Development of New Organocatalytic Methods towards the Synthesis of 2-Deoxy and 2,6-Dideoxy Glycosides

A Dissertation Submitted in partial fulfillment
of the Requirements for the
Degree of Doctor of Philosophy

By

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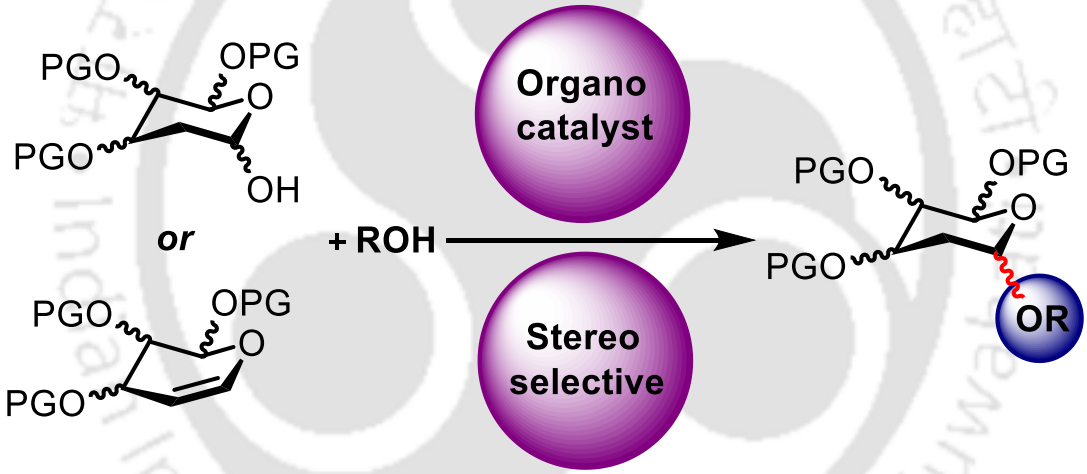
Titli Ghosh



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Department of Chemistry

STATEMENT

The work contained in this thesis entitled "**Development of New Organocatalytic Methods towards the Synthesis of 2-Deoxy and 2,6-Dideoxy Glycosides**" is the outcome of the research work carried out by me under the supervision of Dr. Pavan K. Kancharla, Department of Chemistry, Indian Institute of Technology Guwahati, India. In the present thesis, the general practice of the scientific observations are reported, and whenever needed, the work on the findings of other invesigators are described and thus due acknowledgments have been made.

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CERTIFICATE

This is to certify that the work incorporated in this thesis entitled "**Development of New Organocatalytic Methods towards the Synthesis of 2-Deoxy and 2,6-Dideoxy Glycosides**" which is being submitted to the Department of Chemistry, Indian Institute of Technology Guwahati, India for the award of Doctor of Philosophy in Chemistry by Ms. Titli Ghosh (Roll no: 136122012) was carried out by her under my supervision. The work presented in her thesis is original that has not been submitted elsewhere for a degree.

August 2019

Dr. Pavan K. Kancharla

(Thesis supervisor)

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Dedicated to my parents and family members

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List of Publications and Presentations

Publications:

1. **Ghosh, T.**; Mukherji, A.; Srivastava, H. K.; Kancharla, P. K. ***"Secondary Amine Salts Catalyzed Controlled Activation of 2-Deoxy Sugar Lactols towards Stereoselective Dehydrative Glycosylation"*** *Org. Biomol. Chem.* **2018**, *16*, 2870–2875.
2. **Ghosh, T.**; Mukherji, A.; Kancharla, P. K. ***"Sterically Hindered 2,4,6-Tri-tert-butylpyridinium (TTBPy) Salts as Single Hydrogen Bond Donors for Highly Stereoselective Glycosylation Reactions of Glycals"*** *Org. Lett.* **2019**, *21*, 3490–3495.
3. **Ghosh, T.**; Mukherji, A.; Kancharla, P. K. ***"Open-Close Strategy towards the Organocatalytic Generation of 2-Deoxy-ribofuranosyl Oxocarbenium Ions: Pyrrolidine Salts Catalyzed Synthesis of 2-Deoxy-ribo-furanosides from 2-Deoxy-ribo-furanoses"*** *(Submitted)*.
4. **Ghosh, T.**; Mukherji, A.; Kancharla, P. K. ***"Synergistic Catalysis of DMAP Salts and Schreiner's Thiourea towards Dehydrative Glycosylation of 2-Deoxy Gluco, Galacto, Arabino Hemiacetals"*** *(Submitted)*.

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1. Honored a Best Poster Presentation Award in **Chemconvene – 2017**, held at Indian Institute of Technology, Guwahati, India.
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3. Presented a Poster in **Frontiers in Chemical Sciences (FICS) – 2018**, held at Indian Institute of Technology, Guwahati, India.
4. Presented a Poster in **Organic Molecules As Synthons & Reagents For Innovations (OMSRI) – 2019**, held at Indian Institute of Technology, Roorkee, India.

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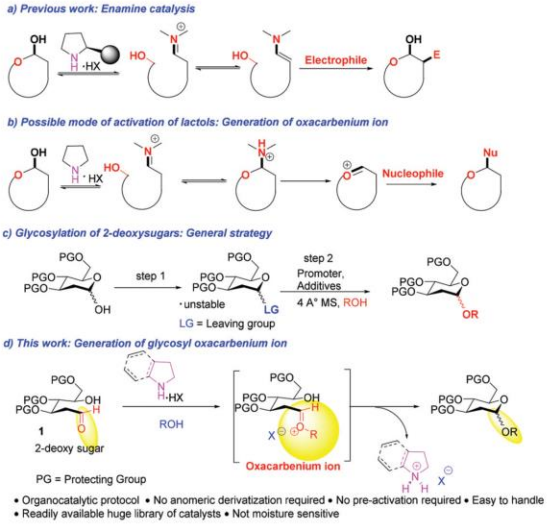
Secondary amine salt catalyzed controlled activation of 2-deoxy sugar lactols towards alpha-selective dehydrative glycosylation†

Titli Ghosh, Ananya Mukherji, Hemant Kumar Srivastava and Pavan K. Kancharla *

A new organocatalytic glycosylation method exploiting the lactol functionality has been disclosed. The catalytic generation of glycosyl oxacarbenium ions from lactols under forcible conditions *via* weakly Brønsted-acidic, readily available secondary amine salts affects the diastereoselective glycosylation of 2-deoxypyranoses and furanoses. This operationally simple iminium catalyzed activation of 2-deoxy hemi-acetals is a potential alternative to the existing cumbersome methods that need specialized handling. The mechanisms for this unique transformation and kinetic/thermodynamic effects have been discussed based on both experimental evidence and theoretical studies.

The formation of iminium ions[1a] by a reaction between secondary amines/amine salts and aliphatic/aromatic aldehydes has been extensively explored since the seminal work by MacMillan *et al.*[2] and Barbas *et al.*[3] In the case of aliphatic aldehydes,[1b] the thus-generated iminium ions tautomerize into the corresponding enamines that are trapped by a multitude of electrophiles (Scheme 1a), whereas iminium ions formed from α,β-unsaturated aldehydes are prone to undergo 1,2 or 1,4-nucleophilic addition reactions. Liu *et al.* have showcased the iminium/enamine catalyzed functionalization of masked aldehydes *i.e.* lactols[4] and cyclic hemi-aminals[5] that react with nitrostyrenes, α,β-unsaturated ketones and ketomalonates.[4b] We envisioned that in the case of lactols, the iminium ions that tautomerize into enamines, under forcible conditions, could be trapped intramolecularly which upon the expulsion of ammonium species could lead to the generation of oxacarbenium ions[6] (Scheme 1b), one of the most important intermediates in organic chemistry. The thus-generated oxacarbenium ions if trapped by nucleophiles like alcohols would lead to the development of a novel organocatalytic method for the synthesis of acetals.



Scheme 1 Organocatalytic dehydrative glycosylation.

We have chosen 2-deoxysugar lactols as substrates to study the hypothesis. 2-Deoxysugar acetals *i.e.* 2-deoxyglycosides are part of several natural products with anticancer[7] and antibiotic properties[7a,8] and it has been shown that these structural motifs are important for their activity.[9] Most of the sugar lactols require the anomeric derivatization prior to glycosylation and 2-deoxysugars are no exception.[10] However, the derivatized 2-deoxysugar donors are relatively unstable[11] and require careful handling. Several direct and indirect methods for the synthesis of 2-deoxyglycosides[12] involving C-2 heteroatom substitutions,[11b,13] 1,2-epoxides,[14] enol ethers,[15] and hemi-acetals[16] have been developed over the past two decades.

Despite the significant advantages, dehydrative glycosylation has not evolved into a commonly used method owing to the unique challenges posed by lactol donors *e.g.* the self-condensation reaction of the lactols often compete with the desired glycosylation product. 2-Deoxy lactols pose a bigger

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Sterically Hindered 2,4,6-Tri-*tert*-butylpyridinium Salts as Single Hydrogen Bond Donors for Highly Stereoselective Glycosylation Reactions of Glycals

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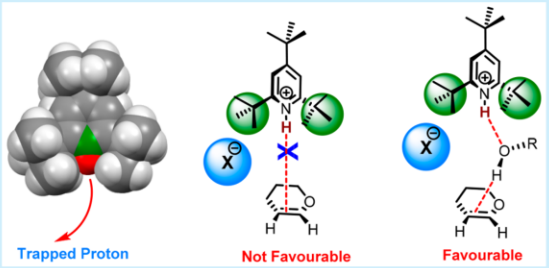
Supporting Information

ABSTRACT: We demonstrate here that the strained and bulky protonated 2,4,6-tri-*tert*-butylpyridine salts serve as efficient catalysts for highly stereoselective glycosylations of various glycals. Moreover, the mechanism of action involves an interesting single hydrogen bond mediated protonation of glycals and not via the generally conceived Brønsted acid pathway. The counteranions also play a role in the outcome of the reaction.



2,4,6-Tri-*tert*-butylpyridine (TTBPy), a highly hindered pyridine derivative, was first synthesized by Mach and Dimroth in 1968 from stable oxonium salts.[1] TTBPy, along with its well-studied analogue, 2,6-di-*tert*-butylpyridine (DTBP),[2−5] are known for their inability to coordinate even to smaller Lewis acids like CH_3^+ or BF_3 except with a proton.[2,6] This typical non-nucleophilic basicity has been exploited in a variety of reactions, in particular, as an acid scavenger or as a buffering agent in studies of reactions of metal ions in aqueous solutions.[6] Effenberger and co-workers used TTBPy in characterizing the concentration of acylium ions in aromatic acylation reactions to exploit its ability to trap the released triflic acid.[7] The profound effect of TTBPy on k_H/k_D values in these reactions has also been studied. Shibata and co-workers used the TTBPy/Tf_2O system for the synthesis of indole triflones.[8] More recently, Berke and co-workers found that the bulky TTBPy in the presence of $B(C_6F_5)_3$ can heterolytically cleave H_2, showing frustrated Lewis pair (FLP) activity (Scheme 1, a). In addition, it was also found that TTBPy can form a stable frustrated Lewis pair with [(acridine)BCl_2]-[$AlCl_4$] that can also heterolytically cleave H_2.[9] Intriguingly, Ingleson and co-workers observed that the position of the hydride from H_2 has been found to be the C9 position of acridine and not the usually expected boron.

The best and the most common use of the 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), has been in glycosylation reactions again as a trap to capture the released sulfonic acids at lower temperatures.[10]

Gin and co-workers introduced the use of excess of TTBPy in the sulfoxide-catalyzed activation of glycosyl hemiacetals (Scheme 1, b).[11,12] However, Crich later introduced TTBP as a potential alternative to TTBPy on the grounds that the former is a nonhygroscopic white crystalline powder unlike the hindered pyridine derivatives.[13] Though the mechanism is not clear, Ye and co-workers observed an intriguing stereoswitch[14] in glycosylation reactions of glucosamine derivatives in the presence and absence of 2,4,6-tri-*tert*-butylpyrimidine.

However, curiosity lingers on the reactivity of these hindered pyridine and pyrimidine compounds as bases. For example, it is known that the aqueous pK_a of DTBP is about ∼2 units lower than expected, though the gaseous state pK_a is in line with predicted values.[4,5] The weak basicity of 2,4,6-tri-*tert*-butylpyridine, similar to that of DTBP or TTBP, is attributed to the inability of TTBPyH to be solvated in aqueous solutions due to high steric shielding and hence behaves as a weak base (pK_a = 3.4). This effect is more pertinent in DMSO in which the 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 ability of the cationic Brønsted acid TTBPyH depends extensively on the hydrogen-bonding character of the solvent. However, we were curious to understand the behavior of TTBPyH in the more generally used solvents like DCE or DCM with low dielectric constants (ε = 10.36 and ε = 8.93, respectively) where it is used as a proton-trapping agent. On the other hand, very recently, it has been shown that Schrenier's thiourea, whose pK_{DMSO} is 8.5, catalyzes the tetrahydropyranylation of alcohols via a Brønsted acid mechanism.[15−24] This led us to question whether TTBPy, whose conjugate acid is a much stronger acid in DMSO, is safe as a non-nucleophilic base in glycosylation reactions, particularly in reactions involving glycals. This thought carries

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Chapter 4. Sterically Hindered 2,4,6-Tri-tert-butylpyridinium (TTBPy) Salts as Single Hydrogen Bond Donors for Highly Stereoselective Glycosylation Reactions of Glycals

Chapter 5. Synergistic Catalysis of DMAP Salts and Schreiner's Thiourea towards Dehydrative Glycosylation of 2-Deoxy Gluco, Galacto, Arabino Hemiacetals

Abbreviation

AcOH	Acetic acid
ACN	Acetonitrile
Ac	Acetyl
Å	Angstrom
α	Alpha
β	Beta
Ag_2O	Silver oxide
BF_3	Boron trifluoride
BF_4	Tetrafluoroborate
Bn	Benzyl
Bz	Benzoyl
BCl_3	Boron trichloride
BSM	Bovine submaxillary mucin
BA_rF	Tetrakis(3,5-bis(trifluoromethyl)phenyl)borate
BINOL	1,1'-Bi-2-naphthol
cat.	Catalytic/Catalyst
°C	Degree Celsius
$CeCl_3$	Cerium(III) chloride
CH_3	Methyl
$CDCl_3$	Deuterated chloroform
C_6D_6	Deuterated benzene
CBr_4	Tetrabromomethane
Cbz	Carboxybenzyl
DCC	N,N'-Dicyclohexylcarbodiimide
DMAP	4-Dimethylaminopyridine
DNA	Deoxyribonucleic acid
DCM	Dichloromethane
DCE	1,2-Dichloroethane

DMF	N,N'-Dimethylformamide
DTBMP	2,6-Di-*tert*-butyl-4-methylpyridine
DIPEA	N,N'-Diisopropylethylamine
DFT	Density functional theory
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
KHMDS	Potassium bis(trimethylsilyl)amide
K_2CO_3	Potassium carbonate
$LiClO_4$	Lithium perchlorate
LiBr	Lithium bromide
mm	Millimetre
MeI	Methyl iodide
MHz	Mega hertz
Ms	Mesyl
min	Minute
Me	Methyl
ml	Millilitre

mg	Milligram
µl	Microlitre
$NOBF_4$	Nitrosyl tetrafluoroborate
$NaHCO_3$	Sodium bicarbonate
$Na_2S_2O_4$	Sodium dithionite
NIS	N-Iodosuccinimide
NaI	Sodium iodide
NaH	Sodium hydride
NMR	Nuclear magnetic resonance
nOe	Nuclear Overhauser effect
Nu	Nucleophile
Ph	Phenyl
PPh_3	Triphenylphosphine
$P(OPh)_3$	Triphenylphosphite
PCC	Pyridinium chlorochromate
ppm	Parts per million
RNA	Ribonucleic acid
rt	Room temperature
ROMP	Ring-opening metathesis polymerisation
$SnCl_4$	Tin(IV) chloride
Tf	Triflate
Ts	Tosylate
TBAF	Tetra-n-butylammonium fluoride
TBAI	Tetra-n-butylammonium iodide
THF	Tetrahydrofuran
TTBP	2,4,6-Tri-*tert*-butylpyridine
TMS	Trimethylsilane
TBDPS	*tert*-Butyldiphenylsilyl
TIPS	Triisopropylsilane
TfOH	Triflic acid

TMSOTf	Trimethyltrifluoromethanesulfonate
TMSBr	Bromotrimethylsilane
TLC	Thin layer chromatography
UV	Ultraviolet
VT	Variable temperature
XRD	X-ray powder diffraction

Abstract

The contents of the thesis entitled "**Development of New Organocatalytic Methods towards the Synthesis of 2-Deoxy and 2,6-Dideoxy Glycosides**" have been divided into five chapters based on the experimental works, results, and calculations during the complete course of the research period. The first chapter of the thesis is the literature review of deoxy glycosides. The second chapter contains the dehydrative glycosylation of 2-deoxy hemiacetals via iminium ion catalysis. The third chapter describes the open-close strategy towards ribo-lactol to form biologically relevant 2-deoxy riboglycosides using pyrrolidinium salts. Chapter four reveals us that protonated sterically hindered TTBPy salts act as a single hydrogen bond donor to activate glycals towards stereoselective glycosylation. The fifth chapter contains the cooperative catalysis of DMAP salts and Schreiner's thiourea towards dehydrative glycosylation of 2-deoxy and 2,6-dideoxy glycosides.

Chapter 1. Literature Survey on Synthesis of Deoxy Sugars

Chapter 1 deals with the basic introduction about deoxysugars, general methods of glycosylation and state of the art literature on 2-deoxysugars.

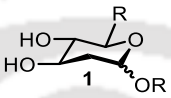
Glycosylation:

Carbohydrates are one of the most essential biomolecules on earth. Our understanding of these biomolecules has tremendously improved over the past decades. However, there is still a need for more studies to decipher the role of these biomolecules in cellular processes like development and growth of tumors, metastasis, or viral and bacterial infections. The tremendous medicinal potential of glycomolecules has been exploited by the development of synthetic carbohydrate-based therapeutic agents. Improved methods of isolation and synthesis of complex carbohydrates have become crucial for the growth of the field of glycoscience. The majority of carbohydrates in nature exists as polysaccharides (cellulose, starch, and chitin) or glycoconjugates (glycopeptides, glycolipids). In recent years, significant progress in the synthesis of oligosaccharides has been achieved. Despite this progress, there are still problems with the direct formation of glycosidic linkages. However, when the glycobiology field is expanding, there is a need for reliable and stereocontrolled glycosylation methods.

Deoxy Sugars:

2-deoxyglycosides are a class of carbohydrates in which the hydroxyl group at C2 position is replaced by a hydrogen atom. For example, 2-deoxy-D-ribose is a crucial component of the sugar backbone of deoxyribonucleic acid (DNA). Besides, 2-deoxy sugars, mainly, 2,6-dideoxy and 2,3,6-trideoxy sugars, widely exist in natural molecules with biological activity and are reported to play an essential role in their bioactivities.

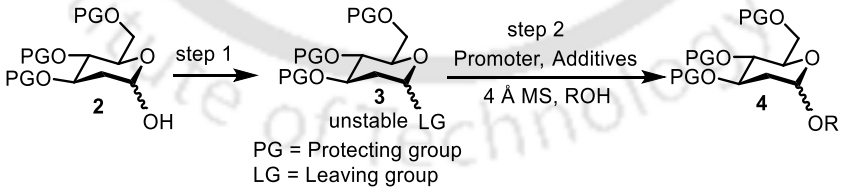
Challenges in the Synthesis of 2-deoxyglycosides:



Stereoseletive synthesis of 2-deoxyglycosides has been a difficult task due to the lack of neighboring group participation from C2 position to regulate the stereochemistry at anomeric carbon. However, moderate selectivity towards thermodynamically more stable α-glycosides is generally achievable with assistance from the 'anomeric effect'. Hence, in order to achieve the synthesis of β-glycosides, there is a need to override the anomeric effect.

General Strategy:

Generally, most of the glycosylation reactions utilize a two-step strategy. The anomeric hydroxyl group is converted to a relatively unstable intermediate latent leaving group that can be activated in the presence of promoters, additives, molecular sieves, etc., in the presence of alcohols as acceptors to achieve the glycosylated products **4** as shown in **Scheme 1**.



Scheme 1: Glycosylation of 2-deoxysugars: General Strategy.

This thesis addresses the challenge of dehydrative glycosylation, which obviates the conversion of anomeric hemiacetals to a leaving group, specifically for 2-deoxyglycosides using a novel organocatalytic strategies.

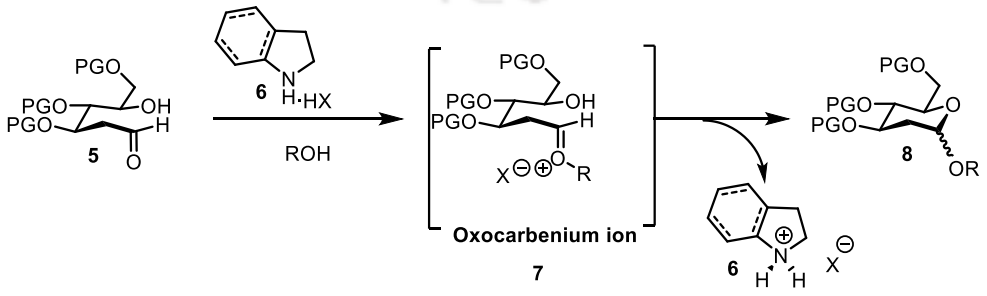
Chapter 2. Secondary Amine Salts Catalyzed Controlled Activation of 2-Deoxy Sugar Lactols towards Stereoselective Dehydrative Glycosylation

Chapter 2 deals with the development of a new organocatatalytic glycosylation method utilizing the benchtop pyrrolidine hydrochloride as a catalyst. This chapter unveils a new mode of reactivity for secondary amines where these amine salts have been used to generate oxocarbenium ions, the most important intermediates in carbohydrate chemistry.

General Introduction:

Formation of iminium ions by the reaction between secondary amines/amine salts and aliphatic/aromatic aldehydes has been extensively explored since the seminal work by MacMillan et al. and Barbas et al. In case of aliphatic aldehydes, the thus generated iminium ions tautomerize into the corresponding enamines that are trapped by a multitude of electrophiles whereas iminium ions formed from α,β-unsaturated aldehydes are prone to undergo 1,2 or 1,4-nucleophilic addition reactions. We envisioned that in the case of lactols, the iminium ions that tautomerize into enamines, under forcible conditions could be trapped intramolecularly which upon the expulsion of ammonium species could lead to the generation of oxocarbenium ions **7**, one of the most important intermediates in organic chemistry. Thus generated oxocarbenium ions **7**, if trapped by nucleophiles like alcohols, would lead to the development of a novel organocatalytic method for the synthesis of acetals **8** (**Scheme 2**).

The novel organocatalytic glycosylation method involves the usage of simple, benchtop secondary amine salts as catalysts. Additional advantages of the present method include the following: 1) No need of an additive, 2) pyrrolidinium organocatalysts **6** being solids can be easily weighed, not moisture sensitive and easy to handle, 3) no need for any stabilizer to drive the reaction, 4) one-step process, 5) the reaction is very quick and α-stereoselective with high yields.



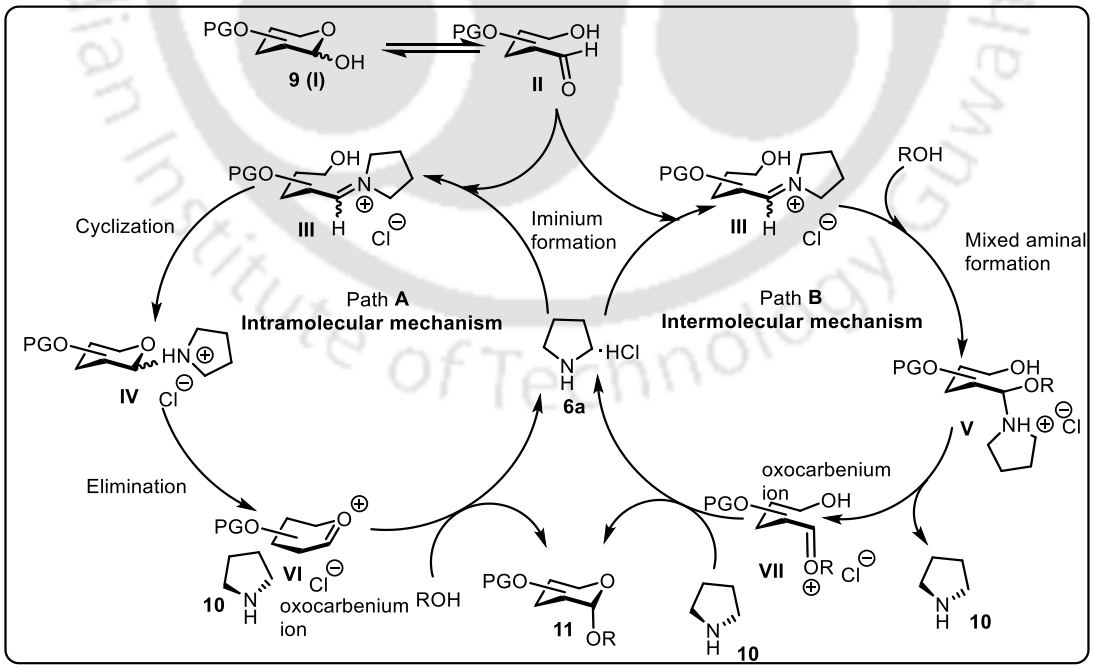
Scheme 2: Proposed Dehydrative Glycosylation Reaction of 2-deoxylactols.

Proposed Mechanism:

Based on the control experiments, the following mechanism has been proposed for the organocatalytic glycosylation. Generation of the iminium ion **III** is dependent on the percentage of sugar lactol existing in its open-chain form (**Scheme 3**, **III**). The generated iminium ion **III** must possess the necessary electrophilicity to react with the unactivated alcohols (**Scheme 3**, **IV** or **V**) and the leaving group ability of pyrrolidinium species facilitates the generation of the oxocarbenium ion (**Scheme 3**, **VI** or **VII**).

Different Derivatives of Glycosylation Reaction using Organocatalyst:

After optimizing the reaction conditions, we screened this method in the presence of various alcohols and donors to make various derivatives. The commercially cheap, robust, and easily accessible pyrrolidine hydrochloride **6a**, was chosen as the optimized catalyst to study the substrate scope. All the non-carbohydrate primary alcohols gave the desired glycosylation products with excellent yields and good to high levels of α-selectivites (**Figure 1**). The sterically demanding cholesterol also gave corresponding glycoside **11c** in 62% yield and 3.5:1 α:β selectivity. The coupling with 1-adamantanol also reacted well under the reaction conditions to provide the glycoside in 71% yield with high α-selectivity (13:1, α:β, **Figure 1**).



Scheme 3: Proposed Mechanistic Pathways for Dehydrative Glycosylation.

Both the alcohols derived from glucose and galactose were successfully coupled with 2-deoxy lactols **9a** (**11s** and **11r**, respectively). However, when no acceptor was used, the armed 2-deoxy lactol **9a** in the presence of catalyst **6a** lead to the corresponding α→α-trehalose analog **11q** as major diastereomer. More strikingly, the coupling reaction between the galacto-configured 2-deoxy lactol **9b** and the galactose derived diacetonide acceptor in the presence of pyrrolidine tosylate **6b** as the catalyst lead to a single diastereomer (only α).

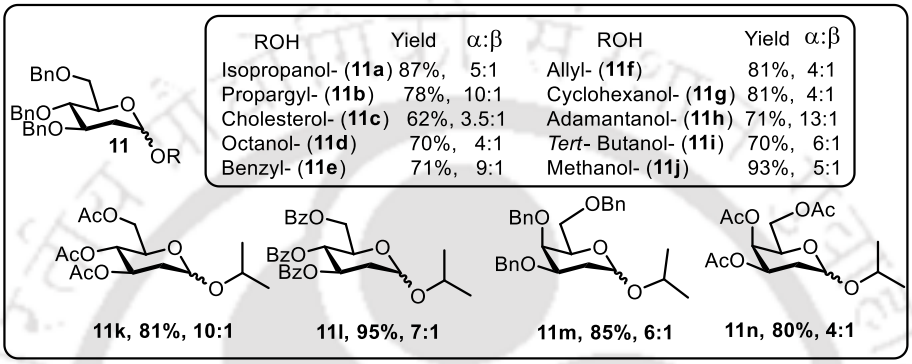


Figure 1: Synthesis of Monosaccharides by using Pyrrolidinium Salts.

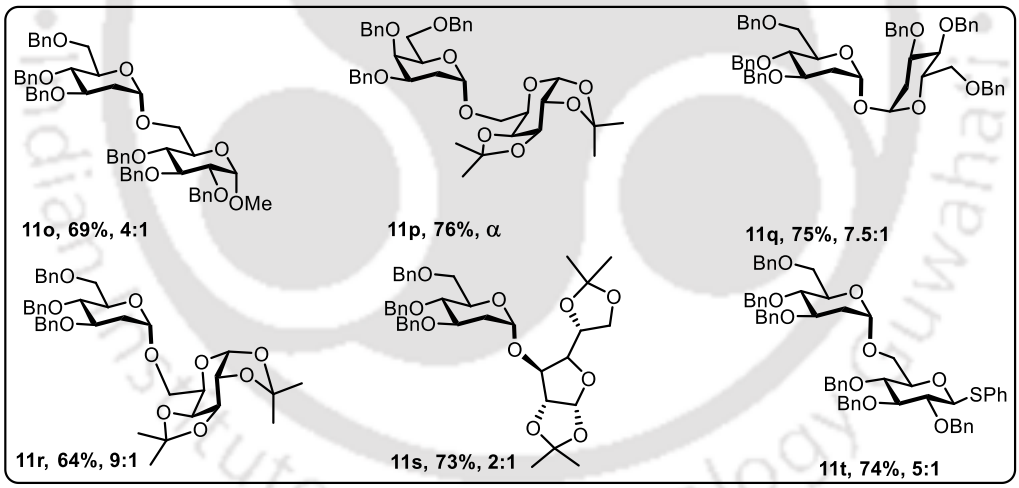


Figure 2: Synthesis of Disaccharides by using Pyrrolidinium Salts.

Detailed studies on the scope of the derivatives and mechanistic studies, including theoretical studies on the possible pathways have been discussed in this chapter.

Chapter 3. Open-Close Strategy towards the Organocatalytic Generation of 2-Deoxy-ribofuranosyl Oxocarbenium Ions: Pyrrolidine Salts Catalyzed Synthesis of 2-Deoxy-ribo-furanosides from 2-Deoxy-ribo-furanoses

Chapter 3 deals with the utilization of the concept developed in **chapter 2** towards the synthesis of 2-deoxy-ribofuranosyl oxocarbenium ions and thereby the respective glycosides.

General Introduction:

2-Deoxy-riboses, a subclass under 2-deoxy-sugars, have great significance in biology being a constituent of DNA. The synthesis and biological studies of *N*-linked 2-deoxy-ribonucleotides and their analogues received great attention. On the other hand, synthesis of *O*-linked 2-deoxy-riboglycosides could be interesting targets for drugs and their structure-activity relationship studies against cancer and viral proliferation and can attract high demand in medicinal

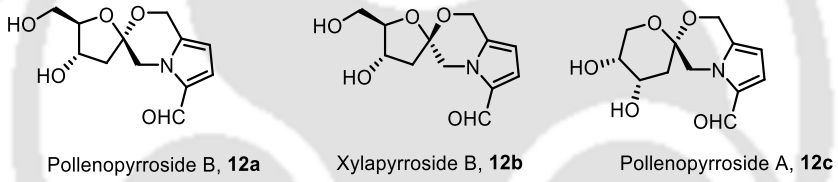
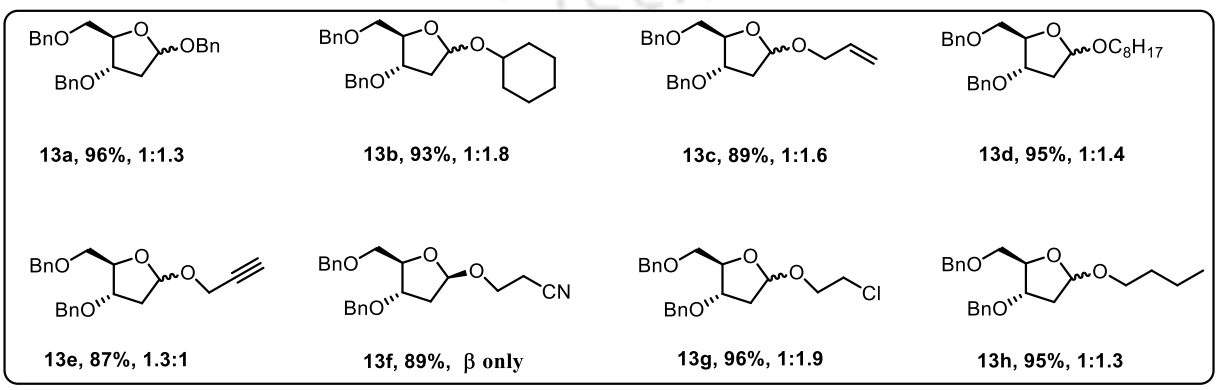


Figure 3: Some Biologically Important Natural Products.

chemistry. Very recently, several natural products constituting 2-deoxyfuranoside skeleton (**Figure 3**, **12a-c**) with antioxidant and antibacterial properties have also been isolated and has attracted the attention of organic and medicinal chemists.

Synthesis of Derivatives from Different Donors and Acceptors:

Building upon the work in chapter 2, we have studied the effect of 2-deoxyfuranose sugars



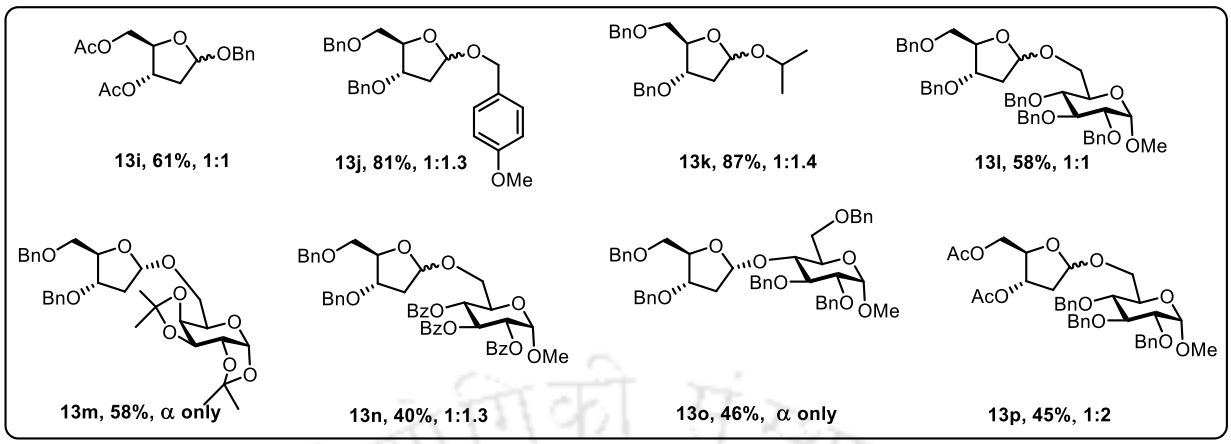
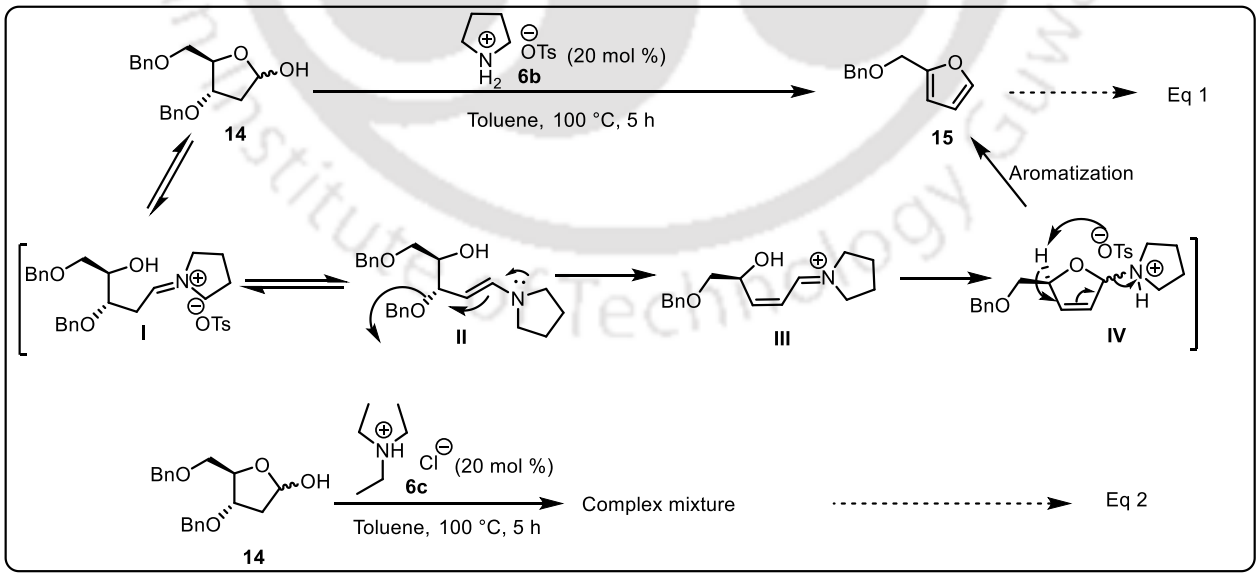


Figure 4: Synthesis of Different Ribofuranoses by using Pyrrolidinium Salts.

towards iminium catalysis and were able to apply the methodology to synthesize several 2-deoxyfuranoglycosides (**Figure 4**, **13a-p**).

Proposed Mechanism:

In order to understand the mechanism, we subjected 2-deoxy-ribo-lactol **14** to the catalytic conditions in the absence of an acceptor. Interestingly, the reaction leads to the formation of a substituted furan derivative **15** (**Scheme 4**, Eq. 1) in 78% yield. It is rather surprising to observe the formation of **15**, as this type of compounds are formed only under strong Brønsted-acidic conditions from ketal derivatives. This leads us to examine the Brønsted acidic nature of the



Scheme 4: Mechanistic Investigation of Dehydrative Glycosylation of 2-deoxyribofuranoses.

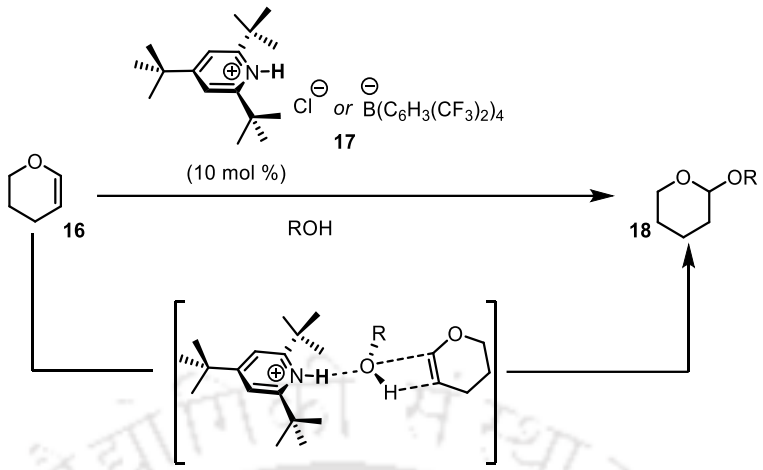
secondary amine salts. Hence, we performed the same reaction with triethylamine hydrochloride **6c** instead of pyrrolidine hydrochloride whose pK_as are close but obviates the formation of iminium or enamine. However, the reaction only leads to a very complex mixture of products (**Scheme 4**, eq. 2) hinting at the unique role of secondary amine catalysis in the former case. The facile formation of the furan derivatives under the secondary amine catalysis could be easily explained via the formation of enamine driven elimination of C-3 *O*-benzyl group, ring-closure to obtain the protonated hemi-aminal, followed by aromatization (**Scheme 4**, eq. 1). These reactions provided a strong evidence for the involvement of iminium ions in the current transformation.

Chapter 4. Sterically Hindered Protonated 2,4,6-Tri-*tert*-butylpyridinium (TTBPy) Salts as Single Hydrogen Bond Donors for Highly Stereoselective Glycosylation Reactions of Glycals

Chapter 4 deals with the discovery of a unique mode of activity for the protonated salts of the sterically hindered 2,4,6-tri-*tert*-butylpyridinium (TTBPy) salts. The conjugate acids of TTBPy, that is generally used as proton trapper/acid quencher has been shown to act as single hydrogen bond donors, thus activating glycals via an amplificative Brønsted acidic mechanism.

General Introduction:

2,4,6-Tri-*tert*-butylpyridine (TTBPy), a highly hindered pyridine derivative was first synthesized by Mach and Dimroth in 1968 from stable oxonium salts. This sterically bulky pyridine, along with its much well studied analogue, 2,6-di-*tert*-butylpyridine, DTBP are known for their inability to coordinate even to smaller Lewis acids like CH_3^+ or BF_3 except a proton. This typical non-nucleophilic basicity has been exploited in a variety of reactions, in particular as an acid scavenger or as a buffering agent in studies of reactions of metal ions in aqueous solutions. The weak basicity of 2,4,6-tri-*tert*-butylpyridine, similar to DTBP or TTBP, is attributed to the inability of TTBPyH to be solvated in aqueous solutions due to high steric shielding and hence behaves as a weak base (p*K*a = 3.4). It is evident that the ability of the cationic Brønsted acid TTBPyH depends extensively on the hydrogen bonding character of the solvent. On the contrary chapter 4 deals with the development of highly stereoselective glycosylation reaction utilizing the sterically hindered TTBPy.HCl **17** as single hydrogen bond donating organocatalyst.



Scheme 5: Stereoselective Glycosylation of Glycals by TTBPy Salts.

Scope of Reactivity of Donors with Different Acceptors:

We focused on the reactivity of different donors and acceptors to see the applicability of this method. It was observed that TBDPS protected donors gave highly stereoselective product **19a-i** towards α-isomer (**Figure 5**).

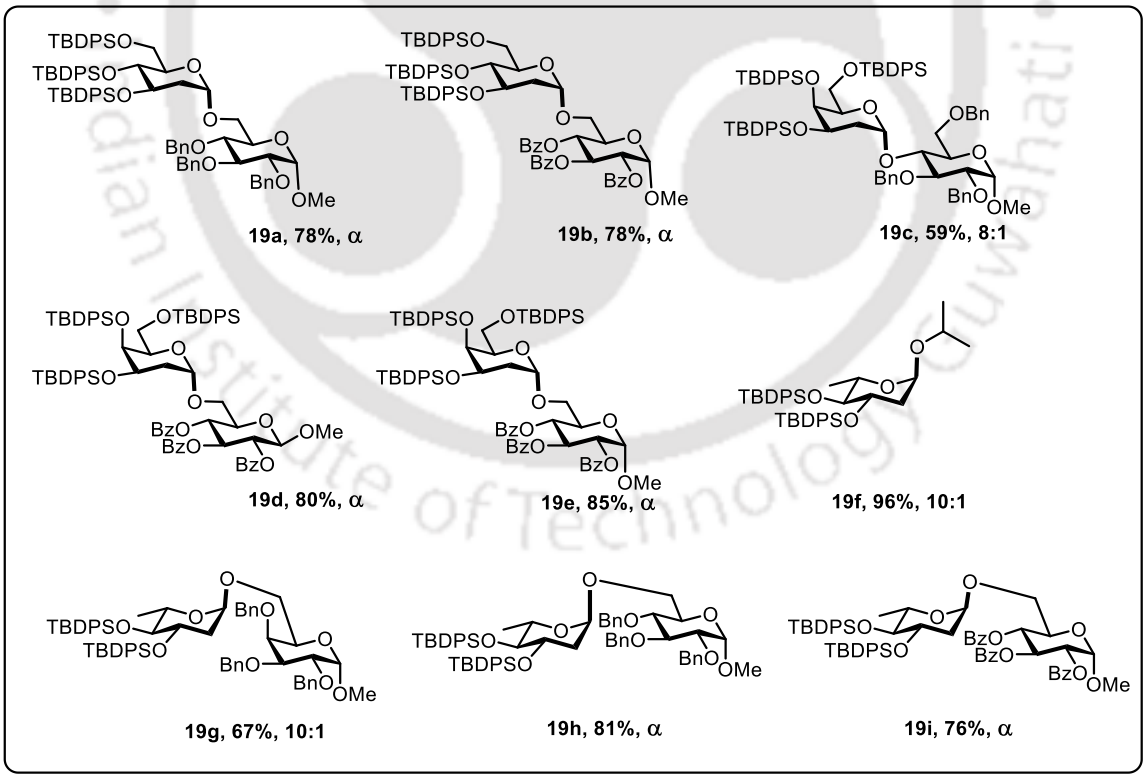


Figure 5: Synthesis of Mono- and Disaccharides by using TTBPyHCl Catalyst.

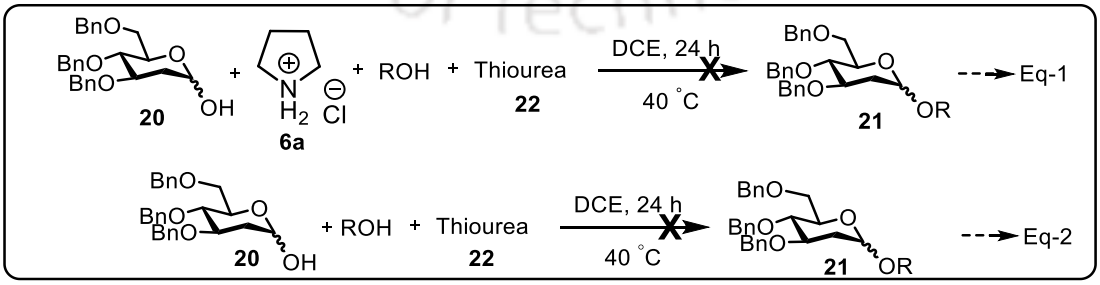
In this chapter, we show that TTBPy salts not only catalyze the glycosylation of glycals but it was very effective with 10 mol % of the catalyst and also in a highly stereoselective fashion leading to the synthesis of various deoxyhexoses. Further, our observations also throw some light onto the mechanism, which reveals that TTBPyH catalyzes the reaction not via a Brønsted acid mechanism (BA) but via its hydrogen bonding assisted activation (HB). Besides, the effect of the catalytic activity also seems to be controlled by the nature of the counter-ion.

Chapter 5. Synergistic Catalysis of DMAP Salts and Schreiner's Thiourea towards Dehydrative Glycosylation of 2-Deoxy Gluco, Galacto, Arabino Hemiacetals

Chapter 5 deals with the development of another organocatalytic method that involves a synergistic/cooperative catalytis of dimethylaminehydochloride (DMAPHCl) and Schreiner's thiourea towards the dehydrative glycosylation.

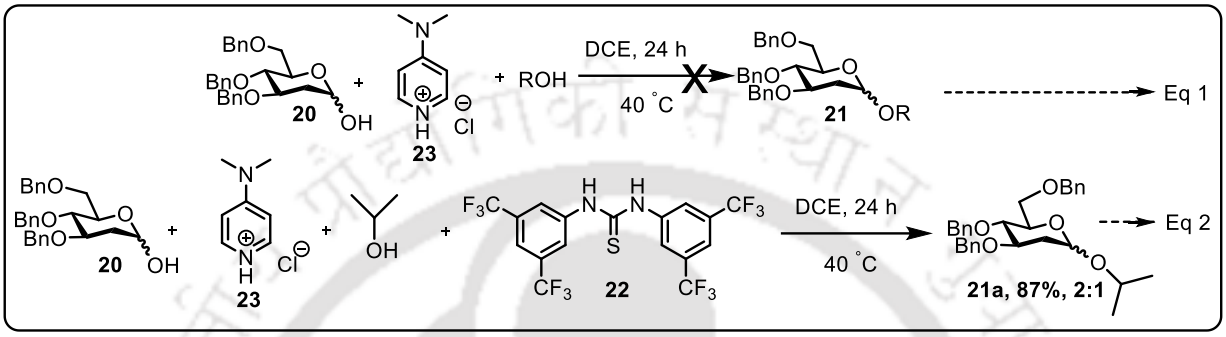
General Introduction:

Chapter 2 dealt with iminium catalyzed dehydrative glycosylation that occurs at elevated temperature. However, our attempts to perform the reaction at moderate temperatures by employing Schreiner's thiourea **22**, an established halide ion binder, thus increasing the activity of secondary amines **6a**, resulted in failure (**Scheme 6**, Eq. 1). A similar result was observed in presence of only thiourea **22** (**Scheme 6**, Eq. 2) that can bind to hydroxyl anions. We then shifted our focus towards developing an organocatalytic dehydrative glycosylation method employing amine salts as Brønsted acid catalysts.



Scheme 6: Initial Studies with Pyrrolidine Hydrochloride Salts.

Wang and coworkers have reported the usage of DMAP. HCl **23** to catalyze the formation of esters from alcohols via the formation of an acylium intermediate. We presumed that the DMAP salt could also catalyze the dehydrative glycosylation by virtue of its cationic Brønsted acidic nature resulting in the generation of a glycosyl DMAP salt, which would further react with alcohols. However, performing a glycosylation reaction with DMAP.HCl **23** and glucose derived



Scheme 7: Catalysis of DMAP Hydrochloride salt and Thiourea.

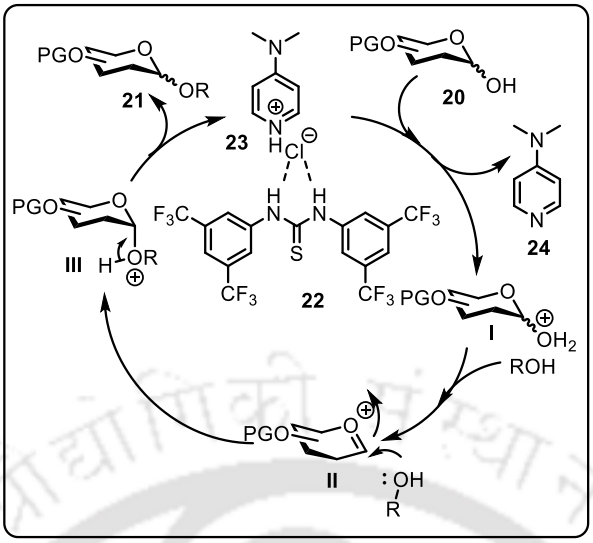
hemiacetal at 40 °C did not give any product (**Scheme 7**, Eq. 1). However, surprisingly enough, reaction when under similar conditions along with the presence of catalytic Schreiner's thiourea **22** lead to the conversion of the lactols into glycosylated products at 40 °C efficiently (**Scheme 7**, Eq. 2).

Proposed Mechanism:

Thiourea **22** has a significant role in binding with halide ion as depicted in **Scheme 8** which in increasing the acidic character of the protonated DMAP. By expulsion of water from intermediate (**I**), the hemiacetal readily forms the corresponding oxocarbenium ion (**II**) which undergoes a nucleophilic addition with the alcohol. Deprotonation of intermediate (**III**) results in the formation of the desired glycosylated product in good yields.

Scope of Reactivity of Different Donors and Acceptors:

Several derivatives using various donors and acceptors have been synthesized to showcase the efficiency of this method (**Figure 6**). Generally, benzyl protected donors were unable to give selectivity more towards the alpha isomer. It was observed that silyl protected donors gave products **21b-k** good yields and selectivities.



Scheme 8: Proposed Mechanism using Thiourea and DMAP hydrochloride Salt.

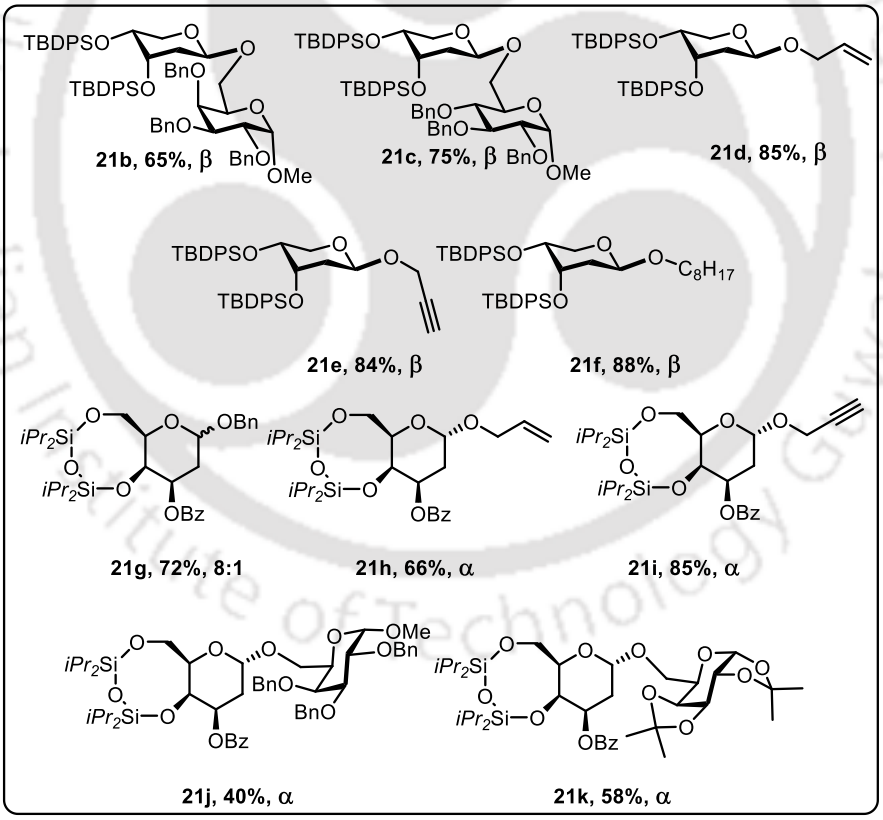


Figure 6: Glycosylation of 2-deoxy Hemiacetals by DMAP hydrochloride salt using Thiourea.

Summary and Perspective:

In conclusion, 2-deoxy hemiacetals as glycosyl donors gave us stereoselective glycosides through the formation of oxocarbenium ion via iminium catalysis. This dehydrative glycosylation also has the potential to convert native and readily available deoxy sugars into the corresponding glycosides with high yields. Afterward, the open-close strategy of protected ribose hemiacetal successfully gave us biologically relevant 2-deoxy riboglycosides. Surprisingly, the formation of furan derivative implied us a clear idea about the mechanism. We found that protonated TTBPy can act as a single hydrogen bond donor to activate the alcohol, thereby driving the glycosylation of glycals in a stereoselective fashion. It is interesting to see that TBDPS protected glycals gave stereoselective products in high yields. The usage of bulky and the superarmed TBDPS along with the sterically congested TTBPy salts allowed to achieve high α-selectivities in the construction of the glycosidic bonds. The effect of the counterions on the structure and reactivity of the cationinc TTBPy has also been thoroughly investigated, and the difference in reactivity was showcased in the glycosylation reactions towards the synthesis of 2-deoxy glycosides as well as the Ferrier glycosyl products. Finally, the use of Schreiner's thiourea in combination with DMAP salts allowed us to perform the dehydrative glycosylation under ambient conditions. Overall, we have developed three different methods for the synthesis of 2-deoxy and 2,6-dideoxy glycosides each following a unique mechanism, and the utility of these methods towards the synthesis of other classes of glycosides will be investigated.

Chapter 1

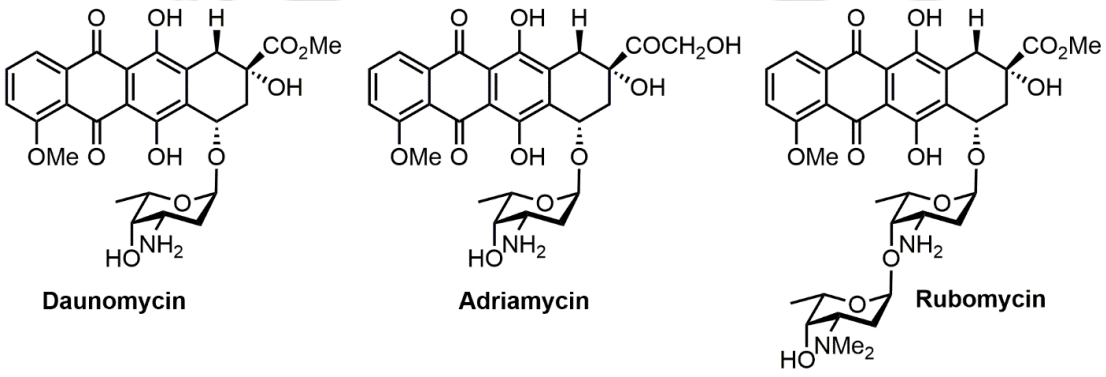
Literature Survey on Synthesis of 2-Deoxy Sugars

1.1 Deoxy Sugars:

Deoxy sugars are a class of carbohydrates in which one or more hydroxyl groups are replaced with hydrogen atoms. Among various available deoxy sugars, 2-deoxy glycosides are essential targets in the medicinal and synthetic field. 2-deoxy-D-ribose is a well-known deoxy sugar, which is the main constituent of deoxyribonucleic acid (DNA). Furthermore, 2-deoxy sugars, 2,6-dideoxy, and 2,3,6-trideoxy sugars are more abundant sugars, and they are present in naturally available and biologically relevant molecules.[1] Fucose or 6-deoxy-L-galactose is the main component of fucoidan of brown algae and found in N-linked glycans. Moreover, rhamnose or 6-deoxy-L-mannose is a type of 2,6-dideoxy sugar and commonly, found in plant glycosides.

1.2 Occurrence and Biological Importance of Deoxy Sugars:

Naturally, 2-deoxy sugars are found in biologically active molecules. Most of them have antitumor activities as well as cancer therapeutics applied in clinics[2] such as anthracycline antitumor antibiotics,[3] aureolic acid derivatives,[4] angucycline group antibiotics,[5,6] avermectins,[7] and enediyne antibiotics.[8] Anthracycline antitumor antibiotics are a class of natural product containing tetracyclic aglycone unit linked to the 2-deoxy sugar moiety. These molecules such as Daunomycin, Adiramycin, and Robumycin (**Figure 1**) form noncovalent complexes with DNA through intercalation and inhibits DNA replication and RNA transcription. Doxorubicin is a well-known drug for antitumor activity. Furthermore, Anthracycline derivatives, e.g. Marcellomycin and Aclacinomycin A containing long carbohydrate chains are less toxic.



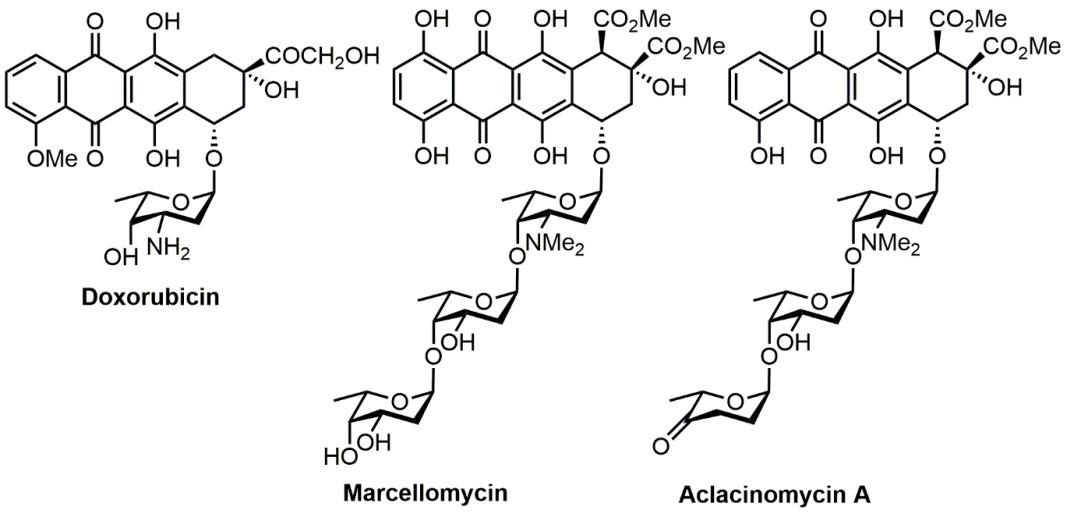


Figure 1: Naturally occurred Anthracycline antibiotics.

The aureolic acid antibiotics including Mithramycin,[9] Chromomycin A_3,[10] Olivomycin A,[11] UCH9[12] are family of glycosylated tricyclic polyketides which are found from various streptomycete species and contain polycyclic chromophore with more than two 2-deoxy glycosides subunits[13] (**Figure 2**). It was observed that they have important antitumor activities and can be applied as chemotherapeutic agents for the treatment of cancer. Moreover, the study of such antibiotics reveals that little change in 2-deoxy subunits leads to a significant effect on their bioactivities.[14]

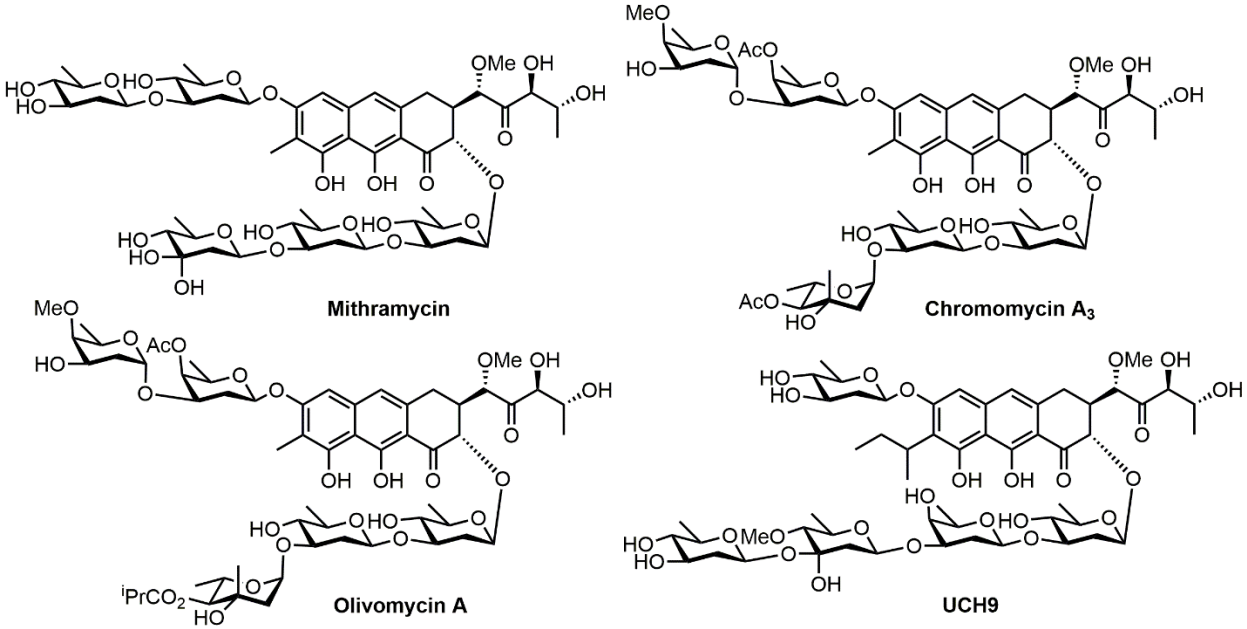


Figure 2: Aureolic acid antitumor antibiotics.

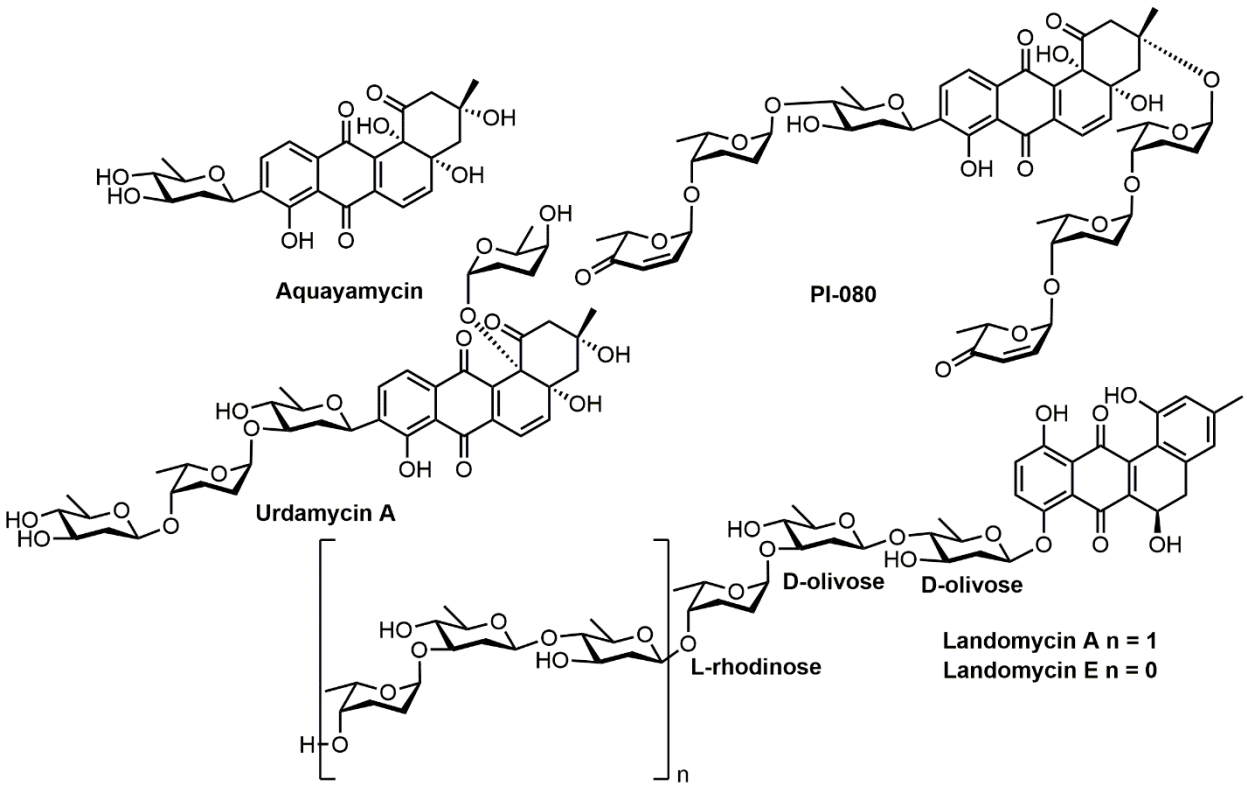


Figure 3: Biologically relevant Angucycline antibiotics.

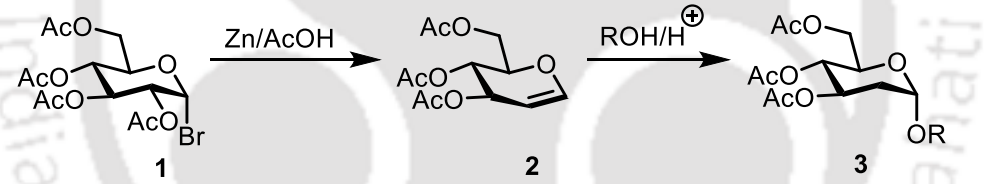
The angucycline antibiotics are glycosylated containing more than two oligosaccharide subunits and show excellent biological activities (**Figure 3**). Acuayamycin[15] can be used as an inhibitor of tyrosine and dopamine β-hydroxylase.[16] The Angucycline Urdamycin A[17,18] can be utilized against gram-positive bacteria and murine leukemia L1210 stem cells. Furthermore, PL-080 antibiotic inhibits platelet aggregation.[19] Landomycin A possess the longest hexasaccharides which are a combination of two repeated trisaccharides [α-L-rhodinose-(1→3)-β-D-olivose-(1→4)-β-D-olivose] and has a potent antitumor activity against a range of 60 cancer cell lines[20,21] which gain a huge attraction towards landomycin family. Moreover, it is known that Landomycin A inhibits the biosynthesis of DNA during the G1/S cell cycle progression.[22] However, it was observed that the cytotoxicity of landomycin family depends on the length of the glycan chain. Therefore, Landomycin E reveals lower biological activity due to the truncation of glycan units.[20, 22-23]

2-Deoxy Sugars:

The importance of 2-deoxy sugar is 2-deoxy-D-erythro-pentose (2-deoxyribose), the main constituent of deoxyribonucleic acids (DNA). Moreover, 2-deoxy-D-arabino-hexose (2-deoxyglucose) has been known as an energy restriction mimetic agent.[24] Besides, synthesis of 2-deoxy sugars is also challenging as they are very tough to handle. Generally, they are very sensitive towards hydrolysis and 1,2-elimination.

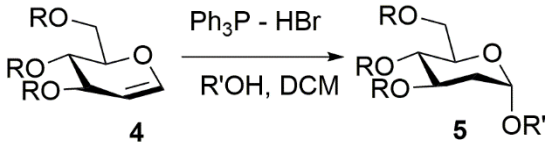
Synthesis

a) Glycosyl halides can be activated by Zn in acetic acid to form glycals, which upon hydrolysis gave corresponding 2-deoxy glycosides. The most well-known process is Fischer's glycal method for the synthesis of 2-deoxy sugars. Acetylated glucosyl bromide **1** converted to corresponding glucal **2**, followed by addition of water or alcohol to double bond in acidic medium afforded 2-deoxy glucosides **3** (**Scheme 1**).[25] Ferrier product was formed as a side product in some of these cases.



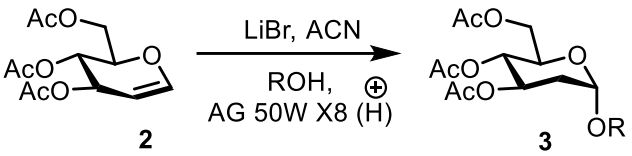
Scheme 1: Preparation of 2-deoxysugar from glycal.

b) Another procedure for the synthesis of 2-deoxy sugar **5** is activation of glucal **4** by triphenyl phosphine in the presence of HBr (**Scheme 2**).[26] However, the formation of Ferrier product was eliminated during this procedure.



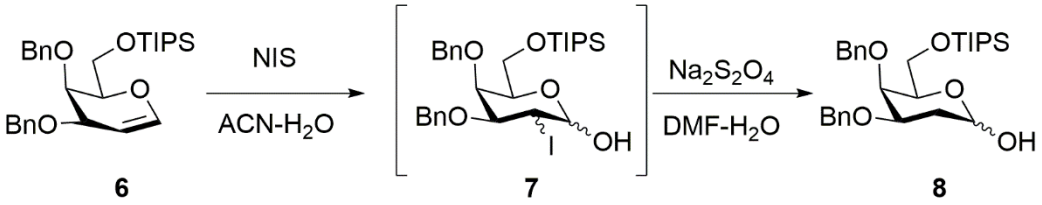
Scheme 2: Synthesis of 2-deoxysugar from glycal in the presence of Ph_3P-HBr.

c) Acetyl protected glucal **2** afforded corresponding deoxy sugars **3** in the presence of acid resin and Lithium bromide to form α-selective glucosides (**Scheme 3**).[27]



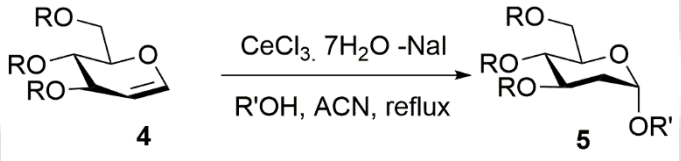
Scheme 3: Synthesis of 2-deoxysugar in the presence of acid resin and LiBr.

d) N-iodosuccinimide in the presence of aqueous acetonitrile activates galactal **6** to transform corresponding 2-iodo pyranoside **7** (**Scheme 4**).[28] This method is relatively mild to acid labile and sensitive silyl and trityl groups.



Scheme 4: Synthesis of 2-deoxy hemiacetals via 2-iodopyranoside.

e) Another mild process to synthesis 2-deoxy pyranoses is a reaction of glycal with lanthanide salts like Lewis acids (**Scheme 5**).[29] It was found that glucal **4** can be activated by $CeCl_3.7H_2O$ – NaI system to form corresponding 2-deoxy glucosides **5** in stereoseletive fashion with high yields. Although, the absence of NaI results the formation of Ferrier product.



Scheme 5: Synthesis of 2-deoxy pyranose from glycal in presence of Lewis acid.

2,6-Dideoxy Sugars:

This class of carbohydrate is highly abundant in nature as a diastereomers having antibiotic and antitumor activity. Among them, 2,6-dideoxy-3-*O*-methyl-hexopyranoses and 2,6-dideoxy-3-amino-hexopyranoses have been utilized as components of natural products in medicinal chemistry.

Occurrence:

D-boivinose was found as a component of a cardenolide glycoside isolated from the seeds of *Corchorus olitorius* L.[30] L-boivinose is the less abundant and found in corn (Zea mays).[31] D-digitoxose is the main constituent of plant cardiac and other steroidal glycosides[32] whereas L-digitoxose has been found from actinomycetes particularly as a unique family of antibiotics, the jadomycins. L-olivose is the main constituent of the trisaccharides chain of the anthracycline

Aclacinomycin A. Interestingly, L-olivose is not available in nature but its 3-*O*-methyl derivative, L-oleandrose has been isolated in oleandomycin, a macrolide antibiotic produced by *Streptomyces antibioticus*.

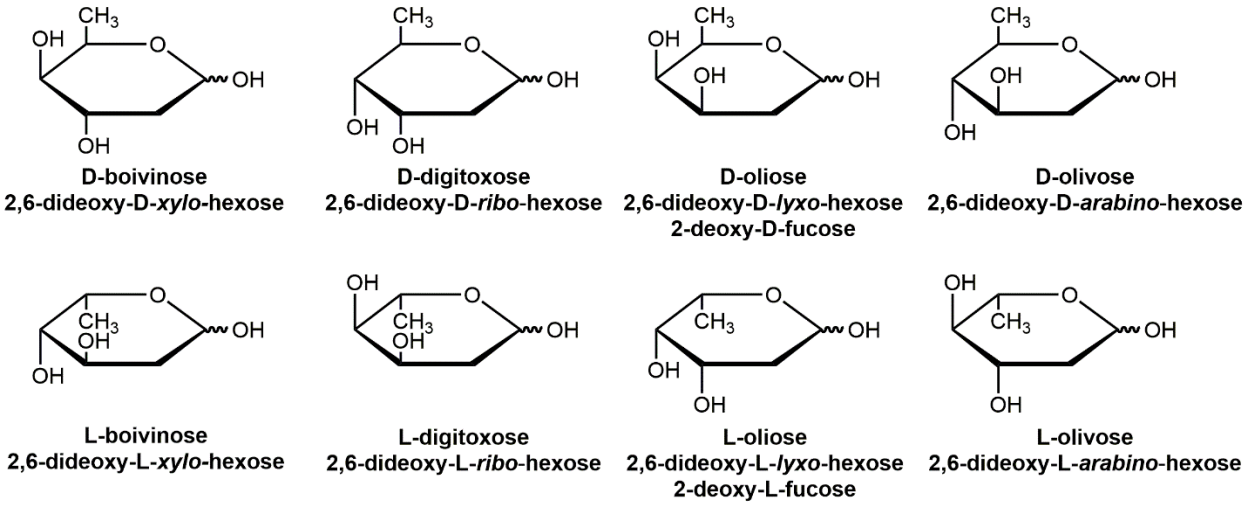
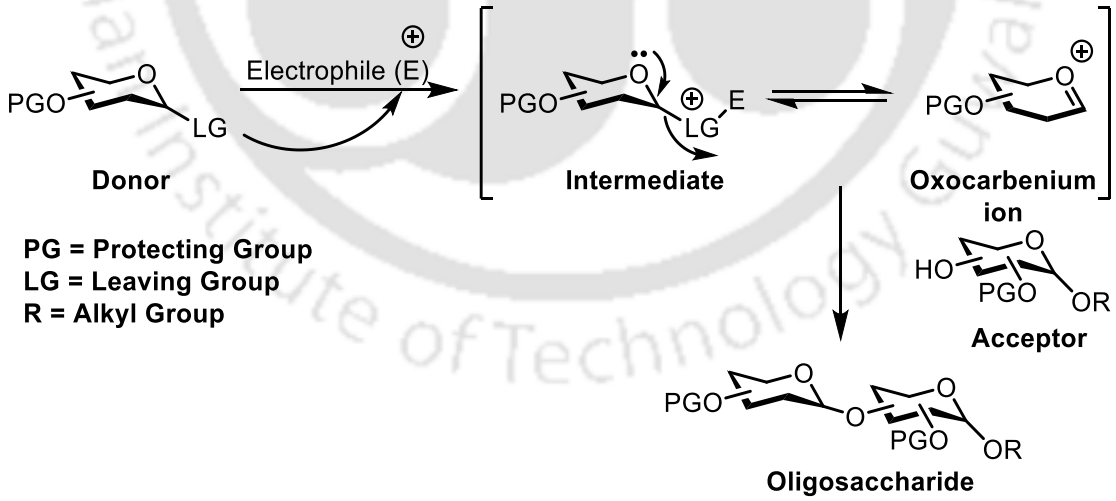


Figure 4: Naturally occurring 2,6-dideoxy sugars.

1.3 Traditional Method for Synthesis of Glycosides:

Initially, the biologically active organic molecules were collected from natural resources, but this extraction method was time-consuming and expensive process also. Most of the cases, the



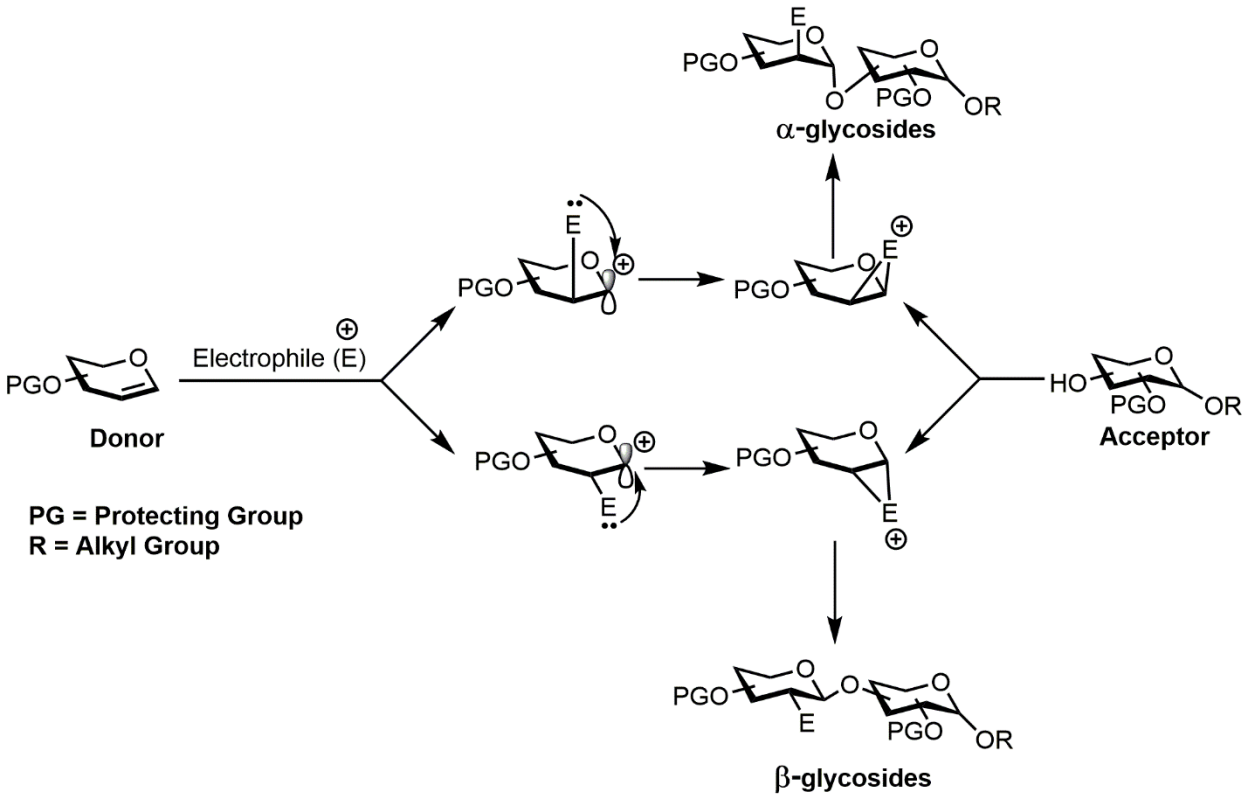
Scheme 6: Traditional synthesis of Glycosides: mono-, oligo- and polysaccharides.

supply of the antibiotics is problematic because of the less stock and limited access. To overcome this issue, there is a necessity for the synthesis of such target molecules to ensure sufficient supply of antibiotics. Hence, there is a requirement in discovery and development in the synthesis of

natural products. After a few decades, the oligosaccharide synthesis was carried out by glycosylation process by reacting glycosyl donor and acceptor to form glycosidic linkage. As depicted in **Scheme 6**, the leaving group of donor was activated by an electrophile acting as a promotor. Then, the generated intermediate remains in equilibrium with oxocarbenium ion. The acceptor acting as a nucleophile reacted with oxocarbenium ion to provide oligosaccharide via the formation of glycosidic bond. It is distinct that there is a possibility for the nucleophile to attack the oxocarbenium ion from both bottom (α) and top (β) faces. Because of sp^2 hybridization of oxocarbenium ion, it adopts trigonal planar geometry and hence, both axial (α), and equatorial (β) isomers of oligosaccharide are formed.

1.4 Influence of Neighboring or Participating Group in Glycosylation:

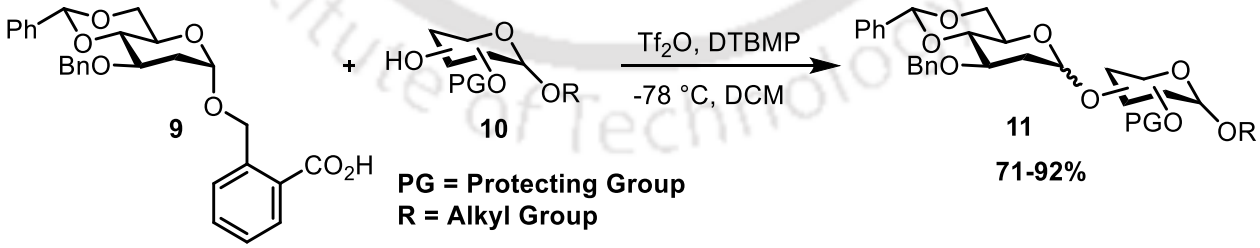
It is evident that axial (α) glycosides are more favored due to the anomeric effect while the synthesis of equatorial (β) isomer is relatively tricky and even more challenging. During the synthesis of 2-deoxy glycosides, there is a difficulty to control the stereochemistry in glycosylation due to the absence of substitution at C2 position in 2-deoxy sugars. Hence, various approaches were discovered for stereochemical control of glycosidation[33], and that can be done either introducing any participating group like electrophile or incorporating any substituent, which has neighboring group participation effect like acetate or benzoate group at C2 position (**Scheme 7**). If the participating group at C2 position stays at the axial position and blocks the top (β) face, then, the hydroxyl group of acceptor attacks from the bottom (α) side to generate axial (α) glycosides. Alternatively, the substitution of the participating group at equatorial position blocks the bottom (α) face then, the acceptor attacks from top (β) side exclusively to construct equatorial (β) glycosides. Normally, halogen, sulfur or selenium[34] was often used as the participating group, and they are introduced to glycal during the reaction or after several steps before construction of glycosides. Finally, the participating group was removed by various synthetic procedures to provide the corresponding glycosides.



Scheme 7: Influence of Neighboring or Participating Group in Glycosylation.

1.5 Literature Preview on Synthesis of 2-Deoxy Glycosides:

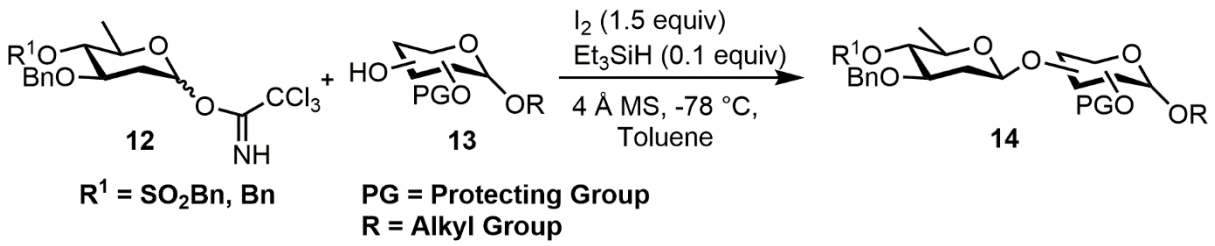
In literature, there are various reports on the synthesis of 2-deoxy glycosides. Kim et al. reported the novel glycosylation of (2'-carboxy)benzyl-4,6-*O*-benzylidene-2-deoxyglucoside **9** (**Scheme 8**) in the presence of triflic anhydride at -78 °C to provide disaccharide **11** with 71-92% yield.[35] In this reaction, the selectivity is more towards β isomer.



Scheme 8: Synthesis of 2-deoxy glycosides by Kim et al.

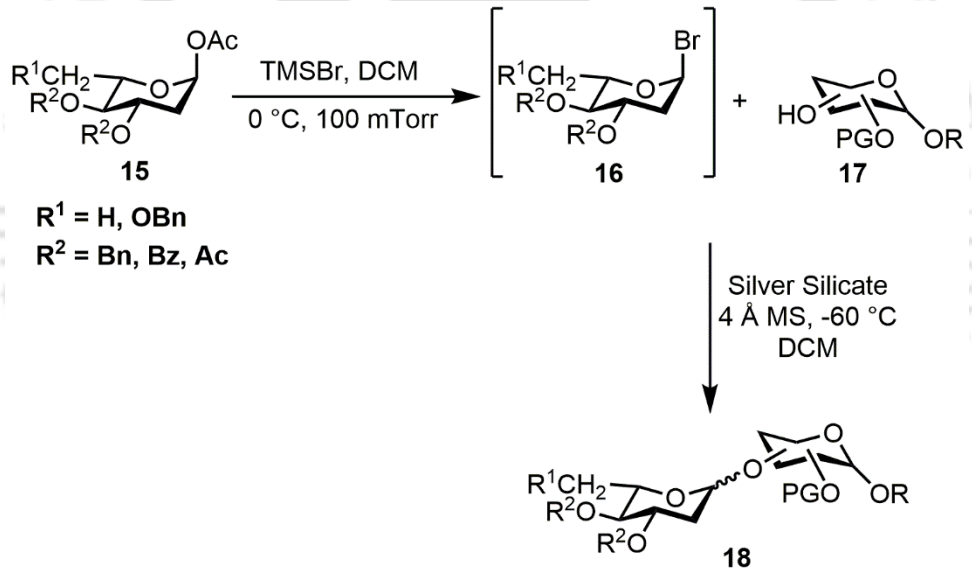
Takahashi and coworkers elucidated the direct synthesis of β-linked oligosaccharide **14** from glycosyl imidates **12** by oxidative activation of the donor (**Scheme 9**).[36] This coupling method can also be applied on 2,6-dideoxy and 2,3,6-trideoxy glycosides to ensure β-selective

glycosides with high yields. Iodine and a catalytic amount of triethylsilane in toluene act as a promotor to activate the donor to provide corresponding product in high yields and selectivity.



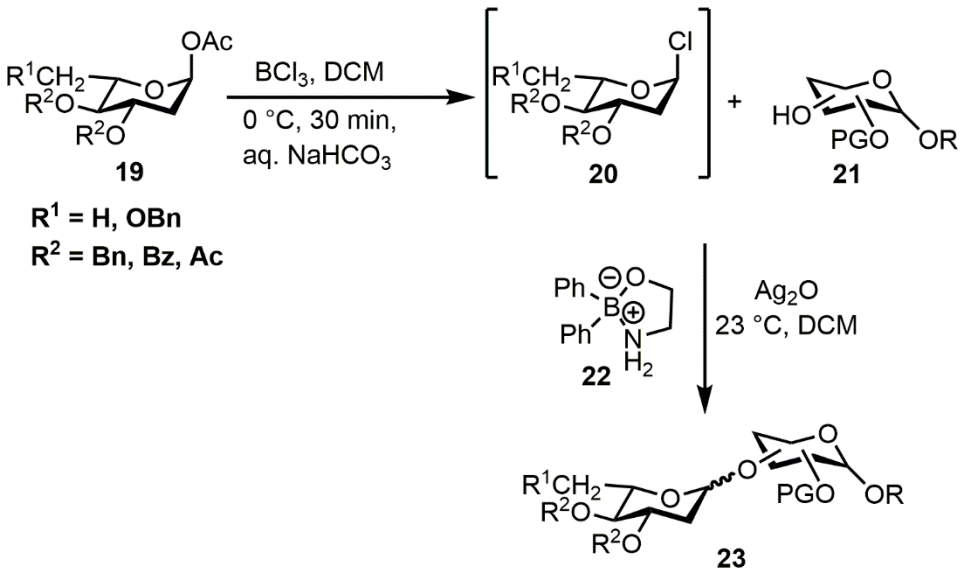
Scheme 9: Synthesis of β-linkage oligosaccharide by T. Takahashi and coworkers.

Herzon and coworkers reported glycosylation of 2-deoxy and 2,6-dideoxy glycosides with acceptor **17** to achieve corresponding oligosaccharides **18** in high yields and towards more β selectivity (**Scheme 10**).[37] The reactive glycosyl bromide **16** was synthesized by coupling between corresponding glycosyl anomeric acetate **15** and TMSBr in DCM.



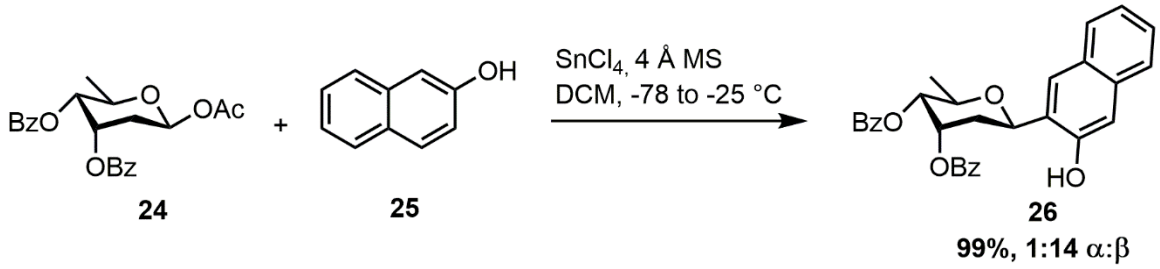
Scheme 10: Glycosylation of deoxy glycosyl bromide by Herzon and coworkers.

In another example, Mark S. Taylor and coworkers reported organo boron-catalyzed glycosylation of 2-deoxy and 2,6-dideoxy glycosyl chloride **20** to provide corresponding oligosaccharides **23** with high yields and β selective (**Scheme 11**).[38] The boron catalyst **22** promotes enhancement of acceptor's **21** nucleophilicity which enables the glycosylation more towards β linkages via S_N2 pathway.



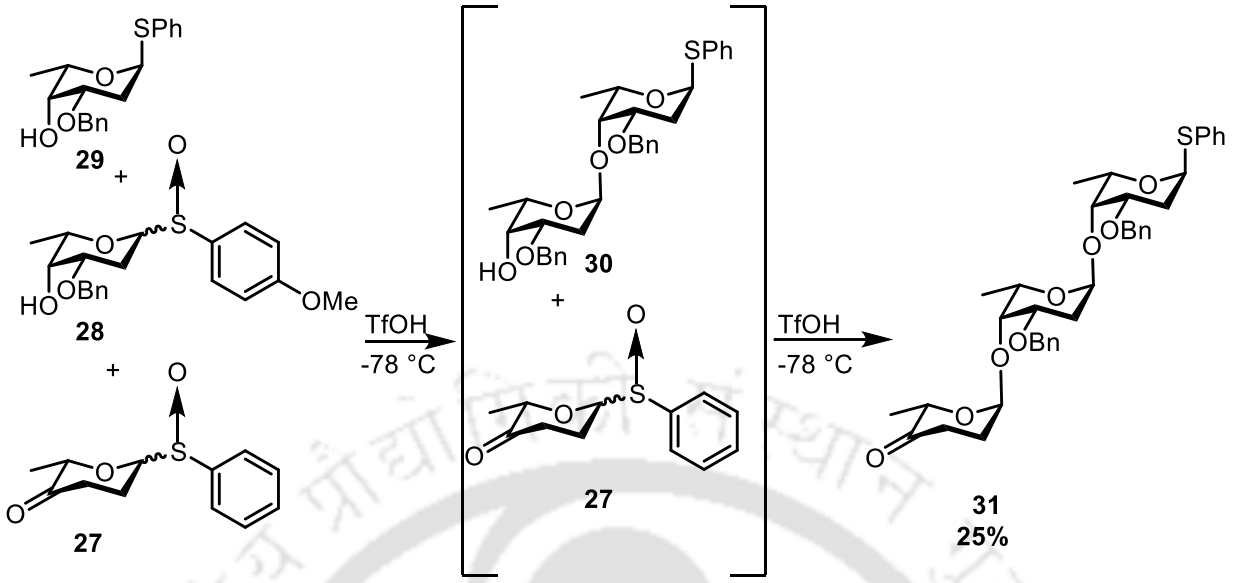
Scheme 11: Organo boron-catalyzed Glycosylation by Mark S. Taylor and coworkers.

Suzuki and co-workers reported a direct conversion of deoxyglycosyl acetates **24** into 2-deoxy *C*-glycosides **26**. In this process, initial *O*-glycosylation was carried out at low temperature followed by warming to afford the corresponding *C*-glycoside (**Scheme 12**).[39]



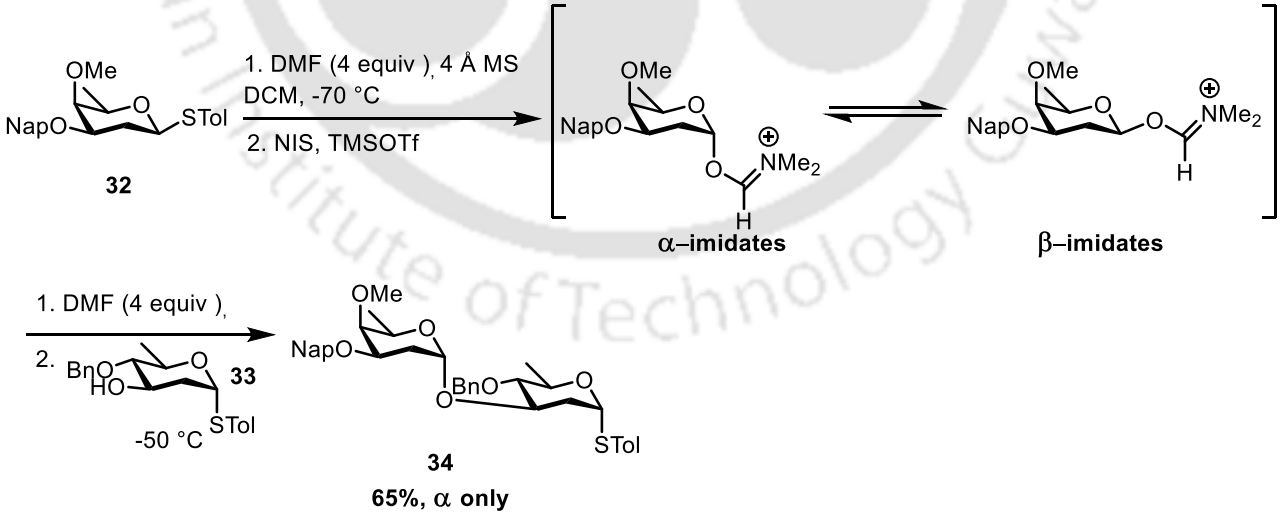
Scheme 12: Synthesis of *C*-glycosides via *O*-glycosylation.

In 1993, Kahne and coworkers reported that there is a huge chemical reactivity difference between OMe and H during one-pot glycosylation to synthesize ciclamycin trisaccharides **31** (**Scheme 13**). The mixture of two 2-deoxysugar sulfoxides donors **27, 28** and 2-deoxythioglycoside **29** as an acceptor with a catalytic amount of triflic acid in the presence of methyl propiolate as a sulfenic acid scavenger afforded the trisaccharides with 25% yield.[40]



Scheme 13: One-Pot Synthesis of the ciclamycin trisaccharide using glycosyl sulfoxides.

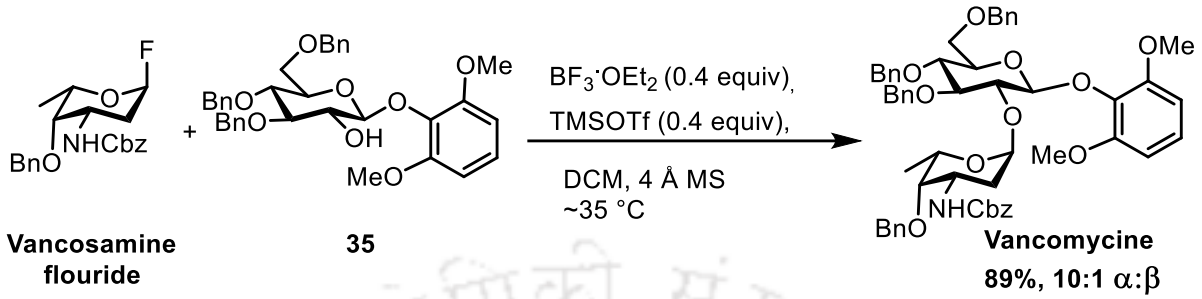
After that, Mong exploited that dimethylformamide (DMF) could be used as a modulator during thioglycoside activation to provide α-selective 2-deoxy glycosides **34** with good yields (**Scheme 14**). The activation of the thioglycoside **32** with NIS/TMSOTf in the presence of DMF (4 to 12 equiv) to afford a glycosyl imidate existing in equilibrium between the more stable α-imidate and more reactive β-imidate. However, β-imidate reacts with acceptor **33** to give products with α-selectivity.[41]



Scheme 14: Use of DMF as a modulator in the α-selective synthesis of 2-deoxyglycosides.

Nicolaou and co-workers showcased the activation of glycosyl fluoride by Lewis acid during the synthesis of vancomycin (**Scheme 15**).[42] They demonstrated that the activation of

vancosamine fluoride by Lewis acid $BF_3{\cdot}OEt_2$ and TMSOTf with glucose derived acceptor **35** to provide the vancomycin disaccharide in 89% yield with 10:1 α:β selectivity.

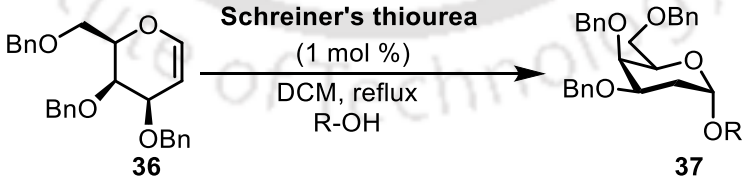


Scheme 15: Synthesis of the vancomycin through $BF_3{\cdot}OEt_2$-TMSOTf.

1.6 Organocatalytic Synthesis of 2-Deoxy Glycosides:

The enantioselective organocatalysis is a powerful synthetic method to catalyze challenging transformations in synthetic organic chemistry. It has an important role in the development of new methods to make chiral molecules with excellent regio-, chemo-, and stereoselective control. The organocatalysis is known to be simple for handle and operational purposes. Organocatalysts, generally are readily available, easy to prepare, and low in toxicity. These valuable features make organocatalysis an attractive method to synthesize complex structures, including oligosaccharides in stereoselective fashion.

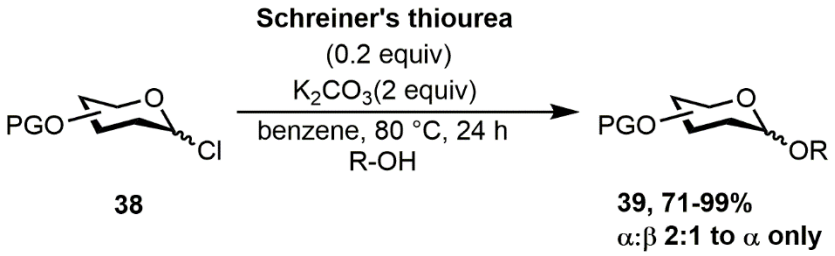
Galan, McGarrigle, and coworkers demonstrated that the reaction of glycals **36** with Schreiner's thiourea provide α-stereoselective 2-deoxygalactosides **37** (**Scheme 16**).[43] It showcased that a range of protecting groups, e.g., ethyl, allyl, benzyl, methoxymethyl ether (MOM) and silyl ether are not affecting during the reaction.



36 **37**

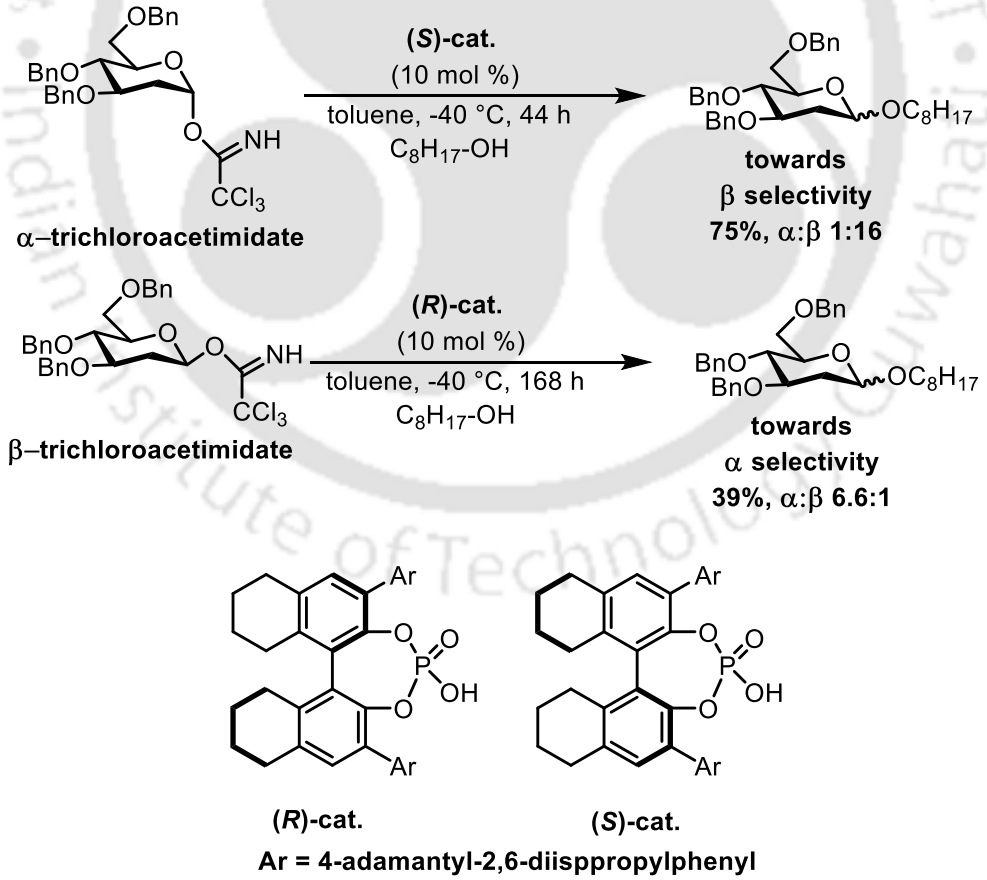
Scheme 16: Synthesis of α-selective glycosides from galactal.

In another report, Ye and coworkers elucidated that protected glycosyl chloride **38** was activated by Koenigs−Knorr activation to afford deoxyglycosides **39** with high yields and more towards α-selectivity (**Scheme 17**).[44] It was found that the combination of thiourea catalyst with K_2CO_3 provided the desired disaccharides after 24 h at 80 °C.



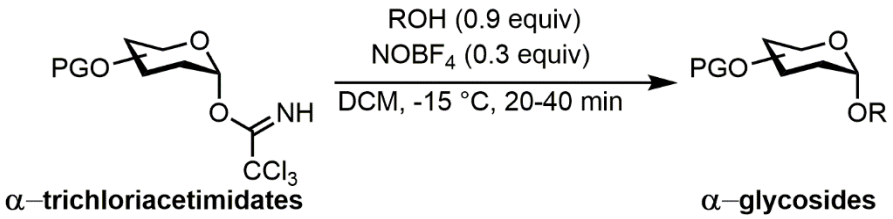
Scheme 17: Stereoselective synthesis of deoxy glycosides from glycosyl chloride by Koenigs-Knorr activation.

Recently, Bennett and co-workers showcased that perbenzylated 2-deoxyglycosyl α- or β-trichloroacetimidate can be activated by chiral BINOL-derived phosphoric acids and afforded the corresponding 2-deoxyglycosides after coupling reactions with 1-octanol (**Scheme 18**).[45] Interestingly, high levels of β-selective glycosides were found (1:16 α:β) when chiral Brønsted acid catalyst (*S*)-cat. and an α-trichloroacetimidate donor was used. Besides, while the reaction involving (*R*)-cat. and β-trichloroacetimidate donor required longer reaction times and afforded the corresponding product more towards α-selective (6.6:1 α:β).



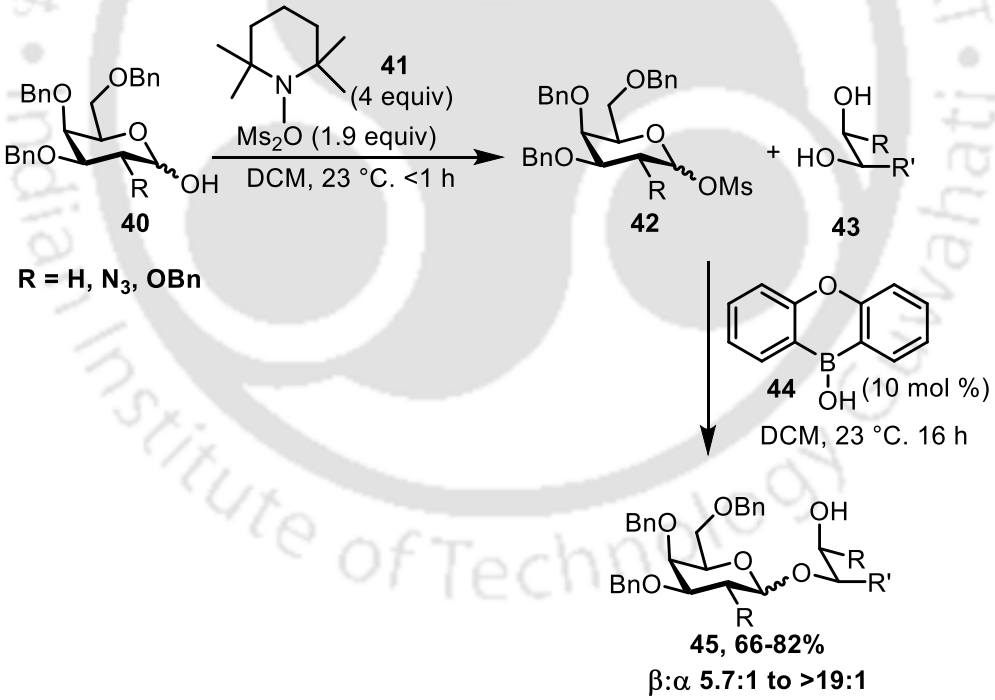
Scheme 18: Synthesis of chiral acid-catalyzed glycosides from trichloroacetimidate.

Furthermore, Misra and coworkers demonstrated that the glycosyl trichloroacetimidate donors could activate by $NOBF_4$ followed by addition of nucleophile provided α-selective glycosides within 20-40 min (**Scheme 19**).[46] The authors proposed that a nitrosyl cation efficiently activates the trichloroacetimidate to form an oxocarbenium ion as an intermediate.



Scheme 19: Synthesis of α-selective glycosides using $NOBF_4$ as a Lewis acid.

The oxaboraanthracene-derived borinic acid catalyst **44** has a great influence in highly stereoselective glycosylations with glycosyl mesylate donors **42** (**Scheme 20**).[47] M. S. Taylor and coworkers demonstrated the in situ formation of glycosyl mesylates **42** by the reaction of glycosyl hemiacetal **40** with methanesulfonic anhydride **41**. The generated glycosyl mesylate **42** was

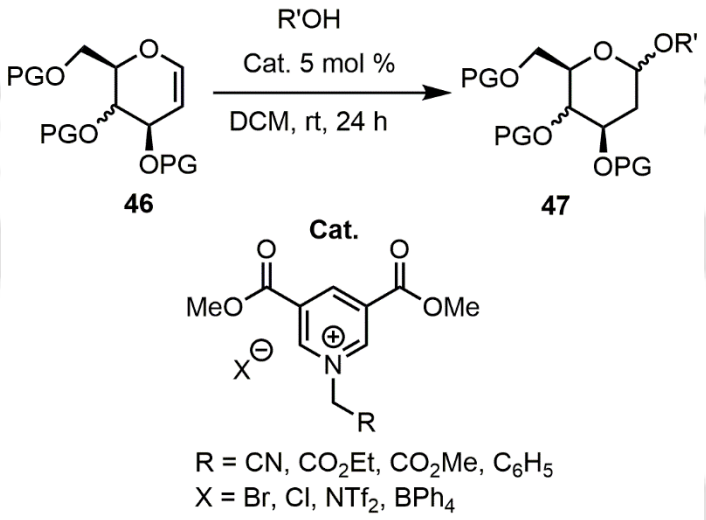


Scheme 20: In situ formation of glycosyl mesylate donors followed by glycosylation using a diarylorganoboron catalyst.

activated with diarylorganoboron catalyst **44** by an organoboron-catalyzed glycosylation in the presence of 1,2- or 1,3-cis-diols **43** as an acceptor. The desired disaccharides **45** were obtained over 16 h in high yields towards β-selectivity and also regioselectivity toward the other free OH.

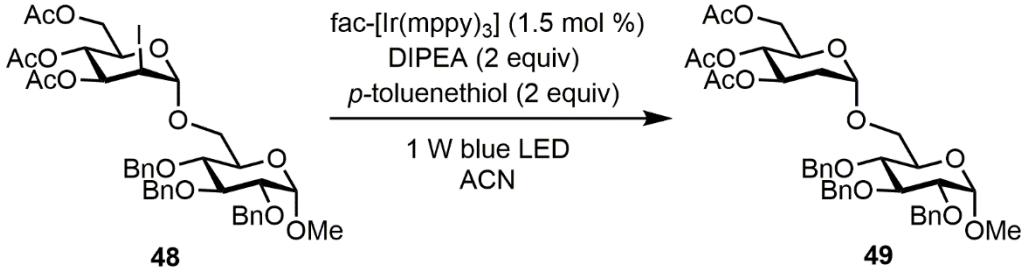
However, when the reactions were carried out in the absence of the organoboron catalyst **44** afforded the products **45** having modest to high α-selectivity and indicated the stereochemical influence shown by the organocatalyst.

Berkessel and coworkers reported that glycals **46** can be activated by electron-deficient pyridinium salts as catalysts to provide 2-deoxyglycosides **47** in the presence of alcohol (**Scheme 21**).[48] They displayed that 1−2 mol % of catalyst was enough for stereoselective glycosylation of glycals. This method was applicable on a series of primary and secondary acceptor and desired product obtained within 14 h in high yields towards α-selective product.



Scheme 21: Electron-deficient pyridinium salt-catalyzed 2-deoxyglycosylation.

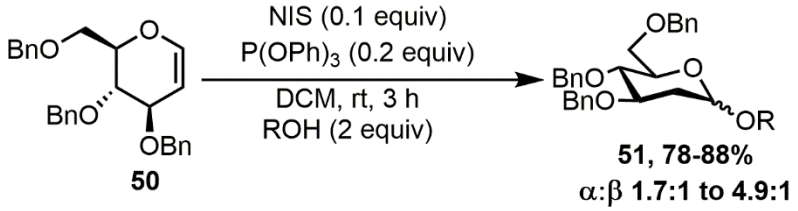
Recently, Wan and coworkers highlighted the deiodination of 2-iodo-2-deoxy glycosides under visible-light irradiation in the presence of an iridium catalyst (**Scheme 22**).[49] They mentioned that this protocol is highly efficient to convert acetate-protected 2-iodo-2-deoxyglycoside **48** to corresponding 2-deoxy-α-glycosides **49** with good yields.



Scheme 22: Visible-light-mediated deiodination of 2-iodo-2-deoxyglycosides.

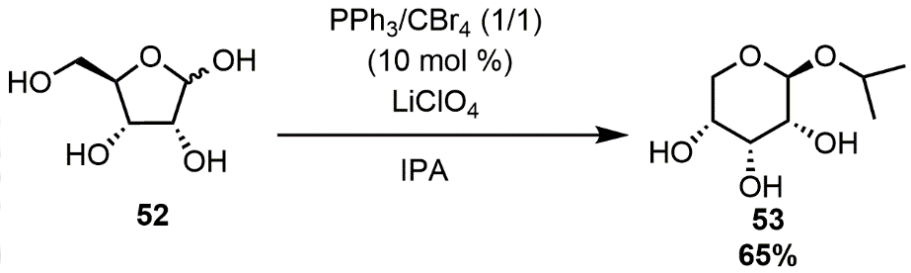
After that, Toshima and coworkers demonstrated the activation of glycals by reactive iodophosphonium ion (**Scheme 23**).[50] They displayed that, in the presence of alcohol, glycal **50**

was activated in the presence of NIS (0.1 equiv) and triphenylphosphite (0.2 equiv) to generate corresponding 2-deoxyglycosides **51** at rt with good yields and selectivities.



Scheme 23: Synthesis of 2-deoxyglycosides using NIS and $P(OPh)_3$.

In another report, Mahrwald and coworkers described the glycosylation of unprotected native sugar **52** to provide 6-deoxyglycosides **53** in a stereoselective way (**Scheme 24**).[51] This protocol involves the activation of unprotected native sugar by using PPh_3/CBr_4 catalytic system.



Scheme 24: Glycosylation of unprotected sugars using PPh_3/CBr_4.

1.7 References:

1. De Lederkremer, R. M.; Marino, C. *Adv. Carbohydr. Chem. Biochem.* **2008,** *61*, 143–216.
2. Weymouth-Wilson, A. C. *Nat. Prod. Rep.* **1997,** *14*, 99–110.
3. Williama Lown, J. *Chem. Soc. Rev.* **1993,** *22*, 165–176.
4. Lombo, F.; Menendez, N.; Salas, J. A.; Mendez, C. *Appl. Microbiol. Biotechnol.* **2006,** *73*, 1–14.
5. Krohn, K.; Rohr, J. Springer: 1997; pp127–195.
6. Rohr, J.; Thiericke, R. *Nat. Prod. Rep.* **1992,** *9*, 103–137.
7. Davies, H.; Green, R. *Nat. Prod. Rep.* **1986,** *3*, 87–121.
8. Nicolaou, K.; Dai, W. M. *Angew. Chem., Int. Ed.* **1991,** *30*, 1387–1416.
9. Wohlert, S. E.; Kunzel, E.; Machinek, R.; Mendez, C.; Salas, J. A.; Rohr, J. *J. Nat. Prod.* **1999,** *62*, 119–121.
10. Ogawa, H.; Yamashita, Y.; Katahira, R.; Chiba, S.; Iwasaki, T.; Ashizawa, T.; Nakano, H. *J. Antibiot.* **1998,** *51*, 261–266.

11. Roush, W. R.; Hartz, R. A.; Gustin, D. J. *J. Am. Chem. Soc.* **1999,** *121*, 1990–1991.
12. Ogawa, H.; Yamashita, Y.; Katahira, R.; Chiba, S.; Iwasaki, T.; Ashizawa, T.; Nakano, H. *J. Antibiot.* **1998,** *51*, 261–266.
13. Katahira, R.; Uosaki, Y.; Ogawa, H.; Yamashita, Y.; Nakano, H.; Yoshida, M. *J. Antibiot.* **1998,** *51*, 267–274.
14. Menendez, N.; Nur-e-Alam, M.; Fischer, C.; Brana, A. F.; Salas, J. A.; Rohr, J.; Mendez, C. *Appl. Environ. Microbiol.* **2006,** *72*, 167–177.
15. Sezaki, M.; Kondo, S.; Maeda, K.; Umezawa, H.; Ohno, M. *Tetrahedron* **1970,** *26*, 5171–5190.
16. Nagatsu, T.; Ayuakawa, S.; Umezawa, H. *J. Antibiot.* **1968,** *21*, 354–357.
17. Drautz, H.; Zahner, H.; Rohr, J.; Zeeck, A. *J. Antibiot.* **1986,** *39*, 1657–1669.
18. Henkel, T.; Ciesiolka, T.; Rohr, J.; Zeeck, A. *J. Antibiot.* **1989,** *42*, 299–311.
19. Kawashima, A.; Kishimura, Y.; Tamai, M.; Hanada, K. *Chem. Pharm. Bull.* **1989,** *37*, 3429–3431.
20. Henkel, T.; Rohr, J.; Beale, J. M.; Schwenen, L. *J. Antibiot.* **1990,** *43*, 492–503.
21. Rohr, J.; Wohlert, S.-E.; Oelkers, C.; Kirschning, A.; Ries, M. *Chem. Commun.* **1997,** 973–974.
22. Crow, R. T.; Rosenbaum, B.; Smith, R.; Guo, Y.; Ramos, K. S.; Sulikowski, G. A. *Bioorg. Med. Chem. Lett.* **1999,** *9*, 1663–1666.
23. Shaaban, Khaled A.; Srinivasan, Sowmyalakshmi; Kumar, Raj; Damodaran, Chendil; Rohr, J. *J. Nat. Prod.* **2011,** *74*, 2–11.
24. Zhu, Z.; Jiang, W.; McGinley, J. N.; Thompson, H. J. *Cancer Res.* **2005,** *65*, 7023–7030.
25. Ferrier, R. J.; Hoberg, J. O. *Adv. Carbohydr. Biochem.*, **2003,** *58*, 55–120.
26. Bolitt, V.; Mioskowski, C.; Lee, S. G.; Falck, J. R. *J. Org. Chem.*, **1990,** *55*, 5812–5813.
27. Sabesan, S.; Neira, S. *J. Org. Chem.*, **1991,** *56*, 5468–5472.
28. Costantino, V.; Imperatore, C.; Fattorusso, E.; Mangoni, A. *Tetrahedron Lett.* **2000,** *41*, 9177–9180.
29. Yadav, J. S.; Reddy, B. V. S.; Reddy, K. B.; Satyanarayana, M. *Tetrahedron Lett.* **2002,** *43*, 7009–7012.
30. Nakamura, T.; Goda, Y.; Sakai, S.; Kondo, K.; Akiyama, H.; Toyoda, M. *Phytochemistry*, **1998,** *49*, 2097–2102.
31. Suzuki, R.; Okada, Y.; Okuyama, T. *J. Nat. Prod.* **2003,** *66*, 564–565.

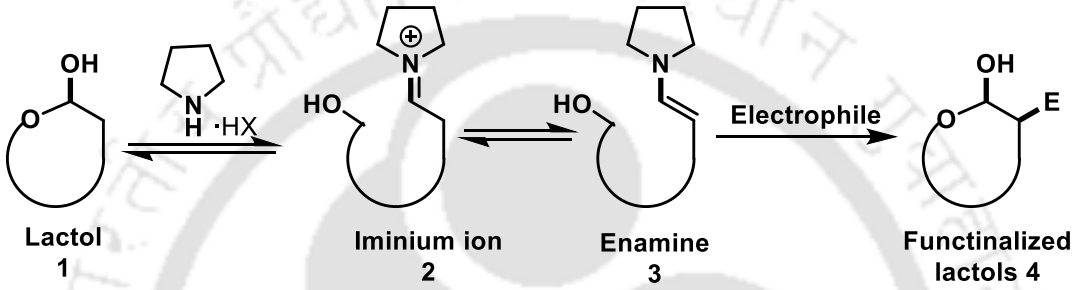
32. Reichstein, T.; Weiss, E. *Adv. Carbohydr. Chem.* **1962,** *17*, 65–120.
33. Hou, D.; Lowary, T. L. *Carbohydr. Res.* **2009,** *344*, 1911–1940.
34. Marzabadi, C. H.; Franck, R. W. *Tetrahedron* **2000,** *56*, 8385–8417.
35. Kim, K. S.; Park, J.; Lee, Y. J.; Seo, Y. S. *Angew. Chem., Int. Ed.* **2003,** *42*, 459–462.
36. Tanaka, H.; Yoshizawa, A.; Takahashi, T. *Angew., Chem., Int. Ed.* **2007,** *119*, 2557–2559.
37. Kaneko, M.; Herzon, S. B. *Org. Lett.* **2014,** *16*, 2776–2779.
38. Beale, T. M.; Moon, P. J.; Taylor, M. S. *Org. Lett.* **2014,** *16*, 3604–3607.
39. Matsumoto, T.; Hosoya, T.; Suzuki, K. *Tetrahedron Lett.* **1990**, *31*, 4629−4632.
40. Raghavan, S.; Kahne, D. *J. Am. Chem. Soc.* **1993**, *115*, 1580–1581.
41. Lu, S.-R.; Lai, Y.-H.; Chen, J.-H.; Liu, C.-Y.; Mong, K.-K. T. *Angew. Chem., Int. Ed.* **2011**, *50*, 7315−7320.
42. Nicolaou, K. C.; Mitchell, H. J.; Jain, N. F.; Bando, T.; Hughes, R.; Winssinger, N.; Natarajan, S.; Koumbis, A. E. *Chem. - Eur. J.* **1999**, *5*, 2648−2667.
43. Balmond, E. I.; Coe, D. M.; Galan, M. C.; McGarrigle, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 9152−9155.
44. Sun, L.; Wu, X.; Xiong, D. C.; Ye, X. S. *Angew. Chem., Int. Ed.* **2016**, *55*, 8041−8044.
45. Liu, D.; Sarrafpour, S.; Guo, W.; Goulart, B.; Bennett, C. S. *J. Carbohydr. Chem.* **2014**, *33*, 423−434.
46. Sau, A.; Santra, A.; Misra, A. K. *Synlett* **2012**, *23*, 2341−2348.
47. D'Angelo, K. A.; Taylor, M. S. *J. Am. Chem. Soc.* **2016**, *138*, 11058−66.
48. Das, S.; Pekel, D.; Neudorfl, J. M.; Berkessel, A. *Angew. Chem., Int. Ed.* **2015**, *54*, 12479−12483.
49. 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*, 17319−17323.
50. Kimura, T.; Takahashi, D.; Toshima, K. *J. Org. Chem.* **2015**, *80*, 9552−9562.
51. Schmalisch, S.; Mahrwald, R. *Org. Lett.* **2013**, 15, 5854−5857.

Chapter 2

Secondary Amine Salts Catalyzed Controlled Activation of 2-Deoxy Sugar Lactols towards Stereoselective Dehydrative Glycosylation

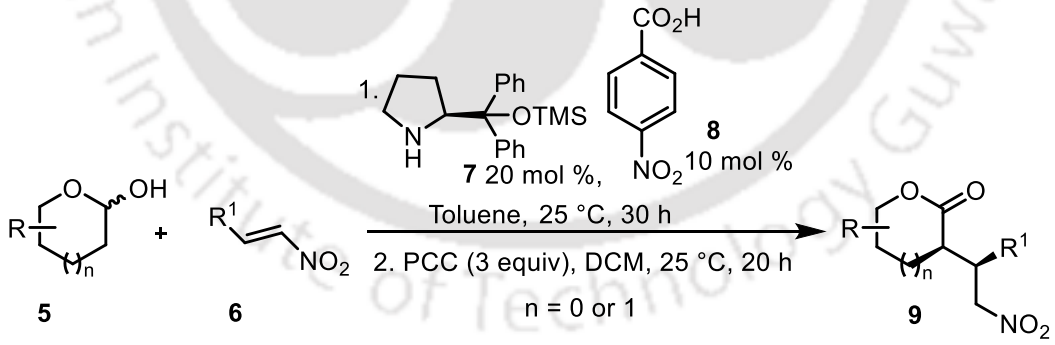
2.1 Introduction:

The formation of iminium ions[1a] by a reaction between secondary amines/amine salts and aliphatic/aromatic aldehydes has been extensively explored since the seminal work by MacMillan et al.[2] and Barbas et al.[3] In the case of aliphatic aldehydes,[1b] the thus-generated iminium ions tautomerize into the corresponding enamines that are trapped by a multitude of electrophiles (**Scheme 1**), whereas iminium ions formed from α,β-unsaturated aldehydes are prone to undergo 1,2 or 1,4-nucleophilic addition reactions.



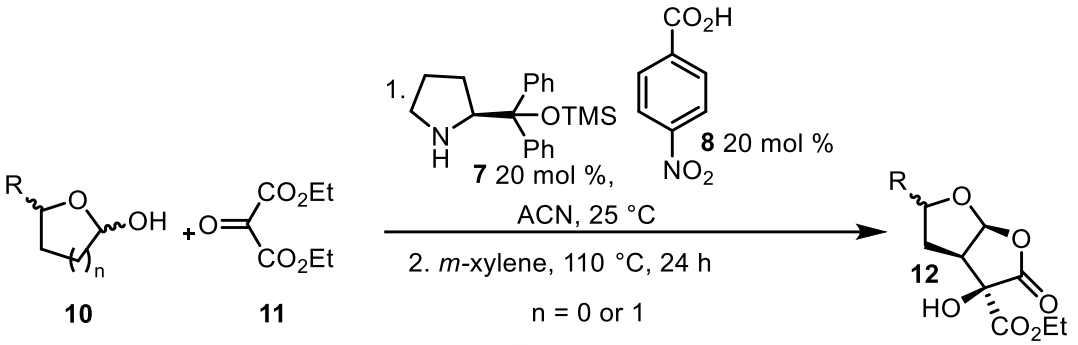
Scheme 1: General iminium/enamine catalysis of lactols.

Liu et al. have showcased the iminium/enamine catalyzed functionalization of masked aldehydes, i.e. lactols[4] **5** and cyclic hemi-aminals[5] that react with nitrostyrenes **6**, α,β-unsaturated ketones, and ketomalonates.[4b] With this open-close strategy in asymmetric catalysis, lactols are



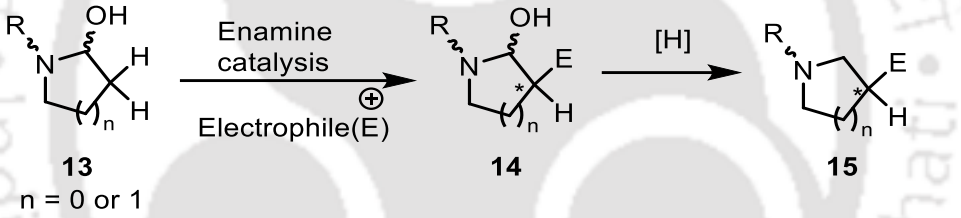
Scheme 2: Iminium/enamine catalysis of functionalized lactols.

directly activated by secondary amine catalyst **7** providing α-functionalized lactols containing two adjacent stereogenic centers. These lactols were further oxidized to their respective lactones **9** to obtain the products as a single diastereomers in good yields and with excellent enantioselectivities (most cases >99%) (**Scheme 2**).



Scheme 3: Asymmetric aldol-desymmetrization method to synthesize bicyclic compounds.

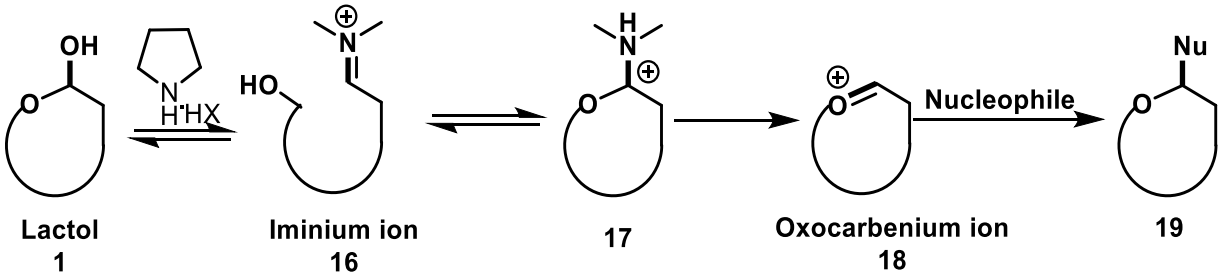
Similarly, Liu and his coworkers reported an asymmetric aldol-desymmetrization approach in the presence of diethyl malonate **11** which provided highly efficient and biologically important bicyclic oxygen-containing compounds with multiple chiral centers and one is a quaternary stereogenic center containing a free hydroxy group (**Scheme 3**). Moreover, the final products were obtained from racemic lactols as two separable diastereomers.



Scheme 4: Enamine-based Asymmetric conjugate addition reaction.

Liu and his group elucidated an enamine-based asymmetric conjugate addition reaction for the synthesis of functionalized nitrogen-containing heterocycles **15** (**Scheme 4**). With this method, cyclic hemiaminals **14** were directly used for the first time as nucleophiles to afford corresponding heterocycles in high yields and enantioselectivities.

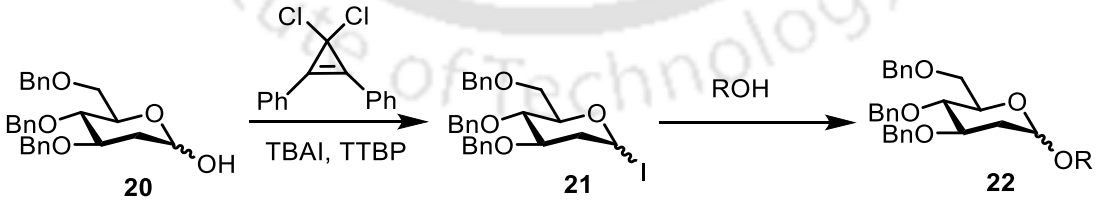
We envisioned that in the case of lactols **1**, the iminium ions **16** that tautomerize into enamines **17**, under forcible conditions, could be trapped intramolecularly which upon the expulsion of ammonium species could lead to the generation of oxocarbenium ions[6] **18** (**Scheme 5**), one of the most important intermediates in organic chemistry. The thus generated oxocarbenium ions if trapped by nucleophiles like alcohols would lead to the development of a novel organocatalytic method for the synthesis of acetals **19**.



Scheme 5: Possible mode of activation of lactols: Generation of oxocarbenium ion.

We have chosen 2-deoxysugar lactols as substrates to study the hypothesis. 2-Deoxysugar acetals, i.e. 2-deoxyglycosides are part of several natural products with anticancer[7,] and antibiotic properties[7a,8] and it has been shown that these structural motifs are important for their activity.[9] Most of the sugar lactols require the anomeric derivatization prior to glycosylation and 2-deoxysugars are no exception.[10] However, the derivatized 2-deoxysugar donors are relatively unstable[11] and require careful handling. Several direct and indirect methods for the synthesis of 2-deoxyglycosides[12] involving C-2 heteroatom substitutions,[11b,13] 1,2-epoxides,[14] enol ethers,[15] and hemi-acetals[16] have been developed over the past two decades.

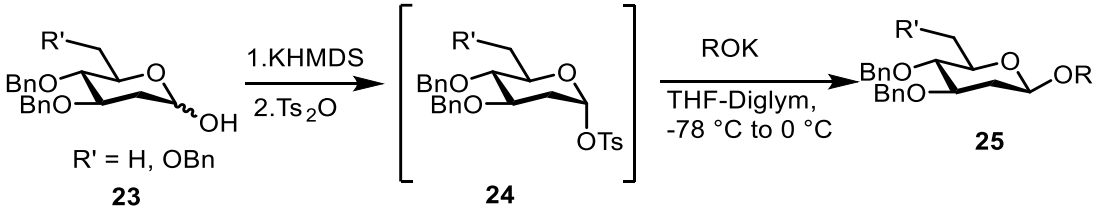
Despite the significant advantages, dehydrative glycosylation has not evolved into a commonly used method owing to the unique challenges posed by lactol donors, e.g. the self-condensation reaction of the lactols often competes with the desired glycosylation product. 2-Deoxy lactols pose a bigger challenge due to their high reactivity/nucleophilicity towards the self-condensation of the substrates. The existing methods, though highly effective, suffer from the requirement of more than one reagent[16c,e,17] and limited applicability.[16a,18] Bennett and coworkers



Scheme 6: Dehydrative glycosylation via glycosyl iodide.

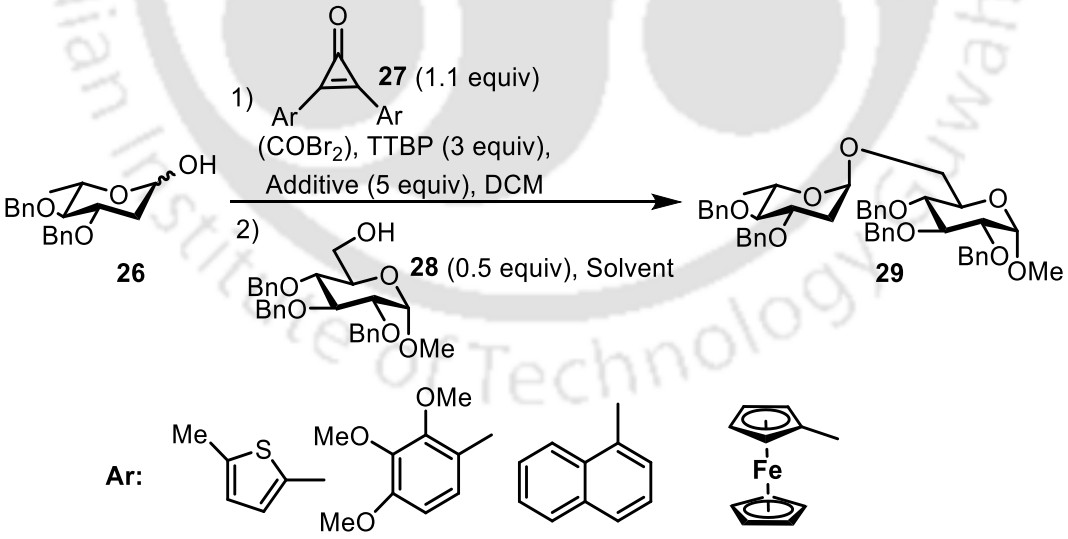
reported a method to convert 2-deoxy hemiacetals **20** into glycosyl iodides **21** in-situ via anomeric cyclopropenium intermediate in the presence of TBAI and TTBP followed by the addition of alcohol to provide the glycosides **22** in high yields (**Scheme 6**). However, the method suffers from

the usage of more than one reagent and also involves the usage of more than stoichiometric amounts of the expensive base TTBP.



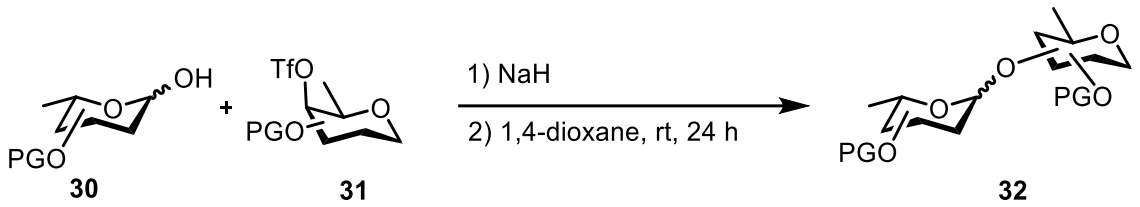
Scheme 7: Dehydrative glycosylation via α-glycosyl tosylate.

Recently, the same group showed that 2-deoxy hemiacetals **23** could be converted into glycosyl tosylates **24** using tosic anhydride in the presence of hindered base KHMDS and this tosylate intermediate was found to be very effective to give β selective glycosides **25** with corresponding alkoxides in high yields via S_N^2 pathway (**Scheme 7**). Although, this method is highly selective, but still, it is a two-step process. For this purpose, the dehydrative glycosylation method in one-step process in which 2,6-dideoxy hemiacetals **26** converted directly to corresponding α-selective glycosides **29** in high yields (**Scheme 8**). Cyclopropenone and tetrabutylammonium iodide (TBAI) were used to activate the hemiacetal and after that, the addition of primary sugar alcohol **28** to it, gave corresponding disaccharide **29** stereoselectively.



Scheme 8: Reagent-controlled α-selective dehydrative glycosylation.

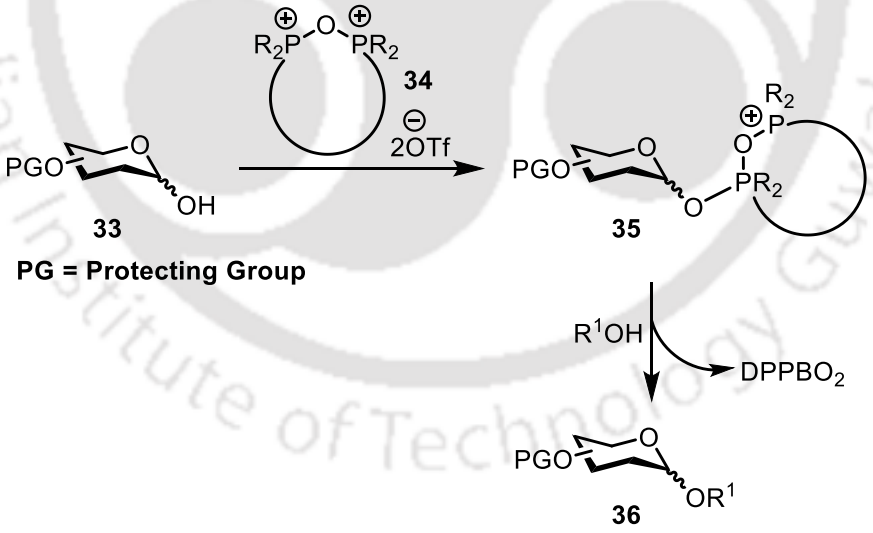
Although, they were getting selectively one isomer in one-step, but they were using so many additives, more than one promoters to drive the reaction.



Scheme 9: Synthesis of 2-deoxy glycoside via anomeric *O*-alkylation.

Alternatively, J. Zhu and coworkers reported a novel approach for the synthesis of 2-deoxy and 2,6-dideoxy glycosides **32** via anomeric *O*-alkylation with secondary electrophiles like glycosyl triflates **31** (**Scheme 9**). This method is performed in a basic condition that is beneficial for acid-labile 2-deoxy glycosides **30**.

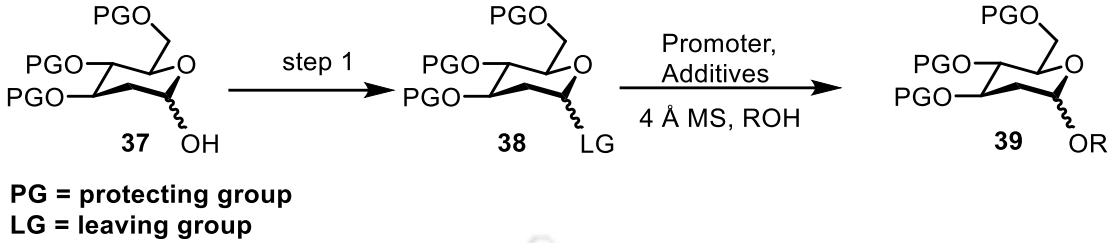
Walczak and his group reported the dehydrative glycosylation of glycosides **33** with cyclic phosphonium anhydride **34** to form phosphonium intermediate **35**, and the corresponding product was formed **36** upon addition of alcohol with high yields (**Scheme 10**). Generally, cyclic phosphonium anhydride is an efficient and versatile reagent for N-, S-, O- and C- glycosylation in excellent yields.



Scheme 10: Dehydrative glycosylation using cyclic phosphonium anhydride.

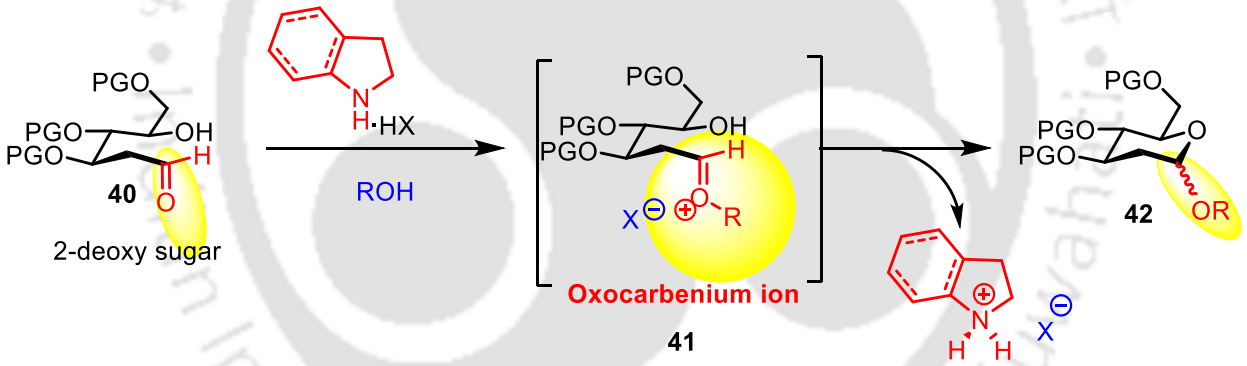
In literature, 2-deoxy sugar lactols **37** are activated in one-step by using several activating agents to form highly reactive intermediate **38**, where hydroxyl group was converted to a conventional leaving group (**Scheme 11**). Finally, this intermediate **38** can be trapped by alcohol

in the presence of more than one additive, promoter, and molecular sieves to achieve corresponding acetals **39**.



Scheme 11: General strategy of glycosylation methods.

Till date, an effective catalytic method for the dehydrative glycosylation with a broad scope towards the synthesis of 2-deoxyglycosides **42** has not been realized. To overcome these difficulties and challenges, a new controlled mode of activation of these substrates is needed. Here, in this chapter, we report an unprecedented and operationally simple organocatalytic protocol for



Scheme 12: Our strategy of dehydrative glycosylation method via generation of oxocarbenium ion.

the direct dehydrative glycosylation of 2-deoxyglycosides **40** using secondary amine salts as catalysts that involve the efficient use of lactol functionality (**Scheme 12**). In this method, preactivation of the substrate is not needed, the reaction is easy to handle and not moisture sensitive. Raw materials for the preparation of catalyst are very cheap, and the process of synthesis of salts is very simple. Dehydrative glycosylation was very common and well-known method in carbohydrate chemistry. So, we should always be aware of the self-condensation product (dimerized product) which is expected byproduct in dehydrative glycosylation method as 2-deoxy lactols had high reactivity/nucleophilicity towards self-condensation of the substrates.

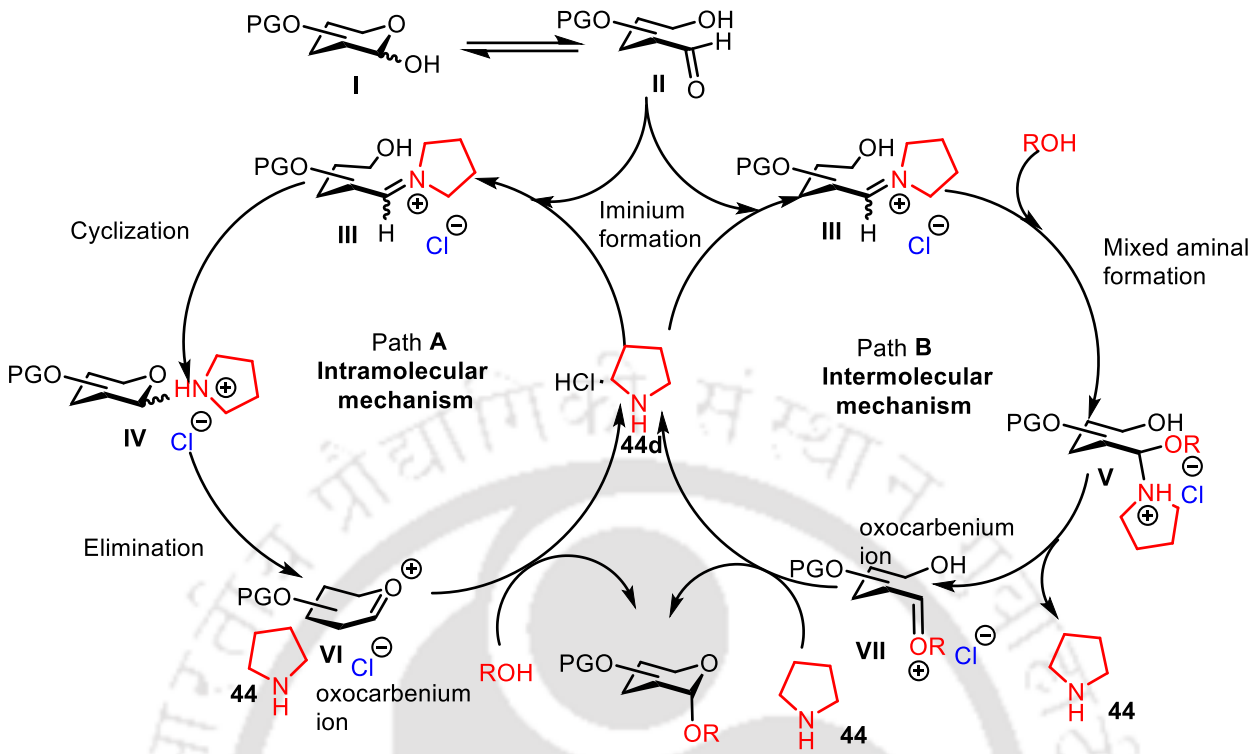


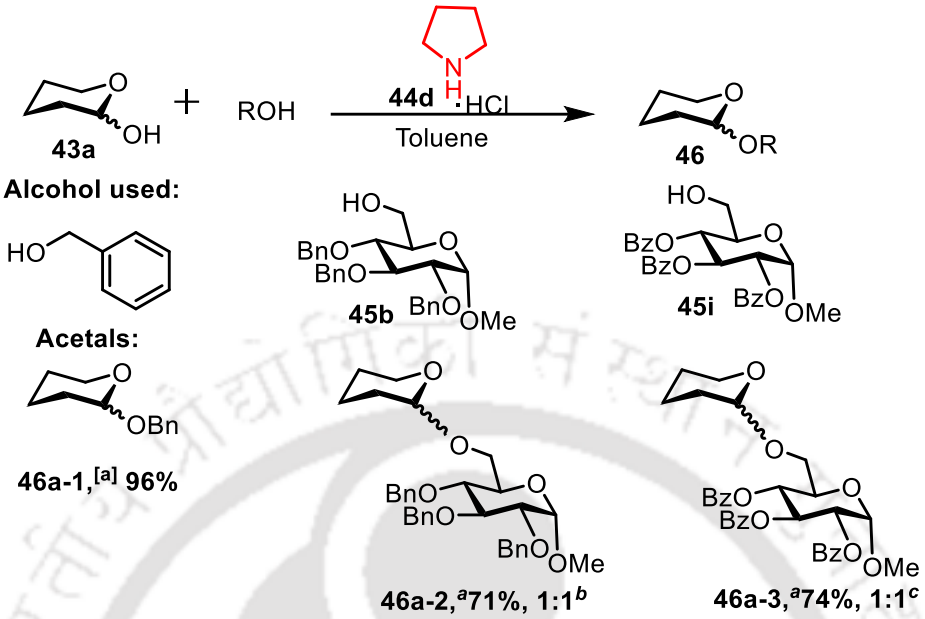
Figure 1: Proposed mechanistic pathways of glycosylation reactions.

Though reminiscent of the recent development of an oxa-Pictet Spengler reaction via oxocarbenium ion catalyzed by pyrrolidine salts,[18] the current strategy involving the sugar lactols has several challenges. 1) Generation of the iminium ion **III** is dependent on the percentage of sugar lactol existing in its open-chain form (**Figure 1**, **III**), 2) The generated iminium ion **III** must possess the necessary electrophilicity to react with the unactivated primary and secondary sugar alcohols (**Figure 1**, **IV** or **V**) and 3) the leaving group ability of pyrrolidinium species to generate the oxocarbenium ion (**Figure 1**, **VI** or **VII**). We embarked upon to test the hypothesis by choosing δ-Valerolactol **43a** and benzyl alcohol as model substrates using simple pyrrolidine hydrochloride **44d** as the organocatalyst (**Scheme 13**).

2.2 Initial Studies:

After a few failed attempts at various temperatures, we were delighted to see that the acetal formation is clean at 100 °C and gave the desired product **46a-1** in 96% yield. Similar reactions were performed with activated and deactivated sugar acceptors **45b** and **45i** that also proceeded

Scheme 13: Initial studies for acetal synthesis using δ-valerolactol.



Reaction conditions: 0.98 mmol of **43a**, 0.13 mmol of benzyl alcohol/**45b**/**45i** and 20 mol % of **44d**, 100 °C, 5 h. [a]No dimerization of **43a** was observed. [b]Anomeric ratios were determined from crude ^{13}C NMR analysis. [c]Anomeric ratios were determined from crude ^{1}H NMR analysis.

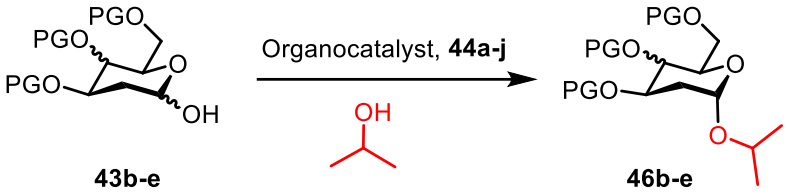
with a yields of 71% and 74% respectively (**Scheme 13, 46a-2, 46a-3**). Surprisingly, contrary to Siedel's work, the reaction leads to decomposition when performed in the presence of thiourea.[19]

2.3 Optimisation Study:

We then swiftly shifted our focus to the more complex 2-deoxysugar lactols as the coupling partners. We have chosen isopropanol to perform the optimization studies with the sugar lactols. Initial attempts with 10 mol % pyrrolidinium hydrochloride **44d** and glycosyl donor **43b** in the presence of isopropanol as the acceptor and toluene as solvent did not lead to any glycosylation product even after 24 h at rt (**Table 1**, entry 2). However, after several attempts at various temperatures (**Table 1**, entries 3-4), the reaction when performed with 1.5 equiv of isopropanol with respect to the lactol donor **43b** in the presence of 20 mol % of the organocatalyst **44d** at 80 °C in toluene as solvent, provided us the glycosylation product **46b** in 63% yield with 2:1 α:β selectivity (**Table 1**, entry 3). The reaction went to completion in 5 h with reasonable α-selectivity without requiring any molecular sieves even at elevated temperature. After further optimization

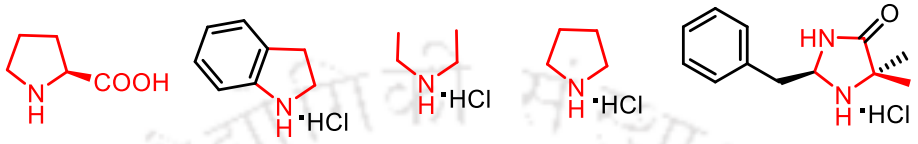
studies, we found that the reaction gives excellent results (**Table 1**, entry 4) with toluene as solvent at 100 ^{o}C with improved α selectivity. Interestingly, the formation of the dimerized product **47d** was not observed under these catalytic conditions. Several other secondary amine salts were tested, but none of them provided further improvements. Moreover, chiral L-proline **44a,** when used (**Table 1**, entry 1), lead to the decomposition of the starting lactol donor **43b**. Diethylamine hydrochloride **44c** (**Table 1**, entry 6) gave almost similar yields and selectivities, albeit a little more hygroscopic than the pyrrolidine hydrochloride. The Macmillian's imidazoline salt **44e** (**Table 1**, entry 8) also resulted in diminished rate of the reaction and yields. Use of a chiral amine salt has shown no bearing on the stereoselectivity of the reaction. Indoline hydrochloride **44b** (**Table 1**, entry 5) afforded the glycosylation product in 46% yield but resulted in considerable formation of the undesired trehalose analogue **47d** (~20%) presumably because of the increased Brønsted acidic nature of the catalyst. In order to examine the effect of the counterion in the present organocatalytic glycosylation, we investigated the coupling reaction with several pyrrolidine salts bearing different counter ions (**Table 1**, entries 9-13). Salts with tetrafluoroborate and the trifluoroacetate anions (**44h** and **44j** respectively, **Table 1**, entries 11, 13) hardly made any difference to the reactivity and yielded the glycosylated product **46b** in almost identical yields and selectivities suggesting that pyrrolidine salts generated with strong acids are ideal for these reactions. However, the reaction with pyrrolidine tosylate **44f** (**Table 1**, entry 9) is slightly sluggish and also effects the anomeric selectivity, whereas the pyrrolidine salts of benzoate **44g** (**Table 1**, entry 10) and 3,4-dinitrobenzoate **44i** (**Table 1**, entry 12) only resulted in the decomposition of the starting materials. Having successfully tested several secondary amine salts, we decided to probe the effect of armed and disarmed 2-deoxy lactol donors in this coupling reaction. The disarmed triacetylglucopyranose derivative **43c** gave the corresponding isopropyl glycoside **46c** with excellent yields (**Table 1**, entry 18) albeit with surprisingly improved anomeric selectivity. The armed tribenzylgalactopyranose **43d** derivative provided the desired product in 85% yield and 6:1 α:β selectivity (**Table 1**, entry 19). All the anomeric configurations/ratios were confirmed after extensive NMR analysis.[20]

Table 1: Optimization studies of organocatalysts using sugar lactols.



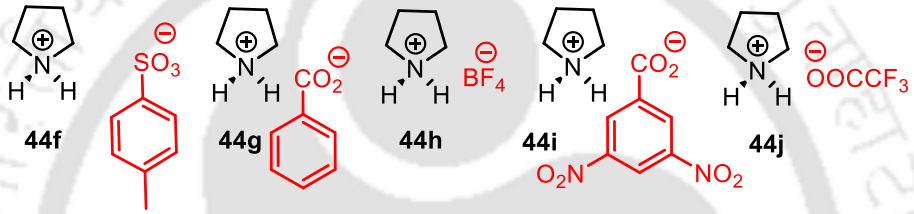
43b-e 46b-e

Different secondary amines



44a **44b** **44c** **44d** **44e**

Different counter ions



44f **44g** **44h** **44i** **44j**

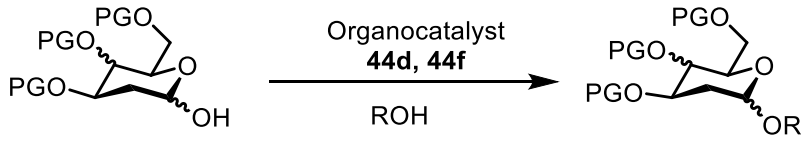
entry	sub	cat.	product	yield(%)	α:β[j]
1	**43b**	**44a**	**46b**	0	-
2[a]	**43b**	**44d**	**46b**	0	-
3[b]	**43b**	**44d**	**46b**	63	2:1
4	**43b**	**44d**	**46b**	87	5:1
5[c]	**43b**	**44b**	**47b**	46	4:1
6	**43b**	**44c**	**46b**	81	4:1
7[d]	**43b**	**44d**	**46b**	47	4:1
8	**43b**	**44e**	**46b**	85	4:1
9	**43b**	**44f**	**46b**	86	5:1
10[e]	**43b**	**44g**	**46b**	0	-
11	**43b**	**44h**	**46b**	77	3:1
12	**43b**	**44i**	**46b**	0	-
13	**43b**	**44j**	**46b**	76	1.5:1
14[f]	**43b**	**44d**	**46b**	38	4:1
15[g]	**43b**	**44d**	**46b**	85	2:1
16[h]	**43b**	**44d**	**46b**	85	2.5:1
17[i]	**43b**	**44d**	**46b**	83	1.5:1
18	**43c**	**44d**	**46c**	81	10:1
19	**43d**	**44d**	**46d**	85	6:1
20	**43e**	**44d**	**46e**	80	4:1

Reaction conditions: 0.12 mmol of **43b-e**, 0.18 mmol of isopropanol and 20 mol % of **44a-j**, toluene, 100 °C, 5 h, (24 h for **46c** and **46e**). [a]rt, 24 h. [b]At 80 °C. [c]1 equiv of **45b** was used. [d]10 mol % of **44d** was used. [e]Anomeric benzoate was observed in HRMS. [f]10 mol % of TBAF was used as an additive. [g]10 mol % of TBAI was used as an additive. [h]80 °C, DCE was used as a solvent. [i]80 °C (1:1 ACN:DCM) was used as a solvent. [j]Anomeric selectivities were determined from crude NMR analysis.

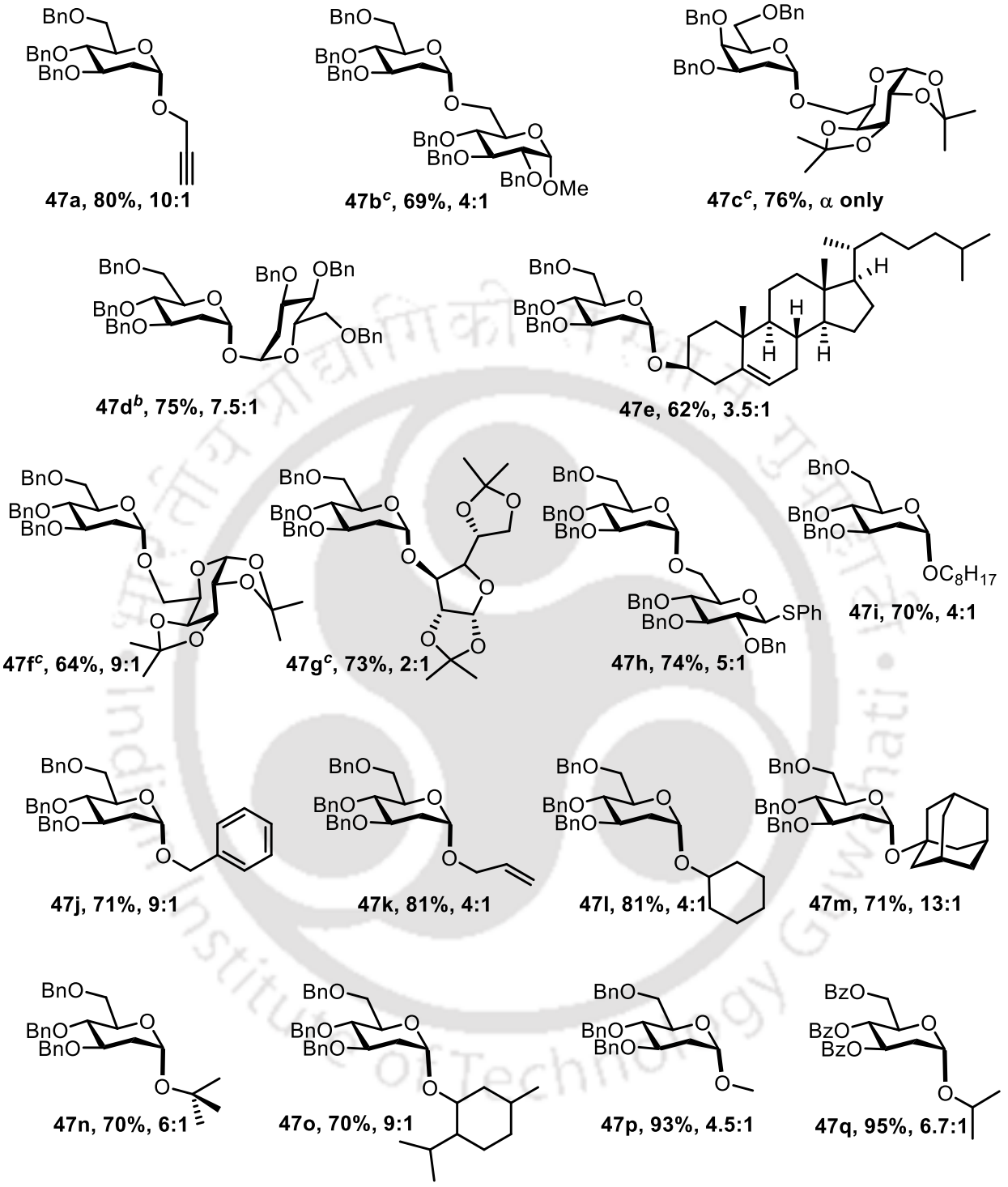
2.4 Scope of Various Derivatives with Different Glycosyl Donors and Acceptors:

In order to understand the scope of the newly developed iminium catalyzed glycosylation, the coupling reaction was performed with a variety of alcohols as acceptors. Again, commercially cheap, robust and easily accessible pyrrolidine hydrochloride **44d**, was chosen as the optimized catalyst to study the substrate scope. All the non-carbohydrate primary alcohols gave the desired glycosylation products with excellent yields and good to high levels of α-selectivities (**Scheme 14**). The sterically demanding cholesterol also gave corresponding glycoside **47e** in 62% yield and 3.5:1 α:β selectivity. The coupling with the tertiary 1-adamantanol also reacted well under the reaction conditions to provide the glycoside in 71% yield with high α-selectivity (13:1, α:β, **Scheme 14**). Both the primary alcohols derived from glucose and galactose were successfully coupled with 2-deoxy lactol **43b** in 69% and 64% yields respectively (**47b** and **47f** respectively). Noteworthy is the fact that these charged neutral amine catalysts did not hamper the stability of the acid-sensitive acetonide protecting group. Similarly, the secondary alcohol diacetonide glucose gave the coupled product **47g** in 73% yield, albeit with **44f** as the catalyst. However, when no acceptor is used, the armed 2-deoxy lactol **43b** in the presence of catalyst **44f** lead to the corresponding α→α-trehalose analogue **47d** as major diastereomer. More strikingly, the coupling reaction between the galacto-configured 2-deoxy lactol **43d** and the galactose derived diacetonide acceptor in the presence of pyrrolidine tosylate **44f** as the catalyst leading to a single diastereomer (only α) in 76% yield. Next, we decided to inspect the orthogonality of these organocatalytic conditions towards the conventional thioglycoside donors. To this end, we treated the donor **43b** under the standard reaction conditions with 6-hydroxythioglycoside **45h**. The coupling reaction proceeded with 74% yield and 5:1 α:β selectivity showing the potentiality of the current organocatalytic glycosylation as an orthogonal method.

Scheme 14: Scope of reactivity with different donors and acceptors.



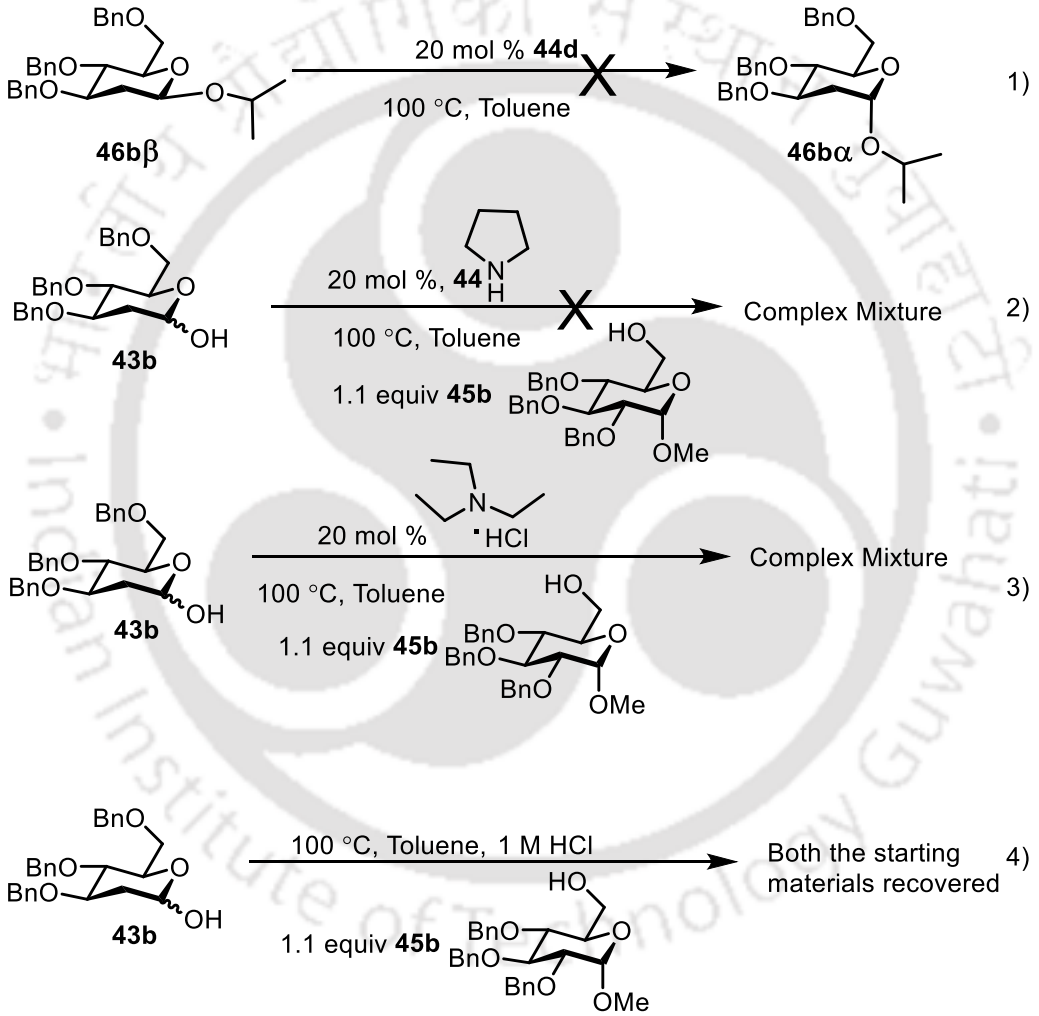
43b, 43d **47a-q**, α:β[a]



Reaction conditions: 0.12 mmol of glycosyl donor **43b**, **43d**, 0.13 mmol of **45b-c**, **45h**, (0.24 mmol of **45g**), and 20 mol % of **44d**, 100 °C, 5 h, (7 h for **47g**, and 16 h for **47d**). [a]Anomeric selectivities α:β ratios were determined from crude NMR analysis. [b]No acceptor was used. [c]20 mol % of **44f** was used for **47c**, **47d**, **47g**, and 0-10% dimerized product **47d** was found.

2.5 Control Experiments:

As depicted in the proposed mechanism (**Figure 1**), the reaction could proceed either via the formation of a cyclic aminal **IV** or a mixed aminoacetal **V**. Attempts to isolate or characterize the cyclic aminal **IV** or the iminium **III** only resulted in failure. A control experiment was performed with simple pyrrolidine **44** (**Scheme 15**, 2) instead of the corresponding salt. The reaction led to an intractable mixture of products, emphasizing the importance of ammonium



Scheme 15: Control experiments to establish the mechanism.

species in catalyzing the reaction. The reaction, when tested with 20 mol % of pyrrolidine benzoate **44g** (*vide supra*) as the catalyst, led to the decomposition of the starting material. However, the mass spectral analysis of the crude reaction mixture revealed the formation of glycosyl benzoate (**Table 1**, entry 10), which suggests the possible intermediacy of oxocarbenium ion in these

reactions. Other possible mechanisms involving the direct generation of oxocarbenium ions catalyzed by the weak Brønsted-acidity of pyrrolidinium species or by the possible release of HCl from secondary amine salts cannot be ruled out. To test this hypothesis, we elected to perform the glycosylation reaction in the presence of triethylamine hydrochloride salt (**Scheme-15**, 3) and 1 M HCl (**Scheme 15**, 4) that obviates the possibility of iminium species. However, the reaction in the former case resulted in an intractable mixture (**Scheme 15**, 3) whereas no reaction happened in the later. All these experiments strengthen the distinctive role of the secondary amine salts catalyzing the reaction. Besides, the anomerization experiment (**Scheme 15**, 1) confirmed the kinetic origins of the observed α-selectivities and thus, further strengthening the unique mode of activation by the secondary amine salts.

2.6 Mechanism and DFT Calculation:

DFT calculations were performed for the estimation of reaction barrier for the formation of cyclic aminal **IV** (intramolecular mechanism, Path A) and mixed aminoacetal **V** (intermolecular mechanism, Path B). Calculated energy profiles for these two paths are depicted in **Figure 2**.

The formation of **IVa** had a much lower reaction barrier (30.98 kcal/mol) compared to the formation of **V** (40.86 kcal/mol). Interatomic distances (O--H, C--N and C--O) in the transition states for **IV** are lower compared to the same for **V**, which probably facilitates the faster formation of **IV**. The stabilization gained by **IV** is around 3 kcal/mol higher compared to the stabilization gained by **V**. In addition, the reverse reaction is preferred for Path B, and the forward reaction is preferred for Path A. Thus, the existence of **V** is energetically not possible. We repeated these calculations at various DFT methods and basis sets and found that the level of the calculations does not affect the trend of the results, **Table S2**. DFT calculations clearly showed that Path A is preferred for the reaction.

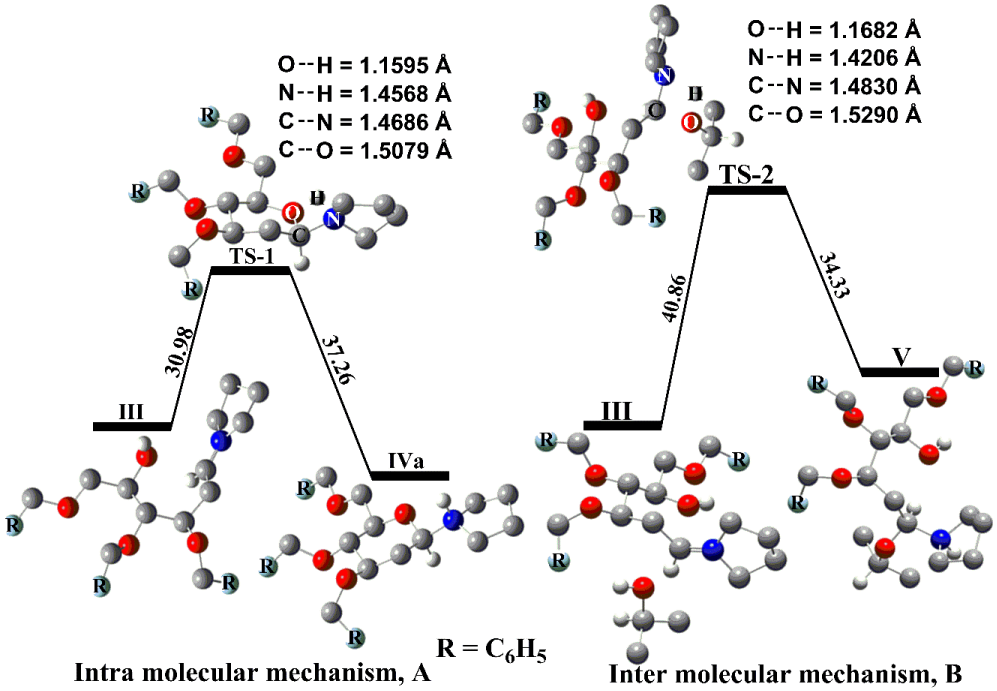
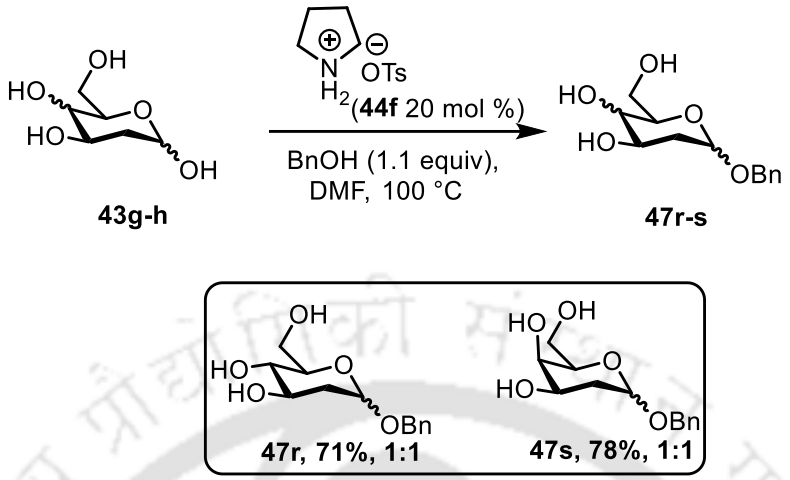


Figure 2: Optimized geometries, important interatomic distances in the transition states, and calculated energy profile for intramolecular mechanism 'A' and intermolecular mechanism 'B'. Energies (in kcal/mol) are obtained at the B3LYP/6-31G(d) level of theory. Only important hydrogen atoms are depicted, and 'C_6H_5' are depicted as 'R' in this figure for the clarity in representation (Please see Figure S1-S6 for detailed representation).

2.7 Glycosylation of Unprotected Sugars:

Unlike the general glycosylation methods that involve the usage of protection and deprotection strategy, glycosylation of unprotected and unactivated sugars avoiding the multistep sequence remains a challenge. The current literature reports for such a transformation either employ alcohol as a solvent (Fischer type glycosylations) under strongly acidic conditions or use ionic liquids as solvents in excess Lewis acidic conditions. Hence, an organocatalytic glycosylation of unprotected sugars would be a great advancement to the field. The secondary amine catalysis showcased in the current chapter also allowed us to convert the unprotected and unactivated native sugars into the corresponding glycosides in good yields (**Scheme 16**). The reaction of 2-deoxyglucose **43g** and 2-deoxygalactose **43h** react with benzyl alcohol in the

Scheme 16: Fischer type of glycosylation of unprotected sugars.



Reaction conditions: 0.122 mmol of **43g-h**, 2.44 mmol of benzyl alcohol, and 20 mol % of **44f**, 100 ºC, 5 h, DMF. Anomeric selectivities α:β ratios were determined from crude NMR analysis.

presence of 20 mol % of pyrrolidine tosylate **44f** in DMF as a solvent to provide the respective glycosides (**47r**, 71%, 1:1 α:β, and **47s**, 78%, 1:1 α:β).

2.8 Conclusion:

In conclusion, we have developed for the first time, an organocatalytic, α-selective direct dehydrative glycosylation method for the synthesis of various 2-deoxyglycosides. The role of secondary amine salts as a source of iminium ions and thereby generating oxocarbenium ions that react with alcohols in a stereoselective mode has been effectively utilized in the current protocol. The orthogonality of this protocol to thioglycosides besides the functional group tolerance has been well depicted. The method successfully gave glycosylated products with primary, secondary, and tertiary alcohols with equal efficiency. DFT calculations at various levels indicated that Path A is preferred. Interestingly, this dehydrative glucosylation can be extended towards unprotected native sugars.

2.9 Experimental Section:

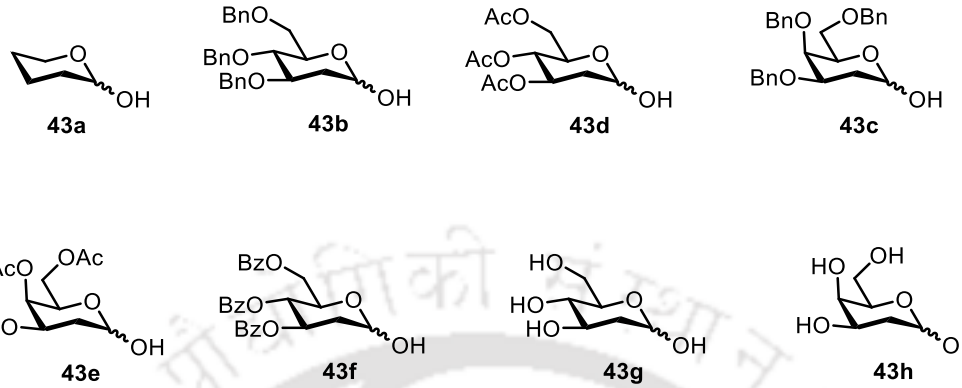
General Information

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

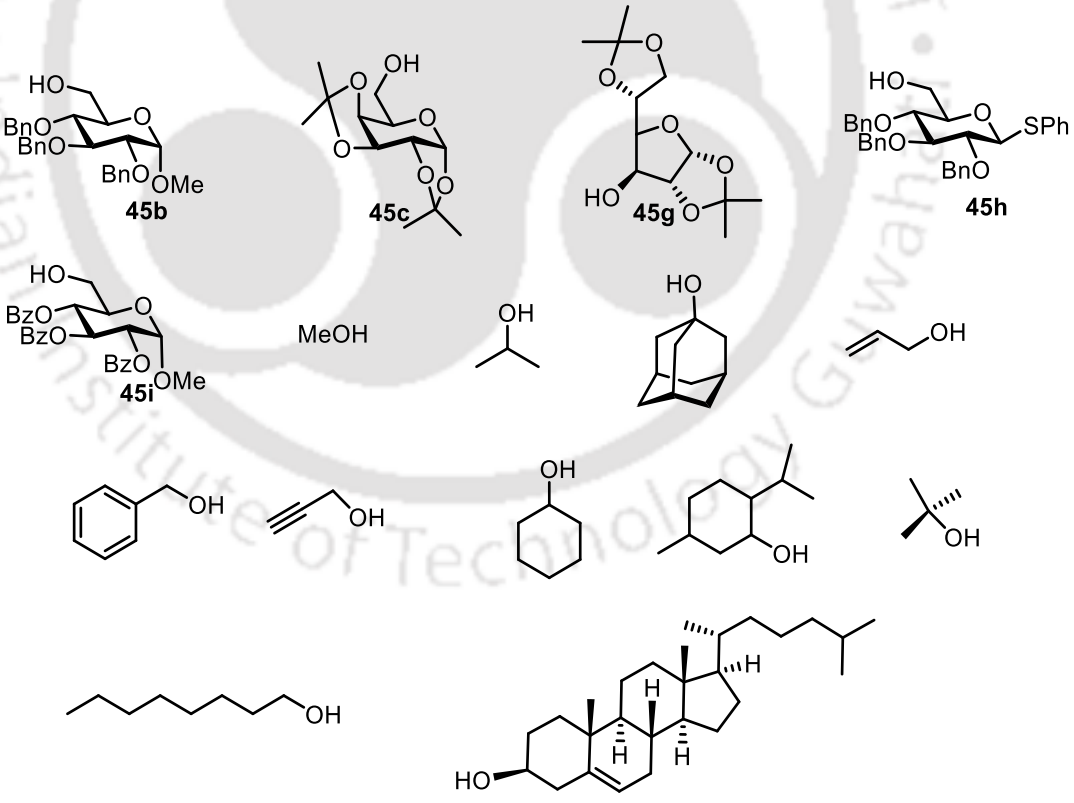
Analysis

Reactions 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 a Büchi rotary evaporator (bath temperatures up to 40 °C) at a pressure of either 15 mmHg (diaphragm pump) and 0.7 mmHg (oil pump), at rt. ^{1}H- and ^{13}C NMR were recorded on a Bruker 600 MHz and Varian 400 MHz spectrometer using $CDCl_3$, DMSO-d_6, C_6D_6 as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 for ^{1}H, δ 77.16 for ^{13}C), (DMSO-d_6: δ 2.58 for ^{1}H, δ 39.52 for ^{13}C), (C_6D_6: δ 7.16 for ^{1}H). Data are reported as follows: chemical shifts (δ), multiplicity (s = singlet, d = doublet, dd = double of doublet, ddd = double of double 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 performed using Agilent technologies mass spectrometer. The diastereomeric ratio calculated from crude NMR. Specific rotation was recorded in Rudolph research analytical polarimeter, the unit of the specific rotation is (deg·mL)/(g·dm), and concentration *c* is given in g/100 ml. Optical rotation values for **43a**, **43b**, **43c**, **43d**, **43e**, **43g**, **45b**, **45c**, **45g**, **45h**, and **45i** were matched with reported data.

Donors Used in this Study:



Acceptors Used in this Study:

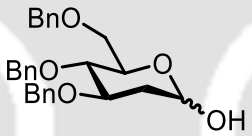


Synthesis of Glycosyl Donors

2-Hydroxytetrahydropyran (43a):

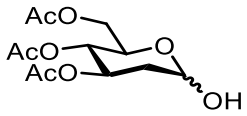
An aqueous solution of 0.2(N) HCI (30 ml) was added dropwise to a cooled solution of 2,3-dihydropyran (9.22 g, 109.600 mmol, 10 ml) under stirring condition. The mixture was stirred at 0 °C for 15 min and for 1 h at rt. It was then extracted with DCM (3x15 ml), and the combined organic layers were washed with saturated $NaHCO_3$ (100 ml), dried over Na_2SO_4 followed by evaporation of the solvent to get as a colourless oil **43a**. R_f- 0.1 (20% ethyl acetate in hexane), amount- 8.1g, yield- 72%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.84 (br s, 1H), 4.00 (m, 1H), 3.49 (m, 1H), 1.87 (m, 2H), 1.50 (m, 4H).[21]

3,4,6-Tri-*O*-benzyl-2-deoxy-α,β-D-glucopyranose (43b):



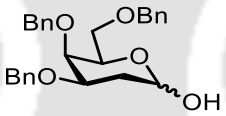
3,4,6-Tri-*O*-benzyl-D-glucal (100 mg, 0.240 mmol, 1.0 equiv) was dissolved in 2 ml of 90:10:1 THF: water: 8(M) HCl and was stirred for 24 h.[22] The reaction mixture was then concentrated and extracted with DCM (3x10 ml). The organic phase was washed with brine (40 ml), dried over anhydrous Na_2SO_4 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 **43b**. R_f- 0.3 (40% ethyl acetate in hexane), amount-82 mg, yield- 79%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.05 (m, 20H), 5.40 (d, *J* = 3.6 Hz, 1H), 4.89 (t, *J* = 10.3 Hz, 1H), 4.63 – 4.50 (m, 7H), 4.06 – 4.02 (m, 2H), 3.67 (d, 2H), 3.51 – 3.46 (m, 2H), 2.96 (s, 1H), 2.35 – 2.33 (m, 1H), 2.29 (dd, *J* = 12.8, 4.8 Hz, 1H), 1.71 – 1.67 (m, 1H). 1.57 (td, *J* = 12.0, 9.9 Hz, 1H). HRMS (ESI) $C_{27}H_{30}O_5NH_4$ $[M+NH_4]^+$- calculated- 452.2431; found- 452.2431.

3,4,6-Tri-*O*-acetate-2-deoxy-α,β-D-glucopyranose (43c):



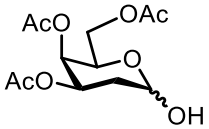
Tri-acetyl-D-glucal (200 mg, 0.730 mmol, 1.0 equiv) was dissolved in acetonitrile (5 ml), followed by addition of LiBr (196 mg, 2.260 mmol, 3.1 equiv) and water (240 µl, 13.330 mmol, 18.0 equiv) at 0 °C.[23] Then, Conc. HCl (10 µl) was added to the reaction mixture and was stirred for 4 h. After the completion of the reaction (as monitored by TLC analysis), it was quenched with saturated $NaHCO_3$ solution (10 ml). The reaction mixture was then evaporated under reduced pressure to remove the solvent, and the residue was extracted with DCM (3x15 ml), and the organic phase was dried over Na_2SO_4, concentrated and purified by column chromatography. The compound **43c** thus obtained was recrystallized in ethyl acetate →cyclohexane. R_f- 0.3 (20% Ethyl acetate in Hexane), amount- 120 mg, yield- 57%. HRMS (ESI) $C_{12}H_{18}O_8Na$ $[M+Na]^+$- calculated- 313.0894; found- 313.0894.

3,4,6-Tri-*O*-benzyl-2-deoxy-α,β-D-galactopyranose (43d):



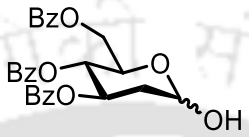
Procedure for the synthesis of **43d** with 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv) as the starting material. White solid. R_f- 0.3 (40% ethyl acetate in hexane), amount- 80 mg, yield- 77%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.23 (m, 26H), 5.36 (d, *J* = 2.1 Hz, 1H), 4.89 (d, *J* = 11.7 Hz, 1H), 4.58 – 4.53 (m, 7H), 4.44 – 4.32 (m, 3H), 4.09 – 4.06 (m, 1H), 3.95 – 3.92 (m, 1H), 3.58 – 3.54 (m, 1H), 3.37 – 3.33 (m, 1H), 2.14 (td, *J* = 12.4, 3.3 Hz, 1H), 1.94 (dd, *J* = 12.5, 4.5 Hz, 1H). HRMS (ESI) $C_{27}H_{30}O_5NH_4$ $[M+NH_4]^+$- calculated- 452.2431; found- 452.9046.

3,4,6-Tri-*O*-acetate-2-deoxy-α,β-D-galactopyranose (43e):



Procedure for the synthesis of **43e** with 3,4,6-tri-*O*-acetate-D-galactal (200 mg, 0.730 mmol, 1.0 equiv) as starting material to afford **43e** as white crystals. R_f- 0.3 (20% ethyl acetate in hexane), amount- 120 mg, yield- 57%. HRMS (ESI) $C_{12}H_{18}O_8Na$ $[M+Na]^+$- calculated- 313.0894; found- 313.1047.

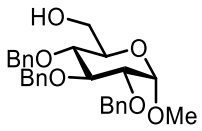
3,4,6-Tri-*O*-benzoyl-2-deoxy-α,β-D-glucopyranose (43f):



Procedure for the synthesis of **43c** with 3,4,6-tri-*O*-benzoyl-D-glucal (100 mg, 0.240 mmol, 1.0 equiv) as starting material and the reaction mixture was stirred for 4 days at 50 °C to give the product as a white solid **43f**. R_f- 0.3 (20% ethyl acetate in hexane), amount- 93 mg, yield- 82%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 – 7.93 (m, 7H), 7.52 – 7.33 (m, 12H), 5.84 – 5.80 (m, 1H), 5.65 (t, *J* = 9.6 Hz, 1H), 5.54 (d, *J* = 2.6 Hz, 1H), 4.63 (dd, *J* = 8.5, 4.2 Hz, 2H), 4.44 (dd, *J* = 12.9, 5.1 Hz, 1H), 3.68 (t, *J* = 6.4 Hz, 1H), 3.55 (t, *J* = 6.6 Hz, 1H), 2.68 – 2.65 (m, 1H), 2.55 (dd, *J* = 12.5, 5.3 Hz, 1H), 2.02 – 1.95 (m, 1H), 1.86 – 1.69 (m, 1H).^{13}C NMR (151 MHz, $CDCl_3$) δ 170.5, 166.5, 166.4, 166.0, 165.9, 165.8, 165.7, 165.6, 133.7, 133.5, 133.5, 133.4, 133.4, 133.2, 133.2, 133.2, 133.2, 130.2, 130.0, 129.9, 129.9, 129.8, 129.8, 129.8, 129.8, 129.8, 129.7, 129.7, 129.5, 129.4, 129.3, 129.3, 129.2, 128.6, 128.5, 128.5, 128.5, 99.7, 97.1, 94.2, 91.9, 72.4, 72.2, 71.6, 71.5, 70.5, 70.4, 70.3, 70.2, 70.0, 69.9, 68.8, 68.4, 67.1, 63.8, 63.7, 63.6, 63.6, 63.5, 62.1, 45.0, 44.9, 44.9, 44.6, 37.9, 36.5, 35.6, 35.4, 30.0, 29.8, 29.5, 29.3, 29.2, 29.1, 27.0, 27.0, 26.1, 21.0. HRMS (ESI) $C_{27}H_{24}O_8NH_4$ $[M+NH_4]^+$- calculated- 494.1809; found- 494.1826, HRMS (ESI) $C_{27}H_{24}O_8NH_4$ $[M+Na]^+$- calculated- 499.1363; found- 499.1366. $[\alpha]_D^{22}$ = +24 (*c* 1.7, $CHCl_3$).

Synthesis of Glycosyl Acceptors

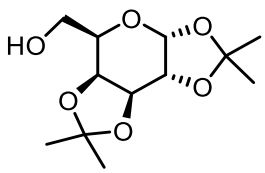
Methyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (45b):



A solution of methyl-α-D-glucopyranoside (6.0 g, 0.03 mol, 1.0 equiv), trityl chloride (11 g, 0.036 mol, 1.2 equiv), triethylamine (8 mL), and DMAP (2 g, 0.015 mol, 0.5 equiv) in DMF (50 ml) was

stirred overnight at rt under nitrogen. After 12 h stirring, the reaction mixture was poured into ice-water (70 ml) and extracted with DCM (3x100 ml). The organic phase was washed with water (150 ml), dried over Na_2SO_4 and purified by column chromatography to obtain yellowish viscous liquid **(I)**. R_f- 0.5 (100% ethyl acetate), amount- 2.1 g, yield- 50%. To a solution of methyl-6-O-trityl-α-D-glucopyranoside **(I)** (2.1 g, 0.005 mol, 1.0 equiv) in DMF (20 ml) at 0 °C NaH was added (0.866 g, 0.023 mol, 4.5 equiv considering 60% in mineral oil). After 30 min, BnBr (2.55 ml, 0.023 mol, 4.5 equiv) was added, and the reaction mixture was stirred overnight at rt. The reaction was then quenched with MeOH (5 ml), and it was extracted with DCM (3x30 ml). The organic extract was washed with brine (100 ml), dried over Na_2SO_4. After removal of the solvents, the residue was purified by column chromatography (5% ethyl acetate in hexane) to afford the compound methyl-2,3,4 tri-O-benzyl-6-O-trityl-α-D-glucopyranoside **(II)** as a white solid (2.3 g, 68%). 1.52 g of methyl-2,3,4 tri-O-benzyl-6-O-trityl-α-D-glucopyranoside was stirred in (80 ml) mixture of acetic acid:water = 9:1 at reflux for 5 h at 90 °C. After 5 h the reaction mixture was extracted with DCM (3x150 ml), then the organic layer was washed with water (170 ml) and saturated $NaHCO_3$ solution (170 ml), dried over Na_2SO_4 and evaporated under reduced pressure to purify in column chromatography to get colourless viscous liquid methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **45b**. R_f- 0.5 (50% ethyl acetate in hexane), amount- 500 mg, yield- 51%.[24] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.23 (m, 15H), 4.99 (d, *J* = 10.9 Hz, 1H), 4.88 (d, *J* = 11.0 Hz, 1H), 4.85 – 4.79 (m, 2H), 4.65 (dd, *J* = 13.7, 11.6 Hz, 2H), 4.57 (d, *J* = 3.5 Hz, 1H), 4.01 (t, *J* = 9.3 Hz, 1H), 3.77 (dd, *J* = 11.8, 2.7 Hz, 1H), 3.70 – 3.68 (m, 1H), 3.66 – 3.63 (m, 1H), 3.54 – 3.49 (m, 2H), 3.36 (s, 3H). HRMS (ESI) $C_{28}H_{32}O_6Na$ $[M+NH_4]^+$- calculated- 482.2537; found- 482.2536. HRMS (ESI) $C_{28}H_{32}O_6Na$ $[M+Na]^+$- calculated- 487.2091; found- 487.2087. HRMS (ESI) $C_{28}H_{32}O_6K$ $[M+K]^+$- calculated- 503.1830; found- 503.1840.

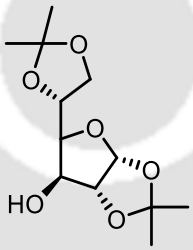
1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (45c):



Anhydrous $ZnCl_2$ (1.25 g, 0.009 mol) and dry acetone (3 g, 0.044 mmol, 3.3 ml) were taken in round bottom flask and stirred under argon. Then to it, conc. H_2SO_4 (20 µl) and D-galactose (300

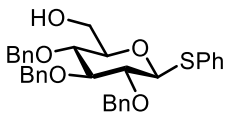
mg, 1.670 mmol, 1.0 equiv) were added and stirred under argon for 24 h.[25] Then it was quenched with Na_2CO_3 solution (10 ml) and filtered. The filtrate was concentrated under reduced pressure to remove excess acetone and extracted with DCM (3x15 ml) and then concentrated under reduced pressure to get colourless viscous liquid **45c**. R_f- 0.5 (20% ethyl acetate in hexane), amount- 150 mg, yield- 50%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.57 (d, *J* = 5.0 Hz, 1H), 4.62 (dd, *J* = 7.9, 2.3 Hz, 1H), 4.34 (dd, *J* = 5.0, 2.4 Hz, 1H), 4.28 (d, *J* = 7.9 Hz, 1H), 3.88 – 3.84 (m, 2H), 3.78 – 3.74 (m, 1H), 2.29 (br s, 1H), 1.54 (s, 3H), 1.46 (s, 3H), 1.34 (s, 6H).[26] HRMS (ESI) $C_{12}H_{20}O_6NH_4$ $[M+NH_4]^+$- calculated- 278.1598; found- 278.1596, HRMS (ESI) $C_{12}H_{20}O_6NH_4$ $[M+Na]^+$- calculated- 283.1152; found- 283.1149.

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose (45g):



D-glucose (1 g, 0.006 mol, 1.0 equiv) was taken in acetone (20 ml) and allowed to stir under ice bath.[25] Then, 0.8 ml of conc.H_2SO_4 was added dropwise and the reaction mixture was stirred under argon at rt. After 24 h, the reaction mixture was neutralized with aq. NaOH solution (25 ml) and filtered. The filtrate was concentrated and extracted with DCM (3x20 ml), the organic layer was washed with water (70 ml), then saturated $NaHCO_3$ solution (70 ml) and finally with brine (70 ml). The combined organic layer was concentrated under reduced pressure and purified by column chromatography to get white solid **45g**. R_f- 0.5 (20% ethyl acetate in hexane), amount- 781 mg, yield- 50%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.90 (d, *J* = 3.6 Hz, 1H), 4.49 (d, *J* = 3.6 Hz, 1H), 4.31 – 4.29 (m, 1H), 4.13 (dd, *J* = 8.6, 6.2 Hz, 1H), 4.02 (dd, *J* = 8.0, 2.8 Hz,1H), 3.97 (dd, *J* = 8.7, 5.2 Hz, 1H), 3.04 (s, 1H), 1.46 (s, 3H), 1.41 (s, 3H), 1.33 (s, 3H), 1.28 (s, 3H).[24] HRMS (ESI) $C_{12}H_{20}O_6Na$ $[M+Na]^+$- calculated- 283.1152; found- 283.1119.

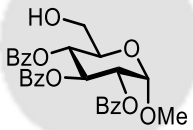
Phenyl-2,3,4-tri-*O*-benzyl-β-D-thioglucopyranoside (45h):



Penta-*O*-acetyl-D-glucpopyranoside (4 g, 0.010 mol, 1.0 equiv) was dissolved in anhydrous DCM (10 ml) and stirred under argon. Then, thiophenol (1.65 g, 1.50 ml, 0.015 mol, 1.5 equiv) was added dropwise. After addition, the reaction mixture was allowed to cool 0 °C and $BF_3.Et_2O$ (3.55 g, 3.2 ml, 0.025 mol, 2.5 equiv) was added dropwise to it. Then, it was allowed to stir at rt. After 24 h, it was treated with saturated aqueous $NaHCO_3$ solution (15 ml) and extracted with DCM (3x20 ml). Then, the organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to purify in column chromatography to get phenyl-2,3,4,6-tetra-*O*-acetyl-β-D-thioglucopyranoside **(I)** as a white solid. R_f- 0.4 (10% ethyl acetate in hexane), amount- 4.14 g, yield- 92%.[21] Then, the compound **(I)** (2.4 g, 0.005 mol, 1.0 equiv) was dissolved in MeOH (64 ml) and kept in an ice bath. Then, Sodium (0.54 g, 0.023 mol, 4.3 equiv) was added to it in stirring condition and stirred for 20 min after which the solvents were removed under reduced pressure to afford the deacetylated thioglycoside **(II)** as a white solid. R_f- 0.1 (10% MeOH in DCM), amount- 1.27 g, yield- 93%.[21] Deacetylated thioglycoside **(II)** (500 mg, 1.840 mmol, 1.0 equiv) was dissolved in pyridine (15 ml) and cooled to 0 °C. After that, DMAP (5 mg, 0.040 mmol, 0.02 equiv) was added followed by addition of TBDMS-Cl (332 mg, 2.200 mmol, 1.2 equiv) and stirred at rt under nitrogen. After 2 h, 5 ml of Et_3N was added to it and stirred for 24 h until the full conversion of starting material. Then, it was extracted with DCM (3x20 ml) and washed with 1(N) HCl solution (80 ml). Then, the organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to purify in column chromatography to get 6-*O*-TBDMS-2,3,4-trihydroxy thioglycoside **(III)** as a colourless liquid. R_f- 0.8 (100% ethyl acetate), amount- 496 mg, yield- 70%.[28] The thioglycoside **(III)** (700 mg, 1.810 mmol, 1.0 equiv) was then dissolved in anhydrous DMF (10 ml) cooled to 0 °C, NaH (174 mg, 7.240 mmol, 4.0 equiv considering 60% in mineral oil) was added and the solution was then stirred at rt for 30 min after which the reaction mixture was cooled back to 0 °C and BnBr (1.1 g, 760 µl, 6.340 mmol, 3.5 equiv) was added dropwise. The solution was then stirred at rt for 16 h, at which time MeOH (5 ml) was added, and the solution was concentrated *in vacuo*. The residue was dissolved in DCM (3x20 ml), washed with water (70 ml), brine (70 ml), dried over Na_2SO_4, filtered and concentrated under reduced pressure to purify in column chromatography to afford 6-*O*-TBDMS-2,3,4-*O*-benzyl thioglycoside **(IV)** as a liquid. R_f- 0.9 (50% ethyl acetate in hexane), amount- 1.1 g, yield- 86%.[29] The 6-*O*-TBDMS-2,3,4-*O*-benzyl thioglycoside **(IV)** (1 g, 0.002 mol, 1 equiv) was then dissolved in a 1M THF solution of TBAF (26 mL) and stirred for 2 h at rt, after which the reaction was diluted with DCM (50 ml) and washed with water (100 ml),

brine (100 ml), dried over Na_2SO_4 and concentrated *in vacuo* followed by purification in column chromatography to afford phenyl-2,3,4-tri-*O*-benzyl-β-D-thioglucopyranoside **45h** as a yellowish white solid. R_f- 0.6 (20% Ethyl acetate in hexane), amount- 520 mg, yield- 48%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53 – 7.50 (m, 2H), 7.40 – 7.38 (m, 2H), 7.35 – 7.28 (m, 16H), 4.91 (dd, *J* = 10.5, 2.9 Hz, 2H), 4.86 (dd, *J* = 10.9, 8.4 Hz, 2H), 4.77 (d, *J* = 10.2 Hz, 1H), 4.72 (d, *J* = 9.8 Hz, 1H), 4.65 (d, *J* = 10.9 Hz, 1H), 3.88 (dd, *J* = 12.0, 2.6 Hz, 1H), 3.76 – 3.67 (m, 2H), 3.58 (t, *J* = 9.5 Hz, 1H), 3.49 (dd, *J* = 9.6, 8.9 Hz, 1H), 3.39 (ddd, *J* = 9.8, 4.9, 2.7 Hz, 1H), 1.85 (s, 1H).[29] HRMS (ESI) $C_{33}H_{34}O_5SNH_4$ $[M+NH_4]^+$- calculated- 560.2465; found- 560.2443.

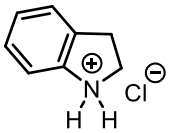
Methyl-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (45i):



Methyl α-D-glucopyranoside (500 mg, 2.570 mmol, 1.0 equiv) was dissolved in pyridine (15 ml) under a N_2 atmosphere. Imidazole (350 mg, 5.140 mmol, 2.0 equiv) and TIPSCl (0.6 mL, 4.700 mmol, 1.8 equiv) were added and the solution was then stirred at rt. After 16 h, BzCl (2.4 ml, 21.000 mmol) was added and the reaction was stirred for 24 h and it was quenched with MeOH (1 ml). The solution was diluted with DCM (3x30 ml), washed with 1M HCl (100 ml), saturated $NaHCO_3$ solution (100 ml), water (100 ml), dried over Na_2SO_4 and concentrated under reduced pressure to afford methyl-2,3,4- tri-*O*-benzoyl-6-*O*-TIPS-α-D-glucopyranoside **(I)**. The **(I)** residue was dissolved in a solution of THF (8 ml), H_2O (3 ml) and TFA (4 ml) and stirred at rt for 18 h after which the solution was concentrated *in vacuo* by azeotroping with toluene followed by purification in column chromatography to afford methyl-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside **45i** as a viscous colourless liquid. R_f- 0.4 (20% ethyl acetate in hexane), amount- 960 mg, yield- 74%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 8.8, 7.4 Hz, 4H), 7.87 (dd, *J* = 13.9, 12.6 Hz, 2H), 7.56 – 7.49 (m, 2H), 7.45 – 7.35 (m, 5H), 7.29 (t, *J* = 7.9 Hz, 2H), 6.23 (t, *J* = 9.7 Hz, 1H), 5.50 (t, *J* = 9.9 Hz, 1H), 5.28 (dt, *J* = 9.0, 3.7 Hz, 2H), 4.06 – 4.00 (m, 1H), 3.83 (dd, *J* = 13.1, 2.0 Hz, 1H), 3.74 (dd, *J* = 13.1, 3.6 Hz, 1H), 3.47 (s, 3H).[29]

Synthesis of Catalysts

Indoline hydrochloride salt (44b):

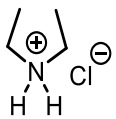


To a solution of indole (250 mg, 2.100 mmol, 1.0 equiv) in acetic acid (20 ml), was added $NaBH_3CN$ (634 mg, 10.000 mmol, 4.8 equiv) in portions and was stirred at rt. Then, the reaction mixture treated with saturated NaOH solution and extracted with DCM (3x30 ml). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure by rotary evaporator and purified by column chromatography in (hexane/ethyl acetate) to afford indoline as pale yellowish oil. R_f– 0.2 (10% ethyl acetate in hexane), amount- 150 mg, yield- 60%.[30] Indoline was dissolved in 4(N) HCl in methanol (5 ml) and white fumes was immediately generated. Then, the solution was stirred at rt under argon.[18] After stirring it for 30 min, the solvent was evaporated under reduced pressure, and the residue was washed with ether (3x5 ml) to afford yellowish solid **44b**. Amount- 250 mg, yield- 96%. ^{1}H NMR (600 MHz, DMSO) δ 11.60 (br s, 2H), 7.47 (d, *J* = 7.1 Hz, 1H), 7.44 – 7.39 (m, 2H), 7.39 – 7.35 (m, 1H), 3.69 (t, *J* = 7.9 Hz, 2H), 3.19 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (151 MHz, DMSO) δ 136.6, 135.6, 129.1, 128.0, 126.0, 119.5, 48.6, 44.7.

Procedure for the Synthesis of 44c and 44d:

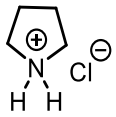
2 ml of acetyl chloride was added dropwise to 2 ml of methanol in an ice bath under argon.[31] After few min, ether (1 ml) solution of secondary amine [(**44c**, 8.220 mmol, 850 µl) and (**44d**, 8.450 mmol, 690 µl)] was added dropwise to it which readily resulted in a turbid solution and the reaction mixture was stirred at 0 °C under argon for 1 h. The solution was then concentrated to get a white solid (**44c** or **44d**). The solid was washed with ether (3x5 ml).

Diethylamine hydrochloride salt (44c):



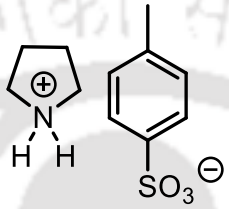
Yield- 93%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.45 (s, 2H), 3.01 (dd, *J* = 12.5, 7.0 Hz, 4H), 1.45 (t, *J* = 7.3 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 42.4, 11.3.

Pyrrolidinium hydrochloride salt (44d):



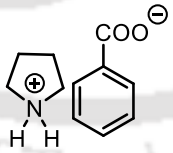
Yield- 99%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.48 (s, 2H), 3.26 (s, 4H), 1.96 (s, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 45.1, 24.4.

Pyrrolidinium tosylate salt (44f):



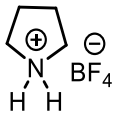
para-toluene sulphonic acid (1.3 g, 7.030 mmol, 1.0 equiv) was dissolved in 10 ml of DCM:MeOH (5:1) and stirred in ice bath, then ether (1 ml) solution of pyrrolidine (500 mg, 582 µl, 7.030 mmol, 1.0 equiv) was added dropwise to it, and it was stirred at 0 °C under argon. Then, after 1 h, it was concentrated under reduced pressure to get solid. It was washed with ether (3x5 ml) to afford the yellowish solid **44f**. Amount- 1.69 g, yield- 99%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.74 (s, 2H), 7.71 (t, *J* = 8.3 Hz, 2H), 7.18 (t, *J* = 8.6 Hz, 2H), 3.25 (d, *J* = 5.5 Hz, 4H), 2.35 (s, 3H), 1.87 (dd, *J* = 14.3, 7.2 Hz, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 141.5, 140.7, 129.1, 125.8, 45.6, 24.2, 21.4.

Pyrrolidinium benzoate salt (44g):



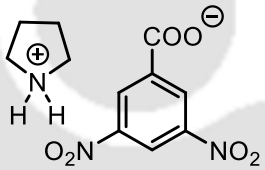
Procedure for the synthesis of **44g** was similar procedure of **44f** by taking benzoic acid (1.7 g, 14.060 mmol, 1.0 equiv) to get white solid **44g**. Amount- 1.3 g, yield- 96%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.2 Hz, 2H), 7.47 (t, *J* = 7.3 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 2H), 3.31 (t, *J* = 7.1 Hz, 4H), 2.02 – 1.91 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.8, 134.5, 131.6, 129.7, 128.2, 45.0, 24.6.

Pyrrolidinium tetrafluoroborate salt (44h):



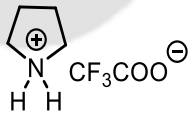
Tetrafluoroboric acid (679 mg, 7.730 mmol, 1.0 equiv) was dissolved in 5 ml of DCM and stirred in an ice bath, then pyrrolidine (500 mg, 582 µl, 7.030 mmol, 1.0 equiv) in ether solution was added dropwise to it, and it was stirred at 0 °C under argon. Then, after 1 h, it was concentrated under reduced pressure to get solid. It was washed with ether (3x5 ml) to afford yellowish white solid **44h**. Amount- 986 mg, yield- 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (s, 2H), 3.30 (s, 4H), 2.00 (s, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 46.7, 23.8.

Pyrrolidinium 3,5-dinitrobenzoate salt (44i):



Procedure for the synthesis of **44i** was similar procedure of **44f** by taking 3,5-dinitrobenzoic acid (597 mg, 2.800 mmol, 1.0 equiv) to get yellowish crystalline solid **44i**. Amount- 1.7 g, yield- 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (d, *J* = 8.3 Hz, 3H), 3.36 (s, 4H), 2.10 (s, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.5, 148.4, 141.6, 129.4, 120.2, 45.2, 24.7.

Pyrrolidinium trifluoroacetate salt (44j):



Procedure for the synthesis of **44j** was a similar procedure of **44f** by taking trifluoroacetic acid (881 mg, 7.730 mmol, 1.0 equiv) to get yellowish liquid **44j**. Amount- 1.06 g, yield- 82%.

