STRATEGIES FOR THE DIASTEREOSELECTIVE SYNTHESIS OF GLYCOSIDES BY CONFORMATIONAL BIAS

A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE

REQUIREMENTS OF THE DEGREE OF

DOCTOR OF PHILOSOPHY

BY

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Dedicated to....

My Parents

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CERTIFICATE

Certified that, the work incorporated in the thesis entitled, "***Strategies for the Diastereoselective Synthesis of Glycosides by Conformational Bias***" submitted by Maidul Islam was carried out by the candidate, under my supervision. The work presented here or any part of it has not been included in any other thesis submitted previously for the award of any degree or diploma from any other University or institution.

Date: 29th May 2017

Pune (MH), India. **Prof. Srinivas Hotha**

DECLARATION

I declare that this written submission represents my ideas in my own words and where others' ideas have been included; I have adequately cited and referenced the original sources. I also declare that I have adhered to all principles of academic honesty and integrity and have not misrepresented or fabricated or falsified any idea/data/fact/source in my submission. I understand that violation of the above will be cause for disciplinary action by the Institute and can also evoke penal action from the sources which have thus not been properly cited or from whom proper permission has not been taken when needed.

Date: 29th May 2017 **Maidul Islam**

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Last, but not the least, I dedicate this achievement to my family members who walked along with me, sharing all ups and downs. Finally, it has been a difficult task to capture and express my feelings for my family members. What I am and intend to be in the future is because of the good will and unstinted support of my grandmother, parents, elder brothers (Ananda), younger brothers (Mijanur), sister (Nargish), sister-in-law (Minhaz da) and niece (Muskan, Sanzida) without knowing much what I am doing exactly, just wishing me all the time with no expectations. No words are enough to acknowledge them for their patience and sacrifice which were always remains a source of inspiration and will remain throughout my life. My success now and always will be dedicated to them.

Maidul Islam

Contents

- ^{1}H NMR spectra were recorded on AV 200, AV 400, DRX-500 MHz, JEOL ECX 400 or Bruker Avance 500 MHz spectrometer using tetramethylsilane (TMS) as an internal standard. Chemical shifts are expressed in ppm units downfield to TMS.
- ^{13}C NMR spectra were recorded on AV 50, AV 100, DRX-125 MHz, JEOL ECX 100 or Bruker Avance 125 MHz spectrometer.
- High resolution mass spectroscopy (HRMS) was performed on Waters Synapt G2 and Maldi-TOF.
- IR spectra were recorded on Perkin-Elmer 1310 and Perkin-Elmer 1600 FT-IR spectrometers with sodium chloride optics and are measured in cm^{-1}.
- Specific rotations were measured on a JASCO P-1020 or Rudolph polarimeter and measured in degree.
- All reactions were monitored by Thin-Layer Chromatography carried out on precoated Merck silica plates (F254, 0.25 mm thickness); compounds were visualized by UV light or by staining with anisaldehyde spray.
- All reactions were carried out under nitrogen or argon atmosphere with dry freshly prepared solvents under anhydrous conditions and yields refer to chromatographically homogenous materials unless otherwise stated.
- All evaporators were carried out under reduced pressure on Büchi and Heildoph rotary evaporator below 45 °C unless otherwise specified.
- Silica gel (100-200) and (230-400) mesh were used for column chromatography.
- All gold and transition metal salts were purchased from multinational commercial vendors.
- Materials were obtained from commercial suppliers and were used without further purification.
- Scheme, Figure and Compound numbers in abstract and individual chapters are different.

Å – Angstrom

Ac – Acetate

AcBr – Acetyl bromide

AcCl – Acetyl chloride

AcOH – Acetic acid

Ac_2O – Acetic anhydride

AG – Arabinogalactan

AIBN – Azobisisobutyronitrile

Ara*f* – arabinofuranosyl / arabinofuranoside

Bn – Benzyl

BnBr – Benzyl bromide

Boc – *t*-butylcarbonyl

Bz – Benzoyl

BzCl – Benzoyl chloride

Calcd – Calculated

Cbz – Carboxybenzyl

cat. – catalytic

$CDCl_3$ – Chloroform-D

$CHCl_3$ – Chloroform

d – days

DBU – 1,8-Diazabicycloundec-7-ene

DDQ – 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone

DEPT – Distortionless Enhancement by Polarization Transfer

DIPEA – N,N-Diisopropylethylamine

DMAP – N,N-Dimethylaminopyridine

DMF – N,N-Dimethyl formamide

D_2O – Deuterium oxide

δ – delta (in PPM)

eq. – equivalents

Et_3N – Triethyl amine

FE-SEM – Field Emission Scanning Electron Microscopy

g – gram

Gal*f* – galactofuranosyl / galactofuranoside

h – hour

HRMS – High-Resolution Mass Spectrometry

HSQC – Heteronuclear Single Quantum Coherence

Hz – Hertz

Im. – Imidazole

IR – Infrared

J – coupling constant

Kg – Kilogram

LAM – Lipoarabinomannan

Man*p* – mannopyranosyl / mannopyranoside

MeOD – Methanol-D4

mg – milligram

min. – minutes

MHz – Megahertz

mL – millilitre

mmol – millimolar

MS – Molecular sieves

Mtb – Mycobacterium tuberculosis

NAP – N-bromomethyl naphthalene

NGP – Neighbouring group participation

NIS – N-Iodosuccinimide

NMR – Nuclear Magnetic Resonance

NNGP – Non-neighbouring group participation

NPG – *n*-Pentenyl glycoside

PMB – *p*-Methoxy benzyl

PMBCl – *p*-Methoxy benzyl chloride

Py – Pyridine

PTSA– *p*-Toluene sulfonic acid

ppm – parts per million

RDAS – Reciprocal-Donor-Acceptor-Selectivity

Rib*f* – ribofuranoside / ribofuranosyl

rt – room temperature

sat – saturated

Tb – tuberculosis

TBAF – tetra-n-Butyl ammonium fluoride

TBAI – tetra-n-Butyl ammonium iodide

TBDMS – *t*-Butyldimethylsilyl

TBDMSCl – *t*-Butyldimethylchloride

TBDPS – *t*-Butyldiphenylsilyl

TBDPSCl – *t*-Butyldiphenylsilylchloride

TCA – trichloroacetimidate

TfOH – Triflouromethanesulfonic acid

THF – Tetrahydrofuran

TLC – Thin Layer Chromatography

TMSOTf – Trimethylsilyltrifluoromethanesulfonate

µg – microgram

µmol – micromolar

µL – microliter

The thesis entitled "***Strategies for the Diastereoselective Synthesis of Glycosides by Conformational Bias***" is divided into five chapters. Chapter one demonstrates brief ideas about the importance of glycoconjugates and oligosaccharide and stereo-selective synthesis of glycoconjugates. Chapter two describes hypervalent iodine mediated stereo- and regio-selective synthesis of C-2-*deoxy* glycosides and amino acid glycoconjugates. In chapter three, we have determined the influence of steric crowding on the diastereoselective arabinofuranosylation. In chapter four, we have exploited Reciprocal-Donor-Acceptor-Selectivity (RDAS) to assemble hencontapentasaccharide (51units) of mycobacterial Lipoarabinomannan. In chapter five, Reciprocal-Donor-Acceptor-Selectivity (RDAS) for the synthesis of four possible hybrid isomers of Ara*f*-Rib*f* glycolipids at disaccharide and pentasaccharide level was described.

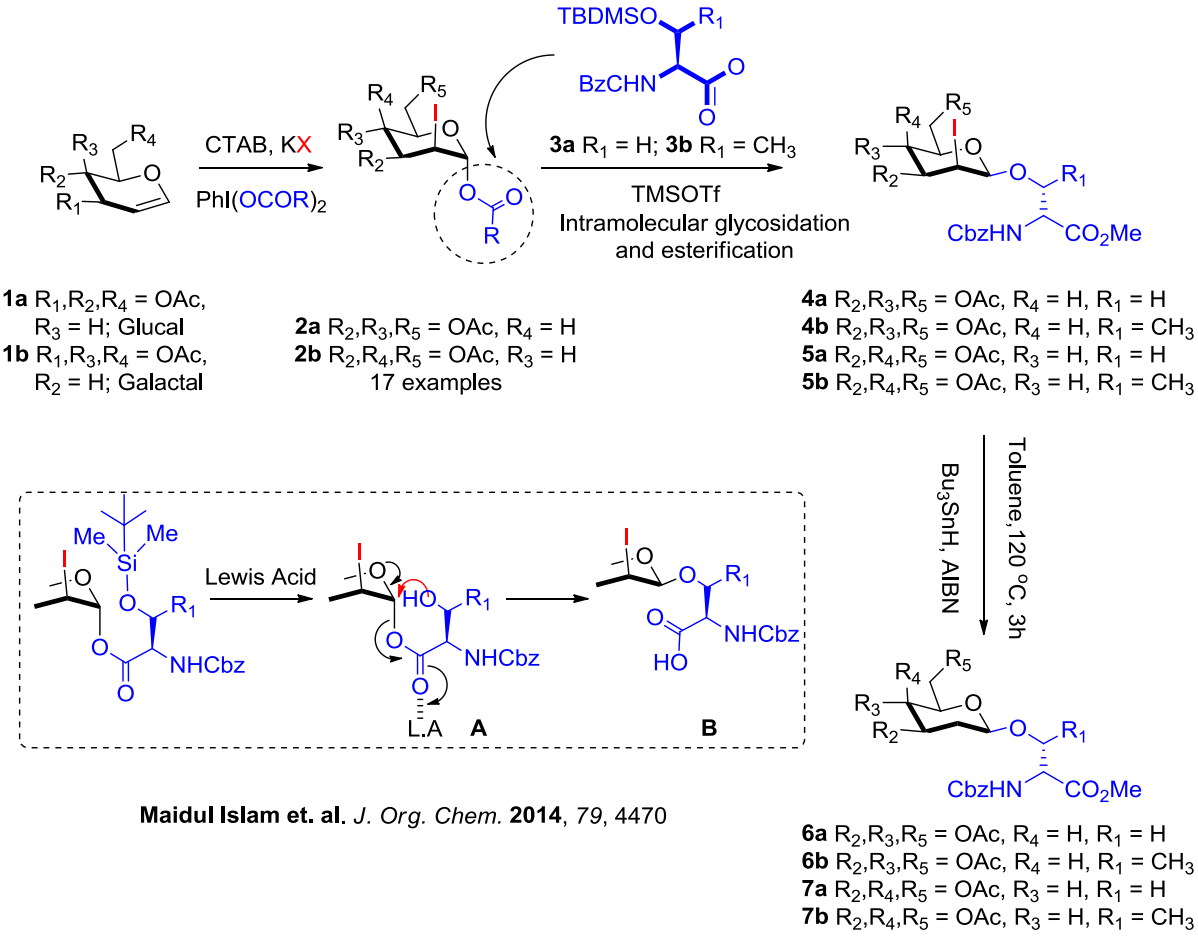
Chapter 1: Introduction to Stereoselective Glycosylation

Glyconjugates and oligosaccharides are the essential parts of naturally occurring, carbohydrate containing compounds including polysaccharides, glycoproteins, proteoglycans and glycolipids. In these glycoconjugates, sugar unit can exist in pyranose, furanose or 2-*deoxy* form which is attached with numerous discrete molecules having different biological activity. Despite the biological and medical importance, glycobiology sub-discipline is suffering from the lack of pure and structurally well-defined glycoconjugates and oligosaccharides. Natural sources provide micro-quantities and as heterogeneous forms which are very difficult to purify and characterize. Therefore, it is clearly evident that chemical synthesis of such complex structures in the laboratory requires access to reliable and high yielding glycosylation methods and novel approaches to construct interglycosydic bond in highly regio- and stereoselective fashion. Last few decades have witnessed development of different types of glycosyl donors; among them, trichloroacetamidate, thiophenyl, n-pentenyl and alkyne glycosyl donors are famous. For stereo- and regioselectivity event, intermolecular and intramolecular approaches are often employed.

Chapter 2: Hypervalent Iodine Mediated Synthesis of C-2 *deoxy* Glycosides and Amino acid Glycoconjugates

Stereo- and regio- selectivities in organic synthesis is of paramount importance and often chiral environment or the template guided asymmetric synthesis are well studied. Reactions in self-assemblies might be yet another avenue for stereo- and regio- selectivities. Therefore

we thought to utilize cetyltrimethylammonium bromide (CTAB) derived reverse micelle nano-reactor as a chiral template for stereo- and regio selective synthesis of 2-*deoxy*-2-iodo



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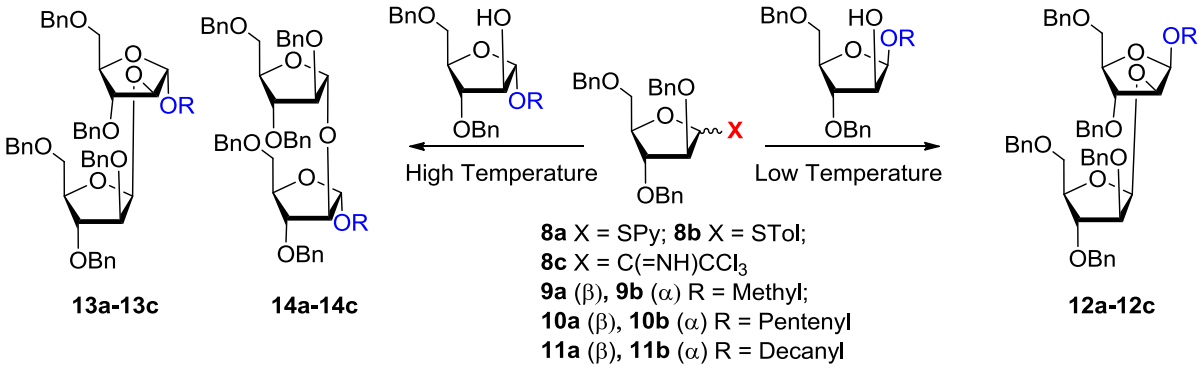
acetate glycosides. The second part of my thesis deals with the synthesis of 2-*deoxy*-2-iodo acetate glycosides and its subsequent conversion to 2-*deoxy*-β glycosides. The π-bond of glycals (**1a**, **1b**) was embedded in CTAB derived reverse micelle, was activated by the electrophilic hypervalent iodine(III) reagent and the intermediate was displaced in S_N^2 fashion by acetate followed by CTAB bound iodide anion to obtaine 2-*deoxy*-2-iodo acetate glycosides. Among the various anomeric esters, serinyl (**3a**) and threonyl (**3b**) esters were converted to 2-*deoxy*-2-iodo-β glycosides (**4a**-**5b**) via intramolecular glycosidation. Radical mediated C-2 deiodination afforded 2-*deoxy*-β serinyl/threonyl glycosides (**6a**-**7b**) in a post-glycosylation synthetic effort.

Chapter 3: Influence of Steric Crowding on the Diastereoselective Arabinofuranosylations

Glycoconjugates and oligosaccharides belong to a class of biomolecules that play pivotal roles in various cellular events. Glycoconjugates contain an oligosaccharide unit or glycan attached to a lipid, peptide and/or steroid in a stereodefined fashion and thus access to oligosaccharides is required. Construction of glycans relies upon two important building



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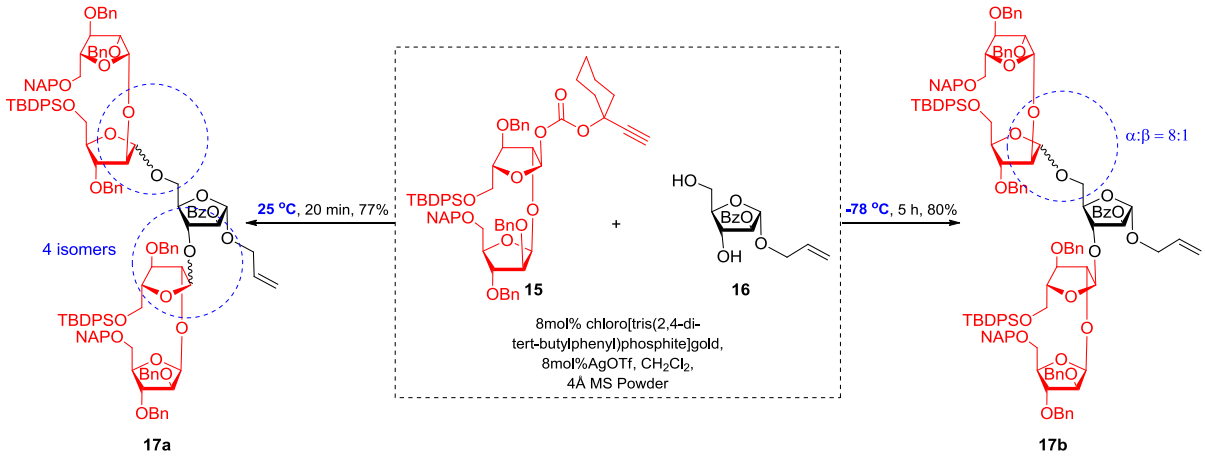
blocks which are called glycosyl donor and glycosyl acceptor (or aglycon). A glycosyl donor is defined as any substance that can donate its glycon to the acceptor through an interglycosidic bond. Activators promote the formation of an intermediate called oxocarbenium ion which will be attacked by a nucleophile present in the form of an aglycon to form glycosides. Most of the studies in the literature consider the stereoelectronic effects of the glycosyl donors only while tuning the stereoselectivity during the glycosidation. However, the fate of the glycosidation reaction also depends on the stereoelectronic effects on the glycosyl acceptor as well. Fraser-Reid coined the term reciprocal donor activity selectivity (RDAS) to explain effects of both donor and acceptor stereoelectronics on the outcome of the glycosidation. Mycobacterial cell wall consists of arabinogalactan (AG) and Lipoarabinomannan (LAM) have an oligoarabinofuranoside having both 1,2-*trans* and 1,2-*cis* furanoside linkages. 1,2-*trans* linkages can be easily prepared by taking advantage of neighbouring group participation (NGP) effect of C-2 benzoyl/acetate protecting group at glycosyl donor. In turn synthesis of 1,2-*cis* furanoside is much more challenging and difficult task. In this regard, we have exploited Reciprocal-Donor-Acceptor-Selectivity (RDAS) for 1,2-*cis* arabinofuranosylation in good yield. Glycosidation of armed arabinofuranosyl donor (**8a**-**8c**) and 1,2-*cis* sterically crowded (less reactive) arabinofuranosyl acceptor (**10a,11a**) (at lower temperature afforded only 1,2-*cis* arabinofuranosyl disaccharides **12b**-**12c**. Although trend in disaccharide level also followed at trisaccharide and hexasaccharide level, however, at hexasaccharide stage we got inseparable mixture of all four isomers of hexasaccharides.

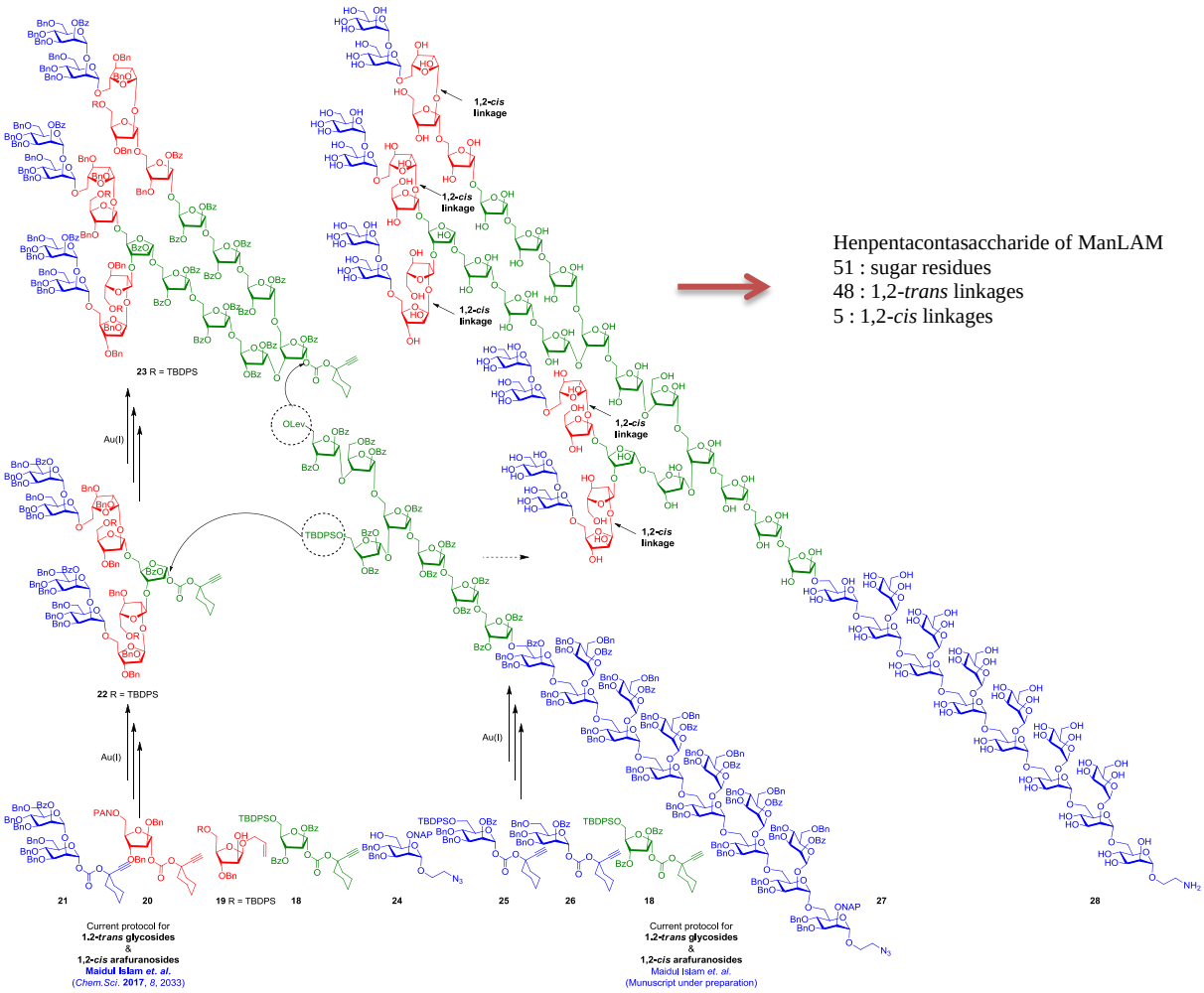
Chapter 4: Expedient synthesis of LAM epitope

Lipoarabinomannan (LAM) is one of the major constituents of Mycobacterium tuberculosis cell wall and active immunogenic molecular scaffold for antituberculosis drug and vaccine development. Although structurally diverse, LAM has a mannan backbone having α-1,2 and α-1,6 linked mannopyranoside residue which is attached to phosphatidylinositol and arabinofuranoside. Further arabinofuranoside consists of highly complex branching having both 1,2-*cis* and 1,2-*trans* linkages and non- reducing end of 1,2-*cis* arabinofuranoside is capped by mannopyranoside. Owing to its intriguing structure and bioactivity, LAM has



received significant attention for synthetic studies. Most of the reports in the literature dealt with the synthesis of arabinan and mannan only and thus far no efforts were visible for the entire construct of arabinomannan by chemical means. In this premise, we envisioned that the gold catalysis discovered in our group could be of great significance for the synthesis of full length arabinomannan of *Mycobacterium tuberculosis*. Our synthetic journey started with the synthesis of most challenging 1,2-*cis* pentasaccharide **17(a, b)**. As discussed earlier, exploiting RDAS, during the synthesis of hexasaccharide, resulted in an inseparable complex mixture of hexasaccharide; hence, we have employed **15** and **16** for gold catalysed glycosylation to obtained pentasaccaride **17**. At room temperature, glycosylation of **15** with **16** afforded inseparable mixture of all four possible pentasaccharides. Surprisingly, when **15** was subjected to glycosylation with **16** at -78 ^{o}C, only two pentasaccharide in α:β = 8:1 ratio was obtained. Next, arabinomannan nonasaccharide carbonate **22** was assembled *via* deprotection of two NAP-ether units in **17b** using DDQ in CH_2Cl_2/MeOH to get pentasaccharide diol which was subsequently glycosylated in presence of Au (I) catalyst with **21**, hydrolysis of allyl group to afford hemiacetal followed by protection of hemiacetal with cyclohexyl carbonate reagent. Iterative glycosylation followed by deprotection generated

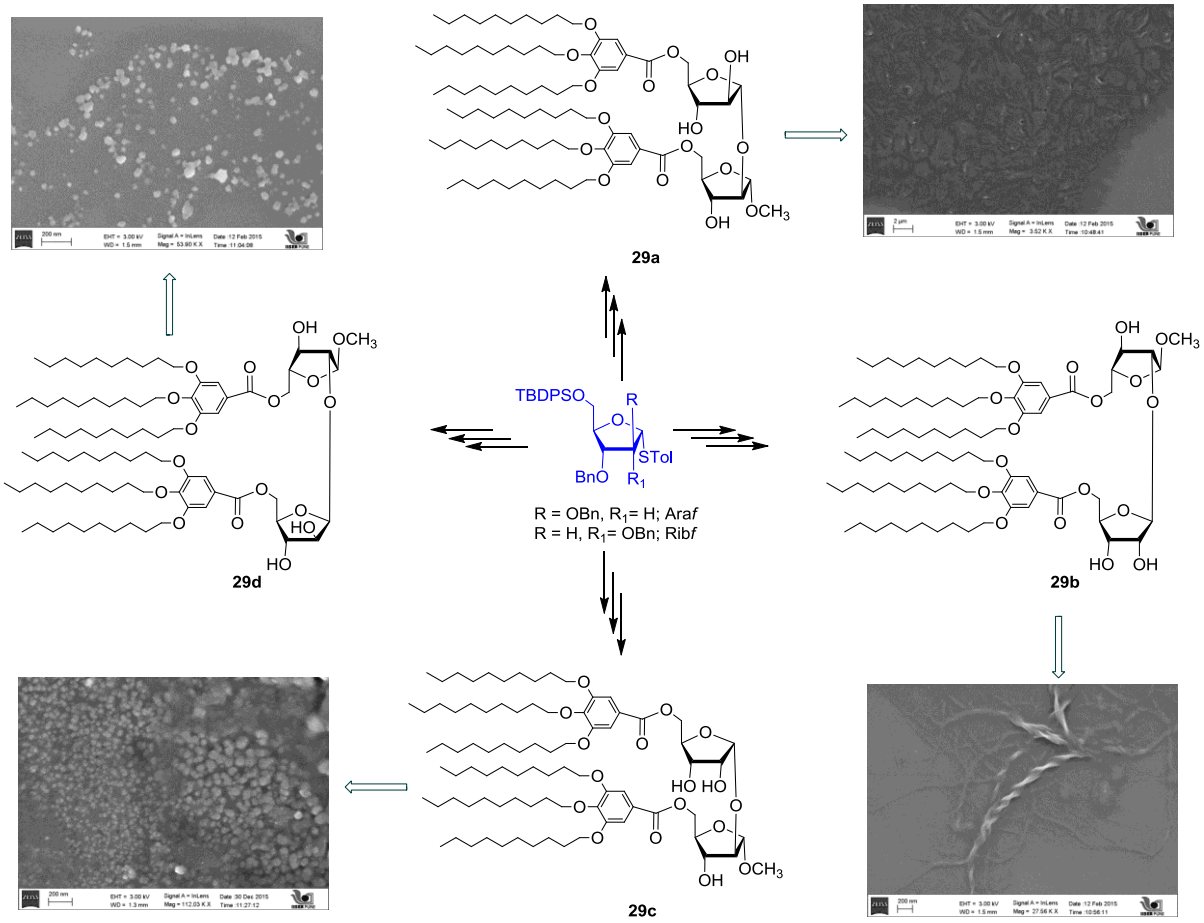
heneicosasaccharyl (**23**) and tetradecasaccharyl (**27**) arabinomannan. Final glycosylation of **27** with **23** and **22** and subsequent global deprotection steps are under progress.



Chapter 5: RDAS to investigate the impact of mycolic acid and furanose ring in Mtb cell wall

Tuberculosis (TB) has plagued mankind for centuries and still continues to kill more than two million lives every year globally. *Mycobacterium tuberculosis* (Mtb) is the etiological agent and pioneering efforts from the Brennan group highlighted two major carbohydrate epitopes *viz.* Lipoarabinomannan (LAM) and Arabinogalactan (AG) in the cell surface of Mtb. Both LAM and AG have an oligoarabinofuranoside which is highly characteristic to the Mtb cell wall. Presence of xenobiotic furanosyl forms of arabinose, galactose and cyclopropanes in the lipids can raise a few questions: (i) why Mtb chose furanoses over pyranoses; (ii) why Mtb chose Ara*f* over other pentoses; (iii) why Mtb requires two extra steps two synthesize

particularly 1,2-*cis* Ara*f*s at the non-reducing end; (iv) why Mtb did not utilise 1,2-*trans* Ara*f* or 1,2-*trans* Rib*f* at the non-reducing end; (v) Is there any relation between arabinolipid of Mtb and its survival under extreme conditions?. To investigate these events, exploiting



RDAS, we have prepared four possible hybrid mixtures of Ara*f*-Rib*f* (**29a**-**29d**) glycolipids at disaccharide level. Preliminary analysis by FE-SEM images disclosed that the glycolipids **29c** and **29d** assembled in particle morphology; whereas **29a** and **29b** showed fibre, helix or sheet morphology that differs depending upon the solvents. To get the better understanding, we have also exploited RDAS to prepare four possible hybrid mixtures of Ara*f*-Ribo*f* glycolipids at pentasaccharide level. Currently, employing modern spectroscopic and microscopic techniques, different physicochemical studies on a library of furanoside lipids are underway.

Chapter: 1

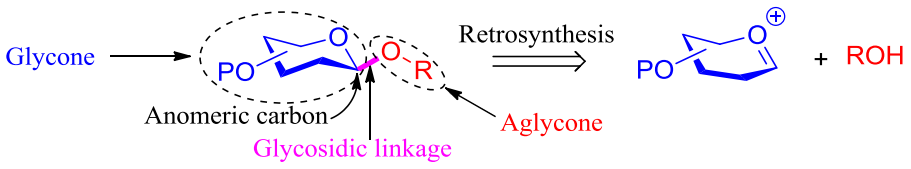
Introduction to stereoselective glycosylations

1.1 Introduction

Among the four biomolecules, glycoconjugates and oligosaccharides are naturally occurring compounds which are increasingly used as probes for biological research and development of drugs and candidate vaccines.[1] Mostly carbohydrates are covalently linked to peptides, proteins, lipids and sugar residues to form dissolved or cell surface respective glyco-peptides, glyco-proteins, glyco-lipids, and poly- or oligosaccharides. Although, carbohydrates are assumed to be for the energy source, in recent decades, they appeared as key players in protein folding, signal transduction, fertilization, blood transfusion, hormonal activity, and cell proliferation.[2] Despite the biological and medicinal importance, glycobiology sub-discipline is suffering from the lack of pure and structurally well-defined glycoconjugates and oligosaccharides. Natural source provides micro-quantities in heterogeneous form of glycoconjugates that are very difficult to purify and characterise.[3] Chemical or chemo-enzymatic synthesis can be employed to obtain good quantities of glycoconjugates which can be easily isolated and characterised.[4] Unlike nucleic acids and protein synthesis, major obstacles for the oligosaccharide and glycoconjugate synthesis are: (i) complex branching and asymmetric nature, (ii) they are assembled by either α- or β-interglycosidic linkages, (iii) multistep protecting group manifestations for oligosaccharides synthesis in chemical approaches and (iv) low abundance of different types glycosyl transferases.

1.2 Glycosylation

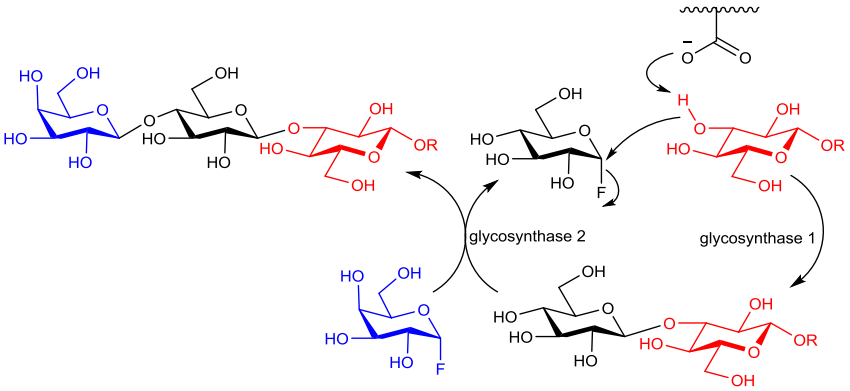
The most crucial aspect in the carbohydrate chemistry is the assembly of sugar units through glycosidic linkages. The reaction is known as glycosylation that can be defined as the activation of the leaving group attached to the anomeric carbon of glycosyl donor in the presence of suitable activators resulting in an oxocarbenium ion intermediate that will be attacked by the acceptor molecule containing one free hydroxyl group or a carbon nucleophile or a thio-nucleophile or some *O*-*N*- or an ester nucleophile. In general, glycosylation reactions can be performed in two approaches *viz.* enzymatic and/or chemical glycosylation (Scheme 1.1).[5]



Scheme1.1 Retrosynthetic analysis of glycosylation

1.2.1 Enzymatic synthesis of glycoconjugates

During the past few decades, enzymatic methods are getting employed to prepare various types of oligosaccharides and glycoconjugates.[6] The salient features of enzymatic approaches are: (i) highly regio- and stereo- selectivity, (ii) catalytic and (iii) very mild reaction conditions. In this premise, in a Nobel winning work, Leloir and co-workers have identified a class of glycosyltransferases to assemble oligosaccharides utilizing sugar nucleotides as glycosyl donors. Although novel glycosyltransferases showcase broad substrate compatibility and high yield, the process becomes complicated by availability and cost of glycosyl transferases. To circumvent the limitation associated with glycosyltransferases, a cheaper substrate compatible (sugar halides and sugar *p*-nitrophenyl) glycosidases have been introduced to obtain glycoconjugates in very low yields. Withers group addressed these problems by introducing glycosynthases, mutants of glycosidases which were obtained by the reinstatement of one of the catalytic aspartic or glutamic acid with another amino acid and subsequently utilized to prepare a series of glycoconjugates from the fluoride glycosyl donors (Scheme 1.2).[7]



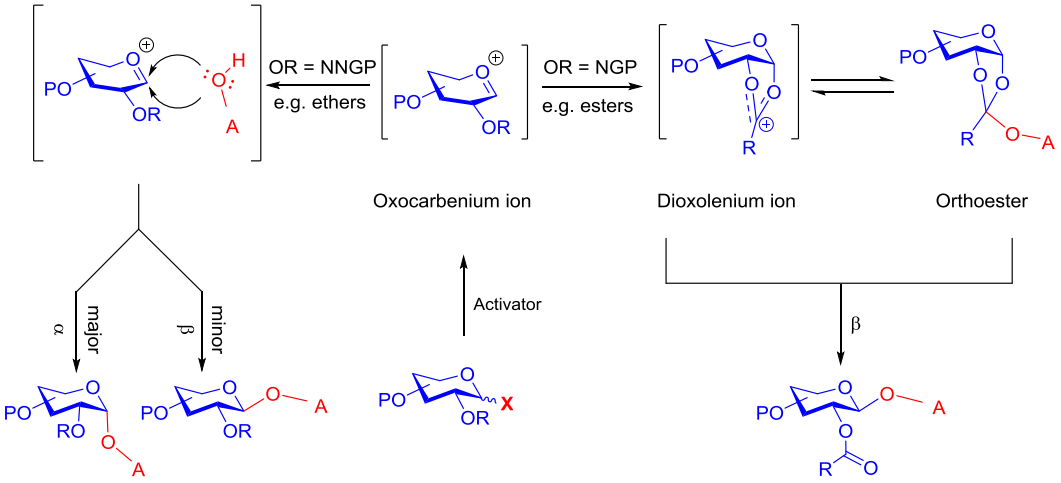
Scheme 1.2 Glycosylation in enzymatic approaches

Recently, few glycan modifying enzymes such as acetyltransferases, oxidases, sulfotransferases and epimerases have been reported for the post-glycosylation modification of glycoconjugates and oligosaccharides.[6b,8] Further, with the advent of automated enzymatic approach, C.-H. Wong and co-workers have assembled a variety of glycoconjugates with solid as well as water soluble polymeric supports. However, major drawbacks in enzymatic approaches are: (i) as specific enzymes are used to access a specific transformation and with huge diversity of the glycosidic linkages, necessitates large collection of different costly and rare enzymes, (ii) compatibility of the enzymes with saccharides having unusual or unnatural

sugar substrate and (iii) minor perturbations of the catalytic site of the enzymes by mutation can hamper the reaction rate. Hence, to avoid this limitation, chemical or chemo-enzymatic approaches to access diverse set glycoconjugates and oligosaccharides would be more advantageous.[9]

1.2.2 Chemical synthesis of glycoconjugates

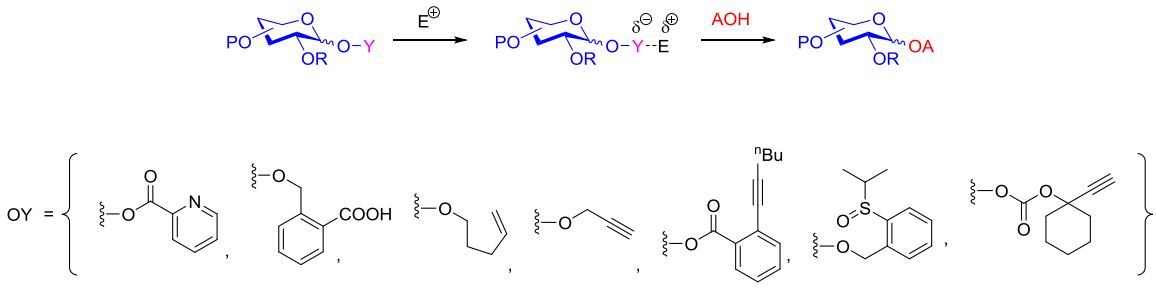
Glycosidic bond can be constructed by nucleophilic displacement of a leaving group (X) present at the anomeric carbon of a sugar unit by other sugar alcohol or any nucleophiles in the presence of suitable activators. During this process, the sugar partner



Scheme 1.3 Glycosylations by chemical approaches

'donating' the sugar unit is called glycosyl donor, while alcohol that 'receives' sugar unit is called as a glycosyl acceptor. In general, promoters or activators help to activate the leaving group and facilitate its departure; activators can be Lewis acids, Brønsted acids or neutral reagents. Along with promoters, some additives such as molecular sieves and sterically hindered base are also used in glycosylation to scavenge respective water and excess acid. The success of any chemical glycosylation relies on numerous factors such as reactivity of glycosyl donor and acceptor, choice of leaving group, activation system, reaction temperature and solvent. Departure of the leaving group generates the half-chair oxocarbenium ion which can undergo nucleophilic attack by the acceptor molecules to afford the desired glycosides. At this stage, chirality or stereoselectivity of newly formed glycosidic bond largely depend on the conformation of acceptor and donor and C2-protecting group of the donor. In the presence of C2-benzoate or acetate, oxocarbenium ion is trapped by C2-ester group by virtue of neighbouring group participation (NGP) to generate dioxolenium ion from which acceptor

can attack from the unhindered phase resulting directly 1,2-*trans* glycosides. Presence of non-neighbouring group participating (NNGP) group at C2-position makes the acceptor molecule access both α- and β- face of the oxocarbenium ion affording α/β mixture of glycosides and the α/β ratio is governed by various electronic and steric factors (Scheme 1.3).



Scheme 1.3.1 Glycosylation in remote activation approaches

Chemical glycosylation can be sub-divided into two groups'*viz.* (i) stoichiometric and (ii) catalytic glycosylation. A stoichiometric approach requires one or more than one equivalents of activators to activate one equivalent of the glycosyl donor whereas catalytic methods as the name suggests employ catalytic quantity of reagents. Hence, possibility of generating side products or waste materials in stoichiometric glycosylation reaction will be more. Further, both stoichiometric and catalytic glycosylation can be further classified into four sub-groups which are described as below.[5b,10]

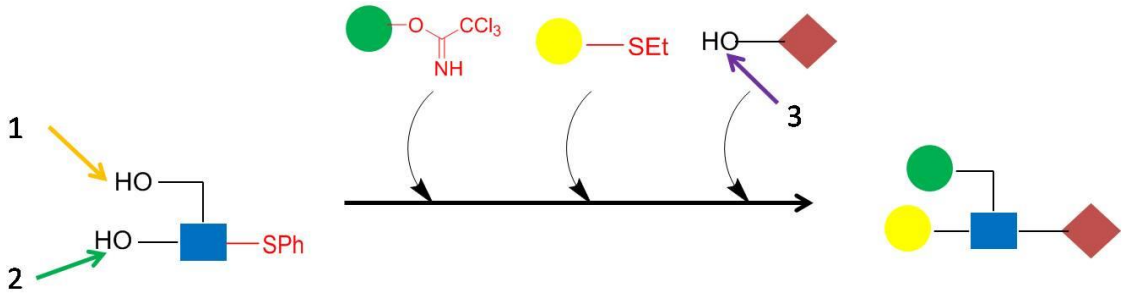
1.2.2.1 Glycosidation by remote activation

Glycosylations by remote activation are milder and are traceless because activation of the functional group Y (olefin, alkyne thio, etc.) will be away from the *O*-ether/*O*-carbonyl/*O*-carbonate anomeric site. The activated remote functionality, in turn, assist to depart the anomeric leaving group in intramolecular fashion to afford oxocarbenium ion which then undergoes subsequent glycosylation with nucleophile or acceptor molecules (Scheme 1.3.1).[11]

1.2.2.2 Glycosidation by one pot orthogonal methods

To expedite the rapid synthesis of oligosaccharides, one pot orthogonal glycosylation has been developed. In this novel glycosylation strategy, a glycosyl donor is chemoselectively activated in the presence of other potential glycosyl donors. Therefore, it is facilitated from classical glycosidation by reducing the number of protection and deprotection steps, in turn, enhances the efficiency and overall yield of the glycosylation reaction. It relies on the

differences in reactivity of different glycosyl donor which may be obtained by varying the electron donating and withdrawing protecting groups on the glycosyl donor to provide armed-disarmed glycosyl donor or by changing chemical nature of leaving groups (Scheme 1.3.2).

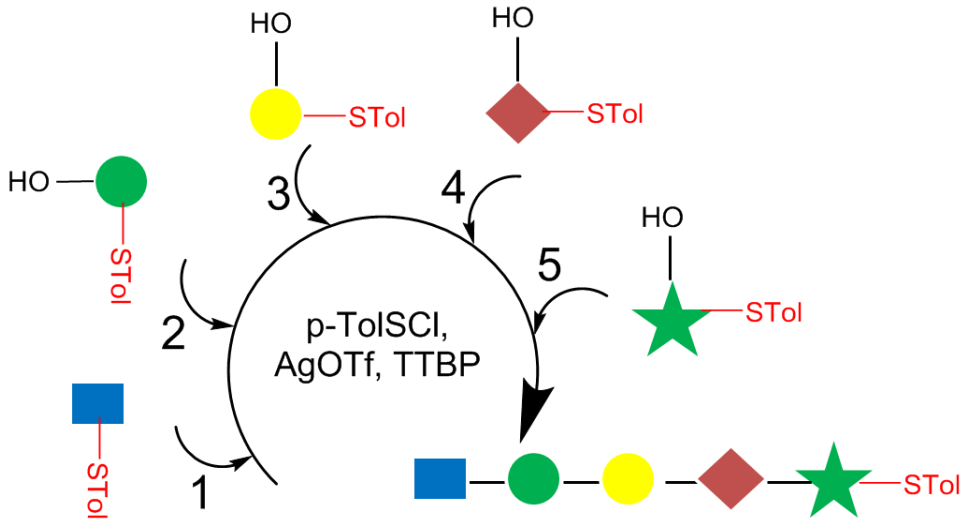


Scheme 1.3.2 Glycosylation in one pot orthogonal approaches

Owing to these elegancies, a series of oligosaccharides were assembled employing this method in the last few decades. For example, S. C. Hung and co-workers have exploited one pot orthogonal glycosylation to prepare tetrasaccharide of proteoglycan (Scheme 1.3.2), while J-S Yang and co-workers have assembled linear and branch type of arabinan as well as galactofuranose fragments of Mycobacterial and Streptococcus cell wall.[12]

1.2.2.3 Glycosylation by preactivation or latent activation

First, the term 'Preactivation' was introduced by Crich and it is very similar to one pot orthogonal approach, except, instead of different leaving groups at the anomeric carbon, identical leaving groups are utilized and activated utilizing identical promoters. It attributes the preactivation of glycosyl donor by suitable promoters to afford reactive intermediate that is actually undergoing glycosylation with acceptor molecule having identical leaving group at the anomeric carbon (Scheme 1.3.3). In this context it is worthy to mention that Crich and co-workers preactivated 4,6-*O*-benzylidine protected mannose sulfoxide using Tf_2O at -78 ^oC and subsequently glycosylated by the acceptor to afford high β-selective mannosides; while premixing activation of glycosyl donor in the presence of acceptor at identical reaction condition resulted in only α-mannosides. Later, Guo and co-workers adopting latent activation glycosylation assembled glycophosphatidyl anchors, arabinogalactan and lipoarabinomannan fragments present in Mtb cell wall. The most striking achievement was gained very recently by X-S Ye *et al.*, by preparing 92-mer of mycobacterial arabinogalactan utilizing the latent activation strategy.[13]



Scheme 1.3.3 Glycosylation in latent/preactivation approaches

1.2.2.4 Glycosylations by De Novo approaches

Due to the immense complexity, stereoselective and efficient assembly of glycoconjugates and oligosaccharides remains a major challenge for carbohydrate community. In this regard, often de novo approaches have been employed to construct biologically relevant complex, rare and unnatural glycosides. In general, de novo glycosylation relied upon the synthesis of the glycosidic bond by a very mild asymmetric reaction followed by the ring expansion or ring cyclization by respective chemical transformations and at last functionalisation of the resulting olefin by dihydroxylation.The main advantages of de novo glycosylations are: (i) high chemo- and stereo-selectivities and (ii) rare and unnatural glycosides are synthesized by asymmetric synthesis unlike classical glycosylation chemistry requires several complicated steps. This approach has been introduced and pioneered by O'Doherty, but utilized effectively by Seeberger and Rhee *et al.* independently by synthesizing a series of rare and complex glycoconjugates and oligosaccharides.[14]

1.2.3 Account of glycosyl donors

As described previously, construction of glycosidic linkage is one of the herculean tasks in assembling glycoconjugates and oligosaccharides. In the last few decades, although many potential glycosyl donors have been developed, even today, there is no universal glycosylation methodology for oligosaccharide synthesis and it is very difficult to predict which glycosylation method would be suitable to prepare a specific glycosidic linkage. Hence, each oligosaccharide synthesis becomes an individual research project which often

requires months or years to furnish the corresponding oligosaccharide successfully. The story of glycosyl donor begins with Fischer glycosylation wherein unprotected cyclic hemiacetal and a large excess of alcohol are refluxed for a long time under acidic condition. To assemble oligosaccharides, Fisher glycosylation is not ideal as employing excess alcohol might be very expensive and it might be difficult to remove excess alcohol at post-glycosylation step. Numerous glycosyl donors are developed for glycoconjugates and oligosaccharide syntheses in order to improve the scope of the glycosidation reaction.

1.2.3.1 Glycosyl halides

The first practical glycosylation donor was developed by Koenigs and Knorr in 1901 wherein glycosyl halides (bromides and chlorides). Varieties of heavy silver salts are identified as promoters in this glycosylation, including AgOTf, Ag_2O, Ag_2CO_3, $AgClO_4$ and $AgNO_3$. Later, Helferich *et al*. enhanced the efficiency of the glycosylation reaction with the introduction of organic solvent soluble metal salts such as $HgBr_2$, $Hg(CN)_2$, HgO, $HgCl_2$ and HgI_2. Glycosyl iodides are less stable; but, are more advantageous over glycosyl chlorides and bromides by virtue of their efficiency, reaction time and stereoselectivity. Glycosyl iodides were first prepared from glycosyl bromide by the treatment of NaI in acetone; however, Gervay-Hague systematically studied the mechanism of α/β-glycosyl iodides formation and subsequently stereoselective glycosylation were conducted. In basic reaction medium, glycosyl iodides can afford β-glycosides whereas *in situ* anomerization can generate α-glycosides. In 1981, most stable glycosyl fluoride was introduced by Mukaiyama *et al*. Over the years, numerous fluorophilic reagents were developed for the activation of glycosyl fluorides such as $SnCl_2$-$AgClO_4$ (Mukaiyama *et al.*), SiF_4 (Noyori *et al.*), TMSOTf (Noyori *et al.*) and $BF_3.OEt_2$ (Nicolaou *et al.*). Despite the tremendous advantages of glycosyl halides as donors, they are not routinely utilized to assemble large scale synthesis of glycosides owing to the involvement of very toxic promoter systems.[10a,15]

1.2.3.2 Glycosyl esters and orthoesters

Helferich and Kochetkov independently introduced glycosyl esters and glycosyl orthoesters as glycosyl donors respectively. Easy accessibility and very good stability of glycosyl esters from readily available precursors is the most advantageous over others. A series of Lewis and Brønsted acids including $ZnCl_2$, $SnCl_4$, $FeCl_3$, $BF_3{\cdot}OEt_2$, TfOH and TMSOTf, were employed to activate glycosyl esters. The utility of glycosyl ester donors, however, was hampered by the low reactivity and the need of stoichiometric quantity of promoters which in turn might

become very harsh for an oligosaccharide synthesis. On the other hand, glycosyl esters on treatment by acid halide generate glycosyl halide which in the presence of base can afford glycosyl 1,2-orthoester. Among the various 1,2-orthoesters, at first, Kochetkov developed *t*ert-butyl orthoester and activated with 2,6-dimethylpyridinium perchlorate to provide desired glycoconjugates. Although, catalytic quantity of promoters can activate 1,2-orthoesters, often direct glycoside as a side product poses limitation.[16]

1.2.3.3 Thioglycosides

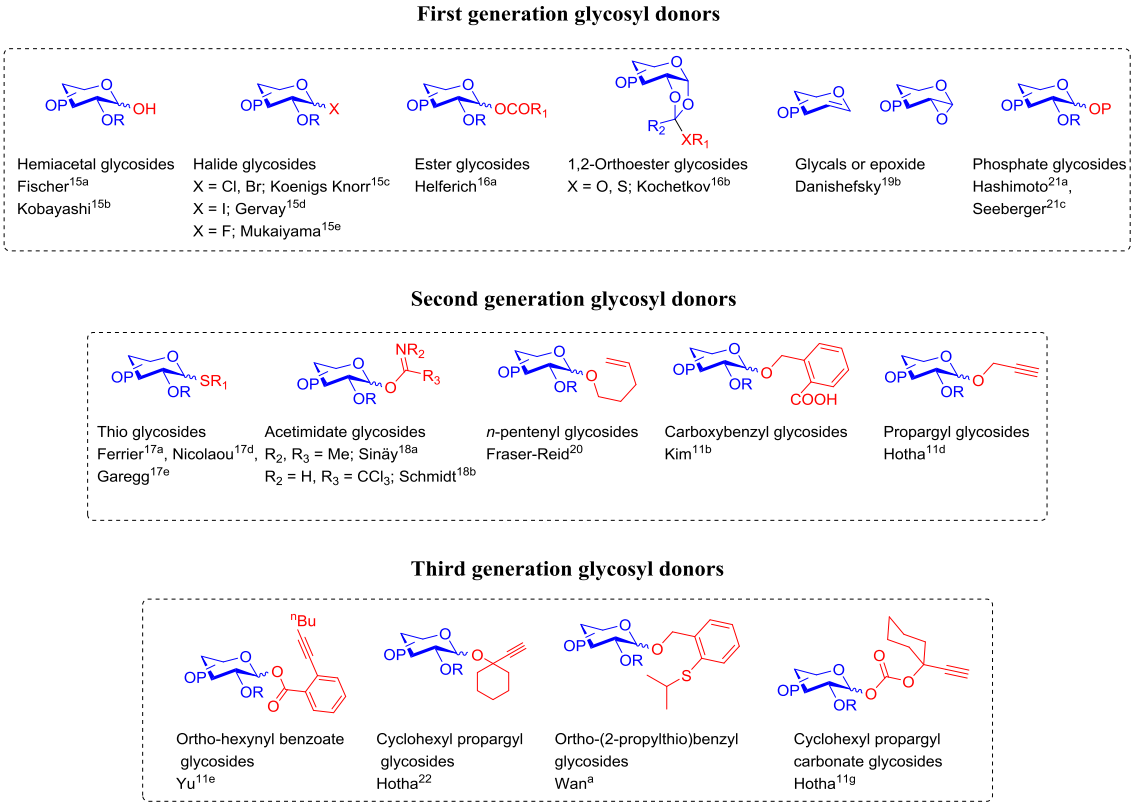
Thioglycosides as glycosyl donors are most stable, diverse and widely used to construct disaccharides to oligosaccharides.They can be easily accomplished either from per-*O*-acetate sugar and a mercaptan in the presence of Lewis acids such as $BF_3.OEt_2$, TMSOTf or $SnCl_4$ (for both pyranose and furanose) or from fully protected sugar hemiacetal by the addition of dithiane and $^{n}Bu_3P$. Traditionally, thioglycosides are activated by NIS-AgOTf/TfOH (Fraser-Reid and Van Boom *et al.*) but they can also be activated by at least seven or eight different orthogonal promoters. The elegancy of thioglycoside donors are: (i) high stability, (ii) can be activated under very mild conditions having temperature range 50 to -90 ^{o}C and (iii) compatible with multiple protecting groups and thus thio-ether becomes a temporary protecting group at the anomeric centre; hence can acts as both glycosyl donor and glycosyl acceptor as well.[17]

1.2.3.4 Glycosyl imidates

The glycosyl imidates as a glycosyl donor was introduced by Sinäy *et al.* in 1976. However, seminal work by Schimdt identified glycosyl trichloroacetamidate (TCA) as more reactive donors and TCA donors excelled Sinäy'sdonors in many aspects.Thermally and chemically stable TCA donors can be obtained by the treatment of glycosyl hemiacetal with trichloroacetonitrile in the presence of NaH, K_2CO_3, Cs_2CO_3 or DBU. The glycosylation reaction can be smoothly performed in the presence of catalytic amount of $BF_3.OEt_2$, TMSOTf, TfOH or PPTS. Apart from aforementioned promoters, very recently TCA was activated by Au-catalysts as well by Kunz and Schmidt. The main drawbacks of TCA donors are the low stability for armed sugar donor and the formation of trichloroacetamide as the side product. To overcome these limitations, Yu *et al.* introduced *N*-phenyl trifluoroacetamidates donor which can be stored for months and in addition undergo catalytic activation by Lewis acids.[18]

1.2.3.5 Glycals

Glycals emerged as very important and versatile glycosyl intermediates to assemble special class of glycosides i.e. 2-*deoxy* or 2,6-*dideoxy* glycosides. In the presence of electrophiles such as I_2/acceptor or $PhI(OAc)_2$/KI, glycals can afford respective 2-*deoxy*-2-iodo glycosides or 2-*deoxy*-2-iodo acetates. Further, Lemieux *et al.* have utilized glycals for the synthesis of 1,2-anhydro sugar to synthesize sucrose glycosides. The breakthrough in the glycal donor chemistry was achieved by Danishefsky and co-workers with the oxidation of glycals using dimethyldioxirane (DMDO) to give 1,2-anhydro sugar which was subsequently treated with $ZnCl_2$ to provide desired glycoconjugates and oligosaccharides.[19]



Scheme 1.3.4 List of three generation of glycosyl donors

1.2.3.5 *n*-Pentenyl glycosides

In 1988, a new and effective *n*-pentenyl glycosyl donor was introduced by Bert Fraser-Reid. Usually, *n*-pentenyl glycosyl (NPG) donors are prepared from glycosyl hemiacetal and *n*-pentenyl alcohol in the presence of acid at elevated temperature or by the treatment of glycosyl acetate with 4-pentene-1-ol in the presence of suitable Lewis acids. During the activation of *n*-pentenyl glycosides employing NIS-TfOH, remote olefin moiety undergoes

iodination followed by cyclization to release tetrahydrofurfuryl iodide and oxocarbenium ion intermediate which is subsequently attacked by the acceptor molecules to afford corresponding glycosides.[20]

1.2.3.6 Carboxybenzyl glycosides

In 2001, Kim and co-workers reported the use of 2-carboxybenzyl (CB) glycosyl donors by activating the remote carboxylic group using Lewis acid to trigger the consecutive glycosylation process. CB donor can be prepared by two successive steps *via* alkylation of glycosyl halide using 2-(benzyloxycarbonyl) benzyl (BCB) in basic medium, followed by hydrogenolysis to convert –COOBn to corresponding carboxylic acid. Glycosylations by CB-donors can be performed under both basic as well as acidic conditions and hence facilitates the one pot and latent activation glycosylation to assemble oligosaccharides.[11b]

1.2.3.7 Phosphate and phosphite glycosides

In 1980s, glycosyl phosphates and phosphites are investigated as glycosyl donors. In this context, Hashimoto and Ikegami developed diphenyl phosphates and diphenyl phosphine imidates as glycosyl donors respectively. Phosphate donors are readily achieved from glycosyl trichloroacetamidates by treating with phosphorous acid. To activate glycosyl phosphates, Seeberger *et al.* screened a series of Lewis acids including TMSOTf, TBSOTf and $BF_3.OEt_2$ in which TMSOTf was found to be more effective. The key disadvantage of the glycosyl phosphates and phosphites is the requirement of stoichiometric quantity of strong Lewis acid TMSOTf.[21]

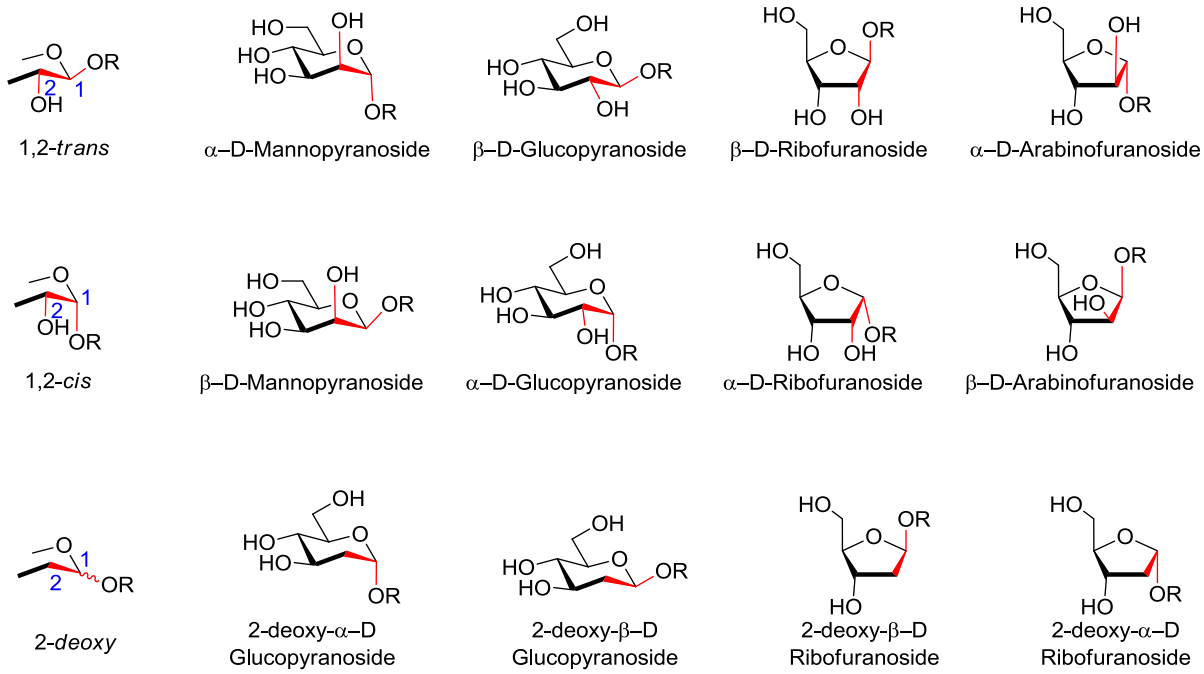
1.2.3.8 Alkyne glycosides

In 2006, Hotha and Kashyap first disclosed the propargyl glycosides as glycosyl donors under Au(III) catalytic conditions. The reaction was carried out on armed per-*O*-benzyl glycosides with different acceptors in acetonitrile solvent at 70 ^{o}C to afford α/β mixture of glycosides. The reaction was facilitated by alkynophilicity of Au(III) halides which activated the remote alkyne moiety resulting in an oxocarbenium ion followed by smooth glycosylation in the presence of acceptors. Later, they have suppressed the elevated reaction temperature by introducing more reactive cyclohexyl propargyl glycoside donors which afforded desired glycosides at 25 ^{o}C. However, aforementioned both alkyne leaving groups were succumbed towards acyl protected glycosyl donors. In the meantime in, Yu *et al.* introduced glycosyl *o*-hexynyl benzoates having both benzyl ethers and ester protecting group, can provide

moderate to good yield of glycosides employing Au(I) catalytic conditions. Difficulties associated with Yu's donors are: (i) low abundance and very expensive leaving group and (ii) requires five to seven steps to prepare the leaving group. To circumvent these limitations, Hotha and co-workers in 2016 developed a highly reactive, catalytically and high yielding cyclohexyl propargyl glycosyl carbonate donor which afforded excellent yields of disaccharides to oligosaccharides using 8mol% each of Au-phosphite and AgOTf in just 15 minutes.[11d-11e,11g, 22]

1.3 Types of glycosidic linkages

Majority of glycoconjugates are assembled through *O*-glycosidic bond; however, there are sugar-*S*, sugar-*N*, sugar-*C*, sugar-carbamate and sugar-*O*-N-linkages are also reported in the literature. Two major obstacles to install these interglycosidic bonds are: (i) the regio-chemistry of newly formed glycosidic bond and (ii) stereochemistry of the resulting glycosidic bond. These linkages are further classified by the nomenclature as α- and β- or to be precise 1,2-*cis* and 1,2-*trans* linkages.[4b]



Scheme 1.4 Representative examples of glycosidic linkages

1.3.1 1,2-*trans* linkages

1,2-*trans* Glycosidic linkages can be easily achieved with the assistance of neighbouring group participation of C-2 esters present in the donor unit. Activation of the glycosyl donor

followed by the departure of leaving group results in an oxocarbenium ion which is further trapped in to a five membered dioxolenium ion intermediate through the anchimeric effect of *C*-2 ester groups. Nucleophiles affect (reactive acceptor) the *trans*-cleavage at *C*-1 of dioxolenium ion to afford desirable 1,2-*trans* glycoside. Less reactive acceptors undergo nucleophilic attack the dioxolenium ion intermediate instead of the C-1 carbon to provide corresponding orthoesters which can further isomerise in the presence of suitable acid to furnish 1,2-*trans* glycosideas delineated above (Scheme 1.3).

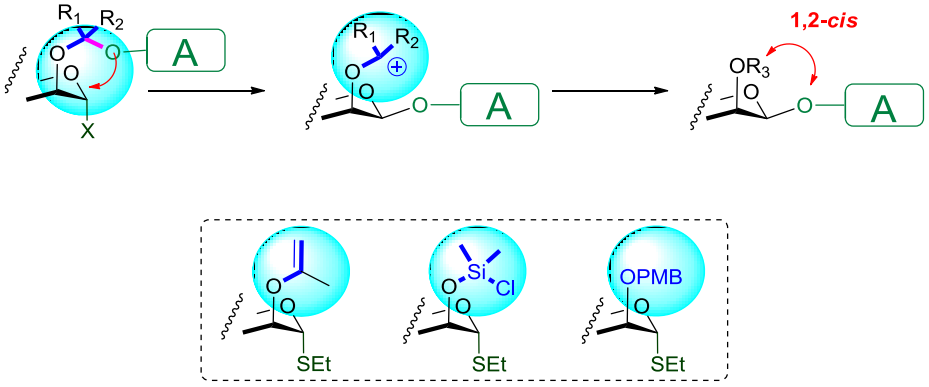
1.3.2 1,2-*cis* linkages

Construction of 1,2-*cis* glycosidic linkages is challenging compared to that of 1,2-*trans* linkages. A first criterion to synthesize 1,2-cis linkages is the presence of non-participating group at C-2 position of glycosyl donor. In the presence of non-participating group, anomeric effect facilitates the 1,2-*cis* glycosides and extent of 1,2-*cis* selectivity relies on the reaction conditions, reactivity of glycosyl donor and acceptor. However, 1,2-*cis*-mannosides cannot be synthesized by exploiting anomeric effect as anomeric effect will favour the 1,2-*trans*-mannosides. Moreover, repulsive interaction between the C2-axial substituent and incoming acceptor will force the acceptor molecule to attack from the axial face affording 1,2-*trans*-(or α)-mannosides.

Development of efficient methods to construct α- and β-2-*deoxy* glycosides stereo-selectively is yet another arduous task in the carbohydrate chemistry. The absence of C-2 substituents diminish the anchimeric assistance and stereoelectronic effects which in turn make the construction of both α- and β- 2-*deoxy* glycosides a herculean task to.

In addition, five membered furanosides are conformationally more flexible compared to the pyranoside sugars due to their inherent flexibility; furanoside oxocarbenium ion can exist in twenty different stable conformations in solution phase. Hence, it is tough to control the 1,2-*cis* stereoselectivity in furanosylations. Tuning of stereoselectivity is further complicated by the lack of anomeric effect in furanosides.

Two most useful approaches for the stereoselective synthesis of 1,2-*cis* linkages are (i) intramolecular approaches and (ii) intermolecular approaches as described below.

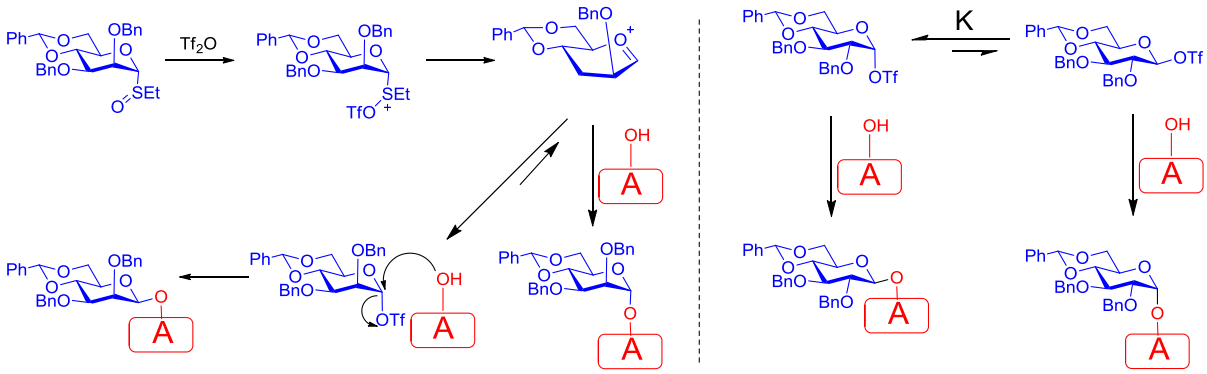


1.3.2.1 Intramolecular approaches

In intramolecular methods, the acceptor molecules itself are attached to the glycosyl donors by virtue of different linker or spacer motifs. Activation of glycosyl donor results in an oxocarbenium ion which is trapped by the acceptor in an intramolecular fashion to afford 1,2-*cis* glycosides. In this endeavour, pioneering work was performed by Hindsgaul *et al.* by introducing isopropylidene linker to tether acceptor molecules. Followed by Hindsgaul, Stork and Ogawa groups have independently proposed chlorosilyl and PMB linkers for 1,2-*cis* glycosylation.[23]

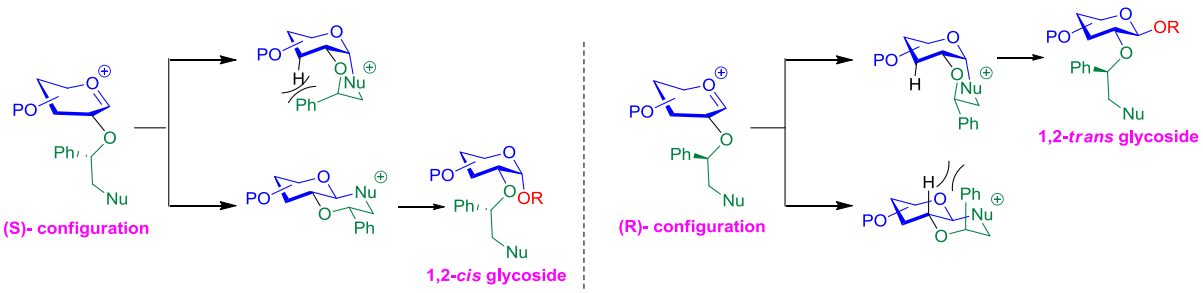
1.3.2.1 Intermolecular approaches

The pioneering work by Crich *et al.* led to the discovery of cyclic 4,6-benzylidene protecting group for 1,2-*cis* mannosylation. The 4,6-benzylidene with the assistance of change in electronic properties and torsional angles deactivated the sulfoxide glycosyl donor and on treatment of Tf_2O stabilized the α-*O*-triflate intermediate at lower temperature.



In the presence of acceptor, α-triflate intermediate undergoes S_N2 displacement to provide 1,2-*cis* mannopyranoside. In contrast, for glucose and galactose substrates, α-triflate intermediate at the lower temperature is very less reactive to undergo S_N2 displacement,

while it isomerizes to more reactive β-triflate that can undergo S_N2 displacement by acceptor to afford 1,2-*cis* glucoside or galactoside. Apart from the cyclic 4,6-benzylidene protecting group, over the last few decades numerous cyclic protecting group have been developed for 1,2-*cis* glycosylation such as 2,3- or 3,4-acetal, 3,5- or 4,6-di-^{t}butylsilylene and 3,5- or 4,6-O-(1,1,3,3-tetra-isopropyl-1,3-disiloxanylidene) are some of them. In this regard, another noteworthy report was carried out by Boons *et al.* by introducing chiral auxiliary as a protecting group in the donor motif itself. *trans*-Decalin intermediate is proposed when the chiral auxiliary is in *S*-configuration. The formation of *trans*-decalin was hypothesized to form in order to avoid steric repulsion in *cis*-decalin intermediate. At the *trans*-decaline intermediate, acceptor molecule can access only axial- or α-face to give 1,2-*cis* glycosides.



In contrast, when the chiral auxiliary is in *R*-configuration, *cis*-decaline intermediate becomes preferred intermediate to afford 1,2-*trans* glycosides. Recently, Demchenko*et al.* unravelled the H-bond mediated-aglycon-delivery (HAD) by employing remote picolinyl (Pic) or picoloyl (Pico) protecting groups in which nitrogen atom can form hydrogen bonding with the incoming acceptor molecule to facilitate *cis*-face of donor for 1,2-*cis* glycosylation.[24]

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Chapter: 2

Synthesis of 2-Deoxy-β-Glycosides

2.1 Introduction

Carbohydrates are not only important as building blocks of life but also have been the focus of potential therapeutic drug development. 2-*d*eoxy Glycosides can defined as those sugarswhereintheC2-hydroxylmoiety is replaced byahydrogen atom. These 2-*d*eoxyglycosides are structural units present in many natural products such as antitumor agents (anthracyclines, aureolic acids), antibiotics against Gram-positive bacteria (erythromycin, orthosomycin) etc.[1-6]

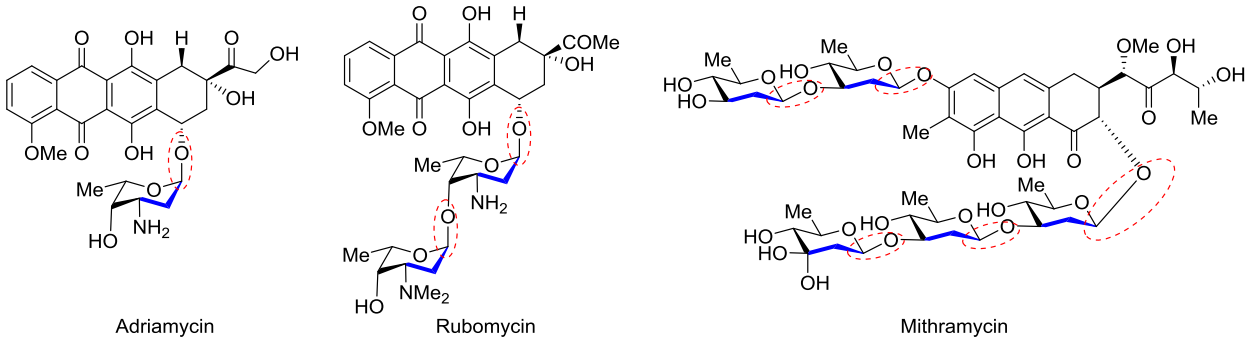


Figure 2.1 Example of biologically active 2-*deoxy*glycoconjugates

The realization that 2-*d*eoxyglycoconjugates are involved in many interesting biological processesled to the stimulation of drug development efforts on the synthesis of 2-*deoxy*glycoconjugatesinsufficient quantities.

2.1.1 Challenges intheSynthesis of 2-*deoxy*glycosides

The absence of any electron withdrawing substituent at the C2-position makes the resulting glycosidic bond very labile in acidic medium and consequent hydrolysis and racemization increasein 2-*deoxy* glycosides compared to their C2-hydroxyl congeners(Figure 2.2). [7]

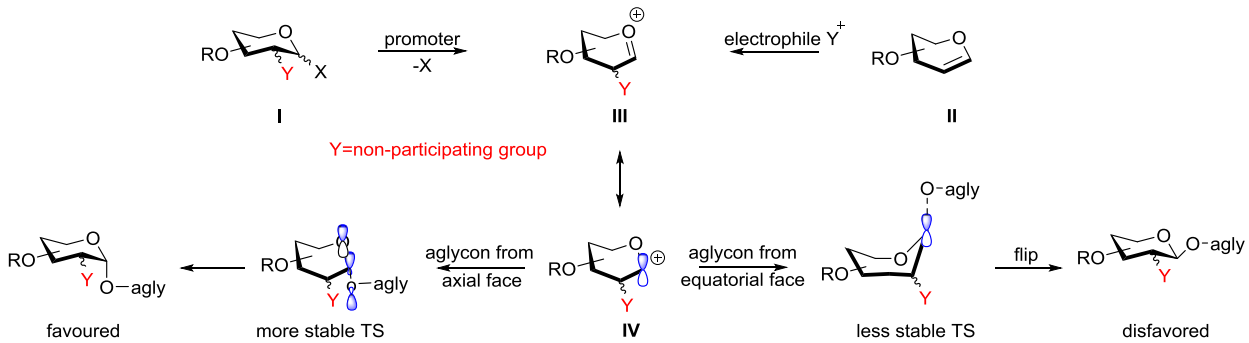


Figure 2.2 Transition state for (α-) and (β-) 2-*deoxy* glycoconjugates

Further, glycosylation of 2-*d*eoxyglycosides and control of the stereoselectivity is more challenging due to the absence of participating group at C-2 position. Leaving group activation of a 2-*d*eoxy donor either by activators or by the activation of glycalsunder acidic conditions generates sp^2 hybridized oxocarbenium ion with trigonal planner geometry (**III**) and therefore acceptor or nucleophile can access both bottom (α-) and top (β-) faces of oxocarbenium ion.[8] In the absence of C2-participating group (Y = H), during the axial face attack by the nucleophile, the transition state is stabilized by hyperconjugation between one of the non-bonding orbital of ring oxygen and anti-bonding orbital of the developing bond to afford α-2-*d*eoxyglycosides (Figure 2.2). In contrast, β-2-*d*eoxy glycosides formation demands the transition state to adopta less stable boat conformation and ring flipping has to happen.Therefore, the synthesis of β-2-*deoxy* glycosides is more challenging compare to the synthesis of α-2-*deoxy* glycosides (Figure 2.2).[9]

2.1.2 Synthesis of 2-*deoxy*-β-glycosides: Direct approaches

In the literature, numerous examples for direct synthesis of 2-*d*eoxy-β-glycosides were explored utilizing carboxy-benzyl (CB), trichloroacetimidate, thiophenyl(-SPh), bromo (–Br), chloro(-Cl) and hemiacetal(-OH) donors (Figure 2.3).[10-15] However, indirect approaches owing to the absence of directing group at C2 position of the 2-*d*eoxy sugars, it is very difficult and challenging to control anomeric stereoselectivity and often a mixture of inseparable α/β-anomers are obtained.[9,16]

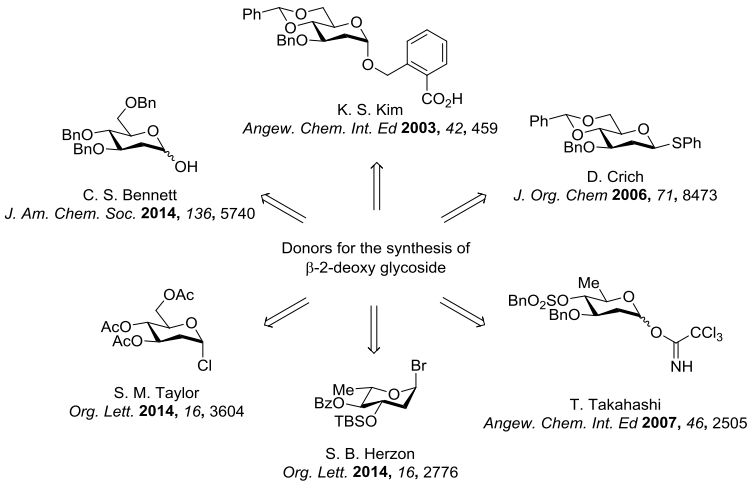
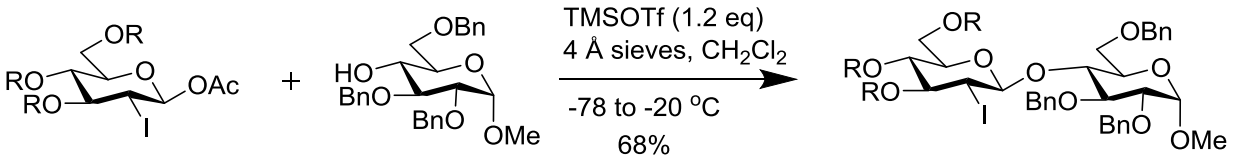


Figure 2.3 Glycosyl donors for the direct glycosylation

2.1.3 Indirect approaches: Synthesis of 2-*d*eoxy-β-glycosides

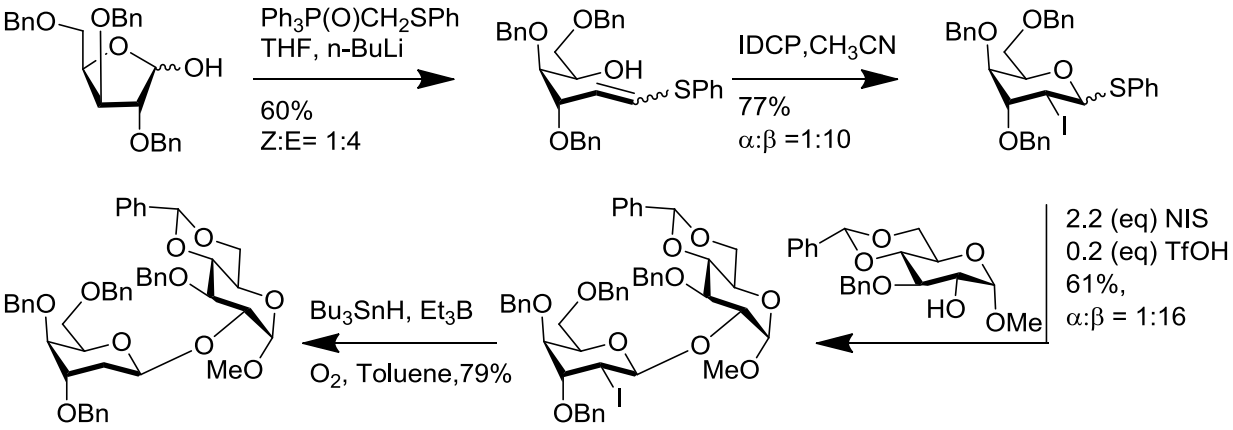
To circumvent stereoselectivity issues associated with the direct approaches, indirect approach of a temporary protecting group at C-2 was considered(e.g. iodo) that canimpart neighboring group participation (NGP) or stereoelectronic effect inthe glycosylation step to control anomeric stereoselectivity.[9]



Scheme 2.1 Indirect glycosylation by Roush and co-workers

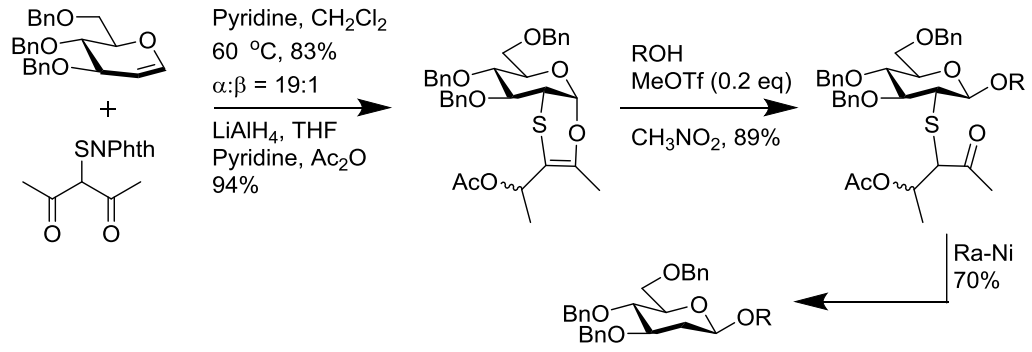
Roush group in pioneering work identified that 2-*d*eoxy-2-iodo-β-D-glucopyranosyl acetate (or trichloroacetimidate) can be an excellent glycosyl donor for obtaining good stereoselectivity of the disaccharide (α:β =1:19) (Scheme 2.1).[17] However, overall efficacy gothamperedbecausethepreparation of 2-*d*eoxy-2-iodo-β-D-glucopyranosyl donor from glycalresults in 1:1 mixture of β-D-gluco and α-D-manno isomers thereby reducing the overall efficiency of the protocol.

Castillōn and co-workers has developed another elegant method to obtain exclusively 2-*deoxy*-2-iodo-glucothiopyranoside with good to moderate β-selectivity (α:β = 1:16 to 1:8) in the glycosylation step (Scheme 2.2).[18]



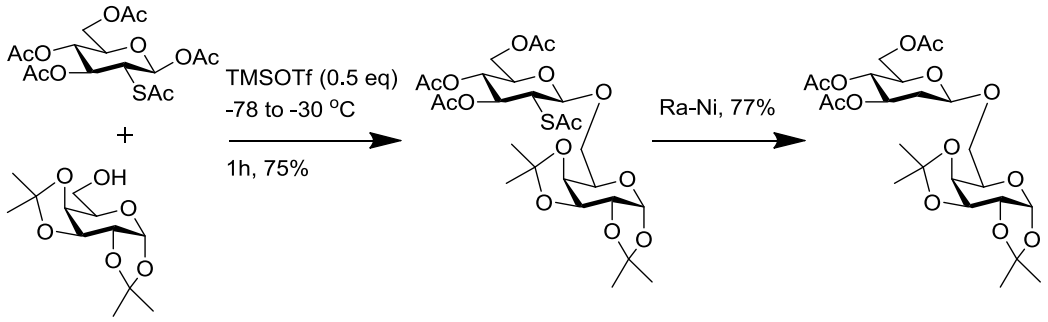
Scheme 2.2 Indirect glycosylation by Castillōn and co-workers

In another effort, Capozzi and co-workers envisioned that carbohydrate fused 1,4-oxathiine, prepared by the cycloaddition of glycals with oxothioheterodienes, are effective donors for the stereospecific synthesis of 2-*d*eoxy-2-thio-β-glycoside which can be converted into 2-deoxy β-D-glucopyranoside by using Ra-Ni (Scheme 2.3).[19]



Scheme 2.3 Indirect glycosylation by Capozzi and co-workers

Latter, Knapp and co-workers found that 1,2,3,4,6-penta-*O*,S,*O*,*O*,*O*-acetyl-2-*deoxy*-2-thio-β-D-glucopyranosecan be used for the synthesis of 2-*deoxy*-β-glycosides in presence of catalytic of TMSOTf with a range of acceptors. The high β-selectivity was rationalized by the formation of oxathioliumintermediate (Scheme 2.4).[20]



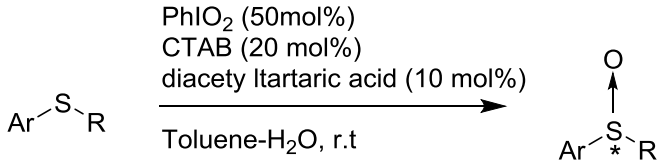
Scheme 2.4 Indirect glycosylation by Knapp and co-workers

Hence, development of an efficient and highly stereo- and regio-selective method for acquisition of 2-*d*eoxy-2-iodo-acetate as well as 2-*deoxy*-β-glycoside is still very attractive in organic synthesis. In this dissertation, we have utilized CTAB nano-reactor as a chiral template for stereo- and regio-selective synthesis of 2-*d*eoxy-2-iodo-acetate which is subsequently converted to 2-*d*eoxy-β-glycoside via intramolecular glycosylation.

2.2 Present work

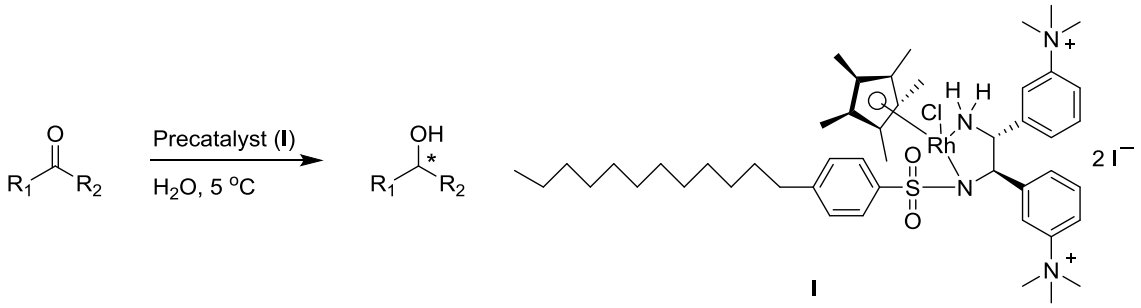
2.2.1 Research Strategy

Stereo- and regio-selectivities in organic synthesis are of paramount importance and often chiral environment or template guided asymmetric synthesis are studied.[21-25] For instance, Kim and co-workers reported catalytic asymmetric oxidation of sulfides to sulfoxides in cetyltrimethylammonium bromide (CTAB) embedded cationic reverse micelle nano-reactor (**Scheme 2.5**).They carried the reaction with aromatic sulfides and hypervalent iodine $PhIO_2$ in the presence of catalyticamoutsof CTAB and chiral diacetyltartaric acid in toluene-water solvent system to afford upto 72% *ee* of chiral sulphoxide.[26]



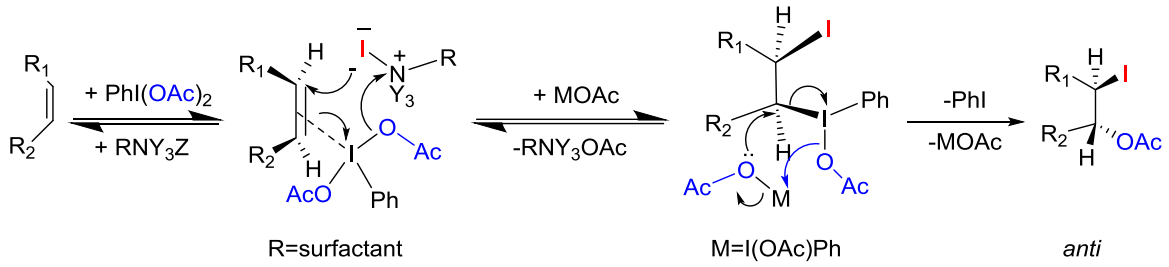
Scheme 2.5 Asymmetric oxidation of sulfide to sulfoxide

In another effort, Deng and co-workers applied a novel chiral surfactant type Rh-catalyst consisting of a chiral cationic ligand for efficient asymmetric transfer hydrogenation of aliphatic ketones. Treatment of $[Cp^*RhCl_2]_2$with cationic ligand generated chiral precatalyst (**I**) which



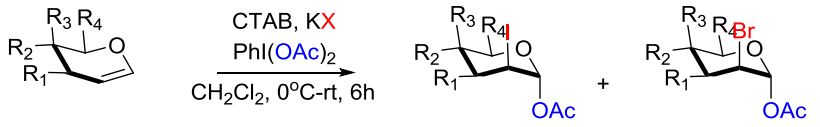
Scheme 2.6 Asymmetric transfer hydrogenation of ketone

assisted in face-selective asymmetric hydrogenation of aliphatic ketones by avoiding steric repulsion between alkyl group of the ketone and the methyl groups of Cp^* present in the catalyst (Scheme 2.6).[27]

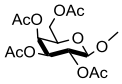


Scheme 2.6 Stereo- and regioSelective heterodifuntionalisation of olefin

Similarly, Maity and co-workers employed cetyltrimethylammonium bromide (CTAB) assembled lipophilic nano-reactors for the heterodifunctionalisation of alkynes and alkenes in water as well as in organic media.[28] They have showed the power of this methodology by preparing α,α-dibromoketones from alkynes and stereo-selective*anti*-halohydrin from alkene in water. High regioselectivity was rationalized by the placement of smaller organic part towards the interface of nano-reactor whereas the high stereoselectivity was attributedtothe*syn*-addition of $PhI(OAc)_2$ and halide followed by the reductive elimination of PhIOAc in a concerted fashion (Scheme 2.6).



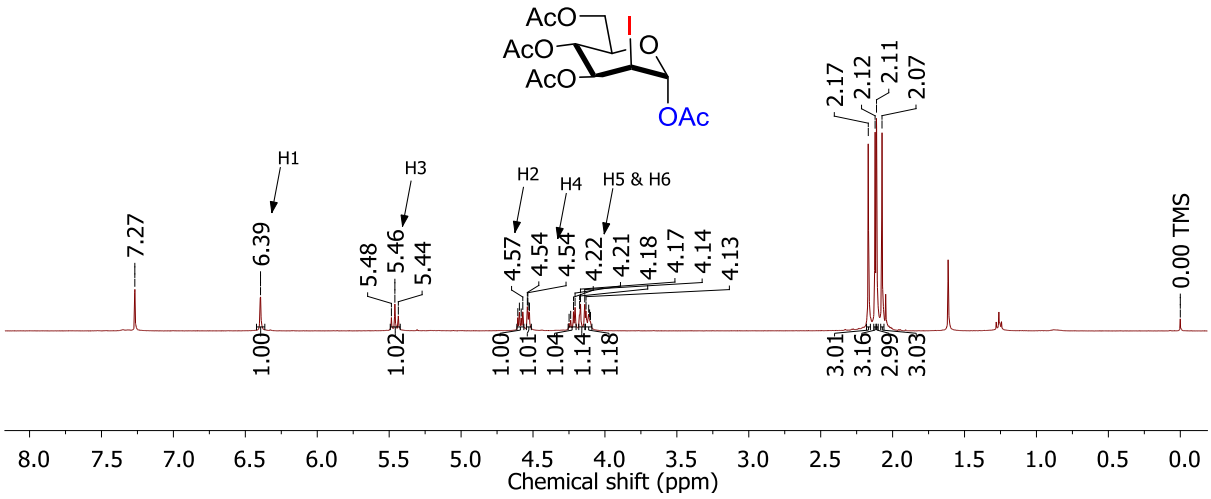
1a-1c **2a-2c** **3a-3c**

No.	R_1	R_2	R_3	R_4	KX	% Yield	Ratio
1a	-OAc	-OAc	-H	$-CH_2OAc$	KI	85	**2a:3a** = 95:5
	-OAc	-OAc	-H	$-CH_2OAc$	KBr	71	**2a:3a** = 0:100
1b	-OAc	-H	-OAc	$-CH_2OAc$	KI	80	**2b:3b** = 94:5
1c	-OAc		-H	$-CH_2OAc$	KI	75	**2c:3c** = 95:5

Scheme 2.7 Synthesis of *C*-2-*deoxy C*-2 iodo anomeric acetates in self assembled structures

The aforementioned discussion ensued us to investigate cetyltrimethylammonium bromide (CTAB) assembled lipophilic nano-reactor for regioselective iodination of glycals in presence of polycoordinated iodine reagents for the synthesis of 2-*d*eoxy-2-iodo acetates. To begin our investigation, per-*O*-acetyl glucal **1a** was activated by $PhI(OAc)_2$, CTAB and KI at 0 ^oC in CH_2Cl_2 solvent to obtain a turbid solution of the reaction mixture. The reaction mixture was

^{1}H NMR Spectrum of compound **2a**



^{13}C NMR Spectrum of compound **2a**

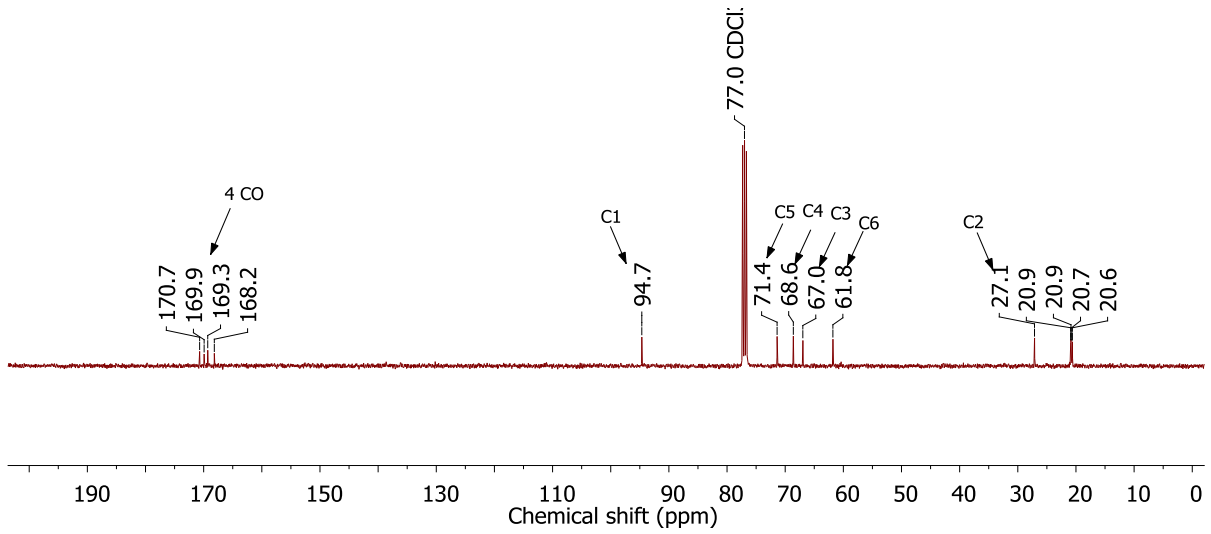


Figure 2.4 ^{1}H and ^{13}C NMR spectrum of 2a

stirred at 25 ^{o}C for 6h to notice the formation of two inseparable products **2a** and **3a** in 95:5 ratio; and surprisingly, no regioisomeric products wereobserved. The structural homogeneity of products was confirmed by the NMR and other spectroscopy analysis (Scheme 2.7). In the ^{1}HNMR spectrum, the H-1 proton was observed as a singlet at δ 6.39 ppm along with other ring protons {H-2 δ 4.59(dd, *J* = 9.5, 4.4 Hz), H-3 δ 5.46(t, *J* = 9.6Hz), H-4 δ 4.53(dd, *J* = 4.3, 1.5

Hz), H-5 δ 4.23(dd, *J* = 12.3, 4.4 Hz), H-6(a) δ 4.16(dd, *J* = 12.3, 4.4 Hz) and H-6(b) δ 4.11(dd, J = 7.4, 4.9 Hz)} and in ^{13}C NMR spectrum, the C-1 carbon was appeared at δ 94.7 ppm and rest of ring carbon appeared δ 27.1-71.4 ppm, (Figure 2.4) confirming the α-D-manno configuration of compound **2a**. To understand the origin of compound **3a**, a control experiment was carried out wherein KI was replaced by KBr and it was observed that the compound **3a** only was formed. In addition, compound **3a** showed similar type of ^{1}HNMR and ^{13}CNMR spectral signatures as in compound **2a**{for H-1 δ 6.32 (d, *J* = 1.5 Hz, 1H) ppmand for C-1 δ 94.3ppm)}further confirming α-D-manno configuration of compound **3a**.Hence, formation of compound**3a**(5%) in the previous reaction can be due to the exchange of halide counterion between CTAB and KI.Further, regioisomeric mixture was ruled out from two isotopic mass peaks of compound **3a** in MS analysis confirming 2-*deoxy*-2-bromo-α-D-manno acetate (**3a**).

FE SEM microscopic images showed the formation of self assembled nano-reactor particles of 200 nm size and we hypothesized that high regio- and stereo- selectivityare due to these assembled nanoreactors.It is important to note that these reactions are to be carried out at the critical micellar concentration (CMC) of CTAB by adding 10 mol% CTAB in 15 ml dichloromethane to get complete regio- and stereo-selective products.

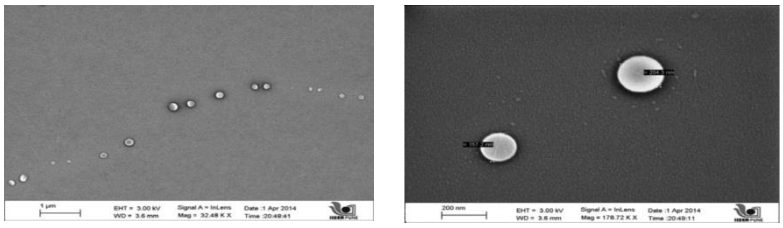
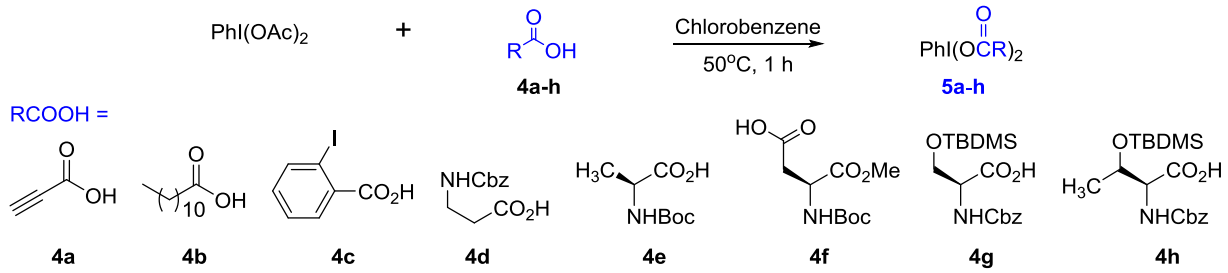


Figure 2.5 FE SEM Images of Reaction Mixture

All four possible isomers were obtained when the reaction was carried out below the CMC value or in the absence of CTAB due to the absence of nano-reactors. In continuation, optimized conditions were employed for activation of galactal (**1b**) and lactal (**1c**), with $PhI(OAc)_2$, CTAB and KI to generate **2b**:**3b** = 95:5 and **2c**:**3c** =95:5 respectively. In the ^{1}HNMR spectrum of **2b** and **2c** characteristic resonances corresponding to both H-1 protons were noticed as doublet at δ 6.44 ppm and δ 6.22 ppm, whereas in the^{13}CNMR spectrum anomeric carbons of **2b** and **2c** were identified at δ 96.0 ppm and 90.7 ppm respectively. In compounds **2a-2c** and **3a-3c**, the presence of anomeric esters are beneficial since they can be easily glycosylated by the addition

of many Lewis acids. In addition, the presence of iodo or the bromine will be beneficial as they can be easily deoxygenated by invoking radical chemistry.



Scheme 2.8 Preparation of iodosobenzene diacylate

One can vary the glycal scaffold, iodo or bromo glycosdes and if possible different esters can be synthesized if one has access to diverse range of phenyliodoso acetates. In this direction, a recent report Koposov*et al.*[29]will be of immense significance as they have showed that diverse set of phenylidoso diacetates can be obtained by from $PhI(OAc)_2$ by simply heating them in chlorobenzene for 1 h at 50 ^oC. Accordingly, acetyl groups of $PhI(OAc)_2$ were exchanged with various aliphatic, aromatic and amino acid carboxylic acids (**4a-h**) by heating equimolar mixture of $PhI(OAc)_2$ and carboxylic acids (**4a-h**) at 50 ^oC at reduced pressure for 1h in chlorobenzene to afford diverse set of modified iodosobenzenediacylates (**5a-5h**).[29]

The scope of the modified iodosobenzenediacylates (**5a-5h**) were investigated first with glucal (**1a**) and later extended for others in the series. Gratifyingly, the glycosylation reaction had undergone smoothly affording glucoside (**6a-6h**) in highly regio- and stereo-selective fashion. In ^{1}HNMR spectra of glycosides **6a-6h**, characteristic resonances corresponding to H-1 protons

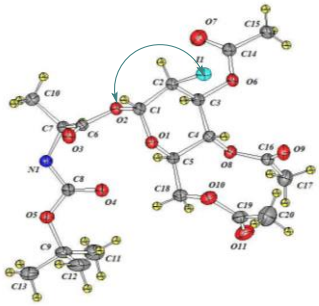
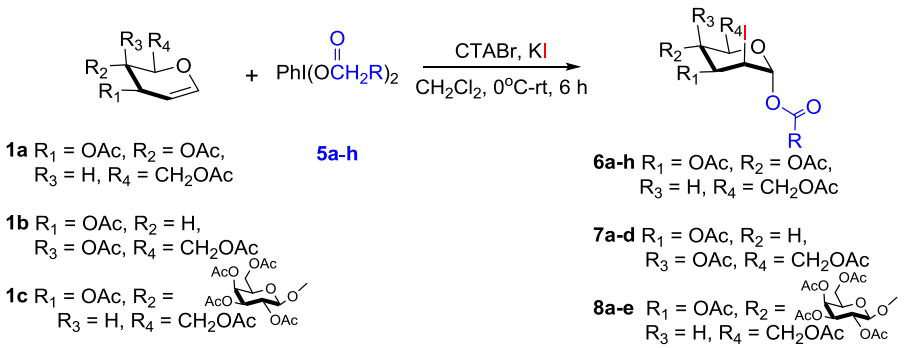


Figure 2.5 Single crystal structure of compound 6e

were noticed in the range of δ 6.38-δ 6.47 ppm and that of C-1 carbons were identified at δ 93.9-δ 96.0 ppm in the ^{13}CNMR spectrum thereby confirming the presence of single diastereomer formation due to the reactions in nano-reactors. Luckily, we were able to obtain single crystals of compound **6e** and diffraction studies unambiguously confirmed the regio- and stereo-selectivityofcompound **6e** (Figure 2.5).

After successfully confirming the regio- and stereo- selective formation of the iodoacetates, we turned our attention to activate other glycal systems in order to test the scope of the method. Accordingly, galactal (**1b**) was treated with **5d**, **5e, 5g-5h** to observe formation of 2-*d*eoxy-2-iodo ester glycosides (**7a-7d**) in very good yield along with the minor amounts (≤ 5%) of bromo esters. However, regio-/stereo-selectivity of glycosides **7a-7d**was not compromised which was confirmed from ^{1}HNMR and ^{13}CNMR spectral signatures of H-1 protons and C-1 carbons.

Similarly,the nano-reactor based protocol was tested on the glycal system of a disaccharide as well. To do so, we have chosen to prepare the lactal which can be easily accessed from the commercially available lactose. Gratifyingly, glycosylated lactal derivatives (**8a-8h**) were obtained from hypervalent iodine reagents (**5d-5h**) in moderate to good yields from lactal **1c**. The structural homogeneity of all lactosides **8a-8h** was confirmed from their respective ^{1}HNMR



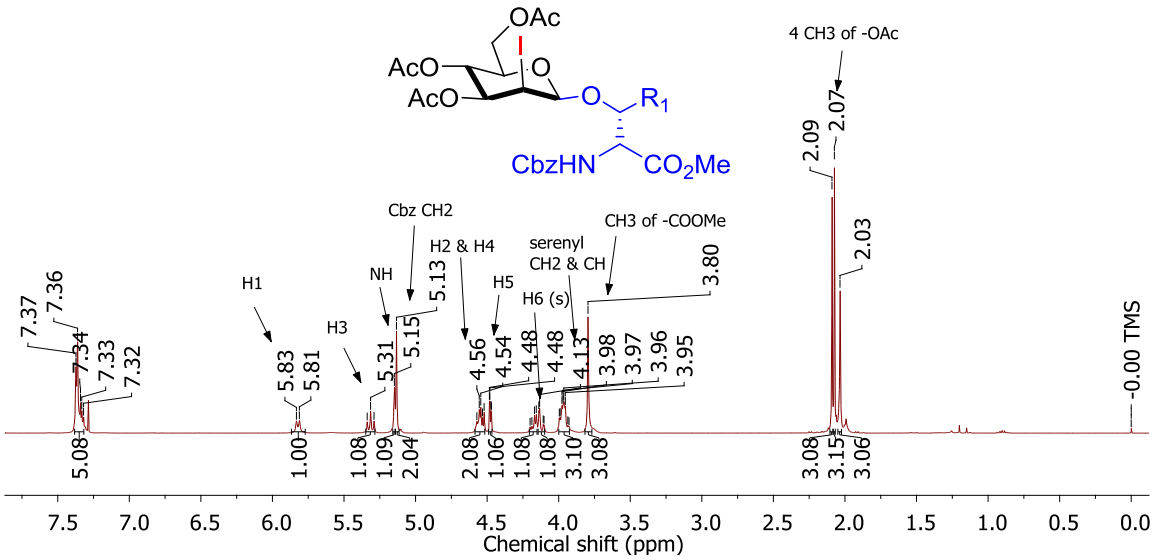
	5a	5b	5c	5d	5e	5f	5g	5h
1a	**6a** (76%)	**6b** (73%)	**6c** (80%)	**6d** (72%)	**6e** (80%)	**6f** (81%)	**6g** (81%)	**6h** (79%)
1b	ND	ND	ND	**7a** (76%)	**7b** (83%)	**ND**	**7c** (74%)	**7d** (90%)
1c	ND	ND	ND	**8a** (76%)	**8b** (83%)	**8c** (80%)	**8d** (80%)	**8e** (77%)

ND = Not determined; Numbers in paranthesis show isolated yields

Scheme 2.9 Preparation of 2-*d*eoxy-2-iodo anomeric esters

And ^{13}CNMR spectral signatures. Amino acid glyconjugates **6g-6h** and **7c-7d** are very interesting among all the 2-*d*eoxy-2-iodo esters as they can be easily converted into *N*-carboxy anhydrides (NCAs) for the preparation of 2-*d*eoxy glycopeptides by the ring opening polymerization.[30-33]

^{1}H NMR Spectrum of compound **9a**



^{13}C NMR Spectrum of compound **9a**

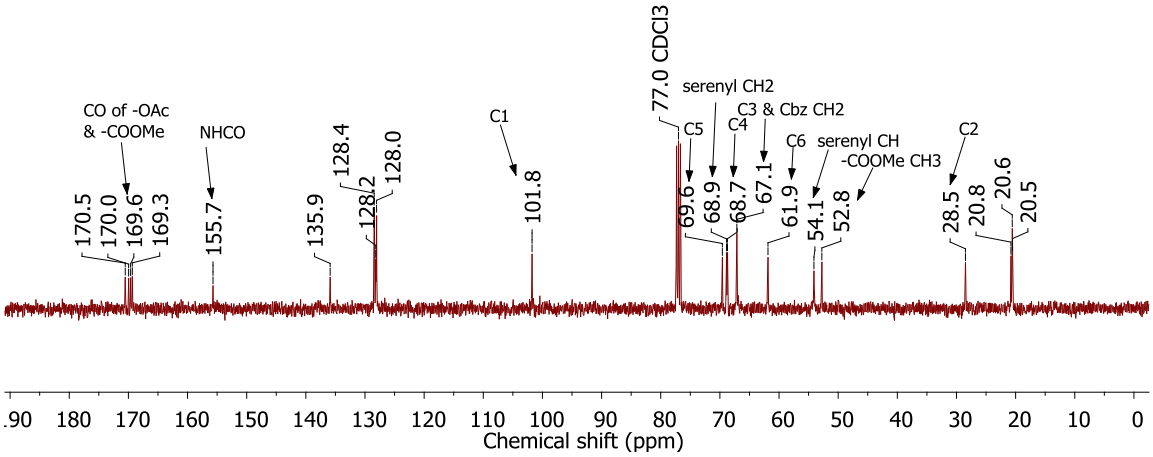
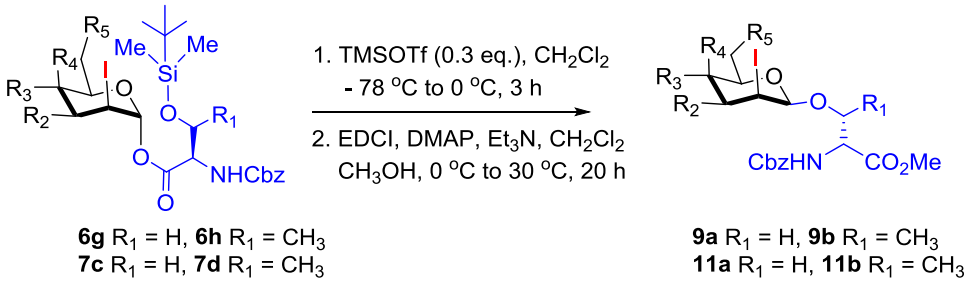


Figure 2.5 ^{1}H and ^{13}C NMR spectrum of 9a

In addition, we hypothesized that the amino acid glycoconjugates **6g**, **6h**, **7c,** and **7d** are strategically oriented to undergo intramolecular glycosylation in presence of suitable Lewis acid

by the activation of the anomeric ester. To decipher intramolecular glycosylation, amino acid glycoconjugate **6g** was activated by the addition of catalytic amount of TMSOTf in dichloromethane at -78 ^{o}C (Scheme 2.10). Resulting carboxylic acids became highly polar and thus methyl esters were prepared under MeOH/EDCI/DMAP conditions to obtain serinyl ester **9a**. The β-configuration of serinyl glucoside **9a** was confirmed by the NMR spectroscopy. In the ^{1}HNMR spectrum of glycoside **9a**, H-1 proton appeared at δ 5.82 ppm as a doublet (J = 8.2 Hz), a singlet for three protons at δ 3.80 ppm confirmed the *O*-methyl ester, broad singlet at δ 5.15 ppm indicated amide proton, benzylic protons were observed at δ 5.14 ppm and characteristic serenylmethyne and methelene protons were noticed at δ 3.92-4.01ppm as a multiplet;whereasC-1 carbon was observed at δ 101.8 ppm in the ^{13}CNMRspectrum along with all other resonances in complete agreement with that of assigned structure (Figure 2.5).



