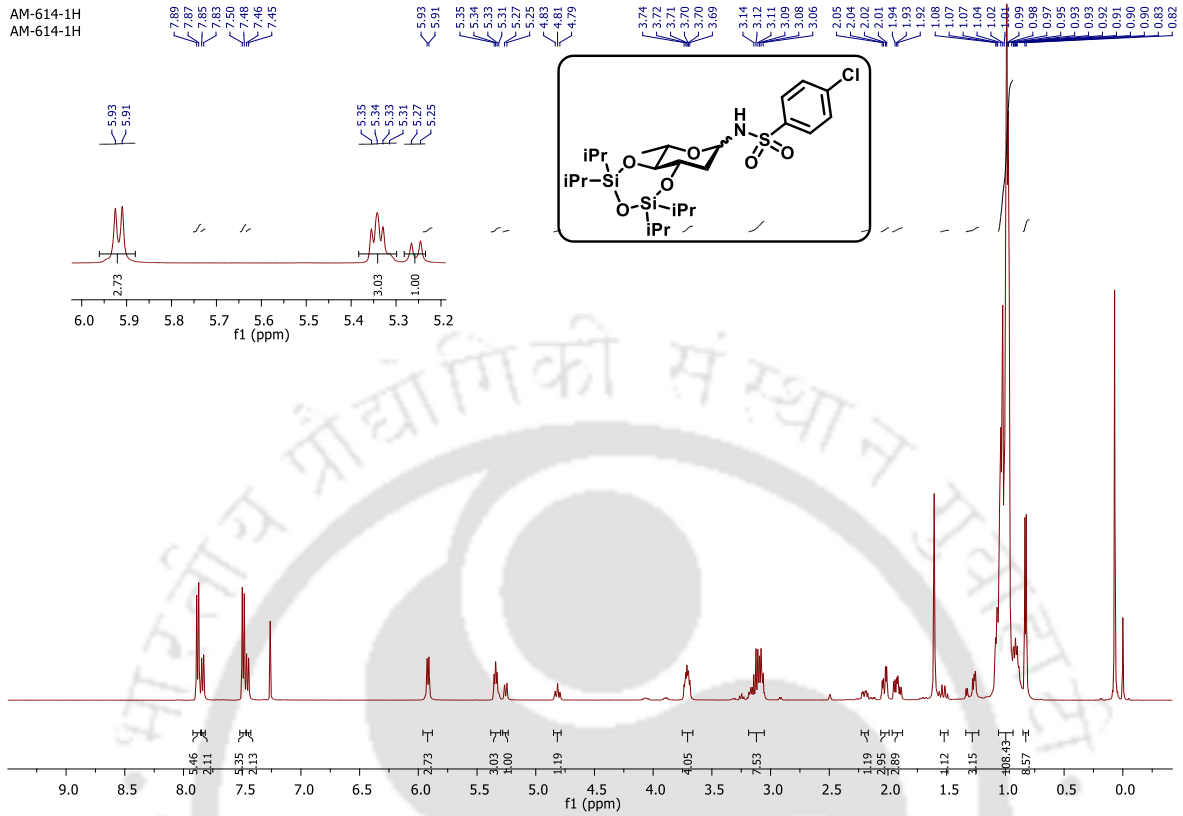
^{13}C NMR of 3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-toluenesulfonamide (23a, 600 MHz, $CDCl_3$):



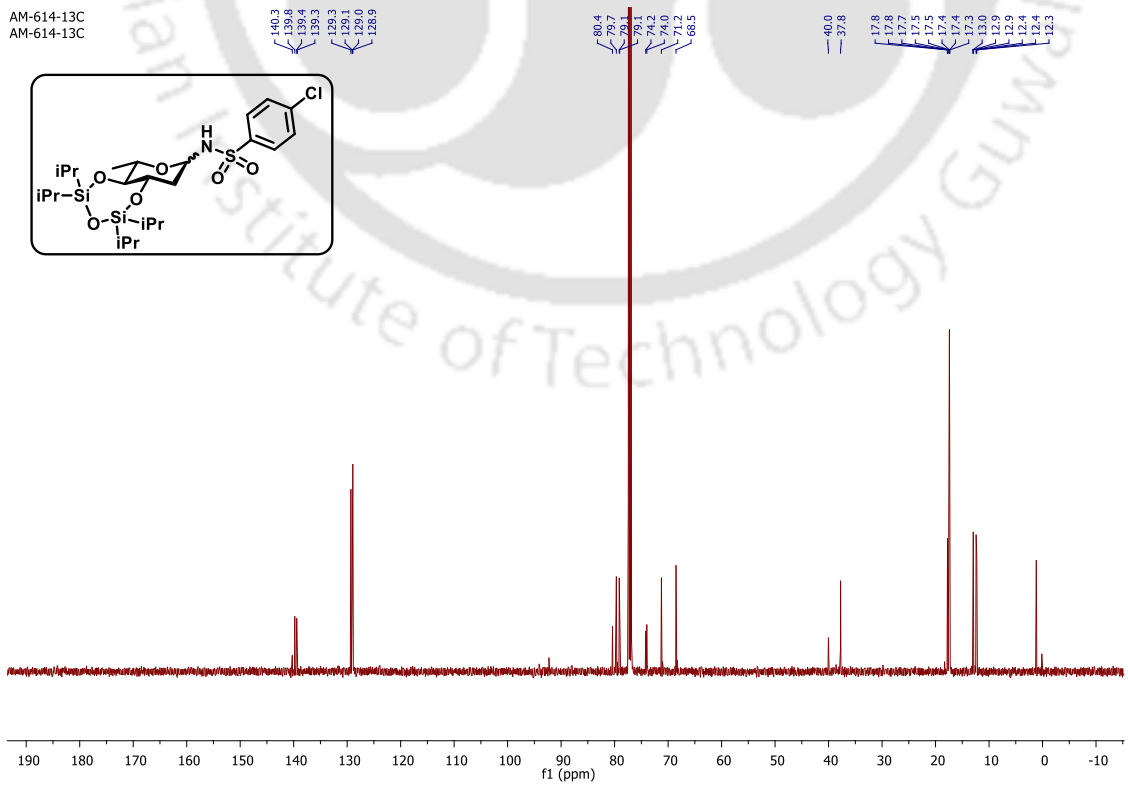
COSY NMR of 3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-toluenesulfonamide (23a, 600 MHz, $CDCl_3$):



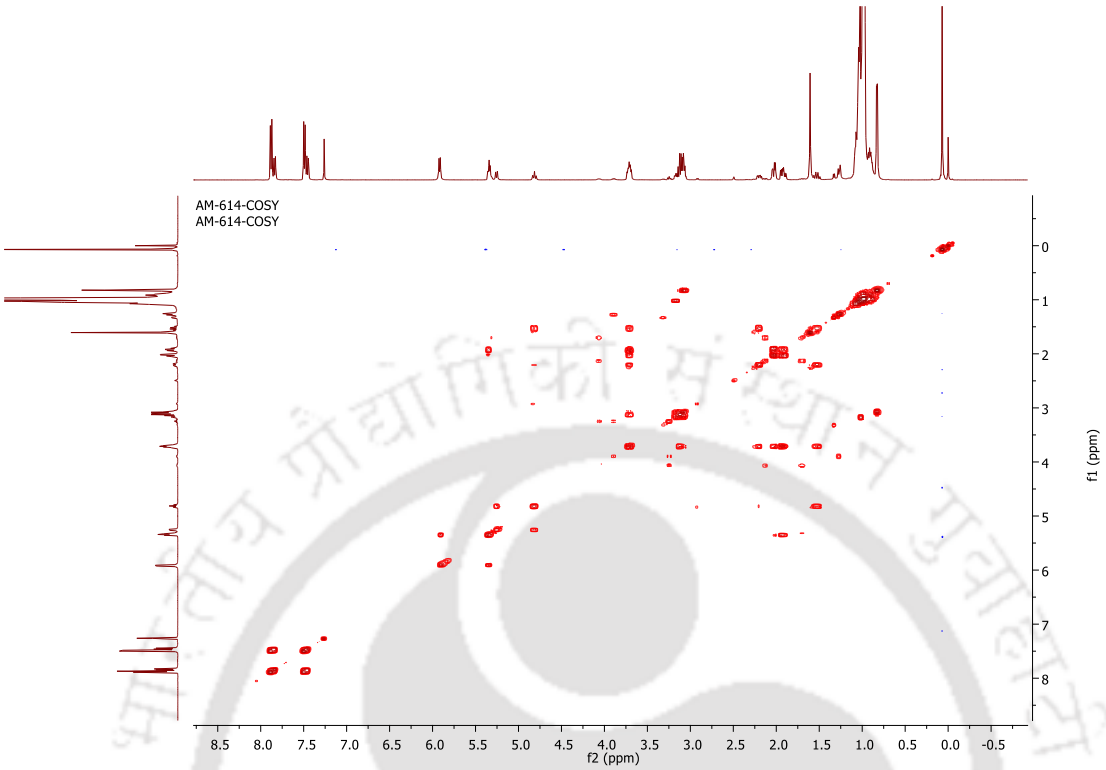
^{1}H NMR of 3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranosyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-chlorobenzene sulfonamide (23b, 500 MHz, $CDCl_3$):



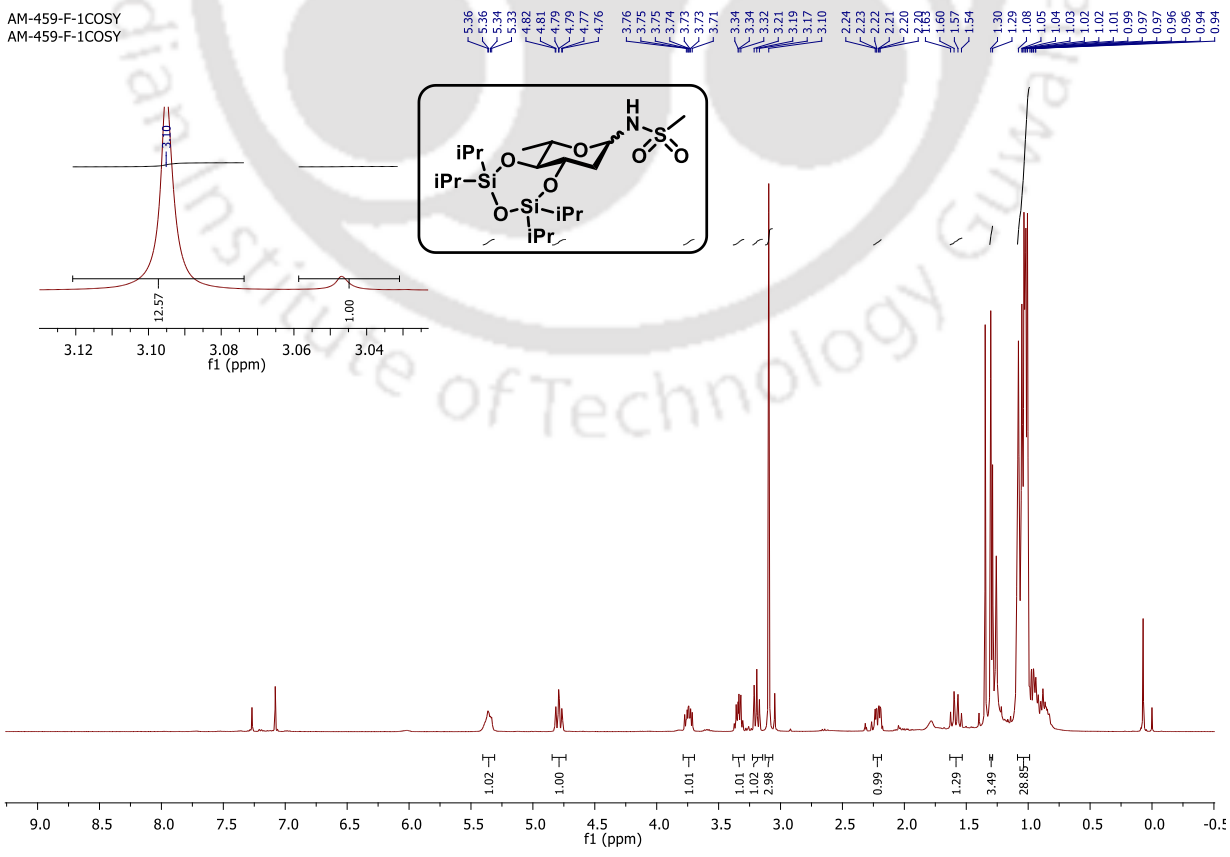
^{13}C NMR of 3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranosyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-chlorobenzene sulfonamide (23b, 500 MHz, $CDCl_3$):



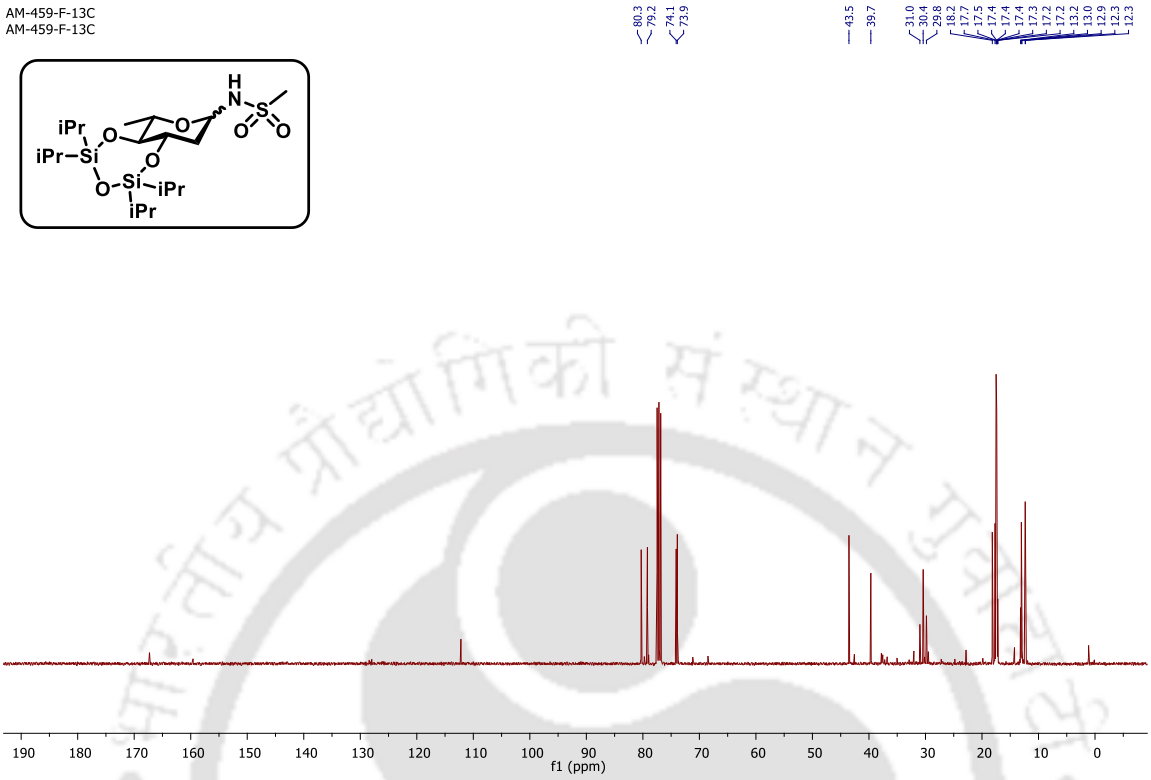
COSY NMR of 3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranosyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-chlorobenzene sulfonamide (23b, 500 MHz, $CDCl_3$):



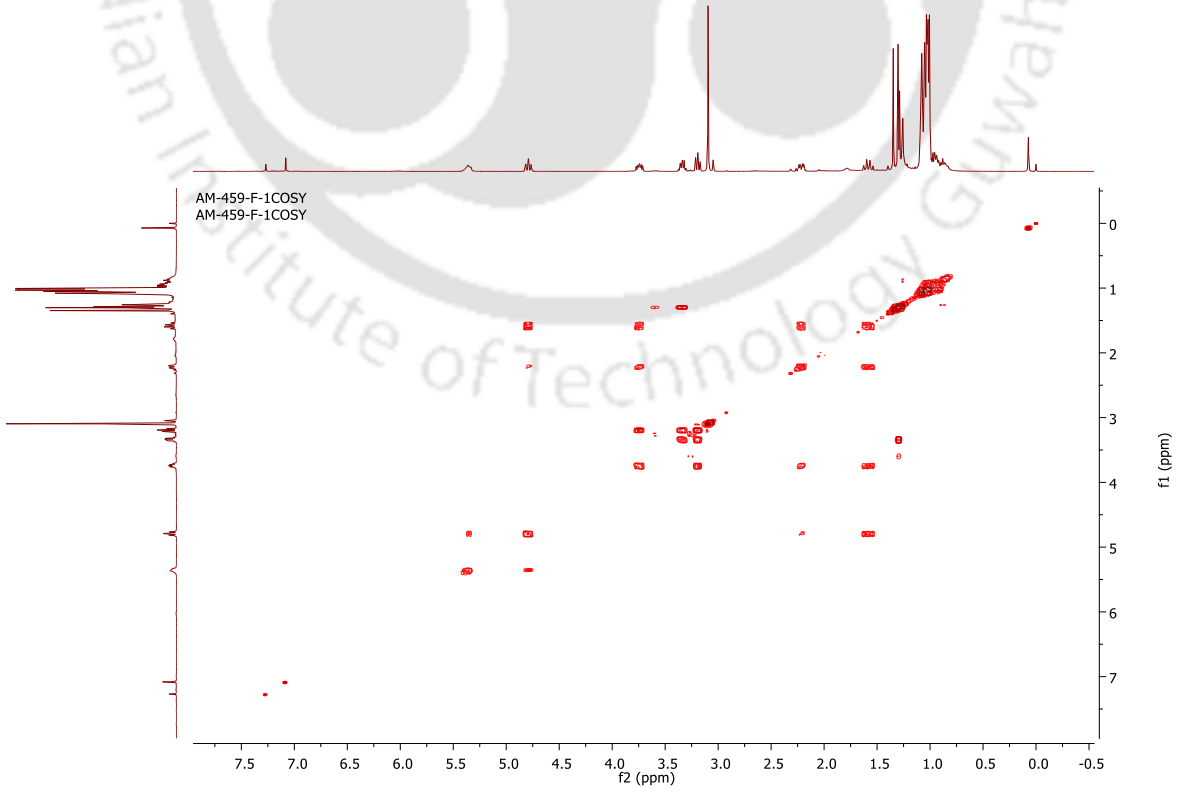
^{1}H NMR of 3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranosyl-2,6-dideoxy-α,β-L-rhamnopyranosyl methanesulfonamide (23c, 400 MHz, $CDCl_3$):



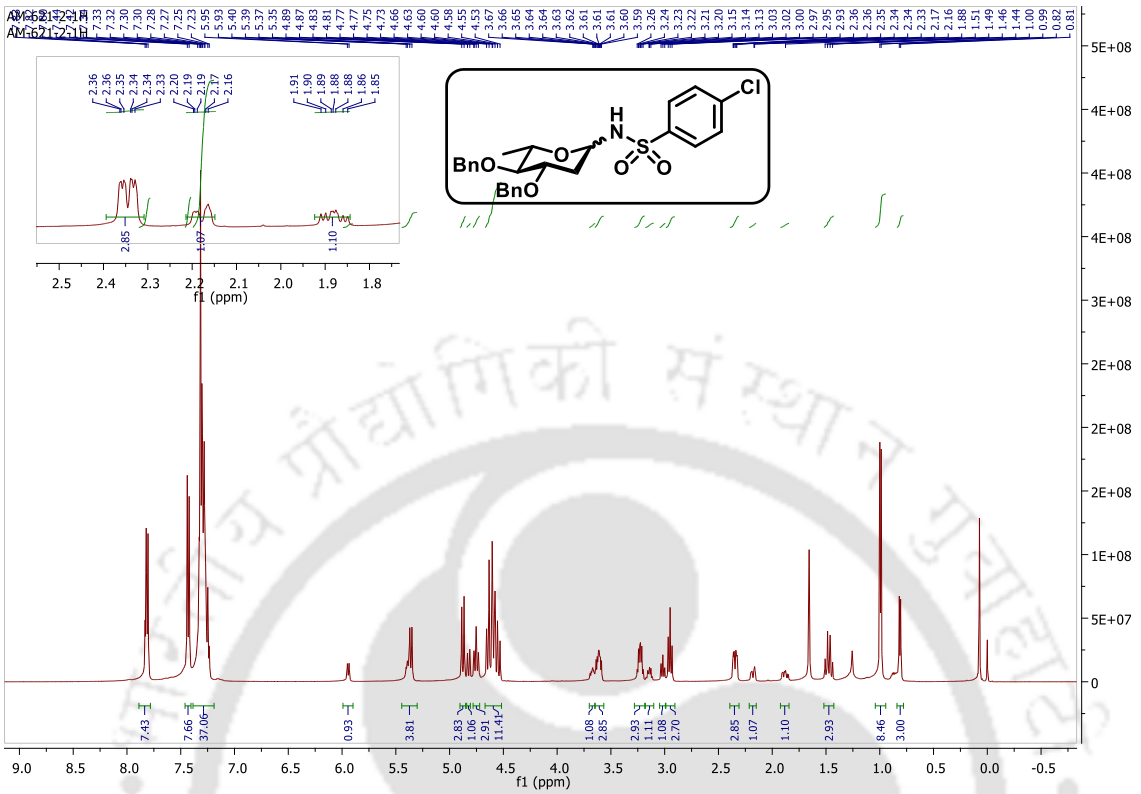
^{13}C NMR of 3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranosyl-2,6-dideoxy-α,β-L-rhamnopyranosyl methanesulfonamide (23c, 400 MHz, $CDCl_3$):



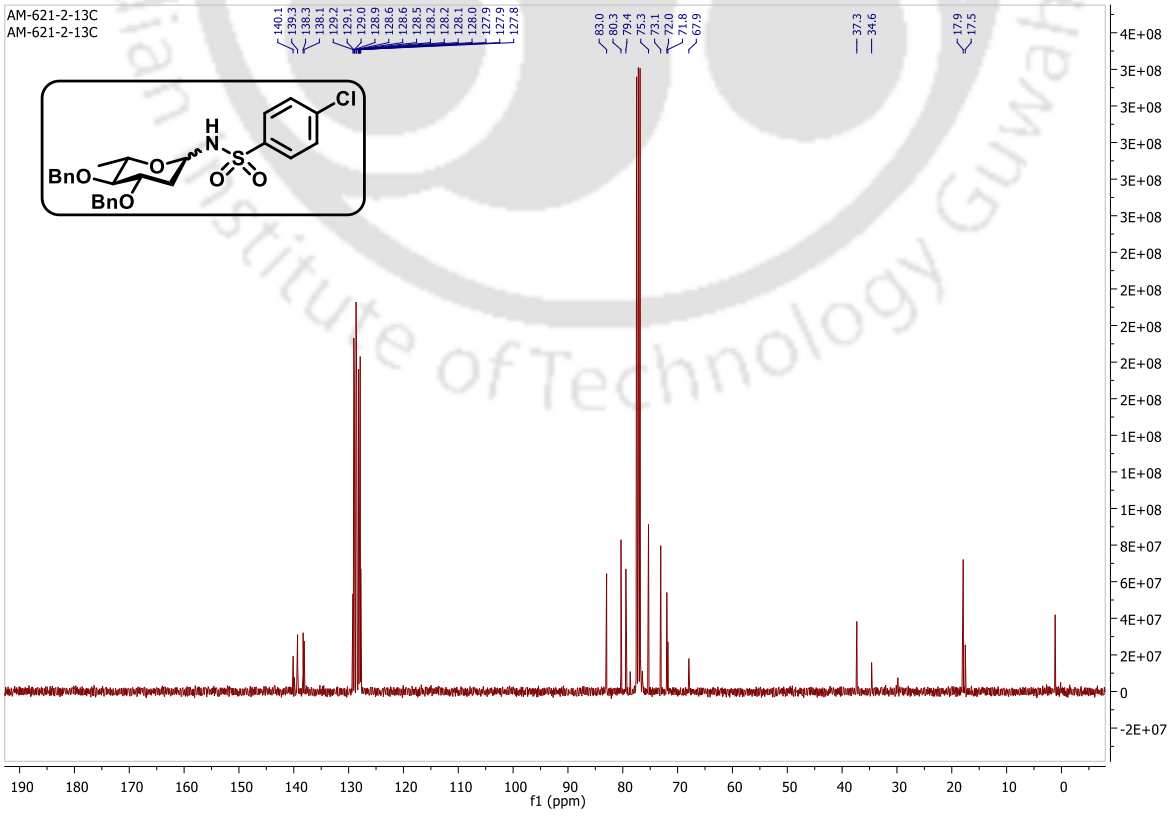
COSY NMR of 3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-erythro-hexapyranosyl-2,6-dideoxy-α,β-L-rhamnopyranosyl methanesulfonamide (23c, 400 MHz, $CDCl_3$):



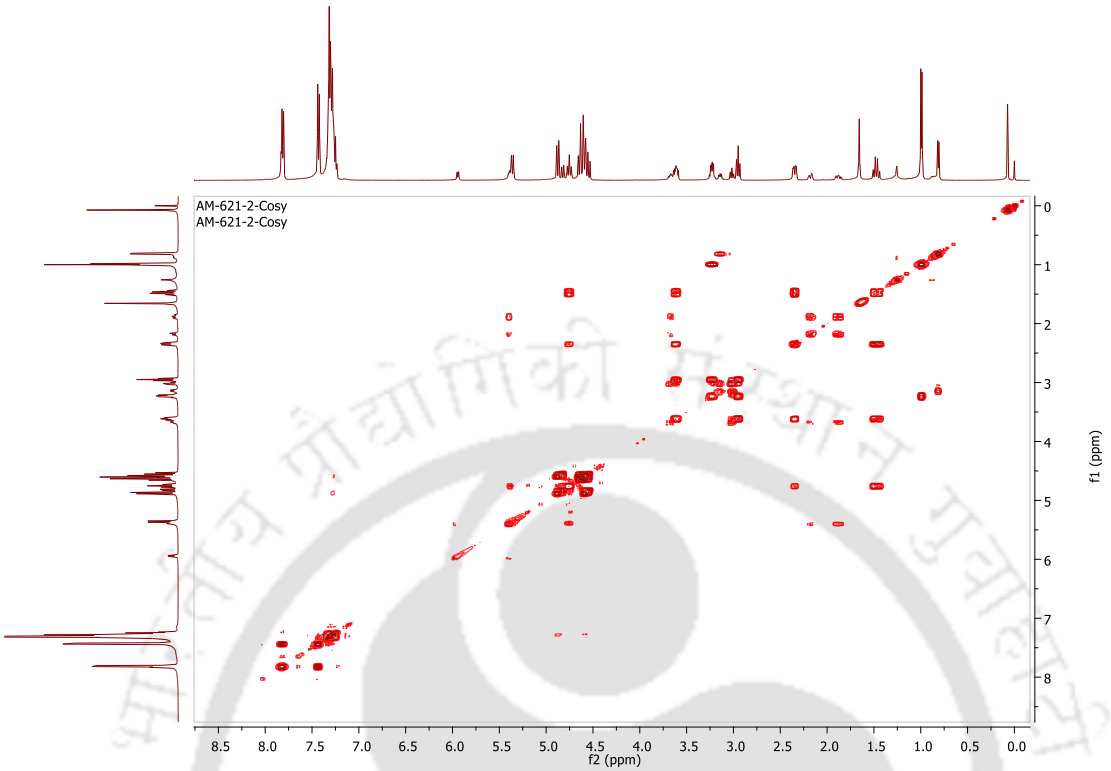
^{1}H NMR of 3,4-di-*O*-benzyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-chlorobenzene sulfonamide (23d, 500 MHz, $CDCl_3$):



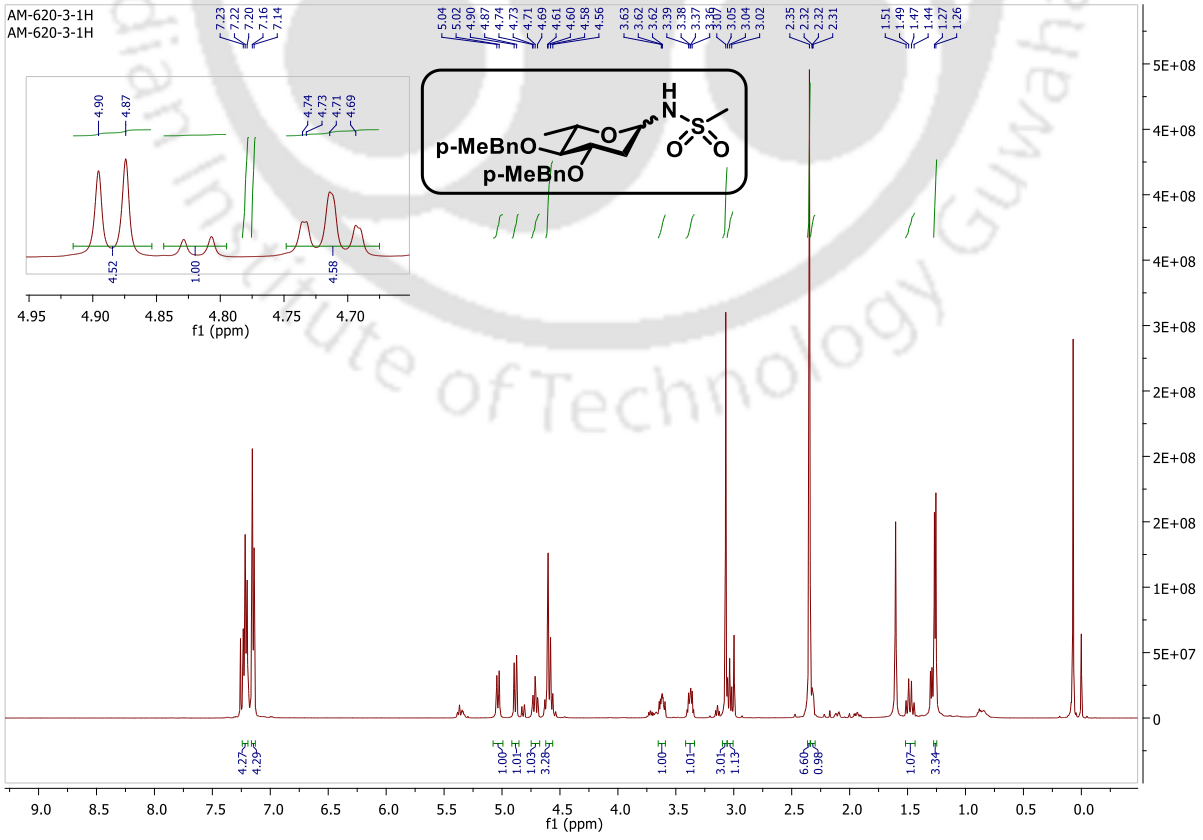
^{13}C NMR of 3,4-di-*O*-benzyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-chlorobenzene sulfonamide (23d, 400 MHz, $CDCl_3$):



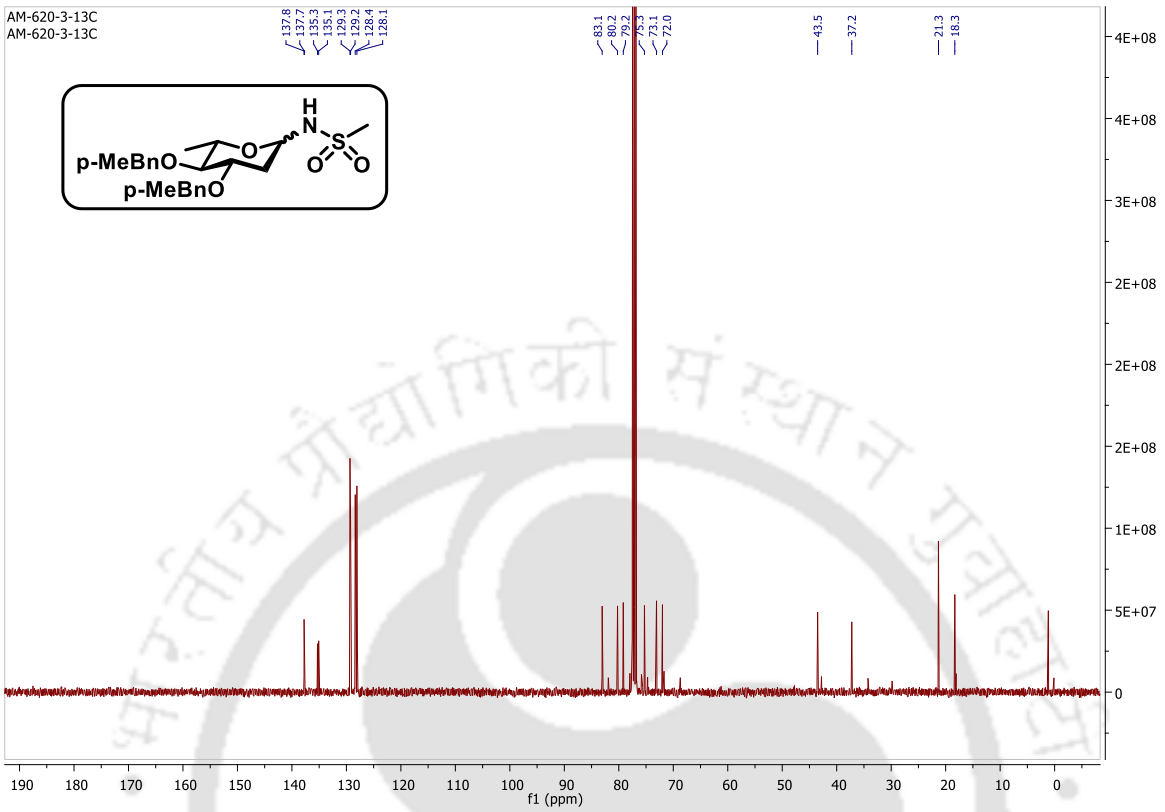
COSY NMR of 3,4-di-*O*-benzyl-2,6-dideoxy-α,β-L-rhamnopyranosyl p-chlorobenzene sulfonamide (23d, 500 MHz, $CDCl_3$):



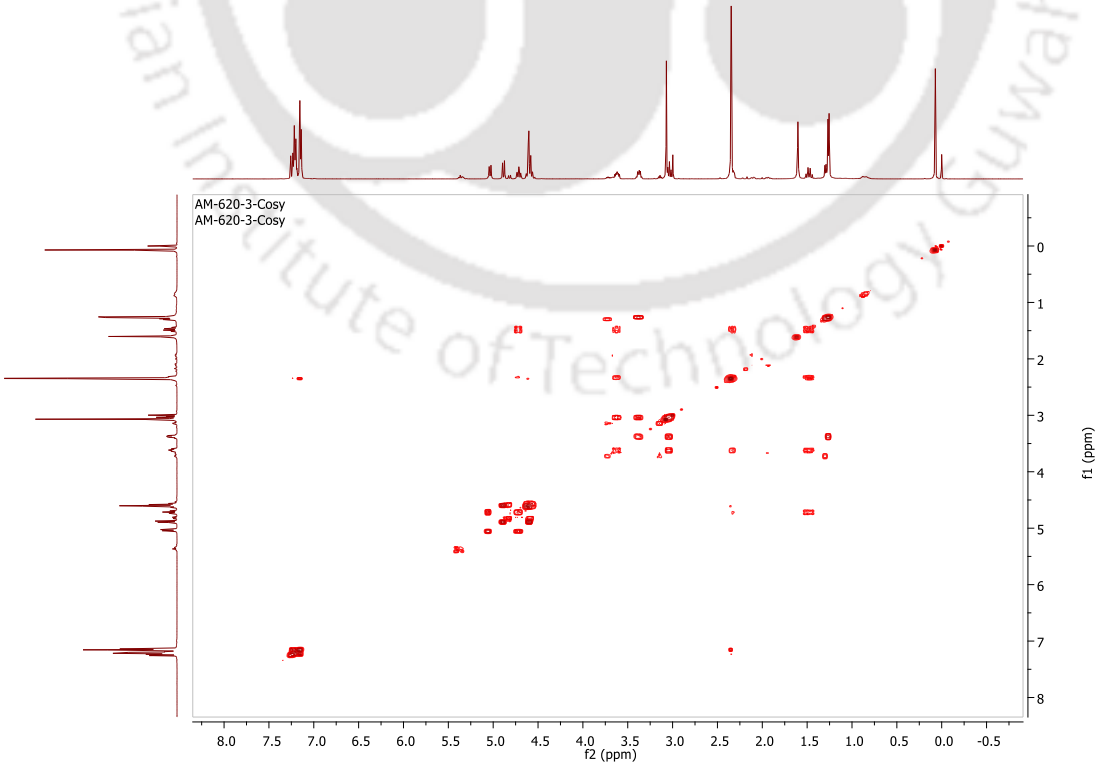
^{1}H NMR of 3,4-di-*O-para*-methylbenzyl-2,6-dideoxy-α,β-L-rhamnopyranosyl methanesulfonamide (23e, 500 MHz, $CDCl_3$):



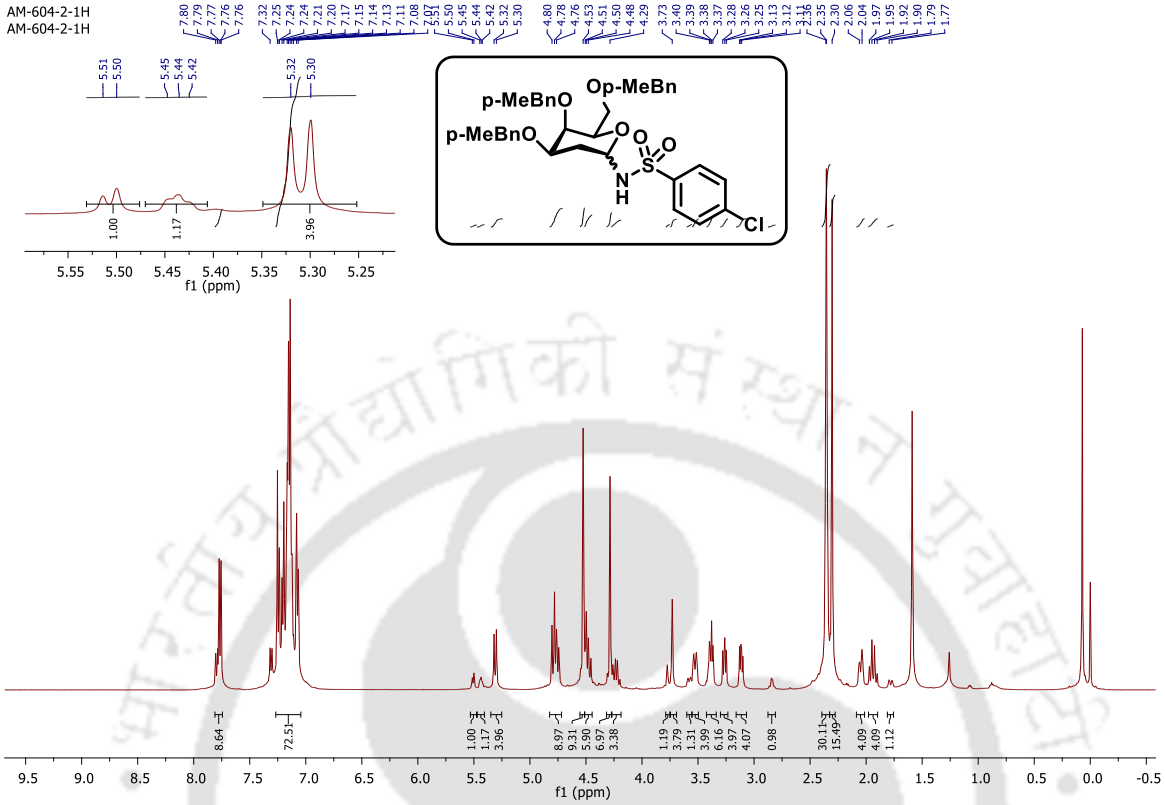
^{13}C NMR of 3,4-di-*O*-*para*-methylbenzyl-2,6-dideoxy-α,β-L-rhamnopyranosyl methanesulfonamide (23e, 400 MHz, $CDCl_3$):



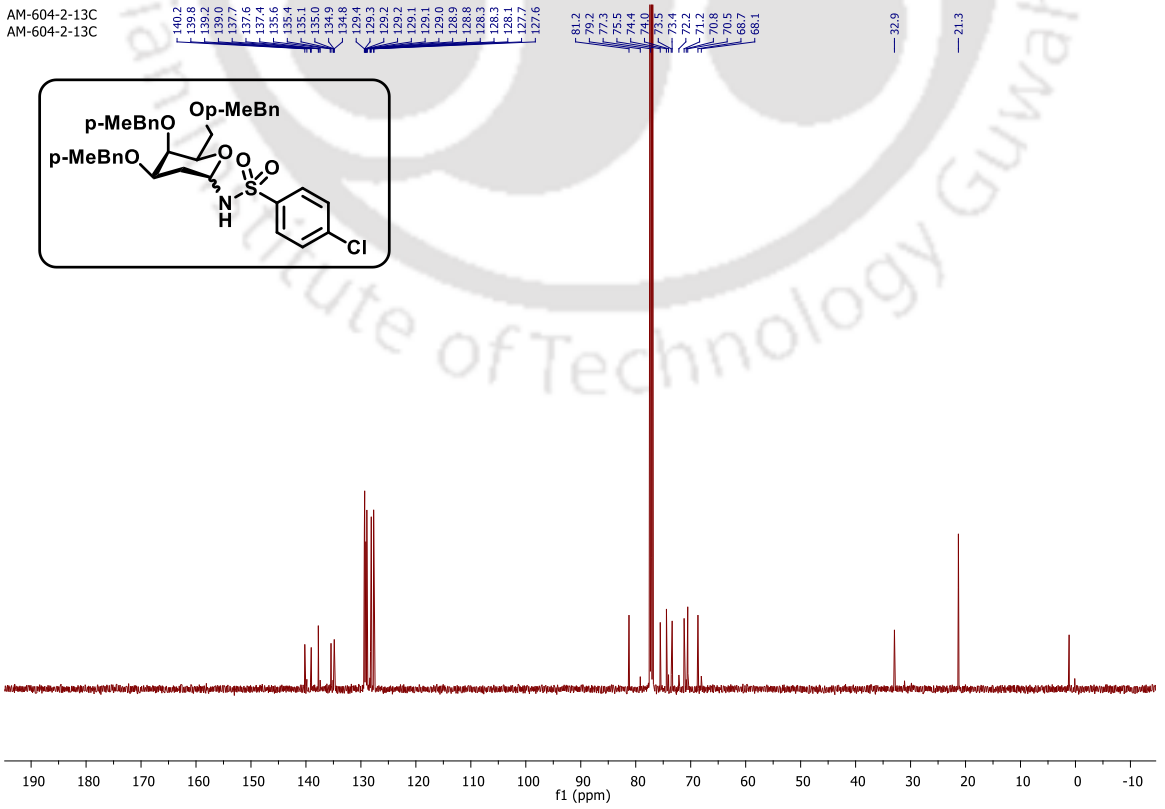
COSY NMR of 3,4-di-*O*-*para*-methylbenzyl-2,6-dideoxy-α,β-L-rhamnopyranosyl methanesulfonamide (23e, 500 MHz, $CDCl_3$):



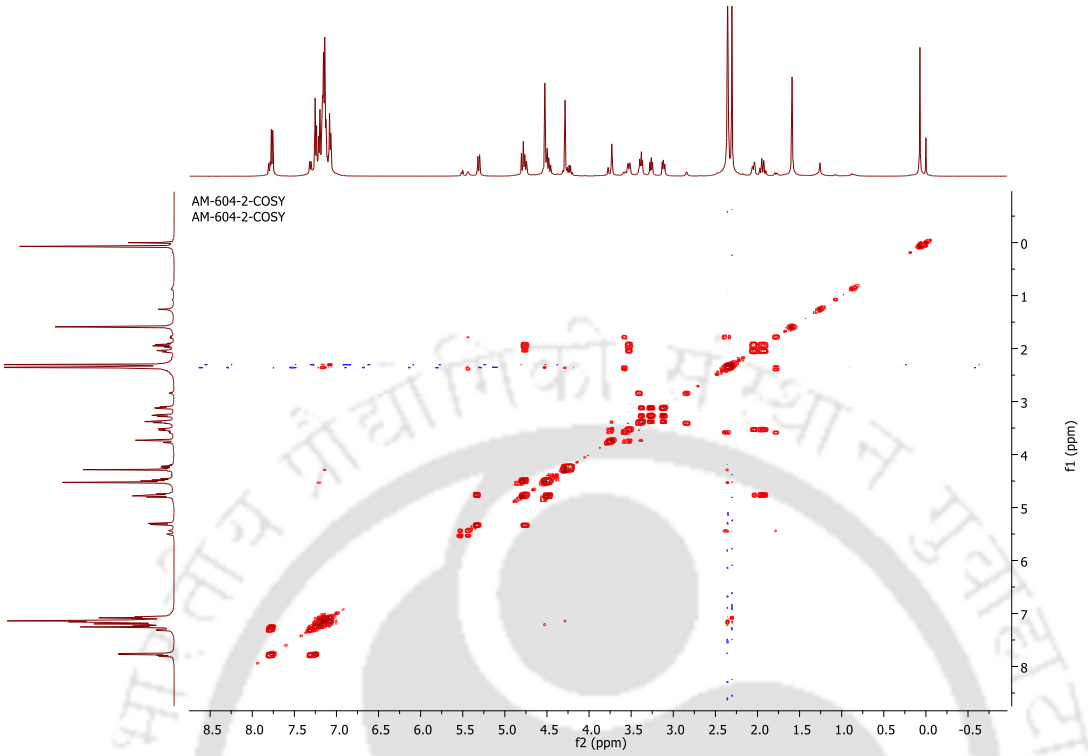
^{1}H NMR of 3,4,6-Tri-O-*para*-methylbenzyl-2-deoxy-α,β-D-galactopyranosyl p-chlorobenzene sulfonamide (23f, 500 MHz, $CDCl_3$):



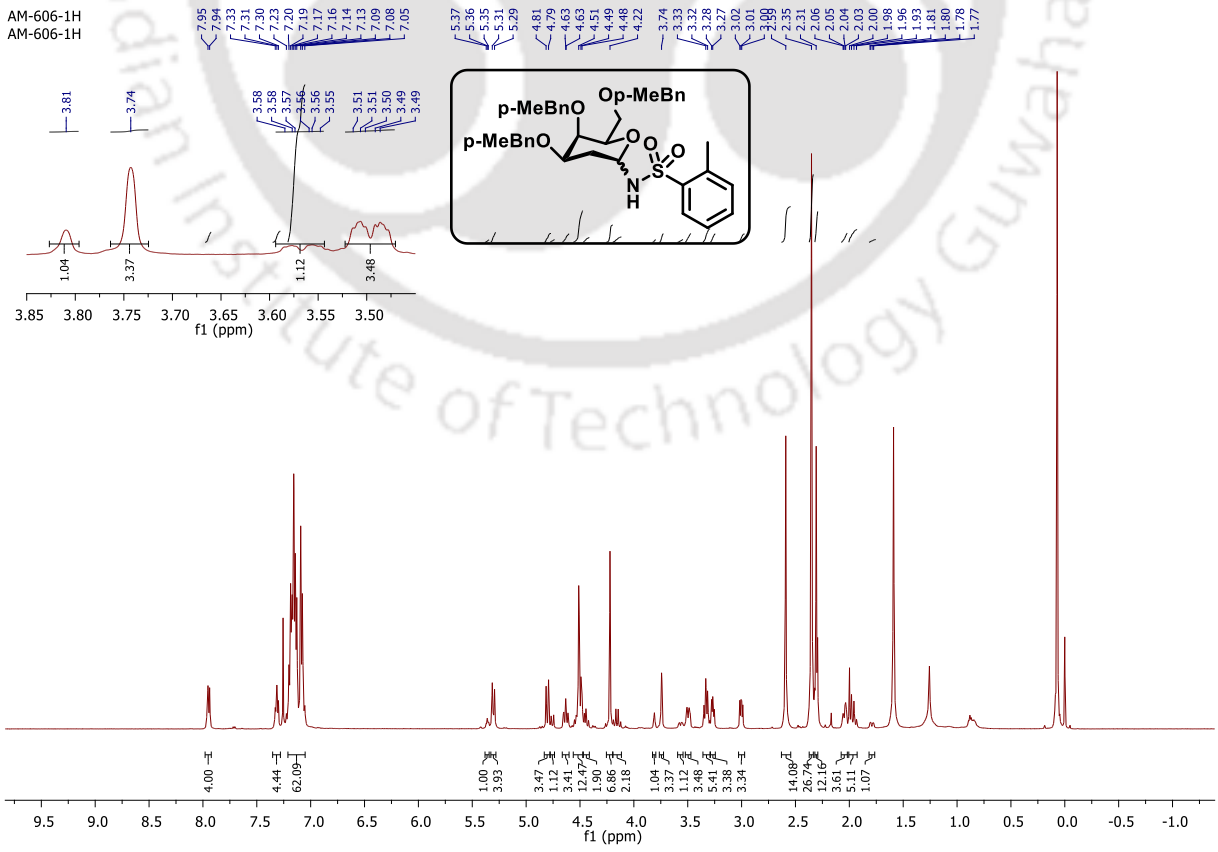
^{13}C NMR of 3,4,6-Tri-O-*para*-methylbenzyl-2-deoxy-α,β-D-galactopyranosyl p-chlorobenzene sulfonamide (23f, 500 MHz, $CDCl_3$):



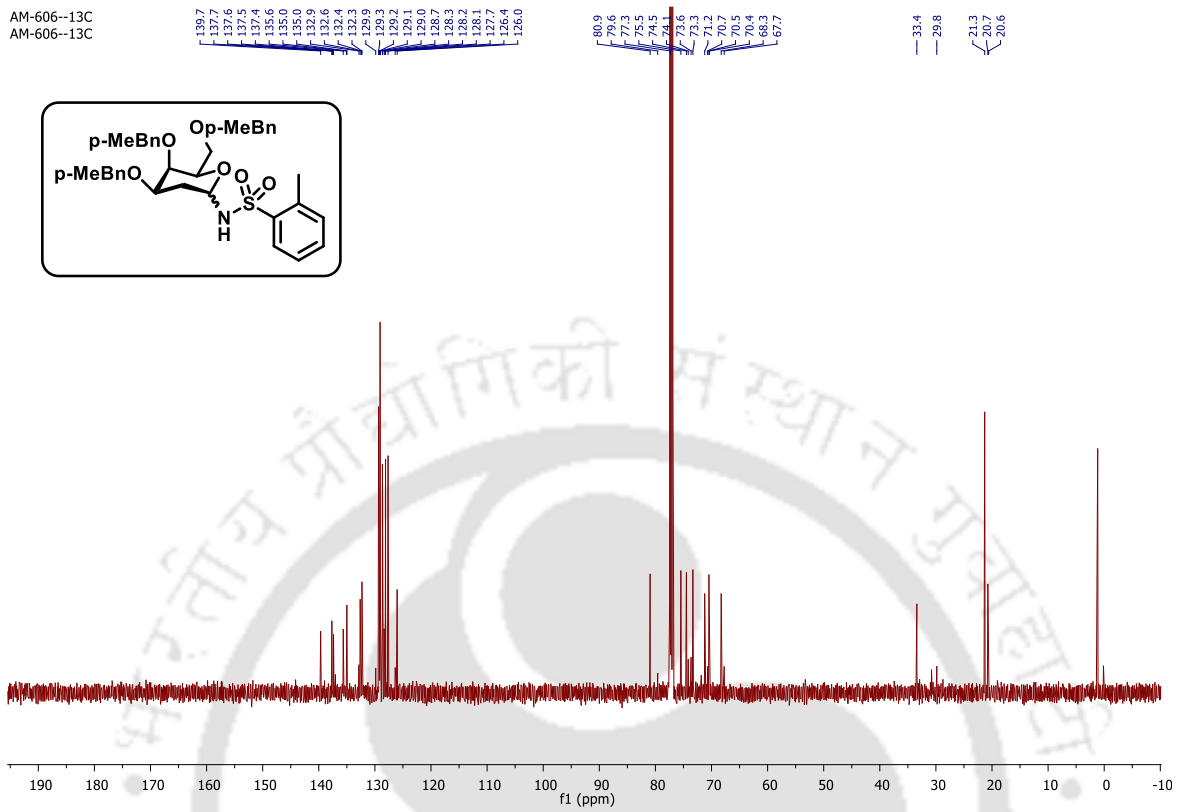
COSY NMR of 3,4,6-Tri-O-*para*-methylbenzyl-2-deoxy-α,β-D-galactopyranosyl p-chlorobenzene sulfonamide (23f, 500 MHz, $CDCl_3$):



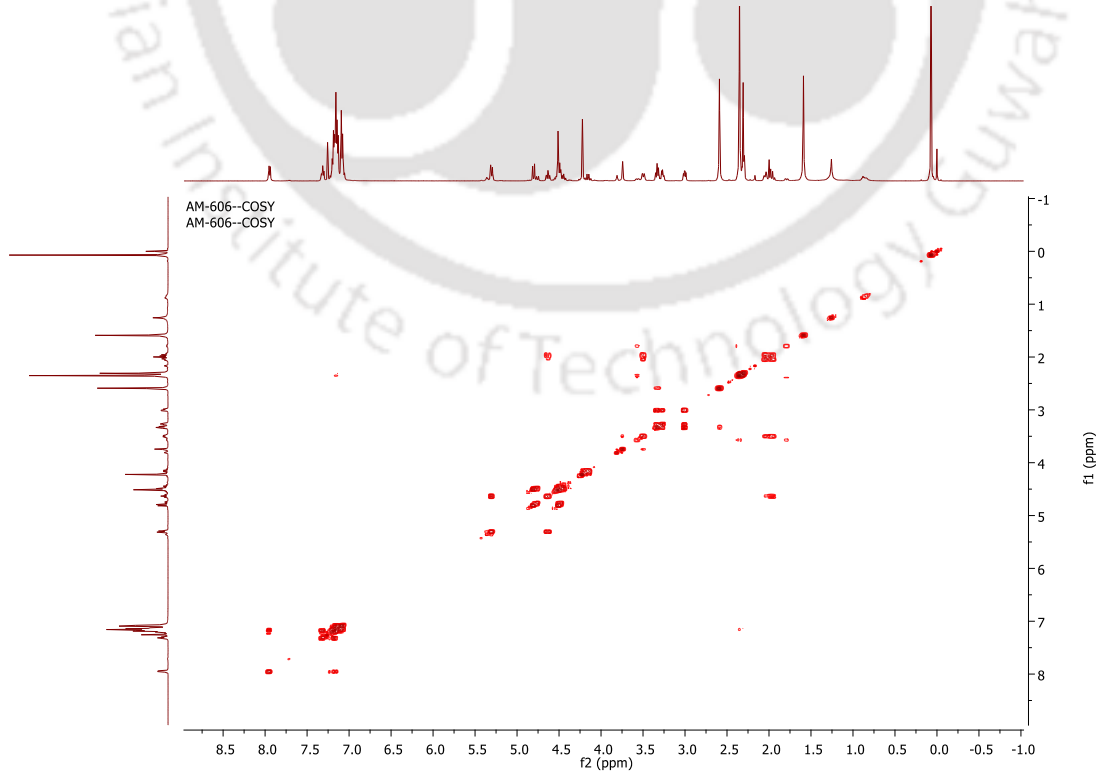
^{1}H NMR of 3,4,6-Tri-O-*para*-methylbenzyl-2-deoxy-α,β-D-galactopyranosyl o-toluenesulfonamide (23g, 500 MHz, $CDCl_3$):



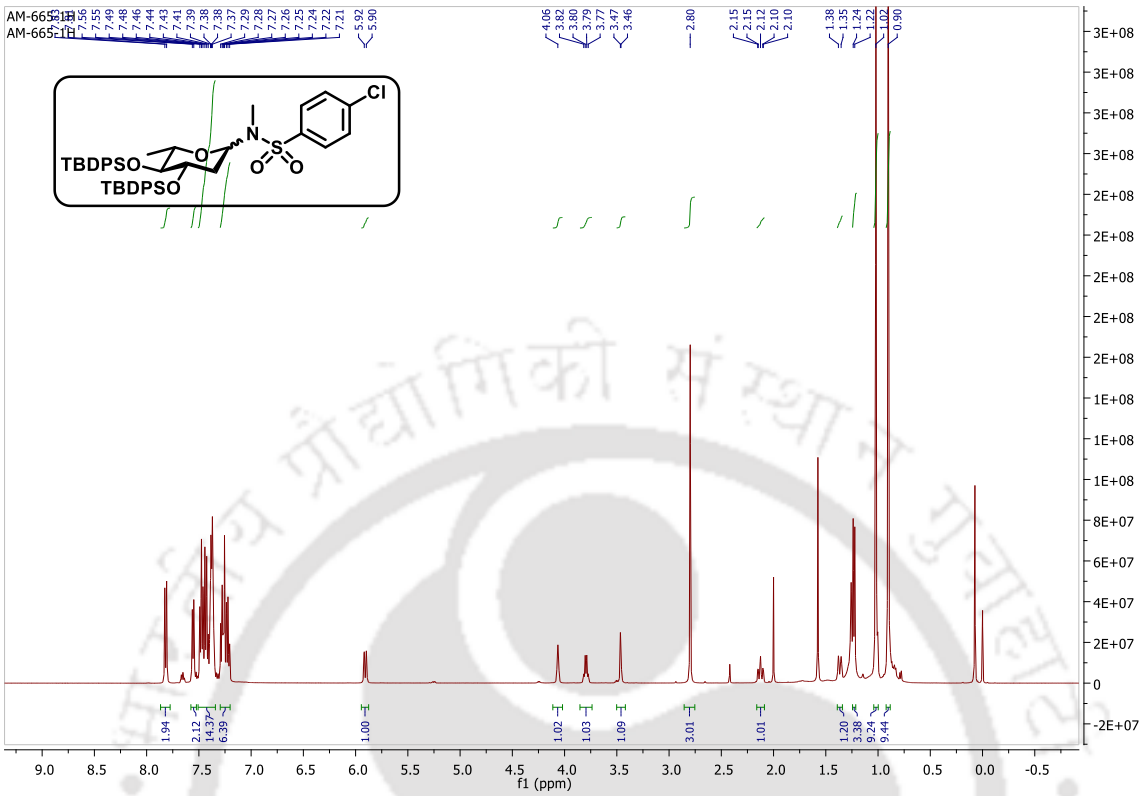
^{13}C NMR of 3,4,6-Tri-O-*para*-methylbenzyl-2-deoxy-α,β-D-galactopyranosyl o-toluenesulfonamide (23g, 500 MHz, $CDCl_3$):



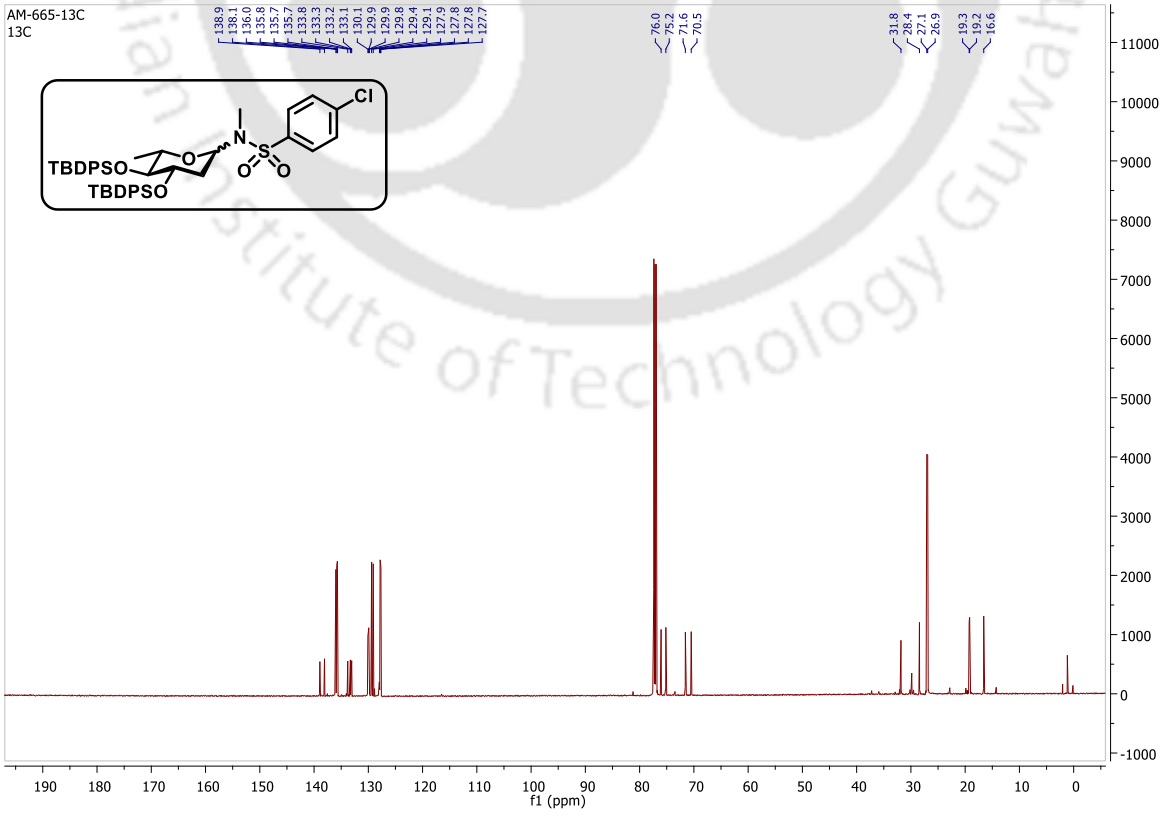
COSY NMR of 3,4,6-Tri-O-*para*-methylbenzyl-2-deoxy-α,β-D-galactopyranosyl o-toluenesulfonamide (23g, 500 MHz, $CDCl_3$):



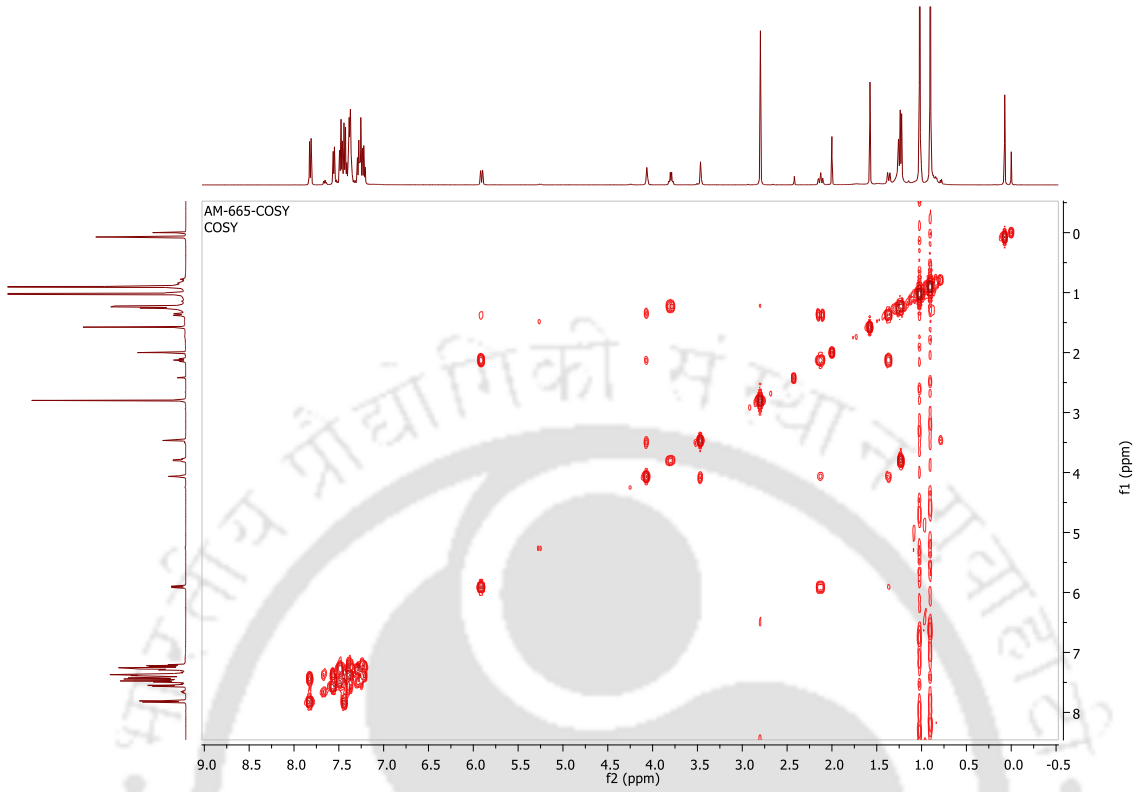
^{1}H NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α-L-rhamnopyranosyl N-methyl-p-chlorobenzene sulfonamide (26)