General Procedure for Glycosylation Reactions

General Procedure A:

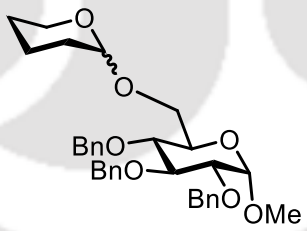
Glycosyl donor (0.980 - 1.220 mmol, 1.0 equiv) was taken in round-bottomed flask, fitted with a reflux condenser and dissolved in 0.5 ml (for 0.980 mmol) of toluene/DMF. Then, pyrrolidinium hydrochloride catalyst was dissolved in 0.5 ml (for 0.980 mmol) of toluene/DMF, and this solution was added to donor solution dropwise slowly to make a homogenous solution. After this, glycosyl

acceptor (1.1 - 2.0 equiv) was added dropwise or pinchwise slowly to it, and it was shaken manually to make a clear solution. Then, this solution was flushed by argon, and it was closed, heated at 80 - 150 °C for 5 - 24 h. After cooling it to rt, the reaction mixture was quenched by water (1 ml for 0.980 mmol), and it was extracted with DCM (3x15 ml for 0.980 mmol), dried over Na_2SO_4 and concentrated by rotary evaporator and purified by column chromatography in hexane/ethyl acetate.

General Procedure B:

Glycosyl donor (0.980 – 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride/pyrrolidinium tosylate catalyst and glycosyl acceptor (1.1 - 2.0 equiv) were taken in a sealed tube and dissolved in 1 ml (for 0.980 mmol) of DCM. Then, this solution was flushed by argon, and it was closed, heated at 80 - 100 °C for 5 - 24 h. After cooling it to rt, the reaction mixture was quenched by water (1 ml for 0.980 mmol), and it was extracted with DCM (3x15 ml for 0.980 mmol), dried over Na_2SO_4 and concentrated by rotary evaporator and purified by column chromatography in hexane/ethyl acetate.

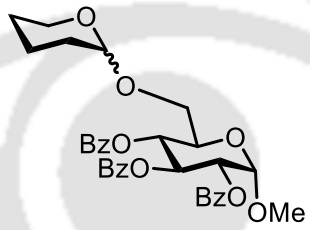
Methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranosidetetrahydropyran (46a-2):



General procedure **A** was followed by adding glycosyl donor **43a** (100 mg, 0.980 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor **45b** (500 mg, 1.080 mmol, 1.1 equiv) at 100 °C for 5 h to get product **46a-2** as a white solid. R_f-0.4 (20% ethyl acetate in hexane), amount- 380 mg, yield- 71%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.21 (m, 30H), 4.97 (t, *J* = 10.6 Hz, 2H), 4.95 – 4.77 (m, 8H), 4.76 – 4.54 (m, 8H), 4.53 – 4.46 (m, 2H), 4.07 – 3.94 (m, 4H), 3.87 – 3.81 (m, 2H), 3.79 – 3.70 (m, 2H), 3.63 (d, *J* = 9.2 Hz, 2H), 3.56 (tdd, *J* = 10.3, 7.5, 3.8 Hz, 4H), 3.51 – 3.44 (m, 2H), 3.41 – 3.33 (m, 6H), 1.86 – 1.42 (m, 12H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9, 138.8, 138.6, 138.5, 138.3, 138.3, 138.2, 130.1,

130.0, 129.9, 128.6, 128.6, 128.6, 128.5, 128.5, 128.3, 128.2, 128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 99.5, 99.3, 98.3, 98.2, 98.1, 82.3, 82.1, 80.1, 78.0, 77.9, 77.5, 75.9, 75.9, 75.2, 75.1, 73.6, 73.5, 70.8, 70.2, 70.1, 66.3, 65.9, 62.7, 62.6, 62.0, 55.3, 55.2, 55.2, 31.1, 30.7, 30.7, 25.5, 25.4, 19.8. HRMS (ESI) $C_{33}H_{40}O_7NH_4$ $[M+NH_4]^+$- calculated- 566.3112; found- 566.3034. $[\alpha]_D^{22}$ = +8 (*c* 0.4, $CHCl_3$).

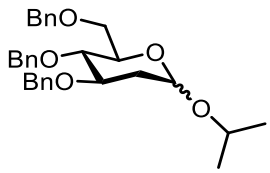
Methyl 2,3,4-tri-*O*-benzoyl-α-D-glucopyranosidetetrahydropyran (46a-3):



General procedure **A** was followed by adding glycosyl donor **43a** (100 mg, 0.980 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor **45i** (550 mg, 1.080 mmol, 1.1 equiv) at 100 °C for 5 h to get product **46a-3** as a white solid. R_f- 0.6 (20% ethyl acetate in hexane), amount- 430 mg, yield- 74%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 – 7.27 (m, 30H), 6.23 (t, *J* = 9.8 Hz, 1H), 6.13 (tt, *J* = 14.9, 7.4 Hz, 1H), 5.67 (t, *J* = 9.9 Hz, 1H), 5.61 (t, *J* = 9.9 Hz, 1H), 5.54 – 5.45 (m, 1H), 5.35 – 5.18 (m, 4H), 4.69 – 4.63 (m, 1H), 4.59 – 4.53 (m, 1H), 4.29 – 4.19 (m, 1H), 4.08 – 4.00 (m, 1H), 3.98 – 3.91 (m, 1H), 3.86 – 3.82 (m, 1H), 3.79 – 3.71 (m, 1H), 3.71 – 3.66 (m, 1H), 3.61 (ddd, *J* = 12.3, 10.5, 7.6 Hz, 1H), 3.50 – 3.43 (m, 6H), 3.40 – 3.31 (m, 1H), 1.90 – 1.34 (m, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.6, 166.0, 166.0, 166.0, 166.0, 166.0, 165.4, 165.4, 133.9, 133.5, 133.5, 133.4, 133.3, 133.2, 133.2, 130.1, 130.1, 130.0, 129.9, 129.9, 129.8, 129.8, 129.8, 129.5, 129.4, 129.3, 129.3, 129.2, 129.2, 128.7, 128.7, 128.6, 128.5, 128.5, 128.4, 128.4, 99.8, 98.4, 97.3, 97.1, 97.0, 72.3, 72.3, 72.2, 70.9, 70.8, 70.2, 69.9, 69.8, 69.7, 69.6, 69.2, 68.6, 66.3, 65.7, 62.4, 61.6, 61.2, 55.8, 55.6, 55.6, 30.5, 30.3, 29.8, 25.5, 25.5, 19.5, 18.9. HRMS (ESI) $C_{33}H_{34}O_{10}NH_4$ $[M+NH_4]^+$- calculated- 608.2490; found- 608.2422. $[\alpha]_D^{22}$= +20 (*c* 0.4, $CHCl_3$).

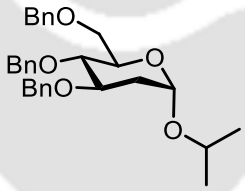
Scope of Derivatives in Glycosylation Reactions

Isopropyl-3,4,6-tri-*O*-benzyl-2-deoxy-α,β-D-glucopyranoside (46b):



General procedure **B** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor isopropanol (11 mg, 14 µl, 0.180 mmol, 1.5 equiv) at 100 °C for 5 h to get product **46b** as a colourless liquid. R_f- 0.9 (20% ethyl acetate in hexane), amount- 50 mg, yield- 87%. HRMS (ESI) $C_{30}H_{36}O_5NH_4$ $[M+NH_4]^+$- calculated- 494.2901; found- 494.2901.

Isopropyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (46bα)

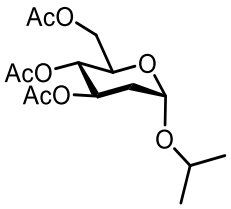


^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 – 7.12 (m, 15H), 5.08 (d, *J* = 2.8 Hz, 1H), 4.96 – 4.84 (m, 1H), 4.66 (qd, *J* = 11.7, 5.8 Hz, 4H), 4.55 – 4.46 (m, 3H), 4.01 (ddd, *J* = 11.5, 8.9, 5.1 Hz, 1H), 3.92 – 3.85 (m, 1H), 3.67 – 3.60 (m, 2H), 2.24 (dd, 1H), 1.75 (td, 1H), 1.16 (d, *J* = 6.3 Hz, 3H), 1.11 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9, 138.6, 138.5, 138.3, 128.5, 128.1, 128.0, 127.8, 127.7, 127.7, 127.6, 95.1, 78.5, 78.0, 75.2, 73.5, 71.9, 70.7, 70.2, 69.0, 68.2, 36.0, 23.4, 21.3.[32] $[\alpha]_D^{22}$= +43 (*c* 2.3, $CHCl_3$). Amount- 41 mg, yield- 71%.

Isopropyl-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranoside (46bβ)

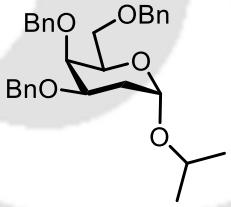
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 15H), 4.90 (d, *J* = 10.8 Hz, 1H), 4.68 (t, *J* = 7.4 Hz, 1H), 4.63 – 4.51 (m, 5H), 4.01 (dt, *J* = 12.4, 6.0 Hz, 1H), 3.78 – 3.73 (m, 1H), 3.71 – 3.60 (m, 2H), 3.52 – 3.44 (m, 1H), 3.41 (ddd, *J* = 9.6, 5.2, 1.9 Hz, 1H), 2.30 (dd, 1H), 1.65 (q, 1H), 1.26 (d, *J* = 6.3 Hz, 3H), 1.15 (d, *J* = 6.0 Hz, 3H).[33] $[\alpha]_D^{22}$= +45 (*c* 2.3, $CHCl_3$). Amount- 9 mg, yield- 16%.

Isopropyl-3,4,6-tri-*O*-acetate-2-deoxy-α-D-glucopyranoside (46c):



General procedure **B** was followed by adding glycosyl donor **43c** (50 mg, 0.170 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (4 mg, 0.034 mmol, 20 mol %) and the glycosyl acceptor isopropanol (16 mg, 20 µl, 0.260 mmol, 1.5 equiv) at 100 °C for 24 h to get product as a colourless liquid **46c**. R_f- 0.5 (20% ethyl acetate in hexane), amount- 46 mg, yield- 81%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.34 (ddd, *J* = 12.4, 10.8, 7.1 Hz, 1H), 5.07 (d, *J* = 3.3 Hz, 1H), 5.01 – 4.97 (m, 1H), 4.30 (dt, *J* = 5.0, 3.8 Hz, 1H), 4.04 (ddd, *J* = 6.7, 5.3, 3.0 Hz, 2H), 3.86 (dq, *J* = 12.5, 6.3 Hz, 1H), 2.17 (dd, 1H), 2.09 (s, 3H), 2.05 (s, 3H), 2.01 (s, 3H), 1.83 (td, 1H), 1.21 (d, *J* = 6.1 Hz, 3H), 1.15 (d, *J* = 5.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 170.4, 170.1, 95.1, 69.8, 69.6, 69.4, 67.9, 62.6, 35.7, 23.4, 21.6, 21.2, 20.9.[23] HRMS (ESI) $[M+NH_4]^+$- calculated- 350.1809; found- 350.1810. HRMS (ESI) $C_{15}H_{24}O_8NH_4$ $[M+Na]^+$- calculated- 355.1363; found- 355.1363. $[\alpha]_D^{22}$= +20 (*c* 0.4, $CHCl_3$).

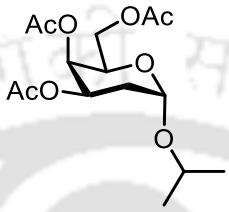
Isopropyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranoside (46d):



General procedure **B** was followed by adding glycosyl donor **43d** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor isopropanol (11 mg, 14 µl, 0.180 mmol, 1.5 equiv) at 100 °C for 5 h to get product as a colourless liquid **46d**. R_f- 0.9 (20% ethyl acetate in hexane), amount- 46 mg, yield- 85%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 – 7.10 (m, 15H), 5.09 (d, *J* = 3.3 Hz, 1H), 4.95 – 4.92 (m, 1H), 4.67 – 4.57 (m, 3H), 4.50 (d, *J* = 11.7 Hz, 1H), 4.44 (dd, *J* = 11.4, 9.2 Hz, 1H), 3.95 (dt, *J* = 12.9, 6.4 Hz, 3H), 3.87 (dq, *J* = 11.8, 5.9 Hz, 1H), 3.64 – 3.59 (m, 1H), 3.58 – 3.53 (m, 1H), 2.24 (td, 1H), 1.94 (dd, 1H), 1.17 (d, *J* = 6.3 Hz, 3H), 1.12 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.1, 139.0, 139.0,

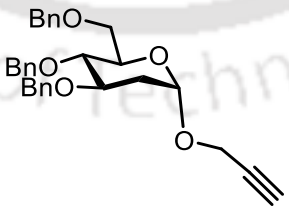
139.0, 138.8, 138.7, 138.6, 138.3, 138.2, 138.2, 128.5, 128.3, 127.8, 127.8, 127.6, 127.4, 127.3, 95.7, 75.2, 74.4, 73.6, 73.2, 70.6, 69.8, 69.7, 68.4, 31.8, 29.8, 23.5, 21.5.[32] HRMS (ESI) $C_{30}H_{36}O_5NH_4$ $[M+NH_4]^+$- calculated- 494.2901; found- 494.2923. $[\alpha]_D^{22}$= +44 (*c* 3.2, $CHCl_3$).

Isopropyl-3,4,6-tri-*O*-acetate-2-deoxy-α-D-galactopyranoside (46e):



General procedure **B** was followed by adding glycosyl donor **43e** (50 mg, 0.170 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (4 mg, 0.034 mmol, 20 mol %) and glycosyl acceptor isopropanol (16 mg, 20 µl, 0.260 mmol, 1.5 equiv) at 100 °C for 24 h to get product as a colourless liquid **46e**. R_f- 0.5 (20% ethyl acetate in hexane), amount- 45 mg, yield- 80%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.36 – 5.26 (m, 1H), 5.13 (d, *J* = 3.2 Hz, 2H), 4.27 – 4.20 (m, 1H), 4.12 – 4.06 (m, 2H), 3.87 (dq, *J* = 12.3, 6.2 Hz, 1H), 2.14 (s, 3H), 2.09 (td, 1H), 2.05 (s, 3H), 1.98 (s, 3H), 1.81 (dd, *J* = 12.5, 4.9 Hz, 1H), 1.21 (d, *J* = 6.2 Hz, 3H), 1.15 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 170.6, 170.3, 95.7, 69.7, 69.6, 67.0, 66.7, 66.5, 62.7, 30.8, 23.3, 21.7, 21.0, 20.9, 20.9.[34] HRMS (ESI) $C_{15}H_{24}O_8NH_4$ $[M+NH_4]^+$- calculated- 350.1809; found- 350.1825. HRMS (ESI) $C_{15}H_{24}O_8NH_4$ $[M+Na]^+$- calculated- 355.1363; found- 355.1371. $[\alpha]_D^{22}$= +23 (*c* 0.5, $CHCl_3$).

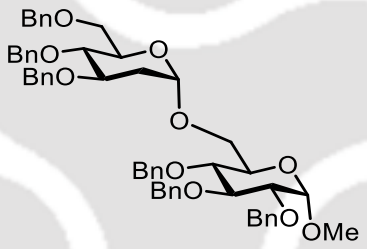
Propargyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (47a):



General procedure **B** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor propargyl alcohol (7 mg, 8 µl, 0.130 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **47a**. R_f- 0.8 (20% ethyl acetate in hexane), amount- 45 mg, yield- 80%. ^{1}H NMR

(600 MHz, $CDCl_3$) δ 7.40 – 7.13 (m, 15H), 5.14 (d, *J* = 2.7 Hz, 1H), 4.89 (dd, *J* = 10.8, 4.1 Hz, 1H), 4.64 (q, *J* = 11.4 Hz, 3H), 4.51 (d, *J* = 11.6 Hz, 2H), 4.18 (dd, *J* = 4.6, 2.4 Hz, 2H), 3.99 (ddd, *J* = 11.5, 8.9, 5.1 Hz, 1H), 3.76 (ddt, *J* = 8.7, 6.4, 4.1 Hz, 2H), 3.67 (dd, *J* = 11.1, 2.6 Hz, 1H), 3.65 – 3.60 (m, 1H), 2.40 (t, *J* = 2.4 Hz, 1H), 2.33 (dd, 1H), 1.77 (td, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8, 138.7, 138.6, 138.2, 128.6, 128.5, 128.5, 128.5, 128.1, 128.0, 128.0, 127.8, 127.8, 127.7, 127.7, 97.9, 96.9, 96.3, 79.4, 78.1, 78.2, 77.4, 77.3, 75.4, 75.1, 74.8, 74.5, 73.6, 72.0, 71.6, 71.4, 69.3, 68.9, 55.5, 54.1, 36.7, 35.3.[39] HRMS (ESI) $C_{30}H_{32}O_5NH_4$ $[M+NH_4]^+$- calculated- 490.2588; found- 490.2588. $[\alpha]_D^{22}$= +8 (*c* 0.2, $CHCl_3$).

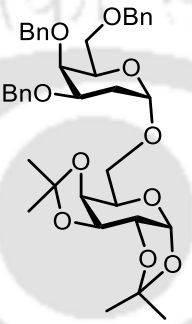
Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-α-D-glucopyranoside (47b):



General procedure **A** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor **45b** (60 mg, 0.130 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **47b**. R_f- 0.2 (20% ethyl acetate in hexane), amount- 73 mg, yield- 69%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.09 (m, 30H), 4.99 (d, *J* = 10.9 Hz, 2H), 4.92 (d, *J* = 11.1 Hz, 1H), 4.87 (d, *J* = 11.1 Hz, 1H), 4.79 (dd, *J* = 11.4, 7.2 Hz, 2H), 4.71 – 4.50 (m, 8H), 4.47 (d, *J* = 11.0 Hz, 1H), 4.40 (d, *J* = 12.2 Hz, 1H), 3.99 (t, *J* = 9.3 Hz, 1H), 3.93 (s, 1H), 3.83 – 3.79 (m, 1H), 3.73 (s, 1H), 3.66 (d, *J* = 10.7 Hz, 1H), 3.61 – 3.56 (m, 2H), 3.53 – 3.47 (m, 2H), 3.34 (s, 3H), 2.30 (dd, *J* = 12.9, 4.7 Hz, 1H), 1.68 (td, *J* = 12.6, 3.3 Hz, 1H).[23] ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9, 138.8, 138.8, 138.7, 138.7, 138.6, 138.5, 138.5, 138.3, 138.2, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 98.0, 97.9, 92.9, 82.4, 80.1, 78.3, 77.9, 75.9, 75.1, 75.0, 75.0, 73.6, 73.5, 73.4, 71.9, 71.8, 71.6, 71.0, 69.9, 68.9,

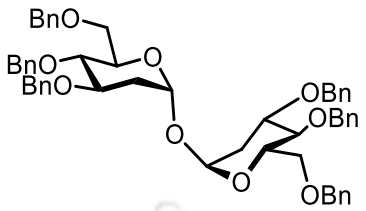
68.8, 65.8, 55.2, 35.4, 29.8.[34] HRMS (ESI) $C_{55}H_{60}O_{10}NH_4$ $[M+NH_4]^+$- calculated- 898.4525; found- 898.4539. $[\alpha]_D^{22}$= +43 (*c* 4.2, $CHCl_3$).

(3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactocopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (47c):



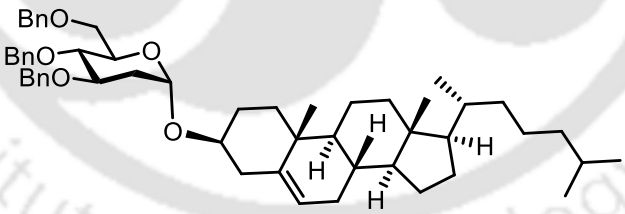
General procedure **A** was followed by adding glycosyl donor **43d** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium tosylate catalyst **44f** (6 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor **45c** (34 mg, 0.130 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **47c**. R_f- 0.5 (20% ethyl acetate in hexane), amount- 62 mg, yield- 76%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 – 7.24 (m, 15H), 5.52 (d, *J* = 5.0 Hz, 1H), 5.03 (d, *J* = 3.5 Hz, 1H), 4.92 (d, *J* = 11.6 Hz, 1H), 4.63 – 4.57 (m, 4H), 4.50 – 4.41 (m, 2H), 4.31 (dd, *J* = 5.1, 2.4 Hz, 1H), 4.21 (dd, *J* = 8.0, 1.9 Hz, 1H), 3.95 (ddt, *J* = 10.6, 7.1, 3.6 Hz, 4H), 3.74 (dd, *J* = 10.7, 6.8 Hz, 1H), 3.64 (ddd, *J* = 13.0, 10.0, 6.9 Hz, 2H), 3.54 (dd, *J* = 9.2, 5.6 Hz, 1H), 2.22 (td, *J* = 12.6, 3.7 Hz, 1H), 2.03 (dd, *J* = 12.8, 4.4 Hz, 1H), 1.51 (s, 3H), 1.42 (s, 3H), 1.33 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 138.7, 138.2, 128.6, 128.5, 128.4, 128.3, 128.0, 127.8, 127.6, 127.5, 109.4, 108.7, 97.6, 96.5, 74.8, 74.5, 73.5, 72.9, 71.2, 70.8, 70.7, 70.5, 69.9, 69.3, 65.9, 65.6, 31.2, 26.3, 26.1, 25.1, 24.7.[29] HRMS (ESI) $C_{39}H_{48}O_{10}NH_4$ $[M+NH_4]^+$- calculated- 694.3591; found- 694.3638. $[\alpha]_D^{22}$= +23 (*c* 1.6, $CHCl_3$).

(3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→1)-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (47d):



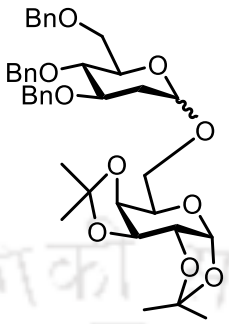
General procedure **A** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44f** (6 mg, 0.024 mmol, 20 mol %) at 100 °C for 16 h to get dimerized[37] product as a colourless liquid **47d**. R_f- 0.8 (20% ethyl acetate in hexane), amount- 73 mg, yield- 75%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 – 7.20(m, 15H), 5.06 (d, *J* = 2.3 Hz, 1H), 4.90 (dd, *J* = 10.9, 5.9 Hz, 1H), 4.68 – 4.62 (m, 3H), 4.52 (dd, *J* = 11.2, 7.5 Hz, 2H), 4.45 (d, *J* = 11.8 Hz, 1H), 4.06– 4.00 (m, 1H), 3.83 – 3.77 (m, 2H), 3.67 – 3.63 (m, 2H), 2.33 (dd, *J* = 13.0, 4.8 Hz, 1H), 1.78 – 1.73 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9, 138.6, 138.3, 138.2, 137.9, 128.5, 128.5, 128.1, 128.1, 128.0, 127.8, 127.8, 96.9, 78.5, 77.9, 75.2, 75.0, 73.6, 72.0, 71.1, 71.0, 69.0, 35.6, 29.8. HRMS (ESI) $C_{54}H_{58}O_9NH_4$ $[M+NH_4]^+$- calculated- 868.4419; found- 868.4432. $[\alpha]_D^{22}$= +6 (*c* 1.5, $CHCl_3$).

Cholesteryl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (47e):



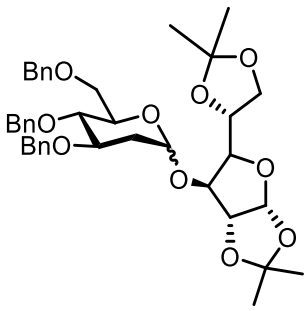
General procedure **B** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor cholesterol (50 mg, 0.130 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **47e**. R_f- 0.9 (20% ethyl acetate in hexane), amount- 60 mg, yield- 62%. ^{1}H NMR and ^{13}C NMR was matched with reported data.[35] HRMS (ESI) $C_{54}H_{74}O_5NH_4$ $[M+NH_4]^+$- calculated- 820.5875; found-820.5770. $[\alpha]_D^{22}$= +27 (*c* 0.2, $CHCl_3$).

(3,4,6-tri-*O*-benzyl-2-deoxy-α,β-D-glucopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (47f):



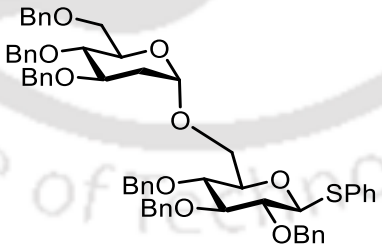
General procedure **B** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor **45c** (34 mg, 0.130 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **47f**. R_f- 0.4 (20% ethyl acetate in hexane), amount- 52 mg, yield- 64%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.13 (m, 15H), 5.51 (d, *J* = 5.0 Hz, 1H), 5.02 (d, *J* = 3.1 Hz, 1H), 4.88 (d, *J* = 10.6 Hz, 1H), 4.69 – 4.63 (m, 3H), 4.62 – 4.57 (m, 2H), 4.54 – 4.48 (m, 3H), 4.31 (dd, *J* = 4.9, 2.4 Hz, 1H), 4.24 – 4.20 (m, 1H), 3.99 (ddd, *J* = 11.5, 9.1, 5.1 Hz, 1H), 3.94 (td, *J* = 6.7, 1.4 Hz, 1H), 3.83 – 3.75 (m, 2H), 3.72 (dt, *J* = 10.9, 6.8 Hz, 2H), 3.69 – 3.62 (m, 3H), 2.33 (dd, *J* = 12.8, 4.7 Hz, 1H), 1.73 (td, 1H), 1.52 (s, 3H), 1.43 (s, 3H), 1.34 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 138.7, 138.3, 128.6, 128.6, 128.5, 128.5, 128.5, 128.1, 128.1, 127.8, 109.4, 108.7, 97.4, 96.5, 78.3, 75.1, 73.6, 71.9, 71.1, 70.8, 68.8, 65.8, 65.5, 35.6, 26.3, 26.1, 25.1, 24.7.[32] HRMS (ESI) $C_{39}H_{48}O_{10}NH_4$ $[M+NH_4]^+$- calculated- 694.3591; found- 694.3592. $[\alpha]_D^{22}$= +14 (*c* 2.3, $CHCl_3$).

(3,4,6-tri-*O*-benzyl-2-deoxy-α,β-D-glucopyranosyl)-(1→3)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranoside (47g):



General procedure **A** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium tosylate catalyst **44f** (6 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor **45g** (63 mg, 0.240 mmol, 2.0 equiv) at 100 °C for 7 h to get product as a colourless liquid **47g**. R_f- 0.6 (20% ethyl acetate in hexane), amount- 59 mg, yield- 73%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 39H), 7.18 – 7.16 (m, 6H), 5.99 (d, *J* = 3.8 Hz, 1H), 5.82 (d, *J* = 3.6 Hz, 2H), 5.25 (d, *J* = 3.4 Hz, 2H), 5.01 (d, *J* = 3.4 Hz, 1H), 4.89 (dd, *J* = 10.7, 8.7 Hz, 4H), 4.68 – 4.60 (m, 13H), 4.57 – 4.48 (m, 9H), 4.30 – 4.18 (m, 5H), 4.16 – 4.05 (m, 7H), 3.99 – 3.91 (m, 5H), 3.80 – 3.69 (m, 11H), 3.63 (dq, *J* = 14.6, 9.1 Hz, 6H), 2.38 – 2.34 (m, 1H), 2.31 – 2.26 (m, 3H), 1.72 (ddt, *J* = 12.8, 11.3, 4.0 Hz, 4H), 1.67 – 1.65 (m, 1H), 1.48 (s, 6H), 1.46 (s, 3H), 1.40 (s, 6H), 1.36 (s, 3H), 1.34 (s, 3H), 1.33 (s, 3H), 1.32 (s, 6H), 1.25 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8, 138.8, 138.6, 138.4, 138.3, 138.3, 138.1, 128.6, 128.5, 128.5, 128.4, 128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 112.3, 112.0, 109.3, 106.5, 106.5, 105.4, 101.0, 98.8, 97.2, 84.1, 83.9, 81.4, 80.3, 79.5, 78.3, 78.2, 75.3, 75.1, 75.0, 73.7, 73.5, 72.6, 72.0, 71.9, 71.8, 71.1, 70.8, 69.0, 68.8, 67.8, 67.1, 35.4, 35.3, 29.8, 27.3, 26.9, 26.7, 26.2, 25.6.[32] HRMS (ESI) $C_{39}H_{48}O_{10}NH_4$ $[M+NH_4]^+$- calculated- 694.3586; found- 694.3580. $[\alpha]_D^{22}$= +47 (*c* 3.9, $CHCl_3$).

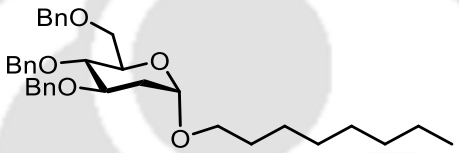
Phenyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4,6-tri-*O*-benzyl-α-D-glucopyranosyl)-β-D-thioglucopyranoside (47h):



General procedure **A** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor **45h** (72 mg, 0.130 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a solid **47h**. R_f- 0.5 (20% ethyl acetate in hexane), amount- 85 mg, yield- 74%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 – 7.14 (m, 35H), 5.04 (d, *J* = 2.9 Hz, 1H), 4.88 (dt, *J* = 13.6, 7.6 Hz, 5H), 4.75 (d, *J* = 10.2 Hz, 1H), 4.68 – 4.56 (m, 5H), 4.50 (d, *J* = 11.0 Hz, 1H), 4.45 (d, *J* = 12.1 Hz, 1H), 3.96 (ddd, *J* = 11.5, 8.9, 5.1

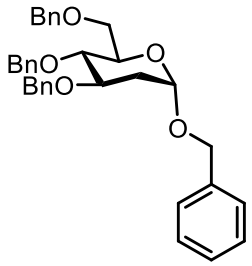
Hz, 1H), 3.81 (dd, *J* = 11.4, 4.8 Hz, 1H), 3.75 (ddd, *J* = 9.9, 3.7, 2.0 Hz, 1H), 3.72 – 3.67 (m, 3H), 3.64 – 3.57 (m, 2H), 3.54 – 3.44 (m, 3H), 2.31 (dd, *J* = 12.9, 5.1 Hz, 1H), 1.72 (td, *J* = 12.9, 3.5 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9, 138.3, 138.1, 133.6, 132.5, 129.1, 128.6, 128.6, 128.6, 128.6, 128.5, 128.4, 128.4, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 98.2, 87.6, 86.9, 81.0, 78.6, 78.3, 77.9, 77.6, 76.0, 75.6, 75.2, 74.9, 73.5, 71.9, 71.0, 68.9, 66.3, 35.5, 29.8. HRMS (ESI) $C_{55}H_{60}O_{10}NH_4$ $[M+NH_4]^+$- calculated- 976.4453; found- 976.4468. $[\alpha]_D^{22}$= +26 (*c* 1.0, $CHCl_3$).

Octanyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (47i):



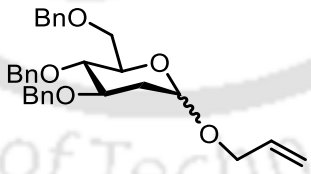
General procedure **B** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor 1-Octanol (17 mg, 20 µl, 0.130 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **47i**. R_f- 0.8 (20% ethyl acetate in hexane), amount- 46 mg, yield- 70%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.14 (m, 15H), 4.94 – 4.86 (m, 2H), 4.71 – 4.62 (m, 3H), 4.55 – 4.49 (m, 2H), 3.97 (ddd, *J* = 11.4, 9.0, 4.7 Hz, 1H), 3.82 – 3.77 (m, 1H), 3.75 (d, *J* = 9.9 Hz, 1H), 3.69 – 3.65 (m, 1H), 3.61 (td, *J* = 9.6, 3.6 Hz, 1H), 3.57 – 3.50 (m, 1H), 3.24 – 3.18 (m, 1H), 2.28 – 2.22 (m, 1H), 1.75 – 1.68 (m, 1H), 1.58 (s, 1H), 1.52 – 1.42 (m, 1H), 1.41 – 1.17 (m, 9H), 0.86 (tdd, *J* = 7.4, 5.6, 3.2 Hz, 6H).[38] ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.9, 138.7, 138.3, 128.5, 128.5, 128.2, 128.1, 128.0, 127.8, 127.7, 127.7, 97.8, 97.8, 78.5, 77.9, 75.2, 73.6, 71.9, 70.9, 70.4, 70.3, 69.1, 39.7, 39.6, 35.8, 30.7, 29.3, 29.2, 24.1, 24.0, 23.2, 14.3, 11.4, 11.2.[42] HRMS (ESI) $C_{35}H_{46}O_5NH_4$ $[M+NH_4]^+$- calculated-564.3684; found- 564.3699. $[\alpha]_D^{22}$= +32 (*c* 0.8, $CHCl_3$).

Benzyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (47j):



General procedure **B** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor benzyl alcohol (14 mg, 14 µl, 0.130 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **47j**. R_f- 0.8 (20% ethyl acetate in hexane), amount- 45 mg, yield- 71%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 – 7.07 (m, 20H), 4.99 (d, *J* = 3.0 Hz, 1H), 4.82 (d, *J* = 10.8 Hz, 1H), 4.61 – 4.55 (m, 4H), 4.45 (dd, *J* = 11.4, 6.6 Hz, 2H), 4.38 (d, *J* = 11.9 Hz, 1H), 3.97 (ddd, *J* = 11.5, 9.0, 5.1 Hz, 1H), 3.75 (d, *J* = 9.8 Hz, 1H), 3.71 (dd, *J* = 10.4, 3.9 Hz, 1H), 3.61 – 3.54 (m, 2H), 2.26 (dd, *J* = 12.7, 4.6 Hz, 1H), 1.69 (td, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.8, 138.6, 138.3, 137.8, 128.5, 128.1, 128.1, 128.0, 127.8, 127.8, 127.7, 127.7, 127.7, 96.9, 78.4, 77.8, 75.1, 73.6, 71.9, 71.8, 71.1, 69.0, 35.6, 29.8.[39] HRMS (ESI) $C_{34}H_{36}O_5NH_4$ $[M+NH_4]^+$- calculated- 542.2901; found- 542.2901. $[\alpha]_D^{22}$= +45 (*c* 3.1, $CHCl_3$).

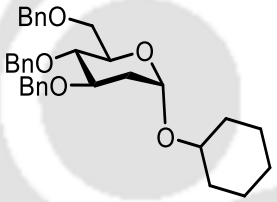
Allyl-3,4,6-tri-*O*-benzyl-2-deoxy-α,β-D-glucopyranoside (47k):



General procedure **B** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor allyl alcohol (8 mg, 10 µl, 0.130 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **47k**. R_f- 0.9 (20% ethyl acetate in hexane), amount- 46 mg, yield- 81%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.13 (m, 15H), 5.92 – 5.85 (m, 1H), 5.29 – 5.23 (m, 1H), 5.16 (dd, *J* = 10.3, 1.2 Hz, 1H), 5.00 (d, *J* = 2.7 Hz, 1H), 4.89 (dd, *J* = 10.9, 3.7 Hz, 1H), 4.70 – 4.61 (m, 3H), 4.52 (d, *J*

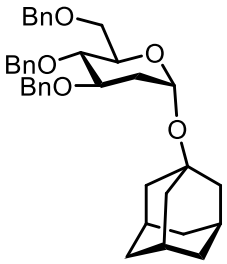
= 2.6 Hz, 1H), 4.50 (s, 1H), 4.15 – 4.09 (m, 1H), 4.05 – 3.98 (m, 1H), 3.95 – 3.90 (m, 1H), 3.78 (dd, *J* = 8.1, 4.3 Hz, 2H), 3.67 (dt, *J* = 8.0, 6.2 Hz, 1H), 3.63 (t, *J* = 9.0 Hz, 1H), 2.31 (dd, 1H), 1.74 (td, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 138.8, 138.7, 138.5, 138.5, 138.3, 134.3, 128.6, 128.5, 128.5, 128.5, 128.5, 128.5, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7, 127.7, 117.5, 117.2, 99.0, 96.8, 79.6, 78.4, 78.3, 77.8, 77.4, 75.4, 75.1, 73.6, 73.6, 71.9, 71.6, 71.0, 69.9, 69.5, 69.0, 67.8, 36.8, 35.6.[40] HRMS (ESI) $C_{30}H_{34}O_5NH_4$ $[M+NH_4]^+$-cal- 492.2744; found-492.2744. $[\alpha]_D^{22}$= +18 (*c* 0.2, $CHCl_3$).

Cyclohexyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (47l):



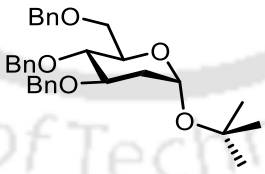
General procedure **A** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor cyclohexanol (13 mg, 14 µl, 0.130 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **47l**. R_f- 0.8 (20% ethyl acetate in hexane), amount- 50 mg, yield- 81%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.14 (m, 15H), 5.12 (d, *J* = 2.9 Hz, 1H), 4.89 (d, *J* = 10.7 Hz, 1H), 4.66 (dt, *J* = 11.5, 9.1 Hz, 3H), 4.50 (d, *J* = 11.4 Hz, 2H), 4.02 (ddd, *J* = 11.5, 8.9, 5.0 Hz, 1H), 3.85 (ddd, *J* = 9.9, 3.7, 2.0 Hz, 1H), 3.80 (dd, *J* = 10.5, 3.9 Hz, 1H), 3.67 (dd, *J* = 10.4, 2.0 Hz, 1H), 3.64 – 3.59 (m, 1H), 3.58 – 3.51 (m, 1H), 2.24 (dd, 1H), 1.89 – 1.78 (m, 2H), 1.74 (td, 1H), 1.70 (s, 2H), 1.51 (d, *J* = 11.2 Hz, 1H), 1.36 – 1.13 (m, 13H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 138.7, 138.4, 128.5, 128.5, 128.5, 128.2, 128.0, 127.7, 127.7, 127.6, 95.2, 78.7, 78.0, 75.2, 74.5, 73.6, 71.9, 70.9, 69.2, 36.2, 33.6, 31.6, 25.8, 24.4, 24.2.[33] HRMS (ESI) $C_{33}H_{40}O_5NH_4$ $[M+NH_4]^+$- calculated- 534.3214; found- 534.3272. $[\alpha]_D^{22}$= +49 (*c* 1.0, $CHCl_3$).

1-Adamantanyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (47m):



General procedure **A** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor 1-adamantanol (20 mg, 0.130 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **47m**. R_f- 0.7 (20% ethyl acetate in hexane), amount- 48 mg, yield- 71%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 12H), 7.24 (s, 1H), 7.21 – 7.15 (m, 2H), 5.40 (d, *J* = 2.6 Hz, 1H), 4.89 (d, *J* = 10.7 Hz, 1H), 4.70 – 4.63 (m, 3H), 4.49 (t, *J* = 11.2 Hz, 2H), 4.06 (ddd, *J* = 11.5, 8.9, 4.9 Hz, 1H), 3.99 (ddd, *J* = 9.9, 3.6, 2.1 Hz, 1H), 3.81 (dd, *J* = 10.4, 3.8 Hz, 1H), 3.66 – 3.59 (m, 2H), 2.13 (dd, 1H), 2.10 (s, 3H), 1.78 (q, *J* = 11.9 Hz, 6H), 1.72 (td, 1H), 1.66 – 1.52 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1, 138.8, 138.5, 128.5, 128.5, 128.5, 128.4, 128.1, 128.1, 128.0, 127.8, 127.7, 127.6, 127.6, 90.6, 78.8, 78.1, 77.4, 75.1, 74.0, 73.6, 71.9, 70.5, 69.3, 42.6, 37.2, 36.5, 30.8, 30.7.[36] HRMS (ESI) $C_{37}H_{44}O_5NH_4$ $[M+NH_4]^+$- calculated- 586.3527; found- 586.3526. $[\alpha]_D^{22}$= +60 (*c* 1.0, $CHCl_3$).

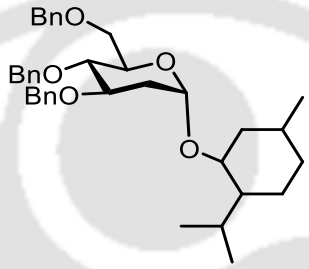
Tertiary-butanyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (47n):



General procedure **A** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor tertiary butanol (10 mg, 12 µl, 0.130 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **47n**. R_f- 0.8 (20% ethyl acetate in hexane), amount- 41 mg, yield- 69%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.14 (m, 15H), 5.27 (d, *J* = 2.7 Hz, 1H), 4.89 (d, *J* = 10.6 Hz, 1H), 4.70 – 4.62 (m, 3H), 4.49 (t, *J* = 11.5 Hz, 2H), 4.04 (ddd, *J* = 11.6, 8.9, 4.9 Hz, 1H), 3.97 – 3.91

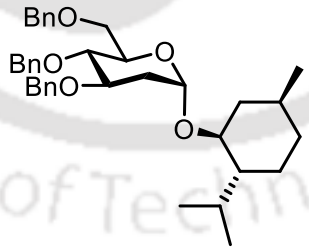
(m, 1H), 3.81 (dd, *J* = 10.4, 3.6 Hz, 1H), 3.67 – 3.58 (m, 2H), 2.12 (dd, 1H), 1.72 (td, *J* = 12.1, 3.6 Hz, 1H), 1.21 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1, 138.8, 138.4, 128.5, 128.5, 128.5, 128.4, 128.2, 128.0, 127.8, 127.7, 127.7, 127.6, 92.1, 78.7, 78.1, 75.1, 74.7, 73.6, 71.9, 70.5, 69.2, 37.2, 28.8.[32] HRMS (ESI) $C_{31}H_{38}O_5NH_4$ $[M+NH_4]^+$- calculated- 508.3057; found- 508.3040. $[\alpha]_D^{22}$= +47 (*c* 1.7, $CHCl_3$).

(±)Menthoyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (47o):



General procedure **A** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor menthol (20 mg, 0.130 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **47o**. R_f- 0.8 (20% ethyl acetate in hexane), amount- 48 mg, yield- 70%. HRMS (ESI) $C_{37}H_{48}O_5NH_4$ $[M+NH_4]^+$- calculated- 590.3840; found- 590.3843.

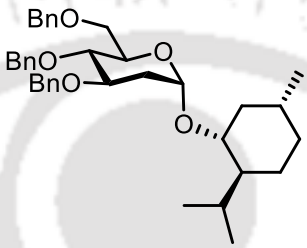
(-)-Menthoyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (47oA)



^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 – 6.98 (m, 15H), 5.20 (d, *J* = 3.4 Hz, 1H), 4.87 (d, *J* = 10.7 Hz, 1H), 4.72 – 4.61 (m, 3H), 4.50 (dd, *J* = 11.4, 6.7 Hz, 2H), 4.02 – 3.90 (m, 1H), 3.83 (dd, *J* = 10.3, 3.2 Hz, 1H), 3.78 (d, *J* = 9.9 Hz, 1H), 3.68 – 3.61 (m, 2H), 3.45 (td, *J* = 10.6, 4.0 Hz, 1H), 2.21 (dd, *J* = 12.3, 4.2 Hz, 1H), 2.11 – 2.04 (m, 1H), 1.79 (td, 1H), 1.63 (dd, *J* = 11.0, 9.2 Hz, 3H), 1.33 (s, 2H), 1.25 (s, 2H), 1.21 (dd, *J* = 12.6, 5.6 Hz, 1H), 0.98 – 0.93 (m, 1H), 0.90 (t, *J* = 7.8 Hz, 3H), 0.87 (t, *J* = 8.9 Hz, 3H), 0.86 – 0.74 (m, 3H), 0.71 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (151 MHz,

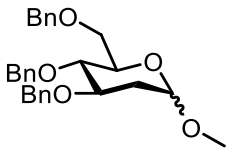
$CDCl_3$) δ 139.0, 138.7, 138.3, 128.5, 128.5, 128.5, 128.3, 128.3, 128.1, 128.1, 127.8, 127.8, 127.7, 127.7, 127.6, 96.4, 93.3, 79.9, 78.7, 78.3, 78.0, 76.4, 75.3, 75.3, 75.1, 74.5, 73.8, 73.7, 71.9, 71.5, 71.3, 69.9, 69.0, 48.1, 48.0, 40.8, 39.9, 37.4, 36.4, 34.6, 34.6, 31.6, 31.5, 31.1, 29.8, 25.3, 25.2, 23.3, 23.0, 22.5, 22.4, 21.4, 21.3, 21.2, 16.0, 15.6.[41] $[\alpha]_D^{22}$= +9 (*c* 1.0, $CHCl_3$). Amount- 25 mg, yield- 36%.

(+)-Menthoyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (47oB)



^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.14 (m, 15H), 5.01 (d, *J* = 3.2 Hz, 1H), 4.89 (d, *J* = 10.8 Hz, 1H), 4.70 – 4.62 (m, 3H), 4.49 (dd, *J* = 11.5, 2.2 Hz, 2H), 3.99 (ddd, *J* = 11.6, 8.9, 4.9 Hz, 1H), 3.96 – 3.91 (m, 1H), 3.79 (dd, *J* = 10.4, 3.9 Hz, 1H), 3.66 (dd, *J* = 10.5, 1.8 Hz, 1H), 3.62 – 3.55 (m, 1H), 3.30 (td, *J* = 10.6, 4.3 Hz, 1H), 2.26 (dd, *J* = 12.2, 5.2 Hz, 1H), 2.10 (d, *J* = 12.1 Hz, 1H), 2.05 – 1.96 (m, 1H), 1.68 (td, *J* = 12.5, 3.7 Hz, 1H), 1.61 (d, *J* = 5.1 Hz, 19H), 1.35 (dd, *J* = 10.5, 6.7 Hz, 2H), 1.25 (s, 1H), 1.16 (dd, *J* = 12.1, 6.5 Hz, 1H), 0.95 (dd, *J* = 12.8, 7.6 Hz, 2H), 0.92 – 0.88 (m, 3H), 0.83 (d, *J* = 6.6 Hz, 4H), 0.79 (dd, *J* = 12.2, 3.2 Hz, 1H), 0.74 (d, *J* = 7.1 Hz, 3H).[33] ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9, 138.7, 138.4, 128.5, 128.5, 128.4, 128.3, 128.1, 128.0, 127.8, 127.7, 127.6, 99.6, 80.7, 78.6, 77.8, 75.1, 73.6, 71.9, 71.0, 69.2, 48.9, 43.1, 36.2, 34.5, 31.8, 25.9, 23.4, 22.4, 21.3, 16.5.[41] $[\alpha]_D^{22}$= -52 (*c* 1.3, $CHCl_3$). Amount- 27 mg, yield- 39%.

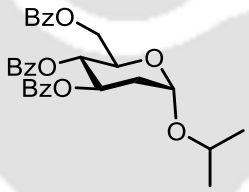
Methyl-3,4,6-tri-*O*-benzyl-2-deoxy-α,β-D-glucopyranoside (47p):



General procedure **A** was followed by adding glycosyl donor **43b** (50 mg, 0.120 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (3 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor

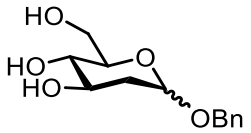
methanol (4 mg, 6 µl, 0.130 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **47p**. R_f- 0.9 (20% ethyl acetate in hexane), amount- 50 mg, yield- 93%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 – 7.12 (m, 15H), 4.89 (dd, *J* = 10.9, 2.7 Hz, 1H), 4.85 (d, *J* = 3.0 Hz, 1H), 4.71 – 4.59 (m, 3H), 4.54 – 4.48 (m, 2H), 3.97 (ddd, *J* = 11.5, 8.8, 5.1 Hz, 1H), 3.77 (dd, *J* = 10.3, 3.9 Hz, 1H), 3.72 (ddd, *J* = 13.4, 8.7, 3.5 Hz, 1H), 3.68 (dt, *J* = 11.7, 3.6 Hz, 1H), 3.61 (dd, *J* = 11.9, 6.9 Hz, 1H), 3.31 (s, 3H), 2.28 (dd, 1H), 1.73 (td, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8, 138.7, 138.5, 138.5, 138.3, 128.6, 128.5, 128.5, 128.4, 128.1, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 100.9, 98.6, 79.5, 78.4, 77.8, 75.3, 75.0, 73.6, 71.9, 71.6, 70.8, 69.5, 69.1, 56.7, 54.7, 36.8, 35.5.[32] HRMS (ESI) $C_{28}H_{32}O_5NH_4$ $[M+NH_4]^+$- calculated- 466.2588; found- 466.2588. HRMS (ESI) $C_{28}H_{32}O_5Na$ $[M+Na]^+$- calculated- 471.2142; found- 471.2118. $[\alpha]_D^{22}$= +63 (*c* 1.9, $CHCl_3$).

Isopropyl-3,4,6-tri-*O*-benzoyl-2-deoxy-α-D-glucopyranoside (47q):



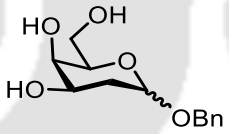
General procedure **A** was followed by adding glycosyl donor **43f** (50 mg, 0.100 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44d** (2 mg, 0.020 mmol, 20 mol %) and glycosyl acceptor isopropanol (7 mg, 10 µl, 0.110 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **47q**. R_f- 0.9 (20% ethyl acetate in hexane), amount- 49 mg, yield- 95%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (dt, *J* = 8.4, 1.4 Hz, 2H), 7.98 (dt, *J* = 8.5, 1.4 Hz, 2H), 7.94 (dt, *J* = 8.4, 1.4 Hz, 2H), 7.57 – 7.52 (m, 1H), 7.49 (tdt, *J* = 7.8, 5.1, 1.3 Hz, 2H), 7.44 – 7.39 (m, 2H), 7.36 (dd, *J* = 10.4, 4.7 Hz, 4H), 5.75 (ddd, *J* = 11.5, 9.6, 5.2 Hz, 1H), 5.56 (t, *J* = 9.7 Hz, 1H), 5.17 (d, *J* = 2.9 Hz, 1H), 4.60 – 4.52 (m, 1H), 4.49 – 4.38 (m, 2H), 3.96 (hept, *J* = 6.2 Hz, 1H), 2.45 (dd, *J* = 12.7, 5.3 Hz, 1H), 2.02 (td, *J* = 12.7, 3.7 Hz, 1H), 1.29 (d, *J* = 6.2 Hz, 3H), 1.19 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 165.9, 165.8, 133.4, 133.2, 133.2, 130.0, 129.8, 129.8, 129.4, 128.5, 128.5, 95.3, 70.7, 70.4, 69.9, 68.4, 63.8, 36.1, 23.5, 21.7. HRMS (ESI) $C_{30}H_{30}O_8NH_4$ $[M+NH_4]^+$- calculated- 536.2279; found- 536.2287. HRMS (ESI) $C_{30}H_{30}O_8Na$ $[M+Na]^+$- calculated- 541.1833; found- 541.1843. $[\alpha]_D^{22}$= +6 (*c* 1.0, $CHCl_3$).

Benzyl-2-deoxy-α,β-D-glucopyranoside (47r):



General procedure **A** was followed by adding glycosyl donor **43g** (200 mg, 1.220 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44f** (59 mg, 0.240 mmol, 20 mol %) and glycosyl acceptor benzyl alcohol (264 mg, 254 µl, 2.440 mmol, 2.0 equiv) at 100 °C for 5 h to get product as a colourless liquid **47r**. R_f- 0.5 (100% ethyl acetate), amount- 220 mg, yield- 71%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 10H), 5.45 (dd, *J* = 5.4, 1.9 Hz, 1H), 5.37 (d, *J* = 5.7 Hz, 1H), 4.82 – 4.79 (m, 2H), 4.74 (d, *J* = 11.7 Hz, 1H), 4.70 (t, *J* = 5.7 Hz, 1H), 4.64 – 4.50 (m, 3H), 4.50 (d, *J* = 11.7 Hz, 1H), 4.25 (q, *J* = 5.9 Hz, 1H), 4.20 (q, *J* = 5.6 Hz, 1H), 3.87 (dt, *J* = 9.2, 5.6 Hz, 2H), 3.77 (dd, *J* = 9.2, 5.5 Hz, 1H), 3.58 (dd, *J* = 9.3, 6.6 Hz, 1H), 2.35 (ddd, *J* = 14.3, 7.5, 1.9 Hz, 1H), 2.24 – 2.20 (m, 1H), 2.16 (dd, *J* = 5.3, 3.4 Hz, 1H), 2.14 (dd, *J* = 5.3, 3.4 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 137.5, 137.1, 128.7, 128.6, 128.3, 128.2, 128.1, 128.0, 128.0, 105.9, 105.5, 84.9, 82.1, 82.0, 80.8, 73.4, 72.0, 71.8, 71.8, 71.1, 69.7, 41.0, 40.8.

Benzyl-2-deoxy-α,β-D-galactopyranoside (47s):



General procedure **A** was followed by adding glycosyl donor **43h** (200 mg, 1.220 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **44f** (59 mg, 0.240 mmol, 20 mol %) and glycosyl acceptor benzyl alcohol (264 mg, 254 µl, 2.440 mmol, 2.0 equiv) at 100 °C for 5 h to get product as a colourless liquid **47s**. R_f- 0.6 (100% ethyl acetate), amount- 242 mg, yield- 78%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 10H), 5.30 (dd, *J* = 5.4, 1.6 Hz, 1H), 5.23 (d, *J* = 5.7 Hz, 1H), 4.99 (ddd, *J* = 7.5, 4.6, 3.2 Hz, 1H), 4.88 (t, *J* = 5.6 Hz, 1H), 4.71 (dd, *J* = 13.6, 11.8 Hz, 2H), 4.56 (d, *J* = 4.9 Hz, 1H), 4.51 (d, *J* = 4.6 Hz, 1H), 4.48 – 4.45 (m, 2H), 4.34 – 4.31 (m, 3H), 3.88 (dd, *J* = 10.1, 3.2 Hz, 1H), 3.81 (d, *J* = 10.1 Hz, 1H), 3.74 (d, *J* = 9.3 Hz, 1H), 2.32 (ddd, *J* = 14.5, 7.4, 1.6 Hz, 1H), 2.25 (d, *J* = 14.7 Hz, 1H), 2.18 – 2.13 (m, 1H), 2.06 (ddd, *J* = 14.5, 5.4, 3.2 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 137.7, 137.6, 128.6, 128.6, 128.1, 128.0, 127.9, 127.8, 104.5, 104.4, 90.6, 87.2, 81.5, 81.4, 77.3, 75.8, 73.8, 72.8, 69.7, 69.4, 40.7, 40.2.

2.10 References:

1. (a) Erkkila, A.; Majander, I.; Pihko, P. M. *Chem. Rev*. **2007**, *107*, 5416–5470; (b) Hong, L.; Sun, W. S.; Yang, D. X.; Li, G. F.; Wang, R. *Chem. Rev*. **2016**, *116*, 4006–4123.
2. MacMillan, D. W. C.; Borths, C. J.; Jen, W. S.; Wiener, J. S.; Paras, N. A.; Wilson, R. M.; *Abstr. Pap. Am. Chem. S.* **2000**, *220*, U122–U122.
3. List, B.; Lerner, R. A.; Barbas, C. F. *J. Am. Chem. Soc.* **2000**, *122*, 2395–2396.
4. (a) Liu, Y. K.; Li, Z. L.; Li, J. Y.; Feng, H. X.; Tong, Z. P. *Org. Lett.* **2015**, *17*, 2022–2025; (b) Li, J. Y.; Yu, K. W.; Xie, C. C.; Liu, Y. K. *Org. Biomol. Chem.* **2017**, *15*, 1407–1417.
5. Feng, H. X.; Tan, R.; Liu, Y. K. *Org. Lett.* **2015**, *17*, 3794–3797.
6. (a) Hosoya, T.; Takano, T.; Kosma, P.; Rosenau, T. *J. Org. Chem*. **2014**, *79*, 7889–7894; (b) Ionescu, A. R.; Whitfield, D. M.; Zgierski, M. Z.; Nukada, T.*Carbohydr. Res.* **2006**, *341*, 2912–2920; (c) Williams, I. H.; Pernia, J. J.; Tunon, I. *Pure Appl. Chem*. **2011**, *83*, 1507–1514.
7. (a) McDonald, L. A.; Lotvin, J. A.; Bailey, A. E.; Carter, G. T. *J. Nat. Prod*. **1998**, *61*, 217–226; (b) Langenhan, J. M.; Peters, N. R.; Guzei, I. A.; Hoffmann, M.; Thorson, J. S. *P Natl. Acad. Sci. USA*. **2005**, *102*, 12305–12310.
8. (a) Peters, K. S. *Chem. Rev*. **2007**, *107*, 859–873; (b) Kong, F. M.; Zhao, N.; Siegel, M. M.; Janota, K.; Ashcroft, J. S.; Koehn, F. E.; Borders, D. B.; Carter, G. T. *J. Am. Chem. Soc.* **1998**, *120*, 13301–13311.
9. (a) Langenhan, J. M.; Engle, J. M.; Slevin, L. K.; Fay, L. R.; Lucker, R. W.; Smith, K. R.; Endo, M. M. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 670–673; (b) Langenhan, J. M.; Griffith, B. R.; Thorson, J. S. *J. Nat. Prod*. **2005**, *68*, 1696–1711.
10. (a) Liu, D.; Sarrafpour, S.; Guo, W.; Goulart, B.; Bennett, C. S. *J. Carbohydr. Chem*. **2014**, *33*, 423–434; (b) Schene, H.; Waldmann, H. *Chem. Commun*. **1998**, 2759–2760.
11. (a) Lloyd, D.; Bylsma, M.; Bright, D. K.; Chen, X. Z.; Bennett, C. S. *J. Org. Chem*. **2017**, *82*, 3926–3934; (b) Roush, W. R.; Gung, B. W.; Bennett, C. E. *Org. Lett.* **1999**, *1*, 891–893.

12. (a) Rodriguez, M. A.; Boutureira, O.; Arnes, X.; Matheu, M. I.; Diaz, Y.; Castillon, S. *J. Org. Chem*. **2005**, *70*, 10297–10310; (b) Roush, W. R.; Narayan, S. *Org. Lett.* **1999**, *1*, 899–902; (c) Bock, K.; Lundt, I.; Pedersen, C. *Carbohydr. Res.* **1984**, *130*, 125–134; d) Bucher, C.; Gilmour, R. *Angew. Chem., Int. Ed.* **2010**, *49*, 8724–8728; (e) Roush, W. R.; Bennett, C. E. *J. Am. Chem. Soc.* **1999**, *121*, 3541–3542.
13. Gervay, J.; Danishefsky, S. *J. Org. Chem*. **1991**, *56*, 5448–5451.
14. (a) Balmond, E. I.; Benito-Alifonso, D.; Coe, D. M.; Alder, R. W.; McGarrigle, E. M.; Galan, M. C. *Angew. Chem., Int. Ed.* **2014**, *53*, 8190–8194; (b) Rosati, O.; Curini, M.; Messina, F.; Marcotullio, M. C.; Cravotto, G. *Catal. Lett*. **2013**, *143*, 169–175; (c) Cui, X. K.; Zhong, M.; Meng, X. B.; Li, Z. J. *Carbohydr. Res.* **2012**, *358*, 19–22; (d) Das, S.; Pekel, D.; Neudorfl, J. M.; Berkessel, A. *Angew. Chem., Int. Ed.* **2015**, *54*, 12479–12483.
15. (a) Roush, W. R.; Lin, X. F. *J. Org. Chem*. **1991**, *56*, 5740–5742; (b) Nguyen, H. M.; Poole, J. L.; Gin, D. Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 414–417; (c) Garcia, B. A.; Gin, D. Y. *J. Am. Chem. Soc.* **2000**, *122*, 4269–4279; (d) Issa, J. P.; Lloyd, D.; Steliotes, E.; Bennett, C. S. *Org. Lett.* **2013**, *15*, 4170–4173; (e) Nogueira, J. M.; Nguyen, S. H.; Bennett, C. S. *Org. Lett.* **2011**, *13*, 2814–2817; (f) Uchiro, H.; Miyazaki, K.; Mukaiyama, T. *Chem. Lett*. **1997**, 403–404; (g) Uchiro, H.; Mukaiyama, T. *Chem. Lett*. **1996**, 79–80; (h) Dyapa, R.; Dockery, L. T.; Walczak, M. A. *Org. Biomol. Chem.* **2017**, *15*, 51–55; i) Mossotti, M.; Panza, L. *J. Org. Chem*. **2011**, *76*, 9122–9126; (j) Zhu, D. Y.; Baryal, K. N.; Adhikari, S.; Zhu, J. L. *J. Am. Chem. Soc.* **2014**, *136*, 3172–3175; (k) Issa, J. P.; Bennett, C. S. *J. Am. Chem. Soc.* **2014**, *136*, 5740–5744; (l) Nogueira, J. M.; Bylsma, M.; Bright, D. K.; Bennett, C. S. *Angew. Chem., Int. Ed.* **2016**, *55*, 10088 – 10092.
16. Smith, A. B.; Hale, K. J.; Rivero, R. A. *Tetrahedron Lett*. **1986**, *27*, 5813–5816.
17. Toshima, K.; Nagai, H.; Matsumura, S. *Synlett* **1999**, 1420–1422.
18. Zhao, C. F.; Chen, S. B.; Seidel, D. *J. Am. Chem. Soc.* **2016**, *138*, 9053–9056.
19. Kotke, M.; Schreiner, P. R. *Synthesis-Stuttgart* **2007**, 779–790.
20. Otte, D. A. L.; Borchmann, D. E.; Lin, C.; Weck, M.; Woerpel, K. A. *Org. Lett.* **2014**, *16*, 1566–1569.
21. Murphy, P. J.; Williams, H. L.; Hibbs, D. E.; Hursthouse, M. B.; Malik, K. M. A.; *Tetrahedron* **1996**, *52*, 8315–8332.
22. Page, P. C. B.; Chan, Y.; Liddle, J.; Elsegood, M. R. J. *Tetrahedron* **2014**, *70*, 7283–7305.

23. Bucher, C.; Gilmour, R. *Angew. Chem., Int. Ed.* **2010**, *49*, 8724–8728.
24. Miao, Y.; Phuphuak, Y.; Rousseau, C.; Bousquet, T.; Mortreux, A.; Chirachanchai, S.; Zinck1, P. *Journal of Polymer Science, Part A: Polymer Chemistry* **2013**, *51*, 2279–2287.
25. Fu, L.; Sun, C.; Yan, L. *ACS. Appl. Mater. Interfaces* **2015**, *7*, 2104–2115.
26. Baek, S. -S.; Hwang, S. -H. *International Journal of Adhesion & Adhesives* **2016**, *70*, 110–116.
27. Kakitsubata, Y.; Aramaki, R.; Nishioka, K.; Wakao, M.; Suda, Y. *Tetrahedron Lett.* **2016**, *57*, 1154–1157.
28. Danishefsky, S. J.; Gervay, J.; Peterson, J. M.; McDonald, F. E.; Koseki, K.; Griffith, D. A.; Oriyama, T.; Marsden, S. P. *J. Am. Chem. Soc.* **1995**, *117*, 1940–1953.
29. Balmond, E. I.; Coe, D. M.; Galan, M. C.; McGarrigle, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 9152–9155.
30. Jiang, X.; Tang, W.; Xue, D.; Xiao, J.; Wang, C. *ACS. Catal.* **2017**, *7*, 1831−1835.
31. Liu, Z.; Ma, Q.; Liu, Y.; Wang, Q. *Org. Lett.* **2014**, *16*, 236–239.
32. Cui, X. -K.; Zhong, M.; Meng, X. -B.; Li, Z. -J. *Carbohydr. Res.* **2012**, *358*, 19–22.
33. Kimura, T.; Takahashi, D.; Toshima, K. *J. Org. Chem.* **2015**, *80*, 9552–9562.
34. Durantie, E.; Bucher, C.; Gilmour, R. *Chem. Eur. J.* **2012**, *18*, 8208–8215.
35. Adhikari, S.; Baryal, K. N.; Zhu, D.; Li, X.; Jhu, J. *ACS. Catal.* **2013,** *3*, 57–60.
36. Nogueira, J. M.; Nguyen, S. H.; Bennett, C. S.; *Org. Lett.* **2011,** *13*, 2814–2817.
37. Kelson, I. K.; Feit, B. -A. *Journal of Carbohydrate Chemistry* **2003,** *22*, 827–841.
38. Toshima, K.; Nagai, H.; Kasumi, K. -I.; Kawahara, K.; Matsumura, S. *Tetrahedron* **2004**, *60*, 5331–5339.
39. Williams, D. B. G.; Simelanea, S. B.; Kinfea, H. H. *Org. Biomol. Chem.* **2012**, *10*, 5636–5642.
40. Morris, W. J.; Shair, M. D. *Org. Lett.* **2009,** *11*, 9–12.
41. Park, Y.; Harper, K. C.; Kuhl, N.; Kwan, E. E.; Liu, R. Y.; Jacobsen, E. N. *Science* **2017,** *355*, 162–166.
42. Rauter, A. P.; Almeida, T.; Vicente, A. I.; Ribeiro, V.; Bordado, J. C.; Marques, J. P.; Ribeiro, F. R.; Ferreira, M. J.; Oliveira, C.; Guisnet, M. *Eur. J. Org. Chem.* **2006**, 2429–2439.

2.11 Variable Temperature ^{1}H NMR:

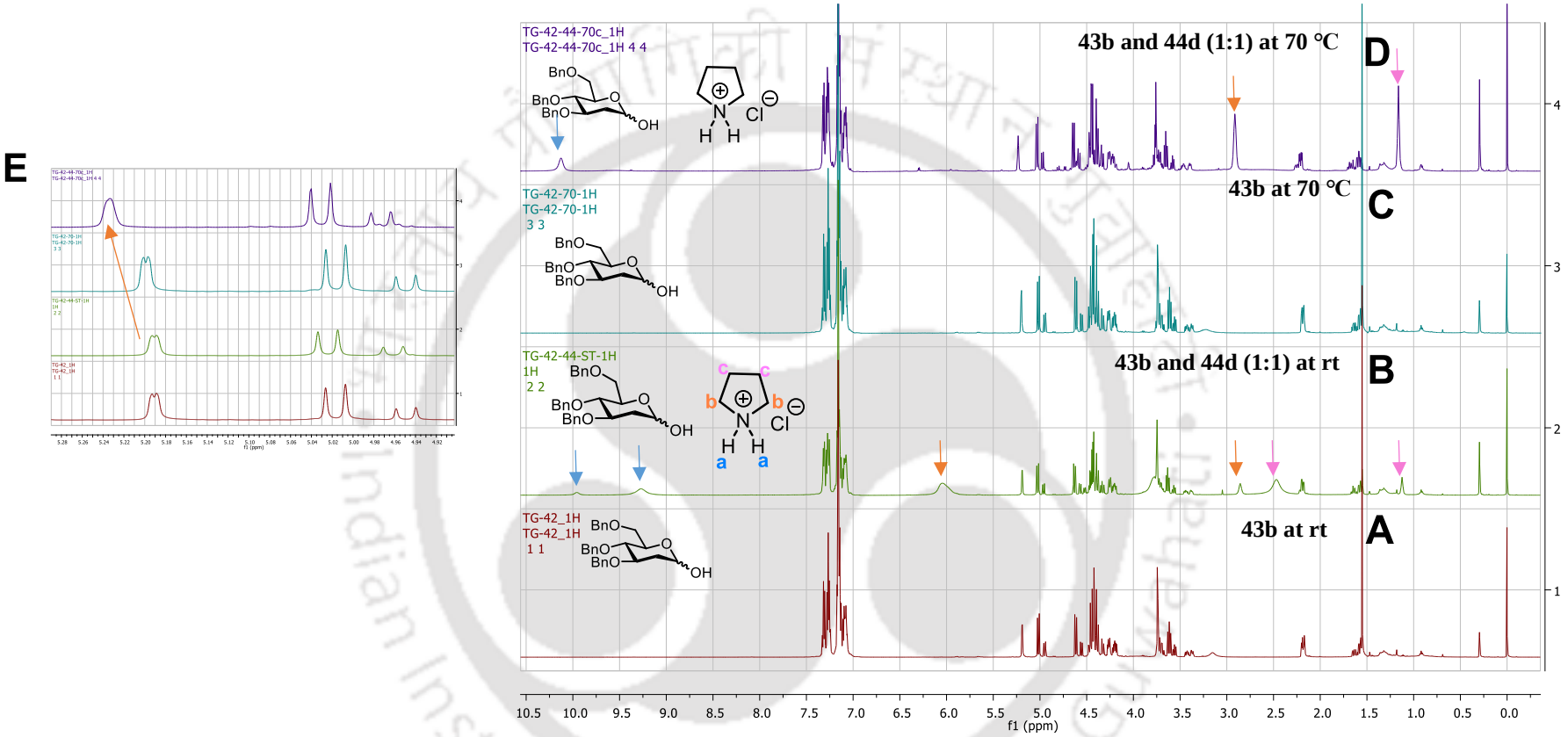
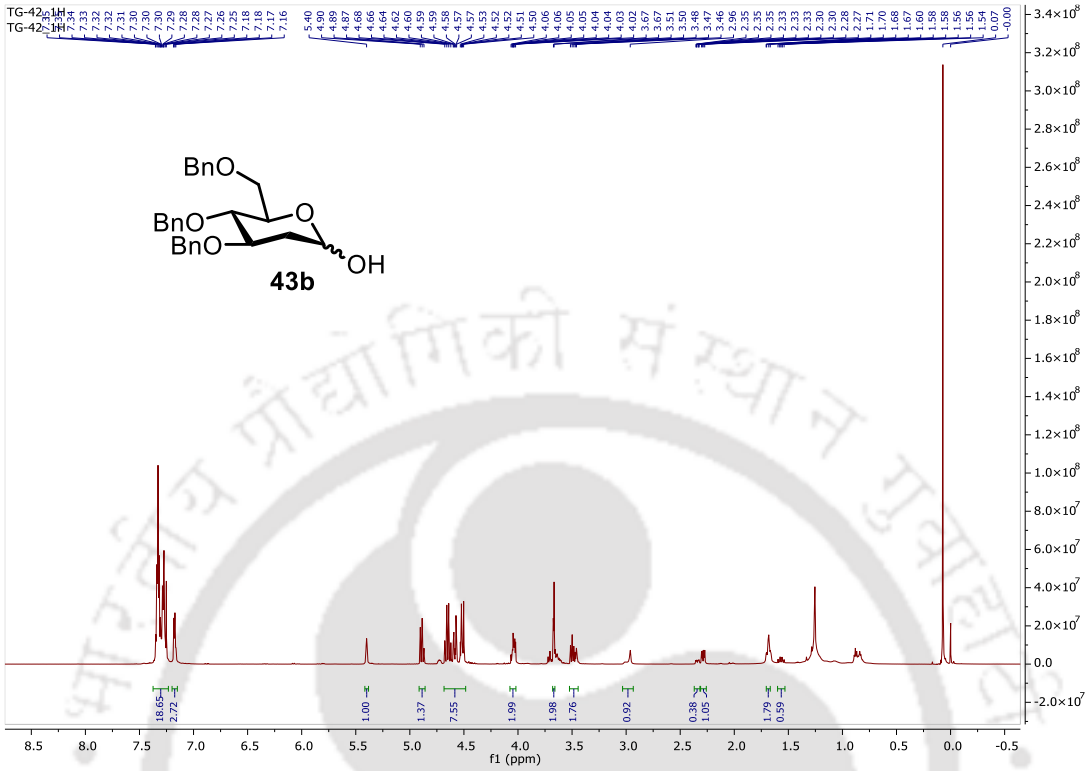
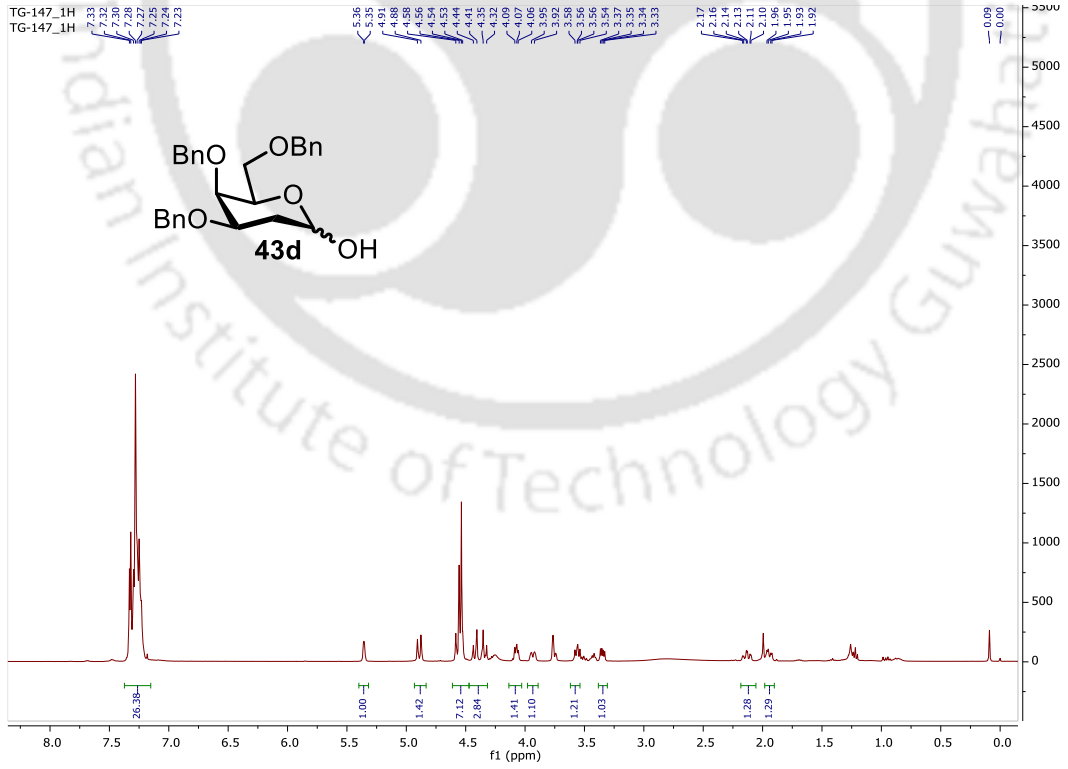
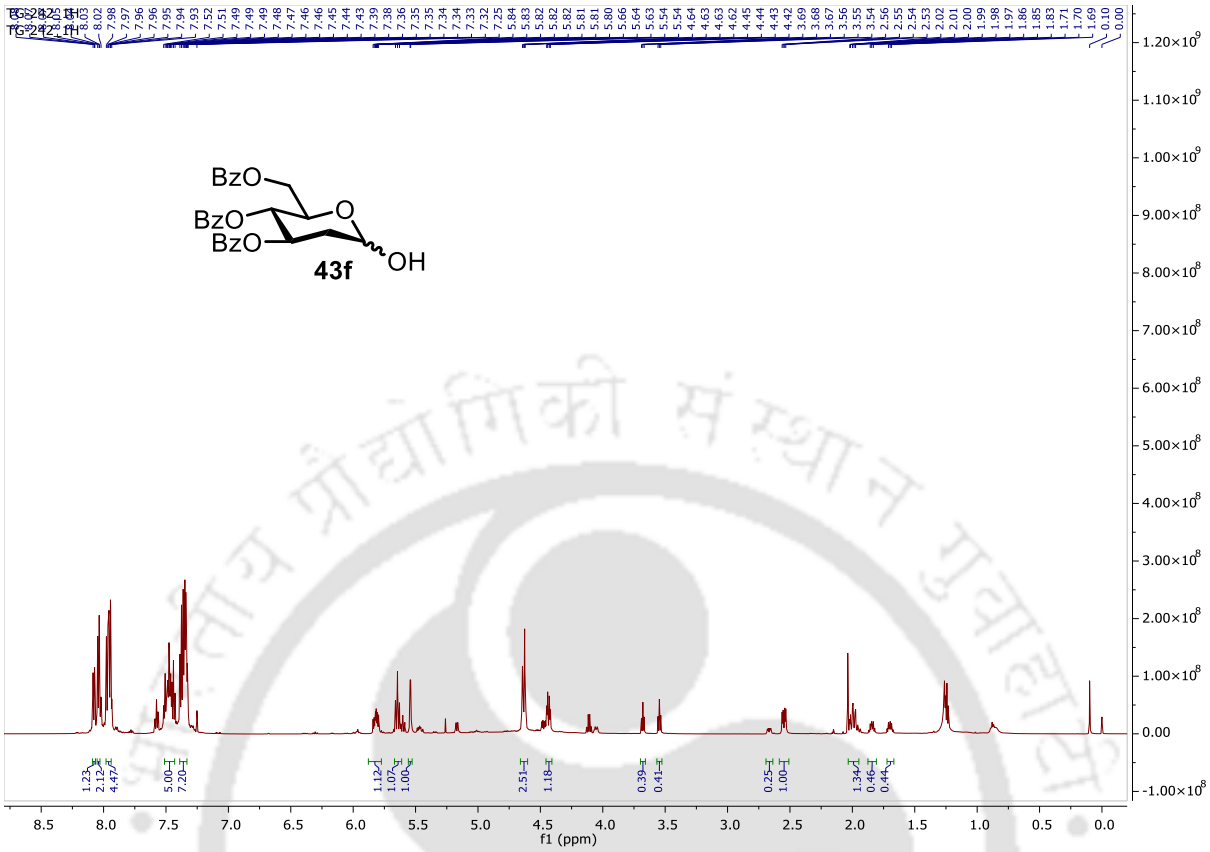


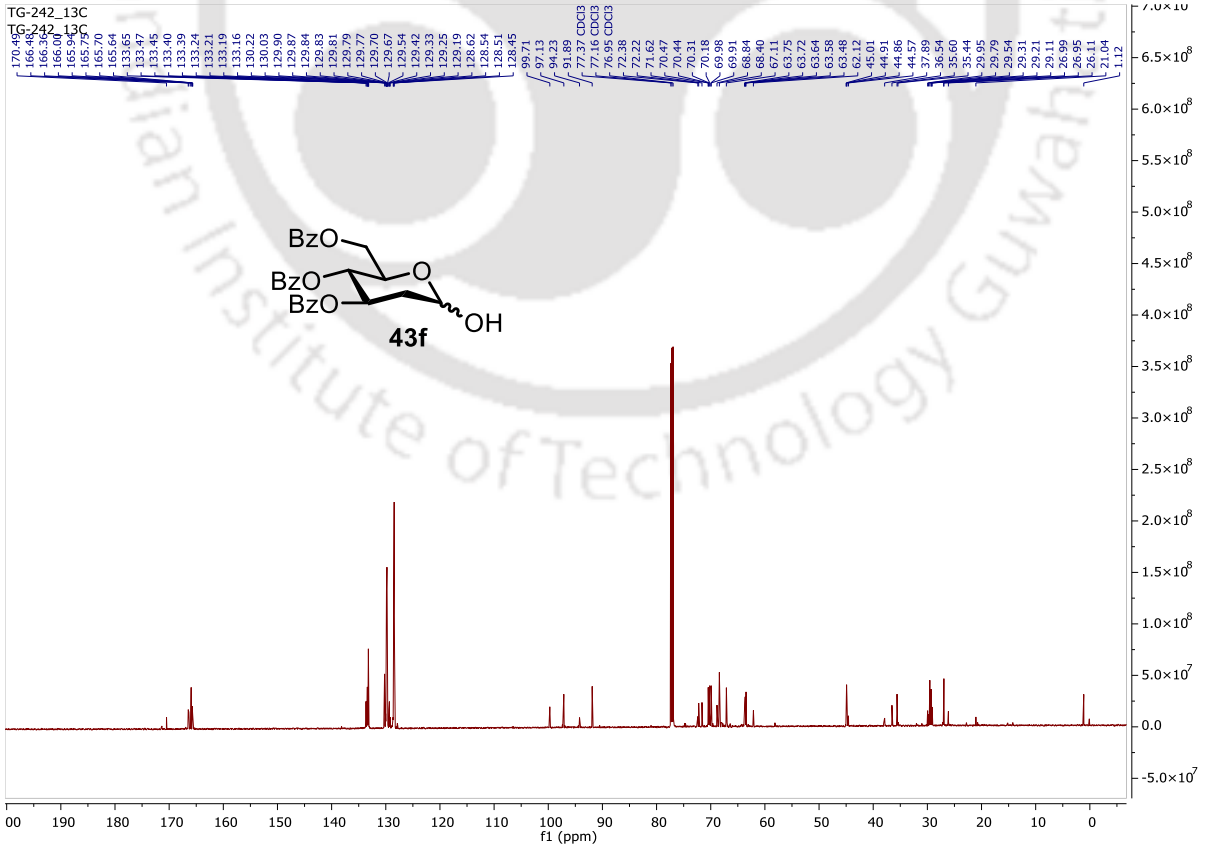
Figure 3: All VT experiments were done on 0.023 mmol scale in 0.6 ml of C_6D_6. A) ^{1}H NMR of donor **43b** at rt. B) ^{1}H NMR of donor **43b** and catalyst **44d** at rt; Strange occurrence of two sets of signals for catalyst **44d** in the presence of **43b** at rt in C_6D_6. C) ^{1}H NMR of donor **43b** at 70 ̊C. D) ^{1}H NMR of donor **43b** and catalyst **44d** at 70 ̊C; only one set of signals for the catalyst **44d**. E) Expansion of anomeric region showing a shift of the anomeric proton by 0.04 ppm at elevated temperature in the presence of catalyst **44d**.

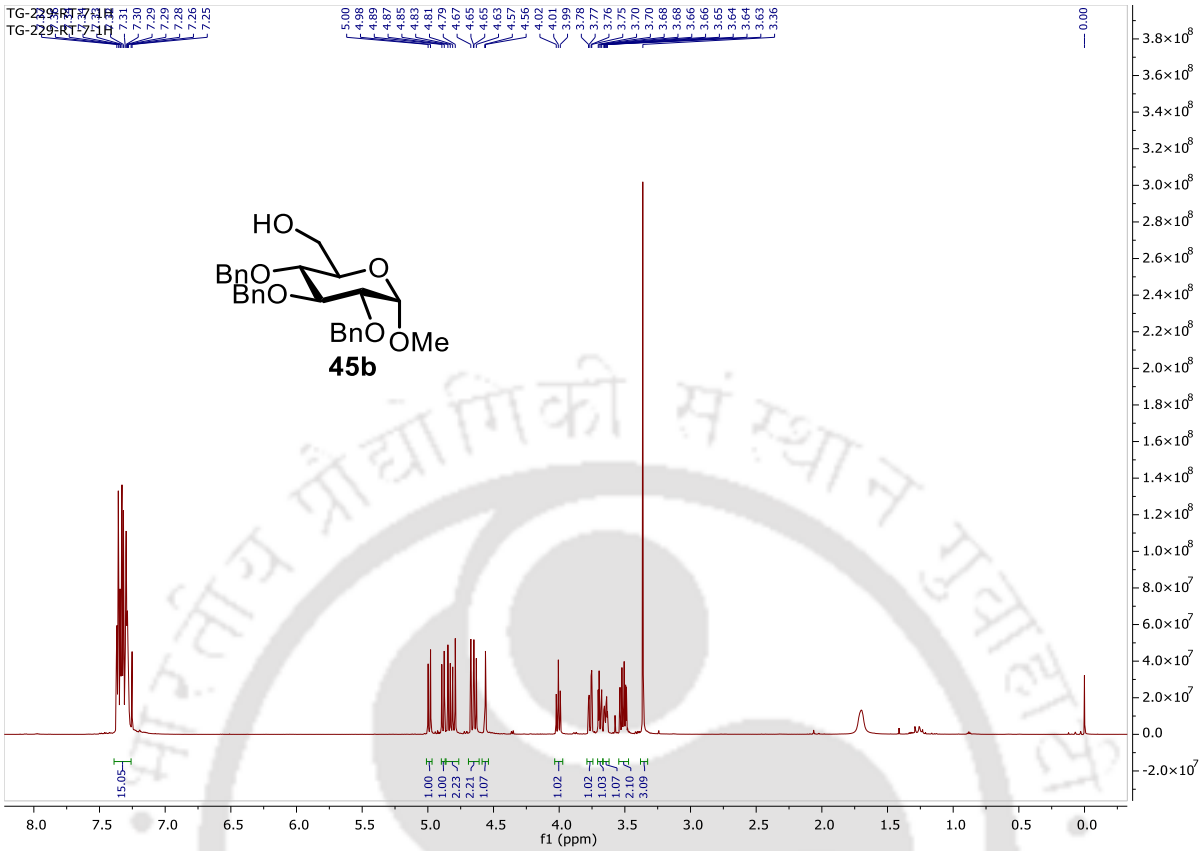
2.12 NMR Spectra:

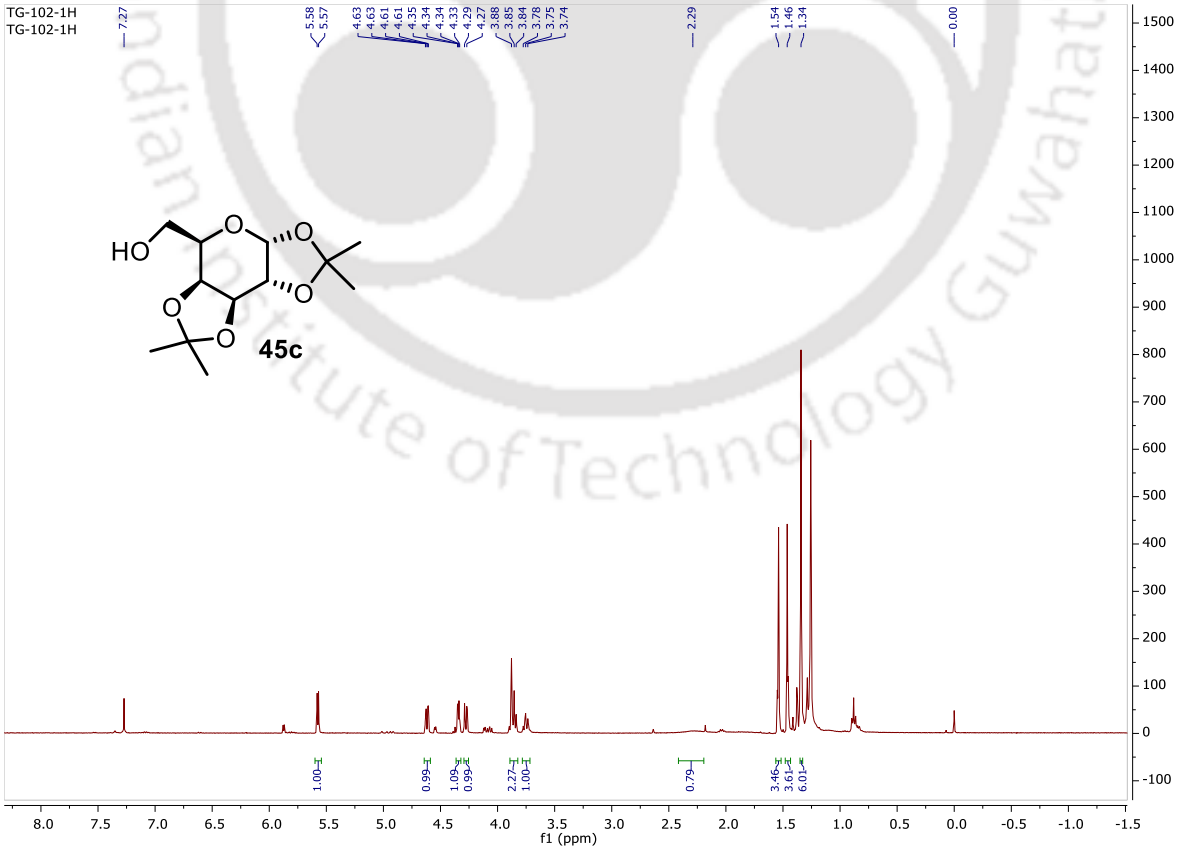


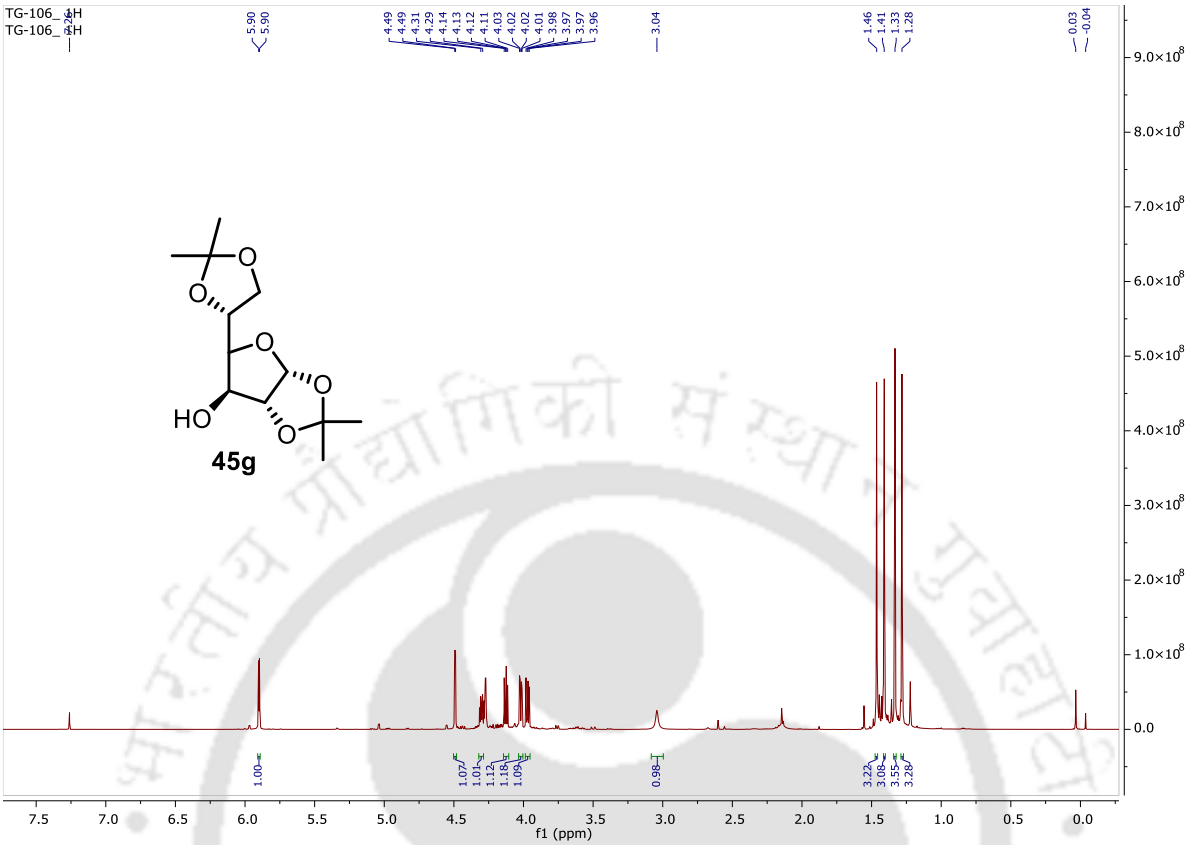


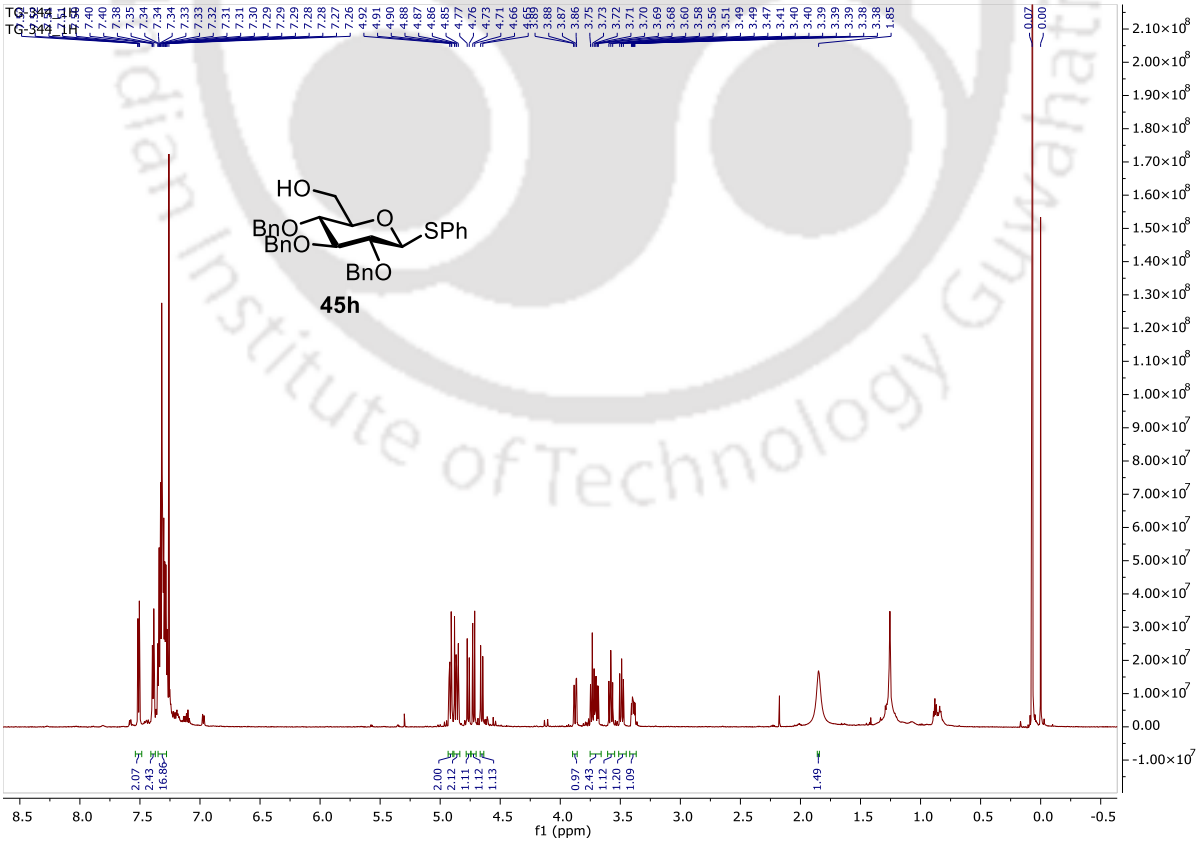


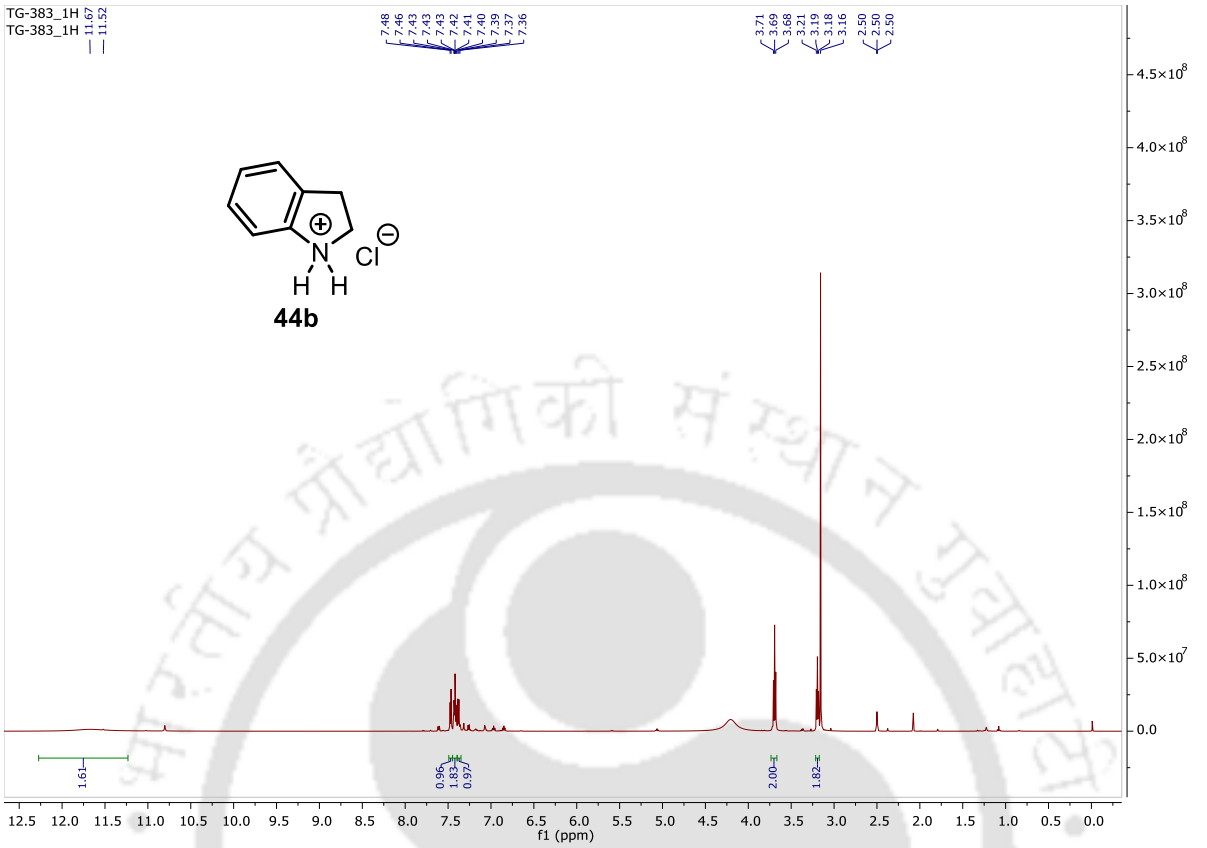


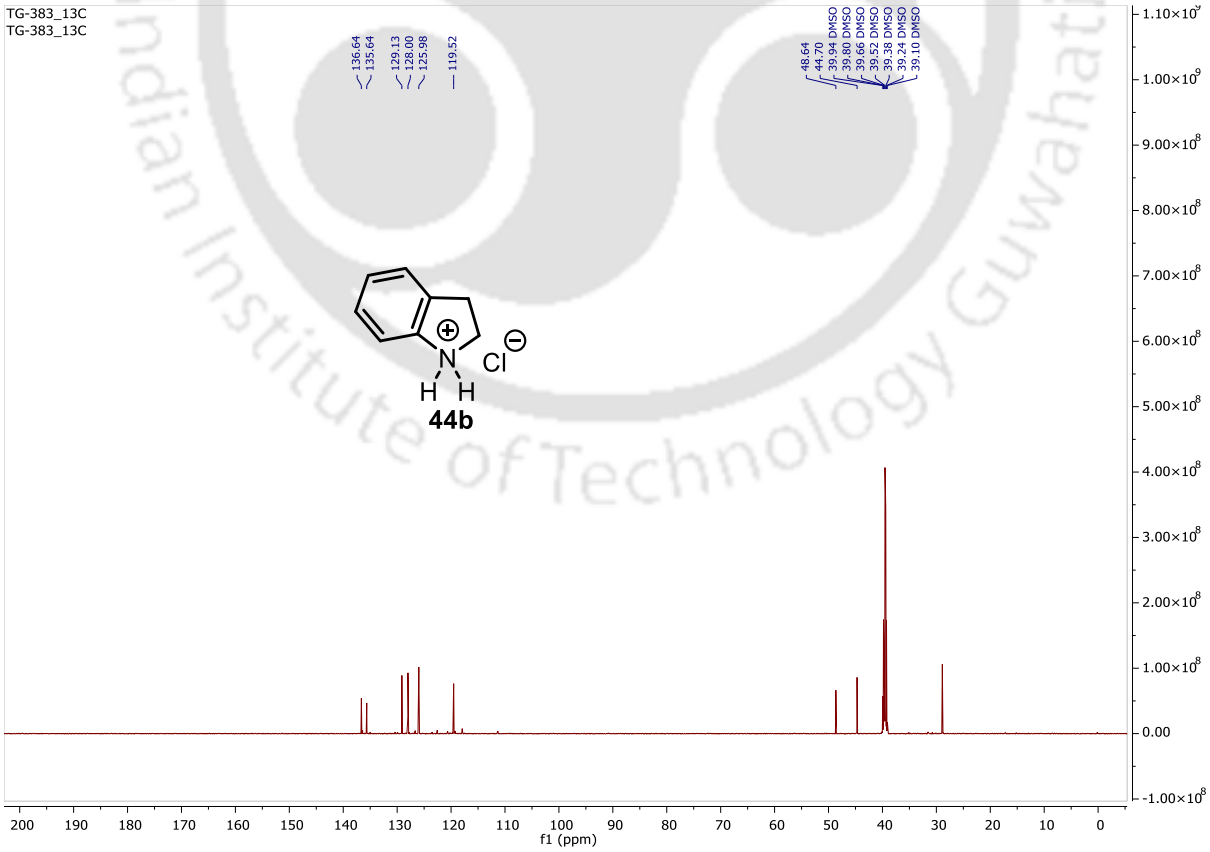


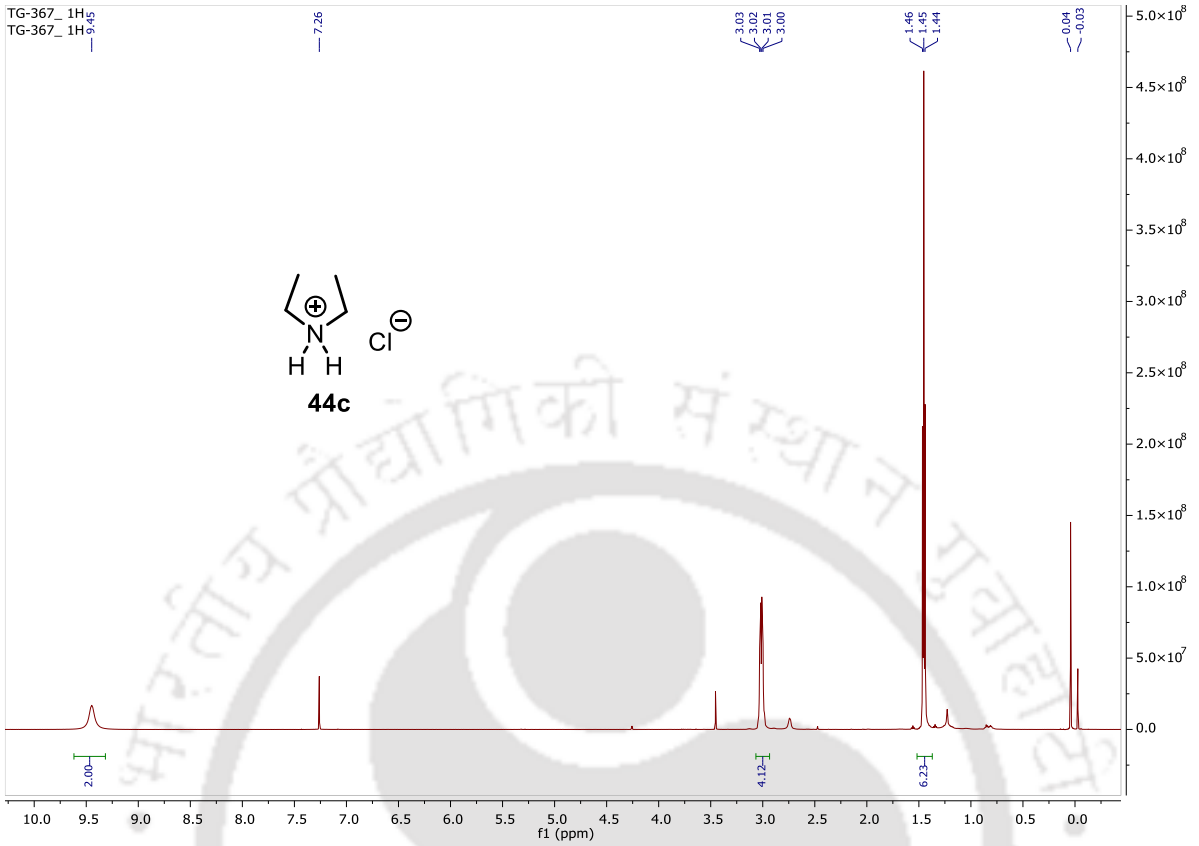


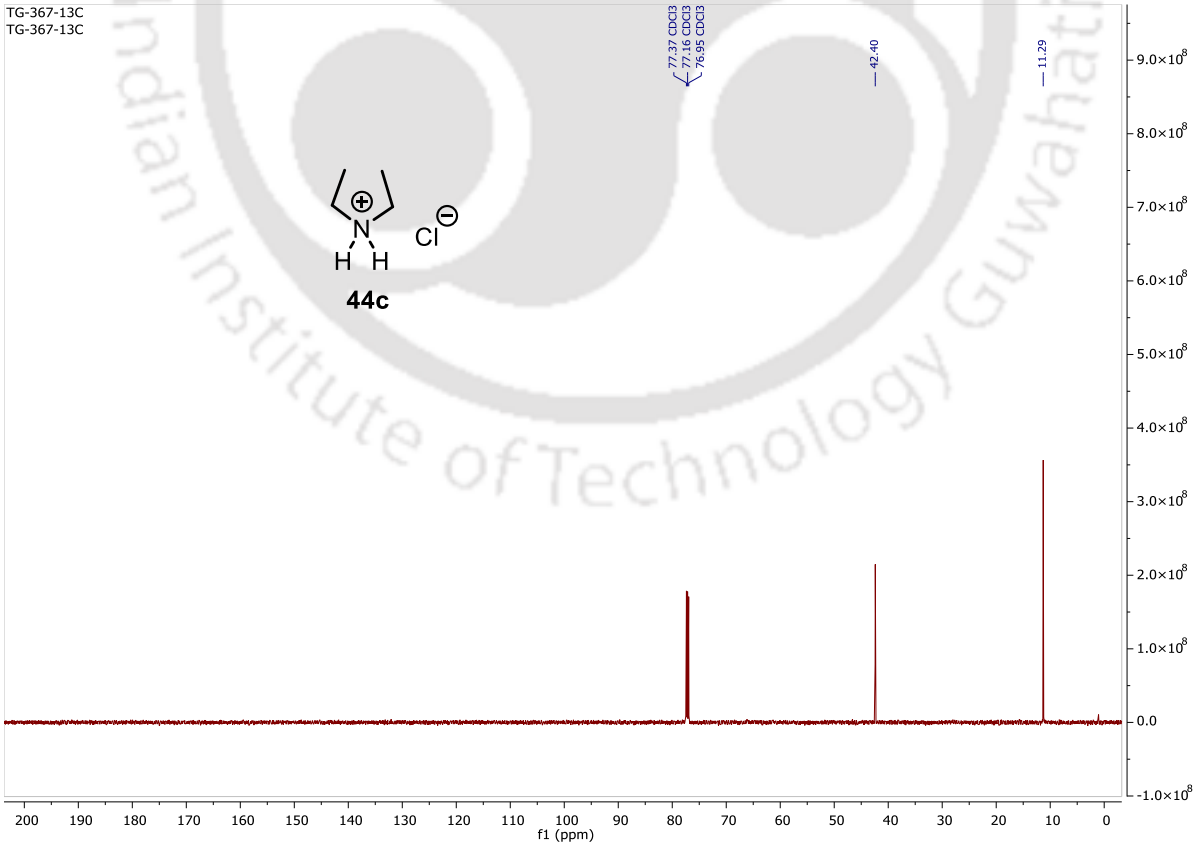


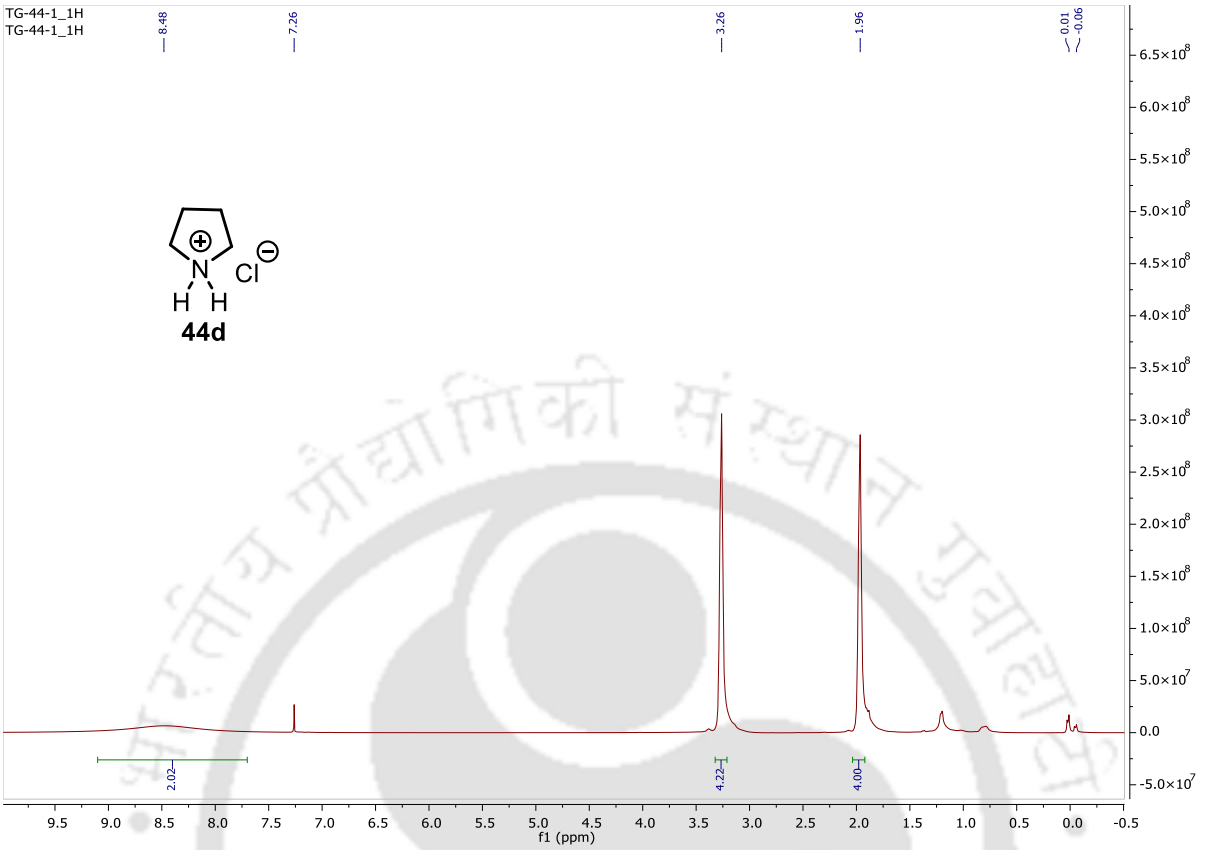


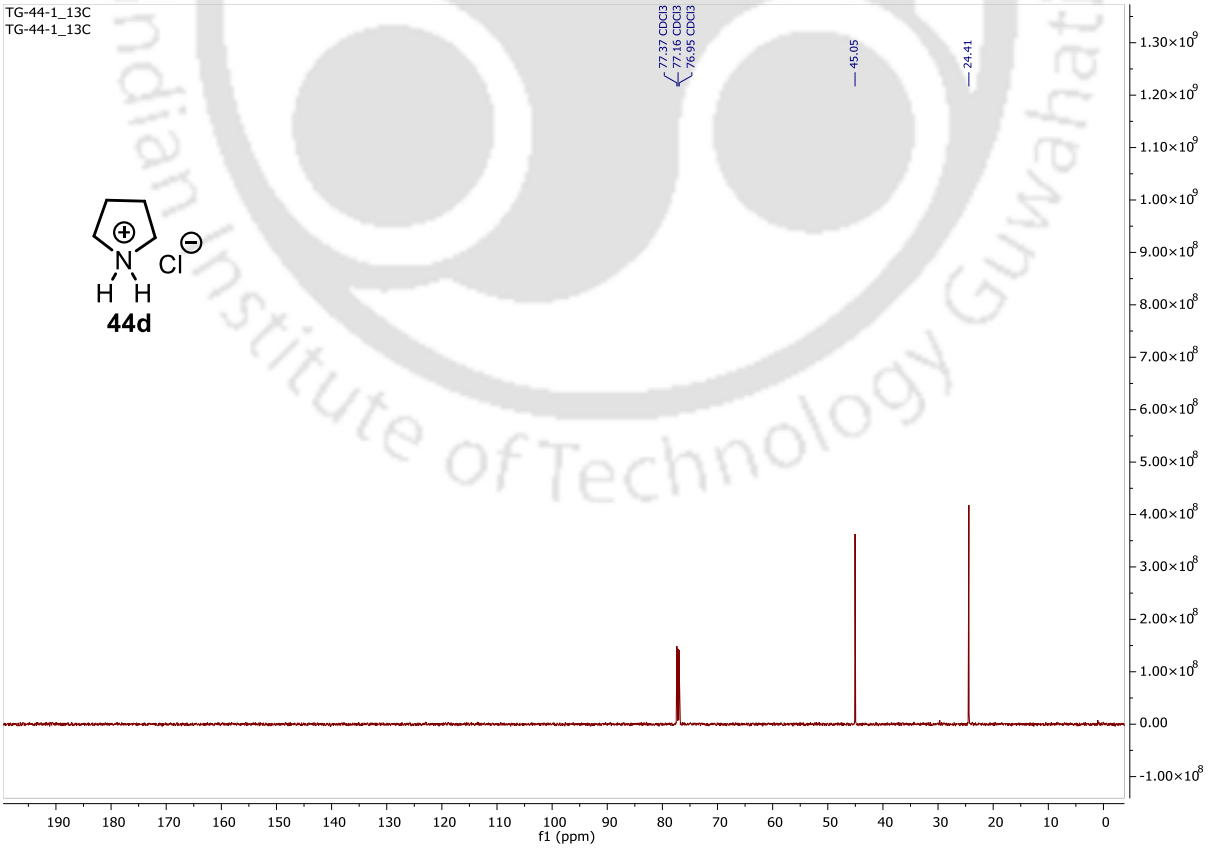


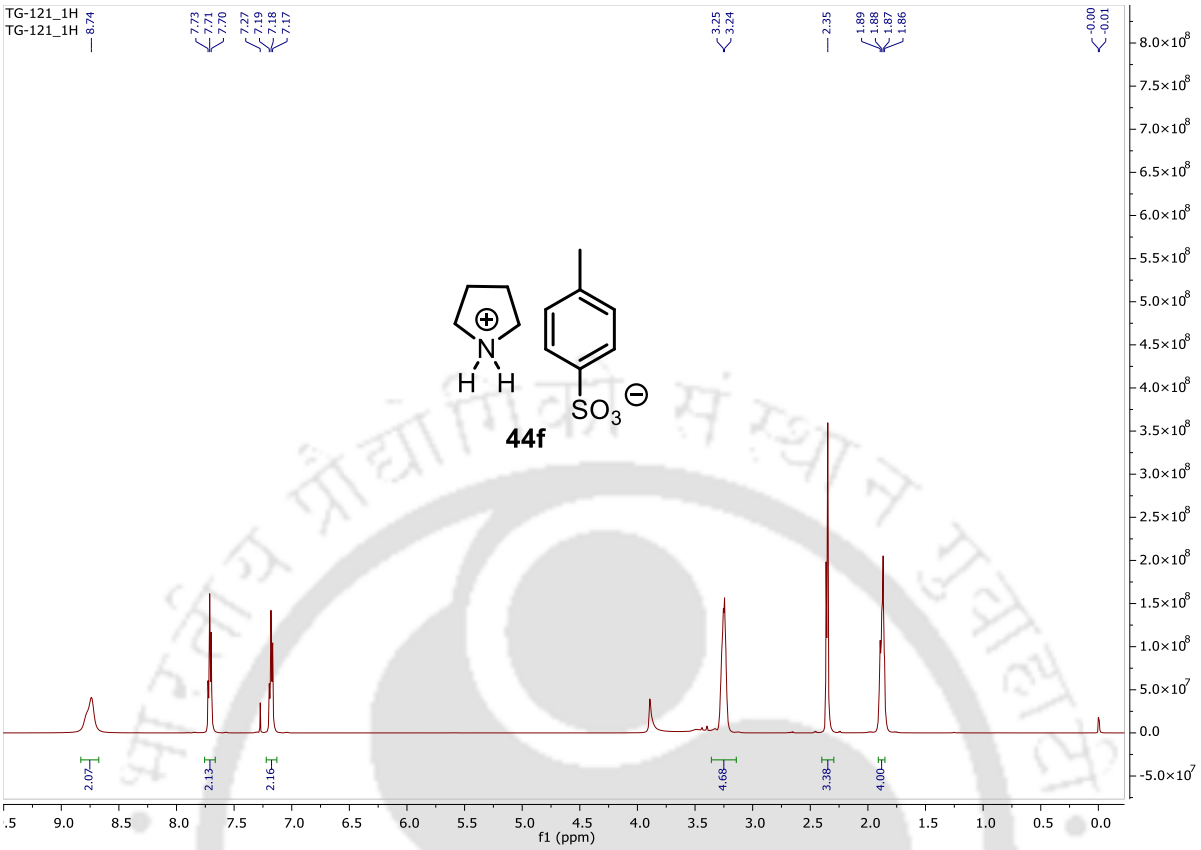


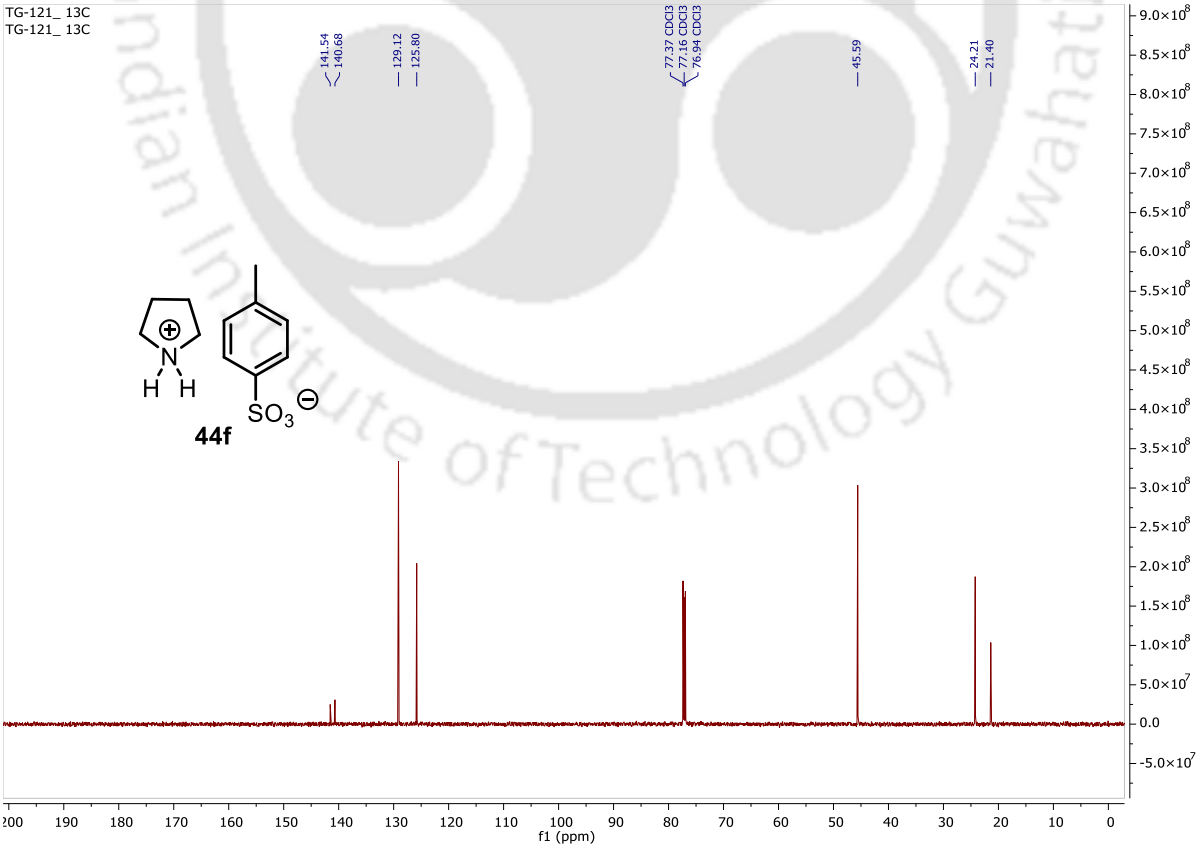


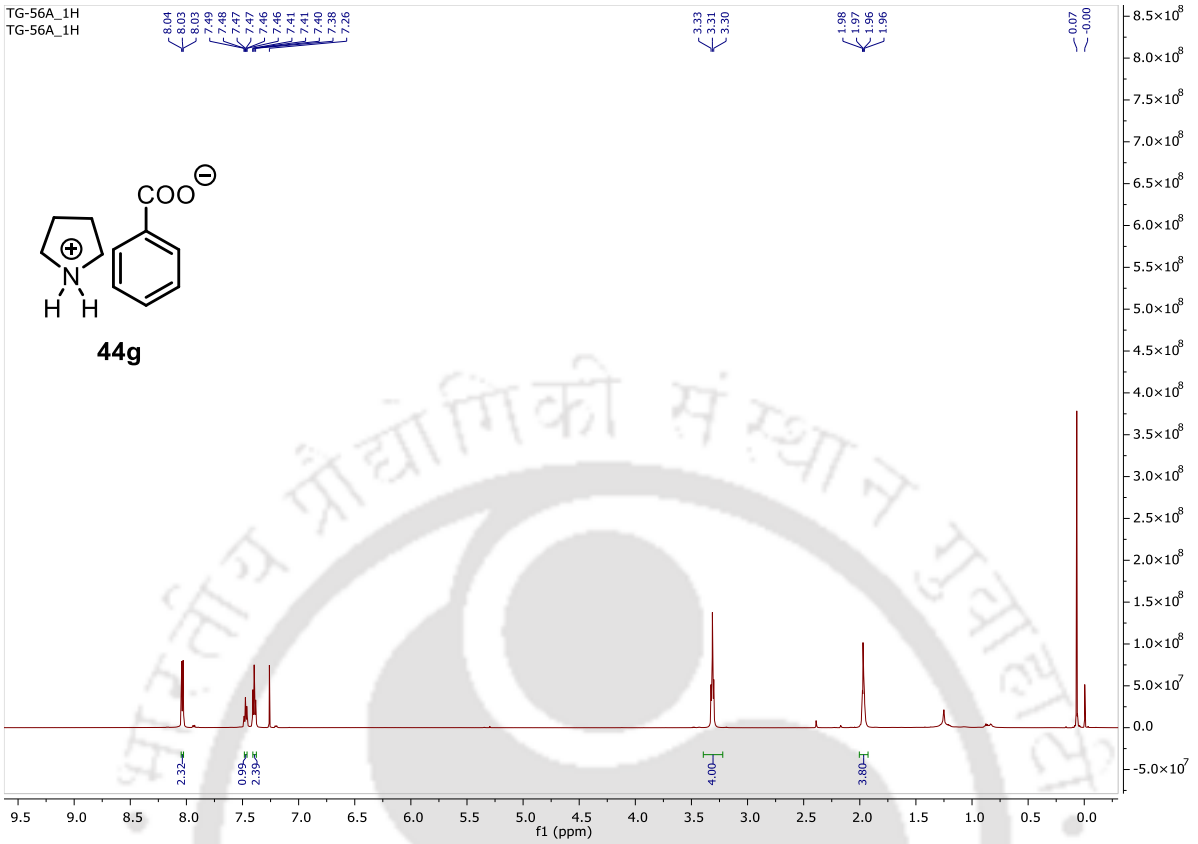


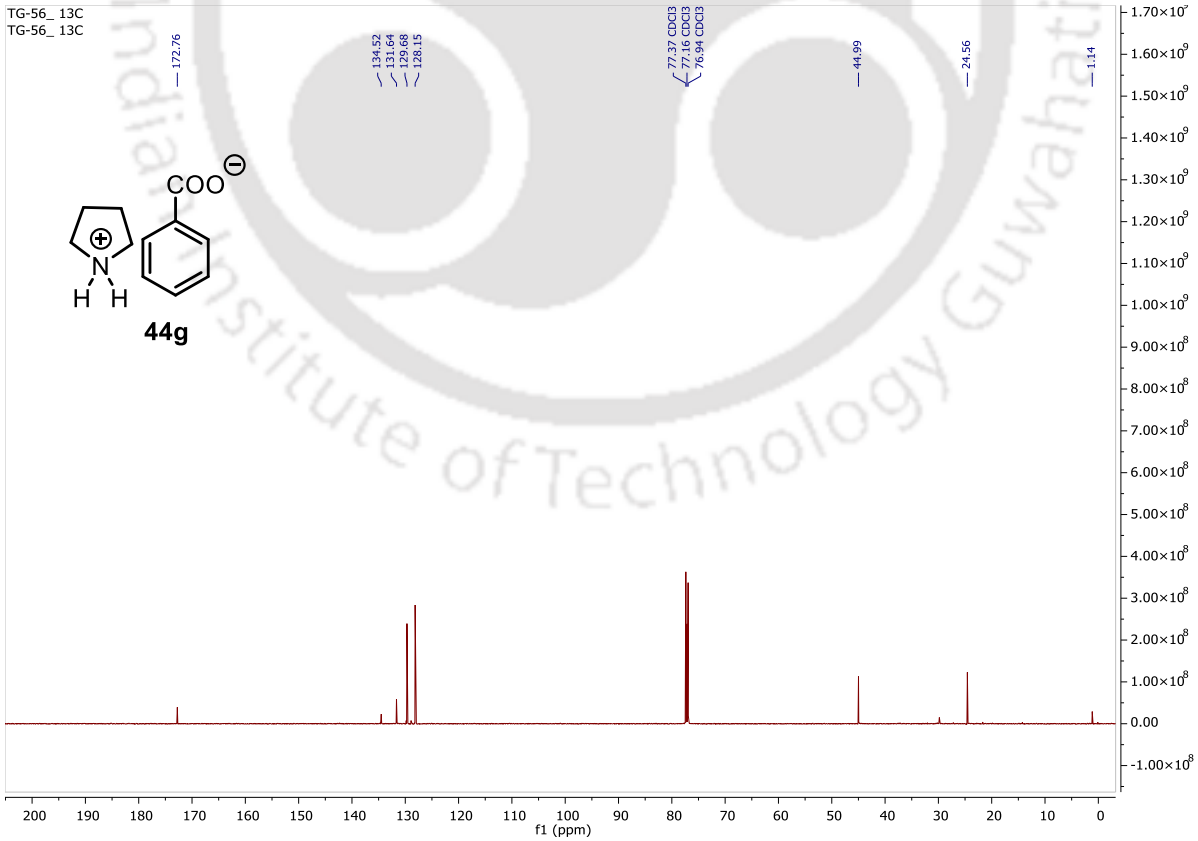


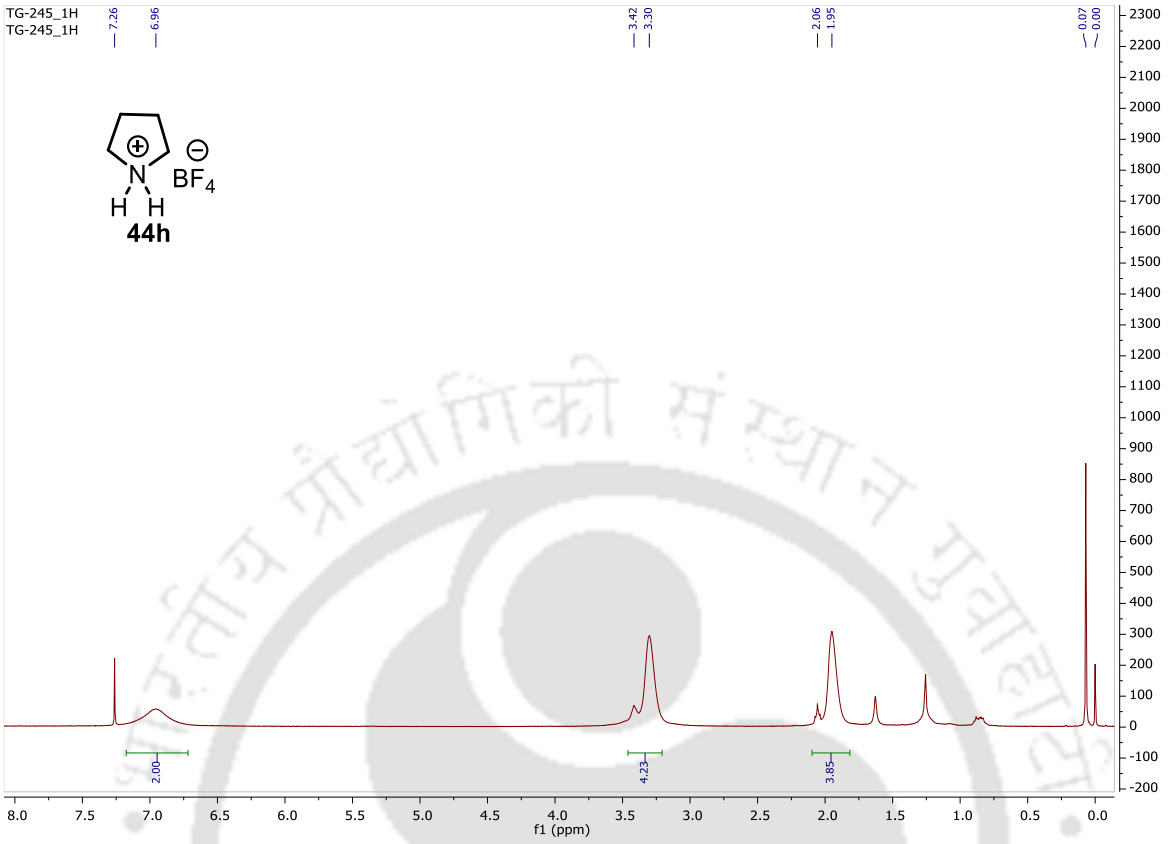


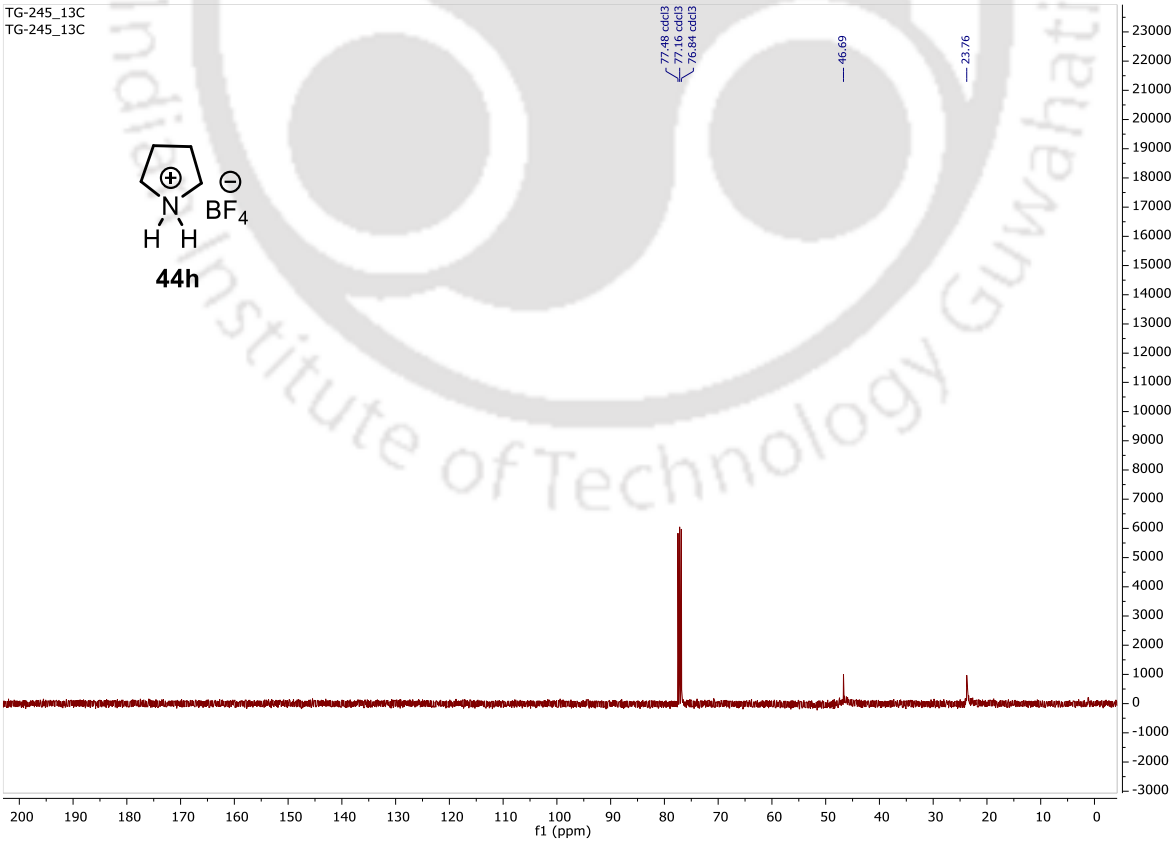


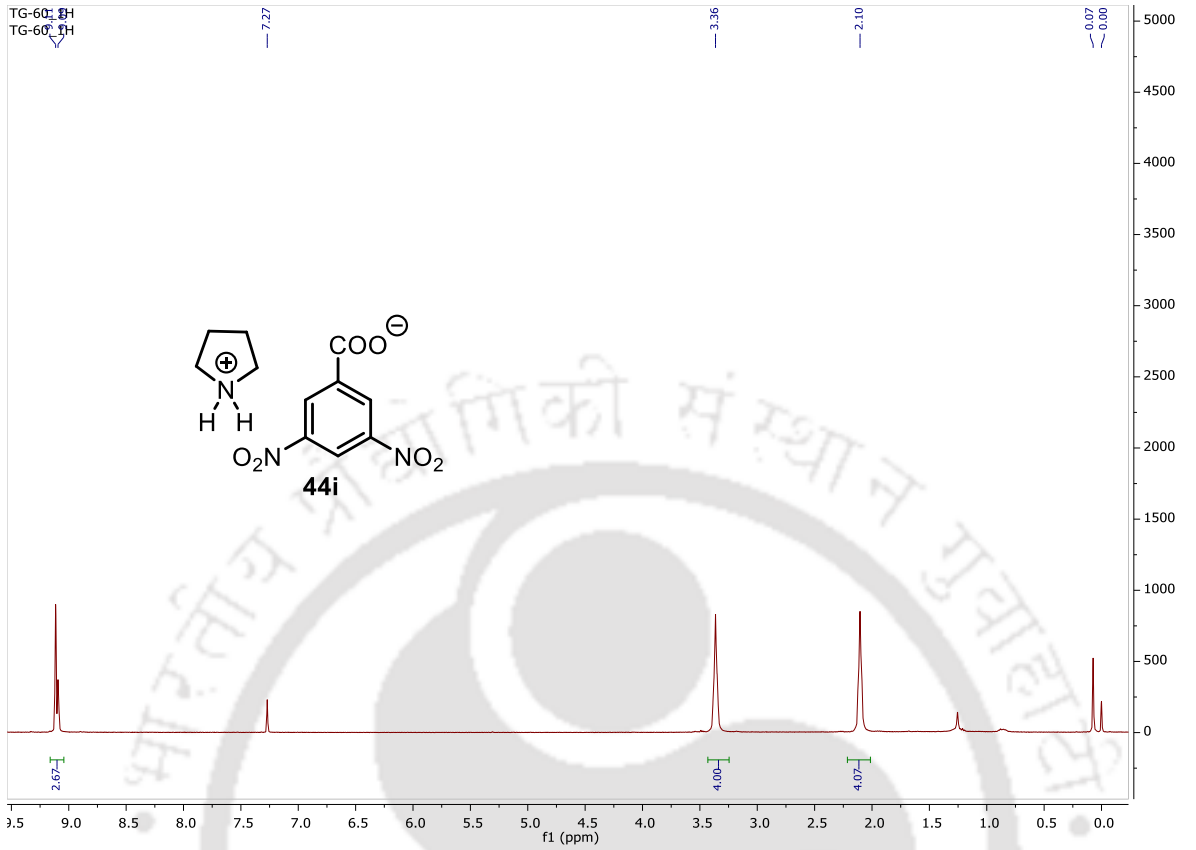


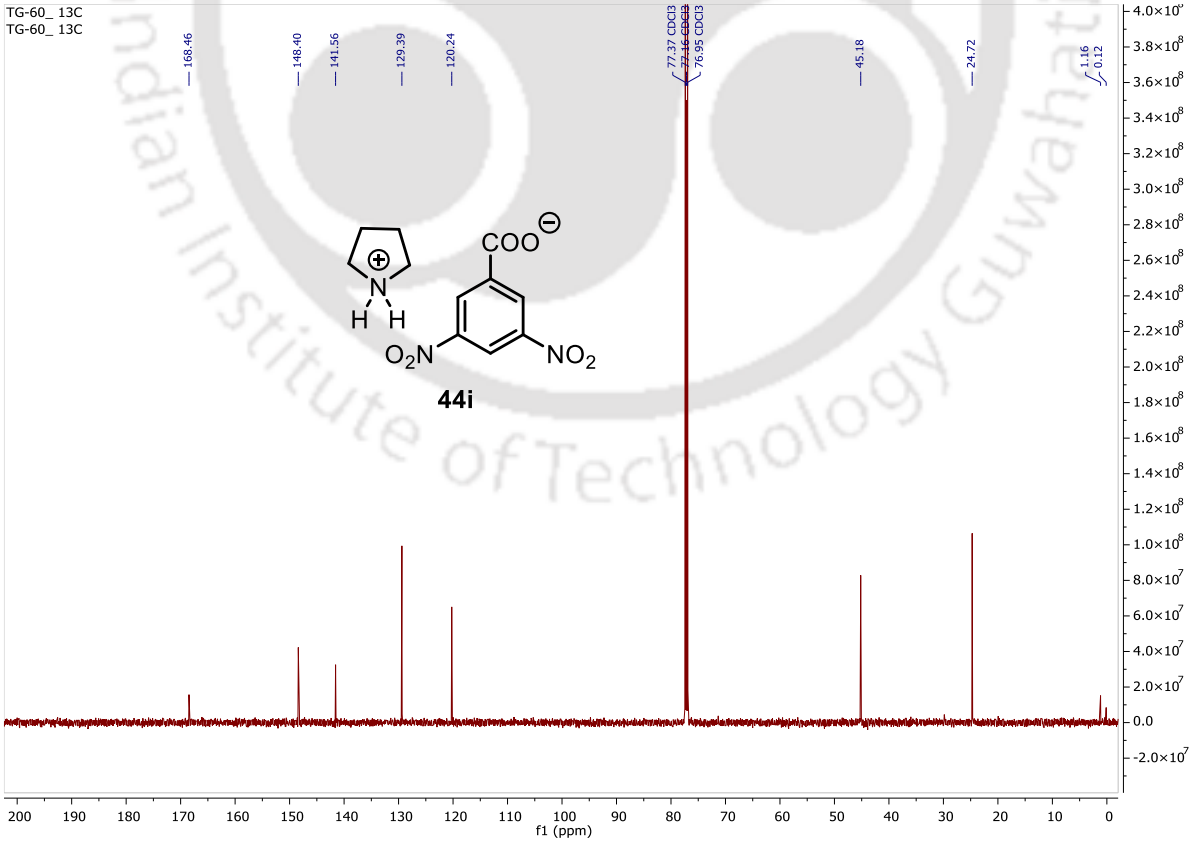


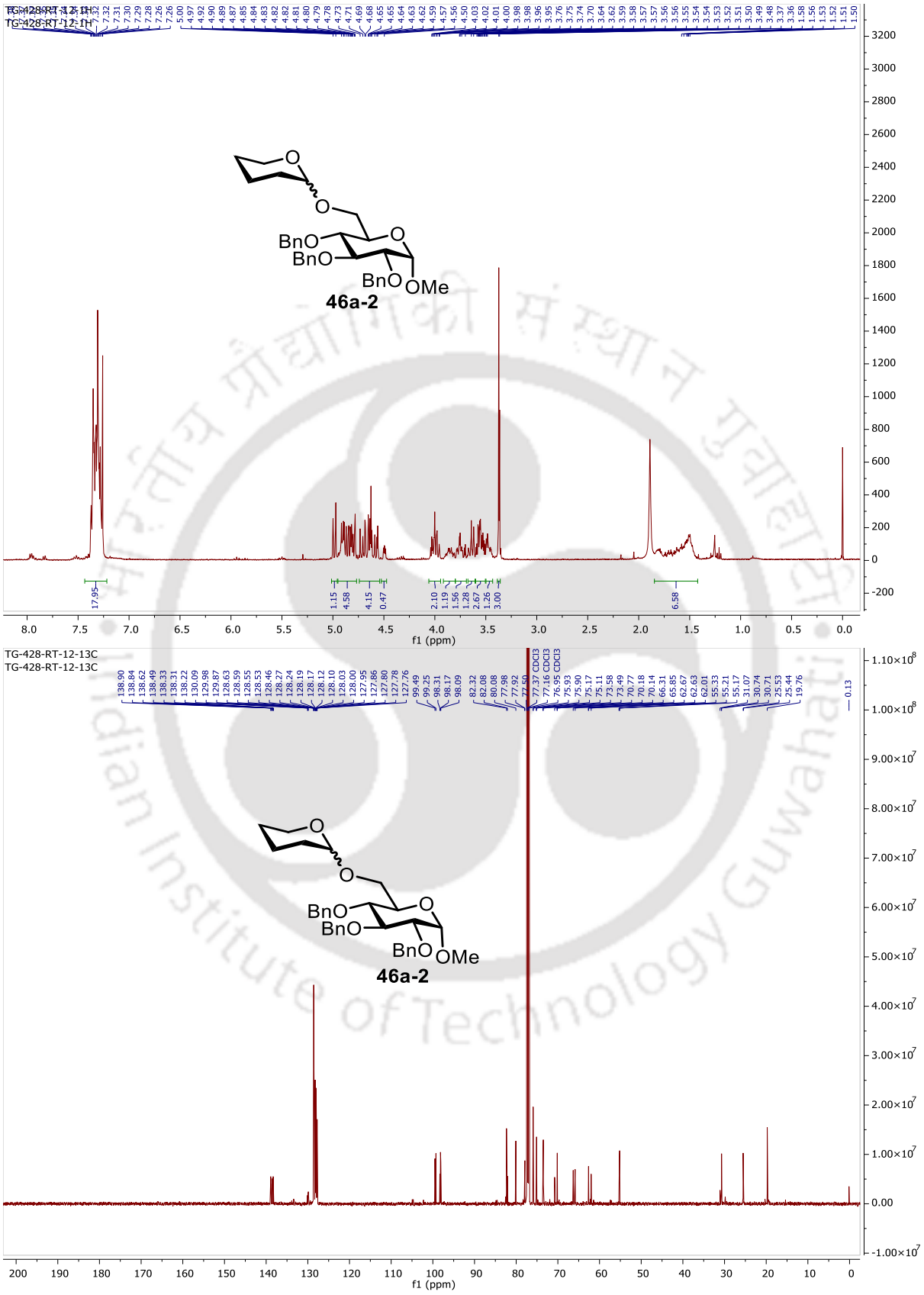




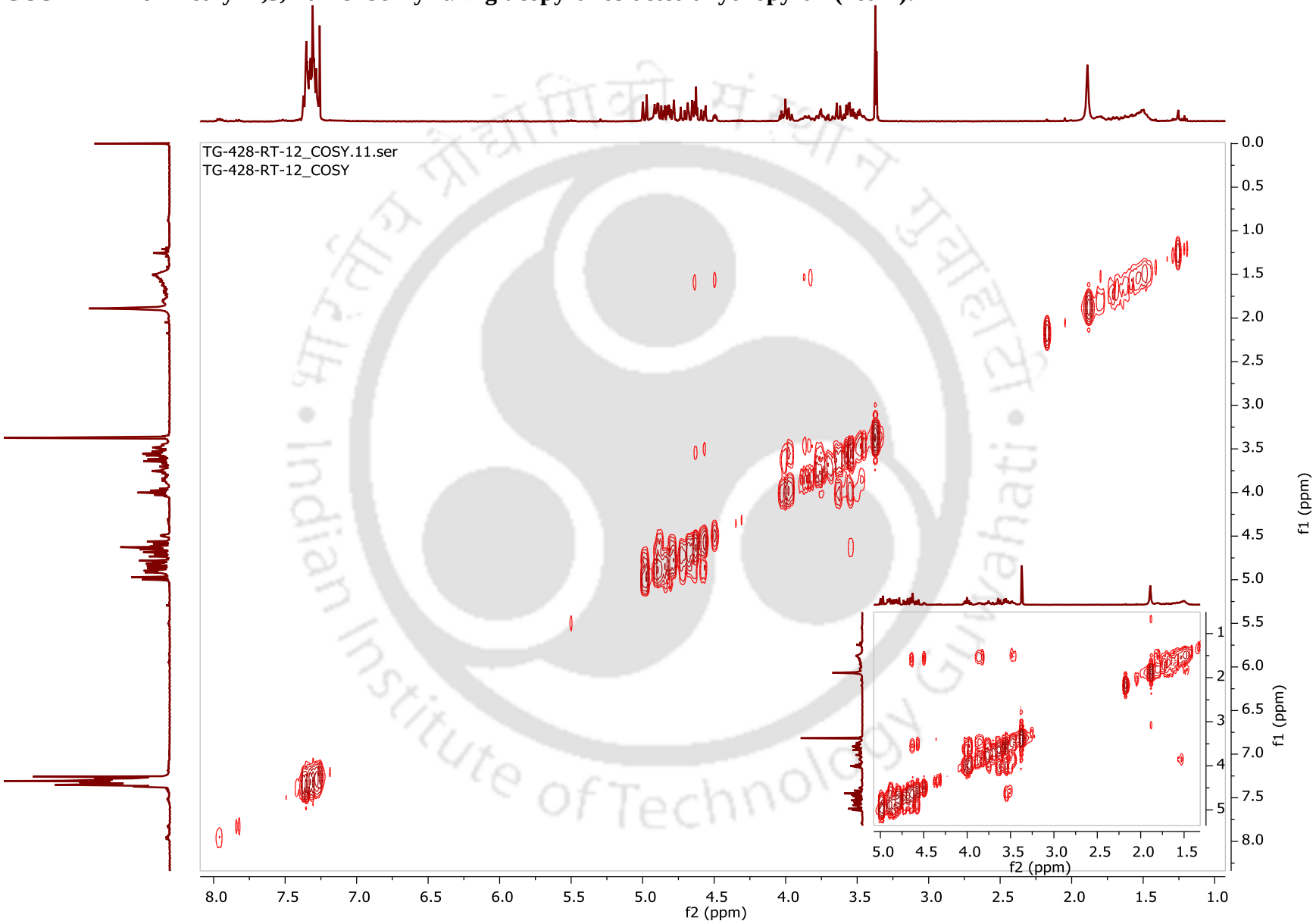


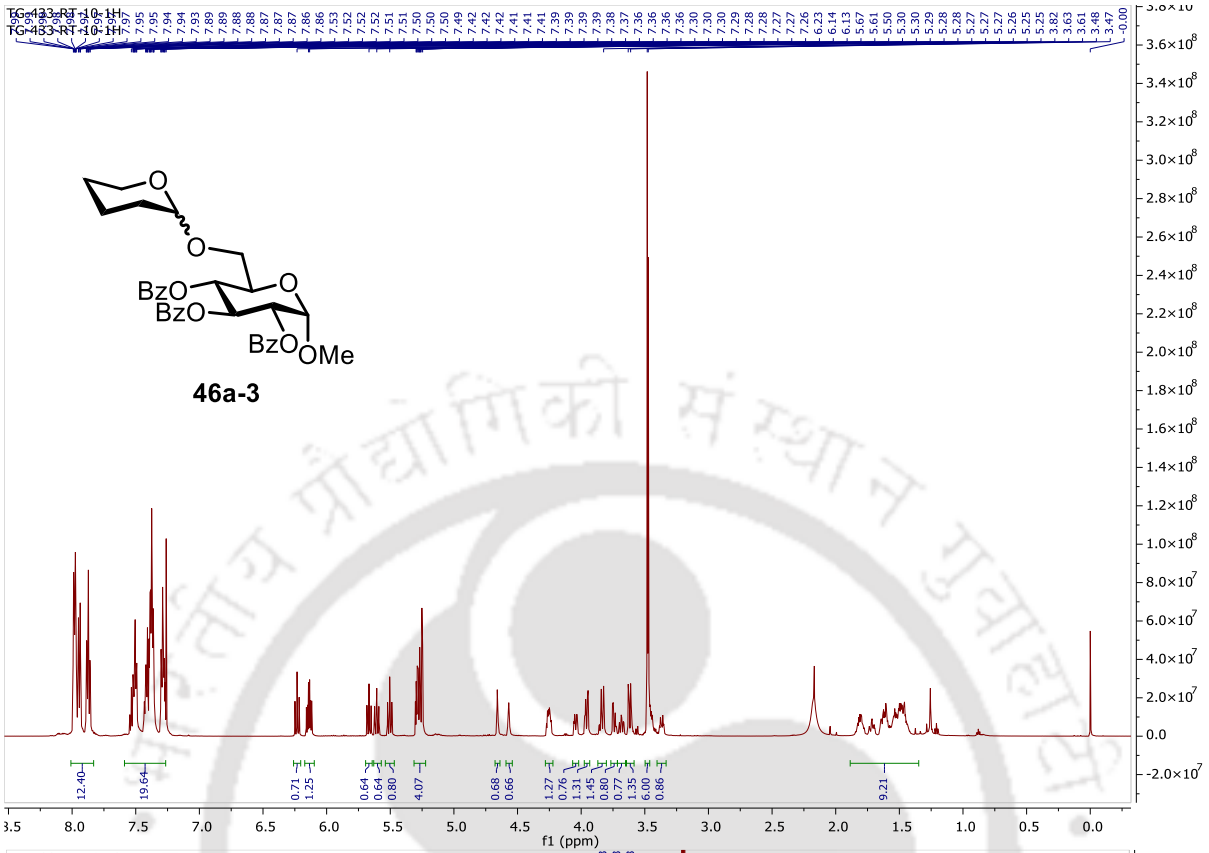


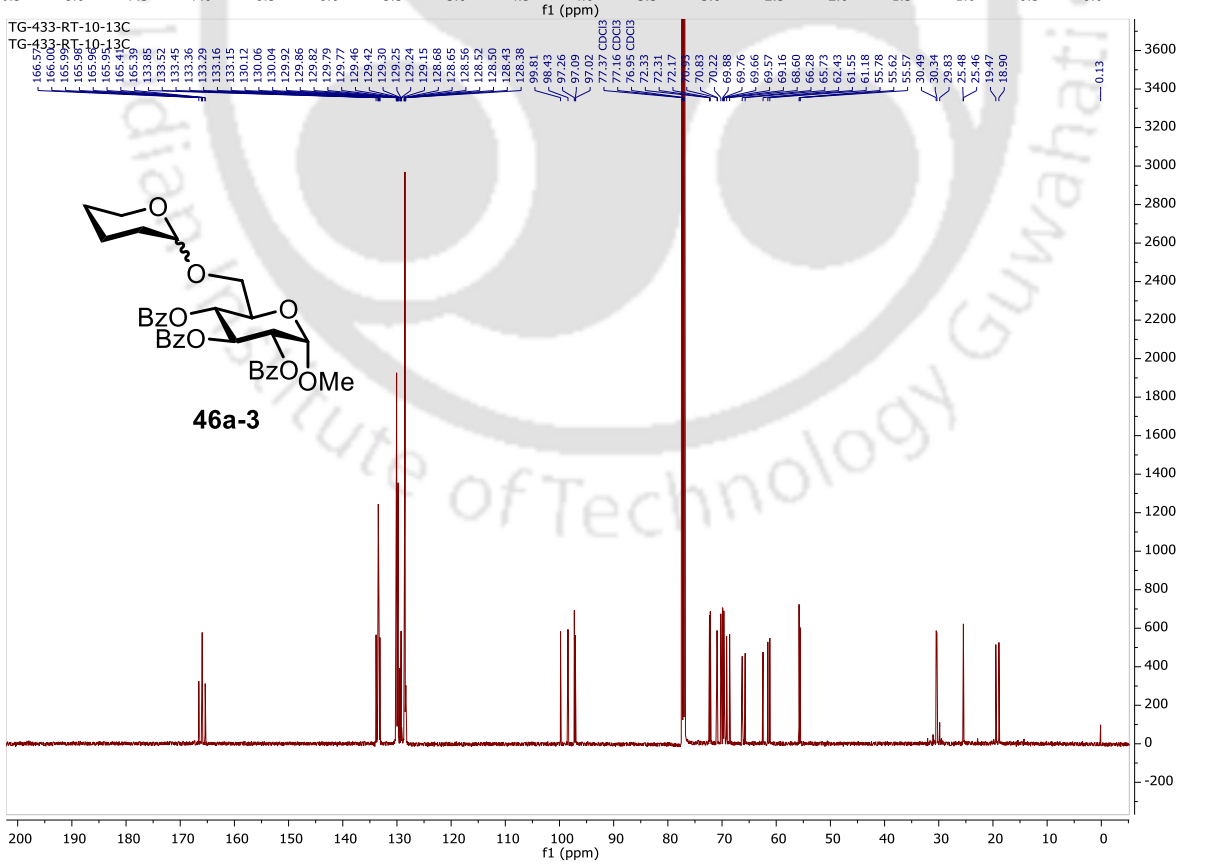




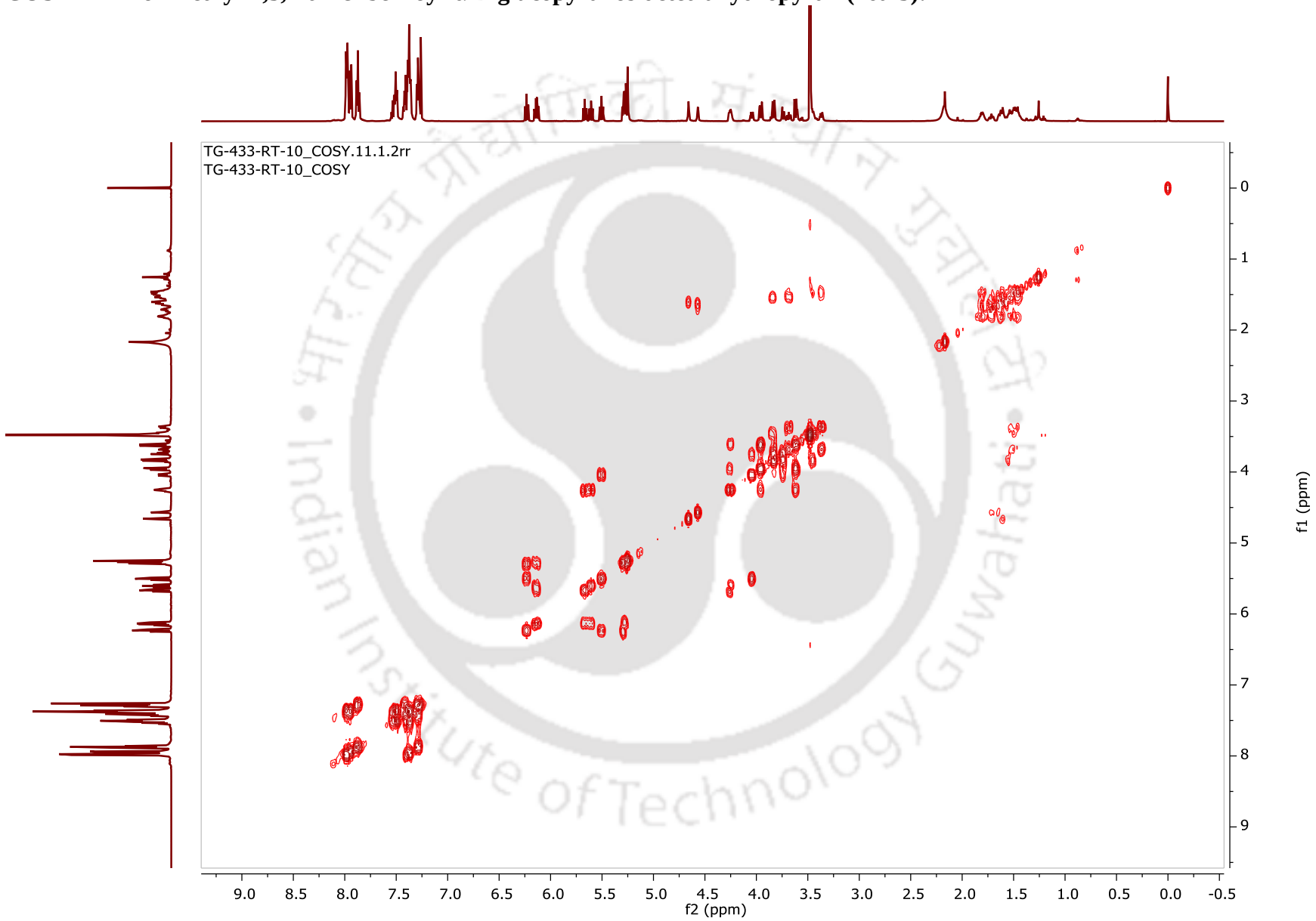
COSY NMR of Methyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranosidetetrahydropyran (46a-2):

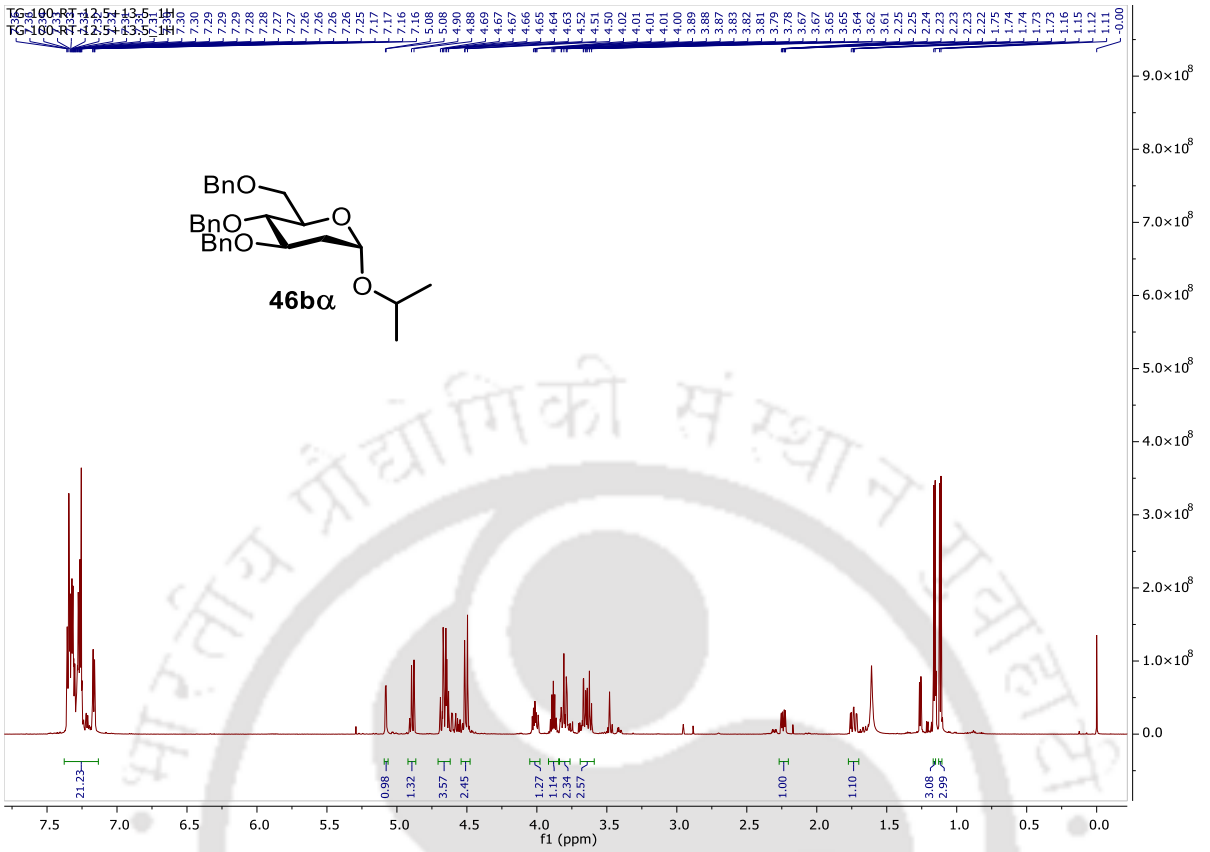


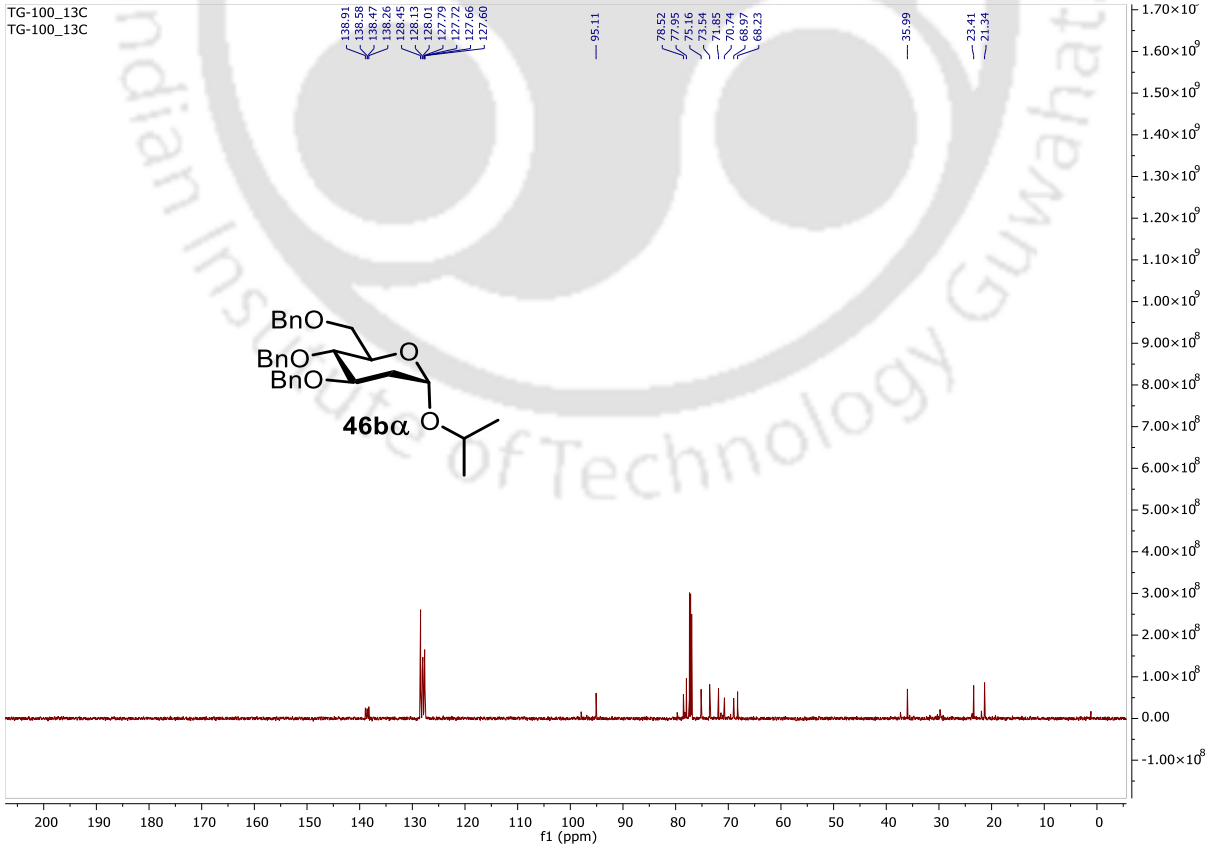


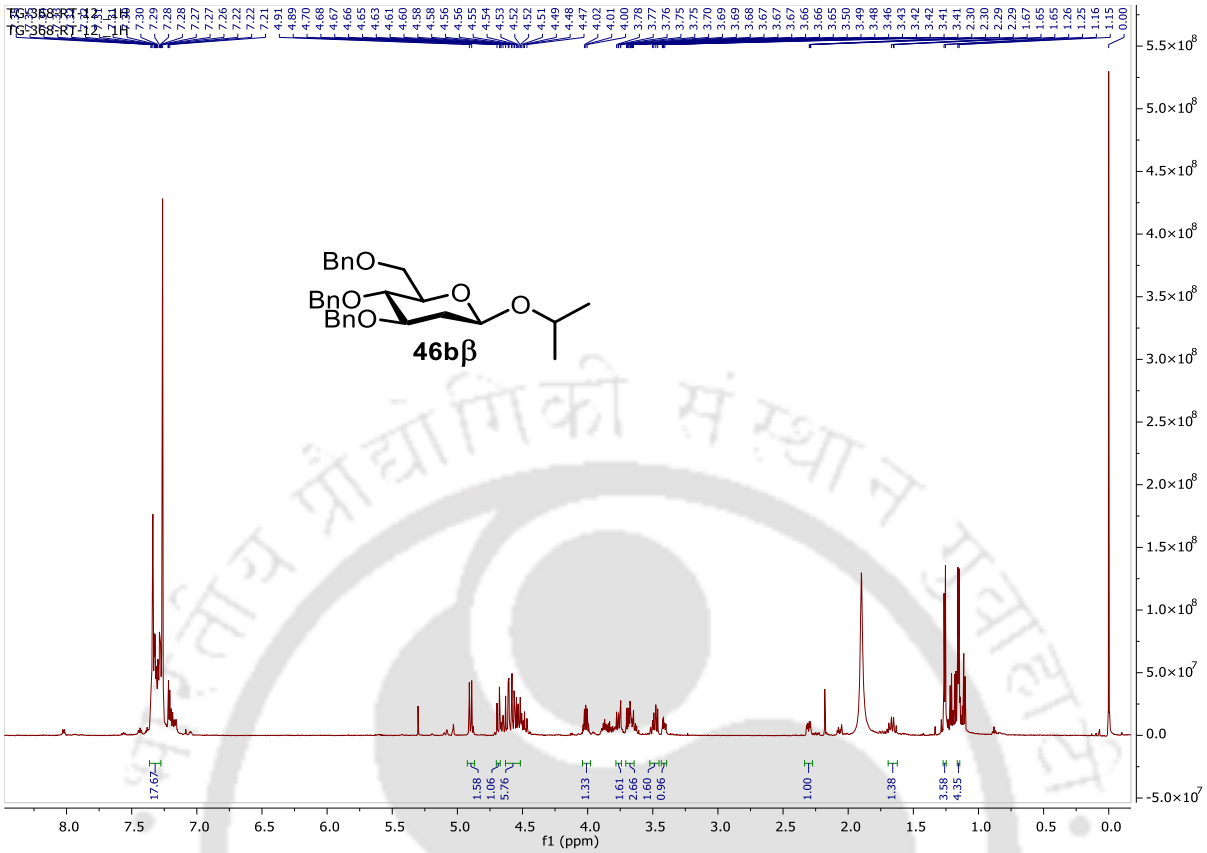


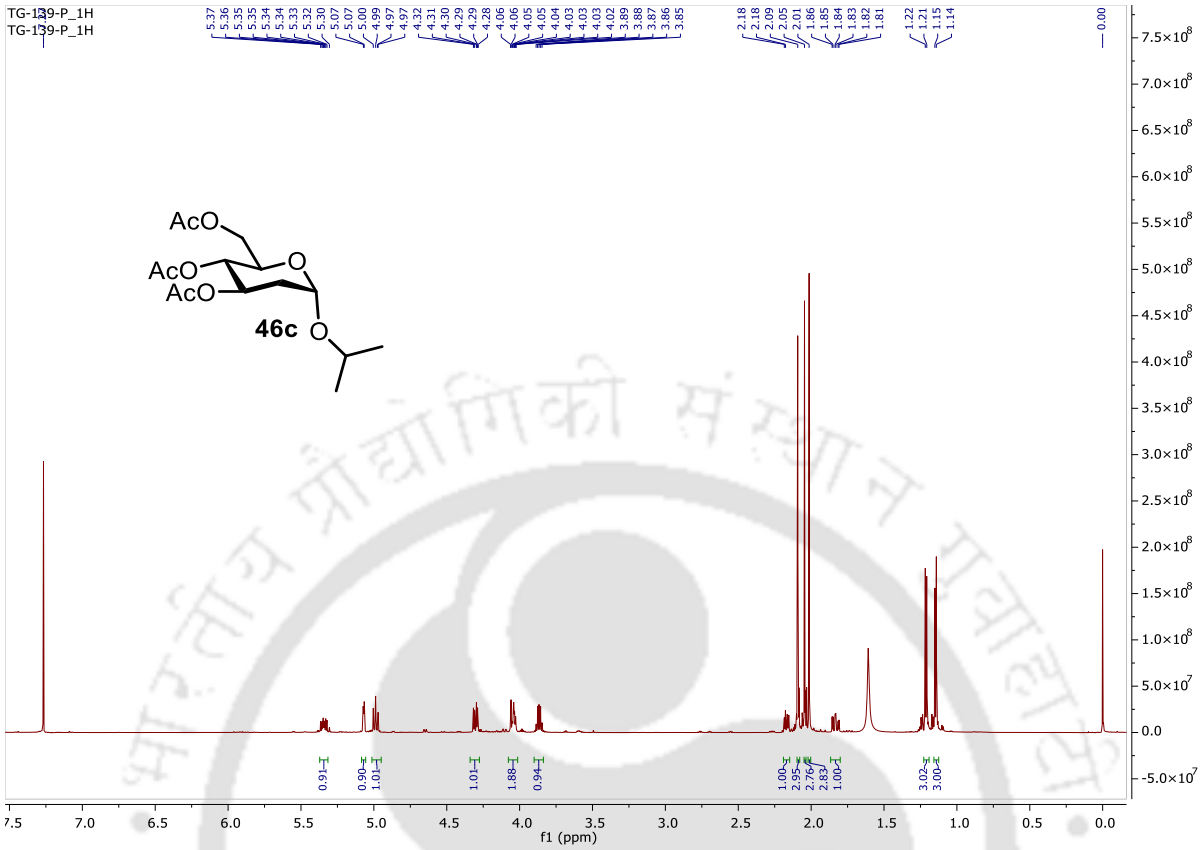
COSY NMR of Methyl-2,3,4-tri-*O*-benzoyl-α-D-glucopyranosidetetrahydropyran (46a-3):

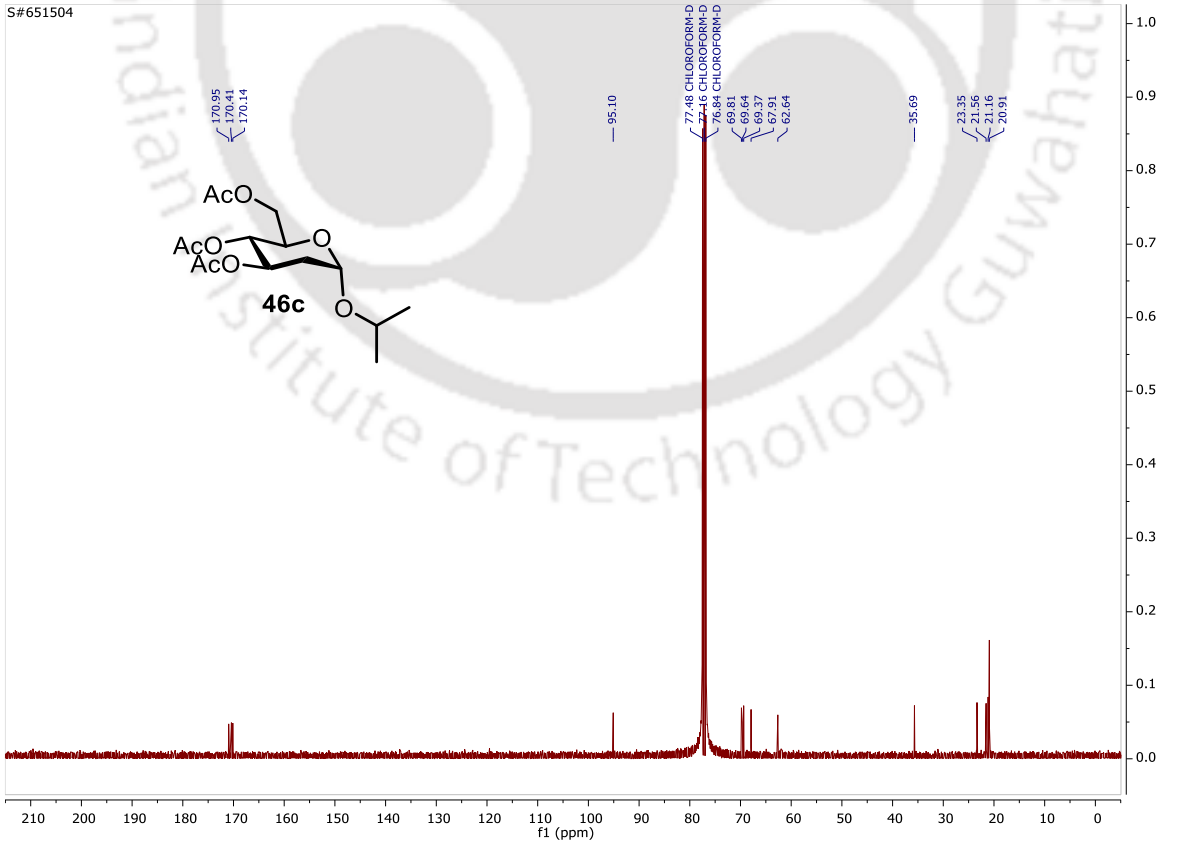


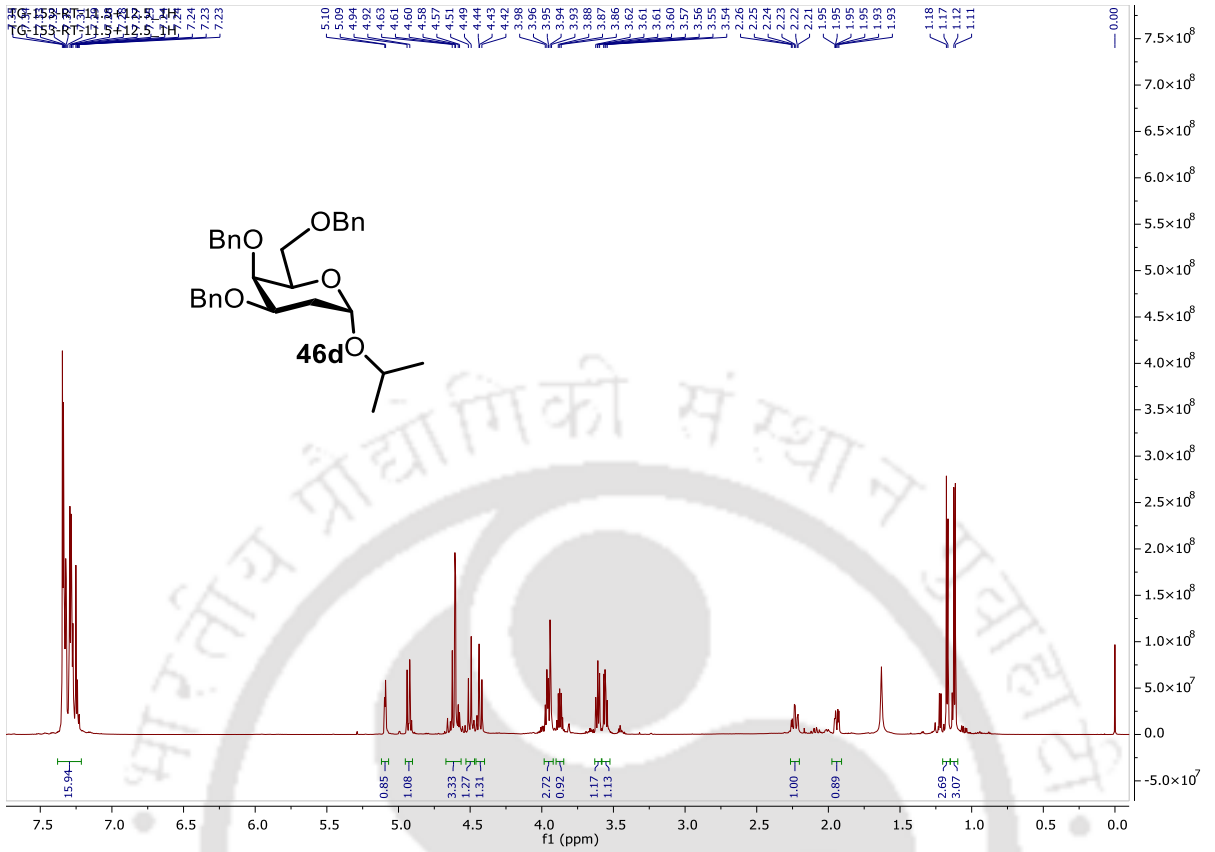


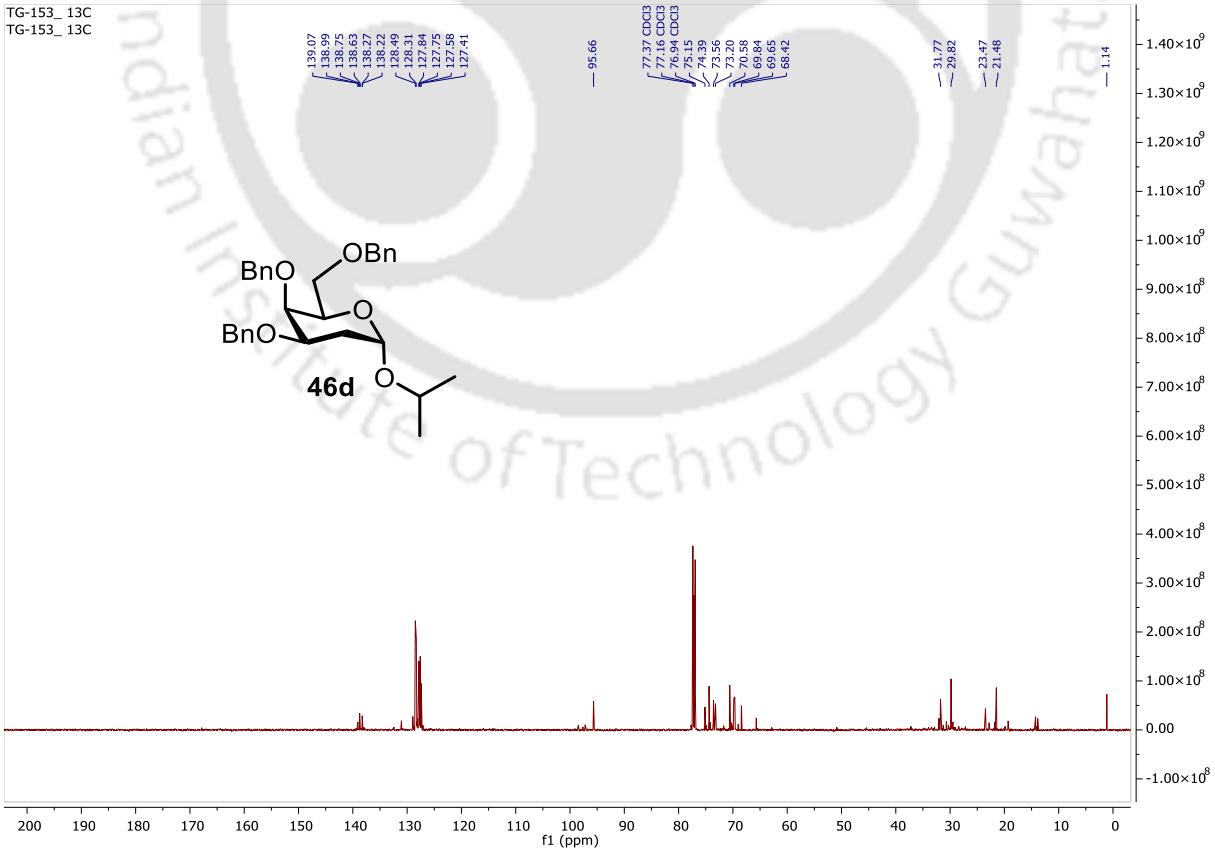


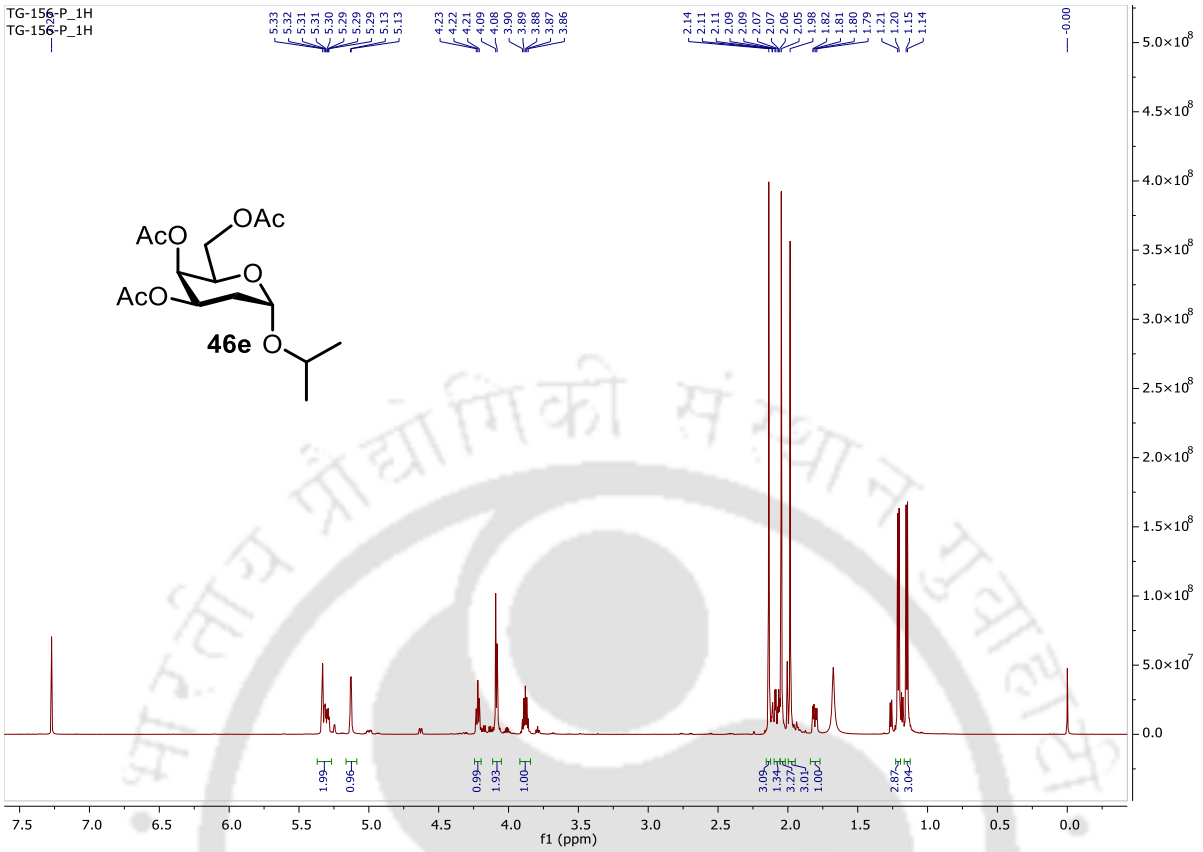


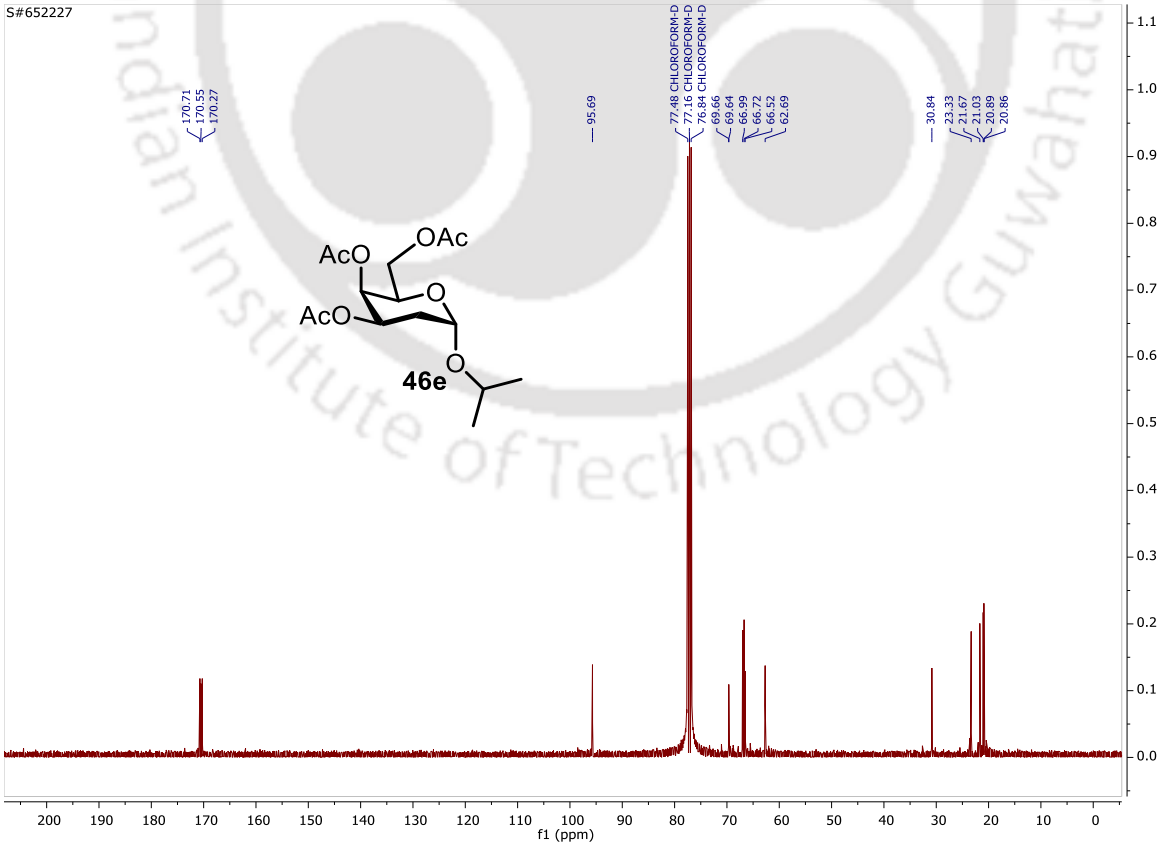


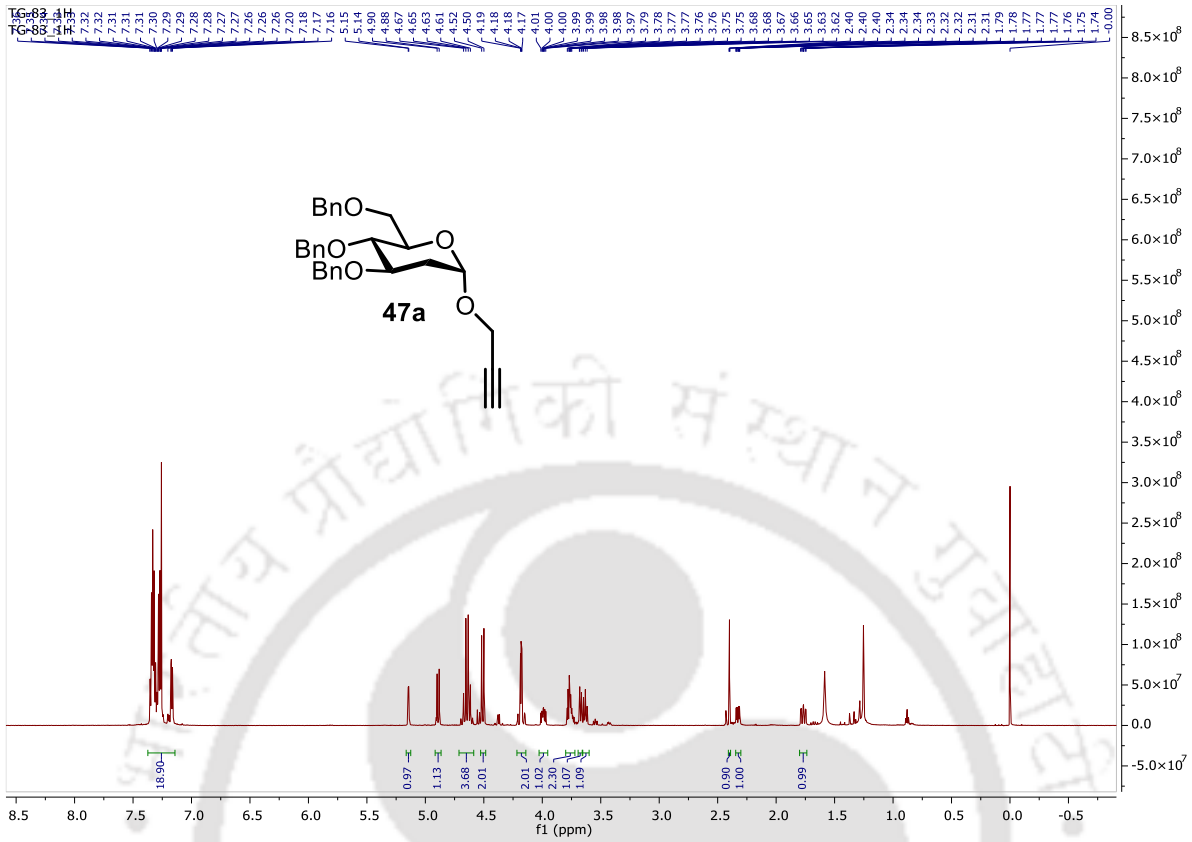




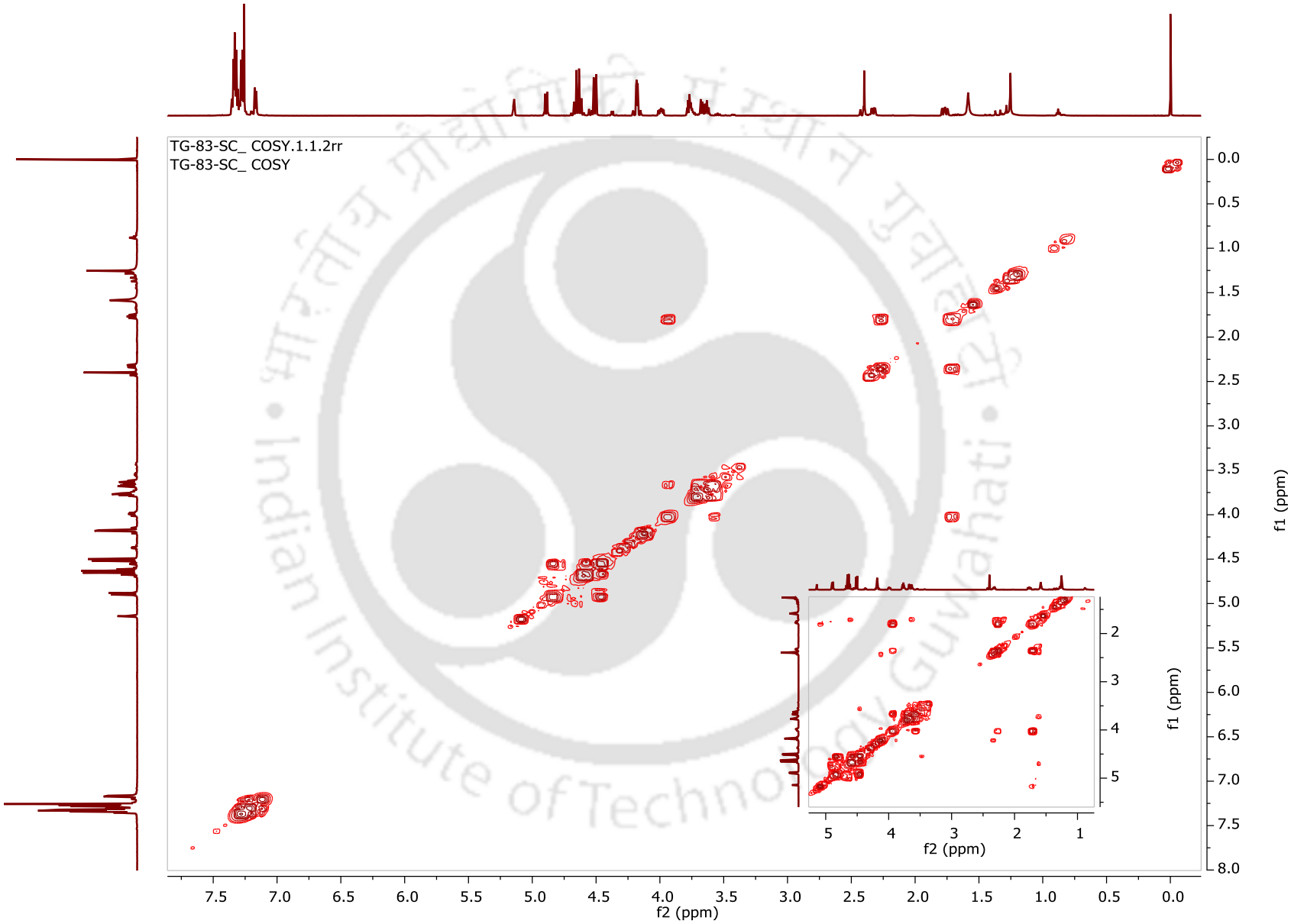


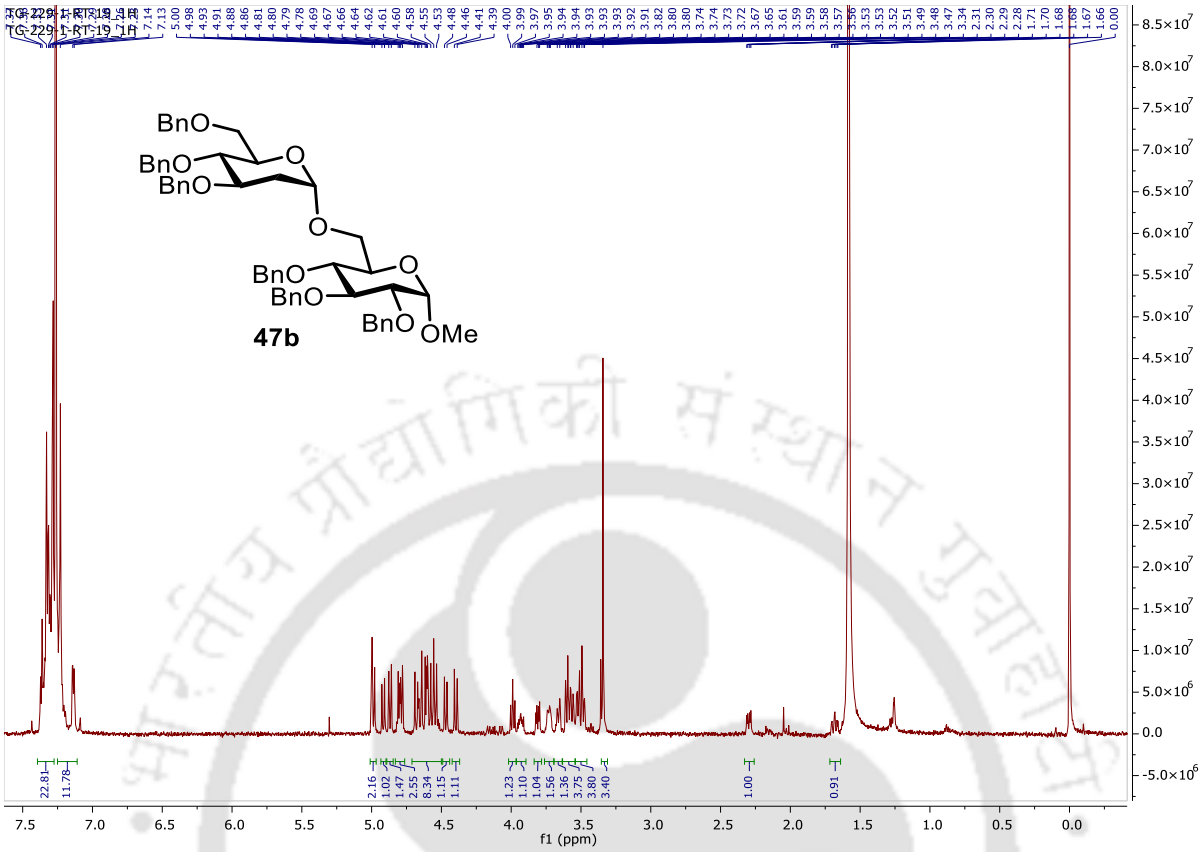


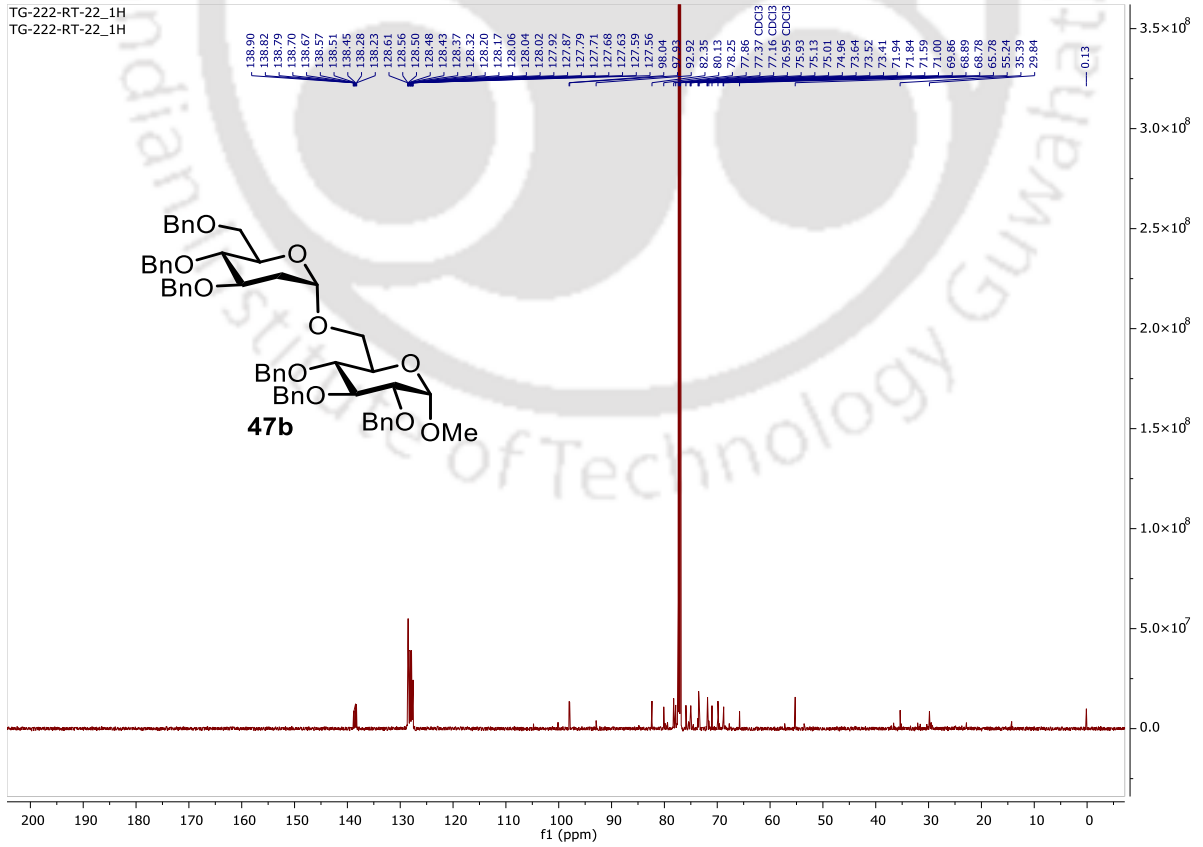


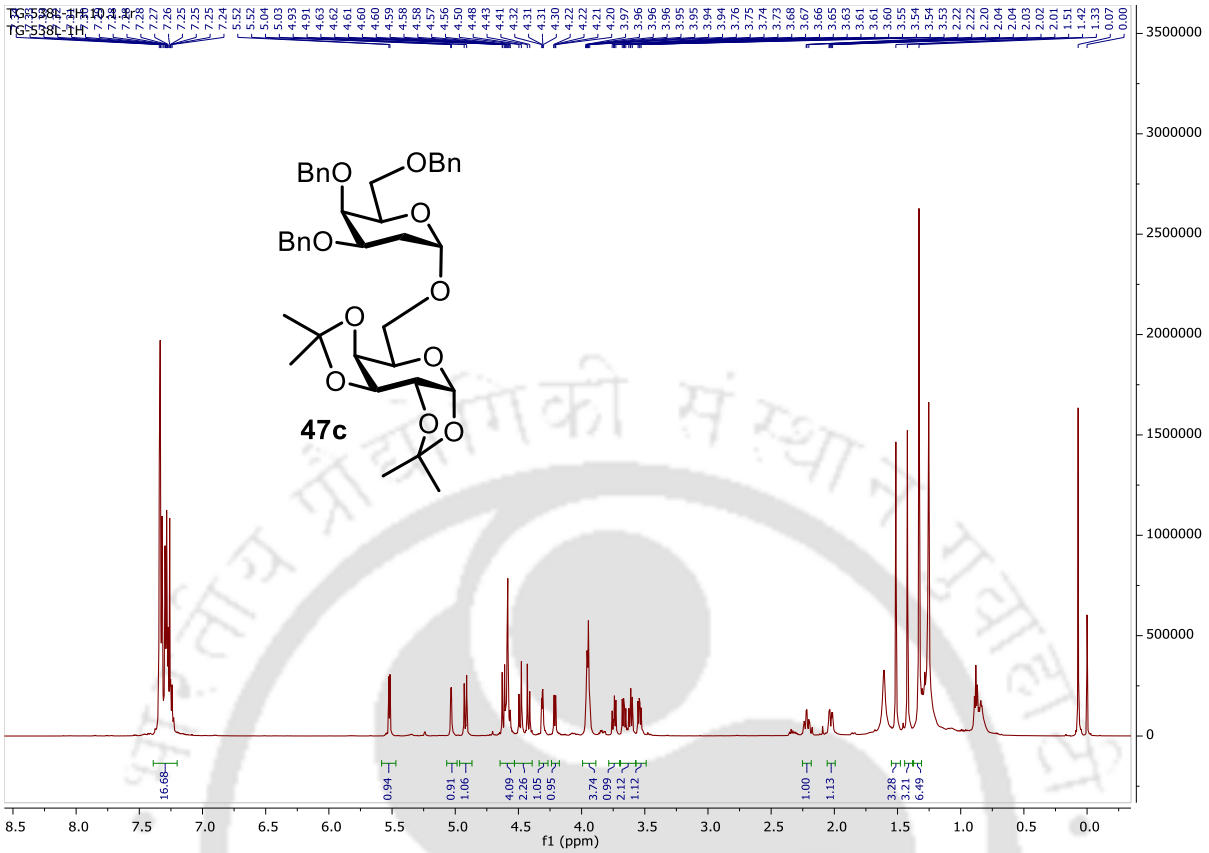


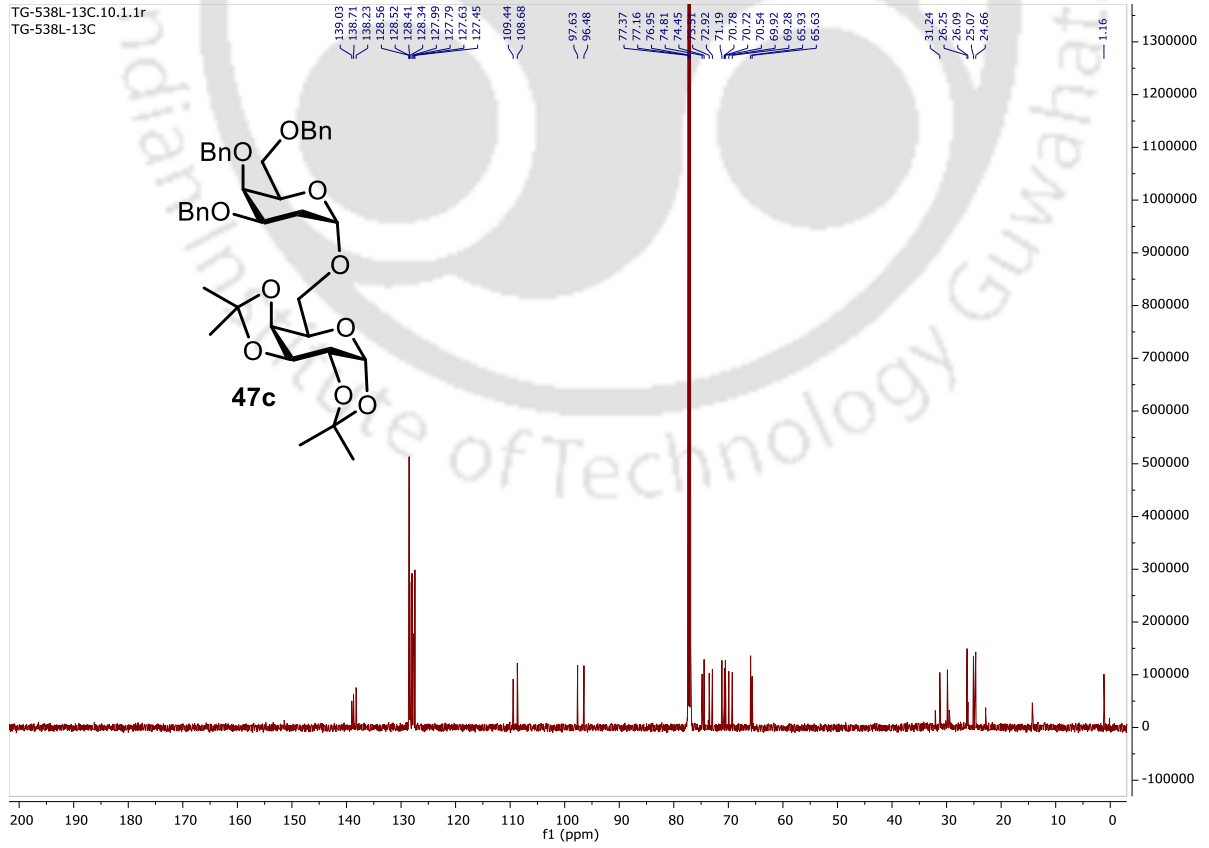
COSY NMR of Propargyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (47a):