6g R_1 = H, **6h** R_1 = CH_3
7c R_1 = H, **7d** R_1 = CH_3

9a R_1 = H, **9b** R_1 = CH_3
11a R_1 = H, **11b** R_1 = CH_3

Substrate	R_2	R_3	R_4	R_5	Product	% Yield
6g	-OAc	-OAc	-H	-CH_2OAc	**9a**	76
6h	-OAc	-OAc	-H	-CH_2OAc	**9b**	73
7c	-OAc	-H	-OAc	-CH_2OAc	**11a**	73
7d	-OAc	-H	-OAc	-CH_2OAc	**11b**	72

Scheme 2.10. Synthesis of 2-*d*eoxy-2-iodo-β-amino acid glycosides

Careful analysis of the thin layer chromatography coupled mass spectral studies (TLC-MS) showed that the TBDMS group was cleaved first by TMSOTf to generate intermediate **A** that underwent intramolecular glycosidation to afford β-glycoside. Mechanistically, TMSOTf disproportionates and generates OTf^{-}that can cleave the Si-O bond giving us a serinyl alcohol (**A**) that can act as a nucleophile if the ester is activated. Being a Lewis acid TMSOTf can activate the carbonyl group of the endocyclic ester to trigger the electron pushing cascade from

the exocyclic oxygen resulting in the carbocation formation at the C-1 position. This carbocation can be easily trapped in a six membered transition state by the serinyl alcohol which is strategically position in order to give the β-serinyl glycoside (Figure 2.6).

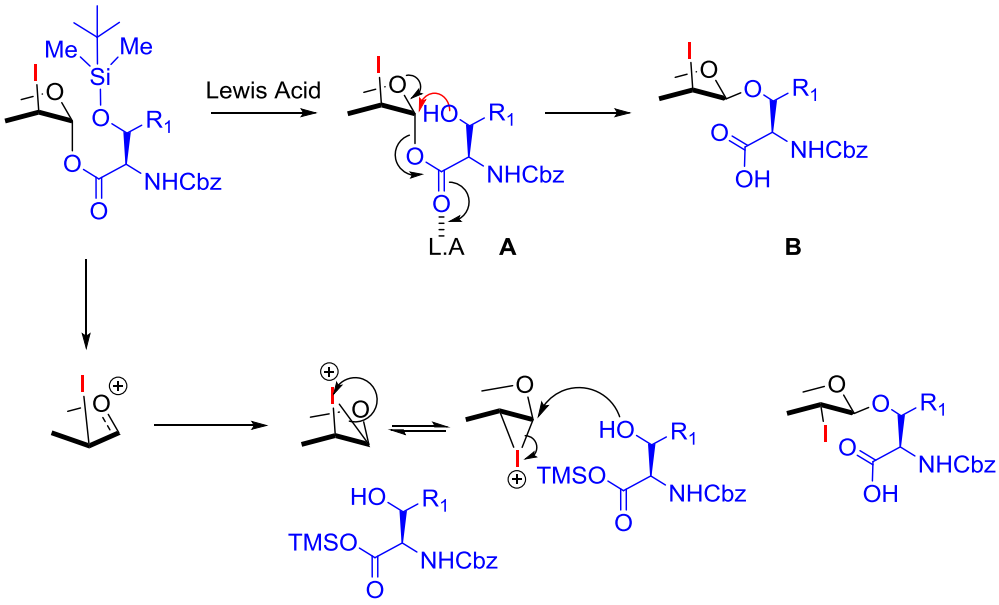
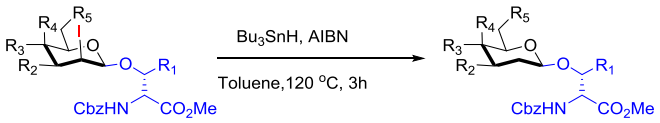


Figure 2.6 Rationale for intramolecular glycosylation

The substrate scope of the intramolecular glycosidation method was extended for other substrates **6h**, **7c** and **7d** prepared *vide supra* to afford respective 2-*d*eoxy-2-iodo-β-amino acid ester glycoconjugates **9b**, **11a,** and **11b**.The β-configuration of **9b**, **11a,** and **11b** isomers was confirmed from the characteristic H-1 and C-1 resonances in the ^{1}HNMR and ^{13}CNMR spectra.

The next important milestone in this endeavor will be the successful deiodination reaction. Towards this effect, we thought of inviting a radical mediated protocol developed long ago. Accordingly, at the post-glycosylation step *C*-2-iodo moiety of serinyl ester **9a** was removed by the use of Bu_3SnH and AIBN in toluene at 100 ^{o}C to give 2-*deoxy*-serinyl β-D-glucoside**10a** in 65% yield.[18]



9a R_1 = H, **9b** R_1 = CH_3
11a R_1 = H, **11b** R_1 = CH_3

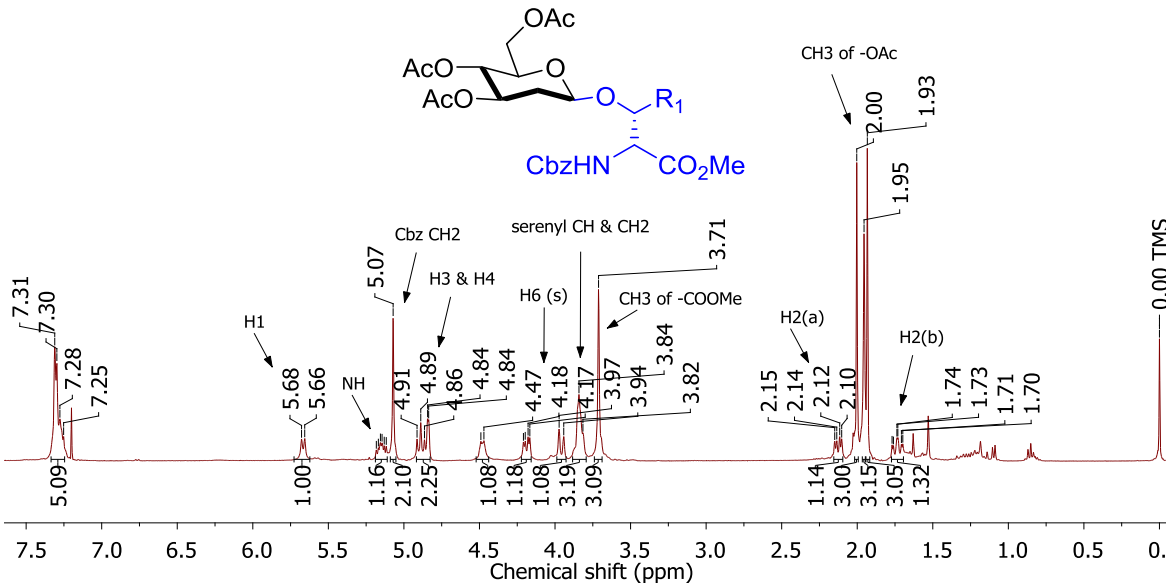
10a R_1 = H, **10b** R_1 = CH_3
12a R_1 = H, **12b** R_1 = CH_3

Substrate	R_2	R_3	R_4	R_5	Product	% Yield
9a	-OAc	-OAc	-H	$-CH_2OAc$	**10a**	65
9b	-OAc	-OAc	-H	$-CH_2OAc$	**10b**	61
11a	-OAc	-H	-OAc	$-CH_2OAc$	**12a**	60
11b	-OAc	-H	-OAc	$-CH_2OAc$	**12b**	63

Scheme 2.11 Preparation of 2-*d*eoxy-β- amino acid glycosides

The ^{1}HNMR spectrum of serinyl ester **10a** was very similar to that of compound **9a** since H-1 proton was noticed at δ 5.67 (d, *J* = 8.4 Hz) with the only difference of two new signals correspond to C-2 hydrogens'at δ 1.73 ppm and δ 2.13 ppm as a multiplet. In ^{13}CNMR spectrum, C-1 carbon resonances were noticed at δ 97.7 ppm andcharacteristic resonances from the C-2-*d*eoxy carbon was observed at δ34.7 ppm.

^{1}H NMR Spectrum of compound **10a**



^{13}C NMR Spectrum of compound **10a**

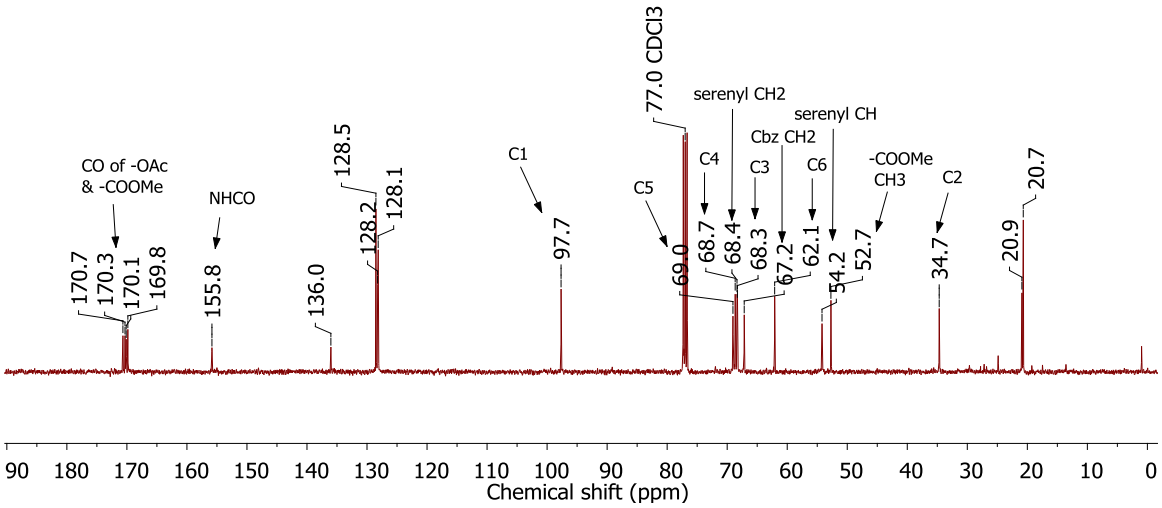


Figure 2.5 ^{1}H and ^{13}C NMR spectrum of 10a

Similarly, C-2 iodo group of **9b**, **11a** and **11b** was removed by Bu_3SnH and AIBN to obtain 2-*deoxy*-glycosides **10b**, **12a** and **12b** respectively and C-2-*d*eoxy nature of **10b**, **12a** and **12b** was confirmed from the characteristic C-2 protons and C-2 carbon resonance in ^{1}HNMR and ^{13}CNMR spectra as delineated above.

In conclusion, an versatile and practical method was developed for the synthesis of 2-*deoxy*-2-iodo glycosides by exploiting salient features of self-assembled reverse micellar nano-reactors. Various 2-*deoxy*-2-iodo glycosyl esters were synthesized in a stereoselective fashion. Intramolecular glycosidation of anomeric serinyl esters afforded β-serinyl glycosides and the radical mediated deiodination at C-2 position resulted in 2-*deoxy*-β-serinyl glycosides. Natural molecules and glycopeptides containing 2-*deoxy* sugar subunits can be easily synthesized by this approach.

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Note: Characterization data and full spectral charts for all compounds can also be found in

J. Org. Chem., **2014**, *79*, 4470.

2.3 Experimental Section

General procedure for activation of glycals

A two-neck round bottom flask containing glucal, **1a** (0.272 g, 1.0 mmol), anhydrous $MgSO_4$ (0.5 g) and CH_2Cl_2 (15 mL) at 0 ^oC was added $PhI(OCOCH_3)_2$ (0.644 g, 2.0 mmol) and CTAB (0.039 g, 10 mole%), KI (0.166 g, 1.0 mmol). The reaction mixture was stirred at 25 ^oC for 6 h and diluted with water and extracted with CH_2Cl_2 (3x25 mL) and the combined organic portions were washed with aq. sodium bicarbonate and brine solution (2x10 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The resulting crude residue was purified by silica gel column chromatography using ethyl acetate and light petroleum ether (bp 60-70 ^oC) to obtain compound **2a** (0.389 g, 85%) as a colourless thick syrup. The Same general procedure was adopted for synthesizing compounds **2a**-**2c**, **6a**-**6h**, **7a**-**7d,** and **8a**-**8e**.

General procedure for intramolecular glycosylation and esterification

To C-2-*d*eoxy-2-iodo amino acid glycoconjugate **6g** (0.750 g, 1.00 mmol) in CH_2Cl_2 (10 mL) was added 4 Å molecular sieves powder (0.5 g) at room temperature. After stirring for 30 min, the reaction mixture was cooled to –78 ºC and TMSOTf (45 µL, 0.25 mmol) was added and stirred for 30 min. The reaction mixture was slowly warmed to 0 ^oC and stirred for 3 h, diluted with CH_2Cl_2 and filtered through Celite. The filtrate was subsequently neutralized with excess

triethylamine, concentrated in vacuo and the residue was purified by silica gel column chromatography to give 2-iodoacid which was directly used for esterification. 2-iodo acid (0.637 g, 1.00 mmol) was redissolved in CH_2Cl_2 (10 mL) and MeOH (61 µL, 1.5 mmol) was added and cooled to 0 ^oC. 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide (EDCI) (0.249 g, 1.30 mmol), Et_3N (181 µL, 1.30 mmol) and DMAP (0.030 g, 0.25 mmol) were added and stirred for 20 h at 25 ^oC. The reaction was quenched with water and extracted with CH_2Cl_2 (2x25 mL), the combined organic layers were washed with saturated $NaHCO_3$, water, brine, dried and concentrated in vacuo to obtain a residue that was purified by silica gel column chromatography using EtOAc and light petroleum (bp 60-70 ^oC) to afford colourless thick syrup of compound **9a** (0.485 g, 76%). The same general procedure was adopted for synthesizing compounds **9b** and **11a-11b**.

Compound 2a: This compound is prepared using the above mentioned general procedure using **1a** (0.272 g, 1 mmol) as the starting material, Yield: (0.389 g, 85%); $[\alpha]_D$ = +31.2 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78 MHz, $CDCl_3$) δ 2.07 (s, 3 H), 2.11 (s, 3H), 2.12 (s, 3H), 2.17 (s, 3H), 4.11 (ddd, 1H, *J* = 7.4, 4.9 Hz), 4.16 (dd, 1H, *J* = 12.3, 4.4 Hz), 4.23 (dd, 1H, *J* = 12.3, 4.4 Hz), 4.53 (dd, 1H, *J* = 4.3, 1.5 Hz), 4.59 (dd, 1H, *J* = 9.5, 4.4 Hz), 5.46 (t, 1H, *J* = 9.6 Hz), 6.39 (s, 1H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 20.6, 20.7, 20.9, 20.9, 27.1, 61.8, 67.0, 68.6, 71.4, 94.7, 168.2, 169.3, 169.9, 170.7; IR ($CHCl_3$) ν 2925, 1747, 1216, 1048 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{14}H_{19}INaO_9$ 480.9971, Found: 480.9979.

Compound 2b: This compound is prepared using the above mentioned general procedure using **1b** (0.272 g, 1 mmol) as the starting material, Yield: (0.367 g, 80%); $[\alpha]_D$ = +43.2 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78 MHz, $CDCl_3$) δ 1.98 (s, 3H), 2.03 (s, 3H), 2.08 (s, 3H), 2.13 (s, 3H), 4.12 (d, 2H, *J* = 6.6 Hz), 4.20 – 4.23 (m, 1H), 4.34 (td, 1H, *J* = 6.7, 1.9 Hz), 4.83 (t, 1H), 5.35 – 5.39 (m, 1H), 6.44 (d, 1H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 18.8, 20.6, 20.8, 20.9, 28.9, 61.4, 64.7, 64.8, 69.0, 96.0, 168.2, 169.6, 170.0, 170.4; IR ($CHCl_3$) ν 2925, 1745, 1219, 1143 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for calcd for $C_{14}H_{19}INaO_9$ 480.9971, found: 480.9979.

Compound 2c: This compound is prepared using the above mentioned general procedure using **1c** (0.560 g, 1 mmol) as the starting material, Yield: (0.560 g, 75%); $[\alpha]_D$ = +17.0 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78 MHz, $CDCl_3$) δ 1.98 (s, 3H), 2.07 (s, 9H), 2.14 (s, 3H), 2.16 (s, 3H), 2.17 (s, 3H), 3.91 – 3.96 (m, 1H), 4.07 (dd, 1H, *J* = 11.1, 6.9 Hz), 4.19 (m, 4H), 4.54 (dd, 1H, *J* =

12.1, 1.8 Hz), 4.60 (d, 1H, *J* = 7.9 Hz), 4.71 (dd, 1 H, *J* = 3.9, 1.6 Hz), 5.00 (dd, 1H, *J* = 10.4, 3.5 Hz), 5.17 (dd, 1H, *J* = 10.4, 8.0 Hz), 5.36 – 5.38 (m, 1H), 5.43 (dd, 1H, *J* = 8.9, 3.9 Hz), 6.22 (d, 1H, *J* = 1.3 Hz); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 20.5, 20.6 (4C), 20.8, 20.8, 22.6, 52.1, 61.1, 61.2, 66.7, 68.3, 69.1, 70.7, 70.9, 72.5, 73.4, 90.7, 101.2, 169.2, 169.4, 170.1, 170.1, 170.1,107.01, 170.3, 170.4;); IR ($CHCl_3$) ν 2930, 1746, 1221, 1053 cm^{-1}; HRMS (TOF) *m/z* [M + Na]$^+$ calcd for $C_{26}H_{35}INaO_{17}$ 769.0817, found: 769.0816.

Compound 3a: This compound is prepared using the above mentioned general procedure using **1a** (0.272 g, 1 mmol) as the starting material, Yield: (0.292 g, 71%); $[\alpha]_D$ = +31.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 2.07 (s, 3H), 2.11 (s, 6H), 2.18 (s, 3H), 4.11 (ddd, 1H, *J* = 10.0, 4.5, 2.5 Hz), 4.15 (dd, 1H, *J* = 12.4, 2.4 Hz), 4.24 (dd, 1H, *J* = 12.4, 4.5 Hz), 4.44 (dd, 1H, *J* = 3.9, 1.7 Hz), 5.20 (dd, 1H, *J* = 9.7, 4.0 Hz), 5.49 (t, 1H, *J* = 9.8 Hz), 6.32 (d, 1H, *J* = 1.5 Hz); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 20.5 , 20.6, 20.7, 20.8, 47.8 , 61.8 , 65.5, 68.7, 71.2, 93.1, 168.0, 169.2, 170.0, 170.6; IR ($CHCl_3$) ν 2925, 1745, 1219, 1143 cm^{-1}; HRMS (TOF) *m/z* [M + Na]$^+$ calcd for $C_{14}H_{19}BrNaO_9$ 433.0110, 435.0090, found: 433.0078, 435.0087.

Compound 6a: This compound is prepared using the above mentioned general procedure using **1a** (0.272 g, 1 mmol) as the starting material, Yield: (0.356 g, 76%); $[\alpha]_D$ = +61.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 2.08 (s, 3H), 2.12 (s, 3H), 2.12 (s, 3H), 3.07 (s, 1 H), 4.13 – 4.19 (m, 2 H), 4.24 (dd, 1H, *J* = 12.7, 4.8 Hz), 4.59 (bs, 1H), 4.60 (d, 1H, *J* = 6.0 Hz), 5.41 – 5.53 (m, 1H), 6.47 (s, 1H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 20.6, 20.7, 20.9, 26.2, 61.6, 66.7, 68.4, 71.8, 73.3, 77.1, 96.0, 149.7, 169.3, 169.8, 170.6; IR ($CHCl_3$) ν 3258, 2950, 1741, 1145, 1059 cm^{-1}; HRMS (TOF) *m/z* [M + Na]$^+$ calcd for $C_{15}H_{17}INaO_9$ 490.9815, found: 490.9825.

Compound 6b: This compound is prepared using the above mentioned general procedure using **1a** (0.272 g, 1 mmol) as the starting material, Yield: (0.437 g, 73%); $[\alpha]_D$ = +25.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 0.82 – 0.92 (m, 3 H), 1.21 – 1.37 (m, 16 H), 1.65 (q, 2H, *J* = 7.3 Hz), 2.07 (s, 3H), 2.11 (s, 3H), 2.11 (s, 3H), 2.40 (t, 1H, *J* = 7.5 Hz), 4.11 (ddd, 1H, *J* = 9.9, 4.6, 2.5 Hz), 4.15 (dd, 1H, *J* = 12.4, 2.4 Hz), 4.22 (dd, 1H, *J* = 12.3, 4.6 Hz), 4.53 (dd, 1H, *J* = 4.4, 1.6 Hz), 4.58 (dd, 1H, *J* = 9.4, 4.4 Hz), 5.45 (t, 1H, *J* = 9.7 Hz), 6.40 (d, 1H, *J* = 1.4 Hz);^{13}C NMR (100.53 MHz, $CDCl_3$) δ 14.0, 20.5, 20.6, 20.7, 22.5, 24.6, 27.2, 28.8, 29.1, 29.2, 29.3, 29.4(2C), 31.8, 33.9, 61.7, 66.9, 68.6, 71.3, 94.3, 169.2, 169.7, 170.5, 170.8; IR ($CHCl_3$) ν 2932, 1745, 1132, 1045 cm^{-1}; HRMS (TOF) *m/z* [M + Na]$^+$ calcd for $C_{24}H_{39}INaO_9$ 621.1536,

found: 621.1547.

Compound 6c: This compound is prepared using the above mentioned general procedure using **1a** (0.272 g, 1 mmol) as the starting material, Yield: (0.517 g, 80%); $[\alpha]_D$ = +27.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 2.07 (s, 3H), 2.12 (s, 3H), 2.12 (s, 3H), 4.14 – 4.33 (m, 3H), 4.75 (d, 1H, *J* = 2.1 Hz), 4.78 (d, 1H, *J* = 4.5 Hz), 5.47 – 5.59 (m, 1H), 6.67 (s, 1H), 7.22 (td, 1H, *J* = 7.6, 1.7 Hz), 7.47 (td, 1H, *J* = 7.6, 1.1 Hz), 7.83 (dd, 1H, *J* = 7.8, 1.6 Hz), 8.04 (dd, 1H, *J* = 7.9, 1.0 Hz);^{13}C NMR (100.53 MHz, $CDCl_3$) δ 20.6, 20.8, 20.9, 27.0, 61.8, 66.9, 68.8, 72.0, 93.9, 96.1, 128.2, 131.6, 133.4, 133.5, 141.6, 163.9, 169.3, 169.9, 170.7; IR ($CHCl_3$) ν 3013, 2931, 1746, 1551, 1441, 1121, 1033, 661 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{19}H_{20}I_2NaO_9$ 668.9094, found: 668.9141.

Compound 6d:This compound is prepared using the above mentioned general procedure using **1a** (0.272 g, 1 mmol) as the starting material, Yield: (0.447 g, 72%); $[\alpha]_D$ = +19.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 2.06 (s, 3H), 2.10 (s, 6H), 2.67 (t, 2H, *J* = 5.8 Hz), 3.51 (q, 2H, *J* = 6.0 Hz), 4.07 – 4.18 (m, 2H), 4.21 (dd, 1H, *J* = 12.4, 4.4 Hz), 4.52 – 4.58 (m, 2H), 5.10 (s, 2H), 5.36 (t, 1H, *J* = 6.1 Hz), 5.46 (t, 1H, *J* = 9.4 Hz), 6.41 (s, 1H), 7.35 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 20.6, 20.7, 20.9, 26.9, 34.3, 36.4, 61.7, 66.8(2C), 68.6, 71.5, 94.9, 128.0-128.5 (5C), 136.2, 156.3, 169.3, 169.8, 169.9, 170.7; IR ($CHCl_3$) ν 3396, 3051, 2958, 1742, 1520, 1130, 1005 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{23}H_{28}INNaO_{11}$ 644.0605, found: 644.0597.

Compound 6e: This compound is prepared using the above mentioned general procedure using **1a** (0.272 g, 1 mmol) as the starting material, Yield: (0.470 g, 80%); mp: 131 ^{o}C; $[\alpha]_D$ = +7.80 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 1.45 (s, 9H), 1.46 (s, 3H), 2.08 (s, 3H), 2.11 (s, 3H), 2.12 (s, 3H), 4.16 (dd, 2H, *J* = 14.0, 11.1 Hz), 4.24 (dd, 1H, *J* = 12.0, 4.0 Hz), 4.31 – 4.40 (m, 1H), 4.51 – 4.60 (m, 2H), 5.02 (d, 1H, *J* = 7.1 Hz), 5.48 (t, 1H, *J* = 9.4 Hz), 6.40 (s, 1H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 18.1, 21.0, 20.7, 20.9, 26.7, 28.2 (3C), 49.0, 61.6, 66.7, 68.7, 71.6, 80.2, 95.5, 155.0, 169.3, 169.8, 170.7, 171.1; IR ($CHCl_3$) ν 3384, 2981, 1747, 1515, 1454, 1160, 1057, 666 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $[C_{20}H_{30}INNaO_{11}$ 610.0761, found: 610.0770.

Compound 6f: This compound is prepared using the above mentioned general procedure using **1a** (0.272 g, 1 mmol) as the starting material, Yield: (0.550 g, 81%); $[\alpha]_D$ = +40.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 1.45 (s, 9H), 2.08 (s, 3H), 2.11 (s, 3H), 2.12 (s, 3H),

2.93 – 3.04 (m, 2H), 3.79 (s, 3H), 4.10 – 4.19 (m, 2H), 4.23 (dd, 1H, *J* = 12.3, 4.4 Hz), 4.53 (dd, 1H, *J* = 9.5, 4.4 Hz), 4.57 – 4.66 (m, 2H), 5.46 (t, 1H, *J* = 9.7 Hz), 5.58 (d, 1H, *J* = 8.0 Hz), 6.38 (s, 1H);^{13}C NMR (100.53 MHz, $CDCl_3$) δ 20.5, 20.6, 20.8, 26.8, 28.2 (3C), 36.9, 49.9, 52.8, 61.6, 66.8, 68.5, 71.6, 80.3, 95.3, 155.1, 168.4, 169.2, 169.7, 170.6, 171.0; IR ($CHCl_3$) ν 3374, 2977, 1745, 1510, 1438, 1162, 1056, 669 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{22}H_{32}INNaO_{13}$ 668.0816, found: 668.0789

Compound 6g: This compound is prepared using the above mentioned general procedure using **1a** (0.272 g, 1 mmol) as the starting material, Yield: (0.603 g, 81%); $[\alpha]_D$ = +8.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 0.03 (s, 3H), 0.04 (s, 3H), 0.85 (s, 9H), 2.05 (s, 3H), 2.09 (s, 3H), 2.11 (s, 3H), 3.88 (dd, 1H, *J* = 10.3, 3.1 Hz), 4.08 – 4.11 (m, 2H), 4.11 – 4.14 (m, 1H), 4.23 (dd, 1H, *J* = 12.5, 4.3 Hz), 4.46 – 4.49 (m, 1H), 4.50 (dd, 1H, *J* = 4.4, 1.5 Hz), 4.58 (dd, 1H, *J* = 9.5, 4.4 Hz), 5.15 (d, 2H, *J* = 10.9 Hz), 5.46 (t, 1H, *J* = 9.8 Hz), 5.58 (d, 1H, *J* = 8.5 Hz), 6.42 (s, 1H), 7.32 – 7.39 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ -5.7, -5.6, 18.2, 20.6, 20.7, 20.8, 25.7 (3C), 26.6, 56.0, 62.0, 63.4, 66.8, 67.3, 68.4, 71.6, 95.6, 128.2-128.6 (5C), 136.0, 155.9, 168.1, 169.3, 170.0, 170.7; IR ($CHCl_3$) ν 3365, 2934, 1747, 1512, 1427, 1117, 1056, 668 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{29}H_{42}INNaO_{12}Si$ 774.1419, found: 774.1423.

Compound 6h: This compound is prepared using the above mentioned general procedure using **1a** (0.272 g, 1 mmol) as the starting material, Yield: (0.605 g, 79%); $[\alpha]_D$ = +5.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 0.00 (s, 3H), 0.05 (s, 3H), 0.82 (s, 9H), 1.24 (d, 3H, *J* = 6.2 Hz), 2.03 (s, 3H), 2.09 (s, 6H), 3.98 – 4.14 (m, 2H), 4.22 (dd, 1H, *J* = 12.8, 4.3 Hz), 4.31 (dd, 1H, *J* = 9.3, 1.7 Hz), 4.40 – 4.62 (m, 3H), 5.16 (d, 2H, *J* = 6.6 Hz), 5.46 (t, 2H, *J* = 9.2 Hz), 6.39 (s, 1H), 7.29 – 7.41 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ -5.4, -4.4, 17.8, 20.5, 20.6, 20.7, 20.8, 25.5(3C), 26.6, 60.0, 61.4, 66.6, 67.3, 68.4, 68.5, 71.5, 95.5, 128.2-128.5 (5C), 135.9, 156.5, 168.4, 169.2, 169.6, 171.0; IR ($CHCl_3$) ν 3445, 2955, 1744, 1512, 1426, 1136, 1063, 698 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{30}H_{44}INNaO_{12}Si$ 788.1575, found: 788.1581.

Compound 7a: This compound is prepared using the above mentioned general procedure using **1b** (0.272 g, 1 mmol) as the starting material, Yield: (0.472 g, 76%); $[\alpha]_D$ = +41.2 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 2.01 (s, 3H), 2.08 (s, 3H), 2.18 (s, 3H), 2.51 – 2.69 (m, 2H), 3.48 (dt, 2H, *J* = 13.6, 6.4 Hz), 4.16 (d, 2H, *J* = 6.6 Hz), 4.30 (d, 1H, *J* = 4.6 Hz), 4.38 (t, 1H, *J* = 5.9 Hz), 4.84 – 4.88 (m, 1H), 5.08 (s, 2H), 5.40 – 5.42 (m, 2H), 6.52 (d, 1H, *J* = 1.2 Hz), 7.31 – 7.37 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 18.6, 20.5, 20.7, 20.8, 34.3, 36.3,

61.4, 64.6, 64.7, 66.7, 69.0, 96.1, 128.0-128.4 (5C), 136.1, 156.2, 169.4, 169.7, 169.9, 170.4; IR ($CHCl_3$) ν 3383, 2951, 1745, 1519, 1427, 1130, 1059, 666 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{23}H_{28}INNaO_{11}$ 644.0605, found 644.0617.

Compound 7b: This compound is prepared using the above mentioned general procedure using **1b** (0.272 g, 1 mmol) as the starting material, Yield: (0.487 g, 83%); $[\alpha]_D$ = +22.4 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78 MHz, $CDCl_3$) δ 1.42 (s, 3H), 1.44 (s, 9H), 2.05 (s, 3H), 2.09 (s, 3H), 2.19 (s, 3H), 4.12 – 4.25 (m, 2H), 4.31 (d, 2H, *J* = 4.3 Hz), 4.47 (t, 1H, *J* = 6.1 Hz), 4.86 – 4.91 (m, 1H), 5.20 (m, 1H, *J* = 7.3 Hz), 5.45 (s, 1H), 6.52 (s, 1H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 17.7, 18.5, 20.5, 20.6, 20.7, 28.1 (3C), 49.0, 61.2, 64.6 (2C), 69.0, 79.9, 96.5, 154.9, 169.2, 169.7, 170.2, 170.8; IR ($CHCl_3$) ν 3372, 2980, 1748, 1515, 1427, 1166, 1060, 670 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{20}H_{30}INNaO_{11}$ 610.0761, found: 610.0771.

Compound 7c: This compound is prepared using the above mentioned general procedure using **1b** (0.272 g, 1 mmol) as the starting material, Yield: (0.556 g, 74%); $[\alpha]_D$ = +20.6 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78 MHz, $CDCl_3$) δ -0.07 (s, 3H), -0.05 (s, 3H), 0.76 (s, 9H), 1.94 (s, 3H), 1.99 (s, 3H), 2.10 (s, 3H), 3.79 (dd, 1H, *J* = 10.3, 3.1 Hz), 3.99 (dd, 1H, *J* = 10.3, 2.7 Hz), 4.07 (dd, 1H, *J* = 15.6, 6.6 Hz), 4.16 (d, 1H, *J* = 4.9 Hz), 4.25 – 4.32 (m, 1H), 4.38 (dt, 1H, *J* = 8.3, 2.8 Hz), 4.71 – 4.79 (m, 1H), 5.05 (d, 2H, *J* = 4.4 Hz), 5.34 (s, 1H), 5.52 (d, 1H, *J* = 8.4 Hz), 6.46 (s, 2H), 7.24-7.30 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ -5.7, -3.7, 18.0, 18.0, 20.5, 20.7, 20.9, 25.6 (3C), 25.7, 61.3, 63.3, 64.5, 64.6, 67.2, 69.3, 97.2, 128.2-128.5 (5C), 136.0, 155.9, 168.1, 169.3, 170.0, 170.3; IR ($CHCl_3$) ν 3367, 2953, 1748, 1513, 1464, 1130, 1058, 670 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{29}H_{42}INNaO_{12}Si$ 774.1419 found: 774.1425.

Compound 7d: This compound is prepared using the above mentioned general procedure using **1b** (0.272 g, 1 mmol) as the starting material, Yield: (0.689 g, 90%); $[\alpha]_D$ = +29.4 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78 MHz, $CDCl_3$) δ -0.05 (s, 3H), 0.00 (s, 3H), 0.78 (s, 9H), 1.20 (d, 3H, *J* = 6.2 Hz), 1.97 (s, 3H), 2.04 (s, 3H), 2.13 (s, 3H), 4.00 – 4.07 (m, 1H), 4.12 (ddd, 1H, *J* = 11.3, 6.5, 1.4 Hz), 4.20 – 4.25 (m, 2H), 4.28 (t, 1H, *J* = 6.6 Hz), 4.35 – 4.43 (m, 1H), 4.77 (t, 1H, *J* = 3.5 Hz), 5.08 – 5.16 (m, 2H), 5.36 (s, 1H), 5.41 (d, 1H, *J* = 8.9 Hz), 6.47 (s, 1H), 7.25 – 7.39 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ -5.4, -4.3, 17.8, 18.1, 20.6, 20.8, 20.9, 20.9, 25.5(3C), 60.0, 61.3, 64.5, 64.6, 67.3, 68.4, 69.3, 97.3, 128.3, 128.6, 136.0, 156.6, 168.6, 169.3, 169.9, 170.3; IR ($CHCl_3$) ν 3446, 2934, 1749, 1511, 1426, 1136, 1067, 699 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{30}H_{44}INNaO_{12}Si$ 788.1575; found 788.1572.

Compound 8a: This compound is prepared using the above mentioned general procedure using **1c** (0.560 g, 1 mmol) as the starting material, Yield: (0.691 g, 76%); $[\alpha]_D$ = +31.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 1.98 (s, 3H), 2.06 (s, 3H), 2.07 (s, 3H), 2.12 (s, 3H), 2.15 (s, 3H), 2.16 (s, 3H), 2.65 (t, 2H, *J* = 5.8 Hz), 3.50 (q, 2H, *J* = 5.9 Hz), 3.92 – 3.98 (m, 1H), 3.99 – 4.14 (m, 4H), 4.18 (dd, 1H, *J* = 11.3, 6.8 Hz), 4.43 (dd, 1H, *J* = 12.1, 1.7 Hz), 4.49 – 4.54 (m, 1H), 4.61 (d, 1H, *J* = 8.0 Hz), 4.67 (dd, 1H, *J* = 7.2, 4.1 Hz), 5.00 (dd, 1H, *J* = 10.5, 3.5 Hz), 5.10 (s, 2H), 5.16 (dd, 1H, *J* = 10.4, 7.9 Hz), 5.30 (t, 1H, *J* = 6.0 Hz), 5.36 – 5.40 (m, 1H), 6.35 (d, 1H, *J* = 2.5 Hz), 7.32 – 7.38 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 20.5, 20.6 (2C), 20.7, 20.8, 21.0, 26.9, 34.4, 36.4, 61.1, 61.7, 66.7, 66.8, 69.0, 69.4, 70.7, 70.9, 71.8, 75.4, 94.7, 101.4, 128.1-128.5 (5C), 136.3, 156.2, 169.3, 169.5, 170.0, 170.1 (2C), 170.4 (2C); IR ($CHCl_3$) ν 3378, 2929, 1747, 1516, 1461, 1133, 1076, 668 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{35}H_{44}INNaO_{19}$ 932.1449, found 932.1443.

Compound 8b: This compound is prepared using the above mentioned general procedure using **1c** (0.560 g, 1 mmol) as the starting material, Yield: (0.727 g, 83%); $[\alpha]_D$ = +25.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 1.44 (s, 9H), 1.98 (s, 3H), 2.03 (s, 3H), 2.08 (d, 6H, *J* = 1.1 Hz), 2.14 (s, 3H), 2.15 (s, 3H), 2.17 (s, 3H), 3.99 (t, 1H, *J* = 6.6 Hz), 4.05 – 4.13 (m, 3H), 4.14 – 4.21 (m, 2H), 4.29 – 4.36 (m, 1H), 4.43 (d, 1H, *J* = 11.8 Hz), 4.50 – 4.55 (m, 1H), 4.64 (d, 1H, *J* = 7.9 Hz), 4.68 (s, 1H), 5.02 (dd, 1H, *J* = 0.4, 3.3 Hz), 5.15 (dd, 1H, *J* = 10.4, 8.1 Hz), 5.23 (d, 1H, *J* = 7.1 Hz), 5.38 (d, 1H, *J* = 3.4 Hz), 6.35 (s, 1H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 17.7, 20.2, 20.3 (2C), 20.4, 20.5, 20.7, 26.7, 28.0 (3C), 48.9, 61.0, 61.4, 66.6, 68.8, 69.1, 70.4, 70.6, 71.6, 75.0, 80.0, 95.0, 101.1, 154.8, 169.0, 169.2, 169.7, 169.8, 170.1 (2C), 171.1; IR ($CHCl_3$) ν 3382, 2981, 1747, 1514, 1453, 1164, 1053, 666 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{32}H_{46}INNaO_{19}$ 898.1606 found 898.1613.

Compound 8c: This compound is prepared using the above mentioned general procedure using **1c** (0.560 g, 1 mmol) as the starting material, Yield: (0.774 g, 80%); $[\alpha]_D$ = +35.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 1.45 (s, 9H), 1.98 (s, 3H), 2.08 (s, 6H), 2.15 (s, 6H), 2.17 (s, 3H), 2.90 – 3.09 (m, 2H), 3.78 (s, 3H), 3.95 (t, 1H, *J* = 6.7 Hz), 4.01 – 4.15 (m, 4H), 4.18 (dd, 1H, *J* = 11.2, 6.7 Hz), 4.46 (dd, 1H, *J* = 12.0, 1.5 Hz), 4.54 (s, 1H), 4.61 (dd, 3H, *J* = 12.1, 7.4 Hz), 5.00 (dd, 1H, *J* = 10.4, 3.5 Hz), 5.15 (dd, 1H, *J* = 10.4, 7.9 Hz), 5.32 – 5.43 (m, 1H), 5.50 (d, 1H, *J* = 8.1 Hz), 6.33 (d, 1H, *J* = 2.0 Hz); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 20.5, 20.6, 20.6, 20.7, 20.8, 20.9, 27.0, 28.2 (3C), 36.9, 49.9, 52.9, 61.1, 61.6, 66.8, 69.0, 69.1, 70.7, 70.9,

72.0, 75.2, 80.4, 95.2, 101.4, 155.2, 168.7, 169.3, 169. 5, 170.0, 170.1, 170.4 (2C), 171.1; IR ($CHCl_3$) ν 3678, 2929, 1746, 1512, 1434, 1164, 1052, 756 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{34}H_{48}INNaO_{21}$ 956.1661, found 956.1667.

Compound 8d: This compound is prepared using the above mentioned general procedure using **1c** (0.560 g, 1 mmol) as the starting material, Yield: (0.832 g, 80%); $[\alpha]_D$ = +18.0 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78 MHz, $CDCl_3$) δ 0.03 (s, 3H), 0.04 (s, 3H), 0.85 (s, 9H), 1.98 (s, 3H), 2.07 (s, 6H), 2.10 – 2.18 (m, 9H), 3.88 (dd, 1H, *J* = 10.4, 3.1 Hz), 3.94 (t, 1H, *J* = 6.7 Hz), 3.97 – 4.04 (m, 1H), 4.07 (m, 4H), 4.18 (dd, 1H, *J* = 11.2, 6.7 Hz), 4.41 (d, 1H, *J* = 13.6 Hz), 4.41 – 4.53 (m, 2H), 4.61 (d, 1H, *J* = 7.9 Hz), 4.72 (dd, 1H, *J* = 7.0, 4.1 Hz), 5.00 (dd, 1H, *J* = 10.4, 3.4 Hz), 5.06 – 5.23 (m, 3H), 5.37 (d, 1H, *J* = 3.2 Hz), 5.58 (d, 1H, *J* = 8.6 Hz), 6.39 (d, 1H, *J* = 2.4 Hz), 7.32 – 7.40 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ -5.6, -5.6, 18.1, 20.5, 20.6, 20.6, 20.7, 20.8, 20.9, 25.7 (3C), 26.5, 55.9, 61.1, 61.6, 63.3, 66.7, 67.2, 69.0, 69.3, 70.7, 70.9, 71.8, 75.4, 95.4 , 101. 4, 128.2-128.5 (5C), 136.1, 155.9, 168.3, 169.2, 169.2, 170.0, 170.1, 170.4 (2C); IR ($CHCl_3$) ν 3369, 2935, 1748, 1514, 1425, 1112, 1057, 699 cm^{-1}; HRMS (TOF) *m/z* $[M + K]^+$ calcd for $C_{41}H_{58}IKNO_{20}Si$ 1078.2003 found 1078.2015.

Compound 8e: This compound is prepared using the above mentioned general procedure using **1c** (0.560 g, 1 mmol) as the starting material, Yield: (0.811 g, 77%); $[\alpha]_D$ = +13.0 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78 MHz, $CDCl_3$) δ -0.07 (s, 3H), -0.02 (s, 3H), 0.75 (s, 9H), 1.17 (d, 3H, *J* = 6.2 Hz), 1.89 (s, 3H), 1.99 (s, 6H), 2.02 (s, 3H), 2.05 (s, 3H), 2.07 (s, 3H), 3.85 – 3.95 (m, 2H), 3.96 – 4.05 (m, 2H), 4.09 (dd, 2H, *J* = 11.2, 6.8 Hz), 4.23 (dd, 1H, *J* = 9.4, 1.6 Hz), 4.35(m, 2H), 4.46 (dd, 1H, *J* = 4.0, 2.2 Hz), 4.55 (d, 1H, *J* = 7.9 Hz), 4.59 (dd, 1H, *J* = 8.0, 4.8 Hz), 4.93 (dd, 1H, *J* = 10.4, 3.3 Hz), 5.00 – 5.14 (m, 3H), 5.29 (d, 1H, *J* = 3.3 Hz), 5.40 (d, 1H, *J* = 9.5 Hz), 6.29 (d, 1H, *J* = 1.9 Hz), 7.23 – 7.36 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ -5.5, -4.4, 17.7, 20.4, 20.4, 20.5, 20.5, 20.6, 20.7, 20.7, 25.4 (3C), 26.8, 59.8, 61.0, 61.4, 66.6, 67.2, 68.4, 68.9, 69.1, 70.5, 70.8, 71.7, 74.9, 95.2, 101.1, 128.1-128.4 (5C), 136.0, 156.4, 168.9, 169.1, 169.1, 169.9, 169.9, 170.2, 170.3; IR ($CHCl_3$) ν 3445, 2932, 1745, 1512, 1462, 1134, 1071, 698 cm^{-1}; HRMS (TOF) *m/z* $[M + K]^+$ calcd for $C_{42}H_{60}IKNO_{20}Si$ 1092.2160 found 1092.2193.

Compound 9a: This compound is prepared using the above mentioned general procedure using **6g** (0.750 g, 1 mmol) as the starting material, Yield: (0.494 g, 76%); $[\alpha]_D$ = +40.7 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78 MHz, $CDCl_3$) δ 2.03 (s, 3H), 2.07 (s, 3H), 2.09 (s, 3H), 3.80 (s, 3H), 3.92 – 4.01 (m, 3H), 4.12 (dd, 1H, *J* = 12.3, 2.3 Hz), 4.18 (dd, 1H, *J* = 12.3, 5.0 Hz), 4.48 (dd,

1H, *J* = 4.3, 1.3 Hz), 4.54 (dt, 2H, *J* = 9.2, 5.6 Hz), 5.15 (s, 1H), 5.14 (s, 2H), 5.31 (t, 1H, *J* = 9.6 Hz), 5.82 (d, 1H, *J* = 8.2 Hz), 7.31 – 7.39 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 20.5, 20.6, 20.8, 28.5, 52.8, 54.1, 61.9, 67.1, 68.7 (2C), 68.9, 69.6, 101.8, 128.0-128.4 (5C), 135.9, 155.7, 169.3, 169.6, 170.0, 170.5; IR ($CHCl_3$) ν 3378, 2930, 1742, 1519, 1452, 1123, 1051, 699 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{24}H_{30}INNaO_{12}$ 674.0710, found 674.0709.

Compound 9b: This compound is prepared using the above mentioned general procedure using **6h** (0.750 g, 1 mmol) as the starting material, Yield: (0.485 g, 73%); $[\alpha]_D$ = +35.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (d, 3H, *J* = 6.4 Hz), 2.05 (s, 3H), 2.07 (s, 3H), 2.09 (s, 3H), 3.78 (s, 3H), 4.06 (ddd, 1H, *J* = 9.8, 5.2, 2.4 Hz), 4.13 (dd, 1H, *J* = 12.2, 2.3 Hz), 4.20 (dd, 1H, *J* = 12.2, 5.3 Hz), 4.32 – 4.39 (m, 2H), 4.44 (dd, 1H, *J* = 9.7, 2.3 Hz), 4.53 (dd, 1H, *J* = 9.3, 4.3 Hz), 5.16 (d, 3H, *J* = 9.4 Hz), 5.31 (t, 1H, *J* = 9.6 Hz), 5.48 (d, 1H, *J* = 9.6 Hz), 7.30 – 7.44 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 17.8, 20.6, 20.6, 20.9, 28.8, 52.7, 58.5, 62.2, 67.3, 67.5, 68.7, 69.7, 77.3, 102.6, 128.2-128.5 (5C), 135.9, 156.5, 169.4, 169.7, 170.6, 170.6; IR ($CHCl_3$) ν 3358, 2950, 1744, 1518, 1452, 1175, 1038, 643 cm^{-1};HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{25}H_{32}INNaO_{12}$ 688.0867, found 688.0861.

Compound 10a. This compound is prepared using the above mentioned general procedure using **9a** (0.400 g, 0.6 mmol) as the starting material, Yield: (0.210 g, 65%); $[\alpha]_D$ = +48.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 1.73 (td, 1H, *J* = 12.9, 3.7 Hz), 1.93 (s, 3H), 1.95 (s, 3H), 2.00 (s, 3H), 2.13 (dd, 1H, *J* = 13.1, 5.3 Hz), 3.71 (s, 3H), 3.84 (s, 3H), 3.96 (d, 1H, *J* = 12.2 Hz), 4.19 (dd, 1H, *J* = 12.2, 4.7 Hz), 4.48 (d, 1H, *J* = 8.0 Hz), 4.82 – 4.93 (m, 2H), 5.07 (s, 2H), 5.15 (td, 1H, *J* = 11.0, 5.4 Hz), 5.67 (d, 1H, *J* = 8.4 Hz), 7.24 – 7.33 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 20.7 (2C), 20.9, 34.7, 52.7, 54.2, 62.1, 67.2, 68.3, 68.4, 68.7, 69.0, 97.7, 128.1-128.5 (5C), 136.0, 155.8, 169.8, 170.1, 170.3, 170.7; IR ($CHCl_3$) ν 3356, 2956, 1740, 1518, 1450, 1132, 1047, 668 cm^{-1};HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{24}H_{31}NNaO_{12}$ 548.1744 found 548.1753.

Compound 10b: This compound is prepared using the above mentioned general procedure using **9b** (0.400 g, 0.6 mmol) as the starting material, Yield: (0.202 g, 61%); $[\alpha]_D$ = +39.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 1.30 (d, 3H, *J* = 6.4 Hz), 1.77 (td, 1H, *J* = 12.7, 3.8 Hz), 2.00 (s, 3H), 2.04 (s, 3H), 2.04 (m, 1H), 2.07 (s, 3H), 3.74 (s, 3H), 3.98 – 4.07 (m, 2H), 4.27 (dd, 1H, *J* = 12.0, 4.9 Hz), 4.34 (dd, 1H, *J* = 6.4, 2.2 Hz), 4.40 (dd, 1H, *J* = 9.7, 2.2 Hz), 4.88 – 5.00 (m, 2H), 5.15 (s, 2H), 5.15 – 5.29 (m, 1H), 5.48 (d, 1H, *J* = 9.8 Hz), 7.31 – 7.43 (m, 5H);

^{13}C NMR (100.53 MHz, $CDCl_3$) δ 18.2, 20.6 (2C), 20.9, 35.1, 52.5, 58.5, 62.2, 67.2, 68.3, 68.5, 69.3, 76.2, 98.4, 128.1-128.4 (5C), 136.0, 156.4, 169.8, 170.1, 170.6, 170.9; IR ($CHCl_3$) ν 3361, 2955, 1742, 1516, 1453, 1128, 1051, 700 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{25}H_{33}NNaO_{12}$ 562.1900 found 562.1909.

Compound 11a: This compound is prepared using the above mentioned general procedure using **7c** (0.750 g, 1 mmol) as the starting material, Yield: (0.474 g, 73%); $[\alpha]_D$ = +35.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 2.03 (s, 3H), 2.07 (s, 3H), 2.16 (s, 3H), 3.79 (s, 3H), 3.97 (s, 2H), 4.12 (d, 1H, *J* = 10.8 Hz), 4.20 (t, 3H, *J* = 9.9 Hz), 4.50 – 4.63 (m, 1H), 4.85 (s, 1H), 5.13 (s, 2H), 5.28 (s, 1H), 5.35 (s, 1H), 5.78 (d, 1H, *J* = 7.5 Hz), 7.29 – 7.40 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 20.6, 20.7, 20.8, 20.9, 23.8, 52.8, 54.1, 61.9, 65.2, 67.1, 67.6, 68.9, 102.8, 128.0-128.5 (5C), 136.0, 155.8, 169.4, 169.9, 170.0, 170.5; IR ($CHCl_3$) ν 3361, 2953, 1744, 1517, 1429, 1119, 1053, 669 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{24}H_{30}INNaO_{12}$ 674.0710 found 674.0708.

Compound 11b: This compound is prepared using the above mentioned general procedure using **7d** (0.750 g, 1 mmol) as the starting material, Yield: (0.478 g, 72%); $[\alpha]_D$ = +40.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 1.31 (d, 3H, *J* = 6.4 Hz), 2.04 (s, 3H), 2.06 (s, 3H), 2.16 (s, 3H), 3.79 (s, 3H), 4.09 (d, 1H, *J* = 5.0 Hz), 4.11 – 4.15 (m, 1H), 4.20 (dd, 1H, *J* = 11.4, 7.2 Hz), 4.30 – 4.35 (m, 1H), 4.37 (dd, 1H, *J* = 6.4, 2.3 Hz), 4.42 (dd, 1H, *J* = 9.7, 2.2 Hz), 4.79 – 4.84 (m, 1H), 5.14 (s, 2H), 5.30 (s, 1H), 5.35 (s, 1H), 5.46 (d, 1H, *J* = 9.7 Hz), 7.31 – 7.41 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 18.0, 20.6, 20.7, 20.8, 20.9, 52.7, 58.5, 62.0, 65.0, 65.3, 67.3 (2C), 77.1, 104.0, 128.1-128.5 (5C), 136.0, 156.5, 169.5, 169.9, 170.4, 170.7; IR ($CHCl_3$) ν 3359, 2951, 1745, 1518, 1452, 1174, 1038, 702 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{25}H_{32}IN\ NaO_{12}$ 688.0867 found 688.0861.

Compound 12a: This compound is prepared using the above mentioned general procedure using **11a** (0.400 g, 0.6 mmol) as the starting material, Yield: (0.193 g, 60%); $[\alpha]_D$ = +62.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 1.76 (dd, 1H, *J* = 12.9, 4.9 Hz), 1.91 (s, 3H), 1.96 (s, 3H), 2.01 (dd, 1H, *J* = 12.8, 3.6 Hz), 2.05 (s, 3H), 3.71 (s, 3H), 3.85 (d, 2H, *J* = 3.0 Hz), 3.99 (m, 3H), 4.44 – 4.54 (m, 1H), 4.90 (d, 1H, *J* = 3.1 Hz), 5.07 (d, 2H, *J* = 1.8 Hz), 5.12 (dt, 1H, *J* = 12.5, 4.2 Hz), 5.24 (d, 1H, *J* = 2.4 Hz), 5.67 (d, 1H, *J* = 8.3 Hz), 7.23 – 7.33 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 20.7, 20.7, 20.8, 29.9, 52.7, 54.2, 62.4, 65.8, 66.4, 67.2 (2C), 68.4, 98.2, 128.1-128.5 (5C), 136.0, 155.9, 170.0, 170.2, 170.4, 170.5; IR ($CHCl_3$) ν 3356, 2956, 1744,

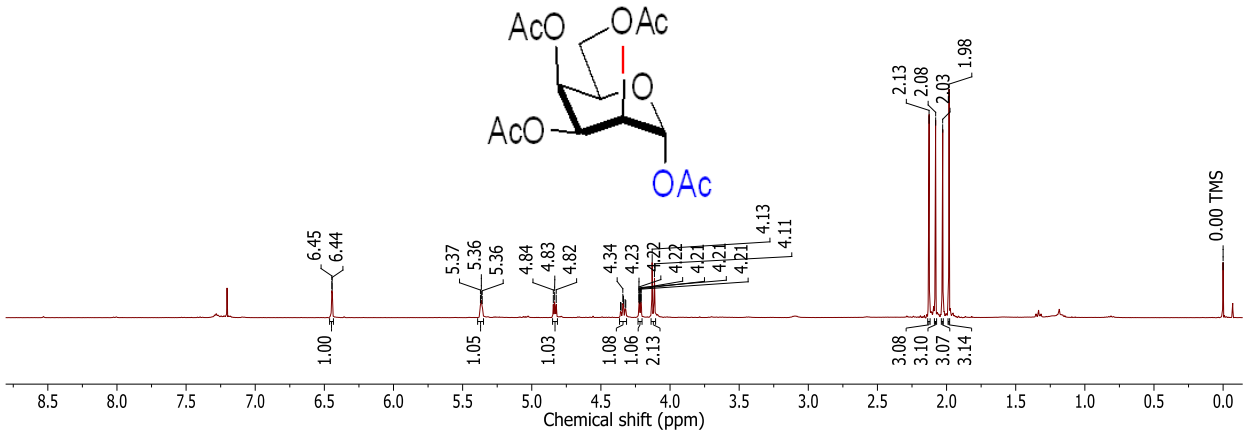
1519, 1449, 1164, 1033, 701 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{24}H_{31}N\ NaO_{12}$ 548.1744 found 548.1754.

Compound 12b: This compound is prepared using the above mentioned general procedure using **11b** (0.400 g, 0.6 mmol) as the starting material, Yield: (0.209 g, 63%); $[\alpha]_D$ = +102.8 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78 MHz, $CDCl_3$) δ 1.30 (d, 3H, *J* = 6.4 Hz), 1.70 (dd, 1H, *J* = 12.7, 5.0 Hz), 1.98 (s, 3H), 2.04 (s, 3H), 2.04 (m, 1H), 2.12 (s, 3H), 3.75 (s, 3H), 4.07 (dd, 2H, *J* = 6.4, 2.2 Hz), 4.18 (t, 1H, *J* = 6.5 Hz), 4.35 (dd, 1 H, *J* = 6.4, 2.1 Hz), 4.39 (dd, 1H, *J* = 9.8, 2.1 Hz), 4.98 (d, 1H, *J* = 3.2 Hz), 5.15 (s, 2H), 5.15 – 5.21 (m, 1H), 5.31 (d, 1H, *J* = 2.1 Hz), 5.44 (d, 1H, *J* = 9.7 Hz), 7.32 – 7.41 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 18.3, 20.6, 20.7, 20.8, 30.2, 52.5, 58.6, 62.5, 65.8, 66.5, 67.1, 67.2, 76.1, 99.1, 128.1-128.5 (5C), 136.0, 156.5, 170.1, 170.2, 170.4, 171.1; IR ($CHCl_3$) : 3358, 2955, 1744, 1517, 1452, 1169, 1028, 701 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{25}H_{33}NNaO_{12}$ 562.1900 found 562.1909.

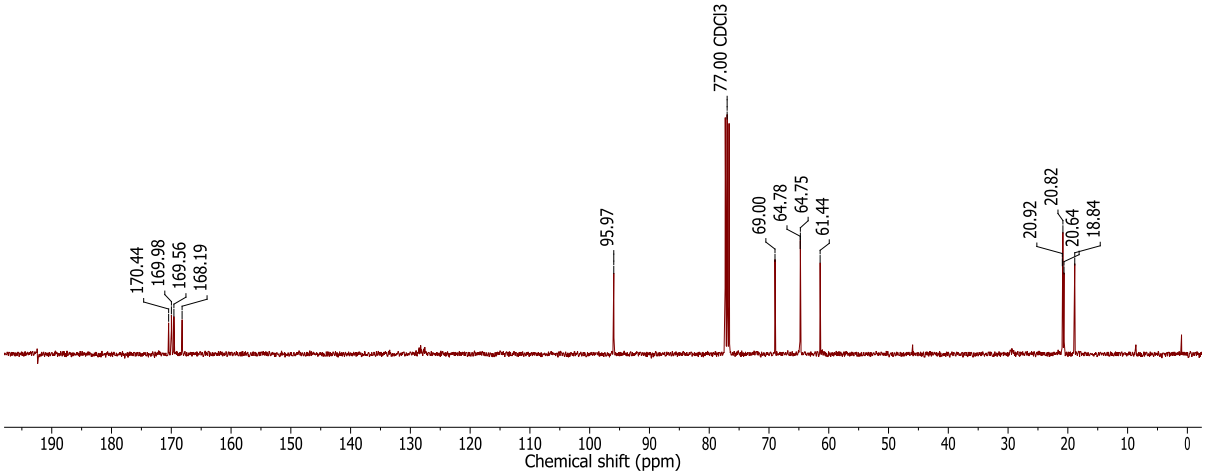
2.4 Spectral Charts of Representative Compounds

{Kindly see the supporting documents file for spectral charts of all compounds}

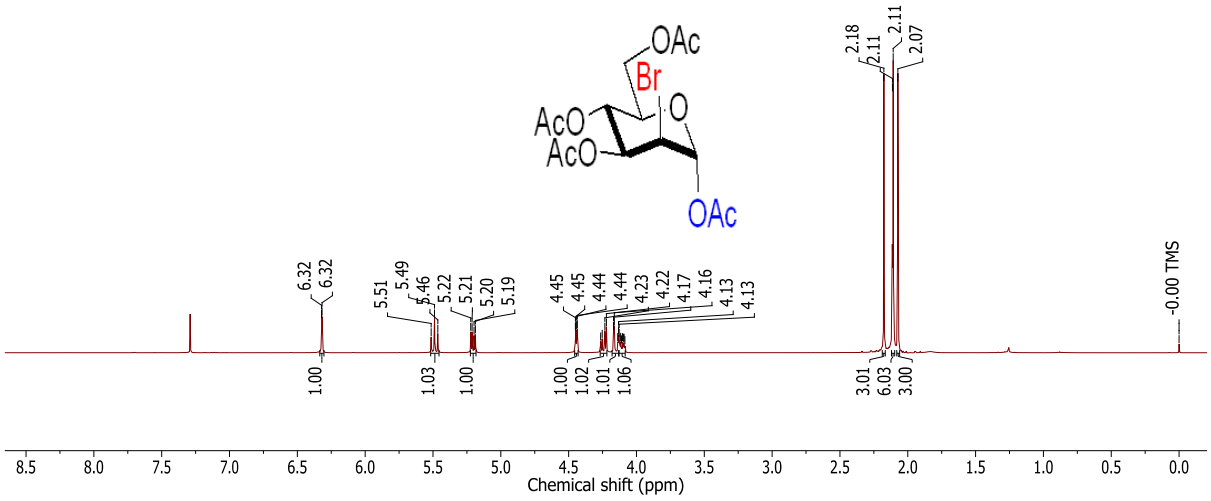
^1H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **2b**



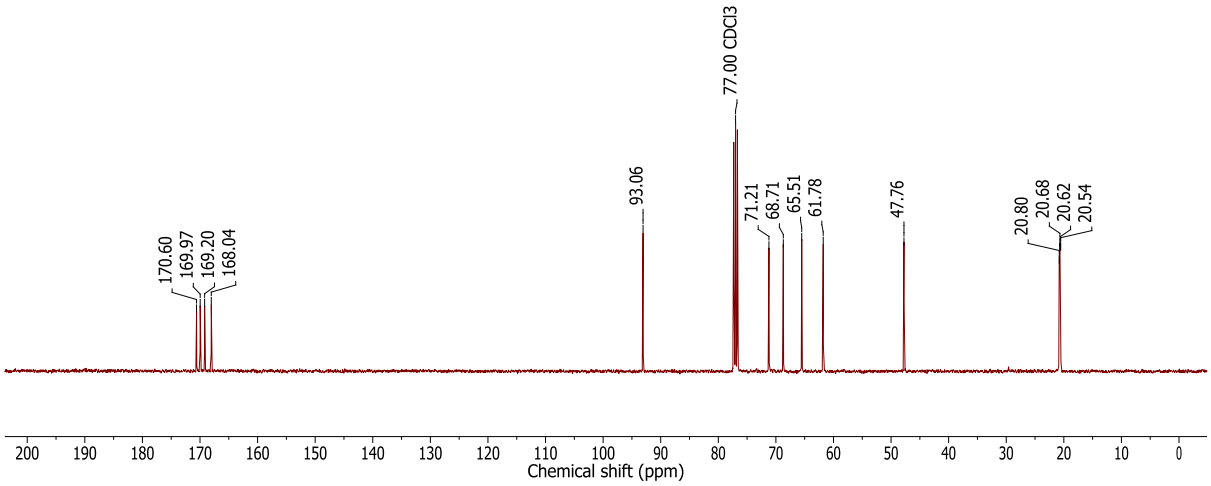
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **2b**



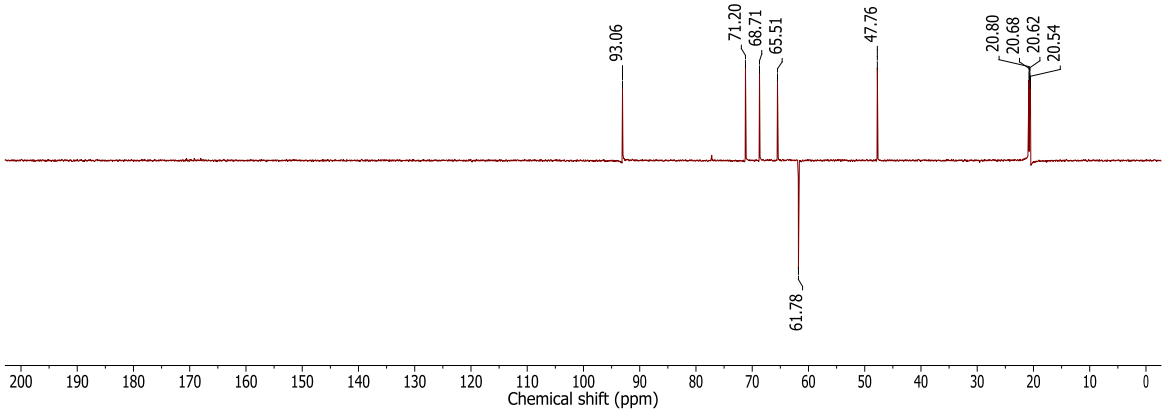
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **3a**



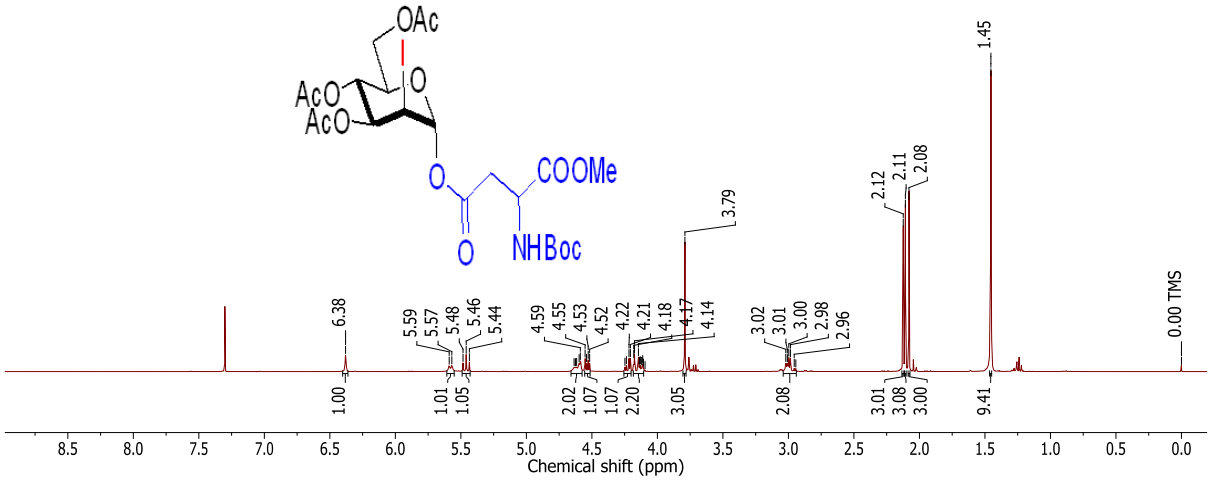
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **3a**



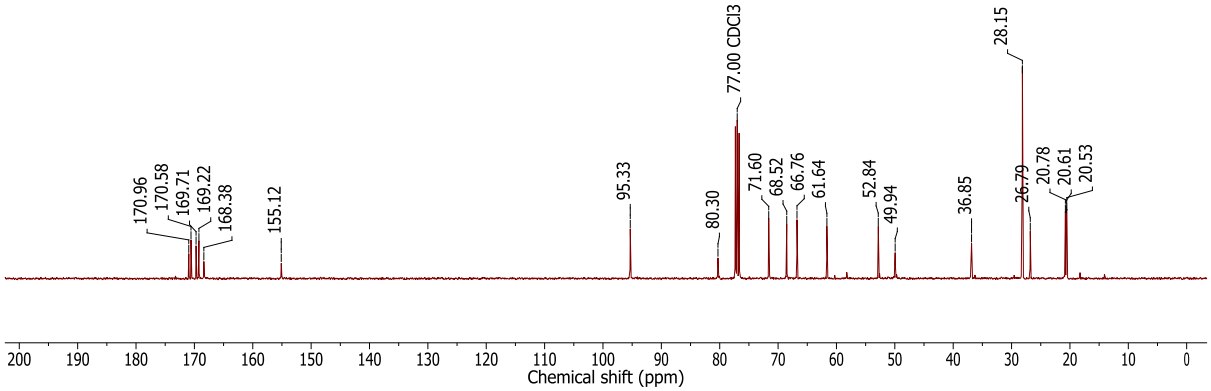
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **3a**



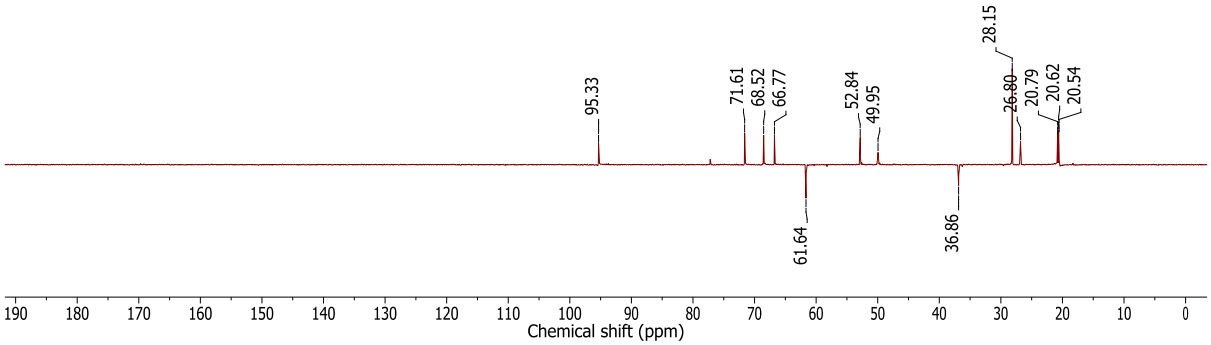
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **6f**



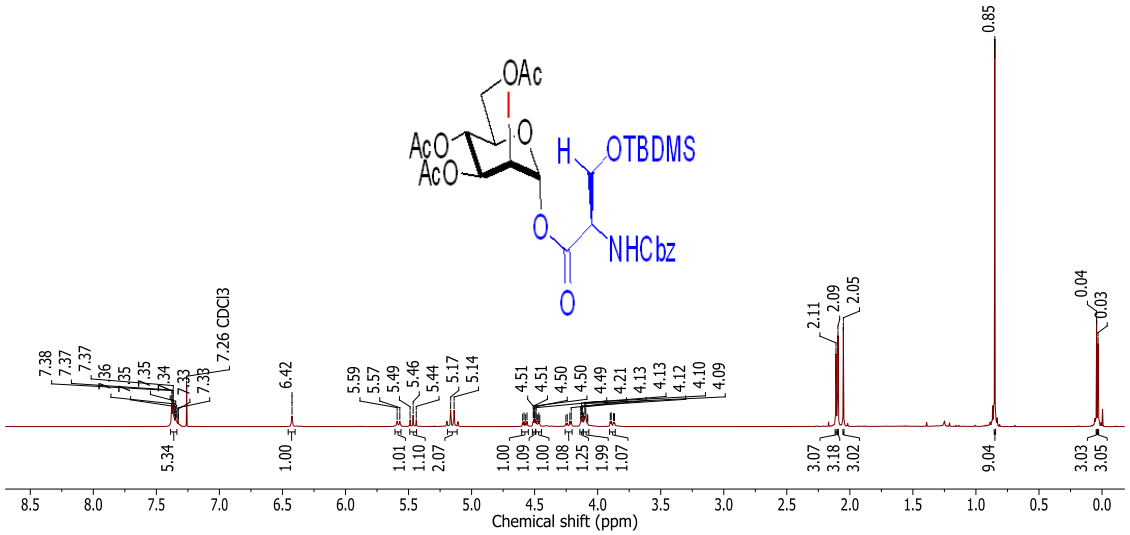
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **6f**



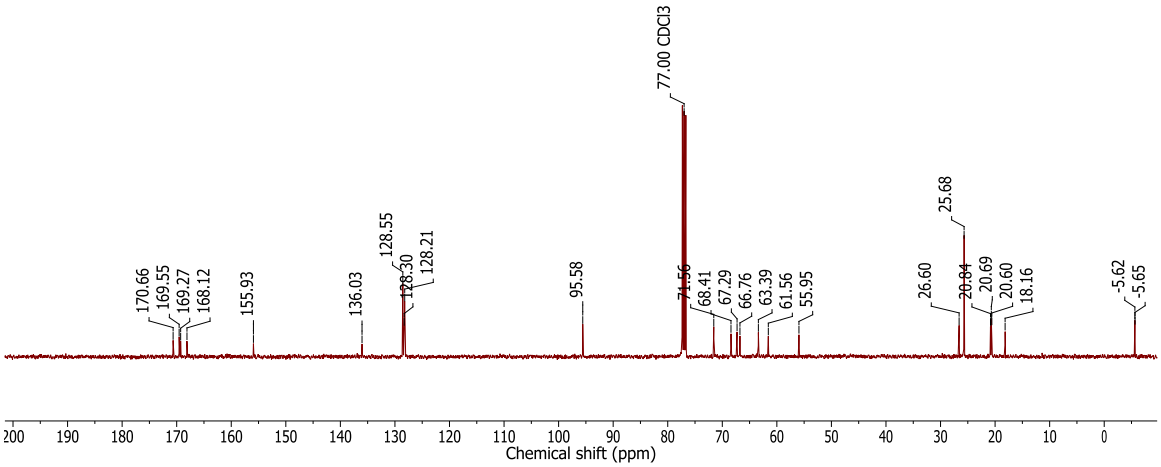
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **6f**



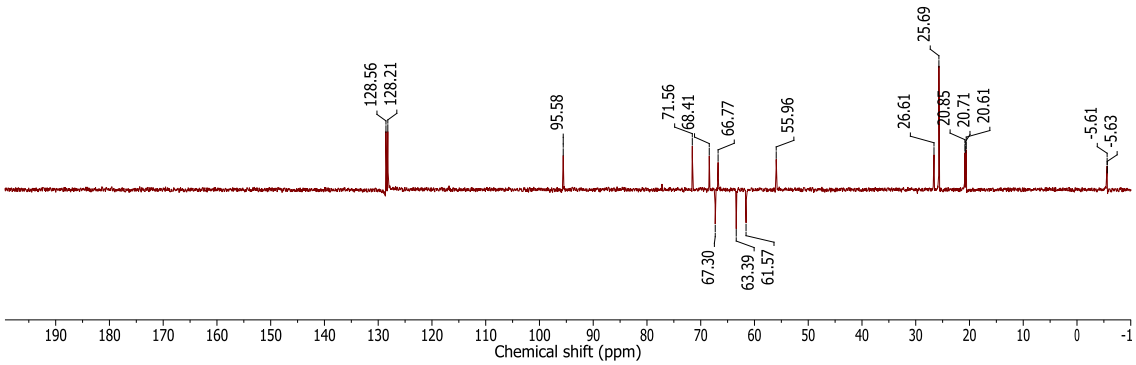
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **6g**



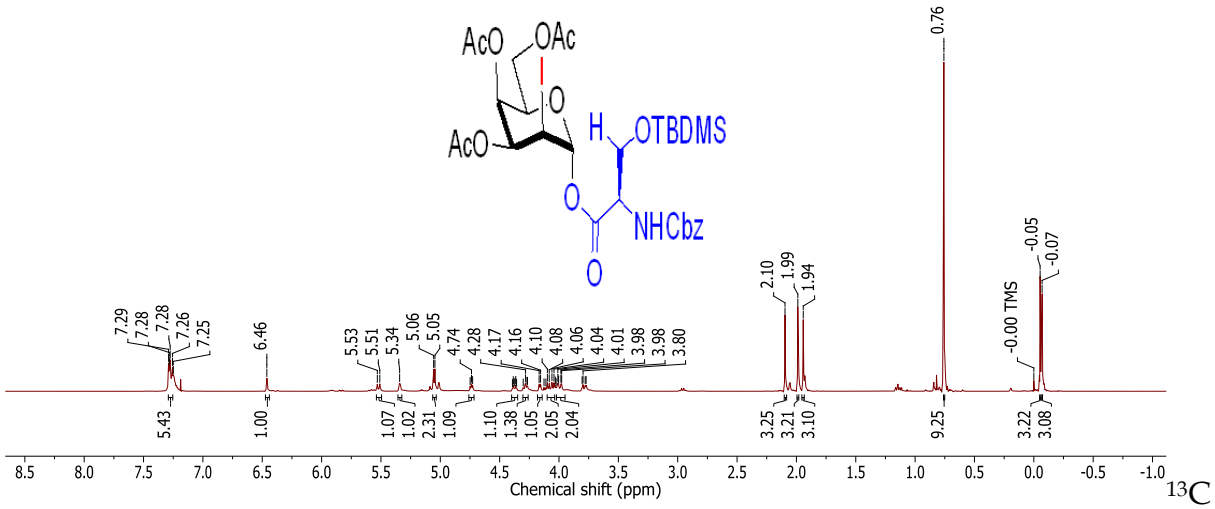
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **6g**



DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **6g**

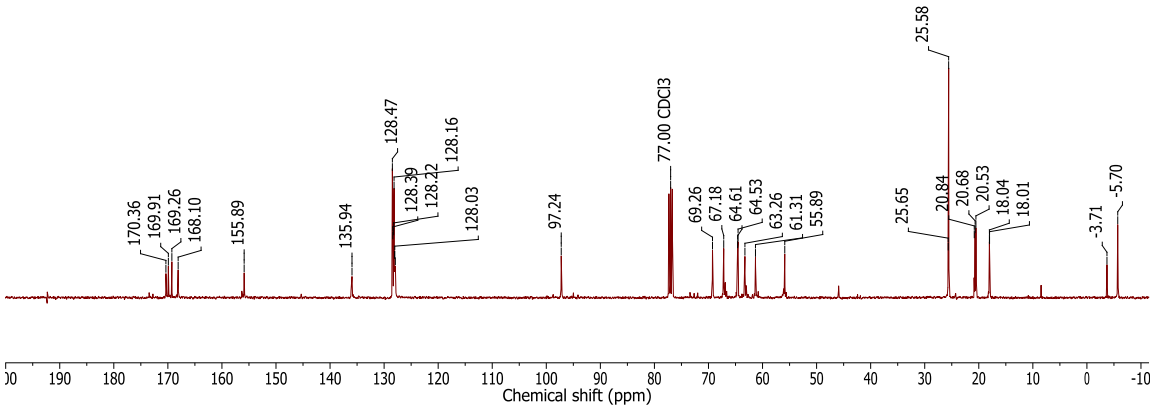


^1H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **7c**

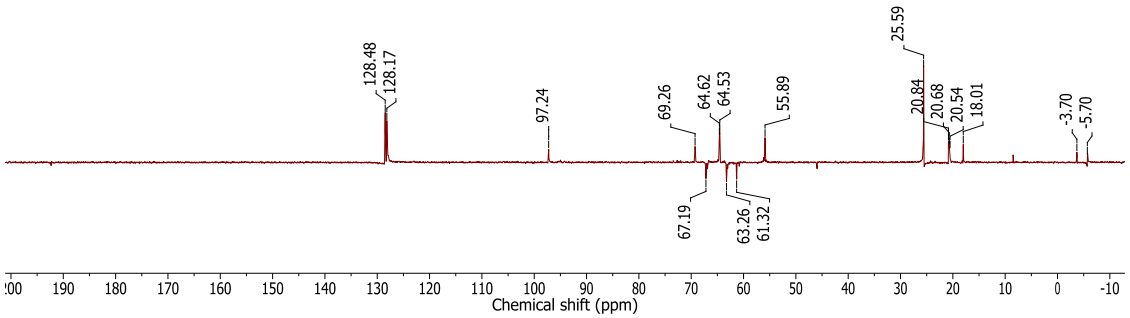


^{13}C

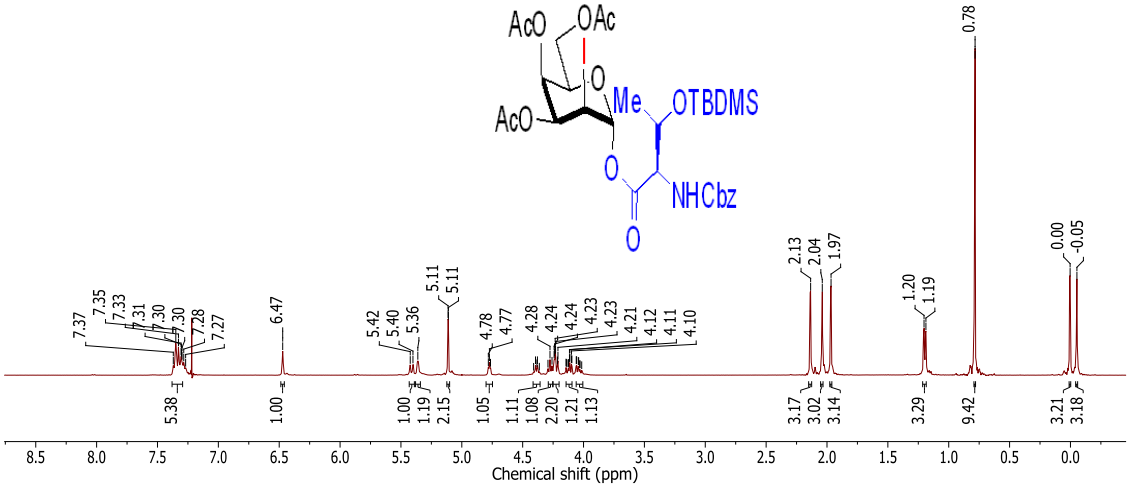
NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **7c**



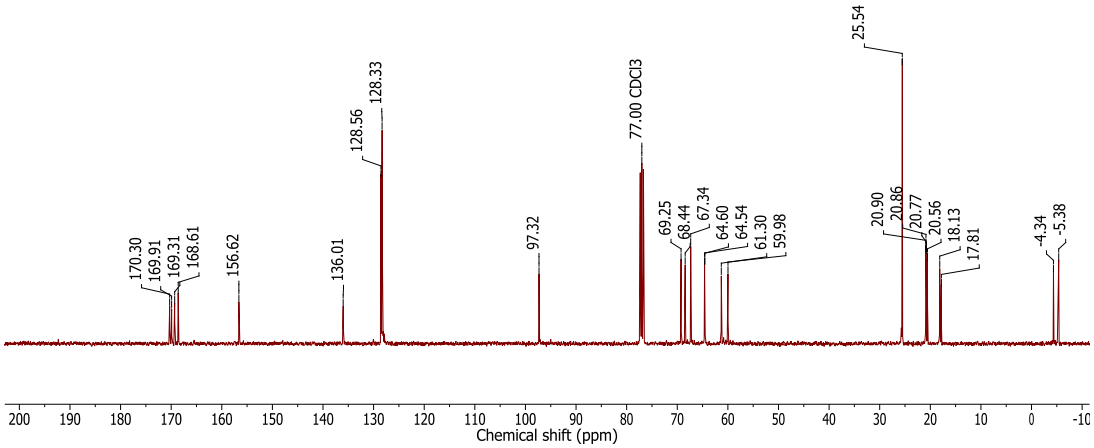
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **7c**



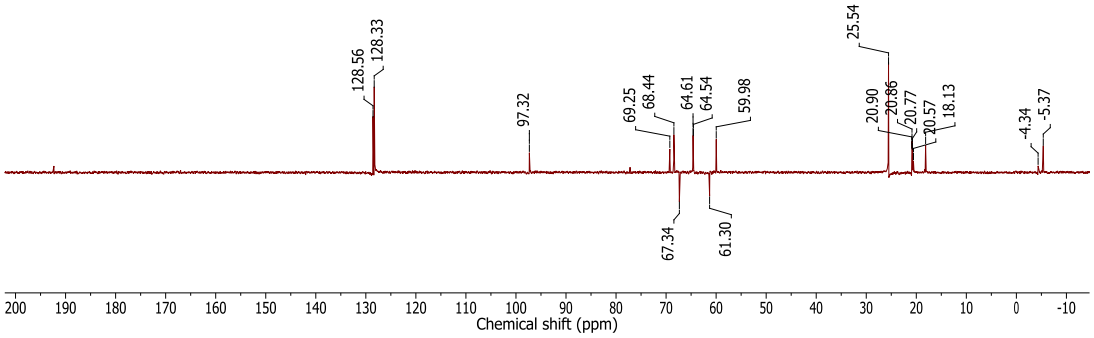
^1H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **7d**



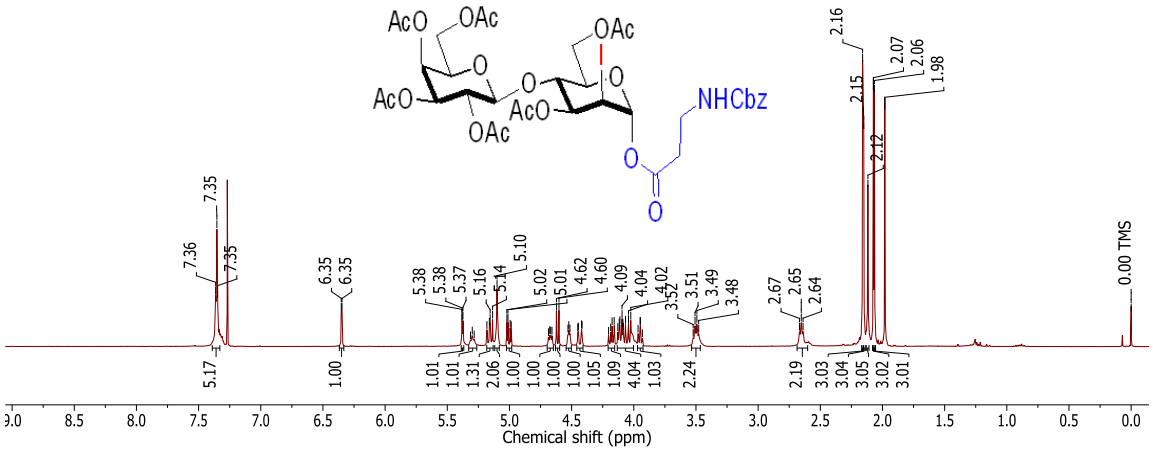
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **7d**



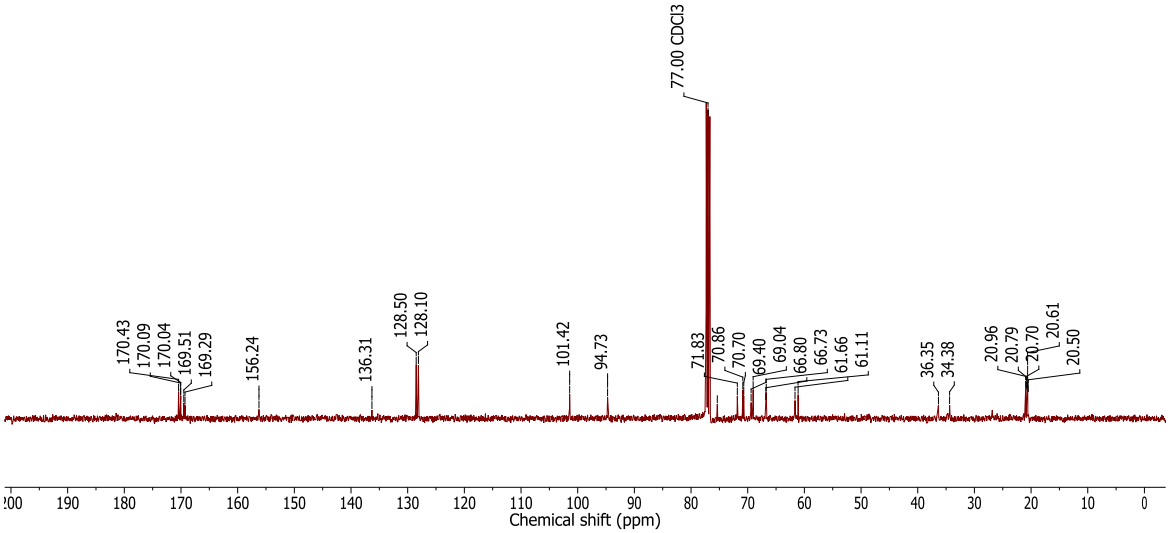
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **7d**



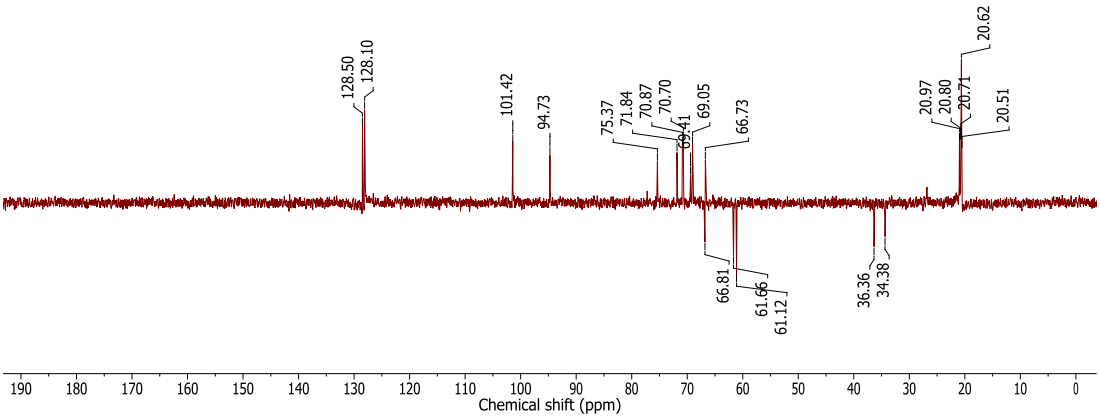
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **8a**



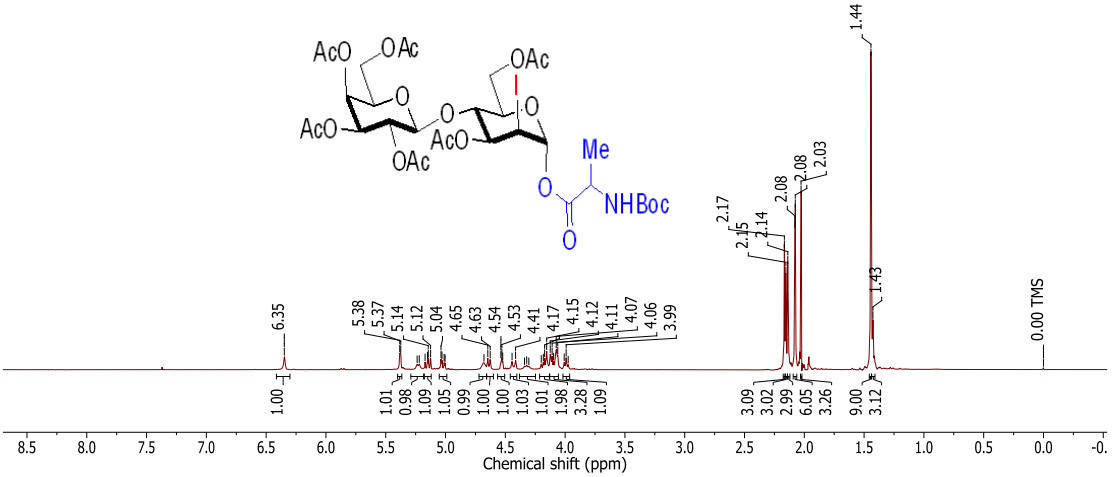
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **8a**



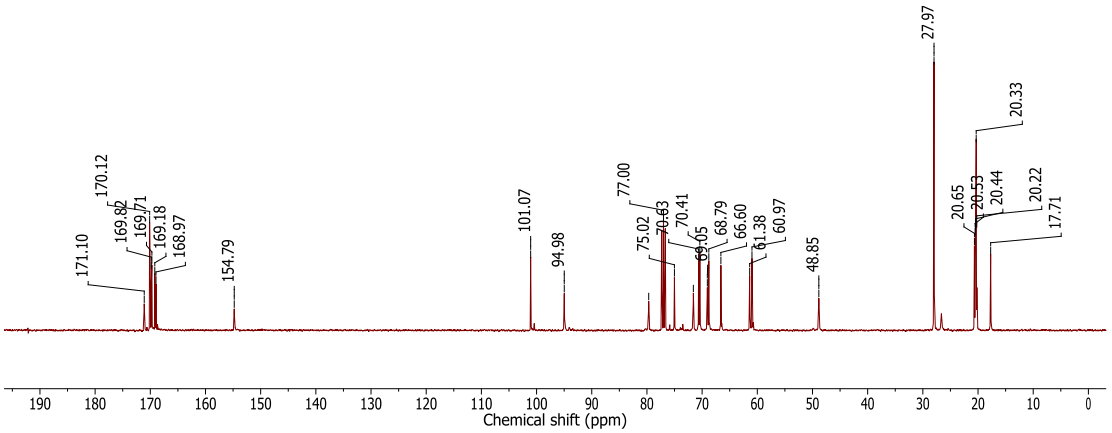
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **8a**



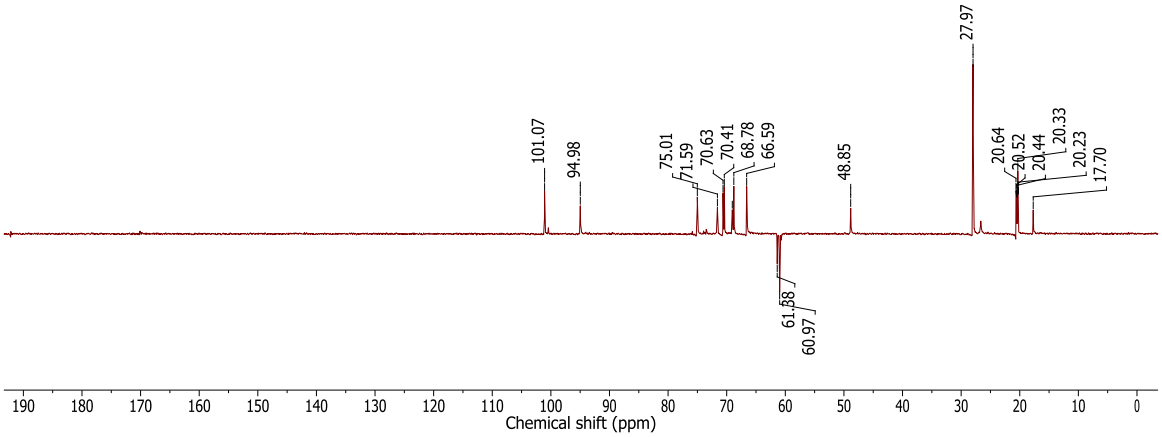
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **8b**



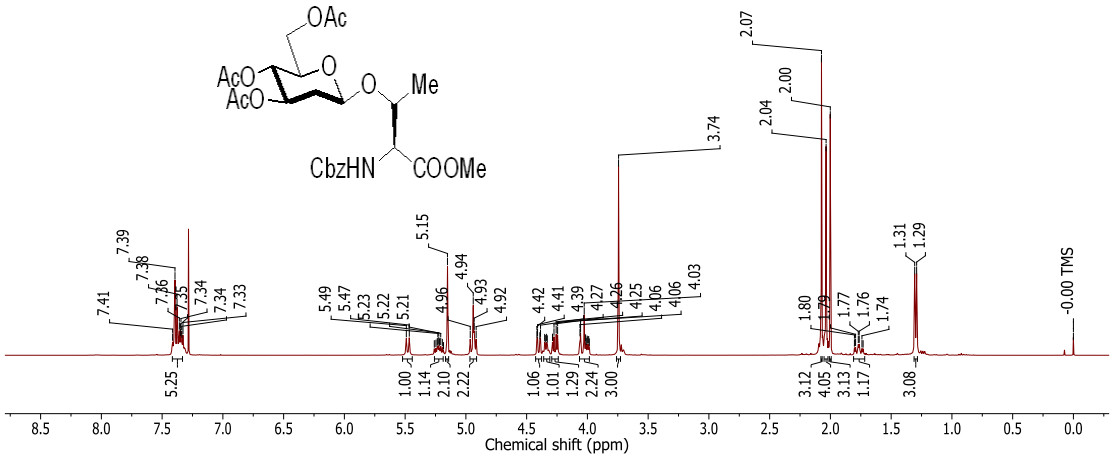
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **8b**



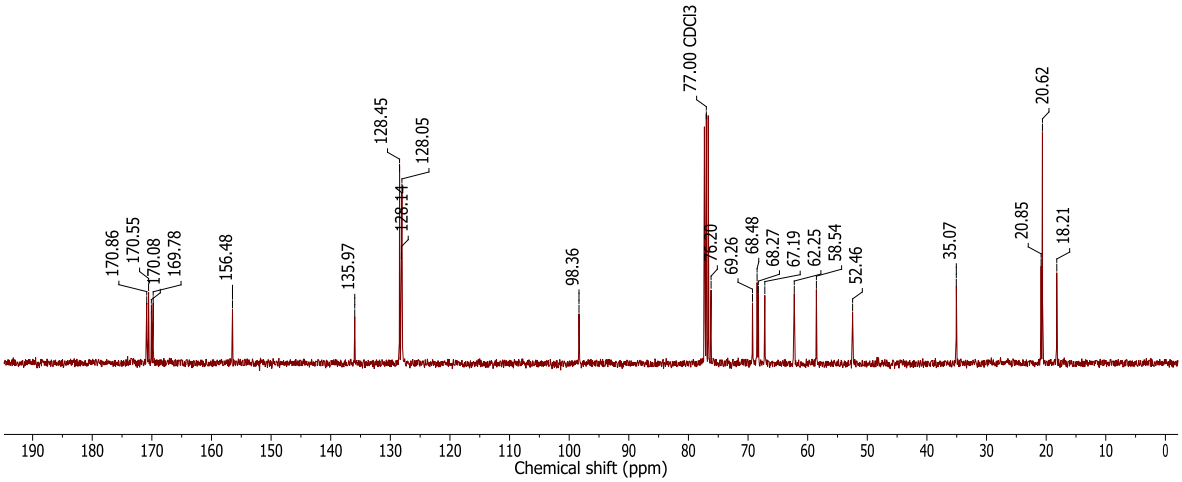
DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **8b**



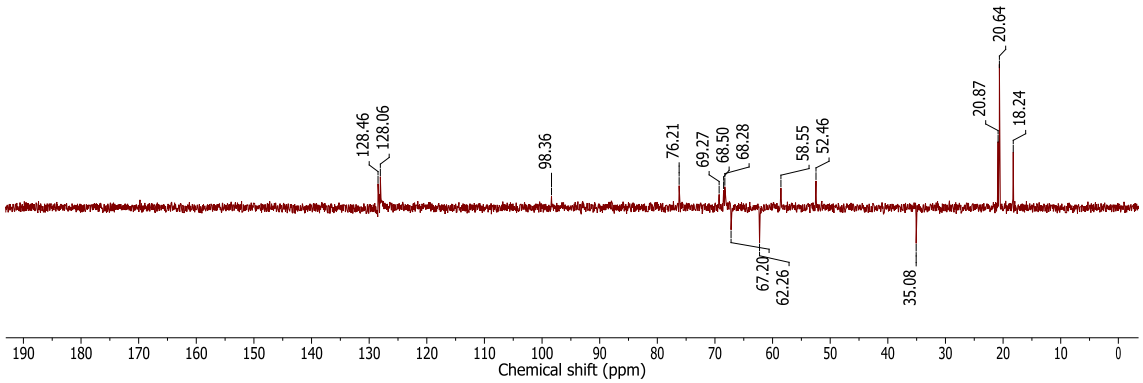
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **10b**



^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **10b**



DEPT NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **10b**



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Chapter: 3

Influence of Steric Crowding on Diastereoselective Arabinofuranosylations

3.1 Introduction

Mycobacterium tuberculosis (Mtb) is the etiological agent of tuberculosis (TB), a bygone disease that has been plaguing Mankind since its emergence.[1a] Highly contagious via air transmission, Mtb has the deadliest impact in developing countries and center of urban decay in the industrialized world predominantly in Asia and Africa (Figure 3.1). In 2011, World Health Organisation (WHO) estimated that a third of the global population is infected with Mtb and reported 1.4 million deaths due to TB.[1b] Further, the situation is also compounded by co-infection with human immunodeficiency virus (HIV) and approximately half million deaths reported owing to HIV co-infection (WHO, 2012).[1c] The global situation even becomes fatal with the re-emergence of TB and rapid spread of multi-drug resistant (MDR)[1d], extensively-drug (XDR) resistant TB strains and recently identified total-drug resistant (TDR) TB strains (Figure 3.2).

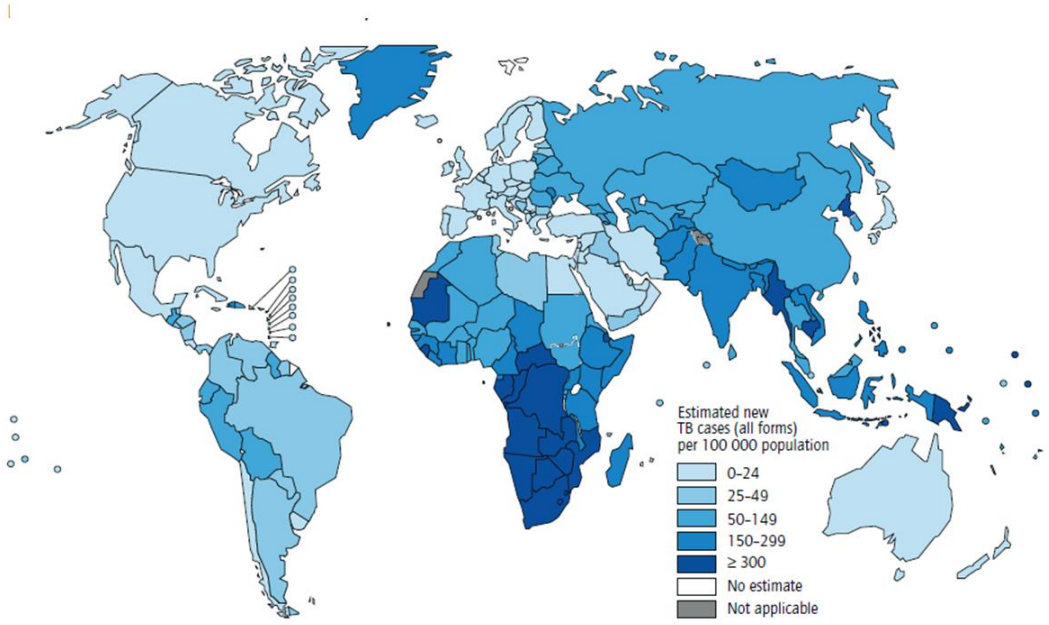


Figure 3.1 Global incidence of tuberculosis in 2011

(Adapted from Global Tuberculosis Report, WHO, 2012)

The classic symptoms associated with TB arechronic cough and sometimes blood-stained sputum, fever, night sweats and weight loss. Tuberculosis treatment basically depends on the vaccination of infants. In 1920, the first milestone for TB treatment was developed by Albert Calmette and Camille Guerin with the discovery of Bacillus-Calmette-Guerin (BCG) vaccine.[2a-b]

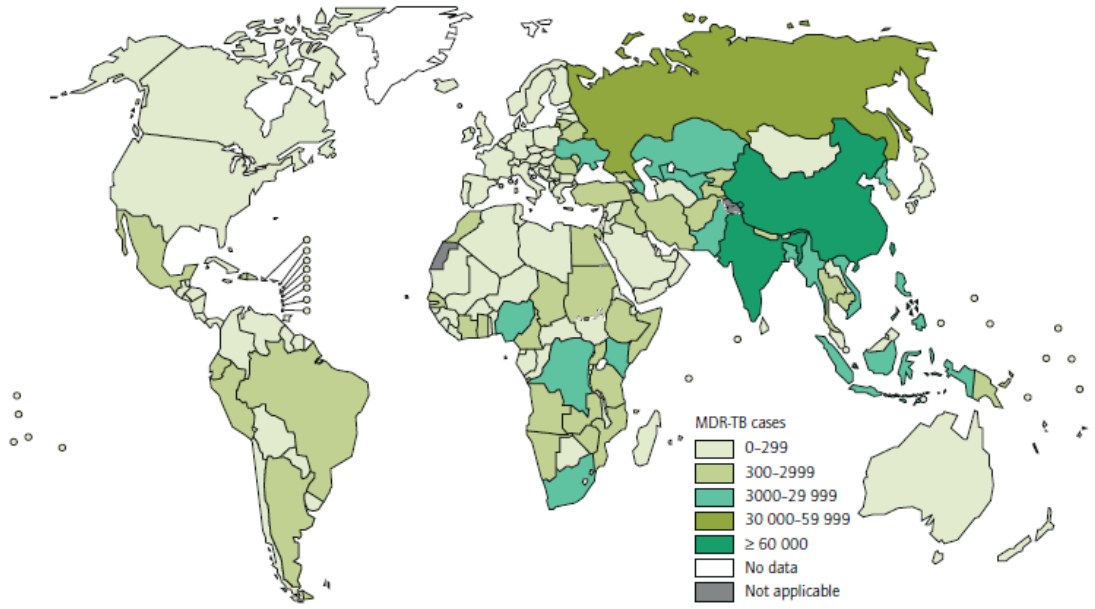


Figure 3.2: Global numbers of cases of multi-drug resistant tuberculosis
(Adapted from Global Tuberculosis Report, WHO, 2012)

However, the efficacy of BCG vaccine is questionable as its protection is highly variable (from 0-80%) in controlled trials in different countries as per the new clinical trials.[3] Prevention of TB based on the killing of mycobacteria employing antibiotics such as streptomycin, rifampicin, isoniazid, pyrazinamide and ethambutol or a combination of one or more of them for the first two months and only rifampicin and isoniazid for the next four months. Furthermore, WHO in 1993 declared TB as a global public health emergency and subsequently launched 'The STOP TB' strategy in 2006. This effort deemed the most effective strategy in combating the spread of TB with the number of new TB cases annually and TB mortality rate dropping by 41% since 1990 (WHO, 2012). Though these efforts stimulated the development of several new molecules to combat TB, but the global burden of TB still remains high due to characteristic Mtb cell wall which acts as hydrophobic facade against foreign molecules.

3.2 Structure of Mtb

After careful analysis, Brenan*et al*[4]completely unravelled the fine structure of Mtb cell wall and they have proposed that major structural components of the cell wall are the (i) mycolyl-arabinogalactan-peptidoglycan complex which contains arabinogalactan (AG) polysaccharide attached at its nonreducing end to mycolic acid and at reducing end to the peptidoglycan and (ii) Lipoglycans, consisting of Lipomannan (LM) and Lipoarabinomannan (LAM) (Figure 3.3).

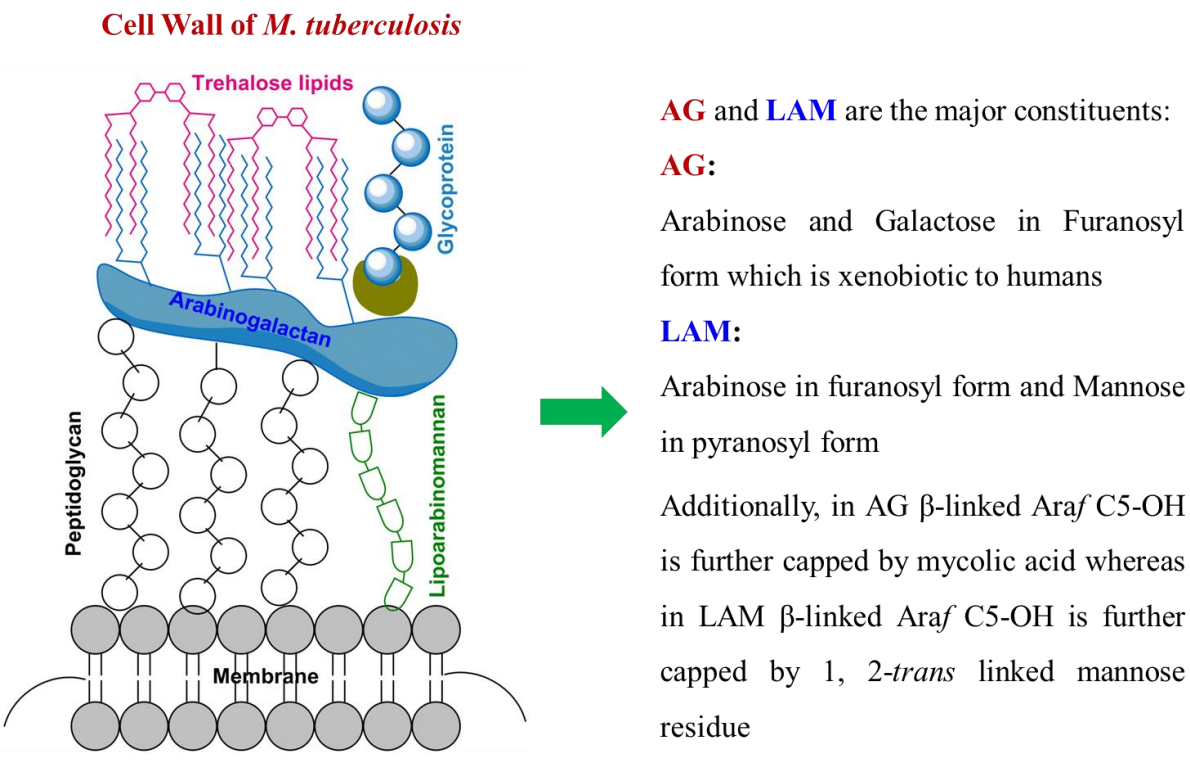


Figure 3.3 Structure of Mtb cell wall

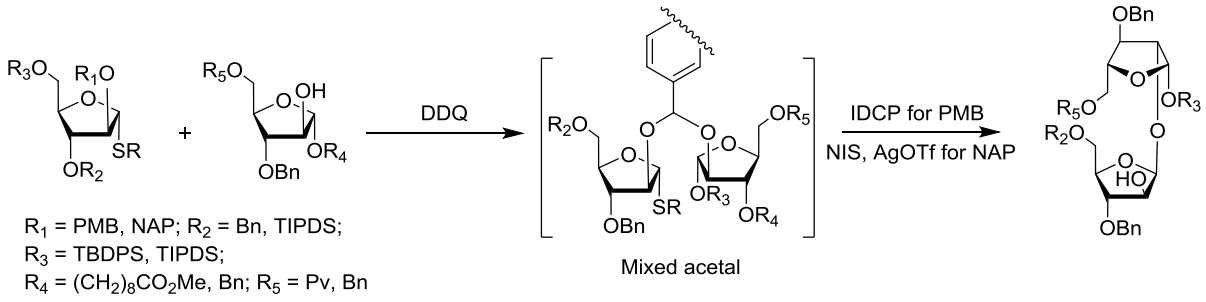
3.3 Synthesis of MTb cell wall and challenges

Both AG and LAM contain similar structure of arabinan domain. However, accumulated evidence suggest that arabinan domain in AG is structurally well defined and homogeneous (consist of 22 residues) whereas in LAM arabinan domain is more complex and heterogeneous in nature.[5a-b] In the biosynthetic step, Ara*f* residues are installed by the mycobacterial arabinofuranosyl transferases (Ara*f*Ts), EmbA, EmbB, and EmbC.[6a-c] Despite the advent of mycobacterial biosynthesis, the process becomes complicated by the production of micro-quantity of arabinan motif and low abundance of mycobacterial transferase enzymes in pure form. To circumvent aforementioned problems associated with enzymatic process to synthesize arabinan motifs, chemical synthesis will be asignificant avenue to access good quantity of pure and authentic samples of these motifs. Therefore, during the last two decades, several innovative arabinofuranosyl donors have been developed to synthesize arabinan motifs.[7a-I] Mycobacterial arabinan contains mainly three types of linkages i.e. 1,5-*trans*-Ara*f*, 1,3-*trans*-Ara*f*, and 1,2-*cis*-Ara*f*. In contrast to 1,5-*trans*-Ara*f*, or 1,3-*trans*-Ara*f* counterparts which can be relatively easily synthesized in a straightforward manner by exploiting neighboring group participation (NGP) of C2-acyl protecting group, the stereoselective 1,2-*cis*-arabinofuranosylation is aquite a challenging task. Further, difficulties

are enhanced due to the absence of anomeric effect in furanoside chemistry and conformational flexibility of furanoside ring compare to the pyranoside ring. Therefore, numerous elegant strategies including direct and indirect approaches have been reported for stereoselective construction of 1,2-*cis*-arabinofuranosides.