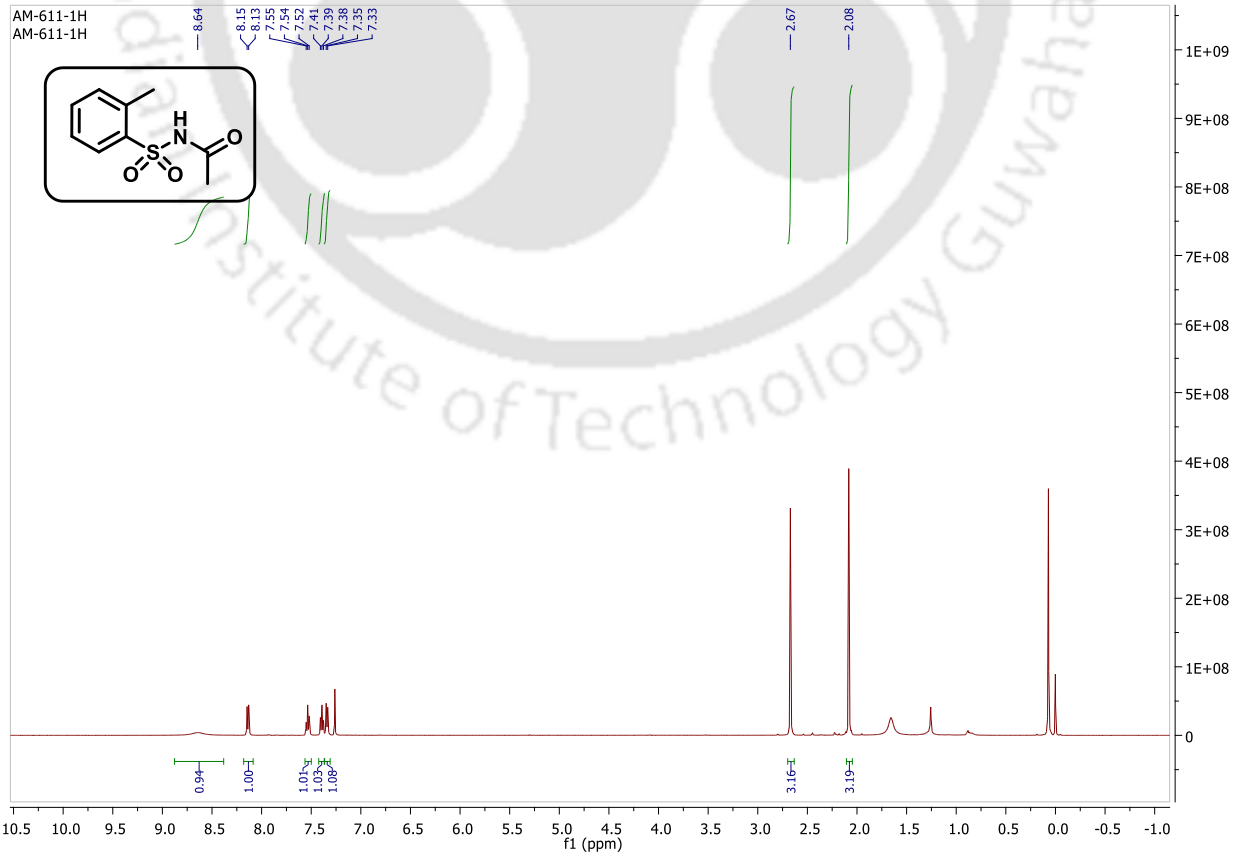
^{13}C NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α-L-rhamnopyranosyl N-methyl-p-chlorobenzene sulfonamide (26)



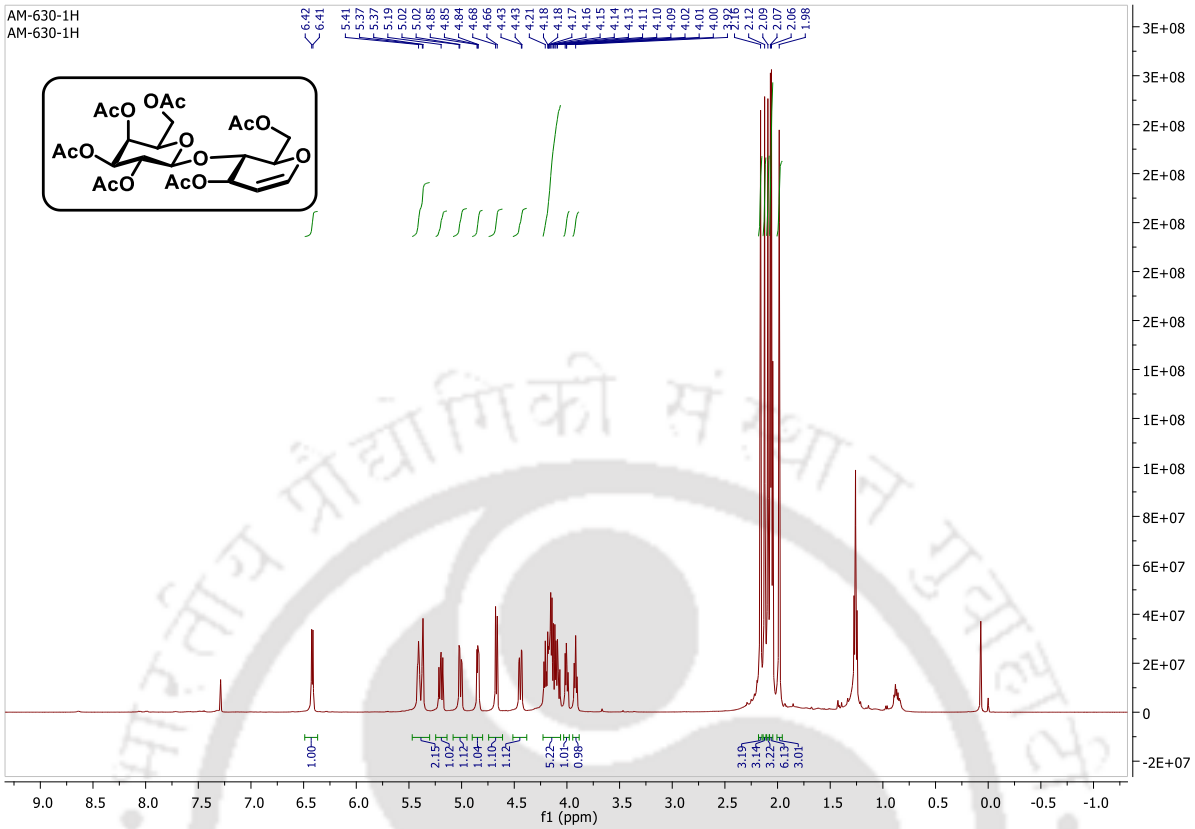
COSY NMR of 3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α-L-rhamnopyranosyl N-methyl-p-chlorobenzene sulfonamide (26)



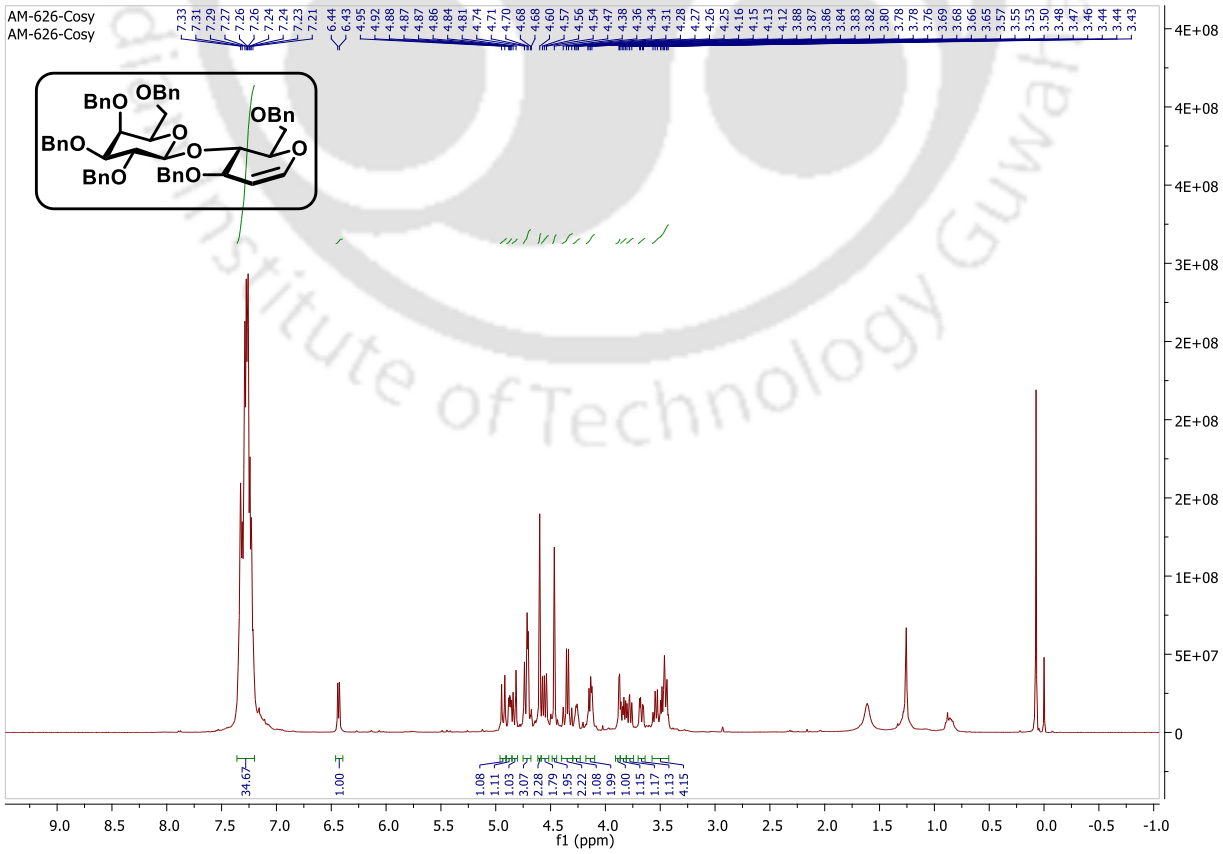
^{1}H NMR of N-(o-tolylsulfonyl)acetamide (21e')



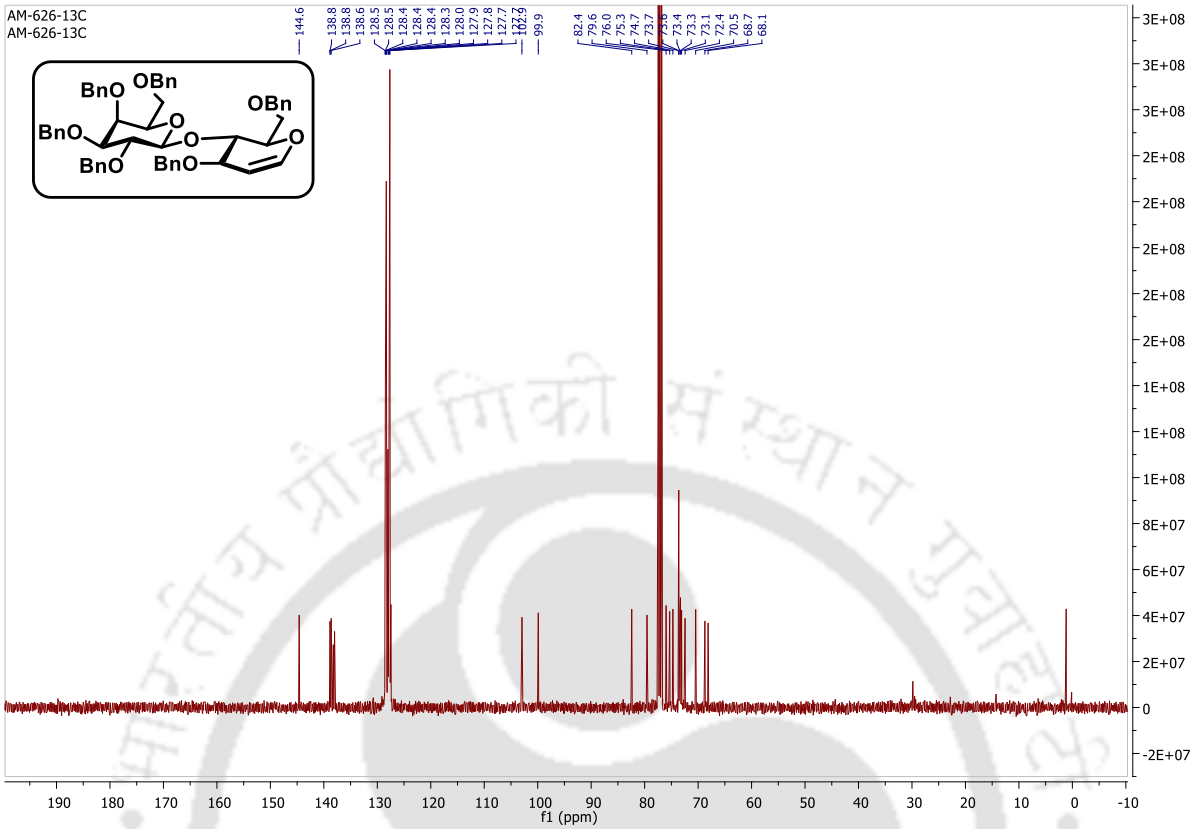
^{1}H NMR of 3,6,2',3',4',6'-Hexa-O-acetyl-D-lactal (20h):



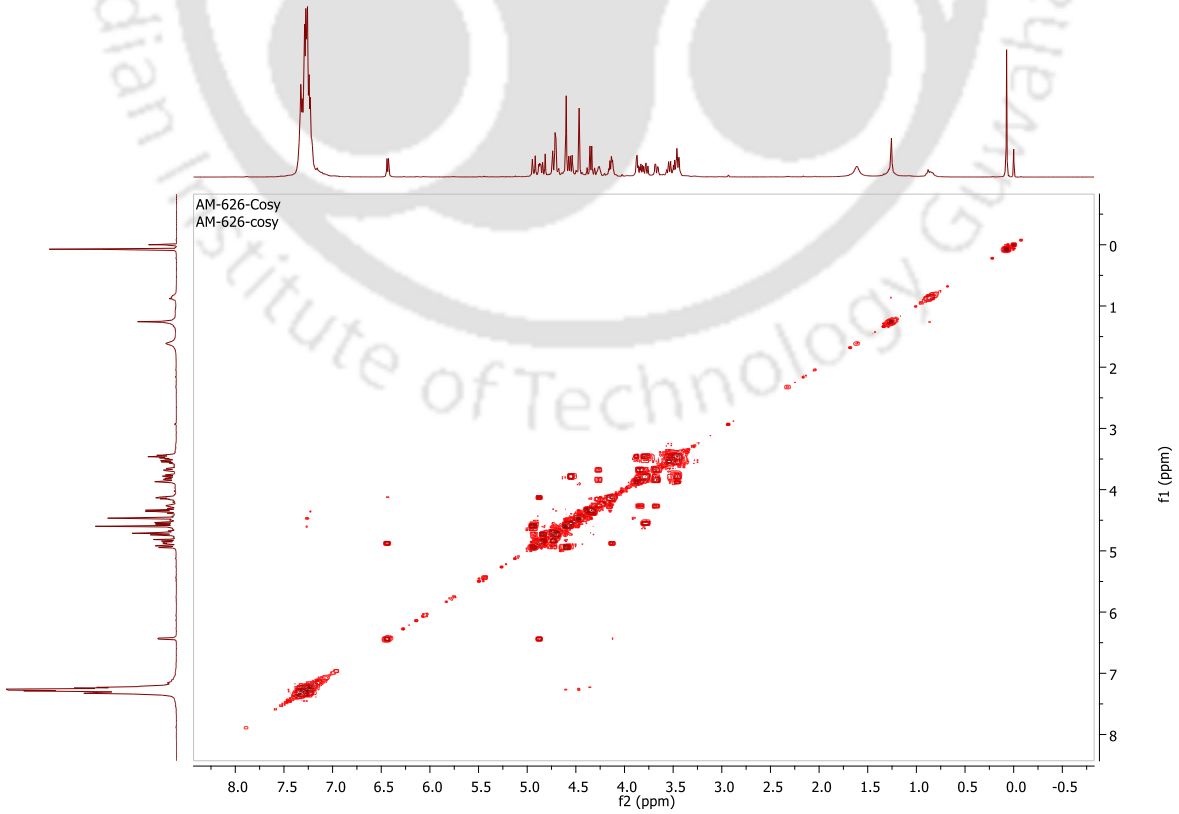
^{1}H NMR of 3,6,2',3',4',6'-Hexa-O-benzyl-D-lactal (20i):



^{13}C NMR of 3,6,2',3',4',6'-Hexa-O-benzyl-D-lactal (20i):



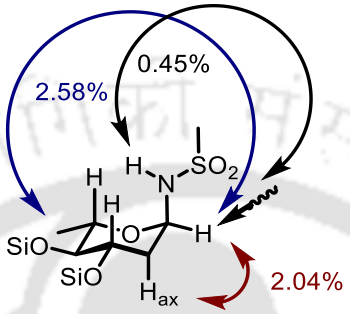
COSY NMR of 3,6,2',3',4',6'-Hexa-O-benzyl-D-lactal (20i):



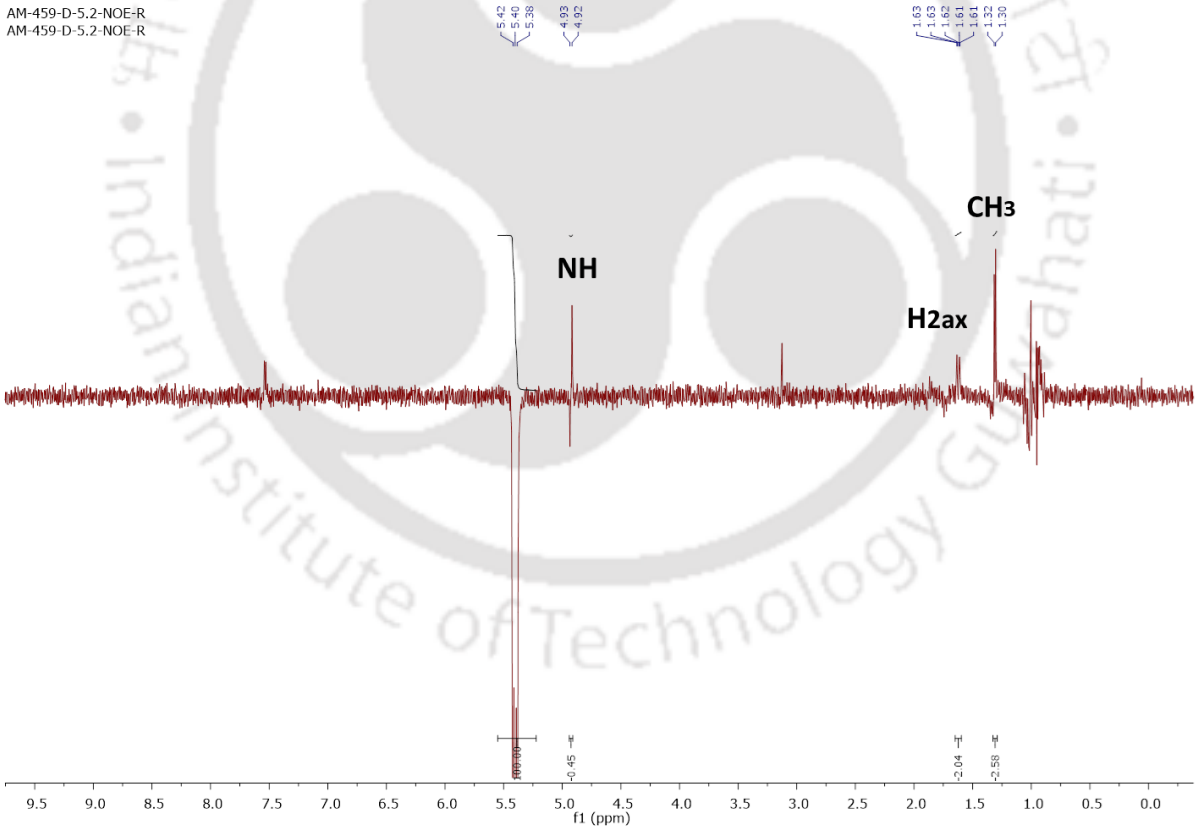
4.11 nOe Experiments

nOe Experiment of 24cα

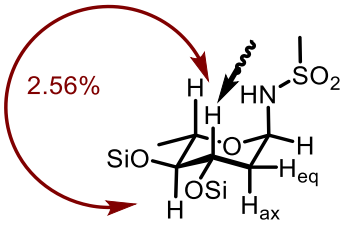
Irradiation of H_1: Upon irradiation of H_1 (at 5.40 ppm), the enhancement on the axial 2-deoxy proton (appearing at 1.62 ppm) is found 2.04%. In addition, NH proton (appearing at 4.93 ppm) and CH_3 protons (appearing at 1.31 ppm) also enhanced by 0.45% and 2.58% respectively. There was no enhancement observed for H_3 (appearing at 4.05 ppm) and H_5 (appearing at 3.90 ppm) proton. Hence, H_1 is trans to both H_3, H_5 and as well as H_{2eq}. Thus, the compound is in alpha configuration.



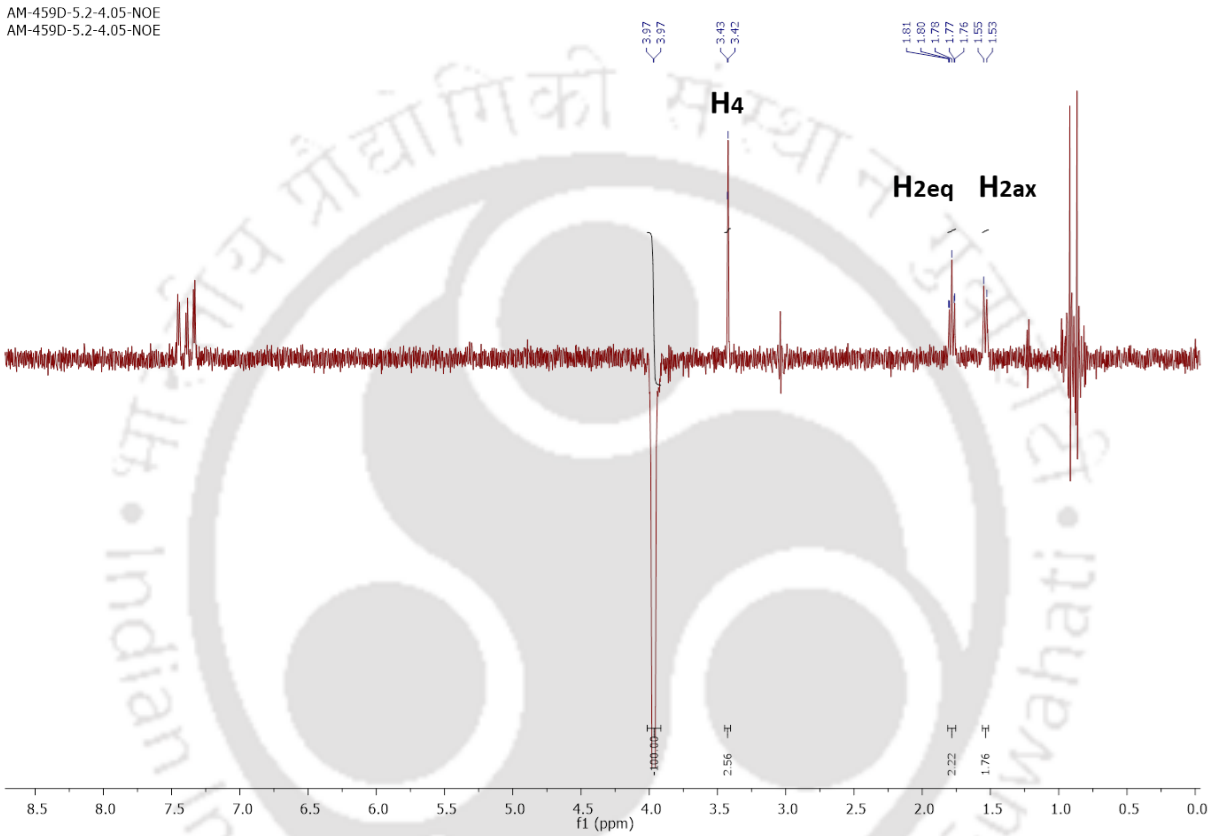
α configuration of **24c**



Irradiation of H_3: Upon irradiation of H_3 (at 4.05 ppm), the enhancement on the axial 2-deoxy proton (appearing at 1.53 ppm) is found 1.76% which is lesser than that of the equatorial 2-deoxy proton (appearing at 1.78 ppm) which is 2.22%. In addition, H_4 is also enhanced by 2.56% but there was no enhancement observed for H_1. Hence, H_3 is trans to H_1. From the above observation it can be concluded that the compound is alpha isomer.

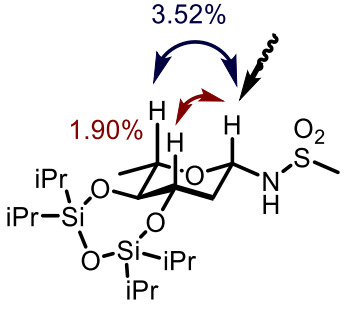


α configuration of **24c**

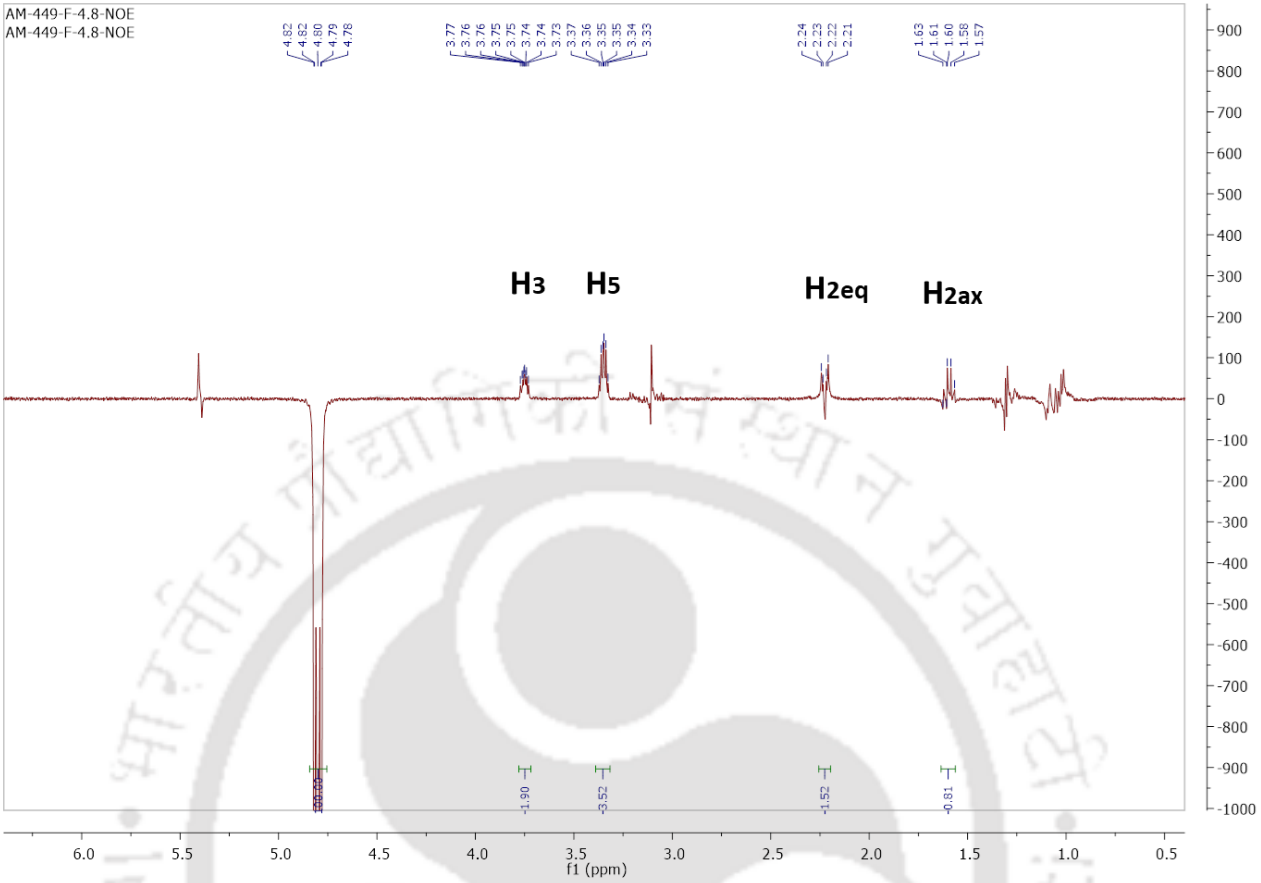


nOe Experiment of 23c

Irradiation of H_1: Upon irradiation of H_1 (at 4.80 ppm), the enhancement on the axial 2-deoxy proton (appearing at 1.60 ppm) is found 0.81% which is lesser than that of the equatorial 2-deoxy proton (appearing at 2.23 ppm) which is 1.52%. In addition, H_3 (appearing at 3.76 ppm) and H_5 (appearing at 3.35 ppm) proton also enhanced by 1.90% and 3.52% respectively.. Hence, H_1 is trans to both H_3, H_5 and as well as H_{2eq}. Thus, the compound is in beta configuration.

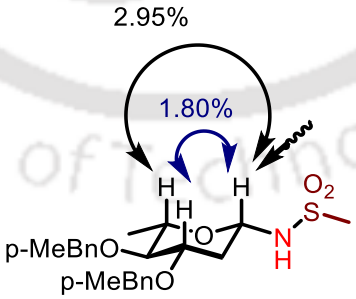


β configuration of **23c**

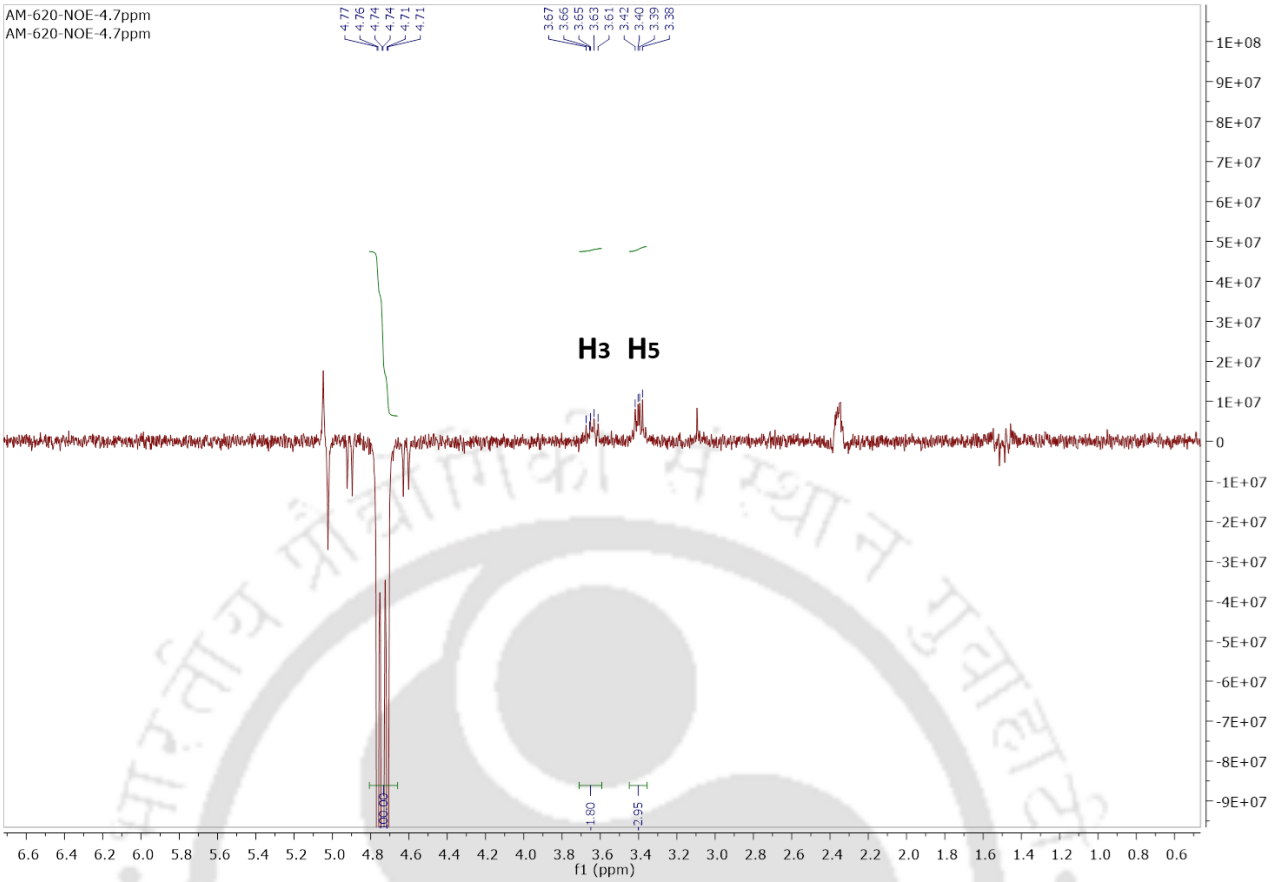


nOe Experiment of 23e

Irradiation of H_1: Upon irradiation of H_1 (at 4.71 ppm), H_3 (appearing at 3.66 ppm) and H_5 (appearing at 3.40 ppm) proton got enhanced by 1.80% and 2.95% respectively. Hence, H_1 is trans to both H_3 and H_5. Thus, the compound is in beta configuration.

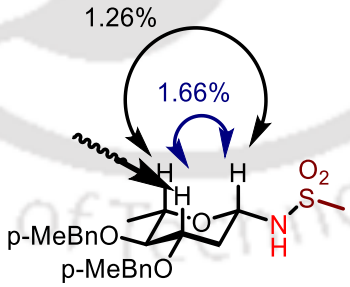


β configuration of **23e**

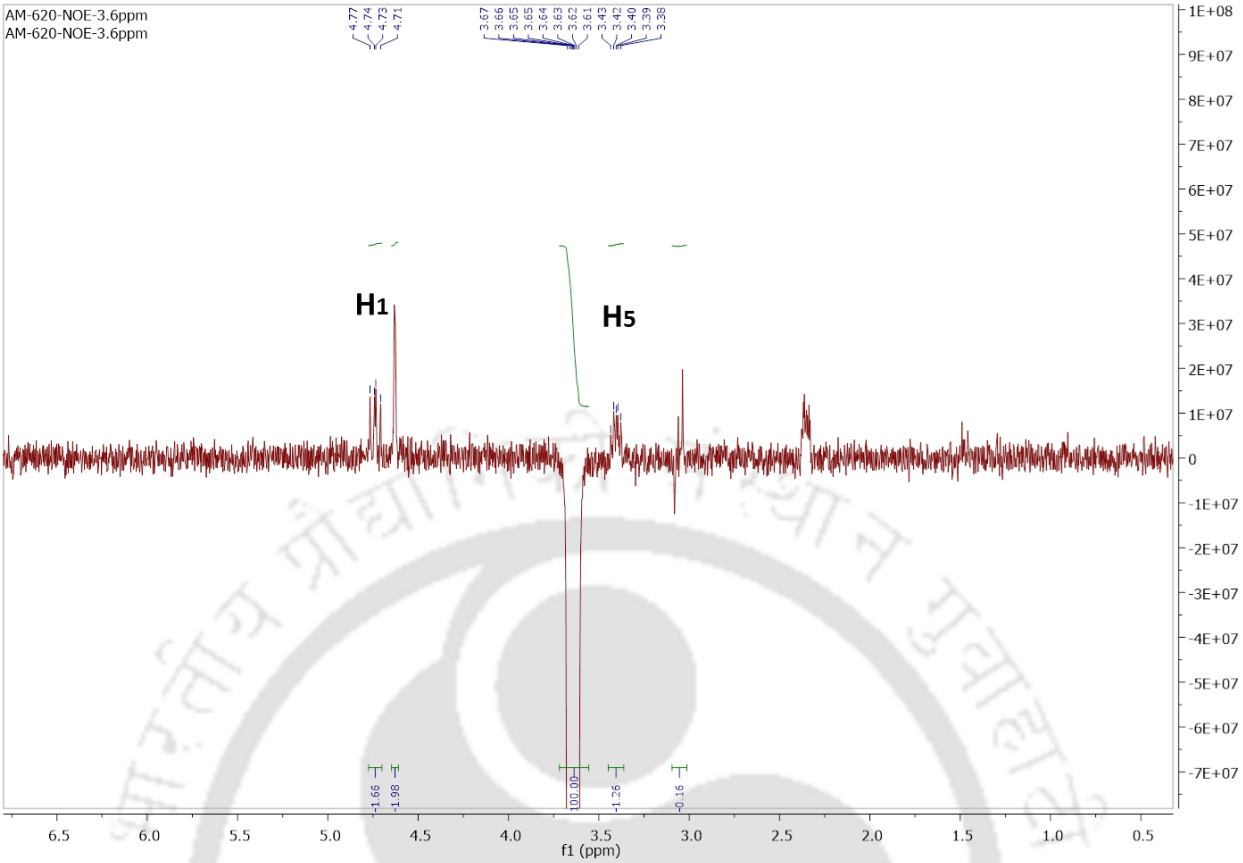


Irradiation of H_3:

Upon irradiation of **H_3** (at 3.63 ppm), **H_1** (appearing at 4.74 ppm) and **H_5** (appearing at 3.40 ppm) proton got enhanced by 1.66% and 1.26% respectively. Hence, **H_3** is trans to both **H_1** and **H_5**. Thus, the compound is in beta configuration.



β configuration of **23e**



4.12 Assignment of Stereochemistry

The α and β stereochemistry of the separated products has been established using nOe technique for some representative examples as shown. Further, analyzing and matching of the chemical shifts and couplings constants analysis of the rest of the compounds with the representative compounds has been undertaken. The stereochemistry has been carefully assigned for all the compounds. In addition, some of the known compounds stereochemistry has also been matched with the literature reports as well. Some of the analysis is provided below.

For compound **24c** nOe experiment was done and compound **24a-e** have has similar ^{1}H-NMR pattern as shown below.

24a- 5.36 (td, *J* = 10.4, 1.9 Hz, H-1), 1.81 (ddd, *J* = 13.2, 10.8, 2.6 Hz, H-2), 1.53 (d, *J* = 13.1 Hz, H-2').

24b- 5.36 (td, *J* = 10.3, 1.9 Hz, H-1), 1.85 – 1.79 (m, H-2), 1.55 (d, *J* = 13.3 Hz, H-2').

24c- 5.38 (td, *J* = 10.7, 1.6 Hz, H-1), 1.87 – 1.83 (m, H-2), 1.60 (d, *J* = 13.1 Hz, H-2').

24d- 5.36 (t, *J* = 10.2 Hz, H-1), 1.84 – 1.79 (m, H-2), 1.56 (d, *J* = 13.3 Hz, H-2').

24e- 5.19 (t, *J* = 9.9 Hz, H-1), 1.87 – 1.82 (m, H-2), 1.53 (d, *J* = 13.2 Hz, H-2').

For compound **23c** nOe experiment was done and compound **23a-c** have has similar ^{1}H-NMR pattern as shown below.

23a- 4.82 (td, *J* = 10.4, 2.0 Hz, H-1), 2.15 (ddd, *J* = 12.6, 4.5, 2.1 Hz, H-2), 1.46 (dd, *J* = 23.4, 10.8 Hz, H-2').

23c- 4.79 (td, *J* = 11.1, 1.9 Hz, H-1), 2.22 (ddd, *J* = 12.8, 5.2, 1.9 Hz, H-2), 1.58 (dd, *J* = 23.9, 11.3 Hz, H-2').

For compound **23e** nOe experiment was done and compound **23d**, **23e** have has similar ^{1}H-NMR pattern as shown below.

23d- 4.76 (dd, *J* = 15.2, 5.6 Hz, H-1), 2.36 – 2.33 (m, H-2), 1.47 (dd, *J* = 23.3, 11.4 Hz, H-2').

23e- 4.72 (dd, *J* = 15.0, 5.9 Hz, H-1), 2.32 – 2.31 (m, H-2), 1.48 (dd, *J* = 23.4, 11.3 Hz, H-2').

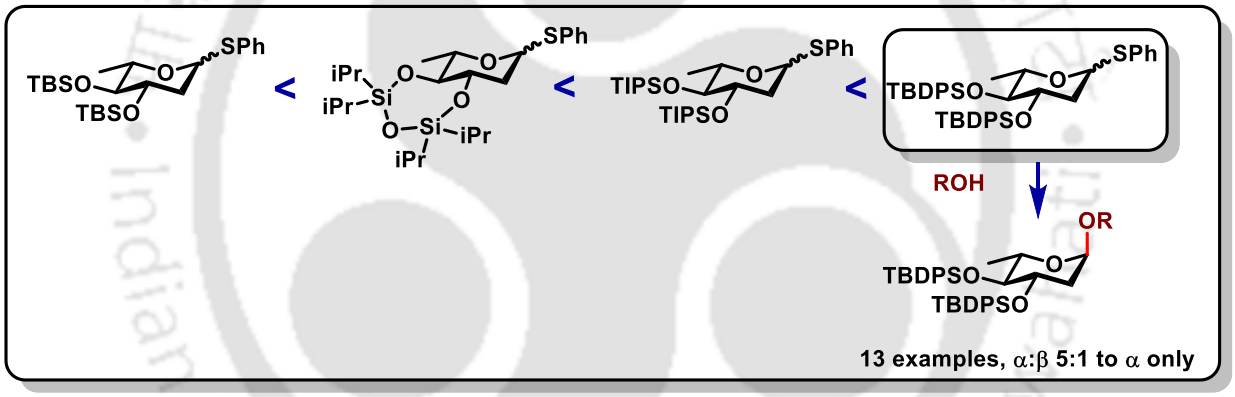
3,4,6-Tri-O-benzyl-2-deoxy-β−D-galactopyranosyl p-toluenesulfonamide is known in literature (*Org. Lett*., **2003**, *5*, 4509-11) and **23f**, **23g** gave similar ^{1}H NMR and based on that analysis was done.

23f- 4.77 (dd, *J* = 19.4, 10.4 Hz, H-1 merged), 2.05 (d, *J* = 11.8 Hz, H-2), 1.94 (dd, *J* = 23.2, 11.6 Hz, H-2').

23g- 4.63 (td, *J* = 10.5, 2.0 Hz, H-1), 2.05 (dd, *J* = 8.9, 3.1 Hz, H-2), 1.97 (dd, *J* = 21.9, 10.4 Hz, H-2' merged).

Chapter V

Influence of Various Silyl Protecting Groups on the Stereo-Selectivity of Rhamnosylation: Stereoselective Synthesis of OTBDPS Protected α-Rhamnosides



Manuscript Under Revision.

Influence of Various Silyl Protecting Groups on the Stereo-Selectivity of Rhamnosylation: Stereoselective Synthesis of OTBDPS Protected α-Rhamnosides

5.1 Introduction:

5.1.1 Importance of 2-Deoxy and 2,6-Dideoxy Glycosides:

As discussed previously in **chapter II**, deoxy sugars are present in several biologically important compounds. In addition, 2-deoxy and 2,6-dideoxy hexoses are an essential class of glycosides due to their presence in a wide range of natural products extending from antibiotics to anticancer agents and also in biologically relevant glycoconjugates.[1,2,7] These glycosides are more challenging to synthesize stereoselectively than their fully oxygenated analogue and their synthesis has been a matter of interest over the past several decades. The synthesis of carbohydrate chains containing deoxyglycosides remains a challenge due to their instability towards hydrolysis. Also, the absence of the C-2 hydroxyl group to control the anomeric selectivity makes the stereoselective construction of 2-deoxyglycosidic linkage even more difficult. Generally, it results in a mixture of anomers during glycosylation reaction.[3,4,5] There are limited studies done on glycosylation of silyl protected 2,6-dideoxysugars.[6] Owing to their biological importance, research efforts in achieving their stereoselective synthesis have received great attention in recent years.[7] The fact that protecting groups play a significant role in carbohydrate reactivity[8] makes it more interesting for us to study the effect of underexplored acid-labile silyl protecting groups on glycosylation with L-rhamnose based sugar donors. Clearly, a comparative study on stereoselective glycosylation of various silyl protected 2,6-dideoxy glycosides is highly desirable.

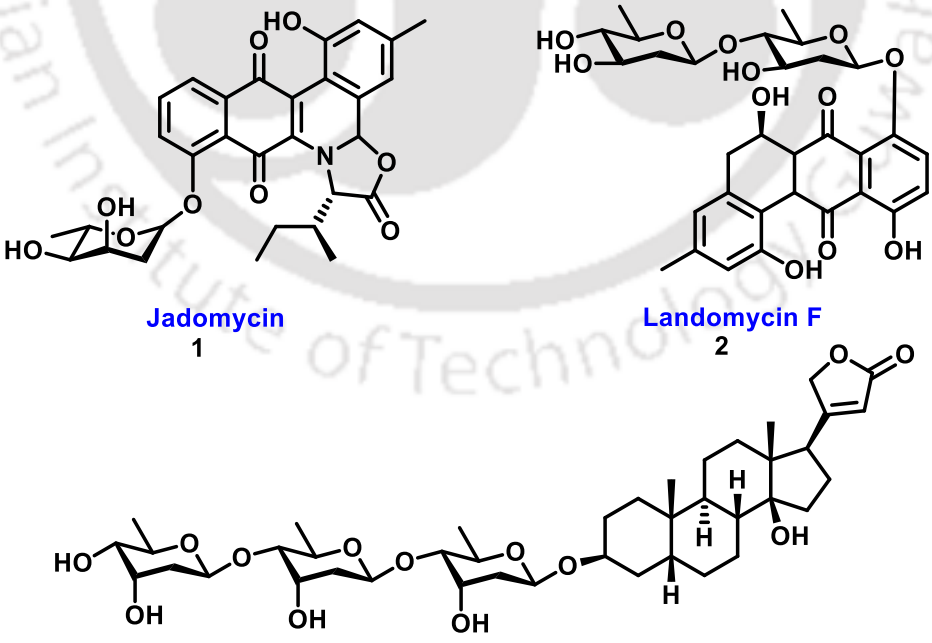


***Fig 1**: Deoxy Sugar Containing Natural Products*

Many of the secondary metabolites possess 2-deoxy oligosaccharides. After further deoxygenation on 2-deoxy sugars (mostly at C-3 and/or C-6 position), we can get its di/trideoxy analogues. These dideoxy or trideoxy sugar units are found in many natural products like angucycline jadomycin, digitoxin, landomycin (angucycline) and mithramycin (anthracycline) etc (Fig 1).

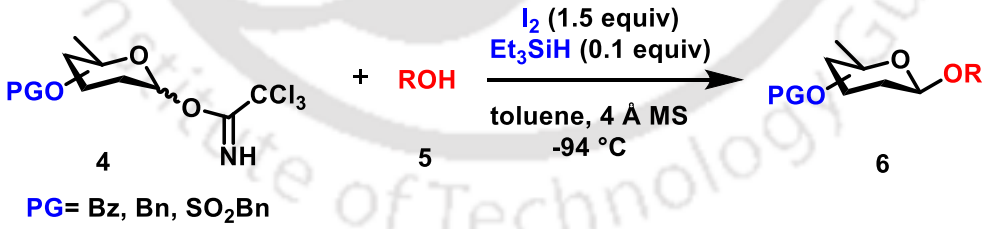
Landomycins, natural products first isolated by Rohr and co-workers are one of well-studied 2-deoxysugar containing class of compounds. Functionalized Landomycins at the C-8 position with a deoxy-sugar chain (with 2 to 6 residue units), possess potent anticancer activity. It has been observed that the activity of these molecules is highly dependent on the length of the deoxy-sugar oligosaccharide chain attached to the aglycone.[9]

5.2 Previous Reports

5.2.1 Literature Reports on Synthesis of 2,6-Dideoxy Glycosides:

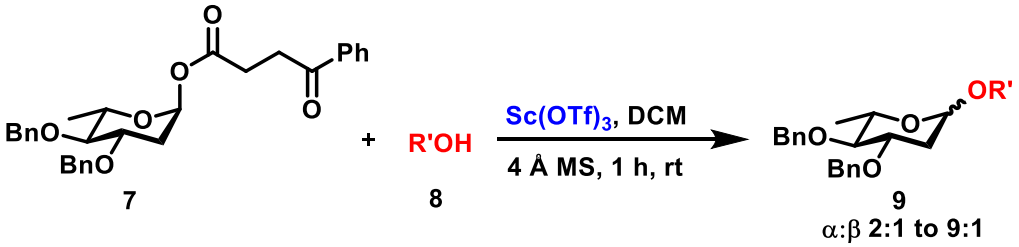
Several research groups have developed new methods for controlling stereo selectivity in glycosylation reactions using 2-deoxy and 2,6-dideoxy sugar donors. Some of the organocatalytic methods to synthesize deoxy glycosides in a stereoselective fashion have been previously discussed in **chapter II**.[10-15]

Glycosylation reactions involving glucals as glycosyl donors shows less stereoselectivity preference than the same with galactal donors and often lead to Ferrier rearrangement side-products.[16] The reason can be the lack of the C-4 OH as the axial substituent, which leads to the attack of the nucleophile from both faces of the ring.[16b] Similarly, reactions with glucal substrates gave products with better stereocontrol than rhamnals, which can be attributed to the conformational preference of the C6-side chain present in glucal donors,[17] which is lacking in the rhamnal donors. Hence, getting a stereoselective glycosylated product derived from rhamnal donors is more challenging. Some of the literature methods developed to synthesize 2,6-dideoxy glycosides or rhamnose based oligosaccharides are discussed below.



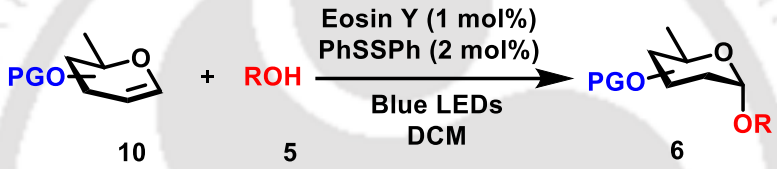
Scheme 1: β-*Selective Glycosylation on Deoxy Hemiacetals*

In 2007, Takahashi and co-workers reported the β-stereoselective synthesis of 2,6-dideoxy and 2,3,6-tri-deoxy glycosides starting from glycosyl trichloro-acetimidates. As discussed previously in chapter I, that β-isomers are relatively difficult to obtain and the β-anomer corresponding to deoxy sugar is even more challenging to synthesize due to absence of any stereo directing group at C-2 position. In this method, they have demonstrated that synthesis of such rare and biologically important compounds can be easily achieved in presence of readily available molecular iodine and catalytic amount of triethylsilane at -94 °C (scheme 1).[18]



Scheme 2: *Lewis-acid Mediated Stereoselective Synthesis of Deoxy-O-glycosides*

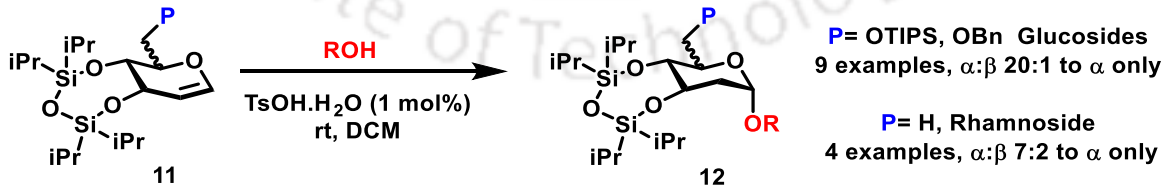
Later on, in 2018, Chandrasekaran and co-workers demonstrated a Lewis acid mediated stereoselective synthesis of 2-deoxy-*O*-glycosides using 2-deoxyglycosyl 3-benzoylpropionates as glycosyl donors (scheme 2).[19] These donors that can be easily obtained from glycals are stable at room temperature and relatively easy to handle. These donors react with all types of acceptors even with the secondary and tertiary alcohols to obtain stereoselective 2-deoxy-glycosides. Furthermore, they have demonstrated the synthesis of biologically important oligosaccharides and trisaccharide.



Scheme 3: *Photoacid Catalysed Activation of Glycals*

In the same year, the photoacid catalyzed synthesis of 2-deoxyglycosides was reported by Wang and coworkers (scheme 3).[20] Along with commercially available photocatalyst eosin Y, several phenol-conjugated acridinium-based organic photoacids were tested for the glycosylation reaction. They have demonstrated that these photoacid catalysts and light could activate glycals towards α-selective glycosylation to afford 2-deoxyglycosides in good yields and with an extensive substrate scope.

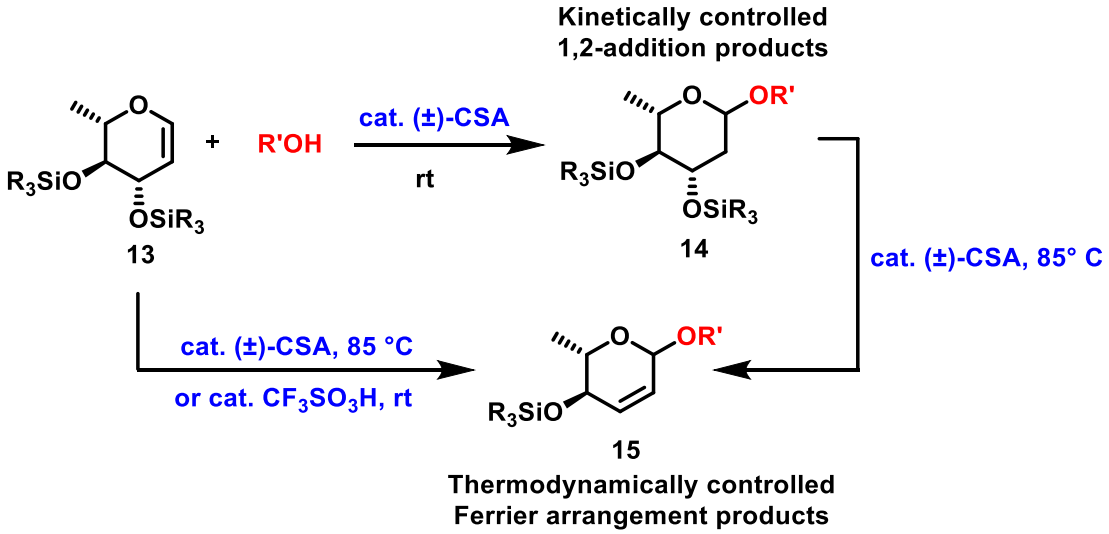
5.2.2 Literature Reports on Stereoselective Synthesis of Silyl Protected 2,6-Dideoxy Glycosides:



Scheme 4: *Tosylic Acid Catalysed Activation of Disiloxane Protected Glycals*

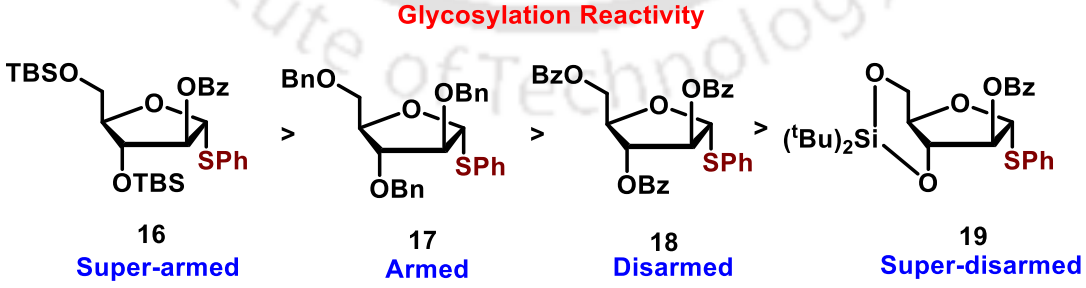
McGarrigle, Galan and coworkers have developed a method for glycosylation of glucals and rhamnals having *trans*-fused cyclic 3,4-*O*-disiloxane protecting group using 1 mol% of TsOH·H_2O as catalyst at room temperature (scheme 4).[21] The high α-selectivity was attributed to the conformational locking of the intermediate oxacarbenium cation. Glucal shows a better selectivity preference towards α-isomer than rhamnal because the C6 side-chain conformation also prefers the selectivity. Although, the reaction proceeds via

oxocarbenium ion intermediate pathway, high α-selectivity was observed in this case due to the conformational restriction imposed by the *trans*-fused 3,4-disiloxane cyclic protecting group. These reactions demonstrate the effect of protecting group on the stereoselectivivities of the glycosylation reactions.



Scheme 5: *Chemoselective Glycosylation of Silyl-protected Rhamnals*

Recently, in 2019, a temperature-controlled chemoselective glycosylation of silyl-protected rhamnals was showcased by Zhang, Chai and co-workers. They have reported a tunable glycosylation to synthesize both 2-deoxyl rhamnosides and 2,3-unsaturated rhamnosides using (±)-CSA as the catalyst (Scheme 5).[22] Kinetially controlled 2-deoxy rhamnosides are obtained at room temperature via 1,2-addition pathway, whereas, thermodynamically controlled 2,3-unsaturated rhamnosides or Ferrier glycosides were obtained at high temperatures using using (±)-CSA or by utilizing a much stronger acid like trifluoromethanesulfonic acid as the catalyst. In this work they have also showcased the effect of protecting group on the chemoselectivity outcome of the glycosylation reaction. Rhamnals with bulky OTBPDS protection yielded the corresponding products under kinetic or thermodynamic conditions in good to excellent yields with high α-stereoselectivity.



Scheme 6: *Effect of Silyl Protecting Groups on the Glycosylation Reactivity*

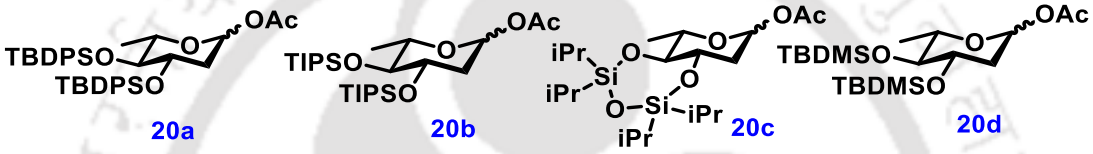
In 2013, Yang's group studied the influence of silyl protecting groups on the glycosylation reactivity of arabinofuranosyl phenyl thioglycoside donors (Scheme 6).[23] They have done their study with C-2-benzoyl substituted arabinosyl donors to focus only on glycosylation reactivity and not on the anomeric stereoselectivity. But a systematical analysis

of the effect of silyl protecting groups on the glycosylation stereoselectivity of rhamnosyl donors has yet to occur.

5.3 Results and Discussion:

As part of our ongoing interest to study the effect of silylethers on the 3,4-positions of the L-rhamnose ring, several well-known literature methods of glycosylation have been employed on various silyl protected L-rhamnose derived glycosyl donors and the stereoselectivity of their related products has been observed. As silyl-ethers are acid labile, these transformations should proceed under relatively mild and neutral conditions, avoiding using Lewis acids or other harsh reaction conditions. Four different silyl protecting groups were chosen to perform this study on L-rhamnose sugar. The stereoselectivity of *O*-, *C*- and *S*-glycoside was monitored in this study.

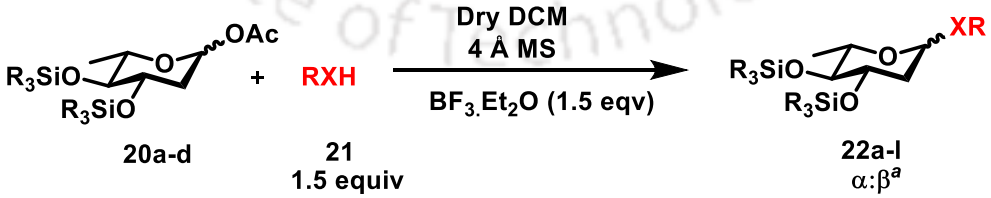
Donors Used in this Method:



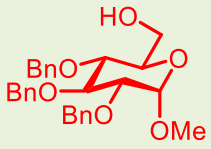
Treatment of L-rhamnal with respective silyl chloride and imidazole gave corresponding silyl glycal, which was converted to hemiacetal by employing TTBPy.HCl catalyst system[24] followed by synthesis of glycosyl acetate **20a-d** using py/ Ac_2O method. Initial studies were done with these anomeric acetates by reacting them with *O*-, *S*- and *C*-glycosyl acceptors using the typical method to convert anomeric acetate donors into their corresponding glycosides by Lewis acid $BF_3.Et_2O$.[25] It was found that 1.5 equivalent of $BF_3.Et_2O$ in dichloromethane at 0 °C in presence of 4 Å MS was the optimum condition to yield the corresponding thioglycoside **22a-d** within 15 mins (Table 1, entry 1-4).

5.3.1 Rhamnosylation of Anomeric Acetate Donors with *O*-, *S*- and *C*- Acceptor:

Table 1. Investigation of Stereoselectivity in Rhamnosylation of Different Donors 20a–d with *O*-, *S*- and *C*- Acceptor.



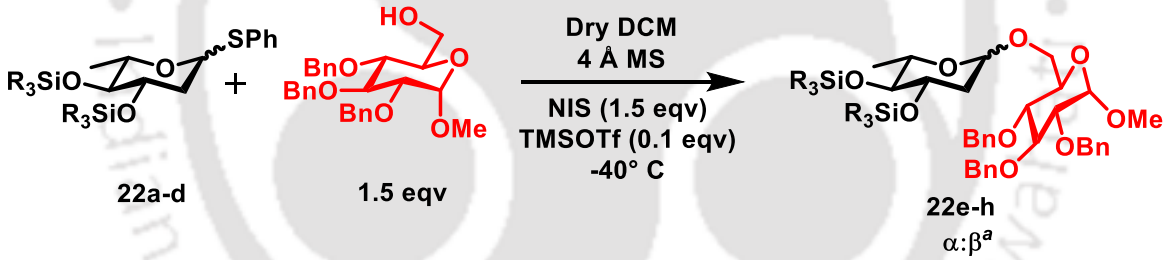
Sl No.	Acceptor	Donor	Product (α: β)
1.	**PhSH, 21a**	**20a**	**22a**, α: β= 13: 1
2.		**20b**	**22b**, α: β= 9: 1
3.		**20c**	**22c**, α: β= 2.2: 1
4.		**20d**	**22d**, α: β= 2: 1

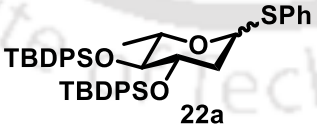
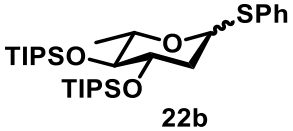
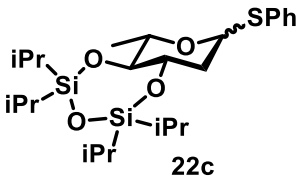
5.	 **, 21b**	**20a**	**22e**, α: β= 10: 1
6.		**20b**	**22f**, α: β=8: 1
7.		**20c**	**22g**, α: β= 3.6: 1
8.		**20d**	**22h**, α: β=1.2: 1
9.[b]	 **, 21c**	**20a**	**22i**, α: β= 1.1: 1
10.[b]		**20b**	**22j**, α: β= 1.5: 1
11.[b]		**20c**	**22k**, α
12.[b]		**20d**	**22l**, α: β= 2: 1

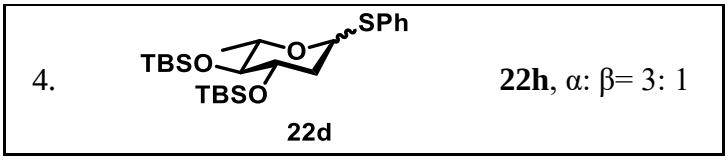
Reaction condition: The reaction was conducted using 0.075-0.24 mmol of **20a-d**, 0.3-0.96 mmol (4 equiv.) of acceptor **21a-c**, 1.5 equiv. of $BF_3.Et_2O$. The yield was determined after column purification. [a]The anomeric ratio was determined by integration of H-1 in the ^1H NMR spectrum of the crude reaction mixture. [b]Isomer analysis was done by nOe experiment and anomeric ratio was obtained from HPLC chromatogram.

5.3.2 Protecting Group Effect on Rhamnosylation

Table 2. Study of Protecting Group Effect on Rhamnosylation in NIS/ TMSOTf Method.



Sl No.	Donor	Product (α: β)
1.	 22a	**22e**, α: β= 18: 1
2.	 22b	**22f**, α: β= 9: 1
3.	 22c	**22g**, α: β= 6: 1

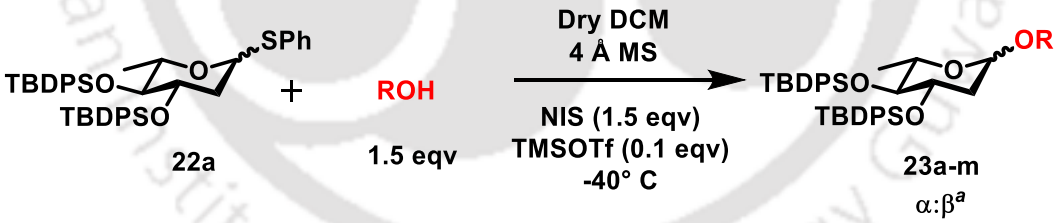


Reaction condition: The reaction was conducted using 0.07-0.106 mmol of **22a-d**, 0.105-0.159 mmol (1.5 equiv.) of acceptor **21b**, 1.5 equiv. of NIS and 0.10 equiv. of TMSOTf. The yield was determined after column purification. [a]The anomeric ratio was determined by integration of H-1 in the ^{1}H NMR spectrum of the crude reaction mixture.