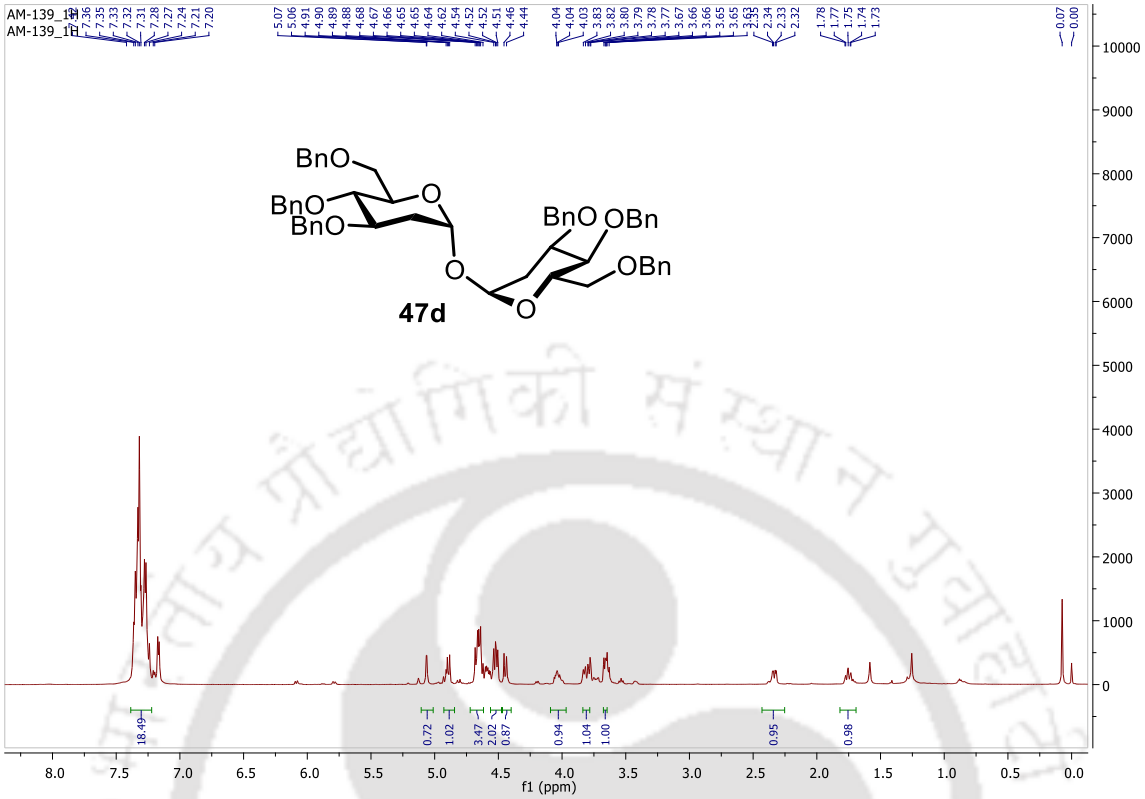


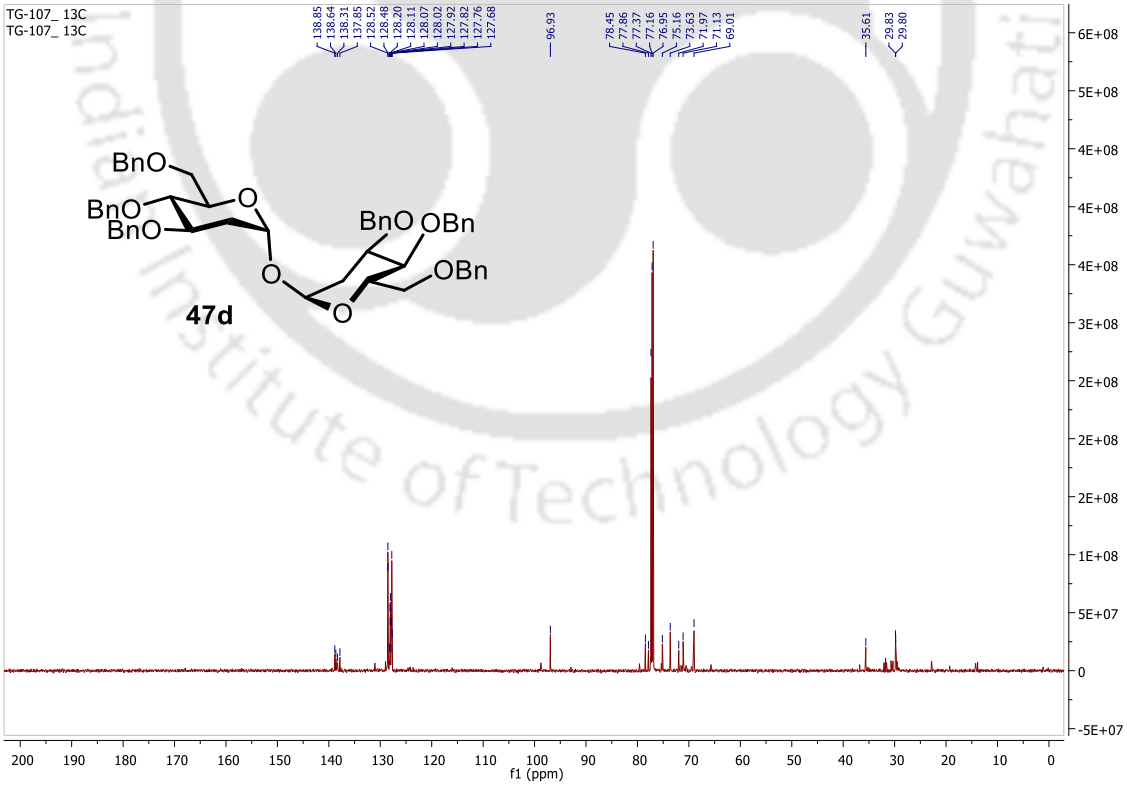


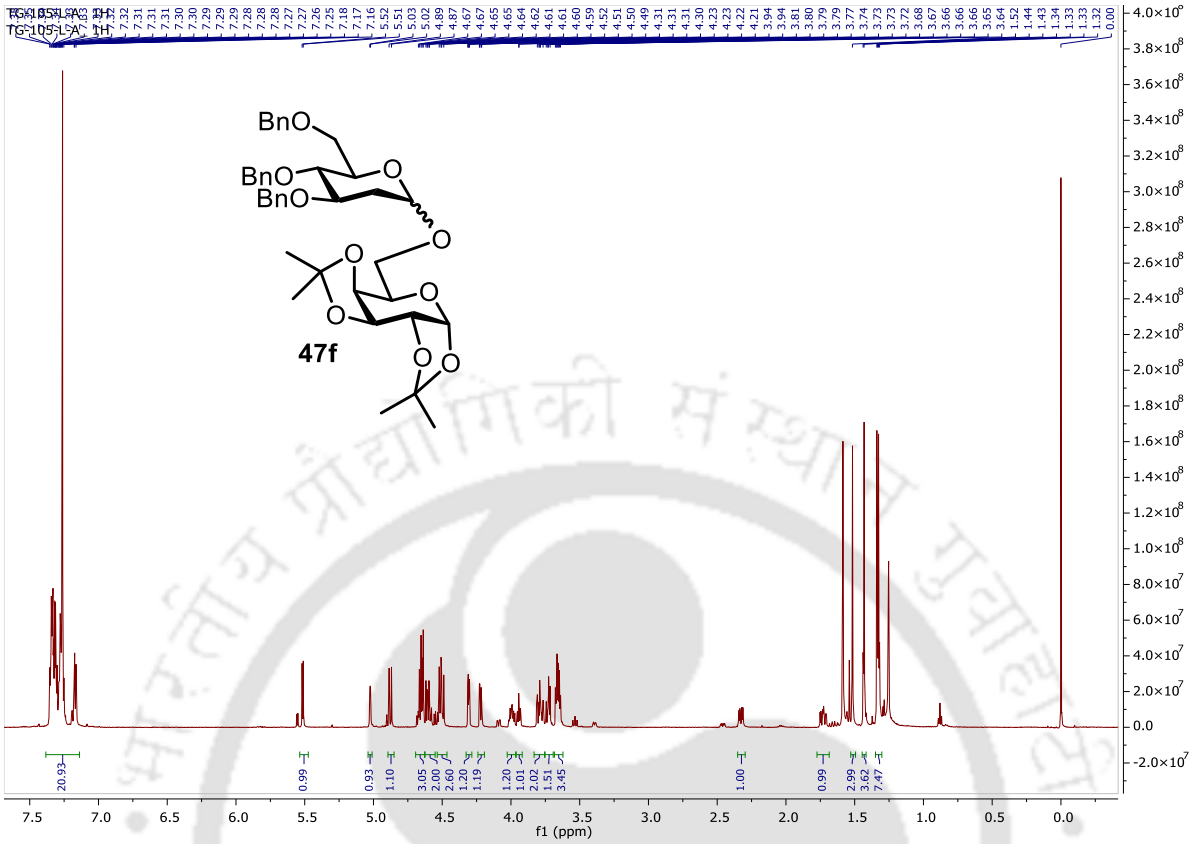


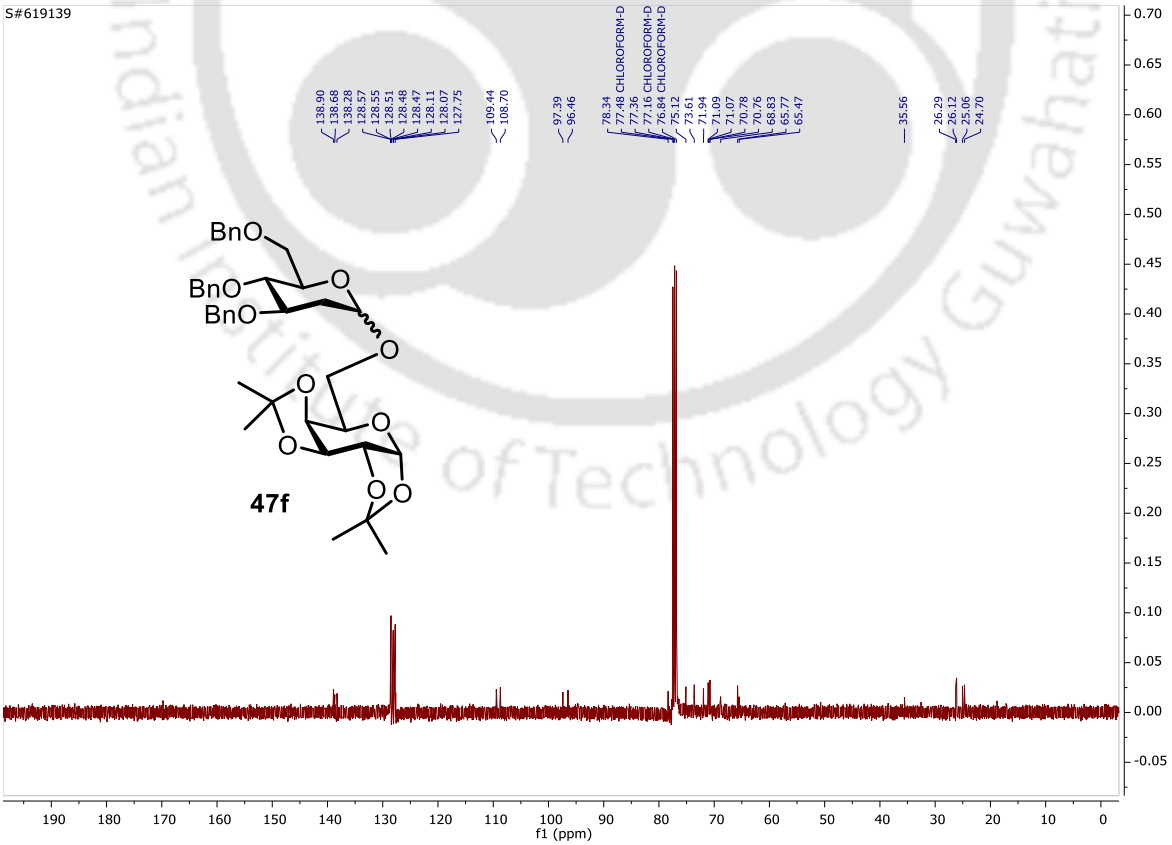


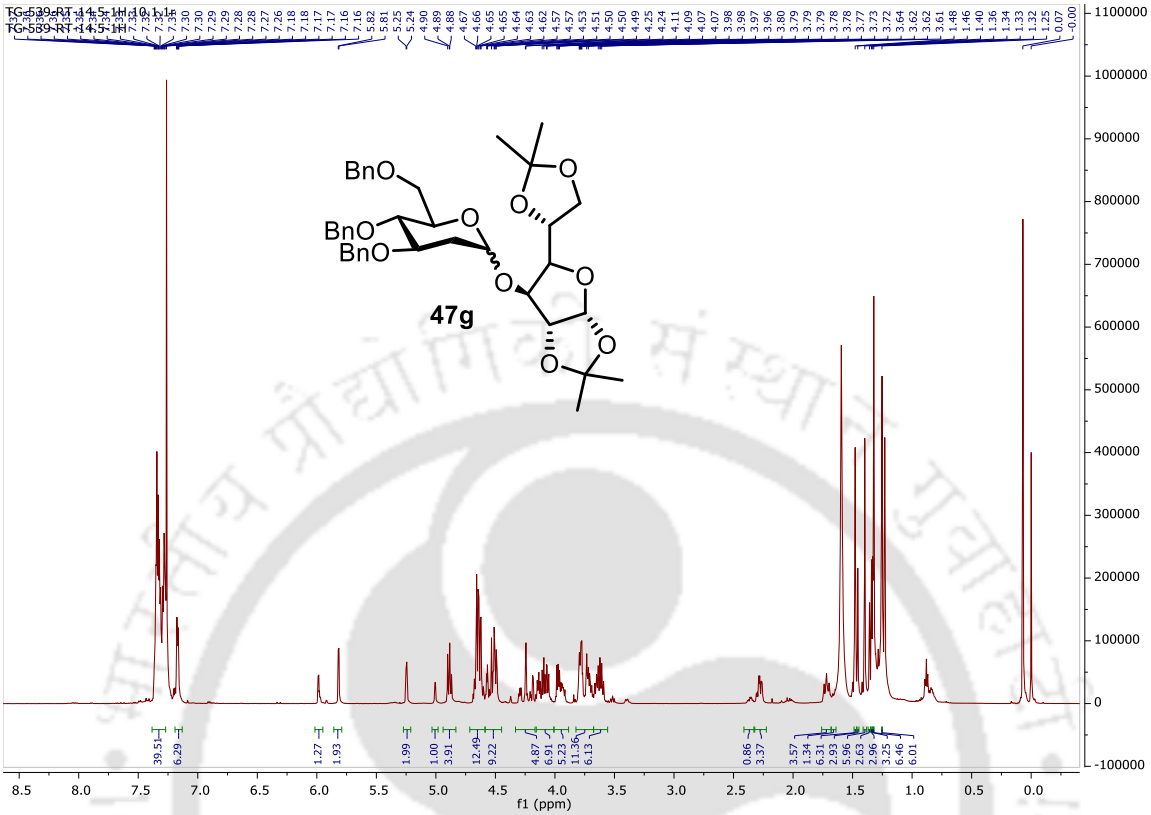


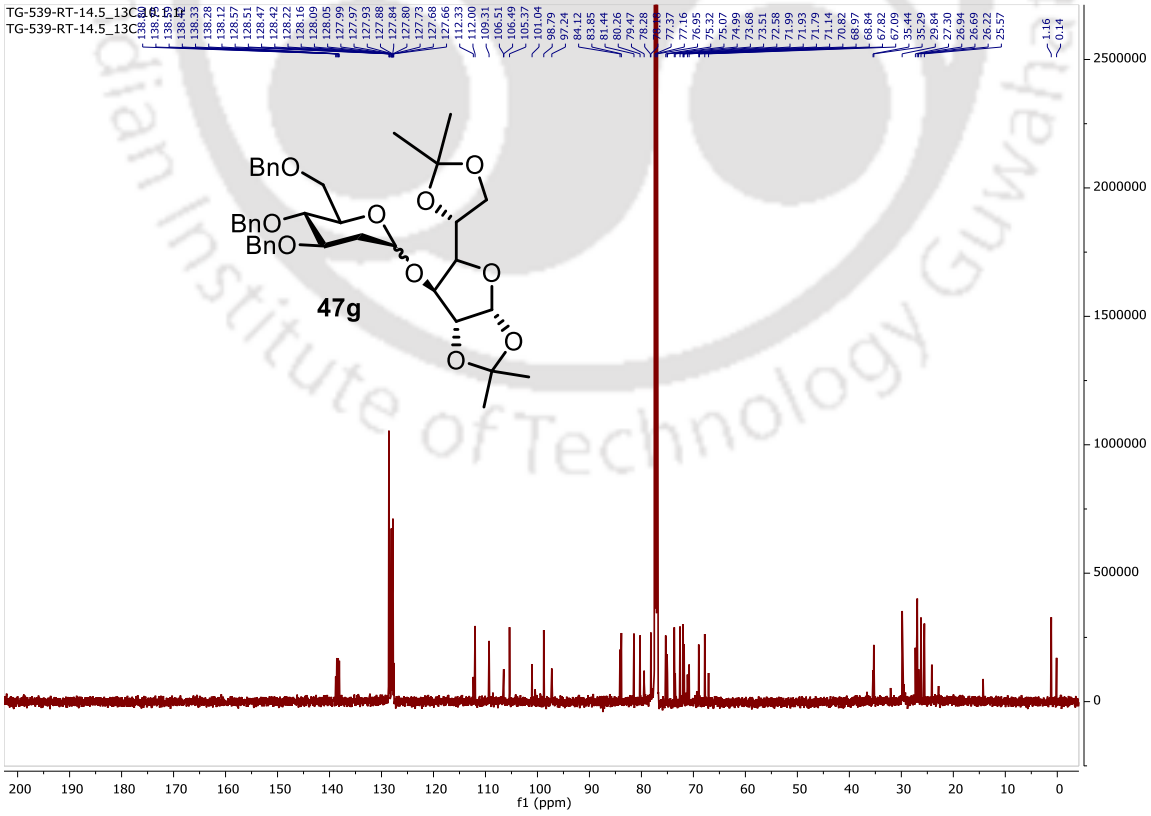


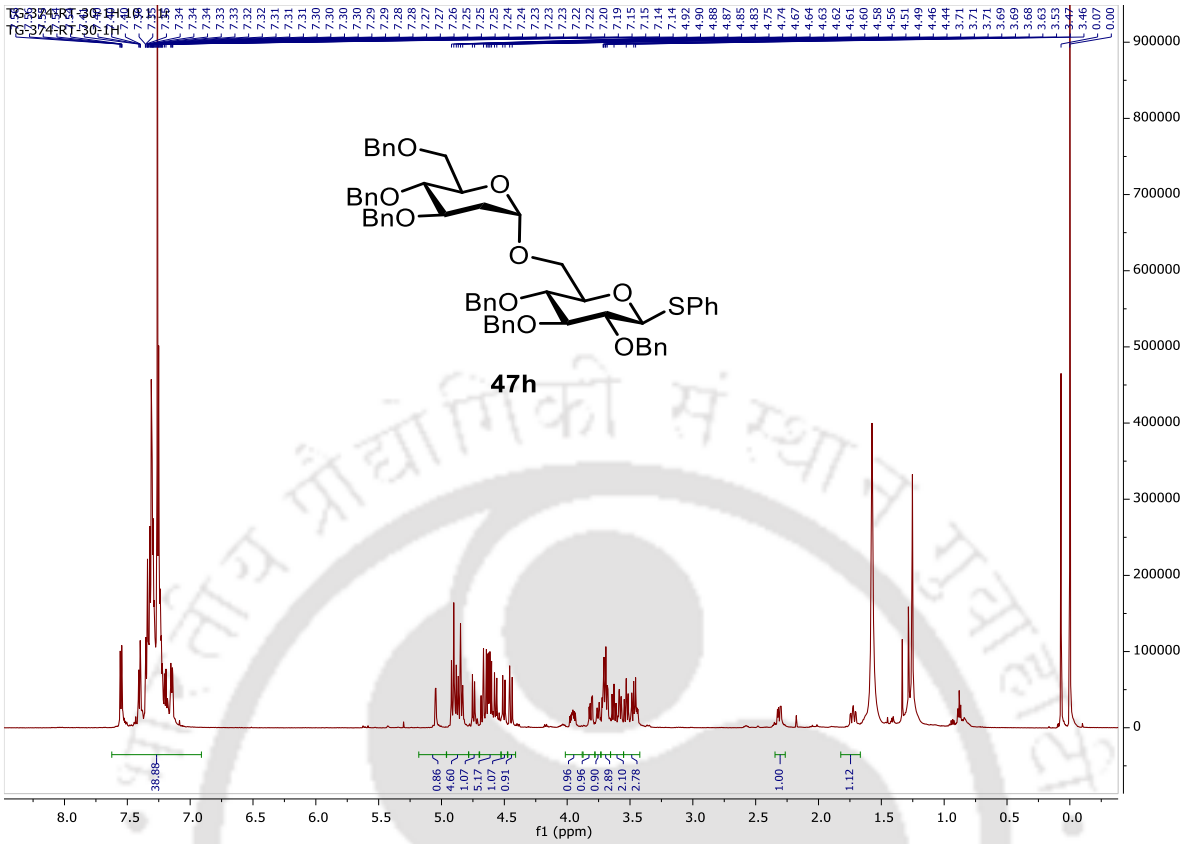


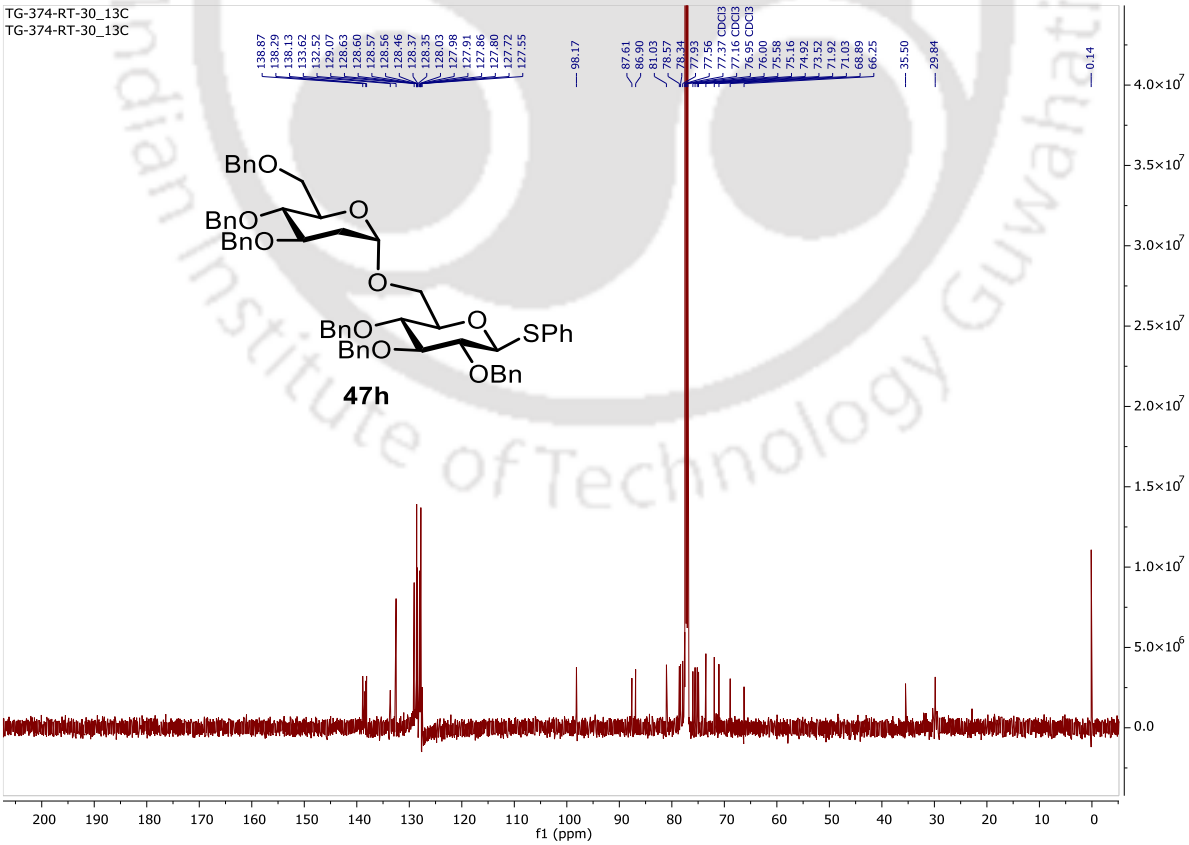


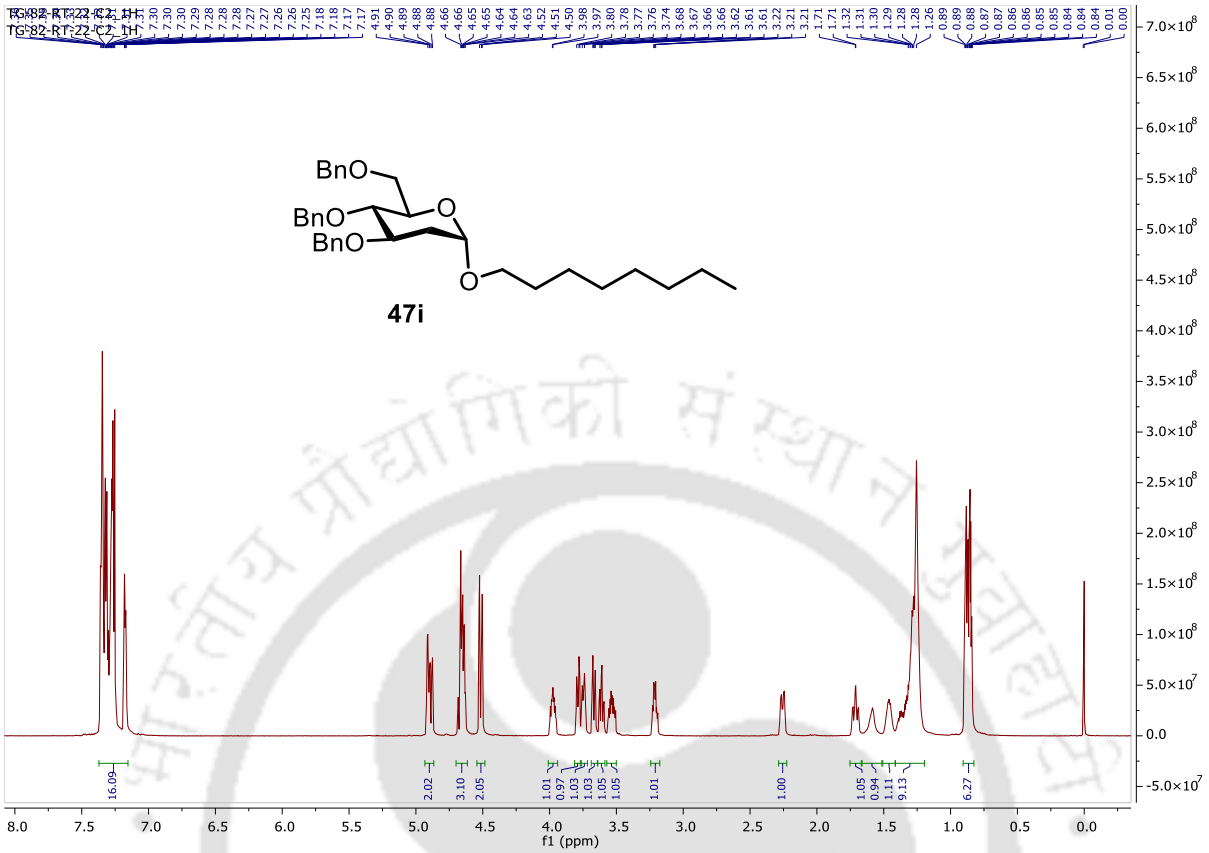


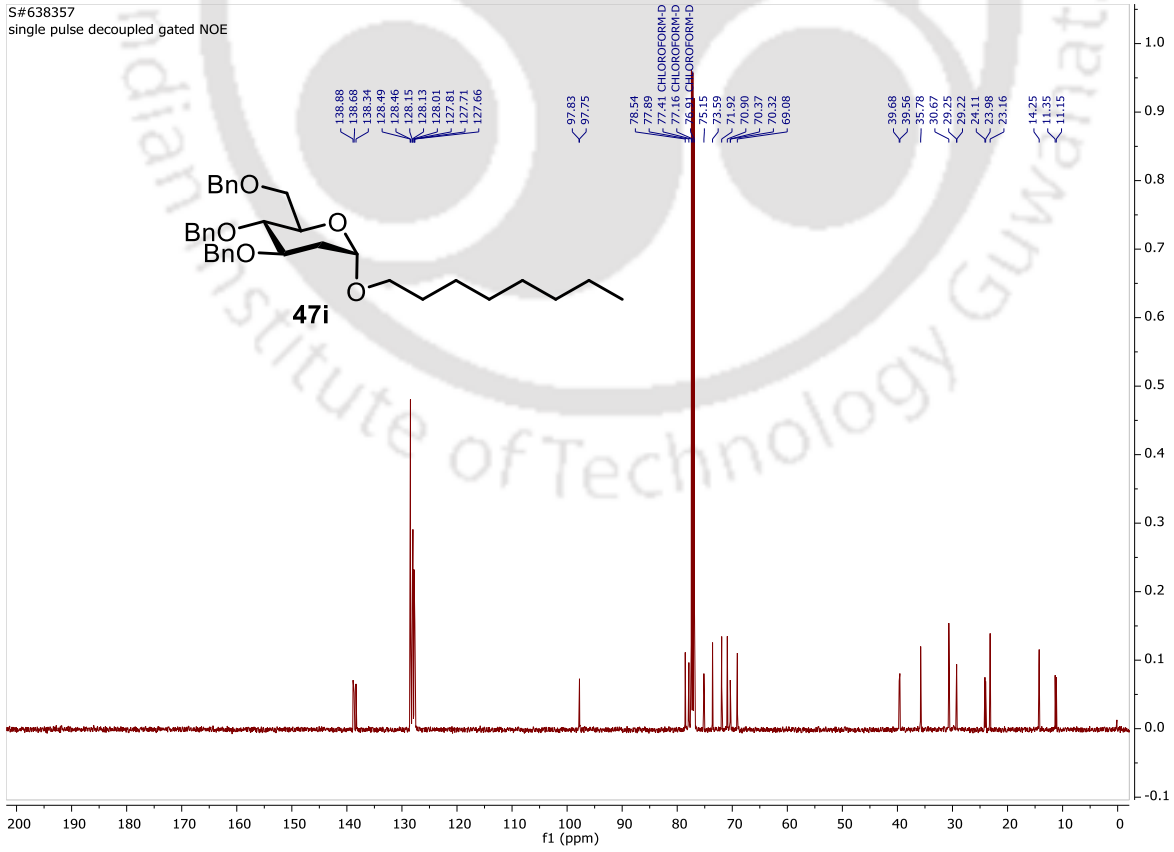


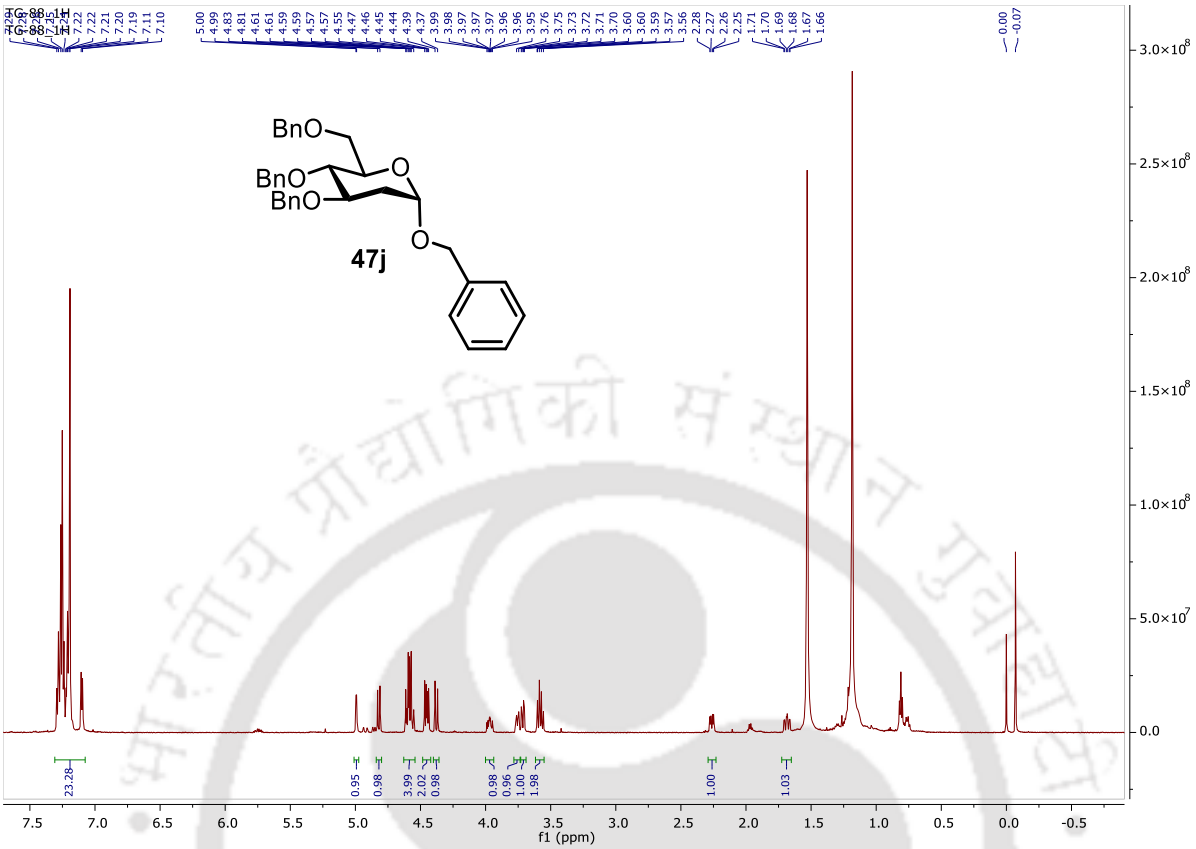


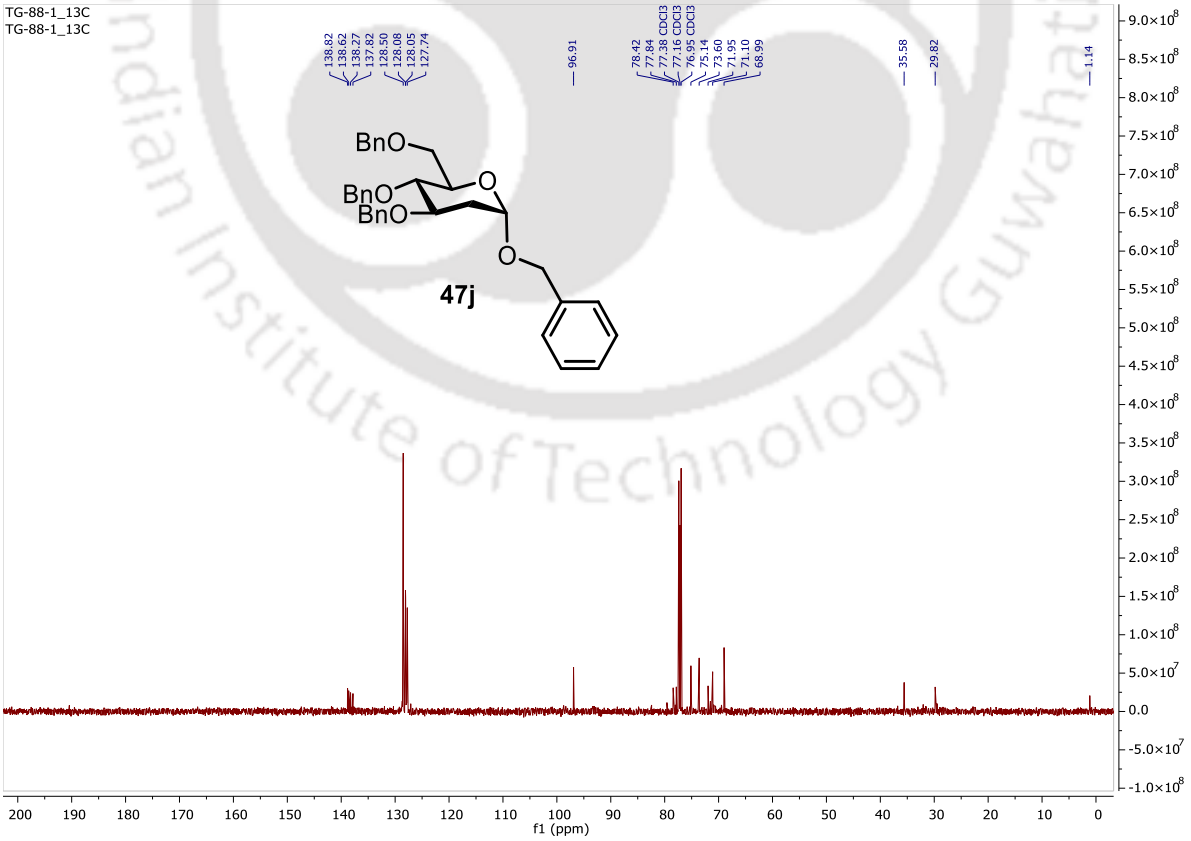




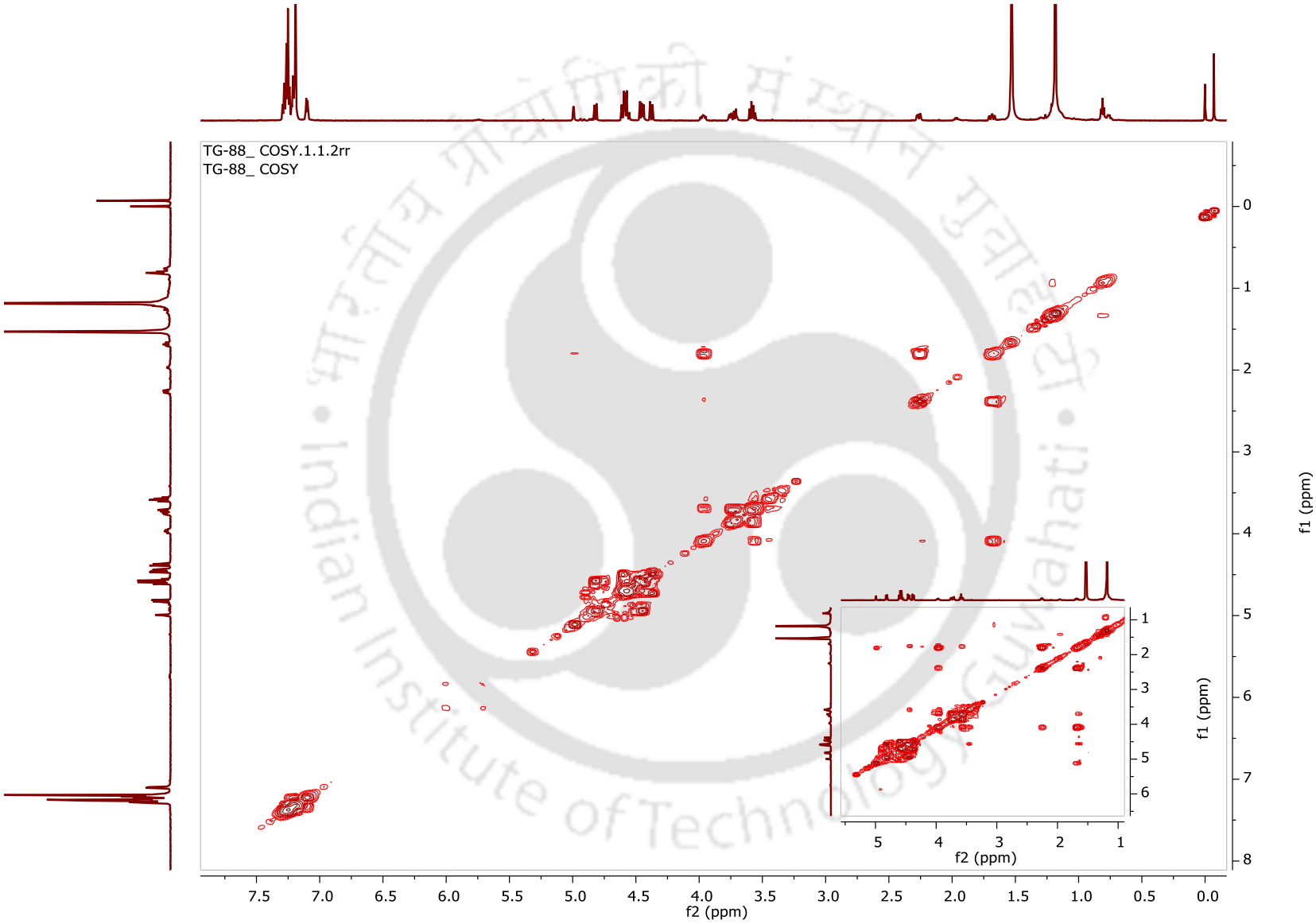


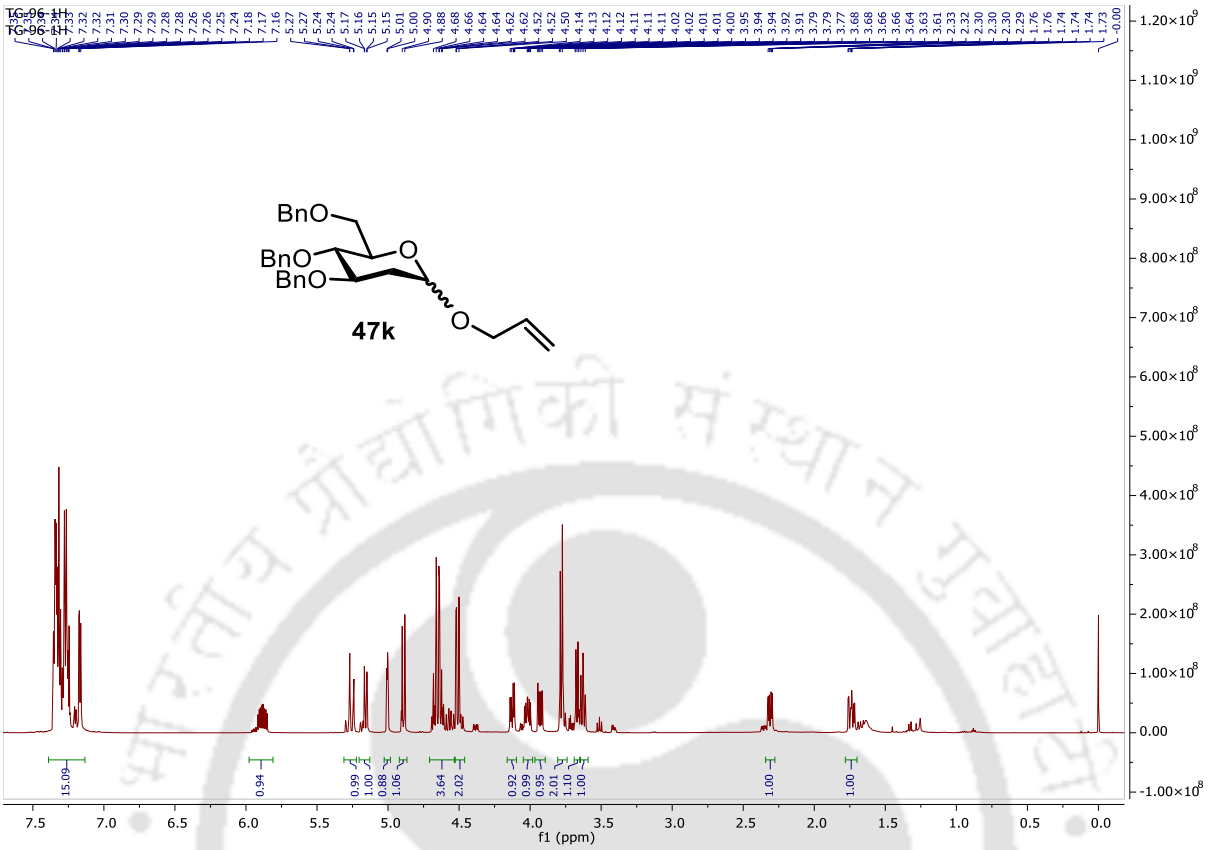


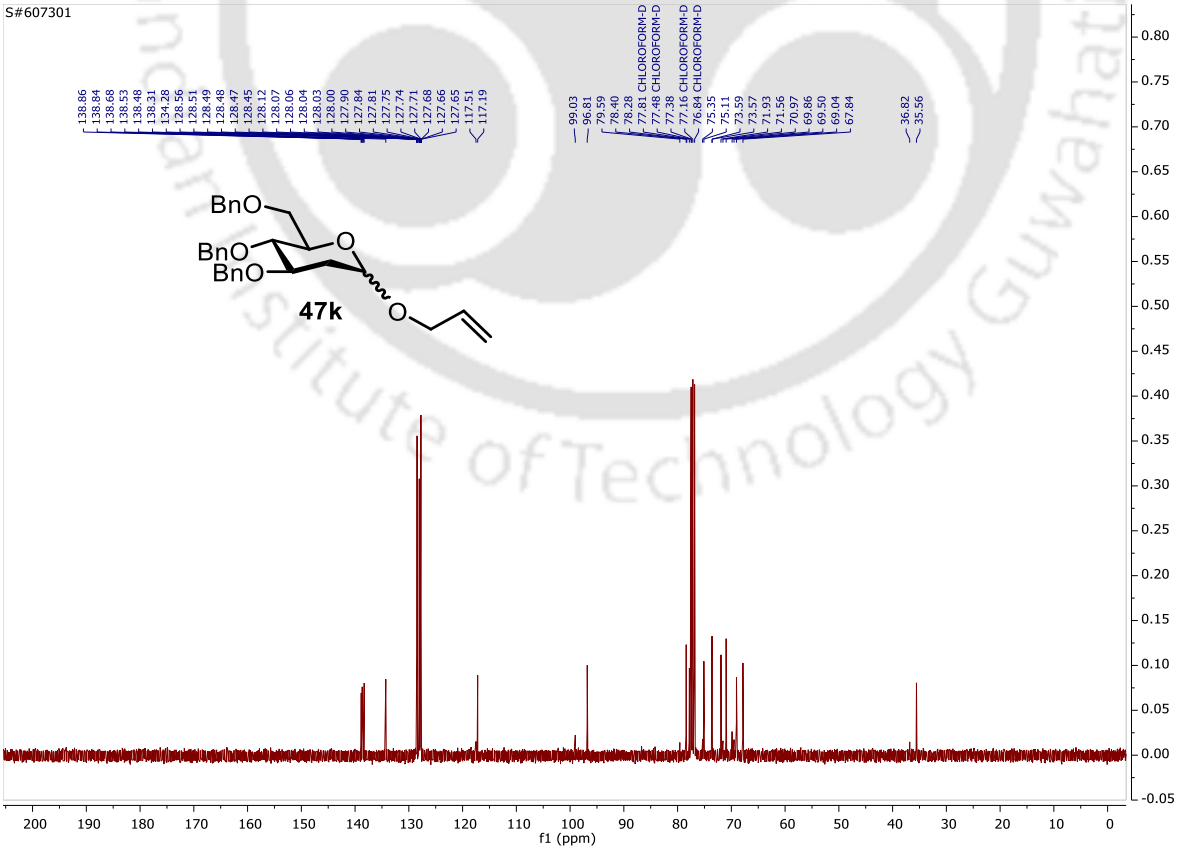




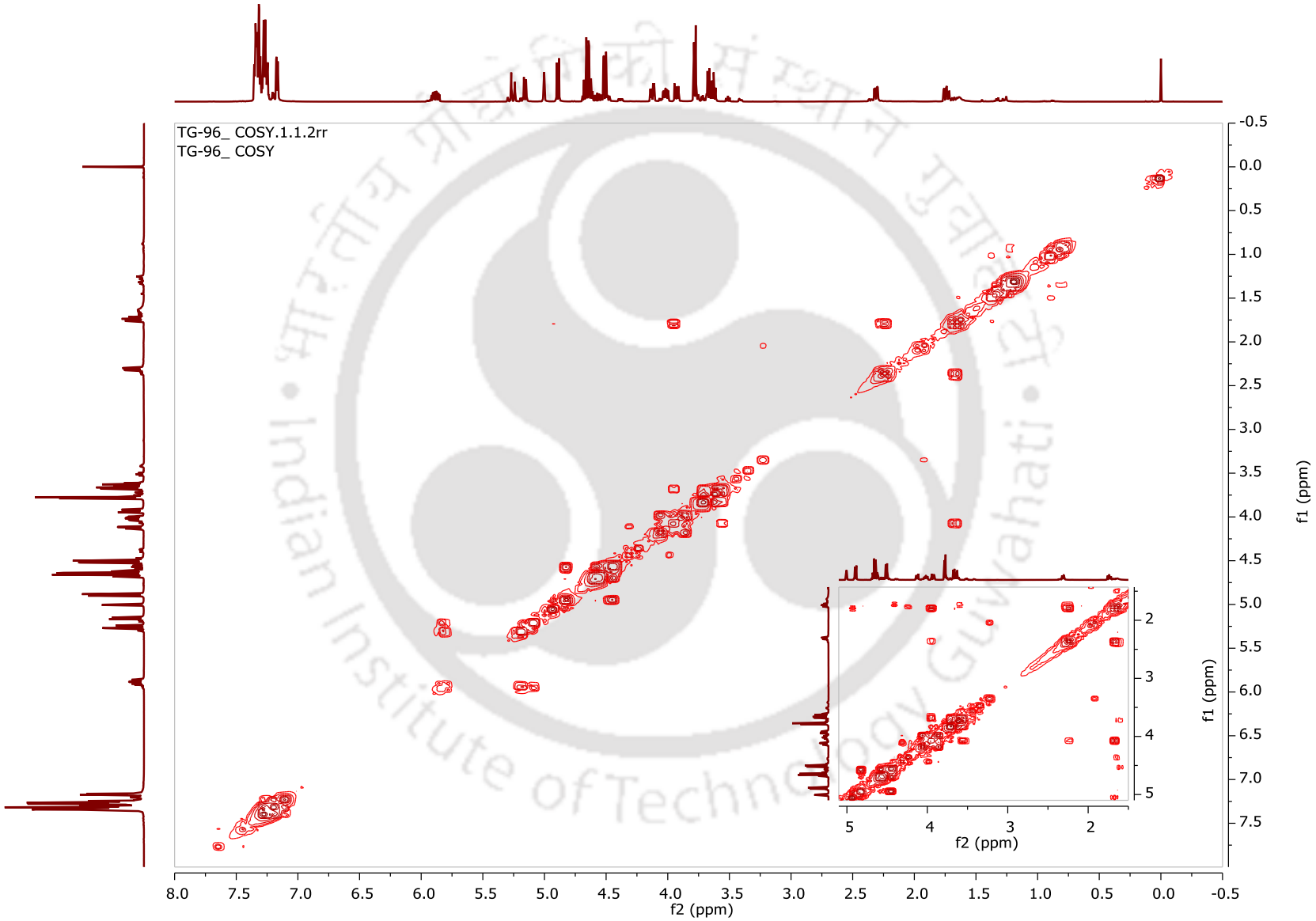
COSY NMR of Benzyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (47j):

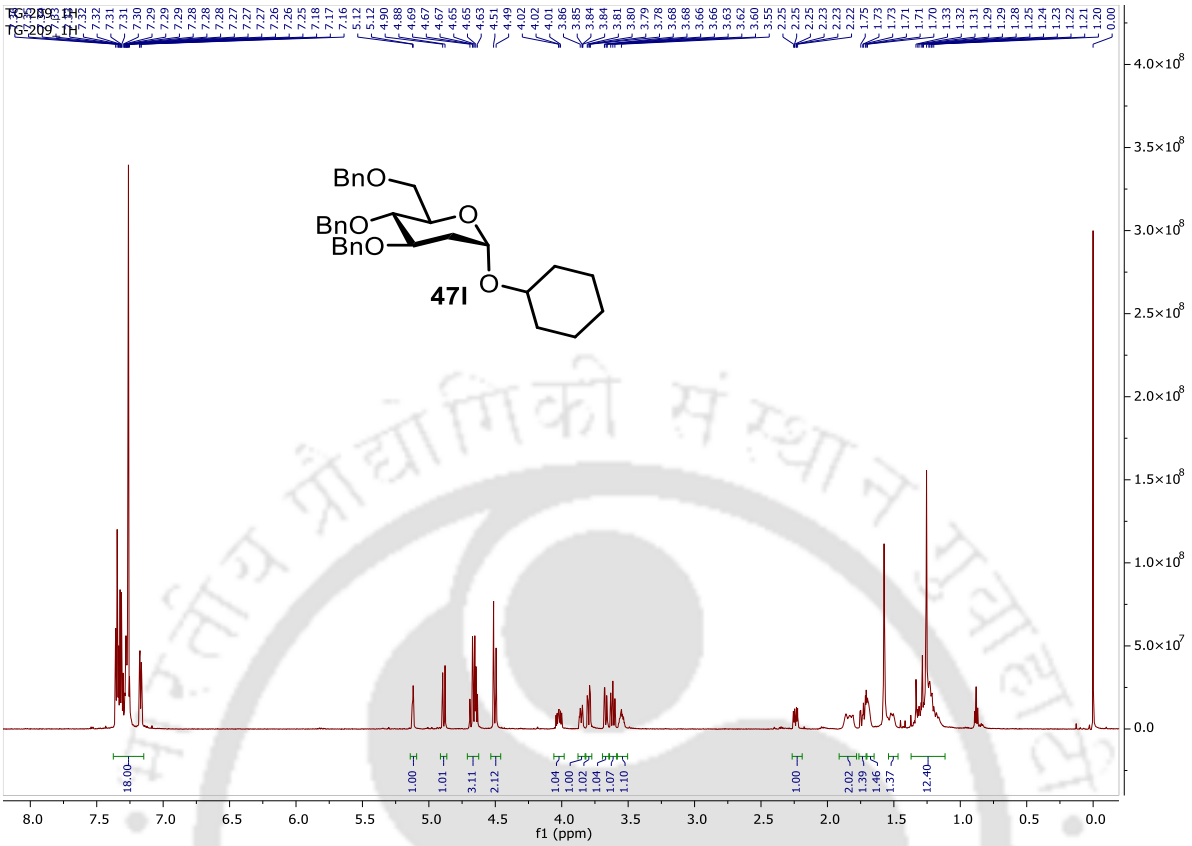


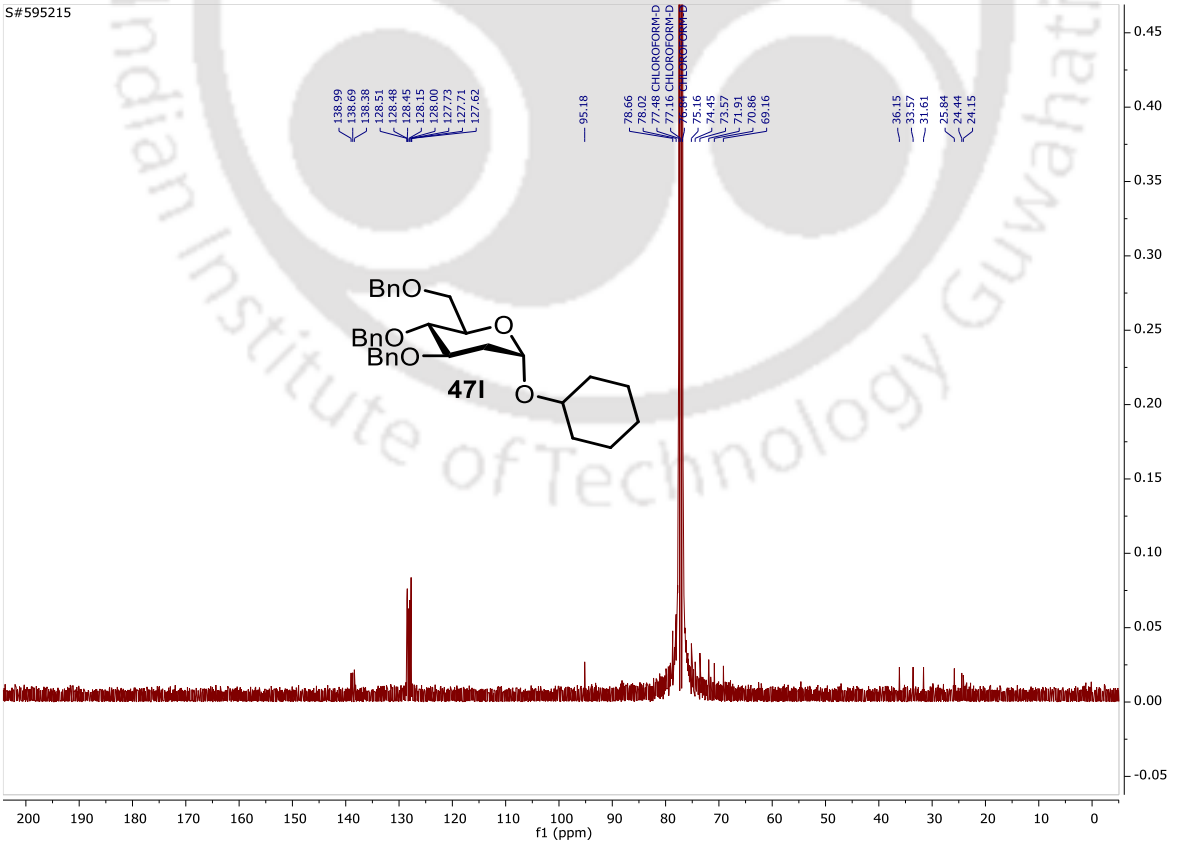


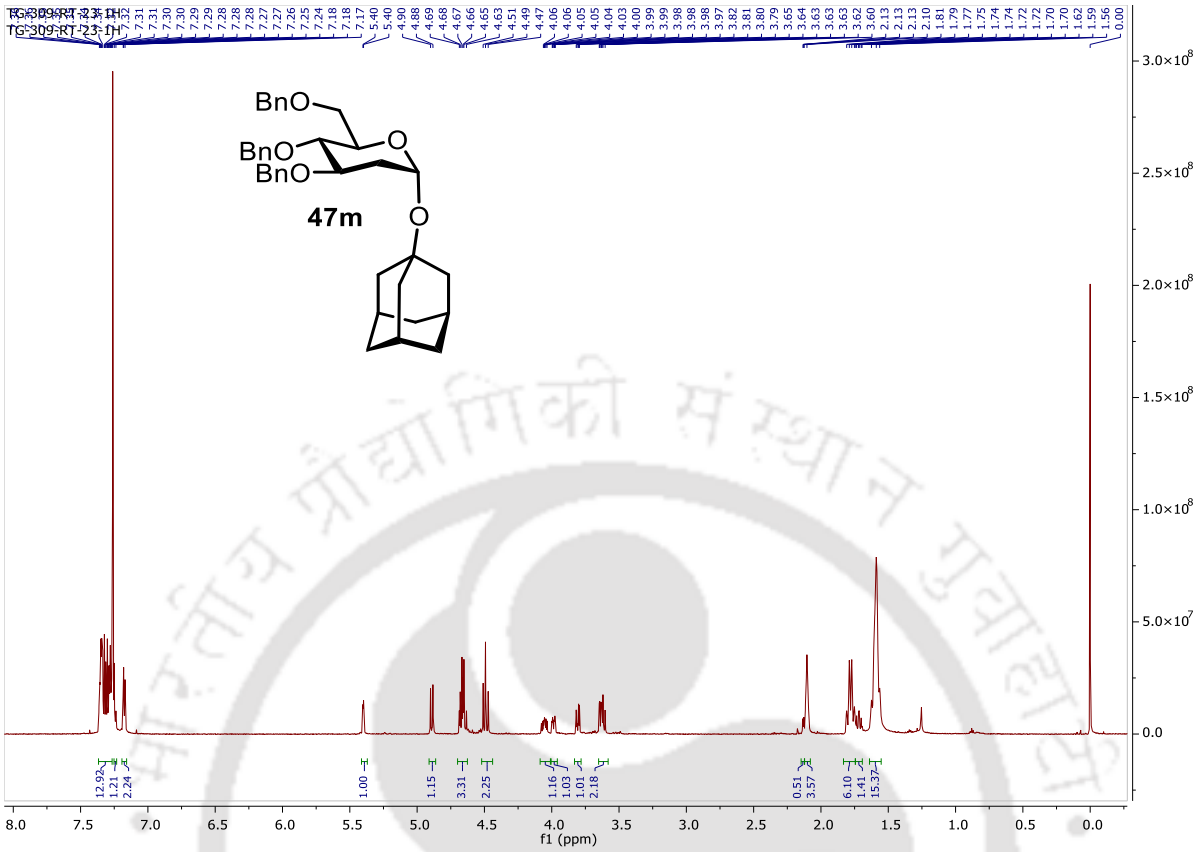


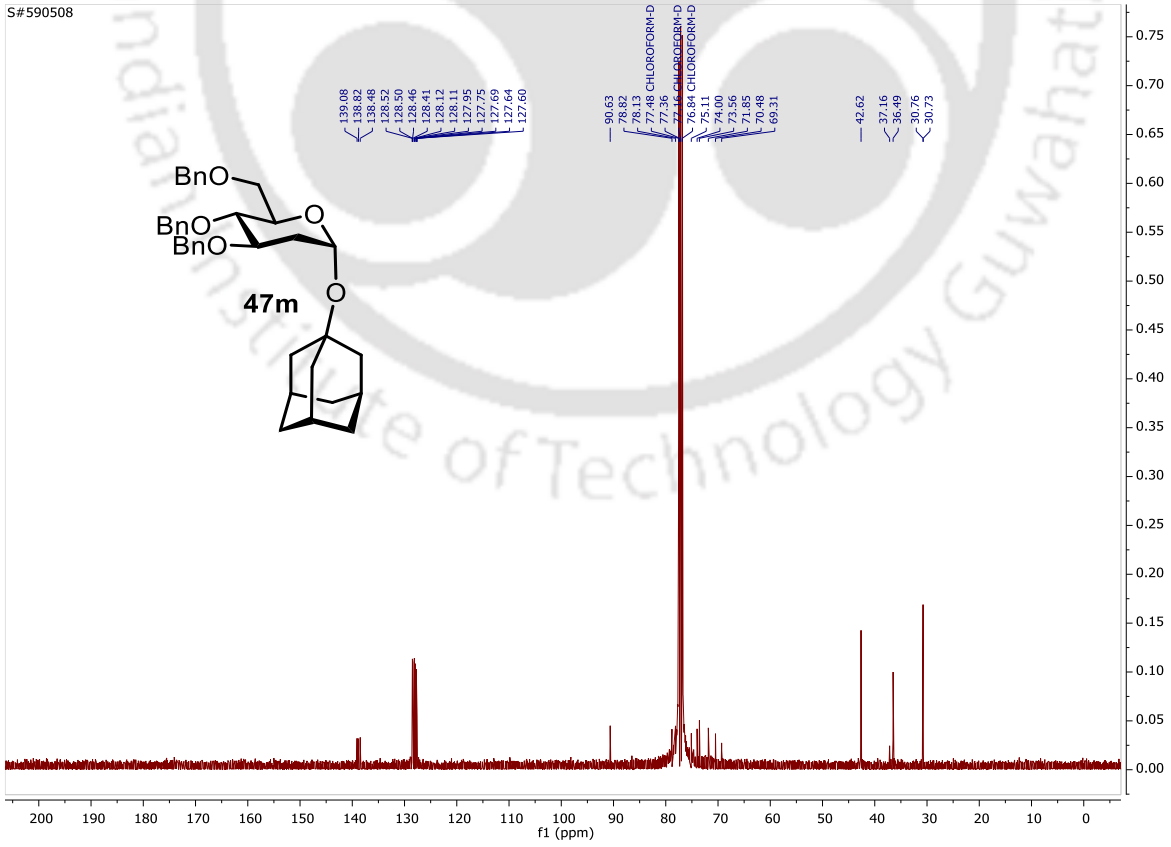
COSY NMR of Allyl-3,4,6-tri-*O*-benzyl-2-deoxy-α,β-D-glucopyranoside (47k):

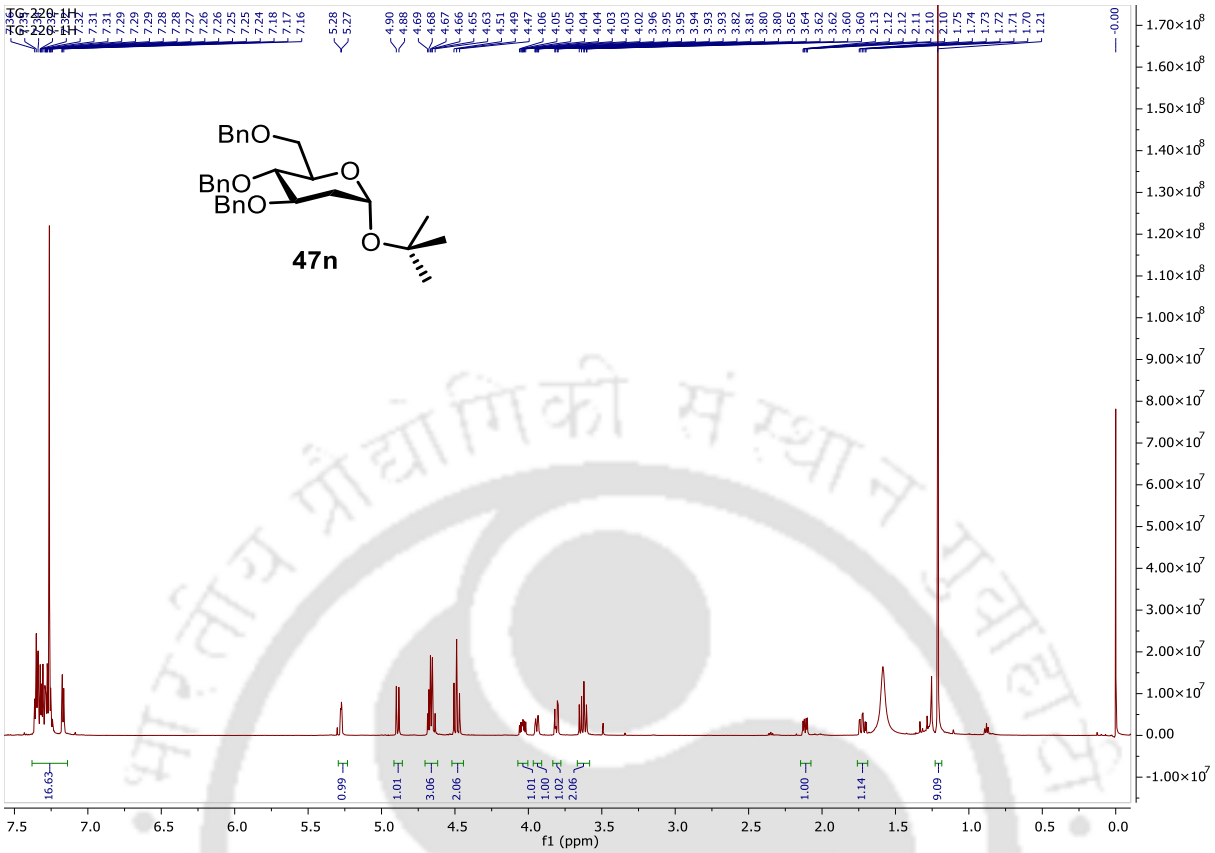


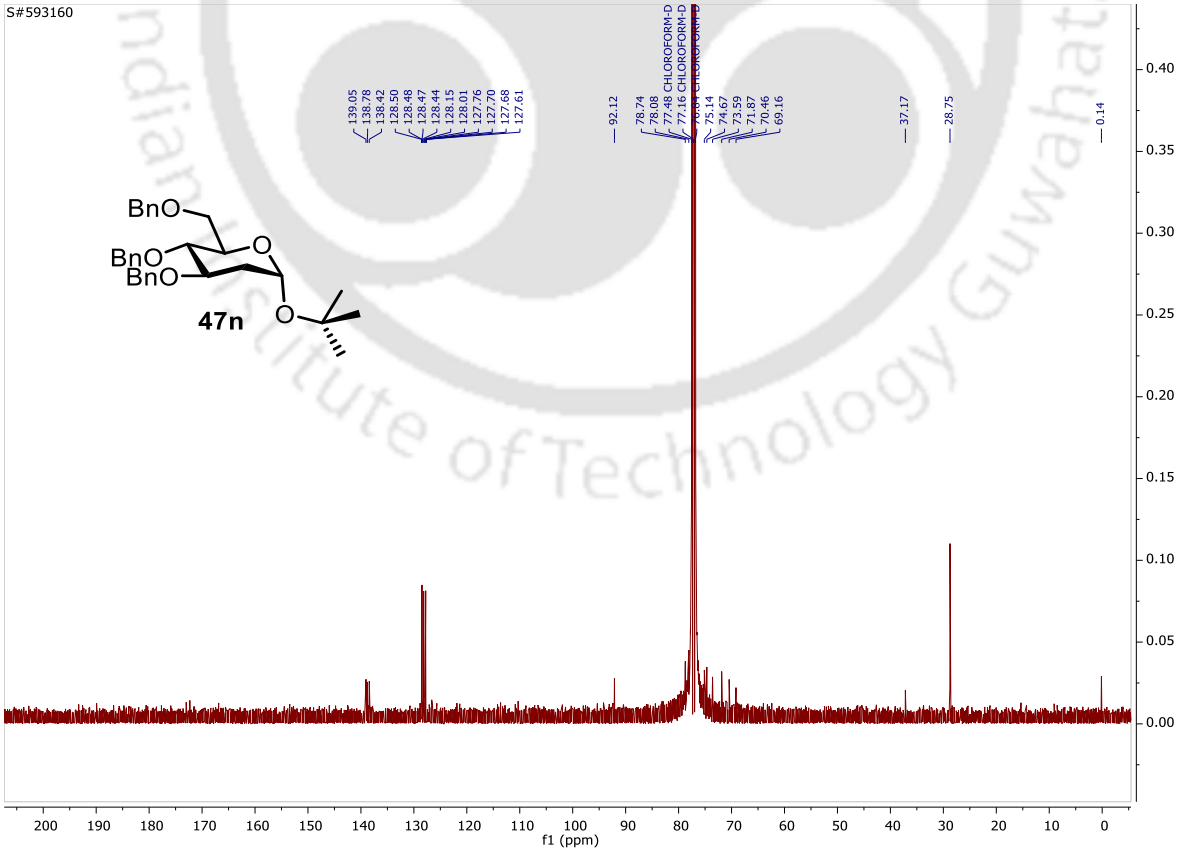


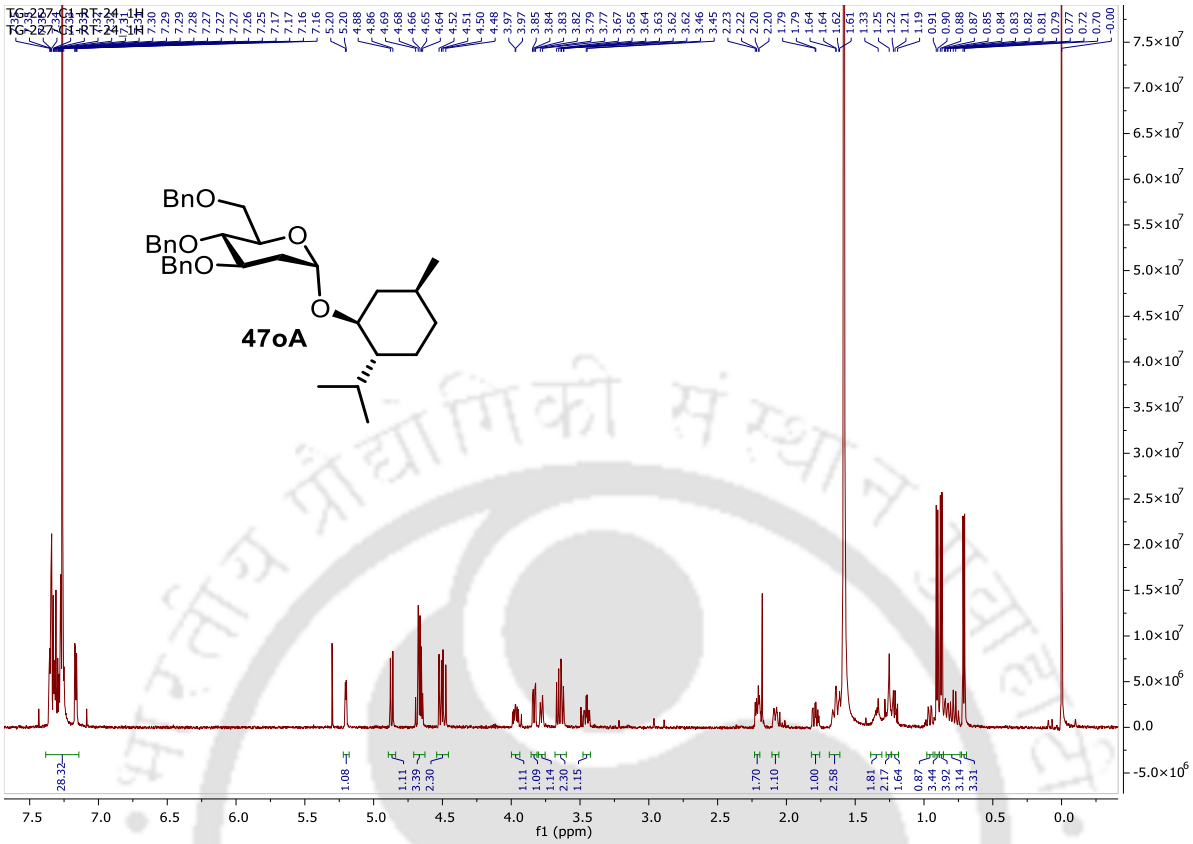


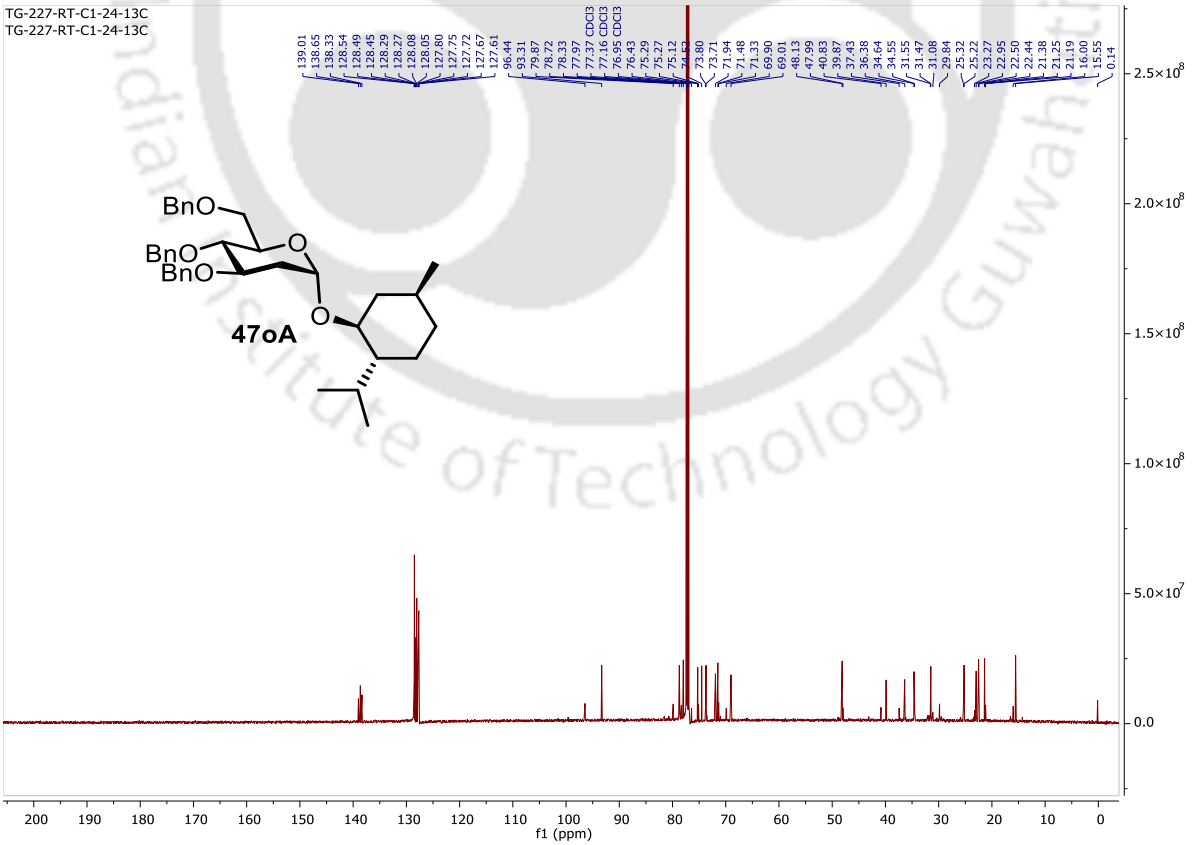


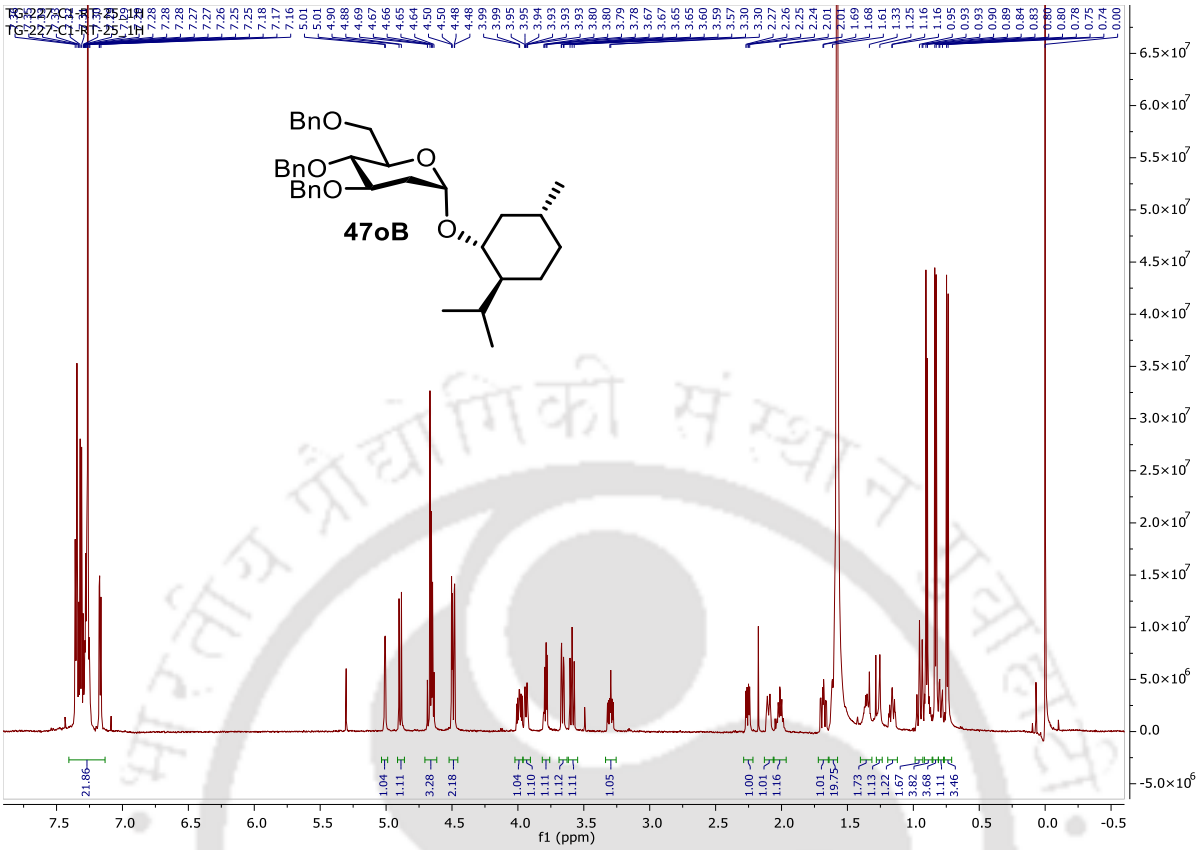


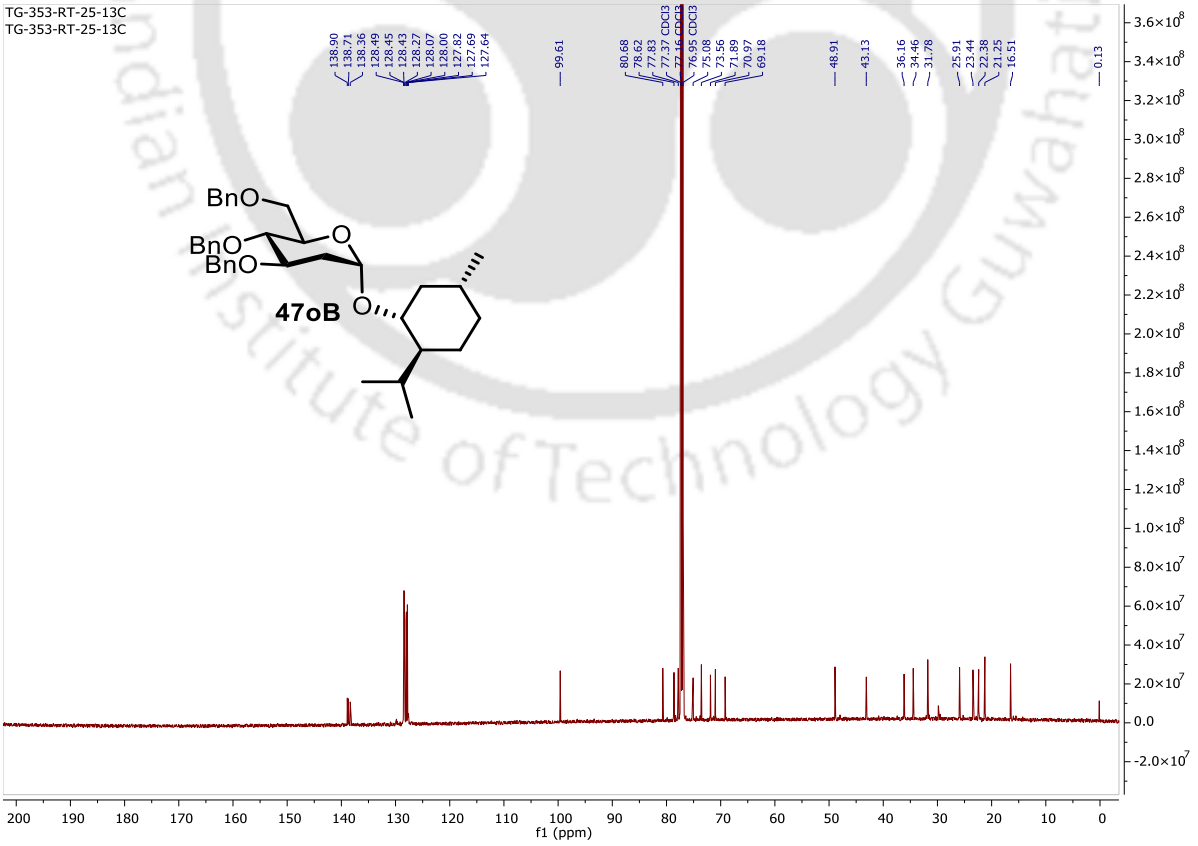


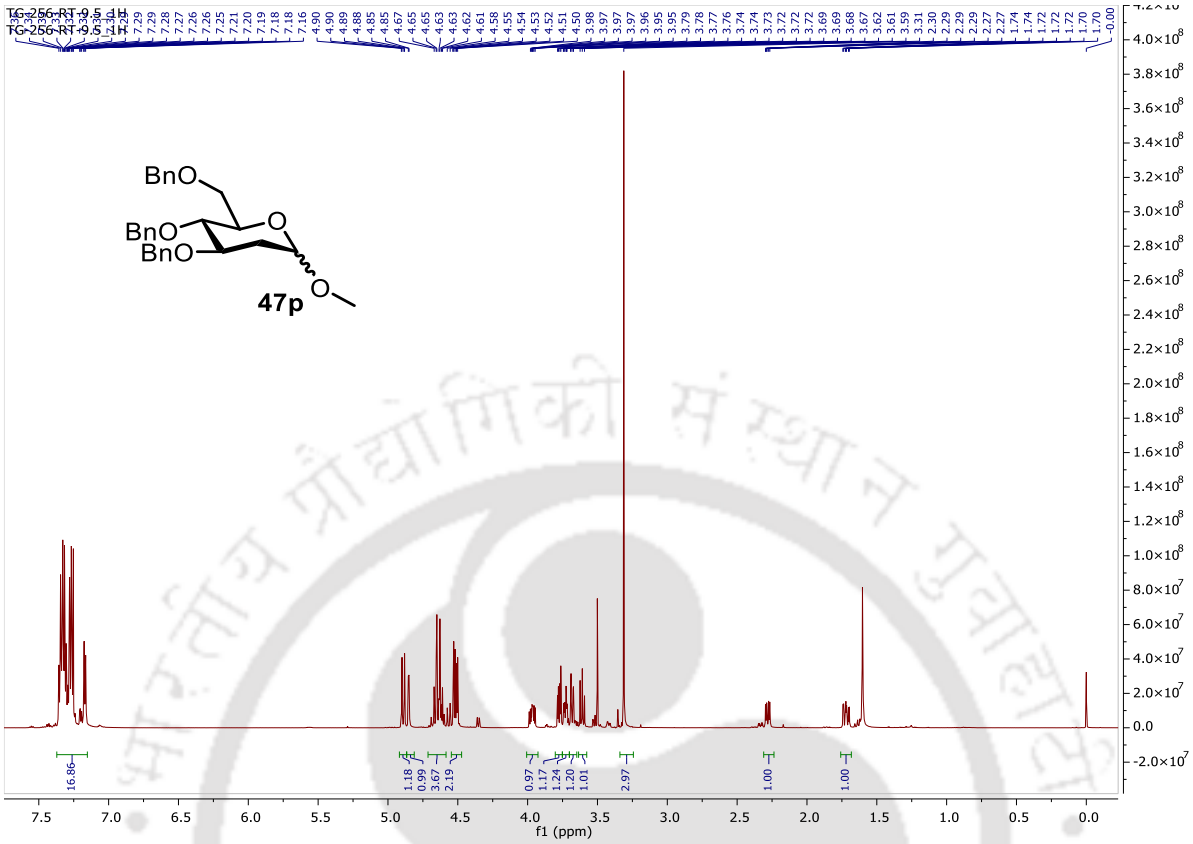


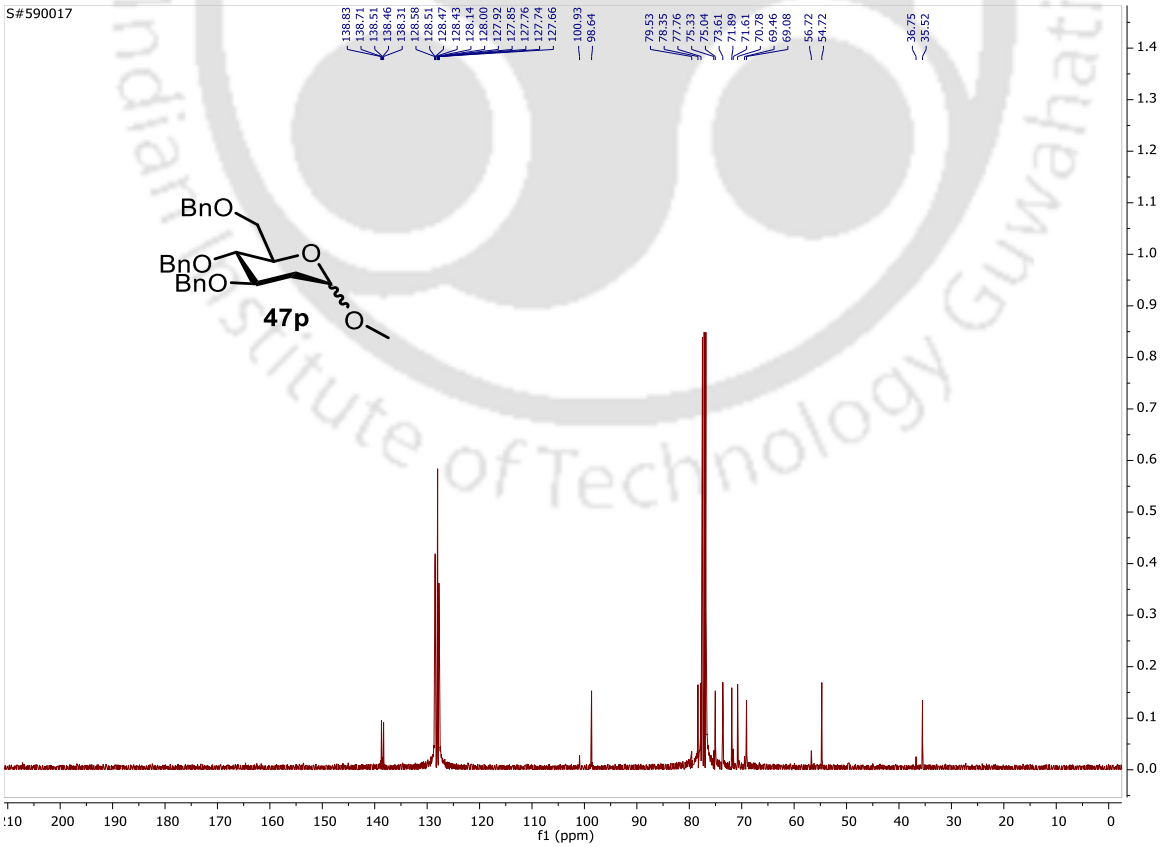


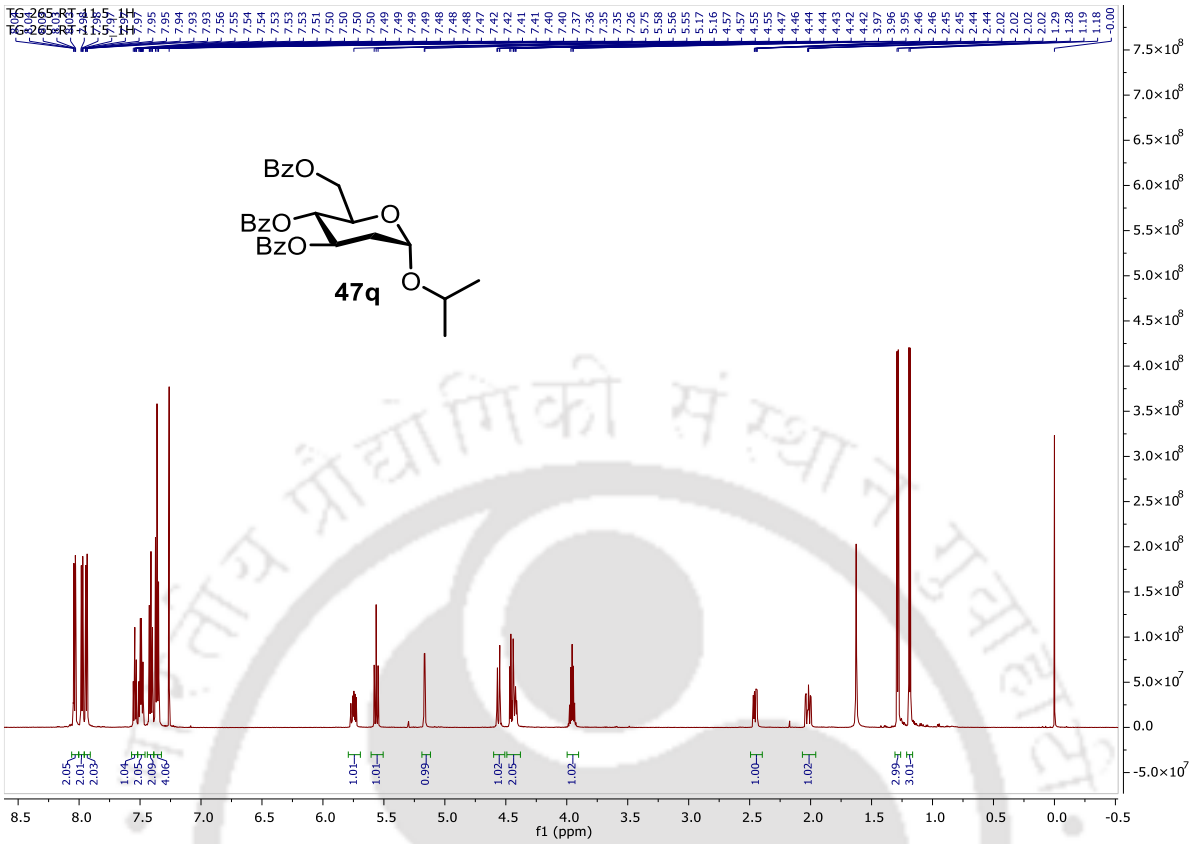


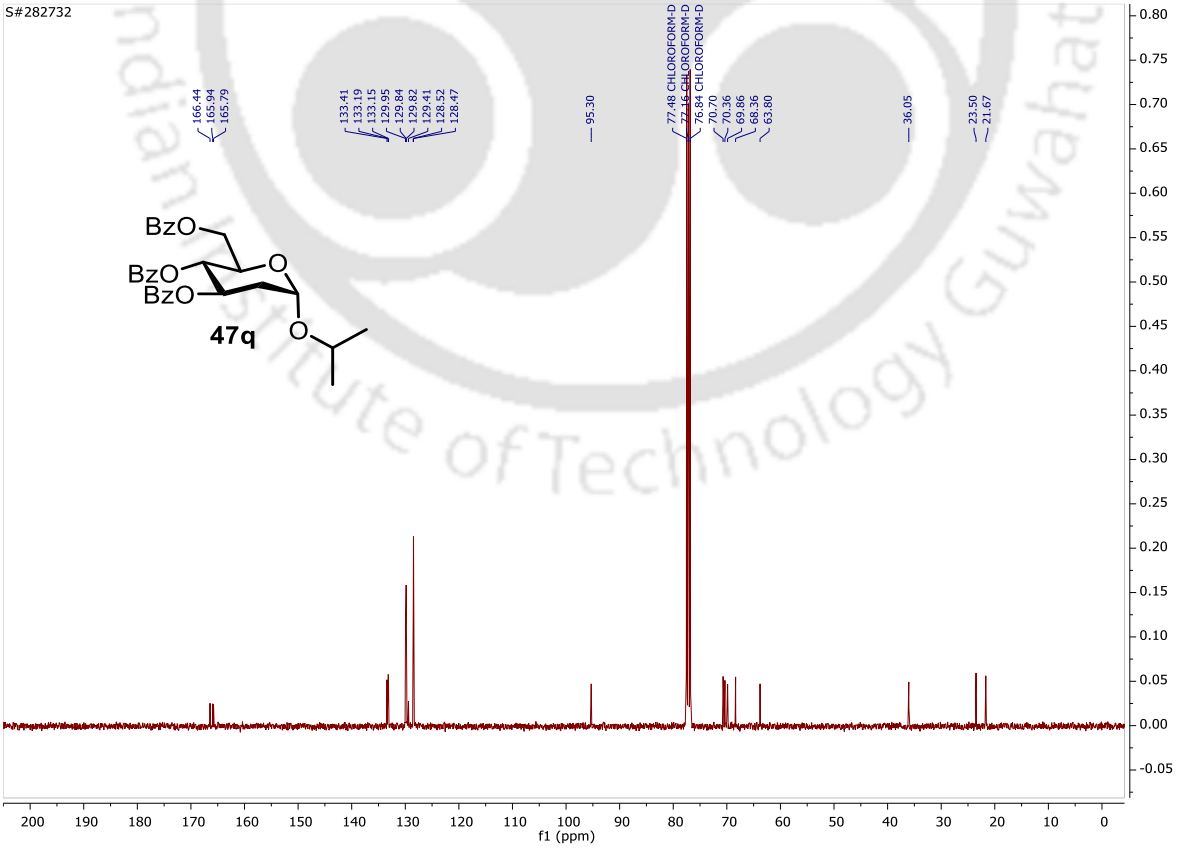




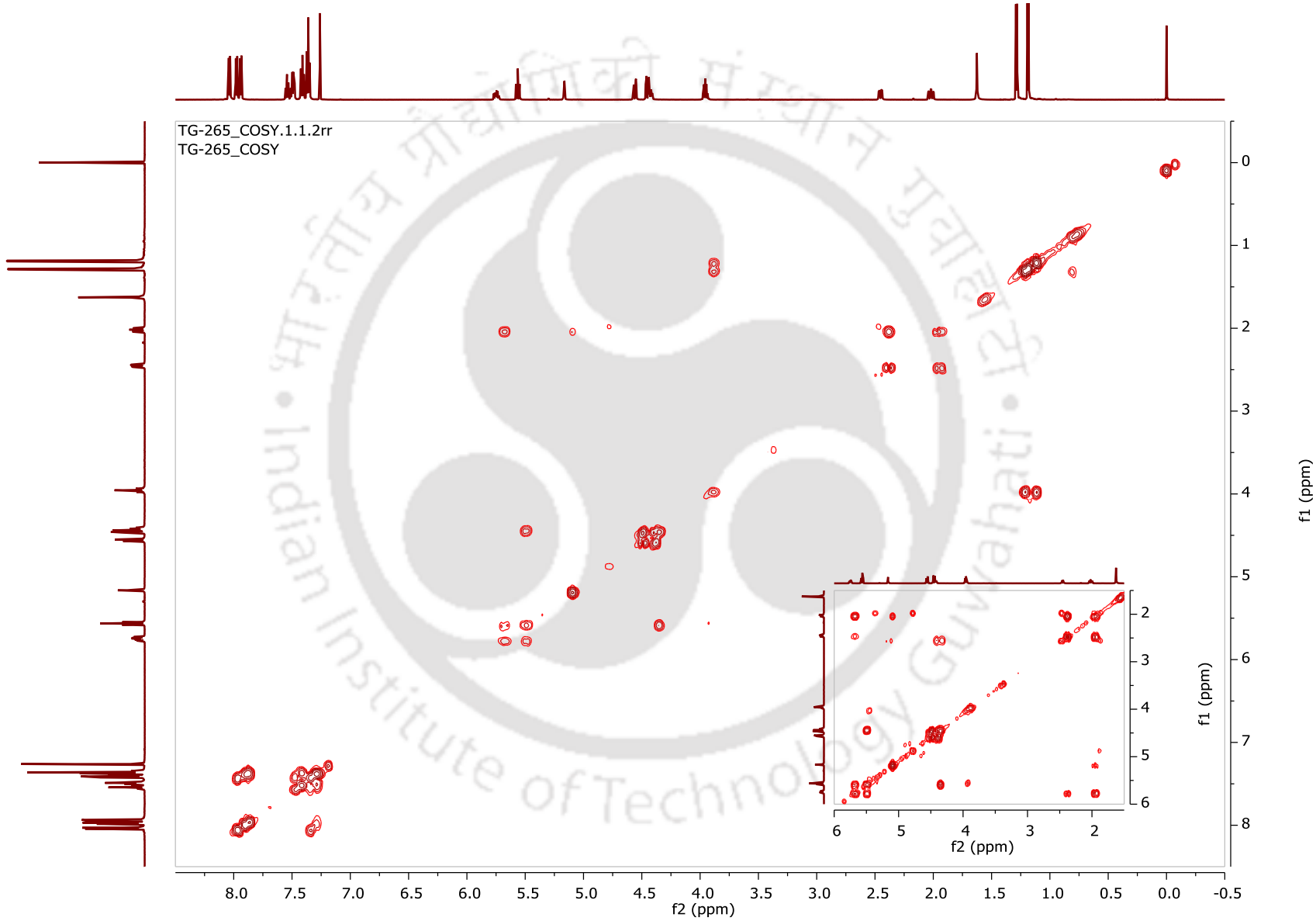


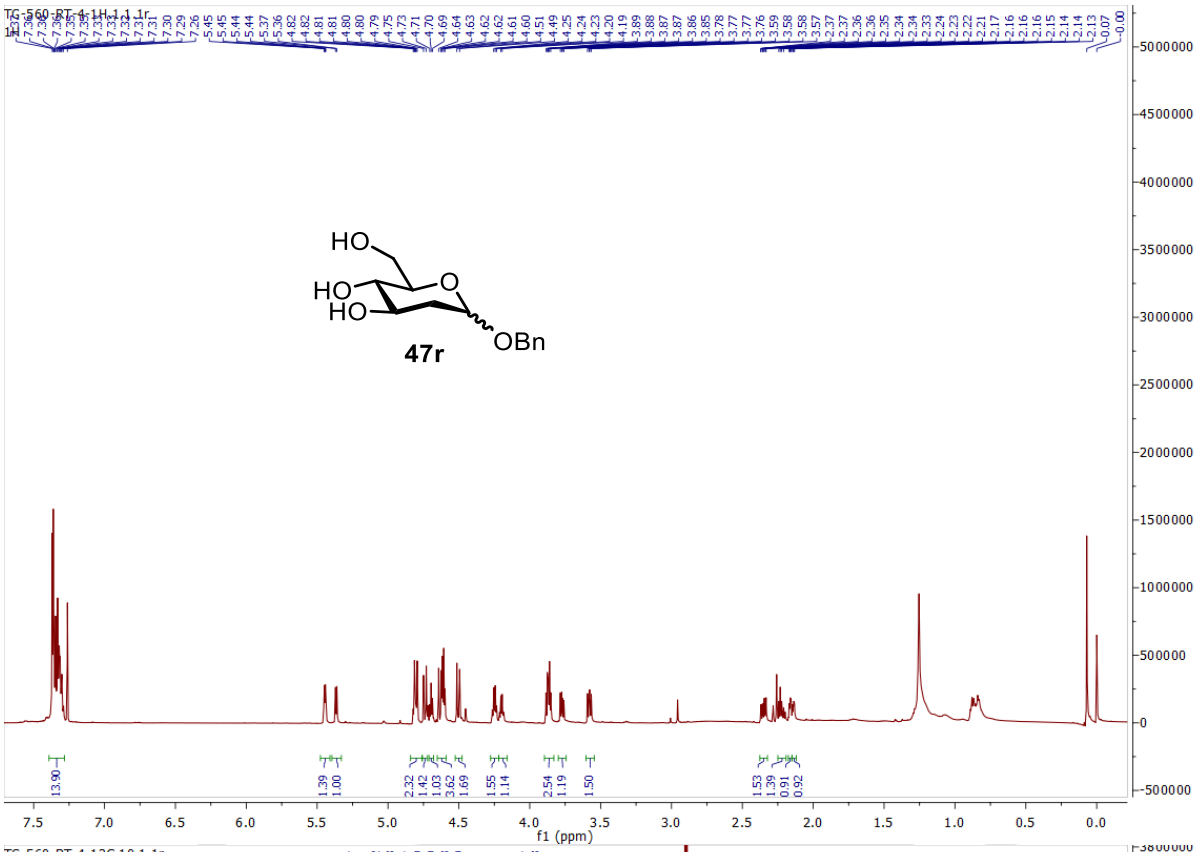


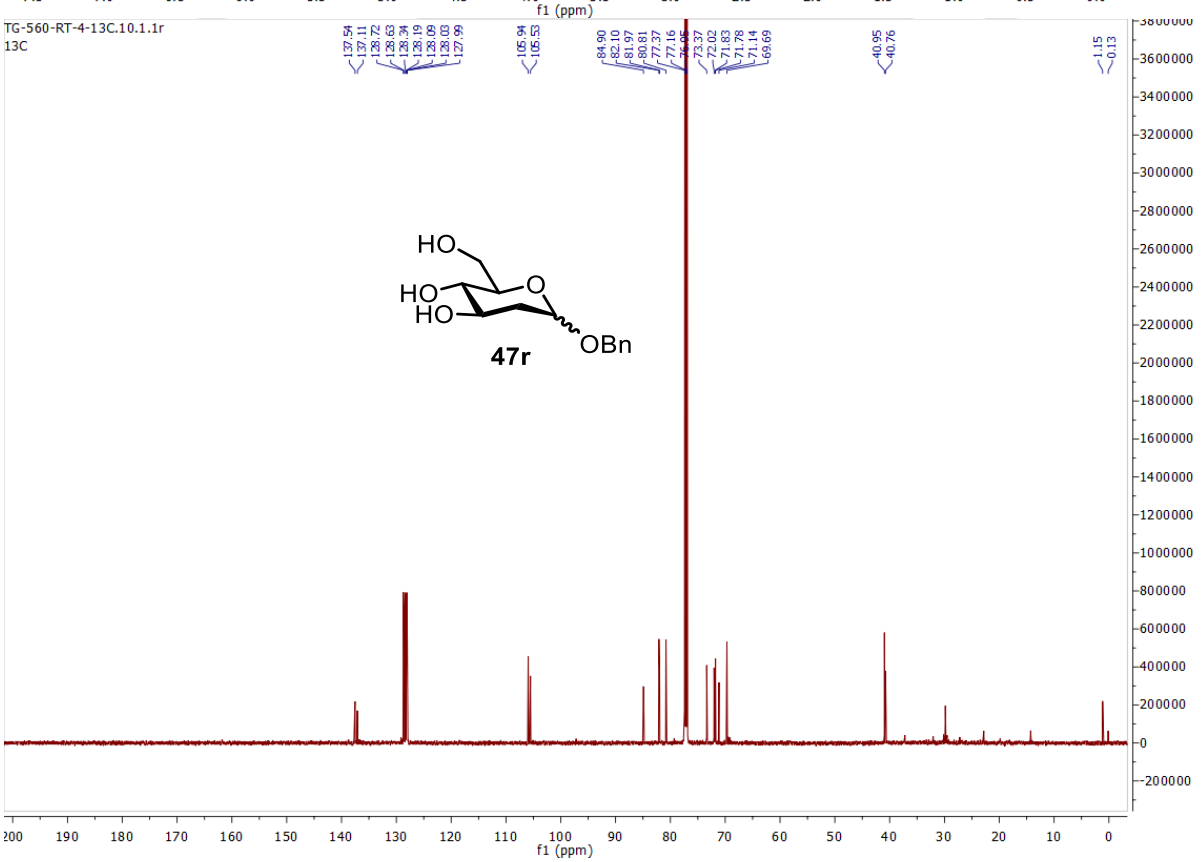


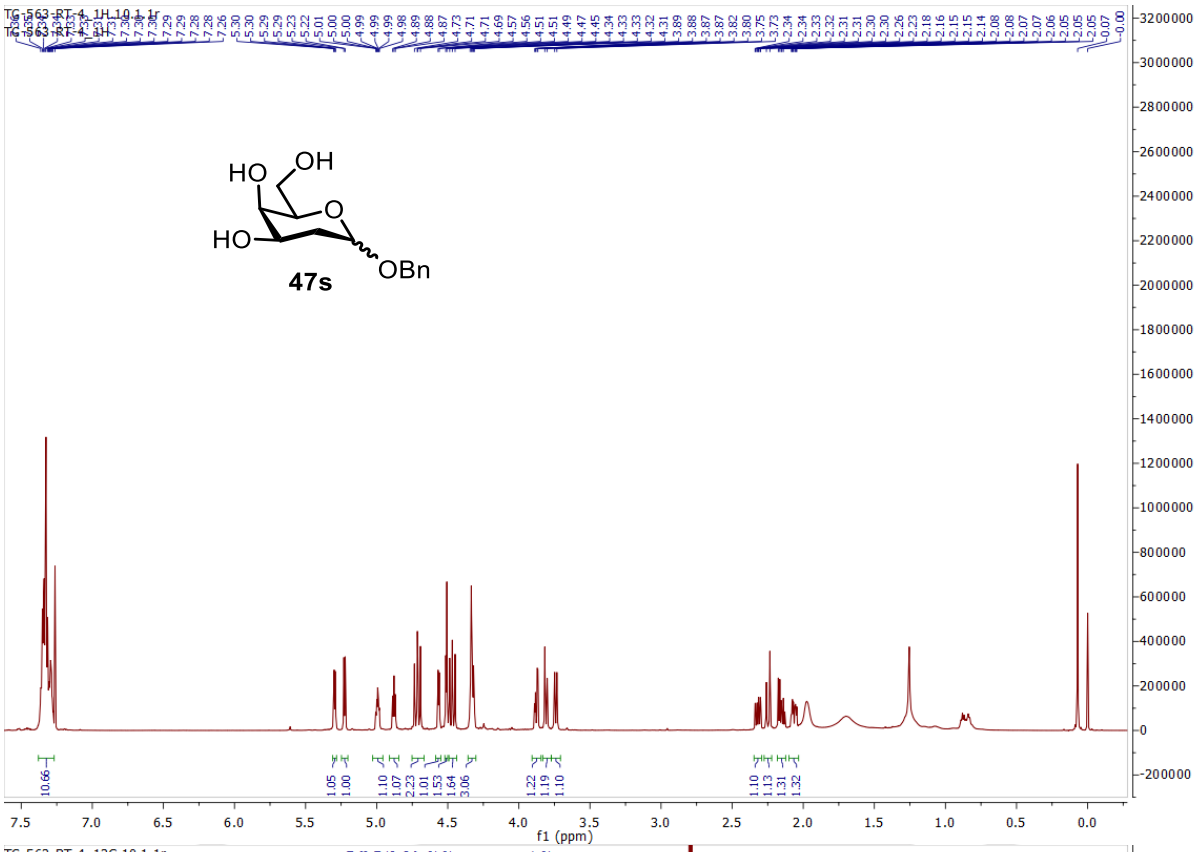


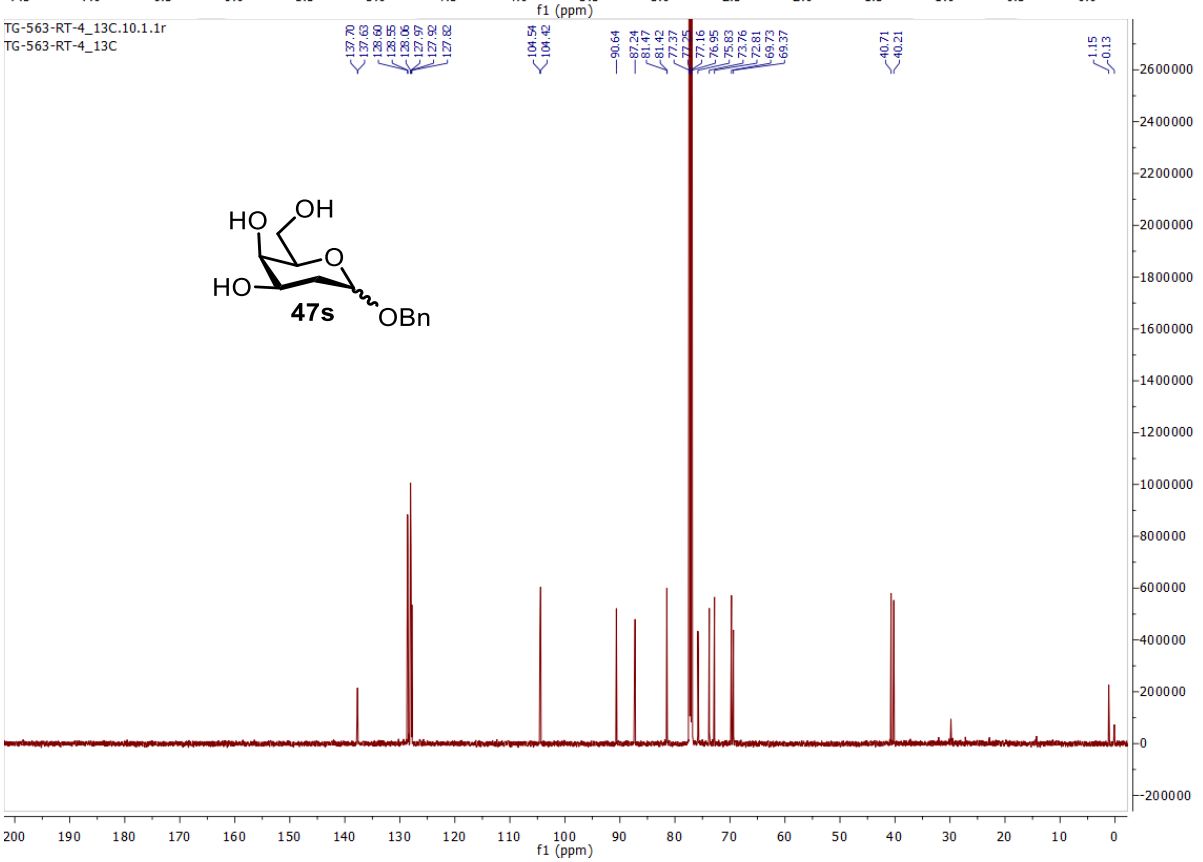
COSY NMR of Isopropyl-3,4,6-tri-*O*-benzoyl-2-deoxy-α-D-glucopyranoside (47q):







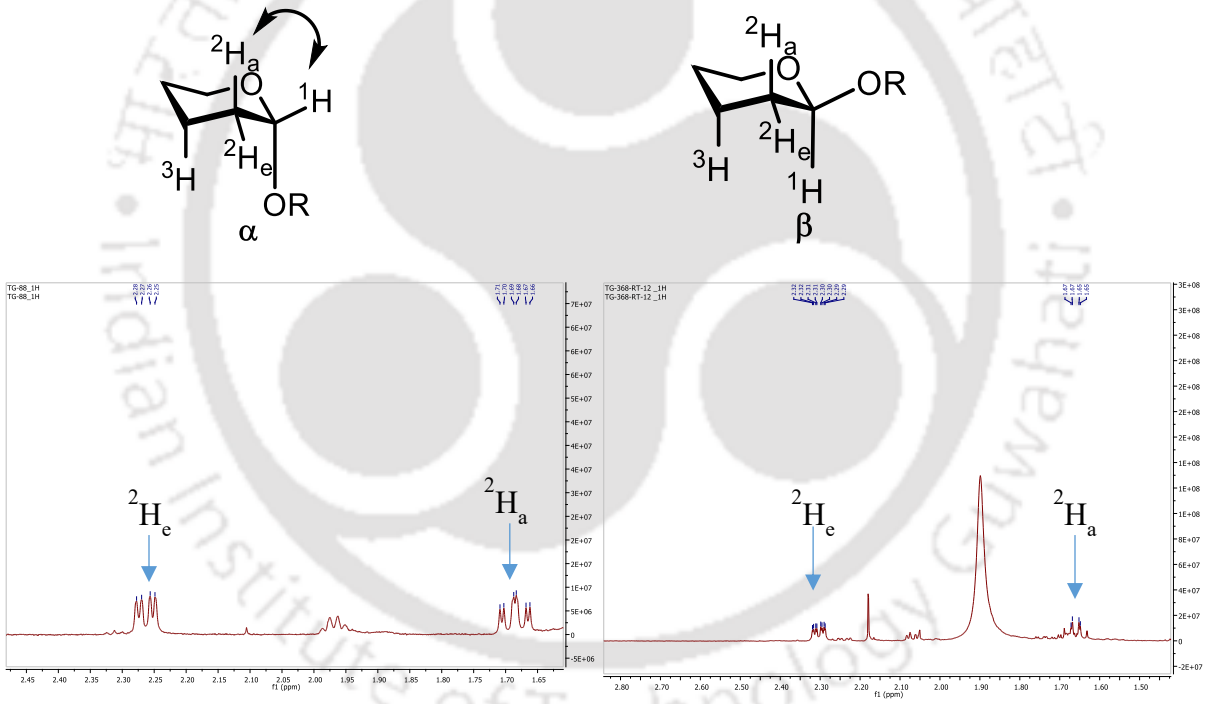

HO
OH
O
HO
OBn
47s
f1 (ppm)


TG-563-RT-4_13C.10.1.1r
TG-563-RT-4_13C
HO
OH
O
HO
OBn
47s
f1 (ppm)

Configuration Analysis of Glycosyl Anomers:

α isomer: In α isomer, anomeric proton ^{1}H appears at ppm range approximately (5.00 – 5.30) ppm as a doublet as equatorial proton appears more downfield than axial one. On the other hand, a 2-deoxy $^{2}H_e$ proton in α isomer comes as doublet of doublet at ppm range approximately 2.21 – 2.24 ppm and $^{2}H_a$ proton appears as triplet of doublet at ppm range approximately (1.71 – 1.76) ppm.

β isomer: In β isomer, anomeric proton appears at ppm range approximately (4.90 – 4.80) ppm. 2-deoxy $^{2}H_e$ proton in β isomer comes as doublet of doublet at ppm range approximately 2.29 – 2.32 ppm and $^{2}H_a$ proton comes as quartet at ppm range approximately (1.65 – 1.67) ppm.



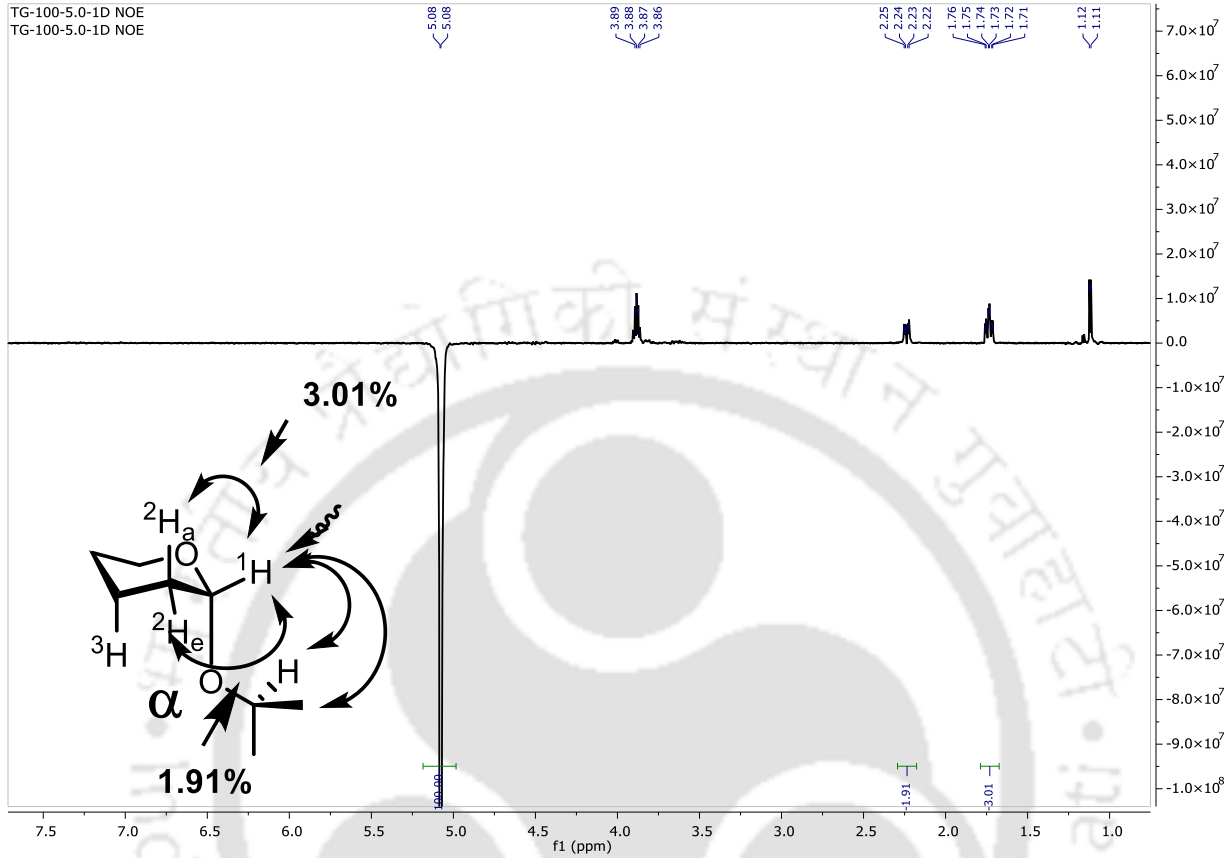


Figure 4: nOe experiment of **46bα** isomer by irradiation of anomeric proton.

2.13 Methodology:

DFT calculations, using B3LYP method and 6-31G(d) basis set, were performed on all the selected intermediates and transition states on the Gaussian-09 program package [1]. Frequency calculations at B3LYP/6-31G(d) level of theory were also performed to confirm the obtained stationary points as minima or transition state on the potential energy surface. Intrinsic reaction coordinate (IRC) calculations, with mass weighted coordinates at the same level of theory, were carried out in forward and reverse directions to validate the reaction path and to follow the reaction profile [2]. We performed single point calculations on B3LYP/6-31G(d) optimized geometries at a few different methods and basis sets (B3LYP/6-311++G(d,p), B3LYP/cc-pVDZ, M06-2X/6-31G(d), M06-2X/6-31++G(d,p), MP2/6-31+G(d), etc.) to confirm that the level of the calculations does not affect the trend of the results, Table **S2**.

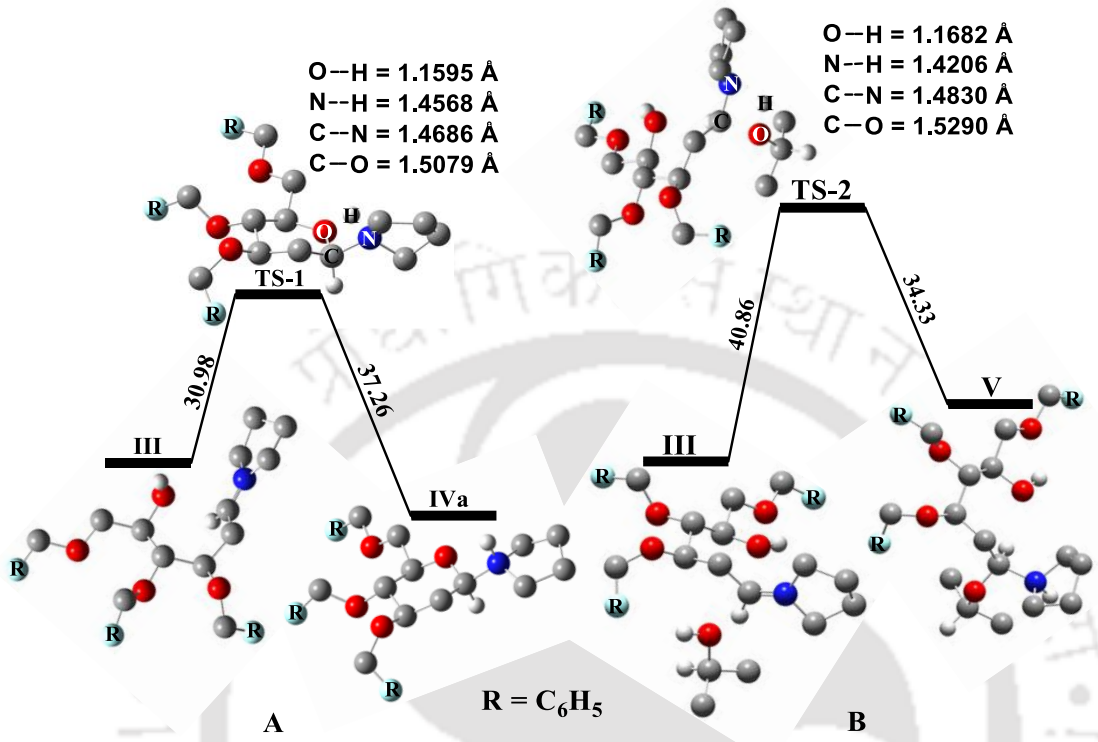


Figure S2: Optimized geometries, important interatomic distances in the transition states and calculated energy for intramolecular mechansim 'A' and intermolecular mechanism 'B'. Energies (in kcal/mol) are obtained at the B3LYP/6-31G(d) level of theory. Only important hydrogen atoms are depicted, and 'C_6H_5' are depicted as 'R' in this figure for the clarity in representation (Please see Figure **S4** & **S5** for detailed representation).

Table S1: Calculated reaction barrier (in kcal/mol) at a few different methods and basis sets

Methods/Basis Sets	III to IVa		III to V	
	TS	Product	TS	Product
B3LYP/6-31G(d)	**30.98**	37.26	**40.86**	34.33
B3LYP/6-31++G(d,p)//B3LYP/6-31G(d)	**31.97**	35.72	**42.09**	31.44
B3LYP/cc-pVDZ//B3LYP/6-31G(d)	**30.89**	34.12	**40.98**	31.87
M06-2X/6-31G(d)//B3LYP/6-31G(d)	**29.64**	39.38	**34.72**	37.84
M06-2X/6-31++G(d,p)//B3LYP/6-31G(d)	**30.10**	37.37	**35.71**	34.85
MP2/6-31+G(d)//B3LYP/6-31G(d)	**29.88**	38.99	**38.34**	35.38
HF/6-31+G(d)//B3LYP/6-31G(d)	**42.95**	50.91	**56.12**	44.66

All the calculations were performed on Gaussian-09 program package.

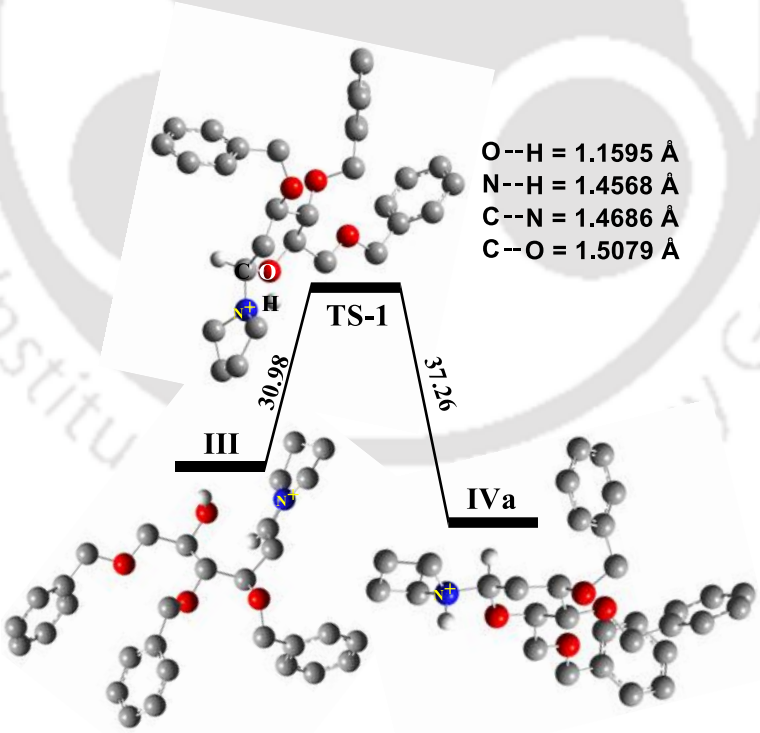


Figure S3: Calculated energy profile for Intramolecular mechanism. Energies (in kcal/mol) are obtained at the B3LYP/6-31G(d) level of theory.

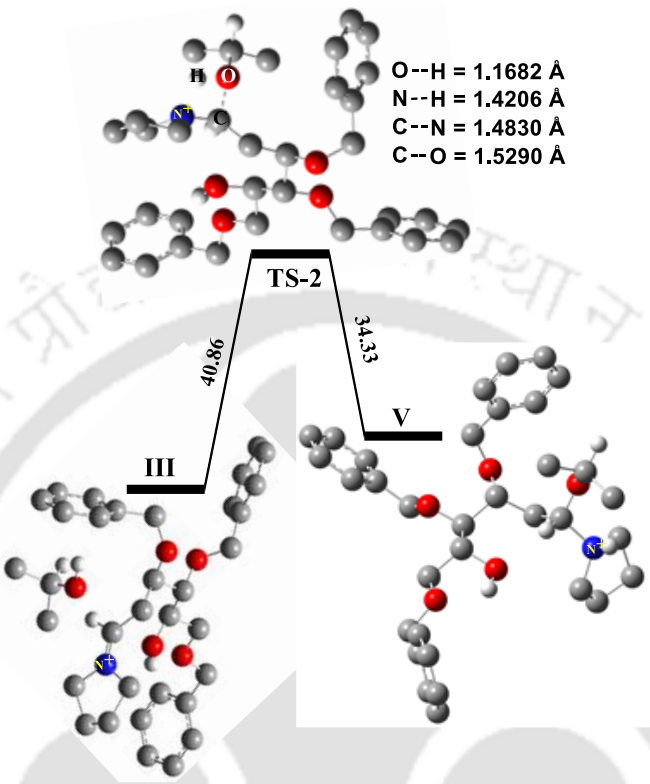


Figure S4: Calculated energy profile for Intermolecular mechanism. Energies (in kcal/mol) are obtained at the B3LYP/6-31G(d) level of theory.

Table S2: Optimized XYZ Coordinates of TS-IIIA at B3LYP/6-31G(d) Level of Theory

1	C	2.85271	-0.49409	-0.65466	38	H	-4.99619	4.70232	0.90545
2	C	2.92078	-1.53710	0.43501	39	C	2.89367	3.25440	-0.20316
3	C	0.25009	-1.42276	0.55244	40	C	4.15248	3.19014	-0.82123
4	C	1.69040	0.47821	-0.39861	41	C	2.80944	3.71716	1.11488
5	C	0.33308	-0.24937	-0.44586	42	C	5.29992	3.58104	-0.13347
6	H	3.27898	-1.14543	1.38895	43	H	4.22500	2.84248	-1.84935
7	H	2.71206	-0.95924	-1.63635	44	C	3.95828	4.11473	1.80495
8	H	3.79194	0.06793	-0.68022	45	H	1.83781	3.78032	1.60016
9	H	1.80346	0.93943	0.59285	46	C	5.20439	4.04496	1.18282
10	H	0.03516	-1.02100	1.54489	47	H	6.26787	3.53898	-0.62568
11	H	0.18383	-0.61771	-1.47130	48	H	3.87710	4.48053	2.82472
12	O	1.56008	-2.13157	0.69742	49	H	6.09798	4.35828	1.71536
13	O	1.71868	1.45801	-1.41445	50	C	-4.39454	-2.37273	0.05109
14	O	-0.67160	0.66627	-0.07455	51	C	-5.01011	-2.11506	1.28329
15	C	-0.73191	-2.54518	0.20671	52	C	-5.04683	-1.99660	-1.12890
16	H	-0.47633	-2.95913	-0.78663	53	C	-6.25508	-1.48894	1.33391
17	H	-0.61661	-3.35771	0.94484	54	H	-4.51337	-2.41075	2.20452
18	C	1.65356	2.82681	-0.95619	55	C	-6.29352	-1.37151	-1.08116
19	H	1.53699	3.40146	-1.87996	56	H	-4.58016	-2.20057	-2.09012
20	H	0.75490	2.96892	-0.34596	57	C	-6.89803	-1.11626	0.15067
21	C	-1.67778	0.94247	-1.07969	58	H	-6.72779	-1.30003	2.29363
22	H	-2.21724	0.01286	-1.29272	59	H	-6.79298	-1.08788	-2.00302
23	H	-1.18388	1.29210	-1.99441	60	H	-7.87074	-0.63425	0.18930
24	O	-2.02816	-2.01680	0.22692	61	H	2.05567	-3.05171	0.19525
25	C	-3.03929	-3.02116	0.00197	62	C	4.28521	-3.05392	-1.15862
26	H	-2.86639	-3.49551	-0.97541	63	C	4.22055	-3.55001	1.21258
27	H	-2.94198	-3.79624	0.77712	64	C	4.76349	-4.79122	0.51260
28	C	-2.60623	1.99375	-0.53640	65	C	5.22800	-4.24220	-0.85200
29	C	-3.51955	1.66637	0.47485	66	H	3.59301	-3.26269	-1.97716
30	C	-2.56416	3.30605	-1.01981	67	H	4.84305	-2.14666	-1.40481
31	C	-4.37290	2.63836	0.99357	68	H	5.03425	-2.91264	1.58285
32	H	-3.55978	0.64674	0.84812	69	H	3.52969	-3.75399	2.03462
33	C	-3.42233	4.27993	-0.50508	70	H	5.57205	-5.26155	1.07701
34	H	-1.86316	3.56577	-1.81035	71	H	3.96551	-5.53152	0.38828
35	C	-4.32619	3.94688	0.50428	72	H	6.26076	-3.88757	-0.78526
36	H	-5.08116	2.37444	1.77410	73	H	5.19291	-4.99835	-1.63944
37	H	-3.38594	5.29419	-0.89279	74	N	3.49546	-2.84806	0.10655

Table S3: Optimized XYZ Coordinates of IIIA at B3LYP/6-31G(d) Level of Theory

1	C	1.69323	0.17337	-0.57282	38	H	-4.79441	4.69549	-0.28674
2	C	3.02385	-0.59631	-0.7249	39	C	2.68266	2.96326	0.13679
3	C	3.27362	-1.65838	0.2852	40	C	4.01735	3.05585	-0.28947
4	C	0.12242	-1.86902	-0.15774	41	C	2.38211	3.23170	1.47688
5	C	0.38459	-0.56907	-0.94566	42	C	5.02589	3.40858	0.60602
6	H	2.72780	-1.63762	1.22471	43	H	4.25761	2.86637	-1.33354
7	H	3.13140	-0.98724	-1.74328	44	C	3.39066	3.59104	2.37601
8	H	3.81968	0.15638	-0.60376	45	H	1.35005	3.17463	1.8159
9	H	1.59858	0.50663	0.47069	46	C	4.71346	3.67754	1.94283
10	H	0.10468	-1.64684	0.91432	47	H	6.05305	3.49206	0.26077
11	H	0.43273	-0.80891	-2.02146	48	H	3.14032	3.80684	3.41101
12	O	1.22280	-2.79482	-0.3427	49	H	5.49769	3.96351	2.63818
13	O	1.81228	1.28594	-1.44405	50	C	-4.62792	-2.00123	0.5764
14	O	-0.64700	0.35755	-0.67782	51	C	-4.52791	-1.67562	1.93634
15	C	-1.17218	-2.61756	-0.50578	52	C	-5.79353	-1.66590	-0.11931
16	H	-1.25002	-2.73887	-1.60383	53	C	-5.57531	-1.02446	2.58537
17	H	-1.08295	-3.62782	-0.07249	54	H	-3.62207	-1.92777	2.48139
18	C	1.59355	2.57903	-0.84123	55	C	-6.84843	-1.02223	0.5313
19	H	1.57583	3.26312	-1.6951	56	H	-5.87917	-1.90954	-1.17572
20	H	0.60878	2.59980	-0.36402	57	C	-6.74022	-0.69917	1.88396
21	C	-1.53453	0.65950	-1.77054	58	H	-5.48806	-0.77679	3.63976
22	H	-2.12227	-0.23708	-2.00826	59	H	-7.74970	-0.76998	-0.02013
23	H	-0.94404	0.93861	-2.65296	60	H	-7.55962	-0.19840	2.39207
24	O	-2.29392	-1.95094	0.01409	61	H	1.17418	-3.12880	-1.25518
25	C	-3.49823	-2.71948	-0.11482	62	C	5.12802	-2.72102	-0.96007
26	H	-3.73269	-2.87645	-1.17858	63	C	4.47725	-3.56672	1.25821
27	H	-3.33139	-3.71242	0.33544	64	C	5.34906	-4.60084	0.53963
28	C	-2.43707	1.79221	-1.3565	65	C	6.14916	-3.75342	-0.46525
29	C	-3.31978	1.62729	-0.28006	66	H	4.53483	-3.09940	-1.80024
30	C	-2.41136	3.01349	-2.03834	67	H	5.56237	-1.75971	-1.24334
31	C	-4.16113	2.66948	0.10453	68	H	5.01357	-3.08322	2.08138
32	H	-3.34173	0.68077	0.25101	69	H	3.52299	-3.95156	1.62306
33	C	-3.25900	4.05637	-1.6574	70	H	5.98592	-5.14790	1.23817
34	H	-1.73096	3.14857	-2.87662	71	H	4.71928	-5.32832	0.01615
35	C	-4.13374	3.88572	-0.5842	72	H	6.98287	-3.24837	0.03424
36	H	-4.84524	2.52824	0.93672	73	H	6.55930	-4.34059	-1.2898
37	H	-3.23470	4.99858	-2.19795	74	N	4.21602	-2.53686	0.20545

Table S4: Optimized XYZ Coordinates of IV at B3LYP/6-31G(d) Level of Theory

1	C	1.73668	0.35643	-0.75925	38	H	-4.78623	4.77995	0.40933
2	C	2.91020	-0.62215	-0.92730	39	C	2.85031	3.13524	-0.23054
3	C	2.66459	-1.84142	-0.05250	40	C	4.19218	3.07334	-0.63789
4	C	0.27627	-1.62865	-0.13351	41	C	2.55614	3.58146	1.06263
5	C	0.37925	-0.33567	-0.97543	42	C	5.21488	3.45272	0.22984
6	H	2.75044	-1.59851	1.01889	43	H	4.42727	2.73730	-1.64526
7	H	2.96365	-0.92669	-1.98120	44	C	3.57966	3.96726	1.93315
8	H	3.84049	-0.10730	-0.66741	45	H	1.51939	3.63850	1.38683
9	H	1.74815	0.75551	0.26521	46	C	4.90974	3.90183	1.51895
10	H	0.22217	-1.35604	0.92975	47	H	6.24946	3.41477	-0.10133
11	H	0.29163	-0.59101	-2.04203	48	H	3.33584	4.31994	2.93148
12	O	1.45380	-2.46489	-0.34745	49	H	5.70621	4.20706	2.19197
13	O	1.91562	1.39515	-1.70032	50	C	-4.42977	-2.21838	0.46379
14	O	-0.61413	0.58419	-0.57904	51	C	-4.47080	-1.92754	1.83470
15	C	-0.89121	-2.56165	-0.46227	52	C	-5.53318	-1.89706	-0.33287
16	H	-0.93271	-2.74066	-1.55042	53	C	-5.59486	-1.32389	2.39553
17	H	-0.69472	-3.53274	0.02264	54	H	-3.61570	-2.17196	2.45996
18	C	1.74578	2.73099	-1.18341	55	C	-6.66415	-1.29994	0.22816
19	H	1.75432	3.35902	-2.07980	56	H	-5.51039	-2.11646	-1.39787
20	H	0.76399	2.82322	-0.70784	57	C	-6.69575	-1.01116	1.59235
21	C	-1.69142	0.80146	-1.51485	58	H	-5.61748	-1.10440	3.45946
22	H	-2.26757	-0.12545	-1.61344	59	H	-7.51601	-1.05825	-0.40103
23	H	-1.27070	1.06849	-2.49359	60	H	-7.57494	-0.54742	2.03083
24	O	-2.08457	-1.99372	0.01625	61	H	3.58273	-3.18808	-1.28812
25	C	-3.21089	-2.87012	-0.13392	62	C	5.14131	-2.53007	-0.05340
26	H	-3.37312	-3.09292	-1.19921	63	C	3.47189	-4.20295	0.50905
27	H	-2.98457	-3.82269	0.37305	64	C	4.79635	-4.93995	0.34005
28	C	-2.55683	1.91421	-0.98700	65	C	5.86195	-3.82114	0.40211
29	C	-3.38682	1.69057	0.11999	66	H	5.53200	-2.09369	-0.97300
30	C	-2.53758	3.18105	-1.58079	67	H	5.13133	-1.75982	0.72000
31	C	-4.18260	2.71895	0.62167	68	H	3.29811	-3.88711	1.54167
32	H	-3.40767	0.70776	0.58234	69	H	2.58603	-4.71266	0.13407
33	C	-3.33797	4.21111	-1.08219	70	H	4.93369	-5.69572	1.11682
34	H	-1.90011	3.36075	-2.44404	71	H	4.82172	-5.45714	-0.62596
35	C	-4.16051	3.98091	0.02109	72	H	6.23190	-3.69378	1.42276
36	H	-4.82737	2.53311	1.47623	73	H	6.72324	-4.04189	-0.23182
37	H	-3.32048	5.18878	-1.55592	74	N	3.68906	-2.93377	-0.29936

Table S5: Optimized XYZ Coordinates of TS-III-B at B3LYP/6-31G(d) Level of Theory

1	C	1.35566	-0.21554	-0.63828	44	C	5.28300	-0.95947	2.42363
2	C	1.04908	-1.64326	-1.15255	45	H	4.19592	0.87890	2.12316
3	C	0.23733	-2.56834	-0.27104	46	C	5.76560	-2.12728	1.83219
4	C	-1.08998	0.64083	-0.23201	47	H	5.92149	-3.26380	0.00491
5	C	0.26360	0.84757	-0.92923	48	H	5.47051	-0.76265	3.47576
6	H	-0.61123	-2.08792	0.2068	49	H	6.33103	-2.84407	2.42121
7	H	0.51368	-1.55940	-2.10498	50	C	-5.66974	1.64769	0.25907
8	H	2.01248	-2.11447	-1.36206	51	C	-6.58564	1.05463	-0.61674
9	H	1.55159	-0.22859	0.44022	52	C	-5.94189	1.64419	1.63359
10	H	-0.92656	0.54782	0.85485	53	C	-7.75703	0.47084	-0.13071
11	H	0.09274	0.86460	-2.01511	54	H	-6.38614	1.05832	-1.68613
12	O	-1.71948	-0.54402	-0.73386	55	C	-7.10820	1.05830	2.12267
13	O	2.53172	0.18857	-1.33797	56	H	-5.23670	2.10656	2.32029
14	O	0.76668	2.10102	-0.47708	57	C	-8.01875	0.47100	1.23998
15	C	-2.04734	1.81548	-0.4617	58	H	-8.46572	0.02251	-0.82146
16	H	-1.71357	2.70878	0.07901	59	H	-7.31297	1.06728	3.18966
17	H	-2.10617	2.05381	-1.53651	60	H	-8.93248	0.02247	1.61987
18	C	3.57898	0.75872	-0.53537	61	H	-2.67125	-0.38809	-0.56499
19	H	4.25290	1.21636	-1.26749	62	C	0.37342	-4.29625	-2.19288
20	H	3.17652	1.55886	0.09465	63	C	-1.64312	-4.14469	-0.91696
21	C	1.11283	3.03621	-1.51063	64	C	-1.79003	-5.34579	-1.88077
22	H	0.19564	3.33367	-2.04486	65	C	-0.36237	-5.61799	-2.41624
23	H	1.77989	2.55786	-2.2369	66	H	0.11940	-3.56600	-2.97109
24	O	-3.30706	1.36044	0.01132	67	H	1.46015	-4.39385	-2.14196
25	C	-4.39546	2.25949	-0.25839	68	H	-1.99771	-4.35128	0.09588
26	H	-4.18831	3.22054	0.23442	69	H	-2.16305	-3.25549	-1.2875
27	H	-4.45874	2.44300	-1.34105	70	H	-2.20448	-6.22205	-1.3768
28	C	1.78184	4.24104	-0.89499	71	H	-2.47187	-5.08820	-2.69555
29	C	1.29959	4.80760	0.29226	72	H	0.12236	-6.41462	-1.84227
30	C	2.87627	4.83446	-1.53412	73	H	-0.35357	-5.91407	-3.46782
31	C	1.90162	5.94573	0.82732	74	N	-0.17271	-3.85854	-0.87653
32	H	0.45918	4.34690	0.80314	75	C	-0.53332	-3.62790	2.63667
33	C	3.47329	5.98037	-1.0052	76	C	0.86143	-3.14534	2.26331
34	H	3.26316	4.40038	-2.45364	77	H	1.61388	-3.84671	2.63292
35	C	2.98781	6.53763	0.17807	78	H	-0.72445	-4.64414	2.27469
36	H	1.52110	6.37423	1.75062	79	H	-0.61584	-3.64966	3.72813
37	H	4.32059	6.43150	-1.51398	80	H	-1.31709	-2.95925	2.26507
38	H	3.45357	7.42663	0.5939	81	C	1.19158	-1.74458	2.74224
39	C	4.32391	-0.26302	0.29997	82	H	2.19220	-1.44109	2.4241
40	C	4.82097	-1.43660	-0.28594	83	H	0.45682	-1.01057	2.39428
41	C	4.56231	-0.03517	1.66047	84	H	1.16693	-1.73736	3.83725
42	C	5.53282	-2.36351	0.47363	85	O	1.10283	-3.25525	0.78582
43	H	4.65588	-1.61176	-1.34634	86	H	0.63305	-4.18007	0.24841

Table S6: Optimized XYZ Coordinates of III-B at B3LYP/6-31G(d) Level of Theory

1	C	1.49570	-0.25291	-1.12040	44	C	4.62670	-1.53038	2.36150
2	C	1.13022	-1.52937	-1.91765	45	H	3.71820	0.40351	2.05523
3	C	0.34585	-2.53089	-1.14916	46	C	5.18266	-2.65709	1.75067
4	C	-0.83953	0.57668	-0.44635	47	H	5.71115	-3.58676	-0.12269
5	C	0.43850	0.87593	-1.23654	48	H	4.58488	-1.46224	3.44561
6	H	0.50305	-2.58593	-0.06862	49	H	5.56396	-3.47409	2.35658
7	H	0.65742	-1.28364	-2.87330	50	C	-5.44040	1.13873	0.41990
8	H	2.08905	-2.01614	-2.15503	51	C	-6.46076	0.60059	-0.37109
9	H	1.61101	-0.51814	-0.06163	52	C	-5.50790	0.99060	1.81206
10	H	-0.58018	0.53274	0.62183	53	C	-7.53620	-0.06959	0.21597
11	H	0.18688	1.01448	-2.29907	54	H	-6.41992	0.71481	-1.45213
12	O	-1.36458	-0.69019	-0.86660	55	C	-6.57625	0.31633	2.40036
13	O	2.73738	0.19819	-1.64978	56	H	-4.71959	1.40827	2.43362
14	O	0.96847	2.07443	-0.69097	57	C	-7.59418	-0.21384	1.60236
15	C	-1.93031	1.63176	-0.63463	58	H	-8.32795	-0.47405	-0.40847
16	H	-1.64508	2.57855	-0.15854	59	H	-6.62218	0.21229	3.48092
17	H	-2.10612	1.81532	-1.70768	60	H	-8.43207	-0.73080	2.06173
18	C	3.70692	0.61472	-0.66921	61	H	-2.29670	-0.66828	-0.56933
19	H	4.51625	1.04687	-1.26595	62	C	-0.77647	-3.51061	-3.12473
20	H	3.28815	1.40577	-0.03956	63	C	-1.13759	-4.46485	-0.89013
21	C	1.38703	3.05384	-1.65689	64	C	-2.28421	-4.87586	-1.81671
22	H	0.49754	3.41440	-2.19941	65	C	-1.65642	-4.76514	-3.21749
23	H	2.06034	2.59263	-2.38787	66	H	-1.32787	-2.59644	-3.36867
24	O	-3.08980	1.07231	-0.03450	67	H	0.12507	-3.55615	-3.73976
25	C	-4.27755	1.86052	-0.20806	68	H	-0.45215	-5.29812	-0.70163
26	H	-4.11852	2.84238	0.26220	69	H	-1.44599	-4.03433	0.06381
27	H	-4.45507	2.02811	-1.28069	70	H	-2.64947	-5.88026	-1.59084
28	C	2.07820	4.19206	-0.94768	71	H	-3.12309	-4.17879	-1.71302
29	C	1.54687	4.73675	0.22903	72	H	-1.03951	-5.64472	-3.43090
30	C	3.24718	4.74380	-1.48341	73	H	-2.39880	-4.67733	-4.01390
31	C	2.17496	5.81200	0.85572	74	N	-0.40545	-3.43320	-1.68217
32	H	0.64641	4.30737	0.65856	75	C	1.05209	-2.82215	4.22950
33	C	3.87125	5.82785	-0.86292	76	C	0.53026	-2.02268	3.03771
34	H	3.67130	4.32643	-2.39413	77	H	0.69564	-0.94973	3.22061
35	C	3.33702	6.36296	0.30932	78	H	2.12249	-2.64359	4.38668
36	H	1.75587	6.22423	1.76963	79	H	0.52975	-2.53680	5.14920
37	H	4.77655	6.24801	-1.29209	80	H	0.90502	-3.89528	4.06465
38	H	3.82294	7.20372	0.79631	81	C	-0.95322	-2.25463	2.77812
39	C	4.22098	-0.53049	0.17988	82	H	-1.28153	-1.70765	1.88718
40	C	4.79034	-1.66312	-0.42077	83	H	-1.15031	-3.32360	2.62935
41	C	4.14311	-0.47631	1.57699	84	H	-1.55255	-1.91544	3.62871
42	C	5.26438	-2.71963	0.35594	85	O	1.22331	-2.39855	1.82857
43	H	4.86740	-1.70761	-1.50466	86	H	2.17656	-2.25441	1.96471

Table S7: Optimized XYZ Coordinates of V at B3LYP/6-31G(d) Level of Theory

1	C	1.24289	-0.34206	-0.58970	44	C	4.64172	-0.46597	3.19051
2	C	0.91882	-1.73419	-1.19663	45	H	3.65462	1.29508	2.43519
3	C	0.41329	-2.74871	-0.17655	46	C	5.15621	-1.72579	2.88135
4	C	-1.11507	0.63013	-0.13631	47	H	5.49182	-3.17673	1.31948
5	C	0.17877	0.73595	-0.95617	48	H	4.70047	-0.08647	4.20696
6	H	-0.39494	-2.33204	0.42811	49	H	5.62258	-2.32973	3.65494
7	H	0.19991	-1.62438	-2.01416	50	C	-5.66924	1.62722	0.60778
8	H	1.85731	-2.10170	-1.61816	51	C	-6.81236	1.17749	-0.06032
9	H	1.30947	-0.41421	0.50391	52	C	-5.64844	1.61172	2.00936
10	H	-0.86152	0.76468	0.92632	53	C	-7.92273	0.72613	0.65683
11	H	-0.06600	0.63691	-2.02488	54	H	-6.83879	1.18692	-1.14774
12	O	-1.71770	-0.65910	-0.32232	55	C	-6.75155	1.15365	2.72690
13	O	2.51194	0.03068	-1.11673	56	H	-4.76247	1.95885	2.53490
14	O	0.69001	2.03372	-0.69077	57	C	-7.89293	0.71190	2.05123
15	C	-2.14622	1.69470	-0.51985	58	H	-8.80797	0.38697	0.12610
16	H	-1.81427	2.69263	-0.20953	59	H	-6.72669	1.14900	3.81318
17	H	-2.30499	1.69965	-1.61123	60	H	-8.75601	0.36300	2.61131
18	C	3.39250	0.72610	-0.21534	61	H	-2.64798	-0.51401	-0.05424
19	H	4.18832	1.10143	-0.86776	62	C	0.63259	-4.75878	-1.83749
20	H	2.88393	1.59107	0.22001	63	C	-1.55771	-3.62599	-1.68856
21	C	1.15489	2.75207	-1.84383	64	C	-1.30089	-4.13430	-3.11200
22	H	0.29276	2.95720	-2.50049	65	C	-0.30995	-5.29277	-2.91490
23	H	1.86324	2.13464	-2.40714	66	H	1.36650	-4.06803	-2.25208
24	O	-3.33884	1.31105	0.14947	67	H	1.15796	-5.51390	-1.25305
25	C	-4.47476	2.13055	-0.15998	68	H	-2.37284	-4.16915	-1.20431
26	H	-4.23895	3.17100	0.11109	69	H	-1.74735	-2.55587	-1.59978
27	H	-4.66735	2.10500	-1.24290	70	H	-2.22988	-4.44189	-3.59825
28	C	1.81108	4.04029	-1.40968	71	H	-0.84964	-3.34630	-3.72500
29	C	1.30762	4.78790	-0.33757	72	H	-0.82757	-6.19490	-2.56787
30	C	2.91951	4.52493	-2.11366	73	H	0.23424	-5.55256	-3.82647
31	C	1.90305	5.99712	0.02113	74	N	-0.27675	-3.96101	-0.90816
32	H	0.45735	4.41342	0.22429	75	C	0.25006	-4.67372	2.20594
33	C	3.50915	5.74032	-1.76254	76	C	1.28360	-3.56975	1.97465
34	H	3.32471	3.94963	-2.94349	77	H	2.27361	-3.95233	2.23421
35	C	3.00264	6.47898	-0.69250	78	H	0.47281	-5.56541	1.60664
36	H	1.50651	6.56581	0.85792	79	H	0.26676	-4.98313	3.25585
37	H	4.36808	6.10425	-2.31946	80	H	-0.77485	-4.33193	2.00333
38	H	3.46331	7.42254	-0.41393	81	C	1.01312	-2.31525	2.79866
39	C	3.97583	-0.15400	0.87234	82	H	1.79489	-1.57030	2.63067
40	C	4.49607	-1.42039	0.57237	83	H	0.03582	-1.87146	2.57377
41	C	4.05062	0.31172	2.19077	84	H	1.01416	-2.57319	3.86311
42	C	5.08024	-2.20191	1.56844	85	O	1.46428	-3.26216	0.55374
43	H	4.44391	-1.78738	-0.44886	86	H	-0.53546	-4.58500	-0.14230

Chapter 3

Open-Close Strategy towards the Organocatalytic Generation of 2-Deoxy-ribofuranosyl Oxocarbenium Ions: Pyrrolidine Salts Catalyzed Synthesis of 2-Deoxy-ribo-furanosides from 2-Deoxy-ribo-furanoses

3.1 Introduction:

2-Deoxy-glycosides are part of several natural products[1] with anticancer and antibiotic properties[2] and has been shown that these structural motifs are important for their activity. Besides, slight modifications in the sugar components through glycorandomization[3] was shown to be an effective technique to alter the biological properties of these natural products. Given the importance, literature has seen a number of methods for the construction of these important class of acetals and their analogues, particularly based on 2-deoxy and 2,6-dideoxy-pyranoses. 2-Deoxy-riboses, a subclass under 2-deoxy-sugars, holds great significance in biology being a constituent of DNA. The synthesis and biological studies of *N*-linked 2-deoxy-ribonucleotides and their analogues received great attention from the scientific community.[4] On the other hand, synthesis of *O*-linked 2-deoxy-riboglycosides that combines the features of 2-deoxy-furanoses and pyranoses, could be interesting targets for drugs and their structure-activity relationship studies against cancer and viral proliferation, received scant attention, presumably because of the instability of donors

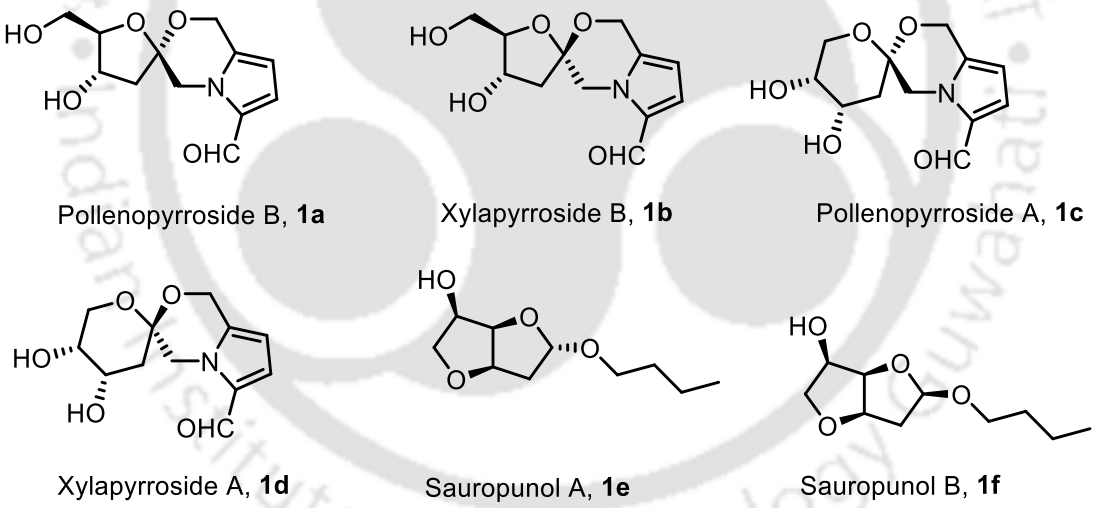
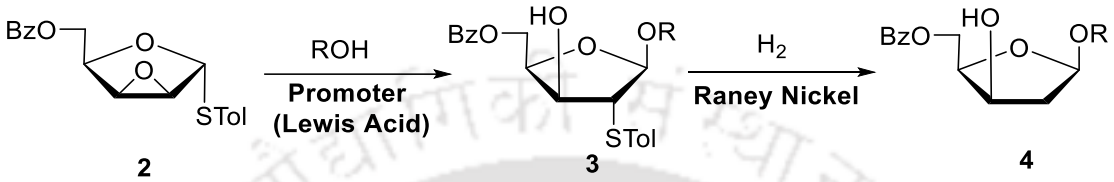


Figure 1: Natural compounds: 2-deoxy furanoside skeleton.

and also the products under the reaction conditions. Very recently, several natural products constituting 2-deoxy-furanoside skeleton (**Figure 1**, **1a-f**)[5] with antioxidant and antibacterial properties have also been isolated and has attracted the attention of organic and medicinal chemists.

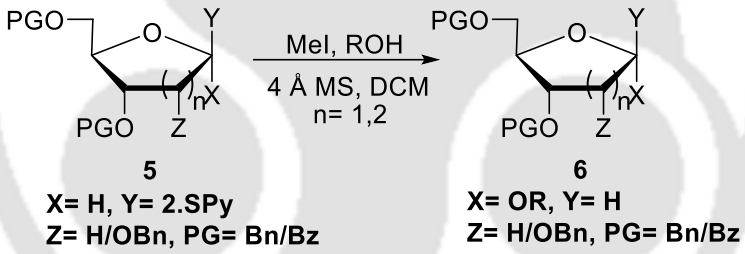
Direct and indirect methods have been developed to achieve the synthesis of 2-deoxy-riboglycosdies. Lowary's usage of 2,3-anhydro-thio-furanoside donors[6] **2** has been a successful

method for the stereoselective synthesis of 2-deoxy ribo-oligosaccharides **4**. It was elucidated that the crucial intermediate 2-thiotolyl-furanoside **3** was transformed into 2-deoxy ribosugar upon hydrogenation with raney nickel (**Scheme 1**). However, this method relies on a two-step process (glycosylation followed by the reduction of aryl thioethers) to achieve the synthesis of these compounds.



Scheme 1: Synthesis of 2-deoxy ribosugar from 2-thiotolyl-furanosides.

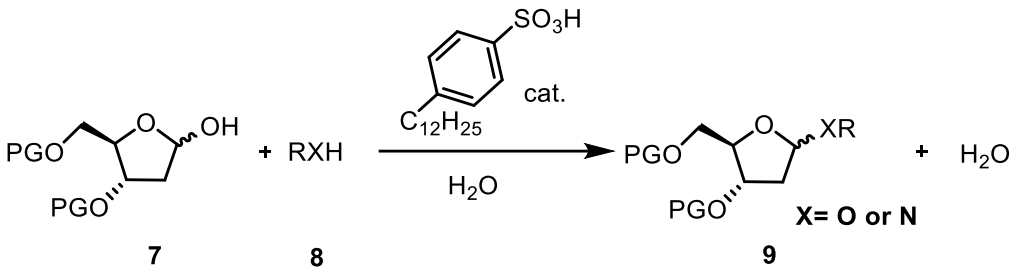
Again, the anomeric mixture of 2-deoxy-2-pyridyl-1-thioglycoside donors **5** were activated by methyl iodide, showcased by Mereyala et al. The corresponding thioglycosides reacted by sugar alcohol to give axially α-linked glycosides **6** (**Scheme 2**). Although it was an effective and one-step direct process, still it requires stoichiometric activation of donors.[7]



Scheme 2: Activation of 2-deoxy-2-pyridyl-1-thioglycosides: synthesis of α-linked glycosides.

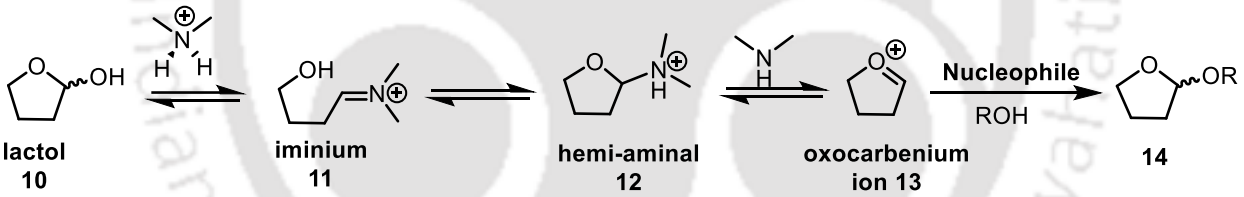
Naohiro and Shu reported Brønsted acid-surfactant-combined dodecylbenzenesulfonic acid (DSBA) catalyzed dehydrative glycosylation[8] that drives the glycosylation in the presence of water as a solvent (**Scheme 3**), but it suffers less substrate scope. Dehydrative glycosylation, utilizing 2-deoxy-ribo-lactols **7**, though an attractive option, has not been explored to its full potential for the synthesis of 2-deoxy-ribo-furanosides **9**.

The ability of secondary amines/amine salts to form iminium ions with aldehydes that tautomerize to enamines to react with a plethora of electrophiles has been well documented. Lactols **10**, that are masked aldehydes have also been showcased to undergo iminium/enamine catalysis towards Michael addition reactions via an open-close strategy.[9] We have envisioned that



Scheme 3: Brønsted acid-surfactant-combined catalyzed dehydrative glycosylation.

the iminium ions **11**, before tautomerization into enamine, could also be trapped intramolecularly, by the suitably placed hydroxyl group leading to the formation of a protonated hemi-aminal **12**. The nucleofugal expulsion of the secondary amine could then lead to the formation of oxocarbenium ions **13**, the putative intermediates in glycosylation reactions. The thus generated oxocarbenium ion **13** via the open-close strategy can be successfully trapped with alcoholic nucleophiles leading to the development of a new glycosylation method. 2-Deoxy-ribo-lactols that are masked aldehydes are excellent substrates to perform the study. Herein, we display the successful execution of the secondary amine catalysis for the synthesis of 2-deoxy-ribofuranosides.



Scheme 4: Organocatalytic dehydrative glycosylation of 2-deoxy ribo-lactol.

3.2 Optimization Studies with Different Catalysts:

We commenced our study by subjecting the easily accesible 3,5-dibenzylated-2-deoxy-ribo-furanose **15a** to the secondary amine catalysis utilizing the commercially available, inexpensive pyrrolidinium hydrochloride. Thus, compound **15a** was reacted with 1.1 equiv of benzyl alcohol as a nucleophile in the presence of 20 mol % of the catalyst **16b** in DCM as solvent at rt. However, no reaction was observed at this temperature, which prompted to raise the temperature gradually. After a failed attempts at various temperatures, the reaction when performed in toluene as solvent at 100 ^{o}C, provided the expected glycosylated product **18a** in 96% yield in 5 h as a mixture of anomers (1:1.3, α:β). The disappearance of the anomeric peaks at (5.56

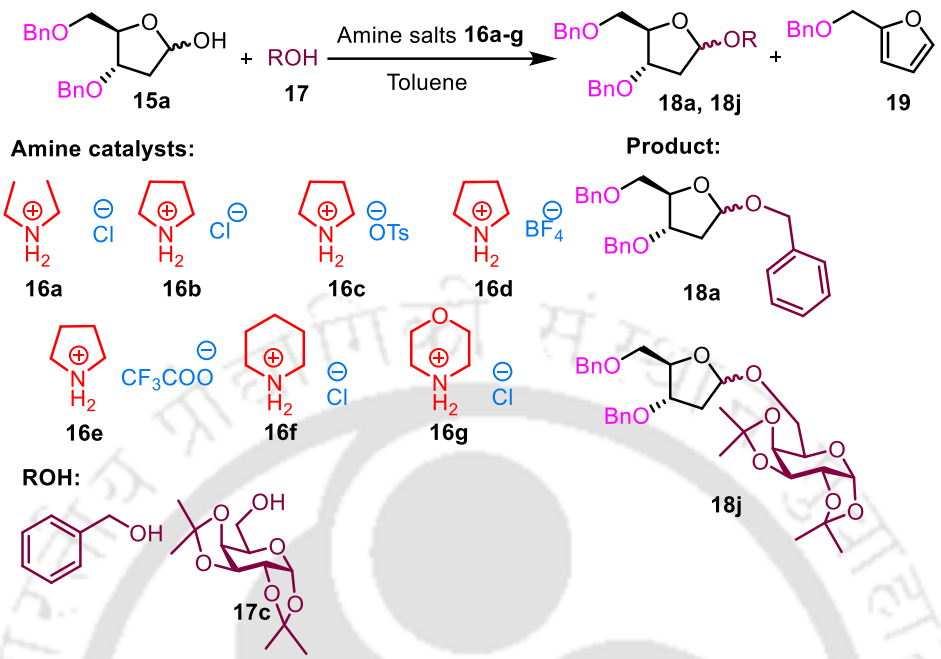
- 5.47) ppm and the appearance of H-1 signals at (5.21 - 5.17) ppm along with the presence of addition benzylic protons confirmed the formation of glycosylated product.

Further optimization study with 2-deoxy ribose **15a** as donor and benzyl alcohol as acceptor in the presence of various secondary amine salts (**Table 1**). The coupling reaction with the flexible diethylamine hydrochloride **16a** gave the desired product in 73% yield with similar anomeric selectivity (**Table 1**, entry 1). Pyrrodiline salts with tosylate and tetrafluoroborate as counter anions (**16c** and **16d**) gave the corresponding glycosylated product in 87% and 93% yields (**Table 1**, entries 3-4) respectively, with comparable selectivities. The secondary amine salt **16e** also afforded the product with a little β-selectivity in 7 h, albeit with a relatively moderate yield of 62% (**Table 1**, entry 5). The observed results points to the fact that the counter ions, particularly the non-nucleophilic anions, do not dictate the outcome of the glycosylation reaction, in agreement with the iminium catalysis.[10] In the presence of 1(N) HCl in toluene and 20 mol % HCl in toluene, the coupling between glycosyl donor **15a** and acetonide protected acceptor **17c** gave the corresponding product **18j** in 63% and 43% yield with exclusively β-selectivity (**Table 1**, entries 6, 12). Surprisingly, 20 mol % *p*-toluene sulphonic acid failed to give the product (**Table 1**, entry 7). Hydrochloride salts of piperidine **16f** and morpholine **16g** gave the corresponding product **18a** in 79% and 66% with 1:1.3 and 1:1.2 α:β selectivity respectively (**Table 1**, entries 8-9). Moreover, in the presence of 3 Å and 4 Å MS, the reaction between benzyl protected donor **15a** and glycosyl acceptor **17c** gave the product **18j** at 50 ^{o}C in mere 14% and 38% yields with 1:1 and 1.1:1 α:β selectivity respectively (**Table 1**, entries10-11). It indicates that there was no drastic improvement in the presence of molecular sieves at a lower temperature. To this end, we have chosen pyrrolidine hydrochloride **16b** as the catalyst of choice to study the glycosylation reaction with various acceptors.

3.3 Scope of Derivatives with Various Glycosyl Donors and Acceptors:

The novel organocatalytic method was then tested with a variety of non-carbohydrate alcohols (**Scheme 5**, **18a-i**, **18m**, **18o**), and excellent yields were obtained in all the cases. However, to our surprise, a very little preference for β-selectivity has been observed in all the cases except in the case of propargyl alcohol (**Scheme 5**, **18e**) where the opposite has been observed. Moreover, the reaction when performed with 2-cyano ethanol as acceptor yielded the β-isomer

Table 1: Optimization Study of different secondary amine salts towards glycosylation.

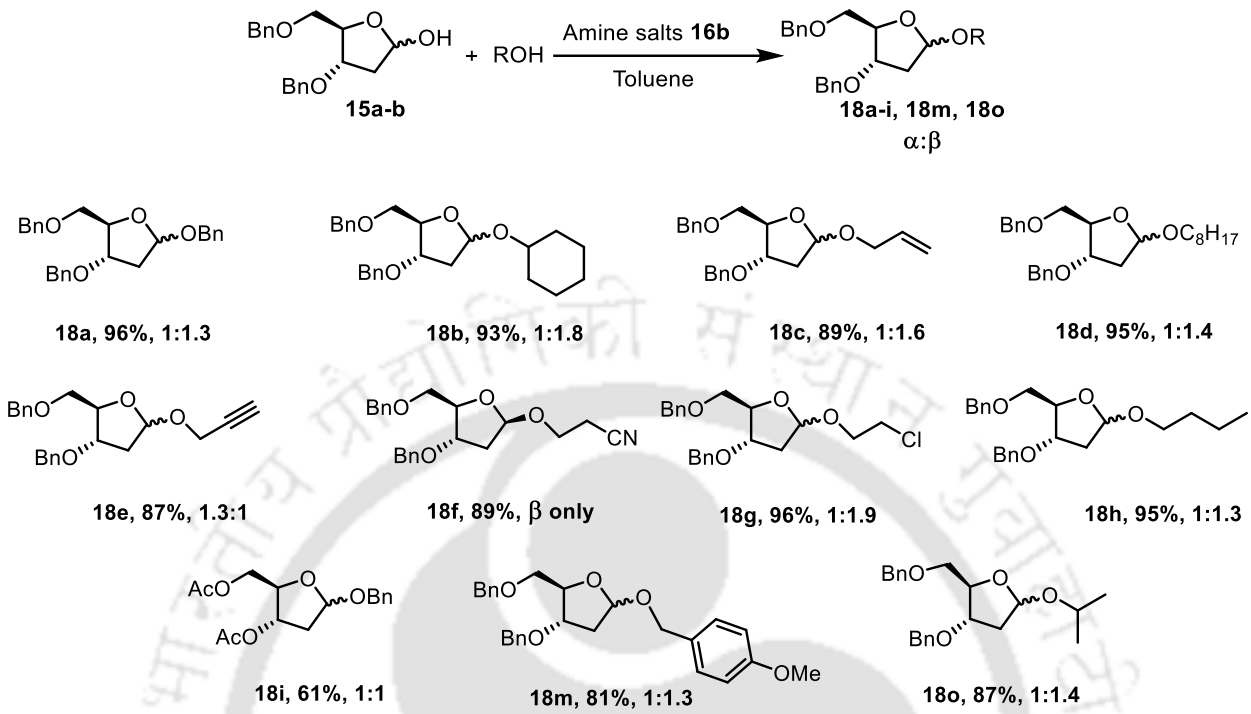


entry	cat.	time	prod.	yield (%)	α:β[e]
1	**16a**	5h	**18a**	73	1:1.3
2	**16b**	5h	**18a**	96	1:1.3
3	**16c**	4h	**18a**	87	1:1.3
4	**16d**	5h	**18a**	93	1:1.2
5	**16e**	7h	**18a**	62	1:1.4
6[a]	**1(N)HCl**	5h	**18j**	63	β
7	**TsOH**	5h	**18j**	0	-
8	**16f**	5h	**18a**	79	1:1.3
9	**16g**	5h	**18a**	66	1:1.2
10[b]	**16b**	5h	**18j**	38	1.1:1
11[c]	**16b**	5h	**18j**	14	1:1
12[d]	**HCl**	5h	**18j**	43	β

Reaction conditions: 1 equiv of **15a**, 1.1 equiv of acceptor and 20 mol % of **16a-g**, toluene, 100 °C. [a]1 ml of 1(N) HCl in toluene was used. [b]200 mg of 4 Å MS was used at 50 °C. [c]200 mg of 3 Å MS was used at 50 °C. [d]20 mol % HCl in toluene was used. [e]Anomeric selectivities were determined from crude NMR analysis.

18f in 89% yield as the only glycosylated product. This could be attributed to the possible intra or intermolecular nitrile effect[11] that could lead to the observed selectivity. In addition, the disarmed donor **15b**, under identical catalytic conditions with benzyl alcohol as acceptor, also lead to the glycsoylation product **18i** in 61% yield, albeit as a 1:1 mixture of anomers.

Scheme 5: Synthesis of monosaccharides through dehydrative glycosylation of 2-deoxy ribose.

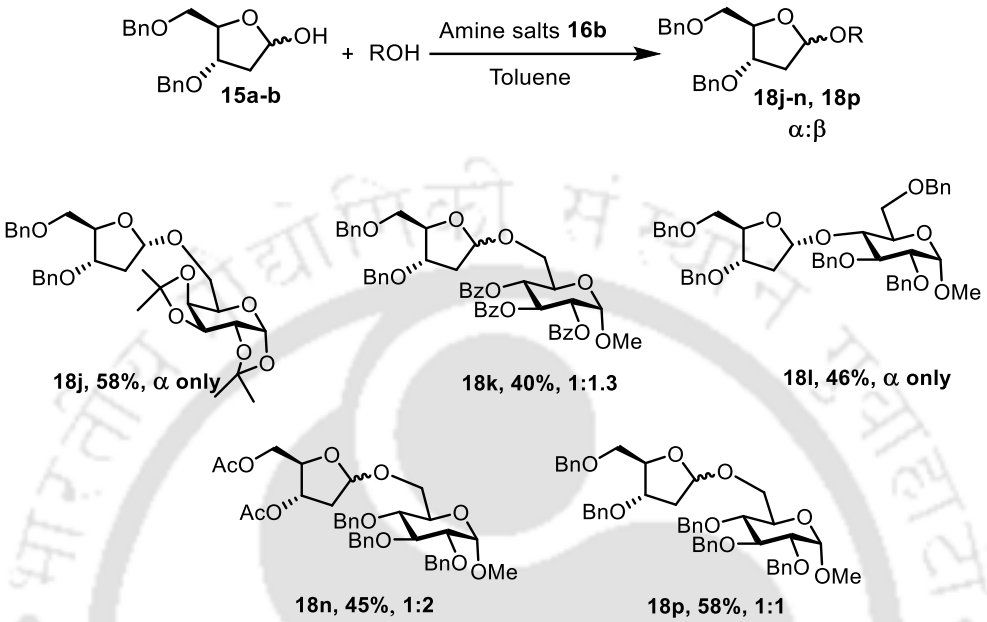


Reaction conditions: 1 equiv of **15a-b**, 1.1 equiv of acceptor and 20 mol % of **16b**, toluene, 100 ^{o}C, 5 h (24 h for **18i**). Anomeric selectivities were determined from crude NMR analysis.

With the successful execution of the organocatalytic method with non-carbohydrate alcohols, we then chose to examine the ability of secondary amine catalysis with challenging carbohydrate alcohols as acceptors. The organocatalysis, however, is only partially effective with the products obtained in moderate yields (**Scheme 6**). Thus, when 1.1 equivalents of the primary sugar alcohol **17c** derived from galactose, treated with 2-deoxy ribose donor **15a** under the optimized conditions gave the corresponding glycosylated product **18j** in 58% yield with exclusive α-selectivity. The disarmed primary sugar acceptor **17d** gave the product **18k** with an α:β selectivity of 1:1.3. Interestingly, secondary alcohol acceptor **17b** also reacted well in this condition to provide the product **18l** in moderate yield of 46% again with exclusive α-selectivity. The coupling between the disarmed donor **15b** and the 6-hydroxy tri-O-benzyl methylpyranoside **17a** has proven to be less effective and gave the expected glycosylated product **18n** in 45% yield with 1:2 α:β selectivity. The reaction between benzyl protected armed donor **15a**, and

electronically rich primary sugar acceptor **17a** afforded the glycosylated product **18p** in 58% yield with 1:1 α:β selectivity.

Scheme 6: Synthesis of disaccharides from 2-deoxy ribose.



Reaction conditions: 1 equiv of **15a-b**, 1.1 equiv of **17a-d** and 20 mol % of **16b**, toluene, 100 ^{o}C, 5 h (24 h for **18n**). Anomeric selectivities were determined from crude NMR analysis.

3.4 nOe Experiments for Determination of Stereochemistry:

The stereochemistry of the anomers has been assigned based on extensive ^{1}H, ^{13}C, COSY, and nOe analysis (**Figure 2**). Thus, in a nOe experiment, irradiation of the signal of $\mathbf{H_1}$ appearing at 5.24 ppm in the isomer **18gα** led to the enhancement of $\mathbf{H_3}$ appearing at 4.01 - 3.98 ppm along with $\mathbf{H_2}$ at 2.28 ppm, confirming that the aglycon is cis to the C-3 –OBn group. Besides, irradiation of the signal for $\mathbf{H_1}$ in the corresponding β glycoside appearing at 5.24 ppm did not lead to the enhancement of $\mathbf{H_3}$ (4.16 ppm) but led to the enhancement of the $\mathbf{H_2'}$ (2.16 ppm) that appears more upfield to $\mathbf{H_2}$, confirming the β-stereochemistry at the anomeric position. This also predicts that the five-membered 2-deoxy-ribo-furanose has adopted the envelope conformation in the solution phase.

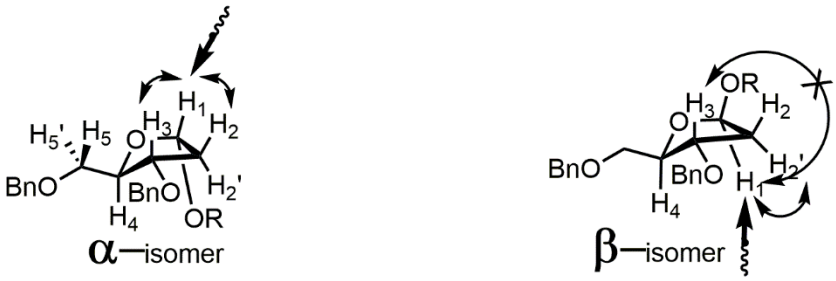


Figure 2: Diagnostic nOe correlation for compounds **18gα** and **18gβ**.

The chemical shifts and the splitting patterns of the characteristic proton signals of the two anomers **18gα** and **18gβ** as depicted in **Table 2** have been correlated with the corresponding signals for all the other compounds to assign the relative stereochemistry.

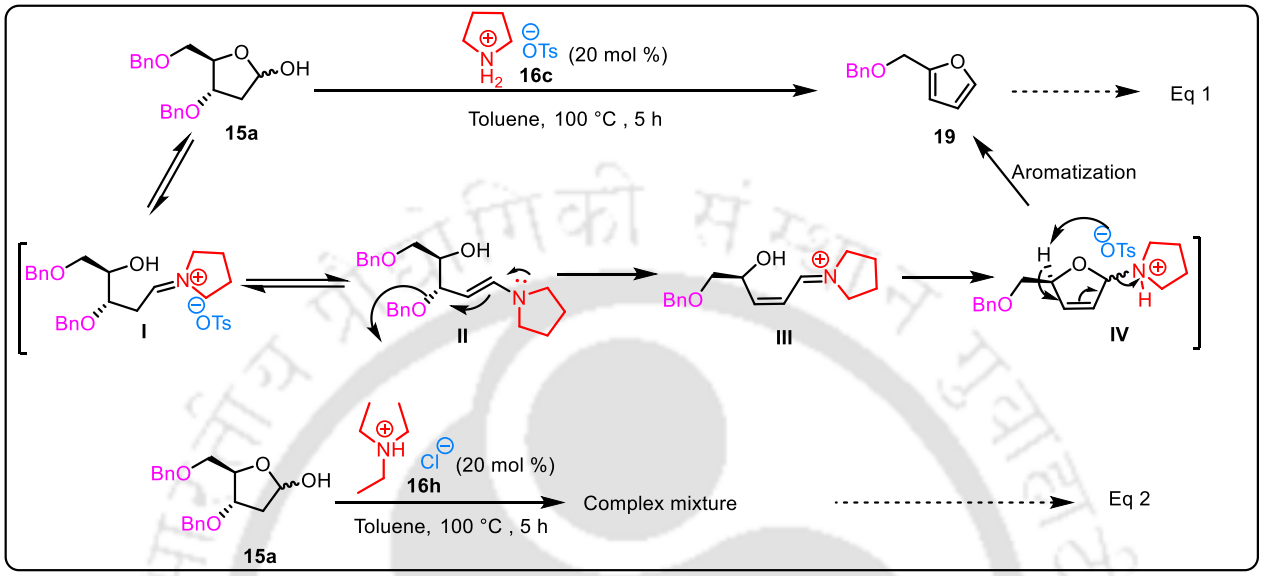
α-isomer ppm (J value)		**β-isomer ppm (J value)**	
Irradiated	**Enhanced**	**Irradiated**	**Enhanced**
H-1 5.24 (dd, *J* = 5.7, 1.4 Hz, 1H)	**H-2** 2.28 (ddd, *J* = 13.7, 8.1, 5.5 Hz, 1H) **H-3** 3.98 (dt, *J* = 11.3, 5.8 Hz, 1H)	**H-1** 5.24 (dd, *J*= 5.5, 1.9 Hz, 1H)	**H-2′** 2.16 (dt, *J* = 13.6, 5.7 Hz, 1H)
H-2 2.28 (ddd, *J* = 13.8, 8.1, 5.6 Hz, 1H)	**H-1** 5.24 (d, *J* = 5.3 Hz, 1H) **H-2′** 2.08 (ddd, *J* = 13.7, 3.4, 1.6 Hz, 1H) **H-3** 4.03 – 3.96 (m, 1H)	**H-2** 2.30 (ddd, *J* = 13.4, 7.0, 1.9 Hz, 1H)	**H-1** 5.25 – 5.23 (m, 1H) **H-2′** 2.15 (t, *J* = 5.6 Hz, 1H) **H-3** 4.16 (d, *J* = 3.8 Hz, 1H)
H-2′ 2.08 (ddd, *J* = 14.1, 3.1, 1.5 Hz, 1H)	**H-2** 2.29 (dd, *J* = 8.0, 5.7 Hz, 1H) **H-3** 4.00 (s, 1H)	**H-2′** 2.16 (dt, *J* = 13.5, 5.6 Hz, 1H)	**H-1** 5.24 (d, *J* = 5.0 Hz, 1H) **H-2** 2.31 (dd, *J* = 7.0, 1.6 Hz, 1H)

Table 2: Comparison of characteristic signals in ^{1}H NMR data of anomers **18gα** and **18gβ**.

3.5 Mechanism:

The observed β-selectivities, albeit low in the case of more reactive non-carbohydrate *O*-glycosyl acceptors, are not consistent with the Woerpel's "inside attack" model[12] of *C*-glycosylation reactions on 2-deoxy-furanosyl oxocarbenium ions (**Figure 3**, B), but fall in line with the Mukaiyama's *O*-glycosyl-ribofuranosides synthesis.[13] However, owing to the high operational temperature, the current method does not provide greater facial descrimination of oxocarbenium ions. On the contrary, the more bulkier and less reactive carbohydrate acceptors

leading to high α-selectivities could be resulting due to the reaction of these acceptors with the more stable low energy pseudo-diaxial conformer (**Figure 3**, B, **VII**) in line with Woerpel's prediction.



Scheme 7: Mechanistic investigation

In order to get insights into the mechanism of the transformation, we subjected 2-deoxy-ribo-leactol **15a** to the catalytic conditions without any acceptor. Interestingly, the reaction leads to the formation of a substituted furan derivative **19** (**Scheme 7**, Eq. 1) in 78% yield, the spectral data of which were in perfect match with the reported data.[14] It is rather surprising to observe the formation of **19**, as such compounds are accessible only under strong Brønsted-acidic conditions from ketal derivatives.[15] This leads us to examine the Brønsted acidic nature of the secondary amine salts. Hence, we chose to perform the same reaction with triethylamine hydrochloride instead of pyrrolidine hydrochloride whose p*K*a's are close but obviates the formation of iminium or enamine. However, the reaction only leads to a very complex mixture of products (**Scheme 7**, Eq. 2) hinting at the unique role of secondary amine catalysis in the former case. The facile formation of the furan derivatives under the secondary amine catalysis could be easily explained via the formation of enamine driven elimination of C-3 *O*-benzyl group, ring-closure to obtain the protonated hemi-aminal, followed by aromatization (**Scheme 7**, Eq. 1). These reactions gave a strong and direct evidence for the involvement of iminium ions in the current transformation. Based on all the above observations, we propose the mechanism for the glycosylation reaction as depicted in (**Figure 3**, A). The open-chain form of the 2-deoxyribofuranose hemi-acetal **15a** can

react with the pyrrolidine hydrochloride to generate iminium ion (**Figure 3**, A, **I**) that undergoes a ring-closure via an intramolecular attack by the tethered hydroxyl group. The thus generated protonated hemi-aminal (**Figure 3**, A, **V**) could lead to the formation of the putative oxocarbenium ion (**Figure 3**, A, **VI**) via a nucleofugal elimination of pyrrolidine. The oxocarbenium ion **VI** is trapped intermolecularly by the alcohols to give the desired 2-deoxy-ribo-furanosides. However, due to rapid conversion of the iminium ions into products, attempts to characterize the formation of iminium ions only resulted in failure.

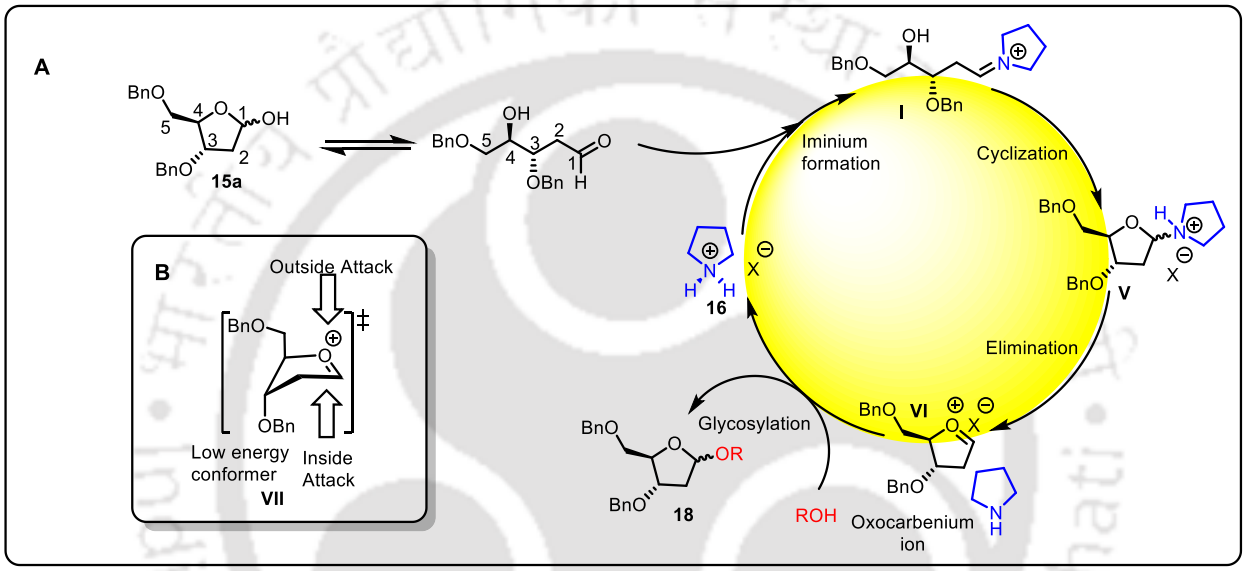


Figure 3: A) Plausible mechanism B) Proposed transition state

3.6 Conclusion:

In summary, we have described here for the first time, a novel organocatalytic protocol for the dehydrative glycosylation of 2-deoxy-ribofuranoses towards the synthesis of biologically relevant 2-deoxy-ribo-furanoside mono and disaccharides. This unprecedented organocatalytic method works extremely well with non-carbohydrate acceptors with excellent yields. Decent yields and high anomeric selectivities have been obtained in the synthesis of disaccharides with bulky sugar acceptors. The formation of furan derivative **19** provided strong evidence for the iminium catalyzed glycosylation reaction. The current protocol being operationally simple besides the availability of a huge library of secondary amines makes an attractive alternative for the synthesis of 2-deoxy-five membered glycosides. Further studies in understanding the mechanism in detail of this novel secondary amine catalysis and thereby to control the anomeric selectivities is under progress in our laboratory.

3.7 Experimental Section:

General Information

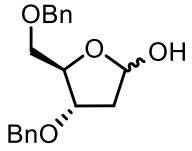
All solvents were purchased in commercial grade and reagents were purchased from Sigma-Aldrich, Merck, Carbosynth, Spectrochem, Alfa Aesar used without further purification for reactions.

Analysis

Reactions were monitored by TLC on Kieselgel 60 F254 (Merck). Detection was done by examination under UV light (254 nm) and by charring with 10% sulfuric acid in water. Purification was performed by both Ultra High Performance Liquid Chromatography (UHPLC) using column [Particle size: (µ) 12, Dim: (mm) 250 x 10] in reverse phase and in normal phase using silica gel [Merck, 60-120 mesh]. Extracts were concentrated *in vacuo* using both Büchi rotary evaporator (bath temperatures up to 40 °C) at a pressure of either 15 mmHg (diaphragm pump) and 0.7 mmHg (oil pump), at rt. ^{1}H- and ^{13}C NMR were recorded on a Bruker 600 MHz and 400 MHz spectrometer using $CDCl_3$ as solvent. Chemical shift values are reported in ppm with the solvent as the internal standard ($CDCl_3$: δ 7.26 for ^{1}H, δ 77.16 for ^{13}C). Data are reported as follows: chemical shifts (δ), multiplicity (s = singlet, d = doublet, dd = double of doublet, ddd = double of double of doublets, dt = doublet of triplet, t = triplet, td = triplet of doublet, q = quartet, m = multiplet) etc., coupling constants J (Hz), and integration. High-resolution mass measurements were performed using Agilent technologies mass spectrometer. The diastereomeric ratio 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. Optical rotation values for **15a, 15b, 17a, 17b, 17c, 17d** were matched with reported value.

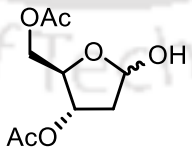
Synthesis of Donors

4-Benzyloxy-5-benzyloxymethyl-tetrahydro-furan-2-ol (15a):



2-deoxy-D-ribose (1 g, 7.000 mmol, 1.0 equiv) was dissolved in MeOH (13 ml) and stirred at rt under nitrogen. Then, acetyl chloride (38 ml) was added dropwise, and it was stirred for 1 h.[16] After completion of reaction, it was quenched by saturated $NaHCO_3$ solution (80 ml), and it was stirred for further 5 min. The solids were filtered through celite and the solvent removed *in vacuo* at 40 °C to give the compound 2-hydroxymethyl-5-methoxy-tetrahydro-furan-3-ol **(I)** as orange oil, R_f- 0.5 (10% MeOH in DCM) (1.05 g, 96%). 1.1 g of **(I)** was dissolved in DMF (20 ml) and stirred in an ice bath under nitrogen. To this solution, NaH (0.65 g, 0.016 mol, 2.2 equiv considering 60% mineral oil) was added pinchwise and stirred for 30 min. Then, benzyl bromide (2.79 g, 1.94 ml, 0.016 mol, 2.2 equiv) was added dropwise to it and stirred at rt for 16 h. The reaction was then quenched with MeOH (5 ml), and it was extracted with DCM (3x40 ml). The organic extract was washed with brine (150 ml), dried over Na_2SO_4. After removal of the solvents under reduced pressure, the residue was purified by column chromatography (ethyl acetate in hexane) to afford the compound 3-benzyloxy-2-benzyloxymethyl-5-methoxytetrahydro-furan **(II)** as a yellow liquid, R_f- 0.8 (20% ethyl acetate in hexane) (2 g, 87%). 1 g of **(II)** was dissolved in (80:20) AcOH:H_2O (77 ml) and heated at 50 °C for 24 h. At this point, additional (80:20) AcOH:H_2O (25 ml) was added, and it was stirred at 50 °C for another 24 h. The reaction mixture was extracted with DCM (3x120 ml), then organic layer was washed with water (150 ml) and saturated $NaHCO_3$ solution (150 ml), dried over Na_2SO_4 and evaporated under reduced pressure to purify in column chromatography (ethyl acetate in hexane) to get 4-benzyloxy-5-benzyloxymethyl-tetrahydro-furan-2-ol **15a** as a yellow liquid. R_f- 0.1 (20% ethyl acetate in hexane), amount- 738 mg, yield- 81%. ^{1}H-NMR data was matched with reported data.

4-Acetyloxy-5-acetyloxymethyl-tetrahydro-furan-2-ol (15b):



1.25 ml of Acetic anhydride was added slowly to the 1 g of 2-hydroxymethyl-5-methoxy-tetrahydro-furan-3-ol **(I)** at 0 °C in dry pyridine (8 ml) and stirred at rt for 17 h under nitrogen. The reaction mixture was extracted with DCM (3x25 ml). The organic extract was washed with saturated $NaHCO_3$ solution (80 ml), dried over Na_2SO_4. After removal of the solvents under reduced pressure, the residue was purified by column chromatography (ethyl acetate in hexane) to

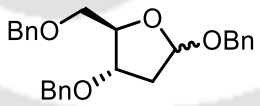
afford the compound 3-acetyloxy-2-acetyloxymethyl-5-methoxytetrahydro-furan **(II)** as a yellow liquid, R_f- 0.8 (10% MeOH in DCM) (1.54 g, 98%). 1.54 g of **(II)** was dissolved in (80:20) AcOH:H_2O (77 ml) and heated at 50 °C for 24 h. At this point, additional (80:20) AcOH:H_2O (25 ml) was added, and it was stirred at 50 °C for another 24 h. The reaction mixture was extracted with DCM (3x120 ml), then the organic layer was washed with water (150 ml) and saturated $NaHCO_3$ solution (150 ml), dried over Na_2SO_4 and evaporated under reduced pressure to purify in column chromatography (ethyl acetate in hexane) to get 4-acetyloxy-5-acetyloxymethyl-tetrahydro-furan-2-ol **15b** as a yellow liquid. R_f- 0.1 (20% ethyl acetate in hexane), amount- 738 mg, yield- 81%. ^{1}H-NMR data was matched with reported data.[16]

General Procedure for Glycosylation Reactions

Glycosyl donor (0.160 – 0.230 mmol, 1 equiv) was taken in round bottomed flask and dissolved in 0.5 ml (for 0.160 mmol) of toluene followed by addition of pyrrolidinium hydrochloride catalyst. After this, glycosyl acceptor was added slowly to it, and it was heated at 100 °C for 5 - 24 h under argon. After cooling it to rt, the reaction mixture was quenched by water (1 ml for 0.160 mmol), and it was extracted with DCM (3x15 ml for 0.160 mmol), dried over Na_2SO_4 and concentrated by rotary evaporator and purified by column chromatography (hexane/ethyl acetate).

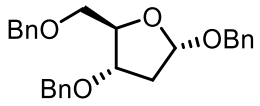
Scope of Derivatives for Glycosylation Reactions

Benzyl-3,5-di-*O*-benzyl-2-deoxy-α,β-D-erythro-pentafuranoside (18a):



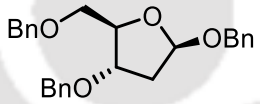
General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.160 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (3 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor benzyl alcohol (20 mg, 20 µl, 0.180 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **18a**. R_f- 0.8 (20% ethyl acetate in hexane), amount- 62 mg, yield- 96%, α:β = 1:1.3. HRMS (ESI) $C_{26}H_{28}O_4NH_4$ $[M+NH_4]^+$- calculated- 422.2326; found- 422.2328.

Benzyl-3,5-di-*O*-benzyl-2-deoxy-α-D-erythro-pentafuranoside (18aα)



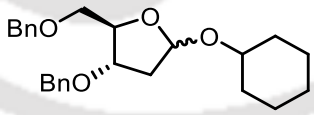
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.26 (m, 15H), 5.26 (dd, *J* = 5.6, 1.5 Hz, 1H), 4.83 (d, *J* = 12.3 Hz, 1H), 4.58 – 4.47 (m, 5H), 4.30 (q, *J* = 4.4 Hz, 1H), 4.02 (ddd, *J* = 7.9, 4.7, 3.1 Hz, 1H), 3.59 – 3.52 (m, 2H), 2.26 (ddd, *J* = 13.8, 8.1, 5.5 Hz, 1H), 2.11 (ddd, *J* = 14.0, 3.1, 1.5 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.4, 138.3, 138.2, 137.1, 128.5, 128.4, 127.1, 127.9, 127.9, 102.1, 82.2, 78.8, 73.6, 71.7, 70.2, 69.0, 38.9. $[\alpha]_D^{22}$ = +85 (*c* 0.11, $CHCl_3$).

Benzyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18aβ)



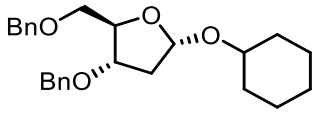
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 – 7.25 (m, 15H), 5.31 (dd, *J* = 5.4, 1.9 Hz, 1H), 4.70 (d, *J* = 11.7 Hz, 1H), 4.57 – 4.49 (m, 4H), 4.42 (d, *J* = 11.7 Hz, 1H), 4.31 (td, *J* = 6.2, 3.7 Hz, 1H), 4.19 (td, *J* = 6.4, 3.8 Hz, 1H), 3.60 – 3.53 (m, 2H), 2.32 (ddd, *J* = 13.4, 7.0, 2.0 Hz, 1H), 2.16 (dt, *J* = 13.5, 5.6 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.3, 138.1, 137.9, 128.5, 128.1, 127.9, 127.8, 103.7, 83.1, 80.2, 73.5, 72.1, 71.7, 69.4, 39.6. $[\alpha]_D^{22}$ = -42 (*c* 0.19, $CHCl_3$).

Cyclohexyl-3,5-di-*O*-benzyl-2-deoxy-α,β-D-erythro-pentafuranoside (18b):



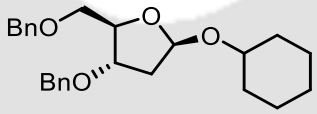
General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.160 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (3 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor cyclohexanol (18 mg, 20 µl, 0.180 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **18b**. R_f- 0.9 (20% ethyl acetate in hexane), amount- 59 mg, yield- 93%, α:β = 1:1.8. HRMS (ESI) $C_{25}H_{32}O_4NH_4$ $[M+NH_4]^+$- calculated- 414.2639; found- 414.2642.

Cyclohexyl-3,5-di-*O*-benzyl-2-deoxy-α-D-erythro-pentafuranoside (18bα)



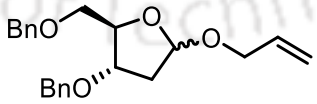
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 10H), 5.33 (dd, *J* = 5.7, 1.8 Hz, 1H), 4.58 – 4.44 (m, 4H), 4.45 (d, *J* = 12.1 Hz, 1H), 4.22 (td, *J* = 5.0, 3.7 Hz, 1H), 3.99 (ddd, *J* = 8.7, 5.3, 3.7 Hz, 1H), 3.60 (dt, *J* = 10.6, 4.2 Hz, 2H), 3.52 (dd, *J* = 10.6, 4.7 Hz, 1H), 2.28 (ddd, *J* = 13.8, 8.3, 5.6 Hz, 1H), 1.98 (ddd, *J* = 13.8, 3.7, 1.8 Hz, 1H), 1.95 – 1.87 (m, 2H), 1.75 – 1.68 (m, 2H), 1.32 – 1.10 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.4, 138.3, 128.5, 128.5, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 101.7, 81.2, 78.7, 75.2, 73.5, 71.6, 70.1, 39.2, 34.1, 31.1, 25.9, 24.6, 24.4. $[\alpha]_D^{22}$ = +5 (*c* 0.13, $CHCl_3$).

Cyclohexyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18bβ)



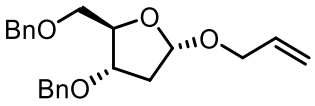
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.26 (m, 10H), 5.38 (dd, *J* = 5.4, 2.5 Hz, 1H), 4.60 – 4.47 (m, 5H), 4.25 (td, *J* = 6.5, 3.6 Hz, 1H), 4.15 (td, *J* = 6.1, 3.5 Hz, 1H), 3.58 – 3.50 (m, 3H), 2.19 (ddd, *J* = 13.4, 7.0, 2.5 Hz, 1H), 2.13 (dt, *J* = 13.5, 5.5 Hz, 1H), 1.90 – 1.80 (m, 2H), 1.69 (dt, *J* = 13.6, 4.0 Hz, 2H), 1.29 – 1.12 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.3, 138.2, 128.5, 128.5, 128.5, 127.9, 127.8, 127.8, 127.8, 102.1, 82.7, 80.5, 75.2, 73.5, 72.4, 71.6, 39.7, 33.9, 31.8, 25.8, 24.5, 24.3. $[\alpha]_D^{22}$ = -33 (*c* 0.18, $CHCl_3$).

Allyl-3,5-di-*O*-benzyl-2-deoxy-α,β-D-erythro-pentafuranoside (18c):



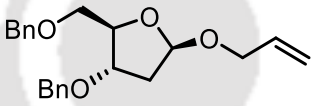
General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.160 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (3 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor allyl alcohol (11 mg, 12 µl, 0.180 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **18c**. R_f- 0.7 (20% ethyl acetate in hexane), amount- 51 mg, yield- 89%, α:β = 1:1.6. HRMS (ESI) $C_{22}H_{26}O_4NH_4$ $[M+NH_4]^+$- calculated- 372.2169; found- 372.2169.

Allyl-3,5-di-*O*-benzyl-2-deoxy-α-D-erythro-pentafuranoside (18cα)



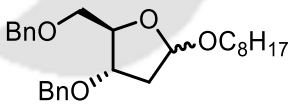
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 10H), 5.96 – 5.87 (m, 1H), 5.32 – 5.15 (m, 3H), 4.57 – 4.46 (m, 4H), 4.28 – 4.24 (m, 2H), 4.04 – 3.98 (m, 2H), 3.58 – 3.50 (m, 2H), 2.27 (ddd, *J* = 13.8, 8.2, 5.6 Hz, 1H), 2.06 (ddd, *J* = 13.9, 3.2, 1.5 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.3, 138.2, 134.8, 128.5, 128.5, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6, 116.1, 103.2, 81.1, 78.6, 73.6, 71.7, 70.1, 68.4, 38.9. $[\alpha]_D^{22}$ = +13 (*c* 0.2, $CHCl_3$).

Allyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18cβ)



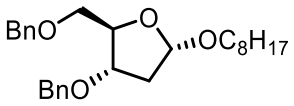
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 10H), 5.88 – 5.82 (m, 1H), 5.25 – 5.13 (m, 3H), 4.59 – 4.48 (m, 4H), 4.28 (td, *J* = 6.3, 3.7 Hz, 1H), 4.18 – 4.14 (m, 2H), 3.92 (ddt, *J* = 12.8, 6.0, 1.4 Hz, 1H), 3.56 – 3.50 (m, 2H), 2.27 (ddd, *J* = 13.5, 7.0, 2.1 Hz, 1H), 2.15 (dt, *J* = 13.6, 5.6 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.3, 138.1, 134.5, 128.5, 127.8, 127.8, 127.8, 117.2, 103.8, 83.0, 80.1, 73.4, 72.2, 71.7, 68.4, 39.5. $[\alpha]_D^{22}$ = -6 (*c* 0.17, $CHCl_3$).

Octanyl-3,5-di-*O*-benzyl-2-deoxy-α,β-D-erythro-pentafuranoside (18d):



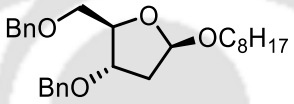
General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.160 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (3 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor 1-octanol (23 mg, 30 µl, 0.180 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **18d**. R_f- 0.8 (20% ethyl acetate in hexane), amount- 65 mg, yield- 95%, α:β = 1:1.4. HRMS (ESI) $C_{27}H_{38}O_4NH_4$ $[M+NH_4]^+$- calculated- 444.3108; found- 444.3109.

Octanyl-3,5-di-*O*-benzyl-2-deoxy-α-D-erythro-pentafuranoside (18dα)



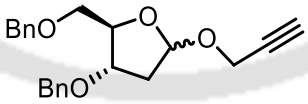
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 – 7.25 (m, 10H), 5.14 (dd, *J* = 5.7, 1.7 Hz, 1H), 4.58 – 4.44 (m, 4H), 4.20 (q, *J* = 5.0, 4.4 Hz, 1H), 4.00 (ddd, *J* = 8.4, 5.2, 3.5 Hz, 1H), 3.65 – 3.52 (m, 3H), 3.28 (td, *J* = 9.3, 5.7 Hz, 1H), 2.26 (ddd, *J* = 13.7, 8.1, 5.5 Hz, 1H), 2.01 (ddd, *J* = 13.8, 3.4, 1.7 Hz, 1H), 1.73 (s, 1H), 1.52 (ddq, *J* = 9.7, 6.1, 3.5, 3.0 Hz, 1H), 1.31 – 1.24 (m, 7H), 0.87 (td, *J* = 7.0, 5.5 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.5, 138.3, 128.5, 128.5, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 104.0, 103.9, 81.6, 78.9, 73.5, 71.6, 70.5, 70.4, 70.2, 39.6, 39.5, 38.8, 30.7, 30.5, 29.2, 29.1, 23.1, 23.9, 23.3, 23.2, 14.3, 11.2, 11.0. $[\alpha]_D^{22}$ = +55 (*c* 0.25, $CHCl_3$).

Octanyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18dβ)



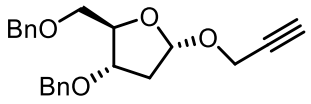
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 10H), 5.18 (dd, *J* = 5.7, 2.1 Hz, 1H), 4.61 – 4.48 (m, 4H), 4.27 (td, *J* = 6.5, 3.5 Hz, 1H), 4.15 (ddd, *J* = 6.9, 5.4, 3.4 Hz, 1H), 3.59 – 3.48 (m, 3H), 3.20 (td, *J* = 9.2, 5.8 Hz, 1H), 2.23 (ddd, *J* = 13.6, 7.0, 2.2 Hz, 1H), 2.14 (dt, *J* = 13.5, 5.4 Hz, 1H), 1.62 (s, 1H), 1.44 – 1.40 (m, 1H), 1.28 – 1.22 (m, 7H), 0.90 – 0.83 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.3, 138.2, 128.5, 128.5, 127.8, 127.8, 127.8, 104.8, 104.7, 82.8, 80.5, 80.4, 73.4, 72.2, 72.2, 71.6, 70.7, 70.7, 39.6, 39.6, 39.5, 30.6, 30.5, 29.2, 29.1, 23.9, 23.8, 23.2, 14.3, 11.2, 11.1. $[\alpha]_D^{22}$ = -48 (*c* 0.15, $CHCl_3$).

Propargyl-3,5-di-*O*-benzyl-2-deoxy-α,β-D-erythro-pentafuranoside (18e):



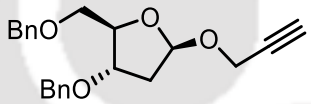
General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.160 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (3 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor propargyl alcohol (10 mg, 12 µl, 0.180 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **18e**. R_f- 0.8 (20% ethyl acetate in hexane), amount- 49 mg, yield- 87%, α:β = 1.3:1. HRMS (ESI) $C_{22}H_{24}O_4NH_4$ $[M+NH_4]^+$- calculated- 370.2013; found- 370.2014.

Propargyl-3,5-di-*O*-benzyl-2-deoxy-α-D-erythro-pentafuranoside (18eα)



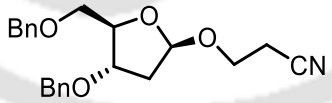
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 10H), 5.42 (dd, *J* = 5.6, 1.2 Hz, 1H), 4.57 – 4.46 (m, 4H), 4.30 (t, *J* = 2.9 Hz, 2H), 4.25 (q, *J* = 4.4 Hz, 1H), 4.00 (ddd, *J* = 7.7, 4.5, 2.8 Hz, 1H), 3.56 – 3.50 (m, 2H), 2.39 (t, *J* = 2.4 Hz, 1H), 2.28 (ddd, *J* = 14.0, 8.0, 5.6 Hz, 1H), 2.08 (dd, *J* = 14.4, 2.4 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.2, 138.1, 128.5, 128.5, 127.1, 127.9, 127.8, 127.6, 102.1, 82.6, 78.6, 74.2, 73.6, 71.7, 70.1, 54.2, 38.8. $[\alpha]_D^{22}$ = +40 (*c* 0.25, $CHCl_3$).

Propargyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18eβ)



^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 10H), 5.37 (dd, *J* = 5.5, 1.8 Hz, 1H), 4.56 – 4.49 (m, 4H), 4.29 (ddd, *J* = 10.1, 7.0, 3.7 Hz, 1H), 4.21 – 4.13 (m, 3H), 3.57 – 3.48 (m, 2H), 2.39 (t, *J* = 2.4 Hz, 1H), 2.30 (ddd, *J* = 13.5, 7.0, 1.8 Hz, 1H), 2.17 (dt, *J* = 13.6, 5.7 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.2, 137.1, 128.6, 128.5, 127.9, 127.8, 102.8, 83.3, 79.8, 74.3, 73.4, 71.9, 71.8, 54.3, 39.4. $[\alpha]_D^{22}$ = -32 (*c* 0.2, $CHCl_3$).

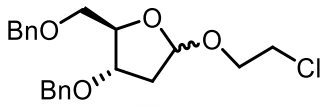
2-Cyanoethyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18fβ):



General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.160 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (3 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor 2-cyano ethanol (13 mg, 12 µl, 0.180 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **18fβ**. R_f- 0.2 (20% ethyl acetate in hexane), amount- 52 mg, yield- 89%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.25 (m, 10H), 5.22 (dd, *J* = 5.5, 2.0 Hz, 1H), 4.59 – 4.46 (m, 4H), 4.28 (td, *J* = 6.0, 3.9 Hz, 1H), 4.16 (ddd, *J* = 6.9, 5.9, 4.0 Hz, 1H), 3.81 (dt, *J* = 9.9, 6.1 Hz, 1H), 3.59 – 3.49 (m, 3H), 2.49 (t, *J* = 6.3 Hz, 2H), 2.28 (ddd, *J* = 13.5, 6.9, 1.9 Hz, 1H), 2.16 (dt, *J* = 13.6, 5.6 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.2, 137.1, 128.6, 128.6, 127.1, 127.9, 118.1, 104.8, 83.4,

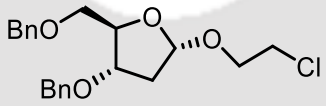
79.6, 73.4, 71.9, 71.7, 62.4, 39.5, 19.1. HRMS (ESI) $C_{22}H_{25}NO_4NH_4$ $[M+NH_4]^+$- calculated- 385.2122; found- 385.2145. $[\alpha]_D^{22}$ = -11 (*c* 0.12, $CHCl_3$).

2-Chloroethyl-3,5-di-*O*-benzyl-2-deoxy-α,β-D-erythro-pentafuranoside (18g):



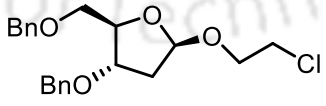
General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.160 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (3 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor 2-chloro ethanol (15 mg, 12 µl, 0.180 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **18g**. R_f- 0.6 (20% ethyl acetate in hexane), amount- 58 mg, yield- 96%, α:β = 1:2. HRMS (ESI) $C_{21}H_{25}ClO_4NH_4$ $[M+NH_4]^+$- calculated- 394.1780; found- 394.1783.

2-Chloroethyl-3,5-di-*O*-benzyl-2-deoxy-α-D-erythro-pentafuranoside (18gα)



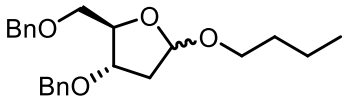
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 10H), 5.24 (dd, *J* = 5.7, 1.4 Hz, 1H), 4.57 – 4.45 (m, 4H), 4.25 (q, *J* = 4.4 Hz, 1H), 4.01 – 3.96 (m, 2H), 3.75 – 3.62 (m, 3H), 3.57 – 3.49 (m, 2H), 2.28 (ddd, *J* = 13.8, 8.1, 5.6 Hz, 1H), 2.08 (ddd, *J* = 14.1, 3.1, 1.5 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.2, 138.1, 128.5, 127.9, 127.9, 127.8, 104.5, 82.3, 78.5, 73.6, 71.7, 70.1, 67.1, 43.1, 38.9. $[\alpha]_D^{22}$ = +87 (*c* 0.2, $CHCl_3$).

2-Chloroethyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18gβ)



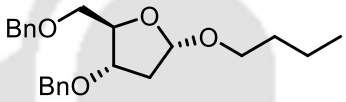
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 10H), 5.24 (dd, *J* = 5.5, 1.9 Hz, 1H), 4.56 – 4.48 (m, 4H), 4.28 (td, *J* = 6.2, 3.8 Hz, 1H), 4.16 (ddd, *J* = 6.9, 5.8, 3.9 Hz, 1H), 3.87 (dt, *J* = 11.0, 5.5 Hz, 1H), 3.63 (ddd, *J* = 11.3, 6.9, 5.0 Hz, 1H), 3.59 – 3.51 (m, 4H), 2.30 (ddd, *J* = 13.4, 7.0, 1.9 Hz, 1H), 2.16 (dt, *J* = 13.5, 5.6 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.2, 138.0, 128.6, 128.5, 127.9, 127.8, 104.8, 83.2, 79.9, 73.5, 71.1, 71.8, 67.9, 43.2, 39.5. $[\alpha]_D^{22}$ = -89 (*c* 0.14, $CHCl_3$).

1-Butyl-3,5-di-*O*-benzyl-2-deoxy-α,β-D-erythro-pentafuranoside (18h):



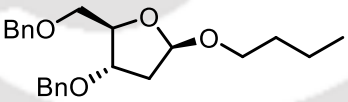
General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.160 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (3 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor 1-butanol (13 mg, 18 µl, 0.180 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **18h**. R_f- 0.7 (20% ethyl acetate in hexane), amount- 56 mg, yield- 95%, α:β = 1:1.3. HRMS (ESI) $C_{23}H_{30}O_4NH_4$ $[M+NH_4]^+$- calculated- 388.2482; found- 388.2495.

1-Butyl-3,5-di-*O*-benzyl-2-deoxy-α-D-erythro-pentafuranoside (18hα)



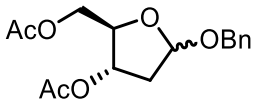
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 10H), 5.17 (dd, *J* = 5.7, 1.7 Hz, 1H), 4.58 – 4.45 (m, 4H), 4.22 (td, *J* = 4.8, 3.7 Hz, 1H), 3.99 (ddd, *J* = 8.3, 5.0, 3.4 Hz, 1H), 3.74 (dt, *J* = 9.6, 6.8 Hz, 1H), 3.59 – 3.51 (m, 2H), 3.42 (dt, *J* = 9.7, 6.6 Hz, 1H), 2.26 (ddd, *J* = 13.9, 8.2, 5.7 Hz, 1H), 2.01 (ddd, *J* = 13.9, 3.4, 1.7 Hz, 1H), 1.60 – 1.55 (m, 2H), 1.41 – 1.34 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.4, 138.2, 128.5, 128.5, 127.9, 127.9, 127.8, 103.8, 81.6, 78.7, 73.5, 71.6, 70.2, 67.6, 38.9, 31.9, 19.5, 14.1. $[\alpha]_D^{22}$ = -69 (*c* 0.5, $CHCl_3$).

1-Butyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18hβ)



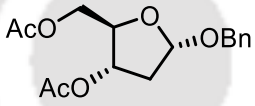
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 10H), 5.19 (dd, *J* = 5.4, 2.1 Hz, 1H), 4.60 – 4.47 (m, 4H), 4.26 (td, *J* = 6.4, 3.6 Hz, 1H), 4.15 (ddd, *J* = 6.9, 5.6, 3.6 Hz, 1H), 3.65 (dt, *J* = 9.5, 6.8 Hz, 1H), 3.55 – 3.48 (m, 2H), 3.33 (dt, *J* = 9.5, 6.6 Hz, 1H), 2.23 (ddd, *J* = 13.4, 7.0, 2.2 Hz, 1H), 2.13 (dt, *J* = 13.5, 5.5 Hz, 1H), 1.51 – 1.45 (m, 2H), 1.34 – 1.27 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.3, 138.2, 128.5, 128.5, 127.8, 104.4, 82.8, 80.3, 73.4, 72.2, 71.7, 67.7, 39.6, 31.8, 19.5, 14.0. $[\alpha]_D^{22}$ = +92 (*c* 0.4, $CHCl_3$).

Benzyl-3,5-di-*O*-acetyl-2-deoxy-α,β-D-erythro-pentafuranoside (18i):



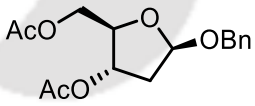
General procedure was followed by adding glycosyl donor **15b** (50 mg, 0.230 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (5 mg, 0.050 mmol, 20 mol %) and glycosyl acceptor benzyl alcohol (27 mg, 26 µl, 0.250 mmol, 1.1 equiv) at 100 °C for 24 h to get product as a colourless liquid **18i**. R_f- 0.4 (20% ethyl acetate in hexane), amount- 43 mg, yield- 61%, α:β = 1:1.1. HRMS (ESI) $C_{16}H_{20}O_6NH_4$ $[M+NH_4]^+$- calculated- 326.1598; found- 326.1597.

Benzyl-3,5-di-*O*-acetyl-2-deoxy-α-D-erythro-pentafuranoside (18iα)



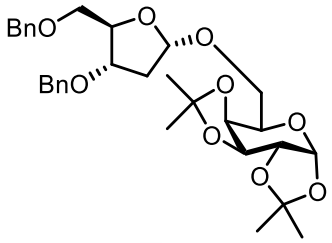
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 5H), 5.31 (d, *J* = 6 Hz, 1H), 5.06 (ddd, *J* = 8.3, 4.1, 2.2 Hz, 1H), 4.80 (d, *J* = 12.1 Hz, 1H), 4.54 (d, *J* = 12.1 Hz, 1H), 4.36 – 4.29 (m, 2H), 4.19 (dd, *J* = 11.8, 4.8 Hz, 1H), 2.41 (ddd, *J* = 14.1, 8.3, 5.3 Hz, 1H), 2.09 (s, 7H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.2, 170.9, 138.1, 128.5, 127.9, 102.9, 80.8, 74.1, 69.1, 64.0, 39.2, 21.2, 21.0. $[\alpha]_D^{22}$ = +52 (*c* 0.2, $CHCl_3$).

Benzyl-3,5-di-*O*-acetyl-2-deoxy-β-D-erythro-pentafuranoside (18iβ)



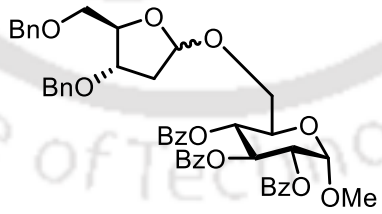
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 5H), 5.35 (dd, J = 5.6, 2.4 Hz, 1H), 5.27 (ddd, J = 7.5, 4.8, 3.1 Hz, 1H), 4.75 (d, J = 11.7 Hz, 1H), 4.47 (d, J = 11.7 Hz, 1H), 4.35 (dt, J = 11.8, 4.2 Hz, 1H), 4.26 (ddd, J = 6.5, 5.3, 3.1 Hz, 1H), 4.16 (dt, J = 11.4, 5.9 Hz, 1H), 2.46 (ddd, J = 14.1, 7.2, 2.4 Hz, 1H), 2.20 (dt, J = 14.2, 5.2 Hz, 1H), 2.06 (d, J = 1.4 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.9, 170.7, 137.6, 128.6, 128.5, 128.1, 127.9, 127.8, 103.8, 82.1, 75.2, 69.8, 64.1, 39.1, 21.1, 21.0. $[\alpha]_D^{22}$ = -26 (*c* 0.3, $CHCl_3$).

3,5-Di-*O*-benzyl 2-deoxyfuranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (18jα):



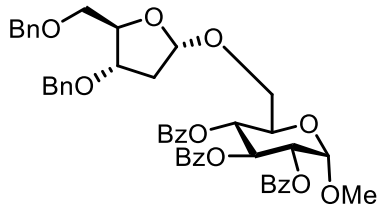
General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.160 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (3 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor **17c** (47 mg, 0.180 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **18jα**. R_f- 0.5 (20% ethyl acetate in hexane), amount- 52 mg, yield- 58%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 10H), 5.54 (d, *J* = 5.0 Hz, 1H), 5.01 (t, *J* = 3.1 Hz, 1H), 4.75 – 4.69 (m, 2H), 4.60 – 4.55 (m, 3H), 4.31 (dd, *J* = 5.0, 2.4 Hz, 1H), 4.19 (dd, *J* = 7.9, 2.0 Hz, 1H), 3.97 (ddd, *J* = 7.1, 5.0, 1.9 Hz, 1H), 3.90 (ddd, *J* = 10.9, 4.4, 2.9 Hz, 1H), 3.80 – 3.72 (m, 3H), 3.69 – 3.59 (m, 2H), 2.24 (ddd, *J* = 12.9, 10.7, 3.4 Hz, 1H), 1.94 (dt, *J* = 12.8, 3.5 Hz, 1H), 1.52 (s, 3H), 1.43 (s, 3H), 1.33 (s, 3H), 1.31 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.8, 138.7, 128.5, 127.9, 127.7, 127.6, 109.4, 108.7, 98.8, 96.5, 72.7, 72.6, 71.5, 71.4, 70.8, 70.6, 70.4, 67.1, 66.9, 61.4, 32.1, 29.9, 26.1, 26.1, 25.1, 24.6. HRMS (ESI) $C_{31}H_{40}O_9NH_4$ $[M+NH_4]^+$- calculated- 574.3011; found- 574.3029. $[\alpha]_D^{22}$ = -48 (*c* 0.1, $CHCl_3$).

3,5-Di-*O*-benzyl 2-deoxyfuranosyl-(1→6)-methyl-2,3,4-tri-*O*-benzoyl-α,β-D-glucopyranoside (18k):



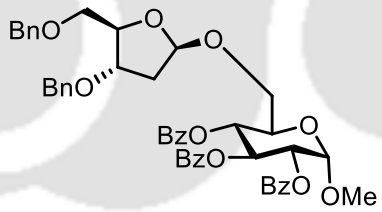
General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.160 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (3 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor **17d** (91 mg, 0.180 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **18k**. R_f- 0.4 (20% ethyl acetate in hexane), amount- 51 mg, yield- 40%, α:β = 1:1.3. HRMS (ESI) $C_{47}H_{46}O_{12}NH_4$ $[M+NH_4]^+$- calculated- 820.3327; found- 820.3325.

3,5-Di-*O*-benzyl 2-deoxyfuranosyl-(1→6)-methyl-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (18kα)



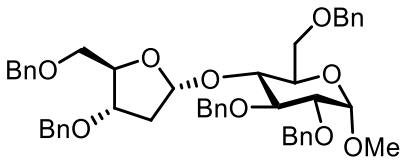
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 – 7.87 (m, 6H), 7.53 – 7.28 (m, 17H), 7.24 (d, *J* = 7.0 Hz, 2H), 6.12 (t, *J* = 9.6 Hz, 1H), 5.66 (t, *J* = 9.8 Hz, 1H), 5.30 – 5.23 (m, 2H), 5.16 (dd, *J* = 5.7, 1.9 Hz, 1H), 4.54 – 4.39 (m, 4H), 4.21 (ddt, *J* = 16.5, 5.4, 3.8 Hz, 2H), 4.01 – 3.96 (m, 2H), 3.68 (dd, *J* = 11.0, 3.3 Hz, 1H), 3.53 – 3.44 (m, 2H), 3.43 (s, 3H), 2.24 (ddd, *J* = 13.9, 8.2, 5.7 Hz, 1H), 1.95 (ddd, *J* = 13.9, 3.9, 1.9 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.0, 166.0, 164.7, 138.4, 133.5, 133.3, 133.1, 130.1, 129.1, 129.9, 129.5, 128.6, 128.5, 128.5, 128.4, 127.9, 127.8, 127.7, 103.7, 97.1, 81.4, 78.2, 73.5, 72.3, 71.6, 70.9, 69.8, 69.5, 68.5, 65.7, 55.7, 38.6, 32.1, 29.9, 29.5. $[\alpha]_D^{22}$ = +42 (*c* 0.06, $CHCl_3$).

3,5-Di-*O*-benzyl 2-deoxyfuranosyl-(1→6)-methyl-2,3,4-tri-*O*-benzoyl-β-D-glucopyranoside (18kβ)



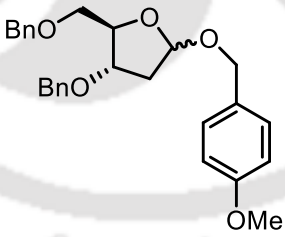
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 – 7.86 (m, 6H), 7.53 – 7.27 (m, 20H), 6.11 (t, *J* = 9.9 Hz, 1H), 5.56 (t, *J* = 9.8 Hz, 1H), 5.30 – 5.19 (m, 2H), 5.16 (dd, *J* = 5.4, 1.9 Hz, 1H), 4.54 – 4.44 (m, 4H), 4.22 (td, *J* = 6.3, 3.8 Hz, 1H), 4.13 (tt, *J* = 13.0, 4.6 Hz, 2H), 3.87 (dd, *J* = 11.4, 2.6 Hz, 1H), 3.57 – 3.48 (m, 3H), 3.42 (s, 3H), 2.30 (ddd, *J* = 13.6, 7.1, 2.0 Hz, 1H), 2.12 (dt, *J* = 13.4, 5.5 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.0, 165.4, 138.3, 138.1, 133.5, 133.2, 130.1, 129.1, 129.8, 129.4, 129.2, 128.6, 128.5, 128.4, 127.8, 105.3, 97.1, 83.2, 79.1, 73.4, 72.3, 72.1, 71.7, 70.7, 69.4, 68.8, 66.2, 55.6, 39.4, 32.1, 29.9, 29.8, 29.8, 29.6, 29.5. $[\alpha]_D^{22}$ = +63 (*c* 0.05, $CHCl_3$).

3,5-Di-*O*-benzyl 2-deoxyfuranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-methylglucopyranoside (18lα):



General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.160 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (3 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor **17b** (82 mg, 0.180 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **18lα**. R_f- 0.2 (20% ethyl acetate in hexane), amount- 56 mg, yield- 46%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 21H), 7.24 – 7.20 (m, 4H), 5.53 (dd, *J* = 5.7, 1.4 Hz, 1H), 4.96 (d, *J* = 11.0 Hz, 1H), 4.77 – 4.55 (m, 6H), 4.48 – 4.41 (m, 4H), 4.07 (q, *J* = 4.2 Hz, 1H), 3.98 – 3.91 (m, 2H), 3.81 – 3.79 (m, 1H), 3.70 – 3.64 (m, 2H), 3.60 – 3.57 (m, 1H), 3.50 (dd, *J* = 9.7, 3.5 Hz, 1H), 3.39 (s, 3H), 3.38 – 3.33 (m, 2H), 2.08 (ddd, *J* = 13.9, 7.9, 5.7 Hz, 1H), 1.93 (ddd, *J* = 14.1, 3.0, 1.5 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9, 138.7, 138.3, 138.2, 138.2, 128.6, 128.5, 128.5, 128.3, 128.3, 128.0, 127.9, 127.8, 105.4, 98.0, 82.6, 82.2, 79.1, 78.8, 75.8, 75.2, 73.6, 73.5, 71.5, 70.2, 69.8, 69.6, 55.2, 38.9, 32.1, 29.8, 22.8, 14.3. HRMS (ESI) $C_{47}H_{52}O_9NH_4$ $[M+NH_4]^+$- calculated- 778.3950; found- 778.3953. $[\alpha]_D^{22}$ = +97 (*c* 0.08, $CHCl_3$).

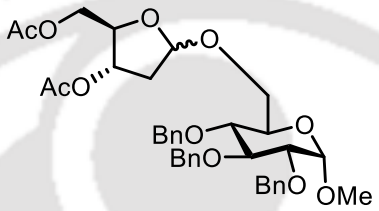
4-Methoxybenzyl-3,5-di-*O*-benzyl-2-deoxy-α,β-D-erythro-pentafuranoside (18m):



General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.160 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (3 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor 4-methoxybenzyl alcohol (25 mg, 22 µl, 0.180 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **18m**. R_f- 0.4 (20% ethyl acetate in hexane), amount- 56 mg, yield- 81%, α:β = 1:1.4. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 20H), 7.19 (d, *J* = 8.6 Hz, 4H), 6.87 – 6.84 (m, 4H), 5.29 (dd, *J* = 5.4, 1.8 Hz, 1H), 5.24 (dd, *J* = 5.6, 1.5 Hz, 1H), 4.75 (d, *J* = 11.9 Hz, 1H), 4.63 – 4.46 (m, 10H), 4.38 (dd, *J* = 13.3, 10.6 Hz, 1H), 4.30 (ddd, *J* = 12.1, 5.9, 4.0 Hz, 2H), 4.19

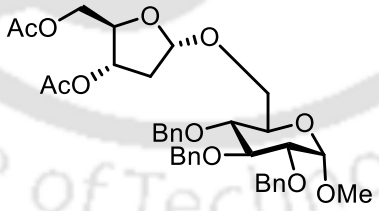
– 4.16 (m, 1H), 4.00 (ddd, *J* = 8.0, 4.8, 3.1 Hz, 1H), 3.79 (s, 6H), 3.60 – 3.52 (m, 4H), 2.31 – 2.27 (m, 1H), 2.26 – 2.22 (m, 1H), 2.14 (dt, *J* = 13.4, 5.6 Hz, 1H), 2.07 (ddd, *J* = 13.9, 3.1, 1.5 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.3, 159.2, 138.3, 138.3, 138.2, 138.1, 129.8, 129.6, 128.5, 128.5, 128.5, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.7, 113.9, 113.8, 103.5, 102.6, 83.1, 82.0, 80.2, 78.7, 73.5, 73.5, 72.2, 71.7, 71.6, 70.2, 69.1, 68.6, 55.4, 55.4, 39.6, 38.9. HRMS (ESI) $C_{27}H_{30}O_5NH_4$ $[M+NH_4]^+$- calculated- 452.2431; found- 452.2446.

3,5-Di-*O*-acetyl 2-deoxyfuranosyl-(1→6)-methyl-2,3,4-tri-*O*-benzyl-α,β-D-glucopyranoside (18n):



General procedure was followed by adding glycosyl donor **15b** (50 mg, 0.230 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (5 mg, 0.050 mmol, 20 mol %) and glycosyl acceptor **17a** (116 mg, 0.250 mmol, 1.1 equiv) at 100 °C for 24 h to get product as a colourless liquid **18n**. R_f- 0.4 (30% ethyl acetate in hexane), amount- 68 mg, yield- 45%, α:β = 1:2. HRMS (ESI) $C_{37}H_{44}O_{11}NH_4$ $[M+NH_4]^+$- calculated- 682.3222; found- 682.3253.

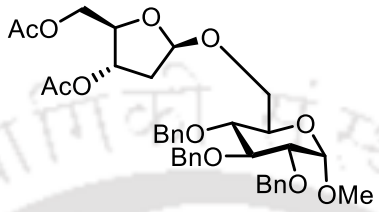
3,5-Di-*O*-acetyl 2-deoxyfuranosyl-(1→6)-methyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (18nα)



^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 15H), 5.28 (d, *J* = 4.9 Hz, 1H), 5.04 – 4.98 (m, 2H), 4.88 – 4.79 (m, 3H), 4.71 – 4.63 (m, 3H), 4.22 – 4.14 (m, 3H), 4.08 – 4.05 (m, 1H), 3.99 (t, *J* = 9.3 Hz, 1H), 3.75 (dt, *J* = 10.0, 2.5 Hz, 1H), 3.66 (t, *J* = 9.5 Hz, 1H), 3.60 (dd, *J* = 11.2, 2.0 Hz, 1H), 3.53 (dd, *J* = 9.6, 3.6 Hz, 1H), 3.37 (s, 3H), 2.40 (ddd, *J* = 14.6, 8.0, 5.5 Hz, 1H), 2.13 – 2.10 (m, 1H), 2.00 (d, *J* = 4.9 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.9, 170.8, 138.9, 138.4, 138.2,

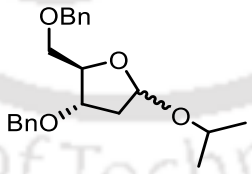
128.7, 128.6, 128.6, 128.3, 128.1, 128.0, 127.9, 127.8, 104.3, 98.4, 82.1, 81.1, 79.9, 77.8, 75.9, 75.2, 74.1, 73.5, 69.8, 65.1, 64.0, 55.3, 39.2, 29.8, 21.1, 20.9. $[\alpha]_D^{22}$ = +47 (*c* 0.09, $CHCl_3$).

3,5-Di-*O*-acetyl 2-deoxyfuranosyl-(1→6)-methyl-2,3,4-tri-*O*-benzyl-β-D-glucopyranoside (18nβ)



^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 15H), 5.21 – 5.18 (m, 1H), 5.08 (dd, *J* = 5.5, 2.2 Hz, 1H), 4.98 (d, *J* = 10.9 Hz, 1H), 4.87 (d, *J* = 11.0 Hz, 1H), 4.81 – 4.77 (m, 2H), 4.67 (d, *J* = 12.0 Hz, 1H), 4.60 (d, *J* = 3.5 Hz, 1H), 4.55 (d, *J* = 11.2 Hz, 1H), 4.25 (d, *J* = 11.3 Hz, 1H), 4.19 (td, *J* = 5.9, 5.5, 3.1 Hz, 1H), 4.12 – 4.09 (m, 1H), 3.98 (t, *J* = 9.3 Hz, 1H), 3.88 (dd, *J* = 10.8, 2.0 Hz, 1H), 3.71 – 3.68 (m, 1H), 3.53 – 3.50 (m, 2H), 3.48 – 3.45 (m, 1H), 3.36 (s, 3H), 2.35 (ddd, *J* = 14.1, 7.3, 2.3 Hz, 1H), 2.10 – 2.08 (m, 1H), 2.05 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 170.7, 138.9, 138.5, 138.3, 128.7, 128.6, 128.6, 128.5, 128.3, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7, 104.7, 98.0, 82.2, 81.9, 80.2, 77.6, 75.9, 75.0, 75.0, 73.4, 69.9, 66.5, 65.1, 55.2, 39.1, 29.8, 21.1, 20.9. $[\alpha]_D^{22}$ = +35 (*c* 0.4, $CHCl_3$).

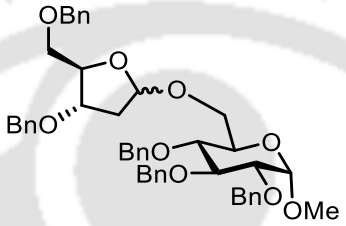
Isopropyl-3,5-di-*O*-acetyl 2-deoxy-α,β-D-erythro-pentafuranoside (18o):



General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.160 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (3 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor isopropanol (11 mg, 14 µl, 0.180 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **18o**. R_f- 0.6 (20% ethyl acetate in hexane), amount- 50 mg, yield- 87%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 20H), 5.33 (dd, *J* = 5.3, 2.6 Hz, 1H), 5.28 (dd, *J* = 5.6, 1.8 Hz, 1H), 4.80 – 4.44 (m, 10H), 4.24 (td, *J* = 6.4, 3.6 Hz, 1H), 4.21 (td, *J* = 4.9, 3.6 Hz, 1H), 4.14 (ddd, *J* = 6.8, 5.5, 3.5 Hz, 1H), 3.98 (ddd, *J* = 8.5, 5.3, 3.6 Hz, 1H), 3.94 (p, *J* = 6.2 Hz, 1H), 3.89 (p, *J* = 6.2 Hz,

1H), 3.60 – 3.48 (m, 5H), 2.27 (ddd, *J* = 13.8, 8.3, 5.7 Hz, 1H), 2.19 – 2.11 (m, 3H), 1.97 (ddd, *J* = 13.8, 3.7, 1.8 Hz, 1H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.14 (d, *J* = 6.1 Hz, 3H), 1.11 (dd, *J* = 9.1, 6.1 Hz, 7H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.5, 138.4, 138.3, 138.3, 128.5, 128.5, 128.5, 128.5, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.7, 127.6, 102.3, 101.8, 82.7, 81.3, 80.5, 78.7, 73.6, 73.5, 72.4, 71.7, 71.7, 70.2, 69.1, 39.7, 39.3, 29.9, 23.9, 23.7, 21.8, 21.6. HRMS (ESI) $C_{22}H_{28}O_4NH_4$ $[M+NH_4]^+$- calculated- 374.2326; found- 374.2386.

3,5-Di-*O*-benzyl 2-deoxyfuranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α,β-D-methylglucopyranoside (18p):



General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.160 mmol, 1.0 equiv), pyrrolidinium hydrochloride catalyst **16b** (3 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor **17b** (82 mg, 0.180 mmol, 1.1 equiv) at 100 °C for 5 h to get product as a colourless liquid **18p**. R_f- 0.3 (20% ethyl acetate in hexane), amount- 70 mg, yield- 58%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.19 (m, 50H), 5.27 (dd, *J* = 5.6, 1.6 Hz, 1H), 4.97 (dd, *J* = 14.7, 10.8 Hz, 2H), 4.88 – 4.73 (m, 8H), 4.71 – 4.60 (m, 5H), 4.58 – 4.43 (m, 7H), 4.36 (d, *J* = 11.8 Hz, 1H), 4.21 (dd, *J* = 11.0, 2.5 Hz, 1H), 4.16 (q, *J* = 4.3 Hz, 1H), 4.01 – 3.94 (m, 3H), 3.88 – 3.84 (m, 2H), 3.77 – 3.63 (m, 6H), 3.57 – 3.43 (m, 7H), 3.35, 3.32 (2 S, 6H), 2.28 (ddd, *J* = 13.6, 7.7, 5.6 Hz, 1H), 2.19 – 2.14 (m, 2H), 1.82 (dt, *J* = 12.8, 3.7 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.1, 138.8, 138.7, 138.7, 138.6, 138.4, 138.3, 138.1, 128.6, 128.6, 128.5, 128.5, 128.4, 128.3, 128.2, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 104.4, 98.5, 98.3, 98.0, 82.5, 82.3, 82.2, 80.0, 79.9, 78.9, 77.8, 77.7, 76.0, 75.8, 75.2, 75.2, 73.6, 73.5, 72.7, 72.3, 71.6, 71.5, 70.5, 70.1, 70.0, 70.0, 66.3, 65.7, 61.2, 55.3, 55.2, 38.8, 32.3. HRMS (ESI) $C_{47}H_{52}O_9NH_4$ $[M+NH_4]^+$- calculated- 778.3950; found- 778.3910.

2-((Benzyloxy)methyl)furan (19):

Glycosyl donor **15a** (50 mg, 0.16 mmol, 1 equiv) and pyrrolidinium tosylate salt **16c** (8 mg, 0.031 mmol, 20 mol %) were dissolved in 0.5 ml of toluene and refluxed at 100 °C for 5 h. After cooling

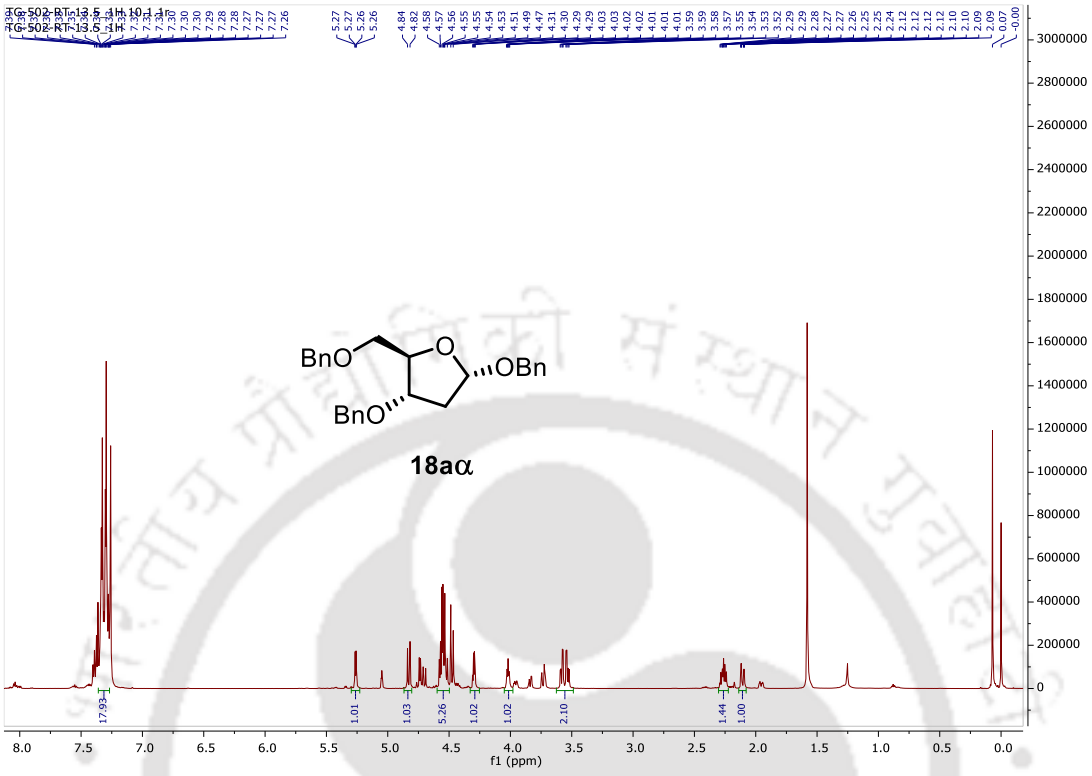
it to rt, the reaction mixture was quenched by water (1 ml) and it was extracted with DCM (3x15 ml), dried over Na_2SO_4 and concentrated by rotary evaporator under reduced pressure and purified by chromatography in hexane/ethyl acetate. The product obtained has R_f- 0.6 (20% ethyl acetate in hexane). From NMR, the product was identified as 2-((Benzyloxy)methyl)furan **19**, amount- 47 mg, yield-78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.17 (m, 5H), 6.27 – 6.26 (m, 2H), 4.48 (s, 2H), 4.41 (s, 2H).

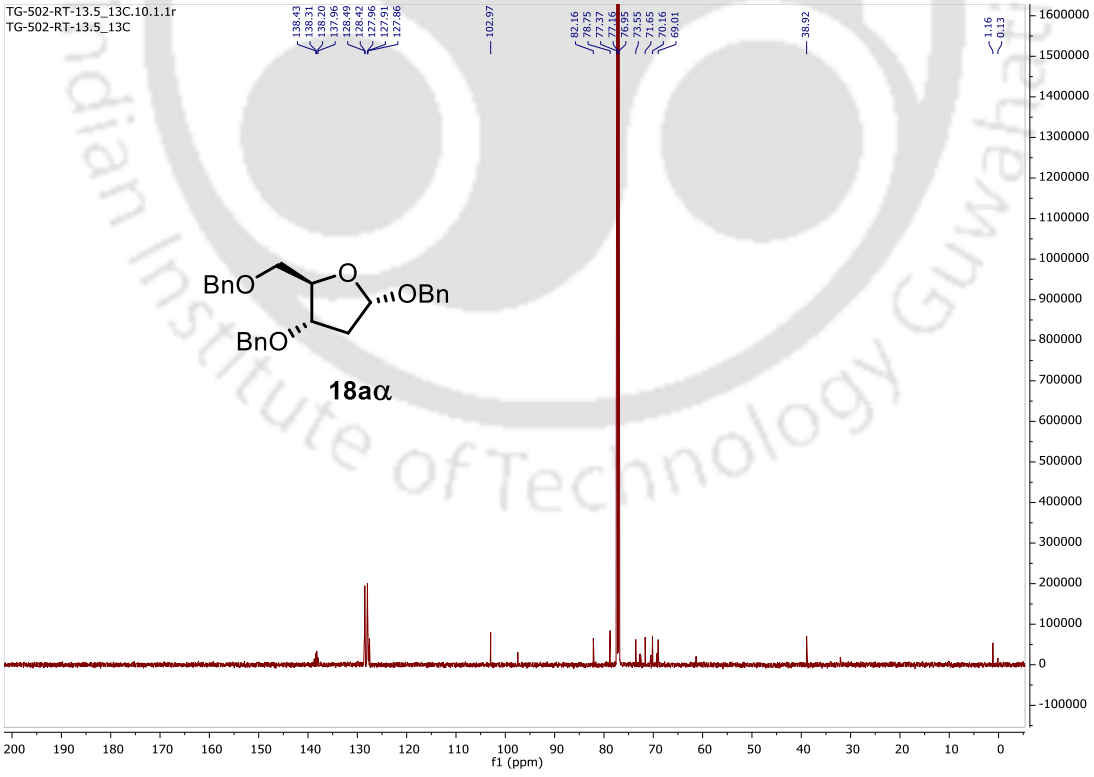
3.8 References:

1. (a) Hansen, M. R.; Hurley, L. H. *Accounts Chem. Res.* **1996,** *29*, 249–258; (b) Hallis, T. M.; Liu, H. W. *Accounts Chem. Res.* **1999,** *32*, 579–588; (c) Riganti, C.; Campia, I.; Kopecka, J.; Gazzano, E.; Doublier, S.; Aldieri, E.; Bosia, A.; Ghigo, D. *Curr. Med. Chem.* **2011,** *18*, 872–885.
2. Kong, F. M.; Zhao, N.; Siegel, M. M.; Janota, K.; Ashcroft, J. S.; Koehn, F. E.; Borders, D. B.; Carter, G. T. *J. Am. Chem. Soc.* **1998,** *120*, 13301–13311.
3. (a) Langenhan, J. M.; Peters, N. R.; Guzei, I. A.; Hoffmann, M.; Thorson, J. S. *P Natl. Acad. Sci. USA.* **2005,** *102*, 12305–12310; (b) Griffith, B. R.; Langenhan, J. M.; Thorson, J. S. *Curr. Opin. Biotech* **2005,** *16*, 622–630.
4. (a) Jung, M. E.; Castro, C. *J. Org. Chem.* **1993,** *58*, 807–808; (b) Kazimierczuk, Z.; Cottam, H. B.; Revankar, G. R.; Robins, R. K. *J. Am. Chem. Soc.* **1984,** *106*, 6379–6382; (c) Lipshutz, B. H.; Hayakawa, H.; Kato, K.; Lowe, R. F.; Stevens, K. L. *Synthesis-Stuttgart* **1994,** 1476–1484.
5. (a) Tong, X. G.; Zhou, L. L.; Wang, Y. H.; Xia, C. F.; Wang, Y.; Liang, M.; Hou, F. F.; Cheng, Y. X. *Org. Lett.* **2010,** *12*, 1844–1847; (b) Wang, C. H.; Li, W.; Liu, H. L.; Wang, J.; Li, G. Q.; Wang, G. C.; Li, Y. L. *Carbohydr. Res.* **2014,** *384*, 99–101.
6. Hou, D.; Lowary, T. L. *Org. Lett.* **2007,** *9*, 4487–4490.
7. Mereyala, H. B.; Kulkarni, V. R.; Ravi, D.; Sharma, G. V. M.; Rao, B. V.; Reddy, G. B. *Tetrahedron* **1992,** *48*, 545–562.
8. Aoyama, N.; Kobayashi, S. *Chem. Lett.* **2006,** *35*, 238–239.
9. Liu, Y. K.; Li, Z. L.; Li, J. Y.; Feng, H. X.; Tong, Z. P. *Org. Lett.* **2015,** *17*, 2022–2025.
10. Hong, L.; Sun, W. S.; Yang, D. X.; Li, G. F.; Wang, R. *Chem. Rev.* **2016,** *116*, 4006–4123.

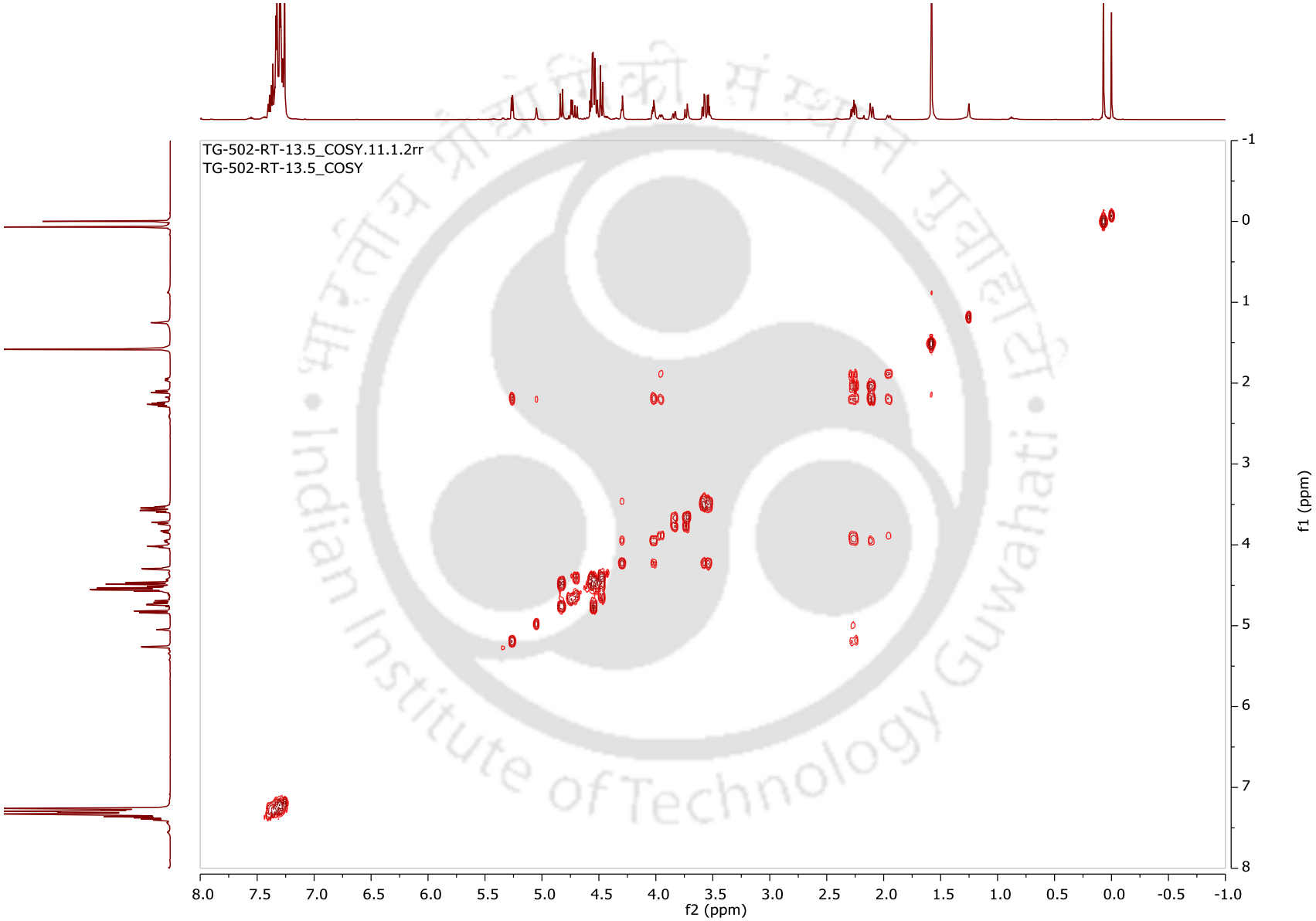
11. Crich, D.; Patel, M. *Carbohydr. Res.* **2006,** *341*, 1467–1475.
12. Larsen, C. H.; Ridgway, B. H.; Shaw, J. T.; Woerpel, K. A. *J. Am. Chem. Soc.* **1999,** *121*, 12208–12209.
13. Shimomura, N.; Saitoh, M.; Mukaiyama, T. *Chem. Lett.* **1994,** *23*, 433–436.
14. Zhong, S.; Hafner, A.; Hussal, C.; Nieger, M.; Brase, S. *Rsc. Adv.* **2015,** *5*, 6255–6258.
15. Reddy, G. M.; Rao, B. U. M.; Sridhar, P. R. *J. Org. Chem.* **2016,** *81*, 2782–2793.
16. Adamo, M. F. A.; Pergoli, R. *Org. Lett.* **2007,** *9*, 4443–4446.

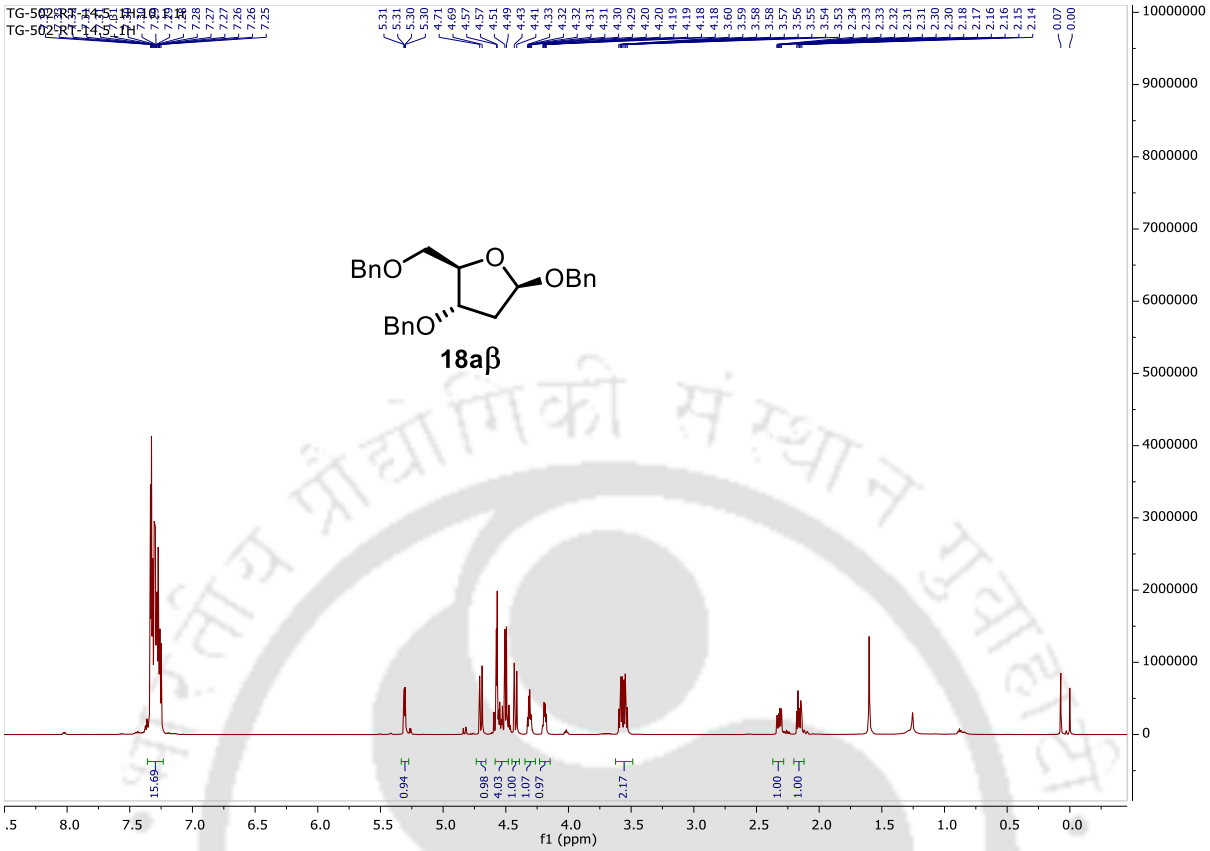
3.9 NMR Spectra:

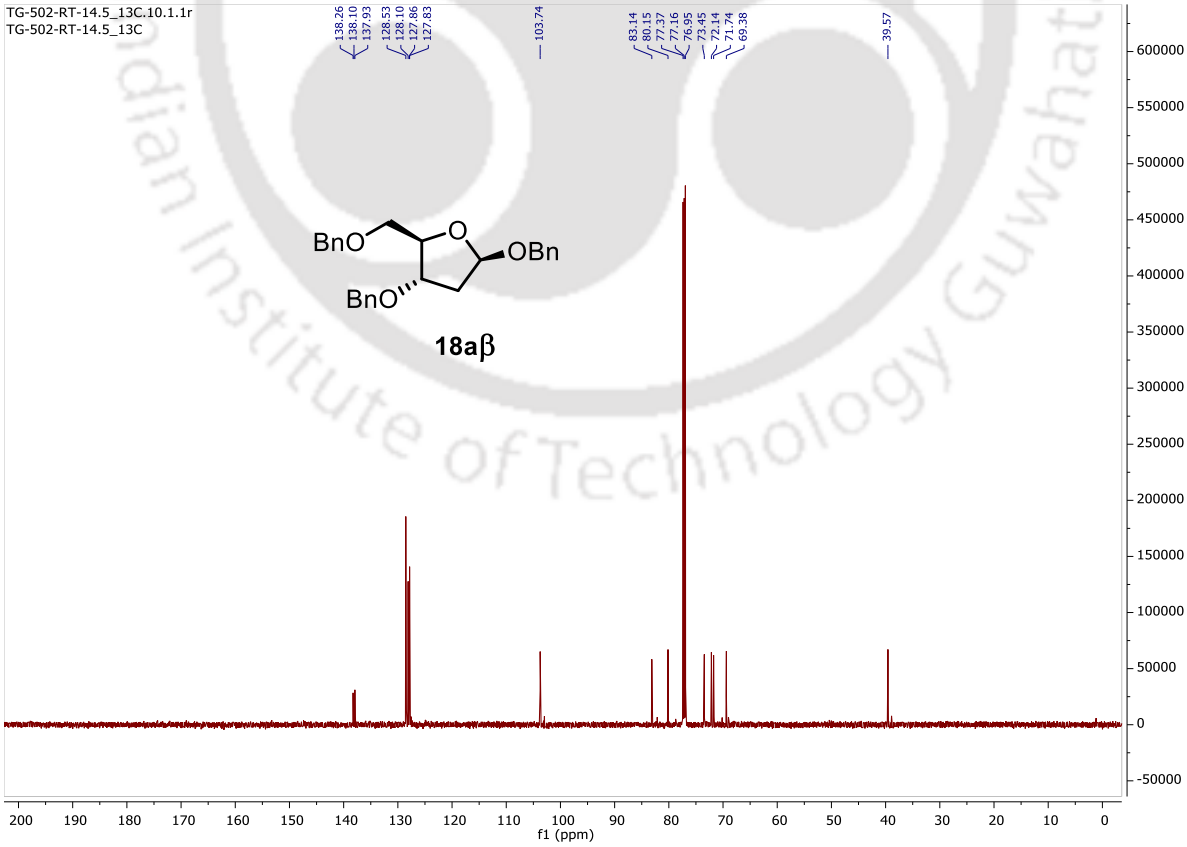




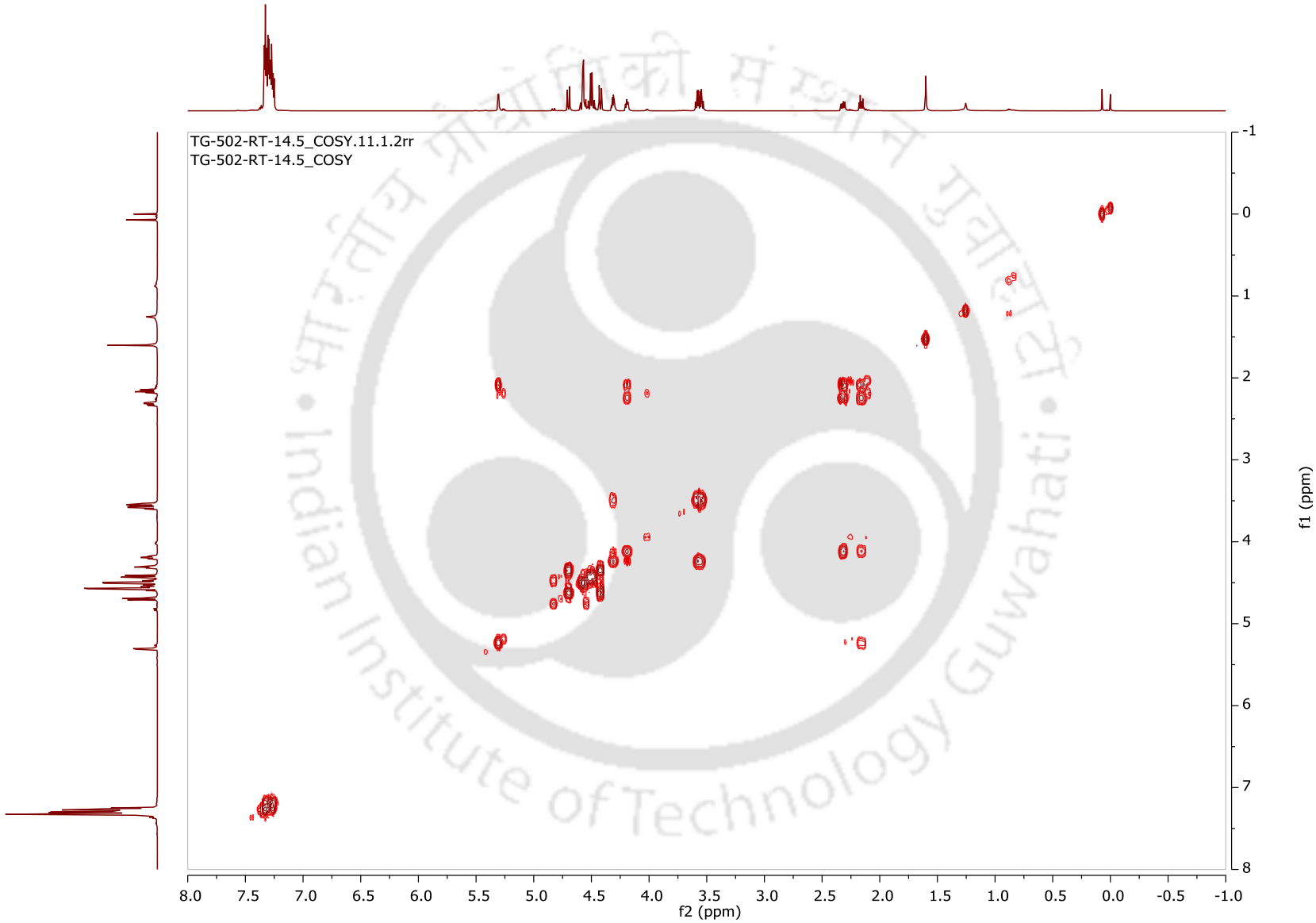
COSY NMR of Benzyl-3,5-di-*O*-benzyl-2-deoxy-α-D-erythro-pentafuranoside (18aα):

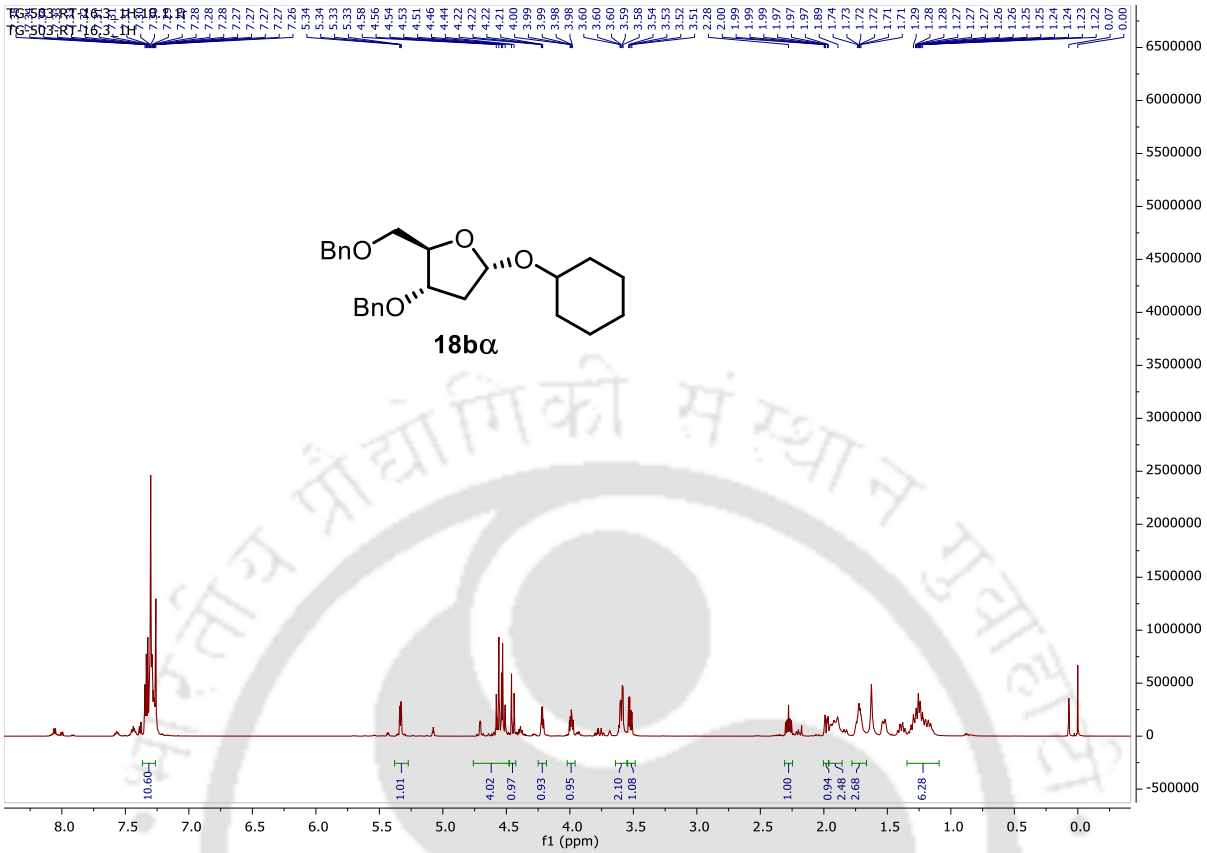


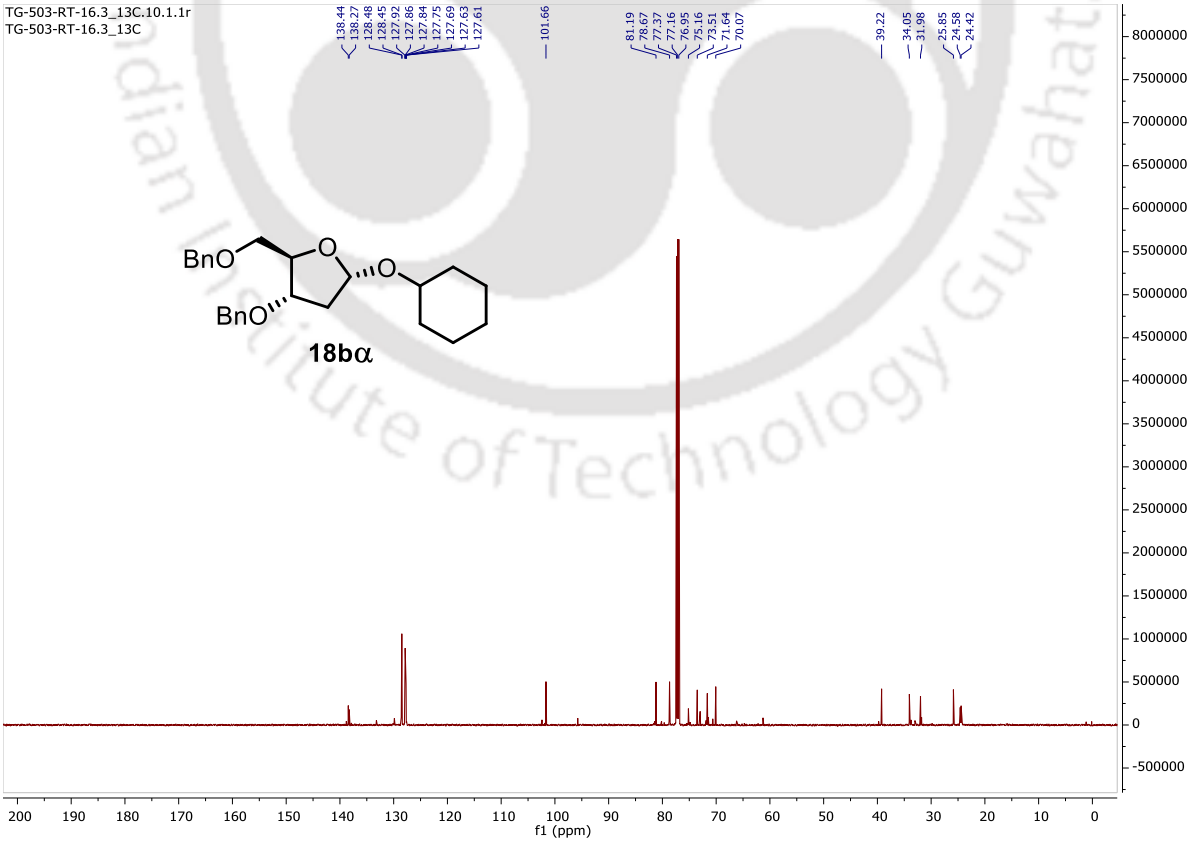




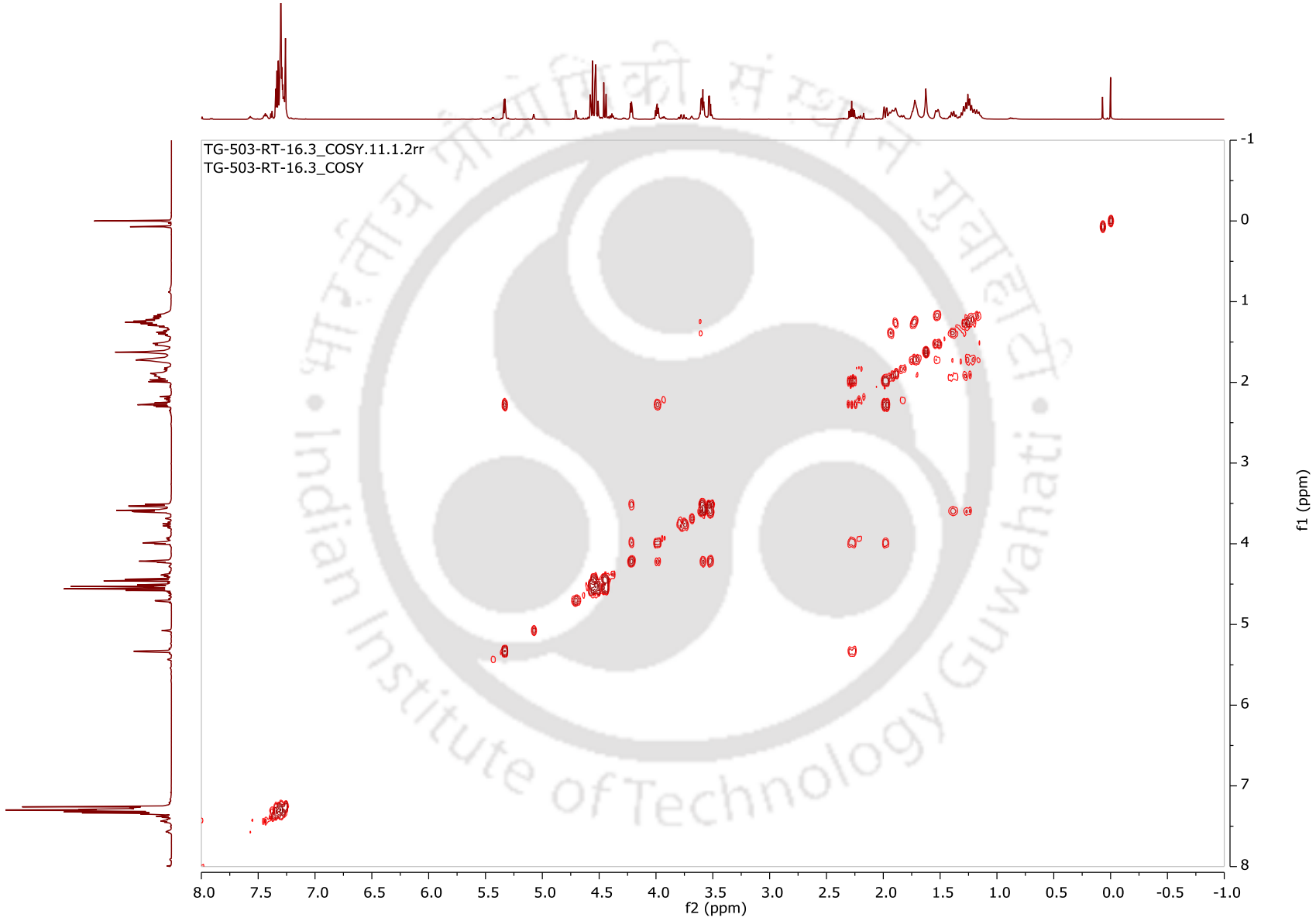
COSY NMR of Benzyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18aβ):

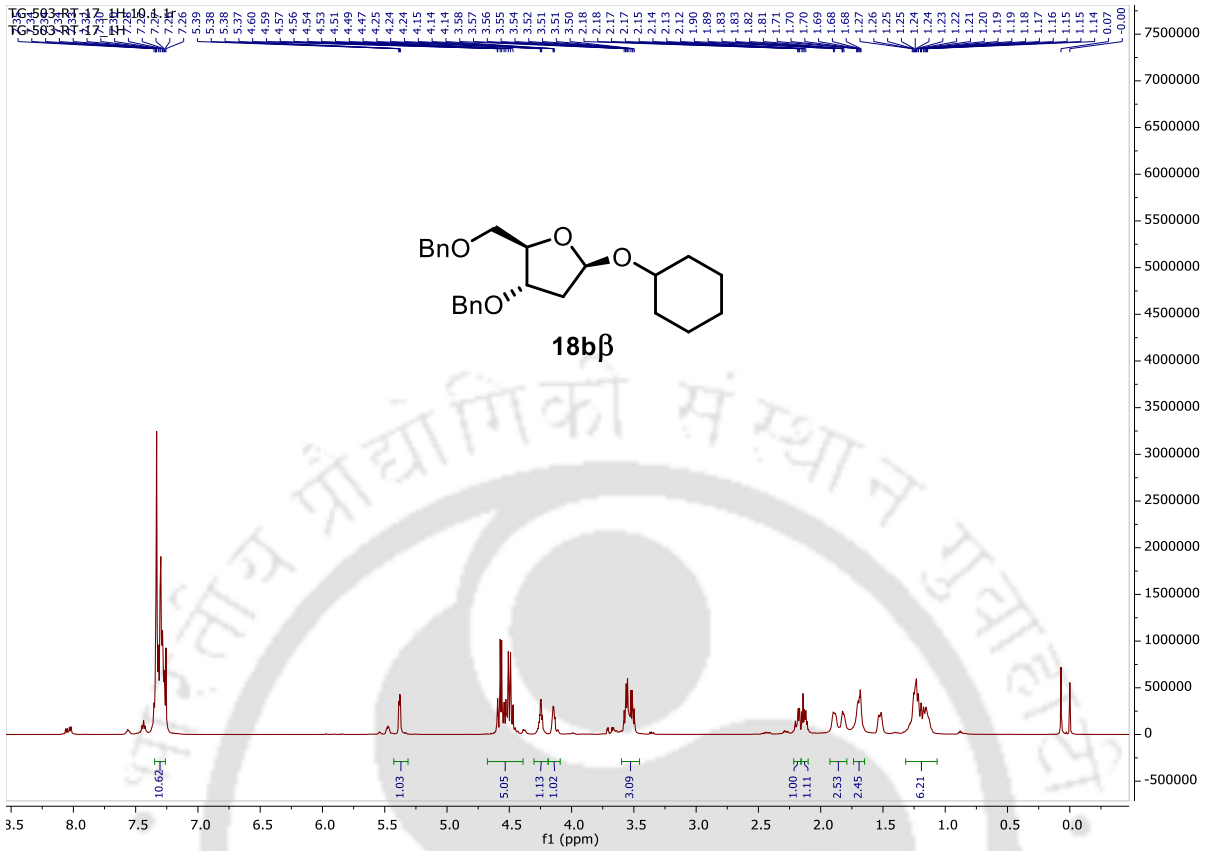


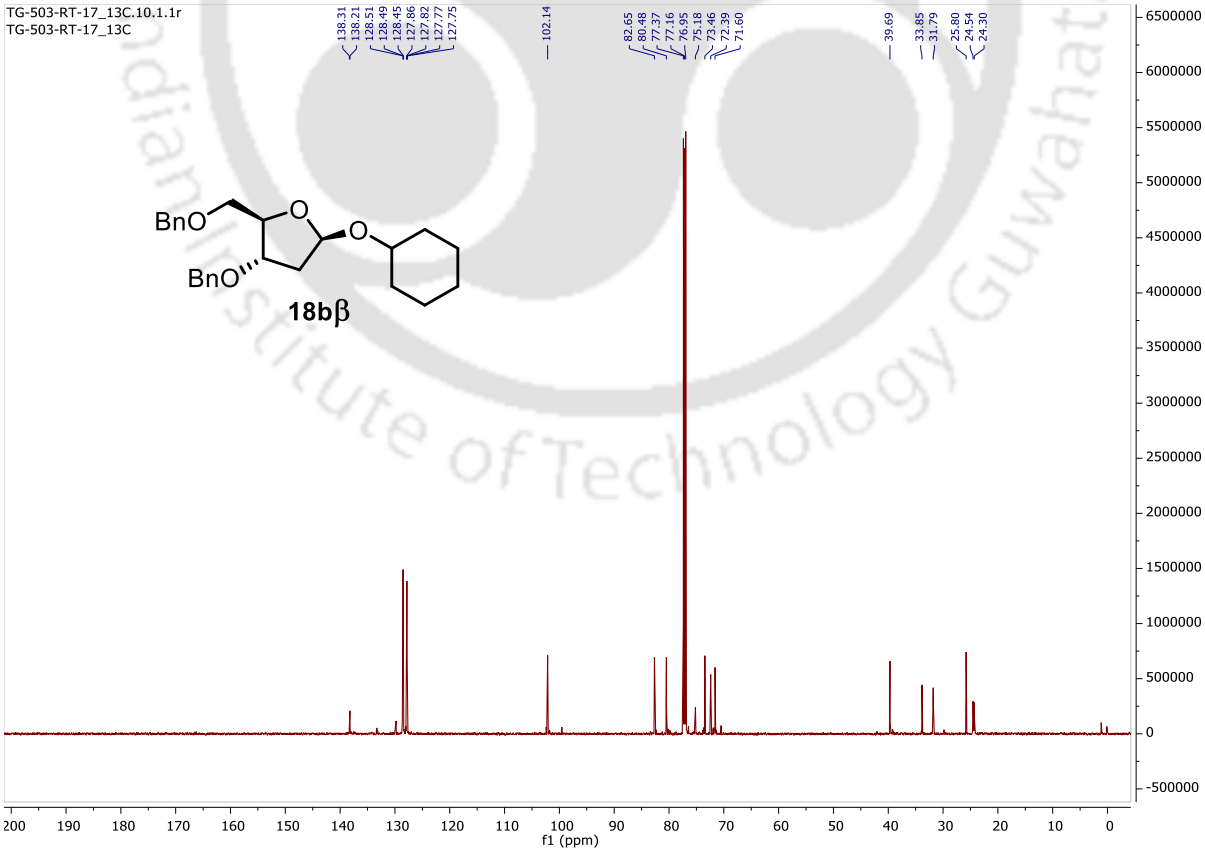




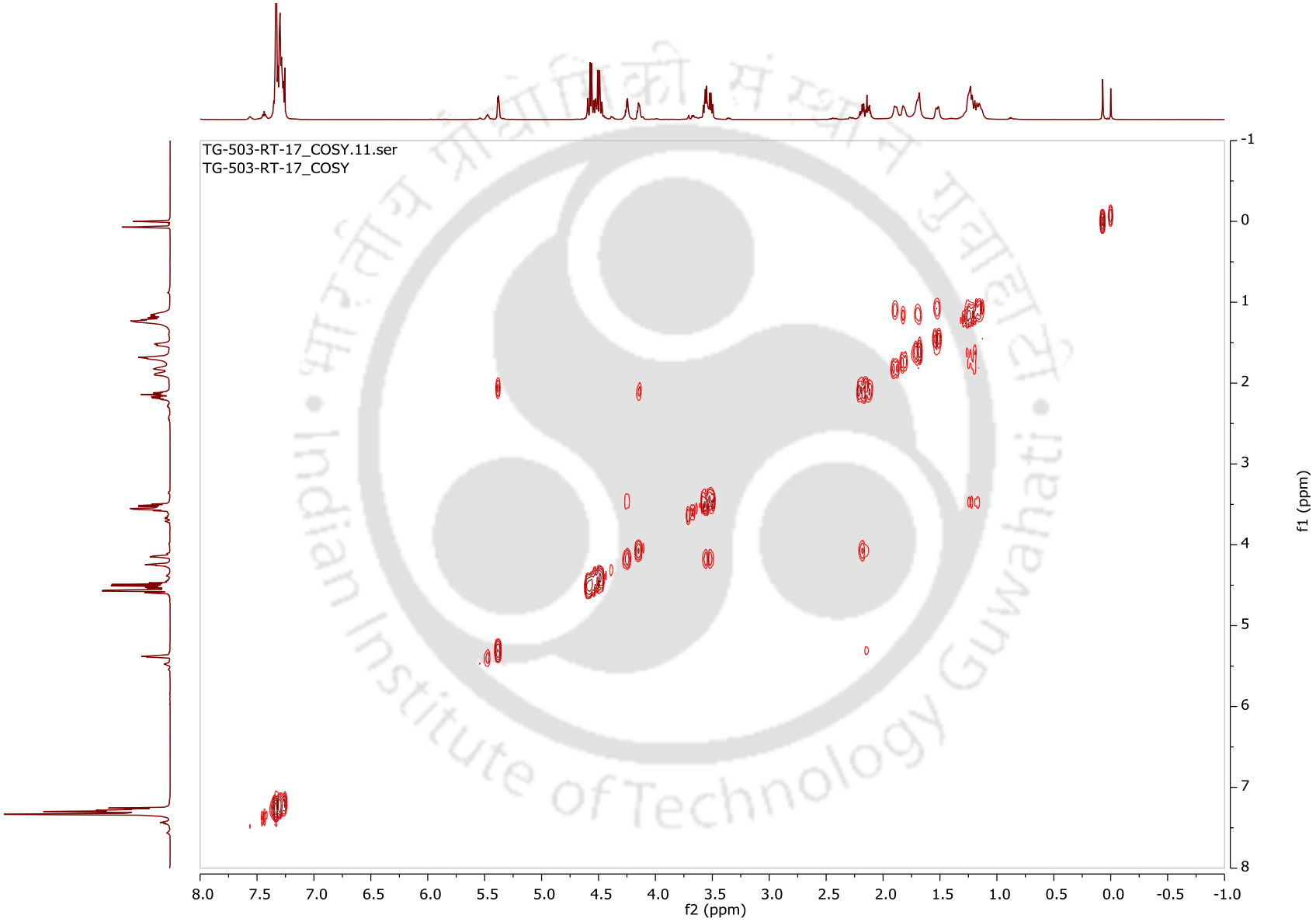
COSY NMR of Cyclohexyl-3,5-di-*O*-benzyl-2-deoxy-α-D-erythro-pentafuranoside (18bα):

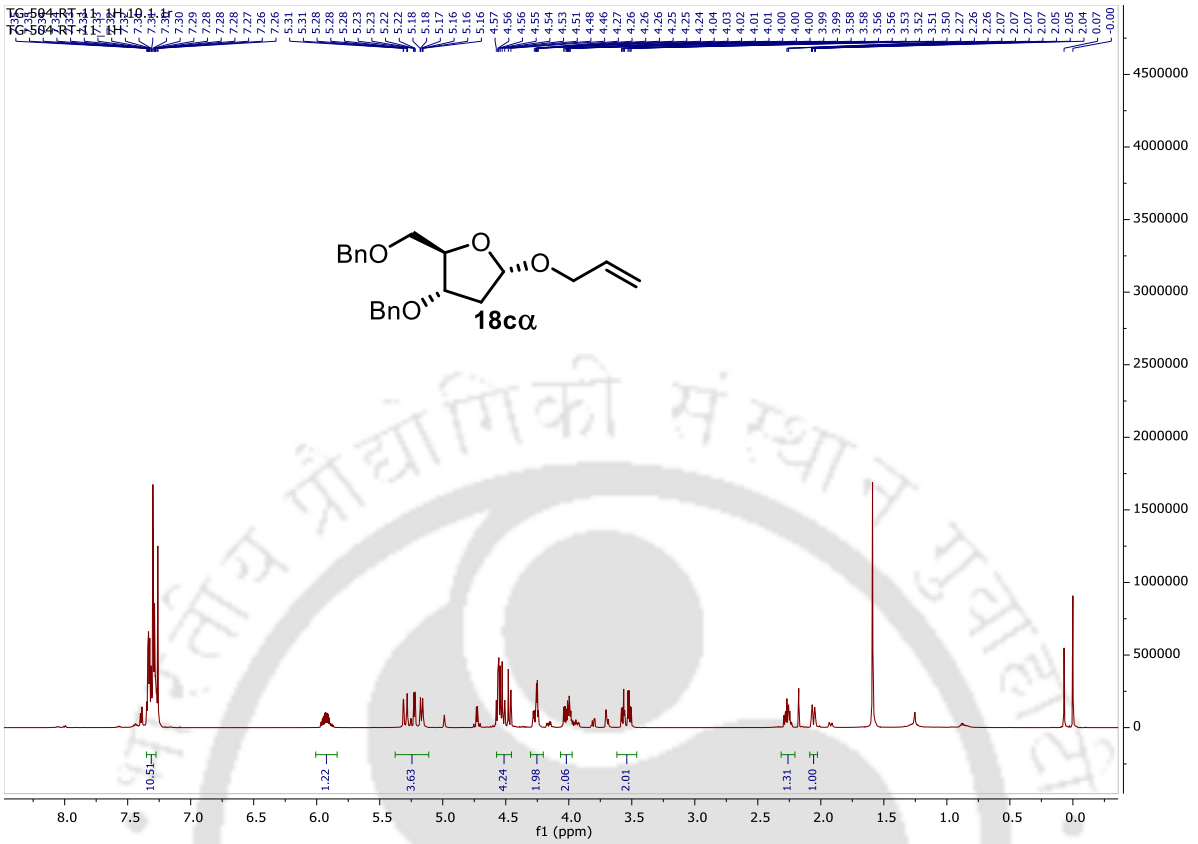


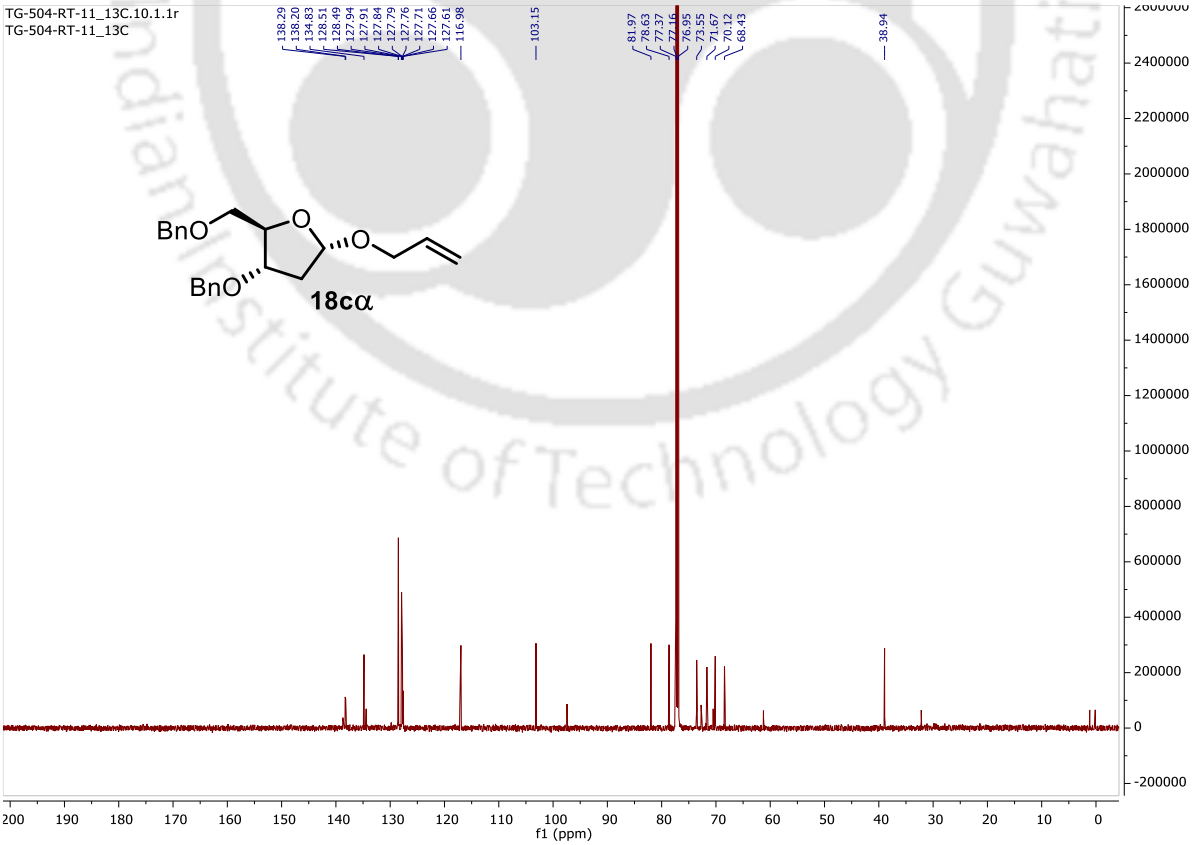




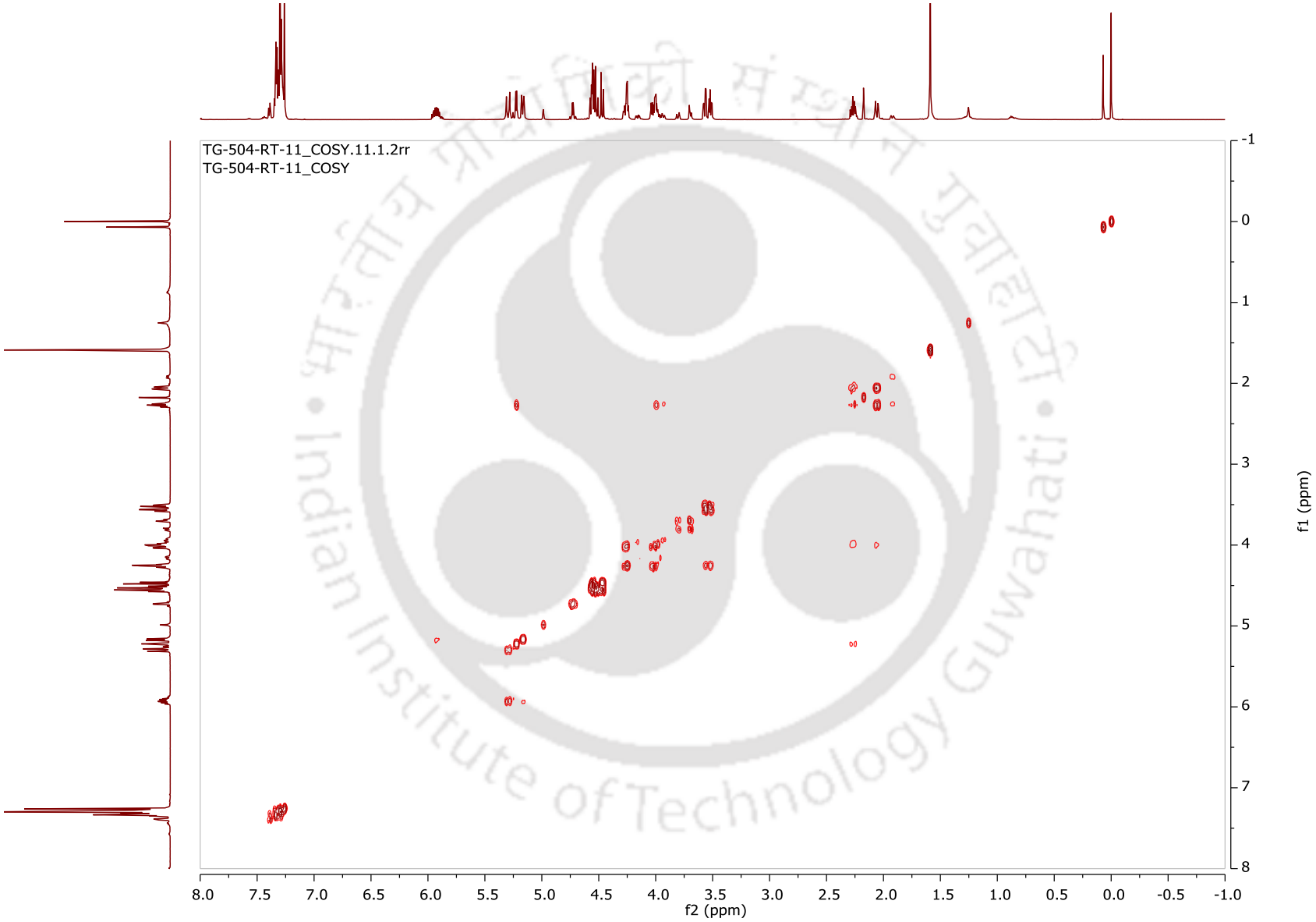
COSY NMR of Cyclohexyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18bβ):

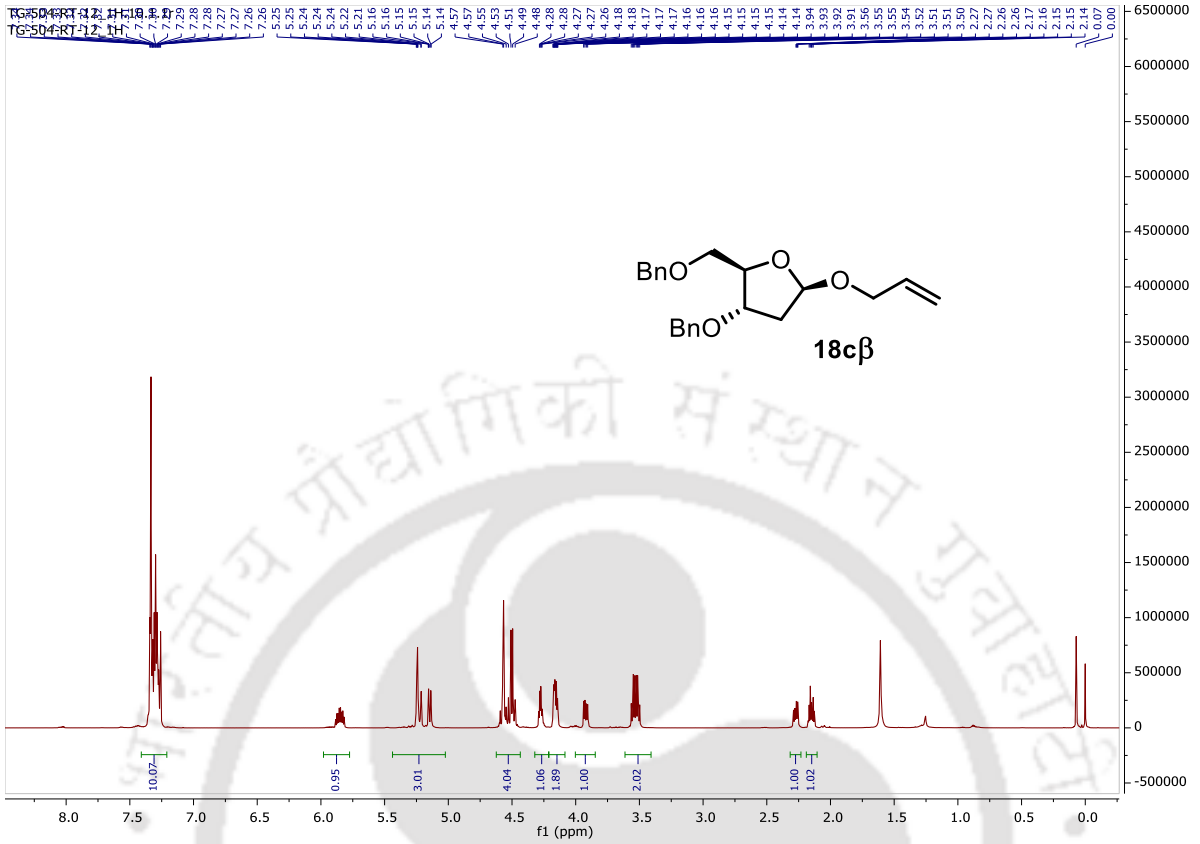


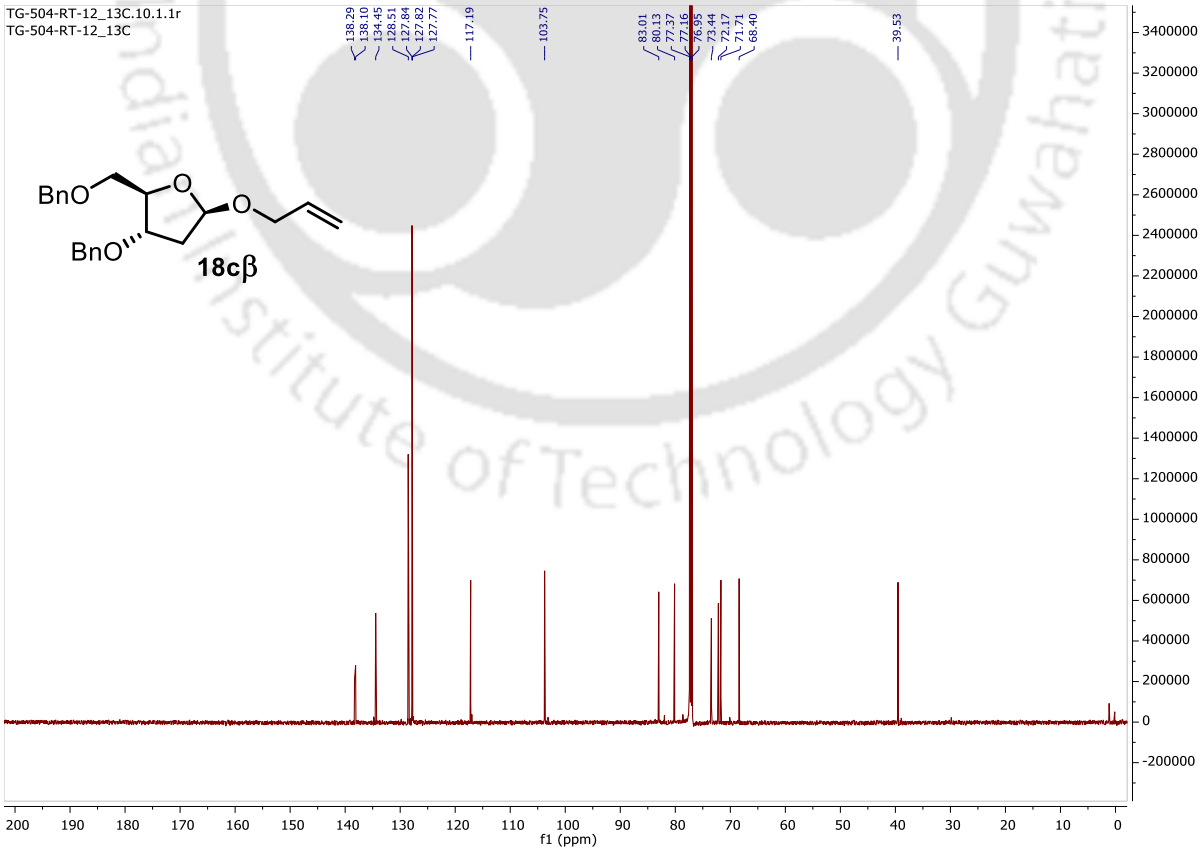




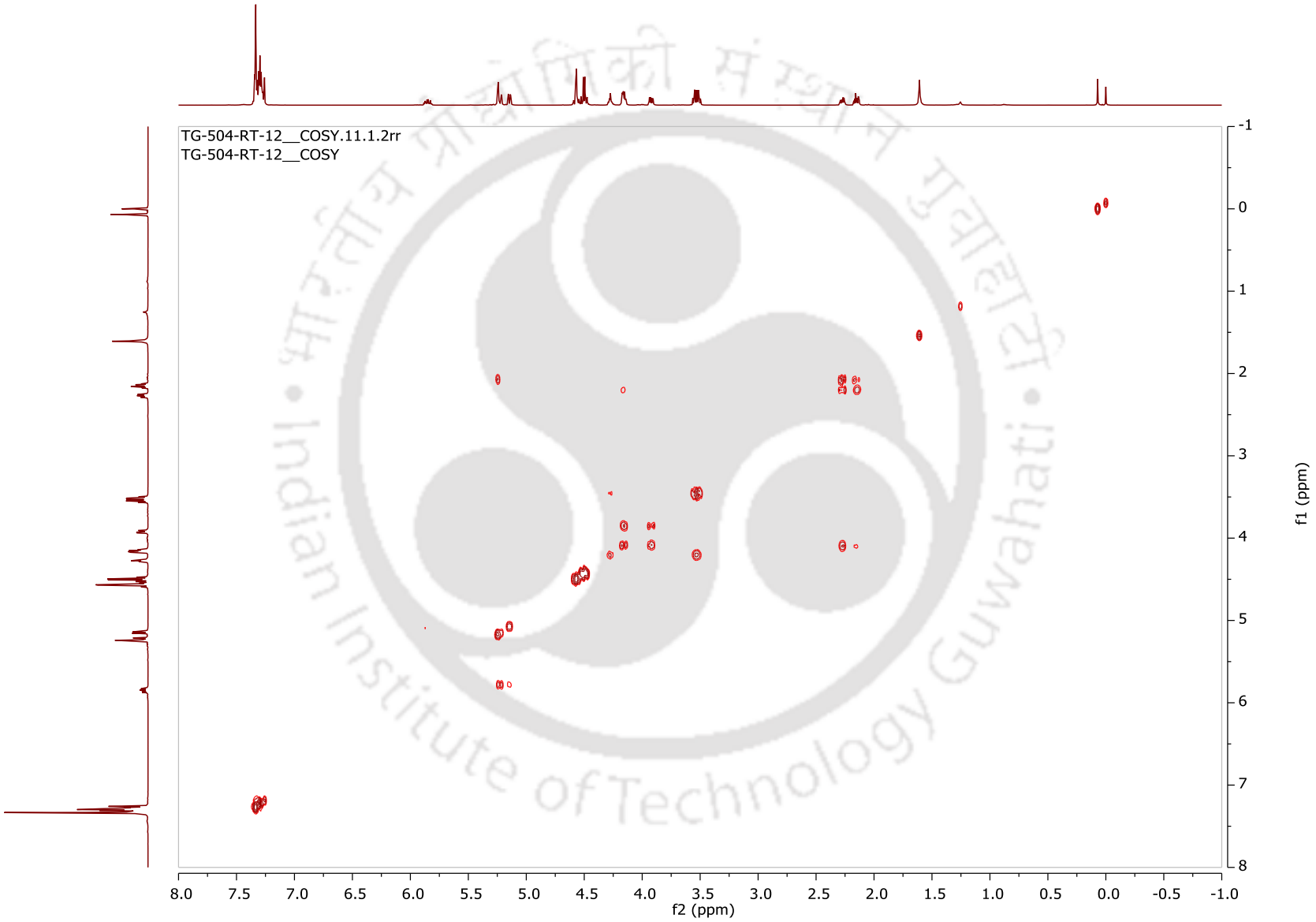
COSY NMR of Allyl-3,5-di-*O*-benzyl-2-deoxy-α-D-erythro-pentafuranoside (18cα):

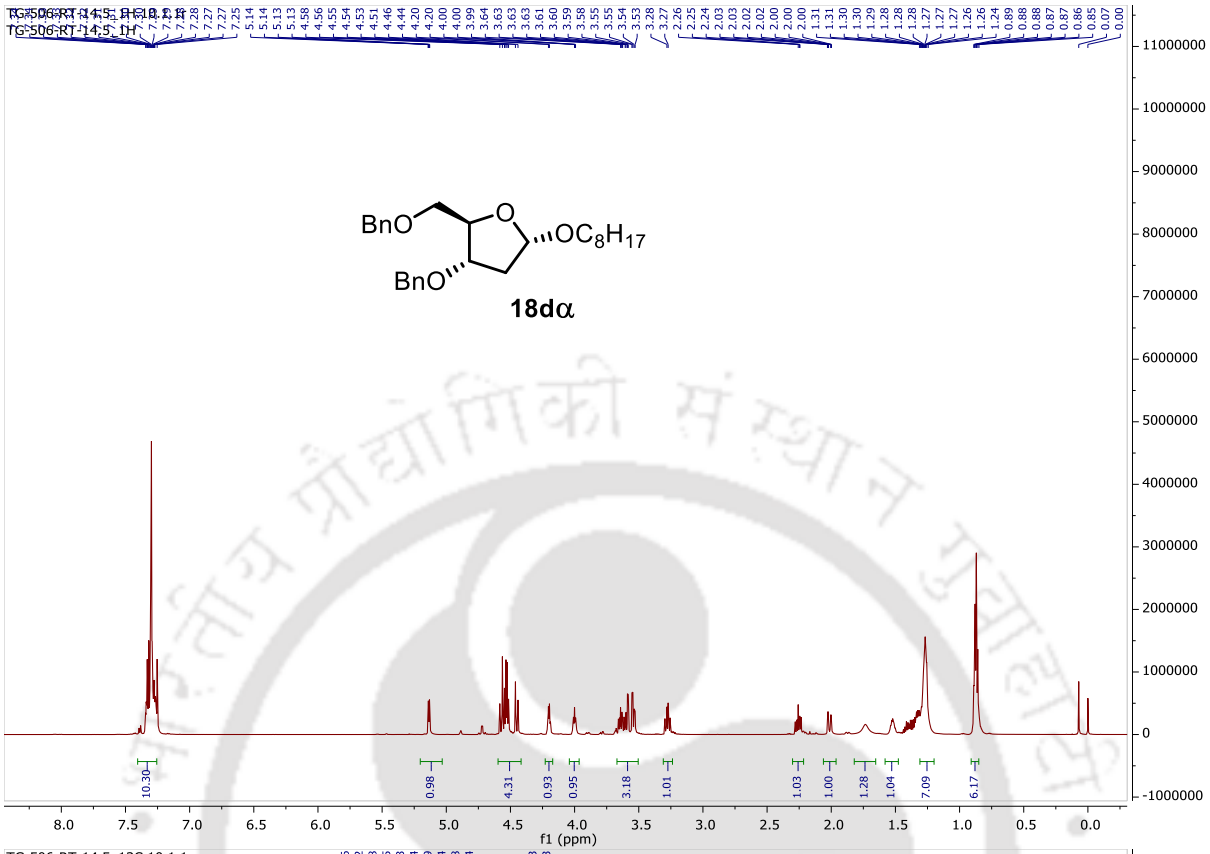


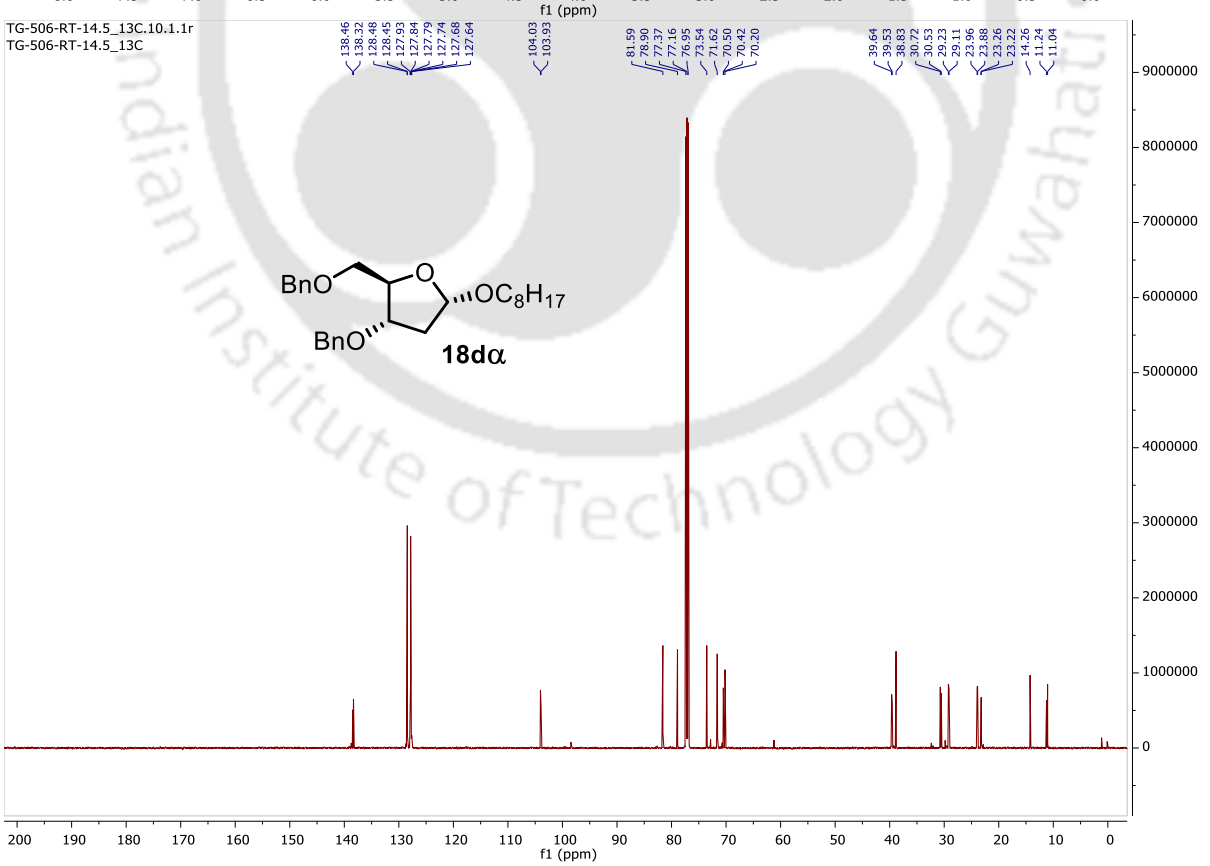




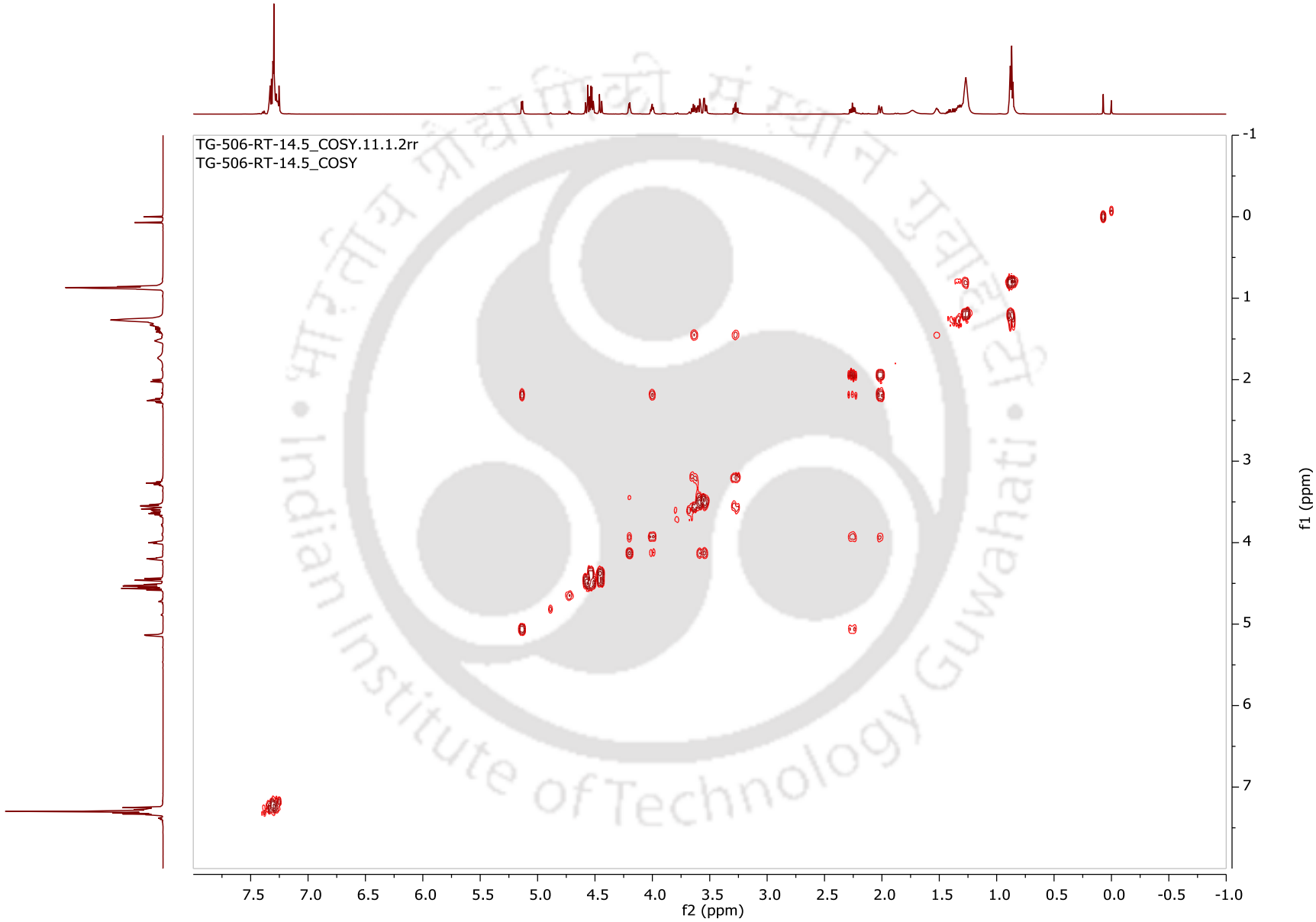
COSY NMR of Allyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18cβ):

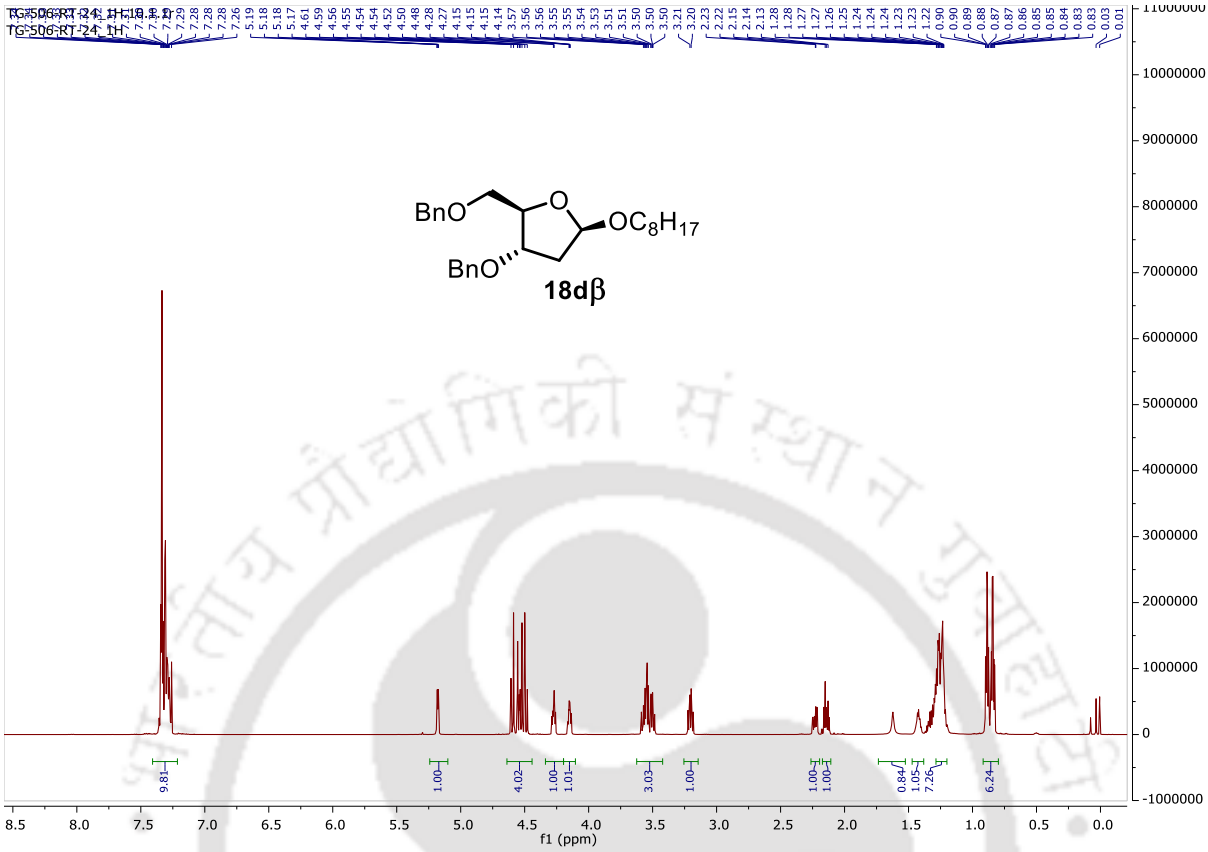


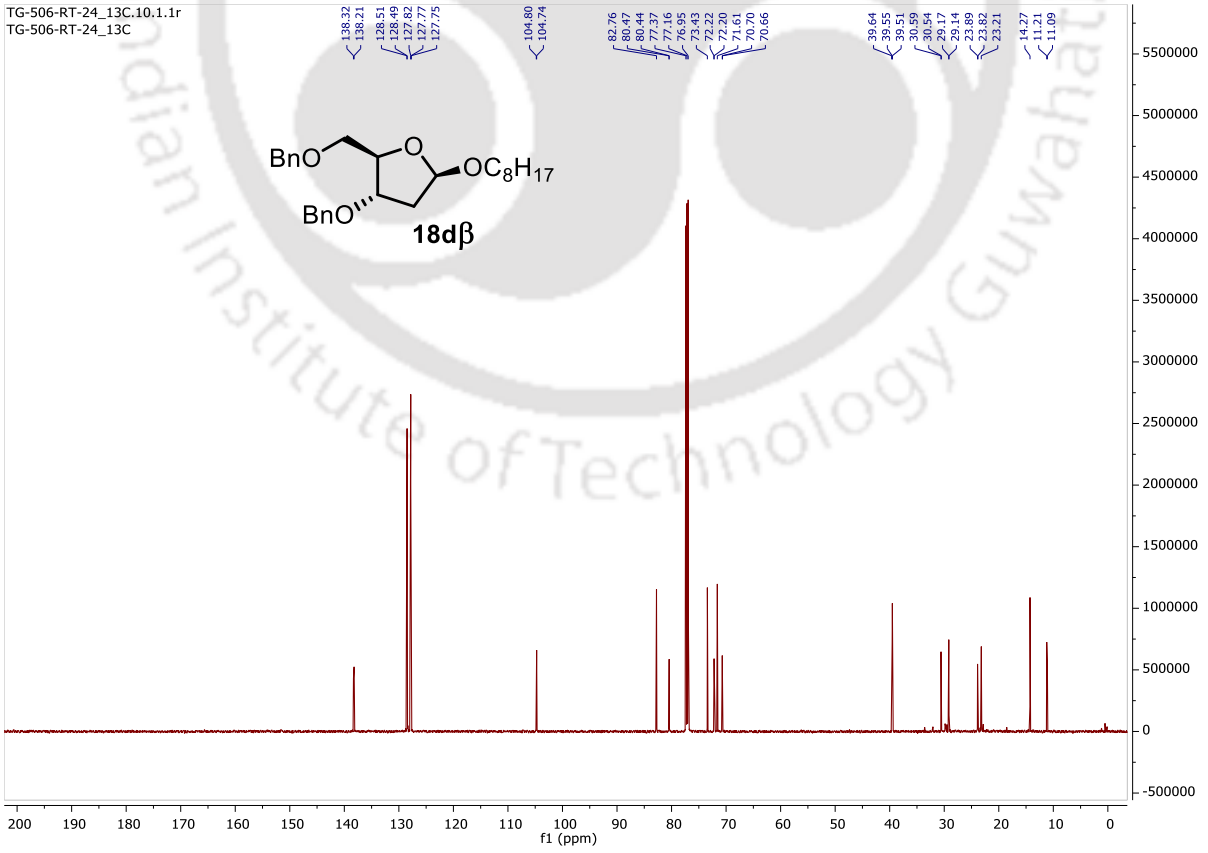




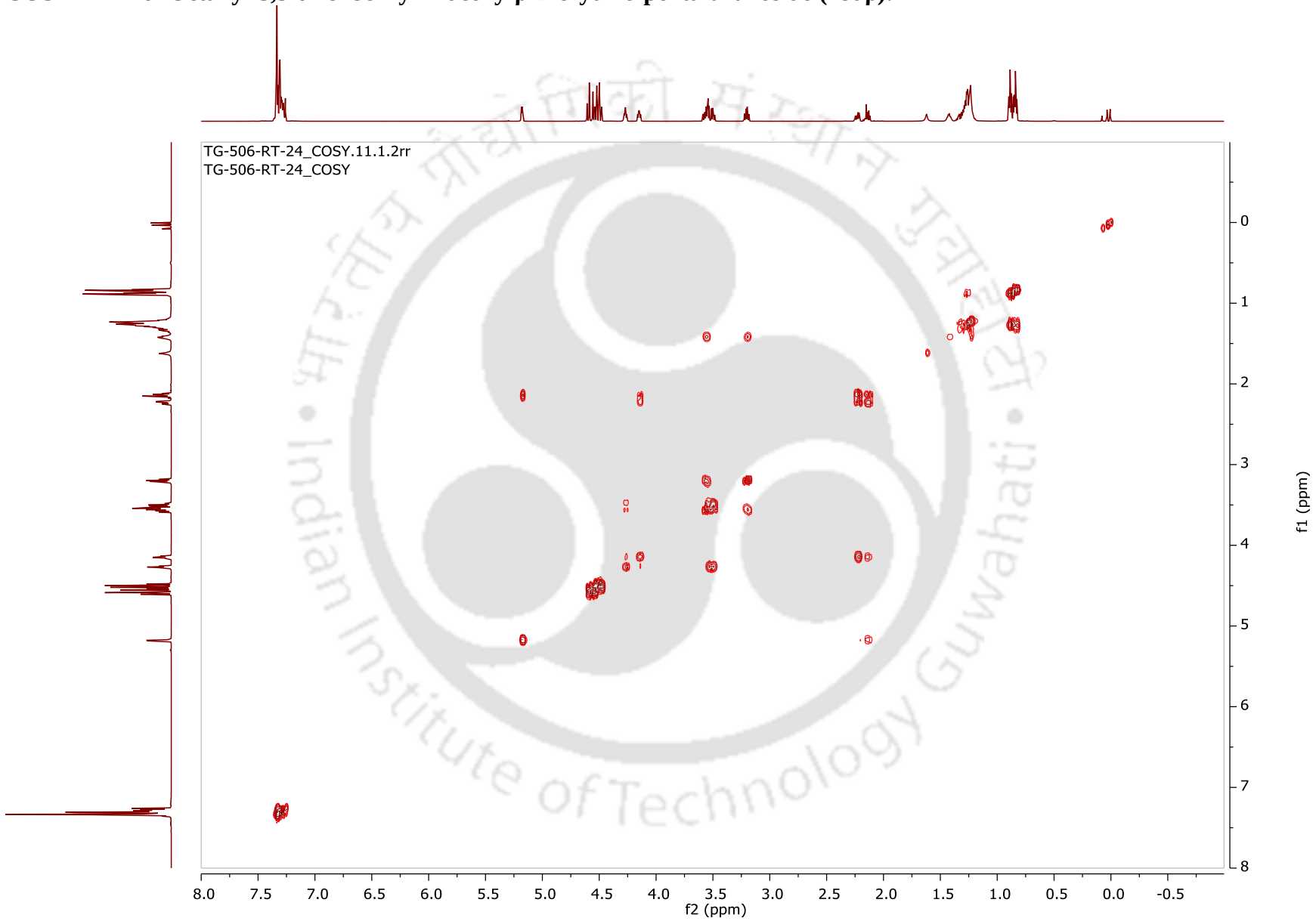
COSY NMR of Octanyl-3,5-di-*O*-benzyl-2-deoxy-α-D-erythro-pentafuranoside (18dα):

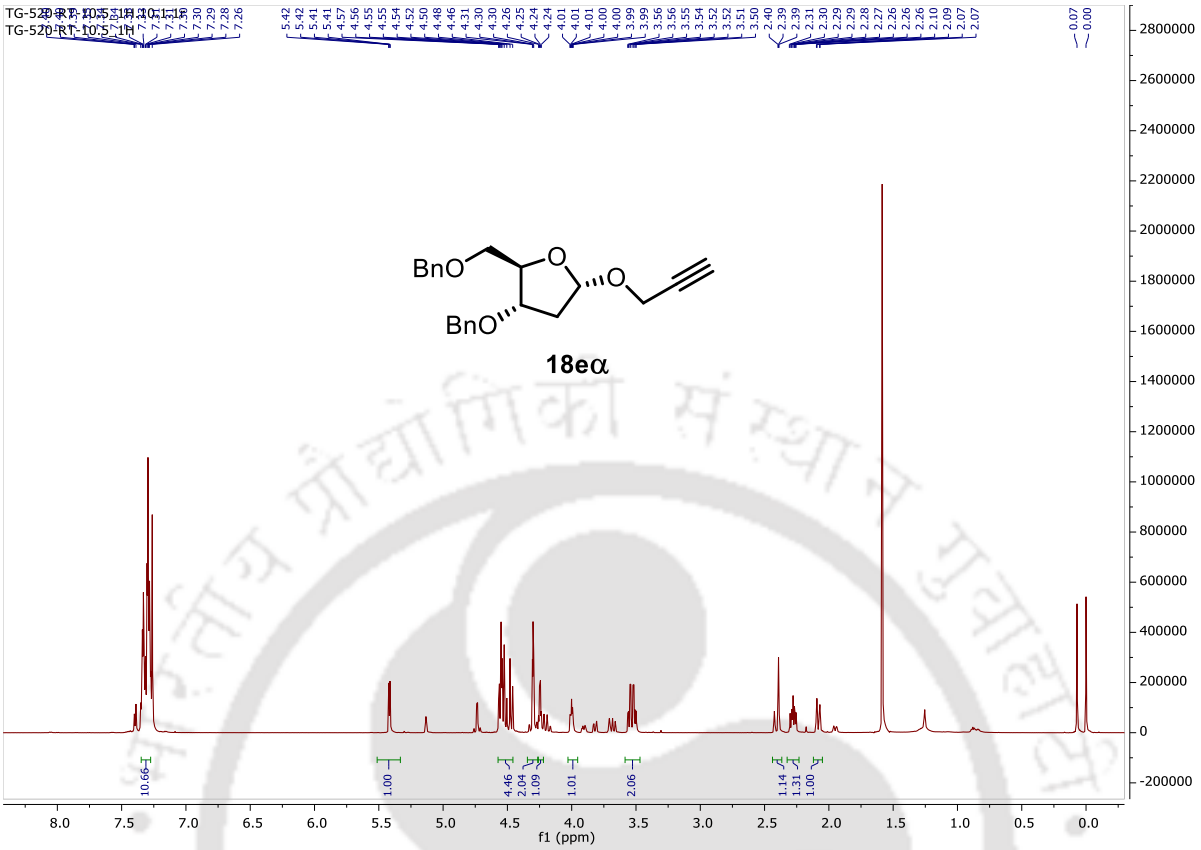


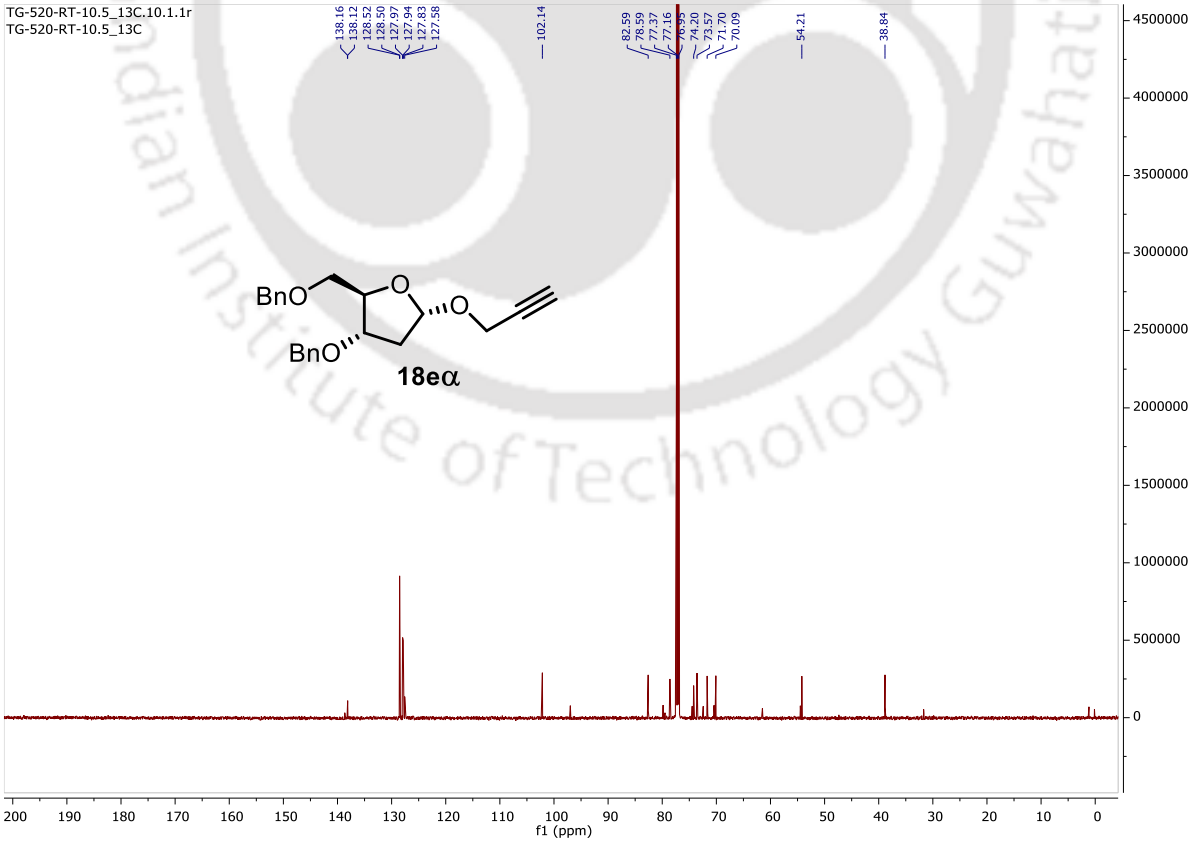




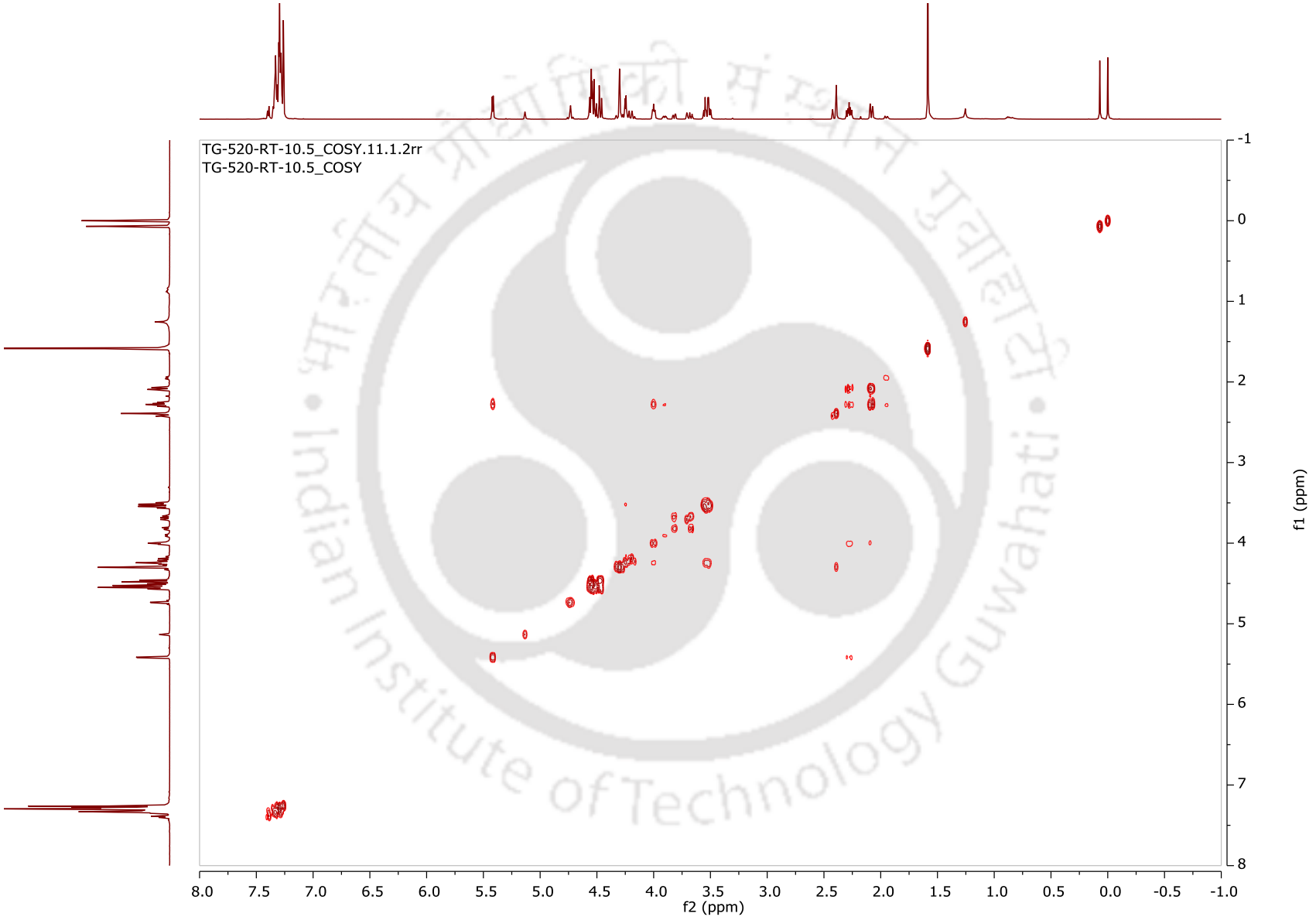
COSY NMR of Octanyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18dβ):

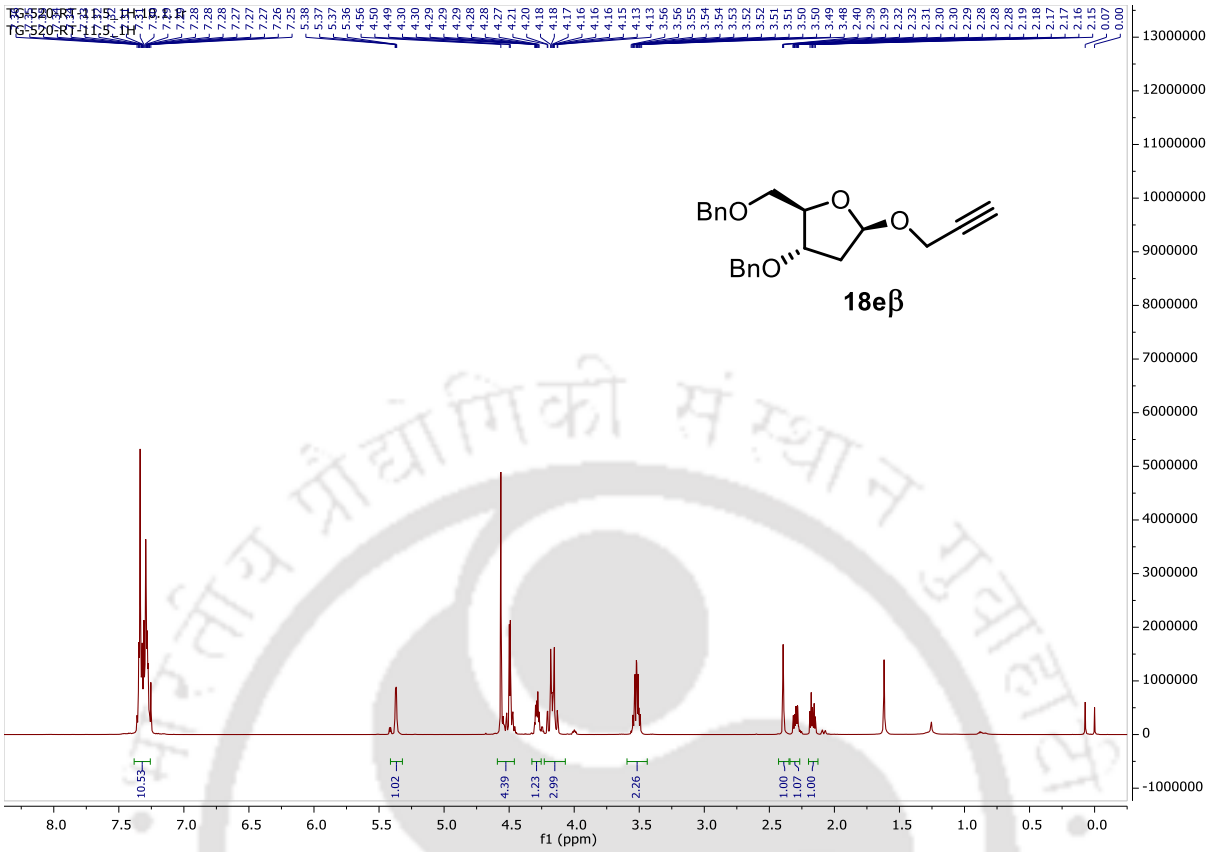


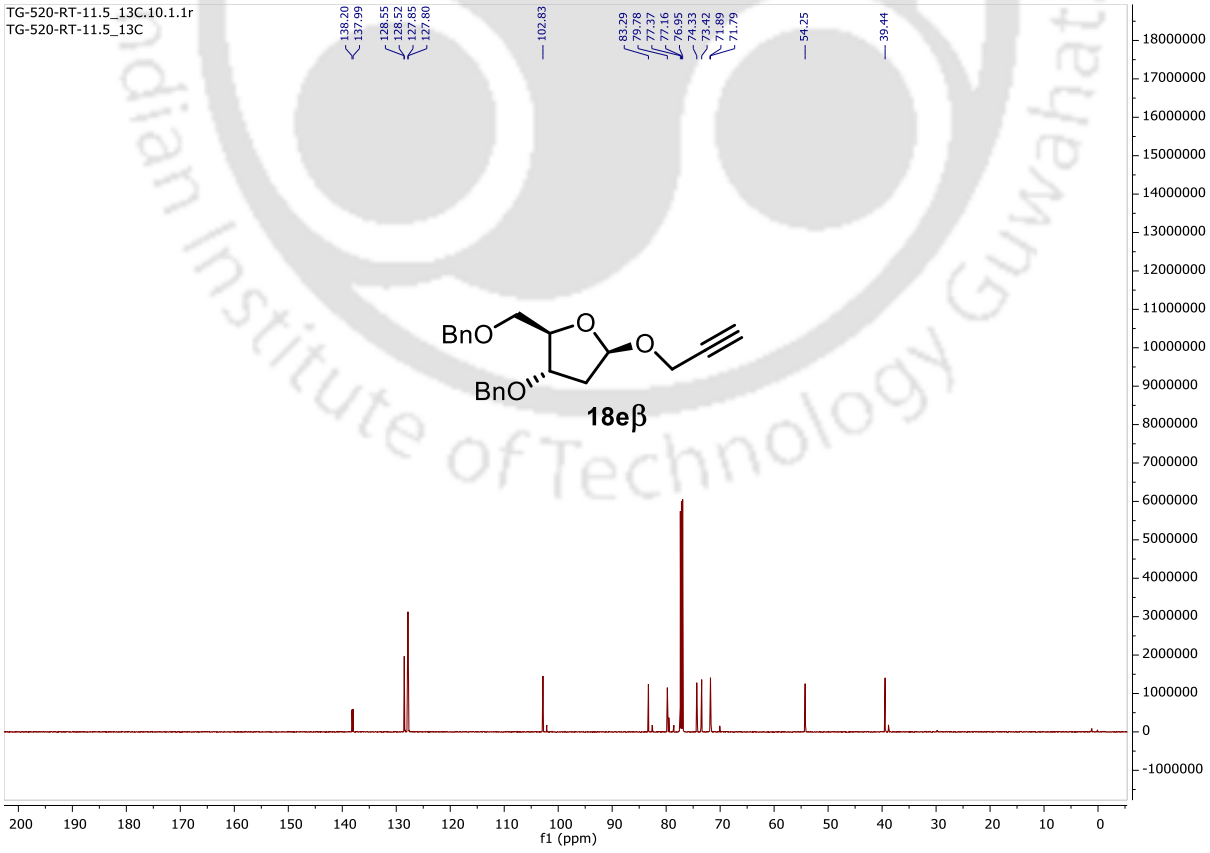




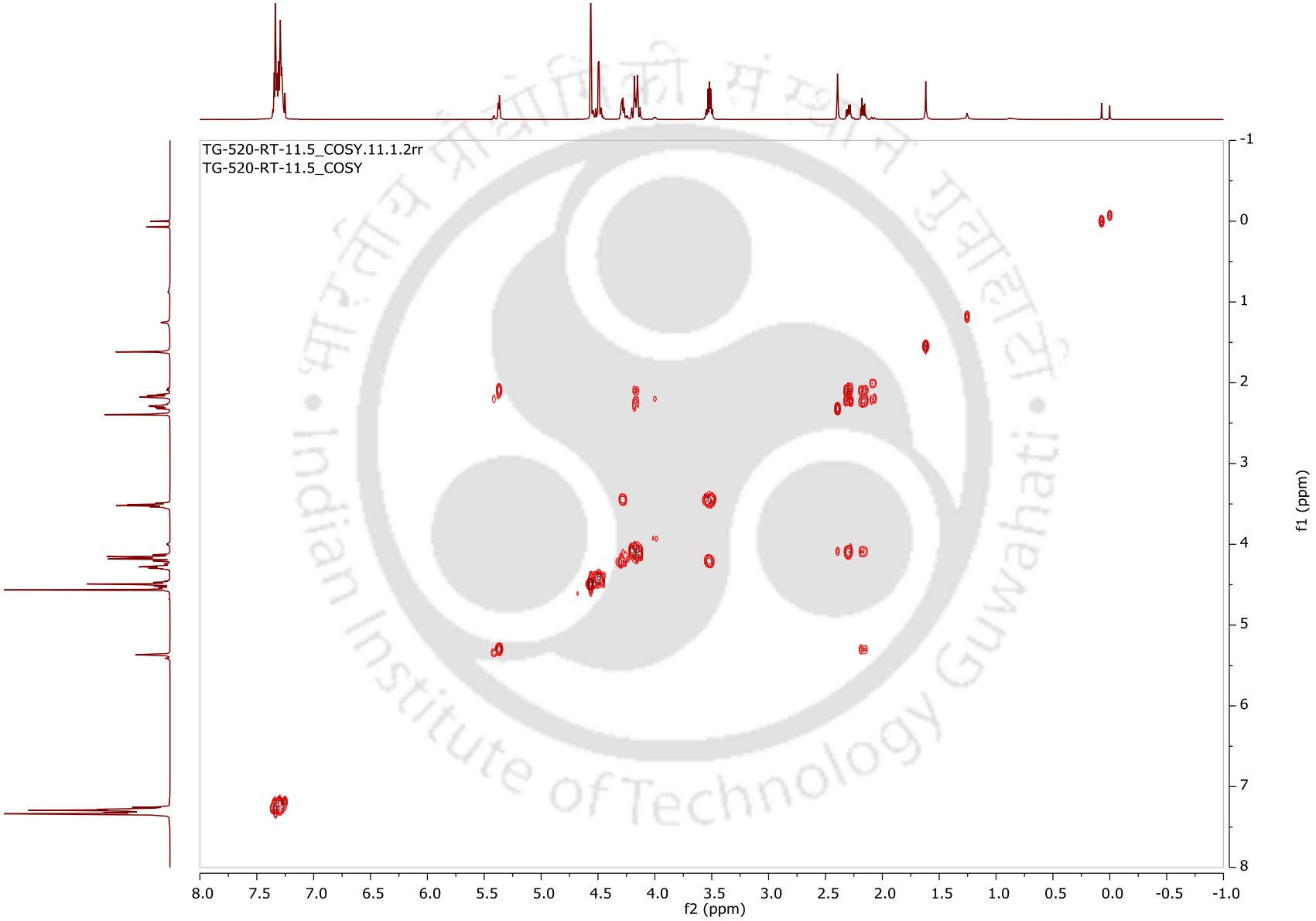
COSY NMR of Propargyl-3,5-di-*O*-benzyl-2-deoxy-α-D-erythro-pentafuranoside (18eα):

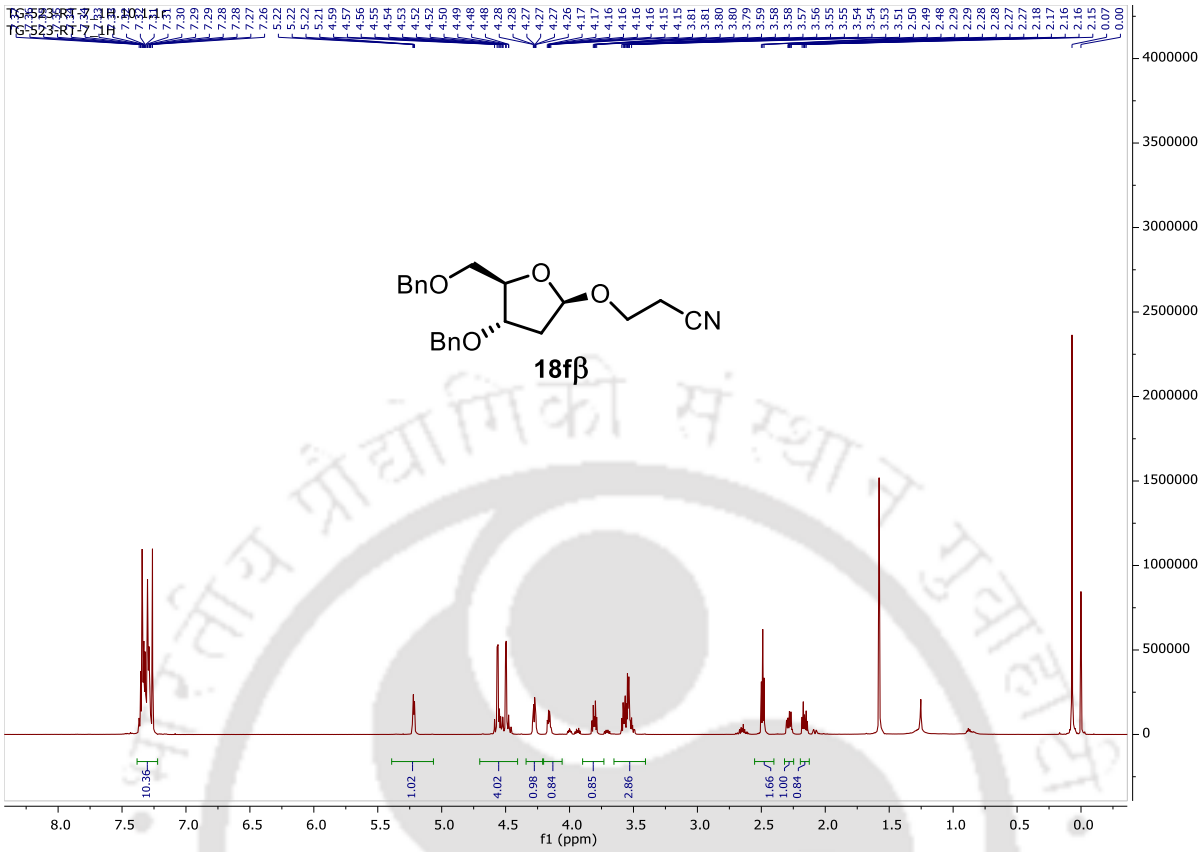


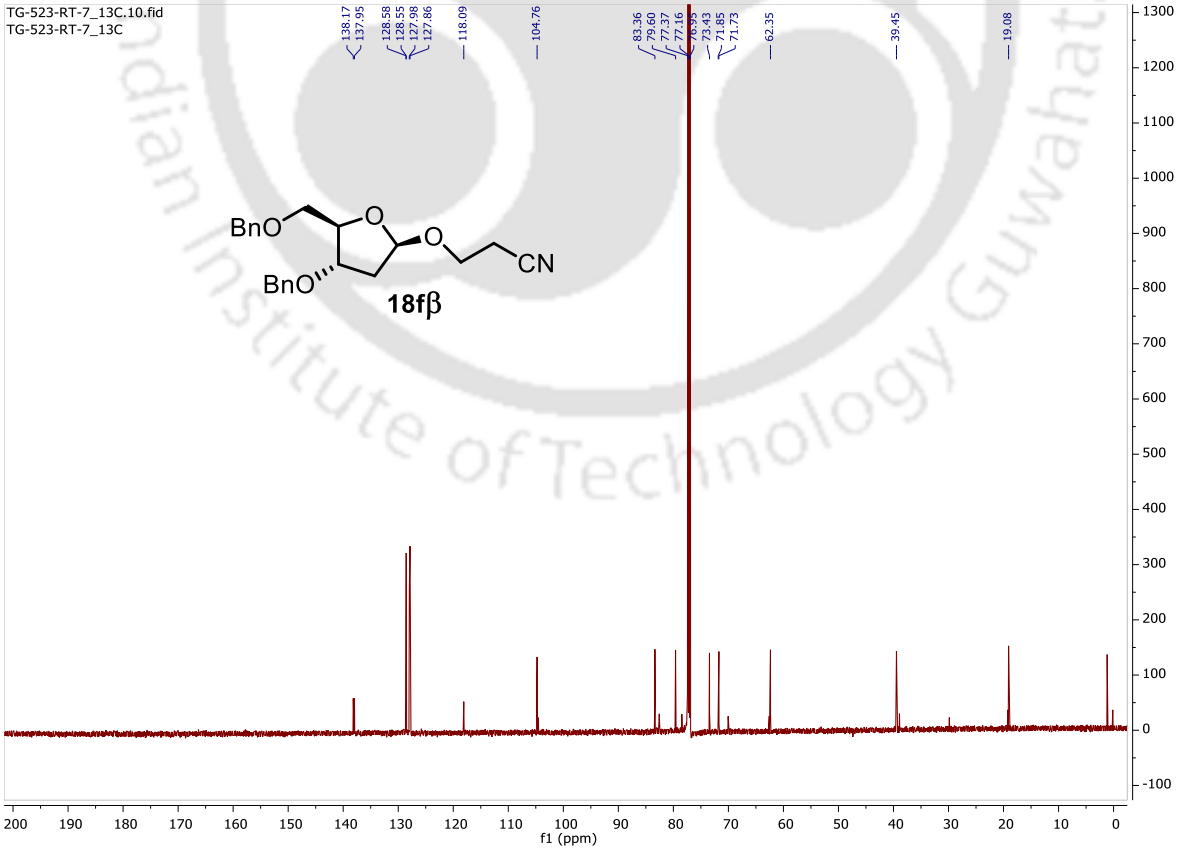




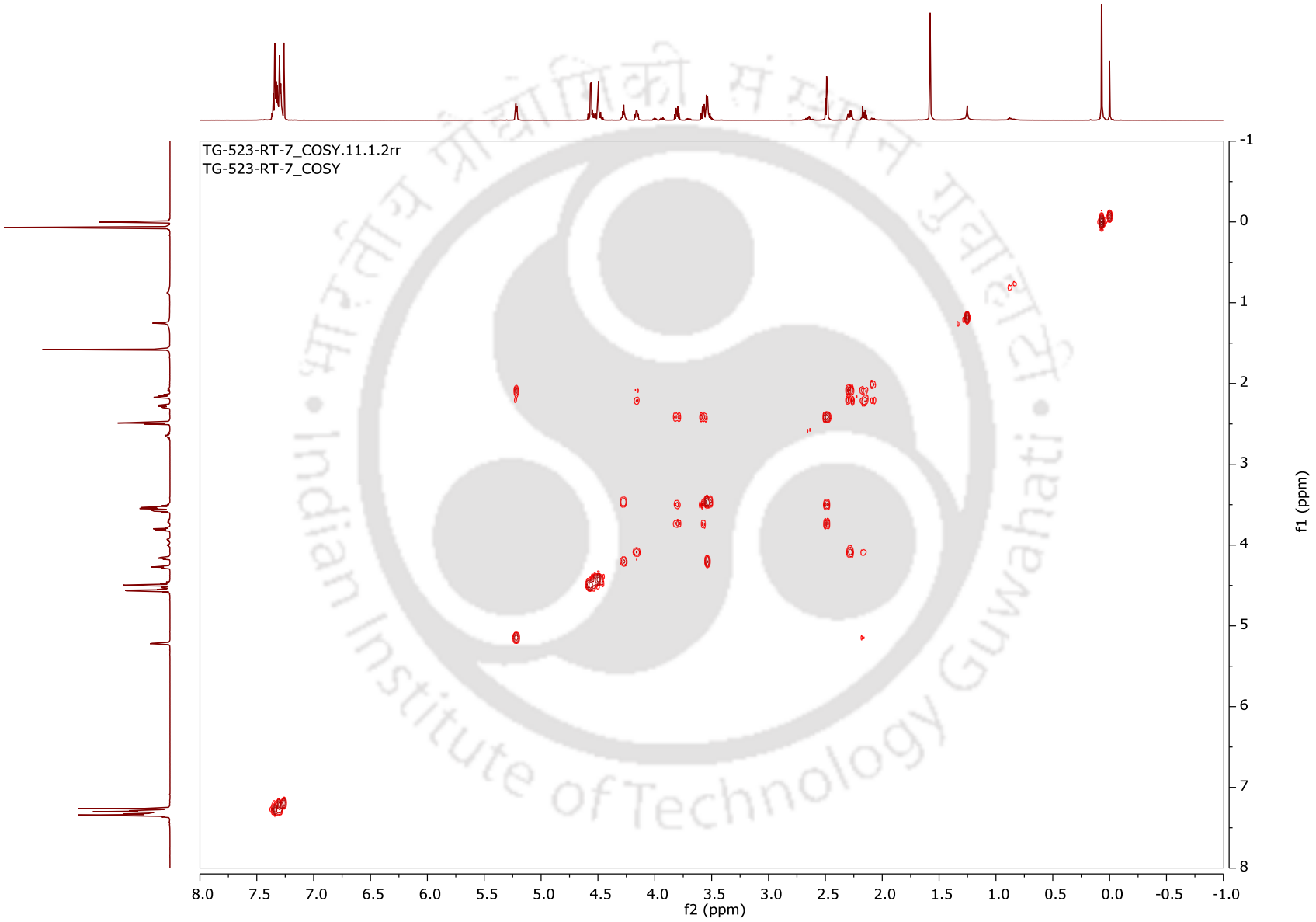
COSY NMR of Propargyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18eβ):

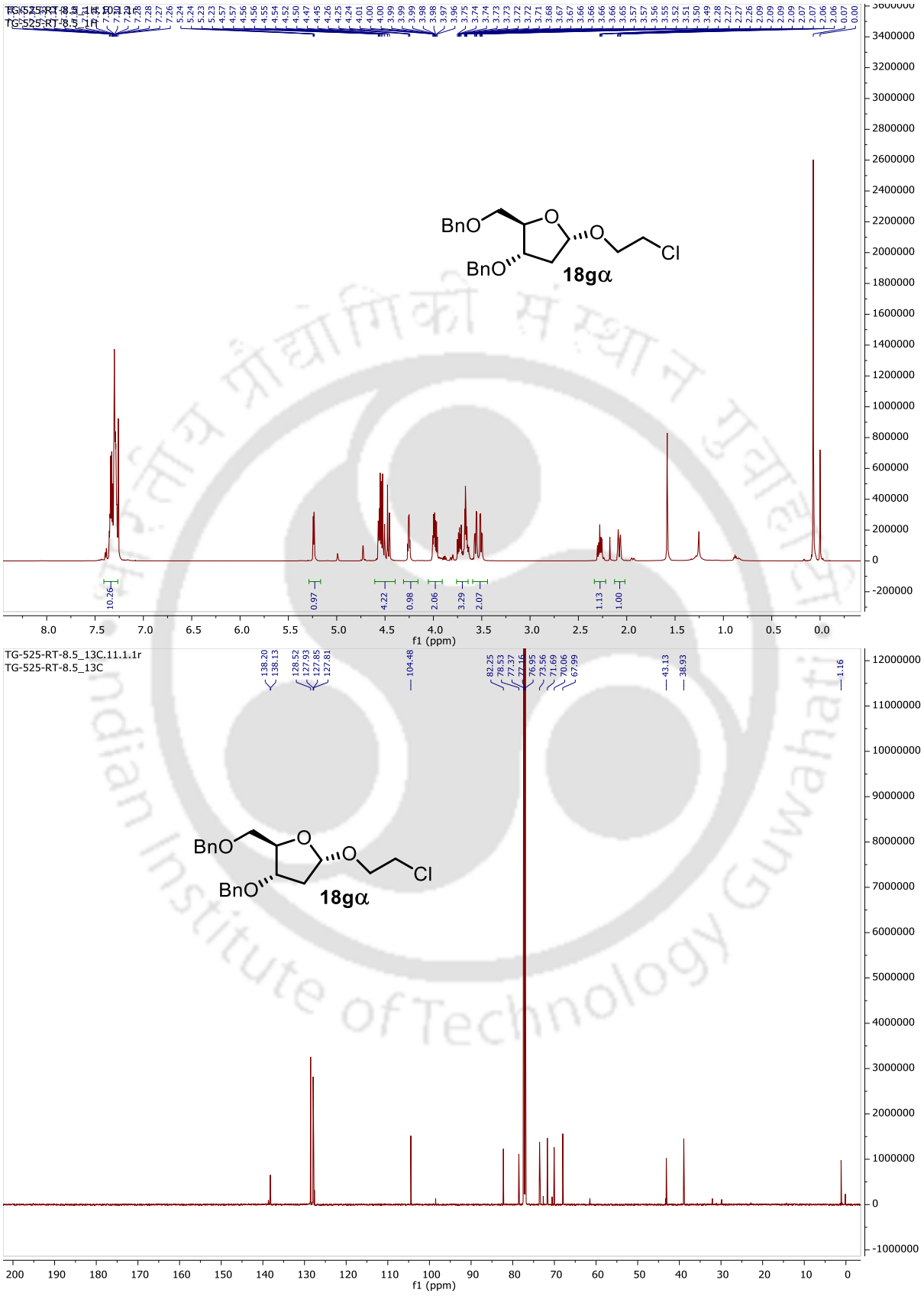




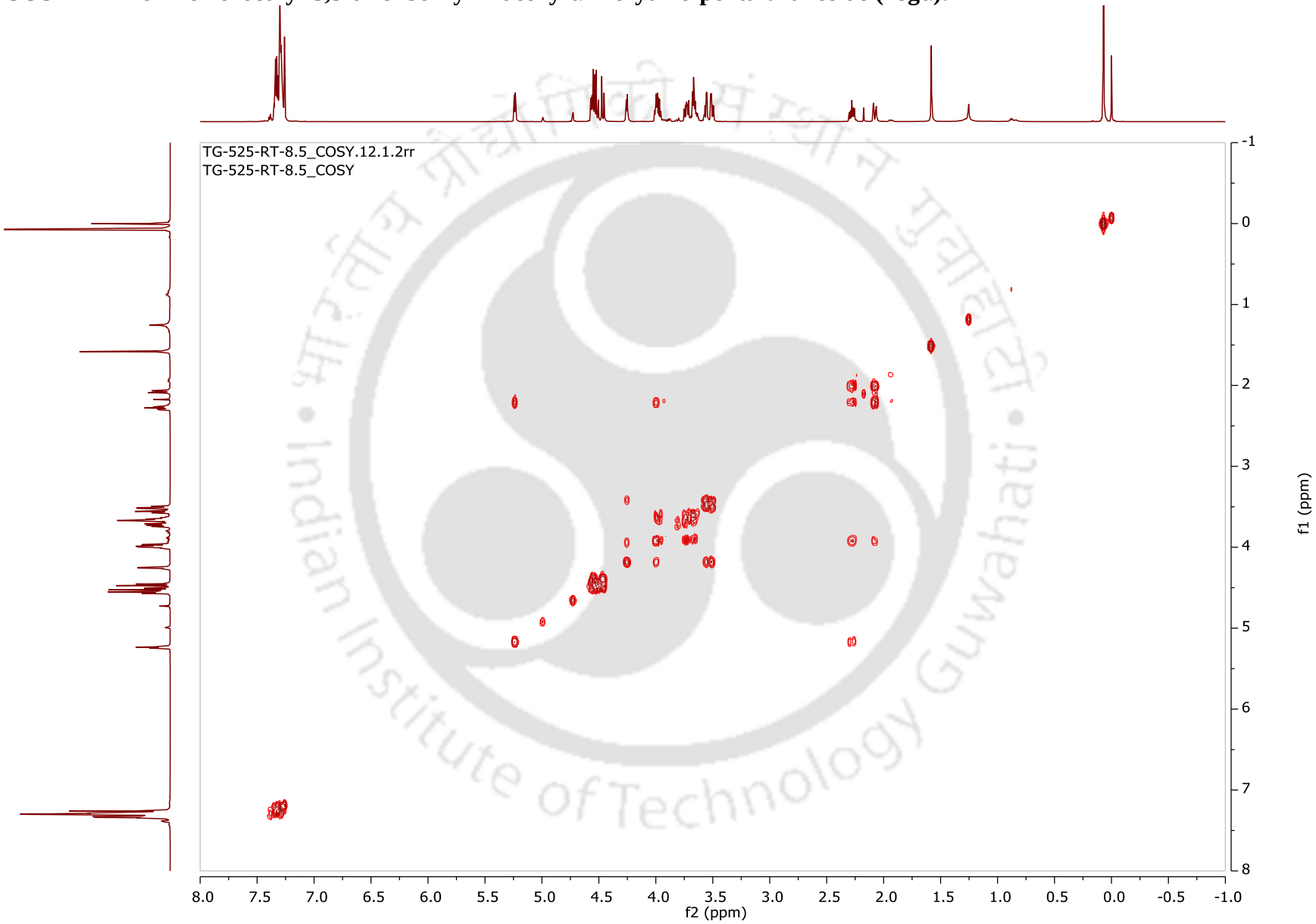


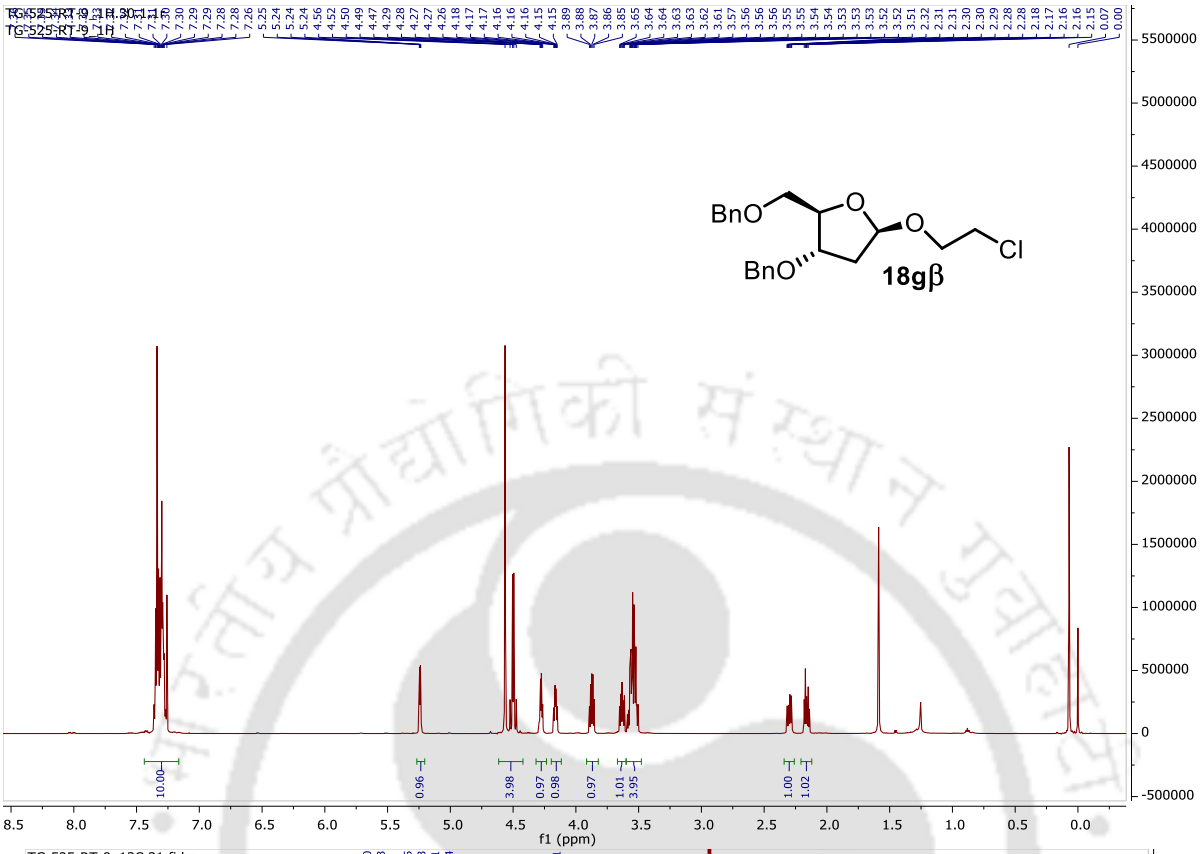
COSY NMR of 2-cyanoethyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18fβ):

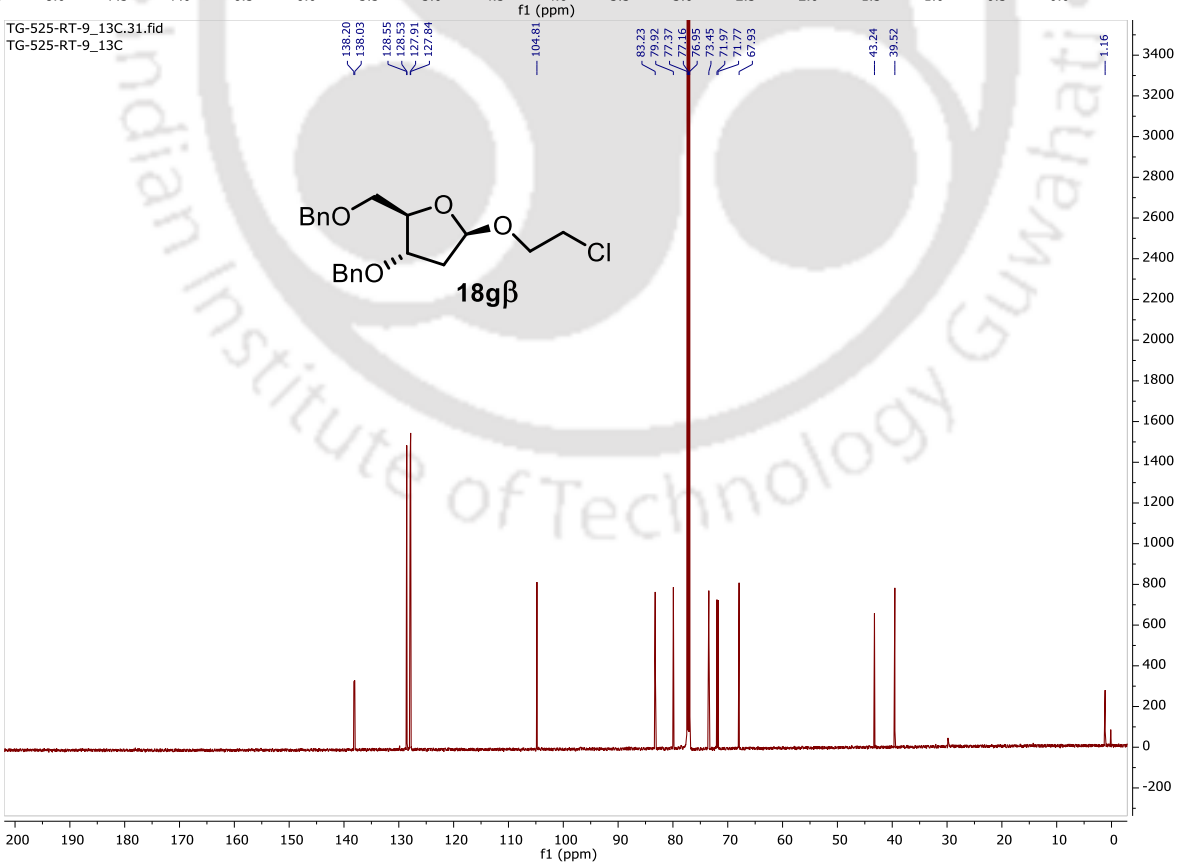




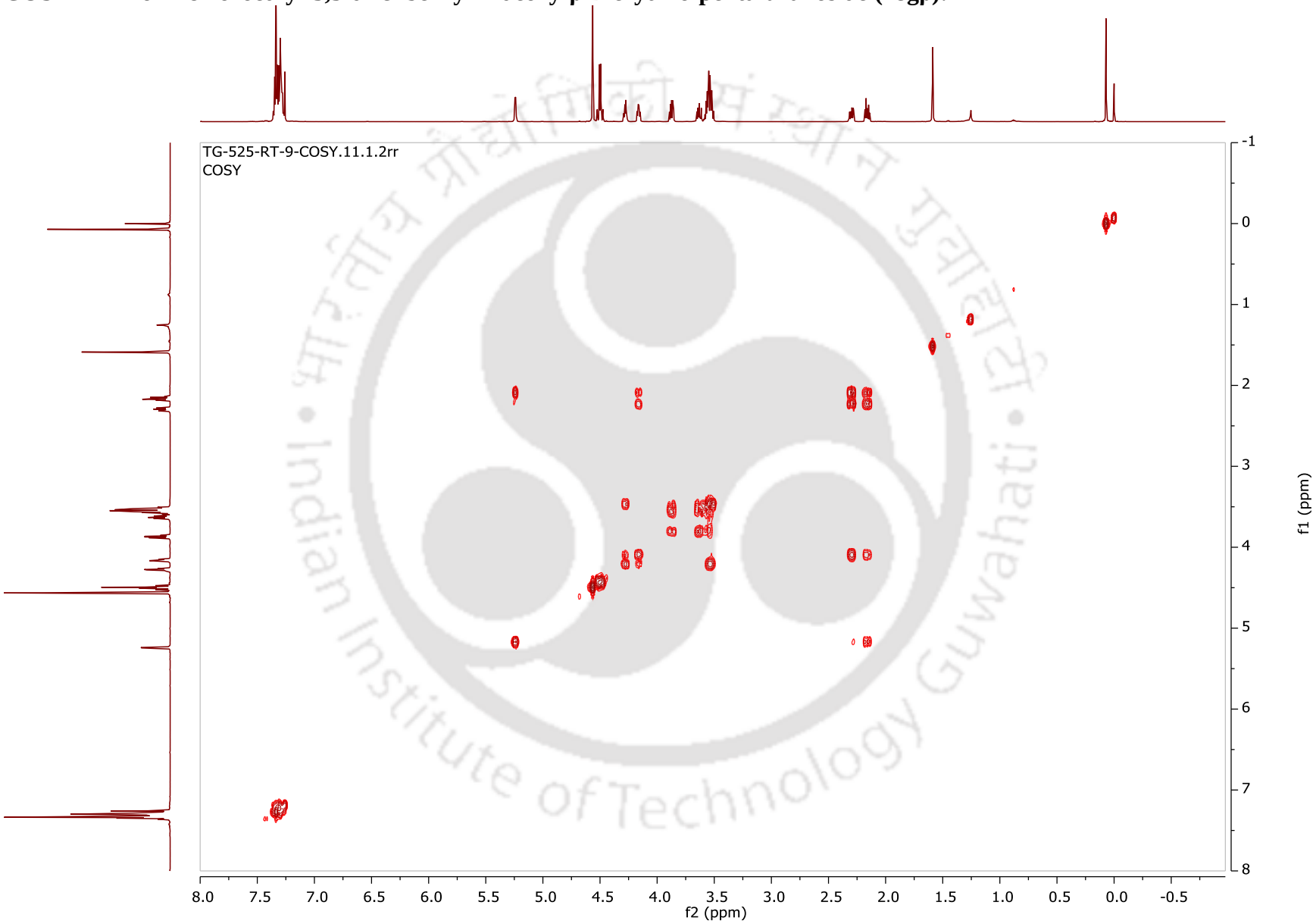
COSY NMR of 2-chloroethyl-3,5-di-*O*-benzyl-2-deoxy-α-D-erythro-pentafuranoside (18gα):

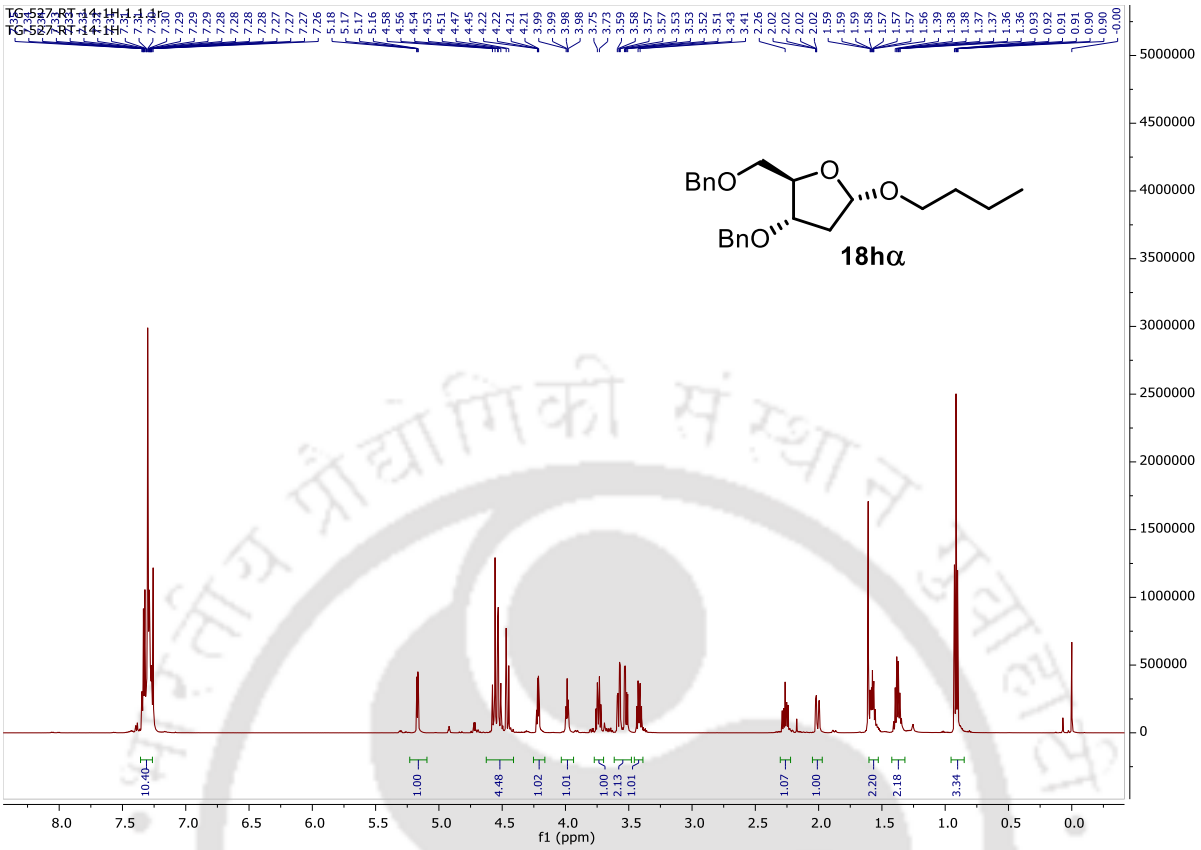


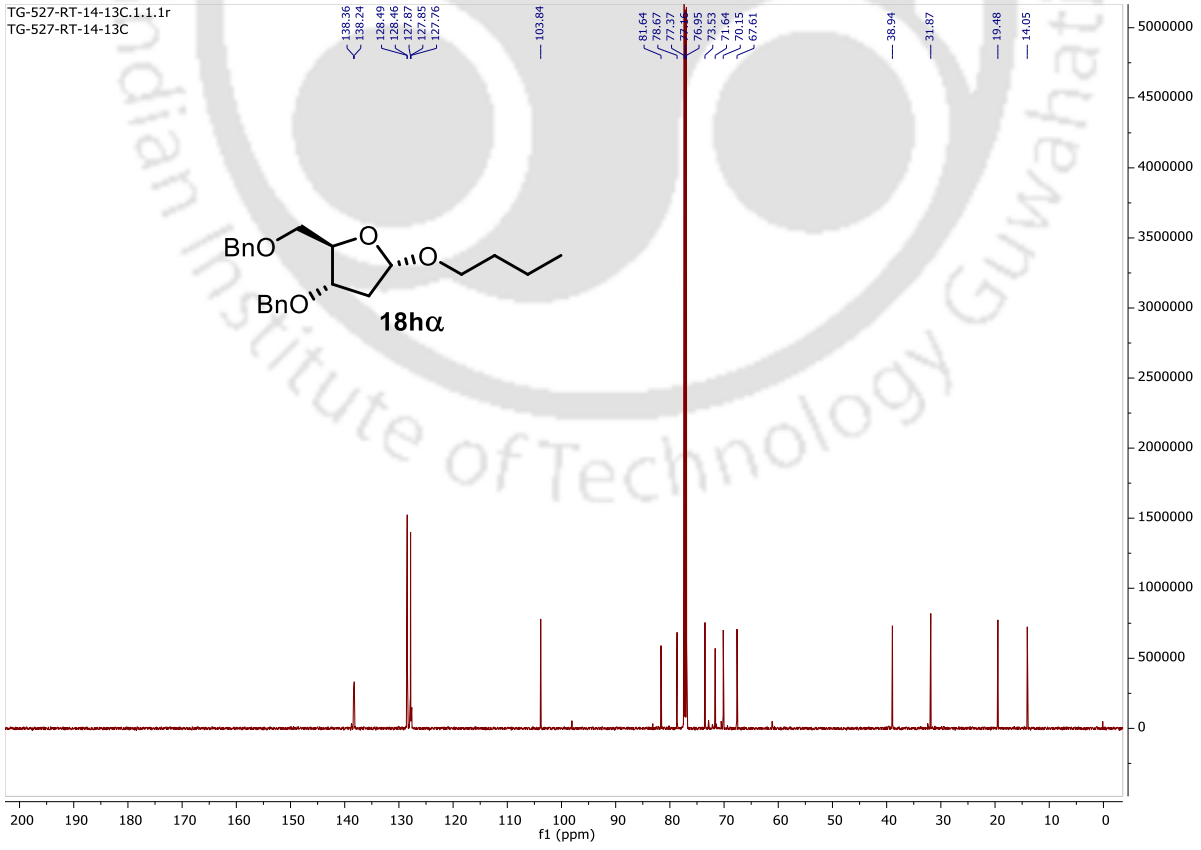




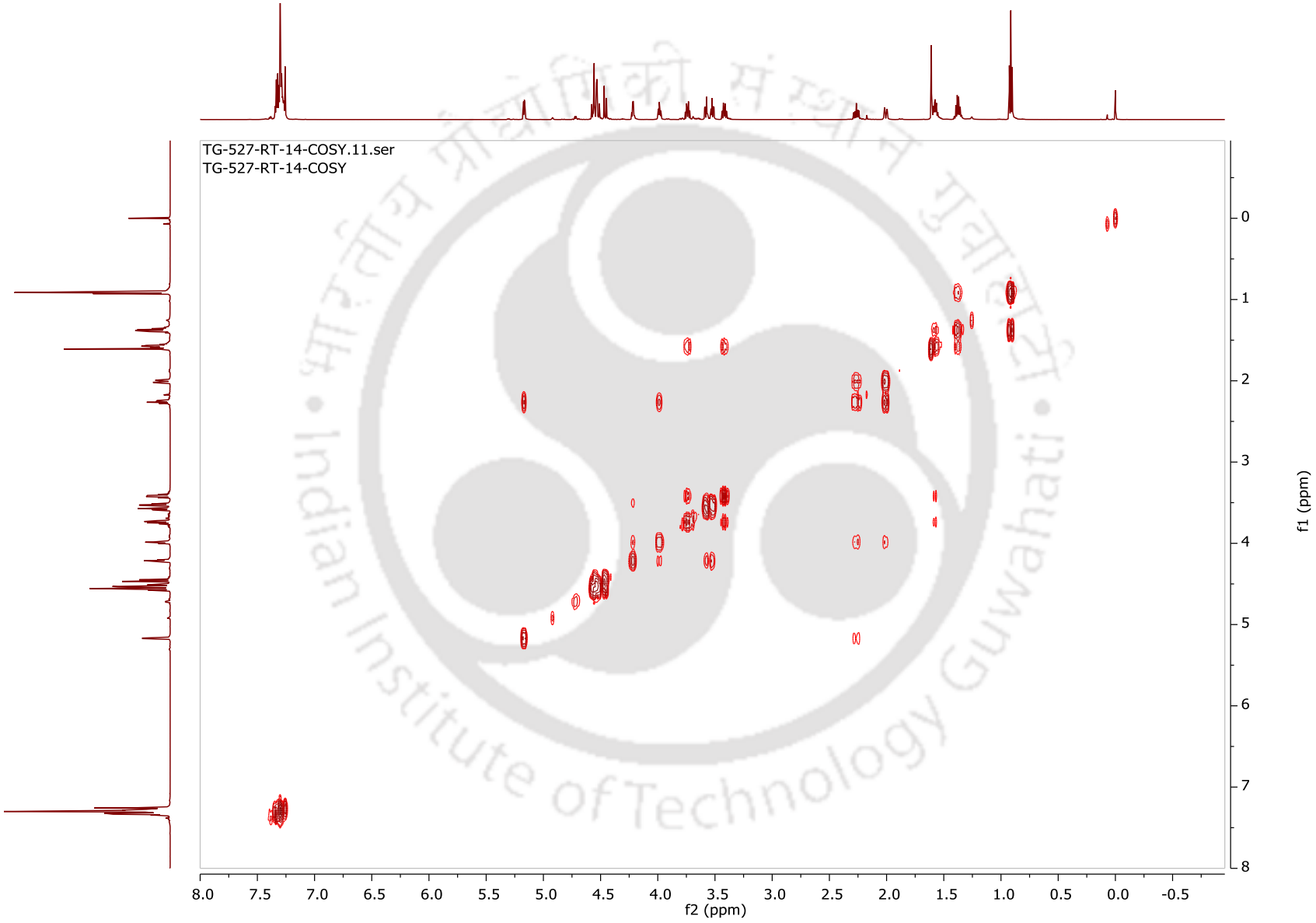
COSY NMR of 2-chloroethyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18gβ):

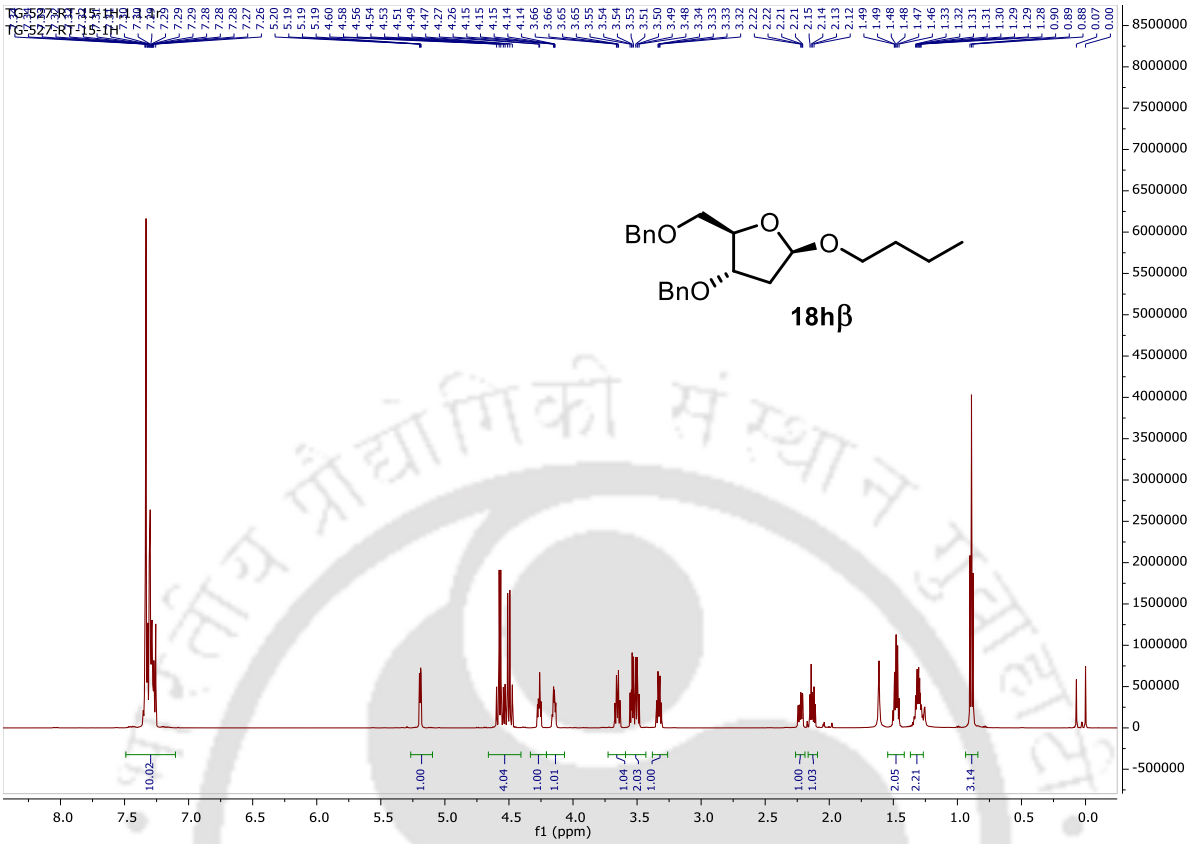


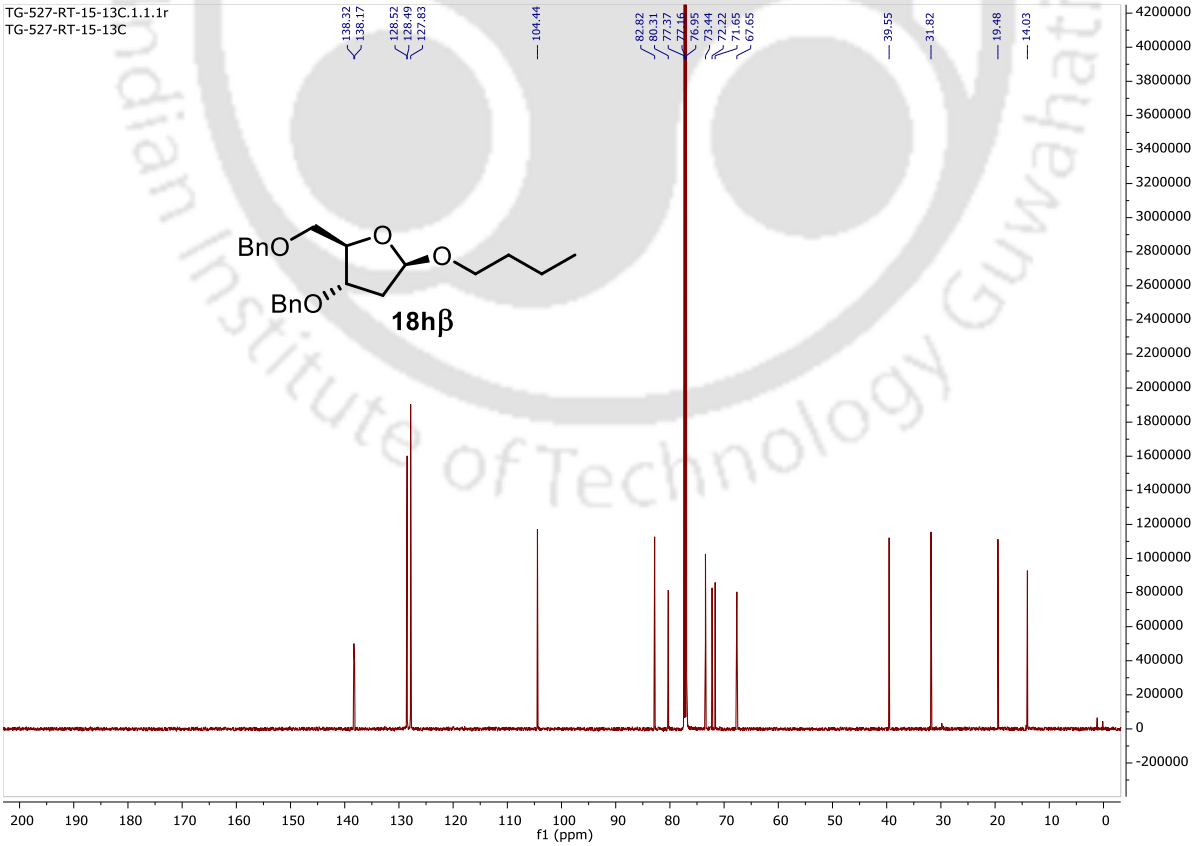




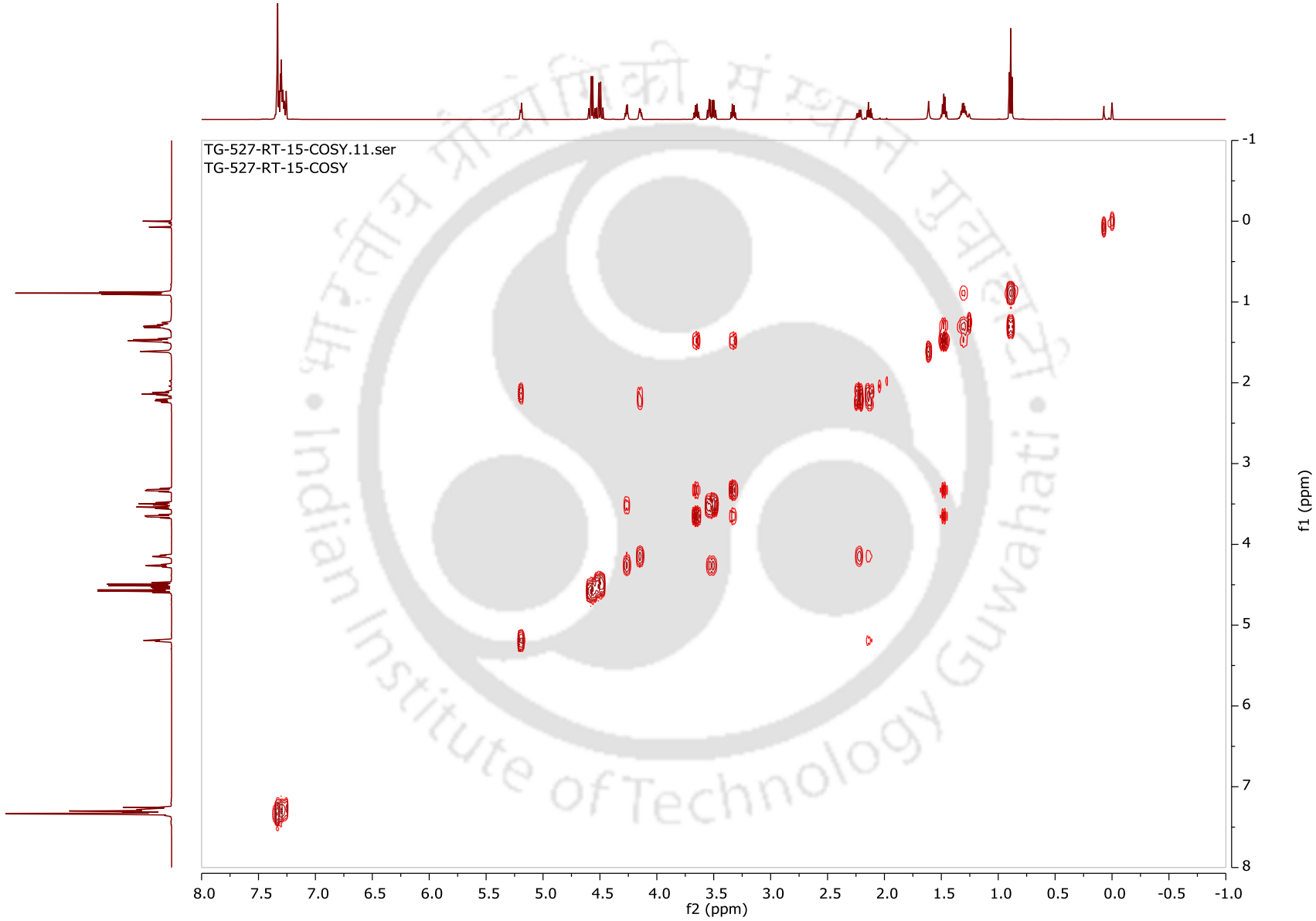
COSY NMR of 1-butyl-3,5-di-*O*-benzyl-2-deoxy-α-D-erythro-pentafuranoside (18hα):

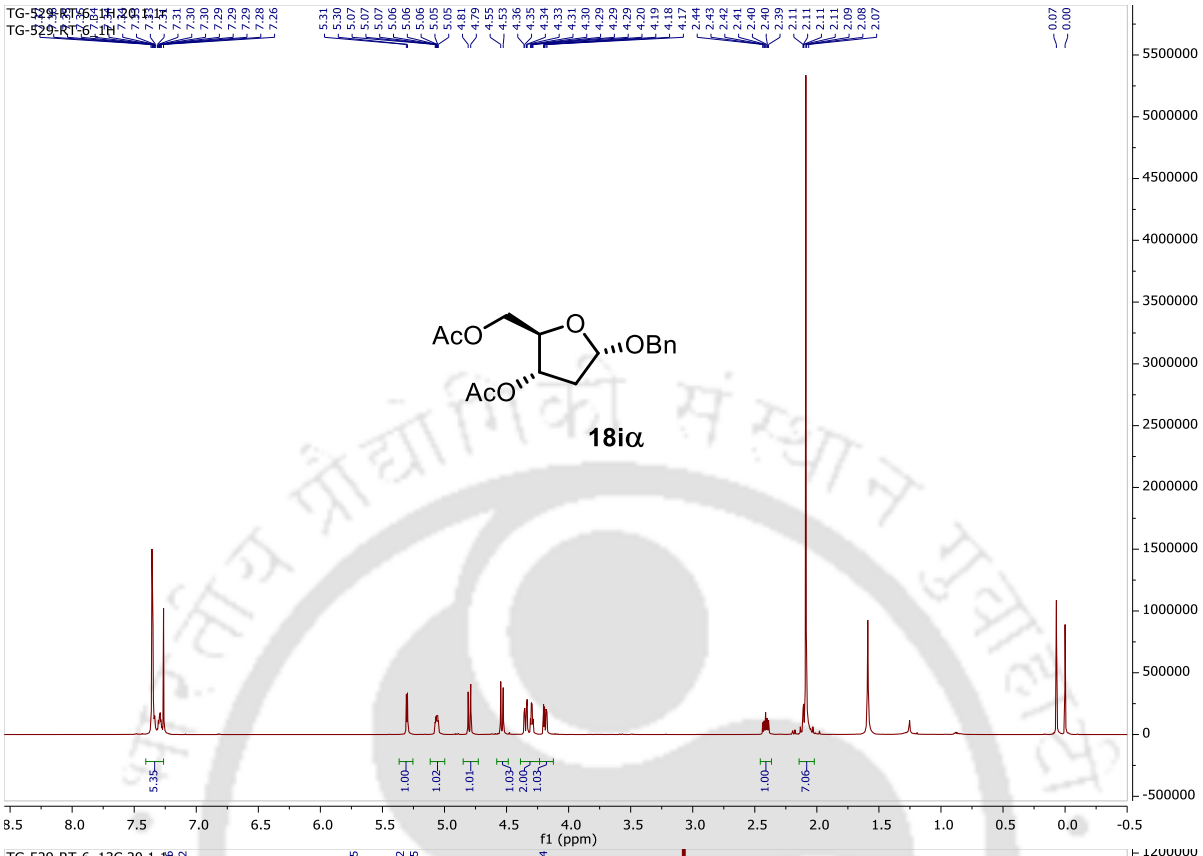


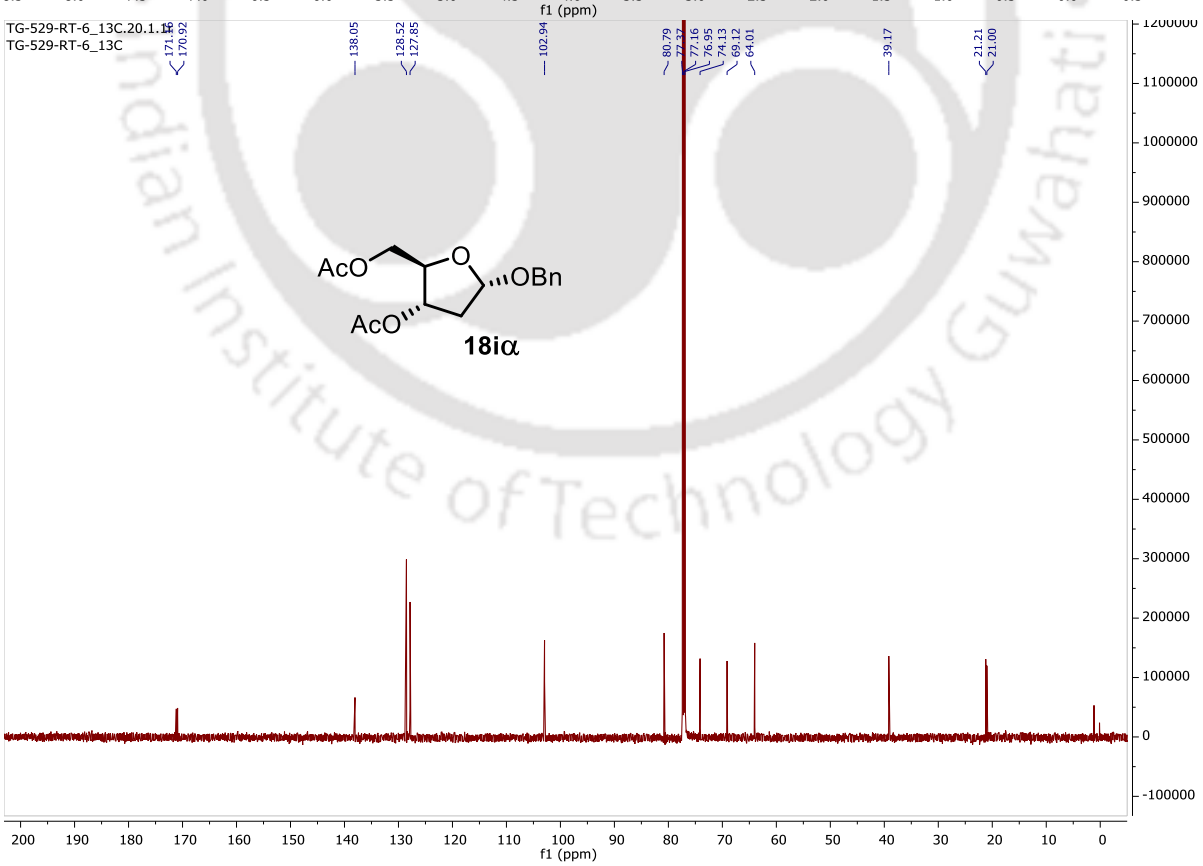




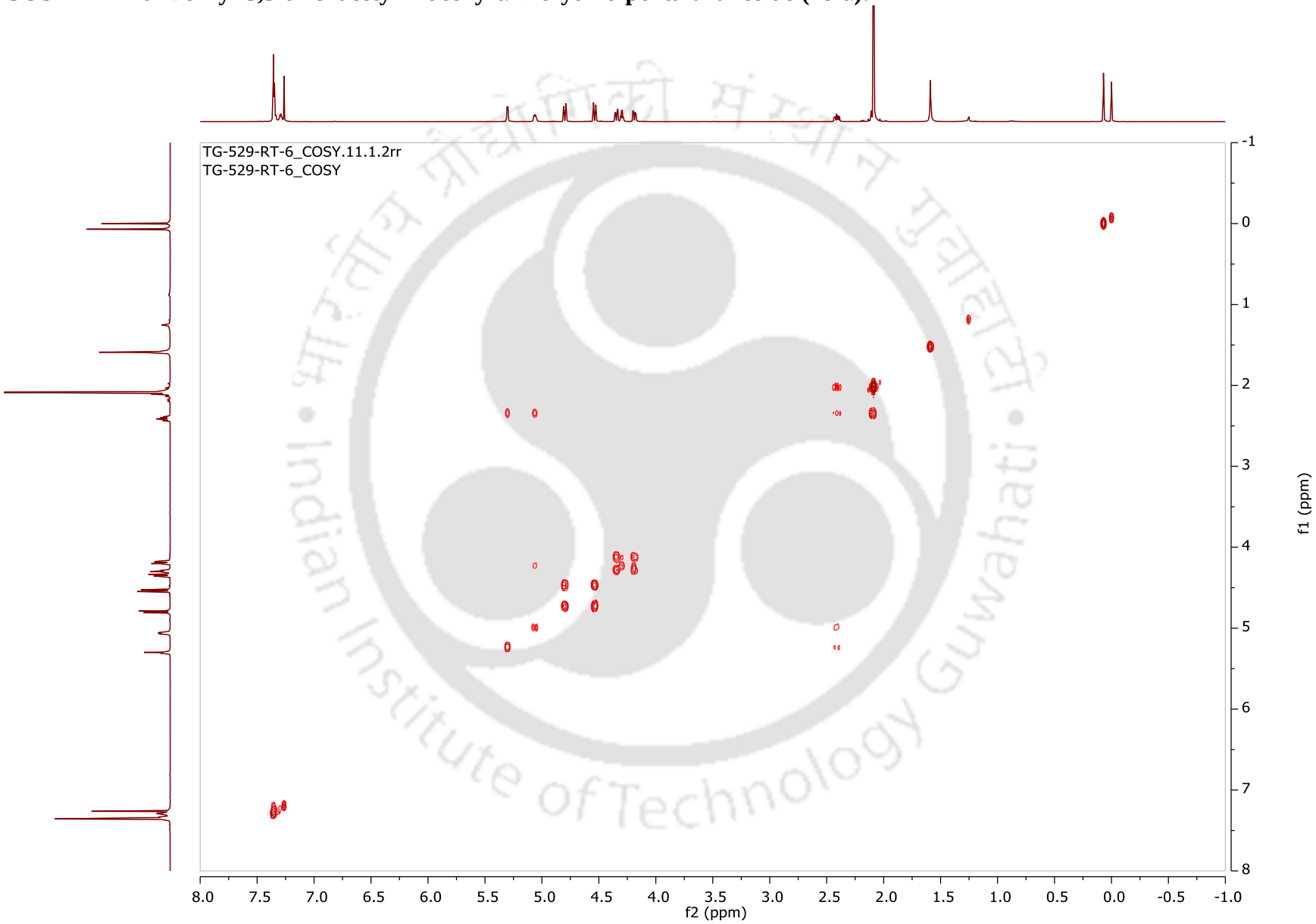
COSY NMR of 1-butyl-3,5-di-*O*-benzyl-2-deoxy-β-D-erythro-pentafuranoside (18hβ):

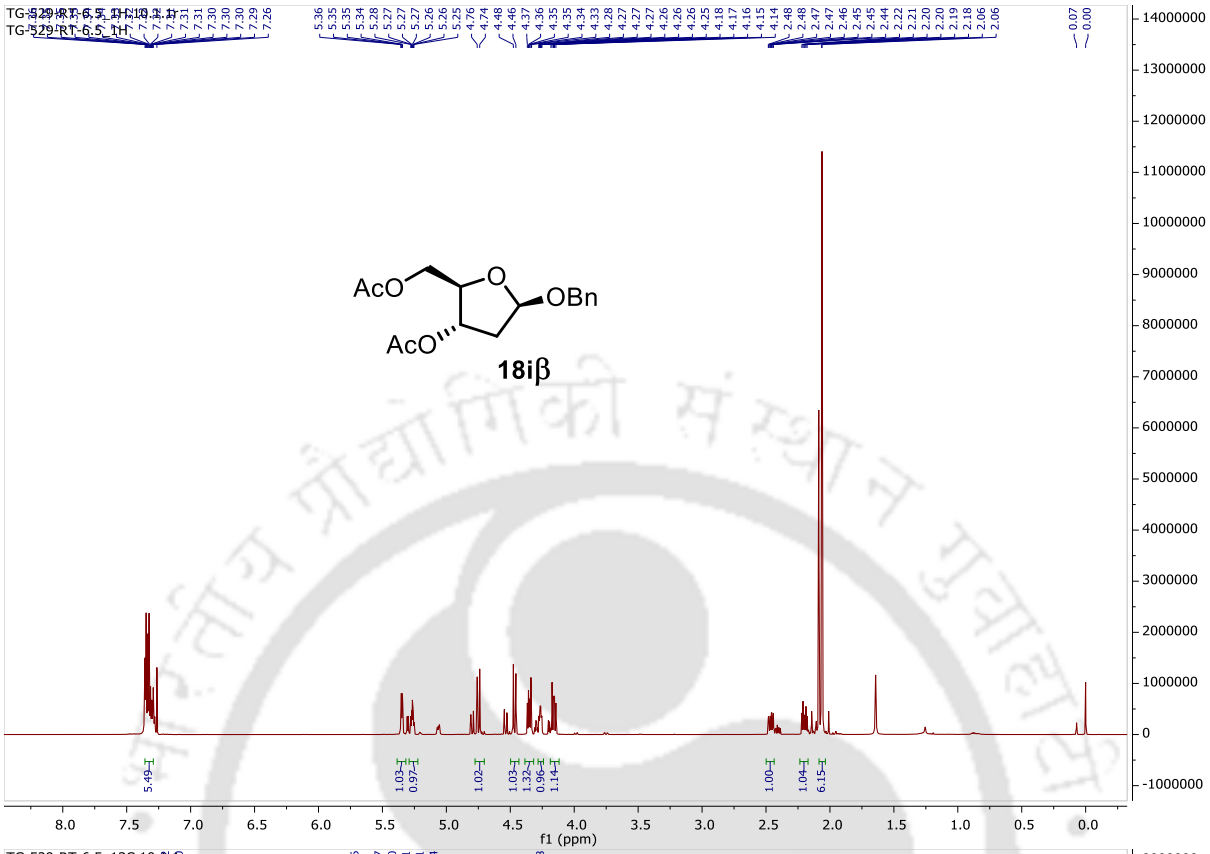


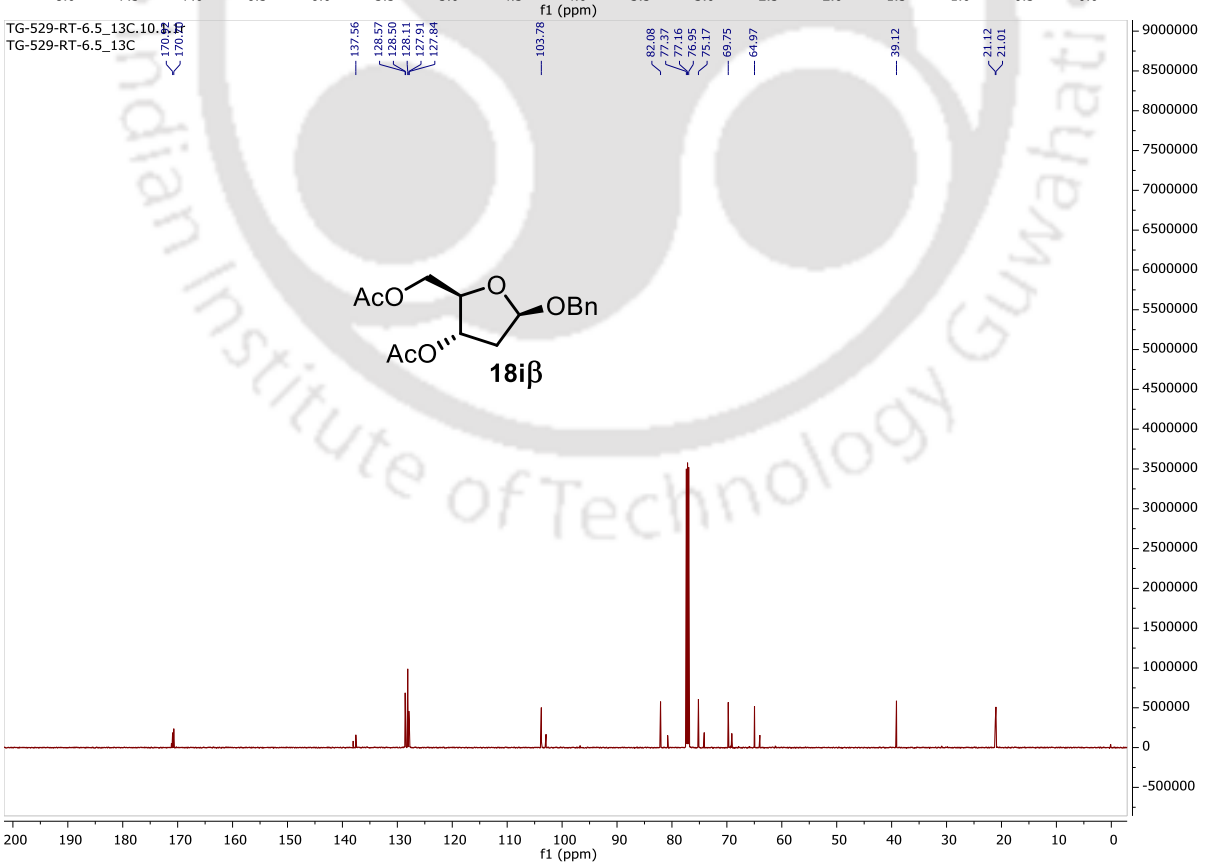




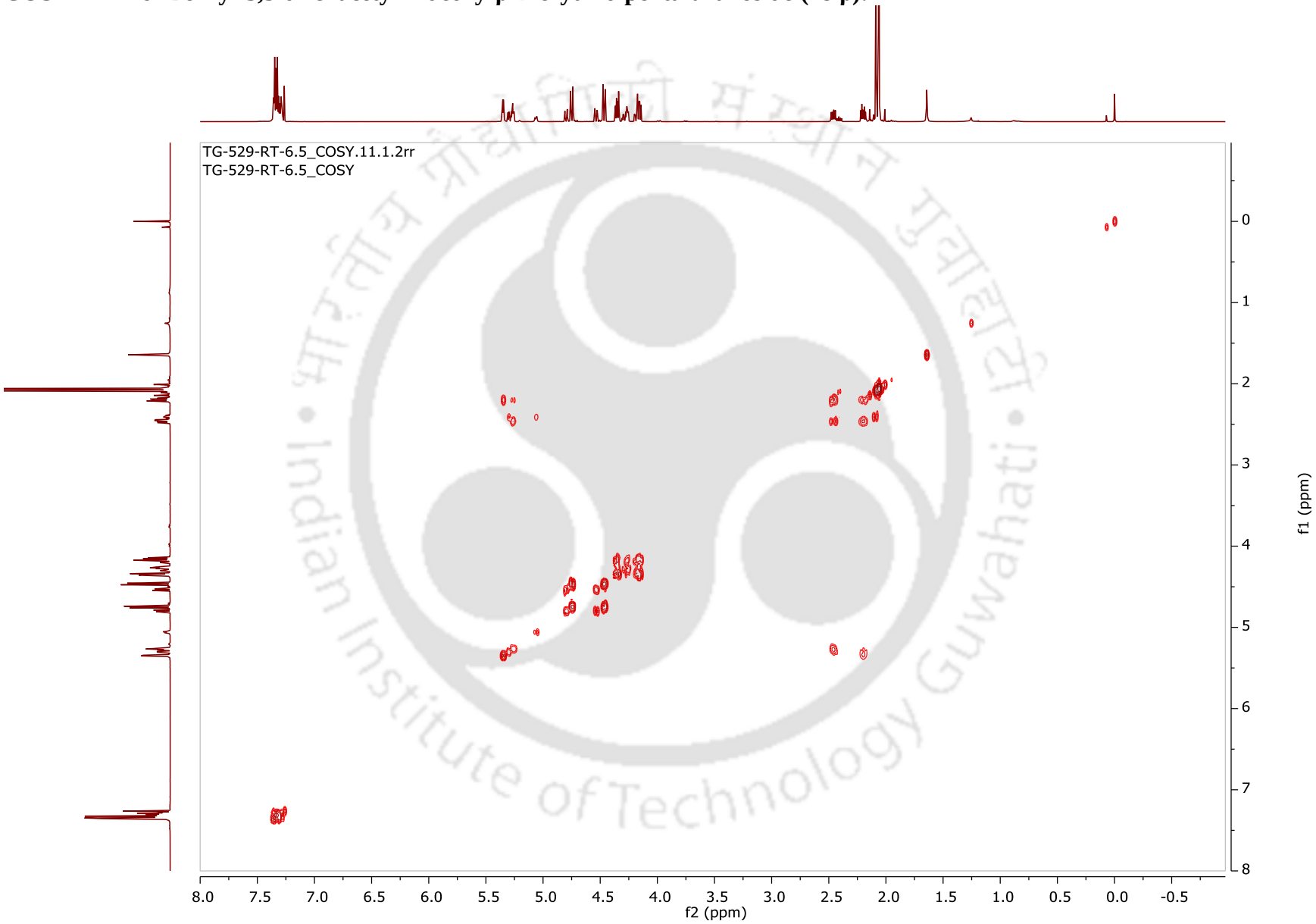
COSY NMR of Benzyl-3,5-di-*O*-acetyl-2-deoxy-α-D-erythro-pentafuranoside (18iα):