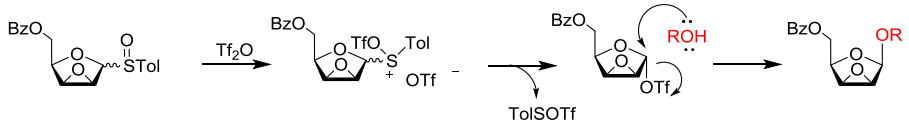
3.3.1 Indirect approaches

In 1999, Jacques Prandi and co-workers first utilized the intramolecular aglycon delivery (IAD) method for 1,2-*cis*-arabinofuranosylation.[7e] To achieve 1,2-*cis*-arabinofuranoside, they performed the reaction with C2-PMB protected arabinofuranosyl donor and glycosylated with C2-OH containing arabinofuranosyl acceptor in presence of DDQ to attain mixed acetal followed by activation of the donor by IDCP to afford 70% 1,2-*cis*-arabinofuranoside disaccharide. In continuation, Ito and co-workers[8] claimed that C2-PMB protected arabinofuranosyl donor at oligosaccharide stage produced very low yield (23%) and therefore they have modified the donor employing C2-NAP protection (Scheme3.1).



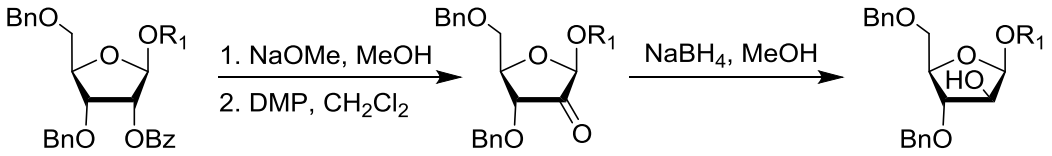
Scheme 3.1 1,2-*cis*-arabinofuranosylation by IAD method

Lowary and co-workers have also studied the stereoselective 1,2-*cis*-arabinofuranosylation utilizing 2,3-anhydro thiotolyl lyxofuranoside.[9a-c] They have conducted the furanosylation using NIS/AgOTf to obtain good to moderate yields of 1,2-*cis* arabinofuranosides. However, with some carbohydrate acceptors, yield and diastereoselectivity were poor and also rearranged product was formed due to migration of thiotolyl group from C1 to C2 postion during the furanosylation step. Subsequently, Lowary group has moved to sulphoxide donors in order to improve the low yield due to the rearranged product. They have carried out a detailed computation and NMR spectroscopic investigations to decipher the high 1,2-*cis*-selectivity and observed that the formationofan α-triflate as the intermediate that undergoes S_N2 displacement by the acceptor to afford 1,2-*cis*-arabinofuranoside (Scheme 3.2).



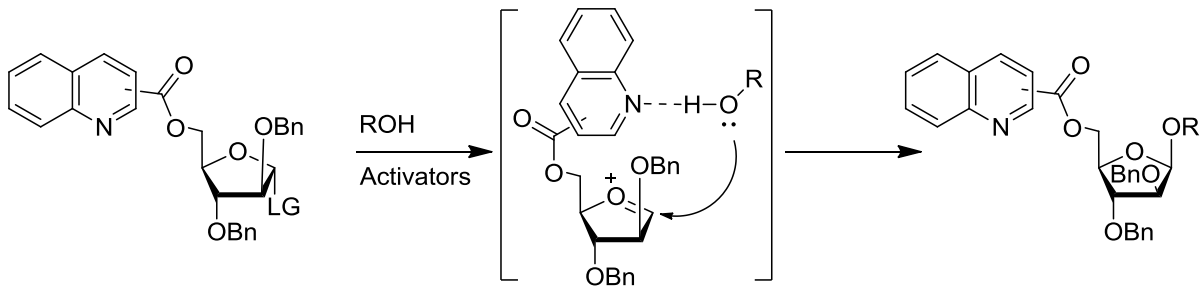
Scheme 3.2 1,2-*cis*-arabinofuranosylation by Lowary method

Recently, Hotha and co-workers[10] have achieved a unique bioinspired route towards the challenging 1,2-*cis*-arabinofuranosylation under catalytic conditions taking clue from the biochemistry of Mtb. At the first step, 1,2-*trans*-ribofuranoside was synthesized by orthoester strategy which resulted in a C2-benzoate that was saponified to afford C2-OH under Zemplén conditions. The resulting C2-OH was oxidized by employing Dess-Martin-periodinane (DMP) to afford the corresponding 2-ribulofuranose followed by the reduction of ketone by $NaBH_4$ to obtain 1,2-*cis*-arabinofuranoside in high diastereoselectivity. Stereo-chemical outcome was explained from the differential steric crowding around the C2-keto group in which ring oxygen, C5-OBn, and C1-furanoside bond prevent the hydride from attacking from *exo*-face of the ketone and hydride attack from only the endo-face to generate 1,2-*cis*-arabinofuranosides stereoselectively(Scheme 3.3).



Scheme 3.3 1,2-*cis*-arabinofuranosylation by Hotha method

In yet another strategy, Yang *et al.* exploited the hydrogen-bonding-assisted glycosylation strategy to construct 1,2-*cis*-arabinofuranoside.[11] In this approach, arabinofuranosy donor was embedded with a directing group at the C5-position in the form of a picolinate which can function as a hydrogen-bond acceptor.

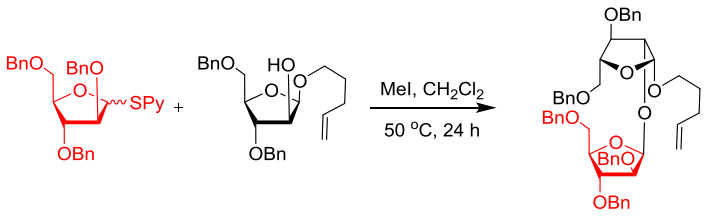


Scheme 3.4 Yang strategy for the 1,2-*cis*-arabinofuranosylation

Among the various C5-O directing groups, C5-O-(2-quinolinecarbonyl) was observed to afford highest 1,2-*cis* selectivity(α:β=1:20). Herein, the high 1,2-*cis* selectivity relies on the intramolecular H-bonding between donor and acceptor in which acceptor can access only *cis*-(or β)-face of the donor to generate 1,2-*cis*-arabinofuranosides (Scheme 3.4).

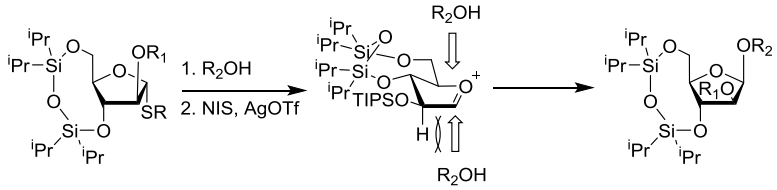
3.3.2 Direct approaches

Mereyala, Hotha and Gurjar reported the first direct approach of the synthesis of 1,2-*cis*-arabinofuranosylation by utilizing thiopyridyl glycosyl donors. They have demonstrated the approach by synthesizing a mycobacterial pentaarabinofuranoside for the first time. However, the origin of the stereoselectivity was not known; but, they could get the desired stereoselectivity (Scheme 3.5).



Scheme 3.5 1,2-*cis*-arabinofuranosylation by thiopyridyl glycosyl donor

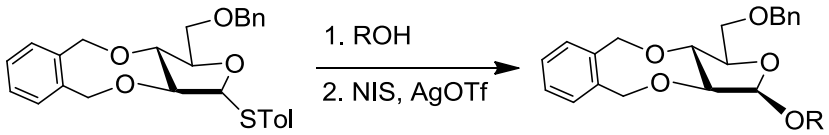
Boons and Ito groups independently investigated 3,5-*O*-di-*tert*-butylsilyene (DTBS) and 3,5-*O*-tetra-isopropyldisiloxanylidine (TIPDS) cyclic protection group respectively for 1,2-*cis*-arabinofuranosylation.[12a-b] For the high 1,2-*cis*-selectivity, they have proposed that nucleophilic attack from α-face is inhibited owing to the1,2-*gauche* steric interaction between the *pseudo* axially oriented C2-H and the incoming nucleophile. However, in case of DTBS protecting group, the 1,2-*cis*-selectivity was low (α:β =1:5) compare to theTIPDS protecting group (α:β=1:20) which was explained based on Woerpel hypothesis;[13] DTBS cyclic protecting group of Ara*f* donor can afford six-five distorted non-chair like bicyclic transition states which diminish the preference for 1,2-*cis*-β-isomer formation whereas for the TIPDS



Scheme 3.6 1,2-*cis*-arabinofuranosylation by DTBS protected donor

cyclic protection group give rise to eight-five bicyclic system favouring 1,2-*cis*-arabinofuranoside formation (Scheme 3.6).

Although aforementioned approaches afford good to excellent 1,2-*cis*-selectivity, tethering of cyclic protecting groups between C3-O and C5-O complicates the synthesis of fragments where C5-O of β-Ara*f* is further capped by the mycolic acid as in AG case or mannose residue as in LAM case.



Scheme 3.7 1,2-*cis*-arabinofuranosylation by 2,3-xylene protected donor

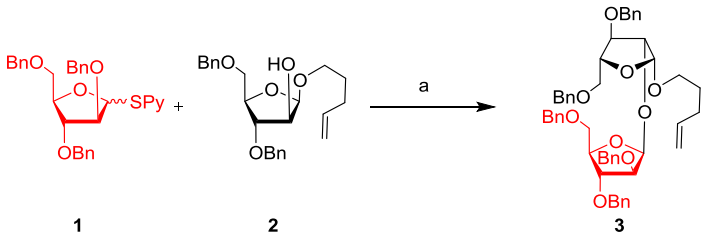
Therefore to avoid such problems, Lowary and co-workers[13] introduced cyclic 2,3-xylene protected Ara*f* donor which upon activation by NIS-AgOTf condition afforded moderate 1,2-*cis*-selectivity (α:β =1:1 to 1:8) (Scheme 3.7).

In both direct and indirect approaches, 1,2-*cis*-selectivity was controlled by the functional group modifications in Ara*f* donors. However, very little is known about acceptors importance or donor-acceptor match/mismatch event for the 1,2-*cis*-arabinofranosylation. Therefore, in this dissertation, we have introduced Reciprocal-Donor-Acceptor-Selectivity (RDAS) for 1,2-*cis*-arabinofuranosylation.

3.4 Present work

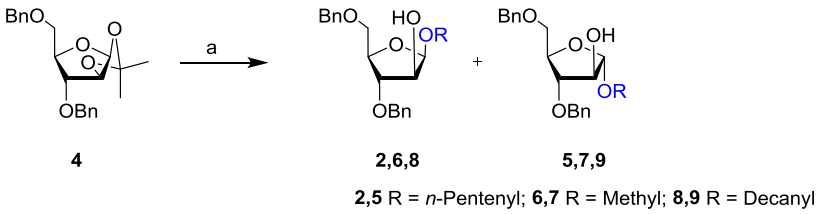
In pyranosylchemistry, the term Reciprocal-Donor-Acceptor-Selectivity (RDAS) was first coined by Bert Fraser-Reid .[15a-b] During three-component double differential glycosylations, they have observed that primary-OH group can be regioselectively glycosylated with orthoester glycosyl (disarmed) donor in the presence of secondary-OH; whereas, secondary-OH can be regioselectively glycosylated with armed glycosyl donor in the presence of primary-OH.[15c] However, very little is known about RDAS in furanosyl chemistry until Kim and co-workers revealed that 1,2-*cis*-Ara*f* can be installed by furanosylation of armed Ara*f* donor and an Ara*f* acceptor having acyl protecting groups.[7f]

In this premise, we studied the importance of stereochemistry and steric crowding around C1- as well as C5-position of acceptors for 1,2-*cis*-arabinofranosylation. As described earlier, although very little was mentioned about the origin of selectivity, in 1998, Gurjar and co-workers noticed that furanosylation of (**1**) and 1,2-*cis*-acceptor (**2**) stereoselectively afforded only 1,2-cis-Ara*f* disaccharide (**3**).[7a] Therefore, to understand this reaction and the origin of stereoselectivity, a set of three Ara*f* acceptors were planned: least sterically crowded (**6,7**), moderately sterically crowded (**2**,**5**) and highly sterically crowded (**8**,**9**).



Scheme 3.8 1,2-*cis*-arabinofuranosylation by Gurjar and co-workers: Reagents a) CH_3I, CH_2Cl_2, 57 ^oC, 24h.

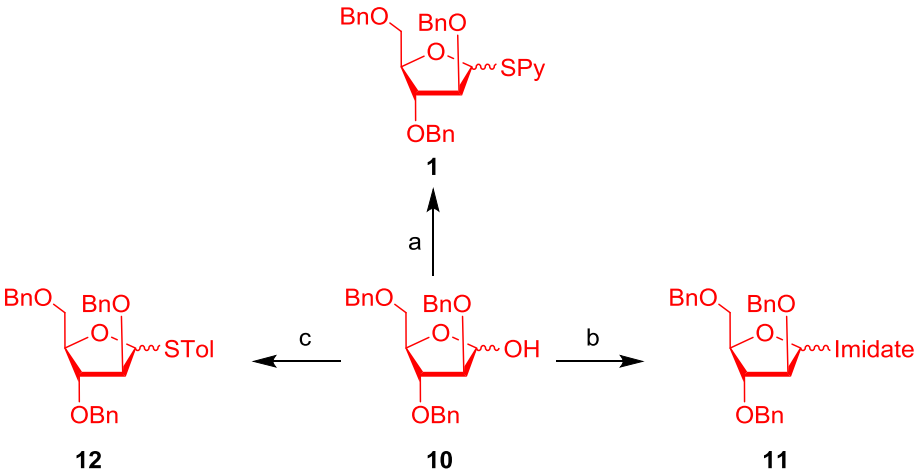
Accordingly, our exploration started with the preparation of these substrates for further furanosylation experiments. All these glycosyl acceptors (**2**,**5-9**) can be easily synthesized from a common precursor compound **4**. The isopropylidene of compound **4** is strategically placed so that the hydrolytic opening of isopropylidene in the presence of an alcohol would result in the formation of both 1,2-*cis* and 1,2-*trans* isomers easily. Hence, 1,2-*O*-Ara*f* acetonide (**4**) was synthesized by a reported procedure[7a] and it was treated in parallel with 4-penten-1-ol, methanol, and decanol in presence of catalytic amount of *p*TSA in CH_2Cl_2 at 50 ^oC to afford 1:1 mixture of **2**,**5-9**. Gratifyingly, 1,2-cis and 1,2-trans isomers of these arabinofuranosides are easily separated on ordinary silica gel column chromatography.



Scheme 3.9 Preparation of 1,2-*cis*(β)-Ara*f* and 1,2-*trans*(α)-Ara*f* acceptors. Reagents: a) *p*TSA (0.2 eq), ROH, CH_2Cl_2, 50 ^oC, 1h, 82-89%.

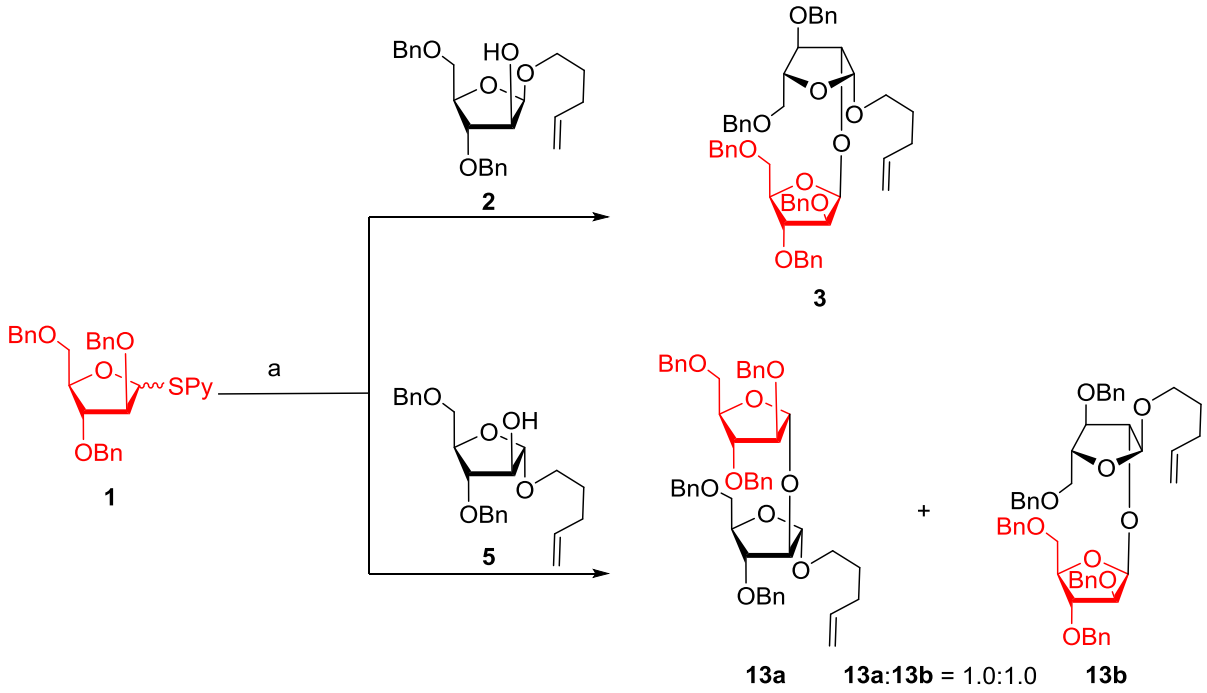
The α and β isomers were confirmed from their respective ^{1}HNMR and ^{13}C NMR spectroscopic investigations. In the ^{1}HNMR spectrum of furanoside **2**, characteristic β-Ara*f* anomeric (H-1) proton was observed at δ 4.95 (d, *J* = 4.6 Hz) ppm whereas the characteristic vinylic C<u>H</u>-proton was noticed as a multipletat δ 5.78 ppm. In the^{13}CNMR spectrum of compound **2**, resonances due to the β-Ara*f* anomeric (C-1) appeared at δ 101.6 ppm. On another hand, the ^{1}HNMR spectrum of compound **5** showed characteristic α-Ara*f* anomeric (H-1) proton was observed as a singlet at δ 5.00 ppm and in the ^{13}CNMR spectrum, resonances due to α-Ara*f* anomeric (C-1) appeared at δ 109.1 ppm. Similarly, Ara*f* acceptors **6**,**7** and **8**,**9** were thoroughly characterized by NMR spectroscopy.

After successful synthesis of Ara*f* acceptors, Ara*f* donors are required *viz*. thiopyridyl, imidate and -STol were chosen as these three donors can be activated at 50 ^oC, 0 ^oC and -50 ^oC respectively. In addition, all the three donors can be obtained from the same precursor hemiacetal **10**.



Scheme 3.10 Preparation of Ara*f*donors. Reagents: a) 2,2'-Dithiopyridine, *n*-tributyl phosphine, CH_2Cl_2, 0 °C-25 ^oC, 30 min, 87%; b) 2,2"-Dithiotoluene, *n*-tributyl phosphine, CH_2Cl_2, 0 °C-25 ^oC, 30 min, 84%; c) CCl_3CN, DBU, CH_2Cl_2, 0 °C-25 ^oC, 76%.

Ara*f* donors **1** and **12** were prepared in presence of *n*-tributyl phosphine by treating the Ara*f* hemiactal (**10**) with respective 2,2'-Dithiopyridine and 2,2'-Dithiotoluene at 0 °C-25 °C under inert atmosphere; whereas, Ara*f* donors **11** was synthesized by the reaction of hemiacetal (**10**) and trichloroacetonitrile in the presence of catalytic DBU in CH_2Cl_2 at 0 °C-25 °C.

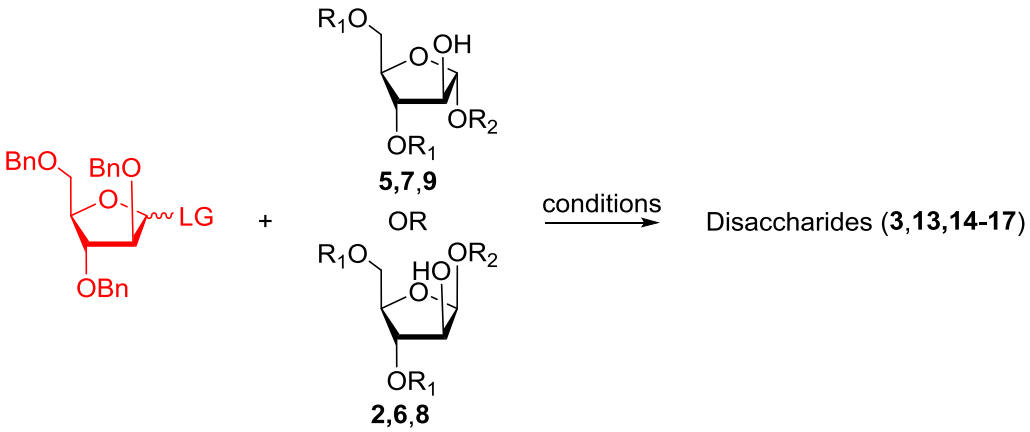


Scheme 3.11 RDAS for arabinofuranosylation. Reagents: a) CH_3I, CH_2Cl_2, 57 °C, 24h.

The furanosylation between **1** and **2** by MeI underwent smoothly to give 1,2-*cis* disaccharide (**3**) only as observed by Gurjar's group; however, to our surprise, furanosylation between donor **1** and acceptor **5** afforded 1:1 mixture of **13a** and **13b**. A possible explanation for the difference of stereoselectivity may be steric environment around the C2-OH group. H-1and H-1' protons of disaccharide **3** appeared at δ 4.95 (d, *J* = 4.1Hz) and 5.09 (d, *J* =4.2 Hz) ppm in ^{1}H NMR and characteristic C-1 and C-1' were noticed at δ 98.4 and 100.0 ppm in the ^{13}C NMR. In contrast, ^{1}HNMR spectrum of disaccharide **13a** revealed H-1and H-1' protons as singlets at δ 5.09 and 5.13 ppm while characteristic C-1 and C-1' were identified at δ 105.6 and 106.9 ppm in the ^{13}C NMR spectrum.^{1}HNMR and ^{13}CNMR spectra of disaccharide **13b** was similar to **13a**, except that in the ^{1}H NMR, a singlet at δ 5.13 ppm was replaced by another signal at δ 5.07 (d, *J* = 4.2 Hz); similarly,^{13}CNMR showed resonances at δ 106.9 ppm were replaced by another signal at δ 100.2 ppm confirming the structural homogeneity.

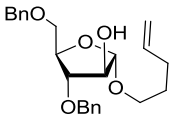
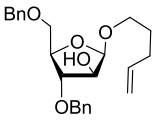
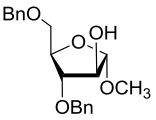
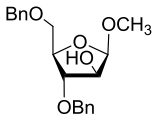
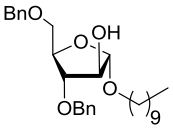
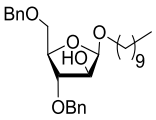
The above delineated experiments clearly showed that stereoselectivity of this furanosidation depends on the steric crowding around the glycosyl acceptors as well and Gurjar's group was just lucky to have carried out the experiment with the 1,2-*cis* pentenyl glycoside only. They would have obtain a diastereomeric mixture had they performed their experiments with the 1,2-*trans* pentenyl glycoside as well. These results clearly suggest that the stereoselectivity during the β-arabinofuranosylation is dependent on the steric crowding.

Encouraged by these results, we turned our attention towards sterically less or more demanding glycosyl acceptors containing methyl and decanyl glycosides at the anomeric position. So, less sterically crowded acceptors (**6** and **7**) and more demanding acceptors (**8** and **9**) were treated with above prepared glycosyl donors **2**, **5**-**9**.



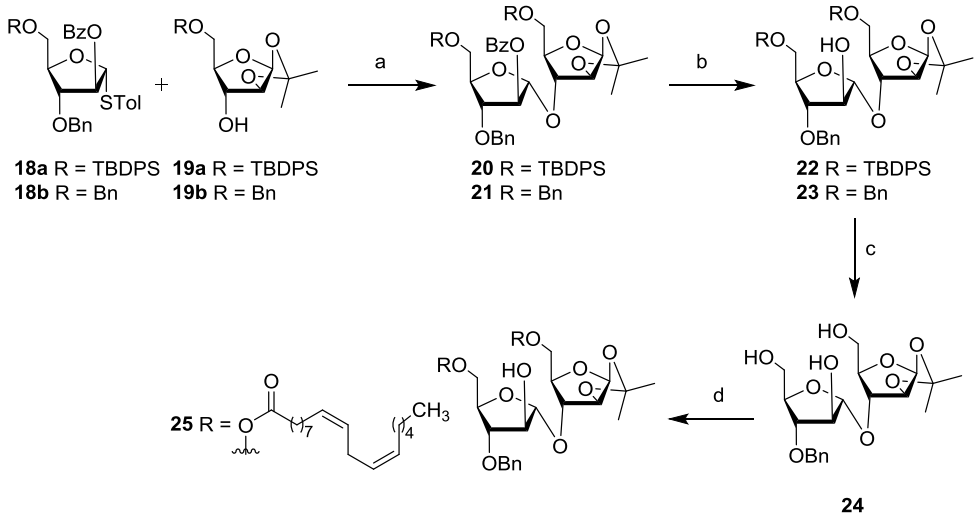
LG = -SPy (**1**); -OC(=NH)CCl_3 (**11**); -STol (**12**)

R_1 = -CH_2Ph; R_2 = -CH_3 (**6**,**7**), -$(CH_2)_3$CH=CH (**2**,**5**), -$(CH_2)_9CH_3$ (**8**,**9**)

Donor	Acceptor											
												
	5		**2**		**7**		**6**		**9**		**8**	
	No.	α:β Ratio	No.	α:β Ratio	No.	α:β Ratio	No.	α:β Ratio	No.	α:β Ratio	No.	α:β Ratio
1[a]	**13**	1.0:1.0	**3**	0.0:1.0	**14**	1.0:0.3	**15**	0.4:1.0	**16**	1.0:1.0	**17**	0.0:1.0
11[b]	**13**	0.1:1.0	**3**	0.0:1.0	**14**	0.3:1.0	**15**	0.1:1.0	**16**	0.0:1.0	**17**	0.0:1.0
12[c]	ND	ND	ND	ND	**14**	1.0:1.0	**15**	0.4:1.0	**16**	0.3:1.0	**17**	0.0:1.0

Scheme 3.12 RDAS for arabinofuranosylation: Reagents a) CH_3I, CH_2Cl_2, 57 ^{0}C, 4 Å MS powder, 15 h, 64-75%; b) TMSOTf, CH_2Cl_2, -78 to -40 ^{0}C; 4 Å MS powder, 1 h, 60-63%; c) NIS, AgOTf, CH_2Cl_2, 0 ^{0}C, 4 Å MS powder, 15 h, 83-86%; ND denotes not determined.

Furanosylation of α-acceptor **7** and **9** with thiopyridyl donor afforded α, β-mixture of disaccharide **14** and **16**. However, the β-selectivity was enhanced from acceptor **7** to **9** that can be attributed to the gradual increase in steric crowding around hydroxyl group of the acceptor. Stereochemistry at the anomeric proton and the carbon of the crude reaction mixture was confirmed by ^{1}HNMR and ^{13}CNMR spectroscopy. The β-isomer showed coupling constants of 4-5 Hz, $\delta_{C\text{-}1}$ around 98-103 ppm; the α-isomers showed coupling constants of 0-3 Hz with $\delta_{C\text{-}1}$ around 104-111 ppm. Further, less steric crowded β-acceptor **6** showed α,β-mixture of disaccharides **15**, whereas the sterically demanding β-decanyl acceptor **8** afforded only β-disaccharide **17** which is very similar to β-pentenyl acceptor **2**. Here again, the β-selectivity was noticed to relies on the overall steric crowding around the hydroxyl acceptor. In the ^{1}HNMR spectrum of compound **15**, appearance of anomeric protons (*H*-1) and (*H*-1') at δ 4.76 (d, *J* = 4.1 Hz) and δ 5.17 (d, *J*= 4.3 Hz) ppm showed β-anomers of disaccharide **15** whereas appearance of C-1 and C-1' at δ 102.0 (2C) ppm in the ^{13}CNMR further endorsed the β-stereochemistry at the anomeric carbon of disaccharide **15** unambiguously. For disaccharide **17**, in the ^{1}HNMR spectrum characteristic (H-1) and (H-1') protons were observed at δ 4.86 (d, *J* = 4.1 Hz) and δ 5.18 (d, *J* = 3.9 Hz) ppm whereas in the ^{13}CNMR spectrum, C-1 and C-1' appeared at δ 101.2 and δ 102.2 ppm confirming the β-stereochemistry of compound **17**. From molecular modeling studies, it was noticed that β-Ara*f* was thermodynamically favored over α-Ara*f* (the total energy of β-linkedproduct was 3.7 kcal/mol lower than that of the α-product).[12b]



Scheme 3.13 Preparation of disaccharide acceptors: Reagents a) NIS, AgOTf, CH_2Cl_2, 0 ^{0}C, 4 Å MS powder, 1h, 86%; b) NaOMe, MeOH, 25^{0}C, 6h, 89%; c) HF-py, Py, 0-25^{0}C, 5h, 91%; d) Linoleic acid, DIC, DMAP, CH_2Cl_2, 0 ^{0}C, 5h, 85%.

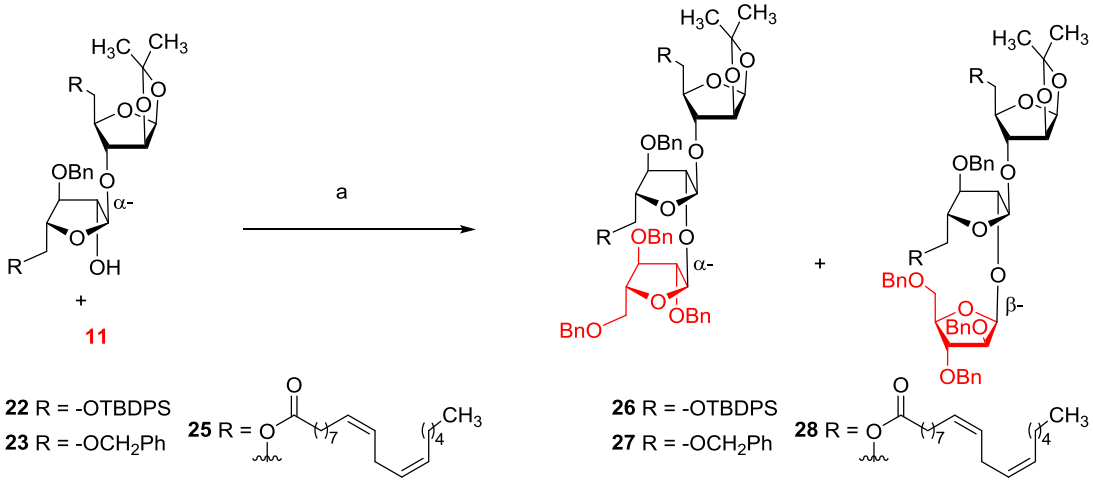
Overall, we noticed subtle changes in the steric environment around the acceptor-hydroxyl moiety alter the stereochemical outcome during the furanosylation reaction in a phenomenal level.

Temperature of the furanosylation is yet another well documented force that can alter the stereochemical outcome due to kinetic and thermodynamic events. Therefore, we have performed these furanosylations at -78^{o}C to -40 ^{o}C and 0 ^{o}C with respective imidate and thiotolyl donor. The effect of -78 to -40 ^{0}C was examined initially. Furanosylation between imidate donor (**11**) and acceptors **5**, **7**, **9** showed increased ratio of β-disaccharide compared to the furanosylation conducted with thiopyridyl donor (**2**) at 57 ^{o}C. On the other hand, furanosylation of **2**, **6** and **8** with imidate donor (**11**) afforded only β-disaccharide. Next, furanosylation was performed at 0 ^{0}C. Here, furanosylation of acceptors **2** and **5** could not carried out as NIS-AgOTf promoter can activate both –Stol and pentenyl donors as well. At 0 ^{0}C, activation of thiotolyldonor with acceptors **6**, **7** and **9** gave mixture of disaccharides whereas sterically demanding acceptor **8** showed only β-disaccharide. Therefore, the stereo-selectivity of Ara*f* was noticed to be influenced by steric demanding around acceptor and the reaction temperature as well.

3.4.1 RDAS at trisaccharide level

In arabinogalactan (AG), the terminal β-Ara*f* residues are further capped with mycolic acid that can in principle tune the reactivity and steric crowding around the hydroxyl moiety of the C2-OH containing acceptor. To probe this intriguing fact, we have synthesized three model disaccharides as acceptors for the study by varying the substituents at the C5-position. Thiotolyl donor **18** was subjected glycosylation with 1,2-acetonide acceptor **19** under NIS-AgOTf condition in CH_2Cl_2 to afford disaccharide **20** and **21**. Subsequent saponification by NaOMe/MeOH afforded disaccharide monoalcohol **22** and **23**. Next, disaccharide **22** on treatment with HF·py to obtain alcohol **24** followed by the protection of C5-OH as linoleate using linoleic acid, DIC, DMAP gave compound **25** (Scheme 3.13). The homogeneity of all three acceptors **22**, **23** and **25** was confirmed by NMR spectroscopy. In the^{1}HNMR spectrumof compound **22**, 1,2-*trans* anomeric proton was observed as a singlet at δ 5.39 ppm and 1,2-*cis* anomeric proton corresponding to the1,2-acetonide residue was noticed at δ 5.96 (d, J = 3.6 Hz) ppm. Further, attendance of two resonances at δ 1.07 (s, 9H) and δ 1.10 (s, 9H) ppm revealed the presence of *t*-butyl of TBDPS group. In the ^{13}CNMR, resonance due to the 1,2-*trans* carbons of C-1 and C-1' corresponding to the 1,2-acetonide fragment appeared

at δ 107.2 and 105.8 ppm respectively. Resonances of *t*-butyl of TBDPS were observed at δ 26.7 (6C) and 19.1 (2C, disappeared in DEPT spectrum) ppm. The ^{1}HNMR and ^{13}CNMR spectrum of compounds **23** and **25** were very similar to compound **22**, the only difference was that in both the cases, the resonances due to *t*-butyl of TBDPS disappeared and new signals corresponding to the characteristic olefinic protons for compound **25** appeared as multiplet at δ 5.35 ppm.



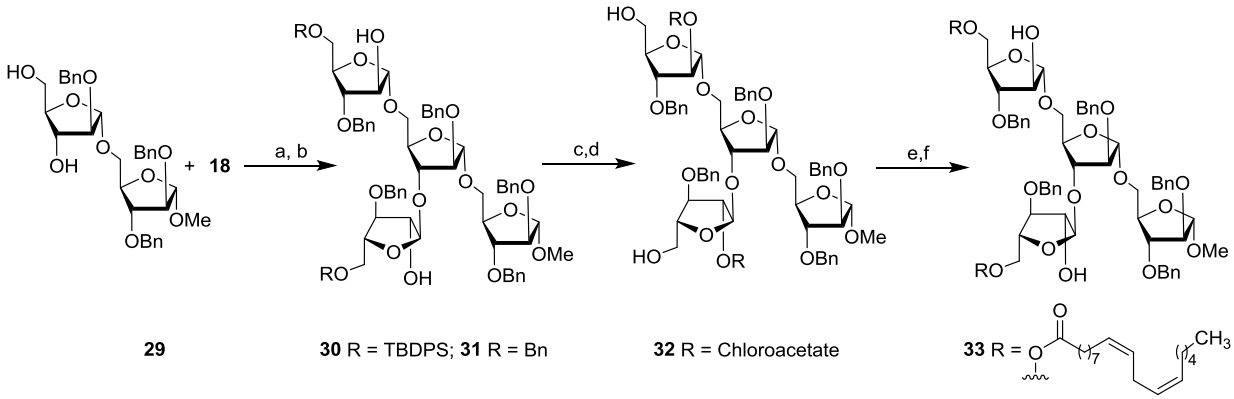
Donor	Acceptor	Product	% Yield	α:β Ratio
11	**22**	**26**	60	0.4:1.0
11	**23**	**27**	64	0.1:1.0
11	**25**	**28**	63	0.0:1.0

Scheme 3.14 RDAS for arabinofuranosylation at the trisaccharide level. Reagents: a) TMSOTf, CH_2Cl_2, -78 to -40 ^{0}C; 4 Å MS powder, 1 h.

Having synthesized all three model acceptors, the first furanosylation was carried out between donor **11** and C5-Osilyl protected acceptor **22** to obtain a α:β mixture (0.4:1.0) of trisaccharides **26**. Further, furanosylation of donor **11** with C5-OBn protected acceptor **23** gave α:β mixture (0.1:1.0) of trisaccharide**s 27** with an increase of β-ratio. Surprisingly, furanosylation between donor **11** and acceptor **25** resulted in β-trisaccharide **28** only (Scheme 3.14). Therefore, from the aforementioned results, we have concluded that overall stereoelectronic environment around the furanosyl acceptor is very important for the final sterochemical outcome of the furanosylation.

3.4.2 RDAS at hexasaccharide level

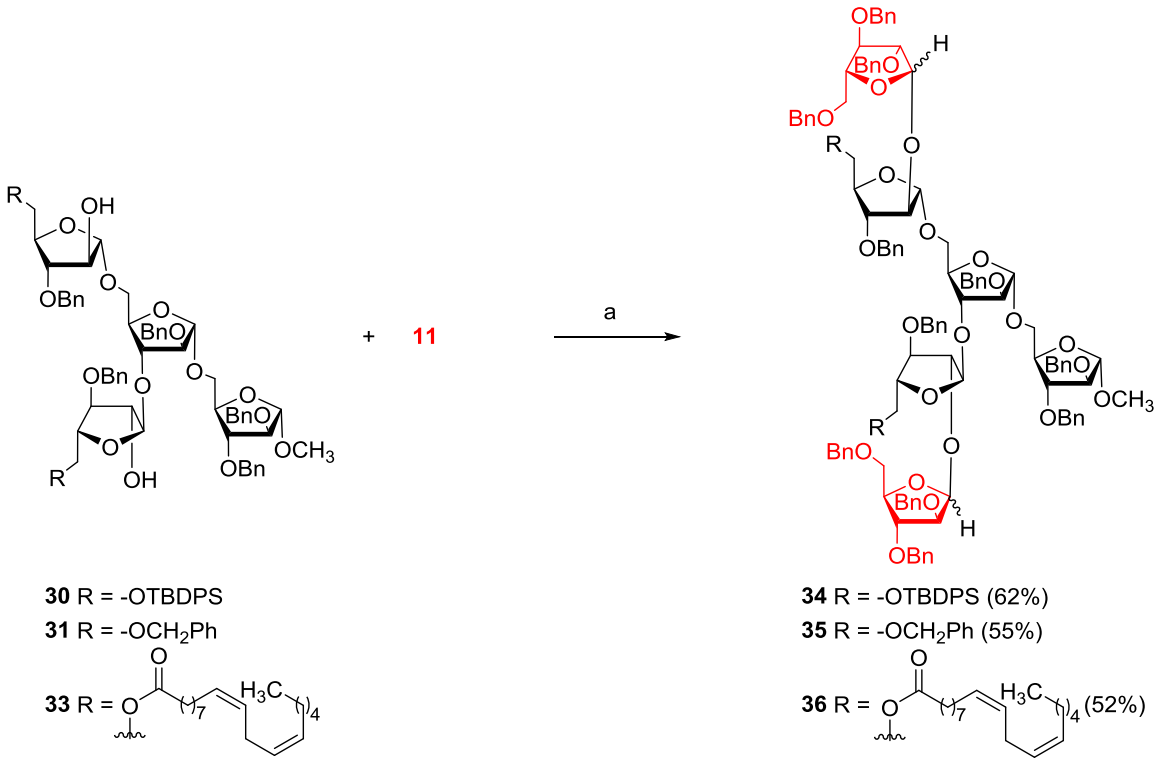
At last, to investigate the validity of RDAS at the hexasccharide level, we have considered yet another three model tetrasaccharide diol acceptors **30**, **31** and **33**. Accordingly, disaccharide diol **29** obtained from the reported procedure.[12b] Furanosylation of acceptor **29** with donor **18** in the presence of NIS-AgOTf activator followed by saponification of two benzoate groups under Zemplén condition (NaOMe-MeOH) resulted in tetrasaccharide diols **30** and **31**.



Scheme 3.15 Preparation of tetrasaccharide acceptors. Reagents: a) NIS, AgOTf, CH_2Cl_2, 0 ^{0}C, 4 Å MS powder, 1h, 86%; b) NaOMe, MeOH, 25^{0}C, 6h, 89%; c) chloroacetic acid, DIC, DMAP, CH_2Cl_2, 0-25^{0}C, 2h; d) HF-py, Py, 0-25^{0}C, 5h, 71% over two steps; e) Linoleic acid, DIC, DMAP, CH_2Cl_2, 0 ^{0}C, 5h; f) $NH_2NH_2.H_2O$, MeOH-AcOH, 40 ^{0}C, 4h, 72% over two steps.

Subsequently, tetrasaccharide diol **33** was obtained from compound **30** in four straightforward steps *viz.* esterification with chloroacetic acid and DIC-DMAP in CH_2Cl_2, deprotection of TBDPS groups by HF·py, protection of C5-OH by linoleic acid and DIC-DMAP and at last deprotection of chloroacetate by hydrazine hydrate in acetic acid (Scheme 3.15) . Compound **30** displayed four 1,2-*trans* anomeric protons at δ 4.97, 5.18, 5.22 and 5.22 ppm as four singlets in the ^{1}HNMR spectrum. A singlet for three protons at δ 3.42 indicated the presence of methyl glycoside at the reducing end and one signal at δ 1.05 (18H) ppm confirmed the presence of two *t*-butyl groups of TBDPS moiety. Other furanoside ring protons along with benzylic protons were noticed between δ 3.37 to 4.65 ppm. In the ^{13}CNMR spectrum, the appearance of four resonances at δ 106.1, 107.1, 107.4, and 108.9 ppm confirmed four 1,2-*trans* arabinofuranosides. Disappearance of resonances at δ 26.6 (6C) ppm and δ 19.1 (2C), in the DEPT spectrum confirmed the presence of *t*-butyl of TBDPS. NMR spectra of both tetrasaccharide acceptors **31** and **33** were similar to acceptor

30, except that in both cases, resonances corresponding to *t*-butyl disappeared and additional characteristic olefin signals appeared in ^{1}HNMR and ^{13}CNMR spectra of compound **33**. In continuation, furanosylation of donor **11** with acceptors **30-33** was performed under aforementioned condition. In all the cases, we got α:β mixture of hexasaccharides **34-36** which could not be separated into individual isomers. However, careful ^{1}H and ^{13}C NMR analysis of hexasaccharides **34-36** indicated gradual increase of β ratio from **34→35→36**, again revealing that the diastereoselectivity of the arabinofuranosylation heavily relies on the steric as well as electronic factors around the acceptor hydroxyl group.



Scheme 3.16 RDAS for arabinofuranosylation at hexasaccharide level. Reagents: a) TMSOTf, CH_2Cl_2, -78 to -40 ^{0}C; 4 Å MS powder, 1 h.

In summary, an efficient approach was developed for 1,2-*cis*-arabinofuranosylation by exploiting Reciprocal-Donor-Acceptor-Selectivity (RDAS) and one can prepare 1,2-*cis*-Ara*f* by performing the furanosylation at a lower temperature having sterically crowded and less reactive acceptor. Further, the utility of the developed method is also applicable to disaccharide as well as tetrasaccharide acceptors.

Note: Characterization data and full spectral charts for all compounds can also be found in

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3.5 Experimental section

a) General procedure for the glycosylation using thiopyridyl donor 1: To a solution of furanosyl acceptor (**2**,**5**,**6-9**) (250 µmol) and donor **1**(326 µmol) in anhydrous CH_2Cl_2 (10 mL) was added freshly activated 4Å molecular sieves powdered (0.40 g) and 5% CH_3I in CH_2Cl_2 at 25 ^{0}C. The reaction mixture was heated to 57 ^{0}C for 15 h, then the reaction mixture was filtered through a pad of Celite®. The filtrate was concentrated *in vacuo* to afford an yellow coloured oil which was purified by silica gel flash column chromatography (*n*-hexane/EtOAc, 9:1, v/v) to obtain furanosides in 64-75% yield.

b) General procedure for the glycosylation using imidate donor 11: To the solution of acceptor (**2**,**5**,**6-9**) (250 µmol) and donor **11** (326 µmol) in anhydrous CH_2Cl_2 (10 mL) was added freshly activated 4Å MS powder (0.400 g) at 25 ^{0}C. After cooling to -78 °C, TMSOTf (37.6 µmol) was added to the reaction mixture and gradually increased the temperature to -40 °C over 5 min. After 1.0 h, the reaction was neutralized by Et_3N and filtered through a bed of Celite®. The filtrate was concentrated in *vacuo* to obtain brown coloured oil that was purified by silica gel flash column chromatography (n-hexane/EtOAc, 9:1, v/v) to afford furanosides in 61-63% yield.

c) General procedure for the glycosylation using *p*-thiotolyl donor 12: To a solution of acceptor (**6-9**) (250 µmol) and donor **12** (326 µmol) in anhydrous CH_2Cl_2 (10 mL) was added freshly activated 4Å MS powder (0.400 g) at 25 ^{0}C. After cooling to 0 °C, NIS (502 µmol) and AgOTf (50 µmol) were added to the reaction mixture and stirred for 1.5h at 0 °C, the reaction was neutralized by Et_3N and filtered through a bed of Celite®. The filtrate was concentrated *in vacuo* to obtain reddish coloured oil that was purified by silica gel flash column chromatography (*n*-hexane/EtOAc, 9:1, v/v) to afford furanosides in 83-88% yield.

4-Pentenyl 3,5-di-*O*-benzyl-β-D-arabinofuranoside (2): Yield: (3.49g, 81%); $[\alpha]_D^{25}$ = -39.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.64 (td, *J* = 15.4, 14.7, 7.6 Hz, 2H), 1.96 – 2.17 (m, 2H), 2.59 (d, *J* = 9.6 Hz, 1H), 3.44 (dt, *J* = 9.6, 6.6 Hz, 1H), 3.52 (d, *J* = 5.9 Hz, 2H), 3.77 (dt, *J* = 9.6, 6.5 Hz, 1H), 3.83 (t, *J* = 5.7 Hz, 1H), 4.14 (q, *J* = 5.6 Hz, 1H), 4.19 – 4.30 (m, 1H), 4.56 (s, 2H), 4.62 (d, *J* = 11.9 Hz, 1H), 4.76 (d, *J* = 11.9 Hz, 1H), 4.93 – 5.04 (m, 3H), 5.78 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 7.27 – 7.35 (m, 10H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 28.3, 29.9, 67.5, 71.5, 71.8, 72.9, 77.6, 80.4, 84.5, 101.3, 114.6, 127.3(2C),

127.4(4C), 128.0(4C), 137.6(2C), 137.7; IR ($CHCl_3$); 3619, 3030, 2921, 1546, 1455, 1212, 1104, 699 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{24}H_{30}NaO_5$ 421.1991, found 421.1989.

4-Pentenyl 2-*O*-[2,3,5-tri-*O*-benzyl β-D-arabinofuranosyl]-3,5-di-*O*-benzyl β-D-arabinofuranoside (3): Yield: (0.122g, 61%); $[\alpha]_D^{25}$ = -43.8 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78 MHz, $CDCl_3$): δ 1.59 (q, *J* = 7.1 Hz, 2H), 2.01 (q, *J* = 7.3 Hz, 2H), 3.38 (dt, *J* = 9.6, 6.6 Hz, 1H), 3.46 – 3.56 (m, 3H), 3.57 – 3.62 (m, 1H), 3.71 (dt, *J* = 9.6, 6.9 Hz, 1H), 4.13 (td, *J* = 9.9, 8.7, 5.7 Hz, 5H), 4.29 (d, *J* = 12.0 Hz, 1H), 4.37 – 4.45 (m, 2H), 4.49 (d, *J* = 11.3 Hz, 1H), 4.52 (s, 2H), 4.57 (s, 2H), 4.60 (d, *J* = 11.8 Hz, 1H), 4.68 (d, *J* = 11.8 Hz, 1H), 4.80 (d, *J* = 11.3 Hz, 1H), 4.90 (t, *J* = 1.2 Hz, 1H), 4.92 – 4.96 (m, 1H), 5.09 (d, *J* = 4.2 Hz, 1H), 5.16 (d, *J* = 2.5 Hz, 1H), 5.70 (ddt, *J* = 17.1, 10.4, 6.6 Hz, 1H), 7.18 – 7.41 (m, 25H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 28.8, 30.2, 67.1, 71.6, 72.2(2C), 72.4, 72.5, 73.0, 73.2, 79.0, 80.2, 80.7, 82.6, 82.9, 83.9, 98.4, 100.0, 114.9, 127.5, 127.5, 127.6(2C), 127.6(2C), 127.7(2C), 127.7(2C), 127.8, 128.0(2C), 128.3(3C), 128.3(3C), 128.3(3C), 128.3(3C), 137.7(2C), 137.8, 137.9, 138.0, 138.0; IR ($CHCl_3$): 3035, 2920, 1550, 1455, 1212, 1104, 699 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd. for $C_{50}H_{56}NaO_9$ 823.3822, found 823.3832.

4-Pentenyl 3,5-di-*O*-benzyl-α-D-arabinofuranoside (5): Yield: (3.49g, 81%); $[\alpha]_D^{25}$ = +97.8 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78MHz, $CDCl_3$): δ 1.70 (dt, *J* = 14.2, 6.9 Hz, 2H), 2.05 – 2.19 (m, 2H), 3.31 (d, *J* = 10.2 Hz, 1H), 3.40 – 3.54 (m, 2H), 3.57 – 3.78 (m, 2H), 3.87 (s, 1H), 4.14 (d, *J* = 9.6 Hz, 1H), 4.26 (s, 1H), 4.50 (t, *J* = 10.8 Hz, 2H), 4.65 (dd, *J* = 22.6, 11.9 Hz, 2H), 4.98 (dt, *J* = 20.9, 10.4 Hz, 3H), 5.82 (td, *J* = 16.7, 16.2, 6.6 Hz, 1H), 7.24 – 7.35 (m, 10H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 28.7, 30.2, 66.9, 69.8, 71.9, 73.7, 77.8, 83.3, 85.2, 109.1, 114.7, 127.7(3C), 127.8(2C), 128.0, 128.4(2C), 128.5(2C), 137.0, 137.9, 138.3; IR ($CHCl_3$): 3615, 3040, 2925, 1546, 1455, 1212, 1104, 712 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{24}H_{30}NaO_5$ 421.1991,found 421.1989.

4-Pentenyl 3,5-di-*O*-benzyl-2-*O*-(2,3,5-tri-*O*-benzyl α-arabinofuranosyl) α-D-arabinofuranoside (13a) [as obtained from the 1:1 mixture of disaccharides 13a,13b]: ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.68 (q, *J* = 7.0 Hz, 2H), 2.10 (p, *J* = 6.9 Hz, 2H), 3.36 – 3.42 (m, 2H), 3.44 (d, *J* = 3.0 Hz, 2H), 3.54 (m, 3H), 3.61 (d, *J* = 3.8 Hz, 2H), 3.73 (dt, *J* = 9.6, 6.6 Hz, 1H), 3.99 (dd, *J* = 6.4, 2.9 Hz, 1H), 4.11 (d, *J* = 2.0 Hz, 1H), 4.20 – 4.23 (m, 2H), 4.28 – 4.49 (m, 10H), 5.09 (s, 1H), 5.13 (s, 1H), 5.72 – 5.81 (m, 1H), 7.24 – 7.33 (m, 25H). ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 28.7, 28.7, 66.9, 69.8, 71.9, 72.0, 72.5, 73.0, 73.3, 77.2, 80.5, 80.8, 83.5, 84.0(2C), 86.3, 88.4, 105.6, 106.9, 114.8, 127.5(2C), 127.6(3C), 127.9(4C), 128.0, 128.1(4C), 128.2(4C), 128.4(4C), 137.4, 137.6, 137.8, 138.2, 138.3.

4-Pentenyl 3,5-di-*O*-benzyl-2-*O*-(2,3,5-tri-*O*-benzyl α-D-arabinofuranosyl) β-D-arabinofuranoside (13b) [as obtained from the 1:1 mixture of disaccharides 13a,13b]: ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.68 (q, *J* = 7.0 Hz, 2H), 2.10 (p, *J* = 6.9 Hz, 2H), 3.36 – 3.42 (m, 2H), 3.44 (d, *J* = 3.0 Hz, 2H), 3.54 (dd, *J* = 8.6, 4.7 Hz, 3H), 3.61 (d, *J* = 3.8 Hz, 2H), 3.73 (dt, *J* = 9.6, 6.6 Hz, 1H), 3.99 (dd, *J* = 6.4, 2.9 Hz, 1H), 4.11 (d, *J* = 2.0 Hz, 1H), 4.20 – 4.23 (m, 2H), 4.28 – 4.49 (m, 10H), 4.98 (s, 1H), 5.07 (d, *J* = 4.2 Hz, 1H), 5.75 – 5.84 (m, 1H), 7.24 – 7.33 (m, 25H). ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 28.7, 30.2, 66.8, 70.0, 72.1, 72.3, 72.4, 73.0, 73.2, 77.2, 79.9, 80.9, 82.8, 83.9(2C), 86.0, 92.2, 100.2, 105.8, 114.6, 127.5(2C), 127.6(3C), 127.9(4C), 128.0, 128.1(4C), 128.2(4C), 128.4(4C), 136.9, 137.1, 137.5, 138.0, 138.1.

Methyl 3,5-di-*O*-benzyl-α-D-arabinofuranoside (7): Yield: (2.90g, 78%); $[\alpha]_D^{25}$ = +122.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 3.39 (s, 3H), 3.43 (m, 2H), 3.63 (dd, *J* = 10.4, 2.5 Hz, 1H), 3.82 (d, *J* = 3.3 Hz, 1H), 4.12 (d, *J* = 6.9 Hz, 1H), 4.21 – 4.29 (m, 1H), 4.48 (dd, *J* = 19.6, 12.1 Hz, 2H), 4.58 (d, *J* = 11.9 Hz, 1H), 4.67 (d, *J* = 12.3 Hz, 1H), 4.89 (s, 1H), 7.22 – 7.35 (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 55.1, 69.6, 71.9, 73.5, 78.0, 83.2, 84.8, 110.2, 127.7(3C), 127.8(2C), 127.9, 128.3(2C), 128.4(2C), 136.9, 137.6; IR ($CHCl_3$):

3618, 3042, 2925, 1550, 1455, 1215, 1100, 688 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{20}H_{24}NaO_5$ 367.1521, found 367.1521.

Methyl 3,5-di-*O*-benzyl-β-D-arabinofuranoside (6): Yield: (2.90g, 78%); $[\alpha]_D^{25}$ = -39.8 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78 MHz, $CDCl_3$): δ 2.67 (bs, 1 H), 3.38 (s, 3H), 3.52 (d, *J* = 5.7 Hz, 2H), 3.84 (t, *J* = 5.8 Hz, 1H), 4.14 (q, *J* = 5.6 Hz, 1H), 4.24 (t, *J* = 5.3 Hz, 1H), 4.55 (d, *J* = 2.2 Hz, 2H), 4.61 (d, *J* = 11.9 Hz, 1H), 4.74 (d, *J* = 11.9 Hz, 1H), 4.83 (d, *J* = 4.7 Hz, 1H), 7.23 – 7.38 (m, 10H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 55.3, 71.8, 72.0, 73.2, 77.9, 80.7, 84.5, 102.6, 127.6(4C), 127.7(2C), 128.3(4C), 137.9, 137.9; IR ($CHCl_3$): 3612, 3032, 2922, 1555, 1455, 1218, 1104, 685 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{20}H_{24}NaO_5$ 367.1521, found 367.1519 .

Decanyl 3,5-di-*O*-benzyl-α-D-arabinofuranoside(9): Yield: (3.81g, 75%); $[\alpha]_D^{25}$ = +91.6 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78MHz, $CDCl_3$): δ 0.81 – 0.93 (m, 3H), 1.16 – 1.38 (m, 14H), 1.59 (q, *J* = 6.7 Hz, 2H), 3.34 – 3.53 (m, 3H), 3.61 – 3.75 (m, 2H), 3.86 (d, *J* = 3.1 Hz, 1H), 4.14 (s, 1H), 4.21 – 4.27 (m, 1H), 4.45 – 4.53 (m, 2H), 4.64 (dd, *J* = 27.6, 12.1 Hz, 2H), 5.00 (s, 1H), 7.21 – 7.39 (m, 10H); ^{13}C NMR (10.53 MHz, $CDCl_3$): δ 14.1, 22.6, 26.0, 29.3, 29.4, 29.5, 29.5, 29.6, 31.8, 67.6, 69.7, 71.8, 73.6, 78.0, 83.0, 85.2, 108.9, 127.6, 127.7(2C), 127.8(2C), 127.9, 128.3(2C), 128.5(2C), 137.0, 137.9; IR ($CHCl_3$): 3622, 3030, 2925, 1552, 1455, 1219, 1104, 683 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{29}H_{42}NaO_5$ 493.2930, found 493.2929.

Decanyl 3,5-di-*O*-benzyl-β-D-arabinofuranoside(8): Yield: (3.66g, 72%); $[\alpha]_D^{25}$ = +39.6 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.8 Hz, 3H), 1.26 (s, 14H), 1.43 – 1.62 (m, 2H), 2.64 (d, *J* = 9.0 Hz, 1H), 3.41 (dt, *J* = 9.5, 6.7 Hz, 1H), 3.53 (d, *J* = 5.9 Hz, 2H), 3.74 (dt, *J* = 9.5, 6.8 Hz, 1H), 3.83 (t, *J* = 5.7 Hz, 1H), 4.14 (q, *J* = 5.7 Hz, 1H), 4.24 (dt, *J* = 9.9, 5.5 Hz, 1H), 4.55 (s, 2H), 4.62 (d, *J* = 11.9 Hz, 1H), 4.76 (d, *J* = 11.9 Hz, 1H), 4.95 (dd, *J* = 4.7, 2.8 Hz, 1H), 7.24 – 7.35 (m, 10H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.1,

22.6, 26.0, 29.3, 29.4, 29.4, 29.5(2C), 31.8, 68.4, 71.7, 72.1, 73.2, 77.9, 80.6, 84.9, 101.5, 127.6(2C), 127.6(4C), 128.3(4C), 138.0(2C); IR ($CHCl_3$): 3625, 3025, 2921, 1548, 1458, 1212, 1113, 698 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{29}H_{42}NaO_5$ 493.2930, found 493.2929.

Methyl 2-*O*-[2,3,5-tri-*O*-benzyl β-D-arabinofuranosyl]-3,5-di-*O*-benzyl α-D-arabinofuranoside (14):An analytical sample for characterization purposes was obtained by purification of the residue resulting from the aforementioned general reaction procedure using the imidate donor (**11**) as the glycosyl donor. Yield: (0.13g, 60%); $[\alpha]_D^{25}$ = -49.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.37 (s, 3H), 3.48 – 3.63 (m, 3H), 3.94 – 4. 01 (m, 1H), 4.09 (dd, *J* = 5.8, 2.5 Hz, 2H), 4.18 – 4.23 (m, 1H), 4.26 (s, 1H), 4.36 (td, *J* = 12.3, 1.7 Hz, 2H), 4.43 – 4.69 (m, 10H), 4.89 (s, 1H), 5.06 (d, *J* = 3.9 Hz, 1H), 7.16 – 7.38 (m, 25H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 54.9, 70.1, 72.0, 72.2, 72.3, 72.5, 73.0, 73.3, 80.0, 81.3, 82.9, 83.9, 84.0, 85.9, 100.2, 106.9, 127.5(3C), 127.5(3C), 127.6, 127.7(5C), 127.9, 128.0(2C), 128.2(2C), 128.3(5C), 128.4(3C), 137.6, 138.0(2C), 138.1(2C); IR ($CHCl_3$): 3033, 2923, 1552, 1459, 1213, 1101, 695 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{46}H_{50}NaO_9$ 769.3353, found 769.3358.

Methyl 2-*O*-[2,3,5-tri-*O*-benzyl β-D-arabinofuranosyl]-3,5-di-*O*-benzyl β-D-arabinofuranoside (15):An analytical sample for characterization purposes was obtained by purification of the residue resulting from the aforementioned general reaction procedure using the imidate donor (**11**) as the glycosyl donor. Yield: (0.14g, 63%); $[\alpha]_D^{25}$ = -7.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.23 (s, 3H), 3.50 (qd, *J* = 9.8, 6.2 Hz, 2H), 3.56 – 3.66 (m, 2H), 4.05 – 4.17 (m, 6H), 4.49 – 4.55 (m, 6H), 4.57 (s, 1H), 4.58 – 4.71 (m, 3H), 4.76 (d, *J* = 4.1 Hz, 1H), 5.17 (d, *J* = 4.3 Hz, 1H), 7.08 – 7.37 (m, 25H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 54.2, 71.9, 72.2, 72.3, 72.5, 72.6, 73.1, 73.3, 79.7, 80.1, 82.9, 83.1, 83.5, 84.2, 102.0(2C), 127.5(2C), 127.6(3C), 127.7(4C), 127.7(5C), 128.3(5C), 128.3(4C),

128.4(2C), 137.4, 137.9(2C), 137.9, 138.1; IR ($CHCl_3$): 3030, 2921, 1546, 1455, 1212, 1104, 699 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{46}H_{50}NaO_9$ 769.3353, found 769.3358.

Decanyl 3,5-di-*O*-benzyl-2-*O*-(2,3,5-tri-*O*-benzyl α-D-arabinofuranosyl) β-D-arabinofuranoside (16):An analytical sample for characterization purposes was obtained by purification of the residue resulting from the aforementioned general reaction procedure using the imidate donor (**11**) as the glycosyl donor. Yield: (0.11g, 62%); $[\alpha]_D^{25}$ = -31.4 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (399.78 MHz, CDCl3): δ 0.87 (t, *J* = 6.8 Hz, 3H), 1.24 (s, 14H), 1.52 – 1.59 (m, 2H), 3.42 (d, *J* = 3.0 Hz, 1H), 3.45 (d, *J* = 2.9 Hz, 1H), 3.83 (dd, *J* = 6.4, 2.8 Hz, 1H), 4.06 (d, *J* = 4.2 Hz, 1H), 4.11 (dt, *J* = 7.5, 4.3 Hz, 3H), 4.14 – 4.27 (m, 5H), 4.45 – 4.61 (m, 10H), 5.02 (d, *J* = 4.3 Hz, 1H), 5.19 (s, 1H), 7.27 – 7.34 (m, 25H). 13C NMR (100.53 MHz, CDCl3): δ 14.1 , 22.7 , 26.1 , 29.3 , 29.4 , 29.6(2C) , 31.9 , 67.8 , 69.1 , 70.0 71.8 , 72.2 , 73.8 , 73.6 , 80.8 , 80.6 , 81.1 , 81.4 , 82.9 , 83.2 , 83.9 , 87.4 , 100.4 , 106.2 , 127.6(3C) , 127.7(4C) , 127.8(2C) , 128.0(2C) , 128.2 , 128.3(3C) , 128.4(4C) , 128.5(2C), 136.9(4C) , 136.9 , 137.1 , 137.6 , 138.1(2C). IR ($CHCl_3$): 3014, 2928, 1555, 1453, 1219, 1117, 696 cm^{-1}. HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{55}H_{68}NaO_9$ 895.4761, found 895.4752.

Decanyl 2-*O*-[2,3,5-tri-*O*-benzyl β-D-arabinofuranosyl]-3,5-di-*O*-benzyl β-D-arabinofuranoside(17):An analytical sample for characterization purposes was obtained by purification of the residue resulting from the aforementioned general reaction procedure using the imidate donor (**11**) as the glycosyl donor. Yield: (0.12g, 63%); $[\alpha]_D^{25}$ = +5.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.8 Hz, 3H), 1.25 (s, 14H), 1.52 (s, 2H), 3.21 – 3.32 (m, 1H), 3.56 (dddd, *J* = 39.9, 18.2, 9.6, 6.4 Hz, 5H), 4.06 – 4.16 (m, 6H), 4.47 – 4.63 (m, 8H), 4.67 (d, *J* = 11.9 Hz, 2H), 4.86 (d, *J* = 4.1 Hz, 1H), 5.18 (d, *J* = 3.9 Hz, 1H), 7.16 – 7.38 (m, 25H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.1, 22.7, 26.3, 29.4, 29.6, 29.6, 29.7, 29.8, 31.9, 67.6, 71.9, 72.4, 72.5, 72.6, 72.9, 73.0, 73.3, 79.5, 80.0, 83.2(2C), 83.5, 84.5, 101.0, 102.2, 127.5, 127.5(5C), 127.6, 127.7(5C), 127.7, 128.3(5C), 128.3(5C),

128.4(2C), 137.7, 137.8, 138.0, 138.1, 138.1; IR ($CHCl_3$): 3012, 2928, 1552, 1455, 1218, 1114, 697 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{55}H_{68}NaO_9$ 895.4761, found 895.4752.

1,2-*O*-Isopropylidene 3-*O*-[3-*O*-benzyl-5-*O*-*tert*-butyldiphenylsilyl-α-D-arabinofuranosyl]-5-*O*-*tert*-butyldiphenylsilyl-β-D-arabinofuranose (22): $[\alpha]_D^{25}$ = +58.2 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78MHz, $CDCl_3$): δ 1.07 (s, 9H), 1.10 (s, 9H), 1.37 (s, 3H), 1.42 (s, 3H), 3.52 – 3.62 (m, 2H), 3.79 – 3.88 (m, 2H), 3.89 – 3.97 (m, 1H), 4.10 (s, 1H), 4.20 (s, 1H), 4.30 (dd, *J* = 10.6, 2.7 Hz, 2H), 4.57 (dd, *J* = 12.1, 1.7 Hz, 1H), 4.67 (s, 1H), 4.69 – 4.75 (m, 2H), 5.28 – 5.39 (s, 1H), 5.96 (d, *J* = 3.6 Hz, 1H), 7.30 – 7.40 (m, 11H), 7.41 – 7.55 (m, 6H), 7.65 – 7.69 (m, 2H), 7.73 (td, *J* = 7.5, 3.9 Hz, 6H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.0, 19.1, 26.0, 26.7(3C), 26.7(3C), 26.9, 63.2, 63.8, 71.8, 77.4, 78.8, 84.6, 84.6, 84.9, 85.9, 105.8, 107.2, 112.4, 127.6(5C), 127.7, 127.9(4C), 128.3(2C), 129.6, 129.6, 130.0, 130.0, 132.0, 132.2, 133.1, 133.2, 135.5(4C), 135.5(5C), 137.8; IR ($CHCl_3$): 3618, 3031, 2921, 1547, 1456, 1212, 1104, 691 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{52}H_{64}NaO_9Si_2$ 911.3987, found 911.3979.

1,2-*O*-Isopropylidene 3-*O*-[3,5-di-*O*-benzyl-α-D-arabinofuranosyl]-5-*O*-benzyl-β-D-arabinofuranose (23): $[\alpha]_D^{25}$ = +42.2 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78MHz, $CDCl_3$): δ 1.32 (s, 3H), 1.52 (s, 3H), 2.34 (s, 1H), 3.60 (td, *J* = 11.8, 11.3, 3.9 Hz, 2H), 3.70 – 3.80 (m, 2H), 3.92 – 3.96 (m, 1H), 3.99 – 4.02 (m, 1H), 4.15 (dd, *J* = 8.7, 3.5 Hz, 2H), 4.17 – 4.20 (m, 1H), 4.41 – 4.60 (m, 7H), 5.16 (s, 1H), 5.85 (d, *J* = 3.9 Hz, 1H), 7.23 – 7.38 (m, 15H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 26.3, 27.1, 62.5, 69.4, 72.1, 72.2, 73.3, 80.4, 80.7, 83.4, 85.5, 86.2, 88.3, 105.2, 105.8, 112.9, 127.6, 127.7(4C), 127.9(4C), 128.3(4C), 128.4(2C), 137.3, 137.6, 137.8; IR ($CHCl_3$): 3617, 3036, 2918, 1549, 1445, 1222, 1114, 689 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{34}H_{40}NaO_9$ 615.2570, found 615.2561.

1,2-*O*-Isopropylidene 3-*O*-[3-*O*-benzyl-5-*O*-(((9*Z*,12*Z*)-octadeca-9,12-dienoyl))-α-D-

arabinofuranosyl]-5-*O*-[(((9*Z*,12*Z*)-octadeca-9,12-dienoyl))]-β-D-arabinofuranose (25): $[\alpha]_D^{25}$ = +49.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 0.87 – 0.89 (m, 6H), 1.20 – 1.37 (m, 35H), 1.53 (s, 3H), 1.59 (d, *J* = 7.2 Hz, 2H), 2.04 (dt, *J* = 14.9, 7.2 Hz, 8H), 2.30 (dt, *J* = 11.4, 7.4 Hz, 4H), 2.77 (t, *J* = 6.4 Hz, 2H), 3.76 (d, *J* = 5.8 Hz, 3H), 4.10 – 4.19 (m, 3H), 4.20 – 4.26 (m, 3H), 4.52 (d, *J* = 12.0 Hz, 1H), 4.64 – 4.72 (m, 2H), 5.10 (d, *J* = 1.7 Hz, 1H), 5.13 (s, 1H), 5.35 (tq, *J* = 7.3, 4.7, 3.6 Hz, 8H), 5.90 (d, *J* = 4.1 Hz, 1H), 7.28 – 7.37 (m, 5H);^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.1, 14.1, 22.5, 22.6, 24.8, 24.8, 25.6, 26.4, 27.2(4C), 29.1(4C), 29.2, 29.3(3C), 29.5, 29.6, 29.7, 29.7, 31.5, 31.9, 34.0, 34.0, 63.3, 63.5, 72.3, 80.1, 80.2, 80.6, 82.6, 85.0, 85.1, 105.4, 107.5, 113.3, 127.7(2C), 127.8, 128.0, 128.0, 128.5(2C), 129.7, 129.7, 130.0, 130.0, 130.0, 130.2, 137.4, 173.2, 173.4; IR ($CHCl_3$): 3627, 3031, 2921, 1753, 1551, 1448, 1218, 1104, 698 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{56}H_{88}NaO_{11}$ 959.6224, found 959.6216.

1,2-*O*-Isopropylidene 3-*O*-[(3-*O*-benzyl-5-*O*-*tert*-butyldiphenylsilyl-α-D-arabinofuranosyl)-2-*O*-(2,3,5-tri-*O*-benzyl β-D-arabnofuranosyl)]-5-*O*-*tert*-butyldiphenylsilyl-β-D-arabinofuranose (26) [resonances for the major β-isomer as obtained from the 0.4:1.0 α,β mixture of trisaccharides]:^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.89 (s, 9H), 0.95 (s, 9H), 1.20 (s, 3H), 1.25 (s, 3H), 3.48 (d, *J* = 5.2 Hz, 2H), 3.67 – 3.73 (m, 4H), 3.98 – 4.02 (m, 1H), 4.02 – 4.06 (m, 2H), 4.12 (dd, *J* = 6.0, 3.2 Hz, 3H), 4.27 (d, *J* = 3.5 Hz, 2H), 4.31 – 4.36 (m, 1H), 4.37 – 4.61 (m, 8H), 4.95 (d, *J* = 4.1 Hz, 1H), 5.05 (s, 1H), 5.74 (d, *J* = 4.0 Hz, 1H), 7.16 – 7.28 (m, 32H), 7.53 – 7.59 (m, 8H). ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.1 , 19.3 , 26.7(3C) , 26.9(3C) , 63.3 , 72.2 , 72.2 , 72.3 , 72.5 , 73.1 , 79.4 , 80.0 , 80.8 , 82.8 , 83.1 , 83.8 , 84.0 , 84.8 , 85.7 , 88.5 , 99.9 , 104.2 , 105.6 , 112.5 , 127.4(2C) , 127.5(5C) , 127.6(13C) , 127.9(3C) , 128.2(2C) , 128.3(2C) , 128.3(2C) , 128.4(2C) , 129.5 , 129.69 , 133.1 , 133.2 , 133.3 , 133.4 , 135.6(9C) , 137.7 , 137.9 , 138.1(2C) .

1,2-*O*-Isopropylidene 3-*O*-[(3,5-di-*O*-benzyl-α-D-arabinofuranosyl)-2-*O*-(2,3,5-tri-*O*-

benzyl β-D-arabnofuranosyl)]-5-*O*-benzyl-β-D-arabinofuranose (27) [resonances for the major β-isomer as obtained from the 0.1:1.0 α,β mixture of trisaccharides]: ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.32 (s, 3H), 1.51 (s, 3H), 3.49 – 3.63 (m, 4H), 3.65 – 3.83 (m, 2H), 3.93 – 4.23 (m, 9H), 4.50 (ddd, *J* = 15.4, 10.0, 2.7 Hz, 12H), 5.12 (d, *J* =3.8Hz,1H), 5.18 (s, 1H), 5.86 (d, *J* = 4.1 Hz, 1H), 7.24 – 7.34 (m, 30H). ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 26.4 , 27.1 , 66.5 , 69.3 , 71.8 , 72.1(3C) , 72.7 , 73.1 , 73.3 , 80.1 , 80.2 , 81.0 , 83.4 , 84.1 , 84.4 , 85.2 , 88.3 , 88.5 , 100.9 , 105.3 , 105.5 , 112.9 , 127.6(6C) , 127.8(4C) , 127.8(4C) , 128.2(5C) , 128.2(5C) , 128.4(6C) , 137.4 , 137.7 , 137.9(2C) , 138.1(2C) .

1,2-*O*-Isopropylidene 3-*O*-[3-*O*-benzyl-5-*O*-(((9*Z*,12*Z*)-octadeca-9,12-dienoyl))-2-*O*-(2,3,5-tri-*O*-benzyl-β-D-arabinofuranosyl)-α-D-arabinofuranosyl]-5-*O*-[(((9*Z*,12*Z*)-octadeca-9,12-dienoyl))]-β-D-arabinofuranose (28): Yield: (90 mg, 63%); $[\alpha]_D^{25}$ = +20.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.64-1.04(m, 6H), 1.23 – 1.34 (m, 35H), 1.51 (s, 3H), 1.56 (d, *J* = 7.2 Hz, 2H), 1.97 – 2.08 (m, 8H), 2.19 – 2.26 (m, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 2.77 (t, *J* = 6.1 Hz, 2H), 3.52 – 3.58 (m, 2H), 3.65 – 3.73 (m, 1H), 3.77 (dd, *J* = 11.2, 4.3 Hz, 2H), 4.07 (dd, *J* = 4.5, 2.3 Hz, 2H), 4.09 – 4.14 (m, 2H), 4.19 (d, *J* = 3.6 Hz, 2H), 4.23 (dd, *J* = 7.0, 3.6 Hz, 2H), 4.47 – 4.55 (m, 4H), 4.55 – 4.60 (m, 2H), 4.65 (dd, *J* = 13.6, 3.9 Hz, 2H), 4.68 – 4.75 (m, 2H), 5.09 (d, *J* = 3.2 Hz, 1H), 5.18 (d, *J* = 3.4 Hz, 1H), 5.28 – 5.42 (m, 8H), 5.90 (d, *J* = 4.1 Hz, 1H), 7.29 (m, 20H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.1, 14.1, 24.8, 25.6, 26.4, 27.0, 27.2(2C), 29.1(3C), 29.2, 29.2, 29.3(3C), 29.5, 29.6, 29.7(2C), 29.7(2C), 31.5(2C), 31.9, 33.9, 34.0, 66.6, 71.9, 72.1(2C), 72.2, 72.6, 73.2(2C), 80.2, 80.4, 80.7, 81.3, 83.1, 83.2, 84.0, 84.2, 85.0, 100.8, 105.4, 105.6, 112.9, 127.5(2C), 127.7(3C), 127.7(3C), 127.8(3C), 127.8, 127.9, 128.1(3C), 128.3(3C), 128.3(3C), 128.4(2C), 129.9, 130.0, 130.0, 130.2, 137.2, 137.8, 138.2(2C), 172.7, 173.3; IR ($CHCl_3$): 3032, 2917, 1749, 1546, 1455, 1212, 1117, 693 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{82}H_{114}NaO_{15}$ 1361.8055 found 1361.8049.

Methyl 2,3-di-*O*-benzyl-5-*O*-[2-*O*-benzyl-3,5-di-*O*-(3-*O*-benzyl-5-*O*-*tert*-butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl]-α-D-arabinofuranoside (30): $[\alpha]_D^{25}$ = +81.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.05 (d, *J* = 2.9 Hz, 18H), 3.37 (d, *J* = 9.3 Hz, 1H), 3.42 (s, 3H), 3.44 (d, *J* = 8.7 Hz, 1H), 3.55 (ddd, *J* = 10.9, 7.5, 2.2 Hz, 2H), 3.72 (t, *J* = 3.2 Hz, 1H), 3.74 (d, *J* = 3.8 Hz, 2H), 3.79 (dd, *J* = 13.2, 2.2 Hz, 1H), 3.93 (dd, *J* = 11.4, 4.3 Hz, 1H), 4.00 – 4.07 (m, 4H), 4.09 (dd, *J* = 6.7, 3.2 Hz, 1H), 4.16 (dd, *J* = 3.1, 1.1 Hz, 1H), 4.17 – 4.27 (m, 6H), 4.42 – 4.48 (m, 2H), 4.48 – 4.54 (m, 2H), 4.56 – 4.63 (m, 5H), 4.65 (dd, *J* = 12. 1, 3.8 Hz, 2H), 4.97 (s, 1H), 5.18 (s, 1H), 5.22 (s, 1H), 5.22 (s, 1H), 7.27 – 7.41 (m, 35H), 7.42 – 7.48 (m, 2H), 7.62 (ddd, *J* = 5.4, 4.0, 1.9 Hz, 4H), 7.66 – 7.70 (m, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.0, 19.0, 26.6(3C), 26.6(3C), 54.9, 63.7, 63.7(2C), 65.7, 71.7(3C), 71.9, 72.2, 77.8, 78.1, 79.0, 80.3, 81.0, 83.0, 83.3, 83.7, 84.1, 84.3, 87.6, 88.3, 106.1, 107.1, 107.4, 108.9, 127.5, 127.6(2C), 127.7(5C), 127.7(3C), 127.7(3C), 127.8(5C),127.8, 127.9(2C), 127.9(3C), 128.3(4C), 128.3(3C), 128.3(3C), 128.4(2C), 129.7, 129.8 (2C), 129.8, 132.4, 132.4, 132.4, 132.5 , 135.5(3C), 135.5, 137.3, 137.4, 137.8(2C), 137.9; IR ($CHCl_3$): 3619, 3035, 2920, 1546, 1455, 1210, 1100, 693 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{88}H_{102}NaO_{17}Si_2$ 1509.6553, found 1509.6548.

Methyl 2,3-di-*O*-benzyl-5-*O*-[2-*O*-benzyl-3,5-di-*O*-(3,5-di-*O*-benzyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl]-α-D-arabinofuranoside (31): $[\alpha]_D^{25}$ = -31.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 3.39 (s, 3H), 3.49 (qd, *J* = 7.1, 6.5, 4.2 Hz, 4H), 3.61 (dd, *J* = 10.5, 2.5 Hz, 1H), 3.65 (d, *J* = 2.4 Hz, 1H), 3.69 (dd, *J* = 11.7, 4.2 Hz, 1H), 3.75 (dd, *J* = 10.8, 5.7 Hz, 1H), 3.85 (dd, *J* = 4.4, 1.8 Hz, 1H), 3.87 – 3.98 (m, 3H), 4.00 – 4.06 (m, 2H), 4.16 (dq, *J* = 10.2, 3.5 Hz, 3H), 4.22 (t, *J* = 5.6 Hz, 2H), 4.26 (d, *J* = 4.0 Hz, 1H), 4.32 (dd, *J* = 6.9, 4.8 Hz, 2H), 4.42 – 4.52 (m, 4H), 4.52 – 4.61 (m, 6H), 4.62 – 4.72 (m, 4H), 4.94 (s, 1H), 5.11 (s, 1H), 5.15 (s, 1H), 5.18 (s, 1H), 7.31 (ddt, *J* = 15.3, 7.3, 4.4 Hz, 35H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 54.9, 66.3, 68.0, 69.6, 69.6, 71.7, 71.8, 71.8, 71.9,

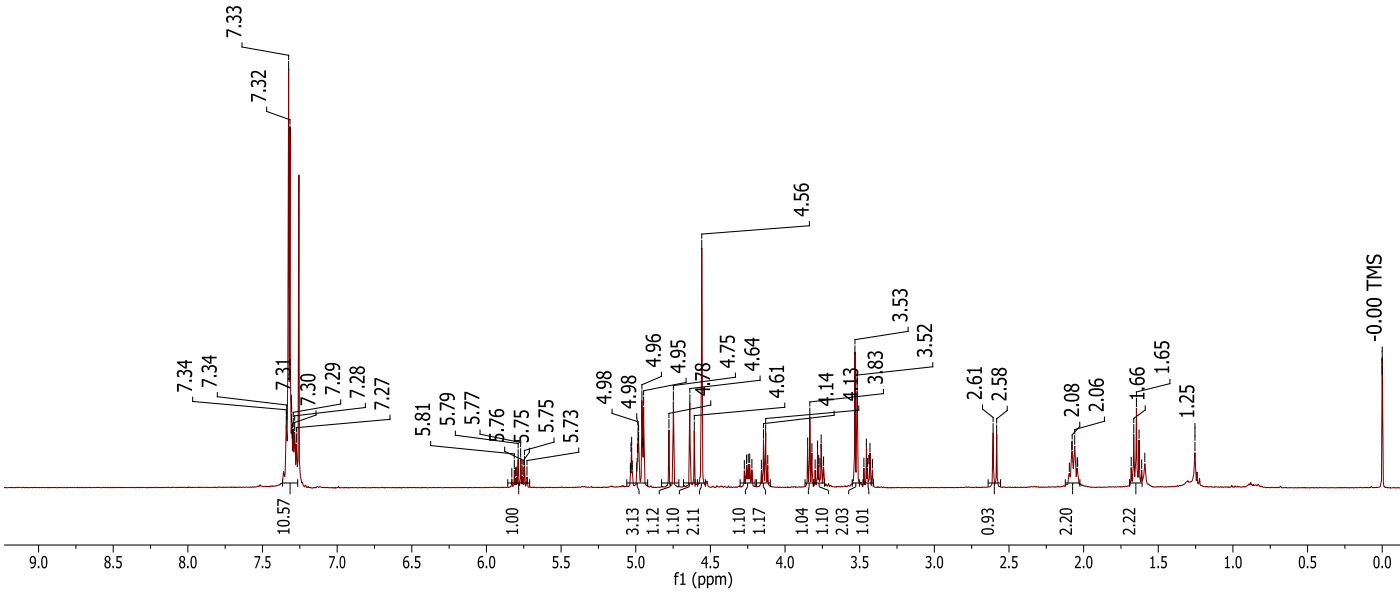
72.2, 73.4, 73.5, 78.3, 78.7, 80.1, 80.4, 82.6, 82.7, 82.8, 83.2, 84.6, 84.8, 88.1, 88.5, 106.4, 107.0, 108.7, 109.1, 127.4, 127.5, 127.6(3C), 127.7(3C), 127.7(6C), 127.8, 127.8(3C), 127.9(3C), 128.1(2C), 128.2(2C), 128.3(6C), 128.4(2C), 128.4(2C), 137.1, 137.2, 137.4, 137.6, 137.8(2C), 137.9; IR ($CHCl_3$): 3621, 3028, 2921, 1556, 1455, 1218, 1111, 699 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{70}H_{78}NaO_{17}$ 1213.5137, found 1213.5134.

Methyl 2,3-di-*O*-benzyl-5-*O*-[2-*O*-benzyl-3,5-di-*O*-(3-*O*-benzyl-5-*O*-(((9*Z*,12*Z*)-octadeca-9,12-dienoyl))-α-D-arabinofuranosyl)-α-D-arabinofuranosyl]-α-D-arabinofuranoside (33): $[\alpha]_D^{25}$ = +80.0 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78MHz, $CDCl_3$): δ 0.88 (t, *J* = 3.5 Hz, 6H), 1.30 (m, 32H), 1.56 (d, *J* = 6.7 Hz, 2H), 1.91 – 2.11 (m, 8H), 2.27 (td, *J* = 7.8, 4.2 Hz, 4H), 2.77 (t, *J* = 6.4 Hz, 2H), 3.35 (s, 3H), 3.63 (dd, *J* = 11.3, 3.1 Hz, 1H), 3.71 (dt, *J* = 9.1, 2.8 Hz, 3H), 3.85 (dd, *J* = 11.3, 3.8 Hz, 1H), 3.92 (dd, *J* = 12.1, 3.5 Hz, 1H), 4.00 (dd, *J* = 3.2, 1.0 Hz, 1H), 4.02 – 4.08 (m, 3H), 4.14 (ddq, *J* = 14.0, 7.0, 2.3 Hz, 6H), 4.18 – 4.19 (m, 1H), 4.21 (dd, *J* = 6.1, 2.4 Hz, 2H), 4.23 – 4.25 (m, 1H), 4.28 (dd, *J* = 5.5, 1.9 Hz, 1H), 4.40 – 4.66 (m, 11H), 4.89 (s, 1H), 4.94 (d, *J* = 1.7 Hz, 1H), 5.01 (d, *J* = 2.5 Hz, 1H), 5.13 (s, 1H), 5.27 – 5.44 (m, 8H), 7.23 – 7.34 (m, 25H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.1, 14.1, 22.5, 22.7, 24.8, 25.6, 27.2(3C), 29.1(2C), 29.1(2C), 29.2, 29.3(2C), 29.3(2C), 29.5, 29.6(2C), 29.7, 29.7, 31.5, 31.9, 34.0, 54.9, 63.4, 63.5, 64.8, 66.6, 71.9, 72.0, 72.2, 72.2, 72.3, 79.0, 79.4, 79.6, 80.0, 80.6, 80.7, 82.3, 82.9, 83.2, 84.3, 86.5, 88.4, 105.7, 106.8, 107.1, 109.1, 127.7(2C), 127.8(2C), 127.8(3C), 127.9(2C), 128.0(2C), 128.1, 128.1, 128.2(3C), 128.2(3C), 128.4(2C), 128.4(2C), 128.42(2C), 128.5(4C), 129.7, 130.0, 130.0, 130.2, 136.9, 137.1, 137.5, 137.7, 137.7, 173.4(2C); IR ($CHCl_3$): 3622, 3031, 2917, 1761, 1546, 1455, 1217, 1104, 699 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$ calcd for $C_{92}H_{126}NaO_{19}$ 1557.8791, found 1557.8787.

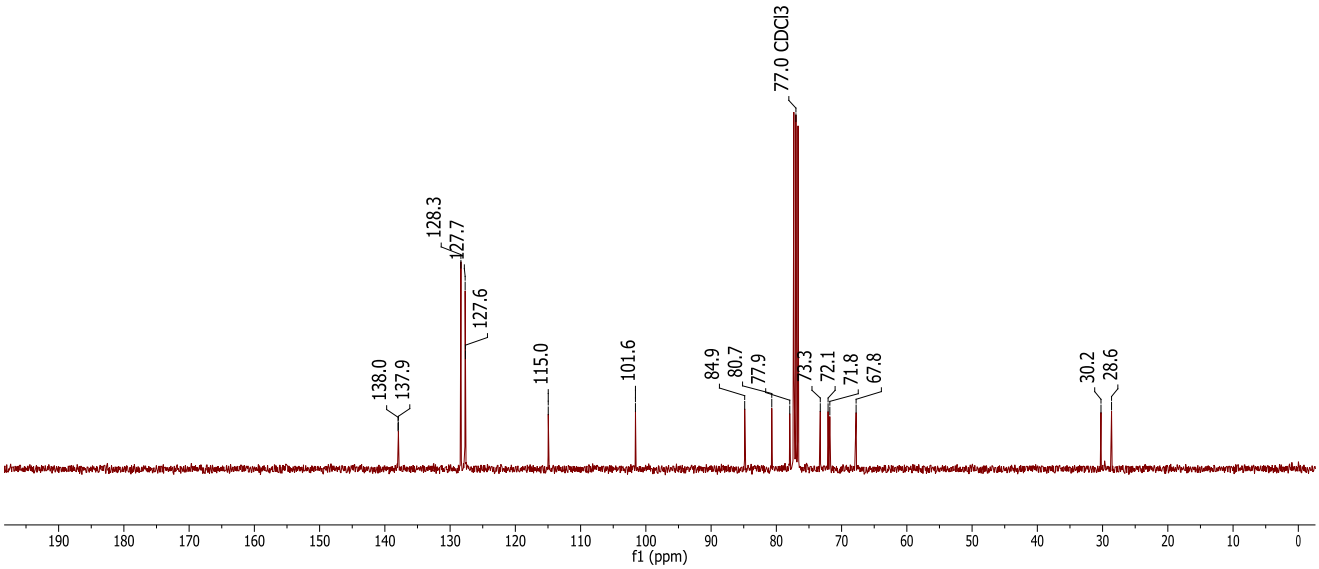
3.6 Spectral charts of representative compounds

{Kindly see the supporting documents file for spectral charts of all compounds}

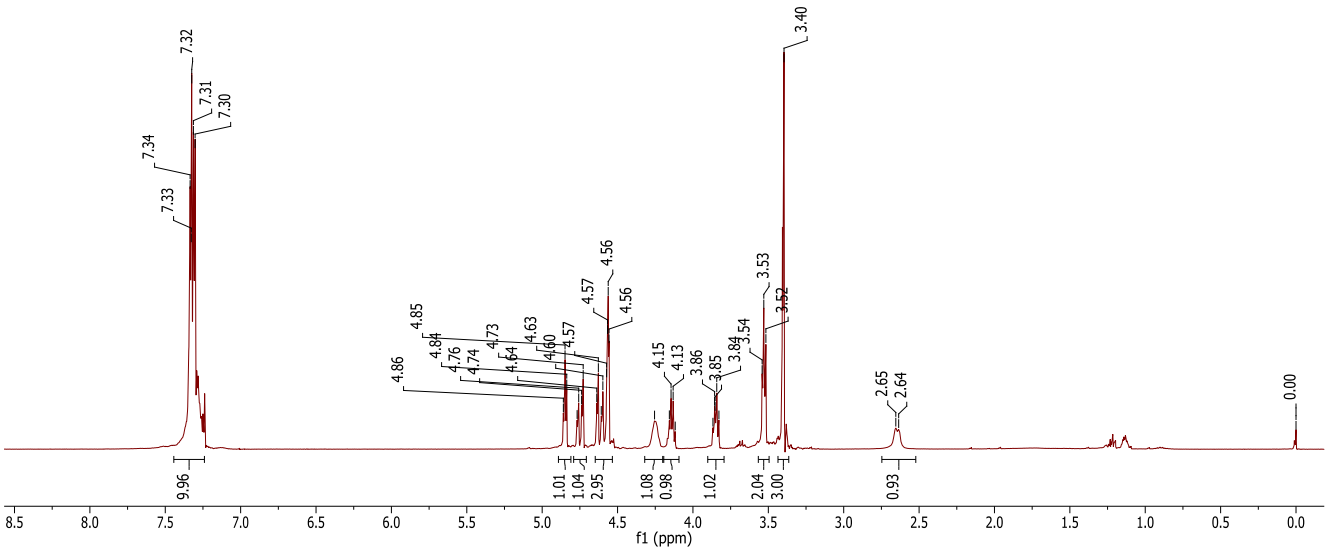
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **2**



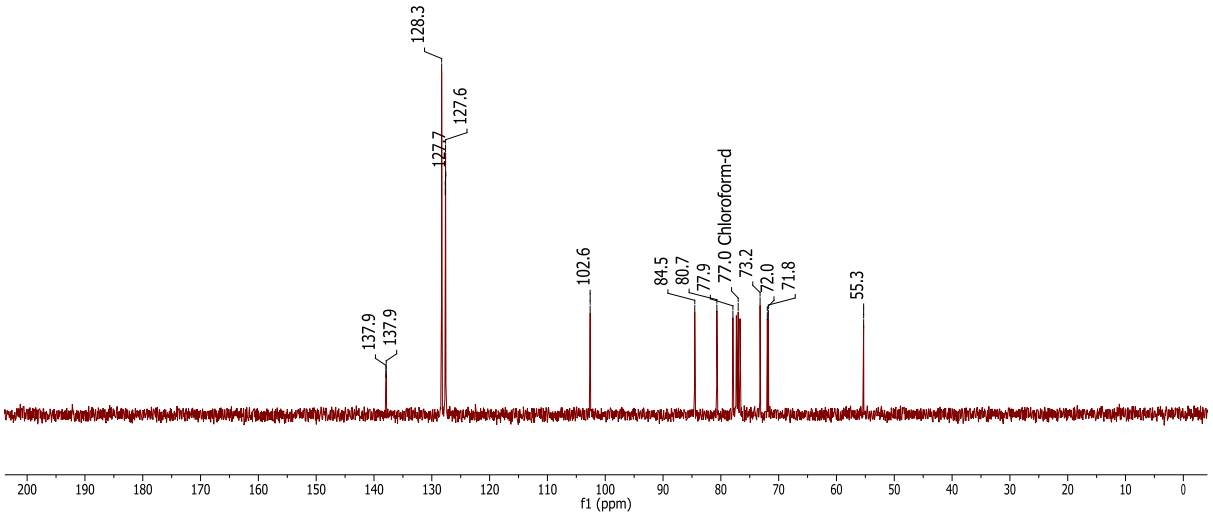
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **2**



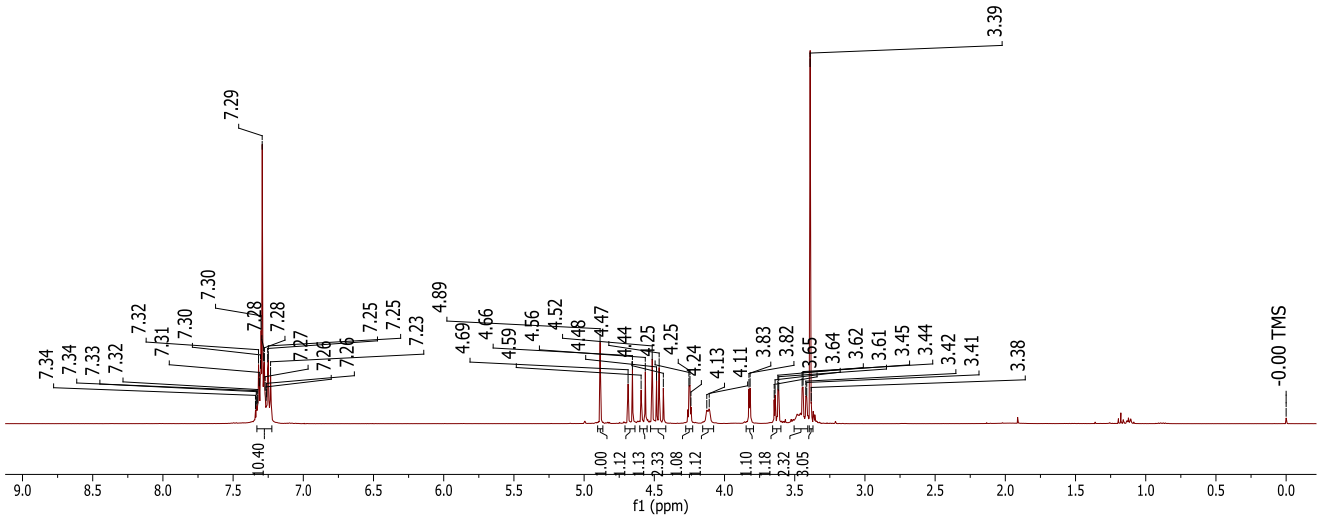
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **6**



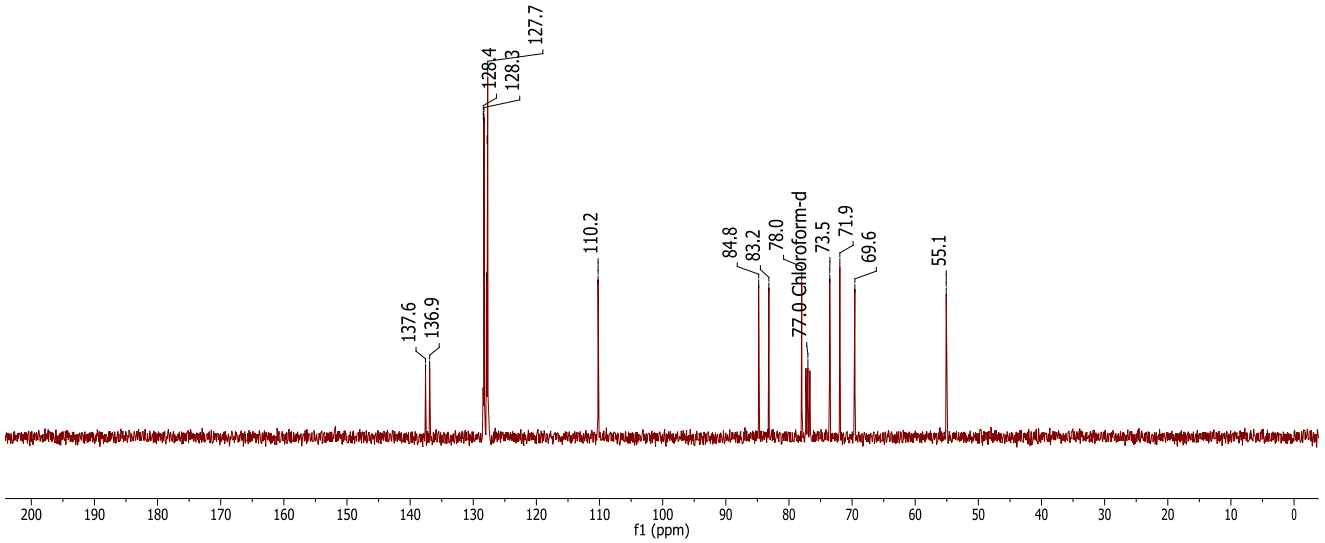
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **6**



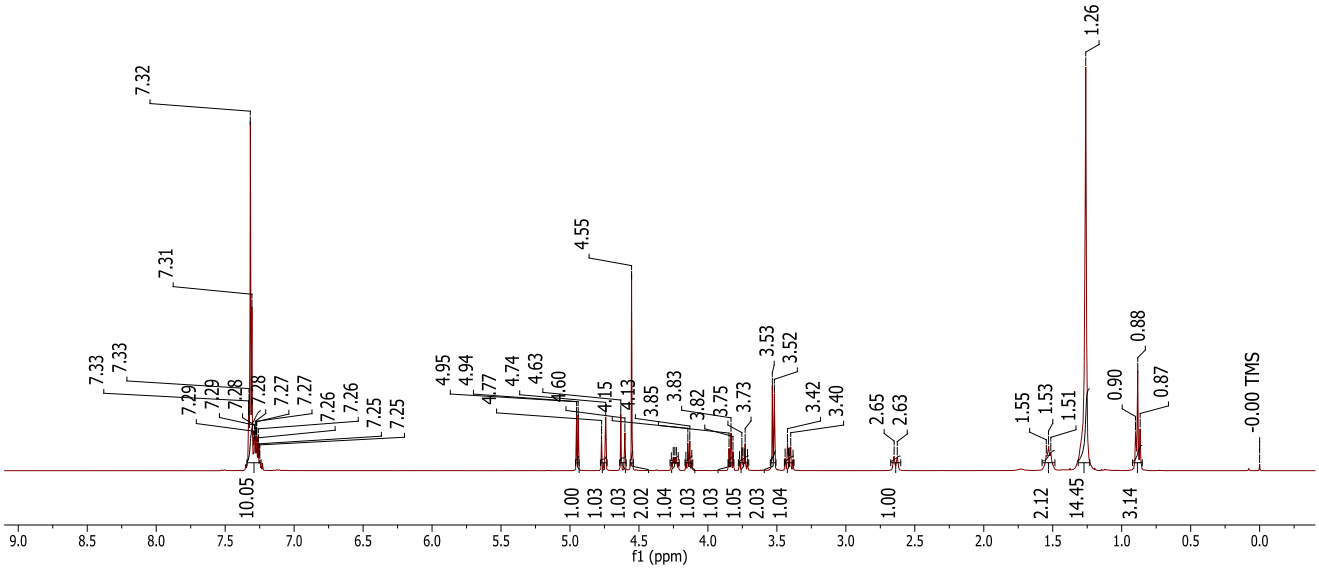
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **7**



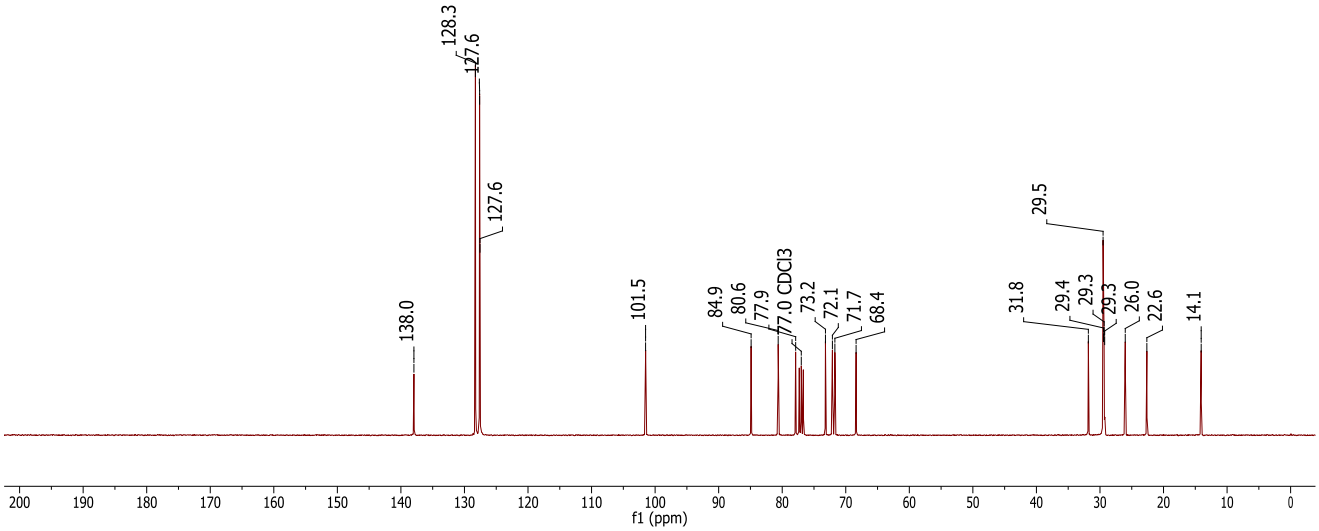
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **7**



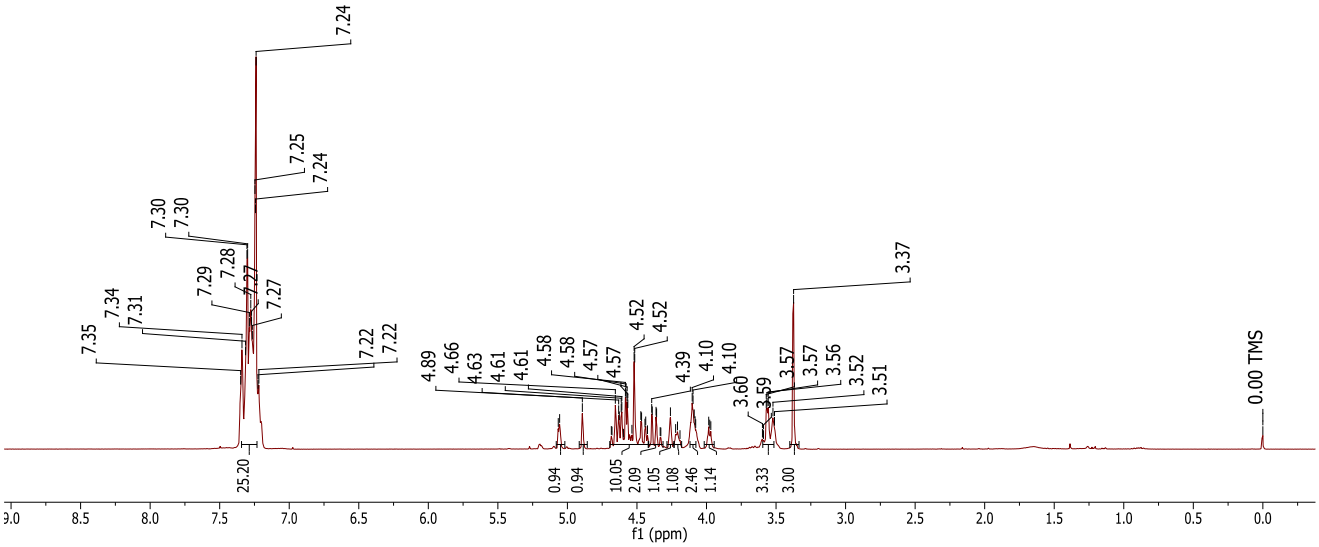
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **8**



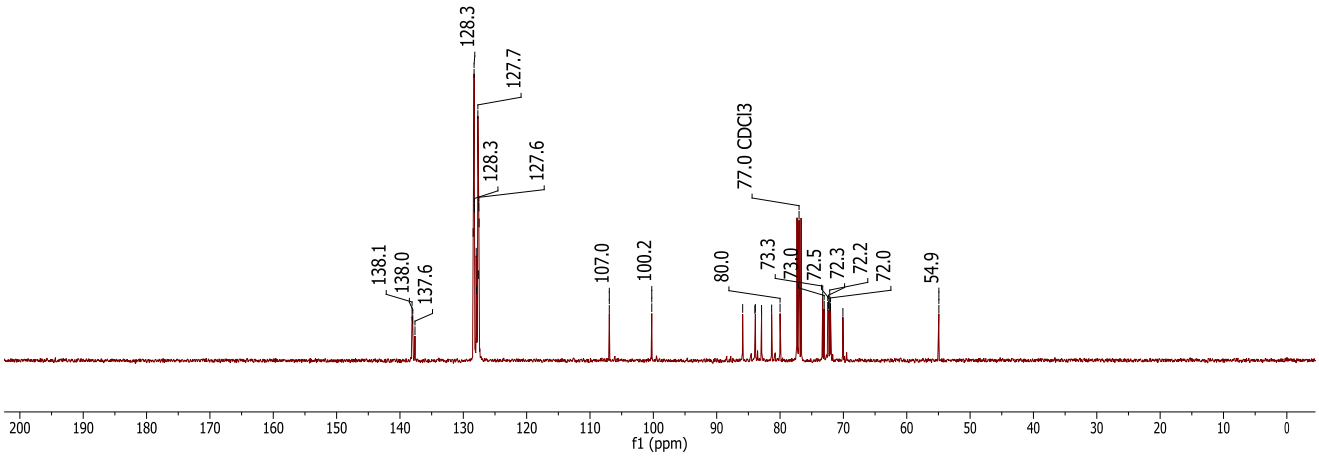
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **8**



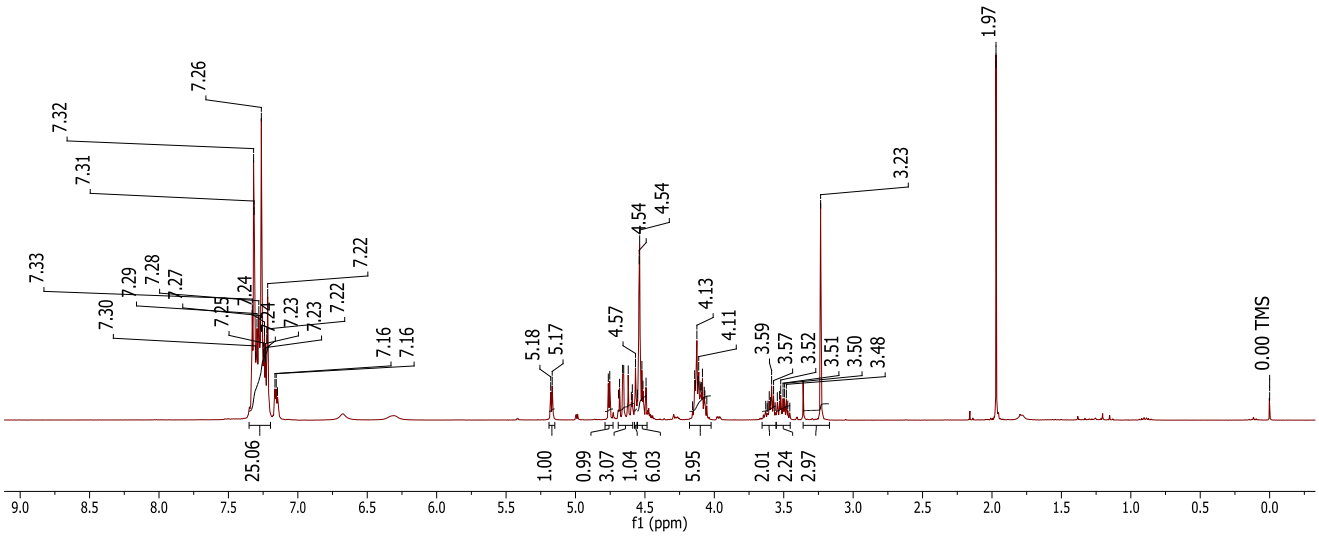
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **14**