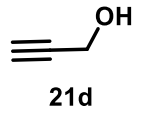
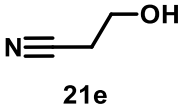
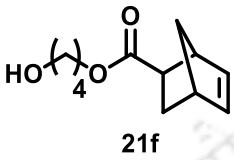
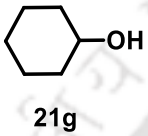
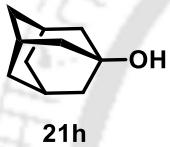
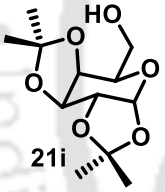
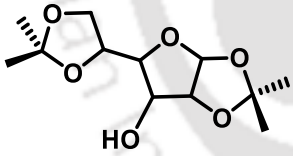
5.3.3 Stereoselective Glycosylation of OTBDPS Protected L-Rhamnosyl Donor

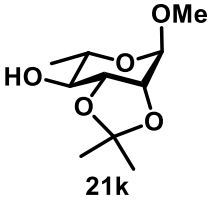
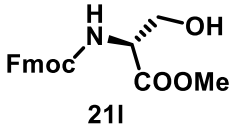
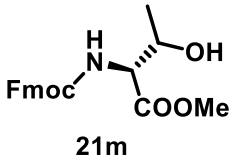
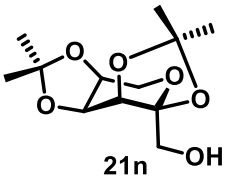
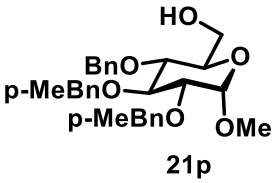
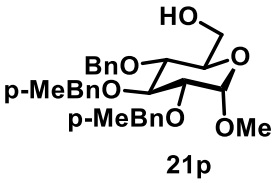
The anomeric acetate corresponding to the OTBDPS protected L-rhamnosyl donor has shown maximum stereoselectivity favouring the α-isomer (α: β=10: 1) followed by the OTIPS protected donor **20b** (α: β=8: 1). Unfortunately, the reaction with cyclic OTIPDS protected donor **20c** shows a sharp decrease in anomeric selectivity (α: β= 3.6: 1) and is then followed by OTBDMS protected donor **20d** (α: β=1.2: 1) in the case of *O*-glycosylation using acceptor **21b** (Table 1, entry 5-8). Among the products obtained in *O*-glycosylation **22e-h,** OTBDPS rhamnose derived *O*-glycoside was obtained with highest α-selectivity (α: β=10: 1). To our surprise, this trend of selectivity was different in the case of *C*-glycosylation with acceptor **21c** (Table 1, entry 9-12). Cyclic OTIPDS protected donor gave complete α-selective *C*-glycosylated product, whereas OTBDPS protected donor **20a** gave the desired product with a nearly equal ratio of both the isomers.

Table 3. Glycosylation of OTBDPS Protected L-Rhamnosyl Donor with Various Glycosyl Acceptors.



Based on the above study on stereoselectivity of various silyl-protected L-rhamnose-derived donors, it can be concluded that OTBDPS protecting group has more preference towards α-selective *O*- and *S*- glycosylation. To check whether this stereoselectivity order is same with a different catalyst system or not, phenyl thioglycoside donors **22a-d** were subjected to NIS/ TMSOTf method[26] of glycosylation with glycosyl acceptor **21b** (Table 2, entry 1-4). We found that 1.5 equivalent of NIS and 0.1 equivalent of TMSOTf in dichloromethane at -40 °C in presence of 4 Å MS was the ideal condition to yield the corresponding *O*-disaccharides **22e-h** within 15 mins. Although the stereoselectivity trend of the silyl protecting groups are in same order but with this method a slight increase in α-selectivity was witnessed in each case and OTBDPS protected disaccharide was obtained almost as a single isomer (α: β=13: 1).

Sl No.	Acceptor	Product (α: β)
1.	 21d	**23a,** 85%, α
2.	 21e	**23b,** 87%, α
3.	 21f	**23c,** 89%, α
4.	 21g	**23d,** 92%, α
5.	 21h	**23e,** 85%, α
6.	 21i	**23f,** 86%, α
7.	 21j	**23g,** 74%, 5:1

Sl No.	Acceptor	Product (α: β)
8.	 21k	**23h,** 78%, α
9.	 21l	**23i,** 88%, α
10.	 21m	**23j,** 83%, α
11.	 21n	**23k,** 79%, α
12.	 21p	**23l,** 82%, α
13.	 21p	**23m,** 78%, α

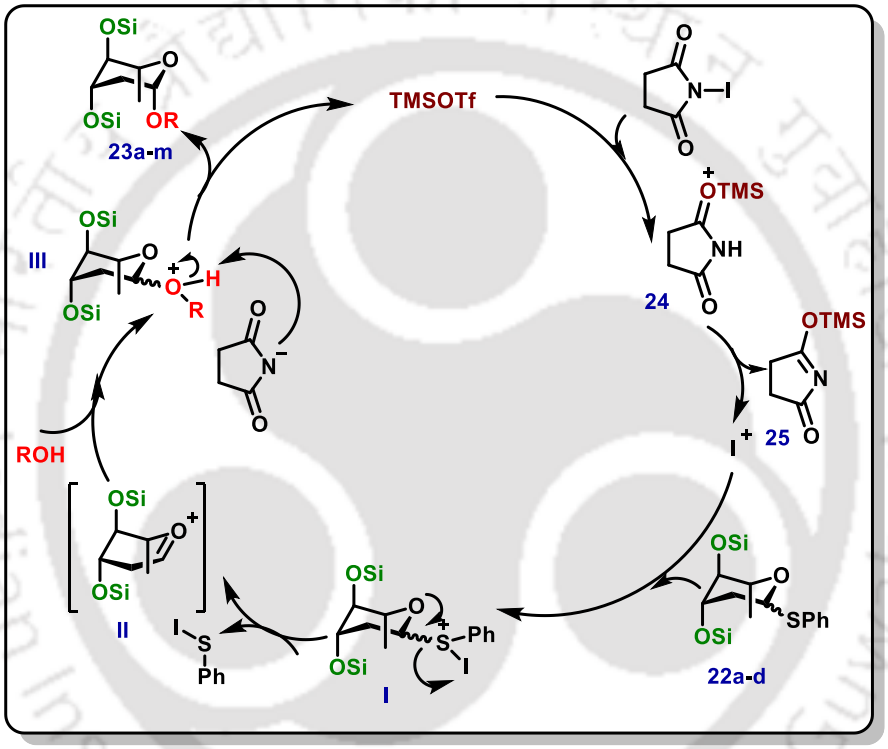
Reaction condition: The reaction was conducted using 0.070 mmol of **22a**, 0.105 mmol (1.5 equiv.) of acceptor **21d-p**, 0.105 mmol (1.5 equiv.) of NIS and 0.10 equiv. of TMSOTf. The yield was determined after column purification. [a]The anomeric ratio was determined by integration of H-1 in the ^{1}H NMR spectrum of the crude reaction mixture.

After establishing the influence of silyl protecting groups on rhamnosylation and examining our observation's generality, various acceptors were tested under the optimized conditions. The studied examples of α-selective 2, 6-dideoxy-*O*-glycosides were showcased in Table 3. Compound **23a-b, 23d** were obtained on reaction with commercially available non-carbohydrate alcohols in exclusive α-selectivity and excellent yields. Despite the presence of nitrile group, which is known for exhibiting α-effect, the reaction, when performed with 2-cyano ethanol as acceptor, yielded the α-isomer **23b** (Table 3) in 87 % yield as the only glycosylated product. Moreover, the coupling with tertiary 1-adamantanol also preceded well under the reaction conditions to provide glycoside **23e** in 85% yield with complete α-selectivity. The primary sugar alcohols derived from glucose, galactose and fructose were successfully coupled with donor **22a** to obtain compounds **23f**, **23k-m** with

good yields and exclusive α-selectivity. Similarly, the sterically congested secondary alcohol diacetonide glucosyl, including rhamnosyl acceptor, were also smoothly coupled with **22a** to furnish the oligosaccharides **23g-h** in 74% and 78% yield, respectively. The fmoc-protected methyl ester of serine **21l** and threonine derivative **21m** was coupled with **3a** to provide the corresponding glycoamino acids **23i-j** as only α product.

5.4 Insights Towards Mechanism:

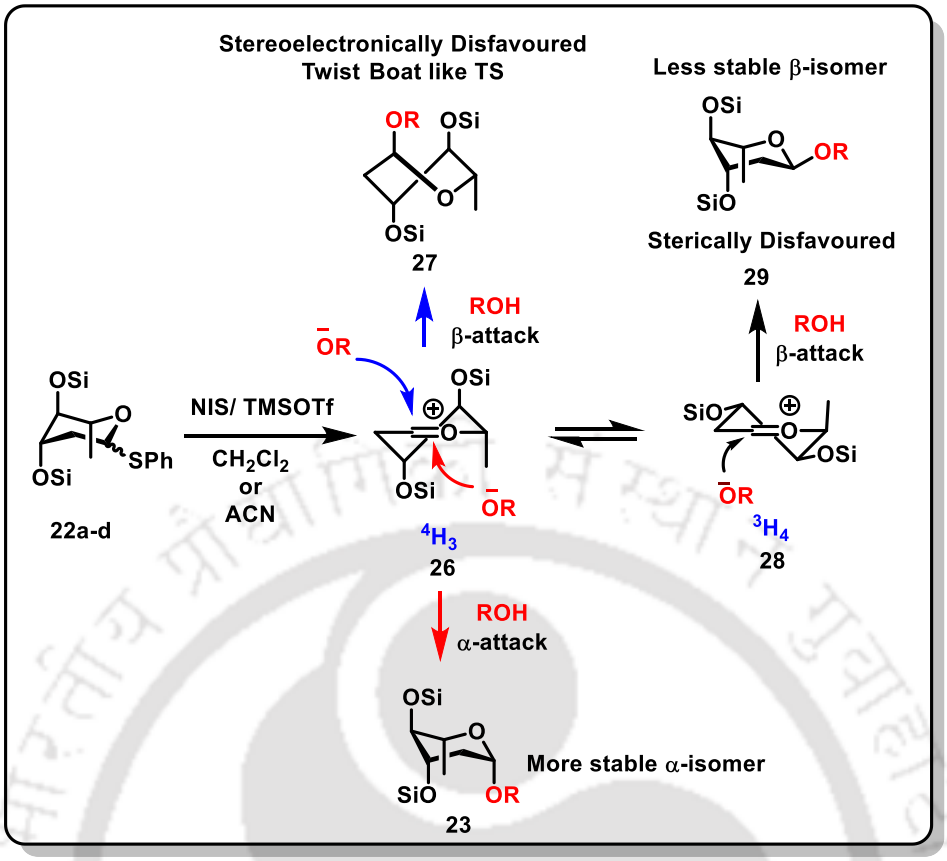
The mechanistic cycle for NIS/TMSOTf thiglycoside activation is shown below (scheme 7). In presence of TMSOTf, NIS acts as a source of iodonium cation. The cooperation of NIS and TMSOTf led to the formation of intermediate iodonium species I, followed by generation of oxocarbenium ion intermediate **II** which finally provides expected glycosylated product in presence of any glycosyl acceptor.



Scheme 7: *Proposed Mechanism*

α- Stereoselectivity :

Following the above mechanistic pathway, in the NIS/TMSOTf mediated glycosylation reaction, we were able to get α-selective glycosylated products almost exclusively. The probable reason is explained schematically below. The oxocarrbenium ion intermediate generated in-situ can exist in equilibrium between $^{4}H_{3}$ and $^{3}H_{4}$ half-chair conformations. β-attack of the nucleophile on the $^{4}H_{3}$ conformation provides stereochemically unstable twist boat like transition state. Although, the β-attack in the $^{3}H_{4}$ conformation generates a stable chair like TS but, due to the presence of sterically bulky silyl protecting groups, β-glycoside is sterically unstable. This explains the formation of sterically stable α-isomer via stable chair like $^{4}H_{3}$ TS.



Scheme 8: *Probable Reason for α-Stereoselectivity Preference*

The 3D structures of oxocarbenium intermediate corresponding to different silyl protected (OTBDMS, cyclic OTIPDS, OTIPS and OTBDPS) rhamnose donors show that due to the maximum crowding in OTBDPS protected rhamnose donor the β-phase is least accessible. This also explains the exclusive α-selective glycoside formation with donor **22a**.

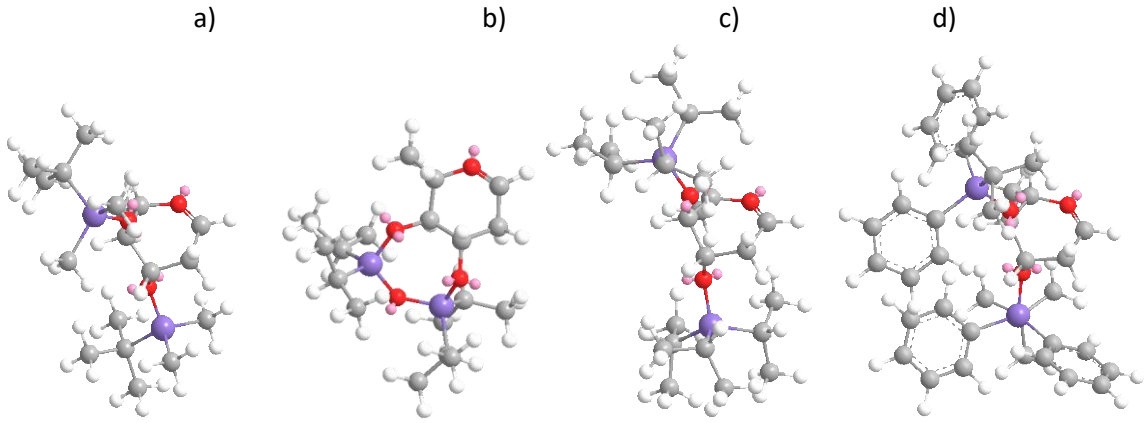
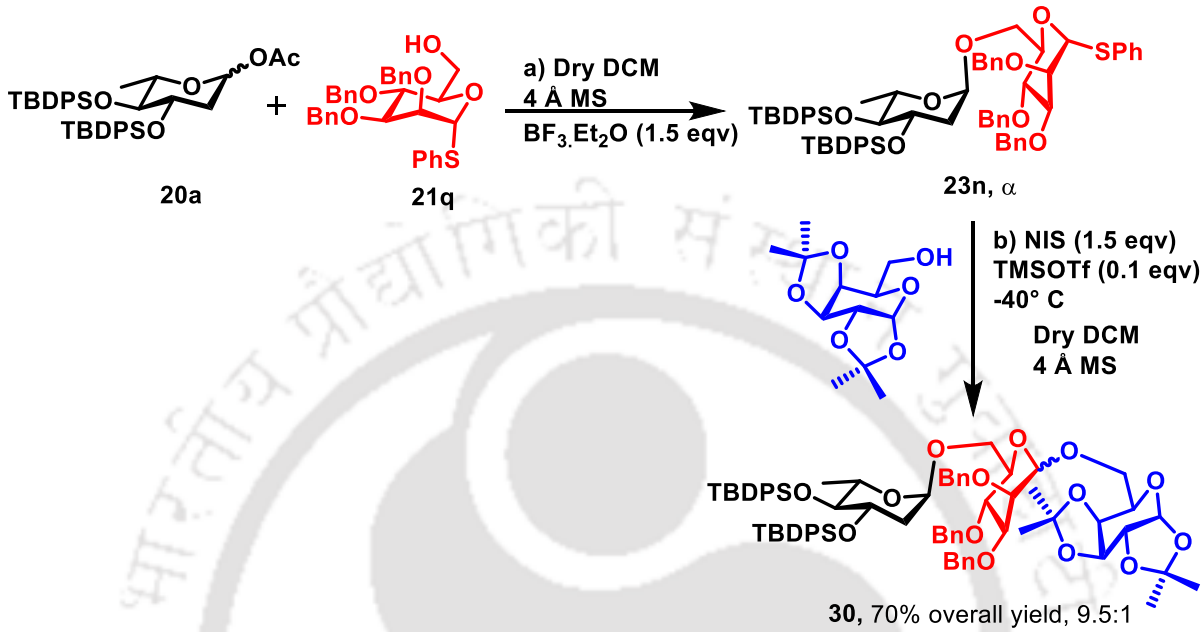


Fig 2. *a), b), c) and d) are 3D structures of oxocarbenium ion corresponding to OTBDMS, cyclic OTIPDS, OTIPS and OTBDPS protected L-rhamnose sugar.*

Towards the end of the project, to showcase the orthogonality, we have synthesized trisaccharide **30** (scheme 9). We have utilized mannose thioglycoside derived 6-OH acceptor

21q under $BF_3.Et_2O$ condition to obtain the disaccharide **23n** as an exclusive α-isomer, which in turn was used for another coupling under NIS/TMSOTf condition to synthesize the trisaccharide **30** in one-pot. Our desired trisaccharide was obtained with an overall yield of 70% as a 9.5:1 α:β mixture.

5.5 Synthesis of Trisaccharide



Scheme 9: *Stereoselective One-pot Trisaccharide Synthesis of Compound 30*

Reaction condition: The reaction was conducted using 0.075 mmol of **20a-d**, 0.3 mmol (4 equiv.) of acceptor **21q**, 0.11 mmol (1.5 equiv.) of $BF_3.Et_2O$. b) The reaction was conducted using 0.043 mmol of **23n**, 0.064 mmol (1.5 equiv.) of acceptor **21i**, 0.064 mmol (1.5 equiv.) of NIS and 0.10 equiv. of TMSOTf.

5.6 Conclusion

In this current work, we have studied the silyl protecting group effect on rhamnosylation. In conclusion, it is observed that OTBDPS protecting group provided better stereo selectivity than OTIPS, cyclic OTIPDS and OTBDMS group on L-rhamnose donors. As an application of this study, stereoselective OTBDPS protected 2, 6- dideoxy L-rhamnosides were synthesized with various glycosyl acceptors with excellent yields. Several non-carbohydrate acceptors, primary and secondary sugar acceptors, and also amino acid derived acceptors were used in this study. Moreover, a trisaccharide was also synthesized where three sugar units are rhamnose, mannose and galactose based respectively. It is observed that α-stereo preference was retained in that case also.

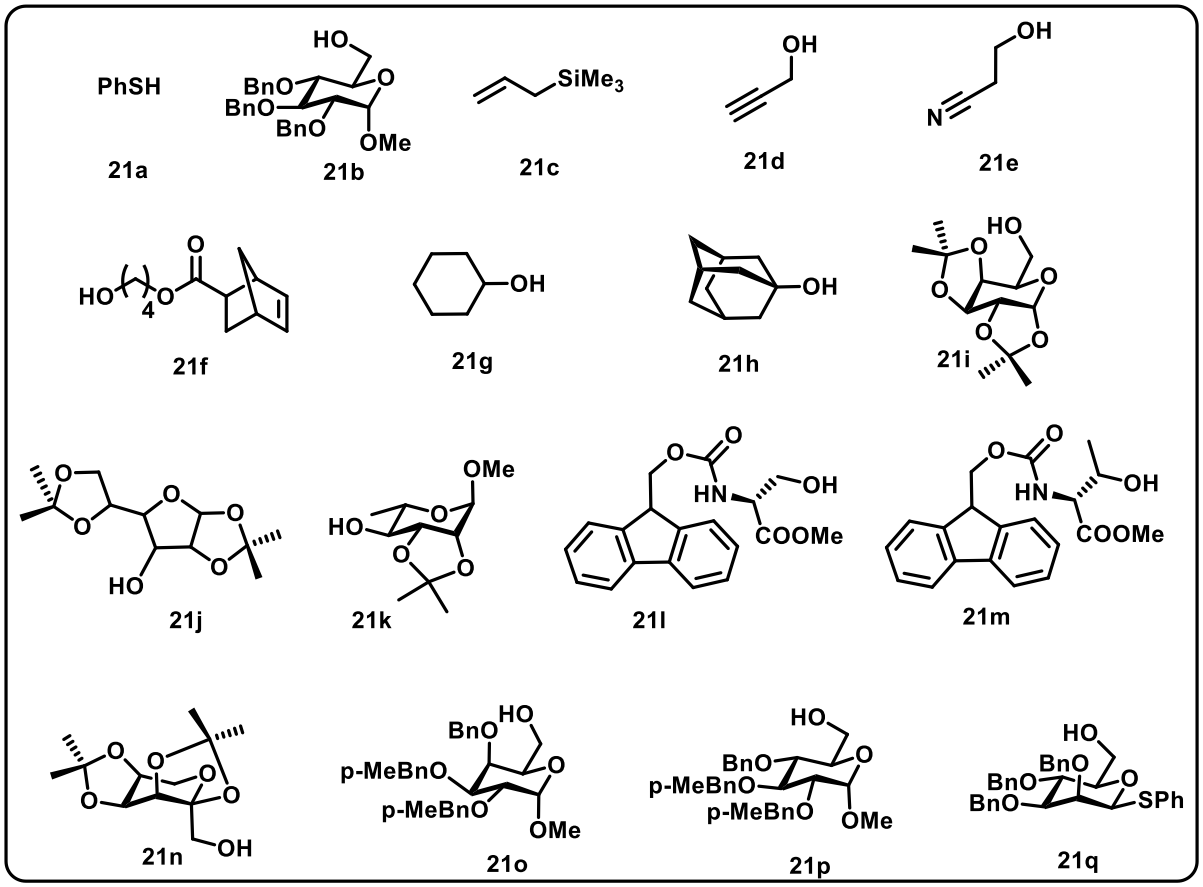
The reaction of OTBDPS protected rhamnose derived thioglycoside donor under NIS/TMSOTf condition proceeds efficiently to afford the corresponding products in good to excellent yields and high stereoselectivity favouring α-glycosides. Therefore, this study has widespread applications in the synthesis of rhamnose-based stereoselective oligosaccharides.

5.7 Experimental Section:

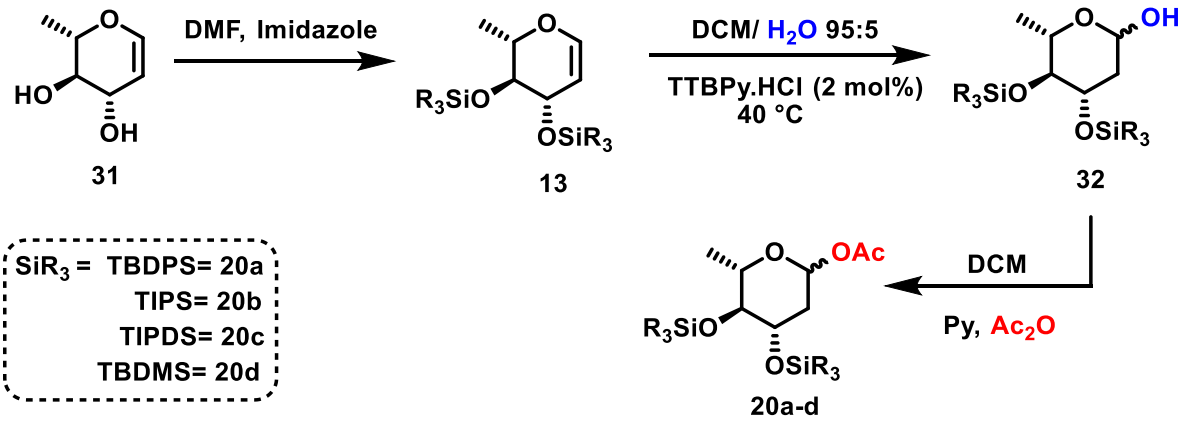
General Information and Analysis:

The general information and analysis section for chapter-V is same as mentioned in chapter-III and chapter-IV. The additional details are given below.

Acceptors Used in this Method:



Synthesis of Donor:



Synthesis of 2,6-dideoxy-3,4-O-bis-(t-butyldiphenylsilyl)-2-deoxy-α,β-L-rhamnopyranosyl-1-acetate (20a):

TBDPSCl (3.03 mL, 11.523 mmol, 3 equiv) was added to a solution of 3,4-dihydro-L-rhamnal (500 mg, 3.841 mmol, 1.0 equiv) and imidazole (785 mg, 11.523 mmol, 3 equiv) in DMF (20 mL). After the reaction mixture was allowed to stir at room temperature for 12 h, most of the reaction solvent was removed under reduced pressure. The residue was dissolved with DCM, and then washed with saturated aqueous $NaHCO_3$. The organic phase was dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography in ethyl acetate/hexane solvent system to give the glycal as a white solid. R_f- 0.5 (50% cyclohexane in hexane), amount- 1.78 g, yield- 76%. Spectroscopic data is in agreement with the reported data.[6a]

Thus synthesized 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnal (500 mg, 0.82 mmol, 1.0 equiv) and catalyst 2,4,6-tri-*tert*-butylpyridinium hydrochloride (5 mg, 0.0164 mmol, 2 mol%) was taken in a round bottomed flask and the flask was then filled with dry DCM and water in 95:5 ratios (10 ml). The mixtures were stirred and heated at 40 °C (using oil bath) in the sealed flask until the reaction was determined to be complete by either TLC or NMR analysis of the crude material. The reaction mixture was quenched by water (20 ml) and it was extracted with DCM, dried over Na_2SO_4 and then concentrated in vacuo and purified by silica gel column chromatography to get the product as a colourless crystalline solid. R_f- 0.5 in 20% EA/hexane, eluent 10% EA in hexane, amount- 412 mg, yield- 80%. Spectroscopic data is in agreement with the reported data. [24]

Thus synthesized 3,4-di-*O*-*tert*-butyldiphenylsilyl-L-rhamnopyranose (500 mg, 0.80 mmol, 1.0 equiv) was taken in DCM and to it pyridine (96 µL, 1.20 mmol, 1.5 equiv) and Ac_2O (115 µL, 1.20 mmol, 1.5 equiv) was added, keeping in ice bath. After the completion of the reaction (monitored by TLC) the reaction mixture was quenched by water (20 ml) and it was extracted with DCM, dried over Na_2SO_4 and then concentrated in vacuo and purified by silica gel column chromatography to get the product **20a** as a colourless oil. R_f- 0.8 in 20% EA/hexane, eluent 5% EA in hexane, amount- 454 mg, yield- 85%. Selectivity α: β= 8: 1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 – 7.52 (m, 4H), 7.50 – 7.44 (m, 4H), 7.39 (ddt, *J* = 9.2, 7.9, 6.9 Hz, 4H), 7.31 (dd, *J* = 15.1, 7.4 Hz, 4H), 7.25 (q, *J* = 7.5 Hz, 4H), 6.23 (dd, *J* = 8.5, 3.7 Hz, 1H), 4.10 (d, *J* = 3.1 Hz, 1H), 3.93 (qd, *J* = 6.8, 3.7 Hz, 1H), 3.57 (t, *J* = 2.9 Hz, 1H), 2.07 (s, 3H), 1.93 (ddd, *J* = 13.3, 8.6, 2.7 Hz, 1H), 1.73 (dt, *J* = 8.1, 3.8 Hz, 1H), 1.18 (d, *J* = 7.0 Hz, 3H), 0.95 (s, 9H), 0.94 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 136.0, 135.9, 135.9, 135.8, 135.8, 133.8, 133.5, 133.5, 133.4, 129.9, 129.8, 129.8, 129.8, 127.8, 127.8, 127.7, 89.4, 74.9, 73.9, 71.9, 32.8, 31.1, 29.8, 27.0, 27.0, 26.9, 21.5, 19.3, 19.2, 17.9. HRMS (ESI-QTOF) $C_{40}H_{50}O_5Si_2Na$ $[M+Na]^+$- calculated- 689.3094; found- 689.3096. $[\alpha]_D^{22}$= -25 (*c* 0.79, $CHCl_3$).

Synthesis of 2,6-dideoxy-3,4-O-bis-(triisopropylsilyl)-2-deoxy-α,β-L-rhamnopyranosyl-1-acetate (20b):

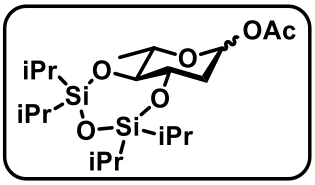
TIPSCl (2.22 ml, 11.523 mmol, 3 equiv) was added to a solution of 3,4-dihydro-L-rhamnal (500 mg, 3.841 mmol, 1.0 equiv) and imidazole (785 mg, 11.523 mmol, 3 equiv) in DMF (20 mL). After the reaction mixture was allowed to stir at room temperature for 12 h, most of the reaction solvent was removed under reduced pressure. The residue was dissolved with DCM, and then washed with saturated aqueous $NaHCO_3$. The organic phase was dried

over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography in ethyl acetate/hexane solvent system to give the glycal as colourless oil. R_f- 0.5 (50% cyclohexane in hexane), amount- 1.43 g, yield- 84%. Spectroscopic data is in agreement with the reported data.[27]

Thus synthesized 3,4-di-*O*-triisopropylsilyl-L-rhamnal (500 mg, 1.13 mmol, 1.0 equiv) and catalyst 2,4,6-tri-*tert*-butylpyridinium hydrochloride (7 mg, 0.0225 mmol, 2 mol%) was taken in a round bottomed flask and the flask was then filled with dry DCM and water in 95:5 ratios (10 ml). The mixtures were stirred and heated at 40 °C (using oil bath) in the sealed flask until the reaction was determined to be complete by either TLC or NMR analysis of the crude material. The reaction mixture was quenched by water (20 ml) and it was extracted with DCM, dried over Na_2SO_4 and then concentrated in vacuo and purified by silica gel column chromatography to get the product 2,6-dideoxy-3,4-O-bis-(triisopropylsilyl)-2-deoxy-α,β-L-rhamnopyranose as a colourless oil. R_f- 0.5 in 20% EA/hexane, eluent 10% EA in hexane, amount- 416 mg, yield- 80%. Selectivity α: β= 2.8: 1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.30 (td, *J* = 7.7, 2.7 Hz, 2.8H), 5.11 – 5.08 (m, 1H), 4.41 (d, *J* = 9.3 Hz, 1H), 4.15 (dd, *J* = 7.0, 3.4 Hz, 2.8H), 4.10 (dt, *J* = 8.8, 5.9 Hz, 3.8H), 3.83 (qd, *J* = 7.1, 3.2 Hz, 1H), 3.75 – 3.74 (m, 1H), 3.59 (t, *J* = 3.0 Hz, 2.8H), 2.88 (d, *J* = 6.9 Hz, 2.8H), 2.31 (dt, *J* = 13.6, 3.3 Hz, 1H), 1.98 (ddd, *J* = 12.9, 8.0, 3.1 Hz, 2.8H), 1.90 – 1.86 (m, 2.8H), 1.84 – 1.79 (m, 1H), 1.50 (d, *J* = 7.2 Hz, 3H), 1.41 (d, *J* = 7.1 Hz, 8.3H), 1.13 – 1.06 (m, 160H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 92.9, 88.5, 75.1, 73.9, 73.6, 73.0, 72.0, 36.9, 34.6, 29.9, 21.4, 18.4, 18.3, 18.3, 18.3, 18.3, 17.9, 13.0, 12.8, 12.8, 12.7.

Thus synthesized 3,4-di-O-triisopropylsilyl-L-rhamnopyranose (500 mg, 1.08 mmol, 1.0 equiv) was taken in DCM and to it pyridine (132 µL, 1.63 mmol, 1.5 equiv) and Ac_2O (154 µL, 1.63 mmol, 1.5 equiv) was added, keeping in ice bath. After the completion of the reaction (monitored by TLC) the reaction mixture was quenched by water (20 ml) and it was extracted with DCM, dried over Na_2SO_4 and then concentrated in vacuo and purified by silica gel column chromatography to get the product **20a** as a colourless oil. R_f- 0.8 in 20% EA/hexane, eluent 5% EA in hexane, amount- 453 mg, yield- 83%. Selectivity α: β= 2: 1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.19 (dd, *J* = 7.0, 3.3 Hz, 2H), 6.03 (t, *J* = 4.0 Hz, 1H), 4.12 (dd, *J* = 8.0, 5.4 Hz, 2H), 4.00 (dd, *J* = 9.2, 4.6 Hz, 1H), 3.97 – 3.95 (m, 2H), 3.87 (qd, *J* = 7.0, 3.3 Hz, 1H), 3.70 – 3.68 (m, 1H), 3.57 (t, *J* = 4.5 Hz, 2H), 2.33 (dt, *J* = 14.0, 4.2 Hz, 1H), 2.13 (ddd, *J* = 13.2, 7.0, 3.2 Hz, 2H), 2.08 (s, 6H), 2.05 (s, 3H), 1.87 (ddd, *J* = 13.2, 5.9, 3.4 Hz, 2H), 1.81 (dt, *J* = 14.0, 4.4 Hz, 1H), 1.47 (d, *J* = 7.1 Hz, 3H), 1.41 (d, *J* = 6.9 Hz, 6H), 1.11 – 1.05 (m, 126H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.3, 169.9, 90.9, 89.9, 75.0, 74.8, 74.7, 73.4, 71.8, 69.5, 34.6, 33.1, 29.9, 21.6, 21.4, 19.9, 18.4, 18.4, 18.3, 18.3, 18.3, 18.1, 18.1, 18.0, 17.9, 17.8, 13.1, 13.0, 12.8, 12.8. HRMS (ESI-QTOF) $C_{26}H_{54}O_5Si_2K$ $[M+K]^+$- calculated- 541.3147; found- 541.3133. $[\alpha]_D^{22}$= -20 (*c* 0.70, $CHCl_3$).

Synthesis of 2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-α,β-L-rhamnopyranosyl-1-acetate (20c):

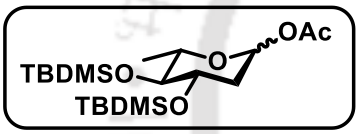


TIPDSCl (1.85 ml, 5.762 mmol, 1.5 equiv) was added to a solution of 3,4-dihydro-L-rhamnal (500 mg, 3.841 mmol, 1.0 equiv) and imidazole (785 mg, 11.523 mmol, 3 equiv) in

DMF (20 mL). After the reaction mixture was allowed to stir at room temperature for 12 h, most of the reaction solvent was removed under reduced pressure. The residue was dissolved with DCM, and then washed with saturated aqueous $NaHCO_3$. The organic phase was dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography in ethyl acetate/hexane solvent system to give the glycal as colourless oil. R_f- 0.5 (50% cyclohexane in hexane), amount- 1.15 g, yield- 82%.

Procedure for the synthesis of **20c** was similar procedure of **20a** with 2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-rhamnal to get the product as a colourless oil. R_f- 0.8 in 20% EA/hexane, eluent 5% EA in hexane, overall yield- 80%. Selectivity α: β= 1.6: 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.15 (d, *J* = 2.8 Hz, 1H), 5.73 (dd, *J* = 10.3, 2.2 Hz, 1.6H), 3.97 (ddd, *J* = 11.5, 8.4, 5.3 Hz, 1H), 3.80 – 3.67 (m, 2.6H), 3.40 (dq, *J* = 9.0, 6.1 Hz, 1.6H), 3.32 – 3.25 (m, 2.6H), 2.20 (ddd, *J* = 12.6, 5.1, 2.1 Hz, 1H), 2.13 – 2.08 (m, 6.7H), 1.87 – 1.83 (m, 1H), 1.80 – 1.71 (m, 1.7H), 1.34 (d, *J* = 6.1 Hz, 4.8H), 1.29 (d, *J* = 6.2 Hz, 3H), 1.09 – 0.90 (m, 73H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 169.4, 92.0, 79.6, 79.2, 73.6, 73.3, 71.2, 70.7, 38.6, 37.4, 21.3, 21.2, 18.2, 18.1, 17.7, 17.7, 17.5, 17.5, 17.5, 17.4, 17.4, 17.3, 17.3, 13.0, 13.0, 12.4, 12.4. HRMS (ESI-QTOF) $C_{20}H_{40}O_6Si_2Na$ $[M+Na]^+$- calculated- 455.2261; found- 455.2261. $[\alpha]_D^{22}$= -22 (*c* 0.79, $CHCl_3$).

Synthesis of 2,6-dideoxy-3,4-di-*O-tert*--butyldimethylsilyl-α,β-L-rhamnopyranosyl-1-acetate (20d):



TBDMSCl (1.74 g, 11.523 mmol, 3 equiv) was added to a solution of 3,4-dihydro-L-rhamnal (500 mg, 3.841 mmol, 1.0 equiv) and imidazole (785 mg, 11.523 mmol, 3 equiv) in DMF (20 mL). After the reaction mixture was allowed to stir at room temperature for 12 h, most of the reaction solvent was removed under reduced pressure. The residue was dissolved with DCM, and then washed with saturated aqueous $NaHCO_3$. The organic phase was dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography in ethyl acetate/hexane solvent system to give the glycal as colourless oil. R_f- 0.5 (50% cyclohexane in hexane), amount- 1.1 g, yield- 80%.

Procedure for the synthesis of **20d** was similar procedure of **20a** with 2,6-dideoxy-3,4-di-*O-tert*-butyldimethylsilyl-L-rhamnal to get the product as a colourless oil. R_f- 0.8 in 20% EA/hexane, eluent 5% EA in hexane, overall yield- 88%. Selectivity α: β= 2: 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.10 – 6.08 (m, 1H), 5.70 (dd, *J* = 9.8, 2.3 Hz, 2H), 3.92 (ddd, *J* = 10.8, 8.1, 4.5 Hz, 1H), 3.72 – 3.66 (m, 3H), 3.41 – 3.32 (m, 2H), 3.19 (dt, *J* = 11.2, 8.4 Hz, 3H), 2.16 (dd, *J* = 4.7, 2.4 Hz, 1H), 2.13 – 2.11 (m, 2H), 2.10 (s, 6H), 2.08 (s, 3H), 1.80 – 1.73 (m, 1H), 1.69 – 1.66 (m, 2H), 1.29 (d, *J* = 6.3 Hz, 6H), 1.24 (d, *J* = 6.4 Hz, 3H), 0.91 – 0.90 (m, 58H), 0.12 – 0.07 (m, 37H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 92.1, 91.6, 77.9, 77.3, 73.9, 72.5, 71.9, 70.5, 39.2, 38.2, 26.4, 26.3, 26.2, 26.2, 25.8, 21.4, 21.3, 21.3, 18.9, 18.8, 18.4, 18.4, 18.2, 18.2, 18.1, 14.3, -2.7, -2.7, -3.0, -3.8, -3.9, -4.1, -4.3, -4.6. HRMS (ESI-QTOF) $C_{20}H_{42}O_5Si_2Na$ $[M+Na]^+$- calculated- 441.2468; found- 441.2467. $[\alpha]_D^{22}$= -22 (*c* 0.77, $CHCl_3$).

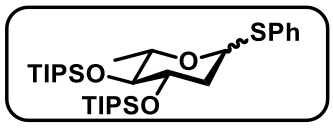
General Procedure A for Glycosylation

Anomeric Acetate donor (0.075-0.24 mmol, 1.0 equiv) was taken in dry DCM and activated 4 Å MS was added to it at 0° C under argon atmosphere. Glycosyl acceptor (0.3-0.96 mmol, 4.0 equiv) was added to it and the reaction mixture was allowed to stir under argon for 30 min followed by addition of $BF_3.Et_2O$ (1.5 equiv). After complete consumption of starting material (monitored by TLC) the reaction mixture was filtered through sintered funnel then quenched by water (20 ml for 0.075 mmol donor) and it was extracted with DCM (3x15 ml for 0.075 mmol donor), dried over Na_2SO_4 and then concentrated in vacuo and purified by column chromatography (Merck 60-120 mesh, 7 gm) and HPLC (using HPLC-grade acetonitrile solvent, flow rate- 5 ml/min).

Synthesis of Phenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (22a):

General procedure **A** was followed by taking 2,6-dideoxy-3,4-O-bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl-1-acetate **20a** (100 mg, 0.15 mmol, 1.0 equiv) in dry DCM and thiophenol **21a** (66 mg, 61 µL, 0.6 mmol, 4.0 equiv) was added to it and then the reaction mixture was allowed to stir under argon for 30 min followed by addition of $BF_3.Et_2O$ (32 mg, 28 µL, 0.22 mmol, 1.5 equiv). After complete consumption of starting material (monitored by TLC) the reaction mixture was filtered through sintered funnel, washed with DCM and excess thiophenol was quenched with 5% NaOH solution. After work up the organic phase was dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography in ethyl acetate/hexane solvent system to give the thioglycoside **22a** as colourless oil. R_f- 0.5 (10% hexane in ethylacetate), amount- 96 mg, yield- 89%. Selectivity α: β= 18: 1. α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.53 (m, 4H), 7.49 – 7.20 (m, 22H), 5.47 (dd, *J* = 11.2, 2.8 Hz, 1H), 4.03 – 3.97 (m, 2H), 3.51 (s, 1H), 2.11 (ddd, *J* = 13.7, 11.4, 2.5 Hz, 1H), 1.69 (dd, *J* = 11.0, 2.7 Hz, 1H), 1.23 (d, *J* = 7.1 Hz, 3H), 0.95 (s, 9H), 0.91 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.9, 135.8, 135.8, 134.6, 133.8, 133.5, 133.5, 133.3, 131.5, 129.9, 129.8, 129.8, 128.8, 127.8, 127.8, 127.7, 127.0, 75.4, 75.2, 72.5, 71.7, 34.0, 27.1, 27.0, 19.3, 19.2, 17.1. HRMS (ESI-QTOF) $C_{44}H_{52}O_3Si_2SNa$ $[M+Na]^+$- calculated- 739.3073; found- 739.3059. $[\alpha]_D^{22}$= -32 (*c* 66, $CHCl_3$).

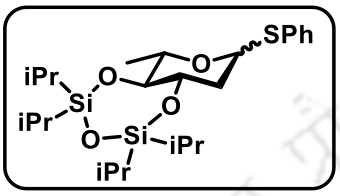
Synthesis of Phenyl 2,6-dideoxy-3,4-O-bis-(triisopropylsilyl)-2-deoxy-α,β-L-arabino-hexapyranoside (22b):



Procedure for the synthesis of **22b** was similar procedure of **22a** with 2,6-dideoxy-3,4-O-bis-(triisopropylsilyl)-2-deoxy-α,β-L-rhamnopyranosyl-1-acetate **20b** (100 mg, 0.20 mmol, 1.0 equiv) as the starting material, thiophenol **21a** (88 mg, 82 µL, 0.80 mmol, 4.0 equiv) as acceptor and $BF_3.Et_2O$ (43 mg, 37 µL, 0.30 mmol, 1.5 equiv) as catalyst to get the product **22b** as a colourless oil. R_f- 0.5 in 10% EA/hexane, eluent 3% EA in hexane, amount- 96 mg, yield- 87%. Selectivity α: β= 9: 1. α-anomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 – 7.51 (m, 1H), 7.39 – 7.33 (m, 1H), 7.28 – 7.25 (m, 2H), 7.21 (ddd, *J* = 7.3, 3.7, 1.1 Hz, 1H),

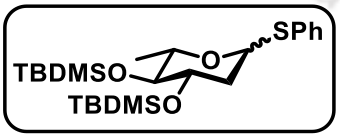
5.45 (dd, *J* = 10.2, 2.8 Hz, 1H), 4.13 (qd, *J* = 7.0, 2.4 Hz, 1H), 4.08 (dd, *J* = 6.8, 3.4 Hz, 1H), 3.59 (t, *J* = 3.0 Hz, 1H), 2.29 (ddd, *J* = 13.1, 8.3, 2.8 Hz, 1H), 1.88 – 1.84 (m, 1H), 1.44 (d, *J* = 7.1 Hz, 3H), 1.13 – 1.02 (m, 42H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.1, 134.8, 131.4, 131.0, 129.2, 128.9, 128.8, 128.7, 126.9, 75.8, 75.6, 72.9, 71.7, 35.2, 32.1, 31.0, 29.9, 29.8, 29.5, 22.8, 18.6, 18.5, 18.5, 18.4, 18.3, 18.3, 18.3, 18.3, 17.9, 17.2, 14.3, 13.8, 12.8, 12.7. HRMS (ESI-QTOF) $C_{30}H_{56}O_3SSi_2K$ $[M+K]^+$- calculated- 591.3126; found- 591.3116. $[\alpha]_D^{22}$= -32 (*c* 0.60, $CHCl_3$).

Synthesis of Phenyl 2,6-dideoxy-3,4-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-α,β-L-arabino-hexapyranoside (22c):



Procedure for the synthesis of **22c** was similar procedure of **22a** with 2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-rhamnopyranosyl-1-acetate **20c** (100 mg, 0.21 mmol, 1.0 equiv) as the starting material, thiophenol **21a** (91 mg, 85 µL, 0.83 mmol, 4.0 equiv) as acceptor and $BF_3.Et_2O$ (44 mg, 38 µL, 0.31 mmol, 1.5 equiv) as catalyst to get the product **22c** as a colourless oil. R_f- 0.5 in 10% EA/hexane, eluent 3% EA in hexane, amount- 93 mg, yield- 83%. Selectivity α: β= 2.2: 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.64 (m, 2H), 7.50 – 7.45 (m, 5H), 7.40 – 7.21 (m, 13H), 5.57 (d, *J* = 5.5 Hz, 2.2H), 4.81 (dd, *J* = 12.1, 1.8 Hz, 1H), 4.15 (dq, *J* = 9.1, 6.2 Hz, 2.2H), 4.00 (ddd, *J* = 11.6, 8.2, 5.1 Hz, 2.2H), 3.74 (ddd, *J* = 11.0, 7.8, 5.4 Hz, 1H), 3.37 – 3.32 (m, 1H), 3.28 (td, *J* = 8.9, 2.6 Hz, 3.2H), 2.30 (dd, *J* = 13.3, 5.2 Hz, 3.2H), 2.13 (ddd, *J* = 13.7, 11.6, 5.7 Hz, 2.3H), 1.85 (dd, *J* = 24.1, 12.1 Hz, 1H), 1.36 (d, *J* = 5.9 Hz, 3H), 1.30 (d, *J* = 6.2 Hz, 7H), 1.11 – 0.93 (m, 92H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 137.1, 135.5, 131.2, 131.1, 129.2, 129.0, 129.0, 128.7, 127.3, 127.1, 84.1, 82.2, 80.3, 79.3, 76.6, 75.2, 72.1, 69.3, 40.0, 39.4, 30.9, 18.5, 18.0, 17.8, 17.6, 17.5, 17.5, 17.4, 17.4, 17.4, 17.4, 13.1, 13.0, 13.0, 12.4, 12.4, 12.3. HRMS (ESI-QTOF) $C_{24}H_{42}O_4SSi_2NH_4$ $[M+NH_4]^+$- calculated- 500.2686; found- 500.2686. $[\alpha]_D^{22}$= -32 (*c* 0.60, $CHCl_3$).

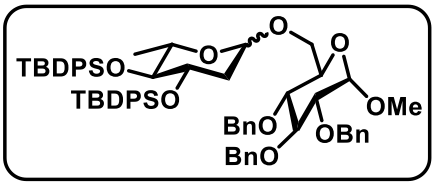
Synthesis of Phenyl 2,6-dideoxy-3,4-bis-*O*-*tert*-butyldimethylsilyl-1-thio-α,β-L-arabino-hexapyranoside (22d):



Procedure for the synthesis of **22d** was similar procedure of **22a** with 2,6-dideoxy-3,4-di-*O*-*tert*-butyldimethylsilyl-L-rhamnopyranosyl-1-acetate **20d** (100 mg, 0.24 mmol, 1.0 equiv) as the starting material, thiophenol **21a** (105 mg, 99 µL, 0.96 mmol, 4.0 equiv) as acceptor and $BF_3.Et_2O$ (51 mg, 44 µL, 0.36 mmol, 1.5 equiv) as catalyst to get the product **22d** as a colourless oil. R_f- 0.5 in 10% EA/hexane, eluent 3% EA in hexane, amount- 96 mg, yield- 86%. Selectivity α: β= 2: 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.46 (ddd, *J* = 5.0, 3.7, 2.0 Hz, 5H), 7.41 – 7.20 (m, 10H), 5.51 (dd, *J* = 5.3, 2.3 Hz, 2H), 4.79 (dd, *J* = 12.0, 1.9 Hz, 1H), 4.13 – 4.05 (m, 2H), 3.95 – 3.90 (m, 2H), 3.70 – 3.63 (m, 1H), 3.30 (tt, *J* = 12.4, 6.2 Hz, 1H), 3.18 (dt, *J* = 15.0, 8.3 Hz, 3H), 2.25 (tdd, *J* = 12.5, 4.6,

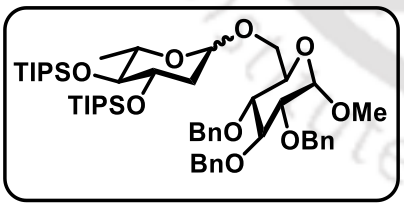
2.1 Hz, 3H), 2.06 – 1.99 (m, 2H), 1.76 (dd, *J* = 23.8, 12.0 Hz, 1H), 1.30 (d, *J* = 2.7 Hz, 3H), 1.25 (d, *J* = 6.4 Hz, 6H), 0.92 (s, 18H), 0.91 (s, 18H), 0.90 (s, 9H), 0.89 (s, 9H), 0.13 – 0.07 (m, 38H). Other Spectroscopic data is in agreement with the reported data.[28]

Synthesis of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α-L-rhamnosyl)-α-D-glucopyranoside (22e):



General procedure **A** was followed by taking glycosyl donor 2,6-dideoxy-3,4-O-bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl-1-acetate **20a** (50 mg, 0.075 mmol, 1.0 equiv) and glycosyl acceptor **21b** (140 mg, 0.3 mmol, 4.0 equiv) and then the reaction mixture was allowed to stir under argon for 30 min followed by addition of $BF_3.Et_2O$ (16 mg, 14 µL, 0.11 mmol, 1.5 equiv). After complete consumption of starting material (monitored by TLC) the reaction mixture was filtered through sintered funnel, washed with DCM and quenched with sat. $NaHCO_3$ solution. After work up the organic phase was dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography in ethyl acetate/hexane solvent system to give product **22d** as colourless oil. R_f- 0.5 (10% hexane in ethylacetate), amount- 63 mg, yield- 79%. Selectivity α: β= 10: 1. α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.53 (m, 2H), 7.44 (t, *J* = 7.4 Hz, 5H), 7.37 – 7.17 (m, 28H), 5.00 – 4.95 (m, 2H), 4.84 – 4.78 (m, 3H), 4.67 (d, *J* = 12.2 Hz, 1H), 4.61 (d, *J* = 3.5 Hz, 1H), 4.50 (d, *J* = 10.7 Hz, 1H), 4.11 (d, *J* = 1.4 Hz, 1H), 4.02 – 3.97 (m, 2H), 3.86 (dd, *J* = 6.8, 4.3 Hz, 1H), 3.77 (dd, *J* = 10.0, 3.3 Hz, 1H), 3.61 (dd, *J* = 11.1, 4.8 Hz, 1H), 3.56 – 3.52 (m, 2H), 3.48 (t, *J* = 9.5 Hz, 1H), 3.35 (s, 3H), 1.93 – 1.88 (m, 1H), 1.69 – 1.63 (m, 1H), 1.09 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 9H), 0.87 (s, 9H). Other Spectroscopic data is in agreement with the reported data. [6a]

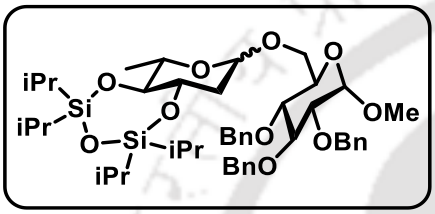
Synthesis of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-triisopropylsilyl-2,6-dideoxy-α-L-rhamnosyl)-α-D-glucopyranoside (22f):



General procedure **A** was followed by taking glycosyl donor 2,6-dideoxy-3,4-O-bis-(triisopropylsilyl)-2-deoxy-α,β-L-rhamnopyranosyl-1-acetate **20b** (50 mg, 0.10 mmol, 1.0 equiv) and glycosyl acceptor **21b** (186 mg, 0.4 mmol, 4.0 equiv) and then the reaction mixture was allowed to stir under argon for 30 min followed by addition of $BF_3.Et_2O$ (21 mg, 19 µL, 0.15 mmol, 1.5 equiv). After complete consumption of starting material (monitored by TLC) the reaction mixture was filtered through sintered funnel, washed with DCM and quenched with sat. $NaHCO_3$ solution. After work up the organic phase was dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography in ethyl acetate/hexane solvent system to give product **22f** as colourless oil. R_f- 0.5 (10% hexane in ethylacetate), amount- 65 mg, yield- 72%. Selectivity α: β= 7: 1. α-anomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.25 (m, 15H), 4.97 (dd, *J* = 10.8, 4.6 Hz, 1H), 4.90 (dd, *J* = 5.6, 3.1

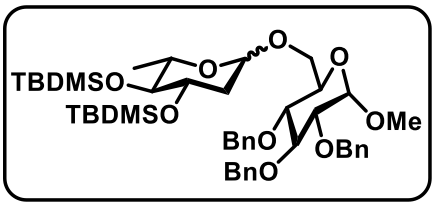
Hz, 1H), 4.85 (dd, *J* = 10.9, 4.1 Hz, 1H), 4.82 – 4.77 (m, 2H), 4.65 (d, *J* = 12.1 Hz, 1H), 4.58 (dd, *J* = 18.2, 7.2 Hz, 2H), 4.07 (t, *J* = 7.4 Hz, 1H), 4.01 – 3.95 (m, 2H), 3.87 – 3.82 (m, 1H), 3.79 (dd, *J* = 10.0, 4.3 Hz, 1H), 3.53 (ddd, *J* = 16.5, 8.9, 4.6 Hz, 2H), 3.49 – 3.44 (m, 2H), 3.36 (s, 3H), 2.10 (ddd, *J* = 13.0, 6.0, 3.5 Hz, 1H), 1.75 (ddd, *J* = 13.0, 6.7, 3.1 Hz, 1H), 1.32 (d, *J* = 6.8 Hz, 3H), 1.06 (dd, *J* = 14.7, 10.3 Hz, 42H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.0, 138.4, 138.4, 128.6, 128.5, 128.5, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 98.0, 96.0, 82.5, 82.2, 80.1, 78.3, 75.9, 75.8, 75.2, 74.8, 74.7, 73.5, 72.5, 72.1, 72.0, 71.8, 70.3, 66.8, 55.1, 36.2, 29.9, 18.5, 18.5, 18.4, 18.4, 18.4, 18.3, 18.3, 18.3, 13.4, 13.3, 13.3, 13.1, 12.4, 12.3. HRMS (ESI-QTOF) $C_{52}H_{82}O_9Si_2NH_4$ $[M+NH_4]^+$- calculated- 924.5841; found- 924.5845. $[\alpha]_D^{22}$= -42 (*c* 0.60, $CHCl_3$).

Synthesis of Methyl 2,3,4-tri-O-benzyl-6-O-(2,6-deoxy-3,4-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-α,β-L-erythro-hexapyranosyl)-α-D-glucopyranoside (22g):



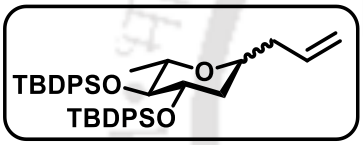
General procedure **A** was followed by taking glycosyl donor 2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-rhamnopyranosyl-1-acetate **20c** (50 mg, 0.11 mmol, 1.0 equiv) and glycosyl acceptor **21b** (204 mg, 0.44 mmol, 4.0 equiv) and then the reaction mixture was allowed to stir under argon for 30 min followed by addition of $BF_3.Et_2O$ (23 mg, 20 µL, 0.17 mmol, 1.5 equiv). After complete consumption of starting material (monitored by TLC) the reaction mixture was filtered through sintered funnel, washed with DCM and quenched with sat. $NaHCO_3$ solution. After work up the organic phase was dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography in ethyl acetate/hexane solvent system to give product **22g** as colourless oil. R_f- 0.5 (10% hexane in ethylacetate), amount- 77 mg, yield- 80%. Selectivity α: β= 3.6: 1. α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.24 (m, 15H), 4.99 (d, *J* = 10.8 Hz, 1H), 4.89 (d, *J* = 11.1 Hz, 1H), 4.82 (d, *J* = 6.3 Hz, 1H), 4.80 (d, *J* = 7.5 Hz, 1H), 4.77 (d, *J* = 3.2 Hz, 1H), 4.66 (d, *J* = 12.1 Hz, 1H), 4.58 (d, *J* = 3.5 Hz, 1H), 4.54 (d, *J* = 11.0 Hz, 1H), 3.97 (ddd, *J* = 11.8, 8.3, 5.7 Hz, 2H), 3.89 – 3.86 (m, 1H), 3.81 – 3.77 (m, 1H), 3.73 – 3.54 (m, 2H), 3.52 – 3.49 (m, 1H), 3.42 – 3.38 (m, 1H), 3.36 (s, 3H), 3.22 (dd, *J* = 11.6, 5.9 Hz, 1H), 2.08 (dd, *J* = 13.1, 5.2 Hz, 1H), 1.66 (ddd, *J* = 17.8, 9.7, 4.0 Hz, 1H), 1.24 (d, *J* = 6.2 Hz, 3H), 1.07 – 0.89 (m, 28H). Other Spectroscopic data is in agreement with the reported data. [24]

Synthesis of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-tertiary-butyldimethylsilyl-2,6-dideoxy-α,β-L-rhamnosyl)-α-D-glucopyranoside (22h):



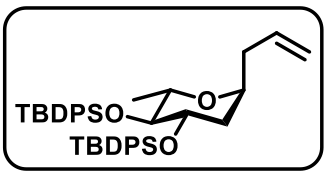
General procedure **A** was followed by taking glycosyl donor 2,6-dideoxy-3,4-di-*O*-*tert*-butyldimethylsilyl-L-rhamnopyranosyl-1-acetate **20b** (50 mg, 0.12 mmol, 1.0 equiv) and glycosyl acceptor **21b** (223 mg, 0.48 mmol, 4.0 equiv) and then the reaction mixture was allowed to stir under argon for 30 min followed by addition of $BF_3.Et_2O$ (26 mg, 22 µL, 0.18 mmol, 1.5 equiv). After complete consumption of starting material (monitored by TLC) the reaction mixture was filtered through sintered funnel, washed with DCM and quenched with sat. $NaHCO_3$ solution. After work up the organic phase was dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography in ethyl acetate/hexane solvent system to give product **22h** as colourless oil. R_f- 0.5 (10% hexane in ethylacetate), amount- 80 mg, yield- 75%. Selectivity α: β= 1.3: 1. α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 15H), 4.99 (d, *J* = 10.8 Hz, 1H), 4.88 (d, *J* = 10.9 Hz, 1H), 4.81 (dd, *J* = 11.4, 5.7 Hz, 2H), 4.71 (d, *J* = 2.0 Hz, 1H), 4.66 (d, *J* = 12.1 Hz, 1H), 4.57 (d, *J* = 3.5 Hz, 1H), 4.53 (d, *J* = 11.0 Hz, 1H), 3.99 (dd, *J* = 15.8, 6.5 Hz, 1H), 3.95 – 3.91 (m, 1H), 3.86 (d, *J* = 11.7 Hz, 1H), 3.78 (dd, *J* = 9.9, 6.4 Hz, 1H), 3.64 – 3.54 (m, 2H), 3.50 (dd, *J* = 9.6, 3.5 Hz, 1H), 3.39 (t, *J* = 5.4 Hz, 1H), 3.36 (s, 3H), 3.12 (t, *J* = 8.5 Hz, 1H), 2.05 (dd, *J* = 12.6, 4.0 Hz, 1H), 1.63 (d, *J* = 3.7 Hz, 1H), 1.17 (d, *J* = 6.4 Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.07 (dd, *J* = 9.7, 5.6 Hz, 12H). Other Spectroscopic data is in agreement with the reported data. [24]

Synthesis of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α,β-L-arabino-non-1-enitol (22iαβ):



General procedure **A** was followed by taking glycosyl donor 2,6-dideoxy-3,4-O-bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl-1-acetate **20a** (50 mg, 0.075 mmol, 1.0 equiv) and glycosyl acceptor **21c** (34 mg, 43 µL, 0.3 mmol, 4.0 equiv) and then the reaction mixture was allowed to stir under argon for 30 min followed by addition of $BF_3.Et_2O$ (16 mg, 14 µL, 0.11 mmol, 1.5 equiv). After complete consumption of starting material (monitored by TLC) the reaction mixture was filtered through sintered funnel, washed with DCM and quenched with sat. $NaHCO_3$ solution. After work up the organic phase was dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography in ethyl acetate/hexane solvent system to give product **22g** as colourless oil. R_f- 0.5 (10% hexane in ethylacetate), amount- 43 mg, yield- 89%. α and β anomers were isolated in HPLC. Selectivity α: β= 1.1:1.

Synthesis of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-non-1-enitol (22iα):



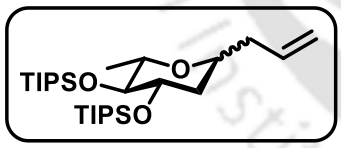
Re-purification was done using HPLC (retention time- 12 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was a colourless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 – 7.55 (m, 2H), 7.52 – 7.51 (m, 2H), 7.47 (d, *J* = 6.9 Hz, 2H), 7.43 – 7.21 (m, 14H), 5.84 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 5.11 – 5.05 (m, 2H), 4.12 – 4.08 (m,

1H), 3.98 (d, *J* = 2.0 Hz, 1H), 3.85 (q, *J* = 7.2 Hz, 1H), 3.51 (d, *J* = 2.7 Hz, 1H), 2.30 (dt, *J* = 12.9, 6.4 Hz, 1H), 2.18 (dt, *J* = 13.8, 7.0 Hz, 1H), 1.79 – 1.75 (m, 1H), 1.32 (d, *J* = 13.5 Hz, 1H), 1.23 (d, *J* = 7.3 Hz, 3H), 0.97 (s, 9H), 0.93 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 135.9, 135.9, 135.8, 135.8, 135.1, 134.2, 133.8, 133.6, 129.8, 129.8, 129.7, 129.7, 127.7, 127.7, 127.7, 127.6, 116.7, 74.7, 71.5, 70.6, 63.2, 40.7, 33.4, 27.1, 27.0, 19.3, 19.2, 16.6. HRMS (ESI-QTOF) $C_{41}H_{52}O_3Si_2Na$ $[M+Na]^+$- calculated- 671.3353; found- 671.3356. $[\alpha]_D^{22}$= 0.02 (*c* 0.1, $CHCl_3$).

Synthesis of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-β-L-arabino-non-1-enitol (22iβ):

Re-purification was done using HPLC (retention time- 13 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was a colourless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 – 7.73 (m, 4H), 7.64 – 7.63 (m, 2H), 7.57 – 7.55 (m, 2H), 7.42 – 7.28 (m, 12H), 5.43 (ddt, *J* = 17.1, 10.2, 7.0 Hz, 1H), 4.82 (d, *J* = 10.1 Hz, 1H), 4.76 (dd, *J* = 17.1, 1.4 Hz, 1H), 4.15 (ddd, *J* = 9.7, 7.1, 5.5 Hz, 1H), 3.65 (t, *J* = 7.3 Hz, 1H), 3.37 – 3.33 (m, 1H), 3.18 – 3.13 (m, 1H), 2.04 (dt, *J* = 13.0, 6.4 Hz, 1H), 1.79 (dt, *J* = 14.0, 7.1 Hz, 1H), 1.59 – 1.56 (m, 1H), 1.10 (dt, *J* = 13.0, 10.4 Hz, 1H), 1.00 (s, 9H), 0.93 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 136.1, 136.1, 136.0, 135.8, 135.7, 135.0, 134.8, 134.3, 134.2, 129.6, 129.5, 129.5, 129.5, 127.7, 127.7, 127.5, 117.0, 79.7, 77.0, 75.8, 73.5, 40.1, 39.5, 27.4, 27.3, 20.4, 19.9, 19.3. HRMS (ESI-QTOF) $C_{41}H_{52}O_3Si_2Na$ $[M+Na]^+$- calculated- 671.3353; found- 671.3356. $[\alpha]_D^{22}$= 0.02 (*c* 0.1, $CHCl_3$).