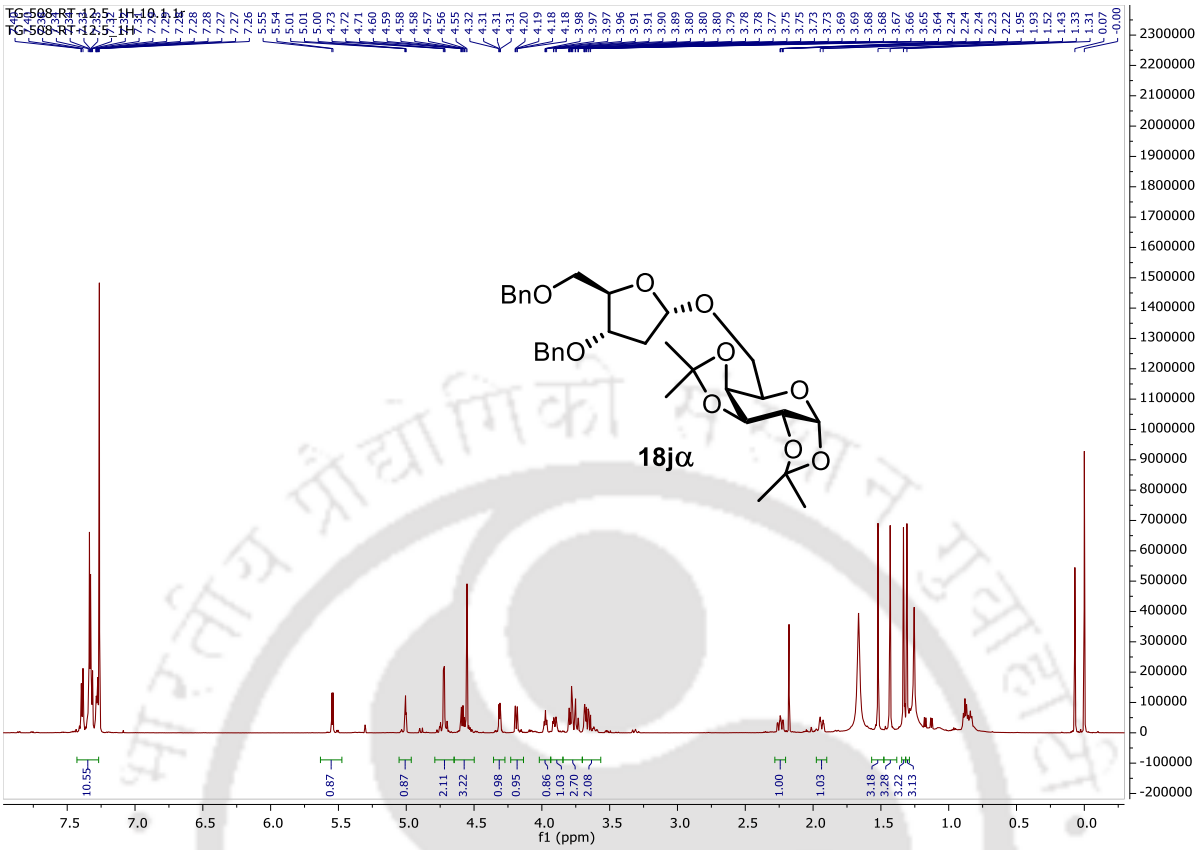


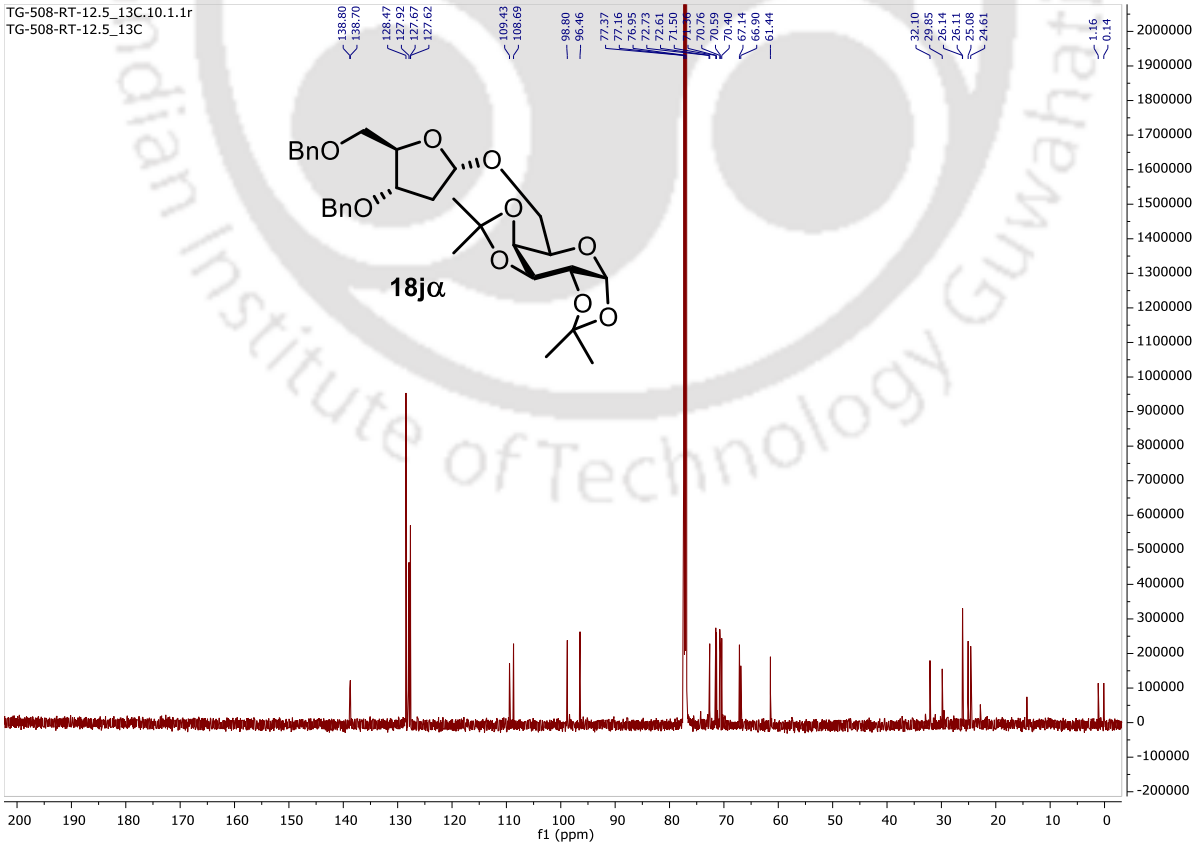




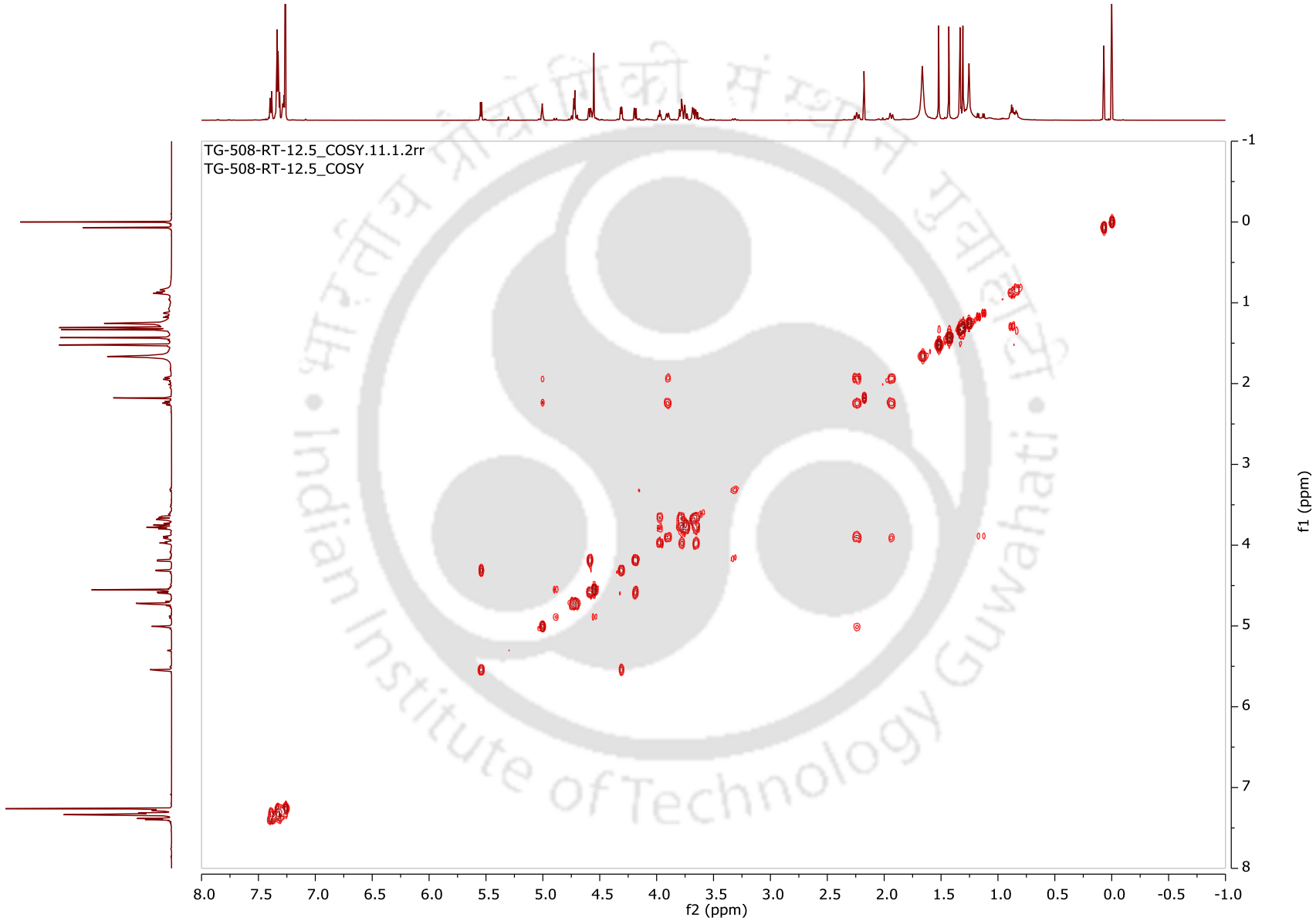
COSY NMR of Benzyl-3,5-di-*O*-acetyl-2-deoxy-β-D-erythro-pentafuranoside (18iβ):

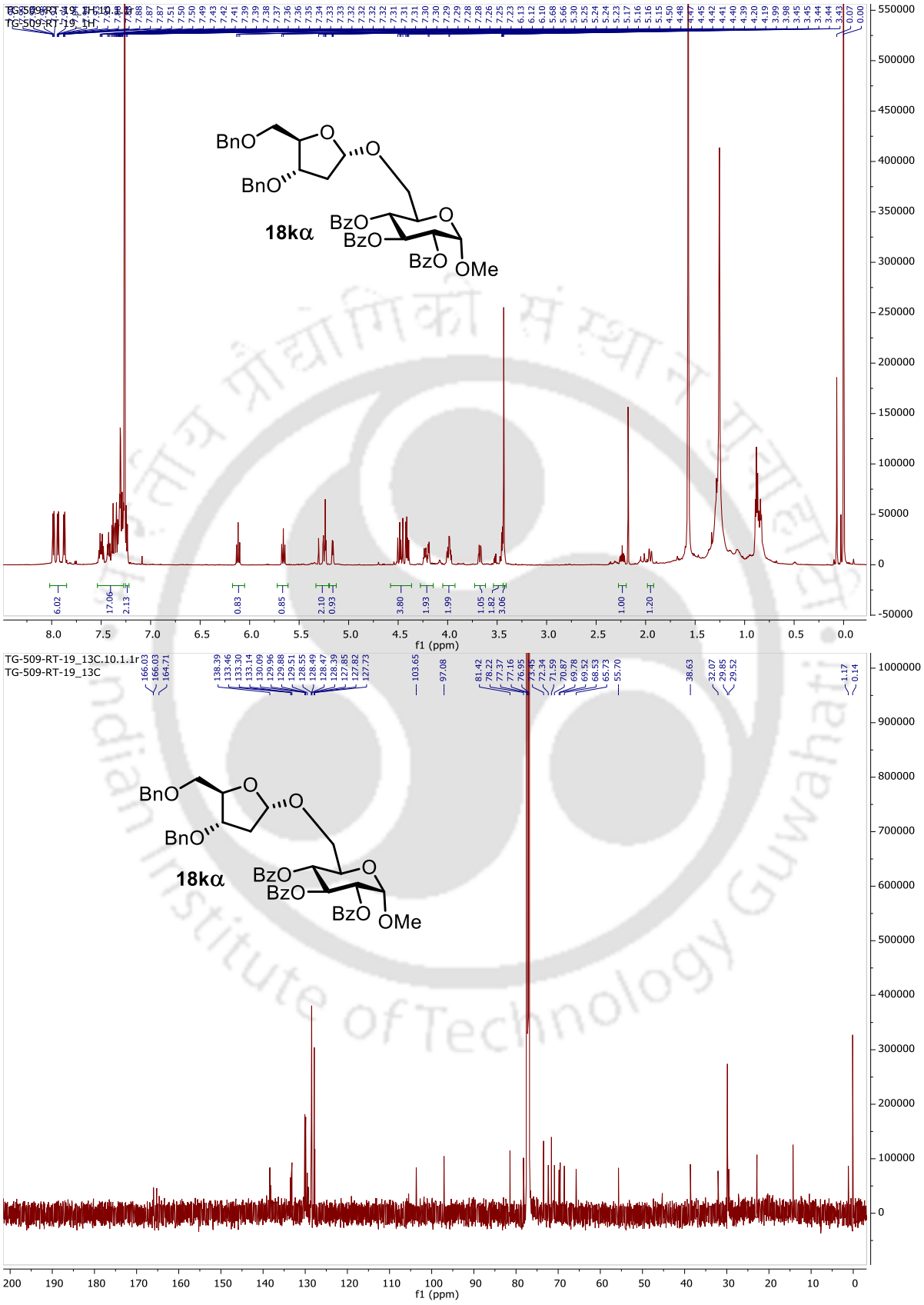




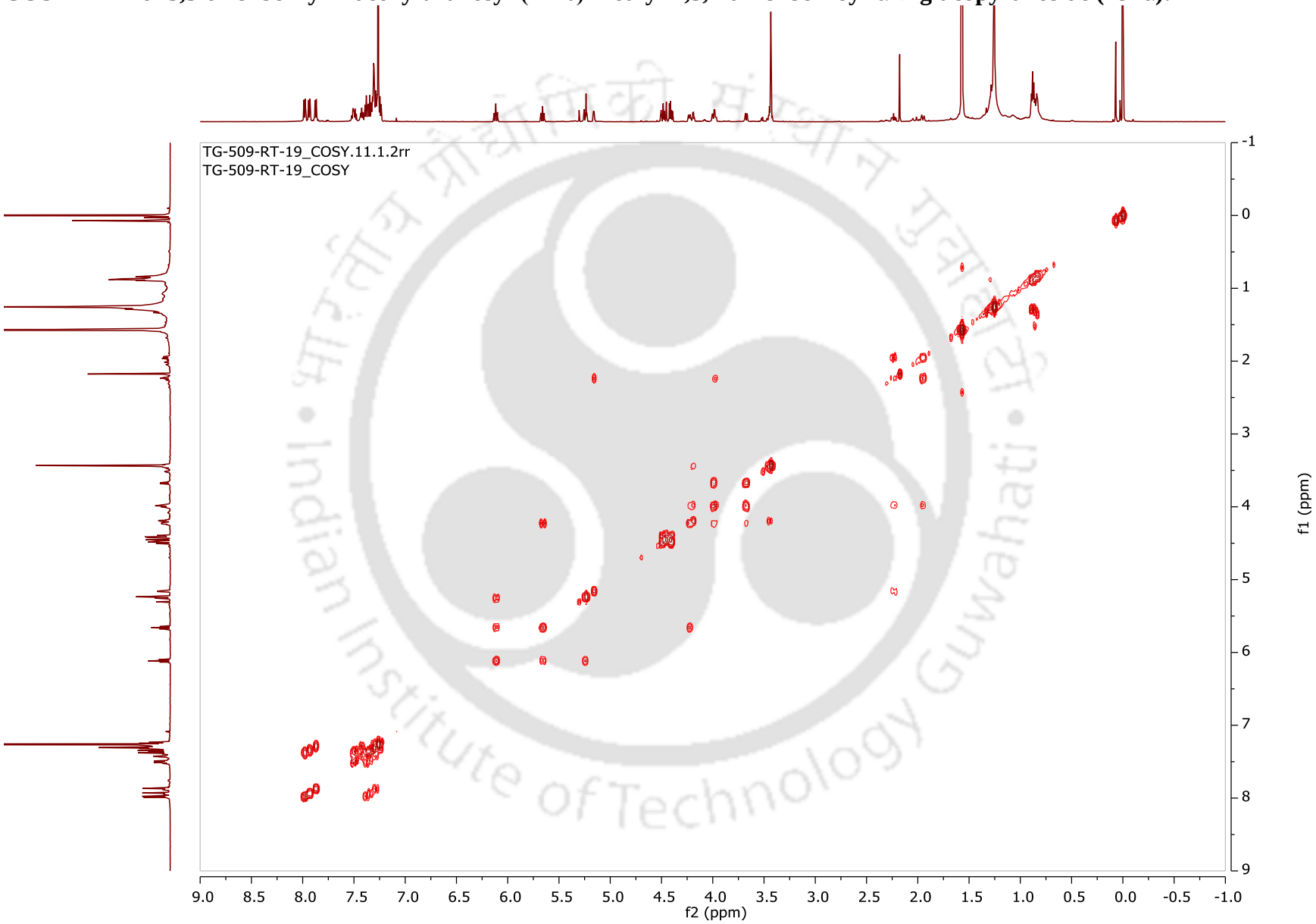


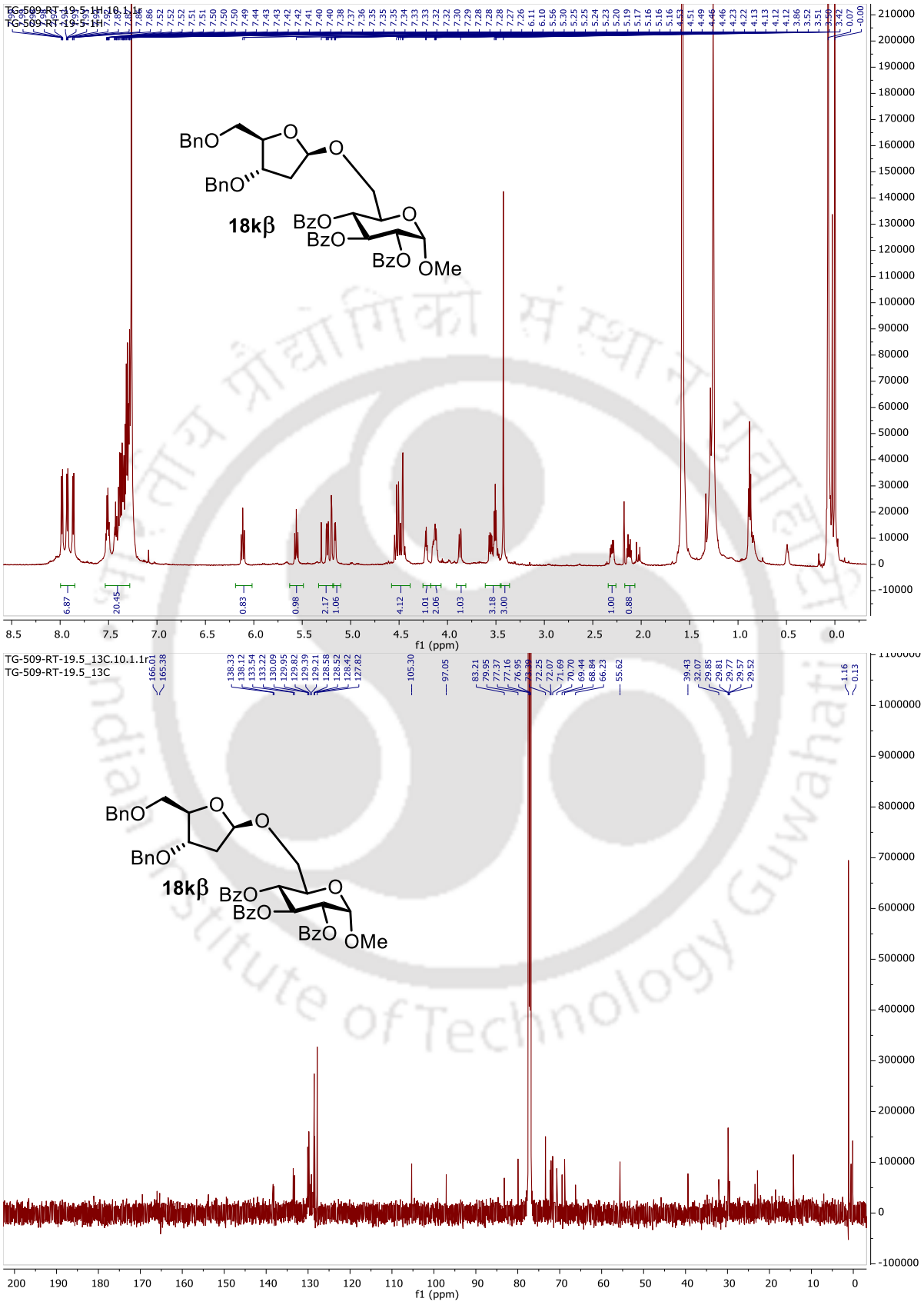
COSY NMR of 3,5-di-*O*-benzyl 2-deoxyfuranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (18jα):



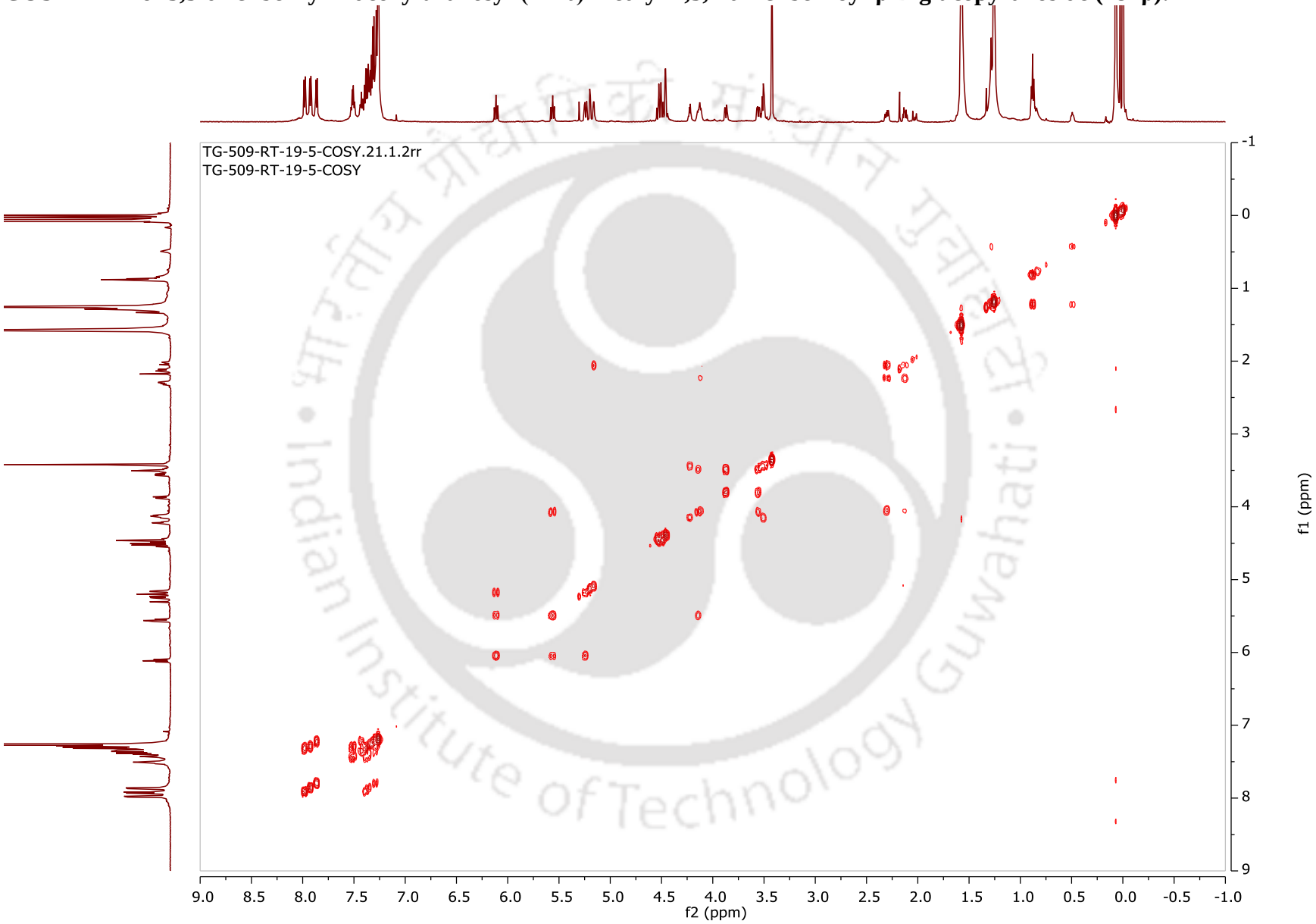


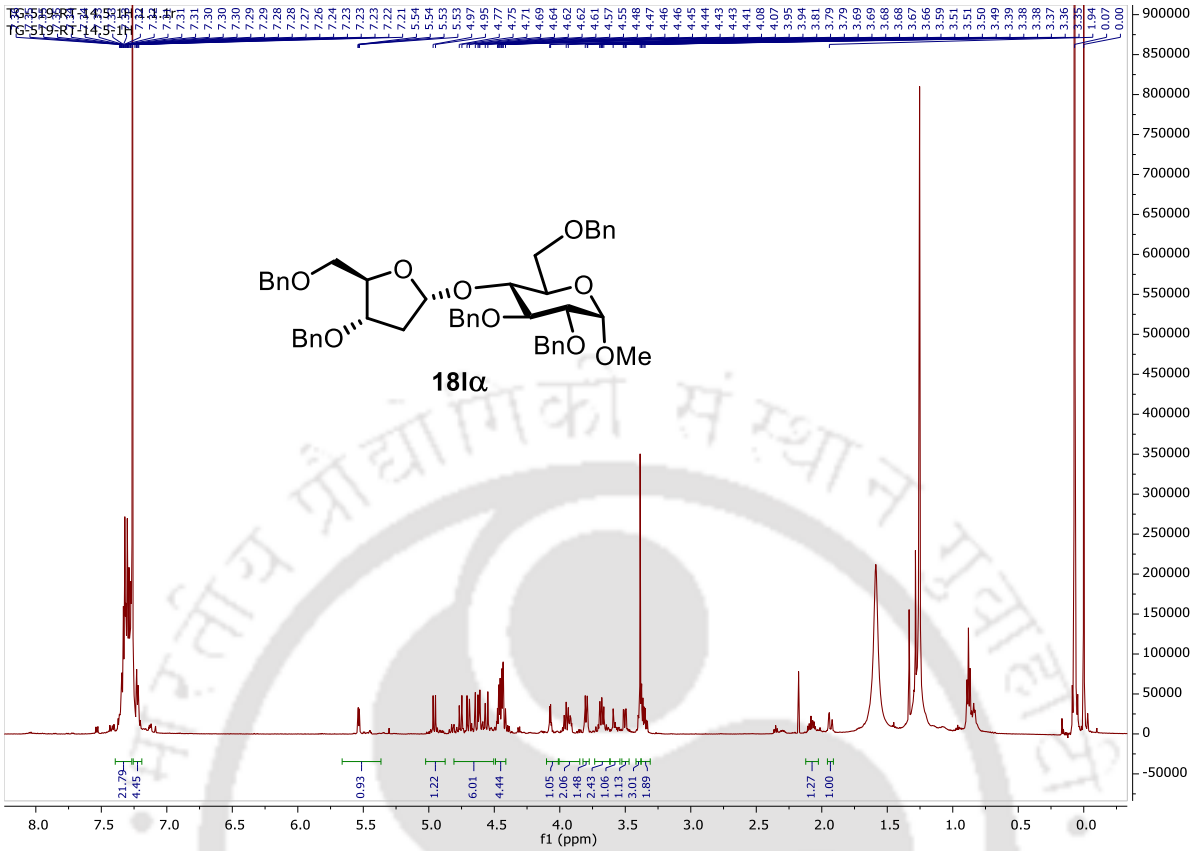
COSY NMR of 3,5-di-*O*-benzyl 2-deoxyfuranosyl-(1→6)-methyl-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (18kα):

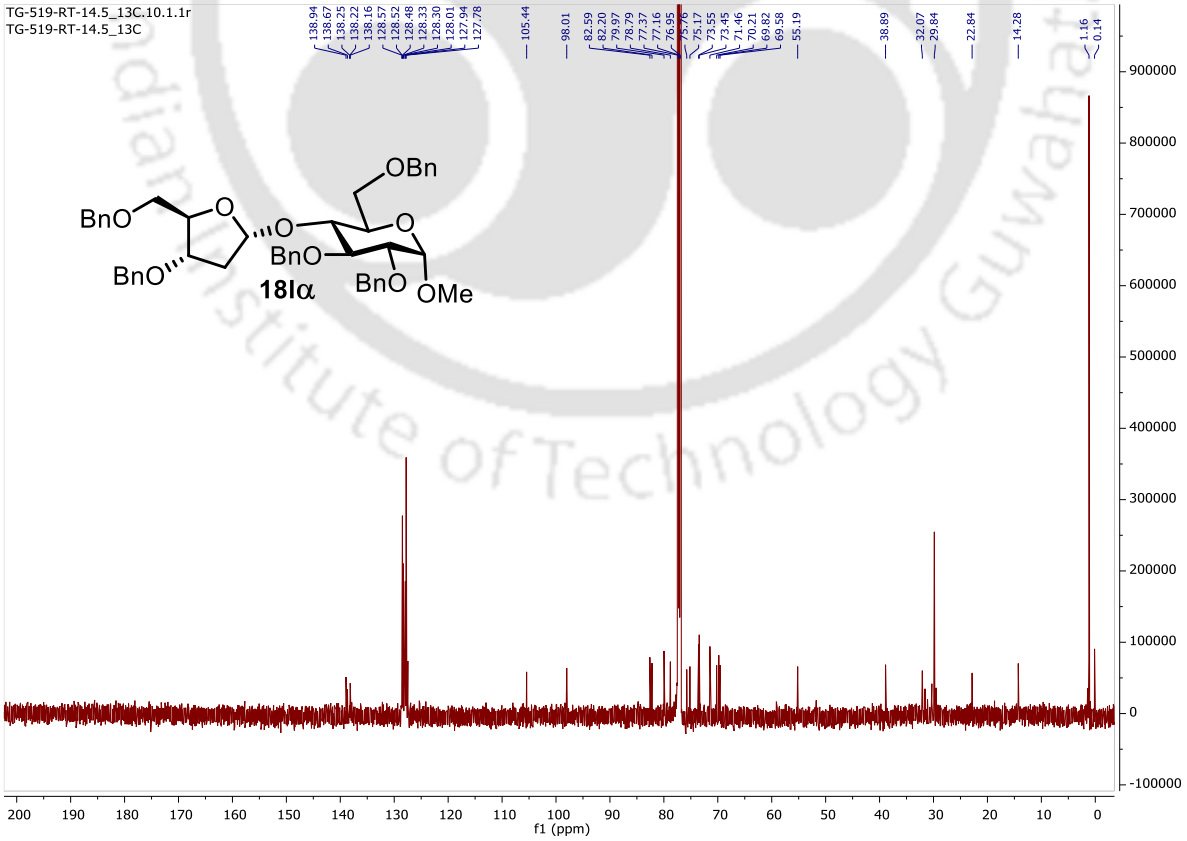


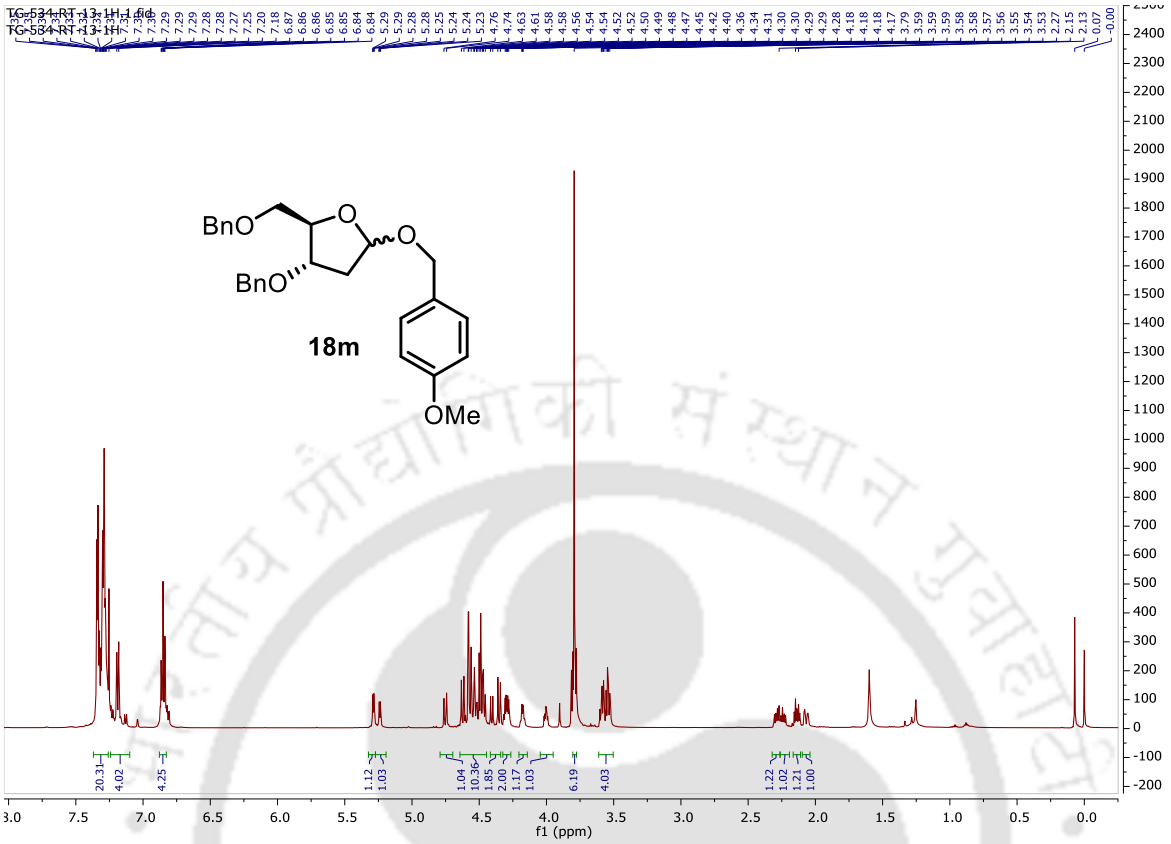


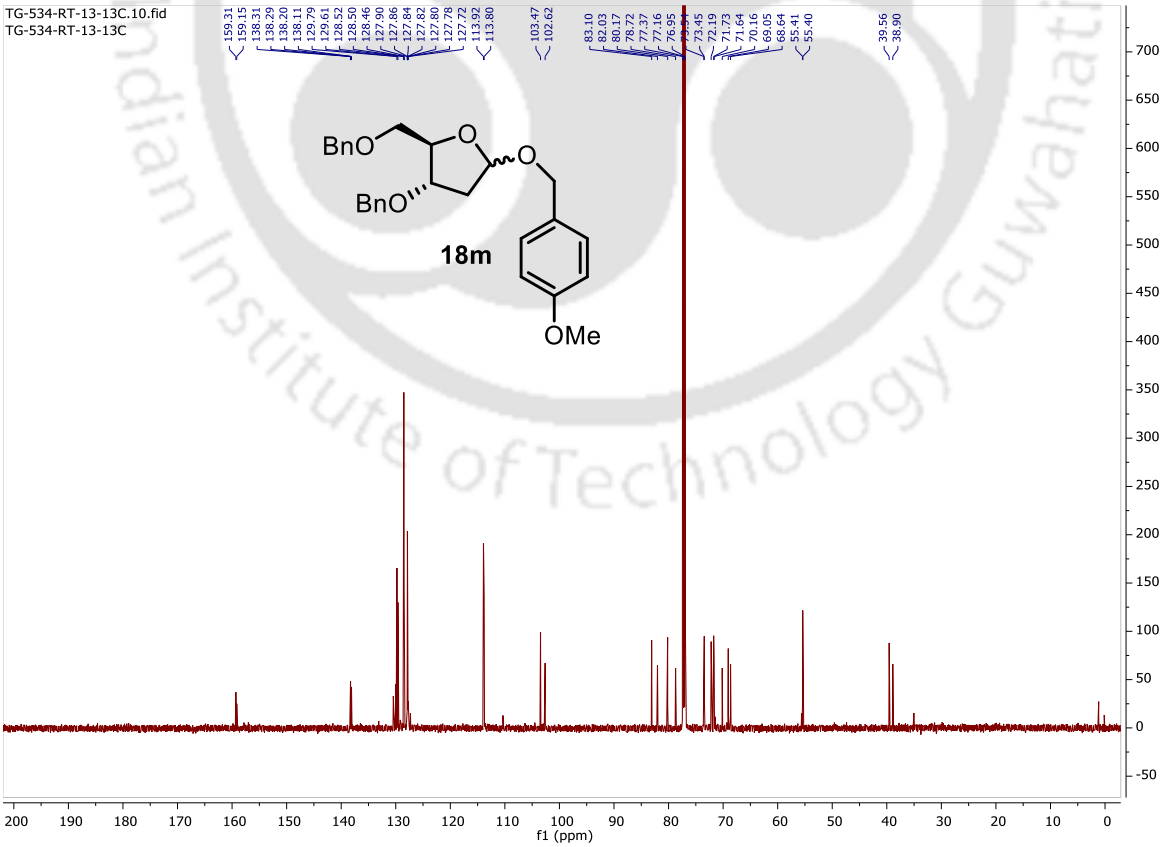
COSY NMR of 3,5-di-*O*-benzyl 2-deoxyfuranosyl-(1→6)-methyl-2,3,4-tri-*O*-benzoyl-β-D-glucopyranoside (18kβ):

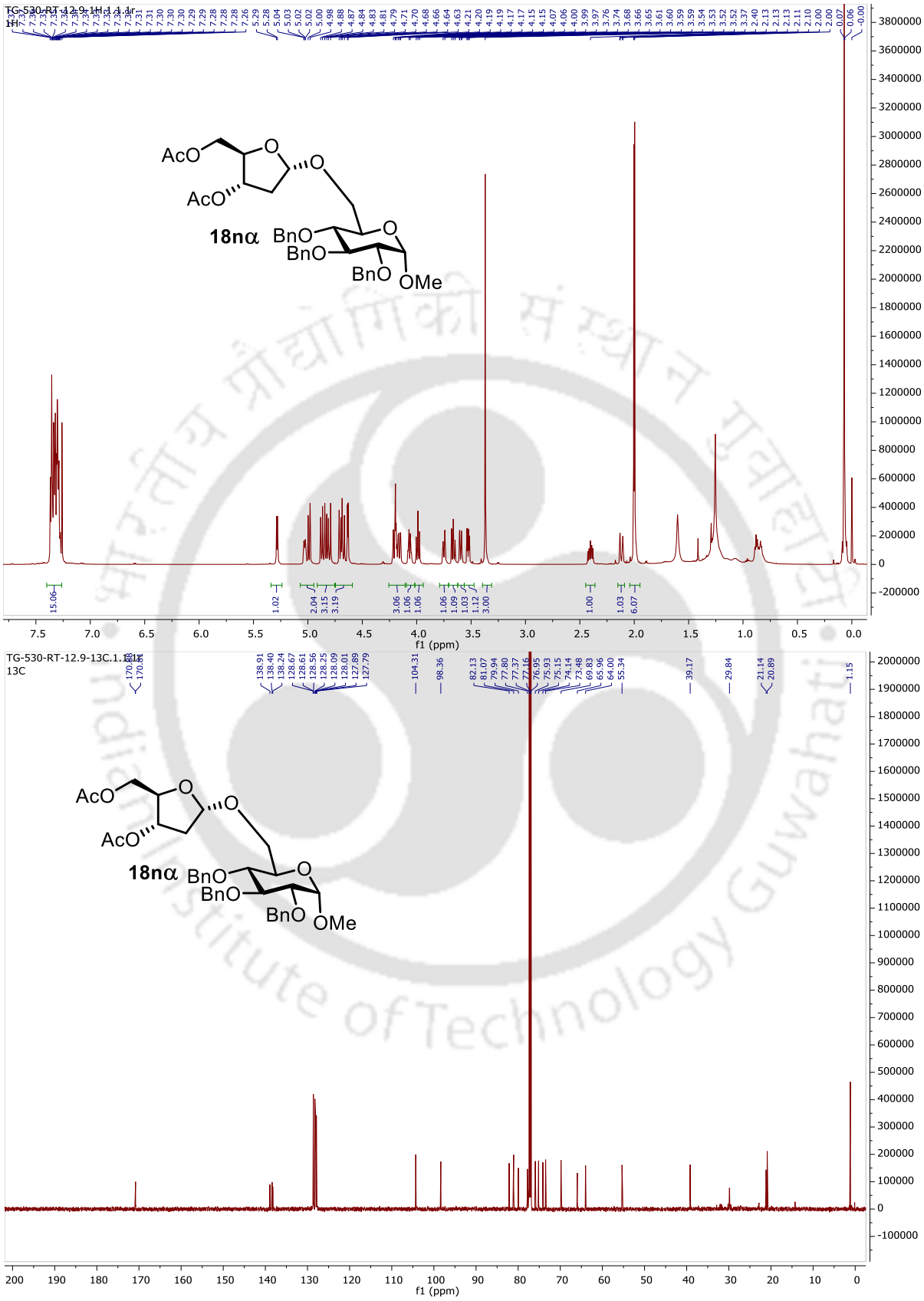




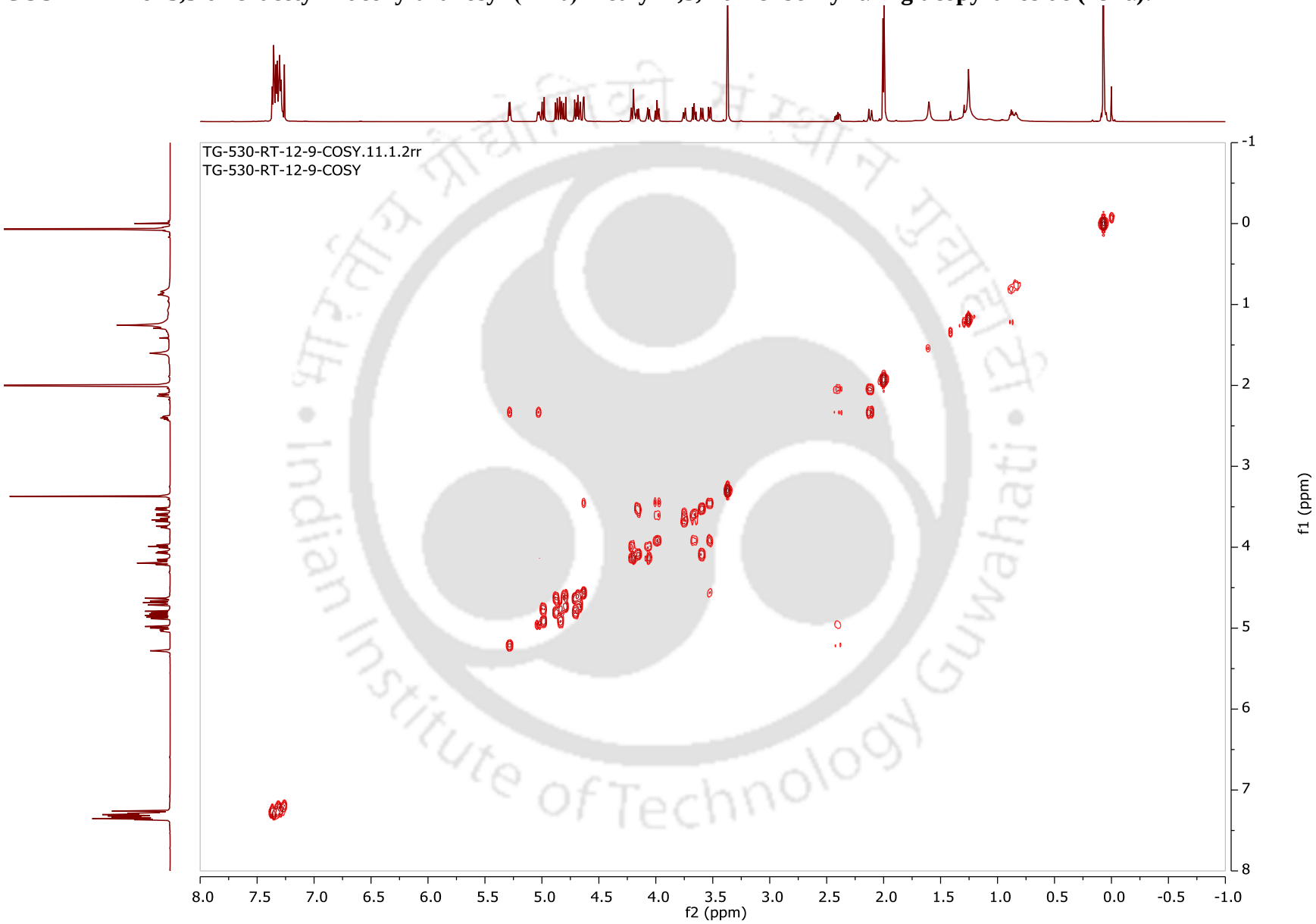


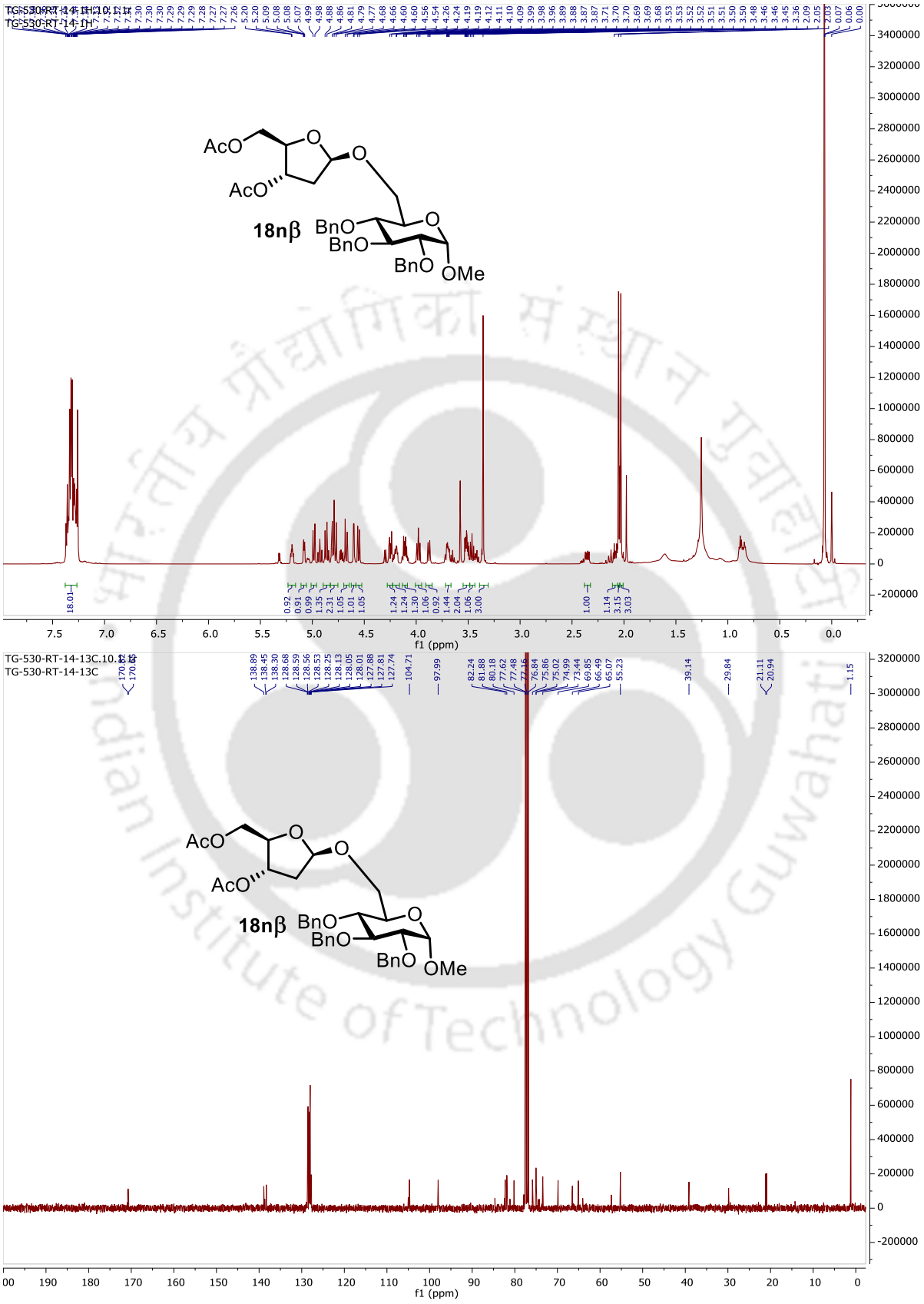




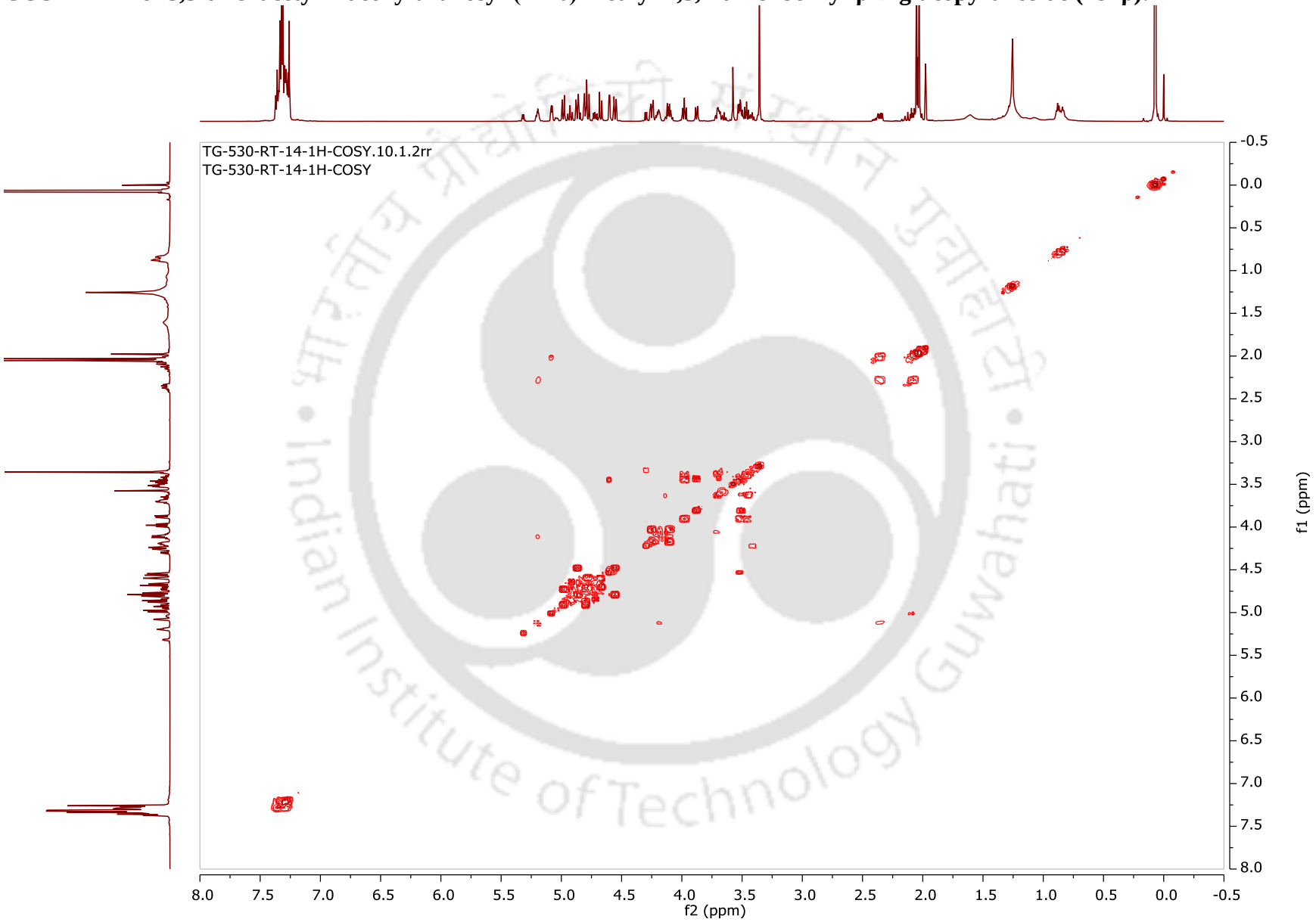


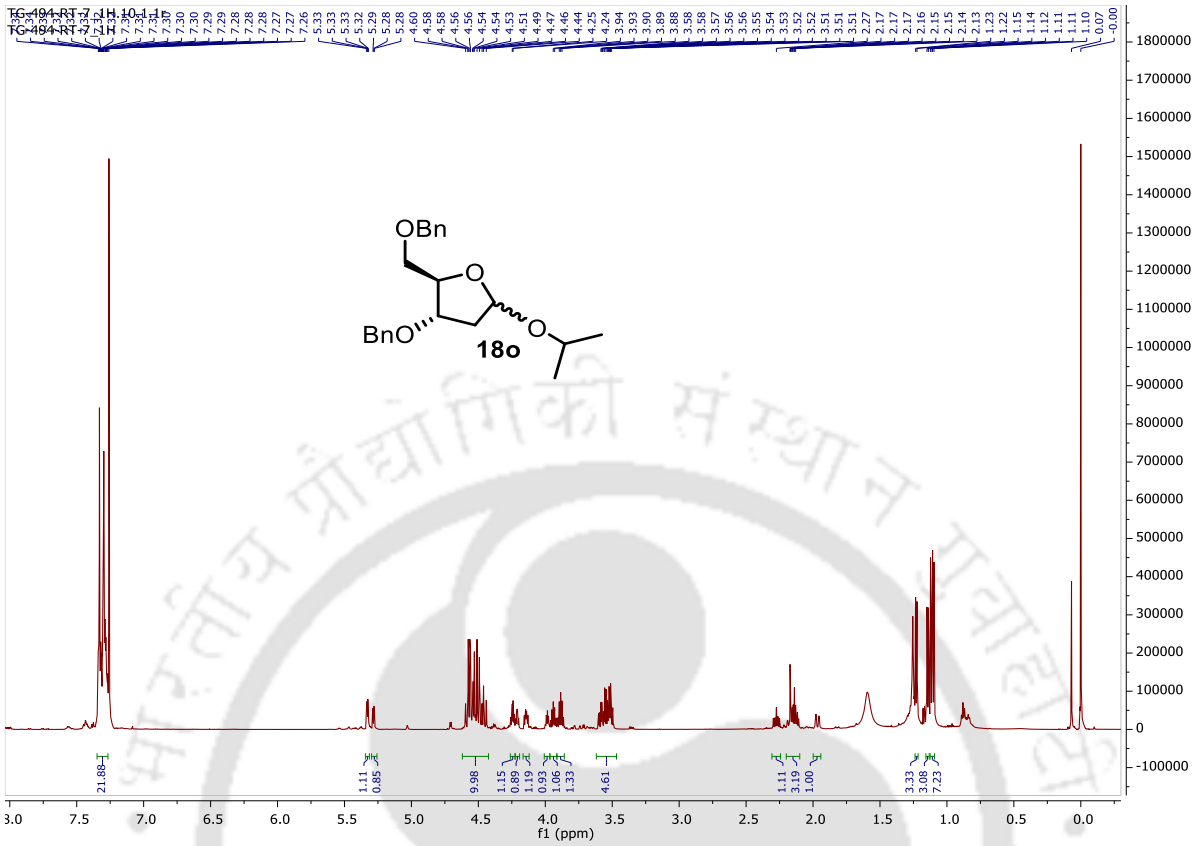
COSY NMR of 3,5-di-*O*-acetyl 2-deoxyfuranosyl-(1→6)-methyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (18nα):

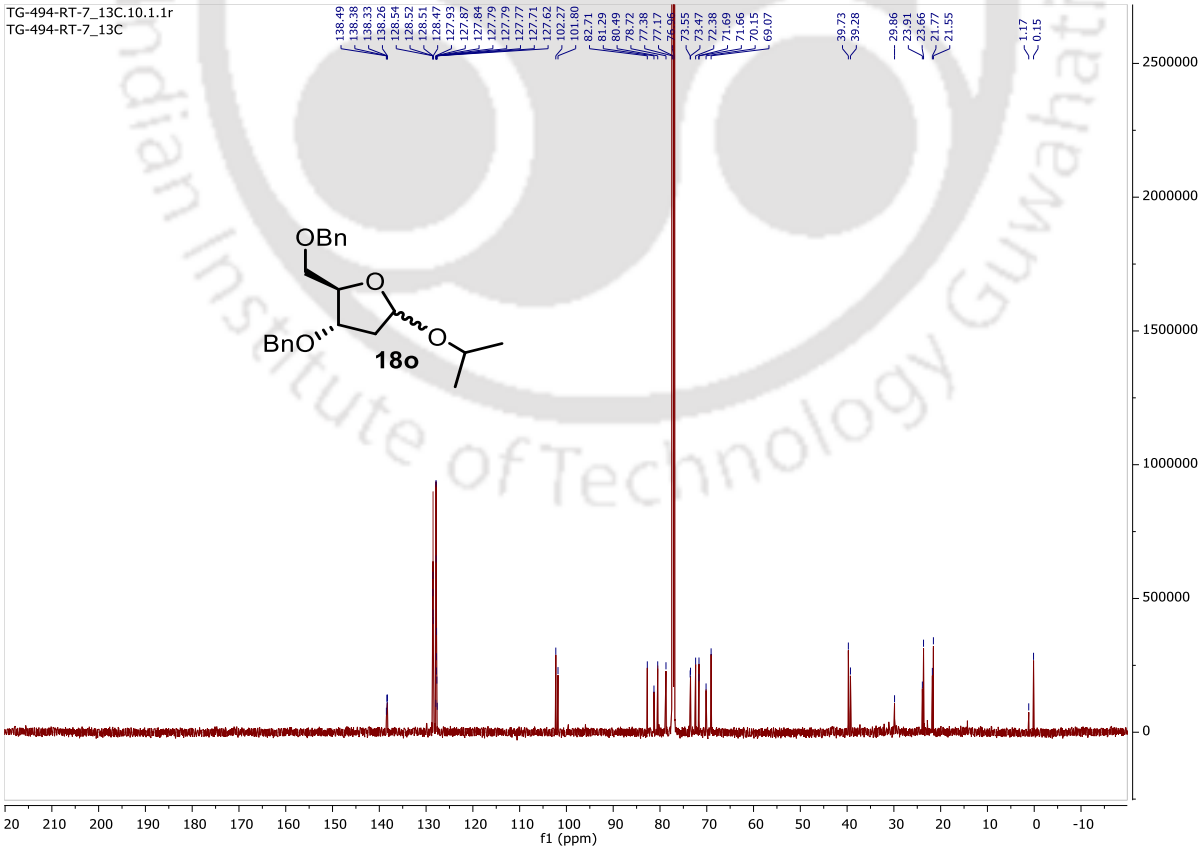




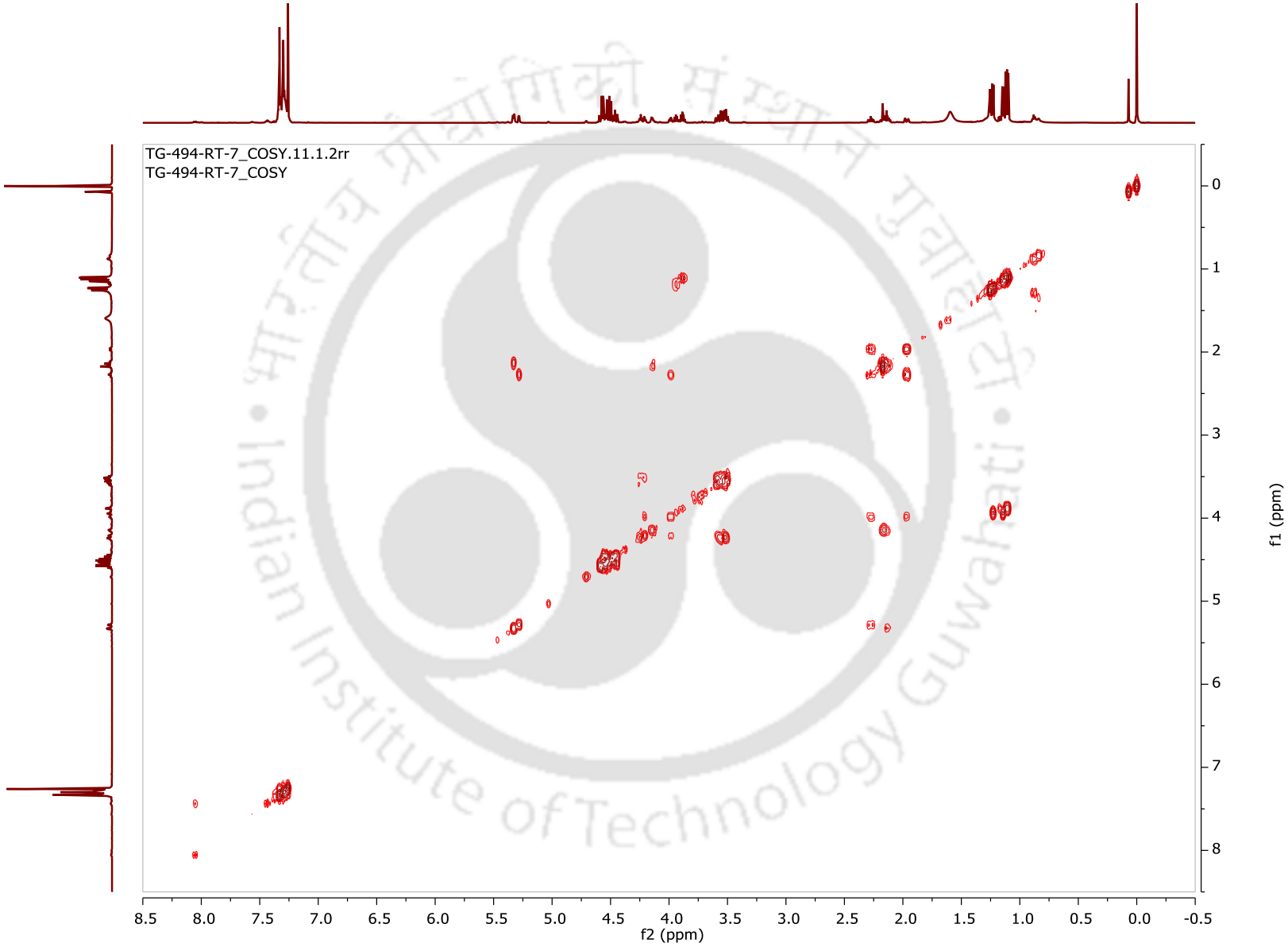
COSY NMR of 3,5-di-*O*-acetyl 2-deoxyfuranosyl-(1→6)-methyl-2,3,4-tri-*O*-benzyl-β-D-glucopyranoside (18nβ):

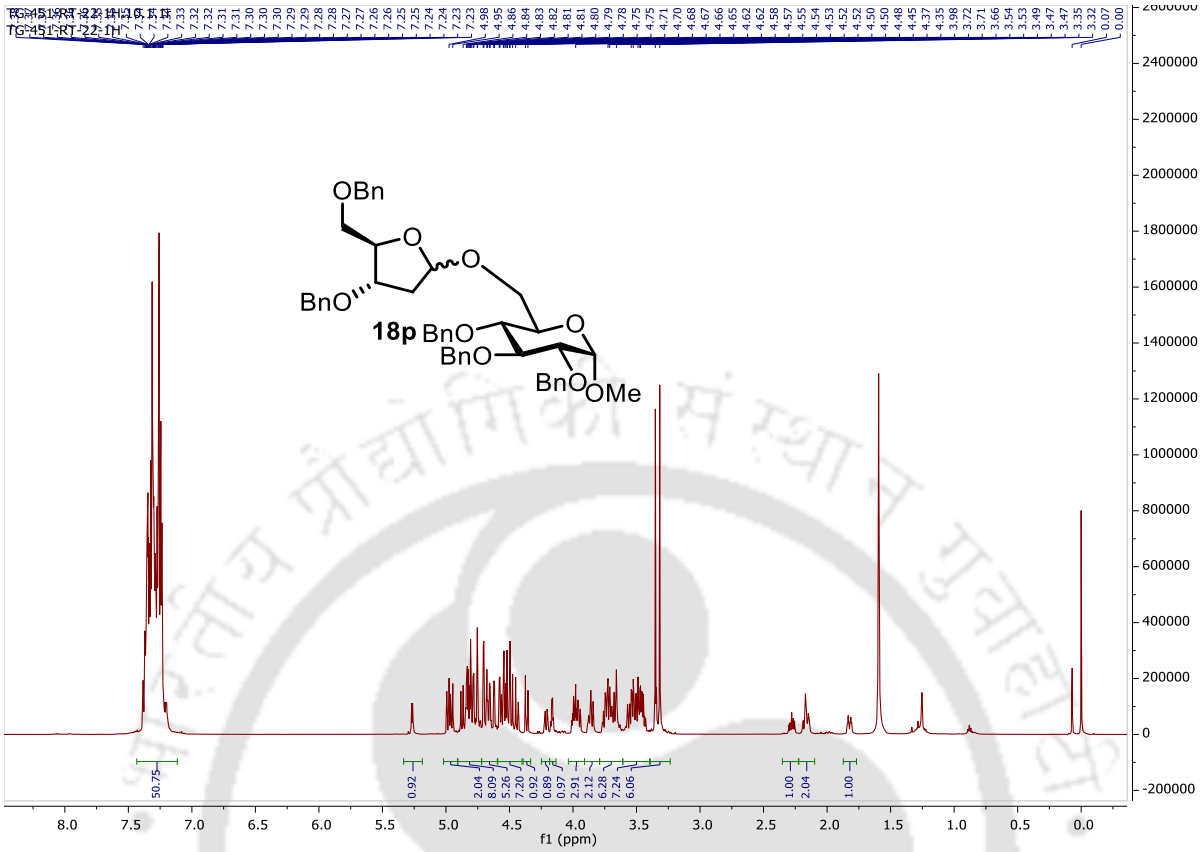


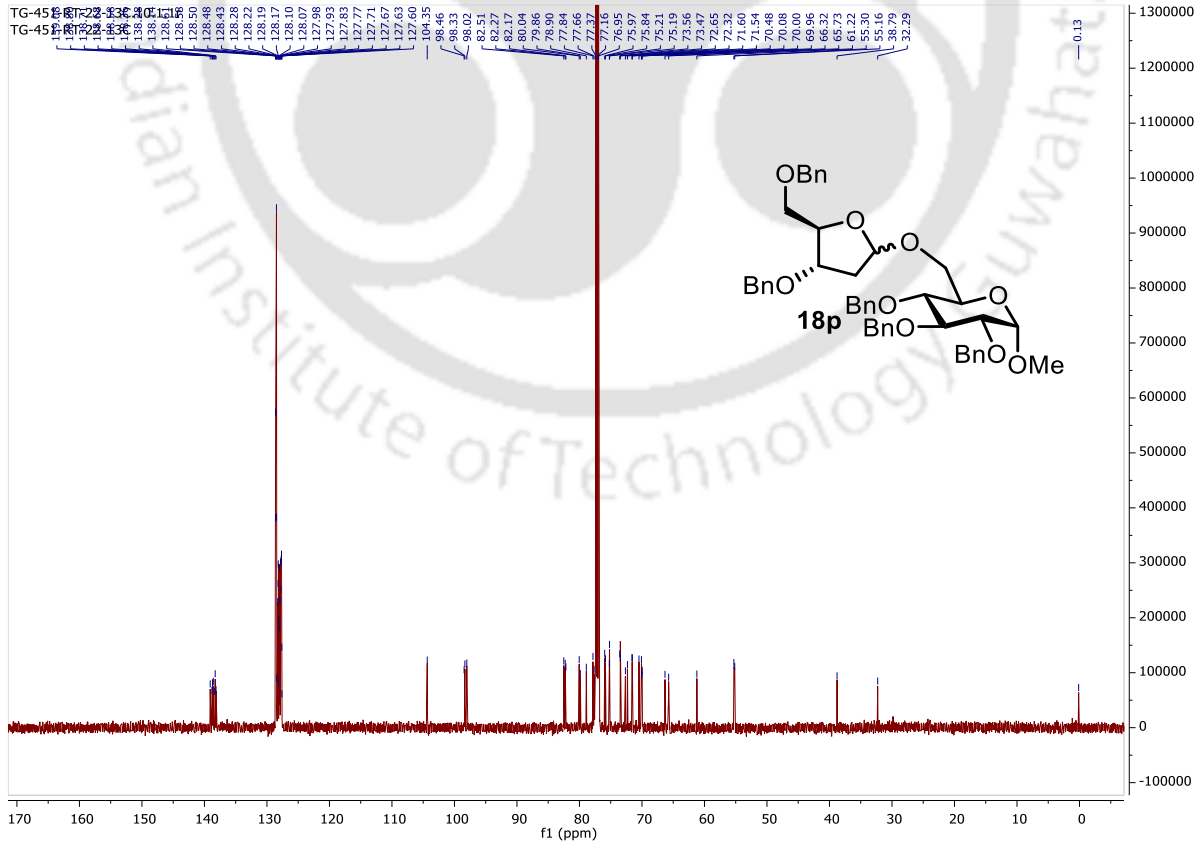




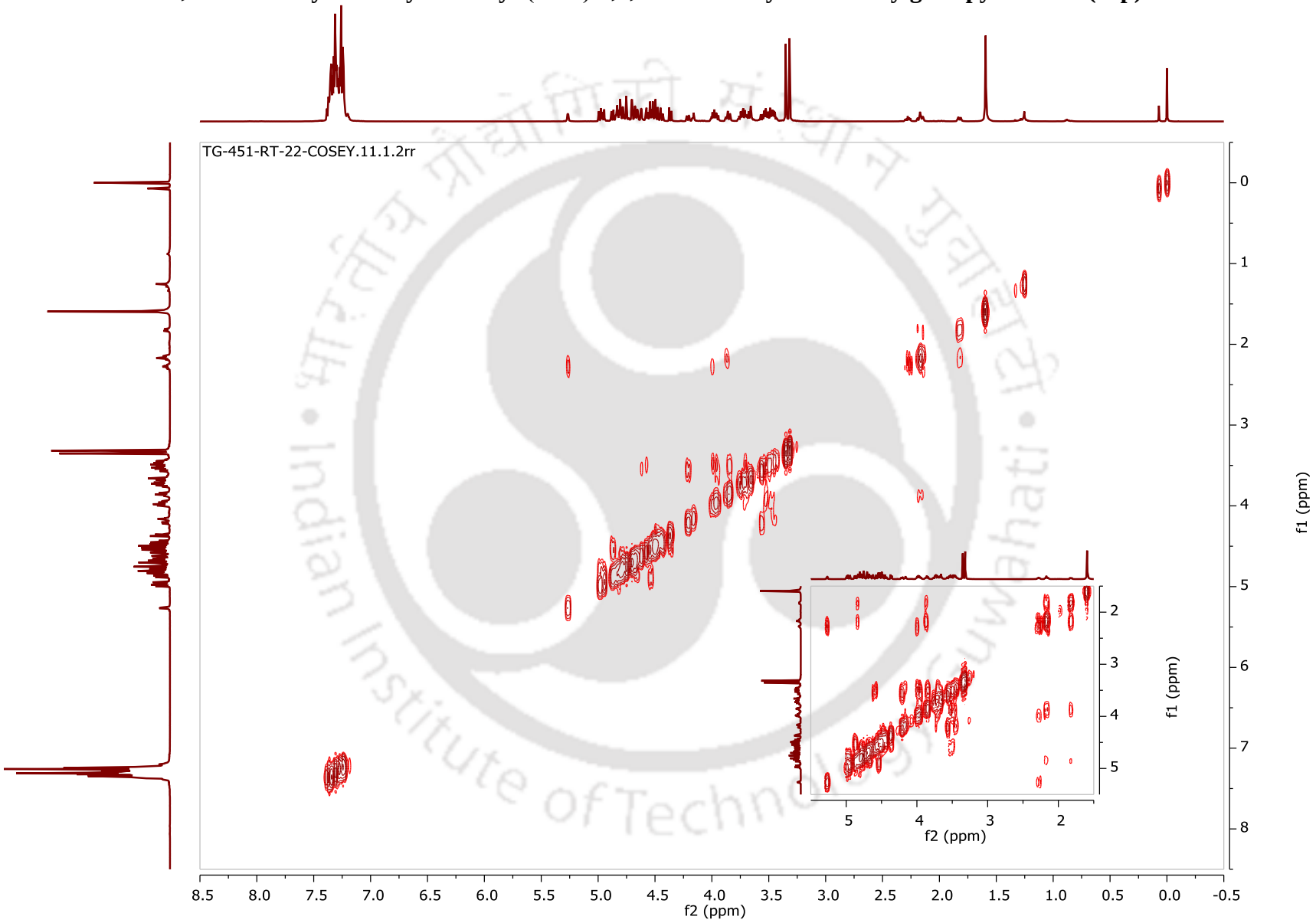
COSY NMR of Isopropyl-3,5-di-*O*-acetyl 2-deoxy-α,β-D-erythro-pentafuranoside (18o):

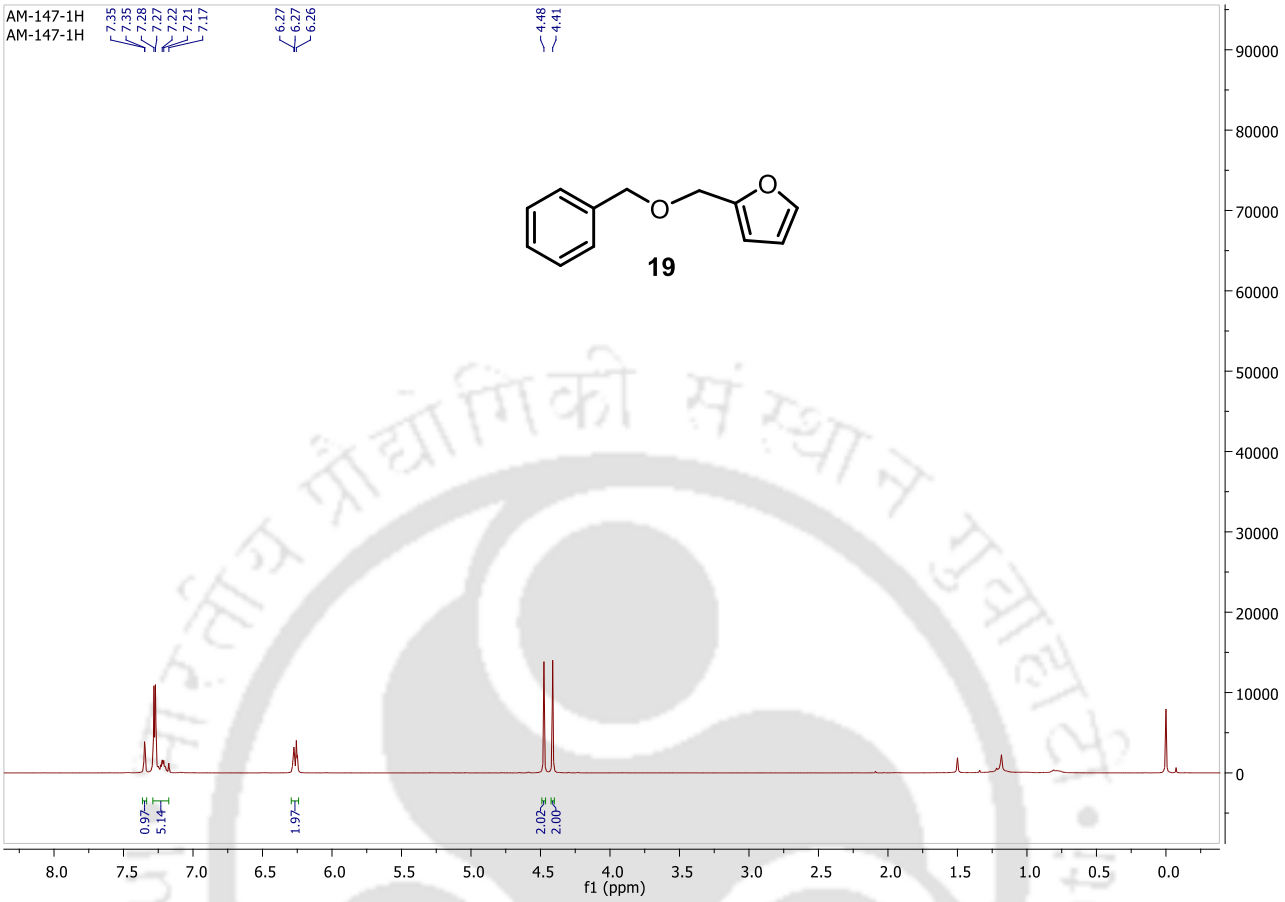






COSY NMR of 3,5-di-*O*-benzyl 2-deoxyfuranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-methylglucopyranoside (18p):





3.10 Determination of Configuration:

α–isomer: Irradiation of anomeric proton of α–isomer, there is an increase of enhancement of one of the 2-deoxy proton at ppm range 2.26 - 2.30 ppm. The enhancement is about 2.58% with respect to another 2-deoxy proton (0.59%). Hence, H_1 proton is cis to H_{2e} proton.

β–isomer: Similarly, irradiation of anomeric proton of β–isomer, there is an increase of enhancement of one of the 2-deoxy proton at ppm range 2.14 - 2.18 ppm with respect to anomeric H_1 proton. The enhancement is about 2.32% with respect to another 2-deoxy proton (0.82%). Hence, H_1 proton is cis to H_{2a} proton.

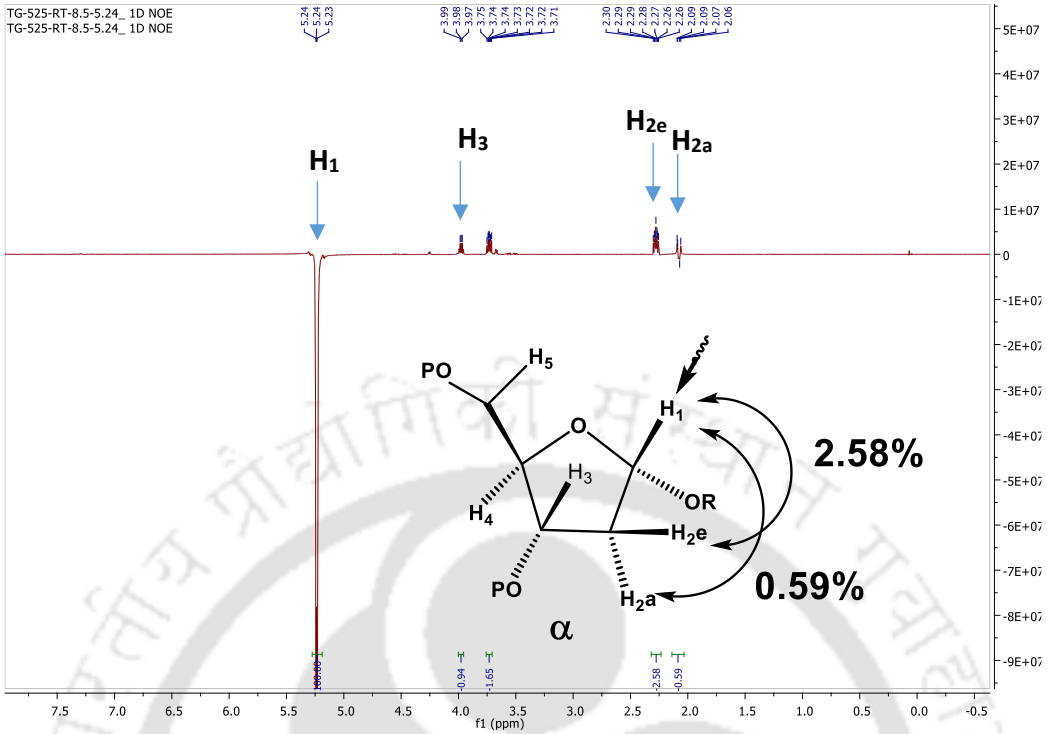


Figure 3: 1D-nOe experiment of α–isomer of **18g**.

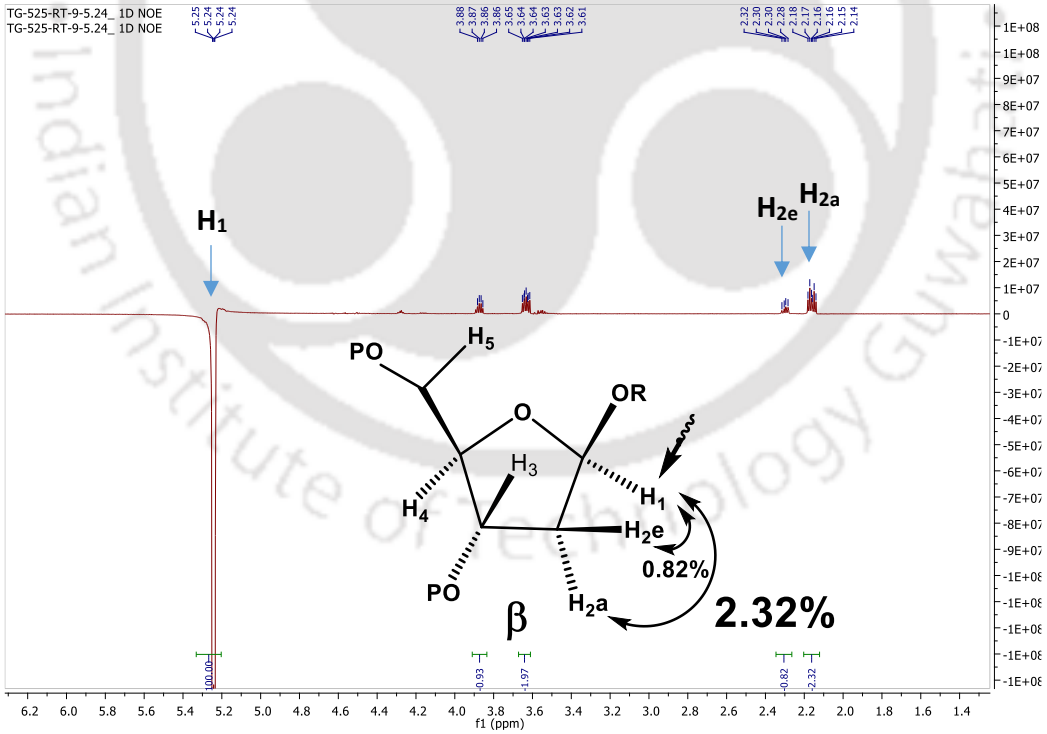


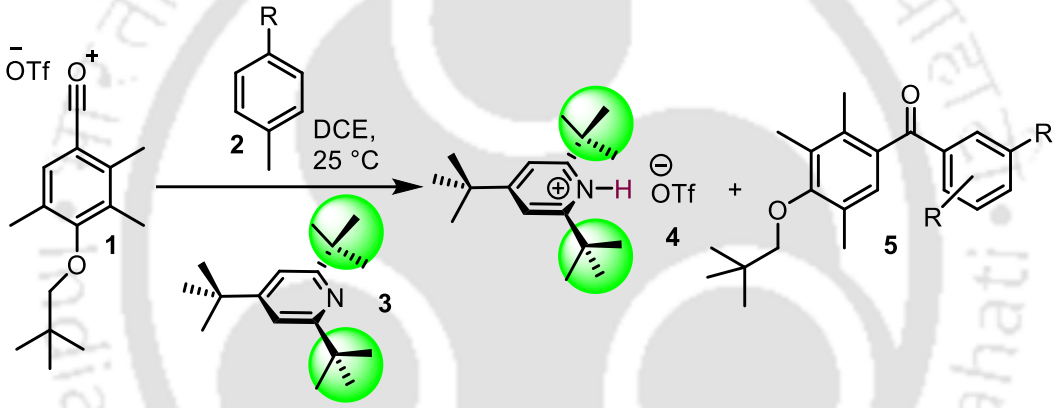
Figure 4: 1D-nOe experiment of β–isomer of **18g**.

Chapter 4

Sterically Hindered 2,4,6-Tri-tert-butylpyridinium (TTBPy) Salts as Single Hydrogen Bond Donor for Highly Stereoselective Glycosylation Reactions of Glycals

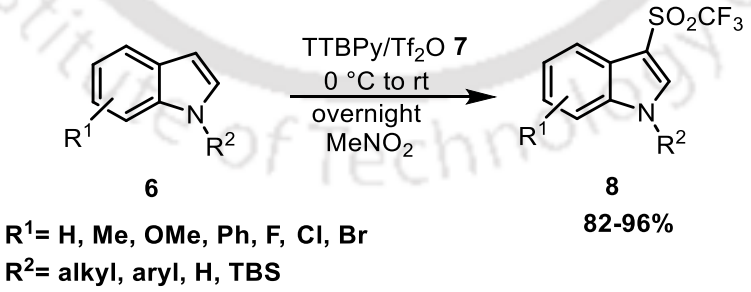
4.1 Introduction:

2,4,6-Tri-*tert*-butylpyridine (TTBPy), a highly hindered pyridine derivative was first synthesized by Mach and Dimroth in 1968 from stable oxonium salts.[1] This sterically bulky pyridine, along with its much well-studied analogue, 2,6-di-*tert*-butylpyridine,[2-5] DTBP are known for their inability to coordinate even to smaller Lewis acids like CH_3^+ or BF_3 except a proton.[2, 6] This typical non-nucleophilic basicity has been exploited in a variety of reactions, in particular as an acid scavenger or as a buffering agent in studies of reactions of metal ions in aqueous solutions.[6] Effenberger and coworkers used TTBPy in characterizing the concentration of acylium ions in aromatic acylation reactions exploiting it's ability to trap the released triflic acid (**Scheme 1**).[7] The profound effect of TTBPy on k_H/k_D values in these reactions has also been studied.



Scheme 1: Acylation of an aromatic compound in the presence of TTBPy.

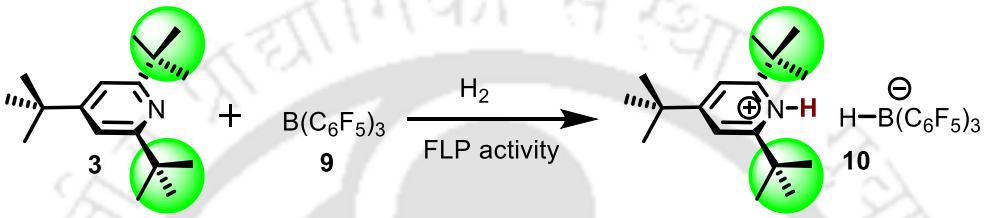
Shibata and coworkers used TTBPy/Tf_2O **7** system for the synthesis of indole triflones[8] **8**



Scheme 2: Synthesis of indole triflones in the presence of TTBPy/Tf_2O system.

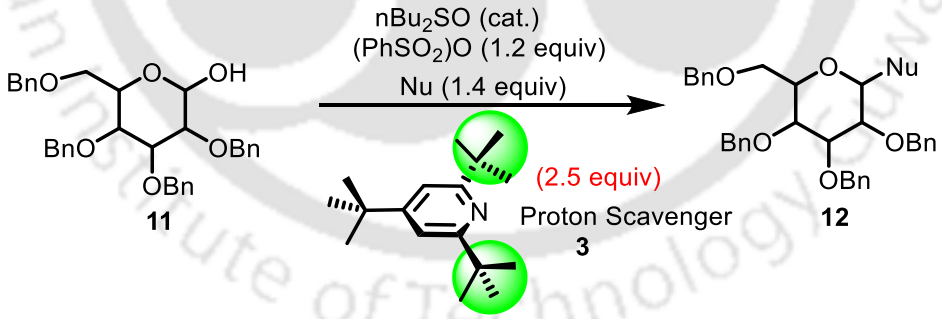
(**Scheme 2**). More recently, Berke and coworkers found that the bulky TTBPy in the presence of $B(C_6F_5)_3$ **9** can heterolytically cleave H_2, showing frustrated Lewis pair FLP activity (**Scheme 3**).[9a] Besides, it was also found that TTBPy can form stable frustrated Lewis pair with

[(acridine)BCl_2][$AlCl_4$] that can also heterolytically cleave H_2.[9b] Intriguingly, Ingleson and coworkers observed that the position of the hydride from H_2 has been found to be the C9 position of acridine and not the usually expected boron. The best and the most common use of the 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) have been in glycosylation reactions again as a trap to capture the released sulfonic acids at lower temperatures.[10]



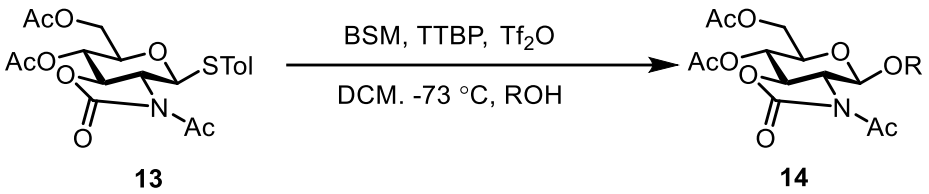
Scheme 3: Heterolytic cleavage of hydrogen by FLP.

Gin and coworkers introduced the use of an excess of TTBPy in the sulfoxide catalyzed activation of glycosyl hemi-acetals[11-12] **11** (**Scheme 4**). TTBPy, being a non-nucleophilic base, is expected to trap the byproduct triflic acid. However, Crich later introduced 2,4,6-tritertiarybutylpyrimidine (TTBP) as a potential alternative to TTBPy on the grounds that the former is non-hygroscopic white crystalline powder, unlike the hindered pyridine derivatives.[13]



Scheme 4: Activation of hemiacetal in the presence of TTBPy/sulfoxide catalytic system.

Ye and coworkers introduced stereoselective glycosylation of 2,3-oxazolidinone thioglycoside **13** as a donor (**Scheme 5**).[14] Though the mechanism is not clear, the authors observed an intriguing stereo-switch in glycosylation reactions of glucosamine derivatives in the presence and absence of 2,4,6-tri-*tert*-butylpyrimidine.



13 **14**

Scheme 5: Activation of hemiacetal in the presence of BSM/TTBP/ Tf_2O catalytic system.

However, curiosity lingers on the reactivity of these hindered pyridine and pyrimidine compounds as bases. For example, it is known that the aqueous pK_a of DTBP is about ~2 units lesser than expected, though the gaseous state pK_a is in-line with predicted values.[4, 5] The weak basicity of 2,4,6-tri-*tert*-butylpyridine, similar to DTBP or TTBP, is attributed to the inability of TTBPyH to be solvated in aqueous solutions due to high steric shielding and hence behaves as a weak base (pK_a = 3.4). This effect is more pertinent in DMSO in which the 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 ability of the cationic Brønsted acid TTBPyH depends extensively on the hydrogen bonding character of the solvent. However, we were curious to understand the behaviour of TTBPyH in the more generally used solvents like DCE or DCM with low dielectric constant (ϵ = 10.36 or 8.93 respectively) where it is used as a proton trapping agent. On the other hand, very recently, it has been shown that the Schreiner's thiourea, whose pK_{DMSO} is 8.5, catalyzes the tetrahydropyranylation of alcohols via a Brønsted acid mechanism.[15-24] This led us to question whether TTBPy, whose conjugate acid is a much stronger acid in DMSO, is safe as a non-nucleophilic base in glycosylation reactions, particularly reactions involving glycals. Contrarily, TTBPy whose conjugate acid is a relatively stronger acid in DMSO, is used as a safe non-nucleophilic base in glycosylation reactions even involving glycals. This thought carries significance as in general, more than one equivalent of TTBPy salts are produced in glycosylation reactions owing to the excess usage of TTBPy as an acid quencher. However, we note in passing that huge difference in reactivity could exist between neutral Brønsted acids versus cationic Brønsted acids, specifically in non-polar solvents like DCM/DCE.[25] It is pertinent to ask if the trapped proton in the TTBPyH, once formed, can behave as a cationic Brønsted acid (**Figure 1**) to protonate the sterically demanding glycal substrates in solvents of poor solvation ability, *or* it forms a tight ion pair with the counter-ion thus showing neutral character.

In this chapter, we show that TTBPy salts not only catalyze the glycosylation of glycals but does it very effectively with 10 mol % of the catalyst and also in a highly stereoselective

fashion leading to the synthesis of various deoxyhexoses (**Scheme 6**). Further, our observations also throw some light onto the mechanism which reveals that TTBPyH catalyzes the reaction *not*

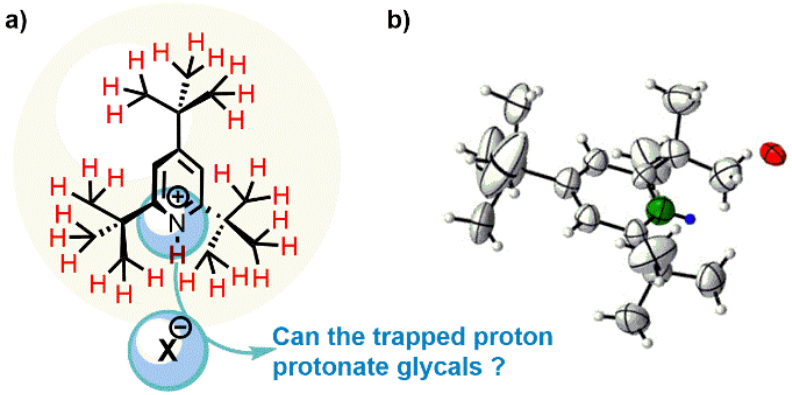
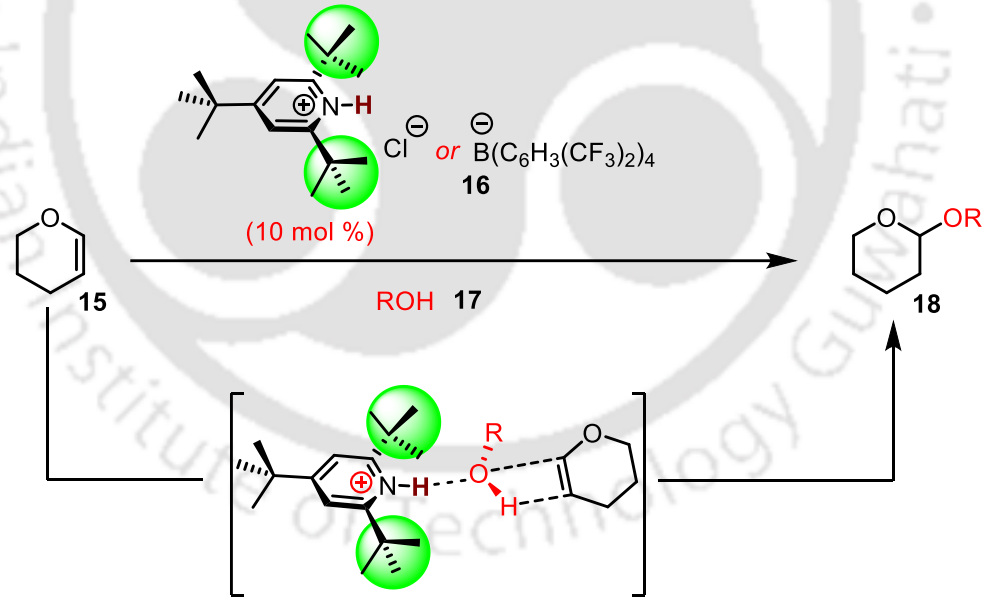


Figure 1: a) Molecular structure and b) ORTEP diagram of TTBPyHCl.

via a Brønsted acid mechanism (BA) but via its hydrogen bonding assisted activation (HB).[26] Besides, the effect of the catalytic activity also seems to be controlled by the nature of the counter-ion.



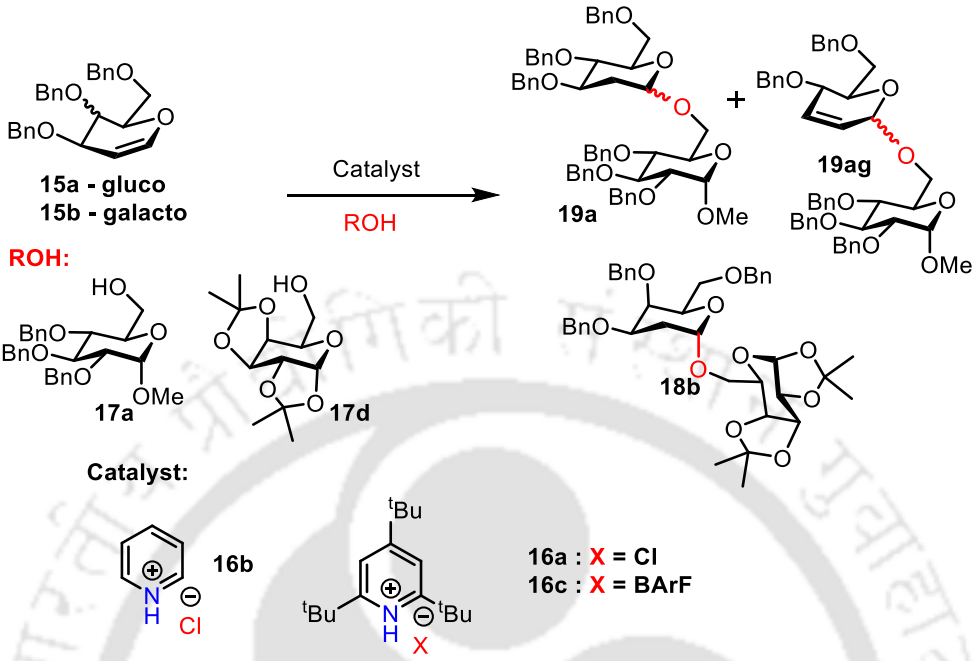
Scheme 6: Stereoselective glycosylation of glycals by TTPPyHCl.

4.2 Optimization Study:

Our study commenced with the synthesis of two TTBPy salts with chloride and BArF as counter anions.[14] The chloride salt of TTBPyH has been achieved by dissolving TTBPy in methanolic HCl and evaporating the solvent to dryness. The BArF salt of TTBPyH is synthesized via a simple anion exchange reaction[15] with the chloride salt triggered by poor dissociation of sodium chloride in DCM.

2-Deoxy and 2,6-dideoxy sugars form a part of several antibiotics and anticancer agents.[16] Despite the recent surge in development of methods for the synthesis of 2-deoxyglycosides,[11d, 11i, 11j, 17] there is still a need to develop a general organocatalytic method for the stereoselective synthesis of various 2-deoxy and 2,6-dideoxyglycosides. Initially, we have reacted glucal **15a** and armed primary sugar acceptor **17a** as substrates using 20 mol % chloride salt of TTBPyH **16a** as the organocatalyst at 40 ^{o}C in DCE as a solvent. Interestingly, this led to the glycosylated product **19a** after 24 h in 86% yield with 4:1 α:β selectivity (**Table 1**, entry 1). 1.1 equivalents of acceptor was sufficient enough to drive the excellent conversion of starting material to glycosylated product. Surprisingly, the organocatalyst **16c** with the weakly coordinating BArF anion[18] in DCM at rt gave corresponding Ferrier[19] glycosylated product **19ag** along with the expected product in presence of primary sugar acceptor with 56% and 34% yields respectively (**Table 1**, entries 5, 7). The difference in reactivity with the change of anion suggests the unique role of cation-anion interactions[20] in the observed catalysis. Besides, catalyst **16c** is active even at temperatures as low as -40 ^{o}C providing decent conversion of glucal to the corresponding products. Since our target molecules are not Ferrier products, we have chosen the chloride salt of TTBPy **16a** for further optimization. Studies to find the right solvent have been performed using the tri-OBn-galactal **15b**, and di-acetonide protected 6-OH acceptor **17d** as coupling partners. A quick study revealed that the chlorinated solvents like DCM and DCE are the best solvents for this cationic Brønsted acid catalyzed glycosylation (**Table 1**, entries 10 - 11). The coupling reaction, when perfomed in DCE, gave the best yields and also led to the exclusive formation of the α-glycosylated product **18b**. However, the same reaction when performed in the presence of only TTBPy instead of it's salt in DCE at 40 ^{o}C for 24 h, did not lead to any glycosylated product thus indicating that this is not a base catalyzed glycosylation reaction.

Table 1: Optimization study of glycosylation of glycals.



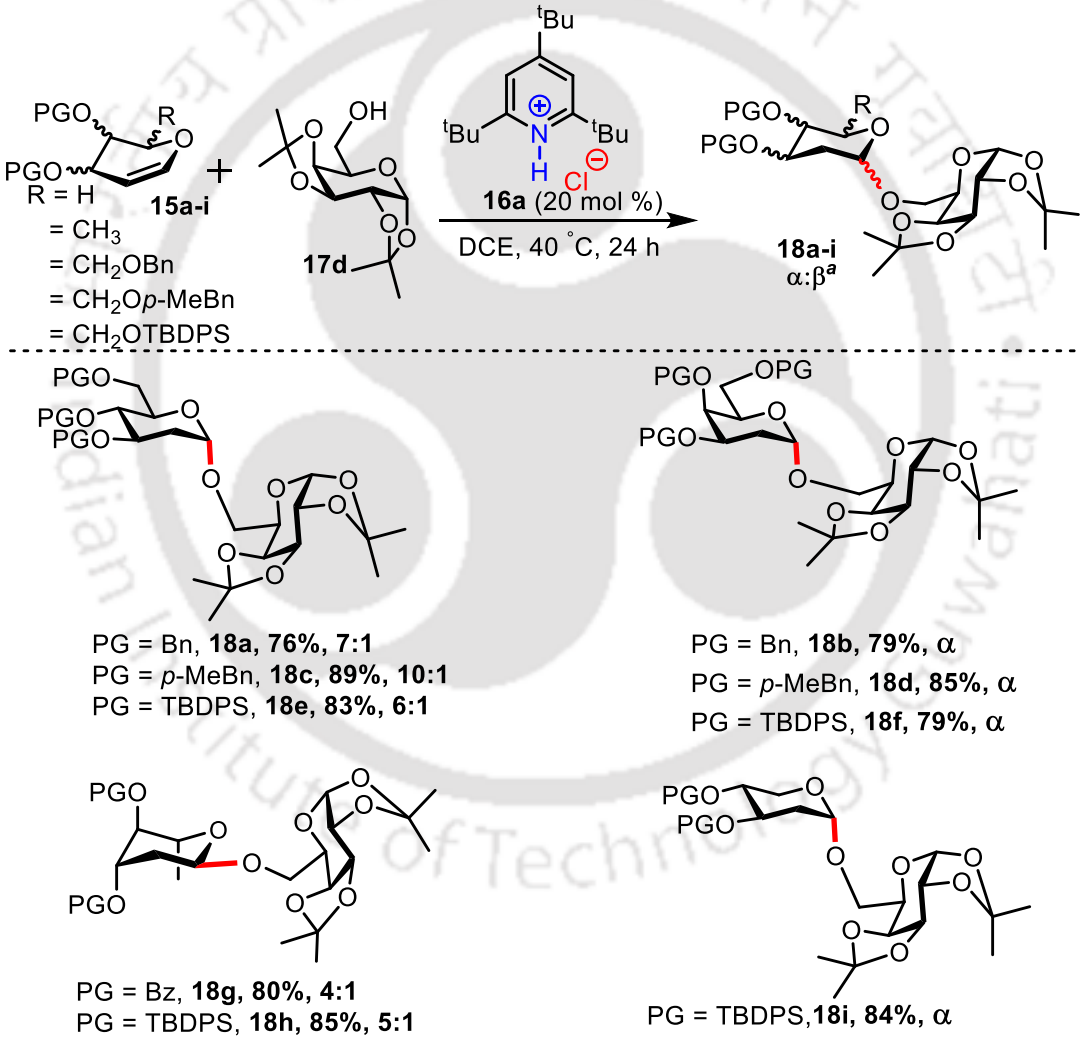
entry	cat.	solvent	compd	yield (%) (α:β)[f]	**19ag** yield (%) (α:β)[f]
1	**16a**	DCE	**19a**	86 (4:1)	-
2	**16b**	DCE	**19a**	58 (2:1)	-
3	TTBPy	DCE	**19a**	-	-
4[a]	**16a**	Et_2O	**19a**	64 (2:1)	-
5	**16c**	DCM	**19a**	56 (1:1)	30 (2:1)
6[b]	**16c**	DCM	**19a**	26 (1:1)	10 (2:1)
7[c]	**16c**	DCM	**19a**	34 (1:1)	21 (3:1)
8[d]	**16c**	Et_2O	**19a**	49 (1:1)	42 (2:1)
9[e]	**16c**	Et_2O	**19a**	46 (2:1)	40 (2:1)
10[d]	**16a**	DCM	**18b**	75 (α)	-
11	**16a**	DCE	**18b**	79 (α)	-
12	**16a**	PhMe	**18b**	44 (α)	-
13	**16a**	ACN	**18b**	40 (α)	-
14	**16a**	*m*-xyl	**18b**	41 (α)	-
15	**16a**	PhH	**18b**	25 (α)	-
16	**16a**	THF	**18b**	67 (α)	-

Reaction conditions: 0.12 mmol of **15a-b**, 0.13 mmol of **17a**, **17d** and 20 mol % of **16a-c** and TTBPy, 24 h [(DCE at 40 °C, for **16a-b** and TTBPy) and (DCM at rt for **16c**)], **15a** for entries 1 - 9 and **15b** for entries 10 - 16. [a]At rt for 7 days. [b]At -40 °C. [c]5 mol % of **16c** was used. [d]At rt. [e]Ether as a solvent at -30 °C. [f]Anomeric selectivities were determined from crude NMR analysis.

4.3 Glycosylation of Benzyl, *p*-methylbenzyl and TBDPS Protected Glycals with Diacetonide Protected Galactosyl 6-OH Acceptor:

With the optimized conditions in hand, we sought to evaluate the ability of the new organocatalysts towards glycals with various protecting groups (**Scheme 7**). The armed benzyl **15a** and *p*-methylbenzyl protected glucal **15g** when reacted with 1.1 equivalents of acetonide

Scheme 7: Glycosylation of benzyl, *p*-methylbenzyl, and TBDPS protected glycals with diacetonide protected galactosyl 6-OH acceptor.



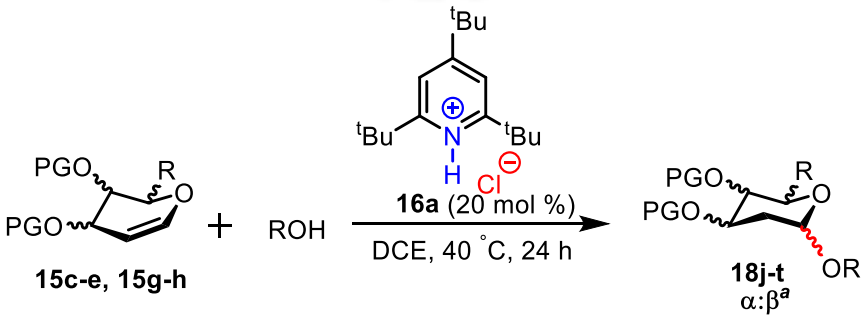
Reaction conditions: 1 equiv of **15a-i**, 1.1 equiv of **17d** and 20 mol % of **16a**, 24 h in DCE at 40 ^{o}C. [a]Anomeric selectivities were determined from crude NMR analysis.

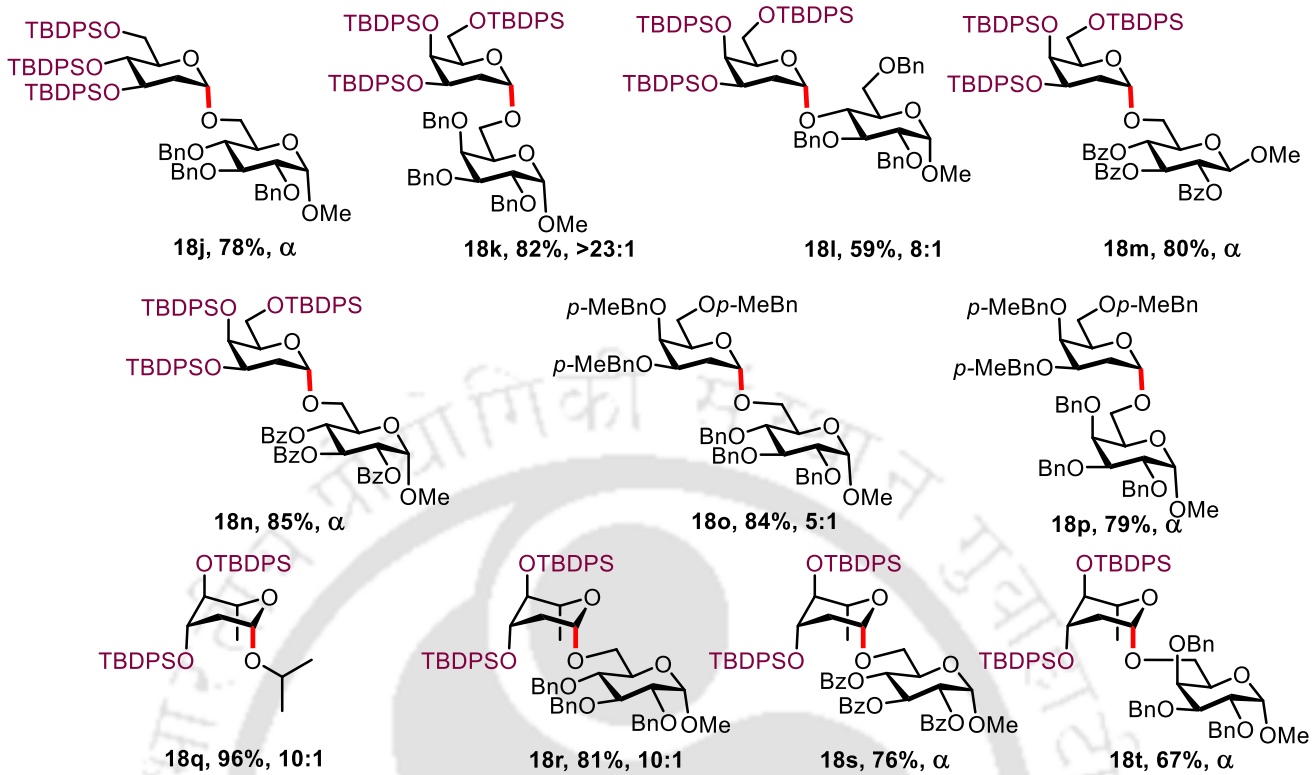
protected primary sugar acceptor **17d** and 20 mol % of **16a** at 40 °C in DCE as a solvent gave the products **18a** and **18c** in 76% and 89% yield with 7:1 and 10:1 α:β selectivity respectively. Remarkably, the sterically bulky TBDPS protected glucal **15c** provided the 2-deoxy-glycosylated product **18e** with 6:1 α:β selectivity in 83% yield. Under similar reaction conditions, benzyl **15b**, *p*-methylbenzyl **15h** and TBDPS protected galactal **15d** reacted with primary sugar acceptor **17d** giving only α-products **18b**, **18d** and **18f** respectively in high yields. We then determined to test the efficiency of the method towards the synthesis of 2,6-dideoxy glycosides also, utilizing the L-rhamnal (**15e** and **15i**) donors. The disarmed benzoyl protected L-rhamnal **15i** gave the coupled product **18g** in 80% yield with 4:1 α:β selectivity whereas the bulky TBDPS protected L-rhamnal **15e** gave the product **18h** in 85% yield with 5:1 α:β selectivity.

4.4 Glycosylation of Protected Glycals with Various Acceptors:

We next focused on the scope of derivatives with different donors and acceptors to investigate the potential applicability of this method. Since it has been observed that bulky TBDPS protecting group in combination with the bulky TTBPy catalyst led to the highly selective glycosylation reactions, all the further studies have been carried out with glycals bearing the same protecting group. TBDPS protected glucal, and galactal donors under the currently developed organocatalytic conditions lead to exclusive formation of α-product with both electronically reactive and deficient acceptors (**Scheme 8**, **18j** to **18n**). The coupling reactions with *p*-MeBn protected galactal **15d** with glucose and galactose derived 6-OH acceptors led to the product **18o** and **18p** in 84% and 79% yield. Synthesis of 2-6-dideoxyglycosides (**Scheme 8**, **18q** to **18t**) has also been achieved in a highly stereoselective fashion under the organocatalytic conditions. The method has also been extended for the synthesis of galactosyl amino acids (**Scheme 9**).

Scheme 8: Glycosylation of protected glycals with several sugar alcohols.



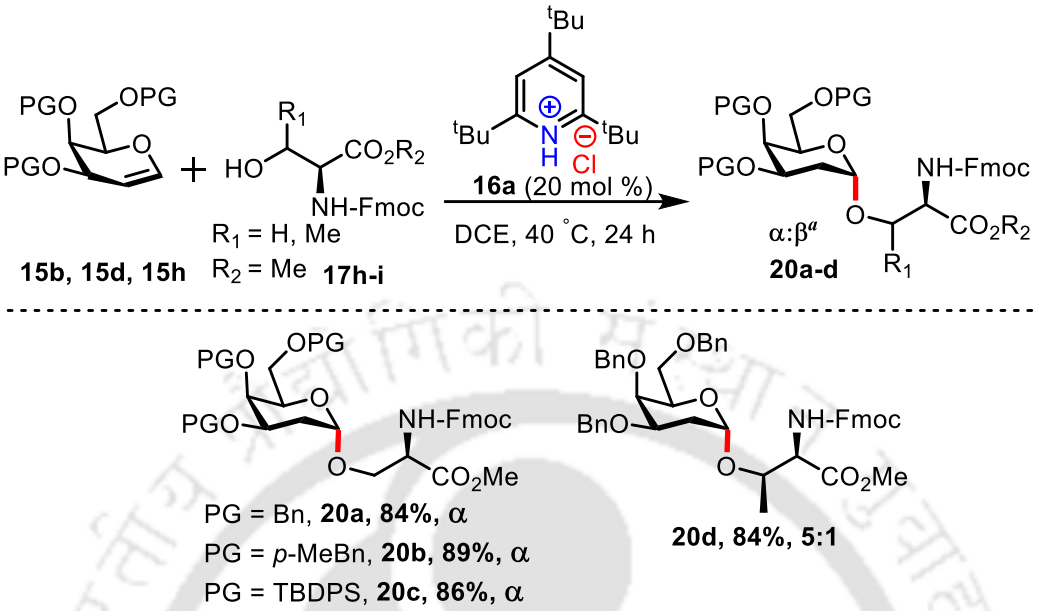


Reaction conditions: 1 equiv of **15c-e**, **15g-h**, 1.1 equiv of **17a-c**, **17e-f** and 20 mol % of **16a**, 24 h in of DCE at 40 ^{o}C. ^{a}Anomeric selectivities were determined from crude NMR analysis.

4.5 Scope of Amino Acid Galactosides:

Fmoc protected methyl ester of serine **17h** was coupled with **15b** providing glycoamino acid **20a** in 84% with α selectivity whereas Fmoc protected methyl ester of threonine **17i** with **15b** gave corresponding glycoamino acid **20d** in good yields with 5:1 α:β selectivity (**Scheme 9**). Similarly, *p*-methylbenzyl and TBDPS protected galactal (**15h** and **15d**) were coupled with serine acceptor **17h** gave corresponding glycoamino acids **20b** and **20c** in 89% and 86% yield respectively, with exclusive α-selectivity.

Scheme 9: Synthesis of glycosyl amino acids.

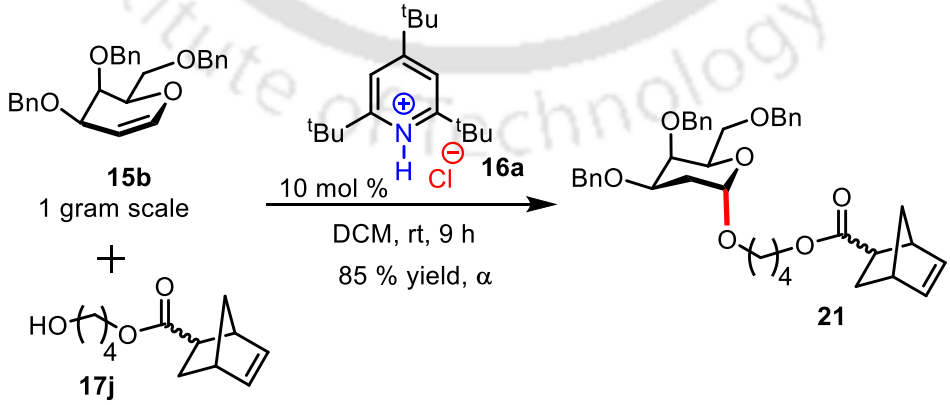


Reaction conditions: 1 equiv of **15b**, **15d**, **15h**, 1.1 equiv of **17h-i** and 20 mol % of **16a**, 24 h in DCE at 40 °C. [a]Anomeric selectivities were determined from crude NMR analysis.

4.6 Gram Scale Synthesis:

The organocatalytic glycosylation method was then applied to gram-scale synthesis (**Scheme 10**). We were delighted to find that 1 gram of benzyl protected galactal **15b** with a norbornene derived ROMP precursor **17j** in the presence of reduced catalytic loading (10 mol %) of **16a** in DCM at rt afforded the corresponding monosaccharide **21** in 85% yield with α selectivity.

Scheme 10: Gram scale demonstration of glycosylation.



Reaction conditions: 1 equiv of **15b**, 2 equiv of **17j**. Anomeric selectivity was determined from crude NMR analysis.

4.7 Proposed Mechanism:

As discussed *vide supra*, the attempted coupling reaction in the presence of only TTBPy and not TTBPy salt, led to no conversion of the starting material suggesting that this is not a base catalysed reaction. In addition, the reaction of stoichiometric amounts of TTBPy·HCl in the absence of any acceptor in ultra-dry DCE failed to provide the expected glycosyl chlorides **22** (**Figure 2**, a). This result signifies that the initiation step is not the proton transfer from TTBPyH to the glycal. The transfer of the trapped proton that is sterically shielded in the bulky TTBPyH, to the bulky sugar enol ethers is highly disfavored thus ruling out the BA mechanism. In order to gain more insights into the mechanism, we focused on NMR experiment in $CDCl_3$. ^1H NMR experiment performed by mixing the catalyst **16a** and 2-propanol in an equimolar ratio, led to a significant shift in the chemical shift of the OH peak of 2-propanol (from δ 1.59 to δ 3.12, **Figure 2**, b-3). Besides, the slight shift has also been observed in α-hydroxy proton $\mathbf{H_D}$ (from δ 4.03 to δ 4.07, **Figure 2**, b-3) and in the methyl doublet $\mathbf{H_E}$ (from δ 1.22 to δ 1.24, **Figure 2**, b-3). The OH peak of 2-propanol shifted downfield whereas the NH peak of the catalyst shifted upfield (from δ 14.25 to δ 14.19) (See experimental section for a detailed analysis). The shift in the non-exchangeable protons albeit present, is slightly less (from δ 4.03 to δ 4.05, **Figure 2**, b-1) when 2-propanol is taken as 6 equivalents (0.108 mmol) with respect to the catalyst **16a** (0.018mmol) in 600 μL of $CDCl_3$ (exactly replicating the concentrations of reaction conditions). These observations strongly suggest a hydrogen bond between TTBPyH and alcohol. We note in passing that a slight change in the chemical shift of $CHCl_3$ peak has been observed in the titration of catalyst **16a** with 2-propanol. Therefore, the ^1H NMR of 2-propanol has been recorded at different concentrations[40] (See experimental section) where it was found that the change in the chemical shift of $CHCl_3$ peak is significant with increasing concentration, revealing the weak hydrogen bonding character of D/$HCCl_3$. Based on the above observations, we propose a hydrogen bond mediated mechanism (HB mechanism) for the observed catalysis as depicted in **Figure 3**. A strong hydrogen bond between the catalyst and the alcohol leading to an increased acidity of the alcoholic OH results in the protonation of glycals, thus forming the oxocarbenium ion. The thus formed oxocarbenium ion is trapped by the alkoxide ion bound to TTBPyH, thereby regenerating the catalyst.

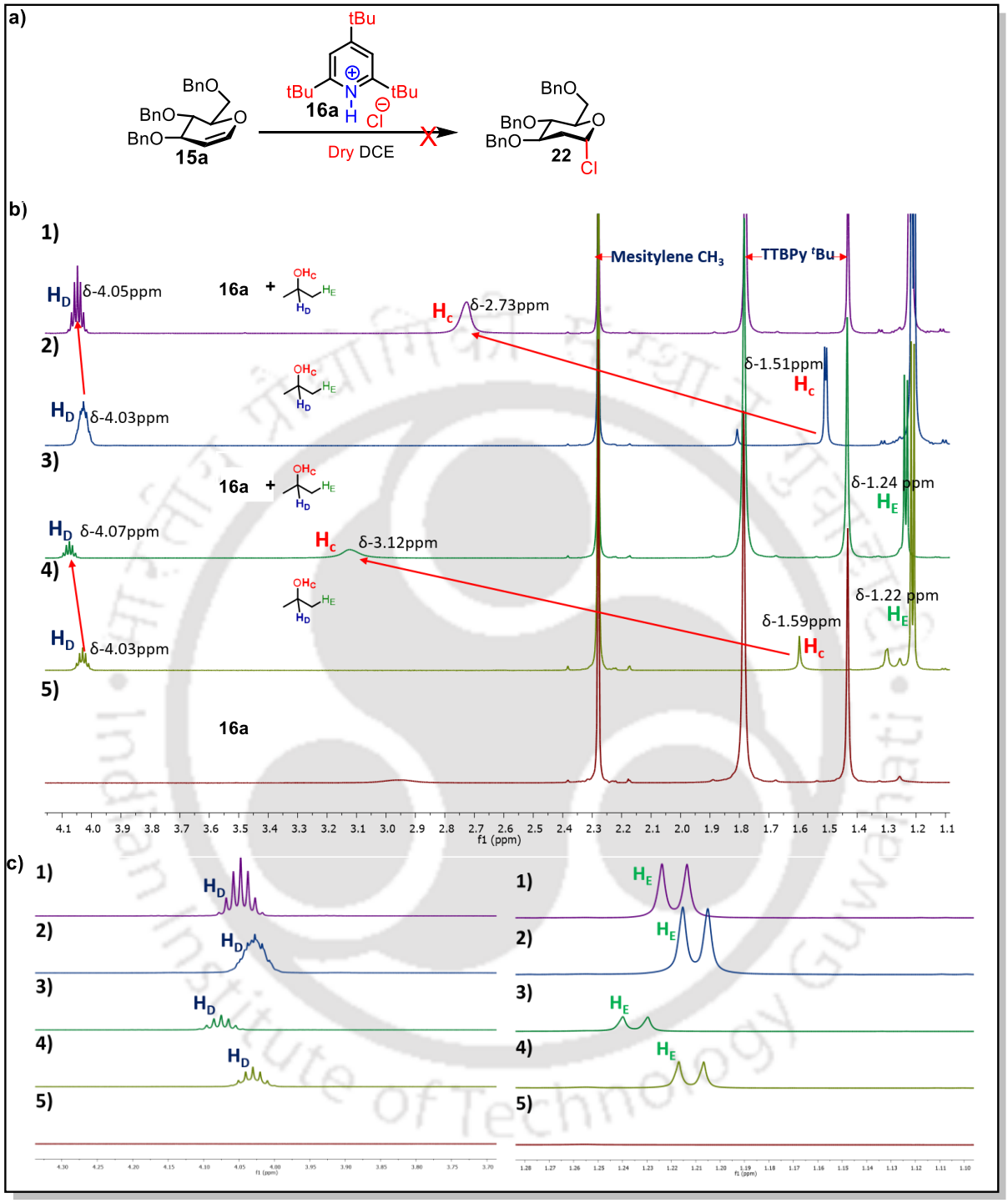


Figure 2: Investigation of the mechanism. a) Control experiment, b) ^{1}H NMR titration of **16a** with 2-propanol in 600 µl of $CDCl_3$. 1) 0.018 mmol of **16a** and 0.108 mmol 2-propanol (1:6 ratio) 2) 0.108 mmol of 2-propanol 3) 0.018 mmol of **16a** and 0.018 mmol of 2-propanol (1:1 ratio) 4) 0.018 mmol of 2-propanol and 5) 0.018 mmol of **16a**. 0.018 mmol of mesitylene is used as an internal standard in all the experiments for the purpose of calibration (See experimental section for more details) c) expanded for **H_D** and **H_E** regions.

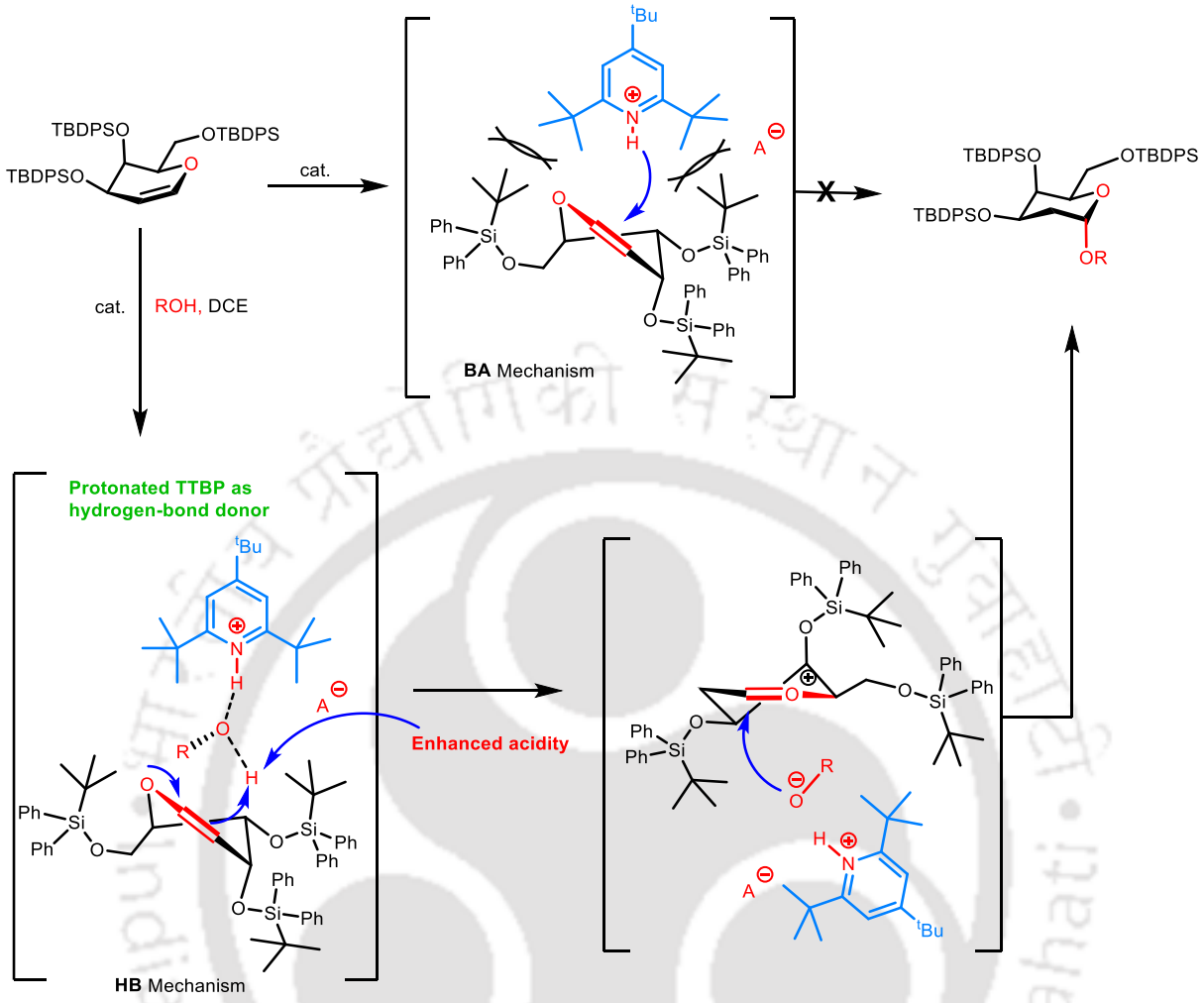


Figure 3: Potential pathways of stereoselective glycosylation of glycals using TTBPy.HCl.

4.8 Conclusion:

In conclusion, we have showcased the utility of the conjugate acids of the sterically bulky 2,4,6-tri-*tert*-butylpyridine as efficient catalysts for the stereoselective synthesis of 2-deoxy and 2,6-dideoxyglycosides. The steric bulk of the organocatalyst in conjunction with the sterically bulky TBDPS protecting group of glycals seems to be working in tandem for the observed stereoselective α-glycosylations. Moreover, despite the low pK_a of the conjugate acids observed in polar solvents like water and DMSO, TTBPy hydrochloride seems to be not acidic enough to protonate glycals via a Brønsted acid mechanism in non-polar solvents like DCM and DCE to generate glycosyl halides. Besides, the catalytic activity of the new organocatalyst happens

through an unprecedented ionic hydrogen bond activation of alcohols as evidenced by the NMR studies and the control experiments. Interestingly, the observed catalytic activity also seems to be influenced by the counter-ion. Further studies on the anionic activity could result in a better understanding of the unique mode of activation. These results will not only be useful for the chemists to judiciously use the bulky base TTBPy as an acid scavenger but also will help design new cationic Brønsted acids.

4.9 Experimental Section:

General Information

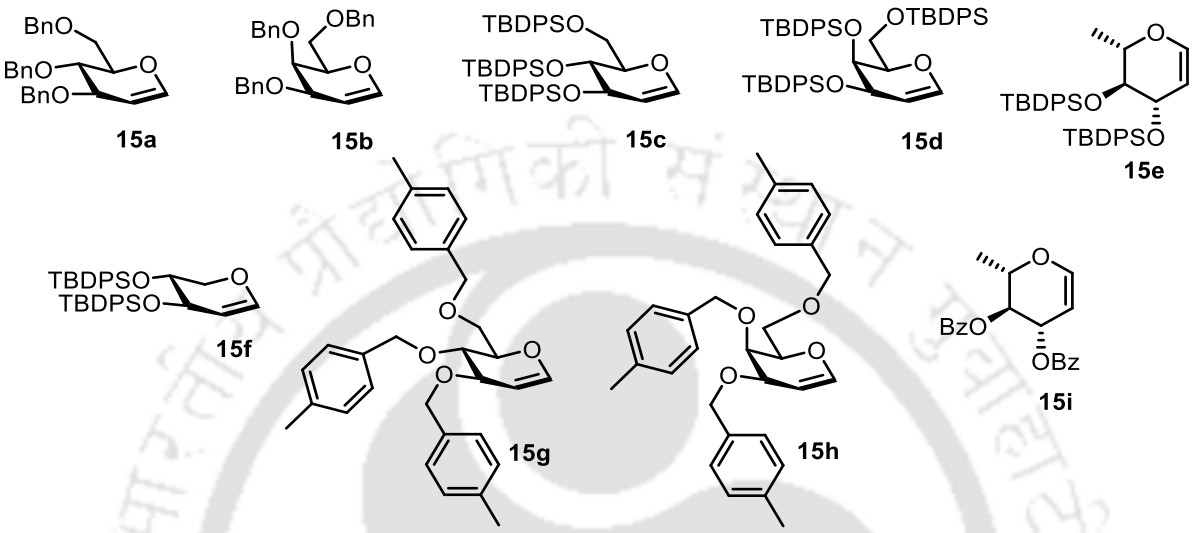
All solvents used were in commercial-grade for the reaction without further purification. Reagents purchased from Sigma-Aldrich, Merck, Spectrochem, Alfa Aesar, Loba and used without further purification.

Analysis

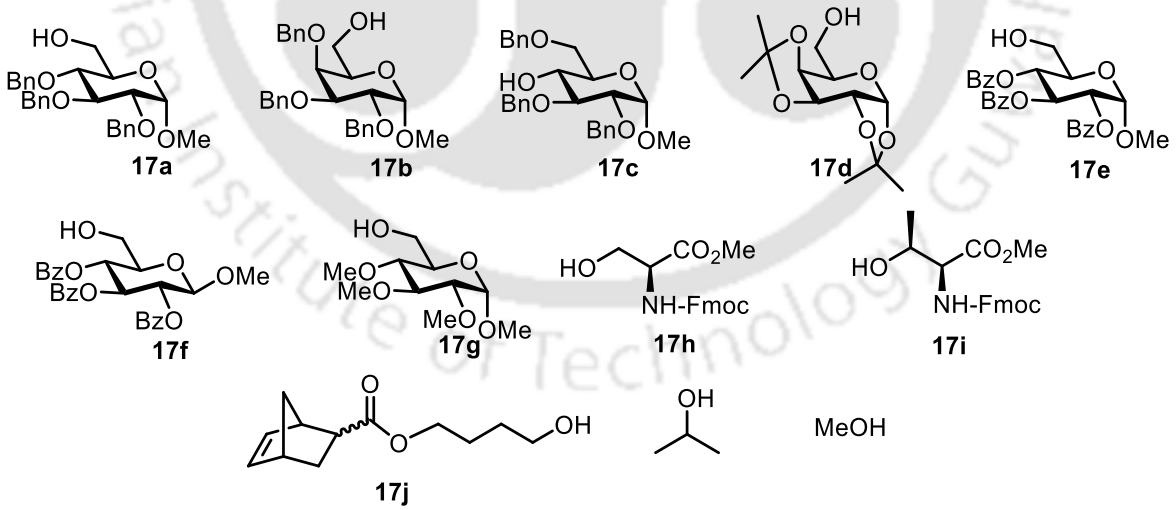
Reactions were monitored by TLC on Kieselgel 60 F254 (Merck). Detection was done by examination under UV light (254 nm) and by charring with 10% sulfuric acid in water. Purification was performed by both Ultra High Performance Liquid Chromatography (UHPLC) using column [Particle size: (µ) 12, Dim: (mm) 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 rt. ^{1}H- and ^{13}C NMR were recorded on a Bruker 600 MHz and 400 MHz spectrometer using $CDCl_3$ as a solvent. Chemical shift values are reported in ppm with the solvent as the internal standard ($CDCl_3$: δ 7.26 for ^{1}H, δ 77.16 for ^{13}C). 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 mass spectrometer. 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.

Donors Used in this Study

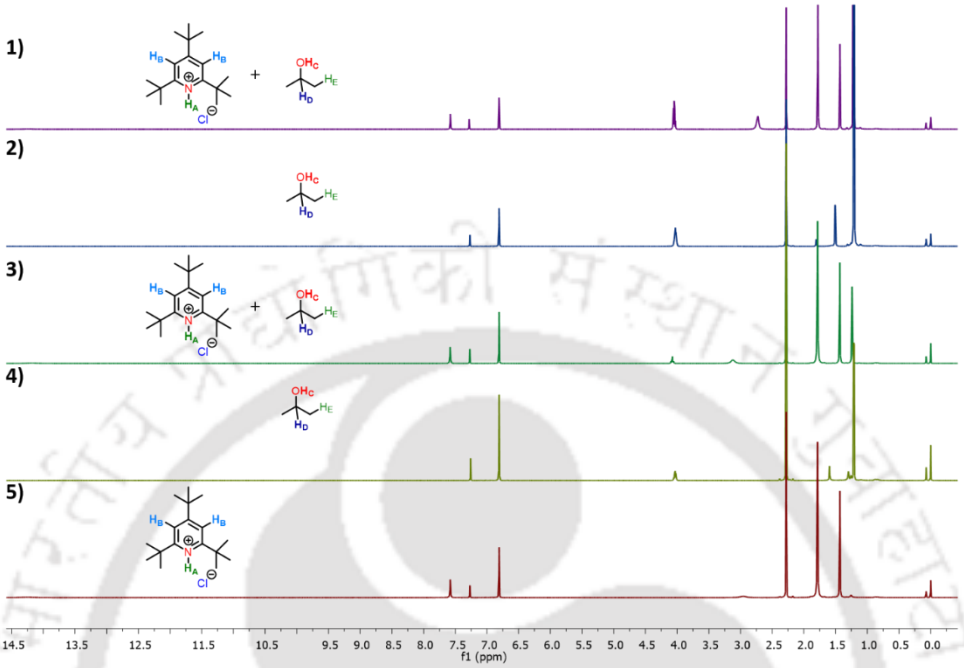


Acceptors Used in this Study



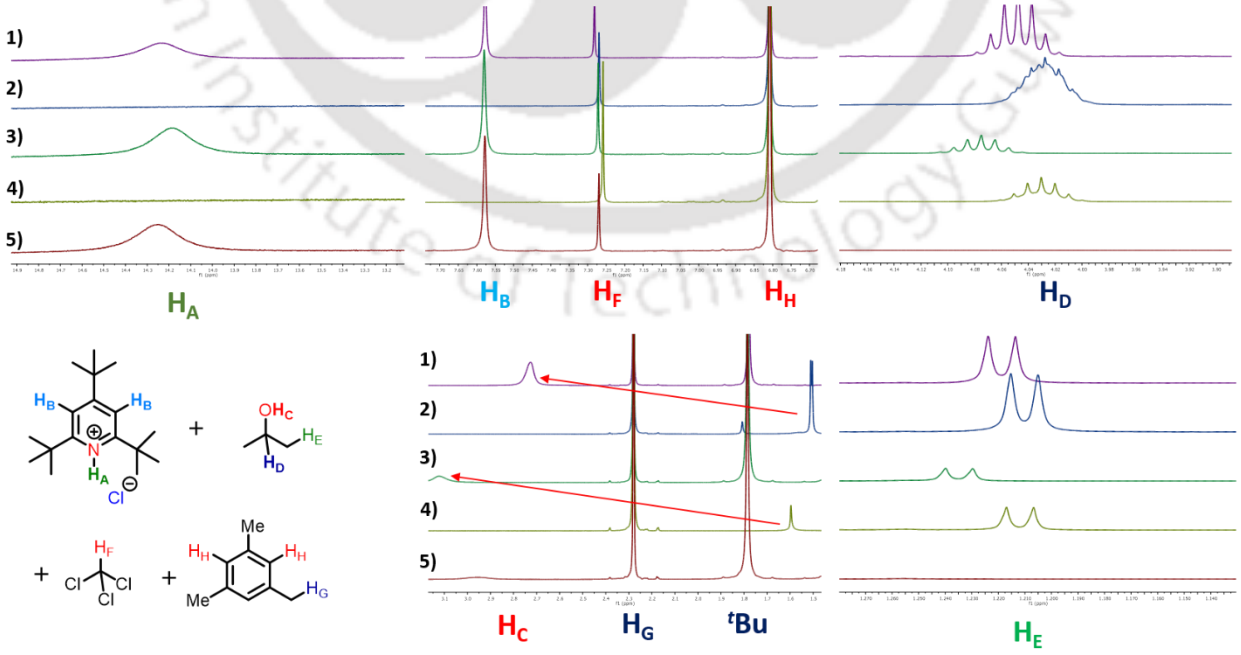
NMR Titration Experiments

^{1}H NMR titration of **16a** with 2-propanol in 0.6 ml solution of $CDCl_3$

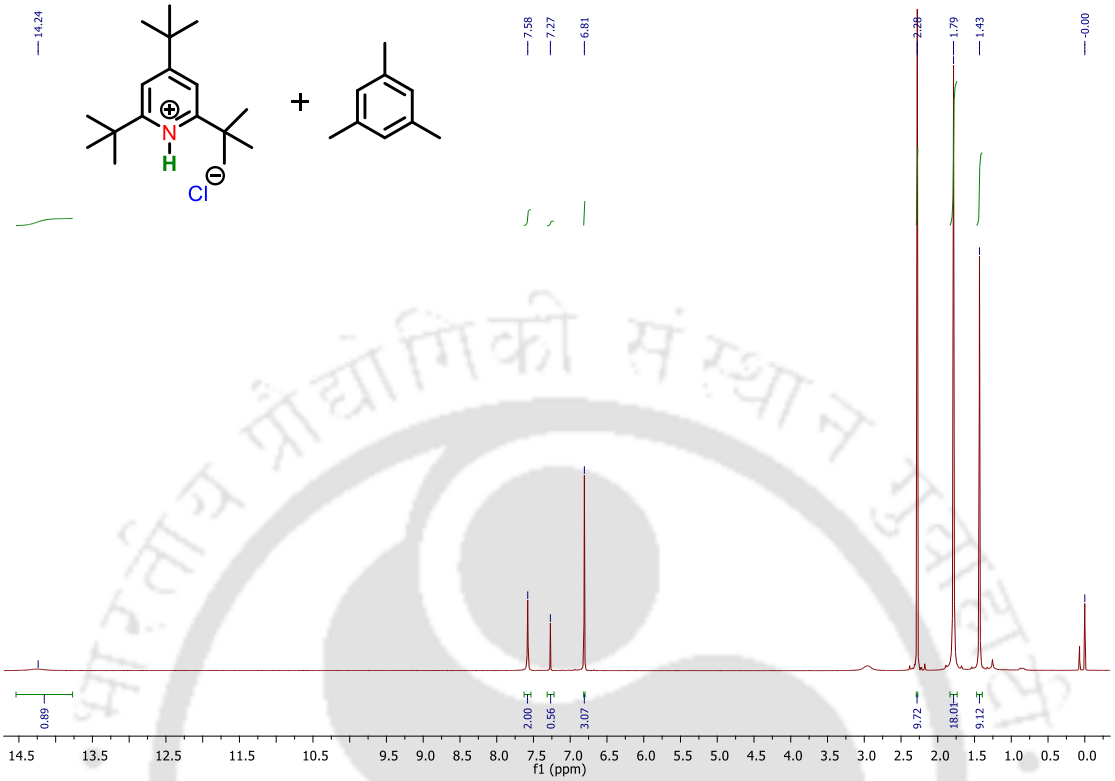


1) 0.018 mmol of **16a** and 0.108 mmol 2-propanol (1:6 ratio), 2) 0.108 mmol of 2-propanol, 3) 0.018 mmol of **16a** and 0.018 mmol of 2-propanol (1:1 ratio), 4) 0.018 mmol of 2-propanol, and 5) 0.018 mmol of **16a**. 0.018 mmol of mesitylene is used as an internal standard in all the experiments for the purpose of calibration.

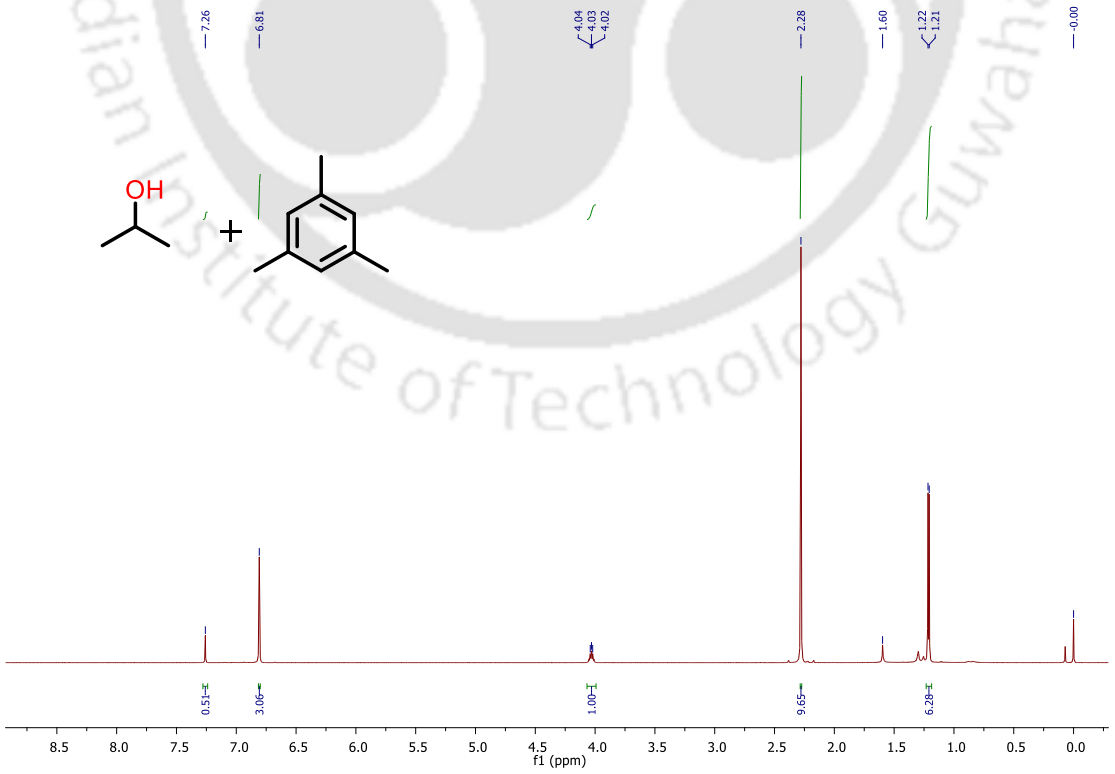
Specific regions expanded



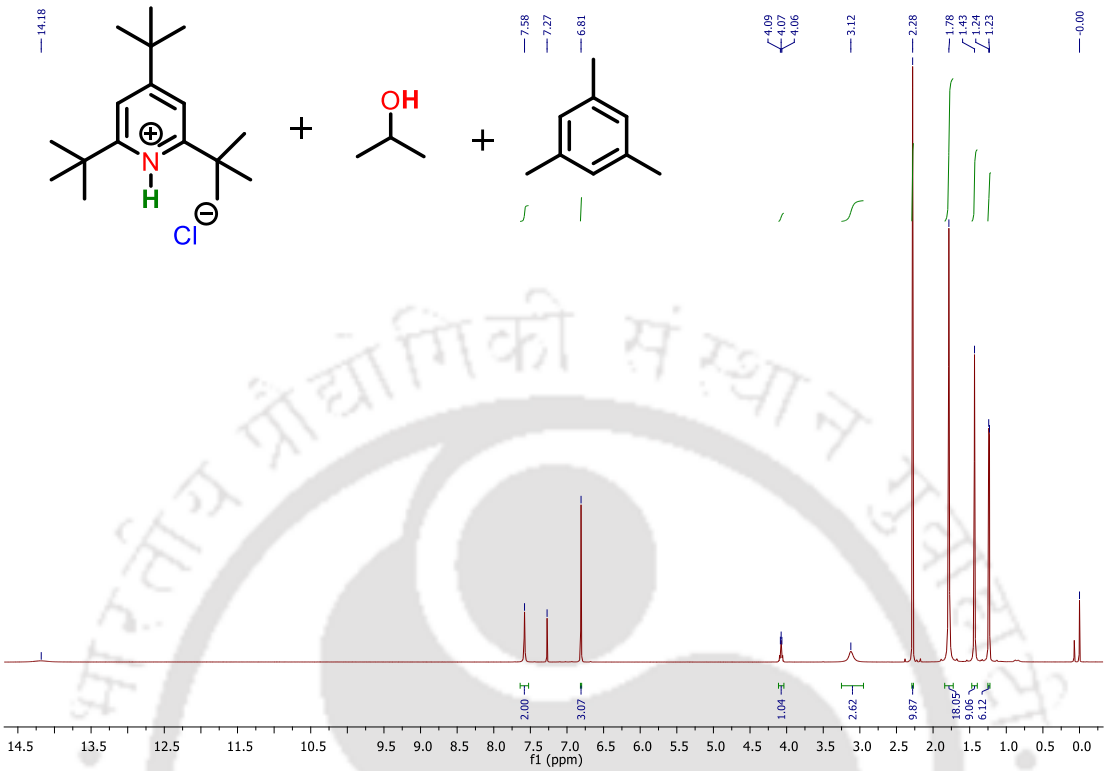
1:1 mixture of **16a** and mesitylene (0.018 mmol of each component in 0.6 ml of $CDCl_3$)



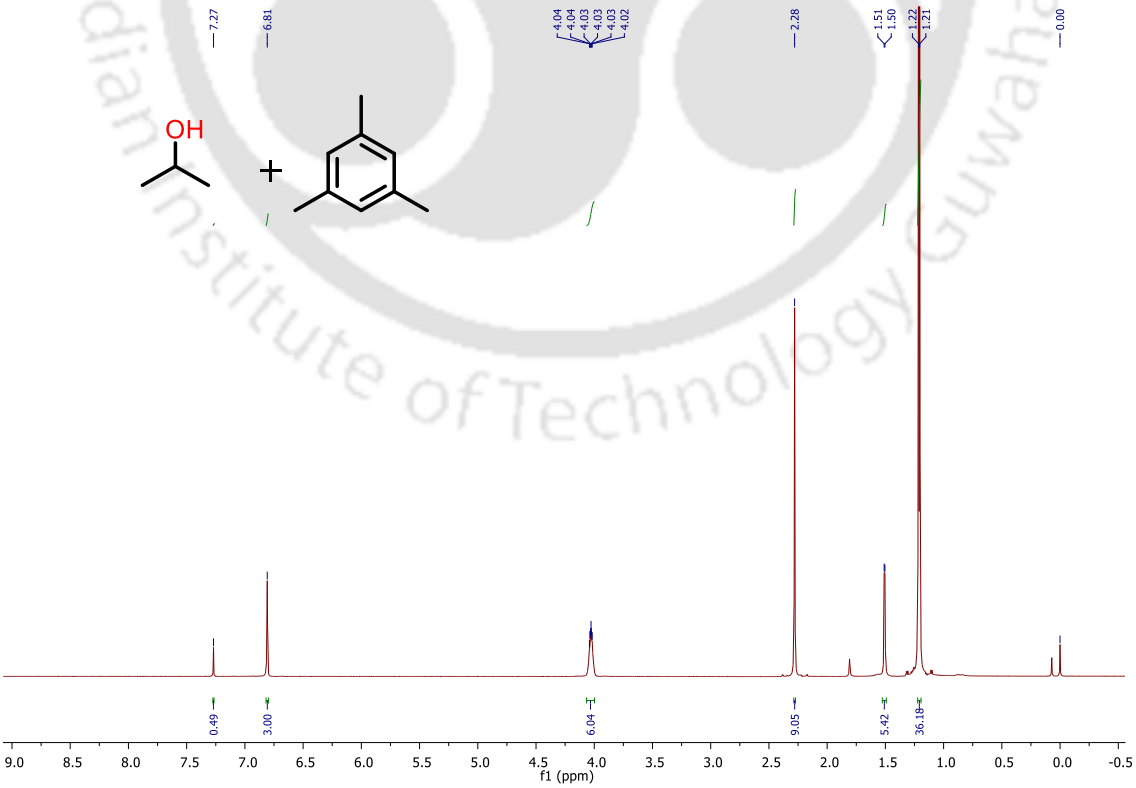
1:1 mixture of 2-propanol and mesitylene (0.018 mmol of each component in 0.6 ml of $CDCl_3$)



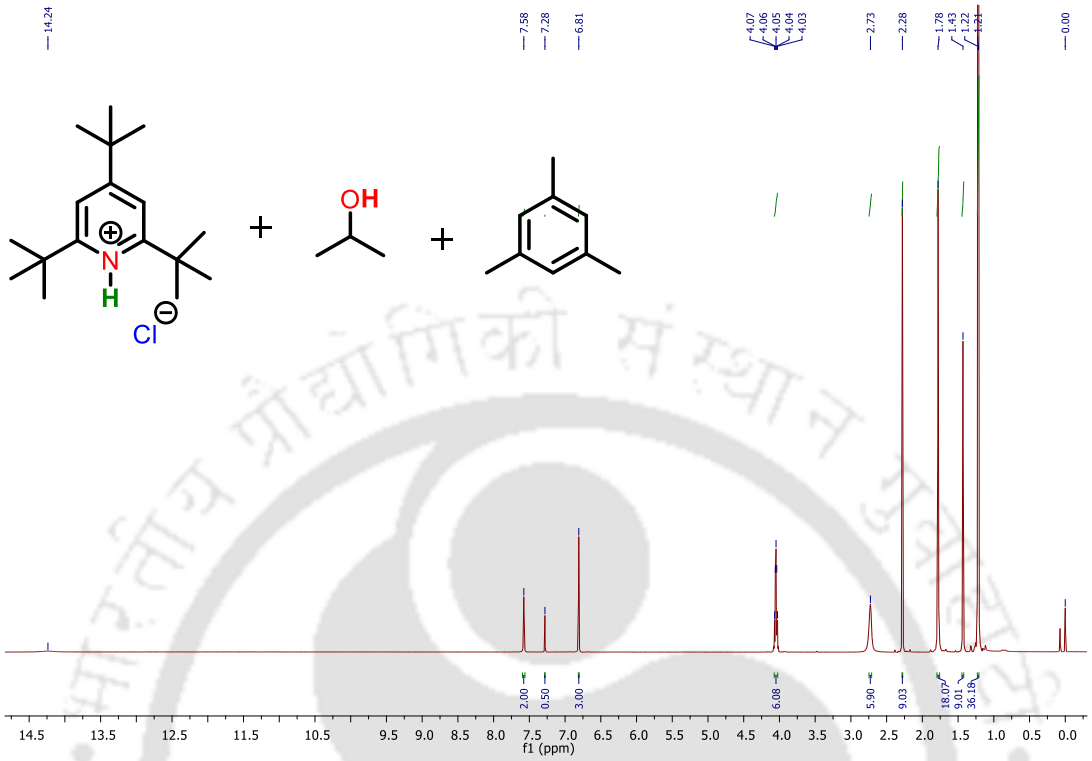
1:1:1 mixture of **16a**, 2-propanol and mesitylene (0.018 mmol of each component in 0.6 ml of $CDCl_3$)



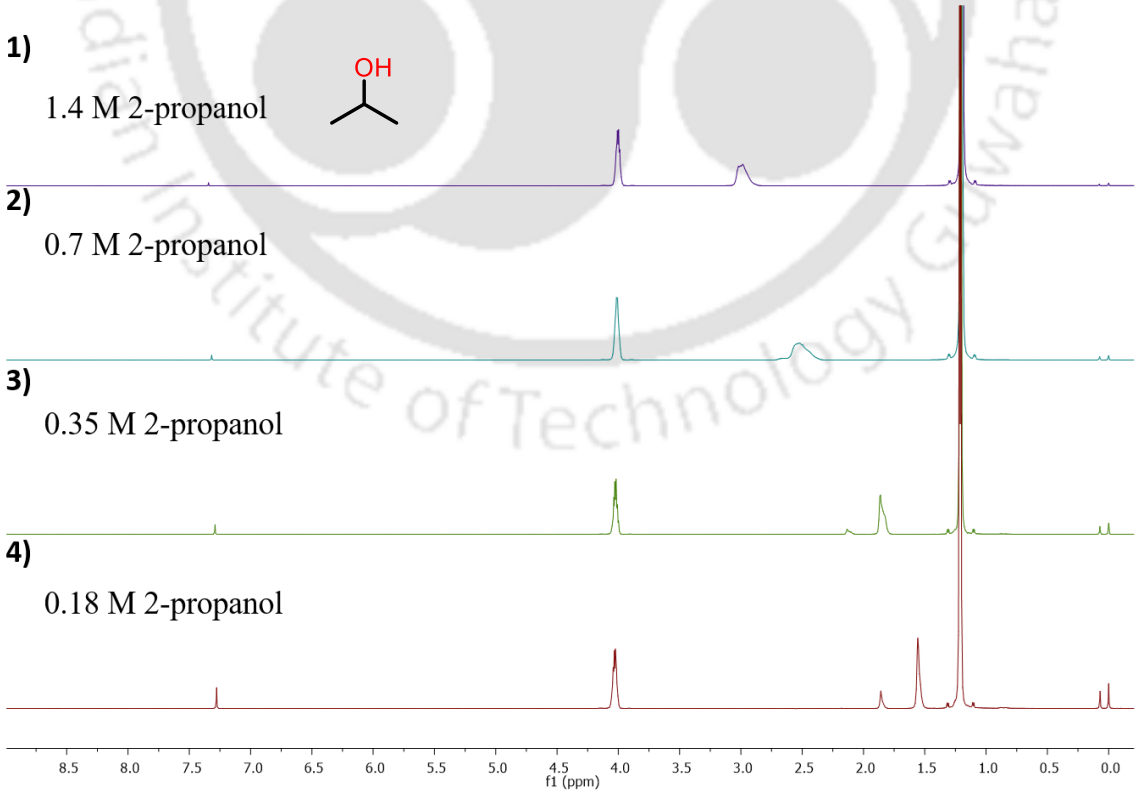
6:1 mixture of 2-propanol and mesitylene (0.018 mmol of mesitylene in 0.6 ml of $CDCl_3$)



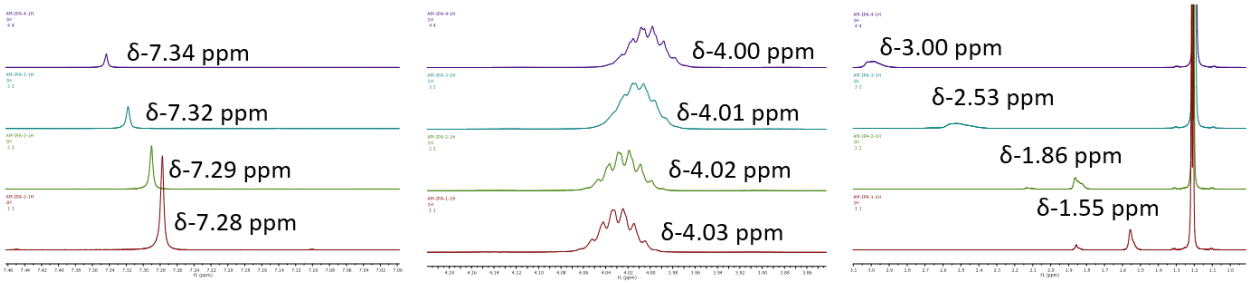
1:6:1 mixture of **16a**, 2-propanol and mesitylene (0.018 mmol of mesitylene in 0.6 ml of $CDCl_3$)

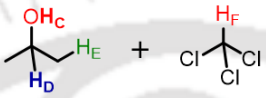


^{1}H NMR of 2-propanol with increasing concentration



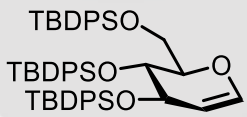
Specific regions expanded





Synthesis of Glycosyl Donors

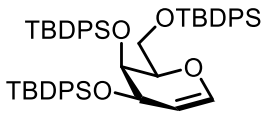
3,4,6-Tri-*O*-tertiary-butyldiphenylsilyl-D-glucal (15c):



D-Glucal (500 mg, 3.421 mmol, 1.0 equiv) was dissolved in 10 ml THF and 5 ml DMF. Then, to it imidazole (815 mg, 11.971 mmol, 3.5 equiv) followed by TBDPSCl (3.29 g, 3.1 ml, 11.969 mmol, 3.5 equiv) were added and this solution was heated at 70 °C for 12 h. [42] 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 in ethyl acetate/hexane solvent system to give the product as a white solid **15c**. R_f- 0.9 (10% ethyl acetate in hexane), amount- 2.6 g, yield- 89%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 (d, *J* = 6.8 Hz, 2H), 7.56 (ddd, *J* = 9.5, 8.0, 1.5 Hz, 4H), 7.43 (d, *J* = 6.8 Hz, 2H), 7.41 – 7.38 (m, 4H), 7.36 – 7.30 (m, 10H), 7.26 (t, *J* = 7.5 Hz, 2H), 7.23 – 7.16 (m, 6H), 6.27 (d, *J* = 6.4 Hz, 1H), 4.41 (ddd, *J* = 6.7, 5.2, 1.8 Hz, 1H), 4.25 (ddt, *J* = 7.6, 3.5, 1.8 Hz, 1H), 4.16 (dd, *J* = 11.6, 8.2 Hz, 1H), 3.95 (q, *J* = 2.0 Hz, 1H), 3.74 – 3.71 (m, 2H), 1.02 (s, 9H), 0.91 (s, 9H), 0.72 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.1, 135.9, 135.8, 135.8, 135.7, 135.5, 134.0, 133.9, 133.8, 133.7, 133.5, 133.3, 129.8, 129.7, 129.7, 129.6, 129.6, 127.9, 127.8,

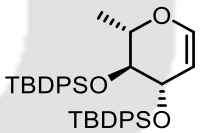
127.7, 127.7, 127.5, 100.3, 79.9, 70.4, 64.8, 62.6, 27.0, 26.9, 26.8, 19.3, 19.3, 18.9. HRMS (ESI) $C_{54}H_{64}O_4Si_3NH_4$ $[M+NH_4]^+$- calculated- 878.4451; found- 878.4456. $[\alpha]_D^{22}$= -21 (*c* 1.1, $CHCl_3$).

3,4,6-Tri-*O*-tertiary-butyldiphenylsilyl-D-galactal (15d):



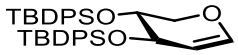
Procedure for the synthesis of **15d** was similar procedure of **15c** with D-galactal (500 mg, 3.421 mmol, 1.0 equiv) as the starting material to afford a white solid. R_f- 0.8 (10% ethyl acetate in hexane), amount- 2.45 g, yield- 84%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.72 – 7.21 (m, 30H), 5.90 (s, 1H), 4.39 (d, *J* = 11.0 Hz, 2H), 4.24 (s, 1H), 3.98 (s, 2H), 3.90 (s, 1H), 1.05 (d, *J* = 4.3 Hz, 18H), 0.80 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.5, 136.4, 136.3, 136.1, 135.8, 135.8, 134.4, 134.0, 133.5, 133.4, 130.3, 129.7, 129.6, 129.6, 129.5, 128.1, 127.8, 127.8, 127.7, 127.6, 127.4, 102.2, 79.3, 70.4, 64.4, 61.6, 27.2, 27.0, 27.0, 19.4, 19.2, 19.1. HRMS (ESI) $C_{54}H_{64}O_4Si_3NH_4$ $[M+NH_4]^+$- calculated- 878.4451; found- 878.4451. $[\alpha]_D^{22}$= -6 (*c* 0.04, $CHCl_3$).

3,4-Di-*O*-tertiary-butyldiphenylsilyl-L-rhamnal (15e):



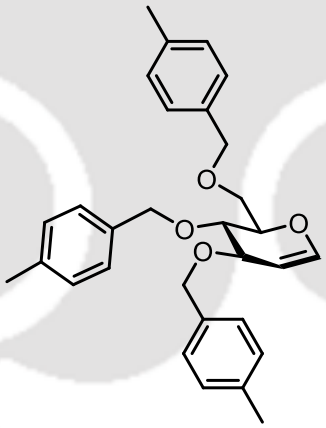
Procedure for the synthesis of **15e** was similar procedure of **15c** with L-rhamnal (500 mg, 3.841 mmol, 1.0 equiv) as the starting material to afford a white solid. R_f- 0.5 (50% cyclohexane in hexane), amount- 1.78 g, yield- 76%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (t, *J* = 7.5 Hz, 4H), 7.49 (t, *J* = 8.3 Hz, 4H), 7.41 – 7.36 (m, 4H), 7.33 (t, *J* = 7.4 Hz, 4H), 7.28 – 7.24 (m, 4H), 6.35 (d, *J* = 6.3 Hz, 1H), 4.56 (ddd, *J* = 6.6, 5.1, 1.8 Hz, 1H), 4.15 (tdd, *J* = 7.2, 5.2, 1.9 Hz, 1H), 3.93 (dt, *J* = 5.5, 2.4 Hz, 1H), 3.87 (d, *J* = 1.9 Hz, 1H), 1.32 (d, *J* = 7.0 Hz, 3H), 0.93 (s, 9H), 0.91 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.8, 136.0, 135.8, 135.8, 135.8, 135.7, 134.3, 134.1, 133.6, 133.6, 129.8, 129.8, 129.7, 129.7, 127.9, 127.7, 127.7, 127.6, 100.2, 74.0, 73.6, 65.7, 27.1, 27.0, 26.9, 26.9, 19.3, 19.2, 16.1. HRMS (ESI) $C_{38}H_{47}O_3Si_2$ $[M+H]^+$- calculated- 607.3058; found- 607.3056. $[\alpha]_D^{22}$= +12 (*c* 0.05, $CHCl_3$).

3,4-Di-*O*-tertiary-butyldiphenylsilyl-D-lyxal (15f):



Procedure for the synthesis of **15f** was similar procedure of **15c** with D-lyxal (500 mg, 4.306 mmol, 1.0 equiv) as the starting material to afford a white solid. R_f- 0.9 (100% in hexane), amount- 2.25 g, yield- 88%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 – 7.58 (m, 4H), 7.52 – 7.49 (m, 4H), 7.41 – 7.37 (m, 4H), 7.35 – 7.31 (m, 4H), 7.28 (q, *J* = 7.8 Hz, 4H), 6.44 (d, *J* = 6.2 Hz, 1H), 4.53 (ddd, *J* = 6.6, 5.2, 1.7 Hz, 1H), 3.95 – 3.93 (m, 1H), 3.87 (dt, *J* = 4.9, 2.1 Hz, 1H), 3.84 – 3.82 (m, 2H), 0.95 (s, 9H), 0.94 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 145.7, 136.0, 135.8, 135.8, 135.8, 134.4, 134.0, 133.8, 133.7, 129.8, 129.8, 129.7, 129.7, 127.8, 127.8, 127.7, 127.7, 127.6, 101.2, 69.8, 65.6, 64.4, 27.0, 27.0, 26.9, 19.3, 19.2. HRMS (ESI) $C_{37}H_{45}O_3Si_2$ $[M+H]^+$- calculated- 593.2902; found- 593.2902. $[\alpha]_D^{22}$= -62 (*c* 0.10, $CHCl_3$).

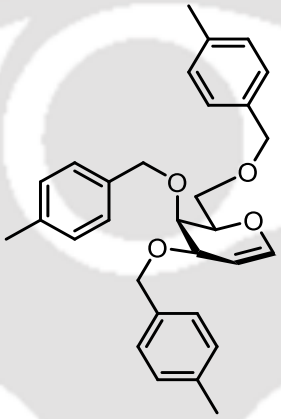
3,4,6-Tri-*O*-*para*-methylbenzyl-D-glucal (15g):



D-glucal (500 mg, 3.421 mmol, 1.0 equiv) was dissolved in DMF (20 ml) and kept in ice bath for 5 mins under argon. Then, to it NaH (480 mg, 20.000 mmol, 3.5 equiv) was added slowly. Then, 4-methyl benzyl bromide (2.2 g, 11.887 mmol, 3.5 equiv) was added dropwise slowly [41] and it was stirred for 24 h. Then, it was quenched with MeOH (5 ml). Now, the solvent was concentrated under reduced pressure 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 **15g**. R_f- 0.8 (20% ethyl acetate in hexane), amount-1.29 g, yield- 82%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 (dd, *J* = 8.1, 2.2 Hz, 4H), 7.14 – 7.10 (m, 8H), 6.40 (dd, *J* = 6.1, 1.4 Hz, 1H), 4.85

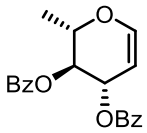
(dd, *J* = 6.2, 2.7 Hz, 1H), 4.77 (d, *J* = 11.0 Hz, 1H), 4.59 – 4.50 (m, 5H), 4.17 (ddd, *J* = 6.3, 2.7, 1.5 Hz, 1H), 4.02 (ddd, *J* = 8.4, 5.2, 2.8 Hz, 1H), 3.81 (dd, *J* = 8.7, 6.2 Hz, 1H), 3.78 – 3.71 (m, 2H), 2.34 (d, *J* = 2.9 Hz, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.8, 137.6, 137.5, 135.4, 135.3, 135.0, 129.2, 129.2, 128.2, 128.1, 128.0, 100.2, 76.9, 75.7, 74.3, 73.7, 73.5, 70.5, 68.4, 21.3. HRMS (ESI) $C_{30}H_{34}O_4NH_4$ $[M+NH_4]^+$- calculated- 476.2795; found- 476.2792. $[\alpha]_D^{22}$= -12 (*c* 0.06, $CHCl_3$).

3,4,6-Tri-*O*-*para*-methylbenzyl-D-galactal (15h):



Procedure for the synthesis of **15h** was similar procedure of **15g** with D-galactal (500 mg, 3.421 mmol, 1.0 equiv) as the starting material to afford a white solid. R_f- 0.7 (20% ethyl acetate in hexane), amount- 1.36 g, yield- 87%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24 – 7.11 (m, 12H), 6.35 (dd, *J* = 6.2, 1.6 Hz, 1H), 4.83 – 4.81 (m, 2H), 4.61 – 4.55 (m, 3H), 4.44 (d, *J* = 11.7 Hz, 1H), 4.35 (d, *J* = 11.7 Hz, 1H), 4.15 – 4.12 (m, 2H), 3.89 (dt, *J* = 4.0, 1.7 Hz, 1H), 3.72 (dd, *J* = 10.1, 7.1 Hz, 1H), 3.58 (dd, *J* = 10.1, 5.1 Hz, 1H), 2.34 (t, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.2, 137.5, 137.5, 137.4, 135.5, 135.4, 135.0, 129.2, 129.2, 129.1, 128.5, 128.2, 127.7, 100.2, 75.8, 73.4, 73.2, 70.8, 70.7, 68.4, 21.3. HRMS (ESI) $C_{30}H_{34}O_4NH_4$ $[M+NH_4]^+$- calculated- 476.2795; found- 476.2812. $[\alpha]_D^{22}$= -9 (*c* 0.05, $CHCl_3$).

3,4-Di-*O*-benzoyl-L-rhamnal (15i):

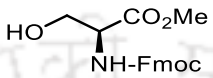


L-rhamnose monohydrate (1.1 g, 6.038 mmol, 1.0 equiv) was taken in DCM (10 ml) and cooled in an ice bath to 0 °C under argon. Then, pyridine (2.11 g, 2.15 ml, 26.675 mmol, 4.4 equiv) followed by benzoyl chloride (3.77 g, 3.11 ml, 26.819 mmol, 4.4 equiv) were added to it and stirred at rt for overnight. The reaction mixture was then concentrated under reduced pressure and extracted with ethyl acetate (3x40 ml). The organic phase was washed with brine (150 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 tetrabenzoate-L-rhamnose as a white solid. R_f- 0.8 (10% ethyl acetate in hexane), amount- 3.3 g, yield- 94%. For bromination, tetrabenzoate-L-rhamnose (3.3 g, 5.683 mmol, 1.0 equiv) was dissolved in DCM (15 ml) and kept in an ice bath at 0 °C under argon. Then, 33% (w/w) HBr in acetic acid (20 ml) was added slowly to it and stirred for overnight. After completion of the reaction, the reaction mixture was then concentrated and extracted with ethyl acetate (3x75 ml). The organic phase was washed with brine (3x100 ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford tribenzoate-L-rhamnosyl bromide as a white solid. R_f- 0.8 (10% ethyl acetate in hexane). After that, zinc (3.34 g, 51.085 mmol, 9.0 equiv) and $CuSO_4.5H_2O$ (1.45 g, 9.084 mmol, 1.6 equiv) were taken, and water (7 ml) followed by acetic acid (16.6 ml) were added slowly to it. Then, 20 ml of ether was added to crude tribenzoate rhamnosyl bromide, and this ether solution was added to that reaction mixture and stirred for 10 h at rt. Then, the reaction mixture was filtered, and the filtrate was extracted with ethyl acetate (3x25 ml). The organic phase was washed with brine (150 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 **15i**. R_f- 0.5 (20% ethyl acetate in hexane), amount- 1.9 g, yield- 83%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 (ddd, *J* = 16.8, 8.4, 1.4 Hz, 4H), 7.58 – 7.52 (m, 2H), 7.42 (dt, *J* = 10.5, 7.8 Hz, 4H), 6.54 (dd, *J* = 6.1, 1.4 Hz, 1H), 5.71 (ddd, *J* = 6.0, 3.2, 1.3 Hz, 1H), 5.51 (dd, *J* = 7.9, 6.0 Hz, 1H), 5.01 (dd, *J* = 6.1, 3.1 Hz, 1H), 4.36 (p, *J* = 6.7 Hz, 1H), 1.45 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.2, 165.6, 146.3, 133.5, 133.3, 130.0, 129.9, 129.8, 129.5, 128.6,

128.5, 98.9, 72.8, 72.1, 68.9, 16.8. HRMS (ESI) $C_{20}H_{18}O_5Na$ $[M+Na]^+$- calculated- 361.1046; found- 361.1050. $[\alpha]_D^{22}$= +82 (*c* 0.06, $CHCl_3$).

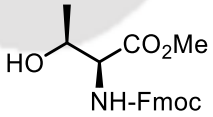
Synthesis of Glycosyl Acceptors

Methyl fmoc-serine (17h):



1 ml of thionyl chloride was added dropwise to 10 ml of methanol in ice bath under argon. After few min, fmoc-serine (500 mg, 1.527 mmol) was added dropwise to it and the reaction mixture was stirred at 0 °C under argon for 4 h. The solution was then concentrated under reduced pressure to get a white solid **17h**. The solid was washed with ether (3x5 ml). Amount- 510 mg, yield- 98%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 2H), 7.60 – 7.58 (m, 2H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 2H), 5.78 (s, 1H), 4.43 (d, *J* = 7.7 Hz, 3H), 4.22 (t, *J* = 6.9 Hz, 1H), 3.99 (d, *J* = 12.3 Hz, 1H), 3.91 (d, *J* = 11.4 Hz, 1H), 3.77 (s, 3H), 2.96 (br s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 156.5, 143.8, 143.7, 141.3, 141.3, 127.8, 127.1, 125.1, 120.0, 67.3, 63.0, 56.1, 52.7, 47.1. HRMS (ESI) $C_{19}H_{20}NO_5$ $[M+H]^+$- calculated- 342.1336; found- 342.1350. $[\alpha]_D^{22}$= +54 (*c* 0.10, $CHCl_3$).

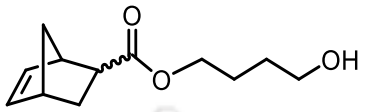
Methyl fmoc-threonine (17i):



1 ml of thionyl chloride was added dropwise to 10 ml of methanol in ice bath under argon. After few min, fmoc-threonine (500 mg, 1.464 mmol) was added dropwise to it and the reaction mixture was stirred at 0 °C under argon for 4 h. The solution was then concentrated under reduced pressure to get a white solid **17i**. The solid was washed with ether (3x5 ml). Amount- 470 mg, yield- 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.61 (t, *J* = 6.0 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 2H), 5.60 (s, 1H), 4.43 (d, *J* = 7.1 Hz, 2H), 4.34 (d, *J* = 7.7 Hz, 2H), 4.24 (t, *J* = 7.0 Hz, 1H), 3.78 (s, 3H), 1.91 (br s, 1H), 1.25 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 156.9, 144.0, 143.9, 141.5, 127.9, 127.2, 125.2, 120.1, 68.1, 67.4, 59.2,

52.8, 47.3, 20.0. HRMS (ESI) $C_{20}H_{22}NO_5$ $[M+H]^+$- calculated- 356.1492; found- 356.1508. $[\alpha]_D^{22}$= -85 (*c* 0.24, $CHCl_3$).

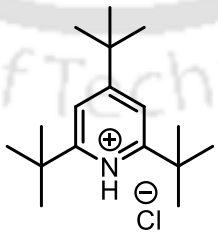
4-Hydroxybutyl-bicyclo[2.2.1]hept-5-ene-2-carboxylate (17j):



A mixture of bicyclo[2.2.1]hept-5-ene-2-carboxylic acid (2.77 g, 20.048 mmol, 1.0 equiv), DCC (6.00 g, 29.079 mmol, 1.45 equiv), DMAP (244 mg, 0.002 mol, 0.1 equiv) and 1,4-butanediol (5.41 g, 5.1 ml, 60.029 mmol, 3.0 equiv) was stirred in dry DCM (150 ml) under argon for 24 h. After removal of the solvent under reduced pressure, the crude product was purified by column chromatography in ethyl acetate/hexane system to give **17j** as transparent oil. R_f- 0.4 (20% ethyl acetate in hexane), amount- 3.20 g, yield- 76%, endo:exo= 6:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 (dd, *J* = 5.6, 3.1 Hz, 1H), 5.92 (dd, *J* = 5.6, 2.8 Hz, 1H), 4.06 (td, *J* = 6.4, 2.8 Hz, 2H), 3.67 (t, *J* = 6.3 Hz, 2H), 2.95 (dt, *J* = 9.2, 3.9 Hz, 1H), 2.91 (s, 1H), 1.93 – 1.87 (m, 2H), 1.73 – 1.67 (m, 2H), 1.66 – 1.61 (m, 2H), 1.44 – 1.39 (m, 2H), 1.29 – 1.26 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.0, 137.9, 132.4, 64.2, 62.4, 49.7, 45.8, 43.5, 42.6, 29.3, 29.3, 25.3. HRMS (ESI) $C_{12}H_{18}O_3Na$ $[M+Na]^+$- calculated- 233.1148; found- 233.1148.

Synthesis of Catalysts

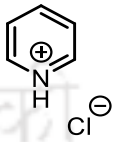
2,4,6-Tri-tertiary-butylpyridinium hydrochloride salt (16a):



2 ml of acetyl chloride was added dropwise to 2 ml of methanol in an ice bath under argon.[33] After few min, ether (1 ml) solution of 2,4,6-tri-tertiary-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 under argon for 1 h. The solution was then concentrated under reduced pressure to get a white

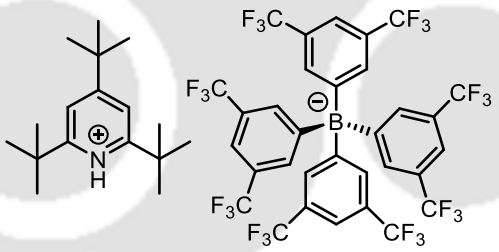
solid. The solid was washed with ether (5x5 ml) to afford **16a**. Amount- 535 mg, yield- 93%.^{1}H NMR (600 MHz, $CDCl_3$) δ 14.50 (br s, 1H), 7.55 (d, *J* = 1.3 Hz, 2H), 1.77 (s, 18H), 1.40 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.5, 165.9, 117.9, 37.7, 36.9, 30.3, 30.1.

Pyridinium hydrochloride salt (16b):



Procedure for the synthesis of **16b** was similar procedure of **16a** with pyridine (500 mg, 510 µl, 6.329 mmol). Amount- 675 mg, yield- 92%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 17.56 (br s, 1H), 8.87 (d, *J* = 5.7 Hz, 2H), 8.48 (t, *J* = 7.7 Hz, 1H), 8.00 (t, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.9, 140.1, 126.8.

2,4,6-Tri-tertiary-butylpyridinium hydrotetrakis[3,5 bis(trifluoromethyl)phenyl]borate salt (16c):



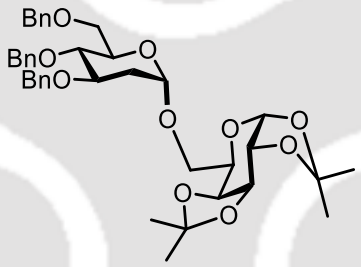
2,4,6-Tri-tertiary-butylpyridinium hydrochloride salt (100 mg, 0.352 mmol, 1.0 equiv) and sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (310 mg, 0.349 mmol, 1.0 equiv) were dissolved in 2 ml of DCM. After that, it was stirred at 0 °C for 1 h and immediately a white precipitate of sodium chloride (NaCl) was observed. Then, the solution was allowed to settle down for few min and after decant the solution, the solution part was then concentrated under reduced pressure to get a white solid **16c**. Amount- 357 mg, yield- 92%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.55 (br s, 1H), 7.69 – 7.65 (m, 10H), 7.51 (s, 4H), 1.43 (s, 18H), 1.37 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.8, 162.6, 162.3, 161.9, 161.6, 161.3, 134.9, 129.3, 129.1, 128.9, 128.7, 127.4, 125.6, 123.8, 121.9, 119.4, 117.6, 37.5, 36.9, 36.8, 30.0, 30.0, 28.9, 28.8.

General Procedure

Glycosyl donor (0.058 – 0.148 mmol, 1.0 equiv) and glycosyl acceptor (1.1 equiv) were taken in round-bottomed flask. Then, the catalyst was added and heated for 24 h in 0.5 ml (for 0.058 mmol) solvent [(at 40 °C in DCE for **16a** and **16b)** and (at rt in DCM for **16c**)] under argon. After cooling it to rt, the reaction mixture was quenched by water (1 ml for 0.058 mmol), and it was extracted with DCM (3x15 ml for 0.058 mmol), dried over Na_2SO_4 and concentrated under reduced pressure and purified by column chromatography in (hexane/ethyl acetate).

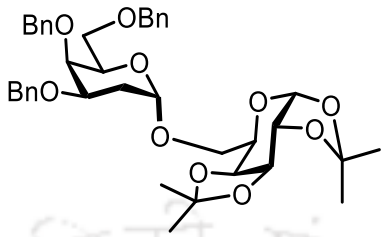
Scope of Derivative

(3,4,6-tri-*O*-benzyl-2-deoxy-α,β-D-glucopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (18a):



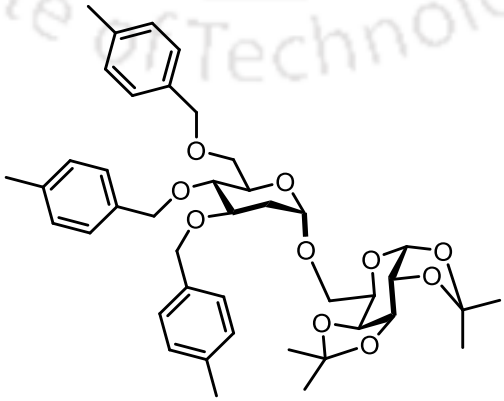
General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.120 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (7 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor **17d** (34 mg, 0.130 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18a**. R_f- 0.4 (20% ethyl acetate in hexane), amount- 62 mg, yield- 76%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.13 (m, 15H), 5.51 (d, *J* = 5.0 Hz, 1H), 5.02 (d, *J* = 3.1 Hz, 1H), 4.88 (d, *J* = 10.6 Hz, 1H), 4.69 – 4.63 (m, 2H), 4.62 – 4.57 (m, 1H), 4.54 – 4.48 (m, 2H), 4.31 (dd, *J* = 4.9, 2.4 Hz, 1H), 4.24 – 4.20 (m, 1H), 3.99 (ddd, *J* = 11.5, 9.1, 5.1 Hz, 1H), 3.94 (td, *J* = 6.7, 1.4 Hz, 1H), 3.83 – 3.75 (m, 2H), 3.72 (dt, *J* = 10.9, 6.8 Hz, 2H), 3.69 – 3.62 (m, 3H), 2.33 (dd, *J* = 12.8, 4.7 Hz, 1H), 1.73 (td, 1H), 1.52 (s, 3H), 1.43 (s, 3H), 1.34 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 138.7, 138.3, 128.6, 128.6, 128.5, 128.5, 128.5, 128.1, 128.1, 127.8, 109.4, 108.7, 97.4, 96.5, 78.3, 75.1, 73.6, 71.9, 71.1, 70.8, 68.8, 65.8, 65.5, 35.6, 26.3, 26.1, 25.1, 24.7.[43] HRMS (ESI) $C_{39}H_{48}O_{10}NH_4$ $[M+NH_4]^+$- calculated- 694.3586; found- 694.3592. $[\alpha]_D^{22}$= +14 (*c* 2.3, $CHCl_3$).

(3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactocopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (18b):



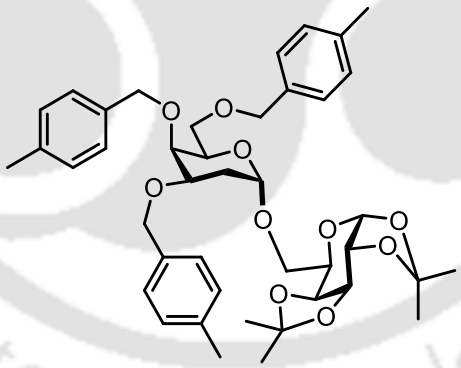
General procedure was followed by adding glycosyl donor **15b** (51 mg, 0.122 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (7 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor **17d** (34 mg, 0.130 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18b**. R_f- 0.5 (20% ethyl acetate in hexane), amount- 64 mg, yield- 79%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 – 7.24 (m, 15H), 5.52 (d, *J* = 5.0 Hz, 1H), 5.03 (d, *J* = 3.5 Hz, 1H), 4.92 (d, *J* = 11.6 Hz, 1H), 4.63 – 4.57 (m, 4H), 4.50 – 4.41 (m, 2H), 4.31 (dd, *J* = 5.1, 2.4 Hz, 1H), 4.21 (dd, *J* = 8.0, 1.9 Hz, 1H), 3.95 (ddt, *J* = 10.6, 7.1, 3.6 Hz, 4H), 3.74 (dd, *J* = 10.7, 6.8 Hz, 1H), 3.64 (ddd, *J* = 13.0, 10.0, 6.9 Hz, 2H), 3.54 (dd, *J* = 9.2, 5.6 Hz, 1H), 2.22 (td, *J* = 12.6, 3.7 Hz, 1H), 2.03 (dd, *J* = 12.8, 4.4 Hz, 1H), 1.51 (s, 3H), 1.42 (s, 3H), 1.33 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.0, 138.7, 138.2, 128.6, 128.5, 128.4, 128.3, 128.0, 127.8, 127.6, 127.5, 109.4, 108.7, 97.6, 96.5, 74.8, 74.5, 73.5, 72.9, 71.2, 70.8, 70.7, 70.5, 69.9, 69.3, 65.9, 65.6, 31.2, 26.3, 26.1, 25.1, 24.7.[43] HRMS (ESI) $C_{39}H_{48}O_{10}Na$ $[M+Na]^+$- calculated- 699.3140; found- 699.3171. $[\alpha]_D^{22}$= +23 (*c* 1.6, $CHCl_3$).

(3,4,6-tri-*O*-*para*-methylbenzyl-2-deoxy-α,β-D-glucopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (18c):



General procedure was followed by adding glycosyl donor **15g** (50 mg, 0.109 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (6 mg, 0.022 mmol, 20 mol %) and glycosyl acceptor **17d** (32 mg, 0.123 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18c**. R_f- 0.6 (20% ethyl acetate in hexane), amount- 70 mg, yield- 89%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 – 7.20 (m, 4H), 7.12 (t, *J* = 7.7 Hz, 4H), 7.07 (d, *J* = 7.6 Hz, 2H), 7.02 (d, *J* = 7.8 Hz, 2H), 5.51 (d, *J* = 5.0 Hz, 1H), 5.01 (d, *J* = 3.5 Hz, 1H), 4.81 (d, *J* = 10.5 Hz, 1H), 4.64 – 4.58 (m, 4H), 4.42 (dd, *J* = 15.1, 11.2 Hz, 2H), 4.30 (dd, *J* = 5.0, 2.4 Hz, 1H), 4.21 (dt, *J* = 8.0, 2.4 Hz, 1H), 3.97 – 3.92 (m, 2H), 3.78 – 3.58 (m, 6H), 2.33 (s, 3H), 2.32 (s, 3H), 2.32 (s, 3H), 2.29 (d, *J* = 5.0 Hz, 1H), 1.73 – 1.68 (m, 1H), 1.51 (s, 3H), 1.43 (s, 3H), 1.33 (d, *J* = 7.9 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 137.4, 137.4, 137.3, 137.3, 135.9, 135.6, 135.1, 129.2, 129.1, 129.1, 129.1, 128.3, 128.3, 127.9, 109.4, 108.7, 97.4, 96.4, 78.1, 77.5, 75.0, 73.4, 71.9, 71.0, 70.7, 70.7, 68.4, 65.7, 65.4, 35.5, 26.3, 26.1, 25.0, 24.7, 21.3, 21.3, 21.3. HRMS (ESI) $C_{42}H_{54}O_{10}NH_4$ $[M+NH_4]^+$- calculated- 736.4055; found- 736.4058. $[\alpha]_D^{22}$= +19 (*c* 0.10, $CHCl_3$).

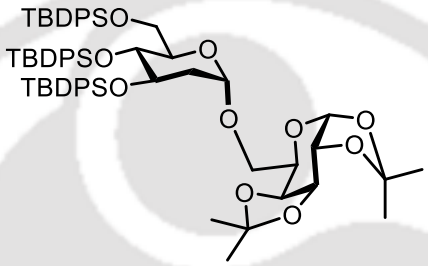
(3,4,6-tri-*O*-*para*-methylbenzyl-2-deoxy-α-D-galactopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (18d):



General procedure was followed by adding glycosyl donor **15h** (52 mg, 0.113 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (6 mg, 0.022 mmol, 20 mol %) and glycosyl acceptor **17d** (32 mg, 0.123 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18d**. R_f- 0.6 (20% ethyl acetate in hexane), amount- 67 mg, yield- 85%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 – 7.08 (m, 12H), 5.51 (d, *J* = 4.9 Hz, 1H), 5.01 (d, *J* = 3.1 Hz, 1H), 4.86 (d, *J* = 11.5 Hz, 1H), 4.80 – 4.50 (m, 4H), 4.43 (d, *J* = 11.6 Hz, 1H), 4.36 (d, *J* = 11.5 Hz, 1H), 4.30 (dd, *J* = 5.0, 2.4 Hz, 1H), 4.21 (dd, *J* = 7.9, 1.9 Hz, 1H), 3.96 – 3.89 (m, 4H), 3.73 (dd, *J* = 10.7, 6.8 Hz, 1H), 3.65 (dd, *J* = 10.7, 6.4 Hz, 1H), 3.57 (dd, *J* = 9.2, 7.5 Hz, 1H), 3.50 (dd, *J* = 9.1,

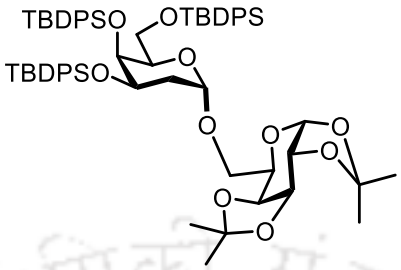
5.6 Hz, 1H), 2.34 (s, 6H), 2.31 (s, 3H), 2.20 (td, *J* = 12.4, 3.6 Hz, 1H), 2.01 – 1.98 (m, 1H), 1.51 (s, 3H), 1.42 (s, 3H), 1.33 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 137.5, 137.3, 137.2, 136.0, 135.7, 135.2, 129.2, 129.0, 128.6, 128.2, 127.6, 109.4, 108.7, 97.7, 96.5, 74.7, 74.2, 73.4, 72.5, 71.2, 70.8, 70.7, 70.4, 70.0, 69.1, 65.9, 65.6, 31.3, 26.2, 26.1, 25.1, 24.7, 21.3. HRMS (ESI) $C_{42}H_{54}O_{10}NH_4$ $[M+NH_4]^+$- calculated- 736.4055; found- 736.4042. $[\alpha]_D^{22}$= +20 (*c* 0.19, $CHCl_3$).

(3,4,6-tri-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (18e):



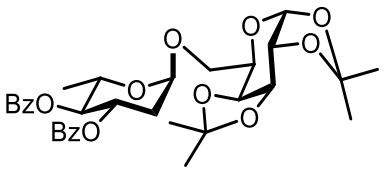
General procedure was followed by adding glycosyl donor **15c** (51 mg, 0.059 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (3 mg, 0.012 mmol, 20 mol %) and glycosyl acceptor **17d** (17 mg, 0.065 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18e**. R_f- 0.7 (10% ethyl acetate in hexane), amount- 56 mg, yield- 83%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63 (d, *J* = 6.8 Hz, 2H), 7.54 – 7.50 (m, 4H), 7.44 – 7.27 (m, 19H), 7.25 – 7.11 (m, 5H), 5.53 (d, *J* = 5.1 Hz, 1H), 5.03 (dd, *J* = 8.5, 3.6 Hz, 1H), 4.60 (dd, *J* = 7.9, 2.4 Hz, 1H), 4.31 (dd, *J* = 5.0, 2.4 Hz, 1H), 4.23 (dd, *J* = 7.9, 1.9 Hz, 1H), 4.03 – 3.99 (m, 3H), 3.92 (dd, *J* = 10.5, 6.5 Hz, 1H), 3.82 (dd, *J* = 10.9, 7.0 Hz, 1H), 3.77 – 3.73 (m, 2H), 3.65 (dd, *J* = 10.9, 4.4 Hz, 1H), 1.86 (ddd, *J* = 13.7, 8.5, 2.7 Hz, 1H), 1.64 (d, *J* = 4.2 Hz, 1H), 1.47 (s, 3H), 1.42 (s, 3H), 1.31 (s, 3H), 1.30 (s, 3H), 0.98 (s, 9H), 0.89 (s, 9H), 0.82 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 135.9, 135.9, 135.8, 135.8, 135.7, 135.7, 135.7, 133.8, 133.7, 133.7, 133.5, 133.4, 129.8, 129.7, 129.6, 129.6, 129.5, 127.7, 127.7, 127.7, 127.6, 109.2, 108.7, 96.5, 95.1, 78.3, 72.0, 71.1, 70.8, 70.8, 70.3, 66.2, 63.3, 33.5, 29.8, 27.0, 26.9, 26.2, 26.1, 25.1, 24.7, 19.3, 19.3, 19.1. HRMS (ESI) $C_{66}H_{84}O_{10}Si_3NH_4$ $[M+NH_4]^+$- calculated- 1138.5711; found- 1138.5714. $[\alpha]_D^{22}$= -91 (*c* 0.37, $CHCl_3$).

(3,4,6-tri-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-D-galactopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (18f):



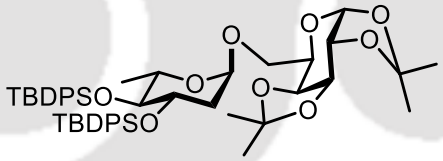
General procedure was followed by adding glycosyl donor **15d** (53 mg, 0.062 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (3 mg, 0.012 mmol, 20 mol %) and glycosyl acceptor **17d** (17 mg, 0.065 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18f**. R_f- 0.6 (10% ethyl acetate in hexane), amount- 53 mg, yield- 79%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 – 7.11 (m, 30H), 5.47 (d, *J* = 4.9 Hz, 1H), 4.89 (d, *J* = 3.4 Hz, 1H), 4.54 (dd, *J* = 7.9, 2.3 Hz, 1H), 4.28 (dd, *J* = 5.0, 2.3 Hz, 1H), 3.99 (ddd, *J* = 11.7, 4.2, 2.1 Hz, 1H), 3.95 (s, 1H), 3.79 (d, *J* = 8.0 Hz, 1H), 3.67 (t, *J* = 7.3 Hz, 1H), 3.54 (dd, *J* = 10.7, 7.1 Hz, 1H), 3.48 (dd, *J* = 9.6, 5.6 Hz, 1H), 3.39 – 3.38 (m, 1H), 3.34 (t, *J* = 9.1 Hz, 1H), 3.17 (dd, *J* = 10.7, 4.4 Hz, 1H), 2.34 (td, *J* = 12.2, 3.8 Hz, 1H), 1.54 (s, 3H), 1.41 (d, *J* = 4.9 Hz, 1H), 1.38 (s, 3H), 1.34 (s, 3H), 1.30 (s, 3H), 1.02 (s, 9H), 1.00 (s, 9H), 0.90 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 136.7, 136.4, 136.3, 136.0, 135.8, 135.6, 134.4, 134.3, 134.1, 133.7, 133.7, 132.8, 129.6, 129.6, 129.5, 129.3, 127.7, 127.6, 127.5, 127.3, 109.0, 108.5, 97.8, 96.5, 74.0, 72.2, 71.0, 70.6, 70.5, 70.0, 65.7, 64.8, 64.7, 33.6, 29.8, 27.3, 27.3, 27.0, 26.4, 26.1, 25.1, 24.6, 20.1, 19.1, 19.0. HRMS (ESI) $C_{66}H_{84}O_{10}Si_3NH_4$ $[M+NH_4]^+$- calculated- 1138.5711; found- 1138.5710. $[\alpha]_D^{22}$= +90 (*c* 1.3, $CHCl_3$).

(3,4-di-*O*-benzoyl-2-deoxy-α-L-rhamnosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (18g):



General procedure was followed by adding glycosyl donor **15i** (50 mg, 0.148 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (9 mg, 0.031 mmol, 20 mol %) and glycosyl acceptor **17d** (43 mg, 0.165 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18g**. R_f- 0.4 (20% ethyl acetate in hexane), amount- 72 mg, yield- 80%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 – 7.92 (m, 4H), 7.55 – 7.47 (m, 2H), 7.37 (dt, *J* = 12.7, 7.8 Hz, 4H), 5.63 (ddd, *J* = 11.5, 9.5, 5.3 Hz, 1H), 5.55 (d, *J* = 5.0 Hz, 1H), 5.22 (t, *J* = 9.7 Hz, 1H), 5.06 (d, *J* = 2.9 Hz, 1H), 4.67 (dd, *J* = 7.9, 2.4 Hz, 1H), 4.40 (dd, *J* = 7.9, 1.9 Hz, 1H), 4.34 (dd, *J* = 5.0, 2.4 Hz, 1H), 4.25 – 4.20 (m, 1H), 4.06 (td, *J* = 6.7, 1.9 Hz, 1H), 3.90 (dd, *J* = 9.8, 7.0 Hz, 1H), 3.62 (dd, *J* = 9.8, 6.3 Hz, 1H), 2.51 (ddd, *J* = 12.9, 5.3, 1.3 Hz, 1H), 1.97 (ddd, *J* = 12.9, 11.6, 3.7 Hz, 1H), 1.60 (s, 3H), 1.46 (s, 3H), 1.38 (s, 3H), 1.36 (s, 3H), 1.26 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.0, 166.0, 133.3, 133.2, 129.9, 129.8, 129.8, 129.8, 129.7, 128.6, 128.5, 128.5, 109.3, 108.8, 96.9, 96.4, 75.1, 71.0, 70.8, 70.7, 70.2, 66.7, 66.1, 65.2, 35.6, 26.3, 26.1, 25.1, 24.6, 17.6. HRMS (ESI) $C_{32}H_{38}O_{11}NH_4$ $[M+NH_4]^+$- calculated- 616.2752; found- 616.2752. $[\alpha]_D^{22}$ = -67 (*c* 0.42, $CHCl_3$).

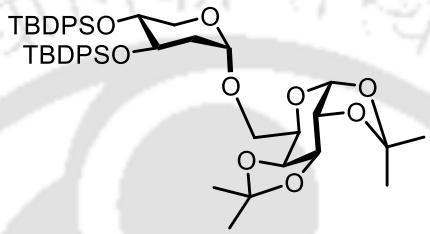
(3,4-di-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-L-rhamnosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (18h):



General procedure was followed by adding glycosyl donor **15e** (51 mg, 0.084 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (5 mg, 0.016 mmol, 20 mol %) and glycosyl acceptor **17d** (23 mg, 0.088 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18h**. R_f- 0.6 (10% ethyl acetate in hexane), amount- 59 mg, yield- 85%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 – 7.21 (m, 20H), 5.53 (d, *J* = 5.0 Hz, 1H), 4.99 (dd, *J* = 7.9, 3.8 Hz, 1H), 4.61 (dd, *J* = 7.9, 2.4 Hz, 1H), 4.31 (dd, *J* = 5.0, 2.4 Hz, 1H), 4.25 (dd, *J* = 7.9, 1.9 Hz, 1H), 4.09 (q, *J* = 3.2 Hz, 1H), 3.97 (ddd, *J* = 7.1, 5.5, 1.9 Hz, 1H), 3.91 (dd, *J* = 10.5, 5.5 Hz, 1H), 3.87 – 3.83 (m, 1H), 3.63 (dd, *J* = 10.5, 6.8 Hz, 1H), 3.54 (t, *J* = 3.6 Hz, 1H), 1.87 (ddd, *J* = 13.6, 7.9, 2.8 Hz, 1H), 1.73 (dt, *J* = 13.5, 4.1 Hz, 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). ^{13}C NMR (151 MHz, $CDCl_3$) δ 135.9, 135.9, 135.8, 135.8,

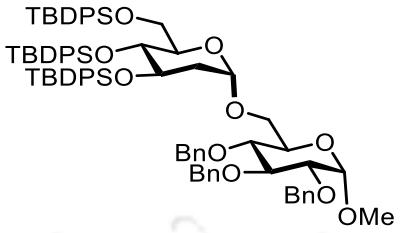
134.0, 133.9, 133.8, 133.7, 129.8, 129.7, 129.7, 127.8, 127.7, 127.7, 127.6, 127.6, 109.3, 108.7, 96.5, 95.1, 75.0, 72.7, 72.5, 71.4, 70.8, 70.7, 67.3, 66.3, 34.1, 27.1, 27.0, 27.0, 27.0, 26.9, 26.3, 26.1, 25.1, 24.6, 19.4, 19.2, 18.4. HRMS (ESI) $C_{50}H_{66}O_9Si_2NH_4$ $[M+NH_4]^+$- calculated- 884.4584; found- 884.4586. $[\alpha]_D^{22}$= -73 (*c* 0.74, $CHCl_3$).

(3,4-di-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-D-lyxosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (18i):



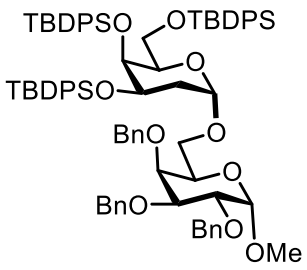
General procedure was followed by adding glycosyl donor **15f** (50 mg, 0.084 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (5 mg, 0.017 mmol, 20 mol %) and glycosyl acceptor **17d** (23 mg, 0.088 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18i**. R_f- 0.4 (10% ethyl acetate in hexane), amount- 57 mg, yield- 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.27 (m, 20H), 5.51 (d, *J* = 5.1 Hz, 1H), 4.76 (dd, *J* = 7.7, 2.3 Hz, 1H), 4.62 (dd, *J* = 8.0, 2.4 Hz, 1H), 4.32 (dd, *J* = 5.0, 2.4 Hz, 1H), 4.26 (dd, *J* = 7.9, 1.9 Hz, 1H), 4.12 (d, *J* = 3.9 Hz, 1H), 4.04 (t, *J* = 7.1 Hz, 1H), 3.77 – 3.68 (m, 2H), 3.59 (dd, *J* = 11.9, 2.1 Hz, 1H), 3.53 – 3.51 (m, 1H), 3.44 (dd, *J* = 11.9, 3.7 Hz, 1H), 1.87 (ddd, *J* = 13.0, 7.9, 3.2 Hz, 1H), 1.62 (dd, *J* = 5.1, 2.3 Hz, 1H), 1.50 (s, 3H), 1.43 (s, 3H), 1.33 (s, 6H), 1.01 (s, 9H), 0.98 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 136.1, 135.9, 135.9, 135.9, 135.8, 134.3, 134.1, 133.8, 133.6, 129.9, 129.8, 129.7, 129.7, 127.8, 127.7, 127.7, 127.6, 109.2, 108.7, 99.2, 96.5, 71.0, 70.9, 70.9, 70.7, 70.2, 67.2, 66.3, 65.1, 35.4, 29.8, 27.1, 27.1, 27.0, 26.2, 26.1, 25.2, 24.6, 19.3, 19.3. HRMS (ESI) $C_{49}H_{64}O_9Si_2NH_4$ $[M+NH_4]^+$- calculated- 870.4427; found- 870.4426. $[\alpha]_D^{22}$= -66 (*c* 0.12, $CHCl_3$).

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4,6-tri-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-D-glucopyranosyl)-α-D-glucopyranoside (18j):



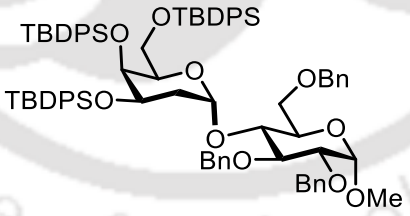
General procedure was followed by adding glycosyl donor **15c** (50 mg, 0.058 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (3 mg, 0.012 mmol, 20 mol %) and glycosyl acceptor **17a** (33 mg, 0.071 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18j**. R_f- 0.6 (10% ethyl acetate in hexane), amount- 62 mg, yield- 78%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 (d, *J* = 6.8 Hz, 2H), 7.52 (d, *J* = 6.8 Hz, 2H), 7.43 – 7.27 (m, 28H), 7.24 – 7.19 (m, 6H), 7.13 – 7.09 (m, 5H), 7.04 (t, *J* = 7.6 Hz, 2H), 5.35 (t, *J* = 4.9 Hz, 1H), 5.07 (dd, *J* = 8.9, 2.9 Hz, 1H), 4.97 (d, *J* = 10.9 Hz, 1H), 4.89 (t, *J* = 10.0 Hz, 2H), 4.82 – 4.75 (m, 2H), 4.67 (d, *J* = 12.2 Hz, 1H), 4.62 (d, *J* = 3.6 Hz, 1H), 4.41 – 4.39 (m, 1H), 3.99 – 3.93 (m, 4H), 3.71 (d, *J* = 5.6 Hz, 2H), 3.61 – 3.58 (m, 2H), 3.53 (dd, *J* = 9.6, 3.6 Hz, 1H), 3.36 (s, 3H), 1.89 (ddd, *J* = 12.4, 9.1, 2.8 Hz, 1H), 1.68 – 1.66 (m, 1H), 0.97 (s, 9H), 0.81 (s, 9H), 0.76 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.2, 138.7, 138.5, 136.2, 135.9, 135.8, 135.7, 135.7, 133.8, 133.7, 133.7, 133.6, 133.5, 133.3, 129.8, 129.7, 129.6, 129.6, 128.6, 128.6, 128.5, 128.5, 128.2, 128.1, 128.0, 128.0, 127.9, 127.7, 127.7, 127.7, 127.6, 127.6, 98.4, 94.1, 82.3, 80.0, 79.5, 77.6, 75.9, 75.3, 73.5, 71.5, 70.4, 69.5, 65.3, 62.6, 55.2, 33.9, 27.0, 26.9, 26.9, 19.3, 19.2, 19.0. HRMS (ESI) $C_{82}H_{96}O_{10}Si_3NH_4$ $[M+NH_4]^+$- calculated- 1342.6650; found- 1342.6650. $[\alpha]_D^{22}$= -59 (*c* 0.06, $CHCl_3$).

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4,6-tri-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-D-galactopyranosyl)-α-D-galactopyranoside (18k):



General procedure was followed by adding glycosyl donor **15d** (52 mg, 0.060 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (3 mg, 0.012 mmol, 20 mol %) and glycosyl acceptor **17b** (33 mg, 0.071 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18k**. R_f- 0.6 (10% ethyl acetate in hexane), amount- 65 mg, yield- 82%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 – 7.06 (m, 45H), 5.01 (d, *J* = 11.6 Hz, 1H), 4.85 – 4.81 (m, 2H), 4.77 (d, *J* = 12.0 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.57 (d, *J* = 3.6 Hz, 1H), 4.51 (d, *J* = 3.5 Hz, 1H), 4.44 (d, *J* = 11.7 Hz, 1H), 4.02 (dd, *J* = 10.0, 3.6 Hz, 1H), 3.90 (dd, *J* = 10.0, 2.9 Hz, 2H), 3.82 (d, *J* = 2.0 Hz, 1H), 3.67 (d, *J* = 2.9 Hz, 1H), 3.58 (dt, *J* = 9.1, 6.3 Hz, 2H), 3.49 (dt, *J* = 8.0, 4.3 Hz, 1H), 3.39 – 3.36 (m, 1H), 3.21 (t, *J* = 8.9 Hz, 1H), 3.16 (s, 3H), 2.99 (dd, *J* = 11.0, 3.5 Hz, 1H), 2.23 (td, *J* = 12.6, 3.9 Hz, 1H), 1.20 (dd, *J* = 12.1, 4.1 Hz, 1H), 1.00 (s, 9H), 1.00 (s, 9H), 0.84 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.1, 138.7, 138.5, 136.6, 136.3, 136.2, 136.0, 135.8, 135.5, 134.2, 134.0, 134.0, 133.7, 133.4, 132.5, 129.7, 129.6, 129.5, 129.4, 129.4, 129.2, 128.6, 128.5, 128.5, 128.3, 128.2, 127.8, 127.7, 127.6, 127.6, 127.5, 127.5, 127.4, 127.3, 98.7, 97.6, 79.4, 74.6, 74.4, 73.9, 73.5, 72.3, 69.9, 68.8, 65.2, 64.3, 55.4, 33.5, 27.3, 27.3, 26.9, 20.1, 19.0, 18.9. HRMS (ESI) $C_{82}H_{96}O_{10}Si_3NH_4$ $[M+NH_4]^+$- calculated- 1342.6650; found- 1342.6663. $[\alpha]_D^{22}$= +28 (*c* 0.19, $CHCl_3$).