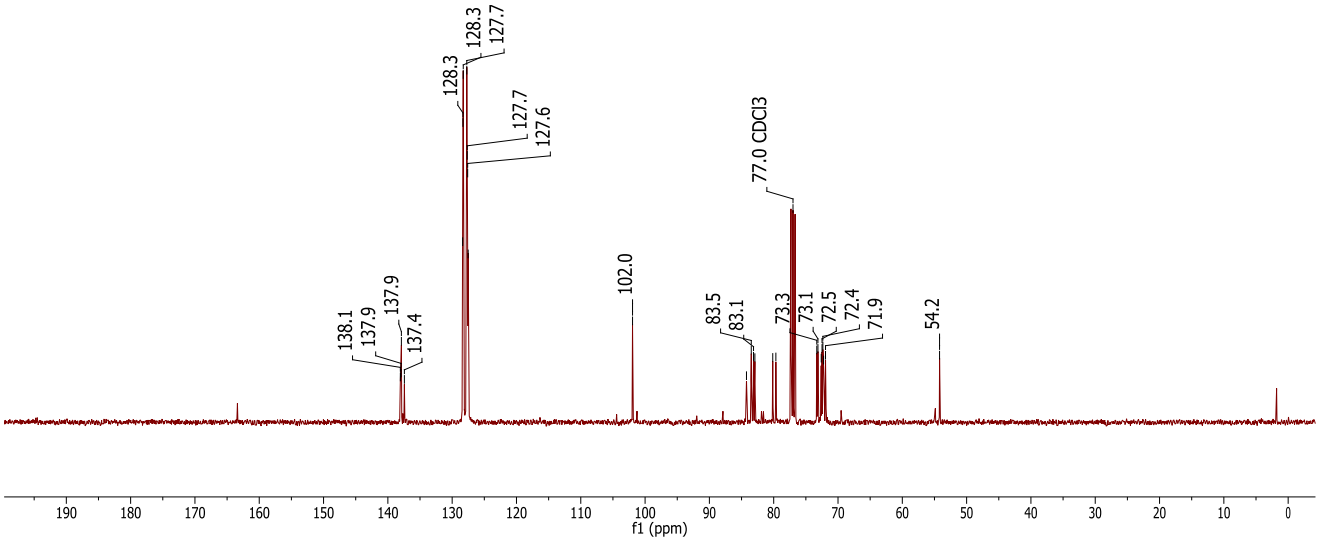
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **14**



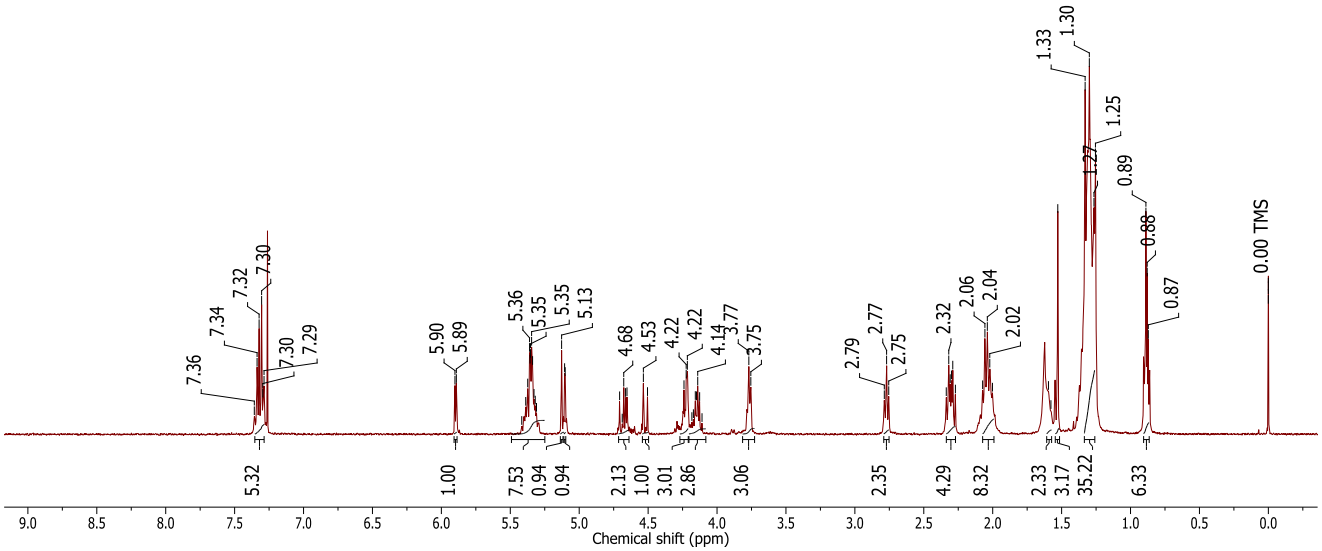
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **15**



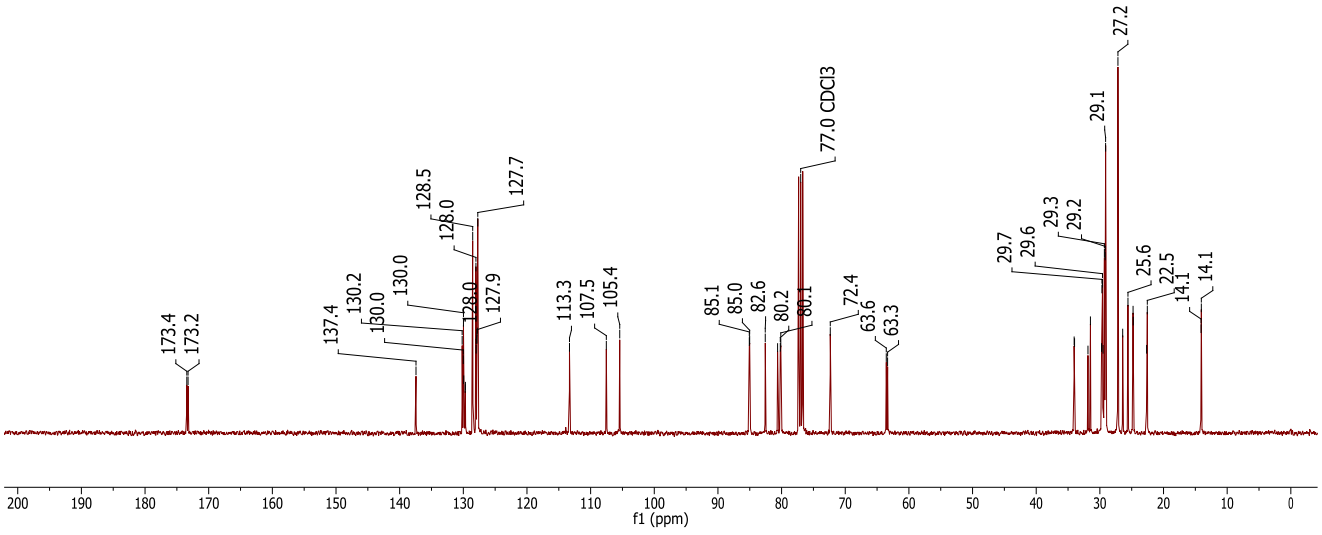
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **15**



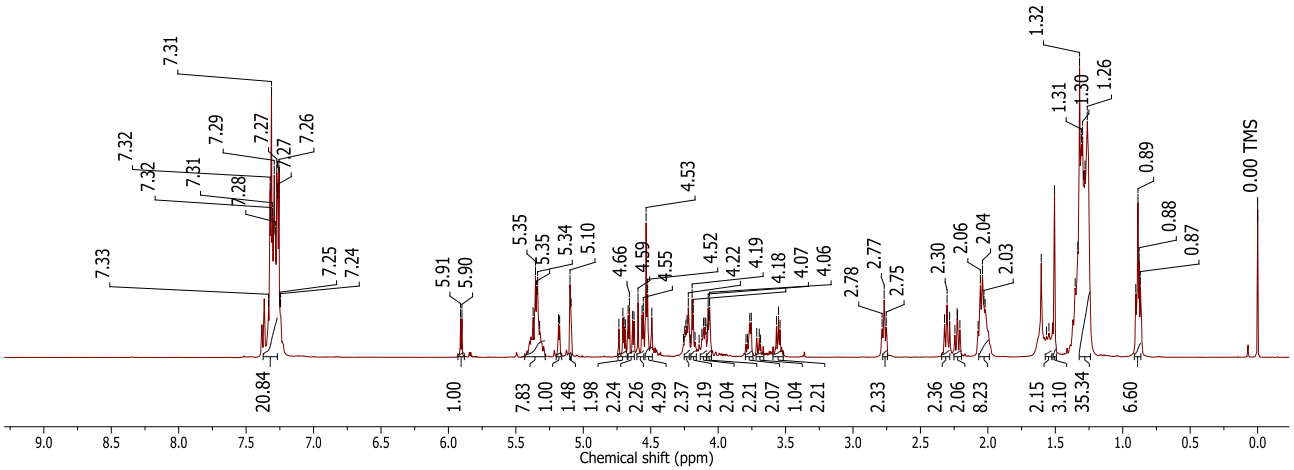
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **25**



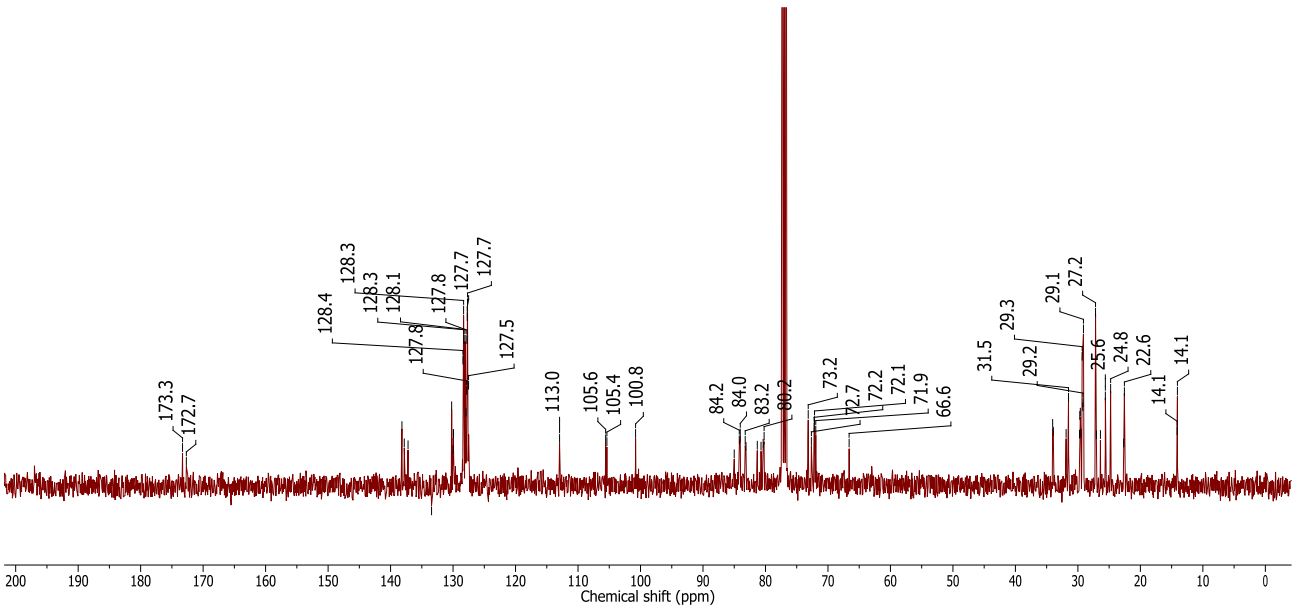
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **25**



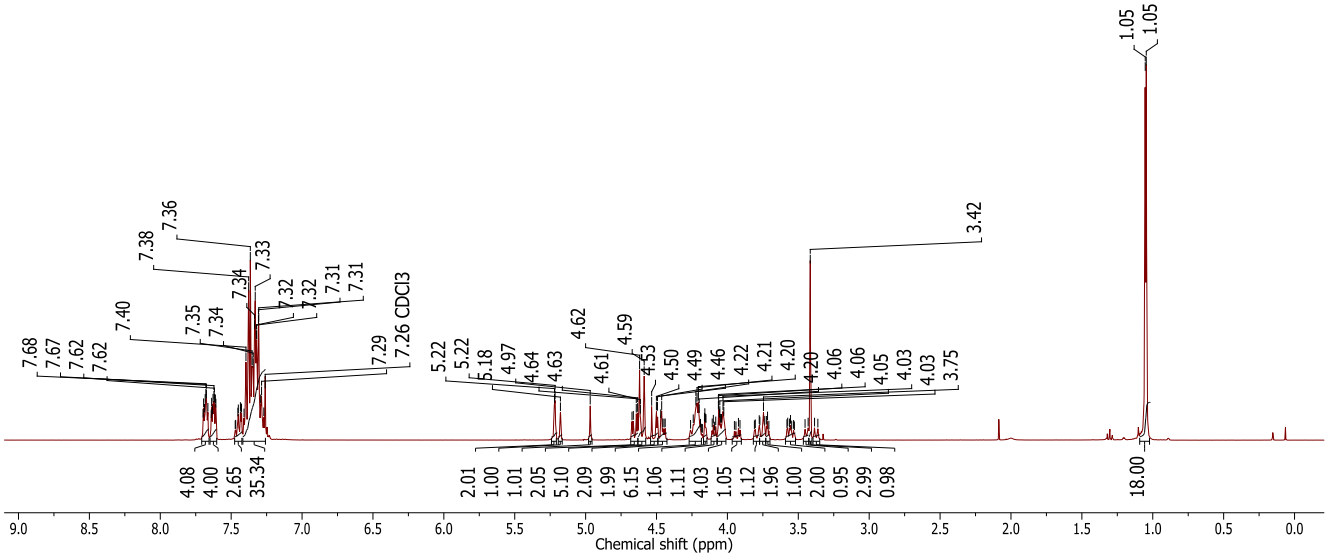
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **28**



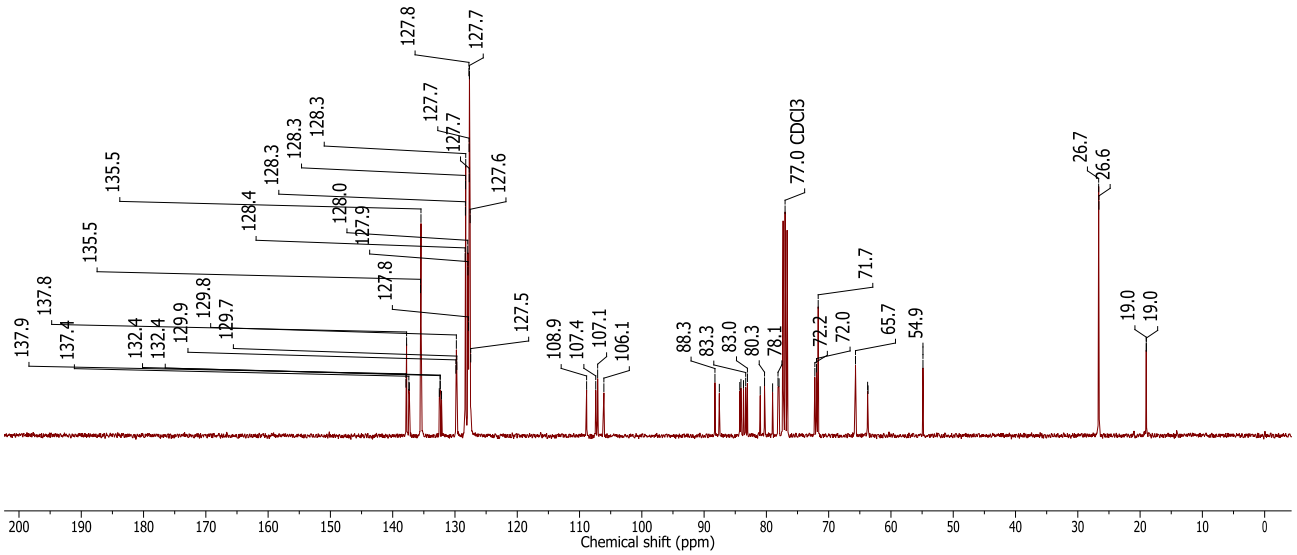
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **28**



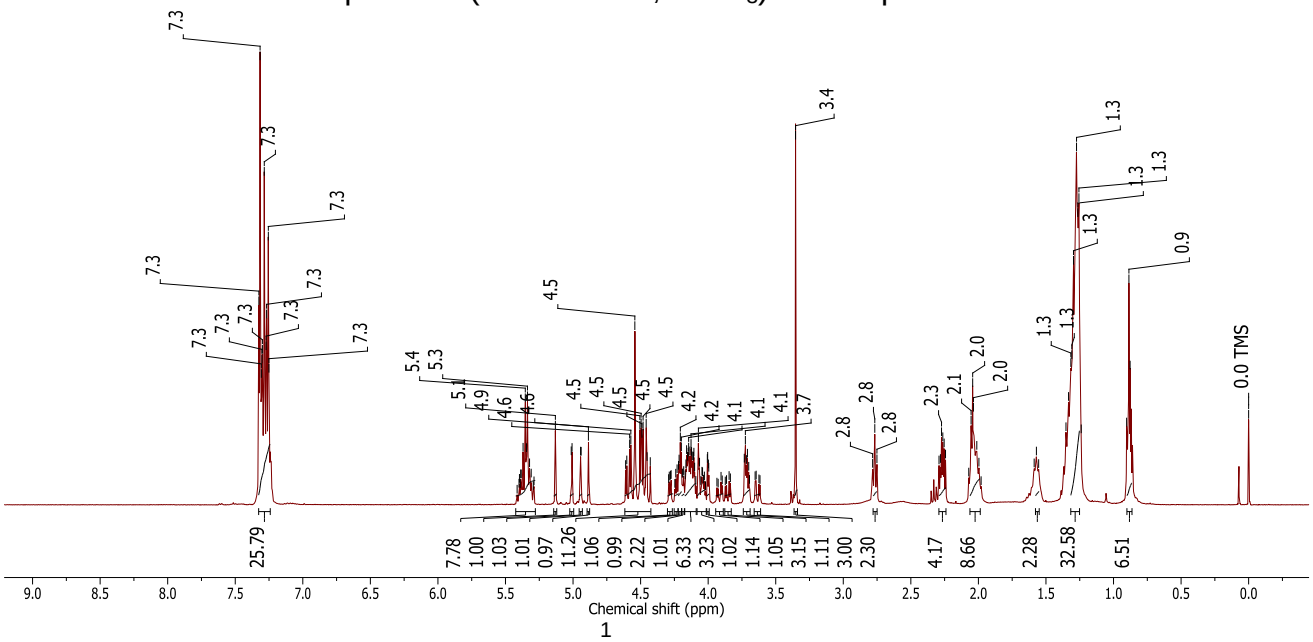
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **30**



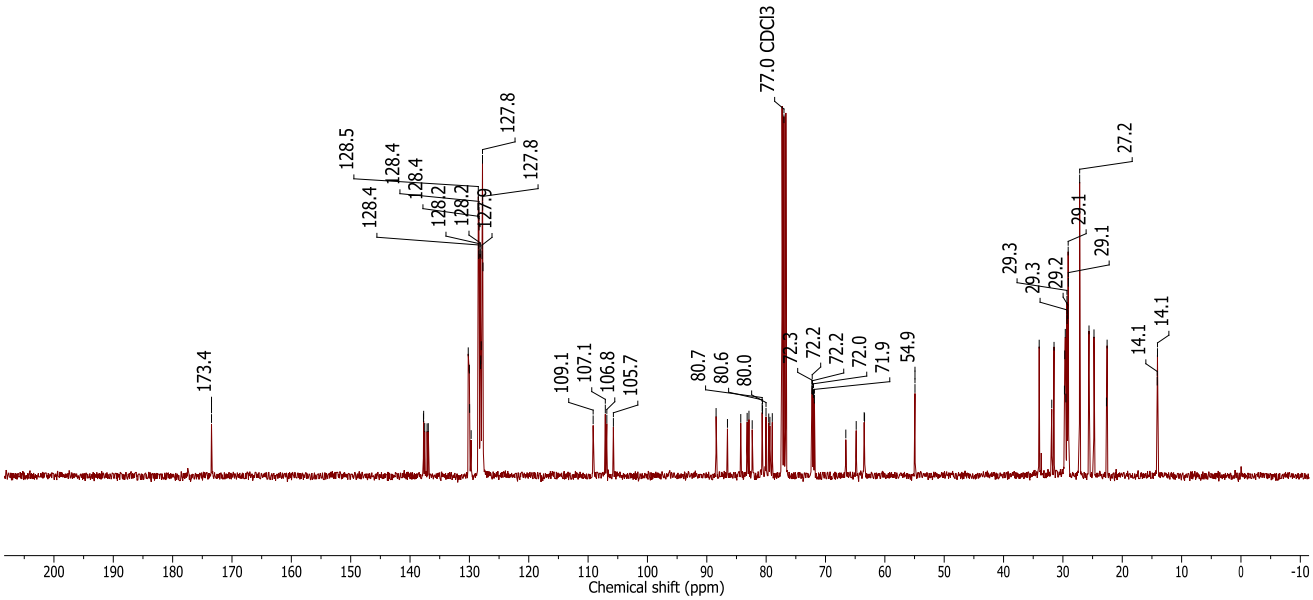
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **30**



^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **32**



^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **32**



3.7 References

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Chapter: 4

Synthesis of Lipoarabinomannan (LAM) and Major Oligosaccharide Epitopes

4.1. Introduction

In 1882, Robert Koch unrevealed the tubercle bacillus, *M. tuberculosis* (Mtb), as the causative agent of tuberculosis (TB) in humans and since then, even today, more than hundred years latter also TB is still a great health problem worldwide. Among the five types of species in Mtb complex, *M. tuberculosis*, *M africanum*, *M. bovis*, *M. bovis BCG* and *M. microti*, first three are the cause of human TB. These three members of Mtb complex are slow growers, with a doubling time of 12-20h at 34-80 ^{o}C and 2-6 weeks is necessary to appear as visible colonies of Mtb on Lowenstein-Jensen (L-J) or 7H10/7H11 Middlebrooks agar.[1,2] The lipid-rich cell wall of Mtb is unique in *Actinomycetes*, including the genera, *Mycobacterium*, *Rhodococcus*, *Corynebacterium*, and *Nocardia*. In addition to mycolyl-arabinogalactan-peptidoglycan, other cell wall components are phosphatidyl –myo-inositol residues (PIMs), lipoglycan, lipomannan (LM), lipoarabinomannan (LAM). [3,4]

4.2 Structure of lipomannan (LM) and lipoarabinomannan (LAM)

In 1930, Masucci *et al.* identified a polysaccharide having building units D-arabinofuranoside (Ara*f*) and Man*p* from *Mycobacterium bovis* and *Mycobacterium bovis* BCG, with the help of electrophoresis has isolated.[5-7] Later, after careful analysis, one of the polysaccharides was classified as arabinogalactan (AG) and other as a pool of immunologically active lipoarabinomannan (LAM) and inactive lipomannan (LM). In both LAM and LM, similar mannan backbone was noticed and it has been observed that mannan backbone was initiated from a C6-O position of inositol of PIMs. The mannan backbone consists of 21-34 linearly linked α-Man*p*(1→6)Man*p* linkages which are further branched by 5-10 mannose units with α-Man*p*(1→2)Man*p* linkages at C2-position in all mycobacterial species except in *M. chelonae*, where branching starts at the C3-position.[8-11]The nonreducing end of the mannan is again extended by arabinan domain comprising of 55-70 Ara*f* units with a linear chain of α-Ara*f*(1→5)Ara*f* linkages which are very similar to those of AG, encompassing two characteristic arabinan motifs (i) hexa arabinoside motif, [β-D-Ara*f*(1→2)-α-D-Ara*f*]$_2$-3,5-α-D-Ara*f*(1→5)-α-D-Ara*f* and (ii) linear tetraarabinofuranoside, β-D-Ara*f*(1→2)-α-D-Ara*f*(1→5)-α-D-Ara*f*(1→5)-α-D-Ara*f*. Hence, the nonreducing end of both hexa- and tetra- arabinans are recognized by Ara*f*-β(1→2)-Ara*f*- distinctive disaccharide units.[13-15]

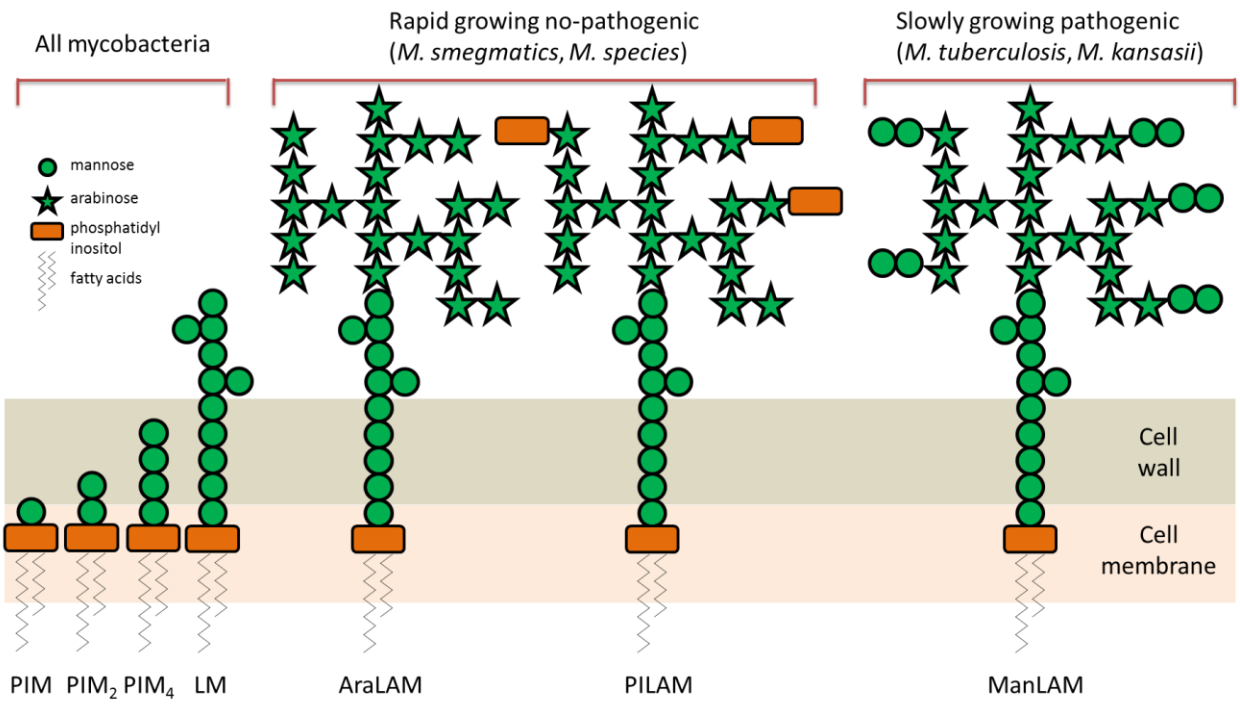


Figure 4.1 Structure of Mycobacterial LM and LAM

Depending upon the mycobacterial species, non-reducing end of β(1→2) linked Ara*f* units in LAM are further capped by different capping motifs; so far, three different capping patterns have been analyzed in mycobacteria i.e. (i) mannose capped LAM (ManLAM), in slow growing and most pathogenic bacteria such as *M. tuberculosis*, *M. bovis*, *M. bovis* BCG, *M. leprae*, *M. avium*, *M. xenopi*, *M. marinum* and *M. kansasii*, (ii) phosphoinositol capped LAM (PI LAM), identified in rapidly growing and non-pathogenic bacteria (*M. smegmatis*, *M fortuitum*) and (iii) uncapped LAM (Ara-LAM), noticed recently in *M. chelonae*. Although, the Man capping in mycobacteria occurs predominately as dimannoside of α (1→2) Man*p*, but single and tri-mannosides can also exist. Apart from caps, ManLAM is further modified with succinyl residues at the C2 of 3,5-di-α-D-Ara*f* units in M. bovis BCG.[14,16-17]

4.3 Biosynthesis of LM and LAM

Investigation of mutant source coupled with experimental evidence disclosed that linear α(1→6) Man*p* backbone was constructed by two enzymes i.e. MptA (*Rv 2174*) and MptB (*Rv 149c*). Also, from recent studies in C. glutamicium suggested that priming of Ac_1/Ac_2-PIM_4 was started by MptB and is responsible for the installation of 12-15 proximal Man*p* residues whereas distal

Man*p* residues are build up by MptA. Further, branching in theα (1→6) mannan core is introduced by MptC (*Rv* 2181) with the addition of α (1→2)Man*p* units to the linear mannan backbone.[18-21]

Open Reading Frame	Function	Role	References No
MptB (*Rv 1459c*)	α (1→6)-Mannopyranosyltransferase	Synthesis of proximal mannan backbone i.e. Ac_1/Ac_2-PIM_{12-17}	22a
MptA (*Rv 2174*)	α (1→6)-Mannopyranosyltransferase	Synthesis of distal mannan backbone i.e. Ac_1/Ac_2-PIM_{22-25}	21
MptC (*Rv 2181*)	α (1→2)-Mannopyranosyltransferase	Adds α(1→2) Man*p* residue on the mannan backbone and also helps to attach the second mannose capp on ManLAM	28
EmbC (*Rv 3793*)	α (1→5)-Arabinofuranosyltransferase	Catalyzes the α(1→5) arabinan motif	22b
AftC (*Rv 2673*)	α (1→3)-Arabinofuranosyltransferase	Involve to add arabinan residues on α(1→5) backbone	23b
AftD (*Rv0236c*)	α (1→5) or α (1→5) Arabinofuranosyltransferase	Involve either for α (1→3) Ara*f* unit addition to the terminal end of α (1→5)arabinan or for the preparation of α(1→5)Ara*f* itself	24a
AftB (*Rv 3805c*)	β (1→2)-Arabinofuranosyltransferase	Associate for the synthesis of β (1→2) Ara*f* at the non-reducing end of hexa- and tetra- arabinan	24b
CapA (*Rv 1635c*)	α (1→5)-Arabinofuranosyltransferase	Adds first mannose cap on non-reducingend of β (1→2) Ara*f*	26a

Table 4.1 for enzymes responsible for biosynthesis of LM and LAM

Initiation of lipoarabinomannan synthesis starts by the extension of core mannan backbone with arabinan domain having 50-70 Ara*f* units. The addition of Ara*f* units to the mannanbackbone is mediated by a class of arabinofuranosyltransferase (Ara*f*T), in which role of EmbC (*Rv 3793*), AftC (*Rv 2673*) and AftD (*Rv 0236c*) was well established.[22-23] Although, priming of mannosecore acceptor in LM with Ara*f* residues to obtain the arabinan core is admitted by an unidentified arabinofuranosyltransferase, sequential installation of 12-16 α(1→5) Ara*f* units is exclusively catalyzed by EmbC. In both AG and LAM, the branching α(1→3) arabinan is attached with the help of AftC and these branched furanosides are further extended by an unidentified α(1→5) arabinofuranosyltransferase. Recently other branching enzymes with α(1→3) Ara*f*T activity have been hypothesized by Skovierova *et.al.*. Again, from the control *in vitro*assay, it was investigated that AftD also will be able to add α(1→3) Ara*f* residues to linear α(1→5) acceptor to afford branching arabinan core. Hence, AftD defines itself as a second branching enzyme. In addition, the branched Ara*f* motif again elongated with characteristic tetra- and hexa- Ara*f* residue in LAM. At last, for arabinan core biosynthesis, the final terminal β(1→2) Araf motif is introduced by AtfB (*Rv 3805c*) in both LAM and AG.[24-26]

In continuation, a careful comparison of the *M. tuberculosis* genome with *M. smegmatis* disclosed that synthesis of mannose caps is initiated in a two-step reaction catalyzed by two distinct manopyranosyltransferases i.e.CapA (*Rv 1635c*) and MptC (*Rv 2181*). At the first step, CapA perceives the non-reducing end of arabinan motif and introduces the first Man*p* unit and in the second step, elongation of the cap with second α(1→2) Man*p* is catalyzed by MptC.[26]

4.4 Importance and biological function of Man-LAM

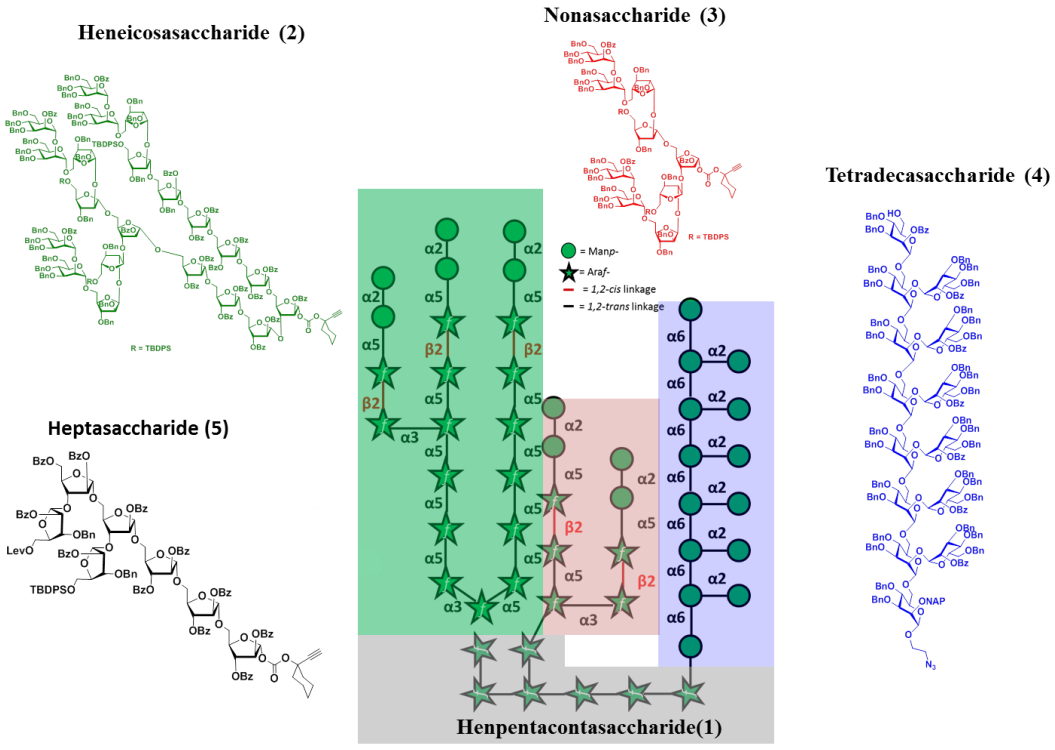
It has been well documented that ManLAM is an important immune-modulating motif affecting the immunological network of the host and hence contributing to the pathogenecity of the mycobacterial infection. It has been observed that LAM isolated from M. tuberculosis and M. leprae exert wide range of effects on the host immune system and also has been shown to attenuate T-cell proliferation.[13,27-29] Further, ESR spectroscopy and spin trapping measurement studies revealed that LAM acts as a free radical scavenger to inhibit protein kinase activity and inhibit synthesis of mRNA encoding interleukin2 (IL2) in human T-cells.[30] Apart from this, ManLAM showed to inhibit production of TNF-α and IL-12 by human dendritic cells and

macrophages *in vitro*to modulate M. tuberculosis mediated macrophage apoptosis. Hence, ManLAM indirectly showed to promote the survival of the bacteria in host macrophages.[31-32]

Therefore, the ideal way to encounter TB infection is the use of the effective preventive vaccine. To combat TB infection, since 1923 the BCG vaccine has been employed throughout the world. As BCG vaccine protects against childhood TB and its effect erode with age, causing insufficient protection against adult pulmonary TB. Hence, compared to BCG, the development of new more effective TB vaccines is one of the top priorities in TB research. The main goal of this dissertation, therefore, was to synthesize the large naturally occurring oligosaccharide motif of ManLAM to augment the development of new vaccines and/or diagnostic tools.

4.5 Present work

Mycobacterium tuberculosis consists of a unique and complex cell wall having two structural components known as arabinogalactan (AG) and lipoarabinomannan (LAM). Between them, LAM is structurally more diverse but found to have a distinctive structure having a phospholipid, a lipidated mannose and an arabinomannan motif linked to the myo-inositol.[4] The mannose backbone attached to the non-reducing end of phosphatidyl inositol motif comprises of α(1→6) and α(1→2) Man*p* residues. In turn, arabinan core composes of α(1→5) Ara*f* linked backbone which is further attached to two types arabinan domains i.e. (i) α(1→5) and β(1→2) linked tetra-Ara*f* and (ii) α(1→5), α(1→3) and β(1→2) hexa Ara*f* motif. In addition, non-reducing end of C5-O of β-linked Ara*f* is terminated by mannopyranosyl cap. It has been well documented that non-reducing end of ManLAM is responsible for mycobacterial infection and various immunomodulatory activities and when this motif is replaced by others oligosaccharide, attenuates its immunogenic activity.[33] Further, exploiting the antigenic property of Man-LAM, very recently a rapid point of care diagnostic kit and carbohydrate based vaccine was developed.[31]

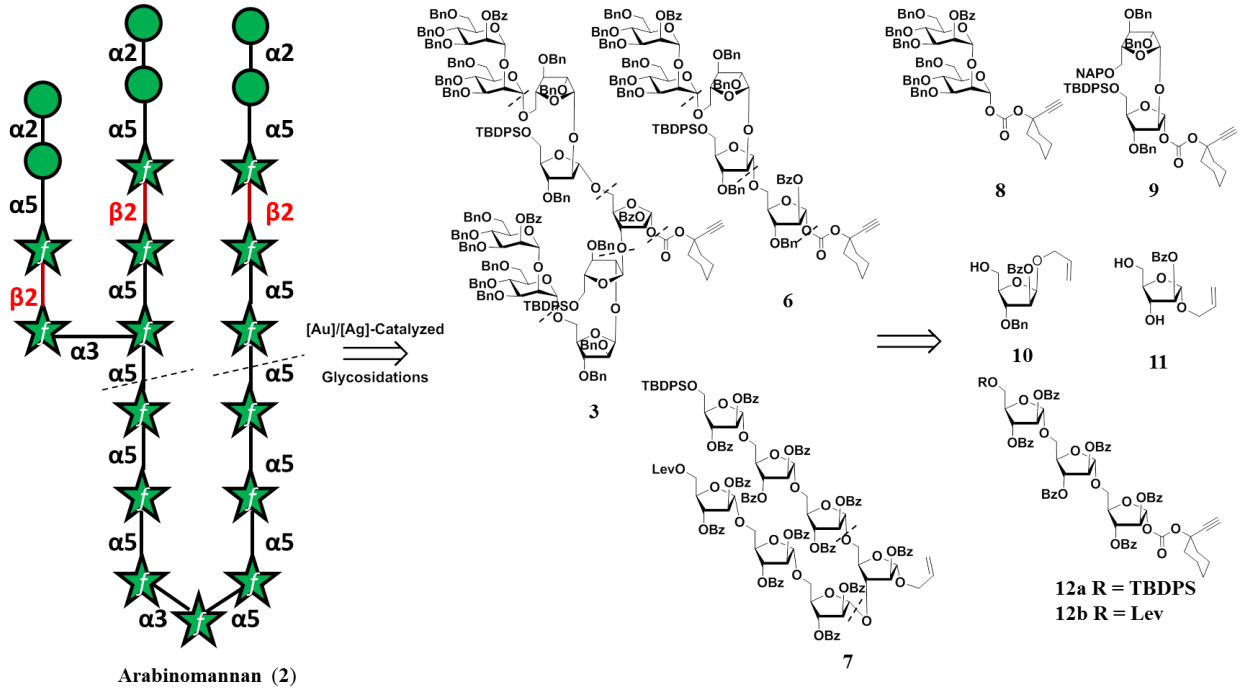


Scheme 4.1 Retrosynthetic analysis of henpentacotasaccharide Man-LAM (1)

The realization of the importance and bioactivity of ManLAM structure stimulated numerous research groups towards the synthesis of variety of LAM fragments, such as arabinomannan, phosphatidylinositol mannosides (PIMs) and lipomannan (LM).[34-37] In most of the studies, they have concentrated only on arabinan motif without mannose residues at the non-reducing end. While our studies are in progress, Guo and coworkers synthesized carrier protein conjugated ManLAM to check their immunological activity.[38] However, far too little attention has been paid to synthesize large oligomeric structures of naturally occurring ManLAM. In this premise, we have targeted henpentacontasaccharyl (containing 51 residues) ManLAM (**1**). It consists of arabinomannan motif having α(1→5), α(1→3) and β(1→2) linked Ara*f*units, C5-O of β-Ara*f* are capped by α(1→2) mannose disaccharide and mannan backbone composing of α(1→6) and α(1→2) Man*p* units. Further, reducing end of mannan domain is stitched with amino group spacer to facilitate conjugation with a carrier protein to evaluate different biological and immunological events.

4.5.1 Retrosynthetic disconnection of henpentacotasaccharide Man-LAM (1)

From the perspective of the types of linkages and branching in the ManLAM (**1**) showcases enough complexity and challenges for its synthesis. For the synthesis of ManLAM (**1**) major obstacles are (i) presence of challenging 1,2-*cis* (β-) arabinofuranosides, (ii) the unsymmetrical nature of the linkages, (iii) synthesis of highly sterically hindered tetradecasaccharide (**4**) mannan backbone and (iv) stereoselective installation of α(1→2) Man*p* residues at C5-O terminal. Considering all these challenges, a careful retrosynthetic analysis was planned which suggested that ManLAM (**1**) can be envisioned from four fragments i.e. heneicosasaccharyl (21-mer) arabinomannan (**2**), nonasaccharyl (9-mer) arabinomannan (**3**), tetradecasaccharyl (14-mer) mannan (**4**) and heptasaccharyl (7-mer) arabinan (**5**). Arabinomannan(**2**) consists of both 1,2-*cis* (β) and 1,2-*trans*(α)interglycosidic linkages. 1,2-*trans* linkages can be easily achieved by exploiting neighboring group participation from the C2-acyl protecting group of the donor. However, synthesis of 1,2-*cis* linkages is more challenging. Therefore, further retrosynthetic analysis of **2** was performed keeping view of previously explored Reciprocal-Donor-Acceptor-Selectivity (RDAS) to get 1,2-*cis* Ara*f*s and salient features of recently developed glycosyl carbonate donor chemistry in the presence of Au(I) and AgOTf catalysts.



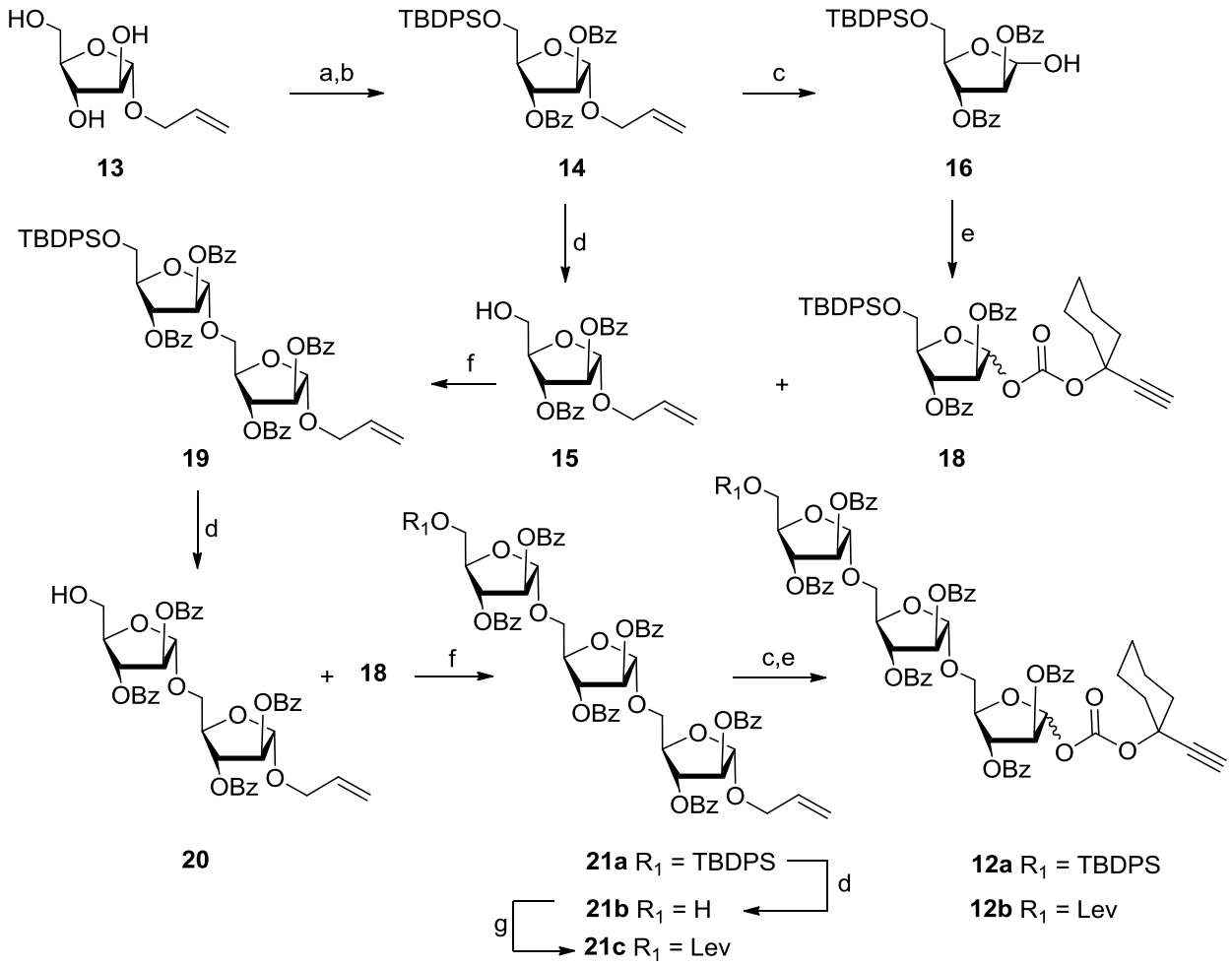
Scheme 4.2 Retrosynthetic analysis of heneicosasaccharyl (21-mer) arabinomannan

Our synthetic endeavor started with the preparation of 21-mer carbonate (**2**) *en route* to ManLAM (**1**). In an effort to achieve heneicosaccharide **2**, we have developed a highly convergent and Split-React-Coupled strategy where both glycosyl donor and glycosyl acceptor can be synthesized from the identical precursor. The precursor can be *split* into two portions and *reacted* individually with appropriate reagents to synthesize glycosyl donor and acceptor, *coupled* to get the desired glycoside. This will be a powerful strategy since it significantly reduces the number of steps required for the preparation of donor, acceptor and offers more convergence to the overall synthesis platform.

Retrosynthetic disconnection plan for oligosaccharide **2** is depicted in scheme 1.2, revealed that saccharide **2** can be prepared from two monosaccharides (**10**, **11**), two disaccharides (**8**, **9**) and two trisaccharides (**12a**, **12b**). Strategically allyl group was kept at the reducing end as it can be suitably converted to hemiacetal that can be extended to the corresponding glycosyl donor. Since saccharide **2** contained mannose disaccharide at the non-reducing end, NAP ether was identified as an orthogonal protecting group to TBDPS, Bz and Bn, which could be easily removed to install mannose disaccharide without affecting other protecting groups. In all the precursors, C2-O was protected as a benzoate ester to ensure 1,2-*trans* selective glycosylation.

4.5.2 Synthesis of trisaccharide carbonates (scheme 4.3)

Trisaccharide building blocks **12a** and **12b** were prepared from easily available allyl arabinoside**13**.[39] C5-*O* -TBDPS protection of **13** using TBDPSCl/Imidazole, followed by dibenzoylation by BzCl/Py/DMAP produced compound **14** which was divided into two fractions and one fraction



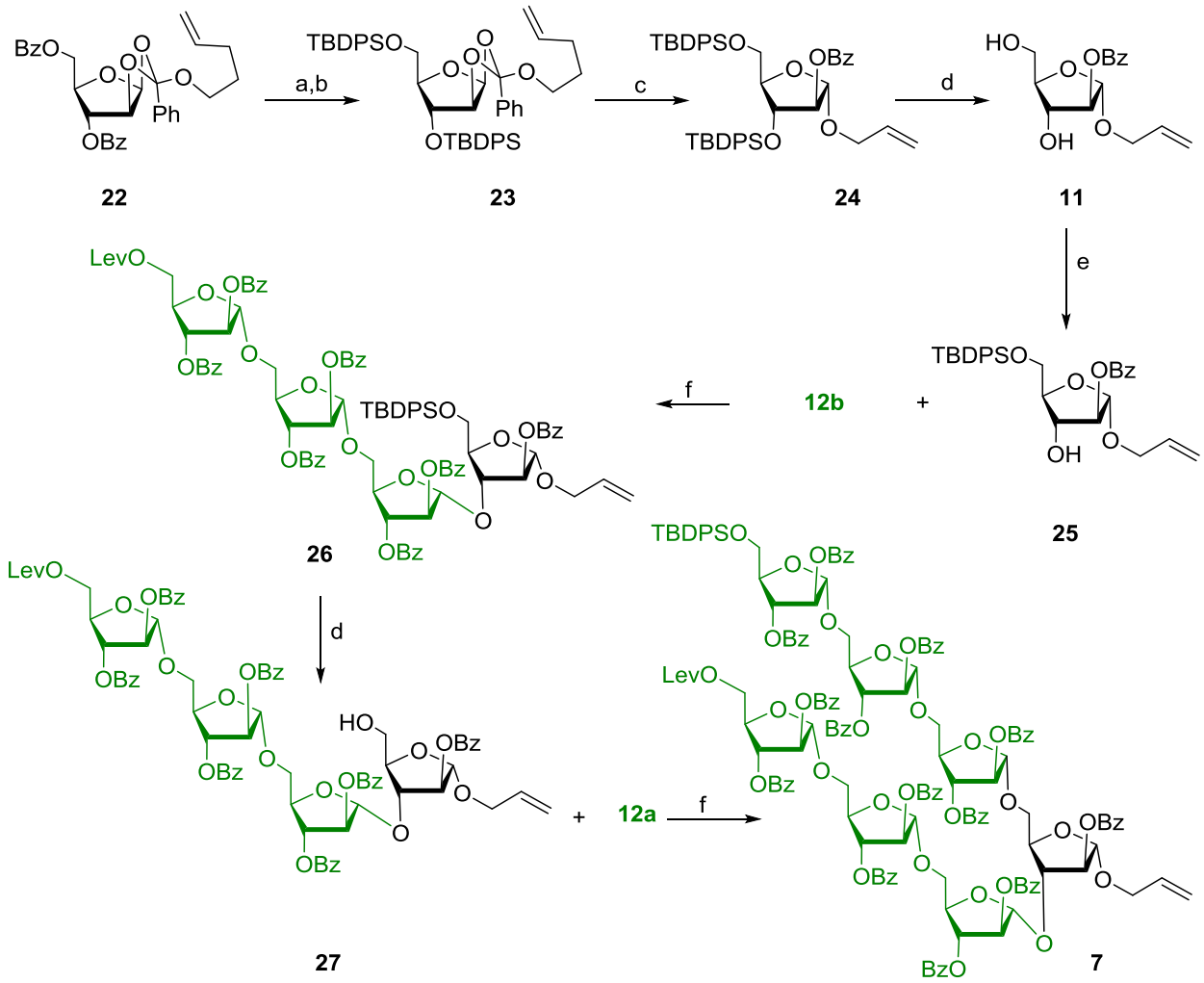
Scheme 4.3 Gold (I) for trisaccharide carabonates. Reagents: a) TBDPS-Cl, Im., DMF, 0 ^{0}C, 1 h, 82%; b) BzCl, pyridine, DMAP, 0-25 ^{0}C, 5 h, 93%; c) $PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 ^{0}C, 4 h, 85%; d) HF·py, pyridine, 0-25 ^{0}C, 5 h, 93% for 15, 91% for 20, 90% for 21b; e) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate (**17**), CH_2Cl_2, DMAP, 0-25 ^{0}C, 3 h, 85% for **18**, 83% for **12a** and 85% for **12b** over two steps respectively; (f) 8mol% chloro[tris(2,4-di-*tert*-

butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ^{0}C, 15 min, 95% for **19**, 92% for **21a**; g) Lev-acid, DIC, DMAP, CH_2Cl_2, 0-25 ^{0}C, 2 h, 95%.

was transformed to the corresponding Ara*f* acceptor (**15**) by reacting with HF·py in THF, while Ara*f* donor (**18**) was accessed from the second fragment by hydrolysis of the allyl group using $PdCl_2$ in CH_2Cl_2/MeOH to obtain hemiacetal **16**, followed by masking of hemiacetal **16** with easily available ethynylcyclohexyl (4-nitro phenyl) carbonate (**17**). The first furanosylation between acceptor **15** and donor **18** employing [Au]/[Ag] combo catalyst in CH_2Cl_2 effortlessly afforded disaccharide **19** in excellent yield. Consecutively, TBDPS group was removed by HF·Py/THF to generate the disaccharide acceptor **20** for further sugar chain elongation. In the ^{1}HNMR spectrum of compound **20**, two 1,2-*trans* Ara*f* anomeric protons appeared as a singlets at δ 5.30 and 5.40 ppm, olefin methine and methylene protons were noticed at δ 5.89 (m) and 5.20 (dq, *J* = 10.5, 1.4 Hz) ppm respectively and the rest of the signals from sugar appeared between δ 4.00-5.64 ppm. In the ^{13}CNMR spectrum, characteristic C1 and C1' carbons were found at δ 104.9 and 105.8 ppm and allylic methylene carbon generated a signal at δ 117.4 ppm. Further, the appearance of four carbonyl peaks at δ 165.2, 165.5, 165.8 and 166.1 ppm disclosed the presence of four benzoate groups. Next, trisaccharide **21a** was achieved by gold-catalyzed furanosylation between acceptor **20** and donor **18**. At this stage again compound **21a**, was *split* into two portions and one portion was converted into corresponding trisaccharide carbonate **12a** by hydrolysis of allyl group and subsequent protection with carbonate **17** with DMAP as a catalyst. On the other hand, trisaccharide **21c**, was obtained from the second portion of compound **21a** by two step sequence started with TBDPS cleavage by HF·pyfollowed by protection under Lev-acid in DIC/DMAP conditions. Later, trisaccharide carbonate **12b** was attained as α/β mixture in 85% yield from compound **21c** by standard aforementioned protecting group manipulations. The structural homogeneity of trisaccharide **21a** and **21c** was thoroughly confirmed by NMR and MS spectroscopy. In the ^{1}HNMR spectrum of trisaccharide **21a**, three distinctive 1,2-*trans* anomeric proton resonances appeared as singlets at δ 5.28, 5.40 and 5.49 ppm, whereas, in the ^{13}CNMR spectrum, 1,2-*trans* characteristic anomeric carbons were noticed at δ 104.9, 105.9 and 106.1 ppm. The ^{1}H and ^{13}C NMR of compound **21c** was almost equal to that of compound **21a** except that the resonances due to the TBDPS group were replaced by Lev group instead.

4.5.3 Synthesis of heptasaccharide (scheme 4.4)

Synthesis of heptasaccharide **7** was initiated with the preparation of diol **11**. Compound **11** was achieved in four steps *viz* saponification of **22** under Zemplén condition (NaOMe/MeOH) followed by di-*O*-TBDPS protection, PTSA mediated ring opening of 1,2-orthoester in the presence of allyl alcohol and at last cleave of both silyl ethers by HF·py/THF to afford diol **11** 58% yield over four steps.



Scheme 4.4 Synthesis of heptasccharide. Reagents: a) NaOMe, MeOH, 25 ^{0}C, 1 h, 95%; b) TBDPS-Cl (2.5 eq.), Im., DMF, 0-25 ^{0}C, 2 h, 85%; c) *p*TSA (0.2 eq.), excess All.OH, CH_2Cl_2, 4Å MS powder, 25 ^{0}C, 1 h, 80%; d) HF·py, pyridine, 0-25 ^{0}C, 6 h, 90% for **11**, 90% for **27**; e) TBDPS-Cl, Im., DMF, 0 ^{0}C, 1 h, 80%; f) 8mol% chloro[tris(2,4-di-*tert*-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ^{0}C, 20 min, 95% for **26** and 92% for **28**.

Regioselective mono C5-*O*-TBDPS protection of diol **11** by the addition of 1 equivalent of TBDPSCl afforded acceptor **25**; subsequent glycosylation under [Au]/[Ag]-catalysis conditions afforded tetrasaccharide **26** in 95% yield. In the ^{1}HNMR spectrum of tetrasaccharide **26**, four 1,2-*trans* anomeric protons were noticed as individual singlets at δ 5.25, 5.35, 5.42 and 5.44 ppm, the resonances at 5.18 (d, J = 10.4 Hz) and 5.95 (ddt, J = 16.7, 10.7, 5.4) correspond to olefinic methylene and methine protons were also identified. In the ^{13}CNMR spectrum, presence of four anomeric carbons at δ 105.0, 105.2, 106.0 and 106.0 ppm and further distinctive methylene carbon at 117.3 ppm confirmed the successful synthesis of the tetrasaccharide **26**. Removal of TBDPS group in tetrasaccharide **26** was performed using HF·py/THF to provide tetrasaccharide mono alcohol **27** which was again glycosylated with donor **12a** under optimized [Au]/[Ag]-conditions to give heptasaccharide **7** in 92% under 20 minutes. In addition to the ^{1}H and ^{13}C NMR spectroscopy (Table 4.2), the successful synthesis of this heptasaccharide **7** was confirmed by mass spectrometric analysis [calculated for $C_{150}H_{138}O_{44}NaSi$, $[M+Na]^{+}$: 2694.8261, found 2694.7383].

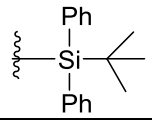
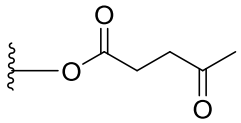
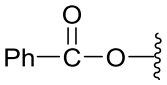
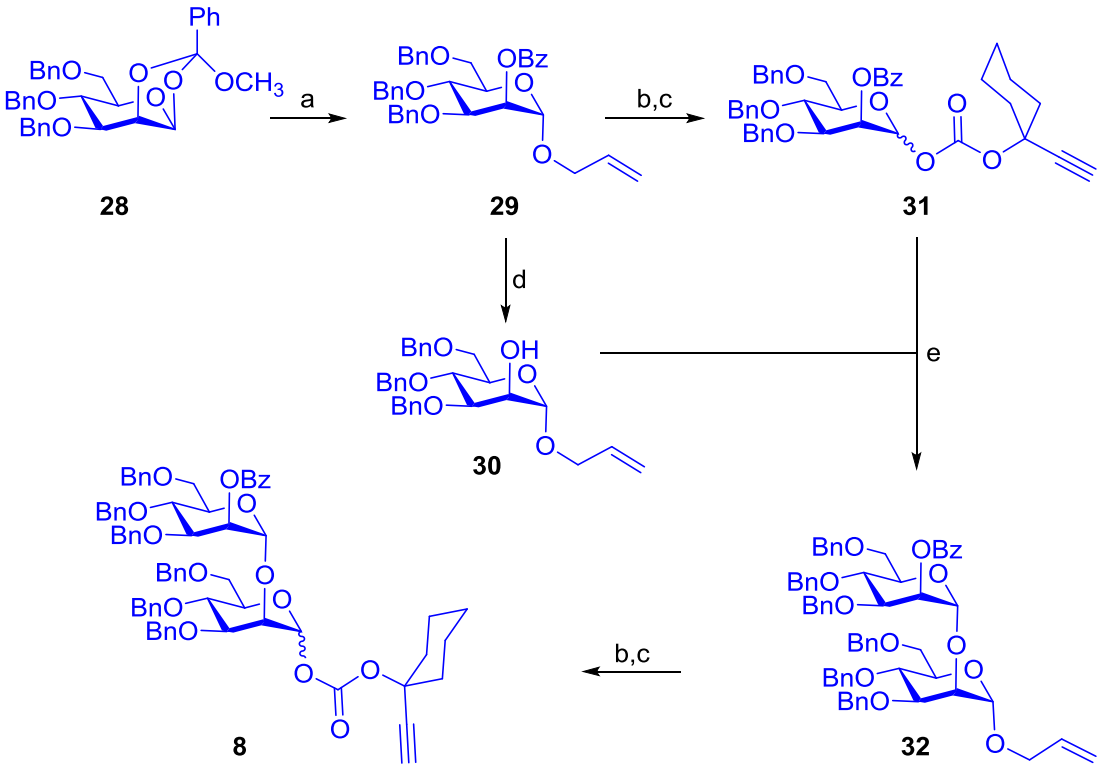
Entry	^{1}HNMR δ ppm	^{13}CNMR δ ppm
H-1/*C*-1	5.23 (s, 1H), 5.30 (s, 1H), 5.32 (s, 1H), 5.36 (s, 1H), 5.37 (s, 1H), 5.41 (s, 1H), 5.52 (s, 1H)	105.1, 105.4, 105.8, 105.9, 105.9, 106.0, 106.0
	1.01 (s, 9H), 7.36-7.98 (m, 10H)	19.4, 26.8 (3C), 127.6-135.7 (12C)
	2.10 (s, 3H), 2.57 (dd, J =6.3, 1.9 Hz, 2H), 2.65-2.70 (m, 2H)	27.9, 29.8, 38.0, 172.5, 206.3
	7.20-8.06 (m, 65H)	127.7-133.9 (78C), 165.1 (3C), 165.2 (2C), 165.2, 165.5, 165.6, 165.6 (4C), 165.7

Table 4.2 Characteristic ^{1}H NMR and ^{13}C NMR signals of heptasaccharide 7

4.5.4 Synthesis of mannose disaccharide carbonate (Scheme 4.5)

Allyl mannoside **29** was prepared from methyl mannose orthoester via *p*TSA mediated ring-opening of orthoester in presence of allyl alcohol. Later, *en route* to the mannose disaccharide

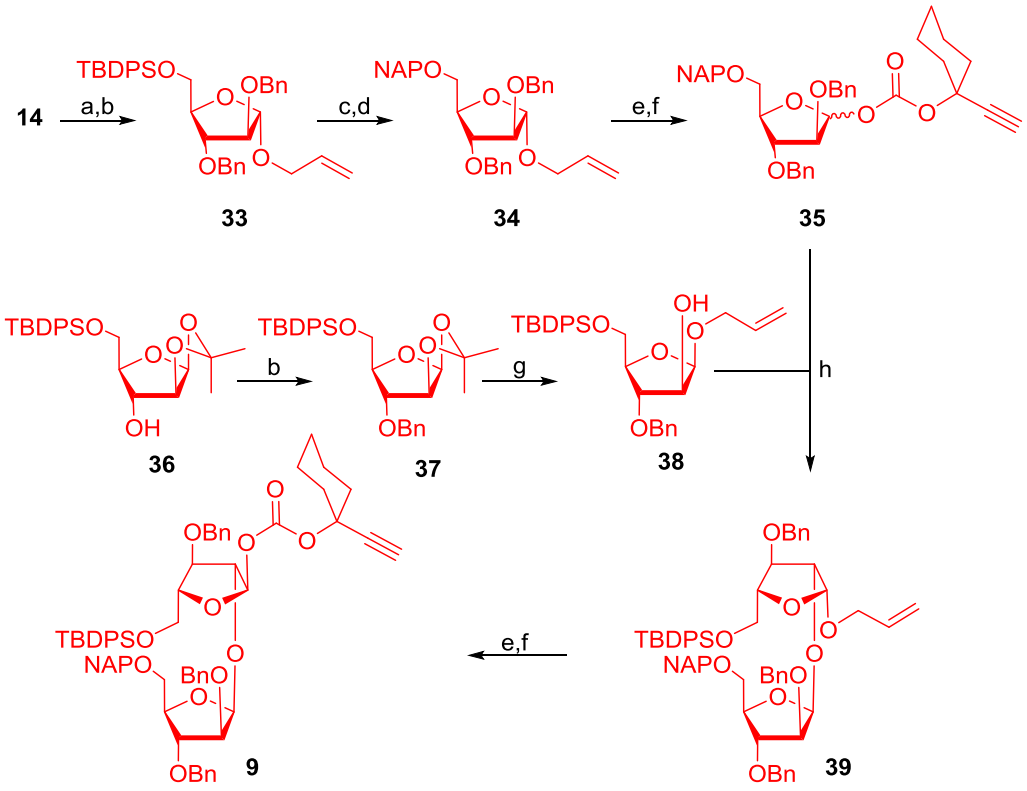
32, allyl mannoside **29** was *split* into two fractions and one fraction was converted to allyl mannose acceptor **30** by *reacting* with NaOMe/MeOH whereas the second portion was transformed to mannose carbonate donor **31** by two successive *reactions* i.e. hydrolysis of the allyl group to obtain hemiacetal followed by the protection of hemiacetal by reagent **17** in the presence of catalytic amount of DMAP. The gold/silver mediated glycosylation between donor **30** and acceptor **31** afforded 93% of mannose disaccharide **32**, which is converted to the corresponding glycosyl carbonate donor **8** by the aforementioned optimized conditions. Although, in the ^{1}HNMR of disaccharide **32**, the resonances due to anomeric protons overlapped with other resonances, we have realized the 1,2-*trans* selectivity by ^{13}CNMR spectrum where anomeric carbons were noticed at δ 98.0 and 99.7 ppm. In addition, 1,2-*trans* selectivity was further confirmed from $^{1}J_{C\text{-}H}$ coupling constants 173 and 175 Hz for those two anomeric carbons.



Scheme 4.5 Gold (I) for mannose disaccharide carbonate. Reagents: a) *p*TSA (0.2 eq.), Allyl.OH, CH_2Cl_2, 4Å MS powder, 25 ^{0}C, 1 h, 86%; b) $PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 ^{0}C, 4 h; c) **17**, CH_2Cl_2, DMAP, 0-25 ^{0}C, 3 h, 78% for **31**, 83% for **8** over two steps; d) NaOMe, MeOH, 25 ^{0}C, 1 h, 94%; e) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ^{0}C, 15 min, 93%.

4.5.5 Synthesis of 1,2-*cis* arabinose disaccharide carbonate (Scheme 4.6)

The synthesis of 1,2-*cis* arabinofuranosyl disaccharide started from compound **14** which was converted to compound **34** through well-known literature procedure,[39] including saponification of compound **14** by NaOMe/MeOH, benzylation utilizing NaH/BnBr, followed by replacement of TBDPS group by successive demployment of HF·py/THF and NAPBr/NaH. Glycosyl carbonate donor **35** was achieved from allyl glycoside **34** in two steps *viz*. first by the $PdCl_2$ mediated hydrolysis of allyl group and next, protection of resulting hemiacetal with reagent **17** and catalytic amount of DMAP. In parallel, compound **36** was converted to benzyl ether **37** by using NaH/BnBr/DMF.

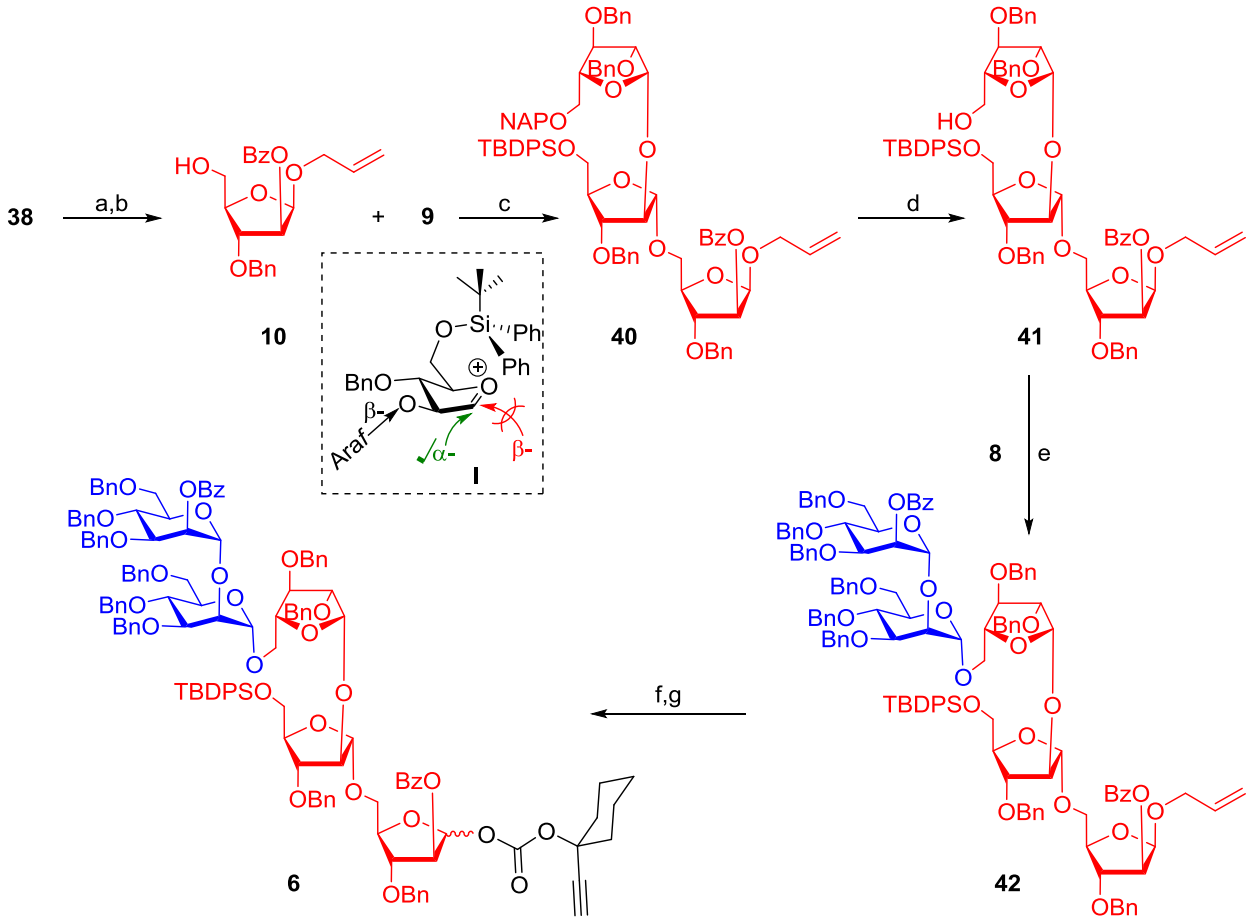


Scheme 4.6 Gold (I) for arabinose disaccharide carbonate. Reagents: a) NaOMe, MeOH, 25 ^{0}C, 1 h, 90%; b) NaH, BnBr, TBAI, DMF, 0-25 ^{0}C, 1 h, 91% for **33** and 93% for **37**; c) HF·py, pyridine, 0-25 ^{0}C, 5 h, 92%; d) NaH, NAPBr, TBAI, DMF, 0-25 ^{0}C, 2 h, 90%; e) $PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 ^{0}C, 4 h; f) **17**, DMAP, CH_2Cl_2, 0-25 ^{0}C, 3 h, 82% for **35**, 78% for **9** over two steps; g) PTSA (0.2 eq.), All.OH, CH_2Cl_2, 50 ^{0}C, 2 h, 45%; h) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, -78 ^{0}C, 5 h, 92%.

Isopropylidene opening of compound **37** in the presence of allyl alcohol under acidic conditions afforded α:β mixture of C2-OH allyl arabinofuranosides. Of these, we have isolated more sterically hindered and less reactive acceptor **38**, owing to our results from the RDAS studies delineated Chapter-3. To recapitulate, less reactive and more sterically crowded Ara*f* acceptors in glycosylation with armed Ara*f* donor, affords only 1,2-*cis* (β) Ara*f* disaccharide. Having synthesized glycosyl donor **35** and acceptor **38**, the furanosylation was carried out with [Au]/[Ag]-catalytic condtions at -78 ^{o}C to furnish 1,2-*cis* or β-disaccharide **39** only. The 1,2-*cis* configuration of **39** was verified by the ^{1}H and ^{13}CNMR spectroscopy. In the ^{1}HNMR spectrum of compound **39**, 1,2-*cis* anomeric protons were noticed at δ 5.2 (d, *J* = 3.9 Hz,2H) ppm while in ^{13}CNMR diagnostic 1,2-*cis* anomeric carbons were recognized at δ 98.7 and 99.0 ppm. In continuation, glycosyl carbonate donor **9** was obtained from disaccharide **39** by aforementioned optimized reaction conditions.

4.5.6 Synthesis of pentasaccharide-carbonate (Scheme 4.7)

Pentasaccharide **42** was assembled by the glycosylation of donor **8** and acceptor **41** under the promotion of gold(I) and AgOTf catalysis. In this direction, monosaccharide **10** was achieved by C2-*O* benzoylation of compound **38** using BzCl/DMAP/Py followed by TBDPS-deprotection utilizing HF·py/THF. At 25 ^{o}C, glycosylation between donor **9** and acceptor **10** showed α:β = 1:1 mixture of trisaccharides, however, upon lowering the temperature of the glycosylation to -78 ^{o}C surprisingly afforded α:β = 8:1 mixture, in favor of the required trisaccharide **40**. The enhanced α-diastereoselectivity can be rationalized by previously reported $^{3}E_{gg}$ conformation of the oxocarbenium ion (**I**) intermediate wherein sterically crowded TBDPS unit shielded the β-face; therefore, incoming acceptor can predominantly access the α-face to generate more α-selective trisaccharide **40**. After isolation of pure **40**, napthyl unit was removed by an oxidative method employing DDQ/CH_2Cl_2-MeOH to furnish trisaccharide acceptor **41** in 82% yield. Although, in the ^{1}HNMR spectrum of **40** anomeric protons overlapped with other sugar protons, the ^{13}C NMR showed, two 1,2-*cis* anomeric carbons at δ 99.6 and 100.2 ppm, while 1,2-*trans* anomeric carbon was noticed at δ 106.0 ppm. The ^{1}H and ^{13}C NMRs of compound **41** were very similar to **40** except the absence of resonances from NAP moiety.



Scheme 4.7 Synthesis of pentasaccharide-carbonate. Reagents: a) BzCl, pyridine, DMAP, 0-25 ^{0}C, 5 h, 93%; b) HF·py, pyridine, 0-25 ^{0}C, 5 h, 94%; c) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, -78 ^{0}C, 5 h, 81%; d) DDQ, CH_2Cl_2-MeOH (1:4), 25 ^{0}C, 4 h, 82%; e) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ^{0}C, 15 min, 76%; f) $PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 ^{0}C, 4 h; g) **17**, DMAP, CH_2Cl_2, 0-25 ^{0}C, 3 h, 75% over two steps.

Subsequently, glycosyl acceptor **41** was subjected to the glycosylation with donor **8** under [Au]/[Ag]-catalyzed conditions to afford 76% of the pentasaccharide **42** which is again transformed to required glycosyl donor **6** via Pd-catalyzed hydrolysis of allyl moiety to hemiacetal followed its conversion to ethynylcyclohexyl carbonate by treating with reagent **17** and DMAP. Pentasaccharide **42** was verified based on the NMR (Table 4.3) and MS

spectroscopic analysis. The observed *m*/*z* value for $C_{130}H_{136}O_{25}NaSi$, 2148.9023 was found to be in excellent agreement with the calculated value 2148.9071.

Entry	^{1}HNMR (δ ppm)	^{13}CNMR (δ ppm)
H-1/*C*-1	4.94 (d, *J* = 1.4 Hz, 1H), 4.94 (s. 1H), 5.15 (d, *J* = 1.4 Hz, 1H), 5.37 (d, *J* = 4.5 Hz, 1H), 5.76 (s, 1H)	98.6, 99.6, 99.7, 100.4, 105.8
TBDPS	1.03 (s, 9H), 7.35-7.98 (m, 10H)	19.4, 27.0 (3C), 127.4-135.8 (12C)
Benzoates	7.24-8.04 (m, 10H)	127.4-133.9 (12C), 165.4, 166.0

Table 4.3 characteristic ^{1}HNMR and ^{13}CNMR of 42

4.5.7 Synthesis of nonasacharide-carbonate (Scheme 4.8)

For the synthesis of nonasaccharide **45**, the most difficult task was the stereoselective introduction of 1,2-*cis* arabinofuranosides. Double glycosylation of diol acceptor **11** with two equivalents of donor **9** under [Au]/[Ag]-conditions at 25 ^{o}C gave inseparable mixture of all four possible isomers of pentasaccharides i.e. α/α, α/β, β/α and β/β; in contrast, glycosylation at -78 ^{o}C afforded separable mixture of two pentasaccharides only in α:β ratio of 8:1. Further, careful analysis of glycosylation disclosed that the mixture of isomers obtained from more reactive C5-OH acceptor only and not from the C3-OH acceptor. Hence, one can argue that glycosylation occurred at more reactive C5-OH at -78 ^{o}C first to attain the α:β = 8:1 trisaccharidesand then, C3-O becomes highly sterically crowded and it can only access the α-face of $^{3}E_{gg}$ oxocarbenium ion (**I**) to afford overall α:β = 8:1 pentasaccharides.

The desired pentasaccharide **43** was isolated by flash column chromatography and characterized thoroughly by NMR and MS spectroscopic studies. In the ^{1}HNMR of pentasaccharide **43**, three 1,2-*trans* anomeric protons resonances were observed as individual singlets at δ 5.19 and 5.32 (2H) ppm whereas anomeric protons corresponding to 1,2-*cis* linkages showed resonances at δ 5.16 (d, *J* = 4.4 Hz) and 5.31(d, *J* = 4.2 Hz) ppm. In the ^{13}CNMR spectrum of compound **43**, distinctive 1,2-*trans* anomeric carbons were noticed at δ 105.1, 105.6 and 106.9 ppm while the appearance of two resonances at δ 99.9 and 100.2 ppm confirmed the presence of two 1,2-*cis* linkages. Later on, two NAP units of **43** were cleaved off by the above mentioned oxidative method using DDQ/CH_2Cl_2-MeOH to afford 75% of pentasaccharide-diol **44** smoothly which was subsequently subjected to [Au]/[Ag]-assisted glycosylation with compound **8** to give 60% of

nonasaccharide **45**. The structural integrity of compound **45** was confirmed by the investigation of ^{13}C NMR spectroscopy (Table1 4.4) and MS spectroscopy. The *m*/*z* for nonasacharide **45** showed $[M+K]^+$at 3816.96 in MALDI (TOF) {calculated for $[M+K]^+$ 3816.59}. At last, the required nonasaccharide carbonate **3** was achieved from nonsaccharide **45** by two well optimized steps.

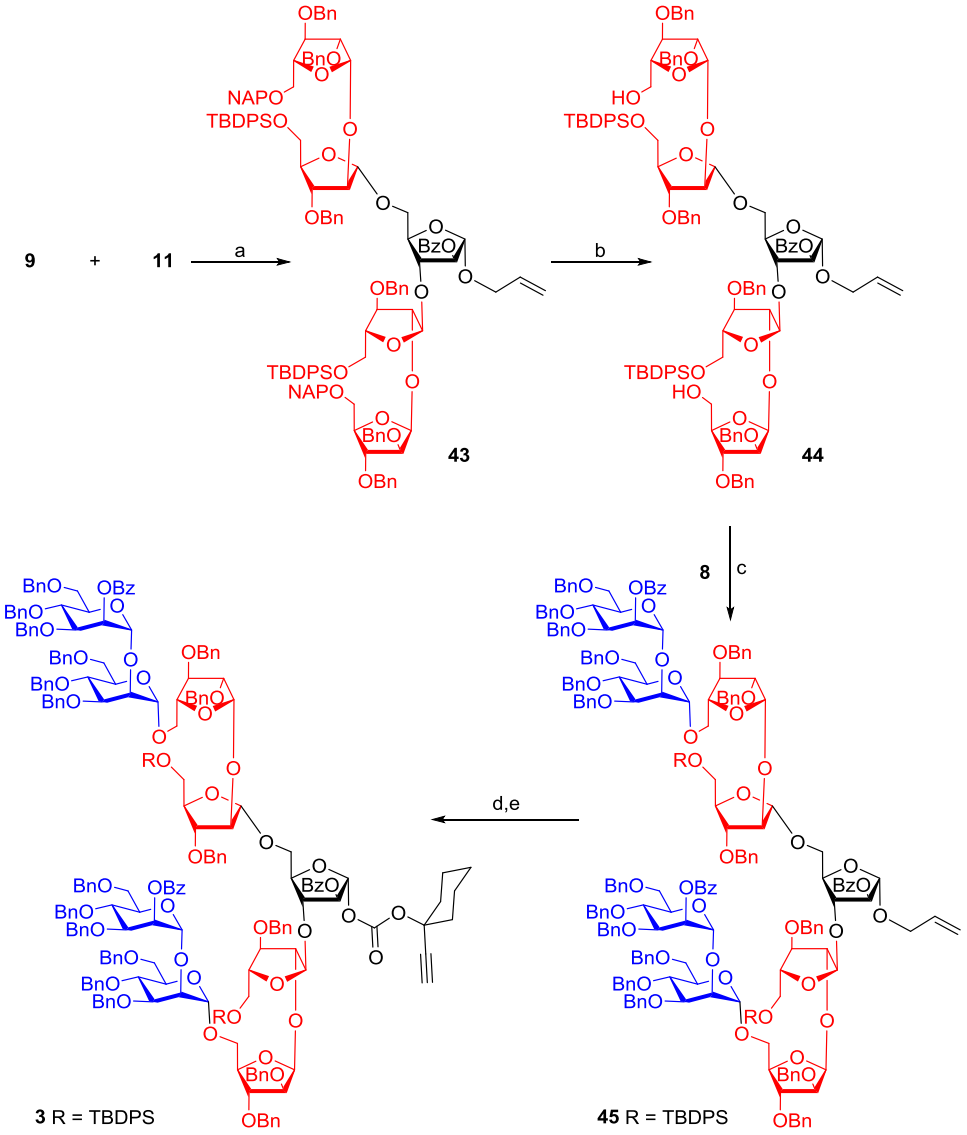
Entry	^{13}CNMR (δ ppm)
C-1	98.6, 98.8, 9 9.7, 99.8, 100.0, 100.5, 105.1, 105.5, 106.8,
TBDPS	19.3, 19.4, 26.9 (3C), 27.0 (3C), 127.4-135.8 (24C)
Benzoates	127.4-134.0 (18C), 165.4, 165.7, 166.0

Table 4.4 Characteristic ^{13}CNMR signals of Nonasaccharide 45

4.5.8 Synthesis of heneicosasaccharide-carbonate (Scheme 4.9)

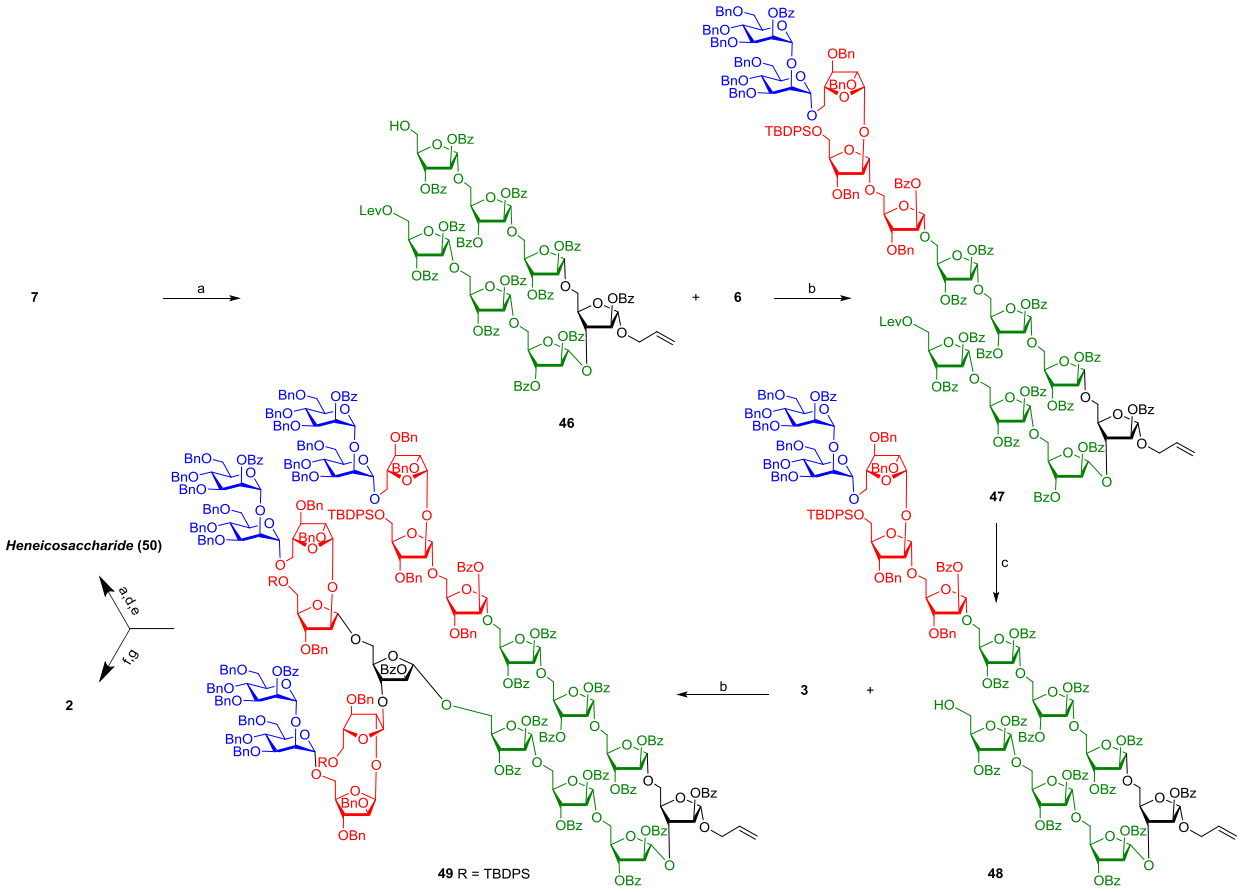
Having synthesized all major fragments, the construction of heneicosacharylarabinomannan **49** was initiated with the removal of TBDPS of compound **7** by HF·py to generate heptasaccharide-acceptor **46** which was subsequently glycosylated with donor **6** in presence of [Au]/[Ag]-activators to give dodechasaccharide **47** in 85% yield. In the ^{1}HNMR spectrum of **47**, owing to the overlap of most of the protons, structural purity was obtained from the ^{13}C NMR and MS spectral studies on dodecasaccharide **47**. In the ^{13}CNMR spectrum of compound **47**, characteristic nine 1,2-*trans* Ara*f* anomeric carbons appeared at δ 105.1, 105.4, 105.9 (2C), 106.0, 106.0, 106.0, 106.2 (2C) ppm whereas anomeric carbons corresponding to 1,2-*trans* Man*p* units showed resonances at δ 98.7 and 100.7 ppm; 1,2-*cis* anomeric Ara*f* carbon was noticed at δ 99.7 ppm. Moreover, two 1,2-*trans* linkages of Man*p* were verified from 172 and 175 $^{1}J_{C\text{-}H}$ coupling constants. In continuation, hydrazine acetate/THF-MeOH mediated hydrolysis of levulinyl ester afforded 80% of alcohol **48** which is further subjected to [Au]/[Ag]-assisted glycosylation with donor **3** to provide heneicosacharylarabinomannan **49** in 80% yield. Here, again in the arabinomannan **49** crowding protons in the anomeric region encouraged us to determine the structural homogeneity by other spectroscopic methods. However, anomeric linkages were gauged from ^{13}CNMR and MALDI (TOF) spectroscopy. In the ^{13}C NMR spectrum of compound **49**, twelve 1,2-*trans* Ara*f* anomeric carbons were observed at δ 105.1, 105.4, 105.9 (4C), 106.0 (2C), 106.2 (2C), 106.4 and 107.3 ppm, six 1,2-*trans* Man*p* anomeric

carbons were noticed at δ 98.8 (2C), 98.8, 100.5 and 100.7 (2C) ppm; three 1,2-*cis*Ara*f* anomeric carbons showed resonances at δ 99.7 and 99.7 (2C) ppm. Further, MALDI (TOF) analysis disclosed *m*/*z* for $C_{484}H_{480}O_{109}NaSi$, 8142.72 which was in good agreement with calculated *m*/*z* value of 8142.12.



Scheme 4.8 Synthesis of nonasaccharide-carbonate. Reagents: a) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, -78 ^{0}C, 5 h, 77%; b) DDQ, CH_2Cl_2-MeOH (1:4), 25 ^{0}C, 4 h, 75%; c) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ^{0}C, 15 min, 60%; d)

$PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 ^{0}C, 4 h; e) **17**, DMAP, CH_2Cl_2, 0-25 ^{0}C, 3 h, 76% over two steps.



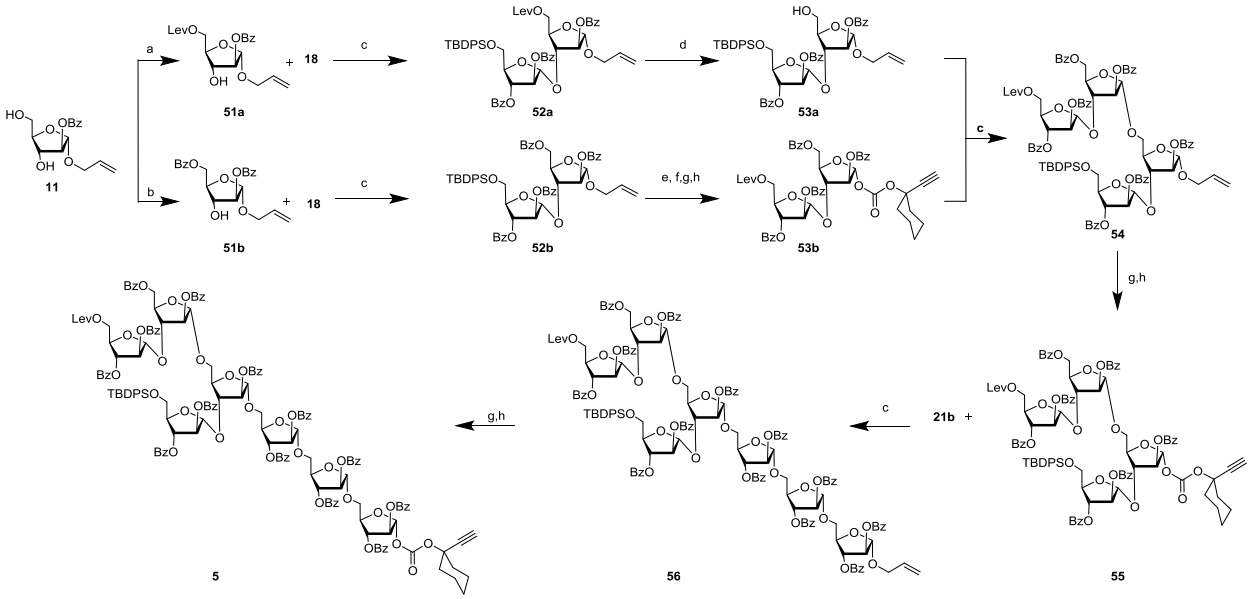
Scheme 4.9 Synthesis of heneicosasaccharide-carbonate. Reagents: a) HF·py, pyridine, 0-25 ^{0}C, 5 h, 83% for **46**; b) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ^{0}C, 30 min, 85% for **47** and 80% for **49**; c) Hydrazine acetate, THF-MeOH (4:1), 25 ^{0}C, 45 min, 80%; d) NaOMe, MeOH, 25 ^{0}C, 15 h, 87%; e) $Pd(OH)_2$, H_2O:THF:CH_3OH = 1:3:3, H_2, 36 h, 90%; f) $PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 ^{0}C, 4 h; g) **17**, DMAP, CH_2Cl_2, 0-25 ^{0}C, 3 h, 68% over two steps.

At this stage, compound **49** was divided into two part and one part was converted into corresponding carbonatedonor **2** by two well known synthetic operations in order to obtain biologically relevant completely deprotected heneicosasaccharide **2** and and check the stability of heneicosasaccharide after global deprotection. Accordingly, cleavage of silyl ethers by employing HF·py/THF, saponification of all benzoate esters using NaOMe/MeOH, and removal

of benzyl ethers by hydrogenolysis employing $Pd(OH)_2/H_2$ in CH_3OH:THF:H_2O = 3:3:1 afforded compound **50** in 66% overall yield after 3 steps.

4.5.9 Synthesis of central heptasaccharide-carbonate (Scheme 4.10)

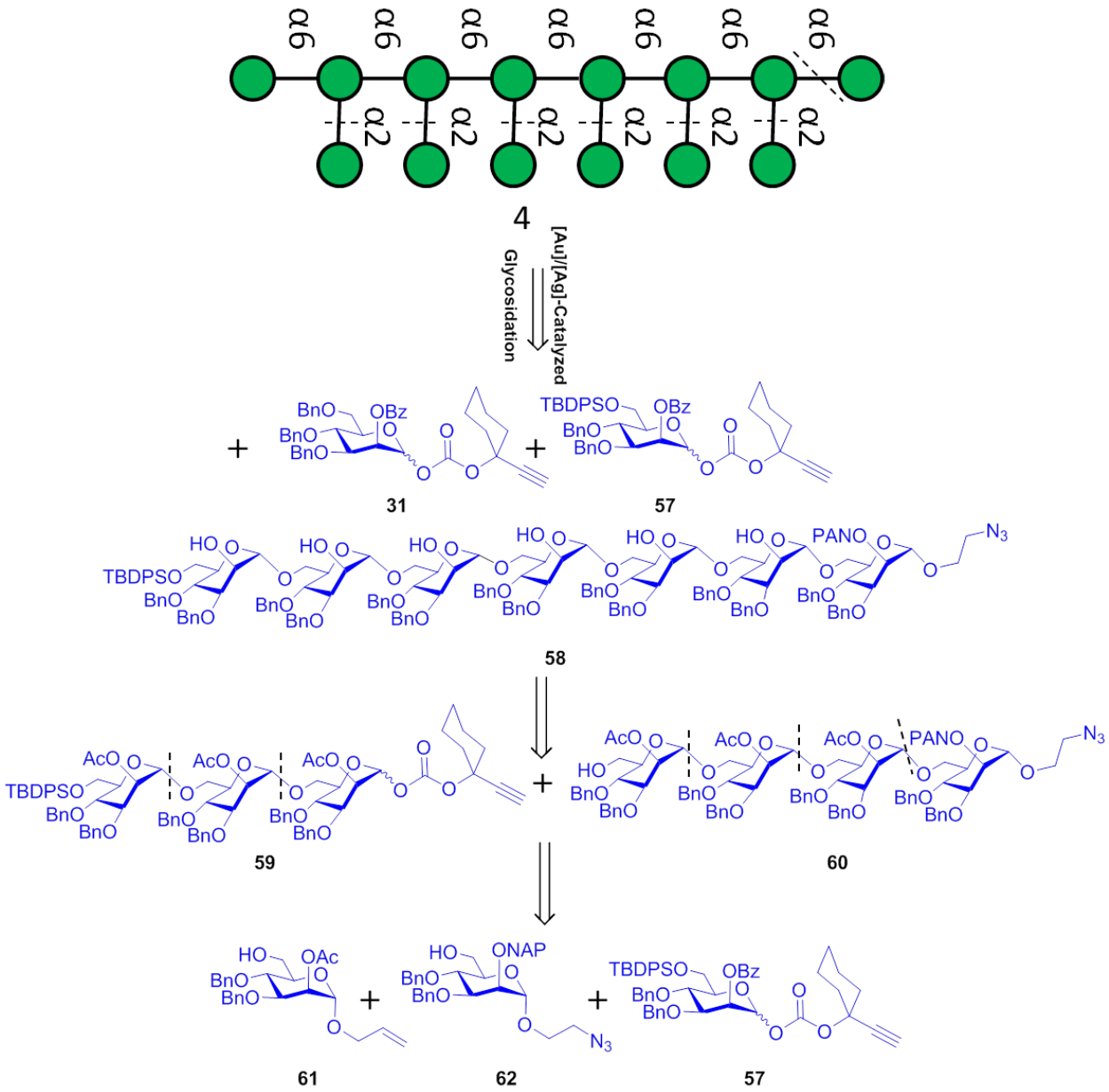
The assembling of middle heptasaccharide-carbonate **5** as depicted in Scheme 4.10 started by the convergent synthesis of tetrasachharide **54**. Accordingly, C5-OH of diol **11** was regioselectively masked by LevCl/py/CH_2Cl_2 and BzCl/Py/CH_2Cl_2 at -30 ^oC to afford monosaccharides **51a** and **51b**. Individual Au/Ag-catalyzed glycosylation of acceptors **51a** and **51b** with furanosyl donor **18** provided respective disaccharide **52a** and **52b**. Hydrazine acetate mediated cleavage of Lev ester afforded disaccharide acceptor **53a** whereas disaccharide carbonate **53b** was achieved in parallel from **52a** *via* four consecutive steps *i.e.* removal of silyl ether by HF·py, protection of C5-OH as levulinoate using Lev-acid/DIC/DMAP, $PdCl_2$ catalyzed hydrolysis of allyl ether to hemiacetal followed by its conversion to the corresponding carbonate with ethenylcyclohexyl carbonate **17** and catalytic amount of DMAP.



Scheme 4.10 Synthesis of heptasaccharide-carbonate. Reagents: a) LevCl, pyridine:CH_2Cl_2 = 1.0:10.0, DMAP, 0-25 ^0C, 5 h, 76%;b) BzCl, pyridine:CH_2Cl_2 = 1.0:10.0, DMAP, 0-25 ^0C, 5 h, 81%;c) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25^0C, 5 h, 95% for **52a**, 96% for **52b**, 92% for **54**, 93% for **56**; d)Hydrazine acetate, THF-MeOH (4:1), 25 ^0C, 45 min, 91%; e) HF·py, pyridine, 0-25 ^0C, 5 h; f) Lev-acid, DIC,

DMAP, CH_2Cl_2, 0-25 ^{0}C, 2 h, 83% over two steps; g)$PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 ^{0}C, 4 h; h) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate (**17**), CH_2Cl_2, DMAP, 0-25 ^{0}C, 3 h, 83% for **53b**, 84% for **55** and 80% for **5** over two steps.

Au/Ag-catalyzed [2+2] glycosylation between acceptor **53a** and acceptor **53b** resulted in tetrasaccharide **54** in 92% yield. In the ^{1}HNMR spectrum of tetrasaccharide **54**, the appearance of anomeric protons as individual singlets at δ 5.20, 5.33, 5.57 and 5.66 ppm revealed the presence of four 1,2-*trans* linkages, whilst ^{13}CNMR revealed anomeric carbons at δ 105.1, 105.3, 105.5 and 106.0 ppm confirming the presence of all four 1,2-*trans* arabinofuranosyl linkages. In continuation, two-step transformation of tetrasaccharide **54** *viz* $PdCl_2$ mediated hydrolysis of allyl glycoside to hemiacetal and subsequent conversion to the tetrasaccharide donor **55** underwent smoothly. Further, acceptor **21b** synthesized *videsupra* was treated with donor **55** to afford the heptasaccharide **56** in 93% yield. The ^{1}HNMR spectrum of **56** showed characteristic anomeric protons; however, they obscured with other C3, C4 protons. In the ^{13}CNMR spectrum of compound **56** anomeric carbons were observed at δ 104.9, 105.0, 105.6 and 105.9 (4C) ppm. Moreover, presentation of thirteen resonances between δ 165.9-166.1 ppm disclosed the existence of thirteen benzoate esters. Apart from this, observation of resonances due to characteristic acetyl ester and ketone at δ 172.5 and 206.4 ppm respectively, confirmed the Lev group whereas resonances at δ 19.4 and 26.8 (3C) verified the TBDPS moiety in heptasaccharide **56**. In continuation, heptasaccharide **56** was subjected to hydrolysis with $PdCl_2$/MeOH-CH_2Cl_2 to generate hemiacetal and subsequently treated with reagent **17** and DMAP to afford desired α/β mixture heptasaccharide-carbonate **5**.

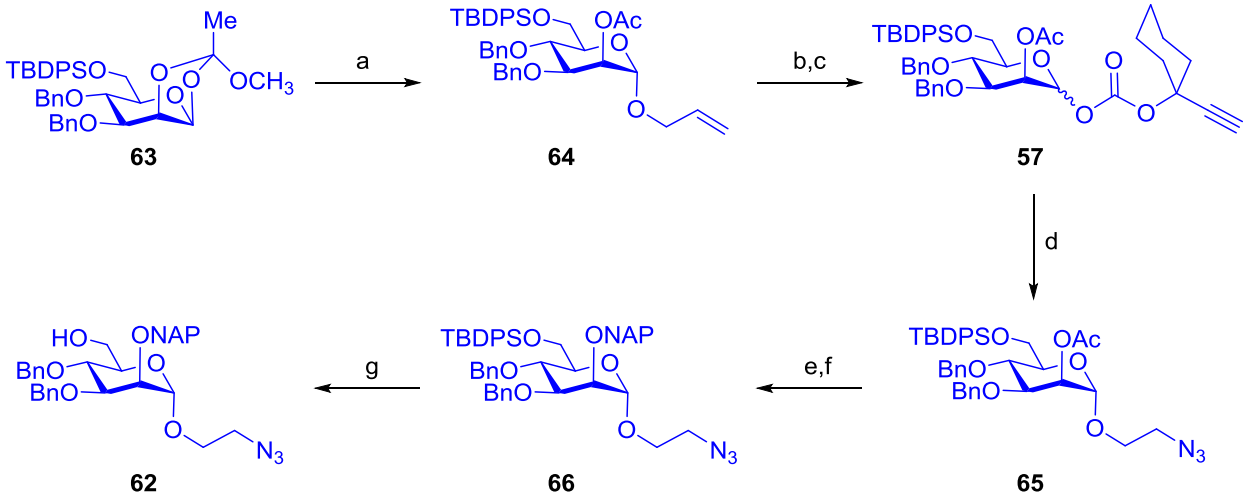


Scheme 4.11 Retrosynthetic analysis of tetradecasaccharidemannan backbone

4.5.10 Retrosynthetic analysis of tetradecasaccharide (Scheme 4.11)

To achieve complex tetradecasaccharide **4** mannancore with maximum branches, we have envisioned highly convergent strategy wherein tetradecasaccharide **4** shall be synthesized from two monosaccharides **31**, **57** and heptasaccharide-hexaol **58** which in turn can be obtained by a [3+4] glycosylation utilizing trisaccaharide carbonate **59** and tetrasaccharide acceptor **60**. Further, **60** can be attained from monosaccharides **57** and **62** whereas heptamannoside **58** can be

assembled from carbonate **57** and aceeptor **61**. The 1,2-*trans*-stereochemistry of each glycosidic bond is ensured by the presence of C2-acetate/benzoate that can impart anchimeric assistance. Along with the benzyl ether as a global protecting group that can be removed in the desired product, we have selected silyl ether and acetyl esters as two orthogonal protecting groups at C6-*O* and C2-*O* respectively for orthogonality. Cleavage of the C6-*O* silyl ether would allow elongating mannan backbone towards 1,6-direction whilst deprotection of acetyl esters would facilitate branching of mannan backbone in 1,2-direction. Apart from this, owing to high stability and catalytic activation of carbonate donor, we have selected carbonate mannosides for the assembly of tetradecasaccharide **4**.



Scheme 4.12 Sythesis of mannopyranoside acceptors. Reagents: a) *p*TSA (0.2 eq.), All.OH, CH_2Cl_2, 4Å MS powder, 25 ^{0}C, 1 h, 84%; b) $PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 ^{0}C, 4 h; c) **17**, CH_2Cl_2, DMAP, 0-25 ^{0}C, 3 h, 76%,over two steps; d) 2-azidoethanol, 8mol% chloro[tris(2,4-di-*tert*-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ^{0}C, 15 min, 93%; e) NaOMe, MeOH, 25 ^{0}C, 1 h; f) NaH, NAPBr, TBAI, DMF, 0-25 ^{0}C, 1 h, 78% over two steps; g) HF·py, pyridine, 0-25 ^{0}C, 5 h, 93%.

4.5.11 Synthesis of monosaccharide acceptor 62 (Scheme 4.12)

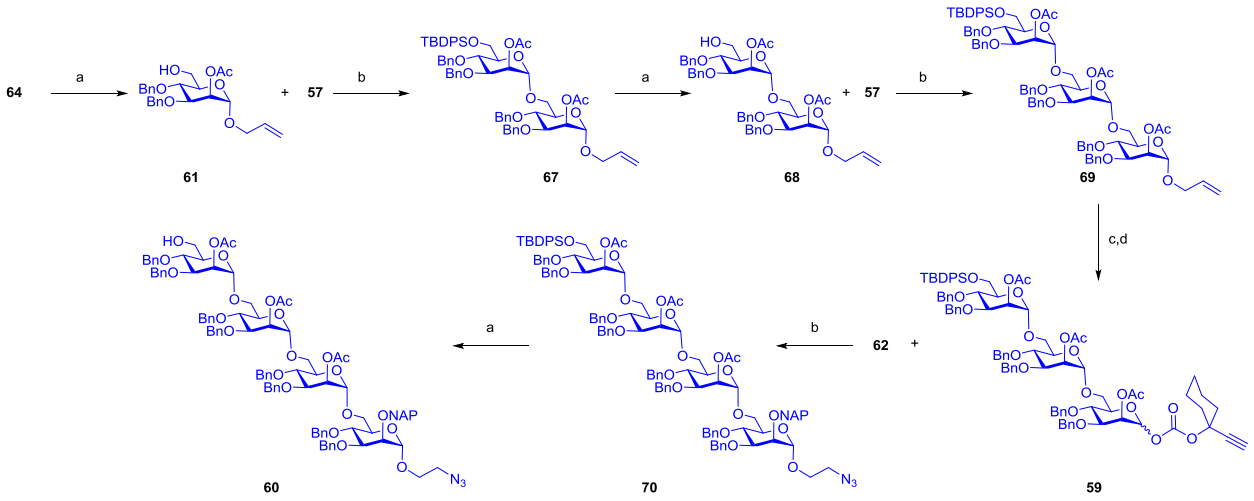
Synthesis of monosaccharide acceptor **62** as outlined in Scheme 4.12 was acquired in seven steps from mannopyranosyl orthoacetate **63**. Ring opening of the orthoester by employing allyl alcohol and *p*TSA gave 84% of allyl mannopyranoside **64** which was further subjected to $PdCl_2$ catalysed hydrolysis to get a hemiacetal followed by its transformation to ethynylcyclohexyl

carbonate donor **57** using reagent **17** and DMAP. Au/Ag-catalyzed glycosylation of donor **57** with 2-azido ethanol afforded azidoethyl mannoside **65** in 93% yield. Next, saponification of azide **65** using NaOMe/MeOH followed by the protection of C2-OH as a NAP-ether employing NAPBr/NaH in DMF generated compound **66** in 78% yield over two steps. Finally, cleavage of silyl ether by HF·py/THF afforded required compound **62** in 93%yield. Homogeneity of compound **62** was supported by NMR and IR spectroscopic analysis. In the ^{13}CNMR spectrum characteristic anomeric carbon was noticed at δ 98.7 ppm whilst IR spectrum showed characteristic asymmetric vibration frequence of azide at 2100 cm^{-1}.

4.5.12 Synthesis of tetrasaccharide mannose acceptor (Scheme 4.13)

The next task was to assemble the mannose tetrasaccharide acceptor **60** and its synthesis commenced with the removal of silyl ether of allyl mannoside **64** using HF·py/THF to obtain alcohol **61**. Stereoselective Au/Ag-catalyzed glycosylation between acceptor **61** and donor **57** in CH_2Cl_2 generated 95% of the disaccharide **67** in which silyl ether was deprotected by HF·py/THF to produce disaccharide acceptor **68** in 88% yield. Formation of disaccharide **67** was verified fromthe regular NMR and MS spectroscopy and anomeric selectivity was confirmed by 2D NMR spectroscopy. In the ^{13}CNMR of disaccharide **67**, distinguishable anomeric carbons were observed at δ 96.7 and 97.8 ppm and in HSQC spectrum, observation of $^{1}J_{C\text{-}H}$ coupling constant of 173 and 174 Hz for anomeric carbons unambiguously confirmed the 1,2-*trans* selectivity of interglycosidic linkages. The NMR spectra of alcohol **68** was very similar to the compound **67** except resonances corresponding to the TBDPS group were absent. In continuation, Au/Ag-catalyzed [2+1] glycosylation between acceptor **68** and donor **57** afforded 90% of the desired trisaccharide **69** which was subsequently converted to respective trisaccharide carbonate **59** *via* aforementioned two-step process. The NMR spectrum of **69** was found to be identical to that of **67**. The only difference was that three anomeric carbons were observed in trisaccharide **69** instead of two anomeric carbons as in disaccharide **67** in ^{13}C NMR spectrum and rest of the ring carbons appeared in the appropriate region. Subsequent treatment of glycosyl donor **59** with acceptor **62** in 8mol% each of gold-phosphite and AgOTf afforded 92% of compound **70** that was subjected to HF·py/THF conditions to obtain tetrasaccharide-alcohol **60** in 90% yield. 1,2-*trans* selectivity of compound **60** was gauged from four anomeric carbon

resonances at δ 97.9, 98.1 and 98.2 (2C) ppm in the ^{13}CNMR spectrum along with $^{1}J_{C\text{-}H}$ coupling constants in the range of 172-175 Hz confirming the structural authenticity of the compound **60**.