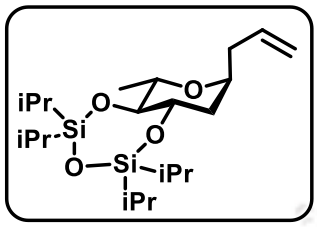
Synthesis of Allyl 2,6-dideoxy-3,4-O-bis-(triisopropylsilyl)-2-deoxy-α,β-L-arabino-non-1-enitol (22jαβ):



General procedure **A** was followed by taking glycosyl donor 2,6-dideoxy-3,4-O-bis-(triisopropylsilyl)-2-deoxy-α,β-L-rhamnopyranosyl-1-acetate **20b** (50 mg, 0.10 mmol, 1.0 equiv) and glycosyl acceptor **21c** (46 mg, 64 µL, 0.40 mmol, 4.0 equiv) and then the reaction mixture was allowed to stir under argon for 30 min followed by addition of $BF_3.Et_2O$ (22 mg, 19 µL, 0.15 mmol, 1.5 equiv). After complete consumption of starting material (monitored by TLC) the reaction mixture was filtered through sintered funnel, washed with DCM and quenched with sat. $NaHCO_3$ solution. After work up the organic phase was dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography in ethyl acetate/hexane solvent system to give product **22j** as colourless oil. R_f- 0.5 (10% hexane in ethylacetate), amount- 43 mg, yield- 88%. Selectivity α: β= 1.3:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.75 (m, 2.3H), 5.02 (d, *J* = 6.9 Hz, 1H), 5.02 – 4.95 (m, 3.3H), 3.96 – 3.94 (m, 3.6H), 3.70 (ddd, *J* = 11.0, 7.7, 5.0 Hz, 1H), 3.54 (d, *J* = 2.7 Hz, 1.3H), 3.34 – 3.29 (m, 1H), 3.26 (t, *J* = 8.1 Hz, 1H), 3.17 (dq, *J* = 12.4, 6.1 Hz, 1H), 2.25 (ddd, *J* = 21.1, 13.4, 6.3 Hz, 2.3H), 2.09 (tt, *J* = 14.0, 6.9 Hz, 2.3H), 1.97 (ddd, *J* = 12.7, 4.8, 1.5 Hz, 1H), 1.82 – 1.77 (m, 1.3H), 1.40 (d, *J* = 13.3 Hz, 1H), 1.34 (d, *J* = 7.3 Hz, 4H), 1.22 (d, *J* = 6.2 Hz, 3H), 1.10 (dd,

J = 14.5, 7.2 Hz, 1.3H), 1.04 – 0.98 (m, 97H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.3, 134.8, 117.0, 116.6, 79.4, 75.6, 75.3, 74.3, 71.7, 70.5, 63.1, 40.7, 40.4, 40.4, 34.0, 19.3, 18.8, 18.6, 18.5, 18.3, 18.3, 18.2, 16.7, 14.1, 14.0, 12.6, 12.4. HRMS (ESI-QTOF) $C_{27}H_{56}O_3Si_2K$ $[M+K]^+$- calculated- 523.3405; found- 523.3393. $[\alpha]_D^{22}$= 0.02 (*c* 0.1, $CHCl_3$).

Synthesis of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-β-L-arabino-non-1-enitol (22k):



General procedure **A** was followed by taking glycosyl donor 2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-rhamnopyranosyl-1-acetate **20c** (50 mg, 0.11 mmol, 1.0 equiv) and glycosyl acceptor **21c** (50 mg, 70μL, 0.44 mmol, 4.0 equiv) and then the reaction mixture was allowed to stir under argon for 30 min followed by addition of $BF_3.Et_2O$ (23 mg, 20 μL, 0.17 mmol, 1.5 equiv). After complete consumption of starting material (monitored by TLC) the reaction mixture was filtered through sintered funnel, washed with DCM and quenched with sat. $NaHCO_3$ solution. After work up the organic phase was dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography in ethyl acetate/hexane solvent system to give product **22i** as colourless oil. R_f- 0.5 (10% hexane in ethylacetate), amount- 39 mg, yield- 82%. Selectivity α. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 – 5.72 (m, 1H), 5.12 – 5.06 (m, 2H), 3.99 (dd, *J* = 14.0, 7.2 Hz, 1H), 3.86 (ddd, *J* = 11.6, 8.3, 5.3 Hz, 1H), 3.47 (dq, *J* = 9.1, 6.1 Hz, 1H), 3.20 (t, *J* = 8.7 Hz, 1H), 2.53 (ddd, *J* = 14.4, 7.8, 6.8 Hz, 1H), 2.33 – 2.26 (m, 1H), 1.92 (dd, *J* = 13.1, 5.0 Hz, 1H), 1.81 (ddd, *J* = 13.4, 11.6, 6.0 Hz, 1H), 1.26 (d, *J* = 6.1 Hz, 3H), 1.09 – 0.89 (m, 28H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 135.0, 117.1, 80.7, 72.6, 71.9, 69.5, 36.1, 35.9, 18.8, 17.7, 17.6, 17.6, 17.5, 17.5, 17.4, 13.1, 13.1, 12.5. HRMS (ESI-QTOF) $C_{21}H_{43}O_4Si_2$ $[M+H]^+$- calculated- 415.2700; found- 415.2688. $[\alpha]_D^{22}$= 0.02 (*c* 0.1, $CHCl_3$).

Synthesis of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-*tert*-butyldimethylsilyl-α,β-L-arabino-non-1-enitol (22lαβ):

General procedure **A** was followed by taking glycosyl donor 2,6-dideoxy-3,4-di-*O*-*tert*-butyldimethylsilyl-L-rhamnopyranosyl-1-acetate **20b** (50 mg, 0.12 mmol, 1.0 equiv) and glycosyl acceptor **21c** (55 mg, 76 μL, 0.48 mmol, 4.0 equiv) and then the reaction mixture was allowed to stir under argon for 30 min followed by addition of $BF_3.Et_2O$ (26 mg, 22 μL, 0.18 mmol, 1.5 equiv). After complete consumption of starting material (monitored by TLC) the reaction mixture was filtered through sintered funnel, washed with DCM and quenched with sat. $NaHCO_3$ solution. After work up the organic phase was dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography in ethyl acetate/hexane

solvent system to give product **22h** as colourless oil. R_f- 0.5 (10% hexane in ethylacetate), amount- 45 mg, yield- 86%. α and β anomers were isolated in HPLC. Selectivity α: β= 2:1.

Synthesis of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-*tert*-butyldimethylsilyl-α,β-L-arabino-non-1-enitol (22lα):

Re-purification was done using HPLC (retention time- 7.5 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.82 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 5.06 (ddd, *J* = 13.7, 11.0, 1.2 Hz, 2H), 3.98 – 3.93 (m, 1H), 3.84 – 3.80 (m, 2H), 3.30 – 3.29 (m, 1H), 2.34 (dt, *J* = 13.4, 6.6 Hz, 1H), 2.17 (dt, *J* = 14.0, 6.8 Hz, 1H), 1.82 (ddd, *J* = 12.9, 9.5, 3.0 Hz, 1H), 1.44 (ddd, *J* = 13.3, 4.4, 2.8 Hz, 1H), 1.34 (d, *J* = 7.1 Hz, 3H), 0.90 (d, *J* = 1.6 Hz, 18H), 0.07 – 0.05 (m, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.3, 116.6, 74.3, 73.2, 70.5, 65.0, 39.7, 34.7, 26.1, 26.0, 18.3, 18.2, 17.4, 1.2, -4.3, -4.4, -4.5, -4.7. HRMS (ESI-QTOF) $C_{21}H_{45}O_3Si_2$ $[M+H]^+$- calculated- 401.2907; found- 401.2906. $[\alpha]_D^{22}$= -43 (*c* 0.52, $CHCl_3$).

Synthesis of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-*tert*-butyldimethylsilyl-α,β-L-arabino-non-1-enitol (22lβ):

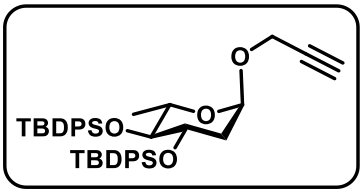
Re-purification was done using HPLC (retention time- 9 min, solvent- HPLC-grade acetonitrile, flow rate- 5 ml/min). The compound obtained was a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 (ddt, *J* = 17.1, 10.2, 7.0 Hz, 1H), 5.06 (dd, *J* = 20.6, 5.1 Hz, 2H), 3.61 (ddd, *J* = 11.3, 8.1, 4.9 Hz, 1H), 3.40 – 3.35 (m, 1H), 3.19 (dq, *J* = 8.6, 6.2 Hz, 1H), 3.09 (t, *J* = 8.5 Hz, 1H), 2.32 (dt, *J* = 13.0, 6.4 Hz, 1H), 2.15 (dt, *J* = 14.0, 6.8 Hz, 1H), 1.93 (ddd, *J* = 13.0, 4.8, 1.7 Hz, 1H), 1.34 (dd, *J* = 24.2, 11.4 Hz, 1H), 1.23 (d, *J* = 6.2 Hz, 3H), 0.90 (s, 9H), 0.90 (s, 9H), 0.08 (t, *J* = 8.5 Hz, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.8, 117.0, 78.7, 74.9, 74.7, 41.1, 40.2, 26.5, 26.3, 19.2, 18.6, 18.3, 1.2, -2.5, -2.7, -3.7, -3.9. HRMS (ESI-QTOF) $C_{21}H_{45}O_3Si_2$ $[M+H]^+$- calculated- 401.2907; found- 401.2906. $[\alpha]_D^{22}$= -43 (*c* 0.52, $CHCl_3$).

General Method B for Glycosylation:

Glycosyl donor **22a** (0.070 mmol, 1.0 equiv) and glycosyl acceptor (0.105 mmol, 1.5 equiv) was taken in a round bottomed flask (10 mL). The starting materials were coevaporated thrice with toluene in rotary evaporator and dried under vacuum. The flask was then filled with dry DCM and activated 4 Å MS and was allowed to stir at 0° C under argon atmosphere. NIS (23 mg, 0.105 mmol, 1.5 equiv) was added to the reaction and it was allowed to stir for 30 min at -40° C under argon, followed by addition of TMSOTf (1.3 µL, 0.1 equiv). After complete consumption of starting material (monitored by TLC) the reaction mixture was quenched by water (20 ml for 0.070 mmol donor) and filtered through sintered

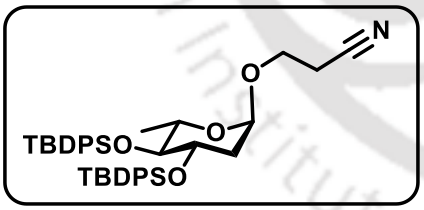
funnel then it was extracted with DCM (3x15 ml for 0.070 mmol donor), dried over Na_2SO_4 and then concentrated in vacuo and purified by column chromatography (Merck 60-120 mesh, 7 gm) and HPLC (using HPLC-grade acetonitrile solvent, flow rate- 5 ml/min).

Synthesis of 1-Propargyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23a):



General procedure **B** was followed by taking glycosyl donor phenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside **22a** (50 mg, 0.070 mmol, 1.0 equiv) and glycosyl acceptor propargyl alcohol **21d** (6 mg, 6 µL, 0.105 mmol, 1.5 equiv) at -40° C to get the product **23a** as a colourless liquid. Rf- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 39 mg, yield- 85%. Selectivity α. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, *J* = 6.9 Hz, 2H), 7.53 (d, *J* = 7.0 Hz, 2H), 7.48 (dd, *J* = 14.6, 7.0 Hz, 4H), 7.43 – 7.40 (m, 4H), 7.33 (dd, *J* = 13.2, 7.2 Hz, 4H), 7.28 – 7.24 (m, 4H), 5.21 (dd, *J* = 8.3, 3.7 Hz, 1H), 4.32 (qd, *J* = 15.7, 2.3 Hz, 1H), 4.10 (s, 1H), 3.90 (td, *J* = 10.7, 6.7 Hz, 1H), 3.57 (s, 1H), 2.44 (t, *J* = 2.3 Hz, 1H), 1.90 (ddd, *J* = 13.4, 8.4, 2.5 Hz, 1H), 1.76 – 1.73 (m, 1H), 1.16 (d, *J* = 6.9 Hz, 3H), 0.96 (s, 9H), 0.93 (s, 9H).^{13}C NMR (151 MHz, $CDCl_3$) δ 135.8, 135.7, 135.7, 135.6, 133.7, 133.5, 133.4, 133.3, 129.7, 129.6, 129.6, 127.6, 127.6, 127.5, 127.5, 93.2, 79.8, 74.6, 74.0, 73.0, 72.3, 54.5, 37.1, 33.4, 31.9, 30.0, 29.7, 29.4, 26.9, 26.8, 22.7, 19.2, 19.1, 18.1, 14.1. HRMS (ESI) $C_{43}H_{58}O_4Si_2Na$ $[M+Na]^+$- calculated- 717.3771; found- 717.3775. $[\alpha]_D^{22}$= -7 (*c* 0.5, $CHCl_3$).

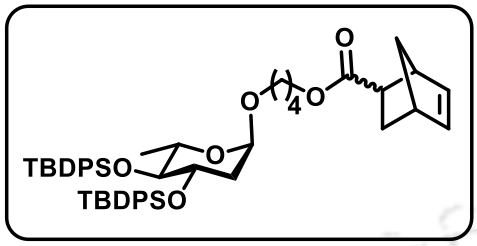
Synthesis of 2-Cyanoethyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23b):



General procedure **B** was followed by taking glycosyl donor phenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside **22a** (50 mg, 0.070 mmol, 1.0 equiv) and glycosyl acceptor 3-hydroxypropionitrile **21e** (7.5 mg, 7 µL, 0.105 mmol, 1.5 equiv) at -40° C to get the product **23b** as a colourless liquid. Rf- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 41 mg, yield- 87%. Selectivity α. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.6 Hz, 2H), 7.51 (d, *J* = 7.5 Hz, 2H), 7.46 (dd, *J* = 13.2, 7.5 Hz, 4H), 7.38 (dd, *J* = 14.3, 6.9 Hz, 4H), 7.33 – 7.29 (m, 4H), 7.27 – 7.22 (m, 4H), 4.96 (dd, *J* = 8.1, 3.8 Hz, 1H), 4.10 (s, 1H), 3.92 (dt, *J* = 10.2, 6.3 Hz, 1H), 3.87 – 3.82 (m, 1H), 3.67 (dt, *J* = 10.1, 6.9 Hz, 1H), 3.55 (s, 1H), 2.61 (td, *J* = 6.5, 3.9 Hz, 2H), 1.86 (ddd, *J* = 13.5, 8.2, 2.4 Hz, 1H), 1.72 (dt, *J* = 13.6, 3.6 Hz, 1H), 1.10 (d, *J* = 6.9 Hz, 3H), 0.95 (s, 9H), 0.92 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.9, 135.9, 135.9, 135.8, 133.9, 133.8, 133.7, 133.6, 129.9, 129.8, 129.8, 127.8, 127.8, 127.7, 127.7, 95.6, 74.9, 72.9, 72.3, 62.8, 33.5, 27.1, 27.0,

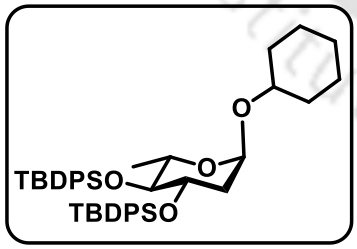
19.4, 19.3, 19.3, 18.4. HRMS (ESI) $C_{42}H_{55}O_4NSi_2Na$ $[M+Na]^+$- calculated- 732.3880; found- 732.3888. $[\alpha]_D^{22}$= -4 (*c* 1.3, $CHCl_3$).

Synthesis of 4-Hydroxybutyl-bicyclo[2.2.1]hept-5-ene-2-carboxylate-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23c):



General procedure **B** was followed by taking glycosyl donor phenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside **22a** (50 mg, 0.070 mmol, 1.0 equiv) and glycosyl acceptor **21f** (22 mg, 0.105 mmol, 1.5 equiv) at -40° C to get the product **23c** as a colourless liquid. Rf- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 50 mg, yield- 89%. Selectivity α. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 – 7.56 (m, 2H), 7.52 – 7.50 (m, 2H), 7.49 – 7.45 (m, 4H), 7.39 – 7.35 (m, 4H), 7.30 (dt, *J* = 12.0, 6.0 Hz, 4H), 7.25 – 7.22 (m, 1H), 6.14 (dd, *J* = 5.6, 2.9 Hz, 1H), 6.10 (dd, *J* = 5.5, 3.0 Hz, 1H), 4.92 (dd, *J* = 8.1, 3.5 Hz, 1H), 4.11 (t, *J* = 6.4 Hz, 3H), 3.88 – 3.84 (m, 1H), 3.78 (dt, *J* = 9.6, 6.3 Hz, 1H), 3.55 (t, *J* = 3.1 Hz, 1H), 3.41 (dt, *J* = 9.6, 6.3 Hz, 1H), 3.04 (s, 1H), 2.91 (s, 1H), 2.22 (dd, *J* = 10.1, 4.4 Hz, 1H), 1.94 – 1.91 (m, 1H), 1.85 (ddd, *J* = 13.5, 8.2, 2.7 Hz, 1H), 1.72 – 1.60 (m, 1H), 1.12 (d, *J* = 6.9 Hz, 3H), 0.94 (s, 9H), 0.92 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.4, 138.2, 136.0, 135.9, 135.9, 135.8, 134.1, 134.0, 133.8, 133.7, 129.8, 129.7, 129.7, 127.7, 127.7, 127.7, 94.8, 74.9, 72.9, 72.6, 67.5, 64.5, 46.8, 46.5, 43.4, 41.8, 34.1, 32.1, 30.5, 30.2, 29.9, 29.5, 27.1, 27.0, 26.5, 25.7, 22.8, 19.4, 19.3, 18.3, 14.3. HRMS (ESI) $C_{50}H_{64}O_6Si_2NH_4$ $[M+NH_4]^+$- calculated- 834.4585; found- 834.4575. $[\alpha]_D^{22}$= -4 (*c* 1.3, $CHCl_3$).

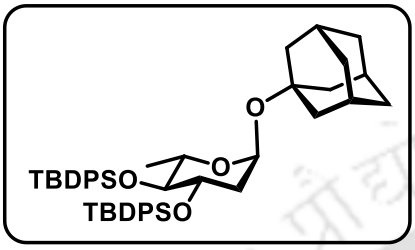
Synthesis of Cyclohexyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23d):



General procedure **B** was followed by taking glycosyl donor phenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside **22a** (50 mg, 0.070 mmol, 1.0 equiv) and glycosyl acceptor cyclohexanol **21g** (11 mg, 11 µL, 0.105 mmol, 1.5 equiv) at -40° C to get the product **23d** as a colourless liquid. Rf- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 44 mg, yield- 92%. Selectivity α. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 6.8 Hz, 2H), 7.53 (d, *J* = 6.8 Hz, 2H), 7.49 (t, *J* = 7.5 Hz, 4H), 7.43 – 7.36 (m, 4H), 7.32 (dd, *J* = 13.0, 7.3 Hz, 4H), 7.27 (dt, *J* = 15.4, 5.5 Hz, 4H), 5.13 (dd, *J* = 8.3, 3.3 Hz, 1H), 4.10 (d, *J* = 3.0 Hz, 1H), 3.94 – 3.90 (m, 1H), 3.61 (td, *J* = 9.3, 4.4 Hz, 1H), 3.55 (t, *J* = 2.9 Hz, 1H), 1.95 – 1.87 (m, 2H), 1.76 – 1.73 (m, 2H), 1.67 – 1.64 (m, 1H), 1.57 –

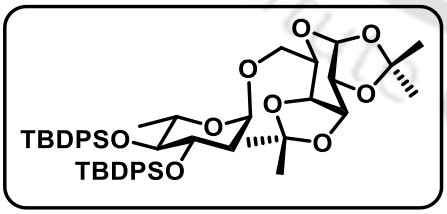
1.55 (m, 1H), 1.38 – 1.19 (m, 6H), 1.16 (d, *J* = 6.9 Hz, 3H), 0.96 (s, 9H), 0.93 (s, 9H).^{13}C NMR (151 MHz, $CDCl_3$) δ 135.8, 135.7, 135.7, 135.7, 133.9, 133.8, 133.5, 133.5, 129.6, 129.5, 129.5, 127.5, 127.5, 127.5, 127.5, 92.0, 75.0, 74.6, 72.8, 72.6, 34.4, 33.8, 32.0, 26.9, 26.8, 25.7, 24.4, 24.2, 19.2, 19.1, 18.1, 1.9. HRMS (ESI) $C_{44}H_{58}O_4Si_2Na$ $[M+Na]^+$- calculated- 729.3771; found- 729.3805. $[\alpha]_D^{22}$= -4 (*c* 1.3, $CHCl_3$).

Synthesis of 1-Adamantanyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23e):



General procedure **B** was followed by taking glycosyl donor phenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside **22a** (50 mg, 0.070 mmol, 1.0 equiv) and glycosyl acceptor 1-Adamantanol **21h** (16 mg, 0.105 mmol, 1.5 equiv) at -40° C to get the product **23e** as a colourless liquid. Rf- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 46 mg, yield- 80%. Re-purification was done using HPLC (retention time- 14 min). Selectivity α. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 – 7.57 (m, 2H), 7.51 – 7.50 (m, 2H), 7.47 – 7.44 (m, 4H), 7.39 – 7.28 (m, 9H), 7.23 (dd, *J* = 7.3, 5.3 Hz, 3H), 5.37 (dd, *J* = 8.7, 2.9 Hz, 1H), 4.08 (d, *J* = 2.8 Hz, 1H), 3.97 (qd, *J* = 7.0, 3.1 Hz, 1H), 3.53 (t, *J* = 2.7 Hz, 1H), 2.12 (s, 3H), 1.89 (ddd, *J* = 13.2, 8.8, 2.6 Hz, 1H), 1.79 (q, *J* = 11.6 Hz, 6H), 1.65 – 1.59 (m, 6H), 1.49 – 1.45 (m, 1H), 1.20 (d, *J* = 7.1 Hz, 3H), 0.95 (s, 9H), 0.92 (s, 9H).^{13}C NMR (126 MHz, $CDCl_3$) δ 136.0, 136.0, 135.9, 135.9, 134.1, 134.1, 133.9, 133.7, 129.8, 129.7, 129.7, 127.7, 127.7, 127.7, 127.6, 86.6, 74.0, 73.9, 73.9, 73.2, 42.8, 36.6, 35.7, 30.9, 27.1, 27.1, 19.4, 19.2, 18.0. HRMS (ESI-QTOF) $C_{49}H_{66}O_4Si_2Na$ $[M+Na]^+$- calculated- 797.4397; found- 797.4399. $[\alpha]_D^{22}$= -74 (*c* 0.73, $CHCl_3$).

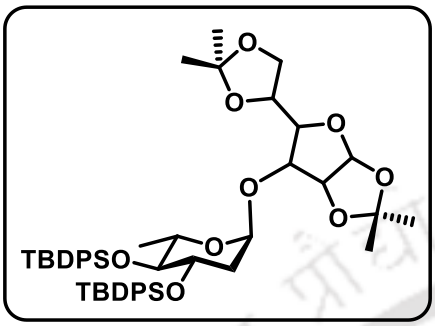
Synthesis of 6-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranoside (23f):



General procedure **B** was followed by taking glycosyl donor phenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside **22a** (50 mg, 0.070 mmol, 1.0 equiv) and glycosyl acceptor **21i** (27 mg, 0.105 mmol, 1.5 equiv) at -40° C to get the product **23f** as a colourless liquid. Rf- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 52 mg, yield- 86%. Re-purification was done using HPLC (retention time- 9 min). Selectivity α. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.0 Hz, 2H), 7.49 – 7.44 (m, 6H), 7.39 – 7.34 (m, 4H), 7.29 (dd, *J* = 15.1, 7.6 Hz, 4H), 7.23 (dt, *J* = 11.1, 7.6 Hz, 4H), 5.53 (d, *J* = 5.0 Hz, 1H), 4.99 (dd, *J* = 7.8, 3.6 Hz, 1H), 4.61 (dd, *J* = 7.9, 2.2 Hz, 1H), 4.31 (dd, *J* = 4.9, 2.3 Hz, 1H), 4.25 (dd, *J* = 8.0, 1.4 Hz, 1H), 4.09 (d, *J* = 3.0 Hz, 1H), 3.97 (t, *J* =

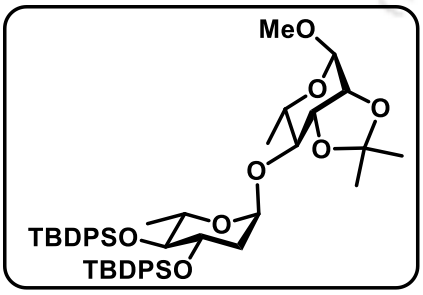
5.4 Hz, 1H), 3.91 (dd, *J* = 10.5, 5.5 Hz, 1H), 3.87 – 3.83 (m, 1H), 3.63 (dd, *J* = 10.4, 6.8 Hz, 1H), 3.53 (t, *J* = 3.2 Hz, 1H), 1.87 (ddd, *J* = 13.3, 8.0, 2.6 Hz, 1H), 1.75 – 1.71 (m, 1H), 1.54 (s, 3H), 1.45 (s, 3H), 1.34 (s, 6H), 1.10 (d, *J* = 6.9 Hz, 3H), 0.93 (s, 9H), 0.91 (s, 9H). Other Spectroscopic data is in agreement with the reported data. [24]

Synthesis of 3-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose (23g):



General procedure **B** was followed by taking glycosyl donor phenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside **22a** (50 mg, 0.070 mmol, 1.0 equiv) and glycosyl acceptor **21j** (27 mg, 0.105 mmol, 1.5 equiv) at -40° C to get the product **23g** as a colourless liquid. Rf- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 45 mg, yield- 74%. Re-purification was done using HPLC (retention time- 9 min). Selectivity α: β=5: 1. α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.55 (m, 2H), 7.49 (dt, *J* = 7.4, 3.9 Hz, 6H), 7.38 (dd, *J* = 6.1, 1.7 Hz, 4H), 7.31 (t, *J* = 7.3 Hz, 6H), 7.25 – 7.23 (m, 2H), 5.82 (d, *J* = 3.6 Hz, 1H), 4.91 (dd, *J* = 7.4, 4.5 Hz, 1H), 4.35 (dd, *J* = 12.5, 6.3 Hz, 1H), 4.31 (t, *J* = 4.1 Hz, 2H), 4.23 (dd, *J* = 6.0, 3.2 Hz, 1H), 4.12 – 4.08 (m, 2H), 4.00 (dd, *J* = 8.4, 6.2 Hz, 1H), 3.84 – 3.81 (m, 1H), 3.59 – 3.58 (m, 1H), 1.76 (ddd, *J* = 13.8, 7.6, 2.8 Hz, 1H), 1.66 (dt, *J* = 8.3, 4.5 Hz, 1H), 1.49 (s, 3H), 1.42 (s, 3H), 1.33 (s, 3H), 1.32 (s, 3H), 1.06 (d, *J* = 6.7 Hz, 3H), 0.93 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.9, 135.9, 135.8, 134.2, 134.0, 133.8, 133.7, 129.8, 127.8, 127.7, 111.9, 108.8, 105.4, 93.4, 82.9, 81.1, 77.3, 76.0, 73.2, 72.5, 72.1, 66.9, 33.9, 27.1, 27.0, 26.8, 26.5, 25.5, 19.4, 19.3, 18.6. HRMS (ESI-QTOF) $C_{50}H_{66}O_9Si_2NH_4$ $[M+NH_4]^+$- calculated- 884.4589; found- 884.4587. $[\alpha]_D^{22}$= -68 (*c* 0.75, $CHCl_3$).

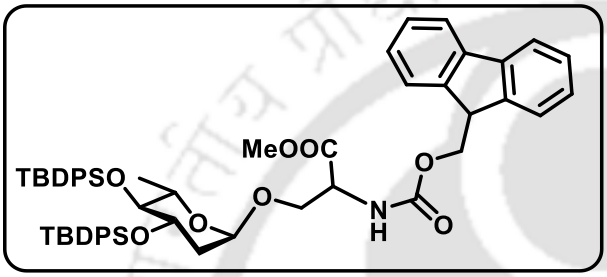
Synthesis of Methyl 6-deoxy-4-O-(3,4-O-bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (23h):



General procedure **B** was followed by taking glycosyl donor phenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside **22a** (50 mg, 0.070 mmol, 1.0 equiv) and glycosyl acceptor **21k** (23 mg, 0.105 mmol, 1.5 equiv) at -40° C to get the product **23h** as a colourless liquid. Rf- 0.4 in 10% EA/hexane, eluent 5% EA in

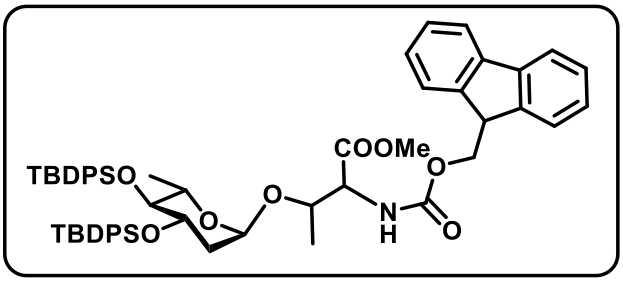
hexane, amount- 45 mg, yield- 78%. Re-purification was done using HPLC (retention time- 9 min). Selectivity α. ^{1}H NMR (500 MHz, D_2O) δ 7.57 (d, *J* = 7.5 Hz, 4H), 7.51 (d, *J* = 7.1 Hz, 2H), 7.45 (d, *J* = 7.2 Hz, 2H), 7.41 – 7.22 (m, 12H), 5.50 (dd, *J* = 8.3, 3.7 Hz, 1H), 4.86 (s, 1H), 4.14 – 4.09 (m, 3H), 3.85 – 3.80 (m, 1H), 3.60 (t, *J* = 5.2 Hz, 1H), 3.52 (s, 1H), 3.37 (s, 3H), 1.84 – 1.79 (m, 1H), 1.76 (dt, *J* = 13.1, 3.2 Hz, 1H), 1.57 (s, 3H), 1.50 (s, 3H), 1.34 – 1.32 (m, 6H), 1.08 (d, *J* = 6.9 Hz, 3H), 0.96 (s, 9H), 0.90 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.0, 135.9, 135.9, 134.2, 133.9, 133.8, 133.7, 129.8, 129.8, 129.7, 129.7, 127.7, 127.7, 127.7, 127.6, 109.3, 98.2, 94.1, 79.0, 77.6, 76.3, 74.7, 72.9, 72.6, 64.7, 54.9, 34.0, 29.9, 28.2, 27.0, 27.0, 26.6, 19.4, 19.3, 18.1, 17.7. HRMS (ESI-QTOF) $C_{48}H_{64}O_8Si_2NH_4$ $[M+NH_4]^+$- calculated- 842.4483; found- 842.4484. $[\alpha]_D^{22}$= -75 (*c* 0.60, $CHCl_3$).

Synthesis of Methyl fmoc-serine-(3,4-O-bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (23i):



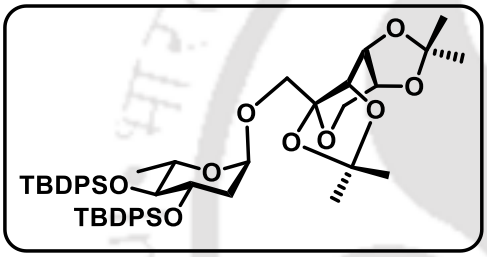
General procedure **B** was followed by taking glycosyl donor phenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside **22a** (50 mg, 0.070 mmol, 1.0 equiv) and glycosyl acceptor **21l** (36 mg, 0.105 mmol, 1.5 equiv) at -40° C to get the product **23i** as a colourless liquid. Rf- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 58 mg, yield- 88%. Re-purification was done using HPLC (retention time- 11 min). Selectivity α. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 – 7.75 (m, 2H), 7.62 (t, *J* = 6.5 Hz, 2H), 7.57 (d, *J* = 7.2 Hz, 2H), 7.50 (dd, *J* = 16.3, 7.7 Hz, 7H), 7.41 – 7.35 (m, 8H), 7.31 (t, *J* = 7.3 Hz, 7H), 5.65 (d, *J* = 8.3 Hz, 1H), 4.86 (dd, *J* = 6.4, 3.5 Hz, 1H), 4.52 – 4.50 (m, 1H), 4.46 (dd, *J* = 10.2, 7.3 Hz, 1H), 4.38 – 4.35 (m, 1H), 4.25 (t, *J* = 7.0 Hz, 1H), 4.15 (dd, *J* = 9.9, 2.6 Hz, 1H), 4.10 (s, 1H), 3.75 (s, 3H), 3.73 (d, *J* = 9.0 Hz, 1H), 3.65 (dd, *J* = 9.6, 2.3 Hz, 1H), 3.57 (s, 1H), 1.79 (dd, *J* = 12.0, 7.1 Hz, 1H), 1.66 (dd, *J* = 9.8, 3.7 Hz, 1H), 1.07 (d, *J* = 6.7 Hz, 3H), 0.93 (s, 9H), 0.92 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.0, 141.5, 135.9, 135.9, 135.8, 134.1, 133.8, 133.7, 129.9, 129.8, 129.8, 127.9, 127.8, 127.7, 127.7, 127.2, 125.3, 120.1, 95.3, 75.6, 72.4, 72.4, 67.3, 67.1, 54.6, 52.6, 47.4, 27.1, 27.0. HRMS (ESI-QTOF) $C_{57}H_{65}NO_8Si_2NH_4$ $[M+NH_4]^+$- calculated- 965.4592; found- 965.4595. $[\alpha]_D^{22}$= -71 (*c* 0.77, $CHCl_3$).

Synthesis of Methyl fmoc-threonine-(3,4-O-bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (23j):



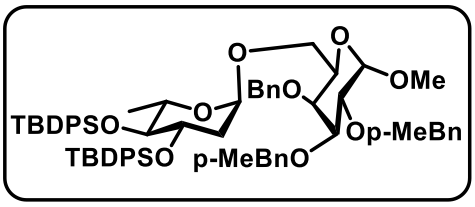
General procedure **B** was followed by taking glycosyl donor phenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside **22a** (50 mg, 0.070 mmol, 1.0 equiv) and glycosyl acceptor **21m** (37 mg, 0.105 mmol, 1.5 equiv) at -40° C to get the product **23j** as a colourless liquid. Rf- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 56 mg, yield- 83%. Re-purification was done using HPLC (retention time- 11 min). Selectivity α. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.64 (t, *J* = 7.8 Hz, 2H), 7.58 (d, *J* = 7.0 Hz, 2H), 7.51 (dd, *J* = 14.4, 7.2 Hz, 5H), 7.40 – 7.24 (m, 17H), 5.63 (d, *J* = 9.0 Hz, 1H), 4.93 (dd, *J* = 7.5, 3.6 Hz, 1H), 4.47 – 4.37 (m, 3H), 4.32 (dd, *J* = 9.1, 2.5 Hz, 1H), 4.27 (t, *J* = 7.1 Hz, 1H), 4.09 (d, *J* = 1.1 Hz, 1H), 3.72 (s, 3H), 3.70 – 3.67 (m, 1H), 3.57 – 3.55 (m, 1H), 1.80 – 1.74 (m, 1H), 1.60 (d, *J* = 4.3 Hz, 1H), 1.16 (d, *J* = 6.3 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 3H), 0.94 (s, 9H), 0.93 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 156.9, 144.0, 141.5, 135.9, 135.8, 135.8, 134.0, 133.6, 129.9, 129.8, 129.8, 129.8, 127.8, 127.8, 127.7, 127.7, 127.2, 125.3, 125.3, 120.1, 92.3, 75.4, 72.6, 72.5, 71.3, 67.3, 59.2, 52.4, 47.4, 27.0, 27.0, 19.4, 19.2, 18.2, 16.8. HRMS (ESI-QTOF) $C_{58}H_{67}NO_8Si_2NH_4$ $[M+NH_4]^+$- calculated- 979.4749; found- 979.4746. $[\alpha]_D^{22}$= -66 (*c* 0.61, $CHCl_3$).

Synthesis of 1-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3:4,5-Di-*O*-isopropylidene-α-D-fructopyranose (23k):



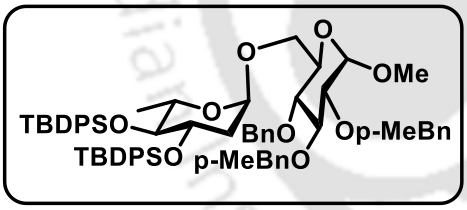
General procedure **B** was followed by taking glycosyl donor phenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside **22a** (50 mg, 0.070 mmol, 1.0 equiv) and glycosyl acceptor **21n** (27 mg, 0.105 mmol, 1.5 equiv) at -40° C to get the product **23k** as a colourless liquid. Rf- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 49 mg, yield- 79%. Re-purification was done using HPLC (retention time- 8 min). Selectivity α. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 6.9 Hz, 2H), 7.48 (dd, *J* = 18.0, 7.2 Hz, 5H), 7.38 (dd, *J* = 12.4, 6.6 Hz, 5H), 7.31 (dd, *J* = 13.7, 7.1 Hz, 4H), 7.26 (d, *J* = 4.8 Hz, 4H), 4.98 (dd, *J* = 7.0, 3.7 Hz, 1H), 4.62 (dd, *J* = 7.8, 2.1 Hz, 1H), 4.43 (d, *J* = 2.4 Hz, 1H), 4.24 (d, *J* = 8.4 Hz, 1H), 4.12 (s, 1H), 3.91 (d, *J* = 11.5 Hz, 1H), 3.84 – 3.82 (m, 1H), 3.80 – 3.77 (m, 1H), 3.74 (d, *J* = 12.8 Hz, 1H), 3.63 (d, *J* = 11.3 Hz, 1H), 3.57 (d, *J* = 3.4 Hz, 1H), 1.84 – 1.80 (m, 1H), 1.72 (dd, *J* = 9.5, 4.0 Hz, 1H), 1.52 (s, 3H), 1.46 (s, 3H), 1.35 (s, 3H), 1.28 (s, 3H), 1.09 (d, *J* = 6.7 Hz, 3H), 0.92 (s, 9H), 0.91 (s, 9H).^{13}C NMR (126 MHz, $CDCl_3$) δ 136.0, 135.9, 135.9, 135.8, 134.1, 134.1, 133.9, 133.7, 129.8, 129.8, 129.7, 129.7, 127.7, 127.7, 127.7, 127.6, 109.3, 109.1, 108.7, 108.6, 102.9, 95.8, 75.6, 72.5, 72.2, 71.3, 71.0, 70.4, 70.2, 70.1, 68.6, 65.8, 61.5, 61.2, 34.0, 27.1, 27.0, 27.0, 27.0, 26.6, 26.1, 25.9, 25.7, 25.5, 24.3, 24.1, 19.4, 19.2, 18.4. HRMS (ESI-QTOF) $C_{51}H_{70}O_9Si_2NH_4$ $[M+NH_4]^+$- calculated- 900.4902; found- 900.4900. $[\alpha]_D^{22}$= -59 (*c* 0.66, $CHCl_3$).

Synthesis of Methyl 6-O-(3,4-O-bis-(t-butyldiphenylsilyl)-2-deoxy-α-L-rhamnopyranosyl)-2,3-di-O-p-methylbenzyl-4-O-benzyl-D-galactopyranoside (23l):



General procedure **B** was followed by taking glycosyl donor phenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside **22a** (50 mg, 0.070 mmol, 1.0 equiv) and glycosyl acceptor **21o** (52 mg, 0.105 mmol, 1.5 equiv) at -40° C to get the product **23l** as a colourless liquid. Rf- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 49 mg, yield- 82%. Re-purification was done using HPLC (retention time- 11 min). Selectivity α. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 (d, *J* = 6.9 Hz, 2H), 7.48 – 7.43 (m, 6H), 7.39 – 7.20 (m, 21H), 7.16 (d, *J* = 7.7 Hz, 2H), 7.12 (d, *J* = 7.8 Hz, 2H), 4.94 (dd, *J* = 11.1, 5.9 Hz, 2H), 4.82 – 4.80 (m, 2H), 4.69 (d, *J* = 11.5 Hz, 1H), 4.64 (dd, *J* = 11.1, 8.5 Hz, 3H), 4.08 (s, 1H), 4.00 (dd, *J* = 10.0, 3.5 Hz, 1H), 3.91 (dd, *J* = 10.1, 2.5 Hz, 1H), 3.86 (s, 1H), 3.85 – 3.80 (m, 2H), 3.72 (dd, *J* = 10.3, 5.5 Hz, 1H), 3.56 (dd, *J* = 10.3, 6.9 Hz, 1H), 3.52 (s, 1H), 3.33 (s, 3H), 2.36 (s, 3H), 2.33 (s, 3H), 1.84 – 1.80 (m, 1H), 1.64 (s, 1H), 1.08 (d, *J* = 6.9 Hz, 3H), 0.92 (s, 9H), 0.90 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.8, 137.4, 137.2, 135.9, 135.8, 135.8, 135.8, 135.6, 133.9, 133.7, 133.6, 133.5, 129.8, 129.7, 129.7, 129.7, 129.2, 129.1, 128.4, 128.4, 128.3, 127.7, 127.7, 127.7, 127.6, 127.6, 127.6, 98.9, 95.2, 79.1, 76.2, 75.5, 74.8, 74.4, 73.6, 73.2, 73.0, 72.3, 69.8, 67.5, 55.3, 34.1, 27.0, 27.0, 26.9, 21.3, 19.3, 19.2, 18.1. HRMS (ESI-QTOF) $C_{68}H_{82}O_9Si_2NH_4$ $[M+NH_4]^+$- calculated- 1116.5841; found- 1116.5846. $[\alpha]_D^{22}$= -62 (*c* 0.79, $CHCl_3$).

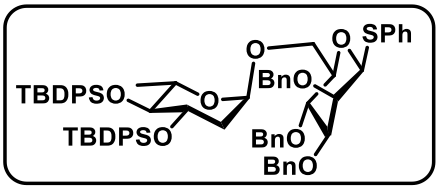
Synthesis of Methyl 6-O-(3,4-O-bis-(t-butyldiphenylsilyl)-2-deoxy-α-L-rhamnopyranosyl)-2,3-di-O-p-methylbenzyl-4-O-benzyl-D-glucopyranoside (23m):



General procedure **B** was followed by taking glycosyl donor phenyl 2,6-dideoxy-3,4-bis-O-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside **22a** (50 mg, 0.070 mmol, 1.0 equiv) and glycosyl acceptor **21p** (52 mg, 0.105 mmol, 1.5 equiv) at -40° C to get the product **23m** as a colourless liquid. Rf- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 47 mg, yield- 78%. Re-purification was done using HPLC (retention time- 12 min). Selectivity α. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 6.9 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 5H), 7.35 (dd, *J* = 12.7, 5.2 Hz, 4H), 7.28 – 7.17 (m, 18H), 7.13 (dd, *J* = 7.4, 5.4 Hz, 4H), 4.95 (dd, *J* = 11.1, 5.0 Hz, 2H), 4.83 (d, *J* = 10.8 Hz, 1H), 4.78 – 4.75 (m, 2H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.56 (d, *J* = 3.4 Hz, 1H), 4.48 (d, *J* = 10.8 Hz, 1H), 4.11 (d, *J* = 1.9 Hz, 1H), 3.97 (t, *J* = 9.4 Hz, 2H), 3.89 – 3.83 (m, 1H), 3.76 (dd, *J* = 9.9, 3.7 Hz, 1H), 3.59 (dd, *J* = 11.0, 5.0 Hz, 1H), 3.54 – 3.49 (m, 2H), 3.44 (t, *J* = 9.5 Hz, 1H), 3.34 (s, 3H), 2.35 (s, 3H), 2.33 (s, 3H), 1.89 (ddd, *J* = 13.2, 7.9, 2.5 Hz, 1H), 1.66 (dt, *J* = 13.5, 3.7 Hz, 1H), 1.09 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 9H), 0.87 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.5, 137.7, 137.3, 136.1, 135.9, 135.9, 135.8, 135.7, 135.4, 134.0, 133.8, 133.8, 133.7, 129.8, 129.7, 129.3, 129.2, 128.5, 128.4, 128.2, 127.9, 127.8, 127.7, 127.7, 127.6, 98.2, 95.8, 82.1, 79.8, 78.1, 75.7, 75.3, 75.1, 73.3, 72.5, 72.5, 70.3, 66.9, 55.1, 34.0, 27.0, 21.3, 21.3, 19.3, 19.2, 18.4.

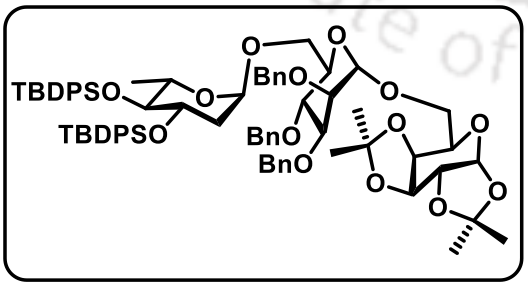
HRMS (ESI-QTOF) $C_{68}H_{82}O_9Si_2NH_4$ $[M+NH_4]^+$- calculated- 1116.5841; found- 1116.5842. $[\alpha]_D^{22}$= -77 (*c* 0.70, $CHCl_3$).

Synthesis of Phenyl 2,3,4-tri-O-benzyl-6-O-(3,4-O-bis-(t-butyldiphenylsilyl)-2-deoxy-α-L-rhamnopyranosyl)-β-D-thioglucopyranoside (23n):



General procedure **A** was followed by taking glycosyl donor 2,6-dideoxy-3,4-O-bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl-1-acetate **22a** (50 mg, 0.075 mmol, 1.0 equiv) and glycosyl acceptor **21q** (163 mg, 0.3 mmol, 4.0 equiv) and then the reaction mixture was allowed to stir under argon for 30 min followed by addition of $BF_3.Et_2O$ (16 mg, 14 µL, 0.11 mmol, 1.5 equiv). After complete consumption of starting material (monitored by TLC) the reaction mixture was filtered through sintered funnel, washed with DCM and quenched with sat. $NaHCO_3$ solution. After work up the organic phase was dried over Na_2SO_4, filtered and concentrated. The crude was purified by column chromatography in ethyl acetate/hexane solvent system to give product **23n** as colourless oil. R_f- 0.5 (10% hexane in ethylacetate), amount- 69 mg, yield- 79%. Selectivity α. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53 (d, *J* = 6.9 Hz, 2H), 7.48 – 7.44 (m, 7H), 7.37 – 7.20 (m, 30H), 5.58 (s, 1H), 4.99 (dd, *J* = 7.7, 3.8 Hz, 1H), 4.92 (d, *J* = 10.7 Hz, 1H), 4.74 (d, *J* = 12.5 Hz, 1H), 4.58 (ddd, *J* = 26.5, 13.6, 8.2 Hz, 4H), 4.33 – 4.31 (m, 1H), 4.11 (d, *J* = 11.4 Hz, 2H), 4.00 (s, 1H), 3.95 (t, *J* = 9.5 Hz, 1H), 3.88 – 3.85 (m, 2H), 3.70 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.53 (d, *J* = 3.2 Hz, 1H), 1.92 (ddd, *J* = 13.2, 7.9, 2.3 Hz, 1H), 1.78 – 1.74 (m, 1H), 1.08 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.88 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.5, 138.3, 137.9, 135.9, 135.8, 135.8, 134.3, 133.9, 133.8, 133.7, 133.6, 132.3, 129.8, 129.7, 129.6, 129.1, 128.5, 128.5, 128.5, 128.1, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 96.0, 85.7, 80.2, 76.0, 75.5, 75.3, 75.3, 72.7, 72.6, 72.1, 72.1, 71.8, 67.2, 33.8, 31.1, 29.9, 19.3, 19.2, 18.5. HRMS (ESI-QTOF) $C_{72}H_{84}O_8SSi_2Na$ $[M+Na]^+$- calculated- 1187.5323; found- 1187.4726. $[\alpha]_D^{22}$= -70 (*c* 0.65, $CHCl_3$).

Synthesis of Trisaccharide (30):



General procedure **B** was followed by taking glycosyl donor **23n** (50 mg, 0.043 mmol, 1.0 equiv) and glycosyl acceptor **21i** (17 mg, 0.064 mmol, 1.5 equiv) at -40° C to get the product **5a** as a colourless liquid. Rf- 0.4 in 10% EA/hexane, eluent 5% EA in hexane, amount- 41 mg, yield- 72%. Re-purification was done using HPLC (retention time- 10 min). Selectivity αα: αβ= 9.5:1. αα-anomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.0 Hz, 2H),

7.46 (t, *J* = 6.4 Hz, 6H), 7.39 (d, *J* = 7.4 Hz, 2H), 7.34 – 7.27 (m, 15H), 7.22 (dd, *J* = 16.2, 8.8 Hz, 10H), 5.52 (d, *J* = 4.6 Hz, 1H), 5.00 (s, 2H), 4.87 (d, *J* = 10.7 Hz, 1H), 4.73 (q, *J* = 12.4 Hz, 2H), 4.60 – 4.58 (m, 3H), 4.52 (d, *J* = 10.6 Hz, 1H), 4.31 – 4.30 (m, 1H), 4.16 – 4.13 (m, 2H), 4.08 (d, *J* = 10.9 Hz, 1H), 3.95 (t, *J* = 6.6 Hz, 1H), 3.90 (d, *J* = 7.4 Hz, 2H), 3.88 – 3.83 (m, 2H), 3.80 – 3.76 (m, 2H), 3.68 (dd, *J* = 10.3, 6.5 Hz, 2H), 3.54 (s, 1H), 1.93 (dd, *J* = 13.3, 8.0 Hz, 1H), 1.75 (d, *J* = 13.4 Hz, 1H), 1.50 (s, 3H), 1.43 (s, 3H), 1.32 (s, 3H), 1.10 (d, *J* = 6.5 Hz, 3H), 0.91 (s, 9H), 0.89 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.8, 138.7, 138.6, 136.0, 136.0, 135.9, 135.8, 134.1, 134.0, 133.8, 133.8, 129.8, 129.7, 129.6, 128.4, 128.1, 128.0, 127.8, 127.7, 127.7, 127.6, 127.6, 109.5, 108.7, 97.4, 96.5, 96.0, 80.2, 75.6, 75.3, 75.2, 74.8, 72.7, 72.5, 72.2, 72.2, 72.2, 71.1, 70.9, 70.8, 67.4, 65.4, 34.0, 27.1, 27.1, 26.3, 26.2, 25.1, 24.8, 19.4, 19.2, 18.6. HRMS (ESI-QTOF) $C_{79}H_{102}O_{14}Si_2H$ $[M+H]^+$- calculated- 1331.6886; found- 1331.6713. $[\alpha]_D^{22}$= -42 (*c* 0.31, $CHCl_3$).

5.8 References

1. (a) He, X. M.; Liu, H. W. *Curr. Opin. Chem. Biol.* **2002**, *6*, 590-7.

(b) Lindhorst, T. K.; Fraser-Reid, B.; Tatsuta, K., *Thiem, J. Eds. Springer: Berlin*, **2001**; 2393.

2. McCranie, E. K.; Bachmann, B. O. *Nat. Prod. Rep.* **2014**, *31*, 1026-42.

3. (a) Balmond, E. L.; Galan, M. C.; McGarrigle, E. M. *Synlett* **2013**, *24*, 2335-9 and references therein.

(b) Issa, J. P.; Lloyd, D.; Steliotes, E.; Bennett, C. S. *Org. Lett.* **2013**, *15*, 4170-3. (c) Zhu, D.; Baryal, K. N.; Adhikari, S.; Zhu, J. *J. Am. Chem. Soc.* **2014**, 136, 3172-5. (d) Kaneko, M.; Herzon, S. B. *Org. Lett.* **2014**, *16*, 2776-9. (e) Chen, J. H.; Ruei, J. H.; Mong, K. K. T. *Eur. J. Org. Chem.* **2014**, *2014*, 1827-31. (f) Issa, J. P.; Bennett, C. S. *J. Am. Chem. Soc.* **2014**, *136*, 5740-4. (g) Wang, H.; Tao, J. Y.; Cai, X. P.; Chen, W.; Zhao, Y. Q.; Xu, Y.; Yao, W.; Zeng, J.; Wan, Q. *Chem. Eur. J.* **2014**, *20*, 17319-23. (h) Das, S.; Pekel, D.; Neudorfl, J. M.; Berkessel, A. *Angew. Chem., Int. Ed.* **2015**, *54*, 12479-83. (i) Medina, S.; Galan, M. C. *Carbohydrate Chemistry; Royal Society of Chemistry: Cambridge, U.K.*, **2016**; *41*, 59. (j) Hsu, M. Y.; Liu, Y. P.; Lam, S.; Lin, S. C.; Wang, C. C. *Beilstein J. Org. Chem.* **2016**, *12*, 1758-64. (k) Hou, D. J.; Lowary, T. L. *Carbohydr. Res.* **2009**, *344*, 1911-40.

4. Benito-Alfonso, D.; Galan, M. C. *Selective Glycosylations- Synthetic Methods and Catalysts*; Bennet, C., Ed.; Wiley-VCH, **2017**, 155-72.

5. (a) Marzabadi, C.H.; Franck, R.W. *Tetrahedron* **2000**, *56*, 8385-417.

(b) Williams, R.; Galan, M. C. *Eur. J. Org. Chem.* **2017**, *2017*, 6247−64.

6.(a) Ghosh, T.; Mukherji, A.; Kancharla, P. K. *Org. Lett.* **2019,** *21*, 3490-5.

(b) Nieto C. P.; Sau, A.; Galan, M. C. *J. Am. Chem. Soc.* **2017**, *139*, 14041−4.

(c) Sau, A.; Nieto, C. P.; Galan, M. C. *J. Org. Chem.* **2019**, *84*, 2415−24.

(d) Nieto, C. P.; Sau, A.; Williams, R.; Galan, M. C. *J. Org. Chem.* **2017**, *82*, 407−14.

7. (a) Thiem, J.; Klafke, W. *Top. Curr. Chem.*, **1990**, *154*, 285.

(b) Toshima, K.; Tatsuta, K. *Chem. Rev.*, **1993**, *93*, 1503-31.

8. (a) Fraser-Reid, B.; Jayaprakash, K. N.; Lopez, J. C.; Gomez, A. M.; Uriel, C. *Frontiers in Modern Carbohydrate Chemistry*; (b) Demchenko, A. V., Ed.; *American Chemical Society: Washington, DC*, **2007**, 91.

9. Rohr, J.; Thiericke, R. *Nat. Prod.* **1992**, *9*, 103−37.

10. Lu, Y. S.; Li, Q.; Zhang, L. H.; Ye. X. S. *Org. Lett.* **2008**, *10*, 3445–48.

11. Beale, T. M.; Moon, P. J.; Taylor, M. S. *Org. Lett.* **2014**, *16*, 3604–07.

12. Nogueira, J. M.; Nguyen, S. H.; Bennett, C. S. *Org. Lett.* **2011**, *13*, 2814–17.

13. Balmond, E. I.; Coe, D. M.; Galan, M. C.; McGarrigle, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 9152−55.

14. Sun, L.; Wu, X.; Xiong, D. C.; Ye, X. S. *Angew. Chem., Int. Ed.* **2016**, *55*, 8041−44.

15. Ghosh, T.; Mukherji, A.; Srivastava, H. K.; Kancharla, P. K. *Org. Biomol. Chem.* **2018,** *16*, 2870–75.

16. a) Ferrier, R. J.; Furneaux, R. H. *J. Chem. Soc. Perk. T. 1* **1977**, 1993-6; b) Hou, D. J.; Lowary, T. L. *Carbohydr. Res.* **2009**, *344*, 1911-40.

17. Dharuman, S.; Crich, D. *Chem. Eur. J.* **2016**, *22*, 4535-42.

18. Tanaka, H.; Yoshizawa, A.; Takahashi, T. *Angew., Chem., Int. Ed.* **2007**, *119*, 2557–59.

19. Bandi, R.; Chalapala, S.; Chandrasekaran, S. *Org. Biomol. Chem.*, **2018**, *16*, 2248–57.

20. Zhao, G.; Wang T.; *Angew. Chem. Int. Ed.* **2018**, *57*, 6120-4.

21. Balmond, E. I.; Alfonso, D. B.; Coe, D. M.; Alder, R. W.; McGarrigle, E. M.; Galan, M. C. *Angew. Chem. Int. Ed.* **2014**, *53*, 8190-4.

22. Wang, J.; Deng, C.; Zhang, Q.; Chai, Y. *Org. Lett.* **2019**, *21*, 1103−7.

23. Liang, X. Y.; Bin, H. C.; Yang J. S. *Org. Lett.* **2013**, *15*, 2834-7.

24. Mukherji, A.; Kancharla, P. K. *Org. Lett.* **2020**, *22*, 2191–5.

25. Sakurai, K.; Kahne. D.; *Tetrahedron Lett.* **2010**, *51*, 3724-7.

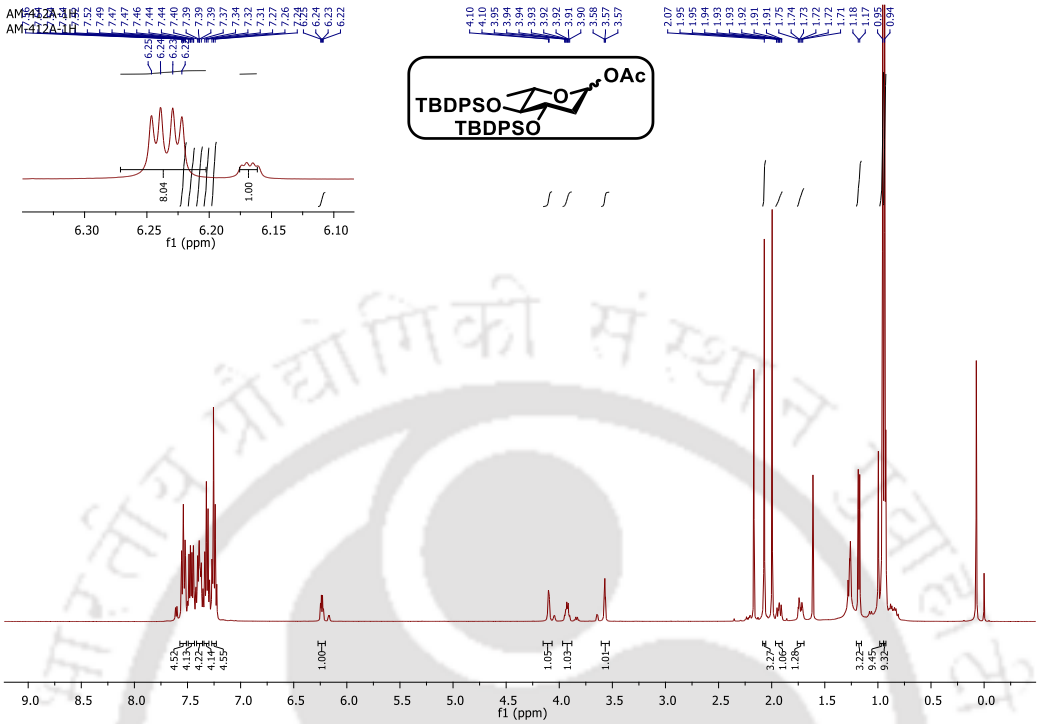
26. Meng, B.; Zhua, Z.; Baker, D. C. *Org. Biomol. Chem*., **2014**, *12*, 5182-91.

27. Shinozuka, T. *ACS Omega* **2020**, *5*, 33196–205.

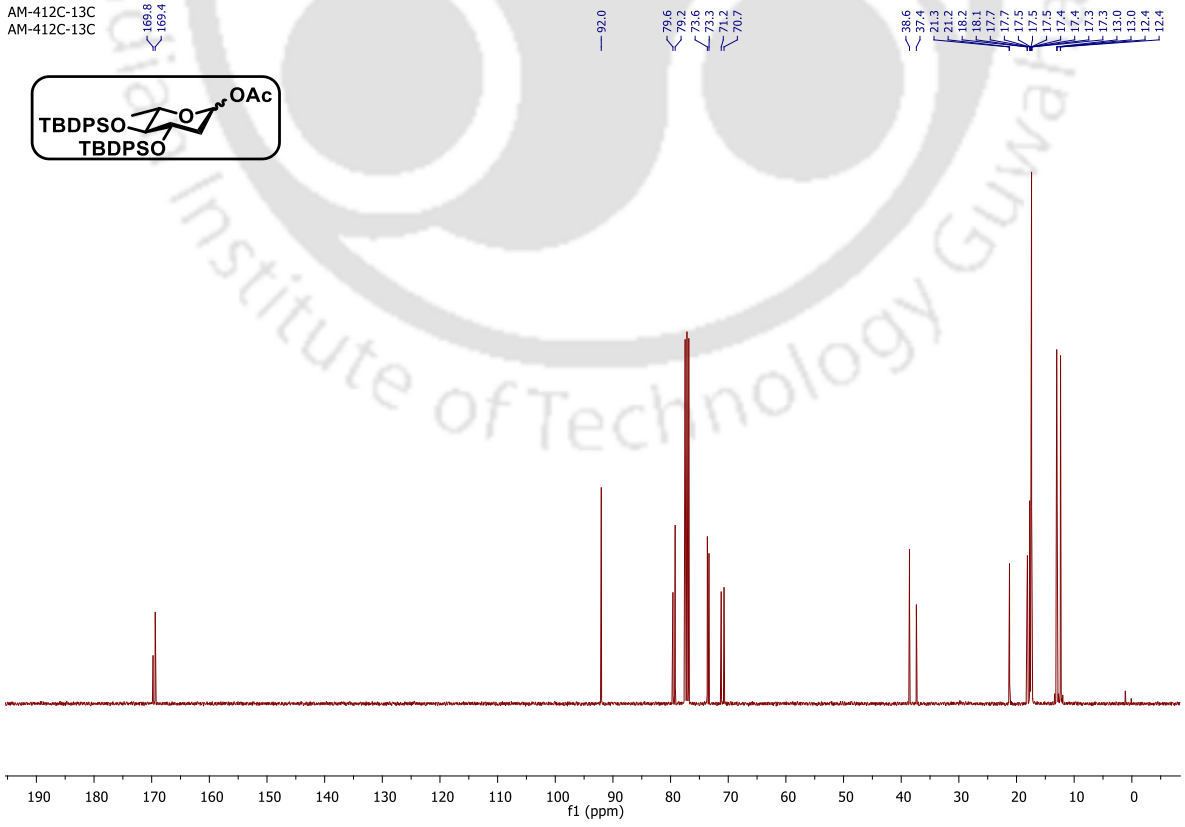
28. Baryal, K. N.; Zhu, D.; Li, X.; Zhu, J. *Angew. Chem. Int. Ed.* **2013**, *52*, 8012-6.