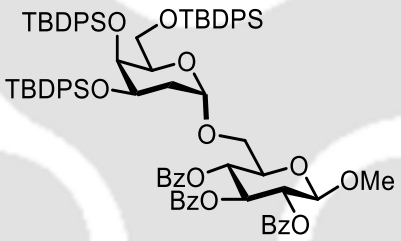
Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(3,4,6-tri-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-D-galactopyranosyl)-α-D-glucopyranoside (18l):



General procedure was followed by adding glycosyl donor **15d** (50 mg, 0.058 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (3 mg, 0.012 mmol, 20 mol %) and glycosyl acceptor **17c** (33 mg, 0.071 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18l**. R_f- 0.7 (10% ethyl acetate in hexane), amount- 62 mg, yield- 59%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.58 (m, 2H), 7.51 – 7.27 (m, 28H), 7.25 – 7.17 (m, 8H), 7.09 – 7.06 (m, 2H), 6.99 – 6.90 (m, 5H), 5.41 (d, *J* = 3.6 Hz, 1H), 4.90 (d, *J* = 11.1 Hz, 1H), 4.70 (d, *J* = 12.0 Hz, 1H), 4.59 – 4.51 (m, 2H), 4.40 (d, *J* = 11.2 Hz, 1H), 4.33 (d, *J* = 12.1 Hz, 1H), 4.15 (d, *J* =

12.1 Hz, 1H), 3.73 (d, *J* = 11.8 Hz, 1H), 3.66 – 3.55 (m, 3H), 3.45 (s, 3H), 3.41 – 3.37 (m, 3H), 3.33 (d, *J* = 10.3 Hz, 1H), 3.19 (dd, *J* = 10.7, 6.1 Hz, 1H), 3.09 (d, *J* = 7.9 Hz, 1H), 2.82 (d, *J* = 10.7 Hz, 1H), 2.23 (td, *J* = 11.7, 3.0 Hz, 1H), 1.28 (d, *J* = 4.1 Hz, 1H), 1.01 (s, 9H), 0.97 (s, 9H), 0.87 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 138.4, 138.2, 136.7, 136.3, 136.2, 136.1, 136.0, 135.8, 134.1, 134.0, 133.7, 133.6, 132.7, 129.9, 129.7, 129.7, 129.4, 129.2, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 127.9, 127.7, 127.7, 127.6, 127.5, 127.2, 97.8, 82.5, 80.2, 77.4, 75.1, 74.7, 73.4, 73.3, 72.9, 72.6, 70.1, 70.0, 69.9, 55.2, 34.0, 27.4, 27.3, 27.1, 20.1, 19.0. HRMS (ESI) $C_{82}H_{96}O_{10}Si_3NH_4$ $[M+NH_4]^+$- calculated- 1342.6650; found- 1342.6653. $[\alpha]_D^{22}$= +47 (*c* 0.12, $CHCl_3$).

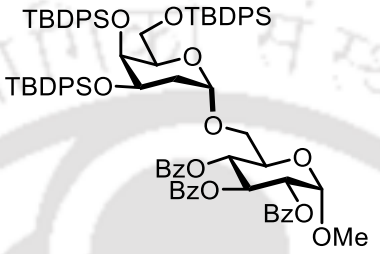
Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(3,4,6-tri-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-D-galactopyranosyl)-β-D-glucopyranoside (18m):



General procedure was followed by adding glycosyl donor **15d** (51 mg, 0.059 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (3 mg, 0.012 mmol, 20 mol %) and glycosyl acceptor **17f** (36 mg, 0.071 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18m**. R_f- 0.4 (10% ethyl acetate in hexane), amount- 66 mg, yield- 80%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.7 Hz, 2H), 7.82 (d, *J* = 7.7 Hz, 2H), 7.75 (d, *J* = 7.7 Hz, 2H), 7.64 (d, *J* = 7.4 Hz, 2H), 7.54 – 7.04 (m, 37H), 5.82 (t, *J* = 9.7 Hz, 1H), 5.43 – 5.36 (m, 2H), 4.91 (d, *J* = 3.5 Hz, 1H), 4.57 (d, *J* = 7.9 Hz, 1H), 4.21 (dt, *J* = 11.4, 3.3 Hz, 1H), 3.81 (s, 1H), 3.77 (dd, *J* = 11.1, 5.1 Hz, 1H), 3.71 (ddd, *J* = 10.1, 5.2, 2.5 Hz, 1H), 3.51 (dd, *J* = 10.7, 8.2 Hz, 1H), 3.43 (dd, *J* = 11.2, 2.5 Hz, 1H), 3.35 (dd, *J* = 8.3, 3.2 Hz, 1H), 3.29 (s, 3H), 2.74 (dd, *J* = 10.8, 3.2 Hz, 1H), 2.32 (td, *J* = 12.5, 3.8 Hz, 1H), 1.49 (dd, *J* = 12.5, 4.2 Hz, 1H), 1.05 (s, 9H), 0.97 (s, 9H), 0.82 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.1, 165.4, 165.2, 136.6, 136.3, 136.2, 136.2, 136.1, 135.8, 135.8, 135.6, 134.3, 134.2, 134.1, 133.7, 133.6, 133.3, 133.2, 132.6, 130.0, 129.8, 129.8, 129.8, 129.5, 129.4, 129.4, 129.2, 129.2, 129.1, 128.5, 128.4, 128.4, 127.6, 127.6, 127.5, 127.3,

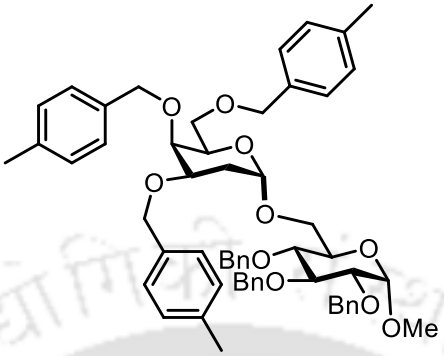
101.9, 97.7, 73.7, 73.6, 73.5, 72.2, 72.0, 69.8, 69.8, 65.1, 64.9, 56.9, 33.3, 29.8, 27.4, 27.3, 26.9, 20.1, 19.2, 18.9. HRMS (ESI) $C_{82}H_{90}O_{13}Si_3NH_4$ $[M+NH_4]^+$- calculated- 1384.6027; found- 1384.6037. $[\alpha]_D^{22}$= +20 (*c* 0.14, $CHCl_3$).

Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(3,4,6-tri-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-D-galactopyranosyl)-α-D-glucopyranoside (18n):



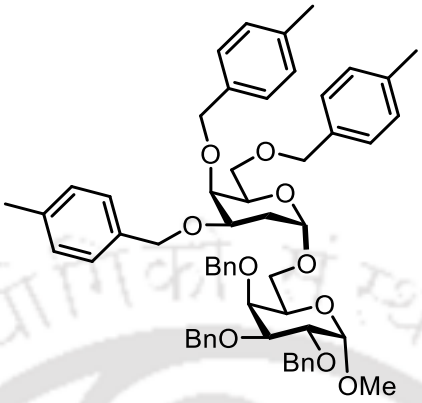
General procedure was followed by adding glycosyl donor **15d** (53 mg, 0.062 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (3 mg, 0.012 mmol, 20 mol %) and glycosyl acceptor **17e** (36 mg, 0.071 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18n**. R_f- 0.8 (10% ethyl acetate in hexane), amount- 70 mg, yield- 85%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.3 Hz, 2H), 7.86 (d, *J* = 7.3 Hz, 2H), 7.76 (d, *J* = 7.6 Hz, 2H), 7.65 (d, *J* = 7.3 Hz, 2H), 7.53 – 7.19 (m, 31H), 7.16 (d, *J* = 7.3 Hz, 2H), 7.07 (t, *J* = 7.5 Hz, 2H), 7.01 (t, *J* = 7.5 Hz, 2H), 6.07 (t, *J* = 9.9 Hz, 1H), 5.44 (t, *J* = 9.9 Hz, 1H), 5.18 (dd, *J* = 10.3, 3.7 Hz, 1H), 5.07 (d, *J* = 3.7 Hz, 1H), 4.94 (d, *J* = 3.4 Hz, 1H), 4.28 (dt, *J* = 11.4, 3.8 Hz, 1H), 3.98 (ddd, *J* = 10.3, 4.8, 2.3 Hz, 1H), 3.82 (d, *J* = 4.8 Hz, 1H), 3.79 (s, 1H), 3.53 (dd, *J* = 10.8, 8.3 Hz, 1H), 3.40 (d, *J* = 11.8 Hz, 1H), 3.37 (d, *J* = 2.9 Hz, 1H), 3.25 (s, 3H), 2.72 (dd, *J* = 10.9, 3.0 Hz, 1H), 2.36 (td, *J* = 12.2, 3.6 Hz, 1H), 1.20 (d, *J* = 4.4 Hz, 1H), 1.07 (s, 9H), 0.95 (s, 9H), 0.79 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.0, 166.0, 165.3, 136.6, 136.3, 136.1, 135.9, 135.6, 134.3, 134.0, 133.7, 133.7, 133.5, 133.2, 133.2, 132.7, 130.1, 129.8, 129.8, 129.7, 129.6, 129.5, 129.4, 129.4, 129.3, 129.2, 128.6, 128.4, 127.6, 127.6, 127.5, 127.5, 127.2, 97.7, 96.9, 73.7, 72.3, 72.1, 71.0, 69.7, 69.3, 68.7, 65.3, 64.7, 55.4, 33.4, 27.5, 27.3, 26.8, 20.1, 19.3, 18.9. HRMS (ESI) $C_{82}H_{90}O_{13}Si_3NH_4$ $[M+NH_4]^+$- calculated- 1384.6027; found- 1384.6026. $[\alpha]_D^{22}$= +89 (*c* 0.73, $CHCl_3$).

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4,6-tri-*O*-*para*-methylbenzyl-2-deoxy-α-D-galactopyranosyl)-α-D-glucopyranoside (18o):



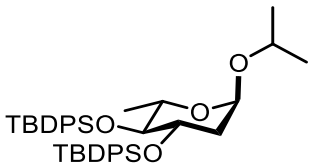
General procedure was followed by adding glycosyl donor **15h** (51 mg, 0.111 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (6 mg, 0.022 mmol, 20 mol %) and glycosyl acceptor **17a** (56 mg, 0.121 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18o**. R_f- 0.6 (20% ethyl acetate in hexane), amount- 85 mg, yield- 84%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.06 (m, 27H), 5.00 (d, *J* = 3.0 Hz, 1H), 4.98 (d, *J* = 10.8 Hz, 1H), 4.86 – 4.77 (m, 4H), 4.67 (d, *J* = 12.1 Hz, 1H), 4.59 (d, *J* = 3.6 Hz, 1H), 4.54 (d, *J* = 11.3 Hz, 1H), 4.55 – 4.51 (m, 3H), 4.36 (d, *J* = 11.6 Hz, 1H), 4.28 (d, *J* = 11.5 Hz, 1H), 3.98 (t, *J* = 9.3 Hz, 1H), 3.83 (q, *J* = 6.4 Hz, 3H), 3.80 (dd, *J* = 11.5, 4.9 Hz, 1H), 3.70 (ddd, *J* = 10.0, 4.7, 1.8 Hz, 1H), 3.60 (dd, *J* = 11.4, 1.9 Hz, 1H), 3.53 – 3.44 (m, 4H), 3.30 (s, 3H), 2.33 (s, 3H), 2.31 (s, 3H), 2.28 (s, 3H), 2.18 (td, *J* = 12.2, 3.6 Hz, 1H), 1.98 (dd, *J* = 12.7, 4.4 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.8, 138.3, 138.3, 138.2, 137.4, 137.4, 137.3, 136.0, 135.9, 135.4, 135.2, 135.2, 129.2, 129.1, 129.0, 128.6, 128.6, 128.5, 128.2, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.7, 98.4, 97.9, 82.3, 80.1, 78.0, 76.0, 75.2, 74.1, 73.4, 73.3, 72.5, 70.2, 69.9, 69.4, 66.1, 55.1, 31.2, 21.3, 21.3. HRMS (ESI) $C_{58}H_{66}O_{10}NH_4$ $[M+NH_4]^+$- calculated- 940.4994; found- 940.4994. $[\alpha]_D^{22}$= +50 (*c* 0.48, $CHCl_3$).

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4,6-tri-*O*-*para*-methylbenzyl-2-deoxy-α-D-galactopyranosyl)-α-D-galactopyranoside (18p):



General procedure was followed by adding glycosyl donor **15h** (50 mg, 0.109 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (6 mg, 0.022 mmol, 20 mol %) and glycosyl acceptor **17b** (56 mg, 0.121 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18p**. R_f- 0.5 (20% ethyl acetate in hexane), amount- 80 mg, yield- 79%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.08 (m, 27H), 4.92 (d, *J* = 11.6 Hz, 1H), 4.88 – 4.80 (m, 3H), 4.74 (d, *J* = 11.7 Hz, 1H), 4.69 (s, 1H), 4.66 – 4.64 (m, 1H), 4.58 – 4.49 (m, 4H), 4.46 – 4.41 (m, 1H), 4.33 (d, *J* = 11.4 Hz, 1H), 4.03 (dd, *J* = 10.0, 3.5 Hz, 1H), 3.92 (dd, *J* = 10.1, 2.6 Hz, 1H), 3.86 – 3.75 (m, 5H), 3.62 (dd, *J* = 9.7, 6.3 Hz, 1H), 3.56 – 3.46 (m, 3H), 3.34 – 3.28 (m, 1H), 3.25 (s, 3H), 2.32 (s, 9H), 2.11 (td, *J* = 12.5, 3.8 Hz, 1H), 1.75 (dd, *J* = 12.7, 4.6 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9, 138.5, 138.5, 137.5, 137.4, 137.3, 135.9, 135.5, 135.0, 129.2, 129.0, 128.6, 128.5, 128.5, 128.4, 128.2, 128.2, 127.9, 127.7, 127.7, 127.5, 98.8, 97.9, 79.3, 76.7, 75.0, 74.7, 74.2, 74.2, 73.7, 73.6, 73.4, 72.4, 70.2, 69.9, 69.2, 68.9, 66.1, 55.3, 31.3, 21.3, 21.3. HRMS (ESI) $C_{58}H_{66}O_{10}NH_4$ $[M+NH_4]^+$- calculated- 940.4994; found- 940.4977. $[\alpha]_D^{22}$= +82 (*c* 0.57, $CHCl_3$).

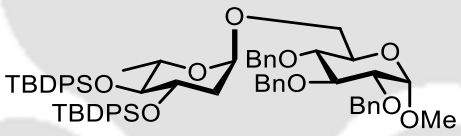
Isopropyl-3,4-di-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-L-rhamnosepyranoside (18q):



General procedure was followed by adding glycosyl donor **15e** (51 mg, 0.084 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (5 mg, 0.016 mmol, 20 mol %) and

glycosyl acceptor isopropanol (5 mg, 8 µl, 0.083 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18q**. R_f- 0.5 (100% in hexane), amount- 51 mg, yield- 96%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, *J* = 6.7 Hz, 2H), 7.51 (d, *J* = 6.8 Hz, 2H), 7.46 (t, *J* = 8.2 Hz, 4H), 7.41 – 7.34 (m, 4H), 7.30 (q, *J* = 7.3 Hz, 4H), 7.27 – 7.21 (m, 4H), 5.07 (dd, *J* = 8.5, 3.4 Hz, 1H), 4.08 (q, *J* = 3.2 Hz, 1H), 3.96 – 3.93 (m, 1H), 3.92 – 3.88 (m, 1H), 3.54 – 3.53 (m, 1H), 1.87 (ddd, *J* = 13.4, 8.6, 2.7 Hz, 1H), 1.63 (dd, *J* = 13.7, 3.5 Hz, 1H), 1.22 (d, *J* = 6.2 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3H), 1.12 (d, *J* = 6.1 Hz, 3H), 0.95 (s, 9H), 0.91 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 135.9, 135.9, 135.9, 135.8, 134.0, 133.9, 133.6, 129.8, 129.7, 129.7, 127.7, 127.7, 127.6, 92.3, 74.5, 73.0, 72.7, 69.3, 34.5, 27.0, 27.0, 23.8, 22.0, 19.3, 19.2, 18.1. HRMS (ESI) $C_{41}H_{54}O_4Si_2NH_4$ $[M+NH_4]^+$- calculated- 684.3899; found- 684.3899. $[\alpha]_D^{22}$= -91 (*c* 0.70, $CHCl_3$).

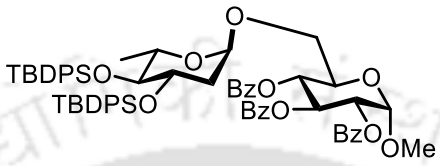
Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-L-rhamnosyl)-α-D-glucopyranoside (18r):



General procedure was followed by adding glycosyl donor **15e** (50 mg, 0.082 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (5 mg, 0.016 mmol, 20 mol %) and glycosyl acceptor **17a** (42 mg, 0.090 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18r**. R_f- 0.4 (10% ethyl acetate in hexane), amount- 69 mg, yield- 81%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 – 7.18 (m, 35H), 4.99 (d, *J* = 10.9 Hz, 1H), 4.96 (dd, *J* = 7.9, 3.7 Hz, 1H), 4.83 (d, *J* = 4.0 Hz, 1H), 4.81 (d, *J* = 3.9 Hz, 1H), 4.79 (s, 1H), 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 (q, *J* = 3.5 Hz, 1H), 4.01 – 3.98 (m, 2H), 3.88 – 3.84 (m, 1H), 3.77 (ddd, *J* = 10.1, 4.9, 1.9 Hz, 1H), 3.61 (dd, *J* = 11.2, 4.9 Hz, 1H), 3.56 – 3.53 (m, 1H), 3.52 (t, *J* = 3.6 Hz, 1H), 3.50 – 3.47 (m, 1H), 3.35 (s, 3H), 1.90 (ddd, *J* = 13.6, 8.0, 2.8 Hz, 1H), 1.68 – 1.64 (m, 1H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.86 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.0, 138.3, 135.9, 135.9, 135.8, 135.7, 133.9, 133.7, 133.7, 133.6, 129.8, 129.7, 129.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.7, 127.7, 127.7, 127.6, 98.1, 95.8, 82.2, 79.9, 78.0, 75.9, 75.2, 75.1, 73.5, 72.6, 72.4, 70.2, 66.8, 55.2, 34.0, 27.1,

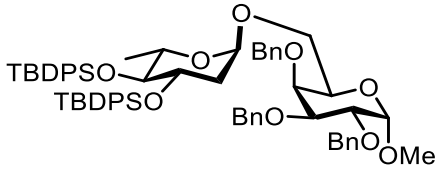
27.0, 19.3, 19.2, 18.3. HRMS (ESI) $C_{66}H_{78}O_9Si_2NH_4$ $[M+NH_4]^+$- calculated- 1088.5523; found- 1088.5521. $[\alpha]_D^{22}$= -16 (*c* 0.27, $CHCl_3$).

Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(3,4-di-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-L-rhamnosyl)-α-D-glucopyranoside (18s):



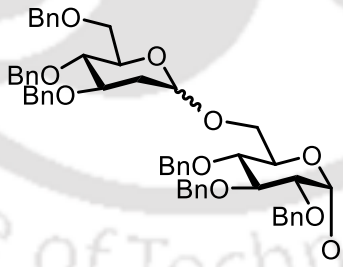
General procedure was followed by adding glycosyl donor **15e** (51 mg, 0.084 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (5 mg, 0.016 mmol, 20 mol %) and glycosyl acceptor **17e** (46 mg, 0.091 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18s**. R_f- 0.3 (10% ethyl acetate in hexane), amount- 68 mg, yield- 76%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 – 7.98 (m, 2H), 7.93 – 7.91 (m, 2H), 7.89 – 7.87 (m, 2H), 7.53 – 7.47 (m, 6H), 7.46 – 7.27 (m, 20H), 7.23 – 7.19 (m, 3H), 6.15 (t, *J* = 9.8 Hz, 1H), 5.53 (t, *J* = 9.9 Hz, 1H), 5.28 (dd, *J* = 10.1, 3.6 Hz, 1H), 5.23 (d, *J* = 3.6 Hz, 1H), 4.97 (dd, *J* = 8.1, 3.8 Hz, 1H), 4.26 (ddd, *J* = 10.3, 6.3, 2.2 Hz, 1H), 4.08 (q, *J* = 3.1 Hz, 1H), 3.94 (dd, *J* = 11.8, 2.3 Hz, 1H), 3.83 – 3.79 (m, 1H), 3.67 (dd, *J* = 11.7, 6.4 Hz, 1H), 3.49 (t, *J* = 3.5 Hz, 1H), 3.44 (s, 3H), 1.89 (ddd, *J* = 13.7, 8.2, 2.8 Hz, 1H), 1.78 (dt, *J* = 13.5, 4.2 Hz, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.0, 166.0, 165.4, 135.9, 135.9, 135.8, 133.9, 133.8, 133.6, 133.6, 133.5, 133.4, 133.2, 130.1, 130.0, 129.8, 129.7, 129.7, 129.5, 129.3, 129.2, 128.6, 128.5, 128.4, 127.7, 127.7, 127.6, 96.9, 96.3, 74.9, 72.6, 72.4, 72.3, 70.8, 69.6, 69.4, 67.0, 55.5, 33.7, 29.8, 27.1, 27.0, 26.9, 19.3, 19.2, 18.3. HRMS (ESI) $C_{66}H_{72}O_{12}Si_2NH_4$ $[M+NH_4]^+$- calculated- 1130.4901; found- 1130.4908. $[\alpha]_D^{22}$= -10 (*c* 0.08, $CHCl_3$).

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-L-rhamnosyl)-α-D-galactopyranoside (18t):



General procedure was followed by adding glycosyl donor **15e** (51 mg, 0.084 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (5 mg, 0.016 mmol, 20 mol %) and glycosyl acceptor **17b** (42 mg, 0.090 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **18t**. R_f- 0.4 (10% ethyl acetate in hexane), amount- 57 mg, yield- 67%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 – 7.20 (m, 35H), 4.97 – 4.95 (m, 1H), 4.94 (s, 1H), 4.84 (d, *J* = 11.8 Hz, 2H), 4.74 (d, *J* = 11.9 Hz, 1H), 4.70 (s, 1H), 4.68 – 4.67 (m, 1H), 4.65 (d, *J* = 11.2 Hz, 1H), 4.08 (d, *J* = 3.5 Hz, 1H), 4.04 (dd, *J* = 9.9, 3.6 Hz, 1H), 3.94 (dd, *J* = 10.0, 2.9 Hz, 1H), 3.90 (d, *J* = 2.9 Hz, 1H), 3.87 – 3.83 (m, 2H), 3.77 – 3.73 (m, 1H), 3.58 (dd, *J* = 10.4, 6.8 Hz, 1H), 3.53 (t, *J* = 3.2 Hz, 1H), 3.34 (s, 3H), 1.84 (ddd, *J* = 13.5, 8.4, 2.7 Hz, 1H), 1.66 (dt, *J* = 13.5, 3.9 Hz, 1H), 1.10 (d, *J* = 6.9 Hz, 3H), 0.93 (s, 9H), 0.90 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9, 138.7, 138.5, 136.0, 135.9, 135.9, 135.8, 135.8, 135.8, 135.7, 133.8, 133.7, 133.6, 133.5, 129.8, 129.8, 129.8, 129.7, 128.8, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 98.7, 95.3, 79.1, 76.5, 75.4, 74.8, 74.2, 73.7, 73.3, 72.3, 69.8, 67.4, 55.3, 34.0, 27.0, 26.9, 19.3, 19.2, 18.0. HRMS (ESI) $C_{66}H_{78}O_9Si_2NH_4$ $[M+NH_4]^+$- calculated- 1088.5523; found- 1088.5523. $[\alpha]_D^{22}$= +45 (*c* 0.04, $CHCl_3$).

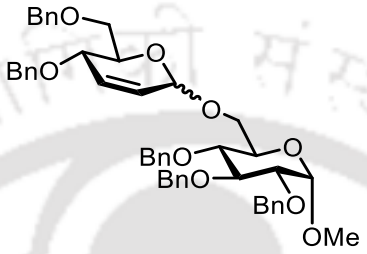
Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-α,β-D-glucopyranosyl)-α-D-glucopyranoside (19a):



General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.120 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (7 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor **17a** (61 mg, 0.131 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **19a**. R_f- 0.2 (20% ethyl acetate in hexane), amount- 91 mg, yield- 86%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.13 (m, 30H), 4.99 (d, *J* = 10.9 Hz, 2H), 4.92 (d, *J* = 11.1 Hz, 1H), 4.87 (d, *J* = 11.1 Hz, 1H), 4.79 (dd, *J* = 11.4, 7.2 Hz, 2H), 4.71 – 4.50 (m, 8H), 4.47 (d, *J* = 11.0 Hz, 1H), 4.40 (d, *J* = 12.2 Hz, 1H), 3.99 (t, *J* = 9.3 Hz, 1H), 3.93 (s, 1H), 3.83 – 3.79 (m, 1H), 3.73

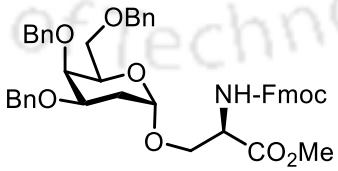
(s, 1H), 3.66 (d, *J* = 10.7 Hz, 1H), 3.58 – 3.56 (m, 2H), 3.51 – 3.48 (m, 2H), 3.34 (s, 3H), 2.30 (dd, *J* = 12.9, 4.7 Hz, 1H), 1.68 (td, *J* = 12.6, 3.3 Hz, 1H).[43]

4,6-Di-*O*-benzyl-2,3-dideoxy-D-erythro-hex-2-enopyranoside-(1→6)-1-methyl-2,3,4-tri-*O*-benzyl-D-glucopyranoside (19ag):



General procedure was followed by adding glycosyl donor **15a** (50 mg, 0.120 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium BArF catalyst **16c** (27 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor **17a** (61 mg, 0.131 mmol, 1.1 equiv) at rt for 24 h in DCM to get product as a colourless liquid **19ag**. R_f- 0.4 (20% ethyl acetate in hexane), amount- 28 mg, yield- 30%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 25H), 6.10 – 6.03 (m, 1H), 5.89 – 5.72 (m, 1H), 4.99 (d, *J* = 10.7 Hz, 1H), 4.89 – 4.77 (m, 4H), 4.68 – 4.60 (m, 4H), 4.57 – 4.49 (m, 3H), 4.46 – 4.34 (m, 2H), 4.01 (t, *J* = 9.3 Hz, 2H), 3.76 (d, *J* = 2.7 Hz, 1H), 3.71 – 3.68 (m, 2H), 3.66 – 3.63 (m, 1H), 3.54 – 3.48 (m, 2H), 3.37 (s, 3H). HRMS (ESI) $C_{48}H_{52}O_9NH_4$ $[M+NH_4]^+$- calculated- 790.3950; found- 790.3952.

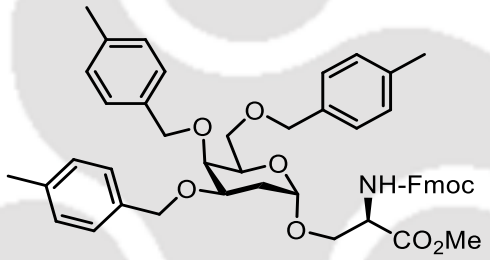
Methyl fmoc-serine-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranoside (20a):



General procedure was followed by adding glycosyl donor **15b** (51 mg, 0.122 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (7 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor **17h** (45 mg, 0.132 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a

colourless liquid **20a**. R_f- 0.4 (20% ethyl acetate in hexane), amount- 76 mg, yield- 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 2H), 7.57 (d, *J* = 7.5 Hz, 1H), 7.39 – 7.22 (m, 20H), 5.92 (d, *J* = 8.7 Hz, 1H), 4.91 (d, *J* = 11.6 Hz, 2H), 4.61 – 4.58 (m, 3H), 4.54 – 4.51 (m, 1H), 4.48 (d, *J* = 11.8 Hz, 1H), 4.40 (s, 1H), 4.38 – 4.35 (m, 2H), 4.20 (t, *J* = 7.1 Hz, 1H), 3.97 (dd, *J* = 10.8, 4.0 Hz, 1H), 3.89 – 3.83 (m, 4H), 3.73 (s, 3H), 3.59 (dd, *J* = 9.5, 6.4 Hz, 1H), 3.53 (dd, *J* = 9.3, 6.5 Hz, 1H), 2.22 (td, *J* = 12.3, 3.8 Hz, 1H), 1.95 (dd, *J* = 12.9, 4.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 156.1, 144.0, 141.4, 138.9, 138.5, 138.1, 128.6, 128.5, 128.5, 128.5, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.5, 127.5, 127.4, 127.2, 125.2, 120.1, 99.3, 74.5, 74.4, 73.5, 72.9, 70.6, 70.6, 69.7, 68.8, 67.2, 54.6, 52.6, 47.3, 31.2. HRMS (ESI) $C_{46}H_{47}NO_9NH_4$ $[M+NH_4]^+$- calculated- 775.3589; found- 775.3589. $[\alpha]_D^{22}$= +96 (*c* 1.5, $CHCl_3$).

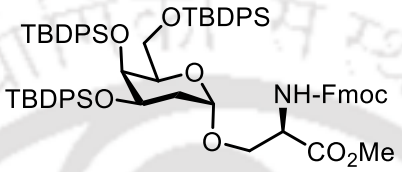
Methyl fmoc-serine-3,4,6-tri-*O*-*para*-methylbenzyl-2-deoxy-α-D-galactopyranoside (20b):



General procedure was followed by adding glycosyl donor **15h** (51 mg, 0.111 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (6 mg, 0.022 mmol, 20 mol %) and glycosyl acceptor **17h** (41 mg, 0.120 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **20b**. R_f- 0.3 (20% ethyl acetate in hexane), amount- 78 mg, yield- 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 2H), 7.58 (d, *J* = 7.5 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.32 – 7.07 (m, 14H), 5.92 (d, *J* = 8.8 Hz, 1H), 4.92 (d, *J* = 3.5 Hz, 1H), 4.85 (d, *J* = 11.4 Hz, 1H), 4.54 (td, *J* = 11.0, 10.3, 7.1 Hz, 4H), 4.43 (d, *J* = 11.7 Hz, 1H), 4.39 – 4.31 (m, 3H), 4.20 (t, *J* = 7.2 Hz, 1H), 3.97 (dd, *J* = 10.9, 3.9 Hz, 1H), 3.87 – 3.78 (m, 4H), 3.74 (s, 3H), 3.55 (dd, *J* = 9.5, 6.1 Hz, 1H), 3.48 (dd, *J* = 9.3, 6.5 Hz, 1H), 2.33 (s, 3H), 2.32 (s, 3H), 2.30 (s, 3H), 2.22 (dd, *J* = 12.4, 3.7 Hz, 1H), 1.93 (dd, *J* = 12.7, 4.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 167.0, 156.2, 144.0, 141.5, 137.4, 137.3, 135.9, 135.5, 135.1, 129.3, 129.2, 129.2, 129.2, 129.0, 128.6, 128.5, 128.4, 128.0, 127.8, 127.6, 127.6, 127.2, 125.3, 120.1, 113.4, 99.3, 74.4, 74.2, 73.4, 72.6,

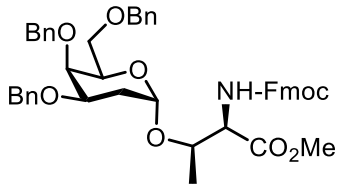
70.7, 70.5, 69.6, 68.8, 67.3, 54.7, 52.6, 47.3, 31.2, 30.2, 21.3, 21.3. HRMS (ESI) $C_{49}H_{53}NO_9NH_4$ $[M+NH_4]^+$- calculated- 817.4059; found- 817.4058. $[\alpha]_D^{22}$= +35 (*c* 0.91, $CHCl_3$).

Methyl fmoc-serine-3,4,6-tri-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-D-galactopyranoside (20c):



General procedure was followed by adding glycosyl donor **15d** (53 mg, 0.062 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (3 mg, 0.012 mmol, 20 mol %) and glycosyl acceptor **17h** (24 mg, 0.070 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **20c**. R_f- 0.5 (10% ethyl acetate in hexane), amount- 62 mg, yield- 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.08 (m, 38H), 4.91 (d, *J* = 9.4 Hz, 1H), 4.78 (d, *J* = 3.4 Hz, 1H), 4.55 (dd, *J* = 10.8, 6.4 Hz, 1H), 4.45 (dd, *J* = 10.8, 6.5 Hz, 1H), 4.32 (dt, *J* = 9.4, 3.3 Hz, 1H), 4.24 (t, *J* = 6.4 Hz, 1H), 3.81 (s, 1H), 3.76 (d, *J* = 11.2 Hz, 1H), 3.65 (s, 3H), 3.59 (d, *J* = 14.5 Hz, 3H), 3.19 (d, *J* = 5.4 Hz, 1H), 3.01 (d, *J* = 10.6 Hz, 1H), 2.30 (dt, *J* = 13.2, 7.1 Hz, 1H), 1.34 (dd, *J* = 12.8, 4.1 Hz, 1H), 1.02 (s, 9H), 1.01 (s, 9H), 0.87 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 156.2, 144.0, 144.0, 141.5, 136.7, 136.3, 136.2, 136.0, 135.8, 135.6, 134.0, 133.6, 132.7, 130.0, 129.8, 129.8, 129.6, 129.4, 127.9, 127.8, 127.7, 127.6, 127.4, 127.2, 125.1, 125.0, 120.2, 120.1, 98.3, 74.5, 72.1, 70.0, 66.9, 66.5, 65.1, 65.1, 54.1, 52.5, 47.4, 33.2, 27.4, 26.9, 20.1, 19.0, 19.0. HRMS (ESI) $C_{73}H_{83}NO_9Si_3NH_4$ $[M+NH_4]^+$- calculated- 1219.5714; found- 1219.5715. $[\alpha]_D^{22}$= +85 (*c* 1.2, $CHCl_3$).

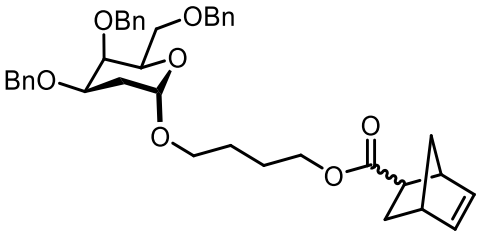
Methyl fmoc-threonine-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranoside (20d):



General procedure was followed by adding glycosyl donor **15b** (50 mg, 0.120 mmol, 1.0 equiv), 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (7 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor **17i** (47 mg, 0.132 mmol, 1.1 equiv) at 40 °C for 24 h to get product as a colourless liquid **20d**. R_f- 0.2 (20% ethyl acetate in hexane), amount- 76 mg, yield- 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (t, *J* = 6.9 Hz, 2H), 7.64 – 7.23 (m, 21H), 5.42 (d, *J* = 9.7 Hz, 1H), 4.94 – 4.91 (m, 2H), 4.65 – 4.57 (m, 3H), 4.51 – 4.41 (m, 4H), 4.36 (dd, *J* = 9.7, 2.2 Hz, 1H), 4.33 – 4.30 (m, 1H), 4.27 (t, *J* = 7.0 Hz, 1H), 3.92 (s, 2H), 3.88 – 3.83 (m, 1H), 3.73 (s, 3H), 3.60 – 3.51 (m, 2H), 2.17 (td, *J* = 12.5, 4.0 Hz, 1H), 1.85 (dd, *J* = 12.6, 4.5 Hz, 1H), 1.24 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.3, 156.8, 144.0, 143.9, 141.5, 141.4, 138.9, 138.5, 138.2, 128.6, 128.5, 128.5, 128.3, 128.3, 128.3, 128.2, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.5, 127.4, 127.2, 125.4, 125.4, 125.2, 125.2, 120.1, 120.0, 99.5, 75.3, 74.4, 73.6, 73.6, 73.1, 70.6, 70.5, 69.6, 67.3, 58.9, 52.5, 47.3, 31.4, 18.6. HRMS (ESI) $C_{47}H_{49}NO_9NH_4$ $[M+NH_4]^+$- calculated- 789.3746; found- 789.3755. $[\alpha]_D^{22}$= +77 (*c* 1.5, $CHCl_3$).

Gram-Scale Synthesis

4-Hydroxybutyl-bicyclo[2.2.1]hept-5-ene-2-carboxylate-2-deoxy-3,4,6-tri-*O*-benzyl-α-D-galactopyranoside (21):



Glycosyl donor **15b** (1.023 g, 2.456 mmol, 1.0 equiv) and glycosyl acceptor **17j** (1.03 g, 4.898 mmol, 2.0 equiv) were taken in round bottomed flask. Then, to it 2,4,6-tri-tertiary-butylpyridinium hydrochloride catalyst **16a** (70 mg, 0.245 mmol, 10 mol %) was added and dissolved in dry DCM (10 ml). The reaction mixture was stirred at rt for 9 h under argon. After cooling it to rt, the reaction mixture was quenched by water (15 ml) and extracted with DCM (3x25 ml). The organic phase was washed with brine (100 ml), dried over Na_2SO_4 and concentrated under reduced pressure. The obtained crude was purified by column chromatography in ethyl acetate/hexane solvent system to get product as a colourless liquid **21**. R_f- 0.5 (20% ethyl acetate in hexane), amount- 1.31 g, yield- 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.24 (m, 15H), 6.18 (dd, *J* = 5.7, 3.0 Hz, 1H), 5.92 (dd, *J* = 5.7, 2.9 Hz, 1H), 4.97 (d, *J* = 3.4 Hz, 1H), 4.93 (d, *J* = 11.6 Hz, 1H), 4.60 (s, 3H), 4.51 (d, *J* = 11.8 Hz, 1H), 4.42 (d, *J* = 11.8 Hz, 1H), 4.03 (q, *J* = 5.6 Hz, 2H), 3.95 – 3.86 (m, 4H), 3.67 – 3.61 (m, 1H), 3.57 (t, *J* = 6.1 Hz, 2H), 3.41 – 3.35 (m, 1H), 2.94 (dt, *J* = 9.8, 4.1 Hz, 1H), 2.89 (s, 1H), 2.22 (td, *J* = 12.5, 3.8 Hz, 1H), 1.98 (dd, *J* = 12.7, 4.4 Hz, 1H), 1.89 (ddd, *J* = 12.3, 9.1, 3.7 Hz, 1H), 1.68 – 1.60 (m, 3H), 1.44 – 1.40 (m, 2H), 1.26 (d, *J* = 7.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.9, 139.0, 138.7, 138.2, 137.9, 132.5, 128.5, 128.5, 128.4, 128.3, 127.9, 127.8, 127.6, 127.5, 97.9, 75.0, 74.4, 73.6, 73.1, 70.6, 70.0, 69.7, 67.0, 64.1, 49.8, 45.9, 43.5, 42.7, 31.3, 29.3, 26.2, 25.9. HRMS (ESI) $C_{39}H_{46}O_7Na$ $[M+Na]^+$- calculated- 649.3136; found- 649.3159. $[\alpha]_D^{22}$= +84 (*c* 0.20, $CHCl_3$).

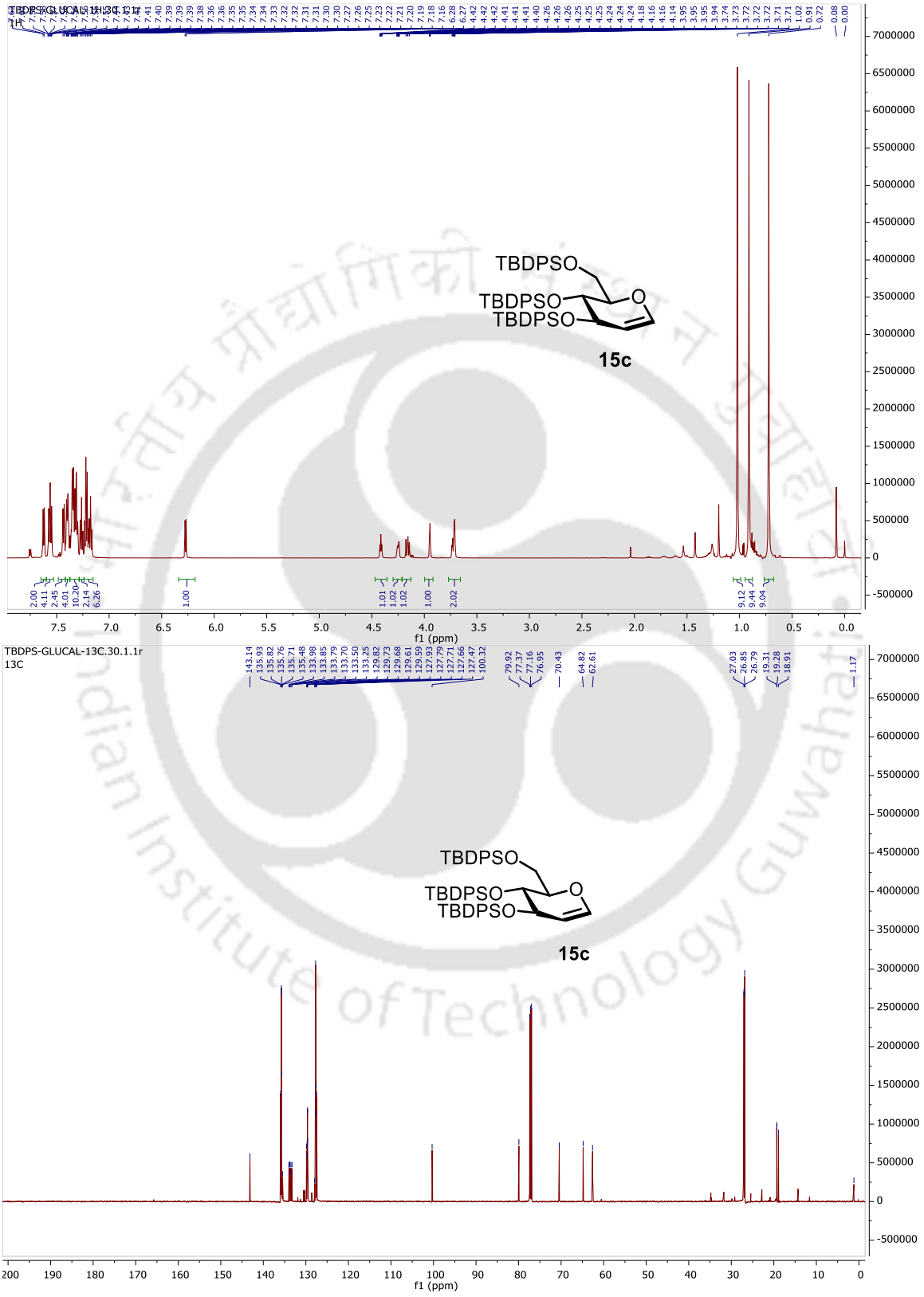
4.10 References:

1. Dimroth, K.; Mach, W. *Angew. Chem., Int. Ed.* **1968,** *80*, 489–490.
2. Brown, H. C.; Kanner, B. *J. Am. Chem. Soc.* **1966,** *88*, 986–992.
3. Benoit, R. L.; Frechette, M.; Lefebvre, D. *Can. J. Chem.* **1988,** *66*, 1159–1162.
4. Vanderplas, H. C.; Koudijs, A. *Recl. Trav. Chim. Pays-Bas*, **1978,** *97*, 159–161.
5. Houriet, R.; Rolli, E. *New J. Chem.* **1987,** *11*, 221–224.
6. Deutsch, E.; Cheung, N. K. V. *J. Org. Chem.* **1973,** *38*, 1123–1126.
7. Effenberger, F.; Eberhard, J. K.; Maier, A. H. *J. Am. Chem. Soc.* **1996,** *118*, 12572–12579.
8. Xu, X. H.; Liu, G. K.; Azuma, A.; Tokunaga, E.; Shibata, N. *Org. Lett.* **2011,** *13*, 4854–4857.

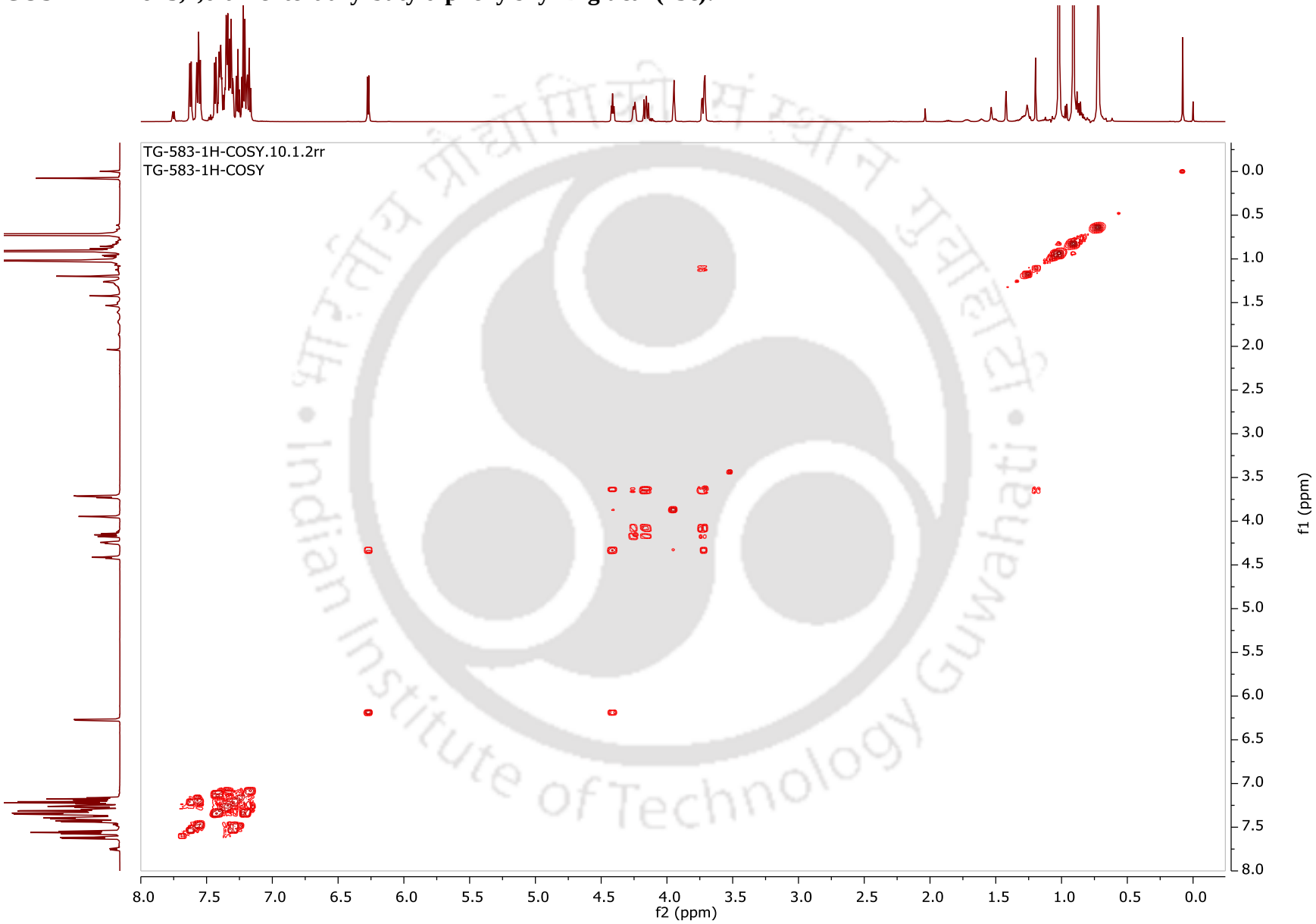
9. (a) Jiang, C.; Blacque, O.; Fox T.; Berke, H. *Organometallics* **2011**, *30*, 2117–2124. (b) Clark, E. R.; Ingleson, M. J. *Organometallics* **2013,** *32*, 6712–6717.
10. Boebel, T. A.; Gin, D. Y. *Angew. Chem., Int. Ed.* **2003,** *42*, 5874–5877.
11. Garcia, B. A.; Gin, D. Y. *Org. Lett.* **2000,** *2*, 2135–2138.
12. Kim, J. Y.; Di Bussolo, V.; Gin, D. Y. *Org. Lett.* **2001,** *3*, 303–306.
13. Crich, D.; Dudkin, V. *J. Am. Chem. Soc.* **2001,** *123*, 6819–6825.
14. Geng, Y.; Zhang, L. H.; Ye, X. S. *Chem. Commun.* **2008**, 597–599.
15. Madarasz, A.; Dosa, Z.; Varga, S.; Soos, T.; Csampai, A.; Papai, I. *ACS. Catal.* **2016,** *6*, 4379–4387.
16. Balthaser, B. R.; McDonald, F. E. *Org. Lett.* **2009,** *11*, 4850–4853.
17. Cox, D. J.; Smith, M. D.; Fairbanks, A. J. *Org. Lett.* **2010,** *12*, 1452–1455.
18. Balmond, E. I.; Galan, M. C.; McGarrigle, E. M. *Synlett* **2013,** *24*, 2335–2339.
19. Kimura, T.; Sekine, M.; Takahashi, D.; Toshima, K. *Angew. Chem., Int. Ed.* **2013,** *52*, 12131–12134.
20. Liu, D. S.; Sarrafpour, S.; Guo, W.; Goulart, B.; Bennett, C. S. *J Carbohydr. Chem.* **2014,** *33*, 423–434.
21. Lee, J.; Borovika, A.; Khomutnyk, Y.; Nagorny, P. *Chem. Commun.* **2017,** *53*, 8976–8979.
22. Palo-Nieto, C.; Sau, A.; Williams, R.; Galan, M. C. *J. Org. Chem.* **2017,** *82*, 407–414.
23. Williams, R.; Galan, M. C. *Eur. J. Org. Chem.* **2017**, 6247–6264.
24. Bennett, C. S.; Galan, M. C. *Chem. Rev.* **2018,** *118*, 7931–7985.
25. Paenurk, E.; Kaupmees, K.; Himmel, D.; Kutt, A.; Kaljurand, I.; Koppel, I. A.; Krossing, I.; Leito, I. *Chem. Sci.* **2017,** *8*, 6964–6973.
26. Farcasiu, D.; Lezcano, M.; Vinslava, A. *New J. Chem.* **2000,** *24*, 199–201.
27. Das, S.; Pekel, D.; Neudorfl, J. M.; Berkessel, A. *Angew. Chem., Int. Ed.* **2015,** *54*, 12479–12483.
28. Butts, M. D.; Scott, B. L.; Kubas, G. J. *J. Am. Chem. Soc.* **1996,** *118*, 11831–11843.
29. He, X. M.; Liu, H. W. *Curr. Opin. Chem. Biol.* **2002,** *6*, 590–597.
30. Sastry, M.; Patel, D. J. *Biochemistry* **1993,** *32*, 6588–6604.
31. Daniel, P. T.; Koert, U.; Schuppan, J. *Angew. Chem., Int. Ed.* **2006,** *45*, 872–893.
32. Langenhan, J. M.; Griffith, B. R.; Thorson, J. S. *J. Nat. Prod.* **2005,** *68*, 1696–1711.

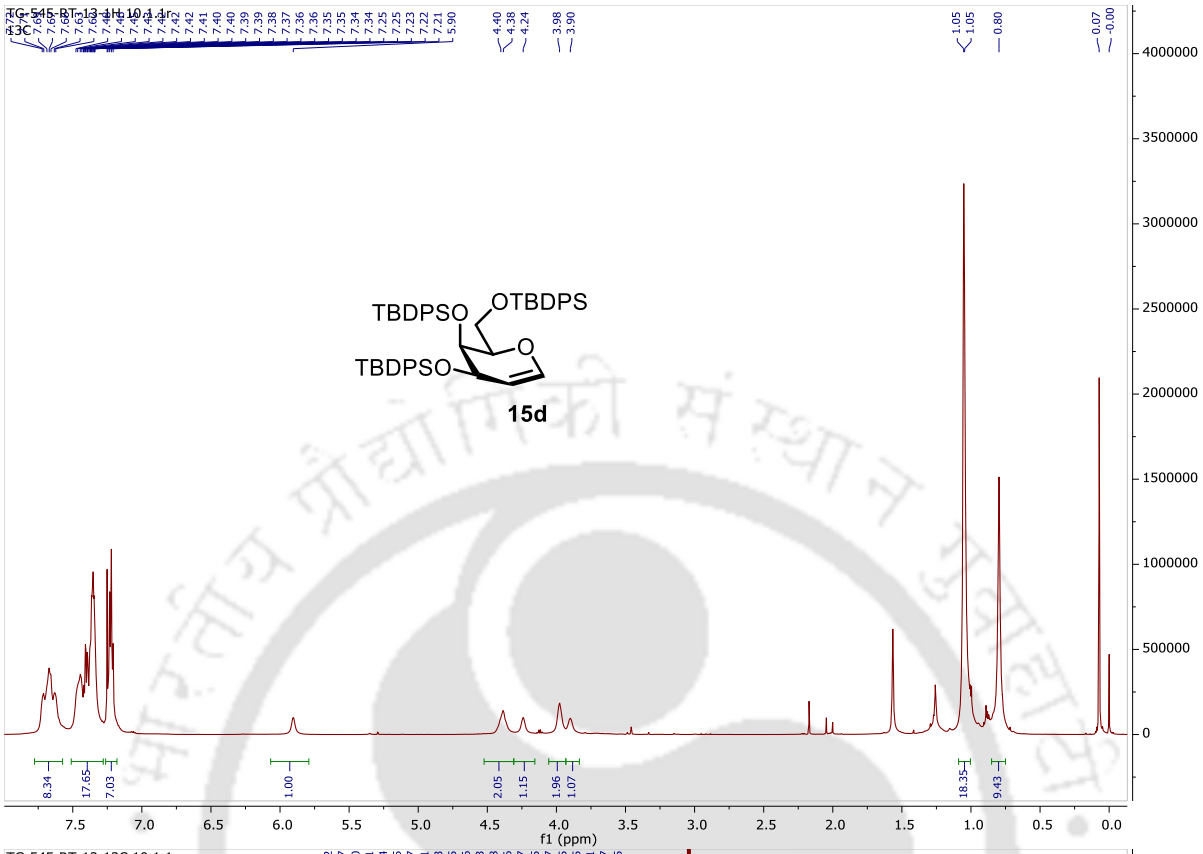
33. Ghosh, T.; Mukherji, A.; Srivastava, H. K.; Kancharla, P. K. *Org. Biomol. Chem.* **2018,** *16*, 2870–2875.
34. Riddlestone, I. M.; Kraft, A.; Schaefer, J.; Krossing, I. *Angew. Chem., Int. Ed.* **2018,** *57*, 13982–14024.
35. Price, C. J.; Chen, H. Y.; Launer, L. M.; Miller, S. A. *Angew. Chem., Int. Ed.* **2009,** *48*, 956–959.
36. Krossing, I.; Raabe, I. *Angew. Chem., Int. Ed.* **2004,** *43*, 2066–2090.
37. Ferrier, R. J. *Glycoscience: Epimerisation, Isomerisation and Rearrangement Reactions of Carbohydrates* **2001,** *215*, 153–175.
38. Gomez, A. M.; Lobo, F.; Uriel, C.; Lopez, J. C. *Eur. J. Org. Chem.* **2013,** *2013*, 7221–7262.
39. Taube, R.; Langlotz, J.; Sieler, J.; Gelbrich, T.; Tittes, K. *J Organomet. Chem.* **2000,** *597*, 92–104.
40. Mitra, A.; Seaton P. J.; Assarpour, R. A.; Williamson, T. *Tetrahedron* **1998**, 54, 15489-15498.
41. Oroszova, B.; Choutka, J.; Pohl, R; Parkan, K. *Chem. - Eur. J.* **2015**, *21*,7043–7047.
42. Chong, P. Y.; Roush, W. R. *Org. Lett.* **2002**, *4*, 4523–4526.
43. Cui, X. -K.; Zhong, M.; Meng, X. -B.; Li, Z. -J. *Carbohydr. Res.* **2012**, *358*, 19–22.

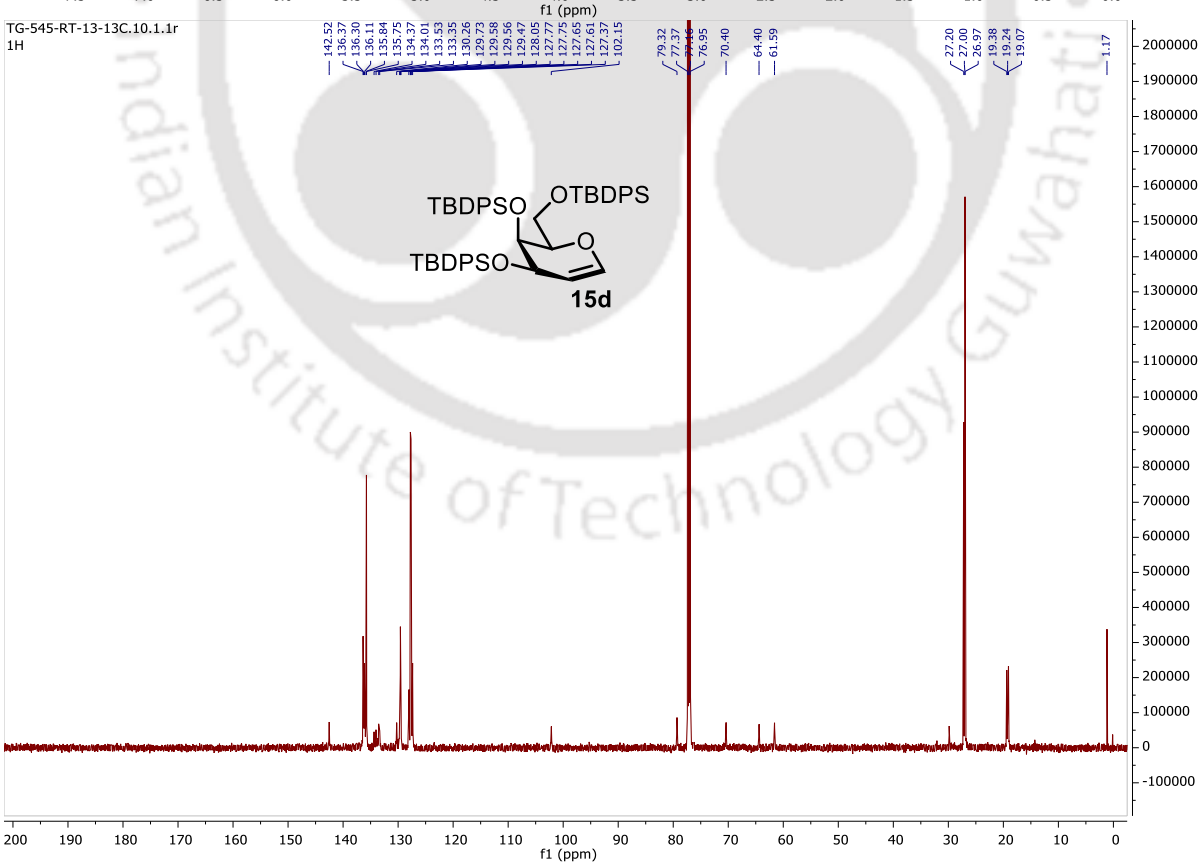
4.11 NMR Spectra:



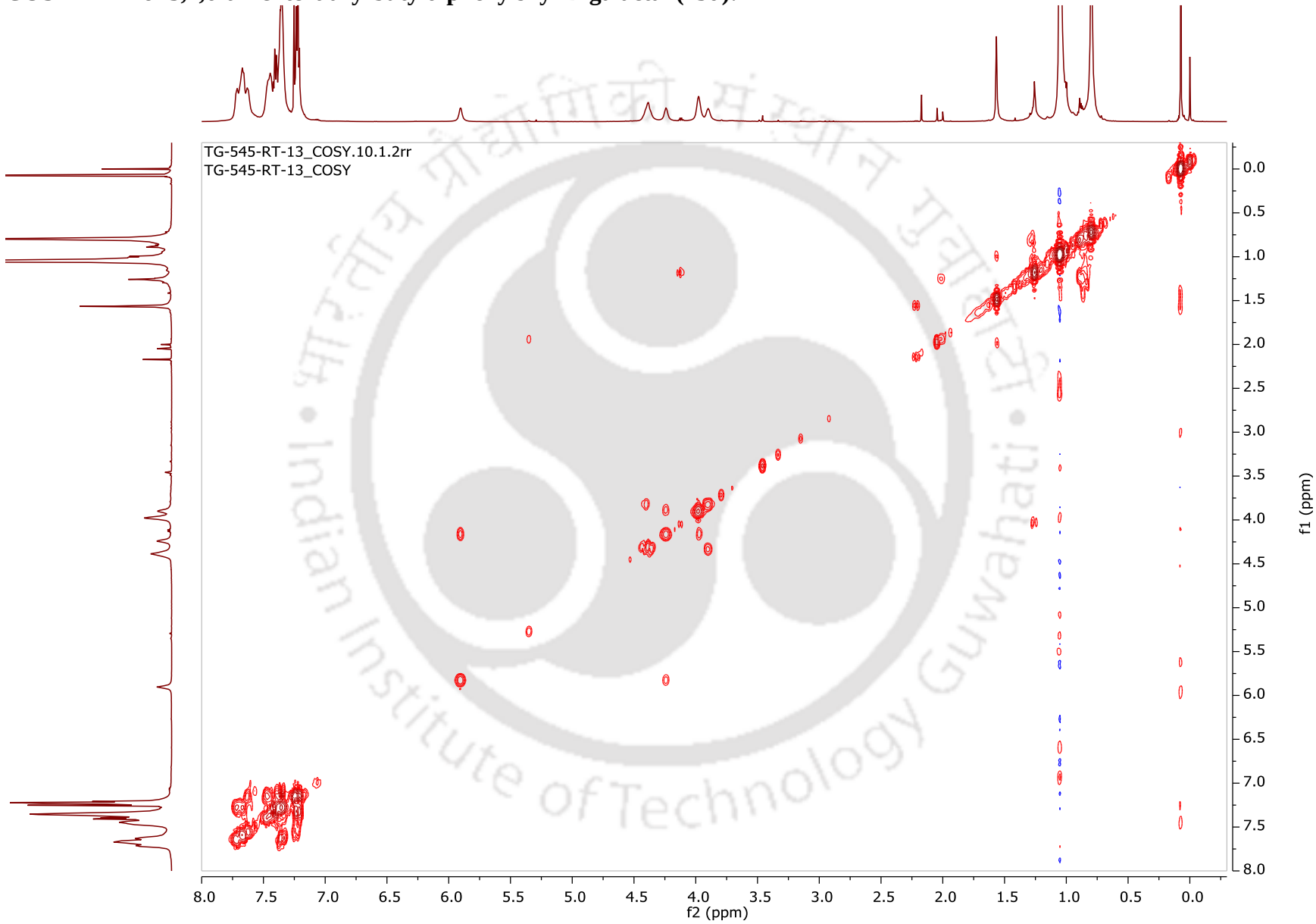
COSY NMR of 3,4,6-tri-*O*-tertiary-butyldiphenylsilyl-D-glucal (15c):

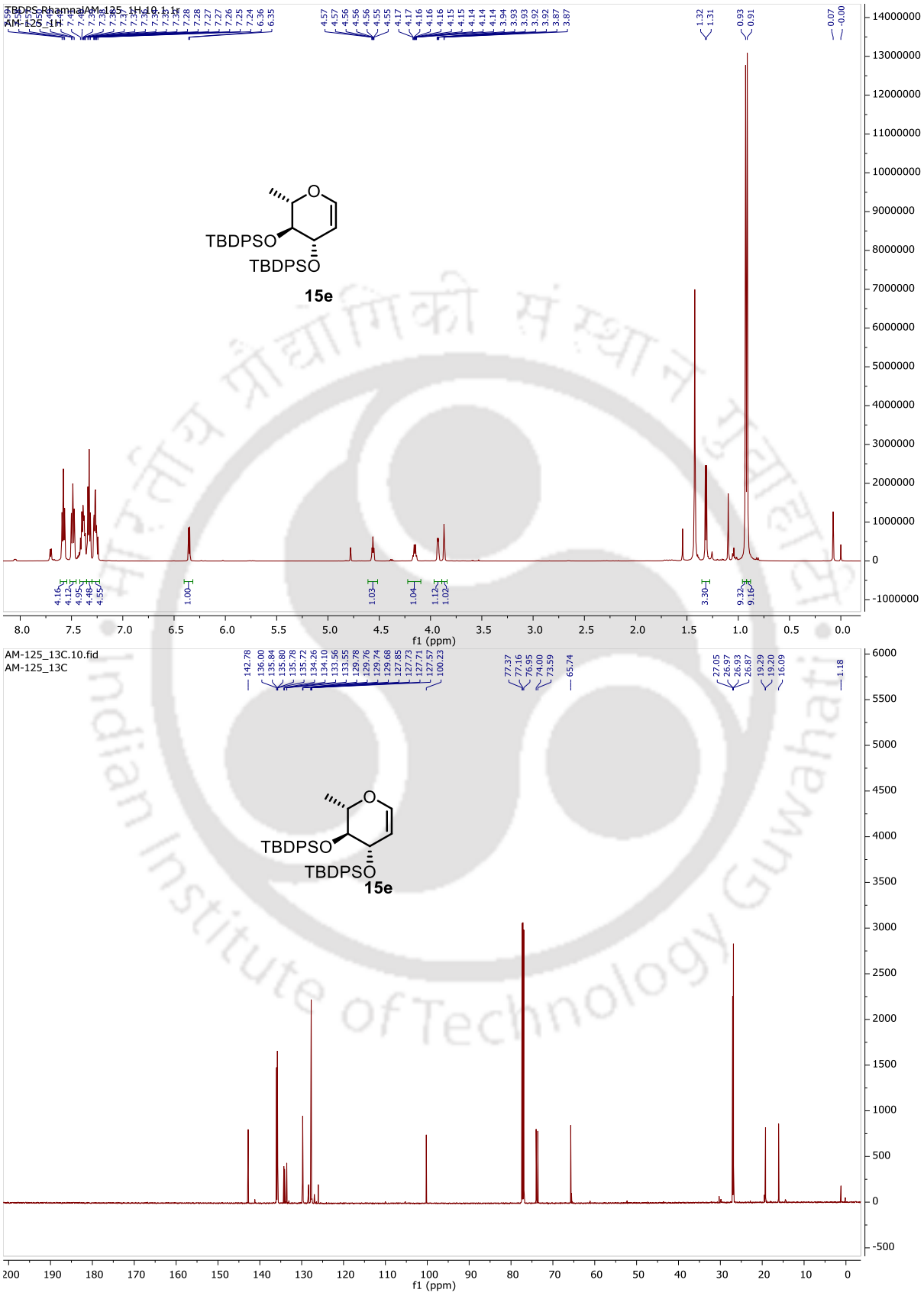


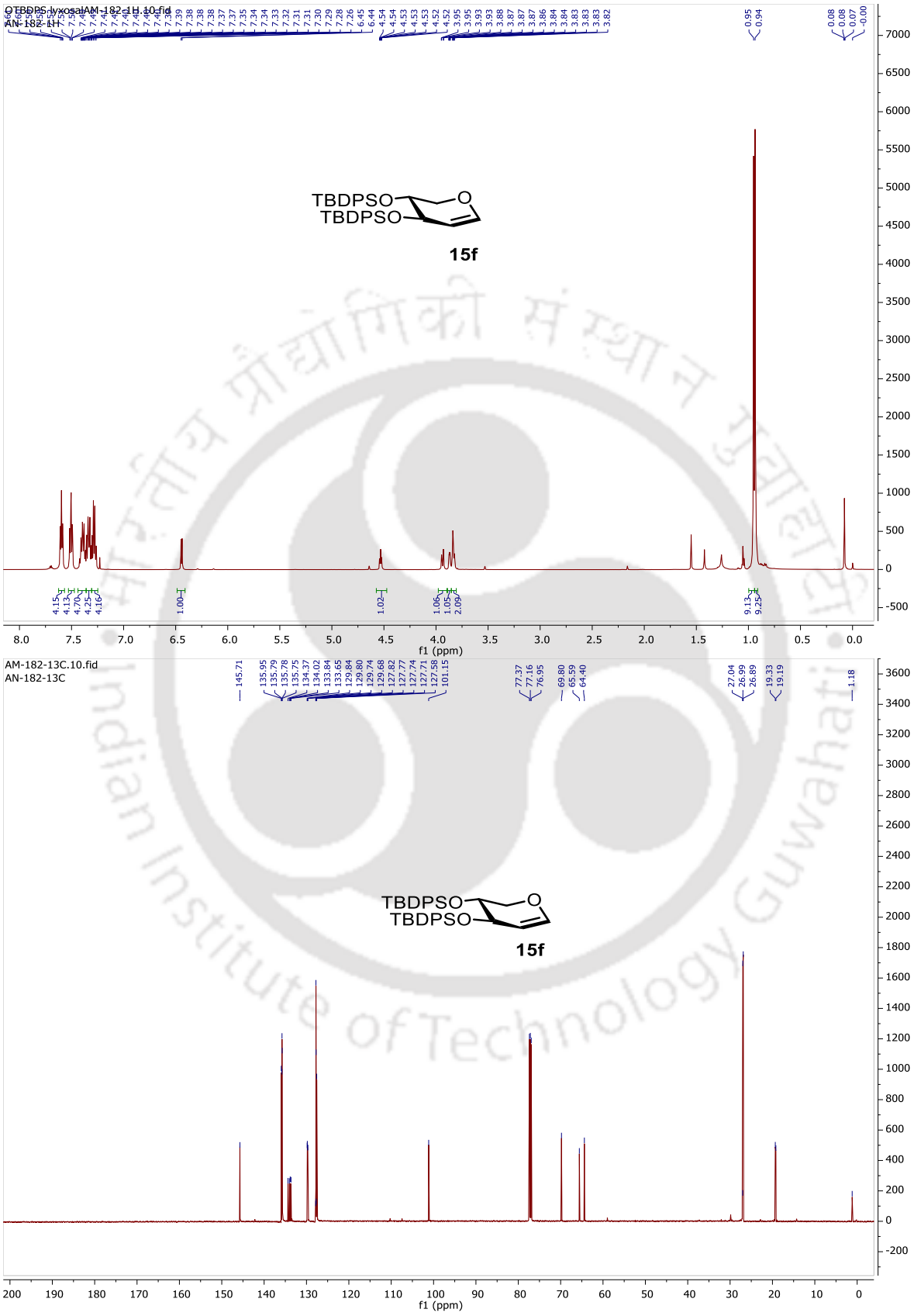


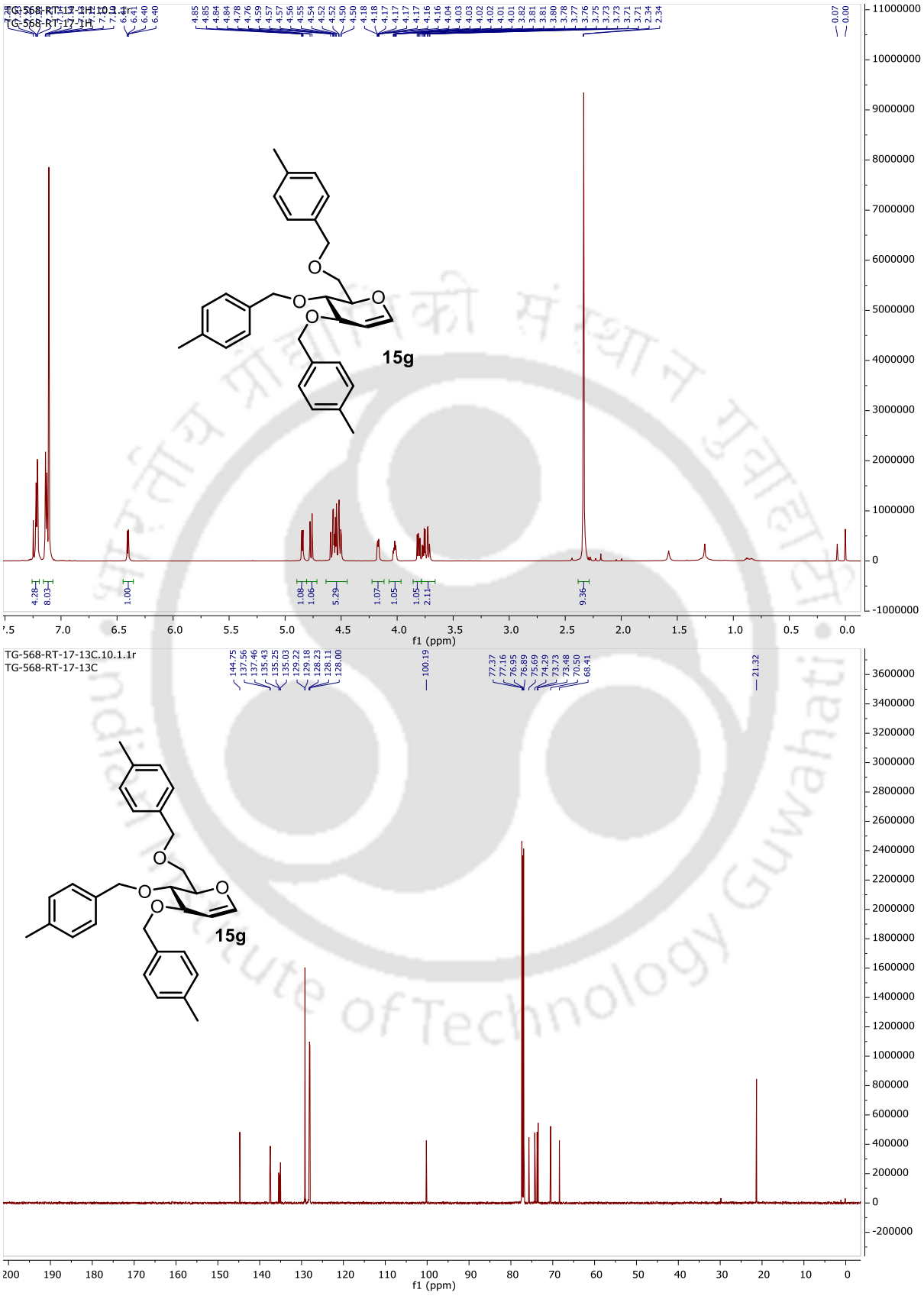


COSY NMR of 3,4,6-tri-*O*-tertiary-butyldiphenylsilyl-D-galactal (15d):

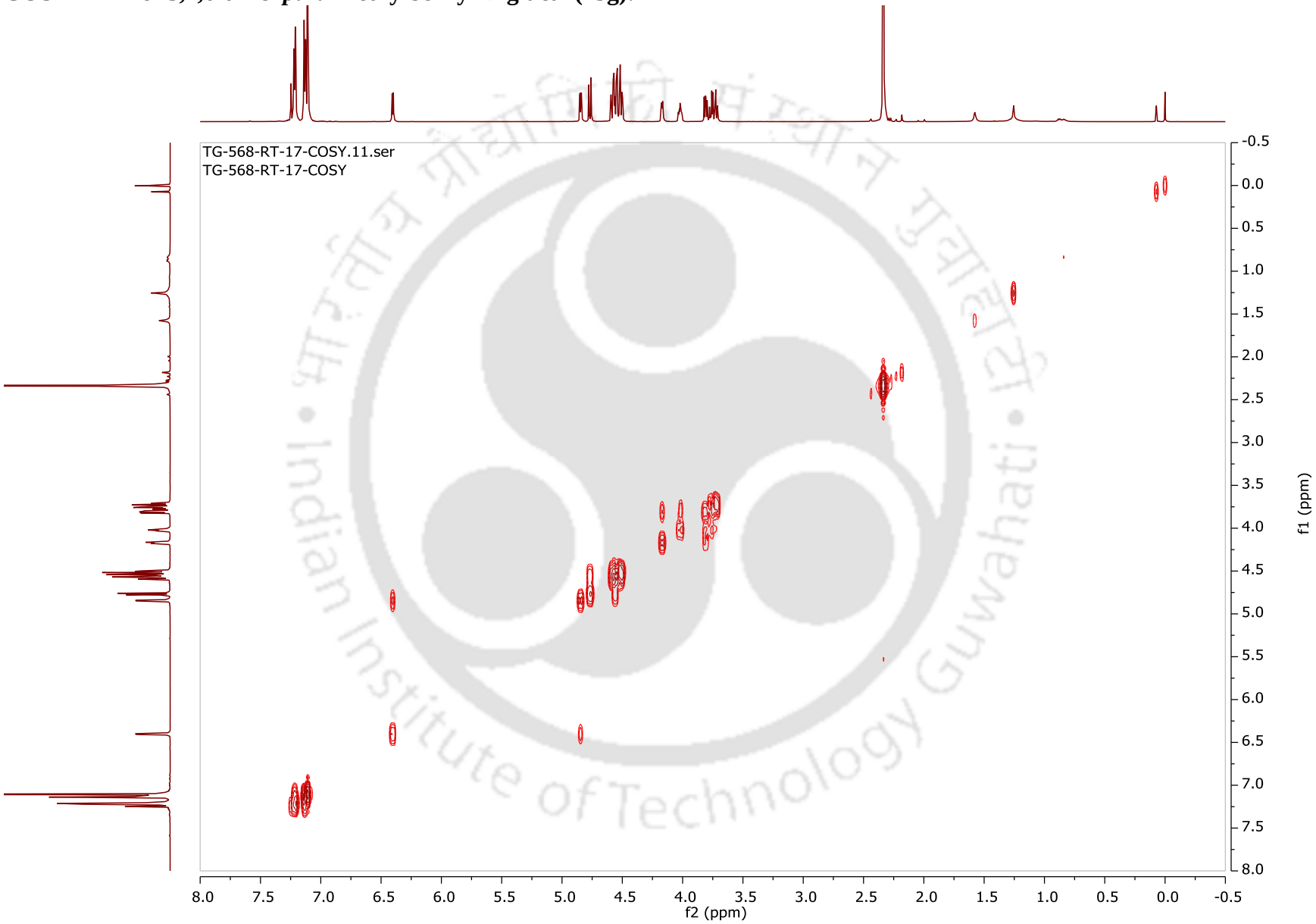


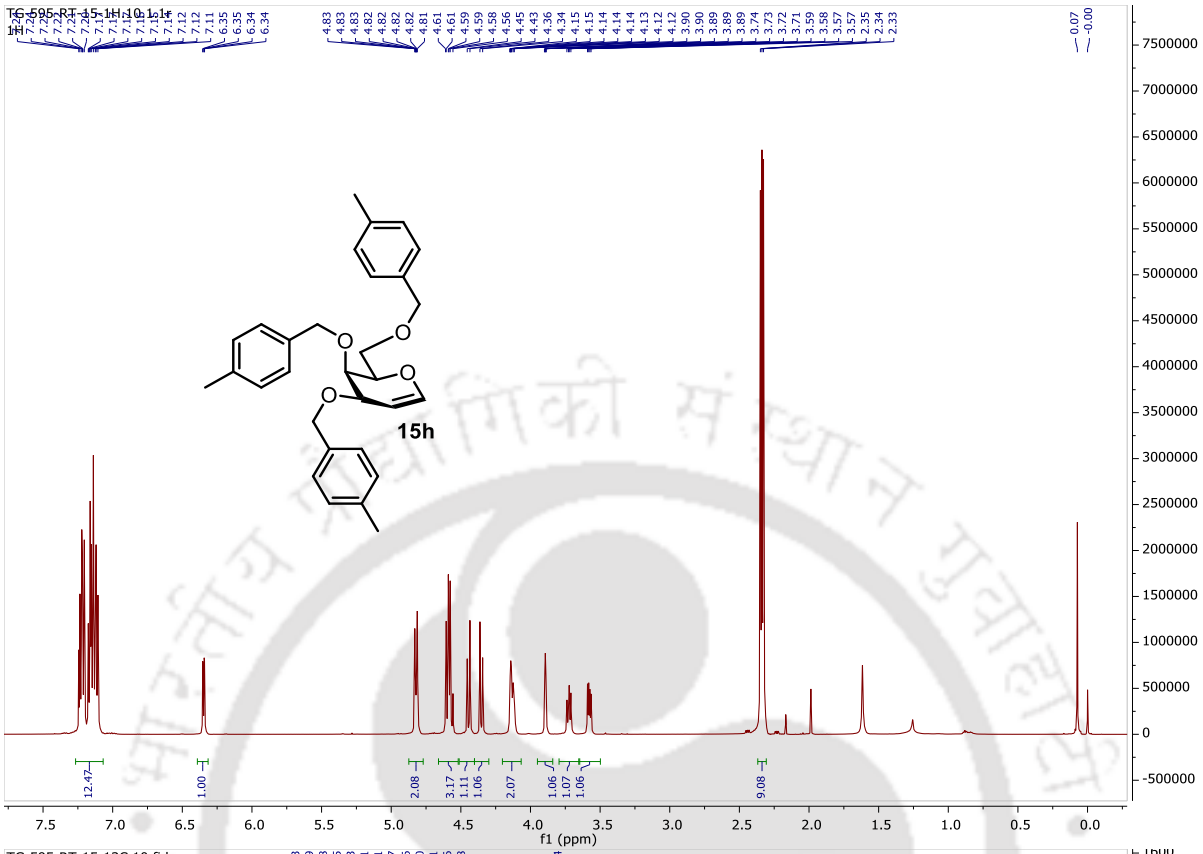


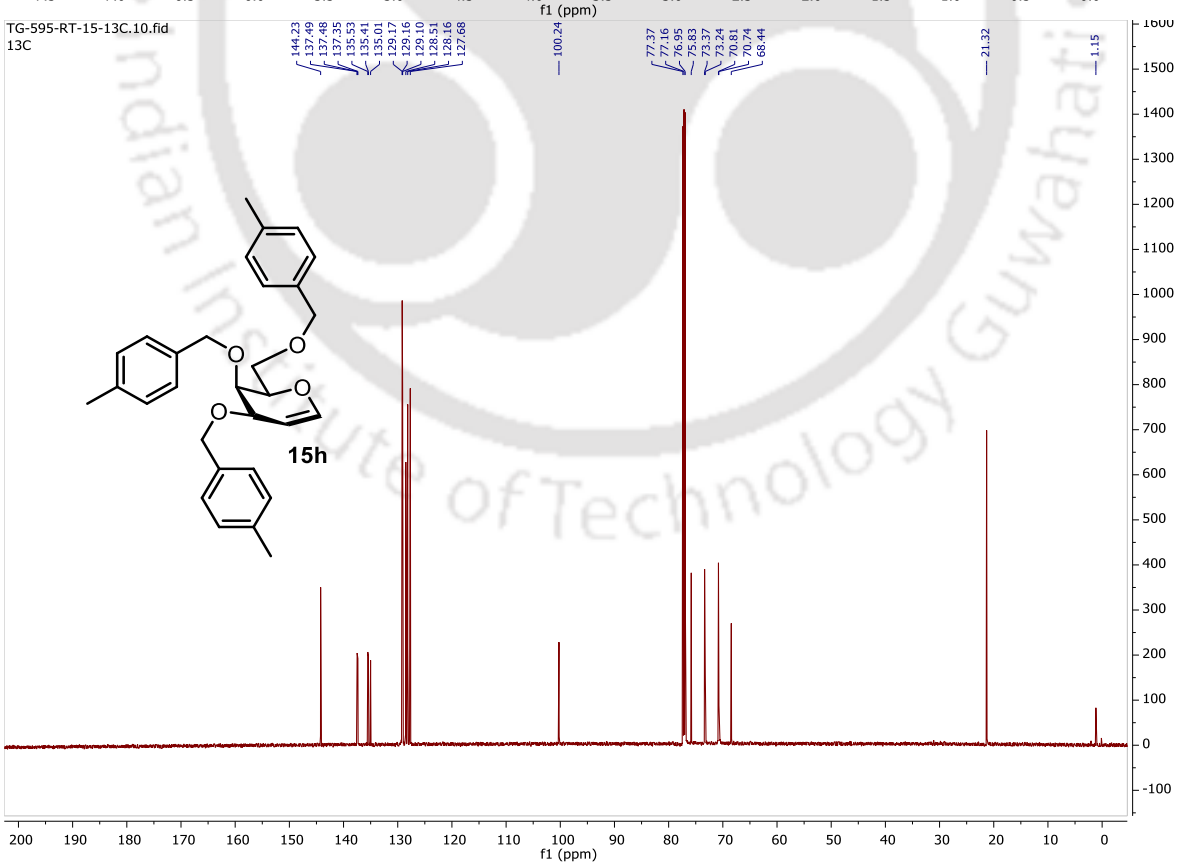




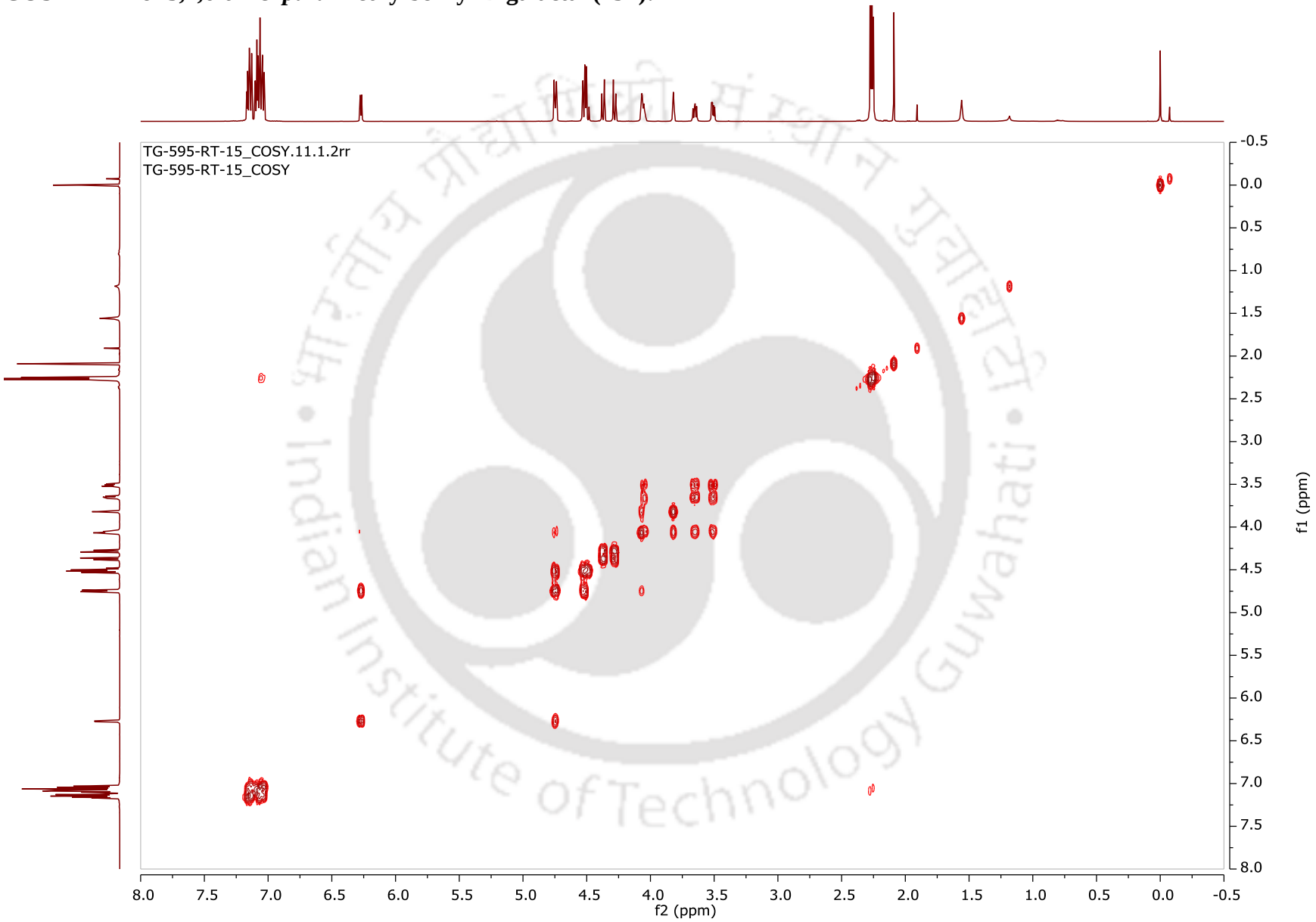
COSY NMR of 3,4,6-tri-*O*-*para*-methylbenzyl-D-glucal (15g):

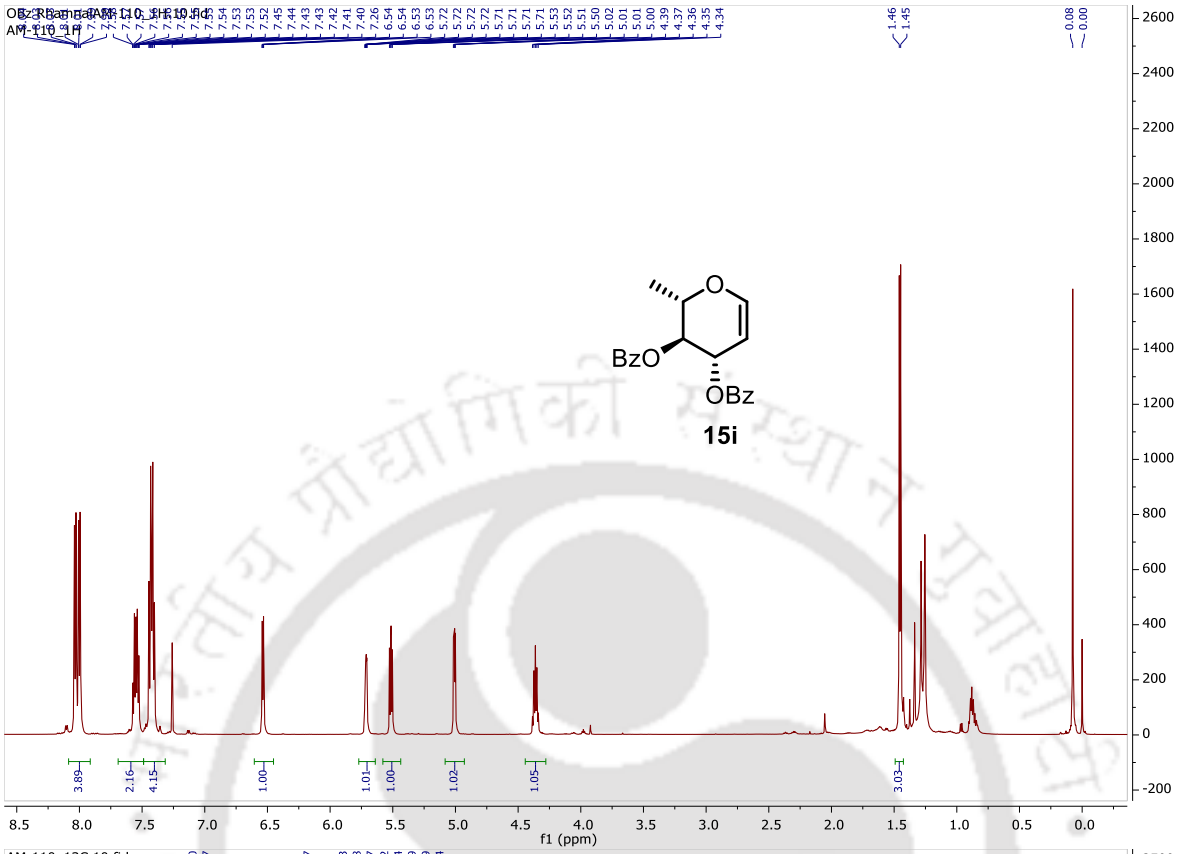


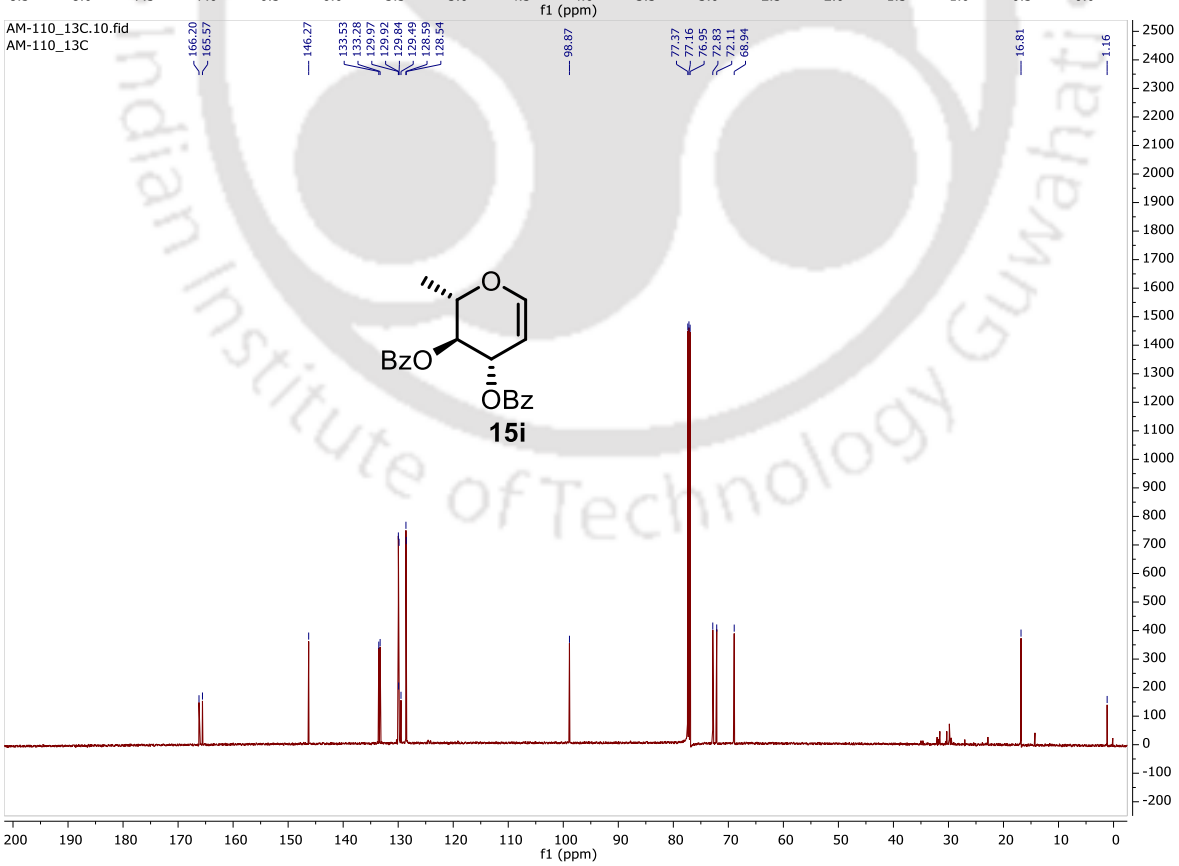


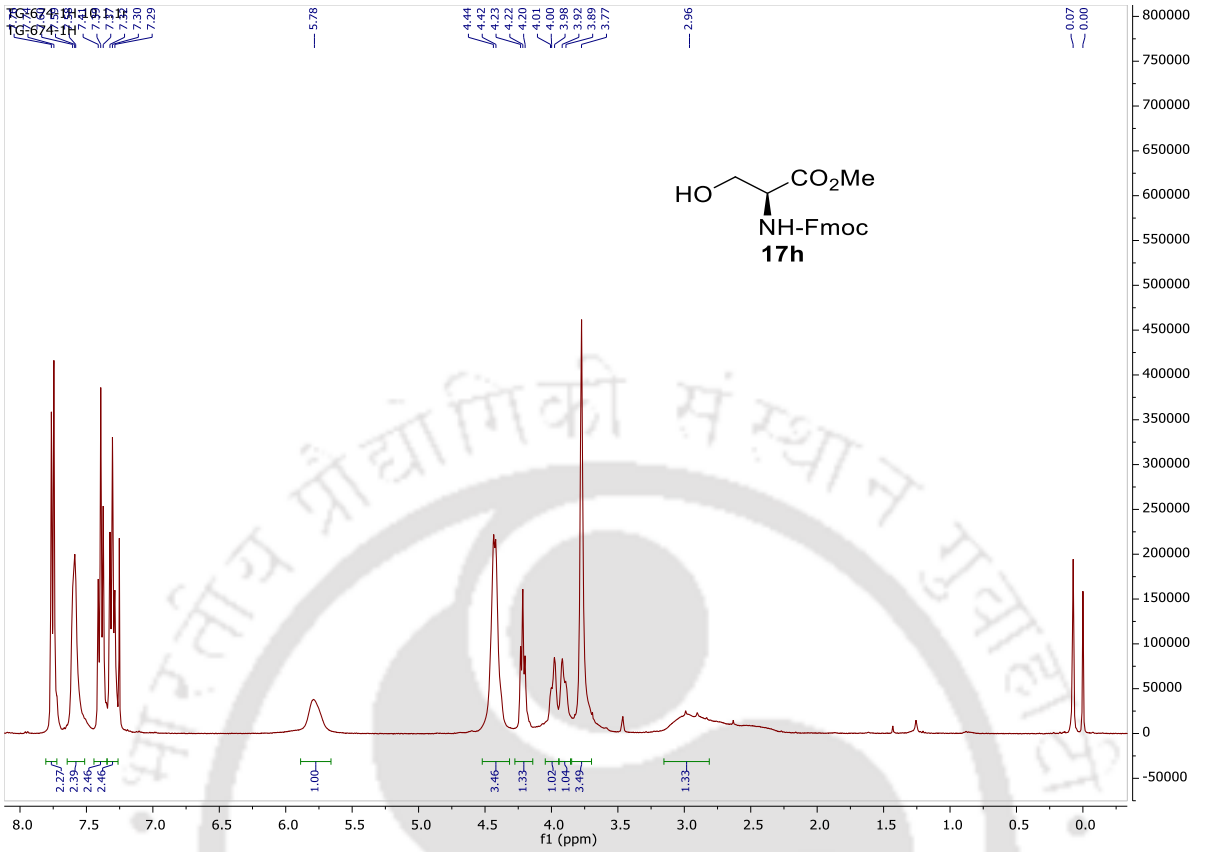


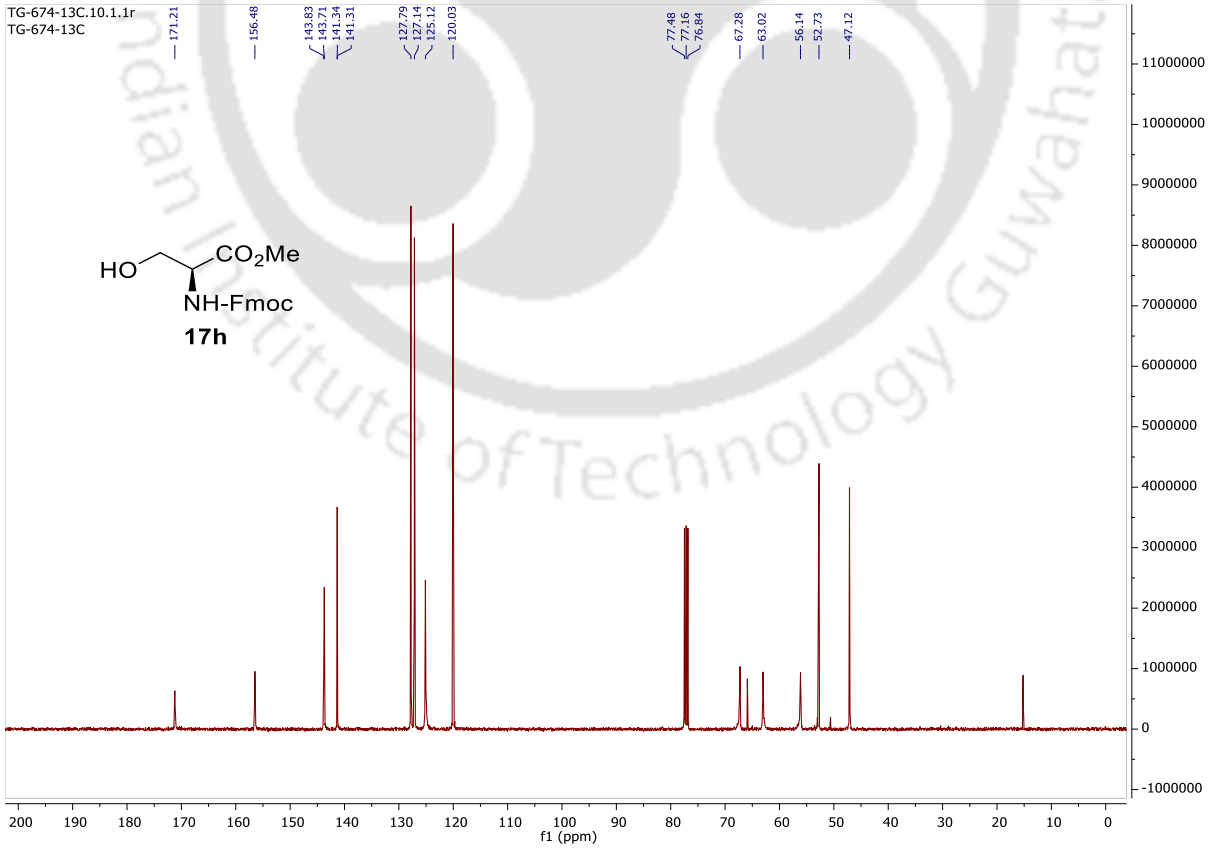
COSY NMR of 3,4,6-tri-*O*-*para*-methylbenzyl-D-galactal (15h):

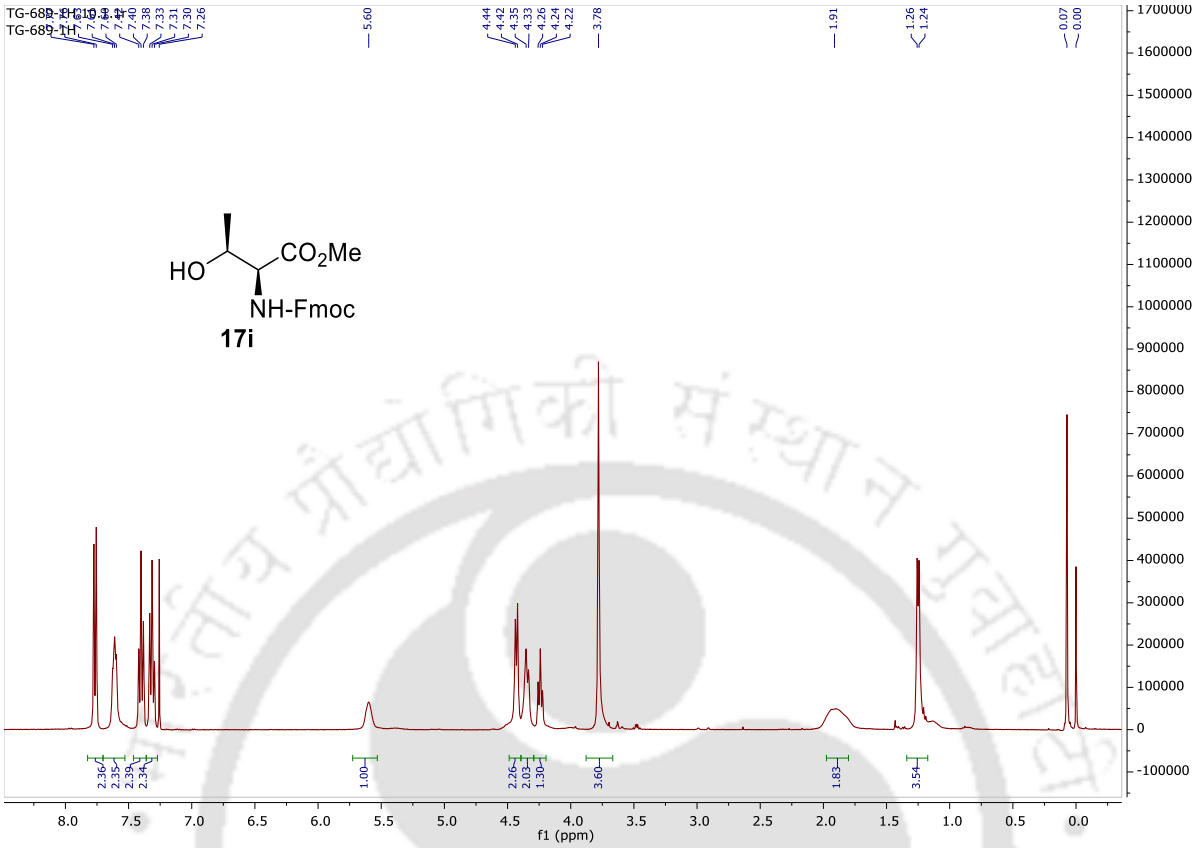


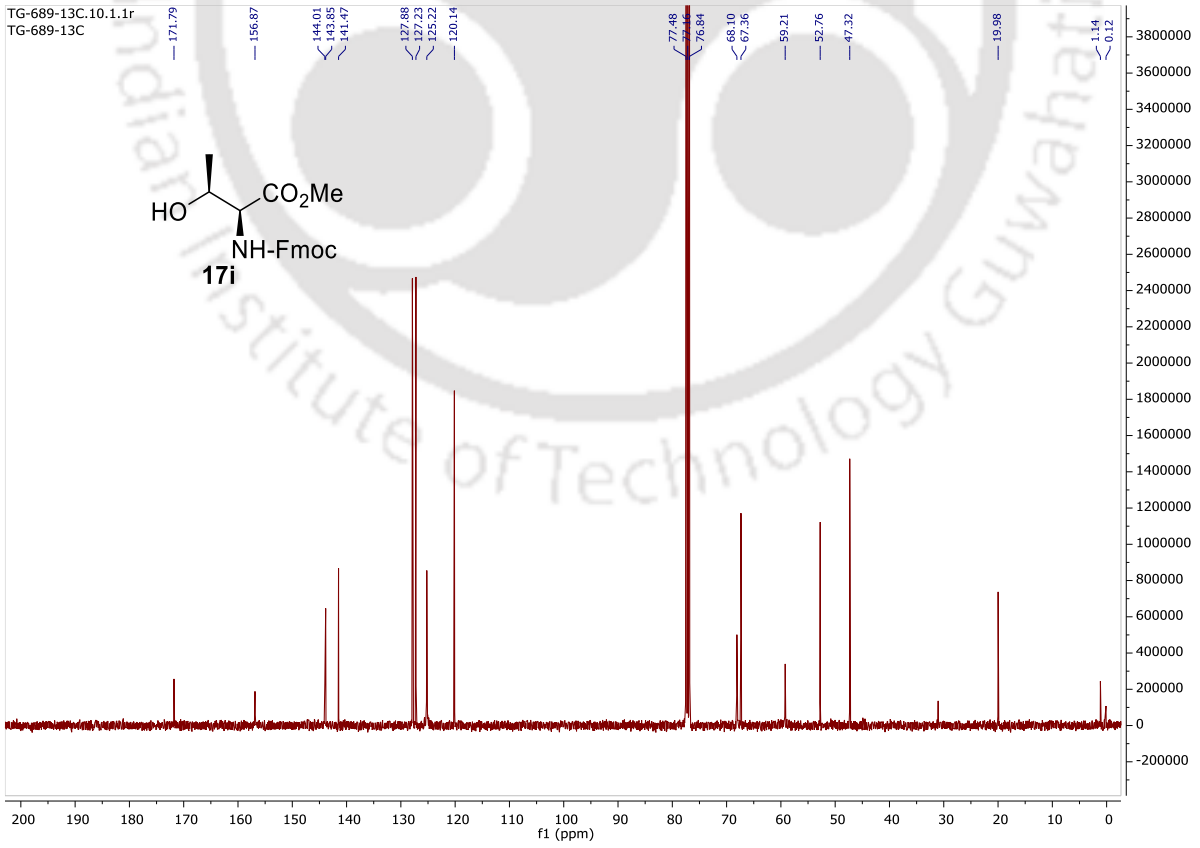


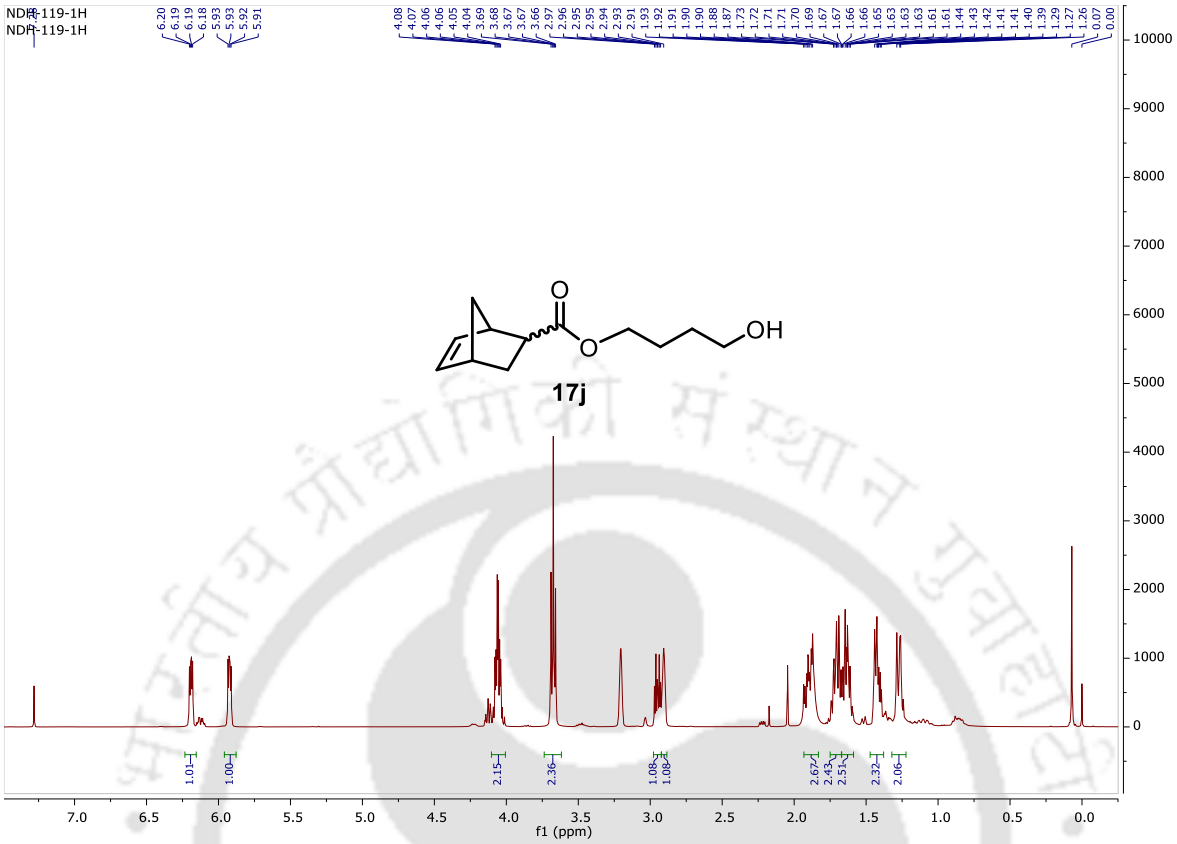


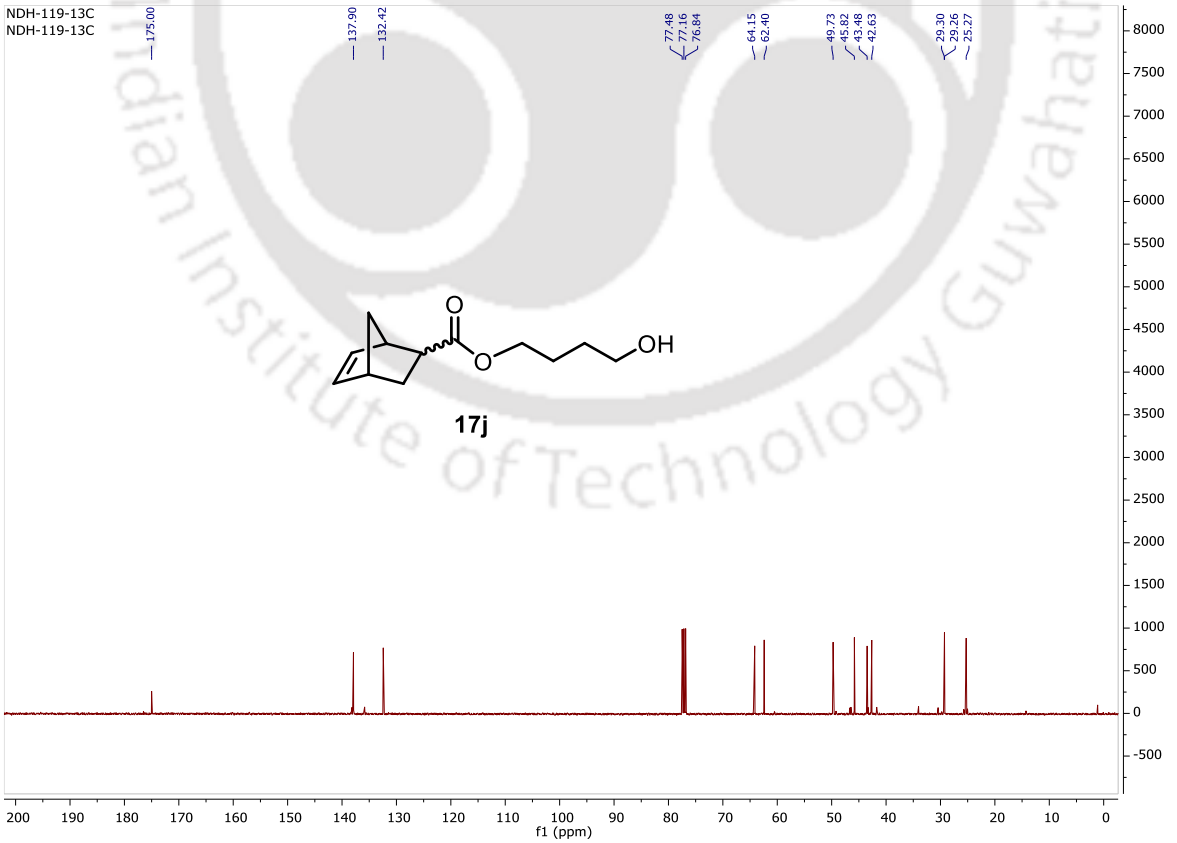


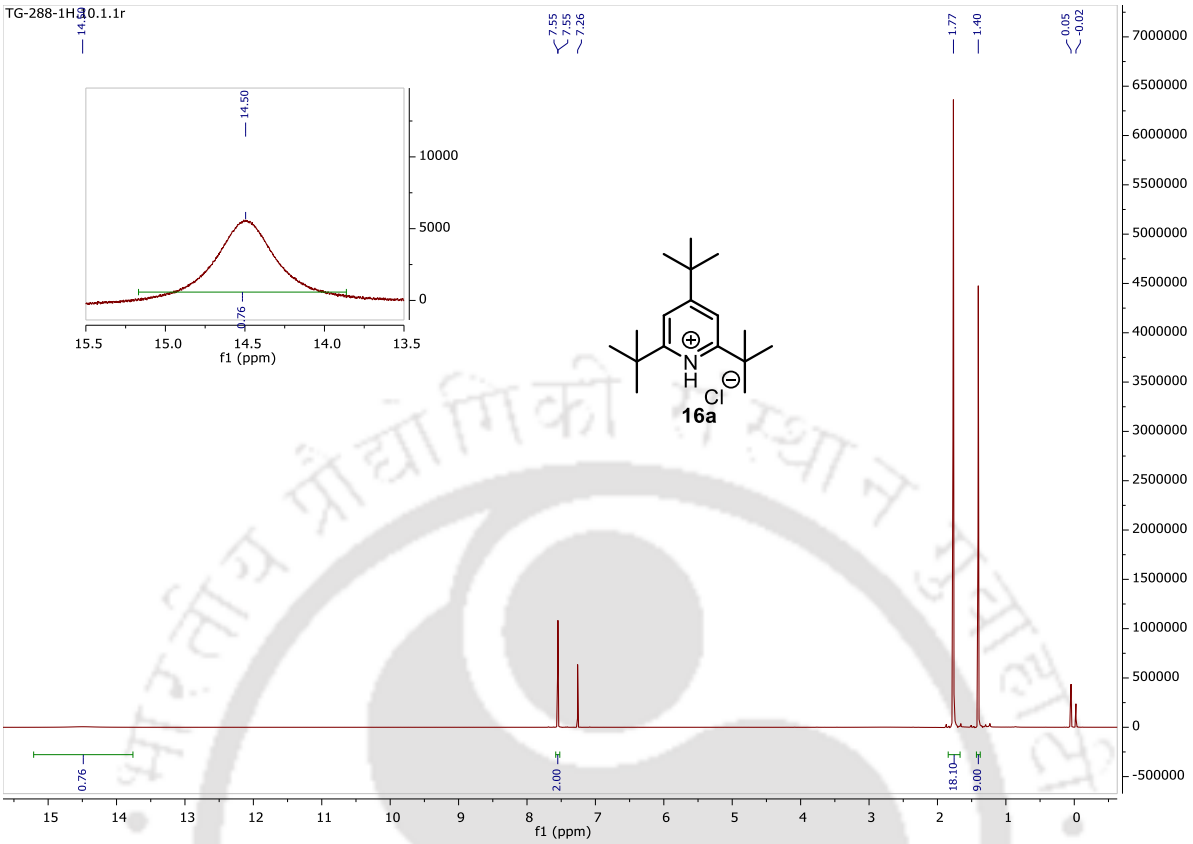


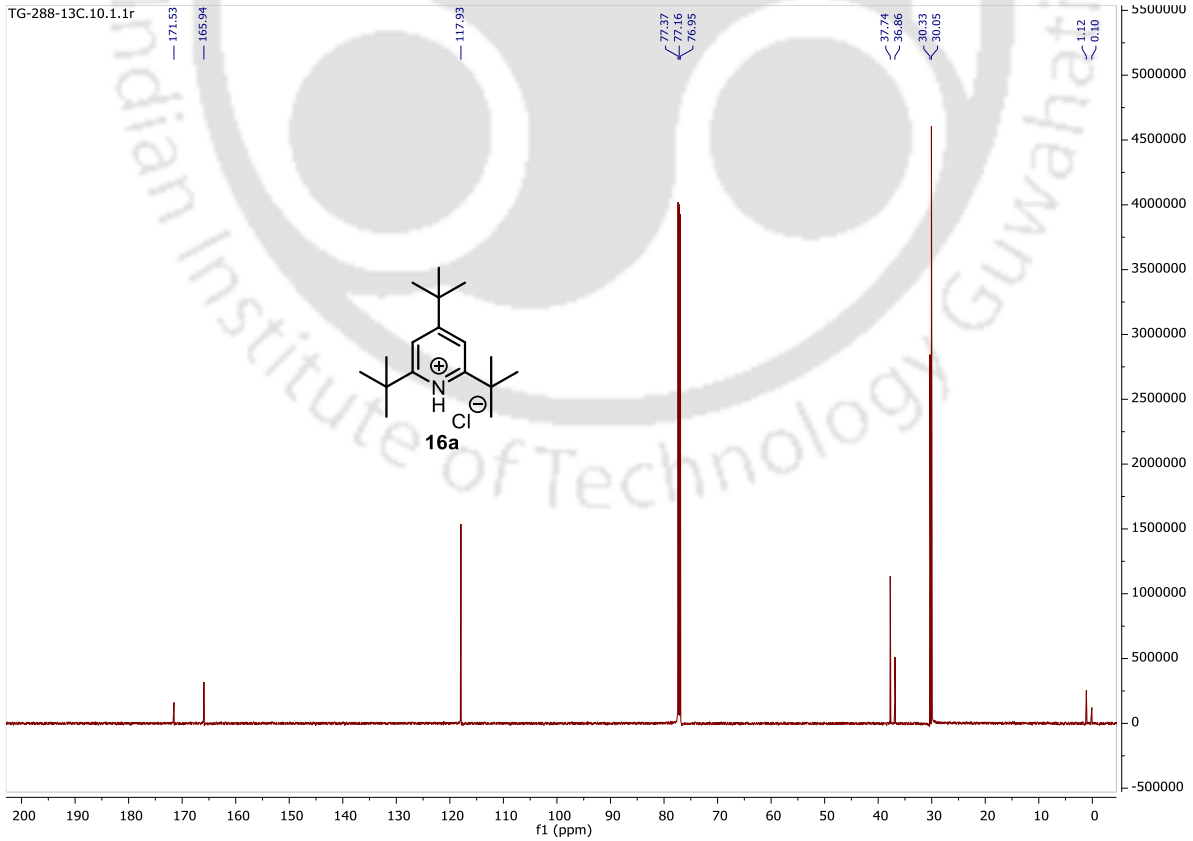


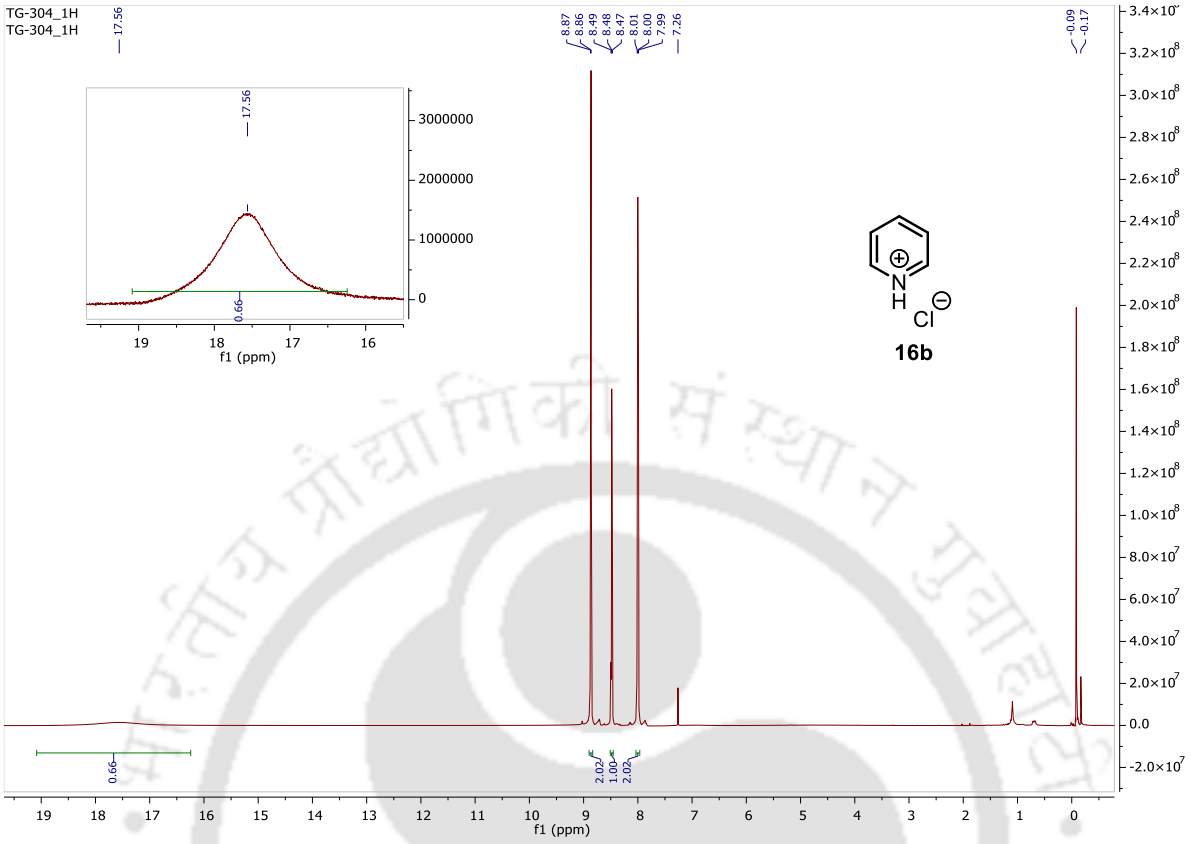


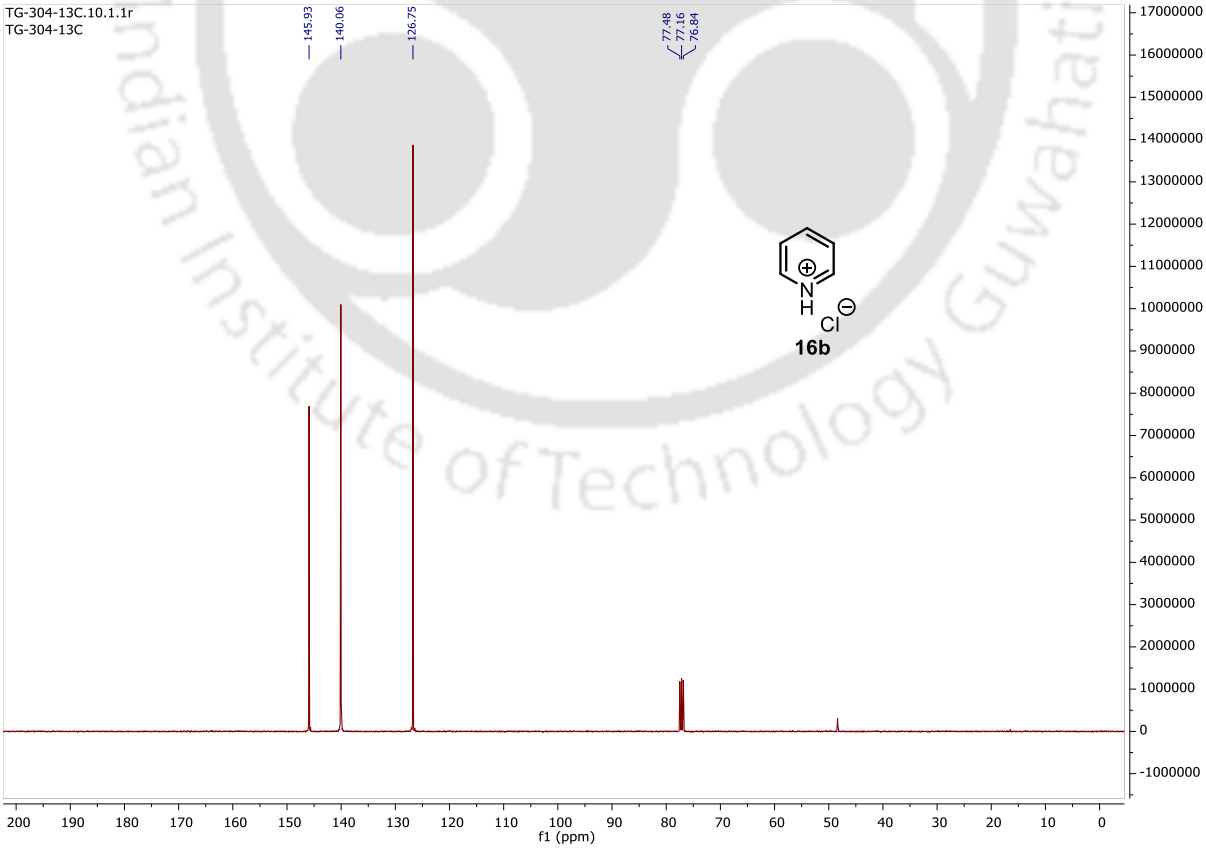


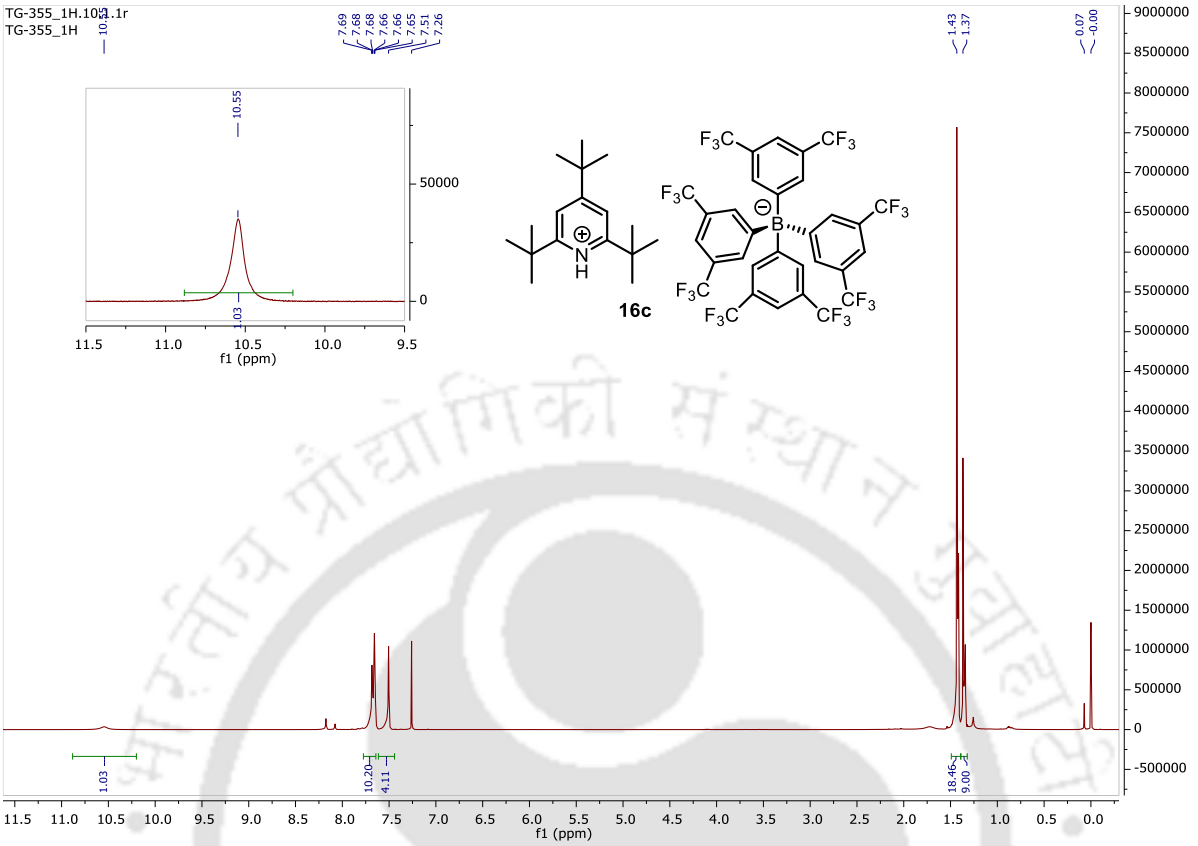


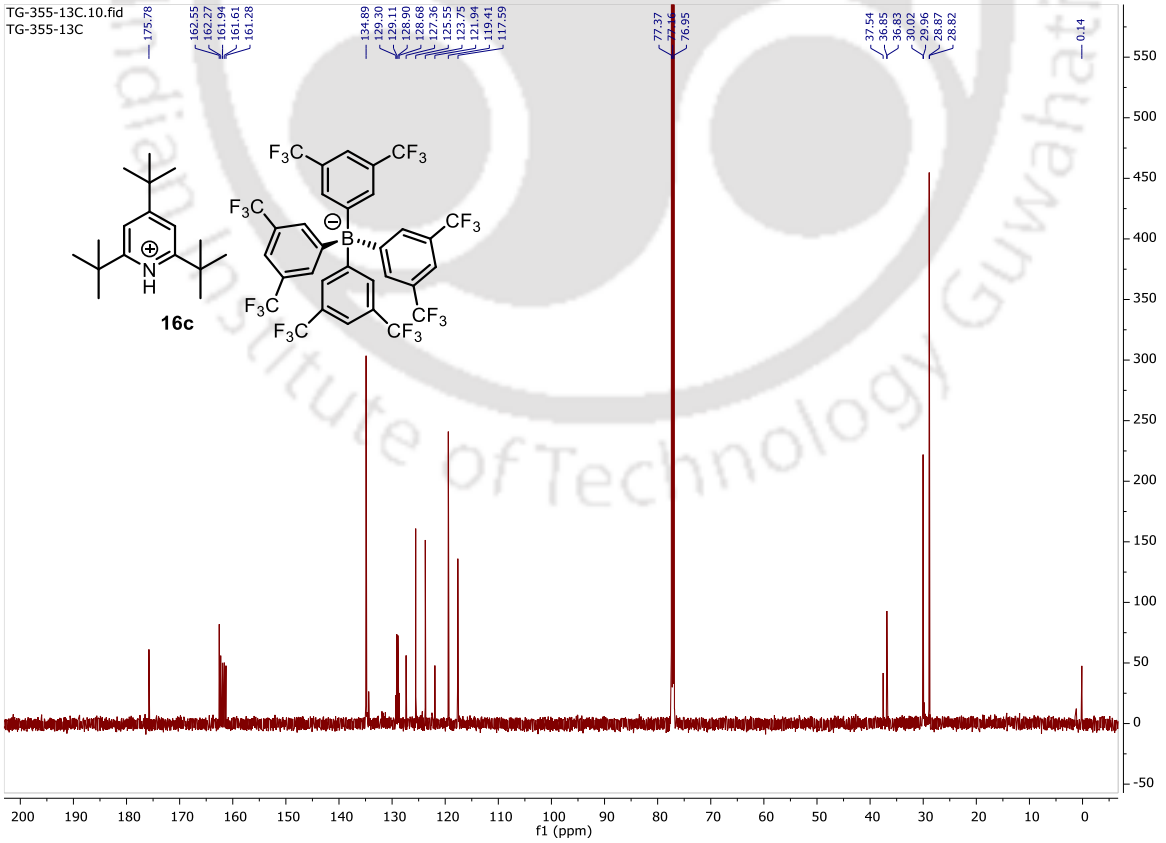


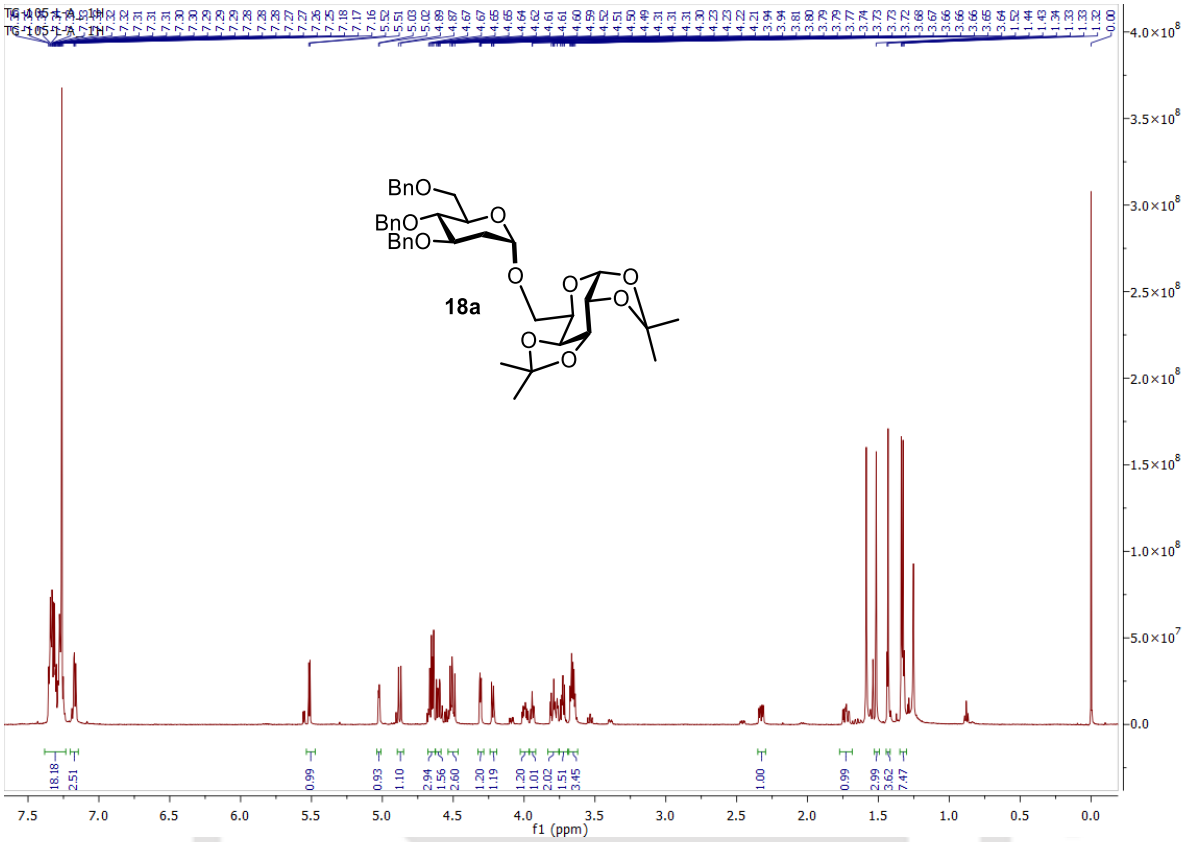


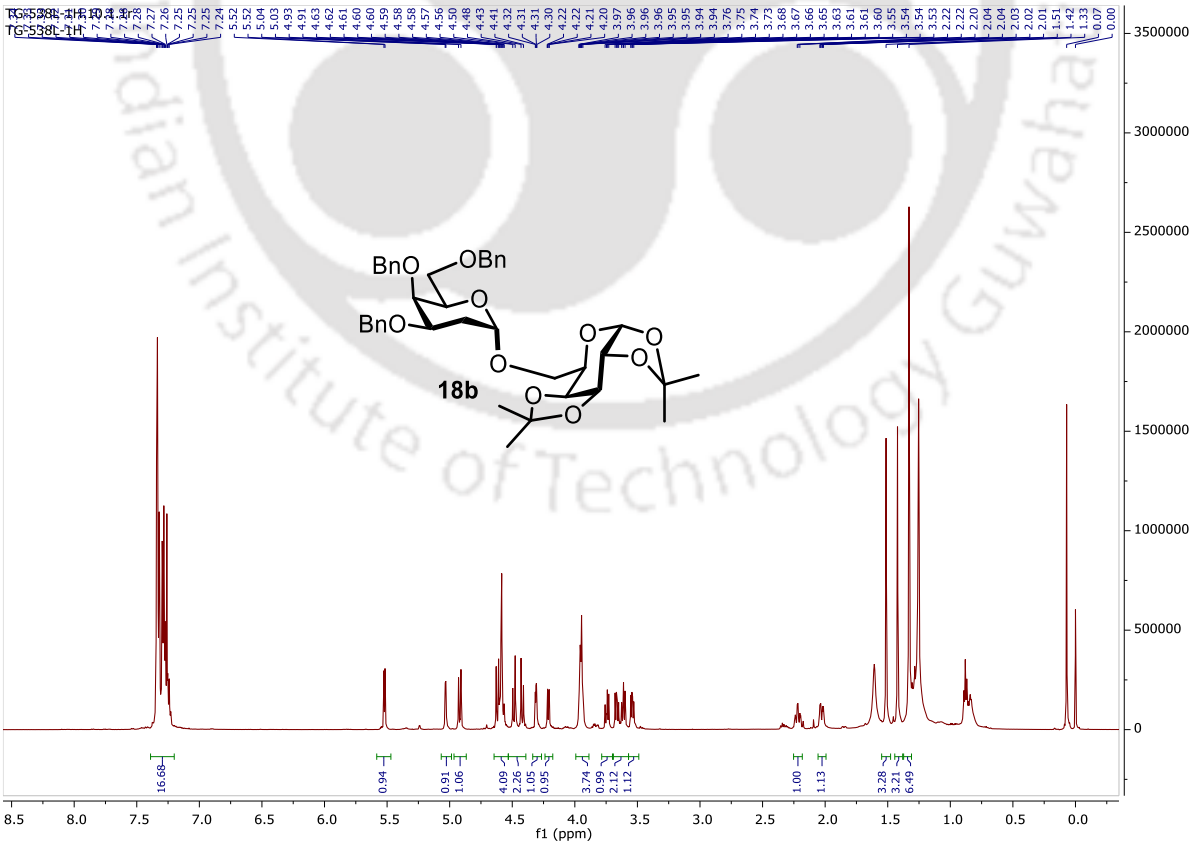


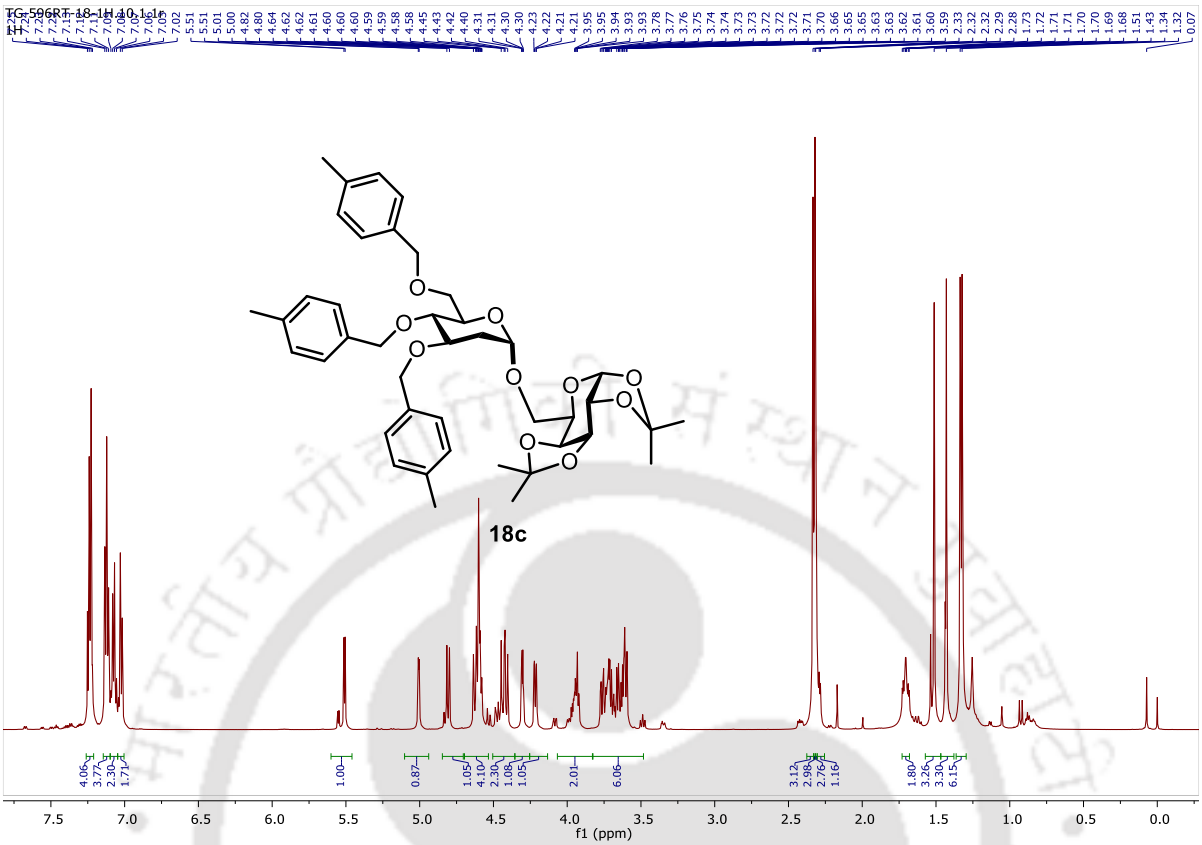


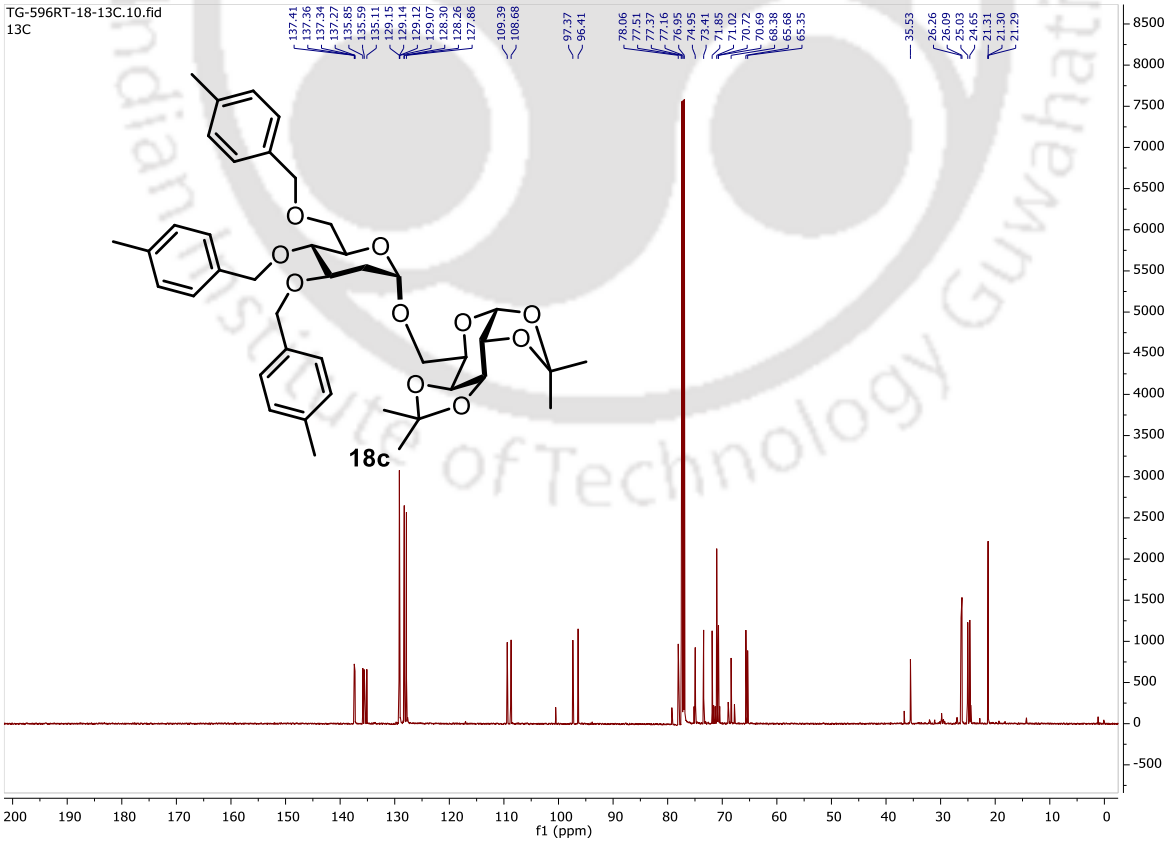




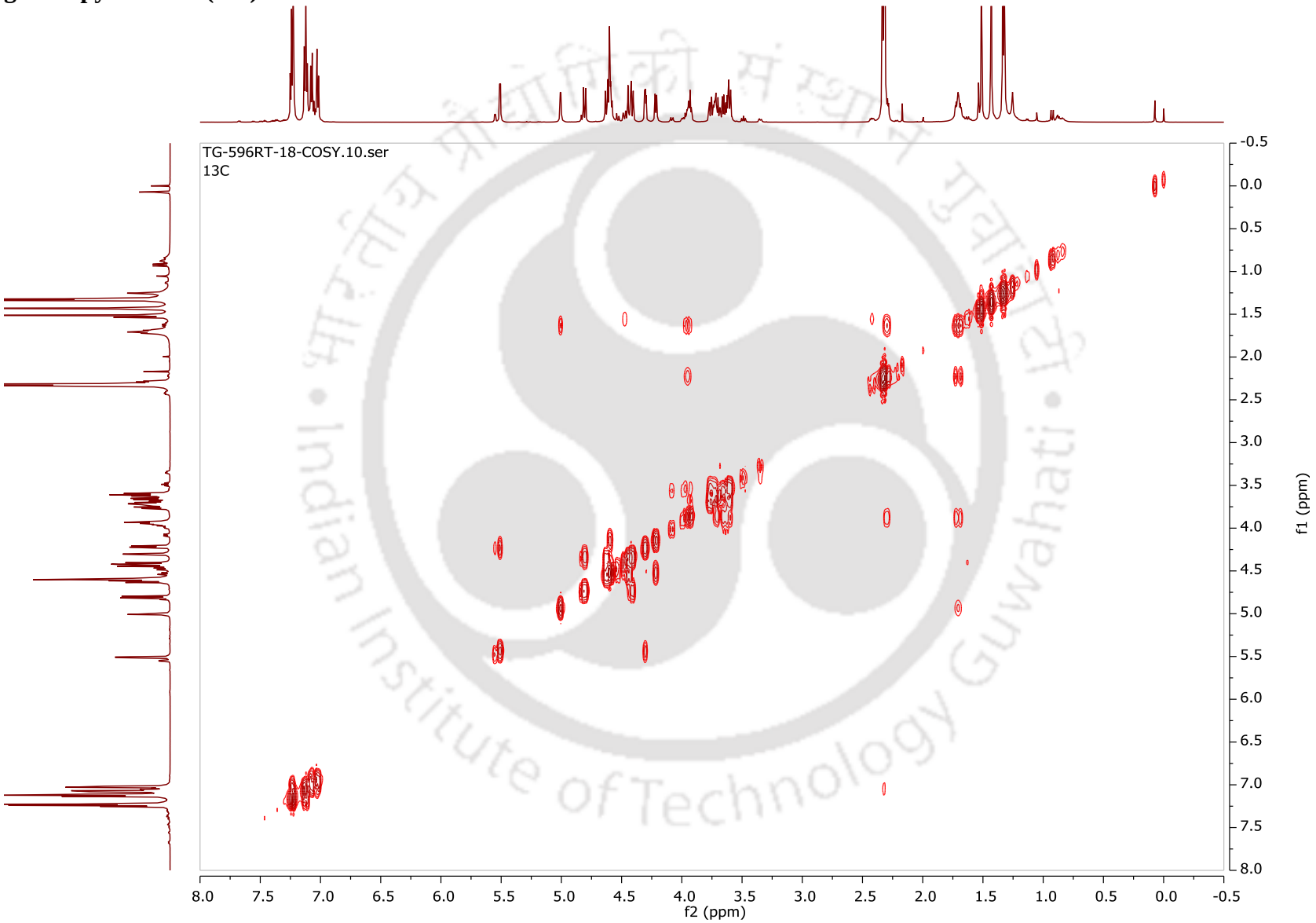


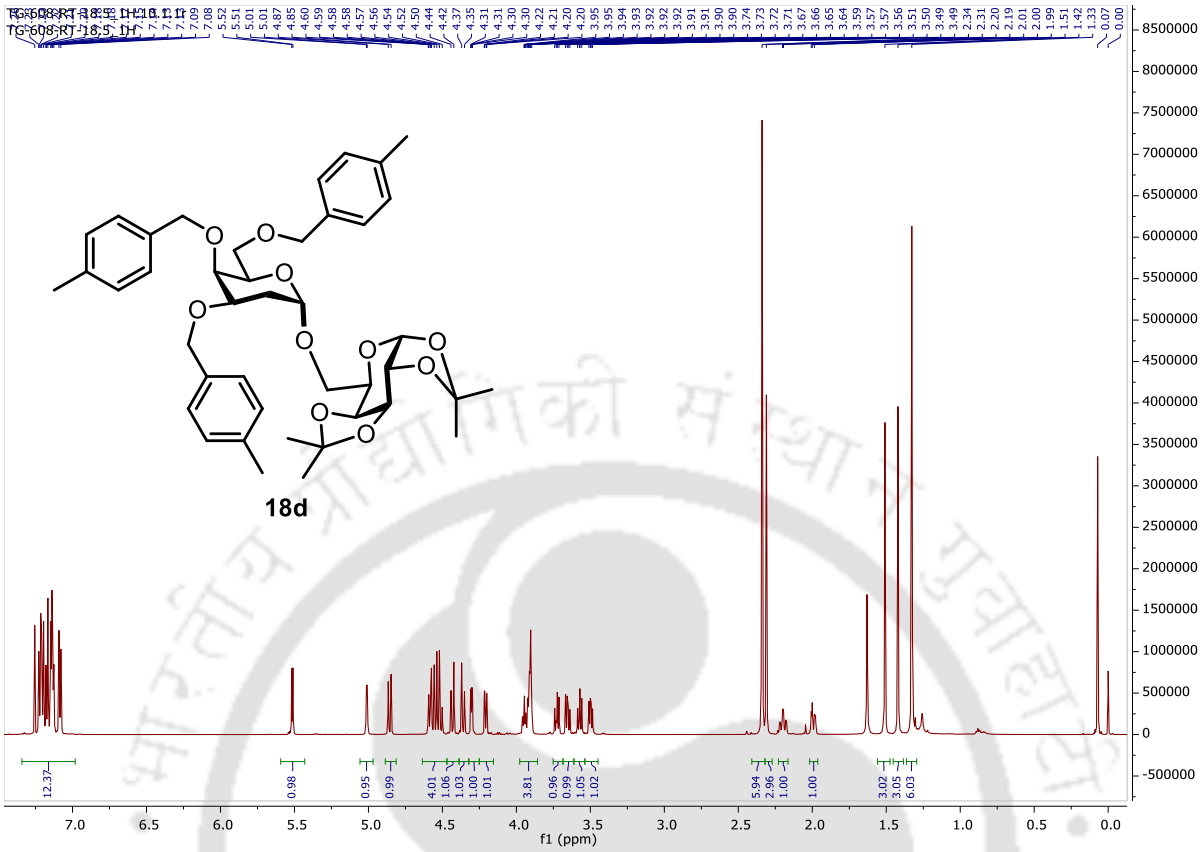


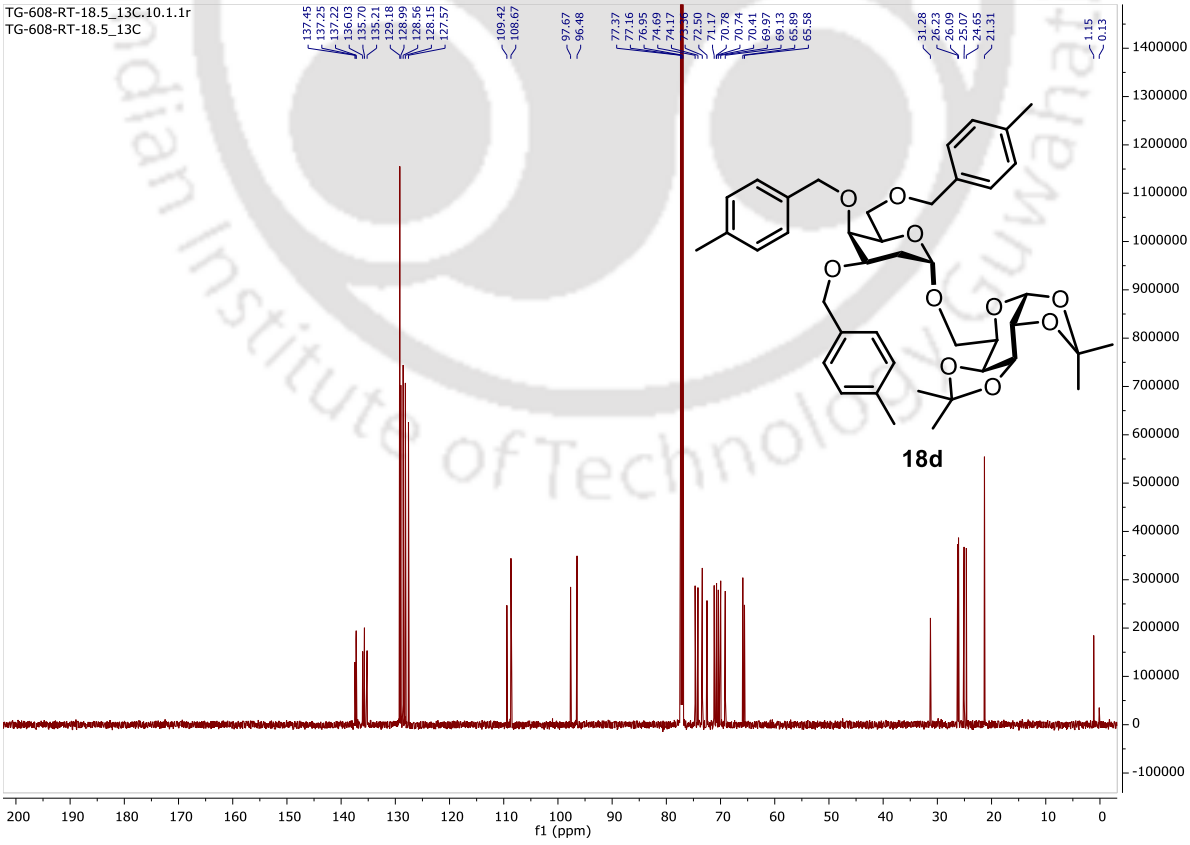




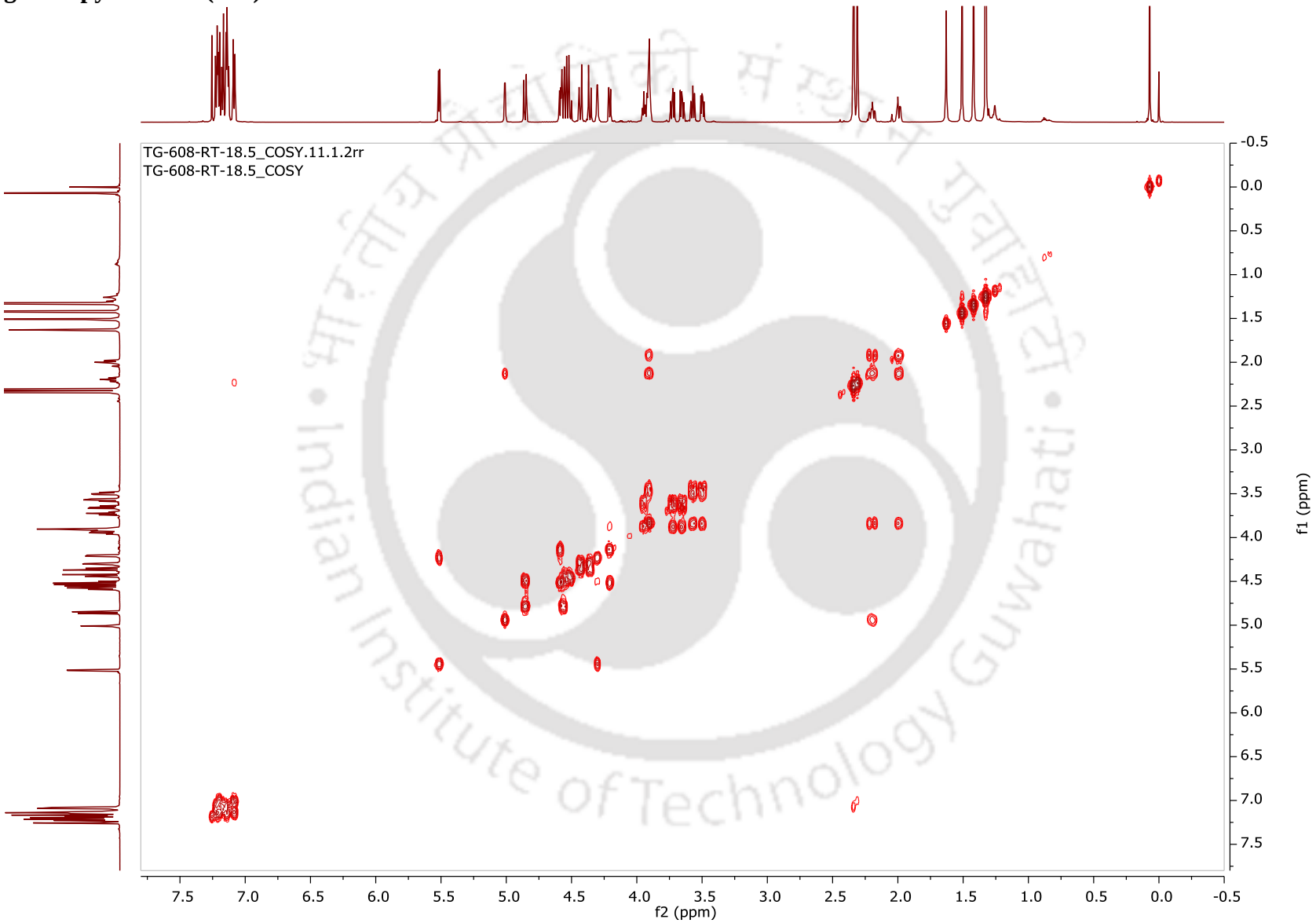
COSY NMR of (3,4,6-tri-*O*-*para*-methylbenzyl-2-deoxy-α,β-D-glucopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (18c):

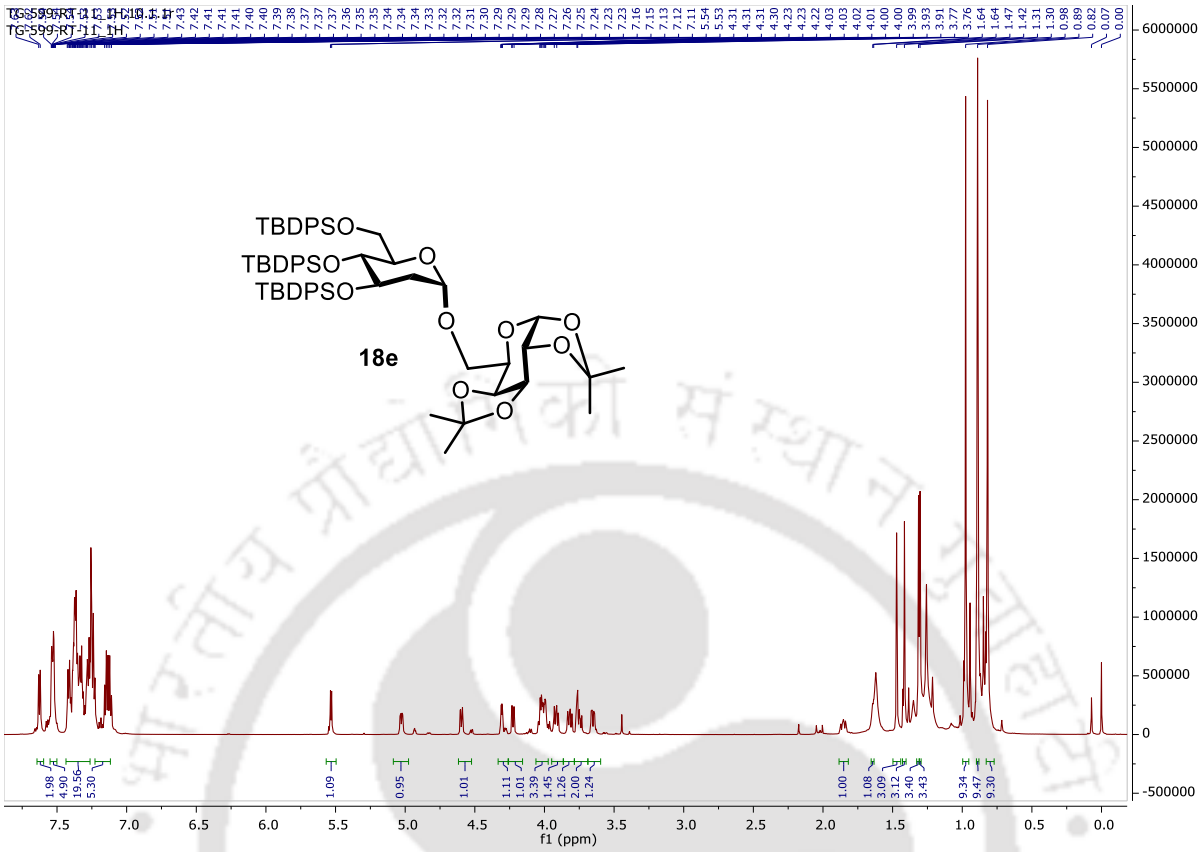


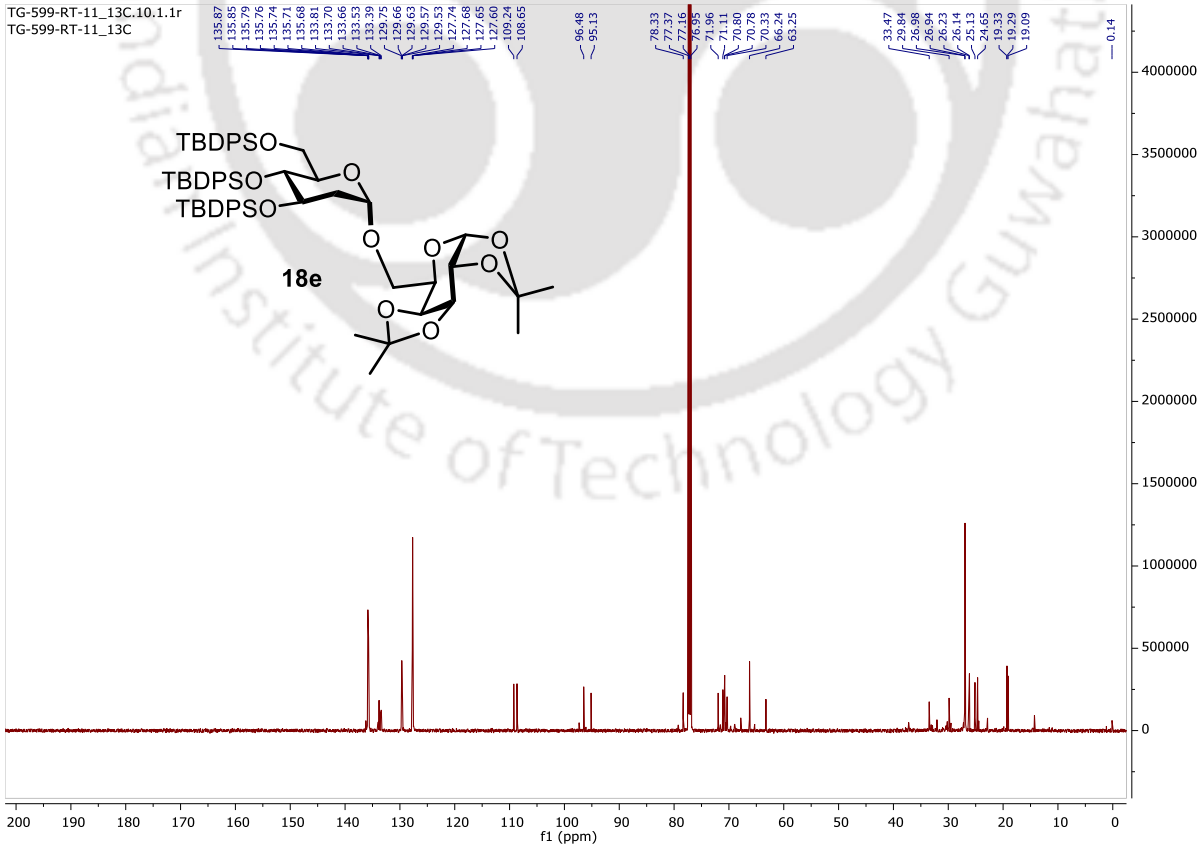




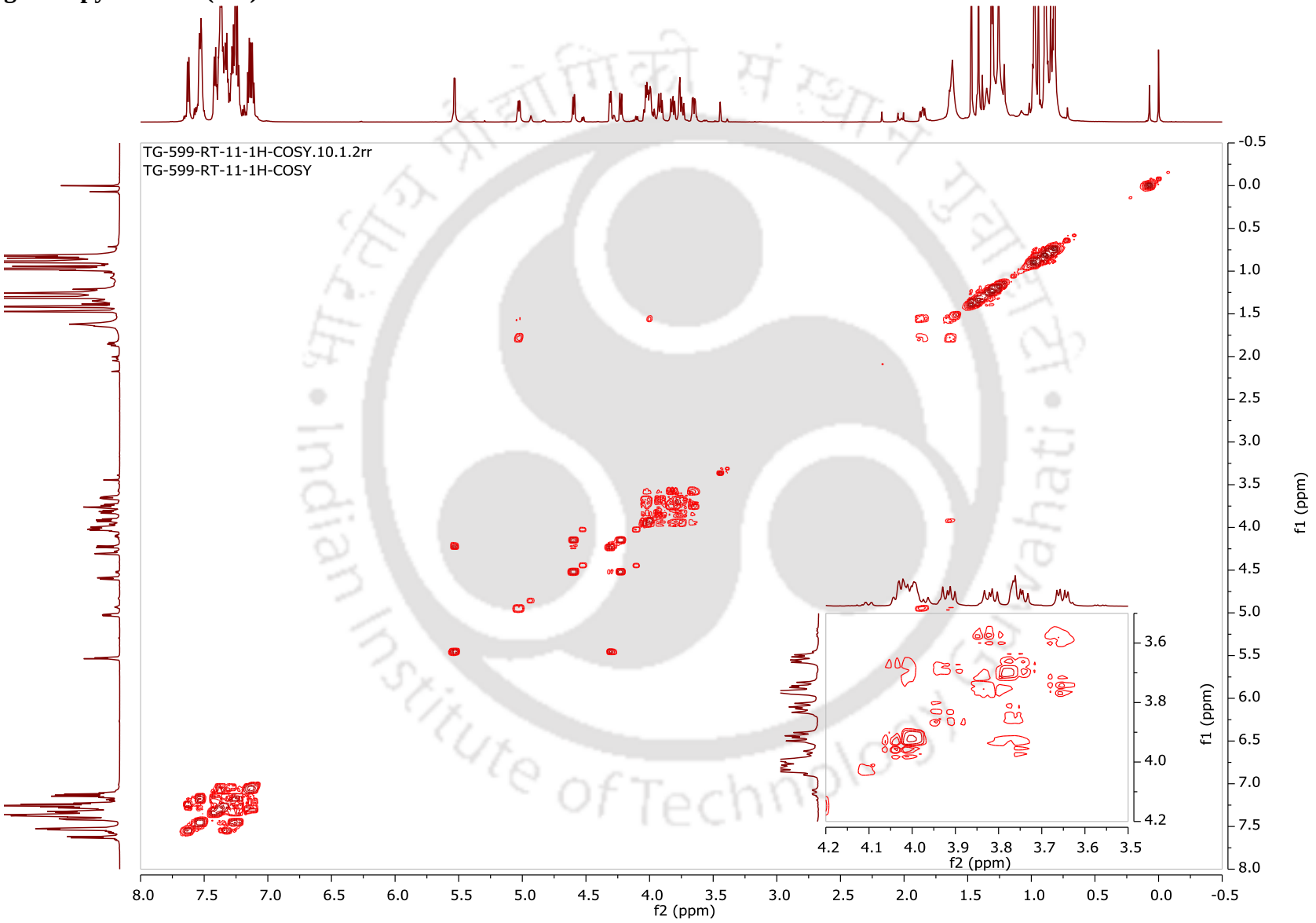
COSY NMR of (3,4,6-tri-*O*-*para*-methylbenzyl-2-deoxy-α-D-galactopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (18d):

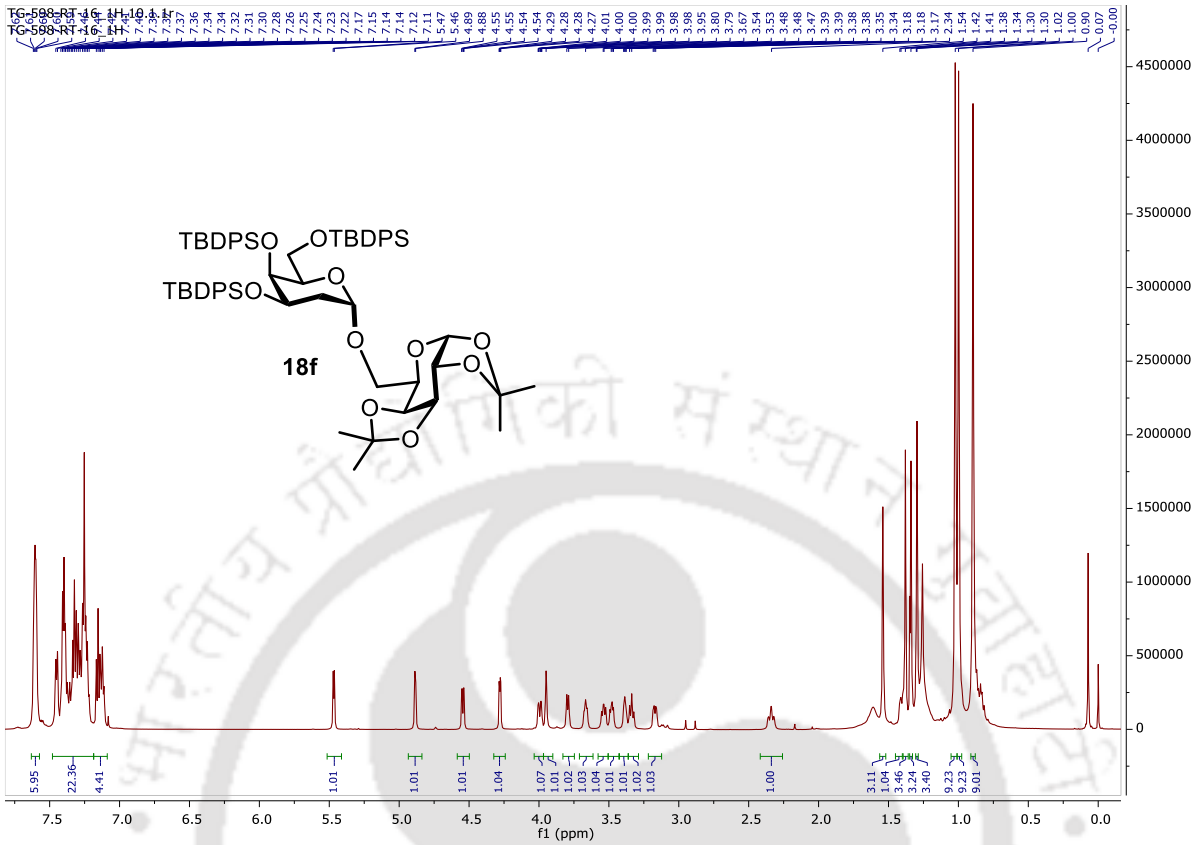


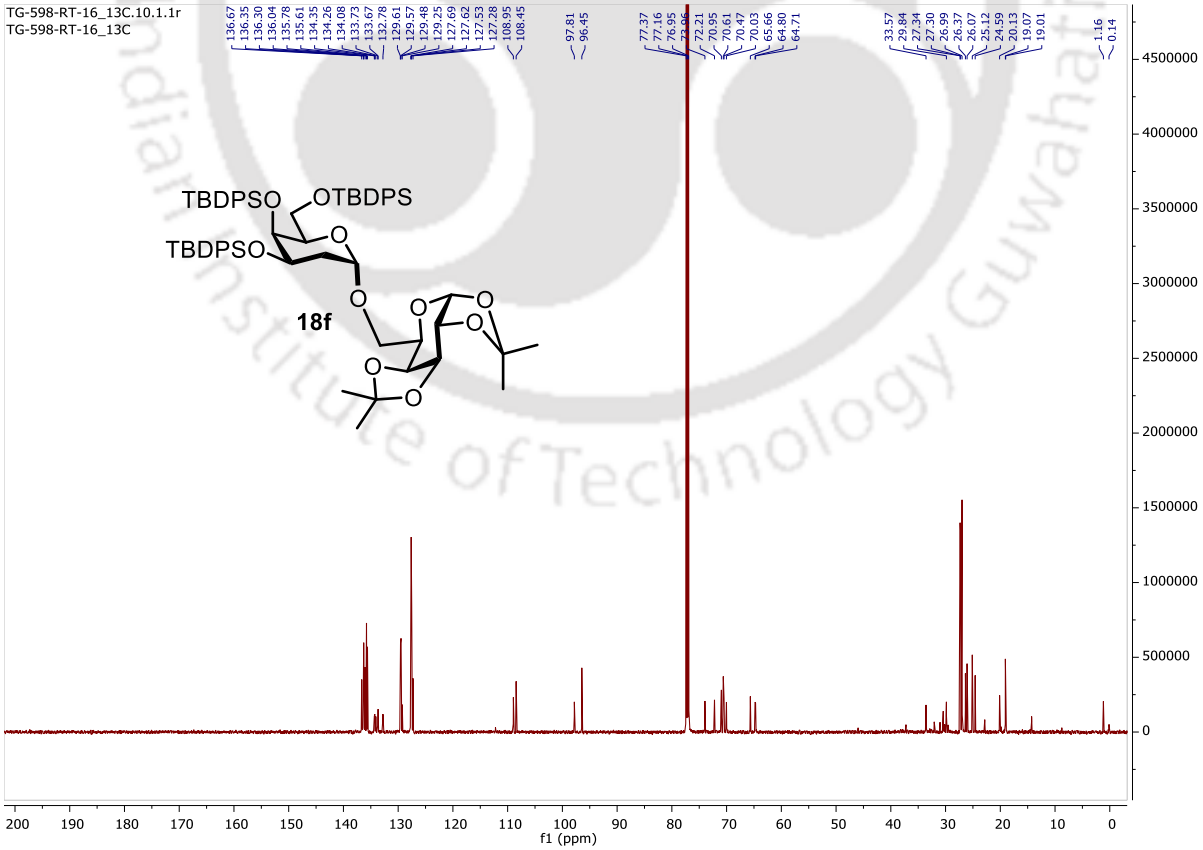




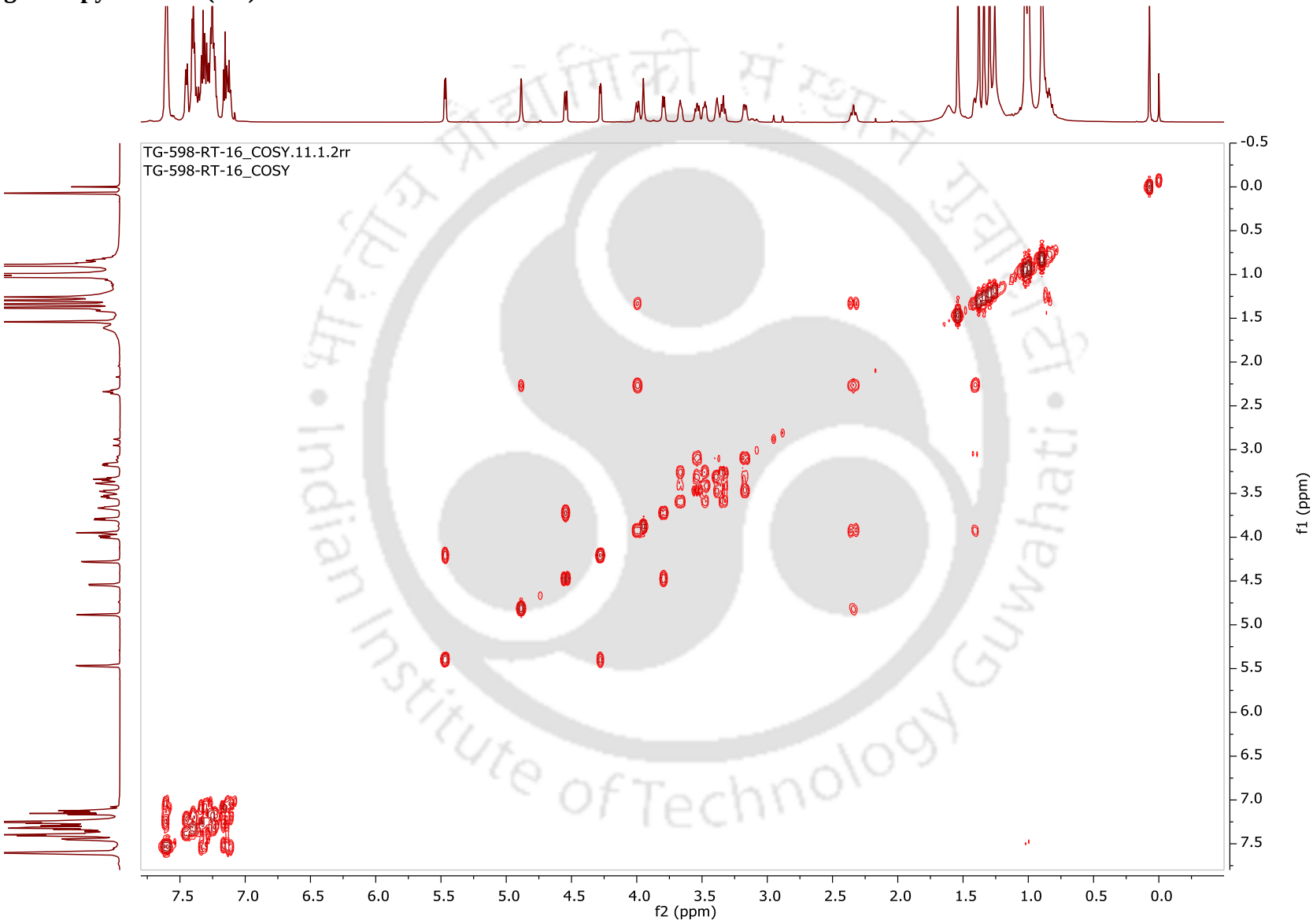
COSY NMR of (3,4,6-tri-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (18e):

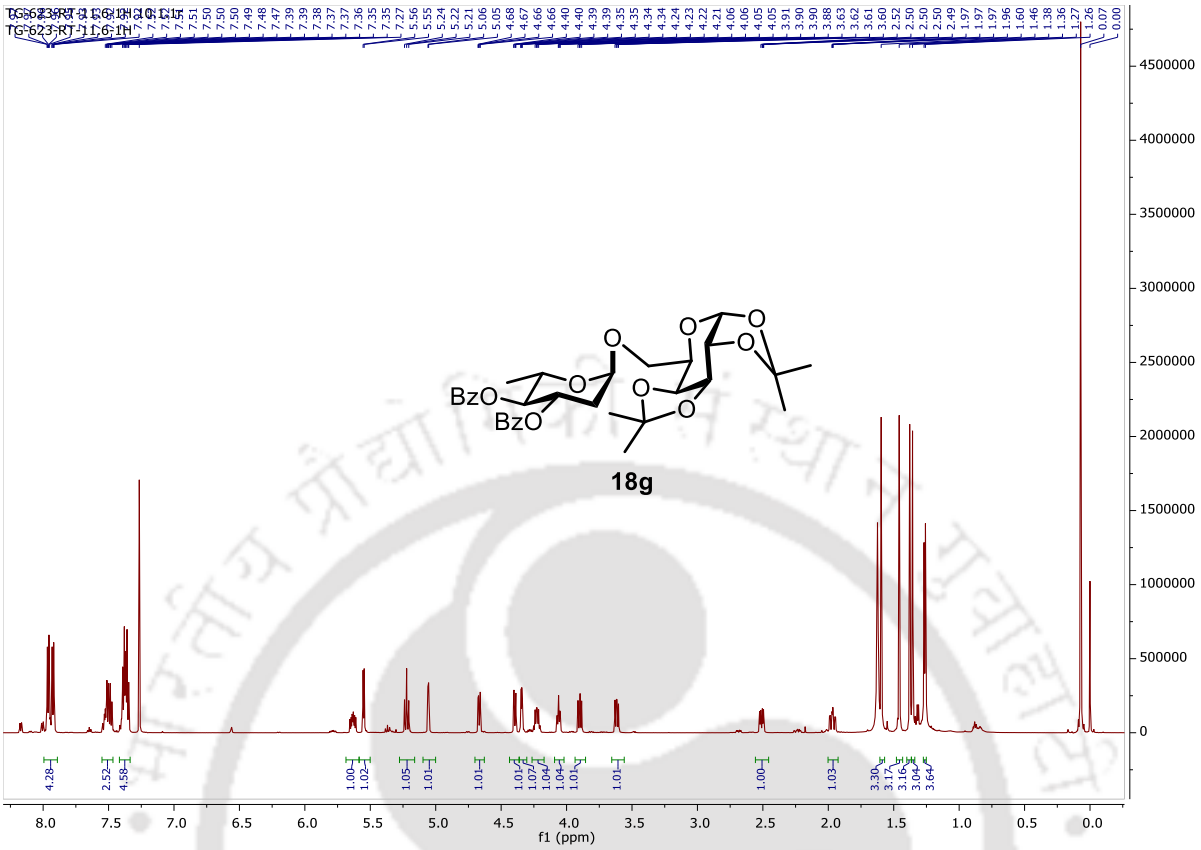


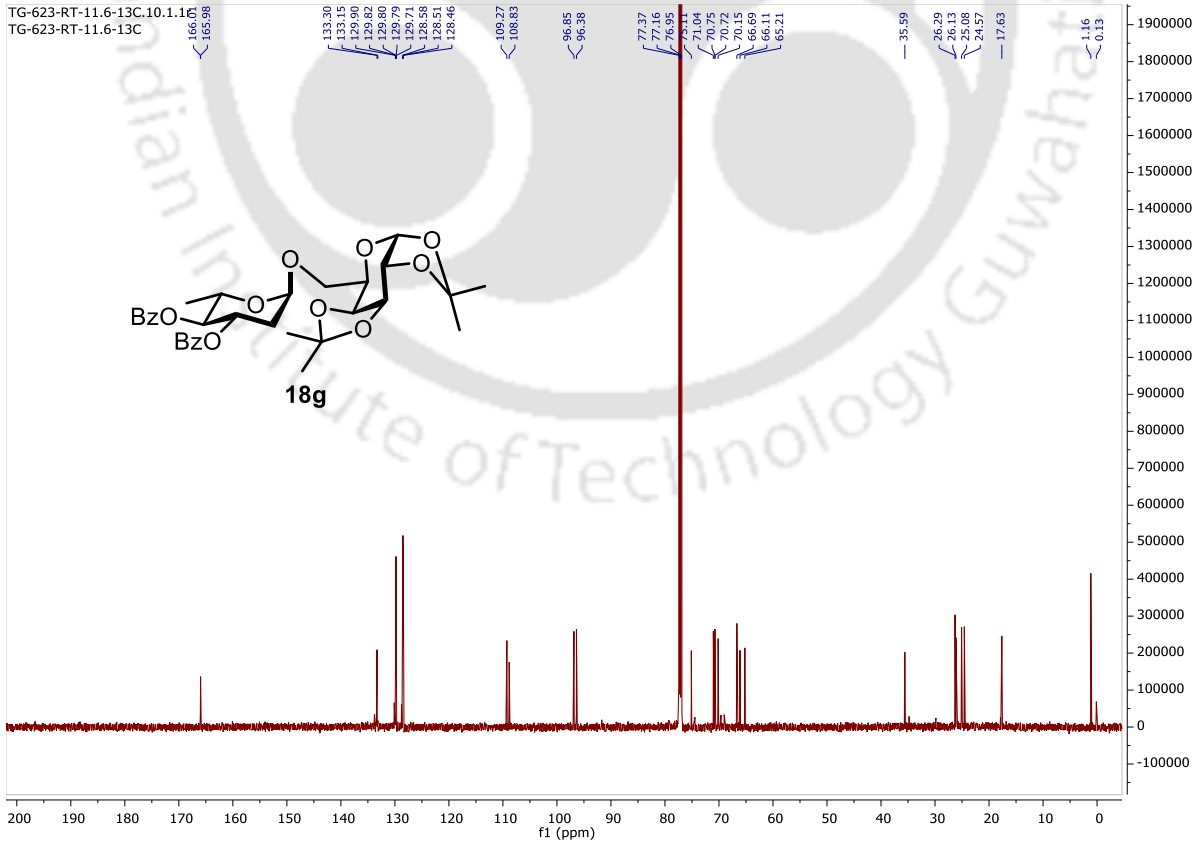




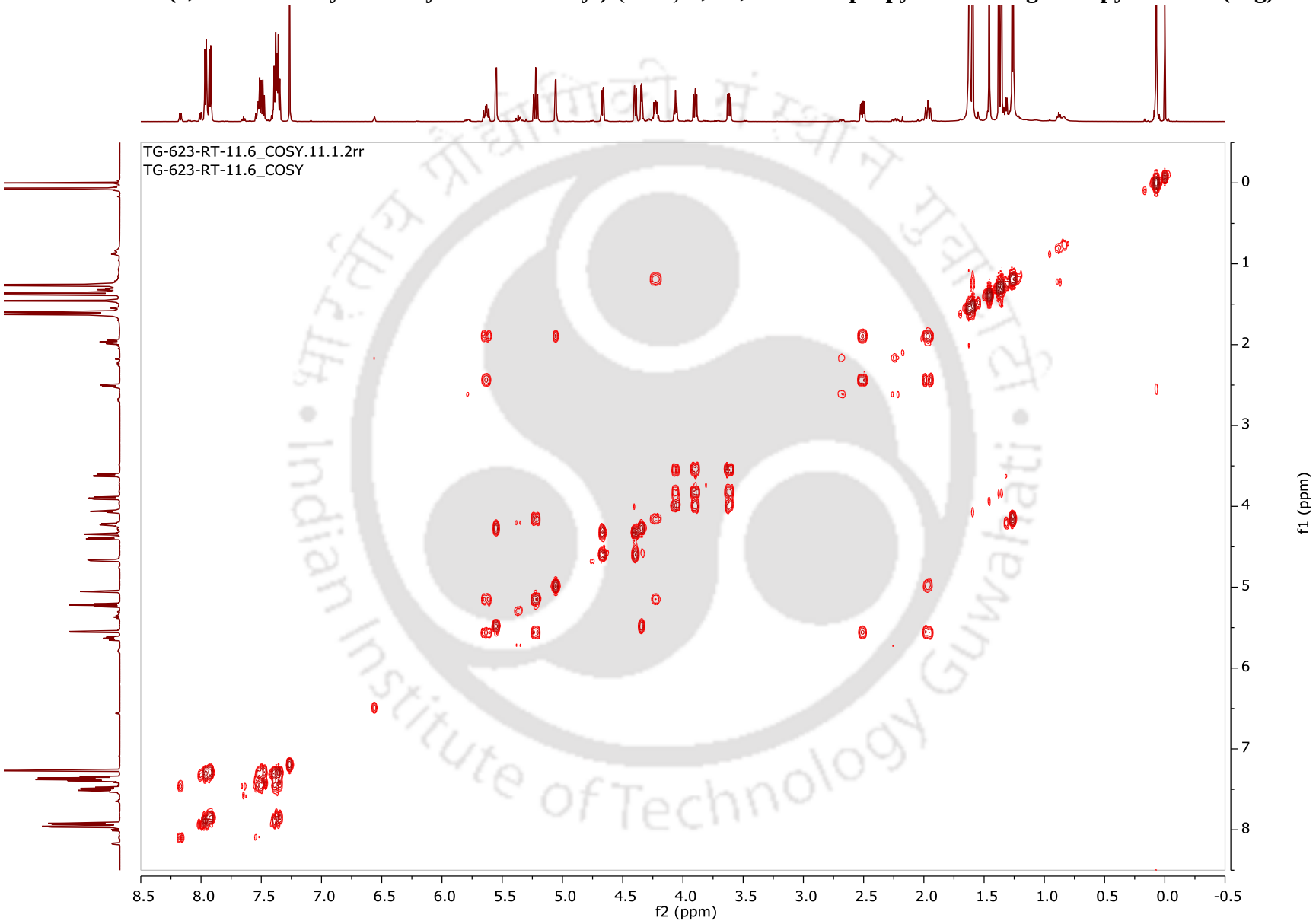
COSY NMR of (3,4,6-tri-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-D-galactopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (18f):

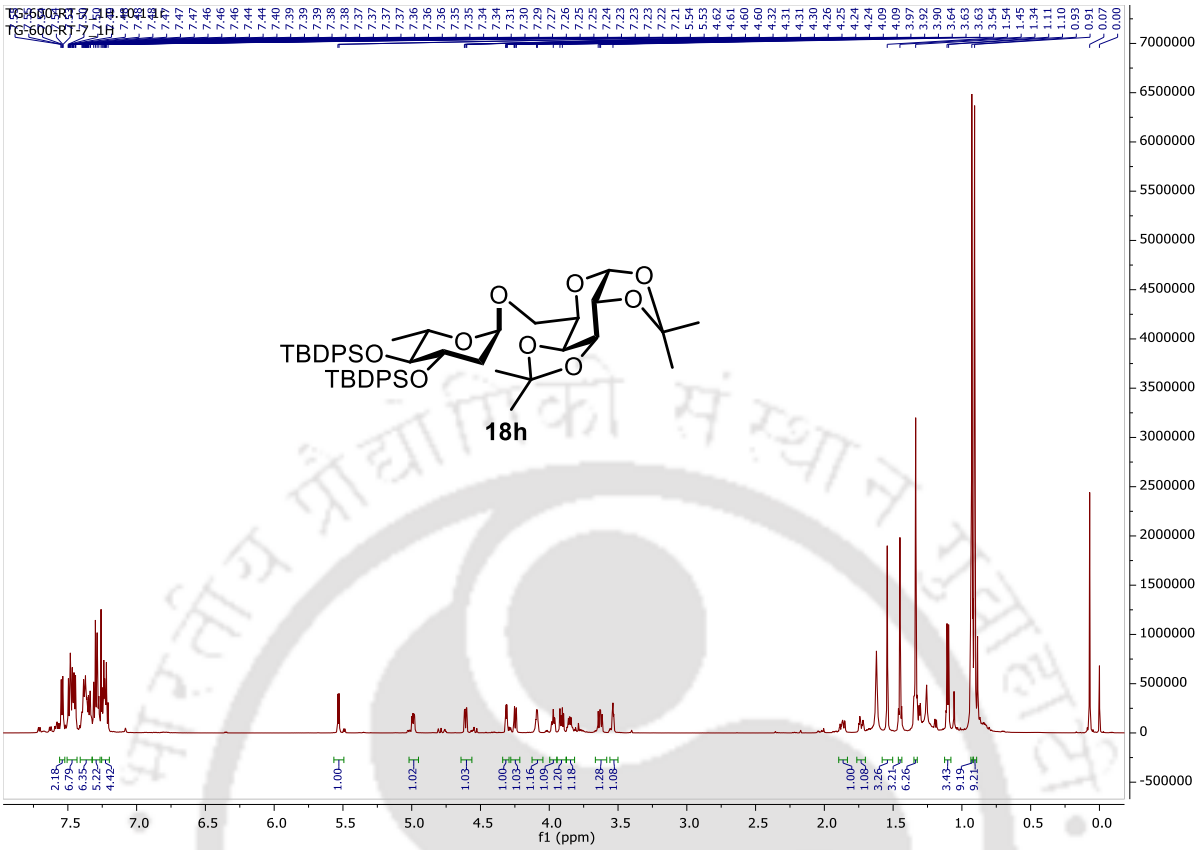


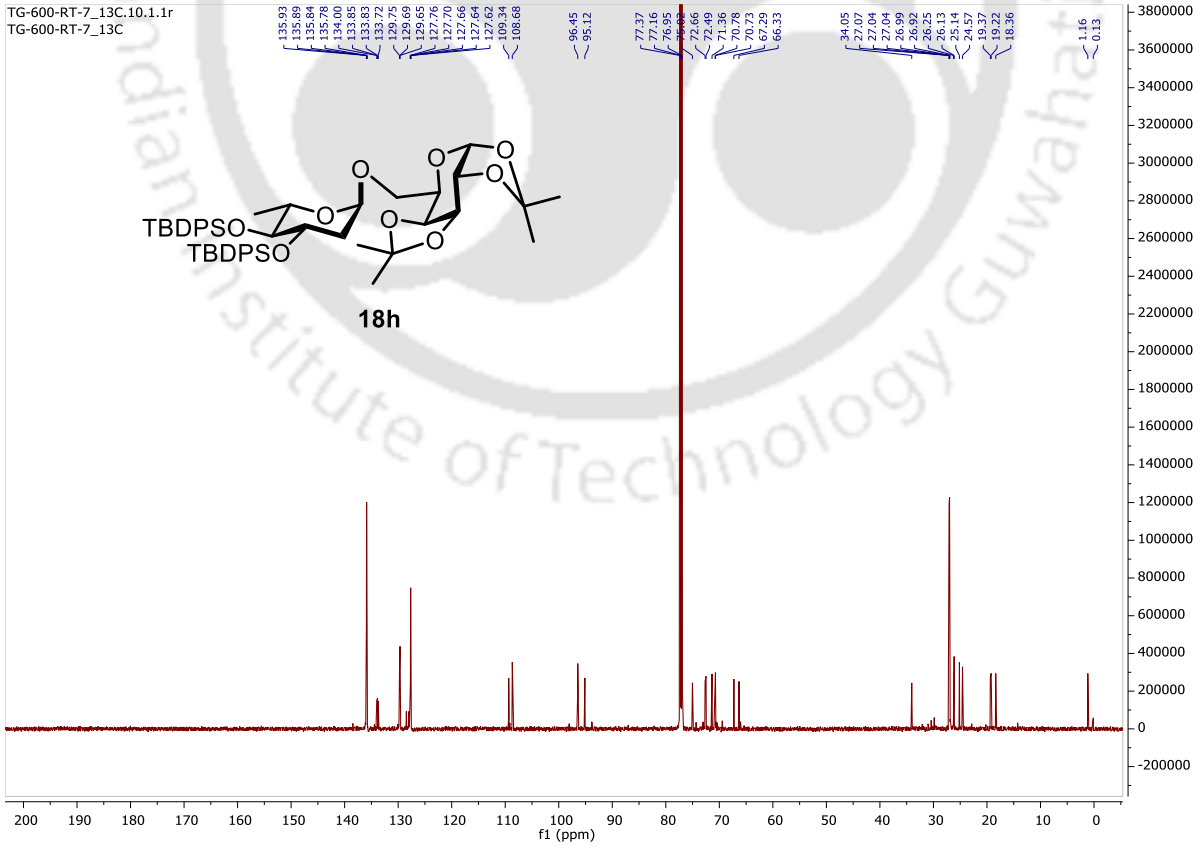




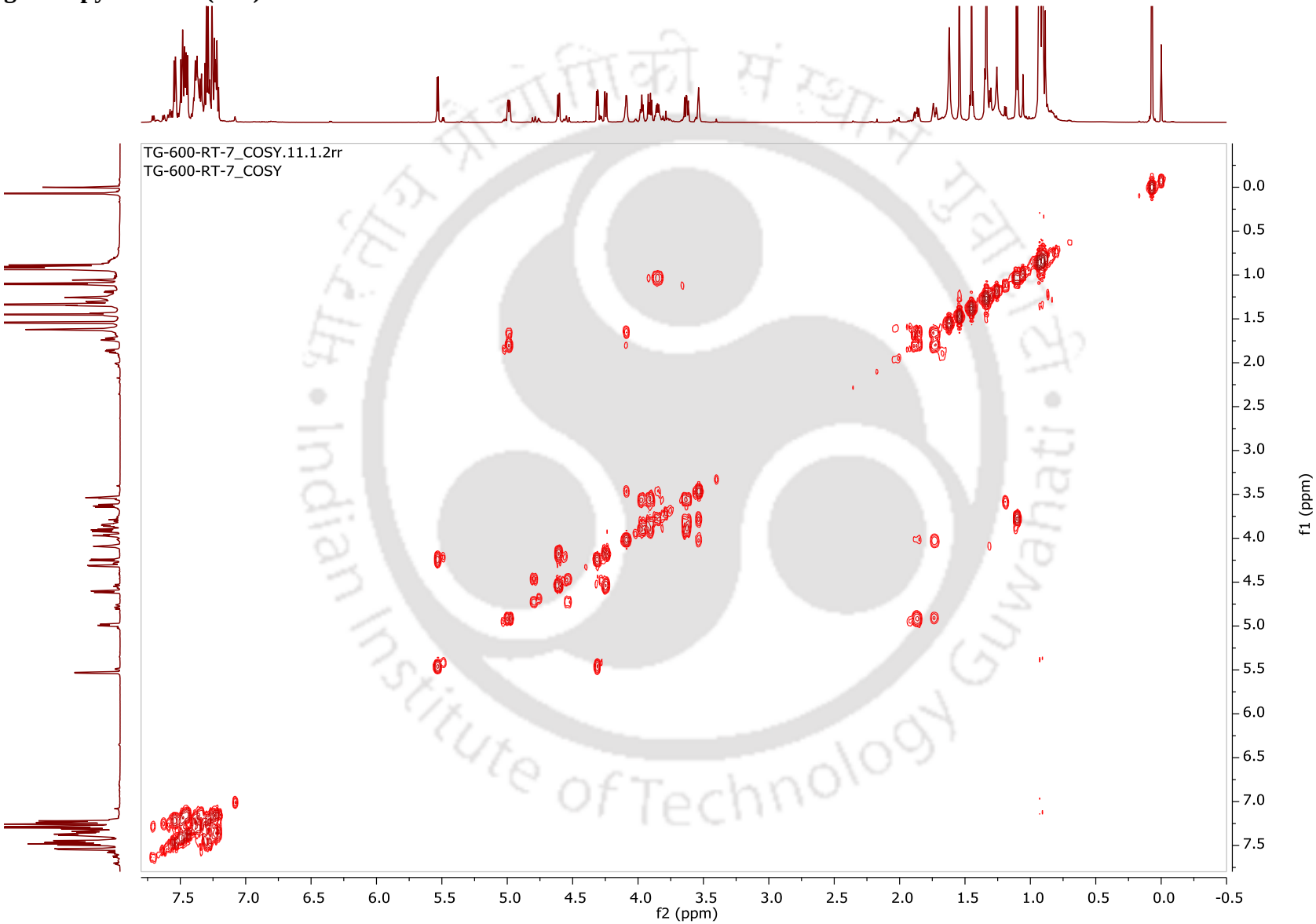
COSY NMR of (3,4-di-*O*-benzoyl-2-deoxy-α-L-rhamnosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (18g):