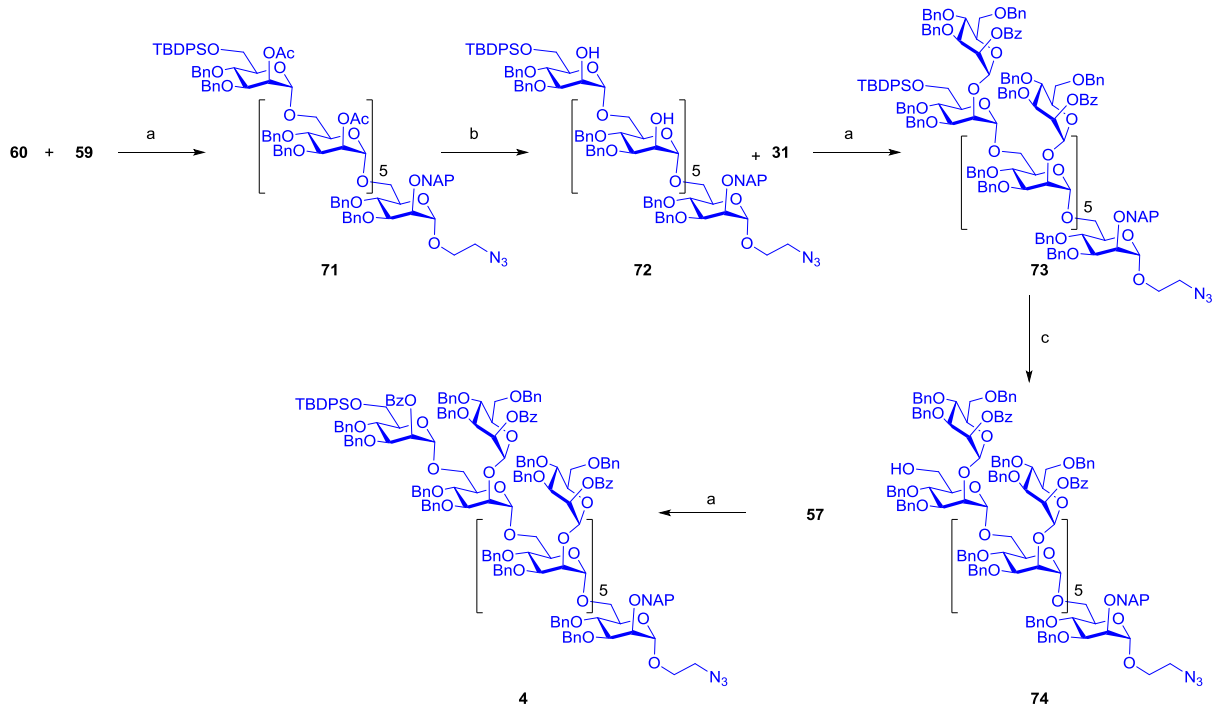


Scheme 4.13 Synthesis of tetrasaccharide acceptor. Reagents: a) HF·py, pyridine, 0-25 ^{0}C, 5 h, 91% for **61**, 88% for **68** and 90% for **60**; b) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ^{0}C, 15 min, 95% for **67**, 90% for **69** and 92% for **70**; c) $PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 ^{0}C, 4 h; d) **17**, CH_2Cl_2, DMAP, 0-25 ^{0}C, 3 h, 73% ,over two steps.

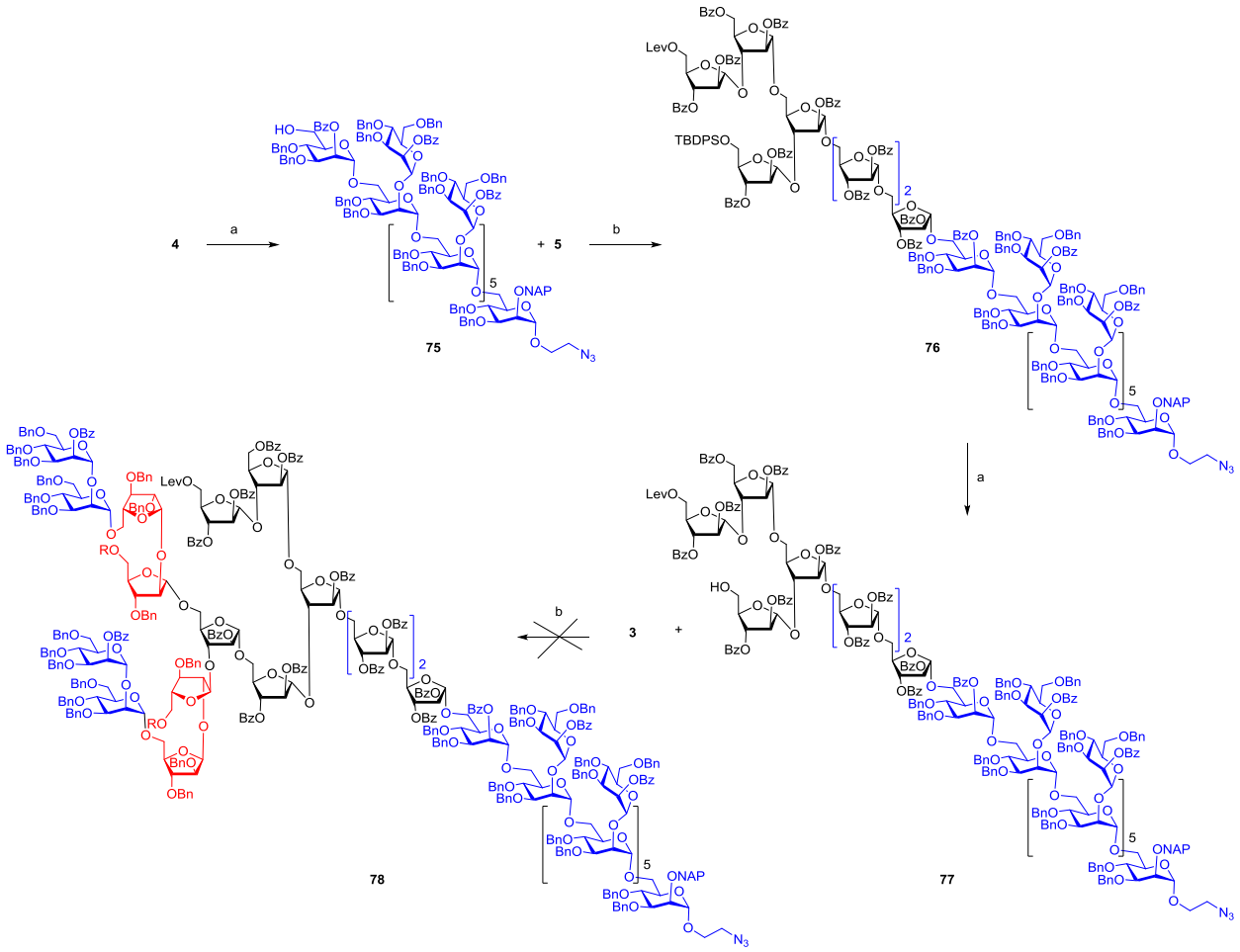
4.5.13 Synthesis of tetradecamannoside (Scheme 4.14)

Having synthesized acceptor **60**, the construction of final tetradecasaccharide **4** was performed by a strategy slightly different to what we employed so far. Our plan was to first synthesize the heptasaccharide acceptor **72** and perform one pot glycosylation in a {7+[6x1]} to obtain tridecasaccharide **73**, followed by [13+1] glycosylation to afford final tetradecasaccharide **4**. In this direction, [3+4] glycosylation of acceptor **60** and donor **59** using Au/Ag-combination gave 88% of the desired heptasaccharide **71**. Formation of heptasaccharide **71** was verified by both 1D and 2D NMR spectroscopy. In the ^{1}HNMR spectrum of saccharide **71**, characteristic seven anomeric protons were noticed at δ 4.9 (1H, overlapped with C3- and C4-sugar protons) and 5.5 (s, 6H) ppm. In the ^{13}CNMR spectrum, appearance of seven resonances at δ 98.0, 98.2 (3C), 98.3 and 98.3(2C) in the anomeric region revealed the presence of seven interglycosidic linkages. Moreover, 1,2-*trans* selectivity was confirmed from gHSQC 2D NMR spectrum wherein all seven anomeric carbons showed $^{1}J_{C\text{-}H}$ coupling constant in the range of 172-175 Hz. Six acetyl

groups were then simultaneously removed by saponification using NaOMe/MeOH to form **72** which was ready for the introduction of branching mannan units at the C2-O position of the mannan backbone. Unfortunately, {7+[6X1]} convergent glycosylation of **72** with seven or more equivalents of donor **31** was not effective and careful analysis of MALDI-TOFspectrum disclosed that even in presence of fifteen equivalents of donor **31**a complex mixture of undecasaccharide and dodecasaccharide without any tridecasaccharide **73** were noticed. To circumvent the problems associated with the direct glycosylation strategy, we have adopted a reverse glycosylation approach wherein acceptor **72** and catalysts were dissolved in CH_2Cl_2 and later donor **31** was added dropwise by syringe infusion pump. Repetition of this for four times of the aforementioned reverse glycosylation strategy, we managed to obtain compound **73** in 70% overall yield. HF·py mediated deprotection of silyl ether generated alcohol **74** which was glycosylated again smoothly with donor **57** using 8mol% of each gold-phosphite and AgOTf catalysts to afford tetradecasaccharide **4** in 84% yield.



Scheme 4.14 Synthesis of tetradecasaccharide. Reagents: a) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ^{0}C, 15 min, 88% for **71**, 70% for **73**, 84% for **4**; b) NaOMe, MeOH, 25 ^{0}C, 1 h, 91%;c) HF·py, pyridine, 0-25 ^{0}C, 5 h, 91%.

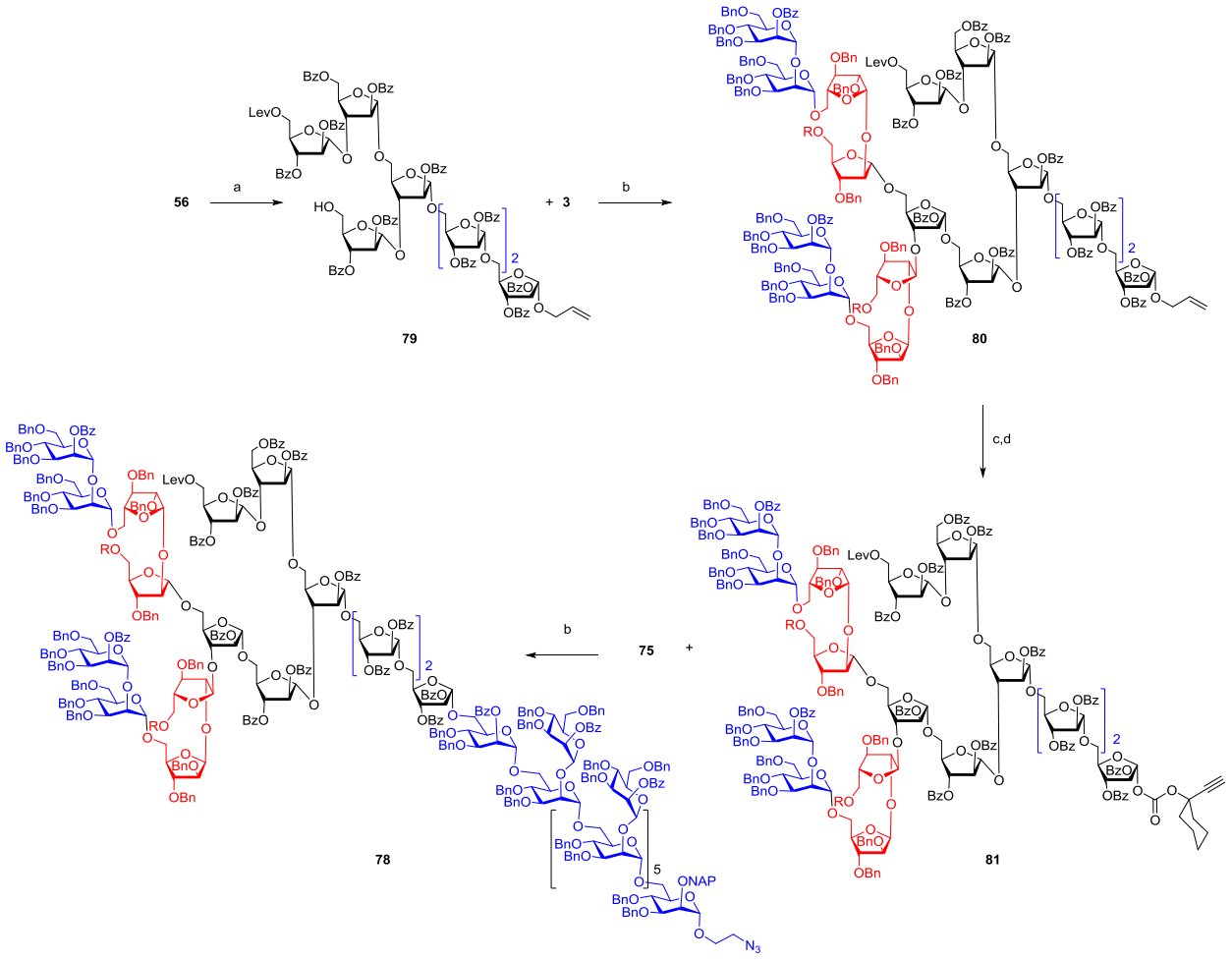


Scheme 4.15a Gold (I) for tricontasaccharide. Reagents: a) HF·py, pyridine, 0-25 ^{0}C, 5 h, 87% for 75, 83% for 77; b) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ^{0}C, 30 min, 85%.

4.5.14 Synthesis of tricontasaccharide (Scheme 4.15)

Having synthesized all the four major fragments **2**,**3**,**4** and **5** and inspired by the high reactivity of ethynylcyclohexyl carbonate donors in presence of gold-phosphite and AgOTf, we tried to assemble these four fragments to accomplish the target henpentacontasaccharide (**1**) of ManLAM. In this respect, silyl-ether of compound **4** was removed using HF·py in THF to afford 87% of tetradecasaccharide acceptor **75** which was further subjected to Au/Ag-catalyzed [14+7] glycosylation with donor **5** to furnish 85% of another heneicosasaccharide **76**. Compound **76** was confirmed thoroughly based on exhaustive NMR and MS analysis. In the ^{13}CNMR spectrum, compound **76** showed two sets resonances in the anomeric region having fourteen resonances

between δ 98.2-99.9 ppm and seven resonances between δ 105.0-106.1 ppm. In addition, appearance of twenty one resonances at δ 164.9, 165.1, 165.2, 165.3(6C), 165.3, 165.4, 165.5(5C), 165.6, 165.7, 166.0, 166.2 and 172.5, suggested presence of twenty-one ester units. Subsequently, removal of silylether in **76** was performed using HF·py/THF afforded alcohol **77** which was further coupled with glycosyl donor **3** in presence of 8mol% of each gold-phosphite and AgOTf to obtain tricontasaccharide **78**. Unfortunately, at this stage productivity of the reaction was not effective; gratifyingly, both the starting materials remained as they after 30 minutes and even after 10 h; later, acceptor **77** was not consumed while donor **3** was converted to the corresponding hemiacetal.



Scheme 4.15b Synthesis of tricontasaccharide. Reagents: a) HF·py, pyridine, 0-25 ^{0}C, 5 h, 94%; b) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å

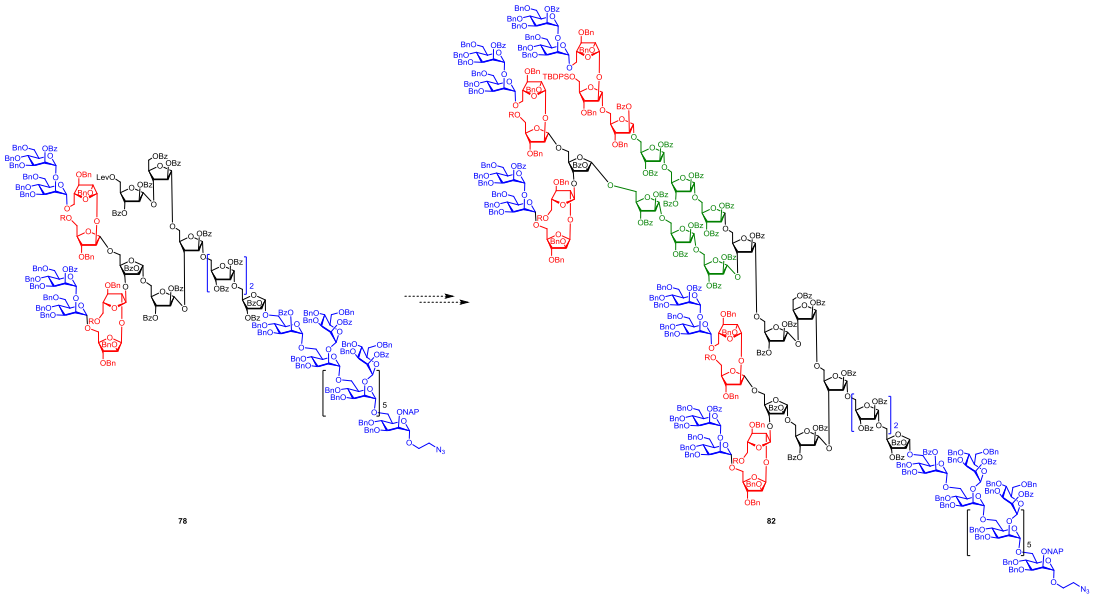
MS powder, 25 ^{0}C, 15 min, 78% for **80** and 70% for **78**;b) $PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 ^{0}C, 4 h; c) 17, CH_2Cl_2, DMAP, 0-25 ^{0}C, 3 h, 68%,over two steps.

Previously during the synthesis of heneicosaarabinomannan carbonate **2,** having similar type of branching at compound **78**, we have observed that Au/Ag assisted [12+9] glycosylation smoothly afforded 80% of heneicosaarabinomannan **49** under 30 minutes. Therefore, we thought during [21+9] coupling stage mannan backbone enhanced the heterogeneity and steric crowding and we have modified the coupling sequences. At first, we have assembled hexadecasaccharide **80**; initiated by cleavage of silyl-ether in compound **56** using HF·py/THF to provide heptasaccharide acceptor **79** which was subjected to the Au/Ag-catalyzed glycosylation with glycosyl donor **3** to generate **80** in 78%. In the ^{13}CNMR of polysaccharide **80**, characteristic two anomeric carbons from 1,2-*cis*-Ara*f* were noticed at δ 99.6 and 99.7 ppm; four anomeric carbons of 1,2-*trans* Man*p* were identified at δ 98.8, 98.8 and 100.8 (2C) ppm; remaining ten 1,2-*trans*-Ara*f* anomeric carbons resonated at δ 104.9, 105.4, 105.6, 105.7, 105.8, 105.9(2C), 106.1, 106.7 and 107.2 ppm. In continuation, hexadecasaccharide donor **81** was achieved from compound **80** by two consecutive steps i.e. $PdCl_2$ mediated hydrolysis of allyl glycoside to hemiacetal, followed by its conversion to respective ethynylcyclohexyl carbonate by the treatment of reagent **17** and DMAP in CH_2Cl_2. Finally, [16+14] glycosylation between donor **81** and acceptor **75** in the presence of 8mol% each of gold-phosphite and AgOTf afforded 70% of the tricontasaccharide **78** in 30 minutes. In the ^{13}CNMR spectrum of tricontasaccharide **78**, characteristic anomeric carbons of 1,2-*cis*-Ara*f* were noticed at δ 99.6, 99.7 ppm; fourteen anomeric carbons of 1,2-*trans* Man*p* were observed between δ 98.3-100.8 ppm; characteristic ten anomeric carbons of 1,2-*trans*-Ara*f* origin showed resonances at δ 104.9, 105.4, 105.6, 105.9, 106.0, 106.1(3C), 106.7 and 107.2 ppm. In addition, MALDI (TOF) spectrum showed *m*/*z* value of tricontasaccharide **78** for $C_{743}H_{735}N_3O_{164}Si_2Na$ at 12424.89 which was in good agreement with calculated m/z value, 12405.89.

4.5.15 Synthesis of henpentacontasaccharide 1 (Scheme 4.16)

The final assembly of henpentacontasaccharide **1** is currently in progress. During these endeavours, enough quantities of heneicosaarabinomannan carbonate **2** and tricontasaccharide **78** are synthesized. After obtaining the henpentacontasaccharide **1**, we need to perform global deprotection of all higher polysaccharides that we synthesized *viz.* henpentacontasaccharide **1**,

heptasaccharide **71**, tetradecasacharide**75**, henicosasaccharide **76** and tricontasaccharide**78** in order to study their immunological significance and other biomedical applications.



Scheme 4.16 Gold (I) for henpentacontasaccharide

In summary, an efficient and convergent strategy was developed for the synthesis of highly branched, hybrid and complex ManLAM of *Mycobacterium tuberculosis*. A split-react-couple strategy was adopted where both glycosyl donor and acceptor were synthesized from the same precursor; therefore reducing the number of synthetic and purification steps and improved the overall synthetic efficiency. Stable ethynylcyclohexyl carbonate donor chemistry was exploited as a versatile glycosyl donor for the synthesis of monosaccharides as well as oligosaccharides. Major advantageous of current methodology were catalytic activation, high yielding, less reaction times and minimal side product.1,2-*trans* Glycosidic linkages were synthesized taking advantage of anchimeric assistance whereas 1,2-*cis* linkages were introduced by exploiting Reciprocal-Donor-Acceptor-selectivity (RDAS). So far, we have prepared heneicosaarabinomannan and tricontasaccharide, final glycosylation steps are currently under progress in our group. Further studies on completion of the targeted henpentacontasaccharide and biophysical studies are currently ongoing.

Note: Characterization data and spectral charts for the compounds can also be found in *Chem. Sci.*, **2017**, *8*, 2033.

4.6 Experimental section

Synthesis of ethynylcyclohexylglycosyl carbonate donors (**2**,**3**,**5**,**6**,**8**,**9**,**12a**,**12b**,**18**,**31**, **35**,**53b**,**57**,**59**,**81**): To a rapidly stirring CH_2Cl_2 solution of arabinofuranosyl or mannopyranosyl hemiacetal (1.0 mmol) and DMAP (1.5 mmol) at 25 ^{0}C, ethynylcyclohexyl(4-nitrophenyl) carbonate (**17**) (1.2 mmol) was added and continued stirring at 25 ^{0}C for 2 h. After complete consumption of the hemiacetal, the reaction mixture was concentrated in *vacuo* and purified by silica gel column chromatography (n-hexane/EtOAc) to afford ethynylcyclohexylglycosyl carbonate donors containing trace quantity of the 4-nitro phenol. Eluents containing the compound are concentrated and redissolved in CH_2Cl_2 and washed with sat.aq. $NaHCO_3$ solution to get 2,3,5,6, 8, 9, 12a, 12b, 18, 31, 35, 53b, 57, 59 and 81 in 85-90% yield.

Glycosylation using ethynylcyclohexylglycosyl carbonate donors (4, 7, 19, 21a, 26, 32, 39, 40, 42, 43, 45, 47, 49, 52a, 52b, 54, 56, 65, 67, 69, 70, 71, 73. 76, 78, 80): To a solution of acceptor (1.0 mmol) and donor (1.0 mmol) in anhydrous CH_2Cl_2 (15 mL) was added freshly activated 4Å MS powder (0.400 g) at 25 ^{0}C. After 10 minutes without stirring, AgOTf (8mol%) and then chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold(I) (8mol%) were added successively to the reaction mixture and immediately stirred for 15-25 minutes if the reaction was carried out at 25 °C and 5-8 h for reactions at -78 °C, the reaction was neutralized by Et_3N and filtered through abed of Celite®. The filtrate was concentrated in *vacuo* and the residue was purified by silicagel column chromatography using n-hexane/EtOAc as mobile phase to afford glycosides in 80-95% yield.

Protection of alcohol using TBDPS-Cl (14, 23, 25, 64): A solution of the alcohol substrates (1 mmol) and imidazole (1.3 mmol) in anhydrous DMF (5 mL) was cooled at 0 °C and tert-butyldiphenylchlorosilane (1.2 mmol) was added dropwise under nitrogen atmosphere. The reaction mixture was gradually warmed up to 25^{o}C and stirred for 2 h. After the completion, the reaction mixture was quenched by adding ice cold water. The whole mixture was transferred to a separatory funnel and extracted with ethylacetate (3x25 mL). The combined organic layers were washed with cold water and brine solution. Organic layer was dried over anhydrous Na_2SO_4, the organic layer was concentrated in *vacuo* and the residue was purified by silica gel column chromatography(ethyl acetate/hexanes) to obtain the desired product.

Deprotection of the TBDPS-ethers (10, 11, 15, 20, 21b, 27, 34, 46, 50, 53b, 60, 61, 62, 68, 74, 75, 77, 79): HF·py (3 mmol) was added dropwise under inert atmosphere to a solution of silyl ether (1mmol) in pyridine (3 times to the volume of HF·py) at 0 ^{o}C. The reaction mixture was stirred for 5 h at 25 ^{o}C, 6N HCl was added to quench the reaction at 0 ^{o}C, diluted with EtOAc (25mL) and washed successively with ice cold water (2x10 mL), saturated solution of $NaHCO_3$(aq), and brine solution. Organic layer was dried anhydrous Na_2SO_4, concentrated in *vacuo* to obtain a residue that was purified by silica gel column chromatography (ethylacetate/hexanes) to furnish the alcohol.

Protection of alcohols as benzyl ethers (33, 37): To a solution of the alcohol (1 mmol) in anhydrous DMF (5 mL) was cooled to 0 °C under nitrogen atmosphere and NaH (60% oil dispersion, 1.3 mmol per alcohol) was added and stirred for 10 minute at 0 ^{o}C, benzyl bromide (1.2 mmol per alcohol) was added dropwise and stirred for 2 h at 25 ^{o}C. The reaction mixture was poured into cold water with vigorous shaking, extraction with ethyl acetate (3x25 mL) and combined EtOAc layers was washed with cold water, brine solution, and dried over Na_2SO_4. The EtOAc solution was decanted and evaporated in *vacuo* to obtain a reddish brown colored residue that was purified by column chromatography (ethyl acetate/hexanes) to obtain the benzyl ether(s) as pale yellow colored syrup.

Synthesis of Allyl glycoside from 1,2-orthoester (24, 29, 64): Ally alcohol (4 mmol) followed by PTSA (0.2 mmol) were added to a vigorously stirred solution of orthoester (1 mmol) in freshly prepared anhydrous CH_2Cl_2 (10 mL) at 25 ^{o}C. After completion of the reaction, Et_3N (2 mL) was added and the solvent was evaporated in *vacuo* and the crude compound was purified by conventional silica gel column chromatography (ethyl acetate/hexanes) to obtain the desired allyl glycoside.

Deprotection of allyl glycosides (14, 21a, 21c, 29, 32, 34, 39, 42, 45, 49, 52b, 54, 56, 64, 69, 80): To the solution of the allyl glycoside (1 mmol) in CH_2Cl_2 (10 mL), $PdCl_2$ (0.2mmol) in MeOH(40mL) was added in five portions at 25 ^{o}C and stirred for 4-5 h. After completion of the reaction, excess amount of Et_3N was added and the solid residue was filtered off through a pad of Celite®. The solvent was evaporated in *vacuo* and the crude compound was purified by conventional silica gel column chromatography (ethyl acetate/hexanes) to obtain the desired hemiacetal.

Protection of levulinoate (21c, 51a, 53b): A solution of the alcohol (1 mmol), DMAP (0.5 mmol) and levulinic acid (1.3 mmol) in dryCH_2Cl_2 (10 mL) was cooled to 0 °C and N,N'-Diisopropylcarbodiimide(1.5 mmol) was added dropwise under nitrogen atmosphere. The reaction mixture was gradually warmed to room temperature and stirred for 2 h. After completion of the reaction, CH_2Cl_2 was evaporated under reduced pressure and the residue was purified by silica gel column chromatography(ethyl acetate/hexanes) to furnish the Lev ester.

Deprotection of levulinoate (46, 53a): Hydrazine acetate (4 mmol) in THF (4 mL) was added to a solution of levulinoate (1 mmol) in MeOH (1 mL) at 25 ^oC and stirred for 45 minutes. The reaction was quenched by adding ice cold 1N HCl solution and washed successively with ethyl acetate (3x25 mL), water, saturated solution of $NaHCO_3$ (aq), and brine solution. After drying over Na_2SO_4, the organic layer was concentrated under diminished pressure and the residue was purified by column chromatography (ethyl acetate/hexanes) to afford the alcohol.

Protection of alcohols as NAPethers (34, 66): To a solution of the alcohol (1 mmol) in anhydrous DMF (5 mL) was cooled to 0 °C under nitrogen atmosphere and NaH (60% oil dispersion, 1.3 mmol per alcohol) was added and stirred for 10 minute at 0 ^oC, 2-bromomethyl naphthalene (1.2 mmol per alcohol) was added dropwise and stirred for 2 h at 25 ^oC. The reaction mixture was poured into cold water with vigorous shaking, extraction with ethyl acetate (3x25 mL) and combined EtOAc layers was washed with cold water, brine solution, and dried over Na_2SO_4. The EtOAc solution was decanted and evaporated in *vacuo* to obtain a reddish brown coloured residue that was purified by column chromatography (ethyl acetate/hexanes) to obtain the benzyl ether(s) as pale yellow coloured syrup.

Deprotection of NAP ethers (40, 43): 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (2 mmol) was added to a rapidly stirred solution of alcohol (1 mmol) in CH_2Cl_2-MeOH (1:4) at 25 ^oC. After 4 h, the reaction mixture was quenched by the addition of Et_3N (reaction mixture turns black from brown) and solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate/hexanes) to furnish the alcohol as a pale yellow colored syrup.

Synthesis of benzoates (10, 14, 51b): A solution of the alcohol (1 mmol) in anhydrous pyridine (10 mL) and DMAP (0.1 mmol) was cooled to 0 °C under nitrogen atmosphere and benzoyl

chloride (1.2 mmol per alcohol) was added dropwise and stirred for 5 h at 25 ^{o}C. The reaction mixture was poured into cold water with vigorous shaking, neutralized by the addition of 6N HCl solution, extracted with ethylacetate (3x50 mL) and combined EtOAc layers was washed with cold water, sat. $NaHCO_3$,brine solution, and dried over Na_2SO_4. The EtOAc solution was decanted and evaporated in *vacuo* to obtain a reddish brown colored residue that was purified by column chromatography (ethyl acetate/hexanes) to obtain the required benzoate.

Saponification of esters (14, 22, 29, 50, 65, 71): Freshly prepared NaOMe (0.1 mmol per benzoate) was added to a solution of the benzoate(1 mmol) in MeOH (10 mL) and stirred for 8 h at 25 ^{o}C. The reaction mixture was concentrated in *vacuo* to obtain a residue that was purified by column chromatography (ethylacetate/hexanes) to obtain alcohol.

Hydrogenolysis of compound (49): To a solution of the compound 46 (30 mg, 5.4 μmol) in 2 mL of MeOH-THF-H_2O (4:3:3) under hydrogen atmosphere (balloon pressure) was added 10% $Pd(OH)_2$ (2mg, 1.0 μmol) and stirred for 36 h at 25 ^{o}C. The reaction mixture was filtered through a pad of Celite® and the filtrate was evaporated in *vacuo* first and subsequently subjected to lyophilisation to afford the target compound 47 (14 mg, 90%) as a white solid.

Synthesis of allyl arabinofuranoside from 1,2-acetonide (38): Allyl alcohol (2.12 mL, 30.8 mmol) was added to a solution of acetonide 25 (8.0 g, 15.4mmol) in CH_2Cl_2 (60 mL), stirred at 60 ^{o}C. After 5 min, PTSA (0.53 g, 3.1 mmol) was added and continued stirring for additional 1 h, the reaction mixture was neutralized by the addition of Et_3N (excess), diluted with water and extracted with CH_2Cl_2 (3x50 mL). Combined CH_2Cl_2 layers was washed with a brine solution, dried over anhydrous sodium sulphate, decanted and concentrated in *vacuo* to obtain a residue that was partially purified by silica gel column chromatography (ethyl acetate/hexanes) to obtain α/β-allyl furanosides which were separated by flash chromatography by obtain diastereomerically pure 26 (3.6 g, 45%) as a pale yellow syrup.

Allyl 2,3-di-*O*-benzoyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranoside (**14**): Yield: (76% over two steps from **7**); $[\alpha]_D^{25}$ = -17.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.05 (s, 9H), 4.01 (d, *J* = 4.8 Hz, 2H), 4.11 (ddt, *J* = 13.1, 6.1, 1.3 Hz, 1H), 4.29 (ddt, *J* = 13.1, 5.0, 1.5 Hz, 1H), 4.40 (q, *J* = 4.7 Hz, 1H), 5.20 – 5.24 (m, 1H), 5.26 (s, 1H), 5.37 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.49 (d, *J* = 1.5 Hz, 1H), 5.62 (dd, *J* = 5.2, 1.4 Hz, 1H), 5.90 – 6.02 (m, 1H), 7.30 – 7.35 (m,

4H), 7.35 – 7.41 (m, 4H), 7.42 – 7.48 (m, 2H), 7.52 – 7.61 (m, 2H), 7.71 (ddd, *J* = 7.8, 3.0, 1.5 Hz, 4H), 7.96 – 8.01 (m, 2H), 8.04 – 8.08 (m, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 26.9(3C), 63.7, 68.0, 77.6, 82.6, 83.1(2C), 105.1, 117.5, 127.8(3C), 128.5(3C), 129.4, 129.6, 129.8(2C), 130.1(3C), 133.3, 133.4(3C), 134.0, 135.8(6C), 165.6, 165.8; IR (CHCl3); 3439, 3029, 2930, 1599, 1454, 1214, 701 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{38}H_{40}O_7NaSi$, 659.2441, found 659.2445.

Allyl 2,3-di-*O*-benzoyl-α-D-arabinofuranoside (**15**): Yield: (93%); $[\alpha]_D^{25}$ = -36.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 2.69 (s, 1H), 4.03 (d, *J* = 12.9 Hz, 2H), 4.11 (ddt, *J* = 13.1, 5.9, 1.3 Hz, 1H), 4.29 (ddt, *J* = 13.1, 4.9, 1.5 Hz, 1H), 4.36 (q, *J* = 4.1 Hz, 1H), 5.21 (dd, *J* = 10.4, 1. 5 Hz, 1H), 5.30 (s, 1H), 5.37 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.43 – 5.50 (m, 1H), 5.57 (d, *J* = 1.3 Hz, 1H), 5.88 – 6.00 (m, 1H), 7.43 (td, *J* = 7.7, 4.5 Hz, 4H), 7.52 – 7.62 (m, 2H), 7.87 – 8.17 (m, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 62.3 , 67.9 , 77.8 , 82.0 , 83.8(2C) , 104.7 , 117.4 , 128.5 , 128.5(2C), 129.1 , 129.2, 129.9 (2C), 129.9(2C), 133.5, 133.6, 133.7, 165.4, 166.2; IR (CHCl3): 3437, 3068, 2927, 1599, 1452, 1262, 1106, 709 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd. for $C_{22}H_{22}O_7Na$, 421.1263, found 421.1265.

Allyl 2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (**19**): Yield: (95%); $[\alpha]_D^{25}$ = -5.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.04 (s, 9H), 3.97 (dd, *J* = 11.2, 2.9 Hz, 1H), 4.02 (dd, *J* = 4.4, 1.8 Hz, 2H), 4.11 (ddt, *J* = 13.2, 5.9, 1.3 Hz, 1H), 4.23 (dd, *J* = 11.2, 4.6 Hz, 1H), 4.30 (ddt, *J* = 13.2, 4.9, 1.5 Hz, 1H), 4.51 – 4.59 (m, 2H), 5.20 (dd, *J* = 10.4, 1.5 Hz, 1H), 5.30 (s, 1H), 5.36 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.41 (s, 1H), 5.58 (d, *J* = 1.2 Hz, 1H), 5.61 (d, *J* = 1.2 Hz, 1H), 5.67 (t, *J* = 5.6 Hz, 2H), 5.88 – 6.03 (m, 1H), 7.28 – 7.47 (m, 16H), 7.51 – 7.58 (m, 2H), 7.72 (ddd, *J* = 7.8, 3.6, 1.7 Hz, 4H), 7.92 – 8.02 (m, 6H), 8.07 (dd, *J* = 8.3, 1.2 Hz, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 26.8(3C), 63.5, 66.1, 67.8(2C), 67.8, 77.5 (2C), 82.0, 82.0, 82.2, 83.3, 104.9, 106.0, 117.4, 127.7(3C), 128.3(2C), 128.4(2C), 128.5(2C), 128.5(2C), 129.1, 129.3, 129.3, 129.4, 129.7(2C), 129.8(2C), 129.9(2C), 130.0(2C), 130.0(2C), 133.2, 133.3, 133.3, 133.4, 133.4(2C), 133.8, 135.7(2C), 135.7(2C), 165.3, 165.4, 165.6, 165.8; IR ($CHCl_3$): 3430, 3029, 2929, 1599, 1444, 1214, 699 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{57}H_{56}O_{13}NaSi$, 999.3387, found 999.3392.

Allyl 2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (**20**): Yield: (91%); $[\alpha]_D^{25}$ = -10.8 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 2.47 (s,

1H), 3.97 (dd, *J* = 11.2, 2.8 Hz, 2H), 4.09 (ddt, *J* = 13.2, 6.0, 1.4 Hz, 1H), 4.21 (dd, *J* = 11.2, 4.6 Hz, 1H), 4.28 (ddt, *J* = 13.2, 4.9, 1.6 Hz, 1H), 4.48 (dt, *J* = 4.7, 2.4 Hz, 1H), 4.51 (q, *J* = 4.2 Hz, 1H), 5.20 (dq, *J* = 10.5, 1.4 Hz, 1H), 5.29 (s, 1H), 5.33 (q, *J* = 1.6 Hz, 1H), 5.37 (q, *J* = 1.6 Hz, 1H), 5.42 (s, 1H), 5.43 – 5.46 (m, 1H), 5.57 (d, *J* = 1.3 Hz, 1H), 5.64 (d, *J* = 5.1 Hz, 1H), 5.66 (d, *J* = 1.3 Hz, 1H), 5.87 – 6.00 (m, 1H), 7.24 – 7.33 (m, 2H), 7.37 – 7.47 (m, 7H), 7.48 – 7.54 (m, 1H), 7.57 (t, *J* = 7.4 Hz, 2H), 7.94 (dd, *J* = 8.3, 1.2 Hz, 2H), 8.00 – 8.10 (m, 6H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 62.4, 66.2, 67.9, 77.4, 77.8, 81.7, 82.0(2C), 83.8(2C), 104.9, 105.8, 117.4, 128.4(2C), 128.5(2C), 128.6(3C), 129.1, 129.1, 129.2, 129.3, 129.9(4C), 129.9(2C), 130.0(2C), 133.4, 133.5, 133.5, 133.6, 133.8, 165.2, 165.5, 165.8, 166.1; IR ($CHCl_3$): 3459, 3067, 2928, 1599, 1452, 1281, 1106, 706 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{41}H_{38}O_{13}Na$, 761.2209, found 761.2211.

Allyl 2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (**21a**): Yield: (92%); $[\alpha]_D^{25}$ = -0.8 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.02 (s, 9H), 3.91 – 4.01 (m, 4H), 4.09 (ddt, *J* = 13.2, 6.0, 1.4 Hz, 1H), 4.21 (ddd, *J* = 11.0, 6.4, 4.5 Hz, 2H), 4.28 (ddt, *J* = 13.2, 4.9, 1.6 Hz, 1H), 4.48 (dt, *J* = 4.7, 2.3 Hz, 1H), 4.51 (q, *J* = 4.7 Hz, 1H), 4.66 (q, *J* = 4.2 Hz, 1H), 5.17 – 5.24 (m, 1H), 5.28 (s, 1H), 5.35 (dd, *J* = 17.2, 1.7 Hz, 1H), 5.41 (d, *J* = 3.9 Hz, 2H), 5.57 (d, *J* = 1.3 Hz, 1H), 5.58 (d, *J* = 1.3 Hz, 1H), 5.62 – 5.67 (m, 4H), 5.93 (dddd, *J* = 17.2, 10.6, 5.9, 4.9 Hz, 1H), 7.25 – 7.40 (m, 17H), 7.41 – 7.57 (m, 7H), 7.70 (ddd, *J* = 7.9, 4.2, 1.7 Hz, 4H), 7.89 – 8.08 (m, 12H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 26.9(3C), 63.5, 66.0, 66.0, 67.9, 77.4(3C), 81.6, 82.0(2C), 82.2, 82.3, 83.3(2C), 104.9, 105.9, 106.1, 117.4, 127.8(3C), 128.3(2C), 128.4 (2C), 128.4(2C), 128.5(2C), 128.5(2C), 128.6(2C), 129.1, 129.2, 129.3, 129.3, 129.4(2C), 129.7(2C), 129.9(4C), 129.9(4C), 130.0(2C), 130.0(2C), 133.1, 133.3, 133.3, 133.4(2C), 133.4, 133.5, 133.5, 133.9, 135.7(2C), 135.7(2C), 165.2, 165.3, 165.5, 165.6, 165.7, 165.8; IR ($CHCl_3$): 3468, 3049, 2938, 1601, 1450, 1230, 1109, 697 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{76}H_{72}O_{19}NaSi$, 1339.4334, found 1339.4347.

Allyl 2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (**21c**): Yield: (88% over two steps); $[\alpha]_D^{25}$ = 0.1 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 2.12 (s, 3H), 2.55 – 2.61 (m, 2H), 2.67 – 2.73 (m, 2H), 3.95 (ddd, *J* = 13.8, 11.3, 2.8 Hz, 2H), 4.09 (ddt, *J* = 13.2, 6.0, 1.4 Hz, 1H), 4.21 (dt, *J* = 11.0, 4.8 Hz, 2H), 4.26 (dt, *J* = 4.9, 1.6 Hz, 1H), 4.30 (dt, *J* =

4.9, 1.6 Hz, 1H), 4.40 (dd, *J* = 11.5, 5.0 Hz, 1H), 4.47 (td, *J* = 4.6, 2.9 Hz, 2H), 4.54 – 4.61 (m, 1H), 4.63 (dt, *J* = 5.8, 2.8 Hz, 1H), 5.20 (dq, *J* = 10.5, 1.4 Hz, 1H), 5.28 (s, 1H), 5.35 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.39 – 5.42 (m, 2H), 5.45 (s, 1H), 5.56 (d, *J* = 1.3 Hz, 1H), 5.60 (d, *J* = 1.1 Hz, 1H), 5.62 – 5.67 (m, 2H), 5.94 (dddd, *J* = 17.1, 10.6, 5.9, 4.9 Hz, 1H), 7.27 (t, *J* = 7.7 Hz, 4H), 7.36 – 7.47 (m, 10H), 7.51 (tdd, *J* = 8.3, 3.5, 2.2 Hz, 2H), 7.58 (dtt, *J* = 10.2, 7.0, 1.3 Hz, 2H), 7.89 – 7.94 (m, 4H), 7.99 – 8.09 (m, 8H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 27.9, 29.9, 40.0, 63.7, 66.0, 66.2, 67.8, 77.4(3C), 77.7, 81.2, 81.5, 81.7, 82.0(2C), 82.1, 104.9, 105.8, 106.0, 117.4, 128.4(2C), 128.4(2C), 128.5(2C), 128.6(4C), 128.6(2C), 129.0, 129.1(2C), 129.2, 129.2, 129.3, 129.8(2C), 129.9(6C), 129.9(2C), 130.0(2C), 133.3, 133.3, 133.5(2C), 133.7, 133.8, 165.1, 165.2, 165.5, 165.7(2C), 165.8, 172.5, 206.3; IR ($CHCl_3$): 3462, 3051, 2939, 1767, 1599, 1451, 1234, 1110, 697 cm^{-1}; HRMS (TOF) m/z [M + Na]$^+$ calcd for $C_{65}H_{60}O_{21}Na$, 1199.3524, found 1199.3525.

Allyl 2-O-benzoyl-α-D-arabinofuranoside (**11**): Yield: (90%); $[\alpha]_D^{25}$ = 99.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 2.24 (s, 1H), 3.51 (s, 1H), 3.80 (d, *J* = 11.8 Hz, 1H), 3.90 – 3.98 (m, 1H), 4.08 (ddt, *J* = 12.9, 6.2, 1.3 Hz, 1H), 4.22 (dd, *J* = 6.1, 2.5 Hz, 2H), 4.29 (ddt, *J* = 12.9, 5.1, 1.4 Hz, 1H), 5.1 3 (d, *J* = 1.5 Hz, 1H), 5.23 (dd, *J* = 10.4, 1.3 Hz, 1H), 5.30 (s, 1H), 5.34 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.87 – 6.01 (m, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.99 – 8.03 (m, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 62.0, 68.4, 76.6, 84.2(2C), 86.3, 104.6, 118.0, 128.7, 129.1, 129.9(2C), 133.7, 133.8, 166.8; IR ($CHCl_3$): 3427, 3074, 2929, 1601, 1451, 1203, 1105, 712 cm^{-1}; HRMS (TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{18}O_6Na$, 317.1007, found 317.1006.

Allyl 2-*O*-benzoyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranoside (**25**): Yield: (30%); $[\alpha]_D^{25}$ = 47.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.04 (s, 9H), 3.09 (d, *J* = 4.1 Hz, 1H), 3.89 (d, *J* = 4.2 Hz, 2H), 4.07 (dd, *J* = 12.9, 6.2 Hz, 1H), 4.21 – 4.31 (m, 3H), 5.14 (s, 1H), 5.22 (dd, *J* = 10.4, 1.4 Hz, 1H), 5.28 (s, 1H), 5.33 (dt, *J* = 17.2, 1.5 Hz, 1H), 5.94 (dddd, J = 16.7, 10.5, 6.1, 5.2 Hz, 1H), 7.31 – 7.44 (m, 8H), 7.56 (d, *J* = 7.4 Hz, 1H), 7.68 (dd, *J* = 7.9, 1.4 Hz, 4H), 7.91 – 7.98 (m, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 26.9(3C), 63.7, 68.3, 77.0, 84.8(2C), 85.8, 104.6, 117.9, 127.8(2C), 127.8(2C), 128.6(2C), 129.3, 129.8(2C), 129.9(2C), 133.4, 133.6, 133.9, 135.7(2C), 135.7(2C), 166.7; IR ($CHCl_3$): 3435, 3027, 2924, 1599, 1454, 1213, 1102, 700 cm^{-1}; HRMS (TOF) m/z [M + Na]$^+$ calcd for $C_{31}H_{36}O_6NaSi$, 555.2178, found 555.2180.

Allyl 2-*O*-benzoyl- 3-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranoside (**26**): Yield: (95%); $[\alpha]_D^{25}$ = 13.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.99 (s, 9H), 2.11 (s, 3H), 2.58 (td, *J* = 7.2, 6.6, 2.2 Hz, 2H), 2.67 – 2.73 (m, 2H), 3.69 (d, *J* = 10.9 Hz, 1H), 3.89 (d, *J* = 3.7 Hz, 2H), 3.94 (d, *J* = 10.3 Hz, 1H), 4.11 (td, *J* = 10.9, 9.4, 4.6 Hz, 2H), 4.19 (dd, *J* = 11.9, 3.1 Hz, 2H), 4.25 – 4.34 (m, 2H), 4.39 (dd, *J* = 11.2, 4.5 Hz, 1H), 4.53 – 4.62 (m, 4H), 5.18 (d, *J* = 10.4 Hz, 1H), 5.25 (s, 1H), 5.35 (s, 1H), 5.38 – 5.41 (m, 2H), 5.42 (s, 1H), 5.44 (s, 1H), 5.57 – 5.64 (m, 5H), 5.69 (d, *J* = 4.3 Hz, 1H), 5.95 (ddt, *J* = 16.7, 10.7, 5.4 Hz, 1H), 7.20 – 7.24 (m, 2H), 7.25 – 7.32 (m , 6H), 7.36 (q, *J* = 7.3 Hz, 10H), 7.43 (d, *J* = 7.4 Hz, 2H), 7.45 – 7.51 (m, 4H), 7.52 – 7.60 (m, 3H), 7.62 – 7.66 (m, 4H), 7.83 (d, *J* = 8.2 Hz, 2H), 7.89 (d, *J* = 8.2 Hz, 2H), 8.01 (ddd, *J* = 26.8, 16.6, 8.0 Hz, 10H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4 , 26.8(3C), 27.9, 29.9, 38.0, 63.2, 63.7, 65.5, 66.1, 67.8(2C), 77.0, 77.3, 77.7, 80.1, 81.2, 81.5(2C), 81.6, 82.1, 82.9, 82.9, 83.5, 105.0, 105.2, 106.0, 106.0, 117.3, 127.7(2C), 127.8(2C), 128.3(2C), 128.4(2C), 128.4(2C), 128.6(6C), 128.6(2C), 129.0, 129.1, 129.1, 129.2, 129.2, 129.4, 129.5, 129.7, 129.8(2C), 129.8, 129.9(5C), 123.0(8C), 133.2 (2C), 133.3(2C), 133.4 (2C), 133.7, 134.2, 135.6(2C), 135.7(2C), 165.1, 165.1, 165.2, 165.6, 165.6, 165.7, 165.7, 172.5, 206.3; IR ($CHCl_3$): 3419, 3035, 2920, 1752,1601, 1455, 1210, 1100, 693 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{93}H_{90}O_{26}NaSi$, 1674.5420, found 1674.5425.

Allyl 2-*O*-benzoyl- 3-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (**27**): Yield: (90%); $[\alpha]_D^{25}$ = 12.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 2.12 (s, 3H), 2.58 (td, *J* = 7.5, 6.8, 2.6 Hz, 2H), 2.67 – 2.72 (m, 2H), 3.82 (d, *J* = 11.4 Hz, 1H), 3.90 – 3.99 (m, 3H), 4.06 – 4.21 (m, 3H), 4.23 – 4.33 (m, 2H), 4.35 – 4.47 (m, 3H), 4.53 – 4.62 (m, 3H), 5.15 – 5.20 (m, 1H), 5.23 (s, 1H), 5.33 (q, *J* = 1.6 Hz, 1H), 5.36 (s, 1H), 5.38 – 5.41 (m, 2H), 5.43 (s, 1H), 5.56 (d, *J* = 4.8 Hz, 1H), 5.59 (s, 3H), 5.63 (d, *J* = 3.6 Hz, 2H), 5.92 (dddd, *J* = 16.7, 10.6, 6.0, 4.9 Hz, 1H), 7.2 7 (q, *J* = 8.2 Hz, 4H), 7.40 (tdd, *J* = 7.4, 6.2, 5.5, 2.8 Hz, 9H), 7.43 – 7.48 (m, 4H), 7.49 – 7.55 (m, 2H), 7.55 – 7.61 (m, 2H), 7.91 (ddd, *J* = 8.4, 3.6, 1.2 Hz, 4H), 7.98 – 8.08 (m, 10H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 27.9, 29.9, 38.0, 62.0, 63.7, 66.1, 66.4, 67.9, 77.2, 77.3, 77.7, 80.8, 81.2, 81.5, 81.5, 81.9, 82.0, 82.5, 83.1, 83.3(2C), 105.0, 105.6, 105.8, 106.0, 117.5, 128.4(5C), 128.6 (8C), 128.6, 129.0, 129.1(2C), 129.1, 129.2,

129.3, 129.4, 129.9(8C), 130.0(5C), 133.3, 133.4, 133.5(4C), 133.7, 133.9, 165.2, 165.3, 165.4, 165.6, 165.7, 165.7, 165.7, 172.6, 206.4; IR ($CHCl_3$): 3426, 3030, 2929, 1741,1599, 1455, 1210, 1100, 693 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{77}H_{72}O_{26}Na$, 1435.4209, found 1435.4193.

Allyl 2-*O*-benzoyl- 3-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(^{t}butyldiphenylsilyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (**7**): Yield: (92%); $[\alpha]_D^{25}$ = 13.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.01 (s, 9H), 2.10 (s, 3H), 2.57 (dd, *J* = 6.3, 1.9 Hz, 2H), 2.65 – 2.70 (m, 2H), 3.79 – 3.92 (m, 5H), 3.95 – 3.99 (m, 2H), 4.00 – 4.09 (m, 2H), 4.14 – 4.28 (m, 5H), 4.35 – 4.44 (m, 3H), 4.46 – 4.54 (m, 3H), 4.59 (ddd, *J* = 11.8, 7.7, 3.6 Hz, 4H), 5.14 (dd, *J* = 10.5, 1.5 Hz, 1H), 5.23 (s, 1H), 5.29 – 5.34 (m, 3H), 5.36 (s, 1H), 5.38 (d, *J* = 5.2 Hz, 2H), 5.41 (s, 1H), 5.45 (d, *J* = 1.5 Hz, 1H), 5.52 (s, 1H), 5.56 (d, *J* = 1.3 Hz, 1H), 5.58 (d, *J* = 1.2 Hz, 2H), 5.60 (d, *J* = 1.1 Hz, 1H), 5.62 (d, *J* = 3.5 Hz, 5H), 5.64 (d, *J* = 5.0 Hz, 1H), 5.69 (d, *J* = 4.6 Hz, 1H), 5.84 – 5.95 (m, 1H), 7.22 – 7.30 (m, 11H), 7.30 – 7.35 (m, 10H), 7.36 – 7.39 (m, 10H), 7.40 – 7.43 (m, 3H), 7.43 – 7.48 (m, 6H), 7.48 – 7.52 (m, 2H), 7.55 (d, *J* = 11.7 Hz, 2H), 7.69 (ddd, *J* = 7.9, 4.1, 1.6 Hz, 4H), 7.84 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.86 – 7.87 (m, 2H), 7.87 – 7.89 (m, 3H), 7.91 (dd, *J* = 6.4, 1.2 Hz, 2H), 7.94 (dd, *J* = 2.7, 1.3 Hz, 2H), 7.96 – 7.97 (m, 5H), 7.98 – 7.99 (m, 5H), 8.00 – 8.06 (m, 6H); ^{13}C NMR (100.53 MHz, $CDCl_3$):) δ 19.4, 26.8(3C), 27.9, 29.8, 37.9, 63.5, 63.7, 65.6, 65.7, 65.8, 66.0, 67.8(2C), 77.0, 77.2, 77.3, 77.3, 77.4(2C), 77.7(2C), 80.7, 81.2, 81.5(3C), 81.6(2C), 82.0, 82.2, 82.2, 82.6, 82.8, 82.9, 83.2, 105.1, 105.4, 105.8, 105.9, 105.9, 106.0, 106.0, 117.4, 127.7(7C), 128.3(2C), 128.3(2C), 128.3(2C), 128.4(2C), 128.4(3C), 128.5(3C), 128.5(3C), 128.6(2C), 129.0, 129.1, 129.1, 129.1(2C), 129.1, 129.2, 129.2, 129.3(2C), 129.3, 129.4, 129.7(2C), 129.8(2C), 129.8(9C), 129.9(12C), 129.9(5C), 130.0(2C), 133.1, 133.2, 133.2, 133.3, 133.3(5C), 133.4(3C), 133.6, 133.9, 135.7(3C), 135.7(3C), 165.1, 165.1, 165.1, 165.2, 165.2, 165.2, 165.5, 165.6, 165.6(4C), 165.7, 172.5, 206.3; IR ($CHCl_3$): 3016, 2918, 1750, 1600, 1454, 1267, 1106, 708 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{150}H_{138}O_{44}NaSi$, 2694.8261, found 2694.7383.

Allyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (**29**): Yield: (86%); $[\alpha]_D^{25}$ = -8.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 3.75 – 3.82 (m, 1H), 3.86 – 3.93 (m, 2H),

4.02 (ddt, *J* = 12.8, 6.0, 1.3 Hz, 1H), 4.06 – 4.16 (m, 2H), 4.20 (ddt, *J* = 12.8, 5.1, 1.5 Hz, 1H), 4.51 – 4.60 (m, 3H), 4.74 (d, *J* = 12.0 Hz, 1H), 4.80 (d, *J* = 11.2 Hz, 1H), 4.87 (d, *J* = 10.7 Hz, 1H), 5.02 (d, *J* = 1.9 Hz, 1H), 5.20 (dq, *J* = 10.6, 1.3 Hz, 1H), 5.28 (dq, *J* = 17.0, 1.6 Hz, 1H), 5.64 (dd, *J* = 2.8, 2.1 Hz, 1H), 5.84 – 5.95 (m, 1H), 7.17 – 7.20 (m, 2H), 7.22 – 7.25 (m, 3H), 7.26 – 7.27 (m, 2H), 7.28 – 7.29 (m, 1H), 7.31 (dq, *J* = 3.3, 1.4 Hz, 3H), 7.32 – 7.34 (m, 1H), 7.34 – 7.40 (m, 5H), 7.55 (ddt, *J* = 8.7, 7.0, 1.3 Hz, 1H), 8.04 – 8.10 (m, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 68.4, 69.2(2C), 71.7, 71.8, 73.6, 74.5, 75.5, 78.4(2C), 97.1, 118.0, 127.7(3C), 127.7, 127.8, 128.2(3C), 128.4(2C), 128.5(3C), 128.5, 128.5, 130.0, 130.1(3C), 133.3, 133.6, 138.2, 138.5, 138.6, 165.9; IR ($CHCl_3$): 3460, 3030, 2920, 1600, 1453, 1203, 1058, 696 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{37}H_{38}O_7Na$, 617.2515, found 617.2509.

Allyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (**30**): Yield: (90%); $[\alpha]_D^{25}$ = 57.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 2.54 (s, 1H), 3.67 – 3.82 (m, 3H), 3.82 – 3.93 (m, 2H), 3.98 (dd, *J* = 12.9, 6.1 Hz, 1H), 4.05 (s, 1H), 4.17 (dd , *J* = 12.9, 5.1 Hz, 1H), 4.51 (t, *J* = 11.8 Hz, 2H), 4.62 – 4.74 (m, 3H), 4.82 (d, *J* = 10.8 Hz, 1H), 4.95 (d, *J* = 1.3 Hz, 1H), 5.14 – 5.20 (m, 1H), 5.25 (dd, *J* = 17.2, 1.5 Hz, 1H), 5.87 (ddt, *J* = 16.6, 10.6, 5.6 Hz, 1H), 7.17 (dd, *J* = 5.0, 2.6 Hz, 2H), 7.31 (ddd, *J* = 16.4, 12.1, 6.9 Hz, 13H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 68.1, 68.5, 69.02, 71.2, 72.1, 73.5, 74.4, 75.3, 80.3(2C), 98.5, 117.6, 127.7, 127.8, 127.9(2C), 128.0(2C), 128.0, 128.0, 128.4(2C), 128.5(2C), 128.6(2C), 133.8, 138.0, 138.3, 138.4; IR ($CHCl_3$): 3460, 3030, 2920, 1600, 1453, 1203, 1058, 696 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{30}H_{34}O_6Na$, 513.2253, found 513.2261.

Allyl 2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (**32**): Yield: (93%); $[\alpha]_D^{25}$ = 2.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.69 – 3.80 (m, 4H), 3.87 (dd, *J* = 11.4, 7.0 Hz, 3H), 3.96 (dd, *J* = 9.2, 2.1 Hz, 1H), 4.00 – 4.06 (m, 3 H), 4.11 (dt, *J* = 8.4, 5.3 Hz, 2H), 4.42 – 4.51 (m, 2H), 4.55 (dd, *J* = 11.7, 6.1 Hz, 3H), 4.64 – 4.79 (m, 5H), 4.86 (dd, *J* = 10.8, 5.9 Hz, 2H), 4.95 (s, 1H), 5.13 (d, *J* = 10.4 Hz, 1H), 5.20 (t, *J* = 8.6 Hz, 2H), 5.78 (m, 1H), 5.80 – 5.91 (m, 1H), 7.14 – 7.22 (m, 11H), 7.23 – 7.29 (m, 12H), 7.35 (dq, *J* = 12.4, 7.1, 6.6 Hz, 9H), 7.55 (t, *J* = 7.4 Hz, 1H), 8.07 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 68.0, 69.2, 69.3, 69.4, 71.8, 72.0, 72.1, 72.3, 73.4, 73.5, 74.5, 74.8, 75.2, 75.3, 75.3, 78.3, 79.9(2C), 98.0, 99.7, 117.3, 127.5, 127.6, 127.6(7C), 127.7, 128.0(2C), 128.2(2C), 128.2(2C), 128.3(2C), 128.4(2C), 128.4(4C), 128.4(4C), 128.5(2C), 130.1(3C), 130.1, 133.1, 133.9, 138.2, 138.4, 138.5(2C), 138.6, 138.6, 165.5; IR ($CHCl_3$): 3455,

3041, 2931, 1599, 1453, 1211, 1058, 697 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{64}H_{66}O_{12}Na$, 1049.4452, found 1049.4449.

Allyl 2,3-di-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranoside (**33**): Yield: (81% over two steps); $[\alpha]_D^{25}$ = 37.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.97 (s, 9H), 3.71 – 3.77 (m, 2H), 3.90 – 3.95 (m, 1H), 3.95 – 3.97 (m, 1H), 3.99 (dd, *J* = 2.9, 1.3 Hz, 1H), 4.08 – 4.11 (m, 1H), 4.12 – 4.18 (m, 1H), 4.38 – 4.51 (m, 4H), 5.02 (d, *J* = 1.0 Hz, 1H), 5.11 (dq, *J* = 10.3, 1.3 Hz, 1H), 5.23 (dq, *J* = 17.3, 1.7 Hz, 1H), 5.79 – 5.92 (m, 1H), 7.15 – 7.22 (m, 6H), 7.23 – 7.29 (m, 8H), 7.30 – 7.36 (m, 2H), 7.60 (td, *J* = 7.4, 6.8, 1.4 Hz, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.5, 27.0(3C), 64.0, 68.3, 72.0, 72.2, 82.5, 83.4(2C), 88.5, 105.4, 117.4, 127.7(3C), 127.8(3C), 127.9(2C), 127.9(2C), 128.5(2C), 128.5(2C), 129.8(2C), 133.6, 134.5, 135.8(2C), 135.8(2C), 137.8, 138.1; IR ($CHCl_3$): 3034, 2928, 1458, 1230, 1103, 698 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{38}H_{44}O_5NaSi$, 631.2855, found 631.2855.

Allyl 2,3-di-*O*-benzyl-5-*O*-(naphthalen-1-yl methyl)-α-D-arabinofuranoside (**34**): Yield: (81% over two steps); $[\alpha]_D^{25}$ = 43.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 3.65 (qd, *J* = 10.7, 4.5 Hz, 2H), 3.94 (dd, *J* = 6.7, 3.1 Hz, 1H), 3.97 – 4.04 (m, 1H), 4.06 (dd, *J* = 3.1, 1.2 Hz, 1H), 4.21 – 4.28 (m, 2H), 4.47 (dd, *J* = 11.9, 3.3 Hz, 2H), 4.55 (d, *J* = 11.7 Hz, 2H), 4.67 – 4.78 (m, 2H), 5.11 (s, 1H), 5.16 – 5.21 (m, 1H), 5.30 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.92 (dddd, *J* = 16.9, 10.9, 6.2, 5.0 Hz, 1H), 7.18 – 7.25 (m, 5H), 7.27 – 7.34 (m, 5H), 7.41 – 7.50 (m, 3H), 7.74 – 7.84 (m, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 68.2, 69.9, 72.1, 72.3, 73.6, 80.9, 83.7(2C), 88.5, 105.5, 117.4, 126.0(2C), 126.2, 126.7, 127.8(2C), 127.9(2C), 128.0, 128.0(2C), 128.3, 128.4(2C), 128.5(2C), 133.1, 133.4, 134.4, 135.7, 137.7, 138.0; IR ($CHCl_3$): 3029, 2917, 1455, 1213, 698 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{33}H_{34}O_5Na$, 533.2303, found 533.2306.

Allyl 3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-β-D-arabinofuranoside (**38**): Yield: (45%); $[\alpha]_D^{25}$ = -23.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.06 (s, 9H), 2.63 (d, *J* = 9.5 Hz, 1H), 3.75 (m, 2H), 3.98 (q, *J* = 6.2 Hz, 2H), 4.08 (q, *J* = 5.5 Hz, 1H), 4.18 (dd, *J* = 12.8, 5.2 Hz, 1H), 4.27 (dt, *J* = 9.8, 5.3 Hz, 1H), 4.62 (d, *J* = 11.8 Hz, 1H), 4 .76 (d, *J* = 11.8 Hz, 1H), 5.01 (d, *J* = 4.7 Hz, 1H), 5.13 (d, *J* = 10.4 Hz, 1H), 5.18 (d, *J* = 17.2 Hz, 1H), 5.80 (ddt, *J* = 16.4, 10.6, 5.7 Hz, 1H), 7.28 (dd, *J* = 14.5, 4.1 Hz, 5H), 7.34 – 7.44 (m, 6H), 7.68 (d, *J* = 7.0 Hz, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 27.0(3C), 65.5, 68.8, 72.0, 78.3, 82.6, 84.7(2C), 100.7, 117.7, 127.7, 127.7(2C), 127.8(2C), 128.5, 129.8, 129.8, 133.4, 133.5, 133.8, 135.7(6C), 138.2; IR

($CHCl_3$): 3451, 3030, 2929, 1455, 1213, 697 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{31}H_{38}O_5NaSi$, 541.2386, found 541.2390.

Allyl 2-O-(2,3-di-*O*-benzyl-5-*O*-(naphthalen-1-yl methyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-β-D-arabinofuranoside (**39**): Yield: (92%) $[\alpha]_D^{25}$ = -69.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.04 (s, 9H) , 3.58 (dd, *J* = 9.7, 4.5 Hz, 1H), 3.65 (td, *J* = 8.3, 7.0, 2.5 Hz, 1H), 3.71 – 3.76 (m, 2H), 3.90 (dd, *J* = 12.1, 6.0 Hz, 1H), 4.06 – 4.22 (m, 5H), 4.27 (td, *J* = 7.1, 6.2, 3.1 Hz, 1H), 4.41 (dd, *J* = 12.3, 2.2 Hz, 1H), 4.44 – 4.51 (m, 2H), 4.53 – 4.63 (m, 4H), 4.70 (dd, *J* = 11.9, 2.4 Hz, 1H), 4.80 (dd, *J* = 11.4, 2.2 Hz, 1H), 5.05 (d, *J* = 10.3 Hz, 1H), 5.12 – 5.19 (m, 3H), 5.69 – 5.81 (m, 1H), 7.23 (s, 10H), 7.29 – 7.38 (m, 11H), 7.39 (d, *J* = 2.0 Hz, 1H), 7.41 – 7.45 (m, 2H), 7.59 (s, 1H), 7.63 – 7.69 (m, 4H), 7.71 – 7.80 (m, 3H); 13C NMR (100.53 MHz, CDCl3): δ 19.4, 27.0(3C), 66.0, 68.2, 71.8, 72.3, 72.4, 72.8, 73.3, 79.5, 81.0(2C), 82.3, 82.9, 83.2, 84.0, 98.7, 99.0, 117.7, 125.8, 125.8, 126.1, 126.4, 127.6, 127.7(2C), 127.7, 127.8, 127.8(4C), 128.0, 128.2(2C), 128.4(2C), 128.4(2C), 128.5(2C), 129.8(2C), 133.1, 133.4, 133.5(2C), 134.0(2C), 135.7(6C), 135.8, 138.1, 138.3, 138.4; IR ($CHCl_3$): 3032, 2931, 1458, 1230, 1103, 698 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{61}H_{66}O_9NaSi$, 993.4374, found 993.4379.

Allyl 2-*O*-benzoyl-3-*O*-benzyl-β-D-arabinofuranoside (**10**): Yield: (87% over two steps); $[\alpha]_D^{25}$ = -115.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$):) δ 2.49 (s, 1H), 3.65 (ddd, *J* = 12.1, 8.2, 4.1 Hz, 1H), 3.79 (dt, *J* = 11.8, 2.5 Hz, 1H), 4.00 (ddt, *J* = 12.9, 5.8, 1.3 Hz, 1H), 4.15 – 4.21 (m, 2H), 4.58 – 4.7 3 (m, 3H), 5.09 (dq, *J* = 10.7, 1.2 Hz, 1H), 5.18 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.23 (dd, *J* = 6.8, 4.9 Hz, 1H), 5.42 (d, *J* = 4.7 Hz, 1H), 5.68 – 5.82 (m, 1H), 7.24 – 7.35 (m, 5H), 7.43 – 7.49 (m, 2H), 7.59 (tt, *J* = 7.0, 1.3 Hz, 1H), 8.02 – 8.08 (m, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 63.5, 69.8, 72.6, 79.7, 79.8, 82.2(2C), 100.0, 117.9, 127.8, 128.0, 128.6(3C), 129.4, 129.9(3C), 133.5(2C), 137.6, 166.0; IR ($CHCl_3$): 3463, 3041, 2929, 1599, 1453, 1276, 1108, 704 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{22}H_{24}O_6Na$, 407.1470, found 407.1465.

Allyl 2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(naphthalen-1-yl methyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)-β-D-arabinofuranoside (**40**): Yield: (81%); $[\alpha]_D^{25}$ = -0.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.06 (s, 9H), 3.55 – 3.63 (m, 3H), 3.77 – 3.86 (m, 2H), 3.93 (d, *J* = 15.1 Hz, 2H), 4.07 – 4.29 (m, 7H), 4.40 – 4.51 (m, 4H), 4.52 (s, 1H), 4.57 (d, *J* = 3.2 Hz, 2H), 4.60 – 4.69 (m, 5H), 4.97 – 5.05 (m, 2H), 5.10 (d, *J* = 4.3 Hz, 2H), 5.22 (d, *J* = 4.6 Hz, 1H), 5.40 (d, *J* = 4.6 Hz, 1H),

5.72 (ddd, *J* = 14.5, 10.5, 4.5 Hz, 1H), 7.18 – 7.22 (m, 6H), 7.24 (dd, *J* = 5.7, 3.3 Hz, 7H), 7.27 – 7.37 (m, 12H), 7.37 (s, 2H), 7.43 (t, *J* = 3.5 Hz, 4H), 7.53 – 7.62 (m, 2H), 7.65 – 7.73 (m, 5H), 7.74 – 7.81 (m, 2H), 8.04 (dd, *J* = 6.4, 2.1 Hz, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 27.0(3C), 64.0, 68.5, 68.9, 72.3, 72.3(2C), 72.4, 72.6, 73.3, 79.7, 79.8, 80.2, 82.3, 82.8, 83.2(2C), 83.9, 84.1, 85.8, 99.6, 100.2, 106.0, 117.1, 125.7, 125.9, 126.1, 126.4, 127.6(3C), 127.8(10C), 127.9, 128.0, 128.1(2C), 128.2, 128.4(2C), 128.4(2C), 128.5(2C), 128.6(2C), 129.6, 129.8(2C), 129.9(2C), 133.0, 133.3, 133.3, 133.5, 133.5, 133.9, 135.5, 135.7(6C), 137.8, 137.9, 138.1, 138.2, 166.0; IR ($CHCl_3$): 3057, 2927, 1598, 1456, 1268, 1107, 698 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{80}H_{84}O_{14}NaSi$, 1319.5527, found 1319.5518.

Allyl 2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)-β-D-arabinofuranoside (**42**): Yield: (76%); $[\alpha]_D^{25}$ = -37.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.03 (s, 9H), 3.53 – 3.66 (m, 4H), 3.70 – 3.87 (m, 8H), 3.88 – 4.01 (m, 4H), 4.02 – 4.13 (m, 6H), 4.14 – 4.25 (m, 3H), 4.39 (dd, *J* = 9.8, 3.2 Hz, 4H), 4.44 – 4.55 (m, 7H), 4.56 – 4.64 (m, 6H), 4.64 – 4.75 (m, 3H), 4.83 (dd, *J* = 10.9, 3.9 Hz, 2H), 4.96 (dd, *J* = 18.4, 1.6 Hz, 2H), 5.00 – 5.09 (m, 2H), 5.11 – 5.23 (m, 3H), 5.37 (d, *J* = 4.5 Hz, 1H), 5.64 – 5.74 (m, 1H), 5.76 (s, 1H), 7.13 – 7.22 (m, 17H), 7.25 (dtd, *J* = 8.6, 5.0, 4.4, 1.9 Hz, 30H), 7.33 – 7.37 (m, 10H), 7.42 (t, *J* = 7.7 Hz, 3H), 7.50 – 7.58 (m, 2H), 7 .66 (td, *J* = 8.1, 1.5 Hz, 4H), 7.98 – 8.08 (m, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 27.0(3C), 64.0, 68.6, 69.1(3C), 71.7, 72.2(3C), 72.2, 72.4, 72.4, 72.7, 73.4(4C), 74.3, 74.4, 75.2, 75.2, 75.3, 78.3, 79.3, 79.7, 79.8, 78.0, 82.2, 82.6, 83.7, 83.9(3C), 85.9, 98.6, 99.6, 99.7, 100.4, 105.8, 117.0, 127.4(3C), 127.4, 127.5(5C), 127.5(3C), 127.6, 127.8(6C), 128.0(3C), 128.1(3C), 128.1(3C), 128.2(3C), 128.3(4C), 128.3(3C), 128.4(4C), 128.4(3C), 128.4, 128.4, 128.5(5C), 128.5, 128.6, 129.6, 129.8(4C), 129.9(3C), 130.1(3C), 130.1, 133.1, 133.3, 133.5, 133.5, 133.9, 135.7, 135.8, 137.7, 138.0, 138.0, 138.0, 138.2, 138.3, 138.6, 138.6, 138.6, 138.6, 165.4, 166.0; IR ($CHCl_3$): 3045, 2929, 1599, 1433, 1253, 1107, 704 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{130}H_{136}O_{25}NaSi$, 2148.9071, found 2148.9023.

Allyl 2-*O*-benzoyl-3,5-di-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(naphthalen-1-yl methyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (**43**): Yield: (77%); $[\alpha]_D^{25}$ = -12.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz,

$CDCl_3$): δ 0.94 (s, 9H), 1.00 (s, 9H), 3.50 – 3.60 (m, 4H), 3.72 (ddd, *J* = 15.6, 8.5, 3.5 Hz, 4H), 3.78 (d, *J* = 10.9 Hz, 2H), 3.96 (s, 1H), 3.99 (dd, *J* = 4.5, 1.8 Hz, 2H), 4.03 – 4.14 (m, 8H), 4.14 – 4.22 (m, 3H), 4.27 (s, 2H), 4.40 (dt, *J* = 9.2, 3.1 Hz, 4H), 4.44 (s, 1H), 4.45 – 4.50 (m, 3H), 4.52 (s, 1H), 4.54 (d, *J* = 4.1 Hz, 2H), 4.57 (d, *J* = 3.1 Hz, 1H), 4.58 – 4.60 (m, 2H), 4.62 (d, *J* = 3.5 Hz, 1H), 4.64 – 4.70 (m, 2H), 5.06 (d, *J* = 1.2 Hz, 1H), 5.13 (dd, *J* = 10.5, 1.5 Hz, 1H), 5.16 (d, *J* = 4.4 Hz, 1H), 5.19 (s, 1H), 5.26 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.32 (d, *J* = 5.4 Hz, 3H), 5.86 (ddt, *J* = 16.7, 10.6, 5.6 Hz, 1H), 7.14 – 7.17 (m, 5H), 7.19 (dd, *J* = 5.9, 3.5 Hz, 6H), 7.22 (s, 10H), 7.24 – 7.26 (m, 7H), 7.26 – 7.30 (m, 11H), 7.33 (dd, *J* = 7.5, 1.9 Hz, 4H), 7.37 – 7.46 (m, 6H), 7.60 (ddd, *J* = 13.8, 7.8, 2.5 Hz, 11H), 7.65 – 7.73 (m, 4H), 7.74 – 7.79 (m, 2H), 7.92 – 8.01 (m, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.3, 19.4, 26.9(3C), 27.0(3C), 63.8, 63.9, 66.3, 67.8, 72.2, 72.3, 72.3, 72.4(3C), 72.6, 72.6, 73.2, 73.3, 77.4, 80.1, 80.1, 81.5, 82.1, 82.3, 82.8, 83.1, 83.5, 83.6, 83.7(2C), 83.9, 84.1, 85.1, 85.8, 99.9, 100.2, 105.1, 105.6, 106.9, 117.6, 125.7, 125.7, 125.9, 125.9, 126.1, 126.1, 126.3, 126.4, 127.5, 127.5(2C), 127.6, 127.7(3C), 127.8(17C), 127.9, 128.0(2C), 128.0(2C), 128.2(3C), 128.2(2C), 128.3(2C), 128.4(3C), 128.4(6C), 128.5(3C), 128.5(2C), 129.5, 129.7(2C), 129.9, 133.0, 133.3, 133.4, 133.5, 133.7, 134.0, 135.7(3C), 135.7(6C), 135.8(3C), 137.8, 138.0, 138.2, 138.3, 138.3, 138.4, 165.8; IR ($CHCl_3$): 3032, 2929, 1601, 1452, 1228, 1107, 695 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{131}H_{138}O_{22}NaSi_2$, 2141.9115, found 2141.8357.

Allyl 2-*O*-benzoyl-3,5-di-*O*-(2-*O*-(2,3-di-*O*-benzyl-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (**44**): Yield: (75%); $[\alpha]_D^{25}$ = -7.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.97 (s, 9H), 1.02 (s, 9H), 2.33 (d, *J* = 23.3 Hz, 2H), 3.47 – 3.61 (m, 3H), 3.67 (d, *J* = 11.4 Hz, 3H), 3.76 (d, *J* = 11.1 Hz, 3H), 3.90 (s, 1H), 3.96 – 4.03 (m, 4H), 4.06 – 4.14 (m, 3H), 4.15 – 4.21 (m, 3H), 4.22 – 4.31 (m, 4H), 4.36 – 4.43 (m, 2H), 4.44 – 4.50 (m, 3H), 4.51 – 4.65 (m, 6H), 4.67 – 4.77 (m, 3H), 5.07 (s, 1H), 5.12 – 5.19 (m, 2H), 5.20 – 5.22 (m, 1H), 5.23 – 5.36 (m, 4H), 5.88 (ddt, *J* = 15.4, 10.4, 4.9 Hz, 1H), 7.18 – 7.37 (m, 44H), 7.45 – 7.51 (m, 1H), 7.56 – 7.67 (m, 8H), 7.9 6 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.3, 19.4, 26.9(3C), 27.0(3C), 63.5, 63.6, 63.7, 63.8, 66.6, 67.9, 72.2, 72.4, 72.4, 72.4, 72.7, 72.7, 80.8(3C), 81.5, 81.8, 82.0, 82.1, 82.2, 82.2, 82.8, 82.8, 83.5, 84.0, 84.1, 84.9, 85.5, 99.4, 99.7, 105.1, 105.2, 106.5, 117.7, 127.6, 127.7(2C), 127.8(11C), 127.8(11C), 128.0(3C), 128.2(2C), 128.4(2C), 128.4(2C), 128.5(3C), 128.5(4C), 128.6(4C), 129.4, 129.8(3C), 129.9(2C), 133.2, 133.4, 133.4, 133.5(2C), 133.9, 135.7, 135.7, 135.8, 137.7,

137.8, 137.9, 138.0, 138.2, 138.2, 165.7; IR ($CHCl_3$): 3461, 3031, 2926, 1597, 1454, 1267, 1106, 701 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{109}H_{122}O_{22}NaSi_2$, 1861.7864, found 1861.7887.

Allyl 2-*O*-benzoyl-3,5-di-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranoside (**45**): Yield: (60%); $[\alpha]_D^{25}$ = -14.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.93 (s, 9H), 0.98 (s, 9H), 3.49 – 3.65 (m, 7H), 3.75 (dd, *J* = 20.5, 10.0 Hz, 14H), 3.87 (d, *J* = 9.0 Hz, 2H), 3.97 (d, *J* = 26.5 Hz, 13H), 4.08 (s, 6H), 4.16 (s, 2H), 4.22 – 4.31 (m, 3H), 4.39 (d, *J* = 12.2 Hz, 9H), 4.48 (d, *J* = 11.0 Hz, 9H), 4.59 (dd, *J* = 25.9, 12.1 Hz, 15H), 4.72 (d, *J* = 11.1 Hz, 2H), 4.80 – 4.93 (m, 6H), 5.04 – 5.12 (m, 2H), 5.13 – 5.25 (m, 4H), 5.30 (d, *J* = 15.0 Hz, 3H), 5.76 (s, 1H), 5.85 (s, 1H), 7.08 – 7.33 (m, 100H), 7.35 (d, *J* = 6.9 Hz, 6H), 7.43 (s, 2H), 7.50 – 7.67 (m, 10H), 7.92 – 8.14 (m, 7H); ^{13}C NMR (10.53 MHz, $CDCl_3$): δ 19.3, 19.4, 26.9(3C), 27.0(3C), 63.7, 63.8, 65.3, 67.8, 69.0, 69.1(3C), 69.6, 69.7, 70.3, 71.5, 71.7(2C), 72.1, 72.3(2C), 72.3(3C), 72.4, 72.5, 73.4(5C), 73.8, 74.3, 74.3, 74.5, 74.5, 74.7, 75.1, 75.2, 75.2, 75.3(2C), 75.3, 76.9, 77.4, 78.3, 78.3, 79.2, 79.4, 80.0(2C), 81.7, 82.2, 82.4, 82.8, 83.4, 83.5, 83.8(2C), 83.8, 83.9, 84.3, 85.1, 86.1, 98.6, 98.8, 9 9.7, 99.8, 100.0, 100.5, 105.1, 105.5, 106.8, 117.6, 127.4(2C), 127.4(2C), 127.5(10C), 127.6(6C), 127.6, 127.7(16C), 128.0, 128.0(6C), 128.1(3C), 128.1(4C), 128.2(2C), 128.2(4C), 128.3(10C), 128.4(17C), 128.5(10C), 128.5(5C), 128.7, 129.4, 129.7(4C), 129.9(2C), 130.1(5C), 133.1, 133.1, 133.3, 133.4, 133.5(2C), 133.6, 134.0, 135.7(3C), 135.7(6C), 135.8(3C), 137.6, 137.7, 137.9, 138.0, 138.1(2C), 138.2(2C), 138.2, 138.3, 138.3, 138.6, 138.6(2C), 138.6, 138.7, 138.7(2C), 165.4, 165.7, 166.0; IR ($CHCl_3$): 3035, 2925, 1599, 1454, 1268, 1106, 699 cm^{-1}; MALDI (TOF) m/z $[M + K]^+$ calcd for $C_{231}H_{242}O_{44}KSi_2$, 3816.59, found 3816.96.

Allyl 2-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (**46**): Yield: (80%); $[\alpha]_D^{25}$ = 12.2 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 2.10 (s, 3H), 2.53 – 2.60 (m, 2H), 2.68 (t, *J* = 6.4 Hz, 2H), 3.78 – 3.94 (m, 6H), 4.03 (dq, *J* = 15.5, 5.3, 4.6 Hz, 3H), 4.13 – 4.19 (m, 4H), 4.23 (dd, *J* = 13.3, 4.8 Hz, 1H), 4.38 (dd, *J* = 9.0, 5.0 Hz, 3H), 4.43 – 4.49 (m, 3H), 4.51 – 4.60 (m, 4H), 5.11 – 5.17 (m, 1H), 5.22 (s, 1H), 5.30 (d, *J* = 6.0 Hz, 2H), 5.35 – 5.41 (m,

6H), 5.43 (s, 1H), 5.50 (s, 1H), 5.58 (d, *J* = 6.5 Hz, 3H), 5.61 (s, 6H), 5.68 (d, *J* = 4.5 Hz, 1H), 5.89 (ddt, *J* = 16.6, 10.6, 5.4 Hz, 1H), 7.18 – 7.29 (m, 8H), 7.32 – 7.50 (m, 28H), 7.53 – 7.59 (m, 2H), 7.81 – 7.93 (m, 10H), 7.95 – 8.06 (m, 17H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 27.9, 29.9, 38.0, 62.4, 63.7, 65.6, 65.7, 66.0, 66.0, 66.1, 67.8(2C), 77.0, 77.2, 77.3, 77.4, 77.7, 77.8(2C), 80.7, 81.2, 81.5(3C), 81.6(2C), 81.8, 82.1, 82.1, 82.6, 82.8, 82.9, 83.7, 105.1, 105.4, 105.8(2C), 105.9, 105.9, 106.0, 117.4, 128.3(2C), 128.3(2C), 128.4(3C), 128.5(2C), 128.5(2C), 128.6(4C), 128.6(7C), 128.6(4C), 129.0, 129.0, 129.1, 129.1(2C), 129.1, 129.1, 129.2, 129.2, 129.2, 129.3, 129.3, 129.3, 129.8, 129.8, 129.8, 129.9(10C), 129.9(9C), 133.2(2C), 133.3, 133.3, 133.4, 133.4(2C), 133.5(2C), 133.5(2C), 133.5(2C), 133.6, 133.7, 133.9(2C), 165.1(2C), 165.2(3C), 165.2, 165.6, 165.7(2C), 165.7, 165.7(2C), 166.1, 172.5, 206.4; IR ($CHCl_3$): 3039, 2925, 1752, 1599, 1448, 1231, 1106, 705 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{134}H_{120}O_{44}Na$, 2455.7049, found 2455.5154.

Allyl 2-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (**47**): Yield: (85%); $[\alpha]_D^{25}$ = 15.2 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.99 (s, 9H), 2.10 (s, 3H), 2.56 (dd, *J* = 10.3, 4.4 Hz, 2H), 2.68 (t, *J* = 6.6 Hz, 2H), 3.44 – 3.57 (m, 2H), 3.62 (dd, *J* = 18.6, 8.4 Hz, 3H), 3.68 – 3.78 (m, 6H), 3.80 (s, 1H), 3.82 – 3.88 (m, 7H), 3.94 (dd, *J* = 14.2, 6.6 Hz, 4H), 4.01 (dt, *J* = 14.4, 5.0 Hz, 6H), 4.09 (s, 4H), 4.17 (d, *J* = 11.3 Hz, 4H), 4.23 (dd, *J* = 13.1, 5.0 Hz, 1H), 4.28 (s, 1H), 4.32 (s, 1H), 4.35 (s, 1H), 4.40 (d, *J* = 11.4 Hz, 7H), 4.44 (d, *J* = 4.0 Hz, 2H), 4.47 (d, *J* = 5.3 Hz, 2H), 4.48 – 4.53 (m, 3H), 4.56 (d, *J* = 10.5 Hz, 8H), 4.62 (d, *J* = 11.5 Hz, 2H), 4.72 (d, *J* = 11.0 Hz, 1H), 4.83 (d, *J* = 10.9 Hz, 2H), 4.90 (s, 1H), 4.99 (s, 1H), 5.07 (d, *J* = 3.4 Hz, 1H), 5.11 – 5.18 (m, 2H), 5.22 (s, 1H), 5.26 – 5.31 (m, 3H), 5.32 – 5.41 (m, 5H), 5.43 (s, 2H), 5.51 (s, 1H), 5.57 (s, 3H), 5.59 – 5.64 (m, 8H), 5.68 (d, *J* = 4.5 Hz, 1H), 5.76 (s, 1H), 5.89 (ddt, *J* = 15.5, 10.4, 5.4 Hz, 1H), 7.08 (d, *J* = 7.3 Hz, 3H), 7.11 (s, 2H), 7.14 (d, *J* = 4. 3 Hz, 7H), 7.17 – 7.20 (m, 13H), 7.21 – 7.27 (m, 29H), 7.28 – 7.30 (m, 7H), 7.32 (d, *J* = 4.0 Hz, 5H), 7.36 (dd, *J* = 11.6, 5.2 Hz, 21H), 7.40 (s, 2H), 7.43 – 7.50 (m, 10H), 7.55 (d,

J = 8.4 Hz, 2H), 7.62 (t, *J* = 8.1 Hz, 4H), 7.85 (t, *J* = 9.5 Hz, 8H), 7.92 (d, *J* = 8.1 Hz, 2H), 7.94 – 8.00 (m, 13H), 8.02 (s, 1H), 8.03 – 8.08 (m, 6H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 27.0(3C), 27.9, 29.8, 38.0, 63.7, 63.9, 65.7, 65.7, 65.8, 65.8, 66.1, 67.8, 69.0, 69.1, 69.1, 69.6, 71.7, 72.1, 72.2(2C), 72.2(2C), 72.3, 72.3, 72.4, 72.4, 73.4(3C), 74.3, 74.5, 75.1, 75.2, 75.3, 76.9, 77.0, 77.3, 77.4, 77.7, 78.3, 79.4, 80.0, 80.8, 81.2, 81.5(3C), 81.7, 81.8, 82.0, 82.1, 82.2, 82.3(2C), 82.6, 82.8, 82.9(2C), 83.1, 83.2, 83.5, 83.8, 84.1, 86.0, 98.7, 99.7, 100.7, 105.1, 105.4, 105.9(2C), 106.0, 106.0, 106.0, 106.2(2C), 117.4, 127.3(3C), 127.5(8C), 127.6(4C), 127.7(2C), 127.7(5C), 127.8(7C), 127.9, 128.0(3C), 128.0(3C), 128.1(3C), 128.2(3C), 128.2(3C), 128.3(8C), 128.4(14C), 128.4(3C), 128.5(3C), 128.5(5C), 128.5(12C), 128.6(3C), 129.0, 129.1, 129.1, 129.1, 129.2, 129.2(2C), 129.2(2C), 129.3(3C), 129.4, 129.6, 129.7(2C), 129.9(16C), 129.9(7C), 130.0(4C), 130.1, 133.1(2C), 133.1, 133.2, 133.3, 133.4(3C), 133.4(3C), 133.5(2C), 133.5, 133.6, 134.0(2C), 135.7, 135.7(3C), 137.7(3C), 137.8, 138.0, 138.1, 138.2, 138.2, 138.5, 138.6, 138.6, 138.6, 165.1(2C), 165.2, 165.2(2C), 165.3, 165.3, 165.4, 165.6(3C), 165.7(3C), 165.7, 172.5, 206.3; IR ($CHCl_3$): 3033, 2928, 1730, 1620, 1453, 1263, 1105, 703 cm^{-1}; MALDI (TOF) m/z $[M + Na]^+$ calcd for $C_{261}H_{250}O_{68}NaSi$, 4524.5839, found 4524.9119.

Allyl 2-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (**48**): Yield: (80%); $[\alpha]_D^{25}$ = 16.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$):) δ 0.99 (s, 9H), 3.52 (dd, *J* = 17.8, 8.7 Hz, 2H), 3.62 (dd, *J* = 18.7, 8.6 Hz, 3H), 3.67 – 3.80 (m, 7H), 3.84 (d, *J* = 7.4 Hz, 8H), 3.91 – 4.04 (m, 12H), 4.06 – 4.11 (m, 4H), 4.12 – 4.17 (m, 3H), 4.18 – 4.26 (m, 2H), 4.27 (s, 1H), 4.39 (d, *J* = 11.4 Hz, 8H), 4.45 (dd, *J* = 17.1, 5.1 Hz, 6H), 4.51 (d, *J* = 6.2 Hz, 2H), 4.54 – 4.64 (m, 8H), 4.72 (d, *J* = 11.0 Hz, 1H), 4.83 (dd, *J* = 10.9, 2.2 Hz, 2H), 4.90 (s, 1H), 4.98 (s, 1H), 5.07 (d, *J* = 3.9 Hz, 1H), 5.11 – 5.17 (m, 2H), 5.21 (s, 1H), 5.26 (s, 1H), 5.30 (s, 2H), 5.32 – 5.40 (m, 5H), 5.43 (s, 2H), 5.48 (s, 1H), 5.58 (dd, *J* = 15.0, 5.7 Hz, 9H), 5.63 (d, *J* = 4.5 Hz, 1H), 5.67 (d, *J* = 4.2 Hz, 1H), 5.76 (s, 1H), 5.88 (dq, *J* = 15.6, 4.9 Hz, 1H), 7.06 – 7.15 (m, 14H), 7.17 – 7.25 (m, 38H), 7.28 (d, *J* = 3.1 Hz, 10H), 7.31 (s, 3H), 7.36 (dt, *J* = 15.4, 7.9 Hz, 24H), 7.43 – 7.50 (m, 9H), 7.54 (t,

J= 7.5 Hz, 2H), 7.61 (t, *J* = 8.1 Hz, 4H), 7.81 – 7.88 (m, 8H), 7.91 (d, *J* = 7.4 Hz, 2H), 7.95 – 8.02 (m, 16H), 8.04 – 8.08 (m, 5H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 27.0, 62.4, 64.0, 65.7(2C), 65.8, 66.0, 66.1, 67.8, 69.0, 69.1, 69.1, 69.6, 71.7(2C), 72.1, 72.2(2C), 72.3(2C), 72.3(2C), 72.3, 72.4, 72.5, 73.4, 73.4, 74.3, 74.5, 75.1, 75.2, 75.3, 77.0, 77.2, 77.2, 77.3, 77.4, 77.8, 78.3, 79.4, 80.0, 80.8, 81.6(3C), 81.7, 81.7, 81.8(2C), 82.0, 82.1, 82.3(2C), 82.6, 82.8(3C), 82.9, 83.2, 83.5, 83.8(2C), 83.8, 84.1, 86.0, 98.7, 99.7, 100.7, 105.1, 105.4, 105.9(4C), 106.0, 106.2(2C), 117.4, 127.4(3C), 127.5(8C), 127.6(5C), 127.7(3C), 127.7(3C), 127.8(2C), 127.8(3C), 127.9, 128.0 (3C), 128.0(3C), 128.1(3C), 128.2(3C), 128.3(2C), 128.3(5C), 128.3(3C), 128.4(8C), 128.4(10C), 128.4(2C), 128.5(4C), 128.5(6C), 128.6(10C), 129.1(2C), 129.1, 129.2, 129.2(2C), 129.3, 129.3(3C), 129.4, 129.6, 129.8(2C), 129.9(20C), 130.0(5C), 130.1(3C), 130.1, 133.1(2C), 133.2, 133.3, 133.3(2C), 133.4(3C), 133.5(4C), 133.6, 133.6, 134.0(2C), 135.7, 135.8, 137.7, 137.9, 138.0, 138.1, 138.2, 138.3, 138.6, 138.6, 138.6, 138.7, 165.2(2C), 165.2(3C), 165.3, 165.4, 165.5, 165.6(3C), 165.7, 165.7(2C), 166.1; IR ($CHCl_3$): 3430, 3030, 2934,, 1590, 1447, 1229, 1105, 694 cm^{-1}; MALDI (TOF) m/z $[M + Na]^+$ calcd for $C_{256}H_{244}O_{66}Na_2Si$, 4426.5471, found 4426.8154.

Allyl 2-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2-*O*-benzoyl-3,5-di-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2-*O*-benzoyl-3-*O*-benzyl-5-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (**49**): Yield: (80%); $[\alpha]_D^{25}$ = 5.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (s, 9H), 0.95 (s, 9H), 0.98 (s, 9H), 3.44 – 3.54 (m, 5H), 3.56 (dd, *J* = 15.0, 6.6 Hz, 4H), 3.60 – 3.65 (m, 4H), 3.68 (dd, *J* = 21.6, 9.0 Hz, 9H), 3.72 – 3.80 (m, 11H), 3.84 (t, *J* = 12.2 Hz, 9H), 3.88 – 3.95 (m, 9H), 3.95 – 4.04 (m, 19H), 4.09 (d, *J* = 16.0 Hz, 12H), 4.13 – 4.24 (m, 5H), 4.27 (d, *J* = 6.7 Hz, 2H), 4.31 (dd, *J* = 10.8, 3.7 Hz, 5H), 4.33 – 4.36 (m, 4H), 4.36 – 4.40 (m, 11H), 4.43 (d, *J* = 8.5 Hz, 5H), 4.44 – 4.47 (m, 4H), 4.48 – 4.51 (m, 7H), 4.52 – 4.57 (m, 16H), 4.60 (dd, *J* = 13.6, 8.2 Hz, 5H), 4.71 (dd, *J* = 10.9, 5.7

Hz, 3H), 4.82 (dd, *J* = 10.4, 6.8 Hz, 6H), 4.85 – 4.89 (m, 3H), 4.98 (s, 1H), 5.06 (s, 2H), 5.09 – 5.18 (m, 6H), 5.20 (s, 2H), 5.26 (d, *J* = 3.6 Hz, 2H), 5.32 (dd, *J* = 21.2, 5.0 Hz, 4H), 5.37 (d, *J* = 11.7 Hz, 2H), 5.42 (s, 2H), 5.53 (d, *J* = 21.6 Hz, 4H), 5.57 – 5.63 (m, 6H), 5.67 (d, *J* = 3.9 Hz, 1H), 5.75 (s, 3H), 5.85 (ddq, *J* = 23.3, 12.6, 6.7, 5.9 Hz, 1H), 7.01 (dt, J = 12.1, 6.5 Hz, 2H), 7.06 (dd, *J* = 14.6, 7.1 Hz, 12H), 7.09 – 7.15 (m, 30H), 7.18 (dq, *J* = 14.1, 7.5, 6.8 Hz, 48H), 7.21 – 7.31 (m, 86H), 7.31 – 7.36 (m, 22H), 7.36 – 7.40 (m, 5H), 7.41 – 7.49 (m, 7H), 7.50 – 7.56 (m, 6H), 7.56 – 7.63 (m, 9H), 7.75 – 7.81 (m, 3H), 7.84 (dd, *J* = 13.0, 7.7 Hz, 4H), 7.88 – 7.93 (m, 4H), 7.97 (dd, *J* = 18.9, 7.6 Hz, 12H), 8.01 – 8.07 (m, 10H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4(3C), 26.9(9C), 63.6, 63.7(2C), 64.0(2C), 65.4, 65.6(2C), 65.6(2C), 65.7(2C), 65.7, 65.8(2C), 65.8(2C), 66.3, 67.8(3C), 69.0(2C), 69.0, 69.1(5C), 69.1, 69.6(2C), 69.7, 71.7(3C), 71.9, 72.0, 72.1, 72.3(7C), 72.3(2C), 72.4, 72.5, 73.4(3C), 73.4(3C), 73.4(4C), 74.3(2C), 74.3, 74.5(2C), 75.0(2C), 75.1, 75.2(2C), 75.3(2C), 75.3, 75.3(2C), 75.3(3C), 78.3, 78.3, 79.2, 79.4, 79.4, 80.0(3C), 81.0, 81.5, 81.6(3C), 81.7, 81.7, 81.8, 81.9, 82.0(2C), 82.3(2C), 82.3, 82.3(2C), 82.5, 82.5, 82.8(2C), 83.0, 83.0, 83.1, 83.4, 83.4, 83.5, 83.8(2C), 83.9, 84.2, 84.2, 84.4(2C), 85.6, 86.0, 86.3, 98.8(2C), 98.8, 99.7, 99.7(2C), 100.5, 100.7(2C), 105.1, 105.4, 105.9(4C), 106.0(2C), 106.2(2C), 106.4, 107.3, 117.4, 127.4(6C), 127.4, 127.5(2C), 127.5(6C), 127.5(12C), 127.5(12C), 127.6(10C), 127.7(3C), 127.7(10C), 127.8(7C), 127.8(7C), 127.8(6C), 127.9, 127.9(2C), 128.0(2C), 128.0(6C), 128.1(5C), 128.1(6C), 128.2(2C), 128.2(6C), 128.3(4C), 128.3(18C), 128.4(14C), 128.4(18C), 128.5(6C), 128.5(5C), 128.5(8C), 128.5(5C), 128.6(4C), 128.6(4C), 128.7, 129.1, 129.1, 129.2, 129.2, 129.2, 129.2(2C), 129.3(2C), 129.3, 129.4, 129.4, 129.5, 129.6(2C), 129.7(3C), 129.8(3C), 129.8(2C), 129.9(3C), 129.9(6C), 129.9(6C), 130.0(2C), 130.0(3C), 130.1(6C), 130.1(2C), 130.2, 133.0, 133.1, 133.1(2C), 133.2(2C), 133.3, 133.4(2C), 133.4(2C), 133.4(2C), 133.5(2C), 133.5, 133.5, 133.6, 134.0(2C), 135.6(2C), 135.7(3C), 135.7(3C), 135.8(3C), 137.7, 137.7, 137.9, 137.9, 138.0, 138.0, 138.1, 138.1, 138.1, 138.2, 138.2, 138.2, 138.2, 138.3(2C), 138.3, 138.6(2C), 138.6(3C), 138.6(2C), 138.6, 138.7(2C), 138.7, 138.7, 139.4, 165.2, 165.2, 165.2(3C), 165.3, 165.3, 165.4, 165.4, 165.5(2C), 165.6(2C), 165.7(4C), 165.7; IR ($CHCl_3$): 3035, 2926, 1600, 1444, 1266, 1106, 699 cm^{-1}; MALDI (TOF) m/z $[M + Na]^+$ calcd for $C_{484}H_{480}O_{109}NaSi_2$, 8147.1390, found 8144.5210.

Propyl 3-*O*-(5-*O*-(5-*O*-(5-*O*-(3,5-di-*O*-(2-*O*-(5-*O*-(2-*O*-(α-D-mannopyranosyl)-α-D-mannopyranosyl)-β-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-5-*O*-(5-*O*-(5-*O*-(5-*O*-(5-

***O*-(2-*O*-(5-*O*-(2-*O*-(α-D-mannopyranosyl)-α-D-mannopyranosyl)-β-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranoside (50)**: Yield: (54%over three steps); $[\alpha]_D^{25}$ = 32.5 (5mg/ml, H_2O:MeOH=4:1); ^{1}H NMR (600 MHz, D_2O): 0.81(t, *J* = 7.4 Hz, 3H), 1.51 (dd, *J* = 14.1, 7.1 Hz, 2H), 3.45 (dd, *J* = 16.3, 6.5 Hz, 1H), 3.52 (dd, *J*= 19.3, 9.6 Hz, 6H), 3.65 – 3.58 (m, 14H),3.68 (dd, *J* = 15.7, 8.4 Hz, 12H), 3.74 (dd, *J* = 11.1,7.3 Hz, 10H), 3.79 (t, *J* = 9.7 Hz, 15H), 3.85 (dd, *J* = 9.9, 6.9 Hz, 4H), 3.92 (s, 15H), 4.06 –3.97 (m, 23H), 4.08 (s, 3H), 4.12 (d, *J* = 3.9 Hz, 7H), 4.19 (d, *J* = 13.9 Hz, 3H), 4.93 (s, 3H),4.96 (s, 1H), 4.99 (s, 6H), 5.02 (s, 1H), 5.06 (d, *J* = 6.5 Hz, 7H), 5.09 (s, 2H), 5.16 (s, 1H);^{13}C NMR (150.99 MHz, D_2O): δ 9.8, 22.0, 58.9, 60.6, 60.6, 60.7(2C), 61.1(2C), 61.7,66.1(2C), 66.2, 66.6, 66.6(2C), 66.6, 66.8, 66.8, 66.9(6C), 67.8, 68.2(3C), 69.9(3C), 70.0,70.1(2C), 70.2(2C), 72.8(2C), 73.2(3C), 74.0(2C), 75.0(3C), 75.0, 75.1, 76.0(3C), 76.5, 76.6,76.6, 76.7, 76.7, 76.7, 76.7, 78.7(2C), 79.1, 79.1(2C), 79.7(2C), 79.7(2C), 80.8, 80.8(4C),80.8, 80.8, 81.0, 81.3, 81.6, 81.7, 82.1, 82.2, 82.3, 82.3(2C), 82.4, 83.1, 83.1(2C), 83.1, 86.9,86.9, 87.0, 87.4, 98.2(3C), 100.4, 100.5, 100.7, 102.3(3C), 105.4, 105.5, 105.6, 107.2, 107.3,107.4, 107.5(2C), 107.5(4C); HRMS (MALDI-TOF) m/z [M + Na]$^+$calcd for $C_{114}H_{188}O_{91}Na$,3037.00, found 3036.55.

Allyl 2-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-α-D-arabinofuranoside (51a): Yield: (81%); $[\alpha]_D^{25}$ = 28.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 2.17 (s, 3H), 2.57 – 2.65 (m, 2H), 2.75 (t, *J* = 6.5 Hz, 2H), 4.09 (ddt, *J* = 12.9, 6.2, 1.3 Hz, 2H), 4.27 – 4.30 (m, 1H), 4.30 – 4.35 (m, 2H), 4.35 – 4.40 (m, 1H), 5.14 (dd, *J* = 2.6, 0.9 Hz, 1H), 5.24 (dq, *J* = 10.4, 1.3 Hz, 1H), 5.30 (s, 1H), 5.35 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.94 (dddd, *J* = 16.6, 10.5, 6.2, 5.2 Hz, 1H), 7.43 – 7.51 (m, 2H), 7.60 (tt, *J* = 7.0, 1.3 Hz, 1H), 8.01 – 8.06 (m, 2H);^{13}C NMR (100.53 MHz, $CDCl_3$): δ 28.0, 29.9, 38.0, 63.7, 68.5, 77.3, 81.8, 85.6(2C), 104.6, 118.0, 128.7, 129.1, 130.0(2C), 133.6, 133.8, 166.7, 172.7, 206.7; IR ($CHCl_3$): 3035, 2926, 1600, 1444, 1266, 1106, 699 cm^{-1}; HRMS (TOF) m/z [M + Na]$^+$ calcd for $C_{20}H_{24}O_8Na$, 415.1369, found 415.1372.

Allyl 2, 5-di-*O*-benzoyl-α-D-arabinofuranoside (51b): Yield: (76%); $[\alpha]_D^{25}$ = 33.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 4.11 (ddt, *J* = 12.9, 6.3, 1.2 Hz, 1H), 4.25 (dd, *J* = 5.7, 2.4 Hz, 1H), 4.32 (ddt, *J* = 13.0, 5.2, 1.4 Hz, 1H), 4.47 (td, *J* = 5.5, 3.9 Hz, 1H), 4.53 (dd, *J* = 11.8, 5.4 Hz, 1H), 4.65 (dd, *J* = 11.8, 3.8 Hz, 1H), 5.16 – 5.20 (m, 1H), 5.24 (dq, *J* = 10.5, 1.3 Hz, 1H), 5.31 – 5.39 (m, 2H), 5.89 – 6.02 (m, 1H), 7.31 – 7.39 (m, 2H), 7.41 – 7.55 (m, 4H), 7.58 – 7.65 (m, 2H), 8.03 (ddd, *J* = 8.7, 2.5, 1.3 Hz, 2H);^{13}C NMR (100.53 MHz, $CDCl_3$): δ

64.0, 68.5, 77.5, 82.1, 85.8(2C), 104.7, 118.1, 128.5, 128.6, 128.7, 129.1, 129.4, 129.9, 130.0, 130.3, 133.3, 133.7, 133.9, 133.9, 166.5, 166.8; IR ($CHCl_3$): 3033, 2926, 1601, 1447, 1255, 1106, 699 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{22}H_{22}O_7Na$, 421.1263, found 421.1268

Allyl 2-*O*-benzoyl-3-*O*-[2, 3-di-*O*-benzoyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl]-5-*O*-(4-oxopentanoyl)-α-D-arabinofuranoside (52a): Yield: (95%); $[\alpha]_D^{25}$ = 15.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.00 (s, 9H), 2.08 (s, 3H), 2.50 – 2.58 (m, 2H), 2.60 – 2.66 (m, 2H), 3.98 (d, *J* = 4.8 Hz, 2H), 4.06 – 4.15 (m, 1H), 4.24 – 4.34 (m, 3H), 4.38 (dt, *J* = 9.4, 5.1 Hz, 2H), 4.46 (dd, *J* = 11.6, 2.8 Hz, 1H), 5.18 (dd, *J* = 10.4, 1.4 Hz, 1H), 5.26 (s, 1H), 5.32 – 5.38 (m, 1H), 5.40 (d, *J* = 1.0 Hz, 1H), 5.53 – 5.61 (m, 3H), 5.86 – 6.00 (m, 1H), 7.27 – 7.39 (m, 8H), 7.45 (dt, *J* = 15.3, 7.8 Hz, 4H), 7.52 – 7.62 (m, 3H), 7.66 – 7.72 (m, 4H), 7.93 (dd, *J* = 8.2, 1.2 Hz, 2H), 8.05 (ddd, *J* = 10.9, 8.4, 1.2 Hz, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 26.8(3C), 27.9, 29.9, 37.9, 63.5, 63.7, 68.0, 77.4, 80.8, 82.0, 82.5, 84.1(2C), 105.1, 105.4, 117.6, 127.8(3C), 128.5(2C), 128.6(2C), 128.6(2C), 129.2, 129.4, 129.6(2C), 129.8, 129.9(2C), 130.0(2C), 130.1(2C), 133.2, 133.3, 133.5, 133.6, 133.9, 135.7(2C), 135.8(2C), 165.3, 165.5, 165.6, 172.6, 206.4; IR ($CHCl_3$): 3031, 2926, 16011, 1446, 1269, 1106, 699 cm^{-1}; MALDI (TOF) m/z $[M + Na]^+$ calcd for $C_{55}H_{58}O_{14}NaSi$, 993.34, found 993.25.

Allyl 2-*O*-benzoyl-3-*O*-[2, 3-di-*O*-benzoyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl]-α-D-arabinofuranoside (53a): Yield: (91%); $[\alpha]_D^{25}$ = 16.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.01 (s, 9H), 3.84 (dd, *J* = 11.9, 3.5 Hz, 1H), 3.93 (dd, *J* = 12.1, 2.6 Hz, 1H), 3.97 (d, *J* = 4.6 Hz, 2H), 4.09 (dd, *J* = 13.3, 6.0 Hz, 1H), 4.23 – 4.30 (m, 2H), 4.32 – 4.37 (m, 1H), 4.43 (d, *J* = 5.7 Hz, 1H), 5.17 (d, *J* = 10.5 Hz, 1H), 5.23 (s, 1H), 5.31 – 5.38 (m, 1H), 5.40 (s, 1H), 5.55 (d, *J* = 5.1 Hz, 3H), 5.92 (ddt, *J* = 17.1, 10.9, 5.6 Hz, 1H), 7.28 – 7.48 (m, 12H), 7.51 – 7.61 (m, 3H), 7.68 (d, *J* = 7.0 Hz, 4H), 7.90 – 7.96 (m, 2H), 7.99 – 8.08 (m, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 26.9(3C), 62.0, 63.8, 67.9, 77.4, 80.7, 82.0, 83.0, 83.3, 84.1(2C), 105.0, 105.7, 117.6, 127.8(3C), 128.5(2C), 128.6(2C), 128.6(2C), 129.2, 129.4, 129.5, 129.8(2C), 129.9(2C), 130.0(2C), 130.1(2C), 133.2, 133.3, 133.5(2C), 133.5, 133.9, 135.7(2C), 135.8(2C), 165.4, 165.6, 165.6; IR ($CHCl_3$): 3033, 2927, 1598, 1442, 1260, 1105, 697 cm^{-1}; MALDI (TOF) m/z $[M + Na]^+$ calcd for $C_{50}H_{52}O_{12}NaSi$, 895.31, found 895.21.