5.9 Spectra

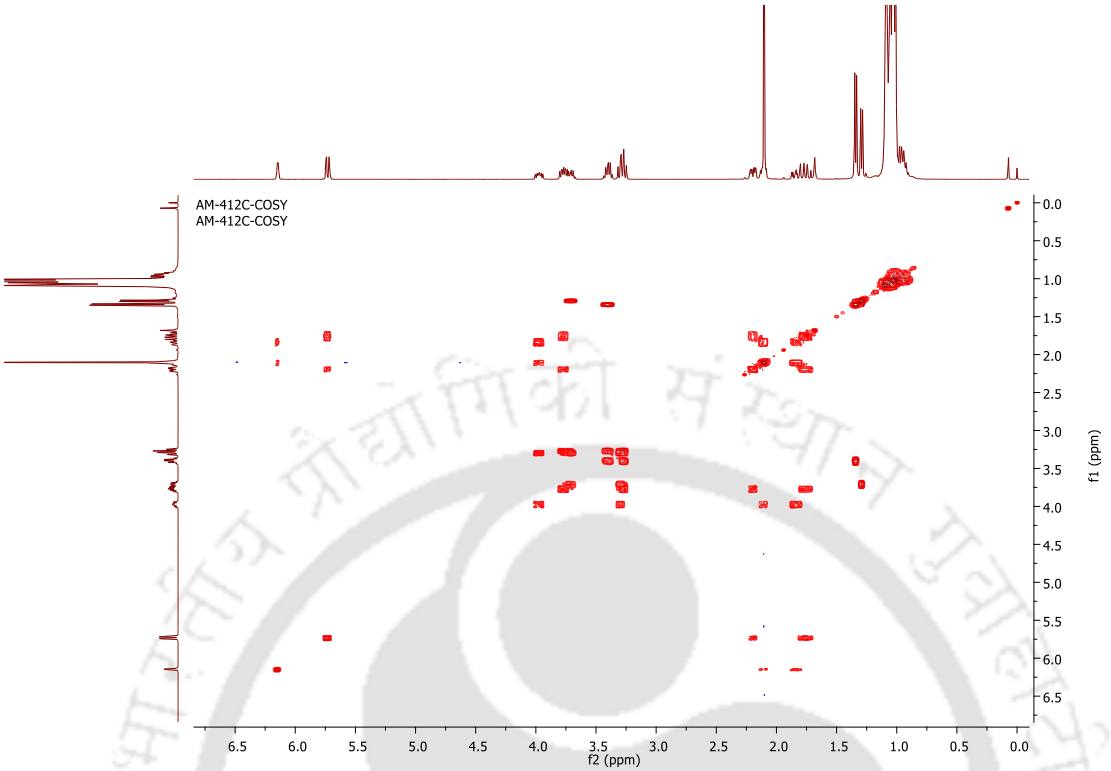
^{1}H NMR of 2,6-dideoxy-3,4-O-bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl-1-acetate (20a, 500 MHz, $CDCl_3$):



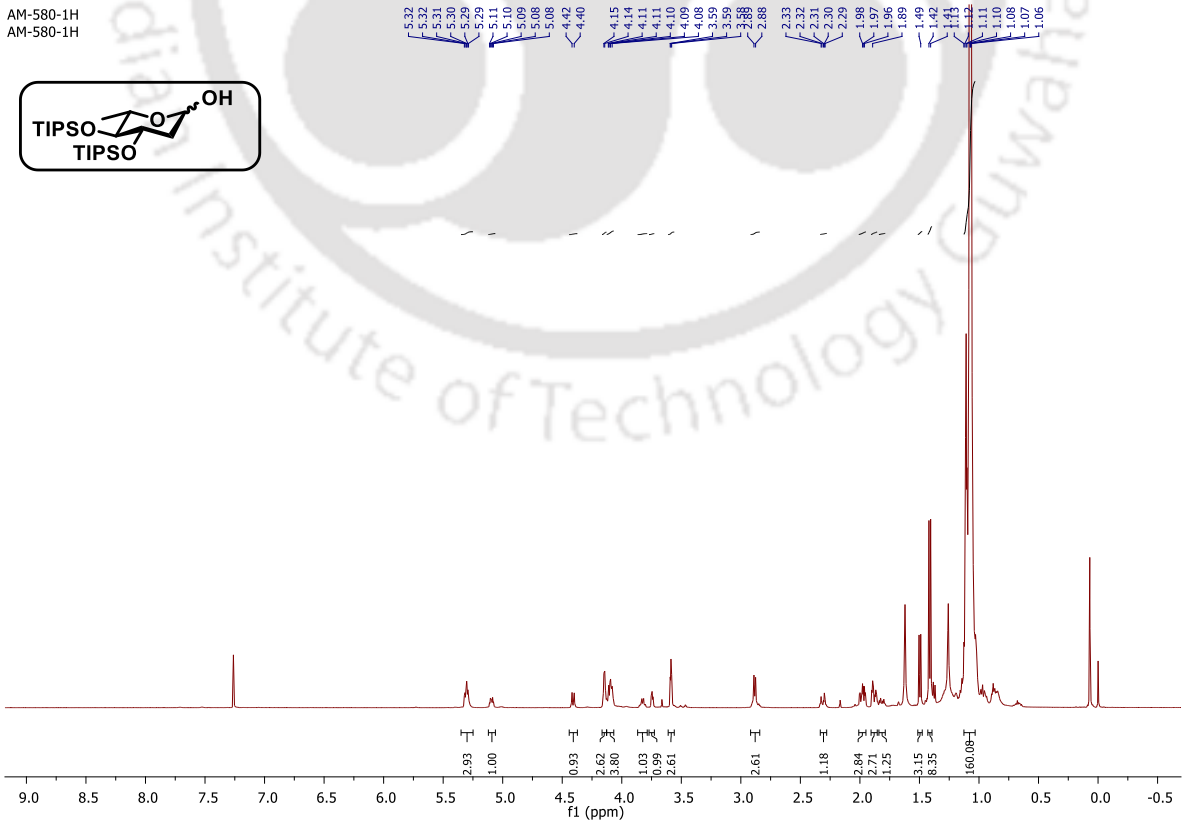
^{13}C NMR of 2,6-dideoxy-3,4-O-bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl-1-acetate (20a, 400 MHz, $CDCl_3$):



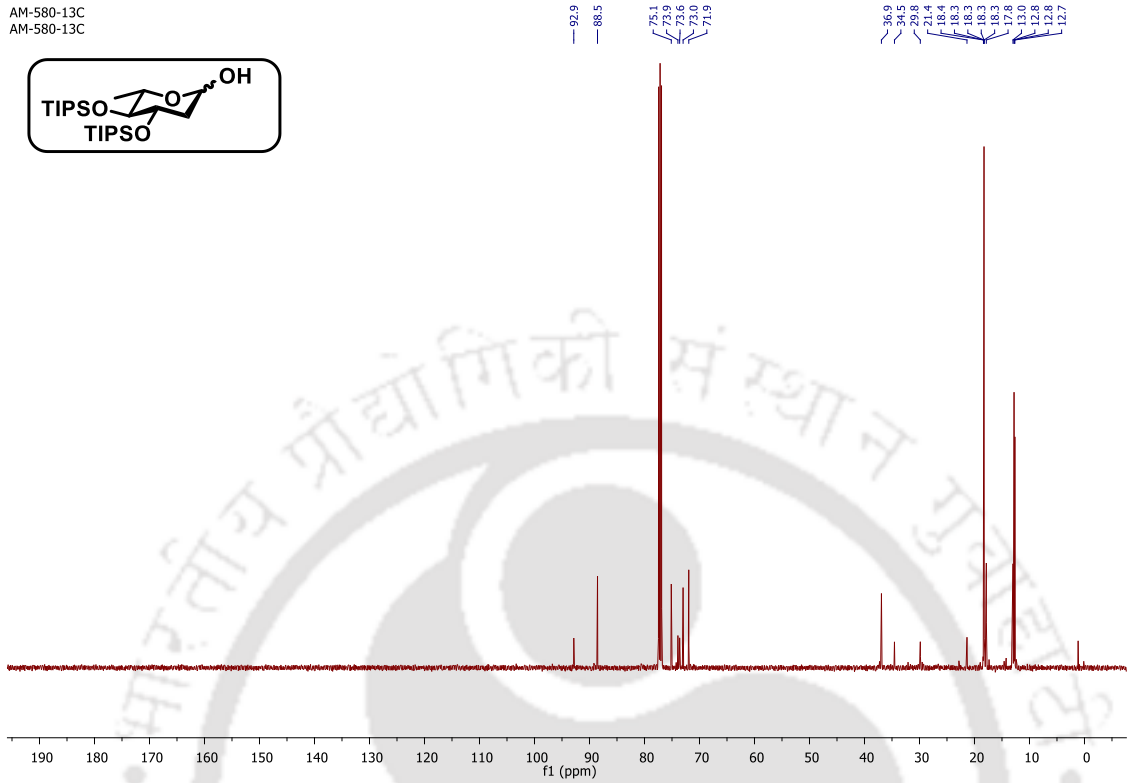
COSY NMR of 2,6-dideoxy-3,4-O-bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl-1-acetate (20a, 400 MHz, $CDCl_3$):



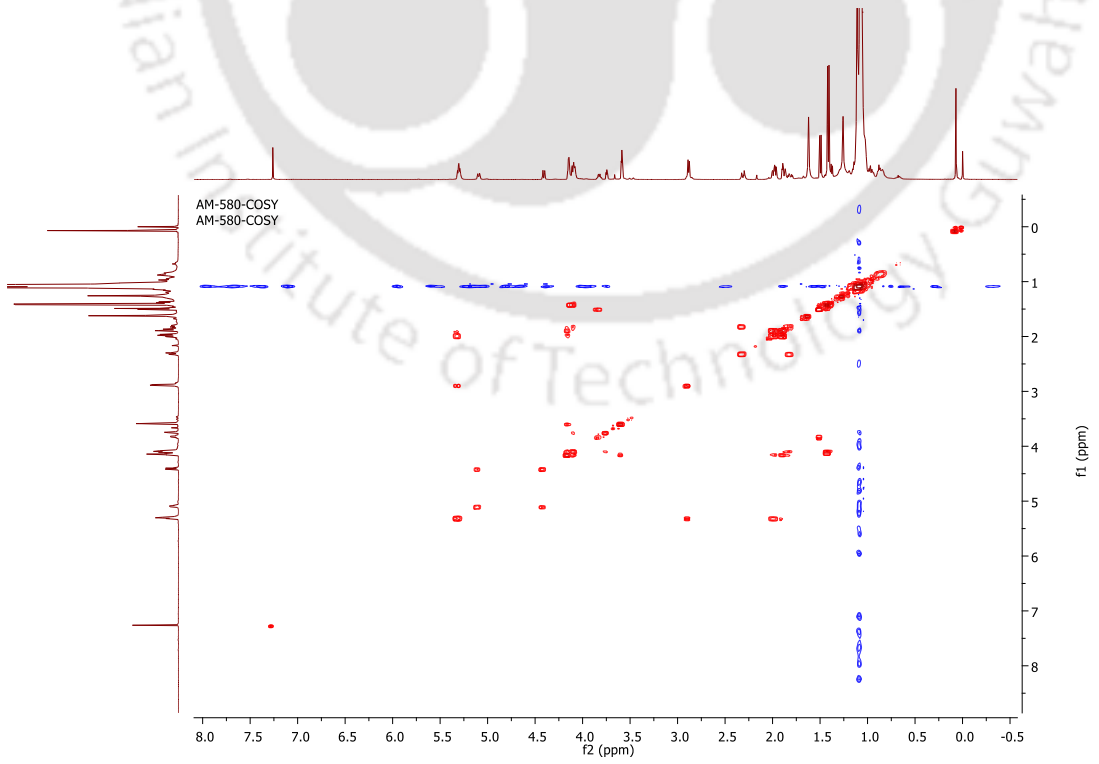
^{1}H NMR of 2,6-dideoxy-3,4-O-bis-(triisopropylsilyl)-2-deoxy-α,β-L-rhamnopyranose (500 MHz, $CDCl_3$):



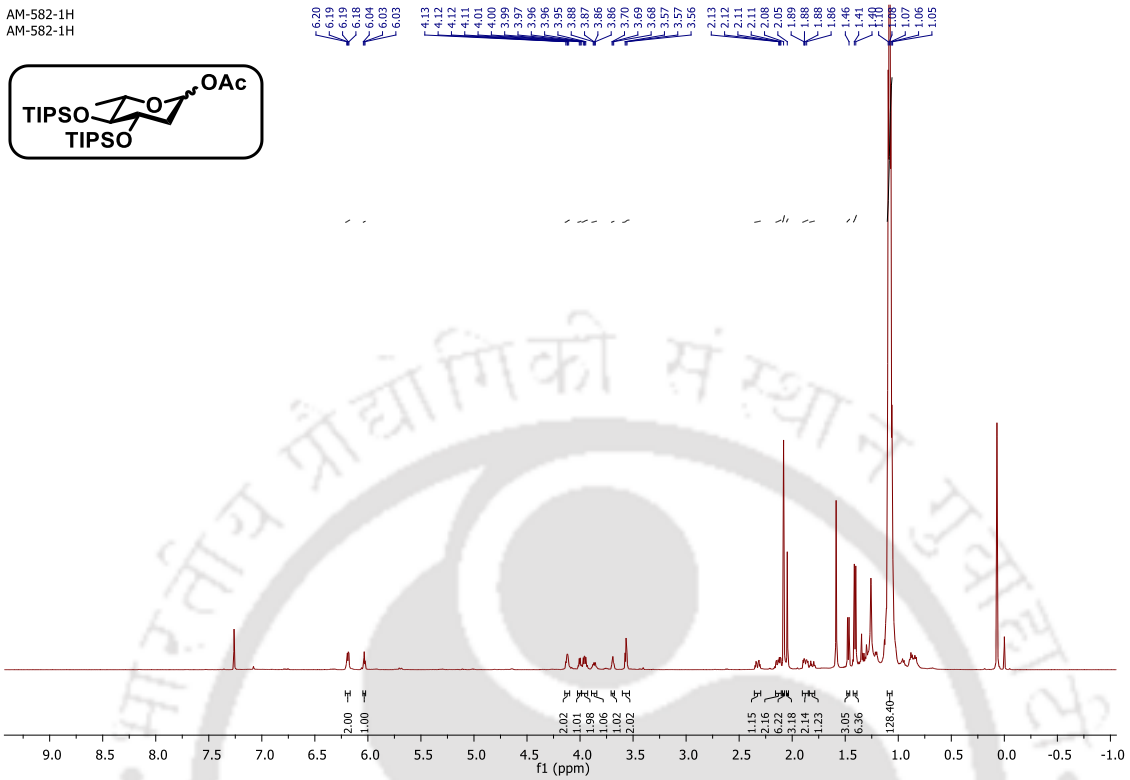
^{13}C NMR of 2,6-dideoxy-3,4-O-bis-(triisopropylsilyl)-2-deoxy-α,β-L-rhamnopyranose (500 MHz, $CDCl_3$):



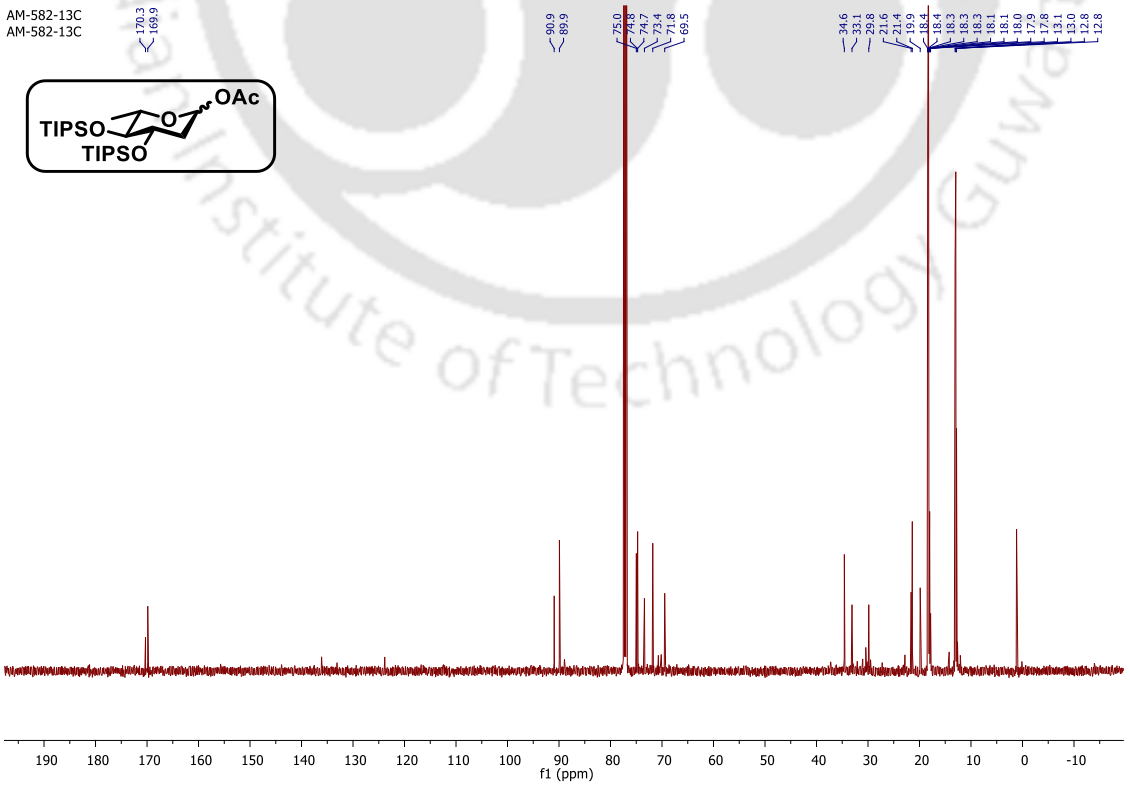
COSY NMR of 2,6-dideoxy-3,4-O-bis-(triisopropylsilyl)-2-deoxy-α,β-L-rhamnopyranose (500 MHz, $CDCl_3$):



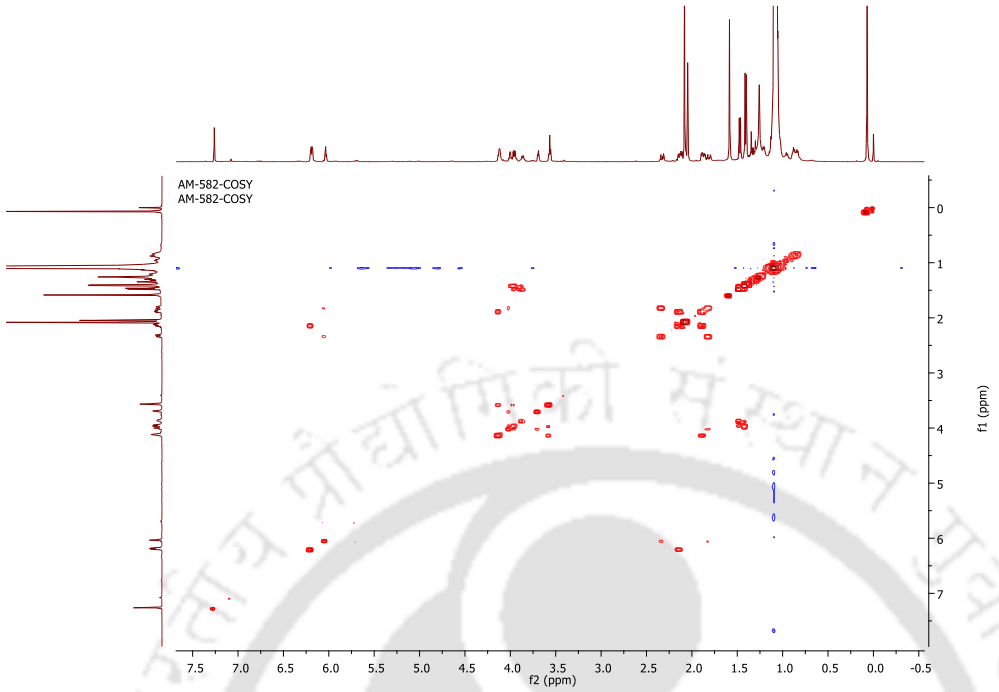
^{1}H NMR of 2,6-dideoxy-3,4-O-bis-(triisopropylsilyl)-2-deoxy-α,β-L-rhamnopyranosyl-1-acetate (20b, 500 MHz, $CDCl_3$):



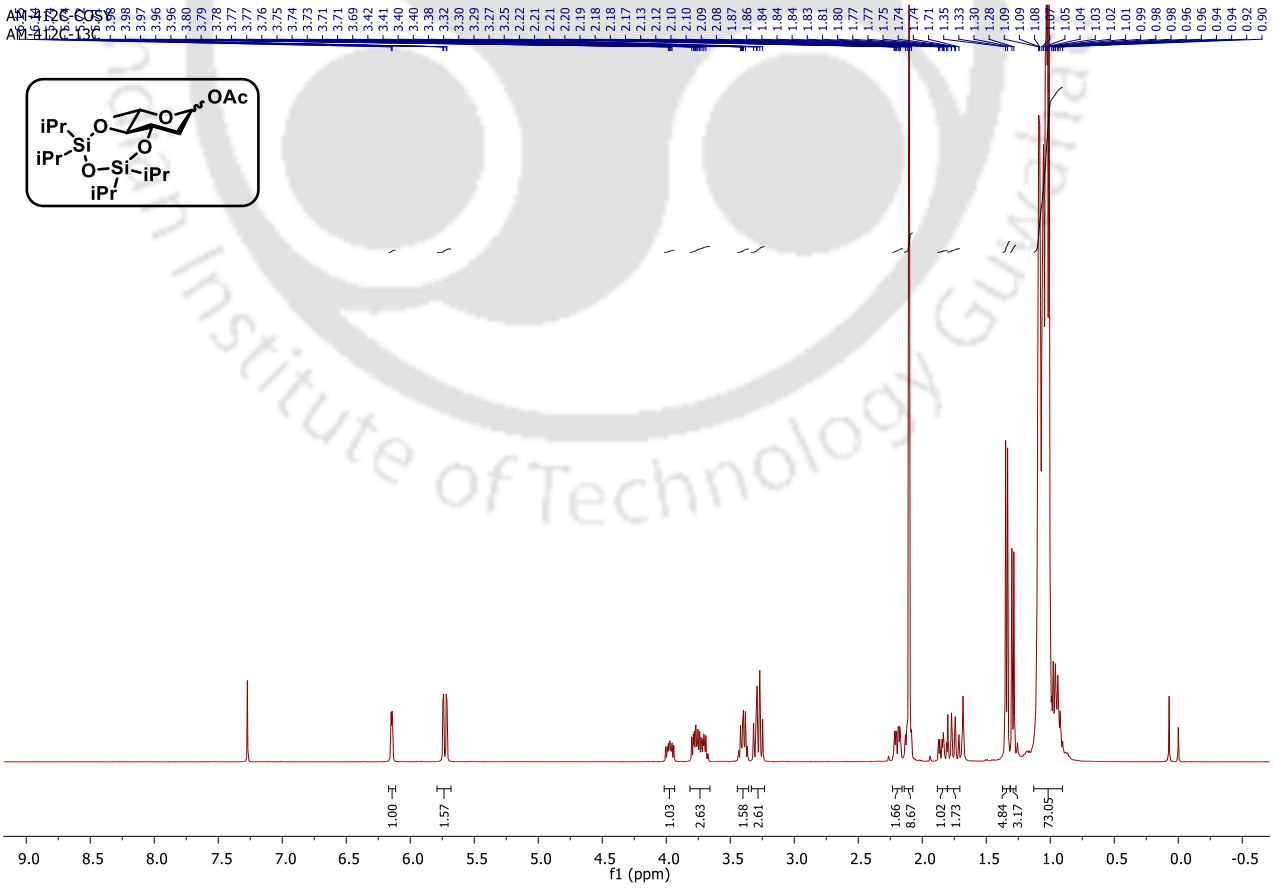
^{13}C NMR of 2,6-dideoxy-3,4-O-bis-(triisopropylsilyl)-2-deoxy-α,β-L-rhamnopyranosyl-1-acetate (20b, 500 MHz, $CDCl_3$):



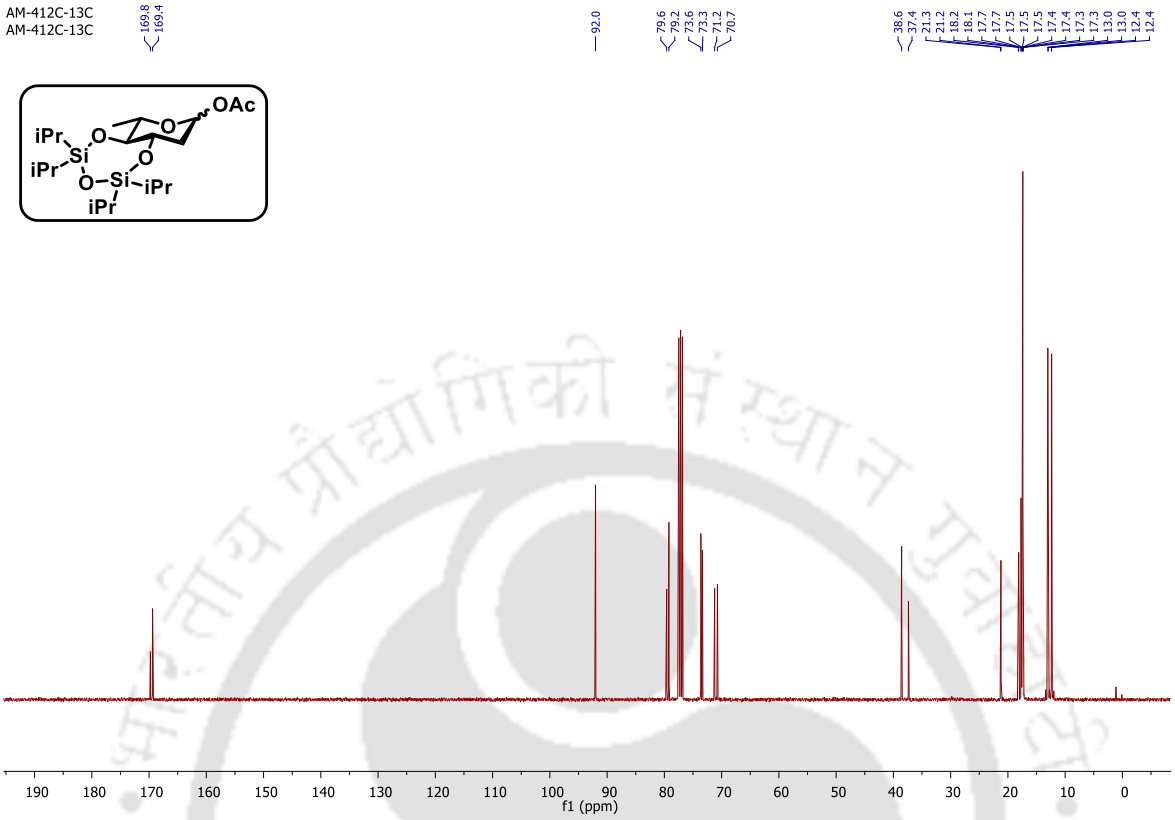
COSY NMR of 2,6-dideoxy-3,4-O-bis-(triisopropylsilyl)-2-deoxy-α,β-L-rhamnopyranosyl-1-acetate (20b, 500 MHz, $CDCl_3$):



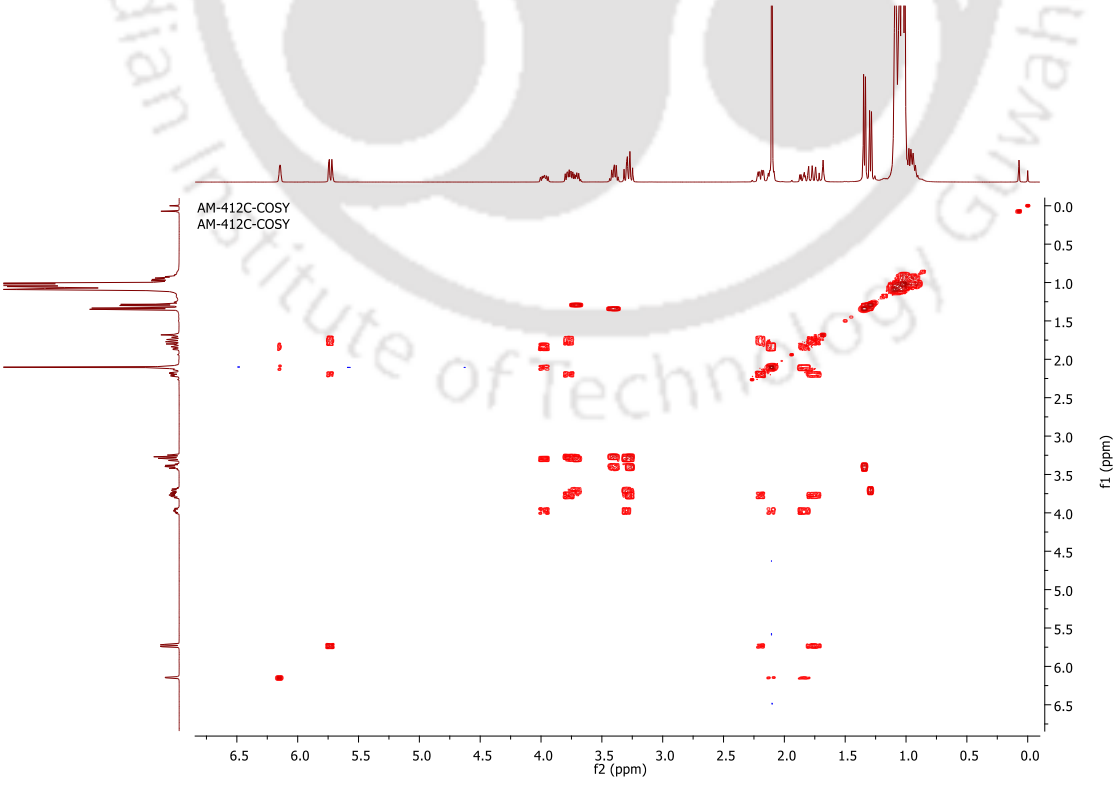
^{1}H NMR of 2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-rhamnopyranosyl-1-acetate (20c, 400 MHz, $CDCl_3$):



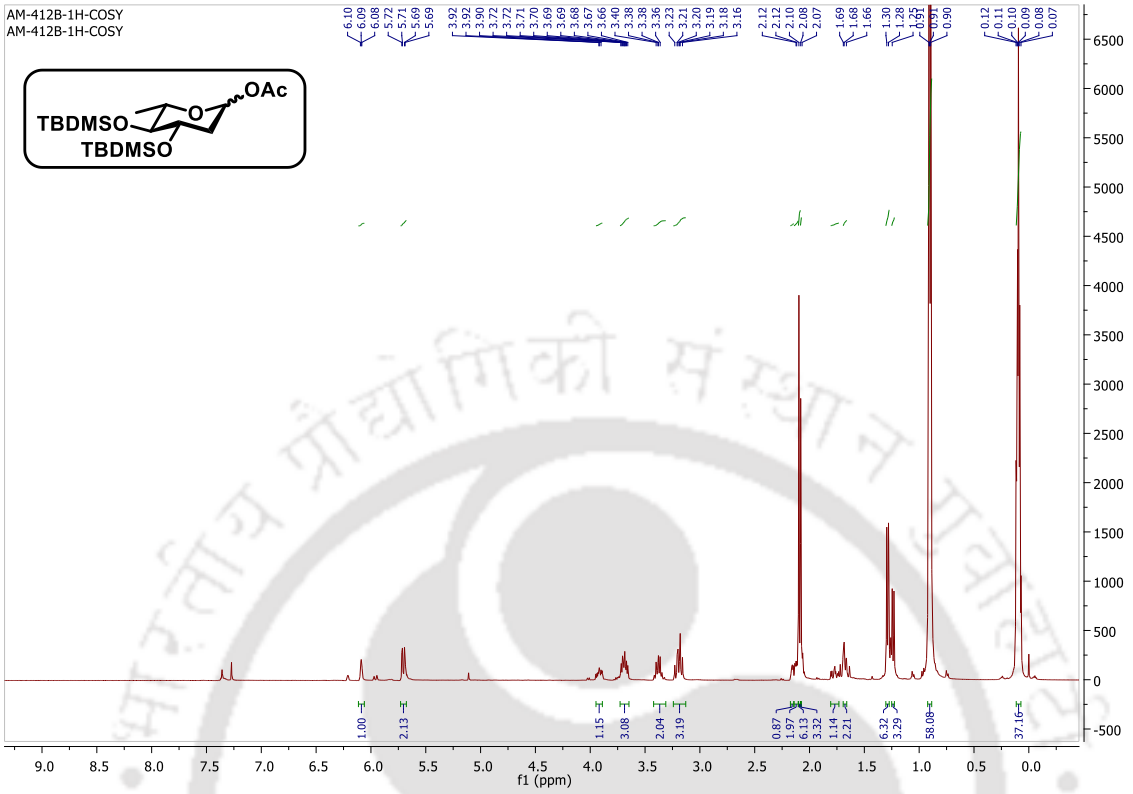
^{13}C NMR of 2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-rhamnopyranosyl-1-acetate (20c, 400 MHz, $CDCl_3$):



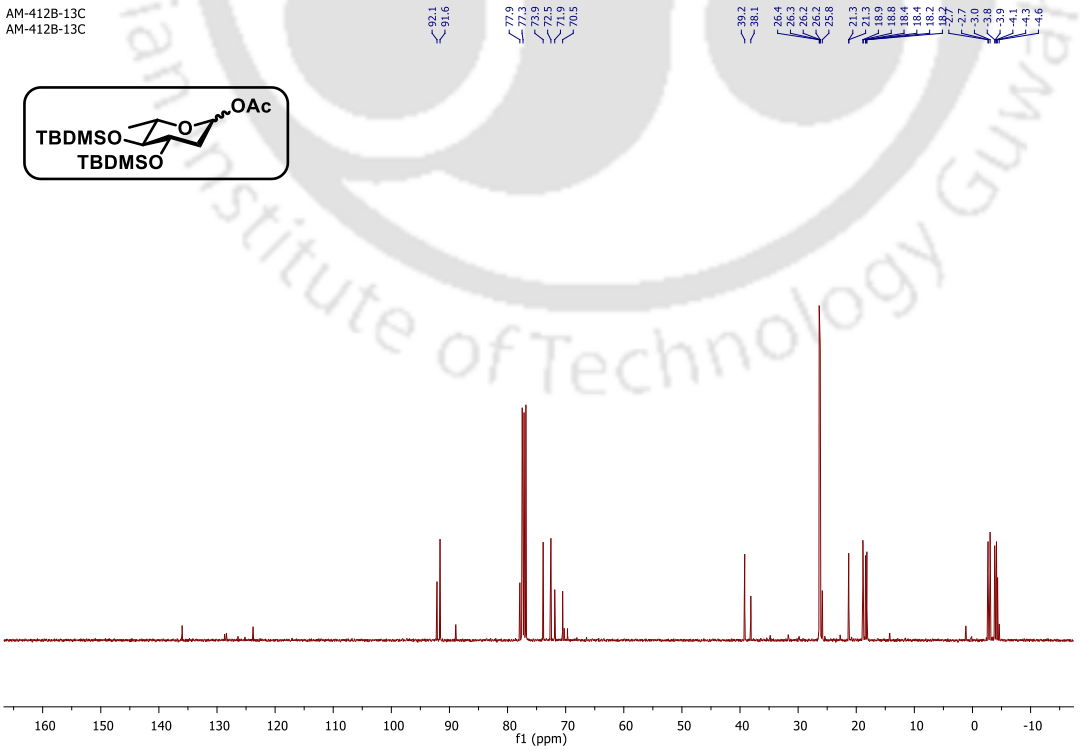
COSY NMR of 2,6-dideoxy-3,4-O-(tetraisopropyldisiloxane-1,3-diyl)-L-rhamnopyranosyl-1-acetate (20c, 400 MHz, $CDCl_3$):



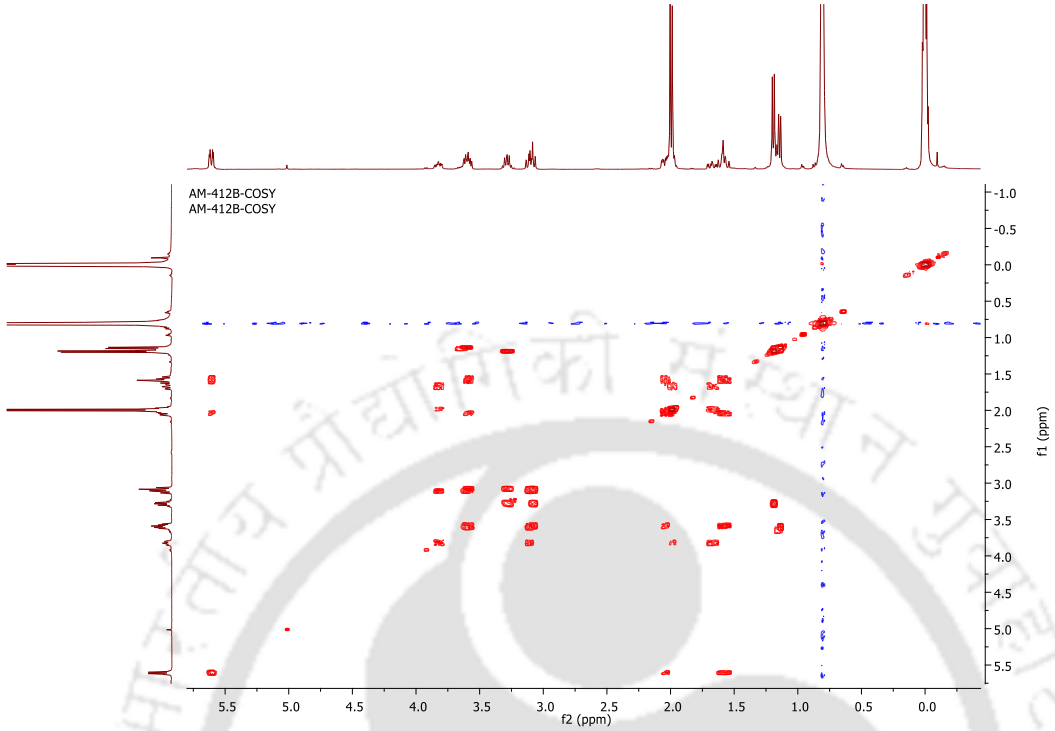
^{1}H NMR of 2,6-dideoxy-3,4-di-*O*-*tert*-butyldimethylsilyl-L-rhamnopyranosyl-1-acetate (20d, 400 MHz, $CDCl_3$):



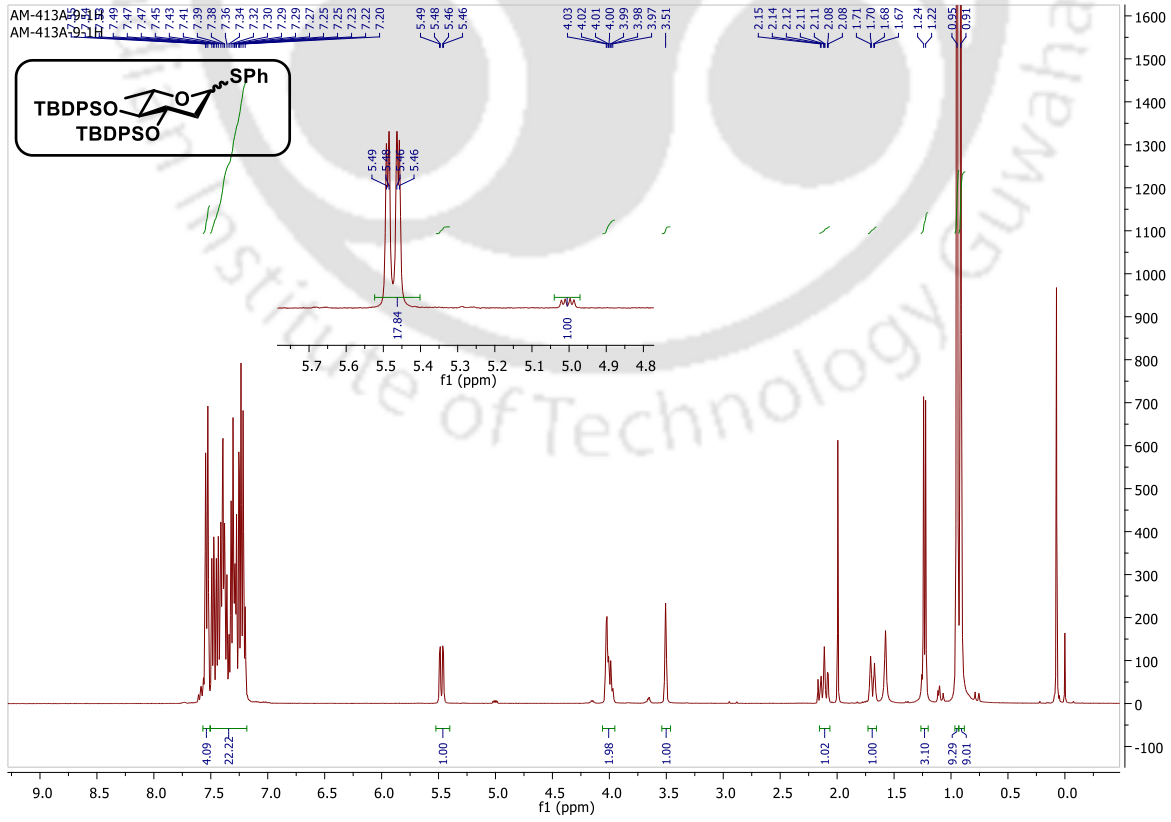
^{13}C NMR of 2,6-dideoxy-3,4-di-*O*-*tert*-butyldimethylsilyl-L-rhamnopyranosyl-1-acetate (20d, 400 MHz, $CDCl_3$):



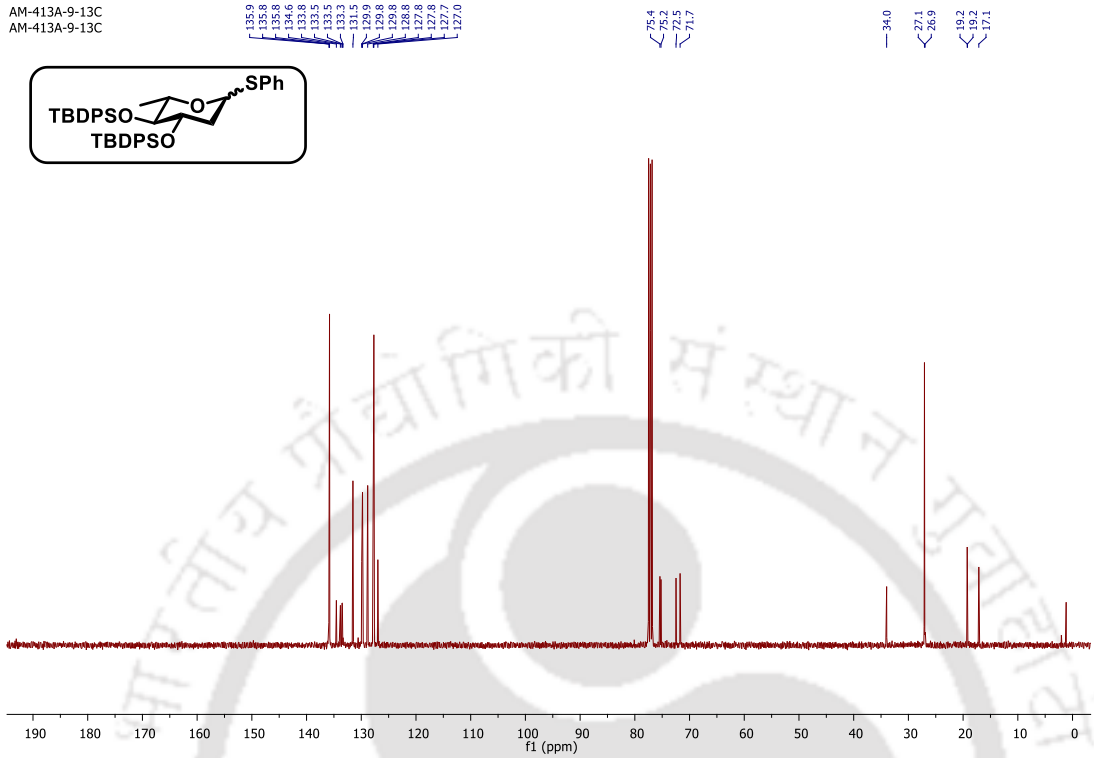
COSY NMR of 2,6-dideoxy-3,4-di-*O*-*tert*-butyldimethylsilyl-L-rhamnopyranosyl-1-acetate (20d, 400 MHz, $CDCl_3$):



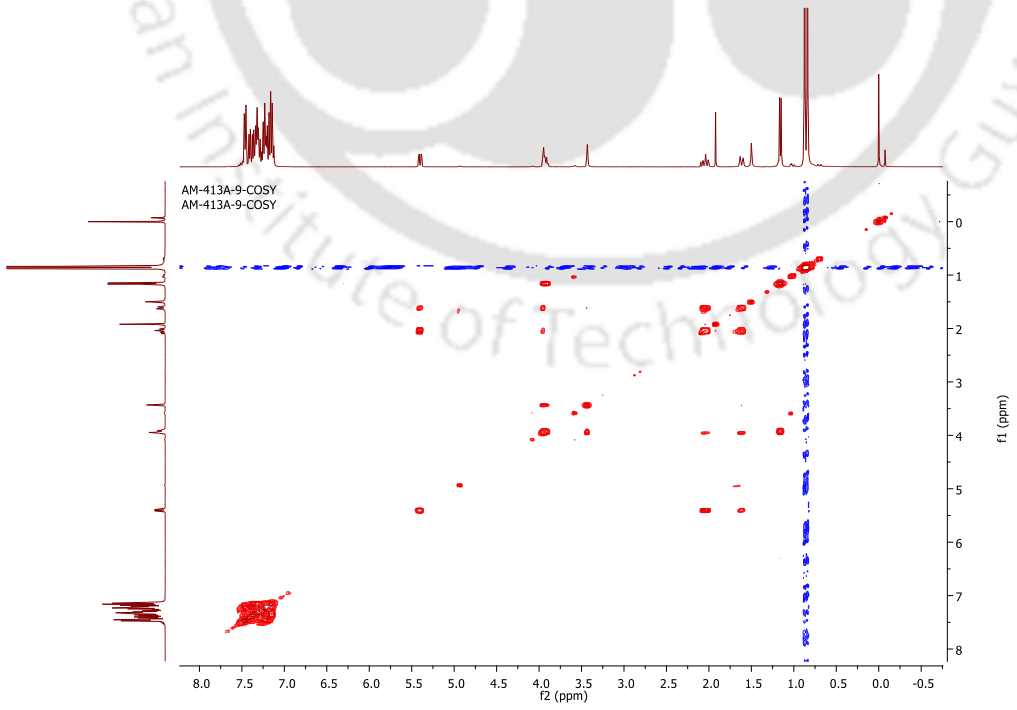
^{1}H NMR of Phenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (22a, 400 MHz, $CDCl_3$):



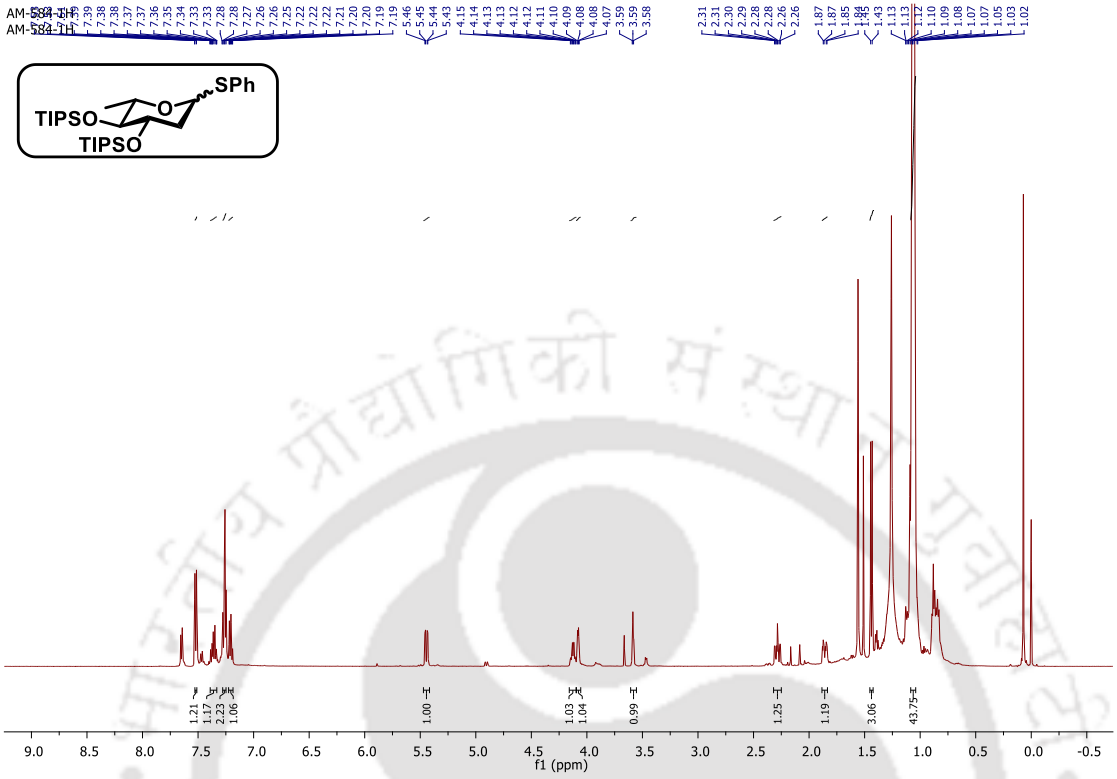
^{13}C NMR of Phenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (22a, 400 MHz, $CDCl_3$):



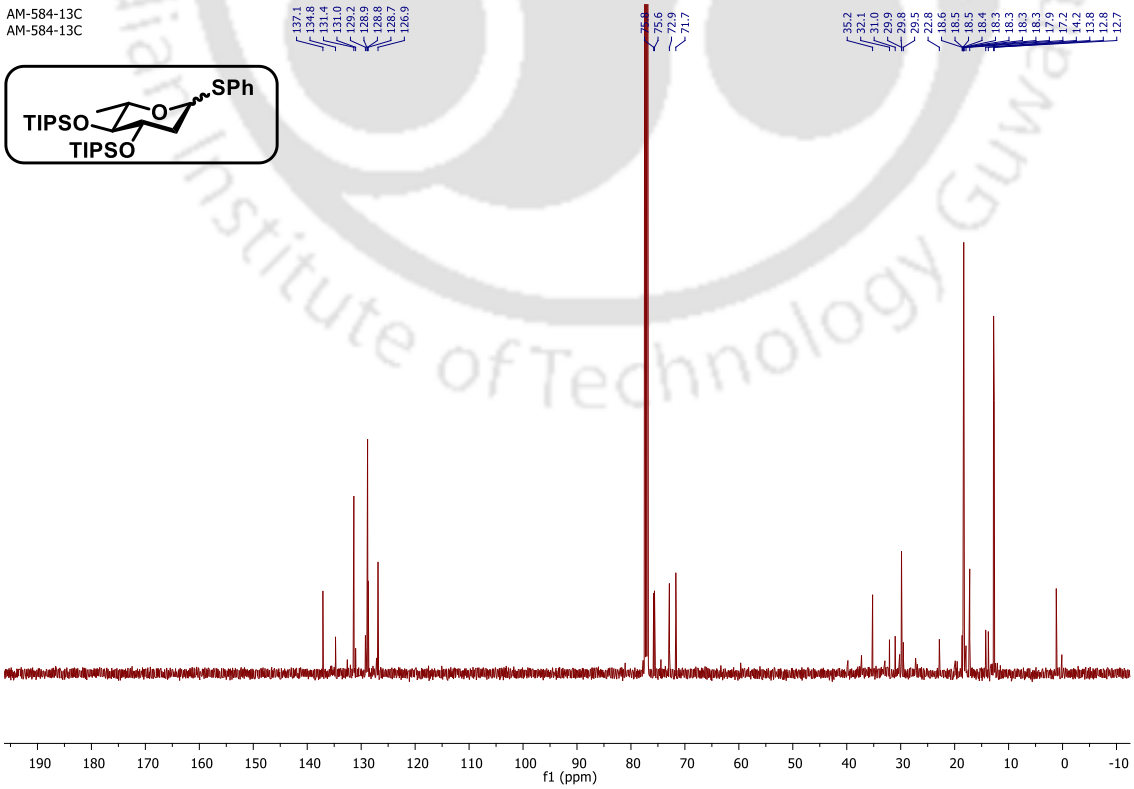
COSY NMR of Phenyl 2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1-thio-α,β-L-arabino-hexapyranoside (22a, 400 MHz, $CDCl_3$):



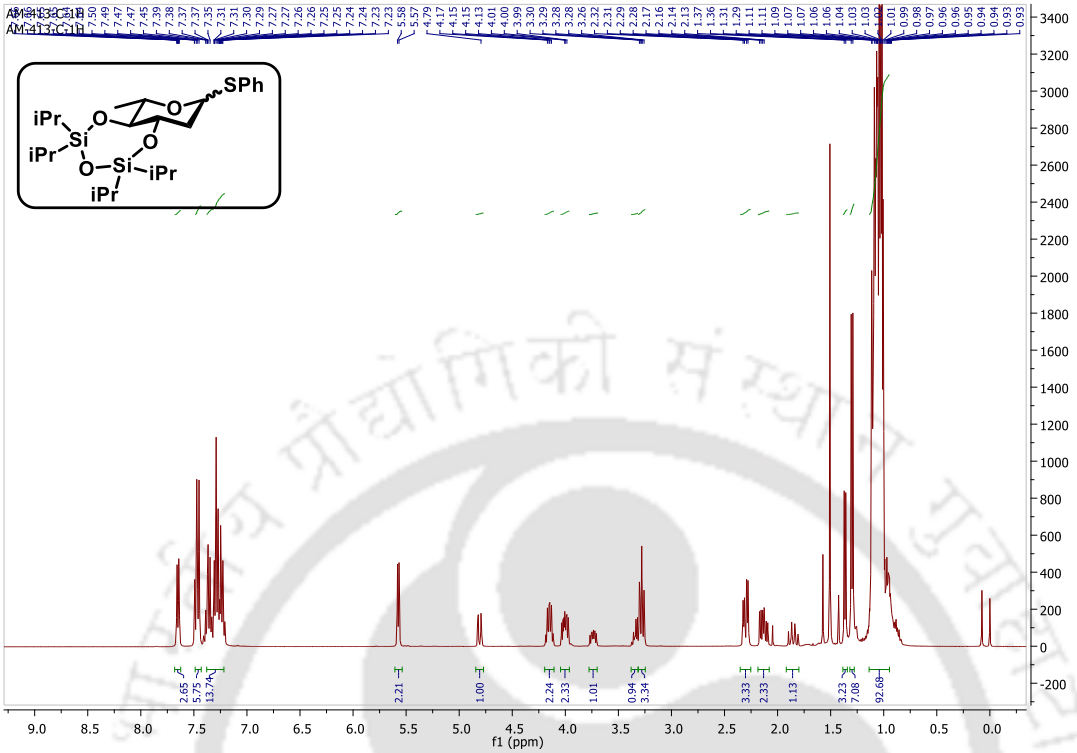
^{1}H NMR of Phenyl 2,6-dideoxy-3,4-O-bis-(triisopropylsilyl)-2-deoxy-α,β-L-arabino-hexapyranoside (22b, 500 MHz, $CDCl_3$):



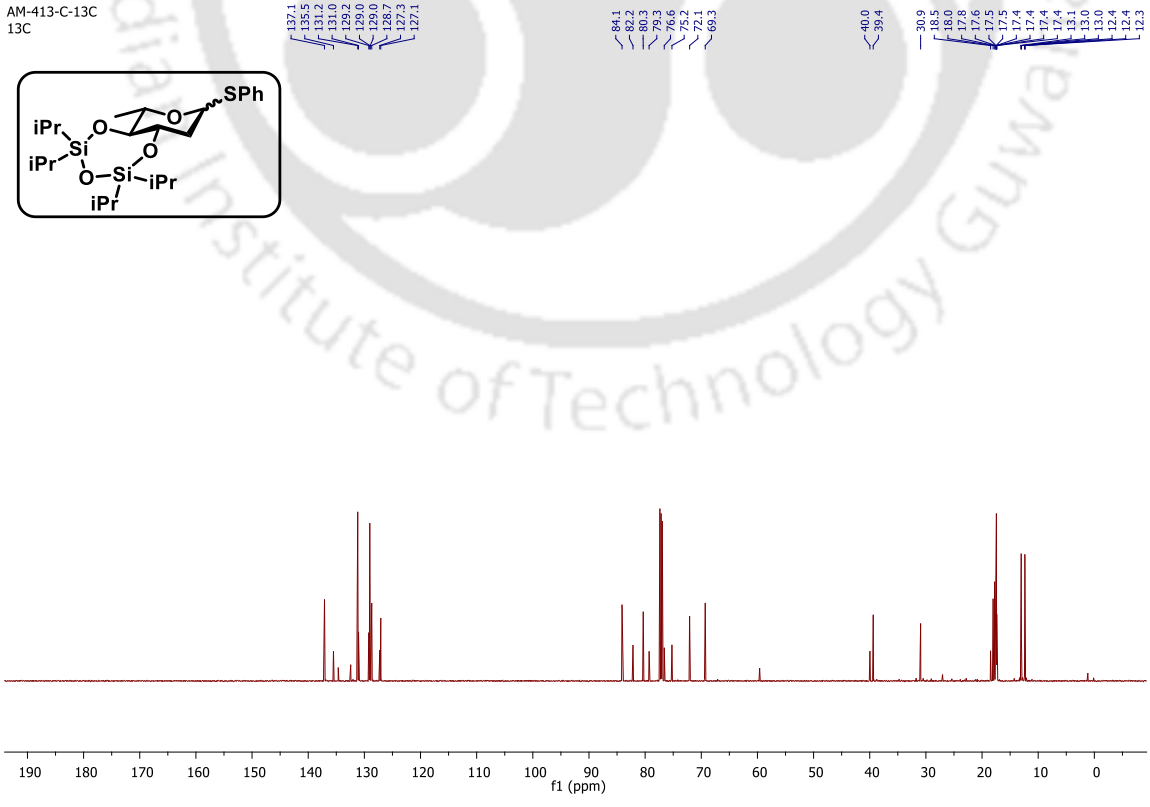
^{13}C NMR of Phenyl 2,6-dideoxy-3,4-O-bis-(triisopropylsilyl)-2-deoxy-α,β-L-arabino-hexapyranoside (22b, 500 MHz, $CDCl_3$):



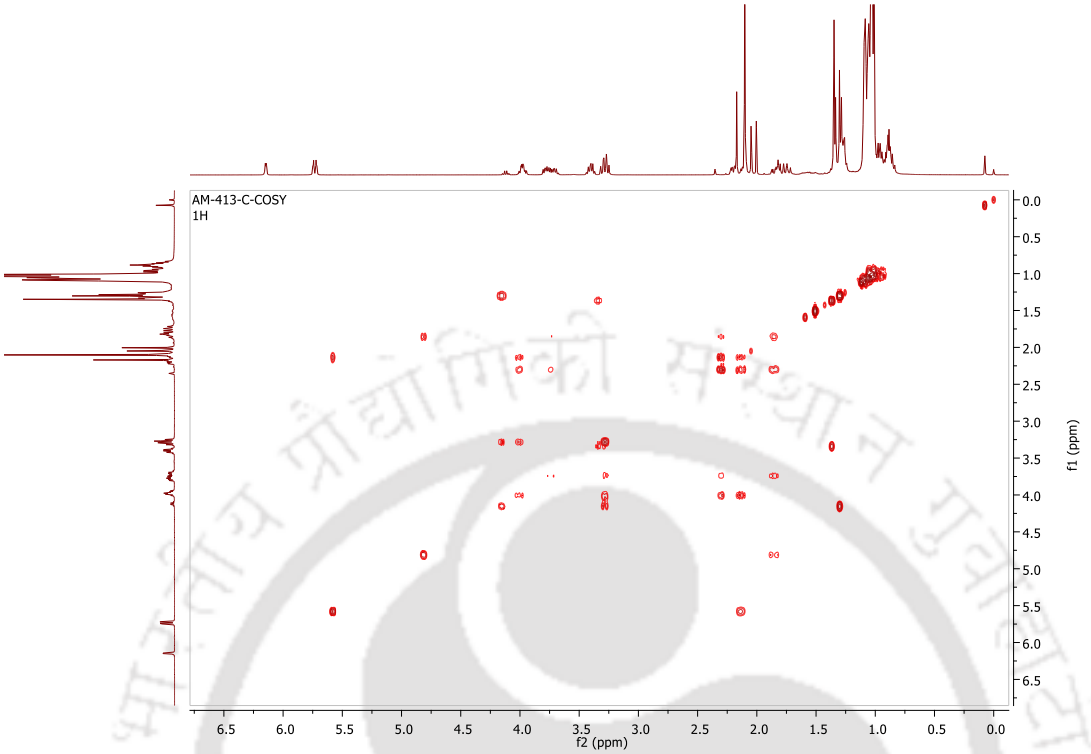
^{1}H NMR of Phenyl 2,6-dideoxy-3,4-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-α,β-L-arabino-hexapyranoside (22c, 400 MHz, $CDCl_3$):



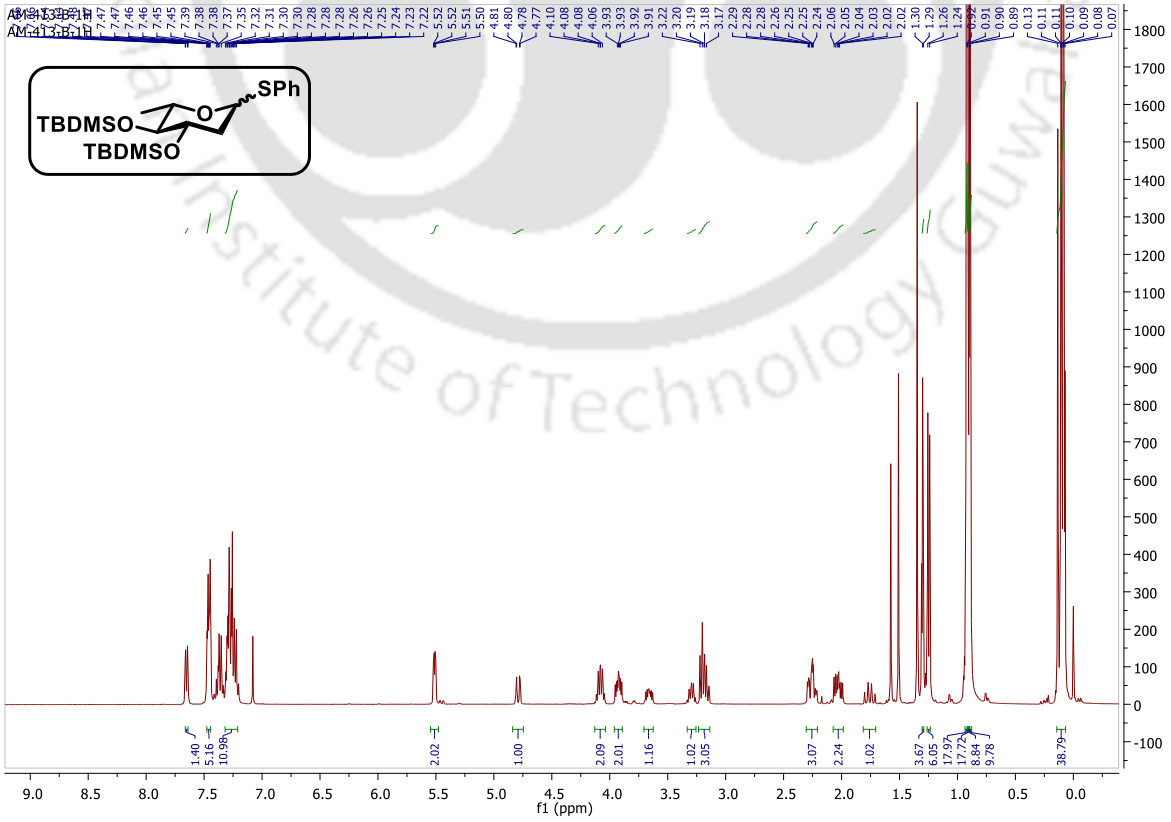
^{13}C NMR of Phenyl 2,6-dideoxy-3,4-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-α,β-L-arabino-hexapyranoside (22c, 600 MHz, $CDCl_3$):



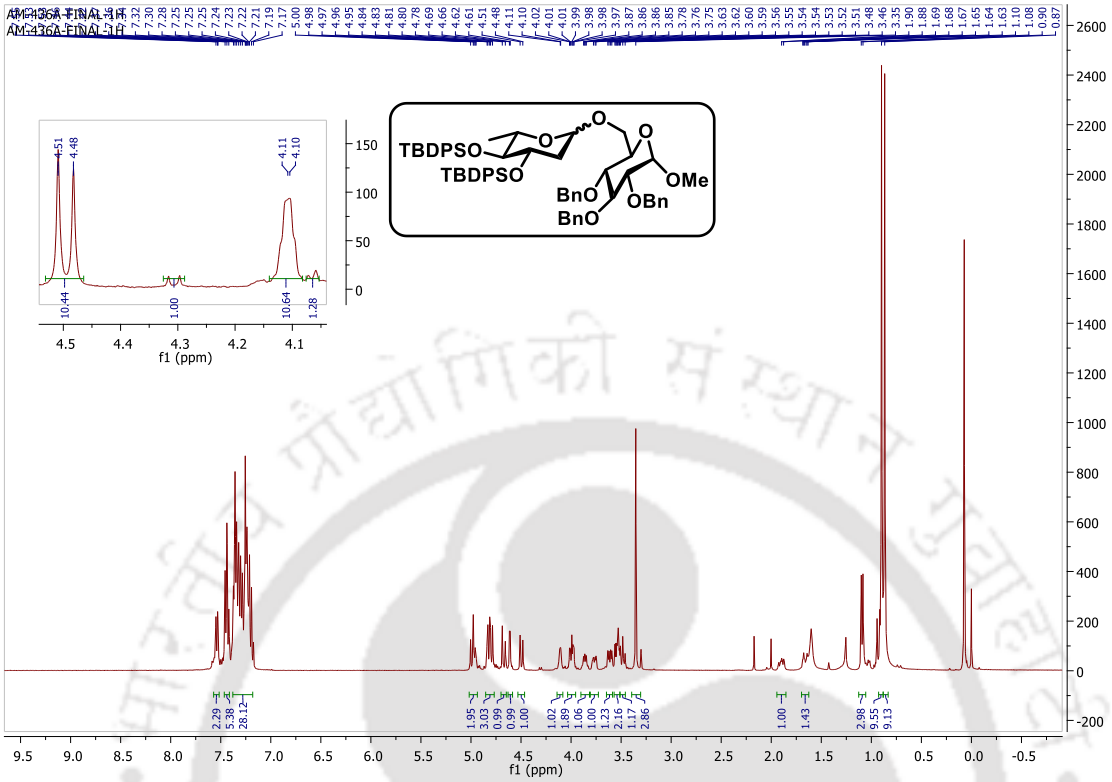
COSY NMR of Phenyl 2,6-dideoxy-3,4-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-1-thio-α,β-L-arabino-hexapyranoside (22c, 400 MHz, $CDCl_3$):



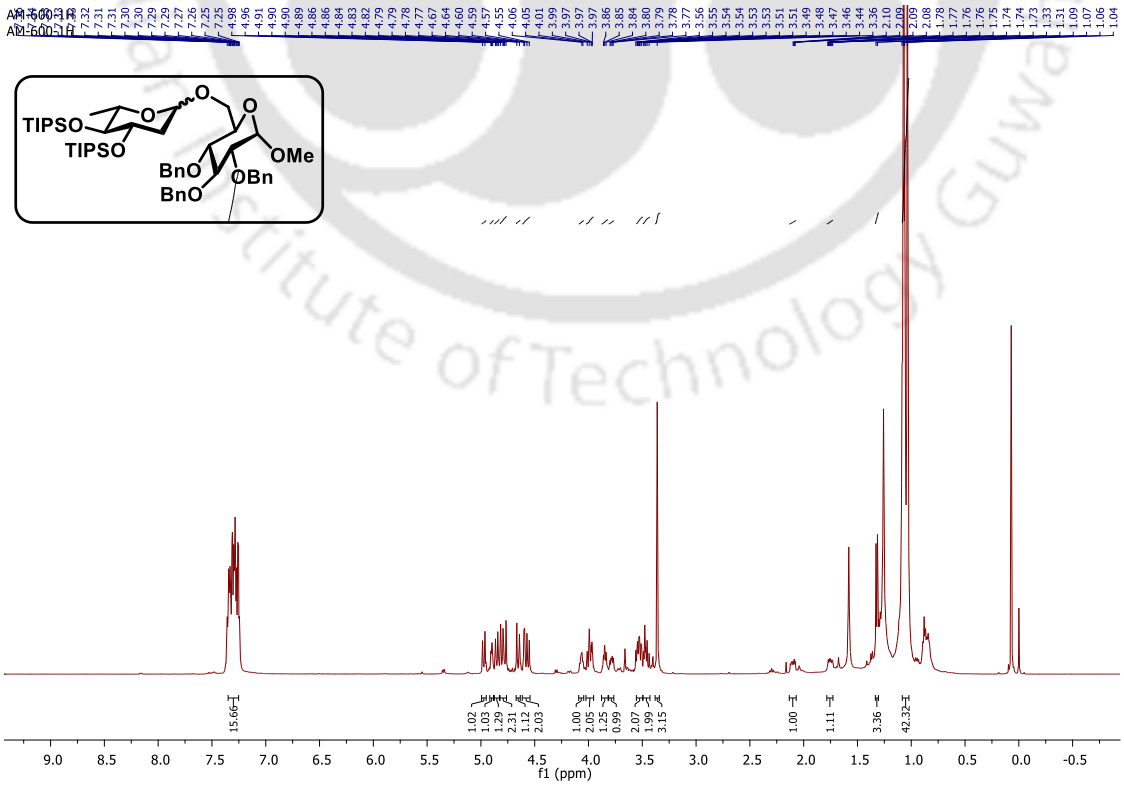
^{1}H NMR of Phenyl 2,6-dideoxy-3,4-bis-*O*-*tert*-butyldimethylsilyl-1-thio-α,β-L-arabino-hexapyranoside (22d, 400 MHz, $CDCl_3$):