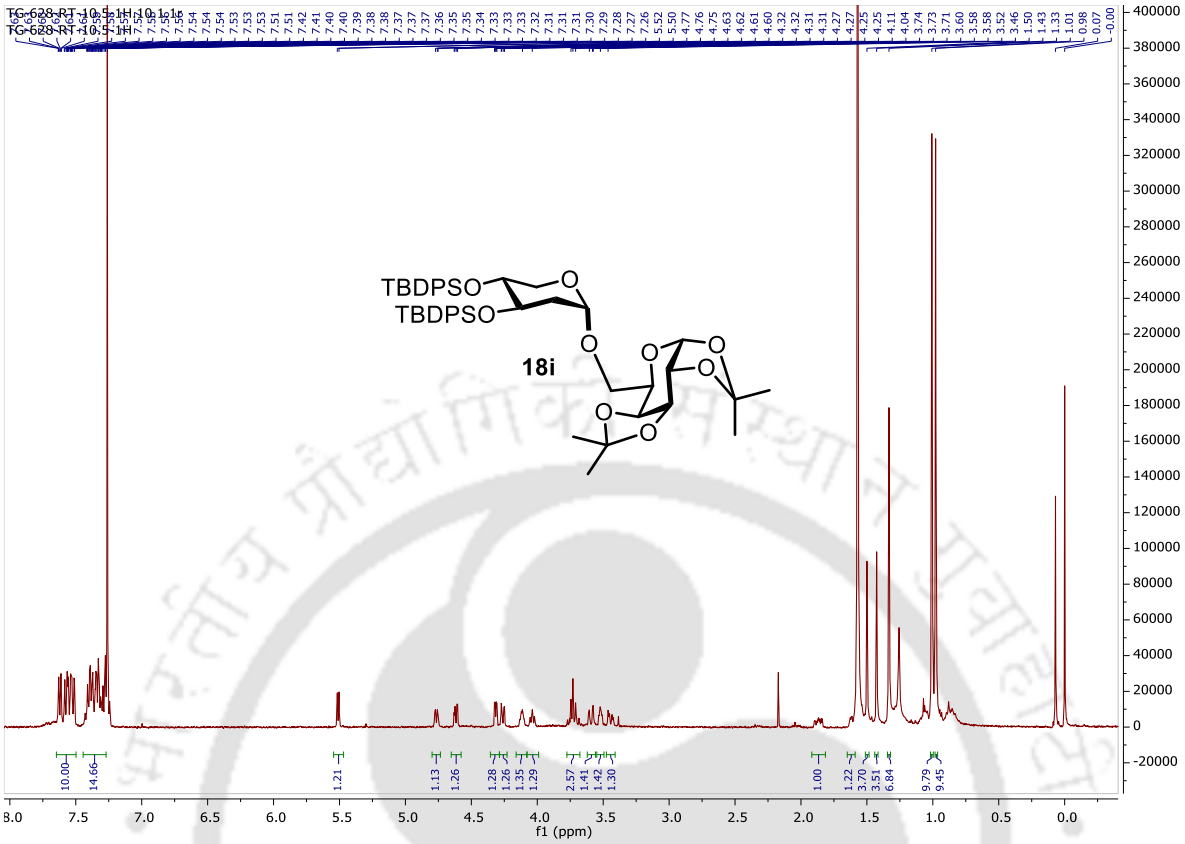


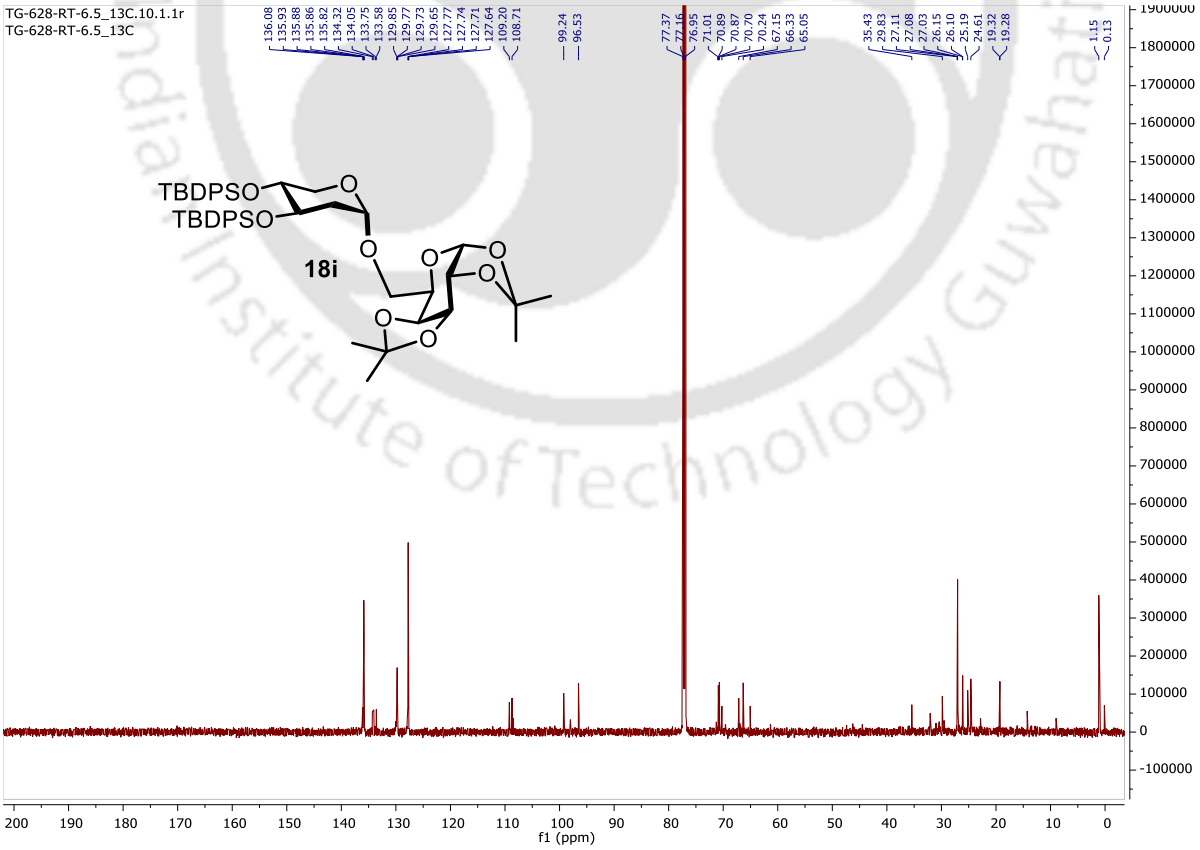


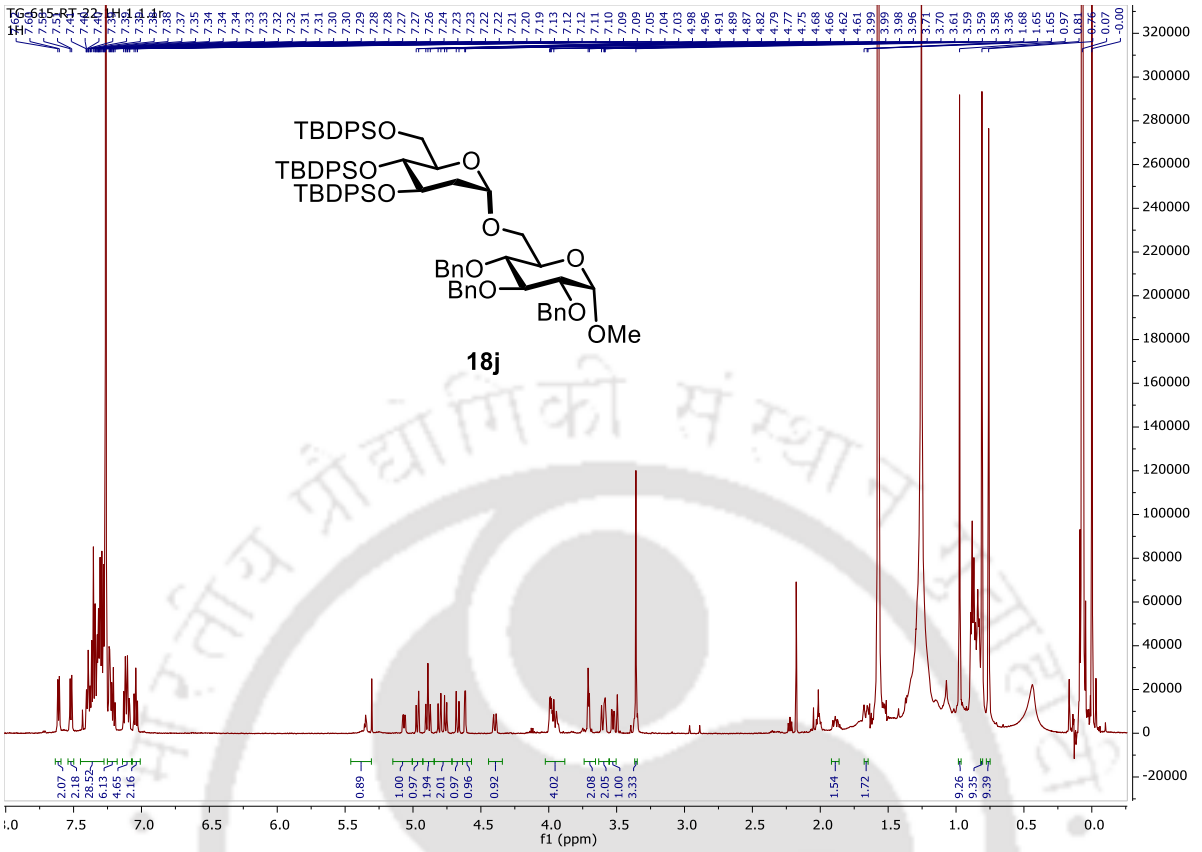


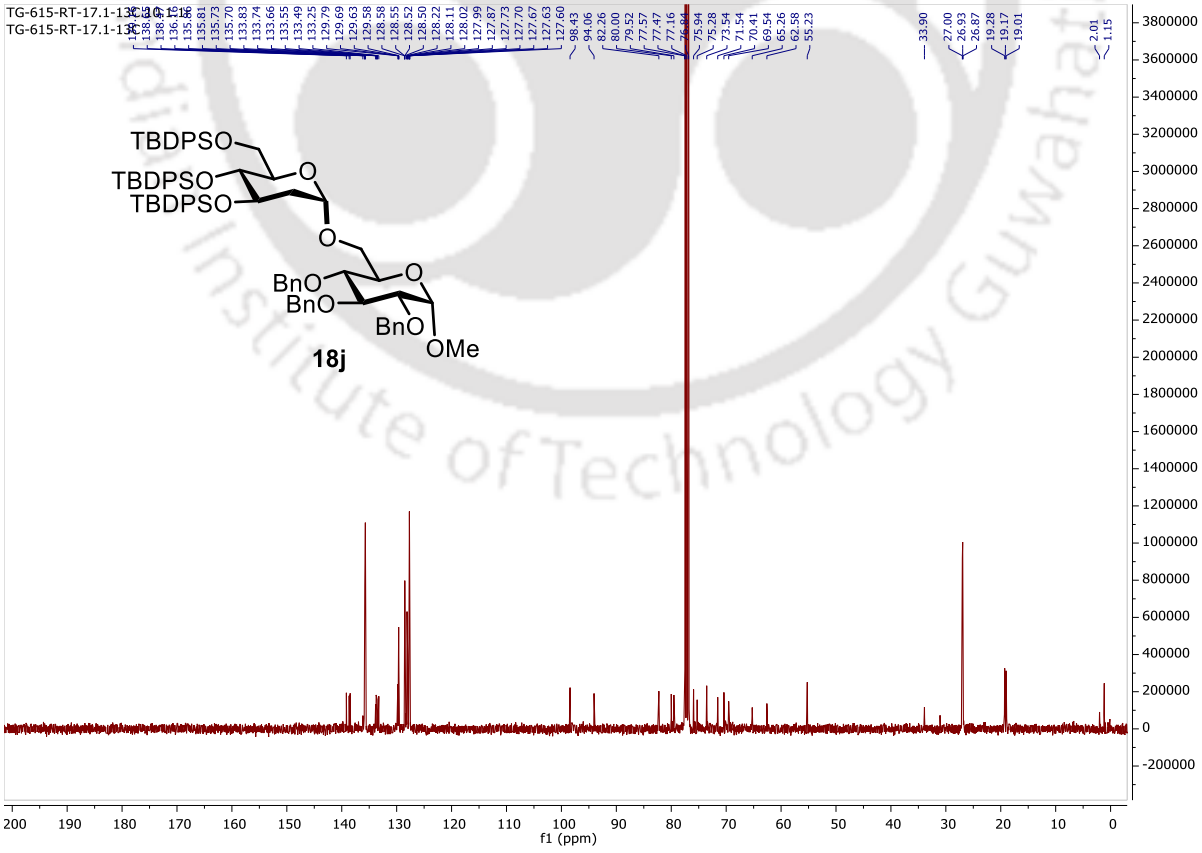
COSY NMR of (3,4-di-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-L-rhamnosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (18h):

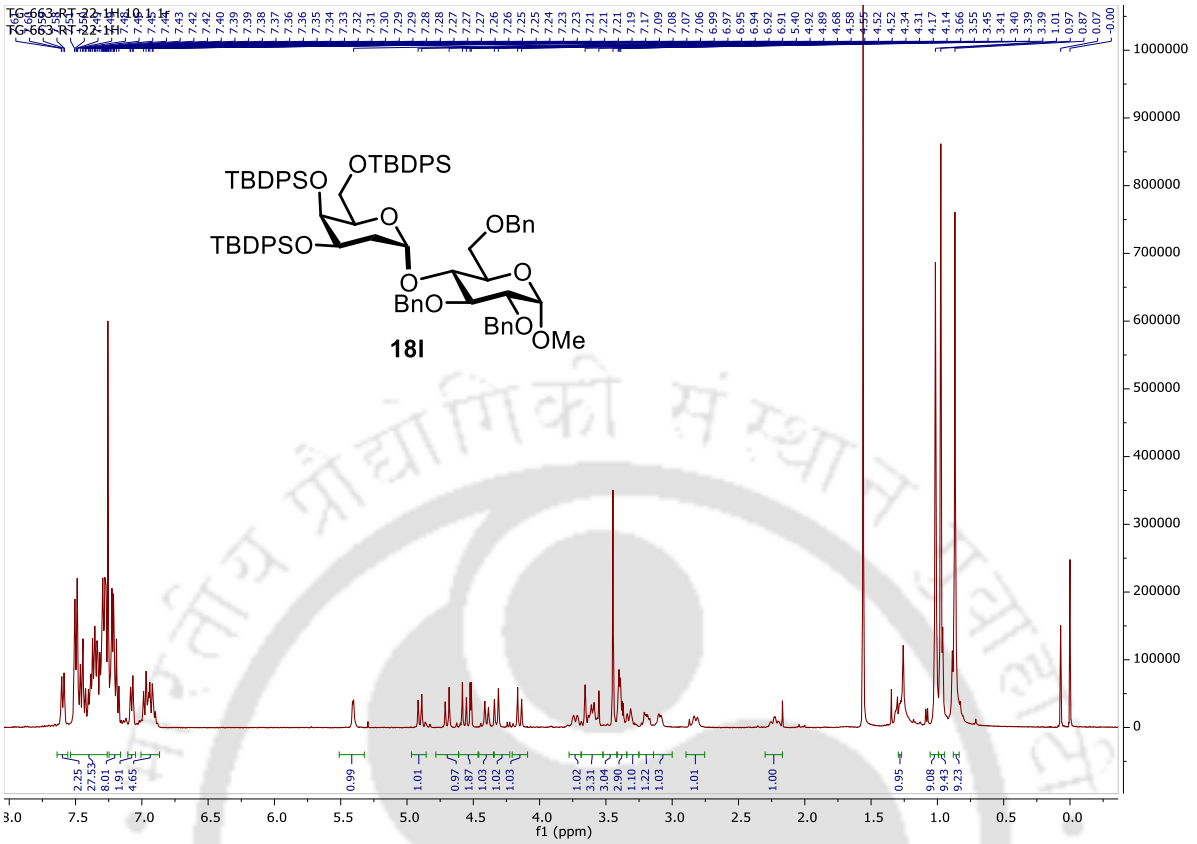


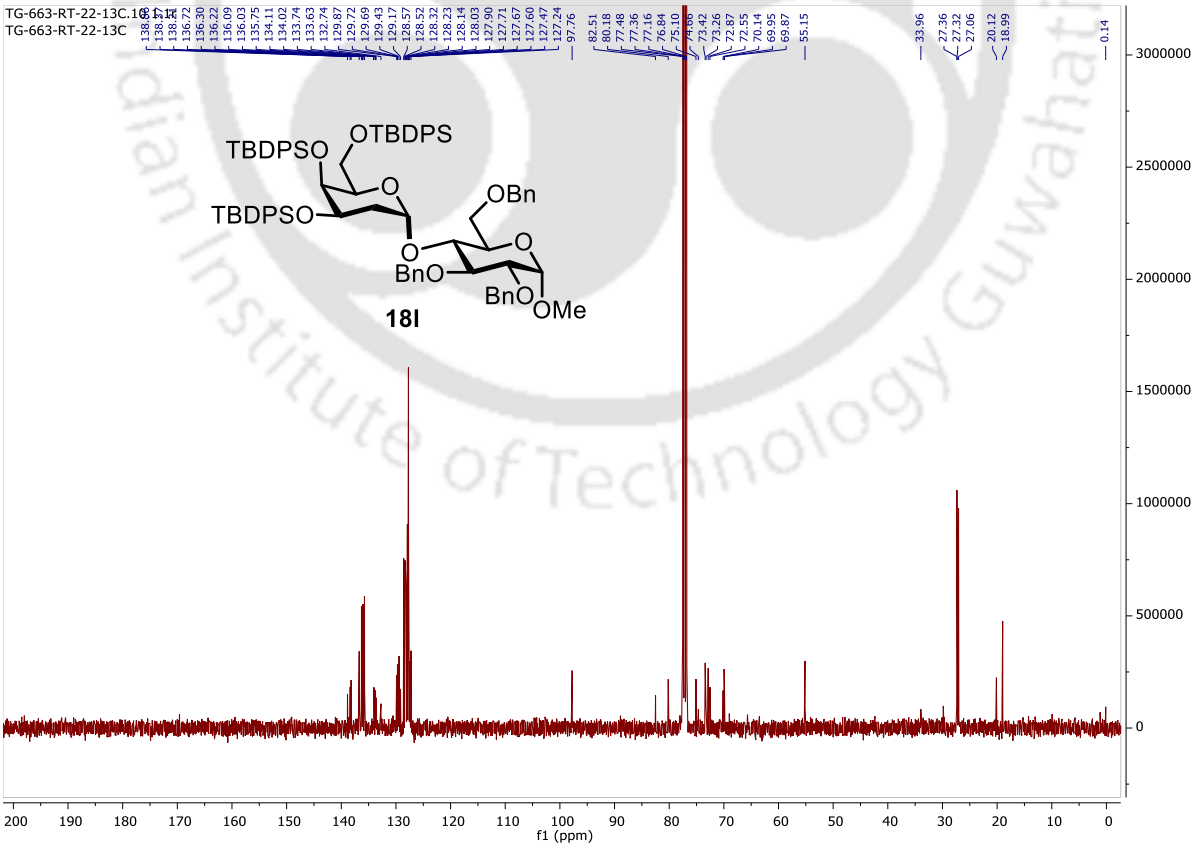


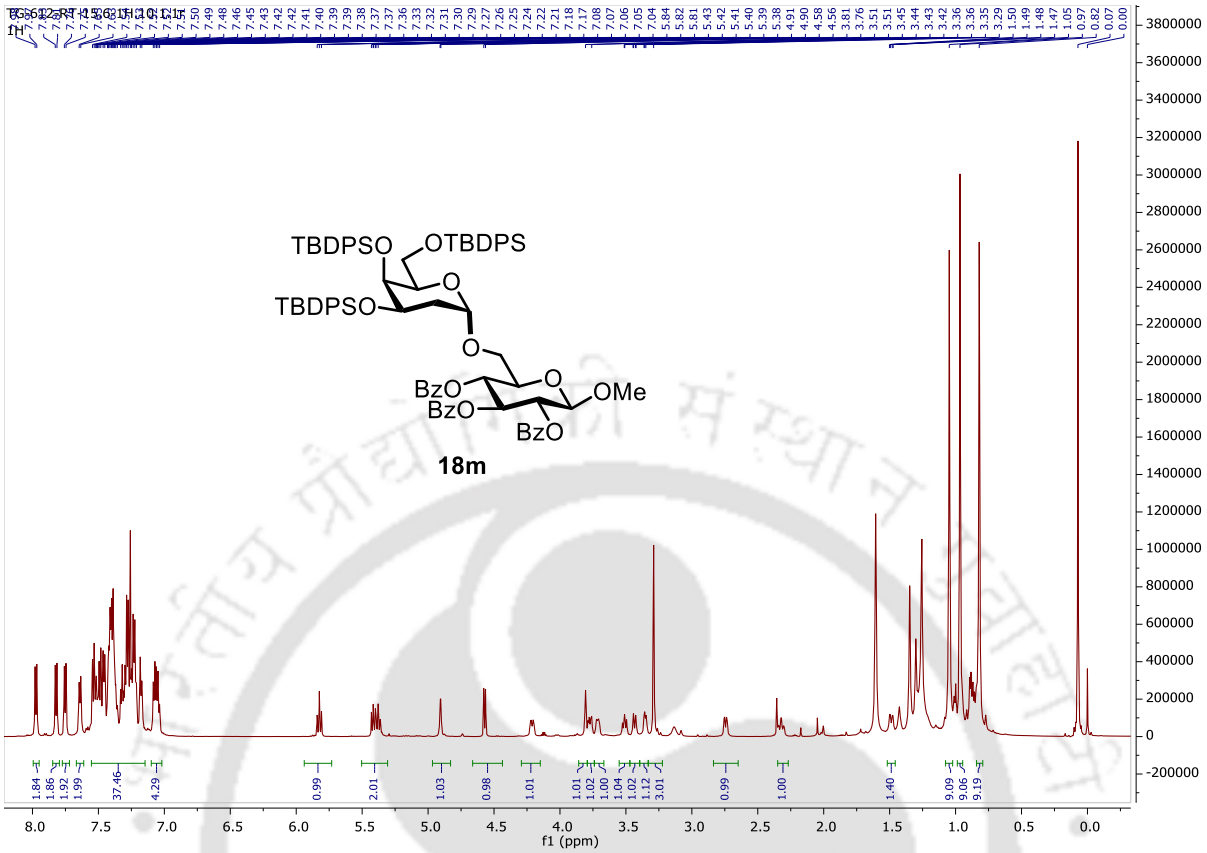


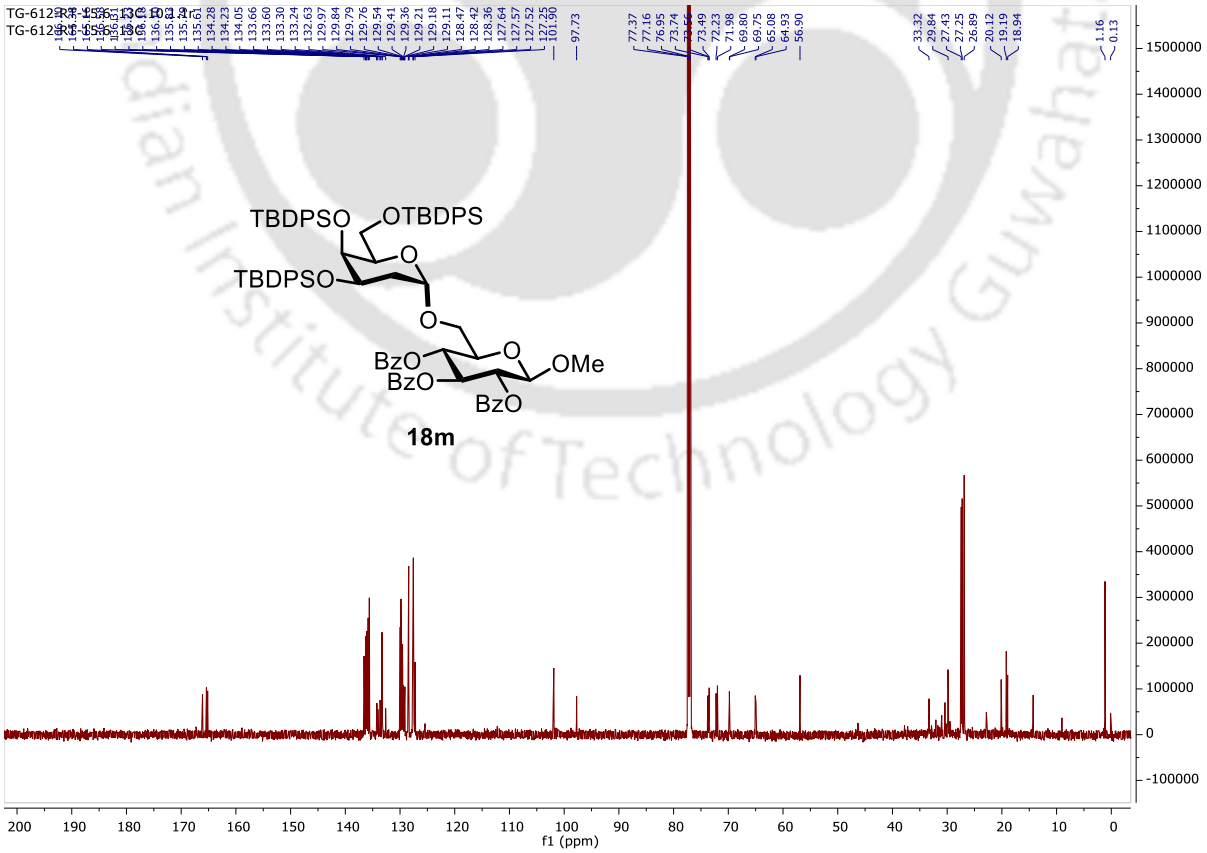




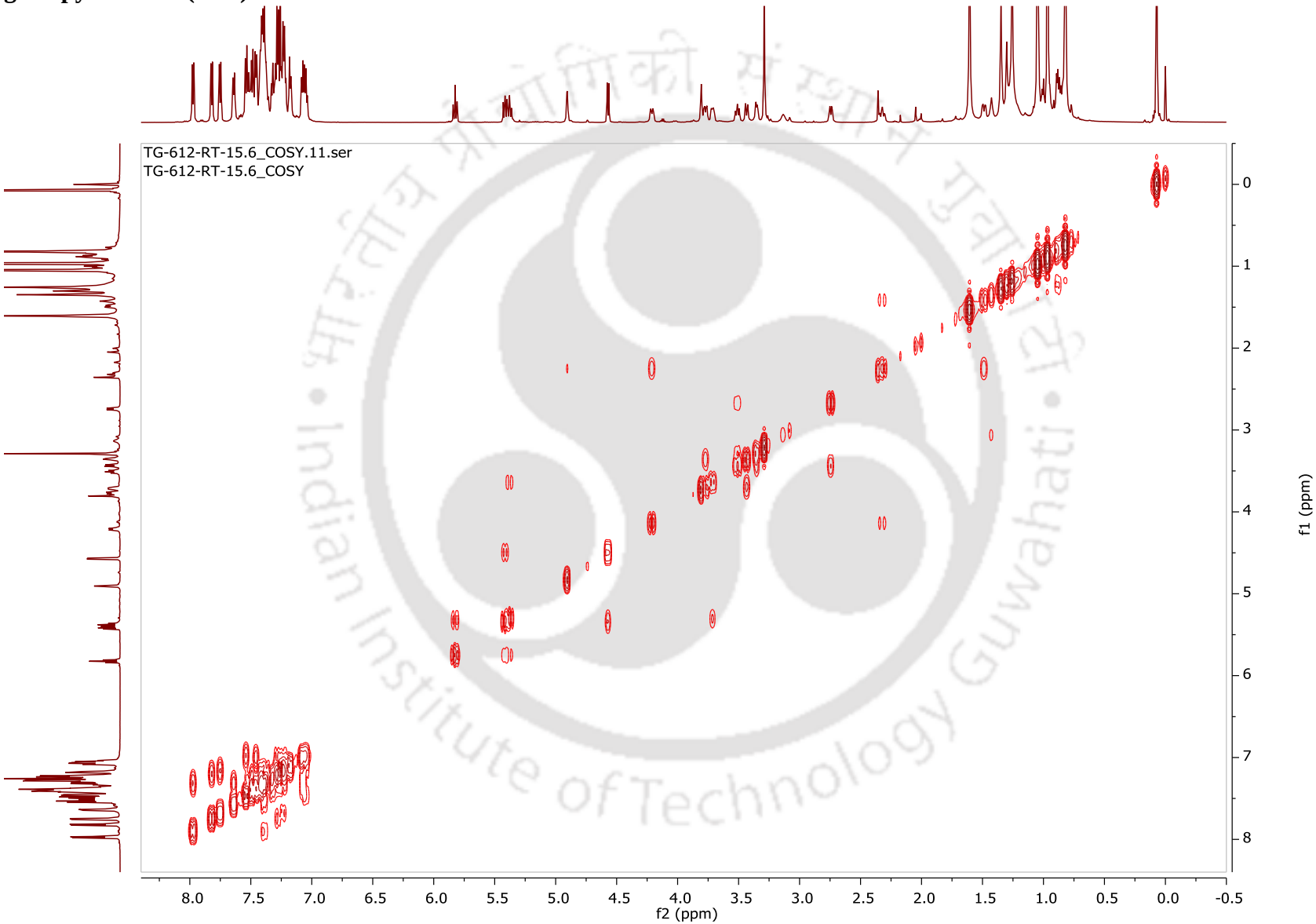


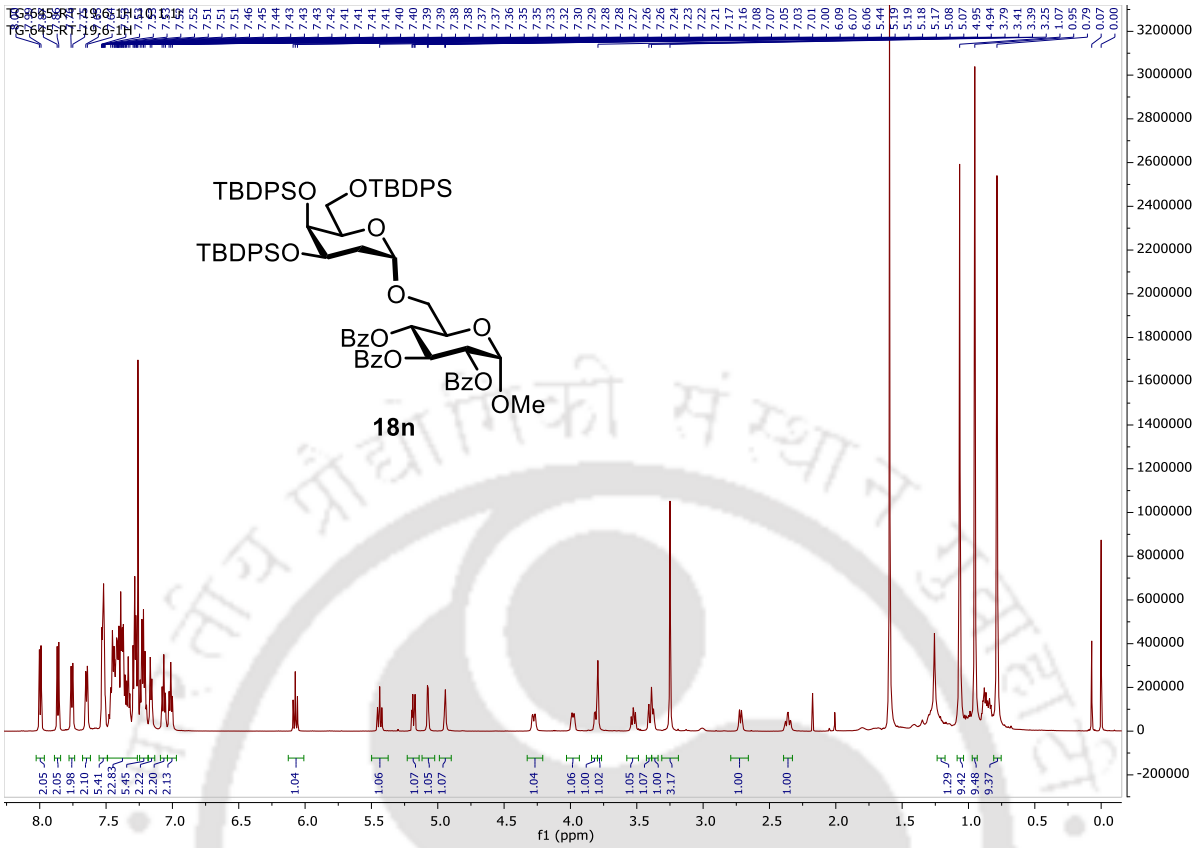


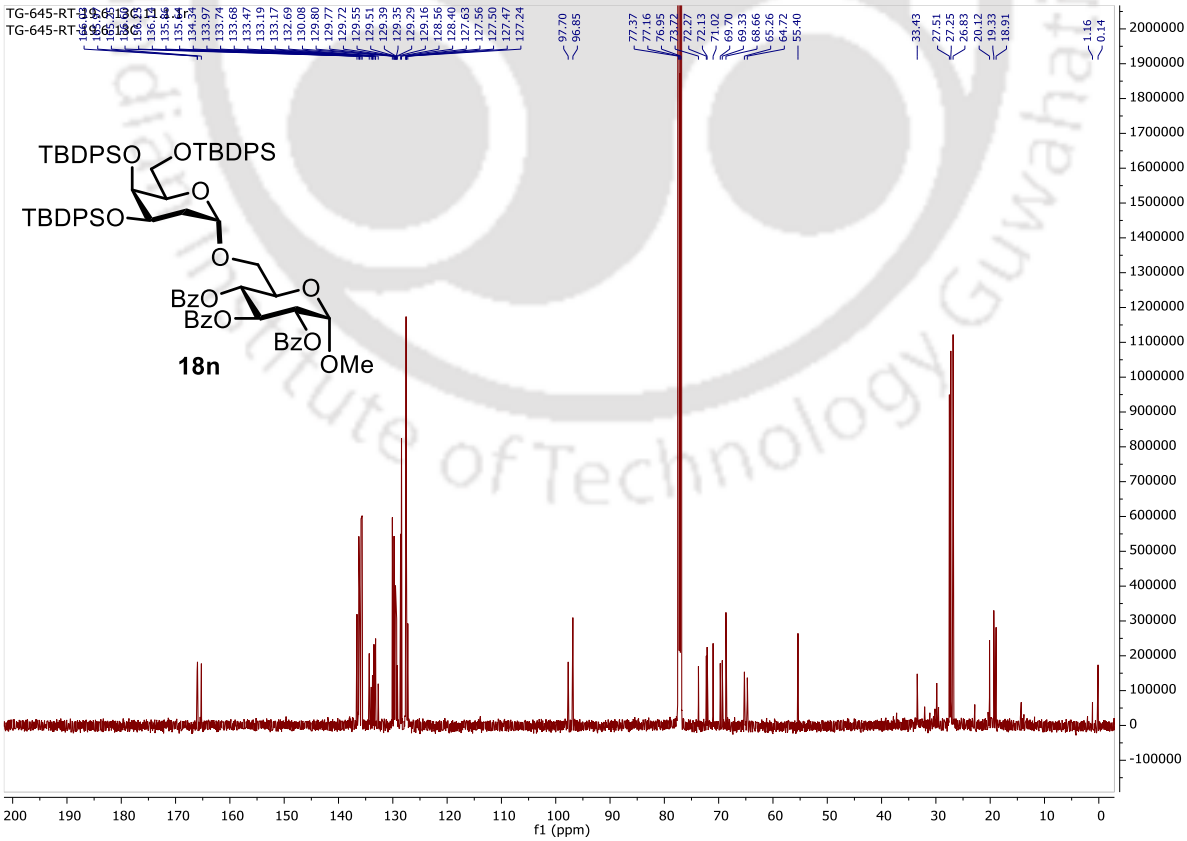




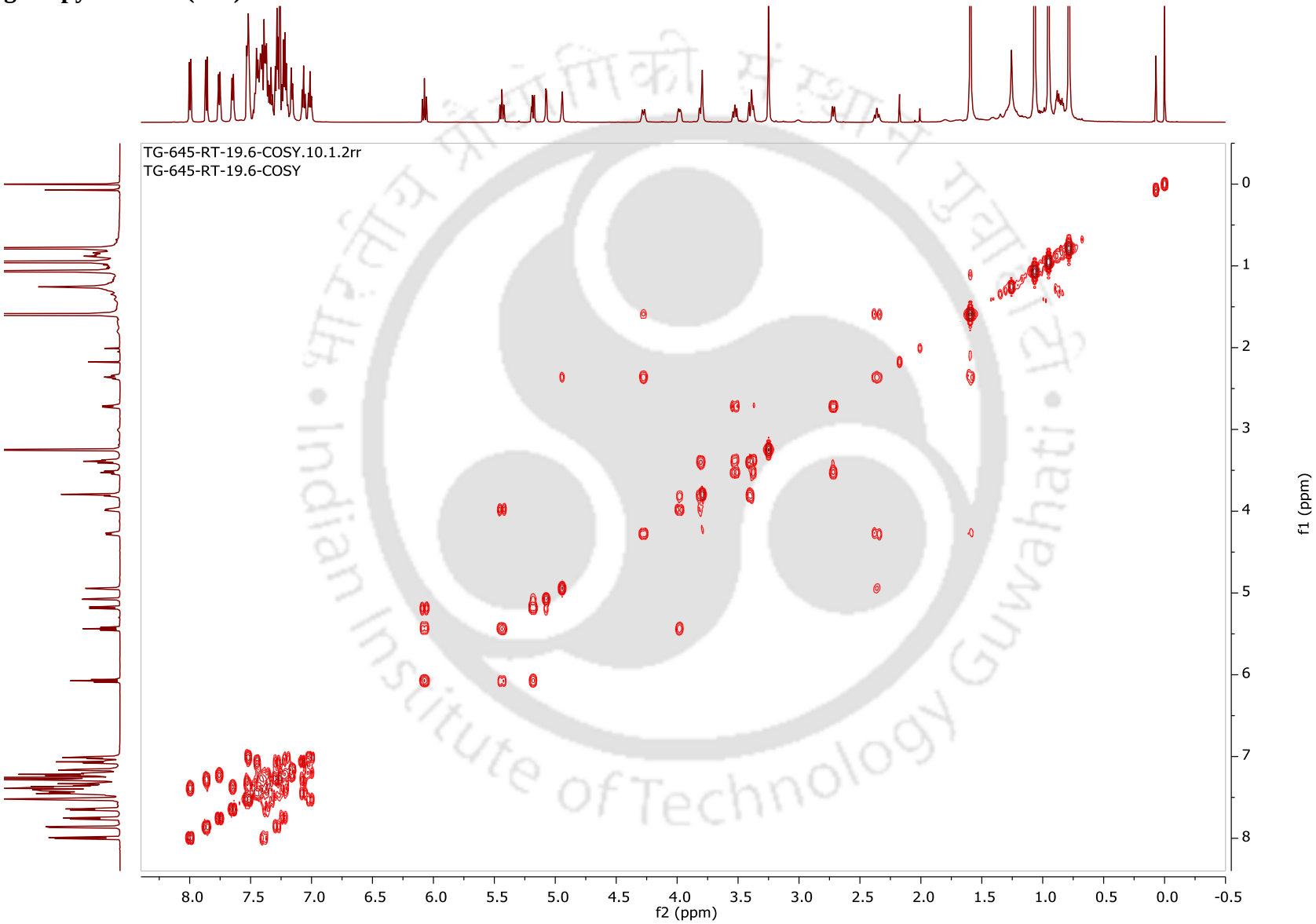
COSY NMR of Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(3,4,6-tri-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-D-galactopyranosyl)-β-D-glucopyranoside (18m):

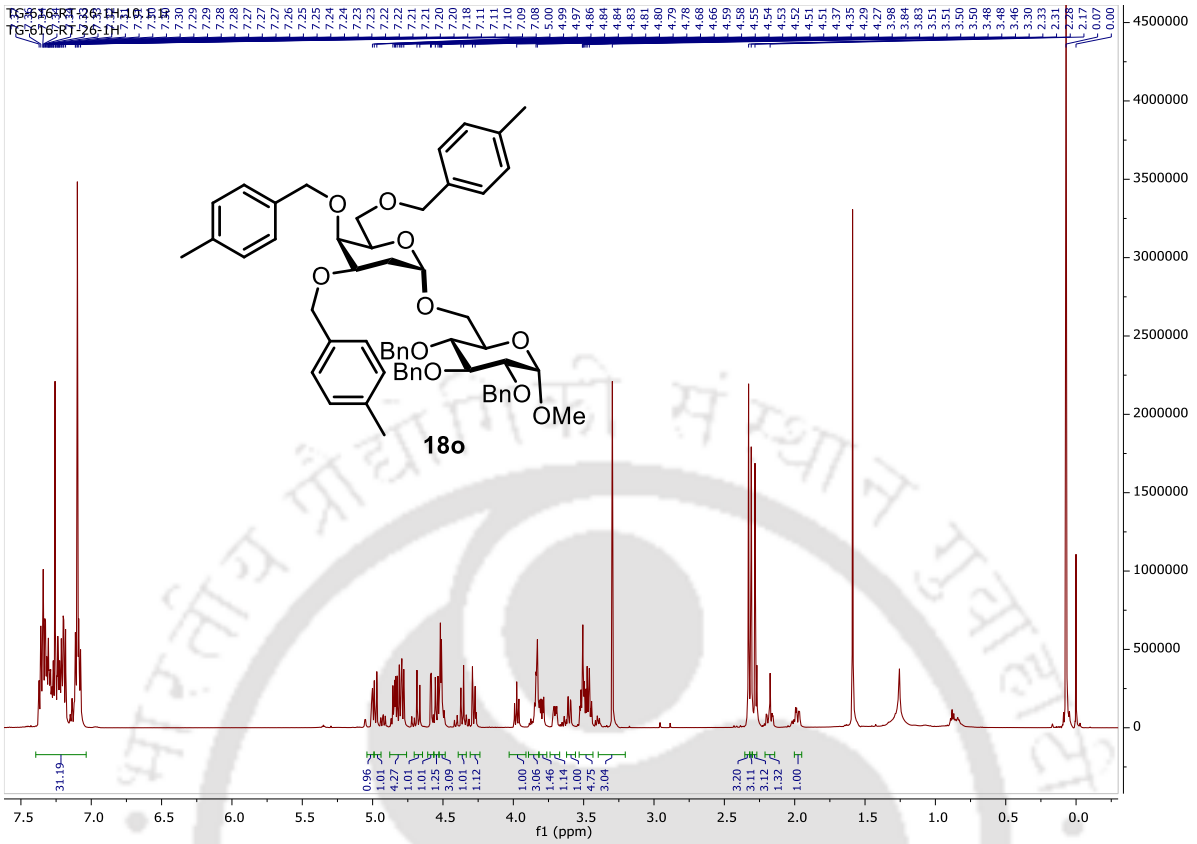


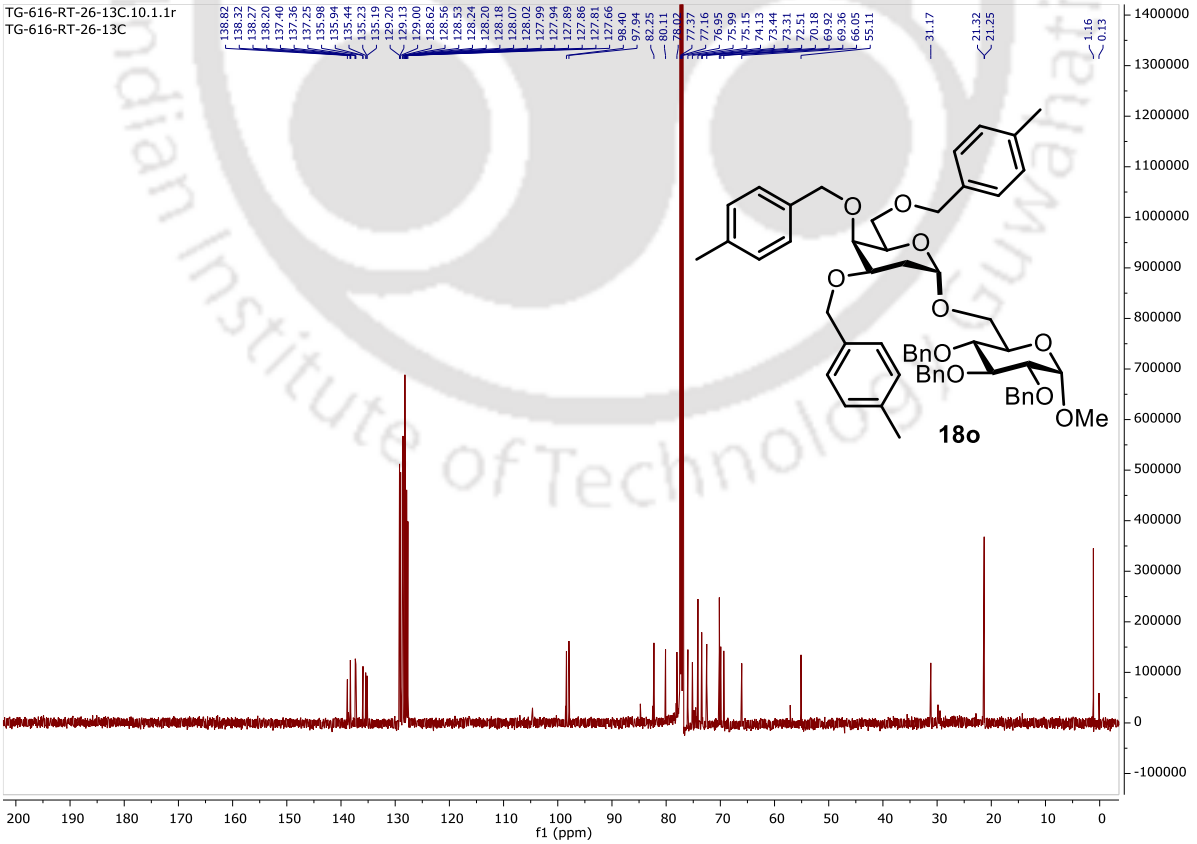




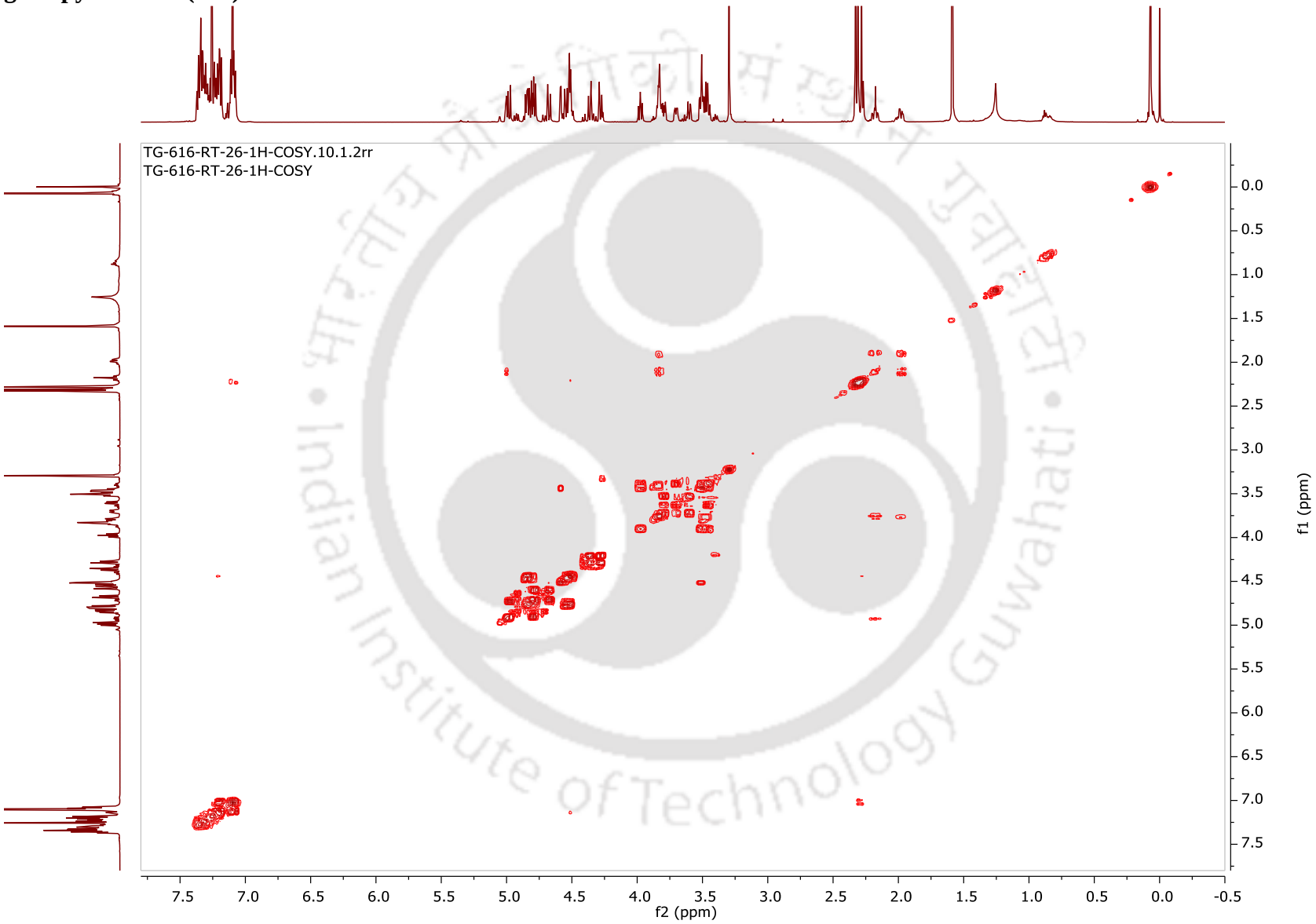
COSY NMR of Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(3,4,6-tri-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-D-galactopyranosyl)-α-D-glucopyranoside (18n):

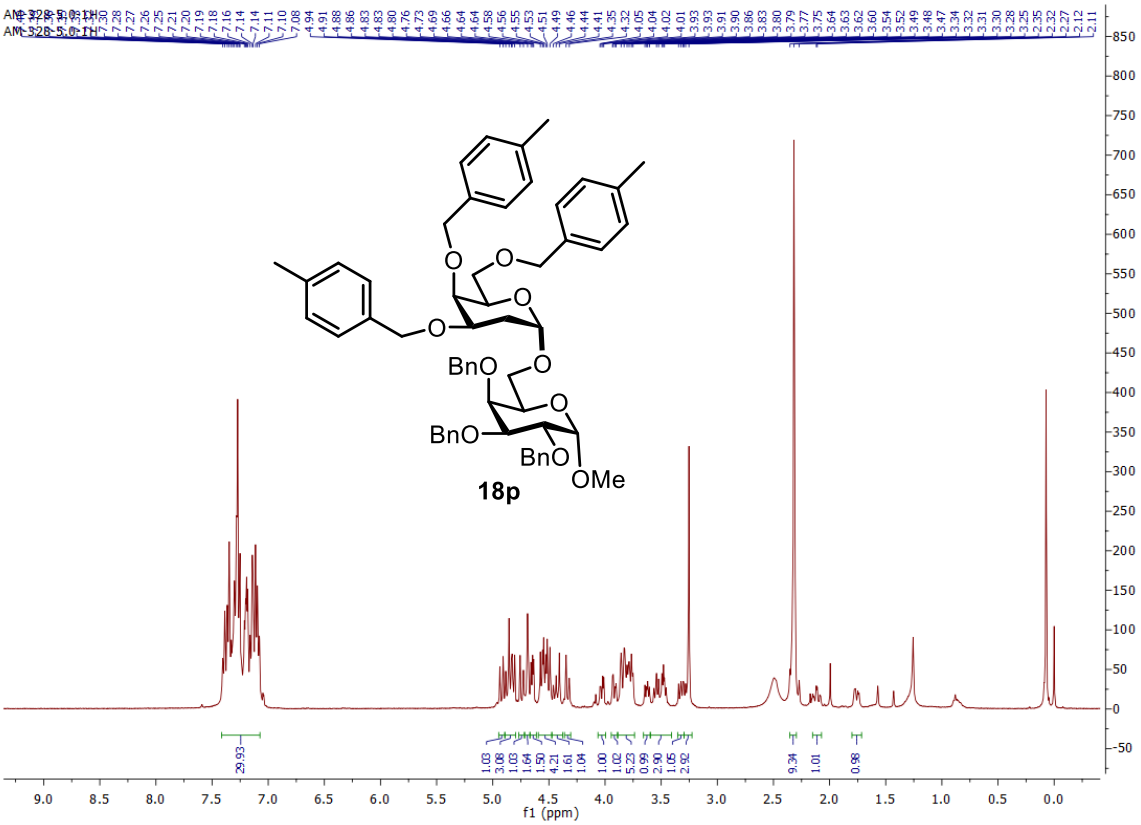


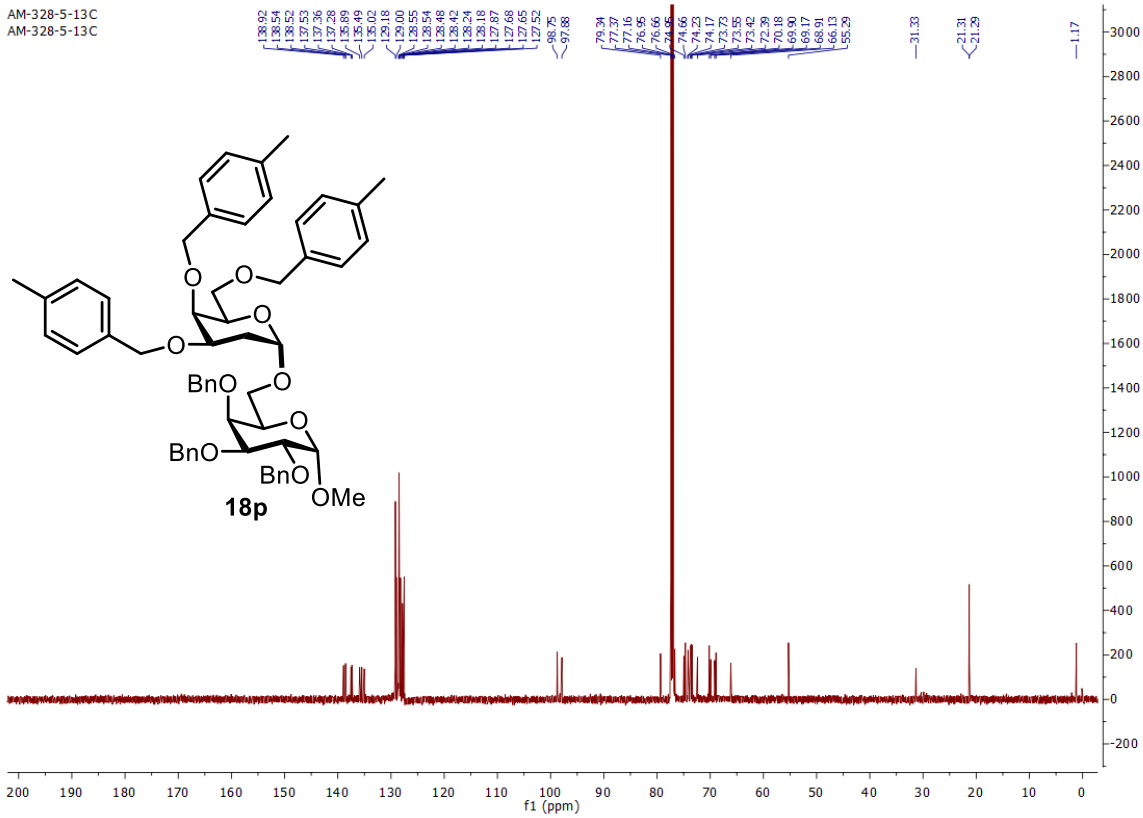


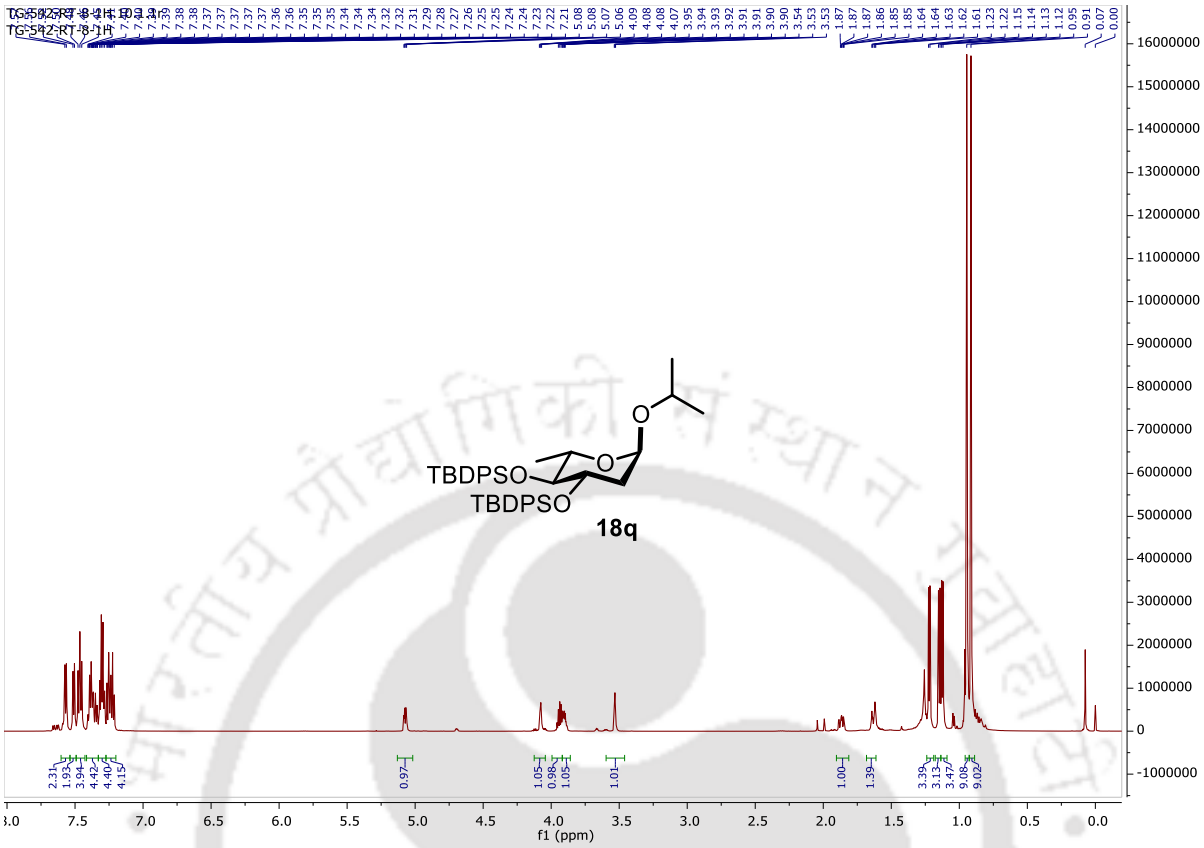


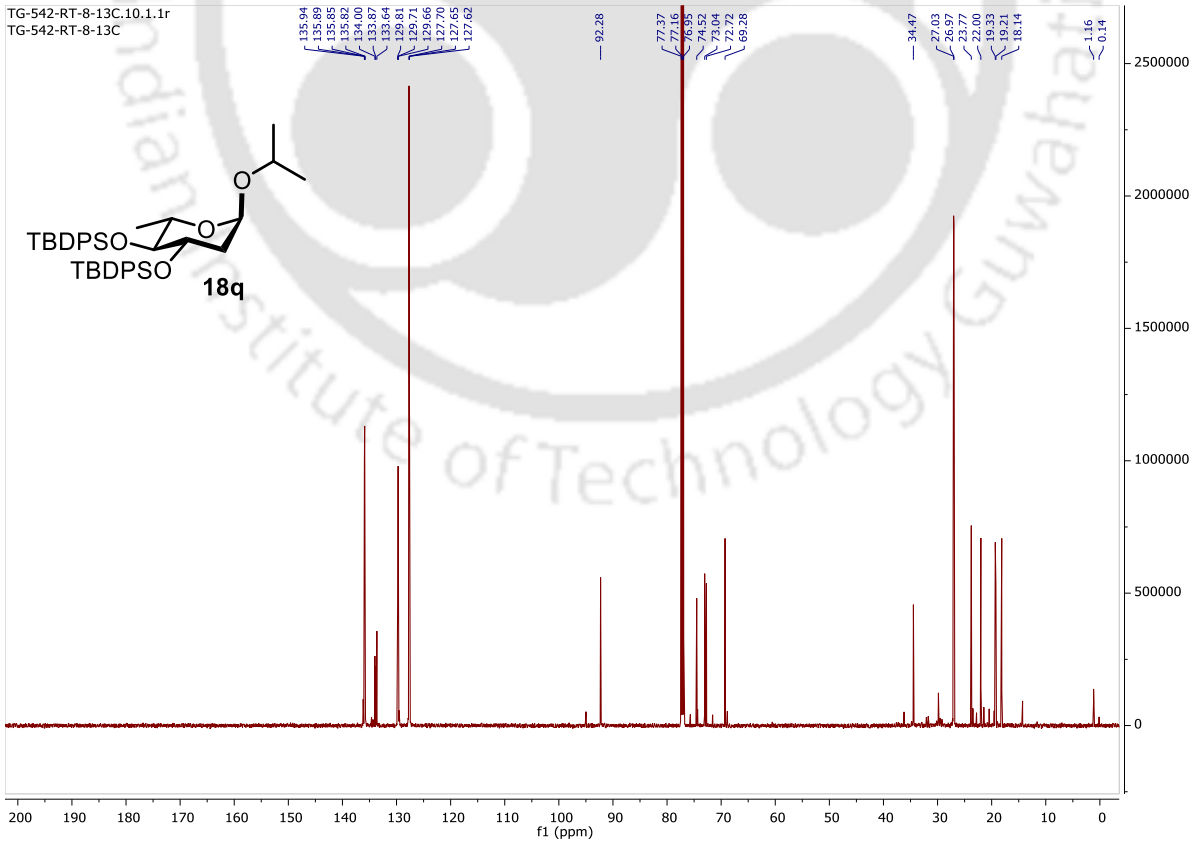
COSY NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4,6-tri-*O*-*para*-methylbenzyl-2-deoxy-α-D-galactopyranosyl)-α-D-glucopyranoside (18o):

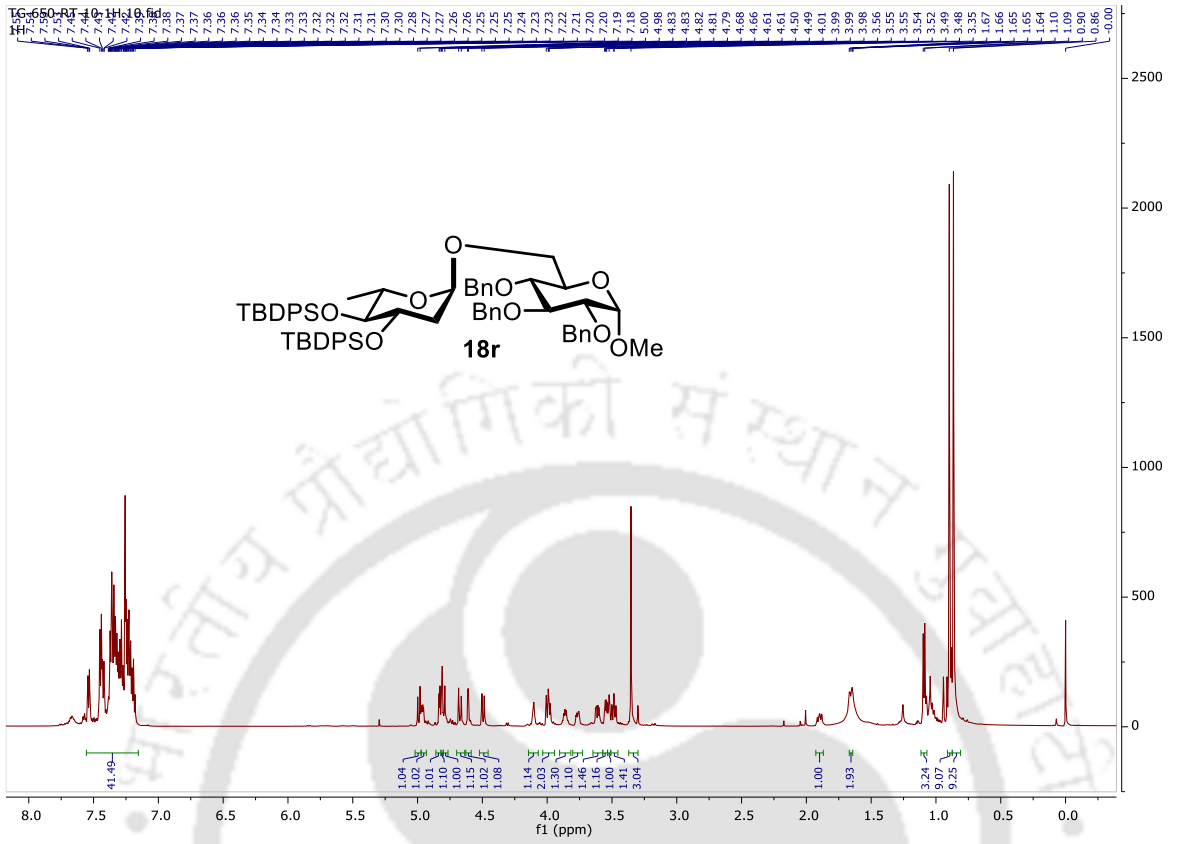


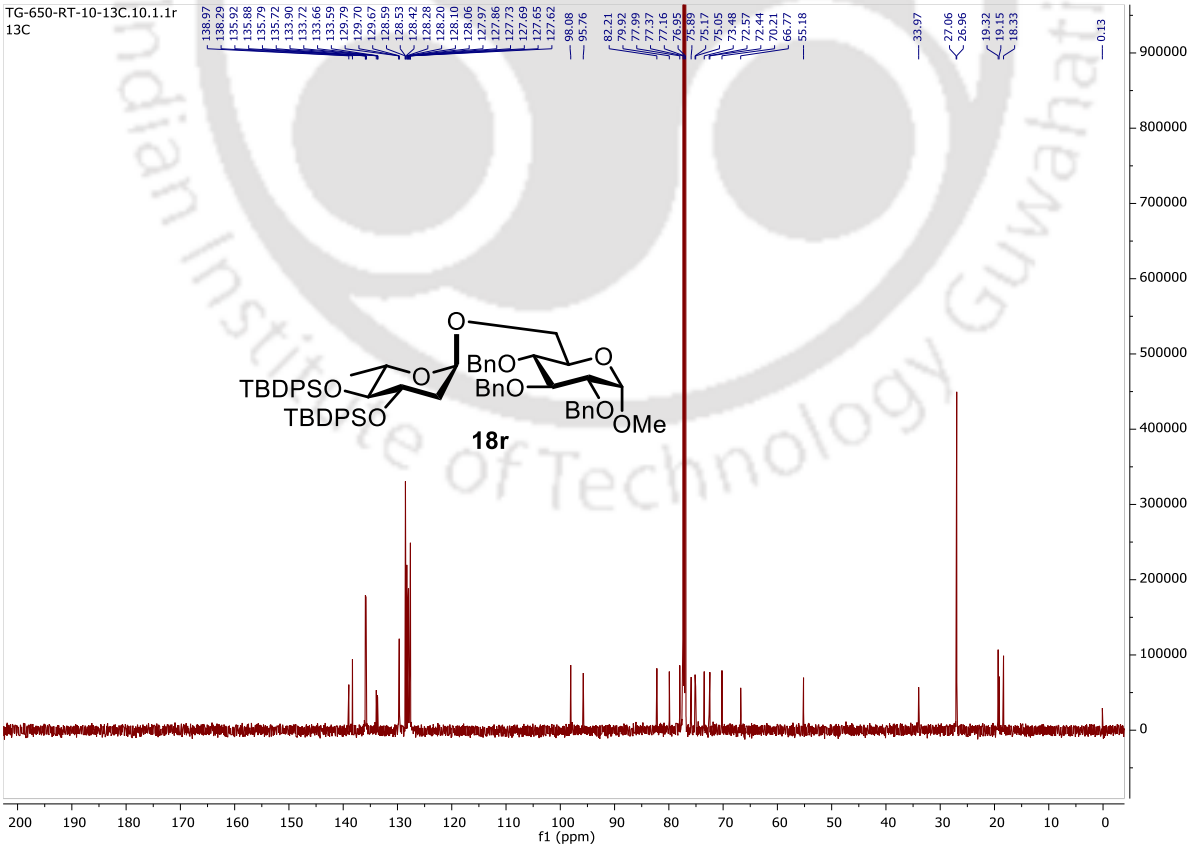




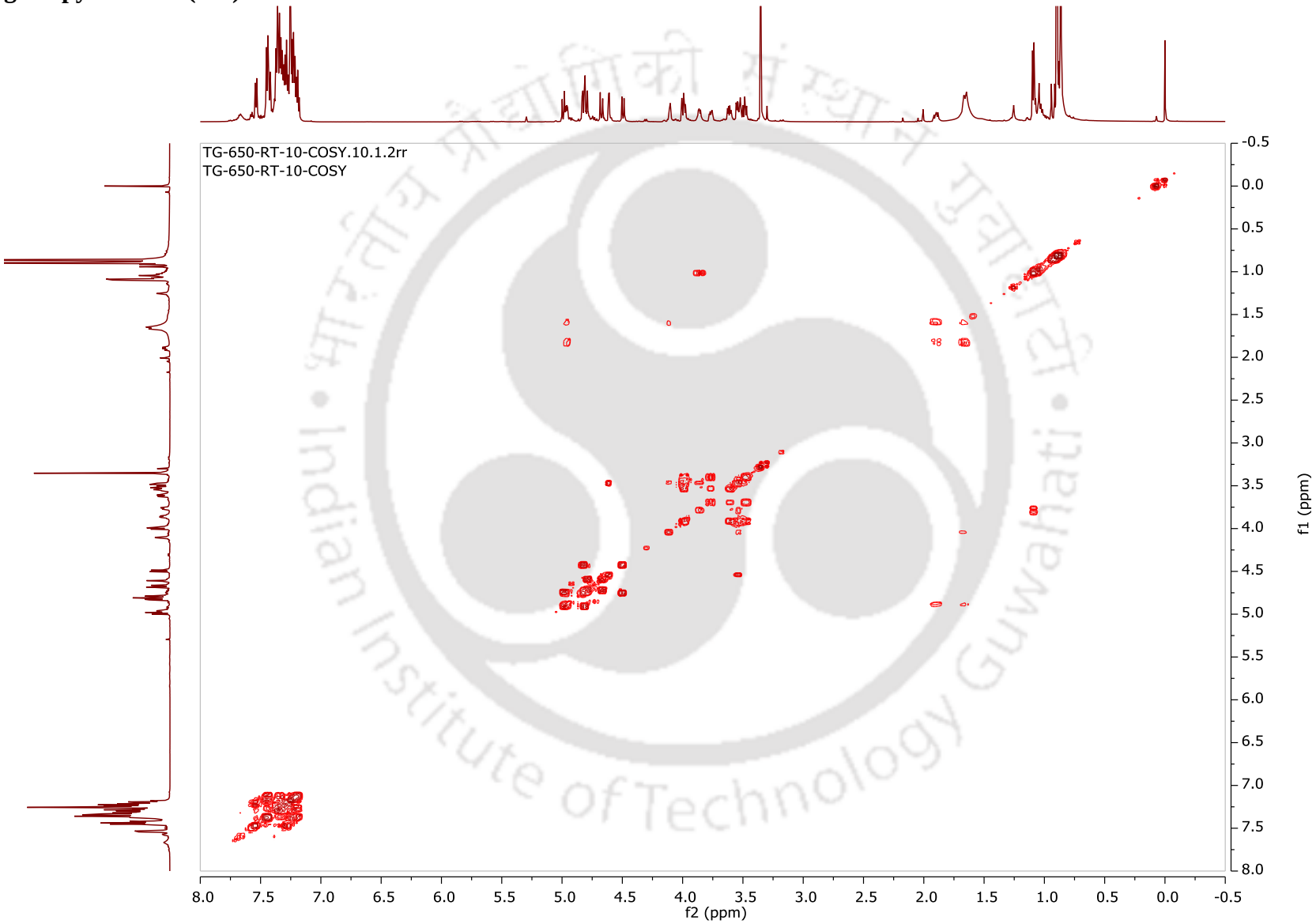


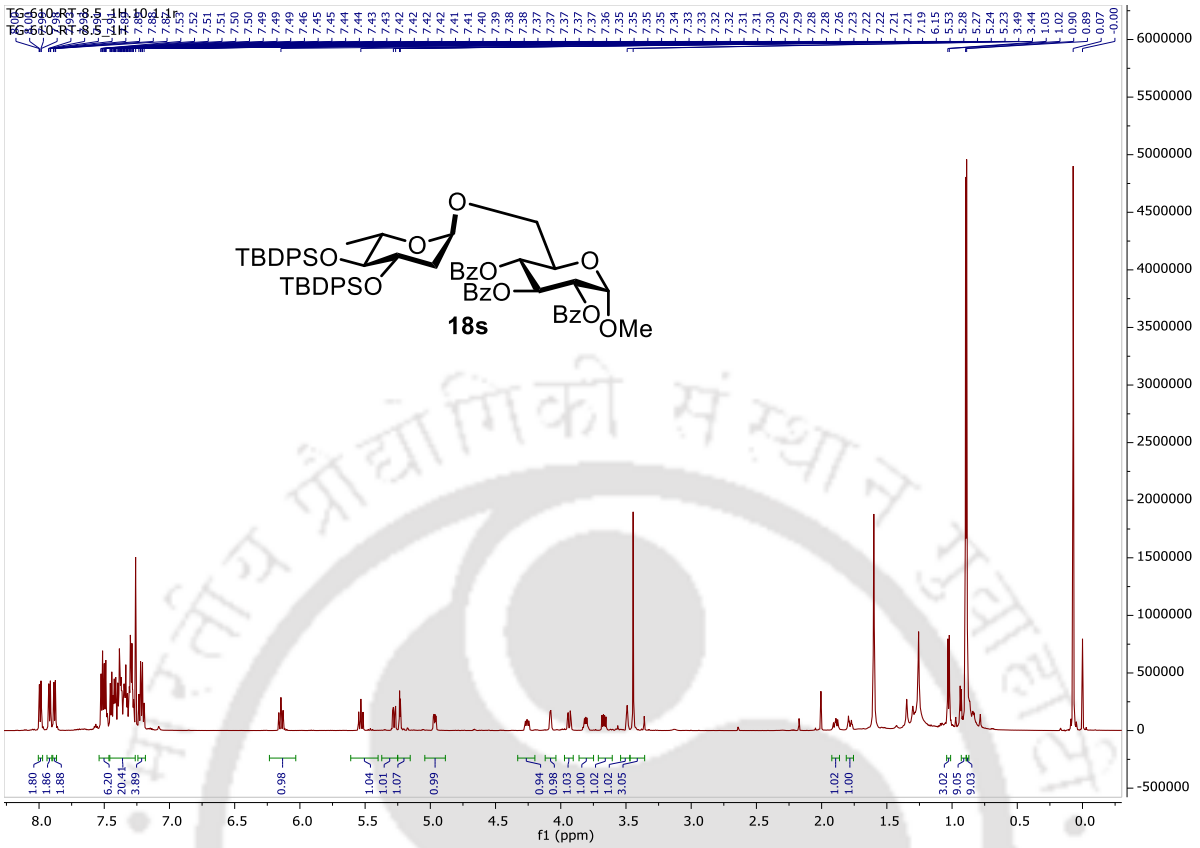


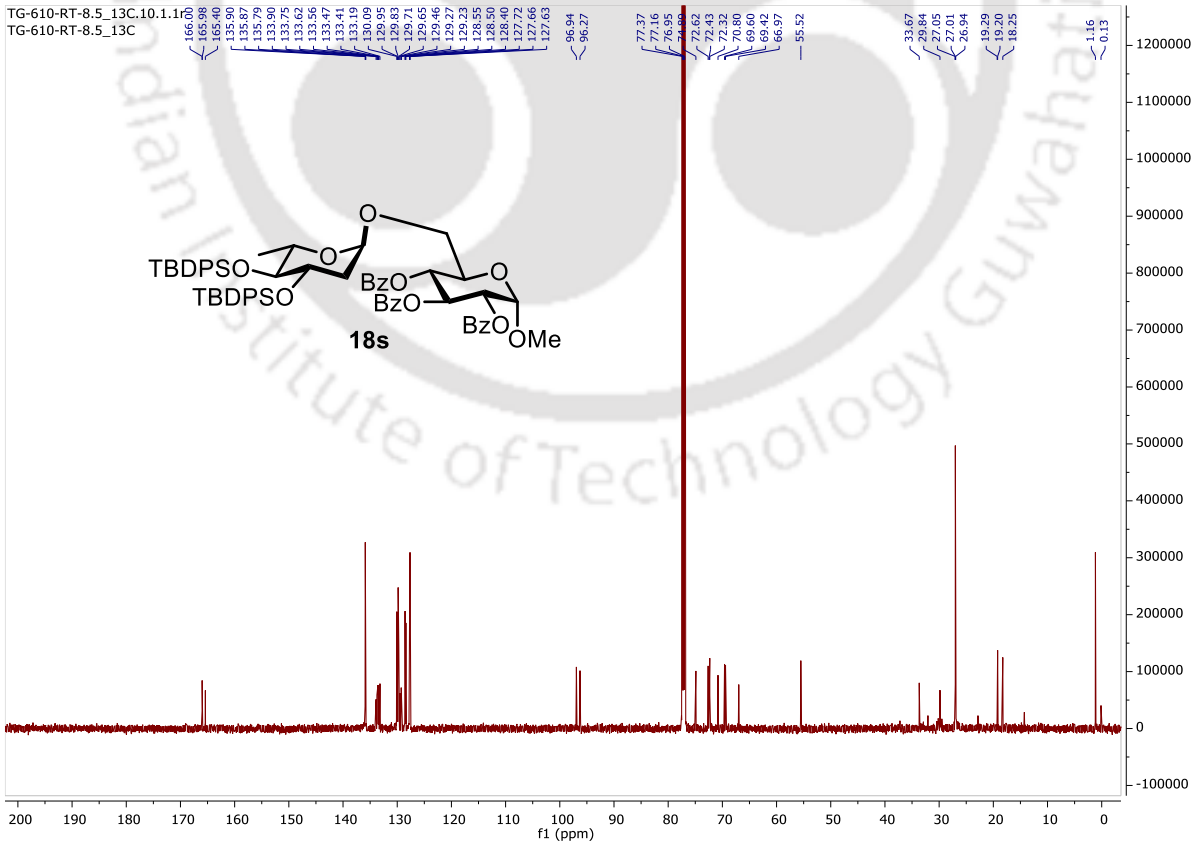




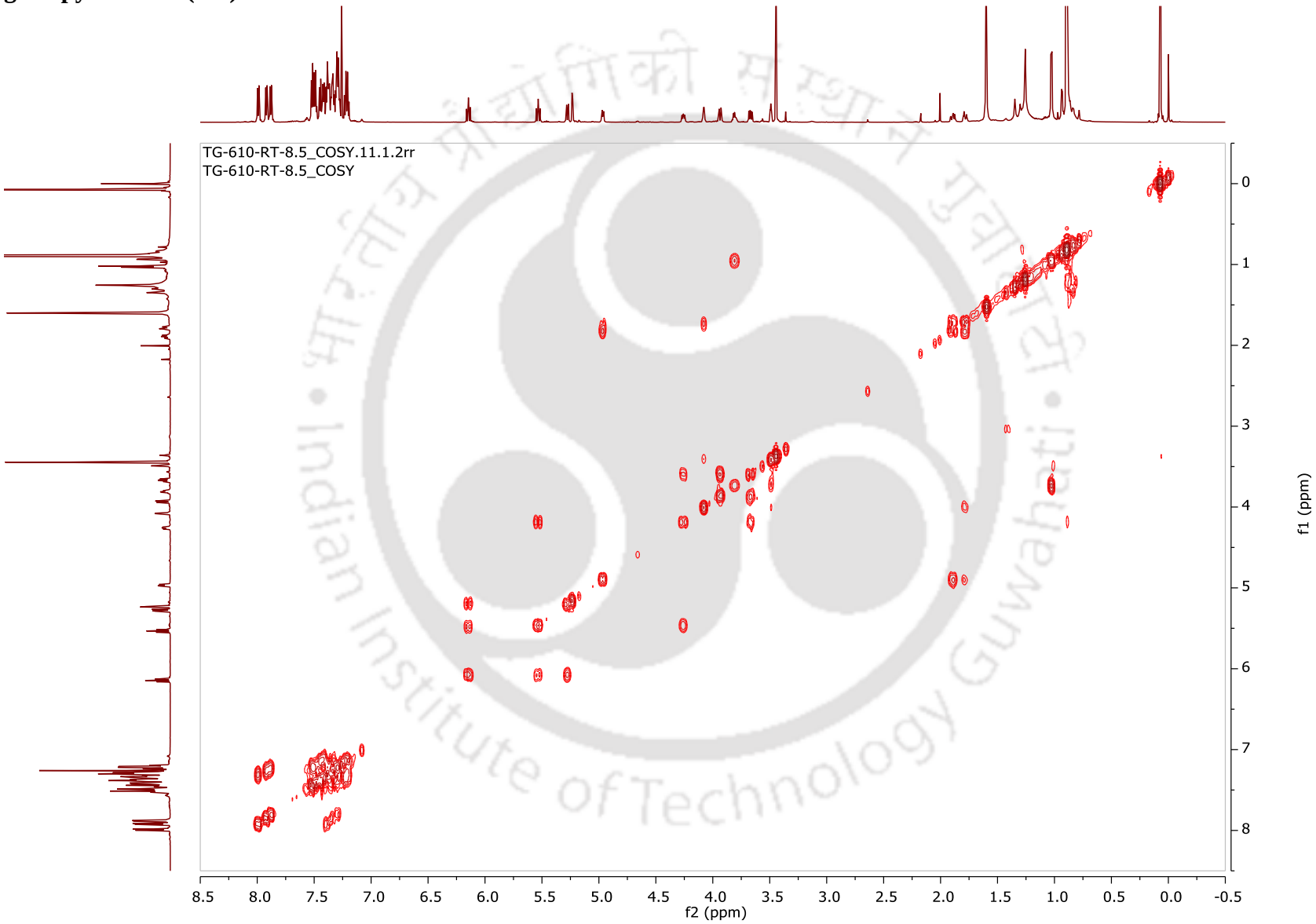
COSY NMR of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-L-rhamnosyl)-α-D-glucopyranoside (18r):

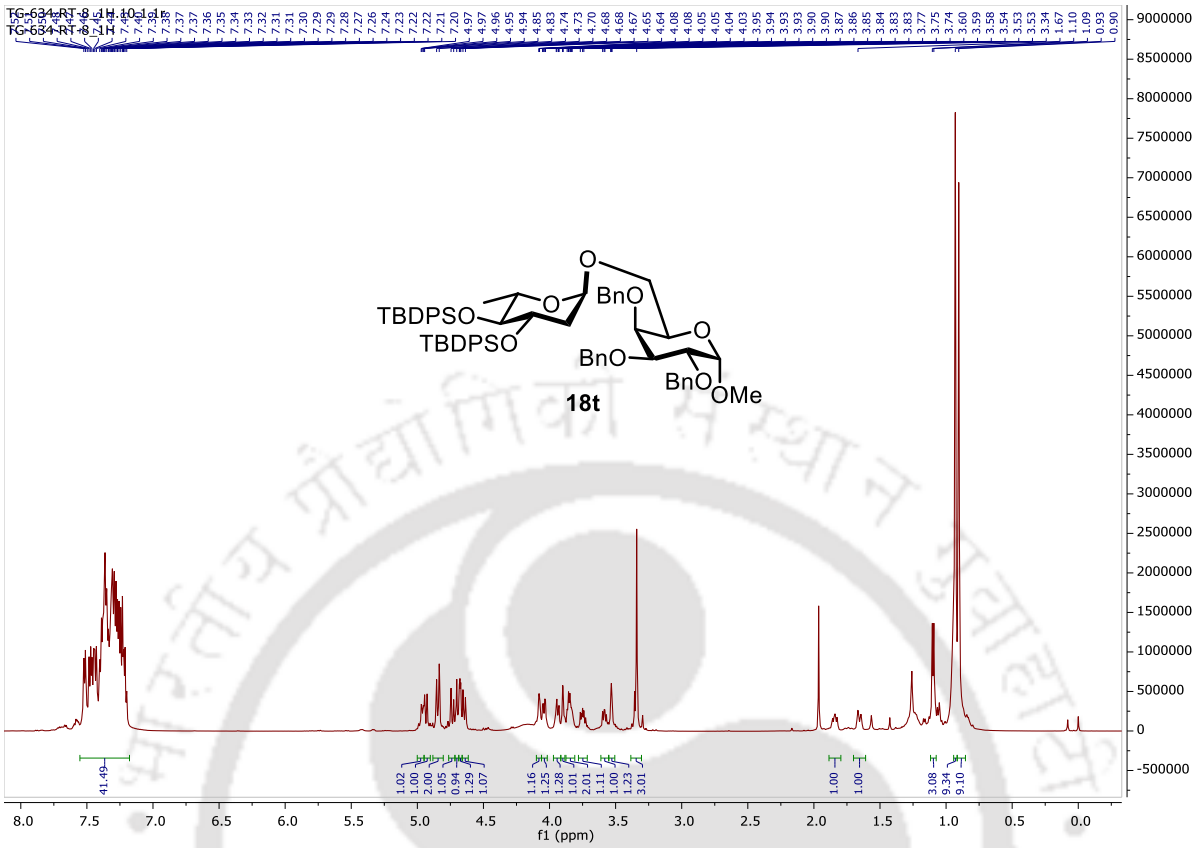


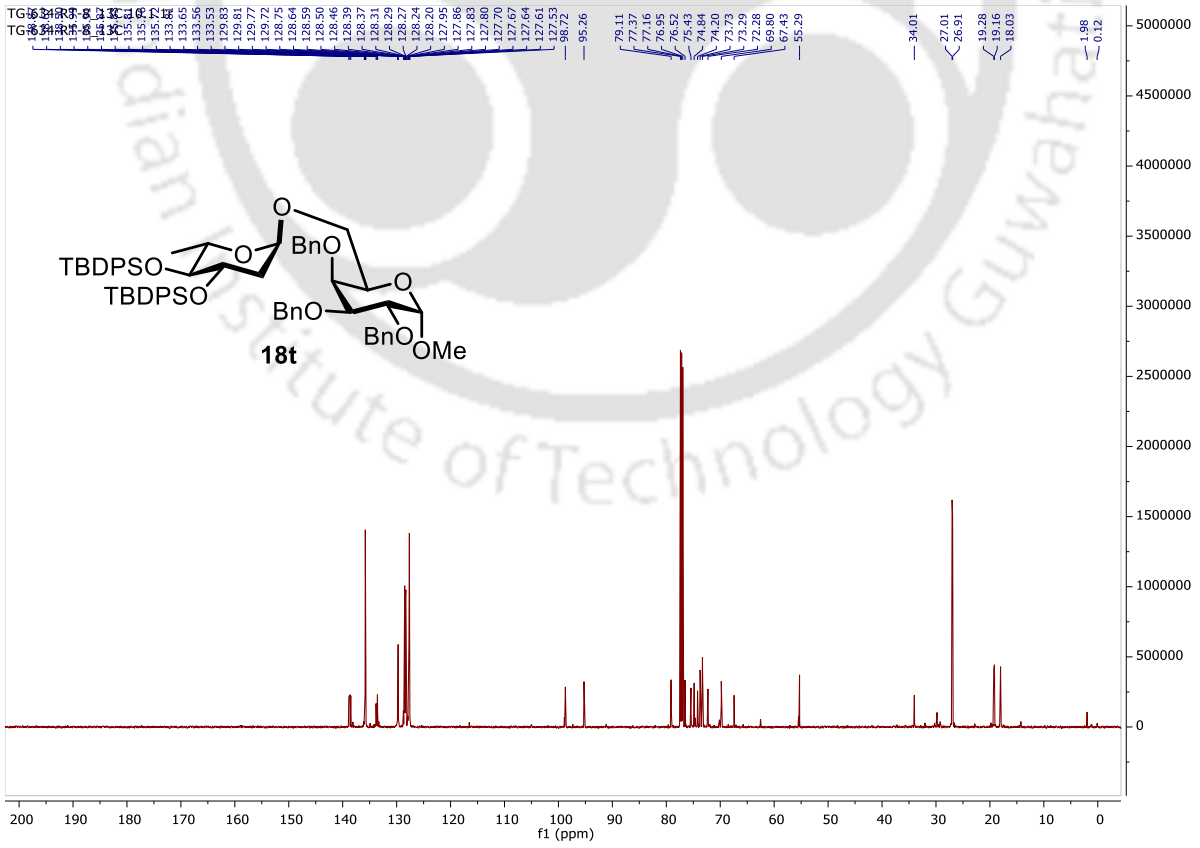


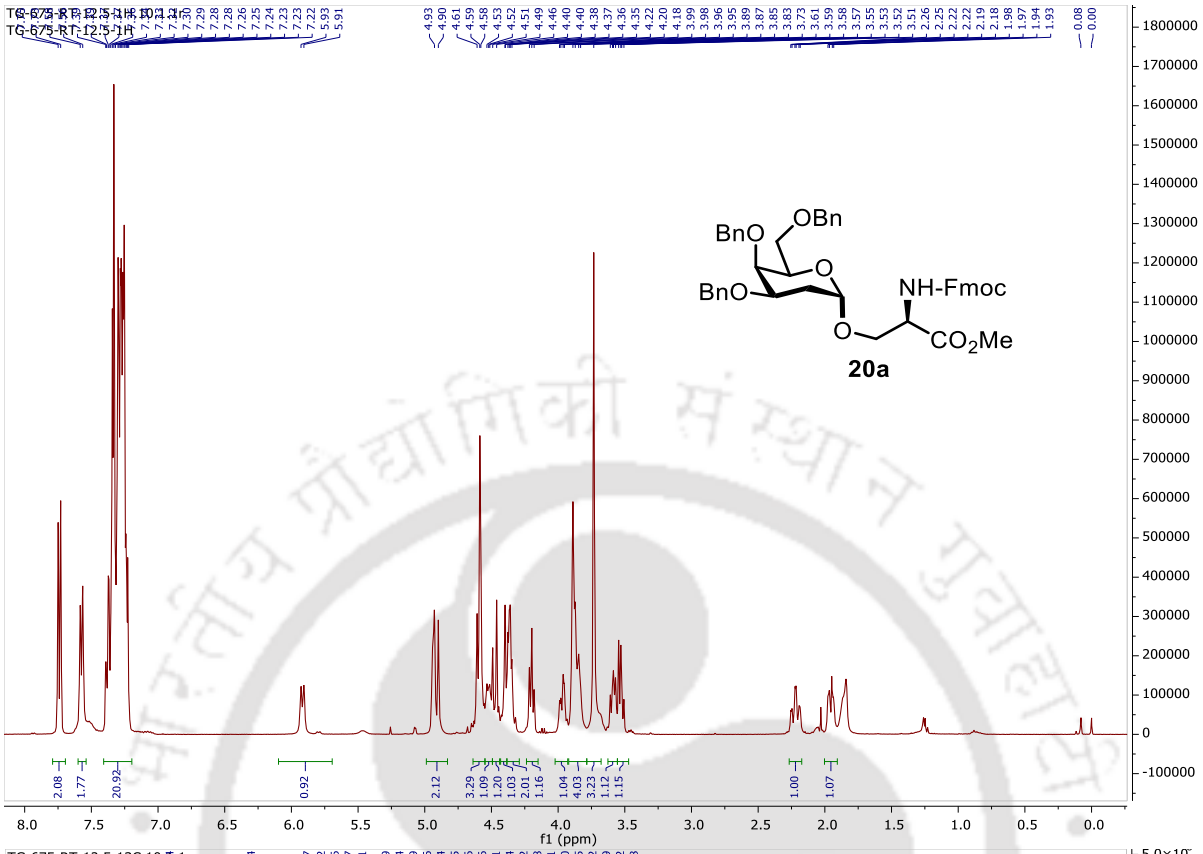


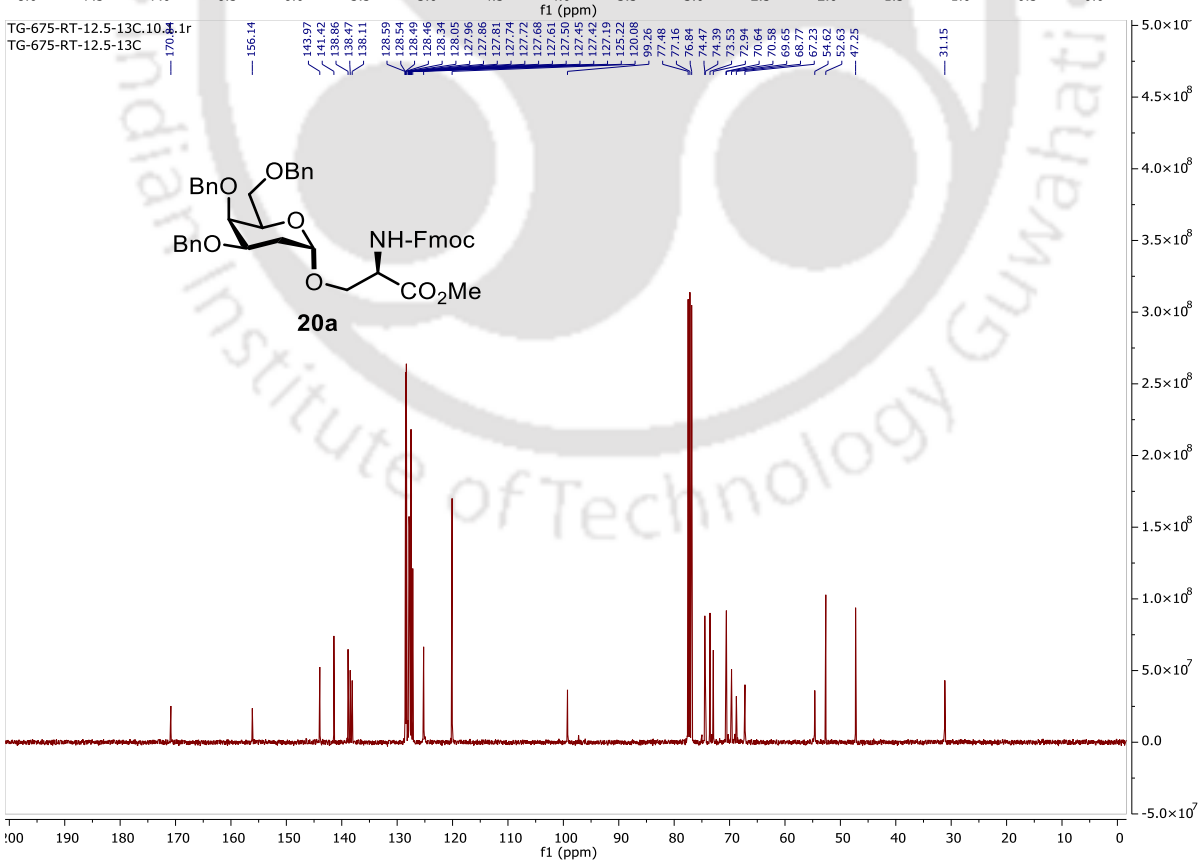
COSY NMR of Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(3,4-di-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-L-rhamnosyl)-α-D-glucopyranoside (18s):



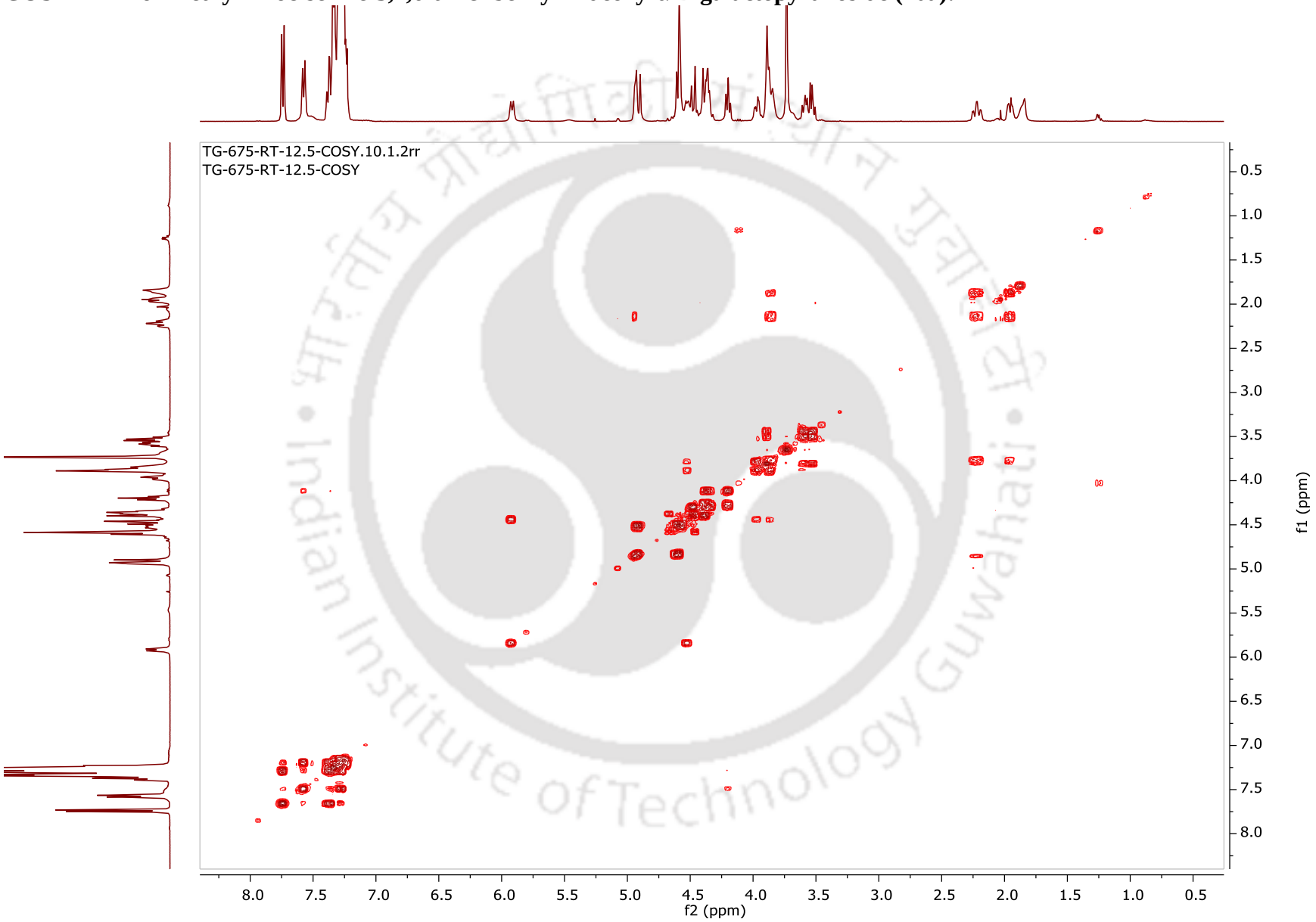


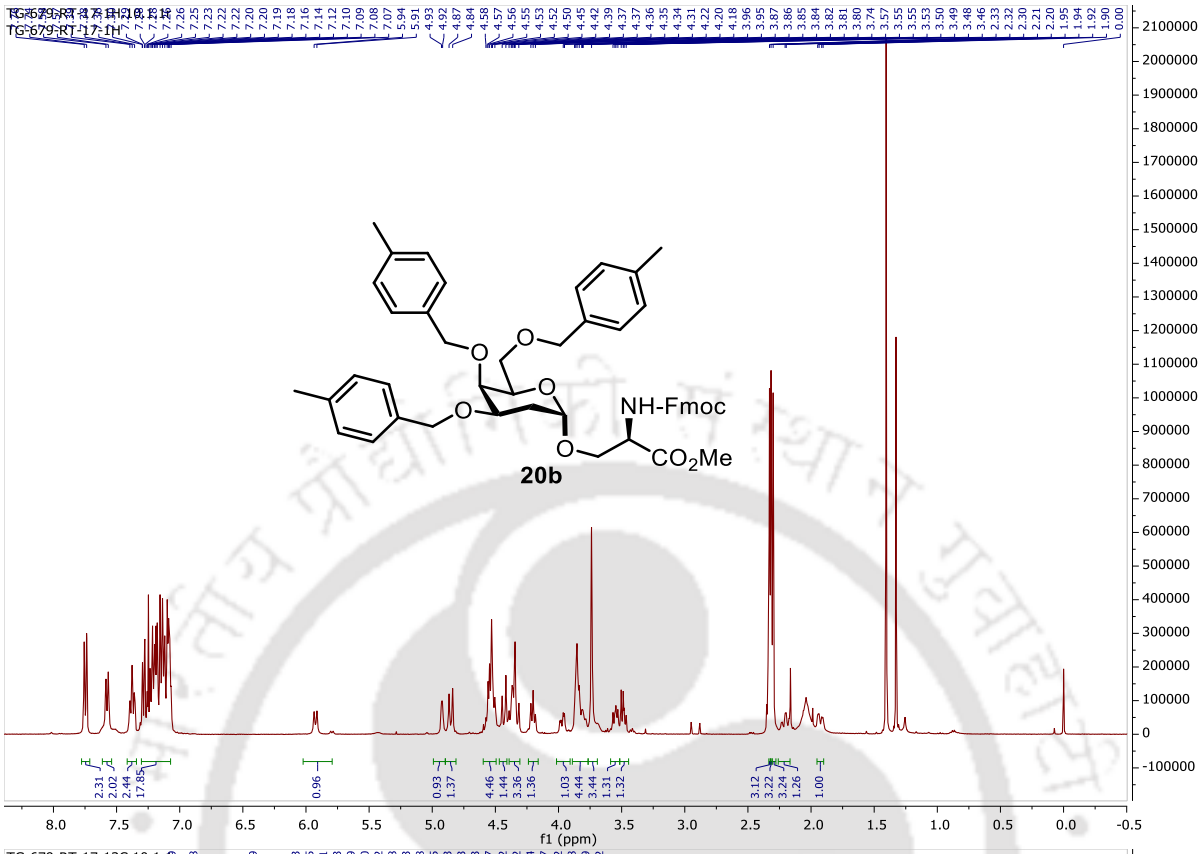


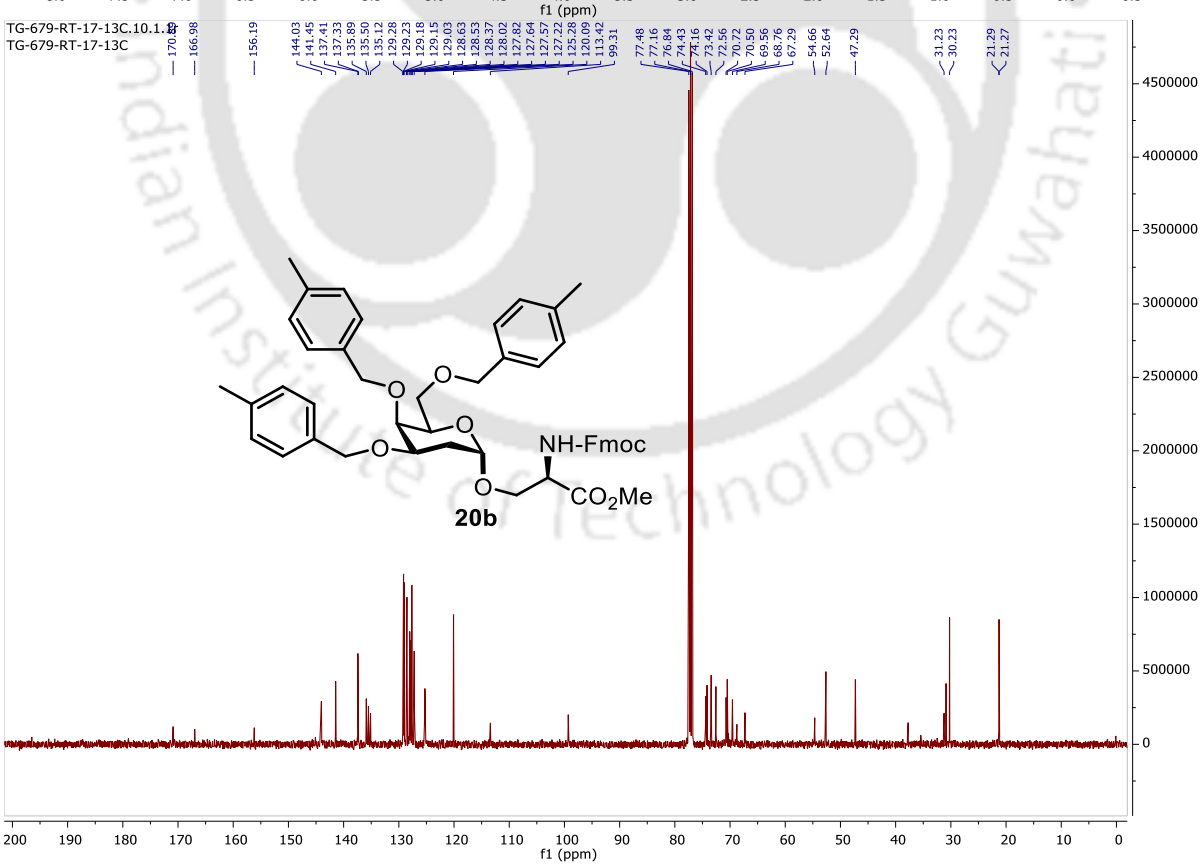


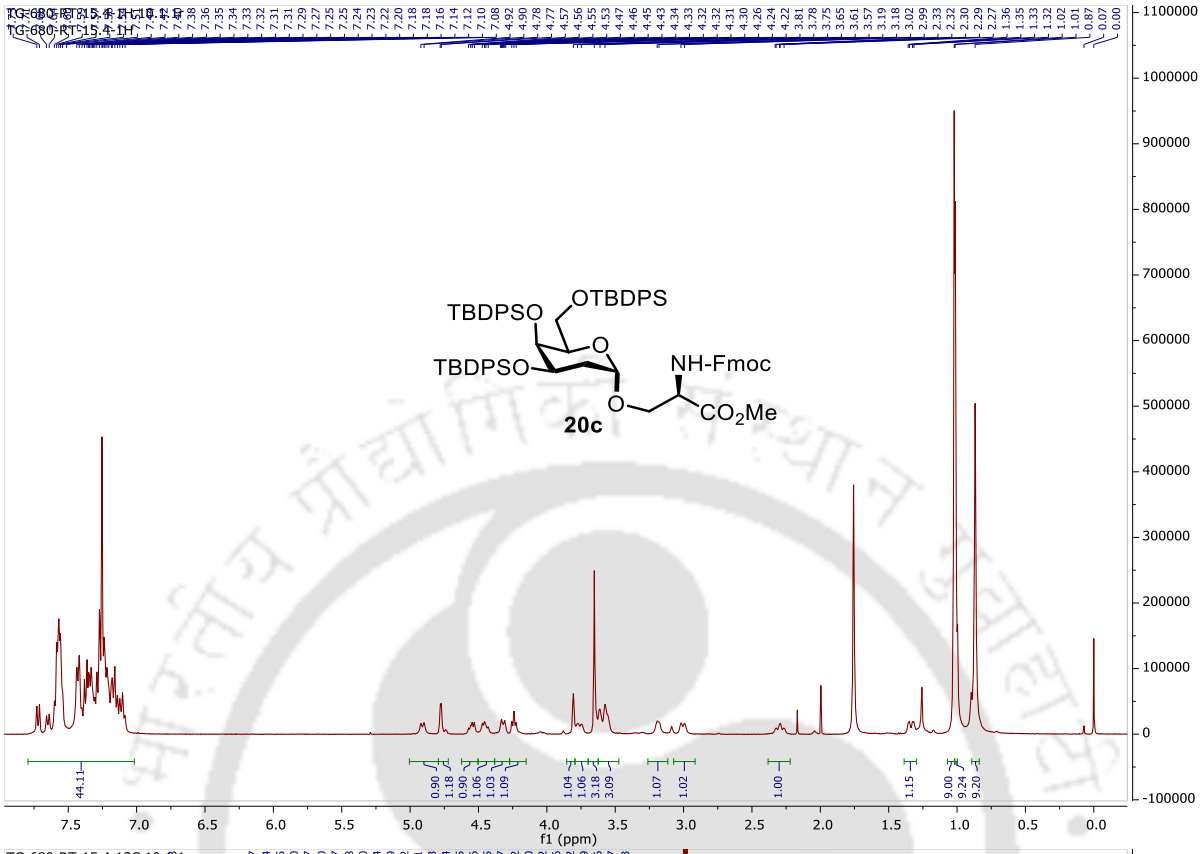


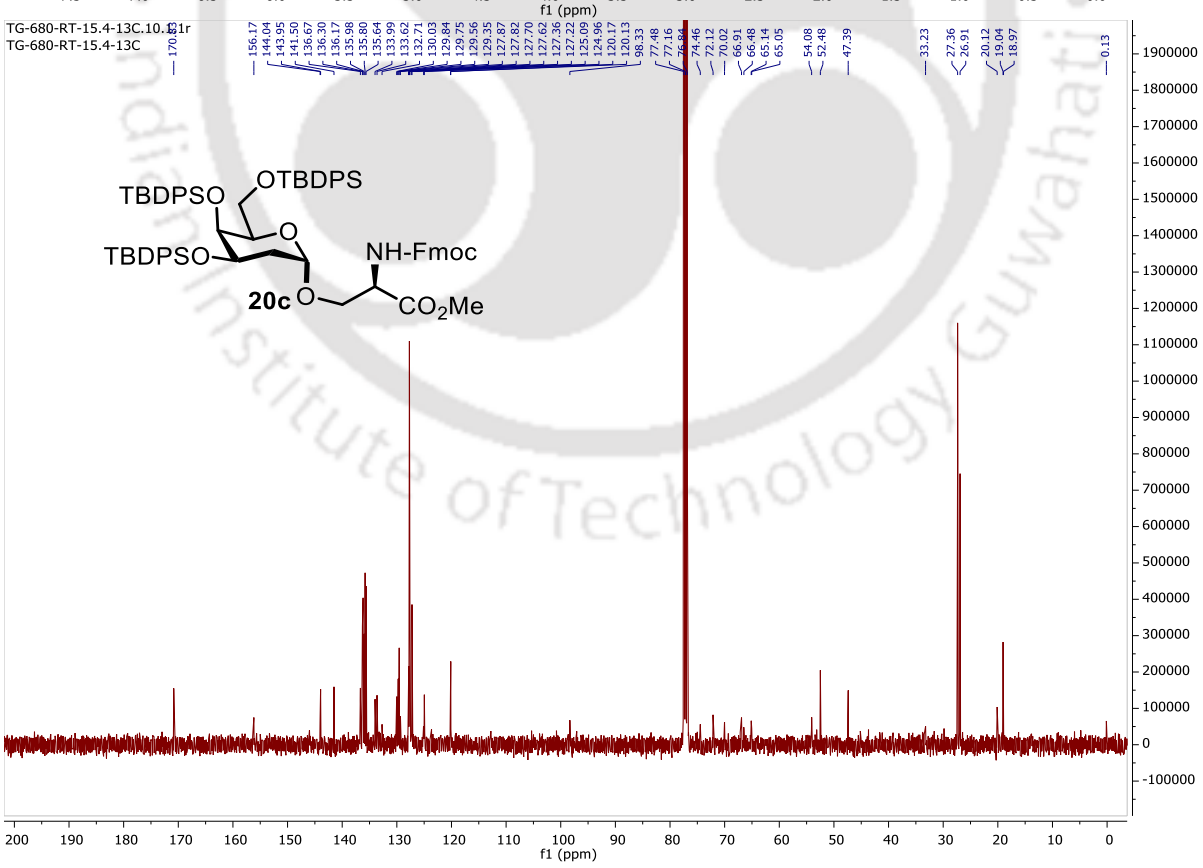
COSY NMR of Methyl fmoc-serine-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranoside (20a):



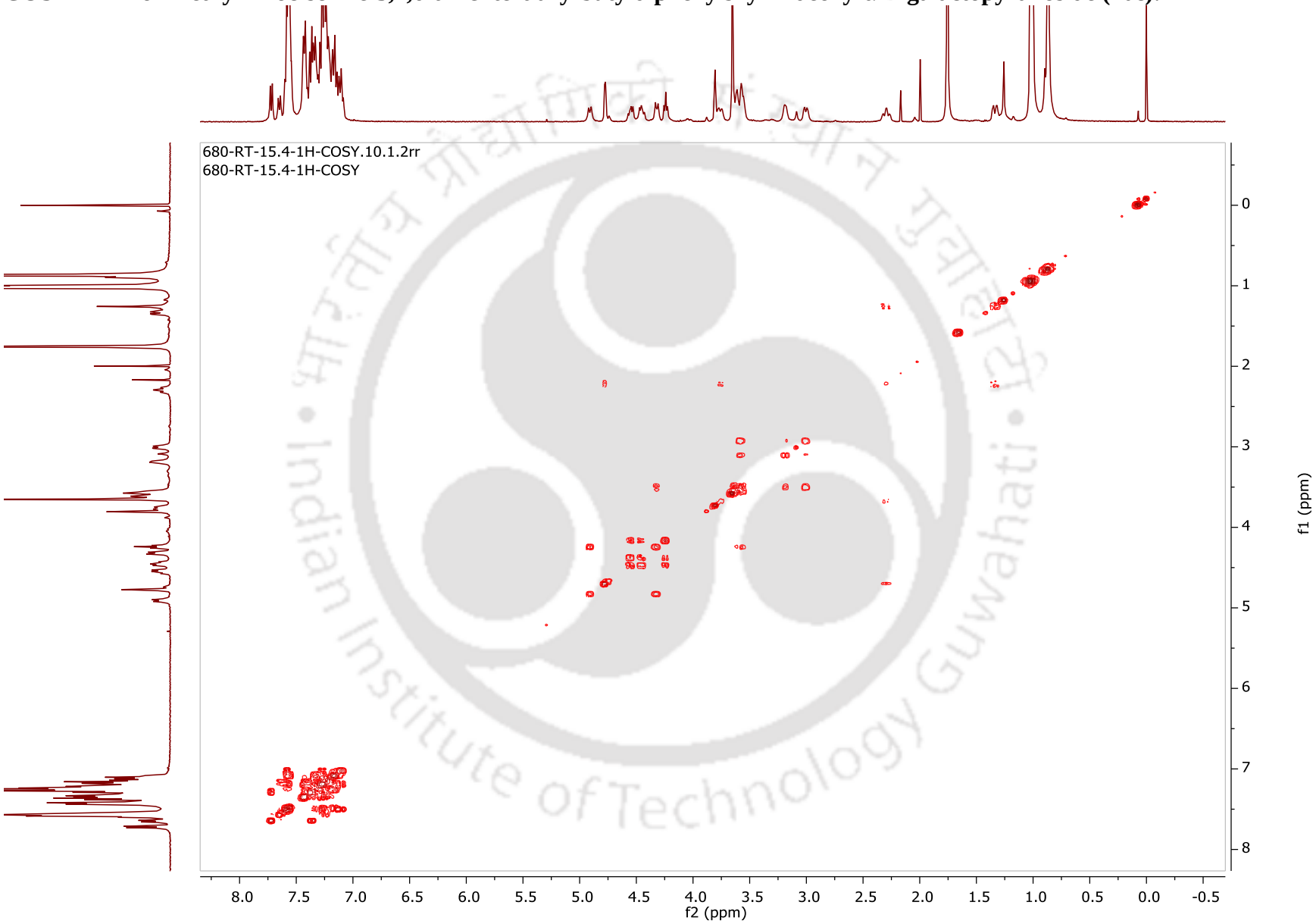


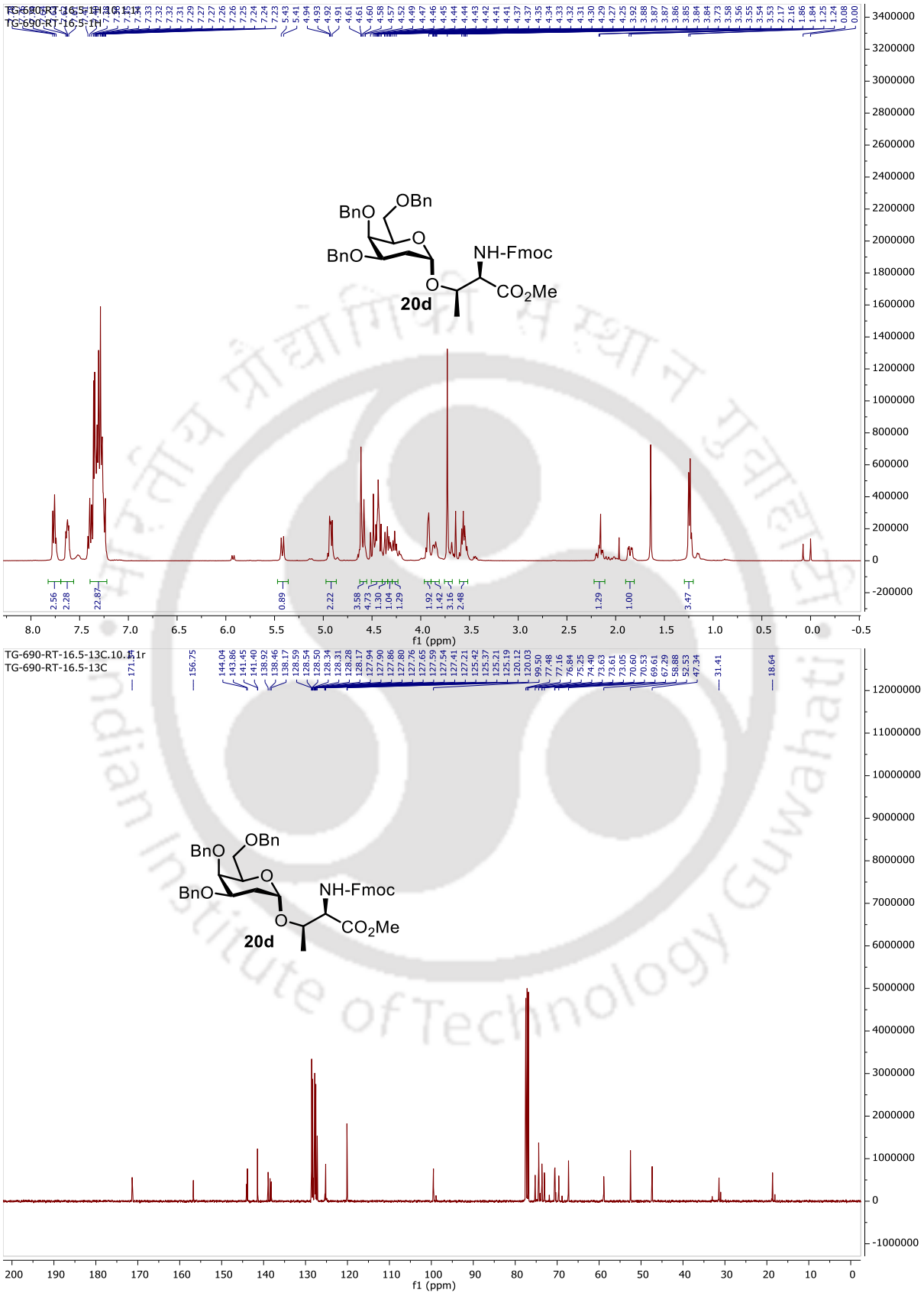


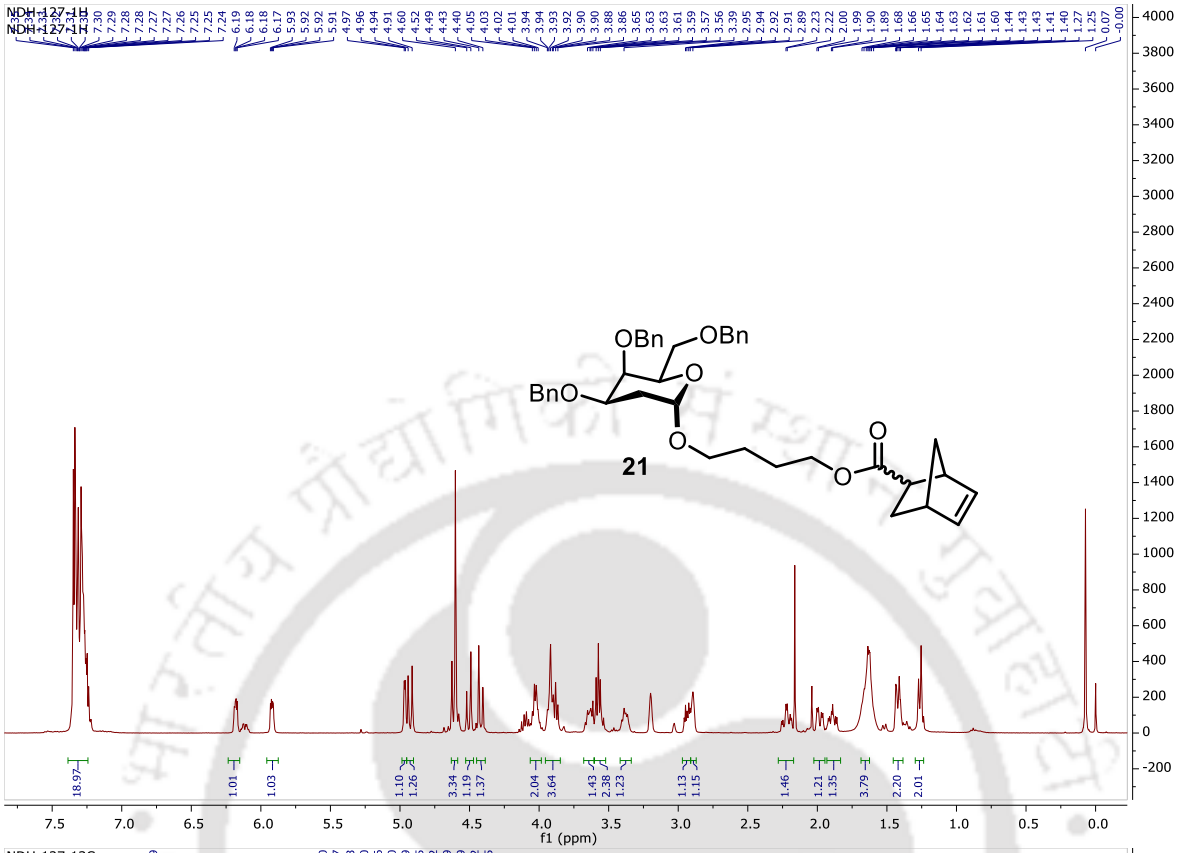


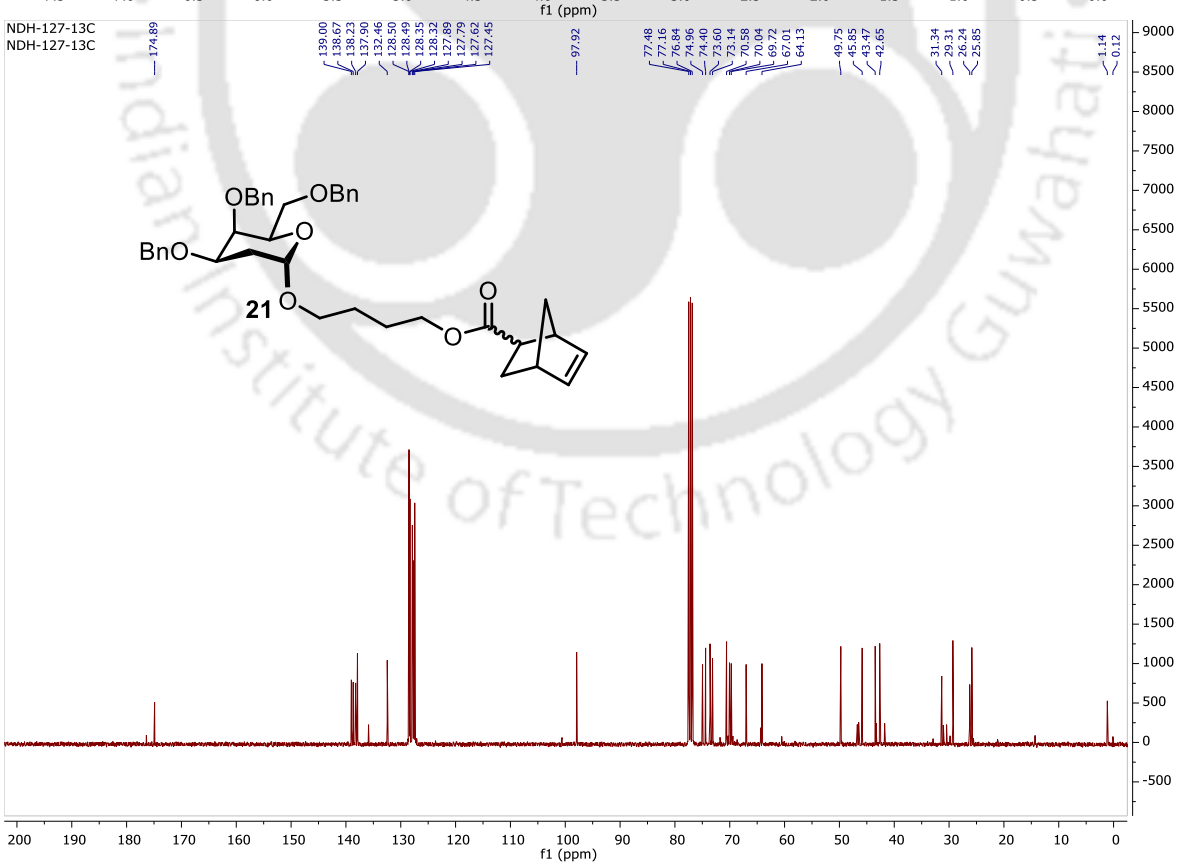


COSY NMR of Methyl fmoc-serine-3,4,6-tri-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-D-galactopyranoside (20c):

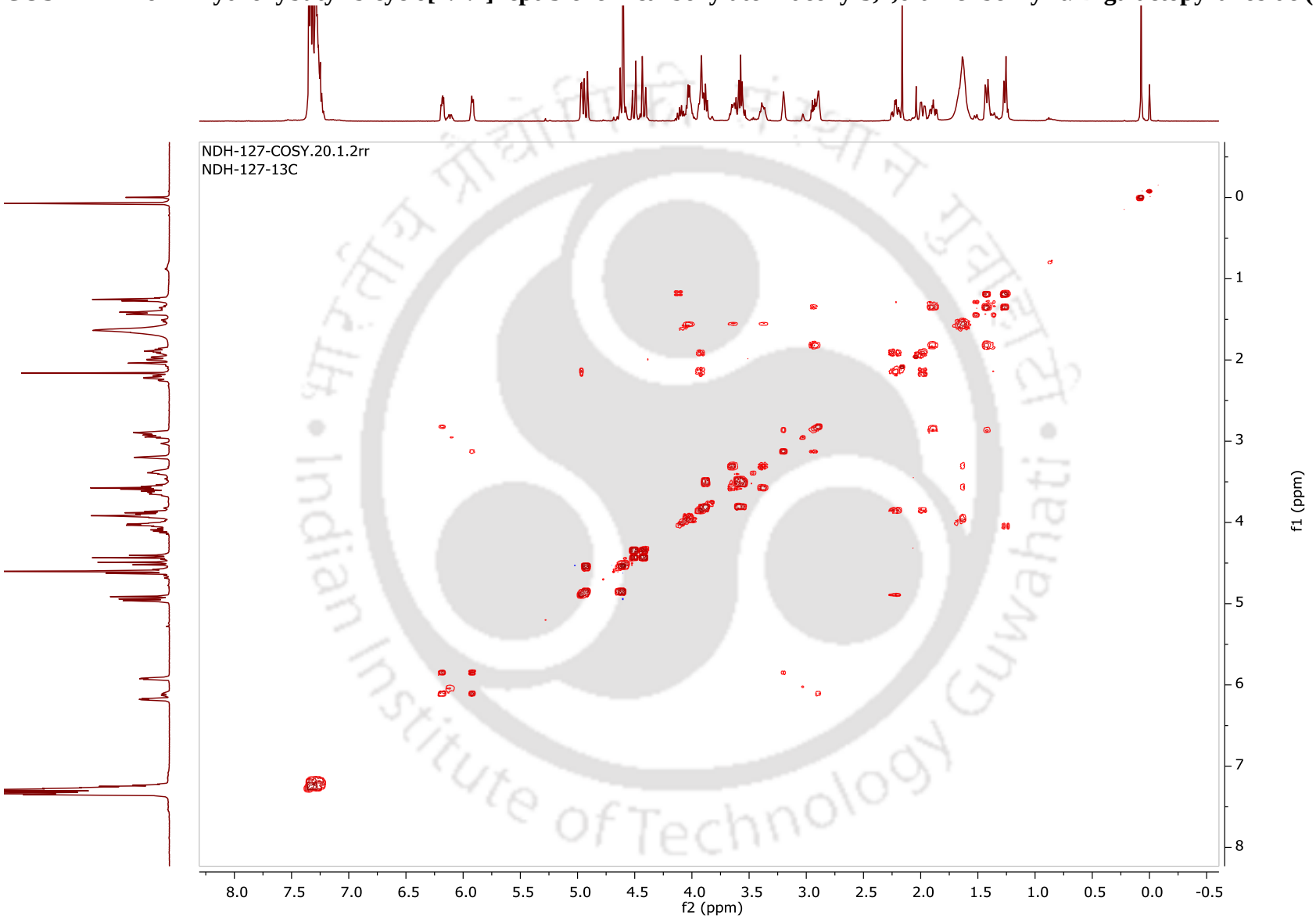






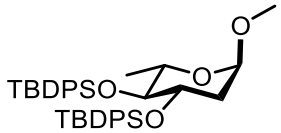


COSY NMR of 4-Hydroxybutyl-bicyclo[2.2.1]hept-5-ene-2-carboxylate-2-deoxy-3,4,6-tri-*O*-benzyl-α-D-galactopyranoside (21):



nOe experiment of 18u

Methyl-3,4-di-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-L-rhamnosepyranoside (18u):



^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.4 Hz, 2H), 7.50 (d, *J* = 7.5 Hz, 2H), 7.47 (dd, *J* = 9.9, 7.6 Hz, 4H), 7.41 – 7.34 (m, 4H), 7.30 (q, *J* = 6.8 Hz, 4H), 7.26 – 7.22 (m, 4H), 4.84 (dd, *J* = 8.3, 3.8 Hz, 1H), 4.09 (d, *J* = 3.5 Hz, 1H), 3.89 – 3.85 (m, 1H), 3.54 (t, *J* = 3.5 Hz, 1H), 3.40 (s, 3H), 1.83 (ddd, *J* = 13.1, 8.2, 2.6 Hz, 1H), 1.68 (dt, *J* = 13.4, 4.2 Hz, 1H), 1.13 (d, *J* = 6.7 Hz, 3H), 0.94 (s, 9H), 0.91 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 135.9, 135.9, 135.9, 135.8, 134.0, 133.8, 133.7, 133.6, 129.8, 129.7, 129.7, 129.7, 127.7, 127.7, 127.7, 127.6, 96.0, 74.8, 72.8, 72.5, 55.6, 33.8, 27.1, 27.0, 19.3, 19.2, 18.3. HRMS (ESI) $C_{39}H_{50}O_4Si_2NH_4$ $[M+NH_4]^+$- calculated- 656.3586; found- 656.3586. $[\alpha]_D^{22}$= -48 (*c* 0.16, $CHCl_3$).

Irradiation of H_1 of 18u:

The anomeric proton **H_1** of **18u** appears at ppm range approximately (4.85 – 4.83). After irradiation of **H_1**, there is a considerable enhancement of C-5 methyl protons coming at ppm range approximately (1.14 – 1.13) and one of the 2-deoxy protons **H_{2eq}** appearing at ppm range approximately (1.70 – 1.66). Thus, it is clear that anomeric proton **H_1** is cis to both C-5 methyl protons and **H_{2eq}**.

Irradiation of H_{2eq} of 18u:

In addition, irradiation of **H_{2eq}** proton results the more enhancement of **H_1** proton and confirms they are cis to each other.

Irradiation of H_{2ax} of 18u:

The other 2-deoxy proton **H_{2ax}** appears at ppm range approximately (1.85 – 1.81). Irradiation of **H_{2ax}**, there is less enhancement of **H_1** proton, and hence, **H_{2ax}** and **H_1** are trans to each other. In addition, it is found that upon irradiation of **H_{2ax}**, there is an enhancement of **H_5** proton coming at ppm range approximately (3.89 – 3.85). Hence, it implies that **H_{2ax}** and **H_5** are cis to each other.

From this above nOe experiments, it is evident that compound **18u** is α-glycosides and adopts the following structure. This experiment helps to determine the configuration of compounds (**18q-t**).

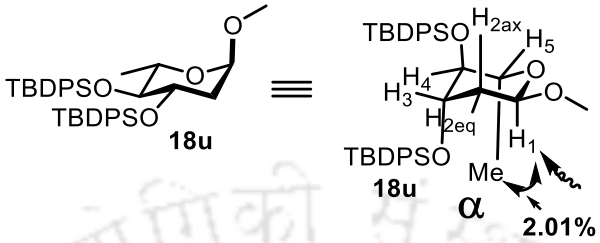
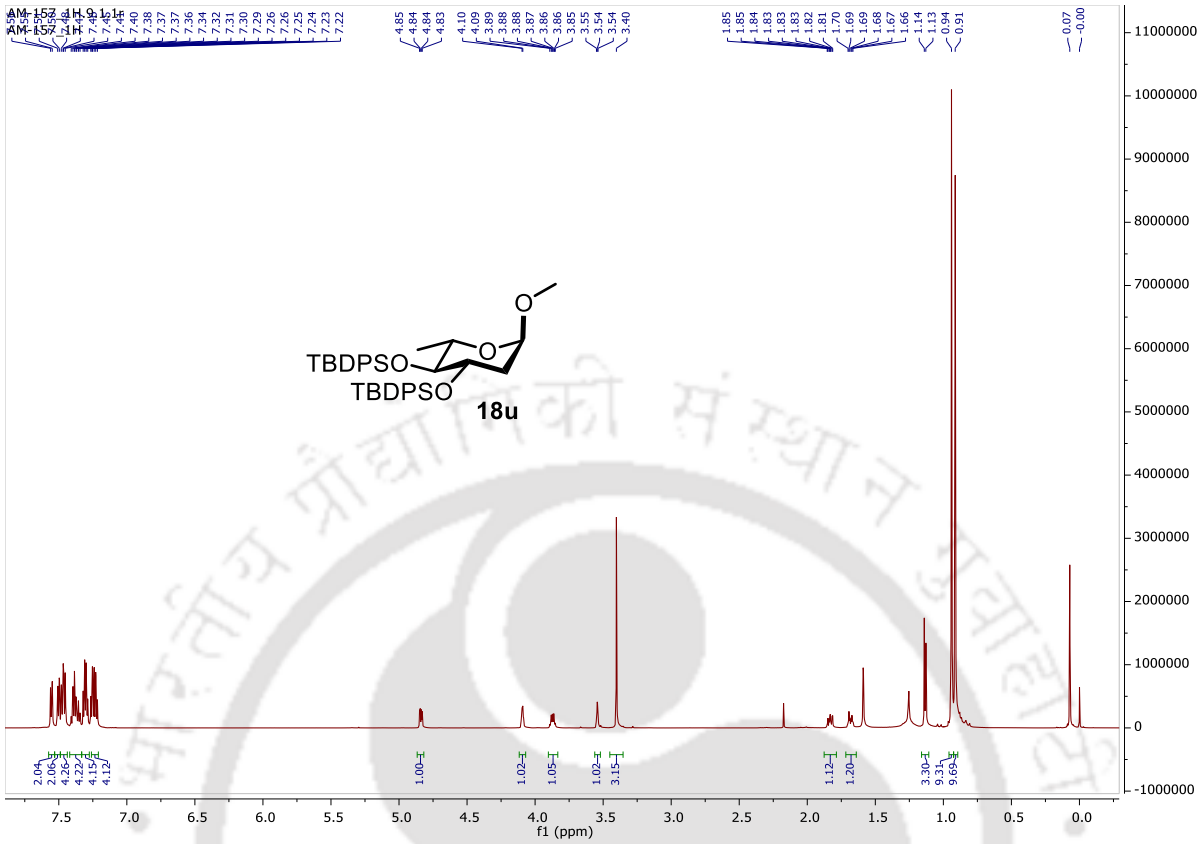
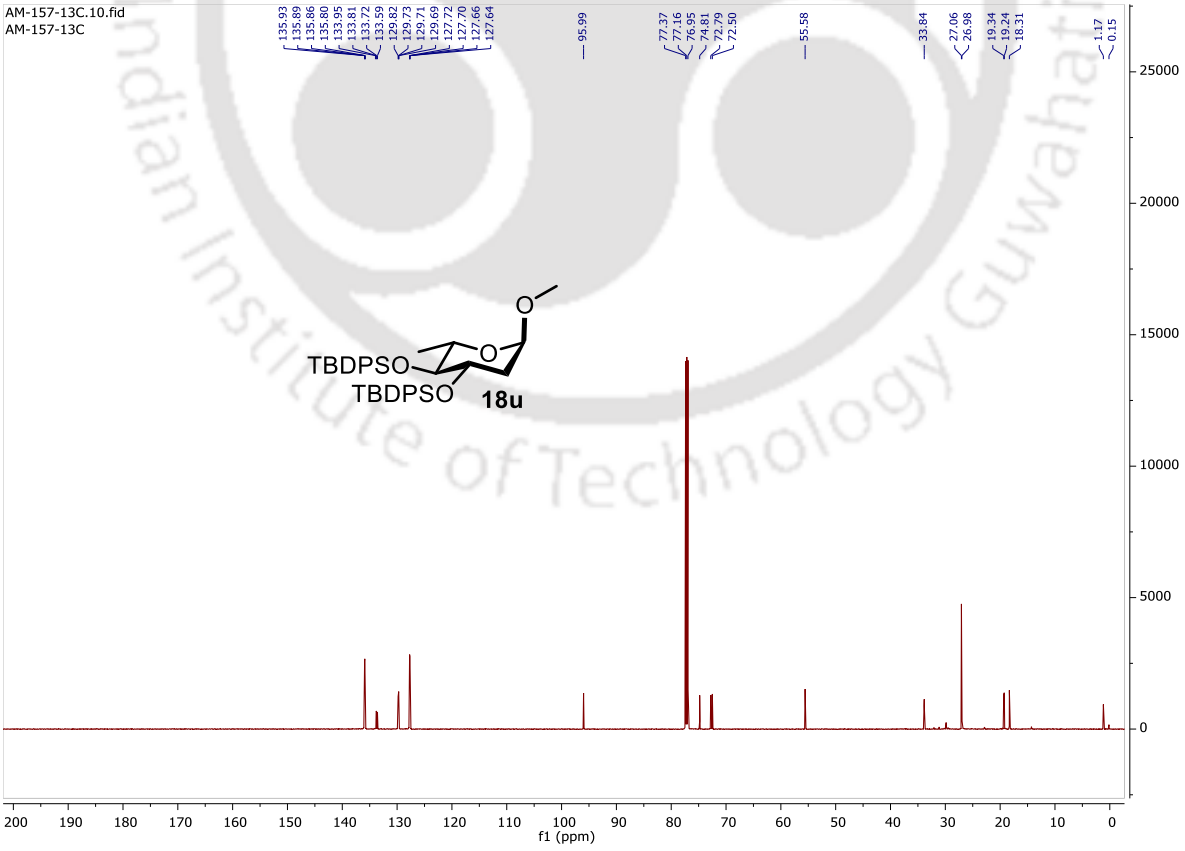
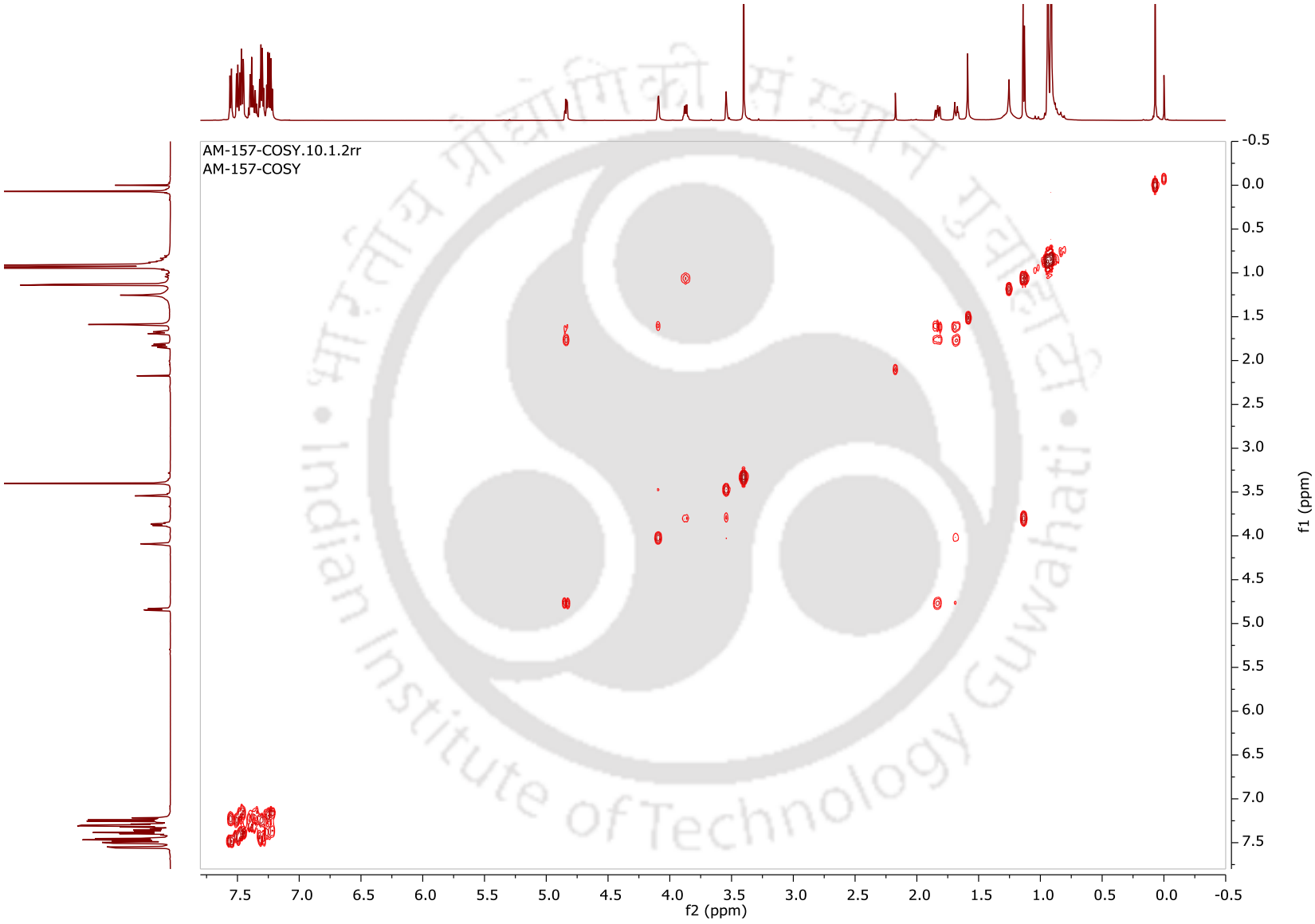


Figure 4: The nOe experiment of **18u**.

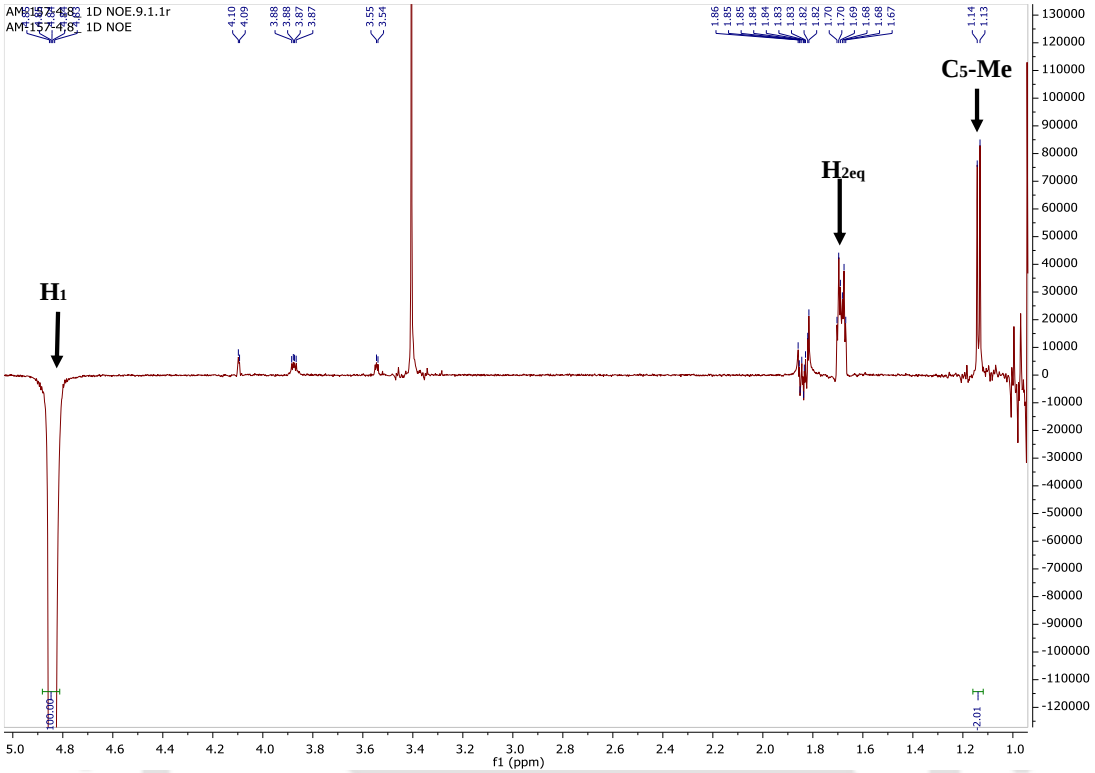




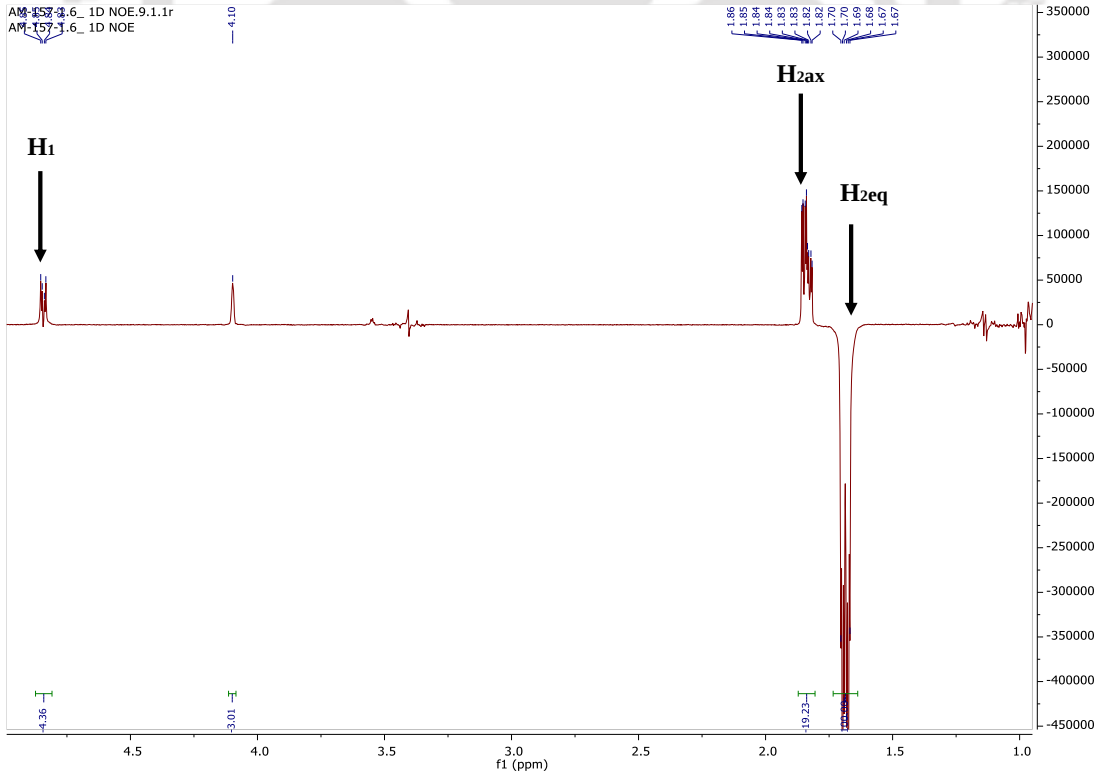
COSY NMR of Methyl-3,4-di-*O*-tertiary-butyldiphenylsilyl-2-deoxy-α-L-rhamnosepyranoside (18u):



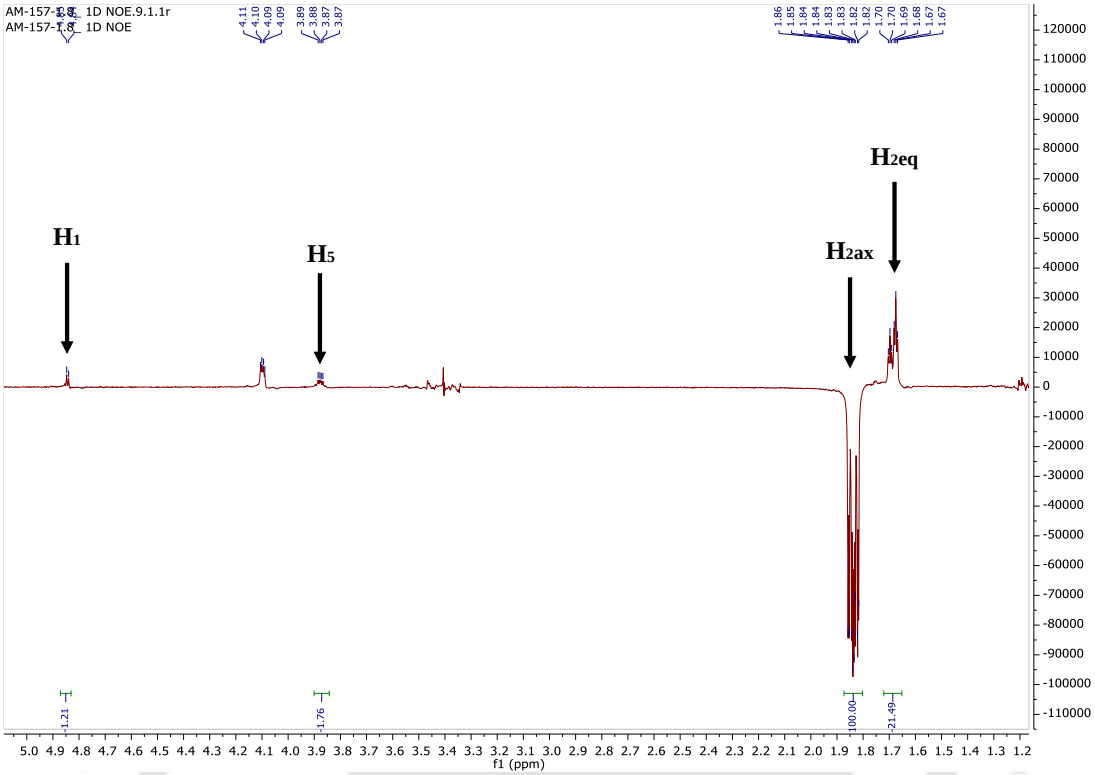
Irradiation of H_1 of 18u:



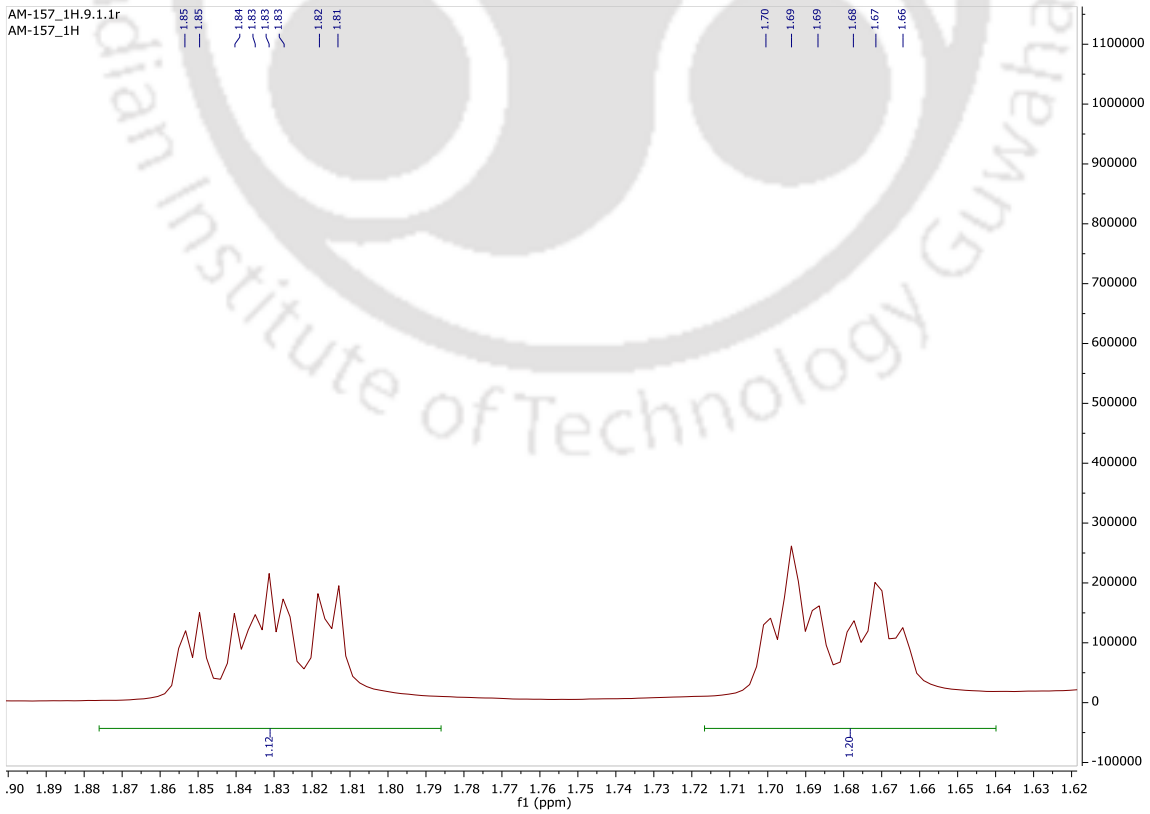
Irradiation of H_{2eq} of 18u:



Irradiation of H_{2ax} of 18u:

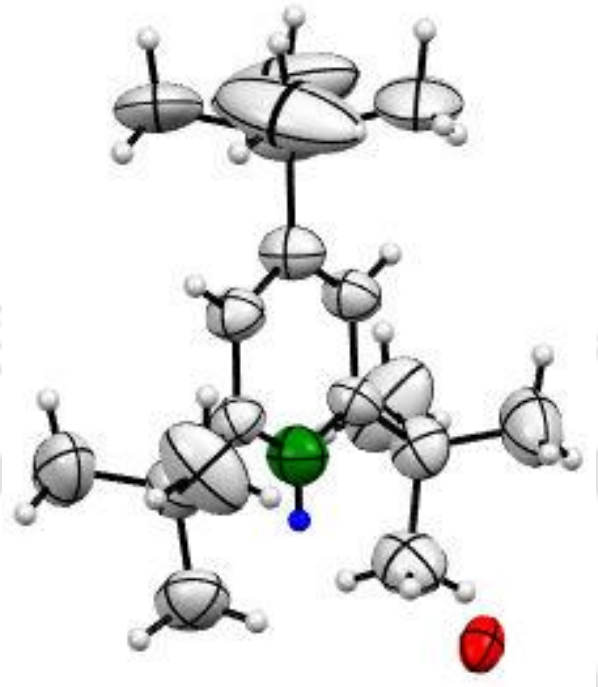


2-deoxy protons of 18u:



4.12 XRD data

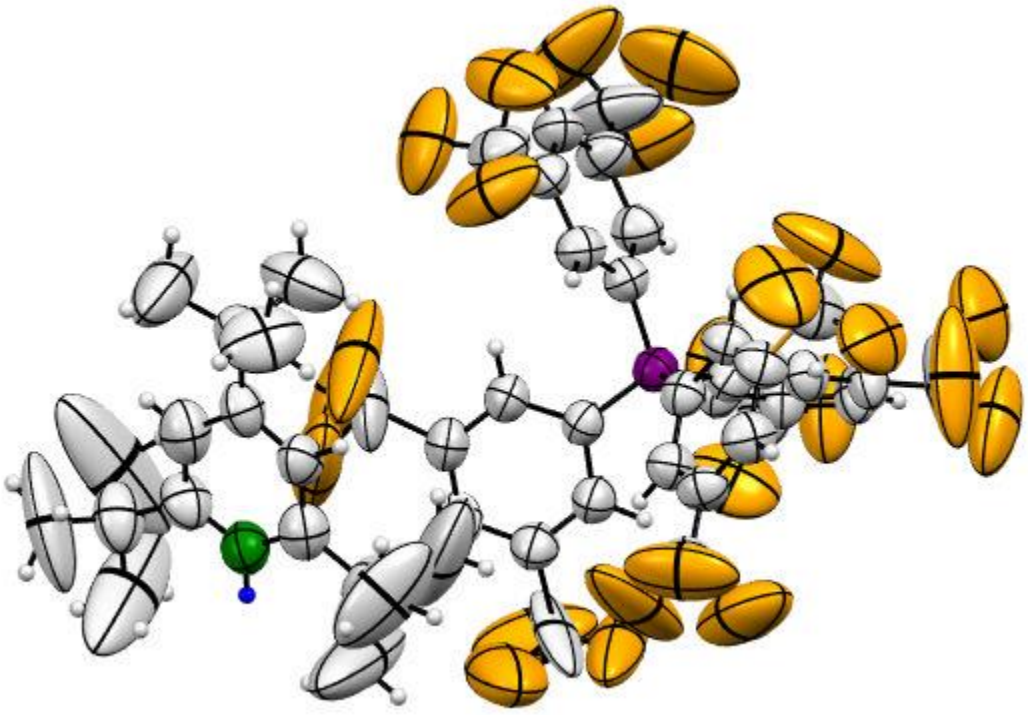
XRD data of 16a (CCDC No: 1897053):



Crystal system	= Orthorhombic	
Bond precision:	C-C = 0.0123 Å	
Wavelength	= 0.71073	
Cell:	a = 10.1384(5) Å	
	b = 18.9027(15) Å	
	c = 11.3925(5) Å	
	α = 90°	
	β = 90°	
	γ = 90°	
Temperature:	293 K	
	Calculated	Reported
Volume	= 2183.3(2) $Å^3$	2183.3(2) $Å^3$
Space group	= P b c n	P b c n
Hall group	= -P 2n 2ab	-P 2n 2ab
Moiety formula	= C16 H27 N, Cl, 2(H2 O), CH3	
Sum formula N0.50 O	= C17 H34 Cl N O2	C8.50 H17 Cl0.50
Mr	= 319.90	159.95

Dx	= 0.973 g cm^{-3}	0.973 g cm^{-3}
Z	= 4	8
Mu	= 0.179 mm^{-1}	0.179 mm^{-1}
F(000)	= 704.0	704.0
F(000')	= 704.84	
Ranges (h,k,l)max	= 12,22,13	12,22,13
Nref	= 1927	1922
Tmin,Tmax	= 0.939,0.949	0.939,0.943
Tmin'	= 0.939	
Correction method	= # Reported	
T Limits:	Tmin = 0.939	
	Tmax = 0.943	
AbsCorr	= Multi-scan	
Data completeness	= 0.997	
Theta(max)	= 25.000	
R(reflections)	= 0.1911(965)	
wR2(reflections)	= 0.4764(1922)	
S	= 1.413	
Npar	= 111	

XRD data of 16c (CCDC No: 1897054):



Crystal system	= Monoclinic	
Bond precision:	C-C = 0.0117 Å	
Wavelength	= 0.71073	
Cell:	a = 14.118(7) Å	
	b = 16.761(8) Å	
	c = 22.755(8) Å	
	α = 90°	
	β = 93.82(3)°	
	γ = 90°	
Temperature:	298 K	
	Calculated	Reported
Volume	= 5373(4) $Å^3$	5373(4) $Å^3$
Space group	= P 21/c	P2(1)/c
Hall group	= -P 2ybc	
Moiety formula	= C32 H12 B F24, C17 H30 N	C32 H12 B F24, C17 H30 N
Sum formula N	= C49 H42 B F24 N	C49 H42 B F24

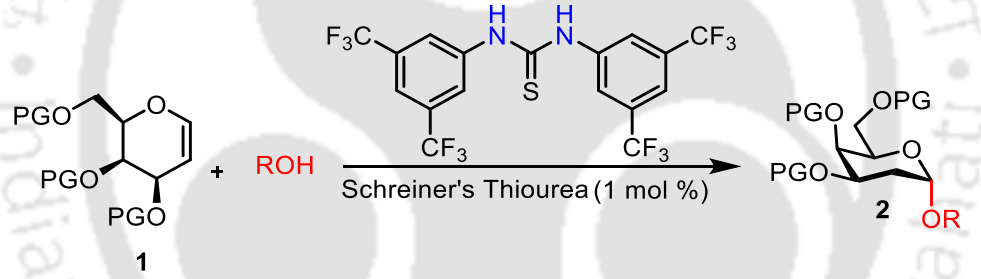
Mr	= 1111.65	1111.65
Dx	= 1.374 g cm^{-3}	1.374 g cm^{-3}
Z	= 4	4
Mu	= 0.138 mm^{-1}	0.138 mm^{-1}
F(000)	= 2256.0	2256.0
F(000')	= 2258.06	
Ranges (h,k,l)max	= 16,19,27	16,19,27
Nref	= 9446	9426
Tmin,Tmax	= 0.963,0.974	0.963,0.974
Tmin'	= 0.962	
Correction method	= # Reported	
T Limits:	Tmin = 0.963	
	Tmax = 0.974	
AbsCorr	= Multi-scan	
Data completeness	= 0.998	
Theta(max)	= 25.000	
R(reflections)	= 0.1160(3390)	
wR2(reflections)	= 0.2831(9426)	
S	= 1.177	
Npar	= 685	

Chapter 5

Synergistic Catalysis of DMAP Salts and Schreiner's Thiourea towards Dehydrative Glycosylation of 2-Deoxy Gluco, Galacto, Arabino Hemiacetals

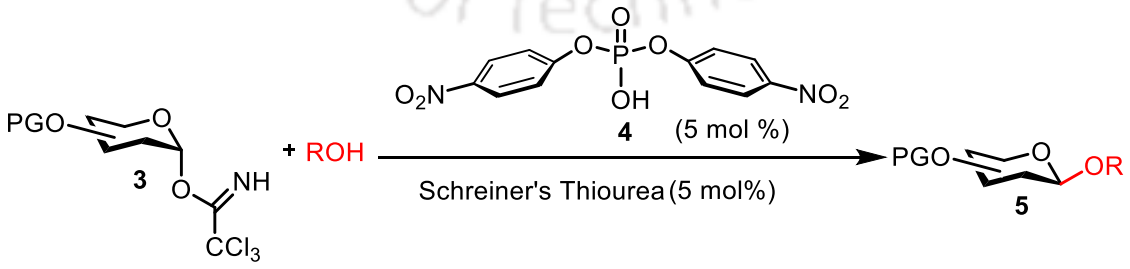
5.1 Introduction:

The impact of Lewis acids has been universal in organic synthesis. The recent surge in the use of hydrogen-bond donors as a source of mild organic Lewis acids instead of metal-based Lewis acids has improved every day in organic chemistry.[1] For example, the dual hydrogen bonding ability of Schreiner's thiourea[2] that can strongly bind with various anions such as chloride,[3] oxyanions,[4] cyanide[5,] and carboxylates[6] along with neutral compounds containing groups which can accurately align to accept two hydrogen bonds, allowed the catalysis of various reactions.[7,8] This concept has been found to have extensive utility in asymmetric synthesis also when performed in the presence of chiral thiourea[9] compounds. This property of Schreiner's thiourea has found potential applicability in carbohydrate chemistry as well and has been exploited towards the development of stereoselective glycosylation methods from glycosyl chlorides, trichloroacetimidates, and glycals. McGarrigle showed that Schreiner's thiourea could catalyze the conversion of glycals **1** into corresponding 2-deoxyglycosides **2** (**Scheme 1**).[10]



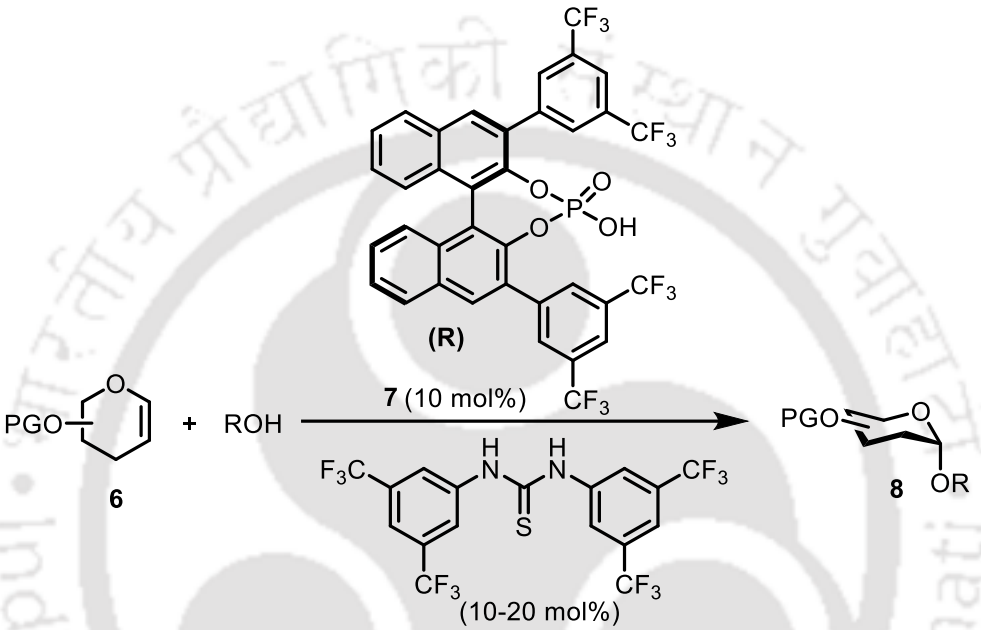
Scheme 1: Glycosylation of glycals **1** in presence of Schreiner's thiourea.

Schmidt and his co-workers reported that *O*-glycosyl trichloroacetimidates **3** afforded corresponding glycosides **5** in the presence of 5 mol % of Brønsted acid **4** and Schreiner's thiourea as a cocatalyst[11] (**Scheme 2**).



Scheme 2: Glycosylation of *O*-glycosyl trichloroacetimidates in the presence of acid catalyst **4** and Schreiner's thiourea as a cocatalyst.

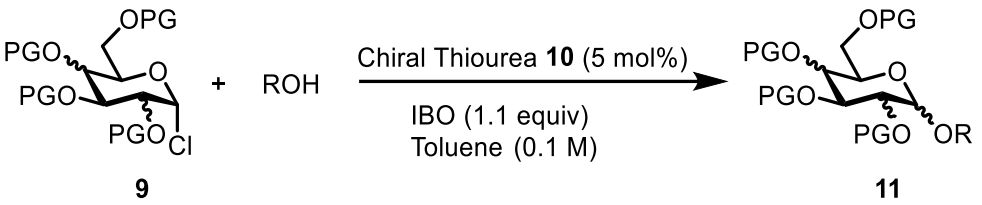
Recently, this cooperative effect of thiourea and acid catalyst was reported by the Galan and co-workers with an increased substrate scope.[12,14] The group demonstrated that the combination of Schreiner's thiourea and chiral BINOL phosphoric acid catalyst **7** was effective for the observed catalysis (**Scheme 3**). Ye et al. reported Koenigs-Knorr glycosylation by urea-mediated hydrogen-bond activation, and anomeric selectivity was observed to improve upon addition of tri-(2,4,6-trimethoxyphenyl) phosphine (TTMPP) on glucose derived donor.[13]



Scheme 3: Glycosylation of glycals **6** in the presence of chiral BINOL phosphoric acid **7** and Schreiner's thiourea.

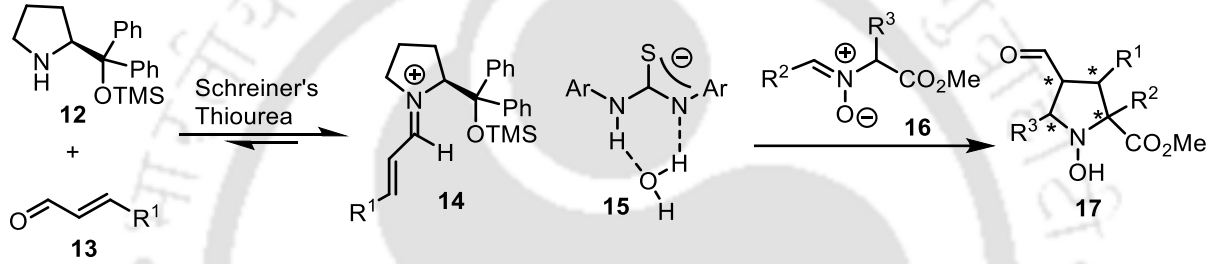
2-deoxysugars are part of several natural products, antibiotics, cancer agents, and carry lots of significance. There are numerous methods for the synthesis of 2-deoxyglycosides emanating from glycosyl acetimidates,[14] fluorides,[6] enol-ethers,[15] and hemiacetals.[16]

Jacobsen and his group discovered macrocyclic chiral bis-thiourea **10** that catalyzes the stereospecific glycosylation reaction of glycosyl chloride **9** to afford corresponding products **11** in high yields (**Scheme 4**).[17] Mechanistic study reveals that both the electrophile and nucleophile are activated in a cooperative way to facilitate the reaction stereoselectively.



Scheme 4: Glycosylation of glycosyl chlorides **9** in the presence of chiral thiourea as a catalyst.

Though enol ethers have been successful substrates for the synthesis of 2-deoxyglycosides, one of the potential pitfalls remains to be the formation of the thermodynamic Ferrier products even with slight variations from the standardized conditions. This can be eliminated by utilizing 2-deoxy hemiacetals as donors. In continuation to our efforts of developing organocatalytic



Scheme 5: Release of hydroxyl group via iminium formation in the presence of Schreiner's thiourea.

methods towards the synthesis of 2-deoxyglcosides, we focused our attention on dehydrative glycosylations.[19] More recently, Schreiner's thiourea has also been found to promote the formation of iminium ions **14** by binding to the released hydroxyl anion (**Scheme 5**)[20] of the hemi-aminal intermediate. We envisaged that glycosyl-hemiacetals might also be activated in a similar fashion leading to the formation of an oxocarbenium ion that can further react with the alcohol nucleophiles. Hence, we performed our initial studies by reacting the 2-deoxy hemiacetal and isopropanol in the presence of 20 mol % of the Schreiner's thiourea (**Table 1**, entry 8). However, this reaction did not lead to the formation of any glycosylated product.

Wang and co-workers reported that DMAP hydrochloride **18a** reacts with acyl chlorides to generate DMAP-acylium (**Figure 1, I**) intermediate that reacts with alcohols to form esters.[18] Taking a cue from above, we were inquisitive to examine whether DMAP hydrochloride **18a**

would react with the reactive 2-deoxy-hemiacetals **20**, leading to the formation of either the oxocarbenium ion or the glycosyl chlorides. Performing a glycosylation reaction with DMAP salt

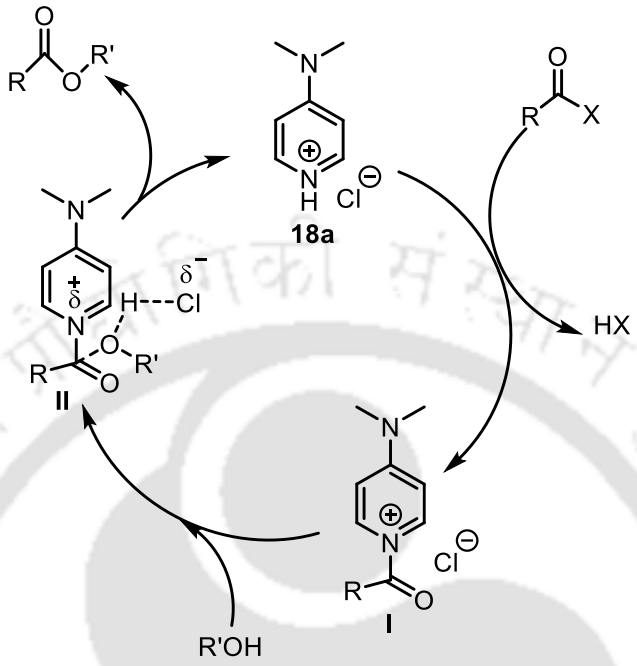
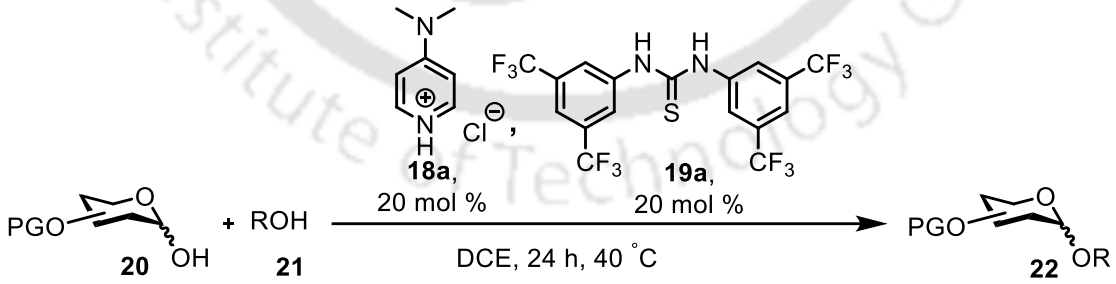


Figure 1: Performance of DMAP.HCl for the synthesis of ester.

18a and 2-dexoyglucose derived hemiacetal **20a** at 40 °C did not yield any product. However, intriguingly, the reaction when performed under similar conditions along with 20 mol % of Schreiner's thiourea **19a** leads to the conversion of the lactols **20** into glycosylated products **22** at 40 °C efficiently (**Scheme 6**).



Scheme 6: Catalysis of DMAP hydrochloride salt and thiourea.

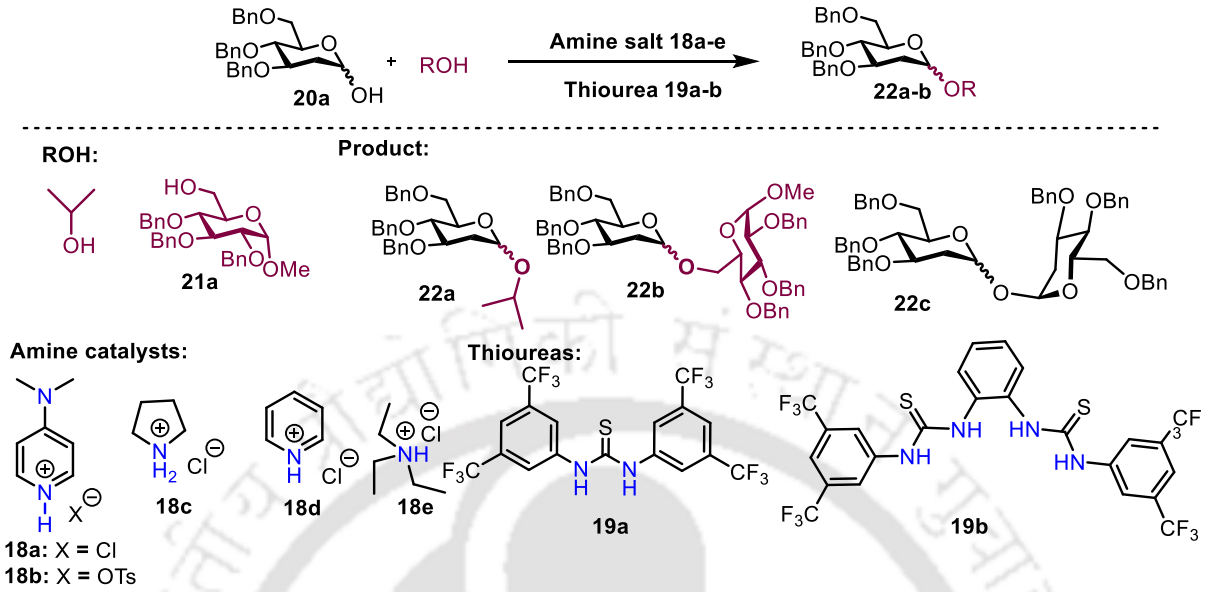
Thiourea and DMAP hydrochloride work synergistically to facilitate the glycosylation of lactols. As discussed vides supra, it is well established that Schreiner's thiourea binds to the chloride via a dual hydrogen bonding and when mixed with an equimolar amount of DMAP

hydrochloride forms a complex leading to a new catalytic site. In other words, the presence of the halide binding thiourea alters the reactivity of the cationic Brønsted acid, in this case, the protonated DMAP. In order to understand if thiourea bound to chloride with its stabilization via the delocalization of the negative charge is indirectly making a weakly coordinating anion, which in turn increases the reactivity of cation, we separately synthesized DMAP-BArF and subjected to the catalysis. However, this did not lead to any glycosylated product.

5.2 Optimization Study:

In chapter 2, we reported that secondary amine salts could catalyze the dehydrative glycosylation of hemiacetals at elevated temperature. Efforts to bring down the elevated temperatures to ambient conditions by employing the thiourea **19a** only resulted in failure (**Table 1**, entries 1 - 2). As discussed above, DMAP hydrochloride salt **18a** as a catalyst in the presence of thiourea as a cocatalyst provided corresponding monosaccharide **22a** under similar reaction condition in 87% yield with 2:1 α:β selectivity (**Table 1**, entry 3). In the presence of primary sugar acceptor **21a**, DMAP hydrochloride **18a** gave efficiently corresponding disaccharide **22b** after 24 h in 66% yield with 4:1 α:β selectivity (**Table 1**, entry 4). No significant improvements have been observed in the yields and selectivities by increasing the amount of thiourea **19a** (**Table 1**, entry 5). When, bis-thiourea **19b**, a stronger halide binding agent[17b] was employed as a cocatalyst instead of thiourea **19a**, it resulted in the formation of the undesired dimerized product **22c** instead of the desired product (**Table 1**, entry 7). Hence, thiourea **19a** was chosen as an optimized cocatalyst for this study. Triethylamine hydrochloride **18e** instead of DMAP hydrochloride lead to no conversion of the starting material (**Table 1**, entry 10). The current method also proved to be sensitive towards the polarity of the solvents as well. Poor yield and selectivity were observed in case of toluene as a solvent (**Table 1**, entry 6), whereas a little drop in selectivity was observed in the presence of 2:1 DCE/ACN solvent system (**Table 1**, entry 14). Hence, DCE has been chosen as an optimized solvent for this organocatalytic method. The pyridine hydrochloride **18d** also afforded corresponding disaccharide **22b** in 55% yield (**Table 1**, entry 9). Surprisingly, the use of molecular sieves (3 Å and 4 Å) terminated the catalytic activity and led to no product (**Table 1**, entries 12 - 13). The DMAP salt with tosylate counter ion **18b** provided the disaccharide **22b** in 52% yield with 1:1 α:β selectivity (**Table 1**, entry 15).

Table 1: Optimization study of glycosylation reaction.



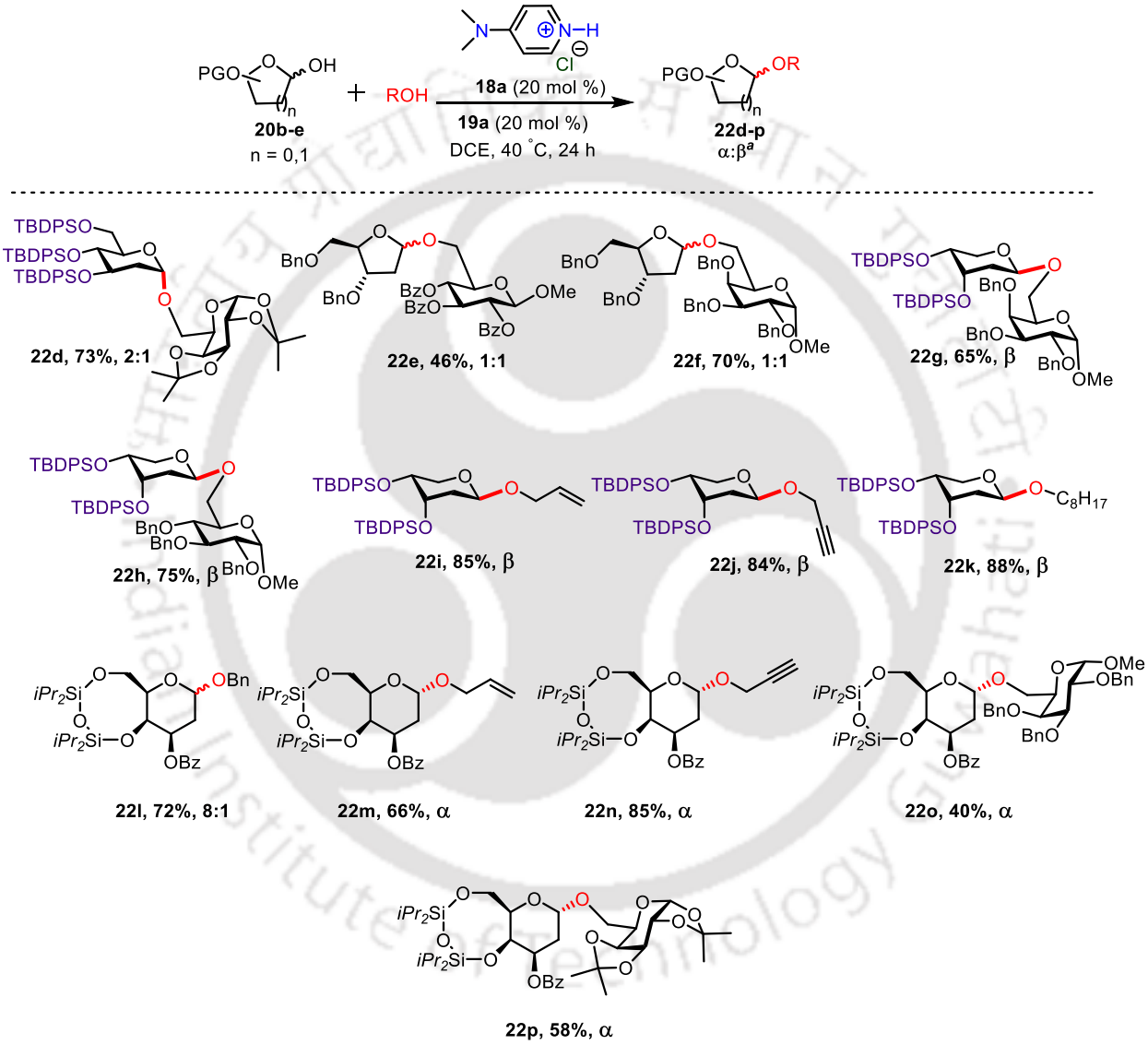
entry	cat.	solvt.	prod.	yield (%)	α:β[j]
1[a]	**18c**	DCM	**22b**	0	-
2[b]	**18c**	DCM	**22a**	0	-
3	**18a**	DCE	**22a**	87	2:1
4	**18a**	DCE	**22b**	66	4:1
5[c]	**18a**	DCE	**22b**	59	2:1
6[d]	**18a**	PhMe	**22b**	61	3:1
7[e]	**18a**	DCE	**22b**	0	-
8	**none**	DCE	**22b**	0	-
9	**18d**	DCE	**22b**	55	1:1
10	**18e**	DCE	**22b**	0	-
11[f]	**18a**	DCE	**22b**	0	-
12[g]	**18a**	DCE	**22b**	0	-
13[h]	**18a**	DCE	**22b**	0	-
14[i]	**18a**	Mix	**22a**	74	2:1
15	**18b**	DCE	**22b**	52	1:1

Reaction condition: 0.12 mmol of **20a**, 0.13 mmol of acceptor IPA and **21a**, 20 mol % of catalyst (**18a-e**), 20 mol % of thiourea **19a-b**, DCE at 40 °C for 24 h. [a]1 equiv of **18c** and 10 mol % of thiourea **19a** were added in DCM at rt. [b]DCM was used as a solvent at rt. [c]50 mol % of thiourea **19a**, and 1.5 equiv of acceptor **21a** were added. [d]Toluene was used as a solvent. [e]20 mol % of thiourea **19b** was used, and 42% of **22c** was found. [f]No thiourea was used. [g]3 Å MS was used. [h]4 Å MS was used. [i](2:1) DCE:ACN was used as a solvent. [j]Anomeric selectivities were determined from crude NMR analysis.

5.3 Scope of Reactivity of Donors with Acceptors:

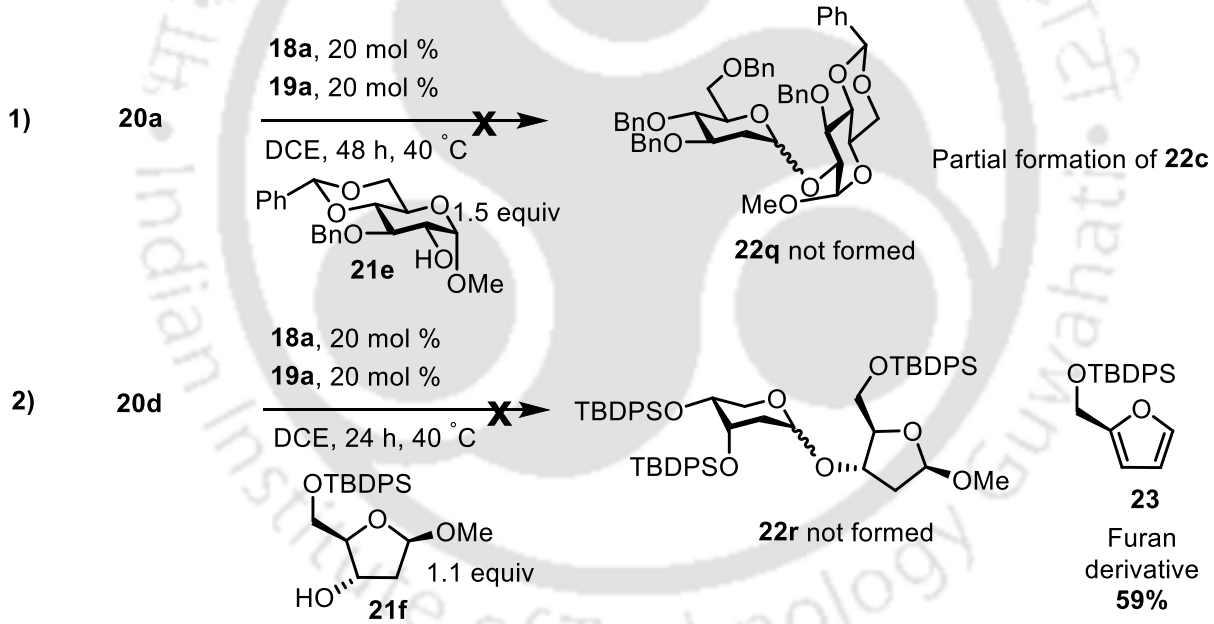
Encouraged by the results, the scope of the methodology has been examined on different donors and acceptors. The coupling of benzyl protected ribose hemiacetal **20b** with electronically

Scheme 7: Scope of monosaccharide and disaccharide.



Reaction condition: 0.12 mmol of **20b-e**, 0.13 mmol of acceptor **21a-d**, 20 mol % of catalyst **18a**, 20 mol % of thiourea **19a**, DCE at 40 °C for 24 h. [a]Anomeric selectivities are determined from crude NMR analysis.

activated and deactivated primary sugar acceptor **21a** and **21d** gave corresponding disaccharides **22f** and **22e** respectively with 1:1 α:β selectivity. TBDPS protected glucose-derived donor **20c** reacted with acetonide protected primary sugar acceptor **21c** to provide the disaccharide **22d** in 73% yield with 2:1 α:β selectivity. However, the reaction of TBDPS protected arabinose hemiacetal **20d** with ally alcohol, propargyl alcohol, and octanol gave efficiently the corresponding monosaccharides **22i**, **22j**, and **22k** respectively with β selectivities and also in high yields (**Scheme 7**). The coupling of TBDPS protected donor **20d** with both benzyl-protected glucose and galactose-derived acceptors **21a** and **21b** provided corresponding disaccharides **22h** and **22g** in 75% and 65% yields respectively with exclusively β selectivity. The coupling between tetraisopropylsiloxane protected galactose derived hemiacetal **20e** with benzyl protected galactose derived primary sugar acceptor **21b**, and acetonide protected 6-OH acceptor **21c** gave the corresponding disaccharides **22o** and **22p** in 40% and 58% yield respectively with α-selectivity.



Scheme 8: Failure attempts with some secondary alcohols.

However, the reaction of **20e** with benzyl, allyl and propargyl alcohol afforded corresponding monosaccharide **22l**, **22m**, and **22n** in high yields 72%, 66%, and 85% respectively. Anomeric ratios were determined by analysis of crude ^{1}H NMR.

Despite many attempts, surprisingly, the current organocatalytic method failed to work with sterically hindered secondary sugar alcohols **21e-f** (**Scheme 8**). Interestingly, the reaction

between **20d** and TBDPS protected ribose derived 3-OH acceptor **21f** led to the formation of TBDPS protected furan derivative **23** (**Scheme 8**, 2).

5.4 Insights towards Mechanism:

Thiourea **19a** is known to bind with a variety Lewis bases and given that there is more than one Lewis base in the reaction mixture, it is challenging to understand the mechanism of activation under the present catalysis. The possible modes of activation have been presented in **Figure 2**.

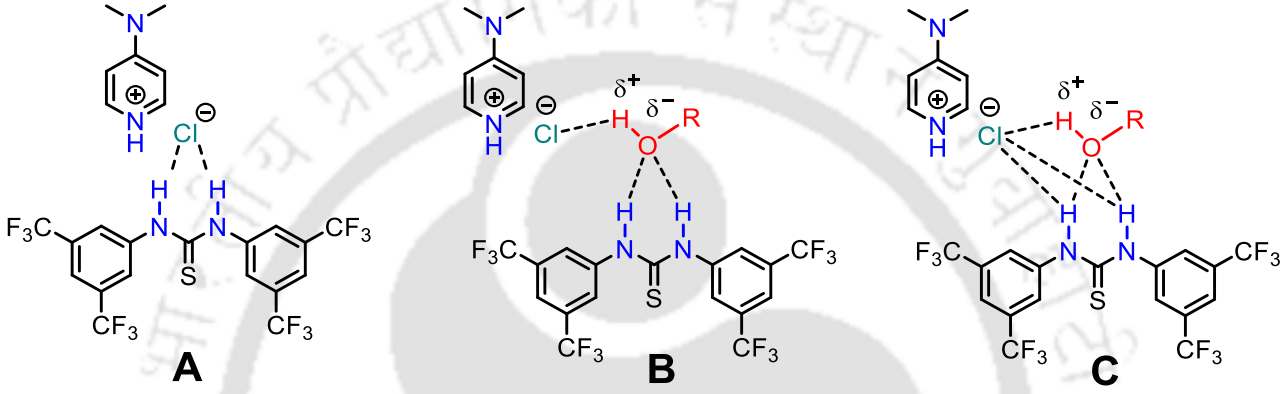


Figure 2: Thiourea A) act as a halide binder of catalyst; B) can form a hydrogen bond with oxyanion; C) Combined interaction of **18a**, **19a**, and alcohol.

^{1}H NMR titration experiment of DMAP hydrochloride **18a** with increasing equivalents of thiourea **19a** lead to a gradual shift in the chemical shift of N-H peak $\mathbf{H_D}$ of DMAP hydrochloride **18a** from δ 15.34 ppm to δ 14.08 ppm (**Figure 5**). In addition, there was a chemical shift of N-H protons of thiourea $\mathbf{H_k}$ from δ 11.00 ppm to δ 10.50 ppm. This signifies the complex formation between DMAP hydrochloride **18a** and thiourea **19a**. On the other hand, when an equimolar isopropanol was added to the mixture, no change in the chemical shifts of both DMAP salt and thiourea has been observed which concludes that halide ions that are more Lewis basic bind strongly to thiourea than the alcohols (**Figure 3**, 4). In addition, there is no involvement of the alcohol in the complex formation of the former two species.

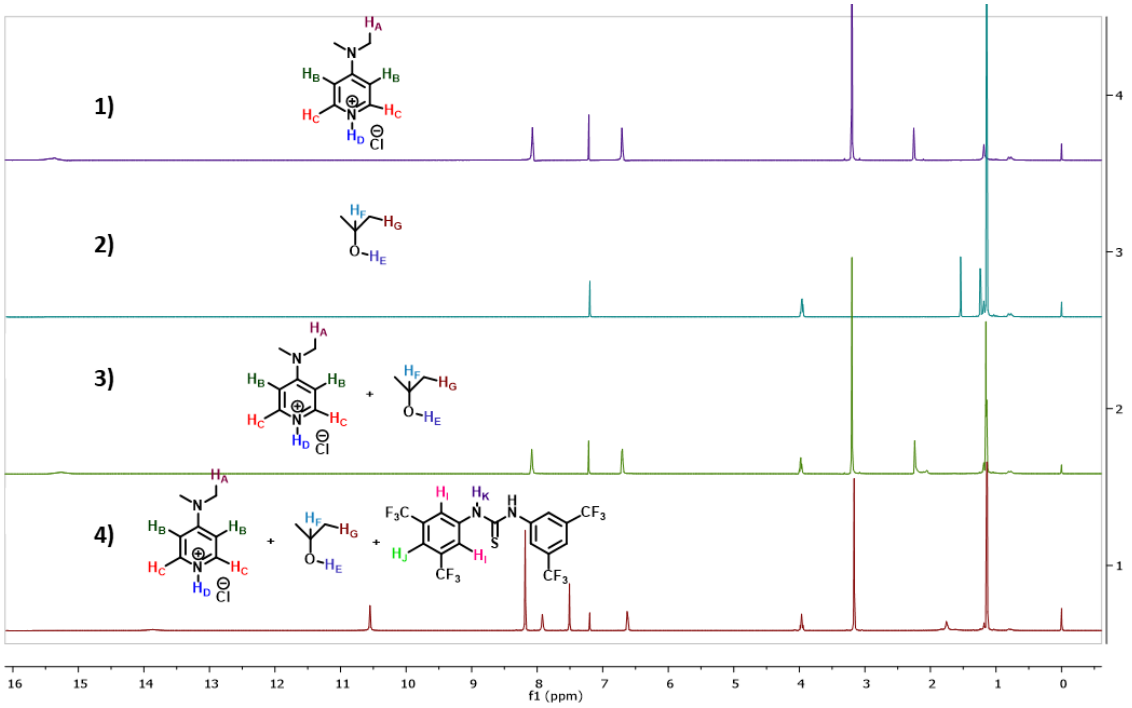


Figure 3: ^{1}H NMR titration of **18a**, **19a** with 2-propanol in 0.6 ml solution of $CDCl_3$. 1) 0.025 mmol of **18a** 2) 0.025 mmol of 2-propanol 3) 0.025 mmol of **18a** and 0.025 mmol of 2-propanol (1:1 ratio) and 4) 0.025 mmol of **18a**, 0.025 mmol of 2-propanol and 0.025 mmol of **19a** (1:1:1 ratio).

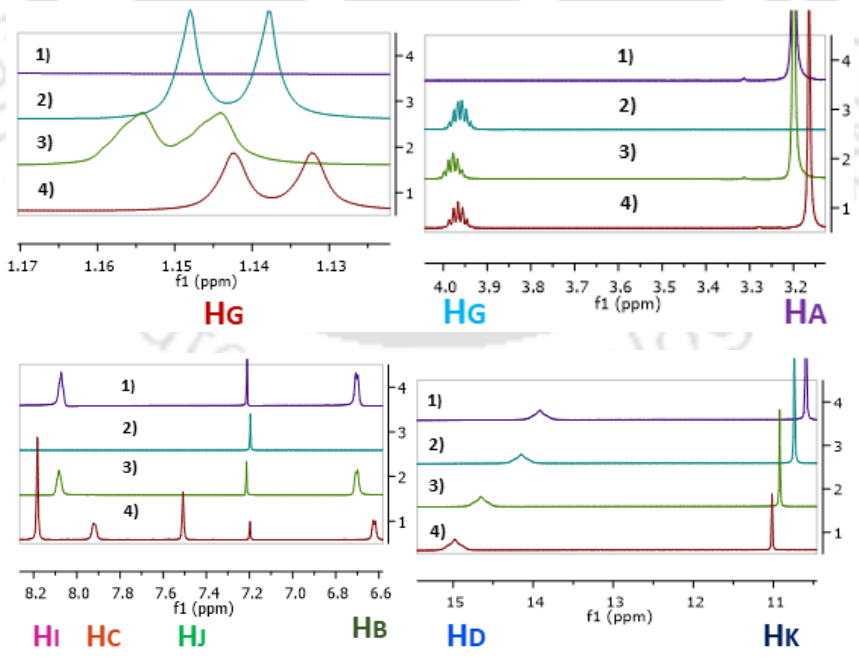


Figure 4: Expanded regions from δ 1.13 – 1.17 ppm, δ 3.20 – 4.00 ppm, δ 6.60 – 8.20 ppm, and δ 11.00 – 15.00 ppm.

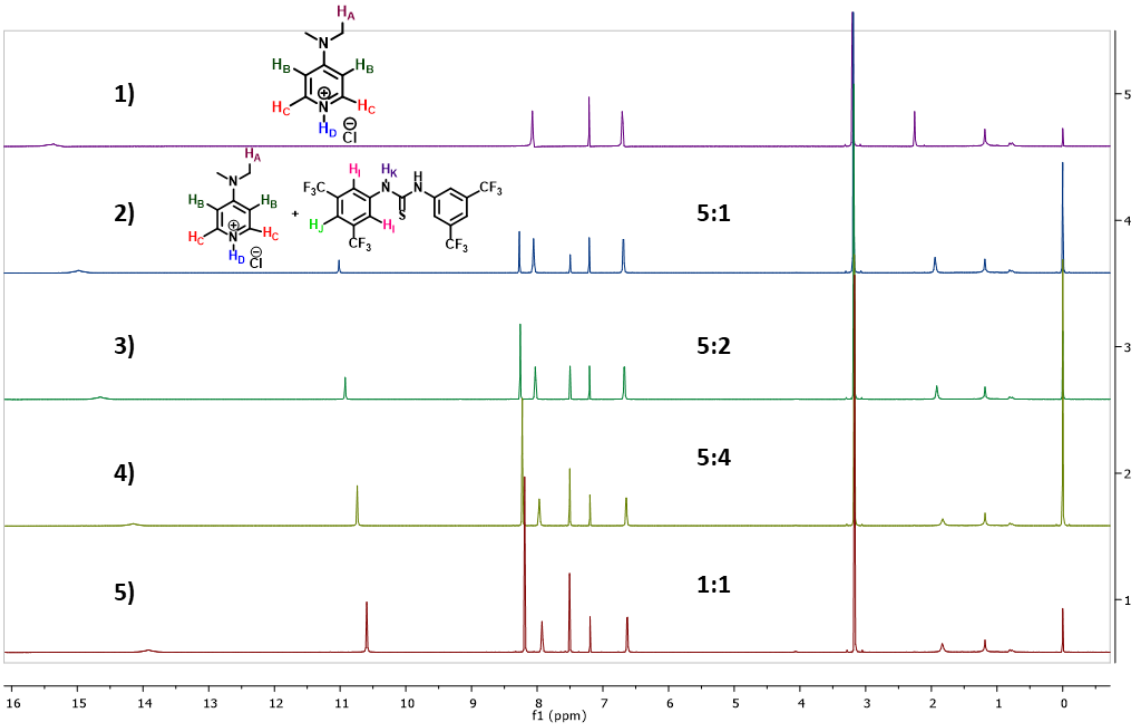


Figure 5: ^{1}H NMR titration of **18a** with **19a** in 0.6 ml solution of $CDCl_3$. 1) 0.025 mmol of **18a** 2) 0.025 mmol of **18a** and 0.005 mmol **19a** (5:1 ratio) 3) 0.025 mmol of **18a** and 0.010 mmol **19a** (5:2 ratio) 4) 0.025 mmol of **18a** and 0.020 mmol **19a** (5:4 ratio) and 5) 0.025 mmol of **18a** and 0.025 mmol of **19a** (1:1 ratio).

Specific regions expanded

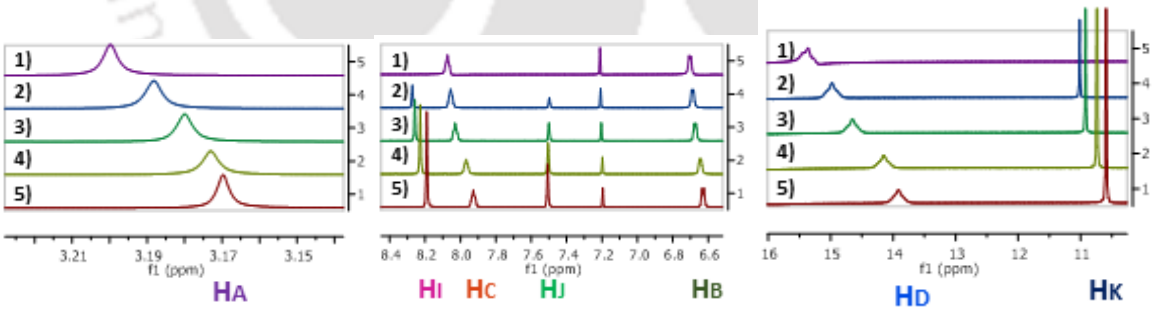
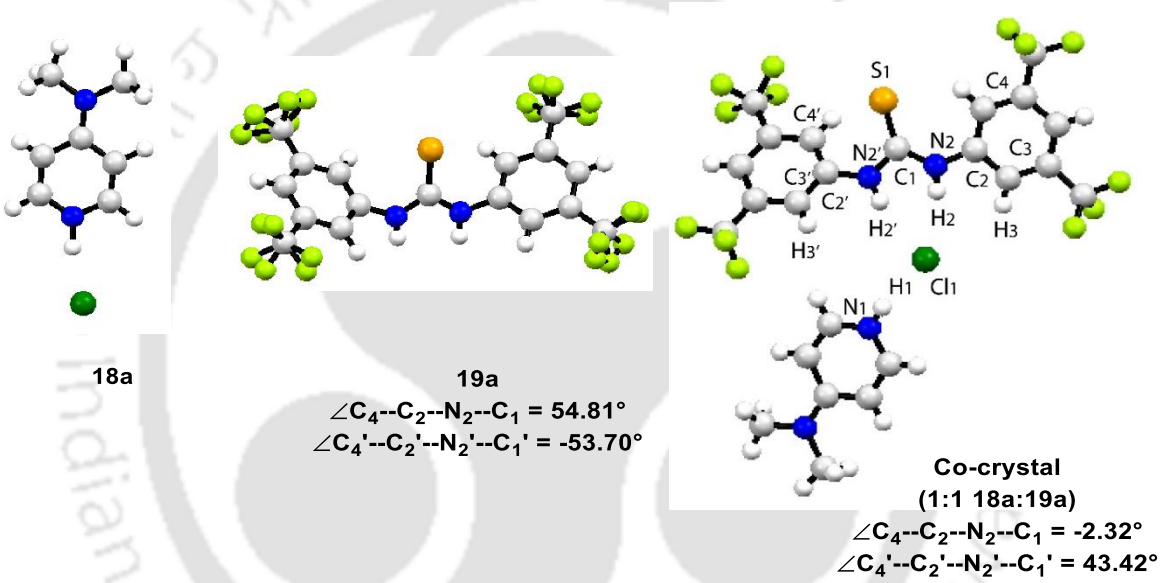


Figure 6: Expanded regions from δ 3.15 – 3.21 ppm, δ 6.60 – 8.40 ppm, and δ 11.00 – 16.00 ppm.

Besides, XRD data of co-crystal (1:1 **18a**:**19a**) reveals that there is a hydrogen bonding between thiourea **19a** and chloride ion of DMAP salt **18a**, (H_2—Cl_1: 2.421Å and $H_{2'}$—Cl_1: 2.307Å, **Table 2**). In addition, there is a shorter in N_1—H_1 bond length in co-crystal as compare to only DMAP.HCl salt **18a** (N_1—H_1: 0.860Å in co-crystal and N_1—H_1: 1.083Å in **18a**, **Table 2**).

Hence, it implies us that negative charge of chloride ion is distributed between the Schreiner's thiourea and the protonated DMAP, which resulted in shrinkage of N_1—H_1 bond length. Moreover, there was also change in bond distances of C—H, C—F, C=S bonds of co-crystal relative to the XRD of Schreiner's thiourea alone (**Table 2**). These observations provide the same information as the ^{1}H NMR which in turn conclude the reactivity differences of the cationic DMAP. We presume that the activated complex of DMAPHCl and thiourea creates an active site akin to the enzymatic cavity allowing a complex between the anomeric hemiacetal and the alcohol, resulting in the coupling. Further experiments need to be performed to decipher the mechanism of activation of the current organocatalytic method.



Bond Distance Data					
DMAP.HCl[18b-c] (**18a**)		Schreiner's Thiourea[1a] (**19a**)		Co-crystal (1:1 **18a**:**19a**)	
Specified bond	Bond Distance (Å)	Specified bond	Bond Distance (Å)	Specified bond	Bond Distance (Å)
N_1—Cl_1	3.065	N_2—H_2	0.775	N_1—Cl_1	3.059
N_1—H_1	1.083	N_2'—H_2'	0.844	N_1—H_1	0.860
H_1—Cl_1	2.013	C_1—S_1	1.678	H_1—Cl_1	2.207
		C_3—H_3	1.068	H_2—Cl_1	2.421
		C_3'—H_3'	0.948	H_2'—Cl_1	2.307
				N_2—H_2	0.860
				N_2'—H_2'	0.860
				C_3—H_3	0.930
				C_1—S_1	1.663

Table 2: Bond distance measurement of Co-crystal of DMAP salt **18a** and thiourea **19a** along with DMAP salt **18a** and Schreiner's thiourea.

Based on the NMR evidence and the control experiments we propose that the increased activity of DMAP salt (Lewis acidity) due to the halide removal by Schreiner's thiourea would transfer the proton to the hemiacetal (**Figure 7, I**) by the expulsion of DMAP. The generated intermediate (**Figure 7**, **II**) liberates one water molecule to convert reactive and crucial oxocarbenium ion intermediate (**Figure 7**, **III**). Upon addition of alcohol, the oxocarbenium ion readily converted to another intermediate (**Figure 7**, **IV)**. After deprotonation of intermediate (**IV**), the desired product (**Figure 7**, **V)** was formed with the regeneration of catalyst due to abstracting the liberated proton by DMAP. Thus, it is obvious that thiourea and DMAP hydrochloride salt act in a synchronous manner to drive the dehydrative glycosylation of hemiacetals.

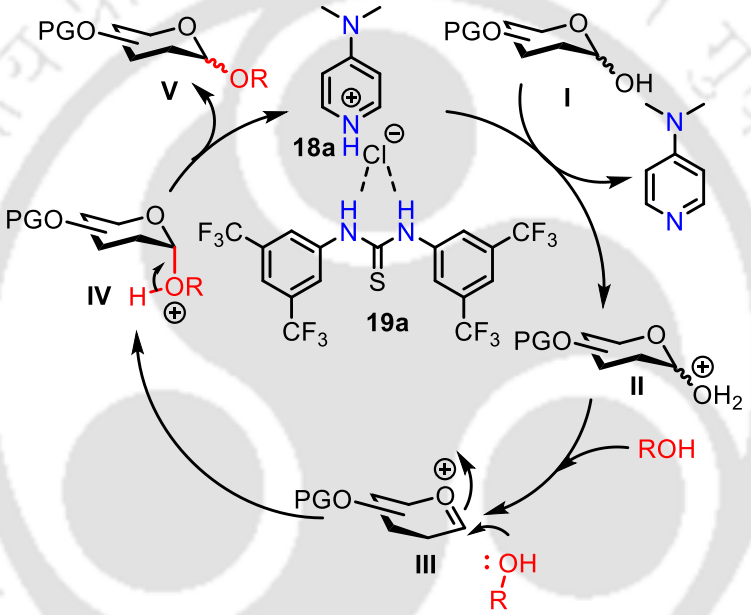


Figure 7: Proposed mechanism for cooperative catalysis of DMAP salt and thiourea.

5.5 Conclusion:

In conclusion, the synergistic activity of Schreiner's thiourea and DMAP salts allowed us to perform the dehydrative glycosylation under ambient conditions. The current cooperative catalysis method is mild enough to selectively activate only 2-deoxy sugar hemi-acetals and does not support the glycosylation of 2-oxy sugars. NMR titration gave us visual evidence about the mechanism where thiourea acts as a halide scavenger in our method by increasing the reactivity of the protonated DMAP catalyst.

5.6 Experimental Section:

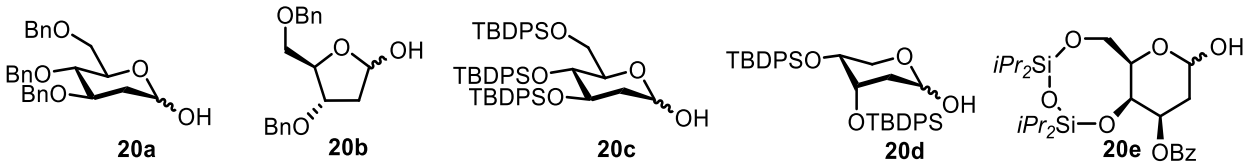
General Information

All solvents and reagents used were in commercial-grade for the reaction without further purification. Reagents were purchased from Sigma-Aldrich, Merck, Spectrochem, Carbosynth, Chempure.

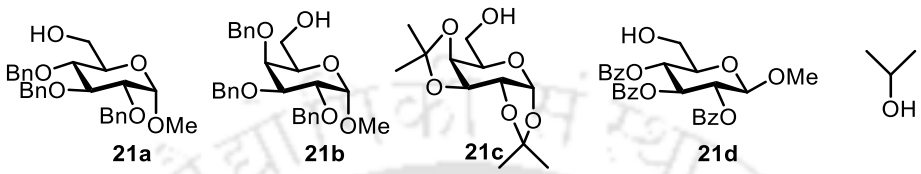
Analysis

Reactions 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 Ultra High Performance Liquid Chromatography (UHPLC) using column [Particle size: (µ) 12, Dim: (mm) 250 x 10] in reverse phase, normal phase using silica gel [Merck, 60-120 mesh] and flash chromatography in normal phase using silica gel [Merck, 230-400 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 rt. ^{1}H- and ^{13}C NMR recorded on a Bruker 600 MHz and 400 MHz spectrometer using $CDCl_3$ as solvent. Chemical shift values reported in ppm with the solvent as the internal standard ($CDCl_3$: δ 7.26 for ^{1}H, δ 77.16 for ^{13}C). 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 performed using Agilent technologies mass spectrometer. The diastereomeric ratio 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.