Allyl 2-*O*-benzoyl-3-*O*-[2,3-di-*O*-benzoyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl]-5-*O*-[2, 5-di-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl]-α-D-arabinofuranoside (54): Yield: (92%); $[\alpha]_D^{25}$ = 30.2 (*c* = 1.0,

$CHCl_3$); ^1H NMR (399.78MHz, $CDCl_3$): δ 0.97 (s, 9H), 2.09 (s, 3H), 2.51 (td, *J* = 7.1, 6.6, 3.6 Hz, 2H), 2.61 – 2.72 (m, 2H), 3.94 (dd, *J* = 15.1, 3.6 Hz, 3H), 4.02 – 4.09 (m, 2H), 4.20 – 4.32 (m, 2H), 4.34 – 4.40 (m, 3H), 4.41 – 4.47 (m, 3H), 4.51 (dt, *J* = 8.0, 3.7 Hz, 2H), 4.61 (dd, *J* = 11.4, 2.4 Hz, 1H), 5.09 – 5.15 (m, 1H), 5.20 (s, 1H), 5.27 – 5.36 (m, 3H), 5.41 (dd, *J* = 3.8, 1.3 Hz, 2H), 5.51 (dd, *J* = 4.8, 1.3 Hz, 2H), 5.54 (d, *J* = 4.5 Hz, 1H), 5.57 (s, 1H), 5.66 (s, 1H), 5.81 – 5.95 (m, 1H), 7.18 (t, *J* = 7.9 Hz, 2H), 7.23 – 7.31 (m, 6H), 7.32 – 7.45 (m, 15H), 7.46 – 7.52 (m, 2H), 7.54 – 7.60 (m, 2H), 7.62 – 7.68 (m, 4H), 7.86 – 7.95 (m, 6H), 7.97 – 8.06 (m, 8H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.3, 26.8, 27.9(3C), 29.9, 38.0, 63.1, 63.7, 63.8, 66.6, 67.9, 77.3, 77.6, 80.9, 81.0, 81.3, 81.5, 81.6, 81.7, 82.0, 82.7, 82.9, 84.2(2C), 105.1, 105.3, 105.5, 106.0, 117.5, 126.2, 127.8(3C), 128.4(2C), 128.5(2C), 128.5(2C), 128.6(2C), 128.6(2C), 128.6(3C), 129.1, 129.1, 129.2, 129.3, 129.4, 129.5, 129.7, 129.7(2C), 129.8(2C), 129.9, 129.9(2C), 130.0(2C), 130.0(2C), 130.0(4C), 130.1(2C), 133.2, 133.2, 133.3, 133.4(2C), 133.5, 133.6, 133.7, 134.0, 135.7(2C), 135.8(2C), 165.1, 165.3, 165.5, 165.6, 165.7(2C), 166.2, 172.6, 206.6; IR ($CHCl_3$): 3034, 2924, 1630, 1442, 1266, 1106, 698 cm^{-1};HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{93}H_{90}O_{26}NaSi$, 1674.5421, found 1674.5426.

Allyl 2,3-di-*O*-benzoyl-5-*O*-[2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-{2-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)-5-*O*-(2, 5-di-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl}-α-D-arabinofuranosyl)-α-D-arabinofuranosyl] -α-D-arabinofuranoside (56): Yield: (93%); $[\alpha]_D^{25}$ = 28.8 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78MHz, $CDCl_3$): δ 0.95 (s, 9H), 2.08 (s, 3H), 2.44 – 2.56 (m, 2H), 2.66 (dt, *J* = 12.2, 7.0 Hz, 2H), 3.87 – 4.00 (m, 6H), 4.02 – 4.11 (m, 2H), 4.18 (dt, *J* = 9.0, 4.4 Hz, 3H), 4.24 – 4.30 (m, 2H), 4.32 – 4.35 (m, 1H), 4.36 – 4.49 (m, 7H), 4.51 – 4.65 (m, 4H), 5.17 – 5.22 (m, 1H), 5.26 (s, 1H), 5.31 (dd, *J* = 4.9, 3.2 Hz, 2H), 5.36 – 5.41 (m, 5H), 5.42 (s, 1H), 5.47 – 5.67 (m, 11H), 5.87 – 6.00 (m, 1H), 7.15 (dt, *J* = 10.4, 7.7 Hz, 5H), 7.21 – 7.30 (m, 14H), 7.31 – 7.42 (m, 20H), 7.46 – 7.57 (m, 6H), 7.61 – 7.69 (m, 4H), 7.82 (dd, *J* = 15.8, 8.0 Hz, 4H), 7.89 (ddd, *J* = 9.6, 5.1, 2.2 Hz, 8H), 7.95 – 8.05 (m, 14H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.3, 26.8(3C), 27.8, 29.9, 37.9, 63.0, 63.5, 63.7, 65.7, 65.9, 66.0, 67.9, 77.3(3C), 77.4(2C), 77.6, 80.6, 80.9, 81.3, 81.4, 81.7(2C), 81.8, 82.0(3C), 82.1, 82.2, 82.3, 82.6, 82.9, 84.0(2C), 104.9, 105.0, 105.6, 105.9(4C), 117.5, 127.7(7C), 128.3, 128.4(8C), 128.6(14C), 129.1(2C), 129.1(2C), 129.2(2C), 129.2(2C), 129.3, 129.3(3C), 129.4, 129.7(7C), 129.8(7C), 129.9(10C), 130.0(7C), 130.0, 133.0, 133.2(2C), 133.2(2C), 133.3, 133.3,

133.5(2C), 133.5(2C), 133.6, 133.9, 135.7, 135.8, 164.9, 165.0, 165.3, 165.3(2C), 165.4, 165.5(2C), 165.6(2C), 165.6, 165.8, 166.1, 172.5, 206.4; IR ($CHCl_3$): 3035, 2931, 1624, 1447, 1268, 1106, 698 cm^{-1}; MALDI (TOF) m/z $[M + Na]^+$ calcd for $C_{150}H_{138}O_{44}NaSi$, 2694.62, found 2694.58.

Allyl 2-*O*-acetyl-3, 4-di-*O*-benzyl-6-*O*- ^{t}butyldiphenylsilyl-α-D-mannopyranoside (64): Yield: (84%); $[\alpha]_D^{25}$ = 17.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.08 (s, 9H), 2.14 (s, 3H), 3.69 – 3.75 (m, 1H), 3.88 – 3.97 (m, 2H), 3.98 – 4.01 (m, 1H), 4.01 – 4.05 (m, 2H), 4.10 – 4.17 (m, 1H), 4.58 (dd, *J* = 15.3, 11.1 Hz, 2H), 4.73 (d, *J* = 11.2 Hz, 1H), 4.88 – 4.94 (m, 2H), 5.15 – 5.20 (m, 1H), 5.24 (dt, *J* = 17.1, 1.4 Hz, 1H), 5.38 – 5.41 (m, 1H), 5.79 – 5.92 (m, 1H), 7.18 (dd, *J* = 5.5, 2.4 Hz, 2H), 7.25 – 7.30 (m, 4H), 7.34 (dddd, *J* = 13.1, 8.6, 4.9, 1.9 Hz, 8H), 7.39 – 7.44 (m, 2H), 7.71 (dt, *J* = 7.8, 1.4 Hz, 2H), 7.74 – 7.77 (m, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.5, 21.2, 26.9(3C), 63.0, 67.9, 69.1, 72.0, 72.8, 74.3, 75.5, 78.4(2C), 96.7, 117.8, 127.7, 127.7, 127.8(2C), 127.9, 128.0(2C), 128.2(2C), 128.5(2C), 128.5(2C), 129.7(2C), 133.3, 133.7, 134.0, 135.7(2C), 136.1(2C), 138.2, 138.6, 170.6; IR ($CHCl_3$): 3031, 2930, 1630, 1444, 1266, 1111, 697 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{41}H_{48}O_7NaSi$, 703.3066, found 703.3065.

2-Azidoethyl 2-*O*-(naphthalen-1-yl methyl)-3, 4-di-*O*-benzyl-α-D-mannopyranoside (62): Yield: (93%); $[\alpha]_D^{25}$ = 37.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 3.27 (dddt, *J* = 19.0, 13.3, 9.3, 3.4 Hz, 2H), 3.49 (ddd, *J* = 10.6, 7.1, 3.5 Hz, 1H), 3.62 – 3.71 (m, 1H), 3.75 – 3.89 (m, 4H), 3.93 – 4.06 (m, 2H), 4.60 – 4.70 (m, 3H), 4.80 – 4.87 (m, 2H), 4.90 – 4.98 (m, 2H), 7.30 (dt, *J* = 10.0, 7.1 Hz, 10H), 7.43 – 7.53 (m, 3H), 7.79 (dd, *J* = 15.5, 6.5 Hz, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 50.5, 62.4, 66.5, 72.5, 72.7, 73.3, 74.8, 74.9, 75.3, 77.2, 80.2, 98.7, 126.0, 126.1, 126.2, 126.8, 127.7, 127.8(3C), 127.9, 128.0, 128.2(2C), 128.3, 128.5(2C), 128.5(2C), 133.1, 133.3, 135.7, 138.4, 138.5; IR ($CHCl_3$): 3033, 2925, 2130, 1449, 1265, 1109, 696 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{33}H_{35}N_3O_6Na$, 592.2424, found 592.2427.

Allyl 2-*O*-acetyl-3, 4-di-*O*-benzyl-α-D-mannopyranoside (61): Yield: (91%); $[\alpha]_D^{25}$ = 34.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 2.14 (s, 3H), 3.71 (dt, *J* = 9.8, 3.5 Hz, 1H), 3.82 (t, *J* = 9.6 Hz, 3H), 3.92 – 3.99 (m, 1H), 4.02 (dd, *J* = 9.3, 3.4 Hz, 1H), 4.14 (ddt, *J* = 12.8, 5.4, 1.4 Hz, 1H), 4.54 (d, *J* = 11.2 Hz, 1H), 4.62 (d, *J* = 10.9 Hz, 1H), 4.71 (d, *J* = 11.2 Hz, 1H), 4.83 (d, *J* = 1.7 Hz, 1H), 4.91 (d, *J* = 10.9 Hz, 1H), 5.16 – 5.22 (m, 1H), 5.26 (dq, *J* = 17.3, 1.5 Hz, 1H), 5.39 (dd, *J* = 3.3, 1.8 Hz, 1H), 5.80 – 5.93 (m, 1H), 7.31 (dtt, *J* = 12.6, 7.9, 4.4 Hz, 10H);

^{13}C NMR (100.53 MHz, $CDCl_3$): δ 21.2, 62.2, 68.3, 68.8, 71.9, 72.0, 74.3, 75.4, 78.2(2C), 97.1, 118.0, 127.8, 127.9, 128.1(3C), 128.5(2C), 128.5(2C), 133.4, 138.0, 138.3, 170.4; IR ($CHCl_3$): 3033, 2931, 1610, 1439, 1263, 1112, 699 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{25}H_{30}O_7Na$, 465.1889, found 465.1888.

Allyl 2-*O*-acetyl-3, 4-di-*O*-benzyl-6-*O*-[2-*O*-acetyl-3.4-*O*-di-benzyl-6-*O*-^{t}butyldiphenylsilyl-α-D-mannopyranosyl]-α-D-mannopyranoside (67): Yield: (95%); $[\alpha]_D^{25}$ = 39.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.07 (s, 9H), 2.12 (s, 3H), 2.14 (s, 3H), 3.72 (dd, *J* = 25.4, 9.3 Hz, 4H), 3.82 (t, *J* = 10.3 Hz, 2H), 3.89 – 3.97 (m, 2H), 3.98 – 4.06 (m, 3H), 4.11 (dd, *J* = 13.1, 5.2 Hz, 1H), 4.45 (d, *J* = 11.1 Hz, 1H), 4.53 (dd, *J* = 11.2, 5.2 Hz, 2H), 4.59 (d, *J* = 10.9 Hz, 1H), 4.71 (dd, *J* = 11.2, 3.5 Hz, 2H), 4.82 (s, 1H), 4.90 (dd, *J* = 21.6, 11.0 Hz, 2H), 4.97 (s, 1H), 5.17 (d, *J* = 10.4 Hz, 1H), 5.25 (d, *J* = 17.2 Hz, 1H), 5.38 (s, 1H), 5.46 (s, 1H), 5.85 (ddt, *J* = 16.3, 10.8, 5.7 Hz, 1H), 7.14 – 7.22 (m, 8H), 7.26 (dd, *J* = 7.8, 4.6 Hz, 6H), 7.30 – 7.36 (m, 10H), 7.37 – 7.43 (m, 2H), 7.68 (d, *J* = 7.6 Hz, 2H), 7.74 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.5, 21.2, 21.2, 26.9(3C), 62.9, 65.7, 68.1, 68.8, 71.2, 71.7, 71.9, 72.8, 74.2, 74.3, 75.2, 75.3, 77.9(2C), 78.49(2C), 96.7, 97.8, 118.1, 127.6, 127.6, 127.7, 127.7(2C), 127.8(2C), 127.8(2C), 127.9, 127.9, 128.2(2C), 128.3(2C), 128.4(2C), 128.4(2C), 128.5(2C), 128.6(2C), 129.7(2C), 133.4, 133.4(2C), 134.0, 135.7, 136.1, 138.0, 138.4, 138.8, 170.4, 170.6; IR ($CHCl_3$): 3033, 2926, 1612, 1447, 1268, 1106, 697 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{63}H_{72}O_{13}NaSi$, 1087.4639, found 1087.4637.

Allyl 2-*O*-acetyl-3,4-di-*O*-benzyl-6-*O*-[2-*O*-acetyl-3.4-di-*O*-benzyl-α-D-mannopyranosyl]-α-D-mannopyranoside (68): Yield: (88%); $[\alpha]_D^{25}$ = 45.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 2.14 (s, 3H), 2.17 (s, 3H), 3.65 – 3.75 (m, 4H), 3.76 – 3.89 (m, 4H), 3.91 – 4.04 (m, 3H), 4.08 – 4.17 (m, 1H), 4.45 – 4.55 (m, 3H), 4.60 (d, *J* = 11.0 Hz, 1H), 4.71 (dq, *J* = 8.8, 3.4, 2.8 Hz, 2H), 4.79 – 4.84 (m, 1H), 4.90 (s, 1H), 4.93 (dd, *J* = 5.1, 2.1 Hz, 2H), 5.14 – 5.21 (m, 1H), 5.22 – 5.30 (m, 1H), 5.37 – 5.42 (m, 1H), 5.45 – 5.50 (m, 1H), 5.78 – 5.91 (m, 1H), 7.23 – 7.35 (m, 20H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 21.1, 62.1, 65.9, 68.2, 68.4, 68.6, 71.0, 71.5, 71.8, 72.0, 74.1, 75.2, 75.2, 77.4, 77.6(2C), 78.3(2C), 96.8, 97.9, 118.0, 127.7(2C), 127.8, 127.9, 128.0(2C), 128.2(4C), 128.4(4C), 128.5(3C), 128.5(3C), 133.4, 137.8, 137.9, 138.4, 170.2, 170.5; IR ($CHCl_3$): 3034, 2929, 1615, 1448, 1266, 1106, 697 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{47}H_{54}O_{13}Na$, 849.3461, found 849.3461.

Allyl 2-*O*-acetyl-3, 4-di-*O*-benzyl-6-*O*-[2-*O*-acetyl-3.4-di-*O*-benzyl-6-*O*-(2-*O*-acetyl-3.4-*O*-di-benzyl-6-*O*-tbutyldiphenylsilyl-α-D-mannopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (69): Yield: (90%); $[\alpha]_D^{25}$ = 44.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.07 (s, 9H), 2.14 (s, 3H), 2.15 (s, 3H), 2.16 (s, 3H), 3.55 – 3.63 (m, 2H), 3.67 – 3.75 (m, 3H), 3.76 – 3.84 (m, 4H), 3.87 (d, *J* = 3.3 Hz, 1H), 3.90 (dd, *J* = 5.8, 2.4 Hz, 1H), 3.92 – 4.01 (m, 3H), 4.02 – 4.14 (m, 3H), 4.42 (d, *J* = 11.3 Hz, 1H), 4.46 – 4.52 (m, 3H), 4.54 (d, *J* = 3.5 Hz, 1H), 4.59 (d, *J* = 10.9 Hz, 1H), 4.68 – 4.74 (m, 3H), 4.83 (d, *J* = 1.6 Hz, 1H), 4.85 – 4.94 (m, 3H), 4.96 (dd, *J* = 4.6, 1.6 Hz, 2H), 5.17 (dd, *J* = 10.3, 1.3 Hz, 1H), 5.25 (dt, *J* = 17.3, 1.6 Hz, 1H), 5.41 (dd, *J* = 3.2, 1.8 Hz, 1H), 5.49 (d, *J* = 2.1 Hz, 2H), 5.78 – 5.90 (m, 1H), 7.16 (tdt, *J* = 7.7, 5.3, 3.0 Hz, 10H), 7.26 (ddt, *J* = 12.2, 7.0, 2.0 Hz, 12H), 7.30 – 7.35 (m, 12H), 7.37 – 7.42 (m, 2H), 7.67 (dd, *J* = 8.0, 1.3 Hz, 2H), 7.75 (dd, *J* = 7.9, 1.4 Hz, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.5, 21.1, 21.2, 26.9(3C), 62.7, 65.4, 65.8, 68.2, 68.2, 68.6, 68.7, 71.2, 71.2, 71.5, 71.6, 71.8, 72.7, 73.9, 74.0, 74.1, 75.0, 75.2, 75.3, 77.8(3C), 78.4(2C), 96.8, 97.9, 97.9, 118.0, 127.4(3C), 127.5, 127.6(2C), 127.6(2C), 127.7(2C), 127.8(2C), 127.9(2C), 127.9, 128.2(3C), 128.3(2C), 128.3(3C), 128.4(2C), 128.4(2C), 128.5(2C), 128.5(3C), 129.6(2C), 133.3, 133.4, 133.9, 135.6(2C), 136.0(2C), 137.7, 137.9, 137.9, 138.4(2C), 138.5, 138.7, 170.3, 170.3, 170.5; IR ($CHCl_3$): 3039, 2927, 1612, 1444, 1269, 1106, 698 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{85}H_{96}O_{19}NaSi$, 1471.6212, found 1471.6240.

2-Azidoethyl 2-*O*-(naphthalen-1-yl methyl)-3, 4-di-*O*-benzyl-6-O-[2-*O*-acetyl-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-acetyl-3.4-di-*O*-benzyl-6-*O*-(2-*O*-acetyl-3.4-*O*-di-benzyl-6-*O*-tbutyldiphenylsilyl-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl] -α-D-mannopyranoside (70): Yield: (92%); $[\alpha]_D^{25}$ = 51.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.05 (s, 9H), 2.12 (s, 3H), 2.14 (s, 3H), 2.16 (s, 3H), 3.25 (dtt, *J* = 19.3, 9.9, 4.6 Hz, 2H), 3.45 – 3.63 (m, 5H), 3.65 – 3.88 (m, 12H), 3.89 – 4.11 (m, 6H), 4.35 – 4.52 (m, 6H), 4.55 – 4.72 (m, 6H), 4.81 – 4.97 (m, 10H), 5.48 (s, 3H), 7.09 (d, *J* = 4.5 Hz, 2H), 7.11 – 7.19 (m, 10H), 7.20 – 7.28 (m, 19H), 7.30 (dd, *J* = 9.9, 4.9 Hz, 13H), 7.35 – 7.40 (m, 2H), 7.43 (dt, *J* = 7.0, 3.4 Hz, 2H), 7.53 (d, *J* = 8.5 Hz, 1H), 7.65 (d, *J* = 7.9 Hz, 2H), 7.70 – 7.80 (m, 6H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.5, 21.2, 26.9(3C), 50.5, 62.7, 65.4, 65.7, 66.5, 66.7, 68.2, 68.4, 68.6, 71.3, 71.3, 71.3, 71.5, 71.6, 71.6, 72.3, 72.7, 73.0, 73.9, 73.9, 74.0, 74.6, 74.6, 75.1, 75.1, 75.1, 75.3, 77.2, 77.4, 77.8, 77.8, 77.9, 80.2(2C), 97.9, 98.1, 98.2(2C), 126.0, 126.2, 126.2, 126.9, 127.5(3C), 127.5(3C), 127.6, 127.6, 127.6(2C), 127.7, 127.8(2C), 127.8(10C), 127.9, 127.9,

128.0, 128.3(2C), 128.4(4C), 128.4(2C), 128.4(2C), 128.5(2C), 128.5(4C), 128.5(2C), 128.6(4C), 129.7, 133.2, 133.3, 133.4, 134.0, 135.7, 135.8, 136.1, 137.8, 137.9, 137.9, 138.5, 138.5, 138.6, 138.6, 138.8, 170.3, 170.4, 170.5; IR ($CHCl_3$): 3031, 2926, 2123, 1614, 1445, 1266, 1106, 699 cm^{-1}; MALDI (TOF) m/z $[M + Na]^+$ calcd for $C_{115}H_{125}N_3O_{24}NaSi$, 1983.83, found 1984.11.

2-Azidoethyl 2-*O*-(naphthalen-1-yl methyl)-3, 4-di-*O*-benzyl-6-O-[2-*O*-acetyl-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-acetyl-3.4-*O*-di-benzyl-6-*O*-(2-*O*-acetyl-3.4-di-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl] -α-D-mannopyranoside (60): Yield: (90%); $[\alpha]_D^{25}$ = 59.7 (*c* = 1.0, $CHCl_3$); ^1H NMR (399.78MHz, $CDCl_3$): δ 2.12 (s, 3H), 2.16 (s, 6H), 3.18 – 3.34 (m, 2H), 3.54 (dt, *J* = 27.3, 13.9 Hz, 4H), 3.62 – 3.88 (m, 14H), 3.90 – 3.97 (m, 5H), 4.40 – 4.52 (m, 6H), 4.54 – 4.61 (m, 3H), 4.66 (dd, *J* = 19.1, 11.7 Hz, 3H), 4.90 (dd, *J* = 21.0, 8.2 Hz, 10H), 5.46 (s, 1H), 5.48 (s, 2H), 7.18 (s, 6H), 7.25 (d, *J* = 8.1 Hz, 21H), 7.28 – 7.33 (m, 13H), 7.42 – 7.47 (m, 2H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 14.7 Hz, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 21.2, 50.5, 62.1, 65.4, 65.8, 66.5, 66.8, 68.3, 68.4, 68.5, 71.2, 71.3, 71.4, 71.6(3C), 72.1, 72.4, 73.1, 73.9, 74.0, 74.2, 74.6, 74.7, 75.1, 75.1, 75.2, 75.3(2C), 77.7, 77.8, 77.9, 80.2(2C), 97.9, 98.2(2C), 98.2, 126.0, 126.2, 126.2, 126.9, 127.5(2C), 127.6, 127.6(2C), 127.7, 127.8, 127.9, 127.9(6C), 128.0, 128.0, 128.0, 128.1(2C), 128.3(2C), 128.4, 128.4, 128.4(6C), 128.5(2C), 128.5(6C), 128.5(2C), 128.6(2C), 128.6(2C), 133.2, 133.4, 135.8, 137.8, 137.8, 137.9, 138.5, 138.5(2C), 138.6, 138.7, 170.1, 170.4, 170.5; IR ($CHCl_3$): 3035, 2926, 2126, 1615, 1449, 1266, 1106, 698 cm^{-1}; MALDI (TOF) m/z $[M + Na]^+$ calcd for $C_{99}H_{107}N_3O_{24}Na$, 1745.71, found 1745.05.

2-Azidoethyl 2-*O*-(naphthalen-1-yl methyl)-3, 4-di-*O*-benzyl-6-*O*-[2-*O*-acetyl-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-acetyl-3.4-*O*-di-benzyl-6-*O*-(2-*O*-acetyl-3.4-*O*-di-benzyl-6-*O*-(2-*O*-acetyl-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-acetyl-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-acetyl-3, 4-di-*O*-benzyl-6-*O*-tbutyldiphenylsilyl-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl] -α-D-mannopyranoside (71): Yield: (88%); $[\alpha]_D^{25}$ = 62.1 (*c* = 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.06 (s, 9H), 2.11 (s, 3H), 2.13 (s, 3H), 2.14 (s, 3H), 2.14 (s, 3H), 2.15 (s, 3H), 2.16 (s, 3H), 3.18 – 3.31 (m, 2H), 3.43 – 3.62 (m, 10H), 3.63 – 3.78 (m, 11H), 3.83 (ddd, *J* = 19.1, 10.7, 5.7 Hz, 8H), 3.93 (dtd, *J* = 11.6, 9.8, 3.2 Hz, 8H), 4.07 (t, *J* = 9.6 Hz, 1H), 4.33 – 4.53 (m, 12H), 4.55 – 4.63 (m, 4H), 4.67 (dt, *J* = 11.7, 6.2 Hz, 5H), 4.80 – 4.95 (m, 16H), 5.48 (s, 6H), 7.05 – 7.09 (m, 2H),

7.10 – 7.19 (m, 19H), 7.21 – 7.27 (m, 32H), 7.27 – 7.32 (m, 21H), 7.35 – 7.40 (m, 2H), 7.43 (dd, *J* = 6.2, 3.2 Hz, 2H), 7.52 (d, *J* = 8.3 Hz, 1H), 7.65 (d, *J* = 6.9 Hz, 2H), 7.70 – 7.82 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 19.5, 21.2(6C), 26.9(3C), 50.6, 62.7, 65.5, 65.7, 65.8, 65.8, 66.5, 66.7, 68.2(2C), 68.3, 68.5, 68.7, 71.3(2C), 71.3(4C), 71.5, 71.6, 71.6(2C), 71.6, 71.7, 72.4, 72.8, 73.0, 73.9(2C), 74.0, 74.0, 74.1, 74.6, 74.7, 75.1(2C), 75.1(4C), 75.1, 75.3, 77.4, 77.8, 77.9(2C), 77.9(2C), 78.0, 80.2(2C), 98.0, 98.2(3C), 98.3, 98.3(2C), 126.0, 126.2, 126.9, 127.4(3C), 127.5(5C), 127.5, 127.5(3C), 127.6, 127.6(4C), 127.6(3C), 127.7, 127.8, 127.8, 127.8(5C), 127.9(5C), 127.9, 128.0(2C), 128.0(2C), 128.0, 128.3(3C), 128.3(3C), 128.4(3C), 128.4(3C), 128.4(5C), 128.4(3C), 128.5(4C), 128.5(4C), 128.5, 128.5(3C), 128.6, 128.6, 128.6(5C), 129.7, 129.7, 133.2, 133.4, 133.4, 134.1, 135.7(2C), 135.8, 136.1(2C), 137.8(2C), 137.8, 137.9, 137.9, 138.0, 138.5, 138.6, 138.6, 138.6, 138.6, 138.7, 138.7, 138.8, 170.3(3C), 170.3(2C), 170.4; IR ($CHCl_3$): 3034, 2925, 2133, 1612, 1444, 1267, 1110, 699 cm^{-1}; MALDI (TOF) m/z $[M + Na]^+$ calcd for $C_{181}H_{197}N_3O_{42}NaSi$; 3136.30, found 3137.32.

2-Azidoethyl 2-*O*-(naphthalen-1-yl methyl)-3, 4-di-*O*-benzyl-6-*O*-[3, 4-di-*O*-benzyl-6-*O*-(3.4-*O*-di-benzyl-6-*O*-(3.4-*O*-di-benzyl-6-*O*-(3, 4-di-*O*-benzyl-6-*O*-(3, 4-di-*O*-benzyl-6-*O*-(3, 4-di-*O*-benzyl-6-*O*-tbutyldiphenylsilyl-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl] -α-D-mannopyranoside (72): Yield: (91%); $[\alpha]_D^{25}$ = 62.1 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.03 (s, 9H), 3.19 (d, *J* = 3.5 Hz, 2H), 3.68 (ddtt, *J* = 58.1, 39.4, 19.0, 9.2 Hz, 36H), 3.93 – 4.15 (m, 10H), 4.40 – 4.53 (m, 6H), 4.62 (dq, *J* = 14.9, 8.8, 7.4 Hz, 13H), 4.81 – 4.99 (m, 15H), 5.08 (s, 1H), 7.16 (s, 5H), 7.16 – 7.28 (m, 49H), 7.32 (d, *J* = 7.4 Hz, 22H), 7.43 (dd, *J* = 5.0, 3.2 Hz, 2H), 7.51 (d, *J* = 8.3 Hz, 1H), 7.66 (d, *J* = 7.9 Hz, 2H), 7.74 (dd, *J* = 12.2, 7.5 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 19.4, 26.9(3C), 50.4, 63.0, 66.0, 66.1, 66.2, 66.3, 66.5, 67.9, 68.0, 68.0, 68.1, 68.3, 70.3, 70.5, 70.6, 70.7, 70.8, 71.4(2C), 71.7, 71.8(4C), 71.8, 72.2, 72.4, 72.5, 73.2, 73.9, 74.0, 74.2(2C), 74.3, 74.4, 74.5, 74.9, 75.0(2C), 75.0(2C), 75.1(2C), 75.1, 77.2, 79.6, 79.9, 80.0, 80.0, 80.1, 80.2(2C), 98.3, 99.1, 99.2, 99.4, 99.5, 99.6, 100.0, 126.0, 126.3, 126.7, 127.5, 127.5(3C), 127.6, 127.6(9C), 127.7(9C), 127.8(9C), 127.9, 128.0(3C), 128.0, 128.0, 128.1(3C), 128.1, 128.3(3C), 128.3(3C), 128.4(3C), 128.4(9C), 128.4, 128.5(3C), 128.6(9C), 128.6, 129.6, 133.1, 133.3, 133.5, 133.9, 135.7(2C), 136.0(3C), 137.7, 137.9, 138.0(2C), 138.1, 138.5(3C), 138.5(3C), 138.6(2C), 138.8; IR ($CHCl_3$): 3033, 2928, 2126,

1447, 1268, 1106, 697 cm^{-1}; MALDI (TOF) m/z $[M + Na]^+$ calcd for $C_{169}H_{185}N_3O_{36}NaSi$, 2884.224, found 2856.71.

2-Azidoethyl 2-*O*-(naphthalen-1-yl methyl)-3, 4-di-*O*-benzyl-6-*O*-[2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3.4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3.4-*O*-di-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-tbutyldiphenylsilyl-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl] -α-D-mannopyranoside (73): Yield: (70%); $[\alpha]_D^{25}$ = 35.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.97 (s, 9H), 3.14 (d, *J* = 11.0 Hz, 4H), 3.24 – 3.44 (m, 8H), 3.50 (d, *J* = 9.8 Hz, 4H), 3.66 – 3.97 (m, 37H), 4.05 – 4.25 (m, 26H), 4.31 – 4.56 (m, 35H), 4.58 – 4.66 (m, 6H), 4.72 (dd, *J* = 24.4, 14.3 Hz, 12H), 4.82 – 4.98 (m, 10H), 4.99 – 5.12 (m, 6H), 5.22 (d, *J* = 28.6 Hz, 6H), 5.79 (s, 7H), 6.83 (d, *J* = 33.4 Hz, 6H), 6.96 – 7.14 (m, 81H), 7.24 (dt, *J* = 26.1, 14.8 Hz, 86H), 7.41 – 7.53 (m, 7H), 7.55 – 7.60 (m, 3H), 7.61 – 7.70 (m, 4H), 7.72 – 7.87 (m, 6H), 7.95 – 8.02 (m, 12H), 8.07 (d, *J* = 6.9 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 19.3, 27.1(3C), 50.4, 62.4, 65.8, 66.4, 66.6, 66.6, 67.0, 67.3, 69.1(3C), 69.2(3C), 69.3, 69.3, 70.0, 70.0, 70.2, 70.2, 70.4, 70.7, 71.0, 71.1, 71.1, 71.3, 71.3, 71.4, 71.5(3C), 71.7(3C), 71.9, 72.1, 72.3(3C), 72.4(3C), 72.9, 73.3(3C), 73.3, 73.4, 73.6, 73.8, 74.0, 74.0, 74.1, 74.4, 74.4, 74.5, 74.6, 74.7, 74.9, 75.1, 75.1(6C), 75.2, 75.3, 75.4, 77.4(4C), 78.5, 78.7, 78.9(6C), 78.9, 79.4, 79.5(4C), 79.6, 79.6, 79.7, 79.9, 80.1, 80.2(4C), 98.3, 99.2, 99.3, 99.3(2C), 99.4, 99.5, 99.7, 99.8, 99.9, 100.0, 100.0, 100.2, 125.9, 126.0, 126.2, 126.5, 126.6, 126.7, 126.8, 126.9, 127.4(6C), 127.4(11C), 127.5(6C), 127.6, 127.6(6C), 127.7(11C), 127.8(11C), 127.8(6C), 127.9(6C), 127.9(6C), 128.0(11C), 128.0(11C), 128.1(11C), 128.2(11C), 128.2(16C), 128.3(24C), 128.4(16C), 128.5(11C), 129.6, 129.6, 130.1(6C), 130.1, 130.1, 130.3, 132.6, 132.7, 133.0, 133.0, 133.0, 133.1, 133.3, 133.5, 133.8, 135.1, 135.6, 135.6, 135.8, 136.0, 137.6, 137.7, 137.9, 137.9(5C), 138.0(2C), 138.3(5C), 138.4, 138.4, 138.5(5C), 138.6, 138.7, 138.8, 138.8(5C), 138.9(2C), 138.9, 138.9, 139.3, 165.3(2C), 165.3(2C), 165.4, 165.5; IR ($CHCl_3$): 3033, 2926, 1606, 1446, 1266, 1109, 699 cm^{-1}; MALDI (TOF) m/z $[M + Na]^+$ calcd for $C_{373}H_{377}N_3O_{72}NaSi$, 6103.56, found 6108.84.

2-Azidoethyl 2-*O*-(naphthalen-1-yl methyl)-3, 4-di-*O*-benzyl-6-*O*-[2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3.4-*O*-di-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3.4-*O*-di-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-benzoyl-3, 4-di-*O*-benzyl-6-*O*-tbutyldiphenylsilyl-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl] -α-D-mannopyranoside (4): Yield: (84%); $[\alpha]_D^{25}$ = 31.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.09 (s, 9H), 3.03 (d, *J* = 42.2 Hz, 2H), 3.17 (s, 4H), 3.24 – 3.44 (m, 5H), 3.52 (s, 3H), 3.74 (d, *J* = 53.4 Hz, 10H), 3.90 (s, 24H), 4.06 – 4.29 (m, 30H), 4.32 – 4.65 (m, 47H), 4.67 – 4.87 (m, 22H), 4.90 – 5.13 (m, 12H), 5.17 – 5.33 (m, 5H), 5.82 (d, *J* = 20.2 Hz, 8H), 6.76 – 6.95 (m, 15H), 7.00 – 7.15 (m, 98H), 7.17 – 7.31 (m, 80H), 7.50 (s, 7H), 7.62 – 7.72 (m, 5H), 7.74 – 7.84 (m, 2H), 8.00 (s, 13H), 8.15 (s, 2H); ^{13}C NMR (150.99 MHz, $CDCl_3$): δ 19.5, 27.0(3C), 50.4, 62.4(2C), 65.3, 65.9, 66.3, 66.4(2C), 66.6(2C), 67.0, 67.2, 68.8, 69.1(8C), 69.2(9C), 70.0, 70.1, 70.1, 70.3, 70.6, 70.9, 71.1(3C), 71.2, 71.3, 71.5(3C), 71.7(8C), 72.0, 72.1, 72.1, 72.3(8C), 72.4, 72.9, 73.3(8C), 73.3, 73.5, 73.6, 73.7, 74.0, 74.0(2C), 74.4(2C), 74.5, 74.7, 74.9, 75.2(6C), 75.3, 75.4, 77.4, 78.0, 78.5, 78.7, 78.9(5C), 79.4, 79.6, 79.7, 79.8, 80.2, 98.3, 98.4, 99.1, 99.3(2C), 99.4, 99.4(2C), 99.7(2C), 99.8, 99.9, 100.0(2C), 126.0, 126.0, 126.2, 126.4, 126.4, 126.6, 126.8, 126.9, 127.0, 127.4, 127.4(31C), 127.8(31C), 128.0(11C), 128.2, 128.3(121C), 128.4, 128.6, 128.8, 129.7, 130.1(8C), 132.6, 132.7, 133.1(8C), 133.2, 133.4, 133.8, 135.6, 135.8(2C), 136.1(2C), 137.5, 137.6, 137.7, 137.7(2C), 137.9(5C), 138.0(8C), 138.2, 138.3(3C), 138.4, 138.4, 138.5(3C), 138.6, 138.7, 138.8(8C), 138.9, 139.2, 165.3(5C), 165.5(2C); IR ($CHCl_3$): 3032, 2929, 2124, 1610, 1448, 1266, 1106, 698 cm^{-1}; MALDI (TOF) m/z $[M + Na]^+$ calcd for $C_{400}H_{403}N_3O_{78}NaSi$, 6550.74, found 6558.92.

2-Azidoethyl 2-*O*-(naphthalen-1-yl methyl)-3, 4-di-*O*-benzyl-6-*O*-[2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3.4-*O*-di-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3.4-*O*-di-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-

mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-benzoyl-3, 4-di-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (75): Yield: (75%); $[\alpha]_D^{25}$ = 33.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.01 – 3.20 (m, 5H), 3.26 – 3.45 (m, 6H), 3.48 – 3.57 (m, 4H), 3.62 – 3.69 (m, 4H), 3.70 – 3.79 (m, 6H), 3.80 – 4.02 (m, 27H), 4.04 – 4.18 (m, 20H), 4.26 (dd, *J* = 23.3, 11.5 Hz, 6H), 4.30 – 4.57 (m, 44H), 4.61 (ddt, *J* = 20.5, 8.3, 5.2 Hz, 5H), 4.67 – 4.76 (m, 13H), 4.82 (ddt, *J* = 16.8, 11.2, 6.7 Hz, 6H), 4.88 – 4.96 (m, 6H), 4.97 – 5.12 (m, 6H), 5.17 – 5.27 (m, 6H), 5.64 (s, 1H), 5.76 – 5.82 (m, 6H), 5.85 (s, 1H), 6.97 – 7.07 (m, 42H), 7.07 – 7.16 (m, 65H), 7.17 – 7.29 (m, 80H), 7.35 – 7.45 (m, 3H), 7.46 – 7.56 (m, 7H), 7.61 – 7.69 (m, 3H), 7.99 (t, *J* = 8.3 Hz, 9H), 8.05 (d, *J* = 7.7 Hz, 3H); ^{13}C NMR (150.99 MHz, $CDCl_3$): δ 50.4, 61.8(2C), 65.5, 66.2, 66.4(2C), 66.6, 66.9, 67.2, 68.7, 69.1(8C), 69.2(8C), 70.1, 70.2, 70.3, 70.6, 70.9, 71.0, 71.0, 71.1, 71.2, 71.5, 71.7(8C), 71.8, 71.9, 72.1, 72.3(8C), 72.3, 72.4, 72.8, 73.2(2C), 73.3(2C), 73.3, 73.3, 73.4, 73.5, 73.5, 73.6, 73.8, 73.9, 73.9, 74.0, 74.0, 74.0, 74.3, 74.4, 74.4, 74.5, 74.7, 74.7, 74.9, 75.1(8C), 75.3, 75.4, 77.4, 77.6, 78.5, 78.7, 78.9(5C), 79.4, 79.4, 79.5, 79.5, 79.8, 80.2, 98.1, 98.2, 99.1, 99.3, 99.3, 99.4, 99.4, 99.4, 99.7, 99.8, 99.9(2C), 100.0(2C), 125.9, 126.0, 126.2, 126.7, 126.7, 126.8, 126.9, 127.1, 127.3(13C), 127.4(3C), 127.4(17C), 127.4, 127.5, 127.6, 127.6, 127.7, 127.8, 127.8, 127.9, 128.0(13C), 128.1(17C), 128.2(16C), 128.2(16C), 128.2(16C), 128.3, 128.3(23C), 128.3(16C), 128.4, 128.4, 128.5, 128.5, 128.5, 128.6(16C), 130.0(8C), 130.1, 130.2, 130.2, 133.0(3C), 133.1(2C), 133.1, 133.2, 135.6, 137.5, 137.5, 137.7, 137.7(2C), 137.8(2C), 137.9(2C), 138.0, 138.0, 138.3, 138.3, 138.3, 138.3, 138.3, 138.4, 138.5(2C), 138.6, 138.6(2C), 138.7(2C), 138.7, 138.7, 138.8(3C), 138.8(2C), 138.8, 138.9, 138.9, 165.3(4C), 165.4(2C), 165.5; IR ($CHCl_3$): 3035, 2926, 2130, 1606, 1449, 1267, 1106, 699 cm^{-1}; MALDI (TOF) m/z $[M + Na]^+$ calcd for $C_{384}H_{385}N_3NaO_{78}Na$, 6312.62, found 6315.54.

2-Azidoethyl 2-*O*-(naphthalen-1-yl methyl)-3, 4-di-*O*-benzyl-6-*O*-[2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3.4-*O*-di-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3.4-*O*-di-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-

mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-benzoyl-3, 4-di-*O*-benzyl-6-*O*-(2,3-di-*O*-benzoyl-5-*O*-[2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-{2-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-α-D-arabinofuranosyl)-5-*O*-(2, 5-di-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl}-α-D-arabinofuranosyl)-α-D-arabinofuranosyl] -α-D-arabinofuranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (77): Yield: (83%); $[\alpha]_D^{25}$ = 24.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.00 (s, 3H), 2.43 (d, *J* = 6.8 Hz, 2H), 2.51 – 2.64 (m, 2H), 3.05 (d, *J* = 25.7 Hz, 1H), 3.15 – 3.48 (m, 7H), 3.54 – 3.71 (m, 12H), 3.80 (t, *J* = 32.4 Hz, 25H), 4.03 (dd, *J* = 70.1, 31.1 Hz, 28H), 4.14 – 4.67 (m, 82H), 4.69 – 5.04 (m, 22H), 5.09 – 5.27 (m, 9H), 5.27 – 5.59 (m, 20H), 5.71 (s, 7H), 5.77 (s, 1H), 6.82 (dd, *J* = 49.7, 22.2 Hz, 7H), 6.95 (dd, *J* = 16.6, 9.3 Hz, 44H), 7.02 (d, *J* = 18.0 Hz, 57H), 7.09 – 7.21 (m, 79H), 7.25 – 7.37 (m, 32H), 7.43 (d, *J* = 25.1 Hz, 10H), 7.52 – 7.61 (m, 3H), 7.66 – 7.76 (m, 6H), 7.78 – 7.97 (m, 36H), 8.05 (s, 2H); ^{13}C NMR (150.99 MHz, $CDCl_3$): δ 14.3, 22.8, 27.8, 38.0, 50.4, 62.6(2C), 63.2(2C), 63.7(2C), 65.2, 65.7, 65.9(2C), 66.4(2C), 66.6, 66.9, 67.2, 68.1, 69.1, 69.2(11C), 70.0, 70.2, 70.6, 70.8, 70.9, 71.0, 71.1, 71.3, 71.5(3C), 71.7(6C), 71.8, 72.0, 72.1, 72.3(6C), 72.4, 72.8, 73.2, 73.3(11C), 73.5, 73.6, 73.9(5C), 74.0, 74.2, 74.3, 74.5, 74.5, 74.7, 74.8, 74.9, 75.1(5C), 75.3, 77.2, 77.2, 77.3(3C), 77.4, 77.5(2C), 77.8(2C), 78.1, 78.5, 78.7, 78.9(3C), 79.0, 79.4, 79.5, 79.6, 79.8, 80.2, 80.7(2C), 80.8, 81.1(2C), 81.6(5C), 81.8, 81.9(2C), 82.1, 82.2(2C), 82.3, 83.0, 83.5, 84.2(3C), 98.2, 98.3, 98.4, 99.2, 99.3, 99.3(2C), 99.4, 99.4, 99.7, 99.8, 99.9(2C), 99.9, 105.0, 105.3, 105.9, 105.9, 106.0, 106.1, 106.1, 125.8, 125.9, 126.0, 126.2, 126.9, 127.2, 127.3(11C), 127.4(21C), 127.6, 127.7, 127.8(9C), 127.9, 127.9, 128.0(21C), 128.0, 128.1, 128.2, 128.2, 128.3(61C), 128.4(21C), 128.5(21C), 128.6(21C), 128.6(21C), 129.0, 129.0, 129.1, 129.1, 129.2, 129.3, 129.3, 129.4, 129.6, 129.7(6C), 129.8(6C), 129.9(21C), 130.0(16C), 133.0(2C), 133.1(3C), 133.1(3C), 133.2(2C), 133.4(2C), 133.4(2C), 133.5(2C), 133.5(2C), 133.6(2C), 135.6, 137.5, 137.5, 137.6(2C), 137.7, 137.8(5C), 138.0(2C), 138.2, 138.3(3C), 138.3, 138.3, 138.4, 138.5(3C), 138.6, 138.7(2C), 138.7, 138.8(2C), 138.8(2C), 138.8(2C), 138.9(2C), 164.9, 165.1, 165.2, 165.3(6C), 165.3, 165.4, 165.5(5C), 165.6, 165.7, 166.0, 166.2, 172.5, 206.5; IR ($CHCl_3$): 3034, 2926, 2129, 1605, 1449, 1267, 1106, 696 cm^{-1}; MALDI (TOF) m/z $[M + Na]^+$ calcd for $C_{515}H_{499}N_3O_{121}Na$, 8688.30, found 8692.78.

4-Pentenyl 2,3-di-*O*-benzoyl-5-*O*-[2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-{2-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2-*O*-benzoyl-3,5-di-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-tbutyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-5-*O*-(2, 5-di-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl}-α-D-arabinofuranosyl)-α-D-arabinofuranosyl] -α-D-arabinofuranoside (80): Yield: (78%); $[\alpha]_D^{25}$ = 13.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.87 (s, 9H), 0.94 (s, 9H), 1.72 (td, *J* = 14.2, 6.4 Hz, 2H), 2.05 (s, 3H), 2.16 (dt, *J* = 14.9, 7.4 Hz, 2H), 2.29 – 2.66 (m, 4H), 3.45 – 3.66 (m, 9H), 3.72 (dt, *J* = 39.5, 10.5 Hz, 11H), 3.82 – 4.20 (m, 32H), 4.20 – 4.64 (m, 50H), 4.69 – 4.74 (m, 2H), 4.83 (q, *J* = 11.9, 10.1 Hz, 5H), 4.92 – 5.07 (m, 4H), 5.12 – 5.29 (m, 8H), 5.36 – 5.65 (m, 17H), 5.76 (d, *J* = 5.5 Hz, 2H), 5.78 – 5.85 (m, 1H), 7.04 (dd, *J* = 14.5, 5.8 Hz, 6H), 7.07 – 7.14 (m, 25H), 7.15 – 7.28 (m, 91H), 7.35 (dtt, *J* = 28.7, 14.8, 7.8 Hz, 29H), 7.53 (ddq, *J* = 24.9, 19.4, 7.1 Hz, 12H), 7.81 (dd, *J* = 15.5, 7.5 Hz, 5H), 7.85 – 7.92 (m, 6H), 7.95 (dd, *J* = 13.4, 7.0 Hz, 6H), 8.03 (dt, *J* = 19.4, 7.9 Hz, 10H); ^{13}C NMR (150.99 MHz, $CDCl_3$): δ 14.3, 19.2, 19.4, 22.8, 26.9(3C), 27.0(3C), 28.9, 30.4, 31.6, 37.9, 63.1, 63.4, 63.6, 63.7, 65.3, 65.8, 66.1, 66.1, 66.8, 68.9, 69.0(2C), 69.6, 69.7, 71.7, 72.0, 72.2(4C), 72.3, 72.3, 73.4(4C), 73.4, 73.4, 74.3, 74.5, 75.0, 75.0, 75.2, 75.3(3C), 75.3, 77.2, 77.3, 77.4, 77.4(2C), 77.5(3C), 78.3, 78.3, 79.3, 79.4, 80.1(2C), 80.5, 81.0, 81.0, 81.3, 81.5, 81.6, 81.7(2C), 81.8, 81.9(5C), 82.0(2C), 82.3, 82.3(3C), 82.4, 82.5, 83.0, 83.1, 83.3(2C), 83.4, 83.8, 83.9, 84.3, 84.4, 84.6, 85.9(2C), 86.3(2C), 98.8, 98.8, 99.6, 99.7, 100.8(2C), 104.9, 105.4, 105.6, 105.7, 105.8, 105.9(2C), 106.1, 106.7, 107.2, 115.0, 127.3(6C), 127.5(26C), 127.6, 127.7(21C), 128.0, 128.0(2C), 128.0(3C), 128.1(2C), 128.2(2C), 128.2(6C), 128.3(11C), 128.4(16C), 128.4(21C), 128.5(6C), 128.5(5C), 128.6(6C), 129.0, 129.1, 129.2(2C), 129.3(33C), 129.3, 129.4, 129.4(2C), 129.5, 129.6, 129.7(3C), 129.7(2C), 129.8, 129.9, 130.0, 130.1(2C), 130.1, 133.0, 133.1, 133.2, 133.3, 133.3, 133.4(3C), 133.5(3C), 133.5(3C), 133.6, 133.6, 133.6, 135.6(2C), 135.7(4C), 135.8(2C), 137.7, 137.8, 137.9, 138.1, 138.2, 138.2(8C), 138.5, 138.6(2C), 138.6, 138.6, 138.7, 138.7, 164.9, 165.0, 165.3, 165.3, 165.4, 165.4, 165.4, 165.5(2C), 165.5(2C), 165.6, 165.6, 165.6, 165.7, 166.0, 172.5, 206.4; IR ($CHCl_3$): 3033, 2929, 1609, 1444, 1269, 1106, 699 cm^{-1}; MALDI (TOF) m/z $[M + Na]^+$ calcd for $C_{364}H_{360}O_{87}NaSi_2$, 6204.32, found 6225.81.

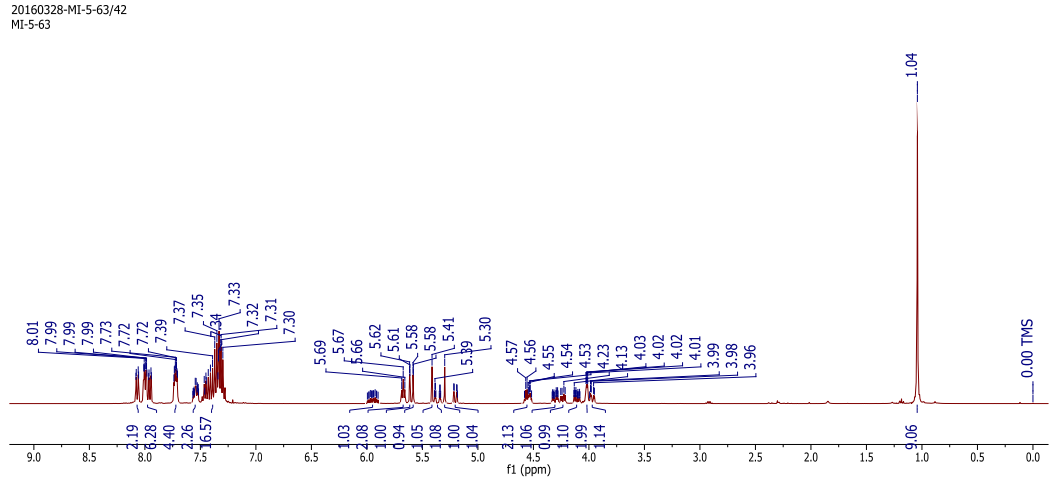
2-Azidoethyl 2-*O*-(naphthalen-1-yl methyl)-3, 4-di-*O*-benzyl-6-*O*-[2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4-*O*-di-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4-*O*-di-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3, 4-di-*O*-benzyl-6-*O*-(2-*O*-benzoyl-3, 4-di-*O*-benzyl-6-*O*-(2,3-di-*O*-benzoyl-5-*O*-[2,3-di-*O*-benzoyl-5-*O*-(2,3-di-*O*-benzoyl-5-*O*-{2-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-5-*O*-(2-*O*-benzoyl-3,5-di-*O*-(2-*O*-(2,3-di-*O*-benzyl-5-*O*-(2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-5-*O*-(2, 5-di-*O*-benzoyl-3-*O*-(2,3-di-*O*-benzoyl-5-*O*-(4-oxopentanoyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl)-α-D-arabinofuranosyl}-α-D-arabinofuranosyl)-α-D-arabinofuranosyl] -α-D-arabinofuranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-mannopyranosyl] -α-D-mannopyranoside (78): Yield: (70%); $[\alpha]_D^{25}$ = 26.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.26 (s, 9H), 1.29 (s, 9H), 2.05 (s, 3H), 2.42 – 2.53 (m, 2H), 2.60 (s, 2H), 2.94 – 3.20 (m, 4H), 3.31 (d, *J* = 66.3 Hz, 6H), 3.40 – 3.59 (m, 12H), 3.60 – 3.79 (m, 29H), 3.79 – 4.04 (m, 48H), 4.11 (d, *J* = 36.0 Hz, 22H), 4.20 – 4.41 (m, 50H), 4.42 – 4.64 (m, 52H), 4.65 – 4.75 (m, 14H), 4.77 – 4.87 (m, 13H), 4.94 (dd, *J* = 39.1, 16.9 Hz, 6H), 5.03 (d, *J* = 17.4 Hz, 6H), 5.10 – 5.28 (m, 13H), 5.37 (dd, *J* = 43.7, 21.1 Hz, 8H), 5.47 – 5.66 (m, 10H), 5.71 – 5.88 (m, 8H), 6.81 – 7.39 (m, 330H), 7.42 (d, *J* = 9.2 Hz, 6H), 7.46 – 7.69 (m, 22H), 7.76 (d, *J* = 7.2 Hz, 4H), 7.82 (s, 4H), 7.85 – 7.91 (m, 6H), 7.91 – 8.17 (m, 30H); ^{13}C NMR (150.99 MHz, $CDCl_3$): δ 14.3, 26.9(3C), 27.0(3C), 30.3, 37.9, 50.4, 60.8, 63.1, 63.4, 63.6, 63.7, 65.2, 65.3, 65.6, 65.7, 65.8, 65.9, 66.0, 66.1, 66.4, 66.6, 66.9, 67.2, 68.1, 69.0(4C), 69.0(9C), 69.1(8C), 69.2(9C), 69.6, 69.7, 70.0, 70.2, 70.6, 70.8, 70.9, 71.0, 71.1, 71.3, 71.5, 71.7(5C), 72.0, 72.1, 72.2(6C), 72.3(7C), 72.3(7C), 72.3(6C), 72.9, 73.3(5C), 73.3(5C), 73.4(10C), 73.4(5C), 73.6, 73.9, 74.0, 74.0, 74.3(2C), 74.5, 74.5(2C), 74.7, 74.8, 74.9, 75.0, 75.1, 75.2(3C), 75.3(3C), 75.3(24C), 75.4(2C), 77.2, 78.1, 78.3(3C), 78.5, 78.7, 78.9(2C), 79.0, 79.3, 79.4(2C), 79.6, 79.7, 79.8, 80.1(2C), 80.2, 80.5, 81.0, 81.0, 81.3, 81.5, 81.6, 81.6, 81.8, 81.8, 81.9, 82.2, 82.3(2C), 82.4, 82.5, 83.0, 83.1, 83.3, 83.4, 83.5, 83.8, 83.9, 84.3,

84.5, 84.6, 86.0, 86.3, 98.3, 98.4, 98.8, 98.8, 99.2, 99.3, 99.3, 99.4, 99.4, 99.5, 99.6(2C), 99.7(2C), 99.7, 99.8, 99.9, 100.0, 100.8(2C), 104.9, 105.4, 105.6, 105.9, 106.0, 106.0, 106.1(2C), 106.8, 107.2, 126.0, 126.0, 126.2, 126.5(2C), 126.6, 126.8, 126.9(2C), 127.2(2C), 127.3(15C), 127.4(15C), 127.5(40C), 127.7(50C), 128.0(10C), 128.1(10C), 128.2(5C), 128.2(5C), 128.2(20C), 128.3(55C), 128.4(55C), 128.5(20C), 128.6(10C), 128.6(10C), 129.0, 129.1, 129.3, 129.4(2C), 129.4, 129.5, 129.6, 129.7(2C), 129.7, 129.8(10C), 129.9(26C), 130.0(4C), 130.1(10C), 130.1(10C), 130.2, 133.1(7C), 133.1(5C), 133.2, 133.3, 133.4(5C), 133.5, 133.6, 133.6, 133.6, 135.6(2C), 135.7(4C), 135.8(2C), 137.5(2C), 137.7, 137.8, 137.9(5C), 137.9, 138.0(2C), 138.1, 138.2(2C), 138.2(5C), 138.3(5C), 138.4, 138.5(2C), 138.6(4C), 138.6, 138.7(4C), 138.7(4C), 138.8, 138.8(7C), 139.2, 139.2, 139.4, 147.2(2C), 147.3, 147.4, 147.8, 147.8, 148.2(2C), 164.9(2C), 165.0, 165.1, 165.2(2C), 165.3(5C), 165.4(4C), 165.4 165.5, 165.5(2C), 165.6(3C), 166.1, 172.5, 206.4; IR ($CHCl_3$): 3030, 2929, 1611, 1441, 1269, 1106, 698 cm^{-1};MALDI (TOF) calculated [M+Na] for $C_{743}H_{735}N_3O_{164}NaSi_2$ 12405.88; observed 12424.89

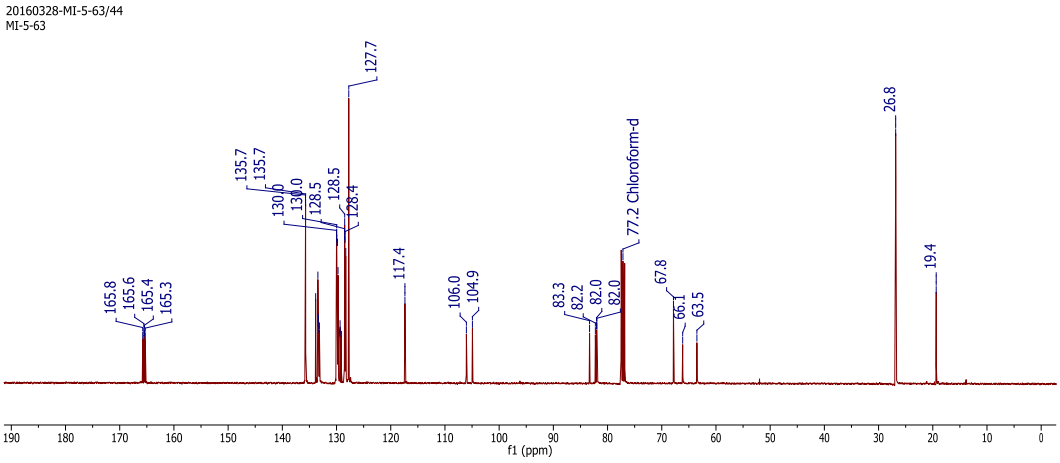
4.7 Spectral charts of representative compounds

{Kindly see the supporting documents file for spectral charts of all compounds}

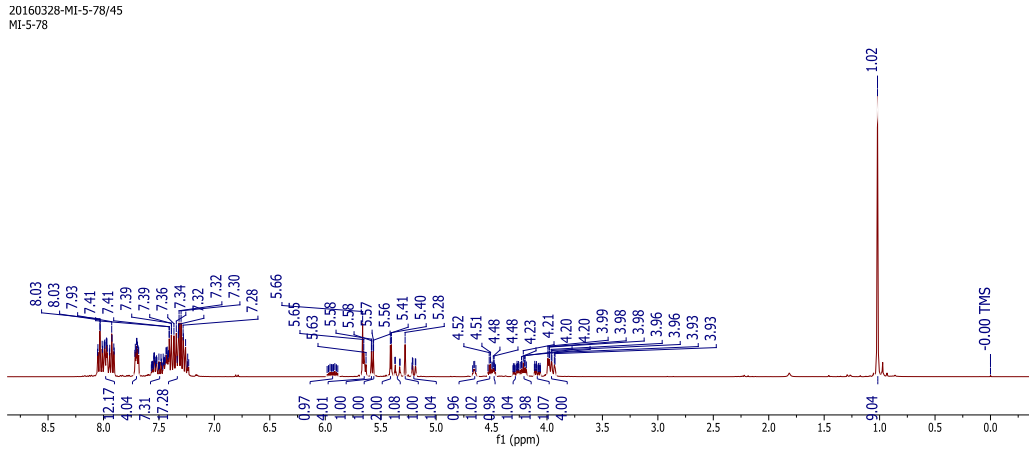
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **19**



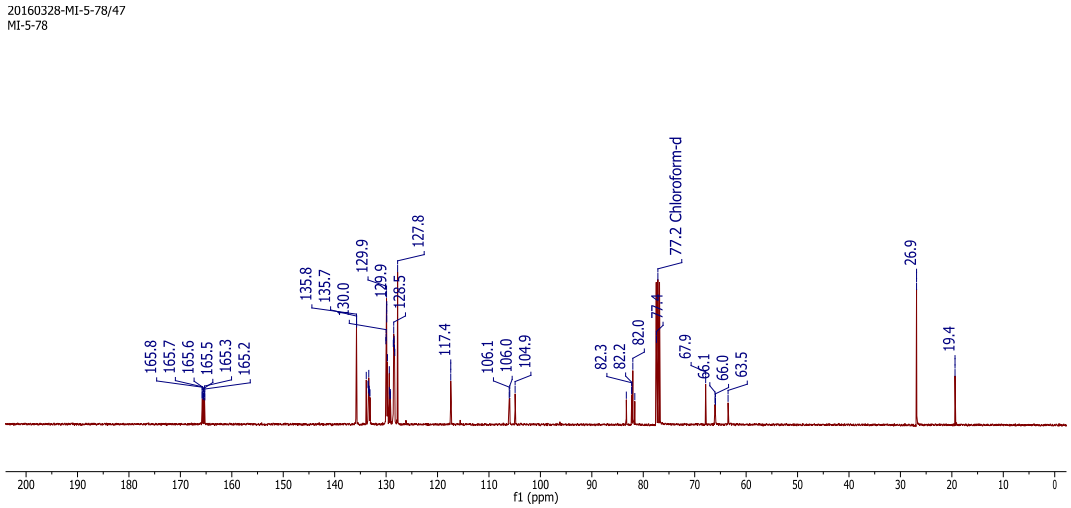
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **19**



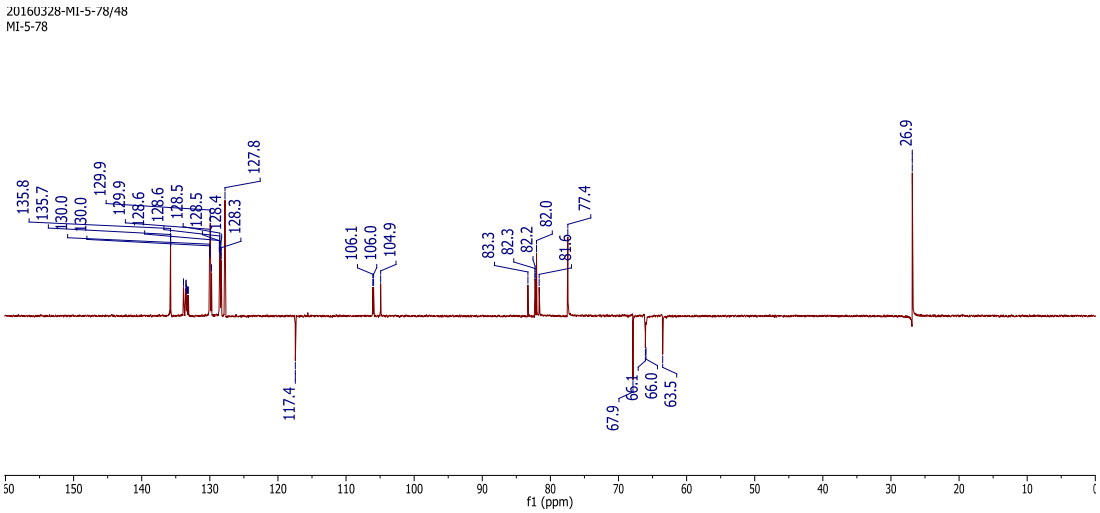
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **21a**



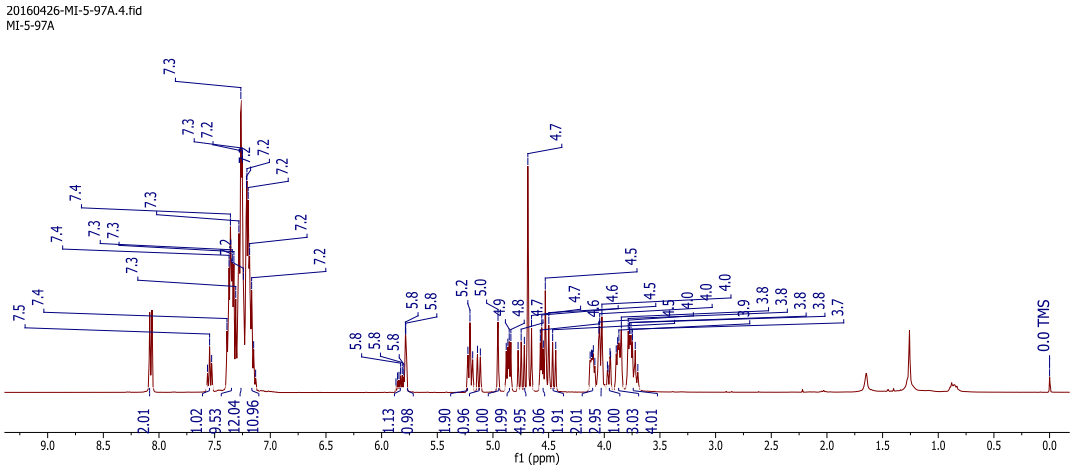
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **21a**



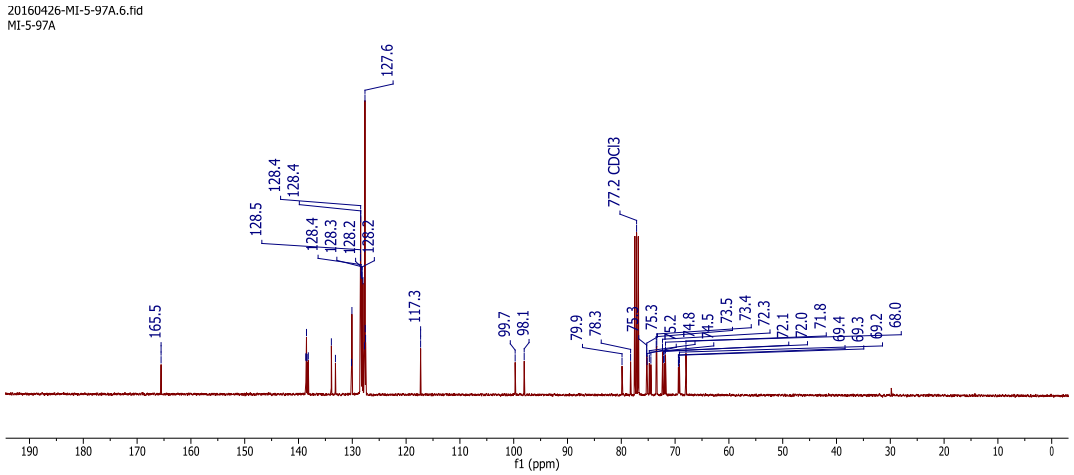
DEPT Spectrum (100.53 MHz, $CDCl_3$) of Compound **21a**



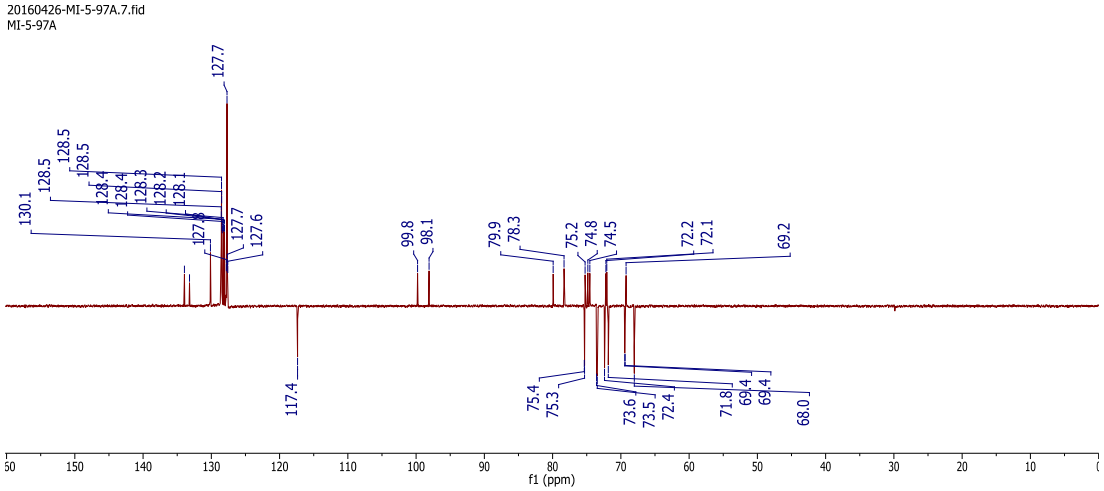
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **32**



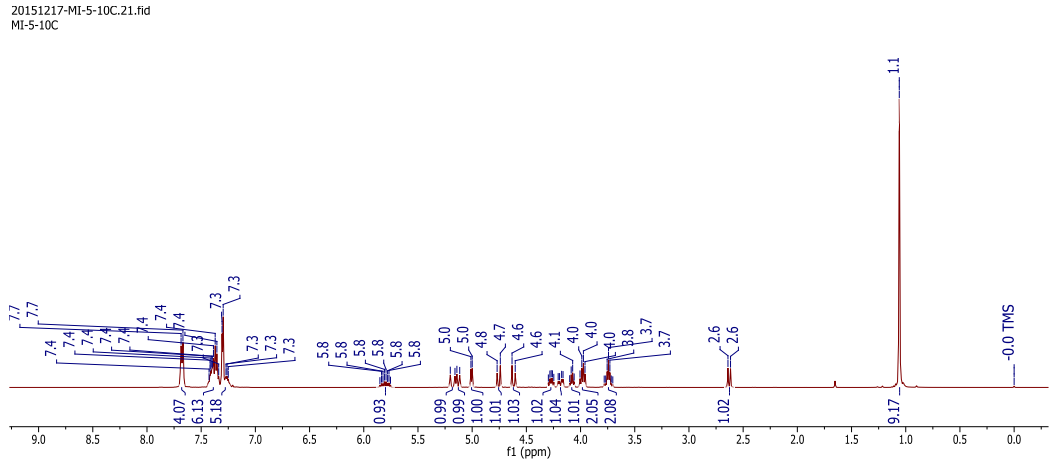
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **32**



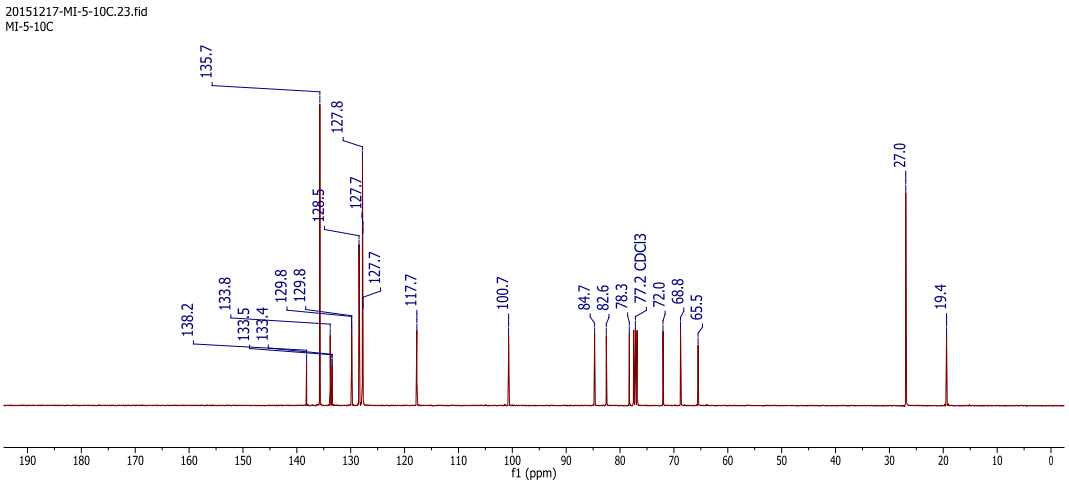
DEPT Spectrum (100.53 MHz, $CDCl_3$) of Compound **32**



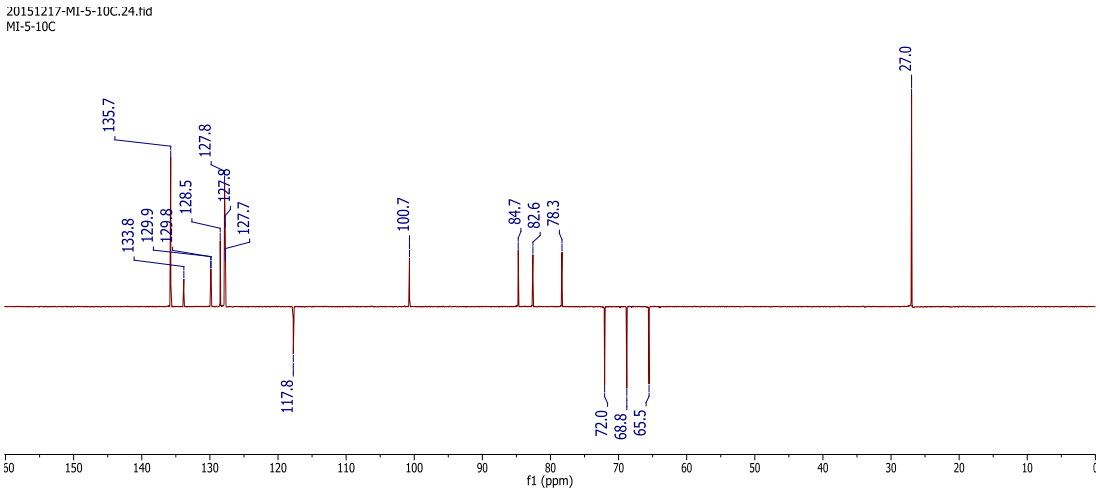
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **38**



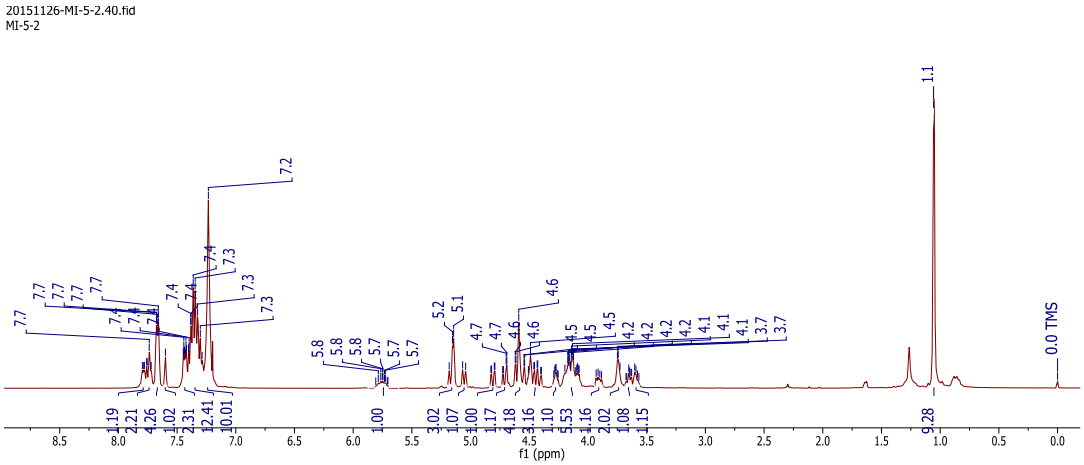
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **38**



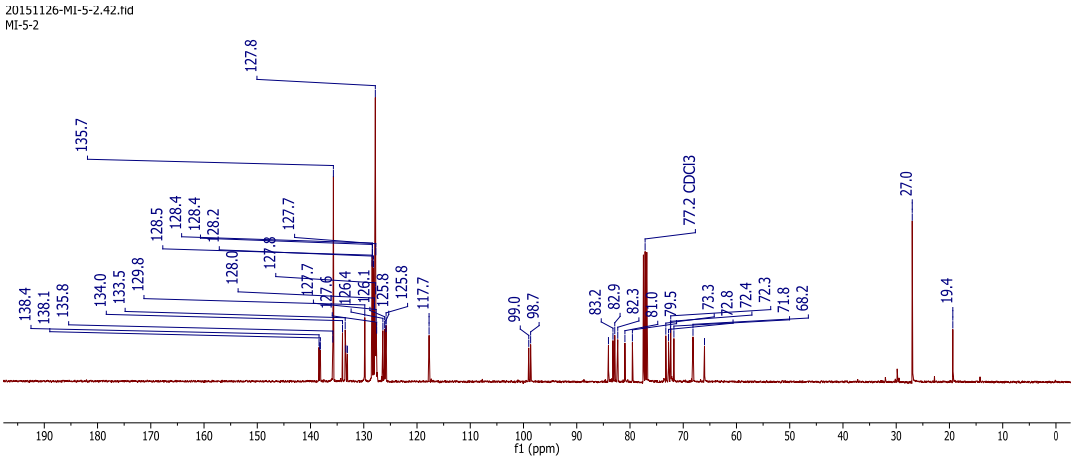
DEPT Spectrum (100.53 MHz, $CDCl_3$) of Compound **38**



^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **39**



^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **39**



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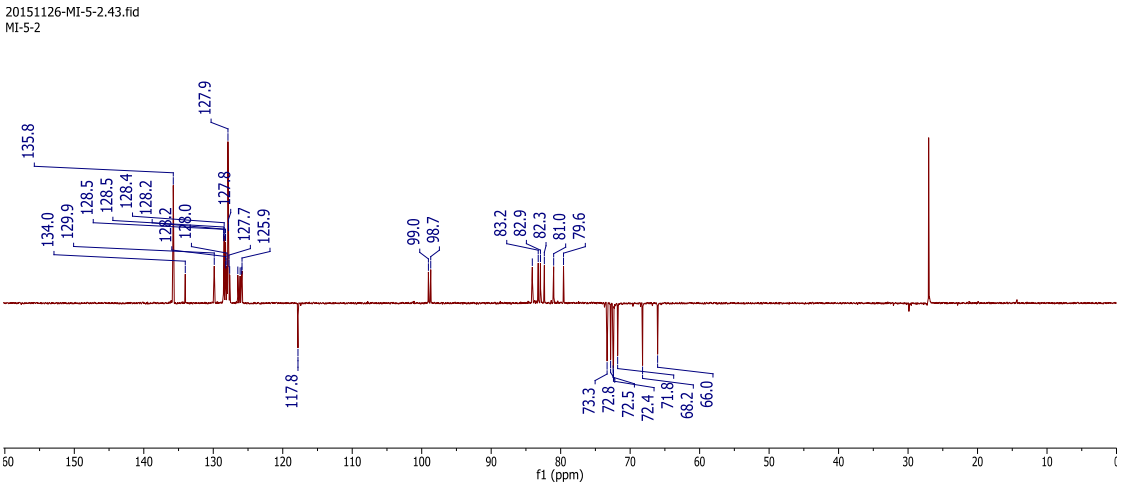

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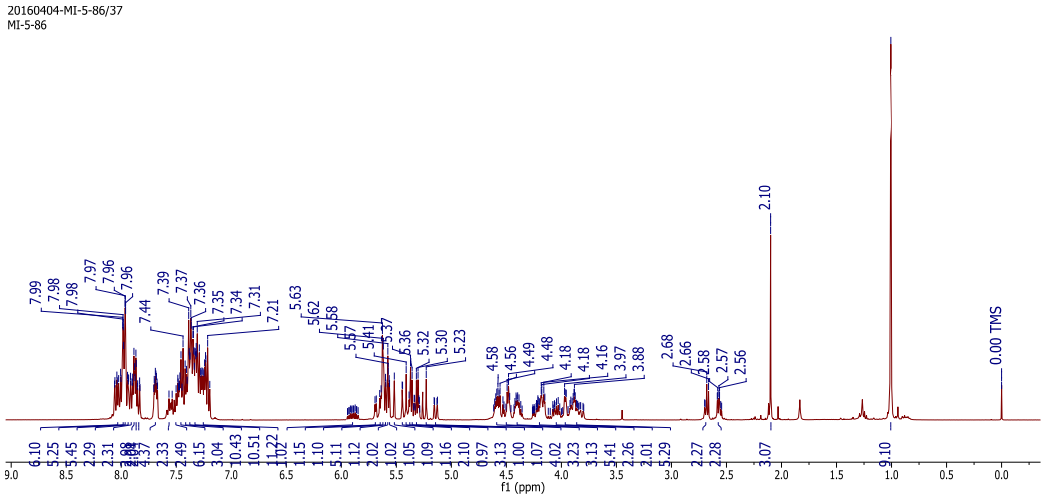

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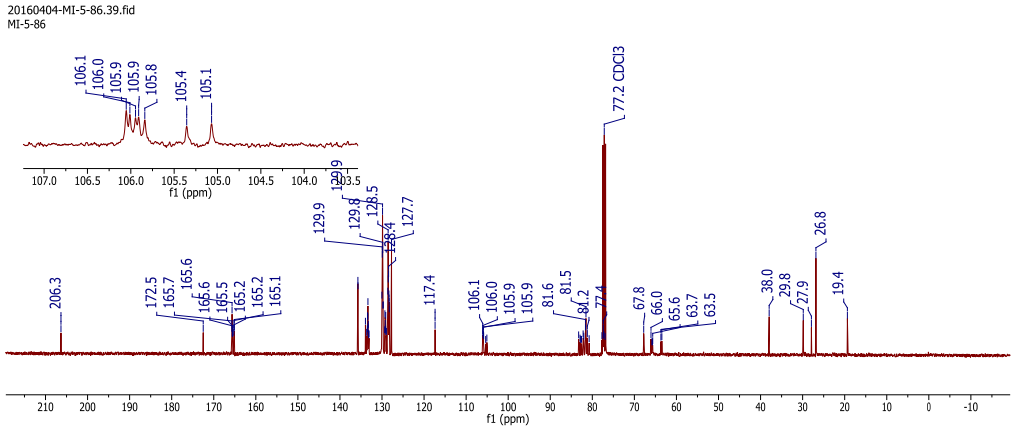
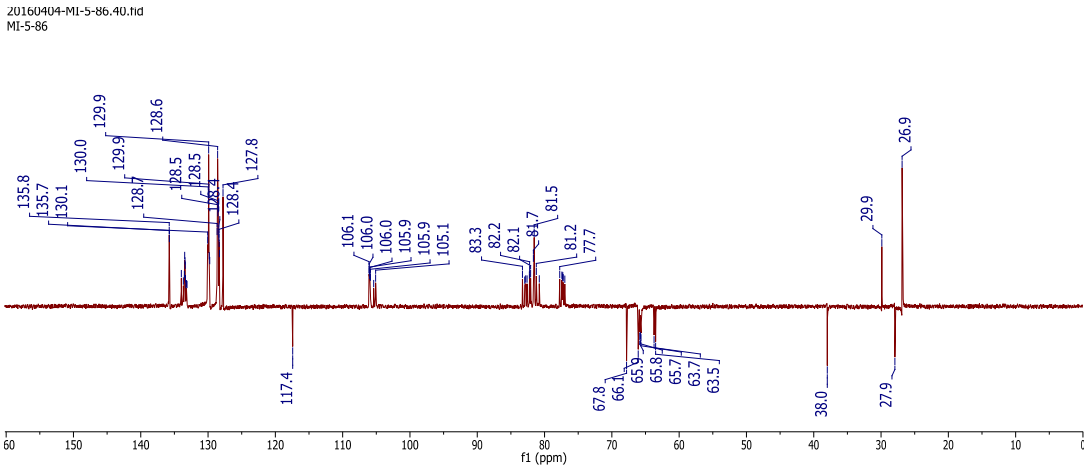


DEPT Spectrum (100.53 MHz, $CDCl_3$) of Compound **7**



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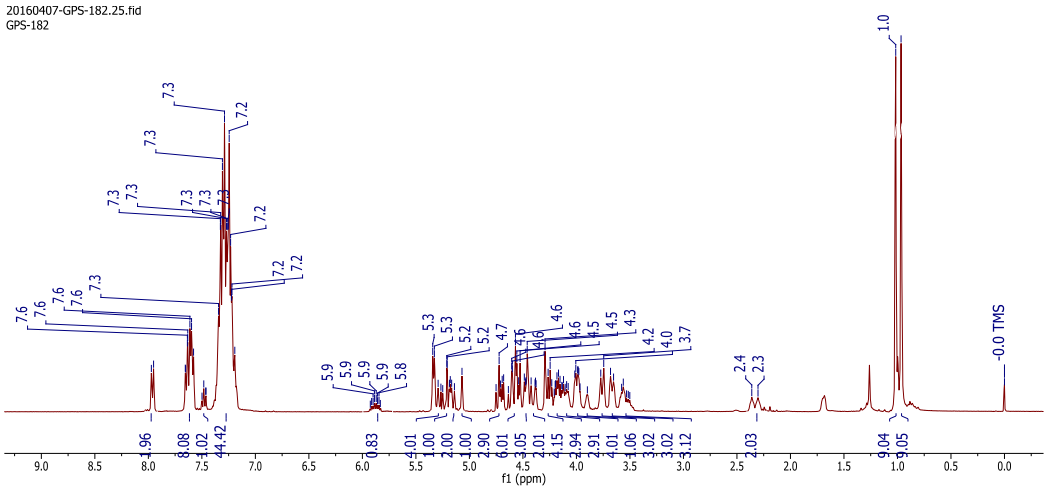

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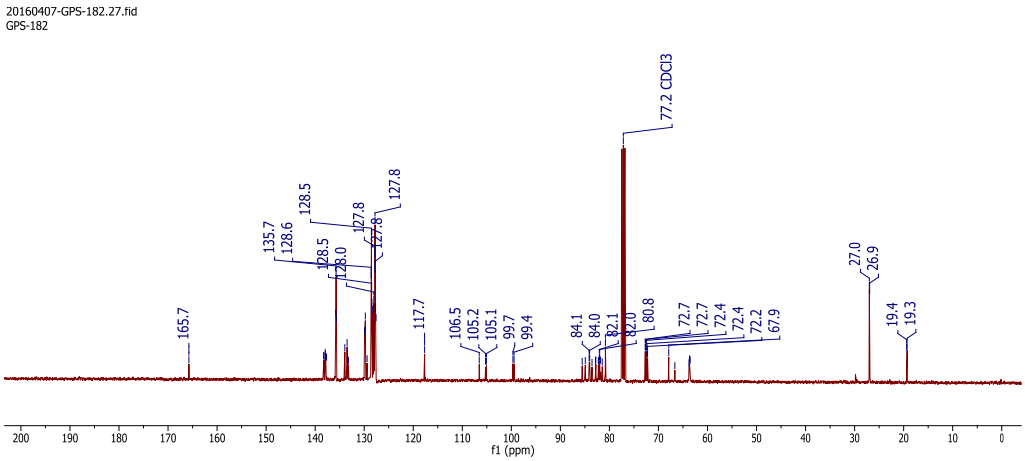

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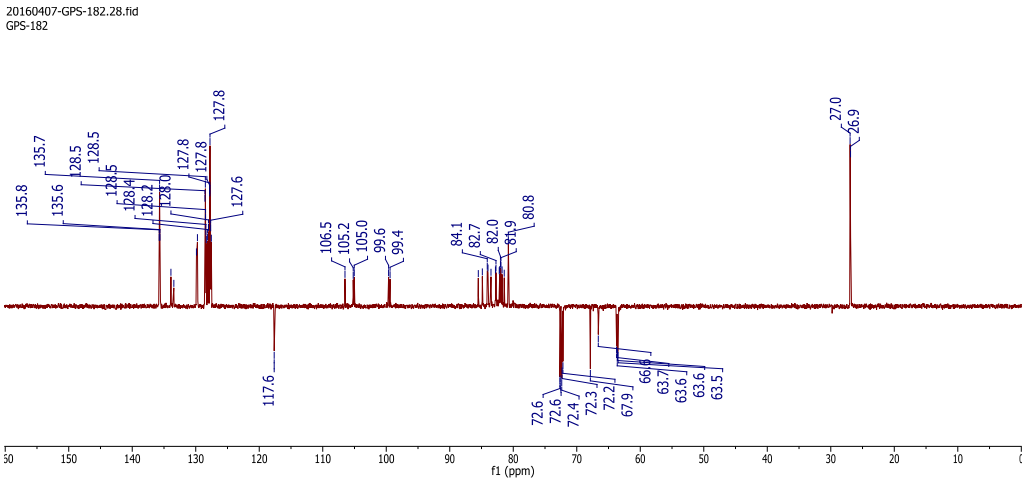

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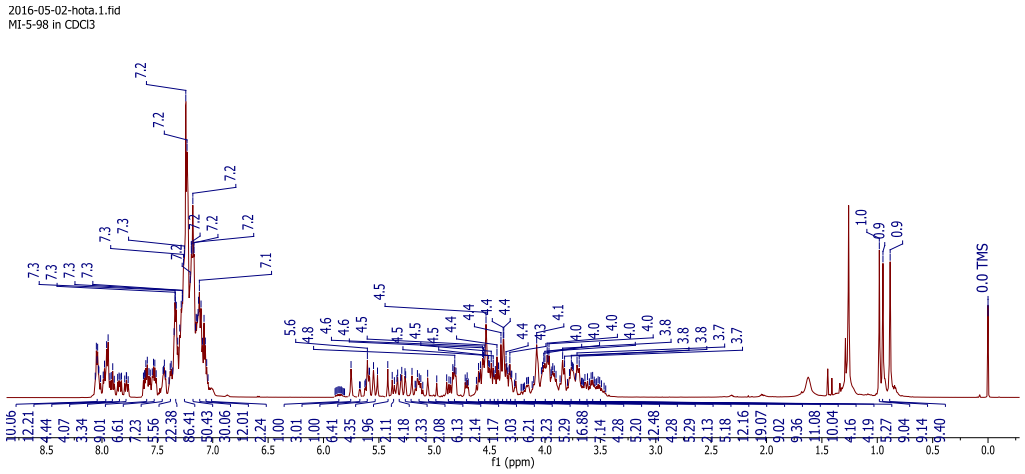

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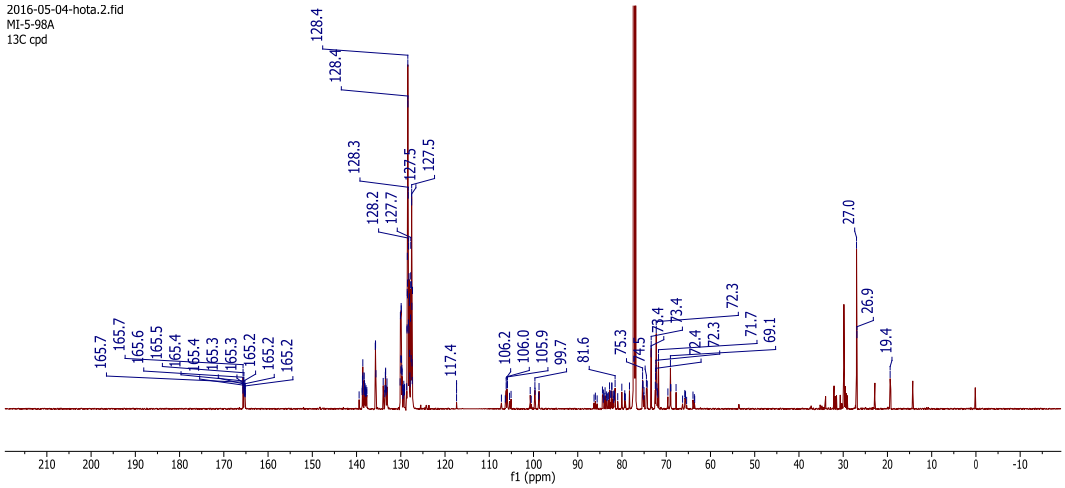

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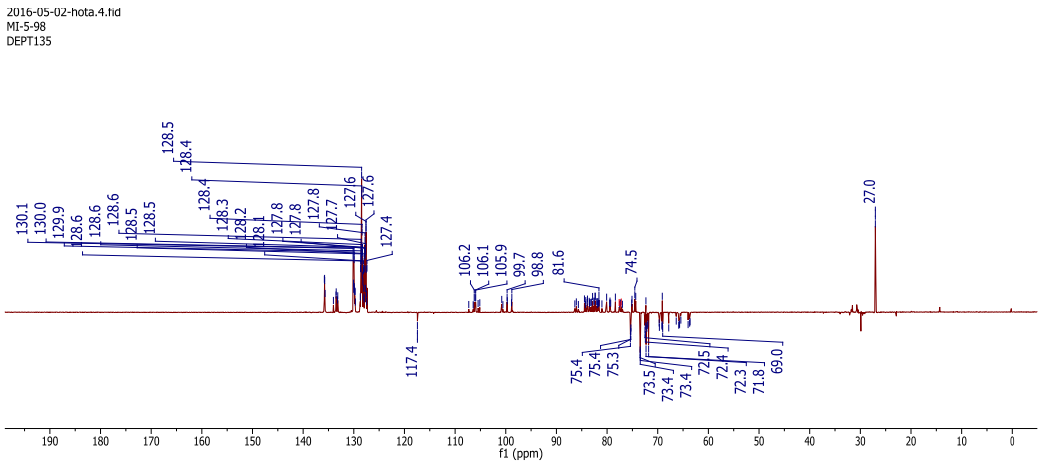

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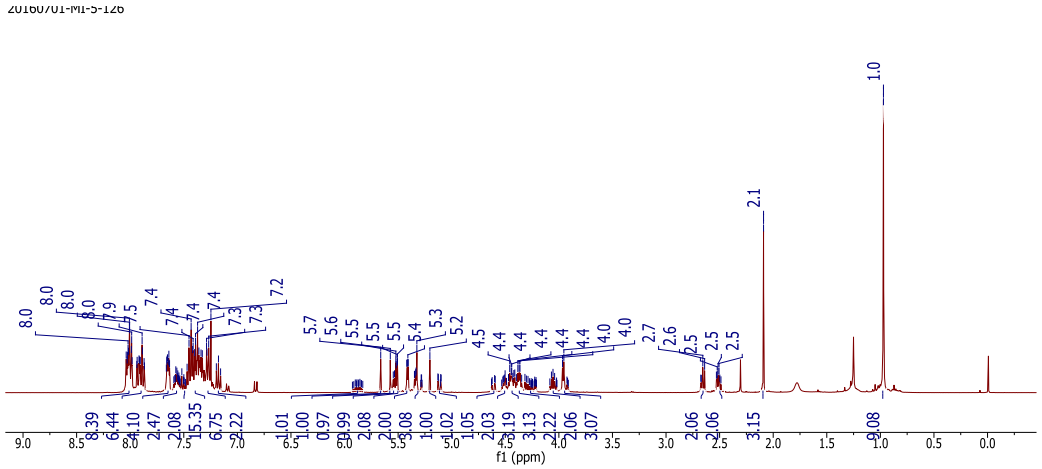

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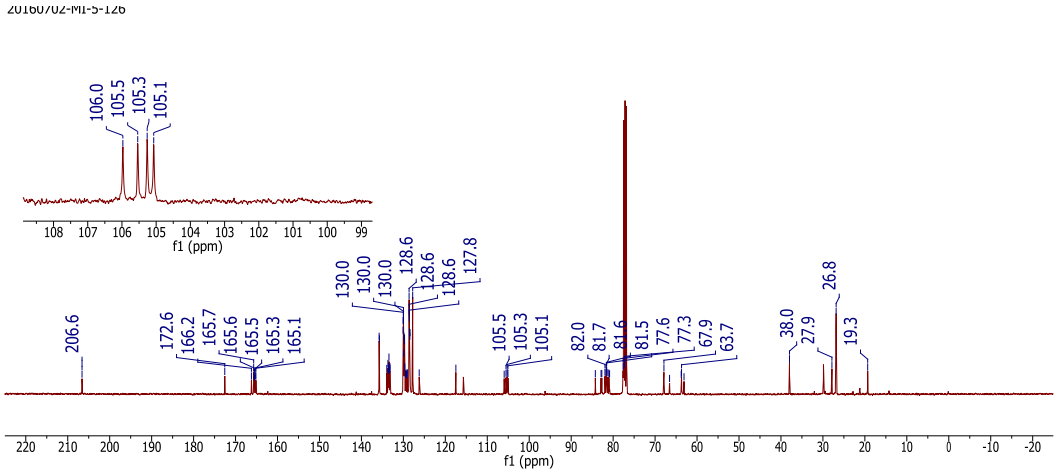
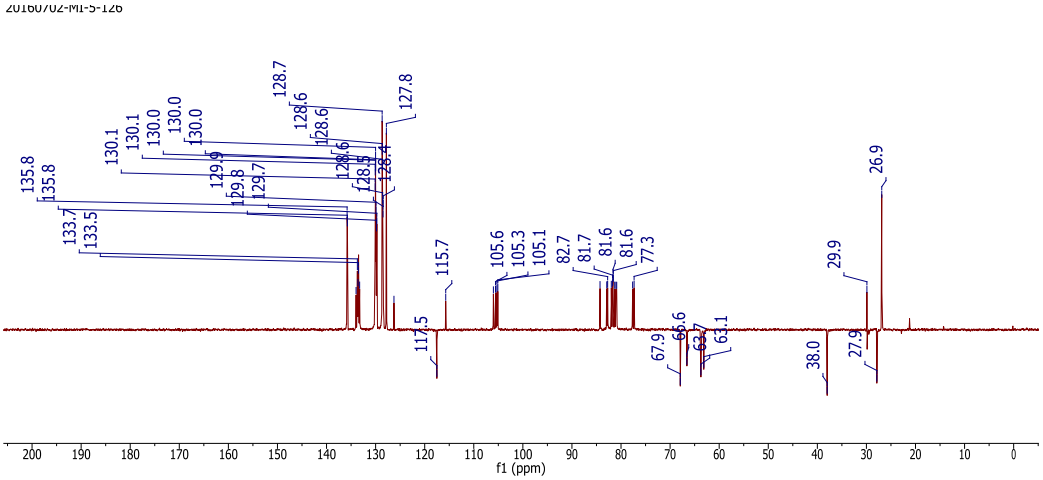


DEPT Spectrum (100.53 MHz, $CDCl_3$) of Compound **54**



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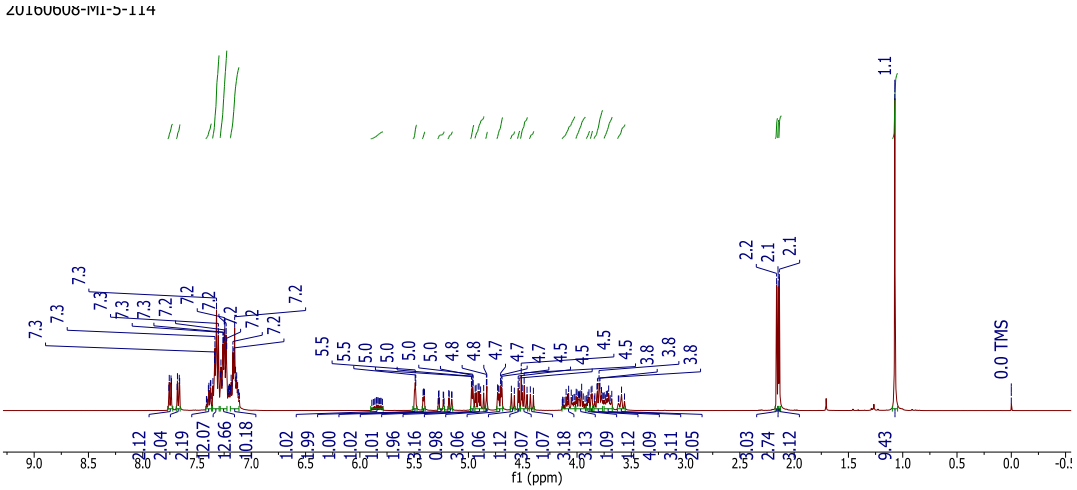

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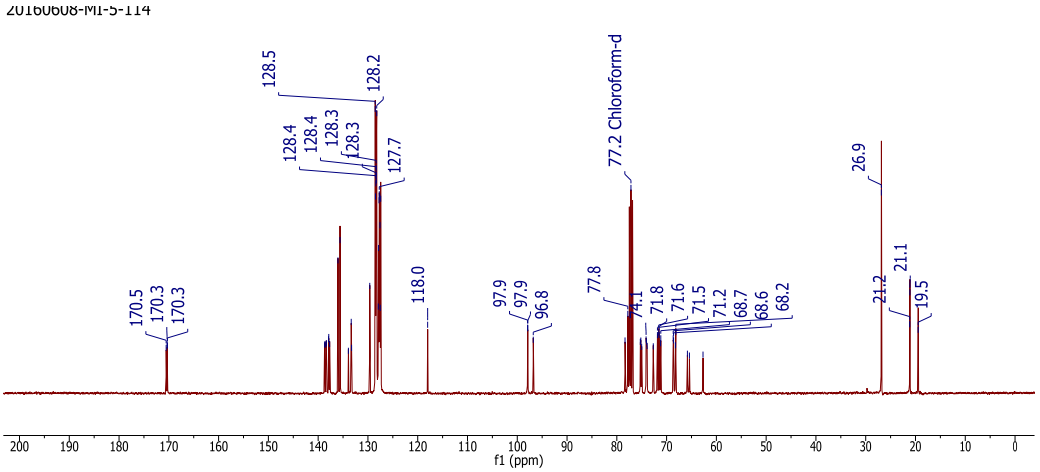

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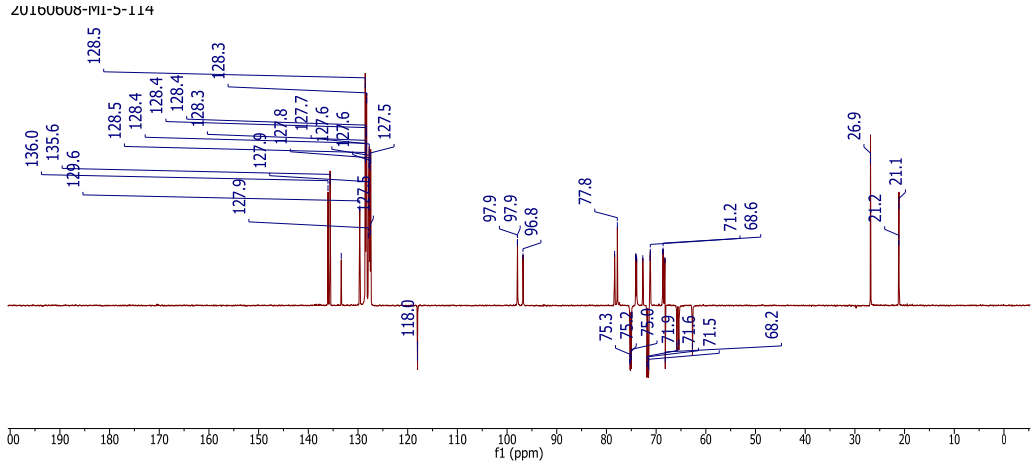

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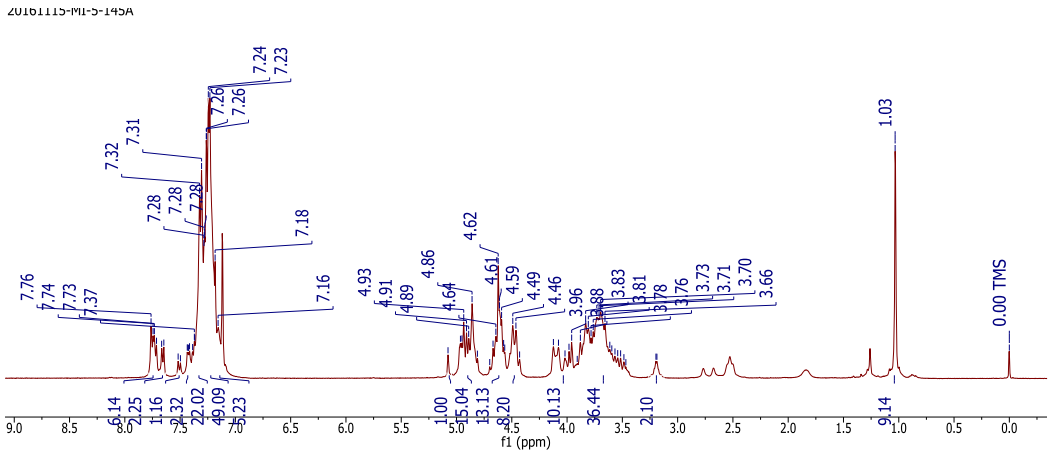

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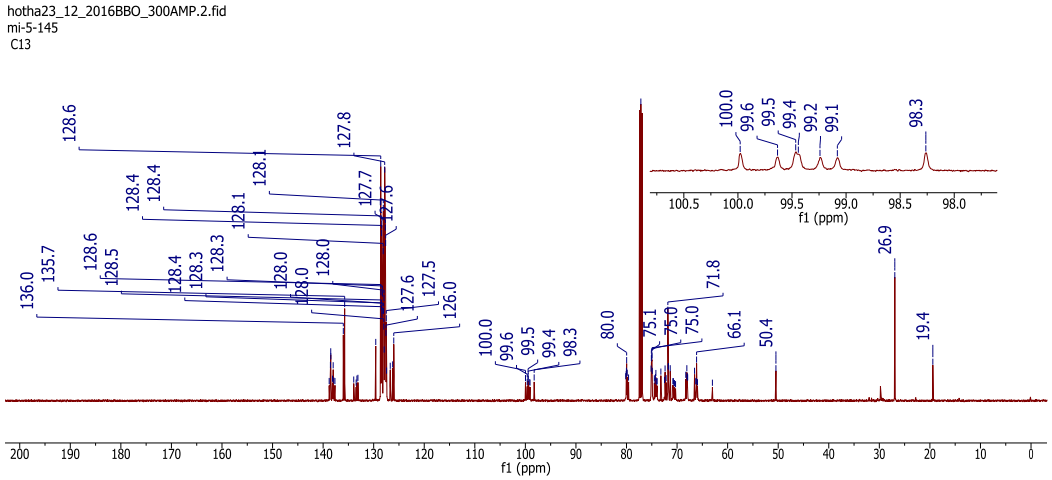
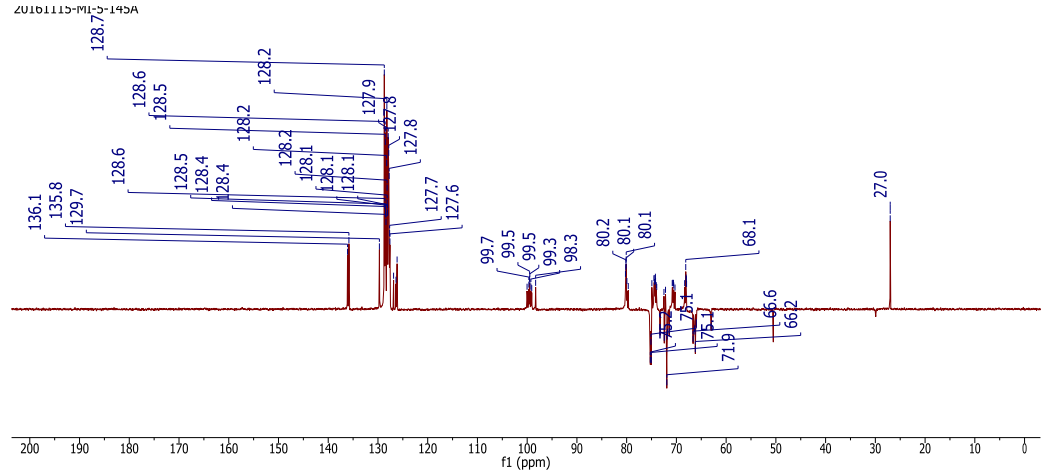


DEPT Spectrum (100.53 MHz, $CDCl_3$) of Compound **72**



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Chapter: 5

Significance of Mycolic Acid and Furanose Ring on the Conformation of *Mycobacterium tuberculosis* Cell Wall

5.1 Introduction

Mycobacterium tuberculosis (Mtb) is known since Robert Koch days as the etiological agent for tuberculosis.[1]Koch also mentioned that the Mtb has a very thick and waxy cell wall which might be the reason for its prolonged dormancy.[1]Fordecades, it was gauged that TB was a disease of the past, but the onset of the HIV epidemicresulted in a significant increase in the number of TB cases;in addition, the emergence of antibiotic resistant Mtbstrains, and the relative ineffectiveness of the BCG vaccine have put TB back on the agenda.With almost two million people being killed by TB each year, the World Health Organizationhas declared it as a global emergency.

Brennan in 1980s came up with a tentative structure of Mtb cell wall by mass spectroscopic studies and showed that there are two major oligosaccharides called Arabinogalactan (AG) and Lipoarabinomannan (LAM).[2]Interestingly, arabinose in LAM/AG and galactose in AG are found to be in the furanosyl form.Further, non-reducing end of AG is capped by mycolic acids.