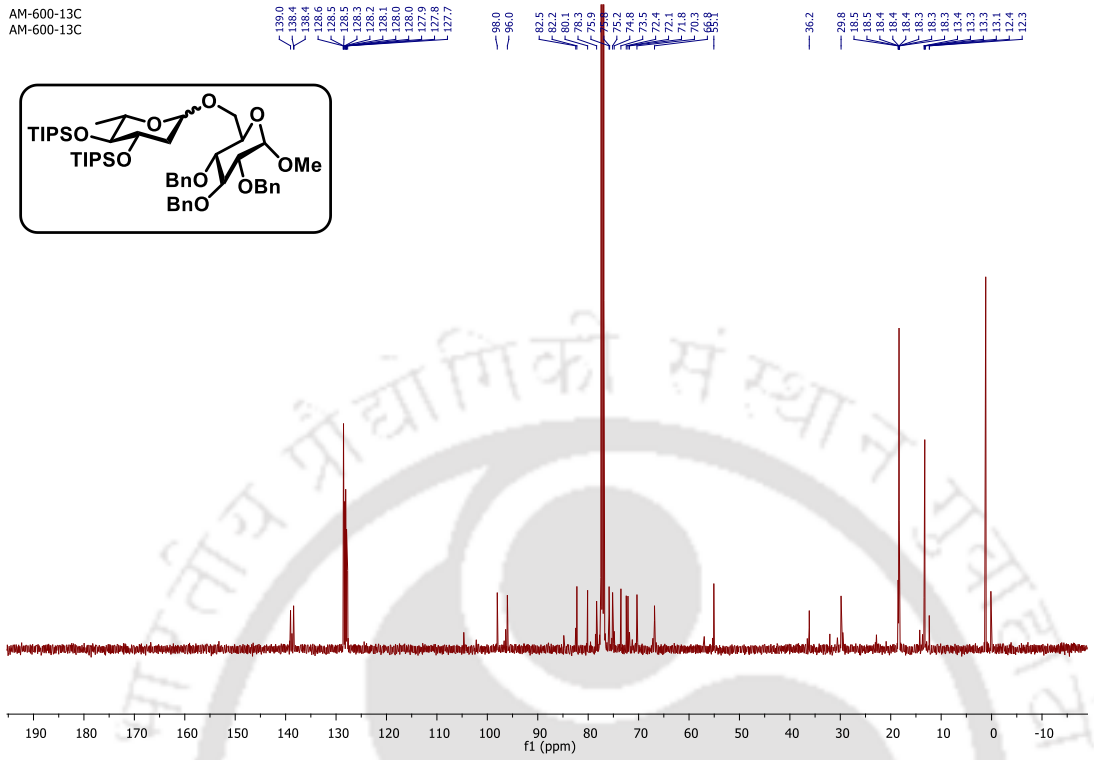
^{1}H NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-α-L-rhamnosyl)-α-D-glucopyranoside (22e, 400 MHz, $CDCl_3$):



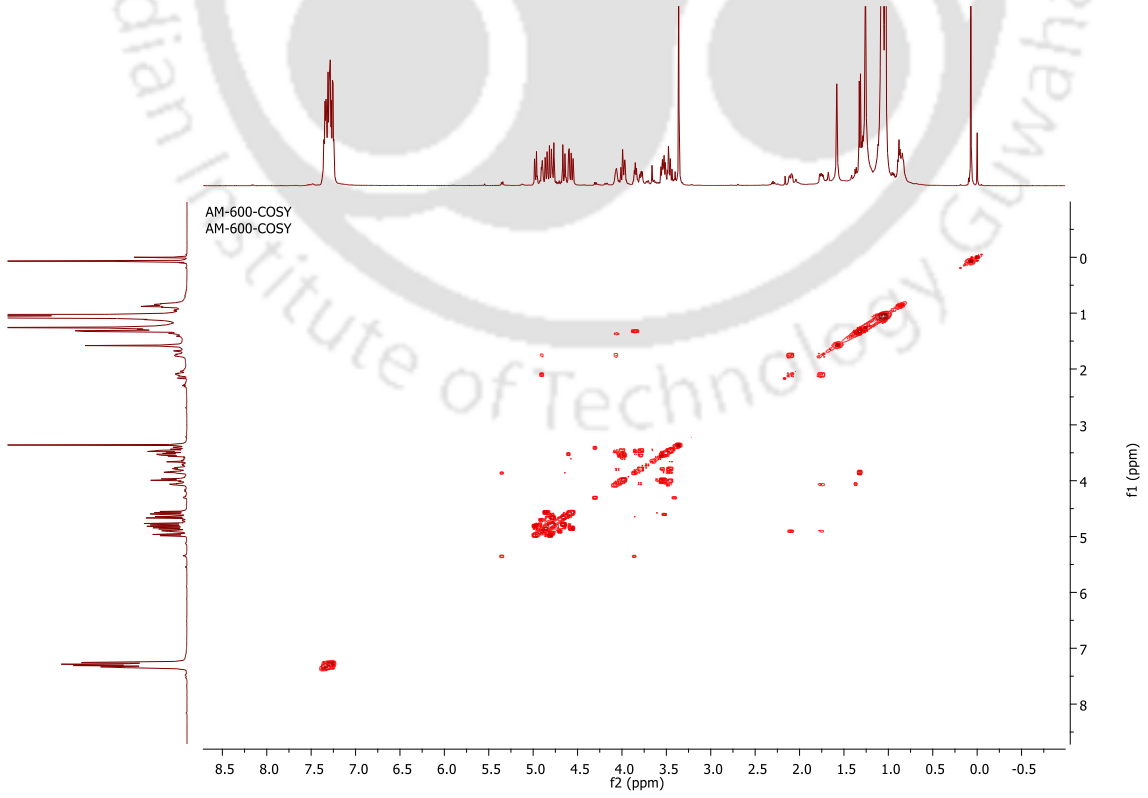
^{1}H NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-triisopropylsilyl-2,6-dideoxy-α-L-rhamnosyl)-α-D-glucopyranoside (22f, 500 MHz, $CDCl_3$):



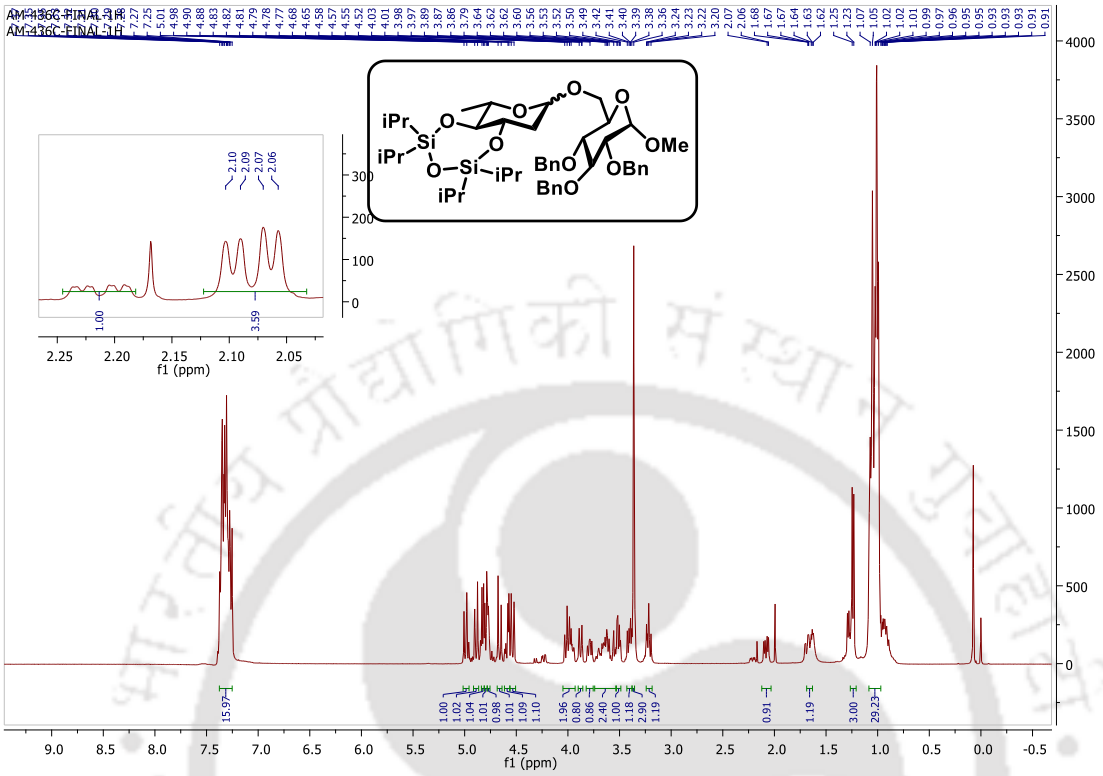
^{13}C NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-triisopropylsilyl-2,6-dideoxy-α-L-rhamnosyl)-α-D-glucopyranoside (22f, 500 MHz, $CDCl_3$):



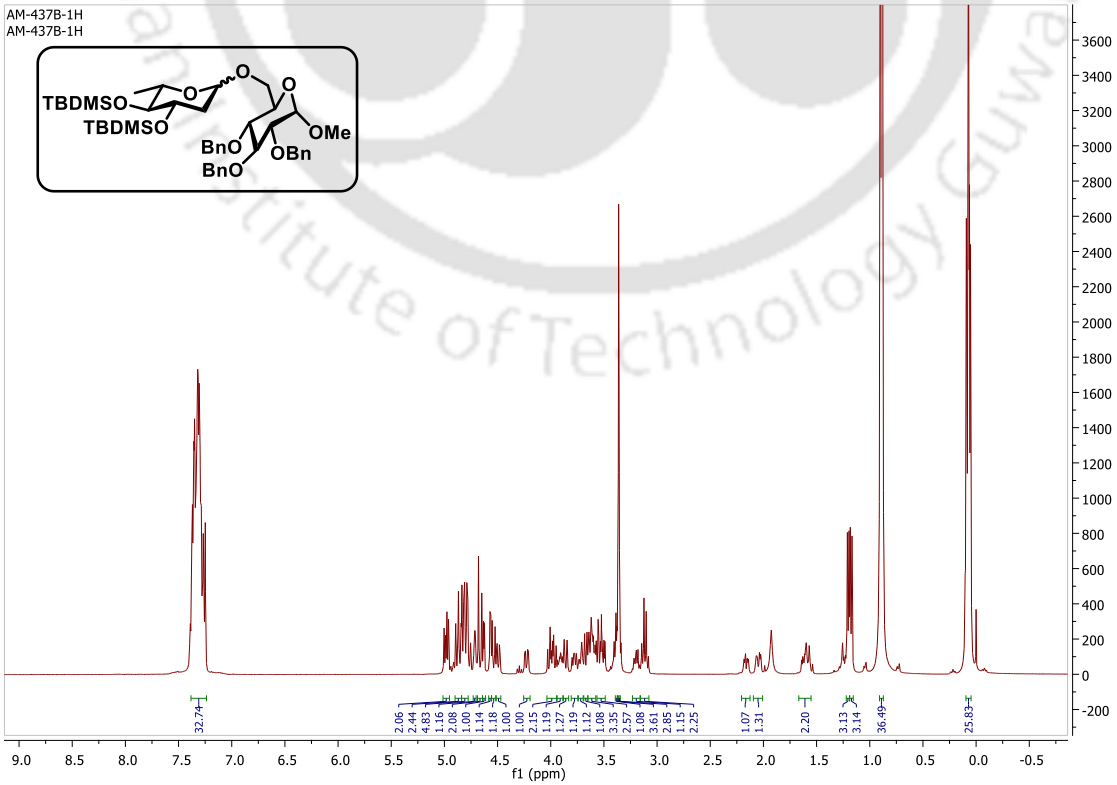
COSY NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-triisopropylsilyl-2,6-dideoxy-α-L-rhamnosyl)-α-D-glucopyranoside (22f, 500 MHz, $CDCl_3$):



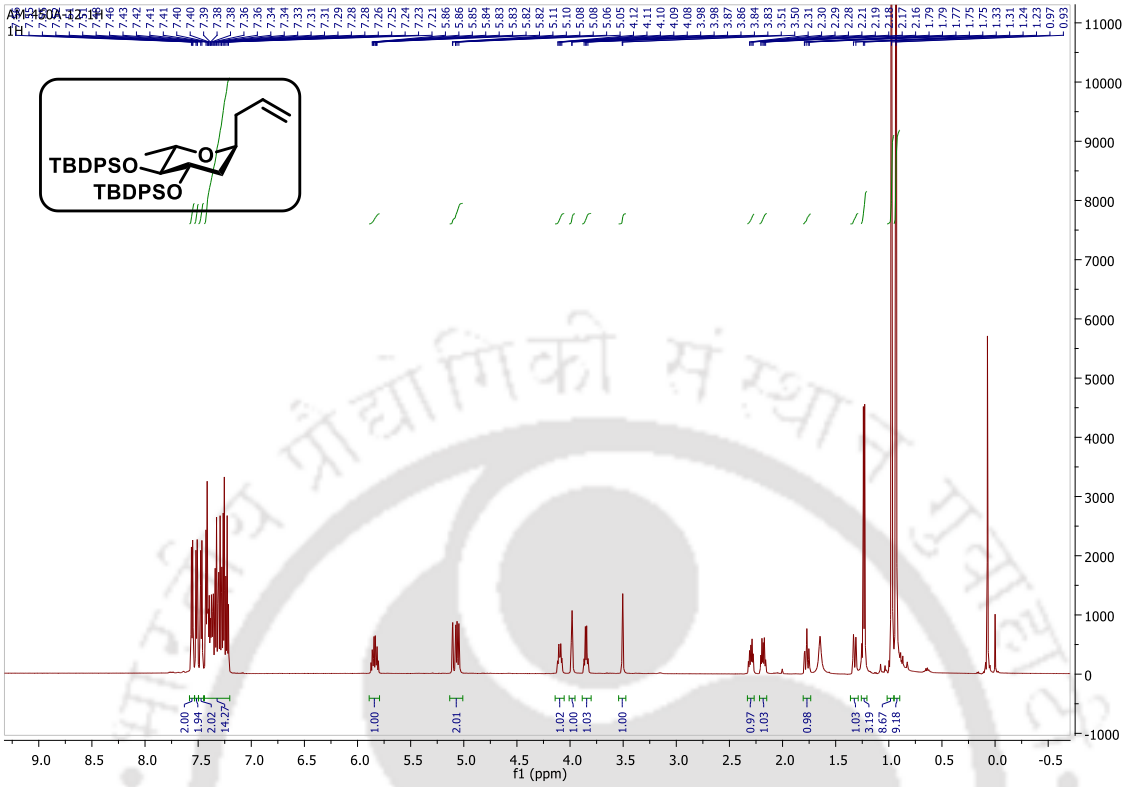
^{1}H NMR of Methyl 2,3,4-tri-O-benzyl-6-O-(2,6-deoxy-3,4-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-α-L-erythro-hexapyranosyl)-α-D-glucopyranoside (22g, 400 MHz, $CDCl_3$):



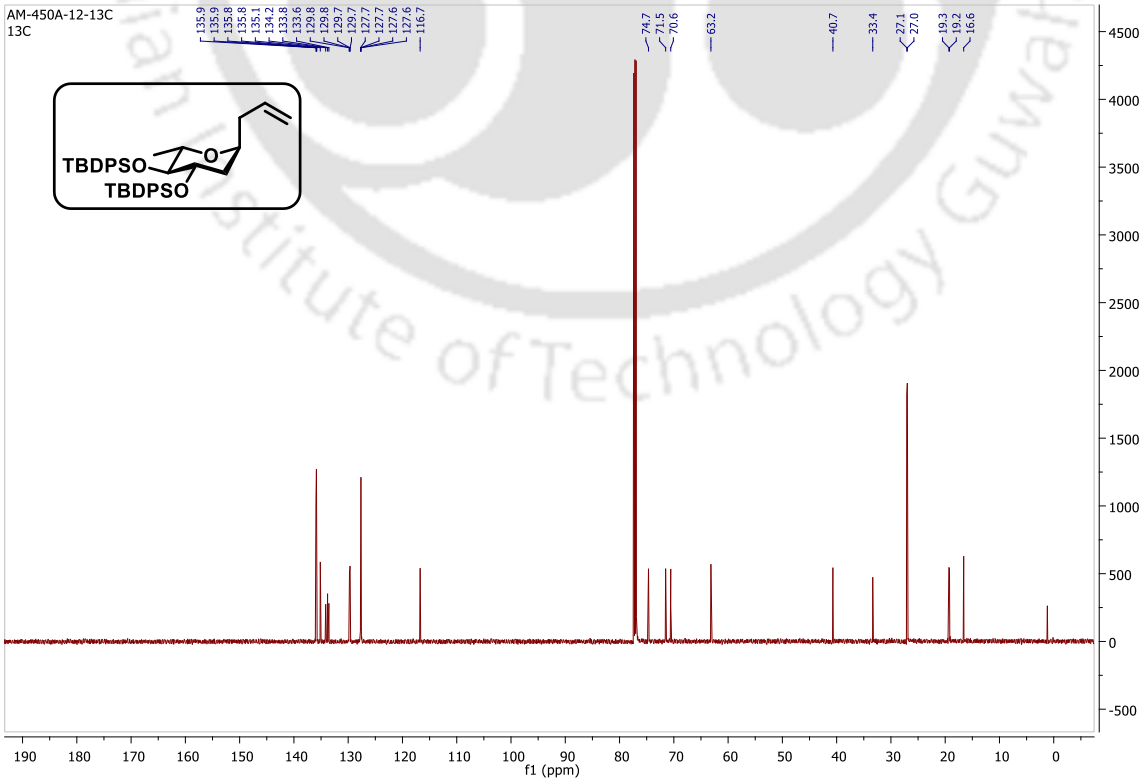
^{1}H NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α-L-rhamnosyl)-α-D-glucopyranoside (22h, 400 MHz, $CDCl_3$):



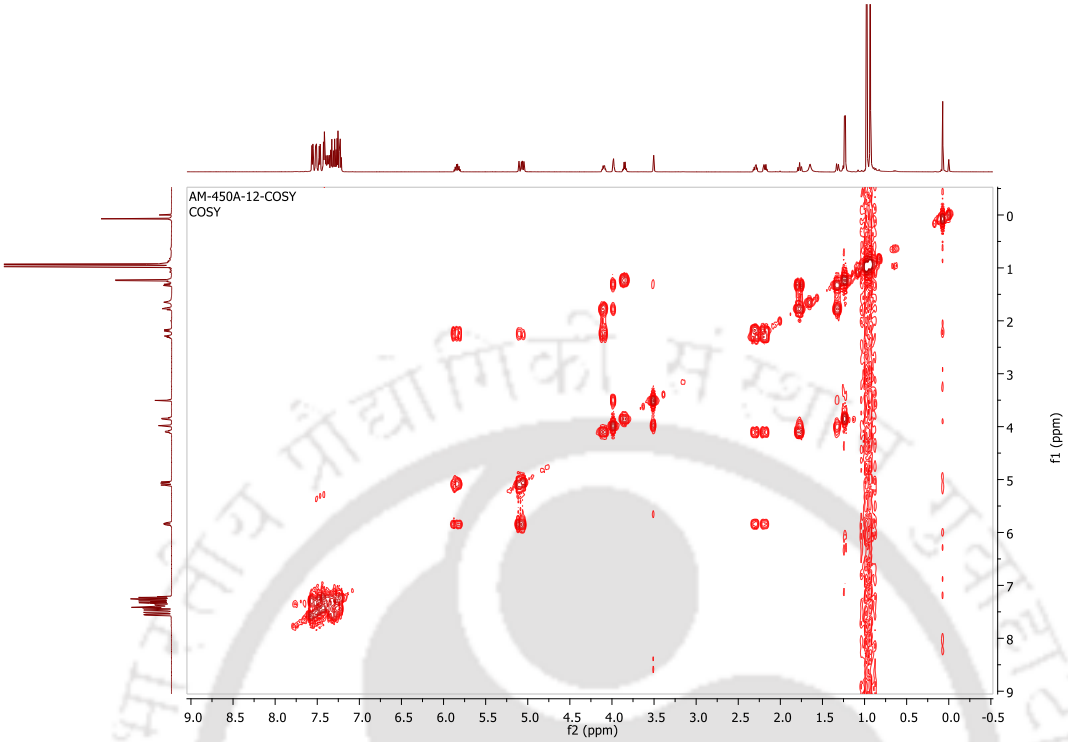
^{1}H NMR of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-non-1-enitol (22i*α*, 600 MHz, $CDCl_3$):



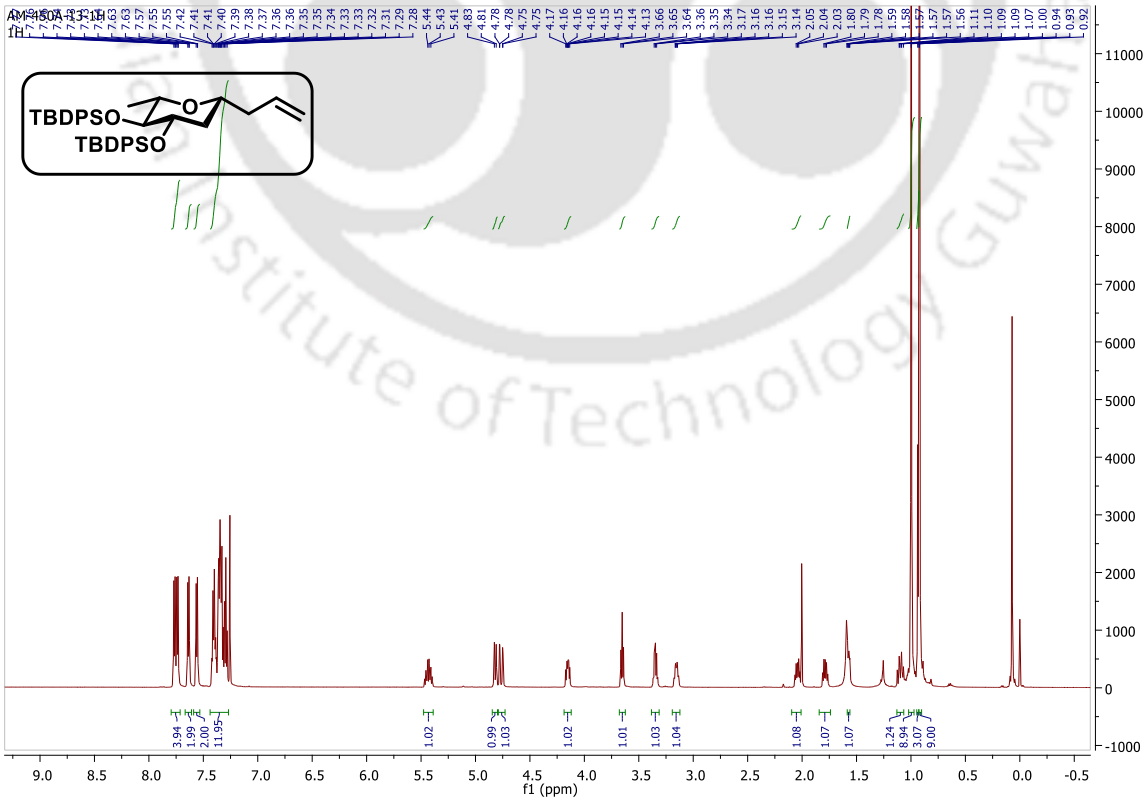
^{13}C NMR of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-non-1-enitol (22i*α*, 600 MHz, $CDCl_3$):



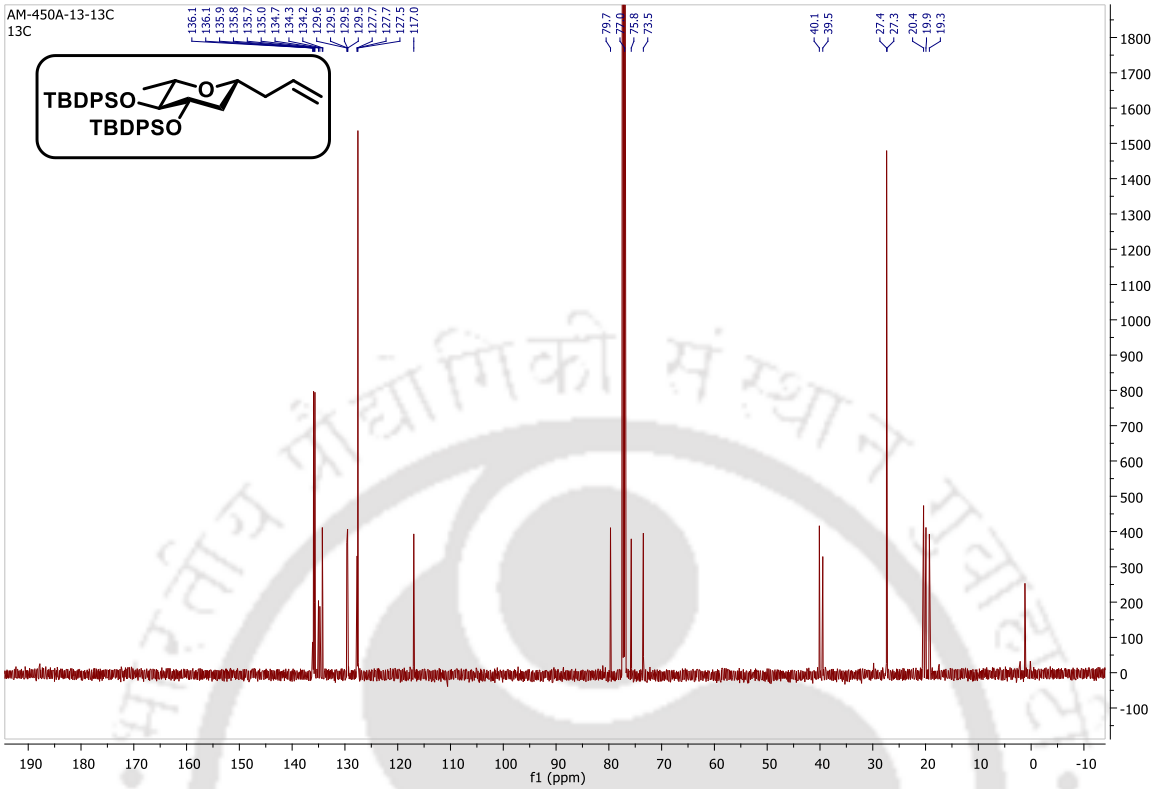
COSY NMR of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-non-1-enitol (22iα, 600 MHz, $CDCl_3$):



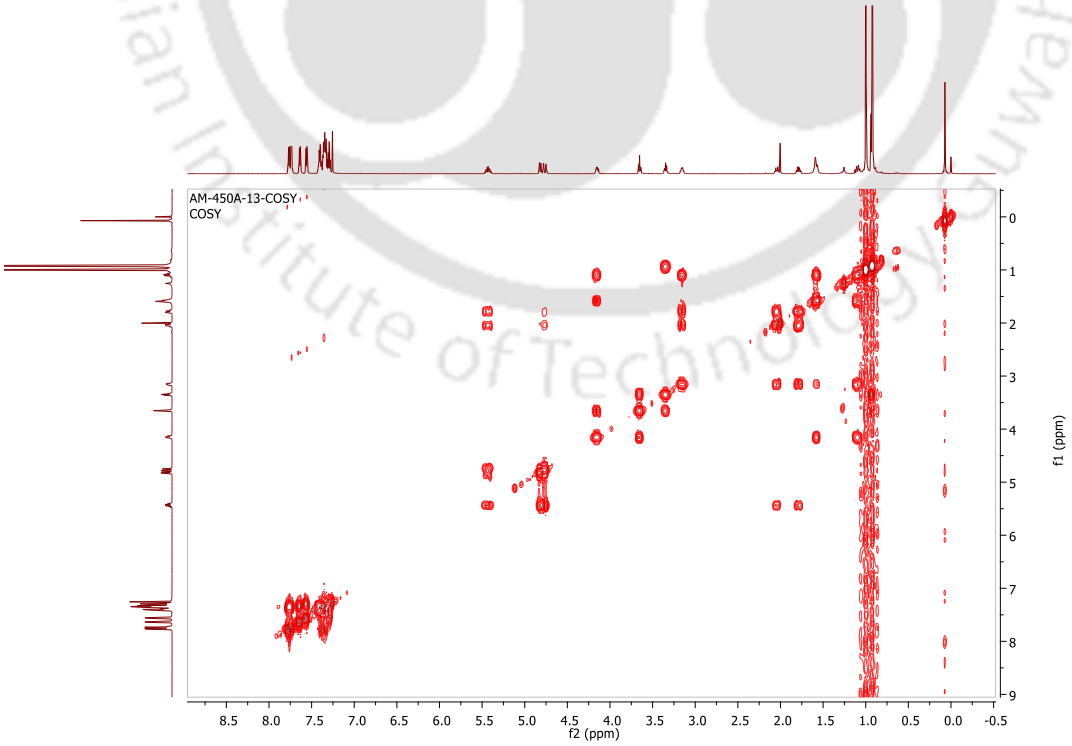
^{1}H NMR of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-β-L-arabino-non-1-enitol (22iβ, 600 MHz, $CDCl_3$):



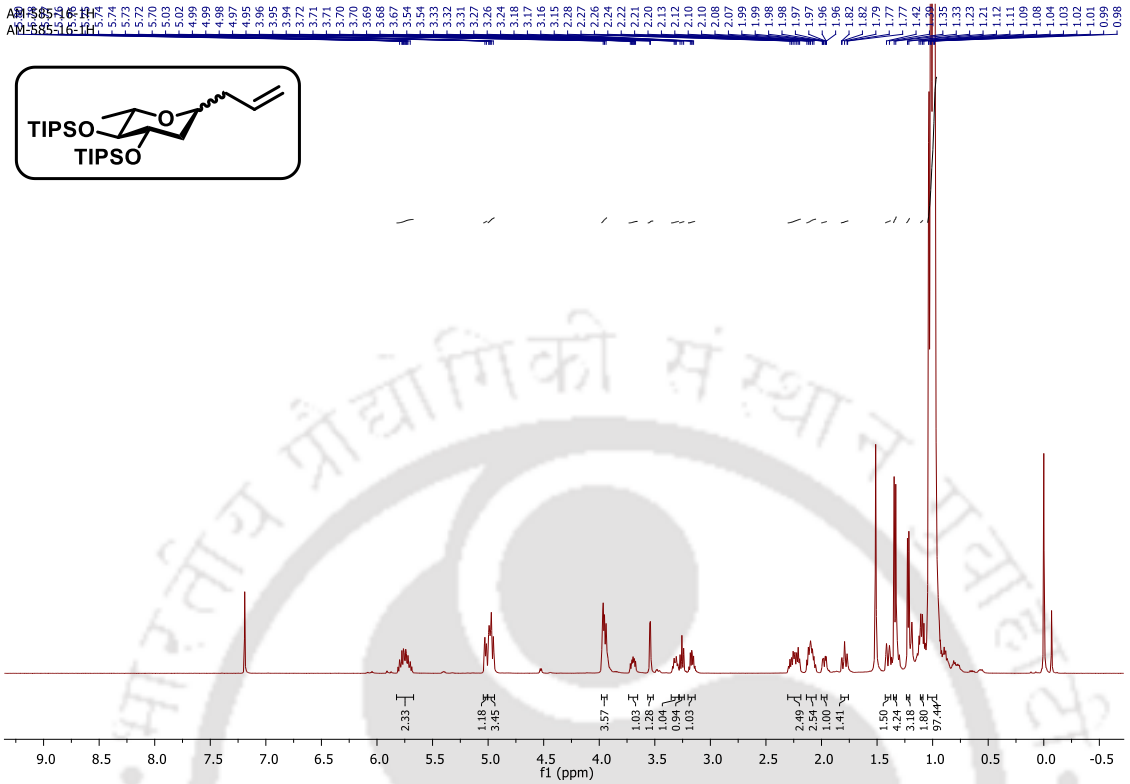
^{13}C NMR of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-β-L-arabino-non-1-enitol (22iβ, 600 MHz, $CDCl_3$):



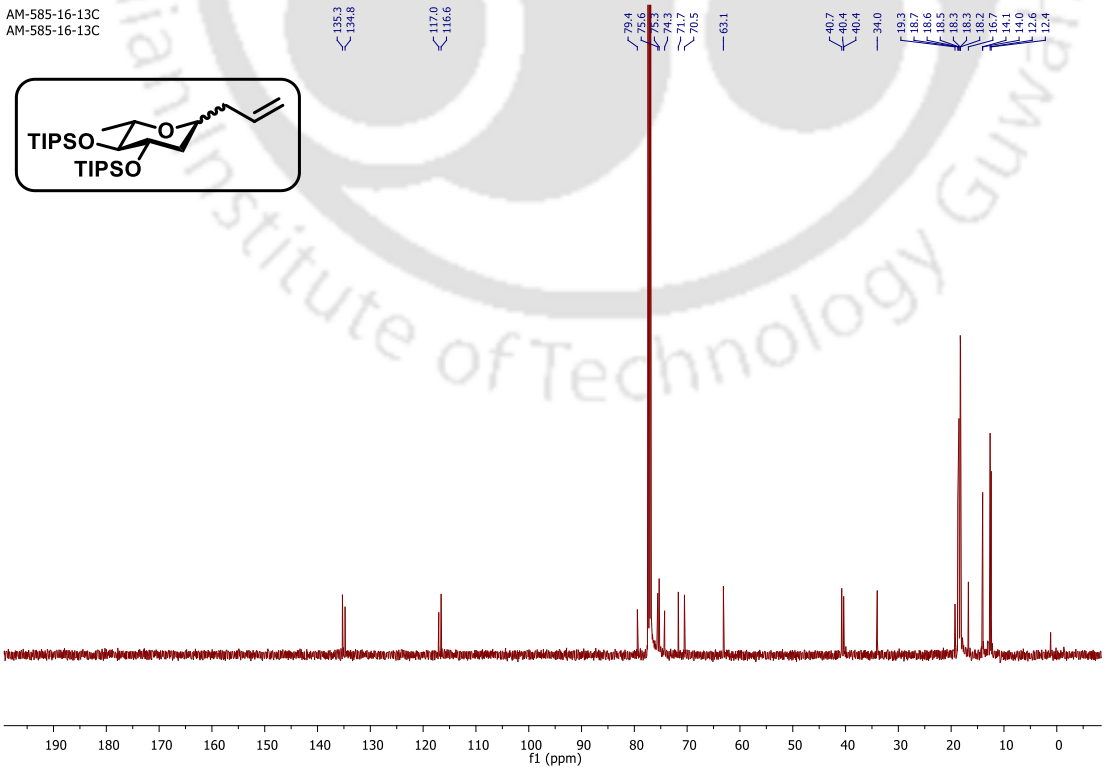
COSY NMR of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-β-L-arabino-non-1-enitol (22iβ, 600 MHz, $CDCl_3$):



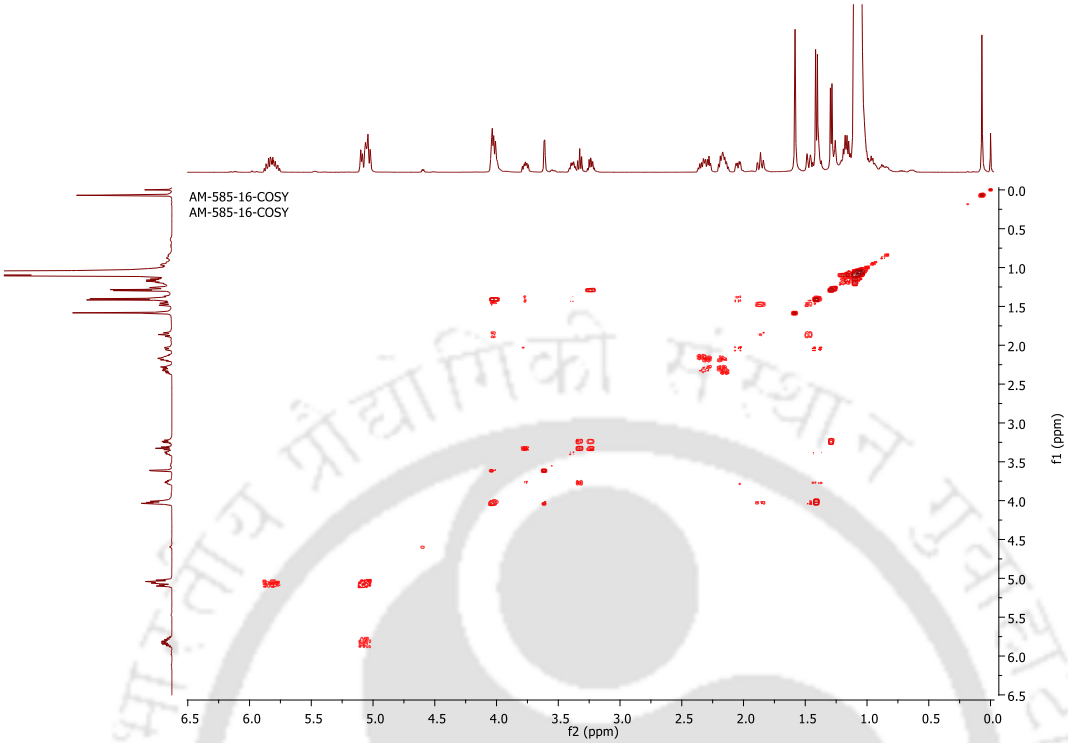
^{1}H NMR of Allyl 2,6-dideoxy-3,4-O-Bis-(triisopropylsilyl)-2-deoxy-α,β-L-arabino-non-1-enitol (22jαβ, 500 MHz, $CDCl_3$):



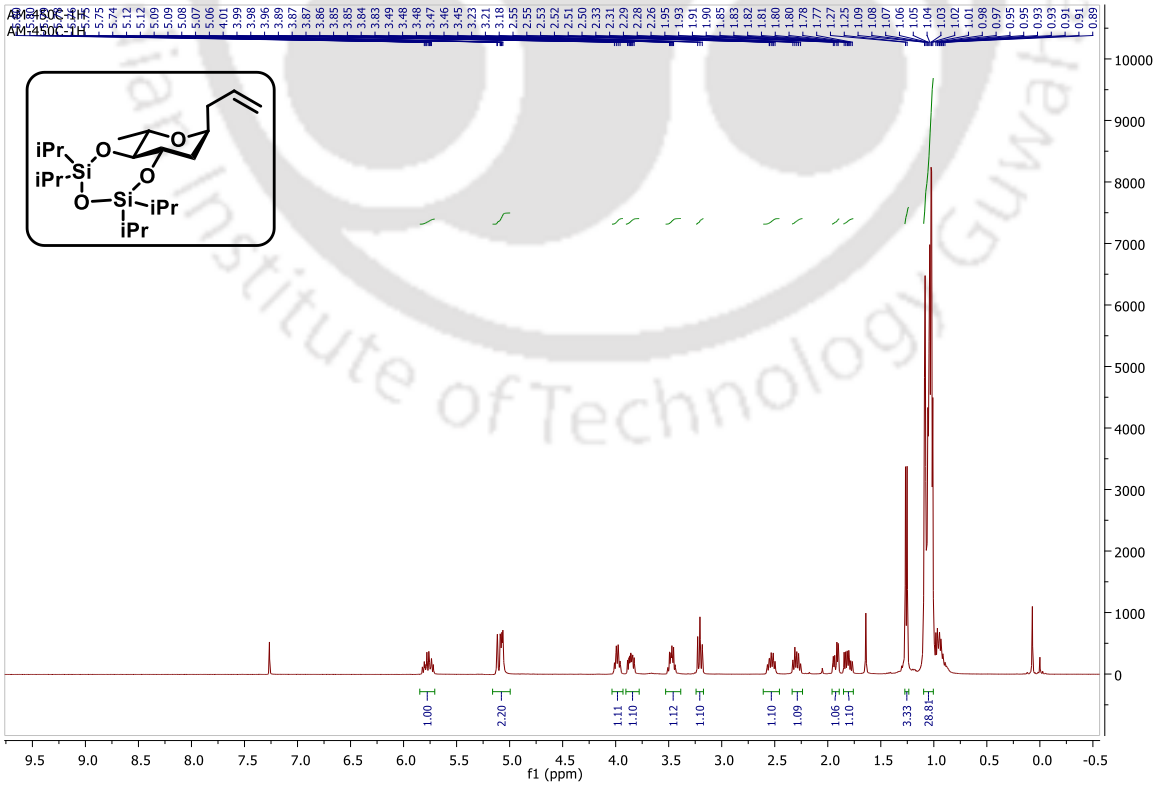
^{13}C NMR of Allyl 2,6-dideoxy-3,4-O-Bis-(triisopropylsilyl)-2-deoxy-α,β-L-arabino-non-1-enitol (22jαβ, 500 MHz, $CDCl_3$):



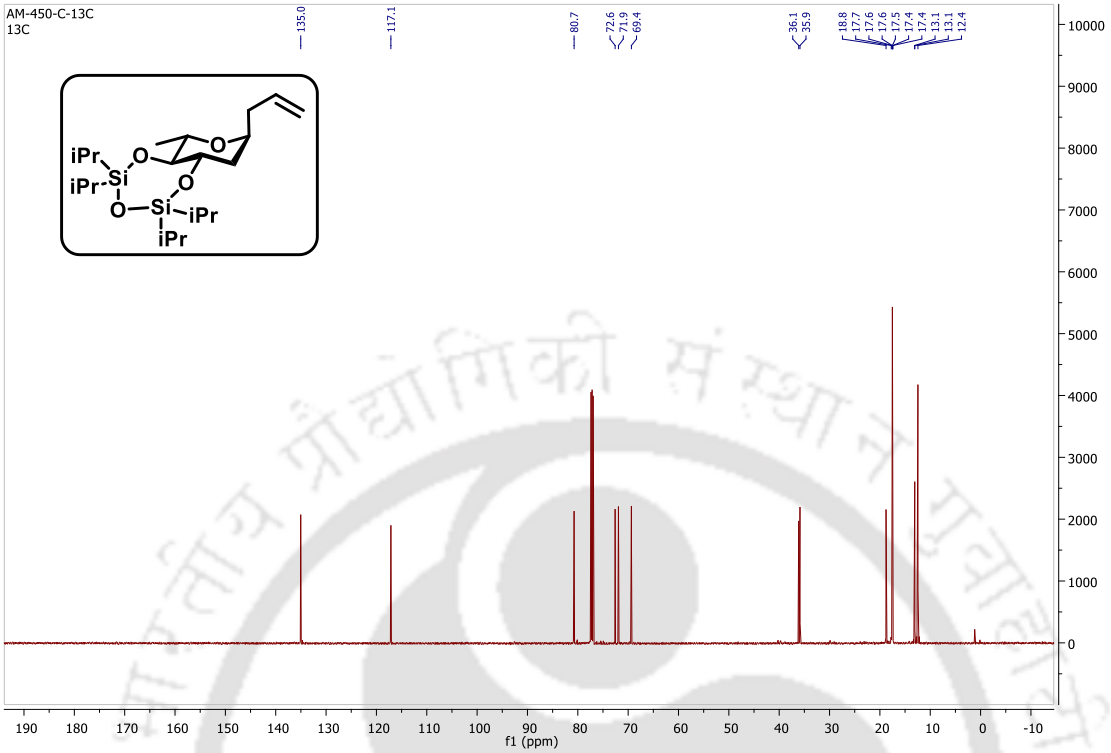
COSY NMR of Allyl 2,6-dideoxy-3,4-O-Bis-(triisopropylsilyl)-2-deoxy-α,β-L-arabino-non-1-enitol (22jαβ, 500 MHz, $CDCl_3$):



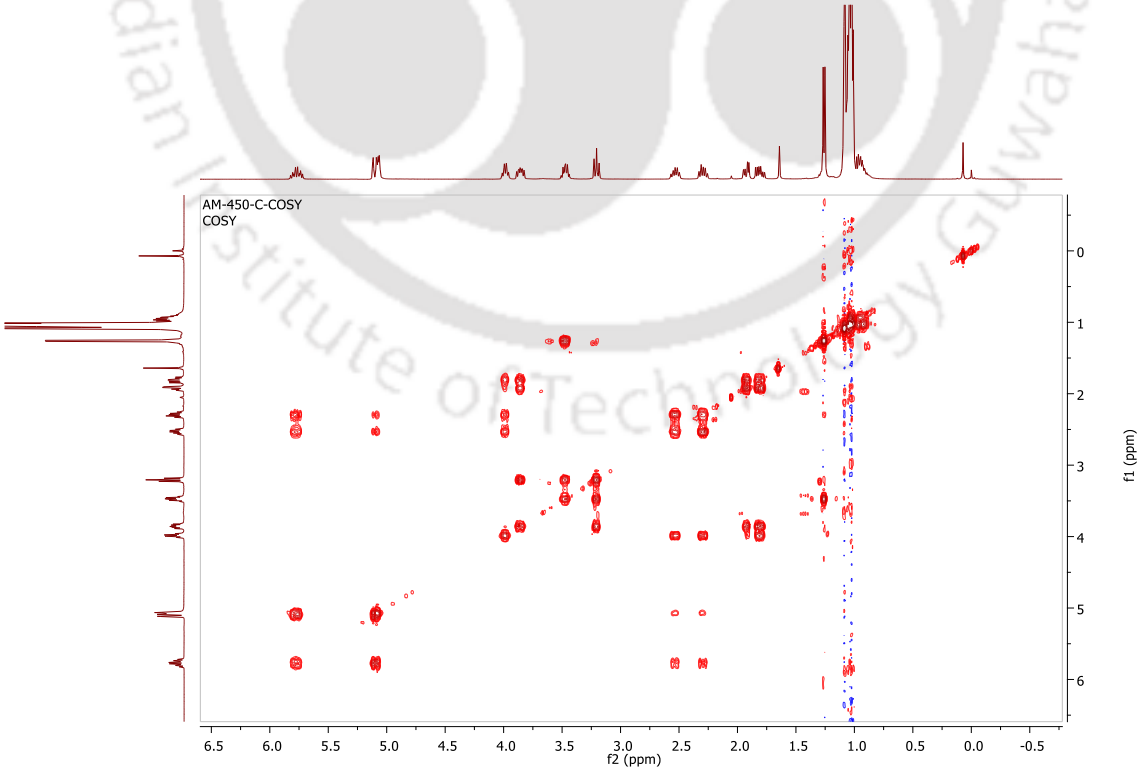
^{1}H NMR of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-β-L-arabino-non-1-enitol (22k, 400 MHz, $CDCl_3$):



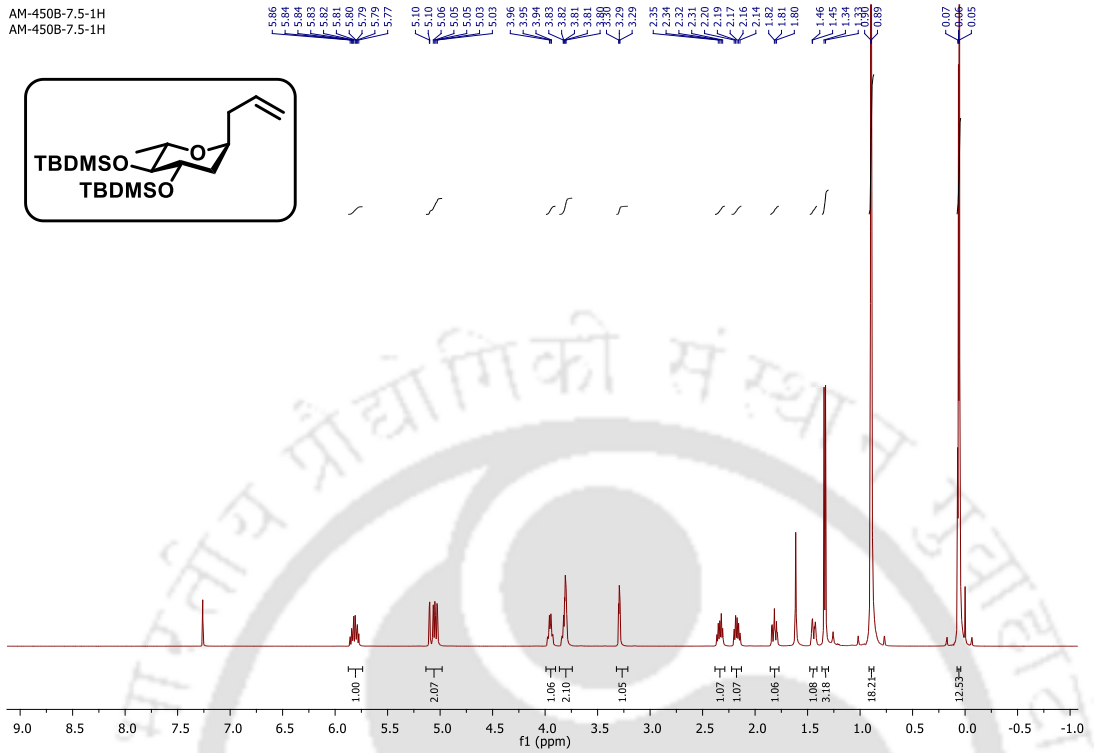
^{13}C NMR of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-β-L-arabino-non-1-enitol (22k, 600 MHz, $CDCl_3$):



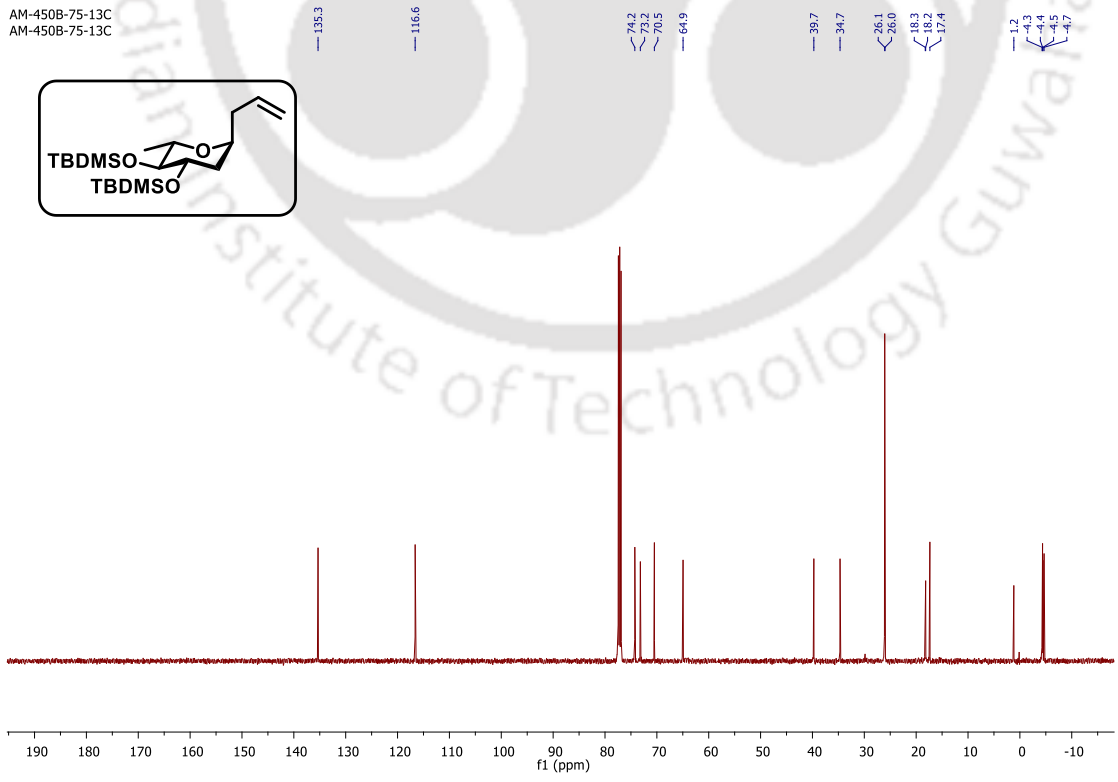
COSY NMR of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-[1,1,3,3-tetrakis(1-methylethyl)-1,3-disiloxanediyl]-β-L-arabino-non-1-enitol (22k, 400 MHz, $CDCl_3$):



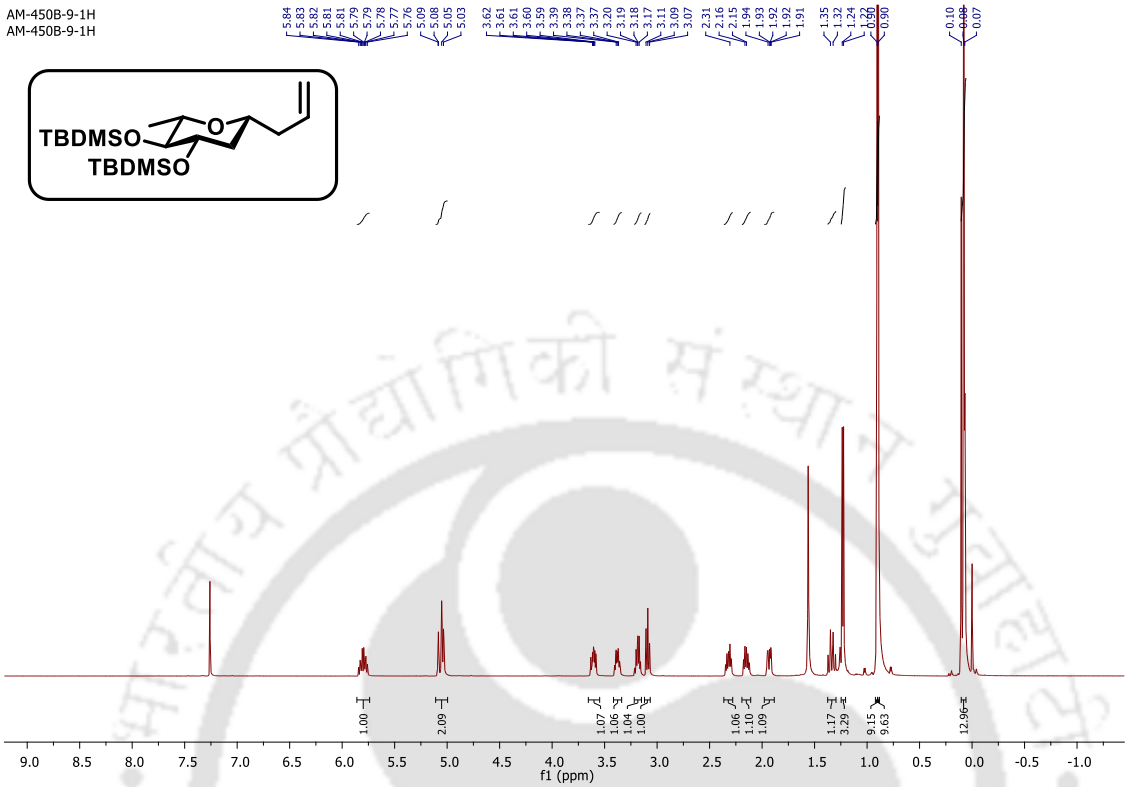
^{1}H NMR of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O-tert*-butyldimethylsilyl-α,β-L-arabino-non-1-enitol (22lα, 500 MHz, $CDCl_3$):



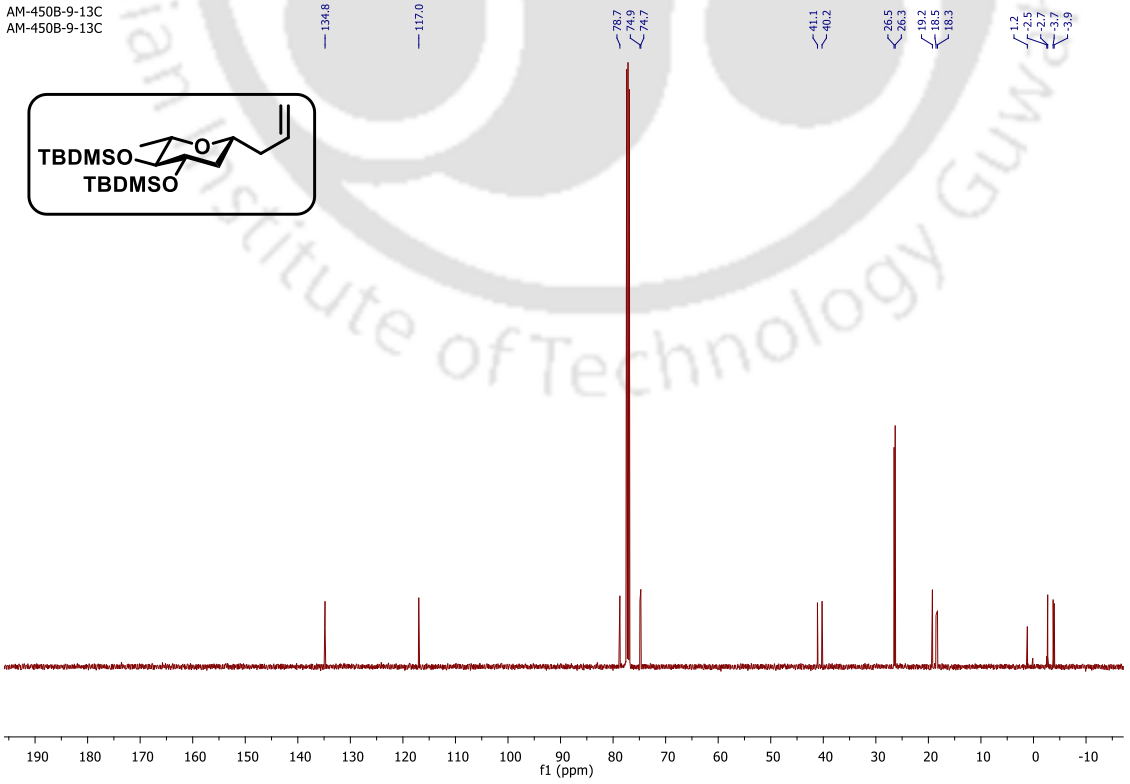
^{13}C NMR of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O-tert*-butyldimethylsilyl-α,β-L-arabino-non-1-enitol (22lα, 500 MHz, $CDCl_3$):



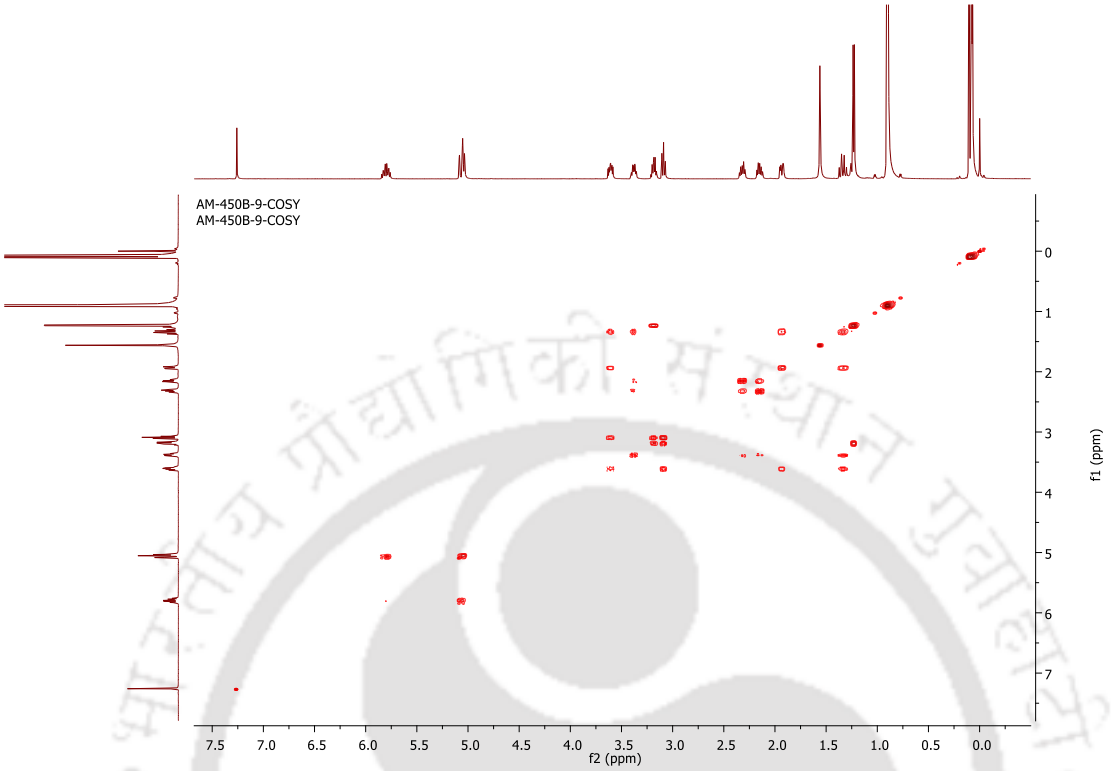
^{1}H NMR of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O-tert*-butyldimethylsilyl-α,β-L-arabino-non-1-enitol (22lβ, 500 MHz, $CDCl_3$):



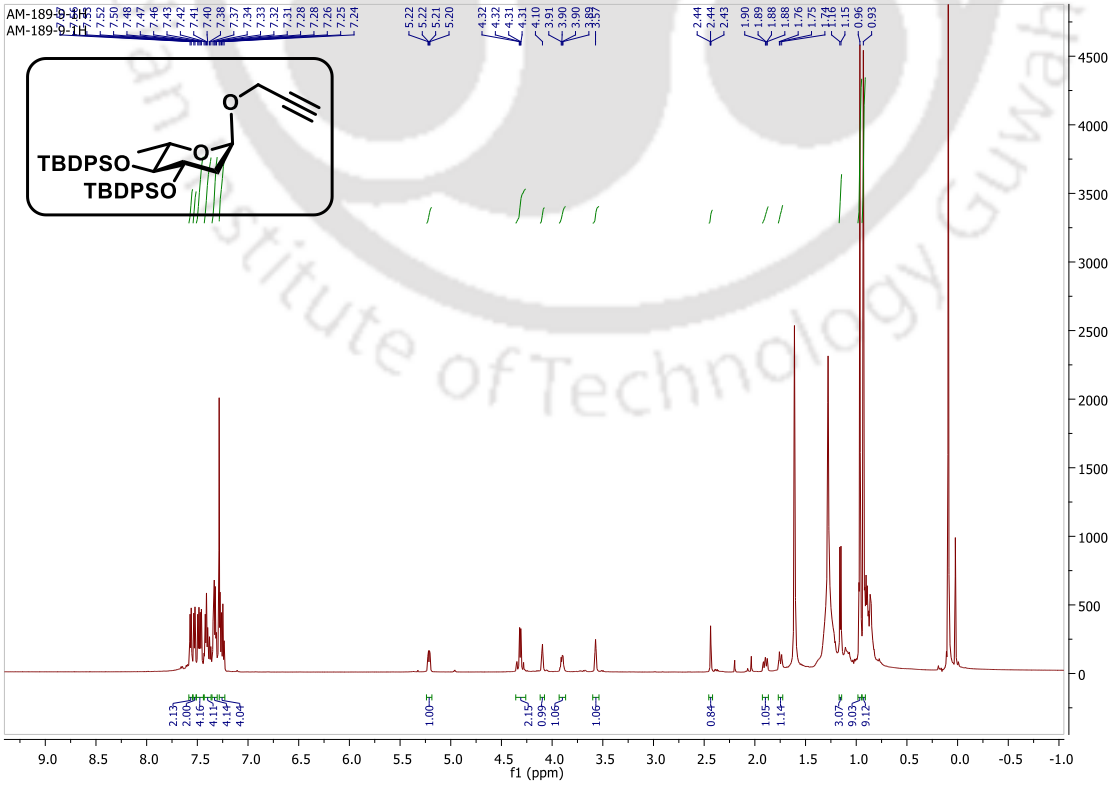
^{13}C NMR of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O-tert*-butyldimethylsilyl-α,β-L-arabino-non-1-enitol (22lβ, 500 MHz, $CDCl_3$):