Glycosyl Donors Used in this Study:

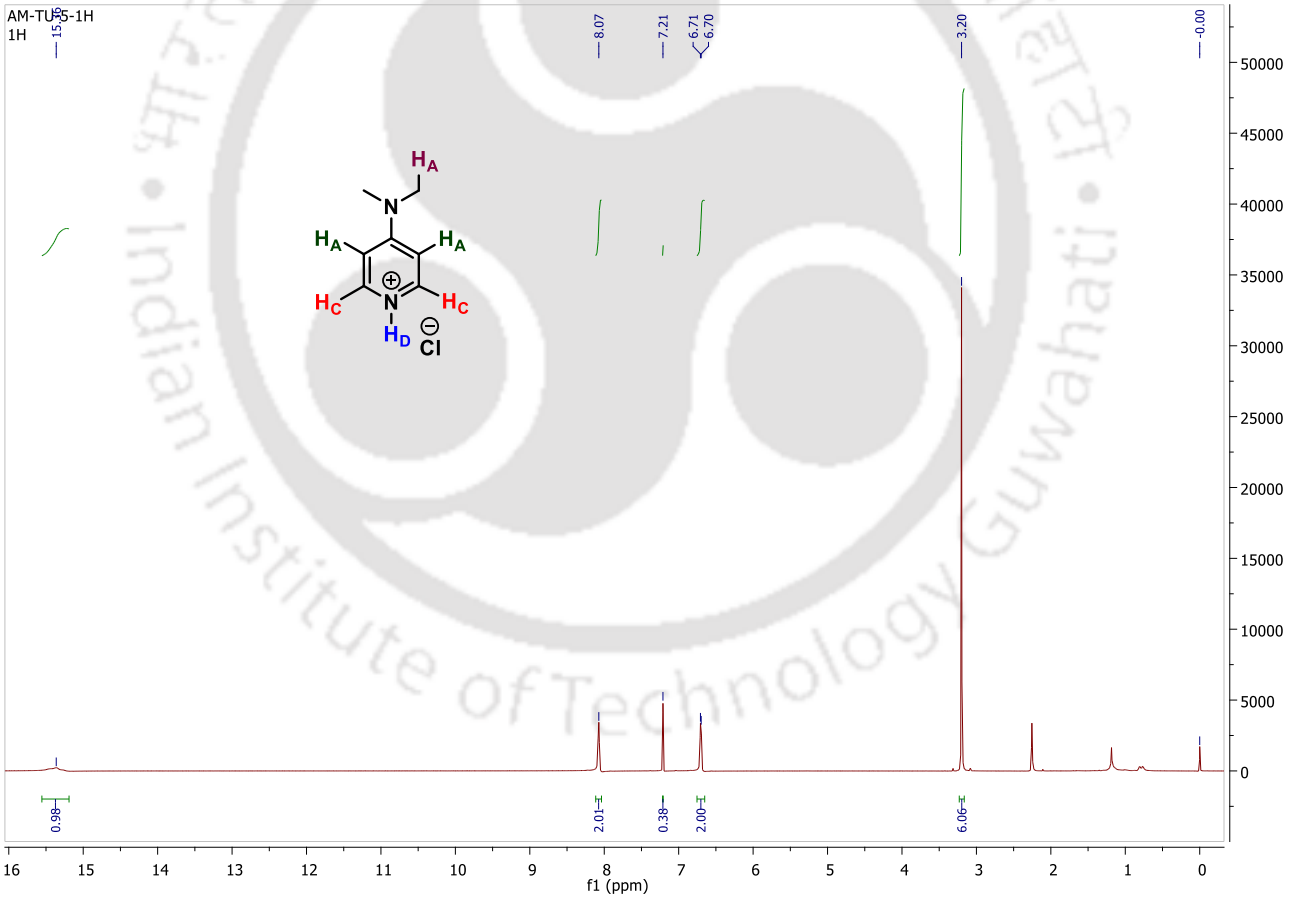


Acceptors Used in this Study:

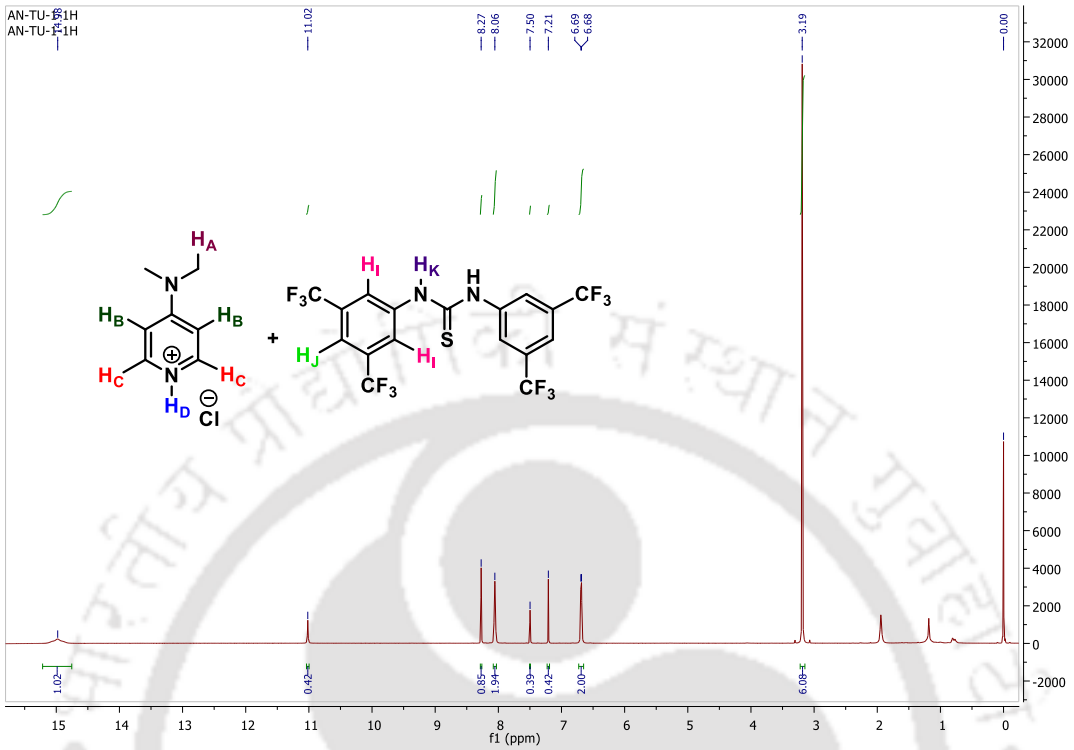


NMR Titration Experments

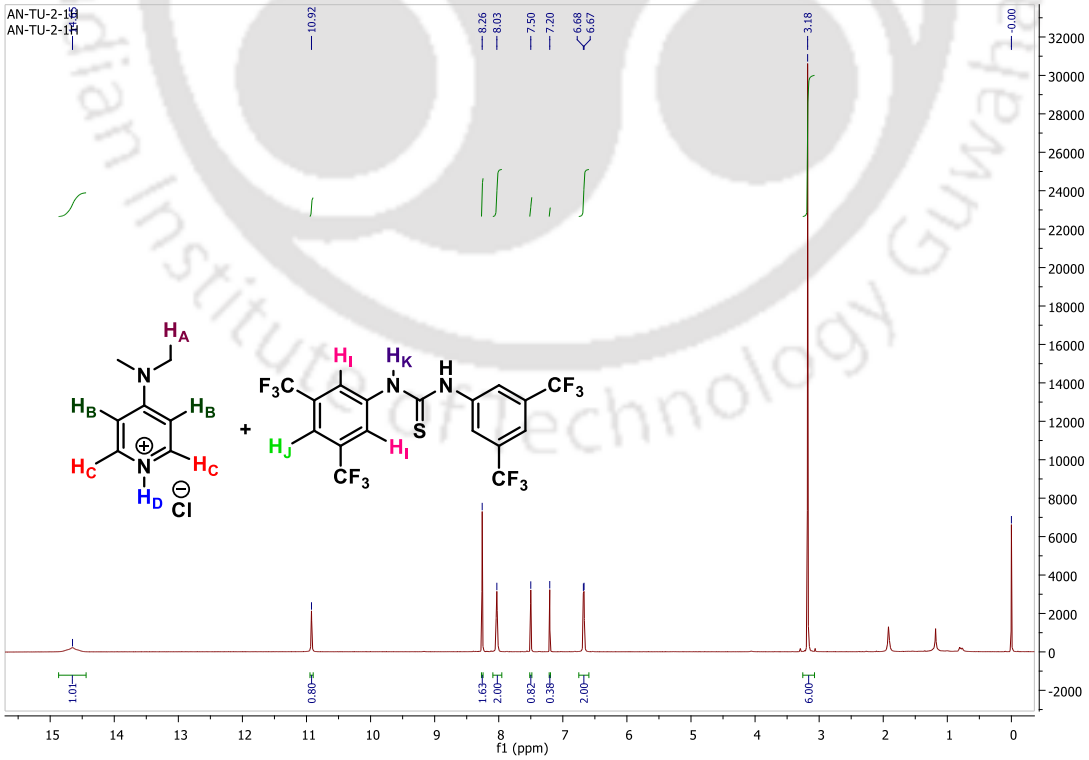
^{1}H NMR of **18a** (0.025 mmol in 0.6 ml of $CDCl_3$)



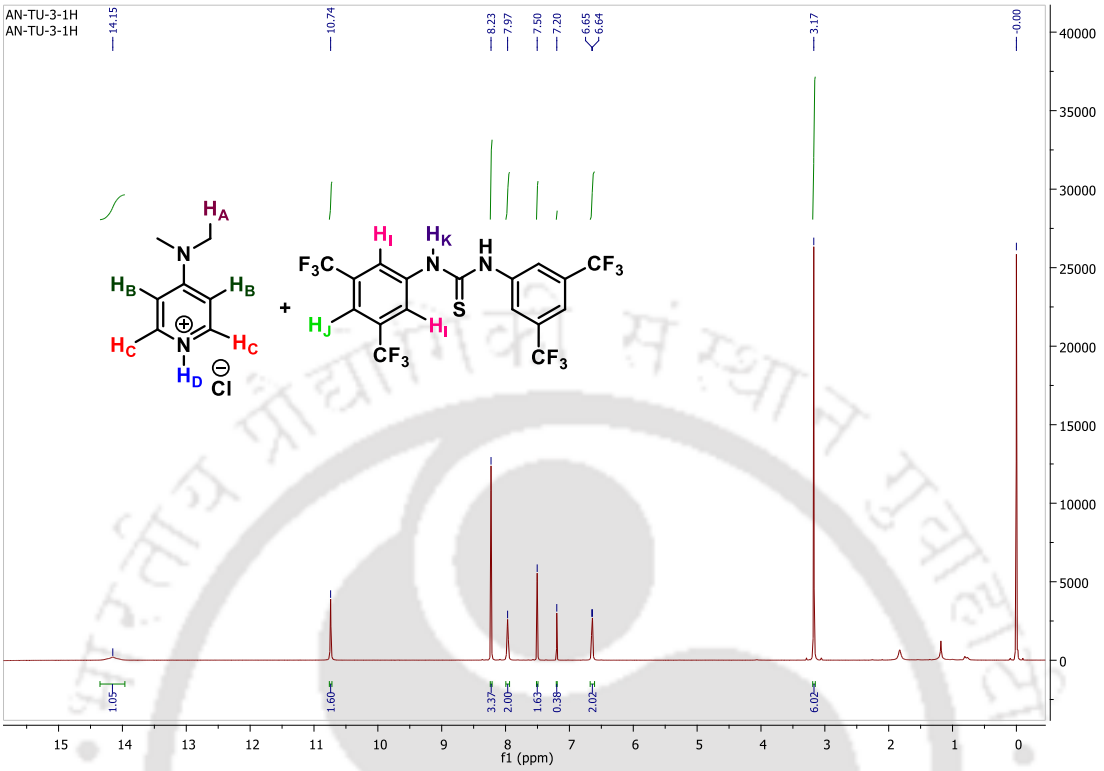
^{1}H NMR of 5:1 mixture of **18a** and **19a** (in 0.6 ml of $CDCl_3$)



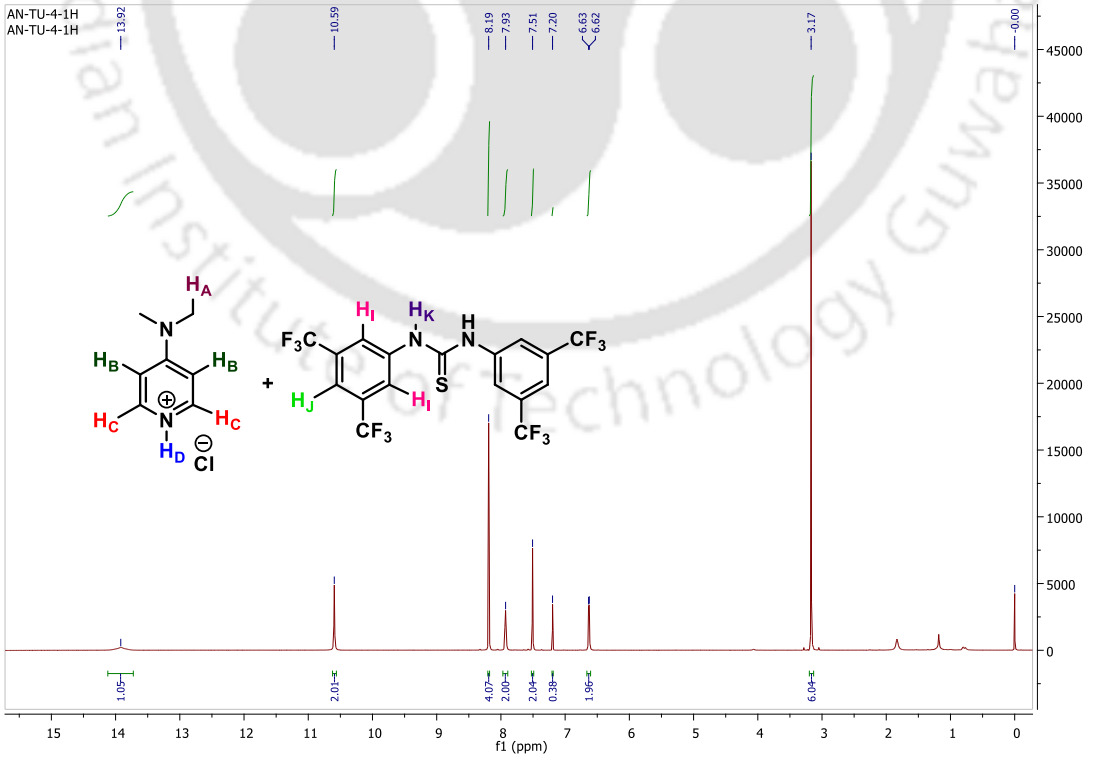
^{1}H NMR of 5:2 mixture of **18a** and **19a** (in 0.6 ml of $CDCl_3$)



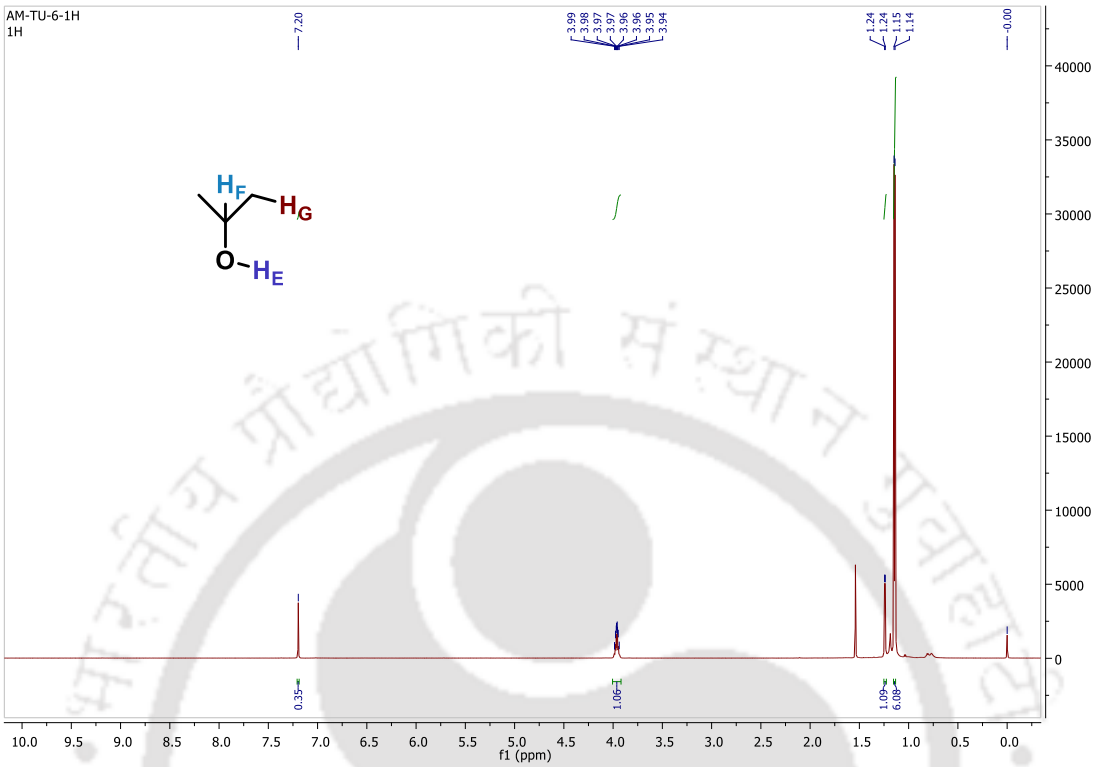
^{1}H NMR of 5:4 mixture of **18a** and **19a** (in 0.6 ml of $CDCl_3$)



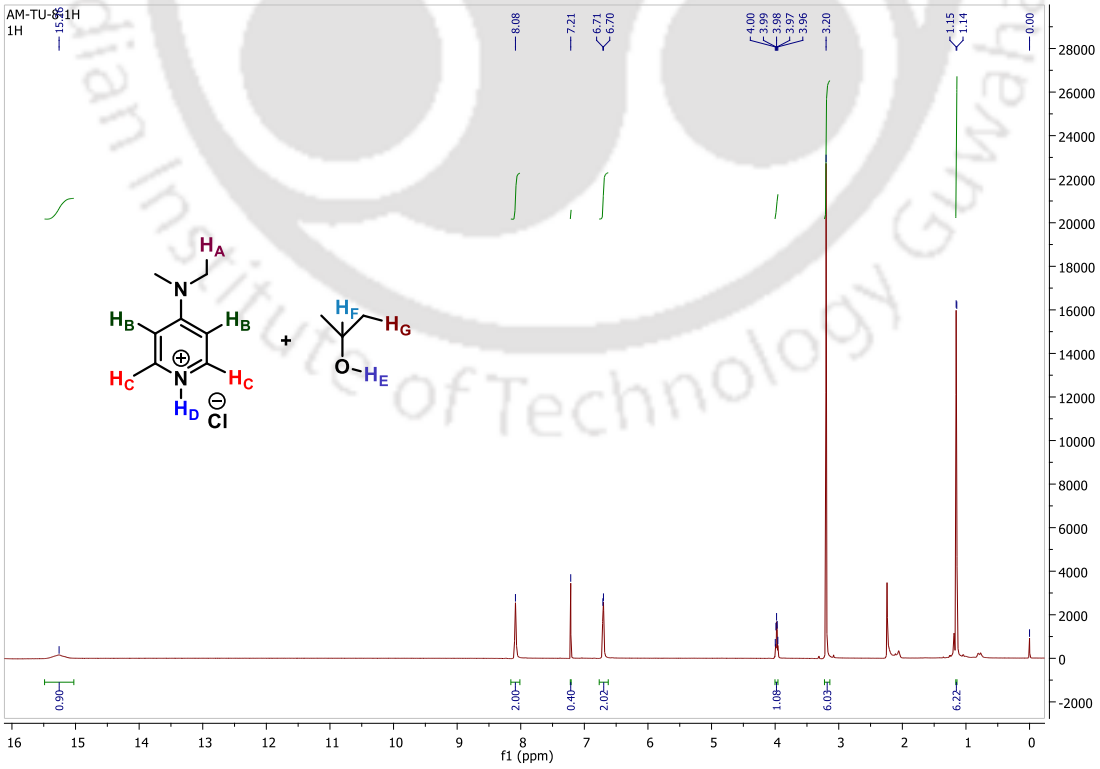
^{1}H NMR of 1:1 mixture of **18a** and **19a** (in 0.6 ml of $CDCl_3$)



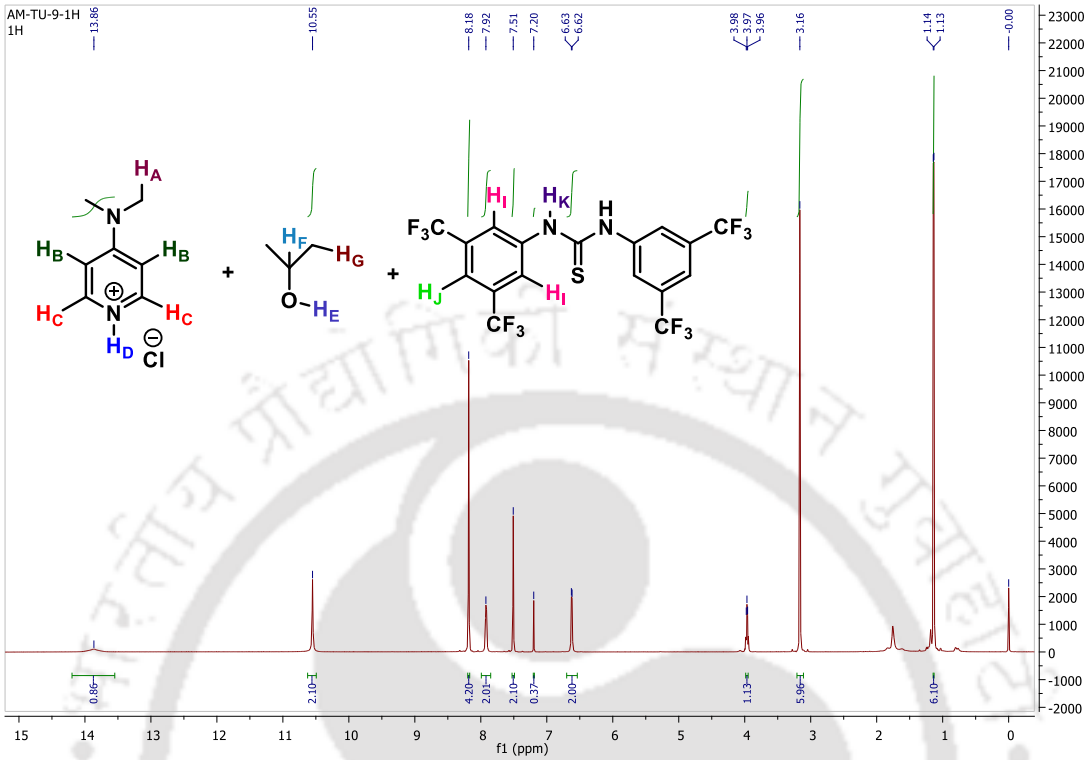
^{1}H NMR of 2-propanol (0.025 mmol in 0.6 ml of $CDCl_3$)



1:1 mixture of **18a** and 2-propanol (in 0.6 ml of $CDCl_3$)

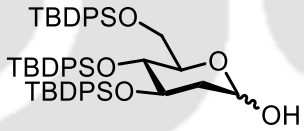


1:1:1 mixture of **18a**, 2-propanol and **19a** (in 0.6 ml of $CDCl_3$)



Synthesis of Donors

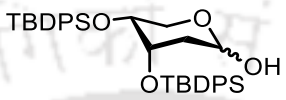
3,4,6-Tri-*O*-tertiarybutyldiphenylsilyl-2-deoxy-α,β-D-glucopyranose (20c):



TBDPS protected D-Glucal (900 mg, 1.050 mmol, 1.0 equiv) dissolved in 10 ml DCM. Then, TTBP hydrochloride (298 mg, 1.050 mmol, 1.0 equiv) was added to it and this solution was stirred at rt for 12 h. The reaction mixture extracted with DCM (3x20 ml). The organic phase washed with brine (80 ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude purified by column chromatography in ethyl acetate/hexane solvent system to give the product as a white solid **20c**. R_f- 0.3 (10% ethyl acetate in hexane), amount- 400 mg, yield- 43%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (d, *J* = 6.8 Hz, 2H), 7.54 (dd, *J* = 13.5, 6.9 Hz, 4H), 7.41 – 7.27 (m, 20H), 7.16 (q, *J* = 7.4 Hz, 4H), 5.01 (t, *J* = 6.4 Hz, 1H), 4.11 (d, *J* = 4.6 Hz, 1H), 4.02 (dd, *J* = 11.0, 7.9 Hz, 1H), 3.90 (d, *J* = 2.4 Hz, 1H), 3.71 (s, 1H), 3.63 (dd, *J* = 11.1, 4.7 Hz, 1H), 2.46 (d, *J* = 6.4 Hz, 1H), 1.74 (ddd, *J* = 12.1, 9.4, 2.6 Hz, 1H), 1.51 (d, *J* = 13.4 Hz, 1H), 0.99 (s, 9H), 0.93

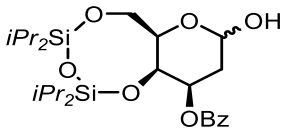
(s, 9H), 0.79 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 136.0, 135.9, 135.9, 135.8, 135.8, 135.7, 133.9, 133.8, 133.6, 133.4, 133.1, 129.9, 129.8, 129.8, 129.7, 129.6, 127.9, 127.9, 127.7, 127.7, 88.4, 81.1, 71.2, 68.9, 62.8, 35.1, 27.0, 27.0, 26.9, 19.3, 19.0. HRMS (ESI) $C_{54}H_{66}O_5Si_3Na$ $[M+Na]^+$- calculated- 901.4110; found- 901.4112.

3,4-Di-*O*-tertiarybutyldiphenylsilyl-α,β-D-arabinose (20d):



Procedure for the synthesis of **20d** was similar procedure of **20c** with TBDPS protected D-arabinal (500 mg, 0.840 mmol, 1.0 equiv) taking TTBP hydrochloride (48 mg, 0.170 mmol, 20 mol %) as the starting material to afford a sticky white solid **20d**. R_f- 0.2 (10% ethyl acetate in hexane), amount- 430 mg, yield- 84%, α:β = 0.7:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.61 (m, 12H), 7.46 – 7.22 (m, 22H), 5.20 (d, *J* = 1.2 Hz 1H), 4.68 (s, 1H), 4.17 (s, 2H), 3.98 (dd, *J* = 11.2, 8.2 Hz, 1H), 3.79 – 3.78 (m, 1H), 3.68 – 3.66 (m, 1H), 3.60 – 3.56 (m, 1H), 3.43 (d, *J* = 9.7 Hz, 1H), 3.09 (dd, *J* = 11.7, 3.2 Hz, 1H), 2.10 (t, *J* = 4 Hz, 1H), 2.03 – 1.98 (m, 1H), 1.54 (d, *J* = 13.6 Hz, 1H), 1.26 (s, 1H), 1.10 (s, 15H), 1.07 (s, 9H), 1.00 (s, 7H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.3, 136.1, 136.1, 136.1, 136.0, 134.5, 134.3, 134.0, 133.9, 133.6, 133.5, 133.1, 132.8, 130.2, 130.0, 129.9, 129.9, 129.9, 129.7, 129.7, 128.0, 127.8, 127.8, 127.8, 127.7, 127.7, 92.8, 92.7, 71.9, 71.0, 70.2, 68.8, 63.9, 36.6, 27.3, 27.2, 27.1, 27.1, 19.5, 19.4, 19.3, 17.6, 17.6, 17.4, 17.3, 17.3. HRMS (ESI) $C_{37}H_{46}O_4Si_2Na$ $[M+Na]^+$- calculated- 633.2827; found-633.2821.

4,6-Di-*O*-(tetraisopropyldisiloxane-1,3-diyl)-3-*O*-benzoyl-2-deoxy-α,β-D-galactopyranoside (20e):

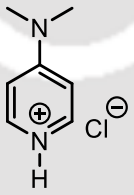


To the ice-cold solution of 4,6-di-*O*-tetraisopropylsiloxane protected D-galactal (4.1 g, 0.01 mol, 1 equiv), pyridine (1.6 g, 1.6 ml, 0.020 mol, 1.5 equiv) followed by benzoyl chloride (2.8 g, 2.3 ml, 0.020 mol, 1.0 equiv) was added slowly and stirred in DCM (20 ml) for overnight at rt. The

reaction mixture was concentrated under reduced pressure and the product **20e** was purified by flash column chromatography as a yellowish solid. R_f- 0.5 (20% ethyl acetate in hexane), amount- 1.6 g, yield- 31%, α:β = 1:0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.2 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.46 – 7.41 (m, 2H), 5.57 – 5.51 (m, 1H), 5.45 (d, *J* = 3.3 Hz, 1H), 4.50 (s, 1H), 4.40 – 4.37 (m, 1H), 4.20 (dd, *J* = 9.9, 5.8 Hz, 1H), 3.87 – 3.74 (m, 2H), 2.41 (td, *J* = 12.4, 3.5 Hz, 1H), 1.92 (dd, *J* = 12.3, 4.6 Hz, 1H), 1.11 – 0.89 (m, 28H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 133.29, 133.1, 130.5, 130.2, 130.0, 129.9, 128.4, 128.3, 94.6, 92.7, 74.6, 72.1, 70.1, 69.7, 65.7, 64.5, 59.8, 59.6, 33.6, 30.2, 17.6, 17.5, 17.5, 17.5, 17.4, 17.3, 17.2, 13.8, 13.5, 13.4, 13.4, 13.3, 12.8. HRMS (ESI) $C_{19}H_{28}O_7SiNH_4$ $[M+NH_4]^+$- calculated- 528.2807; found- 528.2809.

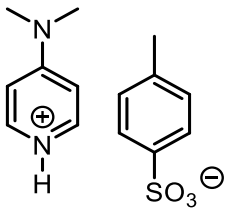
Synthesis of Catalysts

DMAP hydrochloride salt (18a):



2 ml methanol was taken in a round bottom flask and stirred in an ice bath under argon. Then, 2 ml of acetyl chloride added dropwise to it. After a few min, ether (1 ml) solution of DMAP (500 mg, 4.090 mmol, 1.0 equiv) was added dropwise to it and was stirred at 0 °C under argon. After 1 h, it was concentrated under reduced pressure to afford the solid. It was washed with ether (3x10 ml) to get white solid **18a**. Amount- 626 mg, yield- 97%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 15.35 (br s, 1H), 8.14 (t, *J* = 6.5 Hz, 2H), 6.77 (d, *J* = 6.8 Hz, 2H), 3.27 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.4, 139.0, 106.9, 40.4.[18]

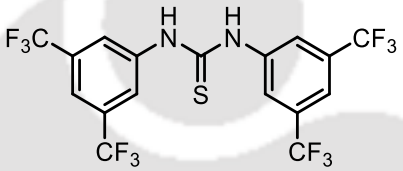
DMAP tosylate salt (18b):



p-toluenesulfonic acid (779 mg, 4.090 mmol, 1.0 equiv) was dissolved in 5 ml of DCM and few drops of methanol. Then, DMAP (500 mg, 4.090 mmol, 1.0 equiv) was added pinch wise to it and it was stirred at 0 °C under argon. After 2 h, it was concentrated under reduced pressure to get the solid. It was washed with ether (3x10 ml) to afford white solid **18b**. Amount- 1.24 g, yield- 98%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 14.21 (br s, 1H), 8.20 (t, *J* = 6.5 Hz, 2H), 7.81 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 7.9 Hz, 2H), 6.74 (d, *J* = 6.9 Hz, 2H), 3.19 (s, 6H), 2.34 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.4, 142.5, 140.0, 139.8, 128.9, 126.1, 106.9, 40.2, 21.4.

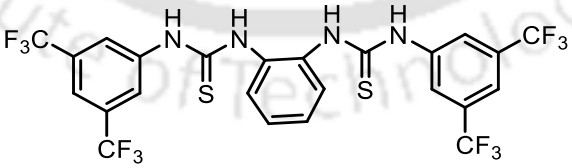
Synthesis of Thiourea

***N*,*N*'-di(3,5-*bis*(trifluoromethyl)phenyl)thiourea (19a):**



A mixture of 3,5-*bis*(trifluoromethyl)phenyl isothiocyanate (68 µl, 0.370 mmol), 3,5-*bis*(trifluoromethyl)aniline (58 µl, 0.370 mmol) and 50 µl of methanol was stirred for 30 min.[21] The solution was concentrated under reduced pressure to get white solid. The product scraped off the walls of the round-bottomed flask affording thiourea **19a** in quantitative yield. ^{1}H and ^{13}C NMR matched with reported data.

1,1'-(1,2-phenylene)bis(3-(3,5-bis(trifluoromethyl)phenyl)thiourea) (19b):



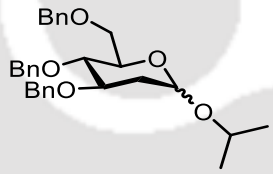
The procedure of **19b** was the similar procedure of **19a** by taking a mixture of 3,5-*bis*(trifluoromethyl)phenyl isothiocyanate (168 µl, 0.620 mmol), o-phenylene diamine (50 mg, 0.460 mmol) and 100 µl of methanol[21] affording thiourea **19b** in quantitative yield. ^{1}H and ^{13}C NMR matched with reported data.

General Procedure

Glycosyl donor (0.060 – 0.160 mmol, 1 equiv) and glycosyl acceptor (1.1 equiv) were taken in round-bottomed flask and dissolved in 0.5 ml (for 0.060 mmol) of DCE. Then, catalyst and thiourea added and heated at 40 °C for 18 – 24 h. After cooling it to rt, the reaction mixture was quenched by water (1 ml for 0.060 mmol), and it was extracted with DCM (3x15 ml for 0.060 mmol), dried over Na_2SO_4, concentrated under reduced pressure and purified by column chromatography in hexane/ethyl acetate.

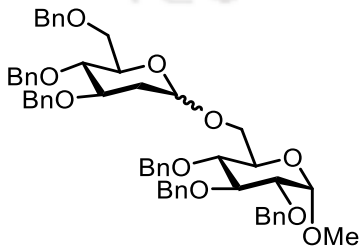
Scope of Derivative

Isopropyl-3,4,6-tri-*O*-benzyl-2-deoxy-α,β-D-glucopyranoside (22a):



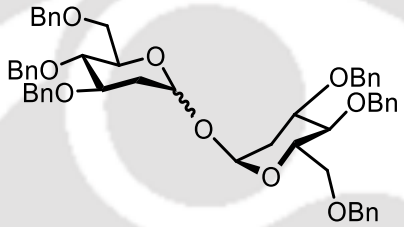
General procedure was followed by adding glycosyl donor **20a** (50 mg, 0.120 mmol, 1.0 equiv), DMAP hydrochloride catalyst **18a** (4 mg, 0.024 mmol, 20 mol %), thiourea **19a** (12 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor isopropanol (11 mg, 14 µl, 0.180 mmol, 1.5 equiv) at 40 °C for 18 h to get product **22a** as a colourless liquid. R_f- 0.9 (20% ethyl acetate in hexane), amount- 50 mg, yield- 87%. ^{1}H NMR, ^{13}C NMR, HRMS, and optical rotation value were matched with reported data.[19]

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-α,β-D-glucopyranosyl)-α-D-glucopyranoside (22b):



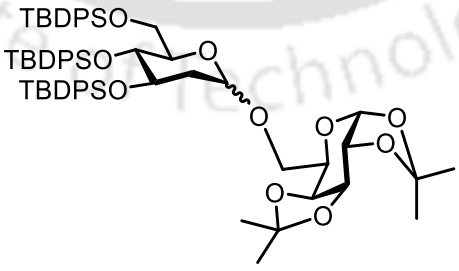
General procedure was followed by adding glycosyl donor **20a** (50 mg, 0.120 mmol, 1.0 equiv), DMAP hydrochloride catalyst **18a** (4 mg, 0.024 mmol, 20 mol %), thiourea **19a** (12 mg, 0.024 mmol, 20 mol %) and glycosyl acceptor **21a** (60 mg, 0.130 mmol, 1.1 equiv) at 40 °C for 24 h to get product **22e** as a colourless liquid. R_f- 0.2 (20% ethyl acetate in hexane), amount- 70 mg, yield- 66%. ^{1}H NMR, ^{13}C NMR, HRMS and optical rotation value were matched with reported data.[22]

(3,4,6-tri-*O*-benzyl-2-deoxy-α,β-D-glucopyranosyl)-(1→1)-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (22c):



General procedure was followed by adding glycosyl donor **20a** (50 mg, 0.120 mmol, 1.0 equiv), DMAP hydrochloride catalyst **18a** (4 mg, 0.024 mmol, 20 mol %) and thiourea **19a** (12 mg, 0.024 mmol, 20 mol %) at 40 °C for 24 h to get dimerized product **22c** as a colourless liquid. R_f- 0.8 (20% ethyl acetate in hexane), amount- 73 mg, yield- 72%. ^{1}H NMR, ^{13}C NMR, HRMS, and optical rotation value were matched with reported data.[19]

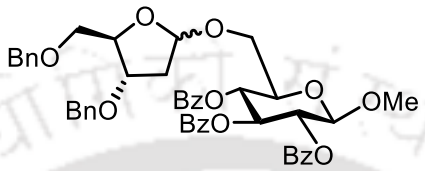
(3,4,6-tri-*O*-tertiarybutyldiphenylsilyl-2-deoxy-α,β-D-glucopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (22d):



General procedure was followed by adding glycosyl donor **20c** (50 mg, 0.060 mmol, 1 equiv), DMAP hydrochloride catalyst **18a** (2 mg, 0.012 mmol, 20 mol %), thiourea **19a** (6 mg, 0.012 mmol, 20 mol %) and glycosyl acceptor **21c** (17 mg, 0.07 mmol, 1.1 equiv) at 40 °C for 24 h to

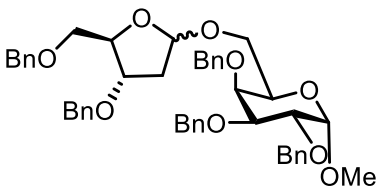
get product **22d** as a colourless liquid. R_f- 0.7 (10% ethyl acetate in hexane), amount- 49 mg, yield- 73%.^{1}H NMR, ^{13}C NMR, HRMS and optical rotation value were matched with reported data.[4]

3,5-Di-*O*-benzyl 2-deoxy-α,β-furanosyl-(1→6)-methyl-2,3,4-tri-*O*-benzoyl-β-D-glucopyranoside (22e):



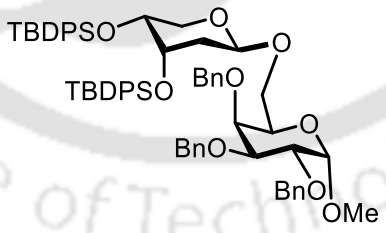
General procedure was followed by adding glycosyl donor **20b** (50 mg, 0.160 mmol, 1.0 equiv), DMAP hydrochloride catalyst **18a** (5 mg, 0.032 mmol, 20 mol %), thiourea **19a** (16 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor **21d** (91 mg, 0.180 mmol, 1.1 equiv) at 40 °C for 24 h to get product **22e** as a colourless liquid. R_f- 0.4 (20% ethyl acetate in hexane), amount- 59 mg, yield- 46%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.27 (m, 25H), 5.82 (t, *J* = 9.7 Hz, 1H), 5.52 – 5.43 (m, 2H), 5.16 (dd, *J* = 5.3, 1.8 Hz, 1H), 4.54 (s, 1H), 4.51 (d, *J* = 4.1 Hz, 2H), 4.47 – 4.45 (m, 3H), 4.24 – 4.20 (m, 2H), 4.13 – 4.10 (m, 2H), 3.92 – 3.87 (m, 1H), 3.51 (s, 3H), 3.43 (d, *J* = 3.9 Hz, 1H), 2.25 (dd, *J* = 14.0, 7.3 Hz, 1H), 2.07 – 2.03 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 166.0, 165.3, 165.3, 138.3, 138.2, 133.5, 133.3, 130.0, 129.9, 129.9, 129.6, 129.2, 129.1, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 127.8, 127.8, 127.8, 127.8, 127.7, 105.3, 104.0, 102.2, 102.0, 100.6, 83.3, 83.0, 81.8, 80.0, 78.5, 73.6, 73.5, 73.4, 73.3, 72.2, 72.1, 72.0, 71.9, 71.7, 71.5, 70.7, 69.9, 66.7, 66.7, 57.3, 57.1, 39.5, 39.3. HRMS (ESI) $C_{47}H_{46}O_{12}NH_4$ $[M+NH_4]^+$- calculated- 820.3327; found- 820.3319. $[\alpha]_D^{20}$ = +33 (*c* 0.04, $CHCl_3$).

3,5-Di-*O*-benzyl 2-deoxy-α,β-furanosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-methylglucopyranoside (22f):



General procedure was followed by adding glycosyl donor **20b** (50 mg, 0.160 mmol, 1.0 equiv), DMAP hydrochloride catalyst **18a** (3 mg, 0.032 mmol, 20 mol %), thiourea **19a** (16 mg, 0.032 mmol, 20 mol %) and glycosyl acceptor **21b** (82 mg, 0.180 mmol, 1.1 equiv) at 40 °C for 24 h to get product **22f** as a colourless liquid. R_f- 0.3 (20% ethyl acetate in hexane), amount- 85 mg, yield- 70%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.23 (m, 50H), 5.21 (dd, *J* = 5.4, 2.6 Hz, 1H), 4.94 (d, *J* = 5.4 Hz, 1H), 4.93 (d, *J* = 3.5 Hz, 1H), 4.91 (d, *J* = 3.2 Hz, 1H), 4.83 – 4.80 (m, 4H), 4.73 – 4.71 (m, 2H), 4.67 – 4.65 (m, 4H), 4.62 – 4.54 (m, 4H), 4.51 (d, *J* = 3.4 Hz, 1H), 4.49 – 4.48 (m, 3H), 4.45 – 4.42 (m, 2H), 4.24 – 4.22 (m, 1H), 4.18 (q, *J* = 4.3 Hz, 1H), 4.14 – 4.11 (m, 1H), 4.04 – 4.01 (m, 1H), 4.00 – 3.97 (m, 3H), 3.94 – 3.91 (m, 2H), 3.90 – 3.87 (m, 1H), 3.77 (d, *J* = 3.0 Hz, 1H), 3.75 – 3.72 (m, 2H), 3.62 (dd, *J* = 10.6, 4.6 Hz, 1H), 3.57 – 3.50 (m, 4H), 3.49 – 3.45 (m, 2H), 3.33 (d, *J* = 1.0 Hz, 6H), 2.21 – 2.10 (m, 3H), 1.91 (dd, *J* = 14.6, 3.0 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9, 138.8, 138.8, 138.6, 138.5, 138.5, 138.2, 138.1, 138.1, 138.0, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 105.0, 104.4, 98.9, 98.7, 82.8, 82.2, 79.8, 79.3, 79.1, 78.8, 76.6, 76.5, 75.7, 74.8, 74.8, 74.7, 73.7, 73.7, 73.6, 73.4, 73.3, 73.2, 71.7, 71.6, 70.0, 69.8, 68.7, 67.7, 66.0, 55.5, 55.3, 39.3, 38.9. HRMS (ESI) $C_{47}H_{52}O_9NH_4$ $[M+NH_4]^+$- calculated- 778.3950; found- 778.3951. $[\alpha]_D^{20}$ = +79 (*c* 0.4, $CHCl_3$).

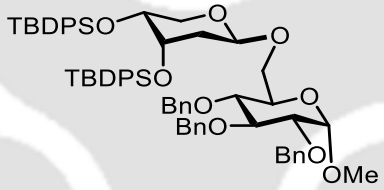
Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-tertiarybutyldiphenylsilyl-2-deoxy-β-D-arabinosyl)-α-D-galactopyranoside (22g):



General procedure was followed by adding glycosyl donor **20d** (50 mg, 0.080 mmol, 1.0 equiv), DMAP hydrochloride catalyst **18a** (3 mg, 0.016 mmol, 20 mol %), thiourea **19a** (8 mg, 0.016 mmol, 20 mol %) and glycosyl acceptor **21b** (42 mg, 0.090 mmol, 1.1 equiv) at 40 °C for 24 h to get product **22g** as a colourless liquid. R_f- 0.6 (10% ethyl acetate in hexane), amount- 55 mg, yield- 65%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71 – 7.69 (m, 4H), 7.62 – 7.61 (m, 2H), 7.56 (d, *J* = 7.3 Hz, 2H), 7.42 – 7.27 (m, 18H), 7.25 – 7.23 (m, 4H), 7.18 – 7.12 (m, 5H), 4.87 (d, *J* = 11.8 Hz, 1H),

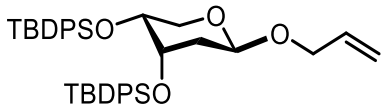
4.83 (d, *J* = 11.3 Hz, 1H), 4.80 – 4.78 (m, 2H), 4.72 (d, *J* = 11.7 Hz, 1H), 4.66 (d, *J* = 12.1 Hz, 1H), 4.61 (d, *J* = 3.6 Hz, 1H), 4.29 (d, *J* = 11.4 Hz, 1H), 4.02 (d, *J* = 9.9 Hz, 1H), 3.98 (dd, *J* = 10.1, 3.6 Hz, 1H), 3.86 (dd, *J* = 10.0, 2.9 Hz, 1H), 3.75 – 3.74 (m, 1H), 3.64 – 3.63 (m, 1H), 3.61 (t, *J* = 6.5 Hz, 1H), 3.43 (dd, *J* = 10.4, 6.4 Hz, 2H), 3.31 (dd, *J* = 10.3, 6.4 Hz, 1H), 3.24 (s, 3H), 3.09 (d, *J* = 11.9 Hz, 1H), 2.23 – 2.21 (m, 1H), 1.47 (d, *J* = 12.5 Hz, 1H), 1.09 (s, 9H), 1.05 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.0, 138.7, 136.3, 136.1, 136.1, 136.0, 134.6, 134.0, 133.7, 129.8, 129.7, 129.6, 128.5, 128.5, 128.3, 128.2, 128.0, 127.9, 127.7, 127.7, 127.6, 127.6, 127.5, 127.5, 98.8, 98.7, 79.3, 76.6, 75.6, 74.8, 73.7, 73.5, 70.9, 69.3, 63.8, 55.3, 37.2, 32.1, 29.9, 27.2, 27.2, 27.1, 19.9, 19.6, 19.4. HRMS (ESI) $C_{65}H_{76}O_9Si_2NH_4$ $[M+NH_4]^+$- calculated- 1074.5366; found- 1074.5369. $[\alpha]_D^{20}$ = -27 (*c* 0.06, $CHCl_3$).

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-tertiarybutyldiphenylsilyl-2-deoxy-β-D-arabinosyl)-α-D-glucopyranoside (22h):



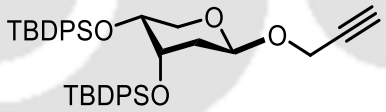
General procedure was followed by adding glycosyl donor **20d** (50 mg, 0.080 mmol, 1.0 equiv), DMAP hydrochloride catalyst **18a** (3 mg, 0.016 mmol, 20 mol %), thiourea **19a** (8 mg, 0.016 mmol, 20 mol %) and glycosyl acceptor **21a** (42 mg, 0.090 mmol, 1.1 equiv) at 40 °C for 24 h to get product **22h** as a colourless liquid. R_f- 0.7 (10% ethyl acetate in hexane), amount- 63 mg, yield- 75%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.12 (m, 35H), 4.99 (d, *J* = 11.0 Hz, 1H), 4.80 (d, *J* = 11.0 Hz, 1H), 4.75 (d, *J* = 12.4 Hz, 1H), 4.70 – 4.66 (m, 3H), 4.51 (d, *J* = 3.5 Hz, 1H), 4.25 (d, *J* = 11.0 Hz, 1H), 4.09 – 4.06 (m, 1H), 3.90 (d, *J* = 9.3 Hz, 1H), 3.86 (s, 1H), 3.64 (d, *J* = 10.6 Hz, 1H), 3.53 – 3.51 (m, 1H), 3.40 – 3.38 (m, 1H), 3.37 – 3.33 (m, 3H), 3.27 – 3.24 (m, 1H), 3.22 (s, 3H), 2.21 (t, *J* = 11.3 Hz, 1H), 1.38 (dt, *J* = 12.6, 3.4 Hz, 1H), 1.10 (s, 9H), 1.03 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.3, 138.5, 138.3, 136.3, 136.1, 136.1, 136.0, 134.1, 133.9, 130.0, 129.8, 129.7, 128.6, 128.5, 128.5, 128.2, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 98.2, 97.9, 82.2, 79.8, 75.7, 75.1, 73.2, 71.1, 69.8, 65.7, 63.6, 55.1, 37.7, 29.8, 27.3, 27.2, 19.6, 19.3. HRMS (ESI) $C_{65}H_{76}O_9Si_2NH_4$ $[M+NH_4]^+$- calculated- 1074.5366; found- 1074.5387. $[\alpha]_D^{20}$ = -86 (*c* 0.08, $CHCl_3$).

Allyl-3,4-di-*O*-tertiarybutyldiphenylsilyl-2-deoxy-β-D-arabinoside (22i):



General procedure was followed by adding glycosyl donor **20d** (50 mg, 0.080 mmol, 1.0 equiv), DMAP hydrochloride catalyst **18a** (3 mg, 0.016 mmol, 20 mol %), thiourea **19a** (8 mg, 0.016 mmol, 20 mol %) and allyl alcohol (5 mg, 6 µl, 0.090 mmol, 1.1 equiv) at 40 °C for 24 h to get product **22i** as a colourless liquid. R_f- 0.6 (10% ethyl acetate in hexane), amount- 44 mg, yield- 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.2 Hz, 4H), 7.67 (d, *J* = 6.4 Hz, 2H), 7.60 (d, *J* = 7.3 Hz, 2H), 7.41 – 7.37 (m, 5H), 7.34 (d, *J* = 7.8 Hz, 3H), 7.28 (d, *J* = 7.3 Hz, 4H), 5.76 – 5.67 (m, 1H), 5.04 (d, *J* = 4.8 Hz, 1H), 5.01 (s, 1H), 4.81 (t, *J* = 3.3 Hz, 1H), 4.16 (dt, *J* = 9.6, 3.3 Hz, 1H), 3.97 (dd, *J* = 13.6, 4.1 Hz, 1H), 3.83 (s, 1H), 3.78 – 3.73 (m, 1H), 3.46 – 3.42 (m, 1H), 3.35 (dd, *J* = 11.8, 2.1 Hz, 1H), 2.20 (t, *J* = 8.6 Hz, 1H), 1.43 (dt, *J* = 12.7, 3.7 Hz, 1H), 1.10 (s, 9H), 1.08 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.3, 136.2, 136.1, 136.1, 134.6, 134.4, 133.8, 129.8, 129.7, 129.6, 127.7, 127.6, 97.7, 71.1, 67.9, 64.0, 27.3, 27.2, 19.6, 19.4. HRMS (ESI) $C_{40}H_{50}O_4Si_2Na[M+Na]^+$- calculated- 673.3140; found- 673.3125. $[\alpha]_D^{20}$ = -76 (*c* 0.2, $CHCl_3$).

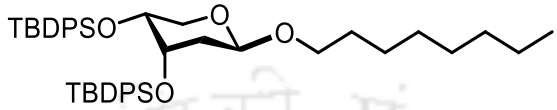
Propargyl-3,4-di-*O*-tertiarybutyldiphenylsilyl-2-deoxy-β-D-arabinoside (22j):



General procedure was followed by adding glycosyl donor **20d** (50 mg, 0.080 mmol, 1.0 equiv), DMAP hydrochloride catalyst **18a** (3 mg, 0.016 mmol, 20 mol %), thiourea **19a** (8 mg, 0.016 mmol, 20 mol %) and propargyl alcohol (5 mg, 5 µl, 0.090 mmol, 1.1 equiv) at 40 °C for 24 h to get product **22j** as a colourless liquid. R_f- 0.4 (15% ethyl acetate in hexane), amount- 43 mg, yield- 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.24 (m, 20H), 5.02 (t, *J* = 3.5 Hz, 1H), 4.13 (dt, *J* = 9.9, 3.1 Hz, 1H), 4.02 (d, *J* = 2.5 Hz, 2H), 3.80 (s, 1H), 3.47 (d, *J* = 9.0 Hz, 1H), 3.32 (dd, *J* = 11.7, 2.1 Hz, 1H), 2.33 (t, *J* = 2.4 Hz, 1H), 2.21 (t, *J* = 10.1 Hz, 1H), 1.44 (dt, *J* = 12.9, 3.8 Hz, 1H), 1.08 (s, 18H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 136.2, 136.1, 136.1, 136.1, 134.5, 134.2, 134.0, 133.7, 129.8, 129.8, 129.7, 129.6, 127.7, 127.7, 127.6, 96.7, 79.7, 74.0, 70.9, 64.2, 54.3, 27.2, 27.1,

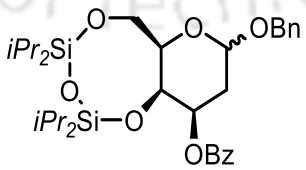
19.5, 19.4. HRMS (ESI) $C_{40}H_{48}O_4Si_2NH_4$ $[M+NH_4]^+$- calculated- 666.3429; found- 666.3435. $[\alpha]_D^{20}$ = -81 (*c* 0.3, $CHCl_3$).

Octyl-3,4-di-*O*-tertiarybutyldiphenylsilyl-2-deoxy-β-D-arabinoside (22k):



General procedure was followed by adding glycosyl donor **20d** (50 mg, 0.080 mmol, 1.0 equiv), DMAP hydrochloride catalyst **18a** (3 mg, 0.016 mmol, 20 mol %), thiourea **19a** (8 mg, 0.016 mmol, 20 mol %) and allyl alcohol (12 mg, 14 µl, 0.090 mmol, 1.1 equiv) at 40 °C for 24 h to get product **22k** as a colourless liquid. R_f- 0.3 (10% ethyl acetate in hexane), amount- 51 mg, yield- 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.25 (m, 20H), 4.73 (d, *J* = 3.0 Hz, 1H), 4.10 (d, *J* = 10.5 Hz, 1H), 3.83 (s, 1H), 3.40 – 3.30 (m, 3H), 3.01 (ddd, *J* = 16.0, 9.3, 5.3 Hz, 1H), 2.23 (s, 1H), 1.41 (dd, *J* = 12.2, 2.6 Hz, 1H), 1.23 – 1.15 (m, 7H), 1.11 (s, 9H), 1.07 (s, 9H), 1.00 (d, *J* = 9.2 Hz, 1H), 0.89 (d, *J* = 8.1 Hz, 1H), 0.83 (t, *J* = 7.0 Hz, 3H), 0.74 (td, *J* = 7.4, 2.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.3, 136.1, 136.0, 134.8, 134.4, 133.9, 129.7, 129.6, 129.6, 127.7, 127.7, 127.7, 127.6, 98.6, 98.5, 71.2, 63.9, 63.9, 39.7, 39.6, 30.5, 30.5, 29.9, 29.2, 29.2, 27.3, 27.2, 23.9, 23.8, 23.2, 23.2, 19.6, 19.3, 14.2, 11.3. HRMS (ESI) $C_{45}H_{62}O_4Si_2Na$ $[M+Na]^+$- calculated- 745.4079; found- 745.4084. $[\alpha]_D^{20}$ = -7 (*c* 0.06, $CHCl_3$).

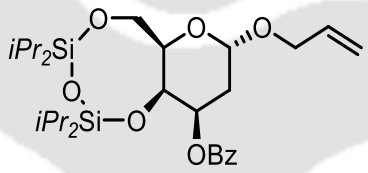
Benzyl-4,6-di-*O*-(tetraisopropyldisiloxane-1,3-diyl)-3-*O*-benzoyl-2-deoxy-α-D-galactopyranoside (22l):



General procedure was followed by adding glycosyl donor **20e** (50 mg, 0.097 mmol, 1.0 equiv), DMAP hydrochloride catalyst **18a** (3 mg, 0.020 mmol, 20 mol %), thiourea **19a** (10 mg, 0.020 mmol, 20 mol %) and benzyl alcohol (12 mg, 12 µl, 0.110 mmol, 1.1 equiv) at 40 °C for 24 h to

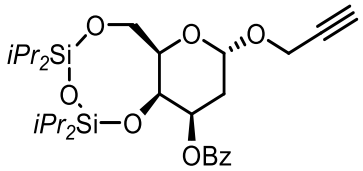
get product **22l** as a colourless liquid. R_f- 0.8 (20% ethyl acetate in hexane), amount- 42 mg, yield- 72%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.2 Hz, 2H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.38 – 7.27 (m, 5H), 5.51 (ddd, *J* = 12.6, 4.5, 2.6 Hz, 1H), 5.07 (d, *J* = 3.3 Hz, 1H), 4.70 (d, *J* = 11.9 Hz, 1H), 4.52 (s, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 4.04 (dd, *J* = 9.9, 5.6 Hz, 1H), 3.88 – 3.77 (m, 2H), 2.45 (td, *J* = 12.4, 3.7 Hz, 1H), 1.96 (d, *J* = 5.0 Hz, 1H), 1.11 – 1.02 (m, 24H), 0.89 – 0.87 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 137.8, 133.1, 130.5, 129.9, 128.6, 128.4, 128.3, 127.9, 127.8, 97.0, 70.3, 70.1, 69.1, 65.6, 59.8, 31.1, 17.6, 17.5, 17.5, 17.4, 17.3, 17.2, 13.8, 13.5, 13.3, 12.8. HRMS (ESI) $C_{26}H_{34}O_7SiNH_4$ $[M+NH_4]^+$- calculated- 618.3277; found- 618.3277. $[\alpha]_D^{20}$ = +21 (*c* 0.06, $CHCl_3$).

Allyl-4,6-di-*O*-(tetraisopropyldisiloxane-1,3-diyl)-3-*O*-benzoyl-2-deoxy-α-D-galactopyranoside (22m):



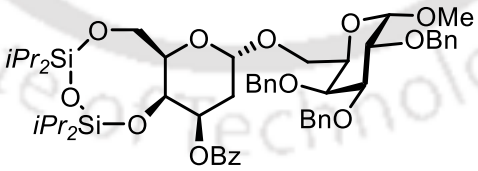
General procedure was followed by adding glycosyl donor **20e** (51 mg, 0.099 mmol, 1.0 equiv), DMAP hydrochloride catalyst **18a** (3 mg, 0.016 mmol, 20 mol %), thiourea **19a** (8 mg, 0.016 mmol, 20 mol %) and allyl alcohol (12 mg, 14 µl, 0.090 mmol, 1.1 equiv) at 40 °C for 24 h to get product **22m** as a colourless liquid. R_f- 0.3 (10% ethyl acetate in hexane), amount- 36 mg, yield- 66%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.2 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 5.91 (ddt, *J* = 16.3, 10.7, 5.6 Hz, 1H), 5.49 (ddd, *J* = 12.5, 4.5, 2.6 Hz, 1H), 5.30 (dd, *J* = 10.2, 1.7 Hz, 1H), 5.19 (dd, *J* = 10.4, 1.6 Hz, 1H), 5.02 (d, *J* = 2.9 Hz, 1H), 4.50 (s, 1H), 4.15 (ddt, *J* = 12.9, 5.1, 1.6 Hz, 1H), 4.01 – 3.94 (m, 2H), 3.86 – 3.75 (m, 2H), 2.44 (td, *J* = 12.4, 3.6 Hz, 1H), 1.91 (dd, *J* = 12.2, 4.5 Hz, 1H), 1.11 – 1.03 (m, 24H), 0.89 – 0.87 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 134.4, 133.1, 130.5, 129.9, 128.3, 117.2, 97.1, 70.2, 70.0, 68.2, 65.6, 59.8, 30.2, 17.6, 17.6, 17.5, 17.5, 17.4, 17.4, 17.3, 17.2, 13.8, 13.5, 13.3, 12.8. HRMS (ESI) $C_{22}H_{32}O_7SiNH_4$ $[M+NH_4]^+$- calculated- 568.3120; found- 568.3145. $[\alpha]_D^{20}$ = +6 (*c* 0.12, $CHCl_3$).

Propargyl-4,6-di-*O*-(tetraisopropyldisiloxane-1,3-diyl)-3-*O*-benzoyl-2-deoxy-α-D-galactopyranoside (22n):



General procedure was followed by adding glycosyl donor **20e** (50 mg, 0.097 mmol, 1.0 equiv), DMAP hydrochloride catalyst **18a** (3 mg, 0.020 mmol, 20 mol %), thiourea **19a** (10 mg, 0.020 mmol, 20 mol %) and propargyl alcohol (6 mg, 8 µl, 0.110 mmol, 1.1 equiv) at 40 °C for 24 h to get product **22m** as a colourless liquid. R_f- 0.3 (10% ethyl acetate in hexane), amount- 45 mg, yield- 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.3 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 5.46 (ddd, *J* = 12.6, 4.5, 2.5 Hz, 1H), 5.18 (d, *J* = 3.5 Hz, 1H), 4.50 (s, 1H), 4.22 (t, *J* = 2.1 Hz, 2H), 3.98 (dd, *J* = 9.9, 5.8 Hz, 1H), 3.86 – 3.76 (m, 2H), 2.48 (dd, *J* = 12.5, 3.7 Hz, 1H), 2.43 (t, *J* = 2.2 Hz, 1H), 1.94 (d, *J* = 5.2 Hz, 1H), 1.11 – 1.02 (m, 24H), 0.89 – 0.87 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 133.1, 130.4, 129.9, 128.3, 96.6, 79.4, 74.5, 70.4, 69.9, 65.5, 59.7, 54.3, 29.8, 17.6, 17.5, 17.5, 17.4, 17.4, 17.4, 17.3, 17.2, 13.9, 13.8, 13.7, 13.4, 13.3, 12.8. HRMS (ESI) $C_{22}H_{30}O_7SiNH_4$ $[M+NH_4]^+$- calculated- 566.2964; found- 566.2959. $[\alpha]_D^{20}$ = +27 (*c* 0.08, $CHCl_3$).

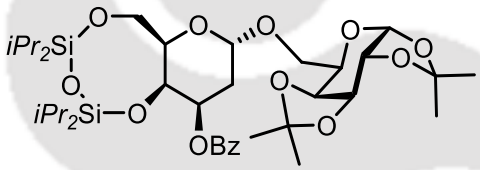
Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(4,6-di-*O*-tetraisopropyldisiloxane-1,3-diyl-3-*O*-benzoyl-2-deoxy-α-D-galactosyl)-α-D-galactopyranoside (22o):



General procedure was followed by adding glycosyl donor **20e** (49 mg, 0.096 mmol, 1.0 equiv), DMAP hydrochloride catalyst **18a** (3 mg, 0.020 mmol, 20 mol %), thiourea **19a** (10 mg, 0.020 mmol, 20 mol %) and glycosyl acceptor **21a** (51 mg, 0.090 mmol, 1.1 equiv) at 40 °C for 24 h to get product **22m** as a colourless liquid. R_f- 0.3 (10% ethyl acetate in hexane), amount- 37 mg, yield- 40%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.19 (m, 20H), 5.31 (ddd, *J* = 12.5, 4.5, 2.7 Hz, 1H), 4.88 (d, *J* = 11.7 Hz, 1H), 4.83 – 4.78 (m, 1H), 4.75 – 4.69 (m, 2H), 4.64 – 4.59 (m, 2H), 4.52

(d, *J* = 11.7 Hz, 1H), 4.38 (s, 1H), 3.98 (dd, *J* = 9.9, 3.6 Hz, 1H), 3.91 – 3.86 (m, 2H), 3.84 – 3.82 (m, 1H), 3.79 – 3.73 (m, 2H), 3.72 – 3.64 (m, 2H), 3.55 (dd, *J* = 9.3, 5.6 Hz, 1H), 3.34 (s, 3H), 3.31 (dd, *J* = 9.2, 1.7 Hz, 1H), 2.24 (td, *J* = 12.3, 3.6 Hz, 1H), 1.61 (dd, *J* = 12.2, 4.6 Hz, 1H), 1.03 – 0.93 (m, 24H), 0.81 – 0.79 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 139.0, 138.8, 138.7, 133.1, 130.5, 129.9, 128.5, 128.5, 128.5, 128.4, 128.3, 127.8, 127.8, 127.7, 127.7, 99.0, 97.8, 79.5, 74.7, 74.7, 73.8, 73.7, 70.0, 70.0, 68.9, 65.9, 65.5, 59.7, 55.7, 30.2, 17.6, 17.6, 17.5, 17.5, 17.4, 17.4, 17.3, 17.2, 13.8, 13.4, 13.3, 12.8. HRMS (ESI) $C_{47}H_{58}O_{12}SiNH_4$ $[M+NH_4]^+$- calculated- 974.4901; found- 974.4921. $[\alpha]_D^{20}$ = +12 (*c* 0.06, $CHCl_3$).

(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 (22p):



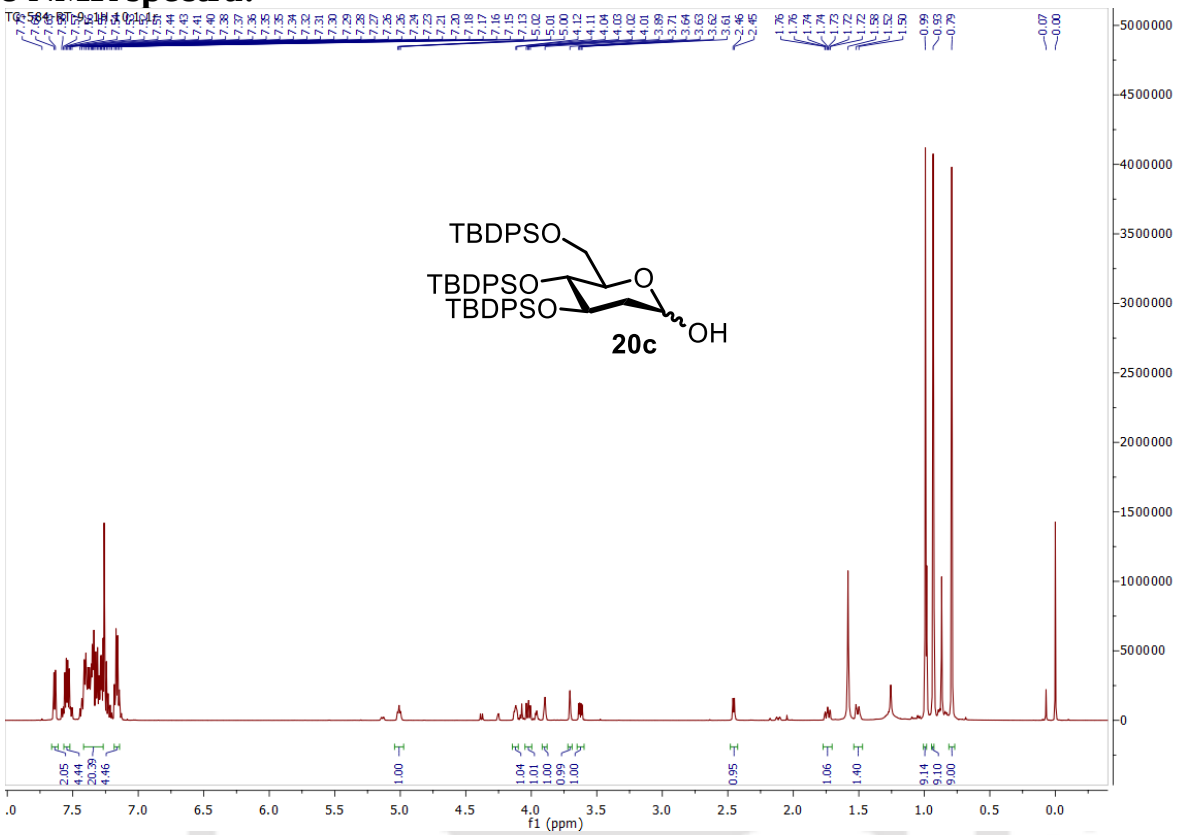
General procedure was followed by adding glycosyl donor **20e** (51 mg, 0.099 mmol, 1.0 equiv), DMAP hydrochloride catalyst **18a** (3 mg, 0.020 mmol, 20 mol %), thiourea **19a** (10 mg, 0.020 mmol, 20 mol %) and glycosyl acceptor **21c** (28 mg, 0.110 mmol, 1.1 equiv) at 40 °C for 24 h to get product **22n** as a colourless liquid. R_f- 0.3 (10% ethyl acetate in hexane), amount- 42 mg, yield- 58%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.1 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 5.53 (d, *J* = 5.0 Hz, 1H), 5.46 (ddd, *J* = 12.4, 4.5, 2.6 Hz, 1H), 5.03 (d, *J* = 3.3 Hz, 1H), 4.62 (dd, *J* = 8.0, 2.4 Hz, 1H), 4.49 (s, 1H), 4.32 (dd, *J* = 5.1, 2.4 Hz, 1H), 4.28 (dd, *J* = 8.0, 1.9 Hz, 1H), 4.00 – 3.95 (m, 2H), 3.85 – 3.73 (m, 3H), 3.65 (dd, *J* = 10.0, 7.7 Hz, 1H), 2.41 (td, *J* = 12.3, 3.7 Hz, 1H), 1.93 (dd, *J* = 12.3, 4.5 Hz, 1H), 1.57 (s, 3H), 1.44 (s, 3H), 1.34 (s, 6H), 1.10 – 1.02 (m, 24H), 0.88 – 0.87 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 133.1, 130.5, 129.9, 128.3, 109.4, 108.8, 98.0, 96.5, 71.0, 70.9, 70.8, 70.2, 70.1, 66.1, 65.8, 65.5, 59.8, 30.1, 26.3, 26.2, 25.1, 24.7, 17.6, 17.5, 17.5, 17.4, 17.3, 17.2, 13.8, 13.4, 13.3, 12.9. HRMS (ESI) $C_{31}H_{46}O_{12}SiNH_4$ $[M+NH_4]^+$- calculated- 770.3962; found- 770.3960. $[\alpha]_D^{20}$ = +14 (*c* 0.10, $CHCl_3$).

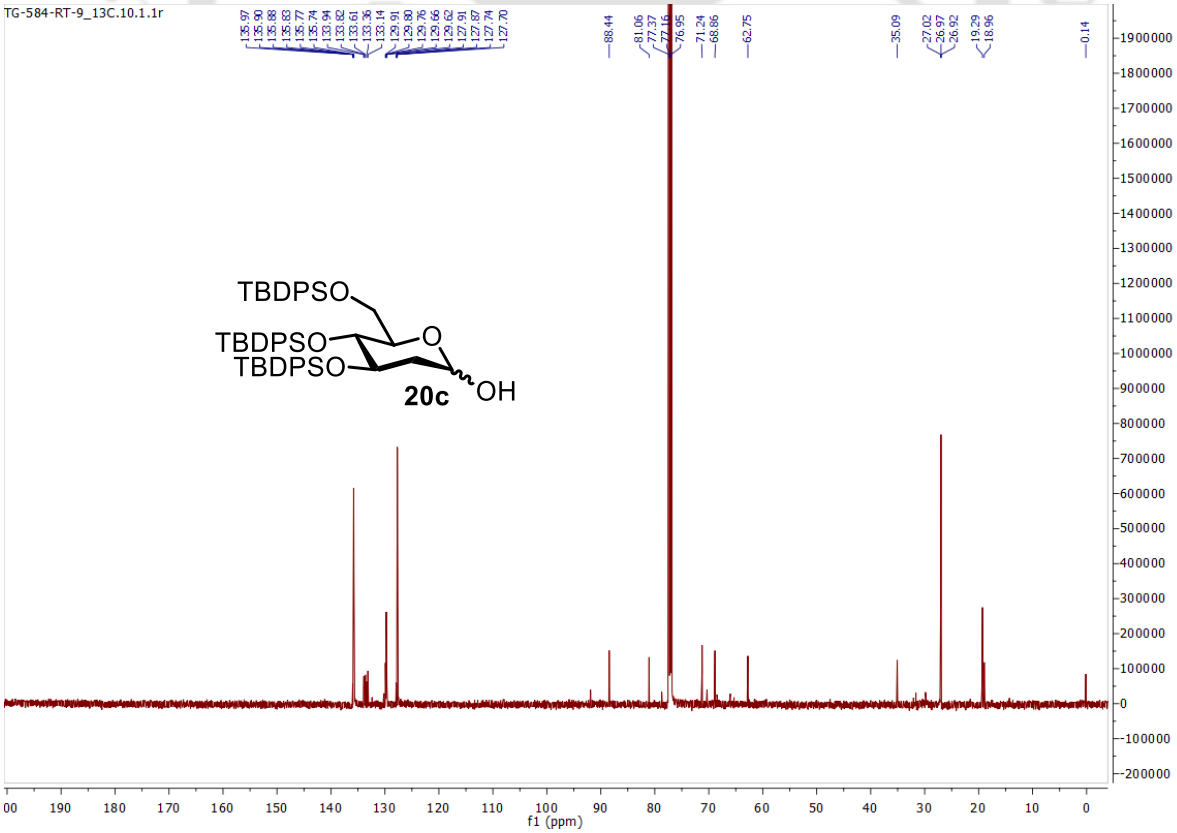
5.7 References:

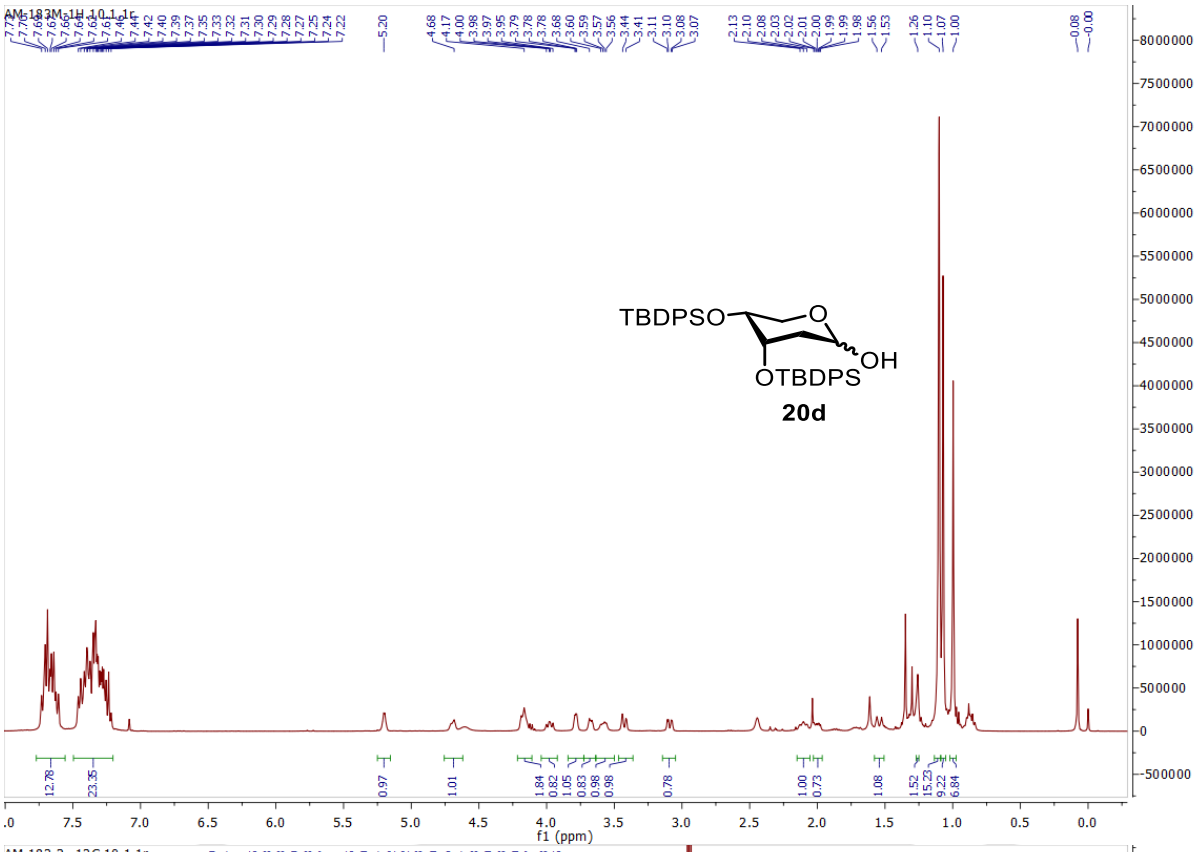
1. a) Schreiner, P. R. *Chem. Soc. Rev.* **2003**, *32*, 289–296; b) Takemoto, Y. *Org. Biomol. Chem.* **2005**, *3*, 4299–4306; c) Connon, S. J. *Chem. Eur. J.* **2006**, *12*, 5418–5427; d) Taylor, M. S.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1520–1543; e) Doyle, A. G.; Jacobsen, E. N. *Chem. Rev.* **2007**, *107*, 5713–5743.
2. Schreiner, P. R.; Wittkopp, A. *Org. Lett.* **2002**, *4*, 217–220.
3. Zhao, C.; Chen, S. B.; Seidel, D. *J. Am. Chem. Soc.* **2016**, *138*, 9053−9056.
4. Zhang, Z.; Schreiner, P. R. Chem. Soc. Rev. **2009**, *38*, 1187–1198.
5. Zuend, S. J.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2009**, *131*, 15358–15374.
6. Murali, M. G.; Vishnumurthy, K. A.; Seethamrajub, S.; Ramamurthy, P. C. *RSC. Adv.* **2014**, *4*, 20592–20598.
7. a) Smith, P. J.; Reddington, M. V.; Wilcox, C. S. *Tetrahedron Lett.* **1992**, *33*, 6085–6088; b) Fan, E.; Vanarman, S. A.; Kincaid, S.; Hamilton, A. D. *J. Am. Chem. Soc.* **1993**, *115*, 369–370; c) Albert, J. S.; Hamilton, A. D. *Tetrahedron Lett.* **1993**, *34*, 7363–7366.
8. Zhang, Z.; Schreiner, P. R. *Chem. Soc. Rev.* **2009**, *38*, 1187–1198.
9. a) Mahlau, M.; List, B. *Angew. Chem., Int. Ed.* **2013**, *52*, 518–533; b) Brak, K.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2013**, *52*, 534–561.
10. Balmond, E. I.; Coe, D. M.; Galan, M. C.; McGarrigle, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 9152–9155.
11. Geng, Y.; Kumar, A.; Faidallah, H. M.; Albar, H. A.; Mhkalid, I. A.; Schmidt, R. R. *Angew. Chem., Int. Ed.* **2013**, *52*, 10089–10092.
12. Kobayashi, Y.; Nakatsuji, Y.; Li, S.; Tsuzuki, S.; Takemoto, Y. *Angew. Chem., Int. Ed.* **2018**, *57*, 3646 –3650.
13. Sun, L.; Wu, X.; Xiong, D.-C.; Ye, X.-S. *Angew. Chem., Int. Ed.* **2016**, *55*, 8041–8044.
14. Palo-Nieto, C.; Sau, A.; Williams, R.; Galan, M. C. *J. Org. Chem.* **2017**, *82*, 407–414.
15. Kotke, M.; Schreiner, P. R. *Synthesis* **2007**, 779–790.
16. a) Issa, J. P.; Lloyd, D.; Steliotes, E.; Bennett, C. S. *Org. Lett.* **2013**, *15*, 4170–4173; b) Nogueira, J. M.; Nguyen, S. H.; Bennett, C. S. *Org. Lett.* **2011**, *13*, 2814–2817; c) Issa, J. P.; Bennett, C. S. *J. Am. Chem. Soc.* **2014**, *136*, 5740–5744.

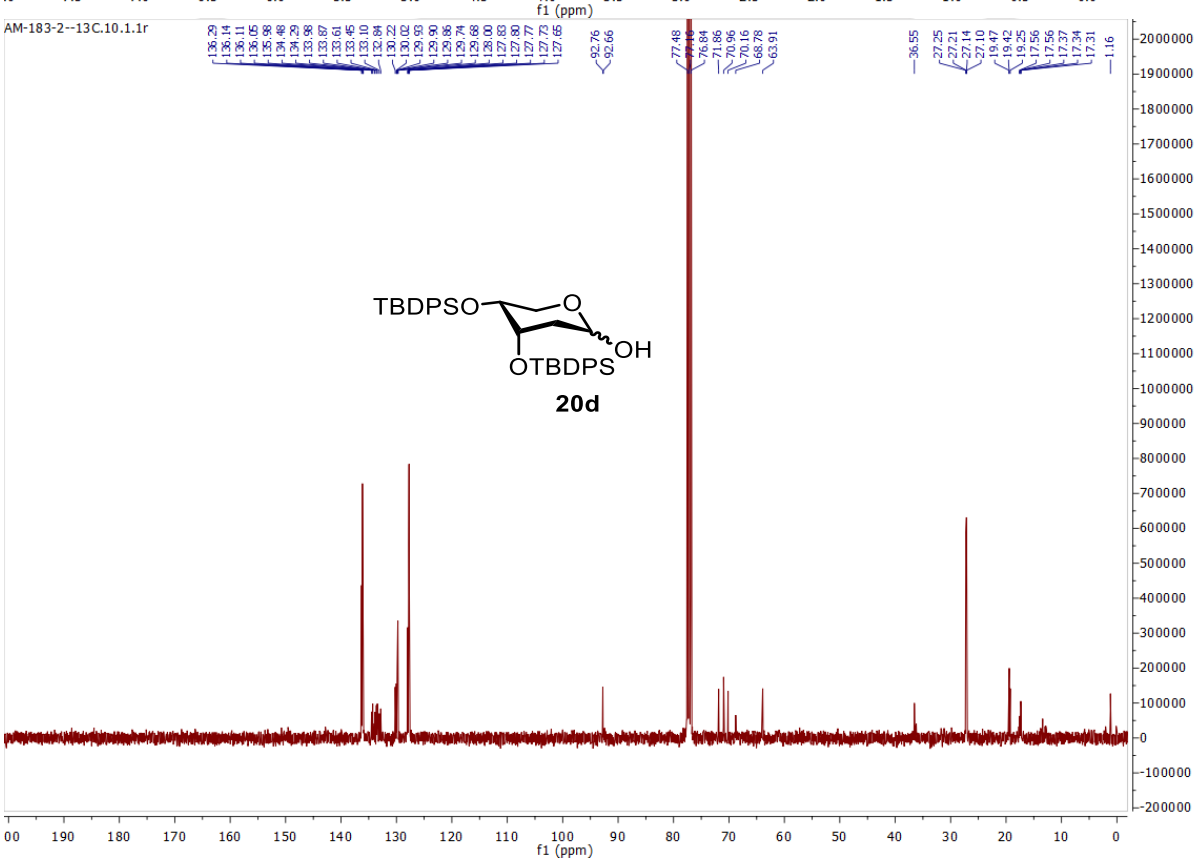
17. a) Park, Y.; Harper, K. C.; Kuhl, N.; Kwan, E. E.; Liu, R. Y.; Jacobsen, E. N. *Science* **2017**, *355*, 162–166; b) Telmesani, R.; Park, S. H.; Tessa, L. -C.; Beeler, A. B. *Angew. Chem., Int. Ed.* **2015**, *54*, 11521–11525.
18. a) Liu, Z.; Ma, Q.; Liu, Y.; Wang, Q. *Org. Lett.* **2014**, *16*, 236−239; b) Chao, M.; Schempp, E.; Rosenstein, R. D. *Acta Cryst.* **1977**, *33*, 1820−1823; c) Bryant, G. L. Jr; King, J. A. Jr. *Acta Cryst.* **1992**, *48*, 2036−2039.
19. Ghosh, T.; Mukherji, A.; Srivastava, H. K.; Kancharla, P. K. *Org. Biomol. Chem.* **2018**, *16*, 2870–2875.
20. Juste-Navarro, V.; Prieto, L.; Delso, I.; Manzano, R.; Tejero, T.; Reyes, E.; Vicario, J. L.; Merinod, P. *Adv. Synth. Catal.* **2017**, *359*, 4122–4128.
21. Strukil, V.; Igrc, M. D.; Maksic, M. E.-; Friscic, T. *Chem. Eur. J.* **2012**, *18*, 8464 – 8473.
22. Ghosh, T.; Mukherji, A.; Kancharla, P. K. *Org. Lett.* **2019**, *21*, 3490–3495.

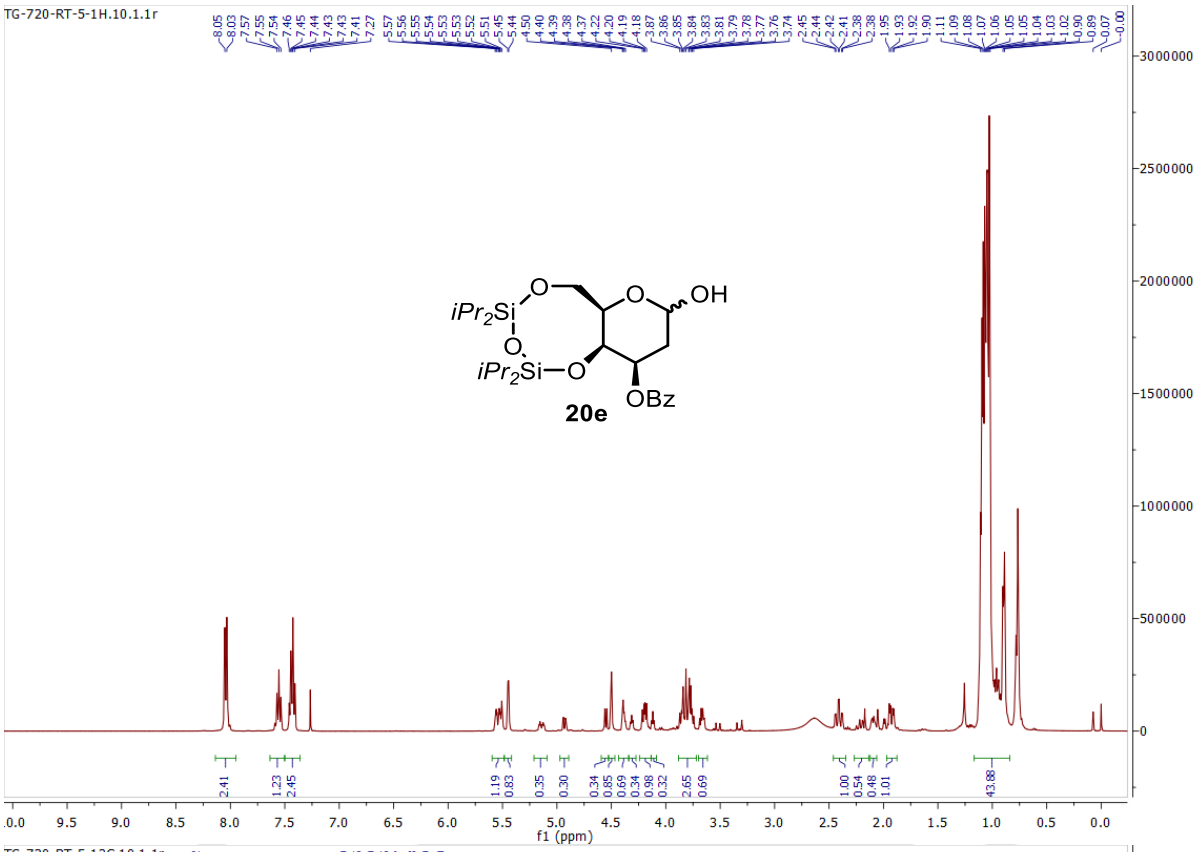
5.8 NMR spectra:







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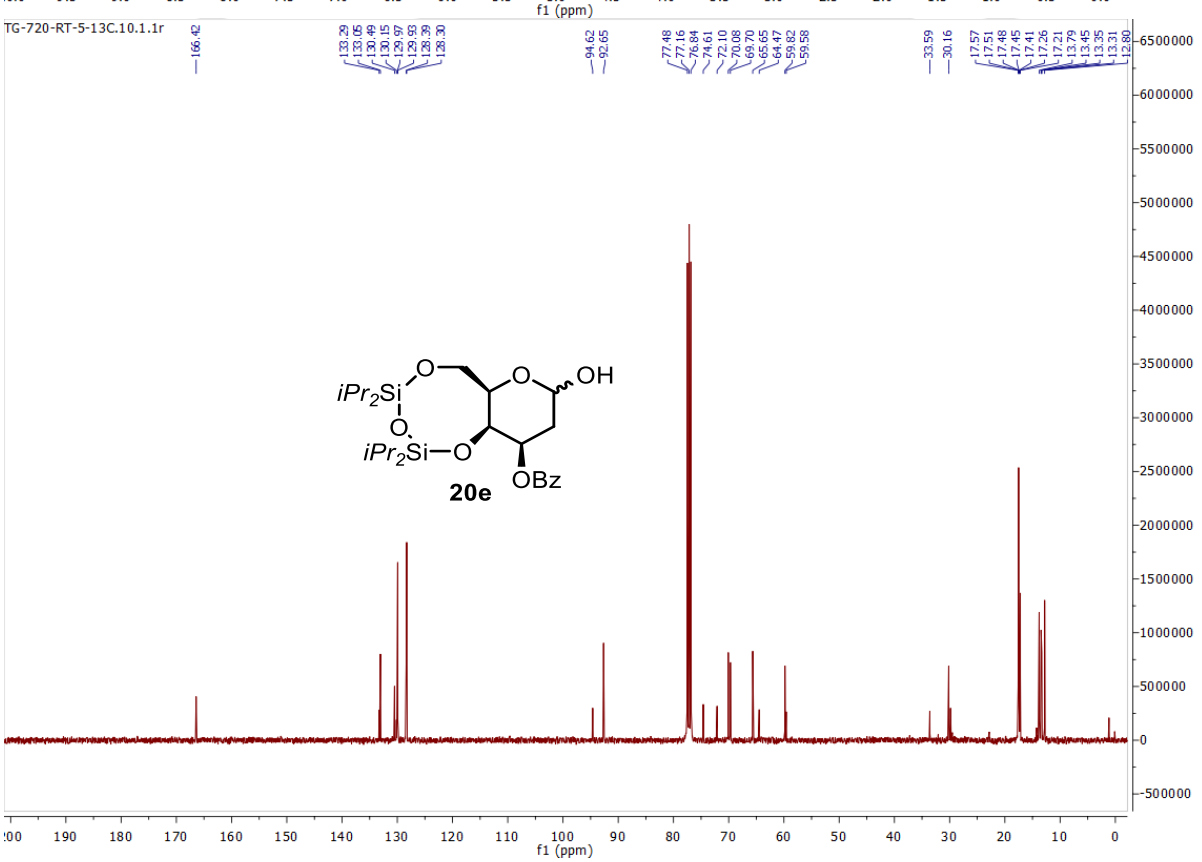
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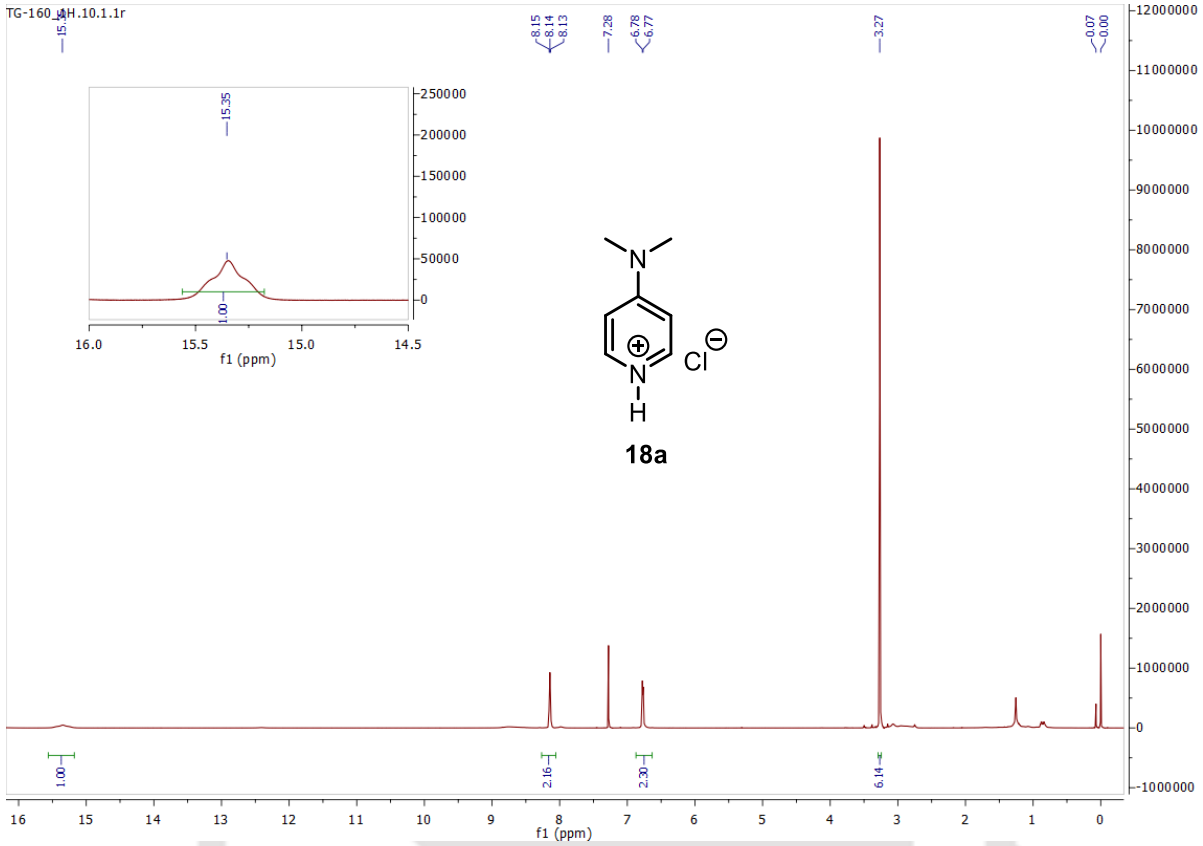

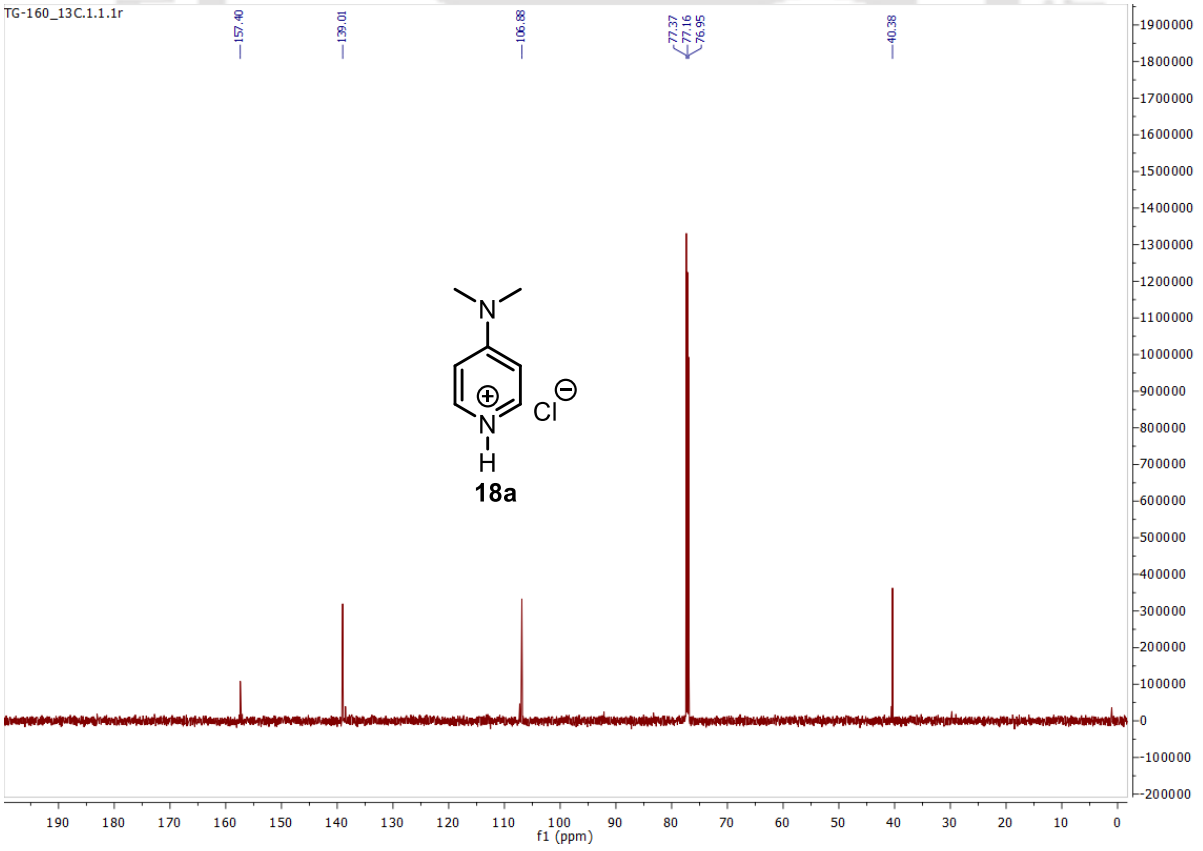

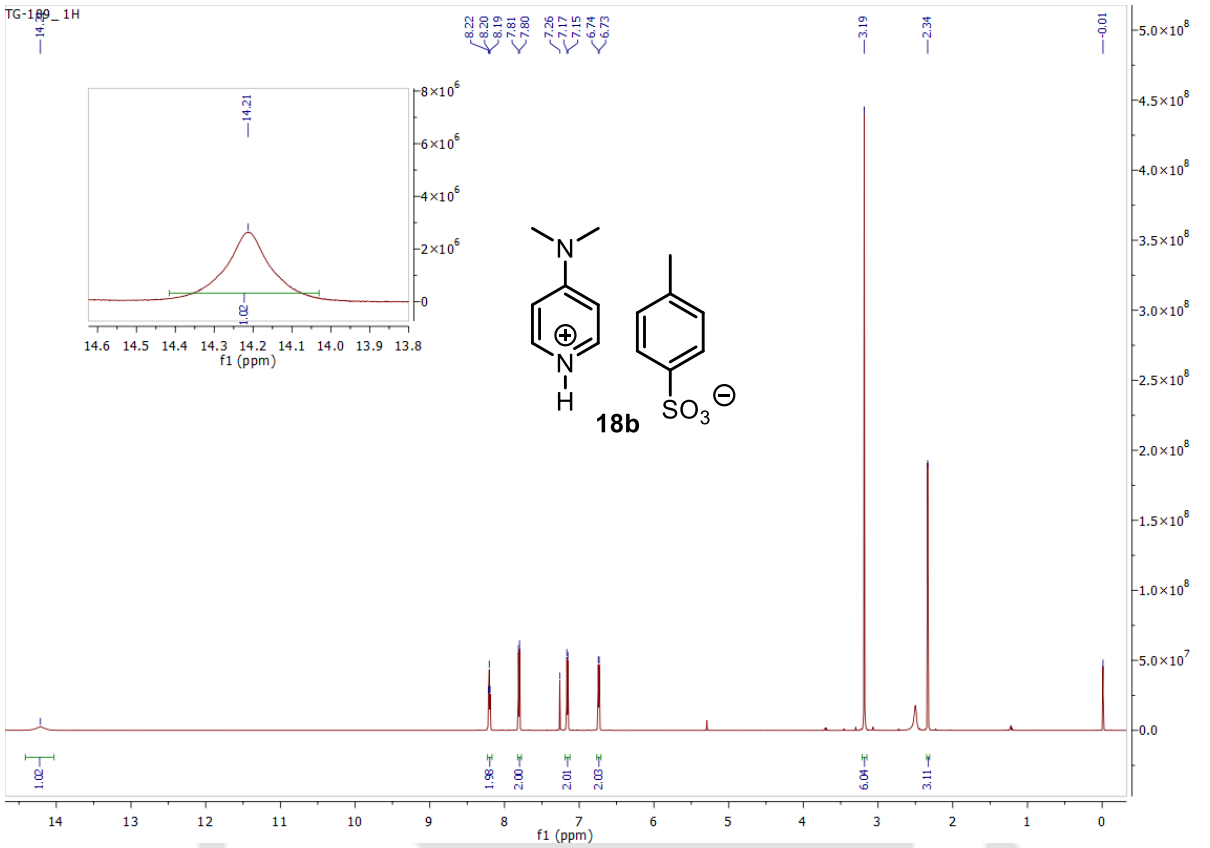
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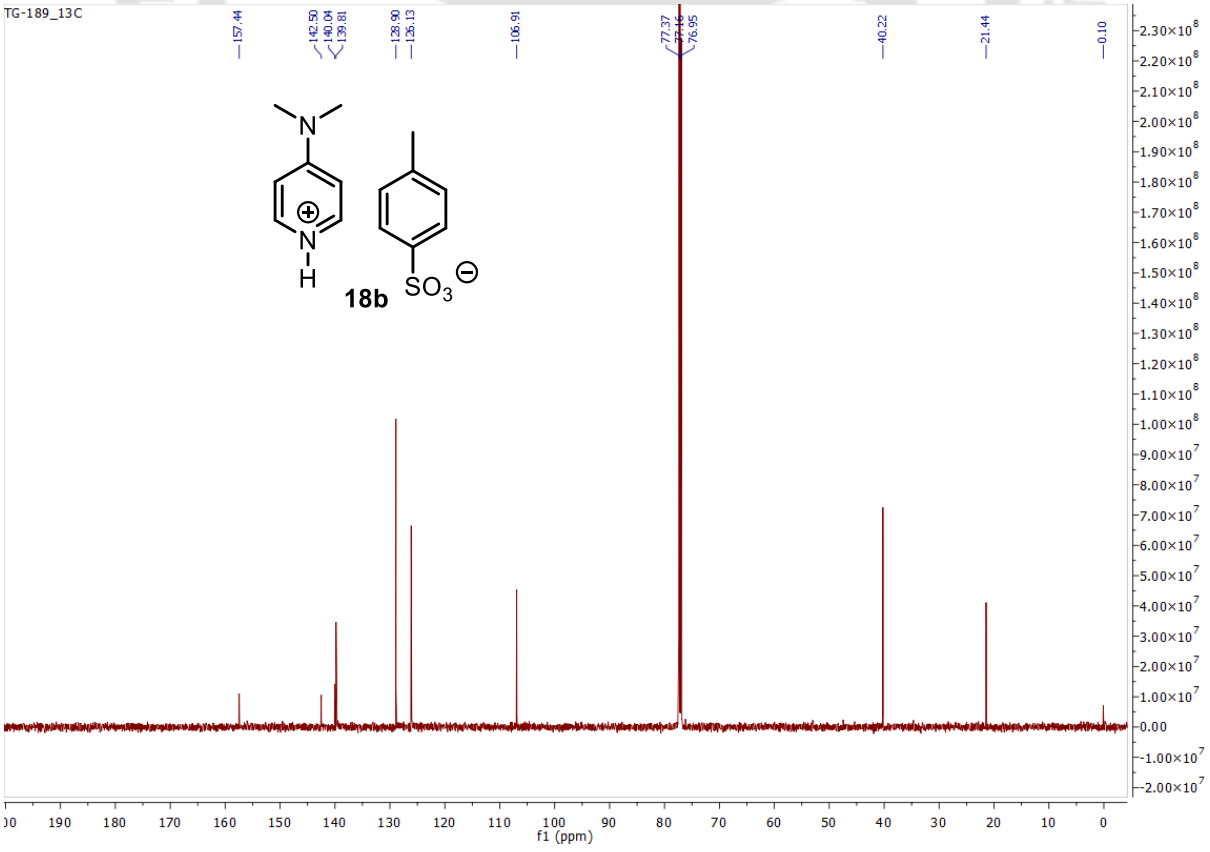
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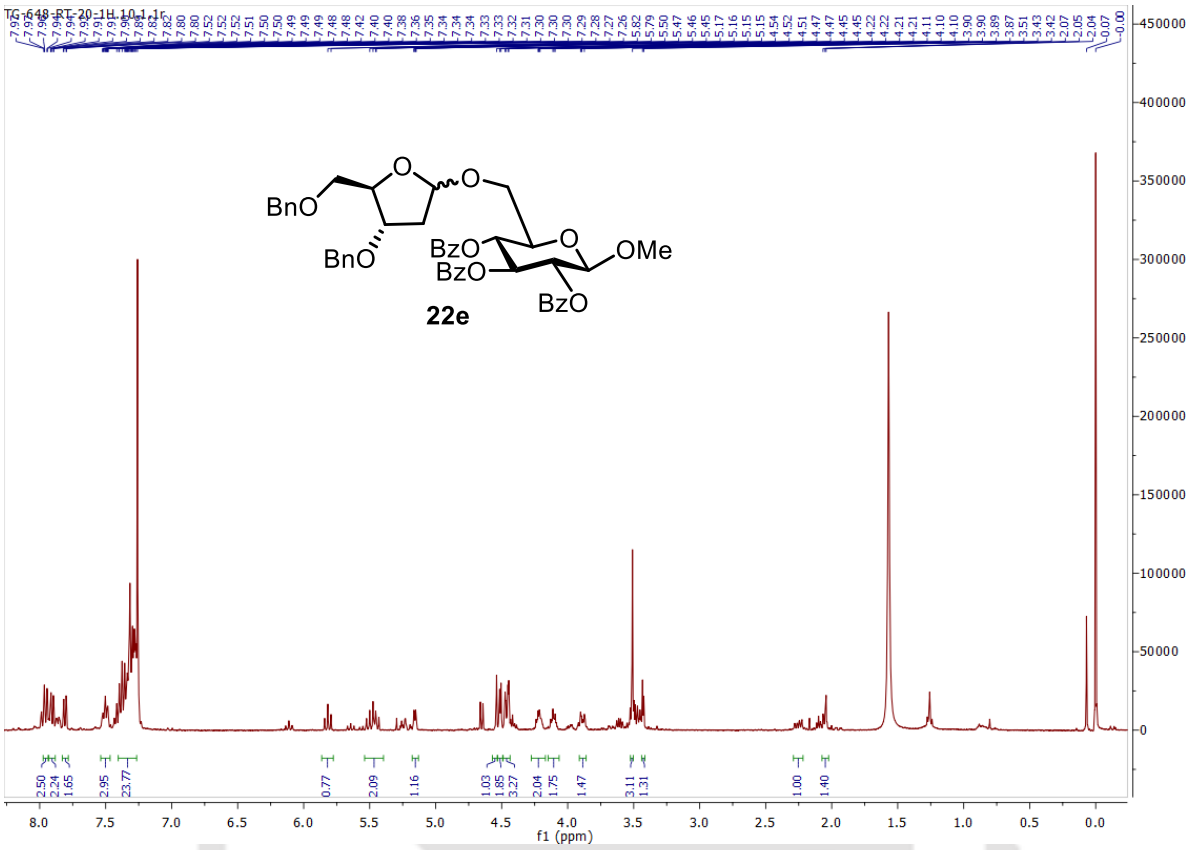

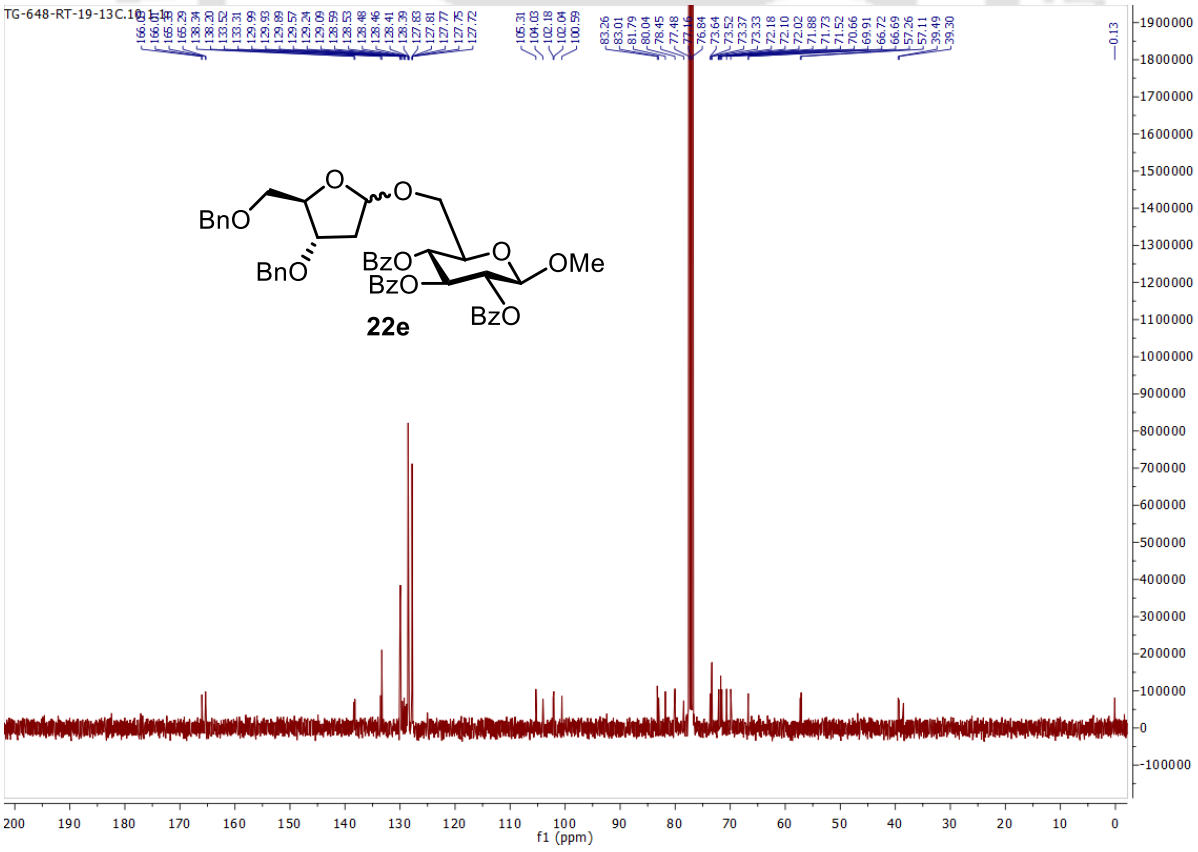

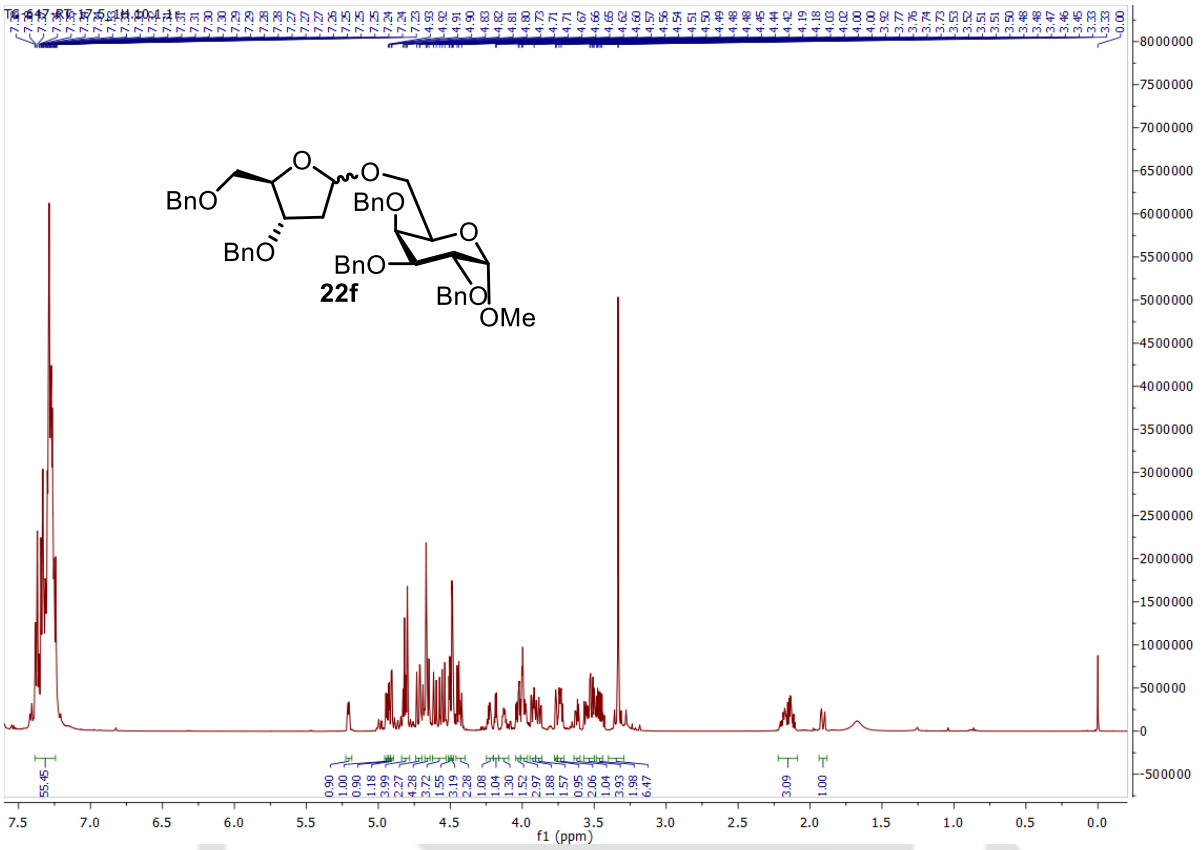
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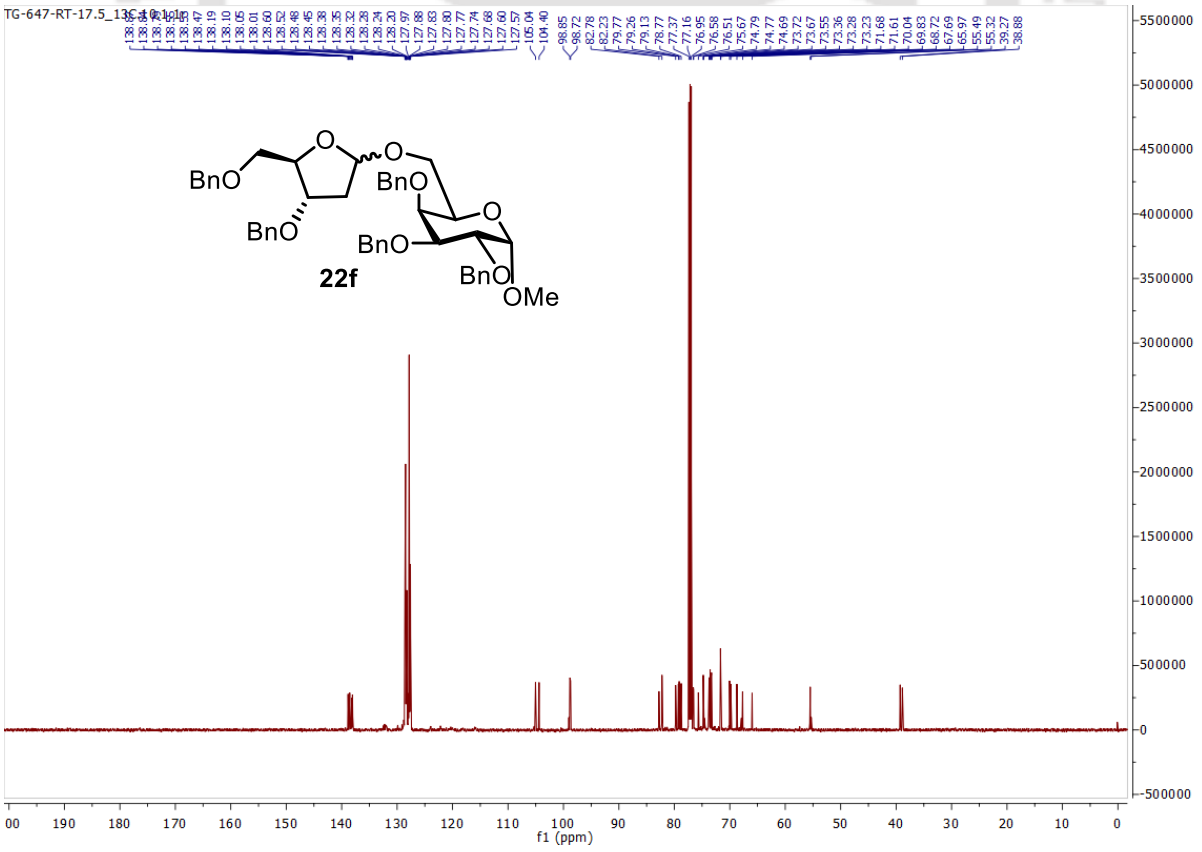
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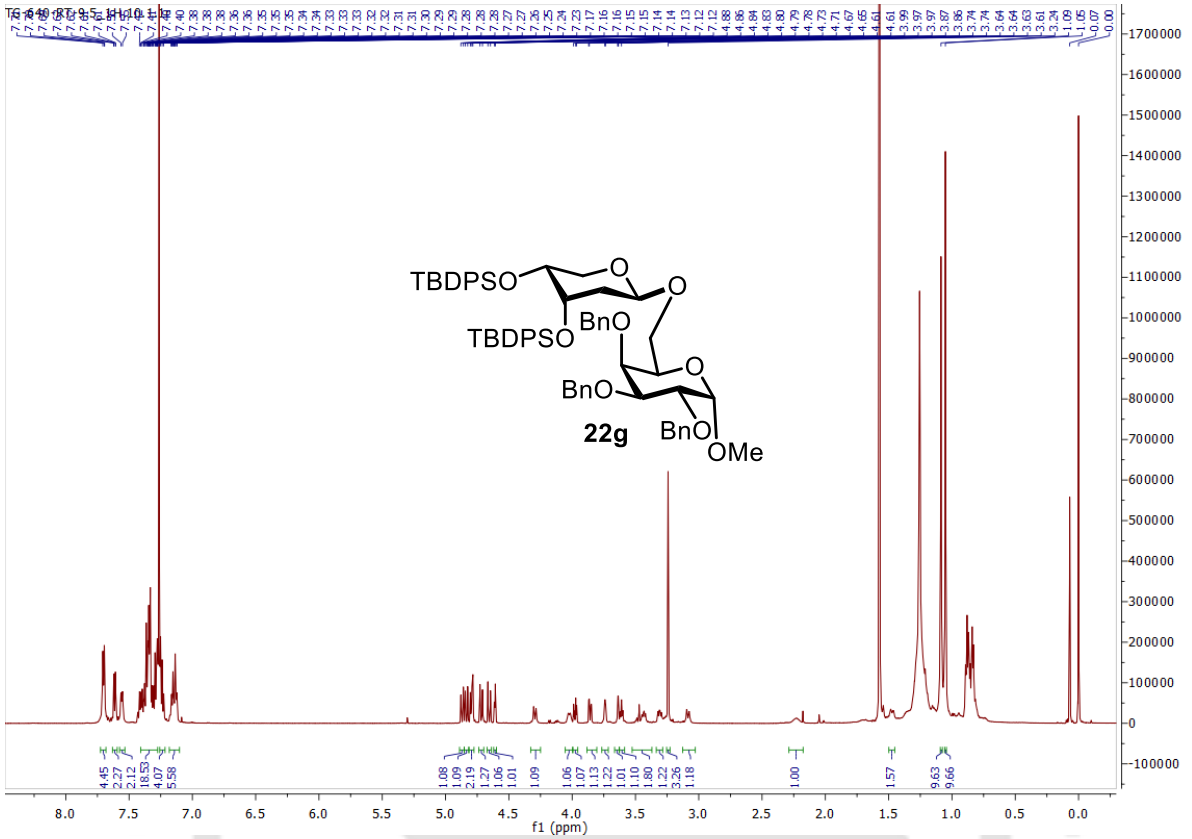
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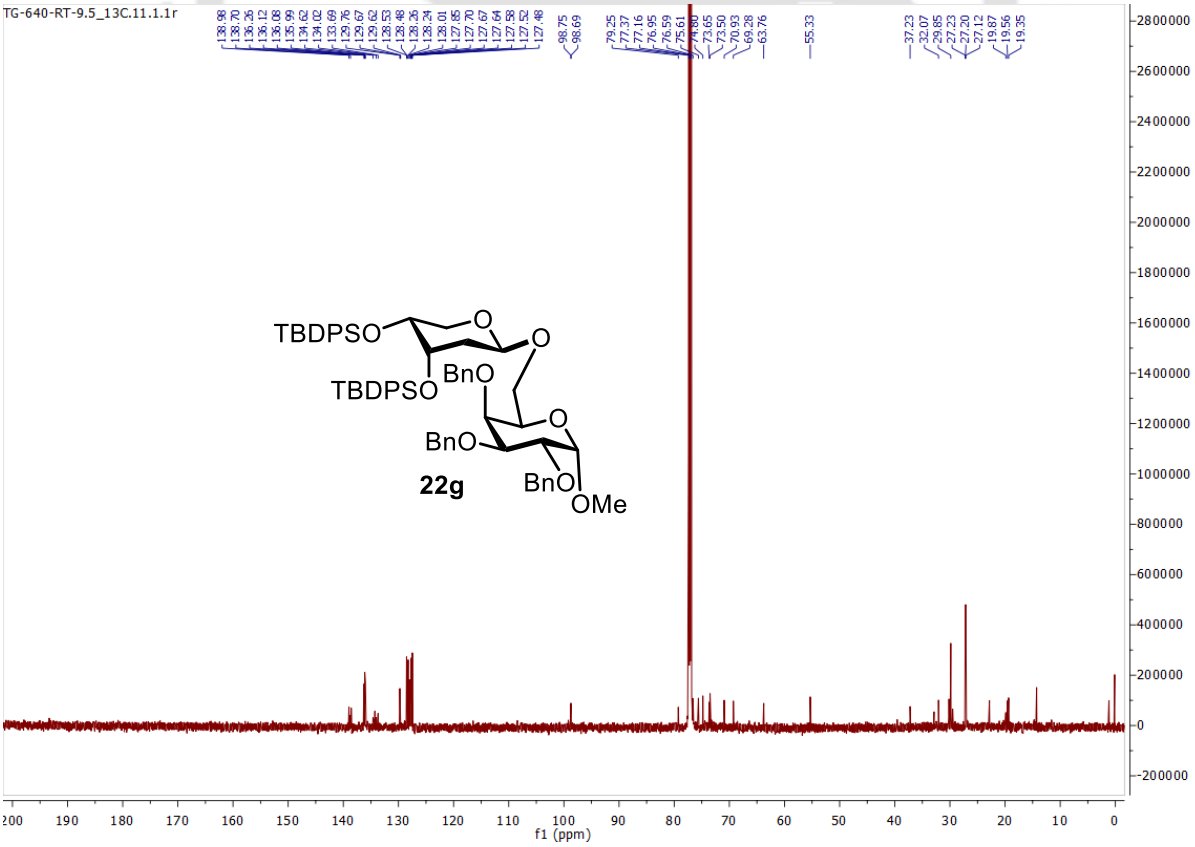
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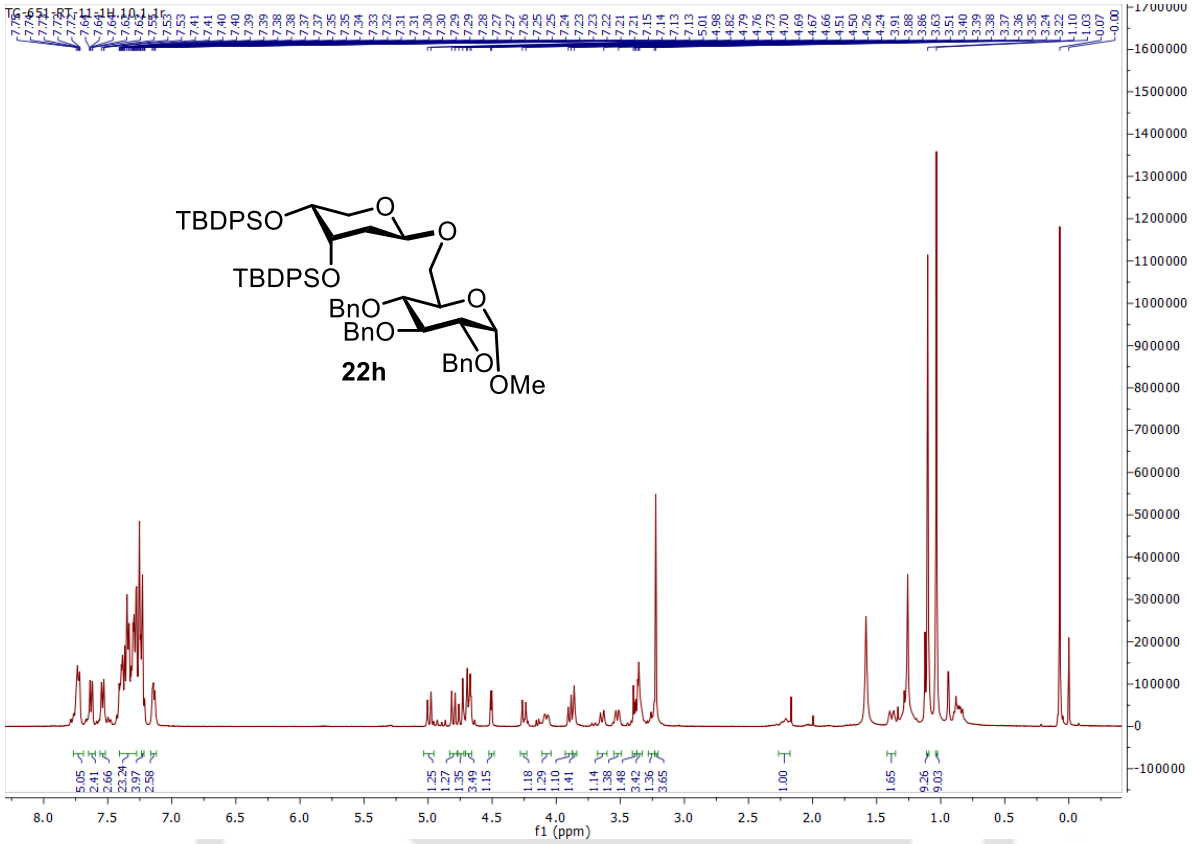
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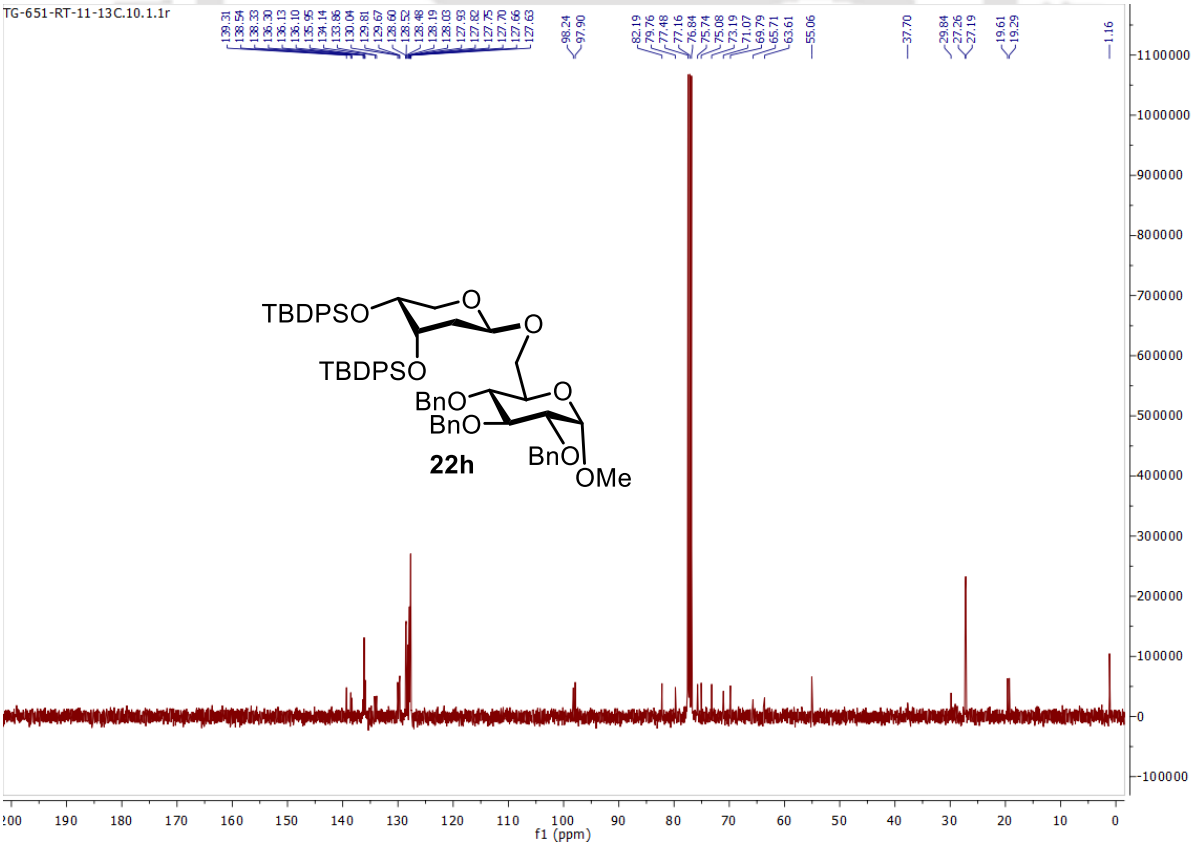
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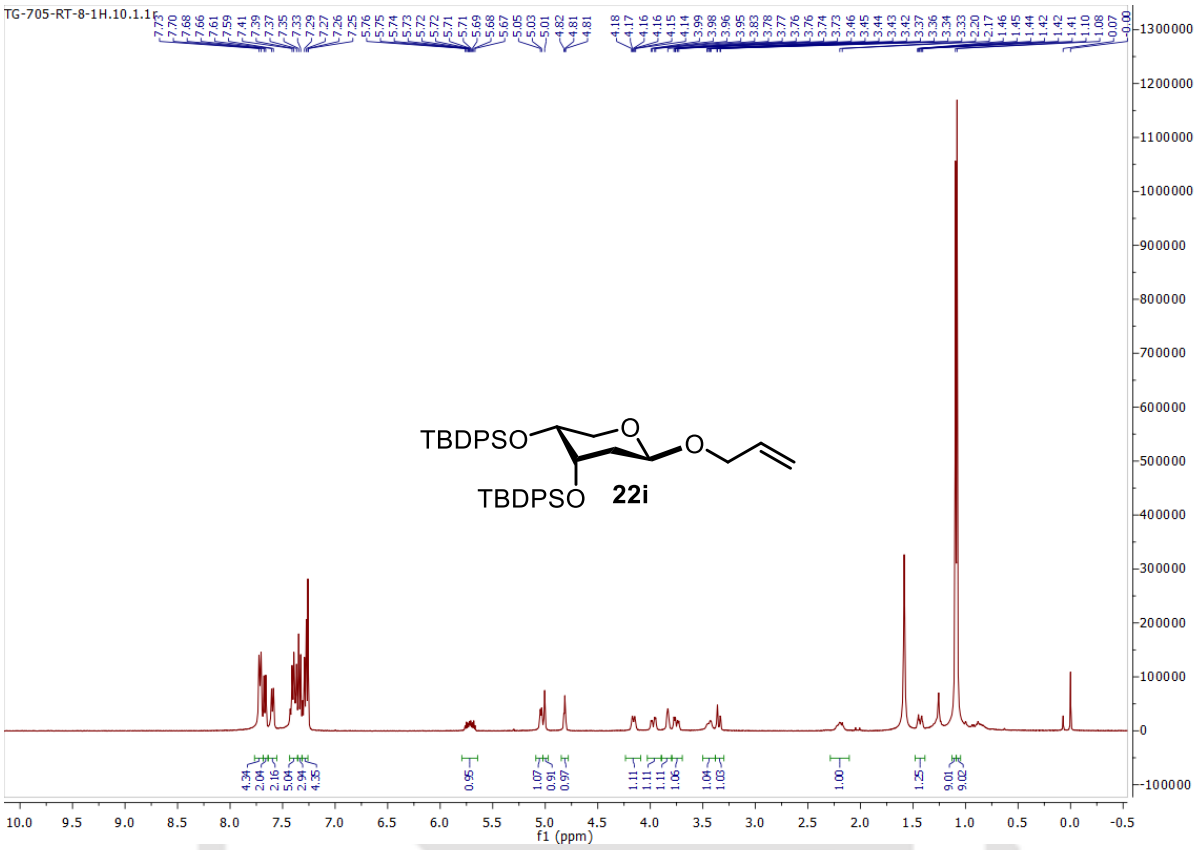
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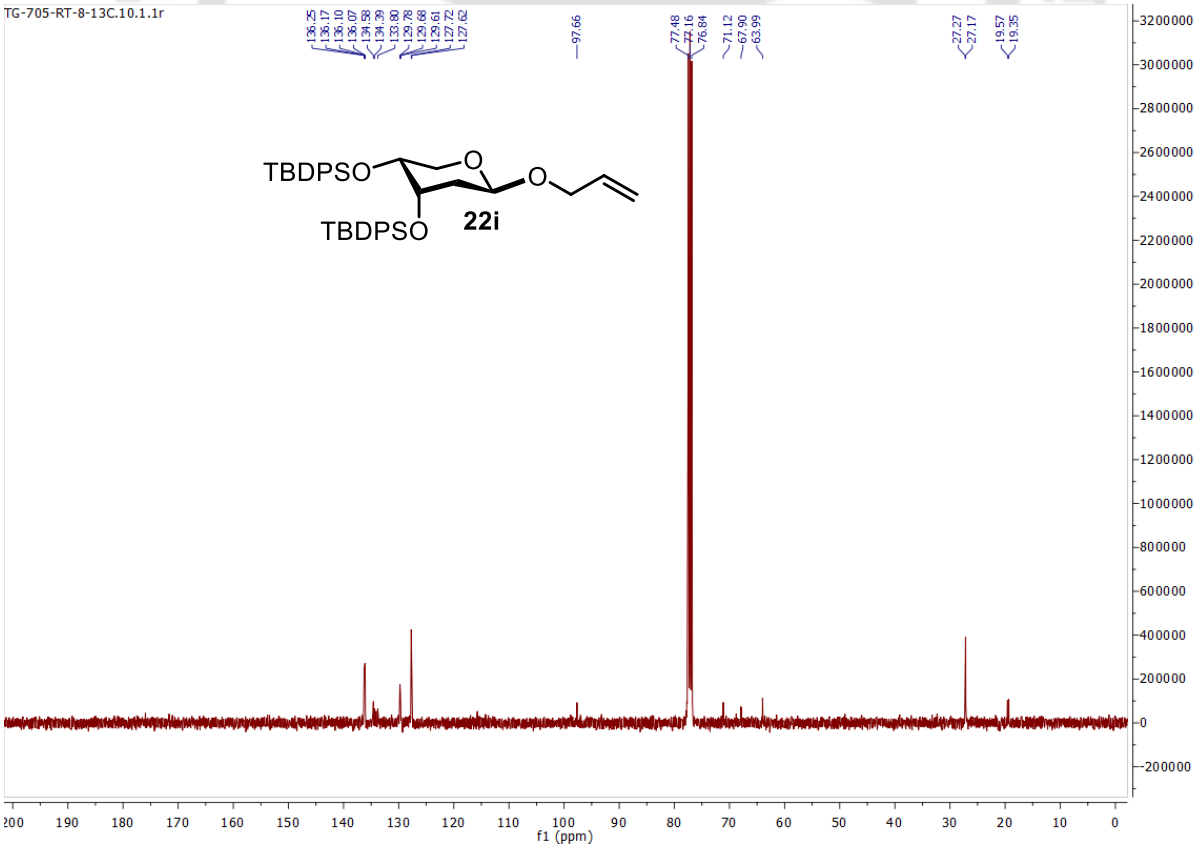
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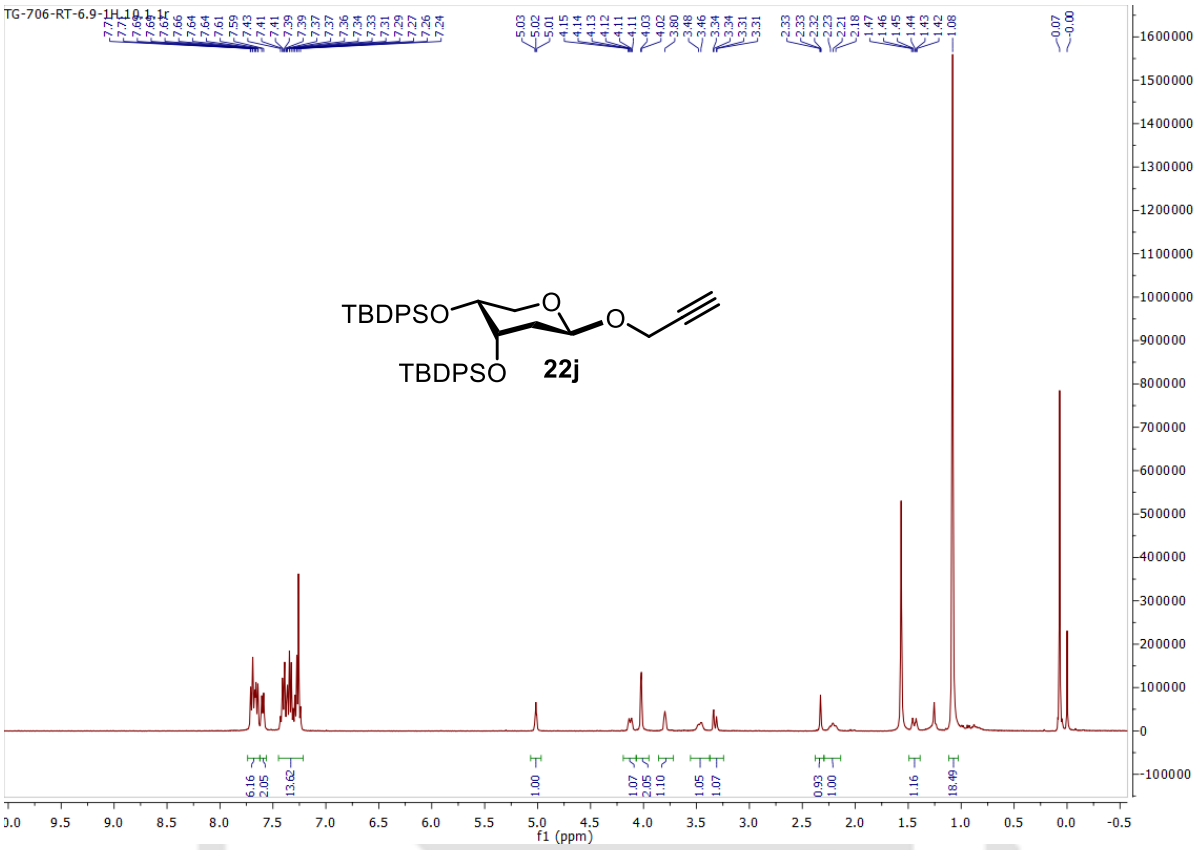
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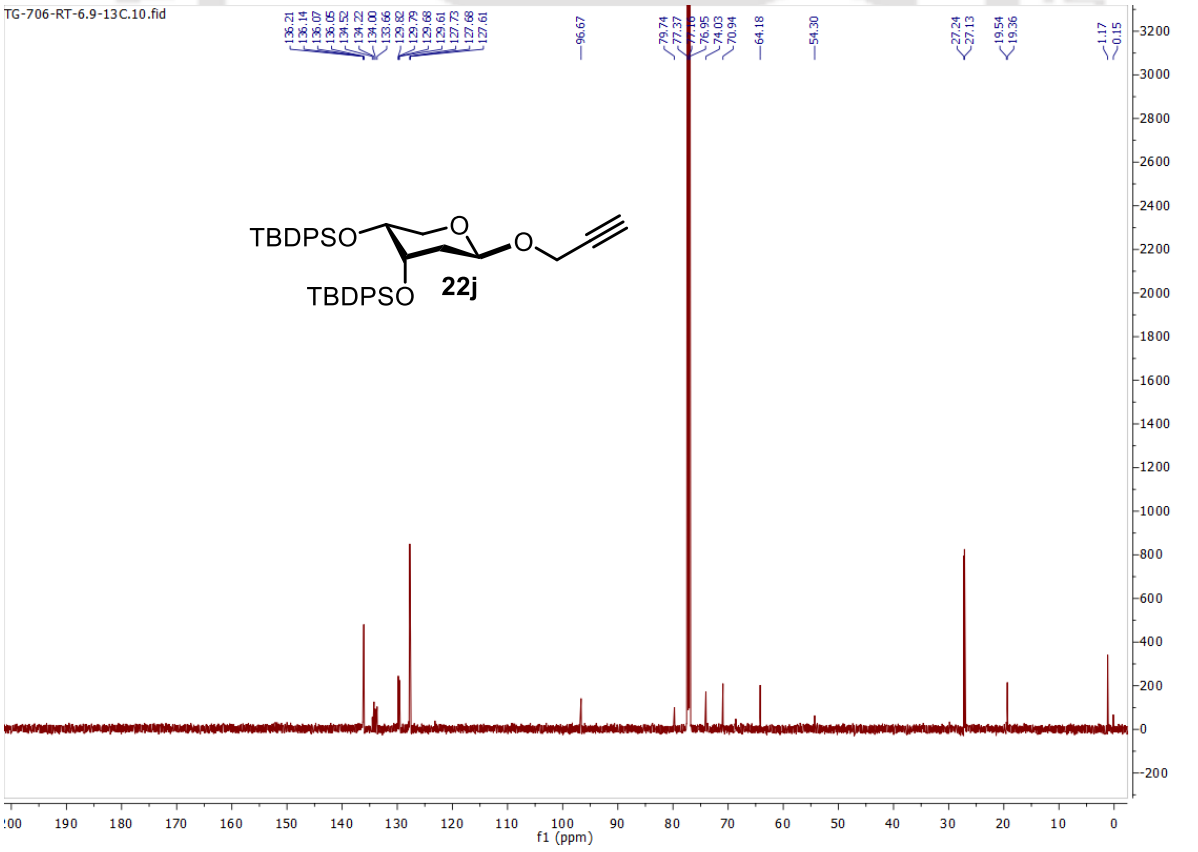
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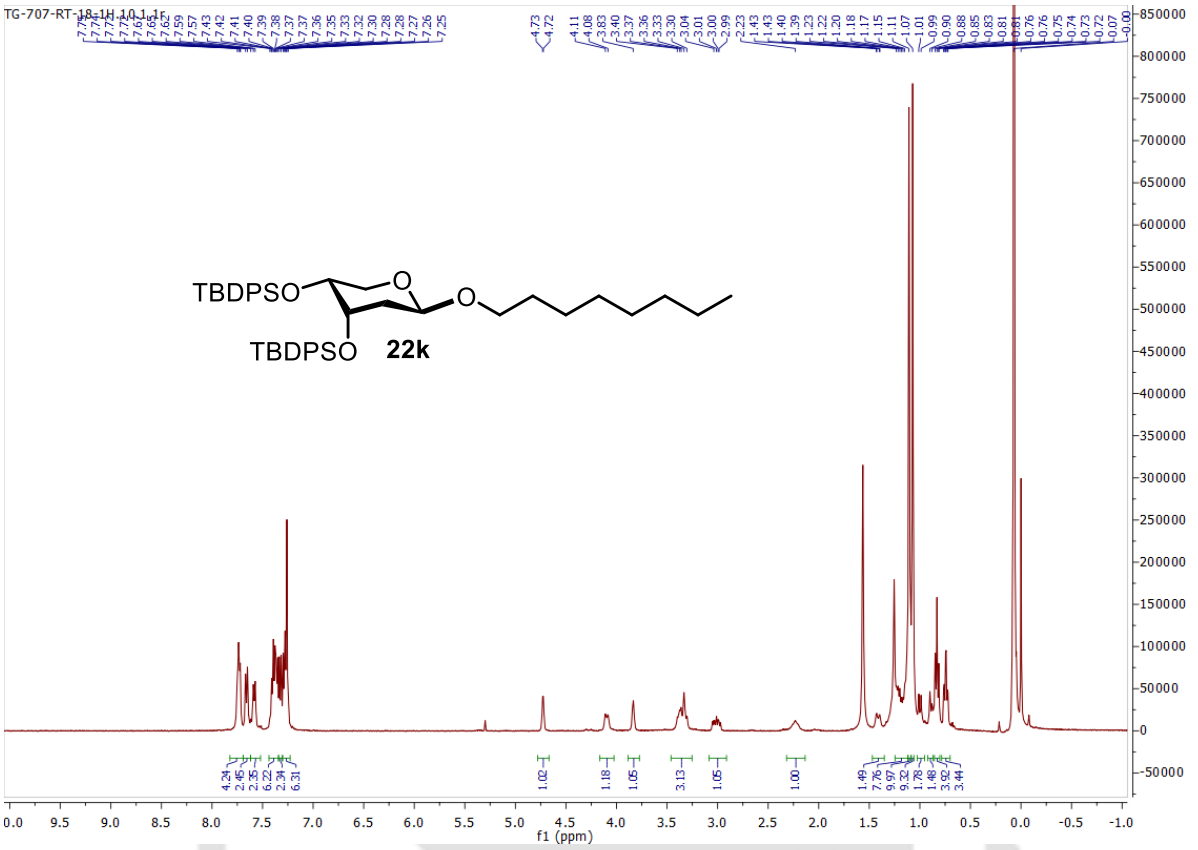
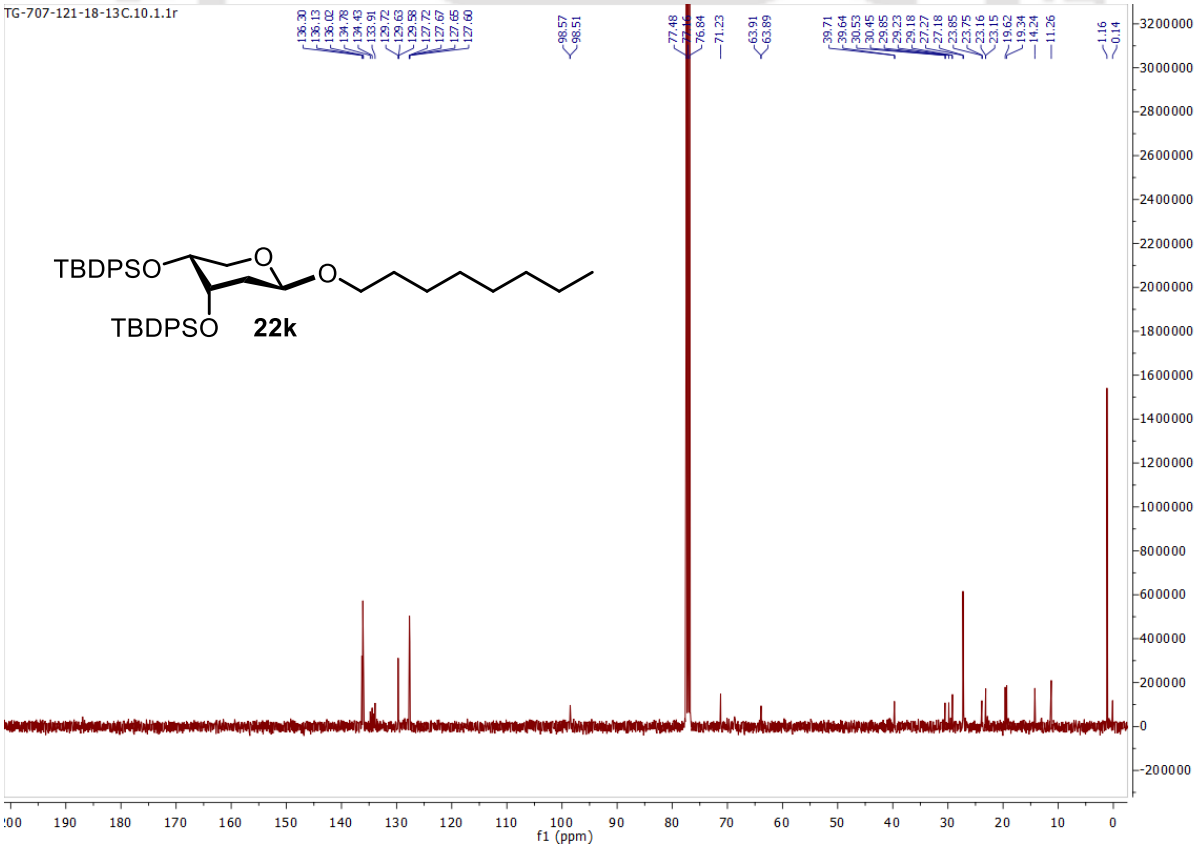
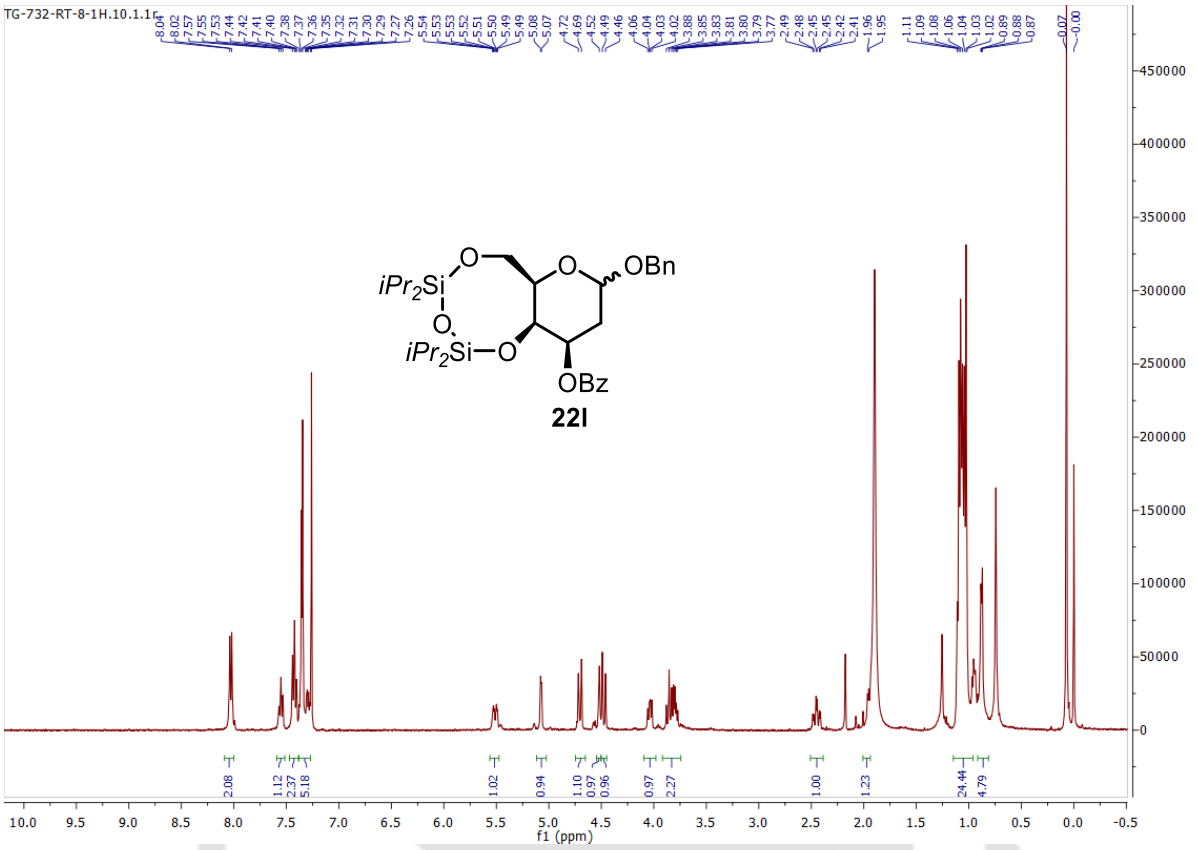
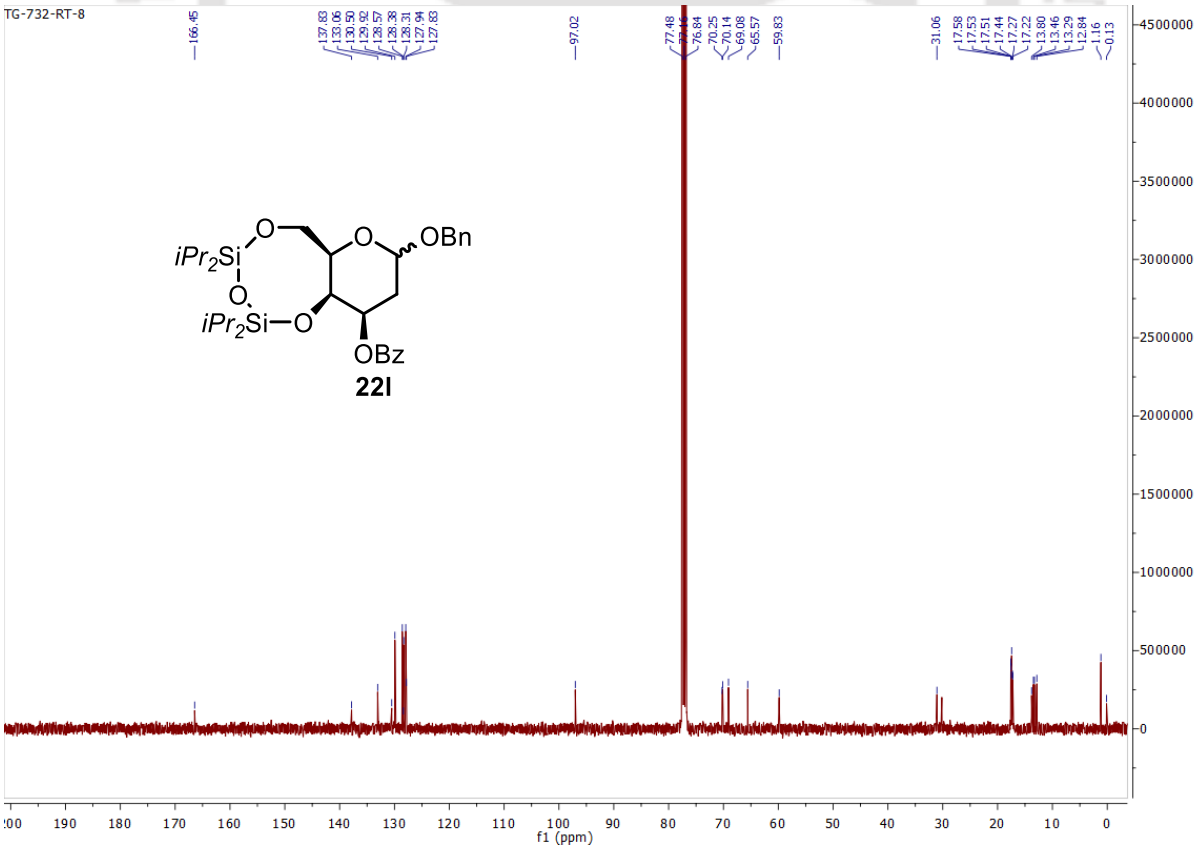
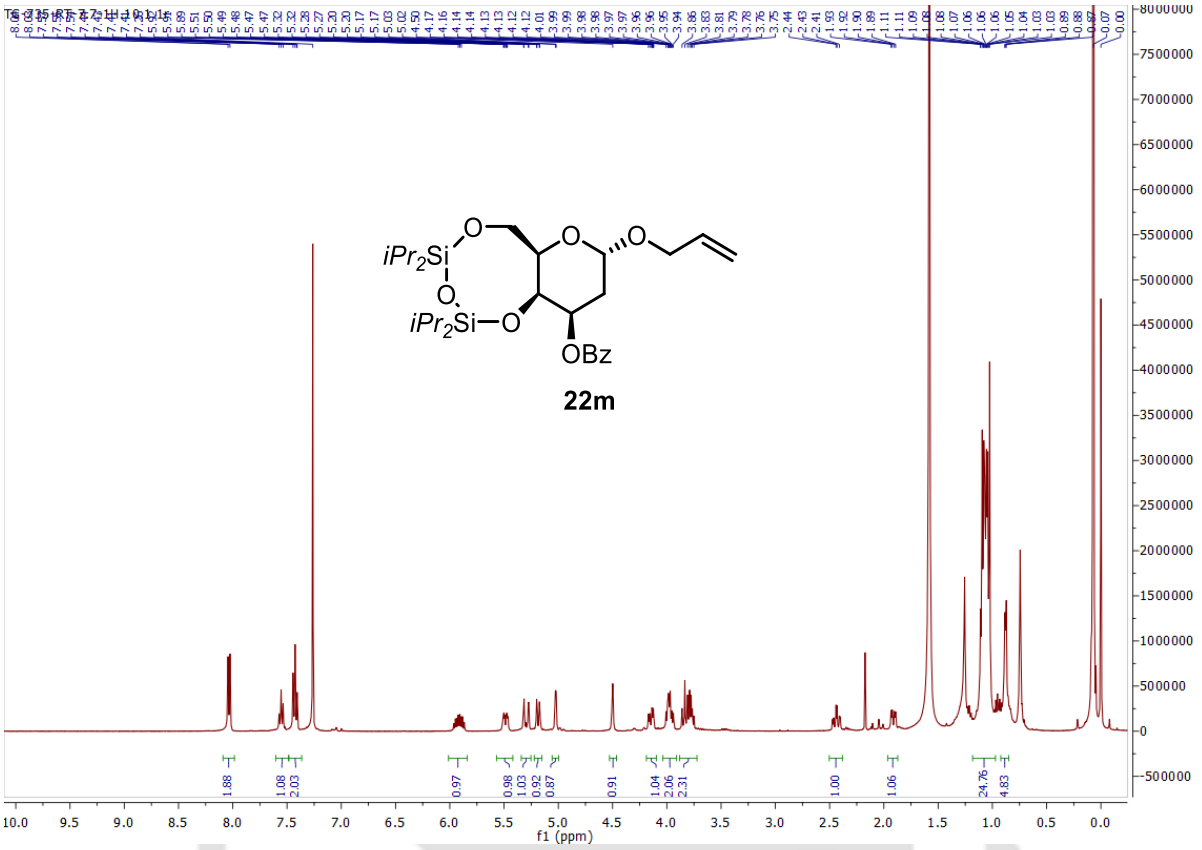
f1 (ppm)

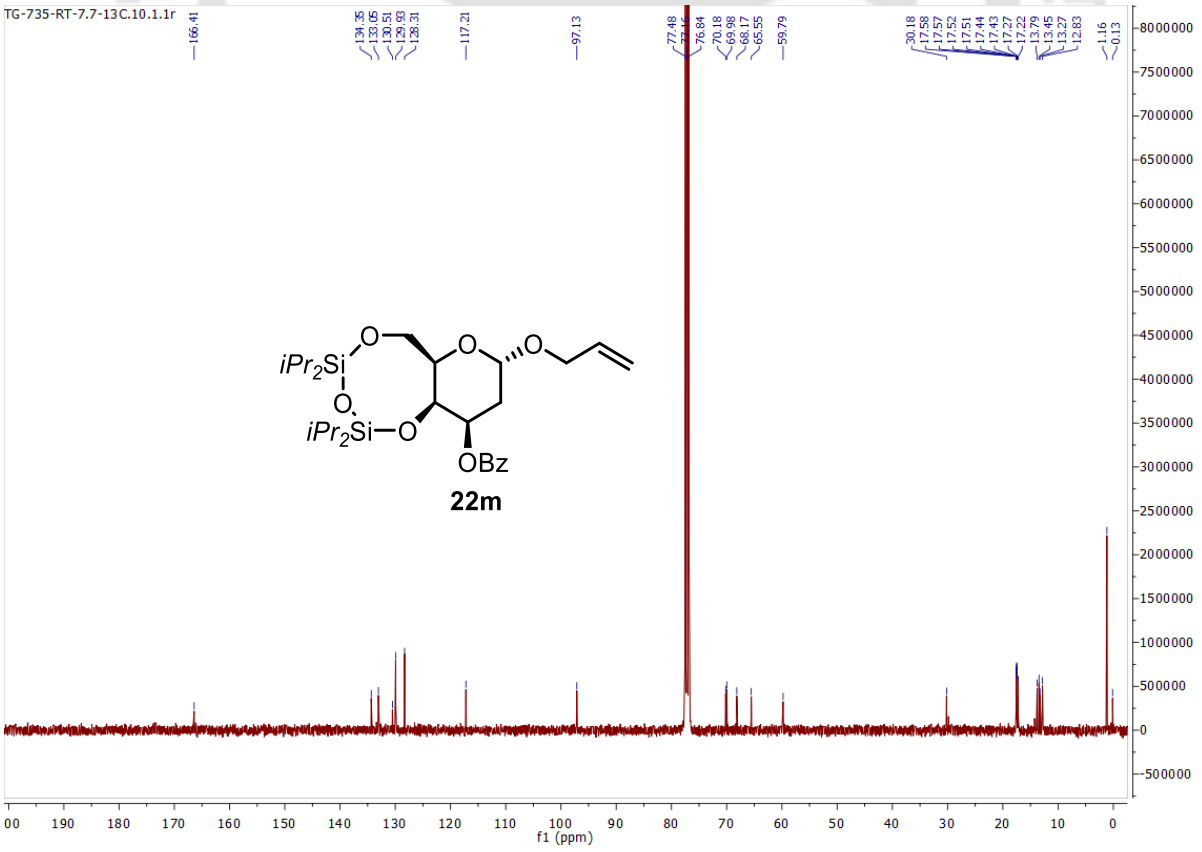


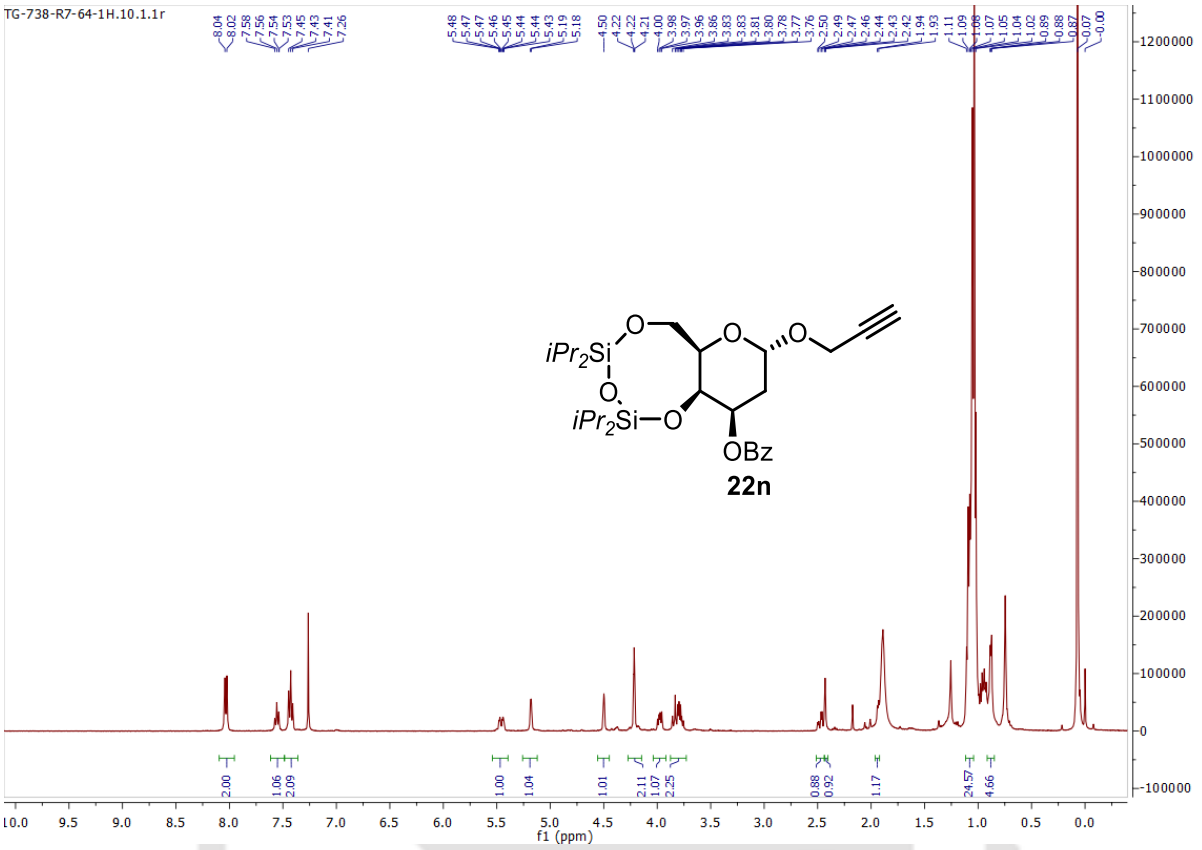


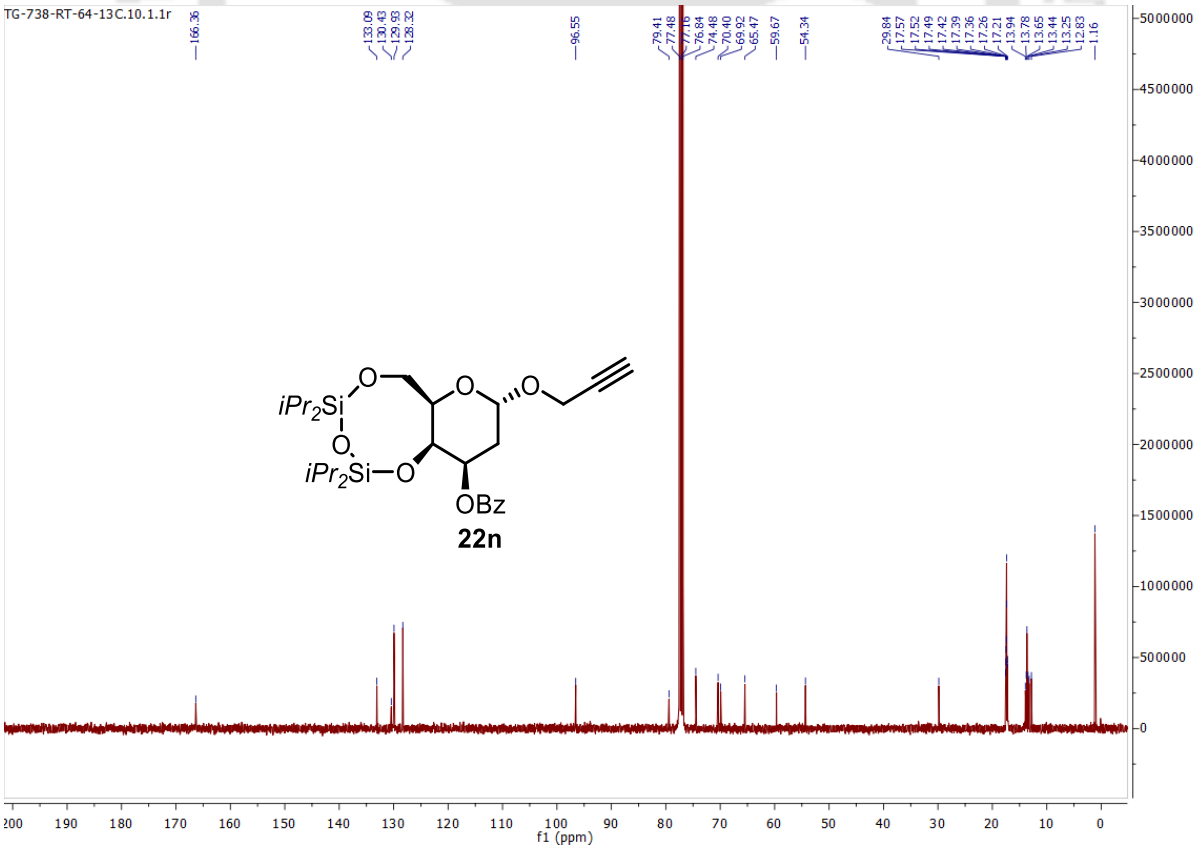

TG-732-RT-8-1H.10.1.1r
OBn
OBz
22l
f1 (ppm)

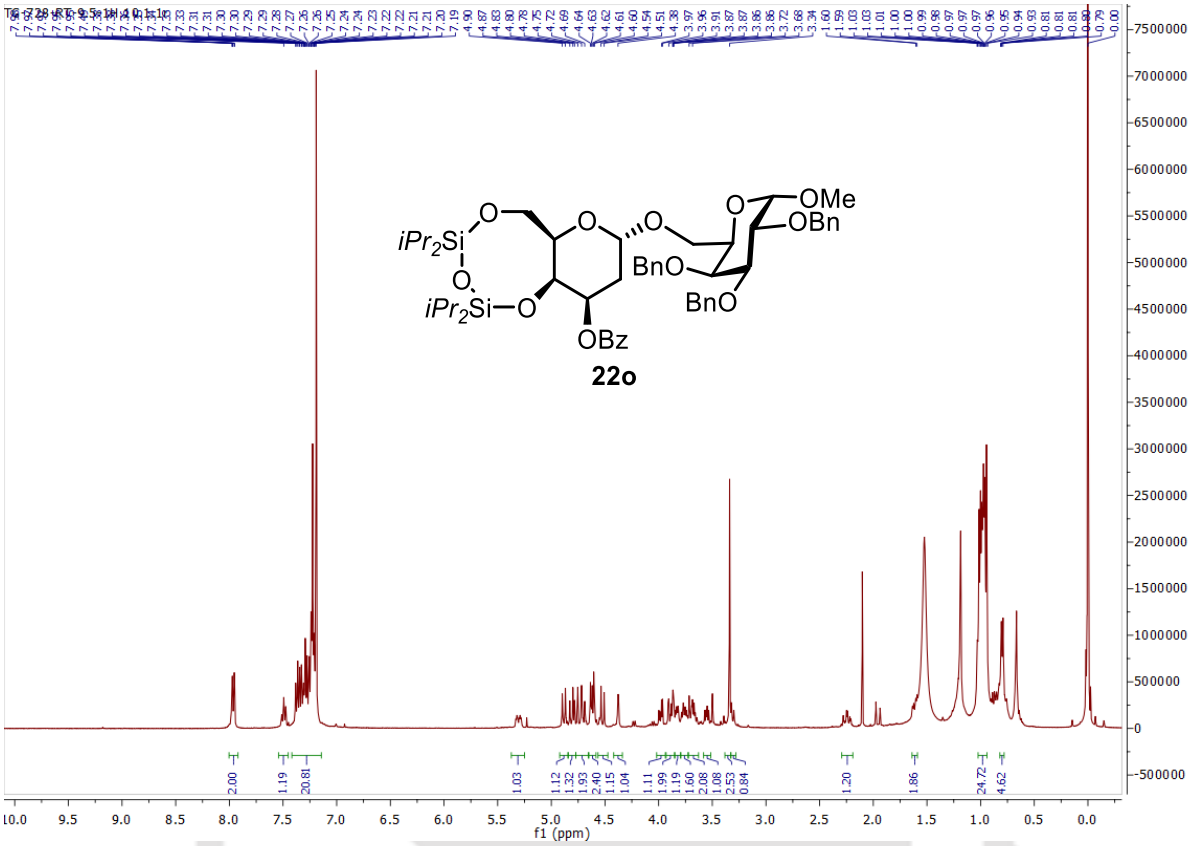

TG-732-RT-8
OBn
OBz
22l
f1 (ppm)

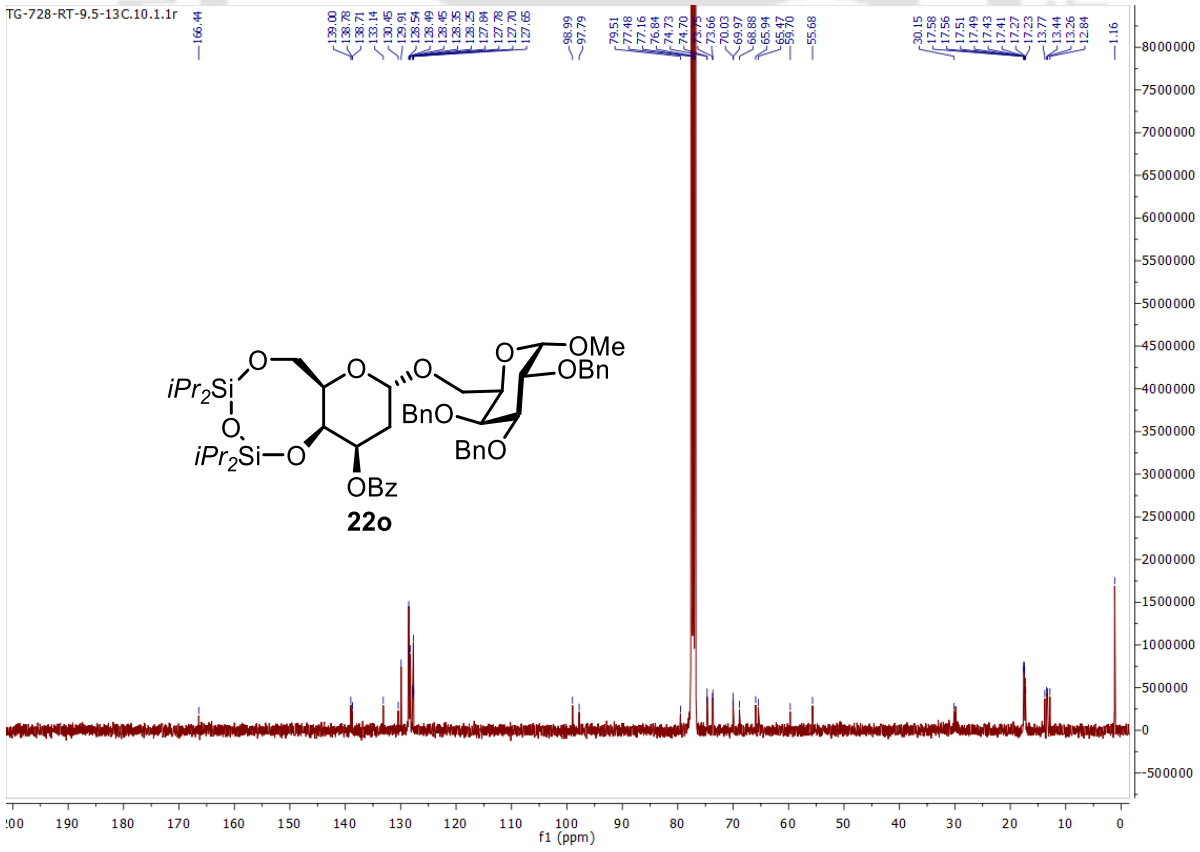

iPr2Si
O
iPr2Si
OBz
22m
f1 (ppm)

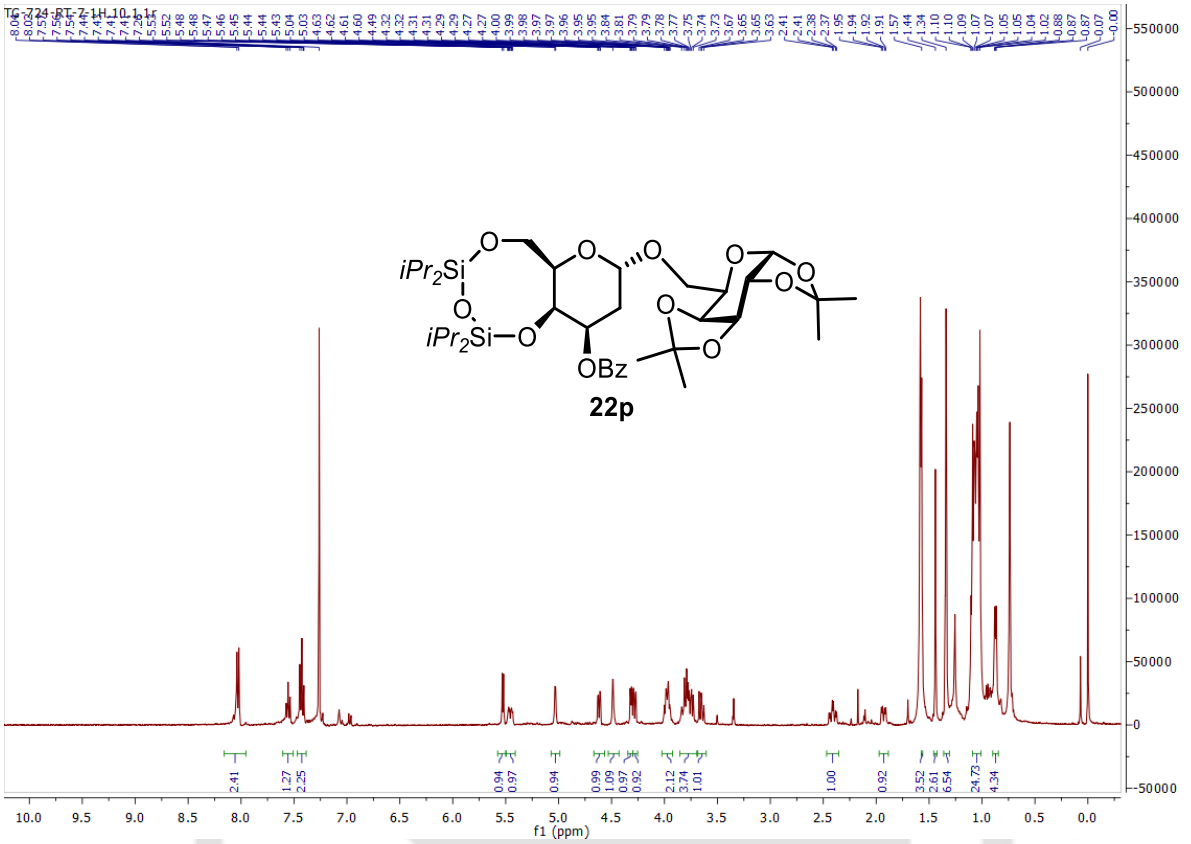

TG-735-RT-7.7-13C.10.1.1r
iPr2Si
O
iPr2Si
OBz
22m
f1 (ppm)

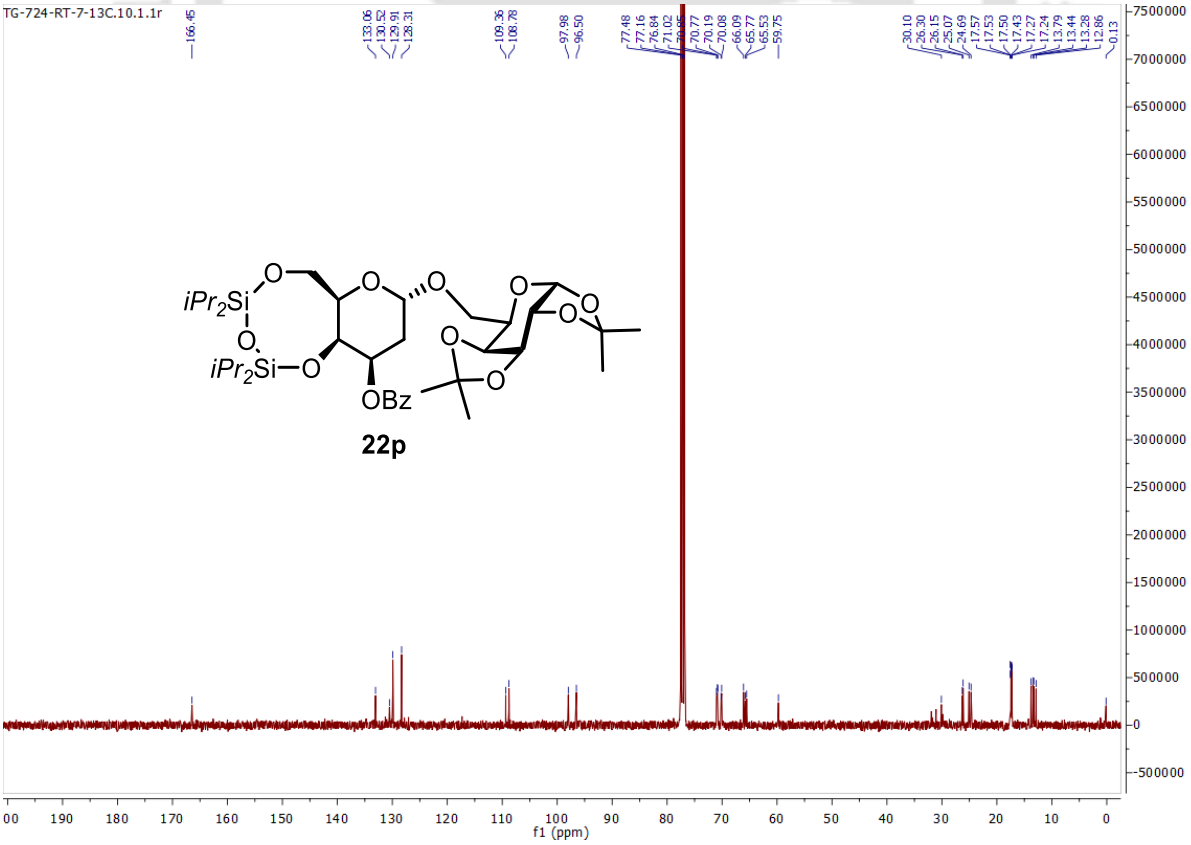

TG-738-R7-64-1H.10.1.1r
OBz
22n


TG-738-RT-64-13C.10.1.1r
OBz
22n






22p


TG-724-RT-7-13C.10.1.1r
22p

nOe Experiment of 22l

Irradiation of H_{2e}:

The anomeric proton **H_1** and **H_3** appear at 5.08 ppm and 5.51 ppm respectively. Upon irradiation of one of the 2-deoxy proton **H_{2e}** appearing at 1.96 ppm, resulted in the enhancement of **H_1**, **H_3**, and other 2-deoxy proton **H_{2a}** coming at 2.45 ppm. It was found that **H_3** proton is more enhanced than **H_1** and therefore, **H_{2e}** proton is cis to **H_3**.

Irradiation of H_{2a}:

Irradiation of other 2-deoxy proton **H_{2a}**, there was an enhancement of only **H_1** proton, and hence, **H_{2a}** is trans to **H_3**.

Irradiation of H_1:

After irradiation of anomeric proton **H_1**, there was an enhancement of only **H_{2a}**, and **H_1** is cis to **H_{2a}**.

Irradiation of H_3:

In addition, the irradiation of **H_3** results in the enhancement of **H_{2e}**, and they are cis to each other.

From the above observation, it can be concluded that **H_1** and **H_3** are trans to each other, and the compound **22l** has the alpha configuration.

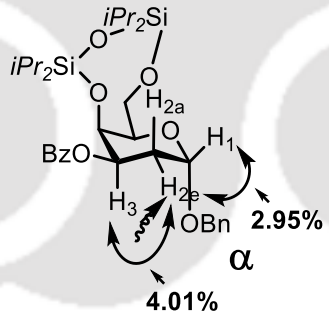
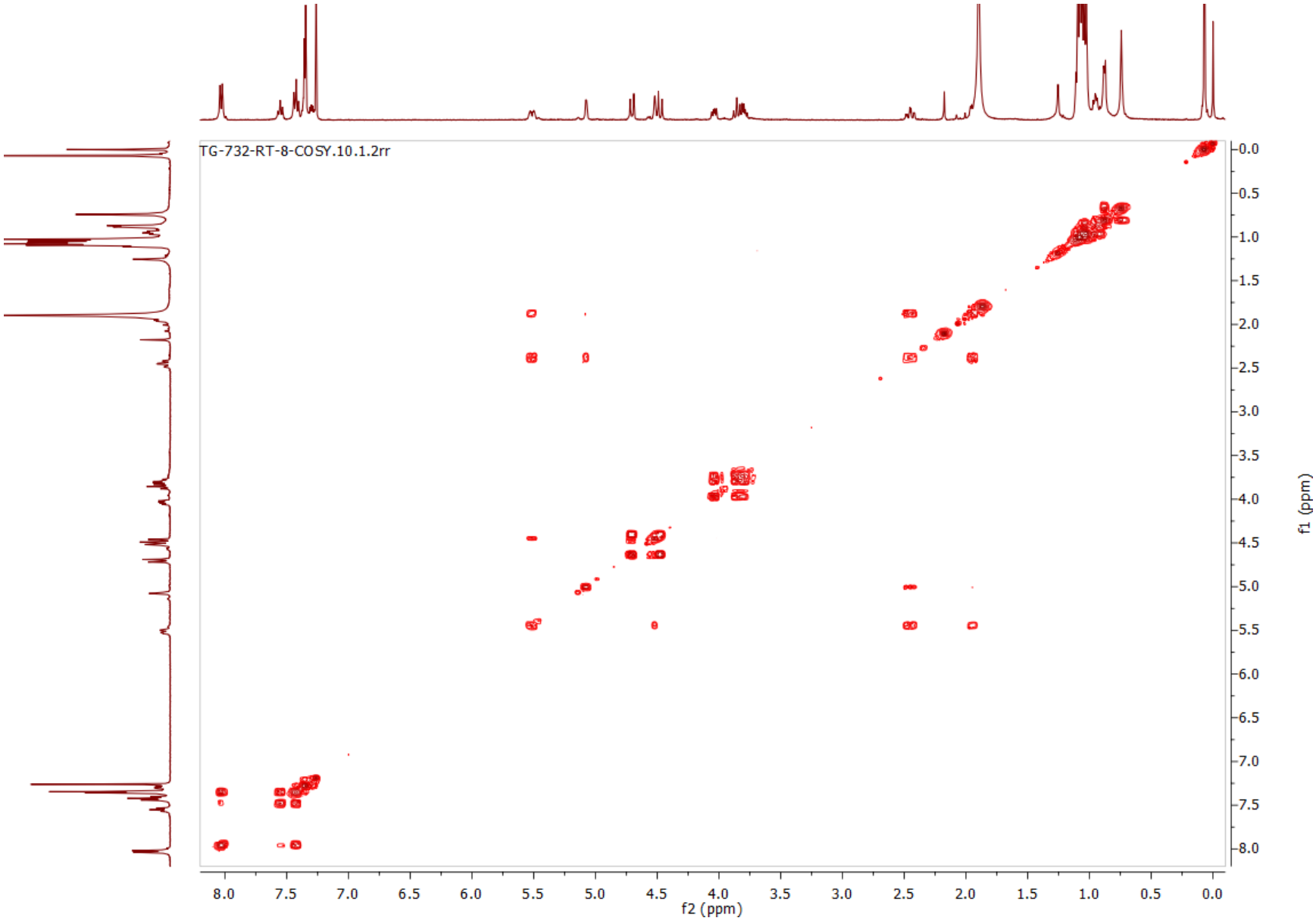


Figure 3: The alpha configuration of **22l**.

COSY NMR of 22l:



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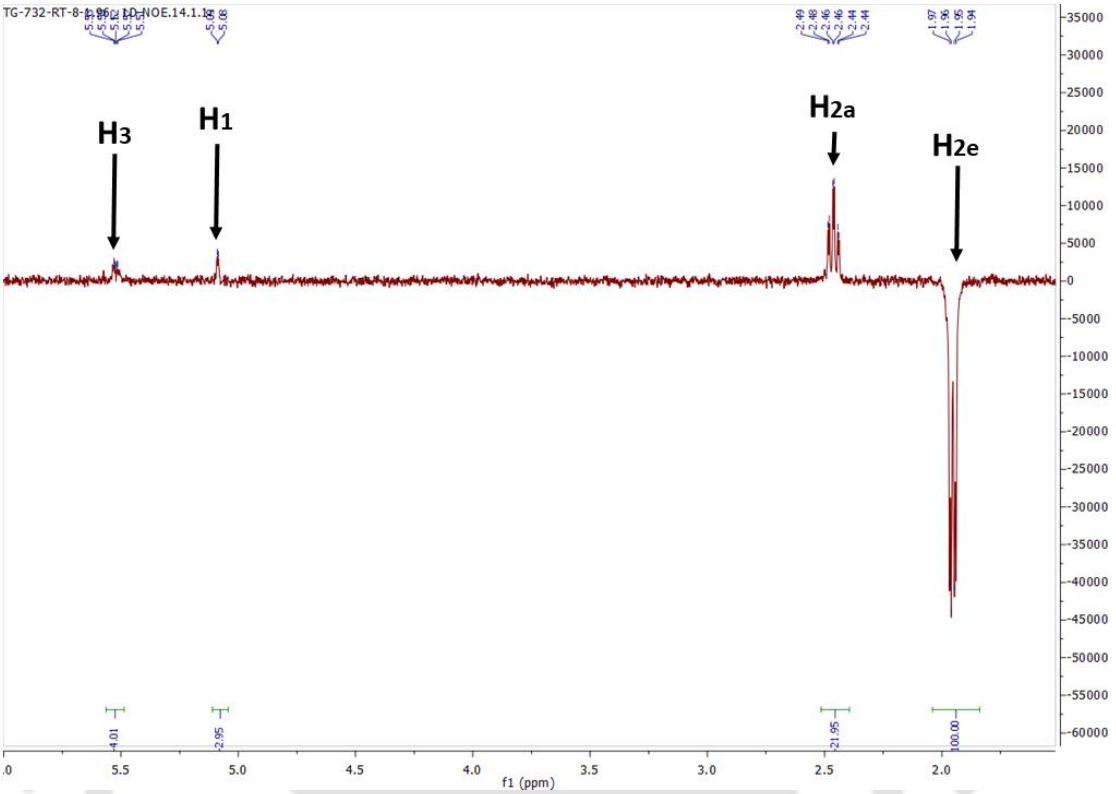
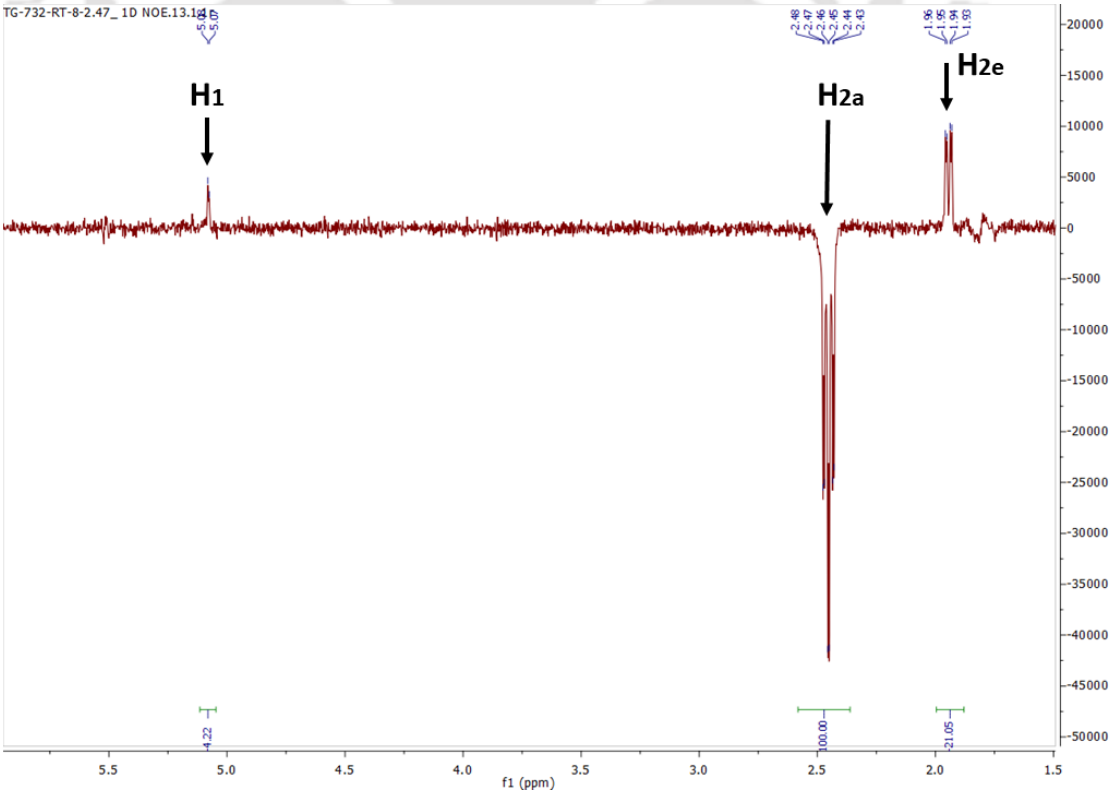
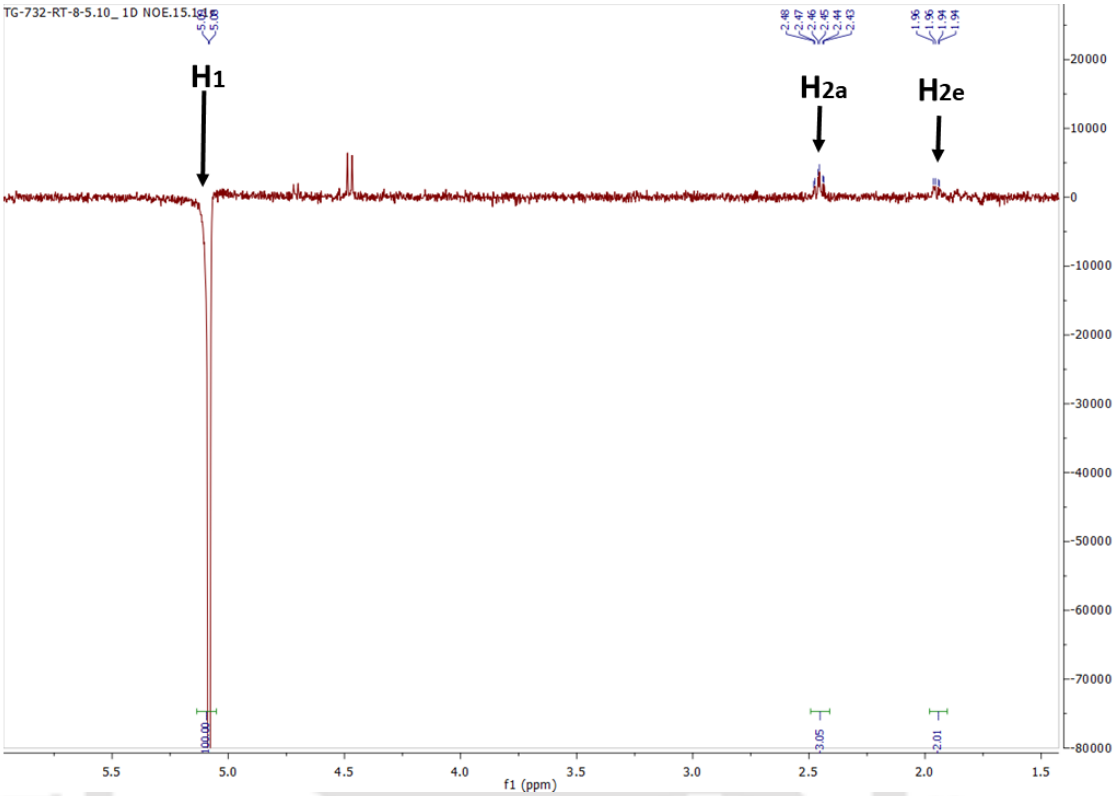
Irradiation of H_{2e} of 22l:



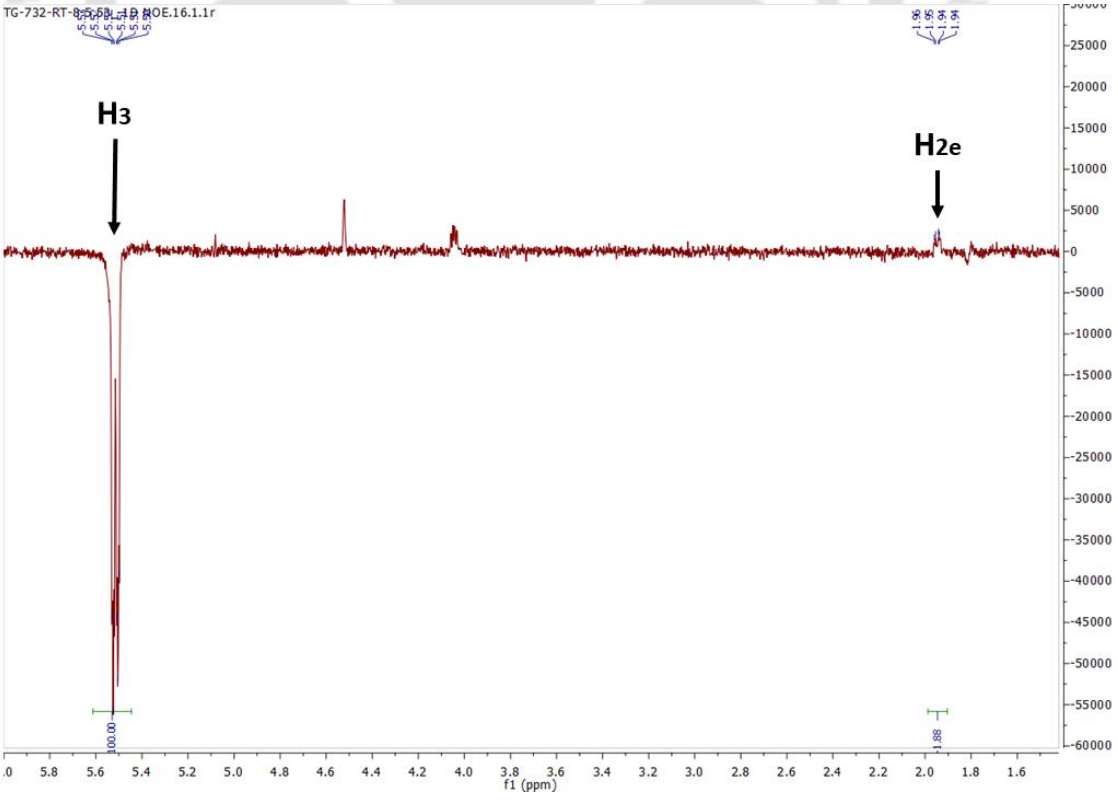
Irradiation of H_{2a} of 22l:

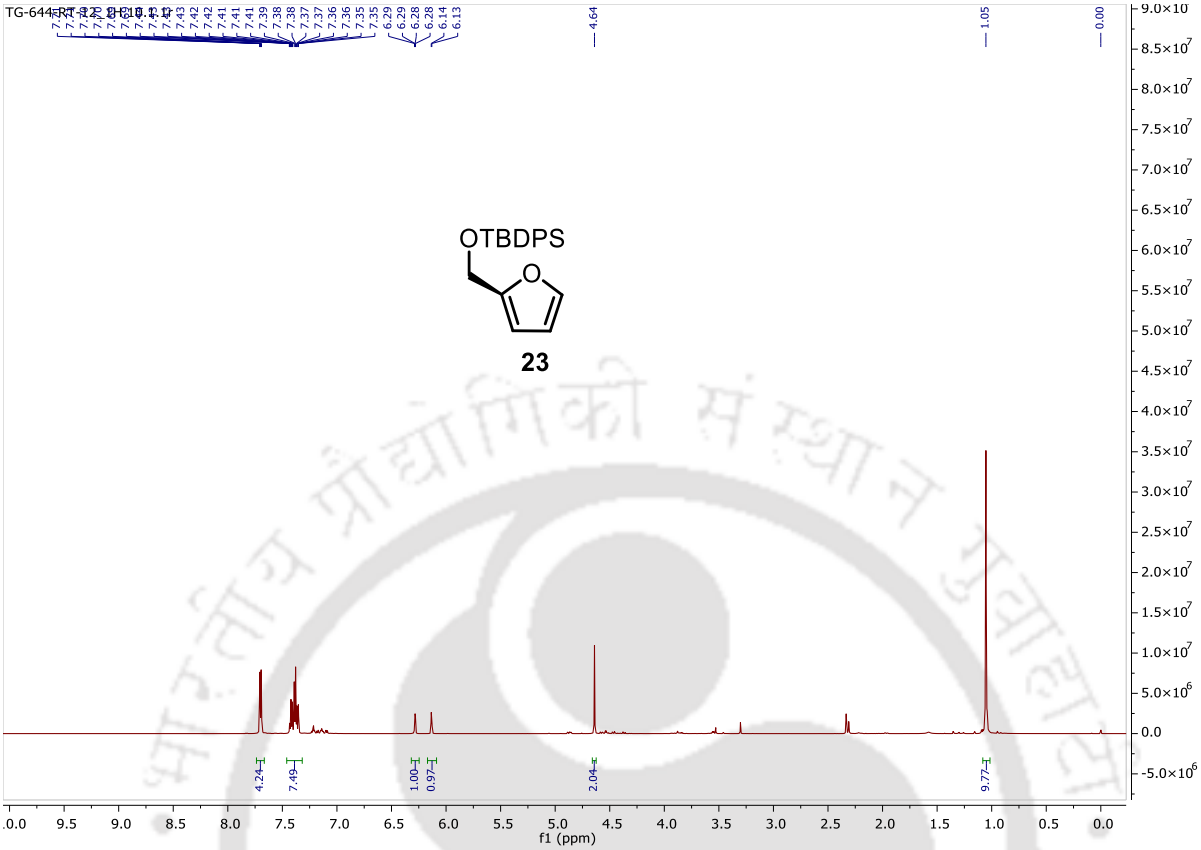


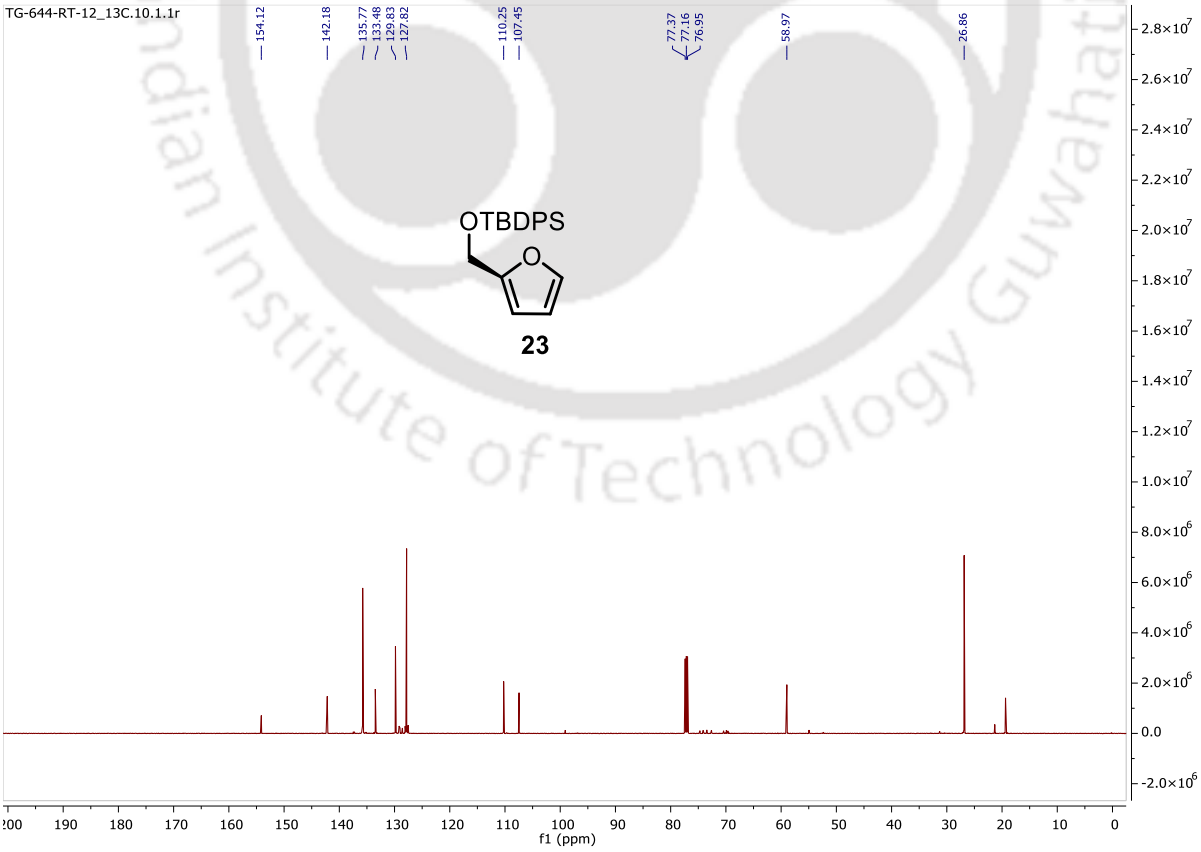
Irradiation of H_1 of 22l:



Irradiation of H_3 of 22l:

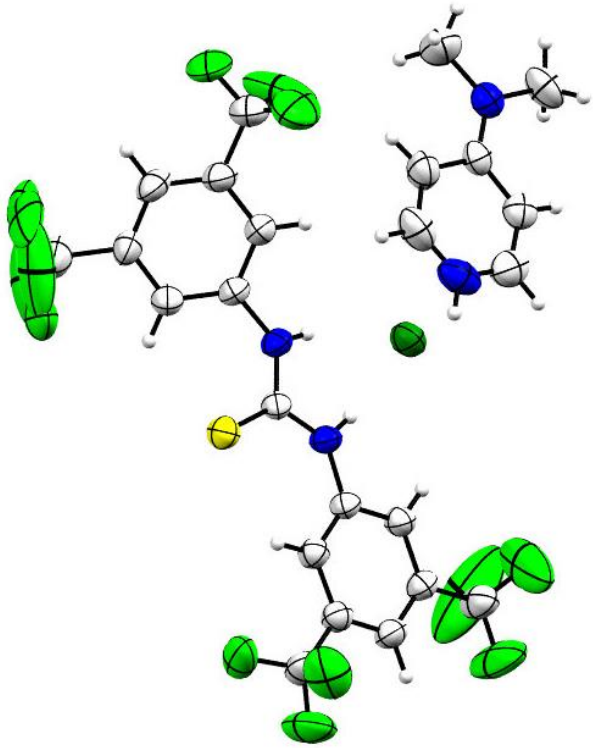






5.9 XRD Data:

Co-crystal (1:1 18a:19a):



Crystal system	= Monoclinic
Bond precision:	C-C = 0.0054 Å
Wavelength	= 0.71073
Cell:	a = 14.7042(6) Å
	b = 22.8325(10) Å
	c = 8.6403(4) Å
	α = 90°
	β = 106.684(1)°
	γ = 90°
Temperature:	273 K
Volume	= 2778.7(2) $Å^3$
Space group	= P 21/c
Hall group	= -P 2ybc
Moiety formula	= C17 H8 F12 N2 S, C7 H11 N2, Cl
Sum formula	= C12 H9.50 Cl0.50 F6 N2 O0 S0.50

Mr	= 329.47
Dx	= 1.575 g cm^{-3}
Z	= 8
Mu	= 0.316 mm^{-1}
F(000)	= 1328.0
F(000')	= 1330.13
Ranges (h,k,l)max	= 17,27,10
Nref	= 4894
Tmin,Tmax	= 0.895, 0.910
Tmin'	= 0.895
Correction method	= # Reported
T Limits:	Tmin = 0.895
	Tmax = 0.910
AbsCorr	= Multi-scan
Data completeness	= 1.000
Theta(max)	= 25.000
R(reflections)	= 0.0650(3895)
wR2(reflections)	= 0.1812(4894)
S	= 1.037
Npar	= 399

Biography

Titli Ghosh *is a post-graduate researcher at the Department of Chemistry, Indian Institute of Technology, Guwahati. She was born to Shri Ganesh Ghosh and Smt. Sabita Ghosh in the metropolitan city of Kolkata, West Bengal, India. She was raised at Kolkata and did her schooling from Kamala Chatterjee School for Girls, Kolkata. She was graduated with Chemistry (Hons.) from Basanti Devi College, affiliation by Calcutta University in 2010. She completed her Master's Degree (M.Sc.) in Organic Chemistry from West Bengal State University, West Bengal in 2012. Later, she enrolled as a research scholar at IIT Guwahati in 2013. She joined the research group of Dr. Pavan K. Kancharla at IIT Guwahati in 2015 and started exploring in development of methodology in Carbohydrate Chemistry. She enjoyed her Ph.D. research work with her lab mates, friends, seniors, and juniors. In the future, she is quite interested in exploring other areas in Chemistry.*