5.2.1 Fine structure of arabinogalactan (AG)

With the assistance of GC-MS, NMR and FABMS spectroscopic techniques, careful analysis of the partially depolymerized polysaccharides revealed that AG mainly compose of arabinan and galactan motifs; in which galactan core consist of approximately 30 linear alternating β(1→5) and β(1→6) galactofuranosides (Gal*f*) residues.[3] Further, galactan core is extended by arabinan chain having approximately 31arabinofuranosides (Ara*f*), at the C5-position of β(1→6)Gal*f* unit. Moreover, from MS spectrometric analysis it has been found that arabinan motifs are attached at 8^{th}, 10^{th} and 12^{th} positions of β(1→6) galactan core.[4] In arabinan, there are linearly arranged α(1→5) linked Ara*f* residues with branching at the C3-positionand having four 1,2-*cis*in total and twenty-six 1,2-*trans*interglycosidic linkages. The non-reducing end of arabinanis terminated by a distinctive hexa-arabinofuranosyl motif i.e. [β-D-Ara*f*-(1→2)-α-D-Ara*f*]$_2$-3,5-α-D-Ara*f*-(1→5)-α-D-Ara*f*], where both terminal 1,2-*cis*Ara*f* as well as penultimate 1,2-*trans*Araf, C5-O are capped by mycolic acids.[5] Apart from the above well define structure; AG has little modification that differs from species to species. For example, in slow growing mycobacteria has non-acylatedgalactosamine (D-GalN) unit at the C2-position of few 3,5-α-D-Ara*f* units, whereas the non-mycolatedarabinan motifs are capped by succinyl residues (Figure 5.1) .[4a, 6]

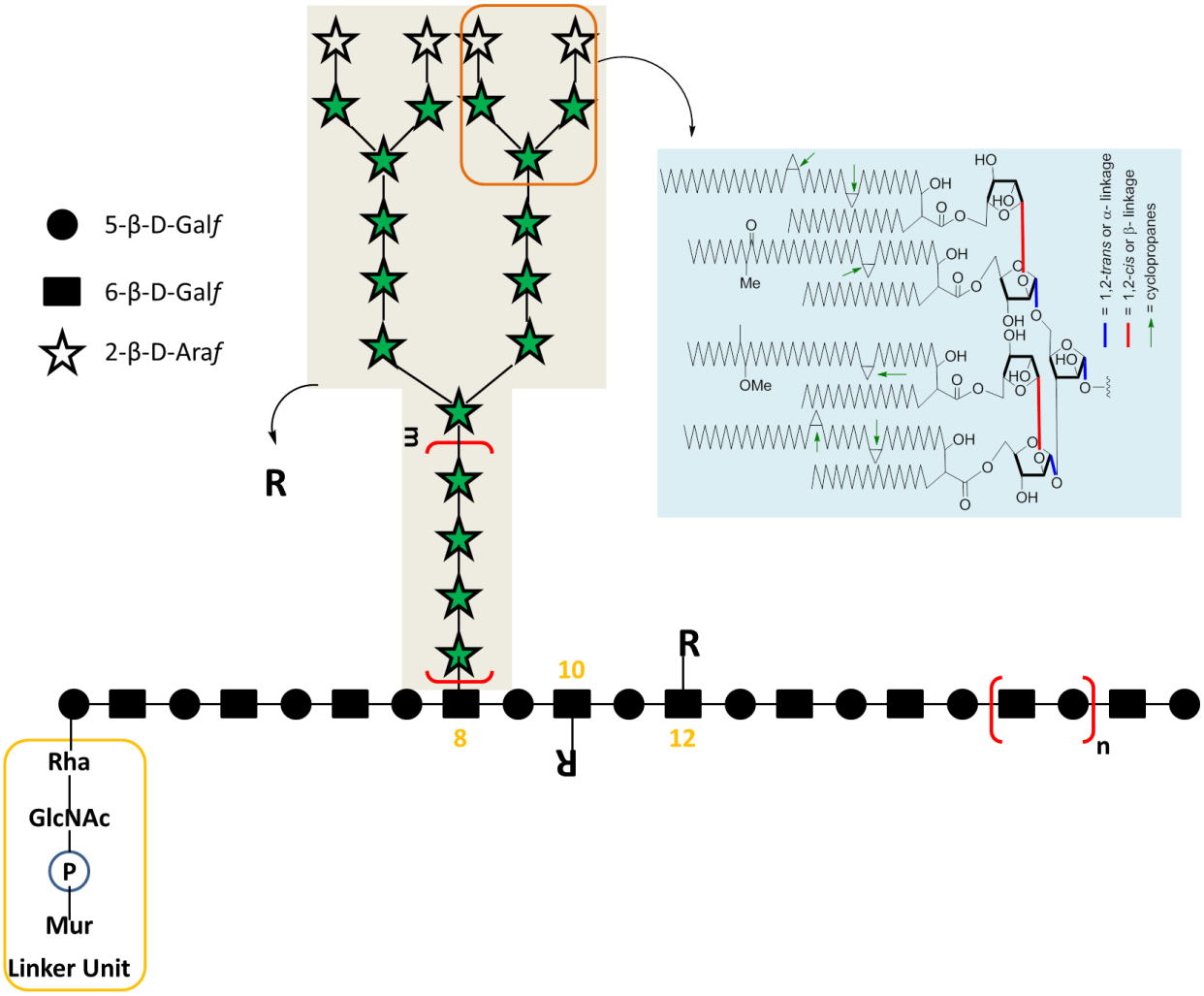


Figure 5.1 Structure of AG

5.2.2Structure of mycolic acid (MA)

Stodola*et al.* from the extract of Mtb first isolated long chain mycolic acids which are attached at the non-reducing end of branched hexa-arabinofuranosides.[3a] Latter on, Asselineau and co-workers claimed that mycolic acid consists of β-hydroxycarboxylic acid with a long α-alkyl side chain.[3b] Further, mycobacterial mycolic acids can be distinguished from the others genera by the fact that (i) they contain approximately 70-90 carbon atoms in which 24 carbons are typically saturated at the α-branch and 40-60 carbons exist in meromycolate chains, (ii) in the meromycolate chain, there are two distinctive positions occupied by double bonds, cyclopropane ringor oxygen-containing functional groups. Based on oxygen-containing functional groups, mycolic acids can be further classified into three subgroups i.e. a) mycolic acid without any

oxygen-containing functional group - α-mycolic acid, b) mycolic acids having methoxy- and keto-functional groups are called methoxy- and keto- mycolic acids respectively (Figure 5.2). The α-mycolic acid is most abundant form (> 70%), while methoxy- and keto-mycolic acids are the minor components (20 to 30%)[7].

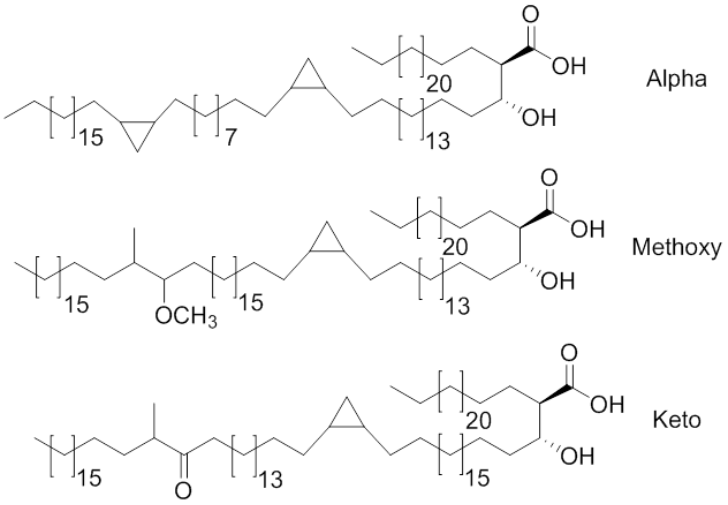
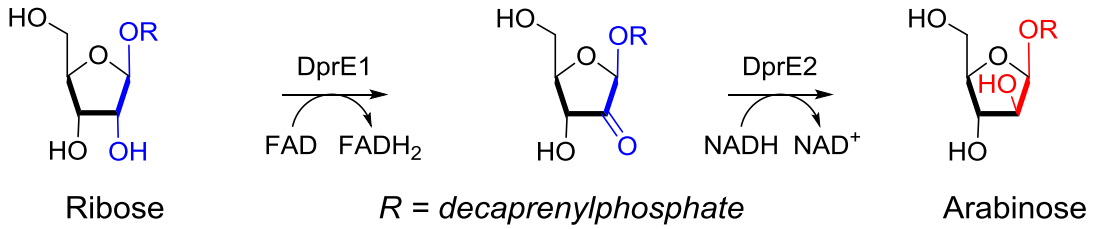


Figure 5.2 Representative examples of mycolic acids found in *Mycobacterium tuberculosis*

5.3Biosynthesis of AG

The biosynthesis of AG is initiated by priming of linker motif. At first, linker unit assembled on decaprenyl-phosphate attaches followed by sequential addition of approximately 30 Gal*f* residues in a linear fashion. The first two Gal*f*residues are added to Rha*p* in the linker unit from UDP-Gal*f*by a galactofuranosyl transferase enzyme GlfT1 (*Rv3782*). The remaining Gal*f* residues are added by a second transferase GlfT2 (*Rv3808c*) and indeed GlfT2 acts as both UDP-Gal*f*:β-D-(1→5) GalT and a UDP-Gal*f*:β-D-(1→6) GalT.[8]Therefore, it is responsible for sequentially polymerizing the bulk of the galactan polysaccharide in alternating β(1→5) and β(1→6) linkages. Next, to the galactan core at 8th, 10th and 12th positions arabinose residues are installed by arabinofuranosyltransferases (Ara*f*Ts) employing the Ara*f* donordecaprenylphosphoryl arabinose(DPA)[4c]. The linear α(1→5) linked Ara*f*s are catalyzed by a novel α(1→5) Ara*f*T, AftA (*Rv3792*). On the other hand, mycobacterial ArafT, AftC (*Rv2673*), introduce α-1, three branches by an addition of α(1→3) linked Ara*f* units to the α(1→5) arabinose chain at the non-reducing end. Recently, it has been observed that in addition to AftC, another Ara*f*Talso exists with α-1,3-branching activity encoded by AftD (*Rv0236c*). In continuation, the transfer of



Scheme 5.1Biosynthesis of 1,2-*cis*Ara*f*

terminal β(1→2) Ara*f* units from DPA onto the arabinan domain is catalyzed by AftB (*Rv3805c*)[9]. In this step, epimerization of decaprenylphosphoryl ribose (Dpr) to DPA is performed by the concerted action of two flavoproteins *viz.* DprE1 and DprE2. DprE1 uses FAD to oxidize DPR to a ketointermediate, which, in turn, is reduced to DPA by DprE2 using NADH as a cofactor (Scheme 5.1).[10] To obtain complete AG structure, final addition of mycolic acids to the non-reducing terminal sugars is catalyzed by the Antigen 85 complex which consists of three closely related proteins FbpA, FbpB and FbpC (*Rv3804c*, *Rv1886c* and *Rv0129c* respectively)[11].

With fine structural details, numerous research groups targetedinhibition of galactofuranosyltransferasesor arabinofuranose transferases in the biosynthesis of AG to develop novel therapeutic agents. For instance, ethambutol and benzothiazinones are the two drugsused for the treatment of TB, found to arrest the arabinan biosynthesis. Currently, glycolipids of Mtb are under investigation as targets for drug discovery. Presence of xenobiotic furanosyl forms of arabinose, galactose and cyclopropanes in the lipids can raise a few questions: (i) why Mtb chose furanoses over pyranoses; (ii) why Mtb chose Ara*f* over other pentoses; (iii) why Mtb cell wall has rare cyclopropanes; (iv) why Mtb requires two extra steps two synthesize particularly 1,2-*cis*Ara*f*s at the non-reducing end; (v) why Mtb did not utilize 1,2-*trans*Ara*f*or 1,2-*trans*Rib*f*at the non-reducing end; (vi) Is there any relation between arabinolipid of Mtb and its survival under extreme conditions?In this section of my thesis, we tried to address some of the above concerning issues through the synthesis of all possible isomers of hybrid mixture of Ara*f*-Rib*f* glycolipids followed by their physicochemical studies on a library of the mixture of Ara*f*-Rib*f* lipids exploiting modern spectroscopic and microscopic techniques.

5.4 Present work

The mycobacterial AG complex is essential for the viability of Mtb.[12]Although, the role of mycolic acidsis still under explored as it exists at the outer cell surface, it was assumed they are responsible for the growth of the bacteria inside the macrophages, effectively hiding from the host immune system. Very recently, with the help of ‘flexible scaffold hypothesis’ proposed that high ring flexibility of furanose rings over pyranose rings facilitates the tight packing of mycolic acids which in turn generates low permeable, dense hydrophobic façade against foreign antibiotics.[7a,13]To investigate the above hypothesis, Lowary[14a] and Jayaraman[14b] groups independently prepared series of arabinofuranosideswith hydrophobic lipids at the non-reducing and reducing end respectively. Lowary*et al.* observed from the NMR experiment that there is very little effect of lipids on the furanose conformation, while Jayraman*et al.* from the biophysical studies claimed hydrophobic alkyl chains are crucial for the mycobacterial growth. However, they have only focused on the arabinofuranosides and very little is known about why mycobacteria chose 1,2-*cis* Ara*f* linkages at the non-reducing end, why not 1,2-*trans* Ara*f*or 1,2-*trans* Rib*f* linkages? To decipher these events, we have prepared four possible hybrid structures of Ara*f*-Rib*f*(**1a-1d)** at the disaccharide level (Figure 5.3).

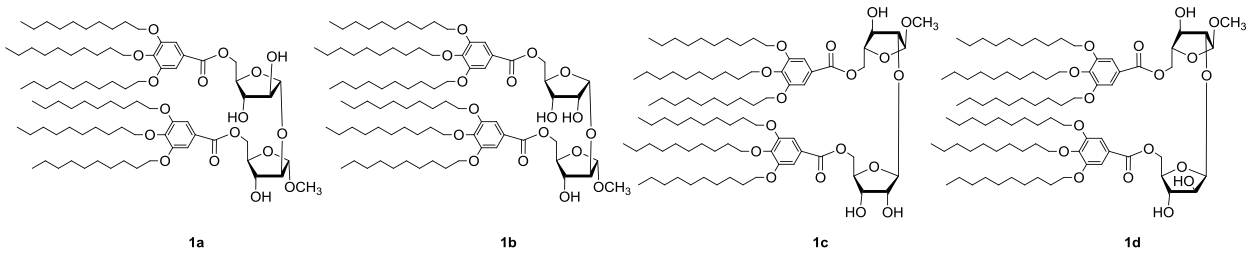
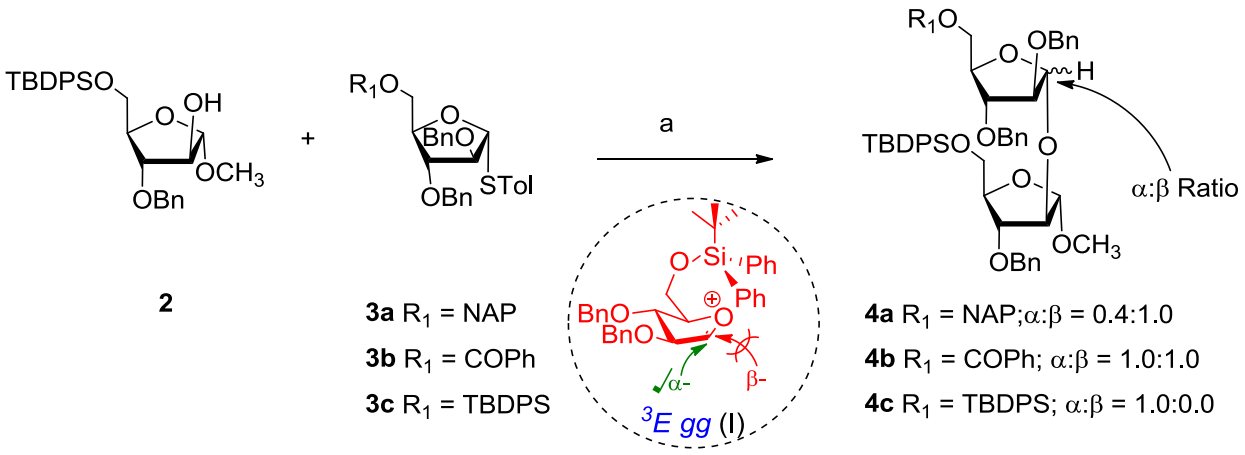


Figure 5.3Structure of hybrid Ara*f*-Rib*f* glycolipids

For the synthesis of glycolipids**1a-1d**, the initial obstacle was to adopt a method which will enable to install 1,2-*cis*Ara*f*, 1,2-*trans*Ara*f*, 1,2-*cis* and 1,2-*trans* Ara*f*-Rib*f* in a stereoselective fashion. Next, to introduce base sensitive ester units at the C5-OH position, its protecting group should be orthogonal to others hydroxyls in the system so that they can be easily cleaved off in the presence of other protecting groups. On the otherhand, C2-O and C3-O should be protected with benzyl ethers which can be removed in the presence of ester moieties at last stage to afford glycolipids**1a-1d**. Keeping these criteria in mind, we have started by optimizing the effect of C5-

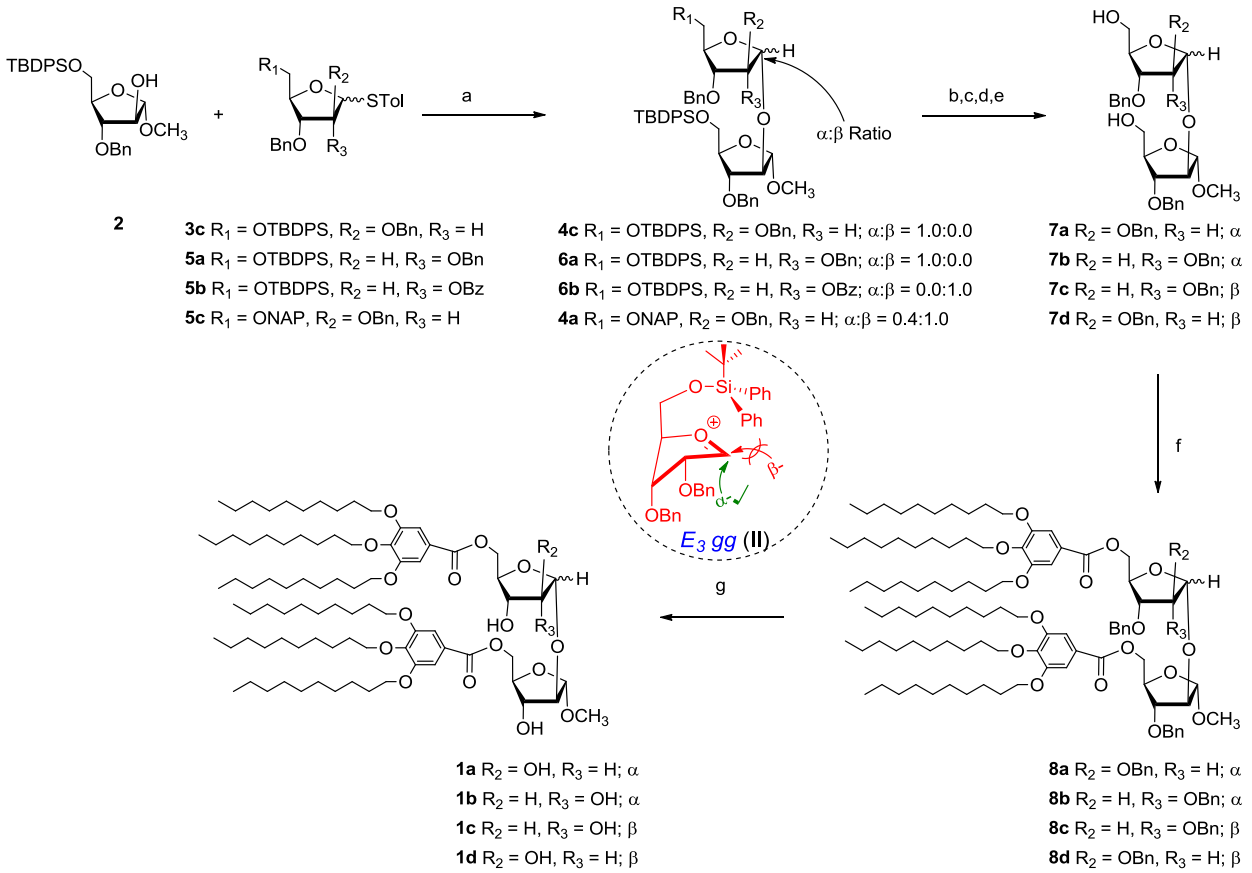
OH protecting groups on the stereoselectivefuranosylation employing glycosyl acceptor **2** and glycosyldonors **3a**-**3c** (Scheme 5.2) which were prepared from the known literature procedures and characterized them thoroughly by MS and NMR spectroscopy.



Scheme 5.2 Optimization for stereoselective arabinofuranosides. Reagents: a)NIS-AgOTf, CH_2Cl_2, 4Å MS, -20^oC, 1h, 85% for 4a, 95% for 4b and 93% for 4c.

Our optimization endeavor started by the glycosylation of acceptor **2** with donor **3a** through the activation by NIS-AgOTf in CH_2Cl_2 at -20 ^oC to give α/β = 0.4:1.0 mixture of disaccharides **4a** in 85% yield. When the glycosylation of acceptor **2** was carried out with donor **3b** having electron withdrawing substituent at C5-OH as OBz, the same reaction conditions generated α/β = 1.0:1.0 mixture of disaccharides **4b** which implies that electron density at the C5-OH is very critical for the stereoselectivefuranosylation.Surprisingly, furanosylation of acceptor **2** with donor **3c**under aforementioned conditions provided only α-disaccharide **4c** in 93% yield.Hence, exploiting Reciprocal Donor-Acceptor Selectivity (RDAS) enabled us to generate 1,2-*trans* as well as 1,2-*cis*furanosides in the absence of NGP effect. The striking difference in the selectivity can be explained by the work reported recently by Codéewho showed from free energy surface (FES) maps, arabinose and ribose oxocarbenium ions were most populated in $^3E_{gg}$ and E_{3gg} conformation at sub-zero temperatures respectively.[15] Hence, during our reaction,bulky C5-OTBDPS strongly undergoes steric repulsion with bulky acceptor **2** and in turn afford only α-isomer. The stereoselectivity of anomeric linkages was confirmed from NMR spectroscopic analysis; α-glycosides, $J_{H1\text{-}H2}$ = 1-2 Hz, $\delta_{C\text{-}1}$= 104-111 ppm, β-glycosides $J_{H1\text{-}H2}$=4-5 Hz, $\delta_{C\text{-}1}$ = 98-102 ppm. In the^{1}HNMR spectrum of compound **4b**, two 1,2-*trans* anomeric protons were

observed as singlets at δ 5.05 and 5.14 ppm; whilst^{13}CNMR spectrum showed characteristic anomeric carbon resonances at δ 105.7 and 108.3 ppm.



Scheme 5.3 Synthesis of hybrid Ara*f*-Rib*f* glycolipids.Reagents: a)NIS-AgOTf, CH_2Cl_2, 4Å MS, -20^oC, 1h, 93% for **4c**, 89% for **6a**, 94% for **6b** and 85% for **4a**; b) HF·py, pyridine, 0-25 ^0C, 5 h, 93% for **7a**, and 91% for **7b**;c) 10% TFA in CH_2Cl_2, 0 ^oC, 30 min, 75% for **7d** over two steps; d) NaOMe, MeOH, 25 ^0C, 1 h; e) NaH, BnBr, TBAI, DMF, 0-25 ^0C, 1 h, 83% *en route* to **7c**; f) 3,4,5-tris(decyloxy)benzoic acid, DIC, DMAP, CH_2Cl_2, 25-90^0C, 2 h, 91% for **8a**, 87% for **8b**, 89% for **8c** and 91% for **8d**; g) $Pd(OH)_2$, EtOAc, H_2, 36 h, 90% for **1a**, 88% for **1b**, 85% for **1c** and 89 % for **1d**.

5.4.1Preparation of hybrid Ara*f*-Rib*f* glycolipids 1a-1d (Scheme 5.3)

Inspired by the above optimized conditions, we have performed the glycosylation of acceptor **2** with donor**5a** using NIS-AgOTf in CH_2Cl_2 to obtain αAra*f*(1→2)Rib*f* disaccharide **6a** which can be rationalized by the E_{3gg} conformation of ribose oxocarbenium ion (**II**). Next, taking advantage

of the NGP effect of benzoate at C-2 position, βAra*f*(1→2)Rib*f***6b** was synthesized by glycosylation betweenacceptor **2** and donor **5b**. In the ^{1}HNMR spectrum of disaccharide**6a**, 1,2-*trans*of and 1,2-*cis* anomeric protons overlapped at δ 5.23 ppm; however, in the ^{13}CNMR spectrum, characteristic 1,2-*cis* and 1,2-*trans* anomeric carbons were observed at δ 101.1 and 108.1 ppm. The NMR spectra of compound **6b** was equivalent to that of compound**6a**, except that, ^{13}CNMR resonances at δ 101.1 ppm were replaced by new resonances at δ 105.6 ppm corresponding to thefreshly formed 1,2-*trans* anomeric carbon.

In continuation, disaccharide diol **7a** and **7b** were accomplished from respective compounds **4c** and **6a** by the treatment of HF·py in THF. Consecutive saponification of compound **6b** using NaOMe/MeOH, benzylation of lone -OH by NaH/BnBr in DMF, followed by the cleavage of

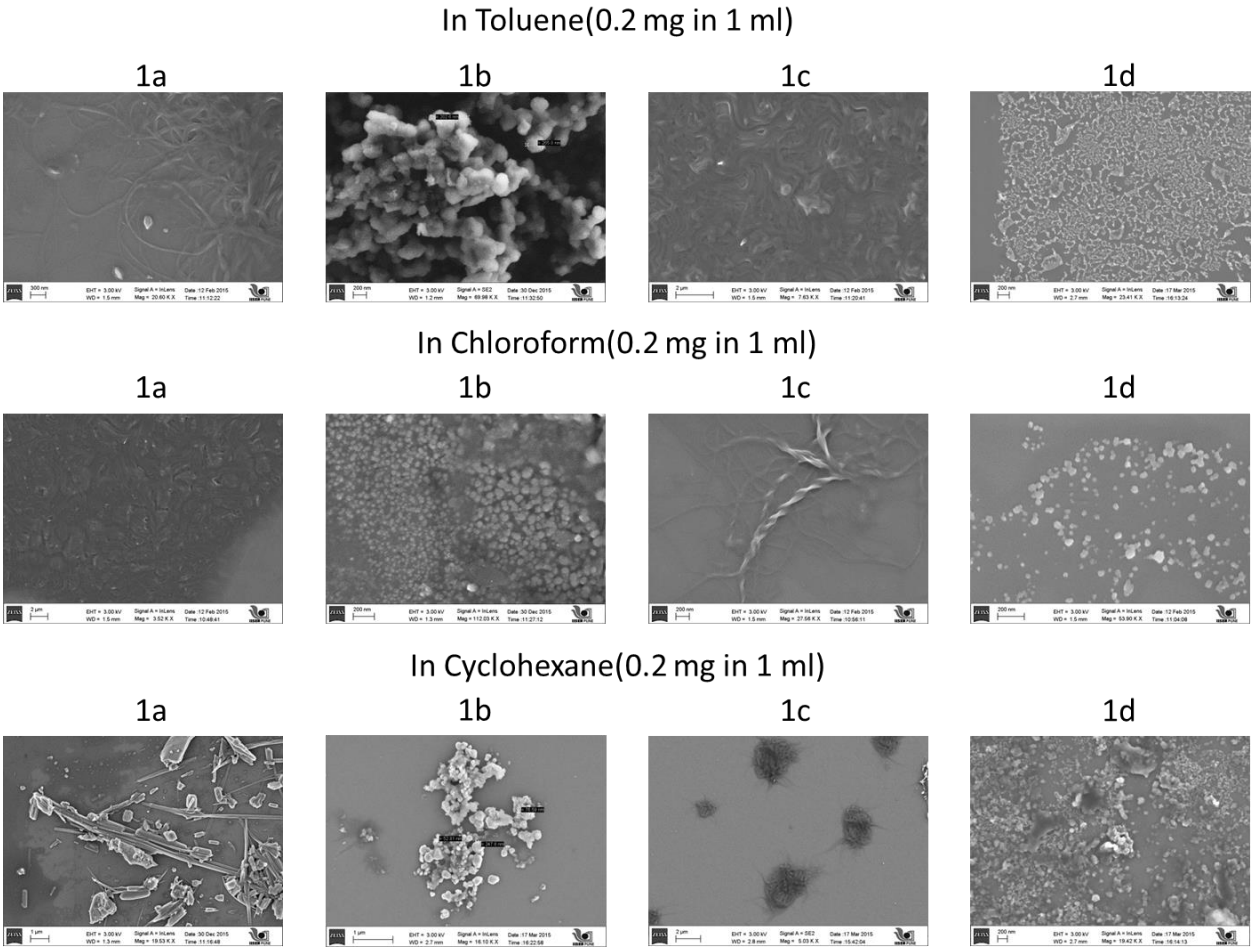
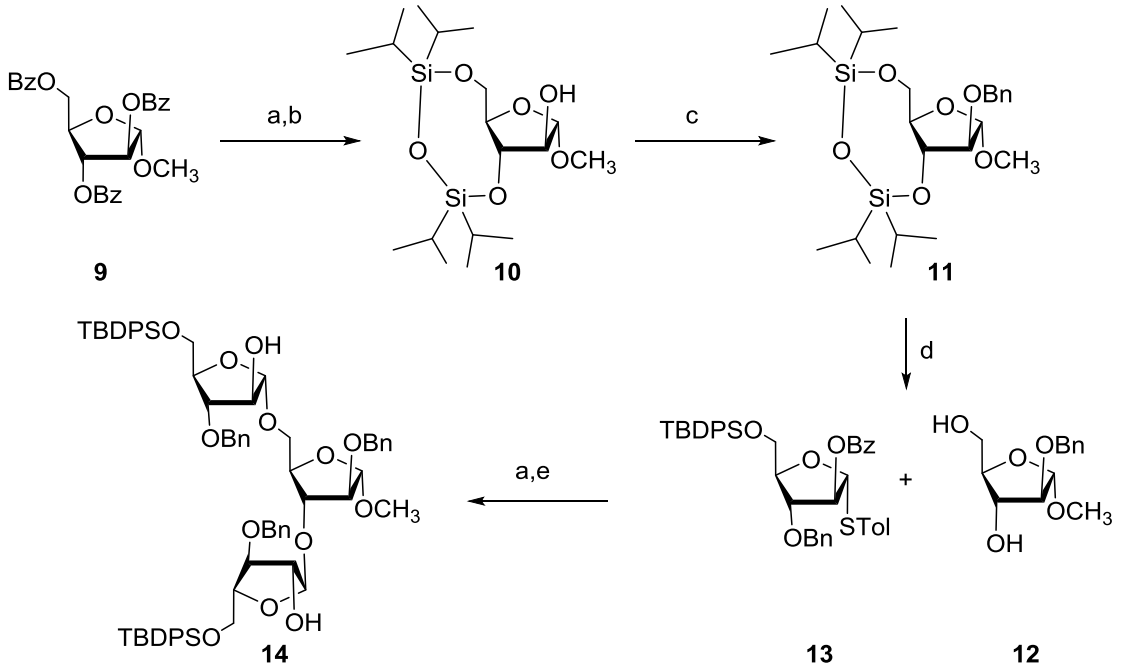


Figure 5.4 FE-SEM images of 1a-1d

two silyl ethers employing HF·py in THF generated another disaccharide diol **7c**. Similarly, compound **4a**was esterified with 3,4,5-tris(decyloxy)benzoic acid by DIC/DMAP in CH_2Cl_2 at 25-90 ^oC to afford respective gallates**8a**-**8d**.

After confirming the homogeneity of **8a**-**8d** by MS and NMR spectroscopy, all gallates were subjected to hydrogenolysis using $Pd(OH)_2/H_2$ in EtOAc for 36 h to result in targeted glycolipids **1a**-**1d**. In the ^1H NMR spectrum, two 1,2-*trans* anomeric protons appeared at δ 5.01, 5.15 (d, *J* = 1.5 Hz) ppm for glycolipid**1a** and δ 5.02, 5.16 ppm for glycolipid**1c**; whereas in the ^{13}CNMR spectrum, characteristic 1,2-*trans* anomeric carbons were noticed at δ 107.6, 107.8 ppm for **1a** and δ 107.6, 107.7 ppm for **1c**.On the other hand, in ^1HNMR spectrum, 1,2-*trans* and 1,2-*cis* anomeric protons were noticed at δ 5.0 and 5.16 (d, *J* = 4.4 Hz) ppm respectively for glycolipid**1b**, δ 4.80 (d, *J* = 1.7 Hz) and 4.96 (d, *J* = 4.2 Hz) ppm for glycolipid **1d**; whilst, ^{13}CNMR spectra of respective 1,2-*cis* and 1,2-*trans* anomeric carbons were observed at δ 102.4 and 107.5 ppm for compound **1b**, δ 101.6 and 106.9 ppm for compound**1d**.



Scheme 5.4Preparation of trisaccharide acceptor. Reagents: a) NaOMe, MeOH, 25 ^0C, 1 h, 96% *en route* to **10** and 90% for **14**; b) 1,3-Dichloro-1,1,3,3-tetraisopropyldisiloxane, Py., 0-25 ^oC, 1h 85%; c) NaH, BnBr, TBAI, DMF, 0-25 ^0C, 1 h, 82%; d) HF·py, pyridine, 0-25 ^0C, 3 h, 95%; e) NIS-AgOTf, CH_2Cl_2, 4Å MS, 0^oC, 1h, 95%.

Successfully synthesizing glycolipids **1a-1d**, we have attempted to check the impact of subtle changes in stereochemistry on self-assembling properties; we have recorded the FE-SEM images (Figure 5.4) of glycolipids**1a-1d** at identical concentration in three different solvents. Careful analysis of SEM images disclosed that the glycolipids **1b** and **1d** assembled in particle morphology in three different solvents; whereas **1a** and **1c** showed fibrillar, helical or sheet like morphology that differs depending upon the solvents further signifying that subtle changes can have big impact on the self-assembling abilities.

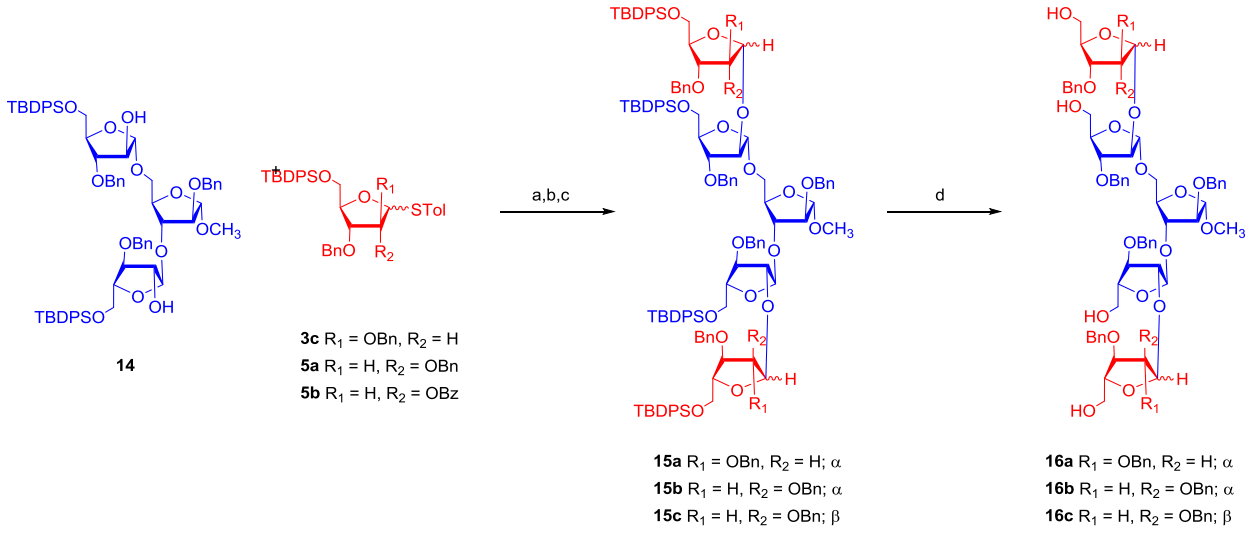
5.4.3 Preparation of trisaccharide acceptor 14 (Scheme 5.4)

With the synthesis of disaccharide glycolipids **1a-1d**, we have also exploited earlierlearnings from RDAS to synthesize four possible hybrid pentasaccharides as well. The assembly of pentasaccharides**15a-15c**commenced with the synthesis of attrisaccharide diol acceptor **14**.*En route* to **14**,monosaccharide diol **12**was achieved in four consecutive steps *viz.* saponification of compound **9** followed by blocking of C3- and C5-OHusing 1,2-dichloro-1,1,3,3-tetraisopropyldisiloxane in pyridine to getdisiloxane**10**. Benzylation of C2-OH using NaH/BnBr in DMF followed by the removal of di-silyl ether by HF·py/THF affordedcompound **12** in 63% overall yield. Subsequently, compound **12** was subjected to glycosylation with donor **13** employing NIS-AgOTfconditions to generate thetrisaccharide in which two benzoate esters were deprotectedunder Zemplén conditions to afford 85% of compound**14**. In the ^{1}HNMR spectrum of compound **14**, three anomeric protons were noticed at δ 4.94, 5.12 and 5.15 ppm as individual singlets and corresponding anomeric carbons were observed at δ 107.3, 107.9 and 109.1 ppm in ^{13}C NMR spectrum which confirmed the 1,2-*trans* selectivity in the trisaccharide**14**.

5.4.4 Preparation of furanosylpentasaccharides16a-16c (Scheme 5.5)

In continuation,trisaccharide acceptor **14** was subjected to glycosylation with donor **3c** using NIS-AgOTf promoters in CH_2Cl_2 at -20 ^{o}C to afford completely 1,2-*trans*pentasaccharide**15a** in 92% yield without any assistance of NGP effect that can be rationalized by $^{3}E_{gg}$ conformation of Ara*f*oxocarbenium ion (**I**).In continuation, glycosylation between compounds **14** and **5a**under similar conditions gave 80% of 1,2-*cis* (α) pentasaccharide**15b**. Further, 1,2-*trans* (β) pentasaccharide**15c** was obtained by the glycosylation of **14** and **5c** using NIS-AgOTf and here 1,2-*trans* selectivity was realized through the NGP effect of C2-OBz in donor **5c**.Finally,

conversion of **15a** and **15b** to respective target molecules **16a** and **16b** was performed by subsequent removal of four silyl ethers utilizing HF·py/THF and target pentasaccharide-tetraol**16c** was obtained from compound **15c** by three successive operations i.e. cleavage of the C2-OBz by saponification underNaOMe/MeOH conditions, benzylation of resulting C2-OH using

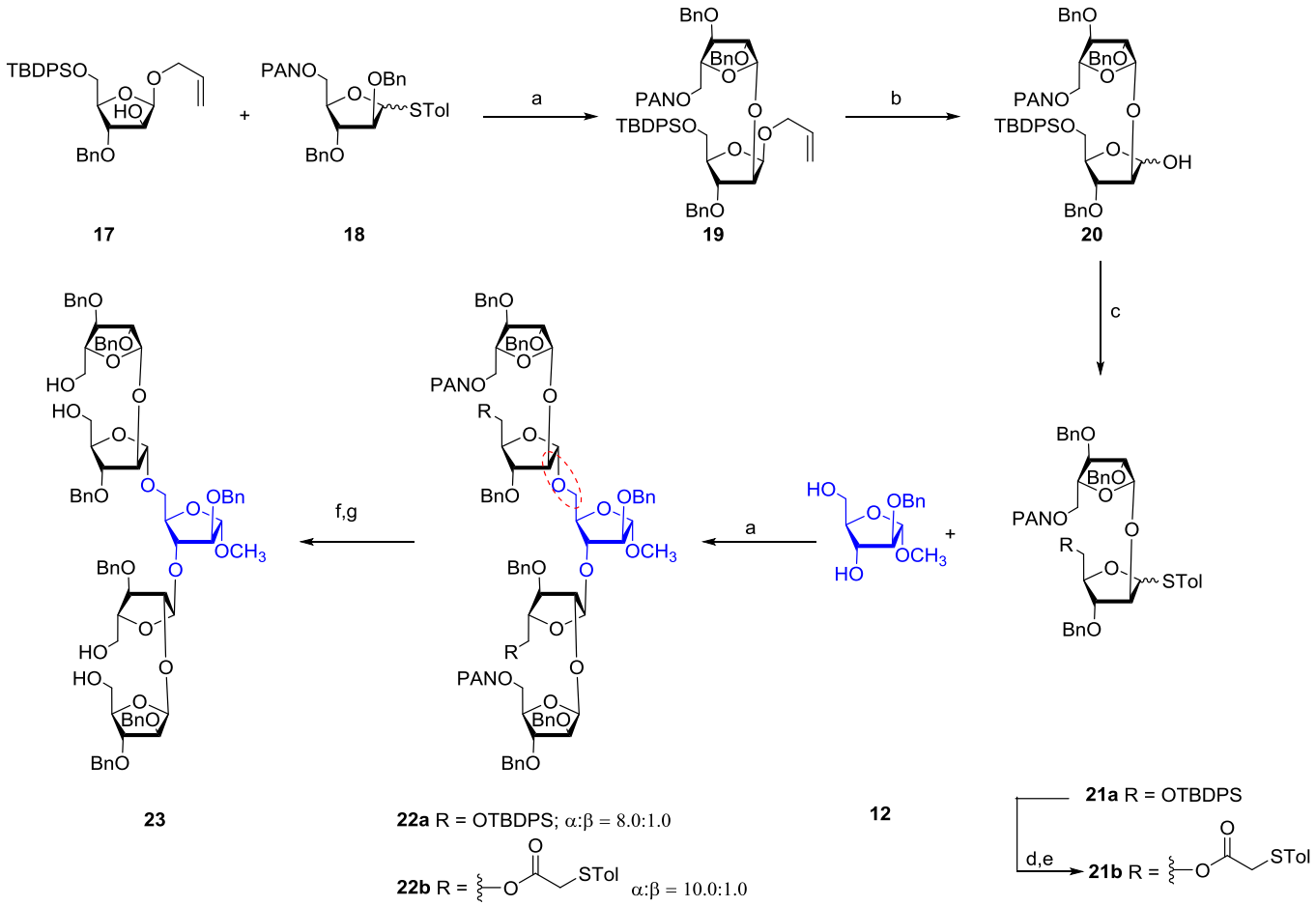


Scheme 5.5Synthesis of hybrid Ara*f*-Rib*f*pentasaccharides.Reagents: a) NIS-AgOTf, CH_2Cl_2, 4Å MS, 0^{o}C, 1h, 92% for 15a, 80% for 15b and 96% *en route* to **15c**; b) NaOMe, MeOH, 25 ^{0}C, 1 h; c) NaH, BnBr, TBAI, DMF, 0-25 ^{0}C, 1 h, 81% for **15c** over two steps; d) HF·py, pyridine, 0-25 ^{0}C, 3 h, 91% for **16a**, 88% for **16b** and 85% for **16c**.

NaH/BnBr, followed by deprotection of silyl ethersusing HF-py/THF.In the ^{1}HNMR spectrum, five 1,2-*trans* anomeric protons showed resonances at δ 4.85, 5.12 (2H), 5.18 and 5.21 ppm for compound **15a**, δ 4.84, 5.09, 5.19, 5.21 and 5.39 ppm for compound **15c**; whilst in ^{13}CNMR characteristic five 1,2-*trans* anomeric carbons appeared at δ 104.8, 105.5, 106.1, 107.1 and 107.4 ppm for compound **15a**, δ 104.6 (2C), 104.9, 106.6 and 107.3 ppm for compound **15c**. In ^{1}HNMR spectrum of compound **15b**, resonances at δ 5.29, 5.33 and 5.60 (d, *J* = 2.8 Hz) ppm suggested the presence of three 1,2-*trans* linkages and two doublets at δ 5.11 (d, *J* = 3.8 Hz) and 5.12 (d, *J* = 4.1 Hz) defined the characteristic two 1,2-*cis* linkages. In addition, ^{13}CNMR showed characteristic three 1,2-*trans* anomeric carbons resonances at δ 105.7, 107.0 and 107.6 ppm whereas two 1,2-*cis* anomeric carbons showed two distinctive resonances at δ 100.6 and 101.5 ppm.

5.4.5 Preparation of furanosylpentasaccharide 23 (Scheme 5.6)

For the synthesis of another target **23**, we have adopted the methodology as described in chapter-4 in which 1,2-*cis*Ara*f* disaccharide was achieved by the glycosylation of sterically crowded and less reactive acceptor with armed glycosyl donor at the lower temperature. Accordingly, 1,2-*cis* acceptor **17** was subjected to the glycosylation with donor **18** employing standard NIS-AgOTf

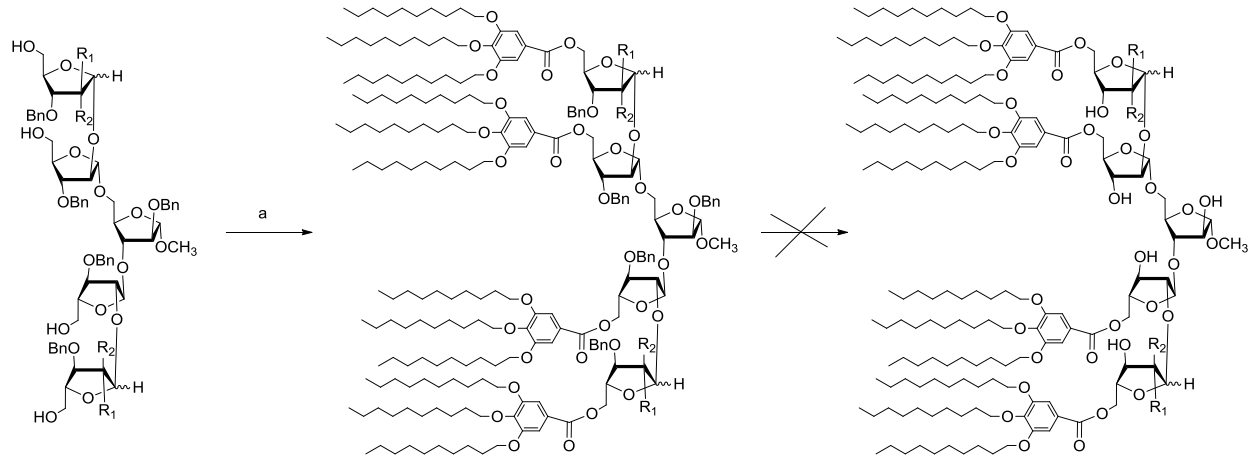


17 **18** **19** **20** **12** **23**

Scheme 5.6Synthesis of 1,2-*cis*Ara*f* pentasaccharide: Reagents a) NIS-AgOTf, CH_2Cl_2, 4Å MS, -78^oC, 1h, 90% for 19, 85% for 22a and 78% for 22b; b) $PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 ^0C, 4 h, 83%; c) p-Tolyl disulfide,tri-n-butylphosphine,CH_2Cl_2, 0 ^oC, 45 min,80%; d) HF·py, pyridine, 0-25 ^0C, 3 h; e) 2-(p-tolylthio)acetic acid,DIC, DMAP, CH_2Cl_2, 25-90^0C, 2 h, 90%; f) NaOMe, MeOH, 25 ^0C, 1 h; g) DDQ, CH_2Cl_2-MeOH (1:4), 25 ^0C, 4 h, 78% over two steps.

activators in CH_2Cl_2 at -78 ^oC to provide 1,2-*cis* disaccharide **19** in 90% yields. $PdCl_2$ catalyzed hydrolysis of allyl glycoside of **19** in CH_2Cl_2/MeOH gave disaccharide hemiacetal **20** which was subsequently converted to the corresponding thiotolyl donor **21a** utilizing p-tolyl disulfide/tri-*n*-

butylphosphine in CH_2Cl_2 at 0 ^oC.At this stage, donor **21a** was divided into two parts - one part was glycosylated with acceptor **12** in NIS-AgOTf conditions to generate α/β = 8:1 mixture of pentasaccharide**22a**in 85% yield. In the second part of donor **21a**, silyl ether was removed using HF-py/THF and then free primary –OHs were esterified with more α-directing 2-(p-tolylthio)acetic acid employing DIC/DMAP in CH_2Cl_2. NIS-AgOTf assisted glycosylation of donor **21b** with acceptor **12** enhanced α-selectivity affording α/β = 10:1 mixture of pentasaccharide**22b**. Later, NAP ethers of compound **22b** and ester moieties were removed by the successive treatment of DDQ in CH_2Cl_2/MeOH, followed by NaOMe/MeOH to result in pentasaccharide-tetraol **23** in 78% over two steps. 1,2-*trans* and 1,2-*cis* linkages of compound **22b** were verified by the NMR spectroscopy. In the ^{1}HNMR spectrum of compound **22b**, three 1,2-*trans* anomeric protons were observed as individual singlets at δ 4.89, 5.09 and 5.15 ppm whereas 1,2-*cis* anomeric protons showed resonances at δ 4.97 (d, *J* = 4.2 Hz) and 5.14 (d, *J* = 4.7 Hz) ppm. In the ^{13}CNMR of compound **22b**, three 1,2-*trans* anomeric carbons appeared at δ 105.5, 106.7 and 107.0 ppm, while two 1,2-*cis* anomeric carbons were noticed at δ 100.0 and 100.3 ppm.



16a R_1 = OBn, R_2 = H; α
16b R_1 = H, R_2 = OBn; α
16c R_1 = H, R_2 = OBn; β
23 R_1 = OBn, R_2 = H; β

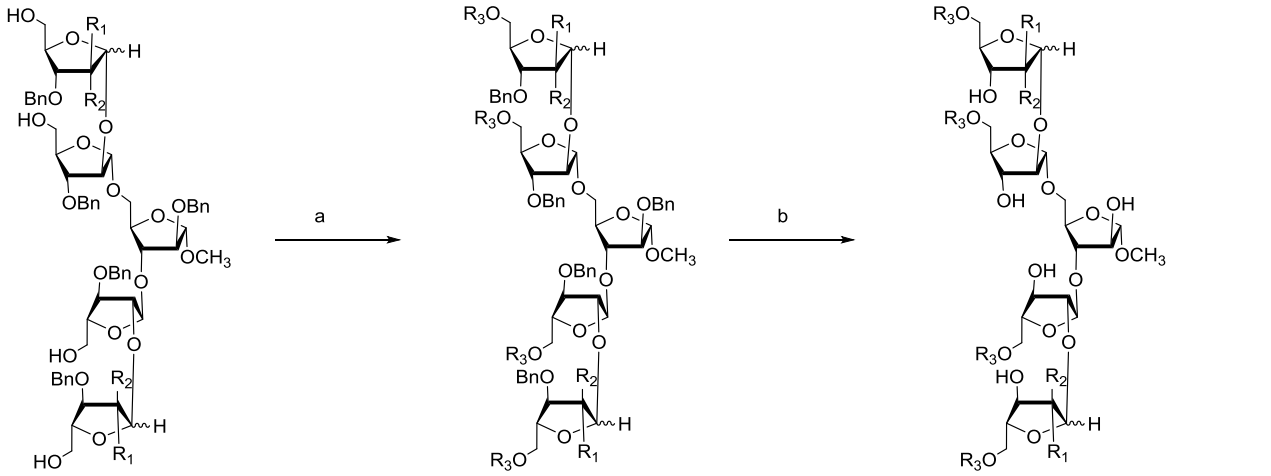
24a R_1 = OBn, R_2 = H; α
24b R_1 = H, R_2 = OBn; α
24c R_1 = H, R_2 = OBn; β
24d R_1 = OBn, R_2 = H; β

25a R_1 = OH, R_2 = H; α
25b R_1 = H, R_2 = OH; α
25c R_1 = H, R_2 = OH; β
25d R_1 = OH, R_2 = H; β

Scheme 5.7Synthesis of hybrid Ara*f*-Rib*f*pentasaccharide glycolipids.Reagents: a) 3,4,5-tris(decyloxy)benzoic acid, DIC, DMAP, CH_2Cl_2, 25-90^{0}C, 2 h, 80% for **24a**, 78% for **24b**, 75% for **24c** and 79% for **24d**; b) $Pd(OH)_2$, CH_2Cl_2-MeOH, H_2, 36-72 h.

5.4.6 Preparation of pentasaccharides glycolipids 27a-27h (Scheme 5.8)

The final set of glycolipids **25a-25d** were accomplishedby esterification of pentasaccharides**16a-16c**,**23** with 3,4,5-tris(decyloxy)benzoic acid using DIC/DMAP in CH_2Cl_2 at 25 ^oC; a complex mixture of mono-, di- and tri-esterified products were obtained. However, coupling reaction at 90 ^oC using DIC/DMAP smoothly afforded desired gallates**24a-24d** (Scheme 5.7). Esterified compounds were next carried forward to hydrogenolysis utilizing $Pd(OH)_2/H_2$ in $EtOAc/CH_2Cl_2$to obtain pentasaccharide glycolipids **25a-25d**; unfortunately, in each case, one or two benzyl ethers did not get removedunder aforementioned reaction conditions. All attempts of optimization during hydrogenolysis using many solvents systems were futile.



16a R_1 = OBn, R_2 = H; α
16b R_1 = H, R_2 = OBn; α
16c R_1 = H, R_2 = OBn; β
23 R_1 = OBn, R_2 = H; β

26a R_1 = OBn, R_2 = H, R_3 = C(O)Ph(O)$C_{10}H_{21}$; α
26b R_1 = OBn, R_2 = H, R_3 = C(O)$C_{12}H_{25}$; α
26c R_1 = H, R_2 = OBn, R_3 = C(O)Ph(O)$C_{10}H_{21}$; α
26d R_1 = H, R_2 = OBn, R_3 = C(O)$C_{12}H_{25}$; α
26e R_1 = H, R_2 = OBn, R_3 = C(O)Ph(O)$C_{10}H_{21}$; β
26f R_1 = H, R_2 = OBn, R_3 = C(O)$C_{12}H_{25}$; β
26g R_1 = OBn, R_2 = H, R_3 = C(O)Ph(O)$C_{10}H_{21}$; β
26h R_1 = OBn, R_2 = H, R_3 = C(O)$C_{12}H_{25}$; β

27a R_1 = OH, R_2 = H, R_3 = C(O)Ph(O)$C_{10}H_{21}$; α
27b R_1 = OH, R_2 = H, R_3 = C(O)$C_{12}H_{25}$; α
27c R_1 = H, R_2 = OH, R_3 = C(O)Ph(O)$C_{10}H_{21}$; α
27d R_1 = H, R_2 = OH, R_3 = C(O)$C_{12}H_{25}$; α
27e R_1 = H, R_2 = OH, R_3 = C(O)Ph(O)$C_{10}H_{21}$; β
27f R_1 = H, R_2 = OH, R_3 = C(O)$C_{12}H_{25}$; β
27g R_1 = OH, R_2 = H, R_3 = C(O)Ph(O)$C_{10}H_{21}$; β
27h R_1 = OH, R_2 = H, R_3 = C(O)$C_{12}H_{25}$; β

Scheme 5.8 Synthesis of hybrid Ara*f*-Rib*f*pentasaccharide glycolipids.Reagents: a) 4-decyloxy benzoic acid or dodecanoic acid, DIC, DMAP, CH_2Cl_2, 25-90^0C, 2 h, 87% for **26a**, 91% for **26b**, 85% for **26c**, 92% for **26d**, 83% for **26e**, 91% for **26f**, 82% for **26g** and 90% for **26h** ; b) $Pd(OH)_2$, EtOAc-$CHCl_3$, H_2, 36 h, 85% for **27a**, 88% for **27b**, 89% for **27c**, 90% for **27d**, 86% for **27e**, 88% for **27f**, 85% for **27g** and 89% for **27h**.

We thought that the reaction must be resulting in the formation of some micellar structures in the reaction mixture to make conditions heterogeneous thereby decreasing the rate of the reaction. To circumvent this limitation, we have replaced the tri-antennary lipids with two different sets of mono-antennary lipids 4-decyloxy benzoic acid and dodecanoic acid. Esterification of **16a**-**16c** and **23** with 4-decyloxy benzoic acid and dodecanoic acid employing DIC/DMAP in CH_2Cl_2 at 25 ^oC gave respective glycolipids **26a**, **26c**, **26e**, **26g** and **26b**, **26d**, **26f**, **26h** which were further subjected to hydrogenolysisunder$Pd(OH)_2/H_2$ in CH_2Cl_2/MeOH to afford targeted glycolipids **27a**-**27h** in moderate to excellent yields. The stereoselectivity of anomeric linkages of **27a**-**27h** were confirmed from the NMR spectroscopy analysis; 1,2-*trans*-glycosides, J_{H1-H2} = 1-2 Hz, δ_{C-1} = 104-111 ppm; 1,2-*cis*-glycosides J_{H1-H2} = 4-5 Hz, δ_{C-1}= 98-102 ppm.

In summary, we have developed efficient approaches for the synthesis of four possible Ara*f*-Rib*f* hybrid glycolipids in disaccharide as well as pentasaccharide levels. The synthesis was highlighted by introducing 1,2-*cis*, 1,2-*trans*Ara*f*s and 1,2-*cis*Ara*f*-Rib*f*interglycosidic bonds exploiting Reciprocal-Donor-Acceptor-Selectivity (RDAS), whereas 1,2-*trans*Ara*f*-Rib*f*was assembled by taking advantage of neighboring group participation (NGP). Preliminary FE-SEM studies on compounds**1a**-**1d** revealed that subtle changes in stereochemistry cause phenomenal changes in the self-assembling property of these glycolipids.Physicochemical studies withthese furanosyl lipids**1a**-**1d** and **27a**-**27h** are currently underway.

5.5 Experimental section

Preparation of *p*-thiotolyl donor from hemiacetal (21a): To a rapidly stirring CH_2Cl_2 solution of arabinofuranosylhemiacetal**20** (1.0 mmol) and *p*-Tolyl disulfide (1.5 mmol) at 0^0C, tri-n-butyl phosphine (1.2 mmol) was added and continued stirring at 0^0C for 40 minutes. After complete consumption of the hemiacetal, the reaction mixture was concentrated in *vacuo* and purified by silica gel column chromatography (n-hexane/EtOAc) to afford p-thiotolyl donor**21a** in 80% yield.

General procedure for the glycosylation using *p*-thiotolyl donor (4a-4c, 6a-6b, 14, 15a-15c, 19, 22a-22b): To a solution of acceptor (1mmol) and donor (1.2 mmol) in anhydrous CH_2Cl_2 (15 mL) was added freshly activated 4Å MS powder (0.400 g) at 25 ^{0}C. After cooling to -20 °C or -78 ^{o}C, NIS (1.5 mmol) and AgOTf or TfOH (0.2 mmol) were added to the reaction mixture and stirred for 1.5h at aforementioned temperature, the reaction was neutralized by Et_3N and filtered through a bed of Celite®. The filtrate was concentrated in *vacuo* to obtain reddish colored oil that was purified by silica gel flash column chromatography (n-hexane/EtOAc) to afford furanosides in moderate to good yield.

Protection of alcohol using 1,3-Dichloro-1,1,3,3-tetraisopropyldisiloxane (10):A solution of the allylarabinofuranoside diol (1 mmol) and imidazole (2.3 mmol) in anhydrousDMF (5 mL) was cooled at 0 ^{0}C and 1,3-Dichloro-1,1,3,3-tetraisopropyldisiloxane(2.2 mmol) was addeddropwise under nitrogen atmosphere. The reaction mixture was gradually warmed up to 25^0C and stirred for 2 h. After the completion, the reaction mixture was quenched by adding icecold water. The whole mixture was transferred to a separatory funnel and extracted with ethylacetate (3x25 mL). The combined organic layers were washed with cold water and brine solution. Organic layer was dried over anhydrous Na_2SO_4, the organic layer was concentrated in *vacuo* and the residue was purified by silica gel column chromatography (ethyl acetate/hexanes) to obtain the desired product.

Deprotection of the TBDPS-ethers (7a-7d, 12, 16a-16c, 21b, 23):HF·py (3 mmol) was added dropwise under inert atmosphere to a solution of silyl ether-furanosides (1mmol) in pyridine (3 times to the volume of HF·py) at 0 ^{0}C. The reaction mixture was stirred for 5 h at 25 ^{0}C, 6N HCl was added to quench the reaction at 0 ^{0}C, diluted with EtOAc (25mL) and washed successively

with ice cold water (2x10 mL), saturated solution of $NaHCO_3$(aq), and brine solution. Organic layer was dried anhydrous Na_2SO_4, concentrated *in vacuo*to obtain a residue that was purified by silica gel column chromatography (ethyl acetate/hexanes) to furnish the alcohol.

Protection of alcohols as benzyl ethers (7c, 11, 15c): To a solution of the alcohol (1 mmol) in anhydrous DMF (5 mL) was cooled to 0 ^{0}C under nitrogen atmosphere and NaH (60% oil dispersion, 1.3mmol per alcohol) was added and stirred for 10 minute at 0 ^{0}C, benzyl bromide (1.2 mmol per alcohol) was added dropwise and stirred for 2 h at 25 ^{0}C. The reaction mixture was poured into cold water with vigorous shaking, extraction with ethyl acetate (3x25 mL) and combined EtOAc layers was washed with cold water, brine solution, and dried over Na_2SO_4. The EtOAc solution was decanted and evaporated in vacuo to obtain a reddish brown colored residue that was purified by column chromatography (ethyl acetate/hexanes) to obtain the benzyl ether(s) as pale yellow colored syrup.

Deprotection of allyl glycosides (20): To the solution of the allyl glycoside**19** (1 mmol) in CH_2Cl_2 (10 mL), $PdCl_2$ (0.2mmol) in MeOH (40mL) was added in five portions at 25 ^{0}C and stirred for 4-5 h. After completion of the reaction, excess amount of Et_3N was added and the solid residue was filtered off through apad of Celite®. The solvent was evaporated in *vacuo* and the crude compound was purified by conventional silica gel column chromatography (ethyl acetate/hexanes) to obtain thedesired hemiacetal**20**in 83% yields.

Esterification of alcohols (8a-8d, 21b, 24a-24d, 26a-26h):A solution of the alcohol (1 mmol), DMAP (0.5 mmol) and lipid carboxylic acid (1.3 mmol) in dryCH_2Cl_2 (10 mL) was cooled to 0 ^{0}C and N, N'-Diisopropylcarbodiimide (1.5 mmol) was added dropwise under nitrogen atmosphere. The reaction mixture was gradually warmed to 25 or 90 ^{0}Cand stirred for 2 h. After completion of the reaction, CH_2Cl_2 was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate/hexanes) to furnish corresponding glycolipids.

Deprotection of NAP ethers (23): 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (2 mmol) was added to a rapidly stirred solution of alcohol (1 mmol) in CH_2Cl_2-MeOH (1:4) at 25 ^{0}C. After 4 h, the reaction mixture was quenched by the addition of Et_3N (reaction mixture turns black from brown) and solvent was evaporated under reduced pressure and the residue was purified by silica

gel column chromatography (ethyl acetate/hexanes) to furnish the alcohol as pale yellow colored syrup.

Saponification of esters (7c, 10, 14, 15c, 23): Freshly prepared NaOMe (0.1 mmol per benzoate) was added to a solution of the esters (1 mmol) in MeOH (10 mL) and stirred for 8 h at 25 ^{0}C. The reaction mixture wasconcentrated in *vacuo* to obtain a residue that was purified by column chromatography (ethyl acetate/hexanes) to obtain alcohol.

Hydrogenolysis of compound (1a-1d, 27a-27h): To a solution of the compound (1mmol) in 5 mL of suitable solvents mixture under hydrogen atmosphere (balloon pressure) was added 10% $Pd(OH)_2$(0.1mmol)and stirred for 36 h at 25 ^{0}C. The reaction mixture was filtered through a pad of Celite® and the filtrate was evaporated in *vacuo* and purified by column chromatography (ethyl acetate/hexanes) to obtain targeted glycolipids.

Methyl-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranoside (2):$[\alpha]_{D25}$ =69.3 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.01 (s, 9H), 3.27 (d, *J* = 10.7 Hz, 1H), 3.43 (s, 3H), 3.53 (d, *J* = 11.2 Hz, 1H), 3.80 (d, *J* = 11.2 Hz, 1H), 3.96 (d, *J* = 2.2 Hz, 1H), 4.12 – 4.22 (m, 2H), 4.54 (d, *J* = 12.4 Hz, 1H), 4.71 (d, *J* = 12.4 Hz, 1H), 4.96 (s, 1H), 7.32 (s, 5H), 7.35 – 7.45 (m, 6H), 7.56 (d, *J* = 7.8 Hz, 2H), 7.66 (d, *J* = 7.6 Hz, 2H).; ^{13}C NMR (100.53 MHz, $CDCl_3$): 19.2, 26.9(3C), 55.4, 64.2, 72.2, 77.9, 84.5, 84.5, 110.3, 128.0(5C), 128.1(2C), 128.6(2C), 130.1, 130.1, 132.4, 132.5, 135.7(2C), 135.8(2C), 137.9; IR ($CHCl_3$): 3032, 2926, 2124, 1441, 1267, 1106, 698 cm-1; HRMS (TOF) m/z [M + Na]+ calcd for$C_{29}H_{36}O_5NaSi$, 515.2230, found 515.2235.

***p*-Tolyl-2,3-di-*O*-benzyl-5-*O*-(naphthalen-1-yl methyl)-1-thio-α-D-arabinofuranoside (3a):** ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 2.30 (s, 3H), 3.64 – 3.75 (m, 2H), 4.05 (dd, *J* = 6.7, 3.3 Hz, 1H), 4.12 (t, *J* = 3.1 Hz, 1H), 4.41 (dt, *J* = 6.7, 4.4 Hz, 1H), 4.45 – 4.53 (m, 2H), 4.54 – 4.65 (m, 2H), 4.66 – 4.75 (m, 2H), 5.55 (d, *J* = 2.8 Hz, 1H), 7.19 – 7.26 (m, 5H), 7.28 – 7.33 (m, 4H), 7.39 – 7.49 (m, 5H), 7.69 – 7.85 (m, 5H).; ^{13}C NMR (100.53 MHz, CDCl3): δ 21.2, 69.2, 72.2, 72.4, 73.5, 80.6, 83.7, 88.5, 90.7, 125.9, 125.9, 126.1, 126.6, 127.8, 127.8, 127.8, 127.9(2C), 128.0(2C), 128.1(2C), 128.2, 128.5(4C), 129.8(2C), 131.1, 132.1(2C), 133.1, 133.3, 135.7, 137.5, 137.5, 137.8.; IR ($CHCl_3$): 3031, 2929, 2124, 1448, 1266, 1106, 699 cm-1; HRMS (TOF) m/z [M + Na]+ calcd for $C_{37}H_{36}O_4NaS$, 599.2232, found 599.2237.

***p*-Tolyl-2,3-di-*O*-benzyl-5-*O*-benzoyl-1-thio-α-D-arabinofuranoside (3b):** $[\alpha]_D^{25}$ = 20.2 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 2.31 (s, 3H), 4.05 (dd, *J* = 6.1, 2.8 Hz, 1H), 4.15 (d, *J* = 2.4 Hz, 1H), 4.44 (dd, *J* = 12.3, 5.8 Hz, 1H), 4.49 – 4.68 (m, 6H), 5.55 (d, *J* = 1.9 Hz, 1H), 7.09 (d, *J* = 7.8 Hz, 2H), 7.23 – 7.36 (m, 11H), 7.37 – 7.42 (m, 3H), 7.52 (t, *J* = 7.4 Hz, 1H), 8.00 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 21.2, 63.8, 72.4, 72.5, 79.1, 83.8, 88.4, 90.8, 127.9(2C), 128.0, 128.1(3C), 128.4(2C), 128.6(4C), 129.8(2C), 129.9(3C), 130.6, 132.5(2C), 133.1, 137.3, 137.5, 137.8, 166.3; IR ($CHCl_3$): 3035, 2923, 2127, 1610, 1445, 1264, 1111, 697 cm-1; HRMS (TOF) m/z [M + Na]+ calcd for $C_{33}H_{32}O_5NaS$, 563.1867, found 563.1868.

***p*-Tolyl-2,3-di-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-1-thio-α-D-arabinofuranoside (3c):**$[\alpha]_D^{25}$ = 79.7 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.04 (s, 9H), 2.31 (s, 3H), 3.84 (qd, *J* = 11.2, 4.4 Hz, 2H), 4.11 – 4.15 (m, 2H), 4.30 – 4.38 (m, 1H), 4.48 – 4.56 (m, 3H), 4.64 (d, *J* = 11.8 Hz, 1H), 5.52 (d, *J* = 3.1 Hz, 1H), 7.08 (d, *J* = 7.9 Hz, 2H), 7.24 – 7.26 (m, 1H), 7.26 – 7.35 (m, 13H), 7.36 – 7.43 (m, 4H), 7.66 (ddd, *J* = 8.1, 6.8, 1.4 Hz, 4H).; ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 21.2, 26.9 (3C), 63.5, 72.2, 72.3, 82.2, 83.4, 88.6, 90.6, 127.7 (2C), 127.8 (5C), 127.9, 128.0 (2C), 128.5 (4C), 129.7 (4C), 131.3, 132.1 (2C), 133.5, 133.5, 135.7, 135.8 (4C), 137.3, 137.6, 138.0.; IR ($CHCl_3$): 3033, 2929, 2127, 1451, 1269, 1106, 699 cm-1; HRMS (TOF) m/z [M + Na]+ calcd for $C_{42}H_{46}O_4NaSSi$, 697.2783, found 697.2775.

Methyl-2-*O*-[2,3-di-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranoside (4c):Yield: (93%); $[\alpha]_D^{25}$ = 53.2 (c = 1.0, $CHCl_3$);^{1}H NMR (399.78MHz, CDCl3): δ 1.08 (d, *J* = 4.5 Hz, 18H), 3.39 (s, 3H), 3.85 (had, *J* = 4.6, 2.9, 1.9 Hz, 4H), 3.94 – 3.98 (m, 1H), 4.03 (dd, *J* = 3.1, 1.3 Hz, 1H), 4.08 (dd, *J* = 6.6, 2.9 Hz, 1H), 4.18 (dt, *J* = 6.9, 3.1 Hz, 2H), 4.25 (d, *J* = 1.8 Hz, 1H), 4.38 – 4.50 (m, 2H), 4.52 – 4.58 (m, 3H), 4.66 (dd, *J* = 12.3, 1.7 Hz, 1H), 5.05 (s, 1H), 5.14 (s, 1H), 7.25 (d, *J* = 1.9 Hz, 3H), 7.27 – 7.33 (m, 12H), 7.35 – 7.45 (m, 12H), 7.71 (ddt, *J* = 7.2, 5.4, 1.6 Hz, 8H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.5, 26.9(3C), 27.0(3C), 55.0, 63.7, 64.1, 72.0, 72.0, 72.2, 82.5, 82.9, 83.3, 85.8, 88.7, 105.7, 108.3, 127.8(14C), 127.9, 128.5(6C), 129.8(4C), 133.4, 133.6, 135.7(3C), 135.8(8C), 137.6, 137.9, 138.0; IR (CHCl3): 3031, 2917, 1546, 1455, 1104, 699 cm-1; HRMS (TOF) m/z [M + Na]+ calcd for $C_{64}H_{74}O_9NaSi_2$, 1065.4768, found 1065.4772.

***p*-Tolyl-2,3-di-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-1-thio-β-D-ribofuranoside (5a):** $[\alpha]_D^{25}$ = -11.7 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.03 (s, 9H), 2.29 (s, 3H), 3.59 – 3.74 (m, 2H), 3.88 (t, *J* = 4.8 Hz, 1H), 4.07 (t, *J* = 5.0 Hz, 1H), 4.22 (q, *J* = 4.4 Hz, 1H), 4.47 – 4.56 (m, 3H), 4.61 (d, *J* = 12.0 Hz, 1H), 5.41 (d, *J* = 4.7 Hz, 1H), 7.27 – 7.32 (m, 8H), 7.33 – 7.37 (m, 6H), 7.39 (ddt, *J* = 6.8, 3.3, 1.4 Hz, 3H), 7.65 (td, *J* = 8.1, 1.4 Hz, 4H), 7.69 – 7.72 (m, 1H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.3, 21.2, 26.7(3C), 27.0, 63.7, 72.2, 72.3, 80.6, 83.3, 89.0, 127.8(4C), 127.9, 128.0(3C), 128.2(2C), 128.5(4C), 129.7(2C), 129.8, 129.8, 130.0, 133.0(2C), 133.3, 133.4, 134.9, 135.8(4C), 137.7, 137.9; IR ($CHCl_3$): 3033, 2929, 2124, 1447, 1267, 1109, 697 cm-1; HRMS (TOF) m/z [M + Na]+ calcd for $C_{42}H_{46}O_4NaSSi$, 675.2964, found 675.2966.

***p*-Tolyl-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-1-thio-β-D-ribofuranoside (5b):** $[\alpha]_D^{25}$ = 3.64 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.08 (s, 9H), 2.29 (s, 3H), 3.67 – 3.78 (m, 2H), 4.23 (s, 1H), 4.32 – 4.39 (m, 1H), 4.45 (d, *J* = 11.6 Hz, 1H), 4.59 (d, *J* = 11.4 Hz, 1H), 5.51 (d, *J* = 3.8 Hz, 1H), 5.55 (s, 1H), 7.06 (d, *J* = 7.1 Hz, 2H), 7.13 – 7.21 (m, 4H), 7.40 (dd, *J* = 17.0, 7.4 Hz, 11H), 7.52 – 7.60 (m, 1H), 7.71 (t, *J* = 7.1 Hz, 4H), 8.08 (d, *J* = 7.1 Hz, 2H). ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 21.3, 26.9, 27.0, 62.5, 63.6, 73.1, 73.2, 73.5, 75.8, 77.2, 81.9, 83.5, 88.9, 90.3, 127.8, 127.8(2C), 127.9(2C), 127.9, 128.0(2C), 128.0, 128.4(2C), 128.5, 128.5(2C), 128.6, 129.4, 129.7, 129.8, 129.9(2C), 130.0, 130.2, 131.7, 133.2(2C), 133.3, 133.4, 135.7, 135.8, 135.8, 137.5, 138.1, 165.7; IR ($CHCl_3$): 3034, 2927, 2125, 1614, 1453, 1265, 1108, 699cm-1; HRMS (TOF) m/z [M + Na]+ calcd for $C_{42}H_{44}O_5NaSSi$, 711.2576, found 711.2579.

Methyl-2-*O*-[2,3-di-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-ribofuranosyl]-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranoside (6a): Yield: (89%); $[\alpha]_D^{25}$ = 30.1 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 1.10 (s, 9H), 1.18 (s, 9H), 3.52 (s, 3H), 3.70 (d, *J* = 11.4 Hz, 1H), 3.77 – 3.85 (m, 1H), 3.92 – 4.00 (m, 3H), 4.10 – 4.16 (m, 2H), 4.28 – 4.44 (m, 3H), 4.59 – 4.87 (m, 6H), 5.23 (s, 2H), 7.33 – 7.42 (m, 14H), 7.44 – 7.53 (m, 13H), 7.73 (ddd, *J* = 11.1, 5.8, 2. 9 Hz, 4H), 7.78 – 7.82 (m, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.3, 19.4, 26.9(3C), 27.0(3C), 55.1, 64.0, 64.6, 72.0, 72.3, 72.6, 75.6, 78.4, 82.2, 83.4, 83.5, 87.4, 101.1, 108.1, 127.6, 127.7, 127.7(4C), 127.8(14C), 128.3(3C), 128.4(2C), 129.6, 129.7, 129.8, 129.8, 133.1, 133.3, 133.6, 133.7, 135.6(2C), 135.7(6C), 138.0, 138.2, 138.6; IR ($CHCl_3$): 3035, 2920, 1455,

1104, 699 cm-1; HRMS (TOF) m/z [M + Na]+ calcd for$C_{64}H_{74}O_9NaSi_2$, 1065.4769, found 1065.4771.

Methyl-2-*O*-[2,3-di-*O*-benzyl-5-*O*-(3,4,5-tris(decyloxy)benzoyl)-α-D-arabinofuranosyl]- 3-*O*-benzyl-5-*O*-(3,4,5-tris(decyloxy)benzoyl)-α-D-arabinofuranoside (8a):Yield: (91%); $[\alpha]_D^{25}$ = 22.1 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.6 Hz, 18H), 1.27 (s, 72H), 1.44 (m, 12H), 1.75 (dd, *J* = 14.8, 6.9 Hz, 12H), 3.34 (s, 3H), 3.94 – 4.03 (m, 16H), 4.20 (d, *J* = 1.8 Hz, 1H), 4.36 – 4.48 (m, 8H), 4.54 (dd, *J* = 12.9, 8.5 Hz, 4H), 4.63 (d, *J* = 12.1 Hz, 1H), 5.01 (s, 6H), 5.08 (s, 1H), 7.19 – 7.33 (m, 19H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.3(6C), 22.8(6C), 26.2(3C), 26.2(3C), 29.4(2C), 29.49(2C), 29.5(7C), 29.5(4C), 29.7(7C), 29.8(4C), 29.8(2C), 29.9(2C), 32.1(6C), 55.2, 69.2(3C), 69.3(3C), 72.3, 72.4, 73.6, 73.7, 79.9, 83.9, 84.0, 85.6, 88.3, 105.2(2C), 108.2, 108.3, 108.3(2C), 124.4, 124.5, 127.8(2C), 127.8(2C), 127.9(2c), 128.0, 128.0, 128.2, 128.6(2C), 128.6(2C), 128.6(2C), 137.3, 137.4, 137.5, 142.6, 142.7, 152.9, 153.4(3C), 166.2, 166.3; IR ($CHCl_3$): 3035, 2920, 1613, 1452, 1109, 699 cm-1; MALDI (TOF) m/z [M + Na]+ calcd for$C_{106}H_{166}O_{17}Na$, 1735.20, found 1735.74.

Methyl-2-*O*-[2,3-di-*O*-benzyl-5-*O*-(3,4,5-tris(decyloxy)benzoyl)-α-D-ribofuranosyl]- 3-*O*-benzyl-5-*O*-(3,4,5-tris(decyloxy)benzoyl)-α-D-arabinofuranoside (8b):Yield: (87%); $[\alpha]_D^{25}$ = 29.4 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.80 (t, *J* = 6.7 Hz, 18H), 1.09 – 1.23 (m, 72H), 1.33 – 1.44 (m, 12H), 1.70 (tdd, *J* = 15.1, 7.6, 4.1 Hz, 12H), 3.29 (s, 3H), 3.74 – 3.82 (m, 2H), 3.88 (td, *J* = 6.4, 4.0 Hz, 8H), 3.94 (q, *J* = 6.2 Hz, 6H), 4.15 (d, *J* = 3.0 Hz, 1H), 4.21 (t, *J* = 4.5 Hz, 2H), 4.27 – 4.32 (m, 1H), 4.32 – 4.41 (m, 2H), 4.51 (td, *J* = 12.4, 12.0, 7.1 Hz, 5H), 4.64 (d, *J* = 12.2 Hz, 1H), 5.02 (d, *J* = 4.0 Hz, 1H), 5.04 (s, 1H), 7.13 – 7.25 (m, 19H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(6C), 22.8(6C), 26.2(2C), 26.2(2C), 26.3(2C), 29.5(8C), 29.6(6C), 29.7(6C), 29.8(4C), 29.8(2C), 29.9(4C), 32.1(6C), 55.3, 69.4(3C), 69.4(3C), 72.4, 72.7, 73.6, 73.7, 75.9, 78.1, 79.2, 80.8, 84.2, 87.9, 101.6, 108.1, 108.4(2C), 108.5(2C), 124.3, 124.6, 127.9, 127.9(2C), 127.9(3C), 128.0(2C), 128.1, 128.5(2C), 128.5(2C), 128.6(2C), 137.6, 137.7, 138.0, 142.8, 143.0, 153.0(2C), 153.0(2C), 166.1, 166.3; IR ($CHCl_3$): 3035, 2929, 1615, 1455, 1111, 698 cm-1; MALDI (TOF) m/z [M + Na]+ calcd for $C_{106}H_{166}O_{17}Na$, 1735.20, found 1735.61.

Methyl-2-*O*-[2,3-di-*O*-benzyl-5-*O*-(3,4,5-tris(decyloxy)benzoyl)-β-D-ribofuranosyl]- 3-*O*-benzyl-5-*O*-(3,4,5-tris(decyloxy)benzoyl)-α-D-arabinofuranoside (8c):Yield: (89%); $[\alpha]_D^{25}$ = 9.5 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.95 (t, *J* = 6.8 Hz, 18H), 1.34 (s, 72H),

1.53 (s, 12H), 1.82 (dtd, *J* = 19.1, 13.3, 6.6 Hz, 12H), 3.43 (s, 3H), 3.96 (q, *J* = 5.8, 5.2 Hz, 6H), 4.05 (dt, *J* = 16.8, 6.4 Hz, 10H), 4.34 (d, *J* = 1.8 Hz, 1H), 4.39 – 4.47 (m, 4H), 4.51 – 4.59 (m, 3H), 4.61 – 4.67 (m, 2H), 4.72 (dd, *J* = 11.8, 4.3 Hz, 2H), 4.87 (s, 1H), 5.18 (s, 1H), 7.24 – 7.43 (m, 19H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(6C), 22.8(6C), 26.2(3C), 26.2(3C), 29.4(4C), 29.5(4C), 29.5(4C), 29.5(4C), 29.7(8C), 29.8(4C), 29.9(2C), 32.0(6C), 54.9, 69.2(3C), 69.3(3C), 72.8, 73.0, 73.6, 79.0, 79.5, 80.2, 80.4, 84.7, 85.7, 105.2, 105.6, 107.2, 108.2(2C), 108.4, 124.3, 124.5, 127.8(2C), 127.9(2C), 128.1, 128.1(2C), 128.2, 128.4(2C), 128.6(3C), 128.6(2C), 137.4, 137.6(2C), 142.6, 142.7, 152.9(4C), 166.2(2C); IR ($CHCl_3$): 3031, 2923, 1612, 1451, 1107, 699 cm-1; MALDI (TOF) m/z [M + Na]+ calcd for $C_{106}H_{166}O_{17}Na$, 1735.20, found 1735.65.

Methyl-2-*O*-[2,3-di-*O*-benzyl-5-*O*-(3,4,5-tris(decyloxy)benzoyl)-β-D-arabinofuranosyl]- 3-*O*-benzyl-5-*O*-(3,4,5-tris(decyloxy)benzoyl)-α-D-arabinofuranoside (8d): Yield: (91%); $[\alpha]_D^{25}$ = -4.57 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.80 (t, *J* = 6.8 Hz, 18H), 1.19 (s, 72H), 1.32 – 1.42 (m, 12H), 1.68 (dt, *J* = 11.4, 6.1 Hz, 12H), 3.29 (s, 3H), 3.81 (t, *J* = 6.4 Hz, 3H), 3.85 – 3.95 (m, 10H), 4.00 – 4.13 (m, 2H), 4.19 – 4.25 (m, 2H), 4.27 – 4.35 (m, 5H), 4.42 – 4.56 (m, 4H), 4.61 (dd, *J* = 11.6, 7.0 Hz, 2H), 4.80 (s, 1H), 5.00 (d, *J* = 4.3 Hz, 1H), 7.10 – 7.29 (m, 19H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(6C), 22.8(6C), 26.2(3C), 26.2(3C), 29.4(4C), 29.5(6C), 29.5(2C), 29.5(4C), 29.7(8C), 29.8(4C), 29.9(2C), 32.0(6C), 55.0, 69.2(3C), 69.3(3C), 72.6, 72.7, 73.6, 79.1, 80.4, 83.0, 84.1, 84.8, 86.1, 100.8, 107.0, 108.2(2C), 108.3(2C), 124.3, 124.5, 127.8(2C), 127.8(3C), 127.9, 128.2(3C), 128.4(2C), 128.5(2C), 128.7(2C), 137.5, 137.6, 137.8, 142.6(2C), 152.9(2C), 152.9(2C), 166.1, 166.2; IR ($CHCl_3$): 3033, 2926, 1615, 1449, 1109, 699 cm-1; MALDI (TOF) m/z [M + Na]+ calcd for $C_{106}H_{166}O_{17}Na$, 1735.20, found 1735.68.

Methyl-2-*O*-[5-*O*-(3,4,5-tris(decyloxy)benzoyl)-α-D-arabinofuranosyl]-5-*O*-(3,4,5-tris(decyloxy)benzoyl)-α-D-arabinofuranoside (1a):Yield: (90%); $[\alpha]_D^{25}$ = 22.5 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.87 (t, *J* = 6.7 Hz, 18H), 1.27 (d, *J* = 7.0 Hz, 72H), 1.46 (p, *J* = 6.9 Hz, 12H), 1.67 – 1.84 (m, 12H), 3.36 (s, 3H), 3.99 (qd, *J* = 6.6, 2.8 Hz, 14H), 4.10 (d, *J* = 2.6 Hz, 1H), 4.12 – 4.15 (m, 1H), 4.28 (qd, *J* = 5.3, 4.9, 3.1 Hz, 2H), 4.45 (ddd, *J* = 27.1, 11.3, 5.2 Hz, 4H), 5.01 (s, 1H), 5.15 (d, *J* = 1.5 Hz, 1H), 7.25 (d, *J* = 4.2 Hz, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(6C), 22.8(6C), 26.2(2C), 26.2(2C), 26.3(2C), 29.5(8C), 29.6(4C), 29.7(6C), 29.8(6C), 29.9(6C), 32.0(2C), 55.3, 69.4(3C), 69.5(3C), 73.7, 73.7, 76.3,

78.0, 81.6, 82.8, 82.9, 86.0, 107.6, 107.8, 108.4(2C), 108.7(2C), 124.1, 124.1, 142.9, 143.1, 153.0(2C), 153.0(2C), 166.7, 166.9; IR ($CHCl_3$): 3034, 2929, 1561, 1459, 698 cm-1; MALDI (TOF) m/z [M + Na]+ calcd for$C_{85}H_{148}O_{17}Na$, 1464.06, found 1464.45.

Methyl-2-*O*-[5-*O*-(3,4,5-tris(decyloxy)benzoyl)-α-D-ribofuranosyl]-5-*O*-(3,4,5-tris(decyloxy)benzoyl)-α-D-arabinofuranoside (1b):Yield: (88%); $[\alpha]_D^{25}$ = 27.7 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.80 (t, *J* = 6.7 Hz, 18H), 1.12 – 1.29 (m, 72H), 1.39 (q, *J* = 7.3 Hz, 12H), 1.69 (dp, *J* = 25.3, 6.7 Hz, 12H), 3.30 (s, 3H), 3.92 (t, *J* = 6.8 Hz, 12H), 3.99 (td, *J* = 6.2, 3.6 Hz, 2H), 4.03 – 4.10 (m, 2H), 4.25 (dq, *J* = 19.8, 5.6, 4.7 Hz, 2H), 4.30 – 4.48 (m, 4H), 5.02 (s, 1H), 5.16 (d, *J* = 4.4 Hz, 1H), 7.15 (s, 2H), 7.19 (s, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(6C), 22.8(6C), 26.2(4C), 26.2(2C), 29.5(10C), 29.5(4C), 29.7(4C), 29.8(8C), 29.8(4C), 32.0(4C), 32.0(2C), 55.3, 69.4(3C), 69.4(3C), 70.8, 71.9, 73.6(2C), 76.3, 82.8, 82.9, 87.0, 102.4, 107.5, 108.4(2C), 108.6(2C), 124.1, 124.2, 143.0, 143.1, 153.0(2C), 153.0(2C), 166.1, 166.8; IR ($CHCl_3$): 3035, 2928, 1556, 1452, 699 cm-1; MALDI (TOF) m/z [M + Na]+ calcd for $C_{85}H_{148}O_{17}Na$, 1464.06, found 1464.49.

Methyl-2-*O*-[5-*O*-(3,4,5-tris(decyloxy)benzoyl)-β-D-ribofuranosyl]-5-*O*-(3,4,5-tris(decyloxy)benzoyl)-α-D-arabinofuranoside (1c):Yield: (85%); $[\alpha]_D^{25}$ = 22.9 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.81 – 0.92 (m, 18H), 1.19 – 1.40 (m, 72H), 1.46 (p, *J* = 6.9 Hz, 12H), 1.66 – 1.85 (m, 12H), 3.37 (s, 3H), 4.00 (qd, *J* = 6.5, 2.8 Hz, 14H), 4.08 – 4.18 (m, 2H), 4.29 (q, *J* = 4.8 Hz, 2H), 4.46 (ddd, *J* = 26.9, 11.4, 5.1 Hz, 4H), 5.02 (s, 1H), 5.16 (s, 1H), 7.25 (d, *J* = 5.8 Hz, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(6C), 22.8(6C), 26.2(2C), 26.2(2C), 26.3(2C), 29.5(10C), 29.6(4C), 29.7(2C), 29.7(4C), 29.8(4C), 29.8(3C), 29.9(3C), 32.1(6C), 55.3, 69.4(3C), 69.5(3C), 73.7, 73.7, 76.2, 77.9, 81.5, 82.9, 83.1, 85.8, 107.6, 107.7, 108.3(2C), 108.7(2C), 124.1, 124.1, 142.9, 143.1, 153.0(2C), 153.0(2C), 166.7, 166.9; IR ($CHCl_3$): 3035, 2929, 1558, 1453, 696 cm-1; MALDI (TOF) m/z [M + Na]+ calcd for $C_{85}H_{148}O_{17}Na$, 1464.06, found 1464.46.

Methyl-2-*O*-[5-*O*-(3,4,5-tris(decyloxy)benzoyl)-β-D-arabinofuranosyl]-5-*O*-(3,4,5-tris(decyloxy)benzoyl)-α-D-arabinofuranoside (1d):Yield: (89%); $[\alpha]_D^{25}$ = 20.0 (c = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.81 (t, *J* = 6.7 Hz, 18H), 1.19 (s,72H), 1.38 (q, *J* = 7.6 Hz, 12H), 1.58 – 1.81 (m, 12H), 3.31 (s, 3H), 3.93 (qd, *J* = 6.6, 2.0 Hz, 12H), 3.97 – 4.13 (m, 5H), 4.21 (td, *J* = 6.4, 3.2 Hz, 1H), 4.29 (dd, *J* = 11.9, 3.1 Hz, 1H), 4.34 – 4.47 (m, 2H), 4.56 (dd,

J = 11.8, 8.1 Hz, 1H), 4.80 (d, *J* = 1.7 Hz, 1H), 4.96 (d, *J* = 4.2 Hz, 1H), 7.17 – 7.21 (m, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(6C), 22.8(6C), 26.2(3C), 26.2(3C), 29.5(8C), 29.5(2C), 29.6(4C), 29.7(6C), 29.8(6C), 29.9(4C), 32.1(6C), 55.4, 69.4(3C), 69.5(3C), 73.7, 73.7, 77.0, 77.4, 77.9, 80.5, 80.9, 88.6, 101.6, 106.9, 108.4(2C), 108.7(2C), 124.0, 124.5, 142.9, 143.1, 153.0(2C), 153.0(2C), 166.4, 166.7; IR ($CHCl_3$): 3033, 2927, 1558, 1455, 698 cm-1; MALDI (TOF) m/z [M + Na]+ calcd for $C_{85}H_{148}O_{17}Na$, 1464.06, found 1464.48.

Methyl-2-*O*-benzyl- α-D-arabinofuranoside (12): Yield: (63% over four steps); $[\alpha]_D^{25}$ = 58.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 3.35 (s, 3H), 3.67 – 3.80 (m, 2H), 3.89 (dd, *J* = 2.6, 0.9 Hz, 1H), 4.04 (q, *J* = 4.5 Hz, 1H), 4.11 (dd, *J* = 4.6, 2.5 Hz, 1H), 4.52 – 4.64 (m, 2H), 4.93 (s, 1H), 7.26 – 7.36 (m, 5H);^{13}C NMR (100.53 MHz, $CDCl_3$): δ 55.0, 62.2, 72.0, 75.5, 85.0, 88.3, 107.0, 128.0(2C), 128.6(2C), 137.2; IR ($CHCl_3$): 3033, 2920, 1452, 1109, 699 cm^{-1}; HRMS (TOF) *m/z* [M + Na]$^+$calcd for $C_{13}H_{18}O_5Na$, 277.1052, found 277.1049.

***p*-Tolyl-2-*O*-benzoyl-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-1-thio-α-D-arabinofuranoside (13):**$[\alpha]_D^{25}$ = 22.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.01 (s, 9H), 2.31 (s, 3H), 3.86 (d, *J* = 4.4 Hz, 2H), 4.24 (d, *J* = 4.9 Hz, 1H), 4.53 (q, *J* = 4.6 Hz, 1H), 4.61 (d, *J* = 12.0 Hz, 1H), 4.80 (d, *J* = 12.0 Hz, 1H), 5.59 (s, 1H), 5.62 (s, 1H), 7.10 (d, *J* = 7.8 Hz, 2H), 7.28 (ddd, *J* = 24.3, 17.2, 7.6 Hz, 9H), 7.38 (q, *J* = 7.0 Hz, 4H), 7.45 (d, *J* = 7.9 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.63 (t, *J* = 6.8 Hz, 4H), 7.95 (d, *J* = 7.7 Hz, 2H).; ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 21.3, 26.9(3C), 63.2, 72.4, 82.6, 83.1, 83.5, 91.6, 127.8(4C), 127.9, 128.0(2C), 128.5(4C), 129.4, 129.8, 129.8(5C), 129.9, 130.8, 132.6(2C), 133.3, 133.5, 135.7, 135.7(4C), 137.6, 137.7, 165.5; IR ($CHCl_3$): 3035, 2927, 1455, 1106, 698 cm^{-1}; HRMS (TOF) *m/z* [M + Na]$^+$calcd for$C_{42}H_{44}O_5NaSSi$, 711.2576, found 711.2579.

Methyl-2-*O*-benzyl-3-*O*-[3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl]-5-*O*-[3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl]-α-D-arabinofuranoside (14):Yield: (89% over two steps); $[\alpha]_D^{25}$ = 76.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.99 (s, 18H), 3.35 (s, 3H), 3.37 – 3.54 (m, 4H), 3.63 – 3.78 (m, 3H), 3.94 – 4.03 (m, 4H), 4.11 – 4.21 (m, 5H), 4.33 – 4.39 (m, 1H), 4.41 – 4.48 (m, 2H), 4.55 – 4.66 (m, 4H), 4.94 (s, 1H), 5.12 (s, 1H), 5.15 (s, 1H), 7.19 – 7.36 (m, 24H), 7.37 – 7.43 (m, 3H), 7.56 (t, *J* = 6.8 Hz, 4H), 7.62 (d, *J* = 5.3 Hz, 4H).; ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.2, 19.2, 26.8(3C), 26.9(3C), 55.0, 64.0, 64.0, 66.1, 71.9, 72.0, 77.7, 78.4, 79.6, 81.1, 83.6, 83.9, 84.7, 84.9, 88.4, 107.3, 107.9, 109.1,

127.7, 127.8, 127.8(3C), 127.9, 127.9(6C), 128.0(6C), 128.1(2C), 128.5(4C), 128.6(2C), 129.9, 130.0, 130.0, 130.1, 132.3, 132.5, 132.6, 132.8, 135.7(5C), 135.8(2C), 137.6, 138.0, 138.1.; IR ($CHCl_3$): 3032, 2925, 1453, 1104, 698 cm^{-1}; HRMS (TOF) *m/z* $[M + Na]^+$calcd for $C_{69}H_{82}O_{13}NaSi_2$, 1197.5191, found 1197.5194.

Methyl-2-*O*-benzyl-3-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl)3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl]-α-D-arabinofuranoside (15a):Yield: (92%); $[\alpha]_D^{25}$ = 58.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 0.98 (s, 18H), 1.02 (s, 18H), 3.20 (s, 3H), 3.72 – 3.77 (m, 7H), 3.79 – 3.88 (m, 3H), 3.94 (s, 1H), 4.00 (t, *J* = 9.1 Hz, 4H), 4.08 (d, *J* = 5.8 Hz, 2H), 4.15 (d, *J* = 7.1 Hz, 3H), 4.18 – 4.22 (m, 2H), 4.26 (s, 1H), 4.31 – 4.37 (m, 4H), 4.38 – 4.51 (m, 10H), 4.57 (d, *J* = 12.2 Hz, 2H), 4.85 (s, 1H), 5.13 (s, 2H), 5.18 (s, 1H), 5.21 (s, 1H), 7.15 – 7.35 (m, 59H), 7.63 (q, *J* = 10.2, 9.0 Hz, 16H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 19.5(3C), 27.0(12C), 54.7, 63.2, 63.4, 63.4, 63.8, 66.8, 71.5, 71.6, 71.8, 71.8(2C), 72.1, 72.2, 80.3, 80.8, 82.6, 82.8, 82.8(2C), 82.9, 83.0, 83.1, 83.3, 84.9, 85.9, 88.2, 88.7(2C), 104.8, 105.5, 106.1, 107.1, 107.4, 127.5, 127.6(8C), 127.7(14C), 127.8(16C), 128.4(10C), 128.5(3C), 129.7(5C), 129.8(3C), 133.4, 133.5, 133.5, 133.6, 133.7, 133.8, 135.7(6C), 135.8(10C), 137.8, 137.8, 137.9, 138.1, 138.2, 138.2, 138.3; IR ($CHCl_3$): 3025, 2921, 1548, 1458, 1212, 1113, 698 cm^{-1}; MALDI (TOF) *m/z* $[M + Na]^+$calcd for $C_{139}H_{158}O_{21}NaSi_4$, 2299.03, found 2298.08.

Methyl-2-*O*-benzyl-3-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*- ^{t}butyldiphenylsilyl-α-D-ribofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-ribofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl]-α-D-arabinofuranoside (15b):Yield: (80%); $[\alpha]_D^{25}$ = 72.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.93 (d, *J* = 5.8 Hz, 18H), 0.99 (d, *J* = 6.4 Hz, 18H), 3.19 (s, 3H), 3.42 (d, *J* = 11.0 Hz, 1H), 3.47 – 3.54 (m, 2H), 3.61 (dd, *J* = 11.2, 2.8 Hz, 1H), 3.79 (ddt, *J* = 15.3, 10.3, 4.8 Hz, 7H), 3.91 (dd, *J* = 11.3, 6.3 Hz, 1H), 4.03 (dt, *J* = 14.9, 7.4 Hz, 4H), 4.08 – 4.13 (m, 3H), 4.15 – 4.26 (m, 4H), 4.28 – 4.35 (m, 2H), 4.37 – 4.45 (m, 3H), 4.48 – 4.57 (m, 7H), 4.59 – 4.64 (m, 4H), 4.87 (s, 1H), 5.12 (t, *J* = 3.3 Hz, 2H), 5.30 (s, 1H), 5.34 (s, 1H), 7.07 – 7.13 (m, 4H), 7.18 (s, 8H), 7.20 – 7.24 (m, 12H), 7.24 – 7.34 (m, 30H), 7.35 – 7.41 (m, 4H), 7.50 – 7.59 (m, 7H), 7.62 (dd, *J* = 8.0, 3.7 Hz, 9H).; ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.3(3C),

19.4, 26.9(9C), 27.0, 54.7, 63.7, 63.9(2C), 64.2, 67.1, 71.5, 71.7, 72.0, 72.2, 72.2, 72.4, 72.5, 75.3, 75.4, 78.5, 78.7, 80.7, 81.2, 81.5, 81.9, 82.8, 83.4(2C), 83.7, 86.9, 88.4, 88.6, 100.5, 101.5, 105.6, 106.9, 107.5, 127.3, 127.5(4C), 127.7(15C), 127.8(15C), 128.3(10C), 128.4(2C), 128.5(2C), 129.6(2C), 129.7(2C), 129.8(4C), 133.0, 133.1, 133.2, 133.3, 133.5, 133.6, 133.7, 133.7, 135.6, 135.7(4C), 135.8, 137.9, 138.0, 138.1, 138.3, 138.5, 138.6, 138.7.; IR ($CHCl_3$): 3030, 2921, 1546, 1455, 1212, 1104, 699 cm^{-1}; MALDI (TOF) *m/z* $[M + Na]^+$calcd for $C_{139}H_{158}O_{21}NaSi_4$, 2299.03, found 2299.07.

Methyl-2-*O*-benzyl-3-*O*-[2-*O*-(2-*O*-benzyl-3-*O*-benzoyl-5-*O*-^{t}butyldiphenylsilyl-β-D-ribofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(2-*O*-benzyl-3-*O*-benzoyl-5-*O*-^{t}butyldiphenylsilyl-β-D-ribofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl]-α-D-arabinofuranoside (15c):Yield: (77% over three steps); $[\alpha]_D^{25}$ = 39.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.99 (d, *J* = 2.6 Hz, 18H), 1.02 (d, *J* = 3.8 Hz, 18H), 3.15 (s, 3H), 3.66 (dd, *J* = 11.3, 4.4 Hz, 1H), 3.70 (d, *J* = 4.3 Hz, 1H), 3.71 – 3.74 (m, 2H), 3.75 – 3.79 (m, 4H), 3.80 – 3.82 (m, 1H), 3.87 (d, *J* = 4.5 Hz, 1H), 3.91 – 3.92 (m, 1H), 3.95 (td, *J* = 6.4, 5.4, 2.5 Hz, 1H), 3.97 – 4.02 (m, 1H), 4.13 (dt, *J* = 5.9, 3.1 Hz, 3H), 4.16 (t, *J* = 3.3 Hz, 2H), 4.19 (s, 1H), 4.20 – 4.23 (m, 1H), 4.23 – 4.26 (m, 1H), 4.29 (dd, *J* = 11.5, 6.1 Hz, 1H), 4.34 (d, *J* = 1.9 Hz, 1H), 4.39 – 4.45 (m, 5H), 4.48 – 4.60 (m, 5H), 4.85 (s, 1H), 5.09 (s, 1H), 5.19 (s, 1H), 5.21 (s, 1H), 5.37 (d, *J* = 4.5 Hz, 2H), 5.40 (d, *J* = 1.4 Hz, 1H), 7.01 (dd, *J* = 12.1, 5.0 Hz, 4H), 7.10 – 7.17 (m, 15H), 7.22 – 7.37 (m, 32H), 7.63 (dddd, *J* = 13.6, 7.1, 3.4, 1.5 Hz, 20H), 8.03 – 8.08 (m, 4H).; ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.3, 19.3, 19.4, 19.4, 26.9(6C), 27.0(6C), 54.6, 63.3, 63.4, 65.9, 65.9, 66.0, 71.4, 72.0, 72.0, 73.0, 73.0, 75.3, 75.4, 78.4, 78.7, 80.3, 81.8, 82.5, 82.5, 82.6, 82.9, 83.5, 84.0, 85.7, 86.0, 87.5, 104.5, 104.9, 106.5, 107.3, 127.4, 127.5, 127.6, 127.7(8C), 127.8(6C), 127.9(17C), 128.2(4C), 128.3(4C), 128.4(2C), 128.5(4C), 129.7(4C), 129.8, 129.8, 129.8, 129.8, 129.9(2C), 130.1(3C), 133.2, 133.2, 133.3, 133.3, 133.3, 133.4(2C), 133.5, 133.6, 133.8, 135.7(12C), 135.8(4C), 137.6, 137.7, 137.8, 138.0, 138.2, 165.7(2C); IR ($CHCl_3$): 3012, 2928, 1552, 1455, 1218, 1114, 697 cm^{-1}; MALDI (TOF) *m/z* $[M + Na]^+$calcd for $C_{139}H_{154}O_{23}NaSi_4$, 2326.98, found 2326.18.

Allyl-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-β-D-arabinofuranoside (17):$[\alpha]_D^{25}$ = -23.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.06 (s, 9H), 2.63 (d, *J* = 9.5 Hz, 1H), 3.75 (h, *J* = 5.3 Hz, 2H), 3.98 (q, *J* = 6.2 Hz, 2H), 4.08 (q, *J* = 5.5 Hz, 1H), 4.18 (dd, *J* = 12.8, 5.2 Hz, 1H), 4.27

(dt, *J* = 9.8, 5.3 Hz, 1H), 4.62 (d, *J* = 11.8 Hz, 1H), 4.76 (d, *J* = 11.8 Hz, 1H), 5.01 (d, *J* = 4.7 Hz, 1H), 5.15 (dd, *J* = 20.9, 13.8 Hz, 2H), 5.80 (ddt, *J* = 16.4, 10.6, 5.7 Hz, 1H), 7.23 – 7.28 (m, 1H), 7.30 (d, *J* = 4.2 Hz, 4H), 7.33 – 7.43 (m, 6H), 7.68 (d, *J* = 7.0 Hz, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 19.4, 27.0(3C), 65.5, 68.8, 72.0, 78.3, 82.6, 84.7, 100.7, 117.7, 127.7(3C), 127.8(3C), 128.5(2C), 129.8, 129.8, 133.4, 133.5, 133.8, 135.7(4C), 138.2; IR ($CHCl_3$): 3451, 3030, 2929, 1455, 1213, 697 cm^{-1}; HRMS (TOF) m/z [M + Na]$^+$calcd for $C_{31}H_{38}O_5NaSi$, 541.2386, found 541.2390.

Allyl-2-O-[2,3-di-O-benzyl-5-O-(naphthalen-1-ylmethyl)-β-D-arabinofuranosyl]-3-O-benzyl-5-O-^{t}butyldiphenylsilyl-β-D-arabinofuranoside (19): Yield: (90%); $[\alpha]_D^{25}$ = -69.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78MHz, $CDCl_3$): δ 1.06 (s, 9H), 3.58 (dd, *J* = 9.7, 4.5 Hz, 1H), 3.65 (td, *J* = 8.3, 7.0, 2.5 Hz, 1H), 3.72 – 3.77 (m, 2H), 3.91 (dd, *J* = 12.1, 6.0 Hz, 1H), 4.07 – 4.22 (m, 5H), 4.27 (td, *J* = 7.1, 6.2, 3.1 Hz, 1H), 4.39 – 4.51 (m, 3H), 4.53 – 4.63 (m, 4H), 4.71 (dd, *J* = 11.9, 2.4 Hz, 1H), 4.81 (dd, *J* = 11.4, 2.2 Hz, 1H), 5.05 (d, *J* = 10.3 Hz, 1H), 5.12 – 5.20 (m, 3H), 5.66 – 5.91 (m, 1H), 7.23 (s, 10H), 7.28 – 7.41 (m, 12H), 7.41 – 7.45 (m, 2H), 7.60 (s, 1H), 7.64 – 7.69 (m, 4H), 7.71 – 7.76 (m, 2H), 7.77 – 7.80 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 19.4, 27.0(3C), 66.0, 68.2, 71.8, 72.3, 72.4, 72.8, 73.3, 79.5, 81.0, 82.3, 82.9, 83.2, 84.0, 98.7, 99.0, 117.7, 125.8, 125.8, 126.1, 126.4, 127.6, 127.7(4C), 127.8(6C), 128.0(2C), 128.2(3C), 128.4(6C), 128.5(3C), 129.8(2C), 133.1, 133.4, 133.5, 134.0, 135.7(4C), 135.8, 138.1, 138.3, 138.4.; IR ($CHCl_3$):3042, 2925, 1550, 1455, 1215, 1100, 688 cm^{-1}; HRMS (TOF) m/z [M + Na]$^+$calcd for $C_{61}H_{66}O_9NaSi$, 993.4374, found 993.4379.

Methyl-2-*O*-benzyl-3-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-(2-(p-tolylthio)acetyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-(2-(p-tolylthio)acetyl)-β-D-arabinofuranosyl)3-*O*-benzyl-5-*O*-^{t}butyldiphenylsilyl-α-D-arabinofuranosyl]-α-D-arabinofuranoside (22b):Yield: (78%); $[\alpha]_D^{25}$ = -2.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 2.27 (d, *J* = 5.8 Hz, 6H), 3.34 (s, 3H), 3.55 (t, *J* = 7.1 Hz, 4H), 3.61 (s, 4H), 3.79 (d, *J* = 11.6 Hz, 1H), 3.94 – 3.98 (m, 3H), 4.00 – 4.04 (m, 3H), 4.15 (dt, *J* = 9.6, 5.9 Hz, 8H), 4.22 (d, *J* = 6.2 Hz, 1H), 4.27 (dd, *J* = 11.5, 6.3 Hz, 3H), 4.37 – 4.43 (m, 5H), 4.44 – 4.52 (m, 3H), 4.55 (d, *J* = 6.3 Hz, 2H), 4.60 (dd, *J* = 11.5, 6.8 Hz, 8H), 4.65 – 4.70 (m, 2H), 4.89 (s, 1H), 4.97 (d, *J* = 4.2 Hz, 1H), 5.09 (s, 1H), 5.14 (d, *J* = 4.7 Hz, 1H), 5.15 (s, 1H), 7.06 (t, *J* = 6.6 Hz, 4H), 7.22 – 7.32 (m, 35H), 7.36 (d, *J* = 4.3 Hz, 4H),

7.38 – 7.41 (m, 2H), 7.46 – 7.49 (m, 4H), 7.68 (d, *J* = 5.5 Hz, 2H), 7.76 (dq, *J* = 9.2, 5.4, 4.4 Hz, 4H), 7.80 – 7.84 (m, 2H).; ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 21.1, 37.0, 37.1, 54.9, 64.7, 64.8, 65.6, 72.0, 72.1, 72.2, 72.3, 72.5, 72.5, 72.5, 72.6, 73.3, 73.3, 80.0, 80.0, 80.1, 80.6, 81.0, 82.8, 83.0, 84.0, 84.1, 85.0, 85.3, 88.5, 100.0, 100.3, 105.5, 106.7, 107.0, 125.8, 125.8, 126.0, 126.0, 126.2, 126.2, 126.5, 126.5, 127.7(3C), 127.8(12C), 127.9(3C), 128.0(2C), 128.1(4C), 128.2(2C), 128.3, 128.3, 128.4(3C), 128.5(7C), 128.6(3C), 129.9(4C), 130.7(4C), 131.4, 131.5, 133.1, 133.1, 133.3, 135.5, 135.6, 137.1, 137.2, 137.6, 137.7, 137.8, 137.9, 138.0, 138.2, 138.3, 169.6, 169.7; IR ($CHCl_3$): 3033, 2923, 1552, 1459, 1213, 1101, 695 cm^{-1}; HRMS (TOF) *m/z* [M + Na]$^+$calcd for $C_{115}H_{118}NaO_{23}S_2$, 1953.7402, found1953.7408.