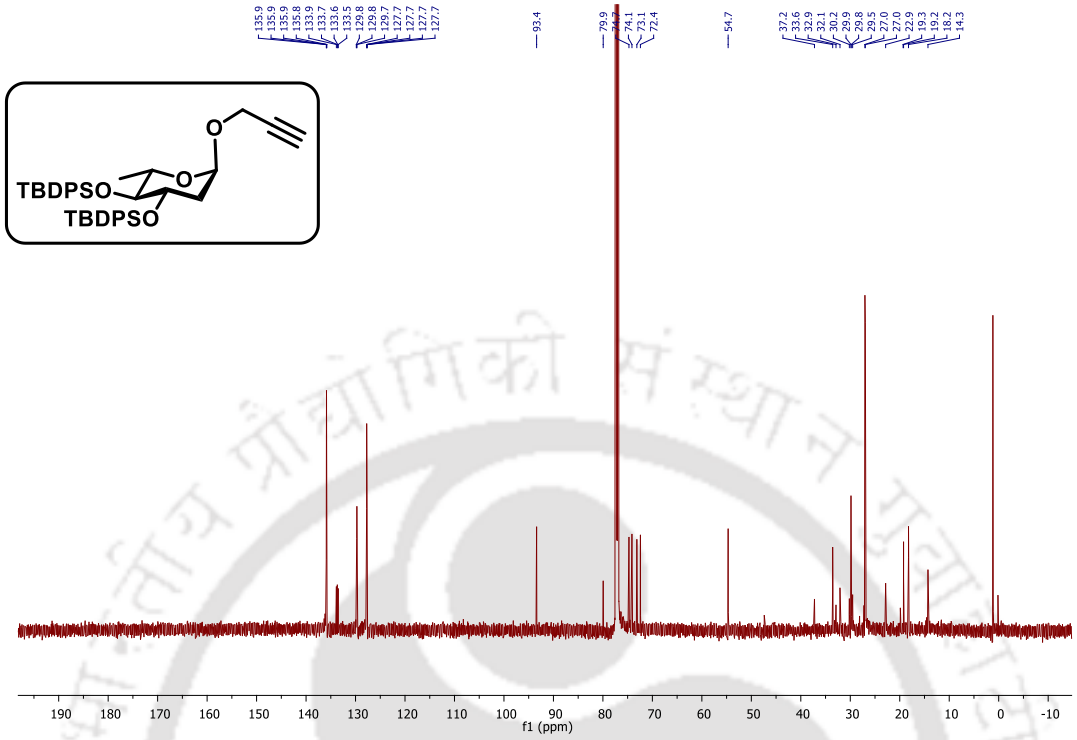
COSY NMR of Allyl 1,2,3,5,8-pentadeoxy-6,7-bis-*O*-*tert*-butyldimethylsilyl-α,β-L-arabino-non-1-enitol (22lβ, 500 MHz, $CDCl_3$):



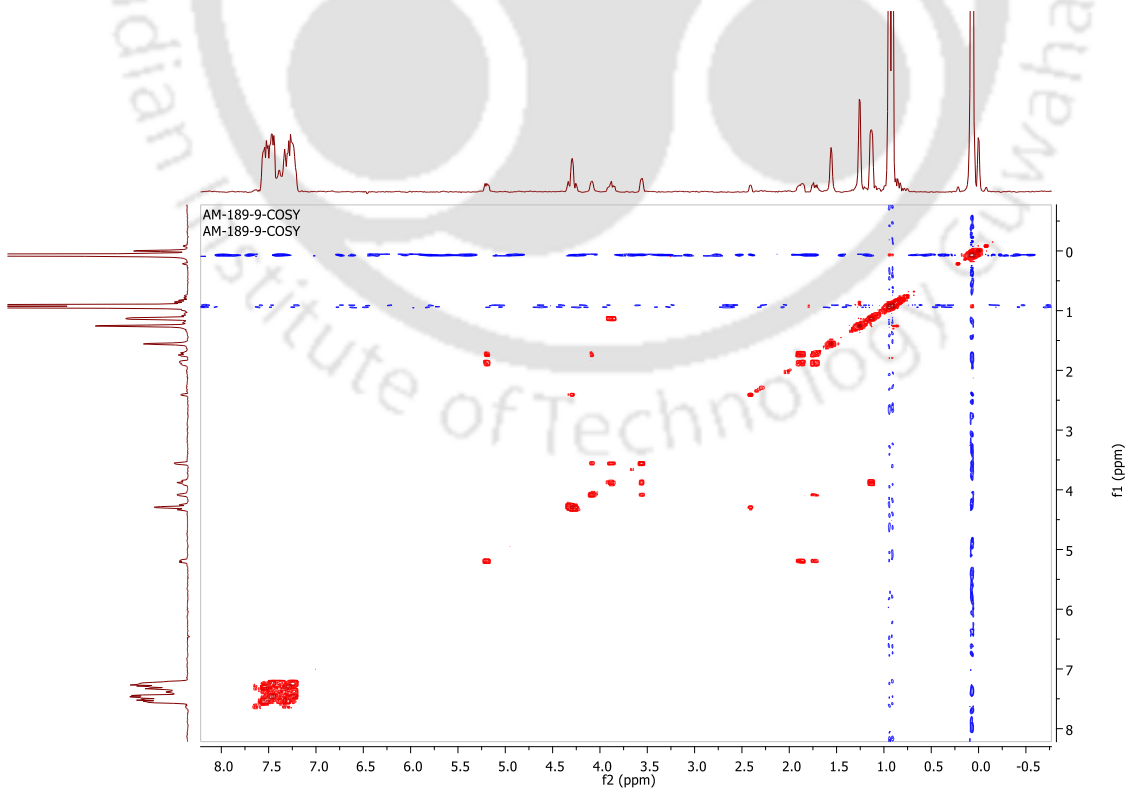
^{1}H NMR of 1-Propargyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23a, 600 MHz, $CDCl_3$):



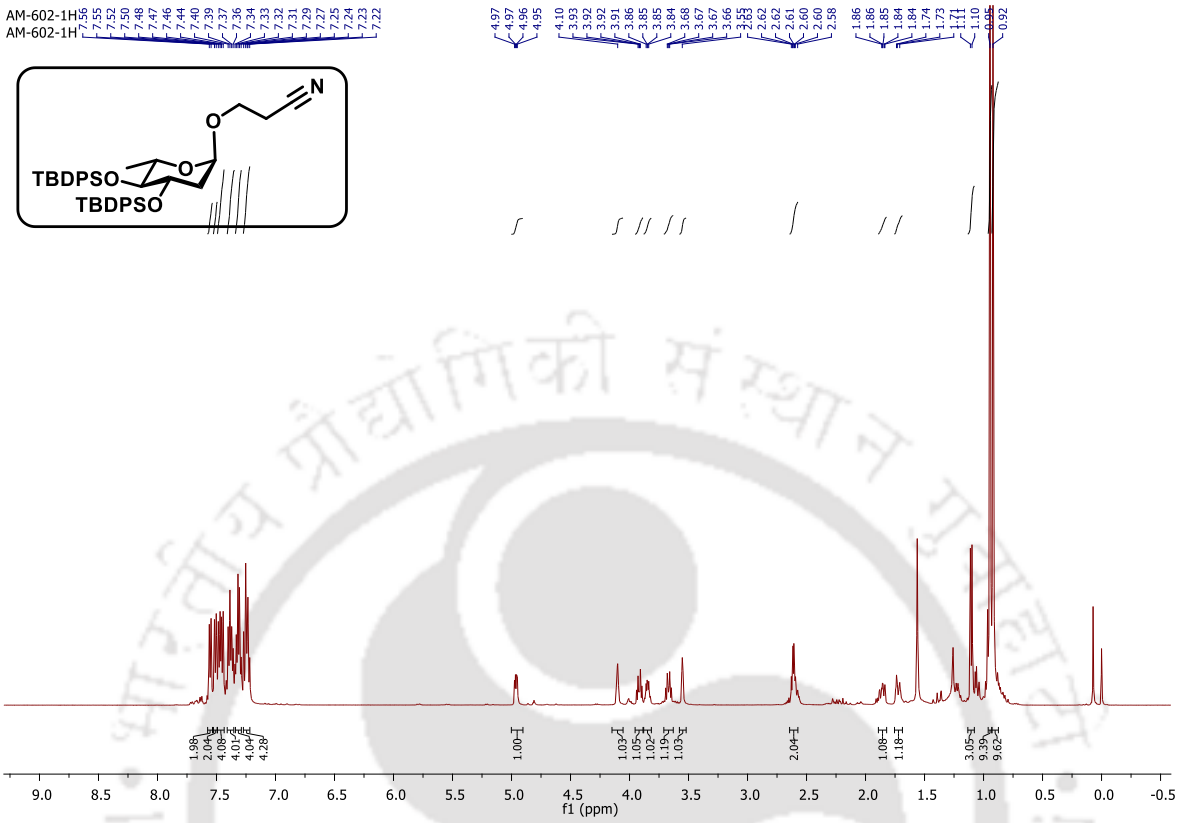
^{13}C NMR of 1-Propargyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23a, 600 MHz, $CDCl_3$):



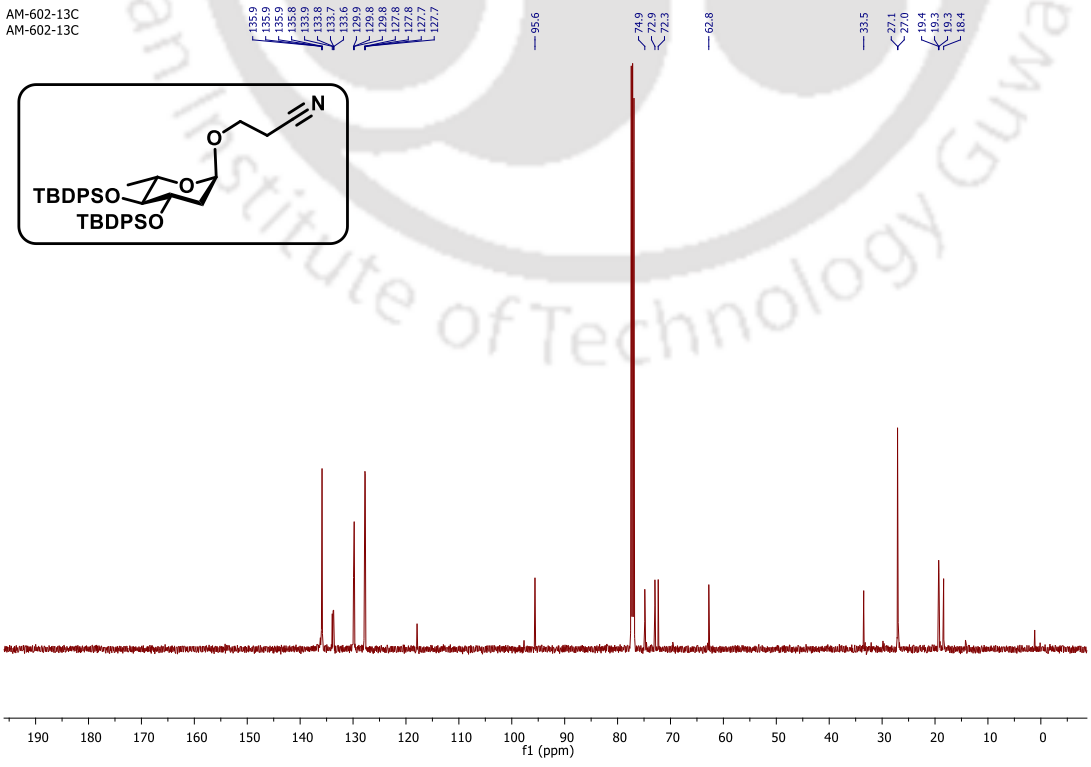
COSY NMR of 1-Propargyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23a, 600 MHz, $CDCl_3$):



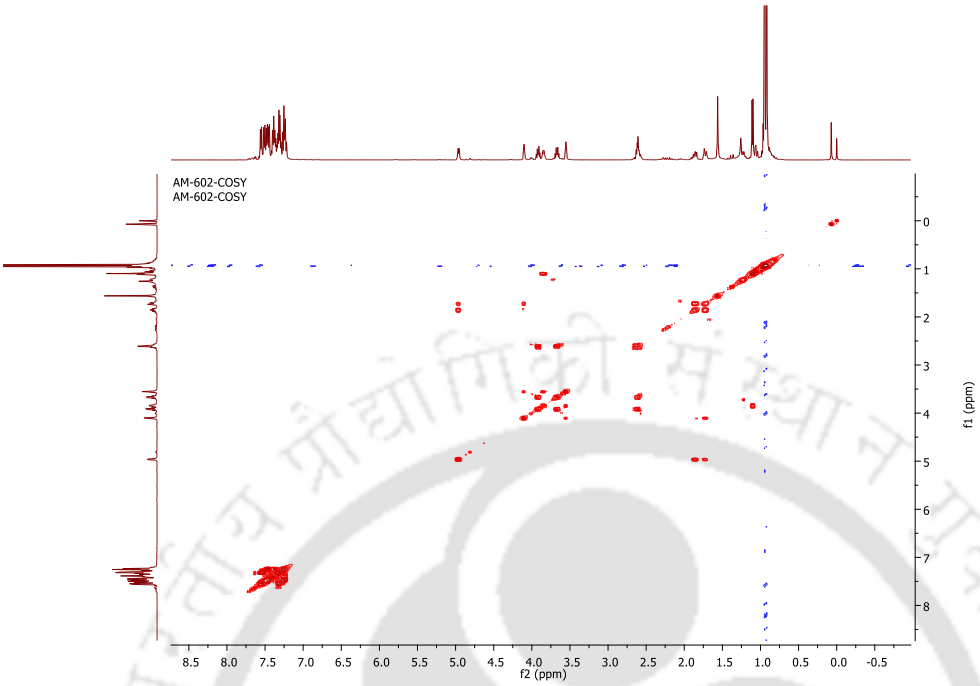
^{1}H NMR of 2-Cyanoethyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23b, 500 MHz, $CDCl_3$):



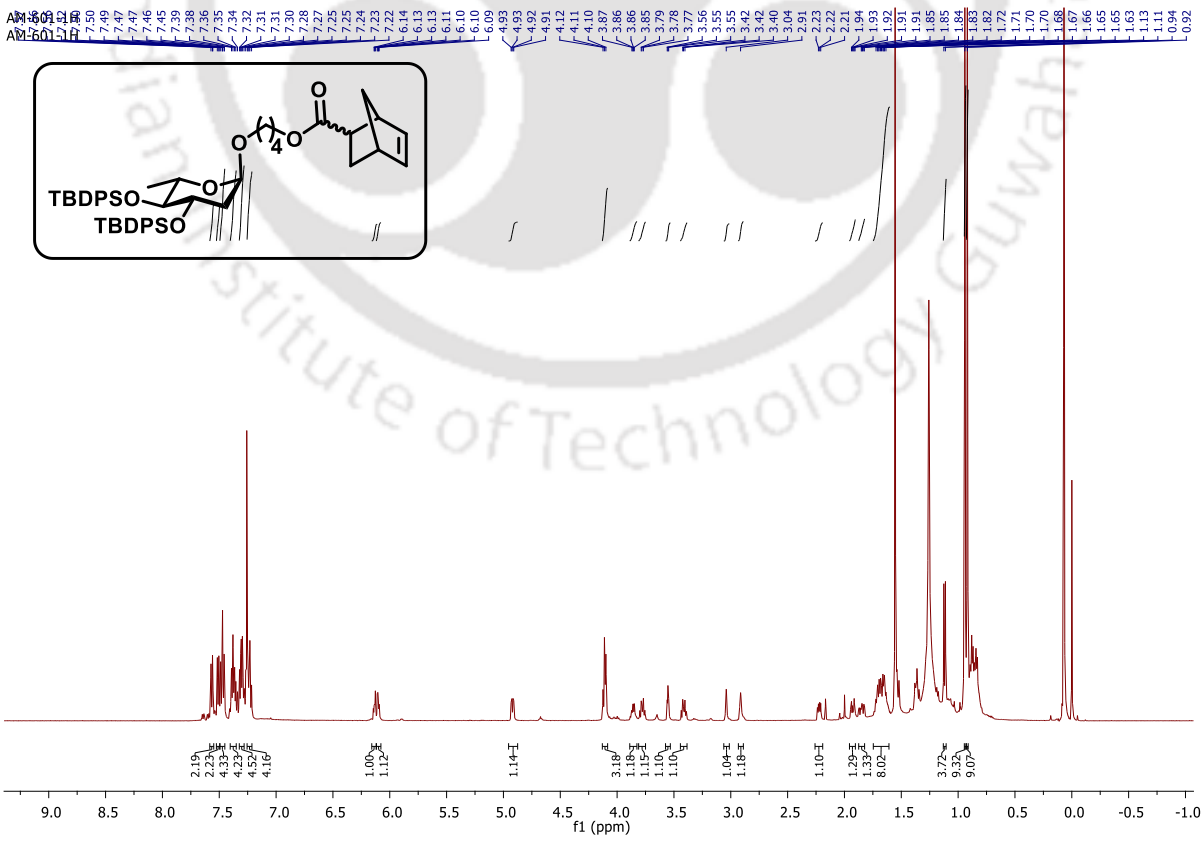
^{13}C NMR of 2-Cyanoethyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23b, 500 MHz, $CDCl_3$):



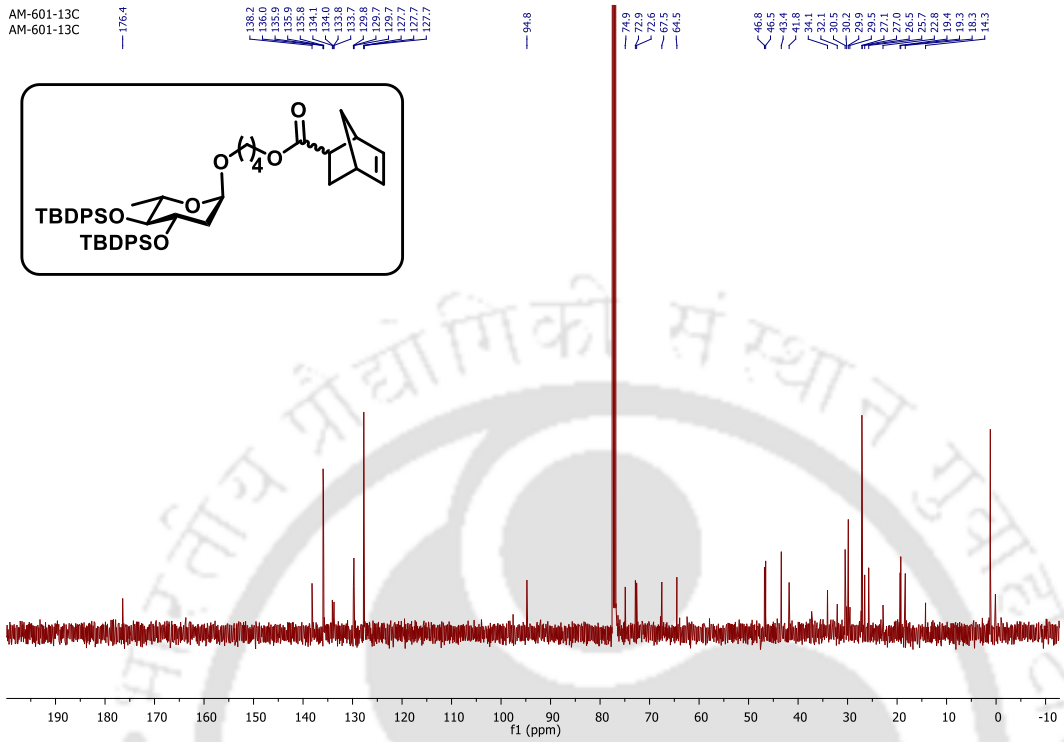
COSY NMR of 2-Cyanoethyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23b, 500 MHz, $CDCl_3$):



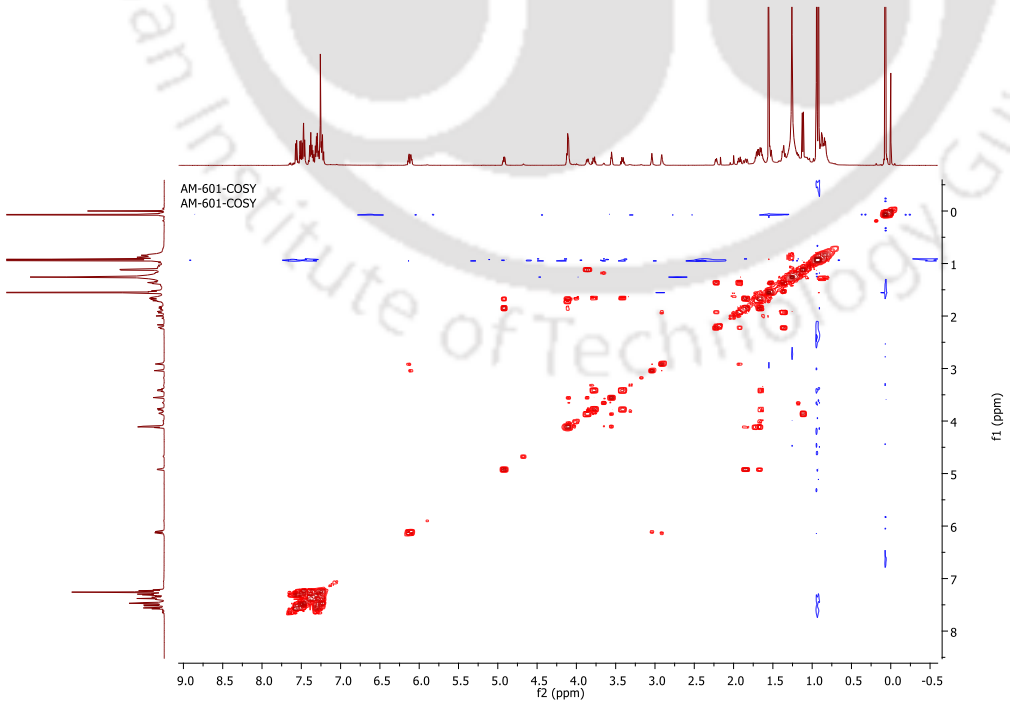
^{1}H NMR of 4-Hydroxybutyl-bicyclo[2.2.1]hept-5-ene-2-carboxylate-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23c, 500 MHz, $CDCl_3$):



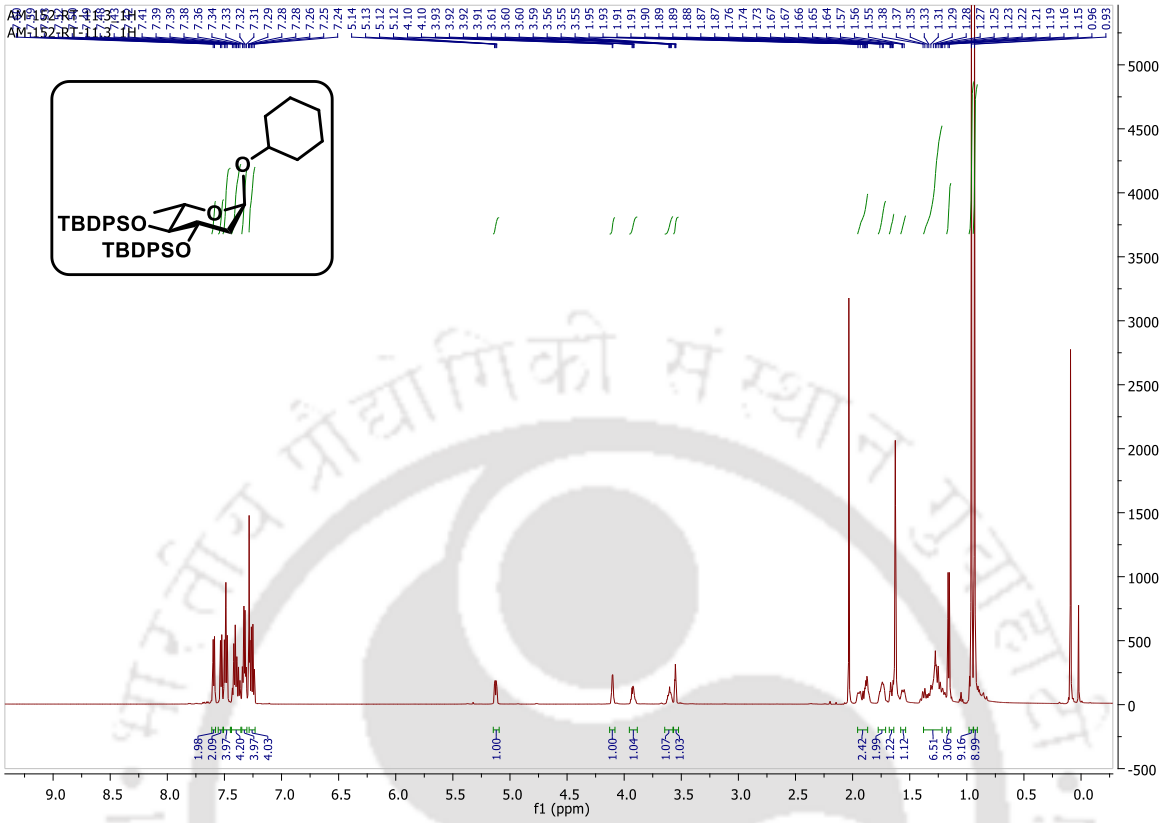
^{13}C NMR of 4-Hydroxybutyl-bicyclo[2.2.1]hept-5-ene-2-carboxylate-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23c, 500 MHz, $CDCl_3$):



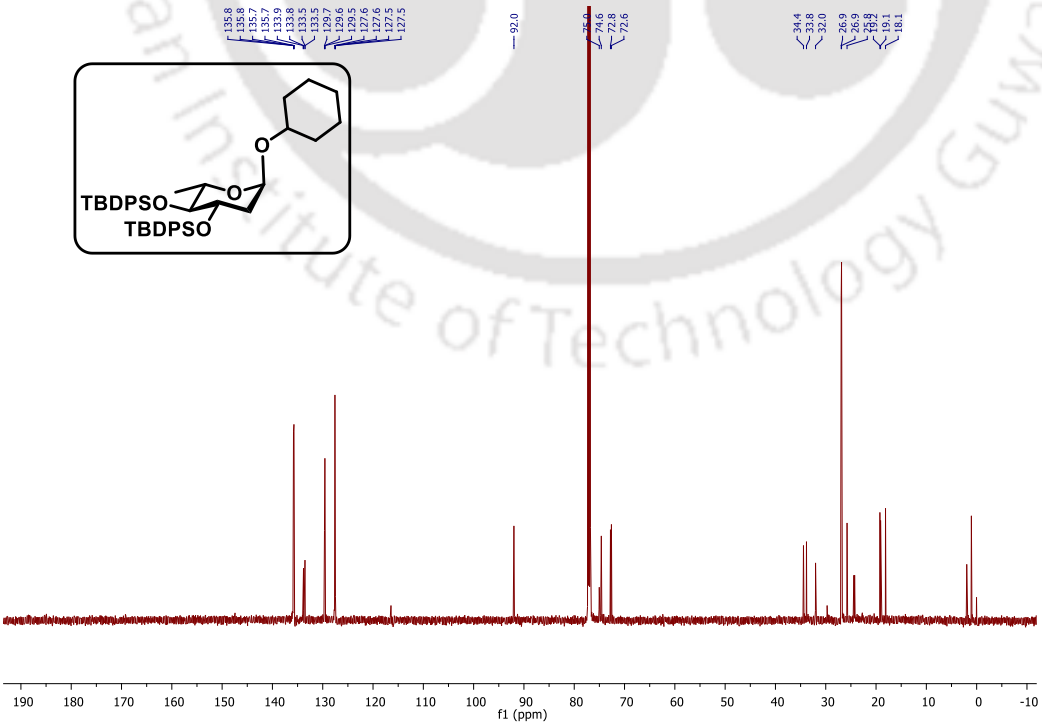
COSY NMR of 4-Hydroxybutyl-bicyclo[2.2.1]hept-5-ene-2-carboxylate-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23c, 500 MHz, $CDCl_3$):



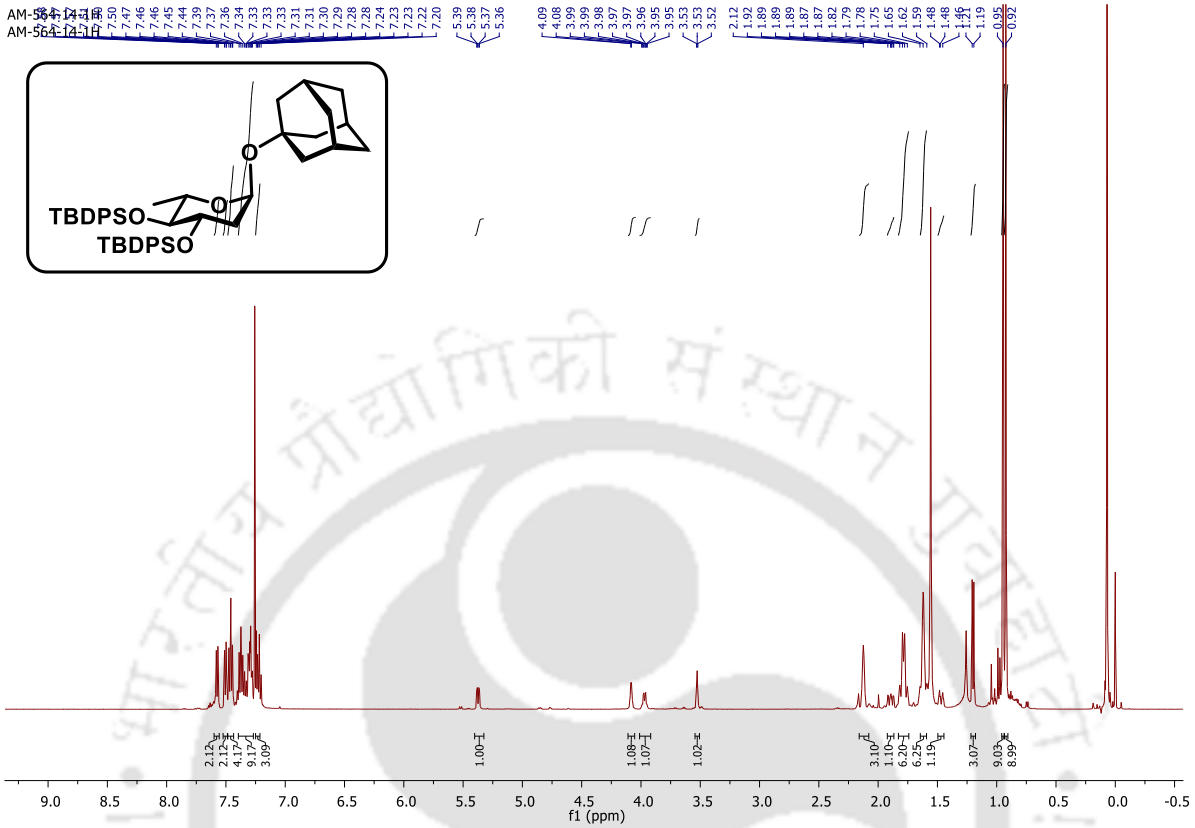
^{1}H NMR of Cyclohexyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23d, 600 MHz, $CDCl_3$):



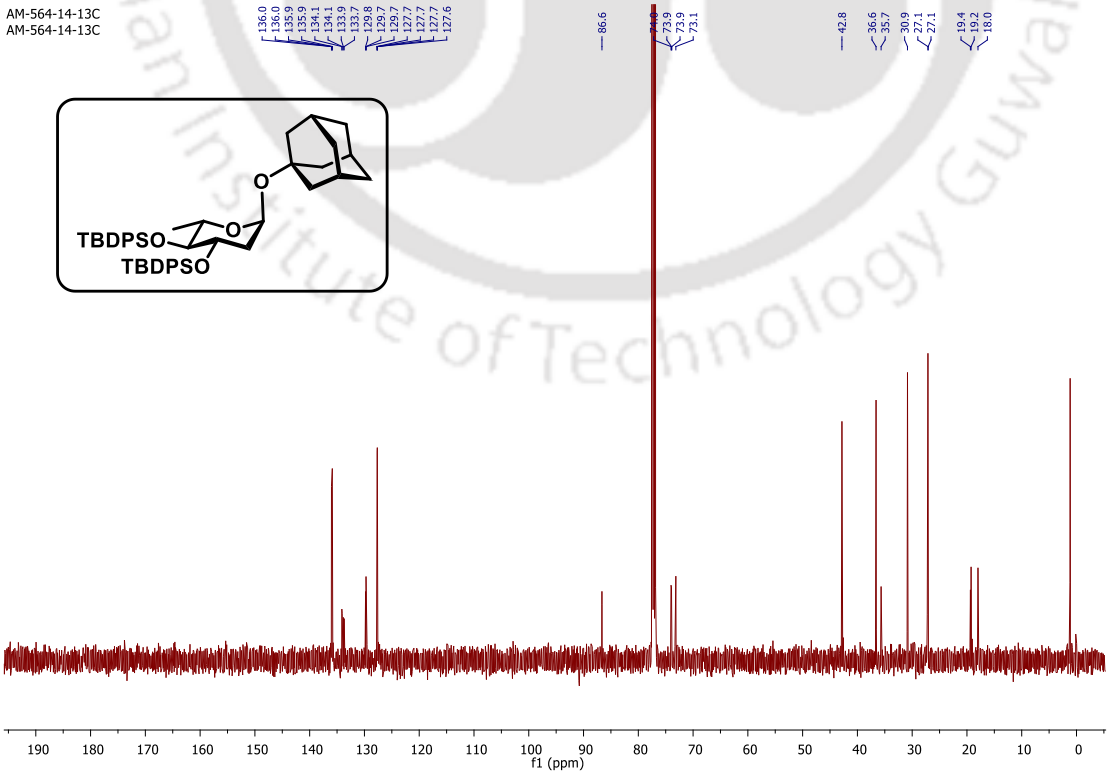
^{13}C NMR of Cyclohexyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23d, 600 MHz, $CDCl_3$):



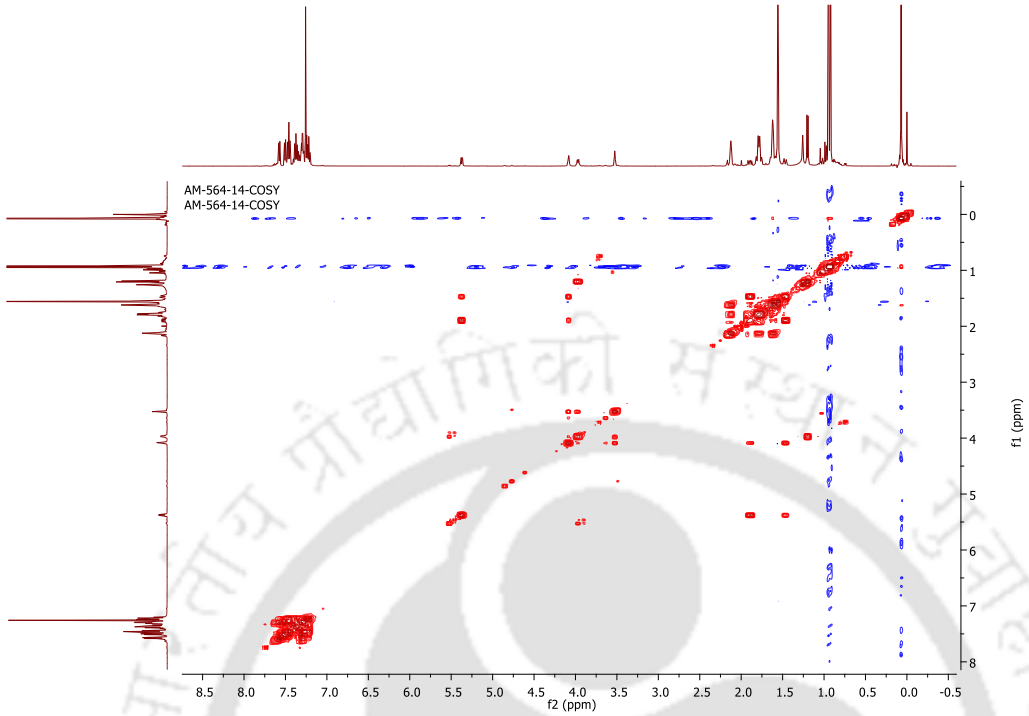
^{1}H NMR of 1-Adamantanyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23e, 500 MHz, $CDCl_3$):



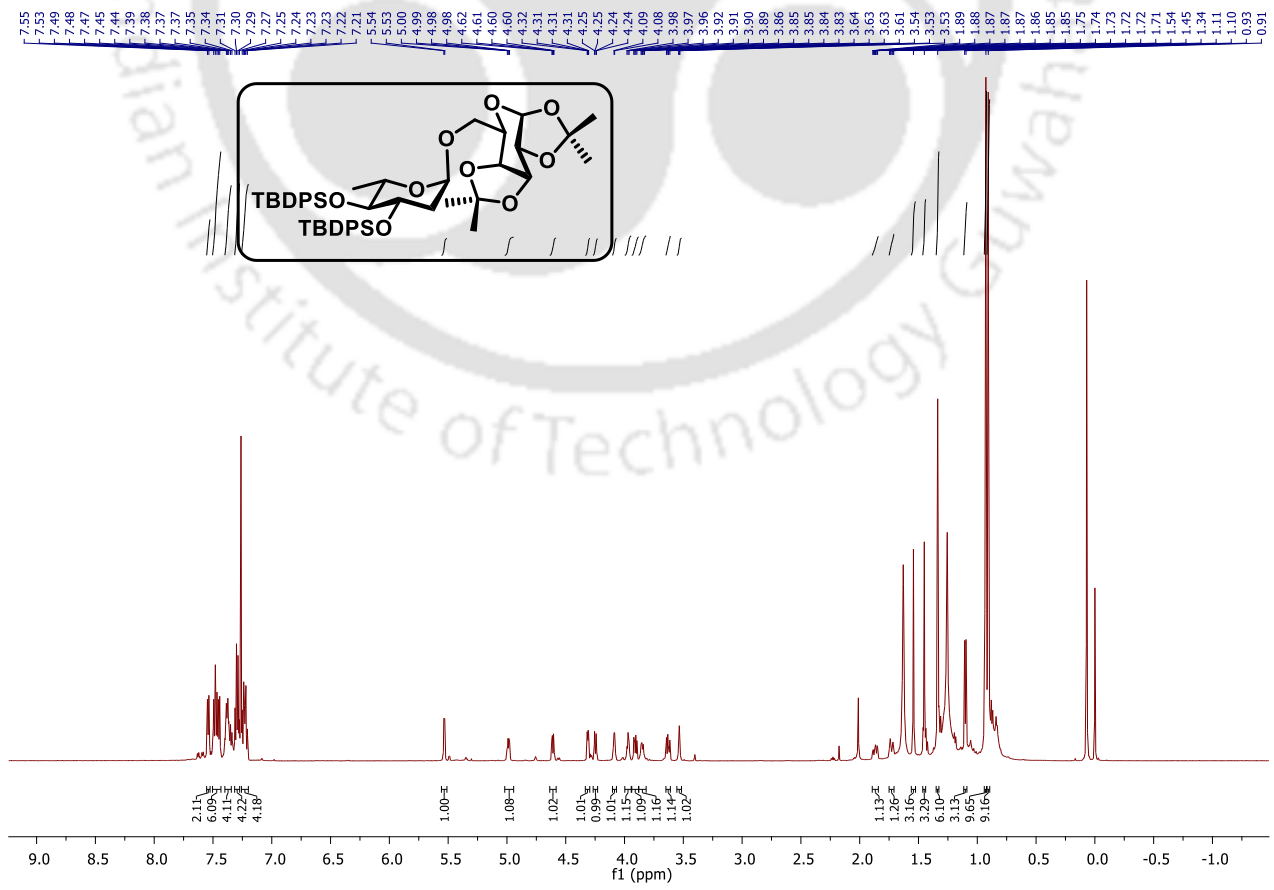
^{13}C NMR of 1-Adamantanyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23e, 500 MHz, $CDCl_3$):



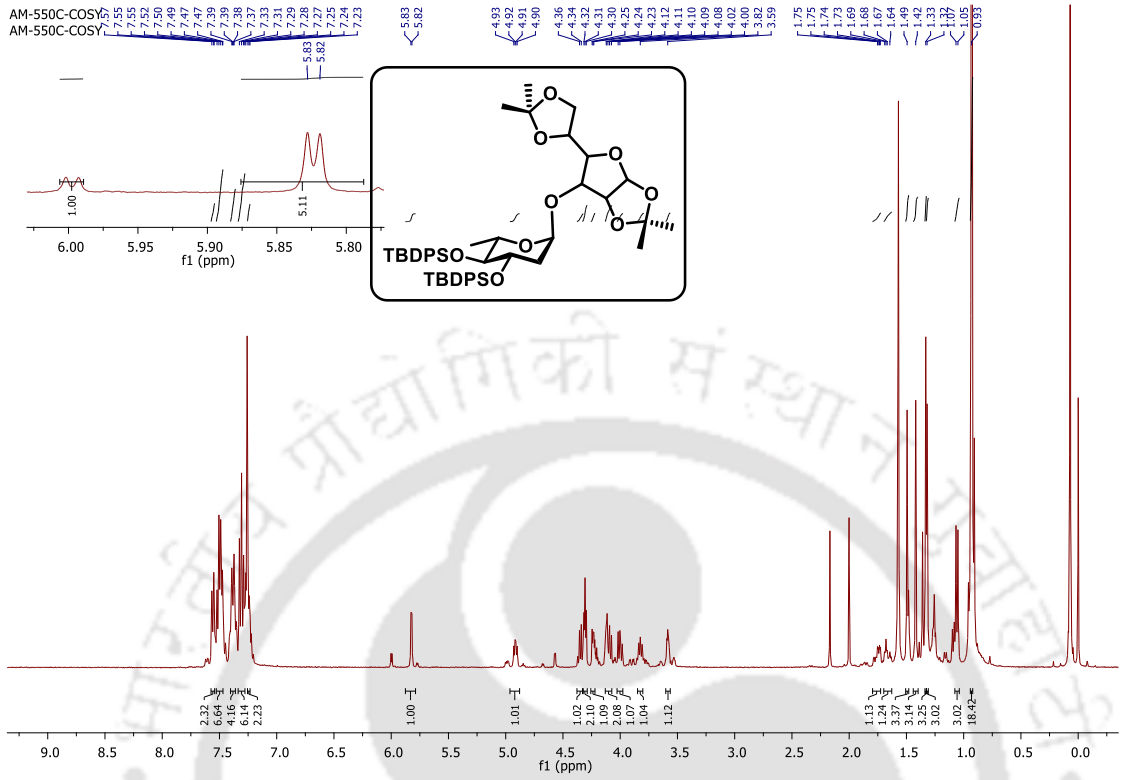
COSY NMR of 1-Adamantanyl-2,6-dideoxy-3,4-bis-*O*-[(1,1-dimethylethyl)diphenylsilyl]-α-L-arabino-hexapyranoside (23e, 500 MHz, $CDCl_3$):



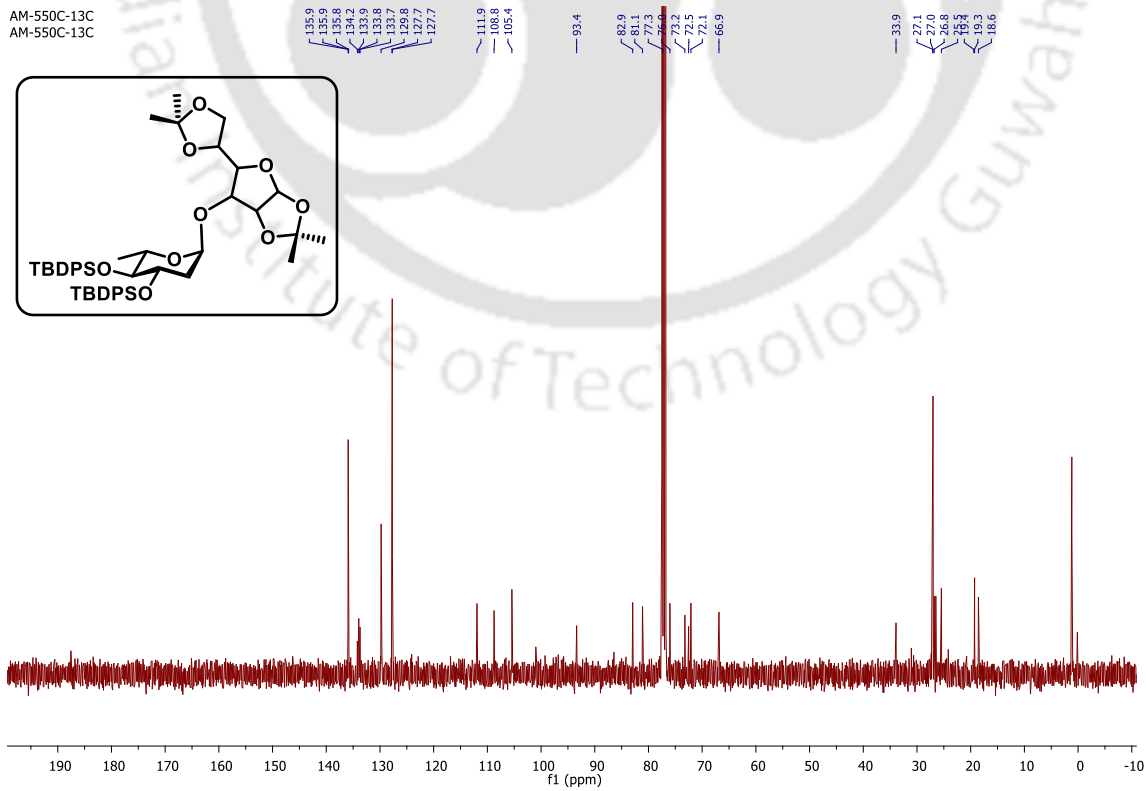
^{1}H NMR of 6-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranoside (23f, 600 MHz, $CDCl_3$):



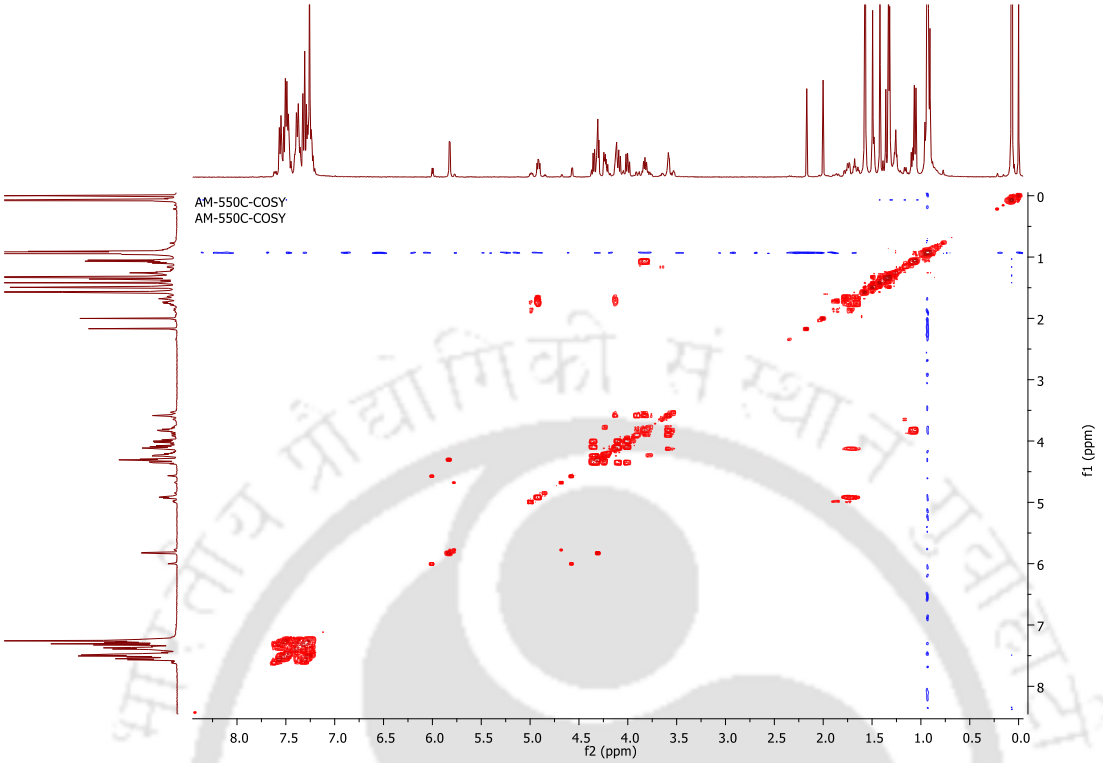
^{1}H NMR of 3-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose (23g, 400 MHz, $CDCl_3$):



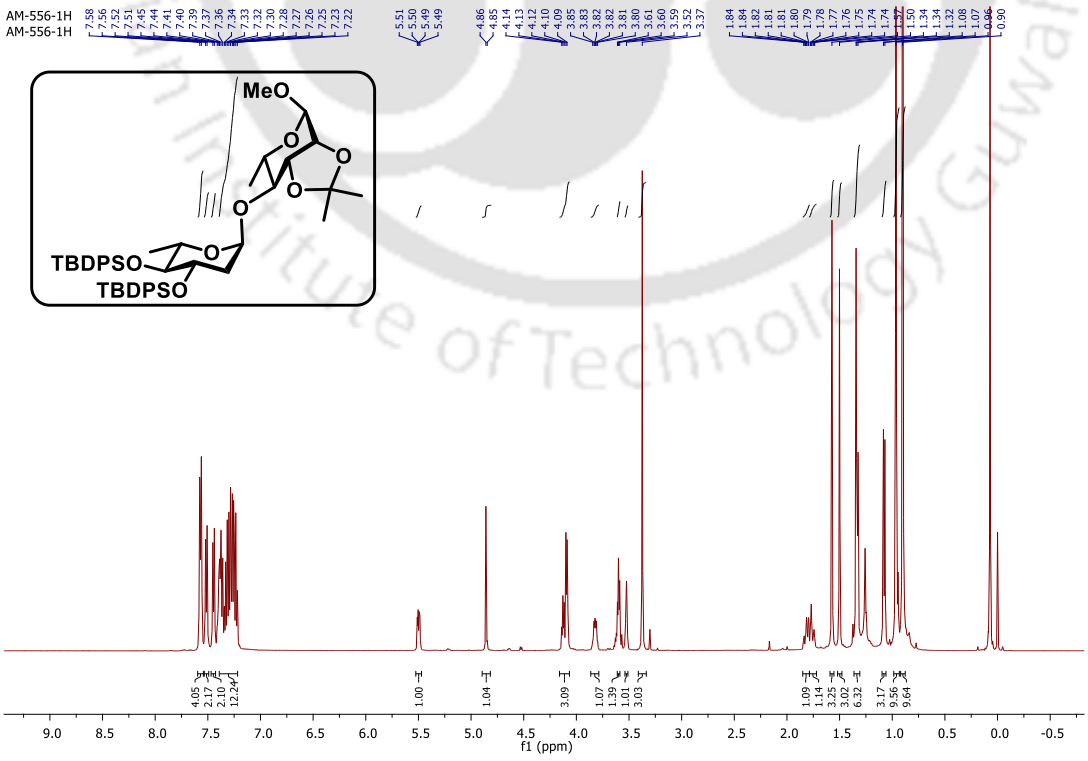
^{13}C NMR of 3-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose (23g, 400 MHz, $CDCl_3$):



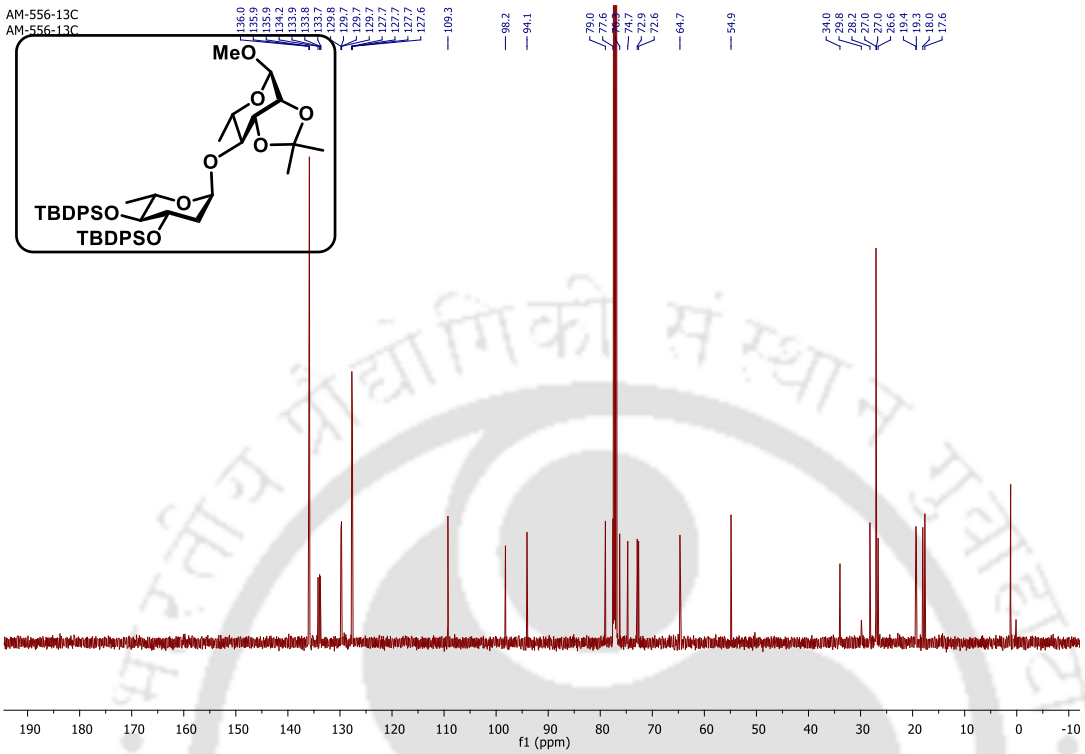
COSY NMR of 3-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose (23g, 400 MHz, $CDCl_3$):



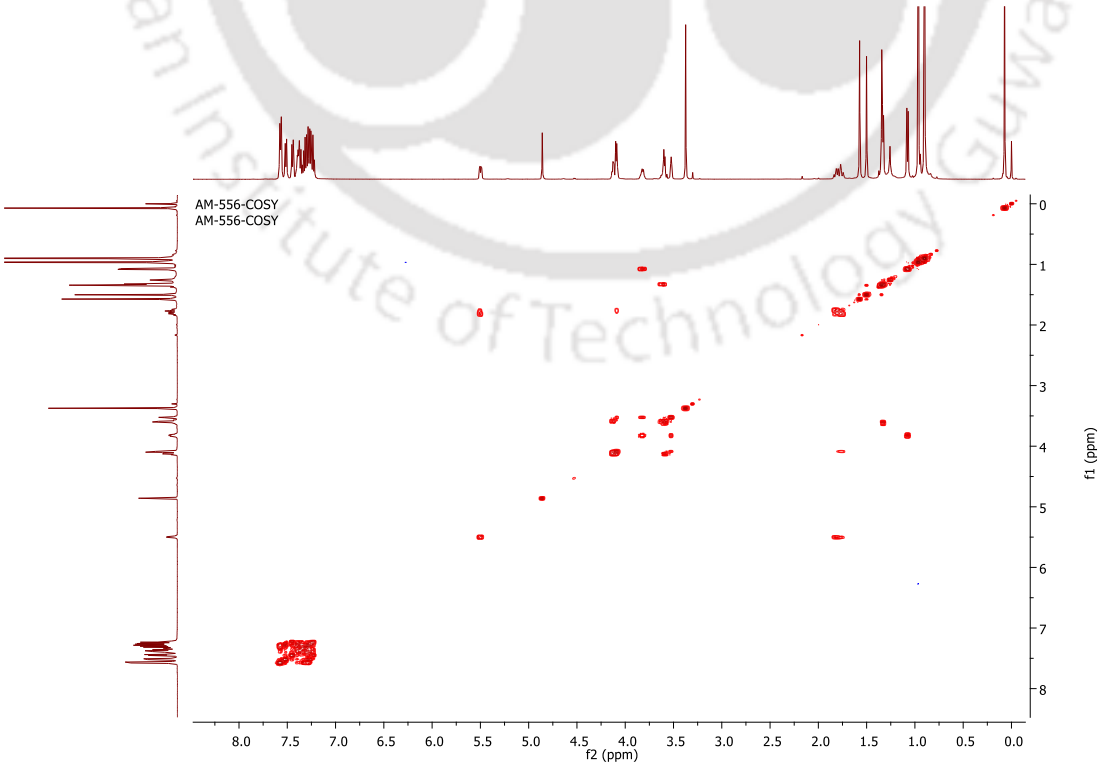
^{1}H NMR of Methyl 6-deoxy-4-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (23h, 500 MHz, $CDCl_3$):



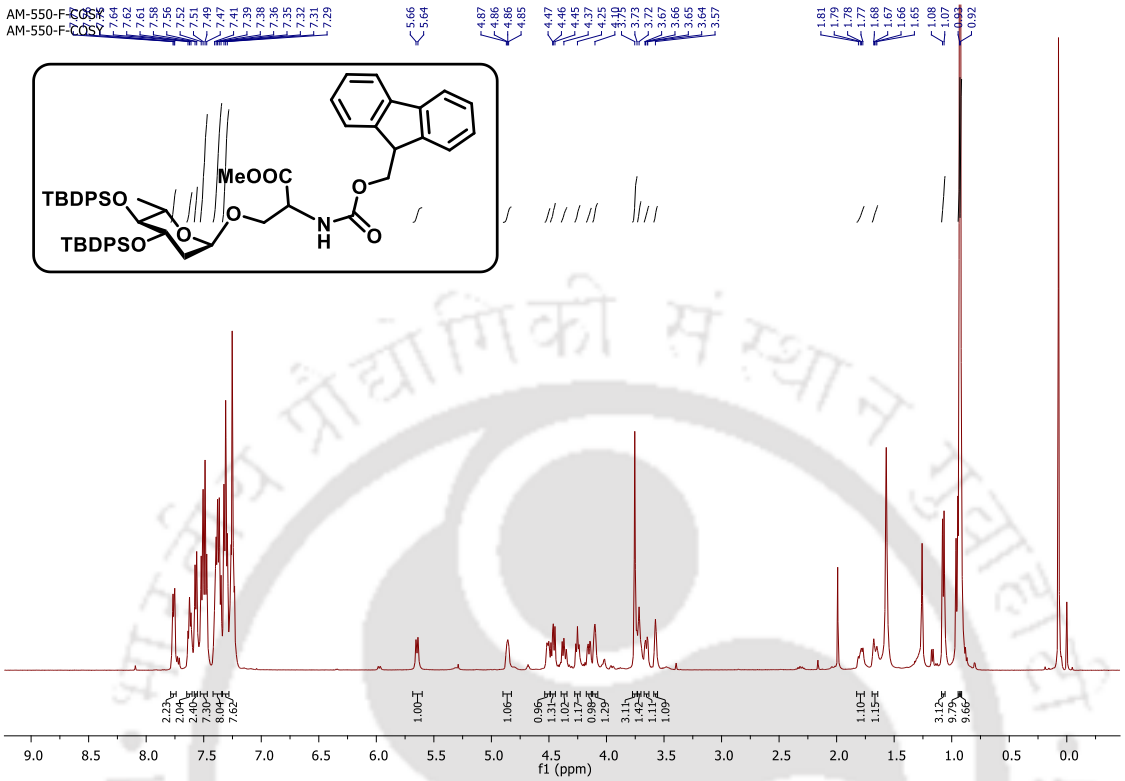
^{13}C NMR of Methyl 6-deoxy-4-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (23h, 500 MHz, $CDCl_3$):



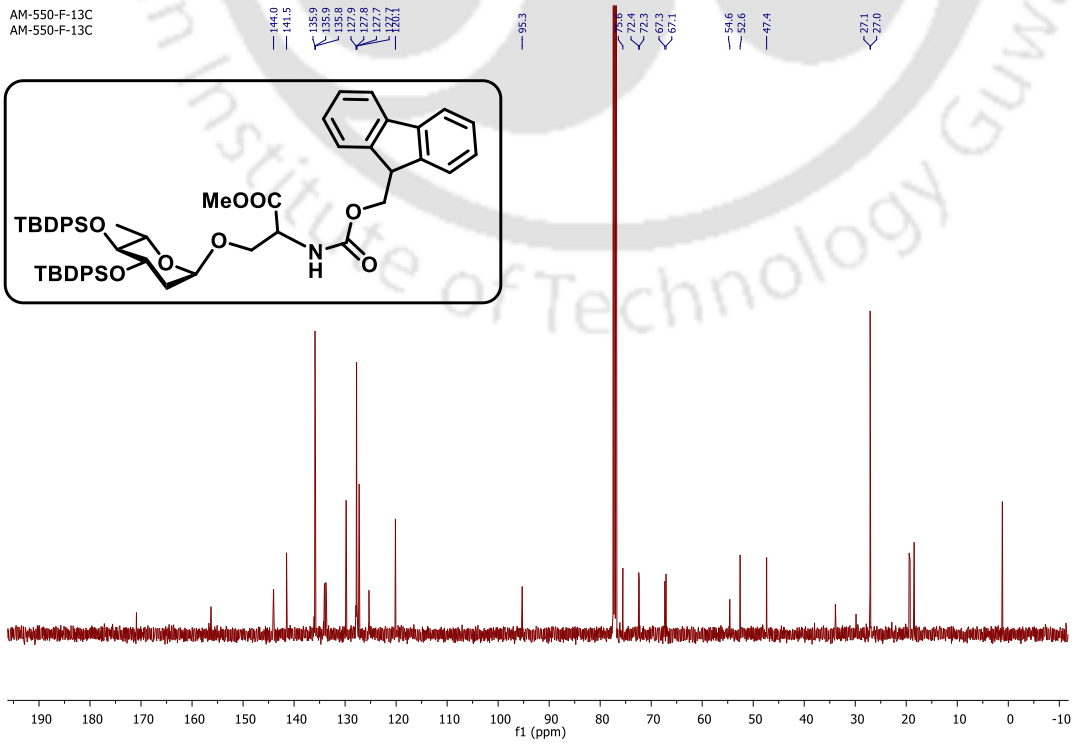
COSY NMR of Methyl 6-deoxy-4-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (23h, 500 MHz, $CDCl_3$):



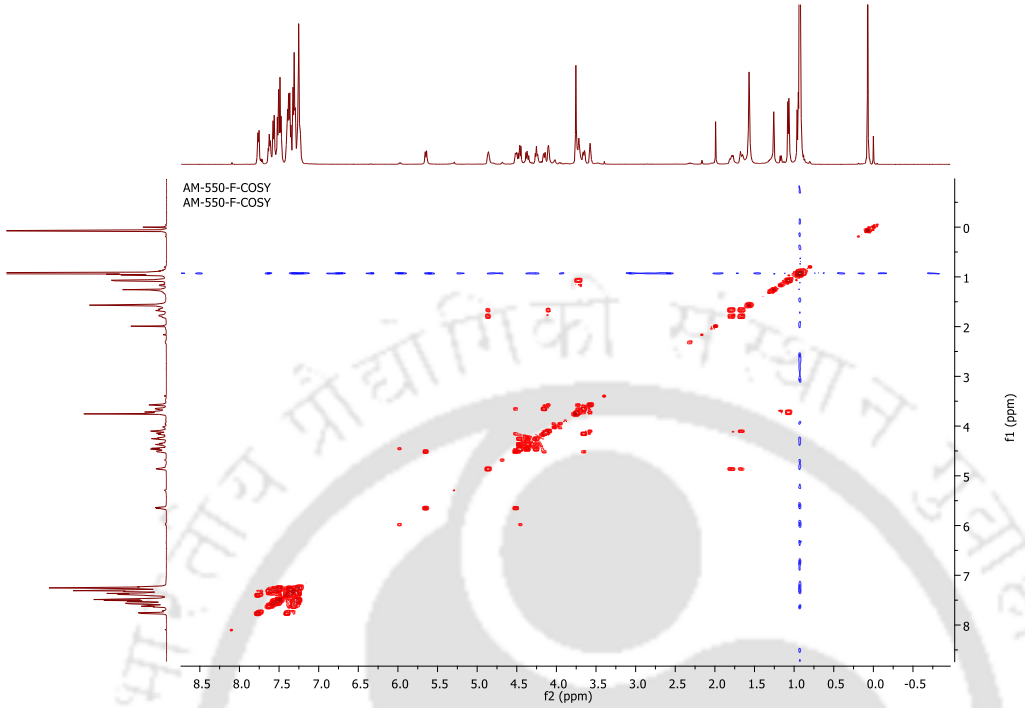
^{1}H NMR of Methyl fmoc-serine-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (23i, 500 MHz, $CDCl_3$):



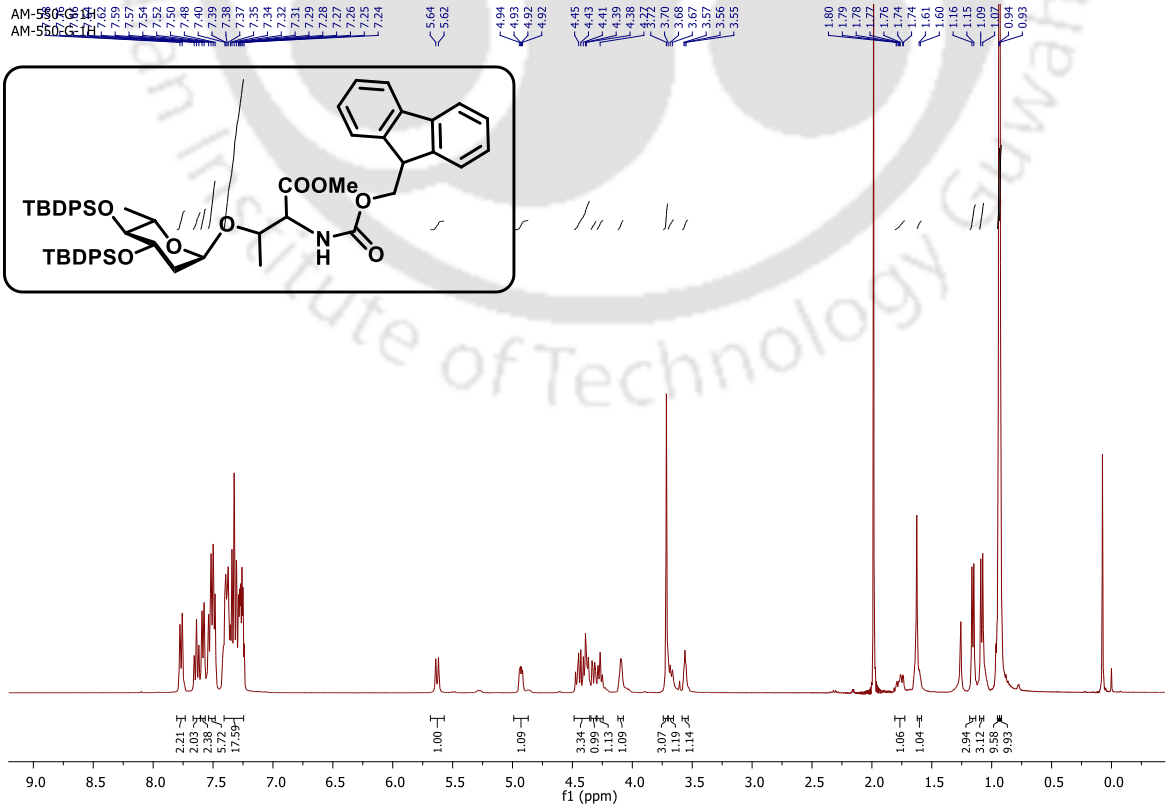
^{13}C NMR of Methyl fmoc-serine-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (23i, 500 MHz, $CDCl_3$):



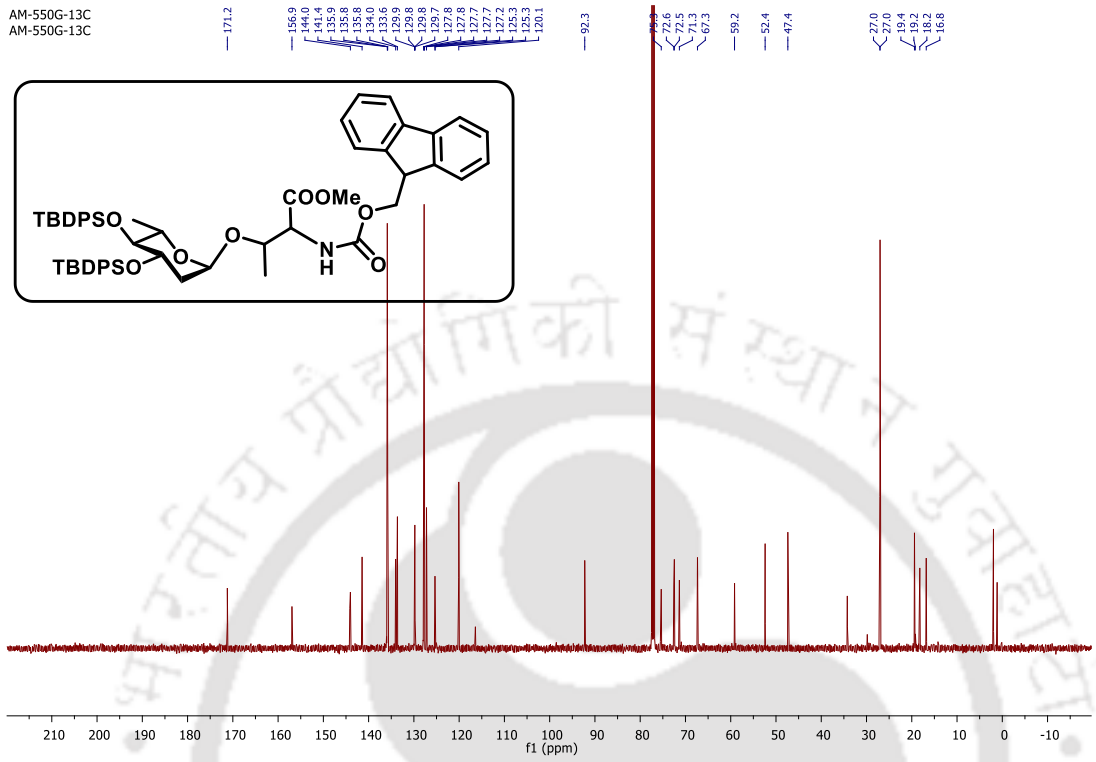
COSY NMR of Methyl fmoc-serine-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (23i, 500 MHz, $CDCl_3$):



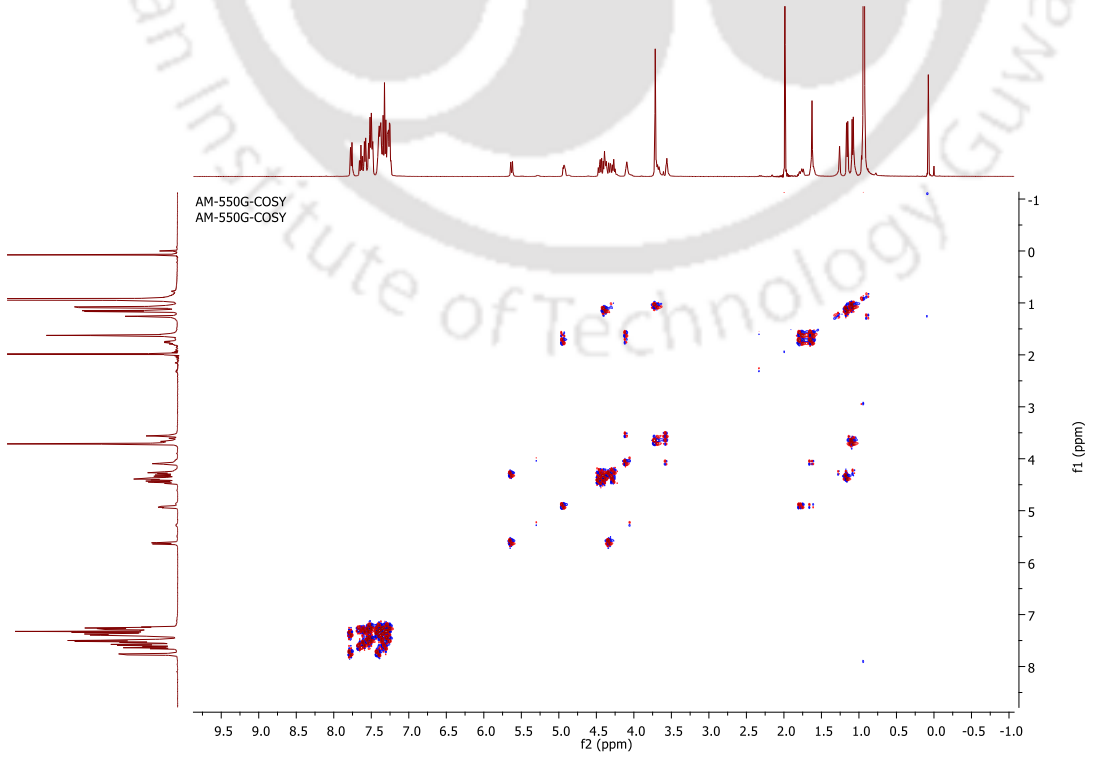
^{1}H NMR of Methyl fmoc-threonine-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (23j, 400 MHz, $CDCl_3$):



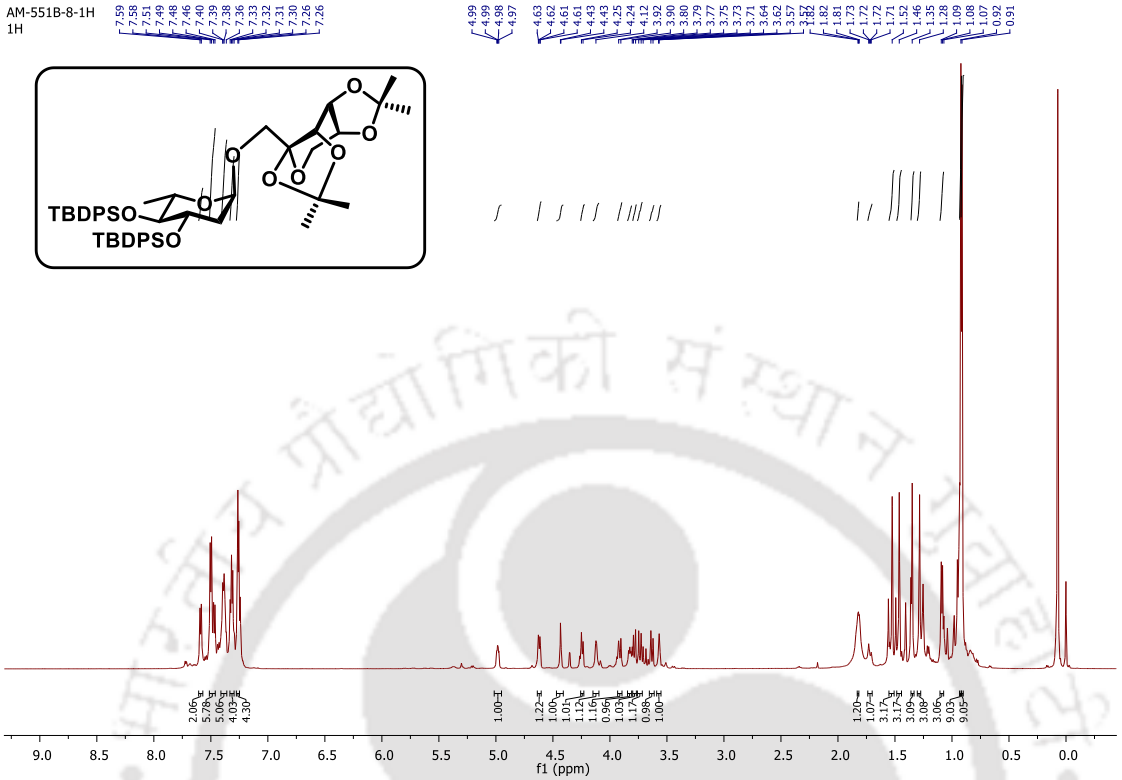
^{13}C NMR of Methyl fmoc-threonine-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (23j, 500 MHz, $CDCl_3$):



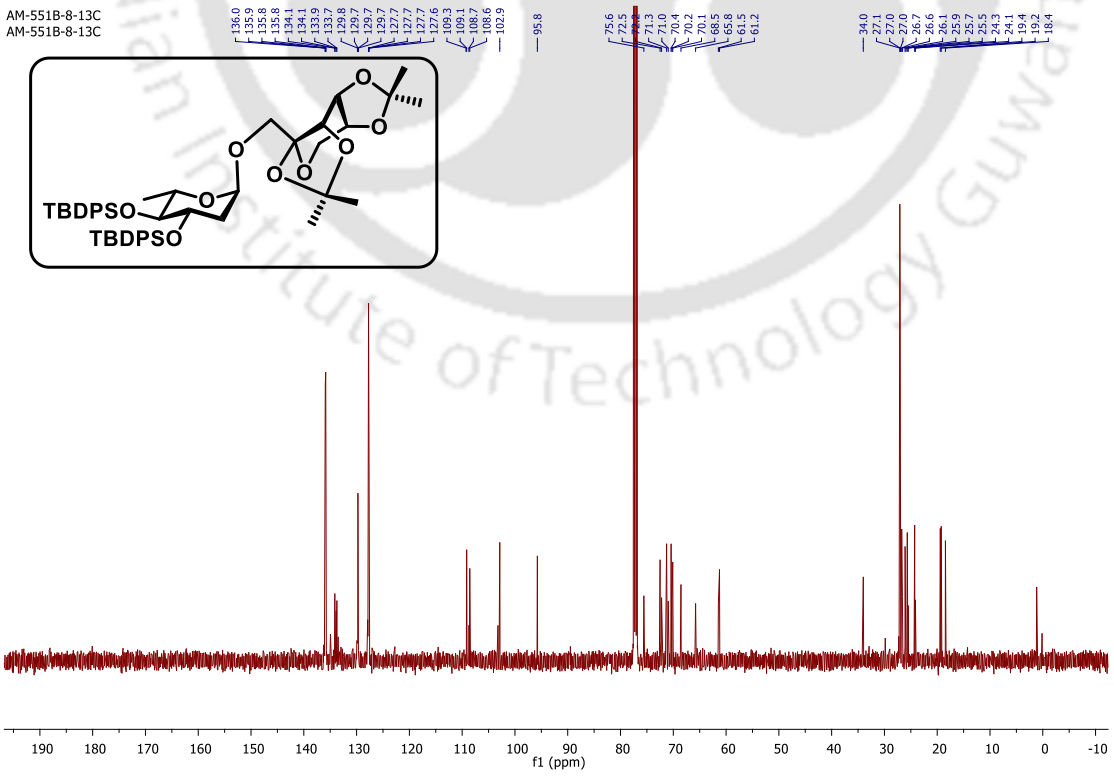
COSY NMR of Methyl fmoc-threonine-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (23j, 400 MHz, $CDCl_3$):



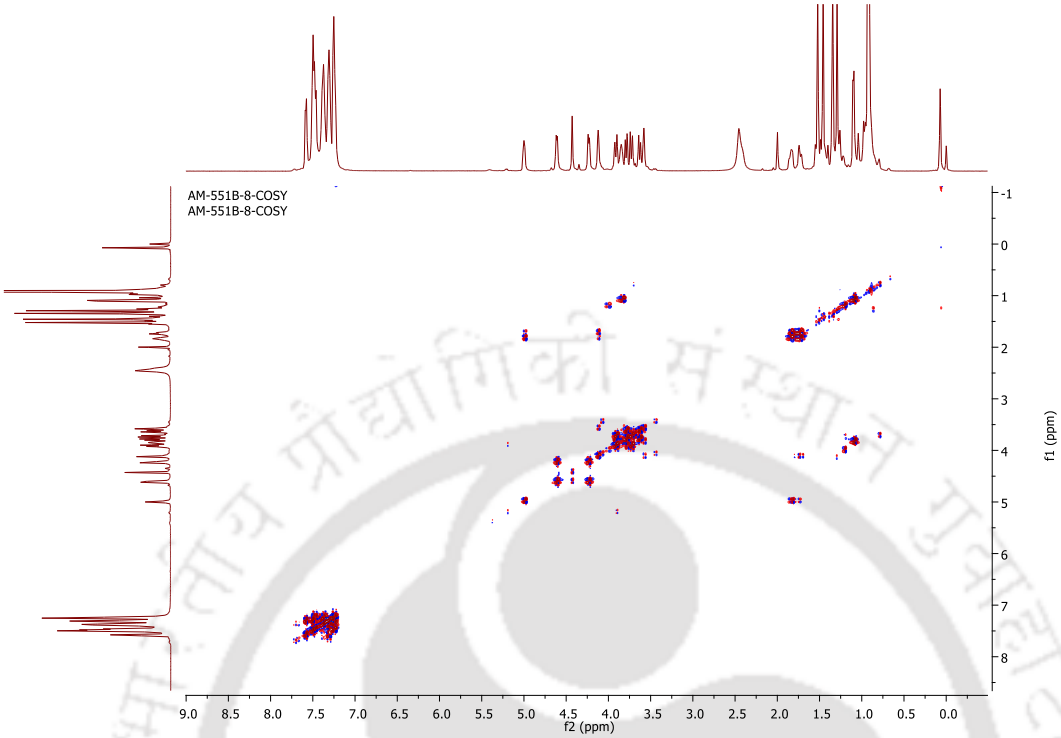
^{1}H NMR of 1-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3:4,5-Di-*O*-isopropylidene-*α*-D-fructopyranose (23k, 600 MHz, $CDCl_3$):



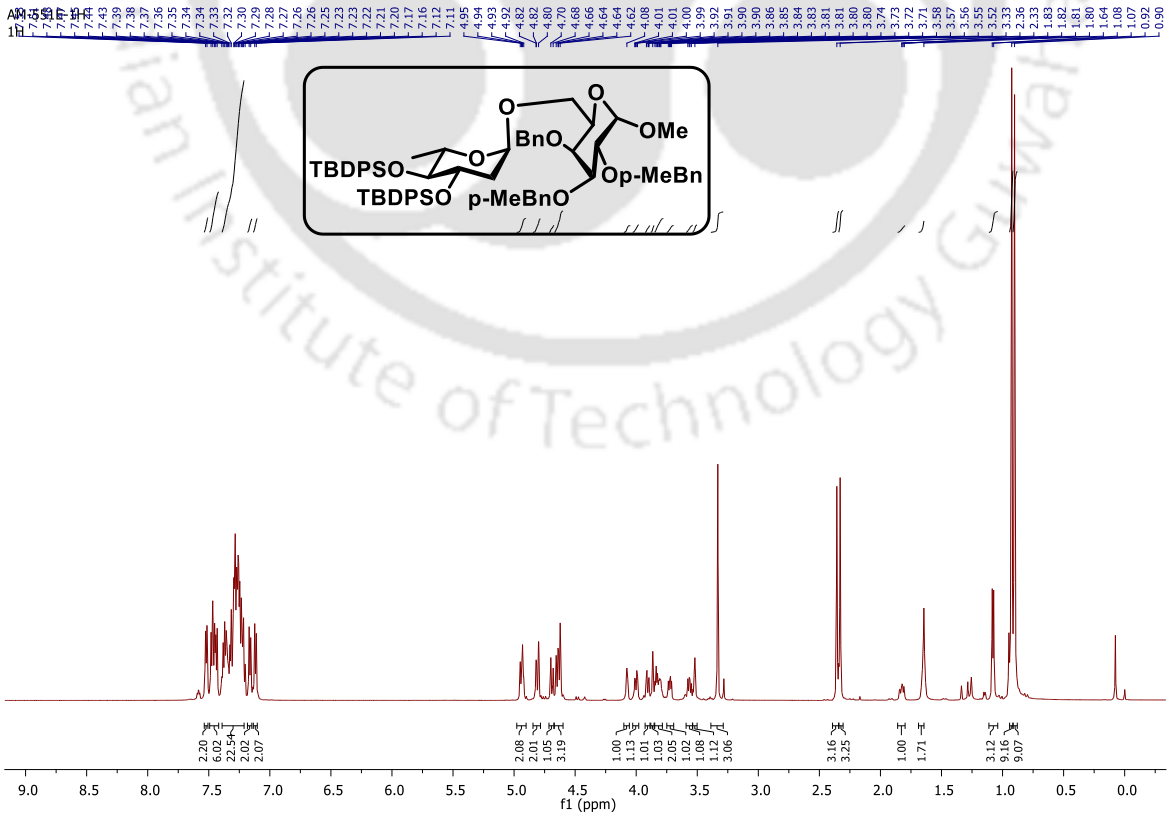
^{13}C NMR of 1-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3:4,5-Di-*O*-isopropylidene-*α*-D-fructopyranose (23k, 500 MHz, $CDCl_3$):



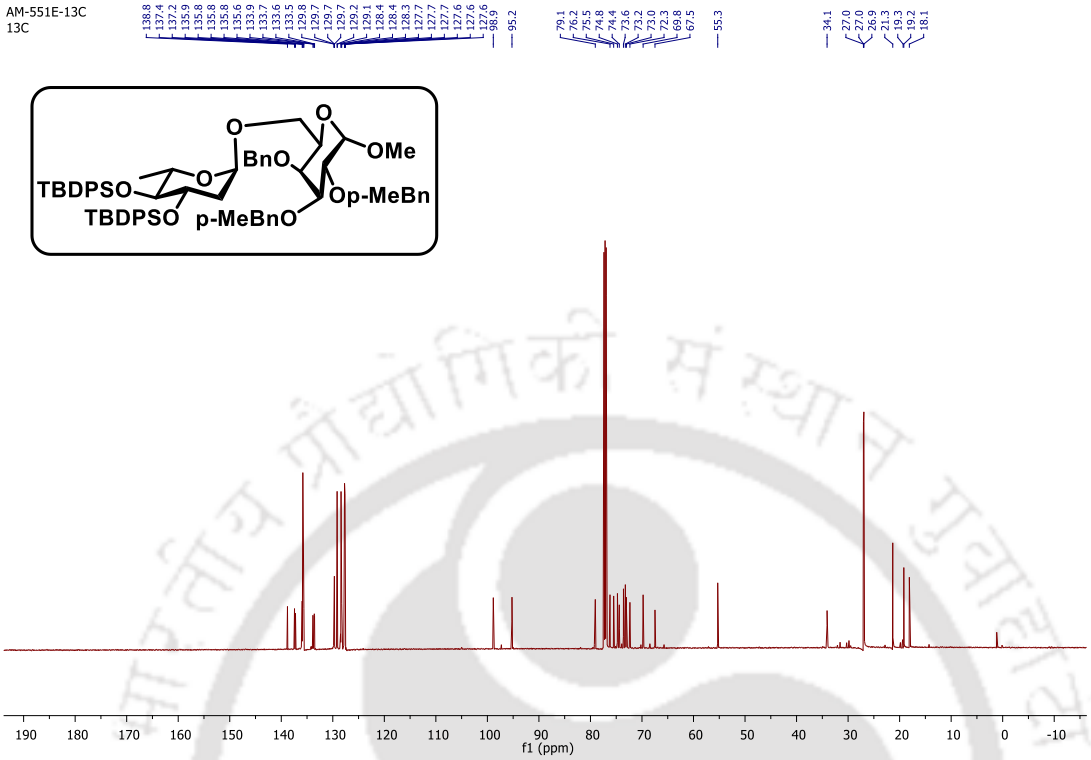
COSY NMR of 1-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3:4,5-Di-*O*-isopropylidene-α-D-fructopyranose (23k, 600 MHz, $CDCl_3$):



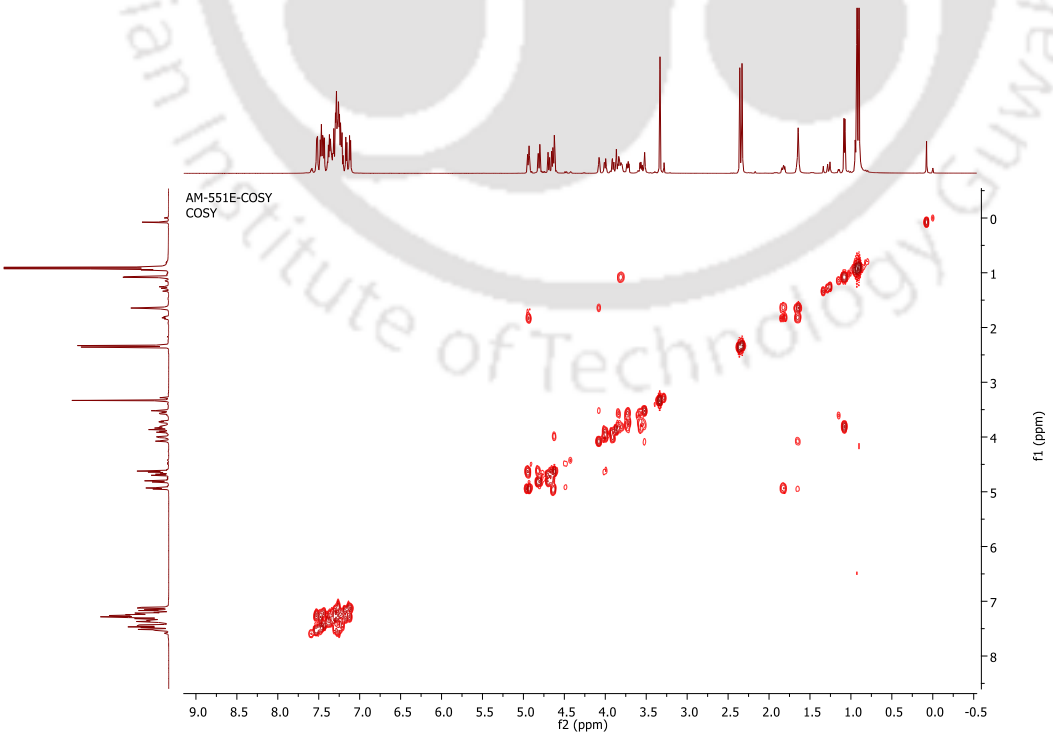
^{1}H NMR of Methyl 6-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-di-O-p-methylbenzyl-4-O-benzyl-D-galactopyranoside (23l, 600 MHz, $CDCl_3$):



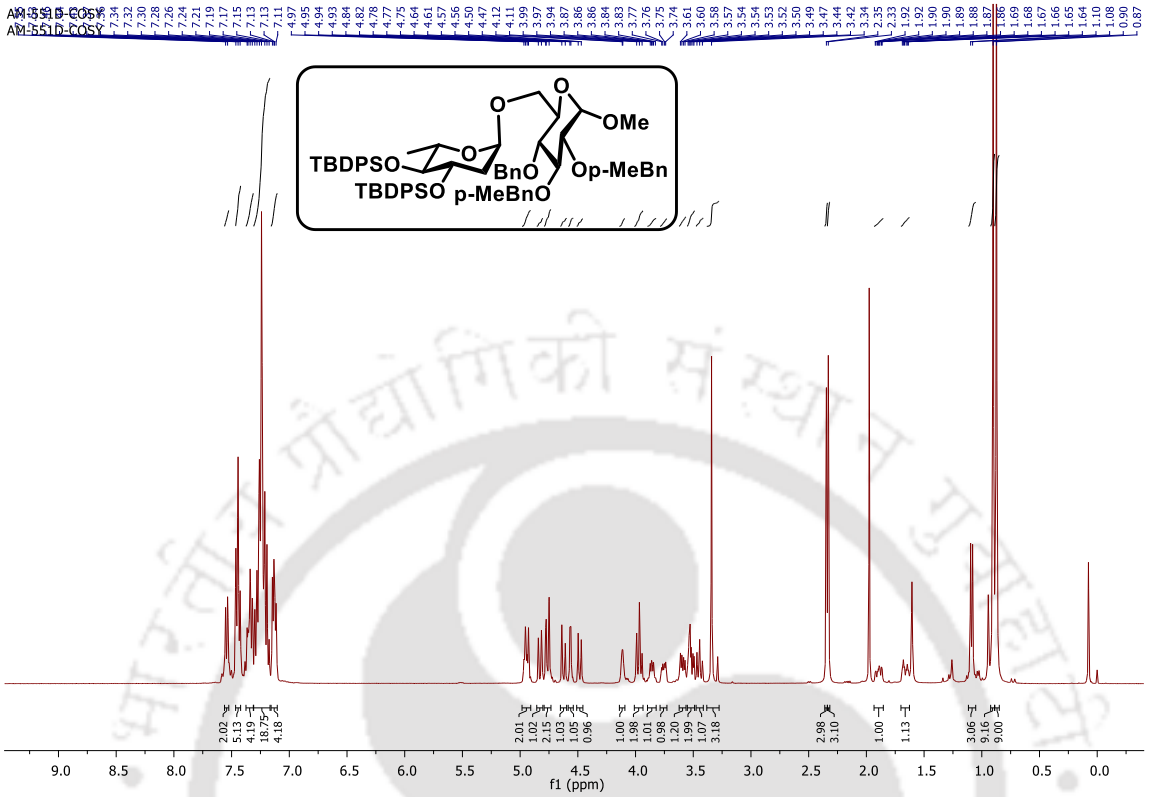
^{13}C NMR of Methyl 6-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-di-O-p-methylbenzyl-4-O-benzyl-D-galactopyranoside (23l, 600 MHz, $CDCl_3$):



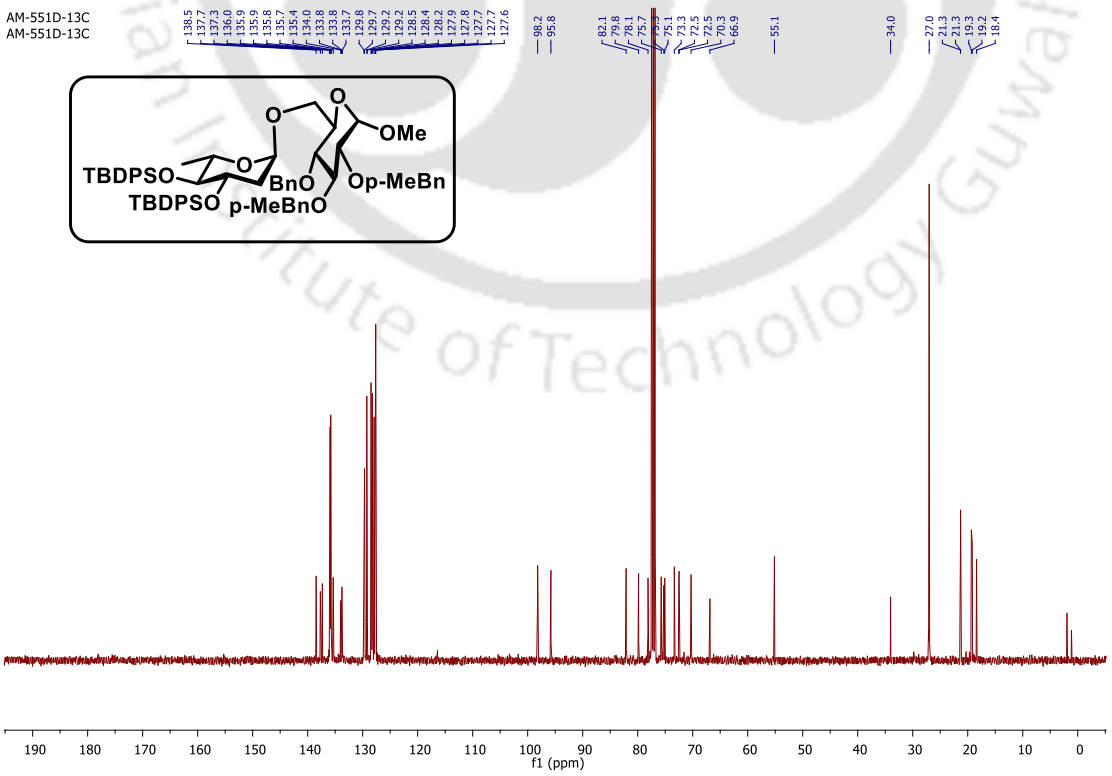
COSY NMR of Methyl 6-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-di-O-p-methylbenzyl-4-O-benzyl-D-galactopyranoside (23l, 600 MHz, $CDCl_3$):



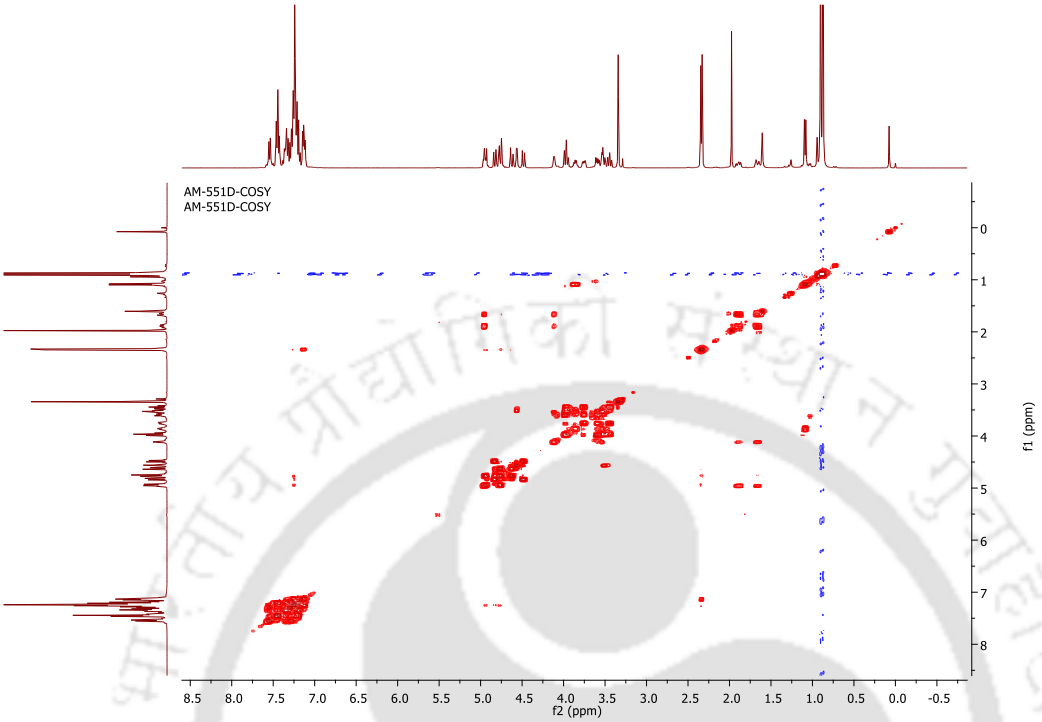
^{1}H NMR of Methyl 6-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-di-O-p-methylbenzyl-4-O-benzyl-D-glucopyranoside (23m, 400 MHz, $CDCl_3$):



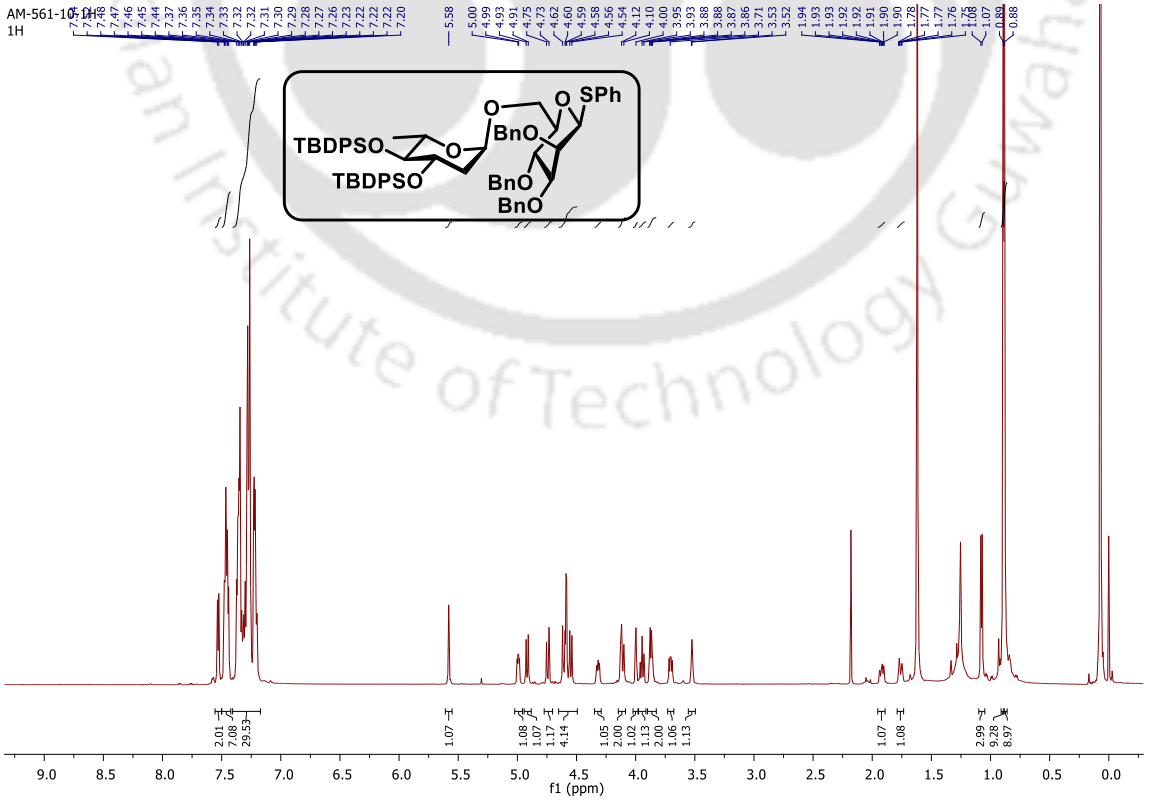
^{13}C NMR of Methyl 6-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-di-O-p-methylbenzyl-4-O-benzyl-D-glucopyranoside (23m, 400 MHz, $CDCl_3$):



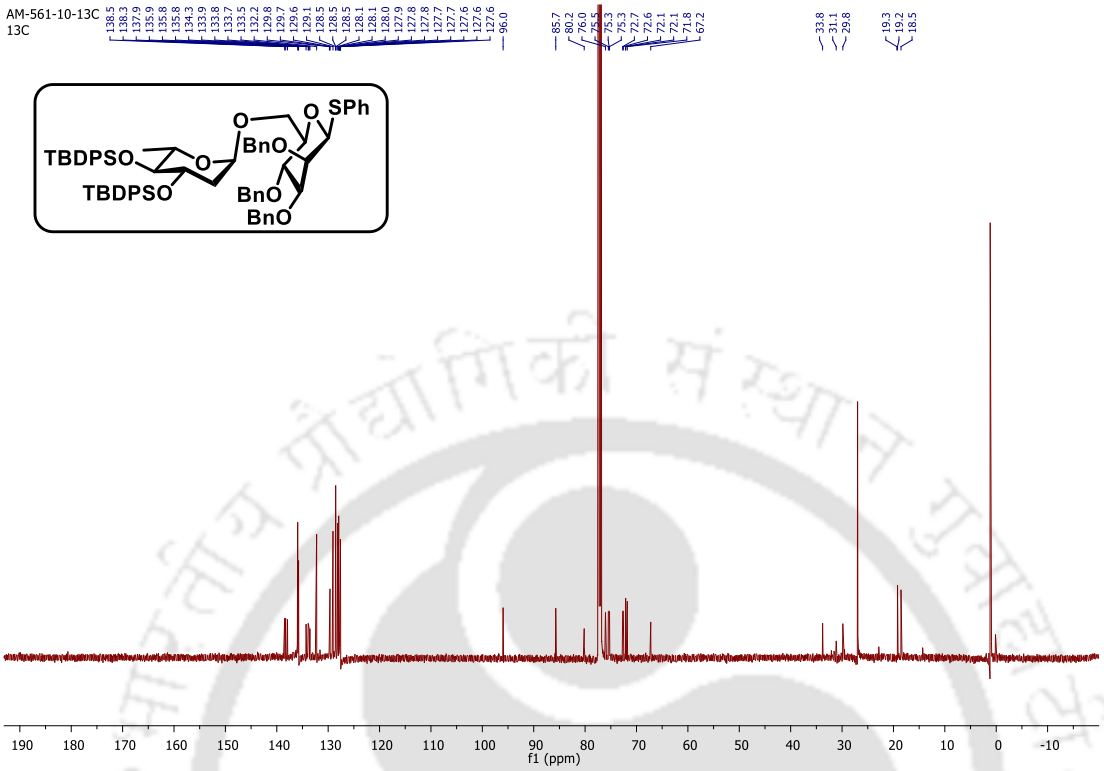
COSY NMR of Methyl 6-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-2,3-di-O-p-methylbenzyl-4-O-benzyl-D-glucopyranoside (23m, 400 MHz, $CDCl_3$):



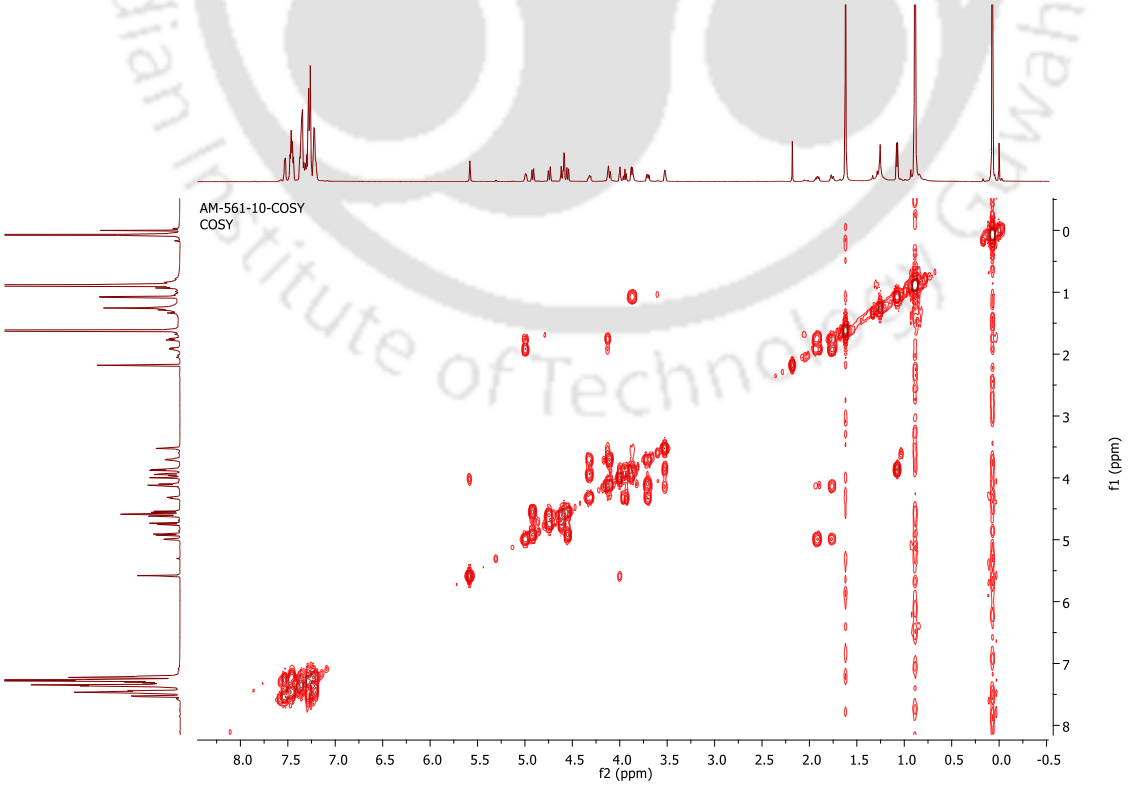
^{1}H NMR of Phenyl 2,3,4-tri-O-benzyl-6-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-β-D-thioglucopyranoside (23n, 600 MHz, $CDCl_3$):



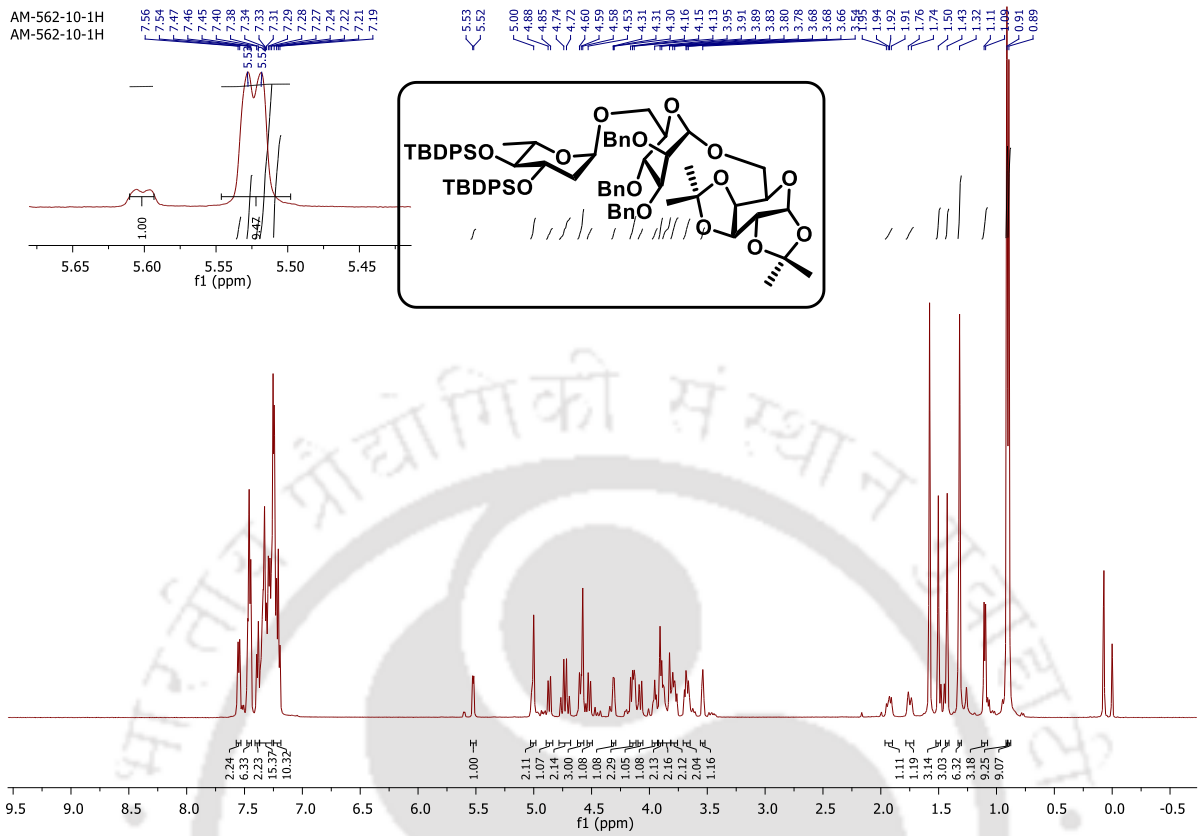
^{13}C NMR of Phenyl 2,3,4-tri-O-benzyl-6-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-β-D-thioglucopyranoside (23n, 600 MHz, $CDCl_3$):



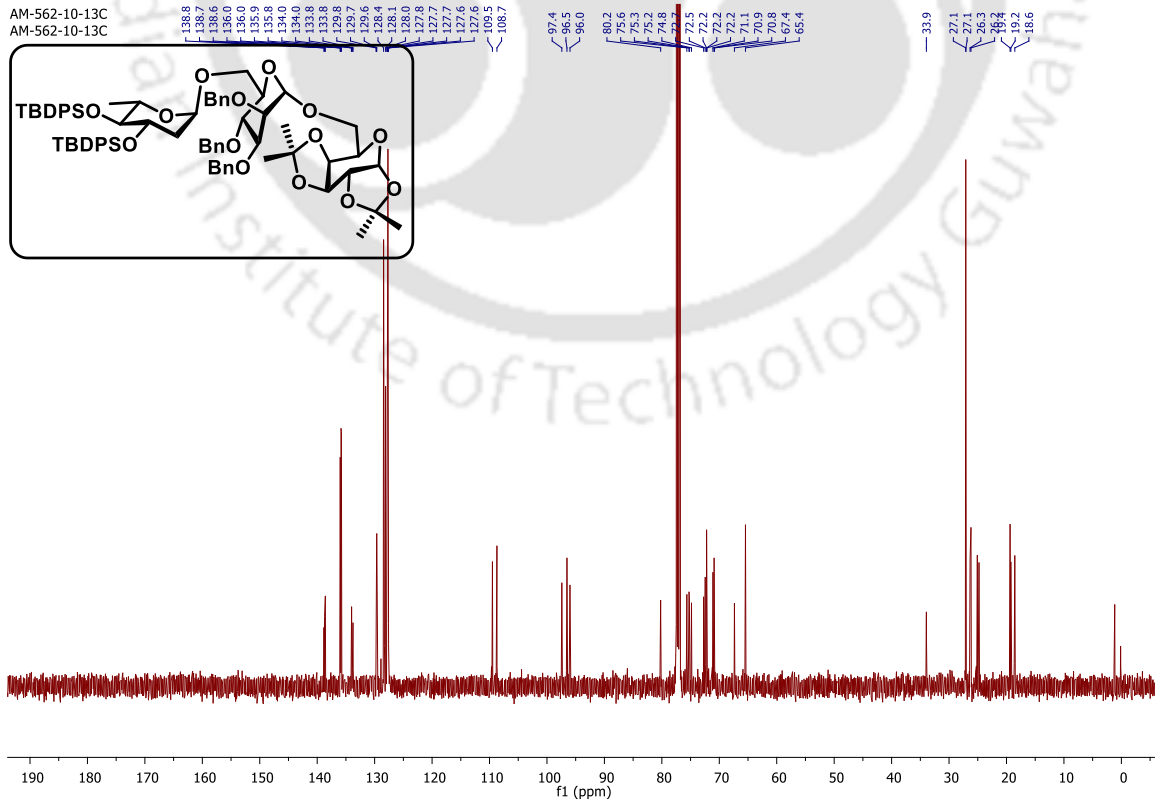
COSY NMR of Phenyl 2,3,4-tri-O-benzyl-6-O-(3,4-O-Bis-(t-butyldiphenylsilyl)-2-deoxy-L-rhamnopyranosyl)-β-D-thioglucopyranoside (23n, 600 MHz, $CDCl_3$):



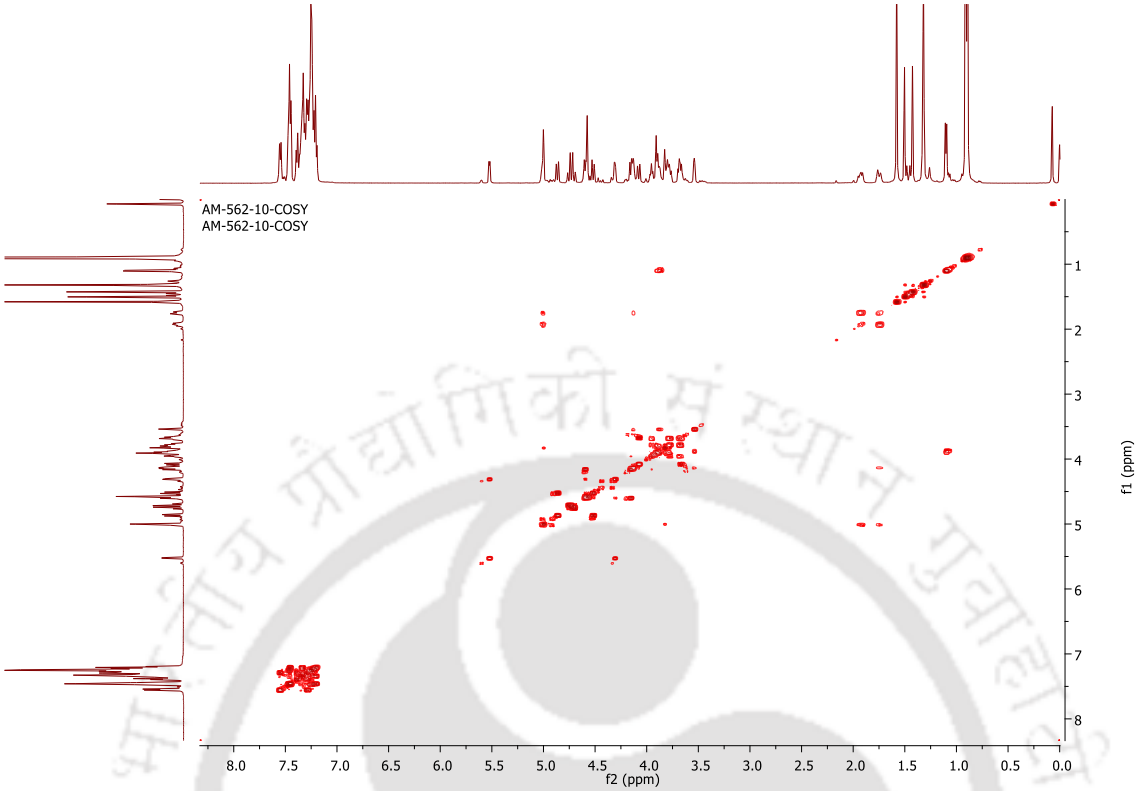
^{1}H NMR of 30 (500 MHz, $CDCl_3$):



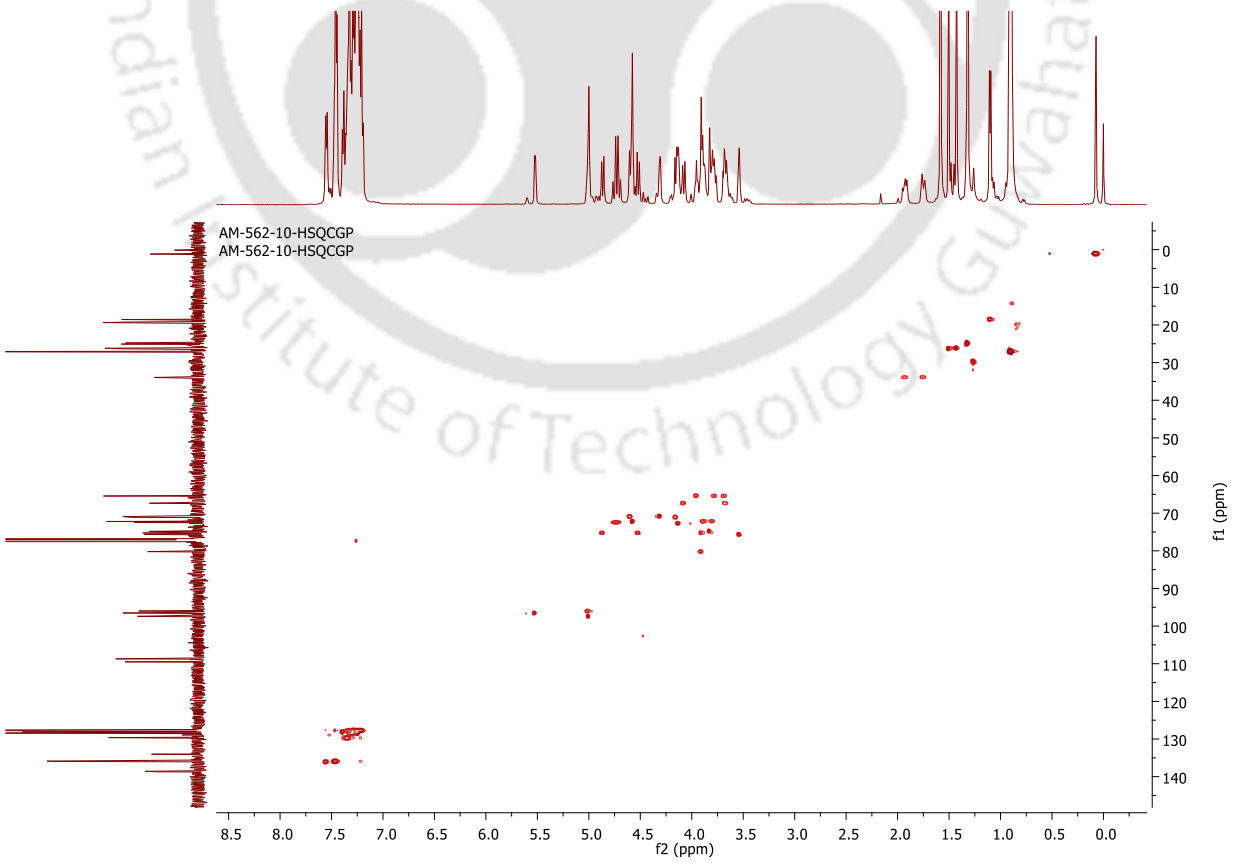
^{13}C NMR of 30:



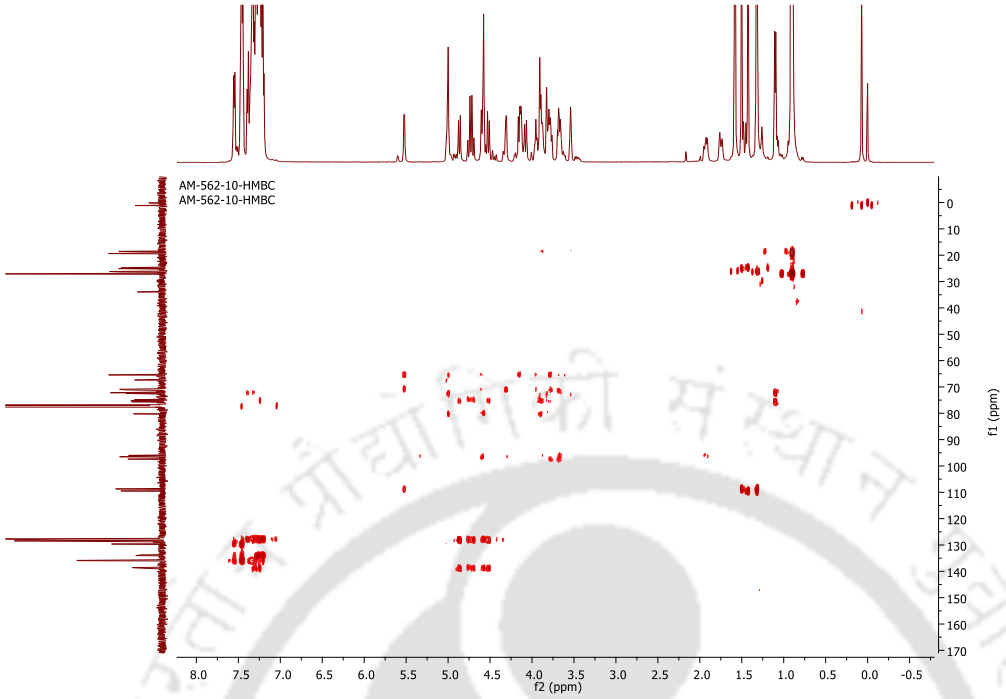
COSY NMR of 30 (500 MHz, $CDCl_3$):



HSQC NMR of 30 (500 MHz, $CDCl_3$):



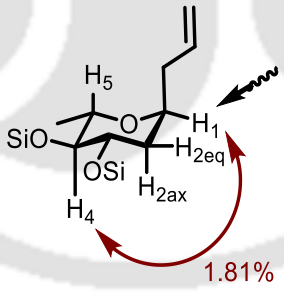
HMBC NMR of 30 (500 MHz, $CDCl_3$):

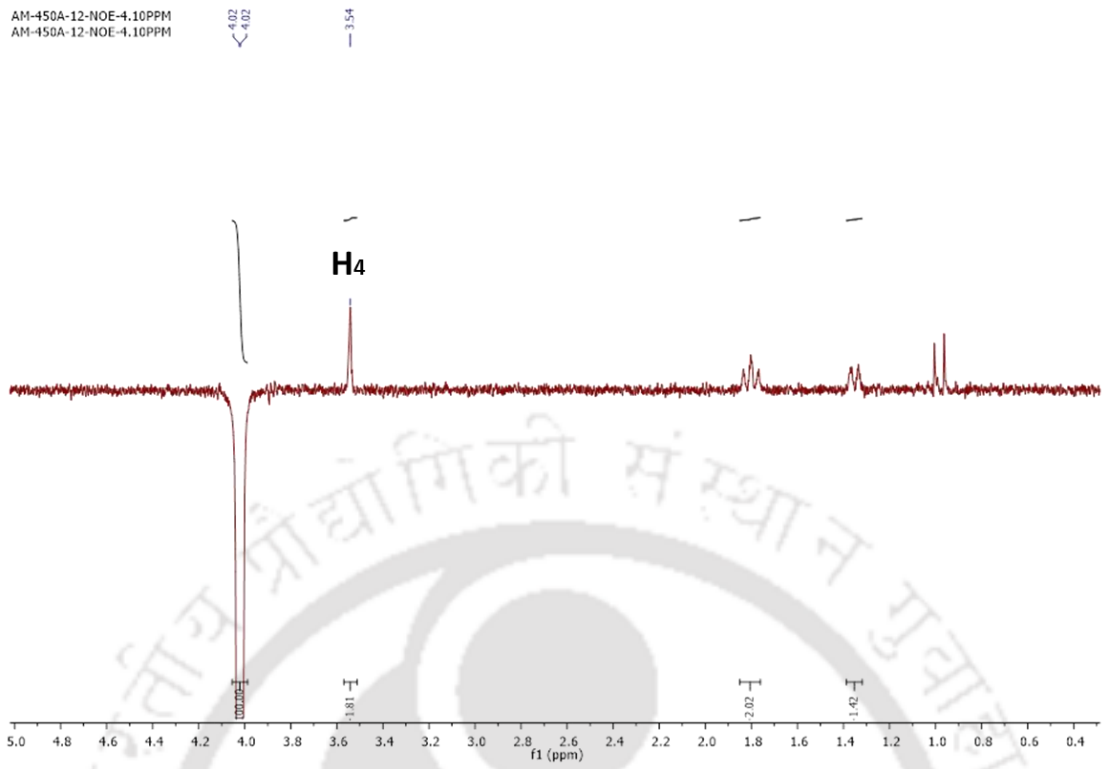


5.10 nOe Experiments

nOe Experiment of 22iα

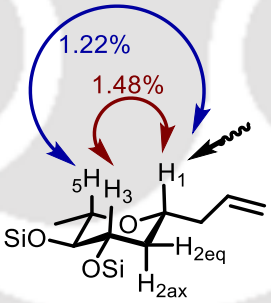
Irradiation of H_1: Upon irradiation of **H_1** the enhancement on **H_4** proton which is appearing at 3.54 is enhanced by 1.81%. Hence, **H_1** is cis to **H_4**. Thus, the compound is in alpha configuration.

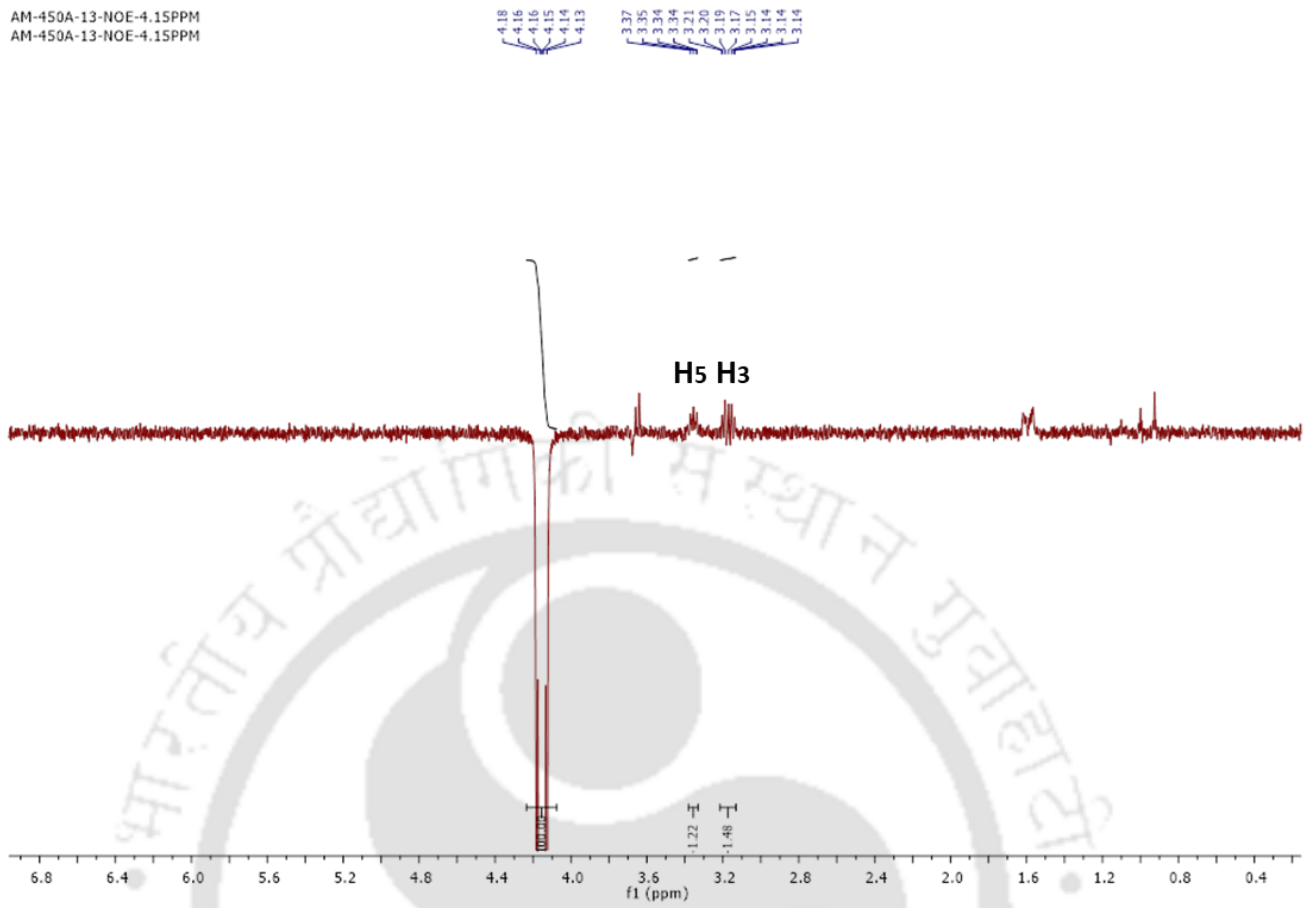




nOe Experiment of 22iβ

Irradiation of H_1: Upon irradiation of **H_1** the enhancement on **H_3** and **H_5** which are appearing at 3.15 and 3.35 respectively are enhanced by 1.48% and 1.22%. Hence, **H_1** is cis to **H_3** and **H_5**. Thus, the compound is in beta configuration.





nOe Experiment of 22k*α*

Irradiation of H_5: Upon irradiation of H_5 the enhancement on allylic protons which are appearing at 2.57 and 2.30 are enhanced by 1.63% and 1.30% respectively. Hence, H_5 is cis to allylic hydrogens. Thus, the compound is in alpha configuration.