Methyl-2-*O*-benzyl-3-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl)3-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-α-D-arabinofuranoside (26a): Yield: (87%); $[\alpha]_D^{25}$ = 57.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.1 Hz, 12H), 1.28 (s, 48H), 1.36 – 1.50 (m, 8H), 1.75 (dq, *J* = 21.7, 7.0 Hz, 8H), 3.28 (s, 3H), 3.78 (d, *J* = 11.5 Hz, 1H), 3.87 (dq, *J* = 6.6, 3.9, 3.3 Hz, 6H), 3.94 (q, *J* = 6.3 Hz, 5H), 4.00 (dt, *J* = 6.8, 3.1 Hz, 5H), 4.19 (dt, *J* = 6.5, 3.4 Hz, 1H), 4.29 (qd, *J* = 6.7, 4.3, 3.6 Hz, 4H), 4.33 – 4.42 (m, 11H), 4.44 – 4.54 (m, 11H), 4.60 (ddd, *J* = 16.3, 8.4, 4.3 Hz, 3H), 4.88 (s, 1H), 5.13 (s, 2H), 5.28 (s, 2H), 6.72 – 6.85 (m, 8H), 7.09 – 7.34 (m, 35H), 7.91 (td, *J* = 9.5, 2.4 Hz, 8H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(4C), 22.8(4C), 26.1(4C), 29.3(2C), 29.5(6C), 29.5, 29.5, 29.7(10C), 32.0(4C), 54.9, 63.5, 63.6, 63.8, 64.1, 66.4, 68.2, 68.3, 68.3, 68.3, 71.6, 71.9, 72.1, 72.2(2C), 72.4(2C), 80.0, 80.1(2C), 80.3, 80.5, 80.8, 83.5, 83.6, 83.7, 83.8, 85.3, 86.1, 88.2, 88.4, 88.5, 105.4, 105.8, 106.3, 107.2, 107.3, 114.1(8C), 122.0, 122.1(2C), 122.1, 127.7, 127.7, 127.7(4C), 127.8, 127.8(5C), 127.9(2C), 127.9(2C), 127.9, 128.0, 128.0, 128.4(2C), 128.5(10C), 128.6(2C), 128.6(2C), 131.9(8C), 137.5, 137.5, 137.6, 137.7, 137.7, 137.7, 137.8, 163.1, 163.1(2C), 163.2, 166.0, 166.1, 166.1(2C); IR ($CHCl_3$): 3033, 2923, 1552, 1459, 1213, 1101, 695 cm^{-1}; MALDI (TOF) *m/z* [M + Na]$^+$calcd for$C_{143}H_{182}O_{29}Na$, 2387.26, found 2387.63.

Methyl-2-*O*-benzyl-3-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-dodecanoyl-α-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-dodecanoyl-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-dodecanoyl-α-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-dodecanoyl-α-D-arabinofuranosyl]-α-D-

arabinofuranoside (26b): Yield: (91%); $[\alpha]_D^{25}$ = 48.2 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.7 Hz, 12H), 1.18 – 1.30 (m, 12H), 1.55 (h, *J* = 6.5, 5.8 Hz, 8H), 2.18 – 2.28 (m, 8H), 3.31 (s, 3H), 3.71 – 3.76 (m, 2H), 3.80 (dd, *J* = 6.1, 2.9 Hz, 1H), 3.87 (dt, *J* = 7.3, 3.9 Hz, 2H), 3.92 (dd, *J* = 11.4, 5.0 Hz, 1H), 3.97 – 4.02 (m, 3H), 4.11 – 4.17 (m, 5H), 4.22 (tq, *J* = 8.8, 3.2 Hz, 8H), 4.27 – 4.33 (m, 2H), 4.37 – 4.63 (m, 14H), 4.90 (s, 1H), 5.10 (s, 1H), 5.11 (s, 1H), 5.18 (s, 1H), 5.20 (s, 1H), 7.21 – 7.36 (m, 35H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(4C), 22.8(4C), 24.8, 24.9, 24.9, 25.0, 29.2, 29.3, 29.3(2C), 29.4, 29.4, 29.5, 29.5(8C), 29.6, 29.6, 29.6, 29.7, 29.8(8C), 29.8, 32.0(4C), 34.0, 34.1(2C), 34.2, 54.9, 63.2, 63.3, 63.4, 63.7, 66.3, 71.6, 71.9, 72.2(2C), 72.2, 72.4(2C), 79.4, 79.6, 79.7, 79.9, 80.5, 80.7, 83.1, 83.4, 83.4, 83.6, 85.3, 86.4, 88.2, 88.3, 88.4, 105.4, 106.0, 106.1, 107.0, 107.4, 127.7(6C), 127.7, 127.8(6C), 127.9(2C), 127.9(2C), 128.0, 128.0, 128.0, 128.1, 128.2, 128.5(2C), 128.5(3C), 128.5(2C), 128.6(2C), 128.6(2C), 128.6(2C), 137.3, 137.4, 137.6, 137.6, 137.7, 137.7, 137.8, 173.6, 173.6, 173.7(2C); IR ($CHCl_3$): 3035, 2925, 1552, 1459, 1213, 1101, 695 cm^{-1}; MALDI (TOF) *m/z* [M + Na]$^+$calcd for$C_{127}H_{182}O_{25}Na$, 2131.29, found 2091.56.

Methyl-2-*O*-benzyl-3-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-α-D-ribofuranosyl)-3-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-α-D-ribofuranosyl)3-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-α-D-arabinofuranoside (26c):Yield: (85%); $[\alpha]_D^{25}$ = 71.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.6 Hz, 12H), 1.28 (d, *J* = 5.4 Hz, 48H), 1.43 (dt, *J* = 22.2, 7.5 Hz, 8H), 1.69 – 1.82 (m, 8H), 3.27 (s, 3H), 3.77 – 3.83 (m, 2H), 3.88 (q, *J* = 6.2 Hz, 6H), 3.98 (td, *J* = 6.5, 3.6 Hz, 5H), 4.03 (d, *J* = 2.4 Hz, 2H), 4.08 (dd, *J* = 7.2, 4.0 Hz, 1H), 4.17 (ddd, *J* = 16.9, 12.2, 3.9 Hz, 4H), 4.29 (dt, *J* = 11.4, 4.1 Hz, 4H), 4.32 – 4.40 (m, 5H), 4.41 – 4.47 (m, 4H), 4.47 – 4.58 (m, 9H), 4.65 (dd, *J* = 19.0, 12.7 Hz, 5H), 4.89 (s, 1H), 5.14 (d, *J* = 3.8 Hz, 2H), 5.36 (s, 1H), 5.39 (s, 1H), 6.80 (dd, *J* = 14.9, 8.5 Hz, 8H), 7.13 – 7.31 (m, 35H), 7.80 (t, *J* = 9.4 Hz, 4H), 7.92 (d, *J* = 8.4 Hz, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(4C), 22.8(4C), 26.1(4C), 29.2(4C), 29.4(4C), 29.5, 29.5, 29.7(10C), 32.0(4C), 54.8, 63.8, 64.2, 64.2, 64.3, 67.0, 68.2, 68.2, 68.3, 68.4, 71.6, 72.1, 72.3, 72.5(2C), 72.6, 72.7, 75.8, 78.0, 78.0, 78.7, 78.9, 80.7, 80.8, 80.9, 81.1, 83.4, 83.4, 87.8, 88.5, 88.7, 101.3, 101.8, 105.8, 107.1, 107.4, 114.1(2C), 114.2(2C), 114.2(4C), 121.8, 121.9, 122.1, 122.2, 127.6(2C), 127.6(2C), 127.7, 127.8, 127.8, 127.9(5C), 127.9(5C), 127.9(2C), 128.0, 128.4(2C), 128.4(5C), 128.4(2C), 128.5(2C), 128.5(2C), 128.6(2C), 131.7(2C), 131.7(2C), 131.9(2C), 131.9(2C),

137.7, 137.8, 137.8, 137.9, 137.9, 138.0, 138.1, 163.0, 163.1, 163.2, 163.2, 165.9, 166.0, 166.1, 166.2; IR ($CHCl_3$): 3031, 2929, 1600, 1452, 1213, 1101, 697 cm^{-1}; MALDI (TOF) *m/z* [M + Na]$^+$calcd for $C_{143}H_{182}O_{29}Na$, 2387.26, found 2387.65.

Methyl-2-*O*-benzyl-3-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-dodecanoyl-α-D-ribofuranosyl)-3-*O*-benzyl-5-*O*-dodecanoyl-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-dodecanoyl-α-D-ribofuranosyl)3-*O*-benzyl-5-*O*-dodecanoyl-α-D-arabinofuranosyl]-α-D-arabinofuranoside (26d): Yield: (92%); $[\alpha]_D^{25}$ = 82.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.6 Hz, 12H), 1.17 – 1.30 (m, 72H), 1.45 – 1.61 (m, 8H), 2.14 (dt, *J* = 15.6, 7.6 Hz, 4H), 2.23 (dd, *J* = 8.5, 6.8 Hz, 4H), 3.31 (s, 3H), 3.75 (dt, *J* = 12.0, 2.8 Hz, 5H), 3.92 (dq, *J* = 5.9, 3.2, 2.6 Hz, 4H), 3.96 – 4.06 (m, 4H), 4.17 (dt, *J* = 8.1, 5.5 Hz, 4H), 4.24 (tt, *J* = 8.4, 3.6 Hz, 6H), 4.31 (dd, *J* = 9.8, 3.5 Hz, 2H), 4.42 – 4.70 (m, 14H), 4.90 (s, 1H), 5.11 (t, *J* = 4.0 Hz, 2H), 5.28 (s, 1H), 5.32 (d, *J* = 1.5 Hz, 1H), 7.20 – 7.33 (m, 35H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(4C), 22.8(4C), 24.8, 24.9, 24.9(2C), 29.2, 29.2, 29.3(2C), 29.3, 29.4(2C), 29.4, 29.5(6C), 29.6, 29.6(4C), 29.7, 29.7(4C), 29.8(4C), 32.0(4C), 33.9, 34.1, 34.1, 34.1, 54.9, 63.3, 63.6, 63.9, 64.0, 66.7, 71.7, 72.0, 72.3, 72.4(2C), 72.6, 72.7, 75.5, 75.5, 77.9, 78.0, 78.3, 78.7, 80.6, 80.7, 80.7, 80.9, 83.1, 83.2, 87.7, 88.7, 88.8, 101.2, 101.9, 105.7, 107.0, 107.4, 127.6(2C), 127.7, 127.7, 127.8, 127.8, 127.8, 127.9(2C), 127.9(6C), 127.9(2C), 127.9, 128.0, 128.0(2C), 128.0, 128.1, 128.4(2C), 128.5(4C), 128.5(2C), 128.5(2C), 128.6(2C), 137.6, 137.7, 137.9, 137.9, 138.0, 138.0, 138.1, 173.3, 173.4, 173.6, 173.7; IR ($CHCl_3$): 3032, 2925, 1557, 1451, 1215, 1106, 698 cm^{-1}; MALDI (TOF) *m/z* [M + Na]$^+$calcd for $C_{127}H_{182}O_{25}Na$, 2131.29, found 2091.57.

Methyl-2-*O*-benzyl-3-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-β-D-ribofuranosyl)-3-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-β-D-ribofuranosyl)3-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-α-D-arabinofuranoside (26e): Yield: (83%); $[\alpha]_D^{25}$ = 44.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.8 Hz, 12H), 1.27 (q, *J* = 4.5, 2.7 Hz, 48H), 1.35 – 1.50 (m, 8H), 1.74 (ddd, *J* = 11.6, 9.2, 5.4 Hz, 8H), 3.28 (s, 3H), 3.79 (dd, *J* = 11.8, 2.4 Hz, 1H), 3.83 – 3.92 (m, 5H), 3.92 (dt, *J* = 6.7, 3.2 Hz, 5H), 3.97 (td, *J* = 3.8, 3.0, 1.9 Hz, 2H), 3.97 – 4.05 (m, 2H), 4.12 (ddd, *J* = 6.7, 4.1, 2.3 Hz, 1H), 4.19 – 4.33 (m, 5H), 4.30 – 4.38 (m, 4H), 4.34 – 4.42 (m, 4H), 4.44 (ddd, *J* = 14.4, 7.9, 4.7 Hz, 6H), 4.46 – 4.69 (m, 11H), 4.91 (d, *J* = 1.3 Hz, 1H), 5.08 (s, 1H), 5.13 (d, *J* = 1.8 Hz, 2H), 5.24 (s, 1H), 6.72 – 6.85

(m, 8H), 7.11 – 7.34 (m, 35H), 7.81 – 7.97 (m, 8H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(4C), 22.8(4C), 26.1(4C), 29.2, 29.2, 29.4(6C), 29.5(2C), 29.7(10C), 32.0(4C), 54.9, 63.9, 64.1, 65.4(2C), 65.8, 68.3(4C), 71.8, 72.2, 72.3, 72.5, 72.6, 72.7, 72.7, 77.4, 78.5, 79.3, 79.4, 79.9, 80.0, 80.5, 80.6, 80.9, 81.1, 84.7, 84.9, 85.8, 85.9, 88.0, 105.7(2C), 105.8, 106.9, 107.1, 114.1(2C), 114.1(4C), 114.2(2C), 121.9, 121.9, 122.1, 122.2, 127.5, 127.6(2C), 127.6(2C), 127.8, 127.9(6C), 128.0, 128.0, 128.0(2C), 128.1(2C), 128.1, 128.3(2C), 128.3(2C), 128.5(5C), 128.5(2C), 128.6(5C), 131.8(2C), 131.8(2C), 131.8(2C), 131.9(2C), 137.5, 137.6, 137.6, 137.7(2C), 137.8, 137.9, 163.1, 163.2(2C), 163.2, 165.9, 166.0(2C), 166.0; IR ($CHCl_3$): 3034, 2926, 1601, 1454, 1211, 11077, 699 cm^{-1}; MALDI (TOF) *m/z* $[M + Na]^+$calcd for $C_{143}H_{182}O_{29}Na$, 2387.26, found 2387.62.

Methyl-2-*O*-benzyl-3-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-dodecanoyl-β-D-ribofuranosyl)-3-*O*-benzyl-5-*O*-dodecanoyl-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-dodecanoyl-β-D-ribofuranosyl)3-*O*-benzyl-5-*O*-dodecanoyl-α-D-arabinofuranosyl]-α-D-arabinofuranoside (26f):Yield: (91%); $[\alpha]_D^{25}$ = 37.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.91 (t, *J* = 6.5 Hz, 12H), 1.28 (d, *J* = 6.6 Hz, 72H), 1.48 – 1.61 (m, 8H), 2.11 – 2.33 (m, 8H), 3.31 (s, 3H), 3.78 (d, *J* = 11.6 Hz, 1H), 3.86 (dt, *J* = 11.5, 5.8 Hz, 4H), 3.95 (dt, *J* = 11.6, 3.5 Hz, 4H), 4.07 – 4.22 (m, 8H), 4.23 – 4.31 (m, 5H), 4.32 – 4.40 (m, 3H), 4.43 – 4.52 (m, 4H), 4.55 – 4.72 (m, 10H), 4.92 (s, 1H), 5.05 (s, 1H), 5.09 (s, 1H), 5.12 (s, 1H), 5.22 (s, 1H), 7.32 (dq, *J* = 11.7, 6.6, 5.9 Hz, 35H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.3(4C), 22.8(4C), 24.8(4C), 29.2(4C), 29.4(4C), 29.5(4C), 29.5(4C), 29.6(4C), 29.7(8C), 32.0(2C), 32.1(4C), 34.1(2C), 34.2(2C), 54.9, 63.6, 63.8, 65.4(2C), 65.8, 71.8, 72.1, 72.2, 72.5, 72.6, 72.7, 72.8, 78.5, 78.5, 79.2, 79.3, 79.8, 80.0, 80.2, 80.4, 81.0, 84.1, 84.3, 85.8, 85.9, 88.1, 105.4, 105.5, 105.6, 107.0, 107.1, 127.8(2C), 127.8(2C), 127.9(2C), 127.9, 127.9(4C), 128.0(2C), 128.1(2C), 128.1, 128.1, 128.1(2C), 128.4(2C), 128.5(2C), 128.5(2C), 128.6(2C), 128.6(9C), 137.5, 137.6, 137.6, 137.7(2C), 137.8, 137.9, 173.5, 173.6(2C), 173.6; IR ($CHCl_3$): 3032, 2929, 1559, 1454, 1216, 1103, 699 cm^{-1}; MALDI (TOF) *m/z* $[M + Na]^+$calcd for $C_{127}H_{182}O_{25}Na$, 2131.29, found 2091.53.

Methyl-2-*O*-benzyl-3-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-β-D-arabinofuranosyl)3-*O*-benzyl-5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-α-D-arabinofuranoside (26g):Yield: (82%);

$[\alpha]_D^{25}$= 10.2 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.6 Hz, 12H), 1.28 (d, *J* = 5.2 Hz, 48H), 1.35 – 1.48 (m, 8H), 1.74 (dq, *J* = 14.7, 7.1 Hz, 8H), 3.29 (s, 3H), 3.85 (q, *J* = 6.2 Hz, 5H), 3.92 (td, *J* = 6.5, 4.4 Hz, 4H), 4.01 (dt, *J* = 12.5, 3.5 Hz, 4H), 4.07 (dt, *J* = 7.2, 3.3 Hz, 2H), 4.12 – 4.20 (m, 4H), 4.24 (dd, *J* = 8.9, 6.9 Hz, 2H), 4.27 – 4.35 (m, 3H), 4.37 – 4.53 (m, 14H), 4.54 – 4.72 (m, 10H), 4.86 (s, 1H), 4.98 (d, *J* = 4.4 Hz, 1H), 5.12 (s, 1H), 5.14 (d, *J* = 4.6 Hz, 1H), 5.19 (s, 1H), 6.68 – 6.82 (m, 8H), 7.13 – 7.34 (m, 35H), 7.81 – 8.01 (m, 8H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(4C), 22.8(4C), 26.1(4C), 29.2(4C), 29.4(4C), 29.5, 29.5, 29.7(10C), 32.0(4C), 54.9, 64.0, 64.0, 65.6, 66.1, 66.2, 68.2, 68.2, 68.3, 68.3, 71.9, 72.4, 72.4, 72.6, 72.7, 72.7, 72.7, 78.8, 78.9, 80.5, 80.6, 80.8, 81.2, 82.5, 82.6, 83.8, 83.9, 84.7, 84.9, 85.8, 86.0, 88.4, 100.6, 100.8, 105.6, 106.7, 107.0, 114.1(4C), 114.2(4C), 121.9, 121.9, 122.0, 122.2, 127.7, 127.7(2C), 127.7(2C), 127.8(2C), 127.8(2C), 127.8, 127.9(2C), 127.9, 128.1, 128.2, 128.2(2C), 128.3(2C), 128.3(2C), 128.4(2C), 128.5(2C), 128.5(5C), 128.6(2C), 128.6(2C), 131.8(2C), 131.8(2C), 131.9(2C), 132.0(2C), 137.5, 137.6, 137.6, 137.8, 137.9, 137.9, 138.0, 163.0, 163.1, 163.2, 163.2, 166.0(2C), 166.0, 166.1; IR ($CHCl_3$): 3031, 2923, 1558, 1451, 1217, 1109, 699 cm^{-1}; MALDI (TOF) *m/z* $[M + Na]^+$calcd for $C_{143}H_{182}O_{29}Na$, 2387.26, found 2387.69.

Methyl-2-*O*-benzyl-3-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-dodecanoyl-β-D-arabinofuranosyl)-3-*O*-benzyl-5-*O*-dodecanoyl-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(2,3-di-*O*-benzyl-5-*O*-dodecanoyl-β-D-arabinofuranosyl)3-*O*-benzyl-5-*O*-dodecanoyl-α-D-arabinofuranosyl]-α-D-arabinofuranoside (26h):Yield: (90); $[\alpha]_D^{25}$ = 5.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.7 Hz, 18H), 1.24 (dd, *J* = 9.9, 5.5 Hz, 72H), 1.56 (ddt, *J* = 36.3, 16.0, 7.9 Hz, 8H), 2.21 (dqd, *J* = 22.8, 7.5, 3.0 Hz, 8H), 3.29 (s, 3H), 3.78 (dd, *J* = 12.0, 2.3 Hz, 1H), 3.96 (dtd, *J* = 11.3, 5.9, 4.8, 3.1 Hz, 7H), 4.03 – 4.15 (m, 10H), 4.17 – 4.23 (m, 4H), 4.24 – 4.29 (m, 2H), 4.33 (d, *J* = 2.7 Hz, 1H), 4.37 – 4.43 (m, 2H), 4.46 (q, *J* = 2.9 Hz, 2H), 4.47 – 4.52 (m, 3H), 4.55 – 4.60 (m, 3H), 4.64 – 4.72 (m, 4H), 4.85 (s, 1H), 4.95 (d, *J* = 4.3 Hz, 1H), 5.05 (s, 1H), 5.11 (d, *J* = 4.4 Hz, 1H), 5.12 (s, 1H), 7.28 (tdd, *J* = 12.2, 7.0, 3.3 Hz, 35H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(4C), 22.8(4C), 24.8, 24.9(3C), 29.2(2C), 29.2(2C), 29.3(2C), 29.4(2C), 29.4(2C), 29.5(6C), 29.5(4C), 29.5(2C), 29.6(2C), 29.6(2C), 29.7(4C), 29.7(2C), 29.8, 32.0(4C), 34.1, 34.1(2C), 34.1, 54.8, 63.6, 63.7, 65.5, 66.1, 66.1, 71.9, 72.4(2C), 72.5(2C), 72.6, 72.6, 78.8, 79.0, 80.0, 80.4, 80.4, 81.2, 82.6, 82.7, 83.8, 84.3, 84.3, 85.5, 85.9, 88.4, 100.4, 100.7, 105.3, 106.7, 107.0, 127.7(2C), 127.7(2C), 127.8(2C), 127.8(2C), 127.8, 127.9(2C), 127.9, 127.9, 128.0, 128.1(4C), 128.2(2C), 128.2, 128.4(2C), 128.5(2C), 128.5(2C), 128.5(4C), 128.6(2C),

128.6(2C), 137.5, 137.6, 137.6, 137.8, 137.8, 137.9, 138.0, 173.5(2C), 173.5, 173.6; IR ($CHCl_3$): 3035, 2926, 1603, 1457, 1217, 1104, 697 cm^{-1}; MALDI (TOF) *m/z* $[M + Na]^+$calcd for $C_{127}H_{182}O_{25}Na$, 2131.29, found 2091.46.

Methyl-3-*O*-[2-*O*-(5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl)-5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl)5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-α-D-arabinofuranoside (27a):Yield: (85%); $[\alpha]_D^{25}$ = 63.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.8 Hz, 12H), 1.26 (s, 48H), 1.39 (h, *J* = 5.9, 5.2 Hz, 8H), 1.73 (dq, *J* = 10.0, 6.2, 5.4 Hz, 8H), 3.26 (s, 3H), 3.84 – 3.93 (m, 8H), 4.00 – 4.09 (m, 4H), 4.16 (dt, *J* = 19.9, 6.9 Hz, 8H), 4.23 – 4.35 (m, 7H), 4.38 – 4.53 (m, 6H), 4.77 (s, 1H), 5.20 (d, *J* = 4.1 Hz, 3H), 5.32 (s, 1H), 6.81 (td, *J* = 5.6, 2.7 Hz, 8H), 7.84 – 7.98 (m, 8H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(4C), 22.8(4C), 26.1(4C), 29.3(2C), 29.5(6C), 29.6(2C), 29.7(10C), 32.0(4C), 55.0, 64.0, 64.2(2C), 64.2, 66.4, 68.4(4C), 76.1, 76.4, 77.4, 77.7, 77.8, 80.5, 81.5, 81.6(2C), 81.9, 82.1, 82.4, 82.5, 84.4, 86.4, 87.0, 106.6, 106.8, 107.6, 107.9, 109.0, 114.3(8C), 121.5, 121.6, 121.6, 121.7, 132.0(8C), 163.4(2C), 163.4, 163.5, 166.8, 166.8, 166.8, 166.9; IR ($CHCl_3$): 3033, 2926, 1559, 1459, 697 cm^{-1}; MALDI (TOF) *m/z* $[M + Na]^+$calcd for$C_{94}H_{140}O_{29}Na$, 1756.94, found 1756.25.

Methyl-3-*O*-[2-*O*-(5-*O*-dodecanoyl-α-D-arabinofuranosyl)-5-*O*-dodecanoyl-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(5-*O*-dodecanoyl-α-D-arabinofuranosyl)5-*O*-dodecanoyl-α-D-arabinofuranosyl]-α-D-arabinofuranoside (27b):Yield: (88%); $[\alpha]_D^{25}$ = 67.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.7 Hz, 12H), 1.27 (d, *J* = 10.1 Hz, 72H), 1.61 (p, *J* = 7.3 Hz, 8H), 2.35 (td, *J* = 7.9, 3.3 Hz, 8H), 3.36 (s, 3H), 3.89 – 4.07 (m, 6H), 4.09 – 4.36 (m, 19H), 4.83 (s, 1H), 5.14 (s, 2H), 5.17 (s, 1H), 5.24 (s, 1H);^{13}C NMR (100.53 MHz, $CDCl_3$):δ 14.2(4C), 22.8(4C), 25.0, 25.0, 29.3(6C), 29.5(4C), 29.5(4C), 29.6(2C), 29.7(2C), 29.8(4C), 32.1(4C), 34.2(2C), 34.2(2C), 55.1, 63.7, 63.8, 63.9, 63.9, 66.4, 66.4, 76.0, 76.3, 77.2, 77.7, 77.7, 80.5, 81.2, 81.2, 81.4, 81.7, 82.1, 82.1, 82.4, 82.6, 82.6, 84.3, 86.3, 86.7, 106.5, 106.7, 107.7, 107.9, 109.1, 174.2, 174.4, 174.4, 174.5; IR ($CHCl_3$): 3034, 2928, 1601, 1454, 698cm^{-1}; MALDI (TOF) *m/z* $[M + Na]^+$calcd for$C_{78}H_{140}O_{25}Na$, 1499.95, found 1499.88.

Methyl-3-*O*-[2-*O*-(5-*O*-(4-(decyloxy)benzoyl)-α-D-ribofuranosyl)-5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(5-*O*-(4-(decyloxy)benzoyl)-α-D-ribofuranosyl)5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-α-D-arabinofuranoside (27c):Yield: (89%);

$[\alpha]_D^{25}$= 61.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.82 – 0.92 (m, 12H), 1.27 (s, 48H), 1.43 (q, *J* = 7.0 Hz, 8H), 1.70 – 1.82 (m, 8H), 3.31 (s, 3H), 3.68 (dt, *J* = 13.6, 5.8 Hz, 3H), 3.89 – 4.00 (m, 8H), 4.04 – 4.17 (m, 7H), 4.18 – 4.28 (m, 4H), 4.30 – 4.43 (m, 8H), 4.48 (dq, *J* = 7.5, 4.2, 2.6 Hz, 3H), 4.80 (s, 1H), 5.22 (d, *J* = 4.0 Hz, 1H), 5.25 (d, *J* = 4.3 Hz, 1H), 5.29 (s, 1H), 5.37 (s, 1H), 6.85 (t, *J* = 9.4 Hz, 8H), 7.85 – 7.99 (m, 8H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(4C), 22.8(4C), 26.1(4C), 29.2(2C), 29.5(6C), 29.5, 29.5, 29.7(10C), 32.0(4C), 55.1, 63.7, 63.8, 63.9, 64.1, 66.4, 68.4(4C), 70.8, 70.8, 72.0, 72.1, 76.0, 76.3, 80.4, 81.5, 83.0, 83.1, 84.4, 86.9, 102.0, 102.1, 106.5, 106.6, 109.1, 114.3(2C), 114.3(2C), 114.3(4C), 121.6, 121.6, 121.7, 121.7, 131.8(2C), 131.8(2C), 132.0(2C), 132.0(2C), 163.4, 163.4, 163.5(2C), 166.2, 166.3, 166.7, 166.7; IR ($CHCl_3$): 3035, 2924, 1557, 1451, 696 cm^{-1}; MALDI (TOF) *m/z* $[M + Na]^+$calcd for $C_{94}H_{140}O_{29}Na$, 1756.94, found 1757.24.

Methyl-3-*O*-[2-*O*-(5-*O*-dodecanoyl-α-D-ribofuranosyl)-5-*O*-dodecanoyl-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(5-*O*-dodecanoyl-α-D-ribofuranosyl)-5-*O*-dodecanoyl-α-D-arabinofuranosyl]-α-D-arabinofuranoside (27d):Yield: (90%); $[\alpha]_D^{25}$ = 72.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.7 Hz, 12H), 1.27 (d, *J* = 9.9 Hz, 72H), 1.61 (dq, *J* = 13.3, 6.9, 6.2 Hz, 8H), 2.30 – 2.39 (m, 8H), 3.36 (s, 3H), 3.91 – 4.05 (m, 6H), 4.06 – 4.33 (m, 19H), 4.83 (s, 1H), 5.21 (t, *J* = 4.1 Hz, 2H), 5.24 (s, 1H), 5.31 (s, 1H);^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.3(4C), 22.8(4C), 25.0(2C), 29.3(2C), 29.3(2C), 29.4(2C), 29.4(4C), 29.5(4C), 29.6(2C), 29.8(6C), 29.8(6C), 32.0(4C), 34.2(2C), 55.1, 63.2, 63.5, 63.6, 63.7, 66.4, 70.7, 70.8, 71.9, 75.9, 76.2, 77.2, 80.2, 81.6, 82.6, 82.8, 82.9, 83.1, 84.4, 86.6, 86.7, 102.0, 102.2, 106.4, 106.6, 109.2, 173.7, 173.8, 174.3, 174.3.IR ($CHCl_3$): 3034, 2925, 1608, 1454, 699cm^{-1}; MALDI (TOF) *m/z* $[M + Na]^+$calcd for$C_{78}H_{140}O_{25}Na$, 1499.95, found 1499.85.

Methyl-3-*O*-[2-*O*-(5-*O*-(4-(decyloxy)benzoyl)-β-D-ribofuranosyl)-5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(5-*O*-(4-(decyloxy)benzoyl)-β-D-ribofuranosyl)-5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-α-D-arabinofuranoside (27e):Yield: (86%); $[\alpha]_D^{25}$ = 47.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.7 Hz, 12H), 1.21 – 1.32 (m, 48H), 1.40 (t, *J* = 7.6 Hz, 8H), 1.73 (ddt, *J* = 14.1, 7.1, 4.3 Hz, 8H), 3.29 (s, 3H), 3.86 – 3.95 (m, 8H), 3.96 – 4.04 (m, 2H), 4.11 (td, *J* = 12.9, 6.1 Hz, 7H), 4.19 – 4.30 (m, 8H), 4.32 – 4.45 (m, 5H), 4.51 (dd, *J* = 11.9, 3.1 Hz, 2H), 4.78 (s, 1H), 5.11 (s, 3H), 5.13 (s, 1H), 6.83 (ddd, *J* = 9.3, 7.5, 2.3 Hz, 8H), 7.91 (td, *J* = 9.0, 2.6 Hz, 8H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.3(4C),

22.8(4C), 26.1(4C), 29.3, 29.3, 29.5(6C), 29.6(2C), 29.7(10C), 32.0(4C), 55.0, 64.0, 64.2, 64.8, 65.1, 66.0, 68.4(4C), 71.8, 71.9, 75.0, 75.1, 75.8, 76.6, 77.4, 80.3, 80.6, 80.7, 82.1, 82.3, 82.5, 83.4, 88.9, 89.4, 106.2, 106.4, 108.0, 108.4, 108.7, 114.1(2C), 114.2(2C), 114.3(4C), 121.5, 121.8, 121.9(2C), 131.9(4C), 131.9(4C), 163.2, 163.3, 163.5, 163.5, 166.4, 166.4, 166.6, 166.7; IR ($CHCl_3$): 3033, 2926, 1559, 1458, 698 cm^{-1}; MALDI (TOF) *m/z* $[M + Na]^+$calcd for $C_{94}H_{140}O_{29}Na$, 1756.94, found 1757.31.

Methyl-3-*O*-[2-*O*-(5-*O*-dodecanoyl-β-D-ribofuranosyl)-5-*O*-dodecanoyl-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(5-*O*-dodecanoyl-β-D-ribofuranosyl)5-*O*-dodecanoyl-α-D-arabinofuranosyl]-α-D-arabinofuranoside (27f):Yield: (88%); $[\alpha]_D^{25}$ = 32.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.85 – 0.91 (m, 12H), 1.26 (s, 72H), 1.61 (dt, *J* = 7.6, 4.9 Hz, 8H), 2.35 (td, *J* = 7.7, 3.5 Hz, 8H), 3.37 (s, 3H), 3.76 (dd, *J* = 12.1, 2.6 Hz, 1H), 3.91 (ddd, *J* = 7.6, 6.0, 3.6 Hz, 2H), 3.96 – 4.02 (m, 2H), 4.04 (dt, *J* = 5.5, 2.8 Hz, 1H), 4.08 – 4.19 (m, 13H), 4.23 – 4.35 (m, 6H), 4.83 (s, 1H), 5.07 (s, 2H), 5.10 (t, *J* = 2.5 Hz, 2H; ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.2(4C), 22.8(4C), 24.8(2C), 25.0, 25.0, 29.2(2C), 29.3(2C), 29.4(2C), 29.5(4C), 29.5(4C), 29.6(2C), 29.7(2C), 29.7(6C), 29.8(4C), 32.1(4C), 34.2(2C), 34.2, 34.3, 55.0, 63.6, 64.8, 65.1, 66.2, 71.9, 72.0, 75.0(2C), 75.5, 76.3, 80.1, 80.5, 81.9, 82.0, 82.7, 83.5, 88.7, 89.2, 106.1, 106.2, 107.8, 108.3, 108.8, 174.0, 174.0, 174.2, 174.3; IR ($CHCl_3$): 3033, 2924, 1606, 1453, 699 cm^{-1}; MALDI (TOF) *m/z* $[M + Na]^+$calcd for$C_{78}H_{140}O_{25}Na$, 1499.95, found 1499.83.

Methyl-3-*O*-[2-*O*-(5-*O*-(4-(decyloxy)benzoyl)-β-D-arabinofuranosyl)-5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(5-*O*-(4-(decyloxy)benzoyl)-β-D-arabinofuranosyl)5-*O*-(4-(decyloxy)benzoyl)-α-D-arabinofuranosyl]-α-D-arabinofuranoside (27g):Yield: (85%); $[\alpha]_D^{25}$ = 55.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.7 Hz, 12H), 1.23 – 1.29 (m, 48H), 1.40 (ddd, *J* = 11.4, 7.8, 4.1 Hz, 8H), 1.68 – 1.78 (m, 8H), 3.28 (d, *J* = 2.7 Hz, 3H), 3.91 (td, *J* = 9.1, 8.0, 5.5 Hz, 8H), 4.03 – 4.07 (m, 2H), 4.09 – 4.17 (m, 9H), 4.19 – 4.31 (m, 6H), 4.37 – 4.53 (m, 9H), 4.76 (s, 1H), 5.01 (d, *J* = 3.1 Hz, 1H), 5.05 (d, *J* = 3.5 Hz, 1H), 5.19 (d, *J* = 2.3 Hz, 1H), 5.26 (d, *J* = 3.2 Hz, 1H), 6.83 (td, *J* = 8.3, 6.3 Hz, 8H), 7.91 (dt, *J* = 9.5, 5.0 Hz, 8H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.3(4C), 22.8(4C), 26.1(4C), 29.3(2C), 29.5(6C), 29.6(2C), 29.7(10C), 32.0(4C), 54.9, 64.3(2C), 64.4, 65.3, 65.5, 68.4(4C), 75.4, 75.5, 75.5, 75.5, 76.0, 77.3, 77.4, 79.8, 80.1, 80.2, 80.2, 80.9, 82.5, 83.7, 89.7, 90.0, 102.3(2C), 105.2, 106.3, 108.7, 114.2(2C), 114.3(4C), 114.4(2C), 121.5, 121.8, 121.9(2C),

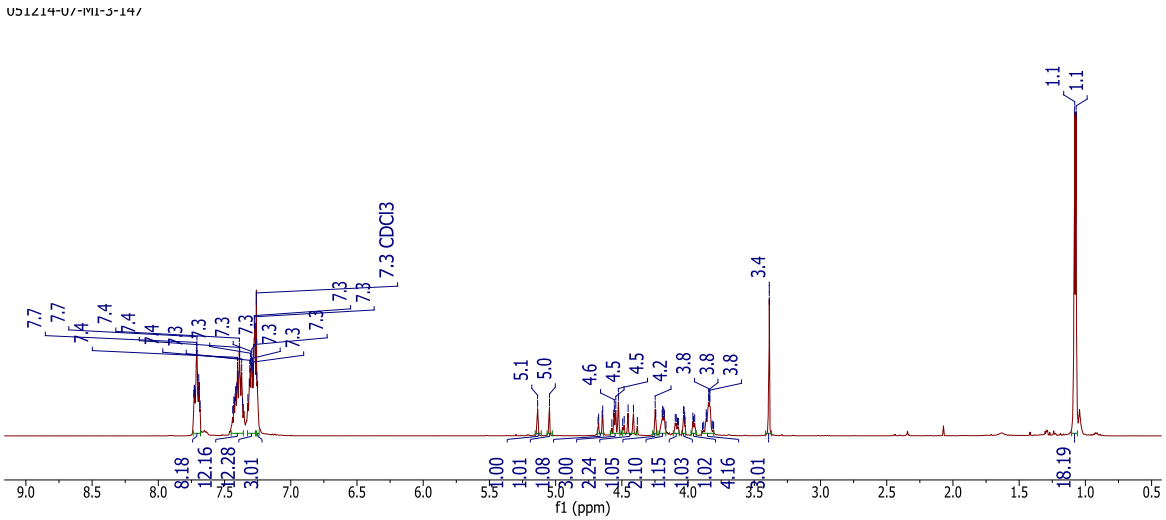
131.9(2C), 131.9(2C), 132.0(4C), 163.2, 163.3, 163.5, 163.6, 166.4, 166.5, 166.7, 166.7; IR ($CHCl_3$): 3035, 2927, 1661, 1463, 697 cm^{-1}; MALDI (TOF) *m/z* $[M + Na]^+$calcd for $C_{94}H_{140}O_{29}Na$, 1756.94, found 1756.27.

Methyl-3-*O*-[2-*O*-(5-*O*-dodecanoyl-β-D-arabinofuranosyl)-5-*O*-dodecanoyl-α-D-arabinofuranosyl]-5-*O*-[2-*O*-(5-*O*-dodecanoyl-β-D-arabinofuranosyl)5-*O*-dodecanoyl-α-D-arabinofuranosyl]-α-D-arabinofuranoside (27h):Yield: (89%); $[\alpha]_D^{25}$ = 58.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.7 Hz, 12H), 1.26 (s, 72H), 1.61 (td, *J* = 7.3, 4.0 Hz, 8H), 2.35 (td, *J* = 7.7, 3.8 Hz, 8H), 3.36 (s, 3H), 4.01 (dq, *J* = 10.5, 3.5 Hz, 6H), 4.10 – 4.34 (m, 19H), 4.81 (s, 1H), 5.04 (d, *J* = 4.5 Hz, 1H), 5.07 (d, *J* = 4.6 Hz, 1H), 5.14 (d, *J* = 3.1 Hz, 1H), 5.21 (d, *J* = 3.1 Hz, 1H); ^{13}C NMR (100.53 MHz, $CDCl_3$): δ 14.3(4C), 22.8(4C), 25.0(2C), 25.0(2C), 29.3, 29.3(4C), 29.4, 29.5, 29.5(5C), 29.6, 29.7(4C), 29.8(5C), 29.8(5C), 29.8, 32.1(4C), 34.2(2C), 34.2, 34.3, 54.9, 63.7(2C), 65.4, 65.6, 65.7, 75.3, 75.7, 75.8, 75.9, 77.4(2C), 79.7, 79.9, 80.0, 80.1, 80.6, 82.5, 83.8, 89.6, 89.8, 102.3(2C), 105.4, 106.0, 108.8, 174.0, 174.0, 174.3, 174.4; IR ($CHCl_3$): 3033, 2929, 1601, 1459, 698 cm^{-1}; MALDI (TOF) *m/z* $[M + Na]^+$calcd for$C_{78}H_{140}O_{25}Na$, 1499.95, found 1499.87.

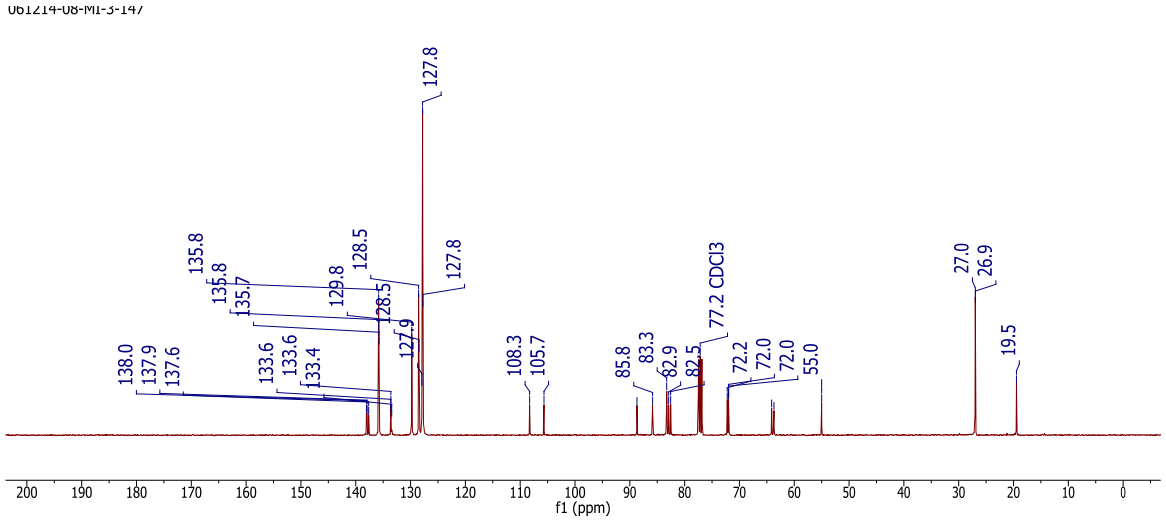
5.6Spectral charts of representative compounds

{Kindly see the supporting documents file for spectral charts of all compounds}

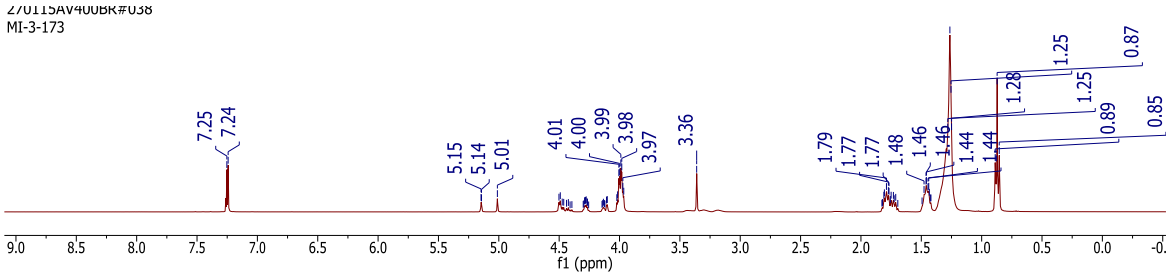
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **4c**



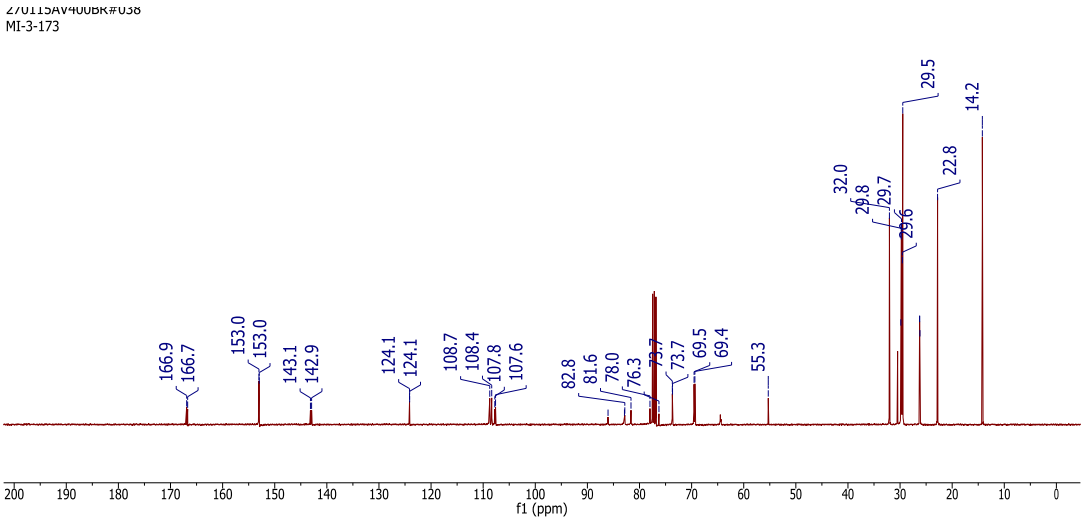
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **4c**



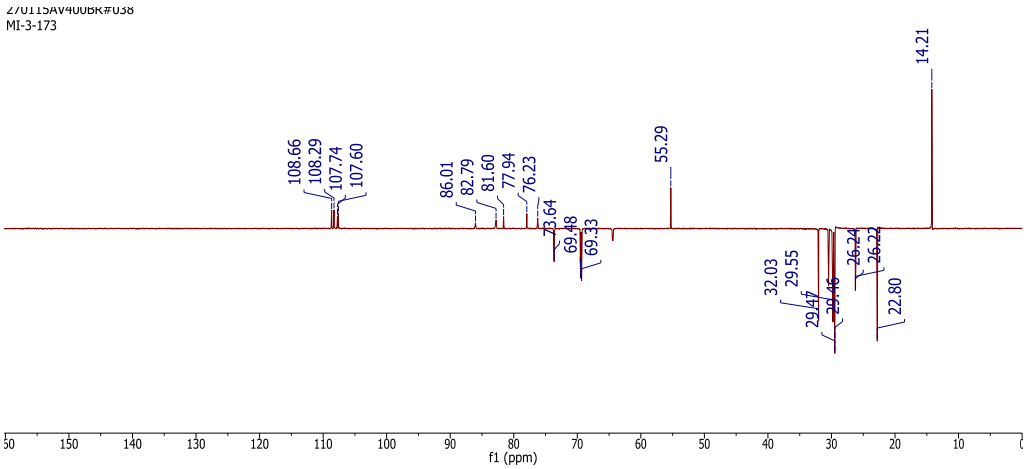
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **1a**



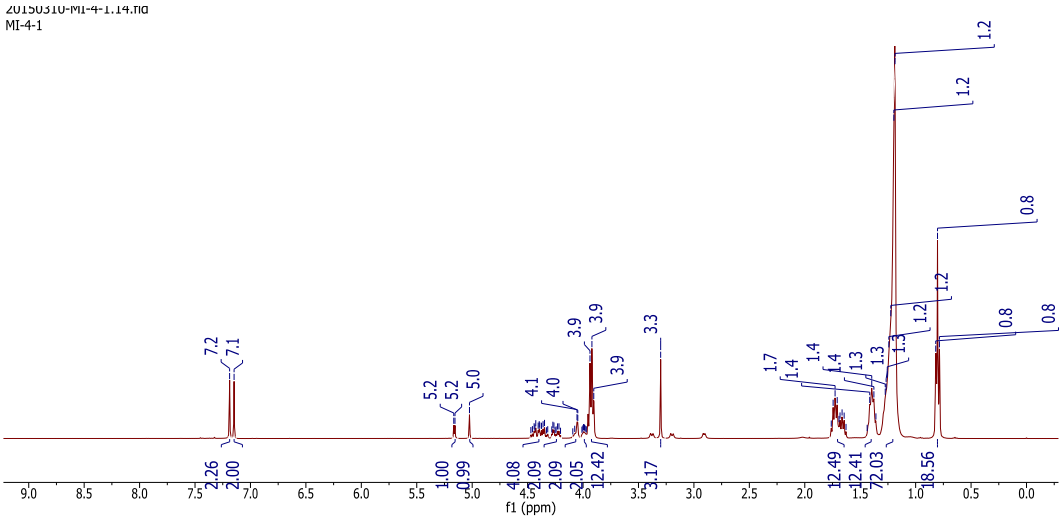
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **1a**



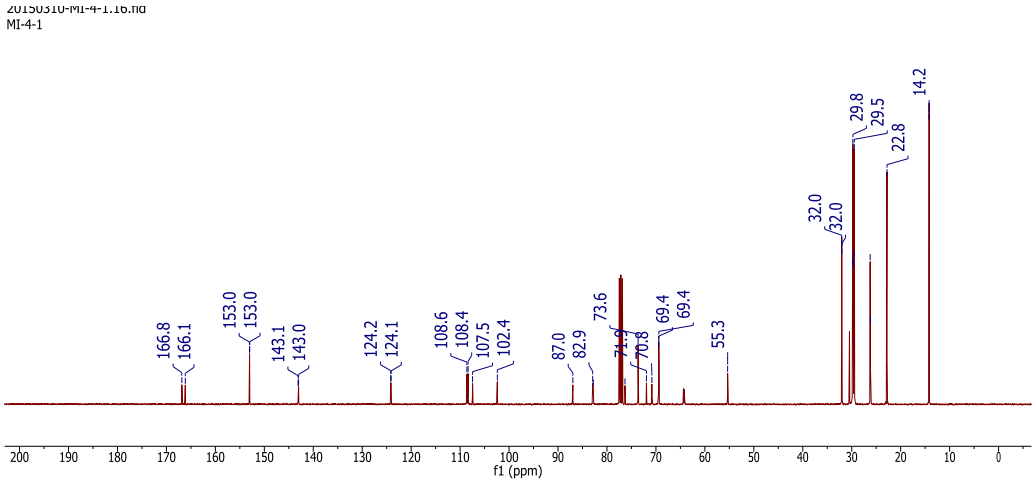
DEPT Spectrum (100.53 MHz, $CDCl_3$) of Compound **1a**



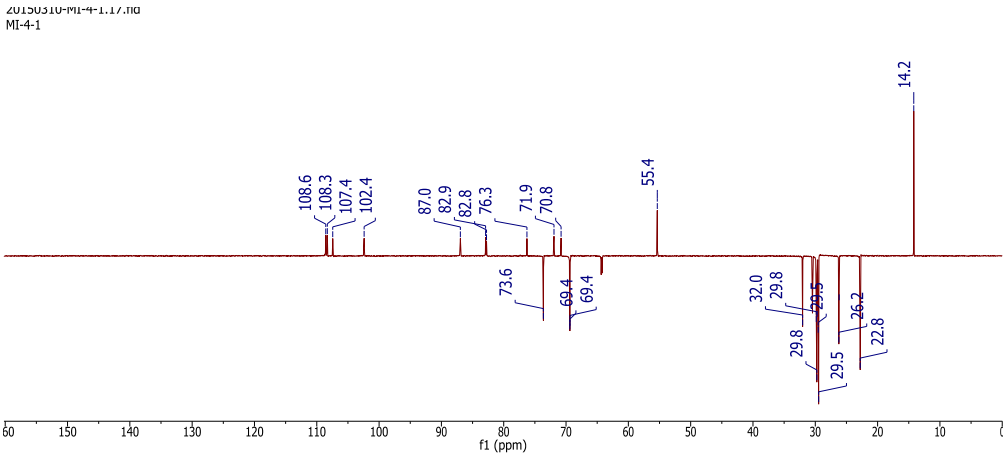
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **1b**



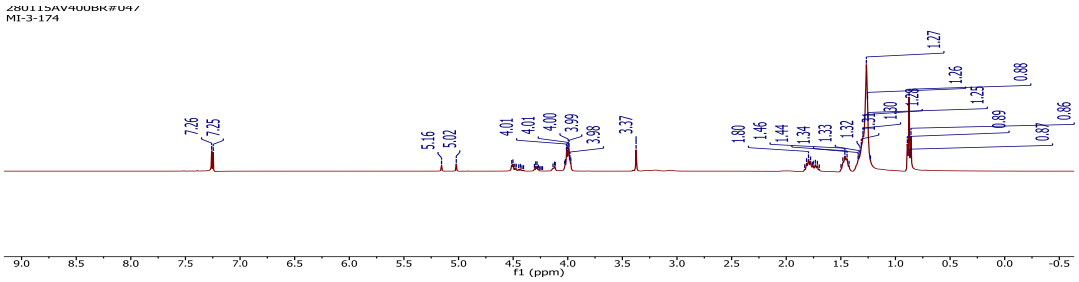
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **1b**



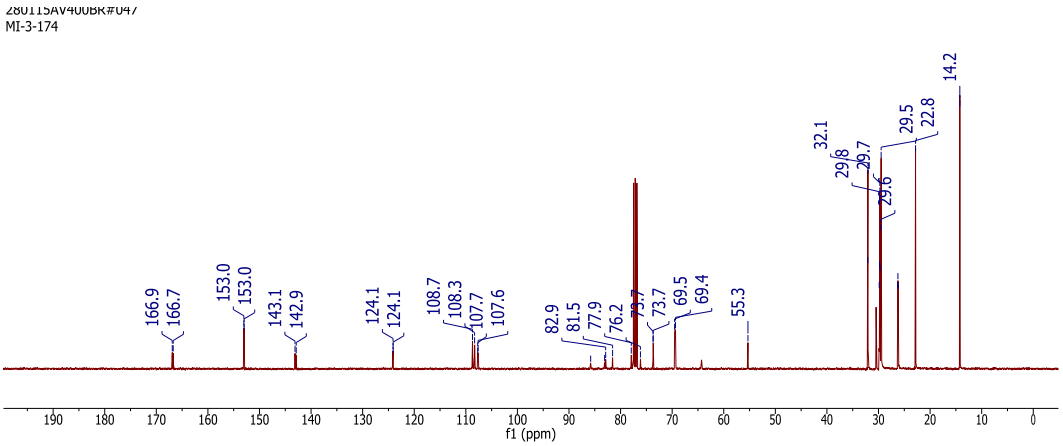
DEPT Spectrum (100.53 MHz, $CDCl_3$) of Compound **1b**



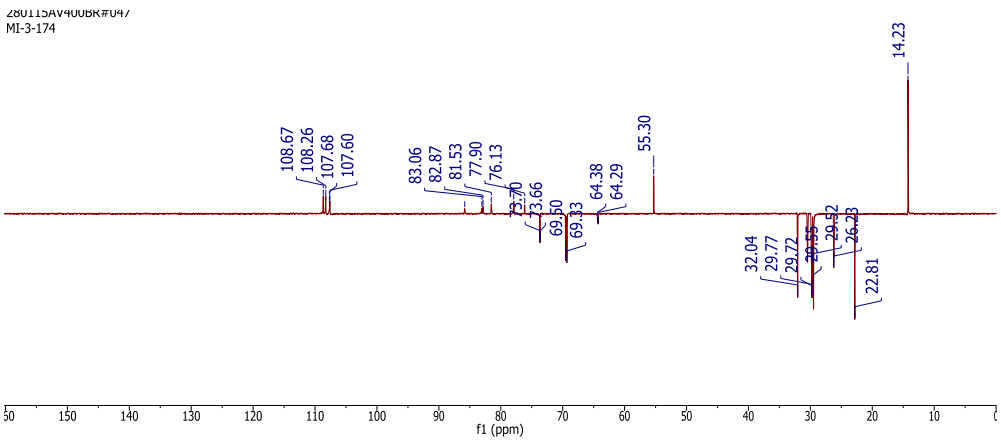
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **1c**



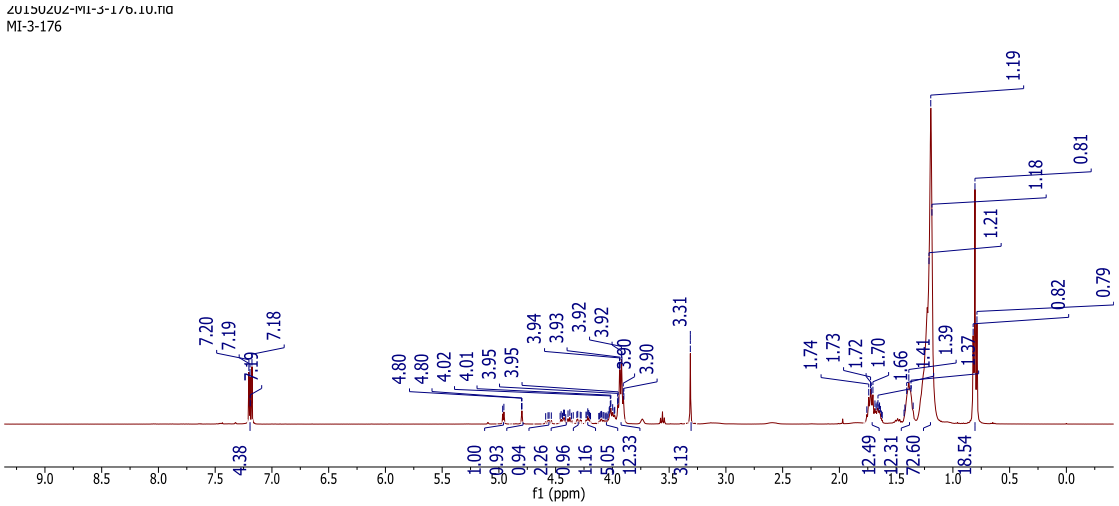
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **1c**



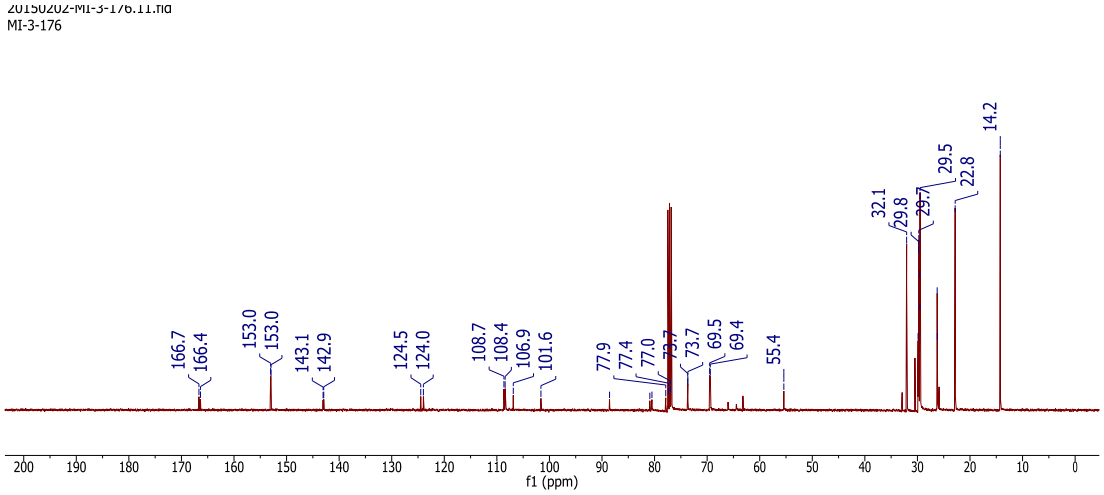
DEPT Spectrum (100.53 MHz, $CDCl_3$) of Compound **1c**



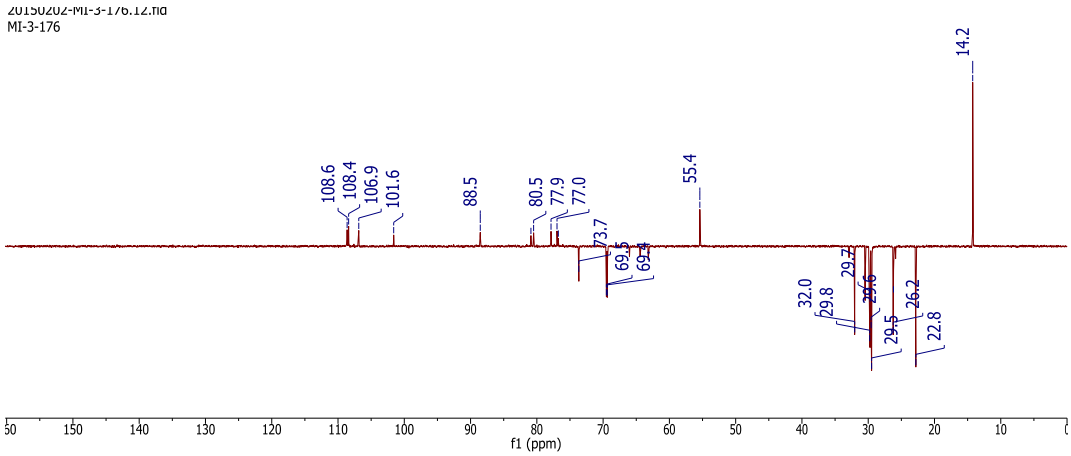
^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **1d**



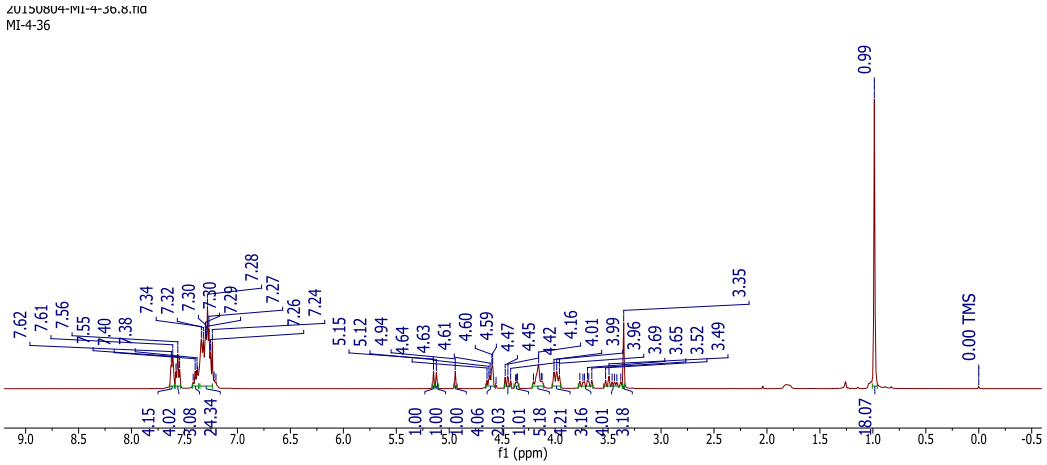
^{13}C NMR Spectrum (100.53 MHz, $CDCl_3$) of Compound **1d**



DEPT Spectrum (100.53 MHz, $CDCl_3$) of Compound **1d**



^{1}H NMR Spectrum (399.78 MHz, $CDCl_3$) of Compound **14**



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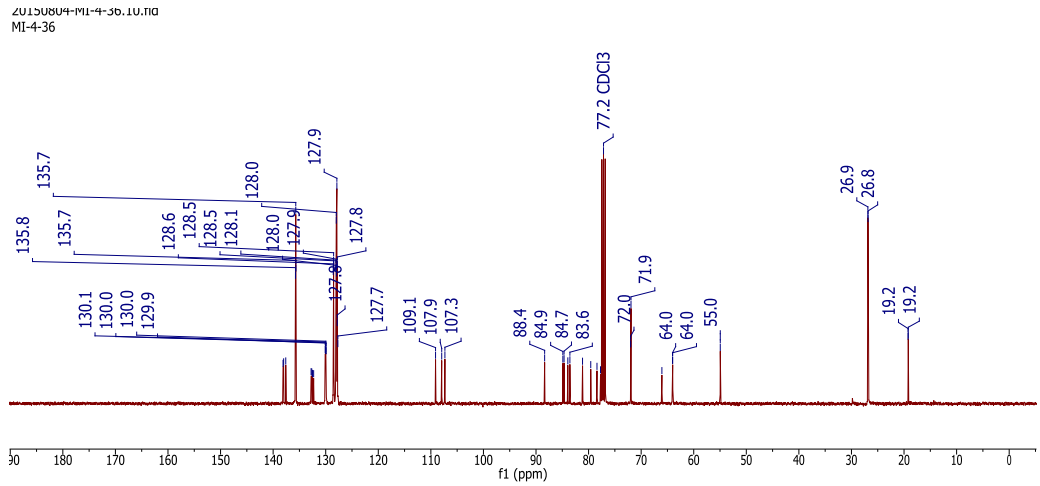

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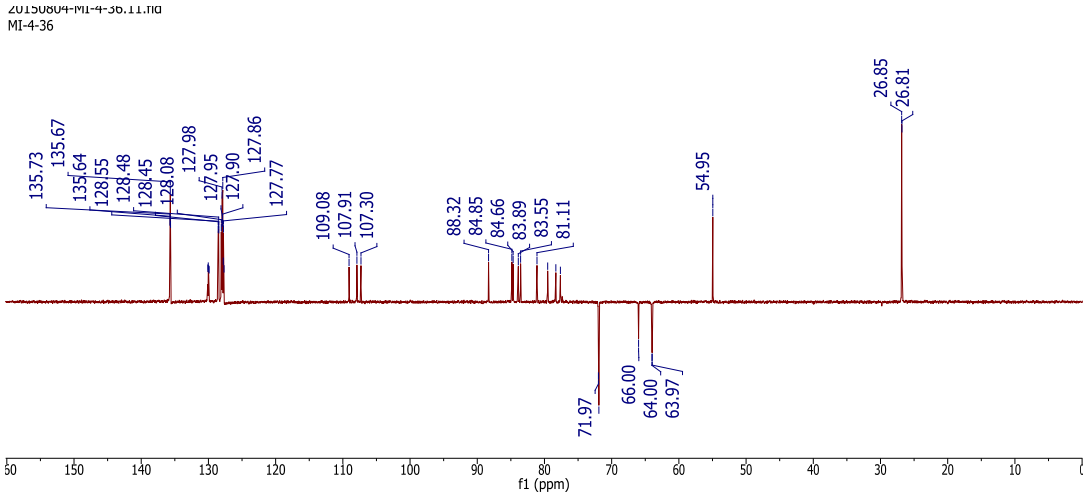

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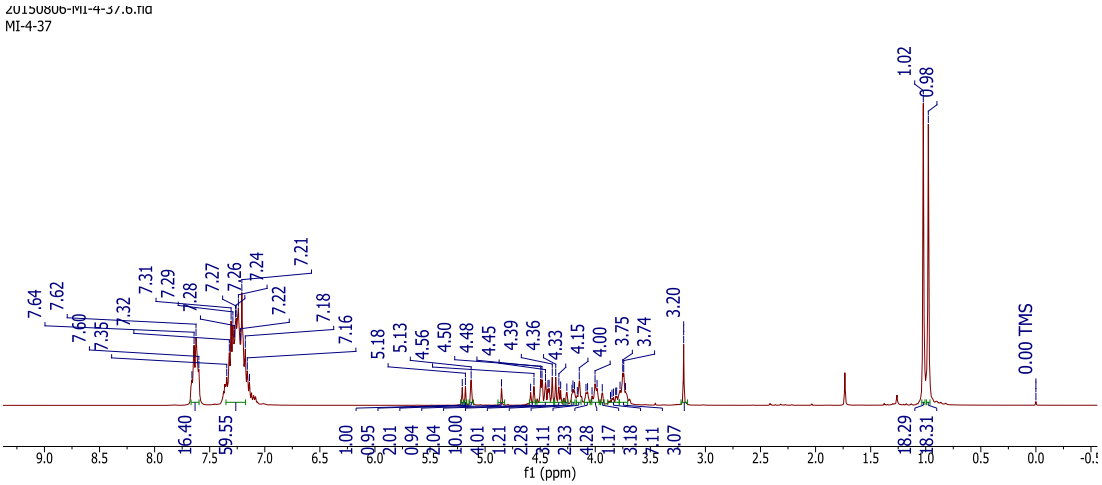

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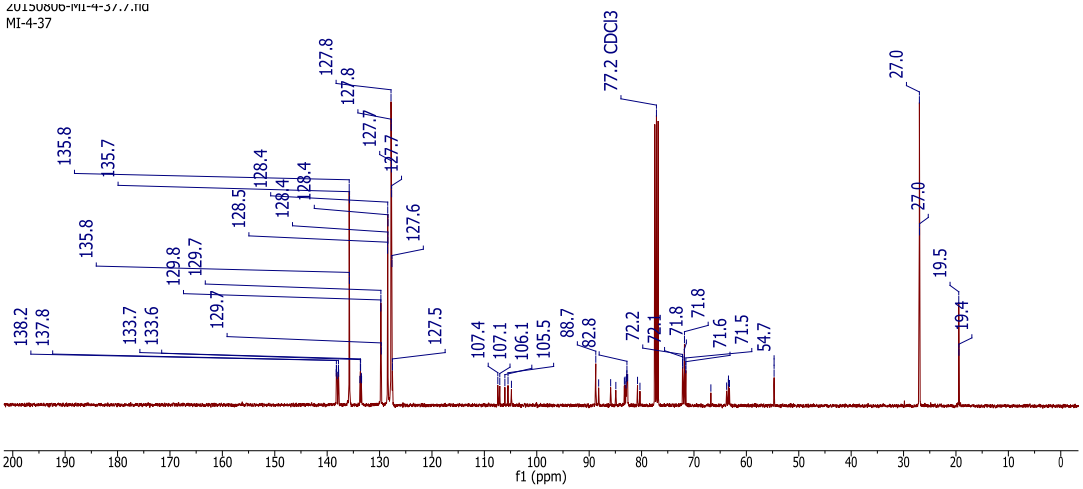

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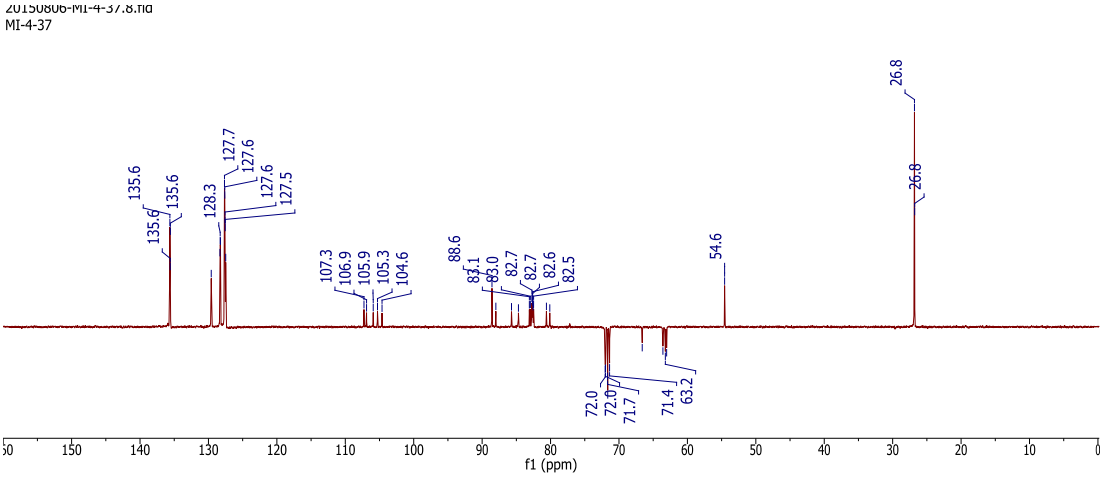

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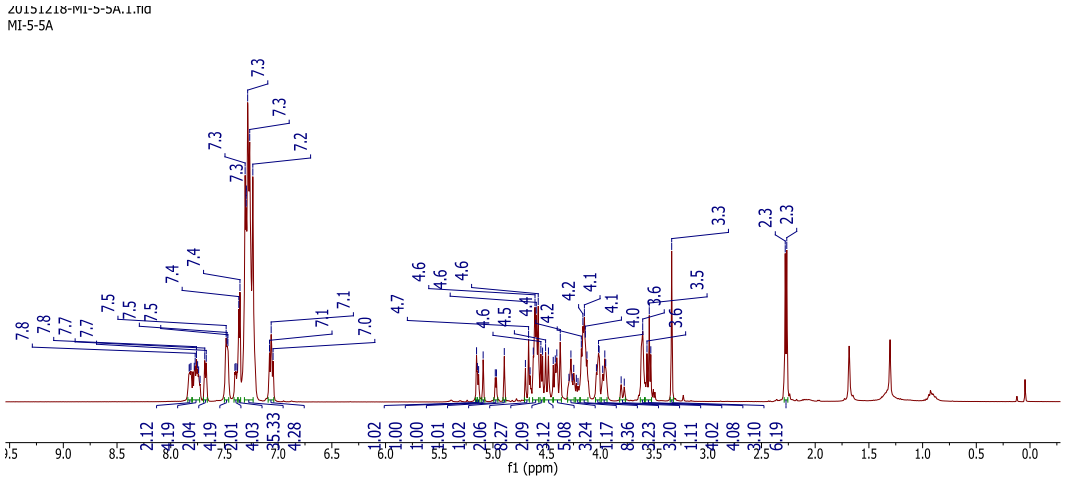

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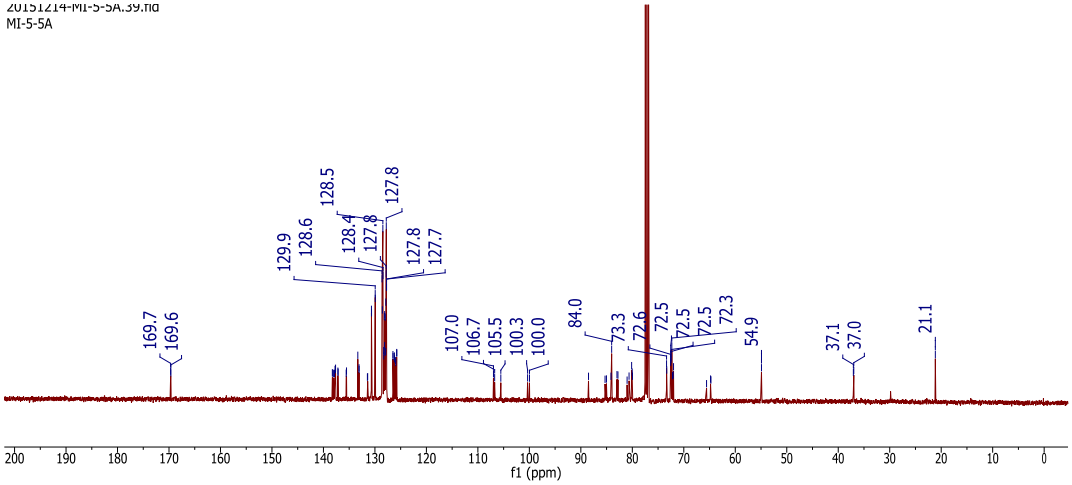

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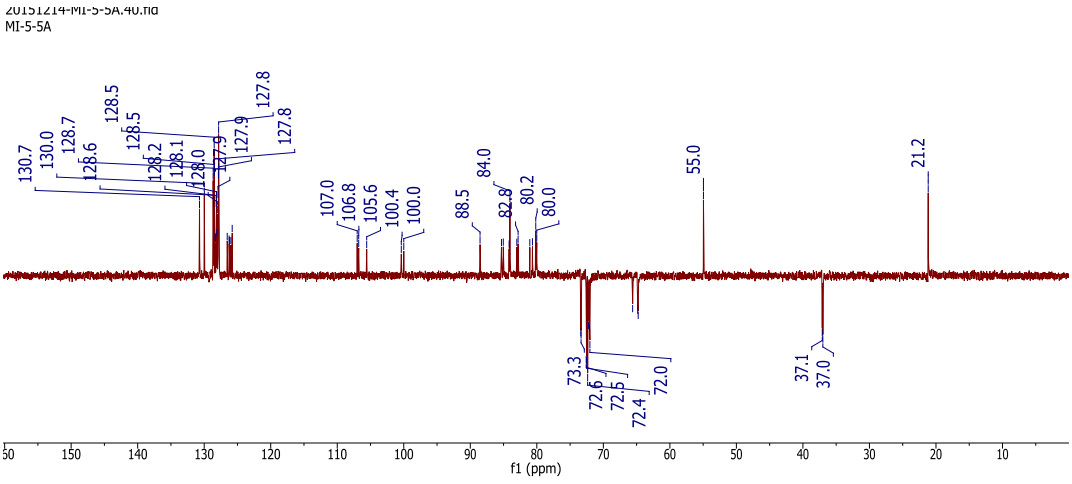

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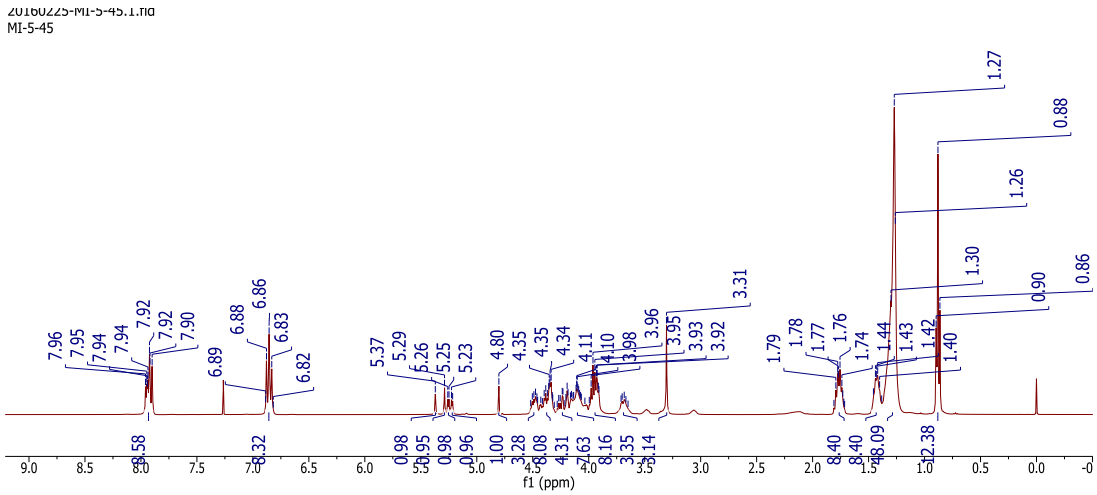

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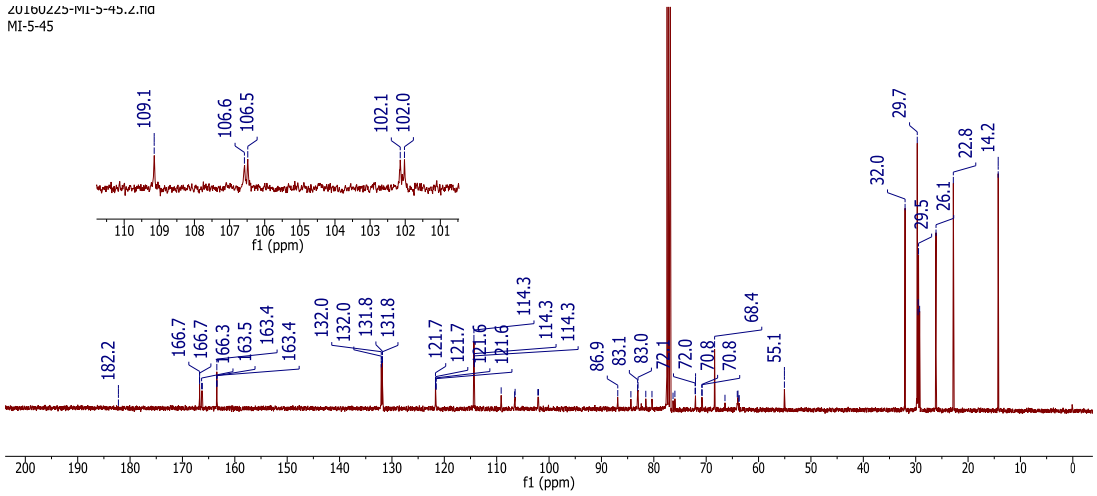
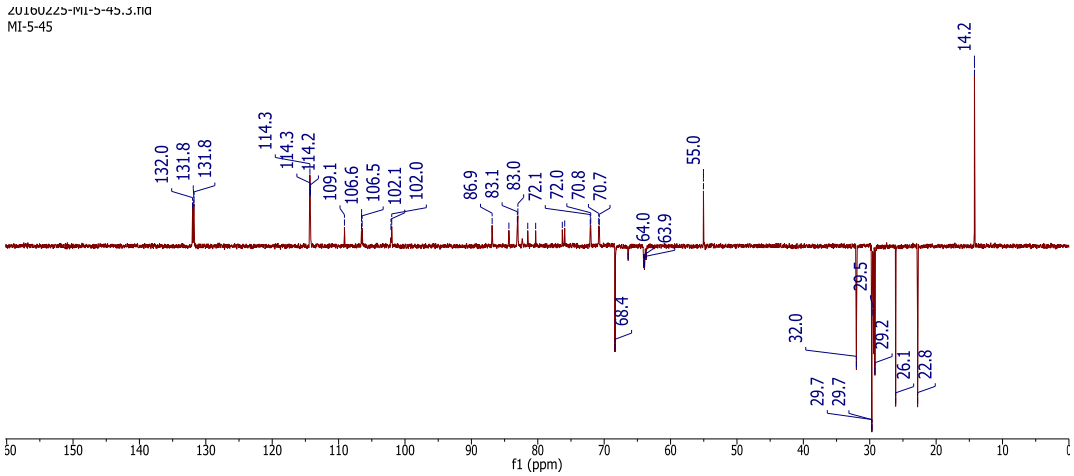


DEPT Spectrum (100.53 MHz, $CDCl_3$) of Compound **27c**



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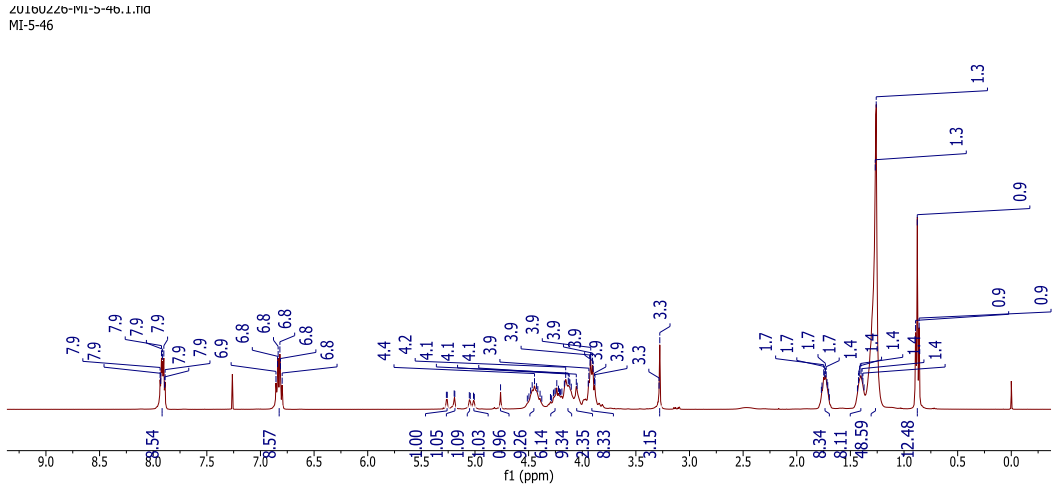

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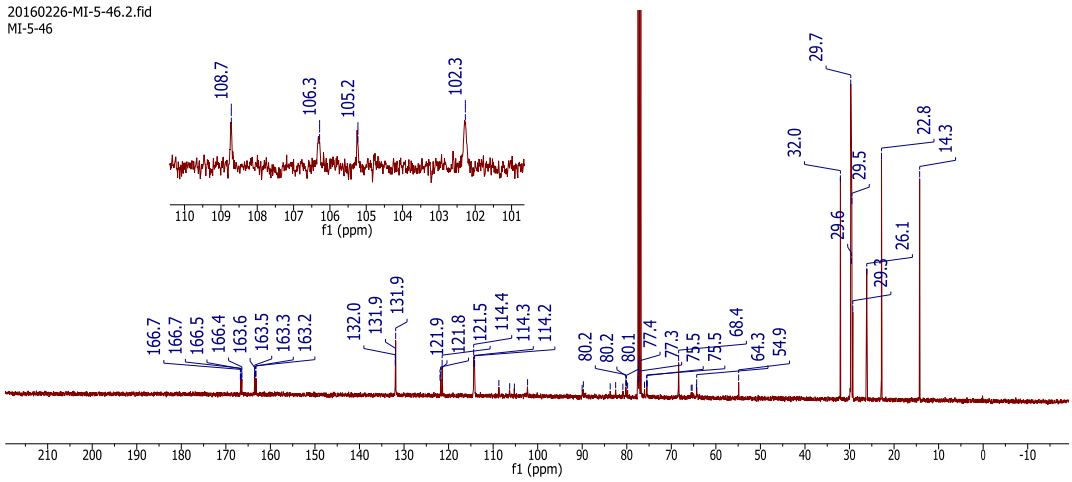
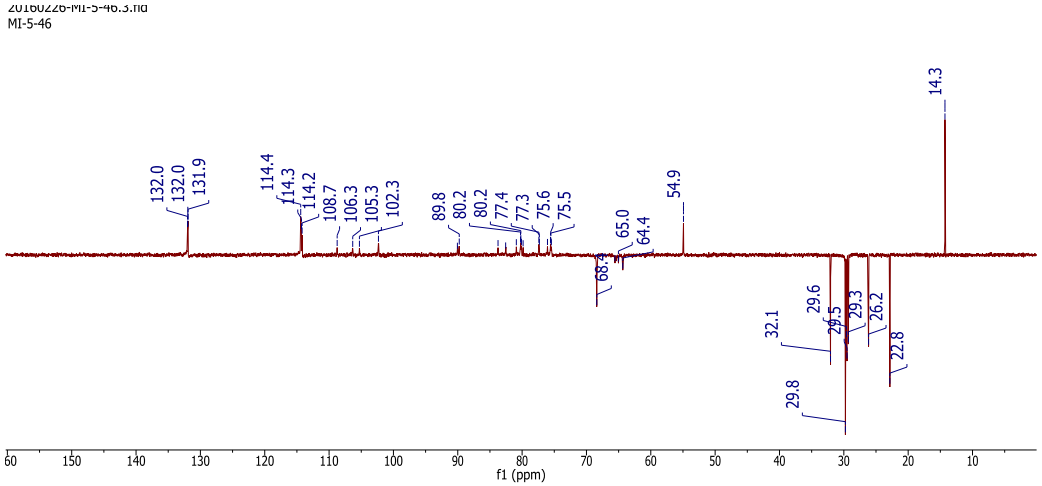


DEPT Spectrum (100.53 MHz, $CDCl_3$) of Compound **27g**



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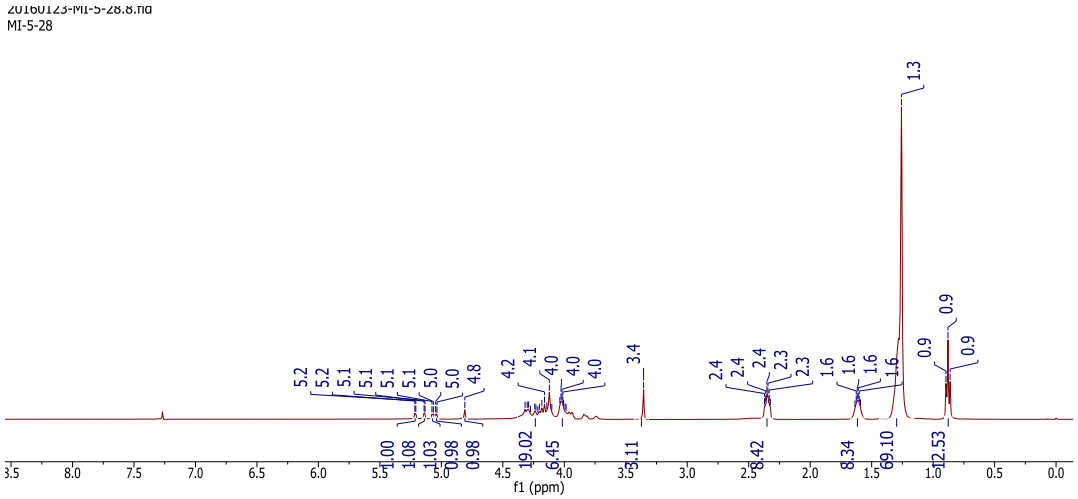

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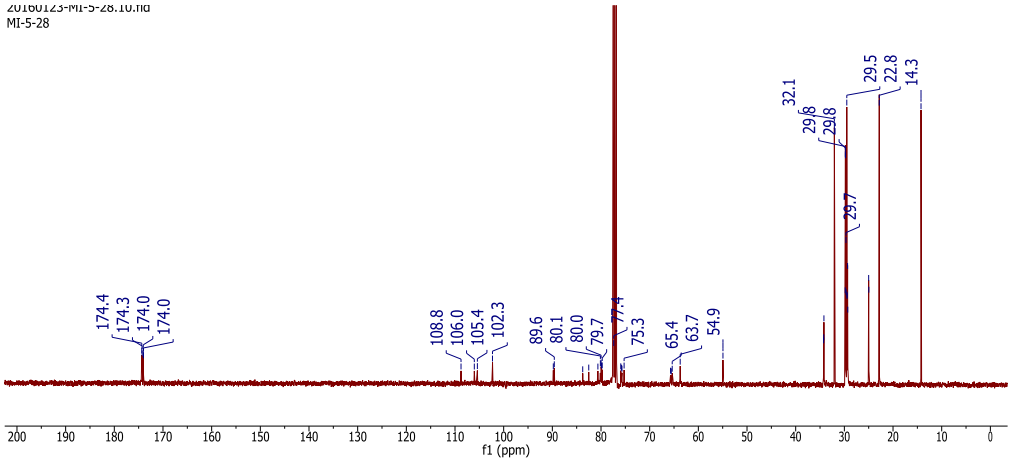

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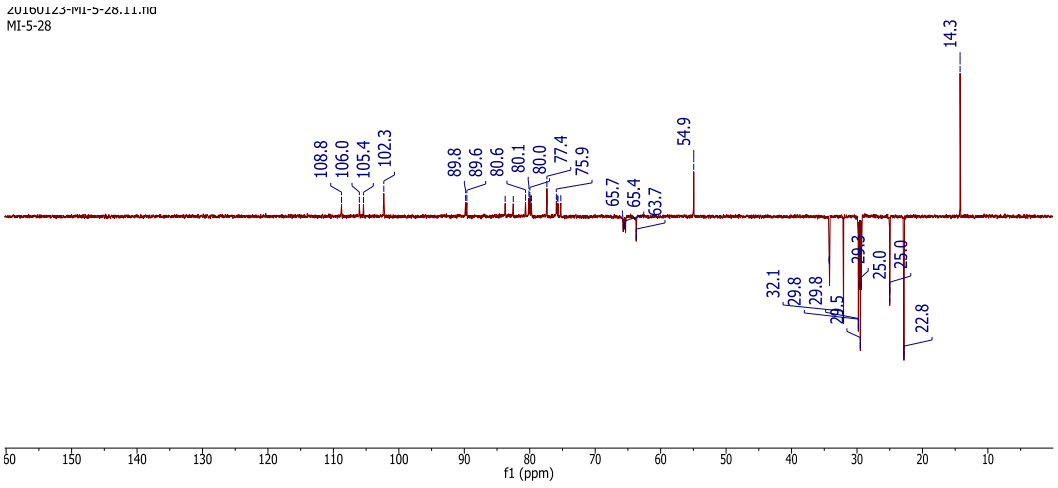

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List of publications:

1. Hypervalent iodine mediated synthesis of C-2- *deoxy* glycosides and amino acid glycoconjugates. **Maidul Islam,** Nishanth D. Tirukoti, Shyamapada Nandi and Srinivas Hotha. *J. Org. Chem.*, **2014**, *79*, 4470.
2. Influence of steric crowding on the diastereoselective arabinofuranosylations. **Maidul Islam**, Gaddamannugu Gayatri, and Srinivas Hotha. *J. Org. Chem.*, **2015**, *80*, 7937.
3. Transition metals for the synthesis of glycopolymers and glycopolypeptides. **Maidul Islam**, Shaikh Ashif Yasin and Srinivas Hotha. *Isr. J. Chem.*, **2015**, *55*, 373.
4. [Au]/[Ag]-catalyzed expedient synthesis of branched Heneicosafuranosyl arabinogalactan motif of Mycobacterium tuberculosis cell wall. Shivaji A. Thadke,# Bijoyananda Mishra,# **Maidul Islam**, Sandip Pasari, Sujit Manmode, Venkateswara Rao Boddu, Mahesh Neralkar, Ganesh P. Shinde, Gulab Walke and Srinivas Hotha. *Nature Commun.* (*In Press*, **doi:10.1038/ncomms14019**) {# equal contribution}
5. Expedient synthesis of Heneicosasaccharyl mannose capped arabinomannan of Mycobacterium tuberculosis cellular envelope by glycosyl carbonate donors. **Maidul Islam**, Ganesh P. Shinde and Srinivas Hotha. *Chem. Sci.*, **2017**, *8*, 2033.
6. Reciprocal donor-acceptor selectivity for synthesis of α-furanoside oligosaccharides and its biophysical studies. **Maidul Islam** and Srinivas Hotha. (**Manuscript under preparation**).
7. Expedient synthesis of the Henpentacontasacaryl arabinomannan of Mycobacterium tuberculosis cellular envelope by glycosyl carbonate donors. **Maidul Islam**, Ganesh P. Shinde, Gulab Walke and Srinivas Hotha. (**Manuscript under preparation**).

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Hypervalent Iodine Mediated Synthesis of *C*-2 *Deoxy* Glycosides and Amino Acid Glycoconjugates

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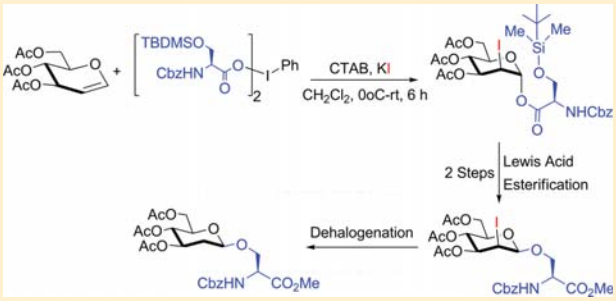
Supporting Information

ABSTRACT: A simple, efficient, and practical method for the synthesis of *C*-2 *deoxy*-2-iodo glycoconjugates in self-assembled structures was found using $PhI(OCOR)_2$. 2-Iodo glycoserinyl esters were intramolecularly converted into 2-iodo serinyl glycosides which upon dehalogenation gave *C*-2 *deoxy* amino acid glycoconjugates.



INTRODUCTION

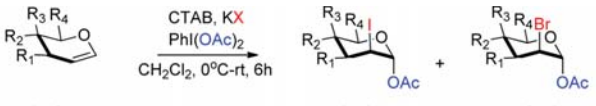
Stereo- and regioselective reactions are well sought after in organic chemistry; frequently, stereo- and regioselectivities are obtained by taking advantage of steric environments such as chiral auxiliaries, reagents, and solvents.[1] The utility of self-assembled structures for the above is a promising alternative.[2] It is desirable that the self-assembled structure (i) is stable at the temperature of the reaction; (ii) does not react with reagents; (iii) does not disassemble during the reaction; and (iv) should be accessible from simple precursors. It is known that cetylammonium bromide (CTAB) forms organic solvent-stable surfactant-assembled lipophilic nanoreactors.[3] Addition of polyvalent iodine reagents onto electron-rich π-systems was found to be suitable for the current investigation since various iodobenzene dicarboxylates react with electron-rich π-systems.[4] Earlier studies showed that indenes can be regioselectively functionalized using $PhI(OAc)_2$ in CTAB derived nano-reactors.[5]

Easily available glycals possess an electron-rich π-bond, and the utility of hypervalent iodine (I^{III}) reagents on glycals was studied for the selective C3-*O*-oxidation, *C*-2 heteroatom substitution, and oxidative glycosidation.[6,7] In this premise, regioselective iodination of glycals has been hypothesized through surfactant-assembled structures by using CTAB and polycoordinated iodine reagents for the synthesis of 2-*deoxy*-2-iodo acetates. Notably, 2-*deoxy*-2-iodo glycopyranosyl acetates are important precursors for the synthesis of 2-*deoxy*-, 2-alkyl, and 2-amino glycosides. Biological significance and their versatility coupled with the challenge of synthesizing 2-*deoxy*-glycopyranosides[7] had attracted many researchers to develop strategies for their synthesis utilizing hypervalent iodine reagent,[7a−h] de novo,[8] and dehydrative[7i] glycosidation. 2-*Deoxy*-glycopyranosides can be accessed through moderately stable C-2 triflates,[9] or by the addition of electrophilic iodine in a poorly regioselective manner to the electron rich π-bond of glycals.[7] Therefore, we thought of studying the reaction of hypervalent iodination on glycals in the presence of CTAB-assembled self-assembled structures for the regioselective synthesis of 2-*deoxy*-glycosides.

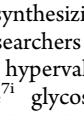
RESULTS AND DISCUSSION

To begin our investigation, a CH_2Cl_2 solution of per-*O*-acetyl glucal **1a** at 0 °C was added to $PhI(OAc)_2$, CTAB, and KI. The resulting turbid solution was stirred at room temperature for 6 h to observe the formation of two inseparable products **2a** and **3a** in a 95:5 ratio which were characterized by NMR and MS analysis (Scheme 1);[10] importantly, no regioisomeric mixture was noticed. The origin of selectivity is attributed to the micellar environment as postulated earlier.[5,10] The formation of compound **3a** is possible due to the halide counterion exchange between CTAB and KI which was confirmed through a control

Scheme 1. Synthesis of *C*-2 *Deoxy* *C*-2 Iodo Anomeric Acetates in Self Assembled Structures



1a-1c 2a-2c 3a-3c

No.	R_1	R_2	R_3	R_4	X	% Yield	Ratio
1a	-OAc	-OAc	-H	$-CH_2OAc$	I	85	**2a:3a** = 95:5
	-OAc	-OAc	-H	$-CH_2OAc$	Br	71	**2a:3a** = 0:100
1b	-OAc	-H	-OAc	$-CH_2OAc$	I	80	**2b:3b** = 94:5
1c	-OAc		-H	$-CH_2OAc$	I	75	**2c:3c** = 95:5

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Influence of Steric Crowding on Diastereoselective Arabinofuranosylations

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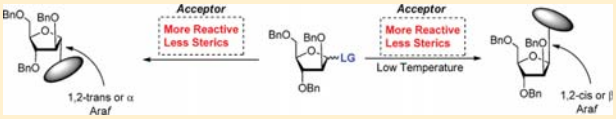
Supporting Information

ABSTRACT: The occurrence of arabinofuranosides on the cell surface of *Mycobacterium tuberculosis* (Mtb) and their significance in controlling disease spurred interest in developing strategies for their diastereoselective synthesis. Mtb uses enzymes to achieve diastereoselectivity through noncovalent interactions. Of the two possible glycosidic linkages, chemically, 1,2-*trans* linkage is relatively easy to synthesize by taking advantage of neighboring group participation, whereas synthesis of the 1,2-*cis* linkage is notoriously difficult. In this article, stereochemical effects on the diastereoselectivity of arabinofuranosidation are investigated with thiopyridyl, imidate, and thiotolyl donors as well as differently crowded glycosyl acceptors; subtle differences in the stereochemical environment of the acceptors were observed to alter the diastereoselectivity of the furanoside formation. Results from this endeavor suggest that 1,2-*cis* arabinofuranosides can be synthesized conveniently by conducting the reaction at lower temperature on sterically demanding and less reactive substrates.



INTRODUCTION

Tuberculosis has plagued mankind for a long time, and it continues to show its socioeconomic impact even now.[1] *Mycobacterium tuberculosis*, the causative agent of tuberculosis, is established to have a thick cell wall, which makes getting small molecules into the cells for eventual killing difficult.[2] Fine structural details of the mycobacterial cell wall have been determined, finding that arabinose and galactose in furanosyl form along with other sugars.[3] Arabinogalactan (AG) and lipoarabinomannan (LAM) are the broad constituents of the mycobacterial cell wall, and the terminal arabinofuranosyl residues of AG are esterified with mycolic acid.[3] The presence of 1,2-*cis* arabinofuranosyl residues at the terminal position of AG is yet another characteristic that distinguishes AG and LAM.

Chemical synthesis of oligosaccharides is important for understanding disease processes and the development of various therapeutic agents.[4a] Chemical synthesis of 1,2-*cis* furanosides is more challenging compared to that of 1,2-*trans* furanosides.[4b] Several approaches have been developed for the synthesis of both 1,2-*trans* and 1,2-*cis* linkages of arabinofuranosides.[5] Various glycosyl donors, such as thio glycosides,[5a−d] alkyl glycosides,[5a,6a] silyl glycosides,[6b] esters,[5g] halo-,[6c,d] imidate,[6e] 1,2-anhydro,[6f,g] and orthoesters[6h−j] were investigated for the synthesis of mycobacterial arabinan fragments. One of the fragments of the mycobacterial cell wall is motif A (**1**), which is a hexaarabinofuranoside containing two 1,2-*cis* and four 1,2-*trans* linkages (Figure 1).[3]

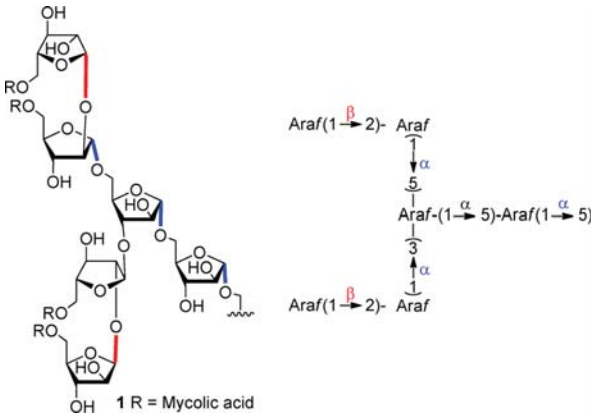


Figure 1. Motif A of the *Mycobacterium tuberculosis* cell wall.

RESULTS AND DISCUSSION

The synthesis of motif A has attracted the attention of many researchers and culminated in the investigation of a variety of glycosyl donors.[7,6a,j,5a,g] A previous report[5a] on the synthesis of pentaarabinofuranosyl motif A of *Mycobacterium tuberculosis* showed stereoselective formation of 1,2-*cis* disaccharide **4** from the thiopyridyl donor **2** and *n*-pentenyl furanoside **3**. However, very little is mentioned about the origin of the selectivity; further investigation on the stereochemical influence of the stereoselectivity might pave the way for a milder and general method for the synthesis of 1,2-*cis* arabinofuranosides. Hence, the initial aim of this research has therefore been to understand the factors that influence stereoselectivity of thiopyridyl-based arabinofuranosidation.

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Review

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Transition Metals for the Synthesis of Glycopolymers and Glycopolypeptides

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Abstract: Glycopolymers and glycopolypeptides are an important class of molecules, which can self-assemble to various interesting biohybrid materials. It is envisaged that the glycans impart good immunological response, and the aliphatic or polypeptide backbone can give tertiary structure for the resulting glycopolymers. The major bottleneck in the synthesis of glycopolymers or glycopolypeptides is the access to suitable building blocks and polymerization methods. This review describes methods that have recently been explored for the successful synthesis of many useful glycomonomers that could be polymerized to afford glycopolymers and/or glycopolypeptides.

Keywords: glycopeptides · polymerization · synthetic methods · transition metals

1. Introduction

Cellular information starts with the replication of DNA, followed by transcription of the information to the RNA, which gets subsequently translated into a protein that further undergoes post-translational modifications, among which glycosidation is the most complicated.[1] Proteins function as enzymes to catalyze reactions to give a variety of polysaccharides, polyketides, and terpenes, which are proven to be of immense benefit to mankind (Figure 1).[1a] Nature exploits extraordinary mechanical properties of abundantly available polysaccharides, such as starch, cellulose, and chitin, for its benefit. Glycans exist as linear or branched forms, and in addition, they can differ by stereochemical linkage at the anomeric or *C*-1 position to generate exceptional diversity.[2] The gigantic structural diversity and information stored in the glycome represents the next challenge of biology, and its potential is still underestimated.[3] Bioinformatic studies estimate that half of the human proteins undergo post-translational glycosylation to form glycoproteins, which are often present on the cell surface.[1a,3]

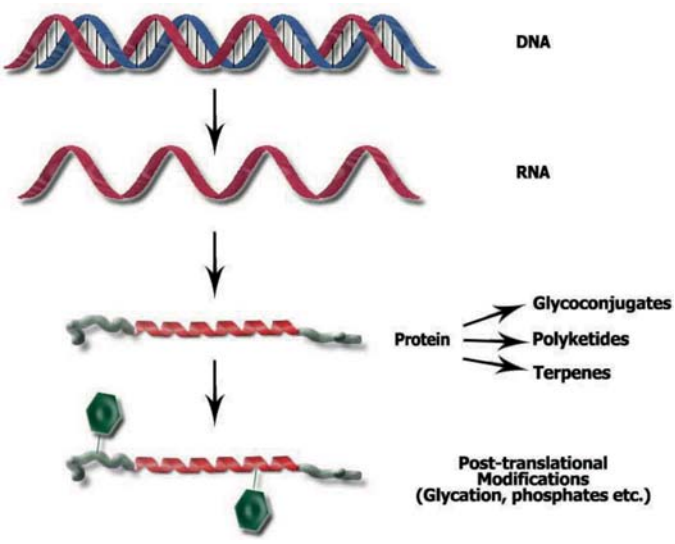

Figure 1. Expanded central dogma of molecular biology.

Cell surface glycans are often attached to either a lipid or a protein, and therefore, are known as glycolipids or glycoproteins, and are broadly referred to as glycoconjugates.[4] Cell surface bound glycoconjugates are found to play pivotal roles in many intracellular and extracellular signal transduction events (Figure 2).[1b] For instance, glycoproteins are demonstrated to be involved in cell-cell communication, cell-cell adhesion, fertilization, viral entry into the cell, bacterial infection, and cell-cell recognition, and hence, they are recognized to have potential applications in therapeutics, diagnostics, and vaccines.[1b] In addition, many biohybrid polymers are currently investigated as novel smart materials, since they are envisaged to have solubility, processability, and scalability, along with much desired chirality and cellular recognition.[5] Isolation of glycoproteins from nature is a daunting task,

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[Au]/[Ag]-catalysed expedient synthesis of branched heneicosafuranosyl arabinogalactan motif of *Mycobacterium tuberculosis* cell wall

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Emergence of multidrug-resistant and extreme-drug-resistant strains of *Mycobacterium tuberculosis* (MTb) can cause serious socioeconomic burdens. Arabinogalactan present on the cellular envelope of MTb is unique and is required for its survival; access to arabinogalactan is essential for understanding the biosynthetic machinery that assembles it. Isolation from Nature is a herculean task and, as a result, chemical synthesis is the most sought after technique. Here we report a convergent synthesis of branched heneicosafuranosyl arabinogalactan (HAG) of MTb. Key furanosylations are performed using [Au]/[Ag] catalysts. The synthesis of HAG is achieved by the repetitive use of three reactions namely 1,2-*trans* furanoside synthesis by propargyl 1,2-orthoester donors, unmasking of silyl ether, and conversion of *n*-pentenyl furanosides into 1,2-orthoesters. Synthesis of HAG is achieved in 47 steps (with an overall yield of 0.09%) of which 21 are installation of furanosidic linkages in a stereoselective manner.

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Expedient synthesis of the heneicosasaccharyl mannose capped arabinomannan of the *Mycobacterium tuberculosis* cellular envelope by glycosyl carbonate donors†

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The global incidence of tuberculosis is increasing at an alarming rate, and *Mycobacterium tuberculosis* (Mtb) is the causative agent for tuberculosis, a disease with high mortality. Lipoarabinomannan (LAM) is one of the major components of the Mtb cellular envelope and is an attractive scaffold for developing anti-tubercular drugs, vaccines and diagnostics. Herein, a highly convergent strategy is developed to synthesize heneicosasaccharyl arabinomannan for the first time. The arabinomannan synthesized in this endeavour has several 1,2-*trans* or α-Ara*f* linkages and three 1,2-*cis* or β-Ara*f* linkages end capped with 1,2-*trans* or α-Man*p* linkages. All the key glycosidations were performed with alkynyl carbonate glycosyl donors under [Au]/[Ag] catalysis conditions, which gave excellent yields and stereoselectivity even for the reactions between complex and branched oligosaccharides. The resultant allyl oligosaccharide was globally deprotected to obtain the heneicosasaccharyl arabinomannan as a propyl glycoside. In summary, heneicosasaccharyl mannose capped arabinomannan synthesis was achieved in 56 steps with 0.016% overall yield.

Introduction

The world-wide resurgence of mycobacterial infections coupled with the emergence of multi- and extreme drug resistance have placed tuberculosis (TB) as a major public health concern.[1–3] The only available protection against tuberculosis is the BCG vaccine; however, multi-centered clinical trials demonstrated variable efficacy.[4] Tuberculosis infections are caused by *Mycobacterium tuberculosis* (Mtb), which has a thick waxy cell wall making it impervious to drugs.[5,6] As a consequence, patients suffering from TB are prescribed a long regimen of multiple drugs. Therefore, TB is an ever growing challenge, and novel strategies to diagnose, control or eradicate it are in great demand.

The chemical structure of the waxy cellular envelope has been identified as a unique glycocalyx comprising mycolic acids, Ara*f*, Gal*f*, Man*p*, Rha*p* and inositols.[7–10]‡ Further investigations revealed that the glycocalyx contains trehalose lipids, lipoarabinomannan (LAM), arabinogalactan (AG) and peptidoglycan.[7–10] Of these, the structure of LAM was noticed to have a key C-3 branched arabinan domain with many α-1 → 5-linked D-Ara*f*s, and a few β-1 → 2-linked D-Ara*f*s capped with α-1 → 2 linked D-Man*p*s at the non-reducing end.[7–10,13] It has been well established that mannose capped LAM (ManLAM) is prevalent in more pathogenic mycobacterial species such as *M. tuberculosis*, *M. leprae*, *M. bovis*.[11–13] ManLAM has been shown to inhibit the production of tumor necrosis factor-α (TNF-α) and interleukin-12 (IL-12) by human dendritic cells and macrophages *in vitro* to modulate *M. tuberculosis* induced macrophage apoptosis.[14,15] Quite recently, a rapid point of care diagnostic kit was developed exploiting the antigenic properties of ManLAM.[16–18] In another study LAM was investigated as a candidate vaccine for mycobacterial diseases. Thus, the non-reducing end portion of LAM is beneficial to various immunological studies, diagnostics and the development of carbohydrate-based tuberculosis vaccines.

Owing to the significance of ManLAM, the synthesis of ManLAM and arabinan fragments has been attempted over the last two decades.[19–27,44] A recent investigation by Guo's group verified the synthetic and immunological potential of protein conjugated ManLAM fragments.[28] However, far too little attention has been paid to synthesizing the large oligomers in ManLAM. The main aim of the current research has therefore been to synthesize naturally occurring large oligosaccharide portions of ManLAM such as arabinomannan **1** (Fig. 1) to facilitate vaccine and diagnostic development.

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